Accreditation Statement: The American College of Rheumatology is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

Designation Statement: The ACR designates this live educational activity for a maximum of 5.25 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

International Physicians: International physicians who register as part of a group and require AMA PRA Category 1 Credit(s)™ must provide the following information to your tour leader: full name, mailing address, telephone and fax numbers and e-mail address. The information will be used to verify your meeting attendance.

The American Medical Association has an agreement of mutual recognition of continuing medical education credit with the European Union of Medical Specialties. International physicians interested in converting AMA PRA Category 1 Credit(s)™ to EACCME credit should contact the UEMS.

Health Professionals: Participants may claim hours to receive a Certificate of Participation for an activity designated for AMA PRA Category 1 Credit(s)™. For non-CME sessions, attendees may also request a certificate of participation.

Disclosure Policy
As an educational provider accredited by the Accreditation Council for Continuing Medical Education, the American College of Rheumatology must ensure balance, independence, objectivity and scientific rigor in all its educational activities. Therefore, all those in a position to control content (e.g., speakers and moderators) participating in an ACR-sponsored activity are required to disclose to the planning committee and audience any financial or other relationships that occurred in the past 12 months. This includes the relationships of spouse/partners. If there are relationships that create a conflict of interest, these must be resolved in accordance with the ACR’s CME Resolution of Conflict policy prior to the participation of the individual in the development or presentation of CME content. Relevant relationships include, but are not limited to:

None: Has no relevant financial relationship to disclose.
1. Stock, stock options or bond holdings in a for-profit corporation or self-directed pension plan;
2. Research grants;
3. Employment (full or part time);
4. Ownership or partnership;
5. Consulting fees or other remuneration;
6. Non-remunerative positions of influence, such as officer, board member, trustee or public spokesperson;
7. Receipt of royalties;
8. Speakers' bureau; or
9. Other.

Abstract author disclosures are published online. Any individual who refuses to disclose relevant financial relationships is ineligible to serve as a planning committee member, presenter or author of an ACR CME activity, and cannot have control of, or responsibility for, the development, management, presentation or evaluation of the CME activity.

Abstract Embargo Policy
Accepted abstracts are made available to the public online in advance of the meeting and are published in a special online supplement of our scientific journal, Arthritis & Rheumatology. Information contained in those abstracts may not be released until the abstracts appear online. Academic institutions, private organizations and companies with products whose value may be influenced by information contained in an abstract may issue a press release to coincide with the availability of an ACR abstract on the ACR/ARHP Annual Meeting Abstract website. However, the ACR continues to require that information that goes beyond what is contained in the abstract (e.g., discussion of the abstract done as part of a scientific presentation or presentation of additional new information that will be available at the time of the meeting) is under embargo until 4:30 PM PT on November 4, 2017.

Violation of this policy may result in the abstract being withdrawn from the meeting and other measures deemed appropriate. Authors are responsible for notifying financial and other sponsors about this policy. If you have questions about the ACR abstract embargo policy, please contact the Annual Meeting abstract staff at abstracts@rheumatology.org.

Copyright Policy
The Annual Meeting is a private event. Programs presented at the meeting are for the education of attendees and purchasers of recorded presentations as authorized by the American College of Rheumatology. The information and materials displayed and presented during this meeting are the property of the ACR and the presenter and cannot be photographed, copied, photocopied, transformed to electronic format, reproduced, or distributed without written permission of the American College of Rheumatology and the presenter. Any use of the program content for commercial purposes, which includes, but is not limited to, oral presentations, audiovisual materials used by speakers, and program handouts, without the written consent of the ACR is prohibited. This policy applies before, during and after the meeting. The ACR will enforce its intellectual property rights and penalize those who infringe upon it.

Media
Credentialed media attend the Annual Meeting to cover stories for consumer, trade and other media outlets and are
easily identified by their black press ribbons. Media has
access to all general sessions and limited access (at the
discretion of speakers) to Meet the Professor and Workshop
sessions. Media may use handheld audio recorders and still
cameras (assuming that intellectual property rights are
respected); moving video recording is also permitted with
the permission of the presenter(s). The exception to this
policy is that no photos or video are allowed in the
Exhibit Hall, or in the Poster Hall without permission
from the poster presenter. Press who would like general
photos of the Exhibit Hall can obtain these after the meeting
from the ACR. Attendees who have questions about the
ACR’s media policies should contact the public relations
department at pr@rheumatology.org.

Photographs and Video Recording Policy
As a courtesy to our presenters, ACR policy does not permit
photographs or recordings during educational sessions,
including poster sessions. The only exception to this is for
registered media, who should review their registration
materials for more information.

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

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

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

- For the purposes of this statement, the term
  “reproduce” includes all forms of reproduction,
  including, but not limited to, print, electronic and
  photographed formats.
- For the purposes of this statement, the term
  “presenting author” refers to the author who is
designated as the individual who will present the
work during the ACR/ARHP Annual Meeting, as
identified through the abstract submission process.

Approval Process for ACR Abstracts

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

Permissions Department
c/o John Wiley & Sons, Inc.
111 River Street
Hoboken, NJ 07030
Fax: 201-748-6008
wiley.com/go/permissions

- Commercial entities seeking permission to reprint
  must obtain all materials from the author and/or
  publisher John Wiley & Sons, Inc. The ACR cannot
  provide any materials.

Approval Process for ACR Posters

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

Reproducing ACR Abstracts and Posters for
Dissemination Prior to the Annual Meeting

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

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

Reproducing ACR Abstracts and ACR Posters for Dissemination After the Annual Meeting

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

- Abstracts and booklets of abstracts (e.g., two or more) must include the following statement on the front of the abstract/booklet:
  Abstract(s) reprinted from the ACR/ARHP Annual Meeting held November 5-8, 2017. The American College of Rheumatology does not guarantee, warrant, or endorse any commercial products or services. Reprinted by (insert name of supporting company).
- Booklets cannot contain corporate or product logos or any advertisements. No exceptions.

ACR Posters
Following approval from the presenting author and the ACR (see approval process above), copies of actual ACR poster presentations (i.e., images from the poster presentation hung in the poster hall) may be reproduced.

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

- IMPORTANT: The ACR does not retain and cannot provide poster presentation images.
- The following statement must be listed under each Poster reprint:
  Reprinted from the ACR/ARHP Annual Meeting held November 5-8, 2017. The American College of Rheumatology does not guarantee, warrant, or endorse any commercial products or services. Reprinted by (insert name of supporting company).

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

Use of the ACR Disclosure Key
It is suggested when referencing disclosures in the reprints, that the ACR’s disclosure key be added to provide adequate context for abstracts:
None: Has no relevant financial relationship to disclose.
  1. Stock, stock options or bond holdings in a for-profit corporation or self-directed pension plan;
  2. Research grants;
  3. Employment (full or part time);
  4. Ownership or partnership;
  5. Consulting fees or other remuneration;
  6. Non-remunerative positions of influence, such as officer, board member, trustee or public spokesperson;
  7. Receipt of royalties;
  8. Speakers’ bureau; or
  9. Other.

Use of the ACR Scientific Program Content
- Information displayed or presented at all sessions during the Annual Meeting is the property of the ACR or the presenter. Information may not be recorded, photographed, copied, photocopied, transferred to electronic format, reproduced or distributed without the prior written permission of the ACR and the presenter.
- Any use of the program content, which includes but is not limited to oral presentations, audiovisual materials used by speakers and program handouts, without the written consent of the ACR is prohibited.
- This policy applies before, during and after the meeting.
- The ACR will enforce its intellectual property rights and penalize those who infringe upon it.
Table of Contents

ACR/ARHP ABSTRACT SESSIONS
SUNDAY, NOVEMBER 5, 2017

8:30 AM - 4:00 PM
ACR Poster Session A
(#1-825)

11:00 AM - 12:30 PM
ACR Plenary Session I: Discovery 2017
(#826-830)

2:30 - 4:00 PM
ACR Concurrent Abstract Sessions
(#831-836) B Cell Biology and Targets in Autoimmune Disease
(#837-842) Epidemiology and Public Health I: Lung, Bone, and Infection Outcomes
(#849-854) Muscle Biology, Myositis and Myopathies
(#855-860) Pain – Basic and Clinical Aspects Oral
(#861-866) Rheumatoid Arthritis – Animal Models
(#867-872) Rheumatoid Arthritis – Clinical Aspects I: Cardiovascular Comorbidities
(#873-878) Sjögren’s Syndrome I: Clinical Assessment and Trial Outcomes
(#879-884) Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment I
(#885-890) Systemic Lupus Erythematosus – Clinical Aspects and Treatment I: Novel and Current Therapies
(#891-896) Vasculitis I: Clinical Trials and Outcomes

ARHP Concurrent Abstract Session
(#843-848) ARHP Psychosocial Impact on Rheumatic Disease

4:30 - 6:00 PM
ACR Concurrent Abstract Session
(#897-901) 2017 Rheumatology Research Foundation, Edmond L. Dubois, MD Memorial Lecture
(#902-906) Biology and Pathology of Bone and Joint
(#907-912) Education
(#913-918) Epidemiology and Public Health II: Non-Genetic Risk Factors for Incident Disease
(#919-924) Healthcare Disparities in Rheumatology
(#931-936) Osteoarthritis – Clinical Aspects I: Pain and Functional Outcomes
(#937-942) Pediatric Rheumatology – Pathogenesis and Genetics
(#943-948) Systemic Sclerosis, Fibrosing Syndromes and Raynaud’s – Clinical Aspects and Therapeutics I
(#949-954) T Cell Biology and Targets in Autoimmune Disease

ARHP Concurrent Abstract Session
(#925-930) ARHP Clinical Practice/Patient Care/Health Services Research

MONDAY, NOVEMBER 6, 2017

8:30 AM - 4:00 PM
ACR/ARHP Poster Session B
(#955-1783)

11:00 AM - 12:30 PM
ACR Plenary Session II: Discovery 2017
(#1784-1789)

2:30 - 4:00 PM
ACR Concurrent Abstract Sessions
(#1802-1807) Patient Outcomes, Preferences, and Attitudes I
(#1808-1813) Reproductive Issues in Rheumatic Disorders
(#1814-1819) Rheumatoid Arthritis – Clinical Aspects II: Treatment Patterns
(#1820-1825) Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy I: Outcomes Therapy
(#1826-1831) Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment II
(#1832-1837) Systemic Lupus Erythematosus – Animal Models
(#1838-1843) Systemic Lupus Erythematosus – Clinical Aspects and Treatment II: Clinical Trial Design and Outcome Measures
(#1844-1849) Vasculitis II: Biomarkers and Disease Activity

ACR/ARHP Combined Abstract Session
(#1850-1855) ACR/ARHP Combined: Orthopedics and Rehabilitation Science

4:30 - 6:00 PM
ACR Concurrent Abstract Sessions
(#1868-1873) Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes
(#1874-1879) Imaging of Rheumatic Diseases I: Novel Imaging and Scoring Systems
(#1880-1885) Miscellaneous Rheumatic and Inflammatory Diseases I
(#1886-1891) Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis
(#1892-1897) Pediatric Rheumatology – Clinical and Therapeutic Aspects I: Autoinflammatory Diseases
(#1898-1903) Rheumatoid Arthritis – Clinical Aspects III: Obesity and Other Comorbidities
(#1904-1909) Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy II: Trials Therapy
(#1910-1915) Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology
(#1916-1921) Systemic Lupus Erythematosus – Clinical Aspects and Treatment III: Biomarkers
(#1922-1927) Systemic Sclerosis, Fibrosing Syndromes and Raynaud’s – Pathogenesis, Animal Models and Genetics

ARHP Concurrent Abstract Session
(#1856-1861) ARHP Education/Community Programs
ACR/ARHP Combined Abstract Session
(#1862-1867) ACR/ARHP Combined: Epidemiology and Public Health: Prevention, Recognition, and Treatment

TUESDAY, NOVEMBER 7, 2017

8:30 AM - 4:00 PM
ACR/ARHP Poster Session C
(#1928-2752)

11:00 AM – 12:30 PM
ACR Plenary Session III: Discovery 2017
(#2753-2758)

2:30 - 4:00 PM
ACR Concurrent Abstract Sessions
(#2759-2764) Antiphospholipid Syndrome
(#2771-2776) Innate Immunity and Rheumatic Disease
(#2777-2782) Patient Outcomes, Preferences, and Attitudes II
(#2783-2788) Rheumatoid Arthritis – Clinical Aspects IV: Medications and Risk
(#2789-2794) Rheumatoid Arthritis – Human Etiology and Pathogenesis I
(#2795-2800) Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy III: Biosimilars Therapy
(#2801-2806) Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment III
(#2807-2812) Systemic Lupus Erythematosus – Clinical Aspects and Treatment IV: Neuropsychiatric Disease and Health Economics
(#2813-2818) Systemic Lupus Erythematosus – Human Etiology and Pathogenesis I

ARHP Concurrent Abstract Session
(#2765-2770) ARHP Rehabilitation Science

4:30 - 6:00 PM
ACR Concurrent Abstract Sessions
(#2825-2830) Genetics, Genomics and Proteomics
(#2831-2836) Health Services Research I: Cost Drivers in Rheumatic Disease
(#2837-2842) Infection-related Rheumatic Disease
(#2843-2848) Metabolic and Crystal Arthropathies I: Gout Risk of Disease Activity, Cardiovascular Disease and Mortality
(#2849-2854) Orthopedics, Low Back Pain and Rehabilitation
(#2855-2860) Pediatric Rheumatology – Clinical and Therapeutic Aspects II: Juvenile Arthritis
(#2861-2865) Rheumatoid Arthritis – Clinical Aspects V: Predicting Treatment Response
(#2866-2871) Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy IV: Pharmacodynamic Markers and Therapeutic Intervention
(#2872-2877) Sjögren’s Syndrome II: Pathogenesis, Autoantibodies and T-Cells
(#2878-2883) Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment IV
(#2884-2889) Systemic Sclerosis, Fibrosing Syndromes and Raynaud’s – Clinical Aspects and Therapeutics II

ARHP Concurrent Abstract Session
(#2819-2824) ARHP: Exemplary Abstracts

WEDNESDAY, NOVEMBER 8, 2017

9:00 AM - 10:30 AM
ACR Concurrent Abstract Sessions
(#2890-2895) Health Services Research II: Methods and Technology in Care and Research
(#2896-2901) Metabolic and Crystal Arthropathies II: Mechanisms of Crystal Inflammation and Metabolism
(#2902-2907) Miscellaneous Rheumatic and Inflammatory Diseases II
(#2908-2913) Rheumatoid Arthritis – Clinical Aspects VI: Comorbidities of Rheumatoid Arthritis
(#2914-2919) Rheumatoid Arthritis – Human Etiology and Pathogenesis II
(#2920-2925) Systemic Lupus Erythematosus – Clinical Aspects and Treatment V: Longterm Outcomes
(#2926-2931) Systemic Sclerosis, Fibrosing Syndromes and Raynaud’s – Pathogenesis, Animal Models and Genetics II
(#2932-2937) Vasculitis III: Pathogenesis

11:00 AM - 12:30 PM
ACR Concurrent Abstract Sessions
(#2938-2943) Imaging of Rheumatic Diseases II: Focus on Rheumatoid Arthritis and Systemic Sclerosis
(#2944-2949) Osteoarthritis – Clinical Aspects II: Structural Progression and Incidence
(#2950-2955) Patient Outcomes, Preferences, and Attitudes III
(#2956-2961) Pediatric Rheumatology – Clinical and Therapeutic Aspects III: Lupus, Dermatomyositis, and Scleroderma
(#2962-2967) Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy V: Imaging and Cardiovascular Outcomes Therapy
(#2968-2973) Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment V
(#2974-2979) Systemic Lupus Erythematosus – Human Etiology and Pathogenesis II
(#2980-2985) Systemic Sclerosis, Fibrosing Syndromes and Raynaud’s – Clinical Aspects and Therapeutics III

ARHP Concurrent Abstract Session
(#2986-2991) ARHP Epidemiology and Public Health

ACR/ARHP Combined Abstract Session
(#2992-2997) ACR/ARHP Combined: Pediatrics

ACR LATE-BREAKING ABSTRACT SESSIONS
TUESDAY, NOVEMBER 7, 2017

8:30 AM - 4:00 PM
ACR Late-Breaking Abstract Poster Session
(#7L-18L) ACR Late-breaking Abstracts Poster
4:30 - 6:00 PM
ACR Late-Breaking Abstract Session
(#1L-6L) ACR Late-breaking Abstracts*

*Please Note: ACR Late-breaking Abstracts are listed below in numeric order instead of presentation order.
Abstract Number: 1

Anti-Phosphatidylserine/Prothrombin Antibodies (aPS/PT) As Potential Diagnostic Markers and Risk Predictors of Venous Thrombosis and Obstetric Complications in Antiphospholipid Syndrome

Hui Shi1, Qiongyi Hu2, Hui Zheng2, Jialin Teng2, Gary Norman3, Jinfeng Zhou4 and Chengde Yang2, 1Department of Rheumatology and Immunology, Ruijin Hospital,Shanghai Jiao Tong University School of Medicine, Shanghai, China, Shanghai, China, 2Ruijin Hospital,Shanghai Jiao Tong University School of Medicine, Shanghai, China, Shanghai, China, 3INOVA Diagnostics, Inc, San Diego, China, 4Werfen China, Shanghai, China

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Antiphospholipid Syndrome Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
The antiphospholipid syndrome (APS) is a thrombophilic disorder characterized by clinical manifestations of vascular thrombosis and obstetric complications associated with the presence of specific antiphospholipid antibodies (aPLs). Most patients with APS can be identified using the conventional laboratory assays for LAC, IgG/IgM anti-cardiolipin (aCL), and IgG/IgM anti-ß2glycoprotein I (ß2GPI) antibodies. Some patients with clinical manifestations highly suggestive of APS however are negative for these classic biomarkers and new biomarkers are needed to identify these “seronegative APS or SNAPS) patients. Anti-Phosphatidylserine/Prothrombin (aPS/PT) antibodies are positive in many SNAPS patients. In the present study we assessed the prevalence and significance of aPS/PT, as well conventional APS biomarkers, in a large cohort of well-characterized patients with APS from the Shanghai region of China.

Methods:
186 Chinese patients meeting the criteria for the classification of APS using the Sydney criteria (67 primary and119 secondary APS), 48 with SNAPS, 176 disease controls ((79 systemic lupus erythematosus (SLE), 29 Šjogren’s syndrome (SS), 30 ankylosing spondylitis (AS), 38 rheumatoid arthritis (RA)), and 90 healthy donors were examined. IgG and IgM aPS/PT, IgG, IgM, IgA anticardiolipin (aCL), and IgG, IgM, IgA anti-ß2-glycoprotein I (anti-ß2GPI) antibodies were tested by QUANTA Lite® ELISA kits (Inova Diagnostics, San Diego, CA). Statistical analyses were performed using SPSS 23.0 (IBM, Chicago, IL, USA) or Analyze-it ver 4.6 (Analyze-it Software, LTD). T-test, Mann-Whitney U test, Kappa test, Fisher’s exact or Chi-square tests were applied.

Results:
160(86.0%) of APS patients were positive for at least one aPS/PT isotype. 135(72.6%) were positive for IgG aPS/PT, 124/186(66.7%) positive for IgM aPS/PT, and 99(53.2%) positive for both. Approximately half of the SNAPS patients were positive for IgG and/or IgM aPS/PT. Highly significant associations between IgG aPS/PT and venous thrombotic events (OR 6.72) and IgG/IgM aPS/PT and pregnancy loss (OR 9.44) were found. Levels of IgM aPS/PT were significantly different in APS patients with thrombotic manifestations and those with fetal loss (p=0.014). The association between IgG/IgM aPS/PT and LAC was highly significant (p<0.001), when both were positive the OR for APS was 101.6. Notably, 91.95%(80/87) of LAC positive specimens were positive for IgG and/or IgM aPS/PT suggesting aPS/PT is an effective option when LAC testing is not available.

Conclusions:
Anti-PS/PT antibody assays demonstrated high diagnostic performance for Chinese patients with APS, detected some APS patients negative for criteria markers, and may serve as potential risk predictors for venous thrombosis and obstetric complications.

Disclosure: H. Shi, None; Q. Hu, None; H. Zheng, None; J. Teng, None; G. Norman, None; J. Zhou, None; C. Yang, None.


Abstract Number: 2
Identifying “Second Hit” Risk Factor(s) Associated with Thrombosis and Pregnancy Morbidity in Ethnically Diverse Antiphospholipid Antibodies Positive Patients

Yu Zuo1, Jennifer Fan2, Ravi Sarode1, Song Zhang2, Una E. Makris1, David Karp3 and Yu-min Shen2, 1University of Texas Southwestern Medical Center, Dallas, TX, 2University of Texas Southwestern Medical Center, dallas, TX, 3Rheumatology, UT Southwestern Med Ctr, Dallas, TX
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Antiphospholipid Syndrome Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The evaluation of thrombotic and pregnancy risks associated with antiphospholipid antibodies (aPL) in individual patients without APS clinical manifestation is challenging. Our aim is to identify potential predictors of thrombosis and pregnancy morbidities among aPL positive patients.

Methods: This study included 229 consecutive persistent aPL positive patients who attended clinic at University of Texas Southwestern Medical Center. All patients had persistent high titer (99 percentiles) aPL. The aPL profiles were assessed with commercial assay. Hypertension (HTN) was classified based on 8th Joint National Committee guidelines. Hyperlipidemia (HLD) was defined as fasting total cholesterol >200 mg/dl. When assessing risk factors associated with pregnancy morbidities, only reproductive age (age<45) female controls were used. Pearson Chi-squared analysis and multivariable logistic regression were used to evaluate correlation between different risk factors and clinical manifestations.

Results: Of the 229 aPL positive patients, 130 (56.8%) patients had criteria APS clinical manifestations and 99 patients did not. 46% were Caucasian, 26% of African descent, 18% Hispanic, 2% Asian, and 8% were unspecified. Among traditional risk factors and signs of endothelial injury, only hypertension demonstrated an independent association with arterial thrombosis (OR=3.826, 95%CI 1.597 – 9.167, P=0.0026), and LA demonstrated an independent association with venous thrombosis (OR=3.308, 95%CI 1.544 – 7.085, P=0.0021). Fisher’s exact test showed a marginally significant association between Caucasian race and thrombosis (P=0.045); however, multivariable analysis did not confirm an independent association. Age, diabetes, hypercholesterolemia, smoking, Raynaud’s phenomenon, livedo reticularis, and triple positive aPLs were not significantly associated with either arterial or venous thrombosis. None of the evaluated risk factors demonstrated a significant association with pregnancy morbidity.

Conclusion: HTN is a potential predictor of arterial thrombosis and the presence of LA is a potential predictor of venous thrombosis in aPL positive patients.

Disclosure: Y. Zuo, None; J. Fan, None; R. Sarode, None; S. Zhang, None; U. E. Makris, None; D. Karp, None; Y. M. Shen, None.


Abstract Number: 3

Burden of Antiphospholipid Syndrome in a Thromboembolic Disease Registry

Aurelia Luissi1, Marina Scolnik1, Maria Florencia Grande Ratti2, Maria Lourdes Posadas Martinez2 and Enrique R. Soriano3, 1Rheumatology Unit, Internal Medicine Service, Hospital Italiano de Buenos Aires, CABA, Argentina, 2Research Unit, Internal Medicine Service, Hospital Italiano de Buenos Aires, CABA, Argentina, 3Rheumatology Unit, Internal Medicine Service, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Antiphospholipid Syndrome Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM
Background/Purpose: Prevalence of antiphospholipid antibodies in general population has been reported in about 5%. Impact of different thrombophilias in clinical thromboembolic disease is difficult to estimate. Our objective was to assess prevalence (global and in patients < 40 years) of Antiphospholipid Syndrome (APS) in a prospective Institutional Registry of Thromboembolic Disease at a tertiary university hospital

Methods: A prospective cohort study evaluated all consecutive incident cases of pulmonary thromboembolism (PTE) and deep vein thrombosis (DVT) confirmed in patients over the age of 18 between January 1st 2011 and December 31st 2014 at a university hospital. All patients with venous thromboembolic disease (VTED), confirmed by venous doppler ultrasound and/or multislice computed tomographic angiography and/or angioMRI and/or ventilation/perfusion scan and/or angiography, were included in the registry after given informed consent. A personal interview was performed and clinical (risk factors, comorbidities, etc) and laboratory data were collected. Patients were contacted annually after incident event in order to assess clinical status, treatments, adverse events, recurrence or death. Electronic medical records of all patients included in the registry were reviewed. APS prevalence was estimated and patients’ characteristics were compared with other VTED etiologies

Results: 1294 patients with VTED were included in the registry in this period [females 54.9%, mean age 68.8 years (SD 15.7)]. VTED was attributed to APS in 23 patients [females 73.9%, mean age 59.6 (SD 18.2)], representing 1.8% of all patients and 3.8% of patients <= 40 years (Table 1). APS was associated with other autoimmune diseases in 7 patients (30.4%) (4 SLE, 2 RA, 1 overlap). Patients with APS and other thrombophilias were younger than patients with other etiologies (p<0.001) (Table 2). Type of event and event mortality were similar across groups (Table 2). Having a prior/recurrent event was more frequent in patients with APS and other thrombophilias. In a multivariate logistic regression analysis, younger age (OR 1.03, CI 1.01-1.06), female sex (OR 1.64, CI 1.06-1.86) and a prior VTED event (OR 6.3, CI 2.5-16.1), were significantly associated with APS as the cause of the event.

Table 1. Registry patients’ characteristics

<table>
<thead>
<tr>
<th></th>
<th>All patients (n=1294)</th>
<th>Patients &lt;= 40 years (n=79)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females, n (%)</td>
<td>713 (54.9)</td>
<td>46 (58.2)</td>
</tr>
<tr>
<td>Mean age at diagnosis, years(SD)</td>
<td>68.8 (15.7)</td>
<td>30.2 (6.6)</td>
</tr>
<tr>
<td>Main cause of DVT/PTE, % (CI 95%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Cancer</td>
<td>34.2 (31.6-36.8)</td>
<td>22.8 (14.8-33.4)</td>
</tr>
<tr>
<td>- Immobility</td>
<td>15.6 (13.7-17.6)</td>
<td>5.1 (1.9-12.8)</td>
</tr>
<tr>
<td>- Major surgery</td>
<td>14.8 (13-16.8)</td>
<td>20.2 (12.7-30.6)</td>
</tr>
<tr>
<td>- Thrombophilias (other than APS)</td>
<td>5.6 (4.5-7)</td>
<td>12.7 (6.9-22)</td>
</tr>
<tr>
<td>- Antiphospholipid syndrome</td>
<td>1.8 (1.2-2.6)</td>
<td>3.8 (1.2-11.2)</td>
</tr>
<tr>
<td>- Recent journey</td>
<td>1.3 (0.8-2.1)</td>
<td>2.5 (0.6-9.6)</td>
</tr>
<tr>
<td>- Oral contraceptives/hormonal replacement</td>
<td>1.2 (0.7-1.9)</td>
<td>10.1 (5.1-19)</td>
</tr>
<tr>
<td>- Pregnancy/puerperium</td>
<td>0.5 (0.2-1)</td>
<td>6.3 (2.6-14.4)</td>
</tr>
<tr>
<td>- Thrombocytosis</td>
<td>0.4 (0.2-0.9)</td>
<td>0</td>
</tr>
<tr>
<td>- Multiple causes</td>
<td>10.3 (8.7-12)</td>
<td>7.6 (3.4-16)</td>
</tr>
<tr>
<td>- Unknown</td>
<td>14.5 (12.7-16.5)</td>
<td>8.9 (0.4-17.5)</td>
</tr>
</tbody>
</table>

Table 2. APS patients’ characteristics in comparison with other etiologies
<table>
<thead>
<tr>
<th></th>
<th>APS patients (n=23)</th>
<th>Other Thrombophilias (n=73)</th>
<th>Other causes of VTED (n=1201)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%)</td>
<td>17 (73.9)</td>
<td>42 (57.5)</td>
<td>654 (54.5)</td>
<td>0.2</td>
</tr>
<tr>
<td>Mean age at diagnosis, years (SD)</td>
<td>59.6 (18.2)</td>
<td>61.3 (17.6)</td>
<td>69.4 (15.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Event type, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- DVT</td>
<td>12 (52.2)</td>
<td>46 (63.1)</td>
<td>687 (57.3)</td>
<td>0.55</td>
</tr>
<tr>
<td>- PTE</td>
<td>6 (26.1)</td>
<td>16 (21.9)</td>
<td>344 (28.7)</td>
<td>0.44</td>
</tr>
<tr>
<td>- DVT + PTE</td>
<td>5 (21.7)</td>
<td>11 (15.1)</td>
<td>167 (13.9)</td>
<td>0.55</td>
</tr>
<tr>
<td>Event mortality, n (%)</td>
<td>0 (0)</td>
<td>4 (5.5)</td>
<td>110 (9.2)</td>
<td>0.18</td>
</tr>
<tr>
<td>On anticoagulation at event time, n (%)</td>
<td>7 (30.4)</td>
<td>14 (19.2)</td>
<td>129 (10.8)</td>
<td>0.002</td>
</tr>
<tr>
<td>Prior event, n (%)</td>
<td>11 (47.8)</td>
<td>24 (32.9)</td>
<td>140 (11.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Type of prior event, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- DVT</td>
<td>6 (26.1)</td>
<td>18 (24.7)</td>
<td>105 (8.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>- PTE</td>
<td>2 (8.7)</td>
<td>3 (4.1)</td>
<td>12 (1)</td>
<td>0.001</td>
</tr>
<tr>
<td>- DVT + PTE</td>
<td>3 (13.1)</td>
<td>3 (4.1)</td>
<td>23 (1.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>Follow-up after event, years, median (IQR)</td>
<td>1.9 (0.1-4.5)</td>
<td>3.2 (0.8-4.5)</td>
<td>1.1 (0.1-3.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Recurrence of any thrombotic event during follow up, n (%)</td>
<td>4 (17.4)</td>
<td>14 (19.2)</td>
<td>40 (3.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Comorbidities, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Hypertension</td>
<td>15 (65.2)</td>
<td>36 (49.3)</td>
<td>780 (65.1)</td>
<td>0.02</td>
</tr>
<tr>
<td>- Diabetes</td>
<td>5 (21.7)</td>
<td>10 (13.7)</td>
<td>190 (15.9)</td>
<td>0.6</td>
</tr>
<tr>
<td>- Dyslipidemia</td>
<td>12 (52.2)</td>
<td>27 (36.9)</td>
<td>483 (40.3)</td>
<td>0.4</td>
</tr>
<tr>
<td>- Active Smoker</td>
<td>6 (26.1)</td>
<td>28 (38.4)</td>
<td>379 (31.6)</td>
<td>0.4</td>
</tr>
<tr>
<td>- Major cardiovascular event</td>
<td>5 (21.7)</td>
<td>6 (8.2)</td>
<td>144 (12.1)</td>
<td>0.2</td>
</tr>
<tr>
<td>- Heart failure</td>
<td>2 (8.7)</td>
<td>3 (4.1)</td>
<td>93 (7.8)</td>
<td>0.5</td>
</tr>
</tbody>
</table>

**Conclusion:** APS-related VTED events represented 1.8% of total events in this registry. Younger age, female sex and having had a prior event were significantly associated with APS.

**Disclosure:** A. Luissi, None; M. Scolnik, None; M. F. Grande Ratti, None; M. L. Posadas Martinez, None; E. R. Soriano, Abbvie, BMS, Novartis, Janssen, Pfizer, Roche, UCB, 2,Abbvie, BMS, Novartis, Janssen, Pfizer, Roche, UCB, 5,Abbvie, BMS, Novartis, Janssen, Pfizer, Roche, UCB, 8.


**Abstract Number:** 4

**Downregulation of microRNAs in Plasmacytoid Dendritic Cells Is Associated with a Type I Interferon Signature in Systemic Lupus Erythematosus and Antiphospholipid Syndrome**

Lucas L. van den Hoogen¹, Joel A.G. van Roon²,³, Ruth D.E. Fritsch-Stork⁴, Cornelis P.J. Bekker¹, Aridaman Pandit¹, Marzia Rossato⁵ and Timothy R.D.J. Radstake¹, ¹Rheumatology and Clinical Immunology, Laboratory of Translational Immunology, University Medical Center Utrecht, Utrecht, Netherlands, ²Department of Rheumatology & Clinical Immunology, University Medical Center Utrecht, Utrecht, Netherlands, ³Laboratory for Translational Immunology, University Medical Center Utrecht, Utrecht, Netherlands, ⁴Department of Rheumatology and Clinical Immunology, University Medical Center Utrecht, Utrecht, Netherlands, ⁵Department of Rheumatology & Clinical Immunology, Laboratory of Translational Immunology, University Medical Center Utrecht, Utrecht, Netherlands

**First publication:** September 18, 2017
The most prominent alteration in the immune system of patients with SLE is a type I interferon (IFN) signature, which we recently also reported in patients with primary APS (PAPS). In SLE and APS, this signature is related to disease activity and vascular disease. Plasmacytoid dendritic cells (pDC) are considered key players in the pathogenesis of SLE and APS as they are major producers of type I IFN. MicroRNAs (miRNAs) are short non-coding RNAs that modulate gene expression through RNA interference and have been implicated in the dysregulation of immune cells in autoimmune diseases. Here we investigated miRNA expression in pDC of patients with SLE and APS in relation to the IFN signature.

Methods:

RNA was extracted from pDCs isolated from the peripheral blood of patients with SLE (n=20), SLE+APS (n=10), PAPS (n=10) and HC (n=12). pDC miRNA and transcriptome profiles were assessed by RT-qPCR by OpenArray and RNA-sequencing (RNAseq) respectively. Patients were stratified by the presence (IFN-high) or absence (IFN-low) of an IFN signature on the basis of RNAseq. pDC stimulated with TLR7 agonists were analyzed for changes in miRNA expression. The frequency of circulating pDC was determined by flow cytometry in patients with SLE (n=49), SLE+APS (n=34) and PAPS (n=27) and healthy controls (HC, n=22)

Results:

Among 131 expressed miRNAs, 36, 17 and 21 miRNAs were differentially expressed (p<0.05) in patients with SLE, SLE+APS and PAPS, respectively, as compared with HC. All but one of these miRNAs were downregulated in the patients versus HC. Only 1 miRNA was differentially expressed when comparing between SLE and SLE+APS patients and between SLE+APS and PAPS patients. No changes in expression of genes related to the biogenesis of miRNAs were observed in the pDC of the patient groups. RNAseq data revealed an IFN signature in pDC, which was strongest in SLE and SLE+APS patients. IFN-high (n=23) patients showed a stronger downregulation of miRNAs as compared with IFN-low (n=17) patients. Activation of pDCs by TLR7 agonists induced a downregulation of miRNAs in pDC, resembling the miRNA expression pattern seen in patients, in particular those with a high type I IFN signature. Pathway enrichment on the overlap of the targets of the top three miRNA (p<0.001) and differentially expressed genes from RNAseq between IFN-high and –low patients indicated that these miRNAs are potentially regulating pathways relevant for pDC function such as TLR signaling, endocytosis and pDC survival. In line with that, the numbers of circulating pDC were reduced in peripheral blood of patients with SLE, SLE+APS and PAPS, in particular in patients with a high type I IFN signature.

Conclusion:

Reduced numbers of circulating pDC and downregulation of miRNAs in pDC are shared between SLE, SLE+APS and PAPS patients and are related to the IFN signature. Our data suggest that the reduced expression of a subset of miRNA underlies pDC dysregulation in SLE, SLE+APS and PAPS patients.

Disclosure: L. L. van den Hoogen, None; J. A. G. van Roon, None; R. D. E. Fritsch-Stork, None; C. P. J. Bekker, None; A. Pandit, None; M. Rossato, None; T. R. D. J. Radstake, None.

Abstract Number: 5

Clinical Utility of the Global Antiphospholipid Syndrome Score (GAPSS) for Risk Stratification: A Pooled Analysis from 2273 Patients

Savino Sciascia1, Massimo Radin2, Giovanni Sama3, Irene Cecchi4, Dario Roccatello5 and Maria Laura Bertolaccini6, 1Center of Research of Immunopathology and Rare Diseases- Coordinating Center of Piemonte and Valle d’Aosta Network for Rare Diseases, Department of Clinical and Biological Sciences, University of Turin, Italy, 2Center of Research of Immunopathology and Rare Diseases- Coordinating Center of Piemonte and Valle d’Aosta Network for Rare Diseases, Department of Clinical and Biological Sciences, University of Turin, Italy, Torino, Italy, 3Department of Clinical and Biological Sciences, Center of Research of Immunopathology and Rare Diseases- Coordinating Center of Piemonte and Valle d’Aosta Network for Rare Diseases, Department of Clinical and Biological Sciences, University of Turin, Italy, Torino, Italy, 4Louise Coote Lupus Unit, Guy's and St Thomas’ NHS Foundation Trust, London, United Kingdom, London, United Kingdom, 5Center of Research of Immunopathology and Rare Diseases- Coordinating Center of Piemonte and Valle d’Aosta Network for
SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Antiphospholipid Syndrome Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Recently, our group conceived a risk score for clinical manifestations of APS [the global APS score or GAPSS] that takes into account the combination of independent cardiovascular risk factors and the aPL positivity profile. These include hyperlipidemia, arterial hypertension, aCL, anti-b2GPI, aPS/PT and the LA. A complementary version, the adjusted GAPSS or aGAPSS, which excludes aPS/PT, was also designed.

Methods:
We pooled data from available cohort studies, including a total of 10 studies, counting for a total of 2273 patients in which the GAPSS score has been applied. A search strategy was developed a priori to identify available cohort that reported findings that investigated the clinical utility of GAPSS or aGAPSS score.

Results:
When pooling together available data, GAPSS/aGAPSS was applied in a total of 2273 patients. Studies characteristics and patients enrolled are summarized in Table 1.

Seven studies used the GAPSS in their cohort, whether three studies used the aGAPSS. In brief, we found a statistically significant difference in the cumulative GAPSS and aGAPSS scores between patients that experienced arterial and/or venous thrombotic event (Cumulative GAPSS 10.6±4.74 and aGAPSS 7.6±3.95), patients without any thrombotic manifestation (Cumulative GAPSS 7.01±5.46 and aGAPSS 4.9±4.33) and patients with pregnancy morbidity (Cumulative GAPSS 8.79±2.59 and aGAPSS 6.7±2.8).

The highest levels of GAPSS were found in patients that experienced arterial thrombosis (mean GAPSS 12.2±5.2) and patients that experienced any recurrences of clinical manifestations of APS (mean GAPSS 13.7±3.1).

Conclusion:
GAPSS may represent a useful tool to assess the thrombosis or pregnancy loss risk in aPL positive patient, switching from the concept of aPL as a sole diagnostic antibody to aPL as risk factors for clinical events. A risk assessment, using appropriate tools as GAPSS, should be implemented to identify and monitor those patients at a higher risk of recurrences and those needing a strict control of all modifiable risk factor for cardiovascular events; in agreement with the above, in the future the management of APS should also modulate according to the GAPSS values.

Table 1. Demographic, clinical and laboratory characteristics of the cohort
<table>
<thead>
<tr>
<th>STUDY</th>
<th>YEAR</th>
<th>STUDY DESIGN</th>
<th>AIM</th>
<th>NUMBER OF PATIENTS</th>
<th>PATIENTS' CHARACTERISTICS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sciascia et al.</td>
<td>2013</td>
<td>Cross-Sectional</td>
<td>To validate the first GAPSS score with a validation cohort</td>
<td>105</td>
<td>SLE</td>
</tr>
<tr>
<td>Sciascia et al.</td>
<td>2014</td>
<td>Prospective</td>
<td>To prospectively and independently validate GAPSS, with a follow-up of mean 32.94 (SD 12.06) months</td>
<td>51</td>
<td>SLE aPL positive patients</td>
</tr>
<tr>
<td>Zuily et al.</td>
<td>2015</td>
<td>Prospective</td>
<td>To investigate the validity of the global APS score (GAPSS) to predict thrombosis in patients with autoimmune diseases, followed up for a mean duration of 43.1 (S.D. 20.7) months</td>
<td>137</td>
<td>patients with aPL and/or SLE</td>
</tr>
<tr>
<td>Oku et al.</td>
<td>2015</td>
<td>Retrospective</td>
<td>To validate the GAPSS independently</td>
<td>282</td>
<td>41 APS (17 PAPS) patients, 88 SLE without APS, 50 rheumatoid arthritis, 16 Sjögren’s syndrome, 21 systemic sclerosis, 10 polymyositis/dermatomyositis and 56 other autoimmune diseases</td>
</tr>
<tr>
<td>Sciascia et al.</td>
<td>2015</td>
<td>Retrospective</td>
<td>To evaluate the clinical relevance of the global APS score (GAPSS) in a cohort of primary APS patients</td>
<td>62</td>
<td>PAPS patients</td>
</tr>
<tr>
<td>Zigon et al.</td>
<td>2016</td>
<td>Retrospective</td>
<td>To evaluate association of different risk factors with thrombosis; and b) to apply GAPSS on a large cohort of unselected Slovenian patients</td>
<td>585</td>
<td>Systemic Autoimmune Diseases</td>
</tr>
<tr>
<td>Sciascia et al.</td>
<td>2016</td>
<td>Retrospective</td>
<td>To evaluate the clinical utility of the GAPSS with the help of APS ACTION Registry</td>
<td>550</td>
<td>APS Patients</td>
</tr>
<tr>
<td>Zu et al.</td>
<td>2016</td>
<td>Retrospective</td>
<td>To evaluate the clinical relevance of aGAPSS in a chinese cohort</td>
<td>89</td>
<td>89 APS Patients</td>
</tr>
<tr>
<td>Fernandez Mosteirin et al.</td>
<td>2017</td>
<td>Retrospective</td>
<td>To independently validate the aGAPSS to predict thrombosis in a cohort of patients with APS and/or autoimmune disease</td>
<td>319</td>
<td>PAPS diagnosed in 130 patients and 89 SAPS patients, and 100 patients with autoimmune disease without APS</td>
</tr>
<tr>
<td>Radin et al.</td>
<td>2017</td>
<td>Retrospective</td>
<td>To investigate the validity of aGAPSS in young patients with myocardial infarction</td>
<td>83</td>
<td>APS Patients</td>
</tr>
</tbody>
</table>
Table 2. GAPSS and aGAPSS between groups

<table>
<thead>
<tr>
<th>Study</th>
<th>Total N</th>
<th>Thrombotic N</th>
<th>GAPSS mean(± SD)</th>
<th>Non-Thrombotic N</th>
<th>GAPSS mean(±SD)</th>
<th>PM N</th>
<th>GAPSS mean(±SD)</th>
<th>CUMULATIVE GAPSS mean(±SD)</th>
<th>CUMULATIVE aGAPPS mean(±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sciascia et al. 2013</td>
<td>105</td>
<td>37</td>
<td>9.6 (4.8)</td>
<td>68</td>
<td>4.9 (5)</td>
<td>22</td>
<td>7.3 (5)</td>
<td>11 (5.4)</td>
<td>9.0 (4.9)</td>
</tr>
<tr>
<td>Sciascia et al. 2014</td>
<td>51</td>
<td>4</td>
<td>10 (5.4)</td>
<td>47</td>
<td>7.13 (5.75)</td>
<td>N/A</td>
<td>N/A</td>
<td>8.15 (5.31)</td>
<td>N/A</td>
</tr>
<tr>
<td>Sciascia et al. 2015</td>
<td>137</td>
<td>16</td>
<td>N/A</td>
<td>121</td>
<td>8.15 (5)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Sciascia et al. 2016</td>
<td>282</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>11</td>
<td>8.7 (3.2)</td>
<td>4.9 (5.46)</td>
<td>4.9 (4.43)</td>
</tr>
<tr>
<td>Sciascia et al. 2017</td>
<td>62</td>
<td>N/A</td>
<td>11.5 (4.6)</td>
<td>44</td>
<td>10.88 (5.06)</td>
<td>11</td>
<td>8.78 (3.2)</td>
<td>9.4 (3.2)</td>
<td>6.58 (3.36)</td>
</tr>
<tr>
<td>Zulli et al. 2015</td>
<td>550</td>
<td>N/A</td>
<td>N/A</td>
<td>419</td>
<td>N/A</td>
<td>419</td>
<td>N/A</td>
<td>10.6 (4.74)</td>
<td>7.6 (3.95)</td>
</tr>
<tr>
<td>Oku et al. 2015</td>
<td>1187</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>9.2 (3.1)</td>
<td>N/A</td>
</tr>
<tr>
<td>Sciascia et al. 2016</td>
<td>98</td>
<td>53</td>
<td>96 (±5)</td>
<td>53</td>
<td>53 (±5)</td>
<td>N/A</td>
<td>N/A</td>
<td>11.5 (4.6)</td>
<td>N/A</td>
</tr>
<tr>
<td>Zu et al. 2016</td>
<td>83</td>
<td>70</td>
<td>500 (±5)</td>
<td>70</td>
<td>500</td>
<td>N/A</td>
<td>N/A</td>
<td>10.6 (4.74)</td>
<td>N/A</td>
</tr>
<tr>
<td>Fernandez et al. 2017</td>
<td>319</td>
<td>201</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>201</td>
<td>N/A</td>
<td>9.2 (3.1)</td>
<td>N/A</td>
</tr>
<tr>
<td>Mosteiro et al. 2017</td>
<td>500</td>
<td>201</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>10.6 (4.74)</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Graph 1. Cumulative GAPSS values between groups

Disclosure: S. Sciascia, None; M. Radin, None; G. Sanna, None; I. Cecchi, None; D. Roccatello, None; M. L. Bertolaccini, None.

Pregnancy Outcomes in a Cohort of Women with Antiphospholipid Syndrome. 25-Years Long-Term Observation

Dana Tegzova¹, Katerina Andelova², Iva Kucerova³, Vera Vlasakova³, Stejskal Jan⁴, Putova Ivana⁵, Marta Olejarova⁶ and Ctibor Dostál⁷, ¹Clinical Department, Institute of Rheumatology and Rheumatological Clinic of 1st Medical Faculty, Charles University, Prague, Czech Republic, ²Institute of Mother and Child Care, Prague, Prague, Czech Republic, ³Dept.of Internal Medicine, City Hospital Ceske Budejovice, Ceske Budejovice, Czech Republic, ⁴1st Medical Faculty, Dpt. of Pathology, Charles University, Prague, Czech Republic, ⁵Institute of Rheumatology, Dpt. of Immunology, Prague, Czech Republic, ⁶Clinical, Institute of Rheumatology and Rheumatological Clinic of 1st Medical Faculty, Charles University, Prague, Czech Republic, ⁷Institute of Rheumatology and Rheumatological Clinic of 1st Medical Faculty, Charles University, Prague, Czech Republic

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Antiphospholipid Syndrome Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The goal of this long-term project was to investigate the course of pregnancy in patients with APS (primary or secondary with SLE) in 1993-2017, to describe the type and severity of it and to explore their relationship with disease-related characteristics. To find specific histological changes in maternal tissue in a subgroup of patients.

Methods: During more than 25 years of systematic observation 80 pregnant women with APS were observed and examined. Secondary APS was in our cohort common with systemic lupus erythematosus (SLE). Patients were evaluated every 3 months by a rheumatologist and a gynaecologist. Basic demographic data were assessed, as well as the duration and type of therapy, autoantibodies, organ involvement and its activity, the number and type of disease flares, thrombosis, the number of abortions and premature labours, new-born weight and presence of complications such as gestational diabetes, hypertension and preeclampsia. In a subgroup of 13 patients (5 with primary APS, 7 with sec.APS/SLE a macroscopic and histological examination of maternal tissue was performed in comparison with a healthy control group.

Results: The group comprised 65 pregnant women with APS, out of which 57% had secondary APS/SLE and 33% primary APS. In the group of primary APS 90% pts were treated with low molecular heparin and/or salicylates. In pts. with sec.APS/SLE 90 % of patients were treated with oral corticosteroids, 8% with cyclosporine A and 16% with azathioprine and 95% with low molecular weight heparin and/or salicylates. 7% of pregnancies were terminated in the first trimester due to missed abortion. 6% of abortions in patients with sec. APS/SLE in second trimester were observed. 57 APS patients delivered 58 newborns, 16% of them before the 37th week of pregnancy and 7% before the 34th week. Out of this group 75% patients delivered prematurely due to hypertension or preeclampsia, 10% due to growth retardation of fetus. Newborn weight was 3020g on average. AV heart block of 3rd degree was observed in 1 newborn with sec.APS/SLE. No congenital malformations were observed in our group. In the group sec.APS/SLE higher number of gestational diabetes was found: 38% of patients, all of which were treated with corticosteroids. Hypertension was found in 33% patients, preeclampsia in 12 % and 60% of patients with preeclampsia had a history of lupus nephritis. Higher score of maternal infarcts and decidual pathological changes with deposits of immunocomplexes were found in microscopic examination in patients with APS in comparison with healthy controls. Rate of weight placenta/fetus was lower. Signs of accelerate aging, nodules and inflammatory infiltration was found in light microscopy and higher score of deposits of immunocomplexes were found.

Conclusion: In spite of the fact that women with APS have a high risk during the course of pregnancy, the results of our long terms study showed a good outcome of pregnancy. Higher rate of complications was found in the group with sec. APS with SLE.

Supported by Research Project Ministry of Health of Czech Republic NO: 000 000 23728

Disclosure: D. Tegzova, None; K. Andelova, None; I. Kucerova, None; V. Vlasakova, None; S. Jan, None; P. Ivana, None; M. Olejarova, None; C. Dostál, None.


Predictive Value for Thrombosis of Double or Triple Positivity in Secondary APS
Depends on the Component Assays and the Type of Thrombosis

Michelle Petri¹, Daniel Goldman² and Laurence S Magder³, ¹Medicine (Rheumatology), Division of Rheumatology, Johns Hopkins University School of Medicine, MD, USA, Baltimore, MD, ²Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, ³Epidemiology and Public health, University of Maryland School of Medicine, Baltimore, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Antiphospholipid Syndrome Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The lupus anticoagulant (LAC) is individually the antiphospholipid antibody (aPL) most associated with thrombotic risk in both primary and secondary APS. Anticardiolipin (aCL) and anti-beta2 glycoprotein 1 may further increase the risk. We investigated the risk for thrombosis in SLE of double or triple positivity for these different aPLs.

Methods: The analysis is based on 1508 SLE patients, (92% female, 51% white, 40% black, and with a mean age at end of follow-up of 46.4 [SD=14.2]). Thrombosis was defined as: arterial thrombosis (CVA, MI, other arterial thrombosis or digital gangrene); and venous thrombosis (DVT, PE or other venous thrombosis).

Results: We looked at the risk of lifetime occurrence of thrombosis as a function of the history of LAC (RVVT confirm), aCL, or anti-beta2 glycoprotein 1 (anti-Beta2). The OR’s in the tables are adjusted for age.

Table 1. History of thrombosis by history of APS.
<table>
<thead>
<tr>
<th>Specific Components</th>
<th>Proportion (%) of patients with a history of any thrombosis</th>
<th>Odds Ratio (relative to those without any APS components)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Any Thrombosis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No aPL</td>
<td>None</td>
<td>100/488 (20%)</td>
<td>1.0 (Ref Group)</td>
</tr>
<tr>
<td>Single Positive</td>
<td>aCL alone</td>
<td>66/369 (18%)</td>
<td>0.8 (0.6, 1.2)</td>
</tr>
<tr>
<td></td>
<td>LAC alone</td>
<td>26/74 (35%)</td>
<td>2.1 (1.2, 3.6)</td>
</tr>
<tr>
<td></td>
<td>anti-Beta2 alone</td>
<td>10/82 (12%)</td>
<td>0.6 (0.3, 1.1)</td>
</tr>
<tr>
<td>Double Positive</td>
<td>Any double positive</td>
<td>105/315 (33%)</td>
<td>1.9 (1.4, 2.6)</td>
</tr>
<tr>
<td></td>
<td>aCL + LAC</td>
<td>61/138 (44%)</td>
<td>2.9 (1.9, 4.4)</td>
</tr>
<tr>
<td></td>
<td>aCL + anti-Beta2</td>
<td>29/147 (20%)</td>
<td>0.9 (0.6, 1.5)</td>
</tr>
<tr>
<td></td>
<td>LAC + anti-Beta2</td>
<td>15/30 (50%)</td>
<td>4.1 (1.9, 8.8)</td>
</tr>
<tr>
<td>Triple positive</td>
<td>All three</td>
<td>89/180 (49%)</td>
<td>3.7 (2.6, 5.4)</td>
</tr>
<tr>
<td><strong>Arterial Thrombosis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No aPL</td>
<td>None</td>
<td>55/488 (11%)</td>
<td>1.0 (Ref)</td>
</tr>
<tr>
<td>Single Positive</td>
<td>aCL alone</td>
<td>40/369 (11%)</td>
<td>0.9 (0.6, 1.5)</td>
</tr>
<tr>
<td></td>
<td>LAC alone</td>
<td>12/74 (16%)</td>
<td>1.5 (0.7, 3.0)</td>
</tr>
<tr>
<td></td>
<td>anti-Beta2 alone</td>
<td>6/82 (7%)</td>
<td>0.6 (0.3, 1.5)</td>
</tr>
<tr>
<td>Double Positive</td>
<td>Any double positive</td>
<td>59/315 (19%)</td>
<td>1.7 (1.1, 2.5)</td>
</tr>
<tr>
<td></td>
<td>aCL + LAC</td>
<td>37/138 (27%)</td>
<td>2.6 (1.6, 4.2)</td>
</tr>
<tr>
<td></td>
<td>aCL + anti-Beta2</td>
<td>18/147 (12%)</td>
<td>1.0 (0.6, 1.9)</td>
</tr>
<tr>
<td></td>
<td>LAC + anti-Beta2</td>
<td>4/30 (13%)</td>
<td>1.3 (0.4, 3.8)</td>
</tr>
<tr>
<td>Triple positive</td>
<td>All three</td>
<td>54/180 (30%)</td>
<td>3.2 (2.1, 5.0)</td>
</tr>
<tr>
<td><strong>Venous Thrombosis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No aPL</td>
<td>None</td>
<td>54/488 (11%)</td>
<td>1.0 (Ref)</td>
</tr>
<tr>
<td>Single Positive</td>
<td>aCL alone</td>
<td>39/369 (11%)</td>
<td>0.9 (0.6, 1.5)</td>
</tr>
<tr>
<td></td>
<td>LAC alone</td>
<td>19/74 (26%)</td>
<td>2.8 (1.5, 5.1)</td>
</tr>
<tr>
<td></td>
<td>anti-Beta2 alone</td>
<td>5/82 (6%)</td>
<td>0.5 (0.2, 1.4)</td>
</tr>
<tr>
<td>Double Positive</td>
<td>Any double positive</td>
<td>72/315 (23%)</td>
<td>2.4 (1.6, 3.5)</td>
</tr>
<tr>
<td></td>
<td>aCL + LAC</td>
<td>42/138 (31%)</td>
<td>3.5 (2.2, 5.6)</td>
</tr>
<tr>
<td></td>
<td>aCL + anti-Beta2</td>
<td>17/147 (12%)</td>
<td>1.0 (0.6, 1.8)</td>
</tr>
<tr>
<td></td>
<td>LAC + anti-Beta2</td>
<td>12/30 (40%)</td>
<td>5.5 (2.5, 12.0)</td>
</tr>
<tr>
<td>Triple positive</td>
<td>All three</td>
<td>60/180 (33%)</td>
<td>3.9 (2.6, 6.0)</td>
</tr>
</tbody>
</table>

The findings in the table confirm that there can be an increase in the point estimate from single, to double positivity. However, it clearly depends on which components are considered, and whether it is arterial or venous thrombosis. The strongest finding is that LAC is the most important component. For arterial thrombosis, however, double positivity with LAC and aCL leads to increased risk.

**Conclusion:** In SLE, lupus anticoagulant is the most important single antiphospholipid test predictive of any thrombosis and venous thrombosis. For arterial thrombosis, aCL and LAC together outperform single tests. For venous thrombosis, the point estimates increase for double positives containing LAC, and for triple positive, although the confidence intervals overlap. In SLE, double, and possibly triple, positivity show promising results. However, different combinations of “double positive” aPLs are important, and differ in arterial vs. venous thrombosis.

**Disclosure:** M. Petri, Anthera Inc, 5,GlaxoSmithKline, 5,EMD Serono, 5,Eli Lilly and Company, 5,Bristol Meyer Squibb, 5,Amen, 5,United Rheumatology, 5,Global Academy, 5,Exagen, 2; D. Goldman, None; L. S. Magder, None.

Antiphospholipid Syndrome Leukocytes Demonstrate Increased Adhesive Potential: a Search for Novel Therapeutic Targets

Gautam Sule1, William J. Kelley1, Srilakshmi Yalavarthi1, Alison Banka1, Omolola Eniola-Adefeso1 and Jason S. Knight2, 1University of Michigan, Ann Arbor, MI, 2, University of Michigan, Ann Arbor, MI
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Antiphospholipid Syndrome Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Adhesion of leukocytes to the endothelium is an initiating event in the thrombosis inherent to antiphospholipid syndrome (APS). Over the years, a number of groups have demonstrated that antiphospholipid antibodies (aPL) upregulate both selectins and integrin receptors on endothelial cells, thereby increasing the adhesive potential of the endothelium. Here, we posit that factors intrinsic to leukocytes may also play a pivotal role in adhesive interactions. For example, transcriptome analysis of APS patient neutrophils has revealed an activated, adhesive signature. Furthermore, leukocyte adhesion in our mouse model of aPL-mediated large vein thrombosis is regulated by leukocyte (more so than endothelial) factors. In this study, we functionally characterize leukocyte adhesion in APS, with the goal of ultimately testing the therapeutic potential of putative targets.

Methods: Patients had primary APS (classified by Sydney criteria), while healthy controls were matched for age and gender. Freshly-isolated human umbilical vein endothelial cells (HUVECs) were used. Anticoagulated whole blood (or purified cellular components) was introduced into a flow channel via a programmable syringe pump, and perfused across an unstimulated HUVEC monolayer in a pulsatile flow profile with wall shear rate set to 1000 s⁻¹. After 15 minutes of perfusion, the chamber was flushed to remove nonadherent cells, and images were captured with an inverted microscope.

Results: Perfusion of APS blood across unstimulated HUVECs resulted in significantly more leukocyte adhesion as compared with control blood (mean 5.0-fold increase; p<0.0001 with n=18 patients). To assess the role of leukocytes themselves (versus plasma factors that might activate HUVECs), leukocytes were washed free of plasma, resuspended in buffer, and then perfused across HUVECs. In this plasma-free context, there was still significantly more adhesion of APS leukocytes (mean 2.2-fold increase; p<0.01 with n=10 patients), suggesting an intrinsic increase and/or activation of leukocyte adhesion factors. Furthermore, treating control leukocytes with APS patient plasma (which was then washed away before perfusion) resulted in increased adhesion of the control leukocytes (mean 2.5-fold increase; p<0.0001 with n=12 plasma samples). Experiments are underway to delineate the factors on the leukocyte surface that dictate the increased adhesive potential (as well as the factors in APS plasma that mediate their upregulation). In particular, we are characterizing both selectin ligands and beta-2 integrins on leukocytes, as even unstimulated HUVECs demonstrate baseline expression of potential binding partners (selectins and ICAM-1, respectively). We are also determining the relative adhesive potential of different leukocyte subpopulations (i.e., monocytes versus neutrophils).

Conclusion: While there is a known role for aPL in increasing the adhesive potential of endothelial cells, we now report that leukocytes themselves have an intrinsic increase in their adhesive potential. The ultimate goal of this work is to identify the most relevant pharmacologic targets on the leukocyte surface.

Disclosure: G. Sule, None; W. J. Kelley, None; S. Yalavarthi, None; A. Banka, None; O. Eniola-Adefeso, None; J. S. Knight, None.

Renal Protective Effect of Antiplatelet Therapy in Antiphospholipid Antibody-Positive Lupus Nephritis Patients without the Antiphospholipid Syndrome

Hironari Hanaoka1, Tomofumi Kiyokawa1, Harunobu Iida1, Yukiko Takakuwa1, Takahiro Okazaki2, Hidehiro Yamada3, Shoichi Ozaki4 and Kimito Kawahata1, 1Division of Rheumatology and Allergology, Department of Internal Medicine, St. Marianna University School of Medicine
SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Antiphospholipid Syndrome Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Lupus nephritis (LN) class III or IV is associated with a poor prognosis for both patient and renal survival. Since antiphospholipid syndrome (APS) is reported to worsen the prognosis of LN, LN patients with APS should be treated with conventional immunosuppressive treatment plus antiplatelet or anticoagulation therapy according to the recommendations for LN management. However it has been unclear whether these therapies would benefit antiphospholipid antibodies (aPL)-positive LN patients not meeting the diagnostic criteria. Here, we evaluated the effect of antiplatelet therapy in addition to conventional immunosuppressive therapy for LN patients positive for aPL without definite APS.

Methods: Patients with biopsy-proven LN class III or IV who did not take hydroxychloriquine were retrospectively evaluated. We selected patients positive for anticardiolipin antibody (aCL) or lupus anticoagulant (LA) who did not meet the criteria for a diagnosis of APS. The patients were divided into two subgroups according to whether antiplatelet therapy was received. The cumulative complete renal response (CR) rate, relapse-free rate, and change in estimated glomerular filtration rate (eGFR) over 3 years after induction therapy were calculated.

Results: We identified 17 patients who received antiplatelet therapy and 21 who did not. Baseline clinicopathological characteristics and immunosuppressive therapy did not show a statistically significant difference between the two groups except for a significantly higher incidence of LN class IV in the treatment group (p = 0.03). There was no significant difference in cumulative CR rate, relapse-free rate, or eGFR change between these subgroups. However, when data on LA-positive patients were assessed, a significant improvement in eGFR was found (p = 0.04) in patients receiving antiplatelet therapy (Figure 1).

Conclusion: Addition of anti-platelet therapy was associated with an improvement of eGFR in LA-positive patients with LN class III or IV. There may be a wider indication for antiplatelet therapy in LN, in addition to its use in patients with a definite APS diagnosis.

Figure 1

<table>
<thead>
<tr>
<th></th>
<th>(A)</th>
<th>(B)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>eGFR (ml/min/1.73m²)</td>
<td>eGFR (ml/min/1.73m²)</td>
</tr>
<tr>
<td>baseline</td>
<td>Year 3</td>
<td>baseline</td>
</tr>
<tr>
<td>LA (+)</td>
<td></td>
<td>LA (-)</td>
</tr>
<tr>
<td>Antiplatelet therapy</td>
<td>Received (n = 11)</td>
<td>Antiplatelet therapy</td>
</tr>
<tr>
<td>Not received (n = 10)</td>
<td></td>
<td>Not received (n = 11)</td>
</tr>
</tbody>
</table>

Disclosure: H. Hanaoka, None; T. Kiyokawa, None; H. Iida, None; Y. Takakuwa, None; T. Okazaki, None; H. Yamada, None; S. Ozaki, None; K. Kawahata, None.


Abstract Number: 10

Arterial Events in Primary Antiphospholipid Syndrome Are Associated with High Values of the Adjusted Global Antiphospholipid Syndrome Score
SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Antiphospholipid Syndrome Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The adjusted Global AntiPhospholipid Syndrome Score (aGAPSS) was described as a tool to estimate the risk of thromboses in patients with APS. The aim of this study is to evaluate if higher values of aGAPSS correlate with the presence of arterial or venous thromboses in thrombotic primary APS patients.

Methods: A cross-sectional study was performed in a group of 72 outpatients who fulfilled thrombotic pAPS classification criteria (Sydney). Clinical and serologic features were collected during visits and by chart review. aGAPSS was calculated for each patient and correlated to arterial and venous thromboses. Statistical analysis was performed using chi-square, Mann-Whitney U and Spearman’s R when applicable. Multivariate regression analysis included age, sex, race and variables with p<0.10 in the bivariate analysis.

Results: Thirty-seven (51.4%) patients had arterial events and 51 (70.8%) had venous thromboses. The mean number of episodes of arterial and venous thromboses was 1.65 and 1.4 per patient, respectively. The median aGAPSS of the 72 patients included in the analysis was 9 (7-13); this was used to divide two groups of patients: low aGAPSS (<10) and high aGAPSS (≥10). Patients with or without arterial thromboses were compared regarding the presence of high aGAPSS. In a bivariate analysis, higher aGAPSS correlated with the presence of arterial thromboses (p=0.018). In a multivariate regression analysis, higher aGAPSS correlated with the presence of arterial thromboses (p=0.018). A one-way analysis of variance (ANOVA) and a new analysis as a variable to detect high risk thrombotic patients, particularly arterial events.

Conclusion: The presence of arterial events was associated with higher values of aGAPSS. aGAPSS seems to be a tool capable to detect high risk thrombotic patients, particularly arterial events.

Table 1: Demographic and clinical characteristics (N=72).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Arterial thromboses (N=37)</th>
<th>No arterial thromboses (N=35)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>46.9±13.5</td>
<td>42.1±11.9</td>
<td>NS</td>
</tr>
<tr>
<td>Female gender</td>
<td>29 (78.4)</td>
<td>31 (88.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Caucasian</td>
<td>23 (62.2)</td>
<td>24 (68.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Time first manifestation (mo)</td>
<td>180 (96-240)</td>
<td>108 (69.5-192)</td>
<td>NS</td>
</tr>
<tr>
<td>aGAPSS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High aGAPSS (value≥10)</td>
<td>20 (54.1)</td>
<td>9 (25.7)</td>
<td>0.013</td>
</tr>
<tr>
<td>Hypertension</td>
<td>17 (45.9)</td>
<td>10 (28.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>20 (54.1)</td>
<td>9 (25.7)</td>
<td>0.018</td>
</tr>
<tr>
<td>Lupus anticoagulant</td>
<td>34 (91.9)</td>
<td>32 (91.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Anticardiolipin</td>
<td>15 (40.5)</td>
<td>13 (37.1)</td>
<td>NS</td>
</tr>
<tr>
<td>Anti-ß2-glycoprotein I</td>
<td>24 (64.9)</td>
<td>15 (42.9)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values showed as N(%) for categorical variables, Mean± SD for normal distribution and Median (interquartil range) for asymmetrical distribution.
Possible Therapeutics for Antiphospholipid Antibody Related Thrombocytopenia: A Systemic Review and Meta-Analysis


First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Antiphospholipid Syndrome Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Despite the pro-thrombotic nature of antiphospholipid antibodies (aPL), thrombocytopenia is frequently observed in patients with antiphospholipid syndrome (APS) or in non-APS patients with aPL. The management of the thrombocytopenia with aPL (aPL related thrombocytopenia; APAT) is often deductive, due to the paradoxical risks of thrombosis and hemorrhage. We have been striving to clarify the mechanisms of APAT and reported its high prevalence of arterial thrombotic events (Nakagawa I, et al. ACR 2014, Abstract #2). In the present study, along with the reconfirmation of the clinical importance of APAT, we aimed to evaluate the efficacy of therapeutic regimes in APAT through a systematic review of the literature with the objective of elaborating a clinical practice guideline for APAT on a consignment project from the Japanese Ministry of Health, Labor and Welfare.

Methods: Four clinical questions were selected for systematic review and redefined using the PICO (Patient, Intervention, Comparison, Outcome) format and prioritized. The four clinical questions were to evaluate the effects of possible therapeutics for APAT; antiplatelet agents, glucocorticoids, and thrombopoietin receptor agonists. Systematic reviews were performed using electronic databases (MEDLINE, EMBASE and CENTRAL) by the Cochrane Japan Centre. Cochrane Collaboration Review Manager software was used to manage and analyze the data collected.

Results: The initial search yielded 1407 citations of which nine were included in our final analysis. There was no randomized controlled trial on treatment for APAT. We identified four case-controlled studies for splenectomy, one for antiplatelet agents and four observational studies for glucocorticoids. Meta-analysis of quantitative data (17/23) showed evidence of an increase in platelet count in patients who underwent splenectomy compared with the patients without splenectomy (mean difference 22.6±10^4/mL, P=0.007) (Figure). Complete remissions of the thrombocytopenia were observed in 18/23 (78%) patients with splenectomy versus 0/23 (0%) without splenectomy. The relapses were occurred in 3/23 (13%) patients with splenectomy. There was no complications due to splenectomy. None of the configured outcomes were susceptible to the antiplatelet and glucocorticoid therapy.

Conclusion: Although splenectomy for APS was previously reported to be a risk of portal vein thrombosis, our systematic review and meta-analysis revealed that it may be performed rather safely and effectively in APAT patients. However, there was no clear evidence to support applications of antiplatelet agents, glucocorticoids, or thrombopoietin receptor agonists as therapeutics of APAT. Further clinical trials are required to establish therapeutic recommendation for APAT.
Abstract Number: 12

Antiphospholipid Syndrome Alliance for Clinical Trials and International Networking (APS ACTION) Clinical Database and Repository Analysis: Pregnancy Outcomes Since Inception

Ecem Sevim¹, Danieli Andrade², Alessandra Banzato³, D. Ware Branch⁴, Ricard Cervera⁵, Guilherme Ramires de Jesus⁶, Jason S. Knight⁷, Pier Luigi Meroni⁸, Maria Tektonidou⁹, Angela Tincani¹⁰, Amaia Ugarte¹¹, Zhang Zhuoli¹², Doruk Erkan¹³ and, on Behalf of APS ACTION ¹⁴, ¹¹¹Urani Research and Training Hospital, Istanbul Health Sciences University, Istanbul, Turkey, ²Rheumatology, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, BR., Sao Paulo, Brazil, ³Department of Cardiac Thoracic and Vascular Sciences, Clinical Cardiology, Thrombosis Centre, University of Padova, Padova, Italy, ⁴Obstetrics and Gynecology, University of Utah and Intermountain Healthcare, Salt Lake City, UT, ⁵Department of Autoimmune Diseases, Institut Clinic de Medicina i Dermatologia, Hospital Clinic de Barcelona, Barcelona, Spain, ⁶Obstetrics, Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil, ⁷., University of Michigan, Ann Arbor, MI, ⁸Istituto Ortopedico Gaetano Pini, University of Milan, Milano, Italy, ⁹First Department of Internal Medicine, School of Medicine, National University of Athens, Athens, Greece, ¹⁰Rheumatology and Clinical Immunology, Spedali Civili and University of Brescia, Brescia, Italy, ¹¹Autoimmune Diseases Research Unit, Department of Internal Medicine, BioCruces Health Research Institute, Hospital Universitario Cruces, University of the Basque Country, Biscay, Spain, ¹²Department of Rheumatology and Immunology, Peking University First Hospital, Peking University First Hospital, Beijing, China, ¹³Rheumatology, Hospital for Special Surgery- Weill Cornell Medicine, New York, NY, ¹⁴., New York, NY

First publication: September 18, 2017

Background/Purpose: APS ACTION Clinical Database and Repository ("Registry") was created to study the natural course of disease over 10 years in persistently antiphospholipid antibody (aPL) positive patients with/without other systemic autoimmune diseases. Our objective was to describe the new pregnancy outcomes of the aPL-positive patients since the inception of the registry.

Methods: A web-based data capture system is used to store patient demographics, history, and medications. The inclusion criteria are positive aPL based on the Updated Sapporo Classification Criteria at least twice within one year prior to enrollment. Patients are followed every 12±3 months with clinical data and blood collection. For this analysis, we identified all patients who were recorded as “pregnant” during the prospective follow-up.

Results: Since the inception of the registry in 5/2012, 45 pregnancies were recorded in 36 aPL-positive patients (mean age 33.4 ± 4.9 y; lupus: 5 [14%]; LA-positive alone: 16 [44%]; triple aPL-positive: 11 [31%]; double aPL-positive: 7 [19%]; obstetric APS [OAPS]: 5 [14%]; thrombotic APS [TAPS]: 10 [28%]; OAPS+TAPS: 12 [33%]; and no history of OAPS/TAPS: 9 [25%]). Of 45 pregnancies (28 patients had one pregnancy, seven had two, and one had three), 23 (51%) resulted in term live birth (preeclampsia [PEC]: 1; and small for gestational age [SGA]: 2), eight (18%) preterm live birth (mean delivery week [w] 33.5 ± 1.7; PEC: 4; and SGA: 1), 12 (27%) (pre) embryonic loss < 10w, one (2%) fetal death > 20w, and one was ongoing at the time of data lock (Table). Term live birth occurred in 12/21 (57%) of pregnancies of patients with history of OAPS (no treatment: 1; Aspirin [ASA]; 1; low-molecular-weight-heparin [LMWH]:2; and ASA+LMWH: 8), compared to 11/24 (46%) of pregnancies of patients without history of OAPS (no treatment: 1; ASA:1; LMWH:2; and ASA+LMWH: 7). (p: 0.38). Pre-term live birth occurred in 3/21 (14%) of pregnancies of patients with history of OAPS (no treatment: 1; and ASA+LMWH: 2), compared to 5/24 (21%) of pregnancies of patients without history of OAPS (ASA+LMWH: 5) (p: 0.70). Similarly, term and preterm live birth rates were not different between patients with and without TAPS.

Conclusion: Fifty percent and 20% of pregnancies in our multi-center international aPL-positive cohort resulted in term and preterm live births, respectively. While 80% of the pregnancies were treated with low dose aspirin +/- LMWH, only 60% had had a history of pregnancy morbidity fulfilling the Updated Sapporo Classification Criteria. Term and preterm live birth rates were similar between patients with and without history of obstetric APS or thrombotic APS; no pregnancy was complicated with fetal loss between 10-20 weeks; and only one with fetal loss after 20 weeks.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/possible-therapeutics-for-antiphospholipid-antibody-related-thrombocytopenia-a-systemic-review-and-meta-analysis
<table>
<thead>
<tr>
<th>Term LB (n: 23)</th>
<th>Preterm LB (n: 8)</th>
<th>(Pre)Emb. Loss&lt;sup&gt;a&lt;/sup&gt; (n: 12)</th>
<th>Fetal Loss&lt;sup&gt;b&lt;/sup&gt; (n:1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of Pregnancy</td>
<td>22 (96%)</td>
<td>6 (75%)</td>
<td>10 (83%)</td>
</tr>
<tr>
<td>History of Pregnancy Morbidity</td>
<td>.</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>≥1 Fetal Loss</td>
<td>10 (45%)</td>
<td>1 (17%)</td>
<td>5 (50%)</td>
</tr>
<tr>
<td>≥1 Preterm Delivery</td>
<td>4 (18%)</td>
<td>1 (17%)</td>
<td>3 (30%)</td>
</tr>
<tr>
<td>≥3&lt;sup&gt;c&lt;/sup&gt; (Pre)Embryonic Loss</td>
<td>2 (9%)</td>
<td>1 (17%)</td>
<td>0</td>
</tr>
<tr>
<td>≥1 (Pre) Embryonic Loss</td>
<td>8 (35%)</td>
<td>2 (34%)</td>
<td>5 (50%)</td>
</tr>
<tr>
<td>No History of Pregnancy Morbidity</td>
<td>.</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>Treatment During Pregnancy</td>
<td>.</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>No ASA/LMWH</td>
<td>4 (17%)</td>
<td>1 (13%)</td>
<td>4 (33%)</td>
</tr>
<tr>
<td>ASA</td>
<td>8 (38%)</td>
<td>1 (13%)</td>
<td>2 (17%)</td>
</tr>
<tr>
<td>LMWH</td>
<td>2 (9%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>ASA + LMWH</td>
<td>9 (39%)</td>
<td>6 (75%)</td>
<td>6 (50%)</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>13 (57%)</td>
<td>4 (50%)</td>
<td>6 (50%)</td>
</tr>
</tbody>
</table>

LB: live birth; ASA: low-dose aspirin; LMWH: low-molecular-weight-heparin; <sup>a</sup>: (pre)embryonic loss < 10 weeks of gestation; <sup>b</sup>: fetal loss > 20 weeks of gestation; <sup>c</sup>: consecutive

Disclosure: E. Sevim, None; D. Andrade, None; A. Banzato, None; D. W. Branch, None; R. Cervera, None; G. Ramires de Jesus, None; J. S. Knight, None; P. L. Meroni, None; M. Tektonidou, None; A. Tincani, None; A. Ugarte, None; Z. Zhuoli, None; D. Erkan, None; O. B. O. A. A., None.

Discipline: Rheumatology


Abstract Number: 13

**Epidemiology of Antiphospholipid Syndrome: A Population-Based Study**

Ali Duarte-Garcia<sup>1</sup>, Michael Pham<sup>1</sup>, Cynthia S. Crowson<sup>2</sup>, Kevin Moder<sup>3</sup>, Rajiv Pruthi<sup>4</sup> and Eric L. Matteson<sup>5</sup>, <sup>1</sup>Mayo Clinic, Rochester, MN, <sup>2</sup>Health Sciences Research, Mayo Clinic College of Medicine and Science, Rochester, MN, <sup>3</sup>Rheumatology, Mayo Clinic, Rochester, MN, <sup>4</sup>Mayo Clinic, R, MN, <sup>5</sup>Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, MN

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Antiphospholipid Syndrome Poster

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The epidemiology of definite antiphospholipid syndrome (APS) in the general population has not been described. A recent meta-analysis (Andreoli L, et al. Arth Care Res 2013;65:1869-73) concluded that it was difficult to determine the frequency of a “clinically significant antiphospholipid (aPL) profile” in patients with aPL-related clinical outcomes due to the lack of robust data; only 4%
of the studies had the current cutoff values for anticardiolipin antibodies (aCL) and less than one fifth of them had confirmation after 6-12 weeks. This study aimed to characterize the epidemiology of definite APS based on the 2006 updated international consensus (Sydney) classification criteria.

**Methods:** An inception cohort of patients with incident APS in 2000-2015 in a geographically well-defined population were identified based on comprehensive individual medical record review. All cases met the definite 2006 Sydney consensus APS criteria, including the laboratory and clinical criteria as well as laboratory confirmation after 12 weeks. Lupus anticoagulant, IgM and IgG aCL and anti-β2 glycoprotein-1 antibodies were tested in a centralized lab (cutoff >40 GPL/MPL). Incidence rates were age and sex adjusted to the US white 2010 population. Prevalence estimates were obtained from the incidence rates assuming no increased mortality associated with APS and assuming migration in/out of the area was independent of disease status.

**Results:** In 2000-2015, 33 cases of incident APS were identified (mean age 54.2 years, 55% female; 97% Caucasian). The annual incidence of definite APS was 2.0 per 100,000 population aged ≥ 18 years (95% confidence interval [CI]: 1.1-3.1 per 100,000). Incidence rates were similar in both sexes (2.1 per 100,000 population in females and 2.0 per 100,000 population in males). The peak incidence was observed in those who were older than 75 years. Significant changes in incidence rates over time were not observed. Six (18%) of the patients had a concurrent diagnosis of systemic lupus erythematosus. Three (17%) patients had obstetric manifestations. During a median follow-up of 8.8 years, 7 patients died (84% survival at 10 years after APS incidence; 95% CI: 69-100%). The overall mortality of patients with APS was not significantly different from the general population (standardized mortality ratio: 1.14; 95% CI, 0.46-2.64). The estimated prevalence of APS adjusted to the US white 2010 population was 50 per 100,000 (95% CI: 42-58) and was similar in both sexes (51/100,000 for females and 48/100,000 for males). Based on this and US census data, an estimated 119,300 persons in the US were affected by APS in 2015.

**Conclusion:** Results from this first ever population based study revealed that definite APS occurred in about 2 persons per 100,000 per year. The estimated prevalence is 50 per 100,000. Overall mortality was not different from the general population. The prevalence of APS in the same population was at least as common as SLE (Jarukitsopa, et al. Arth Care Res 2015;67:817-28).

**Disclosure:** A. Duarte-Garcia, None; M. Pham, None; C. S. Crowson, None; K. Moder, None; R. Pruthi, None; E. L. Matteson, None.


**Abstract Number:** 14

**Abnormalities in Th1, Th2 and Th17 Lymphoid Subpopulations in Long-Term Evolution Primary Antiphospholipid Syndrome**

Gabriela Medina1, Oscar I Florez-Durante2, Laura Arcelia Montiel Cervantes3, Rubiraída Molina Aguilà2, Elba Reyes Maldonado2 and Luis J. Jara4, 1Clinical Research Unit, Hospital de Especialidades Centro Medico La Raza, IMSS, Mexico City, Mexico, 2Escuela Nacional de Ciencias Biológicas, Instituto Politécnico Nacional, Mexico City, Mexico, 3Hematology Laboratory, Hospital de Especialidades Centro Médico La Raza, IMSS, Mexico City, Mexico, 4Direction of Education and Research, Hospital de Especialidades Centro Médico La Raza, IMSS, Mexico City, Mexico

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Antiphospholipid Syndrome Poster  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Primary antiphospholipid antibody syndrome (PAPS) is characterized by recurrent thrombosis and pregnancy morbidity in the presence of antiphospholipid antibodies (aPL). Lymphoid subpopulations and innate and adaptive immune responses have not been fully studied in long-term evolution PAPS.

**Objective:** To analyze the lymphoid subpopulations, Th1, Th2 and Th17 immune response in long-term evolution PAPS patients.

**Methods:** Patients with PAPS >18 years of age, of both genders and a group of healthy blood donors matched for age and sex were included. All patients were receiving oral anticoagulants (Coumadin type). No patient had a recent episode (six months) of thrombosis or other manifestation of APS at the time of the study. Peripheral blood was obtained and lymphoid subpopulations were determined by flow cytometry in order to identify with specific immunological markers, for Treg cells we used: CD4+/CD25+/FoxP3+ and CD8+/CD25+/FoxP3+. The dendritic cells analyzed were: type 1: Lin1-/HLA-DR+/CD11c+; Type 2: Lin1-/HLA-DR+/CD123+; B lymphocytes with CD19+; Monocytes with CD14+; NK: CD3-/CD16+/56+ and NKT: CD3+/CD16+/56+ lymphocytes. Th1 cells were identified by IFN-γ+ positivity; Th2: positivity for IL-4+; Th17: positivity for IL-17+. Parametric statistics and Mann-Whitney U-test were
Results:

A total of 50 patients with PAPS were included, age: 51.9 ± 12.8, evolution time: 12.8 ± 8.9 years and 35 healthy controls. In patients with PAPS there was a decrease in the total CD3 (p<0.001), CD4 (p<0.005) CD8 (p <0.05) count, Monocytes (p<0.03) B lymphocites (p<0.002), iNKT (p <0.001), DC1 (p <0.001) and DC2 (p <0.001) count cells compared to the control group (Table 1). We found significant decrease in Th1, Th2 and Th17 cytokines basal and after activation compared to healthy controls.

<table>
<thead>
<tr>
<th></th>
<th>Patients (N=50)</th>
<th>Controls (N=35)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD3/uL</td>
<td>962</td>
<td>1351</td>
<td>0.001</td>
</tr>
<tr>
<td>CD4/uL</td>
<td>587</td>
<td>786</td>
<td>0.005</td>
</tr>
<tr>
<td>CD8/uL</td>
<td>246</td>
<td>445</td>
<td>0.001</td>
</tr>
<tr>
<td>nk/uL</td>
<td>129</td>
<td>249</td>
<td>0.02</td>
</tr>
<tr>
<td>nkt/uL</td>
<td>33</td>
<td>58</td>
<td>0.02</td>
</tr>
<tr>
<td>14/uL (Monocytes)</td>
<td>140</td>
<td>241</td>
<td>0.03</td>
</tr>
<tr>
<td>19/uL (B Lymphocites)</td>
<td>41</td>
<td>104</td>
<td>0.002</td>
</tr>
<tr>
<td>Tgd/uL</td>
<td>29</td>
<td>45</td>
<td>0.3</td>
</tr>
<tr>
<td>iNKT/uL</td>
<td>8</td>
<td>20</td>
<td>0.001</td>
</tr>
<tr>
<td>DC1/uL</td>
<td>2</td>
<td>5</td>
<td>0.001</td>
</tr>
<tr>
<td>DC2/uL</td>
<td>1</td>
<td>5</td>
<td>0.001</td>
</tr>
<tr>
<td>Treg CD4/uL</td>
<td>17</td>
<td>13</td>
<td>0.5</td>
</tr>
<tr>
<td>Treg CD8/uL</td>
<td>11</td>
<td>13</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Mann Whitney U test

Conclusion:

This study shows profound alterations in innate and adaptive immunity in patients with long-term PAPS, characterized by a decrease in lymphocyte subpopulations and Th1, Th2, and Th17 cytokines with a possible prevalence of other proinflammatory cytokines and inflammasomes. These abnormalities can become new therapeutic targets in order to restore immune imbalance. Our findings may explain in part, the development of thrombosis, accelerate atherosclerosis and other complications, in PAPS patients with long term disease evolution.

Disclosure: G. Medina, None; O. I. Florez-Durante, None; L. A. Montiel Cervantes, None; R. Molina Aguilar, None; E. Reyes Maldonado, None; L. J. Jara, None.

Catastrophic antiphospholipid syndrome (CAPS), a rare disease, is characterized by the rapid onset of widespread thrombosis associated with multi-organ failure in patients meeting the serological criteria for antiphospholipid syndrome. To date, the diagnosis and treatment for CAPS has been based on expert consensus and case-series, not evidence-based guidelines developed with rigorous methodology. One of the main obstacles to guideline development in rare diseases is the sparsity and very low certainty (or quality) of the available evidence. As a prototypical rare disease, CAPS was selected to pilot the application of a guideline development process to a rare disease.

Methods:

The RARE-Best Practices project group in partnership with McMaster University developed a clinical practice guideline on diagnosis and management of patients with CAPS, bringing together a panel of international experts, and using the GIN-McMaster Guideline Development checklist. The evidence for the CAPS guideline was summarized using the GRADE methodology framework. Two novel methods, systematic observation reporting forms and ad hoc registry data analysis, were implemented to supplement the available evidence.

Systematic observation reporting involved collecting standardized contributions from each panel member prior to the panel meeting regarding characteristics and clinical course of previous CAPS patients. The goal was to systematize the process of expert input based on actual experience rather than opinions or anecdotes. Ad hoc analysis of registry data involved calculating raw data for survival estimates for each therapy question from the ‘CAPS Registry’, an international database that has over 500 CAPS patients enrolled.

Results:

Question generation yielded 47 questions, which were prioritized. The top 10 questions were selected by the panel for the guideline process, 3 diagnosis and 7 therapy. The therapy search identified 671 references, of which 8 articles were included in the systematic reviews. The diagnosis search identified 519 references, of which 1 article was included. All of the included studies were considered to be at high risk of bias. Eleven of the 20 panel members submitted systematic observation forms, representing 55 patient cases. The CAPS registry was used to calculate raw mortality for 7 recommendations and impacted the panel’s decision for a treatment recommendation related to rituximab.

Conclusion:

The CAPS guideline initiative met the objective of successful development of a clinical practice guideline in a rare disease using GRADE methodology. The novel methodology was found to be useful for complementing literature-based evidence in informing the recommendations.

Disclosure: K. Legault, Bayer, 9; C. Hillis, None; C. Yeung, None; E. Akl, None; M. Carrier, Leo Pharma, 5, Bayer, 5, Pfizer Inc, 5, Leo Pharma, 9, BMS, 9; R. Cervera, None; M. Crowther, Bayer, 2; F. Dentali, None; D. Erkan, Alexion Pharmaceuticals, Inc., 5; G. Espinosa, None; M. A. Khamashita, None; J. Meerpohl, None; K. Moffatt, None; S. O’Brien, None; V. Pengo, None; J. Rand, None; I. Rodriguez, None; L. Thom, None; H. Schunemann, None; A. Iorio, None.


Abstract Number: 16

Anti-Phosphatidylserine/Prothrombin Antibodies in Primary Antiphospholipid Syndrome

Paola Bermudez-Bermejo1, Gabriela Hernandez-Molina2, Diego Hernández-Ramírez3, Victor Zamora-Legoff2, Elizabeth Olivares-Martínez2, Antonio R. Cabral4 and Carlos Núñez-Álvarez5, 1Immunology and Rheumatology, Instituto Nacional de Ciencias Medicas y Nutricion SZ, Mexico City, Mexico, 2Immunology and Rheumatology, Instituto Nacional de Ciencias Medicas y Nutricion SZ, Mexico City, Mexico, 3Immunology and Rheumatology, Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran, Mexico City, Mexico, 4Department of Medicine. Division of Rheumatology. The Ottawa Hospital.University of Ottawa, Ottawa, ON, Canada, 5Immunology and Rheumatology, Instituto Nacional de Ciencias Medicas y Nutricion S.Z., Mexico city, Mexico

First publication: September 18, 2017
Background/Purpose: Several studies have showed conflicting results regarding the presence and meaning of anti-phosphatidylserine/prothrombin (aPS/PT). However, aPS/PT antibodies seem to be a risk factor for thrombosis. Nevertheless, most of the studies have focused on patients with SLE and secondary antiphospholipid syndrome (APS). We assessed the prevalence of aPS/PT antibodies, as well as their association with other antiphospholipid (aPL) antibodies (specially lupus anticoagulant [LA]) and thrombosis, in a well-established cohort of primary APS from a single center.

Methods: We included 96 consecutive patients with primary APS according the Sydney classification criteria and/or patients with hematological features (thrombocytopenia and hemolytic anemia) attending a referral center in Mexico City. Patients from both groups fulfilled the Sydney laboratory criteria for APS. We registered demographics, disease duration and type of manifestation. aCL (IgG and IgM), antibodies to purified human anti-β2GP-I (IgG and IgM) and aPS/PT antibodies (IgG and IgM) were assessed by ELISA (INOVA Diagnostics). LA was determined by LA/1 screening reactant and a confirmatory test LA/2 according to published guidelines. We used chi-square (χ2) test, Spearman correlation analysis and logistic regression.

Results: Most patients were females (69.7%), mean age 44.5 ± 14.6 and median disease duration 7.3 years. The main clinical features were thrombosis (n=74, 77%), hematologic involvement (n=49 patients, 51%) and obstetric events (n=24, 25%) (non-exclusive groups). The prevalence of LA was 69.8%, aCL-IgG 56.8%, anti-β2GP-I IgG 43.1%, aCL-IgM 31.5% and anti-β2GP-I IgM 21%. The frequency of aPS/PT antibodies was 61.2% and 61.6% for IgG and IgM isotype, respectively. When we compared patients with LA+ (n=58) vs. LA- (n=25), the first group had a higher prevalence of aPS/PT-IgG (79.3% vs. 16%, p=0.0001) and aPS/PT-IgM antibody (81.5% vs. 31.8%, p=0.001), as well as higher titers (aPS/PT-IgG 130.5 U vs. 8.2 U and aPS/PT-IgM 58.5 U vs. 16.6 U, p=0.0001). aPS/PT-IgG antibodies correlated with aPS/PT-IgG (ρ=0.59, p=0.0001), aCL-IgG (ρ=0.62, p=0.0001), anti-β2GP-I IgG (ρ=0.63, p=0.001) and anti-β2GP-I IgM (ρ=0.35, p=0.001). On the other hand, aPS/PT-IgM antibodies correlated with aCL-IgG (ρ=0.57, p=0.0001), aCL-IgM (ρ=0.42, p=0.001), anti-β2GP-I IgG (ρ=0.48, p=0.001) and anti-β2GP-I IgM (ρ=0.59, p=0.0001). We found moderate agreement between the presence of LA and both aPS/PT isotypes (κ= 0.58 p=0.0001 for IgG, and κ=0.47 p=0.001 for IgM). Thrombosis was associated with aPS/PT-IgG antibodies (87.7% vs. 61.1%, p=0.003) but not with aPS/PT-IgM (73.6% vs. 81.8%, p=0.37). At the logistic regression analysis, the aPS/PT IgG antibodies remained associated with thrombosis after adjusting by all other aPL antibodies, OR 8.695% CI 2.1-33.8, p=0.002.

Conclusion: In this cohort of patients with primary APS, aPS/PT antibodies were highly prevalent, correlated with other aPL antibodies and were associated independently with thrombosis.

Disclosure: P. Bermudez-Bermejo, None; G. Hernandez-Molina, None; D. Hernández-Ramírez, None; V. Zamora-Legoff, None; E. Olivares-Martínez, None; A. R. Cabral, None; C. Núñez-Álvarez, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/anti-phosphatidylserineprothrombin-antibodies-in-primary-antiphospholipid-syndrome

Abstract Number: 17

Thrombotic Events in Pediatric Systemic Lupus Erythematosus: A Preliminary Analysis of a Large, Single-Center Cohort

Jennifer Rammel1, Martha Curry2 and Marietta M. de Guzman3, 1Department of Pediatrics, Division of Immunology, Allergy and Rheumatology, Baylor College of Medicine, Houston, TX, 2Pediatric Immunology, Allergy and Rheumatology, Baylor College of Medicine, Houston, TX, 3Immunology, Allergy and Rheumatology, Baylor College of Medicine, Texas Children's Hospital, Houston, TX

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Antiphospholipid Syndrome Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: While pediatric systemic lupus erythematosus (pSLE) represents only 20% of all SLE cases, pSLE patients often have more aggressive disease with multi-organ involvement. These patients can be at significant risk for thrombotic events due to systemic
inflammation, vasculopathy, antiphospholipid antibodies (aPLs) and nephrotic features. Data detailing the timing and nature of thrombotic events in pSLE patients are limited. The objective of this study was to further characterize thrombotic events in a pSLE patient cohort at a large academic medical center.

Methods: A retrospective chart review was completed for patients with pSLE who had a documented thrombotic event. All patients fulfilled the American College of Rheumatology (ACR) classification criteria for SLE. Descriptive statistics were utilized for this preliminary analysis.

Results: Of the 402 patients in this pSLE cohort, there were a total of 45 thrombotic events in 28 patients. The cohort was 89% female, 50% African American, Non-Hispanic and 43% Caucasian, Hispanic. Mean age at pSLE diagnosis was 12.9 years, range was from 6.7 to 17.8 years. 71% (20) had positive APLs at pSLE diagnosis: 60% lupus anticoagulant (LA), 70% anticardiolipin (aCL), and 45% antiβ2glycoprotein1 (αβ2GP1). Mean age at first thrombotic event was 14.9 years, range was from 7.8 to 22.9 years. There was a mean difference of 2.0 years from pSLE diagnosis to thrombotic event, with a range of -4.4 to 10.3 years. Fifteen patients (54%) were diagnosed with pSLE at the time of the initial thrombotic event. Of the 45 thrombotic events, 33% (15) were arterial and 66% (30) were venous. Arterial events included 10 cerebrovascular accidents and 4 transient ischemic attacks. Venous events included 16 deep vein thromboses (DVT), 2 pulmonary emboli (PE) without radiographically identified DVT, and 3 combined DVT/PEs. Seven patients (25%) had multiple thrombotic events. At the time of the thrombotic event, 56% were aPL positive (60% LA, 72% aCL, and 40% aβ2GP1), 11% were negative, and 33% were either not tested or the data was not available.

Conclusion: The majority of the thrombotic events in this cohort were venous, and a single occurrence. More than half of the patients were diagnosed with pSLE as a result of the presenting thrombotic event. Most patients had positive antiphospholipid antibodies both at pSLE diagnosis and at the time of the thrombotic event. Further research plans for this dataset include further analysis of predictive factors for thrombosis and characterizing the variation in establishing initial thrombotic risk, surveillance and management.

Disclosure: J. Rammel, None; M. Curry, None; M. M. de Guzman, None.


Abstract Number: 18

Increased Frequency of Nailfold Videocapillaroscopy Abnormalities in Primary antiphospholipid (PAPS) Patients

Tatiana Sofia Rodriguez-Reyna1, Eduardo Martín Nares2, Paola Bermudez-Bermejo3, Victor Zamora-Legoff4 and Gabriela Hernandez-Molina5, Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, 2Department of Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, 3Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutricion SZ, Mexico City, Mexico, 4Rheumatology and Immunology, Instituto Nacional de Ciencias Médicas y Nutricion SZ, Mexico D.F., Mexico, 5Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición SZ, Mexico City, Mexico

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Antiphospholipid Syndrome Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Primary antiphospholipid syndrome (PAPS) is characterized by venous and arterial thrombosis, obstetric morbidity and the presence of antiphospholipid antibodies. The utility of nailfold videocapillaroscopy in conditions such as scleroderma (SSc) and primary Raynaud’s phenomenon is well known. Whether patients with PAPS have specific findings in nailfold videocapillaroscopy is not well established. Our aim was to evaluate nailfold videocapillaroscopy findings in PAPS patients and their association with clinical and serological features.

Methods: We included 32 PAPS patients according to the modified Sidney criteria and the Alarcón-Segovia criteria for haematologic antiphospholipid syndrome, who regularly attend a tertiary referral center in Mexico City, and 17 healthy controls. We performed nailfold videocapillaroscopy according to the Cutolo technique (Optilia 200x) and obtained: capillary morphology, abnormalities (tortuosity, crossed and dilated capillaries, capillary haemorrhages, neo-angiogenesis) and mean vascular density on 32 images per patient. We collected demographic, clinical (thrombosis, obstetric morbidity, non-criteria manifestations and comorbidities), serological (anticardiolipin antibodies, anti-β2 glycoprotein 1 antibodies and lupus anticoagulant) and treatment information. Analysis was performed used SPSS v.22,
Chi square test was used to compare frequencies and Student’s t test was used to compare means.

**Results:** PAPS patients had higher frequency of at least 1 abnormal finding on videocapillaroscopy (78% vs 12%, p<0.009, OR=26, 95%CI=5-146), higher frequency of dilated capillaries (69% vs 0%, p=0.0001, OR=3.2, 95%CI=1.9-5.3), lower frequency of “perfect normal” pattern (12% vs 59%, p=0.002, OR=0.1, 95%CI=0.02-0.4) than controls, and 8 patients (25%) showed changes compatible with the “early” SSC Cutolo pattern (<4 dilated capillaries/mm, <4 haemorrhages/mm, preserved architecture and no avascular areas). In PAPS patients, capillary haemorrhages were associated with neurologic manifestations (75% vs 14%, p=0.02, OR=19, 95%CI=1.4-248) and with comorbidity with hypertension (75% vs 14%, p=0.02, OR=19, 95%CI=1.4-248), while alterations compatible with “early” pattern were not associated to any clinical or serological variable.

**Conclusion:** PAPS patients frequently show at least one abnormality on videocapillaroscopy. The most frequent abnormalities are dilated capillaries, microhaemorrhages and the presence of an “atypical normal” pattern. Capillary haemorrhages are frequently found in patients with neurologic involvement of PAPS. The coexistence of hypertension or other comorbidities may contribute to the development of capillary abnormalities in PAPS patients.

**Disclosure:** T. S. Rodriguez-Reyna, None; E. Martin Nares, None; P. Bermudez-Bermejo, None; V. Zamora-Legoff, None; G. Hernandez-Molina, None.


Abstract Number: 19

**The Transcription Factor Specificity Protein 1 up-Regulates IL-21 Receptor Expression on B Cells in Rheumatoid Arthritis Leading to Altered Cytokine Production and Maturation**

Elizabeth Dam¹, Alison Maier¹, Anne Hocking¹, Jeffrey Carlin² and Jane H. Buckner¹, ¹Benaroya Research Institute at Virginia Mason, Seattle, WA, ²Rheumatology, Virginia Mason Medical Center, Seattle, WA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** B Cell Biology and Targets in Autoimmune Disease Poster  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Growing evidence suggests that IL-21 has a role in B cell dysfunction in rheumatoid arthritis (RA). Previous studies have reported that IL-21 levels are increased in the serum and synovial fluid of RA subjects and correlate with the 28-joint count disease activity score. While an increase in the percent of IL-21R positive B cells in RA has been described, the significance of this finding in B cells with respect to signaling, B cell differentiation and function has not been investigated. The goal of this study was to address this gap in knowledge and determine the mechanism that leads to increased IL-21R expression on B cells in RA.

**Methods:** We analyzed IL-21 receptor expression in B cells isolated from whole blood and synovial fluid from a cohort of RA subjects and healthy controls matched for age, gender and race. The RA subjects all met the ACR classification criteria and none of the subjects were on biologics at the time of the draw. Flow cytometry was used to quantify protein and mRNA levels of IL-21R, specificity protein 1 (SP1) and to determine cytokine production (IL-6) and maturation status of B cells. IL-21 signaling was assessed by measuring pSTAT3 levels following IL-21 stimulation. IL-21R levels were correlated to serum levels of rheumatoid factor (RF) IgM which was assessed by ELISA. SP1 binding to the IL21R promoter region in B cells was assessed with ChIP-qPCR.

**Results:** We demonstrate an increase in IL-21R expression in total and memory B cells from RA subjects, which correlated with responsiveness to IL-21 as measured by phosphorylation of STAT3. IL-21R expression on memory B cell also correlated with serum rheumatoid factor IgM levels. There was comparable levels of IL-21R expression between memory B cells from peripheral blood and those from synovial fluid in the same subject. In addition, stimulation of naïve B cells from RA subjects with IL-21 and CD40L resulted in an increase in differentiation into plasmablasts. Further investigation showed that IL-21R expression correlated with an increase in the level of the SP1 transcription factor. Mechanistic experiments showed increased binding of SP1 to the IL21R promoter region in B cells in RA.

**Conclusion:** Our results suggest a mechanism by which IL-21 enhances B cell development and function in RA through an SP1 mediated increase in IL-21R expression on B cells. This suggests that therapies for RA may be more efficacious if targeted to memory B cells and/or target SP1.
Low Molecular Weight BAFF Receptor Antagonists Restrain Infiltration of B Cells into Organs of Autoimmune Model Mice By Suppressing B Cell Activation

Keiko Yoshimoto1, Noriyasu Seki2, Katsuya Suzuki3, Kunio Sugahara4 and Tsutomu Takeuchi1, 1Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, 23) Research Unit/Immunology & Inflammation, Mitsubishi Tanabe Pharma Corporation, Yokohama, Japan, 3Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, 4Research Unit/Immunology & Inflammation, Mitsubishi Tanabe Pharma Corporation, Yokohama, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: B Cell Biology and Targets in Autoimmune Disease Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: We have reported that soluble BAFF (sBAFF) robustly increased IL-6 production by peripheral monocytes of patients with primary Sjögren’s syndrome (pSS) and that the expression level of a BAFF receptor (BR3) was significantly elevated in pSS monocytes. In our previous study, we have also demonstrated that the proportion of BR3-positive monocytes to total monocytes was positively and significantly correlated with the serum IgG level of pSS patients. These data collectively suggest that the elevated expression of BR3 on monocytes is involved in IgG overproduction by B cells and that BAFF signaling via BR3 is a possible therapeutic target to treat autoimmune diseases, such as pSS. In addition, we have successfully discovered two pyrrolopyrimidine derivatives, which inhibit BAFF binding to BR3, by a high throughput screening of a low molecular weight compound library. These compounds inhibited not only IL-6 and IL-10 production by BAFF-stimulated monocytes, but also IgG production by B cells in vitro co-cultured with monocytes in the presence of sBAFF possibly by impairing differentiation of B cells. Notably, these compounds suppressed the serum level of an anti-dsDNA antibody in autoimmune disease model mice. In this study, we investigate the effects of these compounds on infiltration of B cells into organs of the model mice.

Methods: A pyrrolopyrimidine derivative, BIK-13, which inhibits BAFF binding to BR3, was administered intraperitoneally to MRL/lpr mice three times a week at a dose of 0.2 mg/kg for 6 months. Serum levels of an anti-ds DNA antibody, IL-6 and IL-10 were measured by ELISA. The proportion of B cell in peripheral blood of the mice was analyzed by FACS. Infiltration of lymphocytes into organs was analyzed by immunohistochemistry.

Results: Administration of BIK13 to MRL/lpr mice for 16 weeks decreased the serum level of an anti-dsDNA antibody. Moreover, serum levels of IL-6 and IL-10, both of which induce B cell activation, in the mice were concomitantly declined as compared to control mice. Notably, immunohistochemistry revealed that infiltration of B lymphocytes was remarkably suppressed in salivary and lacrimal glands and kidney of the mice. In addition, the proportion of B cells in peripheral blood was also decreased in BIK-13-treated mice as compared to the control mice.

Conclusion: These data collectively suggest that BIK-13, a low molecular weight BR3 antagonist, suppress the B cell activation and resultant infiltration into organs in vivo. Suppression of cytokine production by monocytes may be directly or indirectly involved in the molecular mechanism of the suppression of the B cell activation. The compound may provide a novel therapeutic possibility to treat autoimmune diseases.
Producing Effector B Cells Play a Pathogenic Role, While IL-10-Producing Regulatory B Cells Play a Protective Role

Takashi Matsushita1, Yasuhito Hamaguchi1, Minoru Hasegawa2, Manabu Fujimoto3 and Kazuhiko Takehara4, 1Department of Dermatology, Kanazawa University, Kanazawa, Japan, 2Department of Dermatology, University of Fukui, Fukui, Japan, 3Department of Dermatology, University of Tsukuba, Tsukuba, Japan, 4Department of Dermatology, Kanazawa University, Kanazawa, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: B Cell Biology and Targets in Autoimmune Disease Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: IL-10-producing regulatory B (Breg) cells negatively regulate autoimmune diseases. We reported that Breg cells play a protective role in a mouse model of systemic sclerosis (SSc) and in patients. Recent studies indicate that IL-6-producing effector B (Beff) cells have pathogenic effect in autoimmune diseases. IL-6 plays a critical role for the pathogenesis of SSc, and a phase III trial of anti-IL-6R antibody (tocilizumab) is ongoing in patients with SSc. However, the phenotype and function of IL-6-producing Beff cells remains unclear. In this study, we investigated the phenotype of IL-6-producing Beff cells and their role in SSc pathogenesis.

Methods: B cell subsets were sorted and cytokine production was measured by intracellular cytokine staining. We generated mixed bone marrow chimeric mice with a B cell specific deficiency in IL-6 or IL-10 production (B-IL-6−/− or B-IL-10−/−), together with control chimeras (B-WT). Skin fibrosis was assessed 4 weeks after the initiation of bleomycin treatment in mixed bone marrow chimeric mice.

Results: Most splenic IL-6 producing Beff cells were detected within the marginal zone (MZ) B cell subset, while IL-10-producing Breg cells were detected within the MZ B and B1 B cell subsets, but not within the follicular B cell subset (Fig 1). Serum IL-6 levels gradually increased with the development of fibrosis in bleomycin-induced scleroderma mice, while serum IL-10 levels did not. In addition, the frequency of splenic IL-6-producing Beff cells in bleomycin-treated mice was significantly increased. The bleomycin-induced skin fibrosis was attenuated in B-IL-6−/− mice compared with that in B-WT mice. In contrast, B-IL-10−/− mice showed more severe skin fibrosis than B-WT mice (Fig 2).

Conclusion: IL-6-producing Beff cells play a pathogenic role in bleomycin-induced scleroderma model, while IL-10-producing Breg cells play a protective role (Fig 3). Thus, B cells have reciprocal roles in SSc pathogenesis, presenting pathogenic and protective functions.
Disclosure: T. Matsushita, None; Y. Hamaguchi, None; M. Hasegawa, None; M. Fujimoto, None; K. Takehara, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/reciprocal-regulation-of-b-cells-on-bleomycin-induced-scleroderma-model-il-6-producing-effector-b-cells-play-a-pathogenic-role-while-il-10-producing-regulatory-b-cells-play-a-protective-role

Abstract Number: 22

Bone Regulatory Cytokine Production By B Cells in Rheumatoid Arthritis Is Dependent on NF-kb Activation and Autophagy Pathways

Jason Glanzman1, Nida Meednu1, Victor Wang1, Wen Sun2, Lianping Xing3 and Jennifer H. Anolik1, 1Medicine- Allergy, Immunology and Rheumatology, University of Rochester Medical Center, Rochester, NY, 2Nanjing Medical University, Nanjing, China, 3Pathology & Lab Medicine, University of Rochester Medical Center, Rochester, NY

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: B Cell Biology and Targets in Autoimmune Disease Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a systemic autoimmune disease that often leads to joint damage, a process mediated by an imbalance between bone resorption and bone formation. B cells play a role in bone homeostasis in RA, and evidence suggests that B cells can affect function of both osteoblasts (OB) and osteoclasts (OC). In mouse models of RA, B cells were enriched in the subchondral bone marrow (BM) and synovium, and were adjacent to the bone surface. These B cells produce the inflammatory cytokines TNFα and CCL3, which drive dysregulation of bone homeostasis via their OB inhibitory and OC stimulatory effects. In vitro, synergistic production of these cytokines results from co-activation of the B cell receptor (BCR) and toll-like receptor 9 (TLR9). Therefore, we investigated the mechanisms underlying synergistic TNFα/CCL3 production by B cells in response to BCR and TLR9 co-activation.

Methods: Isolated B cells from peripheral blood of healthy controls (HC) were stimulated with 10 µg/mL anti-Ig (A+M+G) and CpG2006 for 4 hours, and production of TNFα and CCL3 was assessed by ELISA and qPCR. Multiple specific inhibitors were used to test the involvement of BCR, TLR9, and NF-κB signaling, as well as autophagy. Data is presented as mean±SEM. Statistical significance was determined by student’s t-test.

Results: Stimulation of B cells with α-Igs and CpG2006 induced significant production of TNFα and CCL3 compared to unstimulated B cells at mRNA and protein levels. Furthermore, cytokine production was significantly higher than levels from α-Igs or CpG2006 stimulations alone, suggesting a synergistic effect (CpG+α-Igs vs. CpG vs. α-Igs (ng/mL): TNFα: 2.71±0.42 vs. 0.33±0.04 (P<0.0001) vs. 0.70±0.23 (P=0.0008), CCL3: 3.69±1.00 vs. 0.77±0.29 (P=0.0031) vs. 0.64±0.18 (P=0.0037)). This synergistic production was dependent on TLR9 and BCR signaling, as blocking B cells with hydroxychloroquine (TLR inhibitor) or PP2 (Src kinase inhibitor) reduced cytokine production to non-synergistic levels. Additionally, blocking BCR internalization with MDC also reduced TNFα and CCL3 production. To investigate signaling downstream of BCR/TLR9 synergy, we tested inhibitors against classical NF-κB (TPCA-1), non-classical NF-κB (NIK inhibitor) and AP-1. We found that BCR/TLR9 synergy was classical NF-κB dependent (CpG+α-Igs vs. CpG+α-Igs+TPCA-1 (ng/mL): TNFα: 2.5±0.44 vs. 0.33±0.14 (P=0.009), CCL3: 1.9±0.3 vs. 0.83±0.08 (P=0.027)). Finally, we inhibited autophagy using class III PI3K inhibitor 3-methyladenine which reduced TNFα and CCL3 production to non-synergistic levels, suggesting that BCR/TLR9 synergy depends on autophagy (CpG+α-Igs vs. CpG+α-Igs+3-MA (ng/mL): TNFα: 1.5±0.25 vs. 0.4±0.04 (P=0.0058), CCL3: 4.1±1.15 vs. 0.82±0.35 (P=0.033)). Investigation of the specific autophagy pathway involved is currently underway.

Conclusion: Dual activation of B cells through the BCR and TLR9 synergistically enhanced TNFα and CCL3 production in a classical NF-κB, and autophagy-dependent manner. These results characterize key mechanistic events in the synergistic production of bone regulatory
cytokines by B cells, a process that contributes to the dysregulation of bone homeostasis in RA.

Disclosure: J. Glanzman, None; N. Meednu, None; V. Wang, None; W. Sun, None; L. Xing, None; J. H. Anolik, None.


Abstract Number: 23

Auto-Reactive B Cells Escape Peripheral Tolerance Checkpoints in Patients with PR3-ANCA Associated Vasculitis

Divi Cornec1, Alvise Berti2, Amber Hummel1, Tobias Peikert1, Jacques-Olivier Pers3 and Ulrich Specks4, 1Mayo Clinic, Rochester, MN, 2Department of Immunology, Rheumatology, Allergy and Rare Diseases, San Raffaele Scientific Institute, Milan, Italy, 3Immunology, Brest University Medical School Hospital, Brest, France, 4Mayo Clinic College of Medicine, Rochester, MN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: B Cell Biology and Targets in Autoimmune Disease Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
While extensive studies have been performed to characterize ANCA, little is known about the auto-reactive B cells that produce these autoantibodies. Indirect evidence previously suggested the presence of circulating PR3-specific B cells in patients with PR3-ANCA-associated vasculitis (AAV). Our objectives here were to develop a method to detect circulating PR3-specific B cells in patients with PR3-AAV, to study their proportion among the different B-cell subsets and to assess their relationship with disease activity.

Methods:
A recombinant PR3 (rPR3) was tagged using FITC or biotin, and we studied its ability to bind specifically to two hybridoma cell lines, MCPR3-2 (producing an anti-human PR3 monoclonal antibody) and MCPR3-13 (producing an anti-mouse PR3 monoclonal antibody, with no cross-reactivity with human PR3). We measured the proportion of PR3-FITC positive B cells among PBMCs in 13 patients with PR3-AAV and 14 healthy controls (HCs) by flow cytometry. We then developed a multi-color flow cytometry including CD19, IgD, CD27, CD38, CD24 and biotinylated rPR3 to measure the proportion of PR3-specific B cells among different B-cell subsets in an independent group of 13 patients with PR3-AAV and 11 HCs.

Results:
rPR3 efficiently bound MCPR3-2 hybridoma cells but not MCPR3-13. Specificity of the staining was confirmed by competition experiments: pre-incubation of MCPR3-2 cells with untagged human rPR3 totally abrogated rPR3-FITC staining, whereas pre-incubation with mouse rPR3 had no effect. Dose-ranging experiments defined the optimal concentration of rPR3 to stain cells expressing anti-PR3 immunoglobulin. The mean (SEM) proportion of rPR3-FITC-stained B cells was higher in patients with PR3-AAV compared to HCs: 2.10% (2.33) vs 0.45% (0.19) respectively, p<0.001. Patients with active disease had numerically higher proportions of PR3-specific B cells than patients in remission: 3.66% (3.28) vs 1.10% (0.52), p=0.09. In HCs, the proportion of PR3-specific B cells was highest among the transitional B-cell subset, and decreased along with the maturation of B cells (figure). Conversely, in patients, the proportion of PR3-specific B cells progressively increased with the maturation of B cells (median 1.9% of naïve B cells, 2.30% of IgD+ memory B cells, 2.37% of IgD-memory B cells, and 3.68% of plasmablasts, p<0.05 for all comparisons with the naïve subset).

Conclusion:
This study describes an original method to detect and study circulating auto-reactive B cells in patients with PR3-AAV, and suggests that PR3-specific B cells are associated with disease activity and may represent a promising biomarker to predict relapse risk in patients in clinical remission. The progressive enrichment in PR3-specific B cells during the B-cell maturation steps in patients suggest that autoimmune B cells are actively selected and escape peripheral tolerance checkpoints.
Abstract Number: 24

**Trafficking of Innate B Cells to the Lungs As a Novel Mechanism in a Model of Pulmonary Lupus and Vasculitis**

Priti Prasad\(^1\), Michael Fishbein\(^2\), Rohan Sharma\(^3\), Ramesh Halder\(^4\), Isela Valera\(^1\) and Ram R. Singh\(^5\), \(^1\)Autoimmunity and Tolerance Laboratory, Division of Rheumatology, Department of Medicine, David Geffen School of Medicine at University of California Los Angeles, Los Angeles, CA, \(^2\)Department of Pathology and Laboratory Medicine, David Geffen School of Medicine at University of California Los Angeles, Los Angeles, CA, \(^3\)Autoimmunity and Tolerance Laboratory, Division of Rheumatology, Department of Medicine, David Geffen School of Medicine at University of California Los Angeles, Los Angeles, CA, \(^4\)Autoimmunity and Tolerance Laboratory, Division of Rheumatology, Department of Medicine, David Geffen School of Medicine at University of California Los Angeles, Los Angeles, CA, \(^5\)Autoimmunity and Tolerance Laboratory, Department of Medicine/Rheumatology, David Geffen School of Medicine at University of California Los Angeles, Los Angeles, CA

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Sunday, November 5, 2017
Session Title: B Cell Biology and Targets in Autoimmune Disease Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

**Background/Purpose:** Lung is involved in up to 50% patients with SLE. Among manifestations of pulmonary lupus, pneumonitis, vasculitis and diffuse pulmonary hemorrhage (DPH) carry a high mortality rate, and are without any effective treatment. Advances in the pathogenesis of pulmonary lupus have been hampered because of the heterogeneity of clinical findings, paucity of access to the affected tissue, and the lack of suitable model systems. Hydrocarbon oils, such as 2,6,10,14-tetramethylpentadecane (TMPD), induce lupus-like autoantibodies, nephritis, arthritis, pneumonitis, and DPH depending on the animals’ genetic background. Previous studies have used this model to show that animals that lack B cells (Igμ\(^{-/-}\)) have a reduced prevalence of DPH. Here, we examined the role of innate B1 B cells in the pathogenesis of pulmonary lupus using the TMPD-DPH model.

**Methods:** We injected TMPD to induce pulmonary lupus in C57BL/6 (B6) mice and analyzed B cells and B cell subsets in the lungs and peritoneal cavity. To determine the role of innate B cells, we injected CD19\(^{-/-}\) mice (deficient in B1a B cells) and wild-type B6 mice with 500 μl TMPD intraperitoneally. Furthermore, we adoptively transferred wild-type peritoneal fluid cells which are enriched in B1 B cells into CD19\(^{-/-}\) and in Igμ\(^{-/-}\) mice (have no B cells). We assessed disease using weight-loss, a semi quantitative scoring system for lung inflammation and hemorrhage, and a quantitative measurement for lung hemorrhage.

**Results:** 73% of 62 TMPD-injected wild-type B6 mice exhibited weight-loss, pneumonitis, vasculitis, and/or DPH compared to none of controls injected with control hydrocarbon oil hexadecane or with PBS or sham. Immunophenotyping revealed abnormalities of all immune cells tested in the diseased lungs. At earlier timepoints prior to histopathological changes, both hexadecane and TMPD caused myeloid cell abnormalities, only TMPD caused lung-infiltration with B-cells that expressed B1 B cell subset markers: CD19\(^+\)CD11b\(^+\)/CD19\(^+\)CD5\(^+\).

Such B1 B cells were simultaneously reduced in their usual location (peritoneal cavity). CD19\(^+\) mice that have less B1a B cells developed less DPH, and less B cell infiltration in the lungs than wildtype mice. The adoptive transfer of wildtype peritoneal fluid cells that are...
A Novel Role for Galectin-3 Binding Protein in B Cell Biology and Antibody Secretion

Shinji Okitsu¹, Melinda Genest¹, Nurudddeen Lewis¹, Evgeni Tzvetkov¹, Yin Wu², Andrew Bender¹, Arnon Arazi³, Thomas Eisenhaure³, Edward Brownë⁴, Alex Rolle⁵, Jonathan Derry⁶, William Pendergraft III⁷, Nir Hacohen⁸, Julie DeMartino⁹ and Jaromir Vlach¹, ¹TIP Immunology, EMD Serono Research and Development Institute, Billerica, MA, ²TIP Immunology, EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA, ³Broad Institute, Cambridge, MA, ⁴Massachusetts General Hospital, Boston, MA, ⁵EMD Serono Research and Development Institute, Billerica, MA, ⁶Iris Bioconsulting, Bainbridge Island, WA, ⁷Kidney Center, University of North Carolina, Chapel Hill, NC, ⁸Harvard Medical School, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: B Cell Biology and Targets in Autoimmune Disease Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Antibodies are important in protection against pathogens, but also harbor the potential to cause autoimmune disease when directed against self-antigens. Systemic lupus erythematosus (SLE) is an autoimmune disease where antibodies recognizing nucleic acids and associated proteins form immune complexes that drive inflammation and disease progression. Consequently, targeting B cells and antibody production is a main focus in SLE drug development and we have endeavored to discover new targets in this pathway.

Methods: Here we show results from screening a secreted protein library for effects on Ig secretion by primary human B cells.

Results: We identified galectin-3 binding protein (G3BP) as a soluble factor that enhances antibody production induced by a variety of stimuli in vitro. In an orthogonal translational study we found that the G3BP gene (LGALS3BP) was one of the most upregulated genes across 14 different immune cell types isolated from lupus nephritis (LN) patient blood. LGALS3BP contains an IRF7 binding site in its promoter and we observed increased expression in TLR7-stimulated PBMCs. SLE is characterized by RNAs that induce type I interferon (IFN) inflammation through the innate receptor TLR7. LGALS3BP expression in LN patients correlated with type I interferon-inducible genes indicating that G3BP is part of this pathological process. Indeed, in support of this hypothesis, other investigators have documented upregulated LGALS3BP in active IFN high SLE patients versus healthy controls (Merrill, J.T. et al., ACR abstract 1809, 2013). We found the same LGALS3BP upregulation and correlation with type I IFN in a mouse model of LN. Moreover, upregulation in mouse kidneys correlated with nephritis development. In in vitro studies we found that antibodies against G3BP led to defects in human B cell survival and loss of antibody production.

Conclusion: We hypothesize that targeting G3BP may be a novel approach to inhibit autoantibody production and may benefit patients suffering from antibody-mediated autoimmune diseases, including lupus nephritis.
Single B Cell Analysis Revealed the Relationship Among the Cytokine Profile, Antibody Affinity, and Pathogenic Roles of Autoantigen-Reactive B Cells in Systemic Sclerosis

Takemichi Fukasawa,1 Ayumi Yoshizaki,2 Satoshi Ebata,1 Kouki Nakamura,1 Ryosuke Saigusa,1 Takashi Yamashita,1 Yoshihide Asano,3 Yutaka Kazoe,4 Kazuma Mawatari,4 Takehiko Kitamori,4 and Shinichi Sato,5 1Dermatology, University of Tokyo, Graduate School of Medicine, Tokyo, Japan, 2Department of Dermatology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan, 3Applied Chemistry, University of Tokyo, Graduate School of Medicine, Tokyo, Japan, 4Applied Chemistry, University of Tokyo, Graduate School of Engineering, Tokyo, Japan, 5Department of Dermatology, Graduate School of Medicine, The University of Tokyo, Bunkyo-ku, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: B Cell Biology and Targets in Autoimmune Disease Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Recent studies have indicated that B cells play critical roles in systemic autoimmunity and disease expression through various functions such as induction of the activation of other immune cells in addition to autoantibody production. Indeed, rituximab, a B cell depleting antibody, can ameliorate some autoimmune diseases including systemic sclerosis (SSc). However, the role of autoreactive B cells is still not clear, because the number of autoreactive B cells is too small to study their functions directly. Although several studies have revealed that B cells play crucial roles in SSc development, autoreactive B cell functions remain totally unclear. In this study, we investigated the role of autoreactive B cells directly using our original micro-ELISA system, which integrates immunoassay into a microchip in order to detect extremely small amounts of analytes and can study autoreactive B cells at a single cell level.

Methods:
Peripheral blood mononuclear cells (PBMCs) were obtained from topoisomerase (topo) I positive SSc patients and healthy controls. Each of topo I-specific B cells was sorted into individual wells of 96 well plates. Their mRNA levels were assessed by single cell PCR. In addition, their cytokine production was analyzed by the micro-ELISA system which realized the analysis of cytokine production in single cells. In mouse studies, we assessed antibody affinities and cytokine production of topo I-specific B cells using topo I and complete Freund’s adjuvant-induced SSc model mice. Furthermore, topo I-specific B cells from topo I and complete Freund’s adjuvant-induced SSc model mice were adoptively transferred to these model mice and then skin and lung fibrosis was assessed.

Results:
Topo I-specific B cells from SSc patients produced higher amounts of IL-6 compared with topo I-non-specific B cells. In addition, IL-10 production of topo I-specific B cells was lower than those of topo I-non-specific B cells.

To reveal the relationship between B cell affinity to the autoantigen and their cytokine production, we analyzed single topo I-immunized SSc model mice and fourth immunized SSc model mice. Single immunized mice had higher frequencies of IL-10-producing topo I-specific B cells than fourth immunized mice, while fourth immunized mice had higher frequencies of IL-6-producing topo I-specific B cells than single immunized mice. The affinity of topo I-specific B cells from fourth immunized mice was higher than those from single immunized mice. Adoptive transfer with high-affinity topo I-specific B cells aggravated skin and lung fibrosis. By contrast, that with low-affinity topo I-specific B cells ameliorated skin and lung fibrosis.

Conclusion:
These results suggest that distinct B cell cytokine production is determined by B cell autoantigen affinity. Autoantigen-reactive B cells with higher autoantigen affinity can be a novel therapeutic target in SSc.

Disclosure: T. Fukasawa, None; A. Yoshizaki, None; S. Ebata, None; K. Nakamura, None; R. Saigusa, None; T. Yamashita, None; Y. Asano, None; Y. Kazoe, None; K. Mawatari, None; T. Kitamori, None; S. Sato, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/single-b-cell-analysis-revealed-the-relationship-among-
Effects of High Titers of Anti-Chimeric Antibodies Following Rituximab

Roberta Fenoglio1, Laura Solfietti1, Savino Sciascia2 and Dario Roccatello1, 1Center of Research of Immunopathology and Rare Diseases- Coordinating Center of Piemonte and Valle d’Aosta Network for Rare Diseases, Department of Clinical and Biological Sciences, University of Turin and S. Giovanni Bo, Turin, Italy, 2Center of Research of Immunopathology and Rare Diseases- Coordinating Center of Piemonte and Valle d’Aosta Network for Rare Diseases, Department of Clinical and Biological Sciences, University of Turin, Italy, Center of Research of Immunopathology and Rare Diseases- Coordinating Center of Piemonte and Valle d’Aosta Network for Rare Diseases, Department of Clinical and Biological Sciences, University of Turin, Italy, Torino, Italy

First publication: September 18, 2017

Background/Purpose:
Monoclonal antibodies (MoAbs) are highly successful in treating various immunological disorders. The development of anti-drug antibodies (ADA) against the therapeutic MoAb is relatively common. In recent years, knowledge of how to assess immunogenicity of biological drugs has improved. ADA are thought to form immune complexes with the MoAb, leading to accelerated MoAB clearance and low decrease levels in the blood stream. Several reports showed an inverse relationship between MoAb levels and anti MoAb antibody formation. Further, patients who develop ADA are more likely to present with infusion-related adverse effects. Acute infusion reactions, including anaphylaxis, develop in a close temporal relationship to MoAb infusion.

Among the others MoAbs, Rituximab (RTX), an anti-CD20 monoclonal antibody, often results in the production of human anti-chimeric antibodies (HACA).

In this study, we aimed to evaluate the presence of HACA in patients with poor response to treatment with RTX

Methods:
We assessed the incidence of anti-drug antibodies (ADA) in patients with autoimmune diseases treated with the RTX and determine the potential relationship with trough drug concentration, efficacy, and patient-reported outcomes.

Results:
When investigating 37 patients treated with RTX, we found very high-titer of HACA (> 1,000 AU) in 5 patients (13.5%): 2 with Systemic Lupus Erythematosus (SLE), 2 with Membranous Nephropathy (MN) and 1 patient with Mixed Cryoglobulinemia (MC). Details are given in table 1. In 4 of them, high titers of HACA were clearly related to unresponsiveness to RTX treatment. In the other case the appearance of high HACA titers was consonant with a severe hypersensitivity reaction during RTX re-treatment.

Conclusion:
HACA detection and monitoring, especially in the cases of RTX re-treatment, could not only assure a safer administration, but also support a more rational strategy of treatment.

<table>
<thead>
<tr>
<th>Case</th>
<th>Disease</th>
<th># of cycles with RTX</th>
<th>steroid-therapy</th>
<th>HACA-Titer (AU)</th>
<th>RTX-level</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>SLE</td>
<td>1</td>
<td>Yes</td>
<td>15,720</td>
<td>ND</td>
</tr>
<tr>
<td>2</td>
<td>SLE</td>
<td>1</td>
<td>Yes</td>
<td>3,719</td>
<td>ND</td>
</tr>
<tr>
<td>3</td>
<td>MC</td>
<td>3</td>
<td>No</td>
<td>14,670</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>MN</td>
<td>1</td>
<td>No</td>
<td>1,007</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>MN</td>
<td>2</td>
<td>No</td>
<td>10,363</td>
<td>0</td>
</tr>
</tbody>
</table>

Tab.I: Patient sample
Sapril and Sbcma As Potential Biomarkers of B Cell Hyperactivation in Rheumatoid Arthritis: A Cluster Analysis Approach

Javier Rodríguez-Carrio1, Mercedes Alperi-López2, Patricia López1, Francisco Javier Ballina-García3 and Ana Suárez1, 1Area of Immunology, Department of Functional Biology, University of Oviedo, Oviedo, Spain, 2Department of Rheumatology, Hospital Universitario Central de Asturias, Asturias, Spain, 3Department of Rheumatology, Hospital Universitario Central de Asturias, Oviedo, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: B Cell Biology and Targets in Autoimmune Disease Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: B cell compartment plays a key role in the pathogenesis of rheumatoid arthritis (RA). Activation and survival of B cell largely rely on the BLyS-APRIL system, including ligands and receptors, both expressed as membrane (m) and soluble (s) forms. The main aim of this study was to analyze the role of the BLyS-APRIL system in RA, with a special focus on its clinical relevance.

Methods: sBLyS, sAPRIL, sBCMA, sTACI, IFNα, MIP1α, TNFα, IL-10, IFNγ, IL-8, IL-37 and GM-CSF levels were measured by immunoassays in serum samples from 104 RA patients (EULAR/ACR 2010 criteria) and 33 healthy controls (HC). The membrane BLyS (mBLyS) expression was assessed on B cells, monocytes (MØ), myeloid (mDC) and plasmacytoid (pDC) dendritic cells and neutrophils (NØ) by flow cytometry in blood samples. A group of biological-naïve RA patients was prospectively followed for 3 months upon TNFα-blockade.

Results: RA patients exhibited increased sAPRIL (p<0.001) and sBCMA serum levels (p=0.002) than HC. sBLyS was higher in patients with early arthritis (recruited at onset) compared to those with long-standing disease (p=0.051) and HC (p=0.024). Levels of sTACI did not differ between patients and controls (p=0.462). mBLyS expression was increased on B cells (p=0.002), MØ (p<0.001), mDC (p=0.001) and NØ (p=0.014) in RA. By means of an unsupervised cluster analysis based on sBLyS, sAPRIL, sBCMA and sTACI, two clusters were identified (clusters I and II), cluster II being hallmarked by increased sAPRIL and sBCMA serum levels. Cluster II was found in 26 (25.0%) RA patients but was not observed in the HC group (p=0.001). Cluster II RA patients showed increased RF (p=0.002) and ACPA (p=0.001) positivity and were less likely to be treated with methotrexate (p=0.028) but more likely with anti-TNFα agents (p=0.013) compared to their cluster I counterparts. Cluster II was associated with higher DAS28 (p<0.050) but no difference in disease duration was observed (p=0.159). Additionally, higher IL-10 (p=0.060), IFNα (p=0.005), MIP1α (p=0.042), TNFα (p=0.006) and GM-CSF (p=0.008) levels were registered in cluster II. Further analyses revealed that sTACI was negatively associated with DAS28 score (r=-0.283, p=0.014) and positively with IL-10 serum levels (r=0.233, p=0.040) in patients within cluster I. On the contrary, in cluster II, APRIL was positively correlated with mBLyS expression on B cells (r=0.786, p=0.036), whereas sBLyS was associated with DAS28 score (r=0.281, p=0.016). Also, IFNα serum levels paralleled those of sTACI (r=0.636, p<0.001) in these patients. Finally, increasing sBLyS (p=0.043) and sBCMA levels (p=0.019) upon TNFα-blockade were associated with poor clinical outcome.

Conclusion: APRIL and sBCMA identify a subset of patients with a more severe disease, probably linked to a B cell hyperactivation status. APRIL and sBCMA may be promising biomarkers for patient stratification to B-cell targeted therapy in RA.

Disclosure: J. Rodríguez-Carrio, None; M. Alperi-López, None; P. López, None; F. J. Ballina-García, None; A. Suárez, None.

BTK Inhibition Ameliorates Lupus-Associated Neuropsychiatric and Skin Disease

Samantha Chalmers1, Jing Wen1, Jessica Doerner1, Ariel Stock2, Carla Cuda3, Hadijat Makinde3, Harris Perlman4, Todd Bosanac5,
SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: B Cell Biology and Targets in Autoimmune Disease Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
The importance of macrophages in the pathogenesis of cutaneous and neuropsychiatric systemic lupus erythematosus (SLE) is well established. Additionally, autoantibodies produced by autoreactive B cells are implicated in both the skin and brain disease associated with lupus. Bruton's tyrosine kinase (BTK) plays an important role in several key macrophage and B cell functions; therefore, we used a novel BTK inhibitor, BI-BTK-1, to target both macrophage and B cell dependent disease pathways in the MRL/lpr murine model of SLE.

Methods:
Starting at 8-9 weeks of age, female MRL/MpJ-Faslpr/J (MRL/lpr) mice were treated with BI-BTK-1, a highly selective BTK inhibitor, via medicated or control chow (Control mice, n=8; BI-BTK-1 treated, n=12). We quantified the development of skin lesions, and additionally assessed neuropsychiatric disease manifestations via comprehensive behavioral testing and immunohistochemical analysis of brain tissue.

Results:
Treatment with BI-BTK-1 significantly attenuated the skin inflammation and cognitive deficits associated with disease in the MRL/lpr strain. Specifically, BI-BTK-1 treated mice had less macroscopic (Fig. 1) and microscopic skin lesions, and reduced cutaneous cellular infiltration. Furthermore, skin from treated mice had significantly diminished inflammatory cytokine expression, including reduced protein levels of TNF, IL-6, IL-17, MCP-1, and GM-CSF. BTK inhibition also significantly improved memory function (p<0.05), and dramatically decreased accumulation of T cells, B cells, and macrophages within the brain, specifically in the choroid plexus (Fig. 2).

Conclusion:
Targeted therapies may improve the response rate in lupus driven target organ involvement, and decrease the dangerous side effects associated with more global immunosuppression. Overall, our results suggest that inhibition of BTK with BI-BTK-1 may be a promising therapeutic option for cutaneous and neuropsychiatric disease associated with SLE.

FIGURE 1:
Specificity of Salivary Gland-Derived Monoclonal Antibodies from Sjogren’s Syndrome Patients Using Proteome Arrays

Sherri Longobardi1, Christina Lawrence2, Kristi A. Koelsch3, Kenneth Smith2, Constantin Georgescu2, Michelle L. Joachims2, Lida Radfar4, Astrid Rasmussen2, Kathy L. Sivils2, Jonathan Wren2, R. Hal Scofield2 and A. Darise Farris2, 1Graduate Program in Biological Sciences, University of Oklahoma Health Sciences Center, Oklahoma City, OK, 2Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 3Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 4Department of Oral Diagnosis and Radiology, University of Oklahoma College of Dentistry, Oklahoma City, OK

First publication: September 18, 2017
ratios ≥ 2.0 SD above the mean value across all arrays and lack of binding by secondary antibody alone. Literature connectivity (IRIDESCENT), interactome and pathways (Ingenuity) bioinformatics analyses were conducted to investigate relationships among the bound antigens.

**Results:** A total of 201 proteins were found to be significantly bound by salivary gland mAbs, including Ro60, La, and Ro52 antigens. These were bound by patient mAbs but not by irrelevant mAbs or secondary antibody alone. Furthermore, of 199 novel non-Ro/non-La antigens identified, 16 were shared between 2 or more subjects on at least 2 arrays. Bioinformatics analyses revealed literature connectivity to the terms “salivary gland” or “Sjögren’s syndrome” among many of the bound antigens. The interactome showed multiple connections between several of the novel antigens; however, the most significant pathway among the shared antigen interactome was the proteasome/ubiquitination pathway.

**Conclusion:** Sixteen novel, non-Ro/La antigens shared between two or more patients were identified as possible targets of autoantibodies in SS. Pathway analysis of the shared interactome supports immune targeting of the proteasome/ubiquitination pathway by SG plasmablasts in SS.

Funding: National Institutes of Health (1P50 AR060804) and Oklahoma Center for the Advancement of Science and Technology (HR 16-055-01)

**Disclosure:** S. Longobardi, None; C. Lawrence, None; K. A. Koelsch, None; K. Smith, None; C. Georgescu, None; M. L. Joachims, None; L. Radfar, None; A. Rasmussen, None; K. L. Sivils, None; J. Wren, None; R. H. Scofield, None; A. D. Farris, None.


**Abstract Number: 31**

**Single Cell Analysis Revealed That the Response to Cyclophosphamide Therapy Is Regulated By B Cells in Systemic Sclerosis-Associated Interstitial Lung Disease**

*Satoshi Ebata¹, Ayumi Yoshizaki², Takemichi Fukasawa¹, Kouki Nakamura¹, Maiko Hirakawa¹, Takashi Yamashita¹, Shunsuke Miura³, Ryosuke Saigusa¹, Megumi Hirabayashi¹, Asako Yoshizaki¹, Kaname Akamata¹, Yoshihide Asano⁴, Yutaka Kazoe³, Kazuma Mawatari⁵, Takehiko Kitamori⁵ and Shinichi Sato⁶, ¹Dermatology, University of Tokyo, Graduate School of Medicine, Tokyo, Japan, ²Department of Dermatology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan, ³University of Tokyo, Graduate School of Medicine, Tokyo, Japan, ⁴Applied Chemistry, University of Tokyo, Graduate School of Medicine, Tokyo, Japan, ⁵Applied Chemistry, University of Tokyo, Graduate School of Engineering, Tokyo, Japan, ⁶Department of Dermatology, Graduate School of Medicine, The University of Tokyo, Bunkyo-ku, Japan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** B Cell Biology and Targets in Autoimmune Disease Poster

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Systemic sclerosis (SSc) is an autoimmune disease characterized by fibrosis of several organs. SSc-associated interstitial lung disease (ILD) is a frequent and severe complication of SSc. SSc-ILD declines the quality of patients' lives and sometimes determines their prognosis. Despite the severity of SSc-ILD, the treatment for SSc-ILD is still debated. The cyclophosphamide (CYC) treatment is the only therapy found to be effective in stabilizing or improving lung function of SSc-ILD in randomized clinical trials, which contained abundant numbers of patients. However, not every SSc-ILD patients treated with CYC recover. We need to know the difference between the responders and the non-responders against CYC. Recent studies indicate that B cells play a critical role in SSc through their function of cytokine production. Indeed, some studies have reported that the B cell depletion therapy with rituximab can be effective for SSc-ILD. However, the relationship between response to CYC therapy and B cell function remains unknown in SSc-ILD. We hypothesized that cytokine-producing effector B cells determine the effectiveness of the CYC treatment in SSc-ILD patients. In this study, we assessed the role of interleukin (IL)-10-producing regulatory B cells and IL-6-producing pathogenic B cells in the responders or non-responders of the CYC treatment.

**Methods:** We cultured human lung endothelial cells (LECs) in a microchannel. Sequentially, B cells from responders or non-responders against the CYC treatment were loaded into the microchannel. After each of B cells which adhered to LECs had produced cytokines, we measured IL-6 and IL-10 production from single B cells by our original micro fluidic-ELISA system. Similarly, we assessed B cells from topoisomerase (topo) I and complete Freund’s adjuvant-induced SSc model mice.
Results: In SSc-ILD patients, the number of B cells adhering to LECs significantly increased relative to healthy controls. B cells adhering to LECs from CYC-responders produced significantly higher amounts of IL-10 and lower amounts of IL-6 than those from CYC-non-responders. After the CYC treatment, the frequency of B cells which adhered to LECs significantly decreased in responders but did not decrease in non-responders. Regarding the cytokine profile of B cells adhering to LECs, the frequencies of IL-10 producing regulatory B cells after the CYC treatment increased in responders and decreased in non-responders. Those of IL-6-producing pathogenic B cells after the CYC treatment decreased in responders and increased in non-responders. In the mouse study, the number of topo I-specific B cells which adhere to LECs significantly increased compared to non-specific conventional B cells. Topo I-specific B cells also showed significantly higher production of IL-6 and lower production of IL-10 than conventional B cells.

Conclusion: These results suggested that the effectiveness of CYC to SSc-ILD patients is associated with the cytokine profile of B cells which interact with LECs. It is likely that IL-6-producing pathogenic B cells which survived the CYC treatment damage the lung function of non-responders.

Disclosure: S. Ebata, None; A. Yoshizaki, None; T. Fukasawa, None; K. Nakamura, None; M. Hirakawa, None; T. Yamashita, None; S. Miura, None; R. Saigusa, None; M. Hirabayashi, None; A. Yoshizaki, None; K. Akamata, None; Y. Asano, None; Y. Kazoe, None; K. Mawatari, None; T. Kitamori, None; S. Sato, None.

Longitudinal Associations between Rheumatoid Factor and Ex Vivo Cytokine Production Reveal Novel Mechanistic Insights into Rheumatoid Arthritis

John M. Davis III1, Cynthia S. Crowson2, Keith L. Knutson3, Sara J. Achenbach4, Terry M. Therneau5, Eric L. Matteson6, Sherine E. Gabriel7 and Peter J. Wettstein8, 1Division of Rheumatology, Mayo Clinic, Rochester, MN, 2Health Sciences Research, Mayo Clinic College of Medicine and Science, Rochester, MN, 3Immunology, Mayo Clinic, Jacksonville, FL, 4Mayo Clinic, Rochester, MN, 5Biostatistics, Mayo Clinic, Rochester, MN, 6Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, MN, 7Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, 8Immunology, Mayo Clinic, Rochester, MN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: B Cell Biology and Targets in Autoimmune Disease Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Positive rheumatoid factor (RF) and/or anti-citrullinated protein antibodies (ACPA) identify a major rheumatoid arthritis (RA) subgroup, characterized by greater propensity to erosive joint damage and extra-articular disease manifestations as compared to seronegative patients. The purpose was to determine the associations between RF/ACPA and changes in functional immune response signatures over 5 years in patients with RA.

Methods:
A longitudinal analysis was performed of baseline and 5-year follow-up data from a prospective study of adult RA patients in a population-based incidence cohort. Data were available for 324 patients at baseline and for 155 patients at 5 years. Peripheral blood leukocytes (PBL) were freshly collected from patients and isolated by Ficoll density gradient centrifugation at both time-points. PBLs were stimulated at 37°C for 48 hrs under six separate conditions: anti-CD3/anti-CD28 monoclonal antibodies (CD3/CD28); phytohemagglutinin (PHA), staphylococcal enterotoxins A and B (SEA/SEB); phorbol myristate acetate and ionomycin (PMA); CpG oligonucleotides (CpG ODN2006); and medium alone. A panel of 17 cytokines and chemokines was analyzed using multiplexed immunoassays (Meso Scale Discovery). RF was measured using the nephelometry (CSL Behring), and ACPA was measured by Quanta Lite CCP IgG (Inova Diagnostics). Factor analysis of normalized data was performed using baseline data on 324 patients to make inferences about underlying cell types based on cytokine profiles. Among the 155 patients with follow-up, Spearman methods were used to assess correlations between RF and/or ACPA seropositivity and longitudinal changes in the factor scores for each stimulus, adjusting for age and sex.

Results:
A total of 109 (70%) of the 155 patients were seropositive at baseline (median age: 57.7 yrs; median disease duration: 9.7 yrs). RF/ACPA
positively associated with CpG factor 1 ($r = 0.28$, $p < .001$), factor 2 ($r = 0.21$, $p = .011$), and factor 3 ($r = 0.20$, $p = .015$). Based on loadings >0.5, CpG factor 1 comprised IL-1β, G-CSF, TNF-α, MIP-1β, and IL-6; factor 2 comprised IFNγ, IL-2, and IL-13; and factor 3 comprised IL-12, and IL-5. Previous studies have shown that the type of CpG used in this study mainly activates B cells. Responses to medium alone paralleled those to CpG, as RF/ACPA positively correlated with medium alone factor 1 ($r = 0.27$, $p < .001$) and factor 3 ($r = 0.29$, $p < .001$) responses. Medium alone factor 1 comprised GM-CSF, MCP-1, IL-17A, IL-6, MIP-1β, TNF-α, and G-CSF; factor 3 comprised IL-1β and TNF-α. Based on this profile, multiple Toll-like receptor (TLR) ligands present in the medium fetal calf serum could have stimulated monocytes or other antigen presenting cells. In contrast, RF/ACPA negatively correlated with CD3/CD28-induced IL-5 ($r = -0.21$, $p = .008$), IL-17A ($r = -0.22$, $p = .009$), and GM-CSF ($r = -0.20$, $p = .013$).

**Conclusion:**

Our findings suggest that sustained stimulation of RF-containing immune complexes increases monocyte and B-cell activation states with increased expression of TLR. This could inform the development of functional assays for CpG and other TLR immune responses as predictors of response to B-cell directed therapy in RA.

**Disclosure:** J. M. Davis III, None; C. S. Crowson, None; K. L. Knutson, None; S. J. Achenbach, None; T. M. Therneau, None; E. L. Matteson, None; S. E. Gabriel, None; P. J. Wettstein, None.


**Abstract Number:** 33

**B Cell Abnormalities in Patients with Chronic Cutaneous Lupus Erythematosus**

Chungwen Wei, Aisha Hill, Kira Smith, Ignacio Sanz, S. Sam Lim and Cristina Drenkard, Medicine, Emory University School of Medicine, Atlanta, GA; Medicine, Emory University School of Medicine, Atlanta, GA; Emory University School of Medicine, Atlanta, GA; Division of Rheumatology, Emory University School of Medicine, Atlanta, GA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** B Cell Biology and Targets in Autoimmune Disease Poster

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Lupus is a spectrum of disease with cutaneous lupus (CLE) without systemic features on one end and systemic lupus erythematosus (SLE) on the other. Among CLE subtypes, chronic cutaneous lupus (CCLE) is deemed less likely to be associated with systemic features. However, 10-20% CCLE will develop SLE throughout their disease course. Little is known regarding the immunological correlates to the disease progression, which we postulate may be accompanied by the emergence of SLE-associated B cell abnormalities. As an initial test for our hypothesis, we compared the B cell phenotypes in a cross-sectional analysis among patients with CCLE, SLE with or without CCLE.

**Methods:** Patients met SLICC and ACR criteria for the classification of CCLE and SLE. Frozen PBMCs were analyzed by flow cytometry from healthy controls (HC) (n=23) and patients with primary CCLE (n=60), SLE (n=58) or CCLE with SLE (n=42). B cell subsets were identified using the following markers: CD19, IgD, CD27, CD24, CD21, CD11c, 9G4, in addition to CD3 and live/dead staining as exclusion markers. Frequencies of the various B cell subsets were compared among the groups using ANOVA followed by Tukey’s multiple comparison statistical tests. To gain a global view of the changes in B cell homeostasis, an unsupervised hierarchical clustering analysis of the B cell profiles was carried out.

**Results:** Several B cell abnormalities have been shown in SLE patients compared to the healthy controls, including a contraction of IgD$^+$CD27$^-$ unswitched memory (USM) and an expansion of IgD$^+$CD27$^+$ double negative (DN) cells. These observations are replicated in this study as well. Furthermore, within the DN population, a subset of cells with an activated phenotype (CD11c$^+$CD21$^-$, termed DN2) is significantly expanded in SLE compared to HC. Its counterpart in the IgD$^+$CD27$^-$ naïve and transitional (N+$T$) compartment – the CD11c$^+$CD21$^-$ activated naïve (aN) B cells – is also expanded in SLE, though not statistically different from HC. Interestingly, CCLE patients share with SLE the characteristic contraction of USM also seen in Sjogren’s and other autoimmune diseases, yet they do not exhibit the expansion of DN, activated DN2 and aN subsets. Instead, CCLE patients show an expansion of the early transitional (T1$+$T2) cells. Globally, an unsupervised hierarchical clustering analysis demonstrates the segregation of HC from SLE (with or without CCLE) on the basis of their B cell profiles. On the other hand, B cell profiles of CCLE patients are heterogeneous and interspersed between HC and SLE patients.
Conclusion: Cross-sectional analysis at baseline reveals that CCLE patients share some SLE abnormalities including contracted USM and expansion of early transitional B cells, but do not display expansions of activated mature B cells (both naïve and isotype switched DN cells), a phenotype that is frequently observed in SLE patients. Moreover, our study demonstrates that from a B cell standpoint, CCLE is a heterogeneous condition thereby opening the door to investigations of correlations between distinct B cell profiles and clinical variables and in particular, with progression to systemic disease. Confirmation awaits the longitudinal follow-up of these patients over the next years.

Disclosure: C. Wei, None; A. Hill, None; K. Smith, None; I. Sanz, None; S. S. Lim, None; C. Drenkard, None.


Abstract Number: 34

IL-23 Regulates Development of Spontaneous Germinal Centers and Pathogenic Autoantibody Production in BXD2 Mice

Huxian Hong1, Qi Wu2, PingAr Yang2, Bao Luo3, Jun Li4, Hao Li5, Daniel Cua6, Hui-Chen Hsu2 and John D. Mountz2,7, 1University of Alabama at Birmingham 1 Division of Clinical Immunology and Rheumatology, Department of Medicine, Birmingham, AL, 2Division of Clinical Immunology and Rheumatology, Department of Medicine, University of Alabama at Birmingham 1 Division of Clinical Immunology and Rheumatology, Department of Medicine, Birmingham, AL, 3Division of Clinical Immunology and Rheumatology, Department of Medicine, University of Alabama at Birmingham 1 Division of Clinical Immunology and Rheumatology, Department of Medicine, Birmingham, AL, 4Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham 1 Division of Clinical Immunology and Rheumatology, Department of Medicine, Birmingham, AL, 5Division of Rheumatology, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, 6Discovery Research, Merck Research Laboratory, Palo Alto, CA, 7University of Alabama at Birmingham and Birmingham VA Medical center, Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: B Cell Biology and Targets in Autoimmune Disease Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Targeting IL-23 to treat autoimmune disease and chronic inflammation is currently in development based on its pro-inflammatory function via regulating the activation of Th17 cells. IL-23 was previously shown to be important for promoting pathogenic autoantibody production in Fas deficient B6-Fas−/− mice, suggesting the positive role of IL-23 in mediating Fas-independent germinal center (GC) responses. In contrast, the lack of IL-23 did not influence conventional GC formation and IgG anti-CII autoantibodies in type II collagen immunized DBA/1 mice. We determined if IL-23 could regulate development of GCs and pathogenic autoantibody production in BXD2 mice.

Methods: The BXD2-IL-23 p19−/− mice were generated by 10 generation crossing the B6-p19−/− with the BXD2 mice. Serum autoantibodies were determined by ELISA. GC development was measured by FACS (GL-7 and Fas) and confocal imaging analyses. Autoantibody class switching was enumerated by the percentage of (IgM IgD+) in GL-7+ B cells. Immune complex deposition (IgM and IgG) in kidney was detected by confocal imaging.

Results: There was lower induction of Il17a in subpopulations of spleen cells from BXD2-p19−/− mice compared to WT BXD2 mice. However, unlike BXD2-Il17ra−/− mice, which developed lower levels of both IgM and IgG autoantibodies, BXD2-p19−/− mice exhibited significantly elevated titer of total IgM and IgM anti-DNA and RF autoantibodies but significantly lower levels of total IgG and IgG anti-histone, compared to WT BXD2 mice. Despite the lower circulating IgG autoantibodies, IgG staining was significantly increased in the glomerulus of BXD2-p19−/− mice compared to BXD2 and normal B6 mice with both an immune complex and linear staining pattern. The number and size of PNA+ GCs and the percent of GL-7+Fas+ GC B cells were increased in BXD2-p19−/− mice comparable to WT BXD2 mice. Abnormal GC development kinetics was confirmed by increased conventional isotype switched IgM IgD+ GL7+Fas+ B cells in BXD2-p19−/− mice compared to BXD2 WT mice.

Conclusion: The present findings provide a potential link to consolidate previous findings on the importance of IL-23 in mediating IgG autoantibody development in B6-Fas−/− mice and the lack of effects in development of IgG anti-CII antibody in CII immunized IL-23 deficient mice. These results extend the paradigm of IL-23 disease beyond the classical IL-23-Th17 axis and suggest IL-23 exhibits a negative effect on development of classical GC B cells that produce highly pathogenic autoAbs.
Abstract Number: 35

**B-Cell Subset Differences in Inflammatory Rheumatic Diseases**

**Joao Lagoas Gomes¹,², Dario Ligeiro³, Alice Lima³, Cristina Teixeira³, Alexandre Sepriano⁴,⁵, Sofia Ramiro⁶, Carina Lopes⁷, Tiago Costa⁸, Manuela Costa⁸, Jaime Cunha Branco¹,² and Fernando Pimentel-Santos¹,²**, ¹Rheumatology, Hospital Egas Moniz, Centro Hospitalar de Lisboa Ocidental, Lisbon, Portugal, ²CEDOC, NOVA Medical School, Lisbon, Portugal, ³Centro de Sangue e Transplantação de Lisboa, Instituto Português do Sangue e Transplantação (IPST), IP, Lisbon, Portugal, ⁴CEDOC, NOVA Medical School, Lisboa, Portugal, ⁵Rheumatology, Leiden University Medical Center, Leiden, Netherlands, ⁶Rheumatology, Department of Rheumatology, LUMC, Leiden, Netherlands, ⁷Hospital de Egas Moniz-CHLO, Lisbon, Portugal, ⁸Rheumatology, Hospital de Egas Moniz, Centro Hospitalar de Lisboa Ocidental, Lisbon, Portugal

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** B Cell Biology and Targets in Autoimmune Disease Poster

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Targeting humoral immunity has been proved effective in several inflammatory rheumatic diseases (IRD). Though clinical trials have shown some efficacy of B-cell depletion in ankylosing spondylitis (AS), results are less convincing. Other studies have revealed an association between mutations and expression of immune regulatory genes suggesting a B-cell dysfunction in the development and progression of AS. Yet, there is still lack of data describing B-cell subsets in AS. The study purpose is to assess and compare the immature, naive and antigen differentiated subsets of peripheral B-cell compartment in AS with those in healthy controls (HC) and other IRD

**Methods:** Patients with AS, RA and SLE according to respective classification criteria were included. Patients under biologic DMARDS were not included. Sociodemographic and clinical variables were recorded and blood samples were collected for quantification of inflammatory markers, immunoglobulin levels and assessment of B-cell immature transitional stages and mature subsets by flow cytometry. Mann-Whitney and Fisher’s exact test were used for statistical analysis

**Results:** Overall, 60 patients and 12 HC were included. All patient groups presented similar and rather low levels of inflammation, as measured by CRP, ESR and immunoglobulins, in addition to a decreased lymphocyte count. There were no differences in the B-cell counts between AS patients and HC, and both groups had higher B-cell counts than RA and SLE patients. Regarding B-cell subsets, the immature transitional compartment of AS patients was found in normal range, but not in RA and SLE. The latter presented a significant decrease in all transitional cell maturity stages (T1-T3). The next step in B-cell differentiation is mature naïve cells, also found to be normal in AS and decreased in RA and SLE. AS patients presented slightly higher counts of CD27+IgD+ MZ-like and class able to switch memory cells with reference to HC and these cell numbers were found to be low in RA and SLE patients. Switched memory CD27+IgD- B-cells were reduced in all patient groups, however, only SLE patients presented highly decreased cell levels

**Conclusion:** We found that while a severe dysfunction is present in the homeostasis of the B-cell compartment in RA and in particular SLE pts, which are lymphopenic in both immature and mature B-cell compartments, it appears that AS patients are not affected in the same way. At this stage, functional studies appear to be necessary in order to identify differences in key mechanisms of B cell development and differentiation that play a role in the aetiology and progression of these inflammatory rheumatic diseases. Our first results, however, establish that pathophysiological mechanisms involving B-cells clearly differentiate AS from RA and SLE
<table>
<thead>
<tr>
<th></th>
<th>AS (n=22)</th>
<th>RA (n=20)</th>
<th>SLE (n=18)</th>
<th>HC (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, Female; n (%)</td>
<td>11 (50); 11 (50)</td>
<td>9 (45); 11 (55)</td>
<td>5 (27.8); 13 (72.2)</td>
<td>3 (25); 9 (75)</td>
</tr>
<tr>
<td>Age; median (IQR)</td>
<td>56 (45.8-65.5)</td>
<td>55 (51-65.5)</td>
<td>44 (37.5-52.5)*</td>
<td>56 (35.3-63.3)</td>
</tr>
<tr>
<td>ESR mm/hour</td>
<td>14 (10-29.3)</td>
<td>21 (10.3-37.8)</td>
<td>23 (6-34.5)</td>
<td>11 (8-22.5)</td>
</tr>
<tr>
<td>CRP mg/dL</td>
<td>1.1 (0.9-1.7)</td>
<td>0.98 (0.7-3.2)</td>
<td>0.6 (0.5-1.6)</td>
<td>-</td>
</tr>
<tr>
<td>HLA B27+; n (%)</td>
<td>11 (68.8)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>With csDMARDs, n (%)</td>
<td>6 (30)</td>
<td>18 (90)</td>
<td>15 (83.3)</td>
<td>0</td>
</tr>
<tr>
<td>IgA seric levels, mg/dl; median (IQR)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IgG</td>
<td>1165 (881.3-1247.5)</td>
<td>1021 (830.3-1265)</td>
<td>1140 (1003-1325)</td>
<td>1033.5 (823.3-1235)</td>
</tr>
<tr>
<td>IgA</td>
<td>230 (158.8-340)</td>
<td>250.5 (164.3-315.3)</td>
<td>261 (205-323)</td>
<td>236.5 (150.3-339.8)</td>
</tr>
<tr>
<td>IgM</td>
<td>95.3 (65.6-119.5)</td>
<td>112 (67.7-164.8)</td>
<td>103 (60.6-131.5)</td>
<td>122 (71.5-158.3)</td>
</tr>
<tr>
<td>Absolute cell counts/μl blood; median (IQR)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>1685</td>
<td>1555</td>
<td>1250 (625-1892.5)</td>
<td>2170 (1830-2377)**</td>
</tr>
<tr>
<td>Total B-cells (CD20+)</td>
<td>186.3 (111-238.6)</td>
<td>96.2 (50.3-180.6)**</td>
<td>65.8 (20.9-116.1)**</td>
<td>182.1 (100.9-269.7)</td>
</tr>
<tr>
<td>Immature Transitional B-cells (CD5⁺CD27⁺IgD⁺), median (IQR)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD24⁺⁺CD38⁺⁺(T1)</td>
<td>2.8 (1.8-3.9)</td>
<td>0.6 (0.1-2.7)**</td>
<td>1.5 (0.2-2.8)**</td>
<td>4.3 (2.3-6.5)</td>
</tr>
<tr>
<td>CD24⁺⁺CD38⁺⁺(T2)</td>
<td>8.3 (5.1-14.9)</td>
<td>2.6 (0.2-8.0)**</td>
<td>3.0 (1.0-8.0)**</td>
<td>13.7 (5.7-18.8)</td>
</tr>
<tr>
<td>CD24⁺CD38⁺⁺(T3)</td>
<td>9.0 (5.5-17.7)</td>
<td>2.2 (0.3-4.6)**</td>
<td>1.9 (0.2-3.7)**</td>
<td>7.7 (4.1-12.3)</td>
</tr>
<tr>
<td>Mature B-Cells, median (IQR)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD27⁺IgD⁺ (naive)</td>
<td>73.2 (49.7-121.7)</td>
<td>40.1 (19.2-76.9)**</td>
<td>27.2(11.9-57.1) †</td>
<td>78.6 (48.4-163.4)</td>
</tr>
<tr>
<td>CD27⁺IgD⁺ (mem. MZ-like)</td>
<td>25.9 (13.6-39.9)</td>
<td>13.0 (3.5-27.2)**</td>
<td>2.6 (1.8-9.6) †</td>
<td>18.9 (11.2-27.1)</td>
</tr>
<tr>
<td>CD27⁺IgD⁺ (switch mem.)</td>
<td>18.8 (12.2-37.9)</td>
<td>13.5 (3.9-37.6)</td>
<td>4.9 (2.2-17.2)***</td>
<td>29.3 (14.51-37.9)</td>
</tr>
<tr>
<td>CD27⁺IgD⁺ (double neg.)</td>
<td>2.4 (1.8-5.2)</td>
<td>3.1 (2.0-6.4)</td>
<td>2.9 (1.0-5.0)</td>
<td>5.2 (2.6-8.1)</td>
</tr>
</tbody>
</table>

Mann-Whitney and the Fisher’s exact test were used for comparison between AS and other groups

* p<0.05; **p<0.02; ***p<0.01; †p<0.0001;

Disclosure: J. Lagoas Gomes, None; D. Ligeiro, None; A. Lima, None; C. Teixeira, None; A. Sepriano, None; S. Ramiro, None; C. Lopes, None; T. Costa, None; M. Costa, None; J. C. Branco, None; F. Pimentel-Santos, None.

GM-CSF-Producing B Cells: A Novel B Cell Subset Involved in the Pathogenesis of Systemic Sclerosis

Kazuhiko Higashioka¹, Yuri Ota¹, Tsuyoshi Nakayama¹, Koji Mishima¹, Masahiro Ayano¹, Yasutaka Kimoto², Hiroki Mitoma¹, Mitsuteru Akahoshi¹, Yojiro Arinobu¹, Koichi Akashi¹, Takahiko Horiuchi³ and Hiroaki Niro⁴, ¹Department of Medicine and Biosystemic Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan, ²Department of Internal Medicine, Kyushu University Beppu Hospital, Oita, Japan, ³Department of Internal Medicine, Kyushu University Beppu Hospital, Beppu, Japan, ⁴Department of Medical Education, Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: B Cell Biology and Targets in Autoimmune Disease Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a T helper type 2 (Th2)-driven autoimmune disease characterized by vasculopathy and fibrosis. There are still unmet needs in the management of SSc, however B-cell depletion therapy has recently been reported to be effective for this disease. Intriguingly here there is no significant correlation between autoantibody titers and the improvement of clinical symptoms, thus highlighting a novel antibody-independent function of B cells, particularly cytokine production, involved in the pathogenesis of SSc. Granulocyte-macrophage colony-stimulating factor (GM-CSF) exerts a wide range of biological effects mainly on myeloid cells, and B cells has recently been reported as another cellular source of GM-CSF that is induced by a Th2 cytokine IL-4. Given a pathological relevance of Th2 cytokines in SSc and association of GM-CSF with fibrotic processes in various rodent models, in the present study we have sought to elucidate a role of GM-CSF-producing B cells in this disease.

Methods: B cell subsets in peripheral blood from healthy donors and patients with SSc were enriched by cell sorting and subjected to the analysis of GM-CSF transcripts and proteins (intracellular staining and ELISA). The relationship between GM-CSF-producing B cells and the clinical features of SSc was also evaluated. To determine the functional impacts of GM-CSF-producing B cells on myeloid cells, B cells cultured under Th2 conditions were co-cultured with CD14+ monocytes.

Results: Among a panel of CD4+ T cell-derived cytokines, Th2 cytokine IL-4 most significantly induced the generation of GM-CSF-producing memory B cells, while T follicular helper (Tfh) cytokine IL-21 remarkably abrogated this process. Intriguingly TGF-b further potentiated IL-4-induced GM-CSF production in memory B cells. GM-CSF-producing effector B cells were positive for CD30, a distinct phenotype from Ab-producing cells induced by IL-21. GM-CSF production in B cells from patients with SSc was more pronounced than that from healthy donors. This trend was also observed in both naïve and memory B cell subsets. A subpopulation of SSc patients with the diffuse type and concomitant IP, in particular, represented enhanced GM-CSF production in memory B cells. Moreover, B cells cultured under Th2 conditions along with TGF-b facilitated the differentiation from CD14+ monocytes to DC-SIGN+CD1a+CD14-CD86+ cells, a novel DC subset previously reported in skin of SSc patients and SSc model mice.

Conclusion: Together, these findings suggest that GM-CSF-producing effector B cells is a novel B cell subset and play a critical role in the pathogenesis of SSc by Ab-independent mechanisms.

Disclosure: K. Higashioka, None; Y. Ota, None; T. Nakayama, None; K. Mishima, None; M. Ayano, None; Y. Kimoto, None; H. Mitoma, None; M. Akahoshi, None; Y. Arinobu, None; K. Akashi, None; T. Horiuchi, None; H. Niro, None.


β2-Glycoprotein I Binds to Necroptotic Cells and Serves As a Target for SLE Autoantibodies

David Salem¹, Rebecca Subang¹, Maziar Divangahi¹, Christian Pineau², Sasha Bernatsky³, Jerrold S. Levine⁴ and Joyce Rauch⁵, ¹Research Institute of the McGill University Health Centre, Montreal, QC, Canada, ²Division of Rheumatology, McGill University Health

Abstract Number: 37
β2-glycoprotein I (β2GPI), a phospholipid-binding protein, binds to apoptotic cells and serves as an antigenic target for autoantibodies from patients with systemic lupus erythematosus (SLE). Here, we determine whether this paradigm can be extended to necroptotic cells. Like apoptotic cells, necroptotic cells express phosphatidylserine on their surface and provide a “scaffold” of cellular self-antigens. We hypothesized that β2GPI should bind to necroptotic cells and serve as a target for anti-β2GPI autoantibodies from patients with SLE.

Methods: We established conditions for inducing necroptotic or apoptotic cell death in murine L929 fibroblast cells. L929 cells treated with vehicle served as the viable cell control. Cells were incubated with human β2GPI and murine monoclonal anti-β2GPI IgG antibody (or isotype control), and bound antibody detected with fluorescently conjugated anti-murine IgG. Similarly, binding of anti-β2GPI autoantibodies from human sera (or IgG isolated from these sera) was detected using fluorescently conjugated anti-human IgG. Human sera were from healthy controls and patients who satisfied the ACR classification criteria for SLE. Antibody binding was analyzed by flow cytometry and confocal microscopy.

Results: Using murine monoclonal anti-β2GPI antibody, we demonstrate that β2GPI binds to necroptotic cells in a similar manner as to apoptotic cells, but not to viable cells. Cells treated with an irrelevant antigen (serum albumin) or isotype control showed little or no antibody binding. Confocal microscopy confirmed monoclonal anti-β2GPI antibody staining of the cell surface of both necroptotic and apoptotic cells. SLE sera positive for anti-β2GPI autoantibodies bound to necroptotic cells and apoptotic cells. In contrast, sera negative for anti-β2GPI autoantibodies behaved similarly to healthy control sera, and showed little or no binding to necroptotic or apoptotic cells. Binding of purified IgG from the sera replicated the findings observed with sera.

Conclusion: Our data demonstrate that β2GPI binds to necroptotic cells and can serve as a target for SLE autoantibodies recognizing β2GPI. Based on these findings, we propose that the paradigm of apoptotic cells serving as a “cellular scaffold” of self-antigens in SLE may be extended to necroptotic cells.

Disclosure: D. Salem, None; R. Subang, None; M. Divangahi, None; C. Pineau, None; S. Bernatsky, None; J. S. Levine, None; J. Rauch, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/%ce%b2-glycoprotein-i-binds-to-necroptotic-cells-and-serves-as-a-target-for-sle-autoantibodies
observations have established the role of metabolic pathways in the diverse array of immune cell functions. It is unknown though how these metabolic pathways influence B cell cytokine production. We sought to elucidate the metabolic programs required for B cell cytokine production.

**Methods:** B cells were isolated from the spleens of C57Bl/6J mice and activated overnight individually by anti-μ antibody, anti-CD40 agonist antibody, polyclonal LPS, R484, and CpG. Supernatants were analyzed for the quantification of cytokines using the Milliplex cytokine kit (EMD Millipore). Real-time analysis of extracellular acidification rates and oxygen consumption rates of activated B cells were performed using the XF-96 Extracellular Flux Analyzer (Seahorse Bioscience). To assess 3-carbon sources for oxidative phosphorylation, inhibitors to fatty acid oxidation (etomoxir), pyruvate transfer to mitochondria (UK-5099), and glutamine usage (BPTES) were used. Amino acids, organic acids, and acylcarnitines were extracted using methanol for targeted metabolomics studies using mass spectroscopy.

**Results:** CpG stimulation of mouse splenic B cells increased both glycolysis and mitochondrial respiration to a larger extent that by other stimuli such as LPS or B cell receptor alone. These processes are highly dependent on glutamine, as inhibition of glutaminolysis with BPTES significantly reduced both processes. Furthermore, glutaminolysis activated mTOR, which was required for glycolysis, mitochondrial respiration, and ATP production in CpG-activated B cells. Quantitative targeted metabolomic studies confirmed CpG-stimulation drove increases in intracellular amino acid levels, aerobic glycolysis and TCA cycle intermediates, all of which were reversed in the presence of BPTES. Production of TNF-α, IL-6, and IL-10 by CpG-stimulated B cells also relied on glutaminolysis and mTOR activation. Interestingly, inhibition of glycolysis alone selectively decreased IL-10 production.

**Conclusion:** B cells undergo metabolic reprogramming when stimulated with CpG, requiring glutaminolysis and mTOR activation, which drove aerobic glycolysis, TCA cycling, and ATP production. Cytokine production is intrinsically linked with this reprogramming, although glycolysis was required for B cell IL-10 production suggesting the possibility that various B cell cytokines differentially rely on specific metabolic pathways. These data are the among first to demonstrate a relationship between B cell effector function and metabolic reprogramming, and suggest that B cell cytokine secretion can be manipulated by altering the local metabolic environment. Manipulating metabolic pathways may represent an interesting therapeutic approach for modulating B cells in autoimmune diseases.

**Disclosure:** M. Cheung, None; D. Huang, None; E. Liu, None; J. Ra, None; A. Kim, Kypha, Inc., 2,Exagen Diagnostics, 5,NIH/NIAMS, 2,Department of Defense, 2,Rheumatology Research Foundation, 2,Doris Duke Foundation, 2,Midwest Strategic Pharma-Academic Research Consortium, 2.


**Abstract Number:** 39

**Protein Array Technology Identifies Rituximab-Treated Non-Responder Rheumatoid Arthritis Patients to Generate New Autoantibody Repertoires during Treatment**

Zoltán Konthur¹, Melvin Michael Wienkes², Thomas Häupt¹, Gerd R. Burmester² and Karl Skriner², ¹Department of Biomolecular Systems, Max Planck Institute of Colloids and Interfaces, Potsdam, Germany, ²Department of Rheumatology and Clinical Immunology, Charité - University Medicine Berlin, Free University and Humboldt University Berlin, Berlin, Germany

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** B Cell Biology and Targets in Autoimmune Disease Poster

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Rituximab (RTX) has shown clinical efficacy but up to 40% of RTX treated rheumatoid arthritis (RA) patients are poor responders (Ann-Rheum-Dis. 2005 Feb;64(2):246-52) and the commonly used RA biomarkers (RF/ACPA) are poor predictors for therapy response. In this study the autoantibody repertoire analysed on protein macorarrays from RA patients under RTX treatment was correlated to clinical DAS28 response.

**Methods:** Screening of RA sera was conducted on 37,830 unique human proteins on protein macorarrays with sera taken before and 24 weeks after treatment. The autoantibody response of different immunoglobulin classes IgD, IgA, and IgG was recorded and bioinformatically evaluated. Response was determined according to DAS28 criteria. DAS 28 scores in the responder group before treatment was from 5.4 – 7.8 and in the non-responder group 5.6 – 6.8. We analyzed 26 RA patient sera (9 responder, 7 non-responder and 10 patients with blinded response classification) investigated the data of found autoantigens in silico and by hierarchical clustering.

**Results:** In the cohort of 26 patients 1292 different autoantigens (IgD,IgA,IgG) were detected. Using protein array we investigated clusters of...
autoantigen responses that disappeared or developed during RTX treatment of RA patients. RA autoantigenic patterns before and 6 month after RTX treatment were patient-specific and no relevant autoantigenic cluster was found that was shared between patients or associated with response. However, RTX reduced the repertoire of autoantibodies after 24 weeks of treatment in the tested RA patient cohort on average by 60%. RA patients which do not respond are generating on average 63% new autoantibodies. In good responders to RTX only 5.5% (+/-3%) new autoantibodies can be detected. The IgA and IgG autoantibody repertoire in the serum after 24 weeks of RTX treatment is reduced (IgA: 41%, IgG:31%) in good responders whereas it is increased (IgA: 1.3%, IgG: 24%) in non responders to RTX.

Conclusion: After 6 month of RTX treatment the autoantibody repertoire in all good responding RA patients is reduced and non-responders to RTX change their autoantibody repertoire directed against new but patient specific antigens. The fast rebuilding of functional B cells is only detected in non-responders to rituximab.

Disclosure: Z. Konthur, None; M. M. Wienkes, None; T. Häupl, None; G. R. Burmester, None; K. Skriner, None.


Abstract Number: 40

B-Cell Attracting Chemokine-1 (BCA-1) and Macrophage Inflammatory Protein-3 Alpha (MIP-3α) Act Synergistically in the Recruitment of B Cells in the Rheumatoid Synovium

Estefanía Armas-González1, María Jesús Domínguez-Luis2, María Teresa Arce-Franco3, Javier Castro-Hernández3, Vanesa Hernandez4, Sagrario Bustabad5, Alberto Cantabrana-Alutiz6 and Federico Diaz-González7, 1Universidad de La Laguna, Departamento de Medicina Física y Farmacología, Facultad de Medicina, La Laguna, Tenerife, Spain, 2Laboratorio de Reumatología. Hospital Universitario de Canarias, La Laguna, Spain, 3Laboratorio de Reumatología. Hospital Universitario de Canarias, La Laguna, Tenerife, Spain, 4Rheumatology, Servicio de Reumatología. Hospital Universitario de Canarias, S/C Tenerife, Spain, 5Rheumatology, Servicio de Reumatología. Hospital Universitario de Canarias, La Laguna, Tenerife, Spain, 6Servicio de Reumatología. Hospital Universitario Nuestra Señora de Candelaria, La Laguna, Tenerife, Spain, 7Servicio de Reumatología. Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: B Cell Biology and Targets in Autoimmune Disease Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: B cells are recognized as key players in the pathogenesis of rheumatoid arthritis (AR) through the production of autoantibodies, the local production of proinflammatory soluble factors and, when acting as antigen-presenting cells, the regulation of T-cell functions. Experimental evidence suggests that B cells should migrate to and accumulate within the synovial microenvironment to exert their pathogenic action in RA. However, little is known about the driving force responsible for the recruitment of B cells in the rheumatoid synovium. Chemokines and their receptors expressed in leucocytes help to control the selective migration and activation of inflammatory cells in the inflamed synovium. Objective: to determine the chemokine or chemokines responsible for the recruitment of B cells in the rheumatoid synovium.

Methods: Surface expression levels of CD27, CCR1, CCR2, CCR3, CCR4, CCR5, CCR6, CCR7, CXCR2, CXCR4, CXCR5 and CXCR7 were assessed by double- or triple-staining flow cytometry analysis in CD20+ mononuclear cells isolated by Ficoll-gradient from the peripheral blood (PB) and synovial fluid (SF) of 15 RA patients. In a sample of patients, the total expression (intra- and extracellular) of specific chemokine receptors was analyzed by flow cytometry in CD20+ cells PB and SF permeabilized mononuclear cells from PB and SF. Transwell experiments were used to study the synergism and migration capabilities of negatively immunoselected PB B-cells from normal donors or in CD20+ mononuclear cells from PB and SF of RA patients in response to a single chemokine or a mix of two chemokines.

Results: B cells from the SF of RA patients showed a significant increase in the surface expression of CCR1 (2.1± 0.1-fold), CCR2 (2.4±0.2 fold), CCR4 (6±2 fold), CCR5 (2±0.1 fold) and CXCR4 (2.5±0.8-fold) with respect to PB. Remarkably, SF B cells expressed consistently lower amounts of CXCR5 (0.15±0.05 fold, p<0.01), CXCR7 (0.7±0.1 fold, p<0.05) and CCR6 (0.75±0.1 fold, p<0.05) with respect to PB. This differential pattern of chemokine receptor expression was not modified by the previous contact of B cells with antigen, as assessed by CD27 expression levels. Flow cytometry results showed a relative increase in the expression of CXCR5 and CCR6 in permeabilized CD20+ cells from SF compared to those from PB, which suggests that both receptors undergo cell internalization in B cells that migrate to the
rheumatoid synovium. In Transwell experiments, MIP-3α and BCA-1, ligands of CCR6 and CXCR5, respectively, caused a significantly higher migration on B cells from PB than in those from the SF of RA patients. Together, the two chemokines synergistically increased B cells migration from PB but not from SF.

**Conclusion:** B cells present in the synovial microenvironment of patients with RA down-regulate the surface expression of CXCR5, CCR6 and CXCR7 via an internalization mechanism. Individually, BCA-1 and MIP-3α show higher chemotactic effects in B cells from PB versus those from SF, while together they exert a synergistic effect in B cells from PB, but not from SF. These results suggest that BCA-1 and MIP-3α might play major roles in RA pathogenesis by acting synergistically in the accumulation of B lymphocytes within the inflamed synovium.

Disclosure: E. Armas-González, None; M. J. Domínguez-Luis, None; M. T. Arce-Franco, None; J. Castro-Hernández, None; V. Hernández, None; S. Bustabad, None; A. Cantabrana-Alutiz, None; F. Díaz-González, None.


**Abstract Number:** 41

**A Fine Bioinformatical Analysis of Lymphocyte Distribution Predicts the Diagnosis of Systemic Autoimmune Diseases**

Quentin Simon1, Bénédicte Rouvière1, Tifenn Martin1, Lucas Le Lann1, Alain Saraux1, Valérie Devauchelle-Pensec1, Concepcion Marañón2, Nieves Varela Hernández2, Aleksandra Dufour3, Carlo Chizzolini4, Ellen de Langhe5, Nuria Barbarroja6, Chary Lopez-Pedrera7, Velia Geri8, Aurelie Degroof9, Julie Ducreu10, Elena Trombettta11, Tianlu Li12, Marta Alarcón-Ríquela13, Christophe Jaman1 and Jacques-Olivier Pers1, 1U1227, Université de Brest, Inserm, Labex IGO, CHU de Brest, Brest, France, 2GENYO, Centre for Genomics and Oncological Research Pfizer, University of Granada, Andalusian Regional Government, Granada, Spain, 3Immunology & Allergy, University Hospital and School of Medicine, Geneva, Switzerland, 4University hospital of Geneva, Geneva, Switzerland, 5Rheumatology, University Hospital KU Leuven, Leuven, Belgium, 6Rheumatology service, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain, 7IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain, 8Department of Rheumatology and Clinical Immunology, Charité University Hospital, Berlin, Germany, 9Pôle de Maladies Rhumatismes, Institut de Recherche Expérimentale et Clinique, Université catholique de Louvain, Brussels, Belgium, 10Pôle de pathologies rhumatismales inflammatoires et systémiques, Institut de Recherche Expérimentale et Clinique, Université catholique de Louvain, Brussels, Belgium, 11Laboratorio di Analisi Chimico Cliniche e Microbiologia - Servizio di Citofluorimetrica, Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico di Milano, Milano, Italy, 12Bellvitge Biomedical Research Institute (IDIBELL), Barcelona, Spain, 13GENYO. Center for Genomics and Oncological Research, Granada, Spain

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** B Cell Biology and Targets in Autoimmune Disease Poster

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** We investigated 194 individuals with SADs (38 primary Sjögren’s syndrome (pSS), 47 rheumatoid arthritis (RA), 46 systemic lupus erythematosus (SLE), 42 systemic sclerosis (SSc) and 21 undifferentiated connective tissue disease (UCTD) patients) and 53 healthy controls (HCs) to determine whether a fine flow cytometry analysis of T and B cell distribution in whole blood could cluster individuals according to disease diagnosis.

**Methods:** Two flow cytometry panels were designed. The first panel was dedicated to T cells and combined CD57, CD45RA, CD62L, CD27, CD38, CD3, CD4 and CD8 mAbs. The second panel was dedicated to B cells and combined IgD, TACI, CD27, CD5, CD38, CD19 and CD24 mAbs. A classical manual gating strategy and the Flow-clustering without K (FLOCK) investigation, a density-based clustering approach to algorithmically identify relevant cell populations from multiple samples in an unbiased fashion, were used.

**Results:** The manual gating strategy allows the identification of 17 distinct lymphocyte subsets. The prediction of the different SADs was determined by discriminant function analysis (DFA). No clustering was found. The FLOCK exploration of the merged HCs identifies 85 distinct subsets of lymphocytes used as reference when compared to SADs. The DFA analysis clearly clusters the HCs and the patients according to each SAD (see figure below).
When compared to HCs, the pSS signature was discriminated by an increase in IgD<sup>hi</sup>CD24<sup>hi</sup>CD38<sup>hi</sup>CD27<sup>-</sup>TACI<sup>-</sup>CD5<sup>hi</sup> transitional B cells, and an increase of CD45RA<sup>-</sup>CD62L<sup>lo/-</sup>CD57<sup>hi</sup> effector CD8<sup>+</sup> T cells.

The SLE signature was discriminated by an increase in IgD<sup>-</sup>CD24<sup>lo</sup>CD38<sup>-</sup>CD27<sup>-</sup>TACI<sup>+</sup>CD5<sup>-</sup> memory like B cells, an increase in CD45RA<sup>-</sup>CD62L<sup>+</sup>CD38<sup>hi</sup> activated central memory CD4<sup>+</sup> T cells.

The RA signature was discriminated by an increase in IgD<sup>hi</sup>CD24<sup>lo</sup>CD38<sup>-</sup>CD27<sup>-</sup>TACI<sup>-</sup>CD5<sup>-</sup> unactivated mature naïve B cells and a decrease in CD45RA<sup>-</sup>CD62L<sup>+</sup>CD38<sup>hi</sup> naïve CD8<sup>+</sup> T cells.

The SSc signature was discriminated by a decrease in CD45RA<sup>-</sup>CD62L<sup>+</sup>CD38<sup>hi</sup> naïve CD8<sup>+</sup> T cells.

Interestingly, patients with UCTD were distributed among the different clusters (28% with HC, 29% with SLE, 29% with SSc, 9% with RA and 5% with pSS clusters).

**Conclusion:** A fine bioinformatical flow cytometry analysis of T and B cell subsets clusterizes patients and HCs suggesting that each SAD can be associated with abnormal specific phenotypical distributions that could be helpful in the diagnosis.

This work has received support from the EU/EFPIA Innovative Medicines Initiative Joint Undertaking PRECISESADS grant no 115565. [www.precisesads.eu](http://www.precisesads.eu)

**Disclosure:** Q. Simon, EFPIA, 2; B. Rouvière, None; T. Martin, None; L. Le Lann, EFPIA, 2; A. Saraux, None; V. Devauchelle-Pensec, Roche-Chugai provided me tocilizumab for the SEMAPHORER study, 2; C. Marañón, EFPIA, 2; N. Varela Hernández, EFPIA, 2; A. Dufour, EFPIA, 2; C. Chizzolini, EFPIA, 2; E. de Langhe, None; N. Barbarroja, None; C. Lopez-Pedrera, EFPIA, 2; V. Gerl, EFPIA, 2; A. Degroof, EFPIA, 2; J. Ducrueux, EFPIA, 2; E. Trombetta, EFPIA, 2; T. Li, EFPIA, 2; M. Alarcón-Riquelme, Genzyme/Sanofi Corporation, 2; C. Jamin, EFPIA, 2; J. O. Pers, EFPIA, 2.
Methods: Flow cytometry and real-time PCR were used to analyze the expression of Sirt1. Sirt1 signaling was modulated with the Sirt1 agonist resveratrol. BALB/c mice were given 0.5 ml of pristane on day 1 by intraperitoneal injection to induce the lupus-like disease and on day 2 the mice received various doses of resveratrol. CD19+ B cells were isolated from the spleen mononuclear cells of the pristane-induced lupus mice and cultured with or without resveratrol in vitro for 3-5 days and B cell activation, plasma B cell differentiation and Prdm1 gene expression were assessed by flow cytometry or real-time PCR.

Results: The expression of Sirt1 in CD19+B cells of SLE patients was significantly decreased when compared to healthy donors (p=0.0071). The expression of Sirt1 negatively correlated with CD19+ B cell frequencies (p=0.0008). In pristane-induced lupus mice, Sirt1 activator-resveratrol dramatically decreased the expression of CD69, CD80, CD86 expression of B lymphocytes in a dose-dependent manner. Resveratrol significantly inhibited CD138+ plasma cell differentiation of B lymphocytes after stimulation with LPS plus anti-CD40 antibody. Finally, resveratrol significantly inhibited the expression of PRDM1(gene encoding Blimp-1) mRNA in B-cells.

Conclusion: Sirt1 is downregulated in SLE patients. The use of resveratrol, Sirt1 agonist may present a novel approach for treatment of SLE by inhibiting B cell activation and plasma cell differentiation.

Disclosure: T. Wang, None; X. Song, None; X. Luo, None; M. Li, None; X. Zeng, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/resveratrol-regulates-sirt1-to-control-b-cells-activation-and-plasma-b-cells-differentiation

Abstract Number: 43

Regulation of TLR7 Signalling By UBE2L3 Dependent Linear Ubiquitination Explains Dimethyl Fumarate Suppression of Autoreactive B Cell Development in SLE

Daniele Mauro1, Victoria Tsang2, Isabelle A. Clayton-Lucey3, Sara Pagani2, Farah Alam2, Elena Pontarini2, Alessandra Nerviani2, Angela Pakozdi4, Andrea Cove-Smith4, Ravindra Rajakariar4, Debasish Pyne5, Timothy J Vyse5, Costantino Pitzalis2 and Myles J. Lewis4,6

1Centre for Experimental Medicine and Rheumatology, William Harvey Research Institute, Barts and The London, School of Medicine and Dentistry, Queen Mary University of London, London, United Kingdom, 2Experimental Medicine & Rheumatology, William Harvey Research Institute, Queen Mary University of London, London, United Kingdom, 3Experimental Medicine & Rheumatology, William Harvey Research Institute, Queen Mary University of London, EC1M 6BQ, United Kingdom, 4Barts Lupus Centre, Barts Health NHS Trust, London, United Kingdom, 5Division of Genetics and Molecular Medicine, King's College London, Guy's Hospital, London, United Kingdom, 6Rheumatology, Centre for Experimental Medicine and Rheumatology, William Harvey Research Institute, Barts and The London, School of Medicine and Dentistry, Queen Mary University of London, London, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: B Cell Biology and Targets in Autoimmune Disease Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
A single risk haplotype spanning UBE2L3 is strongly associated with SLE and multiple autoimmune diseases. The E2 ubiquitin-conjugating enzyme UBE2L3 regulates TNFα and CD40 induced NF-kB activation via regulation of the Linear Ubiquitination Chain Assembly Complex (LUBAC). We have shown that the UBE2L3 risk allele correlates with plasmablast and plasma cell expansion in SLE individuals by regulating NF-κB activation in B cells. Dimethyl Fumarate (DMF), a current oral therapy for multiple sclerosis and psoriasis, has been recently identified as a UBE2L3 inhibitor. Given the known role of excessive TLR7 signalling in SLE, we aimed to determine the effect of UBE2L3 and linear ubiquitination on TLR7 signalling and to explore whether UBE2L3-mediated plasmablast differentiation can be inhibited by DMF.

Methods:
Transient overexpression and shRNA silencing were used in TLR7-HEK293 NF-kB reporter cell line to investigate the effect of UBE2L3/LUBAC on NF-kB activation, gene expression by qPCR and IL-8 secretion by ELISA. Western blot was used to measure linear ubiquitin chain polymerisation, confirmed by confocal microscopy. DMF was administered to CD19+ peripheral blood human B cells cultured in the presence of resiquimod, IFNα, or both for up to 7 days. B cell viability, activation, differentiation and proliferation were analysed by flow cytometry. Immunoglobulin secretion was quantified by ELISA and ANA detected by Hep2 immunofluorescence assay.
Results:

Overexpression of catalytically active LUBAC components increased TLR7-induced NF-kB activation by reporter assay. NF-kB activation, NF-xB target gene expression by qPCR and IL-8 secretion were further enhanced by co-overexpression of UBE2L3 with LUBAC, basally and after TLR7 stimulation, but was abolished by dominant negative mutant UBE2L3(C86S) or HOIP(C885S), and in UBE2L3 silenced cells. TLR7 engagement triggered accumulation of linear ubiquitin chains comparable to TNFα. DMF exerted a dose-dependent suppression of NF-kB activation following TLR7 engagement. DMF reduced human primary B cell survival, and suppressed proliferation of switched and unswitched CD27+ memory B cells. DMF inhibited TLR7 stimulated immunoglobulin secretion by in vitro differentiated B cells. Co-stimulation of B cells with TLR7 ligand resiquimod and IFNa induced anti-nuclear autoantibody production which was suppressed by DMF.

Conclusion:

Our results establish that linear ubiquitination and UBE2L3 regulate TLR7 activation of NF-kB. Silencing UBE2L3/LUBAC, use of dominant negative mutant UBE2L3 or HOIP, or use of the UBE2L3 inhibitor DMF suppressed TLR7 driven NF-kB activation. Excessive TLR7 signaling has been linked to SLE development by impaired checkpoint permissiveness in autoreactive B cells, leading to autoantibody production in the context of type I interferon. DMF demonstrated potent suppression of CD27+ memory B cell differentiation and inhibited TLR7 and IFNa induced autoantibody production. These results suggest that there may be a role for repositioning DMF in the treatment of SLE and autotimmune driven autoimmune diseases.

Disclosure: D. Mauro, None; V. Tsang, None; I. A. Clayton-Lucy, None; S. Pagani, None; F. Alam, None; E. Pontarini, None; A. Nerviani, None; A. Pakozdi, None; A. Cove-Smith, None; R. Rajakariar, None; D. Pyne, None; T. J. Vyse, None; C. Pitzalis, None; M. J. Lewis, None.


Abstract Number: 44

Characterization of Novel Stromal-Derived Autoantigens Recognized By RA Synovial Monoclonal Antibodies

Elisa Corsiero1, Lucas Jagemann1, Costantino Pitzalis2 and Michele Bombardieri3, 1Centre for Experimental Medicine & Rheumatology, William Harvey Research Institute, Queen Mary University of London, London, United Kingdom, 2Centre for Experimental Medicine and Rheumatology, William Harvey Research Institute, Barts and The London, School of Medicine and Dentistry, Queen Mary University of London, London, United Kingdom, 3Centre for Experimental Medicine and Rheumatology, William Harvey Research Institute, Queen Mary University of London, London, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: B Cell Biology and Targets in Autoimmune Disease Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: We previously showed that up to 40% of RA synovial recombinant monoclonal antibodies (RA-rmAbs) generated from germinal center-like structure (GC-LS+) RA synovium recognize citrullinated antigens contained in neutrophils extracellular traps (NETs) (1). The cellular source of other potential autoantigens targeted by the majority of locally differentiated B cells remains undefined. Recently, RA-fibroblast-like synoviocytes (RA-FLS) have been implicated in the release of citrullinated antigens (2, 3). However, whether these cells are targeted by RA-rmAbs is still unknown. Here, we aimed to define i) the RA-rmAbs immunoreactivity towards RA-FLS and ii) identify potential stromal-derived autoantigens.

Methods: 67 RA-rmAbs were generated from single CD19+ B cells FACS-sorted from fresh synovial cell suspensions following IgVH+Vλ genes cloning (1). RA-rmAbs were tested by means of i) cell-based immunofluorescence assays with FLS of RA patients and controls (osteoarthritis (OA)-FLS and RA-dermal fibroblast (RA-DF)), ii) co-localization with stromal specific markers and iii) immunoenzymatic tests with co-localizing antigens. Control rmAbs were also used (Sjögren’s syndrome/healthy donor-IgG rmAbs).

Results: Immunofluorescence on RA-FLS demonstrated reactivity of 22.4% of RA-rmAbs (15/67 rmAbs) towards FLS. Only 4 rmAbs out of 15 were binding both FLS and NETs components. For some RA-rmAbs this reactivity was not specific to RA-FLS since it was also observed for OA-FLS (3% rmAbs). Interestingly, strong co-localization was observed with calreticulin (CRT) which has been shown to bind the RA shared-epitope (SE) ligand and to increase the signalling pathway activated by the SE ligand in its citrullinated form (3). When tested
in ELISA for native vs cit-CRT, 20% (14/67 rmAbs) of the FLS-reactive RA clones showed binding to CRT with 6 out of 14 RA-rmAbs displaying increased immunoreactivity towards cit-CRT. Controls rmAbs showed no reactivity to either FLS or CRT. RA-rmAbs binding to CRT was further confirmed in western blot immunoassays.

**Conclusion:** Here, we provide novel evidence that a subset of locally differentiated B cells within RA synovial GC-LS can react towards RA-FLS derived antigens. Preliminary data suggest that part of this reactivity is directed towards CRT. Identification of immunodominant epitopes within CRT is under investigations.

**References:**
(1) Corsiero et al, ARD 2015  
(2) Sorice et al, Rheumatology 2016  
(3) Ling et al, AR 2013

**Disclosure:** E. Corsiero, None; L. Jagemann, None; C. Pitzalis, None; M. Bombardieri, None.

**Abstract Number:** 45

**BIIB063, a Potent Anti-CD40 Antagonistic Monoclonal Antibody (MAb): Lessons Learned from an Early Development Program.**

**Cristina Musselli,** Claudia Harper, Linda Burkly, Joan Lane, Chase Chen, Dough Donaldson, Million Arefayene, Karen Smirnakis, Devangi Mehta, Dale Morris and Nathalie Franchimont, Biogen, Cambridge, MA

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Sunday, November 5, 2017  
**Session Title:** B Cell Biology and Targets in Autoimmune Disease Poster  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**
CD40/CD40L is a cornerstone pathway for both innate and adaptive immune responses and a suitable target for autoimmune diseases including Sjogren’s. BIIB063 is a high affinity MAb, engineered to reduce Fc effector function and avoid half antibody formation in vivo (IgG4P). BIIB063 has the potential to inhibit germinal center formation, immunoglobulin class switching, T cell activation and cytokine release with a potent inhibition of inflammation and autoimmunity. The results of the first in human and the GLP-toxicology findings are presented.

**Methods:**
In the single ascending dose (SAD) study, 58 healthy volunteers (HV) subjects were assigned to 8 cohorts. Seven cohorts of 4, 6, or 8 subjects were planned to receive increasing single IV doses of BIIB063 (0.003, 0.03, 0.3, 1, 3, 10, and 20 mg/kg) or placebo. One cohort of 8 subjects was planned to receive a single 150 mg SC dose of BIIB063 or placebo. Staggered dosing was used within each cohort to ensure subject safety. Blood samples were analyzed by ELISA for PK and ADA, and flow cytometry for the PD measure of CD40 receptor occupancy (RO). Safety data, including adverse events (AEs) and laboratory tests, were collected. A 26-Week SC and IV Toxicity Study in Cynomolgus Monkeys with a 16-Week Recovery Period was conducted; animals received 10, 30 or 150 mg/kg BIIB063 twice monthly.

**Results:**
In the SAD study, a total of 29 subjects had been enrolled when the study was voluntarily put on hold due to findings from the ongoing 26-week toxicology study where 4 unscheduled terminations occurred. A thorough investigation revealed immune complex (IgM-IgG4) deposits in multiple organs of affected animals, consistent with a type 3 hypersensitivity. This reaction occurred in 44% animals irrespective of the dose level and no NOAEL could be established.

In the SAD, BIIB063 serum concentrations for the lowest two doses (0.003–0.03 mg/kg), were below the LLOQ. BIIB063 Cmax and AUCinf ranged from 3.7 to 22 ug/mL and 100 to 1880 hr*ug/mL following doses of 0.3 and 1 mg/kg, respectively. BIIB063 showed nonlinear PKs
and a dose-dependent CD40 RO and RO duration. There was no significant RO of CD40 at dose levels of BIIB063 <0.3 mg/kg, while full CD40 RO was observed at doses of 0.3 and 1 mg/kg. CD40 RO declined within 96 hr for the 0.3mg/kg dose while CD40 RO lasted 8 days for the 1 mg/kg dose. BIIB063 was generally well tolerated.

No ADA was observed in the 0.003-0.03 mg/kg cohorts where serum concentrations of drug were undetectable, while 67% - 100% subjects had positive ADA in the 0.3-1 mg/Kg cohorts. Interestingly, ADA responses were typically detected several weeks after BIIB063 drug clearance, and in the absence of CD40RO. Hence, the potential impact of ADA on PK and PD was undeterminable.

Conclusion:

BIIB063 administered to HV exhibited a PK profile consistent with an IgG4 molecule. Target engagement as measured by CD40 RO was clearly demonstrated and its duration was dose dependent. ADA response was present in the higher doses cohorts in the SAD. The preclinical toxicology findings and the high immunogenicity of BIIB063 led to the voluntary discontinuation of the trial.

Disclosure: C. Musselli, Biogen Idec, 1, Biogen Idec, 3; C. Harper, Biogen Idec, 3, Biogen Idec, 1; L. Burkly, Biogen Idec, 3; J. Lane, Biogen Idec, 3, Biogen Idec, 1; C. Chen, Biogen Idec, 3, Biogen Idec, 1; D. Donaldson, Biogen Idec, 1, Biogen Idec, 3; M. Arefayene, Biogen Idec, 1, Biogen Idec, 1; K. Smirnakis, Biogen Idec, 1, Biogen Idec, 3; D. Mehta, Biogen Idec, 1, Biogen Idec, 3; D. Morris, Biogen Idec, 1, Biogen Idec, 3; N. Franchimont, Biogen Idec, 3, Biogen Idec, 1.


Abstract Number: 46

Secondary Light Chain Editing and Allelic Inclusion in Antibody Secreting Cells from the Minor Salivary Gland

Kristi A. Koelsch1, Kenneth Smith2, Astrid Rasmussen3, C. Erick Kaufman4, David M. Lewis5, Lida Radfar6, Christopher J Lessard2, Biji T Kurien2, Judith A. James3, Kathy L. Sivils3, A. Darise Farris7 and R. Hal Scofield8, 1Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 2Arthritis and Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, 3Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 4Medicine, University of Oklahoma Health Sciences Center, Oklahoma City, OK, 5Department of Oral Pathology, University of Oklahoma College of Dentistry, Oklahoma City, OK, 6Department of Oral Diagnosis and Radiology, University of Oklahoma College of Dentistry, Oklahoma City, OK, 7Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 8Oklahoma Medical Research Foundation, Oklahoma City, OK

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: B Cell Biology and Targets in Autoimmune Disease Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Heavy and light chain gene usage and mutational analyses of the Ig variable regions (V-regions) enable the identification of gene usage within B cell populations. Within the context of antibody secreting cells (ASC) isolated from the minor salivary glands of Sjogren's syndrome (SS) patients it may give clues to the loss of tolerance that leads to the genesis of autoreactive cells described in these patients.

Methods:

Fourteen subjects were included in this study. Each had symptomatic dry eyes and mouth; 8 subjects met American/European Consensus Group (AECG) primary SS criteria and 1 subject also met the American College of Rheumatology criteria for SLE. Six subjects that did not meet the SS classification criteria (DNMC) served as sicca controls. Labial salivary glands were collected, ASCs were isolated and single-cell sorted using a new method that allows for probing of both kappa and lambda light chains within the same single cells in rare populations. Cells were sequenced and analyzed for V-region gene usage.

Results:
We identified a total of 83 unique heavy/light chain pairs from the SS patient group and 21 from the DNMC control group. No significant differences in the VH- or JH- gene-family usage were noted between SS or DNMC. The Ig VH family usage in both the SS patient and DNMC control groups was dominated by the VH3 and VH4 gene families and JH4 was the predominant JH gene family used by both groups. The light chain analysis revealed that kappa variable region (Vk) gene families, Vk1 and Vk3, were the most frequently used in both groups. The kappa joining (Jk) gene analysis revealed that J-genes, Jk1 through Jk5, were represented in sequences from both groups. The light chain sequence analyses also revealed the incidence of secondary light chain editing in the sequences from 2 pSS subjects and one DNMC, indicated by clonally related heavy chains with different light chain usage. These light chain sequences were unique and not found in any of the other pairs utilized by any of the other subjects. In addition, allelic inclusion, or 1 heavy chain with 2 distinct light chains within the same cell, was identified in 2 instances from the ASCs isolated from one pSS patient. In each case, both a kappa and a lambda light chain sequence were amplified from the same cell.

Conclusion:

In summary, we have developed an improved method for the isolation, characterization and mAb production for rare B cells populations, which has provided data suggesting ASC light chain editing and allelic inclusion not previously reported in SS.

Disclosure: K. A. Koelsch, None; K. Smith, None; A. Rasmussen, None; C. E. Kaufman, None; D. M. Lewis, None; L. Radfar, None; C. J. Lessard, None; B. T. Kurien, None; J. A. James, None; K. L. Sivils, None; A. D. Farris, None; R. H. Scofield, None.

Claudin-11 Regulates Bone Homeostasis Via Bidirectional EphB4-EphrinB2 Signaling

Jong Min Baek1, Chong Hyuk Chung2, Ju-Young Kim3, Wan-Hee Yoo4, Yunjung Choi5, Changhoon Lee6 and Myeung Su Lee7, 1Department of Anatomy, School of Medicine, Wonkwang University, Iksan, Korea, Republic of (South), 2Division of Rheumatology, Department of Internal Medicine, Wonkwang University Hospital, Wonkwang University Hospital, IKSAN, Korea, Republic of (South), 3Imaging Science-based Lung and Bone Diseases Research Center, Wonkwang University, IKSAN, Korea, Republic of (South), 4Division of Rheumatology, Department of Internal Medicine, Chonbuk National University Hospital, Jeonju, Korea, Republic of (South), 5Division of Rheumatology, Department of Internal Medicine, Chonbuk National University Hospital, Jeonju, Korea, Republic of (South), 6Division of Rheumatology, Department of Internal Medicine, Wonkwang University Hospital, Iksan, Korea, Republic of (South), 7Division of Rheumatology, Department of Internal Medicine, Wonkwang University Hospital, Iksan, Chonbuk, Korea, Republic of (South)

First publication: September 18, 2017

Claudins (Cldns) are well-established components of tight junctions (TJs) that play a pivotal role in the modulation of paracellular permeability. Several studies have explored the physiologic aspects of Cldn family members in bone metabolism. However, the effect of Cldn11, a major component of central nervous system myelin, on bone homeostasis has not been reported. This study was performed to identify the effects of Cldn on bone metabolism via regulation of osteoclast and osteoblast differentiation and their function

Methods:

We performed various in vitro and in vivo studies using gain- and loss-of-function of Cldn11 that is belong to the Cldn group. Osteoclast formation from bone marrow cells (BMC) and Osteoblast formation was evaluated in specific condition with over-expression or down-regulation of Cldn11. The expression of osteoclast associated gene and osteoblast related gene mRNA were assessed by RT-PCR. The levels of c-fos and NFATc1 protein were assessed by western blot. Also the mitogen-activated protein (MAPK)s and important signal pathways were measured using Western blot analysis. Osteoclast function was evaluated with resorption pit assay and osteoblastic effects of Cldn11 was evaluated with new bone formation of mouse calvaria. With LPS and co-treated Recombinant protein of Cldn11 on mouse calvaria, we evaluated the effects of Cldn11 on LPS induced bone loss by using histologic analysis.

Results:
We found that Cldn11 played a negative role in receptor activator of nuclear factor kappa B ligand dependent osteoclast (OC) differentiation by downregulating the phosphorylated form of extracellular signal-regulated kinase (ERK), Bruton’s tyrosine kinase, and phospholipase C gamma 2, in turn impeding c-Fos and nuclear factor of activated T cells c1 expression. Osteoblast (OB) differentiation by positive feedback of Cldn11 was achieved through the phosphorylation of Smad1/5/8, ERK, and c-Jun amino-terminal kinase. Importantly, this Cldn11-dependent dual event arose from targeting EphrinB2 ligand reverse signaling into OC and EphB4 receptor forward signaling into OB. In agreement with these in vitro effects, subcutaneous injection of Cldn11 recombinant protein exerted similar effects on local calvarial regions in mice.

Conclusion:

These findings suggest that Cldn11 is a novel regulator in bone homeostasis.

Disclosure: J. M. Baek, None; C. H. Chung, None; J. Y. Kim, None; W. H. Yoo, None; Y. Choi, None; C. Lee, None; M. S. Lee, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/claudin-11-regulates-bone-homeostasis-via-bidirectional-ephb4-ephrinb2-signaling

Abstract Number: 48

Modulation of Subchondral Bone Turnover Is Associated with Alteration of Cartilage Tissue Quality

Cedric Lavet, Isabelle Badoud and Patrick Ammann, Division of Bone Diseases, Geneva, Switzerland

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Biology and Pathology of Bone and Joint Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Osteochondral unit is a bio composite responsible for an optimal distribution of load during movements and axial compression of a joint. Any alteration of tissue mechanical properties (cartilage or bone) could interfere with an optimal function. One obvious question is to understand whether alteration of subchondral bone turnover (i.e. quality) could affect cartilage quality and thus represent a potential risk of OA development.

Methods:

To verify this hypothesis, 15 adult female rats where ovariectomized (OVX, n=10) or SHAM operated (n=5). One group of OVX rats was treated for 8 weeks with pamidronate (APD) at dose of 0.6 mg/kg, 5 days/mo SC to inhibit the increase of bone turnover, and the other two groups received the solvent. At the end of the study, distal femurs were harvested. Bio-indentations (CSM, Switzerland) were performed at the level of the medial condyle at three different area submitted physiologically to different mechanical loading. Elastic modulus (MPa) and indentation depth (mM) were recorded, using different load from 0.05 to 8 mN. Indentation depths were located in the upper third of the hyaline cartilage. Cartilage thickness was evaluated by contrast enhanced computed tomography with ionic contrast agent using (Hexabrix®) at the site of indentation as well as subchondral bone micro architecture. Blood and urine were collected to evaluate bone turnover using measurement of osteocalcin and deoxypyridinoline excretion. Values are mean±SEM; significance of differences was obtained using an ANOVA.

Results:

<table>
<thead>
<tr>
<th></th>
<th>SHAM (n=5)</th>
<th>O VX (n=5)</th>
<th>O VX+APD (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyridinolines/Creat</td>
<td>23.81 ± 3.03°</td>
<td>68.63 ± 11.02*</td>
<td>26.8 ± 2.83°</td>
</tr>
<tr>
<td>BV/T  V (%)</td>
<td>48.0 ± 3.0°</td>
<td>35.0 ± 1.7*</td>
<td>48.7 ± 3.4°</td>
</tr>
<tr>
<td>Tb.Th (mm)</td>
<td>0.074 ± 0.003°</td>
<td>0.063 ± 0.002*</td>
<td>0.079 ± 0.004°</td>
</tr>
<tr>
<td>Modulus (MPa)</td>
<td>2.72 ± 0.22°</td>
<td>1.58 ± 0.14*</td>
<td>3.19 ± 0.32°</td>
</tr>
<tr>
<td>Indentation Depth (mM)</td>
<td>15.87 ± 1.12°</td>
<td>23.7 ± 1.22*</td>
<td>12.5 ± 0.88**</td>
</tr>
</tbody>
</table>

\*p < 0.05
\*\*p < 0.01
An increment of markers of bone turnover was observed in OVX rats and was fully prevented by APD administration. OVX resulted in alteration of bone microarchitecture of the subchondral bone as demonstrated by a reduce bone volume (BV/TV) and trabecular thickness (Tb.Th); all these alterations were fully prevented by APD administration. Hyaline and mineralized cartilage thicknesses were not affected by OVX nor by APD treatments. OVX was associated with alteration of cartilage tissue quality as indicated by a decreased of modulus and increased indentation depth. All these alterations were fully prevented by APD treatment preventing the increment in subchondral bone turnover.

Conclusion:
All together these results demonstrate that in rat, an increment of subchondral bone turnover and/or alteration of the local micro architecture is associated with degradation of the cartilage tissue quality independently of the estrogen deficiency. These results underline the crucial role plays by subchondral bone as “regulator” of cartilage quality.

Disclosure: C. Lavet, None; I. Badoud, None; P. Ammann, None.
BmMSCs lacking GRK3 regulation have impaired S1PR1 internalization.

**Conclusion:** Our work suggests GRK3 regulates S1PR on BmMSCs and lack of such regulation induces increased cellular proliferation and osteogenic differentiation, indicating GRK3 may serve as a potential therapeutic target to alter BmMSC functionality.

**Disclosure:** J. M. Brozowski, None; R. G. Timoshchenko, None; D. S. Serafin, None; J. Koontz, None; B. Allyn, None; A. M. Eudy, None; T. Harris, None; D. Abraham, None; C. T. Rubin, None; J. Rubin, None; N. Allbritton, None; M. J. Billard, None; T. K. Tarrant, None.


**Abstract Number: 50**

**Quality Controls Monitoring As Indicator of Stability in Bone and Cartilage Turnover Markers for Clinical Trials**

Yannick Lhoste, Vanessa Di Cataldo, Philippe Vergnaud and Tanja Schubert, Bioclinica Lab, LYON, France

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Biology and Pathology of Bone and Joint Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Protein biomarkers are widely used in clinical studies to assess drug efficacy, such as bone and cartilage turnover markers in osteoarthritis or rheumatoid arthritis clinical studies. In most of these clinical studies it is highly recommended to analyze as many visits, including all follow-up visits, at the same time, often requiring sample storage below -70°C for an extended period of time. Thus, determination of long-term stability of the biomarkers upon storage is critical.

Typically, long-term stability is measured in samples with a baseline assessment before storage in order to determine the nominal value. Subsequently, samples are assessed in the same condition at frequent intervals, covering different storage periods. However, this method requires numerous samples with a large volume, which is often challenging to obtain. Thus, we suggest an alternative approach by monitoring in-house quality control (QCs) as indication of analyte stability.

**Methods:**

We investigated the long-term stability of the most widely analyzed serum biomarkers in musculoskeletal related clinical trials: carboxyterminal of type 1 collagen (S-CTX-I), osteocalcin (S-OC), aminoterminal propeptide of type 1 collagen (S-PINP), and metalloproteinases 3 and 9 (S-Total-MMP-3 and S-MMP-9). At least 12 serum samples were assayed at baseline and re-assayed after a storage period. Subsequent results were compared to baseline.

Additionally, we monitored the performance of our in-house QC samples for the same biomarkers and compared the data with the stability data previously determined. Urinary carboxyterminal telopeptide of type 2 collagen (U-CTX-II) long-term stability was assessed in samples after QC monitoring to validate our approach. QC monitoring was also performed for serum cartilage oligomeric matrix protein (S-COMP), another cartilage turnover marker.

An analyte is considered stable when the coefficient of variation (CV) and the accuracy (variation from target value) of the QC results are inferior to ± 15%.

**Results:**
Conclusion:

Assay analysis of protein biomarkers for clinical trials require a very stringent and robust quality process, which is based on the use of independent, endogenous QC samples throughout the complete duration of the clinical trial. We proved that long-term stability for biomarkers can be assessed by monitoring in-house QCs as confirmed by the U-CTX-II results.

Thus, based on the data obtained during QC monitoring for S-COMP we suggest that this marker is stable up to 19 months below -70°C. However, these data should be confirmed by a standard validation stability test.

Disclosure: Y. Lhoste, Bioclinica Lab, 3; V. Di Cataldo, Bioclinica Lab, 3; P. Vergnaud, Bioclinica Lab, 3; T. Schubert, Bioclinica Lab, 3.

Irisin Ameliorates Infrapatellar Adiposity in Knee Osteoarthritis Pathogenesis By Orchestrating Adipokine Signaling

Feng-Sheng Wang¹, Yi-Chih Sun¹ and Jih-Yang Ko², ¹Core Facility for Phenomics & Diagnostics, Department of Medical Research, Core Facility for Phenomics & Diagnostics, Department of Medical Research, Kaohsiung Chang Gung Memorial Hospital, Taiwan, Kaohsiung, Taiwan, ²Department of Orthopedic Surgery, Department of Orthopedic Surgery, Kaohsiung Chang Gung Memorial Hospital, Taiwan, Kaohsiung, Taiwan
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Biology and Pathology of Bone and Joint Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Aberrant infrapatellar fat metabolism is a prominent feature that exacerbates inflammation and fibrosis relative to joint deterioration during osteoarthritis (OA). Irisin, a secretory subunit of fibronectin type III domain containing 5 (FNDC5), is found to regulate adipose morphogenesis, energy expenditure, skeletal muscle, and bone metabolism. This study is undertaken to investigate the association of Irisin expression and end-stage knee OA and verify whether Irisin signaling changed infrapatellar fat remodeling and joint homeostasis in the progression of OA.

Methods: Injured articular specimens were harvested from 19 patients with end-stage knee OA and 11 patients with femoral neck fracture (non-OA) who required total hip arthroplasty. Knee joints in mice that overexpressed FNDC5 were subjected to suprapatellar injection of collagenase to provoke OA. Expressions of Irisin, adipokines, and MMPs were probed with RT-quantitative PCR. Infrapatellar adiposity, cartilage damage, and synovial integrity were verified with histomorphometry and immunohistochemistry. Irisin recombinant protein was produced for the treatment of collagenase-affected knees.

Results: Infrapatellar adipose and synovial tissues instead of articular cartilage exhibited distinguishable Irisin immunostaining. Injured specimens from the end-stage OA group showed 40% decline in Irisin expression compared with those in the non-OA group. In vitro, a gain of Irisin function enabled synovial fibroblasts but not chondrocytes to display minor responses to the IL-1β provocation of MMP3 and MMP9 expression. Of note, Irisin signaling enhancement resulted in 85% decrease in adipogenic gene expression and 65% reduction in adipocyte formation of mesenchymal progenitor cells. In collagenase-mediated knee OA pathogenesis, the FNDC5-overexpressing mice showed moderate responses to infrapatellar adipose hypertrophy concomitant with slight synovial hypercellularity and membrane hyperplasia within the affected joints. These adipose-regulatory actions warded off the affected knees from cartilage destruction and gait aberrance. Likewise, administration of Irisin recombinant protein mitigated the development of infrapatellar adiposity and synovitis, a remedial effect that slowed down the progression of articular cartilage erosion and walking profile irregularity. Affected joints and adipocytes responded to the Irisin recombinant protein treatment by reducing the expressions of cartilage-deleterious adipokines IL-6, leptin, and adiponectin through regulating PPARγ function.

Conclusion: Irisin dysfunction is relevant to the occurrence of end-stage knee OA. Irisin signaling protects from excessive adipogenesis of mesenchymal precursor cells and diminishes inflammation and cartilage catabolism actions aggravated by adipocytes and synovial cells. This study sheds an emerging new light on the Irisin signaling stabilization of infrapatellar adipose homeostasis and the prospective of the therapeutic potential of Irisin recombinant protein for deescalating knee OA development.

Disclosure: F. S. Wang, None; Y. C. Sun, None; J. Y. Ko, None.

Abstract Number: 52

In Vivo Effect of Opticin Deficiency in a Surgically Induced Mouse Model of Osteoarthritis

Aina Farran¹, Gladys Valverde-Franco², Laura Tio³, Bertrand Lussier⁴, Hassan Fahna², Jean-Pierre Pelletier², Paul Bishop⁵, Jordi Monfort⁶ and Johanne Martel-Pelletier², ¹Osteoarthritis Research Unit (CRCHUM), Montreal; Inflammation and Cartilage Cellular...
Opticin (OPTC) is a small leucine-rich proteoglycan (SLRP) that has been previously demonstrated to be produced and degraded in osteoarthritic (OA) human cartilage. Here, we further investigated the in vivo effect of OPTC deficiency in OA cartilage.

Methods: OA was induced in 10-week-old Optc−/− (knock-out) and Optc+/+ (wild type) mice by destabilization of the medial meniscus (DMM). Ten weeks post-surgery, cartilage was processed for histology, and immunohistochemistry. SLRP expression was determined in non-operated mouse cartilage at day 3 (P03) and 10 weeks of age. Collagen ultrastructure was analyzed by transmission electron microscopy in 10-week-old non-operated mouse cartilage.

Results: OA Optc−/− mice demonstrated significant protection against cartilage degradation. Data revealed that in non-operated Optc−/− mouse cartilage, the SLRPs lumican and epiphycan were significantly up-regulated at P03 (p≤0.010) and 10 weeks old (p≤0.007), and fibromodulin down-regulated at 10 weeks of age (p≤0.001). Immunohistochemistry of OA mice showed a similar pattern. In OA Optc−/− mouse cartilage, markers of cartilage degradation and complement factors C5b-9 and CCL2 were all down-regulated (p≤0.050). In Optc−/− mouse cartilage, collagen fibers were thinner and better organized (p=0.038) than in OA Optc+/+ mouse cartilage.

Conclusion: This work demonstrates a protective effect of OPTC deficiency during OA, resulting from an overexpression of lumican and epiphycan, known to bind and protect collagen fibers, and a decrease in fibromodulin, contributing to a reduction in the complement activation/inflammatory process. This work suggests that the evaluation of the composition of the different SLRPs in OA cartilage could be applied as a new tool for OA prognosis classification.

Disclosure: A. Farran, None; G. Valverde-Franco, None; L. Tio, None; B. Lussier, None; H. Fahmi, None; J. P. Pelletier, None; P. Bishop, None; J. Monfort, None; J. Martel-Pelletier, None.

Abstract Number: 53

Poly-γ-Glutamic Acid Inhibits RANKL- Induced Osteoclast Differentiation and Prevents Bone Destruction in Rheumatoid Arthritis: Human and CIA Mouse Model

Bitnara Lee1, Jong-Dae Ji2 and Tae-Hwan Kim1, 1Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), 2Rheumatology, Korea University Hospital, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Biology and Pathology of Bone and Joint Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM
Rheumatoid arthritis (RA) is an inflammatory disease that is characterized by chronic inflammation and bone destruction. Osteoclasts, which are bone-resorbing cells, are generally known to play a pivotal role in the pathogenesis of bone destruction in RA. Poly-γ-glutamic acid (γ-PGA), a natural polymer derived from Bacillus subtilis, has anti-inflammatory activity. It is mediated by suppressing differentiation of Th17 cells in asthma model. However, the effects of γ-PGA in RA osteoclast differentiation is unclear. Therefore, we evaluated whether γ-PGA prevents inflammation and joint damage of RA by regulating osteoclast differentiation in human and mice.

Methods:
We tested the inhibitory effect of γ-PGA on osteoclastogenesis in healthy human peripheral blood monocytes, RA synovial fluid macrophages, and mouse bone-marrow-derived macrophages (BMMs). The osteoclastogenesis was assessed by generation of TRAP-positive multinucleated cells and actin ring formation. We analyzed the expressions of essential genes and proteins for osteoclast differentiation by real-time PCR and western blot analysis. We observed whether treatment of γ-PGA efficiently reduces osteoclast formation and bone destruction in animal model of rheumatoid arthritis (collagen-induced arthritis [CIA] in DBA/1J mice).

Results:
Firstly, we showed that γ-PGA strongly inhibits osteoclast differentiation in normal PBMC-derived osteoclast precursors and RA synovial fluid macrophages. γ-PGA suppressed RANK mRNA and protein level by down-regulating of M-CSF receptor protein, which is required for RANK expression. Furthermore, we found that in vitro, treatment with γ-PGA suppressed osteoclastogenesis in wild-type (WT) mice, but the inhibition mechanism of γ-PGA was not TLR4-dependent since γ-PGA still inhibited osteoclast formation in TLR4-deficient mouse BMMs. Reflecting on these in vitro effects, oral administration of γ-PGA markedly reduced bone destruction in CIA mice. Histological analysis confirmed that γ-PGA prevented bone destruction and osteoclast formation in the bone tissues. In addition, treatment with γ-PGA also suppressed the expressions of IL-1β and TNF-α.

Conclusion:
Our results show that γ-PGA markedly suppresses osteoclastogenesis in human and mice. γ-PGA also reduces bone destruction, osteoclast formation, and inflammatory cytokines in animal model of RA. Thus, these data suggest that γ-PGA can be a good candidate for the therapeutic application of joint destruction in RA.

Disclosure: B. Lee, None; J. D. Ji, None; T. H. Kim, None.


Abstract Number: 54

Maintaining Angiogenesis Prevents Glucocorticoid Induced Osteonecrosis

Alanna Dubrovsky¹, Wei Yao¹, Geetha Mohan¹, Mie Jin Lim¹, Yu-An Evan Lay¹, Donald Kimmel² and Nancy E. Lane³,⁴,⁵,⁶,⁷,⁸, ¹UC Davis Center for Musculoskeletal Health, Sacramento, CA, ²Creighton University School of Medicine Osteoporosis Research Center, Omaha, NE, ³Center for Musculoskeletal Health, University of California, Davis School of Medicine, Sacramento, CA, ⁴Internal Medicine, Center for Musculoskeletal Health, UC Davis School of Medicine, Sacramento, CA, ⁵UC Davis Medical Center, Sacramento, CA, ⁶Center for Musculoskeletal Health, Univ of California at Davis, Sacramento, CA, ⁷Medicine, U.C. Davis, Sacramento, CA, ⁸UCDMC, Sacramento, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Biology and Pathology of Bone and Joint Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Atraumatic osteonecrosis (ON) results from reduced bone vascularity. Glucocorticoids (GC) are a major risk factor for ON, as GCs reduce vascular endothelial growth factor, vascular density, and bone mass [Mohan et al CTI 2017]. Mice treated with GCs and either PTH or LLP2A-Ale, a bone targeted therapy that directs mesenchymal stem cells to bone surfaces, showed significantly less GC-induced bone mass changes. The aim of this study was to determine if PTH or LLP2A-Ale co-treatment could prevent or reduce the severity of GC-induced ON.

Methods: Seven-week-old male BALB/c mice were randomized into placebo (PL), PL+GC (4 mg/L dexamethasone in drinking water),
Methods: Seven-week-old male BALB/c mice were randomized into placebo (PL), PL+GC (4 mg/L dexamethasone in drinking water), GC+250 µg/kg or GC+500 µg/kg LLP2A-Ale (subcutaneous (SC), 1X/2 wks), or GC+40 µg/kg PTH (hPTH(1-34), 5x/wk, SC) (n=8 for PL and 16 for all GC groups). Mice were sacrificed on Day 30 or Day 45. Both distal femurs (DF) from each mouse were decalcified, and coronal sections were made and stained with H&E. ON was identified in the DF epiphysis (DFE) using modified criteria [Yang et al., JOR, 2009] (presence of empty osteocyte lacunae, nuclear pyknosis, ghost osteocytes in bone trabeculae, bone marrow/stromal necrosis, > 30% fat in marrow, and fibrin thrombi in blood vessels). ON was diagnosed when three or more of the above features were seen, by three independent, blinded observers, with >80% agreement. Immunohistochemical staining for blood vessels was performed on the DFE using CD31 and endomucin antibodies.

Results: PL+GC mice had 15-20% lower body weight than PL (p<0.05). At Day 30, ON prevalence was 18%, 6%, 0% and 6%, respectively, in PL+GC, GC+LLP2A-Ale (250), GC+LLP2A-Ale (500) and GC+PTH groups. At Day 45, ON prevalence was 81%, 25%, 18% and 12%, respectively, in PL+GC, GC+LLP2A-Ale (250), GC+LLP2A-Ale (500), and GC+PTH. Blood vessels (anti-CD31/endomucin) appeared more intact in GC+LLP2A-Ale and GC+PTH groups than in PL+GC at both times (p<0.05). At Day 45, both GC+LLP2A-Ale and GC+PTH groups had 50% greater sinusoid density, and 50% lower adipocyte density at the DFE compared to PL+GC alone (p<0.05).

Conclusion: Co-treatment of murine GC-induced ON with PTH or LLP2A-Ale reduced the prevalence of ON after 45 days. Additional studies to ascertain the mechanism by which these agents prevent GC-induced ON are warranted.

Disclosure: A. Dubrovsky, None; W. Yao, LLP2A-Ale, 4; G. Mohan, None; M. J. Lim, None; Y. A. E. Lay, None; D. Kimmel, None; N. E. Lane, LLP2A-Ale, 4.

Abstract Number: 55

Nrf2 Inhibits Apoptosis and Suppresses Oxidative Stress By Activating NOX4/ERK1/2/ELK1 Signaling Axis in Human Chondrocytes

Mohammad N. Khan1, Imran Ahmad1, Mohammad Y Ansari2 and Tariq M Haqqi1, 1Anatomy & Neurobiology, Northeast Ohio Medical University, Rootstown, OH, 2Anatomy & Neurobiology, Northeast Ohio Medical University, Roostown, OH

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Biology and Pathology of Bone and Joint Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Nrf2 is a redox sensitive transcription factor that regulates the expression of phase II antioxidant enzymes and cytoprotective genes and is crucial for maintaining the cartilage integrity. However, mechanisms underlying the cartilage/chondroprotective effects of Nrf2 remains largely unknown. Here, we examined the critical role of Nrf2 in protecting human OA chondrocytes against oxidative damage and induction of apoptosis under pathological conditions.
Methods:

Deidentified and discarded OA cartilage was obtained at the time of total joint arthroplasty and chondrocytes were prepared by enzymatic digestion. qRT-PCR and immunoblotting with validated antibodies were used to assess the gene and protein expression respectively. Nrf2 activation was determined by luciferase reporter assay. Chondrocytes were transfected with Nrf2 overexpression plasmid, ARE reporter vector or siRNAs using nucleofection. ROS levels were measured by H$_2$DCF-DA staining. Apoptosis was measured by TUNEL assay. Agarose gel electrophoresis was used to analyze DNA fragmentation.

Results:

Expression of Nrf2 and its downstream targets HO-1, NQO1, and SOD2 was significantly higher in damaged OA cartilage compared with the smooth cartilage of the same patient. A luciferase reporter assay demonstrated that IL-1β-stimulation was a potent inducer of Nrf2 activity in OA chondrocytes. Interestingly, pretreatment of OA chondrocytes with antioxidants significantly inhibited the IL-1β-mediated activation of Nrf2/ARE signaling indicating that the activity was due to oxidative stress. Over-expression of Nrf2 in OA chondrocytes significantly suppressed the IL-1β-mediated generation of ROS, production of H$_2$O$_2$ and expression of NOX4 whereas Nrf2 knockdown significantly enhanced the basal as well as induced levels of ROS and expression of NOX4. OA chondrocytes with overexpression of Nrf2 showed inhibition of both the extrinsic and intrinsic apoptotic pathways as IL-1β-induced DNA fragmentation, activation of Caspase-3, cleavage of PARP, cleavage of Caspase-8,-9, release of cytochrome-c, suppression of mitochondrial ROS production and mitochondrial dysfunction were not observed. Further, enhanced expression of Nrf2 stimulated the expression of anti-apoptotic proteins-Bcl2, Bcl-xl and Mcl-1 and significantly suppressed the expression of pro-apoptotic proteins-Bax, Bad and Bid-in IL-1β stimulated OA chondrocytes. Nrf2 overexpression enhanced the phosphorylation of ERK1/2 and its downstream target proteins-Elk-1, P70S6K and P90RSK in OA chondrocytes, whereas pharmacological inhibition of ERK1/2 activation enhanced the ROS generation and increased apoptosis in IL-1β-stimulated OA chondrocytes.

Conclusion: Taken together, these results show that Nrf2 is a stress response protein in OA chondrocytes with an anti-apoptotic function. IL-1β-induced stress causes activation of Nrf2 which activates the ERK1/2/ELK1-P70S6K-P90RSK signaling pathway to inhibit apoptosis of OA chondrocytes. These activities of Nrf2 make it a promising candidate for the development of novel therapies for the management of OA.

Disclosure: M. N. Khan, None; I. Ahmad, None; M. Y. Ansari, None; T. M. Haqqi, None.


Abstract Number: 56

Baicalein, a Plant-Derived Small Molecule, Activate Nrf2/Autophagy Signaling Axis Via MEK1/2-ERK1/2-Elk1 Pathway to Suppress the Expression of IL-6 in Human Osteoarthritis Chondrocytes

Mohammad N. Khan$^1$, Imran Ahmad$^1$, Mohammad Y. Ansari$^2$ and Tariq M Haqqi$^1$, $^1$Anatomy & Neurobiology, Northeast Ohio Medical University, Rootstown, OH, $^2$Anatomy & Neurobiology, Northeast Ohio Medical University, Roostown, OH

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Biology and Pathology of Bone and Joint Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Inflammation is an important component of osteoarthritis (OA) pathogenesis. IL-6 is implicated in OA pathogenesis as it suppresses anabolic factors and upregulate the expression of catabolic proteins. Here, we used an in vitro model of inflammation in OA to investigate the potential of Baicalein, a natural flavonoid found in root extract of Scutellaria baicalensis, to suppress the expression of IL-6 and determined the molecular mechanism by investigating the role of Nrf2 and autophagy activation in human OA chondrocytes.

Methods: Primary human OA chondrocytes were prepared by enzymatic digestion of deidentified and discarded cartilage from donors with OA who underwent total knee arthroplasty. Autophagy activation was investigated by immunoblotting for LC3-I and LC3-II, ATG5, autophagic flux and immunofluorescence staining for LC3 puncta. Expression and activation of Nrf2 was determined by immunoblotting and by a luciferase reporter assay, respectively. mRNA and protein expression of Nrf2 regulated genes HO-1, NQO1, SOD2 was studied by qPCR and immunoblotting, respectively. Total protein levels and activation of ERK1/2 and its upstream and downstream signaling molecules were assayed by immunoblotting. For molecular docking studies using the Glide tool in Schrödinger Maestro suite, the crystal structure of...
Keap1 protein in complex with a small chemical compound K67 (PDB CODE: 4ZY3) was extracted from the Protein Data Bank and used as docking structure template.

Results:

OA chondrocytes showed high levels of IL-6 expression upon stimulation with IL-1β. However, pre-treatment of OA chondrocytes with Baicalein, in a dose dependent manner, abolished the IL-1β-induced upregulation of IL-6 expression. Baicalein induced macro-autophagy in OA chondrocytes in vitro as indicated by significantly (p<0.05) increased expression of LC3, ATG5, ATG3, enhanced autophagy flux and increased number of autophagic puncta in OA chondrocytes. Baicalein treated OA chondrocytes also showed enhanced activity of Nrf2/ARE as revealed by a Nrf2/ARE reporter assay. Molecular docking studies indicated that Baicalein activates Nrf2 by disrupting the Keap-1/Nrf-2 interaction by blocking the Nrf-2 binding site in the Keap-1 protein. Additionally, OA chondrocytes treated with Baicalein, and in a dose dependent manner, showed enhanced expression, both at mRNA and protein levels, of Nrf2 target genes HO-1, NQO1, and SOD2. We next determined the molecular events involved in Baicalein mediated activation of Nrf2 and it was found that treatment of OA chondrocytes with Baicalein activated MEK1/2-ERK1/2-Elk-1 signaling in a time dependent manner. Inhibition of ERK1/2 activation or inhibition of autophagy using small molecules or siRNA mediated depletion of target genes expression abolished the protective effects of Baicalein in OA chondrocytes under pathological conditions.

Conclusion: The present study indicates that Baicalein act, at least in part, by activating Nrf2/autophagy axis and increased expression of HO-1, NQO1 and SOD2 in OA chondrocytes. This property indicates that Baicalein could be developed as an effective adjunct therapy for the suppression of OA pathogenesis.

Supported by USPHS/NIH grants

Disclosure: M. N. Khan, None; I. Ahmad, None; M. Y. Ansari, None; T. M. Haqqi, None.


Abstract Number: 57

Accelerated Development of Aging-Associated and Instability-Induced Osteoarthritis in 12/15-Lipoxygenase Deficient Mice

Lauris Habouri1, Yassine Ouhaddi1, Gadid Guedi1, Jean-Pierre Pelletier2, Johanne Martel-Pelletier2, mohamed benderdour1 and Hassan Fahmi2, 1Medicine, CRCHUM, Montreal, QC, Canada, 2Osteoarthritis Research Unit, University of Montreal Hospital Research Centre (CRCHUM), Montreal, QC, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Biology and Pathology of Bone and Joint Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
12/15-Lipoxygenase (12/15-LOX) catalyzes the generation of various anti-inflammatory lipid mediators, and has been implicated in several inflammatory and degenerative diseases. However, there is currently no evidence that 12/15-LOX has a role in osteoarthritis (OA). The aim of this study was to investigate the role of 12/15-LOX in the pathogenesis of OA.

Methods:
The development of aging-associated and destabilization of the medial meniscus (DMM)-induced OA were compared in 12/15-LOX-deficient (12/15-LOX-/-) and wild-type (WT) mice. The extent of cartilage damage was evaluated by histology. The expression of OA markers was evaluated by immunohistochemistry and RT-PCR. Cartilage explants were stimulated with IL-1α in the absence or presence of the 12/15-LOX metabolites, 15-HETE, 13-HODE or LXA4, and the levels of MMP-13, NO and PGE2 were determined. The effect of LXA4 on the progression of OA was evaluated in WT mice.

Results:
The expression of 12/15-LOX in cartilage increased during the progression of DMM-induced OA and with aging in WT mice. Cartilage degeneration was more severe in 12/15-LOX-/- mice compared to WT mice in both models of OA, and this was associated with increased
expression of MMP-13, ADAMTS5, iNOS, and mPGES-1. Treatment of cartilage explants with 12/15-LOX metabolites, suppressed IL-1α-induced production of MMP-13, NO and PGE₂, with LXA4 being the most potent. Intra-peritoneal injection of LXA4 reduced the severity of DMM-induced cartilage degradation.

Conclusion:

These data suggest an important role of 12/15-LOX in the pathogenesis of OA. They also suggest that activation of this pathway may provide a novel strategy for prevention and treatment of OA.

Disclosure: L. Habouri, None; Y. Ouhaddi, None; G. Guedi, None; J. P. Pelletier, None; J. Martel-Pelletier, None; M. benderdour, None; H. Fahmi, None.

Abstract Number: 58

Cartilage-like Tissue Generation By 3D-Bioprinting of Induced Pluripotent Stem Cells

Rocío Castro-Viñuelas¹, Alna Forsman², Erdem Karabula³, Erik Romberg³, Camilla Brantsing², Mats Brittberg⁴, Anders Lindahl², Paul Gatenholm³ and Stina Simonsson², ¹Cell Therapy and Regenerative Medicine research group. Rheumatology Division. Institute of Biomedical Research of A Coruña (INIBIC). Dep. of Biomedical Sciences, Medicine and Physiotherapy, University of A Coruña, A Coruña, Spain, ²Institute of Biomedicine at Sahlgrenska Academy, Department of Clinical Chemistry and Transfusion Medicine, University of Gothenburg., Gothenburg, Sweden, ³3D Bioprinting Center, Dept. of Chemistry and Chemical Engineering, Chalmers University of Technology, Gothenburg, Sweden, ⁴Cartilage Repair Unit, University of Gothenburg, Region Halland Orthopaedics, Kungsbacka Hospital, Kungsbacka, Sweden

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Biology and Pathology of Bone and Joint Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Cartilage lesions due to traumatic or pathological conditions slowly grow over the time and may lead to osteoarthritis (OA). As a prospective treatment for such lesions, it has been shown that human-derived induced pluripotent stem cells (iPSCs) can be 3D bioprinted and directed to form cartilage-like tissue (Nguyen et al. 2017). The advantages of using an established iPSC line are unlimited cell source with regeneration capacity and chondrogenic differentiation potential. The aim of this study was to improve the generation of cartilage-like tissue when 3D bioprinting of iPSCs by using molecularly modified nanocelullose/alginate bioink to resemble natural environment found in the tissue.

Methods: In this study the chondrocyte-derived iPSc line “A2B” was used (Borestrom et al. 2014). These cells were bioprinted in combination with a modified bioink composed by nanocellulose and alginate. One week after bioprinting, the constructs were cultured in chondrogenic medium in order to stimulate cell differentiation towards chondrocytes. Cell number and viability was studied. Histological analyses of the 3D printed constructs were performed. Furthermore, expression of pluripotency and chondrogenic specific genes was assessed by Taqman qPCR before and after differentiation.

Results: High viability of the iPSCs inside the constructs was found after bioprinting. 3D printed constructs were positively stained for alcian blue van gieson staining, showing proteoglycans presence inside the prints. Molecular analyses showed high relative expression levels of the pluripotency-related gene Oct4 before initiating the differentiation protocol. Cells inside the constructs express chondrogenic specific genes, such as collagen type 2 and Sox9 after 6 weeks of differentiation. Moreover, 3D printed constructs showed cartilage-resembles (Figure 1).

Conclusion : Modified Nanocelullose/alginate bioink allowed 3D printing of the iPSCs and the in vitro generation of cartilage-like tissue. This approach could be used in the future to model OA disease or to perform screenings of different therapeutic compounds.
Cartilage mimic by 3D bioprinting iPSCs differentiated for 6 weeks in modified bio ink.

Disclosure: R. Castro-Viñuelas, None; A. Forsman, None; E. Karabulut, None; E. Romberg, None; C. Brantsing, None; M. Brittberg, None; A. Lindahl, None; P. Gatenholm, None; S. Simonsson, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/cartilage-like-tissue-generation-by-3d-bioprinting-of-induced-pluripotent-stem-cells

Abstract Number: 59

Abaloparatide, a Novel PTHrP Analog, Increased Bone Mass and Density at Cortical and Trabecular Sites in an Orchiectomized Rat Model of Male Osteoporosis

Heidi Chandler1 and Gary Hattersley2, 1Research, Radius Health Inc, Waltham, MA, 2Radius Health, Inc., Waltham, MA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Biology and Pathology of Bone and Joint Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Male osteoporosis, a disease of reduced bone mass leading to an increased risk of fragility fractures, often results from androgen deficiency caused by hypogonadism or androgen deprivation therapy. Abaloparatide (ABL) is an anabolic PTHrP analog that reduced the incidence of new vertebral and nonvertebral in postmenopausal women with osteoporosis at a high risk for fractures by increasing bone formation and bone mineral density (BMD)1. These attributes suggest ABL may have utility for increasing bone mass and strength in men with osteoporosis. The effects of ABL on bone mass were studied in orchiectomized (ORX) rats, a commonly used preclinical model of male osteoporosis.

Methods: 40 Male SD rats underwent sham or ORX surgery at 4 months of age. After an 8-week bone depletion period, ORX rats received vehicle (VEH) or ABL at 5 (ABL5) or 25 (ABL25) μg/kg/d by daily sc injection for 8 weeks (n = 10/group), while sham controls (n = 10) received VEH. Animals underwent dual X-ray absorptiometry (DXA) and peripheral quantitative computed tomography (pQCT) scans after 0, 4, and 8 weeks of treatment, followed by necropsy.

Results: DXA conducted 8 weeks after surgery showed the VEH group had significantly lower areal bone mineral content (aBMC) and density (aBMD) at the whole body, lumbar spine, total femur, and proximal femur (including the hip) vs Sham controls, indicating ORX-induced osteopenia at the treatment baseline (BL). Between BL and week 8, whole body aBMD increased by 13.8% and 17.3% in the ABL5 and ABL25 groups, respectively, versus 6.3% in VEH controls (both \(P < 0.001\)). Lumbar spine aBMD increased from BL to week 8 by 24.5% and 29.1% in the ABL5 and ABL25 groups, versus 7.6% in VEH controls (both \(P < 0.001\)). Total femur aBMD increased by 19.3% and 26.0% from BL to week 8 in the ABL5 and ABL25 groups, versus 7.2% in VEH controls (both \(P < 0.001\)). Proximal femur aBMD (including the hip) increased from BL to week 8 by 16.9% and 23.2% in the ABL5 and ABL25 groups, vs 5.0% in VEH controls (both \(P < 0.001\)). By treatment week 8, aBMD values for all four of these sites in the ABL5 and/or ABL25 groups were fully restored to the levels of Sham controls. pQCT of the tibial diaphysis showed significantly greater gains from BL to week 8 in cortical thickness for the ABL5 (7.3%) and ABL25 (7.1%) groups compared with VEH controls (0.9%; both \(P < 0.05\)). Tibial diaphysis cortical volumetric BMC (vBMC) was also significantly increased from BL to week 8 in the ABL5 (11.7%) and ABL25 (13.2%) groups compared with VEH controls (6.3%; both \(P < 0.05\)). pQCT of the proximal tibial metaphysis showed greater gains in trabecular vBMD in the ABL5 (96.4%) and ABL25 (163.0%) groups from BL to week 8 compared with VEH controls (6.9%; both \(P < 0.05\)).

Conclusion: Androgen deficiency via ORX led to significant deficits in bone mass for the whole body and for axial and appendicular sites in mature male rats. Abaloparatide fully reversed the ORX-related deficit in whole body bone mass by promoting the accrual of cortical and trabecular bone. These data provide preclinical support for investigations into the effects of abaloparatide in men with osteoporosis.
Low and Moderate Intensity Exercise Suppresses Inflammatory Responses in an Acute Mouse Model of Gout and Suggests Therapeutic Efficacy

Nicholas A. Young1, Kyle Jablonski2, Juhi Sharma1, Evelyn Thomas1, Brian Snoad1, Jeffrey Hampton3, Wael Jarjour1 and Naomi Schlesinger1, 1Department of Internal Medicine, Division of Immunology and Rheumatology, The Ohio State University Wexner Medical Center, Columbus, OH, 2The Ohio State University Wexner Medical Center, Columbus, OH, 3Immunology and Rheumatology, The Ohio State University Wexner Medical Center, Columbus, OH, 4Medicine, Rutgers-Robert Wood Johnson Medical School, New Brunswick, NJ

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Biology and Pathology of Bone and Joint Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Little is known regarding the potential benefits of exercise on managing acute gout. Consequently, recent clinical practice guidelines released by the American College of Rheumatology (2012) and the American College of Physicians (2016) contain no recommendations regarding exercise in gout patients. Currently, many rheumatologists recommend resting the involved joints during an acute attack based on animal studies performed nearly a half century ago. Since the potential for exercise to suppress gouty inflammation is an area of study that has yet to be researched sufficiently, the aim of this study was to determine the efficacy of exercise in an acute mouse model.

Methods: BALB/C-Tg(NFκB-RE-luc)-Xen mice, which contain a firefly luciferase cDNA reporter gene under the regulation of NFκB, were exercised by daily treadmill walking (45 min/day for 2 weeks) at low intensity (35% VO2 max; 8 m/min), moderate intensity (55% VO2 max; 11 m/min), and high intensity (75% VO2 max; 15 m/min). At the end of the 2 week conditioning period, monosodium urate (MSU) crystal-induced arthritis was induced by intra-articular injection of MSU (0.5 mg) into the tibio-tarsal joint (ankle) under anesthesia. Localized NFκB activity was measured using the Xenogen in vivo imaging system (IVIS 200). Serum was collected to measure cytokine expression and tissue was collected for histological analysis.

Results: Histopathology of feet/ankle regions demonstrated a decrease in cellular infiltrate into the joint spaces by H&E staining and a marked decrease in macrophage and neutrophils, as indicated by immunohistochemistry and quantification in mice exercised at low intensity (8 m/min) when compared to non-exercised controls. Low intensity exercise also significantly suppressed serum expression of IL-12, KC/GRO, TNF-α, and IL-6 in MSU-induced gout mice relative to non-exercised and wild-type controls. Caliper measurements of foot pads revealed a significant reduction in swelling with both low and moderate exercise when compared to non-exercised controls, while no difference was observed with high intensity exercise. Additionally, IVIS measurements of the injected ankles demonstrated that NFκB activity was significantly reduced with low and moderate exercise, but slightly elevated following the high intensity regimen relative to non-exercised control mice.

Conclusion: Our results from an acute gout mouse model suggest that low and moderate exercise may be effective in decreasing gouty inflammation. Thus, these data could support a change in the conventional exercise recommendations provided by Rheumatologists in gout patients. Further studies are needed to more comprehensively evaluate this potentially important observation and to elucidate the mechanism responsible for this observation.
Disclosure: N. A. Young, None; K. Jablonski, None; J. Sharma, None; E. Thomas, None; B. Snoad, None; J. Hampton, None; W. Jarjour, None; N. Schlesinger, AstraZeneca, 2,AstraZeneca, Horizon, Pfizer, BMS, Celgene, 5,AstraZeneca, Horizon, Pfizer, BMS, Celgene, 5.


Abstract Number: 61

Resolution of Systemic Joint Inflammatory Processes and Regeneration of Existing Bone Damage upon TNF Blockade As Monitored By In Vivo Multimodal PET-CT Imaging in Progressed Experimental Arthritis

Silvia Hayer1, Markus Zeilinger2,3, Volker Weiss3,4, Markus Seibt5, Birgit Niederreiter1, Tetyana Shvets6, Monika Dumanic6, Florian Pichler6, Marcus Hacker6, Josef S. Smolen7, Kurt Redlich8 and Markus Mitterhauser6, 1Department of Internal Medicine III, Division of Rheumatology, Medical University of Vienna, Vienna, Austria, 2Faulty of Engineering, University of Applied Sciences, Winer Neustadt, Austria, 3Department of Biomedical Imaging and Image-guided Therapy, Medical University of Vienna, Vienna, Austria, 4Faculty of Engineering, University of Applied Sciences, Wiener Neustadt, Austria, 5Department Internal Medicine III, Division Rheumatology, Medical University of Vienna, Vienna, Austria, 6Medical University of Vienna, Vienna, Austria, 7Medical University Vienna, Division of Rheumatology, Department of Internal Medicine III, Vienna, Austria, 8Division of Rheumatology, Medical University of Vienna, Vienna, Austria

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Biology and Pathology of Bone and Joint Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: To use in vivo multimodal [18F]FDG (fluoro-D-glucose, tracer for inflammation) and [18F]Sodium Fluoride (bone tracer) positron emission tomography/computed tomography (PET-CT) imaging for the monitoring of systemic inflammatory and bone remodeling processes as well as colocalized bone destructions before and after TNF blockade in human tumor necrosis factor transgenic (hTNFtg) mice, an established mouse model of chronic inflammatory, erosive polyarthritis.

Methods:
**Nerve growth factor (NGF) as a key regulator of bone repair in experimental arthritis.**

**Background/Purpose:**

Nerve growth factor (NGF) is a key regulator of bone repair and pain in experimental arthritis. NGF therapy reduces osteoarthritis (OA) associated pain, and anti-NGF therapy is associated with rapid progression of OA (RPOA) [1]. In hip OA, there is a 5-fold increase in mesenchymal stem cells (MSCs) from MRI bone marrow (BM) lesions, areas associated with OA progression [2]. MSCs in such lesions are uniformly positive for the NGF receptor, p75, which is also linked to chemotaxis and proliferation in other stromal cell compartments [3]. We therefore sought to evaluate anti-NGF treatment in moniodoacetate (MIA) induced OA and test whether NGF influences human BM-MSC function.

**Methods:**

8 week-old hTNFtg mice were treated with anti-TNF antibodies (Infliximab, i.p., 3x times per week, 10mg/kg body weight) for 4 weeks. Before and after the treatment period mice received [18F]FDG or [18F]Sodium Fluoride (~25MBq) static PET scans (45min post injection) followed by whole-body and high resolution leg CT scans (800kV, 500µA, 800ms, 360 projections) using an Inveon PET/CT/SPECT multimodality system (Siemens Medical Solutions). PET reconstructions were conducted with OSEM3D/MAP, FBP algorithm. Standard uptake values (SUV) were calculated using PMOD software. Radiographic damage score was evaluated by in vivo CTs using InveonResearchWorkplace software. Joints were further analyzed by ex vivo µCT scans (Scanco µCT35) and H&E, TRAP and TB stained paraffin-sections.

**Results:**

Before therapeutic intervention, we observed an increased accumulation of [18F]FDG in various joints of hTNFtg mice including knees, ankles and shoulders compared to wt littermates indicating ongoing systemic inflammatory processes. Moreover, existing bone destructions were detected by in vivo CTs. However, [18F]Sodium Fluoride was equally accumulated within bone tissues such as long bones, in particular at growth plates, and vertebrae between both genotypes. After four weeks, placebo-treated hTNFtg animals showed significantly increased [18F]FDG SUVs as well as progressive bone destruction in knees, ankles and shoulders as shown by in vivo CTs. In contrast, TNF-blockade led to a significant decrease in [18F]FDG SUVs suggesting complete resolution of inflammatory processes in those individuals. Comparison of repeated in vivo CT images demonstrated a significant reduction in radiographic bone damage score and reversal of existing bone destructions upon TNF blockade. Histological analysis demonstrated regeneration processes of former bone erosion sites present as refillings of cartilaginous or fibro-cartilaginous tissue as well as signs of endochondral ossifications or even intact bone surfaces upon TNF blockade. Surprisingly, we found no marked changes in [18F]Fluoride SUVs in joints between both hTNFtg groups and wt mice suggesting that age-related high [18F]Fluoride accumulations in growth plates interfere, thus preventing to monitor inflammatory bone damage.

**Conclusion:**

In vivo small animal multimodal [18F]FDG, but not [18F]Fluoride, PET-CT imaging provides an objective, non-invasive imaging tool for the longitudinal monitoring of (I) reversibility of ongoing inflammatory processes in various joints and (II) regeneration of existing bone erosions during therapeutic intervention in TNF-driven experimental arthritis.

**Disclosure:**

S. Hayer, None; M. Zeilinger, None; V. Weiss, None; M. Seibt, None; B. Niederreiter, None; T. Shvets, None; M. Dumanic, None; F. Pichler, None; M. Hacker, None; J. S. Smolen, AbbVie, Amgen, Astra-Zeneca, Astro, BMS, Celgene, Celltrion, Chugai, Gilead, Glaxo, ILTTO, Janssen, Eli Lilly and Company, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi-Aventis, UCB, 5,AbbVie, Janssen, Eli Lilly and Company, MSD, Pfizer, Roche, 2,AbbVie, Amgen, Astra-Zeneca, Astro, BMS, Celgene, Celltrion, Chugai, Gilead, Glaxo, ILTTO, Janssen, Eli Lilly and Company, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi-Aventis, UCB, 8; K. Redlich, None; M. Mitterhauser, None.

**Abstract Number:** 62

**Convergence of Joint Repair and Pain Pathways Via Nerve Growth Factor and p75**

**Expressing Mesenchymal Stem Cells in Established Osteoarthritis**

**Thomas Baboolal**

1, Saraiaiy Al Hinai2, Elena Jones2, Jill Reckless3, Martyn Foster4, Rachel Doyle5, Kerry af Forselles4, Simon Westbrook4 and Dennis McGonagle2, 1PhD, Leeds, United Kingdom, 2Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom, 3Rxcelerate Ltd, Cambridge, United Kingdom, 4Levicept Ltd, Ramsgate, United Kingdom, 5Tetrad Discovery Ltd, Ramsgate, United Kingdom

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Biology and Pathology of Bone and Joint Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM
Methods:

Human tibial plateau (TP) bone was isolated from patients undergoing total knee replacement. OA was induced in male Wistar rats (n=6) by intra-articular injection of 0.3 mg MIA. Each animal was treated with subcutaneous injection of control human IgG or anti-NGF (3 mg/kg) on Days 30, 35, 39, 45 and 50. Human and animal tissues sections were prepared for histological analysis using H&E staining and immunohistochemistry (IHC) using anti-p75 and anti-NGF antibodies. BM-MSCs were isolated from iliac crest aspirates and cultured under normal conditions. Expression of p75 was induced following overnight incubation with 400mM ethanol (EtOH) and confirmed by flow cytometry. Proliferation and chemotaxis was assessed with and without induction of p75 and in the presence of 0-1 μg/ml NGF.

Results:

Regions adjacent to cartilage loss in human TP showed abundant stromal proliferation, NGF and p75 immunoreactivity. In the MIA model, by Day 28 there was substantial loss of cartilage, bone remodelling and stromal proliferation mimicking human disease and animals demonstrated unequal weight-bearing (p<0.05). Anti-NGF provided sufficient analgesia to normalise weight-bearing by Day 42. Features associated with joint damage and MIA treatment such as fibrogranular reactions and palisading osteoblasts were strongly p75 immunopositive. NGF positive staining was widespread in naïve and MIA-injected knees. To investigate increased p75 positivity in knee OA, we restored p75 expression loss in expanded cell, to 97% of BM-MSCs (n=3) using EtOH. Increased MSC proliferation was seen at Days 6 and 9 (26%, p=0.03 and 30%, p=0.01 increase respectively, n=7) for 1 μg/ml NGF in the presence of EtOH compared to control (no NGF). In cultures without EtOH induction (absent p75) NGF had no effect. NGF was not chemotactic for MSCs with or without the induction of p75.

Conclusion:

TP bone from OA patients and rat MIA-treated subchondral bone contains p75 positive staining in regions of cartilage destruction and associated NGF positivity. In vitro, NGF increased BM-MSC proliferation, suggesting NGF may be involved in the stromal proliferation seen at sites of OA damage. Thus, NGF may regulate MSC function. Complete blockade represents a novel mechanism for accelerated joint destruction in OA.

Reference:


Disclosure: T. Baboolal, None; S. Al Hinai, None; E. Jones, None; J. Reckless, None; M. Foster, Levicept Ltd, 5; R. Doyle, None; K. af Forselles, None; S. Westbrook, Levicept Ltd, 1,Levicept Ltd, 3; D. McGonagle, None.

Abstract Number: 63

**MiR-146a a Key Player in Bone Metabolism**

Victoria Saferding1, Melanie Hofmann1, Julia S. Brunner2, Antonia Puchner1, Melanie Timmen3, Richard Stange3, Josef S. Smolen4 and Stephan Blüni4, 1Medical University of Vienna, Austria, Vienna, Austria, 2Vascular Biology and Thrombosis research, Medical University of Vienna, Austria, Vienna, Austria, 3Institute for Experimental Muskuloskeletal Medicine, University Hospital Muenster, Muenster, Germany, 4Medical University Vienna, Division of Rheumatology, Department of Internal Medicine III, Vienna, Austria

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Biology and Pathology of Bone and Joint Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Micro RNAs (miRNAs) play a crucial role in the regulation of bone metabolism. MiR-146a, an important anti-inflammatory miRNA, was found to negatively impact osteogenesis and bone regeneration *in vitro*, by controlling the differentiation of mesenchymal stem cells. But to date the role of miR-146a in bone remodelling, its influence on bone stability and development of osteoporosis is not known.

Abstract Number: 63

**MiR-146a a Key Player in Bone Metabolism**

Victoria Saferding1, Melanie Hofmann1, Julia S. Brunner2, Antonia Puchner1, Melanie Timmen3, Richard Stange3, Josef S. Smolen4 and Stephan Blüni4, 1Medical University of Vienna, Austria, Vienna, Austria, 2Vascular Biology and Thrombosis research, Medical University of Vienna, Austria, Vienna, Austria, 3Institute for Experimental Muskuloskeletal Medicine, University Hospital Muenster, Muenster, Germany, 4Medical University Vienna, Division of Rheumatology, Department of Internal Medicine III, Vienna, Austria

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Biology and Pathology of Bone and Joint Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Micro RNAs (miRNAs) play a crucial role in the regulation of bone metabolism. MiR-146a, an important anti-inflammatory miRNA, was found to negatively impact osteogenesis and bone regeneration *in vitro*, by controlling the differentiation of mesenchymal stem cells. But to date the role of miR-146a in bone remodelling, its influence on bone stability and development of osteoporosis is not known.

Abstract Number: 63

**MiR-146a a Key Player in Bone Metabolism**

Victoria Saferding1, Melanie Hofmann1, Julia S. Brunner2, Antonia Puchner1, Melanie Timmen3, Richard Stange3, Josef S. Smolen4 and Stephan Blüni4, 1Medical University of Vienna, Austria, Vienna, Austria, 2Vascular Biology and Thrombosis research, Medical University of Vienna, Austria, Vienna, Austria, 3Institute for Experimental Muskuloskeletal Medicine, University Hospital Muenster, Muenster, Germany, 4Medical University Vienna, Division of Rheumatology, Department of Internal Medicine III, Vienna, Austria

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Biology and Pathology of Bone and Joint Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Micro RNAs (miRNAs) play a crucial role in the regulation of bone metabolism. MiR-146a, an important anti-inflammatory miRNA, was found to negatively impact osteogenesis and bone regeneration *in vitro*, by controlling the differentiation of mesenchymal stem cells. But to date the role of miR-146a in bone remodelling, its influence on bone stability and development of osteoporosis is not known.

Abstract Number: 63

**MiR-146a a Key Player in Bone Metabolism**

Victoria Saferding1, Melanie Hofmann1, Julia S. Brunner2, Antonia Puchner1, Melanie Timmen3, Richard Stange3, Josef S. Smolen4 and Stephan Blüni4, 1Medical University of Vienna, Austria, Vienna, Austria, 2Vascular Biology and Thrombosis research, Medical University of Vienna, Austria, Vienna, Austria, 3Institute for Experimental Muskuloskeletal Medicine, University Hospital Muenster, Muenster, Germany, 4Medical University Vienna, Division of Rheumatology, Department of Internal Medicine III, Vienna, Austria

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Biology and Pathology of Bone and Joint Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Micro RNAs (miRNAs) play a crucial role in the regulation of bone metabolism. MiR-146a, an important anti-inflammatory miRNA, was found to negatively impact osteogenesis and bone regeneration *in vitro*, by controlling the differentiation of mesenchymal stem cells. But to date the role of miR-146a in bone remodelling, its influence on bone stability and development of osteoporosis is not known.
Methods:

Systemic bone, tibiae and femur, of wt and miR-146a deficient animals was assessed histologically and via µCT analysis, over a period of 3 to 18 months of age. Serum cytokine levels were analysed by Elisa. mRNA expression levels in bone were analysed by qPCR. To induce osteoporosis, ovariectomty (OVX) induced bone loss was performed.

Results:

When we analysed bone volume of long bones histologically as well as with µCT analysis we detected significantly increased trabecular bone mass in miR-146a deficient compared to wt animals, starting at an age of 6 months. However, cortical thickness of systemic bones from miR-146a knock out animals was significantly reduced compared to control mice. Analysis of serum in aged miR-146a deficient animals displayed elevated activity of bone resorbing osteoclasts as amounts of CTX I in miR-146a−/− mice were significantly increased compared to wt animals. Q-PCR analysis of important osteoclast as well as osteoblast marker genes in bones ex vivo displayed elevated expression of signature molecules of both cell types in aged miR-146a deficient mice, suggesting a regulatory role of miR-146a in both osteoclasts as well as osteoblasts. When we induced osteoporosis using the OVX disease model, histological analysis of long bones showed significant trabecular bone loss in ovariectomized wt mice. In contrast, we detected no trabecular bone loss in ovariectomized miR-146a knock out animals, suggesting that loss of miR-146a deficiency protects bone loss induced by estrogen deficiency.

Conclusion:

MiR-146a seems to control bone turnover and miR-146a deficient mice accrue bone over time. Moreover this miRNA has a negative influence on bone loss occurring during oestrogen loss induced osteoporosis. Therefore miR-146a could be possibly used as a therapeutic target in the treatment of osteoporosis.

Disclosure: V. Saferding, None; M. Hofmann, None; J. S. Brunner, None; A. Puchner, None; M. Timmen, None; R. Stange, None; J. S. Smolen, None; S. Blüml, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/mir-146a-a-key-player-in-bone-metabolism

Abstract Number: 64

The Effect of Adenosine A2A Receptor Stimulation on Mitochondrial Metabolism in the Pathogenesis and Treatment of Osteoarthritis

Cristina Castro1, Carmen Corciulo2 and Bruce Cronstein3, 1Medicine, NYU School of Medicine, New York, NY, 2Department of Medicine, Division of Rheumatology, NYU School of Medicine, New York, NY, 3Rheumatology, New York University School of Medicine, Division of Rheumatology, New York, NY

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Biology and Pathology of Bone and Joint Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Osteoarthritis (OA) is the most common form of arthritis, affecting nearly 10% of the US population. There is no therapy to prevent the progression of or reverse OA pathology. Endogenous adenosine 2A receptor (A2AR) stimulation is crucial for chondrocyte viability and cartilage homeostasis as its downstream signaling mediates inflammation. In recent preliminary studies we have found that mice lacking the A2AR or ecto-5'nucleotidase (CD73, an ectoenzyme critical for extracellular adenosine production) develop spontaneous OA. These findings suggest that diminished extracellular adenosine levels promote the development of OA. Since human OA chondrocytes have been found to have diminished mitochondrial content, we propose to test the hypothesis that OA pathogenesis deregulates A2AR signaling at least in part by affecting the cell's capacity for ATP production via reduced number or functionality of mitochondria.

Methods: A human chondrocyte cell line, TC28a2, was used to determine the effects of IL1B–induced inflammation and A2AR stimulation in vitro. Cells were treated with IL1B (5ng/mL) and with the A2AR-specific agonist, CGS21680 (CGS; 1uM). Mitochondrial content was measured by mtDNA to nDNA ratios and MitoTracker mean cellular intensity. Mitochondrial health and functionality was assessed by mean pixel intensity (MPI) of a fluorescent probe for monitoring mitochondrial membrane potential, TMRM, and by measuring oxygen consumption rates (OCR) on Seahorse Mito Stress Kit Assays. The role of A2AR ligation on mitochondrial health was also studied by histology for 8hydroxyguanosine (8OH-G) residues as a marker for reactive oxygen species (ROS) in A2ARKO mice and Sprague Dawly rats that underwent ACL rupture (post-traumatic OA model) and subsequently received CGS-filled liposomal injections.
Results: A2AR agonism increases mitochondrial content in vitro. IL1B incubation for 3 hours followed by A2AR ligation increases mitochondrial membrane potential (2867±165.5 MPI) compared to control (1582±183.9 MPI), IL1B alone (1483±120.6 MPI) and CGS alone (1788±137.8 MPI) as measured by TMRM staining (p≤0.0001). IL1B incubation for 4 hours with a last hour of A2AR stimulation increases basal oxygen consumption rate and maximal respiratory rate. IL1B+CGS treated cells had significantly increased ATP production (113.04±13.44 of OCR) than the control (83.86±12.80 of OCR), IL1B (81.00±12.80 of OCR) and CGS (76.04± 23.52 of OCR) treated cells as measured by one-way ANOVA (p values =**0.0088, *0.0128, and *0.0259 respectively). A2ARKO mice exhibit increased 8OG-G staining in histology as early as 8 weeks. A2AR stimulation after ACL rupture in rats, results in preserved cartilage volumes, improved OARSI scores (p<0.001) and reduced ROS as seen by reduced 8OH-G staining in histology.

Conclusion: A2AR ligation improves mitochondrial functionality during inflammation and OA progression. Increased mitochondrial function is not seen when the chondrocytes are treated with IL1B or CGS alone; perhaps suggesting that A2AR stimulation is necessary to maintain homeostasis when cells are already under physiological or pathological stress.

Disclosure: C. Castro, None; C. Corciulo, None; B. Cronstein, NIH grant, 2,Arthritis foundation grant, 2,AstraZeneca, 2,Celgene, 2,Eli Lilly & Co., 5,AstraZeneca, 5,Canfite Biopharma, 1.


Abstract Number: 65

RA-Associated Antibodies Targeting Post Translational Modification Have Different Osteoclastogenetic Potential

Akilan Krishnamurthy1, Johanna Steen2, Caroline Grönwall3, Gustaf Wigerblad4, Camilla Svensson5,6, Heidi Wähämaa1, Vivianne Malmström1, Bence Rethi1 and Anca I. Catrina1, 1Rheumatology Unit, Department of Medicine, Karolinska Institute, Karolinska University Hospital, Stockholm, Sweden, 2Dept. of Medicine, Rheumatology Unit, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, 3Dep. of Medicine, Rheumatology Unit, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, 4Department of Medicine, Solna, Karolinska Institutet, Stockholm, Sweden, 5Dept. of Physiology & Pharmacology, Karolinska Institutet, Stockholm, Sweden, 6Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Biology and Pathology of Bone and Joint Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Some but not all antibodies against citrullinated modified proteins (ACPA) promote osteoclastogenesis and bone destruction in vitro and in vivo. We aimed to investigate the ACPA specificity pattern that is related to this effect and if this effect is limited to ACPA or encompasses also other RA-associated antibodies.

Methods:

Polyclonal ACPA IgG and IgGs others than ACPA were obtained from the peripheral blood of RA patients by purification on a G column followed by an anti-CCP2 column. Monoclonal ACPA, anti-MDA and rheumatoid factor (RF) IgGs were generated from either single plasma cells isolated from the synovial fluid or tetramer-positive sorted single B-cell isolated from the plasma of RA patients. Osteoclasts were generated from CD14+ monocytes of healthy individuals or bone marrow cells of Fc gamma III or Fc gamma chain knockout mice, in the presence or absence of polyclonal ACPA, monoclonal antibodies (ACPA, and anti-MDA antibodies and RF) and IgG controls. TRAP positive multinucleated cells were counted and bone erosion assay was done in parallel.

Results:

Polyclonal ACPA increased osteoclastogenesis, by a fold of 1.6±0.03One out of 4 tested plasma cell derived monoclonals ACPAs and one out of the five tested tetramer positive B-cell derived monoclonals have similar effects (with a fold increase of 1.63 ±0.15 for the plasma cell derived antibody and 1.4± 0.16 for the tetramer positive B-cell derived) have similar OC effects. Two additional tetramer positive B-cell derived monoclonals inhibited osteoclastogenesis while the remaining had no significant effect. All monoclonal ACPA were relatively highly cross-reactive to several citrullinated epitopes but not to native arginine peptides. Anti-MDA monoclonals antibodies displaying somatic hypermutations and low reactivity had significant in vitro functional properties and enhanced osteoclastogenesis (fold increase of for
Somatic hypermutations and low reactivity had significant in vitro functional properties and enhanced osteoclastogenesis (fold increase of for one antibody 4.0±0.76 and fold increase of for the second one 2.3±0.2), while the natural antibody related high-reactivity anti-MDA antibody did not. Anti MDA antibodies had no cross reactivity to other antigen modifications such as citrullination or carbamylation. Monoclonal RF had no direct effect on osteoclastogenesis but were able to significantly increase ACPA-mediated osteoclastogenesis (fold increase of 1.68 ±0.03 for ACPA alone and for the combination of ACPA and RF 3.15±0.24). Dimeric Fab fragments of polyclonal ACPA increased OC numbers by a fold of 1.78, suggesting that epitope recognition is involved in the observed osteoclastogenetic effect of ACPA. Interestingly however while ACPA increased osteoclastogenesis from bone marrow precursors of wild type mice, it had no effect on the bone marrow precursors of the Fc gamma chain knockout and Fc gamma III mice bone marrow samples, implying a more complex mechanism than epitope recognition alone that involves Fc receptors.

Conclusion:

We demonstrate that RA-associated antibodies targeting different post translational modifications have the capacity to increase osteoclastogenesis while others have not. The mechanism is mediated through both Fc dependent and independent mechanisms.

Disclosure: A. Krishnamurthy, None; J. Steen, None; C. Grönwall, None; G. Wigerblad, None; C. Svensson, None; H. Wählmaa, None; V. Malmström, None; B. Rethi, None; A. I. Catrina, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/ra-associated-antibodies-targeting-post-translational-modification-have-different-osteoclastogenetic-potential

Abstract Number: 66

Genome-Wide DNA Methylation Profiling of OA PBMCs Reveals Slowed Epigenetic Aging Among Rapid Radiographic Progressors: Data from the Osteoarthritis Initiative (OAI)

Alexander Rivas1, Madison Andrews2 and Matlock A. Jeffries3, 1Rheumatology, Immunology, and Allergy, University of Oklahoma Health Sciences Center, Oklahoma City, OK, 2College of Medicine, University of Oklahoma Health Sciences Center, Oklahoma City, OK, 3Department of Medicine, Division of Rheumatology, Immunology, and Allergy, University of Oklahoma Health Sciences Center, Oklahoma City, OK

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Biology and Pathology of Bone and Joint Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Extensive evidence has correlated epigenetic alterations in articular tissues with both the presence and progression of human osteoarthritis. A recent study demonstrated that accelerated DNA methylation aging was present in OA cartilage compared to controls but not in peripheral blood samples from a mixed population of knee, hip, and hand OA patients. To further clarify epigenetic age changes specifically in knee OA, we examined the DNA methylation aging rate in peripheral blood mononuclear cells (PBMCs) at baseline from knee OA patients with rapid radiographic progression compared to well-matched nonprogressors enrolled in the Osteoarthritis Initiative (OAI).

Methods: Peripheral blood mononuclear cell (PBMC) DNA was obtained from baseline blood draws of 64 OA patients enrolled in the Osteoarthritis Initiative (OAI) longitudinal study. 32 rapidly-progressive OA patients, defined as ≥1.0mm radiographic joint space loss or joint replacement within the first 24 months of follow-up were compared to 32 non-progressive OA patients defined as ≤0.5mm radiographic joint space loss over 48 months of follow-up. There were no differences in age, sex, race, BMI, baseline K/L grade, or calculated PBMC subset composition between rapid- and non-progressors. DNA methylation was quantified with Illumina HumanMethylation 450k arrays. Epigenetic age was estimated with the algorithm described by Horvath et. al., using 353 age-associated CpG sites. This epigenetic age was compared to chronological age to calculate epigenetic-chronological age discordance (ΔAge) and group differences compared with a Student t-test. ΔAge was correlated with individual CpG methylation sites of rapid progressors, and Pearson values calculated. Correlation was considered significant if Pearson’s r values were ≤-0.55 or ≥0.55 (p≤0.001). Pathway analysis of correlated genes was performed with the Ingenuity Pathway Analysis (IPA) system.

Results: The baseline DNA methylation aging rate in rapidly progressive (RP) knee OA patients was decelerated compared to nonprogressors (NP) and to chronological age (ΔAge-RP: -4.9±1.4 vs. ΔAge-NP: -0.071±1.3 mean±SEM years less than chronological age, p=0.015). 1165 CpG sites were correlated with ΔAge in rapid progressors, corresponding to 755 genes. Ontologic analysis of highly correlated genes showed association of the STAT3 pathway (p=6E-4), Notch signaling (p=1E-3), axonal guidance signaling (p=7E-3), CREB signaling (p=2E-2), NFAT signaling (p=2E-2), and autophagy (p=4E-2) among others. Associated upstream regulators included FGF2
Conclusion: Our data reveal that a decelerated peripheral blood differential DNA methylation age epigenotype is present at baseline in rapidly progressive knee OA patients, but not in nonprogressive knee OA patients. The genes correlated with this methylation age deceleration cluster in pathways previously associated with OA in articular tissues. Our data reinforce the notion that OA is a heterogeneous disease composed of distinct subgroups, and suggests that future epigenetic investigation of immune cell subsets may be beneficial in unraveling OA pathogenesis.

Disclosure: A. Rivas, None; M. Andrews, None; M. A. Jeffries, None.

Abstract Number: 67

The Oxygen Sensor PHD1 Is an Indispensable Regulator of Arthritis Development

Katelijne De Wilde, Peggy Jacques and Dirk Elewaut

Inflammation Research Center - VIB UGhent, Molecular Immunology and Inflammation Unit, Ghent, Belgium, Ghent University Hospital, Ghent, Belgium, VIB Inflammation Research Center, University of Ghent, Ghent, Belgium

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Biology and Pathology of Bone and Joint Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Oxygen supply is a fundamental requirement for all living tissues. Some tissues such as articular joints are characterized by a physiological state of hypoxia. Interestingly, under conditions of inflammation such as in arthritic disease, this level of hypoxia is even further enhanced. However, the functional significance of these observations and the molecular mechanisms involved remain poorly characterized to date. We therefore examined the role of 3 known oxygen sensors, prolyl hydroxylase domain (PHD) proteins: PHD1, PHD2 and PHD3. They are enzymes whose function is essentially controlled by oxygen. Their expression pattern varies between either of them and all of them have been ascribed specific roles in a myriad of biological processes. Our goal was to examine the role of oxygen sensors PHD1, PHD2 and PHD3 in preclinical models of rheumatoid arthritis, and to delineate the cellular source involved.

Methods: We subjected the collagen antibody induced arthritis (CAIA) model (resembling rheumatoid arthritis) to hypoxic (10% O2) and normoxic conditions (21% O2), respectively. Furthermore, the CAIA-model was induced in mice with germline deficiency of the specific PHD’s and in mice with a myeloid cell-specific PHD1 deficiency versus controls. Arthritis development was assessed by clinical scoring of paw swelling, histopathology of knee joints and μCT.

Results: Mice kept in hypoxic conditions during CAIA experiments showed markedly less arthritis (both by clinical and histopathological assessment) compared to mice in normoxic conditions. Furthermore, we demonstrated that PHD1 knock-out (KO) mice had significantly less joint inflammation compared to wildtype mice. PHD1 KO mice were also protected against inflammation induced bone loss as evidenced by μCT. By contrast, no differences were found between PHD2 heterozygous (PHD2 KO mice are not viable) or PHD3 KO mice and littermate controls. Because myeloid cells are considered critical effector cells upon passive transfer of arthritogenic antibodies in the CAIA model we also generated myeloid cell specific PHD1 deficiency versus controls. Arthritis development was assessed by clinical scoring of paw swelling, histopathology of knee joints and μCT.

Conclusion: Our data are consistent with a new paradigm that the oxygen sensor PHD1 is a critical regulator of myeloid cell function in arthritic disease. Overall, the data suggest that PHD1 is a potential target in the treatment of arthritis.

Disclosure: K. De Wilde, None; P. Jacques, None; D. Elewaut, Scientific Research Flanders; Research Council Ghent University; Interuniversity Attraction Pole., 2,Boehringer Ingelheim; Pfizer; UCB; Merck; Novartis; Janssen; Abbvie, 5.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-oxygen-sensor-phd1-is-an-indispensable-regulator-of-arthritis-development

Abstract Number: 68
Tankyrase/Wnt Inhibitor Upregulates Osteoclastogenesis and Osteoblastogenesis Via SH3BP2

Shunichi Fujita1, Tomoyuki Mukai1, Takafumi Mito1, Shoko Kodama1, Akiko Nagasu1, Mizuho Kittaka2, Yasuyoshi Ueki3 and Yoshitaka Morita1, 1Department of Rheumatology, Kawasaki Medical School, Kurashiki, Okayama, Japan, 2Department of Oral and Craniofacial Sciences, School of Dentistry, University of Missouri-Kansas City, Missouri-Kansas City, MO, MO, 3Department of Oral and Craniofacial Sciences, School of Dentistry, University of Missouri-Kansas City, Missouri-Kansas City, MO

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Biology and Pathology of Bone and Joint Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Tankyrase is a poly (ADP-ribose) polymerase that leads to ubiquitination and degradation of target proteins. Since tankyrase inhibitors increase Axin protein, a negative regulator of Wnt pathway, they are widely used as Wnt inhibitors. Tankyrase inhibitors have attracted the attention as a promising drug candidate for cancer and fibrotic diseases, in which Wnt pathways are critical in the pathogenesis. Tankyrase has recently been reported to degrade an adaptor protein SH3BP2 (SH3 domain-binding protein 2). We have previously shown that SH3BP2 gain-of-function mutation enhances RANKL-induced osteoclastogenesis in murine bone marrow-derived macrophages (BMMs). Though the interaction between tankyrase and SH3BP2 has been reported, it is not fully elucidated whether tankyrase is involved in bone metabolism. In this study, we investigated the effect of tankyrase inhibition in bone metabolism in vitro and in vivo.

Methods: Primary murine BMMs from wild-type (WT) mice and SH3BP2 knockout (KO) mice and human peripheral blood mononuclear cells (PBMCs) were treated with tankyrase inhibitors (IWR-1 or G007-LK) in the presence of RANKL. Osteoclasts formation, function and intracellular signaling were analyzed by TRAP staining, resorption assay and western blotting, respectively. Primary calvarial osteoblasts from WT mice and SH3BP2 KO mice were also cultured with tankyrase inhibitors. Osteoblast differentiation and intracellular signaling were analyzed by qPCR, Alizarin red staining and western blotting. To examine in vivo effect of the tankyrase inhibitor, 7-week-old WT male mice were treated with G007-LK for 4 weeks, and then tibias and lumber vertebrae were analyzed by micro-CT.

Results: In murine BMMs and human PBMCs culture, both tankyrase inhibitors enhanced osteoclast formation and function. Tankyrase inhibitors increased SH3BP2 protein and augmented phosphorylation of Syk and nuclear localization of NFATc1 in response to RANKL. Moreover, in SH3BP2 KO BMMs culture, tankyrase inhibitors did not promote osteoclast formation, indicating that the osteoclast-inducing effect is mediated by SH3BP2. Next, in primary calvarial osteoblasts culture, tankyrase inhibitors significantly increased osteoblast-associated genes expression and enhanced mineralization even though they have Wnt inhibitory effect. The osteogenic effect of tankyrase inhibitors were diminished by SH3BP2 deficiency, suggesting increased SH3BP2 expression enhanced osteoblastogenesis by surpassing the Wnt inhibitory effect. Finally, in vivo experiment, the administration of G007-LK significantly decreased trabecular bone volume of both tibias and vertebrae.

Conclusion: Tankyrase inhibition upregulates both osteoclastogenesis and osteoblastogenesis through the accumulation of SH3BP2. Our findings highlight the role of tankyrase as the novel regulator of bone metabolism. Also, we demonstrated that in vivo administration of the tankyrase inhibitor induces bone loss. This indicates that we should carefully evaluate the potential adverse effect on bone when tankyrase inhibitors are applied to patients with cancer or fibrotic diseases.


View Abstract and Citation Information Online - http://acrabstracts.org/abstract/tankyraselwnt-inhibitor-upregulates-osteoclastogenesis-and-osteoblastogenesis-via-sh3bp2

Abstract Number: 69

The Effect of Myostatin Inhibition on Bone Loss in Murine Osteoporosis Models

Tomoyuki Mukai1, Takafumi Mito1, Shunichi Fujita1, Shoko Kodama1, Akiko Nagasu1, Teruki Sone2, Shinichiro Nishimatsu3, Yutaka...
Myostatin, also called as growth differentiation factor-8 (GDF-8), is a secreted member of TGF-β superfamily. Myostatin is a negative regulator of skeletal muscle mass as shown by increased muscle mass in myostatin-deficient mice. A recent study reported the regulatory role of myostatin on bone metabolism (Dankbar B, et al. Nat Med 2015). The study showed that myostatin directly regulates osteoclastogenesis and its inhibition reduces inflammatory joint destruction in murine arthritis models. In contrast to this, another group reported that myostatin inhibition by the administration of anti-myostatin antibody did not affect bone mass of femur and vertebra in wild-type mice (Bialek P, et al. Bone 2014). Therefore, it is still controversial whether myostatin inhibition could regulate bone mass. Here, we report the effect of genetic inhibition of myostatin on bone loss in murine osteoporosis models.

Methods:

We used mutant myostatin transgenic (Mstn\textsuperscript{Pro}) mice, in which myostatin prodomain, an endogenous myostatin suppressor, is excessively expressed and subsequently inhibits myostatin activity. For a RANKL-induced osteoporosis model, 1 mg/kg of RANKL was injected intraperitoneally at day 0 and 1, and the sera and bones were collected at day 2. For a tail-suspension unloading model, the tails of mice were suspended for 2 weeks. At the end of the period, the sera and bones were collected. Serum TRAP5b and P1NP levels were measured by ELISA. Bone properties of vertebra and tibia were determined by micro-CT. For cell culture experiments, bone marrow cells were isolated from long bones of wild-type (WT) and Mstn\textsuperscript{Pro} mice. Bone marrow-derived macrophages (BMMs) were treated with RANKL, and then osteoclast differentiation and function were determined by TRAP staining and resorption assay.

Results:

Mstn\textsuperscript{Pro} mice exhibited increased muscle mass similarly to the previously reported myostatin null mice. RANKL injection induced severe bone loss in Mstn\textsuperscript{Pro} mice to the similar extent to that seen in WT mice (WT: 31.0 ± 10.0% reduction, Mstn\textsuperscript{Pro}: 42.8 ± 9.6% reduction compared to control mice of each genotype). Serum TRAP5b and P1NP levels were also comparable between RANKL-treated WT and Mstn\textsuperscript{Pro} mice. In the tail-suspension model, genetic inhibition of myostatin did not also prevent bone loss. In WT BMMs culture, myostatin stimulation slightly enhanced RANKL-induced osteoclastogenesis. Osteoclast formation and resorbed area in response to RANKL were comparable between WT and Mstn\textsuperscript{Pro} BMMs.

Conclusion:

Genetic inhibition of myostatin did not alleviate bone loss in the osteoporosis models we tested. The role of myostatin inhibition might vary in different pathological conditions (e.g. inflammatory or non-inflammatory conditions). Further research will be required to clarify the clinical implications of myostatin inhibition in various disease settings.


View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-effect-of-myostatin-inhibition-on-bone-loss-in-murine-osteoporosis-models

Abstract Number: 70

Excessive Cyclic Compressive Stress Increases Susceptibility to IL-1 in 3D-Cultured
Chondrocytes

Yuki Takeda¹, Yasuo Niki², Yusuke Fukuhara², Yoshitsugu Fukuda², Kazuhiko Udagawa², Toshiyuki Kikuchi², Takeshi Miyamoto², Morio Matsumoto² and Masaya Nakamura², ¹Department of Orthopaedic Surgery, Keio University, Tokyo, Japan, ²Keio University, Tokyo, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster I: The Variable World of Intercellular Signalling
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The mechanism of chondrocyte mechanotransduction is not fully understood. Recently, transient receptor potential vanilloid 4 (TRPV4) has been reported to transduce dynamic compressive loading in articular chondrocytes. The expression of the IL-1 receptor 1 (IL-1R1) on the surface of chondrocytes can be stimulated by compressive stress, and such increment of IL-1 susceptibility has been implicated in the OA pathology. The purpose of this study was to examine mechanical induction of IL-1R1 by chondrocytes in three-dimensional (3D) culture, and the effects of TRPV4 channel regulation on IL-1R1 expression.

Methods: Mouse embryonal carcinoma-derived clonal cell line (ATDC5) was used and cultured in alginate beads with the growth medium for 6 days. These cells were collected and seeded in collagen gels and scaffolds, which maintained chondrogenic phenotype in 3D environment (Fig.1). Cyclic compressive loading of 40 kPa at 0.5Hz was applied to this 3D constructs using a cyclic load bioreactor for 3 hours. Thereafter, the PGE2 concentration and mRNA expressions of Col-II, ADAMTS4 and IL-1R1 were measured in real-time PCR. The effects of subtle amount of IL-1beta (1pg/ml) was determined with or without compressive stress, and the effects of TRPV4 agonist/antagonist on IL-1-induced ADAMTS4 was determined.

Results: The PGE2 production in culture media and mRNA levels of ADAMTS4 and IL-1R1 were substantially increased by the excessive compressive stress. Compressive stress plus IL-1beta (1pg/ml) upregulated ADAMTS4 and IL-1R1 expressions by 3-fold and 8-fold, respectively, but IL-1beta alone failed to do so (Fig.2). TRPV4 agonist suppressed upregulation of ADAMTS4 and IL-1R1 mRNAs by cyclic compressive stress, conversely, TRPV4 antagonist rather accelerated these mRNA expressions (Fig.3).

Conclusion: In chondrogenic 3D environment, the cells gained IL-1 susceptibility under excessive cyclic compressive stress. In this context, the cells would produce ADAMTS4 and MMPs in response to subtle level of IL-1 derived from synovia or cartilage itself, whereas TRPV4 downregulated expression of IL-1R1 and control IL-1 susceptibility to maintain cartilage homeostasis. To control IL-1 susceptibility is a key to prevent the development of OA, when excessive mechanical stress is applied on the articular cartilage.

Fig.1 Alginate beads culture
The Critical Role of Interleukin-33 in Promoting Angiogenesis and Regulates Inflammation through Mast Cells in Takayasu Arteritis

Anne-Claire Desbois, Patrice Cacoub, Aurélie LEROYER, Edwige Tellier, Marlène Garrido, Anna Maciejewski-Duval, Cloé Comarmond, Stéphane Barret, Michel Arock, Edwige Tellier, Marlène Garrido, Anna Maciejewski-Duval, Cloé Comarmond, Stéphane Barete, Michel Arock, Patrick Bruneval, Jean-Marie Launay, Pierre Fouret, Ulrich Blank, Michelle Rosenzwajg, David Klatzman, Mohamed Jarraya, Philippe Cluzel, Fabien Koskas, Gilles Kaplanski, and David Saadoun.

1 Hôpital Pitié-Salpêtrière, Internal Medicine and Clinical Immunology, Paris, France, 2 Department of Internal Medicine and Clinical Immunology, Groupe Hospitalier Pitié-Salpêtrière, Paris, France, 3 Faculté de Pharmacie, Marseille, France, 4 Université Marseille, Marseille, France, 5 I3 laboratory, Pitié-Salpétrière, Paris, France, 6 GHPS, Paris, France, 7 DHU 2iB Internal Medicine Referral Center for Autoimmune diseases Pitie Hospital, Paris, France, 8 HEGP, Paris, France, 9 Hôpital Lariboisière, Paris, France, 10 Hôpital La Pitié Salpêtrière, Paris, France, 11 Hôpital Bichat, Paris, France, 12 UPMC Université Paris 06, UMR 7211, Paris, France, 13 Hôpital Saint Louis, Paris, France, 14 Department of cardiovascular imagery, Assistance Publique-Hôpitaux de Paris (AP-HP), Groupe Hospitalier Pitié Salpêtrière, 83 Boulevard de l’Hôpital, 75013, Paris, France, 15 Department of vascular surgery, Assistance Publique-Hôpitaux de Paris (AP-HP), Paris, France, 16 Aix-Marseille Université - Internal Medicine hospital conception - F-13000 Marseilles, Marseille, France, 17 Sorbonne Universités, UPMC Univ Paris 06, UMR 7211, and Inflammation-Immunopathology-Biotherapy Department
Large vessel vasculitis (LVV) include Takayasu arteritis (TA) and giant cell arteritis (GCA). Arterial lesions in LVV result from chronic inflammation and neoangiogenesis. IL-33, a cytokine involved in angiogenesis and vascular permeability has been previously found overexpressed in arteries of large vessel vasculitis. We aimed at assessing its effects on the regulation of immune response and angiogenesis.

Methods:

In vitro studies on angiogenesis were performed by using human endothelial cells to assess migration, proliferation and angiogenesis. Vascular permeability was assessed in vivo, using Miles assay. The effects of IL-33 on immune response were determined by assessing the production of cytokines by Multiplex in cultures of peripheral mononuclear cells (PBMC) with or without IL-33 stimulation and the proportion of regulatory T cells in cultures of mast cells and CD4+ T cells with or without IL-33 stimulation.

Results:

We identified increased IL-33 levels in serum and in inflammatory lesions of TA and GCA patients as compared to controls. Sera from TA patients have angiogenic properties by promoting HUVECs proliferation, tube and sprout formation and were also able to induce vessel permeability in vivo. The addition of neutralizing anti-IL-33 antibody inhibits neoangiogenesis, migration of endothelial cells in vitro and vascular permeability in vivo. As mast cells are one of the main targets of IL-33, we repeated these experiments in mast-cells deficient mice in which in vivo effects were abolished. Significant increased number of mast cells was observed in aorta lesions of both diseases as compared to non-inflammatory aorta controls. IL-33 overexpression was accompanied by an increased expression of Th2-related cytokines in which in vivo effects were abolished. Significant increased number of mast cells was observed in aorta lesions of both diseases as compared to non-inflammatory aorta controls. IL-33 overexpression was accompanied by an increased expression of Th2-related cytokines by enhancing the secretion of IL-5 and IL-4. IL-33 also promoted the regulatory immune response by increasing the proportion of regulatory T (Tregs) cells. Consistently, IL-33 and mast cells dramatically increased the proportion of Tregs and the activity of indoleamine 2 3-dioxygenase (IDO).

Conclusion:

IL-33/ST2 axis, through its interaction with mast cells, has a critical role in the pathogenesis of LVV.

Disclosure: A. C. Desbois, None; P. Cacoub, None; A. LEROYER, None; E. Tellier, None; M. Garrido, None; A. Maciejewski-Duval, None; C. Comarmond, None; S. Barete, None; M. Arock, None; P. Bruneval, None; J. M. Launay, None; P. Fouret, None; U. Blank, None; M. Rosenzwajg, None; D. Klatzman, None; D. Jarraya, None; P. Cluzel, None; F. Koskas, None; G. Kaplanski, None; D. Saadoun, None.
**Session Title:** Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster I: The Variable World of Intercellular Signalling  

**Session Type:** ACR Poster Session A  

**Session Time:** 9:00AM-11:00AM  

**Background/Purpose:** Tumor-necrosis factor (TNF)-α plays a key role in the pathophysiology of rheumatoid arthritis (RA) and membrane bound TNFα is sufficient to induce arthritis in mice [1]. Zhang [2] demonstrated membrane bound TNFα on extracellular vesicles (EVs) derived from RA synovial fibroblasts. EVs are stable in body fluids and mediate intercellular communication over short and long distances. In this study we want to determine whether TNFα is also present on circulating EVs from RA patients and not in healthy individuals.

**Methods:** pEVs were obtained from 28 RA patients and 24 healthy controls (HC) by size exclusion chromatography. Protein content was measured by micro-BCA, size and concentration by Nanoparticle Tracking. TNFα was detected by bead-based multiplex immunoassays (BBI) and flowcytometry (FC). To control for specificity, pEVs were preincubated with anti-TNFα (etanercept and certolizumab pegol). Immunoglobulin M rheumatoid factor (IgM-RF) was measured in pEVs by ELISA. RF+ and RF- pEVs were preincubated with Protein L beads to bind RF-IgM before TNFα was measured by FC.

**Results:** Particle size and protein content per particle were significantly higher in RA-pEVs as compared to HC (154nm, 484fg and 116nm, 216fg, resp) while particle concentration was not statistically different between RA patients and HC (0.89, 2.59 x10^{10}/ml, resp). In 13 out of 28 RA patients TNFα (220 pg/ml) was detectable in pEVs by BBI whereas in HC TNFα was undetectable. Presence of TNFα on RA-pEVs was confirmed by FC. Preincubation of pEVs with anti-TNFα antibodies (etanercept) fully blocked TNFα detection. Unexpected, after preincubation with anti-TNFα Fab fragments (certolizumab pegol) TNFα was still detectable which suggested aspecific binding of the TNFα detection antibody. By ELISA IgM-RF was detectable on pEVs in 9 out of 13 RA patients. By preincubation with Protein-L coupled magnetic beads, to scavenge RF, TNFα levels on pEVs isolated from RF^{+} RA patients were reduced to background.

**Conclusion:** This study shows for the first time that IgM-RF is present on pEVs in a subpopulation of RA patients and this impedes with immunodetection of TNFα. To obtain conclusive evidence for the presence of TNFα other laboratory techniques are needed. However, the presence of RF on EVs could be important in the immunopathophysiology of RA by directing putative immunoregulatory and potentially inflammatory EVs to sites of immune-complex formation.

1: Keffer. EMBO J. (1991)  

**Disclosure:** O. J. Arntz, None; B. C. H. Pieters, None; R. Thurlings, None; P. M. van der Kraan, Contract research UCB, 2; F. van den Hoogen, None; F. A. J. van de Loo, None.


**Abstract Number:** 73

**Regulation of Th17 Cell Responses By IL-25**

Sophie Archer, Ash Maroof, Meryn Griffiths and Stevan Shaw, UCB Pharma, Slough, United Kingdom  

**First publication:** September 18, 2017

**SESSION INFORMATION**  

**Session Date:** Sunday, November 5, 2017  

**Session Title:** Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster I: The Variable World of Intercellular Signalling  

**Session Type:** ACR Poster Session A  

**Session Time:** 9:00AM-11:00AM  

**Background/Purpose:** IL-17A is a Th17 proinflammatory cytokine that contributes to the pathophysiology of several immune-mediated inflammatory diseases including PsA; while previously underestimated, there is increasing evidence supporting a similar proinflammatory role for IL-17F. IL-17E (IL-25), another IL-17 cytokine, is implicated in Th2 responses, and signals via the IL-17RA/RB receptor complex, sharing the IL-17RA subunit with IL-17A and IL-17F. Extending upon previous work, we hypothesized that IL-25 indirectly regulates production of Th17 cell cytokines, and a broad range of other inflammatory mediators through effects on polyfunctional T cells. Consequently, selectively targeting IL-17A and IL-17F may offer a therapeutic alternative, in the treatment of immune-mediated inflammatory diseases, to targeting broader
signaling pathways by interfering with IL-25. The aim of this study was to investigate the effects of IL-25 on Th17 and polyfunctional T cell responses.

Methods:

Isolated human Th17 cells or peripheral blood mononuclear cells (PBMCs) were either stimulated with Th2 cytokines (IL-4, IL-5 and/or IL-13, IL-25) or Th2-cytokine neutralizing antibodies (10 µg/mL) for 72 hrs, to assess their modulatory effect on Th17 cells in addition to other Th cell subsets. Cytokines in cell supernatant and intracellular cytokines were measured using ELISA and flow cytometry, respectively. To investigate how IL-25 or IL-4 affected polyfunctional T cell responses, PBMCs were stimulated with these cytokines for 72 hrs and intracellular cytokine production was assessed by mass cytometry.

Results:

While IL-25 did not effectively inhibit IL-17A production in stimulated PBMCs, IL-25 did elevate levels of IL-4 in treated versus untreated PBMCs. In contrast to IL-25, IL-4 effectively reduced the percentage of PBMCs expressing IL-17A and IL-17F and inhibited the secretion of IL-17A; the opposite effect was observed using anti-Th2-cytokine antibodies. Both IL-25 and IL-4 inhibited polyfunctional T cell production of the proinflammatory molecules IL-17A, IL-17F, TNF, and IFNγ (Figure 1).

Conclusion: Taken together these data show that IL-25, via IL-4, indirectly modulates IL-17A and IL-17F production, as well as production of a variety of other proinflammatory molecules (including TNF and IFNγ), through effects on Th17 and polyfunctional T cells. Targeted dual neutralization of IL-17A and IL-17F may therefore produce optimal inhibition of inflammatory signaling responses in immune-mediated inflammatory diseases, without interfering with the regulatory role of IL-25.

1Liu et al. Sci Rep 2016;6(36002)

Figure 1: IL-4 and IL-25 (10 ng/mL) regulate production of proinflammatory cytokines from polyfunctional T cells.

Disclosure: S. Archer, Crescendo Biologics, Cambridge, 3,UCB Pharma, 3; A. Maroof, UCB Pharma, 3,UCB Pharma, 9; M. Griffiths, UCB Pharma, 3; S. Shaw, UCB Pharma, 3,UCB Pharma, 9.

Abstract Number: 74

IL-17 Blockade Attenuates Osteoblastic Activity and Differentiation in Ankylosing Spondylitis

Sungsin Jo1, Ye-Soo Park2, Il-Hoon Sung3 and Tae-Hwan Kim1, 1Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), 2Orthopaedic, Hanyang University Guri Hospital, Guri, Korea, Republic of (South), 3Orthopaedic, Hanyang University Seoul Hospital, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster I: The Variable World of Intercellular Signalling
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Ankylosing spondylitis (AS) is a chronic inflammatory bone disease mediated by proinflammatory cytokine secreted by specialized T cells population. The mechanism by which the development of and function of Th17 cells and emerging IL-23/IL-17 axis may be involved in the pathogenesis of AS. However, the effect of IL-17 and IL-23 in osteoblast remain to be elucidated.

Methods:

AS patients satisfying the modified New York criteria were recruited for the study. Healthy donor, rheumatoid arthritis patients and osteoarthritis patients were included as controls. TNFa, IL-17, and IL-23 level were quantized by ELISA in the serum and synovial fluid. Bone tissues were obtained at surgery from facet joints of 10 patient with AS and 26 patients with noninflammatory spinal disease from traffic trauma or spinal compression disease, who served as controls. Immunohistochemistry and RNA level of bone tissue and isolated primary osteoprogenitor cells were performed to identify dominant JAK2 expression. IL-17 cytokine or patient serum with AS stimulated primary osteoprogenitor cells was analyzed by intercellular alkaline phosphatase (ALP) activity, mineralization, real-time PCR, and immunoblotting.

Results:

IL-17 and IL-23 basal level were significantly elevated in serum and synovial fluid of AS patients compared to those of the controls. Expression of JAK2 was enriched in bone tissues and isolated primary osteoprogenitor cells of AS patient. An addition of IL-17 cytokine in osteogenic differentiation exhibited an increase in ALP activity and calcium deposit in cellular level and sustained phos-JAK2 and phos-STAT3, and C/EBPβ in molecular level. Furthermore, adding IL-17A blockade in presence of patient serum with AS upon differentiation exhibited reduced intercellular ALP activity, mineralization, and phos-JAK2 expression in both control and AS osteoprogenitor cells. Intriguing, AG490, a JAK2 specific inhibitor, suppressed ALP activity despite the presence of patient serum with AS.

Conclusion:

This study supports a role of IL-17A in the pathogenesis of AS and attempts to provide a link between proinflammatory cytokine and osteoblast activity in an unexplored cellular system. Blocking of IL-17 could attenuate bony ankyloses in AS.

Disclosure: S. Jo, None; Y. S. Park, None; I. H. Sung, None; T. H. Kim, None.


Factors Associated with TNF Receptor 2 Levels Above the Measurable Range in Rheumatoid Arthritis

Michelle Frits1, Gary Bradwin2, Nancy A. Shadick1, Christine Iannaccone3, Michael Weinblatt1, Nader Rifai2 and Katherine P. Liao4, 1Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 2Laboratory Medicine, Childrens Hospital Boston, Boston, MA, 3Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA, 4Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster I: The Variable World of Intercellular Signalling
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Tumor necrosis factor-alpha (TNFa) is involved in the pathogenesis of RA and is increasingly being studied as a biomarker of cardiovascular disease (CVD). While TNF receptor 2 (TNFR2) and TNFa levels are correlated, TNFR2 is used more frequently as a biomarker in studies because of its stability in stored blood samples. We investigated whether TNF inhibitor (TNFi) use may influence measured TNFR2 levels. Since the mechanism of action for TNFi is binding TNFa, a component of these drugs is a TNF receptor. Thus, we hypothesize that there may be cross-reactivity between specific TNFi’s and the TNFR2 assay.

Methods: All subjects were part of a CVD sub-study performed in a large prospective RA cohort study with blood samples collected annually, data on treatment and C-reactive protein (CRP). TNFR2 was measured using a commercial ELISA kit (R&D Systems, Minneapolis, MN). We categorized TNFR2 levels into 3 groups: (1) >46 and £10,000 pg/mL, typical range; (2) >10,000 pg/mL and ≤100,000 pg/mL, samples requiring 200-fold dilution; (3) >100,000 pg/mL, levels exceeding measurable values. We examined the
association individual TNFi’s and having a TNFR2 level in group 3. Additionally, we assessed the correlation between natural log transformed CRP and TNFR2.

**Results:** We studied 190 RA subjects, mean age 60 years, 84% female, 73% anti-CCP positive and CRP ranged from 0.31-310 mg/L. Subjects on TNFi comprised 47% of the study: 14% on adalimumab, 26% on etanercept, and 8% on infliximab (no subjects on certolizumab or golimumab). All subjects with TNFR2 exceeding measurable levels (group 3) were on etanercept (Table). Samples that required 200-fold dilution (group 2) not on etanercept therapy had higher levels of CRP compared to those on etanercept (Table). We observed no significant correlation between CRP and TNFR2 for all subjects, r=0.05, p=0.51. After excluding subjects on etanercept, the correlation was significant, r=0.46, p=0.0001 (Figure). We observed no significant changes in the correlation between CRP and TNFR2 after excluding patients on adalimumab or infliximab.

**Conclusion:** Our data suggest cross-reactivity between etanercept and the TNFR2 assay, as 100% of subjects on etanercept had levels of TNFR2 above measurable levels. Of the TNFi’s, only etanercept has a TNF binding domain modeled after TNFR2. Thus, it is plausible that the TNFR2 assay has a high affinity for the TNFR portion of etanercept. These data should be considered when designing studies using TNFR2 in populations where etanercept is a treatment option.

**Table.** TNFR2 levels stratified by etanercept use.

<table>
<thead>
<tr>
<th>TNFR2 category</th>
<th>Total, n</th>
<th>Etanercept (%)</th>
<th>No etanercept (%)</th>
<th>CRP mg/L, median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group 1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Typical range</td>
<td>134</td>
<td>0</td>
<td>100</td>
<td>17.9 (4.7, 26.8)</td>
</tr>
<tr>
<td>≤1000 pg/mL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Group 2</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>200-fold dilute</td>
<td>13</td>
<td>54</td>
<td>46</td>
<td>30.2 (21.5, 35.6)</td>
</tr>
<tr>
<td>10000 to 100000</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥10000 pg/mL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Group 3</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exceeds measurable level values &gt;10000 pg/mL</td>
<td>43</td>
<td>100</td>
<td>0</td>
<td>15.8 (2.2, 26.6)</td>
</tr>
</tbody>
</table>

**A) ALL MEASUREMENTS**

![Figure](image1)

**B) EXCLUDE SUBJECTS ON ETANERCEPT**

![Figure](image2)

**Figure.** (A) Correlation between TNFR2 and CRP for all subjects (n=190); (B) Correlation between TNFR2 and CRP excluding subjects on etanercept (n=140).

**Disclosure:** M. Frits, None; G. Bradwin, None; N. A. Shadick, Mallinckrodt, 2,Amgen, Bristol-Myers Squibb, 2,UCB, 2,DxTerity, 2,Sanofi, 2,Crescendo Biosciences, 2,Bristol-Myers Squibb, 5; C. Iannaccone, None; M. Weinblatt, Amgen, BMS, Crescendo Bioscience, UCB, Genzyme, 2,AbbVie, BMS, Eli Lilly and Company, Genentech, Merck, Pfizer, Novartis, Roche, UCB, Crescendo Bioscience, Genzyme, Samsung, 5; N. Rifai, None; K. P. Liao, None.


**Abstract Number:** 76

**TNF-α Potentiates Uric Acid-Induced Interleukin-1β Secretion in Human Neutrophils**

**Shuzo Sato**, 1, Makiko Yashiro1, Tomoyuki Asano1, Tomohiro Koga2, Eiji Suzuki1, Hiroko Kobayashi1, Hiroshi Watanabe1 and Kiyoshi Migita1, 1Rheumatology, Fukushima Medical University School of Medicine, Fukushima, Japan, 2Department of Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, 3Fukushima Medical University School of Medicine, Fukushima, Japan

**First publication:** September 18, 2017
SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster I: The Variable World of Intercellular Signalling
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Gout is an inflammatory arthropathy due to the deposition of uric acid (monosodium urate: MSU) crystals in synovial tissue. MSU leads to activate nucleotide-binding oligomerization domain-like receptor family pyrin domain containing 3 (NLRP3) inflammasome and following IL-1beta secretion via caspase-1 activation in human monocytes. Synthesis of mature IL-1beta is a 2-step processes. In the 1st step, microbial-derived signals (binding of bacterial products such as LPS) up-regulate pro-IL-1beta, resulting in synthesis of pro-IL-1beta. However, priming signals for NLRP3 inflammasome pathway had not been completely elucidated in sterile inflammatory arthritis including gout. In this study, we investigated the role of TNF-alpha on MSU-mediated IL-1beta induction in human neutrophils.

Methods: Venous peripheral blood was collected from healthy volunteers. Human neutrophils were stimulated with MSU (200 µg/ml), in the presence or absence of TNF-alpha priming (2 to 50 ng/ml). The cellular supernatants were analyzed for IL-1beta, IL-18 and caspase-1 by ELISA. Pro-IL-1beta mRNA expressions in human neutrophils were analyzed by real-time PCR.

Results: TNF-alpha stimulation induced pro-IL-1beta mRNA expression, however, MSU stimulation alone did not induce pro-IL-1beta mRNA expression in neutrophils. TNF-alpha alone or MSU stimulation did not result in efficient IL-1beta secretion. Whereas MSU stimulation to TNF-alpha-primed neutrophils resulted in a marked IL-1beta (Figure 1) as well as IL-18 secretion. TNF-alpha-primed neutrophils secreted cleaved caspase-1 (p20) with MSU stimulation.

Conclusion: These results indicate that priming of human neutrophils with TNF-alpha promotes uric acid-mediated NLRP-3 activation and IL-1beta secretion in the absence of microbial stimulation, that provide new insights into the neutrophils-mediated inflammatory processes in gouty arthritis.

Figure 1. MSU induces IL-1beta synthesis from TNF-alpha-pretreated neutrophils.

Disclosure: S. Sato, None; M. Yashiro, None; T. Asano, None; T. Koga, None; E. Suzuki, None; H. Kobayashi, None; H. Watanabe, None; K. Migita, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/tnf-%ce%b1-potentiates-uric-acid-induced-interleukin-1%ce%b2-secretion-in-human-neutrophils

Abstract Number: 77

Platelets Induce IL-1b Production in Human Monocytes through NLRP3 Inflammasome Activation
SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster I: The Variable World of Intercellular Signalling
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Recent studies have revealed that platelets play pivotal roles in inflammation in addition to hemostasis. The thrombus induces subsequent local inflammation and reversely the local inflammation results in the formation of thrombus. Therefore, to suppress activation of platelets is important for preventing tissue damages. In this study, we aim to reveal effects of activated platelets on IL-1b production in human PBMCs and to clarify the mechanism.

Methods: We investigated whether IL-1b production is enhanced by co-culture of PBMCs and platelets compared to PBMCs alone. We analyzed the production of IL-1b in co-culture of each fraction of PBMCs, T cells, B cells, NK cells and monocytes with platelets. NLRP3, or caspase-1 was knocked down by shRNA in THP-1 monocytes, and IL-1b production induced by co-culture with platelets were compared among shRNA-cell lines and scramble controls. We investigated mediators derived from platelets that induced IL-1b production from monocytes, using inhibitors and neutralization antibodies. Furthermore, we compared CD16 positive monocytes with CD16 negative monocytes, regarding IL-1b productivities, expression levels of NLRP3 and caspase-1 mRNA, and platelets-monocytes-aggregates (PMA) ratios. Activation of platelets in inflammatory diseases, rheumatoid arthritis (RA) and Behcet's disease (BD) were analyzed using CD62P and PMA ratio.

Results: IL-1b production was enhanced by co-culture of PBMCs with platelets compared to PBMCs alone. Among PBMCs, monocytes showed the most prominent IL-1b production by co-culture with platelets. NLRP3- and caspase-1-knockdown THP-1 cells showed significantly lower IL-1b production in co-culture with platelets than scramble controls. CCR5 inhibitor and ATP inhibitor significantly attenuated IL-1b production of monocytes from monocytes, using inhibitors and neutralization antibodies. Furthermore, we compared CD16 positive monocytes with CD16 negative monocytes, regarding IL-1b productivities, expression levels of NLRP3 and caspase-1 mRNA, and platelets-monocytes-aggregates (PMA) ratios. Activation of platelets in inflammatory diseases, rheumatoid arthritis (RA) and Behcet's disease (BD) were analyzed using CD62P and PMA ratio.

Conclusion: Platelets stimulate monocytes and have the ability to enhance IL-1b production via CCL 5 and ATP. They activate NF-kB pathway and NLRP3 inflammasomes in monocytes and enhance IL-1b production. Among monocytes, CD16-positive monocytes are highly bound to platelets and produce IL-1b. Activated platelet may be involved in disease progression of inflammatory diseases.

Disclosure: S. Nakano, None; H. Mitoma, None; S. Kawano, None; S. Inokuchi, None; M. Ayano, None; Y. Kimoto, None; M. Akahoshi, None; Y. Arinobu, None; K. Akashi, None; T. Horiuchi, None; H. Niro, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/platelets-induce-il-1b-production-in-human-monocytes-through-nlrp3-inflammasome-activation

Abstract Number: 78

IL-37 Is Associated with Increased Atherogenesis in Patients with Rheumatoid Arthritis

Barbora Sumova1,2, Tereza Lennerova1,2, Lucie Andres Cerezo1, Hana Hulejova1, Romana Jandova1, Karel Pavelka1,2, Jiri Vencovsky1,2 and Ladislav Senolt1,2, 1Institute of Rheumatology, Prague, Czech Republic, Prague, Czech Republic, 2Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, Prague, Czech Republic
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster I: The Variable World of Intercellular Signalling
Background/Purpose: Interleukin-37 (IL-37) is one of few anti-inflammatory cytokines belonging to the IL-1 cytokine family. It is mainly produced by immune cells of innate immunity such as monocytes and dendritic cells. Recent data suggest its role in several autoimmune and cardiovascular diseases. The aim of this study was to analyse the expression of IL-37 in synovial tissue, synovial fluid (SF) and serum of patients with established rheumatoid arthritis (RA) and osteoarthritis (OA) and to analyse its potential role in the pathogenesis of RA.

Methods: Serum and synovial fluid levels of IL-37 were determined in 52 patients with established RA and 49 control subjects with osteoarthritis (OA) by ELISA. All RA patients fulfilled the 2010 ACR/EULAR criteria for RA. Disease activity was assessed based on the Disease Activity Score of 28 joints (DAS28-ESR). For in vitro studies, fibroblast-like synoviocyte (FLS) were obtained from patients with RA and OA (n=6-9). Serum C-reactive protein (CRP) and lipid profile were determined. Immunofluorescence and immunohistological staining was used to localize IL-37 protein expression in synovial tissue cells (n=4-6) and FLS.

Results: The expression of IL-37 was upregulated in synovial tissue of patients with RA compared to OA, and co-localized with B-lymphocyte, T-lymphocyte, fibroblast-like synoviocyte (FLS) and macrophage specific markers. Further, stimulation with lipopolysacharide (LPS) increased the nuclear expression of IL-37 in synovial fibroblasts cell cultures. The serum levels of IL-37 were significantly higher compared to synovial fluid levels of RA and OA patients (77.50 ± 56.73 vs. 51.50 ± 43.17, p<0.001; 57.00 ± 73.25 vs. 27.00 ± 38.38, p<0.001, respectively). Further, the synovial fluid levels, but not the serum levels, of IL-37 were significantly higher in RA patients compared to OA patients (77.50 ± 56.73 vs. 75.00 ± 73.25, p<0.01) and there was a significant correlation between serum and synovial fluid IL-37 levels in RA patients (r=0.55, p<0.001). Although, neither serum nor synovial fluid IL-37 levels were associated with disease activity, synovial fluid IL-37 levels positively correlated with a leukocytes count in SF (r=0.33, p<0.05) and serum levels of CRP (r=0.31, p<0.05). Interestingly, serum levels of IL-37 negatively correlated with high density lipoprotein (HDL) levels (r=-0.33, p<0.05) and positively with atherogenic index (r=0.34, p<0.05), but not with low density lipoprotein (LDL)-cholesterol, triacylglycerol (TAG) or total cholesterol levels.

Conclusion: Our data suggest possible role of IL-37 in accelerated atherosclerosis and increased cardiovascular burden in patients with RA.

Acknowledgement: This study was supported by Research Project No. 00023728.

Disclosure: B. Sumova, None; T. Lennerova, None; L. Andres Cerezo, None; H. Hulejova, None; R. Jandova, None; K. Pavelka, None; J. Vencovsky, Samsung Bioepis Co., Ltd., Biogen, 5; L. Senolt, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/il-37-is-associated-with-increased-atherogenesis-in-patients-with-rheumatoid-arthritis

Abstract Number: 79

Functional Analysis of the Novel G58V Mutation in the TNFRSF1A Gene Identified in a Family with TNF Receptor-Associated Periodic Syndrome (TRAPS)

Shoko Kodama1, Hidenori Matsuzaki2, Tomoyuki Mukai1, Akiko Nagasu1, Masanori Iseki3, Nami Kurosaki1, Takafumi Mito1, Shunichi Fujita1, Takahiko Horiuchi2, Ryuta Nishikomori5 and Yoshitaka Morita1, 1Department of Rheumatology, Kawasaki Medical School, Kurashiki, Okayama, Japan, 2Department of Hygiene, Kawasaki Medical School, Kurashiki, Okayama, Japan, 3Department of Immunology and Molecular Genetics, Kawasaki Medical School, Kurashiki, Okayama, Japan, 4Department of Internal Medicine, Kyushu University Beppu Hospital, Beppu, Japan, 5Department of Pediatrics, Kyoto University Graduate School of Medicine, Kyoto, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster I: The Variable World of Intercellular Signalling
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Mutations in the TNFRSF1A, which encodes tumor necrosis factor receptor 1 (TNFR1), are associated with the autosomal dominant disease TNF Receptor- Associated Periodic Syndrome (TRAPS). TRAPS is an autoinflammatory disease characterized by intermittent self-limited inflammatory episodes of fever. More than 100 heterozygous TNFRSF1A mutations associated with TRAPS or TRAPS-like clinical phenotype have been reported. T50M mutation and cysteine mutations are reported to cause intracellular accumulation of TNFR1 and exhibit a severe disease phenotype. Single nucleotide polymorphism in TNFR1, such as T61I and R92Q mutations, occurs in
1-5% of the general population and can be associated with a TRAPS-like phenotype. Therefore, there are multiple responsible mechanisms to induce inflammation in patients with TRAPS, and the molecular pathogenesis is not yet fully understood. Recently we have identified a novel mutation, G58V (p.G87V) in TNFRSF1A, in two individuals in a family. They also had T61I mutation, and had suffered from recurrent episodes of intermittent fever and abdominal pain. In this study, we functionally characterized this novel G58V TNFRSF1A mutation.

**Methods:** The possible pathogenicity of the G58V mutation was analyzed using the four online prediction tools (SIFT, Polyphen2, PROVEAN and PANTHER). Wild-type (WT) or mutated TNFRSF1A (T50M, G58V, T61I, R92Q) constructs were generated by cloning the individual cDNAs into the pcDNA3.1 vector. The TNFR1 constructs were transfected into HEK-293 cells. Expression levels of the TNFR1 were examined by western blotting. To evaluate the NF-κB promoter activity, HEK-293 cells were transfected with the TNFR1 constructs along with NF-κB promoter-driven luciferase plasmid and the secreted alkaline phosphatase control vector pSEAP. NF-κB activation levels at 24 hours after the transfection were measured by the dual-luciferase reporter assay.

**Results:** The novel G58V mutation was predicted to be a highly damaging amino acid substitution that could cause a disease. The result is similar to those of pathogenic T50M and cysteine mutations. Expression levels of the WT and mutated TNFR1 proteins are comparable in the whole cell lysates of HEK-293 cells. NF-κB promoter activities in the T50M or the G58V TNFR1-expressing cells were significantly decreased compared to those in WT TNFR1-expressing cells (mean±SD; T50M 29.6±7.5% vs. WT 100±11.5%, p<0.001; G58V 40.1±0.9% vs. WT, p<0.001). The T61I mutation showed a small but significant reduction in NF-κB promoter activity (67.4±18.8%, p<0.05 vs. WT). In contrast, the R92Q mutation did not suppress NF-κB promoter activity (93.2±18.4%).

**Conclusion:** Consistent with a previous report (Blood 2006;108:1320-1327), the T50M mutation suppressed spontaneous NF-κB promoter activity, in spite of the clinical inflammatory features of TRAPS. The newly identified G58V mutation developed the similar phenotype to the pathogenic T50M mutation. These findings indicate that G58V could be a responsible mutation causing TRAPS.

**Disclosure:** S. Kodama, None; H. Matsuzaki, None; T. Mukai, Takeda Pharmaceutical Co., Ltd., 2,Pfizer Japan Inc., 2,Mitsubishi Tanabe Pharma Co., 2,Chugai Pharmaceutical Co., Ltd., 2,AbbVie GK, 2,TEIJIN Pharma Ltd., 2,Astellas Pharma Inc., 2,Japan Blood Products Organization, 2,Shionogi & Co., Ltd., 2,Actelion Pharmaceuticals Japan Ltd., 2,Eli Lilly Japan K.K., 2,DAIICHI SANKYO Co., Ltd., 2,UCB Japan Co. Ltd., 2; A. Nagasu, None; M. Iseki, None; N. Kurosaki, None; T. Mito, None; S. Fujita, None; T. Horuchi, None; R. Nishikomori, None; Y. Morita, Takeda Pharmaceutical Co., Ltd., 2,Pfizer Japan Inc., 2,Mitsubishi Tanabe Pharma Co., 2,Chugai Pharmaceutical Co., Ltd., 2,AbbVie GK, 2,TEIJIN Pharma Ltd., 2,Astellas Pharma Inc., 2,Japan Blood Products Organization, 2,Shionogi & Co., Ltd., 2,Actelion Pharmaceuticals Japan Ltd., 2,Eli Lilly Japan K.K., 2,DAIICHI SANKYO Co., Ltd., 2.


Abstract Number: 80

### Production and Characterization of Human Interferon-Epsilon and Interferon-Kappa to Investigate Their Potential Role in Lupus

**Bethany D. Harris**1, Jessica Schreiter2, Matteo Cesaroni3, Marc Chevrier3, Jarrat Jordan3, Jacqueline Benson3 and Mark R. Walter1,

1Microbiology, University of Alabama at Birmingham, Birmingham, AL, 2Estrela Lupus Venture, Janssen Research and Development, LLC., Spring House, PA, 3Janssen Research and Development, LLC., Spring House, PA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster I: The Variable World of Intercellular Signalling

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** IFNε and IFNκ are members of the type-I IFN family that also consists of 12 IFNα subtypes, IFNb, and IFNω. IFNε and IFNκ share approximately 35% sequence identity with each other and the other 14 IFN proteins. In contrast, IFNα subtypes and IFNω share 60%-95% sequence identity. The role of human IFNε and human IFNκ in autoimmune disease in general, and SLE in particular, is unknown. However, the unique expression of IFNε in vaginal tissues, and IFNκ in the skin, are consistent with the sex bias and extensive cutaneous manifestations of lupus. Work to understand the role of IFNε/κ in SLE has been hampered by a paucity of quality reagents for biochemical and biological analysis. To overcome this problem, we have produced and purified human IFNε and IFNκ from E. coli for biochemical and functional studies.

**Methods:** The IFNs were expressed, refolded, and purified from E.coli, and characterized using SDS-PAGE gel electrophoresis, mass spectrometry, surface plasmon resonance, gene expression using reporter cells lines and PCR, and ELISAs performed using serum for Lupus
Results: Purified IFNε and IFNκ bind to the IFNAR receptors and induce reporter cell gene activation. Gene expression induced by IFNε, or IFNκ, was neutralized by anti-IFNAR neutralizing antibodies, but not by the anti-IFNα neutralizing antibodies examined. IFNε and IFNκ both induced a type-I IFN gene signature in human whole blood. ELISA studies suggest serum from some SLE patients contain antibodies that recognize IFNε or IFNκ.

Conclusion: Taken together, these data suggest IFNε and IFNκ may be contributing to the dysregulated type-I IFN environment observed in some lupus patients, making them putative targets for anti-IFN therapy.


Abstract Number: 81

Selective Inhibition of the Immunoproteasome Subunit LMP7 Is Not Sufficient for Blocking Cytokine Production or Attenuating Progression of Experimental Arthritis

Eric Lowe1, Janet Anderl1, R Andrea Fan1, Henry W. B. Johnson2, Christopher J Kirk3 and Tony Muchamuel4, 1Biology, Kezar Life Sciences, South San Francisco, CA, 2Medicinal Chemistry, Kezar Life Sciences, South San Francisco, CA, 3Kezar Life Sciences, South San Francisco, CA, 4Pharmacology and Toxicology, Kezar Life Sciences, South San Francisco, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster I: The Variable World of Intercellular Signalling
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
The proteasome inhibitor (PI) PR-957/ONX 0914 blocks cytokine production in vitro and attenuates disease progression in experimental models of rheumatoid arthritis (RA) (Nature Medicine 2009 15;781-788). While these anti-inflammatory effects were demonstrated to be due to inhibition of the immunoproteasome versus the constitutive proteasome, there remained a question as to which immunoproteasome subunits, LMP7, LMP2, or MECL-1, were necessary and sufficient for these effects. Here we utilize subunit-selective PIs to address this question.

Methods:
Proteasome subunit inhibition was measured in mice following administration and/or in MOLT-4 cells (human leukemia) and human PBMCs following exposure to the immunoproteasome subunit-selective inhibitors, ONX 0914 (LMP7, LMP2, MECL-1), KZR-329 (LMP7), KZR-504 (LMP2), and KZR-082 (MECL-1), via a subunit active site occupancy assay (ProCISE). Cytokine release (TNF-α, IL-6, IL-12/23p40 [p40], and IFN-γ) was measured in human PBMCs stimulated with either endotoxin (LPS) or antibodies to CD3 and CD28 (anti-CD3/CD28) via Meso Scale Discovery electrochemiluminescent detection (MSD). Cell viability was measured by CellTiter-Glo. The therapeutic effect of selective inhibitors alone or in combination was evaluated in the Collagen Antibody-Induced Arthritis (CAIA) mouse model of RA.

Results:
Consistent with previous studies, at a concentration that inhibited multiple immunoproteasome subunits, ONX 0914 blocked secretion of all cytokines tested in stimulated PBMCs. KZR-329 partially blocked secretion of p40 following LPS stimulation and IFN-γ following anti-CD3/CD28 stimulation, but had minimal effect on TNF-α and IL-6. KZR-504 and KZR-082 had no effect on cytokine production. A combination of KZR-329 and either KZR-504 or KZR-082 resulted in a blockade of cytokine release similar to that of ONX 0914. Blockade of all 3 immunoproteasome subunits resulted in enhanced cytokine inhibition compared to the combination of any 2 selective inhibitors, although the triple combination also resulted in a slight decrease in cell viability. In the CAIA model, KZR-329 resulted in a slight attenuation of disease progression, while KZR-504 treatment had no effect. However, in combination, these two inhibitors prevented disease
potency to arthritis such as RA and IBD. Our new agent CKD-506 has a strong inhibitory effect on histone deacetylase 6 (HDAC6), which is a regulatory enzyme in the development of autoimmune disease. Herein, we introduce a novel inhibitor CKD-506 of HDAC6, which can be used as a novel therapeutic drug for RA and IBD.

**Methods:** The inhibitory activity and selectivity of CKD-506 for HDAC6 were determined by enzyme assay. The acetylation of tubulin in PBMCs by CKD-506 was determined by western blot. The in vivo efficacy of CKD-506 in RA or IBD was evaluated in adjuvant (AIA)- and collagen (CIA)-induced arthritis or DSS- and CD45RB+B6 T cell adaptive transfer-induced colitis animal model respectively. To test the effect of CKD-506 on T cell function, CFSE-labeled effector T cells (Teff) from mouse splenocytes were co-cultured with Teff in the presence of CKD-506 and Teff proliferation was analyzed by flow cytometry. The ex vivo anti-inflammatory effect of CKD-506 was tested with peripheral mononuclear cells (PBMCs) or synovocytes from RA patients. The effect of CKD-506 on inflammatory mediators in T cell adaptive transfer colitis was screened by real time RT-PCR.

**Results:** CKD-506 was a potent and selective inhibitory activity on HDAC6 with an IC50 of 5 nM. CKD-506 highly induced acetylation of tubulin in a substrate for HDAC6 in human PBMCs and lymphoid tissue collected from normal rat. In the arthritis animal models, CKD-506 inhibited severity of arthritis in a dose dependent manner and showed stronger synergistic efficacy with methotrexate combination. The proliferation of Teff was suppressed by CKD-506. Interestingly, the CKD-506 significantly inhibited TNF α but induced IL-10 production in PBMCs. CKD-506 inhibited IL-1b induced CCL-2, CXCL-8, CXCL-10 production in fibroblast-like synovocytes from RA patients. In IBD animal models, CKD-506 significantly repressed disease progression and highly inhibited the expression of inflammatory mediators in colon tissues of T cell adaptive transferred colitis animal. (Current status: Phase I in EU, EudraCT number: 2016-002816-42)
Conclusion: The novel HDAC6 inhibitor, CKD-506 had a therapeutic potential in autoimmune disease such as RA and IBD through the inhibition of inflammatory mediators and the regulation of T cell functions.

Disclosure: J. Shin, Chond Kun Dang Research Institute, 2; N. Ha, Chong Kun Dang Research Institute, 2; D. Bae, Chong Kun Dang Research Institute, 2; D. H. Suh, Chong Kun Dang Research Institute, 2; Y. J. Jang, Chong Kun Dang Research Institute, 2; S. Shon, CKD Research Institute, 2; J. Y. Baek, Chong Kun Dang Research Institute, 2; J. H. Jun, Chong Kun Dang Research Institute, 2; Y. J. Lee, Chong Kun Dang Research Institute, 2; C. Lee, Chong Kun Dang Research Institute, 2; S. H. Kim, Chong Kun Dang Research Institute, 2; H. Yu, Chong Kun Dang Research Institute, 2; Y. I. Choi, CKD Research Institute, 2; K. H. Ryu, Chong Kun Dang Research Institute, 2; S. M. Lee, Chong Kun Dang Research Institute, 2; Y. W. Song, CKD Research Institute, 2; S. K. Seo, Chong Kun Dang Research Institute, 2; S. K. Kim, Chong Kun Dang Research Institute, 2.


Abstract Number: 83

Whole Blood Stimulations Identify Elevated T Cell Cytokines and Altered Granulocyte/Dendritic Cell Signaling in SLE Patients with Variable Disease Activity

Samantha Slight-Webb1, Krista M. Bean1, Holden T. Maeccker2, Paul J. Utz3, Judith A. James4 and Joel M. Guthridge5, 1Arthritis and Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, 2Division of Immunology and Rheumatology, Stanford University School of Medicine, Stanford, CA, 3Medicine, Stanford University School of Medicine, Stanford, CA, 4Arthritis & Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 5Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK.

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster I: The Variable World of Intercellular Signalling
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is characterized by loss of immune tolerance to self-antigens and periods of waxing and waning disease. The clinical aspects of SLE differ significantly from individual to individual and are altered during periods of heightened disease activity. Activation of innate and adaptive signaling pathways, such as endosome expressed TLR3, TLR7 and TLR9, are linked to SLE development, yet differences in innate and adaptive immune signaling and responding cytokine production during variable disease activity remains unclear.

Methods: Peripheral whole blood samples of 10 African American healthy controls and 12 SLE patients with either high (SLEDAI=4) or low (SLEDAI=4) disease activity were stimulated with T-cell receptor (TCR), B-cell receptor (BCR), and Toll-like receptor (TLR) ligands for either 4 minutes (TLR and BCR) or 30 minutes (TCR) for phospho-protein analysis, and 24 hours for cytokine analysis of cell culture supernatants. Phospho-protein analysis was assessed by mass cytometry and analyzed using Cytobank. Plasma cytokine and soluble mediator concentrations of stimulated cell culture supernatants were determined by 37-plex assay by ELISA, Spotfire (version 6.0.1) and GraphPad Prism 5.04 for Windows (GraphPad Software, San Diego, CA) was used for analysis and Mann-Whitney test was used to compare non-normally distributed data. All SLE patients met ACR classification criteria.

Results: SLE patients with high disease activity had a significantly increased fold change in T cell associated cytokines following overnight stimulation, namely sCD40L (p=0.045), IL-2 (p=0.041), and IL-13 (p=0.045) in response to TLR4, TLR7/8 and PMA-Ionomycin compared to patients with low disease activity. In general, most SLE patient cytokines had a decreased fold change in response to stimulation compared to healthy controls (p<0.05). CD4+ T cells and CD8+ T cells exhibited no significant differences in immune signaling following CD3/CD28 stimulation between SLE patients with high and low disease activity. TLR3, TLR4 and TLR9 stimulation drive heightened phosphorylation of STAT5 (p<0.0061) and PLCδ2 (p<0.045) in granulocytes of high SLE disease activity patients compared to low disease activity following Poly I:C, LPS, and CpG, respectively. In contrast, dendritic cells had a reduced signaling response to TLR7/8, TLR9 and BCR stimulation with lower pSTAT3 (TLR7/8) (p=0.0427), pp38 (TLR9) (p=0.0285), and Syk (p=0.0080), pSTAT1 (p=0.046) and pSTAT5 (p=0.0106) (BCR) in high disease activity patients compared to low disease activity. B cells also had reduced phosphorylation of p38 (p=0.0427) in response to TLR4 stimulation of high disease activity patients compared to low disease activity patients.

Conclusion: Our results suggest that altered signaling in response to TLRs in granulocyte and antigen presenting cells may contribute to elevated SLE disease activity by driving T cell proliferation and cytokine production.
Physiological Autoantibodies Against the Endothelin Receptor Type-a Are Critically Involved in the Homeostasis of Immune Cells

Otávio Cabral-Marques¹, Harald Heidecke², Frank Petersen³, Xinhua Yu⁴ and Gabriela Riemekasten⁵, ¹Department of Rheumatology, Vasculitis Center UKSH, University of Lübeck, Luebeck, Germany, ²CellTrend GmbH Luckenwalde, Luckenwalde, Germany, ³Research Centre Borstel, Borstel, Germany, ⁴Lung Centre Borstel, a Leibniz institute, Borstel, Germany, ⁵Department of Rheumatology, Universitatsklinikum Schleswig-Holstein, Lubeck, Germany

First publication: September 18, 2017

Background/Purpose:
G protein-coupled receptors (GPCRs) are a family of integral membrane proteins mediating cell trafficking and cellular homeostasis. In the last decades, several functional autoantibodies (ab) against GPCR have been described to be involved in the pathogenesis of various diseases including systemic sclerosis. As suggested by our studies for the autoantibodies against angiotensin and endothelin receptors, anti-GPCR ab may also be present in healthy individuals. However; the role of autoantibodies in physiology is under debate.

Methods:
Antibodies against 10 different GPCR were analysed in 198 healthy donors, 249 patients with SLE, 376 patients with SSc, 47 patients with rheumatoid arthritis, and 128 patients with granulomatosis with polyangiitis (GPA) by ELISA. In patients with SSc, we also have analysed the ab levels against 31 targets including GPCR, growth factors, and signalling molecules. Possible functional interactions of the 31 autoantibody target molecules were studied by STRING, DAVID, and enriched Gene Ontology. Migration assays were performed as well as cell culture experiments stimulating PBMC with IgG from healthy donors. C56Bl/6 mice were immunized with ETAR and the cellular homeostasis was studied by flow cytometry, histology, and compared with the ab levels against anti-ETAR ab.

Results: The detection of antibodies against 10 different GPCR revealed either increased or decreased antibody levels in a disease-specific manner when compared to healthy donors. Antibodies against ETAR were increased in patients with SSc and SLE and decreased in patients with GPA. In addition to the disease-specific ab signatures, we identified SSc-specific correlations between the 31 target antibodies. Possible functional interactions of the 31 autoantibody revealed a network of GPCR, growth factors, and signalling molecules with endothelin receptor type A (ETAR) in the centre. Migration and locomotion were suggested to be the most significant functions regulated by an assumed antibody network. Accordingly, IgG from healthy donors induced both IL-8 expression in PBMC as well as, depending on the anti-ETAR ab levels, migration of neutrophils and lymphocytes, which was specifically diminished by the ETAR blocker sitaxentan. In vivo, increased anti-ETAR ab levels were associated with an altered homeostasis of innate and adaptive immune cells in different tissues.

Conclusion: As indicated for anti-ETAR antibodies, anti-GPCR antibodies reveal physiological levels in healthy donors and specific alterations in different autoimmune diseases. The antibodies are involved in the homeostasis of immune cells and could contribute to disease pathogenesis.
Enhanced IFN-γ STAT1 Signaling in CD4 T Cell Populations and Attenuated IL-2 STAT5 Signaling Contribute to the Pathogenesis of Rheumatoid Arthritis (RA)

Brandon Pope1, Vishal Sharma2, Molly Boland2, Richard Reynolds2, S. Louis Bridges Jr.3 and Chander Raman4, 1Medicine, University of Alabama at Birmingham, Birmingham, AL, 2University of Alabama at Birmingham, Birmingham, AL, 3Clinical Immunology & Rheum, Univ of Alabama, Birmingham, AL, 4Medicine/Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster I: The Variable World of Intercellular Signalling
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Type I (IFN-α) and type II (IFN-γ) interferons are important mediators of autoimmunity. However, there is conflicting evidence regarding the contribution of IFN-γ to the pathogenesis of RA. We recently showed a strong association of IFN-γ receptor 1 (Ifngr1) expression and of IFN-γ receptor 2 (Ifngr2) expression in peripheral blood mononuclear cells (PBMC) with the presence of RA and its radiographic severity, respectively (Arthritis Rheumatol. 2015 67:1165). IL-2 has essential regulatory function in inflammatory diseases and is considered as a potential therapy for autoimmune disease. In this study, we tested the hypothesis that RA is associated with alterations in IFN-γ and IL-2 STAT signaling within certain subsets of PBMCs.

Methods:

We used a high-definition phospho-flow approach to evaluate the activation of STAT1 (assessed using antibody to phosphorylated tyrosine at position 701 [pY701]), STAT3 (pY705) and STAT5 (pY694) after stimulation with IFN-γ or IL-2. We analyzed subsets of PBMCs from 35 RA patients and 12 healthy controls (HC) as shown in Table.

<table>
<thead>
<tr>
<th>Subset</th>
<th>Markers</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 T cells</td>
<td></td>
</tr>
<tr>
<td>Naïve</td>
<td>CD45RA+CCR7+</td>
</tr>
<tr>
<td>Central Memory</td>
<td>CD45RA-CCR7+</td>
</tr>
<tr>
<td>Effector Memory</td>
<td>CD45RA-CCR7-</td>
</tr>
<tr>
<td>Follicular Helper T cells (Tfh)</td>
<td>CD4+PD1+CX3CR5+</td>
</tr>
<tr>
<td>Regulatory T cells (Treg)</td>
<td>CD4+CD25hiCD127lo</td>
</tr>
<tr>
<td>CD8 T cells</td>
<td></td>
</tr>
<tr>
<td>Naïve</td>
<td>CD45RA+CCR7+</td>
</tr>
<tr>
<td>Central Memory</td>
<td>CD45RA-CCR7+</td>
</tr>
<tr>
<td>Effector Memory</td>
<td>CD45RA-CCR7-</td>
</tr>
<tr>
<td>B cells</td>
<td>CD20+</td>
</tr>
<tr>
<td>Monocytes</td>
<td>CD14+CD11b+</td>
</tr>
</tbody>
</table>

Table. Subsets of PBMCs analyzed in this study.

Results:

We found that IFN-γ induced STAT1 activation was significantly greater in naïve, central memory, Tfh and Treg subsets of CD4+ T cell populations from RA patients compared to HC (p<0.05). IFN-γ induced STAT1 activation in RA was similar to HC in effector memory CD4 T cells, all CD8 T cell populations, B cells and monocytes. Phosphatases dephosphorylate STATs to regulate the activation of cytokine induced signals. We found that phenyl-arsine oxide (PAO), a broadly active phosphatase inhibitor, had no effect on IFN-γ induced STAT1 activation in any T cell population from RA or HC. This result indicates that IFN-γ induced acute activation of STAT1 is not regulated by a phosphatase in RA or HC. IFN-γ did not activate STAT3 any mononuclear cell population among RA or HC. IL-2 very efficiently activated STAT5 in all T and B cell populations in RA and HC. The activation of STAT5 in RA was significantly greater than HC in only one population: effector memory CD4 T cells (p<0.01). Remarkably, treatment with PAO greatly enhanced IL-2 induced activation of STAT5 in RA, but not HC CD4 T cell populations (naïve, central memory effector memory, Treg, Tfh). PAO had no effect on STAT5 activation in CD8
T cell populations from RA and HC. This result suggests that the regulatory activity of IL-2 in RA CD4 T cell populations is attenuated by a STAT5-specific phosphatase.

Conclusion:

Our results indicate that CD4 T cell subpopulation dependent enhanced IFN-γ STAT1 signals and attenuated IL2-STAT5 signals (possibly due to a phosphatase inhibitor) contribute to the pathogenesis of RA. Future studies will focus on stratifying patients by disease activity and other covariates.

Disclosure: B. Pope, None; V. Sharma, None; M. Boland, None; R. Reynolds, None; S. L. Bridges Jr., None; C. Raman, None.


Abstract Number: 86

Regulation of Interleukin-1β Signaling By Inhibition of O-Glc-Nacase in Rheumatoid Arthritis Synovial Fibroblasts

Mahamudul Haque1, Anil Singh2, Kelly Kopczynski1 and Salahuddin Ahmed1, 1Department of Pharmaceutical Sciences, Washington State University, College of Pharmacy, Spokane, WA, 2Washington State University, College of Pharmacy, Spokane, WA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster I: The Variable World of Intercellular Signalling
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: O-GlcNAcylation is an important post-translational modification of nuclear and cytosolic proteins involved in the cytokine signaling networks. Studies show both pro- and anti-inflammatory roles of O-linked N-acetyl glucosamine (O-GlcNAc) depending on different cell types and diseases. However, the role of O-GlcNAcylation in chronic inflammatory diseases such as rheumatoid arthritis (RA) is yet to be explored.

Methods: Human normal SFs (NLSFs) and RASFs were isolated from healthy synovial tissues and RA synovial tissues, respectively, under the IRB-approved protocol. Cell lysates and tissue homogenates were used to determine the differences in the expression of the O-GlcNAcylation in NLSFs and RASFs by Western immunoblotting. Effects of IL-1β (10 ng/ml) on O-GlcNAcylation and two enzymes that control glycosylation (O-GlcNAc transferase, OGT and O-GlcNAcase, OGA) in human RASFs were studied. The effect of OGT inhibitor (OSMI-1; 5-50 µM) or OGA inhibitor (Thiamet-G; 1-10 µM) was evaluated on IL-1β-induced IL-6 and IL-8 production and the underlying mechanisms were studied. In rat adjuvant-induced arthritis (AIA) model, ankle, liver, and spleen homogenates from naïve and AIA rats were analyzed to determine the temporal expression pattern of O-GlcNAcylation.

Results: The expression of O-GlcNAc is upregulated in RA synovial tissues compared with healthy synovial tissues, and also showed a similar trend in SFs isolated from these tissues. We also observed IL-1β stimulation resulted in the upregulation of O-GlcNAc levels in RASFs in vitro. Interestingly, pretreatment of RASFs with OGA inhibitor (Thiamet-G) inhibited IL-1β-induced IL-6 and IL-8 production, whereas OGT inhibitor (OSMI-1) had no inhibitory effect, suggesting that OGA inhibition may be of potential therapeutic value in RA. Evaluation of the IL-1β signaling proteins (TAK1, TAB1, or NF-κBp65) that are critical in relaying downstream signaling showed a marked increase in O-GlcNAc levels upon IL-1β stimulation. Thiamet-G pretreatment showed a protective role of OGA inhibition in regulating inflammation. Similarly, in rat AIA model, we observed a higher O-GlcNAc expression pattern in rat joint homogenates, whereas no change in O-GlcNAc expression was observed in liver. Surprisingly, O-GlcNAcylation in spleen homogenates elicited differential expression at the onset of arthritis (day 8) and at the established arthritis (day 18) compared to naive, which correlated with the clinical scores and splenomegaly in arthritic animals. Interestingly, O-GlcNAc levels of protein such as NF-kBp65 was found to be downregulated in spleen microenvironment whereas that of NF-kBp50 remained the same.

Conclusion: Our findings point to an important mediatory role of O-GlcNAc in stabilizing IL-1β signaling proteins to activate downstream inflammatory proteins. OGA inhibition may serve as a potential therapeutic target in regulating synovial inflammation in RA.

Disclosure: M. Haque, None; A. Singh, None; K. Kopczynski, None; S. Ahmed, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/regulation-of-interleukin-1%ce%b2-signaling-by-inhibition-of-oglcnacase-in-rheumatoid-arthritis-synovial-fibroblasts
A Novel Histone Deacetylase 6 Inhibitor, CKD-M808, Regulates the Adhesion and Migration of Fibroblast-like Synoviocytes, and Enhances Suppressive Function of Regulatory T Cells in Rheumatoid Arthritis

Sehui Shon¹, Ji Soo Park¹, Shin Eui Kang¹, Jeong Yeon Kim¹, Dong-Hyeon Suh², Daekwon Bae², Nina Ha², Young Il Choi², Jin Kyun Park¹,³, Eun Young Lee³, Eun Bong Lee³ and Yeong Wook Song³,⁴

¹Department of Molecular Medicine and Biopharmaceutical Sciences, Graduate School of Convergence Science and Technology, and College of Medicine, Seoul National University, Seoul, Korea, Republic of (South), ²Research Institute of Chong Kun Dang Pharmaceutical Corporation, Yongin, Korea, Republic of (South), ³Division of Rheumatology, Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea, Republic of (South), ⁴Department of Molecular Medicine and Biopharmaceutical Sciences, Graduate School of Convergence Science and Technology, Seoul National University, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster I: The Variable World of Intercellular Signalling
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease characterized by bone and cartilage destruction with leukocyte infiltration and activation at synovial tissue. Recently, upregulated histone deacetylase (HDAC) activity has been reported in peripheral blood mononuclear cells (PBMCs) from RA patients. In addition, it has been reported that HDAC inhibitor (HDACi) improved cancers, neurological diseases and inflammatory diseases by suppressing pro-inflammatory cytokines such as TNF-α and IL-6. Previously, we reported that a novel histone deacetylase 6 inhibitor (HDAC6i), CKD-M808 (M808) decreased clinical score in adjuvant induced arthritis (AIA) rat model. Here, we investigated the effect of M808 on cell adhesion, migration and suppressive function of regulatory T cells (Treg) derived from RA patients.

Methods:
Fibroblast-like synoviocytes (FLS) were isolated from synovial tissues of RA patients, and treated with HDAC6i such as tubastatin A and M808 under IL-1β stimulation. The expression of α-tubulin, acetylated tubulin, intracellular adhesion molecule (ICAM)-1 and vascular cell adhesion molecule (VCAM)-1 were measured in RA FLS by western blotting. The levels of CCL2, CXCL8 and CXCL10 were measured in culture supernatant. Wound healing assay were performed to confirm cell migration ability. The adhesion of U937 or Jurkat cells onto RA FLS was measured by cell adhesion assay. CD4+CD25- T cells (effector T cells, Teff) were isolated from RA PBMCs, and differentiated into induced Treg (iTreg) under differentiating media. After the differentiation, Foxp3 and CTLA-4 were analyzed by flow cytometry. iTreg were also co-cultured with carboxyfluorescein succinimidyl ester (CFSE)-labeled Teff derived from healthy donor. The proliferation of Teff was analyzed by flow cytometry.

Results:
M808 increased the acetylation of tubulin in RA FLS. The number of migrated cell was decreased in M808-treated RA FLS without the change in cell viability. The expression of ICAM-1 and VCAM-1 were decreased in HDAC6i-treated groups in a dose-dependent manner. M808 reduced the levels of chemokines including CCL2, CXCL8 and CXCL10 in RA FLS. In addition, M808 attenuated the adhesion of U937 and Jurkat cells on RA FLS. The suppressive function of iTreg were significantly increased in M808-treated groups.

Conclusion:
M808 increased the acetylation of tubulin, and decreased the migration of RA FLS. M808 also decreased the expression of ICAM-1, VCAM-1 and chemokines such as CCL2, CXCL8 and CXCL10. The adhesion between RA FLS and U937 or Jurkat cells was decreased in the presence of M808. M808 increased the suppressive function of iTreg derived from RA PBMCs. The novel HDAC6i, M808, may provide a new therapeutic option in RA patients.
Mind Map Use in Rheumatology Education

Alex Papou, Rheumatology, Consultant Rheumatologist, North West Anglia NHS Foundation Trust, Peterborough City Hospital, Peterborough, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Education Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Medical knowledge is a constantly expanding and changing field. One of the challenges for healthcare professionals, including doctors in training, is to be able to find the most relevant source of reliable information with minimal reasonable efforts. Search for information is often time-consuming and each educational resource has limitations. Traditional forms of study such as textbooks are often out-of-date and inaccessible at work; internet-based information is often too abundant, and can be disorganized, not relevant to clinical practice, and inaccurate; direct learning from seniors is limited in a busy hospital environment; ward experience learning can lead to mistakes. There is an unmet need for a unified resource that will serve the purpose of being accessible wherever you are, comprehensive, reliable, up-to-date, and easily searchable.

Methods: A simple way to organize information is to use mind maps. A mind map is a tree-like structure that consists of radial nodes when the next level can be expanded or collapsed by a mouse click or a tap. Within a few clicks you can reach any information you need, visual hierarchical approach is intuitive and allows easy search, associated topics can be linked, and a web-based application offers easy modification and update of the mind map or its adjustment according to the needs of a trainee.

Results: We have developed a free mind mapping educational resource for health care professionals (www.rheumatologymindmap.com, www.rheumatologymindmap.co.uk, images 1-3). It is based on current rheumatology practice in the United Kingdom and is being updated in accordance with the new information and feedback received from the UK trainees. The mind map has direct online links to appropriate British, European, and American guidelines, incorporates downloadable templates, has hyperlinks to online calculators and to websites providing advice for doctors and patients. The mind map works in desktop and mobile browsers and can be transferred to other platforms including Android and iOS.

Conclusion: Mind mapping can offer a new structured approach in medical training and clinical practice, with fast access to the relevant information. The rheumatology mind map can become an important practical tool and its main benefits are accessibility, intuitive interface, easy search, and modifiability.
The CLASS-Rheum (Critical Literature Assessment Skills Support – Rheumatology) Question-Based Tool Is Associated with Sustained Improvement in Knowledge of Relevant Epidemiology and Biostatistics in Rheumatology Fellows

Lisa A. Mandl1, Julie Schell2, Karina Torralba3, Pascale Schwab4, Christopher E. Collins5, Lisa Criscione-Schreiber6, Anne R. Bass1, Jessica R. Berman1, Alexa Adams7, Michael D. Tiongson8, Stephen A. Page9, Jackie Szymonifka10 and Juliet Aizer1, 1Rheumatology, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY; 2The University of Texas at Austin, Austin, TX; 3Rheumatology, Loma Linda University, Loma Linda, CA; 4Rheumatology, Oregon Health and Science University, Portland, OR; 5Medicine, MedStar Washington Hospital Center/Georgetown University Medical Center, Washington, DC; 6Internal Medicine, Duke University Medical Center, Durham, NC; 7Hospital for Special Surgery/Weill Cornell Medicine, New York, NY; 8Hospital for Special Surgery, New York, NY; 9Division of Rheumatology, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY; 10Rheumatology, Hospital for Special Surgery, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Education Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Understanding epidemiology and biostatistics (epi/biostats) is crucial for rheumatologists to interpret literature and make appropriate data-driven clinical decisions. Based on retrieval-enhanced learning theory, we developed CLASS-Rheum, a cloud-based modular assessment tool to support learning of epi/biostats relevant to rheumatology fellows. In this study we test whether sequential administration of isomorphic Question Sets is associated with sustained learning.

Methods:
CLASS-Rheum Question Sets are organized into 10 modules, each focused on a concept in epi/biostats, framed in rheumatologic context. Administration via Learning Catalytics® allows access on web-enabled devices. With IRB-exemption, 6 rheumatology programs of varying size across the US participated in sequential administration of 2 Question Sets. Question Set 2 (QS2) was comprised of 56 unique questions assessing the same content and learning objectives as Question Set 1 (QS1). We examined face and construct validity, item difficulty, psychometrics, and change in knowledge with sequential administration of Question Sets. Fellows providing individual responses to > 50% of questions were included in the quantitative analysis. Mean change in percent correct and change in Likert-scale ratings were compared with paired-t tests and Wilcoxon Signed-Rank tests, respectively. Mixed effects modeling was used to examine whether year of fellowship impacted percent correct (SAS v9.4).

Results:
From 2/2016-5/2017, 51 rheumatology fellows enrolled in CLASS-Rheum. 39 provided individual responses to >50% of questions and were included in the quantitative analysis. 67% of participating fellows were women. At enrollment, 10% had degrees in epi/biostats, 61% reported being very interested in epi/biostats, and 65% considered their understanding of epi/biostats average compared to other rheumatology fellows. 28 fellows’ data were analyzed in QS1 (all first time takers), and 25 fellows’ in QS2 (11 first time takers). 14 fellows completed both Question Sets, with mean interval between pairs of isomorphic modules of 260 days (SD 70.7).

Difficulty was similar between modules. Mean percent correct for first time takers was 64.4% (SD 15.1%) for QS1 vs. 64.8 (SD 11.9%) for QS2 (p = 0.93). Point biserial correlations were positive for 93% of questions from QS1 and QS2, suggesting strong psychometrics. Based on data from QS1 and QS2, 3rd year fellows had statistically higher average scores than 1st year fellows (p=0.032).

Among the 14 fellows completing QS1 and QS2, mean percent correct increased from 61.8% to 67.9% (p = 0.036). 14% of fellows’ scores increased >20%. Upon completing QS1, 14/14 fellows described CLASS-Rheum as “very useful/useful” in learning epi/biostats, as did 13/14 after completing QS2 (p=0.75).

Conclusion:
Two psychometrically sound modular Question Sets (“CLASS-Rheum”) covering important concepts in epi/biostats, framed in a rheumatologic context, were successfully administered to fellows in diverse rheumatology training programs. Sustained increases in knowledge were demonstrated with sequential administration of isomorphic Question Sets over 15 months. CLASS-Rheum will be evaluated in additional programs.

Disclosure: L. A. Mandl, None; J. Schell, None; K. Torralba, None; P. Schwab, None; C. E. Collins, None; L. Criscione-Schreiber, None; A. R. Bass, None; J. R. Berman, None; A. Adams, None; M. D. Tiongson, None; S. A. Paget, None; J. Szymonifka, None; J. Aizer, None.


Abstract Number: 90

Developing a Pediatric Rheumatology Curriculum for Pediatric Residents

Miriah Gillispie1,2 and Amanda Brown3, 1Texas Children's Hospital, Houston, TX, 2Pediatrics, Department of IAR, Baylor College of Medicine, Houston, TX, 3Allergy, Immunology and Rheumatology, Texas Children's Hospital, houston, TX

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Education Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM
Background/Purpose: The purpose of this project was to develop a curriculum to teach residents these skills. Due to a paucity of pediatric rheumatologists and the growing patient population, pediatricians must be able to recognize and begin a basic work up for suspected autoimmune disease. The project includes 30-minute case based lectures on the topics of systemic lupus erythematosis (SLE), juvenile idiopathic arthritis (JIA), periodic fever, aphthous stomatitis, pharyngitis, adenitis (PFAPA), Kawasaki Disease (KD), juvenile dermatomyositis (JDM), and Henoch Schönlein purpura (HSP).

There are 300,000 children in the US with rheumatic conditions and the incidence is increasing with better recognition of this subset of chronic diseases. This makes rheumatic disease one of the most common chronic illnesses in pediatrics. Most recent estimates from 2015 show that there are 407 pediatric rheumatologists in the country and of those, many have very little clinical time are involved more heavily in research. Sadly, most recent estimates suggest that up to 10% of pediatric rheumatologists will be retiring within the next several years and that demand exceeds supply by 25-50%. Many children who do have access to a pediatric rheumatologist travel >4 hours to see a subspecialist and wait times at many centers are several weeks to months. As a result, the practicing pediatric rheumatologists often must rely heavily on generalists and those in other subspecialties to help manage these patients. However, 40% of residency programs do not have access to an onsite pediatric rheumatologist and 11 states are still without a board certified/eligible pediatric rheumatologist. Even within institutions who have access to a pediatric rheumatologist, exposure is limited with estimates of approximately 5 hours of teaching time for the residents who do not rotate with rheumatology as an elective at our institution. This is similar to exposure in other institutions who have pediatric rheumatology.

Methods: All pediatrics and med-peds residents at our institution were anonymously surveyed to get their opinion on which topics in rheumatology they thought were most important and also on their preference for content delivery. Based on responses, a series of six lectures were composed in a case based, interactive format. Second year pediatrics and third year med-peds residents rotate through the inpatient rheumatology service and received this curriculum. Pre and post surveys were used to evaluate improvement in comfort level with rheumatology topics.

Results: Per self-assessment from the residents’ comfort level with laboratory work up, musculoskeletal exam, and referrals improved after working through cases in the curriculum while on the inpatient rotation.

Conclusion: Although exposure to pediatric rheumatology is limited in our institution, we were able to effectively increase comfort level with regards to work up and diagnosis of autoimmune diseases. Ideally, exposure to patients in both the inpatient and outpatient setting would also help increase comfort level with this subset of patients, but ACGME guidelines for residency training do not require exposure to pediatric rheumatology during residency training.

Disclosure: M. Gillispie, None; A. Brown, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/developing-a-pediatric-rheumatology-curriculum-for-pediatric-residents

Abstract Number: 91

Development of Musculoskeletal Physical Examination Checklists: A Formal Consensus Project Involving National Educators

Andrea Barker1, Arben Brahaj2, Paula Carvalho3, Analia Castiglioni4, Dan Doan5, Krista Gage6, Karen E. Hansen7, Micheline Hearth-Holmes8,9, Laura Kim10, Antonio A. Lazzari11, Tiffany F. Lin12, Christopher Olson13, Vanessa C. O sting14, Mary M. Pearson15, Noelle A. Rolle4, Bernadette C. Siaton16,17, Joan Marie Von Feldt18, Yasuharu Okuda19 and Michael J. Battstone1. 1Veterans Affairs Salt Lake City Health Care System and University of Utah School of Medicine, Salt Lake City, UT; 2VA New England Healthcare System, Bedford, MA; 3Boise VAMC, Boise, ID; 4Orlando VAMC and University of Central Florida, Orlando, FL; 5VA Puget Sound Healthcare System and University of Washington, Seattle, WA; 6San Francisco VAMC, San Francisco, CA; 7Department of Medicine, Division of Rheumatology, University of Wisconsin School of Medicine and Public Health, Madison, WI; 8Internal Medicine/Rheumatology Division, Univ. of Nebraska Medical Center, Omaha, NE; 9Internal Medicine, Omaha VA Medical Center and University of Nebraska Medical Center, Omaha, NE; 10Orlando VAMC and VHA SimLEARN National Center, Orlando, FL; 11VA Boston Healthcare System & Boston University School of Medicine, Boston, MA; 12VHA Madison & University of Wisconsin, Madison, WI; 13JA Haley Veterans Hospital, Tampa, FL; 14JA Haley Veterans Hospital & University of South Florida, Tampa, FL; 15San Francisco VAMC & University of California, San Francisco, San Francisco, CA; 16Baltimore VAMC, Baltimore, MD; 17Rheumatology, University of Maryland School of Medicine, Baltimore, MD; 18Rheumatology, University of Pennsylvania/Philadelphia VAMC, Philadelphia, PA; 19VHA SimLEARN National Center, Orlando, FL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Background/Purpose:
Musculoskeletal (MSK) physical exam checklists for a Veterans Affairs (VA) continuing professional development (CPD) course were developed and validated in a broad educational effort for primary care providers (PCPs). These tools were introduced to national leaders in MSK education in the VA National Simulation, Learning, Education and Research Network (SimLEARN) MSK Master Educator course. The aim of this project is to further enhance these through a statistically guided consensus effort.

Methods:
Twenty MSK educators attending the 2017 MSK Master Educator course were invited to participate in a 3-step Delphi process. Step 1 involved review of current versions of the 21-item shoulder and 26-item knee checklists with invitation to suggest additional items. In step 2, each educator rated every item’s importance to be included in a curriculum for PCPs, using a 5-point Likert scale (1 = not at all important; 5 = extremely important). In the 3rd step, educators were given the groups’ average rating for each item, reminded of their own initial rating, and asked to make a final 5-point rating. Individual responses to each step remained anonymous. After the final step, items meeting the predetermined criteria of mean ≥4 and standard deviation ≤1 were retained; these items defined the consensus checklists.

Results:
Eighteen educators (90%; 16 physicians, 1 physician assistant, 1 nurse practitioner) completed the project. Nine educators’ practice area was primary care; 9 were in specialty care, of which 7 were rheumatologists.

In step 1, 11 items were added to the shoulder and 14 to the knee checklists. There were no significant differences in ratings from step 2 to step 3, though standard deviations were significantly smaller for both shoulder and knee (p < 0.005) in step 3, after respondents were provided with the groups’ mean ratings from step 2.

Final ratings for the shoulder and knee are listed in the figures below:

<table>
<thead>
<tr>
<th>Item</th>
<th>Original Examination Maneuver</th>
<th>Not at all important for primary care</th>
<th>Slightly important for primary care</th>
<th>Somewhat important for primary care</th>
<th>Very important for primary care</th>
<th>Extremely important for primary care</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Abduction apprehension</td>
<td>4.8 (3.0)</td>
<td>4.1 (3.2)</td>
<td>4.1 (3.3)</td>
<td>4.8 (4.0)</td>
<td>Yes</td>
</tr>
<tr>
<td>2.</td>
<td>General observation – symmetry/alignments</td>
<td>4.0 (3.5)</td>
<td>4.1 (3.7)</td>
<td>4.2 (3.8)</td>
<td>4.4 (3.9)</td>
<td>Yes</td>
</tr>
<tr>
<td>3.</td>
<td>Observe for sequestering</td>
<td>3.1 (3.0)</td>
<td>3.3 (3.4)</td>
<td>3.4 (3.6)</td>
<td>3.6 (3.8)</td>
<td>No</td>
</tr>
<tr>
<td>4.</td>
<td>Palpate sternoclavicular joint</td>
<td>3.8 (3.4)</td>
<td>3.6 (3.7)</td>
<td>3.7 (3.8)</td>
<td>3.8 (3.8)</td>
<td>No</td>
</tr>
<tr>
<td>5.</td>
<td>Palpate sternoclavicular joint</td>
<td>3.9 (3.8)</td>
<td>3.6 (3.7)</td>
<td>3.7 (3.8)</td>
<td>3.6 (3.8)</td>
<td>No</td>
</tr>
<tr>
<td>6.</td>
<td>Palpate biceps tendon – big head</td>
<td>4.8 (3.5)</td>
<td>4.3 (3.6)</td>
<td>4.4 (3.7)</td>
<td>4.3 (3.5)</td>
<td>Yes</td>
</tr>
<tr>
<td>7.</td>
<td>Palpate subacromial bursal tendon</td>
<td>3.8 (3.5)</td>
<td>3.6 (3.7)</td>
<td>3.5 (3.7)</td>
<td>3.5 (3.6)</td>
<td>No</td>
</tr>
<tr>
<td>8.</td>
<td>Estimate range of motion – abduction plane</td>
<td>3.0 (3.5)</td>
<td>3.5 (3.7)</td>
<td>3.5 (3.6)</td>
<td>3.5 (3.6)</td>
<td>No</td>
</tr>
<tr>
<td>9.</td>
<td>Subscapularis strength – empty can test</td>
<td>3.5 (3.5)</td>
<td>3.5 (3.6)</td>
<td>3.5 (3.6)</td>
<td>3.3 (3.6)</td>
<td>No</td>
</tr>
<tr>
<td>10.</td>
<td>Interosseous ROM – active external rotation</td>
<td>3.0 (3.0)</td>
<td>3.0 (3.0)</td>
<td>3.0 (3.0)</td>
<td>3.0 (3.2)</td>
<td>No</td>
</tr>
<tr>
<td>11.</td>
<td>Infraspinalus strength – external rotation against resistance</td>
<td>3.0 (3.0)</td>
<td>3.0 (3.0)</td>
<td>3.0 (3.0)</td>
<td>3.0 (3.0)</td>
<td>No</td>
</tr>
<tr>
<td>12.</td>
<td>Supraspinatus strength – full press test</td>
<td>4.0 (4.0)</td>
<td>4.0 (4.0)</td>
<td>4.0 (4.0)</td>
<td>4.0 (4.0)</td>
<td>Yes</td>
</tr>
<tr>
<td>13.</td>
<td>Subscapularis ROM – active internal rotation against plane</td>
<td>3.3 (3.5)</td>
<td>3.3 (3.5)</td>
<td>3.3 (3.5)</td>
<td>3.3 (3.5)</td>
<td>Yes</td>
</tr>
<tr>
<td>14.</td>
<td>Subscapularis strength – lift off test</td>
<td>4.5 (4.0)</td>
<td>4.4 (4.0)</td>
<td>4.4 (4.0)</td>
<td>4.4 (4.0)</td>
<td>Yes</td>
</tr>
<tr>
<td>15.</td>
<td>Teras minor ROM</td>
<td>3.9 (3.5)</td>
<td>3.6 (3.7)</td>
<td>3.6 (3.7)</td>
<td>3.5 (3.6)</td>
<td>Yes</td>
</tr>
<tr>
<td>16.</td>
<td>Teres minor strength – biceps’ test</td>
<td>4.5 (4.0)</td>
<td>4.4 (4.0)</td>
<td>4.4 (4.0)</td>
<td>4.4 (4.0)</td>
<td>Yes</td>
</tr>
<tr>
<td>17.</td>
<td>Hawkins’ test</td>
<td>4.4 (4.0)</td>
<td>4.4 (4.0)</td>
<td>4.4 (4.0)</td>
<td>4.4 (4.0)</td>
<td>Yes</td>
</tr>
<tr>
<td>18.</td>
<td>Neer’s test</td>
<td>4.4 (4.0)</td>
<td>4.4 (4.0)</td>
<td>4.4 (4.0)</td>
<td>4.4 (4.0)</td>
<td>Yes</td>
</tr>
<tr>
<td>19.</td>
<td>Sulcus’ test</td>
<td>3.3 (3.0)</td>
<td>3.3 (3.0)</td>
<td>3.3 (3.0)</td>
<td>3.3 (3.0)</td>
<td>No</td>
</tr>
<tr>
<td>20.</td>
<td>Yergason’s test</td>
<td>3.4 (3.0)</td>
<td>3.4 (3.0)</td>
<td>3.4 (3.0)</td>
<td>3.4 (3.0)</td>
<td>Yes</td>
</tr>
<tr>
<td>21.</td>
<td>Cross arm test</td>
<td>4.4 (4.0)</td>
<td>4.4 (4.0)</td>
<td>4.4 (4.0)</td>
<td>4.4 (4.0)</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Total items retained: 20 (95%)

<table>
<thead>
<tr>
<th>Item</th>
<th>Examination Items added from Step 1</th>
<th>Not at all important for primary care</th>
<th>Slightly important for primary care</th>
<th>Somewhat important for primary care</th>
<th>Very important for primary care</th>
<th>Extremely important for primary care</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Observation – note posture</td>
<td>3.4 (3.0)</td>
<td>3.3 (3.0)</td>
<td>3.0 (2.9)</td>
<td>3.8 (3.9)</td>
<td>No</td>
</tr>
<tr>
<td>2.</td>
<td>Overhead ROM screening – AC joint vs. muscle disease</td>
<td>3.0 (3.0)</td>
<td>2.9 (3.0)</td>
<td>2.9 (3.0)</td>
<td>3.0 (3.0)</td>
<td>No</td>
</tr>
<tr>
<td>3.</td>
<td>Biceps tendon ROM screening for joint vs. muscle disease</td>
<td>2.9 (3.0)</td>
<td>2.9 (3.0)</td>
<td>2.9 (3.0)</td>
<td>3.0 (3.0)</td>
<td>No</td>
</tr>
<tr>
<td>4.</td>
<td>Palpation – bicipital tubercle</td>
<td>3.3 (3.0)</td>
<td>3.3 (3.0)</td>
<td>3.3 (3.0)</td>
<td>3.3 (3.0)</td>
<td>No</td>
</tr>
<tr>
<td>5.</td>
<td>Palpation – bicipital tubercle</td>
<td>3.3 (3.0)</td>
<td>3.3 (3.0)</td>
<td>3.3 (3.0)</td>
<td>3.3 (3.0)</td>
<td>No</td>
</tr>
<tr>
<td>6.</td>
<td>ROM – specific passive ROM for each movement</td>
<td>3.3 (3.0)</td>
<td>3.3 (3.0)</td>
<td>3.3 (3.0)</td>
<td>3.3 (3.0)</td>
<td>No</td>
</tr>
<tr>
<td>7.</td>
<td>Shoulder MDI with elbow flexed to 90° and external rotation</td>
<td>3.0 (3.0)</td>
<td>2.9 (3.0)</td>
<td>2.9 (3.0)</td>
<td>3.0 (3.0)</td>
<td>No</td>
</tr>
<tr>
<td>8.</td>
<td>Snowing test</td>
<td>3.3 (3.0)</td>
<td>3.3 (3.0)</td>
<td>3.3 (3.0)</td>
<td>3.3 (3.0)</td>
<td>Yes</td>
</tr>
<tr>
<td>9.</td>
<td>Shoulder internal rotation lag test</td>
<td>3.0 (3.0)</td>
<td>3.0 (3.0)</td>
<td>3.0 (3.0)</td>
<td>3.0 (3.0)</td>
<td>No</td>
</tr>
<tr>
<td>10.</td>
<td>Internal rotation lag test</td>
<td>3.3 (3.0)</td>
<td>3.3 (3.0)</td>
<td>3.3 (3.0)</td>
<td>3.3 (3.0)</td>
<td>No</td>
</tr>
<tr>
<td>11.</td>
<td>Lutken palpation testing</td>
<td>2.8 (3.0)</td>
<td>2.8 (3.0)</td>
<td>2.8 (3.0)</td>
<td>2.8 (3.0)</td>
<td>No</td>
</tr>
</tbody>
</table>

Total items retained: 0
When stratifying ratings by practice area, significant differences were seen between ratings by those in primary care and those in specialty care, for both shoulder (p = 0.03) and knee (p = 0.004).

**Conclusion:**

This is a feasible method for a national group of experts to create statistically guided educational tools. The differences between specialist and primary care educators’ ratings of item importance suggest these groups may have different expectations for CPD programs. These findings should inform future educational initiatives, ensuring that both subject matter experts and those familiar with the clinical duties of target learners are included in consensus projects.

**Disclosure:** A. Barker, None; A. Brahaj, None; P. Carvalho, None; A. Castiglioni, None; D. Doan, None; K. Gager, None; K. E. Hansen, None; M. Hearth-Holmes, None; L. Kim, None; A. A. Lazzari, None; T. F. Lin, None; C. Olson, None; V. C. Osting, None; M. M. Pearson, None; N. A. Rolle, None; B. C. Siaton, None; J. M. Von Feldt, None; Y. Okuda, None; M. J. Battistone, None.

**View Abstract and Citation Information Online - http://acrabstracts.org/abstract/development-of-musculoskeletal-physical-examination-checklists-a-formal-consensus-project-involving-national-educators**

**Abstract Number: 92**

**Hospital for Special Surgery Academy of Rheumatology Medical Educators: 5 Year Outcomes Demonstrate the Value of Supporting Education Research in the Academic Environment**

Jessica R. Berman1, Juliet Aizer1, Anne R. Bass2, Edward Parrish1, Laura Robbins3, Michael D. Tiongson4 and Stephen A. Paget1,

1Rheumatology, Hospital for Special Surgery Weill Cornell Medical College, New York, NY, 2Rheumatology, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, 3Education & Academic Affairs, Hospital for Special Surgery, New York, NY, 4Hospital for Special Surgery, New York, NY
Background/Purpose: It has been previously demonstrated that educators do not receive the same recognition as their colleagues in clinical and basic science, and financial support for education research is often inadequate. With this in mind, in 2011 the Academy of Rheumatology Medical Educators was founded at Hospital for Special Surgery (HSS) in order to: 1) create a stimulating academic environment for educators that enhances the quality of teaching and 2) award pilot grants to educators interested in research.

Methods: Directed fund-raising was earmarked specifically for annually awarded education grants to serve as a hospital wide impetus for the development of new teaching programs and curricular change through new or improved opportunities for teaching and learning. A request for proposals (RFP) was sent out yearly from 2011-2016 to the HSS rheumatology faculty. One year the RFP was extended to the entire hospital offering matching funds with departments such as nursing and anesthesia. Grants of up to $50,000 a year were awarded to applications with merit that met the requisite funding priorities. All grants were reviewed and scored according to Glassick’s criteria for scholarship by individuals nationally recognized for their education expertise and reviewed by the HSS Education Council, which provides ongoing oversight of the Academy’s activities.

Results: To date, 23 grants have been awarded for a total of $690,695 in funding. The awardees have produced 19 national meeting abstracts, given 24 presentations (11 posters, 13 oral) at national meetings and written 7 manuscripts (5 published, 2 submitted) and 2 editorials. Funding has resulted in the creation of 8 unique curricula and two iBooks. Diverse topics have been represented such as the assessment of professionalism, new pedagogical techniques for teaching epidemiology to fellows, use of technology in education, an inter-professional gout education program for patients and a hospital based mentorship program.

Conclusion: The HSS Rheumatology Academy aims to create a stimulating academic educational environment that enhances the quality of teaching and promotes teaching careers and education research. The formation of the education research funding pilot highlights the talents of heretofore unsupported and unrecognized teaching faculty by allowing them to distinguish themselves academically. This emphasizes the clear advantages of such a formalized structure to achieve the hospital’s heightened educational goals and demonstrates the importance of recognizing the quality of education research as equivalent with clinical and basic science research.

Disclosure: J. R. Berman, None; J. Aizer, None; A. R. Bass, None; E. Parrish, None; L. Robbins, None; M. D. Tiongson, None; S. A. Paget, None.


Abstract Number: 93

Peer-Developed E-Learning Resource Can Address Rheumatology Knowledge Gaps in Junior Learners

Larissa Petriw1, Tabitha Kung2 and Mala Joneja2, 1Internal Medicine, Queen's University, Kingston, ON, Canada, 2Rheumatology, Queen's University, Kingston, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Education Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The symptoms related to Rheumatologic diseases are responsible for one third of visits to general practitioners, yet medical students and residents remain inadequately prepared to approach and manage Rheumatologic problems (Freedman and Bernstein, 2002). There are few resources available to junior learners in Rheumatology. Several handbooks written by Canadian Rheumatologists exist, though none combine clinical images, interactivity and case-based learning in an electronic format. Electronic learning (e-learning) provides a highly flexible medium for information presentation, multimedia and self-assessment in a mobile, searchable, user-friendly platform. Evidence suggests that peer-generated e-learning adds value, though most residents do not have extensive software expertise in developing e-
resources. Here we present an interactive, peer-developed case-based Rheumatology iBook produced by residents for learners in Rheumatology aimed to address these gaps.

**Methods:** Our iBook was written in the free, easy-to-use program “iBooks Author”. The target audience was medical students and residents completing a rotation in Rheumatology. Key learning objectives for a Rheumatology rotation were identified and addressed as the main sections of the iBook. Sections include approaches to common rheumatologic presentations, case presentations of rheumatologic conditions commonly encountered over a rotation or general practice, and appendices, including approaches to serology, medications and joint aspiration. Clinical images and self-assessments add interactivity. The iBook was evaluated in a survey of learners rotating through Rheumatology at Queen’s University, with pre- and post-rotation surveys.

**Results:** The survey is ongoing, however preliminary data shows high satisfaction with our resource and improvement in learners’ knowledge. All learners surveyed agree or strongly agree the iBook is user-friendly (75% strongly agree), well organized (75% agree, 25% strongly agree), and has an appropriate level of material and cases (75% strongly agree). All participants found the iBook useful for rotation preparation (50% agree, 50% strongly agree) and would recommend it to a colleague (57% agree, 43% strongly agree). All participants improved their comfort with Rheumatology topics on a Likert scale pre- and post-assessment. Pre-intervention global comfort level was 2.3/4 and post-intervention was 3/4, with similar trends of improvement in the specific topics surveyed. The iBook itself was free and easy to create without additional training in computer programming.

**Conclusion:** We present the first peer-developed e-learning resource of its kind in Rheumatology that can be used as a rotation resource for junior learners across the country. Although content writing remains labour-intensive, the iBook modality allows easy updating and minimal knowledge of programming by the writers. Conversion to non-iBook format is possible for further distribution across platforms. The iBook structure can easily be adapted to other medical education topics and is a user-friendly method of e-publication for busy residents interested in medical education.

**Disclosure:** L. Petriw, None; T. Kung, None; M. Joneja, None.

**View Abstract and Citation Information Online** - [http://acrabstracts.org/abstract/peer-developed-e-learning-resource-can-address-rheumatology-knowledge-gaps-in-junior-learners](http://acrabstracts.org/abstract/peer-developed-e-learning-resource-can-address-rheumatology-knowledge-gaps-in-junior-learners)

**Abstract Number:** 94

**Validity Evidence for an Objective Structured Clinical Examination Station to Assess Knee Arthrocentesis Skill**

**Tawnie Braaten**1, Andrea Barker2, J. Peter Beek3 and Michael J. Battistone2, 1University of Utah, Salt Lake City, UT, 2Veterans Affairs Salt Lake City Health Care System and University of Utah School of Medicine, Salt Lake City, UT, 3Orthopaedics, Salt Lake City VA Medical Center and University of Utah, Salt Lake City, UT

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017
**Session Title:** Education Poster
**Session Type:** ACR Poster Session A
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

We developed an objective structured clinical examination (OSCE) station to guide preceptors’ observations of trainees’ performance of simulated knee arthrocentesis and to organize feedback in preparation for performing these procedures in patient care. The aim of this project was to examine the evidence for validity of this OSCE.

**Methods:**

**Content:**

An orthopedic surgeon, a rheumatologist, and a primary care provider with expertise in musculoskeletal (MSK) medicine developed a checklist to guide rater observations in evaluating arthrocentesis technique. Content was proposed by faculty, supplemented by literature review, and finalized through consensus.

**Response Process**
A multi-disciplinary cohort of 71 learners (53 postgraduate trainees, 12 physician assistant students, 5 advanced practice nursing students, and one university undergraduate student) participated in the OSCEs in 2016-2017. To promote accuracy of the simulated patient (SP) responses to assessment prompts, one faculty member served as the SP and another as rater; ratings were recorded in real time.

- **Internal Structure**

Two faculty members independently rated a portion of the cases. Percent agreement was calculated and Cohen’s kappa corrected for chance agreement on binary outcomes.

- **Relations to other variables**

Relationship to self-assessment of confidence and competence to perform knee arthrocentesis was explored by written surveys utilizing a 5-point Likert scale. Response scores were compared with OSCE scores through Pearson’s correlation coefficient.

**Results:**

Checklists were developed for knee arthrocentesis (19 items). The checklist was scored by assigning one point for each error observed, in order to capture multiple errors; thus a score of 0 indicated no errors were noted. Mean score was 3.7 (range = 0-8; s.d. = 1.9). Frequency distribution of scores is reported in the Figure:

![Frequency Distribution of Errors](image)

Inter-rater agreement was near perfect at 93% (k = 0.8), as shown in the Table:

<table>
<thead>
<tr>
<th></th>
<th>Rater 1</th>
<th>Rater 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No Error Noted</td>
<td>Error Noted</td>
</tr>
<tr>
<td>Rater 1</td>
<td>116</td>
<td>5</td>
</tr>
<tr>
<td>Rater 2</td>
<td>6</td>
<td>31</td>
</tr>
<tr>
<td>Total</td>
<td>122</td>
<td>26</td>
</tr>
</tbody>
</table>

Observed Agreement = (116 + 31)/158 = 0.93

Chance Agreement = 0.64

Cohen’s kappa = 0.8

Pearson’s coefficient indicated no correlation between self-assessment and OSCE performance (-0.002).

**Conclusion:**

Validity evidence supports use of this OSCE in educational programs preparing learners for clinical settings where MSK procedures may be performed. Evidence for validity includes systematic development of content, response process control, and demonstration of acceptable interrater agreement. Lack of correlation with self-assessments suggests that the OSCE measures a construct different than self-perceived ability.

**Disclosure:** T. Braaten, None; A. Barker, None; J. P. Beck, None; M. J. Battistone, None.
Globalisation of Paediatric Musculoskeletal Matters’ (PMM)

Nicola Smith1, Sharmila Jandial2, Ruth Wyllie2, Christine English3, Barbara Davies5, Raju Khubchandani4, Mercedes Chan5, Jane Munro6, Virginia Ferriani7, Claudia Saad Magalhães8, Ricardo Russo9, Jacqueline Yan10, Chris Scott11, Sirirat Charuvanij12, Khulood Khawaja13, Jelena Vojinovic14, Tim Rapley15 and Helen Foster16. 1Institute of Cellular Medicine, Newcastle University, Newcastle Upon Tyne, United Kingdom, 2Paediatric Rheumatology, Great North Children’s Hospital, Newcastle Upon Tyne, United Kingdom, 3Department of Nursing, Midwifery and Health, Northumbria University, Newcastle Upon Tyne, United Kingdom, 4Department of Paediatrics, Jasloks Hospital and Research Center, Mumbai, India, 5Paediatric Rheumatology, University of Alberta, Edmonton, AB, Canada, 6Paediatric Rheumatology, Royal Children's Hospital, Victoria, Australia, 7Department of Paediatrics, Ribeirão Preto Medical School, University of São Paulo (USP-RP), Sao Paulo, Brazil, 8Department of Pediatrics, São Paulo State University (UNESP), Botucatu, Brazil, 9Service of Immunology/Rheumatology, Hospital de Pediatria Garrahan, Buenos Aires, Argentina, 10Paediatric Rheumatology, Starship Children’s Health, Auckland, New Zealand, 11Department of Paediatrics, University of Cape Town, Cape Town, South Africa, 12Department of Pediatrics, Siriraj Hospital, Mahidol University, Bangkok, Thailand, 13Department of Immunology/Rheumatology, Al-Mafraq Hospital, Abu Dhabi, United Arab Emirates, 14Paediatric Rheumatology, Faculty of Medicine, University of Nis, Nis, Serbia, 15Institute of Health and Society, Newcastle University, Newcastle Upon Tyne, United Kingdom, 16Institute of Cellular Medicine and Paediatric Rheumatology, Newcastle University and Great North Children’s Hospital, Newcastle Upon Tyne, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Education Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: paediatric musculoskeletal matters’ (PMM–www.pmmonline.org) is a free, evidence-based and peer reviewed open e-resource for paediatric musculoskeletal (MSK) medicine targeting non-MSK specialists. Since launch (Nov-2014) PMM has reached 183 countries with >57,000 users, >194,000 hits. Users who have declared their training background on the website are mainly non-MSK specialists. Feedback from users has requested further content to reflect international healthcare systems. PMM India was developed in collaboration with the Indian Academy of Paediatrics (IAP; Sept-2015, >2,200 users, 14,000 hits to date) and showcases successful partnership with local clinicians in developing PMM with local context. Further ‘internationalisation’ is now ongoing with additional global partners to develop ‘PMM International’. Here, we describe the process for international development.

Methods: Paediatric rheumatologists in countries around the world were approached to identify additional PMM content to reflect MSK medicine in their health care systems (e.g. case mix, clinical presentations, care pathways), with the focus on maintaining the level of knowledge relevant for non-MSK specialists. New content was developed by local teams identified by the paediatric rheumatologist(s) who then collated and provided expert overview before submission for editorial review. All contributions were provided in English. Additional cases and images were included with appropriate consent.

Results: PMM International additions to the original website brings new content predominately focused on infections / infection-related disease with MSK features or as differential diagnoses for rheumatic disease. Most content is in English with requests for translation of some content (e.g. pGALS which will be available in >7 languages). PMM International will be further peer reviewed with open access to all. A PMM app is planned to facilitate access where internet capacity is limited.

Conclusion: Rapid globalisation necessitates appropriate e-resources with content that reflect international health care contexts. PMM International targets non-MSK specialist audiences to raise awareness and early recognition of MSK pathology. Our work reflects strong collaborative global partnerships within the paediatric rheumatology community. PMM has been endorsed by PReS as an educational resource to aid teaching and learning. Implementation of PMM International has yet to be formally evaluated, but PMM data so far, supports wide reach and positive uptake from the target audience user groups.

Disclosure: N. Smith, None; S. Jandial, None; R. Wyllie, None; C. English, None; B. Davies, None; R. Khubchandani, None; M. Chan, None; J. Munro, None; V. Ferriani, None; C. S. Magalhães, None; R. Russo, None; J. Yan, None; C. Scott, None; S. Charuvanij, None; K. Khawaja, None; J. Vojinovic, None; T. Rapley, None; H. Foster, Pfizer, BioMarin, Sobi, Genzyme, 9.
Impact of a Student Led Rheumatology Interest Group on Medical Student Interest in Rheumatology

Sonia Silinsky Krupnikova1, Adey Berhanu2, Sean McNish3, Derek Jones1 and Victoria K. Shanmugam2, 1The George Washington University, Washington, DC, 2Rheumatology, The George Washington University, Washington, DC, 3Division of Rheumatology, The George Washington University, Washington, DC

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Education Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Based on data from the Rheumatology Workforce Study, there are currently insufficient rheumatologists to serve the needs of the population. The purpose of this longitudinal observational study is to investigate the impact of developing a student-led Rheumatology Interest Group on medical student interest in rheumatology at a single institution. We report updated longitudinal follow-up data on the impact of this intervention at the two year follow-up stage.

Methods: A student-led Rheumatology Interest Group was established at our institution in April 2015. The Interest Group runs several meetings per year, including a session on careers in rheumatology, finding research projects and mentors, and joint injection workshops. To assess the impact of the Interest Group on medical student interest in rheumatology we collected data prior to and subsequent to development of the Interest Group based on three parameters: the number of medical student abstract submissions to the University Research Day, the number of medical students enrolling in the rheumatology elective, and the number of manuscripts published by faculty with medical students. The mean number of student-rheumatology interactions per 6 months in the pre and post intervention periods was assessed for each parameter. Data lock for the current analysis was in April 2017 and analysis was performed using GraphPad Prism version 5.00 for Windows (GraphPad Software, San Diego, CA).

Results: Analysis of the two years of follow up data indicates that there continues to be a significant increase in medical student enrollment in the rheumatology elective following the Interest Group development, with a mean number of students per 6 months of 2.0 ± 0.89 in the pre-intervention period and 5.25 ± 2.06 in the post-intervention period (p=0.0083). The number of abstract submissions also significantly increased from 0.5 ± 0.84 to 6.5 ±4.65 (p=0.0131). Finally, the number of manuscripts submitted by student-faculty dyads increased from 0.17 ± 0.41 to 1.5 ± 0.58 (p=0.0026).

Conclusion: Based on data at two years of follow-up, a simple and low cost intervention of developing a student-led interest group has dramatically increased ongoing student engagement with rheumatology at a single institution.

Disclosure: S. S. Krupnikova, None; A. Berhanu, None; S. McNish, None; D. Jones, None; V. K. Shanmugam, Multiple, 9.


Medical Student Interest in Rheumatology As a Career

Peter Berger1, Adey Berhanu2, Derek Jones1, Sean McNish3 and Victoria K. Shanmugam2, 1The George Washington University, Washington, DC, 2Rheumatology, The George Washington University, Washington, DC, 3Division of Rheumatology, The George Washington University, Washington, DC

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Education Poster
Session Type: ACR Poster Session A
Background/Purpose:

Based on data from the Rheumatology Workforce Study, there are insufficient rheumatologists to serve the needs of the population. Little is currently known about factors that contribute to career choices of graduating medical students. The purpose of this study was to investigate medical student interest in rheumatology at the time of graduation, and to assess factors which drive career choices.

Methods:

This prospective survey study was IRB approved and conducted at a single center. A web-based REDCap survey was sent to graduating medical students via listserv approximately 1 month prior to graduation. Students self-reported demographics, information on whether and when they decided on their career specialty, how likely they were to consider a career in rheumatology, and what factors appealed to them about rheumatology as a specialty.

Results:

From the graduating class of 208 students, 52 matched into internal medicine or pediatrics. The survey was completed by 28 students (response rate 13.5%). Respondents were 64% female and 36% male; 57% Caucasian and 28% of African American descent. All respondents reported that they had decided on a specialty at the time of survey completion, with 78.5% reporting that they decided during their third or fourth year of medical school. While only one respondent reported planning a career in rheumatology, factors which appealed to the students about rheumatology as a specialty included: favorable work hours (78.5%), work-life balance (78.5%) and interest in complex medical care (54%). Of the experiences that stimulated their interest in rheumatology as a specialty, the most frequent response was the exposure to rheumatology teaching during their second year musculoskeletal block (36%). Interest in a specialty was the primary driver of career choice (85.7%) while earning potential, student debt, and length of training did not play a role.

Conclusion:

In this survey of medical students at a single US medical school, the majority of respondents decided their specialty during their clinical years. Interest in the specialty was the most important factor that drove career choice for this graduating class. Rheumatology teaching during the second year module was the most frequently reported exposure during which interest in rheumatology as a specialty was stimulated.

Disclosure: P. Berger, None; A. Berhanu, None; D. Jones, None; S. McNish, None; V. K. Shanmugam, Multiple, 9.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/medical-student-interest-in-rheumatology-as-a-career

Abstract Number: 98

Impact of a Lung Ultrasound Course for Rheumatology Specialist (IMPACT-2)

Christopher Gasho1, Karina Torralba2, David Chooljian3, Cong-Bin Wang4 and Vi Dinh4, 1Pulmonary and Critical Care Medicine, Loma Linda Medical Center, 12354 Anderson St, CA, 2Division of Rheumatology, Department of Internal Medicine, Loma Linda University, Loma Linda, CA, 3Loma Linda Veteran Affairs Hospital, Loma Linda, CA, 4Loma Linda University Medical Center, Loma Linda, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Education Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Although much emphasis is focused on lung ultrasonography(US) within the critical care field, there is a growing interest in the use of lung US and its role in diagnosis and monitoring of Interstitial Lung Disease(ILD). A large burden of ILD is attributed to connective tissue disorders(CTD) and often presents symptomatically after irreversible fibrosis has ensued. With increasing use of point-of-care musculoskeletal US among rheumatologists, translation of this expertise towards lung US places the rheumatologist in a unique position to screen for asymptomatic lung involvement among patients with CTD. Despite recent evidence of the feasibility and utility of using lung US in screening of patients with CTD-ILD, the field is relatively immature and standardized training curriculum for the rheumatology community is lacking. The aim of this study is to determine the effectiveness of a formalized lung US training course for Rheumatology fellows and attending physicians in incorporating and improving skills and attitudes in lung US.

Methods: Four rheumatology fellows and four board-certified rheumatologists were enrolled in a 4-hour training session including didactics, live models and simulation experience. Pre-course, post-course and 6-month follow-up surveys evaluated participant perceptions towards
previous US experience, training, clinical utility and attitudes toward dedicated lung US. Written exams (21 multiple-choice questions) were completed before, after training, and at 6 months to evaluate basic knowledge in ultrasound physiology, lung US anatomy, artifact and pathology recognition. In addition, a 30-point practical exam using live models and simulation, evaluated competency in machine setup, anatomical, artifact and pathology recognition.

**Results:** The results of this study show overall improvement in written test scores (43% v 66% p<0.001) Considerable improvement was also noted in overall practical skill score following training course. (16.8% v 93.4% p<0.001). Sub category improvements were seen in ultrasound setup and anatomical landmark identification (18.8% v 94.4% p<0.001) identification of pulmonary artifact (15.6% v 91% p<0.001) and pulmonary pathology identification (29% v 91% p<0.001). 6 month retention rate was excellent for: Written Scores (92.3%) , Practical Skills (93%) , Setup/Landmark Identification (88%) Artifact Identification (100%).

**Conclusion:** Dedicated lung ultrasonography training can be integrated into a rheumatology fellowship program for potential screening of CTD-ILD.

**Disclosure:** C. Gasho, None; K. Torralba, None; D. Chooljian, None; C. B. Wang, None; V. Dinh, None.

---

**Abstract Number: 99**

**A Pilot Study of the Use of a Validated Gout Script Concordance Test Assessment in an Interdisciplinary Musculoskeletal Education Program**

Bernadette C. Siaton¹, Andrea Barker² and Michael J. Battistone², ¹Rheumatology, University of Maryland School of Medicine, Baltimore, MD, ²Veterans Affairs Salt Lake City Health Care System and University of Utah School of Medicine, Salt Lake City, UT

**First publication:** September 18, 2017
Background/Purpose: A validated script concordance assessment (SCT) for gout was created for use in the internal medicine residency program at the University of Maryland Medical Center (UMMC). The assessment demonstrated high reliability and large effect size in a population of 143 learners. The aim of this pilot study was to explore the feasibility of using this tool with interprofessional, multilevel groups of learners at the Center of Excellence in MSK Care and Education (MSK COE) at the Salt Lake City Veterans Affairs Medical Center (SLC VAMC), to inform full implementation of the SCT in July, 2017.

Methods: A convenience sample of 19 learners (14 students or trainees; 5 practicing primary care providers (PCPs)) participating in programs at the SLC VAMC MSK COE, were asked to complete the SCT before and after a didactic session on gout. They were then sent emails containing the URL to access the SCT before and after the didactic. Time to complete the survey was not provided during the course. SCT was scored using an aggregate scoring method based on the results of an expert panel. Average pre- and post-test scores were calculated. A one-way ANOVA was used to compare pre- and post-test scores.

Results: Nine learners (47%) completed both the pre- and post-didactic SCT. The maximum possible SCT score was 50.16 points. For reference, the average score of the expert panel was 40.65 (SD=1.72) points. The average pre- and post-test scores for the UMMC population were 31.32 (SD=3.12) points and 33.98 (SD=2.72) points, respectively. The average pre-test score for the SLC VAMC population was 29.71 (SD=5.08) points. The average post-test score was 32.04 (SD=2.73) points. SLC VAMC learners did not show a statistically significant increase in scores after didactics, p=0.243. Individual learner demographics, pre-test scores, and post-test scores are below.

<table>
<thead>
<tr>
<th>Learner Type</th>
<th>Pre-test Score</th>
<th>Post-test Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nurse Practitioner</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Student</td>
<td>31.74</td>
<td>35.72</td>
</tr>
<tr>
<td>Physician Assistant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Student</td>
<td>31.86</td>
<td>30.99</td>
</tr>
<tr>
<td>Medicine Resident</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>30.84</td>
<td>34.95</td>
</tr>
<tr>
<td>Medicine Resident</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>17.18</td>
<td>28.67</td>
</tr>
<tr>
<td>Medicine Resident</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>30.12</td>
<td>32.12</td>
</tr>
<tr>
<td>Physician</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>32.95</td>
<td>33.76</td>
</tr>
<tr>
<td>Nurse Practitioner</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>26.87</td>
<td>31.60</td>
</tr>
<tr>
<td>Physician</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>32.65</td>
<td>33.05</td>
</tr>
<tr>
<td>Nurse Practitioner</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>33.16</td>
<td>27.48</td>
</tr>
</tbody>
</table>

Conclusion: This pilot study demonstrates feasibility of implementing a validated SCT to assess knowledge of gout in a different institution, across an interprofessional and multilevel group of learners. The response rate was low, indicating that different methods of interfacing with this instrument, including confirmation of participation, are needed with our learner groups. The larger pre-course variance, relative to the reference population, may reflect the comparative diversity of our learners, but the small sample size and response rate limit the validity of statistical inferences. We will continue to use the SCT assessment in the MSK Education Week curriculum and accrue additional learners in order to better understand its use as an assessment.


Disclosure: B. C. Siaton, None; A. Barker, None; M. J. Battistone, None.


Abstract Number: 100

Improving Internal Medicine Resident’s Knowledge through a Web-Based Musculoskeletal Educational Module

Uzma Haque1,2, Clifton O. Bingham III3 and Allan C. Gelber4, 1Rheumatology, Johns Hopkins School of Medicine, Lutherville, MD,
Musculoskeletal (MSK) complaints account for 15-30% of the ambulatory care visits in the United States. MSK training during Internal Medicine (IM) residency remains suboptimal, and residents report low self-confidence in managing MSK conditions. To address this gap, we developed an internet-based MSK module to improve IM residents’ knowledge and skills in evaluation and management of ambulatory MSK complaints. We examined the effectiveness of this educational intervention using data from the first 150 residents who completed this module.

Methods: The MSK module was disseminated on Physician Education and Assessment Center (PEAC), a web-based extramural ambulatory curriculum, currently used by 50% (194 out of 389) of the accredited IM Programs in the US and available to 11,000 IM residents as a key component to their ambulatory curricula. The module “Approach to a Patient with a Joint Complaint” was based on pretest-case based didactics-posttest format. The goal of this module was to give IM residents foundational knowledge and a systematic initial approach to a patient with a joint complaint, which leads to an appropriate initial diagnostic differential and work-up. Didactics and content was written to address the specific cognitive/knowledge objectives of the module, such as “to distinguish arthralgia from arthritis”. MSK knowledge was assessed using pre-tests and post-tests. We compared scores between first (PGY-1), second (PGY-2) and third year (PGY-3) residents to assess baseline knowledge, pretest and posttest scores among different years of training. Analyses were performed using SPSS v24.

Results: Of 151 residents completing the module, 32% were program year (PGY)-1, 32% were PGY-2, and 36% were PGY-3. The programs were 23.2% university training programs, 59.6% were community training programs, 7.3% were “other” training programs, and 9.9% were unknown training programs. Baseline mean (SD) pre-test scores were 59.4% (23.4). Pre-test scores were significantly higher when comparing PGY3 to PGY1 (p=0.02) only, but not between other years. The mean post-test score was 91.2% (11.2). Completion of the MSK module led to significant improvement from pre- to post-test scores (mean improvement =31.84% (SD=24.53). There was no difference in the post-test scores among the three years of trainees.

Conclusion: Web-based modules can be effective in augmenting and disseminating MSK knowledge to IM trainees. Additional modules and topics are being implemented. Further studies are required to evaluate whether knowledge gained from this intervention translates into improved care for patients with MSK complaints.

Disclosure: U. Haque, None; C. O. Bingham III, None; A. C. Gelber, None.

Rime (Reporter-Interpreter-Moderator-Educator) Evaluation Tool to Assess Fellows in Rheumatology

Michelene Hearth-Holmes1,2, Amy C. Cannella3 and Alan R. Erickson4, 1Internal Medicine/Rheumatology Division, Univ. of Nebraska Medical Center, Omaha, NE, 2Internal Medicine/Rheumatology Division, University of Nebraska Medical Center, Omaha, NE, 3Section of Rheumatology, University of Nebraska Medical Center, Omaha, NE, 4Omaha VA Medical Center and University of Nebraska Medical Center, Omaha, NE

First publication: September 18, 2017
Rheumatologists in academic settings strive to be excellent teachers and educators. The ACR reinforces this perspective by bestowing yearly education awards for outstanding clinician educators who assist in maintaining and increasing the workforce. The RIME method of evaluation is a teaching tool used to gauge medical students and residents in multiple clinical settings, focusing on whether a student has mastered the subjects of reporting and interpreting data followed by the ability to teach medical information. The ability to teach medical information enhances a student’s ability to recall information during standardized testing. The purpose of this study is to assess if rheumatology fellow performance on RIME evaluations can predict improvement in in-service examination scores from year 1 to year 2 of their fellowship.

Methods:

An evaluation tool using RIME format was adapted to assess four domains (presentation quality, presentation skills, analysis, critical thinking). Fellows were given a number score for each domain as well as a total score (1-does not meet expectations; 2-meets expectations; 3-exceeds expectations). Seven teaching faculty were trained on the use of the tool to determine a RIME designation of reporter, interpreter, moderator, or educator. Every presentation given during the two-year fellowship was evaluated. The in-service scores were from first and second year rheumatology fellow examinations. All fellows’ ITE scores improved in absolute numbers and percentile rank from year 1 to year 2. RIME scores for each domain were tabulated and compared to the in-service scores. The RIME score was calculated as the mean of the 4 separate domains using a 1-3 scale. The overall RIME score was calculated as the mean of the four sections scored. These scores were compared against the year 1, year 2, and the mean ITE scores for years 1 and 2. All presentations were completed and evaluated prior to the year 2 ITE. Statistical models used were generalized estimating equation models with an exchangeable variance structure to account for repeated measurements within fellows.

Results:

Data was collected on eight fellows over four years. There were a total of 34 encounters with an average of four encounters per fellow. This data was compared to in-service examinations from years 1 and 2. Year 1 ITE scores and mean year 1 and 2 ITE scores were not significantly associated with RIME scores (p=0.194; p=0.083). Year 2 ITE scores were significantly associated with RIME scores (p=0.036). RIME designations noted that of the 29 completed encounters, 21 presentations were marked as educator, 4 each as interpreter or moderator and none were marked as reporters. Five encounters were not completely scored and were excluded from the analysis.

Conclusion:

(1) Only the 2nd year ITE scores were significantly associated with RIME scores.

(2) RIME scores for year 1 and the combined years 1 and 2 ITE scores did not correlate.

(3) This data would suggest that RIME feedback to the fellows during their training program prior to year 2 ITE (approximately 19 months), reinforces the skills needed to master, retain, and communicate medical knowledge.

(4) RIME, as well as ITE, is an important tool in the training and evaluation of rheumatology fellows.

Disclosure: M. Hearth-Holmes, None; A. C. Cannella, None; A. R. Erickson, Amgen, 2.

Abstract Number: 102

Incorporating Temporal Artery Ultrasound in a UK District General Hospital with No Prior Colour Doppler Sonography Service: An Encouraging Preliminary Analysis

Othman Kirresh1, Chintu Gademsetty2 and Charles Li1, 1Rheumatology, NHS Royal Surrey County Hospital, Surrey, United Kingdom, 2Radiology, NHS Royal Surrey County Hospital, Surrey, United Kingdom

First publication: September 18, 2017

SEASON INFORMATION

Session Date: Sunday, November 5, 2017

Session Title: Education Poster

Session Type: ACR Poster Session A

Session Time: 9:00AM-11:00AM

Background/Purpose:
Temporal Arteritis (TA) is the most common large vessel vasculitis, affecting adults over the age of 50. It is associated with significant morbidity due to ischemic manifestations such as blindness and stroke.\textsuperscript{1} The gold standard for diagnosis has always been temporal artery biopsy (TAB) and although highly specific (98%) it lacks sensitivity, and can yield false-negative results in up to 60% of cases. The emergence of CDS in the diagnosis of GCA has now been widely acknowledged, further supported by meta-analyses confirming its validity.\textsuperscript{2} Prospective postulate a better sensitivity compared to TAB.\textsuperscript{3} For hospitals with no prior experience in TA-CDS a common validity concern lies in the procedures intra-operator reliability.

**Methods:**

A temporal arteritis (TA) pathway incorporating CDS was introduced into a small UK district general hospital serving a population of 200,000. It was presented at a local hospital medical meeting attended by all doctors to raise awareness. Subsequently the pro forma was distributed throughout the trust including medical wards, Accident and Emergency (A&E) and the Medical assessment unit (MAU).

As part of the pathway every patient who was referred for a TAB (performed by the Maxillofacial surgeons), also underwent a CDS. The latter was-performed by one musculoskeletal (MSK) Consultant Radiologist who was blinded in terms of patient symptoms i.e. side of headache. Crucially the radiologist although experienced (n= 20,000 MSK Ultrasound studies) has not been trained specifically in temporal artery ultrasound. Patients would then be followed up in Rheumatology Outpatients with the results of the investigations within 4 weeks.

**Results:**

<table>
<thead>
<tr>
<th>Table 1: Referrals</th>
</tr>
</thead>
<tbody>
<tr>
<td>N= 20</td>
</tr>
<tr>
<td>Treated for TA</td>
</tr>
<tr>
<td>13/20</td>
</tr>
<tr>
<td>Gender</td>
</tr>
<tr>
<td>Male: 10/20</td>
</tr>
<tr>
<td>Female: 10/20</td>
</tr>
<tr>
<td>Age Range</td>
</tr>
<tr>
<td>56- 85</td>
</tr>
<tr>
<td>Mean Age</td>
</tr>
<tr>
<td>71</td>
</tr>
<tr>
<td>Mean time prior to TAB on GC</td>
</tr>
<tr>
<td>10.2 Days</td>
</tr>
<tr>
<td>Mean time prior to CDS on GC</td>
</tr>
<tr>
<td>5.1 Days</td>
</tr>
<tr>
<td>Mean duration of GC Neg for TA</td>
</tr>
<tr>
<td>5.7 weeks</td>
</tr>
<tr>
<td>Average initial GC dosage</td>
</tr>
<tr>
<td>42.3mg</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CDS Positive</th>
<th>CDS Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAB positive</td>
<td>TAB Negative</td>
</tr>
<tr>
<td>3/12 (3/13)</td>
<td>7/20 (7/13)</td>
</tr>
<tr>
<td>0/20 (0/13)</td>
<td>2/20 (2/13)</td>
</tr>
</tbody>
</table>

**TAB had a specificity of 100% in contrast the sensitivity was 23% (Sensitivity 84% for CDS).**

**Conclusion:**

TA can be a challenging diagnosis for clinicians to make; hence diagnostic investigations are important. Our results demonstrate the critical role and value of CDS in the diagnosis and management of TA. When clinical suspicion is high for TA our data shows CDS as specific as TAB, but more importantly even when a radiologist is new to the procedure significantly higher sensitivity when compared to TAB (84%, P<0.023). Despite non familiarity of the operator the procedure adds to the diagnostic process. Our study data is line with existing data,\textsuperscript{2,3} and highlights the necessity to incorporate CDS in the diagnosis of TA.

**References**

Teaching Musculoskeletal Examination to Internal Medicine Residents in Digital Age

Sonam Kiwalkar and Odunayo Olorunfemi, Internal Medicine, Rochester General Hospital, Rochester, NY
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Education Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The resident-run internal medicine clinic at our community hospital caters to an inner city population. Lower back pain and knee pain are among the top 5 presenting complains. We have a heterogeneous group of residents who graduated from medical school from different parts of the world, who vary in experience of practicing medicine before residency, many of whom were exposed to a minimal or unstructured musculoskeletal (MSK) curriculum in medical school affecting their confidence in performing MSK exam. Our objectives were to improve resident knowledge, skills and engage a heterogeneous group of residents in an active learning classroom activity designed to improve MSK exam skills.

Methods: We designed a MSK workshop incorporated into our mandatory ambulatory curriculum. There were 2 sessions (upper & lower extremity), 2 hours each, that all 58 residents completed. Based on a flipped classroom design, pre-classwork was assigned including review articles and short videos. Classwork comprised of case discussions and peer led MSK skill demonstration and practice sessions. A pretest multiple choice questions was conducted 5 weeks prior to the first session, a post test immediately after and another after 6 months. Pre and post surveys measured levels of confidence and engagement in this active learning experience compared to passive learning. T-test and Chi was used to analyze data.

Results: Residents did better on posttest compared to pretest (p<0.0001). PGY3 sustained their scores even after 6 months. Mean increase in scores were higher for PGY 1 compared to seniors (p<0.0081). Self-reported confidence in MSK exam increased across the board (p<0.004). Those who practiced medicine before joining residency and those who demonstrated MSK skills to their peers sustained this confidence even after 6 months. Use of smart phone during this active workshop compared to traditional classroom passive teaching is shown in Figure 1 & 2, which was used as a marker of resident engagement.

Conclusion: The data suggests that a flipped classroom based MSK curriculum improves medical knowledge and skills of performing a MSK exam in a heterogeneous group of Internal Medicine residents. Moreover, it was successful in capturing attention of residents in a digital age. The reason that PGY 3 did better on knowledge component after 6 months may be attributed to their preparation for boards. Compared to similar endeavors in the past, we had a 100% retention rate because our sessions were mandatory. We hope to enhance our curriculum by embedding standardized patients and observed structured clinical assessments.
Utility of a Virtual Rheumatology Clinic for Community Based Internal Medicine Residency Program

Sonam Kiwalkar¹ and Bethany A. Marston², ¹Internal Medicine, Rochester General Hospital, Rochester, NY, ²Rheumatology, University of Rochester, Rochester, NY

First publication: September 18, 2017

Background/Purpose: At our mid-sized community hospital, internal medicine residents have little routine access to subspecialty rheumatology faculty clinical and didactic teaching, which has been reflected in below-average in-training exam scores in recent years. We needed an active learning resource to disseminate practical aspects of rheumatologic diagnoses and management. Hence, we partnered with the University of Rochester, and collaborated to further develop the ‘Virtual Rheumatology Clinic’ Tool. University residents had found the online tool as an engaging, interactive and user friendly series of virtual patients, which we felt would benefit residents and students at Rochester General. Our primary outcome was to improve confidence in diagnosis and treatment of rheumatologic conditions. Our secondary outcomes were to improve knowledge base in rheumatology and obtain user feedback for these modules.

Methods: We had a total of 58 participants (19 PGY 1, 20 PGY 2, 19 students) using the tool. Login instructions were sent via email. 6 modules (lupus, lower back pain, gout, myositis, giant cell arteritis and osteoporosis) were completed over 3 months. Knowledge was assessed by a pretest and posttest covering a broad range of rheumatology topics. Confidence and usefulness of the tool was determined by pre and post surveys. Data was analyzed by T test and Chi square test.

Results: Self-reported confidence in diagnosis and treatment of rheumatologic diseases was below average to average among students and residents before using the modules (P=0.560). Students gained more confidence compared to residents after completing the modules (P=0.04). There was no difference in pretest and posttest scores across the board (P=0.08). Improvement was greater in those concepts covered by the modules compared to those which were not (P=0.001), Residents had a greater mean increase in scores compared to students (P=0.001). Perceived usefulness of modules is shown in Figure 1.

Conclusion: The modules seem to be more appropriate for residents than students, based on overall improvement in objective test scores. Students and residents both acknowledged the usefulness of the modules. Improvement in global post-tests were not detected, likely in part because these were not limited to topics covered; sub scores on covered diagnoses did improve. Our future goals would be to expand the range of topics covered to include rheumatoid arthritis and psoriatic arthritis, expand access to other trainee groups such as family medicine residents and compare utility among groups, and compare the in-training exam scores for cohorts who used this tool to historic cohorts.
Disclosure: S. Kiwalkar, None; B. A. Marston, None.


Abstract Number: 105

**Tweeting the Meeting: Analysis of Twitter Use during the American College of Rheumatology 2016 Annual Meeting**

Mosaab Mohameden¹, Victoria Malkhasyan², Baker Alkhairi³, Najla Aljaberi⁴ and Candice Yuvienco⁵, ¹Internal Medicine, University of California San Francisco - Fresno Medical Education Program, Fresno, CA, ²University of California San Francisco - Fresno Medical Education Program, Fresno, CA, ³Internal Medicine, Blake Medical Center, Bradenton, FL, ⁴Cincinnati Children’s Hospital Medical Center, Cincinnati, OH, ⁵Internal Medicine, Division of Rheumatology Director, University of California San Francisco, Fresno Medical Education Program, Fresno, CA

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Sunday, November 5, 2017
Session Title: Education Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The American College of Rheumatology (ACR) annual meeting is the premier rheumatology research and education event of the year. The ACR adopted the use of social networks to spread medical knowledge. Twitter is a popular social network site with hundreds of millions of users and over 500 million Tweets being sent each day, there is a great opportunity for ideas to reach a global audience of new and existing professionals and patients. The ACR has specifically used and encouraged the use of twitter for such purpose and to promote its events and disseminate news and educational tweets from the annual meeting. In this study, we aim to analyze the use of twitter at the 2016 ACR annual meeting.

Methods: The Sympular Signals, a specialized healthcare social media analytics platform was used to analyse the hashtag #ACR16, the official hashtag of the ACR 2016 meeting. The analysis was conducted on tweets during the meeting days November 11th-16th of 2016. The number of tweets, participants, impressions, average tweets per hour and average tweets per participant was determined. Advanced search on Twitter was also conducted using the hashtag #ACR16 with timeframe between November 11th-16th. The resulted tweets were sorted by category “top tweets” which are the most popular tweets according to Twitter. The top 50 tweets were categorized by content to scientific, social, administrative, industry promotion, or irrelevant.

Results: The 2016 ACR annual meeting had over 16,000 attendees from around the world. The number of people who participated in the hashtag #ACR16 was 3,298 (about 20% of the attendees) sending 16,796 tweets during the meeting days, with an average of 5 tweets per participant and 117 tweets per hour, leaving 50,302 million impressions. The hashtag activity reached a peak of 4146 tweets on the 4th day of the meeting, November 14th. Seventy percent of the top tweets were by physicians, 10% by medical journals, 10% by patient advocate groups, and 10% by non-medical patient advocate individuals.

Forty two percent of the top 50 tweets had scientific content ranging from disease progression to treatment options. Whereas 28% had social content such as selfies and group photos to commemorate the event. Irrelevant tweets were mostly appreciation tweets addressed to some of the presenters at the meeting and represented 26%. Surprisingly, only 2% of content was industrial promotions and 2% were administrative tweets.
Conclusion: Twitter has facilitated communication between attendees and helped in delivering valuable information to them and to the public efficiently and free of cost. Most of the tweets were posted by physicians and the posts were mostly scientific. A more targeted approach can be implemented to increase tweets generally and scientific posts specifically by attendees, and to encourage industrial companies to tweet about their products. This is a useful and cost-effective way to deliver valuable information and knowledge to a much further audience than just attendees.

Disclosure: M. Mohameden, None; V. Malkhasyan, None; B. Alkhairi, None; N. Aljaberi, None; C. Yuvienco, None.

Abstract Number: 106

Rheumatology Fellows Teaching in a Consult Setting: Pilot Project at Two Training Hospitals

Holly Smith¹, Sarah Kazzaz¹, Anju Mohan² and Jammie Barnes¹, ¹Rheumatology, UT Health, McGovern Medical School Houston, Houston, TX, ²Internal Medicine, UT Health, McGovern Medical School Houston, Houston, TX

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Education Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Subspecialty consults in a hospital setting often contribute to disjointed patient care and frustrated providers. Miloslavsky et al (1) previously demonstrated improvement in rheumatology fellows’ ability to teach in a consult setting in a standardized learner environment. We sought to perform a similar intervention in a pilot real-world setting at our two teaching hospitals. Our goals were to improve fellows’ ability to teach, create interest in the field, and facilitate more collaborative patient care.

Methods:
A 10-question pre-intervention survey was administered to residents on internal medicine teams at each of the 2 training hospitals. The survey utilized a 5-point Likert scale to address 7 aspects of rheumatology fellows’ ability to teach, overall effectiveness and approachability, as well as quantifying percentage of time recommendations were shared in person. Our intervention included: a workshop for fellows on adult learning theory and self-directed learning; provision of pocket card containing medicine team locations, contact numbers, and prompt questions; monthly email reminders of the project goals to attendings and fellows. Rheumatology attendings standardized consult rounds by visiting teams following patient evaluations to relay our recommendations; fellows were instructed to lead the discussion. We employed this strategy for four months, after which the same survey was administered to residents on medicine teams. There was no randomization or blinding due to the nature of the study.

Results:
There were 33 pre-intervention and 15 post-intervention completed surveys. Mean scores on each of the 10 questions improved from pre- to post-intervention. Overall teaching effectiveness improved from mean of 3.55 to 4.4 (on 5-point scale). Prior to the intervention, 9% of respondents reported receiving in-person recommendations at least 50% of the time compared to 60% of respondents after the intervention.
Conclusion:

The findings of our pilot project are similar to the “Rheumatology Fellows as Teachers” project by Miloslavsky et al (1). With a simple teaching intervention and standardization of the workflow, we improved perceived teaching skills in all areas measured. Our limitations included few survey respondents and inability to control for improvements in fellow teaching due to increased experience. Despite these limitations, our findings suggest that having a standardized process for consultation that fosters a positive teaching interaction and collaboration can have far reaching effects on resident fellow interactions as well as patient care. Future studies could include other consult services, and a paired pre- and post-intervention analysis.


Disclosure: H. Smith, None; S. Kazzaz, None; A. Mohan, None; J. Barnes, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/rheumatology-fellows-teaching-in-a-consult-setting-pilot-project-at-two-training-hospitals

Abstract Number: 107

A Blended Learning Approach to Clinical Skills Teaching: E-Learning for Paediatric Gait, Arms, Legs and Spine Examination (pGALS)

Sarah Cope1, Sharmila Jandial2 and Helen E. Foster3, 1Paediatric Rheumatology, Great North Children's Hospital, Royal Victoria Infirmary, Newcastle upon Tyne, Paediatric Rheumatology, Great North Children's Hospital, Newcastle upon Tyne, United Kingdom, 2Department of paediatric rheumatology, Great North Children's hospital, Royal Victoria Infirmary, Newcastle upon Tyne, Department of paediatric rheumatology, Great North Children's hospital, Royal Victoria Infirmary, Newcastle upon Tyne, Newcastle upon Tyne, United Kingdom, 3Institute of Cellular Medicine and Paediatric Rheumatology, Newcastle University and Great North Children's Hospital, Newcastle Upon Tyne, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Education Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Musculoskeletal (MSK) presentations in childhood are common and often present initially to clinicians who are not specialists in paediatric MSK medicine.

Many doctors report lack of confidence and competence in paediatric MSK clinical skills relating to lack of teaching both at undergraduate (1) and postgraduate levels (2). The paediatric Gait, Arms, Legs and Spine (pGALS) examination is a clinical skill targeting non-specialists and is widely taught (3).

One of the ongoing challenges in paediatric MSK education is the reliance on MSK specialists to deliver teaching yet often this resource is limited. Blended learning combines face-to-face with digital resources, and allows greater reach to learners. Using an evidence-based approach, we have developed an e-learning module focused on paediatric MSK clinical skills to complement pGALS teaching, and describe the development and evaluation process.
Methods:

Identification of the learning needs for this module came from previous research with medical students and family medicine clinicians, alongside curriculum review and qualitative work with medical students. In conjunction with web-developers we developed an interactive, case-based module using key e-learning strategies such as question & answer, click and reveal, and reiteration of key learning points. The module focused on key elements; MSK history, pGALS manoeuvres and common abnormalities found, red flags, next steps (investigations and management) and links to Paediatric Musculoskeletal Matters website (www.pmmonline.org) for more information.

The evaluative strategy focused on qualitative methods including pre-testing and focus groups to allow a greater understanding of the user experience of both the module and perceptions of e-learning in general. Focus groups were audio-recorded, transcribed and underwent thematic analysis.

Results:

The final e-module had 22 pages, taking 30 minutes to complete. Emergent themes from the focus groups were positive and related to navigation and usability, content and language, application and reach, learning styles and use of technology. An iterative approach to the module development gave greater clarity to the case and presentation of key learning points. The students valued case based learning and the use of questioning to re-inforce learning. They deemed the variety of modalities useful for their learning.

Conclusion:

Iterative development of this e-learning module, in conjunction with learners, has led to a well-received resource as part of blended learning to complement face-to-face teaching. The module will be openly available to support teaching and learning of paediatric MSK clinical skills. Further e-module development is planned.

References:


Disclosure: S. Cope, None; S. Jandial, None; H. E. Foster, None.

Impact of Antiphospholipid Syndrome Ibook on Medical Students’ Improvement of Knowledge: An International Randomized Controlled Experimental Study

Stephane Zuily1, Laurent Phialy2, Eloïse Germain2, Ozan Unlu3, Virginie Dufrost4, Isabelle Clerc-Urmès4, Jessica R. Berman5, Michael Lockshin6, Denis Wahl7 and Doruk Erkan8. 1Regional Competence Center For Rare Vascular And Systemic Autoimmune Diseases, CHRU de Nancy, Vascular Medicine Division and Regional Competence Center for Rare Vascular and Auto-Immune Diseases; Inserm U1116; Lorraine University, Nancy, France, 2Lorraine University, Nancy School of Medicine, Nancy, France, 3Barbara Volcker Center for Women and Rheumatic Diseases, Hospital for Special Surgery, Weill Cornell Medicine, New York, NY, 4Nancy Academic Hospital, Nancy, France, 5Rheumatology, Hospital for Special Surgery, New York, NY, 6Hospital for Special Surgery, NYC, NY, 7CHU de Nancy, Vascular Medicine Division and Regional Competence Centre For Rare Vascular And Systemic Autoimmune Diseases; and UMR_S U1116 Research Unit, Nancy, France, 8Rheumatology, Hospital for Special Surgery- Weill Cornell Medicine, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Education Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM
Background/Purpose: iBooks, a free electronic book application by Apple, is well-suited for publishing interactive medical texts. To date, no iBook on Antiphospholipid Syndrome (APS) exists, and the utility of an Apple iBook for medical students as a teaching method in APS has never been assessed. Our objective was to assess medical students’ improvement of knowledge and satisfaction with an interactive APS iBook, in comparison with conventional teaching methods.

Methods: The APS iBook was developed both in French and English by a professional iBook developer (LP) with the guidance of a medical team. Second year medical students, who were naïve of lectures regarding APS, were enrolled from two institutions (Nancy University, France; Weill Cornell Medicine, New York, NY). For the “teaching intervention”, following IRB approvals, participants were randomly distributed to three groups: a) APS iBook with interactive capability (Group A); b) printed copy of the material contained in the interactive APS iBook (Group B); and c) classroom presentation of the material contained in the APS iBook (Group C) by a physician (SZ or DE). A standardized medical questionnaire about APS (total score: 10 points) was filled by the participants before and after teaching interventions. Furthermore, participants were asked to fill out a standardized satisfaction survey (max: 10). Recall capability of students was tested four months after the intervention (score: 10 pts).

Results: 233 second-year medical students were enrolled (iBook group: 73; print group: 79, and lecture group: 81). Mean improvement of knowledge was significantly higher in the lecture group in comparison to the iBook group. Satisfaction was significantly higher in both the lecture and the iBook groups, compared to the print group on several dimensions including overall quantitative satisfaction, subjective enhanced knowledge, interactivity, quality of content, comprehensibility, and pleasure of learning. Recall capability of students (n=109) was not significantly different among groups (Table).

Conclusion: Based on our international two-center randomized control study of medical students, a classroom APS lecture is the most effective method in improving medical students’ knowledge, when compared to self-learning methods, i.e., APS iBook or APS printed material. Among these two self-learning methods, medical students were more satisfied with the APS iBook, although both resulted in the same degree of improvement of knowledge. Given the complexity of the spectrum and the management of aPL-related clinical manifestations, we hope that our APS iBook will help medical students in their curriculum and increase the awareness of APS among the community.


<table>
<thead>
<tr>
<th></th>
<th>Group A (iBook)</th>
<th>Group B (Print)</th>
<th>Group C (Lecture)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improvement of Knowledge*</td>
<td>3.65±2.47</td>
<td>4.19±3.21</td>
<td>5.06±3.21</td>
<td>A vs B: 0.54</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>A vs C: 0.003</td>
</tr>
<tr>
<td>Satisfaction Score</td>
<td>5.7±3.0</td>
<td>4.0±2.6</td>
<td>6.4±4.0</td>
<td>A vs B: &lt;0.0001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recall Capability**</td>
<td>7.9±2.0</td>
<td>7.8±2.1</td>
<td>7.6±2.0</td>
<td>A vs B vs C: 0.86</td>
</tr>
</tbody>
</table>

*Increased # of correct answers pre- and post-intervention medical questionnaires

**# of correct answers

Disclosure: S. Zuily, None; L. Phialy, None; E. Germain, None; O. Unlu, None; V. Dufrost, None; I. Clerc-Urmès, None; J. R. Berman, None; M. Lockshin, None; D. Wahl, None; D. Erkan, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/impact-of-antiphospholipid-syndrome-ibook-on-medical-students-improvement-of-knowledge-an-international-randomized-controlled-experimental-study

Abstract Number: 109

The Creation of a Structured Curriculum Outline for the Expansion of a Rheumatology Practice to Include Nurse Practitioners and Physician Assistants

Benjamin J Smith1, Marcy B. Bolster2, Barbara Slusher3, Christine A. Stamatos4, Jeanne Scott5, Heather Benham6, Salahuddin Kazi7, Elizabeth A. Schlenk8, Daniel Schaffer9, Vikas Majithia10, Calvin Brown Jr11, Joan Marie Von Feldt12, Joseph Flood13, David Haag14 and Karen Smarr15, 1School of Physician Assistant Practice, Florida State University College of Medicine School of Physician Assistant Practice, Tallahassee, FL, 2Rheumatology, Allergy and Immunology, Endocrine Associates, Massachusetts General Hospital, Boston, MA, 3Physician Assistant Studies, University of Texas Medical Branch, League City, TX, 4Rheumatology, Northwell Health, Great Neck, NY, 5Rheumatology, Cheshire Medical Clinic, Keene, NH, 6Pediatric Rheumatology, Texas Scottish Rite Hospital for Children, Dallas, TX, 7University of Texas Southwestern, Dallas, TX, 8School of Nursing Room 415, University of Pittsburgh, Pittsburgh, PA, 9Rheumatology, Mayo Clinic, Rochester, MN, 10Division of Rheumatology, University of Mississippi, Jackson, MS, 11Rheumatology Division, Northwestern
SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Education Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Rheumatology practices are expanding to include non-physician healthcare providers, such as nurse practitioners and physician assistants (NP/PAs). To date, there has not existed a structured curriculum for NP/PAs for the acquisition of rheumatology knowledge. The Association of Rheumatology Health Professionals (ARHP), a division of the American College of Rheumatology (ACR), charged a task force (TF) to recommend ways to facilitate the preparation of NP/PAs to work in a rheumatology practice setting.

Methods: The TF, consisting of private practice and academic rheumatologists, NPs and PAs, including those in adult and pediatric settings, assimilated information from many sources and resources to develop mechanisms for NP/PAs to acquire rheumatology knowledge. Through face-to-face and webinar meetings, the TF designed a Rheumatology Curriculum Outline (RCO), incorporating stakeholder’s feedback, to provide a framework for the training of NP/PAs new to rheumatology practice.

Results: The core competencies, from the Accreditation Council for Graduate Medical Education (ACGME) Core Competencies, Nurse Practitioner Core Competencies, and Competencies for the Physician Assistant Profession, of patient care, medical knowledge, systems-based learning, practice-based learning and improvement, professionalism, and interpersonal and communication skills, served as a framework for the RCO creation. (Table 1) Informed by stakeholder’s feedback, a NP/PA RCO was developed, endorsed by the ACR Board of Directors and is ready for use by community-based and academic rheumatology practices, whether pediatric or adult, who desire to add a NP/PA to their practice. The RCO includes a Rheumatology Toolbox for Suggested Learning Activities and Assessments to facilitate the development of a robust learning environment for the NP/PA new to rheumatology practice. The Toolbox is an amalgam of resources that were identified by the task force as important and useful for the development and experience of the early NP/PA rheumatology provider. Foundational knowledge, skills and attitudes embodied in the RCO are generally believed to be attainable within one year for NP/PAs. Realizing the needs of individual practices vary, foundational and aspirational expectations are included in the RCO, allowing for flexibility in the application of the RCO to specific practice settings.

Conclusion: The ACR/ARHP NP/PA Rheumatology Curriculum Outline is a valuable tool to facilitate efficient and effective training of a NP/PA new to rheumatology and incorporate him/her proficiently as a patient care provider. Increasing the number of NP/PAs trained in rheumatology assists in closing the workforce gap, thus providing access to care for more persons with rheumatic disease.

Table 1

<table>
<thead>
<tr>
<th>Competency</th>
<th>Patient Care</th>
<th>Medical Knowledge</th>
<th>Systems-Based Learning &amp; Improvement</th>
<th>Interpersonal &amp; Communication Skills</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Professional</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medicine</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Physical</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Social</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Cognitive</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Disclosure: B. J. Smith, None; M. B. Bolster, None; B. Slusher, None; C. A. Stamatos, None; J. Scott, None; H. Benham, None; S. Kazi, None; E. A. Schlenk, None; D. Schaffer, None; V. Majithia, None; C. Brown Jr, None; J. M. Von Feldt, None; J. Flood, None; D. Haag, None; K. Smarr, None.
Consensus-Building on a Rheumatology Musculoskeletal Ultrasound Scanning Protocol for Rheumatology Fellowship Programs

Karina Torralba1,2, Midori Jane Nishio3, Ralf G. Thiele4, Robert Fairchild5, Kristal Choi6, Lorena Salto6, Amy C. Cannella7 and Eugene Y. Kissin8, 1Internal Medicine/Rheumatology, Loma Linda University, Loma Linda, CA, 2Division of Rheumatology, Department of Internal Medicine, Loma Linda University, Loma Linda, CA, 3John Muir Hospital, Walnut Creek, CA, 4Medicine, University of Rochester Medical Center, Rochester, NY, 5Stanford University, Palo Alto, CA, 6Loma Linda University, Loma Linda, CA, 7Section of Rheumatology, University of Nebraska Medical Center, Omaha, NE, 8Boston University, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Education Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Musculoskeletal ultrasound (MSUS) is currently taught at 95% of adult United States Rheumatology fellowship programs. Only 30 (41%) programs have a formal curriculum. MSUS curriculum development for rheumatology fellowship programs is ongoing with ACR support. In 2011, at Rochester NY, a group of rheumatology MSUS experts developed a document on documentation, scanning conventions, and tier designations (1, Rheumatology sonographers need to know and need to perform routinely; 2, Rheumatology sonographers need to know but do not need to perform routinely; 3, Rheumatology sonographers may know about & may perform based on individual practice focus) for each view of the major joints. The objective of this study is to update consensus of the 2011 Rochester document to serve as the foundation for the development and implementation of a rheumatology MSUS curriculum for fellowship training programs.

Methods: A 96-item IRB-approved survey was developed for use in a Delphi study. Apart from demographics (8), there were 86 questions testing for agreement/disagreement on documentation (5), scanning conventions (5), and tier designations for 8 peripheral joint-specific areas (76). 108 lead faculty at 113 rheumatology fellowship programs were identified based on prior surveys. 101 respondents (including the 38 who developed the 2011 document) were selected based on selected criteria including lead MSUS faculty experience, course instruction, ACR-RhMSUS certification, or publication in MSUS. The survey was disseminated via Qualtrics®. Survey initiation and completion indicated consent for study participation.

Results: 55 (55%) rheumatologists responded: 39 (71%) were full time academic faculty, 40 (73%) had certification, with a third of the respondents certified via ACR-RhMSUS pathway. 51 (59%) questions achieved high (>85%) agreement. Questions with less than 85% agreement all concerned tier designations. 13 questions with 30-60% disagreement favored tier 1 designation over 2011 tier 2. Table 1 lists areas of disagreement.

Conclusion: Initial phase of consensus-building reveals 41% disagreement on areas related to anatomic-region tier designation. Many respondents favored Tier 1 over Tier 2 for many of those items, indicating a shift in overall expert opinion towards including more views in the MSUS mastery requirements. Further clarification through subsequent rounds of this Delphi study is needed to resolve areas of disagreement, and facilitate development of a standardized MSUS fellowship curriculum.
<table>
<thead>
<tr>
<th>Joint Views</th>
<th>Tier</th>
<th>2011 Agree, n (%)</th>
<th>2017 Disagree, n (%)</th>
<th>Tier</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Shoulder</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acromio-clavicular joint, longitudinal</td>
<td>2</td>
<td>34 (61%)</td>
<td>20 (36%)</td>
<td>1</td>
</tr>
<tr>
<td>Posterior transverse</td>
<td>2</td>
<td>46 (83%)</td>
<td>8 (14%)</td>
<td>1</td>
</tr>
<tr>
<td>Dynamic impingement</td>
<td>2</td>
<td>41 (74%)</td>
<td>12 (21%)</td>
<td>1</td>
</tr>
<tr>
<td>Suprascapular transverse</td>
<td>2</td>
<td>36 (65%)</td>
<td>17 (30%)</td>
<td>3</td>
</tr>
<tr>
<td>Axillary longitudinal</td>
<td></td>
<td>37 (67%)</td>
<td>18 (31%)</td>
<td>3</td>
</tr>
<tr>
<td><strong>Elbow</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Olecranon bursa</td>
<td>2</td>
<td>46 (83%)</td>
<td>8 (14%)</td>
<td>1</td>
</tr>
<tr>
<td>Posterior transverse medial</td>
<td>2</td>
<td>44 (80%)</td>
<td>6 (10%)</td>
<td>3</td>
</tr>
<tr>
<td>Posterior longitudinal medial</td>
<td>2</td>
<td>45 (81%)</td>
<td>8 (14%)</td>
<td>3</td>
</tr>
<tr>
<td><strong>Wrist</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scapholunate ligament, dorsal transverse</td>
<td>2</td>
<td>39 (70%)</td>
<td>15 (27%)</td>
<td>1</td>
</tr>
<tr>
<td>Radial orthogonal compartment 1 tendons</td>
<td>2</td>
<td>39 (70%)</td>
<td>15 (27%)</td>
<td>1</td>
</tr>
<tr>
<td>Ulnar transverse</td>
<td>2</td>
<td>33 (60%)</td>
<td>20 (36%)</td>
<td>1</td>
</tr>
<tr>
<td>Volar longitudinal median nerve</td>
<td>2</td>
<td>34 (61%)</td>
<td>21 (38%)</td>
<td>1</td>
</tr>
<tr>
<td>Dorsal orthogonal extensor compartments 2-5</td>
<td>2</td>
<td>39 (70%)</td>
<td>14 (25%)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Hand</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dorsal orthogonal MCP joint/PIP joint in flexion</td>
<td>2</td>
<td>45 (81%)</td>
<td>7 (12%)</td>
<td>3</td>
</tr>
<tr>
<td>MCP radial/ulnar orthogonal</td>
<td>2</td>
<td>35 (63%)</td>
<td>20 (36%)</td>
<td>1</td>
</tr>
<tr>
<td>PIP joint transverse (dorsal and volar)</td>
<td>2</td>
<td>43 (78%)</td>
<td>12 (21%)</td>
<td>1</td>
</tr>
<tr>
<td>Hand inflammatory arthritis scan set</td>
<td>2</td>
<td>33 (60%)</td>
<td>20 (36%)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Hip</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior transverse femoral neck</td>
<td>2</td>
<td>37 (67%)</td>
<td>18 (32%)</td>
<td>1</td>
</tr>
<tr>
<td>Lateral hip transverse</td>
<td>2</td>
<td>45 (81%)</td>
<td>10 (18%)</td>
<td>1</td>
</tr>
<tr>
<td>Snapping hip dynamic scan</td>
<td>3</td>
<td>46 (83%)</td>
<td>8 (14%)</td>
<td>2</td>
</tr>
<tr>
<td>Transverse sacral iliac joint</td>
<td>2</td>
<td>25 (45%)</td>
<td>28 (50%)</td>
<td>3</td>
</tr>
<tr>
<td><strong>Knee Views</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior transverse suprapatellar</td>
<td>2</td>
<td>22 (40%)</td>
<td>33 (60%)</td>
<td>1</td>
</tr>
<tr>
<td>Anterior transverse in maximum flexion</td>
<td>1</td>
<td>45 (81%)</td>
<td>10 (18%)</td>
<td>2</td>
</tr>
<tr>
<td>Anterior transverse infrapatellar</td>
<td>2</td>
<td>37 (67%)</td>
<td>18 (32%)</td>
<td>1</td>
</tr>
<tr>
<td>Medial longitudinal</td>
<td>2</td>
<td>29 (52%)</td>
<td>26 (47%)</td>
<td>1</td>
</tr>
<tr>
<td>Lateral longitudinal</td>
<td>2</td>
<td>32 (58%)</td>
<td>23 (41%)</td>
<td>1</td>
</tr>
<tr>
<td>Posterior transverse medial</td>
<td>2</td>
<td>41 (74%)</td>
<td>13 (23%)</td>
<td>1</td>
</tr>
</tbody>
</table>
Disclosures: K. Torralba, None; M. J. Nishio, None; R. G. Thiele, Amgen, 8, AbbVie, 8, BioClinica, 5, Fujifilm SonoSite, 9; R. Fairchild, None; K. Choi, None; L. Salto, None; A. C. Cannella, None; E. Y. Kissin, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/consensus-building-on-a-rheumatology-musculoskeletal-ultrasound-scanning-protocol-for-rheumatology-fellowship-programs

Focused Musculoskeletal Ultrasound Teaching: Effect on Medical Students’ Physical Examination Skills

Bhavna Seth1, Lorraine Stanfield2 and Eugene Y. Kissin3, 1Internal Medicine, Boston University Medical Center, Boston, MA, 2Internal Medicine, Boston Univeristy, Boston, MA, 3Boston University, Boston, MA

First publication: September 18, 2017
to instruction group using a standardized checklist, that included key inspection, palpation, and maneuvers for joint exams. The study was exempted from review by the local IRB. Participant confidentiality was maintained with anonymized codes. The Mann-Whitney-Wilcoxon test was used to analyze the results given the small sample and non-normal distribution of the scores.

**Results:**

The maximum score for knee and shoulder examinations were 14 and 15 respectively. For the knee examination, the mean score of the USG (10.38±2.35) was significantly higher than the non-USG group (8.95±2.14) p=0.013. There was a non-significant trend towards improved performance of shoulder examination in the USG (12.58±1.82) compared to non-USG (11.59±2.49) group (p=0.11).

Since ultrasound visualization is more likely to improved inspection and palpation components, we analyzed them separately. For knee examination, the USG group fared significantly better (7.5±1.72 vs. 6.10±1.67, p=0.003); a similar trend towards improved performance in the shoulder examination, did not reach significance in the USG group (4.96±0.99 vs. 4.49±1.12, p=0.075).

In sub-components of the knee exam, significant improvement was seen in the USG-aided group in palpation of the lateral collateral ligament (p=0.016), popliteal space for Baker’s cysts (p=0.017), and the patellofemoral shrug test (p=0.004). For sub-components of the shoulder exam, improvement was significant in the USG-aided group for shoulder inspection (p=0.043), palpation of the sternoclavicular joint (p=0.008), acromioclavicular joint (p=0.043), and shoulder range of motion (p=0.045).

**Conclusion:**

Incorporation of ultrasound into musculoskeletal exam curriculum demonstrated short-term improvement in knee examination performance, with a trend toward improvement in shoulder exam in second-year medical students.

Table: Knee and Shoulder Exam- ultrasound vs. non-ultrasound group scores

<table>
<thead>
<tr>
<th>Subcomponent</th>
<th>USG group (mean scores)</th>
<th>Non-USG group (mean scores)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee Examination - Ultrasound dependent skills</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inspection (2)</td>
<td>1.71</td>
<td>1.51</td>
<td>0.43</td>
</tr>
<tr>
<td>Palpation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quadriceps poplite tendon, tibial tubercle (1)</td>
<td>0.82</td>
<td>0.89</td>
<td></td>
</tr>
<tr>
<td>Patellar anserineus (1)</td>
<td>0.79</td>
<td>0.72</td>
<td>0.51</td>
</tr>
<tr>
<td>Lateral &amp; Medial joint line (3)</td>
<td>0.58</td>
<td>0.56</td>
<td>0.88</td>
</tr>
<tr>
<td>Lateral collateral ligament (1)</td>
<td>0.79</td>
<td>0.79</td>
<td>0.016</td>
</tr>
<tr>
<td>Patellar/ Bakers cyst (1)</td>
<td>0.87</td>
<td>0.59</td>
<td>0.017</td>
</tr>
<tr>
<td>Demarcation of lateral suprapatellar injection site for knee joint injection (1)</td>
<td>0.58</td>
<td>0.54</td>
<td>0.72</td>
</tr>
<tr>
<td>Total (9)</td>
<td>2.5±1.72</td>
<td>6.10±1.67</td>
<td>0.003</td>
</tr>
<tr>
<td>Knee Examination - Ultrasound independent skills</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manoeuvers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patellofemoral shrug sign (3)</td>
<td>0.71</td>
<td>0.33</td>
<td>0.004</td>
</tr>
<tr>
<td>Bridge sign (1)</td>
<td>0.58</td>
<td>0.33</td>
<td>0.05</td>
</tr>
<tr>
<td>Abduction (1)</td>
<td>0.66</td>
<td>0.46</td>
<td>0.14</td>
</tr>
<tr>
<td>External rotation (1)</td>
<td>0.83</td>
<td>0.62</td>
<td>0.84</td>
</tr>
<tr>
<td>Anterior Cruciate Ligament (1)</td>
<td>0.65</td>
<td>0.82</td>
<td>0.52</td>
</tr>
<tr>
<td>Posterior Cruciate Ligament (1)</td>
<td>0.82</td>
<td>0.87</td>
<td>0.07</td>
</tr>
<tr>
<td>Total Knee exam (14)</td>
<td>10.38±2.35</td>
<td>8.95±2.14</td>
<td>0.013</td>
</tr>
<tr>
<td>Shoulder Examination - Ultrasound dependent skills</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inspection (1)</td>
<td>1.00</td>
<td>0.84</td>
<td>0.043</td>
</tr>
<tr>
<td>Palpation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sternoclavicular joint (1)</td>
<td>0.85</td>
<td>1.00</td>
<td>0.008</td>
</tr>
<tr>
<td>Acromioclavicular joint (1)</td>
<td>0.85</td>
<td>0.64</td>
<td>0.04</td>
</tr>
<tr>
<td>Biceps tendon (1)</td>
<td>0.83</td>
<td>0.84</td>
<td>0.50</td>
</tr>
<tr>
<td>Coracoid process (1)</td>
<td>0.92</td>
<td>0.87</td>
<td>0.56</td>
</tr>
<tr>
<td>Glenohumeral Injection site (1)</td>
<td>0.35</td>
<td>0.28</td>
<td>0.44</td>
</tr>
<tr>
<td>Total (8)</td>
<td>4.96±0.05</td>
<td>4.49±0.2</td>
<td>0.075</td>
</tr>
<tr>
<td>Shoulder Examination - Ultrasound independent skills</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range of Motion (8)</td>
<td>2.92</td>
<td>2.4</td>
<td>0.045</td>
</tr>
<tr>
<td>Motor-related internal/external rotation, Empty can (3)</td>
<td>2.29</td>
<td>2.4</td>
<td>0.62</td>
</tr>
<tr>
<td>Hawkins Test (1)</td>
<td>0.87</td>
<td>0.69</td>
<td>0.35</td>
</tr>
<tr>
<td>Neer’s Test (1)</td>
<td>0.87</td>
<td>0.77</td>
<td>0.26</td>
</tr>
<tr>
<td>Yergsens’s Test (1)</td>
<td>0.65</td>
<td>0.86</td>
<td>0.01</td>
</tr>
<tr>
<td>Total Shoulder exam (15)</td>
<td>12.58±1.82</td>
<td>11.59±2.48</td>
<td>0.11</td>
</tr>
</tbody>
</table>

Disclosure: B. Seth, None; L. Stanfield, None; E. Y. Kissin, None.
A Qualitative Assessment of a CME “City Rounds” Workshop Educational Program to Meet the Educational Needs of Rheumatologists

John J. Cush1, Leonard H. Calabrese2, Greg Salinas3 and Sergio Schwartzman4, 1Baylor Scott & White Research Institute, Dallas, TX, 2Rheumatic & Immunologic Disease and Infectious Disease, Cleveland Clinic Foundation, Cleveland, OH, 3CE Outcomes, Birmingham, AL, 4Hospital for Special Surgery, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Education Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: An Annual Rheumatology & Therapeutics Review for Organizations & Societies (ARTHROS) initiative called “City Rounds” was created to meet the educational needs of rheumatologists with regard to advances in therapeutic s in Rheumatoid arthritis. The program was designed to introduce and assess advances in diagnosis, therapeutic s and safety through an interactive roundtable, small-group format wherein rheumatologists would interact and discuss case based issues with local and national RA experts.

Methods: These, roundtable programs were delivered in 16 US cities and attended by 5-15 rheumatologists using a case-based workbook covering three topics: Targeted Therapies in RA, Immunopathogenesis of RA, and Safety Issues in RA Management. ARTHROS partnered with CE Outcomes to qualitatively evaluate the impact of the City Rounds on rheumatologists using structured interviews with 12 randomly chosen participants. Transcripts of the interviews were analyzed to identify common themes and compare practices reported by interviewees to evidence-based guideline recommendations and learning objectives of the City Rounds program.

Results: The findings of the qualitative analysis demonstrate the City Rounds program enabled rheumatologists to provide more thorough patient education. Participant interviews showed the following: 94% of participants believed that these educational objectives impacted their knowledge; 98% of the participants indicated that this activity enhanced their effectiveness in treating; 91% of participants indicated that this activity will change in their practice behavior; 24% of participants indicated they will create or revise policies for patient care; 55% of participants indicated they will change their management and treatment of RA; 24% of participants indicated they will create or revise policies for patient care; 55% of participants indicated they will change their management and treatment of RA; 38% of participants indicated that they have no barriers in implementing changes learned in this education. Several interviewees reported greater confidence in managing hard-to-treat patients after participating in the education. The City Rounds program also reinforced rheumatologist use of evidence-based care in several key areas, including: selection of tests and exams for diagnosis and monitoring; active use of evidence-based guidelines; and selection of treatments for patients with high RA disease activity who have failed methotrexate. The findings of the assessment also suggest that, despite the positive impact of the program, educational gaps in these same areas persist among some rheumatologists.

Conclusion: Small group, workshop or roundtable style educational programs are highly impactful as they: a) well attended by a wide variety of practitioners (from trainees to professors; urban and suburban); b) allow for intense, impactful interactions between colleagues and experts on important teaching points and practice issues; and c) are a conduit for the introduction and integration of guidelines and standards of care into daily practice.

Disclosure: J. J. Cush, Pfizer, Janssen, Abbvie, Celgene, Novartis, AstraZeneca, Genentech, 2Janssen, Abbvie, Novartis, Amgen, Genentech, Lilly, Horizon, 5; L. H. Calabrese, Celgene, Crescendo, 2Celgene, Crescendo, 5,Celgene, Crescendo, 8; G. Salinas, CE Outcomes, 5; S. Schwartzman, Abbvie, Genentech, Janssen, Novartis, Pfizer, UCB, Sanofi, Regeneron, 2Abbvie, Janssen, Genentech, Pfizer, UCB, Crescendo, Novartis, 8,Crescendo Biosciences, Discus Analytics, National Psoriasis Foundation, 9.

A Primer on Exercise: An Interactive, Online Educational Module Incorporating Spaced Education to Supplement the ACR Core Curriculum Outline for Rheumatology

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/a-primer-on-exercise-an-interactive-online-educational-module-incorporating-spaced-education-to-supplement-the-acr-core-curriculum-outline-for-rheumatology
Fellowship Programs

Amit Patel and Kenneth O'Rourke, Department of Internal Medicine, Section on Rheumatology and Immunology, Wake Forest School of Medicine, Winston-Salem, NC

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Education Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
The 5 topics in rehabilitative rheumatology (RR) included in the ACR Core Curriculum Outline include exercise, adaptive equipment, orthotics, thermal modalities and splinting. A 2004 survey of Program Directors (PD) led to a subsequent increase in RR clinical symposia at ACR Annual Meetings. Fellowship program instruction in RR is still felt to be under-represented.

Methods:
An online needs assessment survey of PD (107), therapy providers (34), and physicians with an interest in RR (31) yielded response rates of 37%, 27% and 16%, respectively. For PD respondents, 56% did not offer a RR rotation, 71% had no one interested in leading a group teaching session, but 93% said self-study could be part of teaching resources. There was consensus among all respondents that exercise should be the first RR content to be addressed. Using certain software, we created a two-part, interactive, online educational module on exercise. The first part addresses exercise modalities, CDC exercise recommendations and creating an exercise prescription, and the second part presents current literature for self-directed study on exercise applications in selected rheumatic diseases.

An educational trial of the content in the first part of the exercise module was completed with fellows in the Carolina Fellows Collaborative as our study participants. Fellow level of confidence in, and frequency of, prescribing exercise, as well as providing an exercise prescription for a simulated patient, was assessed during a rheumatology OSCE (ROSCE) station. Fellows were then asked to provide an exercise prescription immediately after, and 6 weeks after completion of the module. In a randomized subset of fellows, spaced education by email was used as a means to improve retention during the 6 weeks between the second and third prescription assignments. All prescriptions were scored using the same metrics applied during the ROSCE station.

Results:
18 fellows (85.7%) participated in the ROSCE. 4 of 21 fellows (19.0%) completed the exercise prescriptions immediately following completion of the module and 5 fellows (23.8%) completed the prescriptions 6 weeks after completion of the module, 1 of which had participated in the spaced education program. Only 2 fellows (9.5%) completed all 3 sets of prescriptions, none of which had completed the spaced education program. The average correct responses paralleled level of training, overall increasing from 70.94% to 85.42% with the introduction of the module content. At 6-week follow-up, the average score had fallen to 67.91%. Fellow confidence in prescribing exercise, assessed on a 6-point Likert-type scale, increased over the study from an average rating of somewhat unconfident to somewhat confident.

Conclusion:
We have created an online primer on exercise for use as part of a mini-curriculum on RR. In a pilot trial, completion of the module led to an immediate improvement in the completeness of an exercise prescription, but this improvement was not durable in the short-term, most likely due to the low participation rate and small sample sizes. A larger study including the effect of faculty supervision of learner participation is warranted.

Disclosure: A. Patel, None; K. O'Rourke, ACR Curriculum Subcommittee, 6.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/a-primer-on-exercise-an-interactive-online-educational-module-incorporating-spaced-education-to-supplement-the-acr-core-curriculum-outline-for-rheumatology-fellowship-programs

Abstract Number: 114

Early Diagnosis and Treatment of RA: Clinical Performance and Economic Outcomes from a Continuing Education Initiative

David Gazeley¹, Michael Weinblatt² and Stephen Bender³, ¹Medicine, Medical College of Wisconsin, Milwaukee, WI, ²Rheumatology,
SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Education Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
The CME initiative RAPID® (Rheumatoid Arthritis: Primary Care Initiative for Improved Diagnosis and Outcomes) is a 7-year series of activities that used national-scope aggregated healthcare claims data to identify primary care clinicians who diagnose and refer patients for RA at a low frequency. Medical claims data have been used since 2008 to measure the implementation of the diagnostic and referral clinical strategies resulting from the RAPID activities by analyzing performance changes of participants. Since its inception, over 65,516 physicians have completed the RAPID educational activity. We have reported statistically significant improvements in the participants’ diagnostic and referral performance (Bender S, et al. CE Measure, 2016;10:10-15).

Methods:
Rates of increased RA diagnoses and referral among providers were determined for a sample of the RAPID initiative (RAPID III) using a national-scope administrative healthcare claims database representing over 870,000 US clinicians. New RA diagnoses were defined as the number of unique patients with a diagnosis of RA (ICD-9 codes 714.X) who had a claim from both a primary care provider and a rheumatologist (shared patients) in the time period prior to, or after the CME activity date [2011] and who had been prescribed (and filled) a prescription for an appropriate RA therapy. Comparisons were made among highly matched controls of non-participants, with approximately 40 non-participant controls for every participating clinician. The follow period was approximately 2.5 years. An exploratory predictive model was used to estimate the economic impact of earlier diagnosis and treatment of RA. The model estimated how many patients with moderate/high disease activity were likely to transition to remission and the associated costs averted by decreased healthcare utilization and productivity losses. Prevention of joint arthroplasty was also predicted. Deterministic and probabilistic sensitivity analyses were performed to evaluate the influence of model parameters on the estimated outcomes of the model.

Results:
A sample of 3,919 RAPID III participants (n=1,691) was evaluated. These participants managed 265,834 patients and had 1,837 newly diagnosed patients with RA. There was a statistically significant 11% increase in the proportion of RA diagnoses by learners following participation in the CME initiative. All referred patients received appropriate therapy for RA. There was no change in the proportion of RA diagnoses among the control group. The estimated costs averted when newly diagnosed patients underwent treatment leading to remission were $11,618,483 (95% CI; $3,954,798 to $24,547,314).

Conclusion:
A CME initiative improved the post-activity performance of targeted learners significantly more than non-targeted providers. Analysis of medical claims data is a useful tool for assessing performance change in CME initiative participants. Earlier diagnosis and treatment of RA may be associated with decreased costs.

Disclosure: D. Gazeley, None; M. Weinblatt, FACTORx and the RAPID CME initiative, 5; S. Bender, None.

Abstract Number: 115

Training the Next Generation of Investigative Rheumatologists: Results of the Usbji’s Young Investigator Initiative for Academic Rheumatologists

Nancy E. Lane, Ann Rosenthal, Howard Hillstrom and Edward Puzas, 1Center for Musculoskeletal Health, University of California, Davis School of Medicine, Sacramento, CA, 2Division of Rheumatology, Medical College of Wisconsin, Milwaukee, WI, 3orthopedics, Hospital for special surgery, New York City, NY, 4Orthopedic Surgery, University of Rochester School of Medicine, Rochester, NY

First publication: September 18, 2017
SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Education Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The success of a physician scientist in academic rheumatology requires effective skills to obtain peer-reviewed funding. The number of NIH-funded junior investigators is low in proportion to the prevalence of musculoskeletal (MSK) diseases. As well-conceived and structured research is more likely to be funded, in 2005 the U.S. Bone and Joint Decade/Initiative (USBJI) and Bone and Joint Canada initiated a grant mentoring and career development program for junior faculty in all fields of MSK research in the US/Canada who had not obtained an Independent Peer Reviewed Research Grant (RO1/equivalent) in order to foster the next generation of investigators. The purpose of this study was to determine the outcomes of Rheumatologists who attended the program 2005-2016.

Methods: The Young Investigator Initiative (YII) program included two 2-day workshops held 12-18 months apart with training in specific aspects of the development of well-founded research studies and grantsmanship (specific aims, experimental design, budget, collaborations), benefitting from multi-disciplinary perspectives on their proposed studies. Each mentee was assigned 2-4 experienced external mentors from the YII faculty to complement their institutional mentors until the Young Investigator obtained funding. Mentors made themselves available to assigned mentees for review of specific aims, evaluating grant drafts, and discussing research strategies. External mentors’ research expertise across the MSK disciplines included rheumatology, epidemiology, orthopaedics, bioengineering, biology, PTs, OTs.

Results: The YII is a competitive, peer-reviewed program. Of 736 applicants 2005-2016, 364 (49.5%) were accepted, including 59 Rheumatologists developing studies in common and less common forms of Rheumatic disease. Program metrics are tabulated in Table 1. Total external funding obtained by YII Rheumatology participants 2005-2016 is $48.5 million, from a combination of NIH/Canadian Institutes of Health Research/Foundations/Granting Agencies/Institutions, including the ACR-RRF; 34/59 (58%) received peer-reviewed funding.

Conclusion: The YII program has been successful in assisting junior investigators in academic rheumatology obtain peer-reviewed funding by providing education and external mentoring on grant structure and writing until funding is obtained.

Disclosure: N. E. Lane, LLP2A-Ale, 4; A. Rosenthal, None; H. Hillstrom, None; E. Puzas, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/training-the-next-generation-of-investigative-rheumatologists-results-of-the-usbjis-young-investigator-initiative-for-academic-rheumatologists
Immunotherapy-Induced Rheumatic Disease: How Prepared Are Rheumatologists to Address This Emerging Condition?

Laura Cappelli¹,², Cassandra Calabrese³, Leonard H. Calabrese³ and Clifton O. Bingham III⁴, ¹Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, ²Medicine/Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, ³Rheumatic & Immunologic Disease, Cleveland Clinic Foundation, Cleveland, OH, ⁴Rheumatology, Johns Hopkins University, Baltimore, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Education Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Cancer immunotherapy targeting immune checkpoints represents a major advance in oncology, yet has been associated with immune-related adverse events (IRAEs) affecting many organ systems, including an expanding range of rheumatic manifestations. Rheumatologists are new to this field, and we sought to examine their awareness, experience, clinical confidence, and educational needs regarding IRAEs by surveying rheumatology practitioners.

Methods: In the 2nd quarter of 2016, questionnaires were sent via email to health care provider cohorts at Johns Hopkins University (JHU) and Cleveland Clinic (CC). The survey population came from their Continuing Medical Education (both) and Rheumatology Website (JH) databases. Both cohorts had physicians and advanced practitioners. Survey questions addressed domains of awareness, clinical experience, and interest in IRAE-specific medical education.

Results: Response rates were 114/2198 (5.2%) at CC and 39/789 (5.0%) at JHU. Male physicians from private practices and academic institutions predominated (table 1). Only 24.1% reported familiarity with IRAEs, with most unaware of IRAEs or lacking sufficient knowledge on the topic (table 2). Only 14.8% had seen a patient with an IRAE, with inflammatory arthritis the most common. Most (60.7%) did not feel confident managing IRAEs. All but one participant indicated interest in educational activities on IRAEs, with description/recognition of IRAEs perceived as the biggest educational need.

Conclusion: We conclude that most respondents 1) had limited experience with rheumatic IRAEs, 2) lacked confidence in clinically addressing IRAEs, and 3) had a strong expressed desire for targeted education. Although limited by response rate, responder bias, and the timing of the survey shortly after the approval of these drugs, the results suggest a considerable need for rheumatology-specific education around this topic.
<table>
<thead>
<tr>
<th>Table 1. Demographic Variables (N = 153)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex: N (%)</strong></td>
</tr>
<tr>
<td>Male: 93 (61%)</td>
</tr>
<tr>
<td>Female: 60 (39%)</td>
</tr>
<tr>
<td><strong>Age: mean (SD)</strong></td>
</tr>
<tr>
<td>55.0 (12.4)</td>
</tr>
<tr>
<td><strong>Degree: N (%)</strong></td>
</tr>
<tr>
<td>MD/DO: 127 (83%)</td>
</tr>
<tr>
<td>NP: 8 (5.2%)</td>
</tr>
<tr>
<td>PA: 4 (2.6%)</td>
</tr>
<tr>
<td>RN: 9 (5.9%)</td>
</tr>
<tr>
<td>Other: 5 (3.3%)</td>
</tr>
<tr>
<td><strong>Years in medical practice: mean (SD)</strong></td>
</tr>
<tr>
<td>22.1 (12.9)</td>
</tr>
<tr>
<td><strong>Practice Setting: N (%)</strong></td>
</tr>
<tr>
<td>Academic: 43 (28.1%)</td>
</tr>
<tr>
<td>Private Practice: 68 (44.4%)</td>
</tr>
<tr>
<td>Hospital-based Practice: 25 (16.3%)</td>
</tr>
<tr>
<td>Industry: 5 (3.3%)</td>
</tr>
<tr>
<td>Other: 9 (5.9%)</td>
</tr>
<tr>
<td>Table 2. ICI/IRAE provider experience</td>
</tr>
<tr>
<td>--------------------------------------</td>
</tr>
<tr>
<td>Familiarity with ICIs</td>
</tr>
<tr>
<td>(N= 133)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Awareness of IRAEs</td>
</tr>
<tr>
<td>(N= 130)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Have seen a patient with an IRAE</td>
</tr>
<tr>
<td>(N = 122)</td>
</tr>
<tr>
<td>Types of IRAEs seen</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Confidence in management of IRAEs (N = 122)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

Disclosure: L. Cappelli, Bristol-Myers Squibb, 2; C. Calabrese, None; L. H. Calabrese, Bristol-Myers Squibb, 5; C. O. Bingham III, Bristol-Myers Squibb, 2,Bristol-Myers Squibb, 5.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/immunotherapy-induced-rheumatic-disease-how-prepared-are-rheumatologists-to-address-this-emerging-condition](http://acrabstracts.org/abstract/immunotherapy-induced-rheumatic-disease-how-prepared-are-rheumatologists-to-address-this-emerging-condition)

Abstract Number: 117

Using Goutpro to Make Medical Trainees Gout Pros- a Single Blinded Randomized Control Study

Linh Ngo¹, Eric Miller², Peter A. Valen³ and Alisa Duran⁴, ¹Division of Rheumatology, University of Minnesota, Minneapolis, MN, ²Medicine, Hennepin County Medical Center, Minneapolis, MN, ³Rheumatology/ Dept of Medicine, University of Minnesota/Minneapolis VAMC, Minneapolis, MN, ⁴Department of Medicine, University of Minnesota, Minneapolis, MN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: ARHP Education Poster
Session Type: ACR Poster Session A  
Session Time: 9:00AM-11:00AM

**Background/Purpose:** Gout is the most common type of inflammatory arthritis in the U.S., affecting 4% of the population. Despite modern advancements and the availability of reference tools, the current care from primary care providers is felt to be suboptimal in the U.S. One barrier to improving care in gout includes limited education during medical training.

To address limited education during training, we developed a digital adjunctive teaching tool, GoutPro, on the topic of gout. Utilizing a clinically integrative model proposed by Khan et al, it takes into consideration different learning styles, current guidelines on gout, interactive activities and clinical problem solving. In our pilot study, we obtained positive subject feedback through survey. To assess objective trainee improvement of gout knowledge, a single-blinded randomized controlled study assessing knowledge prior to and after GoutPro intervention was conducted.

**Methods:** We recruited a total of 19 medical trainees from Hennepin County Medical Center to participate in our study. Trainees included medical students of MS 3-4 training levels and residents of PGY 1-4 training levels. All trainees registered via an online registration form and consent forms were signed digitally. Registered participants were randomized proportionally according to level of training into the control and the study group via a novel automated cloud based system to keep the investigators blinded. Correspondence with participants was also managed by the automated system. All participants were sent an e-mail with a link to a pre-test of 14 questions on crystalline arthropathy based on recommendations from the 2012 ACR Gout Guidelines and MKSAP 17. The study group was instructed to attend a live session led by the investigators that utilized GoutPro. The control group was provided both the ACR Guidelines and UpToDate reference articles on crystalline arthropathy for review. All participants received an identical post-test 27 days later to avoid coinciding with trainee change of rotations. 15 out of 19 subjects completed the post-test. Our primary outcome was difference in pre- and post-quiz scores between the control and study group. The Student's t-test was used for analysis.

**Results:**

<table>
<thead>
<tr>
<th>Average Scores</th>
<th>Control Group (n=10)</th>
<th>Study Group (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Quiz</td>
<td>38%</td>
<td>52%</td>
</tr>
<tr>
<td>Post-Quiz</td>
<td>41%</td>
<td>59%</td>
</tr>
<tr>
<td>% Improvement</td>
<td>3%</td>
<td>7%</td>
</tr>
</tbody>
</table>

**Conclusion:**

1) The study group had a slightly higher percent improved test scores (7%) compared to those in control group (3%). The results did not reach statistical significance due to the small study size ($P=0.99$).

2) At baseline, medical trainees in the study demonstrated low knowledge on gout demonstrating the need for improved gout curriculum.

3) Future GoutPro studies with larger sample size from multiple centers will be needed.

4) Utilization of a novel cloud-based automated system to randomize and communicate with study subjects was an effective cost-efficient way to recruit, organize and manage study subjects while maintaining investigator blindness.

**Disclosure:** L. Ngo, None; E. Miller, None; P. A. Valen, None; A. Duran, None.


**Abstract Number:** 118

**Experiences and Perceptions of Patients with Rheumatoid Arthritis Participating in an Online Support Group: The Use of Social Media**

Jude K. A. des Bordes1, Jessica Foreman1, Susan K. Peterson2, Maria A. Lopez-Olivo3, Tiffany Westreich-Robertson4, Catherine Hofstetter5, Anne Lyddiatt6, Amye L. Leong7 and Maria Suarez-Almazor3, 1Section of Rheumatology and Clinical Immunology, Department of General Internal Medicine, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA, Houston, TX, 2Department of Behavioral Science, The University of Texas MD Anderson Cancer Center, Houston Texas, USA, Houston, TX, 3Section of Rheumatology and Clinical Immunology, Department of General Internal Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX,
SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: ARHP Education Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Providing social support is an important component in the management of chronic diseases. In rheumatoid arthritis (RA), peer support is particularly important for coping with the psychosocial aspects of the disease. The aim of this study was to assess the participation, experiences, and perceptions of patients in an online support group for patients with RA using social media.

Methods: A private online support group was created on Facebook including 105 participants who were 18 years or older, residing in the United States or Canada and had been diagnosed with RA for less than 10 years. Each week, a moderator posted a topic for discussion, however, participants could also share other disease-relevant information not directly related to the discussion of the week. We analyzed participants' posts in the first 5 weeks, their reaction to responses of other participants, and how often and what information was being shared outside the main discussion topics.

Results: Most participants were female and non-Hispanic white (94% and 87.6%, respectively). Nearly two-thirds (65%) were married or lived with a significant other or partner and 62 (59%) had a Bachelor’s or higher degree. The mean age was 52.7 years. Although nearly all participants visited the forum, only an average of about 50 (48%, range 42-62) actively participated in the discussions each week, with the most and least participation recorded respectively in the first and fifth weeks. About 10 percent of participants never contributed to the discussions. Topics discussed included physical challenges, emotional health, self-care, exercise, and socializing. Discussion on physical challenges attracted the highest number of posts (n=311) while self-care had the least (n=120). Other information shared by participants outside the discussion topics included their disease experiences, medications, social lives, other websites on RA, frustrations and messages of encouragement. They also shared pictures of themselves, their families, pets and satirical depictions of their disease experience. Many participants expressed excitement and thankfulness for the social support provided by the group.

Conclusion: Participants were generally enthusiastic about the online support group. Social media based groups may provide an alternative means of facilitating education and peer support that is so often lacking in traditional models of care. However, more research is needed to find better ways to encourage more participation and to sustain participant interest.

Disclosure: J. K. A. des Bordes, None; J. Foreman, None; S. K. Peterson, None; M. A. Lopez-Olivo, None; T. Westrich-Robertson, None; C. Hofstetter, None; A. Lyddiatt, None; A. L. Leong, None; M. Suarez-Almazor, Rheumatology Research Foundation, 2.


Abstract Number: 119

Occupational Exposure to Asbestos and Risk of Rheumatoid Arthritis

Anna Ilar1, Per Gustavsson1, Pernilla Wiebert1, Camilla Bengtsson1, Lars Klareskog2 and Lars Alfredsson1, 1The Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden, 2Rheumatology unit, Department of Medicine, Karolinska Institutet, Stockholm, Sweden
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Epidemiology and Public Health Poster I: Rheumatoid Arthritis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Due to the known association between silica dust and rheumatoid arthritis (RA), we wanted to study the association between RA and another
silicate mineral; asbestos. The aim was to estimate the risk of seropositive or seronegative RA from ever occupational asbestos exposure as well as years with exposure.

Methods:

The study base consisted of men and women living in Sweden between 2006 and 2013. RA patients were identified from the Swedish Rheumatology Quality Register (SRQ). We matched ten controls from the national population register per case on age, county and sex. Data on occupational histories were collected from the national population and housing censuses carried out in 1960, 1970, 1975, 1980 and 1990. A job-exposure matrix (JEM) containing historical exposure estimates from 1955-1995 to asbestos was applied to the study participants’ occupational histories. We used conditional logistic regression to assess the odds ratios (ORs) and 95 % confidence intervals (CIs) of RA associated with ever exposure and years of exposure to asbestos. ORs were adjusted for ever exposure to respirable crystalline silica dust and household disposable income divided into quartiles.

Results:

9 704 cases and 90 271 controls were included in the analysis. Ever vs. never asbestos exposure resulted in an OR of 1.35 (95 % CI: 1.22-1.48) among men and 1.10 (95 % CI: 0.94-1.29) among women for seropositive RA. The ORs decreased to 1.12 (95 % CI: 1.01-1.25) and 1.02 (95 % CI: 0.86-1.22) for men and women respectively after adjusting for silica exposure and household disposable income. Asbestos exposed men were more likely than women to have worked with asbestos for a longer period of time and their risk of seropositive RA increased with years with the exposure. Male participants with more than 20 years of asbestos exposure at work had an adjusted OR of 1.27 (1.06-1.53, p for trend: 0.008).

Conclusion:

Asbestos exposure is associated with seropositive RA among men. The increased risk remained after adjustments for potential confounding from silica exposure and household disposable income.

Disclosure: A. Ilar, None; P. Gustavsson, None; P. Wiebert, None; C. Bengtsson, None; L. Klareskog, None; L. Alfredsson, None.


Abstract Number: 120

Patients with Rheumatoid Arthritis Have Higher Lifetime Professional and Non-Professional Exposure to Silica Dust Particles Compared to General Population

Luca Semerano1,2,3, Catherine Cavalin4,5,6, Odile Macchi4,7, Sara El Rharras3, Mylene Petit3, Patrice Decker8,9, Emma André10, Paul André Rosental4,11 and Marie-Christophe Boissier12, 1UMR 1125, Inserm, Bobigny, France, 2EA4222, University of Paris 13, Sorbonne Paris Cité, Bobigny, France, 3Service de Rhumatologie, Assistance Publique – Hôpitaux de Paris (AP-HP) Groupe hospitalier Avicenne - Jean Verdier – René Muret, Bobigny, France, 4SILICOSIS project, ERC Advanced Grant, Centre for European Studies, Sciences Po, Paris, France, 5Centre for Employment and Labour Studies (CNAM), Noisy-le-Grand, France, 6Laboratory for Interdisciplinary Evaluation of Public Policies (LIEPP, Sciences Po, Paris), Paris, France, 7Centre for Historical Research, CNRS-EHESS, Paris, France, 8Li2P, University of Paris 13, Sorbonne Paris Cité, Bobigny, France, 9UMR 1125, INSERM, Bobigny, France, 10UMR1125, Inserm, Bobigny, France, 11National Institute for Demographic Studies (INED), Paris, France, 1274 rue Marcel Cachin, INSERM, Bobigny, France

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Epidemiology and Public Health Poster I: Rheumatoid Arthritis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Occupational exposure to silica dust has been associated with increased risk of developing ACPA positive Rheumatoid arthritis (RA)1,2,3. Little is known about non-occupational exposure, as there are no available tools to assess it in clinical practice.

The Dust Exposure Life-Course Questionnaire (DELCQ) longitudinally quantifies lifetime occupational and non-occupational (e.g. body care; hobbies such as DIY, woodworking, stone cutting etc..).
The DELCQ, developed within a European Research Council Advanced Grant, provides clinical research with a tool derived from social sciences. In the DELCQ, the identification of situations likely to put people at risk of exposure is grounded on an extensive list of products and activities summed up by the International Agency on Research on Cancer IARC and on a wide overview of the literature that in medicine, epidemiology and industrial hygiene has been addressing silica exposure and silica-related (or suspected-to-be-related) diseases.

The aim of this study was to use this novel tool to explore occupational and non-occupational silica exposure in a series of consecutive RA patients and to explore the association of quantified silica dust exposure with major disease features (ACPA positivity) or outcomes (erosive disease).

**Methods:**

The DELCQ was administered to 97 consecutive RA patients (77F, 20M, mean age 59.1+/− 13.3 yrs., 75 ACPA positives, 66 with erosive disease) attending the department of rheumatology of the Avicenne teaching Hospital (Bobigny, FRANCE). The DELQQC scores of patients were compared to those of 261 controls, matched for sex, age and smoking status, from a 825-subject national cohort, representative of the general French population (ELIPSSilice). Within RA subjects, the association of the scores with ACPA positivity and with erosive disease was assessed after adjustment for tobacco exposure.

**Results:**

RA patients had higher scores of total (median [Q1, Q3]: 25 [13, 36] vs. 9 [4, 19]), occupational (10 [0, 17] vs. 0 [0, 4]) and non-occupational (15 [8, 20] vs. 7 [0, 15]) exposure vs. controls (p<0.0001 for all comparisons). Amongst RA patients, male vs. female patients had higher occupational scores of exposure (12 [2, 18] vs. 0 [0, 3] p<0.005), while non-occupational exposure was not significantly different (12 [3, 25] vs. 8[4, 15]). After adjusting for smoking (ever smokers vs. nonsmokers), neither professional nor non-professional scores were associated with erosive disease, despite a strong negative interaction with tobacco exposure.

**Conclusion:**

By using a tool developed in collaboration of social sciences, this work shows for the first time that RA patients have higher nonprofessional lifetime exposure to silica dust compared to age and sex-matched subjects from the general population. Moreover, higher occupation exposure in RA is confirmed, in accordance with previous literature. Neither occupational nor non-occupational exposure was associated with ACPA positivity or erosive disease, likely due to the high prevalence of ACPA positivity and severe disease in the patient series.

**Disclosure:** L. Semerano, None; C. Cavalin, None; O. Macchi, None; S. El Rharras, None; M. Petit, None; P. Decker, None; E. Andre, None; P. A. Rosental, None; M. C. Boissier, None.

**View Abstract and Citation Information Online** - [http://acrabstracts.org/abstract/patients-with-rheumatoid-arthritis-have-higher-lifetime-professional-and-non-professional-exposure-to-silica-dust-particles-compared-to-general-population](http://acrabstracts.org/abstract/patients-with-rheumatoid-arthritis-have-higher-lifetime-professional-and-non-professional-exposure-to-silica-dust-particles-compared-to-general-population)

**Abstract Number:** 121

### Depression As a Risk Factor for the Development of Rheumatoid Arthritis: A Population-Based Cohort Study

**Isabelle Vallerand**1, Ryan Lewinson2, Mark Lowerison1, Alexandra Frolkis3, Gilaad Kaplan3, Andrew Bulloch4, Scott Patten1 and Cheryl Barnabe5, 1Department of Community Health Sciences, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada, 2Biomedical Engineering Program, Schulich School of Engineering, University of Calgary, Calgary, AB, Canada, 3Department of Medicine, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada, 4Department of Physiology & Pharmacology, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada, 5Division of Rheumatology, University of Calgary, Calgary, AB, Canada

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Epidemiology and Public Health Poster I: Rheumatoid Arthritis  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The underlying risk factors for the development of Rheumatoid Arthritis (RA) remain poorly understood; however, prospective studies have demonstrated that individuals with elevated Tumor Necrosis Factor alpha (TNFα), a pro-inflammatory cytokine, are at increased risk of subsequently developing RA. It remains unknown whether elevated TNFα by means of a different disease process can subsequently increase the risk of developing RA. Recently, major depressive disorder (MDD) has been identified to have a direct effect on
cytokines, including increased serum concentrations of TNFα relative to healthy controls independent of underlying inflammatory disease. Based on this, our hypothesis is that exposure to MDD may increase the risk of subsequently developing RA. In this study using a large population-based cohort, we assessed if patients with MDD were at increased risk of subsequently developing RA compared to the general population without MDD.

**Methods:** A retrospective cohort study was conducted using The Health Improvement Network (THIN) Database between the years 1986-2012 for up to 26 years of follow-up. The MDD cohort comprised patients with a diagnostic (Read) code for MDD and the remainder of patients formed the referent cohort. Both cohorts were followed until patients developed RA or were censored. Cox proportional hazards models were used to determine the risk of developing RA among patients with MDD, as reported using Hazard Ratios (HRs) and 95% confidence intervals (CIs) (α=0.05). A backward elimination procedure was used to determine the presence of effect modification (using a Wald test) or confounding by age or sex.

**Results:** A cohort of 403,932 patients with MDD and a referent cohort of 5,339,399 patients without MDD were identified in THIN. A total of 2,192 (0.54%) patients with MDD developed RA, and 24,021 (0.45%) patients without MDD developed RA over this period. Cox proportional hazards models identified a confounding effect by sex and a significant interaction by age (p<0.0001), whereby younger patients with MDD (age<40) had a 42% increased risk of developing RA (sex-adjusted HR=1.42, 95%CI: 1.31 – 1.53). In older patients (age>40), the risk of developing RA among those with MDD was lower but demonstrated a 14% increased risk (sex-adjusted HR=1.14, 95%CI: 1.08-1.21).

**Conclusion:** MDD was found to be a risk factor for the development of RA. This risk was highest among younger patients with MDD, and the risk was only somewhat increased among older patients with MDD. These results provide support the hypothesis that MDD may be associated with the development of RA.

**Disclosure:** I. Vallerand, Canadian Rheumatology Association and Novartis, 3; R. Lewinson, None; M. Lowerison, None; A. Frolkis, None; G. Kaplan, None; A. Bulloch, None; S. Patten, None; C. Barnabe, None.


**Abstract Number:** 122

**Poor Prognostic Factors at the Start of Methotrexate Therapy Are Not Associated with Worse Treatment Response: Results from the Rheumatoid Arthritis Medication Study**

**JM Gwinnutt¹, Kimme L. Hyrich¹, M Lunt¹, Darren Plant¹, M Brazl², R Postema², Anne Barton¹ and Suzanne M Verstappen¹**, ¹Manchester Academic Health Science Centre, Manchester, United Kingdom, ²Bristol-Myers Squibb, Uxbridge, United Kingdom

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Epidemiology and Public Health Poster I: Rheumatoid Arthritis  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** As anti-citrullinated protein antibody positivity (+), RF+ and erosions are independently associated with poor outcomes in patients (pts) with RA, clinicians may use these prognostic factors in treatment decisions. However, it is not known whether pts with these poor prognostic factors respond equally well to conventional synthetic DMARD therapy. The aim of this analysis was to compare clinical and pt-reported outcomes (DAS28 [CRP], HAQ) of pts with RA with poor prognostic factors (RF+ and/or anti-cyclic citrullinated peptide antibody 2+ [anti-CCP2+] and erosions) vs those without over 1 year. **Methods:** Pts with RA in the UK starting MTX therapy were recruited to the Rheumatoid Arthritis Medication Study (RAMS), a 1-year, prospective cohort study. RF was determined from baseline blood samples, and data about anti-CCP status and erosions were obtained from medical notes. Pts who were anti-CCP2+ and/or RF+ and had erosions were classified as having poor prognosis (PP), while those not were classified as not having poor prognosis (NPP). For this analysis, pts were excluded if they were recruited >2 years following symptom onset or had missing data for any of the three prognostic factors. At baseline, 6-month and 12-month demographic and clinical data were recorded by a research nurse and pts completed the HAQ. The association between prognosis group and longitudinal DAS28 (CRP) and HAQ at 6 and 12 months was assessed using linear and negative binomial regression, respectively. The association between prognosis group and longitudinal DAS28 (CRP) and HAQ was assessed using linear and negative binomial random effects models, respectively. Baseline age, sex and symptom duration were included in the models as covariates. **Results:** In total, 545 pts with RA were included (PP, n=79 [14.5%]; NPP, n=466 [85.5%]). At baseline, PP pts were older, but other characteristics were similar (Table). DAS28 (CRP) and HAQ scores were similar between groups at 6 months (median [interquartile range (IQR)] DAS28 [CRP]: PP, 3.03 [2.4, 4.1] vs NPP, 3.2 [2.3, 4.3], coefficient –0.11, 95% CI –0.52, 0.29; HAQ: PP, 0.88 [0.25, 1.50] vs NPP, 0.63 [0.13, 1.25], incidence rate ratio [IRR] 1.12, 95 CI 0.76, 1.64) and 1 year (median [IQR] DAS28 [CRP]: PP, 2.98 [2.25, 3.75] vs
Conclusion: Treatment response is similar in pts with and without poor prognostic factors. These results suggest that, at this early stage of disease, baseline poor prognostic factors do not predict treatment response to conventional synthetic DMARDs, nor do they indicate that RA disease is reported as worse at 6 or 12 months in pts with vs without these poor prognostic factors.

Table. Patient Demographic and Clinical Data at Baseline

<table>
<thead>
<tr>
<th></th>
<th>Total cohort (N=545)</th>
<th>PP (n=79)</th>
<th>NPP (n=466)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at onset, years</td>
<td>57 (47, 66)</td>
<td>60 (48, 71)</td>
<td>56 (47, 66)</td>
<td>0.03†</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>354 (65.0)</td>
<td>49 (62.0)</td>
<td>305 (65.5)</td>
<td>0.54‡</td>
</tr>
<tr>
<td>Symptom duration (months)</td>
<td>6 (4, 12)</td>
<td>7 (4, 11)</td>
<td>6 (4, 12)</td>
<td>0.93‡</td>
</tr>
<tr>
<td>Smoking status, n (%)</td>
<td>201 (37.2) 208 (38.5)</td>
<td>31 (39.7) 30 (38.5)</td>
<td>170 (36.8) 178 (38.5)</td>
<td>0.83‡</td>
</tr>
<tr>
<td>Never Ex-smoker Current</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SJC (28)</td>
<td>4 (2, 9)</td>
<td>4 (2, 9)</td>
<td>4 (2, 9)</td>
<td>0.72‡</td>
</tr>
<tr>
<td>TJC (28)</td>
<td>6 (2, 12)</td>
<td>5.5 (2, 9)</td>
<td>6 (2, 12)</td>
<td>0.56†</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>0.88 (0.38, 1.50)</td>
<td>1.00 (0.38, 1.75)</td>
<td>0.88 (0.38, 1.50)</td>
<td>0.25†</td>
</tr>
<tr>
<td>DAS28</td>
<td>4.25 (3.25, 5.20)</td>
<td>4.30 (3.55, 4.80)</td>
<td>4.20 (3.25, 5.25)</td>
<td>0.96†</td>
</tr>
<tr>
<td>HAQ</td>
<td>0.88 (0.38, 1.50)</td>
<td>1.00 (0.38, 1.75)</td>
<td>0.88 (0.38, 1.50)</td>
<td>0.25†</td>
</tr>
<tr>
<td>RF status, n (%)</td>
<td>372 (68.3) 173 (31.7)</td>
<td>74 (93.7) 5 (6.3)</td>
<td>298 (64.0) 168 (36.1)</td>
<td>&lt;0.001‡</td>
</tr>
<tr>
<td>Positive Negative</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-CCP2 status, n (%)</td>
<td>344 (63.1) 201 (36.9)</td>
<td>66 (83.5) 13 (16.5)</td>
<td>278 (59.7) 188 (40.3)</td>
<td>&lt;0.001‡</td>
</tr>
<tr>
<td>Positive Negative</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erosions, n (%)</td>
<td>98 (18.0) 447 (82.0)</td>
<td>79 (100.0) 0 (0.0)</td>
<td>19 (4.1) 447 (95.9)</td>
<td>&lt;0.001‡</td>
</tr>
<tr>
<td>Positive Negative</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other csDMARD at baseline, n (%)</td>
<td>66 (12.3) 22 (3.9)</td>
<td>13 (16.5) 4 (5.1)</td>
<td>53 (11.6) 18 (3.9)</td>
<td>0.22‡</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steroids at baseline, n (%)</td>
<td>104 (19.2)</td>
<td>14 (18.0)</td>
<td>90 (19.4)</td>
<td>0.76‡</td>
</tr>
</tbody>
</table>

Data are median (IQR) unless otherwise stated *p-values resulting from comparison of baseline score across the two prognosis groups †Mann–Whitney U test ‡Chi-square test CCP=cyclic citrullinated peptide; IQR=interquartile range; NPP=patient group not having poor prognosis; PP=patient group with poor prognosis; csDMARD=conventional synthetic DMARD

Disclosure: J. Gwinnutt, None; K. L. Hyrich, None; M. Lunt, None; D. Plant, None; M. Brazil, Bristol-Myers Squibb, 1,Bristol-Myers Squibb, 3; R. Postema, Bristol-Myers Squibb, 1,Bristol-Myers Squibb, 3; A. Barton, Roche-Chugai, Celgene and Boehringer Engelheim, 5,Bristol-Myers Squibb, 2; S. M. Verstappen, None.


Abstract Number: 123

Relationship between Shift Work and the Onset of Rheumatoid Arthritis; Results from a Swedish Case-Control Study

Lars Alfredsson1, Anna Karin Hedström2, Torbjörn Åkerstedt3 and Lars Klareskog4, 1The Institute of Environmental Medicine, Karolinska
Background/Purpose: Shift work has previously been associated with increased RA risk in females. The aim of this study was to investigate the potential association between permanent night shift work, rotating shift work, and day oriented shift work, and risk of developing anti-citrullinated peptide antibodies (ACPA) positive and ACPA negative RA.

Methods: The present report is based on a Swedish population-based, case-control study with incident cases of RA (1951 cases, 2225 matched controls). Using logistic regression, occurrence of RA among subjects who have been exposed to different kinds of shift work was compared with that among those who have never been exposed, by calculating the odds ratio (OR) with a 95% confidence interval (CI).

Results: Rotating shift work and day oriented shift work were associated with a 30% increased risk of developing ACPA positive RA, but not ACPA negative RA (OR 0.7, 95% CI 0.6-0.9) and ACPA negative RA (OR 0.8, 95% CI 0.6-1.0) (table 1). For both subsets of RA, significant trends showed a lower risk of developing RA with increasing duration of permanent night shift work (table 2).

Conclusion: Sleep restriction as a consequence of shift work is associated with several biological effects among which changes in melatonin production may be involved. The present epidemiological findings of a complex relationship between sleep patterns and different forms of RA may be of importance for increasing the understanding of the pathophysiology of RA.

Disclosure: L. Alfredsson, None; A. K. Hedström, None; T. Åkerstedt, None; L. Klareskog, None.

Abstract Number: 124
Background/Purpose: Smoking is one of the most established risk factors for rheumatoid arthritis (RA). The aim of this study was to estimate how age at smoking debut, smoking cessation, duration, intensity, and cumulative dose of smoking influence the risk of developing ACPA positive and ACPA negative RA.

Methods: The present report is based on a Swedish population-based, case-control study with incident cases of RA (3655 cases, 5883 matched controls). Using logistic regression models, subjects with different smoking habits were compared regarding risk of developing the two subsets of RA, by calculating odds ratios (OR) with 95% confidence intervals (CI).

Results: Smoking increased the risk of developing both ACPA positive (OR 1.9, 95% CI 1.7-2.1) and ACPA negative RA (OR 1.3, 95% CI 1.2-1.5). For both subsets of RA, a cumulative dose of smoking less than five pack years was not significantly associated with increased disease risk. A dose-response association was observed between cumulative dose of smoking (exceeding five pack years) and risk of developing both ACPA positive and ACPA negative RA (p values for trend <0.0001) (table 1). Duration of smoking had a higher influence on the association between smoking and RA than did intensity of smoking (table 2). Among both subsets of RA, the detrimental effect of smoking decreased after smoking cessation. Twenty years after smoking cessation, there was no longer an association between smoking and risk of ACPA negative RA, whereas the association between smoking and ACPA positive RA risk persisted and was dependent on the cumulative dose of smoking (table 3).

Conclusion: Smoking increases the risk of both subsets of RA with a more pronounced influence on the risk of ACPA positive RA. Preventive measures in order to reduce smoking are essential and may result in a decline in RA incidence.
Disclosure: L. Alfredsson, None; A. K. Hedström, None; C. Bengtsson, None; L. Klareskog, None.


Abstract Number: 125

Exposure to Passive Smoking and RA Risk; Results from a Swedish Case-Control Study

Lars Alfredsson1, Anna Karin Hedström2 and Lars Klareskog3, 1The Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden, 2Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden, 3Dept. of Medicine, Rheumatology Unit, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Epidemiology and Public Health Poster I: Rheumatoid Arthritis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Smoking has consistently been associated with increased risk of developing rheumatoid arthritis (RA). We investigated the influence of passive smoking on the risk of developing ACPA positive and ACPA negative RA.

Methods: A population-based case-control study using incident cases of RA was performed in Sweden, and the study population in this report was restricted to include never smokers (589 cases, 1764 controls). Cases and controls answered an extensive questionnaire. The incidence of RA among never smokers who had been exposed to passive smoking was compared with that of never smokers who had never been exposed, by calculating the odds ratio (OR) with a 95% confidence interval (CI) employing logistic regression.

Results: No association was observed between exposure to passive smoking and risk of ACPA positive or ACPA negative RA, regardless if the exposure took place within 10 years prior to index, or earlier in life.

There was no suggestion of a trend between duration of passive smoking and RA risk. Long term exposure to passive smoking for 20 years or longer was not significantly associated with increased disease susceptibility (table 1).

Conclusion: No association was observed between exposure to passive smoking and risk of ACPA positive or ACPA negative RA among never smokers. Our finding may be explained by a threshold below which no association between smoke exposure and RA occurs.
Smoking Is Causally Associated with Disease Activity in Rheumatoid Arthritis

Milena Gianfrancesco¹, Laura Trupin², Stephen Shiboski³, Mark van der Laan⁴, Jonathan Graf⁵, John B. Imboden Jr.⁶, Jinoos Yazdany² and Gabriela Schmajuk⁷, ¹Medicine/Rheumatology, University of California, San Francisco, San Francisco, CA, ²Medicine/Rheumatology, University of California San Francisco, San Francisco, CA, ³Department of Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, CA, ⁴University of California, Berkeley, Berkeley, CA, ⁵Department of Medicine, Division of Rheumatology Zuckerberg San Francisco General Hospital, University of California, San Francisco, San Francisco, CA, ⁶Medicine, University of California, San Francisco, San Francisco, CA, ⁷San Francisco VA Medical Center, University of California San Francisco, San Francisco, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Epidemiology and Public Health Poster I: Rheumatoid Arthritis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The association between smoking and risk of rheumatoid arthritis (RA) has been well documented; however, the relationship between smoking and RA disease activity is less clear. Previous studies have indicated a null association between smoking and pain, swollen joint count, physical function, and radiographic joint damage, while others have demonstrated an inverse association. Inconsistent findings may be ascribed to heterogeneous study designs or biases in statistical analyses. We examined the causal association between smoking and RA outcomes using methods that account for time-varying confounding and loss to follow-up.

Methods: We used electronic health record data from a safety-net health system between 2013-2017. We included individuals with a diagnosis of RA and at least 2 clinic visits within 12 months (n=291). Timepoints during the study period were defined in 3-month intervals. We assessed smoking status (yes/no) at each timepoint; additional covariates included sex, race/ethnicity, age, obesity (BMI > 30 kg/m²), and medications. We also controlled for depression among a subset of patients (n=165) who had completed the Patient Health Questionnaire (PHQ-9). We used longitudinal targeted maximum likelihood estimation to estimate the causal effect of smoking on disease activity as measured by the clinical disease activity index (CDAI) and patient global assessment (PGA) at 30 months (or 2.5 years). We also accounted for time-varying covariates and informative missingness of data.

Results: Patients were 82% female, with a mean age 59.2 ± 12.2 and 91% racial/ethnic minorities. Eleven percent of patients were smokers
and the mean BMI was 29.0 + 6.9 (Table 1). Smoking was associated with a CDAI score of 16.67 at 30 months compared to a score of 12.05 for non-smoking after adjusting for covariates. Conversely, smoking was associated with a lower PGA score compared to non-smoking over the same period (40.53 vs. 45.42, respectively; p<0.001). However, additional control for depression based on the PHQ-9 did not change the association between smoking and disease activity based on CDAI (p<0.001), but eliminated the significant inverse relationship between smoking and PGA (p=0.24).

**Conclusion:** Smoking may be causally associated with higher levels of disease activity over time as measured by the CDAI. Differences in CDAI between smokers and non-smokers are likely clinically meaningful for individuals with low to moderate disease activity. Patient reported outcomes such as PGA may be influenced by other factors such as depression. These methods may be useful for investigations of additional exposures on longitudinal outcome measures in rheumatologic disease.

**Table 1. Baseline characteristics of rheumatoid arthritis patients included in the study (n=291)**

<table>
<thead>
<tr>
<th></th>
<th>N (%) or Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>238 (82)</td>
</tr>
<tr>
<td>Age</td>
<td>59.16 (12.2)</td>
</tr>
<tr>
<td>White, non-Hispanic</td>
<td>26 (9)</td>
</tr>
<tr>
<td>Asian</td>
<td>84 (29)</td>
</tr>
<tr>
<td>Black, non-Hispanic</td>
<td>23 (8)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>158 (54)</td>
</tr>
<tr>
<td>Current Smoker</td>
<td>31 (11)</td>
</tr>
<tr>
<td>BMI</td>
<td>29.04 (6.9)</td>
</tr>
<tr>
<td>CDAI Score</td>
<td>14.17 (12.6)</td>
</tr>
<tr>
<td>PGA Score</td>
<td>48.65 (27.9)</td>
</tr>
<tr>
<td>Prescribed Biologic</td>
<td>52 (18)</td>
</tr>
<tr>
<td>Prescribed Synthetic</td>
<td>230 (79)</td>
</tr>
</tbody>
</table>

**Disclosure:** M. Gianfrancesco, None; L. Trupin, None; S. Shiboski, None; M. van der Laan, None; J. Graf, None; J. B. Imboden Jr., None; J. Yazdany, None; G. Schmajuk, None.


**Abstract Number:** 127

**Diet Change and Omega-3 Supplementation in the First Three Years Following a Diagnosis with Rheumatoid Arthritis in Sweden**

Maxine Lancelot1,2, Olivier Grimaud3, Saedís Saevardsdóttir4, Johan Asklings5, Lars Klareskog6, Lars Alfredsson7 and Camilla Bengtsson8, 1IMM, Karolinska Institutet, Stockholm, Sweden, 2EHESP, Paris, France, 3EHESP, Rennes, France, 4Rheumatology Unit, Department of Medicine, Karolinska University Hospital and Karolinska Institutet, Stockholm, Sweden, 5Unit of Clinical Epidemiology, Department of Medicine, Karolinska University Hospital and Karolinska Institutet, Stockholm, Sweden, 6Dept. of Medicine, Rheumatology Unit, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, 7The Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden, 8Inst of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden

**First publication:** September 18, 2017
Background/Purpose:
Major dietary modification and omega-3 supplements are often promoted on patient counseling websites for those with RA. Given uncertainty regarding such approaches, we aim to study the frequency and characteristics of patients who undertake these complementary measures.

Methods:
Included were 810 participants in the Epidemiological Investigation of Rheumatoid Arthritis (EIRA) in Sweden who answered questionnaires including diet (normal/Mediterranean/vegetarian/vegan/low glycemic index/other) and omega-3 supplement use at diagnosis, 1 year, and 3 years post-diagnosis. Prevalence of diet changes and supplement use were assessed. Logistic regression was used to analyze associations between changing diet post-diagnosis, omega-3 supplement use, and the lifestyle/demographic characteristics of education, sex, age, BMI, smoking, and pre-diagnosis diet.

Results:
Between 1999 and 2016, 810 EIRA participants (women: 74%, median age at inclusion: 58 (min 17-max 85), median BMI at inclusion 25.1 (min 15.5-max 50.1), university degree holders: 30%). The proportion of participants with a non-normal diet increased from 23% in 2008 to 30% in 2013. 26% reported a major change in diet within 3 years post-diagnosis (Table). Those who made a change were more likely to be younger (OR 0.98 per year of age, 95% CI 0.96-0.99), have a university education (OR 1.89, 95% CI 1.28-2.80), be women (OR 1.77, 95% CI 1.28-2.80), be obese (OR 2.28, 95% CI 1.38-3.78), and have an non-normal diet at baseline (OR 2.81, 95% CI 1.36-5.79 for vegetarian; OR 10.12, 95% CI 5.79-17.71 for Mediterranean; OR 24.82, 95% CI 8.09-76.1 for others). Omega-3 supplement use increased from 20.4% at baseline to 30.9% at one year and decreased to 11.9% three years post-diagnosis. Participants were more likely to both change diets and use omega-3 supplements if they were younger (OR 0.98 per year increase, 95% CI 0.96-0.99), following an alternative diet at baseline (12.0, 95% CI 6.61-21.6), or obese (OR 2.05, 95% CI 1.09-3.88).

<table>
<thead>
<tr>
<th>Description of diet change</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maintained same diet for 3 years</td>
<td>650 (74.4)</td>
</tr>
<tr>
<td>Maintained normal diet</td>
<td>550 (66.2)</td>
</tr>
<tr>
<td>Maintained another diet</td>
<td>50 (6.20)</td>
</tr>
<tr>
<td>Changed diet between baseline and 1 year, then maintained new diet at 3 years</td>
<td>61 (7.57)</td>
</tr>
<tr>
<td>Changed to normal diet at 1 year</td>
<td>24 (2.96)</td>
</tr>
<tr>
<td>Changed to another diet at 1 year</td>
<td>37 (4.68)</td>
</tr>
<tr>
<td>Changed diet between 1 and 3 years</td>
<td>173 (21.5)</td>
</tr>
<tr>
<td>Changed to normal diet at 3 years</td>
<td>51 (6.33)</td>
</tr>
<tr>
<td>Changed to another diet at 3 years</td>
<td>122 (15.1)</td>
</tr>
</tbody>
</table>

Conclusion:
Many RA patients change their diets or use supplements after diagnosis. To better target messaging about these complementary therapies, it may be beneficial to consider them by the sociodemographic and lifestyle characteristics that distinguish them.

Disclosure: M. Lancelot, None; O. Grimaud, None; S. Saevarsdottir, None; J. Askling, MSD, BMS, Pfizer, AbbVie, SOBI, UCB, Roche, Lilly, AstraZeneca, 2; L. Klareskog, None; L. Alfredsson, None; C. Bengtsson, None.


Abstract Number: 128

Use of Machine Learning and Traditional Statistical Methods to Classify RA-Related Disability Using Administrative Claims Data

Jeffrey R. Curtis¹, Huifeng Yun², Carol J. Etzel³, Shuo Yang⁴ and Lang Chen⁴, ¹Rheumatology & Immunology, University of Alabama at Birmingham, Birmingham, AL, ²University of Alabama at Birmingham, Birmingham, AL, ³Departments of Epidemiology and Biostatistics,
Background/Purpose: Administrative claims and electronic health record (EHR) data are commonly used to assess outcomes in rheumatoid arthritis (RA). However, direct measures of functional status are typically not available in these data sources to control for confounding in comparative effectiveness research.

Methods: Corrona registry data linked to Medicare claims (2006-2014) were used to build a claims-based disability classifier, measured by HAQ. Eligible patients had RA per Corrona rheumatologist, and >=1yr prior coverage. Demographics, socioeconomic factors, comorbidities, healthcare utilization, and medications from claims data were included as predictors.

In separate analyses, HAQ was classified dichotomously (<1, ≥1), as 3 categories (0, <0.5, ≥0.5–<1.5, and ≥1.5–3), and as a continuous variable, converted to corresponding HAQ category. Generalized logistic regression (GenLogit) with LASSO for variable selection and results were compared with machine learning methods including RandomForests, using a forest of 2000 trees. Separate models were run classifying each of the 8 HAQ subdomains separately, and then summing to form the composite HAQ score. Misclassification rates were compared and the area under the receiver operator curves (AUROC) was described.

Results: A total of 2,788 RA patients were eligible, classifying 52% of patients with low (n=1448) and 48% with high (n=1340) HAQ; and as 3 categories, low (n=887), moderate (n=1109), and high (n=792). Univariable analysis showed higher HAQ was associated with older age, being disabled (per Medicare), rural residence, and greater comorbidity burden, and higher healthcare utilization.

Variables selected by various methods were similar (Table). In the 2 category HAQ models, overall misclassification was 29% (RandomForests), 28% , and 38% (LASSO), with an AUROC of 0.84. In the 3 category HAQ models, RandomForests yielded misclassification of ~48% that did not meaningfully differ across the 3 HAQ categories. Misclassification of the GenLogit model varied widely by HAQ category. When misclassification did occur in the 3 category analysis, patients were usually 1 category off; more extreme misclassification (categorizing low HAQ patients as high, or vice-versa) was uncommon (<8%). The median (IQR) difference in the (observed – predicted) HAQ was 0.00 (-0.45, 0.41) units. Ongoing work is refining these models, reducing the misclassification rate, and validating the approach.

Conclusion: Results from this preliminary analysis suggest that administrative claims and EHR data might be useful to classify RA-related disability as measured by the HAQ with reasonable accuracy. Larger datasets and richer information in EHR data likely will improve the accuracy of these methods.
Table: Key variables from administrative claims data selected by machine learning methods to classify HAQ category*

<table>
<thead>
<tr>
<th>Variable</th>
<th>RandomForests</th>
<th>Generalized logistic regression with LASSO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Number of rheumatology visits</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Number of AHRQ CCS comorbidities</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Number of unique medications (any type)</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Number of outpatient physician visits</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Baseline steroid use</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Median household income</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Elixhauser comorbidity index</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Wheelchair</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Disable</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

*results shown for 3 category HAQ models

Disclosure: J. R. Curtis, AbbVie, Roche/Genentech, BMS, UCB, Myraid, Lilly, Amgen, Janssen, Pfizer, Corrona, 5,Amgen, Pfizer, Crescendo Bio, Corrona, 9; H. Yun, Bristol-Myers Squibb, 2; C. J. Etzel, Corrona, LLC, 3,Merck Human Health, 9; S. Yang, None; L. Chen, None.


Abstract Number: 129

Impact of the Multi-Biomarker Disease Activity Score Results on Whether Rheumatologists Changed Biologic Therapy for RA Patients

Jeffrey R. Curtis1, Kerri Ford2, Lang Chen3, Huifeng Yun3 and Fenglong Xie4, 1Rheumatology & Immunology, University of Alabama at Birmingham, Birmingham, AL, 2Crescendo Bioscience Inc., South San Francisco, CA, 3University of Alabama at Birmingham, Birmingham, AL, 4Division of Clinical Immunology & Rheumatology, University of Alabama at Birmingham, Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Epidemiology and Public Health Poster I: Rheumatoid Arthritis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The multi-biomarker disease activity (MBDA) score is a validated test used to assess disease activity for patients with rheumatoid arthritis (RA). How it is used in clinical practice in the U.S. is unclear. We evaluated the likelihood that rheumatologists would add or switch biologic therapies based on the MBDA test result.

Methods: Using previously published methods, we linked results of MBDA tests obtained as part of routine clinical care to 2012-2014 Medicare fee for service claims data for RA patients. We characterized patients as being on a biologic or targeted synthetic DMARD in the 90 days prior to the MBDA test and evaluated biologic/tofacitinib treatment changes in the 90 days following the MBDA test. MBDA test scores were classified as low (<30), moderate (30-44), and high (>44). The unit of analysis was the 90-day interval before and after each MBDA test score. Alternating logistic regression was used to compute odds ratios (OR) to quantify the likelihood that patients made any change (add or switch), accounting for the clustered nature of the data (intervals nested within patients, and patients nested within doctor
practices) and physician-level variability, controlling for patient age and sex. Sensitivity analyses used a 6-month interval for outcome ascertainment after the MBDA test.

**Results:** Using previously validated methods, a total of 27,621 unique RA patients were linked to 44,438 MBDA test scores. For the 27,256 intervals where RA patients were not on biologic therapy when the MBDA score was obtained, a total of 13.2% of patients added a biologic. Patients with high MBDA scores were significantly more likely to add a biologic (Table). For the 17,182 intervals where RA patients were already on a biologic, a total of 19.1% of patients switched or stopped the biologic that they were taking. Patients with lower MBDA scores were significantly more likely to stay on their therapy, whereas those with higher scores were more likely to stop and/or switch biologics.

After adjustment, results from the regression analyses showed that patients with moderate MBDA scores were 1.47 (95% CI 1.29-1.67)-fold more likely to add or switch biologics, and those with high MBDA scores were 2.54 (95% CI 2.19-2.94)-fold more likely to add or switch biologics. Men (OR=0.90, 95% CI 0.82-0.98) and older patients (OR=0.92 per 5 year increment, 95% CI 0.91-0.93) were less likely to add or switch therapy, even after controlling for variability between physicians (OR = 1.10, 95% CI 1.02-1.19). These results were robust and ORs were numerically larger when extending the interval to 6 months.

**Conclusion:** Results from the MBDA score were significantly associated with the likelihood that a physician added or switched biologic therapies, with either type of change being more frequent when the MBDA score was high. Further evaluation of outcomes after switching, conditional on the MBDA score, is warranted.

| Table: Proportion of patients who added or switching biologics after the MBDA test |
|------------------------------------|----------------------------------|----------------------------------|----------------------------------|
| MBDA Score                        | Non-biologic users who added a biologic after the MBDA test | Biologic Users Who Switched or Stopped their Current Biologic after the MBDA test |
| Low (<30)                         | N=27,256                         | N=17,182                        |
| Moderate (30-44)                  | 8.4%                             | 14.0%                           |
| High (>44)                        | 10.8%                            | 16.2%                           |
| Chi-square p value                | <0.0001                          | <0.0001                          |

**Disclosure:** J. R. Curtis, AbbVie, Roche/Genentech, BMS, UCB, Myriad, Lilly, Amgen, Janssen, Pfizer, Corrona, 5,Amgen, Pfizer, Crescendo Bio, Corrona, 9; K. Ford, Myriad Genetics, Inc., 1,Crescendo Bioscience Inc., 3; L. Chen, None; H. Yun, BMS, 2; F. Xie, None.


**Abstract Number:** 130

**Availability of Clinical Measures for Patients with Rheumatoid Arthritis in Integrated Delivery Networks Who Receive a Biologic or Targeted Synthetic Disease-Modifying Antirheumatic Drug: A Real-World Analysis of an Electronic Health Records Database**

Benjamin Chastek¹, Chieh-I Chen², Toshibo Kimura³, Jonathan Fay², Stephanie Korrer³ and Stefano Fiore⁴, ¹Optum, Eden Prairie, MN, ²Regeneron Pharmaceuticals, Inc., Tarrytown, NY, ³Health Economics and Outcomes Research, Optum, Eden Prairie, MN, ⁴Clinical Science, Sanofi Genzyme, Bridgewater, NJ

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Epidemiology and Public Health Poster I: Rheumatoid Arthritis

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** In patients with rheumatoid arthritis (RA), ACR treatment guidelines recommend treating to targets based on quantitative endpoints, with modification of therapy as needed to achieve those targets. Integrated Healthcare Delivery Networks (IDNs) collect data in electronic health records (EHR), which can be used to assess quality of care, manage costs, and support treatment decisions. This study examined the availability of clinical measures across IDNs among patients with RA who received a biologic or a targeted
Methods: In this retrospective analysis of the Optum One EHR database, patients were 18 years or older, had RA diagnoses ≥7 days apart between June 30, 2008 and July 31, 2015. For patients who switched from a tumor necrosis factor inhibitor (TNFi) to a different medication, the index date was the switch date. Among other patients with a prescription for a biologic or tsDMARD, the index date was the first prescription written. Analysis periods were “baseline” (1 year pre-index), or “follow-up” (1 year post-index). EHR reporting rates were determined for quantitative measures to guide treatment decisions: clinical measurements (height, weight, blood pressure, cholesterol, erythrocyte sedimentation rate [ESR], C-reactive protein [CRP], or tuberculosis [TB] test) and validated disease severity instruments (Routine Assessment of Patient Index Data [RAPID3], Disease Activity Score [DAS28], or Clinical Disease Activity Index [CDAI]). Mean ESR and CRP in follow-up were summarized.

Results: The 29,829 patients were 76.8% female, 80.1% age ≥45 years, and 83.8% Caucasian. Baseline TB reporting rate in EHRs was 18.8%. EHR reporting rates in follow-up (median, 6 office visits) were: 49.0% ESR or CRP; and 6.5% ≥1 disease severity measure (5.8% RAPID3, 0.2% DAS28, 0.6% CDAI). Data reporting in EHRs varied significantly across the 10 largest IDNs, including a range of 0.0% to 25.2% for disease severity measure reporting in follow-up. Mean±SD values for ESR and CRP in follow-up were 13.9±8.0 mm/hr and 5.7±4.2 pcg/mL, respectively; variations in ESR and CRP values were less pronounced than variations in EHR reporting rates.

Table. EHR reporting rates and reported ESR/CRP values, by IDN

<table>
<thead>
<tr>
<th>IDN Rank</th>
<th>Baseline (N=29,829)</th>
<th>Follow-up (N=7,455)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≥1 TB Test in EHR, %</td>
<td>≥1 ESR or CRP Test in EHR, %</td>
</tr>
<tr>
<td>Total</td>
<td>18.8%</td>
<td>49.0%</td>
</tr>
<tr>
<td>IDN Rank 1</td>
<td>22.0%</td>
<td>52.9%</td>
</tr>
<tr>
<td>IDN Rank 2</td>
<td>19.3%</td>
<td>55.4%</td>
</tr>
<tr>
<td>IDN Rank 3</td>
<td>13.6%</td>
<td>41.0%</td>
</tr>
<tr>
<td>IDN Rank 4</td>
<td>22.7%</td>
<td>38.5%</td>
</tr>
<tr>
<td>IDN Rank 5</td>
<td>9.1%</td>
<td>43.9%</td>
</tr>
<tr>
<td>IDN Rank 6</td>
<td>27.9%</td>
<td>60.7%</td>
</tr>
<tr>
<td>IDN Rank 7</td>
<td>14.7%</td>
<td>23.4%</td>
</tr>
<tr>
<td>IDN Rank 8</td>
<td>13.3%</td>
<td>65.1%</td>
</tr>
<tr>
<td>IDN Rank 9</td>
<td>44.6%</td>
<td>70.4%</td>
</tr>
<tr>
<td>IDN Rank 10</td>
<td>20.5%</td>
<td>65.1%</td>
</tr>
<tr>
<td>Other IDN (N=7,455)</td>
<td>15.8%</td>
<td>46.3%</td>
</tr>
</tbody>
</table>

p-value*<0.001<0.001<0.001<0.001<0.001

Conclusion: In this analysis of EHR reporting of clinical data among RA patients in IDNs who switched from a TNFi or received a biologic or tsDMARD, approximately 1 in 5 had a TB test reported pre-index and half had ESR and/or CRP reported post-index. Validated measures of disease severity (RAPID3, DAS28, or CDAI) were reported infrequently, and EHR reporting was highly variable across IDNs. With greater emphasis on a treat-to-target approach, more consistent and more complete EHR reporting is recommended to assist rheumatologists in tracking whether treatment targets for RA are being met with biologic or tsDMARD therapy appropriately.

Disclosure: B. Chastek, Optum, 3; C. I. Chen, Regeneron Pharmaceuticals, 3,Regeneron Pharmaceuticals, 1; T. Kimura, Regeneron Pharmaceuticals, 3,Regeneron Pharmaceuticals, 1; J. Fay, Regeneron Pharmaceuticals, 3,Regeneron Pharmaceuticals, 1; S. Korrer, Optum, 3; S. Fiore, Sanofi, 3,Sanofi, 1.


Abstract Number: 131

What Does It Mean to Have Rheumatoid Arthritis Now? a Current Burden of Disease Assessment in the United States

Rebecca Schumacher1, A Dominique2, Sofia Pedro1, TA Simon2 and Kaleb Michaud1-3, 1National Data Bank for Rheumatic Diseases, Wichita, KS, 2Bristol-Myers Squibb, Princeton, NJ, 3University of Nebraska Medical Center, Omaha, NE
Known since 1859, RA is the most common inflammatory joint disease with 0.5-1% worldwide prevalence. Currently, there is a larger number of medications and strategies for treating RA earlier and more aggressively, which also necessitates a greater understanding of the current burden of RA. Our objective is to measure the impact of RA on the individual and society through patient reported outcomes using a large US registry.

Methods:
We performed descriptive statistics of a random observation from RA patients enrolled in the National Data Bank for Rheumatic Diseases (NDB), a longitudinal US-wide study with comprehensive 6-month questionnaires from 1998-2017. We limited analysis to observations in the last decade (2007-2017) with a comparison to the previous 8 years (1998-2006). Health-related Quality of Life measures examined included HAQ, EQ5D, SF-36, activities of daily living, economic factors, and illness-related employment. With each of these individual testing measures, a total of 65 variables were considered for comparable analysis.

Results:
Our study included 18,168 participants in the last decade with 82.2% female, mean (SD) age of 60.6 (13.5) and RA duration of 15.7 (12.1) years. The 1998-2006 cohort included 20,412 patients, with 77.1% female, age of 60.4 (13.5) and RA duration of 14.2 (11.0) years. Descriptive item responses are detailed in Table. Patient reported consequences of the burden within the 2007-2017 cohort show a slight improvement in HAQ, pain, fatigue, and SF-36 physical component score (PCS), but a worsening in global severity, sleep, SF-36 mental component score (MCS), quality of life (QOL) scale, health satisfaction, and functional limitations. When stratified by RA duration (Figure), patients with a duration of ≤2 years had the lowest HAQ, pain, PCS, comorbidities, functional limitations and a higher QOL while duration of >20 years had the lowest fatigue, sleep and MCS score. Patients that took a DMARD or Biologic showed a definite improvement over patients that did not take any or prednisone. Conclusion:
Even in this era of effective new treatments, we found the burden of RA to still be severe and important. Current analyses show that HrQOL measures appear to be less related to type of treatment than decade of RA onset. Further analysis will be performed evaluating biologic vs. non-biologic treatments.
Table. Characterization of RA patients by decade.

<table>
<thead>
<tr>
<th>Variable</th>
<th>2007-2017 Mean</th>
<th>SD</th>
<th>1998-2006 Mean</th>
<th>SD</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>60.6</td>
<td>13.5</td>
<td>60.4</td>
<td>13.4</td>
<td>0.2</td>
</tr>
<tr>
<td><strong>Sex (% male)</strong></td>
<td>17.8</td>
<td></td>
<td>22.9</td>
<td></td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Disease duration (years)</strong></td>
<td>15.7</td>
<td>12.1</td>
<td>14.1</td>
<td>11.0</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Married (%)</strong></td>
<td>65.8</td>
<td></td>
<td>67.9</td>
<td></td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Total Income (US dollars)</strong></td>
<td>54771.73</td>
<td>944973.72</td>
<td>54771.49</td>
<td>944973.72</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>HAQ (0-3)</strong></td>
<td>1.0</td>
<td>0.7</td>
<td>1.1</td>
<td>0.7</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Pain (0-10)</strong></td>
<td>3.9</td>
<td>2.8</td>
<td>4.0</td>
<td>2.8</td>
<td>0.3</td>
</tr>
<tr>
<td><strong>Global severity (0-10)</strong></td>
<td>3.8</td>
<td>2.5</td>
<td>3.7</td>
<td>2.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Fatigue (0-10)</strong></td>
<td>4.4</td>
<td>3.0</td>
<td>4.5</td>
<td>3.0</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Sleep disturbance (0-10)</strong></td>
<td>4.1</td>
<td>3.2</td>
<td>3.8</td>
<td>3.1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Physical component score (SF-36)</strong></td>
<td>36.9</td>
<td>11.2</td>
<td>35.9</td>
<td>11.1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Mental component score (SF-36)</strong></td>
<td>48.0</td>
<td>11.8</td>
<td>49.1</td>
<td>11.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Comorbidity Index (0-9)</strong></td>
<td>2.0</td>
<td>1.7</td>
<td>1.7</td>
<td>1.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>VAS QOL scale (0-100)</strong></td>
<td>64.6</td>
<td>20.8</td>
<td>66.0</td>
<td>20.8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Health satisfaction (0-4)</strong></td>
<td>1.9</td>
<td>1.3</td>
<td>1.8</td>
<td>1.2</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Function Limitations</strong></td>
<td>7.4</td>
<td>5.4</td>
<td>7.1</td>
<td>5.3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Function Now compared to 6 Months</strong></td>
<td>2.9</td>
<td>1.0</td>
<td>2.9</td>
<td>0.9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Pain Now compared to 6 Months</strong></td>
<td>3.0</td>
<td>1.0</td>
<td>2.9</td>
<td>1.0</td>
<td>0.1</td>
</tr>
<tr>
<td><strong>Health Aides</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cane</strong></td>
<td>0.3</td>
<td>0.4</td>
<td>0.2</td>
<td>0.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Crutches</strong></td>
<td>0.0</td>
<td>0.1</td>
<td>0.0</td>
<td>0.1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Walker</strong></td>
<td>0.1</td>
<td>0.3</td>
<td>0.1</td>
<td>0.3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Wheelchair</strong></td>
<td>0.1</td>
<td>0.3</td>
<td>0.0</td>
<td>0.2</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Person Help-Dressing &amp; Grooming</strong></td>
<td>0.1</td>
<td>0.3</td>
<td>0.1</td>
<td>0.3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Person Help-Arising</strong></td>
<td>0.1</td>
<td>0.3</td>
<td>0.1</td>
<td>0.3</td>
<td>0.3</td>
</tr>
<tr>
<td><strong>Person Help-Eating</strong></td>
<td>0.0</td>
<td>0.1</td>
<td>0.0</td>
<td>0.1</td>
<td>0.9</td>
</tr>
<tr>
<td><strong>Person Help-Walking</strong></td>
<td>0.1</td>
<td>0.3</td>
<td>0.1</td>
<td>0.3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Economic</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Employed at Onset of Disease</strong></td>
<td>0.8</td>
<td>0.4</td>
<td>0.8</td>
<td>0.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Retired Early due to Arthritis or Pain</strong></td>
<td>0.3</td>
<td>0.5</td>
<td>0.3</td>
<td>0.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Retired Early due to Other Medical</strong></td>
<td>0.1</td>
<td>0.3</td>
<td>0.1</td>
<td>0.3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Days Limited Activity in 6 Months</strong></td>
<td>40.2</td>
<td>56.9</td>
<td>44.8</td>
<td>0.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Days Health kept from Usual Activities (30 days)</strong></td>
<td>8.0</td>
<td>10.1</td>
<td>7.5</td>
<td>10.0</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Able to Perform Activities Completely</strong></td>
<td>2.6</td>
<td>1.1</td>
<td>2.6</td>
<td>1.1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Financial Problem After Insurance (No/Limited. Moderate. Great)</strong></td>
<td>1.6</td>
<td>0.7</td>
<td>1.6</td>
<td>0.7</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Patient or Family Member Pay for All or Part Insurance</strong></td>
<td>0.7</td>
<td>0.4</td>
<td>0.7</td>
<td>0.4</td>
<td>0.4</td>
</tr>
</tbody>
</table>
Problem of Paying for Medical Insurance
(No/Slight/Moderate/Great) 0.9 1.0 0.9 1.0 0.5

<table>
<thead>
<tr>
<th>Medications</th>
<th>Mean</th>
<th>SD</th>
<th>Mean</th>
<th>SD</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMARD or biologic (%)</td>
<td>84.2</td>
<td>83.8</td>
<td>&lt;0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DMARD (%)</td>
<td>71.4</td>
<td>77.0</td>
<td>&lt;0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biologic (%)</td>
<td>49.2</td>
<td>34.8</td>
<td>&lt;0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current DMARDs (count)</td>
<td>0.9</td>
<td>0.7</td>
<td>1.1</td>
<td>0.8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>No DMARD/biologic or prednisone (%)</td>
<td>12.0</td>
<td>12.2</td>
<td>0.7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure. Means of health-related Quality of Life measures by decade and RA duration.

Disclosure: R. Schumacher, National Data Bank for Rheumatic Diseases, 3; A. Dominique, Bristol Myers Squibb, 3; S. Pedro, National Data Bank for Rheumatic Diseases, 3; T. Simon, Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1, 9; K. Michaud, National Data Bank for Rheumatic Diseases, 3.


Abstract Number: 132

**Occupational Physical Workload and Development of Anti-Collagen Type II Antibodies in Rheumatoid Arthritis Patients**

Pingling Zeng1, Lars Alfredsson2, Lars Klareskog3, Mohammed Mullazehi4, Saedis Saevarsdottir5, Camilla Bengtsson6 and Johan Römelid7, 1Institute of Environmental Medicine, Institute of Environmental Medicine, Karolinska Institute, Stockholm, Sweden, Stockholm, Sweden, 2The Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden, 3Dept. of Medicine, Rheumatology Unit, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, 4Department of Immunology, Genetics and Pathology, Uppsala University, Uppsala, Sweden, 5Karolinska Institute and Karolinska University Hospital, Stockholm, Sweden, 6Inst of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden, 7Department of Immunology Genetics and Pathology, Uppsala University, Uppsala, Sweden

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Epidemiology and Public Health Poster I: Rheumatoid Arthritis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: We have previously observed an association between exposure to occupational physical workload (PW) and risk of
developing rheumatoid arthritis (RA)[1]. We posit that PW could impose mechanical stress on the joints leading to neo-epitope formation and immune activation. The major solid component of the articular cartilage is collagen type II (CII). Elevated level of anti-CII antibodies do not predate RA development, but are transiently found in 6-9% early RA patients. These antibodies are associated with acute RA onset and HLA-DRB1*01 and *03, yet predict good long-term prognosis[2]. We hypothesized that exposure to PW especially in the period closely predating RA diagnosis would associate with anti-CII positive RA but not anti-CII negative RA.

**Methods:** Data involving 1396 incident RA cases and 5935 controls from the Swedish population-based case-control study, Epidemiological Investigation of Rheumatoid Arthritis (EIRA), were analyzed. Information on self-reported exposure to occupational PW was collected through questionnaire. Anti-CII was measured using ELISA. The odds ratio (OR) with 95% confidence interval (CI) of developing anti-CII positive RA or anti-CII negative RA associated with PW exposure was calculated using logistic regression. Adjustment for sex, age, residential area, educational level, alcohol consumption, body mass index, cigarette smoking, silica exposure and occupational class did not substantially change the estimates.

**Results:** The ORs observed for the association between anti-CII positive RA and different types of PW ranged from 1.0 (95% CI, 0.4-2.4) to 2.3 (95% CI, 1.3-4.0). There was no difference in the ORs for PW exposure at diagnosis or five years earlier (table1). The ORs for the association between anti-CII negative RA and PW ranged from 1.0(95% CI, 0.8-1.3) to 1.8(95% CI, 1.5-2.1). No statistically significant difference was observed between the ORs for anti-CII positive RA and the ORs for anti-CII negative RA (all p-values > 0.2). Stratification for HLA-DRB1*01/*03 or symptom duration did not change the results.

**Conclusion:** Since physical workload is associated with rheumatoid arthritis irrespective of anti-CII status or the presence of anti-CII associated HLA alleles, and regardless of whether the timing of PW exposure was close to the appearance of anti-CII. We found no evidence suggesting an association between PW and development of anti-CII in RA.

**References**


**Disclosure:** P. Zeng, None; L. Alfredsson, None; L. Klæreskog, None; M. Mullazehi, None; S. Saevarsdottir, None; C. Bengtsson, None; J. Rönnelid, None.


**Abstract Number:** 133

**Impact of the Five Components of the Euroqol 5-Dimensions Instrument on Healthcare and Work-Loss Costs in Rheumatoid Arthritis: Observational Data from Southern Sweden**

Anders Gülle1, Tor Olofsson1, Jonas K Söderling2, Martin Neovius2 and Johan K Wallman1, 1Department of Clinical Sciences Lund, Rheumatology, Lund University, Lund, Sweden, 2Department of Medicine, Clinical Epidemiology Unit, Karolinska Institutet, Stockholm, Sweden

First publication: September 18, 2017
SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Epidemiology and Public Health Poster I: Rheumatoid Arthritis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Healthcare and work-loss costs are markedly higher in RA patients than in the general population. The EuroQol 5-Dimensions (EQ-5D) instrument, commonly applied to measure utility and quality-adjusted life-years (QALYs) in health-economic evaluations, is based on a questionnaire, asking respondents to value 5 health dimensions (mobility; self-care; usual activities; pain/discomfort; anxiety/depression) on a 3-leveled scale. In this study, we aimed to compare how these 5 EQ-5D components relate to healthcare, work-loss, and total societal costs in RA.

Methods: Clinical visits of anti-TNF treated RA patients, monitored in the observational South Swedish Arthritis Treatment Group register 2005-2011, were included (11674 visits in 2246 patients; >95% fulfillment of 1987 ACR criteria in a prior validation). EQ-5D questionnaire responses at visits were linked to register-derived costs of anti-rheumatic drugs, out- and inpatient care, and work-loss due to sick leave or disability pension from 30 days before to 30 days after each visit. Associations of the 5 EQ-5D components to healthcare (patient care and drugs), work-loss (in patients <65 years), and total societal costs (healthcare + work-loss costs; <65 years) were studied in separate, adjusted, generalized estimating equations regression models, comparing standardized β coefficients by nonparametric bootstrapping to assess which component best reflects costs.

Results: The strongest associations with both healthcare and work-loss (and thus also societal) costs were observed for the usual activities component (p<0.05 vs. all other components; Figure). Apart from that, the mobility and self-care components were more closely associated with healthcare costs than anxiety/depression, while stronger associations with work-loss costs were revealed for mobility and anxiety/depression than for pain/discomfort. For comparison, cost associations with the composite EQ-5D utility score (United Kingdom preference set) were (standardized β (95%CI)): -0.11 (-0.14 to -0.09) for healthcare, -0.07 (-0.08 to -0.05) for work-loss, and -0.12 (-0.15 to -0.09) for societal costs.

Conclusion: Of the 5 EQ-5D components, problems to perform one’s usual daily activities was most strongly related to both healthcare and work-loss (as expected) costs. Moreover, the associations of the usual activities component to costs were on par with those observed for the composite EQ-5D utility score, making it an interesting simple marker of total societal costs in RA. Somewhat unexpectedly, relatively weak cost associations were observed regarding the pain/discomfort component.

Disclosure: A. Gülfe, None; T. Olofsson, None; J. K. Söderling, AbbVie, Merck, Novartis, Shire, 5; M. Neovius, Schering-Plough, AstraZeneca, Novo Nordisk, Pfizer, Roche, 2,Pfizer, Abbott, 5; J. K. Wallman, AbbVie, Celgene, Novartis, UCB, 5.

Abstract Number: 134

Baseline Characteristics and Rates of Hospitalized Infections in Patients with Rheumatoid Arthritis Treated with Non-TNF Inhibitors in Denmark and Sweden
Kathrine Lederballe Grøn, Elizabeth V. Arkema, Bente Glintborg, Johan Askling, and Merete Lund Hetland, 1The DANBIO registry and the Danish Departments of Rheumatology, Copenhagen, Denmark, 2Clinical Epidemiology Unit, Department of Medicine, Karolinska University Hospital and Karolinska Institutet, Stockholm, Sweden, 3Unit of Clinical Epidemiology, Department of Medicine, Karolinska University Hospital and Karolinska Institutet, Stockholm, Sweden, 4The DANBIO registry and the Danish Departments of Rheumatology, Glostrup, Denmark

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Epidemiology and Public Health Poster I: Rheumatoid Arthritis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Hospitalized infections during treatment with biologic disease modifying drugs (bDMARDs) in rheumatoid arthritis (RA) are a concern. This has mainly been studied in patients (pts) treated with tumor necrosis factor inhibitors (TNFi), and only to a limited degree in pts treated with non-TNFi (abatacept (ABA), rituximab (RTX), tocilizumab (TCZ)). The aims of this interim report, which is part of an ongoing collaborative project between Denmark (DK) and Sweden (S), were to explore a) baseline characteristics and b) 12-month risks of hospitalized infections in RA pts treated with ABA, RTX and TCZ in routine care.

Methods: Observational, prospective cohort study conducted in parallel in DK and S. RA pts who started treatment with a non-TNFi between Jan 2010 and 2015 (DK: July 2015 and S: Dec 2015) were identified in the Danish DANBIO(1) and the Swedish ARTIS/SRQ registries(2). By use of unique identification codes, information on pts’ baseline clinical characteristics from the registers was enriched with information on previous malignancies, hospitalizations and hospitalized infections from the National Patient Registries (NPR). Information on hospitalized infections during follow-up was obtained from the NPRs. Follow-up was 12 months after treatment start or 90 days after withdrawal, whichever came first. Crude incidence rates (IR) of hospitalized infections were calculated for each drug in each country. For the current interim analysis, no formal comparisons of rates were conducted.

Results: 8931 treatment series were identified. The numbers of ABA/RTX/TCZ treatment series were 830/718/1098 in DK and 1872/2630/1783 in S, respectively (Table). Age, gender, functional status and disease activity were typical for RA pts, but a pattern of higher age, more frequent previous cancer, hospitalizations or hospitalized infections in RTX treated patients was observed in both countries (Table). The crude 12-month hospitalized infection rates were 5.84-8.76 in DK and 4.28-6.81 in S (Table).

Conclusion: This collaborative project between DK and S included >8000 treatment series of RA pts treated with ABA, RTX and TCZ in routine care, and it demonstrated some channeling of patients to certain treatments, as reflected in differences in baseline characteristics. Variation in crude rates of hospitalized infections was observed across drugs and countries. Further analyses will explore underlying reasons that might explain differences in rates between the countries, as well as the impact of channeling, on the risk of hospitalized infections associated with each drug under study.

Table Baseline characteristics of Danish and Swedish RA patients starting a non-TNFi between Jan 2010 and 2015, stratified according to drug and country.

Table

<table>
<thead>
<tr>
<th></th>
<th>Denmark</th>
<th>Sweden</th>
<th>Norway</th>
<th>Switzerland</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of treated series</td>
<td>830</td>
<td>718</td>
<td>1098</td>
<td>1872</td>
</tr>
<tr>
<td>Age (years)</td>
<td>65 (58-71)</td>
<td>64 (58-71)</td>
<td>61 (58-71)</td>
<td>62 (58-71)</td>
</tr>
<tr>
<td>Gender (female)</td>
<td>49%</td>
<td>50%</td>
<td>51%</td>
<td>51%</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>7 (3-15)</td>
<td>7 (3-15)</td>
<td>7 (3-15)</td>
<td>7 (3-15)</td>
</tr>
<tr>
<td>DAS28 at baseline</td>
<td>5.6 (4.0-6.6)</td>
<td>5.6 (4.0-6.6)</td>
<td>5.6 (4.0-6.6)</td>
<td>5.6 (4.0-6.6)</td>
</tr>
<tr>
<td>DMARDs at baseline</td>
<td>36%</td>
<td>36%</td>
<td>36%</td>
<td>36%</td>
</tr>
<tr>
<td>Corticosteroids at baseline</td>
<td>16%</td>
<td>16%</td>
<td>16%</td>
<td>16%</td>
</tr>
<tr>
<td>Number of hospitalizations at baseline</td>
<td>538</td>
<td>434</td>
<td>750</td>
<td>1,260</td>
</tr>
<tr>
<td>Hospitalizations per 1,000 patients</td>
<td>65 (63-67)</td>
<td>65 (63-67)</td>
<td>65 (63-67)</td>
<td>65 (63-67)</td>
</tr>
<tr>
<td>Hospitalizations per 1,000 patient years</td>
<td>0.65 (0.65-0.65)</td>
<td>0.65 (0.65-0.65)</td>
<td>0.65 (0.65-0.65)</td>
<td>0.65 (0.65-0.65)</td>
</tr>
</tbody>
</table>

References 1)Ibfelt et al. Clin Epi 2016;8:737-42

ADDIN EN.REFLIST

Disclosure: K. Lederballe Grøn, None; E. V. Arkema, None; B. Glintborg, Abbvie, Biogen, 2; J. Askling, MSD, BMS, Pfizer, AbbVie,
Comorbidity Measures Differentially Predict Longitudinal Disease Activity, Remission, and Disability in Rheumatoid Arthritis

Bryant R. England1, Harlan Sayles2, Kaleb Michaud2, Grant Cannon3, Andreas Reimold4, Liron Caplan5, Gail S. Kerr6, Namrata Singh7, Gleb Haynatzki8, Michael D. George9, Joshua Baker10 and Ted R. Mikuls11, 1Division of Rheumatology & Immunology, Department of Internal Medicine, Nebraska-Western IA VA Health Care System & University of Nebraska Medical Center, Omaha, NE, 2University of Nebraska Medical Center, Omaha, NE, 3Salt Lake City VA Medical Center and University of Utah, Salt Lake City, UT, 4Hospital of Southern Norway, Kristiansand, Norway, 5Division of Rheumatology, University of Colorado School of Medicine, Aurora, CO, 6VAMC, Georgetown University, Washington, DC, 7Internal Medicine, University of Iowa Hospitals and Clinics and Iowa City VA, Iowa City, IA, 8Biostatistics, University of Nebraska Medical Center, Omaha, NE, 9Division of Rheumatology, University of Pennsylvania, Philadelphia, PA, 10Rheumatology, University of Pennsylvania, Philadelphia, PA, 11Internal Medicine, Division of Rheumatology, University of Nebraska Medical Center, Omaha, NE

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Epidemiology and Public Health Poster I: Rheumatoid Arthritis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Comorbidity frequently complicates rheumatoid arthritis (RA) leading to poor long-term outcomes. However, whether comorbidity influences measures of RA activity over time is less well established. The purpose of this study was to examine the association of different comorbidity assessments with longitudinal disease activity and functional status.

Methods: Participants were enrollees in a multicenter, longitudinal observational cohort of US veterans with RA. Comorbid conditions were collected at enrollment by treating rheumatologists and modeled using the Rheumatic Disease Comorbidity Index (RDCI) score, comorbidity count (range 0-53), or by the individual comorbid conditions. Disease activity (DAS28) and functional status (MD-HAQ) were assessed at routine clinic visits. Associations of comorbidity measures with disease activity and functional status over the initial 3 years of follow-up were examined using multivariable linear mixed effects models. Comorbidity measures were examined as main effects as well as by using interaction terms with time, the latter to examine whether a given measure was associated with diverging disease activity and functional status trajectories over follow-up. The odds of ever achieving DAS28 remission (<2.6) were examined using multivariable logistic regression.

Results: Among 2,516 participants with mean age of 64 (SD 11) years, RA duration 11 (11) years, 90% male, 79% RF positive, 78% anti-CCP positive, and 80% with smoking history, 75% had a RDCI ≥1. Hypertension (53%), hyperlipidemia (41%), lung (20%), and cardiovascular (CV) disease (19%) were the most prevalent comorbidities. Comorbidity, measured by RDCI ≥1, count, or RDCI score, was not associated with longitudinal disease activity or remission (Table 1, Figure 1) although comorbidity count and RDCI score were associated with reduced physical function (Table 1). Select individual comorbidities, including CV, lung, and psychiatric disease, were more closely associated with unfavorable longitudinal disease activity, remission achievement, and physical function (Table 1, Figure 1). CV and interstitial lung disease (ILD) were the only comorbidities with a significant time-interaction term (DAS28 models), suggesting a widening gap in disease activity over time for these conditions.

Conclusion: CV, lung, and psychiatric comorbidities, but not composite comorbidity scores, are associated with higher measures of disease activity and lower odds of achieving remission in RA. Specific comorbidities and composite measures are associated with longitudinal functional status.
Table 1. Associations of comorbidities with longitudinal disease activity and functional status.

<table>
<thead>
<tr>
<th></th>
<th>log DAS28 (Std Error)</th>
<th>MD-HAQ (Std Error)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Composite measures</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RDCI *i</td>
<td>-0.017 (0.025)</td>
<td>0.034 (0.039)</td>
</tr>
<tr>
<td>RDCI score</td>
<td>0.002 (0.006)</td>
<td>0.048 (0.010)**</td>
</tr>
<tr>
<td>Comorbidity count</td>
<td>0.000 (0.002)</td>
<td>0.016 (0.003)**</td>
</tr>
<tr>
<td><strong>Individual conditions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung disease</td>
<td>-0.002 (0.023)</td>
<td>0.109 (0.035)**</td>
</tr>
<tr>
<td>Interstitial lung disease (ILD)</td>
<td>-0.093 (0.042) ±</td>
<td>0.032 (0.064)</td>
</tr>
<tr>
<td>ILD x time (years)</td>
<td>0.079 (0.012)**</td>
<td>-</td>
</tr>
<tr>
<td>COPD</td>
<td>0.021 (0.025)</td>
<td>0.132 (0.037)*</td>
</tr>
<tr>
<td>Cardiovascular (CVD)</td>
<td>-0.012 (0.024) ±</td>
<td>0.081 (0.036)*</td>
</tr>
<tr>
<td>CVD x time (years)</td>
<td>0.044 (0.016)**</td>
<td>-</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.001 (0.024)</td>
<td>0.079 (0.036)*</td>
</tr>
<tr>
<td>Hypertension</td>
<td>-0.013 (0.020)</td>
<td>0.021 (0.030)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>-0.039 (0.019)</td>
<td>0.047 (0.029)</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>0.006 (0.044)</td>
<td>0.094 (0.066)</td>
</tr>
<tr>
<td>Cancer</td>
<td>-0.030 (0.030)</td>
<td>0.006 (0.044)</td>
</tr>
<tr>
<td>PTSD</td>
<td>0.177 (0.038)**</td>
<td>0.206 (0.058)**</td>
</tr>
<tr>
<td>Depression</td>
<td>0.093 (0.031)**</td>
<td>0.157 (0.046)**</td>
</tr>
</tbody>
</table>

Covariates: RF, current smoking, DMARD, biologic DMARD, prednisone + (DAS28) smoking*time (MD-HAQ) education, race, disease duration.

* p < 0.05, ** p < 0.01

† Result from model with a significant comorbidity x time interaction term

Abbreviations: RDCI Ð rheumatic disease comorbidity index; COPD Ð chronic obstructive pulmonary disease; PTSD Ð post-traumatic stress disorder

Disclosure: B. R. England, None; H. Sayles, None; K. Michaud, None; G. Cannon, Amgen, 2; A. Reimold, Bristol-Myers Squibb,
Prevalence of Rheumatoid Arthritis and Associated Comorbidities in the 2011-2015 Medicare Population

Suying Li, Julia T. Molony, Yi Peng, Kimberly M. Nieman and David T. Gilbertson, Minneapolis Medical Research Foundation, Chronic Disease Research Group, Minneapolis, MN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Epidemiology and Public Health Poster I: Rheumatoid Arthritis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a systemic inflammatory disease affecting about 1.5 million adults in the US (Helmick et al., 2008). Patients with RA have an increased burden of comorbidity such as cardiovascular disease (CVD), diabetes, cancer, and other inflammatory diseases. This study aimed to update prevalence estimates of RA and associated comorbidity in the US.

Methods: This was a retrospective descriptive study using the 2010-2015 20% Medicare sample data. Yearly prevalent RA cohorts (2011-2015) were defined based on ICD-9 diagnosis code 714.0 with the addition of ICD-10 codes for the 2015 cohort. For each cohort year, included patients were required to have Medicare Part A and Part B coverage with no Medicare Advantage, and to be alive for the entire year preceding a cohort year and through the first month of the cohort year. RA was defined if a diagnosis code was present in at least 1 inpatient claim or 2 or more outpatient claims, separated by at least 30 days. The baseline period was 1 year preceding the cohort year and was used to define comorbidity, including CVD, diabetes, hypertension, hyperlipidemia, cancer, anemia, and other inflammatory conditions such as psoriasis, psoriatic arthritis, non-alcoholic fatty liver disease (NAFLD), and cirrhosis. Prevalence of comorbidity was presented as a percentage of RA patients.

Results: This study included approximately 6 million Medicare beneficiaries in each year, 2011-2015; average RA prevalence was about 2.0% (Table 1). RA patient demographics were similar across years, with mean age 72.4 years; 77.0% were female, 83.4% white, and 10.7% black in the 2015 cohort. Common comorbid conditions in the 2015 RA cohort included hypertension (prevalence 67.3%), hyperlipidemia (48.5%), diabetes (26.6%), anemia (26.4%), arteriosclerotic heart disease (21.5%), peripheral artery disease (17.2%), congestive heart failure (13.2%), and cancer (8.8%) (Table 1). Prevalence of inflammatory conditions increased across years; for example, NAFLD was 0.96% in 2011 and 1.36% in 2015; corresponding values were 0.04% and 0.07% for cirrhosis, 1.14% and 1.45% for psoriasis, and 1.58% and 1.81% for psoriatic arthritis.

Table 1. Prevalence of RA and Associated Comorbid Conditions in 2011-2015 Medicare Patients
Cohort Year | 2011 | 2012 | 2013 | 2014 | 2015
--- | --- | --- | --- | --- | ---
N Medicare patients in the 20% sample | 5,845,175 | 5,859,826 | 5,906,084 | 5,975,397 | 6,324,354
N with RA in the 20% sample | 117,014 | 117,494 | 118,660 | 120,448 | 123,137
% with RA | 2.0 | 2.0 | 2.0 | 2.0 | 2.0

Baseline characteristics in RA patients

Mean age in years (SD) | 71.8 (11.6) | 71.8 (11.5) | 71.7 (11.5) | 71.8 (11.4) | 72.4 (11.4)
% of Female | 75.8 | 75.9 | 75.7 | 75.5 | 77.0
Race, %
White | 82.2 | 82.3 | 82.3 | 82.5 | 83.4
Black | 11.7 | 11.6 | 11.5 | 11.2 | 10.7
Other | 6.1 | 6.1 | 6.2 | 6.3 | 6.0

Comorbidity (%) in RA patients

Diabetes | 26.7 | 27.2 | 27.1 | 27.2 | 26.6
Hypertension | 65.9 | 66.5 | 66.6 | 66.8 | 67.3
Hyperlipidemia | 45.5 | 47.3 | 47.8 | 48.1 | 48.5
CVD
ASHD | 21.9 | 22.1 | 21.9 | 21.6 | 21.5
CHF | 13.2 | 13.4 | 13.0 | 12.8 | 13.2
CVA/TIA | 8.5 | 8.7 | 8.6 | 8.6 | 8.8
PVD | 16.2 | 16.7 | 16.4 | 16.7 | 17.2
Other cardiac | 13.6 | 14.5 | 14.0 | 14.1 | 14.7
Cancer | 8.5 | 8.8 | 8.7 | 8.8 | 8.8
Anemia | 26.8 | 27.7 | 27.0 | 26.7 | 26.4
GI bleeding | 3.2 | 3.4 | 3.2 | 3.2 | 3.2
Liver | 1.76 | 1.87 | 1.89 | 2.03 | 2.08
NAFLD | 0.96 | 1.05 | 1.19 | 1.27 | 1.36
Cirrhosis | 0.04 | 0.04 | 0.05 | 0.05 | 0.07
Psoriasis | 1.14 | 1.30 | 1.36 | 1.43 | 1.45
Psoriatic arthritis | 1.58 | 1.69 | 1.77 | 1.84 | 1.81
RA | 69.7 | 71.2 | 71.6 | 72.0 | 73.7

RA=Rheumatoid arthritis; CVD=Cardiovascular disease; ASHD=Arteriosclerotic Heart Disease;
CHF=Congestive heart failure; CVA/TIA=Cerebrovascular Accidents/Transient Ischemic Attack;
PVD=Peripheral artery disease; NAFLD=Non-alcoholic fatty liver disease

**Conclusion:** Hypertension, CVD, hyperlipidemia, diabetes, anemia, and cancer are common in RA patients. Other inflammatory conditions increased over the years studied. Further analysis should evaluate the effect of RA treatment and of secondary prevention in patients with other inflammatory conditions.

**Disclosure:** S. Li, None; J. T. Molony, None; Y. Peng, None; K. M. Nieman, None; D. T. Gilbertson, None.


**Abstract Number:** 137

**Rheumatoid Arthritis and the Risk for Interstitial Lung Disease: A Comparison of Risk Associated with Biologic and Conventional Dmards**
Background/Purpose: Interstitial Lung Disease (ILD) is a rare but often severe consequence of several rheumatologic conditions including rheumatoid arthritis (RA). The comparative risk of incident ILD between RA therapies remains undetermined.

Methods: A retrospective cohort study using 2006-2014 Medicare and 2010-2015 Market Scan data was conducted to assess the risk of ILD among biologic and conventional DMARDs (cDMARDs) users. Adults with at least one ICD-9-CM RA diagnosis code from rheumatologist, initiated at least one biologic or cDMARDs were included. Patients had to have at least 1 year of full coverage (medical and pharmacy) prior to their RA treatment. Those with a diagnosis code for prevalent ILD, malignancy, HIV or organ transplantation (MHO), or prior oxygen use (suggesting treatment for pre-existing ILD) were excluded. Patients initiating cDMARDs with prior exposure to biologic or synthetic DMARDs (all available data) were also excluded. Follow up started at the initiation date of each therapy and ended at the earliest of: event, loss of full coverage, end of exposure (with 90 days extension), switch to other biologic or synthetic DMARDS, diagnosis of MHO (except for lung transplant), or end of study. ILD was defined as: one or more hospital discharge diagnosis code (any position) or 2 outpatient diagnosis codes from a physician visit with diagnostic tests for chest CT or lung biopsy. Incidence rates (IR) of ILD were calculated using Poisson regression; hazard ratios (HR) were calculated using COX regression, accounting for the clustering of RA treatments within patients. Among patients who developed ILD, initiation of home oxygen and death (Medicare only) were reported.

Results: A total of 150,225 RA patients with 208,641 initiations of biologics or DMARDs were eligible for analysis. A total of 958 patients developed ILD among 199,739 person years, resulting in an overall IR of 4.78 per 1,000 person years. The crude IRs for ILD ranged from a low of 3.05 (95%CI: 1.15-8.14) for tofacitinib to a high of 8.37 (7.29-9.61) for infliximab (INF) in Medicare (Table 1); and a low of 0.58 (0.08-4.13) for certolizumab (CER) to 3.87(2.08-7.19) for INF in Market Scan. Compared to abatacept (ABA), the adjusted HR ranged from 0.82 (0.30-2.22) for tofacitinib to 2.07 (1.62-2.64) for INF in Medicare; from 0.41 (0.05, 3.41) for CER to 2.85 (1.03-7.89) for INF in Market Scan.

Among 880 Medicare patients with ILD, 359 (41%) died after a mean (SD) 529 (640) days since diagnosis; 328 (37%) initiated home oxygen, at a mean (SD) of 177 (418) days. Among 78 Market Scan patients with ILD, 22 (28%) initiated oxygen at a mean (SD) of 114(262) days.

Conclusion: Compared to ABA, INF, rituximab, adalimumab, tocilizumab and etanercept were associated with increased risk of ILD, although the absolute IR differences between therapies were small. Initiation of home oxygen and mortality was high among RA patients with incident ILD.
### Table: Incidence Rates of Interstitial Lung Disease and Adjusted Hazard Ratio in RA Patients

<table>
<thead>
<tr>
<th>DMARDs</th>
<th>Medicare</th>
<th>Market Scan</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of patients=104,870</td>
<td>Number of patients=45,355</td>
</tr>
<tr>
<td></td>
<td>Number of initiations=143,540</td>
<td>Number of initiations=65,101</td>
</tr>
<tr>
<td></td>
<td>Event Person Years IRs aHR* (95% CI)</td>
<td>Event Person Years IRs aHR* (95% CI)</td>
</tr>
<tr>
<td>ABATACEPT</td>
<td>99 23,939 4.14 (3.40-5.04) Reference</td>
<td>6 4,154 1.44 (0.65-3.21) Reference</td>
</tr>
<tr>
<td>ADALIMUMAB</td>
<td>82 13,382 6.13 (4.94-7.61) 1.77 (1.32-2.38)</td>
<td>14 7,268 1.93 (1.14-3.25) 1.42 (0.54-3.72)</td>
</tr>
<tr>
<td>CERTOLIZUMAB</td>
<td>14 4,306 3.25 (1.93-5.49) 0.83 (0.48-1.46)</td>
<td>1 17,198 0.58 (0.08-4.13) 0.41 (0.05-3.41)</td>
</tr>
<tr>
<td>ETANERCEPT</td>
<td>75 14,038 5.34 (4.26-6.70) 1.47 (1.09-1.99)</td>
<td>10 76,838 1.30 (0.70-2.42) 0.98 (0.35-2.7)</td>
</tr>
<tr>
<td>GOLIMUBAB</td>
<td>15 2,683 5.59 (3.37-9.27) 1.55 (0.90-2.67)</td>
<td>2 16,118 1.24 (0.31-4.96) 0.93 (0.19-4.64)</td>
</tr>
<tr>
<td>HCQ, LEF, or SSZ</td>
<td>115 25,221 4.56 (3.80-5.47) 1.03 (0.78-1.38)</td>
<td>10 6,877 1.45 (0.78-2.70) 1.00 (0.34-2.89)</td>
</tr>
<tr>
<td>INFILXIMAB</td>
<td>202 24,136 8.37 (7.29-9.61) 2.07 (1.62-2.64)</td>
<td>10 2,584 3.87 (2.08-7.19) 2.85 (1.03-7.89)</td>
</tr>
<tr>
<td>METHOTREXATE</td>
<td>174 30,747 5.66 (4.88-6.57) 1.28 (0.97-1.68)</td>
<td>14 8,751 1.60 (0.95-2.70) 1.04 (0.37-2.93)</td>
</tr>
<tr>
<td>RITUXIMAB</td>
<td>63 7,968 7.91 (6.18-10.12) 1.93 (1.41-2.65)</td>
<td>3 1,519 1.98 (0.64-6.13) 1.16 (0.28-4.71)</td>
</tr>
<tr>
<td>TOCILIZUMAB</td>
<td>37 5,666 6.53 (4.73-9.01) 1.69 (1.16-2.47)</td>
<td>4 2,637 1.52 (0.57-4.04) 1.03 (0.29-3.67)</td>
</tr>
<tr>
<td>TOFACITINIB</td>
<td>4 1,310 3.05 (1.15-8.14) 0.82 (0.30-2.22)</td>
<td>4 1,540 2.60 (0.97-6.92) 1.68 (0.47-5.99)</td>
</tr>
<tr>
<td>All exposure</td>
<td>880 153,395 5.74 (5.37-6.13) 178 46,344 1.68 (1.35-2.10)</td>
<td></td>
</tr>
</tbody>
</table>

CI: Confidence interval; aHR: Adjusted hazard ratio; IR: Incidence rate, per 1000 years.

* Adjusted for age, sex, systemic sclerosis, systemic lupus erythematosus, Sicca syndrome, Hemiplegia or paraplegia, Diabetes, hypertension, Pneumonia, Chronic pulmonary disease, Myocardial infarction, Coronary heart disease, Peripheral vascular disorder, Cerebrovascular disease, Dementia, Liver disease.
Disclosure: F. Xie, None; N. Annapureddy, None; L. Chen, None; J. L. Lobo, None; J. C. Oates, None; A. Shah, None; H. Yun, Bristol-Myers Squibb, 2; S. Yang, None; J. R. Curtis, AbbVie, Roche/Genentech, BMS, UCB, Myraider, Lilly, Amgen, Janssen, Pfizer, Corrona, 5,Amgen, Pfizer, Crescendo Bio, Corrona, 9.


Abstract Number: 138

**Prediction of Cardiovascular Events in Rheumatoid Arthritis Patients Using a Multi-Biomarker of Disease Activity**

Fenglong Xie¹, Lang Chen², Huifeng Yun² and Jeffrey R. Curtis³, ¹Division of Clinical Immunology & Rheumatology, University of Alabama at Birmingham, Birmingham, AL, ²University of Alabama at Birmingham, Birmingham, AL, ³Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Sunday, November 5, 2017  
**Session Title:** Epidemiology and Public Health Poster I: Rheumatoid Arthritis  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The ACC/AHA recommends preventive strategies for patients with a high predicted risk of atherosclerotic cardiovascular disease (CVD). RA patients are at higher risk for CVD events, yet the role of systemic inflammation and the influence of traditional CVD risk factors is unclear with respect to risk prediction in RA. A simple and accurate algorithm for predicting CVD event risk that includes systemic inflammation might help risk assessment for RA patients and optimize preventive care.

**Methods:** We derived a U.S. cohort of RA patients with multi-biomarker disease activity (MBDA) test results linked to Medicare claims data. Patients had to have ≥1 year baseline with Medicare coverage prior to the first MBDA test. Exclusions were past MI, PCI/CABG, stroke, or cancer. Follow-up ended at the earliest of 1) CVD event; 2) other than CVD cause of death; 3) loss of coverage; or 4) 12/31/2014. The composite CVD event comprised of incident MI, stroke or fatal CVD event, using validated algorithms. MBDA scores were grouped as low (<30), moderate (30-44), and high (>44). Other predictors included demographics, healthcare utilization, and comorbidities. Three separate models were developed using Cox regression. Model 1 included age, sex and race. Model 2 included age, sex race, 9 comorbidities and CVD medication classes, plus interaction terms. Model 3 included age, sex, and race plus categorized MBDA score. We calculated the net reclassification index (NRI) for model 2 and 3 compared to model 1. We also plotted the observed vs. predicted probability of CVD event for each model, with risk categorized as low (<7.5), moderate (7.5-<15) and high (≥15) per 1000 person-years based upon annualized ACC/AHA cutpoints.

**Results:** A total of 15,757 RA patients were included; mean (SD) age 68.6(10.8) years, 80% female, 80% white. A total 209 CVD events occurred in 14,843 person years (1.41/100 py). The median (IQR) follow up time was 0.84 (0.41, 1.27) year. The maximum event time was at 2.7 year. All models had reasonable discrimination and calibration; model 3 was better than models 1 and 2 and observed vs predicted risk is shown (Figure). The sum of the absolute difference between observed and predicted probability was 0.56, 0.57 and 0.33 for models 1, 2 and 3 respectively. Compared to model 1, model 2 resulted in a positive overall NRI of 0.214 (non-event NRI=0.173, event NRI=0.041); model 3 resulted in positive overall NRI of 0.279 (non-event NRI=0.092, event NRI=0.187), consistent with more accurate CVD event classification.

**Conclusion:** Preliminary results from this analysis suggest that a simple algorithm consisting only of age, sex and race plus a multi-biomarker score can provide an accurate method to predict short term CVD risk in RA. Further validation with more extended time frames should improve the utility of this approach.

Figure: Observed vs. Predicted One-Year CVD Risk per 1000 person-years in RA Patients, using only Age, Sex, Race, and MBDA score (Model 3)
No Effect of Tumor Necrosis Factor-a Inhibitors on Renal Function in Patients with Rheumatoid Arthritis from Kobio Registry from 2012 to 2016

Seong-Kyu Kim¹, Jung-Yoon Choe², Sung-Hoon Park³ and Hwajeong Lee², ¹Rheumatology, Catholic University of Daegu School of Medicine, Daegu, Korea, Republic of (South), ²Catholic University of Daegu School of Medicine, Daegu, Korea, Republic of (South), ³Internal Medicine, Catholic University of Daegu School of Medicine, Daegu, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Epidemiology and Public Health Poster I: Rheumatoid Arthritis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Renal disease is prevalent in patients with rheumatoid arthritis (RA), although the precise prevalence of RA has not been determined. Increased mortality in patients with RA is associated with concurrent renal diseases. Impaired renal function in patients with RA is likely due to a chronic inflammatory response, antirheumatic drug toxicity, and renal involvement of RA itself. The effect of biological disease-modifying antirheumatic drugs (bDMARDs) on renal function in patients with RA has not been well established. We assessed whether tumor necrosis factor (TNF) inhibitors could affect renal function in RA.

Methods: A total of 2110 patients with RA enrolled in the Korean College of Rheumatology Biologics (KOBIO) registry were analyzed. All patients were taking bDMARDs or conventional synthetic DMARDs (csDMARDs). Renal function was evaluated by calculating the estimated glomerular filter rate (eGFR) using the Modification of Diet in Renal Disease (MDRD) equation. Renal insufficiency was defined as eGFR < 60 mL/min/1.73 m². Differences in eGFR changes between different types of DMARDs were assessed at each follow-up time using the generalized linear model (GLM) method. Risk factors for renal insufficiency were identified using binary logistic regression analysis.

Results: The changes of eGFR values in patients treated with TNF inhibitors were not significantly different from those with csDMARDs alone or non-TNF inhibitors in all RA patients regardless of renal function. Among patients with renal insufficiency, GLM analysis revealed that the changes of eGFR values by TNF inhibitors were also compatible to those treated with csDMARDs alone or non-TNF inhibitors. Older age (> 55 years), longer disease duration (> 5 years), and use of methotrexate were identified as clinical determinants for renal insufficiency.

Conclusion: TNF inhibitors did not influence the change of renal function during RA treatment. TNF inhibitors may be a safe treatment option irrespective of renal function.
Estimating Prevalence and Cost of Depression Among Japanese RA Patients: A Retrospective Claims Data Base Analysis

Rosarin Sruamsiri1, Jörg Mahlich2 and Yuko Kaneko3, 1Health Economics, Janssen Pharmaceutical KK,, Tokyo, Japan, 2Health Economics, Janssen Pharmaceutical KK, Tokyo, Japan, 3Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan

First publication: September 18, 2017

Background/Purpose:

Significant evidence in the scholarly literature suggests that depression is a common comorbidity among patients with rheumatoid arthritis (RA) causing significant burden for the healthcare system. However, no studies are available for Japan and, hence, this is the first attempt to systematically assess the cost of depression in an RA patient cohort.

Methods:

We used a large administrative claims data base (JMDC) to calculate prevalence and associated costs of depression within RA patients between March 2009 and September 2015. Descriptive statistics is used to describe baseline characteristics of included patients, healthcare utilization and total health care cost. Propensity score matching is applied to eliminate confounding effects (potential imbalances in baseline covariates) using 1:4 matching type.

Results:

We identified 101,512 patients in the database with neither RA or depression diagnosis. 6,838 were diagnosed with RA but not with depression and 473 had a co-diagnosis of depression and RA indicating a prevalence of depression within RA patients of 6.5%. After matching, RA patients with depression had 55% more outpatient visits (p=0.010) and caused 46% higher health care costs than those without depression (p=0.000). Mean healthcare costs per patient per month was 102,101 JPY for the former and 70,079 JPY for the latter population.

Conclusion:

A co-morbidity of RA patients with depression adds significant costs to the healthcare system and rheumatologists should be aware of this co-morbidity to ensure timely treatment initiation when necessary.


Refractory Disease in Rheumatoid Arthritis: Results from the British Society of Rheumatology Biologics Register for Rheumatoid Arthritis

Lianne Kearsley-Fleet1, Diederik De Cock1, Kath Watson1, Maya H. Buch2, John D Isaacs3 and Kimme L. Hyrich1,4, 1Arthritis Research
Background/Purpose: Biologic therapy has revolutionised treatment pathways and improved outcomes for patients with Rheumatoid Arthritis (RA) who do not tolerate or respond to conventional synthetic therapies. However, for some patients on biologics, disease control remains elusive with so-called refractory disease. The aim was to quantify the frequency of biologic resistant disease and identify factors, measured at the start of first biologic, associated with resistant disease.

Methods: Patients with RA starting first-line TNFi (previously failed ≥2 DMARDs) in the BSRBR-RA were included if they had a full 10 years of study follow-up (N=5755). Patients were classified as “refractory” if they had used ≥3 classes of biologic, and were compared with “persistent” patients who remained on first TNFi for 10 years. Stop reasons were investigated. HAQ was assessed at 3 years (end of patient follow-up) and DAS28 at 10 years. Associations with age, gender, disease duration, baseline DAS28 and components, comorbidities, HAQ and refractory disease were analysed in a multivariable logistic analysis. Multiple imputation was used to account for missing data.

Results: Of the whole cohort, 2147 (37%) were classed as persistent TNFi patients, and 272 (5%) as refractory (Table 1). Refractory patients remained on their first TNFi for a mean of 2.9 years, and 51% stopped for inefficacy. Refractory patients had also used rituximab (94%), tocilizumab (77%), and other classes (48%), whilst 74% had also used >1 TNFi. In the refractory cohort, 34% reported recurrent drug inefficacy only, 8% recurrent adverse events only and 50% a combination of reasons for repeated drug failures (with reasons missing in 8%). Disease activity was higher among patients with refractory disease (DAS28 5.0 vs 3.7; HAQ 2.0 vs 1.6). In multivariable analysis, older patients (>50 years, OR 0.5 (95% CI 0.4, 0.7)) and those with longer disease duration (>10 years, OR 0.7 (95% CI 0.6, 0.95)) had reduced odds of refractory disease. In addition, greater baseline HAQ (OR 1.8 (95% CI 1.4, 2.4)), and patient global assessment (OR 1.1 (95% CI 1.0, 1.2)) had increased odds of refractory disease (Table 2).

Conclusion: In this real-world cohort of patients with RA, followed for 10 years, approximately 5% had biologic resistant disease, with 2/3 reporting lack of response to any biologic. This may be an under-estimate as many patients in this study may have died before alternative non-TNFi biologics became available. Higher disability at the start of first TNFi predicted resistant disease but in general persistent and resistant patients were similar at the outset of therapy.
<table>
<thead>
<tr>
<th>Table 1: Baseline Characteristics.</th>
<th>Multiple Failures [N=272]</th>
<th>Persistent First Users [N=2147]</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First TNFi, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Etanercept: 115 (42%)</td>
<td>Etanercept: 1045 (49%)</td>
<td>P=0.1</td>
<td></td>
</tr>
<tr>
<td>Infliximab: 74 (27%)</td>
<td>Infliximab: 511 (24%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adalimumab: 83 (31%)</td>
<td>Adalimumab: 591 (28%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Females, n (%)</strong></td>
<td>222 (82%)</td>
<td>1612 (75%)</td>
<td>P=0.02</td>
</tr>
<tr>
<td><strong>Age (years), median (IQR)</strong></td>
<td>51 (43, 58)</td>
<td>55 (47, 62)</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td><strong>Disease Duration (years), median (IQR)</strong></td>
<td>9 (4, 17)</td>
<td>11 (6, 18)</td>
<td>P=0.01</td>
</tr>
<tr>
<td></td>
<td>N=2125</td>
<td>N=2143</td>
<td></td>
</tr>
<tr>
<td><strong>Rheumatoid Factor Positive, n (%)</strong></td>
<td>175 (64%)</td>
<td>1331 (62%)</td>
<td>P=0.5</td>
</tr>
<tr>
<td></td>
<td>N=2143</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fulfilled RA ACR criteria at baseline, n (%)</strong></td>
<td>272 (100%)</td>
<td>2147 (100%)</td>
<td>-</td>
</tr>
<tr>
<td><strong>On concurrent methotrexate, n (%)</strong></td>
<td>165 (61%)</td>
<td>1377 (64%)</td>
<td>P=0.3</td>
</tr>
<tr>
<td><strong>On steroids at baseline, n (%)</strong></td>
<td>116 (43%)</td>
<td>848 (40%)</td>
<td>P=0.3</td>
</tr>
<tr>
<td><strong>Total Comorbidities</strong></td>
<td></td>
<td></td>
<td>P=0.2</td>
</tr>
<tr>
<td>None</td>
<td>128 (47%)</td>
<td>1137 (53%)</td>
<td></td>
</tr>
<tr>
<td>1 comorbidity</td>
<td>95 (35%)</td>
<td>711 (33%)</td>
<td></td>
</tr>
<tr>
<td>2 comorbidities</td>
<td>38 (14%)</td>
<td>241 (11%)</td>
<td></td>
</tr>
<tr>
<td>3+ comorbidities</td>
<td>11 (4%)</td>
<td>58 (3%)</td>
<td></td>
</tr>
<tr>
<td><strong>SF-36 scores [range 0 (worse) to 100], median (IQR)</strong></td>
<td>N=221</td>
<td>N=1707</td>
<td></td>
</tr>
<tr>
<td>Physical Component Score</td>
<td>14 (9, 19)</td>
<td>16 (11, 23)</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Mental Component Score</td>
<td>40 (33, 49)</td>
<td>43 (35, 53)</td>
<td>P=0.007</td>
</tr>
<tr>
<td><strong>Disease Activity, median (IQR)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tender Joint Count (range 0 - 28)</td>
<td>17 (12, 24)</td>
<td>15 (10, 21)</td>
<td>P=0.002</td>
</tr>
<tr>
<td>N=265</td>
<td>N=2095</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Swollen Joint Count (range 0 – 28)</td>
<td>12 (7, 17)</td>
<td>11 (7, 15)</td>
<td>P=0.05</td>
</tr>
<tr>
<td>N=265</td>
<td>N=2096</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient Global Assessment, cms (range 0 – 10)</td>
<td>8.0 (6.9, 9.0)</td>
<td>7.5 (6.0, 8.5)</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>N=264</td>
<td>N=2091</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESR (mm/hr)</td>
<td>38 (23, 69)</td>
<td>38 (22, 59)</td>
<td>P=0.8</td>
</tr>
<tr>
<td>N=253</td>
<td>N=2011</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DAS28 (range 0 – 10)</td>
<td>6.8 (6.0, 7.5)</td>
<td>6.5 (5.8, 7.2)</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>N=2124</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HAQ (range 0 – 3)</td>
<td>2.1 (1.9, 2.5)</td>
<td>2.0 (1.5, 2.4)</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>N=266</td>
<td>N=2034</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Total comorbidities = hypertension, ischemic heart disease, stroke, lung disease, renal disease, diabetes, depression, liver disease.

Tumour Necrosis Factor inhibitor (TNFi), interquartile range (IQR), Rheumatoid Arthritis (RA), American College of Rheumatology (ACR), 36-item Short Form Survey for quality of life (SF-36), erythrocyte sedimentation rate (ESR), 28-joint Disease Activity Score (DAS28), Health Assessment Questionnaire (HAQ)
Table 2: Multivariable analysis (imputed data, 71 datasets), odds ratios for having refractory disease compared with persistent first users.

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio</th>
<th>P-value [mean]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females</td>
<td>1.3 (0.95, 1.8)</td>
<td>P=0.1</td>
</tr>
<tr>
<td>Age Groups (&gt;-50 years vs ≤ 50 years)</td>
<td>0.5 (0.4, 0.7)</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Disease Duration Groups (&gt;10 years vs ≤ 10 years)</td>
<td>0.7 (0.6, 0.95)</td>
<td>P=0.02</td>
</tr>
<tr>
<td>Tender Joint Count</td>
<td>1.0 (1.0, 1.1)</td>
<td>P=0.07</td>
</tr>
<tr>
<td>Swollen Joint Count</td>
<td>1.0 (1.0, 1.0)</td>
<td>P=0.6</td>
</tr>
<tr>
<td>Patient Global Assessment (cpps)</td>
<td>1.1 (1.0, 1.2)</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>ESR (mm/hr)</td>
<td>1.0 (1.0, 1.0)</td>
<td>P=0.4</td>
</tr>
<tr>
<td>DAS28 (whole unit)</td>
<td>0.9 (0.5, 1.5)</td>
<td>P=0.6</td>
</tr>
<tr>
<td>HAQ (whole unit)</td>
<td>1.8 (1.4, 2.4)</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Total Comorbidities*  (vs none)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 comorbidity</td>
<td>1.2 (0.9, 1.6)</td>
<td>P=0.3</td>
</tr>
<tr>
<td>2 comorbidities</td>
<td>1.3 (0.9, 2.0)</td>
<td>P=0.2</td>
</tr>
<tr>
<td>3+ comorbidities</td>
<td>1.6 (0.8, 3.1)</td>
<td>P=0.2</td>
</tr>
</tbody>
</table>

*Total comorbidities = hypertension, ischemic heart disease, stroke, lung disease, renal disease, diabetes, depression, liver disease.

Erythrocyte sedimentation rate (ESR), 28-joint Disease Activity Score (DAS28), Health Assessment Questionnaire (HAQ).

Disclosure: L. Kearsley-Fleet, None; D. De Cock, None; K. Watson, None; M. H. Buch, Pfizer Ltd, 2,Roche Pharmaceuticals, 2,Abbott Immunology Pharmaceuticals, 5,Sandoz, 5; J. D. Isaacs, None; K. L. Hyrich, None.


Abstract Number: 142

Incidence of Hip Fracture in Rheumatoid Arthritis: British Columbia, Canada

C. Allyson Jones1, Pierre Guy2, Hui Xie3, Eric C. Sayre4 and Diane Lacaille5,6, 1Physical Therapy, University of Alberta, Edmonton, AB, Canada, 2Department of Orthopaedics, University of British Columbia / Centre for Hip Health and Mobility, Vancouver, BC, Canada, 3Biostatistics, Faculty of Health Sciences, Simon Fraser University / Arthritis Research Canada, Burnaby, BC, Canada, 4Arthritis Research Canada, Richmond, BC, Canada, 5Arthritis Research Canada/ University of British Columbia, Vancouver, BC, Canada, 6University of British Columbia, Arthritis Research Canada, Richmond, BC, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017

Session Title: Epidemiology and Public Health Poster I: Rheumatoid Arthritis

Session Type: ACR Poster Session A

Session Time: 9:00AM-11:00AM

Background/Purpose: Hip fractures have serious long-term effects, including a high 1-year mortality rate (usually 20-30%) and poor functional recovery, with approximately 50% not attaining pre-fracture functional status. Although risk of hip fractures is known to be increased in rheumatoid arthritis (RA), few studies specifically look at the incidence of hip fractures in patients with RA compared to general population controls. We estimated the incidence of hip fractures in a population-based cohort including all incident RA cases in a Canadian province, using administrative health data.

Methods: Using physician billing data and a previously published RA definition, we assembled an incident cohort of all cases with RA onset between 1997 and 2009. Controls (with no diagnosis of RA or other inflammatory arthritis) selected randomly from the general population were matched 2:1 to RA patients on birth year, gender and index year. RA and controls with prior hip fractures, pathological fractures or Paget’s disease were excluded. Hip fractures (ICD9-CM codes 820.0, 820.2; ICD10-CA codes S72.0, S72.1, S72.2) were identified using hospitalization data (includes ≤25 codes defining reason for admission or complications during hospitalization). Crude incident rates were
Results: A total of 60,101 RA patients and 120,462 controls (mean age 57.2 yrs; 68% females for each cohort) were followed to December 2014, yielding 0.596 million PY and 1.23 million PY, resp. Incident hip fractures were observed in 2463 RA and 3566 controls. Mean (SD) age at time of fracture was 78.9 (10.9) yrs in RA and 82.1 (9.0) yrs in controls. Crude incidence rate was 4.1 and 2.9 per 1000 PY for RA and controls, resp., yielding an incidence rate ratio (IRR) of 1.42 [95% CI 1.35, 1.50]. Crude IRRs decreased with age and did not differ by sex (Figure 1). Adjusting for age and sex, persons with RA had 48% greater risk of hip fracture than persons without (HR 1.48, 95%CI 1.41, 1.56).

Conclusion: Risk of hip fractures in persons with RA is higher than age/sex matched controls particularly at younger ages. Given the impact of hip fractures, this has important implications for functional status and quality of life of people with RA. Further work on course of recovery, mortality and health services use post-fracture is needed.

Disclosure: C. A. Jones, None; P. Guy, None; H. Xie, None; E. C. Sayre, None; D. Lacaille, None.


Abstract Number: 143

Patient Rheumatoid Arthritis Data from the Real World (PARADE) Study: Preliminary Results from an Apple Researchkit™ Mobile App-Based Real World Study in the United States

Rachel Williams¹, Emilia Quattrocchi², Sarah Watts³, Sherry Wang⁴, Pam Berry⁴ and Michelle Crouthamel¹, ¹Real World Evidence and Epidemiology, GSK, Collegeville, PA, ²R&D Immunoinflammation, GSK, Middlesex, United Kingdom, ³GSK, Stevenage, United Kingdom, ⁴GSK, Collegeville, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Epidemiology and Public Health Poster I: Rheumatoid Arthritis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Smartphone apps and sensors enable researchers to design novel endpoints and collect real world data directly from patients in a cost-effective, fast, and patient-focused approach. ResearchKit™, created by Apple in 2015, is an iOS-based, open-source platform for researchers to conduct App-based studies. We were the first pharmaceutical company to utilize the ResearchKit™ by conducting the Patient Rheumatoid Arthritis Data from the Real World (PARADE) Study. The objectives were to investigate the feasibility of utilizing a mobile app to recruit and enroll patients into a study and to gain insights about Rheumatoid Arthritis (RA) in a real world setting.

Methods: The PARADE study was conducted in the United States (US) using a customized Apple ResearchKit™ App. The PARADE App included study video, eligibility screen, electronic informed consent, and data collection. The enrolment period was July 12 through August 12, 2016. Recruitment was enhanced with advertisement on various targeted social media platforms. Participants could enroll if they were 21 years or older, spoke English, lived in the US, and had been diagnosed with RA by a doctor. Participants were asked to provide demographics, comorbidities, medications, and RA symptoms including pain, fatigue, mood and morning stiffness. Additionally, over the course of 12 weeks, participants were asked to complete validated questionnaires routinely used in RA clinical trials, namely HAQ, FACIT,
Results: There were 1170 downloads of the PARADE App with 428 consents to participate in the study. Of these, 399 participants provided analyzable data, defined as those completing all demographic questions. The study population was 80% female, 81% Caucasian, mean age 47.9 years, and 77% college graduates. The duration of diagnosed RA included 122 (30.6%) participants with RA for <2 years, 91 (22.8%) for 2-5 years, 91 (22.8%) for 5-10 years and 95 (23.8%) for >10 years. Most bothersome RA symptoms included joint pain (87.5%), fatigue (73.5%), morning stiffness (57.5%), poor sleep (52.4%), walk and balance (32.8%), and mood variations (23.7%). Mean pain score was 4.4 (SD 0.14) on a numerical rating scale of 0 (no pain) to 10 (worst pain imaginable). Mean scores for validated questionnaires were HAQ-DI, 1.1 (SD 0.04); Patient Global Assessment of Disease Activity, 5.4 (SD 0.14) (0=I don’t feel arthritis to 10=Arthritis affects me severely); EQ-5D, 0.6983 (SD 0.00822), and FACIT, 25.5 (SD 0.66). RA medications are listed in the Table.

Conclusion: The PARADE study was the first Pharma-sponsored study in which real world patients could self-recruit, consent, enroll, and report data entirely via their iPhone using a ResearchKit™ App. This study successfully demonstrated the feasibility of this novel technology to gather insights into RA from a real world perspective.

<table>
<thead>
<tr>
<th>Current RA medications among PARADE study participants</th>
<th>Proportion of population that answered this question (n=388)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Painkillers</td>
<td>170 (43.8%)</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>194 (50.0%)</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>117 (30.2%)</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>155 (39.9%)</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>5 (1.3%)</td>
</tr>
<tr>
<td>Auranofin</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>Chloroquine</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>107 (27.6%)</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>30 (7.7%)</td>
</tr>
<tr>
<td>Mycophenolate</td>
<td>3 (0.8%)</td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>29 (7.5%)</td>
</tr>
<tr>
<td>Abatacept</td>
<td>29 (7.5%)</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>42 (10.8%)</td>
</tr>
<tr>
<td>Certolizumab</td>
<td>10 (2.6%)</td>
</tr>
<tr>
<td>Etanercept</td>
<td>34 (8.8%)</td>
</tr>
<tr>
<td>Golimumab</td>
<td>11 (2.8%)</td>
</tr>
<tr>
<td>Infliximab</td>
<td>16 (4.1%)</td>
</tr>
<tr>
<td>Rituximab</td>
<td>11 (2.8%)</td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>13 (3.4%)</td>
</tr>
<tr>
<td>Tofacitinib</td>
<td>18 (4.6%)</td>
</tr>
<tr>
<td>Others</td>
<td>40 (10.3%)</td>
</tr>
</tbody>
</table>

Disclosure: R. Williams, GSK, 3; E. Quattrocchi, GSK, 3; S. Watts, gsk, 3; S. Wang, gsk, 3; P. Berry, gsk, 3; M. Crouthamel, gsk, 3.


Abstract Number: 144

Are RA Patients at a Higher Risk for Car Accidents?

Kaleb Michaud¹,², Sofia Pedro¹ and Ted R. Mikuls³, ¹National Data Bank for Rheumatic Diseases, Wichita, KS, ²University of Nebraska Medical Center, Omaha, NE, ³Internal Medicine, Division of Rheumatology, University of Nebraska Medical Center, Omaha, NE

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017

Session Title: Epidemiology and Public Health Poster I: Rheumatoid Arthritis

Session Type: ACR Poster Session A

Session Time: 9:00AM-11:00AM

Background/Purpose:
Automobile driving is an important instrumental activity of daily living with heightened importance among arthritis sufferers who are disproportionately reliant on driving for the preservation of health, well-being, and quality of life. Despite its importance to patients, scant data exists regarding the impact of arthritis on driving performance. We investigated occurrences of motor vehicle accidents (MVA) in patients with RA and how clinical function measures may be associated with MVA.

Methods:

Using a large US observational cohort, the National Data Bank for Rheumatic Diseases (NDB), we compare RA and adult non-RA rheumatic disease patients who had a validated MVA. Within each group, we also compare patients with and without a MVA measured at a random observation before the accident or at any time for those without an accident. Patients with <2 questionnaires were excluded. MVAs were identified by validated hospitalizations (code 162) and by death codes (ICD9, E81*). We conducted a principal component analysis (PCA) using the 20 items from the HAQ. Scree plot and the Kaiser criterion were used to select the number of components.

Results:

From a total of 37,743 patients, we found 142 MVA, 103 recorded as hospitalizations and 39 as deaths. From the 26,905 RA adults, 90 (0.33%) had a MVA while the 10,838 non-RA patients had somewhat higher number of 52 (0.48%) (P=0.037). There was no statistical difference in demographic or clinical outcomes between those with or without a MVA in patients with RA, though there was an association with the number of individuals living the patient's household with those in MVA having fewer (p=0.02). Non-RA patients with MVA were older than patients with no accidents or compared to RA patients (Table). Scree plot analysis and Kaiser criterion identified the first two components as being the most associated with MVA (Figure). Component 1 (overall disability score) accounted for 56% of the variance in MVA risk while Component 2 (individual HAQ items) accounted for an additional 8% of variance. Of note, Component 2 included HAQ response items focused on upper extremity function / mobility (i.e. opening a car door, eating, opening a jar) and did not include items focused on lower extremity function (Figure).

Conclusion:

These findings provide evidence that reduced functional independence and hand mobility, outcomes associated with RA disease activity, may be linked to poor driving and/or future vehicle accidents.

Table –Comparison between RA and non-RA patients with and without car accidents

<table>
<thead>
<tr>
<th>Variables</th>
<th>RA patients (N=26,905)</th>
<th>Non-RA patients (N=10,838)</th>
<th>P-value for car accidents RA vs non-RA</th>
</tr>
</thead>
<tbody>
<tr>
<td>mean (sd) or %</td>
<td>No car accidents (N=26,815)</td>
<td>Car accidents (N=90)</td>
<td>No car accidents (N=10,786)</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>60.81 (13.31)</td>
<td>60.17 (13.25)</td>
<td>0.65</td>
</tr>
<tr>
<td>Sex (%)</td>
<td>0.21 (0.41)</td>
<td>0.22 (0.42)</td>
<td>0.72</td>
</tr>
<tr>
<td>Employed (%)</td>
<td>0.34 (0.47)</td>
<td>0.26 (0.44)</td>
<td>0.12</td>
</tr>
<tr>
<td>Educational level (yrs)</td>
<td>13.67 (2.38)</td>
<td>13.36 (2.47)</td>
<td>0.21</td>
</tr>
<tr>
<td>Dependency</td>
<td>1.23 (0.96)</td>
<td>0.42 (0.94)</td>
<td>1.17 (0.97)</td>
</tr>
<tr>
<td>None of the time (%)</td>
<td>29.27</td>
<td>19.70</td>
<td>29.78</td>
</tr>
<tr>
<td>A little of the time (%)</td>
<td>41.46</td>
<td>36.36</td>
<td>33.14</td>
</tr>
<tr>
<td>Some of the time (%)</td>
<td>14.63</td>
<td>31.82</td>
<td>28.70</td>
</tr>
<tr>
<td>Most of the time (%)</td>
<td>12.20</td>
<td>12.12</td>
<td>7.33</td>
</tr>
<tr>
<td>All of the time (%)</td>
<td>2.44</td>
<td>0.00</td>
<td>1.05</td>
</tr>
<tr>
<td>Number of person in household</td>
<td>2.21 (1.05)</td>
<td>0.82</td>
<td>2.19 (1.07)</td>
</tr>
</tbody>
</table>
Causes-Specific Mortality in a Large Population-Based Cohort of Rheumatoid Arthritis Patients in Italy

Francesca Ometto\textsuperscript{1}, UGO FEDELI\textsuperscript{2}, ELENA SCHIEVANO\textsuperscript{2}, Costantino Botsios\textsuperscript{3}, MARIA CHIARA CORTI\textsuperscript{1} and Leonardo Punzi\textsuperscript{4},
\textsuperscript{1}Rheumatology Unit, Department of Medicine - DIMED, University of Padova, PADOVA, Italy, \textsuperscript{2}Epidemiological Department, Veneto Region, VENETO, Italy, \textsuperscript{3}Rheumatology Unit, Department of Medicine - DIMED, University of Padova, Padova, Italy, \textsuperscript{4}Rheumatology Unit, Department of Medicine DIMED, University of Padova, Padova, Italy

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Epidemiology and Public Health Poster I: Rheumatoid Arthritis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Studies on mortality in RA from Italy are completely lacking. The aim of our study was to investigate cause-specific mortality in RA subjects living in the Veneto Region (Italy).

Methods: We identified in the electronic archive of the Veneto Region patients aged 20-89 years who were exempt from copayment for RA in January 2010, and linked them with the archive of causes of deaths of the period 2010-2015. Causes of death were coded according to the International Classification of Diseases, 10th Edition. The selection of the underlying cause of death (UCOD) was performed by means of the Automated Classification of Medical Entities (US National Center for Health Statistics). Each subject was followed from 1st January 2010 until death, or 90 years of age, or 31st December 2015, whichever came first. Standardized Mortality Ratios (SMRs) with 95% confidence intervals were computed as the ratios between deaths observed in the cohort, and those expected according to age- and gender-specific regional mortality rates.

Results: Overall 16,098 residents diagnosed with RA and aged 20-89 years were enrolled in the cohort (Figure 1). The overall follow-up amounted to 88,599 person-years, with 2,142 registered decedents. The most common causes of death were circulatory diseases (36.6%), neoplasms (24.2%), and respiratory diseases (8.3%). Overall SMR in RA subjects was 1.42 (1.36-1.48). Mortality was significantly increased from circulatory (SMR=1.56, 1.45-1.67), respiratory (SMR=1.83, 1.57-2.12), digestive (SMR=1.93, 1.60-2.32), infectious (SMR=2.34, 1.88-2.89), and hematological diseases (SMR=3.22, 2.04-4.83), and falls (SMR=1.95, 1.19-3.01) (Table I). Particularly SMR for circulatory diseases was higher in patients aged <65 years: SMR 1.86 (1.06-3.02) in males, and 2.07 (1.23-3.28) in females. RA was selected as the UOCD in 6.1% of all deaths in the cohort and was mentioned in 25.4% of death certificates. Diseases often reported in the certificate without being selected as the UCOD where sepsis, pneumonia, diabetes mellitus, and hypertensive diseases (Table II).

Conclusion: In the Veneto Region, a 42% excess risk of death was observed among subjects with RA compared to the general population. Adverse effects of therapy and comorbidities should be identified and adequately monitored in RA subjects.
Figure 1. Demographics of the study population at the beginning of follow-up: 18,698 patients with rheumatoid arthritis aged 20-89 years, Veneto Region (Italy), January 2010.
<table>
<thead>
<tr>
<th>Condition</th>
<th>Deaths</th>
<th>SMR (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Certain infectious and parasitic diseases</td>
<td>88</td>
<td>2.34 (1.88-2.89)</td>
</tr>
<tr>
<td>(A00-B99)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septicemia (A40-D41)</td>
<td>66</td>
<td>3.07 (2.37-3.90)</td>
</tr>
<tr>
<td>Neoplasms (C00-D48)</td>
<td>519</td>
<td>0.98 (0.90-1.07)</td>
</tr>
<tr>
<td>Malignant neoplasm of stomach (C16)</td>
<td>25</td>
<td>1.04 (0.67-1.54)</td>
</tr>
<tr>
<td>Malignant neoplasms of colon, rectum and anus</td>
<td>51</td>
<td>0.96 (0.71-1.26)</td>
</tr>
<tr>
<td>(C18-C21)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malignant neoplasm of pancreas (C25)</td>
<td>45</td>
<td>1.04 (0.76-1.39)</td>
</tr>
<tr>
<td>Malignant neoplasms of trachea, bronchus and</td>
<td>102</td>
<td>1.10 (0.89-1.33)</td>
</tr>
<tr>
<td>lung (C33-C34)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malignant neoplasm of breast (C50)</td>
<td>44</td>
<td>0.87 (0.63-1.16)</td>
</tr>
<tr>
<td>Non-Hodgkin's lymphoma (C82-C85)</td>
<td>21</td>
<td>1.36 (0.84-2.08)</td>
</tr>
<tr>
<td>Leukemia (C91-C95)</td>
<td>22</td>
<td>1.31 (0.82-1.99)</td>
</tr>
<tr>
<td>Diseases of the blood and blood-forming organs</td>
<td>23</td>
<td>3.22 (2.04-4.83)</td>
</tr>
<tr>
<td>(D50-D89)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endocrine, nutritional and metabolic diseases</td>
<td>57</td>
<td>0.96 (0.73-1.25)</td>
</tr>
<tr>
<td>(E00-E90)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus (E10-E14)</td>
<td>43</td>
<td>0.93 (0.67-1.26)</td>
</tr>
<tr>
<td>Mental and behavioural disorders (F00-F99)</td>
<td>50</td>
<td>0.90 (0.67-1.18)</td>
</tr>
<tr>
<td>Dementia (F00-F03)</td>
<td>44</td>
<td>0.86 (0.62-1.15)</td>
</tr>
<tr>
<td>Diseases of the nervous system (G00-G99)</td>
<td>61</td>
<td>0.89 (0.68-1.14)</td>
</tr>
<tr>
<td>Alzheimer's disease (G30)</td>
<td>27</td>
<td>0.90 (0.59-1.31)</td>
</tr>
<tr>
<td>Diseases of the circulatory system (I00-I99)</td>
<td>783</td>
<td>1.56 (1.45-1.67)</td>
</tr>
<tr>
<td>Hypertensive diseases (I10-I15)</td>
<td>101</td>
<td>1.51 (1.23-1.83)</td>
</tr>
<tr>
<td>Ischemic heart diseases (I20-I25)</td>
<td>247</td>
<td>1.51 (1.33-1.71)</td>
</tr>
<tr>
<td>Other heart diseases (I00-I09, I26-I51)</td>
<td>201</td>
<td>1.64 (1.42-1.88)</td>
</tr>
<tr>
<td>Cerebrovascular diseases (I60-I69)</td>
<td>182</td>
<td>1.43 (1.23-1.65)</td>
</tr>
<tr>
<td>Diseases of the respiratory system (J00-J99)</td>
<td>177</td>
<td>1.83 (1.57-2.12)</td>
</tr>
<tr>
<td>Pneumonia (J12-J18)</td>
<td>61</td>
<td>2.22 (1.70-2.86)</td>
</tr>
<tr>
<td>Chronic lower respiratory diseases (J40-D47)</td>
<td>54</td>
<td>1.47 (1.10-1.92)</td>
</tr>
<tr>
<td>Interstitial pulmonary diseases (J84)</td>
<td>20</td>
<td>3.47 (2.12-5.36)</td>
</tr>
<tr>
<td>Diseases of the digestive system (K00-K93)</td>
<td>117</td>
<td>1.93 (1.60-2.32)</td>
</tr>
<tr>
<td>Vascular disorders of intestine (K55)</td>
<td>21</td>
<td>2.40 (1.48-3.66)</td>
</tr>
<tr>
<td>Diseases of liver (K70-K76)</td>
<td>20</td>
<td>0.95 (0.58-1.47)</td>
</tr>
<tr>
<td>Diseases of the musculoskeletal system (M00-M99)</td>
<td>149</td>
<td>17.3 (14.7-20.4)</td>
</tr>
</tbody>
</table>
| Rheumatoid arthritis (M05-M06)                 | 130    | 63.3 (52.9-
Table 2. Number of deaths and standardized mortality ratio (SMR) with 95% Confidence Interval (CI), by gender and age class.

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>SMR (CI)</td>
</tr>
<tr>
<td>All causes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-64 yrs</td>
<td>62</td>
<td>1.50 (1.15-1.93)</td>
</tr>
<tr>
<td>65-74 yrs</td>
<td>141</td>
<td>1.30 (1.10-1.54)</td>
</tr>
<tr>
<td>75-89 yrs</td>
<td>452</td>
<td>1.32 (1.20-1.45)</td>
</tr>
<tr>
<td>Neoplasms (C00-D48)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-64 yrs</td>
<td>21</td>
<td>1.03 (0.64-1.58)</td>
</tr>
<tr>
<td>65-74 yrs</td>
<td>50</td>
<td>0.91 (0.67-1.20)</td>
</tr>
<tr>
<td>75-89 yrs</td>
<td>117</td>
<td>1.03 (0.85-1.23)</td>
</tr>
<tr>
<td>Circulatory system</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(I00-I99)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-64 yrs</td>
<td>16</td>
<td>1.86 (1.06-3.02)</td>
</tr>
<tr>
<td>65-74 yrs</td>
<td>43</td>
<td>1.62 (1.17-2.18)</td>
</tr>
<tr>
<td>75-89 yrs</td>
<td>179</td>
<td>1.48 (1.27-1.71)</td>
</tr>
<tr>
<td>Respiratory system</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(J00-J99)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-64 yrs</td>
<td>3</td>
<td>2.94 (0.59-8.59)</td>
</tr>
<tr>
<td>65-74 yrs</td>
<td>6</td>
<td>1.31 (0.48-2.85)</td>
</tr>
<tr>
<td>75-89 yrs</td>
<td>54</td>
<td>1.76 (1.33-2.30)</td>
</tr>
</tbody>
</table>

Disclosure: F. Ometto, None; U. FEDELI, None; E. SCHIEVANO, None; C. Botsios, None; M. C. CORTI, None; L. Punzi, None.


Abstract Number: 146

**Major Cardiovascular Events Among an Inception Cohort of Seniors with Rheumatoid Arthritis**

Jessica Widdifield¹ ², Michael Paterson², Anjie Huang², Bindee Kuriya³, Carter Thorne⁴, Janet E. Pope² and Sasha Bernatsky⁶, ¹Clinical Epidemiology, Research Institute of the McGill University Health Centre, Montreal, ON, Canada, ²Institute for Clinical Evaluative Sciences, Toronto, ON, Canada, ³Sinai Health System, University of Toronto, Toronto, ON, Canada, ⁴Southlake Regional Health Centre, Newmarket,
We previously observed that incident RA patients have an increased risk of cardiovascular (CV) mortality relative to the general population in Ontario. Our aim was to evaluate the incidence and factors associated with major CV events subsequent to RA diagnosis.

Methods:
We studied incident RA patients within the population-based Ontario Rheumatoid Arthritis Database (ORAD). We analyzed all individuals who were diagnosed with RA after their 65th birthdate (ensuring comprehensive drug coverage) between 2000 and 2013. Our primary outcome was a composite measure which included acute myocardial infarction (AMI), stroke, congestive heart failure (CHF), revascularization with either percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) surgery. All patients were followed from cohort entry until major CV event, censored on death, out-migration, or end of study period (Dec 2013), whichever occurred first. Factors associated with experiencing a major CV event during follow-up were analyzed using multivariable Cox regression to estimate hazard ratios (HRs), exploring the effects of baseline and time-varying medication exposures (including methotrexate, other DMARDs, anti-TNFs, COXIBs, NSAIDs, glucocorticosteroids, statins, antihypertensives), baseline comorbidities, time-varying development of extrarticular manifestations (as proxy for disease severity), healthcare use, and demographics (age, sex, rurality, socioeconomic status).

Results:
Among 23,994 incident RA patients, 67% were female. Patients had a high CV risk burden at the time of diagnosis (70% had pre-existing hypertension, 23% diabetes, 16% coronary artery disease, 3% previous AMI and 1% cerebrovascular disease). During 115,453 person-years of follow-up, 3,294 (14%) patients experienced a CV event for a crude rate of 28.5 events (95% CI 27.6,29.5) per 1,000 person-years [24.6 events (95% CI 23.5,25.7) among females and 37.4 events (95% CI 35.5,39.5) among males]. In our multivariable analysis, we did not observe clear associations with use of anti-rheumatic treatment during follow-up. Greater use of statins was associated with a lower CV event risk [HR 0.96 (95% CI 0.94,0.98)], whereas greater cumulative exposure to glucocorticosteroids was associated with an increased risk [HR 1.08 (95% CI 1.05,1.11)]. The strongest independent risk factors for a major CV event were pre-existing comorbidities at time of RA diagnosis, including coronary artery disease [HR 1.72 (95% CI 1.57,1.87)], prior AMI [HR 1.53 (95% CI 1.32,1.76)], renal disease [HR 1.43 (95% CI 1.20,1.70)], diabetes [HR 1.41 (95% CI 1.30,1.52)], cerebrovascular disease [HR 1.36 (95% CI 1.03,1.80)], and hypertension [HR 1.16 (95% CI 1.05,1.28)].

Conclusion:
Senior RA patients have a high CV risk burden at the time of RA diagnosis. Risk of experiencing a subsequent major CV event during follow-up was high. Pre-existing co-morbidities and glucocorticosteroids were positively associated with CV events, while statins were protective. This clearly highlights strategies to decrease CV events in RA.

Disclosure: J. Widdifield, None; M. Paterson, None; A. Huang, None; B. Kuriya, None; C. Thorne, AbbVie, Aمنgen, Celgene, Lilly, Novartis, Pfizer, Sanofi, and UCB; has served as a consultant for AbbVie, Aمنgen, Celgene, Centocor, Genzyme, Hospira, Janssen, Lilly, Medexus/Medac, Merck, Novartis, Pfizer, Sanofi, and UCB, 2.Medexus/Medac, 8; J. E. Pope, AbbVie, Aمنgen, Bayer, BMS, Celtrion, Eli Lilly and Company, Merck, Novartis, Pfizer, Roche, UCB, 5.Aمنgen, Bayer, BMS, GSK, Merck, Novartis, Pfizer, Roche, UCB, 2; S. Bernatsky, None.

Abstract Number: 147

Performance of Cardiovascular Risk Age and Vascular Age Estimations in Predicting Cardiovascular Events in Rheumatoid Arthritis

Grunde Wibetoe1, Cynthia S. Crowson2, Joseph Sexton3, Silvia Rollefstad1, Eirik Ikdahl1, George D. Kitas4, Piet van Riel5, Sherine E.
Disease duration and/or glucocorticoid treatment may influence the performance of risk age estimations.

Conclusion: Disease duration was preserved in these additional analyses. The trend of reduced concordance among women, glucocorticoid users and RA patients with short disease duration was observed. Additional analyses including RA patients on cardio preventive ranged from 0.71 to 0.73 with standard errors of 0.03. Across prediction models, the lowest observed concordance was found among women. Overall, the C-index across risk models in subgroups of RA patients based on disease characteristics.

Methods: RA patients were included from an international consortium, aged 30-70 years at baseline. Those with prior CVD, diabetes and/or users of lipid-lowering and/or antihypertensive therapy at baseline were excluded. Cardiovascular risk age was estimated based on chronologic age, smoking status, total cholesterol and systolic blood pressure at baseline. Vascular age was derived from the 10-year risk of fatal CVD events. Two risk age models based on the Systematic Coronary Risk Evaluation (SCORE) algorithm have been developed; the cardiovascular risk age and the vascular age. However, the performance of these models has not been compared. Using longitudinal data on CVD events in RA patients, we aimed to compare the discriminative ability of cardiovascular risk age and vascular age among RA patients and in subgroups of RA patients based on disease risk characteristics.

Results: Among the 1867 RA patients included, 74% were female, median (inter-quartile range) age and disease duration were 52.0 (44.0, 59.9) and 0.6 (0.1, 6.4) years, 72.5% were rheumatoid factor positive, 24.7% were using glucocorticoids and 10.3% were using biologics at baseline. Overall, 144 CVD events occurred and median follow-up time was 5.0 (2.6, 9.3) years. Median difference between estimated risk age and chronologic age was 4.0 to 6.7 years, depending on the specific risk age model applied. Overall, the C-index across risk models ranged from 0.71 to 0.73 with standard errors of 0.03. Across prediction models, the lowest observed concordance was found among women. Additional analyses including RA patients on cardio preventive therapy yielded slightly lower c-indexes. Since SCORE was developed for use in Europe, we performed analyses on European RA patients, which yielded similar results. The trend of reduced concordance among women, glucocorticoid users and RA patients with short disease duration was preserved in these additional analyses.

Conclusion: The cardiovascular risk age and vascular age models have comparable performance in predicting CVD in RA patients. Sex, disease duration and/or glucocorticoid treatment may influence the performance of risk age estimations.
Disclosure: G. Wibetoe, None; C. S. Crowson, None; J. Sexton, None; S. Rollefstad, None; E. Ikdahl, None; G. D. Kitas, None; P. van Riel, None; S. E. Gabriel, None; T. K. Kvien, AbbVie, Biogen, BMS, Celltrion, Eli Lilly and Company, Janssen, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Samsung, Sandoz, UCB, 5,AbbVie, Biogen, BMS, Celltrion, Eli Lilly and Company, Janssen, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Samsung, Sandoz, UCB, 8; K. Douglas, None; A. Sandoo, None; E. Arts, None; S. Wällberg-Jonsson, None; S. Rantapää Dahlqvist, None; G. Karpouzas, None; P. H. Dessein, None; L. Tsang, None; H. El-Gabalawy, None; C. A. Hitchon, None; V. Pascual-Ramos, None; I. Contreras-Yañez, None; P. P. Sfikakis, None; E. Zampeli, None; M. A. González-Gay, None; A. Corrales, None; L. J. Colunga-Pedraza, None; D. A. Galarza-Delgado, None; J. R. Azpiri-Lopez, None; A. G. Semb, None.


Abstract Number: 148

Lack of Screening By Rheumatologists and Primary Care Physicians for Childhood Sexual Abuse in Patients with Fibromyalgia-Depression Overlap: An Unrecognized Crisis?

M. Anthony Albornoz1, Christian Albornoz2 and Daniel J. Clauw3, 1Rheumatology, Riddle Memorial Hospital/Mainline Health System, Media, PA, 2Temple University School of Medicine, Philadelphia, PA, 3Chronic Pain & Fatigue Research Center, University of Michigan, Ann Arbor, MI
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Depression is reported in as many as 71% of patients with Fibromyalgia (FM). An association between Childhood Sexual Abuse (CSA) and FM has been well documented and is responsible for inducing disturbing levels of chronic physical and psycho-affective morbidity. Based on the 28-year experience of the lead author, the frequency of CSA in patients with Fibromyalgia-Depression Overlap (FDO) is thought to be highly underestimated, principally due to the underutilization of validated screening questions by Rheumatologists (RH), Internists and Family Medicine Physicians (PCP). We primarily sought to determine the frequency of CSA screening by RH and PCP in patients with FDO and the incidence of CSA in new patients with FDO. Additional clinical and psychosocial variables were secondarily assessed.

Methods: A retrospective analysis conducted over a 12 month period in an outpatient, community-based, solo private practice setting of 131 consecutive new adult patients diagnosed with FM by one RH. All patients were screened for depression, anxiety and CSA using validated tools(PHQ-9, GAD-7,Gen Hosp Psychiatry. 2007 Jan-Feb;29(1):8-13). CSA patients were asked whether past and/or present PCP and past RH inquired about sexual abuse: active and/or past PCP 15 (83%) and past RH 9 (100%); Psychiatric/Psychological care given in 18 (100%) of CSA patients; 18 (100%) of CSA patients experienced past

Results: All data is summarized in Table. Noteworthy clinical findings included: Of the 131 FM patients, 100% were female, 82 (63%) were diagnosed with FDO and 18 (22%) of FDO patients revealed they were victims of CSA; CSA was not encountered in the non-FDO population; CSA mean age was 42 with an age range of 18-74; mean age at time of abuse 13; oldest age when CSA first divulged was 74; 16 (89%) of CSA patients were under age 65 and of these 13 (81%) were either on disability or unemployed; 6 (33%) family member(s) did not believe claim of CSA; 14 (78%) of CSA patients requested that abuse history not be included in the medical record; 11 (61%) of assailants were 1st degree relatives; CSA patients never queried by physicians about sexual abuse: active and/or past PCP 15 (83%) and past RH 9 (100%); Psychiatric/Psychological care given in 18 (100%) of CSA patients; 18 (100%) of CSA patients experienced past
suicidal ideations and 11 (61%) active suicidal ideations; 8 (44%) attempted suicide; 18 (100%) had active depression and 16 (89%) had active anxiety; 15 (83%) active severe depression; 14 (78%) active severe anxiety; 16 (89%) active panic attacks.

Conclusion: The structure and small sample size of this investigation limits our ability to draw definitive conclusions. However, these data reveal that in an alarmingly high number of FDO patients previously evaluated by RH and PCP, CSA escaped detection. The results of this analysis highlights that patients with FDO-CSA likely represent a particularly at-risk population who are in need of greater physician awareness and a more focused assessment. A multi-state study addressing this topic is in progress.

Disclosure: M. A. Albornoz, None; C. Albornoz, None; D. J. Clauw, Abbott Pharmaceutical, 5, Aptinyx, 5, Astellas Pharmaceutical, 5, Cerephex, 5, Daiichi Sankyo, 5, Pfizer Inc, 5, Pierre Fabre, 8, Samumed, 5, Theravance, 5, Tonix, 5.


Abstract Number: 149

Effect of Vitamin D Supplementation in Chronic Widespread Pain: A Systematic Review and Meta-Analysis

Wai Chung Yong, Anawin Sanguankeo and Sikarin Upala, Bassett Medical Center, Cooperstown, NY
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Abstract

Background/Purpose: Chronic non-specific widespread pain (CWP) including fibromyalgia (FM) is characterized by widespread pain, reduced pain threshold and multiple tender points on examination, causing disability and decreased quality of life. Vitamin D has been proposed as an associated factor in CWP. This meta-analysis aimed to explore the benefit of vitamin D supplementation in the management of CWP.

Methods: A comprehensive search of the CENTRAL, MEDLINE and EMBASE databases was performed from inception through January 2017. The inclusion criterion was the randomized clinical trials’ evaluating the effects of vitamin D treatment in adult subjects with CWP or fibromyalgia. CWP was defined as chronic recurrent musculoskeletal pain without secondary causes; fibromyalgia patients met the American College of Rheumatology criteria for fibromyalgia. Study outcome was assessed using visual analog scale (VAS) of pain intensity. Pooled mean difference (MD) of VAS and 95% confidence interval (CI) were calculated using a random-effect meta-analysis. Meta-regression analysis using random-effects model was performed to explore the effects of change in vitamin D in the treatment group on difference in mean of VAS. Sensitivity analysis was performed to evaluate the robustness of results. The between-study heterogeneity of effect-size was
Results: Data were extracted from 4 randomized control trials involving 287 subjects. Pooled result demonstrated a significant lower VAS in CWP patients who received vitamin D treatment compared with those who received placebo (MD=0.46; 95% CI: 0.09 – 0.89, I² = 48%). Meta-regression analysis revealed no significant relationship between the changes of vitamin D and VAS with a coefficient = 0.04 (95% CI: -0.01 to 0.08), p=0.10.

Conclusion: In this meta-analysis, we conclude that vitamin D supplementation is able to decrease pain scores and improve pain despite no significant change in VAS after increasing serum vitamin D level. Further study needs to be conducted in order to explore the improvement of functional status, quality of life, and the pathophysiological change that improves chronic widespread pain.

Disclosure: W. C. Yong, None; A. Sanguankeo, None; S. Upala, None.
Abstract Number: 150

Effects of Taping Therapy in the Management of Fibromyalgia: A Randomized Controlled Study

Hae Joo Suh1 and Sang Tae Choi2, 1Seoul National University Hospital, Seoul, Korea, Republic of (South), 2Internal Medicine, Chung-Ang University College of Medicine, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Fibromyalgia is a medical condition characterized by chronic widespread musculoskeletal pain, accompanied by fatigue, insomnia, cognitive problems, psychiatric symptoms and various somatic symptoms. While a number of pharmacological and nonpharmacological therapies are attempting to treat the patients with fibromyalgia, fibromyalgia is still difficult to manage. Taping therapy has been reported to be effect in relieving pain in a variety of musculoskeletal diseases. However, there were no reports of the patients with fibromyalgia. Therefore, in this study, we aimed to evaluate the effectiveness of taping therapy in fibromyalgia management.

Methods: This is a randomized controlled trial, and total 60 patients with fibromyalgia were enrolled in this study. All patients were met the 2010 American College of Rheumatology (ACR) diagnostic criteria for fibromyalgia. Participants were randomized into the Kinesio taping group (n = 30) and the inelastic paper taping group (n = 30) as control. Kinesio taping therapy or inelastic paper taping was performed twice a week for three weeks in both groups. Three weeks later, Kinesio taping was applied to the control group for additional three week. To assess the effect, the widespread pain index (WPI), severity score (SS) and fibromyalgia impact questionnaire (FIQ) by ACR were used to measure pain, disease severity and dysfunctions in daily life. The Beck depression inventory (BDI) was used to assess depression, and quality of life was assessed by the EQ-5D INDEX and EQ-5D VAS by EurQol group.

Results: There were no significant differences between the two groups in mean ages, sex ratio and type of medications including anti-depressants and muscle relaxants. The Kinesio taping group showed significant improvement in pain (WPI, 10.50 ± 3.98 vs. 5.70 ± 2.73, p < 0.001), symptom severity (SS, 7.93 ± 2.24 vs. 5.27 ± 1.98, p < 0.001), dysfunction in daily life (FIQ, 65.03 ± 18.75 vs. 43.25 ± 18.87, p < 0.001), depression (BDI, 18.17 ± 8.55 vs. 13.00 ± 6.75, p < 0.001) and QoL (EQ-5D INDEX, 9.10 ± 1.54 vs. 7.67 ± 1.40, p < 0.001; EQ-5D VAS, 38.33 ± 24.65 vs. 56.67 ± 27.93, p < 0.001), respectively. In the control group, however, the significant difference was noted only in pain (WPI, 10.53 ± 3.87 vs. 9.27 ± 3.57, p = 0.014). The changes in the Kinesio taping group before and after treatment showed significant differences compared to the control group; WPI (p < 0.001), SS (p < 0.001), FIQ (p < 0.001), BDI (p = 0.001), EQ-5D INDEX (p < 0.001), and EQ-5D VAS (p < 0.001), respectively. After changing from inelastic paper taping to Kinesio taping, all parameters have been significant improved (WPI, p <0.001; SS, p <0.001; FIQ, p <0.001; BDI, p <0.001; EQ-5D INDEX, p <0.001; EQ-5D VAS, p <0.001, respectively). There was no serious adverse event to all participants.

Conclusion: This randomized controlled study showed that Kinesio taping therapy is effective in pain, symptom severity, dysfunctions in daily life, depression, and quality of life in patient with fibromyalgia. Taping therapy could be a useful treatment modality in the management of fibromyalgia.

Disclosure: H. J. Suh, None; S. T. Choi, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/effects-of-taping-therapy-in-the-management-of-fibromyalgia-a-randomized-controlled-study

Abstract Number: 151

Prevalence of Fibromyalgia in Nurses; A Cross Sectional Study

Sarah Alajmi1, Faisal Shahwan1, Yazeed Bajuaifer1, Rand Al Ohaly2, Maha Edrees2, Alanood Asiri2 and Mohammed Omair3, 1Internal Medicine, King Saud University Medical City, Riyadh, Saudi Arabia, 2King Saud University Medical City, Riyadh, Saudi Arabia, 3Division of Rheumatology, Department of Medicine, King Saud University, Riyadh, Saudi Arabia

First publication: September 18, 2017
SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Nurses are at increased of developing pain sensitization syndromes due to stress and interrupted sleep. The prevalence of fibromyalgia (FM) in nurses is unknown. The aim of this study is to evaluate the prevalence of FM in nurses using different screening tools.

Methods:
This was a cross-sectional study conducted in King Saud University Medical City (KSUMC). Nurses were invited to fill a questionnaire. The fibromyalgia Rapid Screening tool (FIRST), Fibromyalgia Survey Questionnaire (FSQ) and London Fibromyalgia Epidemiology Study Screening Questionnaire (LFESSQ) were used to identify patients with FM. Descriptive analysis was used for demographics. Non-parametric tests were to compare PIT with and without FM.

Results:
A total of 335 nurses completed the questionnaire. They were mostly females (93.7%), married (64.5%) with a median (interquartile range) age and body mass index of 32 (10) years and 24.8 (4.7) respectively. Of those, 121 (36.1%) nurse admitted having body pain. The prevalence of FM using the FIRST, FSQ and LFESSQ were (1.8%), (0.6%) and (19.4%) respectively. None of them fulfilled the 3 criteria concurrently. Using the LFESSQ criteria, nurses with FM were more likely to complain from irritable bowel syndrome ($p=0.018$), dry mouth ($p=0.026$), chest pain ($p=0.002$) and headache ($p<0.001$). the underlying specialty had an impact on the prevalence of FM based on specialty was; emergency department (23.1%), clinics (17.2%), intensive care (10.6%), ward (5.3) and operation room (4.3%).

Conclusion: The prevalence of FM is variable among nurses based on the used screening tool. Educational programs and screening clinics are justified.

Disclosure: S. Alajmi, None; F. Shahwan, None; Y. Bajuaifer, None; R. Al Ohaly, None; M. Edrees, None; A. Asiri, None; M. Omair, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/prevalence-of-fibromyalgia-in-nurses-a-cross-sectional-study

Abstract Number: 152

**Patients Failing to Fulfill 2016 Criteria for Fibromyalgia Represent a Truly Different Population Subset**

Marco Antivalle$^{1,2}$, Maria Chiara Ditto$^3$, Alberto Batticciotto$^3$, Rossella Talotta$^3$, Maria Chiara Gerardi$^3$, Alessandra Mutti$^3$, Fabiola Atzeni$^3$ and Piercarlo Sarzi-Puttini$^3$, $^1$Rheumatology, Rheumatology Unit, ASST Fatebenefratelli - Sacco, L. Sacco University Hospital, Milano, Italy, $^2$Rheumatology Unit, ASST Fatebenefratelli - Sacco, L. Sacco University Hospital, Milan, Italy, $^3$Rheumatology Unit, ASST Fatebenefratelli - Sacco, L. Sacco University Hospital, Milano, Italy

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The 2010/2011 fibromyalgia (FMS) diagnostic criteria (1) were recently revised, with the addition of a generalized pain criterion in order to avoid misclassification of regional pain syndromes; furthermore, the diagnosis of fibromyalgia is now valid irrespective of other diagnoses. Aim of the present study was to evaluate whether patients classified as having (2016+) or not having (2016–) FMS by 2016 revised criteria truly represent different populations.

Methods: 334 patients (306 F and 28 M) with a diagnosis of FMS according to 2011 criteria were included in the study; mean age was
46.82 yrs (range 16 – 75), and mean disease duration 6.25 yrs (range 3 months -34 yrs). Widespread Pain Index (WPI) and Symptom Severity Scale (SSS) were assessed by a localized version of the Fibromyalgia Survey Questionnaire; furthermore, patients were asked to report the presence or absence -in the last 7 days- of each of the 41 somatic symptoms suggested by the original 2010 classification paper (2). An evaluation of overall pain level in the last 7 days (0-10 numeric rating scale, NRS), and of fatigue by the FACIT-Fatigue questionnaire were available in 101 and 137 patients respectively. Statistical analysis was performed by IBM SPSS v 22. Differences of mean values and of proportions were evaluated by parametric or non-parametric methods as appropriate.

**Results:** the diagnosis of FMS was confirmed by 2016 criteria in 290 (86.8%) patients, and not confirmed in 44 (13.2%) patients. Mean age (47.62 ± 10.6 yrs vs 46.69 ± 11.7 yrs, p=0.625), mean disease duration (6.27 ± 6.37 vs 6.25 ± 6.10 yrs, p=0.982), the percentage of females (93.2% vs 91.4%, p=0.688), and the association with other clinically relevant diseases (27.3% vs 18.6%, p=0.179) were not different in the 2016- group as compared to 2016+ group. 2016- patients had significantly lower values of polysymptomatic distress scale (PSD: 16.59 ± 2.4 vs 21.86 ± 4.5 p < 0.001), and of pain-related variables (WPI: 7.57 ± 2.1 vs 12.66 ± 3.4, p< 0.001; TP: 10.54±5.4 vs 13.28 ± 4.3, p<0.001; NRS: 5.64 ± 2.9 vs 7.46 ± 1.9 p=0.022). SSS was similar in the 2 groups (9.03 ± 1.9 vs 9.20 ± 1.9 p=0.599), but the number of somatic symptoms reported was significantly lower in 2016- patients (14.44 ± 5.0 vs 17.49 ± 6.6 p=0.005, Fig. 1), which reported higher levels of fatigue (FACIT-Fatigue 28.3 ± 10.8 vs 21.17 ± 10.0, p=0.010).

**Conclusion:** The rate of disagreement between 2011 and 2016 criteria (13.2%) in our study is very close to the results (13.8%) reported in the only comparison study published to date (3). Patients failing to meet 2016 criteria seem to represent a truly different population, characterized by lower polysymptomatic distress, lower overall pain, and fewer somatic symptoms.

![Fig 1. Prevalence of somatic symptoms according to 2011 and 2016 FMS diagnostic criteria](image)

References:

Disclosure: M. Antivalle, None; M. C. Ditto, None; A. Batticciotto, None; R. Talotta, None; M. C. Gerardi, None; A. Mutti, None; F. Atzeni, None; P. Sarzì-Puttini, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/patients-failing-to-fulfill-2016-criteria-for-fibromyalgia-represent-a-truly-different-population-subset](http://acrabstracts.org/abstract/patients-failing-to-fulfill-2016-criteria-for-fibromyalgia-represent-a-truly-different-population-subset)

Abstract Number: 153

**Prevalence of Fibromyalgia in Physician in Training; A Cross Sectional Study**

Sarah Alobud1, Nour Alsultan1, Abeer Alhazzani1, Yasmin Altymani1, Muneera Albugami1, Maha Omair2 and Mohammed Omair3. 1King Saud University, Riyadh, Saudi Arabia, 2Department of Statistics, College of Science, King Saud University, Riyadh, Saudi Arabia, 3Division of Rheumatology, Department of Medicine, King Saud University, Riyadh, Saudi Arabia

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster I
Background/Purpose: Physicians in training (PIT) are at increased risk of developing pain sensitization syndromes due to stress and interrupted sleep. The prevalence of fibromyalgia (FM) in PIT is unknown. The aim of this study is to evaluate the prevalence of FM in PIT using different screening tools.

Methods: This was a cross-sectional study conducted in King Saud University Medical City. PIT were invited to fill a questionnaire which included the fibromyalgia Rapid Screening tool (FIRST), Fibromyalgia Survey Questionnaire (FSQ) and London Fibromyalgia Epidemiology Study Screening Questionnaire (LFESSQ) to identify patients with FM. Non-parametric tests were used for the analysis.

Results: A total of 183 PIT completed the questionnaire. They were predominantly males (56.8%), single (56.3%) and at resident level (86.3%). The median (interquartile range) age and body mass index were 28 (4) years and 26.3 (7.86) respectively. Seventy-two (39.3%) PIT admitted having generalized body pain. The prevalence of FM using the FIRST, FSQ and LFESSQ were (8.2%), (11.5%) and (8.2%) respectively. Seven (3.8%) of them fulfilled the 3 criteria concurrently. Using the LFESSQ criteria, PIT with FM were more likely to have a family history of FM (37.5% vs 3.5%; \( p < 0.001 \)), complain from irritable bowel syndrome (\( p < 0.001 \)), non-specific headaches (\( p = 0.001 \)), migraines (\( p < 0.001 \)), interrupted sleep (\( p = 0.003 \)), snoring (\( p = 0.046 \)), and impaired concentration (0.045). Surgical residents had the highest prevalence (14.8%) followed by anesthesia (14.3%) and medical residents (13.4%).

Conclusion: The prevalence of FM is increased among PIT regardless of the used screening tool. Educational programs and screening clinics are justified.

Disclosure: S. Alobud, None; N. Alsultan, None; A. Alhazzani, None; Y. Altymani, None; M. Albugami, None; M. Omair, None; M. Omair, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/prevalence-of-fibromyalgia-in-physician-in-training-a-cross-sectional-study

Abstract Number: 154

Frequency of Fibromyalgia in Patients with Antiphospholipid Syndrome. a Cross-Sectional Study

Nicole Mouneu Ornelas¹, Laura-Aline Martinez-Martinez², Vijaya Rivera³, Ricardo Alberto Venegas Yañez⁴, Victor Alejandro Escamilla Gomez⁵, Gumaro Acosta Peña⁶, Luis H. Silveira⁷, Angelica Vargas Guerrero³, Luis M. Amezcua-Guerra³ and Manuel Martinez-Lavin³,
¹Internal Medicine, Instituto Nacional de Cardiología - Ignacio Chávez, IGNACIO CHÁVEZ, Mexico, ²Rheumatology, Instituto Nacional de Cardiología Ignacio Chavez, Mexico City, TX, Mexico, ³Rheumatology, Instituto Nacional de Cardiología Ignacio Chavez, Mexico City, Mexico, ⁴Reumatología, Instituto Nacional de Cardiología "Ignacio Chavez", Ciudad de México, Mexico, ⁵Rheumatology, Instituto Nacional de Cardiología - Ignacio Chávez, Mexico City, Mexico, ⁶Instituto Nacional de Cardiología, Ciudad de Mexico, Mexico, ⁷Rheumatology, Instituto Nacional de Cardiología Ignacio Chavez, Mexico City DF, Mexico

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The observation of several cases with coexistent antiphospholipid syndrome (APS) and fibromyalgia led us to this investigation. The objective was to define the frequency of fibromyalgia in a group of patients with antiphospholipid syndrome.

Methods:
From March 24th to June 8th 2017 we studied all APS patients attending our outpatient rheumatology clinic. All of them fulfilled the Sapporo and/or Sydney APS classification criteria. The Institutional Ethics Committee approved the protocol. All patients underwent a history + physical examination with emphasis on musculoskeletal features. All filled-out the following questionnaires: the Revised Fibromyalgia Impact Questionnaire (FIQ-R), the 2016 revision of Wolfe’s Fibromyalgia Diagnostic Criteria, and the quality of life EuroQol 5D-5L. The Damage Index in Thrombotic Antiphospholipid Syndrome (DIAPS) was also obtained. Spearman method was used to correlate APS clinical
features with fibromyalgia questionnaire scales. Chi square to compare categorical variables.

**Results:**

Sixty one patients with APS were included. Their mean age: 44 ± 15 years, 70% are female and 54% have primary APS. The prevalence of fibromyalgia was different when using the 1990 ACR diagnostic criteria (4.9%) compared to Wolfe’s criteria (16.4%) \(p<0.0001\). The frequency of fibromyalgia was not different in patient with primary vs. secondary APS. In those patient who had concurrent APS and fibromyalgia according to Wolfe’s criteria (\(n = 10\)), there was a correlation between total number of thrombotic events with headache, depression, and abdominal pain \((r=0.636, p=0.048)\), as well as with FIQ-R balance problems \((r=0.754, p=0.012)\). Oddly, cumulative organ damage measured by DIAPS inversely correlated with FIQ-R quality of sleep \((r=-0.820, p=0.004)\). Quality of life measured by Euro Qol is poorer in APS + fibromyalgia patients \((85\pm16 \text{ vs } 64\pm12, p<0.001)\).

**Conclusion:**

In this cohort of patients with APS, more individuals can be classified as having concurrent fibromyalgia when the 2016 revised Wolfe’s criteria is used. Recurrent thrombosis is associated to several fibromyalgia symptoms such as headache, depression and abdominal pain. Patients with APS and concurrent fibromyalgia have poorer quality life.

**Disclosure:** N. M. Ornelas, None; L. A. Martínez-Martínez, None; V. Rivera, None; R. A. Venegas Yañez, None; V. A. Escamilla Gomez, None; G. Acosta Peña, None; L. H. Silveira, None; A. Vargas Guerrero, None; L. M. Ameza-Guerra, None; M. Martínez-Lavín, None.


Abstract Number: 155

**Xerostomia in Patients with Fibromyalgia**

Nicolas Lloves\(^1\), Anastasia Secco\(^2\), Virginia Durigan\(^3\), Santiago Scarafia\(^2\), Felix Romanini Sr.\(^4\) and Marta Mamani\(^4\), \(^1\)Rheumatology Department, Hospital Rivadavia, Buenos Aires, Argentina, \(^2\)Hospital Bernardino Rivadavia, CABA, Argentina, \(^3\)Reumatology, Hospital Bernardino Rivadavia, CABA, Argentina, \(^4\)Hospital Rivadavia, Buenos Aires, Argentina

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster I  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**  
Fibromyalgia (FM) is a rheumatic disease characterized by diffuse, chronic musculoskeletal pain, of non-articular origin, which is evidenced by the palpation of painful points in specific anatomical areas and is usually accompanied by non-repairing sleep, Tiredness, morning stiffness, cognitive alterations, among others. FM affects approximately 0.5 -5% of the population, having a maximum prevalence between 40 and 50 years. No racial or socioeconomic predisposition has been determined to date. Sjicca syndrome whose term encompasses xerophthalmia, xerostomia, xeroderma and xerovagina, has been described in patients with FM. Xerostomia is the sensation of dry mouth due to lack or decrease of saliva. There are no clinical studies that determine the prevalence of xerostomia in patients with FM and on the other hand the reduction of salivary flow in these patients has not been studied with objective tests. The aim of this study was to determinate the frecuency of xerostomia in patients with diagnosis of Fibromyalgia and describe their clinical and epidemiologic characteristics.

**Methods:** Patients were included according 1990 and 2010 ACR Classification criteria. Patients taking drugs that cause xerostomia were excluded as well as the ones presenting other rheumatologic diseases. Xerostomia was assessed by interrogation and physical examination, and a sialometry was performed in order to determinate the decrease of salival flow. A sialometry was positive if the saliva flow was under 1.5 ml in 15 minutes. In case of presenting positive sialometry patients were studied to rule out Sjogren Syndrome with laboratory and minor salivary gland biopsy.

**Results:** 50 patients were recruited during the study. The 100 % of them were women. The mean age was 47 years old (DS±8.5), while the mean time of evolution of FM was 6 years. 29 patients reported xerostomia of which 4 presented positive sialometry. No positive sialometry was found in the group that did not referred xerostomia. Smoking was more prevalent in patients with FM who did not report xerostomia with respect of those who reported xerostomia (31.8% vs 6.9%, \(p 0.02\)). There were not associations between xerostomia and hypothyroidism,
Conclusion: The prevalence of xerostomia was 51%. No statistically significant associations were found in patients who reported xerostomia. A decrease in objective salivary flow was not demonstrated in patients with FM.

Disclosure: N. Lloves, None; A. Secco, None; V. Durigan, None; S. Scarafia, None; F. Romanini Sr., None; M. Mamani, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/xerostomia-in-patients-with-fibromyalgia

Abstract Number: 156

Unexpectedly High Prevalence of Immunoglobulin Deficiency in Fibromyalgia – II

Xavier J. Caro1,2 and Earl F. Winter2, 1Northridge Hospital Medical Center, Northridge, CA, 2Southern California Fibromyalgia Research and Treatment Center, Northridge, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: We have recently reported that 70% of an unselected FM cohort (n = 107) had subtle laboratory findings of Primary Immune Deficiency (PID), usually consisting of one or more immunoglobulin subclass deficiencies (Arthritis Rheum 2014;55(11): S905). To better understand this finding we surveyed a second cohort of FM subjects for laboratory evidence of PID, and – additionally - any clinical evidence of recurrent infections. Our results are reported here.

Methods: We retrospectively reviewed serum Ig concentration values on all FM subjects seen between December 2013 and May 2017 in an outpatient, rheumatology office setting. No other diagnosis precluded inclusion in the study unless it was likely that it might predispose to Ig deficiency. A total of 81 consecutive FM subjects, meeting 2010 ACR criteria, were screened; 4 were excluded (i.e., alcohol abuse; prior cancer chemotherapy; age < 18 yrs.). Data on 77 remaining FM subjects were reviewed; 43 of these had coincident RA (26 % seropositive). Ig deficiency was defined as an Ig value below the lower limits of normal (LLN) suggested by Paul’S Fundamental Immunology ( ); all deficient specimens were tested in duplicate. Ig abnormalities were confirmed by repeat analysis 6 - 9 weeks later. We also reviewed the prevalence of deficient or low mannose binding lectin in these subjects (deficient < 50 ng/ml; low < 500 ng/ml). In an attempt to further ascertain the role of Ig deficiency in FM we also studied the prevalence of any Ig level > LLN but within the lower most quartile of normal values (range / 4). We also collected data regarding a ÔLifetime History of InfectionsÔ on all FM subjects and 26 ÔApparently HealthyÔ aged-matched, community volunteers (± 5 years).

Results: Our findings are listed below:

Serum Ig Deficiency in 77 FM Subjects Compared to Literature Based Controls

<table>
<thead>
<tr>
<th>Immunoglobulin</th>
<th>No. with Ig deficiency</th>
<th>No. with-out Ig deficiency</th>
<th>Prevalence of FM Ig Deficiency</th>
<th>Estimated Normal Prevalence</th>
<th>P-value (2-tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG Subclass 1</td>
<td>27</td>
<td>50</td>
<td>35%</td>
<td>1/1200</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>IgG Subclass 2</td>
<td>12</td>
<td>65</td>
<td>16%</td>
<td>1/1200</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>IgG Subclass 3</td>
<td>37</td>
<td>40</td>
<td>48%</td>
<td>1/1200</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>IgG Subclass 4</td>
<td>34</td>
<td>43</td>
<td>44%</td>
<td>1/1200</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>IgA Subclass 1</td>
<td>20</td>
<td>57</td>
<td>26%</td>
<td>1/500</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>IgA Subclass 2</td>
<td>11</td>
<td>66</td>
<td>14%</td>
<td>3/100</td>
<td>0.002</td>
</tr>
<tr>
<td>IgM</td>
<td>1</td>
<td>76</td>
<td>1%</td>
<td>3/100</td>
<td>NS</td>
</tr>
<tr>
<td>IgE</td>
<td>11</td>
<td>66</td>
<td>14%</td>
<td>2.5/100</td>
<td>0.002</td>
</tr>
<tr>
<td>Any Ig</td>
<td>64</td>
<td>13</td>
<td>83%</td>
<td>1/1200</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>


Ed: Paul, WE. Lippincott, New York 2013. Analysis was by Chi-square test.
Of 71 FM subjects in whom Mannose Binding Lectin (MBL) was measured 18 (23 %) had levels <500 ng/ml, and 12 (16%) had levels <50 ng/ml. The prevalence any Ig in FM subjects being within our estimate of PaulÖs () lowest quartile for normal Ig levels ranged from 40% to 74%. There was no significant difference in the prevalence of Ig deficiency in FM subjects with concomitant RA compared to those without RA. A history of recurrent sinus infections was not significantly more common in our FM subjects compared to controls, but a history of recurrent serious, non-sinus infections was more prevalent for FM (P(1) = 0.009), and FM + RA (P(1) = < 0.0001).

**Conclusion:** Our study shows that clinically significant Ig deficiency, particularly IgG subclass deficiency, is a common accompaniment to FM. It also strengthens the argument that FM may be a disorder associated with immune dysregulation. The precise mechanism of this interaction remains unclear, but deserves further investigation.

**Disclosure:** X. J. Caro, None; E. F. Winter, None.

**Abstract Number:** 157

**A Systematic Review of the Upper Limb Soft Tissue Comorbidities in Patients with Type 2 Diabetes Mellitus**

Michelle C Papandony1, Anita E Wluka2, Ar Kar Aung3, Yuanyuan Wang1, Sultana Monira Hussain4 and Flavia M Cicuttini1, 1Monash University, Department of Epidemiology and Preventive Medicine, Melbourne, Australia, 2Australia, Armadale, Australia, 3Department of General Medicine, Alfred Health, Melbourne, Australia, 4Monash University, Department of Epidemiology and Preventative Medicine, Melbourne, Australia

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Soft tissue disorders affecting the upper limb are not commonly thought of as “classic” complications of type 2 diabetes mellitus. However, the majority of upper limb disorders including adhesive capsulitis, carpal tunnel syndrome, Dupuytren’s disease, flexor tenosynovitis, limited hand mobility and rotator cuff tendinitis are more frequent in patients with type 2 diabetes mellitus compared to the general population. With population aging and increasing obesity, the epidemic of type 2 diabetes mellitus is expected to grow. As such, targeting upper limb soft tissue diseases, which contribute to difficulty performing activities of daily living, increased morbidity, poorer health outcomes and higher health service related costs will be important.

The aim of this systematic review is to determine the type and magnitude of upper limb soft tissue comorbidities in patients with type 2 diabetes mellitus compared to the general population.

**Methods:**

A systematic literature review of the MEDLINE and EMBASE databases was performed. Any study describing upper limb soft tissue disease in patients with type 2 diabetes mellitus was included. A risk of bias assessment was performed. Where the prevalence of a condition was available, the median and range was presented.

**Results:**

8035 manuscripts were identified by the search strategy. 31 articles were eligible for inclusion. Most studies were cross sectional in design. The risk of bias assessment was high. We found that upper limb soft tissue disease is common in type 2 diabetes mellitus (median 32.1%, range 19-57.7%).

Based on data from two studies, the prevalence of any hand abnormality was higher in T2DM compared to controls (median prevalence 45% (range 20.5-69.5%) and 4.9% respectively). Limited hand mobility in type 2 diabetes mellitus was common, with a median prevalence of 26.7% (range 0-80%) (data from 19 studies). Dupuytren’s disease was more common in type 2 diabetes mellitus, with a median prevalence 18.8%, (range 0-43.4%), compared to 8% (range 0-39%) in controls (data from 18 studies). Carpal tunnel syndrome was also more common in type 2 diabetes mellitus compared to controls, with a median prevalence of 14% (range 0.32-83.3%) and 3.1% (range 0-17.5%) respectively. The median prevalence of flexor tenosynovitis in type 2 diabetes mellitus was 7.2% (range 2-16.7%) compared to 2% (range0-
The prevalence of any shoulder abnormality in type 2 diabetes mellitus was 19.5% compared to 4.4% in controls (data from one study). Adhesive capsulitis in type 2 diabetes mellitus was more common (median prevalence was 14.6%, range 7-29%) compared to 2.5% (range 0.5-17%) in controls (data from 8 studies). The median prevalence of rotator cuff tendinitis in type 2 diabetes mellitus was also higher (23.3% (range 9.5-43.3%)) compared to 8.7% (range 0.8-50%) in controls (data from 3 studies).

Conclusion:
This systematic review has demonstrated that upper limb soft tissue disease is more prevalent in patients with type 2 diabetes mellitus compared to the general population. These associations need to be further investigated and targeted in patients with type 2 diabetes mellitus in order to optimize health outcomes.

Disclosure: M. C. Papandony, None; A. E. Wluka, None; A. K. Aung, None; Y. Wang, None; S. M. Hussain, None; F. M. Cicuttini, None.

Abstract Number: 158

Is Lu Eight-Brocades Exercise Beneficial for Patients with Fibromyalgia?

Juan Jiao1, Irwin Jon Russell2, Wen Wang3, Ya-yun Zhao4, Rou-man Zhang4, Jing Wang4 and Quan Jiang5, 1Rheumatism Department, Guang’anmen Hospital, China Academy of Chinese Medical Sciences, Beijing, China, 2Affiliated with Arthritis & Osteoporosis Center of South Texas, Medical Director, Fibromyalgia Research and Consulting, San Antonio, Texas, San Antonio, TX, 3JCW Education Consulting, Conway, AR, 4Guang’anmen Hospital, China Academy of Chinese Medical Sciences, Beijing, China, 5Rheumatology Department, Guang’anmen Hospital, China Academy of Chinese Medical Sciences, Beijing, China

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Fibromyalgia is a chronic debilitating musculoskeletal pain syndrome that causes substantial physical and psychological impairments. With the release of the 2016 revised EULAR recommendations for the management of fibromyalgia, there is a growing interest in developing new exercise program aiming to improve patients’ physical function and wellbeing. The Eight Brocades (EB) is an eight-section Qigong physical exercise, originated more than eight-hundred years ago in China, and it has been used by people to improving their general health or existing health issues. Lu Eight Brocades (LEB) is a modified EB, adapted by Chinese Medicine Master Zhi-zhen Lu, which is specifically tailored for patients with rheumatic diseases and is simple and easy to learn. The clinical study reported here was aimed to evaluate the effectiveness of LEB in the management of fibromyalgia in Chinese patients in China.

Methods: In this randomized blank-control study, 62 patients with fibromyalgia were assigned to LEB or control group by computer using the SAS system with a ratio of 1:1. Trained and guided by LEB certified physicians, patients practiced LEB one hour, twice a week for 12 weeks in GUAN AN MEN hospital. The primary outcome measure is Visual Analogue Scales for pain (pain VAS), and the secondary outcomes include the followings: Revised Fibromyalgia Impact Questionnaire (FIQR), Multidimensional Assessment of Fatigue (MAF), Pittsburgh Sleep Quality Index (PSQI), Beck Depression Inventory (BDI), Perceived Stress Scale (PSS), and Tender Points Count (TP). The outcome measures were assessed at baseline and at the end of week 4, 8, 12. As compensation, patients in blank-control group received LEB training for additional 12 weeks after the end of the study. Statistical analyses were conducted by a statistician using intention to treat analysis set.

Results: Sixty-two subjects were mostly women (55, 87.7%), mean age was 51.2 years (SD 10.6 years, range: 29-69 years), and mean duration was 32.1 months (SD 26.3 months, range: 4-128 months). At the baseline, there were no significant differences on demographics and disease characteristics between LEB and control groups. At the week 4, except for BDI and PSS, improvement of pain VAS, FIQR, MAF, PSQI, and TP were greater in LEB group compared to those in the control group (Ps ≤0.046). At week 8, all above the measures further improved in LEB group than those in control group (Ps ≤0.033). At the week 12, all the outcome measures were improved in LEB group compared with control (Ps ≤0.004). There were no complaints about side effects of LEB exercise during the study period using the side-effect report form.

Conclusion: This pilot study demonstrated the effectiveness of physician-guided LEB practice for 12 weeks in improving all spectrum of debilitation symptoms and the feeling of wellbeing in fibromyalgia participants. The study suggests LEB exercise could be a potential
valuable nonpharmacological treatment for patients with fibromyalgia, thus warrants for further larger scale investigations.

Disclosure: J. Jiao, None; I. J. Russell, None; W. Wang, None; Y. Y. Zhao, None; R. M. Zhang, None; J. Wang, None; Q. Jiang, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/is-lu-eight-brocades-exercise-beneficial-for-patients-with-fibromyalgia

Abstract Number: 159

The Use of “Fibromyalgia Rapid Screening Tool” for Detection of Fibromyalgia in Patients with Chronic Arthritis Treated with Full and Tapered Biological Disease-Modifying Antirheumatic Drugs

Larissa Valor1, Diana Hernández-Flórez2, Tamara del Río2, Juan Gabriel Ovalles-Bonilla3, Julia Martínez-Barrio4, Iustina Jiană5, Belen Serrano6, Claudia Saez2, Roberto Gonzalez2, Juan Carlos Nieto5, Carlos M Gonzalez5, Indalecio Montenegro5 and Francisco Javier López Longo7, 1Rheumatology, Hospital general Universitario Gregorio Marañón, Madrid, Spain, 2Rheumatology, Gregorio Marañón University General Hospital, Madrid, Spain, 3Instituto de Investigación Sanitaria Gregorio Marañón, Madrid, Spain, 4Servicio de Reumatología, Hospital General Universitario Gregorio Marañón, Madrid, Spain, 5Rheumatology, Hospital General Universitario Gregorio Marañón, Madrid, Spain, 6Rheumatology, Hospital General Universitario Gregorio Marañón, Genoa, Italy, 7Facultad de Medicina, Universidad Complutense de Madrid, Madrid, Spain

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The coexistence of fibromyalgia (FM) and chronic arthritis is a challenge for an accurate identification of signs and symptoms associated with rheumatoid arthritis (RA), psoriatic arthritis (PsA), peripheral (PerSpA) and axial spondyloarthropathies (AxSpA). The Fibromyalgia Rapid Screening Tool (FiRST) is a validated questionnaire with high sensitivity and moderate specificity to identify 89% of FM cases, even when it is accompanied by anxiety, depression or functional disability. The use of full or tapered biological disease-modifying antirheumatic drugs (bDMARD) depends in many cases on the reliability of clinical indices which can be altered by the subjectivity of the patient and/or concomitant pathologies. Objective: To evaluate the prevalence of FM using the FiRST questionnaire in patients diagnosed with chronic arthritis and treated with bDMARD.

Methods: This cross-sectional study included 325 patients [178 (54.8%) females and 147 (45.2%) males] diagnosed of chronic arthritis and treated with bDMARDs. They were consecutively recruited in the Biological Therapy Unit from January to March 2015, all patients were in full or tapered bDMARD for at least 1 year. The dosage tapering had been made in patients with a maintained remission according to their rheumatologist attendant and the patient approval. All patients self-completed the FiRST questionnaire and a score> 5/6 was considered positive. The clinical assessment was always performed by the same investigator. Demographic, clinical and laboratory variables were collected and clinical indices related to each pathology were calculated (DAS28-ESR, DAS28-CRP, SDAI, CDAI, BASDAI, BASFI, ASDAS-CRP). Patients were classified as peripheral arthritis (PerAR: RA, PsA, PerSpA) and axial spondyloarthropathies (AxSpA).

Results:

A total of 68/325 (21%) patients had a FiRST>5/6. The time since diagnosis and the number of previous used bDMARD were not significant respect to FiRST<5/6. In the PerRA vs. AxSpA group we observed that 19% (n=43) and 35% (n=25) had FiRST>5/6, respectively (p=NS). Fifteen % of patients with tapered bDMARD had FiRST>5/6 vs. 85% of patients in full bDMARD dosage (p=0.001). Patients in clinical remission were higher in the PerAR group with tapered bDMARD dosage according to DAS28-ESR, SDAI and CDAI [96%, 94% and 94%] (p=0.01, p=0.04, p=0.032), respectively. In the PerAR subgroups, we found an association between tapered bDMARD and remission only in patients with RA according to DAS28-VSG, SDAI and CDAI (p=0.026, p=0.04, p=0.043, respectively). In the AxSpA group with tapered bDMARD dosage 86% of patients were in clinical remission according to BASDAI (p=0.019).

Conclusion: There was no difference between PerAR and AxSpA groups regarding FiRST>5/6. Patients with tapered bDMARD dosage had a lower proportion of FiRST>5/6, therefore early detection of patients with FiRST>5/6 might help us to better understand clinical activity in chronic arthritis and to improve diagnostic and therapeutic approaches of FM in these patients treated with bDMARD in terms of its efficacy and cost-effectiveness.
Fibromyalgia Screening Form in the Diagnosis of Concomitant Fibromyalgia

Robert S. Katz1 and Jessica L. Polyak2, 1Rush University Medical Center, Chicago, IL, 2Rheumatology Associates S.C., Chicago, IL
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: We have found that patients with a variety of rheumatic diseases who have concomitant fibromyalgia more frequently fail therapies for the underlying inflammatory rheumatic disease and osteoarthritis. Based on the 2010 ACR criteria for the diagnosis of fibromyalgia, a screening form was developed at the time of the study for accurate diagnosis. The screening assessment form is filled in by patients. It includes 19 pain areas as well as questions concerning sleep, energy, cognition, headache, abdominal pain, and depression. Adding this fibromyalgia screening questionnaire to the patient’s initial visit can also help validate the diagnosis in the minds of patients and also clinicians. We had patients in a rheumatology office practice complete this diagnostic form.

Methods: There are 19 pain areas listed. Patients checked a box next to the areas of pain during the last 7 days and replied to questions for the other symptoms- sleep (0-3), energy (0-3), cognition (0-3), and abdominal pain (0-1), headaches (0-1) and depression (0-1). A score of 12 and above is consistent with fibromyalgia.

Results: 60 patients with various rheumatic diseases, but excluding primary fibromyalgia, filled out the assessment form developed for the 2010 ACR diagnostic criteria. In those patients with an underlying inflammatory rheumatic disease diagnosis, without known fibromyalgia, 14 (23.3%) had a finding of 12 or more points using the fibromyalgia diagnostic screening form.

Conclusion: The fibromyalgia screening form developed in conjunction with the ACR 2010 criteria for fibromyalgia diagnosis can be quite helpful in determining the presence of concomitant fibromyalgia. 23.3% of a group of patients with inflammatory arthritis, lupus, and osteoarthritis also had fibromyalgia, according to the screening form results.

This form can be used to suggest the possibility of concomitant fibromyalgia in patients with other rheumatic diseases. Concomitant fibromyalgia and an inflammatory rheumatic disease may be a reason for the failure of biologic modifier and other therapy aimed at reducing pain and improving global well-being.

Disclosure: R. S. Katz, None; J. L. Polyak, None.

The Effectiveness of Medications for Fibromyalgia Based on Patient Experiences

Robert S. Katz and Frank Leavitt, Rush University Medical Center, Chicago, IL
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster I
Background/Purpose: To assess patients’ global assessment of frequently used treatments for the fibromyalgia syndrome (FMS), we asked patients with fibromyalgia to rank medications they have tried in the order of their effectiveness.

Methods: 95 patients (mean age of 50.5) diagnosed with fibromyalgia based on the 2011 ACR criteria, 88 females and 7 males, completed an in-office questionnaire regarding the effectiveness of various medications often used to treat fibromyalgia. The study ranked 9 medications, which include pregabalin, gabapentin, duloxetine, Muscle Relaxants, Sleep Aids, Stimulants, ADD Medications, Pain Medications, and NSAIDS. Patients rated the medications using this scale: 1=minimally helpful, 2=somewhat helpful, 3=moderately helpful, 4=very helpful.

Results: The three medications that were most positively rated by patients were opiate pain meds (mean=2.8), meds to improve sleep (mean=2.8), and ADD stimulants for fibro fog symptoms (mean=2.6).

Effectiveness ratings by fibromyalgia patients for other medications included: gabapentin (mean=0.73); duloxetine (mean=1.02); pregabalin (mean=1.26). 59.1% of FMS patients reported little or no help from pregabalin, and 83.3 % found gabapentin to be little help.

Conclusion: Fibromyalgia patients rated the effectiveness of various medications that had tried. Pain medication, sleep aids and stimulants given for the attention deficit component of fibro fog were judged by patients to be the most helpful.

Disclosure: R. S. Katz, None; F. Leavitt, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-effectiveness-of-medications-for-fibromyalgia-based-on-patient-experiences-2

Abstract Number: 162

Depression Versus Frustration

Robert S. Katz1 and Jessica L. Polyak2, 1Rush University Medical Center, Chicago, IL, 2Rheumatology Associates S.C., Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Patients with fibromyalgia may feel depressed. But is it a clinical depression, suggesting the need for SSRI, SNRI, or other medication, or is it frustration related to the presence of the symptoms of the disease?

Methods: 115 fibromyalgia syndrome (FMS) patients, meeting the 2010 ACR criteria for the diagnosis, completed a questionnaire in a rheumatology office practice asking whether they were depressed and also whether they felt frustrated. The 62 FMS patients who responded yes to having depression also filled out a Patient Health Questionnaire-9 (PHQ-9) for depression. The PHQ-9 asked the following questions: little interest in doing things; feeling down/depressed; trouble with sleep; feeling tired/low energy; poor appetite; feeling bad about oneself; poor concentration; moving and speaking slowly or excessively fidgety; and thoughts of hurting oneself. Patients were asked to rate these questions based on how they felt over the last two weeks, as follows: 0 for not at all, 1 for several days, 2 for "more than half the days and 3
for nearly every day. A score of 5-9 minimal symptoms, 10-14 minor depression, 15-19 major depression, moderate; and >20 major depression, severe.

The Patient Health Questionnaire (PHQ-9)

<table>
<thead>
<tr>
<th>Over the past 2 weeks, how often have you been bothered by any of the following problems?</th>
<th>Not at all</th>
<th>Several Days</th>
<th>More Than Half the Days</th>
<th>Nearly Every Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Little interest or pleasure in doing things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Feeling down, depressed or hopeless</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3. Trouble falling asleep, staying asleep, or sleeping too much</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4. Feeling tired or having little energy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5. Poor appetite or overeating</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6. Feeling sad about yourself or that you’re a failure or have let yourself or your family down</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7. Trouble concentrating on things, such as reading the newspaper or watching television</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>8. Moving or speaking so slowly that other people could have noticed. Or, you felt so fidgety or restless that you have been moving around a lot more than usual</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>9. Thoughts that you would be better off dead or of hurting yourself in some way</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

Results: 96 FMS patients responded yes to the question “are you frustrated?” When asked, “Are you depressed?”, 62 FMS patients answered yes. Scores of the PHQ-9 in the 62 FMS patients feeling depressed were as follows: 12 (19.3%) that scored in the 5-9 range (“minimal symptoms”), 18 (29.2%) that scored in the 10-14 range (“minor depression”), 22 (35.4%) that scored in the 15-19 range (Major depression, moderate), and 10 (16.1%) that scored in the >20 range (Major depression, severe).

Conclusion: Of 115 patients with fibromyalgia, 62 reported depression. Using the PHQ-9 depression questionnaire 22 of these patients had a moderate major depression and 10 severe major depression. The great majority of patients with fibromyalgia express frustration but don’t
meet the criteria for depression, based on the PHQ-9 questionnaire. Psychotherapy, including ventilation of the patient’s symptoms in the rheumatologist’s office, and continued in a psychologist’s or psychiatrist’s office, can be important. Separating depression, with the possibility of prescribing antidepressant medications, and frustration can be clinically and therapeutically important.

Disclosure: R. S. Katz, None; J. L. Polyak, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/depression-versus-frustration

Abstract Number: 163

Fibromyalgia Patients Identify More Causes of Disease Flare Ups Than RA Patients

Robert S. Katz1, Lauren Kwan2 and Jessica L. Polyak2, 1Rush University Medical Center, Chicago, IL, 2Rheumatology Associates S.C., Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: We compared patients with the Fibromyalgia Syndrome (FMS) and Rheumatoid Arthritis (RA) patients with respect to stresses that the patients believe may have caused their diseases to flare.

Methods: 201 office patients with FMS or RA (150 FMS:130 women and 20 men; mean age 51±12, 61 RA:45 women and 16 men; mean age 55±15) completed a questionnaire as to whether the following conditions caused their disease to flare: lack of sleep, fatigue, emotional stress, physical stress, depression, anxiety, traumatic events, overdoing it, being overworked, feeling overwhelmed, illness, personal changes, and confrontations with friends or family members. The chi-square test of association was done to compare FMS and RA patients with respect to their responses, using a 0.05 significance level.

Results: FMS patients were significantly more likely than RA patients to report that stress caused their disease to flare including, with regard to frequency, emotional stress (58% vs. 43%, p= 0.042), physical stress (54% vs. 34%, p= 0.010), and also lack of sleep (53% vs. 33%, p= 0.007), concomitant illness (39% vs. 12%, p < 0.001), anxiety (31% vs. 16%, p= 0.027), depression (25% vs. 10%, p = 0.012), and traumatic events (25% vs. 12%, p = 0.026).

Conclusion: FMS patients were significantly more likely to be sensitive to a variety of factors compared with RA patients. Fibromyalgia patients recognize many things that tend to aggravate their symptoms. Stress reduction strategies might help fibromyalgia patients.

Disclosure: R. S. Katz, None; L. Kwan, None; J. L. Polyak, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/fibromyalgia-patients-identify-more-causes-of-disease-flare-ups-than-ra-patients-3
Association of Natural Killer Cell Ligand Polymorphism, HLA-C Asn80Lys, with the Development of Anti-SSA/Ro Associated Congenital Heart Block

Hannah C. Ainsworth1, Miranda C Marion1, Antonio Brucato2, Nathalie Costedoat-Chalumeau3, Tiziana Bertero4, Rolando Cimaz5, Micaela Fredi6, Patrick M. Gaffney7, Jennifer A. Kelly7, Kateri Levesque8, Alice Maltret8, Nathalie Morel6, Véronique Ramoni9, Amelia Ruffatti10, Carl D Langelfield11, Jill P. Buyon11 and Robert M Clancy11, 1Wake Forest University, Winston Salem, NC, 2Ospedale Papa Giovanni XXIII, Bergamo, Italy, 3Service de médecine interne Pôle médecine, Hôpital Cochin, Centre de référence maladies auto-immunes et systémiques rares de l’île de France, Paris, France, 4Ospedale Mauriziano, Torino, Italy, 5Department of Paediatrics, University of Florence and Anna Meyer Children's Hospital, Florence, Italy, Florence, Italy, 6Department of Rheumatology and Clinical Immunology, Rheumatology and Clinical Immunology, Spedali Civili of Brescia, Brescia, Italy, 7Oklahoma Medical Research Foundation, Oklahoma City, OK, 8Université Paris Descartes-Sorbonne Paris Cité, Paris, France, 9Ospedale Papa Giovanni XXIII of Bergamo, Policlinico San Matteo of Pavia, Bergamo, Pavia, Italy, 10Unità di Reumatologia, Dipartimento di Medicina-DIMED, Università di Padova., Padova, Italy, 11NYU Langone Medical Center, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Genetics, Genomics and Proteomics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Fetal exposure to maternal anti-SSA/Ro antibodies is necessary but insufficient for the development of congenital heart block (CHB), suggesting the potential of a fetal genetic predisposition. Prior studies identified an association of HLA and CHB risk providing a possible avenue into pathogenesis involving an interactive genetic effect between 6p21 and 19q13 wherein HLA-C acts as a ligand for the checkpoint receptor killer cell immunoglobulin-like receptors (KIR). A dimorphism at position 80 in HLA-C creates two epitope subgroups, defined by their KIR interactions: C1 (Asn80) and C2 (Lys80). We tested whether C2, which binds with high affinity to an inhibitory KIR rendering an NK cell incapable of restricting inflammation, contributes to CHB.

Methods:
192 pedigrees from the US, Italy, and France (194 CHB, 91 unaffected siblings, 152 fathers, 167 mothers) and 1073 out-of-study controls were genotyped on the Immunochip single nucleotide polymorphism (SNP) microarray. There were 79 discordant CHB sibling pairs. HLA-C Asn80Lys and KIR imputation was completed. Tests for association used logistic regression, and matched analyses between affected and unaffected children employed McNemar’s test.

Results:
The C1 allele was enriched (and C2 allele reduced) in mothers compared to female controls (P=0.0014; OR=0.63). In contrast, C2 was increased in fathers compared to male controls (P=0.0123; OR=1.40). This gender-by-C2 interaction was statistically significant (P=0.0002). CHB offspring had comparable C2 frequencies to the fathers (affected offspring frequency=0.42; fathers frequency=0.45) while unaffected C2 offspring frequencies were comparable to the mothers (unaffected frequency=0.31; mothers frequency=0.29). Formal assessment of C2 differences within a pedigree showed a significant increase in the C2 allele in affected vs. unaffecteds (P=0.0027; OR=4.00). Results were comparable in the CHB discordant sibling pairs in which mothers were homozygous for C1 (n=46 pairs, P=0.07; OR=2.75). When the paired-sibling analysis was stratified by geographic region the results remained significant in each stratum (U.S. P=0.0325; OR=3.67; Europe P=0.0348; OR=4.50). There was no difference in the inhibitory KIR genotype (AA KIRs) between affected and unaffected children (P=0.55).

Conclusion:
The HLA-C–encoded supertypic epitope C2 was significantly enriched in CHB vs. unaffected offspring, establishing C2 as a novel genetic risk factor associated with disease. This observation supports a model in which anti-SSA/Ro exposed fetuses expressing C2 ligands may have impaired NK surveillance resulting in unchecked cardiac inflammation and scarring.

Disclosure: H. C. Ainsworth, None; M. C. Marion, None; A. Brucato, None; N. Costedoat-Chalumeau, None; T. Bertero, None; R. Cimaz, None; M. Fredi, None; P. M. Gaffney, None; J. A. Kelly, None; K. Levesque, None; A. Maltret, None; N. Morel, None; V. Ramoni, None; A. Ruffatti, None; C. D. Langelfield, None; J. P. Buyon, None; R. M. Clancy, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/association-of-natural-killer-cell-ligand-polymorphism-
**Rheumatoid Arthritis Risk Polymorphisms in CCR6, SNP and Estrogen-Dependent Response to Immune Mediator Gene Expression, and NF-κB Transcriptional Activity: Crosstalk between the Immune and Endocrine Systems**

Ming-Fen Ho\(^1\), Tim Bongartz\(^2\), James N. Ingle\(^3\), Liewei Wang\(^1\) and Richard M. Weinshilboum\(^1\), \(^1\)Department of Molecular Pharmacology and Experimental Therapeutics, Mayo Clinic, Rochester, MN, \(^2\)Emergency Medicine, Vanderbilt University, Nashville, TN, \(^3\)Department of Medical Oncology, Mayo Clinic, Rochester, MN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Genetics, Genomics and Proteomics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
The rheumatoid arthritis (RA) risk locus CCR6 rs3093024 SNP is associated with increased risk of RA in a sex-specific pattern in Asian populations. Specifically, the variant allele was associated with increased RA disease risk in ACPA-positive women. This SNP is in tight linkage disequilibrium with rs3093023, which has been associated with both RA risk and increased serum IL17 levels. We previously reported that these two SNPs altered estrogen receptor binding to estrogen response elements and resulted in the induction of CCR6 by estradiol (E2) in a SNP-dependent fashion. Specifically, CCR6 expression could be induced by E2 only in cells carrying the variant genotype. Strikingly, IL17A and IL17RA responded in a parallel fashion. The present study was designed to study mechanisms underlying the CCR6 SNP effect on the estrogen-dependent regulation of immune mediators in relation to the pathogenesis of RA—a disease for which 2/3 of patients are women.

Methods:
“Human Variation Panel” lymphoblastoid cell lines (LCLs) consisting of LCLs from 300 subjects were used to obtain genome-wide mRNA expression and genome-wide SNP data, and to perform functional genomic studies including site-directed mutagenesis, luciferase reporter assays, qPCR, NF-κB reporter assays and co-immunoprecipitation.

Results:
A reporter construct with variant genotypes for the CCR6 SNPs increased luciferase activity in response to E2 treatment as compared to wild-type (p<0.001), providing direct evidence for the functional role of these SNPs in the regulation of CCR6 transcription. Use of the LCL model system allowed us to determine global mRNA expression profiling for functional study. We then performed pathway analysis using genes correlated with CCR6 expression with p≤1E-08 and found that those genes were enriched in immunological regulation pathways. Next, we validated genes significantly correlated with CCR6 expression, with a focus on immunological genes, including cytokines, chemokines and toll-like receptors, all of which have been implicated in the pathogenesis of RA. CCR6 knock down using LCLs with known CCR6 SNP genotypes resulted in significant changes (p<0.05) in the expression of CCL20, IL7R, IL7, IL17RA, IL17A, IL6R, IL6, TLR2, TLR4 and NF-κB p65. Additionally, significant induction for IL17RA, TLR2, TLR4 and NF-κB p65 in response to E2 treatment was observed only in variant genotype cells (p<0.05). In parallel, NF-κB transcriptional activity responded in a CCR6 SNP and E2-dependent fashion. Finally, CCR6 could physically interact with NF-κB p65 as determined by co-immunoprecipitation. These results suggest that NF-κB signaling might be associated with CCR6 SNP and estrogen-dependent effects.

Conclusion:
CCR6 SNPs are functionally relevant to the pathogenesis of RA. CCR6 is estrogen inducible in a SNP-dependent fashion, resulting in downstream effects modulating the expression of proinflammatory cytokines and NF-κB transcriptional activity. Our results provide a mechanistic explanation for the results of previous genome-wide association studies that have linked these SNPs in the CCR6 gene to RA risk and the differential effects of these SNPs on E2 treatment.

Disclosure: M. F. Ho, None; T. Bongartz, None; J. N. Ingle, None; L. Wang, None; R. M. Weinshilboum, None.

Integrative Systems Biology Approach Identifies Key Transcription Factors and Novel Rheumatoid Arthritis (RA) and Individualized Therapeutic Targets

Richard Ainsworth¹, Kai Zhang², Gary S. Firestein³ and Wei Wang⁴, ¹UC San Diego, La Jolla, CA, ²UCSD School of Engineering, San Diego, CA, ³Medicine, University of California San Diego, La Jolla, CA, ⁴Chemistry and Biochemistry, UC San Diego, La Jolla, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Genetics, Genomics and Proteomics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The search for novel targets in RA requires novel computational methods and in silico systems to identify non-obvious pathways that account for the diversity of responses to targeted agents. We developed and applied a novel integrative systems biology method that identifies transcription factors (TFs) central to regulatory patterns in RA fibroblast-like synoviocytes (FLS) and significant variations in gene networks between RA patients.

Methods: Our whole genome ATAC-seq and RNA-seq data (from 11 RA and 11 osteoarthritis [OA] FLS lines) were evaluated for overlaps between ATAC-seq peaks and known gene promoter regions (4kb upstream and 1kb downstream from the TSS). ATAC-seq peaks not assigned to promoters were considered as enhancer regions and linked with the nearest gene. TF binding motifs were curated from the CIS-BP database. 745 TFs had binding sites within 150-bp regions in ATAC-seq peak summits. 22 unique network topologies were constructed by forming directed edges between any parent node TF and child node gene or child node TF. Via the integration of RNA-seq expression data for each sample, the Personalized PageRank (PPR) algorithm was developed and run measure the global influence of each node and variance between RA patients.

Results: Initial analysis focused on differences between RA and OA. The mean PPR was calculated for TFs from RA and OA samples and were ranked based on the largest absolute difference between RA and OA (DPPR). Of these, 33 TFs were significantly different for RA vs. OA (p < 0.05). For example, the glucocorticoid receptor NR3C1 was the highest rank DPPR (p value = 0.03). BACH1, which regulates osteoclastogenesis, was the second highest rank DPPR (p = 0.0005). Other high DPPR genes included STAT1, YY1 (JAK-STAT signaling) and SP1. We then looked within RA for inter-RA patient differences to understand individual network profiles. The intersection of the 33 significant RA vs OA TFs with TFs that have the highest variance of normalized PPR within the RA networks, yielded 15 hits. MGA (MAX gene-associated protein), which regulates the expression of MYC-MAX and T-box family target genes, had the highest intra-RA variance with a high rank DPPR (p = 0.024) suggesting that this TF defines differences in RA pathogenesis between patients. Another high intra-RA variance gene within the intersection includes TBX2, which participates in mesenchymal cell differentiation. A smaller subset of RA patients (~30%) have high PPR values for ID1. ID family genes play a role in cell proliferation and angiogenesis in RA.

Conclusion: This systems biology approach not only defines disease specific TFs that contribute to the RA phenotype but also distinguishes patient-to-patient differences. The unique computational approach identifies novel targets and helps elucidate the mechanism of differential responses to highly targeted agents in RA. Key transcription factors, including well known genes such as NR3C1 and STAT1, along with novel patient-specific TFs targets like MGA emerge from this in silico method to individualize treatment.

Disclosure: R. Ainsworth, None; K. Zhang, None; G. S. Firestein, None; W. Wang, None.


Differentially Co-Expressed Gene Networks in Previously DMARD-Naïve Patients with Early RA Achieving Sustained Drug-Free Remission after Step-up Methotrexate Therapy

Xavier M Teitsma¹, Johannes WG Jacobs¹, Michal Mokry², Attila Pethö-Schramm³, Michelle EA Borm⁴, Jacob M. van Laar⁵, Johannes
SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Genetics, Genomics and Proteomics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: According to current standards, methotrexate (MTX) is an anchor drug in the treatment of rheumatoid arthritis (RA) and should be used in the initial line of treatment in newly diagnosed patients. Some of these patients do not need additional therapy to reduce disease activity and even achieve sustained drug-free remission (sDFR) after tapering and stopping MTX. To identify these patients, we performed network analyses within differentially expressed genes (DEGs) and identified clusters (i.e. modules) of co-expressed genes associated with achieving sDFR.

Methods: Data was used from DMARD-naïve patients with early RA who in the U-Act-Early trial were randomized to initiate treat-to-target MTX therapy. MTX was given at a starting dose of 10 mg/week orally and was increased with 5 mg every 4 weeks until 30 mg or the maximum tolerable dose. When the treatment target, sustained remission (defined as disease activity score assessing 28 joints (DAS28) <2.6 with ≤4 swollen joints for ≥24 weeks), was achieved, therapy was tapered and hereafter stopped if remission was maintained. Patients achieved sDFR if they remained ≥3 months in remission while being drug-free. Blood samples were collected of those achieving sDFR (n=13) and those not able to discontinue medication (n=11) as controls. Hereafter ‘cluster of differentiation 4’-positive (CD4+) T Helper cells and CD14+ monocytes were isolated and analyzed using RNA sequencing. DEGs were identified and weighted gene co-expression network analysis was used to identify clusters (i.e. modules) of co-expressed genes.

Results: Nine modules were identified in CD4+ cells and the module best correlated with achieving sDFR (Pearson correlation coefficient 0.60, p=0.012) included 49 co-expressed genes. Within this module, when performing pathway analyses in the Gene Ontology (GO) database, 304 terms were significantly overrepresented. Of these, response to bacterium (p=1.92E-07), response to external biotic stimulus (p=6.11E-07), and response to other organism (p=6.11E-07) were the most significant. In addition, two significant enriched pathways were found in the Kyoto Encyclopedia of Genes and Genomics database: “p53 signaling pathway” (p=8.44E-06) and “Jak-STAT signaling pathway” (p=2.22E-04). The down-regulated SESN3 and ZNF585B and the upregulated CPXM1 genes showed the highest intramodular connectivity and are therefore considered as signature genes (Fig. 1). Network analyses in CD14+ cells yielded no significant modules.

Conclusion: By network analyses of differentially expressed genes, several pathways were identified important for achieving sDFR in DMARD-naïve with early RA after initiation of an MTX-based strategy. SESN3, ZNF585B and CPXM1 were identified as signature genes that might be used as biomarkers for RA outcome.

Disclosure: X. M. Teitsma, None; J. W. Jacobs, None; M. Mokry, None; A. Pethö-Schramm, F Hoffmann-La Roche, 3; M. E. Borm, Roche Nederland BV, 3; J. M. van Laar, MSD, Pfizer, Eli Lilly, and BMS, 5; J. W. J. Bijlsma, Roche, AbbVie, Bristol-Myers Squibb,
Identification of Novel Susceptibility Loci in a Large UK Cohort of Juvenile Idiopathic Arthritis (JIA) Cases

Samantha Smith1, John Bowes1, Joanna Cobb2, Anne Hinks1, Sunil Sampath1, Annie Yarwood1, Lucy R Wedderburn2, Kimme L. Hyrich4 and Wendy Thomson1, 1Arthritis Research UK Centre for Genetics and Genomics, Centre for Musculoskeletal Research, Manchester Academic Health Sciences Centre, The University of Manchester, Manchester, United Kingdom, 2NIHR Manchester Musculoskeletal Biomedical Research Unit, Manchester Academic Health Science Centre, Central Manchester Foundation Trust, Manchester, United Kingdom, 3Arthritis Research UK Centre for Adolescent Rheumatology, UCL GOS Institute of Child Health, University College London, London, United Kingdom, 4Arthritis Research UK, Centre for Epidemiology, Centre for Musculoskeletal Research, Manchester Academic Health Sciences Centre, The University of Manchester, Manchester, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Genetics, Genomics and Proteomics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Juvenile idiopathic arthritis (JIA) is a group of chronic arthropathies of unknown cause affecting children under 16yrs, and is the most common childhood inflammatory rheumatic diagnosis, affecting 1 in 1,000 UK children. In recent years great advances in dissecting the genetic basis of JIA have been made. In one landmark study, conducted on the two most common subtypes (oligoarthritis and RF-negative polyarthritis), 17 susceptibility loci were identified at genome-wide significance (p-value<5x10^{-08}) with a further 11 reaching suggestive significance (p-value<1x10^{-06}). These findings were the results of a large international collaboration using the ImmunoChip array, which targets 186 known loci in 12 autoimmune diseases. However, one limitation to the afore-mentioned study was that the analysis was limited to the selected loci; large genome-wide studies are now needed. The aim of this work is to identify novel genetic loci associated with disease susceptibility using a large cohort of UK JIA cases.

Methods:

Whole-genome genotyping data was generated using four platforms (Illumina). Following stringent quality control common variants to all four platforms were extracted from the individual datasets before merging together. Imputation was performed using the Haplotype Reference Consortium panel on the Michigan Imputation Server using Minimac3 software. SNPs with imputation accuracy (r^2>0.5), minor allele frequency>1% and Hardy-Weinberg p-value>1x10^{-03} were retained for analysis. Association was conducted using logistic regression; using the top three principal components as covariates. Bioinformatics analysis was performed using in-house Capture Hi-C data, to study long-range interactions, to elucidate the potential function of the associated SNPs.

Results:

Post-QC, 2,585 cases and 5,181 controls were available for analysis with ~7.4 million SNPs. Analysis conducted within oligoarthritis and RF-negative polyarthritis cases, (n=1,617) confirmed 13 previously identified JIA risk loci and identified more than 20 potentially novel regions above suggestive significance (2.25 x 10^{-05}). Of these, rs7874896, an intergenic SNP located between TNFSF15 and TNFSF8 on chromosome 9 was one of the most strongly associated (p-value 3.67x10^{-07}). TNFSF15 in particular is interesting, as it has been found that TNFSF15 drives expression of pro-inflammatory cytokines (IFNγ) and TNFα from CD4+CD161+ T-cells, yet these cells were found to be resistant treatment with an anti-TNF; suggesting that blockade of TNFSF15 may possess therapeutic benefit in JIA. Further investigation of associated SNPs using Capture Hi-C data has yielded potentially interesting interactions within T- and B-cell lines.

Conclusion:

This study represents the largest GWAS conducted in JIA to date and our preliminary results have identified novel associations with the most common subtypes of the disease and may have highlighted a potentially novel therapeutic target.
New Autoinflammatory Phenotype Associated with Homozygous AGBL3 Variant

Ahmet Gül, Neslihan Abaci and Sema Sirma Ekmekci, 1Department of Internal Medicine, Division of Rheumatology, Istanbul University, Istanbul Faculty of Medicine, Istanbul, Turkey, 2Department of Genetics, Istanbul University Institute for Experimental Medical Research, Istanbul, Turkey

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Genetics, Genomics and Proteomics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: To identify new genes/pathways associated with autoinflammatory phenotype.

Methods: We screened genomic variations by whole exome sequencing in 3 families presented with autoinflammatory gene mutations. A systematic search was carried out specifically for identification of deleterious genetic variants in genes involved in novel inflammatory pathways.

Results: We identified a deleterious mutation in the AGBL3 (ATP/GTP binding protein-like 3) gene, in a consanguineous family of Assyrian origin. Index case, now 22-year-old male, presented to our outpatient clinic with recurrent attacks of fever, urticarial rash on the extremities and trunk, conjunctival injections and arthralgia. His attacks started when he was 13, and two to three day lasting attacks recurred more frequently during warm weather conditions or following hot baths. He had highly elevated CRP and ESR during attacks, but his acute phase response did not return to normal values in between the flares. Low C3 and C4 values were also observed during asymptomatic periods. He responded partially to corticosteroids as well as canakinumab and anakinra treatments, and he is currently on low dose steroids and 200 mg/day anakinra. Whole exome sequencing revealed homozygous c.769C>T mutation in AGBL3 gene, which results in early termination of the protein (p.Gln257Ter) and deletion of carboxypeptidase domain. This protein belongs to metallocarboxypeptidases that mediate both deglutamylation and deaspartylation of target proteins. AGBL3 is suggested to catalyze the deglutamylation of polyglutamate side chains, especially in proteins such as tubulins. Also, STRING search revealed interaction of AGBL3 with complement regulatory proteins, such as CD46, CD55, and CD59, which are potent inhibitors of the complement membrane attack complex.

We searched databases from Turkey and other sources, and we could not identify this variant in other individuals.

Conclusion: This study identifies the AGBL3 metallocarboxypeptidase gene as a potential autoinflammatory gene involved in a novel pathway, and its loss of function mutations may result in a potent innate inflammatory response associated with lower complement levels and a partial response to IL-1 blockade.

Disclosure: A. Gül, None; N. Abaci, None; S. Sirma Ekmekci, None.
Finding Transcriptional Regulators Central to RA with Transcriptomics of IL17 Dose Response, Time Series, and siRNA Silencing in Stromal Cells

Kamil Slowikowski¹, Hung Nguyen², Gerald Watts², Fumitaka Mizoguchi³, Erika H. Noss⁴, Michael Brenner⁵ and Soumya Raychaudhuri⁶

¹Harvard University, Boston, MA, ²Brigham and Women's Hospital, Boston, MA, ³Department of Rheumatology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University (TMDU), Tokyo, Japan, ⁴Division of Rheumatology, University of Washington, Seattle, WA, ⁵Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ⁶Division of Medicine and

Abstract Number: 171
Background/Purpose: Rheumatoid arthritis (RA) is characterized by immune cell infiltration into the synovial membrane of the joint, where they engage stromal cells such as synovial fibroblasts in a persistent proinflammatory feedback loop. Tumor necrosis factor alpha (TNF) and interleukin 17 (IL17) are elevated in RA and activate synovial fibroblasts. Chronically activated fibroblasts proliferate, degrade joint cartilage, and recruit additional immune cells. We found that stimulation of fibroblasts with IL17 alone produced little response compared to TNF, but the combination of IL17 and TNF synergistically increased chemokine and cytokine gene expression. The purpose of this study is to define the transcriptional network controlling the synergistic response to IL17 and TNF.

Methods: We assessed transcriptional changes over time and IL17 doses. We did 175 Smart-seq2TM RNA-seq experiments on synovial fibroblast cell lines from knee joint tissues obtained from 4 RA and 3 osteoarthritis (OA) donors. For each donor, we did a time series with 8 time points over 24 hours and 3 IL17 doses (0, 1, and 10 ng/mL) in combination with TNF (1 ng/mL). We repeated a subset of these RNA-seq experiments after siRNA silencing of specific transcription factors, this time with fewer time points and independent cell lines.

Results: We identified 813 genes at 5% false discovery rate (FDR) and >1.5 fold change between RA and OA, including two homeobox genes HOXC10 and HOXD11. Statistical analysis with linear models revealed 34 genes at 5% FDR and >1.5 fold change that respond to IL17 in a dose dependent manner, 10 of which are also differently expressed between RA and OA. We identified motifs enriched in these 34 genes' promoters representing binding sites for known transcription factors (TFs) such as NFKB p65 (Rel A) and CEBP. We also found a novel transcription factor, CUX1. Two CUX1 target genes, CXCL2 and CXCL3, are highly dose-responsive to IL17 and these targets have CUX1 peaks in their promoters in ENCODE ChIP-seq data. Finally, exon level differential expression analysis revealed IL17 dose-dependent exon inclusion of 38 exons in 21 genes at 5% FDR, including an exon in Nfkbiz inhibitor zeta (NFKBIZ) for an ankyrin repeat that likely binds to NFKB. Analysis of siRNA silencing experiments is ongoing.

Conclusion: IL17 and TNF costimulation activates a different transcriptional network than TNF or IL17 alone. A specific set of genes responds to dose of IL17, and putative transcription factors controlling these genes include NFKB p65 (Rel A), CEBP, and CUX1.
Disclosure: K. Slowikowski, None; H. Nguyen, None; G. Watts, None; F. Mizoguchi, None; E. H. Noss, None; M. Brenner, None; S. Raychaudhuri, Pfizer Inc, 2, Roche Pharmaceuticals, 2.

Optimizing Precision Medicine By Using Genetics to Assign Diagnostic Prior Probabilities to Patients with Synovitis

Rachel Knevel1,2,3,4, Chikashi Terao5,6,7, Jing Cui1,8, Kamil Slowikowski2,9,10, TWJ Huizinga3, Elizabeth Karlson11 and Soumya Raychaudhuri1,2,12,13, 1 Division of Medicine and Rheumatology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, 2Medical and Population Genetics Program, Broad Institute of MIT and Harvard, Cambridge, MA, 3Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, 4Division of Genetics, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, 5Laboratory for Statistical Analysis, RIKEN Center for Integrative Medical Sciences, Yokohama, Japan, 6Clinical Research Center, Shizuoka General Hospital, Shizuoka, Japan, 7Department of Rheumatology and Clinical Immunology, Kyoto University Graduate School of Medicine, Kyoto, Japan, 8Division of Genetics, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, 9Division of Medicine and Rheumatology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, 10Division of Genetics, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, 11Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 12Department of Institute of Inflammation and Repair, University of Manchester, Manchester, United Kingdom, 13Division of Genetics, Brigham and Women's Hospital, Harvard Medical School, Boston, MA

First publication: September 18, 2017

Background/Purpose:
As the cost of genome-wide genotyping plummets, and biobanking efforts integrating medical records and genetics are rapidly expanding, many patients will have genotyping available in medical records prior to patient visits. The question emerges: how informative this data is in a rheumatology clinic.

This study tests the potential for genetics to assign prior probabilities for six synovitis phenotypes; ACPA positive rheumatoid arthritis, ACPA negative rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis, psoriatic arthritis and gout.

Methods:
Risk allele information was obtained from Immunobase and GWAS publications. The genetic probability (GP) for each phenotype was calculated using Bayesian theorem with the summation of the risk alleles times the risk effects of each genetic variant as the likelihood and the sex adjusted disease prevalence as the prior. The GPs were normalized so that the total of the six probabilities for each individual was one. If GPs are accurate we expect that the percent of individuals that have a disease tracks with GP.

I Benchmarking performance by simulation

We simulated a population of one million people with random genotypes using minor allele frequencies from the 1000 genome project. We randomly assigned phenotypic status based on the known genetic risk alleles, sex, and disease prevalence. We then scored all individuals with disease for posterior probabilities.

II Validation

We selected clinical cases on their ultimate diagnosis from BostonOs Partners BIOBANK, using a rule-based algorithm based on clinical notes, lab tests and medication prescriptions.

Results:

In the simulation data set we observed that GPs were concordant with the phenotypic status, demonstrating that our model works in a
We identified 297 out of the 15,000 patients in the BIOBANK that had one of the six diseases of interest. We used these individuals and assessed the performance of the GP.

We observed that there was a high positive correlation between the GP and the clinical case risk for the phenotypes ($r^2 = 0.95$). A high GP correctly corresponded with the clinical phenotypes: in all cases where the probability > 0.9, the patient indeed had that phenotype. More importantly, the GP could discard phenotypes: GPs < 0.1 correctly corresponded with a clinical disease risk of < 10%, whereby for all individuals 1-4 phenotypes could be effectively ruled out. We note however that the GP (mean 0.24) somewhat overestimated the clinical risk (mean 0.16).

**Conclusion:**

In a cohort of synovitis patients, genetic information can facilitate decision making in early disease by ruling out and pointing towards the most likely phenotype. Seeing the importance of an early diagnosis in patients presenting with synovitis, genetics can be considered as part of a patient's medical history and as such it can inform us about the most likely diagnosis, without having to wait for more symptoms to arise.

**Disclosure:**

R. Knevel, None; C. Terao, None; J. Cui, None; K. Slowikowski, None; T. Huizinga, Abbott Laboratories, Biotest AG, Bristol-Myers Squibb, Crescendo Bioscience, Novartis Pharmaceuticals Corporation, Pfizer Inc, Roche, sanofi-aventis, Schering-Plough, UCB, Eli Lilly, 5,METEOR Board, 6,EU & Dutch Arthritis Foundation, 2,Abbott Laboratories, Biotest AG, Bristol-Myers Squibb, Novartis Pharmaceuticals Corporation, Pfizer Inc, Roche, sanofi-aventis, Schering-Plough, 8,Abbott Laboratories, Roche, 9; E. Karlson, None; S. Raychaudhuri, Pfizer Inc, 2,Roche Pharmaceuticals, 2.


**Abstract Number:** 173

**Applying Urine Proteomics for Discovery of Lupus Nephritis Damage Biomarkers in a Pediatric Cohort**

Jessica Turnier1, Bruce Aronow2, Kenneth Greis3, Michael Bennett4, Wendy Haffey5, Sherry Thornton5, Gaurav Gulati6, Michael Wagner7, David Witte8, Prasad Devarajan9 and Hermine I. Brunner10, 1Pediatric Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 2Computational Medicine, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 3University of Cincinnati College of Medicine, Cincinnati, OH, 4Nephrology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 5Division of Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 6Division of Immunology, Allergy and Rheumatology, University of Cincinnati College of Medicine, Cincinnati, OH, 7Biomedical Informatics, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 8Pathology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 9Nephrology, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH, 10Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Genetics, Genomics and Proteomics Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Non-invasive biomarkers of lupus nephritis (LN) damage are needed to guide treatment decisions and determine risk for kidney failure. Urinary proteomics has advanced as a tool for novel biomarker discovery in recent years. Specifically, Isobaric Tags for Relative and Absolute Quantification (iTRAQ) is an advanced proteomics technique that quantifies and compares protein expression among samples by mass spectrometry in a single experiment. We aimed to use iTRAQ for discovery of candidate urine biomarkers (CUBMs) for LN
chronicity in a pediatric lupus cohort and then further pursued validation of CUBMs.

**Methods:** For the initial discovery cohort, urine was collected from children with LN (n=21) at the time of kidney biopsy. LN damage was characterized as per the NIH chronicity index (NIH CI, score range: 0-12) and categorized as none (0), low (1), moderate (2), or high (≥3). iTRAQ experiments compared protein composition in four urine samples from different LN damage categories, respectively. The relative expression of differentially excreted proteins was tested for significant differences using a log-rank test. We then generated heat maps and performed network analysis to identify proteins associated with LN damage, also considering concurrent histological LN activity (NIH activity index scores). Upon identification of CUBMs from the discovery cohort, specific commercial ELISAs were performed on urine samples from children with varying levels of LN chronicity in a separate validation cohort (n=41). Analysis of Variance was performed to detect statistical differences between each of the CUBMs and LN chronicity, with adjustment for clinical LN activity.

**Results:** Overall, iTRAQ detected 112 proteins from the urine sample sets of the discovery cohort, and 51 proteins were quantifiable in all replicate sample runs. Initial log-rank test revealed 4 differentially expressed proteins with p-values <0.05. Further evaluation by heat map and network analysis led to identification of 7 CUBMs for LN chronicity: Afamin (AFM), Immunoglobulin Heavy Constant Alpha 1 (IGHA1), Alpha-1-Antichymotrypsin (SerpinA3), Transthyretin (TTR), Retinol Binding Protein 4 (RBP4), Alpha-1-Acid Glycoprotein, Type 2 (ORM2) and Transferrin (TF). In the validation cohort, only SerpinA3 was found to be different based on degree of LN chronicity after adjustment for concurrent LN activity. SerpinA3 levels were found to increase with higher degrees of LN chronicity.

**Conclusion:** Using advanced proteomic techniques followed by confirmation using specific ELISAs, we identified SerpinA3 as a potential urine biomarker to help quantify the degree of tissue damage from LN. Elevated levels of SerpinA3, a known inhibitor of neutrophil cathepsin G and angiotensin II production, could serve as both a danger signal and protective mechanism from further kidney damage. Further validation of SerpinA3 as an LN damage biomarker in an independent cohort is needed to determine its ability to guide treatment and predict prognosis.

**Disclosure:** J. Turnier, None; B. Aronow, None; K. Greis, None; M. Bennett, None; W. Haffey, None; S. Thornton, None; G. Gulati, None; M. Wagner, None; D. Witte, None; P. Devarajan, NIDDK, 2; H. I. Brunner, NIDDK, 2.


**Abstract Number:** 174

**Transcriptional Profiling of Synovial Macrophages from RA Patients to Capture Disease Heterogeneity**

Philip J. Homan¹, Arthur M. Mandelin II², Salina Dominguez³, Emily Bacalao³, S. Louis Bridges Jr.⁴, Joan M. Bathon⁵, John Atkinson⁶, David Fox⁷, Eric L. Matteson⁸, Chris Buckley⁹, Costantino Pitizalis¹⁰, Deborah Parks¹¹, Laura Hughes¹², Laura Geraldino-Pardilla¹³, Robert Ike¹⁴, Kristine Phillips¹⁵, Kerry Wright¹⁶, Andrew Filer¹⁷, Stephen Kelly¹⁸, Eric M. Ruderman¹⁹, Carla Cuda¹, Hiam Abdala-Valencia¹, Alexander Misharin³, G. R. Scott Budinger³, Richard M. Pope¹⁹, Harris Perlman²⁰ and Deborah R. WInter¹, ¹Department of Medicine Division of Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL, ²Rheumatology, Northwestern University, Chicago, IL, ³Northwestern University, Chicago, IL, ⁴Clinical Immunology & Rheum, Univ of Alabama, Birmingham, AL, ⁵Division of Rheumatology, Columbia University Medical Center, New York, NY, ⁶Washington University in St. Louis, St. Louis, MO, ⁷Department of Medicine [Division of Rheumatology], University of Michigan Medical System, Ann Arbor, MI, ⁸Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, MN, ⁹University of Birmingham, Birmingham, United Kingdom, ¹⁰Centre for Experimental Medicine and Rheumatology, William Harvey Research Institute, Barts and The London, School of Medicine and Dentistry, Queen Mary University of London, London, United Kingdom, ¹¹Washington University School of Medicine in St. Louis, St. Louis, MO, ¹²University Alabama Birmingham, Birmingham, AL, ¹³Columbia University, New York, NY, ¹⁴Division of Rheumatology, University of Michigan, Ann Arbor, MI, ¹⁵University of Michigan, Ann Arbor, MI, ¹⁶Rheumatology, Mayo Clinic, Rochester, MN, ¹⁷Institute of Inflammation and Ageing (IIA), University of Birmingham, Birmingham, United Kingdom, ¹⁸William Harvey Research Institute, London, United Kingdom, ¹⁹Medicine/Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL, ²⁰Department of Medicine, Division of Rheumatology, Northwestern University Feinberg School of Medicine, Northwestern University Feinberg School of Medicine., Chicago, IL

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Genetics, Genomics and Proteomics Poster I

**Session Type:** ACR Poster Session A
Background/Purpose: In a given patient with rheumatoid arthritis (RA), it is difficult to predict disease progression or identify to which treatments they will respond. Macrophages have been strongly implicated in the pathogenesis of RA and reduction in the number of macrophages in the synovial sublining of the joint is a key biomarker for better outcomes. However, without a deeper knowledge of the genes regulated in vivo, such as provided by unbiased high-throughput sequencing, it is difficult to discern the function of these macrophages in RA. Here, we describe our work to profile the genome-wide transcriptome of synovial macrophages in RA patients. 

Methods: We used tissue obtained from synovial biopsies of the wrist joints in RA patients for histology and cell sorting via FACS. We gated for CD45+Lin−CD64+CD11b+CD14+HLA-DR+ macrophages and distinguished 2 populations based on the expression of CD206. As a comparison, we also collected and sorted macrophages from OA patients via surgical discards. We processed all macrophage populations for RNA-seq and sequenced the libraries on an Illumina NextSeq 500 to an average depth of 5 million reads. The reads were aligned and mapped to genes using bowtie and HTseq, respectively, followed by bioinformatic analysis as described below. 

Results: The quality of the RNA-seq data from RA macrophages was comparable to OA, confirming the feasibility of our approach. Next, we assessed the ability of our macrophage-specific RNA-seq to identify differentially expressed genes between RA and OA by fold-change, as compared with RNA-seq of the unprocessed whole synovial tissue. While the approaches generally agreed, we found many genes that were differentially expressed only in macrophages, supporting the value of cell-specific RNA-seq to uncover gene pathways that would be obscured in whole tissue RNA-seq. Next, we considered the heterogeneity of macrophages across RA patients by calculating the pairwise correlation between samples. We found that there were significant differences between RA transcriptional profiles that were best explained by classification of patients into lymphoid, myeloid, or pauci-immune phenotypes based on the dominant cell type. In order to overcome this difficulty in identifying genes associated with RA pathology, we focused on clustering genes into co-regulated modules based on their expression across samples. This allowed us to identify pathways with significant expression patterns, even if the relevant genes were up-regulated in only a portion of RA samples. For example, we found that a subset of RA patients demonstrated over-expression of certain cytokine-mediated pathways (including IL3, IL5, and IL13), while another subset was enriched for type 1 interferon signaling. Similarly, we found that Dock2, a gene involved in actin remodeling that was not significant at the whole-tissue level, was preferentially expressed in RA macrophages that also expressed Ccr1.

Conclusion: Together, these results help us to understand the role of different macrophage populations in RA heterogeneity. Our goal is to use these studies as the basis for predicting clinical outcomes and choosing between therapeutic options for treatment.

Disclosure: P. J. Homan, None; A. M. Mandelin II, None; S. Domínguez, None; E. Bacalao, None; S. L. Bridges Jr., None; J. M. Bathon, Regeneron, 5; J. Atkinson, None; D. Fox, None; E. L. Matteson, None; C. Buckley, None; C. Pitzalis, None; D. Parks, None; L. Hughes, None; L. Geraldino-Pardilla, None; R. Ike, None; K. Phillips, None; K. Wright, None; A. Filer, None; S. Kelly, None; E. M. Ruderman, AbbVie, Amgen, BMS, GSK, Janssen, Eli Lilly and Company, Novartis, Pfizer, Roche/Genentech, 5; C. Cuda, None; H. Abdala-Valencia, None; A. Misharin, None; G. R. S. Budinger, None; R. M. Pope, None; H. Perlman, None; D. R. Winter, None.

Abstract Number: 175

Precisely Controlled Differential Gene Expression System to Investigate the Effect of eQTL

Xiaoming Lu, PhD1,2, Xiaoting Chen1, Carny Forney1, Connor Schroeder1, John B. Harley1, Matthew Weirauch3 and Leah C. Kottyan4, 1Center for Autoimmune Genomics and Etiology (CAGE), Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 2Immunobiology Graduate Program, University of Cincinnati College of Medicine, Cincinnati, OH, 3Center for Autoimmune Genomics and Etiology (CAGE) and Divisions of Biomedical Informatics and Developmental Biology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 4Center for Autoimmune Genomics and Etiology (CAGE), Division of Allergy and Immunology, Cincinnati Children's Hospital, Cincinnati, OH

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Genetics, Genomics and Proteomics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Genome-wide association studies and large-scale sequencing studies identify many non-coding genetic variants that...
increase disease risk. At least 60% of these loci have been associated with genotype-dependent expression of nearby genes. It remains to be determined that 50-100% expression differences are biologically relevant in specific immune cell types. We focus on the expression quantitative trait loci (eQTL) at the ETS1 lupus-risk locus. Patients with lupus have 50% less peripheral blood mononuclear cell mRNA expression of ETS1 than people without SLE, and people with the risk haplotype at the ETS1 locus have 50% less mRNA expression than people with the non-risk haplotype. Since ETS1 is a transcription factor, differential ETS1 expression could have easily measurable consequences on transcription factor binding and downstream gene expression. There are nearly 800 genes that are known to be dysregulated in subjects with SLE.

**Methods:** We developed a system combining the Clustered regularly interspaced short palindromic repeats (CRISPR) Homology-directed Repair technique with Tet-inducible Controlled Gene Expression technique to precisely control gene expression. This system allows us to mimic the differential gene expressions caused by genetic variants.

**Results:** Our analyses of these genes using publically available ChIP-seq data sets from B cell line GM12878 and epithelial cell line K562 indicates that 191 and 151 of these genes, respectively, have ETS1 binding sites proximal to the transcription start site (enrichment of 3-4 fold compared to randomly chosen gene sets, p<10^-46). We hypothesize that these changes in ETS1 levels are important in 1) ETS1 binding throughout the genome, 2) expression of ETS1 downstream target genes (such as BLIMP1), and 3) immunological dysfunction and hyperactivity of B cells. We test these hypotheses by analyzing the binding of ETS1 (ChIP-seq) and the changes to the transcriptome of cells with 2-fold differences in ETS1 expression (RNA-seq). Our CRISPR system successfully mimics the differential gene expressions.

**Conclusion:** The investigation of the ETS1 eQTL will allows us to make important progress in the field of human genetics and especially complex genetic disease etiology.

**Disclosure:** X. Lu, PhD, None; X. Chen, None; C. Forney, None; C. Schroeder, None; J. B. Harley, NowDiagnostics, 1; M. Weirauch, None; L. C. Kottyan, None.

---

**SEC16A and Antigen Presentation Abnormalities in the Pathogenesis of Axial Spondyloarthritis**

Fanxing Zeng1, Vidya Ranganathan2, Proton Rahman3, Darren O’Rielly4 and Nigil Haroon5, 1University Health Network, Toronto, ON, Canada, 2University of Toronto, Toronto, ON, Canada, 3Rheumatology, St Claires Mercy Hospital, St Johns, NF, Canada, 4Memorial University, St John's, NF, Canada, 5Rheumatology, Toronto Western Hospital, University of Toronto, Spondylitis Clinic, Toronto, ON, Canada

**First publication:** September 18, 2017

**SESSION INFORMATION**

Session Date: Sunday, November 5, 2017  
Session Title: Genetics, Genomics and Proteomics Poster I  
Session Type: ACR Poster Session A  
Session Time: 9:00AM-11:00AM

**Background/Purpose:** Axial Spondyloarthritis (AxSpA) is a chronic inflammatory rheumatic disease of axial skeleton. Our group recently identified a novel rare mutation of the SEC16A gene that strongly tracked with AxSpA in a multiplex family. Remarkably, all individuals with HLA-B27 and the SEC16A mutation had or went on to develop AxSpA. Sec16a is an important player in the ER-Golgi transport pathway with potential effects on antigen presentation and the pathogenesis of AxSpA. We have previously shown that the SEC16A mutation hinders the assembly of COPII vesicles budding from the ER that leads to abnormal MHC I trafficking and ER stress. In this study we explore the functional impact of Sec16A abnormalities on CD8+ T cell immune response. In addition, protein-protein interaction assays followed by pathway analysis help us understand the impact of SEC16A mutation on different cellular processes.

**Methods:** AxSpA patients from the multiplex family (N=9) had both SEC16A mutation and HLA-B27. Controls (N=5) were family members with no disease and had HLA-B27 and wild-type (WT) SEC16A. B cell lines were generated from patients and controls by EBV transformation. For validation, SEC16A was silenced in B-lymphoblastoid cells with stable HLA-B27 expression (CIR-B27) and assays repeated. Total protein was extracted from B cells and the formation of HLA free heavy chain homodimer (FHC) was studied using HC-10 western blot under non-

---

reducing and reducing conditions. HLA-B27 mediated immune response was assessed by cytotoxic T-lymphocyte assay. NP383-391 specific CTL clones were generated from HLA-B27 positive donor. The GFP-ubiquitin-NP383-391 construct was introduced by DNA transfection in B cells. Two days after transfection, B cells were incubated with NP383-391 specific CTL at a ratio of 1:10 for 4 hours. CTL activity was evaluated using caspase 3 cleavage in target cells. Pathway analysis assessed by protein-protein interaction was carried out to investigate the interactome of SEC16A variants.

Results:

Both SEC16A mutation in patients’ B cells and Sec16a deficiency (90% suppression) in C1R-B27 significantly (P<0.01 and P<0.001 respectively) increased the level of HLA-B27 FHC homodimers. This is likely due to a general disruption of MHC I trafficking by Sec16A abnormalities as we previously reported. GFP-ubiquitin-NP383-391 constructs were stably expressed in EBV-B cells at a similar level without having an effect on HLA-B27 surface expression. However, the cytotoxicity of NP 383-391 specific T cells were significantly lower against EBV-B cells with mutant SEC16A compared to EBV-B cells with WT SEC16A (p<0.01). T cell cytotoxicity was almost completely abolished in SEC16A-suppressed C1R-B27 cells. Using protein-protein interaction and pathway analysis, we found that mutant Sec16a had lower affinity to interactors involved in ER-to-Golgi vesicle mediated transport, membrane budding, vesicle organization, and antigen processing/presentation.

Conclusion:

Sec16a abnormalities can affect HLA-B27 intracellular transport, dimerization, antigen presentation and cytotoxic T cell responses. These changes can potentially play a role in AS pathogenesis.

Disclosure: F. Zeng, None; V. Ranganathan, None; P. Rahman, Janssen Pharmaceutica Product, L.P., 8,Amgen, AbbVie, BMS, Celgene, Pfizer, Janssen, Wyeth, EliLiiy, Novartis, 8,Amgen, AbbVie, BMS, Celgene, Pfizer, Janssen, Wyeth, EliLiiy, Novartis, 5; D. O’Rielly, None; N. Haroon, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/sec16a-and-antigen-presentation-abnormalities-in-the-pathogenesis-of-axial-spondyloarthritis

Abstract Number: 177

Intronic Variants of the B-Cell Proliferator RASGRP3 Affect Its Expression, and Might Contribute to Lupus Risk

Bhupinder Singh1, Philip Borden2, Julio Molineros3, Celi Sun3, Loren Looger2 and Swapn Nath1, 1Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 2Howard Hughes Medical Institute, Ashburn, VA, 3Oklahoma Medical Research Foundation, Oklahoma City, OK

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Genetics, Genomics and Proteomics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic lupus erythematous (SLE) is an inflammatory autoimmune disease with complex genetic underpinnings. Variants from RASGRP3 (RAS Guanyl Releasing Protein 3) is one of the most consistently replicated SLE susceptibility genes. We recently reported that two intronic variants (rs13385731 and rs12612030) explained RASGRP3-SLE association in Asians [Sun et al. 2016, Nat Genet]. However, the “causal” functional variants and the genetic mechanism(s) by which associated variants contribute to disease are largely unknown. We hypothesized that these intronic variants affect epigenetic regulation and modulate RASGRP3 expression.

Methods: First, we used in-silico bioinformatics and epigenetic analyses to define the potential regulatory effects of the candidate variants on gene expression using data on several histone marks, DNase-1 hypersensitivity, and eQTLs across multiple tissues from ENCODE, ROADMAP and GTEx data bases. Luciferase reporter assays in HEK293 cells were used to measure the effects of risk and non-risk variants/haplotypes on gene expression. Next, we used a combination of DNA pulldown, Electrophoretic Mobility Shift Assay (EMSA), Super-shift, Western blot and Mass Spectrometry to identify DNA-bound proteins followed by quantitative chromatin immunoprecipitation-PCR (ChIP-qPCR) to assess the allele-specific binding of interacting proteins. To assess the effect of risk alleles/haplotypes on cis-regulatory elements we also performed ChIP-qPCR with H3K27Ac and P300. Finally, using EBV-transformed cell lines, RASGRP3 mRNA and protein expressions were compared between risk and non-risk alleles/haplotypes.

Results: Bioinformatics predicted that these variants are located in active chromatin and have the potential to be dual enhancers/promoters.
We also predicted allele-specific binding to PARP1 and IRF1 at rs13385731. We observed significant (p<0.005) difference in RASGRP3 transcript and protein levels with increased expression in rs13385731 risk genotype (TT). Luciferase assays demonstrated significant (p<0.005) allele-specific enhancer and promoter activities. DNA pulldown and EMSA suggested allele-specific binding protein ~100 kD, which was identified as PARP1 protein by Mass Spectrometry and later confirmed by super shift and Western blot. We also verified differential allele-specific binding of PARP1 and IRF1 against rs13385731 using ChiP-qPCR. Interestingly, while PARP1 binding affinity is higher with risk (TT) genotype, IRF1 binding shows strong binding affinity with non-risk (CC) genotype of rs13385731.

Conclusion: Our results showed that rs13385731 is an eQTL, and the risk (TT) genotype is associated with increased RASGRP3 expression. Furthermore, this variant showed significant allele-specific binding to H3K27Ac, P300, PARP1 and IRF1 proteins, which might alter expression of RASGRP3, contributing to SLE risk. The activity of this variant provides insight into the molecular mechanisms underlying its association with SLE.

Disclosure: B. Singh, None; P. Borden, None; J. Molineros, None; C. Sun, None; L. Looger, None; S. Nath, None.

Abstract Number: 178

Genome-Wide DNA Methylation Study in Lupus in an Admixed Mexican Population

Maria Teruel1, Patrick Coit2, Mikhail Dozmarov3, Mario Cardiel4, Ignacio Garcia-De La Torre5, Marco A Maradiaga-Ceceña Sr.6, José Francisco Mocetzezama7, María Teresa Tusié-Luna8, Marta Alarcón-Riquelme9,10 and Amr H Sawalha2, 1GENYO, Center for Genomics and Oncological Research Pfizer/University of Granada/Andalusian Regional Government, Granada, Spain, 2Division of Rheumatology, University of Michigan, Ann Arbor, MI, 3Department of Biostatistics, Virginia Commonwealth University, Richmond, VA, 4Centro de Investigación Clínica de Morelia SC, Morelia, Mexico, 5Inmunología & Rheumatology, Centro de Est. de Invest. Bas. y Clin., S.C., Guadalajara, JAL, Mexico, 6Hospital General de Culiácan, Culiácan, Mexico, 7Servicio de Reumatología, Hospital General de México, Ciudad de Mexico, Mexico, 8Medicina Genómica y Toxicología Ambiental, Universidad Nacional Autonoma de Mexico, Ciudad de Mexico, Mexico, 9Uppsala University, Uppsala, Sweden, 10Centro de Genomica e Investigación Oncológica, Pfizer-University of Granada-Junta de Andalucía, Granada, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Genetics, Genomics and Proteomics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Our knowledge about the pivotal role DNA methylation plays in the pathogenesis of SLE has significantly increased in the last few years. However, we still have a relatively poor idea about the role of this epigenetic mark in the development of SLE in admixed populations. In addition, we do not yet understand the role of DNA methylation in explaining the higher prevalence and severity of SLE in these populations. To achieve these goals, we have conducted a genome-wide DNA methylation case-control study on individuals with different degrees of Amerindian ancestry.

Methods: Whole blood DNA from 60 females SLE patients and 59 female healthy individuals from Mexico were included in the study. The Native American ancestry was estimated using STRUCTURE and a set of ancestry informative markers (AIMs), and data from 1000 Genomes populations and a set of individuals of Nahua population were used as reference panel. In order to minimize the effect of other minor ancestries, all individuals were selected to have less than 10% of Asian and African ancestries. DNA methylation data were generated using the Infinium MethylationEPIC BeadChip (Illumina). Differential methylation between groups was estimated by beta regression after adjusting for age, technical variables and estimated cell type composition. SLE patients were stratified according to clinical manifestations. Functional annotations were performed using DAVID/Panther.

Results: Differential DNA methylation pattern was observed among individuals with different degrees of native Amerindian ancestry. The probe cg03693186 located in DAPK1 gene had the most significant signal detected (p-value =3.0 E-19). In a case-control association analysis, an overall hypomethylation in lupus was observed, especially in genes involved in the type I interferon response and regulation such as IFIH1, IF44, IF44L, MX1 and NLRCS5, consistent with findings in other populations. When comparing DNA methylation changes associated with lupus nephritis, a significant enrichment in the canonical WNT/β-catenin signaling pathway (p-value adjusted= 1.1 E-7) was found among hypomethylated genes. Hypermethylated genes in lupus nephritis show a significant enrichment in Angiotensin II-stimulated signaling through G proteins and beta-arrestin (p-value adjusted= 0.0034).

**Conclusion:** Differential methylation of interferon-regulated genes is associated with SLE in an admixed Amerindian population from Mexico, consistent with the epigenetic interferon signature observed in other ethnicities. The Amerindian association found for DAPKI gene, a positive mediator of gamma-interferon induced programmed cell death, might provide clues to explain the higher SLE prevalence and severity observed in these populations. In addition, our results also identify other biological pathways associated with lupus nephritis that might help to clarify the high prevalence and severity of lupus nephritis in admixed populations.

**Disclosure:** M. Teruel, None; P. Coit, None; M. Dozmorov, None; M. Cardiel, None; I. Garcia-De La Torre, None; M. A. Maradiaga-Ceceña Sr., None; J. F. Moctezuma, None; M. T. Tusié-Luna, None; M. Alarcón-Riquelme, Genzyme/Sanofi Corporation, 2; A. H. Sawalha, None.

**Abstract Number:** 179

**Mass Spectrometry Imaging of Synovium: A Novel Approach to Classify the Rheumatoid and Psoriatic Arthritis Patients**

**Beatriz Rocha**¹,², Berta Cillero-Pastor³, Gert Eijkel³, Lennart R. Huizing³, Cristina Ruiz-Romero¹,⁴, Andrea Cuervo⁵,⁶, Ron M A Heeren³, Juan D. Cañete⁵,⁶ and Francisco J Blanco¹,⁶,¹Rheumatology Division, ProteoRed/ISCIII Proteomics Group, INIBIC - Hospital Universitario de A Coruña, A Coruña, Spain, A Coruña, Spain,²The Maastricht Multimodal Molecular Imaging Institute (M4I), Division of Imaging Mass Spectrometry, Maastricht University, The Netherlands, Masstricht, Netherlands,³The Maastricht Multimodal Molecular Imaging Institute (M4I), Division of Imaging Mass Spectrometry, Maastricht University, The Netherlands, Maastricht, Netherlands,⁴CIBER-BBN Instituto de Salud Carlos III, INIBIC-CHUAC, A Coruña, Spain, A Coruña, Spain, A Coruña, Spain,⁵Arthritis Unit, Rheumatology Department, Hospital Clinic, IDIBAPS, Barcelona, Spain, Barcelona, Spain,⁶RIER-RED de Inflamación y Enfermedades Reumáticas, INIBIC-CHUAC, A Coruña, Spain, A Coruña, Spain

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Genetics, Genomics and Proteomics Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Psoriatic arthritis (PsA) and Rheumatoid arthritis (RA) are immune-mediated chronic inflammatory diseases. Synovial membrane is the initial site of inflammation in PsA and RA joints. This tissue can be used for diagnostic purposes since pathophysiological events occurring in the synovial are more likely than dispersed serum factors to reflect the clinical status and outcome in patients. Even though both tissues are morphologically similar, we hypothesize that there are differences in the molecular signature of the PsA and RA synovial membranes that can be employed for an accurate diagnosis of both pathologies. The purpose of this study is to create a new method for arthritic patient classification based on the spatially resolved molecular profiles detected by mass spectrometry imaging (MSI).

**Methods:**

Synovial membrane slices obtained from 10 PsA and 10 RA patients were analyzed by matrix-assisted laser desorption/ionization fourier-transform ion cyclotron resonance mass spectrometry imaging (MALDI-FT-ICR-MSI) to characterize the specific profile and distribution of metabolites. Images of differentially expressed metabolites were generated with FlexImaging 4.1 software. Principal component analysis (PCA) and discriminant analysis (DA) were used to look for the metabolites with the highest differences between PsA and RA synovial membranes. Annotation of the detected metabolites was performed by matching accurate mass with METLIN and Human Metabolome Databases.

**Results:**

PsA and RA synovial membranes were discriminated based on their metabolic signature using discriminant analysis. Sugars including N-acetylgalactosamine 6-sulfate (m/z 282,0276), glucuronic acid 1-phosphate (m/z 273,0026), N-acetylaceuraminic acid (m/z 290,0876) and different small lipids were identified and localized. Fatty acids and lysophosphatidic acids (LPAs) showed a higher expression in PsA compared to RA (Figure 1). On the contrary, all sugars displayed a stronger intensity in RA synovial tissues when compared to PsA. N-acetylaceuraminic acid showed a higher abundance in the synovial sublining layer whereas glucuronic acid 1-phosphate was specifically localized in the lining layer (Figure 2).
Conclusion:
We have localized and identified for the first time metabolites from human PSA and RA synovial membranes using MALDI-FT-ICR-MSI. Our results provide a fast and reliable classification of patients affected by PsA and RA.

Figure 1. Spatial distribution of small lipids in synovial tissues after MALDI-FT-ICR-MSI measurements. MALDI-MSI images of m/z 435,2516, m/z 419,2566, m/z 417,2402 and m/z 283,2636 identified as LPA(18:1) (A), LPA(18:0) (B), a different adduct of LPA(18:1) (C) and stearic acid (D), respectively.
Identification of a Functional Susceptible Variant in Distal Enhancer of Mir-146a By CRISPR-Cas9

Guojun Hou1, Jing Zeng2, Yuanjia Tang3 and Nan Shen4,5, 1Institute of Health Sciences, Shanghai Institutes for Biological Sciences (SIBS), Chinese Academy of Sciences (CAS) &Shanghai Jiao Tong University School of Medicine (SJTUSM), ShangHai, China, 2Shanghai Institute of Rheumatology, Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China, 3Shanghai Institute of Rheumatology, Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China, 4Shanghai Institute of Rheumatology, Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China, Shanghai, China, Shanghai, China, 5The Center for Autoimmune Genomics and Etiology (CAGE), Cincinnati Children’s Hospital Medical Center, Cincinnati, Ohio, United States of America, Cincinnati, OH

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Genetics, Genomics and Proteomics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM
**Background/Purpose:** The majority of trait-associated SNPs occur in noncoding regions and are enriched in enhancers. GWAS have identified numerous genetic variants associated with Systemic Lupus Erythematosus (SLE), but mechanistic insights remain limited, particular for noncoding polymorphisms. miR-146a is a negative regulator of the interferon pathway. In SLE patients, the expression of miR-146a is low and contributes to the abnormal activation of interferon pathway. rs2431697 is associated with the miR-146a expression level and located approximately 15.3 kb upstream of miR-146a exon 1, but how this risk variant regulates miR-146a expression and functionally contributes to the underlying pathogenesis is still unclear. Now, the application of CRISPR-Cas9 for genome engineering provides a new approach to study the function of disease susceptibility variants. This study was undertaken to investigate the role of rs2431697-containing region in the regulation of miR-146a expression by CRISPR-Cas9 technology.

**Methods:** To confirm whether rs2431697-containing region is a distal enhancer, we carried out ATAC-seq and formaldehyde-assisted isolation of regulatory elements (FAIRE) to test chromatin accessibility of this region. Chromatin immunoprecipitation (ChIP) followed by qRT–PCR (ChIP-qRT–PCR) was adopted to probe the enrichment of active enhancer makers H3K4me1 and H3K27ac. SAM system is a dCas9-based transcription activation system comprising of dCas9-VP64 and MS2–p65–HSF1 complex, which can transactivate target genes from distal enhancers. We also take this system to test the function of this region. To detect whether rs2431697-containing region is actually involved in the regulation of miR-146a expression, CRISPR-Cas9 technology was used to generate a 30 bp-deletion of the genomic region containing rs2431697 in U937 cells and miR-146a expression was analyzed by TaqMan microRNA assay. We also generated rs2431697 T allele and rs2431697 C allele containing cell clone in U937 cells by CRISPR-Cas9 induced homology-directed repair, and using bioinformatics to predict the SNP-specific binding transcription factor.

**Results:** ChIP-qRT–PCR analysis showed that rs2431697-containing region was enriched with H3K27ac and H3K4me1 modification. ATAC-Seq and FAIRE-qRT–PCR indicated that the region was open. Additionally, dCas9-vp64-SAM system could activate miR-146a expression based on the guide RNAs around this region. Importantly, the generation of 30 bp-deletions comprising rs2431697 dramatically reduced the miR-146a expression at transcriptional level of up to 10-fold, but had no effect on the expression of the neighbor gene PTTG1. rs2431697 T allele and C allele comprising cell clone had different miR-146a expression level at both native and TNFα stimulation. Bioinformatics analysis suggested that rs2431697 T and C allele may have differential RelA binding.

**Conclusion:** Using CRISPR-Cas9 technology, we first indicate that rs2431697-containing region participates in the regulation of miR-146a expression. We also demonstrate that rs2431697 is located in a distal enhancer and has differential transcription factor binding that modulates miR-146a expression involving in the pathogenesis of SLE.

**Disclosure:** G. Hou, None; J. Zeng, None; Y. Tang, None; N. Shen, None.


**Abstract Number:** 181

**Identification of Disease-Susceptible Lncrna Contributed to Abnormal Activation of Type I Interferon Pathway in Systemic Lupus Erythematosus**

Nan Shen1,2, Yuanjia Tang3, Zhixin Xue3 and Chaojie Cui4,1 Shanghai Institute of Rheumatology, Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China, Shanghai, China, 2The Center for Autoimmune Genomics and Etiology (CAGE), Cincinnati Children’s Hospital Medical Center, Cincinnati, Ohio, United States of America, Cincinnati, OH, 3Shanghai Institute of Rheumatology, Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China, 4Shanghai Institute of Rheumatology, Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Genetics, Genomics and Proteomics Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Dysregulation or dysfunction of some key moleculars in signaling pathway is involved in disease pathogenesis. Long non-coding RNA (lncRNA), as a regulator of gene expression, plays great role in signaling pathway. The majority of susceptible single nucleotide polymorphisms (SNPs) of systemic lupus erythematosus (SLE) identified in GWAS studies are located in noncoding regions of the human genome. We hypothesized that disease-related functional SNP linked to lncRNA may affect expression or function of lncRNA and involve in key signaling pathway of SLE.
Methods:

Deep sequencing of human renal samples to screen differential expression of lncRNAs between LN patients and healthy donors and mining GWAS data were applied to get candidate lncRNAs. RNA-FISH was used to identify subcellular location of lncRNA. Reporter gene assay was applied to ascertain effect of disease-related SNP on lncMKLN1 transcription. Stimulation in human renal mesangial cells (HRMC) by all kinds of TLR ligands, IFNs, and TNFα, and transfection in HRMC cells by antisense oligonucleotides (ASOs), and quantitative real-time polymerase chain reaction (RT-qPCR) were used to analyze the relative genes expression. LncMKLN1 transcription was activated or inhibited through CRISPR-dCas9 system in Hela cell line. RNA-seq was executed to examine the gene expression profile after changing lncMKLN1 expression, and western blot was applied to determine the key signaling molecules of IFN pathway.

Results:

LncMKLN1, dominantly located in nucleus, was up-regulated in lupus patients compared to healthy donors, and could be induced by IFNα and TLR ligands in HRMC. GWAS data showed that there were two lupus-related SNPs located within proximal region of lncMKLN1 promoter. Promoter constructs containing susceptible allele have higher activity of transcription compared to another allele. Silencing lncMKLN1 significantly reduced the expression of a group of interferon-inducible genes, including IFIT3, OAS1, CXCL10, etc. We used lose-of-function and gain-of-function strategy through CRSIPR system to confirm that lncMKLN1 positively regulated type I interferon pathway. Furthermore, it was identified the involvement of lncMKLN1 in interferon signaling pathway was through regulating the expression of STAT1, IRF9 and phosphorylation of IRF9 and STAT1 although its mechanism is also needed to investigate.

Conclusion:

Functional susceptible SNP enhances lncMKLN1 expression, resulting in abnormal activation of interferon pathway of SLE.

Disclosure: N. Shen, None; Y. Tang, None; Z. Xue, None; C. Cui, None.

Abstract Number: 182

Genetic Determinants of Fatigue in Primary Sjögren’s Syndrome – a Genome Wide Association Study

Katrine Norheim1, Andrei Alexsson2, Juliana Ingenberg-Kreuz3, Johan Gorgas Brun4,5, Roland Jonsson6, Wan-Fai Ng7,8, Elke Theander9, Thomas Mandl10, Kathy L. Sivils11, Lars Rönnblom12, Gunnel Nordmark13 and Roald Omdal5,14, 1Clinical Immunology Department, Stavanger University Hospital, Stavanger, Norway, 2Rheumatology and Science for Life Laboratory, Department of Medical Sciences, Uppsala University, Uppsala, Sweden, 3Department of Medical Sciences, Uppsala University, Uppsala, Sweden, 4Section for Rheumatology, Haukeland University Hospital, Bergen, Bergen, Norway, 5Department of Clinical Science, University of Bergen, Bergen, Norway, 6Department of Clinical Science, Broegelmann Research Laboratory, University of Bergen, Bergen, Norway, 7Newcastle-upon-Tyne Hospitals NHS Foundation Trust, Newcastle-upon-Tyne, UK, Newcastle-Upon-Tyne, United Kingdom, 8Musculoskeletal Research Group, Institute of Cellular Medicine, Newcastle University, Newcastle-Upon-Tyne, UK, Newcastle-Upon-Tyne, United Kingdom, 9Dept of Rheumatology, Skane University Hospital Malmo, Lund University, Malmö, Sweden, 10Department of Rheumatology, Skåne University Hospital, Malmö, Sweden, Lund, Sweden, 11Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 12Department of Medical Sciences, Section of Rheumatology, Uppsala University, Uppsala, Sweden, 13Rheumatology, Department of Medical Sciences, Uppsala University, Sweden, Uppsala, Sweden, 14Clinical Immunology Unit, Department of Internal Medicine, Stavanger University Hospital, Stavanger, Norway

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Genetics, Genomics and Proteomics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Fatigue is common in primary Sjögren’s syndrome (pSS), but the mechanisms that lead to fatigue are not fully understood. We hypothesized that there is a genetic basis for fatigue, and that specific gene-variants (single nucleotide polymorphisms – SNPs) influence the severity of
fatigue. To investigate this further we performed a genome wide association study (GWAS) of 367 Scandinavian pSS patients.

Methods:

PSS patients from 4 sites in Norway and Sweden were collected through the Scandinavian Sjögren’s syndrome network. Genotyping was performed at the SNP&SEQ platform, Uppsala University, Sweden using the Illumina Human OmniExpressExome array. All included cases fulfilled the American-European Classification Criteria for pSS. Fatigue was assessed using the fatigue Visual Analogue Scale or the European Sjögren’s Syndrome Patient Reported Index. Imputation was performed using SHAPEIT2 and IMPUTE2. After genotype and sample quality control and imputation a total of 365 samples and 4,966,159 SNPs remained for analysis. A linear regression analysis of fatigue scores versus minor alleles was performed.

Results:

The pSS patients were 92% females, mean age 57 years with a median fatigue score of 66 (range 0-100). Our analysis revealed five SNPs exceeding the genome wide significance (GWS) threshold of p=5E-8 with a beta coefficient of 12.8. All five SNPs were in linkage disequilibrium and two of the SNPs, rs7626469 and rs73182503, were in the gene Receptor Transporter Protein 4 (RTP4), in which the minor allele was associated with less fatigue. RTP4 encodes a Golgi chaperone, involved in the cell surface expression of opioid receptors. In addition, 58 SNPs in 4 genes (Endoplasmatic Reticulum to Nucleus Signaling 1 (ERN1), Long intergenic non-protein coding RNA 1553 (LINC01553), Long intergenic non-protein coding RNA 1184 (LINC01184) and RP11-15I11.2) reached a suggestive significance level (p<1E-5).

Conclusion:

We identified genetic variants in RTP4 exceeding the GWS level for association with fatigue. Notably, this gene encodes a protein involved in pain processing. Pain is known to influence fatigue, and this finding could point to a possible molecular explanation. The present study is the largest GWAS of fatigue in autoimmune disease, and adds further evidence to a genetic regulation of fatigue.

Disclosure: K. Norheim, None; A. Alexsson, None; J. Ingemerg-Kreuz, None; J. G. Brun, None; R. Jonsson, None; W. F. Ng, None; E. Theander, None; T. Mandi, None; K. L. Sivils, None; L. Rönnblom, None; G. Nordmark, None; R. Omdal, None.


Abstract Number: 183

Allele-Dependent Binding of a Viral Protein to Autoimmune Disease-Associated Genetic Variants

Matthew Weirauch1, Daniel Miller2, Leah C. Kottyan3, Ignacio Ibarra4, Arthur Lynch2, Sayeed Syed5, Xiaoting Chen2, Erin Zoller2, Conner Schroeder2, Josh Lee2, Albert Magnusen6, Ally Yang7, Timothy R. Hughes7, Joo-Seop Park8, Charles Vinson5 and John B. Harley2,9, 1Center for Autoimmune Genomics and Etiology (CAGE) and Divisions of Biomedical Informatics and Developmental Biology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 2Center for Autoimmune Genomics and Etiology (CAGE), Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 3Center for Autoimmune Genomics and Etiology (CAGE), Division of Allergy and Immunology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 4Center for Autoimmune Genomics and Etiology (CAGE), Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 5Structural and Computational Biology Unit, European Molecular Biology Laboratory, Heidelberg, Germany, 6NCI, Bethesda, MD, 7Center of Autoimmune Genomics and Etiology (CAGE), Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 7University of Toronto, Toronto, ON, Canada, 8Divisions of Urology and Developmental Biology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 9US Department of Veterans Affairs Medical Center, Cincinnati, OH

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Genetics, Genomics and Proteomics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Risk factors are known for many diseases, but the etiologies of most autoimmune diseases remain unknown and are idiopathic. Pathogenesis of disease likely involves complex interplay between genetic and environmental risk factors. Specifically, Epstein Barr virus (EBV) has suggestive associations with many autoimmune diseases, and EBV infection is nearly ubiquitous in adults. The molecular mechanisms underlying these associations, however, remain unclear.
Methods: We tested the hypothesis that some autoimmune variants might act by altering the binding of the EBV-encoded transcription factor Zta, consequently resulting in downstream changes in gene expression. To this end, we comprehensively characterized the DNA binding of Zta to both methylated and unmethylated DNA sequences using protein binding microarrays (PBMs). Based on these data, we identified plausible causal variants for multiple sclerosis (MS), systemic lupus erythematosus (SLE), and juvenile idiopathic arthritis (JIA) predicted to alter Zta binding. From among these, we identified variants located within likely regulatory regions in EBV-infected B cells using publically available functional genomic datasets. We screened these candidate variants using electrophoretic mobility shift assays (EMSAs) to identify general differential binding of nuclear factors, and validated differential Zta binding using EMSA-supershift and DNA Affinity Precipitation Assays coupled with Western blots (DAPA-Westerns).

Results: These experiments revealed three genetic variants, associated with MS, SLE, and JIA, respectively, exhibiting stronger Zta binding to the risk allele. We provide data showing that each of these variants is associated with genotype-dependent expression in EBV-transformed B cell lines. Using luciferase reporter assays, we further demonstrate that the MS risk allele in the RGS14 promoter results in greater promoter activity, and that this activity is significantly diminished in cell lines lacking EBV.

Conclusion: Collectively, these data demonstrate for the first time that differential binding of a viral protein to a disease-associated genetic variant can result in altered levels of host gene expression in ways that are predicted to influence autoimmune disease. Since Zta is a viral protein, and is expressed throughout human life subsequent to EBV infection, but only in virally infected cells, these results offer a potential therapeutic target for multiple autoimmune diseases.

Disclosure: M. Weirauch, None; D. Miller, None; L. C. Kottyan, None; I. Ibarra, None; A. Lynch, None; S. Syed, None; X. Chen, None; E. Zoller, None; C. Schroeder, None; J. Lee, None; A. Magnusen, None; A. Yang, None; T. R. Hughes, None; J. S. Park, None; C. Vinson, None; J. B. Harley, None.

Abstract Number: 184

An Epigenome-Guided Approach to Causal Variant Discovery in Autoimmune Disease

Richard C. Pelikan1, Jennifer A. Kelly2, Yao Fu2, Caleb Lareau3, Graham B. Wiley1, Stuart Glenn1, Martin Aryee3,4, Courtney Montgomery2 and Patrick Gaffney2, 1Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 2Arthritis and Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, 3Department of Biostatistics, Harvard T.H. Chan School of Public Health, Charlestown, MA, 4Department of Pathology, Harvard Medical School, Boston, MA, 5Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Genetics, Genomics and Proteomics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Genome-wide association studies have identified thousands of genetic associations with complex human diseases and traits. However, establishing the truly causal regions of risk haplotypes is complicated by the correlation of many non-causal variants to genetic associations through linkage disequilibrium (LD). This has made translating genetic findings into functional mechanisms an inefficient, resource-intensive task.

Methods: Here, we expedite causal variant discovery for autoimmune diseases by identifying genetic variants (epiQTLs) that leave an epigenomic footprint of allelic imbalance in sequencing reads recovered by chromatin immunoprecipitation of enhancer marks (H3K4me1 and H3K27ac ChIP-seq). We aligned sequencing reads using the WASP pipeline to control for reference genome bias. We used the combined haplotype test (CHT) to statistically test for robust footprints of allelic imbalance. We also characterized the three-dimensional chromatin interaction topography among H3K27ac-marked active enhancers of our cell lines by HiChIP.

Results: We discovered a total of 6261 epiQTLs across 25 patient-derived EBV-transformed B-cell lines. We overlaid these epiQTLs onto risk haplotypes from 21 autoimmune (AI) diseases and found that 145 reported AI risk haplotypes contained one or more of our epiQTLs. A total of 14 epiQTL SNPs matched AI risk SNPs reported in the NHGRI GWAS catalog, while 180 epiQTLs were proxies of these reported SNPs. We found that epiQTLs located on disease risk haplotypes disproportionately influence gene expression variance, beyond what can be expected by random chance, over non-epiQTL variants in tight linkage disequilibrium. A majority (78%) of epiQTLs were located in chromatin loop anchors. Using a generalized linear model, we identified 571 epiQTLs – not associated with autoimmune disease - that
modify gene expression from 68 previously established AI disease risk haplotypes through chromatin looping at FDR ≤5%. Expanding this analysis to include both risk haplotypes and independent eQTLs increased the number of epiQTLs with significant (FDR ≤ 5%) modifier effects on gene expression to 1062. Of these gene expression modifying interactions, 717 (68%) increased eQTL-driven gene expression by the epiQTL, while 345 (32%) suppressed eQTL-driven gene expression.

Conclusion: Our data suggest that the epiQTL approach can facilitate the decomposition of risk haplotypes into specific regions that are highly likely to contain functional causal variants. Moreover, epiQTLs not associated with disease haplotypes function to modify gene expression from risk haplotypes and eQTLs through long-range allele-dependent epigenetic mechanisms.

Disclosure: R. C. Pelikan, None; J. A. Kelly, None; Y. Fu, None; C. Lareau, None; G. B. Wiley, None; S. Glenn, None; M. Aryee, None; C. Montgomery, None; P. Gaffney, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/an-epigenome-guided-approach-to-causal-variant-discovery-in-autoimmune-disease

Abstract Number: 185

Effect of Pre-Appointment Consult Triage on Patient Selection and Revenue Generation in a University Rheumatology Practice

Sterling West1, Duane Pearson1, Christopher C. Striebich2, Ryan Goecker1 and Jason Kolfenbach1, 1Division of Rheumatology, University of Colorado School of Medicine, Aurora, CO, 2Division of Rheumatology, University of Colorado School of Medicine, Aurora, CO

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Health Services Research Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Academic hospital leadership puts a priority on all patients (pts) having access to subspecialists. Often the demand for rheumatology consultation exceeds the ability to see pts promptly. This necessitates a consult triage system to ensure timely appointments for pts with inflammatory rheumatic diseases (IRD). The aim of this study was to evaluate the effectiveness of pre-appointment consult screening to identify pts with potential IRD who need timely access and the revenue implications of caring for these IRD pts compared to non-IRD pts.

Methods: During a 9 month period, all pts referred by a healthcare provider to our University rheumatology practice were screened and classified as either possible IRD or non-IRD based on a pre-appointment records request and review by a rheumatologist. Pts with possible IRD were scheduled for an appointment and diagnosis after clinical evaluation was recorded. Using the 2015 Medicare fee schedule, revenue generated through the care of pts accepted for evaluation was recorded for the subsequent 12 months after initial consultation (Table 1). Outpatient services necessary for initial diagnosis and subsequent patient monitoring were analyzed. Costs of medications, surgical procedures, and hospitalizations were not included. Revenues between IRD and non-IRD pts were compared using a Student’s t-test. Pts categorized as non-IRD based on pre-appointment screening and denied evaluation received subsequent care through their referring provider and clinical outcome at one year was recorded if available.

Results: Of the 961 referrals, 673 pts (70%) were classified after consult review as possible IRD pts and scheduled for evaluation. Of the 597 pts who presented for initial evaluation (average time to first appointment 13 days, range 1-31), 357 pts (60%) were found to have an IRD (139 RA, 83 SLE/SSc/UCTD/ Sjogren’s, 44 crystal dz, 38 spondylo, 34 vasculitis/myositis, 19 other) and 240 pts (40%) had a non-IRD. Of the 288 pts who were denied evaluation, 128 had follow-up data for at least one year with only six (0.5%) developing an IRD. The sensitivity of consult screening to identify IRD was 98% with a positive predictive value of 60%. Complete revenue data was available for 510 pts (318 pts with IRD, 192 pts with non-IRD); analysis demonstrated that care of pts with IRD generated 5.6 times more revenue compared to non-IRD pts (p<0.05).

Conclusion: Pre-appointment consult screening is an effective method to identify pts with IRD. This allows for timely access to care for pts in highest need of evaluation and for significantly more revenue generation.

Table 1: Total revenue (dollars) generated by patients with IRD versus non-IRD over 12 months
<table>
<thead>
<tr>
<th>Care modality/Service</th>
<th>IRD (318 pts)</th>
<th>Non-IRD (192 pts)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Followup visits/Provider fees</td>
<td>68,580</td>
<td>1,620</td>
</tr>
<tr>
<td>Labs/radiology/rheumatology procedures</td>
<td>108,980</td>
<td>15,495</td>
</tr>
<tr>
<td>Specialty consults/PT/OT</td>
<td>38,500</td>
<td>6,300</td>
</tr>
<tr>
<td>Total</td>
<td>216,060; 679/pt</td>
<td>23,415; 122/pt</td>
</tr>
</tbody>
</table>

Disclosure: S.West, None; D.Pearson, None; C.Striebich, None; R.Goecker, None; J.Kolfenbach, None

Disclosure: S. West, None; D. Pearson, None; C. C. Striebich, None; R. Goecker, None; J. Kolfenbach, None.


Abstract Number: 186

**Paediatric Musculoskeletal (MSK) Triage in the Community – Rightpath – a Pilot Study**

Nicola Smith¹, Sharmila Jandial², Jill Firth³, Helen Light³, Katharine Kinsey³, Neil Snowden³, Judith McNaught⁴, Tim Rapley⁵, Alan Nye³ and Helen E. Foster⁵. ¹Institute of Cellular Medicine, Newcastle University, Newcastle Upon Tyne, United Kingdom; ²Paediatric Rheumatology, Great North Children’s Hospital, Newcastle Upon Tyne, United Kingdom; ³Pennine MSK Partnership Ltd, Oldham, United Kingdom; ⁴Physiotherapy, South Tyneside NHS Foundation Trust, South Shields, United Kingdom; ⁵Institute of Health and Society, Newcastle University, Newcastle Upon Tyne, United Kingdom; ⁶Institute of Cellular Medicine and Paediatric Rheumatology, Newcastle University and Great North Children's Hospital, Newcastle Upon Tyne, United Kingdom

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Health Services Research Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

We are piloting a children and young people (CYP) community-based triage (called Rightpath) based on a validated adult MSK triage model developed by Pennine MSK Partnership Ltd (PMSKP), Greater Manchester. Rightpath aims to promptly identify CYP with MSK pathology and triage them to the appropriate service (rheumatology, orthopaedics, neurodisability or urgent care), and to manage those who do not need specialist referral appropriately within the community. Triage and referral guidance has been developed in partnership with MSK specialists and this study aims to test its safety, feasibility and acceptability in the community, and through application across two geographical areas in the UK to assess transferability.

**Methods:**

Piloted first at PMSKP, with iteration of the triage guidance and process followed by roll out at a second site (South Tyneside NHS Trust). Using mixed methods, evaluation focused on key areas:

- **Implementation** – workshops with service providers (triagers and clinicians) held at two time points to refine triage guidance and process.

- **Training** – for triagers based on their weekly log of triage experiences and regular case based discussions and feedback.

- **Evaluation** – (i) Parent/ patient questionnaire, incorporating the ‘Friends and Family’ test and ‘Collaborate’ (a patient reported measure of shared decision-making), completed immediately after consultation to explore expectations and satisfaction; (ii) Service providers weekly log documenting experiences and training needs; (iii) Routine patient data including demographic details, referral information, triage outcome, ultimate diagnosis/outcome and communication between triage teams and health care providers; (iv) Service providers signposted to key areas for self-directed learning (paediatric musculoskeletal matters [PMM] – [PMMonline.org](http://pmmonline.org)) and usage monitored.

This study had ethical approval.
Results:

Total triaged 05/09/16 - 30/04/17 (101 to Rightpath, 264 to specialist paediatric services). The most common CYP MSK referrals from the community were knee pain, foot pain, flat feet and back pain; the most common conditions triaged to Rightpath were foot pain, knee pain, flat feet, and in-toeing. No significant pathology has been triaged inappropriately so far to Rightpath. Feedback from 66 Rightpath family participants was positive (no complaints or requests for onward specialist referral); 100% would recommend the service, with satisfaction (1-10) scores about community providers being high (1=’no’ and 9=’every’ effort made); ‘helped understand your/your child’s health issues’ (8.9), ‘listened to things that matter most to you about your/your child’s health’ (8.9), ‘included what matters most to you in choosing what to do next’ (8.9). Community therapists and podiatry described the clinical workload to be appropriate for their existing skills. Triage staff deemed the triage process manageable (57% of decisions ‘easy/very easy’) and triage guidance to be useful commenting that paediatric experience was important to support decision-making.

Conclusion:

Initial data shows Rightpath to be feasible, safe and acceptable. Phase 2 of the pilot is in progress at the second site.

Disclosure: N. Smith, None; S. Jandial, None; J. Firth, None; H. Light, None; K. Kinsey, None; N. Snowden, None; J. McNaught, None; T. Rapley, None; A. Nye, None; H. E. Foster, None.


Abstract Number: 187

Improved Identification of Pseudogout in Electronic Medical Records By Adding Text String Searching to a Billing Code Algorithm

Sara K. Tedeschi, Kazuki Yoshida and Daniel H. Solomon, Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Health Services Research Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Calcium pyrophosphate deposition disease (CPPD) has a spectrum of manifestations, of which pseudogout is the most acute inflammatory phenotype. To facilitate clinical research on CPPD, an ICD-9 algorithm for “definite or probable CPPD” (per Ryan and McCarty’s diagnostic criteria) was developed at a Veterans’ Administration (VA) Medical Center. The algorithm includes ≥1 ICD-9 code 275.49 (“other disorders of calcium metabolism”) or 712.1-712.39 (“chondrocalcinosis” due to dicalcium phosphate crystals, pyrophosphate crystals, or cause unspecified). We hypothesized that the algorithm would be suboptimal for identifying pseudogout, and aimed to enhance its ability to identify pseudogout in electronic medical records (EMR).

Methods: Following the published methods, we applied the ICD-9 algorithm to patients with ≥1 encounter at our non-VA academic medical center over 2 years (1/1/15-12/31/16). 100 patients were randomly selected for EMR review from date of 1st qualifying ICD-9 code through 5/1/17. We evaluated whether patients fulfilled each of 3 clinical definitions: “definite or probable CPPD”—which the algorithm was designed to identify—and 2 pseudogout definitions (Table). We calculated the positive predictive value (PPV) and 95% confidence intervals (CI) of the ICD-9 algorithm for identifying each phenotype. We then modified the ICD-9 algorithm to include text string searching for “pseudogout” or “calcium pyrophosphate crystals” in narrative notes and re-assessed test performance characteristics.

Results: 55% of 100 patients were female; mean age was 68.6 (+13.9) years. Joint pain was present in 86% and synovitis in 34%. The published algorithm had 68% (59-77%) PPV for “definite or probable CPPD” in our sample (Table), compared to 91% (88-94%) PPV in the VA derivation study. The published algorithm identified only 18% (10-26%) of patients with crystal-proven pseudogout. In our sample of 100 patients, 50 had a positive text string search. Of these, 17 had crystal-proven pseudogout per EMR review, producing a PPV of 34% (25-43%) and NPV of 98% (95-100%). Text string searching was 94% sensitive (89-99%) and 60% specific (50-70%) for crystal-proven pseudogout in the sample.

Conclusion: Adding text string searching to a published ICD-9 CPPD algorithm improved PPV for identifying crystal-proven pseudogout from 18% to 34%, with excellent sensitivity and moderate specificity. The accuracy of identifying pseudogout in EMR data might be further improved using more advanced text searching methodology, such as natural language processing.


Positive predictive value (PPV) of a published ICD-9 algorithm* for identifying CPPD or pseudogout in an electronic medical record dataset

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>PPV% (95% CI) for phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>Published CPPD definition</td>
<td></td>
</tr>
<tr>
<td>Ryan and McCarty “definite or probable CPPD”**</td>
<td>68 (59-77)#</td>
</tr>
<tr>
<td>Pseudogout definitions</td>
<td></td>
</tr>
<tr>
<td>Crystal-proven pseudogout+</td>
<td>18 (10-26)</td>
</tr>
<tr>
<td>Modified EULAR acute CPP crystal arthritis++</td>
<td>25 (17-34)</td>
</tr>
</tbody>
</table>

*Algorithm for Ryan and McCarty “definite or probable CPPD”: ≥1 ICD-9 code 275.49 or 712.1-712.39

#PPV 91% reported by Bartels et al.¹ at Milwaukee VA Medical Center

**Joint pain, and either synovial fluid with calcium pyrophosphate crystals or chondrocalcinosis in any joint, or both

+Synovitis (pain, swelling and tenderness) in the affected joint and synovial fluid with calcium pyrophosphate crystals

++Synovitis in the knee, wrist or shoulder reaching maximum intensity in 6-24 hours and either (1) age >65 or (2) chondrocalcinosis in any joint. Modified from Zhang et al.²

Disclosure: S. K. Tedeschi, None; K. Yoshida, None; D. H. Solomon, None.


Abstract Number: 188

Lupus Low Disease Activity State Is Associated with Reduced Direct Medical Costs in Patients with Systemic Lupus Erythematosus

Ai Li Yeo¹, Rachel Koelmeyer², Rangi Kandane-Rathnayake¹, Vera Golder², Alberta Y. Hoi², Edward R. Hammond³, Henk Nab⁴, Molla Huq⁵, Mandana Nikpour⁶ and Eric F Morand⁷, ¹Rheumatology, Monash University, Melbourne, Australia, ²Centre for Inflammatory Diseases, Monash University, Melbourne, Australia, ³AstraZeneca, Gaithersburg, MD, ⁴AstraZeneca, Cambridge, United Kingdom, ⁵Department of Medicine (Rheumatology), Melbourne University, Melbourne, Australia, ⁶Melbourne University, Melbourne, Australia, ⁷Monash University, Melbourne, Australia

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Health Services Research Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: High health care utilization and direct costs have been documented in multiple studies of SLE. The recently described lupus low disease activity state (LLDAS) has been associated with reduced flares and damage accrual. We hypothesized that LLDAS attainment would be associated with reduced healthcare cost.

Methods: This study utilized data from a single tertiary centre cohort of SLE patients (ACR criteria) between October 2013 and June 2016. Baseline demographics, and per visit disease activity (SLEDAI-2K, physician global and flare index) and medication use were matched to
healthcare utilization and cost data obtained from hospital information systems. LLDAS was defined as described (Franklyn K, et al. Ann Rheum Dis 2016;75:1615). Statistical analyses were performed using Stata version 14.

Results: 200 SLE patients (88% female, median age 42 years) were followed for 357.8 person-years. A history of lupus nephritis was present in 42%, anti-dsDNA antibodies in 70%, and SLICC damage index (SDI)>0 at study commencement in 57.3%. During the observation period, median (range) time adjusted mean SLEDAI was 4.0 (0–16.9), there were 571 hospitalizations (24.2% multi-day), and 31% of patients had at least one emergency room attendance. The mean (standard deviation) annual direct medical cost per patient was US$7,413 (US$13,133)/year. Patients in the highest quartile of annual cost were more likely to accrue new damage during the observation (34 vs 11%, p<0.001) and had significantly more physician visits, hospitalizations, and emergency room visits (all p<0.001). Mean annual costs were significantly greater in patients with baseline SLEDAI >6 or SDI>0, or who during observation had time-adjusted mean SLEDAI >6, renal disease activity, or used corticosteroids (all p<0.01). In multivariable analysis, baseline organ damage, and moderate–high corticosteroid use (>7.5 mg/day) were significantly associated with increased cost (see table). In contrast, meeting LLDAS criteria for >50% of the observed time was associated with a 25% reduction in annual direct medical cost (p=0.041).

Association of LLDAS with Annual Direct Medical Cost

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Ratio of Geometric Means</th>
<th>P Value for Association</th>
<th>Estimated Increment/Decrement in Annual Direct Cost (%)</th>
<th>Estimated Incremental/Decremental in Annual Direct Cost (US$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;50% time spent in LLDAS</td>
<td>0.74</td>
<td>0.041</td>
<td>-25.6</td>
<td>-895</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Annual prednisolone dosage</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low dosage (≤7.5 mg/day)</td>
<td>1.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate dosage (&gt;7.5–15 mg/day)</td>
<td>1.56</td>
<td>0.018</td>
<td>56.5</td>
<td>1975</td>
</tr>
<tr>
<td>High dosage (&gt;15 mg/day)</td>
<td>3.0</td>
<td>&lt;0.001</td>
<td>203.7</td>
<td>7123</td>
</tr>
<tr>
<td>Damage</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Organ damage present at baseline</td>
<td>1.43</td>
<td>0.008</td>
<td>42.7</td>
<td>1493</td>
</tr>
</tbody>
</table>

# Adjusted for variables in table and geographic distance from the treating centre.

Conclusion: As in previous studies, baseline organ damage, high disease activity, and corticosteroid use were associated with increased cost. Our findings demonstrate that LLDAS attainment is associated with significantly reduced health care cost among patients with SLE. # Adjusted for variables in table and geographic distance from the treating centre.

Disclosure: A. L. Yeo, None; R. Koelmeyer, None; R. Kandane-Rathnayake, None; V. Golder, None; A. Y. Hoi, None; E. R. Hammond, AstraZeneca, 3; H. Nab, AstraZeneca, 3; M. Huq, None; M. Nikpour, None; E. F. Morand, AstraZeneca, 2,AstraZeneca, 5.


Abstract Number: 189

Challenges and Opportunities of Implementing a Patient-Reported Measure of Physical Function through an Online Electronic Health Record Patient Portal in Routine Rheumatology Practice
Jing Li1, Jinoos Yazdany2, Laura Trupin2, Zara Izadi3, Milena Gianfrancesco1, Sarah Goglin1 and Gabriela Schmajuk4,
1Medicine/Rheumatology, University of California, San Francisco, San Francisco, CA, 2Medicine/Rheumatology, University of California San Francisco, San Francisco, CA, 3Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, CA, 4San Francisco VA Medical Center, University of California San Francisco, San Francisco, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Health Services Research Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Despite significant interest in the collection of patient-reported outcomes (PROs) to make care more patient-centered, few studies have evaluated implementation efforts to collect PROs in real-world practice settings that serve diverse patient populations. In this study, we assessed the collection of PROs from rheumatoid arthritis (RA) patients in an academic rheumatology clinic, using a paper form and subsequently, an online form through the electronic health record (EHR) patient portal.

Methods:
We identified patients seen at the clinic from June 2012-July 2016 with at least 2 face-to-face encounters with a rheumatology provider and ICD codes for RA, ≥30 days apart. In February 2013, the clinic implemented a paper version of the Patient Reported Outcome Measurement Information System (PROMIS) physical function (PF) form that was administered to patients upon their check-in at the clinic; in January 2015, an online version of the form became available via the EHR patient portal to patients with active portal accounts. We queried our EHR’s SQL server to obtain demographic information, paper and online PROMIS scores, and their dates of completion. We compared the proportion of visits with documented PROMIS scores across age, race/ethnicity, and language, using chi-square and ANOVA tests and p-chart.

Results:
We included 1,078 patients with RA with 7,049 in-person encounters at the rheumatology clinic over 4 years, with an average of 168 visits/month. 80% of patients were female; mean age was 55 (SD 16). Overall PROMIS PF score documentation increased from 60% of visits in 2013 to 74% in 2016. Online score documentation increased from 10% in 2015 to 19% in 2016 (Figure 1). Most users of the online form used it only once, reverting to the paper form in subsequent visits. African Americans were less likely to have any PROMIS PF recorded (63% vs. 81% for other racial groups, p<0.001). Compared with Whites, both African American and Hispanics were less likely to have active online EHR portal accounts (50% and 57% respectively, vs. 84% of Whites; p<0.001) and, once activated, less likely to use the online survey (14% and 18% respectively, vs. 31% of Whites; p=0.02). There was no significant difference in the proportion of any PROMIS PF recorded between Non-English vs. English speakers. However, Non-English speakers were less likely to use the online survey, likely because the online survey existed only in English (7% vs. 23% of English speakers; p<0.001). No significant differences were found across age or gender.

Conclusion:
PROMIS PF form completion improved overall over 4 years, but lagged among racial/ethnic minorities and non-English speaking patients. Future studies should address issues of portal access, enrollment, satisfaction and persistence, and focus on developing PRO implementation strategies that accommodate the needs and preferences of diverse populations.
Opioid Dispensation Among Systemic Lupus Erythematosus (SLE) Patients Who Persistently Frequent the Emergency Department (ED)

Jiha Lee¹, Lisa Gale Suter²,³ and Liana Fraenkel³,⁴, ¹Rheumatology, Yale University School of Medicine, New Haven, CT, New Haven, CT, ²Medicine, Rheumatol., TAC S541, Rheumatology, VA Connecticut Healthcare System, West Haven, CT, New Haven, CT, ³Rheumatology, Rheumatology, Yale University School of Medicine, New Haven, CT, New Haven, CT, ⁴Medicine, Section of Rheumatology, Rheumatology, VA Connecticut Healthcare System, West Haven, CT, New Haven, CT

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Health Services Research Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Patients who persistently frequent the ED are more likely to be prescribed opioids for pain, and opioid initiation in the ED has been found to increase the risk of long-term opioid therapy (LOT). Pain is frequently experienced by SLE patients, and a major cause of ED use. We sought to understand the prevalence of, and factors associated with opioid dispensation among SLE patients who persistently frequent the ED to identify opportunities to improve quality of care.

Methods: We identified SLE patients who persistently frequented the ED from 2013-2016 at a large urban academic medical center. Persistent use was defined as having three or more ED visits during the 12 months in a calendar year, for at least two out of the four years, consecutive or non-consecutive, during the study period. We collected patient-level variables including demographics and LOT use. Each encounter was categorized as either SLE-, infection-, pain-related or other. Additional encounter-level variables such as healthcare resource utilization and disposition were recorded. We used mixed effects logistic regression to analyze patient- and encounter-level factors associated with opioid administration in the ED and opioid prescription upon discharge from the ED. Variables with p-value <0.1 in univariate analysis were included in a multivariate model.

Results: Seventy-seven SLE patients had 1143 ED encounters. Opioids were administered in the ED for 38.4% of all encounters. In multivariate analysis, Medicaid, LOT use, MD as the ED provider (proxy measure for higher acuity), more imaging tests, and rheumatology evaluation were associate with increased odds of opioid administration in the ED (Table 1). Opioids were prescribed on discharge for 16.8% of encounters discharged from the ED. In multivariate analysis, African American patients, those on Medicaid, and patients utilizing the ED for SLE-related activity/complications were more likely to receive an opioid prescription upon discharge from the ED, than their respective counterparts (Table 2).
Conclusion: Opioids are commonly dispensed from the ED for SLE patients, even for those utilizing the ED for lupus-related activity/complications. Further study is warranted to inform how best to decrease opioid use in SLE patients both in the ED and upon discharge.

Table 1:
Multivariate analysis of factors associated with opioid administration in the ED

<table>
<thead>
<tr>
<th>Variables</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient level measures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>1.66 (0.64-4.31)</td>
<td>0.294</td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>0.47 (0.18-1.21)</td>
<td>0.120</td>
</tr>
<tr>
<td>Insurance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medicaid</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Medicare</td>
<td>0.85 (0.41-1.76)</td>
<td>0.665</td>
</tr>
<tr>
<td>Private/Commercial</td>
<td>0.22 (0.06-0.78)</td>
<td>0.019</td>
</tr>
<tr>
<td>Long-term opioid therapy</td>
<td>4.03 (1.99-8.15)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Encounter level measures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ED Provider type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MD</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Mid-level with MD supervision</td>
<td>1.33 (0.92-1.92)</td>
<td>0.129</td>
</tr>
<tr>
<td>Mid-level only</td>
<td>0.39 (0.21-0.74)</td>
<td>0.003</td>
</tr>
<tr>
<td>No. of Imaging</td>
<td>1.72 (1.42-2.08)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Rheumatology Evaluation</td>
<td>2.78 (1.42-5.45)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Odds ratio, 95% CI; *p*-value

Table 2:
Multivariate analysis of factors associated with opioid prescription upon discharge

<table>
<thead>
<tr>
<th>Variables</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient level measures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>0.22 (0.06-0.82)</td>
<td>0.025</td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>0.57 (0.21-1.53)</td>
<td>0.265</td>
</tr>
<tr>
<td>Insurance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medicaid</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Medicare</td>
<td>1.07 (0.55-2.06)</td>
<td>0.830</td>
</tr>
<tr>
<td>Private/Commercial</td>
<td>0.19 (0.04-0.79)</td>
<td>0.023</td>
</tr>
<tr>
<td>Area of Deprivation Index</td>
<td>1.00 (0.97-1.03)</td>
<td>0.792</td>
</tr>
<tr>
<td>No. of co-morbidities</td>
<td>1.17 (0.93-1.48)</td>
<td>0.181</td>
</tr>
<tr>
<td>Long-term opioid therapy</td>
<td>1.39 (0.73-2.66)</td>
<td>0.319</td>
</tr>
<tr>
<td>Encounter level measures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Encounter category group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>“Other”</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>SLE-related</td>
<td>8.44 (1.53-46.51)</td>
<td>0.014</td>
</tr>
<tr>
<td>Infection-related</td>
<td>1.51 (0.64-3.53)</td>
<td>0.342</td>
</tr>
<tr>
<td>Pain-related</td>
<td>2.00 (1.18-3.40)</td>
<td>0.010</td>
</tr>
</tbody>
</table>

Odds ratio, 95% CI; *p*-value

Disclosure: J. Lee, None; L. G. Suter, CMS, 3; L. Fraenkel, None.

Is the Nature of Rheumatology Practice Changing? Damage and Distress Contribute a Greater Proportion to Decision-Making Than Inflammation in Contemporary Care
Background/Purpose: Inflammation generally is regarded as the primary concern of rheumatologists, and measures of inflammation, such as laboratory tests and pooled indices, usually are the only quantitative data recorded in routine care. Structural damage to joints and other organs, as well as patient distress seen as fibromyalgia, depression, etc., are recognized, but not quantitated routinely in clinical care. In recent years, advances in control of inflammation, along with increases of degenerative diseases in an aging population, and recognition of a high prevalence of fibromyalgia, may have shifted rheumatology patient mix and decision-making more toward damage and distress vs inflammation. We sought to analyze the importance of inflammation, damage, and distress in care of individual rheumatology patients, by quantifying levels on 0-10 visual analog scales (VAS) and estimating their relative contributions to management decisions.

Methods: As part of routine care, rheumatologists at one academic site complete a 0-10 physician global assessment (DOCGL) VAS, as well as 3 further 0-10 VAS to assess inflammation (reversible disease) (DOCINF), joint and other organ damage (irreversible disease) (DOCDAM), and patient distress (fibromyalgia, depression), etc. (DOCSTR). The proportion of clinical management decisions attributed to inflammation, damage, and distress (total=100%) also is estimated. Mean values were analyzed in a cross-sectional study of 570 patients, and compared in subgroups of 98 with rheumatoid arthritis (RA), 131 with osteoarthritis (OA) and 89 with fibromyalgia (FM), using t tests and analysis of variance (ANOVA).

Results: Mean 0-10 DOCGL scores were 4.4 in all patients, 4.4 in OA, 4.6 in RA, and 5.2 in FM (Table) (p=0.04). Highest mean scores were seen for DOCINF in RA, DOCDAM in OA, and DOCSTR in FM, and differing significantly in each diagnosis (Table), confirming face validity. Importantly, damage VAS scores (DOCDAM) were higher than inflammation (DOCINF) scores in all groups, including in RA, and mean estimates of the proportion of clinical management decisions attributed primarily to damage were greater than to inflammation in all conditions (Table). Scores for DOCSTR were higher than for DOCINF in all patients and subgroups, other than in RA.

Mean VAS Scores and % of clinical management decision attributed to inflammation, damage, and distress in patients with rheumatic diseases

<table>
<thead>
<tr>
<th></th>
<th>ALL</th>
<th>RA</th>
<th>OA</th>
<th>FM</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>570</td>
<td>98</td>
<td>131</td>
<td>89</td>
<td></td>
</tr>
<tr>
<td>Mean VAS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scores</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOCGL</td>
<td>4.4 (1.6)</td>
<td>4.6 (1.8)</td>
<td>4.4 (1.5)</td>
<td>5.2 (1.6)</td>
<td>0.04</td>
</tr>
<tr>
<td>DOCINF</td>
<td>1.8 (2.0)</td>
<td>2.8 (2.4)</td>
<td>0.7 (1.1)</td>
<td>0.8 (1.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DOCDAM</td>
<td>3.1 (2.2)</td>
<td>3.8 (2.3)</td>
<td>4.4 (1.8)</td>
<td>1.7 (1.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DOCSTR</td>
<td>2.1 (2.9)</td>
<td>1.2 (2.2)</td>
<td>1.5 (2.5)</td>
<td>6.0 (2.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>P (DOCINF vs</td>
<td>0.001</td>
<td>0.01</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>DOCDAM)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P (DOCINF vs</td>
<td>0.11</td>
<td>&lt;0.001†</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>DOCSTR)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean % of</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>clinical</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>management</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>decision</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>attributed to:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>%inflammation</td>
<td>29 (31)</td>
<td>39 (29)</td>
<td>12 (19)</td>
<td>6 (11)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>%damage</td>
<td>48 (35)</td>
<td>52 (30)</td>
<td>73 (31)</td>
<td>18 (23)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>%distress</td>
<td>22 (34)</td>
<td>9 (20)</td>
<td>15 (27)</td>
<td>76 (27)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*ANOVA - RA vs OA vs FM

† - only comparison in which DOCINF higher than DOCSTR

Conclusion: Physician VAS scores and attributions to clinical decisions in individual patients were higher for damage than for inflammation in all groups seen in a rheumatology setting, even in RA patients as a group. Control of inflammation remains the primary concern for rheumatologists, but has improved considerably in recent years, as damage and distress may have become more prominent in routine patient care, and systematic quantitation appears of value.

Disclosure: T. Pincus, Theodore Pincus, 7; I. Castrejón, None; J. A. Block, None.
Patient Education Materials in Rheumatology: Only Adequate at Best

Aleksander Lenert and Sujin Kim, 1 Internal Medicine, Div. of Rheumatology, University of Kentucky, Lexington, KY; 2 Division of Biomedical Informatics, College of Medicine, University of Kentucky, Lexington, KY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Health Services Research Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Low health literacy and reading ability of rheumatologic patients is associated with poor outcomes [1]. In practice, patient education is commonly delivered via patient education materials (PEMs). However, readability of PEMs has been reported to be high and PEMs remain poorly understood [2]. We sought to determine the suitability of PEMs used in rheumatology practice.

Methods: Sixteen PEMs from 2 resources (ACR 2015 & UpToDate Basics 5-2017) were analyzed. PEMs on 4 diseases (OA, RA, SLE, vasculitis) and 4 treatments (abatacept, hydroxychloroquine, NSAIDs, rituximab) were scored for clinical complexity by 16 clinical rheumatologists. Suitability assessment of materials (SAM), a validated method to assess health-related educational resources, was used to score PEMs by 3 reviewers [3]. SAM scores were categorized and mean scores reported. Readability was measured by validated methods. PEMs were additionally assessed with 2 novel tools: information entropy and medical subject heading (MeSH) complexity. These methods provide further insight into information quantity and content complexity of PEMs. We compared means for ACR and UpToDate PEMs by Student t-test (1-sided alpha=0.05).

Results: Sixteen PEMs were rated by SAM: 3 were superior (with 2/3 on OA) and 13 were adequate (Figure 1). The mean SAM score for disease-PEM was highest for OA and lowest for vasculitis, and for therapy-PEM was highest for NSAIDs and lowest for abatacept. Mean SAM, information entropy and MeSH complexity scores did not significantly differ between ACR and UpToDate (p>0.05) (Table 1). Readability was at 6th grade for only 4 PEMs (all UpToDate) while it was >8th grade level for 12 PEMs; 4 ACR PEMs had readability >12th grade. Mean readability grade was significantly higher for ACR compared to UpToDate (p=0.002).

Conclusion: The suitability of PEMs in rheumatology is adequate at best for less complex topics but remains low for clinically complex topics. The majority of PEMs exceed the recommended 6th-grade reading level, especially PEMs by ACR. Development of personalized PEMs in rheumatology is needed to improve patient health literacy and impact outcomes.

References:


Evaluation of a Diversionary Back Pain Service

Lynden Roberts, Rheumatology, Monash Medical Centre, Clayton, Australia

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Health Services Research Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Surgical treatment of spinal pain is rarely indicated. Nevertheless, primary care clinician referrals to spinal surgeons for evaluation of spinal pain conditions are common. In the publicly funded hospital system in Australia, more than 90% of those referred to spinal surgeons with back pain do not receive surgery. It may be more appropriate for many people with spinal pain to be diagnosed and managed under a different model of health care.

Methods: A weekly spinal pain clinic was established at a publicly funded hospital. The clinic was staffed by a rheumatologist and 4 physiotherapists. All spinal pain referrals to the hospital’s spinal surgeons were diverted to the new clinic, with the exception of referrals assessed as likely spinal cord compression or cauda equina syndrome. Patients with previously diagnosed chronic spinal pain were not seen in the new clinic. Clinical and administrative data was prospectively and routinely collected including clinical diagnosis, Short Form of the Örebro Musculoskeletal Pain Screening Questionnaire, and clinical outcomes including whether spinal surgery was done. An 11-point Likert scale (0-10) was used to collect the patient satisfaction with the clinic following the encounter.

Results: A total of 575 face-to-face patient encounters occurred in the first 12 months of the service including 363 new patients. Low back
pain with radiculopathy was the commonest diagnosis. Average Örebro score was 67%. The failure-to-attend rate was 7%. Nearly half of the patients were discharged to community physiotherapy management, 2% to a chronic pain service, and 9% to a spinal surgeon. For patients referred to a spinal surgeon, 80% underwent spinal surgery. Average patient satisfaction was 9.2.

Conclusion: A novel model of care involving the substitution of spinal surgeons with a rheumatologist and physiotherapists for the assessment of patients with spinal pain was established. The patients assessed had a high estimated risk for future work disability. Efficient clinical care and a high patient satisfaction was demonstrated.

Disclosure: L. Roberts, None;

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/evaluation-of-a-diversionary-back-pain-service

Abstract Number: 194

Kinesiophobia Moderates the Association between Anxiety and Disability in Chronic Low Back Pain

Jenna Goesling1, Stephanie Moser2, Jennifer Pierce1 and Christian Bolton3, 1Department of Anesthesiology, University of Michigan, Ann Arbor, MI, 2Anesthesiology, University of Michigan, Ann Arbor, MI, 3University of Michigan, Ann Arbor, MI

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Health Services Research Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
- Low back pain is a debilitating and costly condition with complex biological, psychological, and social factors contributing to the development of chronic low back pain (CLBP).
- Kinesiophobia is defined as an “excessive, irrational, and debilitating fear of physical movement and activity resulting from a feeling of vulnerability to painful injury or re-injury” (1).
- According to cognitive behavioral models of fear and avoidance, maladaptive thoughts may lead to avoiding activity, which in turn may lead to illness behavior and increased disability.
- Previous research suggests that depression, anxiety and kinesiophobia contribute to pain perception and physical function.
- Yet, little is known about how kinesiophobia and anxiety and depression may interact to predict disability.
- The objective of the present study was to explore the moderating effect of kinesiophobia on the relationship between depression and anxiety and disability in a sample of adults with chronic low back pain (CLBP).

Methods:
- The study included 283 new patients seeking treatment for chronic pain.
- New patients completed the Oswestry Disability Index, the Hospital Anxiety and Depression Scale, and the Tampa Scale of Kinesiophobia (TSK). High kinesiophobia was defined as a score greater than 37 on the TSK.

Results:
- High kinesiophobia was reported in 64% (N=181) of participants.
- Kinesiophobia, depression and anxiety were associated with greater disability.
- The moderated effect of depression was nonsignificant.
- Kinesiophobia modified the association between anxiety and disability (Table 1). Namely, anxiety contributed to greater disability at high levels, but not low levels, of kinesiophobia (Figure 1).
Conclusion:

- Kinesiophobia, anxiety, and depression were associated with greater disability. However, kinesiophobia moderated the relationship between anxiety and disability, such that having anxiety and high kinesiophobia was associated with a worse outcome.

- Kinesiophobia and anxiety are both modifiable psychological factors that can be addressed using cognitive restructuring and exposure based behavioral interventions.

References:


Table 1

<table>
<thead>
<tr>
<th>Depression Predictor (n = 255)</th>
<th>Coeff.</th>
<th>SE</th>
<th>p</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-.01</td>
<td>.06</td>
<td>.92</td>
<td>[-.12,.11]</td>
</tr>
<tr>
<td>Gender</td>
<td>2.26</td>
<td>1.79</td>
<td>.21</td>
<td>[-1.26, 5.78]</td>
</tr>
<tr>
<td>Depression</td>
<td>13.97</td>
<td>1.96</td>
<td>&lt;.001</td>
<td>[10.11, 17.89]</td>
</tr>
<tr>
<td>Kinesiophobia</td>
<td>.87</td>
<td>.12</td>
<td>&lt;.001</td>
<td>[.45,.91]</td>
</tr>
<tr>
<td>Depression X Kinesiophobia</td>
<td>-.35</td>
<td>.21</td>
<td>.10</td>
<td>[-.77,.07]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Anxiety Predictor (n = 254)</th>
<th>Coeff.</th>
<th>SE</th>
<th>p</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>.00</td>
<td>.06</td>
<td>.98</td>
<td>[-.13,.12]</td>
</tr>
<tr>
<td>Gender</td>
<td>2.70</td>
<td>1.89</td>
<td>.15</td>
<td>[-1.02, 6.42]</td>
</tr>
<tr>
<td>Anxiety</td>
<td>5.90</td>
<td>2.18</td>
<td>.01</td>
<td>[1.00, 10.21]</td>
</tr>
<tr>
<td>Kinesiophobia</td>
<td>.44</td>
<td>.13</td>
<td>.001</td>
<td>[.19,.69]</td>
</tr>
<tr>
<td>Anxiety X Kinesiophobia</td>
<td>.54</td>
<td>.23</td>
<td>.02</td>
<td>[.08,1.00]</td>
</tr>
</tbody>
</table>

Note. Sample sizes vary due to missing data.

Figure 1: Interaction of Anxiety and Kinesiophobia on Disability

Disclosure: J. Goesling, NIH Project #1K23DA038718-01A1, 2; S. Moser, None; J. Pierce, None; C. Bolton, None.


Abstract Number: 195

Health Care Costs of Patients with Systemic Lupus Erythematosus (SLE) Versus Control Patients As a Function of Disease Severity: Analysis of the
Betriebskrankenkassen German Sickness Fund

Edward R. Hammond¹, Heiko Friedel², Elena Garal-Pantaler², Marc Pignot³, Erica Velthuis⁴, Xia Wang¹, Henk Nab⁵, Barnabas Desta¹ and Andreas Schwarting⁶, ¹AstraZeneca, Gaithersburg, MD, ²Team Gesundheit GmbH, Essen, Germany, ³Kantar Health GmbH, Munich, Germany, ⁴Evidera PPD, Utrecht Area, Netherlands, ⁵AstraZeneca, Cambridge, United Kingdom, ⁶Universitätsmedizin der Johannes Gutenberg-Universität Mainz, Mainz, Germany

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Health Services Research Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: SLE is a chronic, debilitating, multisystem autoimmune disorder of connective tissue. In developing new treatment options, the economic burden of SLE should be quantified as a function of disease severity.

Methods: Anonymized data from the Betriebskrankenkassen (BKK) German Sickness Fund Database were used to perform analyses of real-world claims of patients (pts) with SLE. Health care utilization and resource use and costs were assessed annually for 2009–2014 for confirmed pts with SLE identified in 2009 (using repeated claims with SLE diagnosis, co-diagnosis codes, laboratory tests, or prescription treatment and specialty of diagnosing physician) and compared with those of matched controls. Pts were ≥18 years of age and had data available for 2009 and ≥3 years prior to index quarter in 2009. SLE cases were matched to controls by age, sex, and baseline Charlson Comorbidity Index (CCI). Continuous outcomes were compared with a nonparametric test (e.g., Wilcoxon–Mann-Whitney), because most outcome distributions were positively skewed.

Results: Of the 3,290,701 persons with evidence of 3 years of insurance prior to 2009, 1,228 were identified as SLE cases in 2009, representing a prevalence of 37.32 per 100,000 and an incidence of 5.96/100,000 per year. The prevalence increased during the next 5 years to 47.36 per 100,000 in 2014. The final sample included 1,160 confirmed pts with SLE who were ≥18 years of age and had data for 2009. Pts with SLE were 84% female, and had a mean age of 52 years and a baseline CCI range of 1–13. 85% who qualified for the cohort in 2009 had already been diagnosed with SLE before 2009. A combined approach of International Classification of Diseases-10 GM and medication/procedures codes classified SLE disease severity as mild for 148, moderate for 484, and severe for 528 pts. Pts with SLE had significantly greater mean annual total medical costs in 2009 than did matched controls (€6,895 vs. €3,692, p<0.0001), and in all subsequent years evaluated. Moreover, pts with moderate and severe SLE had significantly greater mean annual total medical costs in 2009 than did matched controls (moderate SLE: €4,867 vs. €3,380, p<0.0001; severe SLE: €10,001 vs. €4,239, p<0.0001), and in all subsequent years. Mean costs and numbers of outpatient visits, hospital stays, outpatient prescriptions and other benefits, and total number of hospital days, were significantly greater for the full SLE population and the moderate and severe SLE subpopulations than for matched controls. For example, mean costs for hospital stays, outpatient prescriptions, and other benefits in 2009 were €4335 vs. €1414, €2582 vs. €1087, and €1068 vs. €691, respectively, for pts with mild, moderate and severe SLE vs. controls.

Conclusion: In this analysis, the economic burden of moderate and severe SLE was greater than that of socio-demographically and morbidity–adjusted controls. Pts with SLE were greater users of the health care system and incurred greater total annual medical costs than did matched controls. Health care utilization by pts with SLE increased with disease severity, with the greatest burden for those with severe SLE. New treatments could reduce health care resource use and help alleviate economic burden.

Disclosure: E. R. Hammond, AstraZeneca, 3; H. Friedel, None; E. Garal-Pantaler, None; M. Pignot, None; E. Velthuis, None; X. Wang, AstraZeneca, 3; H. Nab, AstraZeneca, 3; B. Desta, AstraZeneca, 3; A. Schwarting, None.

Abstract Number: 196

Patient Assistance Program Outcomes in a Community Clinic Setting

Stephanie Cerritos¹, Yanira Ruiz-Perdomo¹, Natalie Tobar¹, Ann Biehl² and James D. Katz³, ¹National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, ²Department of Pharmacy, National Institutes of Health Clinical Center, Bethesda, MD, ³National Institute of Arthritis, Musculoskeletal and Skin Disease (NIAMS), Bethesda, MD

First publication: September 18, 2017
Background/Purpose:

Uninsured rheumatic disease patients are at risk for inadequate treatment due to issues with access to care, such as medication costs that average at least $1659/patient/10 weeks (Costs for medications obtained using government prime vendor pricing). Pharmaceutical companies created patient assistance programs (PAPs) as one way to address these barriers. However, the process of getting assistance is resource-intensive because eligibility requirements are not standardized across these foundations. This study aims to understand one aspect of direct care costs in a community health clinic population.

Methods:

A clinical team was created to aid patients needing assistance for high-cost biologics. Patients were followed for about a year. We determined the rates of successful PAP approvals and stratified our analysis based on a diagnosis of Rheumatoid Arthritis (RA) or Other Autoimmune diseases (OTHER). We also catalogued reasons why some patients were unable to renew enrollment.

Results:

Data collected from 6/2016-5/2017 revealed a 94% PAP success rate for our patients with identified need (Table 1). RA patients had a 93% success rate. Success rates were higher in OTHER patients. PAP denial was often due to inadequate income documentation. Delay was often due to eligibility for Medicaid/Medicare.

Table 1. Biological Therapy Access Rates

<table>
<thead>
<tr>
<th>Category</th>
<th>Patients in need (#)</th>
<th>Successful Procurement Rate (#)</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Patients</td>
<td>75</td>
<td>71</td>
<td>94.6%</td>
</tr>
<tr>
<td>RA</td>
<td>59</td>
<td>55</td>
<td>93.2%</td>
</tr>
<tr>
<td>Other Autoimmune</td>
<td>16</td>
<td>16</td>
<td>100%</td>
</tr>
</tbody>
</table>

Furthermore, analysis of patients enrolled in PAP from 6/2016-5/2017 revealed a 68% renewal success rate. Reasons for lack of renewal were: newly acquired health insurance, personal choice, insufficient income documentation, and enrollment in Medicare. Overall savings for our patient population, was estimated to be $1.2 million per year. Our teams invest in counseling time with the patient, phone time with sponsoring foundations, computer resources for implementing a program renewal database, and pharmacy handling of infusion medications.

Conclusion:

This study addresses the impact of a dedicated effort, within a community clinic setting, to expedite access to medications through a streamlined PAP. Outpatient drug costs for rheumatic diseases are important to target when containing overall direct health care costs. Our observations take this further to show a dedicated health care team can assist limited resource patients with accessing high cost biologics. Benefits from our program extend beyond immediate financial relief – there is educational value for rheumatology trainees and protected free time for clinical pharmacists which can used for teaching, clinical oversight, and academic scholarship.

In conclusion, investing resources to support individuals with limited resources in securing of assistance is a successful endeavor. Further research is necessary to capture the downstream benefits of this effort.

Disclosure: S. Cerritos, None; Y. Ruiz-Perdomo, None; N. Tobar, None; A. Biehl, None; J. D. Katz, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/patient-assistance-program-outcomes-in-a-community-clinic-setting

Abstract Number: 197

Process Evaluation of the Making It Work Program, an Online Program to Help People with Inflammatory Arthritis Remain Employed

Kathy Tran¹, Xi yuan Li², Xiang Chain Seah³, Catherine Backman⁴, Brendan vanAs³, Pam Rogers², Monique Gignac⁵, John M. Esdaile³, Carter Thorne⁶, Linda Li² and Diane Lacaille⁷, ¹Simon Fraser University, Arthritis Research Canada, Richmond, BC, Canada, ²Rheumatology, Arthritis Research Canada, Richmond, BC, Canada, ³Arthritis Research Canada, Richmond, BC, Canada, ⁴Rehab Medicine,
SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Health Services Research Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Inflammatory arthritis (IA) commonly affects ability to work, yet few arthritis services exist addressing employment. We report on the process evaluation of the Making it Work program, an online self-management program to help people with IA deal with employment issues, performed in the context of a RCT testing its effectiveness at preventing work disability and improving at-work productivity.

Methods: Participants, recruited from rheumatology practices, a consumer organization (Arthritis Consumer Experts) and advertisements, were eligible if they had IA, were currently employed, aged 18-59, concerned about their ability to work. The program consists of five e-learning modules; five on-line group meetings using video conferencing led by a vocational rehabilitation counsellor (VRC); individual consults with an occupational therapist (OT) for an ergonomic work assessment and with a VRC.

Results:
All program participants by 06/17 were included (N=236) [80% female, mean(SD) age: 45(10) years, RA:52%, AS:19%, PsA:15%, SLE:14%]. All participants Jan-Dec 2016 completed a feedback survey post program (n=69). Group meetings were successfully conducted online. Overall, participation was good. Median(25;75Q) no. group meetings attended: 4(3;5), with highest attendance in the first (86%) and lowest in the fourth (63%) meetings. Reasons for not attending included work obligations, health issues, family commitments, or other time constraints. 91% and 88% met with the OT and VRC. Completion of e-learning modules [Median(25;75Q) % of total slides viewed] ranged from 73(0-100)% for module 4, to 100(30;100)% for modules 1 & 2. Not all content is relevant to all, depending on disease and job characteristics.

Overall, participants were highly satisfied with the program. 94% would recommend it to others. Median [25Q;75Q] usefulness ratings (0-10, 0=not at all, 10=very useful) were: 8 [7;10] for online modules; 9[7.5;10] for group meetings; 8 [7;10] each for ergonomic & VRC assessments. Median time to complete each module was 60 min. Satisfaction with online group meetings was high: 93% were satisfied with facilitation; 87% with group dynamic; 84% were comfortable with the online format. Median [25Q;75Q] ratings (1-10) for ability to follow group discussion: 10 [9;10]; getting to know other participants: 7 [7;10]; feeling listened to and understood: 9 [8;10]; feeling that group was supportive: 9 [7;10].

Conclusion:
Overall, online delivery of the Making it Work program was feasible and participants were highly satisfied. Our study demonstrates that self-management programs can be successfully delivered using an online format, which facilitates wider dissemination, greater convenience to patients, and lower costs.

Disclosure: K. Tran, None; X. Y. Li, None; X. C. Seah, None; C. Backman, None; B. vanAs, None; P. Rogers, None; M. Gignac, None; J. M. Esdaile, None; C. Thorne, None; L. Li, None; D. Lacaille, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/process-evaluation-of-the-making-it-work-program-an-online-program-to-help-people-with-inflammatory-arthritis-remain-employed

Abstract Number: 198

The Impact of Electronic Consults (E-Consults) on Positive ANA Referrals in a Veteran Population

Veena Patel1,2, Diana Stewart2,3 and Molly Horstman1,2,4, 1Internal Medicine, Baylor College of Medicine, Houston, TX, 2Internal Medicine, Michael E. DeBakey VA Medical Center, Houston, TX, 3Internal Medicine and Pediatrics, Baylor College of Medicine, Houston, TX, 4Center for Innovations in Quality, Effectiveness and Safety (iQUEST), Houston, TX
First publication: September 18, 2017
Background/Purpose: Referrals to rheumatology for positive ANA in the absence of clinical signs and symptoms is a common practice, which may lead to unnecessary resource use and contribute to delays in patients seeing a rheumatologist. The electronic consult (E-consult) was developed for specialists to review a patient’s medical record and make recommendations without an in-person visit in an effort to improve access to timely care. The aims of this project are to assess how E-consults for positive ANA are being used in clinical practice, examine their impact on resource use, and evaluate if the introduction of E-consults improved wait times for in-person rheumatology visits.

Methods: Charts were reviewed for Veterans referred to the Houston VA outpatient rheumatology clinic from 1/2015-3/2017 with “positive ANA” as the reason for consult. Demographic data, referral information, relevant rheumatologic labs and imaging were recorded. Veterans’ final diagnoses were organized into the following categories: AARD (ANA-associated rheumatic disease), ORD (other rheumatic disease), no AARD or ORD, lost to follow-up or no definitive diagnosis at time of review. Lab costs for Veterans with no AARD or ORD were calculated using the cost to the Houston VA. The costs of consults were estimated using the 2017 Medicare National Fee Schedule. Imaging costs were estimated from the Healthcare Bluebook. An XmR control chart was created using average wait times for in-person clinic visits per month.

Results: A total of 139 Veterans had positive ANA outpatient consults. Figure 1 shows the number of patients with positive ANA consults and their final diagnosis category. 55/139 (40%) of Veterans received E-consults. 73% of patients with consults (86/139) did not have an AARD or ORD (n=43 E-consults, n=43 in-person visits). Of these, E-consults spent $1,992 more on lab tests, while clinic visits spent $5,074 more on imaging studies. Clinic visits were more likely to schedule follow-up visits and on average billed $99 more per visit. Figure 2 is a control chart showing special cause variation with >7 points below the line of central tendency (circled graph points), indicating that E-consults have made an impact on decreasing in-person visit wait times.

Conclusion: E-consults are an effective way to address positive ANA consults, which has helped decrease wait times for in-person rheumatology visits. E-consults did spend more on lab tests, but had less follow-up appointments and imaging use. Future studies should address patient satisfaction and PCP satisfaction with the E-consult process.
Disclosure: V. Patel, None; D. Stewart, None; M. Horstman, None.


Abstract Number: 199

**Incremental Direct Medical Costs of Systemic Lupus Erythematosus Patients in the Years Preceding Diagnosis and the Impact of Sex: A General Population-Based Study**

Natalie McCormick\(^1,2\), Carlo Marra\(^3\) and J. Antonio Avina-Zubieta\(^4\), \(^1\)Arthritis Research Canada, Richmond, BC, Canada, \(^2\)Pharmaceutical Sciences, The University of British Columbia, Vancouver, BC, Canada, \(^3\)School of Pharmacy, University of Otago, Dunedin, New Zealand, \(^4\)Division of Rheumatology, Department of Medicine, University of British Columbia, Vancouver, BC, Canada

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Sunday, November 5, 2017  
Session Title: Health Services Research Poster I  
Session Type: ACR Poster Session A  
Session Time: 9:00AM-11:00AM  

**Background/Purpose:**

Little is known about the healthcare costs of systemic lupus erythematosus (SLE) patients in the years leading up to SLE diagnosis. We estimated the incremental (extra) direct medical costs of a general population-based cohort of incident SLE for five years before diagnosis, and examined the impact of sex on these costs.

**Methods:**

Data Source: Our administrative data captured all provincially-funded outpatient encounters and hospitalisations (1990-2013), and all dispensed medications, for ALL residents of the province of British Columbia, Canada.

Sample: We assembled a population-based cohort of incident SLE: those with a new diagnosis of SLE from at least one hospitalisation or rheumatologist visit, or two non-rheumatologist visits, between Jan 2001 and Dec 2010, and no prior SLE diagnosis between Jan 1990 and Dec 2000. For each SLE case, we matched up to 5 non-SLE from the general population on age (±2 years), sex and calendar year of diagnosis. All persons had ≥ 5 years’ follow-up in the databases before index date (first SLE-coded encounter; random date for non-SLE).

Cost Calculation: Outpatient and prescription costs were summed directly from billing data. Case-mix methodology was used for hospitalisations.
Analysis:

We estimated the unadjusted incremental costs of SLE (difference in per-person costs between SLE and non-SLE) for the five pre-diagnosis/pre-index years (Y-5 to Y-1) and index year (Y0).

Generalised linear models were used to further adjust for socioeconomic status (SES), urban/rural and comorbidities between SLE and non-SLE, and evaluate the impact of sex on costs.

Results:

We included 3,632 incident SLE (86% female, mean age 49.6 years) and 18,152 non-SLE. Index-year (Y0) costs for SLE averaged $12,019 per-person (2013 CDN): 59% from hospitalisations, 24% outpatient, and 18% medications. Costs increased by 35% per year, on average, with the biggest increases in the two years before diagnosis (see Table). Adjusted cost ratios between SLE and non-SLE rose from 1.7 in Year -3 (Y-3) to 1.9 (Y-2), 2.4 (Y-1), and 4.0 in Y0.

Among non-SLE, adjusted costs were higher for females than males, but among SLE, males had higher costs, controlling for age, SES and previous year’s comorbidity score. SLE males had higher odds of hospitalisation than SLE females in Y-1 (OR=1.44, 95% CI=1.18-1.76), while non-SLE males had 15% lower odds. In Years -2 & -1, encounters with primary diagnosis of diabetes, or renal or cardiovascular disease accounted for 11% of costs for SLE males, vs. 5% for SLE females.

Adjusted M/F cost ratios in SLE were 1.15 (95% CI 1.03-1.29) in Y-2, 1.22 (1.11-1.35) in Y-1, and 1.44 (1.29-1.61) in Y0. When comparing costs of SLE and non-SLE, the Male*SLE interaction term was significant in all years.

Conclusion:

The incremental costs of SLE are considerable, even in the years prior to diagnosis. Unlike the general population, SLE males had higher costs than females, potentially from early comorbidities.
<table>
<thead>
<tr>
<th>N</th>
<th>Mean (SD) Age</th>
<th>Mean (SD) Baseline Charlson-Romano Comorbidity Score</th>
<th>Year Before SLE Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Year -5</td>
</tr>
<tr>
<td>All SLE</td>
<td>3,632</td>
<td>49.6 (15.9)</td>
<td>$3,073</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.42 (0.49)</td>
<td>($2,872-$3,273)</td>
</tr>
<tr>
<td>All Non-SLE</td>
<td>18,152</td>
<td>49.8 (15.4)</td>
<td>$1,709</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.14 (0.35)</td>
<td>($1,645-$1,772)</td>
</tr>
<tr>
<td>Cost difference</td>
<td>0.18</td>
<td></td>
<td>$1,364</td>
</tr>
<tr>
<td>SLE Females</td>
<td>3,111</td>
<td>49.1 (15.6)</td>
<td>$3,042</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.40 (0.49)</td>
<td>($2,826-$3,257)</td>
</tr>
<tr>
<td>Non-SLE Females</td>
<td>15,547</td>
<td>49.2 (15.1)</td>
<td>$1,746</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.13 (0.34)</td>
<td>($1,677-$1,815)</td>
</tr>
<tr>
<td>Cost difference</td>
<td>0.18</td>
<td></td>
<td>$1,296</td>
</tr>
<tr>
<td>SLE Males</td>
<td>521</td>
<td>52.9 (17.1)</td>
<td>$3,258</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.50 (0.50)</td>
<td>($2,710-$3,806)</td>
</tr>
<tr>
<td>Non-SLE Males</td>
<td>2,605</td>
<td>53.0 (17.0)</td>
<td>$1,485</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.17 (0.37)</td>
<td>($1,328-$1,641)</td>
</tr>
<tr>
<td>Cost difference</td>
<td>0.18</td>
<td></td>
<td>$1,773</td>
</tr>
</tbody>
</table>

Disclosure: N. McCormick, None; C. Marra, None; J. A. Avina-Zubieta, None.


Abstract Number: 200

Implementation and Evaluation of a Novel Nurse-Led Telemedicine Intervention for Dose Escalation of Urate-Lowering Therapy in Gout: A Clinical Practice Improvement Project

Sen Hee Tay1,2, Bernadette Poh Lee Low3, Pamela Shi Hui Tan2, Zhi Wei Khong2, Siew Hwa Chong4, Amelia Santosa1,2, Anita Yee Nah Lim1,2 and Gim Gee Teng2,5, 1 Division of Rheumatology, Department of Medicine, National University Hospital, National University Health System, Singapore, Singapore, Singapore, 2 Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore, Singapore, 3 Division of Primary Care, Department of Care Integration and Alliance, National University Hospital, National University Health System, Singapore, Singapore, Singapore, 4 Clinical Nursing Unit, National University Hospital, National University Health System, Singapore, Singapore, Singapore, 5 Division of Rheumatology, University Medicine Cluster, National University Health System, Singapore, Singapore, Singapore
Urate-lowering therapy (ULT) is the mainstay of gout treatment. In our clinics, time to achieve target serum urate (SU) level during ULT titration was 37 weeks, during which 15% of patients developed gout attacks requiring hospitalization and the time from last outpatient visit to incident hospitalization was 16 weeks. The suboptimal management may be due to infrequent follow-up during ULT. We implemented and evaluated the efficacy and safety of a novel nurse-led telemedicine intervention for dose escalation (DE) of ULT for gout patients in a real-life clinical practice.

Methods:
Consecutive gout patients fulfilling indications for ULT whose SU ≥ 360 µmol/L were approached. Patients with estimated GFR < 30 mL/min, cognitive impairment and immobility were excluded. A bundle of care was designed to support telemedicine as the main intervention led by a nurse. The bundle components included: nurse education; a safety program (SP) with 6 fortnightly phone calls for adverse drug reactions (ADRs); hotline service and virtual monitoring clinic (VMC) appointments. The VMC consisted of 6-weekly laboratory investigations at government clinics or hospital, protocolized DE of ULT and courier services for ULT. Patient satisfaction and adherence were assessed using a questionnaire survey of patient experience and Medication Adherence Report Scale (MARS-5), respectively. The primary outcome was the time to achieve target SU < 360 µmol/L, variables that trended towards a significant association (p < 0.1) were examined in a multivariable Cox regression model.

Results:
We recruited 100 gout patients from July 2016 to March 2017 with a median age of 52.5 years and 90% men; 53.0% were on pre-existing ULT. The median time to target SU was 19.0 weeks (IQR 17.5-20.5), with no hospitalizations for gout attacks. One patient had an ADR, 3 SP phone calls were made to the patient and allopurinol was stopped immediately after the rash developed. The average Likert summed scores were high and similar to the overall patient satisfaction. Cox regression model revealed that high levels of education (university versus primary), absence of gout attacks, lower baseline SU and number of VMC appointments in 6 months were associated with attainment of target SU.

Conclusion:
Our study is the first to describe the utility of telemedicine in gout care. A nurse-led telemedicine intervention is effective, safe and well-accepted for the management of patients with gout. Telemedicine has the potential to improve access to care for gout patients, thereby decreasing burden of disability and overall healthcare utilization.
Table 1. Results of a bundled telemedicine intervention for the management of gout. Data are median (95% CI or IQR).

<table>
<thead>
<tr>
<th>Time to achieve target SU (weeks)</th>
<th>19.0 (17.5-20.5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All gout patients</td>
<td></td>
</tr>
<tr>
<td>Gout patients naïve to ULT</td>
<td>20.0 (16.4-23.6)</td>
</tr>
<tr>
<td>Gout patients on ULT</td>
<td>14.0 (8.0-20.0)</td>
</tr>
<tr>
<td>Duration of follow-up (weeks)</td>
<td>14.0 (8.0-23.0)</td>
</tr>
<tr>
<td>No. of VMC appointments</td>
<td>2.0 (1.0-3.0)</td>
</tr>
<tr>
<td>No. of ULT dose escalations</td>
<td>2.0 (1.0-3.0)</td>
</tr>
<tr>
<td>Gout patients achieving target SU</td>
<td>64 (64.0)</td>
</tr>
<tr>
<td>No. of VMC appointments to achieve target SU in 6 months</td>
<td>3.8 (2.7-4.8)</td>
</tr>
<tr>
<td>All gout patients</td>
<td></td>
</tr>
<tr>
<td>Gout patients naïve to ULT</td>
<td>3.8 (2.5-4.4)</td>
</tr>
<tr>
<td>Gout patients on ULT</td>
<td>4.0 (2.8-4.8)</td>
</tr>
<tr>
<td>No. of ULT DIs to achieve target SU in 6 months</td>
<td>3.7 (2.1-4.4)</td>
</tr>
<tr>
<td>All gout patients</td>
<td></td>
</tr>
<tr>
<td>Gout patients naïve to ULT</td>
<td>3.9 (2.8-4.4)</td>
</tr>
<tr>
<td>Gout patients on ULT</td>
<td>3.1 (1.9-2.3)</td>
</tr>
<tr>
<td>Gout attacks</td>
<td>35 (35.0)</td>
</tr>
<tr>
<td>No. of gout attacks</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>65 (65.0)</td>
</tr>
<tr>
<td>1</td>
<td>26 (26.0)</td>
</tr>
<tr>
<td>2</td>
<td>6 (2.0)</td>
</tr>
<tr>
<td>3</td>
<td>2 (2.0)</td>
</tr>
<tr>
<td>4</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Hospitalizations for gout attacks</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>No. of SP phone calls</td>
<td>6 (4.0-6.0)</td>
</tr>
<tr>
<td>ADRs detected by SP</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Patient satisfaction</td>
<td></td>
</tr>
<tr>
<td>Average Likert summed score (1-5)</td>
<td>3.92 (3.67-4.46)</td>
</tr>
<tr>
<td>Overall satisfaction score (1-5)</td>
<td>4.00 (4.00-5.00)</td>
</tr>
<tr>
<td>MARS-5 (5-25)</td>
<td>24.0 (23.00-25.00)</td>
</tr>
</tbody>
</table>

Table 2. Multivariable analysis of factors associated with achieving SU < 360 μmol/L.

<table>
<thead>
<tr>
<th></th>
<th>Adjusted HR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group &lt; 40 years (≤ 40 years to referent)</td>
<td>1.58 (0.75-3.35)</td>
<td>0.223</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chinese</td>
<td>0.55 (0.16-1.80)</td>
<td>0.311</td>
</tr>
<tr>
<td>Malay</td>
<td>0.75 (0.17-3.24)</td>
<td>0.699</td>
</tr>
<tr>
<td>Indian</td>
<td>2.23 (0.33-15.32)</td>
<td>0.414</td>
</tr>
<tr>
<td>Others</td>
<td>1</td>
<td>0.227</td>
</tr>
<tr>
<td>Educational level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nil</td>
<td>0.56 (0.18-1.73)</td>
<td>0.312</td>
</tr>
<tr>
<td>Primary</td>
<td>0.33 (0.12-0.88)</td>
<td>0.027</td>
</tr>
<tr>
<td>Secondary or equivalent</td>
<td>0.62 (0.27-1.40)</td>
<td>0.250</td>
</tr>
<tr>
<td>Pre-university or polytechnic</td>
<td>0.51 (0.21-1.27)</td>
<td>0.150</td>
</tr>
<tr>
<td>University and above</td>
<td>1</td>
<td>0.232</td>
</tr>
<tr>
<td>Pre-existing ULT</td>
<td>1.90 (1.00-3.60)</td>
<td>0.050</td>
</tr>
<tr>
<td>Gout attacks</td>
<td>0.50 (0.27-0.94)</td>
<td>0.031</td>
</tr>
<tr>
<td>Baseline SU</td>
<td>0.99 (0.99-1.00)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>No. of VMC appointments in 6 months</td>
<td>2.63 (1.95-3.35)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Disclosure: S. H. Tay, None; B. P. L. Low, None; P. S. H. Tan, None; Z. W. Khong, None; S. H. Chong, None; A. Santosa, None; A. Y. N. Lim, None; G. G. Teng, None.


Abstract Number: 201
Computer Learning (artificial intelligence) to Create a Computer-Based Triage Tool Classifying Referrals As Inflammatory or Non-Inflammatory Requiring Only Patient Reported Information

Cindy Kim1, Tanner Bohn2, Charles X. Ling3, Nikhil Chopra4 and Janet E. Pope5, 1Faculty of Medicine, University of Western Ontario, London, ON, Canada, 2University of Western Ontario, London, ON, Canada, 3Computer Sciences, University of Western Ontario, London, ON, Canada, 4Rheumatology, Private Practice, London, ON, Canada, 5Department of Medicine, Division of Rheumatology, University of Western Ontario, St Joseph’s Health Care, London, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Health Services Research Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: To determine if a computer-based triage tool can accurately classify referrals as inflammatory or non-inflammatory using information obtained from the patient; not requiring assessment by healthcare workers.

Methods: Patient referrals to a single rheumatologist were studied. Patient lists for 11 commonly encountered diagnoses [rheumatoid arthritis (RA), psoriatic arthritis, lupus, osteoarthritis, gout, soft tissue rheumatism (i.e. arthralgia NYD, tendonitis, mechanical low back pain), ankylosing spondylitis (AS), polymyalgia rheumatica (PMR), and fibromyalgia] were created. The diagnoses of RA, lupus, AS, PMR, and other seronegative spondyloarthopathies were classified as inflammatory arthritis (non-crystalline) (IA). At least five patient charts for each diagnosis were reviewed and eligible for study if a self-reported patient pain diagram was also completed. The following patient-reported information was collected from each referral: age, sex, symptom duration, and pain diagram. Lab results for ESR, CRP, ANA, ENA, anti-DNA, anti-CCP antibodies, urate, and rheumatoid factor were also collected where available. Machine learning techniques were used to create a logistic regression model to classify referrals as inflammatory or non-inflammatory. Backward feature selection was used to enhance model performance by identifying features most predictive of referral state. Leave-one-out cross-validation was used to predict model performance. The models were subsequently evaluated on prospectively collected patient data from 20 new referrals seen after the creation of the triage tool, where data was coded blindly to patients’ diagnosis.

Results: In creation of the triage tool, 168 patient charts were used; 73 were classified as IA after being seen by a rheumatologist. The triage tool correctly classified 65 of 73 referrals as inflammatory using patient-reported information (model 1) (sensitivity 89%, specificity 52%). When the referral tool was reevaluated using laboratory markers in addition to the information obtained from the patient (model 2), 67 referrals were correctly classified as inflammatory (sensitivity 92%, specificity 63%). When model 1 was tested on 20 prospective patients, all 6 patients with IA were correctly classified (sensitivity 100%, specificity 52%). Model 2 correctly classified 14 patients (who had lab values present) including 5 patients with IA (sensitivity 83%, specificity 64%). The results are shown in table. Further prospective multi-site testing is ongoing.

Conclusion: A referral tool that can be entered into a database for computer assessment has good sensitivity to detect high priority referrals from data that can be obtained directly from patients and ascertained by non-healthcare workers. This may be of benefit in areas of limited resources and long waiting lists to see a rheumatologist.

<table>
<thead>
<tr>
<th></th>
<th>Model 1</th>
<th></th>
<th>Model 2</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Predicted (N=168)</td>
<td>Actual (N=20)</td>
<td>Predicted (N=168)</td>
<td>Actual (N=20)</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>89.0%</td>
<td>100%</td>
<td>91.8%</td>
<td>83.3%</td>
</tr>
<tr>
<td>Specificity</td>
<td>51.6%</td>
<td>35.7%</td>
<td>63.2%</td>
<td>64.3%</td>
</tr>
<tr>
<td>NPV</td>
<td>86.0%</td>
<td>100%</td>
<td>90.9%</td>
<td>90.0%</td>
</tr>
<tr>
<td>PPV</td>
<td>58.6%</td>
<td>40.0%</td>
<td>65.7%</td>
<td>50.0%</td>
</tr>
<tr>
<td>IA Referrals Correctly Classified</td>
<td>65/73</td>
<td>6/6</td>
<td>67/73</td>
<td>5/6</td>
</tr>
</tbody>
</table>

Disclosure: C. Kim, None; T. Bohn, None; C. X. Ling, Director of Data Mining and Business Intelligence Lab, 6; N. Chopra, Amgen, Novartis, UCB, AbbVie, Janssen, 5; J. E. Pope, AbbVie, Amgen, Bayer, BMS, Celtrion, Eli Lilly and Company, Merck, Novartis, Pfizer, Roche, UCB, 5;Amgen, Bayer, BMS, GSK, Merck, Novartis, Pfizer, Roche, 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/computer-learning-artificial-intelligence-to-create-a-computer-based-triage-tool-classifying-referrals-as-inflammatory-or-non-inflammatory-requiring-only-patient-reported-information
Analysis of Provider-to-Provider Variability in the Use of Biologics: Data from the Rheumatology Informatics System for Effectiveness Registry

Douglas White

Michael Evans

Gabriela Schmajuk

Rachel Myslinski

Salahuddin Kazi

Jinoos Yazdany

Gundersen Health System, Onalaska, WI

University of California San Francisco, San Francisco, CA

San Francisco VA Medical Center, University of California San Francisco, San Francisco, CA

Practice, Advocacy, & Quality, American College of Rheumatology, Atlanta, GA

University of Texas Southwestern, Dallas, TX

Medicine/Rheumatology, University of California San Francisco, San Francisco, CA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017

Session Title: Health Services Research Poster I

Session Type: ACR Poster Session A

Session Time: 9:00AM-11:00AM

Background/Purpose: Variations in biologic prescribing habits by rheumatology providers may account in part for variability in direct cost of care for patients with rheumatoid arthritis (RA). We used data from the Rheumatology Informatics System for Effectiveness (RISE) registry to estimate variability in biologic use among US rheumatologists.

Methods: RISE is a national, EHR-enabled registry that passively collects and houses data on all patients seen by participating practices and thereby avoids sampling bias. As of December 2016, RISE was connected to 632 providers (99.5% of which were physicians) representing an estimated 16% of the US workforce. We calculated, on a per-provider basis, the proportion of RA patients prescribed a biologic or tofacitinib at least once between January and December 2016 (inclusive). The population of patients in the denominator, numbering 58,055 across all participating practices, was defined as those assigned an ICD code for RA in at least two separate encounters in 2016. Consistent with other national performance analyses, providers who saw fewer than 30 RA patients (315 of the 632 RISE-connected providers) were excluded. Few patients saw >1 provider, but in those instances prescriptions were attributed only to the provider with the plurality of RA-coded visits; therefore, each patient was attributed to only one provider.

Results: Provider-to-provider variability in the proportion of RA patients who received a biologic prescription is shown in Figure 1. Across the US in 2016, an average of 38% of each provider’s RA patients were prescribed a biologic but the fraction of patients prescribed a biologic ranged from 0 to 79%. A regional breakdown is shown in Table 1 and demonstrates statistically significant geographic variability as well.

Conclusion: These data estimate the degree to which biologic prescription patterns vary across the US. In light of existing data indicating that biologics account for the majority of the direct cost in providing care for US patients with RA, and ongoing initiatives such as the Merit Incentive Payment System to incorporate measures of resource utilization in payment reform, this study provides initial benchmarking information for rheumatology providers in the US. Our study does not address quality of care. Future studies adjusted for case mix and disease activity will be required to estimate variability in the value (quality divided by cost) of care.

Figure 1. Fraction of RA patients prescribed biologics, by provider. Red line indicates the mean.

Table 1. Fraction of RA patients prescribed biologics, on a per-provider basis, by region.
### Intensive Care Unit Admissions Among Patients with Rheumatic Diseases at a Tertiary Care Center

Ali Al-Marzooq¹, Mohammed Al-Charakh¹, Sumediah Nzounkwelle², Bikash Bhattarai³, Mark McPherson² and Konstantinos Parperis⁴,
¹Internal Medicine, Maricopa Integrated Health System, Phoenix, AZ, ²Maricopa Integrated Health System, Phoenix, AZ, ³Research, Maricopa Integrated Health System, phoenix, AZ, ⁴Rheumatology, Maricopa Integrated Health System and University of Arizona College of Medicine, Phoenix Campus, phoenix, AZ.

**First publication:** September 18, 2017

### SESSION INFORMATION

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Health Services Research Poster I  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Patients with autoimmune rheumatic diseases have higher risk of developing organ failure and may require admission to intensive care unit (ICU), however there are only few studies in the US addressing this topic. The aim of our study is to determine reasons of admission to the ICU, identify potential risk factors associated with mortality and assess outcomes of patients with rheumatic disease admitted to the ICU.

**Methods:**

We conducted a retrospective chart review of patients admitted to the ICU from 2011 to 2016 using ICD-9/ICD-10 codes for morbidities. We identified patients with new or established diagnosis of a rheumatic disease. Patient’s data included demographics, ICU admission diagnoses, co-morbidities, organ involvement, laboratory studies, length of stay in ICU/hospital, complications and immunosuppressive regimen. Short-term (ICU/30-day post-ICU) stay and long-term (1-year post) outcomes were assessed.

**Results:**

A total of 80 rheumatic disease patients were identified with mean age of 48.8 (range 19-84), 67% were female, 56% were Hispanic. Most common disease associated with ICU admission was SLE in 34 patients (42%), followed by RA 21(26%). 10(12%) had Systemic Vasculitis.
Sepsis was the leading cause of ICU admission with 25 patients (31%), followed by acute hypoxemic respiratory failure due to pneumonia 8 (10%) and congestive heart failure/CHF 8 (10%). Others were respiratory failure due to underlying disease 6 (8%) and cardiac tamponade 6 (8%). Less common included cerebrovascular events (4), metabolic disturbances (3), Steven’s Johnson (3), meningoencephalitis (3), encephalopathy (3), pulmonary hypertension (2), diffuse alveolar hemorrhage (2), pancreatitis (2), cardiac arrest (2), anemia (1), hypertensive emergency (1) and pulmonary embolism (1).

45% of patients required mechanical ventilation and 31% vasopressor support. Mean ICU stay was 7 days and hospital stay 13.7 days. 16 of 80 patients (20%) died in ICU, 4 (5%) died 30 days post-ICU and 6 (7.5%) within 1-year of ICU stay, resulting into an overall mortality of 33% by the end of 1-year. Higher mortality found in patients with DM (40%) and SLE (24%). Predictors of increased mortality during ICU stay were cardiovascular involvement (p=0.01), renal involvement (p=0.032) and requirement for mechanical ventilation (p<0.01). Worse outcome 30 days post ICU stay was influenced by development of venous thromboembolic disease (VTE) during hospitalization (p=0.03). At 1-year post ICU-stay, survival for patients with CHF was 76.5% compared to 95.7% without CHF (p=0.041).

Conclusion:

Our findings indicated that SLE is the most common rheumatic disease associated with ICU admission, followed by RA. Sepsis, respiratory failure due to pneumonia/CHF were the most common causes leading to ICU admission. Factors associated with higher mortality were requirement for mechanical ventilation, renal and cardiovascular involvement on admission, development of VTE and history of CHF.

Disclosure: A. Al-Marzooq, None; M. Al-Charakh, None; S. Nzuonkwelle, None; B. Bhattarai, None; M. McPherson, None; K. Parperis, None.


Abstract Number: 204

Healthcare Utilization Among Young Adults Transitioning from Pediatric to Adult Care in a Safety Net Population

Nicole Bitencourt1, Una E. Makris1,2, Tracey Wright3,4 and E. Blair Solow1, 1UT Southwestern Medical Center, Dallas, TX, 2Department of Medicine, VA North Texas Health Care System, Dallas, TX, 3Pediatrics/Rheumatology, UT Southwestern Medical Center, Dallas, TX, 4Texas Scottish Rite Hospital for Children, Dallas, TX

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Health Services Research Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

The transition from pediatric to adult care for young adults with chronic illness is a vulnerable period especially among socioeconomically disadvantaged populations. As part of a quality improvement project, we sought to characterize patterns of healthcare utilization, namely hospitalizations and emergency department (ED) visits during the transfer period between pediatric and adult rheumatologic care in a large public safety net healthcare system.

Methods:

Using an electronic medical record, 95 patients were identified as being between 17 and 21 years of age at the time of referral to adult rheumatology between 3/2014 and 4/2017. Following chart review, 65 of these patients were confirmed as transitioning between pediatric and adult care. Data on disease categories, demographics, medical coverage, and referring provider were extracted and comparisons made regarding hospitalizations and ED visits (excluding visits which were clearly unrelated to an underlying rheumatic disease) by using unpaired t-test and one-way analysis of variance.

Results:
Among the 65 patients transitioning to adult care, 72% were female, 74% were Hispanic, 49% had a connective tissue disease (CTD), 49% had juvenile idiopathic arthritis (JIA), 75% had Medicaid, and 74% were referred by a pediatric rheumatologist (Table 1). Hospitalizations and ED visits were common (20% and 28% of patients, respectively) during the transfer period, and were more common among those with a CTD (compared to JIA), and in blacks (compared with Hispanics and whites) (Figure 1). Those with a lapse in medical coverage during the transfer period and lack of coverage at the time of initial referral had significantly higher healthcare utilization than those with consistent medical coverage. Those referred to adult care by a pediatric rheumatologist had significantly fewer hospitalizations and ED visits than those referred by other clinicians (Figure 2).

Conclusion:

Hospitalizations and ED visits are especially prevalent among patients transitioning from pediatric to adult rheumatologic care. Factors associated with high utilization included having a CTD, black race, lapse in medical coverage during the transfer period, lack of coverage at initial referral to adult care, and being referred by someone other than a pediatric rheumatologist.

<table>
<thead>
<tr>
<th>Table 1 Demographic Data</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>18 (28)</td>
</tr>
<tr>
<td>Female</td>
<td>47 (72)</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>48 (74)</td>
</tr>
<tr>
<td>White</td>
<td>8 (12)</td>
</tr>
<tr>
<td>Black</td>
<td>7 (11)</td>
</tr>
<tr>
<td>Asian</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Age at referral, mean, years</td>
<td></td>
</tr>
<tr>
<td>Referred by pediatric rheumatology</td>
<td>18.5</td>
</tr>
<tr>
<td>Referred by another clinician</td>
<td>19.6</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
</tr>
<tr>
<td>CTD (SLE, JDM, scleroderma, Sjogren’s)</td>
<td>32 (49)</td>
</tr>
<tr>
<td>JIA</td>
<td>32 (49)</td>
</tr>
<tr>
<td>Periodic Fever Syndrome</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Medical coverage at first referral</td>
<td></td>
</tr>
<tr>
<td>Medicaid</td>
<td>49 (75)</td>
</tr>
<tr>
<td>Title V Maternal &amp; Child Health Grant</td>
<td>6 (9)</td>
</tr>
<tr>
<td>Children’s Health Insurance Program (CHIP)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Dallas County/Parkland support</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Affordable Health Care Act Plan</td>
<td>1 (2)</td>
</tr>
<tr>
<td>None</td>
<td>5 (8)</td>
</tr>
<tr>
<td>Referring physician</td>
<td></td>
</tr>
<tr>
<td>Pediatric rheumatology</td>
<td>48 (74)</td>
</tr>
<tr>
<td>All other clinicians (ED physician, hospitalist, primary care)</td>
<td>17 (26)</td>
</tr>
</tbody>
</table>

CTD: connective tissue disease, JIA: juvenile idiopathic arthritis, SLE: systemic lupus erythematosus, JDM: juvenile dermatomyositis
What Is the Value of the Prior Authorization Process in Specialty Drug Therapy?

Shally Alendry1, Melad Qodsi1, Travis Hunerdossse1 and Eric M. Ruderman2,3, 1Northwestern Medicine, Chicago, IL, 2Northwestern University Feinberg School of Medicine, Chicago, IL, 3Medicine/Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Health Services Research Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: As the use of specialty pharmacy drugs has grown, many insurers have instituted strict prior authorization requirements, ostensibly to ensure that the right patients get the right medications at the right point in their disease process. Rheumatologists, dermatologists, and patients, however, often question whether this process creates logistical barriers that delay treatment. Northwestern Medicine established a specialty pharmacy in 2014 to provide medication directly to patients at the institution. Rheumatology and dermatology clinics began working with this specialty pharmacy in 2015 and now utilize it for all new specialty drug prescriptions. When possible, medications are filled directly through the health system pharmacy. When insurers require use of an alternative specialty pharmacy, the prescription is transferred, but the NM specialty pharmacist continues to help guide the prior authorization steps. We analyzed the number of prescriptions approved or denied through this process, hypothesizing that few medications requiring prior authorization were ultimately denied.

Methods: We reviewed prior authorization requests from 6/1/2015 through 6/12/2017. We included primarily prescriptions for approved indications, at labeled doses. Indications included ankylosing spondylitis, juvenile idiopathic arthritis, psoriatic arthritis, rheumatoid arthritis, and psoriasis.

Results: Of the 3192 prescriptions handled by the specialty pharmacy, 840 did not require prior authorization. A total of 2,352 prior authorizations were submitted; 2,113 of these were approved with the initial request, and 239 (10.1%) were denied. Appeals were submitted for 126 of these denials in rheumatology; the denial was overturned in 83 cases, upheld in 40, and 3 are pending. Dermatologists appealed fewer denials. As of the data cut, 2196 (93.4%) of the prescriptions submitted for prior authorization had been approved and filled. Results for individual diseases are shown in Table 1.

Conclusion: In our academic medical practice, rheumatology and dermatology specialty medications prescribed for approved indications are seldom denied, and most of the denials are reversed when appealed. These findings suggest that the time spent on prior authorizations, at
substantial cost to the practices involved, may be unnecessary, as appropriate treatments are rarely denied. Insurers may have other interests in the prior authorization process besides the stated reason of restricting inappropriate or unnecessary prescriptions. There appears to be little value in the prior authorization process for rheumatology- or dermatology-specific specialty drugs prescribed in an academic practice. A more streamlined approach could limit wasted time and effort, suggesting a need for exploration of alternative methods in partnership with payers.

Table 1. Prior Authorization Status for Specialty Drugs in Rheumatology and Dermatology

<table>
<thead>
<tr>
<th>Disease</th>
<th>Approved</th>
<th>Denied</th>
<th>Not Needed</th>
<th>Appeal Granted</th>
<th>Appeal Denied</th>
<th>Appeal Pending</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ankylosing Spondylitis</td>
<td>133</td>
<td>11</td>
<td>45</td>
<td>2</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Juvenile Idiopathic Arthritis</td>
<td>17</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>648</td>
<td>103</td>
<td>288</td>
<td>8</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Psoriatic Arthritis</td>
<td>253</td>
<td>31</td>
<td>78</td>
<td>20</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
<td>1062</td>
<td>92</td>
<td>425</td>
<td>51</td>
<td>24</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>2113</td>
<td>239</td>
<td>840</td>
<td>83</td>
<td>40</td>
<td>3</td>
</tr>
</tbody>
</table>

Disclosure: S. Alendry, None; M. Qodsi, None; T. Hunerdossse, None; E. M. Ruderman, Pfizer Inc, 5,Roche Pharmaceuticals, 5,Seattle Genetics, 5,Abbott Immunology Pharmaceuticals, 5,Amgen, 5,Pfizer Inc, 2,Bristol-Myers Squibb, 5,Janssen Pharmaceutica Product, L.P., 5,Eli Lilly and Company, 5,Novartis Pharmaceutical Corporation, 5.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/what-is-the-value-of-the-prior-authorization-process-in-specialty-drug-therapy

Abstract Number: 206

Real World IGRA Testing in Rheumatology Practice

Paul DeMarco\textsuperscript{1,2}, Megan Bishop\textsuperscript{3}, Ashling Smith\textsuperscript{4}, Herbert S. B. Baraf\textsuperscript{4,5}, Andrew Gregory DeMarco\textsuperscript{6}, Temitope Ademola\textsuperscript{7}, Deborah Contreras\textsuperscript{8}, Adalisa Enriquez RMA\textsuperscript{1}, Lisa Klein\textsuperscript{1}, Kayra Perez\textsuperscript{1}, Sandra Ventura\textsuperscript{1}, Janice Whyte-Whitworth\textsuperscript{1}, Vince Calhoun\textsuperscript{1}, Theresa Bass Goldman\textsuperscript{1} and Alan K Matsumoto\textsuperscript{1,9}, 1The Center for Rheumatology and Bone Research, Wheaton, MD, 2Division of Rheumatology, Department of Medicine, Georgetown University School of Medicine, Washington, DC, 3Clinical Trials, The Center for Rheumatology and Bone Research, Wheaton, MD, 42730 University Blvd West, Suite 306, The Center for Rheumatology and Bone Research, Wheaton, MD, 5Department of Medicine, George Washington University School of Medicine, Washington, DC, 6Department of Biochemistry and Molecular Cellular Biology, Georgetown University Department of Biochemistry and Molecular Cellular Biology, Washington, DC, 7The Center for Rheumatology and Bone Research, Washington, DC, 82730 University Boulevard West, Suite 306, The Center for Rheumatology and Bone Research, Wheaton, MD, 9Department of Medicine, Division of Rheumatology, Johns Hopkins School of Medicine, Baltimore, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Health Services Research Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Mycobacterium tuberculosis (MTb) screening is routine for clinical trial protocols, & authorization for immunomodulators use by health insurances. Real world data is needed to guide clinicians and researchers in appropriate test choice. The two interferon gamma release
assays (IGRAs) available to screen for MTb, QuantiFERON TB Fold In-Tube test (QFT-G) & SPOT TB (T-Spot), rely on an uncompromised immune system. Both, however, have a “+,” “−,” & “indeterminate (IND)” or in TSpot, “borderline” result. IND or borderline values have been theorized to result from an immunocompromised state, but the literature varies with regard to the effect of immunomodulation, particularly with corticosteroids, disease-modifying anti-rheumatic medications (DMARDs) and biologic response modifiers (BRMs).

**Methods:** The Center for Rheumatology and Bone Research (CRBR) obtained IRB review / waiver to conduct a retrospective chart review from 2014 to 2016. CRBR focused on care provided by Arthritis and Rheumatism Associates P.C. regarding medication use at the time of an IGRA. Data included IGRA type, test result (“+”, “−” & IND/borderline), & medication use. Medications were divided by corticosteroid (prednisone or methylprednisolone), DMARD use (including but not limited to hydroxychloroquine, sulfasalazine, MTX, azathioprine, leflunomide, cyclosporine) and exposure to a BRM (aka anti-TNFα therapy [such as etanercept, adalimumab, infliximab, certolizumab, golimumab], tocilizumab, abatacept rituximab and tofacitinib). A medication was considered active at the time of the laboratory if there were evidence of use within 1 month of testing. Statistical Analysis was performed using a student’s z-test as well as Chi-square analysis.

**Results:**

A total of 796 IGRAs were reported. There were 722 QTF-G tests and 74 Tspot drawn. Negative QTF-G values occurred in 643/722 (89%), equally distributed between those on & off immunomodulators. Positive QTF-G values occurred in 41/722 (5.6%), equally distributed between those on & off immunomodulators. IND QFT-G occurred in 38/722 (5.9%); the distribution was imbalanced. IND QTF-G occurred in 24/38 (63 %) on immunomodulators while IND QTF-G occurred in 14/38 (37%) with p=0.0087. IND QTF-G were more likely to occur during corticosteroid + DMARD / BRM treatment, occurring in 19/38 (50%) vs.DMARD ± BRM without corticosteroid, which occurred in 5/38 (13%) with p<0.025. This effect was not seen in non-steroid DMARD or non-steroid BRM treated cohort. This effect was not observed in the Tspot cohort, as IND / border line values occurred in 1/74 on immunomodulators while 2/72 subjects were not exposed to immunomodulators.

**Conclusion:**

Our cohort demonstrated positive, negative and IND rate similar to other published studies. However, our large QTF-G cohort demonstrated a statistically significant difference in IND values while taking immunomodulators, largely related to steroid exposure. Our smaller Tspot cohort did not demonstrate this effect, but this may have related to the cohort size. Further study to guide IGRA choice is warranted, but clinicians should consider Tspot over QTF-G when the subject is exposed to corticosteroid within a month of testing.

**Disclosure:** P. DeMarco, None; M. Bishop, None; A. Smith, None; H. S. B. Baraf, None; A. G. DeMarco, None; T. Ademola, None; D. Contreras, None; A. Enriquez RMA, None; L. Klein, None; K. Perez, None; S. Ventura, None; J. Whyte-Whitworth, None; V. Calhoun, None; T. Bass Goldman, None; A. K. Matsumoto, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/real-world-igra-testing-in-rheumatology-practice](http://acrabstracts.org/abstract/real-world-igra-testing-in-rheumatology-practice)

**Abstract Number:** 207

**Direct Medical Costs of Systemic Lupus Erythematosus in South Korea**

So-Yeon Park¹ and Sang-Cheol Bae², ¹Department of Rheumatology, Myongji Hospital, Seonam university, Goyang, Korea, Republic of (South), ²Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South)

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Health Services Research Poster I  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Systemic lupus erythematosus (SLE) has very high economic burdens on society and healthcare system. The aim of this study was to estimate the annual direct costs and predictors of cost in Korean patients with SLE.

**Methods:** This study used a national insurance claims database during the period from 2006 to 2010. Information was taken from the Korea National Health Insurance (KNHI) Claims Database of the Health Insurance Review and Assessment Service (HIRA). Factors associated with the direct medical costs were analyzed by using multiple regression and multivariate logistic regression.

**Results:** A total of 13,047 SLE patients were mainly analyzed. The estimated total annual direct medical costs amounted to $2,240 (2010 US dollars), of which 47.1% was accounted for by inpatient costs and 52.9% by outpatient costs. Among the cost domains for total direct medical costs, the biggest component was the costs of medication. The mean medication costs were $983, which accounted for 43.9% of the
total healthcare costs, followed by costs for diagnostic procedures and tests, accounting for 32.8% of the total. For the type of insurance, national health insurance were 92%, and medical aid were 8%. Total reimbursement rates of patients with SLE were 86.4%, and copayment comprised 13.6%, respectively. Reimbursement rates have shown a tendency to increase, whereas, out-of-pocket was decreasing gradually each year between 2006 and 2010. In the multivariate regression analyses, the predictors of increased direct costs were male sex, medical aid-insurance type, more comorbidity disease, and the use of immunosuppressant including steroids.

Conclusion: We have reported on the first population-based cost study of SLE patients in South Korea. The results of this study will contribute to a better understanding of the economic burden of SLE, and should provide information that is useful when allocating healthcare resources.

Table 1. Annual direct medical costs* in patients with SLE, 2006–2010 (US $)

<table>
<thead>
<tr>
<th></th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=9,878)</td>
<td>(n=10,555)</td>
<td>(n=11,375)</td>
<td>(n=12,103)</td>
<td>(n=13,047)</td>
</tr>
<tr>
<td>Outpatient</td>
<td>940</td>
<td>1,017</td>
<td>1,046</td>
<td>1,118</td>
<td>1,184</td>
</tr>
<tr>
<td>Inpatient</td>
<td>993</td>
<td>1,065</td>
<td>1,138</td>
<td>1,039</td>
<td>1,056</td>
</tr>
<tr>
<td>Total direct costs</td>
<td>1,993</td>
<td>2,082</td>
<td>2,184</td>
<td>2,157</td>
<td>2,240</td>
</tr>
</tbody>
</table>

*Medical costs except non-reimbursement

Table 2. Multiple linear regression model of annual direct medical costs in 13,047 patients with SLE in 2010* Medical costs except non-reimbursement

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariate coefficient</th>
<th>p</th>
<th>Multivariate coefficient</th>
<th>p</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>age</td>
<td>-147</td>
<td>0.9428</td>
<td>2,465</td>
<td>0.0939</td>
<td></td>
</tr>
<tr>
<td>sex (male=1)</td>
<td>203,811</td>
<td>0.0168</td>
<td>266,052</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>insurance type (National health insurance=1)</td>
<td>-1,308,571</td>
<td>&lt;0.0001</td>
<td>-471,980</td>
<td>&lt;0.0001</td>
<td>56.99</td>
</tr>
<tr>
<td>CCI*</td>
<td>329,655</td>
<td>&lt;0.0001</td>
<td>103,740</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Surgical procedure</td>
<td>5,148,455</td>
<td>&lt;0.0001</td>
<td>3,109,270</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Number of visits</td>
<td>117,016</td>
<td>&lt;0.0001</td>
<td>89,275</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Length of stay, days</td>
<td>124,607</td>
<td>&lt;0.0001</td>
<td>98,597</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Use of immunosuppressant</td>
<td>1,704,733</td>
<td>&lt;0.0001</td>
<td>1,001,006</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Dosage of glucocorticoid</td>
<td>1,665</td>
<td>&lt;0.0001</td>
<td>648</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
</tbody>
</table>

*Charlson comorbidity index

Disclosure: S. Y. Park, None; S. C. Bae, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/direct-medical-costs-of-systemic-lupus-erythematosus-in-south-korea

Abstract Number: 208

Influence of Depression on Healthcare Expenditures Among Adults with Spondylosis, Intervertebral Disc Disorders and Other Back Problems in the United States

Jawad Bilal¹, Adam Berlinberg¹, Jaren Trost¹, Sandipan Bhattacharjee² and Irbaz Bin Riaz¹, ¹Banner University Medical Center, Tucson, AZ, ²Department of Pharmacy, University of Arizona, Tucson, AZ

First publication: September 18, 2017

SESSION INFORMATION
Epidemiologic Subsets Drive a Differentiated Thoracic and Extrathoracic Presentation of Sarcoidosis: Analysis of 1082 Patients from the Sarcogeas-SEMI Registry

Soledad Retamozo1,2,3, Roberto Pérez-Alvarez4, Guadalupe Fraile5, Ricardo Gómez De La Torre6, Miguel López Dupla7, Begoña De Escalante Yangüela8, Ana Alguacil9, Joel Chara-Cervantes10, Jose Velilla Marco10, Francisco Javier Rascón11, Jose Salvador García Morillo12, Carles Tolosa13, Eva Fonseca Aizpuru14, Mariona Bonei15, José Luis Callejas16, Gloria De la Red17, Eva Calvo Beguería18, Cristina Soler i Ferrer19, Enrique Peral Gutiérrez De Ceballos20, Jorge Francisco Gómez Cerezo21, Gracia Cruz Caparrós22, Patricia Perez Guererro23, Sergio Rodríguez Fernández24, Blanca Pinilla25, Alberto Gato Diez26, Miriam Akasbi27, Angel Robles28, Inmaculada Ojeda29, María José Vives30, César Morcillo31, María Penadés Vidal32, Moisés De Vicente33, Belchín Kostov34, Manuel Ramos-Casals35, Lucio Pallarés36 and Pilar Brito-Zerón37, 1Instituto de Investigaciones en Ciencias de la Salud, Universidad Nacional de Córdoba, Consejo Nacional de Investigaciones Científicas y Técnicas (INICSA-UNC-CONICET), Cordoba, Argentina, 2Laboratory of Systemic Autoimmune Diseases “Josep Font”, CELLEX, Institut d’Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Department of Systemic Autoimmune Diseases, ICMID, Hospital Clinic, Barcelona, Barcelona, Spain, 3Rheumatology Unit, Hospital Privado Universitario de Córdoba, Institute University of Biomedical Sciences University of Córdoba (IUBCC), Cordoba, Argentina, 4Department of Internal Medicine, Hospital Alvaro Cunqueiro, Vigo, Vigo, Spain, 5Autoimmune Diseases Department, Hospital Ramón y Cajal, Madrid, Spain, 6Department of Internal Medicine, Hospital Universitari Joan XXIII, Tarragona, Tarragona, Spain, 7Department of Internal Medicine, Hospital Clínico, Zaragoza, Zaragoza, Spain, 8Department of Internal Medicine, Hospital Virgen de la Salud, Toledo, Toledo, Spain, 9Department of Internal Medicine, Hospital Universitario Miguel Servet, Zaragoza, Zaragoza, Spain, 10Department of Internal Medicine, Hospital Son Espases. Palma de Mallorca, Palma de Mallorca, Spain, 11Department of Internal Medicine, Hospital Virgen del Rocio, Sevilla, Sevilla, Spain, 12Department of Internal Medicine, Corporación Sanitaria Universitaria Parc Taulí, Barcelona, Spain, 13Department of Internal Medicine, Hospital de Cabueñes, Gijón, Gijón, Spain, 14Department of Internal Medicine, Althaia, Xarxa Assistencial de Manresa, Manresa, Spain, 15Department of Internal Medicine, Hospital Clínico San Cecilio, Granada,

Abstract Number: 209

Epidemiologic Subsets Drive a Differentiated Thoracic and Extrathoracic Presentation of Sarcoidosis: Analysis of 1082 Patients from the Sarcogeas-SEMI Registry

Soledad Retamozo1,2,3, Roberto Pérez-Alvarez4, Guadalupe Fraile5, Ricardo Gómez De La Torre6, Miguel López Dupla7, Begoña De Escalante Yangüela8, Ana Alguacil9, Joel Chara-Cervantes10, Jose Velilla Marco10, Francisco Javier Rascón11, Jose Salvador García Morillo12, Carles Tolosa13, Eva Fonseca Aizpuru14, Mariona Bonei15, José Luis Callejas16, Gloria De la Red17, Eva Calvo Beguería18, Cristina Soler i Ferrer19, Enrique Peral Gutiérrez De Ceballos20, Jorge Francisco Gómez Cerezo21, Gracia Cruz Caparrós22, Patricia Perez Guererro23, Sergio Rodríguez Fernández24, Blanca Pinilla25, Alberto Gato Diez26, Miriam Akasbi27, Angel Robles28, Inmaculada Ojeda29, María José Vives30, César Morcillo31, María Penadés Vidal32, Moisés De Vicente33, Belchín Kostov34, Manuel Ramos-Casals35, Lucio Pallarés36 and Pilar Brito-Zerón37, 1Instituto de Investigaciones en Ciencias de la Salud, Universidad Nacional de Córdoba, Consejo Nacional de Investigaciones Científicas y Técnicas (INICSA-UNC-CONICET), Cordoba, Argentina, 2Laboratory of Systemic Autoimmune Diseases “Josep Font”, CELLEX, Institut d’Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Department of Systemic Autoimmune Diseases, ICMID, Hospital Clinic, Barcelona, Barcelona, Spain, 3Rheumatology Unit, Hospital Privado Universitario de Córdoba, Institute University of Biomedical Sciences University of Córdoba (IUBCC), Cordoba, Argentina, 4Department of Internal Medicine, Hospital Alvaro Cunqueiro, Vigo, Vigo, Spain, 5Autoimmune Diseases Department, Hospital Ramón y Cajal, Madrid, Spain, 6Department of Internal Medicine, Hospital Universitari Joan XXIII, Tarragona, Tarragona, Spain, 7Department of Internal Medicine, Hospital Clínico, Zaragoza, Zaragoza, Spain, 8Department of Internal Medicine, Hospital Virgen de la Salud, Toledo, Toledo, Spain, 9Department of Internal Medicine, Hospital Universitario Miguel Servet, Zaragoza, Zaragoza, Spain, 10Department of Internal Medicine, Hospital Son Espases. Palma de Mallorca, Palma de Mallorca, Spain, 11Department of Internal Medicine, Hospital Virgen del Rocio, Sevilla, Sevilla, Spain, 12Department of Internal Medicine, Corporación Sanitaria Universitaria Parc Taulí, Barcelona, Spain, 13Department of Internal Medicine, Hospital de Cabueñes, Gijón, Gijón, Spain, 14Department of Internal Medicine, Althaia, Xarxa Assistencial de Manresa, Manresa, Spain, 15Department of Internal Medicine, Hospital Clínico San Cecilio, Granada,

Abstract Number: 209

Epidemiologic Subsets Drive a Differentiated Thoracic and Extrathoracic Presentation of Sarcoidosis: Analysis of 1082 Patients from the Sarcogeas-SEMI Registry

Soledad Retamozo1,2,3, Roberto Pérez-Alvarez4, Guadalupe Fraile5, Ricardo Gómez De La Torre6, Miguel López Dupla7, Begoña De Escalante Yangüela8, Ana Alguacil9, Joel Chara-Cervantes10, Jose Velilla Marco10, Francisco Javier Rascón11, Jose Salvador García Morillo12, Carles Tolosa13, Eva Fonseca Aizpuru14, Mariona Bonei15, José Luis Callejas16, Gloria De la Red17, Eva Calvo Beguería18, Cristina Soler i Ferrer19, Enrique Peral Gutiérrez De Ceballos20, Jorge Francisco Gómez Cerezo21, Gracia Cruz Caparrós22, Patricia Perez Guererro23, Sergio Rodríguez Fernández24, Blanca Pinilla25, Alberto Gato Diez26, Miriam Akasbi27, Angel Robles28, Inmaculada Ojeda29, María José Vives30, César Morcillo31, María Penadés Vidal32, Moisés De Vicente33, Belchín Kostov34, Manuel Ramos-Casals35, Lucio Pallarés36 and Pilar Brito-Zerón37, 1Instituto de Investigaciones en Ciencias de la Salud, Universidad Nacional de Córdoba, Consejo Nacional de Investigaciones Científicas y Técnicas (INICSA-UNC-CONICET), Cordoba, Argentina, 2Laboratory of Systemic Autoimmune Diseases “Josep Font”, CELLEX, Institut d’Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Department of Systemic Autoimmune Diseases, ICMID, Hospital Clinic, Barcelona, Barcelona, Spain, 3Rheumatology Unit, Hospital Privado Universitario de Córdoba, Institute University of Biomedical Sciences University of Córdoba (IUBCC), Cordoba, Argentina, 4Department of Internal Medicine, Hospital Alvaro Cunqueiro, Vigo, Vigo, Spain, 5Autoimmune Diseases Department, Hospital Ramón y Cajal, Madrid, Spain, 6Department of Internal Medicine, Hospital Universitari Joan XXIII, Tarragona, Tarragona, Spain, 7Department of Internal Medicine, Hospital Clínico, Zaragoza, Zaragoza, Spain, 8Department of Internal Medicine, Hospital Virgen de la Salud, Toledo, Toledo, Spain, 9Department of Internal Medicine, Hospital Universitario Miguel Servet, Zaragoza, Zaragoza, Spain, 10Department of Internal Medicine, Hospital Son Espases. Palma de Mallorca, Palma de Mallorca, Spain, 11Department of Internal Medicine, Hospital Virgen del Rocio, Sevilla, Sevilla, Spain, 12Department of Internal Medicine, Corporación Sanitaria Universitaria Parc Taulí, Barcelona, Spain, 13Department of Internal Medicine, Hospital de Cabueñes, Gijón, Gijón, Spain, 14Department of Internal Medicine, Althaia, Xarxa Assistencial de Manresa, Manresa, Spain, 15Department of Internal Medicine, Hospital Clínico San Cecilio, Granada,
Granada, Spain, 17Department of Internal Medicine, Hospital Esperit Sant, Badalona, Badalona, Spain, 18Hospital General San Jorge, Huesca, Huesca, Spain, 19Department of Internal Medicine, Hospital de Santa Caterina, Girona, Girona, Spain, 20Department of Internal Medicine, Hospital Virgen Macarena, Sevilla, Sevilla, Spain, 21Department of Internal Medicine, Hospital Infanta Sofia, San Sebastián, San Sebastian, Spain, 22Department of Internal Medicine, Hospital de Poniente El Ejido, Almería, Almería, Spain, 23Department of Internal Medicine, Hospital Universitario Puerta del Mar, Cádiz, Cadiz, Spain, 24Department of Internal Medicine, Hospital da Barbanza, A Coruña, A Coruña, Spain, 25Department of Internal Medicine, Hospital Gregorio Marañón, Madrid, Madrid, Spain, 26Department of Internal Medicine, Complejo Hospitalario Albacete, Albacete, Albacete, Spain, 27Department of Internal Medicine, Hospital Infanta Leonor, Madrid, Madrid, Spain, 28Internal Medicine, Hospital La Paz, Madrid, Spain, 29Department of Internal Medicine, Hospital Valle del Guadiato, Córdoba, Córdoba, Spain, 30Department of Internal Medicine, Parc Sanitari San Joan de Déu, San Boi de Llobregat, Barcelona, Spain, 31Department of Medicine, Hospital CIMA-Santas, Barcelona, Barcelona, Spain, 32Department of Internal Medicine, Hospital De Manises, Valencia, Valencia, Spain, 33Department of Internal Medicine, Hospital Nuestra Señora del Prado, Talavera, Talavera, Spain, 34Primary Care Research Group, IDIBAPS, Centre d’Assistència Primària ABS Les Corts, CAPSE, Barcelona, Barcelona, Spain, 35Laboratory of Systemic Autoimmune Diseases “Josep Font”, CELLEX, Institut d’Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Department of Systemic Autoimmune Diseases, ICMID, Hospital Clinic, Barcelona, Spain, Barcelona, Spain

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Health Services Research Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** To analyse whether epidemiologic factors (such as gender or age at diagnosis of the disease) are associated with particular disease expressions and define specific epidemiological subsets in patients with sarcoidosis.

**Methods:** In January 2016, the Autoimmune Diseases Study Group (GEAS-SEMI) created a national registry (SARCOGEAS) of patients with sarcoidosis. Sarcoidosis was diagnosed in agreement with the criteria proposed by the American Thoracic Society/European Respiratory Society/World Association of Sarcoidosis and Other Granulomatous Disorders (WASOG) 1999 statement on sarcoidosis. Organ involvement was retrospectively determined in each patient at the time of diagnosis using the 2014 WASOG organ assessment instrument. Ethnicity was defined according to the FDA classification.

**Results:** The cohort consisted of 1082 patients (82% biopsy-proven), including 618 (57%) women and 464 (43%) men, with a mean age at diagnosis of 47.2 ± 15.5 years. One hundred forty (13%) patients were born outside Spain. With respect to the FDA ethnic classification, 965 (89%) patients were classified as White, 69 (6%) as Hispanic, 30 (3%) as Black/African American and 18 (2%) as Asian. Thoracic involvement was retrospectively determined in each patient at the time of diagnosis using the 2014 WASOG organ assessment instrument. Ethnicity was defined according to the FDA classification.

In the multivariate analysis models, women showed a lower frequency of thoracic involvement (87% vs 93% in men, p=0.019) and a higher frequency of cutaneous (42% vs 26%, p<0.001) and ocular (13% vs 9%, p=0.012) WASOG involvements, patients with a younger disease onset (<35 years) were more frequently born out of Spain (17% vs 11%, p=0.027), had a higher frequency of thoracic disease (94% vs 88%, p=0.008) and a lower frequency of kidney involvement (3% vs 6%, p=0.041), and patients with an elderly onset (age>70 years) were more frequently born in Spain (99% vs 86%, p=0.007) and had a lower frequency of thoracic (81% vs 90%, p=0.006) and cutaneous (23% vs 37%, p=0.001) involvements and a higher frequency of bone marrow involvement (12% vs 4%, p=0.004).

**Conclusion:** This is one of the largest series of sarcoidosis reported out of the US, predominantly composed by White patients in nearly 90% of cases. Thoracic and extrathoracic involvements at disease presentation were strongly influenced by specific epidemiologic features such as gender, age and ethnicity.

**Disclosure:** S. Retamozo, None; R. Pérez-Alvarez, None; G. Fraile, None; R. Gómez De La Torre, None; M. López Dupla, None; B. De Escalante Yanguela, None; A. Alguacil, None; J. Chara-Cervantes, None; J. Veilla Marco, None; F. J. Rascón, None; J. S. García Morillo, None; C. Tolosa, None; E. Fonseca Alipzuru, None; M. Bonet, None; J. Lúis Callejas, None; G. De la Red, None; E. Calvo Begueria, None; C. Soler i Ferrer, None; E. Peral Gutiérrez De Ceballos, None; J. F. Gómez Cerezo, None; G. Cruz Caparrós, None; P. Perez Guerrero, None; S. Rodríguez Fernández, None; B. Pinilla, None; A. Gato Diez, None; M. Akashi, None; A. Robles, None; I. Ojeda, None; M. J. Vives, None; C. Morcillo, None; M. Penadés Vidal, None; M. De Vicente, None; B. Kostov, None; M. Ramos-Casals, None; L. Pallarés, None; P. Brito-Zerón, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/epidemiologic-subsets-drive-a-differentiated-thoracic-](http://acrabstracts.org/abstract/epidemiologic-subsets-drive-a-differentiated-thoracic-).
Pharmacovigilance Surveillance of Autoimmune Diseases Induced By Biological Agents: A Review of 12013 Cases (aeBIOGEAS-SEMI Registry)

Soledad Retamozo1,2,3, Manuel Ramos-Casals4,5, Marta Pérez de Lis6, Alejandra Flores-Chavez7,8,9, Sofia Arteaga10,11, Celeste Galcerán-Chaves1,2, Belchin Kostov13, Roberto Pérez-Alvarez6 and Pilar Brito-Zerón2,14. 1Instituto de Investigaciones en Ciencias de la Salud, Universidad Nacional de Córdoba, Consejo Nacional de Investigaciones Científicas y Técnicas (INICSA-UNC-CONICET), Córdoba, Argentina, 2Laboratory of Systemic Autoimmune Diseases “Josep Font”, CELLEX, Institut d’Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Department of Systemic Autoimmune Diseases, ICMID, Hospital Clinic, Barcelona, Barcelona, Spain, 3Rheumatology Unit, Hospital Privado Universitario de Córdoba, Instituto University of Biomedical Sciences University of Córdoba (IUCBC), Córdoba, Argentina, 4Laboratory of Systemic Autoimmune Diseases “Josep Font”, CELLEX, Institut d’Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Department of Systemic Autoimmune Diseases, ICMID, Hospital Clinic, Barcelona, Spain, Barcelona, Spain, 5Department of Medicine, University of Barcelona, Barcelona, Spain., Barcelona, Spain, 6Department of Internal Medicine, Hospital Alvaro Cunqueiro, Vigo, Vigo, Spain, 7Department of Autoimmune Diseases, ICMiD, Hospital Clinic Barcelona, Spain., Barcelona, Spain, 8Unidad de Investigación Biomédica 02 (Unidad de Investigación en Epidemiología Clínica), UMAE, Hospital de Especialidades, Centro Médico Nacional de Occidente, Instituto Mexicano del Seguro Social, Jalisco, Mexico, 9Programa de Doctorado en Ciencias Médicas, Centro Universitario de Investigaciones Biomédicas (CUIB), Universidad de Colima, Colima, Mexico, Mexico, Mexico, 10Residente de Reumatología II año, Universidad de Antioquia, Medellín, Colombia, Medellín, Colombia, 11(d) Department of Autoimmune Diseases, ICMiD, Hospital Clinic Barcelona, Spain., Barcelona, Spain, 12Neurosciences Clinical Institute, Hospital Clinic, Barcelona, Spain, Barcelona, Spain, 13Primary Care Research Group, IDIBAPS, Centre d’Assisténcia Primària ABS Les Corts, CAPSE, Barcelona, Barcelona, Spain, 14Autoimmune Diseases Unit, Department of Medicine, Hospital CIMA- Sanitas, Barcelona., Barcelona, Spain

First publication: September 18, 2017

SESSiON INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Health Services Research Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The increasing use of biological agents has been linked with the paradoxical development of autoimmune processes. The scenario has dramatically change in recent years due to the increased number and the emerging use of biologics in solid cancers.

Methods: In 2006, the Study Group on Autoimmune Diseases (GEAS) of the Spanish Society of Internal Medicine created the aeBIOGEAS Registry (autoimmune events) designed to collect data on autoimmune diseases secondary to the use of biologic agents though a systemic and yearly MEDLINE search. The baseline analysis identified in 2017 nearly 200 cases of autoimmune diseases triggered overwhelmingly anti-TNF. We present the updated results of the aeBIOGEAS Registry (cases included until May 31, 2017).

Results: The aeBIOGEAS Registry currently includes 12013 cases of autoimmune diseases related to the administration of biological agents, including more than 50 different systemic and organ-specific autoimmune processes; the most frequently reported were psoriasis (n=6377), inflammatory bowel disease -IBD- (n=783), demyelinating CNS diseases (n=453), lupus (n=369), interstitial lung diseases -ILD- (n=378), peripheral neuropathies (n=328), vasculitis (n=291) and hypophysitis (n=207). The main biological agents identified consisted of anti-TNF agents in 9220 cases (mainly adalimumab in 4051, infliximab in 3109 and etanercept in 2148). The main biological agents identified consisted of ant-TNF agents in 9220 cases (mainly adalimumab in 4051, infliximab in 3109 and etanercept in 1496). B-cell targeted therapies in 729 (mainly rituximab in 664), immune checkpoint inhibitors in 552 (mainly ipilimumab in 426 and nivolumab in 77) and vascular endothelial growth factor inhibitors in 504 cases (bevacizumab). With respect to the biologic, the main associations were reported for the development of lupus and hepatitis in patients treated with infliximab (44% and 45% of the reported cases of induced lupus and hepatitis, respectively), demyelinating CNS diseases, sarcoidosis, uveitis and IBF in patients treated with etanercept (47%, 41%, 67% and 83%, respectively), psoriasis in patients treated with adalimumab (56%), ILD in patients treated with rituximab (49%) and hypophysitis in patients treated with ipilimumab (96%). With respect to the underlying disease for which the patient received the biological agent, the main associations were reported for the development of lupus, vasculitis and sarcoidosis in patients with RA (68%, 84% and 47% of the reported cases of induced lupus, vasculitis and sarcoidosis, respectively), uveitis and IBF in patients with JIA (60% and 41%, respectively), psoriasis in patients with IBF (33%), hypophysitis in patients with melanoma (90%) and IBF in patients with hematological neoplasia (50%).

Conclusion: As the use of biological therapies expands, the number and diversity of induced autoimmune disorders is increasing exponentially. Management of these biologic-induced autoimmune diseases will be an increasing clinical challenge in the daily practice in the next years.
Disclosure: S. Retamozo, None; M. Ramos-Casals, None; M. Pérez de Líz, None; A. Flores-Chavez, None; S. Arteaga, None; C. Galcerán-Chaves, None; B. Kostov, None; R. Pérez-Alvarez, None; P. Brito-Zerón, None.


Abstract Number: 211

Hopes and Fears of Patients with Axial Spondyloarthritis in Spain. the Value of Patient Opinion: Results from the Spanish Atlas

Marco Garrido-Cumbrera1, Pedro Plazuelo-Ramos2, Olta Brace1, David Galvez-Ruiz1 and Jorge Chacon-Garcia1, 1Universidad de Sevilla, Seville, Spain, 2CEADE, Madrid, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Health Services Research Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Not much attention has been paid to listening to the opinions of patients in most scientific studies on Spondyloarthritis, despite their opinions playing an increasingly important role in decision-making alongside clinical and public health criteria. To assess the opinions of patients with Axial Spondyloarthritis (ax-SpA) using qualitative information.

Methods: A sample of 680 patients diagnosed with ax-SpA was interviewed during 2016 as part of the Spanish Atlas, which aims to promote early referral and improve healthcare and the use of effective treatments in patients with ax-SpA. The Atlas is a CEADE initiative (Spanish Coordinator of Patients with ax-SpA in Spain) developed by the University of Seville and Max Weber Institute in collaboration with GRESSER (Spanish Rheumatology Society spondyloarthritis study group). Responses to qualitative items about patients' hopes and fears for their disease and their personal aims regarding their treatment were analysed.

Results: 53% were females, mean age 46 years and 77.1% were HLA-B27+. The five main hopes of patients are: stopping the disease, dream of a cure, elimination of pain, improve their quality of life and live without limitations. Additionally, patients has expectations on the medical research outcomes. Thus, 81% of patients hope that the research will make possible to find the cause and a cure for ax-SpA, developing more efficient biologic therapies (11%), and finding new techniques or medication (8%). The following stand out among drug treatment-related concerns: having more effective treatments (32%), sustaining the results of biologic therapies (29%), being able to start on biologics (8%), the public health system funding non-drug treatments for AS (8%), eliminating secondary effects (15%), reducing prices (4%), and correct use (4%). With respect to their fears, patients stated that their main concern was mobility loss (31%), followed by loss of independence (23%), disability (22%), stiffness (12%), structural damage (3%), organ damage (3%), other illnesses and diseases related (3%), physical decline (3%), and sight loss (1%). Patients who expressed fear regarding their disease listed their greatest concern was that they would not overcome or tolerate pain (56%), followed by the fear that the disease would develop (32%), along with
apprehension about flare-ups (7%), and tiredness (5%). With respect to patients’ personal objectives in terms of their treatments, they
highlighted the wish that their treatment would, first, help them to reduce and eliminate pain, increasing their in mobility, improved quality of
life, the avoidance of structural damage and the disease eventually being cured.

Conclusion: Analysis of patient opinion using qualitative information has enabled the identification of important concerns for patients such as
discovering the cause of the disease, reducing pain and structural damage, loss of self-sufficiency and disability.

Disclosure: M. Garrido-Cumberera, None; P. Plazuelo-Ramos, None; O. Brace, None; D. Galvez-Ruiz, None; J. Chacon-Garcia, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/hopes-and-fears-of-patients-with-axial-spondyloarthritis-
in-spain-the-value-of-patient-opinion-results-from-the-spanish-atlas

Abstract Number: 212

Treatment Patterns in Large Vessel Arteritis (Giant Cell Arteritis and Temporal Arteritis): Findings from a Large Contemporaneous Real-World Cohort in the US

Zhaohui Su1, Vandana Menon1, Richard Gliklich2 and Tom Brecht1, 1 Research, OM1, Inc, Cambridge, MA, 2 OM1, Inc, Cambridge, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Health Services Research Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Giant cell arteritis (GCA) is the most common form of primary systemic vasculitis with annual incidence as high as 27 per 100,000 in
persons over the age of 50 years. Key issues in management after a diagnosis of GCA include prompt initiation of therapy, prevention and
treatment of adverse effects related to treatment, and close monitoring for disease flares. Glucocorticoids are the mainstay of therapy and are
used for induction and maintenance of remission. However, there is little consensus on the optimal treatment strategies for GCA. We present
treatment patterns in a large real-world population of patients with GCA managed by rheumatologists across the US.

Methods:
The OM1 platform collects, links, and leverages, structured and unstructured data from electronic medical records (EMR) and other sources
in an ongoing and continuously updating manner to create a next generation registry-a novel approach to real world evidence. The OM1 GCA
Cohort includes data who met our definition of at least two GCA related diagnosis codes [ICD-10: M31.6, M31.5, M31.4; ICD-9:446.7,
446.5] within a 1 year period, treated by rheumatologists, between 2013 and 2016.

Results:
The cohort included 1,567 patients with a mean age of 72 + 10 years, three quarters were Caucasian (78%) and female (76%). Median
follow up time was 24 months with a mean of 12 rheumatology ambulatory encounters. Nearly a third of the cohort had a concomitant
diagnosis of polymyalgia rheumatica (33%) and 17% had rheumatoid arthritis. A majority of the patients had at least one erythrocyte
sedimentation rate (ESR) and C-reactive protein (CRP) measurement. Median ESR at baseline was 21mm/hr (IQR: 8, 48) and median CRP
was 1mg/L (0.3, 4.0). Only 6% of patients had a documented temporal artery biopsy. Patient reported pain scores were available in 26% of
the patients with a median duration of 6 months between first and last assessment. The majority of patients received glucocorticoids (85%),
22% were treated with methotrexate, 8% with hydroxychloroquine, 5% with aspirin, 5% with tocilizumab and 3.5% with azathioprine; 14%
were treated with more than one drug concurrently.

Conclusion:
We present findings from a large, representative, cohort of real-world patients seen in routine clinical practice. There are wide variations in
patient profile and treatment practices which may reflect the lack of clarity around value of additional steroid-sparing agents to avoid the
common glucocorticoid adverse effects and to reduce time to remission.

Disclosure: Z. Su, None; V. Menon, None; R. Gliklich, None; T. Brecht, None.


Abstract Number: 213

Perception of Access to Mental Health Services in Publicly Insured Vs Privately Insured Patients with Rheumatic Diseases

Elizabeth Soto-Cardona, Jackie Szymonifka and Robert F. Spiera, Rheumatology, Hospital for Special Surgery, New York, NY
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: ARHP Health Services Research Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: To assess perception of access to mental health services (MHS) and utilization of those services based on participant’s insurance type. We compared responses of participants with public insurance (Medicare and Medicaid) and private insurance receiving rheumatologic care at an urban academic medical center.

Methods: Patients with rheumatic diseases seen in clinic and in private practices at a tertiary care academic medical center underwent a standardized interview by a single interviewer. Patient reported utilization of medical care and mental health services, as well as perceptions of access to those services was assessed using a standardized questionnaire. Socio-demographic variables were collected. Health characteristics included rheumatological diagnosis, physical functional status and mental health, measured by the SF36. High scores, reported on a scale from 0 to 100, define a more favorable health state. Responses from patients with public health insurance were compared to those with private commercial insurance.

Results: Participants with private insurance were more likely to be white (p=.037), married (p=.001) and home owners (p <.001), whereas participants with public insurance where more likely to be disabled (p=.074) and diagnosed with RA (p=.022) or SLE (p=.022). Those with private insurance scored higher on the SF-36 and were less likely to recognize role limitations due to emotional problems (p=.028), score lower for pain (p=.019) and to report worse physical function (p=.006). [Table 1]

Conclusion:
Of the 52 participants only 34 had received MHS in the past, 13/34 (38%) of public insurance patients, and 21/34 (61%) of private patients. Patients with public insurance were less likely to perceive barriers to access to mental health services than were those with private insurance, although that difference did not reach statistical significance (59% vs 24%, p = 0.227). In terms of relative ease of access to MHS vs physical health specifically, 38% of participants with public insurance felt they had less access to MHS than to medical services in general where as 61% of private practice patients reported perceiving less access to MHS (p=.041) than to medical services in general. The majority of participants in both private (76%) and clinic settings (76%) felt access to MHS was important to their well-being. Conclusion: Patients with rheumatic diseases commonly value the importance of mental health services, but frequently perceive barriers to access those services. Perhaps surprisingly, patients with public insurance were less likely to perceive such barriers than those privately insured. Future investigations should focus on identifying those specific barriers to mental health access for private and publicly insured patients in order to facilitate provision of such services.

Table 1. SF-36 component scores by insurance type
SF-36 component | All patients (n=52) | Medicare or Medicaid (n=25) | Private insurance (n=27) | p-value
--- | --- | --- | --- | ---
Emotional well-being | 74 [54, 88] | 72 [56, 88] | 76 [48, 88] | 0.912
Energy/fatigue | 48 [30, 73] | 50 [30, 70] | 45 [30, 75] | 0.854
General health | 43 [25, 60] | 50 [25, 60] | 40 [25, 60] | 0.497
Pain | 51 [23, 73] | 33 [20, 68] | 58 [45, 78] | 0.019
Physical functioning | 43 [25, 70] | 35 [25, 50] | 60 [40, 80] | 0.006
Role limitations due to emotional problems | 100 [0, 100] | 33 [0, 100] | 100 [33, 100] | 0.028
Role limitations due to physical health | 0 [0, 50] | 0 [0, 25] | 25 [0, 100] | 0.070
Social functioning | 63 [50, 88] | 63 [38, 75] | 75 [50, 88] | 0.570

Disclosure: E. Soto-Cardona, None; J. Szymonifka, None; R. F. Spiera, None.


Abstract Number: 214

Ambulatory and Hospital Care for Arthritis and Related Conditions in Ontario, Canada

Y. Raja Rampersaud1, J. Denise Power2, Anthony V. Perruccio2, Michael Paterson3, Christian Veillette2, Elizabeth M. Badley4 and Nizar Mahomed2, 1Arthritis Program, Krembil Research Institute, University Health Network, Toronto, ON, Canada, 2Arthritis Program, Krembil Research Institute, University Health Network, Toronto, ON, Canada, 3Institute for Clinical Evaluative Sciences, Toronto, ON, Canada, 4Health Care & Outcomes Research, Krembil Research Institute, University Health Network, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: ARHP Health Services Research Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Ontario, Canada’s most populous province, has publicly funded, universal health insurance covering medically necessary hospital and physician services with no copayments. The purpose of this study was to quantify the burden of arthritis and related conditions (A&R) on the Ontario health care system, according to service type (ambulatory vs. inpatient care) physician specialty (primary care, rheumatology, orthopedics), and hospital setting (emergency department (ED), day surgery, inpatient care).

Methods: Administrative health data were analyzed for fiscal 2013/14 for Ontarians aged 18+ years (N=10,841,302). Data sources included: the Ontario Health Insurance Plan (OHIP) Claims History Database, which captures data on in- and out-patient physician services; the Canadian Institute for Health Information (CIHI) Discharge Abstract Database, which records diagnoses and procedures associated with all inpatient hospitalizations; and the CIHI National Ambulatory Care Reporting System, which captures data on all ED and day surgery encounters. Services associated with A&R were identified using the International Classification of Diseases (ICD) diagnosis code identified on each physician service claim as the “main reason” for each outpatient physician visit and the “most responsible” ICD diagnosis code recorded on each hospitalization, ED visit and day surgery record. Patient visit rates and numbers of patients and visits were tabulated according to care setting, patient age and sex, and physician specialty for the grouping of all A&R, as well as for specific diagnoses, such as osteoarthritis (OA) and rheumatoid arthritis (RA).

Results: Overall, 1.3 million adult Ontarians (11.9%) made 2.7 million outpatient physician visits for A&R in 2013/14, with 62% of these visits occurring in primary care. Patient visit rates for A&R increased with age and were higher in women than men; women accounted for 60% of all A&R visits. Approximately 5% of adult Ontarians made an outpatient physician visit specifically for OA, with about 1% making at least 1 visit for RA. 63% of outpatient visits for OA, and 35% for RA, were in primary care. Just over 25% of adult Ontarians who saw a physician for OA consulted an orthopaedic surgeon at least once and 58% who made a visit for RA consulted a rheumatologist at least once. Just over 1% of adult Ontarians made an ED visit for which the most responsible diagnosis was A&R, for a total of 142,000 visits. Rates of hospitalization and day surgery for A&R were 410 and 190 per 100,000 population, respectively. The highest rate of inpatient hospitalization was associated with OA, at 340 per 100,000, which accounted for 82% of all A&R-related hospital admissions.
Conclusion: A&R place a significant burden on the health care system, particularly in primary care. As the population ages, it will be essential that health system planning takes into account the large demand for arthritis care, both in terms of health human resources planning and implementation of clinically and cost-effective models of care.

Disclosure: Y. R. Rampersaud, None; J. D. Power, None; A. V. Perruccio, None; M. Paterson, None; C. Veillette, None; E. M. Badley, None; N. Mahomed, None.

Abstract Number: 215

Clinical Pharmacist As Part of the Interprofessional Team Improves Quality of Care in Patients with Rheumatic Disease

Jessica Farrell¹, Lee S. Shapiro¹ and Mitchell Miller², ¹The Center for Rheumatology, Albany, NY, ²Albany College of Pharmacy and Health Sciences, Albany, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: ARHP Health Services Research Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Successful multidisciplinary models exist for the management of chronic diseases such as diabetes, cardiovascular disease, infectious diseases, kidney disease and psychiatric illnesses. A multidisciplinary team including a pharmacist in the ambulatory care setting has shown to improve patient and population outcomes for various chronic disease states. Rheumatology healthcare providers recognize the burden of rheumatic disease requires an integrated, multidisciplinary team including a pharmacist. Recent data suggests pharmacists can improve adherence and health outcomes in the management of gout. This type of pharmacist-led intervention can easily be extrapolated to other rheumatic diseases. The addition of a pharmacist to the healthcare team can have many benefits, including improving patient compliance and education, serving as a drug information resource, and obtaining insurance coverage. This includes establishing patient relationships, gathering medication histories, preventing, identifying and resolving medication related problems, educating patients and other healthcare providers, monitoring patients and medication effects, and contributing to continuity of care for all patients. Clinical pharmacy services at The Center for Rheumatology (TCFR) have expanded over the past 8 years.

Methods:
The aim of our project is to 1) provide billable pharmacy consult services which systematize practice-wide medication initiation and safety monitoring, 2) provide additional support to practice-wide procedures/protocols related to medication therapy and insurance authorizations, 3) provide evidence of improved patient and population outcomes when a pharmacist is part of the interdisciplinary team in a rheumatology practice, 4) serve as a business model of an innovative practice in pharmacy. Outcome measures include number of reimbursable visits, assessments of medication prior authorizations, denials and peer-to-peer calls, and provider, support staff and patient surveys.

Results:
The pharmacist provides face-to-face problem/medication focused visits which are reimbursed through incident-to billing. Visits are focused on initiation and safety monitoring for high-risk DMARD and osteoporosis therapies. The drug information consult services and insurance authorization assistance have been shown to save providers and support staff time, ranging from 1-3+ hours per week per provider. Providers report the addition of a pharmacist allows them to provide a higher level of care focused on medication therapy and safety, and helps improves patient compliance and anxiety related to medications.

Conclusion:
The addition of a pharmacist to the multidisciplinary team in a rheumatology practice can improve the quality of care delivered to patients, specifically related to medication safety and access by assisting in the prior authorization process and serving as patient advocates. The addition of clinical pharmacy services sets the practice apart from others by improving patient care and serving as an innovative business model for rheumatology practices to include a clinical pharmacist as part of their healthcare team.
Disclosure: J. Farrell, None; L. S. Shapiro, None; M. Miller, None.


Abstract Number: 216

**Creation of the First Massive Open Online Course for Patients with Rheumatoid Arthritis**

**Sonia Tropé**¹, Jean-David Cohen², Catherine Beauvais³, Didier Poivret⁴, Alain Saura⁵, Danielle VACHER⁶, Hervé Barkatz⁷, Pascal Lacoste⁷, Valérie Weil⁸ and Gérard Thibaud⁹.


First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** ARHP Health Services Research Poster

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** People with chronic conditions face the disease more effectively when they develop psychosocial skills and self-care. Health authorities thus recommend the organization of therapeutic patient education (TPE). Suffering from different limitations, a patient organization had the idea to develop a digital training solution, accessible everywhere, complementary to TPE, for patients with rheumatoid arthritis.

**Methods:** The choice was made for an online training program such as Massive Open Online Courses (MOOC). A preliminary survey was carried out among the patients via an electronic questionnaire via social networks and an emailing to the organisation members.

A steering committee (COPIL) made up of representatives of the patients' association, expert patients and rheumatologists with the support of a specialized agency, determined the timetable, the educational objectives, the contents, the speakers and the evaluations.

**Results:** The initial investigation was stopped at 100 responses, obtained in 3 days.

The majority of respondents planned to follow the MOOC on their computer (85.9%), but to meet the needs of all, the device is responsive.

More than half of respondents (61%) had never participated in a TPE program and 94% were interested in joining MOOC to learn new information about the disease (78.8%), treatments (71.7%), have expert views (67.7%), share experience with other patients (56.6%), and better live with the disease (50.5%).

Respondents would like to have a weekly webconference lasting from 1 hour to 1h30.

About the MOOC:

- Using the Learning Management System platform drspoc.com
- Intervention of the experts via videos and live courses, evaluation of the achievements and, during two annual sessions, tutoring by patients trained specifically.

At the beginning and end of the session, learners are invited to answer different questionnaires (knowledge, skills, satisfaction).

The MOOC includes the following modules:

- Introduction and background on MOOC
- Understanding Rheumatoid Arthritis
- Explore the care pathway, current events and treatment prospects
- Everyday life with rheumatoid arthritis
• Manage pain and fatigue.

COPIL identified 15 experts (patient-experts, rheumatologists, occupational therapist, physiotherapist, nutritionist, social worker, psychologist, sexologist, nurse) who wrote the content of their speech. All texts have been validated by a pedagogical engineer and the director of the association.

215 people pre-registered during the month preceding the launch, 148 persons active during the first session.

41 responses recorded to the voluntary assessment questionnaire.

Conclusion: This is the first digital training strategy for people with rheumatoid arthritis. This project proved to be useful to patients, offering an alternative or complement to TPE.

It will be necessary to evaluate the impact of this MOOC on the quality of life of the patients and their perception on its usefulness after several sessions. An update is planned according to patient feedback and possible changes in content.

Disclosure: S. Tropé, None; J. D. Cohen, None; C. Beauvais, None; D. Poivret, None; A. Saraux, None; D. VACHER, None; H. Barkatz, None; P. Lacoste, None; V. Weill, None; G. Thibaud, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/creation-of-the-first-massive-open-online-course-for-patients-with-rheumatoid-arthritis

Abstract Number: 217

Keeping a Balance: Social Engagement and Care Giving

Elizabeth M. Badley1,2, Dov Millstone2 and Anthony V. Perruccio2,3,4, 1Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada, 2Health Care & Outcomes Research, Krembil Research Institute, University Health Network, Toronto, ON, Canada, 3Arthritis Program, Krembil Research Institute, University Health Network, Toronto, ON, Canada, 4Institute of Health Policy, Management & Evaluation, Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: ARHP Health Services Research Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Arthritis is associated with pain and disability. As a result there has been some interest in examining the receipt of care among those with arthritis. What has garnered less attention is care giving in this population. The purpose of this study was to describe both care giving and care receipt, and social engagement, in a nationally representative sample of later working age (age 45-64 years) people with arthritis.

Methods:
Analysis was based on the first wave data from the Canadian Longitudinal Study on Aging (CLSA), a nationally representative sample of people aged 45-85. The questionnaire covers socio-demographic, health, functioning, social, and work variables. Analyses were limited to participants aged 45-64 (n=12,319).

Results:
Overall, 30% reported arthritis: 4% reported RA, 17% OA, and 9% other arthritis. Arthritis was reported more frequently by women than men. Most people with arthritis were married (75%), and 70% had more than a high school education. A significant proportion (70%) of people with arthritis were overweight or obese. The majority of individuals with arthritis (68%) reported difficulty with at least one daily activity - most frequently were crouching, kneeling or stooping; standing up after sitting; and standing for a long period. More than 85% were currently in the labour force, and most were socially connected (e.g. 80% took part in community-based activities at least once a week).

Taking both informal and formal care together, around 20% of people arthritis in this age group received some form of care, with the majority of care being informal only. A small proportion received professional care - most often assistance around the house (3%) and medical care (2.5%). Overall, 18% received some kind of non-professional assistance: 14% around the house, 11% with transportation, and 10% with
meal preparation. Nearly 60% of the informal care received came from someone living in the same household, and a similar proportion was provided by men and women. Almost half of care had been received for 6 months or less, although 22% reported receiving care for 5 years or more. Over half of individuals with arthritis (53%) reported providing some kind of care to others: 39% gave assistance with transportation, 31% assistance around the house, 25% assistance with meal preparation. Care was most frequently provided to individuals living in another household. Care was provided for a median of 12 weeks in the past year and 5 hours per week. People reporting RA were slightly more likely to report receiving care than those with OA. There was no difference in the proportion with RA and OA giving care.

Conclusion:

Against a backdrop of substantial limitations in activities, the majority of people with arthritis in the later decades of working life were in the work force and engaged in the community. At the same time, more than half provided care to others, far more than the proportion that received care. The need to provide care and at the same time balance work and a social and family life for individuals with arthritis may impact their ability to care for themselves.

Disclosure: E. M. Badley, None; D. Millstone, None; A. V. Perruccio, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/keeping-a-balance-social-engagement-and-care-giving

Abstract Number: 218

Social Factors and Racial Disparities in Total Hip Arthroplasty Outcomes

Susan M. Goodman1, Bella Y. Mehta2, Meng Zhang3, Jackie Szymonifka4, Joseph T. Nguyen3, Yuo-Yu Lee3, Mark P. Figgie5, Michael L. Parks5, Shirin A. Dey4, Daisy B. Crego4, Linda A. Russell6, Lisa A. Mandl7 and Anne R. Bass4, 1Medicine, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, 2Rheumatology, Hospital for Special Surgery/Weill Cornell Medicine/Mailman School of Public Health, New York, NY, 3Epidemiology and Biostatistics, Hospital for Special Surgery, New York, NY, 4Rheumatology, Hospital for Special Surgery, New York, NY, 5Orthopaedic Surgery, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, 6Rheumatology, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, 7Rheumatology, Hospital for Special Surgery Weill Cornell Medical College, New York, NY

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Healthcare Disparities in Rheumatology Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Socioeconomic factors such as poverty may mediate racial disparities in health outcomes including those of total hip arthroplasty (THA), and confound analyses of differences between blacks and whites.

Methods: Using data from a large institutional THA registry, we compared pain and function 2 years after surgery between blacks and whites. The census tract variable “percent of the population with Medicaid insurance coverage” was used to measure community deprivation. We used geocoding to link patients to census tracts, built models that incorporated both individual patient and census tract data, and analyzed the interaction between race and percent of population with Medicaid coverage and its association with patient-reported outcomes 2 years after THA.

Results: Black patients, comprising 145/4170 (3%) of THA cases, had worse pain and function scores both at baseline and at 2 years after THA compared to whites (Table 1). There was a strong positive correlation between census tract Medicaid coverage and percent living below the poverty line (rho = 0.69; p<0.001). Racial disparities in 2-year WOMAC pain and function were magnified in communities with a high percentage of the population covered by Medicaid (Table 2). For blacks in these communities, 2-year WOMAC function scores were predicted to be 5.54 points lower (80.42 vs. 85.96) than in blacks from communities with a low prevalence of Medicaid coverage, while scores for whites did not differ between communities. Pain scores were also lower for blacks living in deprived areas, but the difference was not significant.

Conclusion: WOMAC pain and function 2 years after THA are similar among blacks and whites in communities with little deprivation (measured as percent of the population with Medicaid insurance coverage). WOMAC function at 2 years is worse among blacks in areas of higher deprivation, whereas this poverty gradient does not impact outcomes among whites.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total</th>
<th>White</th>
<th>Black</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>4170 (100%)</td>
<td>4025 (97%)</td>
<td>145 (3%)</td>
<td></td>
</tr>
<tr>
<td>Age at surgery (years), mean (SD)</td>
<td>65.29 (11.01)</td>
<td>65.42 (10.98)</td>
<td>61.69 (11.23)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>2311 (55.42%)</td>
<td>2219 (55.13%)</td>
<td>92 (63.45%)</td>
<td>0.048</td>
</tr>
<tr>
<td>BMI (kg/m²), mean (SD)</td>
<td>27.75 (5.48)</td>
<td>27.68 (5.44)</td>
<td>29.74 (6.33)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Hispanic, n (%)</td>
<td>75 (1.80%)</td>
<td>73 (1.81%)</td>
<td>2 (1.38%)</td>
<td>1.00</td>
</tr>
<tr>
<td>One or more comorbidities, n (%)</td>
<td>1013 (24.29%)</td>
<td>956 (23.75%)</td>
<td>57 (39.31%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>College or above, n (%)</td>
<td>2805 (68.35%)</td>
<td>2721 (68.69%)</td>
<td>84 (58.74%)</td>
<td>0.012</td>
</tr>
<tr>
<td>Insurance payer, n (%)</td>
<td>53 (1.27%)</td>
<td>2257 (56.07%)</td>
<td>60 (41.38%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Medicaid</td>
<td>2317 (55.56%)</td>
<td>1738 (43.18%)</td>
<td>62 (42.76%)</td>
<td></td>
</tr>
<tr>
<td>Medicaid</td>
<td>1800 (43.17%)</td>
<td>1392 (34.83%)</td>
<td>47 (33.09%)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0.033</td>
</tr>
<tr>
<td>I-II</td>
<td>3387 (81.26%)</td>
<td>3279 (81.51%)</td>
<td>108 (74.48%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>III-IV</td>
<td>781 (18.74%)</td>
<td>744 (18.49%)</td>
<td>37 (25.52%)</td>
<td></td>
</tr>
<tr>
<td>Hospital for Special Surgery Expectations Score, mean (SD)</td>
<td>83.30 (16.46)</td>
<td>83.17 (16.52)</td>
<td>86.64 (14.42)</td>
<td>0.043</td>
</tr>
<tr>
<td>WOMAC pain at baseline, mean (SD)</td>
<td>53.58 (17.85)</td>
<td>53.84 (17.72)</td>
<td>46.48 (20.04)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>WOMAC pain at 2 Years, mean (SD)</td>
<td>93.63 (11.39)</td>
<td>93.81 (11.13)</td>
<td>88.60 (16.39)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Delta WOMAC pain, mean (SD)</td>
<td>40.04 (19.14)</td>
<td>39.97 (18.95)</td>
<td>42.15 (23.75)</td>
<td>0.144</td>
</tr>
<tr>
<td>WOMAC function at baseline, mean (SD)</td>
<td>49.93 (18.04)</td>
<td>50.19 (18.00)</td>
<td>42.78 (17.80)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>WOMAC function at 2 Years, mean (SD)</td>
<td>90.86 (13.21)</td>
<td>85.43 (16.09)</td>
<td>77.80 (22.42)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Delta WOMAC function, mean (SD)</td>
<td>40.93 (19.31)</td>
<td>40.89 (19.12)</td>
<td>41.93 (24.22)</td>
<td>0.351</td>
</tr>
<tr>
<td>Percent Below Poverty Level, n (%)</td>
<td>3363 (80.69%)</td>
<td>3303 (82.10%)</td>
<td>60 (41.38%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>&lt;10%</td>
<td>626 (15.02%)</td>
<td>585 (14.54%)</td>
<td>41 (28.28%)</td>
<td></td>
</tr>
<tr>
<td>10%-20%</td>
<td>102 (2.45%)</td>
<td>82 (2.04%)</td>
<td>20 (13.79%)</td>
<td></td>
</tr>
<tr>
<td>20%-30%</td>
<td>11 (2.22%)</td>
<td>33 (0.82%)</td>
<td>18 (12.41%)</td>
<td></td>
</tr>
<tr>
<td>30%-40%</td>
<td>26 (0.62%)</td>
<td>20 (0.50%)</td>
<td>6 (4.14%)</td>
<td></td>
</tr>
<tr>
<td>&gt;40%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent with Medicaid Coverage, n (%)</td>
<td>3128 (75.85%)</td>
<td>3086 (76.71%)</td>
<td>42 (32.31%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>&lt;=10%</td>
<td>679 (16.46%)</td>
<td>644 (16.12%)</td>
<td>35 (26.92%)</td>
<td></td>
</tr>
<tr>
<td>10%-20%</td>
<td>194 (4.70%)</td>
<td>167 (4.18%)</td>
<td>27 (20.77%)</td>
<td></td>
</tr>
<tr>
<td>20%-30%</td>
<td>97 (2.35%)</td>
<td>77 (1.93%)</td>
<td>20 (15.38%)</td>
<td></td>
</tr>
<tr>
<td>30%-40%</td>
<td>26 (0.63%)</td>
<td>20 (0.50%)</td>
<td>6 (4.62%)</td>
<td></td>
</tr>
</tbody>
</table>
Table 2: WOMAC pain and function 2 years after total hip arthroplasty: interaction between race and percent of Medicaid coverage at census-tract level

<table>
<thead>
<tr>
<th>Percent of Medicaid Coverage at Census-Tract Level</th>
<th>Race</th>
<th>WOMAC Pain at 2 Years*</th>
<th>WOMAC Function at 2 Years**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Estimate (Standard Error)</td>
<td>Estimate (Standard Error)</td>
</tr>
<tr>
<td>10%</td>
<td>Black</td>
<td>88.44 (1.59)</td>
<td>85.96 (1.78)</td>
</tr>
<tr>
<td></td>
<td>White</td>
<td>90.43 (1.05)</td>
<td>87.59 (1.22)</td>
</tr>
<tr>
<td>20%</td>
<td>Black</td>
<td>87.54 (1.28)</td>
<td>87.59 (1.22)</td>
</tr>
<tr>
<td></td>
<td>White</td>
<td>90.13 (1.08)</td>
<td>87.59 (1.22)</td>
</tr>
<tr>
<td>30%</td>
<td>Black</td>
<td>86.63 (1.38)</td>
<td>82.27 (1.49)</td>
</tr>
<tr>
<td></td>
<td>White</td>
<td>89.82 (1.16)</td>
<td>87.23 (1.31)</td>
</tr>
<tr>
<td>40%</td>
<td>Black</td>
<td>85.72 (1.81)</td>
<td>80.42 (1.93)</td>
</tr>
<tr>
<td></td>
<td>White</td>
<td>89.52 (1.28)</td>
<td>86.87 (1.45)</td>
</tr>
<tr>
<td>50%</td>
<td>Black</td>
<td>84.81 (2.41)</td>
<td>78.57 (2.56)</td>
</tr>
<tr>
<td></td>
<td>White</td>
<td>89.21 (1.44)</td>
<td>86.51 (1.63)</td>
</tr>
<tr>
<td>60%</td>
<td>Black</td>
<td>83.91 (3.07)</td>
<td>76.73 (3.28)</td>
</tr>
<tr>
<td></td>
<td>White</td>
<td>88.91 (1.61)</td>
<td>86.15 (1.83)</td>
</tr>
</tbody>
</table>

*Estimation based on linear mixed-effect model assessing the effect of interaction between race and percent of Medicaid coverage at census-tract level on WOMAC pain at 2 years after THA, using the following assumptions: WOMAC pain at baseline=53; age at surgery=65; BMI=28/kg/m²; HSS expectation score=83; sex=female; comorbidities=0; insurance=Medicaid; education=college and above.

** Estimation based on linear mixed-effect model assessing the effect of interaction between race and percent of Medicaid coverage at census-tract level on WOMAC function at 2 years after THA, using the following assumptions: WOMAC function at baseline=49; age at surgery=65; BMI=28/kg/m²; HSS expectation score=83; sex=female; comorbidities=0; insurance=Medicaid; education=college and above.

Figure 1 – New York City % Medicaid Coverage for THA Study Participants
Disparities in Patients’ Expectations of Foot and Ankle Surgery

Mackenzie T. Jones¹, Elizabeth A. Cody¹, Shirin A. Dey², Jackie Szymonińska², Michael L. Parks³, Lisa A. Mandl⁴, Susan M. Goodman⁵ and Scott J. Ellis⁶, ¹Hospital for Special Surgery, New York, NY, ²Rheumatology, Hospital for Special Surgery, New York, NY, ³Orthopaedic Surgery, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, ⁴Rheumatology, Hospital for Special Surgery Weill Cornell Medical College, New York, NY, ⁵Medicine, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, ⁶Hospital for Special Surgery/Weill Cornell Medicine, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Healthcare Disparities in Rheumatology Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
A previous study examining patients’ expectations of elective foot and ankle surgery found that race is significantly associated with expectations. In this study, using a patient-derived institutional Foot & Ankle Surgery Expectations Survey, we aimed to examine the relationship between patients’ preoperative expectations and census tract (CT) socioeconomic factors in addition to race.

Methods:
All adult patients scheduled for elective foot or ankle surgery by one of six orthopedic surgeons were screened for inclusion between August 2015 and March 2016. Preoperatively, patients completed the Foot & Ankle Surgery Expectations Survey, which contains 23 expectations categories, each rated on a 5-point Likert scale ranging from “I do not have this expectation” to “complete improvement expected”, with higher scores (range 1-23) indicating greater expectations. Using geocoding, individual-level registry data was linked to US census tracts data through patient addresses. Simple and multiple linear regression were used to model expectations scores as a function of individual race, and CT median income, Gini coefficient, and percentages of blacks, Hispanics, residents living below poverty, residents living alone, residents with insurance coverage, and residents with Medicaid coverage. The multiple linear regression model used backward selection methodology, requiring 0.05 significance to remain in the final model. An interaction between race and CT poverty was assessed.

Results:
352 patients (mean age 55±14 years, 66% female) were included in this study. Factors that were significantly associated with higher expectations in univariate modeling were non-Caucasian race, female sex, and census tract percentage of blacks, census tract percentage of Hispanics, census tract percentage of residents with Medicaid insurance, census tract poverty level, and census tract Gini coefficient (all p<0.05, Table 1). In multivariable modeling, females scored 5 points higher (5.00±1.93, p=0.01) on the Expectations Survey than males. Caucasians scored nearly 11 points lower (-10.98±3.13, p<0.001) than non-whites. There were no community CT variables that remained significant, and there was no interaction between race and CT poverty (p=0.7).

Conclusion:
Among patients undergoing diverse procedures in foot and ankle surgery, we found that female sex and non-Caucasian race were independently associated with higher expectations, but community social factors were not significant. These findings may help inform surgeons’ preoperative discussions as they address patients’ expectations. Future studies are needed to explore whether preoperative expectations scores correlate with postoperative satisfaction, and whether the factors that affect expectations also affect satisfaction.
### Table 1

<table>
<thead>
<tr>
<th>Univariate Factor</th>
<th>Beta coefficient ± SE</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, per 10 years</td>
<td>-0.63 ± 0.69</td>
<td>0.358</td>
</tr>
<tr>
<td>Sex: female (reference=male)</td>
<td>4.73 ± 2.09</td>
<td>0.024</td>
</tr>
<tr>
<td>BMI, per 1 kg/m²</td>
<td>0.21 ± 0.17</td>
<td>0.220</td>
</tr>
<tr>
<td>Race: white (reference=non-white)</td>
<td>-12.48 ± 3.35</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Marital status: married (reference=not married)</td>
<td>-3.46 ± 2.09</td>
<td>0.100</td>
</tr>
<tr>
<td>FAOS* Pain, per 10 points</td>
<td>-2.40 ± 0.43</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FAOS Symptoms, per 10 points</td>
<td>-1.47 ± 0.44</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FAOS ADL, per 10 points</td>
<td>-2.57 ± 0.41</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FAOS Sports, per 10 points</td>
<td>-1.70 ± 0.33</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SF-12 overall, per 10 points</td>
<td>-2.76 ± 0.42</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PCS, per 5 points</td>
<td>-2.69 ± 0.41</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MCS, per 5 points</td>
<td>-1.14 ± 0.44</td>
<td>0.010</td>
</tr>
<tr>
<td>Census tract data</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent black, per 1 percent</td>
<td>0.19 ± 0.09</td>
<td>0.036</td>
</tr>
<tr>
<td>Percent Hispanic, per 1 percent</td>
<td>0.22 ± 0.09</td>
<td>0.017</td>
</tr>
<tr>
<td>Percent single mothers, per 1 percent</td>
<td>0.55 ± 0.46</td>
<td>0.237</td>
</tr>
<tr>
<td>Percent live alone, per 1 -0.07 ± 0.92</td>
<td>0.942</td>
<td></td>
</tr>
<tr>
<td>Percent insured, per 1 percent</td>
<td>-0.32 ± 0.18</td>
<td>0.066</td>
</tr>
<tr>
<td>Percent Medicaid, per 1 0.42 ± 0.13</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Percent below poverty, per 1 percent</td>
<td>0.53 ± 0.18</td>
<td>0.003</td>
</tr>
<tr>
<td>Median income, per $10,000</td>
<td>-0.36 ± 0.23</td>
<td>0.114</td>
</tr>
<tr>
<td>Gini coefficient, per 10 -3.39 ± 1.38</td>
<td>0.015</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Multivariable Factor</th>
<th>Beta coefficient ± SE</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex: female (reference=male)</td>
<td>5.00 ± 1.93</td>
<td>0.010</td>
</tr>
<tr>
<td>Race: white (reference=non-white)</td>
<td>-10.98 ± 3.13</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FAOS ADL, per 10 points</td>
<td>-1.50 ± 0.52</td>
<td>0.004</td>
</tr>
<tr>
<td>PCS, per 5 points</td>
<td>-1.71 ± 0.52</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*FAOS = Foot and Ankle Outcome Score

---

**Disclosure:** M. T. Jones, None; E. A. Cody, None; S. A. Dey, None; J. Szymonifka, None; M. L. Parks, Zimmer Biomet, Inc., 5; L. A. Mandl, Boehringer Ingelheim, 2; American College of Physicians, 3, Up To Date, 7; S. M. Goodman, None; S. J. Ellis, None.


**Abstract Number:** 220

**English Language Proficiency and Total Joint Replacement Outcomes: Is There a Relationship?**
Bella Y. Mehta, Jackie Szymonifka, Shirin A. Dey, Stephen Grassia, Lisa A. Mandl, Anne R. Bass, Linda A. Russell, Michael L. Parks, Mark P. Figgie, Yuo-Yu Lee, Joseph T. Nguyen and Susan M. Goodman, 1Hospital for Special Surgery/Columbia University Mailman School of Public Health, New York, NY, 2Rheumatology, Hospital for Special Surgery, New York, NY, 3Medicine, Hospital for Special Surgery, New York, NY, 4Rheumatology, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, 5Orthopaedic Surgery, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, 6Epidemiology and Biostatistics, Hospital for Special Surgery, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Healthcare Disparities in Rheumatology Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Healthcare disparities are recognized for surgical outcomes in patients with Limited English Proficiency (LEP) (1). The purpose of this study is to assess the association of LEP on Total Knee (TKR) and Total Hip Replacement (THR) outcomes.

Methods:
Individual patient-level variables – namely, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain and function scores at baseline and 2 years after elective TKR and THR – were collected from a single institution registry between 5/07 and 2/11 and analyzed. We used census tract LEP -“Less than very well” as recommended for screening individuals. We obtained census level data using patients’ geocodable addresses (2). Only patients from closest states (NY, NJ and CT) were included (Figure 1). Data was analyzed using univariate and multivariable linear mixed effects models, with census tracts variables treated as random effects.

Results:
Table 1 describes the characteristics of the patients with THR and TKR. In univariable analyses, for every percent increase in LEP, the WOMAC scores at baseline and 2 year decreased significantly (p-value<0.001). However when adjusted for neighborhood poverty age, BMI, sex, comorbidities, and the Gini coefficient these changes were not statistically significant, suggesting potential confounders (Table 2). While women had worse baseline and 2-year WOMAC pain and function scores (all p≤0.04), this difference was not significantly influenced by neighborhood LEP (all p_interaction=NS).

Conclusion:
Patients from LEP neighborhoods have worse pain and function scores in unadjusted models. However when adjusted for potential confounders, the difference is not significant. Community factors contributing to healthcare disparities are multidimensional; thus, further studies examining individual LEP data would be warranted.

Figure 1
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total Hip Replacement</th>
<th>Total Knee Replacement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N=4009)</td>
<td>(N=3898)</td>
</tr>
<tr>
<td><strong>Patient demographics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at surgery (years), mean ± SD</td>
<td>65.6 ± 10.6</td>
<td>67.8 ± 9.5</td>
</tr>
<tr>
<td>Sex: female, n (%)</td>
<td>2160 (53.9%)</td>
<td>2346 (60.2%)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.9 ± 5.4</td>
<td>30.0 ± 5.9</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>3794 (94.6%)</td>
<td>3568 (91.5%)</td>
</tr>
<tr>
<td>Black</td>
<td>131 (3.3%)</td>
<td>174 (4.5%)</td>
</tr>
<tr>
<td>Asian</td>
<td>25 (0.6%)</td>
<td>74 (1.9%)</td>
</tr>
<tr>
<td>Other</td>
<td>43 (1.1%)</td>
<td>56 (1.4%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>16 (0.4%)</td>
<td>26 (0.7%)</td>
</tr>
<tr>
<td>Hispanic ethnicity, n (%)</td>
<td>102 (2.5%)</td>
<td>129 (3.3%)</td>
</tr>
<tr>
<td><strong>Patient status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASA class</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I–II</td>
<td>3307 (82.5%)</td>
<td>3124 (80.1%)</td>
</tr>
<tr>
<td>III–IV</td>
<td>700 (17.5%)</td>
<td>773 (19.8%)</td>
</tr>
<tr>
<td>One or more comorbidities</td>
<td>895 (22.3%)</td>
<td>1057 (27.1%)</td>
</tr>
<tr>
<td><strong>Census tract characteristics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poverty, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 10%</td>
<td>3325 (82.9%)</td>
<td>2787 (71.5%)</td>
</tr>
<tr>
<td>10% – &lt; 20%</td>
<td>507 (12.7%)</td>
<td>511 (13.1%)</td>
</tr>
<tr>
<td>20% – &lt; 30%</td>
<td>115 (2.9%)</td>
<td>129 (3.3%)</td>
</tr>
<tr>
<td>30% – &lt; 40%</td>
<td>49 (1.2%)</td>
<td>56 (1.4%)</td>
</tr>
<tr>
<td>≥ 40%</td>
<td>13 (0.3%)</td>
<td>27 (0.7%)</td>
</tr>
<tr>
<td>Percent poverty, mean ± SD</td>
<td>6.2 ± 6.5</td>
<td>6.6 ± 7.2</td>
</tr>
<tr>
<td>Limited English Proficiency (LEP), n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 10%</td>
<td>2981 (74.4%)</td>
<td>2787 (71.5%)</td>
</tr>
<tr>
<td>10% – &lt; 20%</td>
<td>614 (15.3%)</td>
<td>650 (16.7%)</td>
</tr>
<tr>
<td>20% – &lt; 30%</td>
<td>209 (5.2%)</td>
<td>251 (6.4%)</td>
</tr>
<tr>
<td>30% – &lt; 40%</td>
<td>120 (3.0%)</td>
<td>113 (2.9%)</td>
</tr>
<tr>
<td>≥ 40%</td>
<td>85 (2.1%)</td>
<td>97 (2.5%)</td>
</tr>
<tr>
<td>Percent LEP, mean ± SD</td>
<td>8.6 ± 9.6</td>
<td>9.2 ± 10.0</td>
</tr>
<tr>
<td>Gini coefficient, mean ± SD</td>
<td>0.45 ± 0.07</td>
<td>0.45 ± 0.07</td>
</tr>
<tr>
<td><strong>Patient-reported outcomes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline survey results, mean ± SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WOMAC pain</td>
<td>53.3 ± 17.8</td>
<td>54.4 ± 17.5</td>
</tr>
<tr>
<td>WOMAC function</td>
<td>49.5 ± 18.0</td>
<td>53.7 ± 17.6</td>
</tr>
<tr>
<td>2-year survey results</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WOMAC pain, mean ± SD</td>
<td>93.7 ± 11.3</td>
<td>87.9 ± 15.6</td>
</tr>
<tr>
<td>WOMAC function, mean ± SD</td>
<td>91.1 ± 13.1</td>
<td>85.6 ± 16.1</td>
</tr>
</tbody>
</table>

**Methodology:** Categorical variables are summarized as frequency (percent). Continuous variables are summarized as mean ± standard deviation.
Table 2. Impact of every 10% change in neighborhood limited English proficiency on WOMAC pain and function

<table>
<thead>
<tr>
<th>Time-point</th>
<th>WOMAC pain</th>
<th>p-value</th>
<th>WOMAC function</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimate ± SE</td>
<td></td>
<td>Estimate ± SE</td>
<td></td>
</tr>
<tr>
<td><strong>Total Hip Replacement</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline (Univariate)</td>
<td>-1.4 ± 0.3</td>
<td>&lt;0.001</td>
<td>-1.7 ± 0.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2-year (Univariate)</td>
<td>-0.9 ± 0.2</td>
<td>&lt;0.001</td>
<td>-1.2 ± 0.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline (Multivariable)</td>
<td>-0.6 ± 0.3</td>
<td>0.10</td>
<td>-0.6 ± 0.3</td>
<td>0.07</td>
</tr>
<tr>
<td>2-year (Multivariable)</td>
<td>-0.4 ± 0.2</td>
<td>0.054</td>
<td>-0.6 ± 0.3</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Total Knee Replacement</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline (Univariate)</td>
<td>-1.7 ± 0.3</td>
<td>&lt;0.001</td>
<td>-1.8 ± 0.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2-year (Univariate)</td>
<td>-1.0 ± 0.3</td>
<td>&lt;0.001</td>
<td>-1.1 ± 0.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline (Multivariable)</td>
<td>-0.8 ± 0.3</td>
<td>0.02</td>
<td>-0.5 ± 0.3</td>
<td>0.13</td>
</tr>
<tr>
<td>2-year (Multivariable)</td>
<td>-0.2 ± 0.3</td>
<td>0.43</td>
<td>-0.2 ± 0.3</td>
<td>0.54</td>
</tr>
</tbody>
</table>

**Methodology:** Univariate and multivariable linear mixed-effects models were analyzed, with census tracts treated as random effects. In addition to neighborhood Limited English Proficiency, variables included in the model were: age, BMI, sex, ≥ 1 comorbidity, neighborhood percent poverty (<10%, 10% - < 20%, 20% - < 30%, 30% - < 40%, ≥ 40% [reference group]), neighborhood Gini coefficient was also included.

**Disclosure:** B. Y. Mehta, None; J. Szymonifka, None; S. A. Dey, None; S. Grassia, None; L. A. Mandl, Boehringer Ingelheim, 2.American College of Physicians, 3.Up To Date, 7; A. R. Bass, Pfizer, 9,Abbot, 9; L. A. Russell, None; M. L. Parks, Zimmer Biomet, Inc., 5; M. P. Figgie, Lima, 7,Mekanika, 1; Y. Y. Lee, None; J. T. Nguyen, None; S. M. Goodman, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/english-language-proficiency-and-total-joint-replacement-outcomes-is-there-a-relationship

Abstract Number: 221

**Do Immigrant Communities Play a Role in Total Knee Arthroplasty (TKA) Outcomes?**

Bella Y. Mehta1, Jackie Szymonifka2, Shirin A. Dey2, Stephen Grassia3, Lisa A. Mandl4, Anne R. Bass4, Linda A. Russell4, Michael L. Parks5, Mark P. Figgie5, Yuo-Yu Lee6, Joseph T. Nguyen6 and Susan M. Goodman4, 1Hospital for Special Surgery/Columbia University Mailman School of Public Health, New York, NY, 2Rheumatology, Hospital for Special Surgery, New York, NY, 3Medicine, Hospital for Special Surgery, New York, NY, 4Rheumatology, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, 5Orthopaedic Surgery, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, 6Epidemiology and Biostatistics, Hospital for Special Surgery, New York, NY

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Sunday, November 5, 2017

Session Title: Healthcare Disparities in Rheumatology Poster

Session Type: ACR Poster Session A

Session Time: 9:00AM-11:00AM
Background/Purpose: Social factors affect TKA (total knee arthroplasty) outcomes in osteoarthritis, both at the individual and neighborhood levels. However, prior studies have not evaluated the influence of the proportion of foreign-born individuals within a neighborhood, as reported for other high-cost procedures (1). Our objective was to determine the association of neighborhood foreign-born resident proportion (FBRP) on Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain and function scores at baseline and 2 years after elective TKA. We examined if this is different between sexes.

Methods: Individual patient-level variables were obtained from a single institution TKA registry from 5/07-1/11, including demographics, baseline and 2 year WOMAC pain and function, and geocodable US addresses. We only included patients living in the hospital’s catchment area - i.e. New York, Connecticut and New Jersey (Figure 1). Individual patient-level variables were then linked to US Census Bureau data at the census tract level. Data was analyzed using univariate and multivariable linear mixed effects models, with census tracts variables treated as random effects. A separate linear mixed-effects model was used to assess the interaction between neighborhood FBRP and gender.

Results: Table 1 describes the 3,898 TKA cases analyzed. In multivariable analyses, patients from neighborhoods with low FBRP (< 10%) had slightly higher baseline and 2-year WOMAC pain and function scores than those with high FBRP (≥ 40%), but these differences were not statistically significant (Table 2). While women had worse baseline and 2-year WOMAC pain and function scores (all p ≤ 0.04), this difference was not significantly influenced by neighborhood FBRP (all pinteraction NS).

Conclusion: Patients coming from high (>40%) FBRP neighborhoods present with worse baseline pain and function. Two years later, worse pain and function persist; however, the difference is not significant. Although sex differences favoring males are notable, these differences are not associated with FBRP. Social factor contributions to healthcare disparities are multidimensional, and future studies examining immigration-related neighborhood characteristics may be warranted.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>FBRP* &lt;10%</th>
<th>FBRP* ≥10% - ≤40%</th>
<th>FBRP* &gt; 40%</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=1032)</td>
<td>(n=2527)</td>
<td>(n=339)</td>
<td>(≤ 10% v. &gt; 40%)</td>
</tr>
<tr>
<td><strong>Patient demographics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at surgery (years), mean ±SD</td>
<td>67.0±9.2</td>
<td>68.1±9.6</td>
<td>67.8±9.6</td>
<td>0.16</td>
</tr>
<tr>
<td>Sex: female, n (%)</td>
<td>568 (55.0%)</td>
<td>1538 (60.9%)</td>
<td>240 (70.8%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (kg/m²), mean±SD</td>
<td>30.1±5.7</td>
<td>29.9±6.0</td>
<td>31.0±6.6</td>
<td>0.03</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>White</td>
<td>1012 (98.1%)</td>
<td>2297 (90.9%)</td>
<td>259 (76.4%)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>5 (0.5%)</td>
<td>128 (5.1%)</td>
<td>41 (12.1%)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>9 (0.9%)</td>
<td>47 (1.9%)</td>
<td>18 (5.3%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>5 (0.5%)</td>
<td>35 (1.4%)</td>
<td>16 (4.7%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (0.1%)</td>
<td>20 (0.8%)</td>
<td>5 (1.5%)</td>
<td></td>
</tr>
<tr>
<td>Ethnicity, n (%)</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hispanic</td>
<td>5 (0.5%)</td>
<td>35 (1.4%)</td>
<td>16 (4.7%)</td>
<td></td>
</tr>
<tr>
<td><strong>Patient status</strong></td>
<td>0.81</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASA class</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I–II</td>
<td>828 (80.2%)</td>
<td>2026 (80.2%)</td>
<td>270 (79.7%)</td>
<td></td>
</tr>
<tr>
<td>III–IV</td>
<td>203 (19.7%)</td>
<td>501 (19.8%)</td>
<td>69 (20.4%)</td>
<td></td>
</tr>
<tr>
<td>One or more comorbidities</td>
<td>267 (25.9%)</td>
<td>674 (26.7%)</td>
<td>116 (34.2%)</td>
<td>0.003</td>
</tr>
<tr>
<td><strong>Sociodemographic characteristics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education level (highest), n (%)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Some high school, high school graduate or some college</td>
<td>359 (36.0%)</td>
<td>849 (35.1%)</td>
<td>158 (49.4%)</td>
<td></td>
</tr>
<tr>
<td>College graduate or Masters, professional or doctorate degree</td>
<td>639 (64.0%)</td>
<td>1569 (64.9%)</td>
<td>162 (50.6%)</td>
<td></td>
</tr>
<tr>
<td>Lives alone, n (%)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>863 (84.4%)</td>
<td>1881 (75.9%)</td>
<td>229 (69.0%)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>159 (15.6%)</td>
<td>598 (24.1%)</td>
<td>103 (31.0%)</td>
<td></td>
</tr>
<tr>
<td><strong>Census tract characteristics</strong></td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poverty, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 10%</td>
<td>975 (94.5%)</td>
<td>2078 (82.2%)</td>
<td>122 (36.0%)</td>
<td></td>
</tr>
<tr>
<td>10% – &lt; 20%</td>
<td>48 (4.7%)</td>
<td>300 (11.9%)</td>
<td>163 (48.1%)</td>
<td></td>
</tr>
<tr>
<td>≥ 20%</td>
<td>9 (0.9%)</td>
<td>149 (5.9%)</td>
<td>54 (15.9%)</td>
<td></td>
</tr>
<tr>
<td><strong>Patient-reported outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline survey results, mean ±SD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WOMAC** pain</td>
<td>54.9±17.6</td>
<td>54.7±17.3</td>
<td>51.0±18.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>WOMAC** function</td>
<td>54.2±16.9</td>
<td>54.1±17.7</td>
<td>49.1±17.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2-year survey results</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WOMAC** pain, mean±SD</td>
<td>89.3±14.7</td>
<td>87.5±15.7</td>
<td>86.5±17.5</td>
<td>0.01</td>
</tr>
<tr>
<td>WOMAC** function, mean±SD</td>
<td>86.7±14.9</td>
<td>85.4±16.2</td>
<td>83.6±17.9</td>
<td>0.005</td>
</tr>
</tbody>
</table>

*FBRP – Foreign Born Resident Proportion, **WOMAC-Western Ontario and McMaster Universities Osteoarthritis Index

**Methodology:** Categorical variables are summarized as frequency (percent). Continuous variables are summarized as mean ± standard deviation. Comparisons of categorical variables were made using chi-squared test. Continuous variables were compared using t-tests (for ≤ 10% v. > 40%) or ANOVA tests (for 3-group comparisons).
Table 2. Impact of neighborhood foreign born resident proportion (FBRP) on WOMAC pain and function.

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>WOMAC** pain estimate ± SD</th>
<th>p-value</th>
<th>WOMAC** function estimate ± SD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>0.36</td>
<td></td>
<td>0.24</td>
<td></td>
</tr>
<tr>
<td>FBRP* &lt; 10%</td>
<td>52.30 ± 3.26</td>
<td></td>
<td>51.71 ± 3.28</td>
<td></td>
</tr>
<tr>
<td>FBRP* ≥ 40%</td>
<td>51.19 ± 3.33</td>
<td></td>
<td>50.31 ± 3.36</td>
<td></td>
</tr>
<tr>
<td>2-year</td>
<td>0.80</td>
<td></td>
<td>0.97</td>
<td></td>
</tr>
<tr>
<td>FBRP* &lt; 10%</td>
<td>85.08 ± 3.02</td>
<td></td>
<td>85.95 ± 3.11</td>
<td></td>
</tr>
<tr>
<td>FBRP* ≥ 40%</td>
<td>84.81 ± 3.09</td>
<td></td>
<td>85.90 ± 3.18</td>
<td></td>
</tr>
</tbody>
</table>

*FBRP – Foreign Born Resident Proportion, **WOMAC- Western Ontario and McMaster Universities Osteoarthritis Index

Methodology: Multivariable models adjusting for age, sex, ≥ 1 comorbidity, neighborhood poverty percentage (<10%, 10% - < 20%, 20% - < 30%, 30% - < 40%, ≥ 40% [reference group])

Disclosure: B. Y. Mehta, None; J. Szymonifka, None; S. A. Dey, None; S. Grassia, None; L. A. Mandl, Boehringer Ingelheim, 2, American College of Physicians, 3, Up To Date, 7; A. R. Bass, Pfizer, 9, AbbVie, 9; L. A. Russell, None; M. L. Parks, Zimmer Biomet, Inc., 5; M. P. Figgie, Lima, 7, Mekanika, 1; Y. Y. Lee, None; J. T. Nguyen, None; S. M. Goodman, None.

Abstract Number: 222

Characterization of Unexpected Autoantibody Specificities in American Indian SLE Patients

Joseph M. Kheir1, Tim Gross1, Carla J. Guthridge1, Krista Bean1, Virginia C. Roberts1, Joel M. Guthridge2, M. Sohail Khan3, Fabio Mota4, Michael Peercy5, Bobby Saunkeah6 and Judith A. James7, 1Arthritis and Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, 2Arthritis & Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, 3Cherokee Nation Health Services, Tahlequah, OK, 4Chickasaw Nation Medical Center, Ada, OK, 5Epidemiology, Chickasaw Nation Department of Health, Ada, OK, 6Chickasaw Nation Department of Health, Ada, OK, 7Arthritis & Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK.

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Healthcare Disparities in Rheumatology Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

System Lupus Erythematosus (SLE) is an autoimmune disease that is over-represented in the American Indian (AI) population and often manifests as a more severe disease. Although the clinical manifestations can be diverse, nearly all patients share the presence of autoantibodies, including anti-dsDNA and anti-Sm which have high specificity for the disease. American Indian SLE patients often lack reactivity to autoantigens commonly found in SLE patients of other ethnicities. We have observed that sera from 41% of AI SLE patients contain unidentified autoantigenic reactivity by precipitin testing compared to 24% for AA, 17% for EA, and 23% for HA. Therefore the goal...
of this study is to identify non-traditional autoantibody specificities associated with disease in AI SLE patients.

Methods:
The sera from 100 AI SLE patients, 37 AI unaffected controls, 16 AI unaffected family members, and 17 AI patients with other systemic autoimmune diseases were screened using a 128 autoantigen protein array. Antigen reactivity based on a mean fluorescence intensity three standard deviations above the average of the unaffected negative controls for that antigen were considered positive. Hierarchical clustering of these data was used to identify shared autoantibody reactivities.

Results:
Twenty-two percent (n=22) of all of the positive SLE patients, 19% (n=3) of all positive unaffected family members, and 24% (n=4) of all positive other autoimmune disease samples had reactivity to the M2 mitochondrial antigen typically associated with primary biliary cirrhosis (PBC), an autoimmune liver disease. Furthermore, 91% (n=20) of the M2 positive SLE samples also contained 1 or more autoantibodies specific for or associated with myositis, whereas only 33% (n=1) of M2 positive unaffected family member samples, and 50% (n=2) of the M2 positive samples from individuals with other autoimmune disease contained myositis specific or associated autoantibodies.

Conclusion:
This study suggests that M2 and myositis autoantibodies are associated with disease in American Indian SLE patients. Although SLE patients are often diagnosed with more than one autoimmune disease, the coexistence of SLE and PBC or myositis is rare. The study was funded in part by Native American Research Centers for Health.

Disclosure: J. M. Kheir, None; T. Gross, None; C. J. Guthridge, None; K. Bean, None; V. C. Roberts, None; J. M. Guthridge, None; M. S. Khan, None; F. Mota, None; M. Peercy, None; B. Saunkeah, None; J. A. James, None.

Abstract Number: 223

Decreased Medication Adherence Is a Major Cause for Increased Risk of Hospitalizations Among High Risk Lupus Patients

Caroline Thirukumaran¹, Katherine McCarthy², Jessica Patel³ and Allen P. Anandarajah⁴, ¹orthopedics, University of Rochester Medical Center, Rochester, NY, ²Pharmacy, University of Rochester Medical Center, Rochester, NY, ³Allergy, Immunology and Rheumatology, University of Rochester Medical Center, Rochester, NY, ⁴Dept of Rheumatology, Univ of Rochester Medical Ctr, Rochester, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Healthcare Disparities in Rheumatology Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Low medication adherence in lupus has been associated with increased hospitalizations, more severe disease activity, and irreversible multi-organ damage. While lower socioeconomic levels, education, depression and polypharmacy have been identified as common determinants of non-adherence among patients with chronic diseases, few studies have investigated the rates of medication adherence with lupus.

Purpose: To compare medication adherence among patients with lupus at high risk for multiple admissions with all admissions for lupus.

Methods: We previously identified 171 lupus patients with a confirmed diagnosis that were admitted to Strong Memorial Hospital between July 1st of 2013 and June 30th of 2015. We then classified a high risk group of 28 lupus patients who had required ≥ 3 admissions/ year over the 2 years. For this study we linked the database of all lupus patients with pharmacy claims database for the same period to calculate the medication possession ratio (MPR), an indicator of whether a patient had adequate medication supply in a given time frame. For the bivariate analysis, we used t-tests and chi-square tests to check for the differences in distribution of patient demographics and MPR across the high-risk and non-high risk group. For the multivariate analyses, we estimated hierarchical linear regression models and controlled for the clustering of refills by patient and medication. We also controlled for patient demographics and medication details. We used two-tailed hypothesis tests and p-value<0.05 to indicate statistical significance.

Results: The high-risk group was significantly younger (mean age 39.64 years [SD: 19.09] as compared to mean age of 47.57 years in non-
high risk group, \( p=0.03 \), 82% were females compared to 92% in the non-high risk group and the group had significantly higher proportion of African Americans 61% as compared to 41% in the non-high risk group \( p=0.05 \) see Table 1. Complete pharmacy data was available for 102 patients. The mean MPR was lower among the high-risk group (73.40% as compared to 79.93% in the non-high risk group). Our multivariate analysis showed that after controlling for relevant confounders, on average high-risk patients had 10 percent point lower MPR as compared to non-high risk patients (Estimate: -10.41, 95% CI: [-21.36 to 0.54], \( p=0.06 \)).

**Conclusion:** Medication non-adherence is a major cause of increased risk for admissions among patients with lupus. Targeting measures to improve medication adherence is an important component of the management of patients with lupus.

<table>
<thead>
<tr>
<th></th>
<th>All lupus patients (n=143)</th>
<th>High risk lupus (n=28)</th>
<th>Total (n=171)</th>
<th>p-value (Fischer/chi-square)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age: mean (SD)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>47.57 (17.32)</td>
<td>39.64 (19.09)</td>
<td>46.27 (17.81)</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>Females: n (col%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>132 (92.31)</td>
<td>23 (82.14)</td>
<td>155 (90.64)</td>
<td>0.09</td>
</tr>
<tr>
<td><strong>Race: n (col%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>2 (1.40)</td>
<td>2 (7.14)</td>
<td>4 (2.34)</td>
<td>0.13</td>
</tr>
<tr>
<td>Caucasian</td>
<td>58 (40.56)</td>
<td>17 (60.71)</td>
<td>75 (43.86)</td>
<td>0.05</td>
</tr>
<tr>
<td>Hispanic</td>
<td>76 (53.15)</td>
<td>8 (28.57)</td>
<td>84 (49.12)</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>7 (4.90)</td>
<td>1 (3.57)</td>
<td>8 (4.68)</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>Average number of medications: mean (SD)</strong></td>
<td>2.12 (1.02)</td>
<td>2.74 (1.15)</td>
<td>2.24 (1.06)</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Average number of fills per medication: mean (SD)</strong></td>
<td>6.64 (5.78)</td>
<td>5.29 (4.82)</td>
<td>6.39 (5.62)</td>
<td>0.35</td>
</tr>
<tr>
<td><strong>Average MPR: mean (SD)</strong></td>
<td>79.93 (25.02)</td>
<td>73.40 (22.80)</td>
<td>78.71 (24.64)</td>
<td>0.30</td>
</tr>
<tr>
<td><strong>Average MPR for top 4 medications: mean (SD)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prednisone</td>
<td>78.51 (36.42)</td>
<td>69.31 (29.02)</td>
<td>76.67 (35.06)</td>
<td>0.38</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>78.78 (22.58)</td>
<td>76.19 (25.39)</td>
<td>78.29 (22.98)</td>
<td>0.71</td>
</tr>
<tr>
<td>Mycophenolate</td>
<td>83.83 (32.15)</td>
<td>62.22 (38.18)</td>
<td>77.87 (34.63)</td>
<td>0.14</td>
</tr>
</tbody>
</table>

Table: 1 Descriptive data of lupus cohorts
<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Confidence interval</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non high risk</td>
<td>Reference</td>
<td>-10.41</td>
</tr>
<tr>
<td>High risk</td>
<td>-10.41</td>
<td>0.06</td>
</tr>
<tr>
<td>Age</td>
<td>0.15</td>
<td>[-0.11,0.41]</td>
</tr>
<tr>
<td>Female</td>
<td>Reference</td>
<td>[-23.50,6.66]</td>
</tr>
<tr>
<td>Male</td>
<td>-8.42</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>Reference</td>
<td>[-13.29,5.26]</td>
</tr>
<tr>
<td>African American</td>
<td>-4.01</td>
<td>[-0.84,56.06]</td>
</tr>
<tr>
<td>Asian</td>
<td>27.61</td>
<td>[-39.08,7.06]</td>
</tr>
<tr>
<td>Hispanic</td>
<td>-16.01</td>
<td></td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>Reference</td>
<td>[-14.33,21.32]</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>3.50</td>
<td>[-73.77,37.32]</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>-18.23</td>
<td>[-21.82,87.26]</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>32.72</td>
<td>[-21.54,88.78]</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>33.62</td>
<td>[-12.84,44.74]</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>15.95</td>
<td>[-16.81,16.35]</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>-0.23</td>
<td>[-10.94,16.02]</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>2.54</td>
<td>[-11.77,11.88]</td>
</tr>
<tr>
<td>Mycophenolate</td>
<td>0.06</td>
<td>[-8.97,8.62]</td>
</tr>
<tr>
<td>Prednisone</td>
<td>-0.18</td>
<td>[1.11,65.94]</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>33.52*</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Multivariate analysis of medication possession ratio

Disclosure: C. Thirukumaran, None; K. McCarthy, None; J. Patel, None; A. P. Anandarajah, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/decreased-medication-adherence-is-a-major-cause-for-increased-risk-of-hospitalizations-among-high-risk-lupus-patients

Abstract Number: 224

Patterns of Methotrexate Use in African Countries with Low Versus Medium/High Human Development Index: Preliminary Results of Semi-Structured Interviews

Carol A Hitchon1, Yan Liu2, Steven Shi3, Girish M Mody4, Candace H. Feldman5, Michael Weinblatt6 and Ines Colmegna7, 1 Internal Medicine, University of Manitoba, Winnipeg, MB, Canada, 2McGill University, Montreal, QC, Canada, 3University de Montreal, Montreal, QC, Canada, 4Dept of Rheumatology, University of Kwa Zulu-Natal, Durban, South Africa, 5Brigham and Women’s Hospital, Division of Rheumatology, Immunology and Allergy, Boston, MA, 6Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 7Division of Rheumatology, Department of Medicine, Division of Experimental Medicine, McGill University, Montreal, Quebec, Canada, Montreal, QC, Canada

First publication: September 18, 2017

SESSION INFORMATION
**Background/Purpose:** Methotrexate (MTX) is standard therapy for rheumatoid arthritis (RA) and also used to treat other rheumatic diseases. Existing guidelines for RA treatment/MTX use did not contemplate the realities of resource limited countries. We aimed to understand MTX use patterns and barriers in African countries to inform the development of culturally appropriate guidelines.

**Methods:** We identified African physicians (MDs) from countries classified as low Human Development Index (LHDI) and medium/high HDI (MHDI) by the United Nations Development Programme and who self-identified as MTX prescribers. Each MD participated in a 45 minute semi-structured interview by phone in either English or French regarding their MTX practices.

**Results:** 29 MDs (23 rheumatologists; 6 internists) from 29 African countries were interviewed (17 LHDI; 12 MHDI) representing a population of 1,000.4 million; (LHDI 673.8 million; MHDI 326.6 million). The median (range) of rheumatologists/ million population in these countries was only 0.17 (0-9.4). LHDI countries had significantly fewer rheumatologists/ million population than MHDI (0.1 (0-0.66) vs 1.1(0-9.43) p=0.004). MTX was prescribed by non-rheumatologists in 93% LHDI and 67% MHDI countries. Most MDs practised in capital cities and served adult patients. 88% LHDI and 67% MHDI MDs also provided pediatric care. The main indication for MTX use was RA with connective tissue diseases and psoriatic arthritis as secondary indications. Prior to prescribing MTX, most MDs (97%) evaluated patients for pulmonary, hepatic and renal dysfunction and excluded cytopenias. Screening was performed for TB (with CXR) by 62%, HIV by 55% and Hepatitis B/C by 52%. Pregnancy screening was usually by patient self-report (86%). Discussing alcohol consumption was considered pertinent to the local consumption by 42% of MDs. MTX dosing was similar between LDHI and MDHI countries, and usually given with folate (83%). Only 55% of countries had parenteral MTX. 55% of MDs reported barriers to MTX use due to drug availability or costs. Compared to MHDI countries, LHDI countries were more likely to have an inconsistent MTX supply throughout the year (82% LHDI vs 42% MHDI (p=0.05) and less likely to have MTX available in the hospital pharmacy (35% LHDI vs 83% MHDI; p=0.02). Major contributors to MTX non-adherence included drug cost or availability (85%), lack of prescribers (15%) and patients’ beliefs/education/tolerance (37%).

**Conclusion:** The challenges of treating RA patients in African countries with low HDIs are unique. Costs of medical care and drugs, limited subspecialist availability, patient specific beliefs, and lack of MTX are significant challenges faced by MDs treating patients with rheumatic disease. Understanding the African LHDI reality is critical for the development of guidelines to improve care quality and outcomes. Table: Patterns of MTX prescription in Africa. All values are % or median (range)
Population (2015)  
Total n=29  
LHDI n=17  
MHDI n=12  
P value  
1,000,446,000-673,839,000-326,607,000  
P=0.47

Rheumatologists/million  
0.17 (0-9.4)  
0.8 (0-0.66)  
1.1 (0-9.4)  
P=0.004

Rheumatologic indications for methotrexate  
Main reason RA (% reporting)  
100  
100  
100  
P=1

Second reasons CTD/ PsA/ JIA  
43/14  
44/38/19  
42/50/8  
P=0.7

Pre-methotrexate evaluation  
Lung, liver, kidney, hematology  
97%  
94%  
100%  
P=1

Xray done  
58%  
65%  
50%  
P=0.4

TB screen CXR done  
62%  
71%  
50%  
P=0.3

HIV done  
55%  
59%  
50%  
P=0.6

Hepatitis B/C done  
52%  
41%  
67%  
P=0.3

Pregnancy screen by self-report only  
86%  
88%  
83%  
P=1

Methotrexate prescription  
Starting dose (mg/wk)  
10(2.5-15)  
10(7.5-15)  
10(2.5-15)  
P=0.5

Maximum dose (mg/wk)  
25(12.5-30)  
25(15-25)  
22.5(12.5-30)  
P=0.5

Folate prescribed  
83%  
82%  
83%  
P=1

Prescribing challenges  
Cost for 1 month (10-15 mg/wk) USD  
17(0.5-27)  
17.25 (1-27)  
10(0.5-27)  
P=0.7

Injectable formulation available  
55%  
52%  
58%  
P=0.8

Inconsistent MTX supply  
66%  
42%  
42%  
P=0.05

MTX in hospital pharmacy  
55%  
82%  
83%  
P=0.02

Adherence challenges  
Cost/drug availability  
85%  
94%  
73%  
P=0.3

Lack of prescribers  
15%  
13%  
18%  
P=1

Patient belief/education/intolerance  
37%  
44%  
27%  
P=0.4

Disclosure:  
C. A. Hitchon, None;  
Y. Liu, None;  
S. Shi, None;  
G. M. Mody, None;  
C. H. Feldman, None;  
M. Weinblatt, None;  
I. Colmegna, None.

View Abstract and Citation Information Online -  

Abstract Number: 225

Barriers to the Use of Methotrexate in Ethiopia: Survey of Pharmacy Providers

Carol A Hitchon1, Yvon de Jong2, Michele Meltzer3, Rosie Scuccimarri4, Birhanu D Desyibelew5, Addisu Melkie5, Yewondwosen Mengistu6 and Ines Colmegna6,7, 1University of Manitoba, Winnipeg, MB, Canada, 2Ecumenical Pharmaceutical Network, Nairobi, Kenya, 3Thomas Jefferson University, Philadelphia, PA, 4Department of Pediatrics, McGill University Health Centre, Montreal, QC, Canada, 5Addis Ababa University, Addis Ababa, Ethiopia, 6Division of Rheumatology, Department of Medicine, Division of Experimental Medicine, McGill University, Montreal, Quebec, Canada, Montreal, QC, Canada, 7Rheumatology, McGill University Health Centre, Montreal, QC, Canada

First publication: September 18, 2017
Background/Purpose:

African countries with a low Human Development Index (LHDI) based on life expectancy, education and income per capita, face competing social, economic, health and poverty related issues that distract from the treatment of chronic conditions such as Rheumatoid Arthritis (RA). Methotrexate (MTX) is standard of care for RA and used for other rheumatic diseases. We sought to determine MTX availability and MTX dispensing practices of pharmacy providers (PP) in Ethiopia, an LHDI country, in order to inform the development of culturally appropriate guidelines for using MTX to treat rheumatic diseases.

Methods:

The Ecumenical Pharmaceutical Network and the Ethiopian Catholic – Social and Development commission (ECC-SDCO) is the second largest health institution in Ethiopia (next to the public health system) and oversees 83 health institutions of which 52 have a pharmacy department (includes 4 hospitals, 16 health centers and 32 clinics). In September 2016, PP attending the Essentials of Pharmacy Practice course provided by ECC-SDCO were invited to participate in an anonymous survey regarding their experience with dispensing MTX for the treatment of rheumatic conditions. We also conducted a 45 minute semi-structured interview for pharmacists serving the country’s sole public rheumatology clinic in Ethiopia. Descriptive statistics are reported from the survey and interview notes.

Results:

Twenty-three PP (18 pharmacy technicians; 5 pharmacists) from hospitals and health centers of 9 regional states and 2 chartered cities of Ethiopia completed the survey (18/23 were located outside Addis). Seven (32%) worked in a hospital based pharmacy, 12 (55%) in a health centre pharmacy and 3 (14%) in other areas (i.e. clinic pharmacy). The number of years of practice (median (range)) was less for pharmacy technicians compared to pharmacists (4 (1-8) vs 10(6-15) p<0.0001). Methotrexate was available in only 3/23 pharmacies (2 were hospital pharmacies) and was only available as oral tablets. Five PP reported that MTX was available in the hospital pharmacy of their region. Only 2/23 PP had dispensed MTX and in both cases it was not for rheumatic conditions. Only 3 (13%) PP reported feeling comfortable educating patients on how to take methotrexate, (2 had counseled on MTX, 1 had not, 1 counselled but without confidence). Counselling included need for blood work (n=3), folic acid (n=3) and alcohol intake (n=1). No PP counselled on contraception. While interviewed pharmacists were confident regarding counselling patients on MTX, contraception was not consistently discussed. Additional barriers to prescribing MTX identified by interviewed PP included inconsistent supply and prioritizing use of MTX for non-rheumatologic conditions.

Conclusion:

Bridging the gap of RA treatment between developed and emerging countries is both a need and a responsibility. The survey and interview identified two key aspects limiting the use of MTX in Ethiopia: a) availability of the drug in pharmacies, and b) confidence of designated pharmacists in supplying and counseling patients for methotrexate. Improved MTX access and recommendations for counselling are needed to increase the confidence of pharmacists in dispensing MTX.
Background/Purpose: Multiple epidemiological studies ascertained that GCA is one of the most common systemic vasculitis in western countries. But, there is only one study based on 2 patients in Tennessee to assess the low incidence of GCA in African descent (AD) populations. Moreover, very few series are devoted to these patients in the literature. Our objective was to describe the characteristics of GCA and study the incidence in the Afro-Caribbean (AC) population of Martinique, a French region of the West Indies where inhabitants are more than 90% of AD and have free access to health care including a regional competence center for systemic vasculitis.

Methods: Population based retrospective study in Martinique. Computed files of the 2 pathology units of the island (public and private) were analyzed to find all patients with a positive temporal arteritis biopsy. All medical files were reviewed to assess the incidence, but only AC patients (self-declared) were included to describe the disease in an African descent cohort.

Results: 40 patients had a biopsy proven GCA between 1991 and 2016. Mean age at GCA diagnosis was 75.7 years (SD±7.4; range: 63-91). Main manifestations at diagnosis of the 38 patients of AC origin (30 women, 8 men) were: fever 9.1% (3/33), asthenia 64.5% (20/31), weight loss 75.7% (25/33), headache 69.4% (25/36), jaw claudication 36.3% (12/33), scalp tenderness 35.2% (12/34), anterior ischemic optic neuropathy 31.4% (11/35), stroke 2.9% (1/34), and polymyalgia rheumatica 35.2% (12/34). C-reactive protein was over normal value for 96.8% (n=31; mean value 106.5, range: 7-283). ESR was positive in 86.3% (19/22). Available for 15 patients, CT scan of the aorta and its branches revealed one aortitis and one arteriopathy of lower limbs. All patients were treated by steroids. Twenty three patients (60.5%) were followed >18 months and mean follow up duration was 43.7 months. Eleven patients relapsed. Six patients died (15.8%). Kaplan Meier analysis found 93.9%, 84.6%, 75% survival rates at respectively 6, 12 and 24 months. Crude mean annual incidence of GCA in Martinique was 3.12 cases for 10^6 inhabitants from 1991 to 2016. Mean number of GCA gradually increased from 0.5 patient/year between 1991 and 2000, 1.6 between 2001 and 2010 to 3.8 between 2011 and 2016, parallel to the increasing proportion of elderly in the martinican population (13% was over 60 years old in 1990, 23% in 2016 and official estimation is 39.6% in 2032).

Conclusion: This is the first population based description of GCA in an AD population. The features in Martinique are similar to the literature, except for the ischemic complications that seem less frequent in our population. Our data confirm the low frequency of GCA in AD populations compared to Caucasians. The retrospective nature of the study and the absence of negative biopsy GCA could weaken conclusion. We note a progressive increase of annual number of cases during the 25 years of survey, parallel to the accelerated ageing of the martinican population. We could hypothesize that low incidence of GCA in AD populations is at least partially related to the low rate of elderly in most of these populations around the world, and could also increase in the future.

Disclosure: F. Moinet, None; V. Molinie, None; K. Polomat, None; H. Merle, None; M. Blettery, None; L. Brunier-Agot, None; M. DeBandt, None; C. Deligny, None.

Abstract Number: 227

Chinese-American Rheumatology Patients Who Use Traditional Chinese-Medicine Have Worse Patient Reported Outcomes

Kai Sun1, Jackie Szymonifka2, Henghe Tian3, Ya Ju Chang4, Jennifer Leng5 and Lisa A. Mandl6, 1Hospital for Special Surgery/Weill Cornell medicine, New York, NY, 2Rheumatology, Hospital for Special Surgery, New York, NY, 3Internal Medicine, New York University School of Medicine, New York, NY, 4Mount Sinai Beth Israel, New York, NY, 5Immigrant Health and Cancer Disparities laboratory, Memorial Sloan Kettering Cancer Center, New York, NY, 6Rheumatology, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY

First publication: September 18, 2017
Background/Purpose: Chinese-Americans are a fast growing US immigrant group, and many use Traditional Chinese Medicine (TCM). Ethnic Chinese patients also have worse outcomes in SLE and RA compared to Caucasians. In order to optimally care for this growing population with rheumatic diseases, rheumatologists must have some understanding of patients’ traditional cultural beliefs and practices, which may influence medication taking behaviors, and thus ultimately outcomes. TCM use by Chinese-American rheumatology patients has not previously been studied, and whether patient-reported outcomes differ between TCM users and nonusers is unknown.

Methods: Subjects were recruited from two rheumatology clinics that serve a predominantly Chinese-American immigrant population. Inclusion criteria were English or Mandarin Chinese fluency and being actively treated for a systemic rheumatic disease. Questionnaires were used to assess TCM use, acculturation, and demographics. Self-reported health status was assessed using Patient-Reported Outcome Measurement Information System (PROMIS®) short forms. Chart review was performed to gather clinical data. Parametric and nonparametric statistics were performed as appropriate. Multivariable logistic regression using step-wise selection was used to examine factors independently associated with TCM use.

Results: 230 enrolled, median age 55 years (range 20-97), 65% female, 71% ≤ high school education, 70% Medicaid, and 22% reported English fluency. 50% reported TCM use in the past year, most frequently tuina massage (47%), acupuncture (45%), and herbs (37%). 60% of TCM users used TCM to treat rheumatic disease, but only 34% discussed TCM use with the rheumatologist. TCM users had worse scores in PROMIS® anxiety, depression, pain interference, fatigue, physical function, and social health. There was no difference in PROMIS® scores between herb users and nonusers; however more frequent TCM users and those using TCM to treat rheumatic disease had worse pain and function. In multivariable analysis, older age (Odds Ratio [OR]1.03, p=0.04), female sex (OR 2.3, p=0.02), ≥ some college education (OR 2.1, p=0.04), US residence for ≥20 years (OR 2.2, p=0.03), more anxiety (OR 1.05, p=0.004), fewer years since rheumatic disease diagnosis (OR 1.1, p=0.01), reporting western medicine to be ineffective (OR 5.3, p=0.003), and belief in TCM (OR 2.8, p=0.01) were independently associated with TCM use.

Conclusion: In this group of Chinese-American rheumatology patients with low education, low socioeconomic status, and poor acculturation, TCM use is common (50%) and is independently associated with older age, female sex, better education, longer US residence, higher levels of anxiety, more recent rheumatic disease diagnosis, perceived ineffectiveness of western medicine, and stronger belief in TCM. Providers should ask Chinese-American patients about TCM use because it may be a proxy for unmet therapeutic needs in this population, as TCM users have worse patient-reported outcomes across many important domains.

Disclosure: K. Sun, None; J. Szynonifika, None; H. Tian, None; Y. J. Chang, None; J. Leng, None; L. A. Mandl, Boehringer Ingelheim, 2, American College of Physicians, 3, Up To Date, 7.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/chinese-american-rheumatology-patients-who-use-traditional-chinese-medicine-have-worse-patient-reported-outcomes

Abstract Number: 228

Characterizing Indigenous Community Engagement Patterns in Published Arthritis Studies: A Systematic Review of the Literature

Chu-Yang Lin1, Kelle Hurd1, Cheryl Barnabe2 and Adalberto Loyola-Sánchez3, 1University of Calgary, Calgary, AB, Canada, 2Division of Rheumatology, University of Calgary, Calgary, AB, Canada, 3Rheumatology, University of Calgary, Calgary, AB, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Healthcare Disparities in Rheumatology Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Indigenous populations in Canada, Australia, New Zealand and the United States of America have a higher prevalence of arthritis conditions and experience worse outcomes. Research can play a pivotal role in identifying and addressing care gaps, and community engagement (CE) approaches are the most promising ways for achieving positive and sustainable impacts. This systematic review characterizes CE patterns in arthritis studies involving Indigenous populations from four countries.

Methods: We performed a secondary systematic review (MEDLINE, EMBASE, CINAHL and Indigenous-specific online indexes up to May 2016) that characterized the epidemiology, clinical outcomes, mortality and health services utilization for arthritis in Indigenous populations of the four countries (n=5,269 titles and abstracts). 159 studies met inclusion criteria for the relevant outcomes. Included studies were evaluated for their descriptions of CE at inception of research, data collection, and data usage (i.e. results interpretation and dissemination). Extraction was performed in duplicate using standardized criteria. Descriptions were subsequently mapped onto a CE spectrum adapted from the Beacon for Public Engagement, ranging from the lowest to highest level of engagement: inform, consult, involve, collaborate or empower.
had less impairment (mean 48.0) compared to Filipinos (mean 42.1, p=0.02) or other Asians (mean 42.3, p=0.04).

Comparing outcomes among the Asian subgroups, the only significant differences were in the SF-36 PF scores, for which Chinese patients scored higher LSI scores than whites, as did Latinos and African Americans. However, Asians did not differ from whites in SLICC, SLEDAI or SF-36 PF.

In Table 1, we show the mean and SD of SLE severity, damage and function measures are shown in the table, along with results from the regression models. Asian Americans in all subgroups had significantly higher disease activity and damage indices compared to whites, and higher physical function scores compared to whites. Furthermore, compared to whites, Filipinos had higher disease activity and damage indices, lower physical function scores, and higher fatigue scores.

Results: Of the 159 included studies, 127 were CAN/USA publications and 32 were AUS/NZ publications. Only 32% (n=51) of the 159 included studies reported any description of CE (n=43 CAN/USA, n=8 AUS/NZ). Few studies report CE activities at the inception of research (n=6, 12%), with consultation described in 3 studies and collaboration discussed in 3 studies. In comparison, 98% (n=50) of studies described CE at the data collection stage, which also had the highest frequency of MCE compared to other research stages (n=11 studies).

Here, the majority of studies (n=30) reported community consultation, while 11 studies reported involvement or collaboration. Nine studies recruited community members to aid data collection. During data usage, ten studies (20%) described CE, including 4 studies where Indigenous communities were informed or consulted with, and 6 where Indigenous communities were involved or collaborated with. Regionally, the reporting of MCE was concentrated in CAN/USA, with MCE described in all stages of research, whereas publications from AUS/NZ only reported MCE at data collection.

Conclusion: The reporting of CE in Indigenous arthritis studies in the specified countries is limited in frequency, with few studies reaching the higher end of the CE spectrum (i.e. collaboration and empowerment). CE was most frequently reported during the data collection stage and is mostly described as consultation, which can be reached merely by obtaining informed consent. This reflects researchers’ adherence to ethical guidelines rather than a CE effort. Regional differences in CE reporting are likely explained by differences in research policies for Indigenous research. We call for CE guidelines specific to Indigenous rheumatology research.

Disclosure: C. Y. Lin, None; K. Hurd, None; C. Barnabe, None; A. Loyola-Sánchez, None.

Abstract Number: 229

Divergent Measures of Lupus Disease Damage and Severity Among Asians in an Ethnically Diverse Cohort

Laura Trupin1, Patricia P. Katz2, Cristina Lanata2, Lindsey A. Criswell2, Charles G. Helnick3, Maria Dall’Era2 and Jinoos Yazdany1,

1Medicine/Rheumatology, University of California San Francisco, San Francisco, CA, 2Medicine/Rheumatology, University of California, San Francisco, San Francisco, CA, 3Centers for Disease Control and Prevention, Atlanta, GA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Healthcare Disparities in Rheumatology Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is not well characterized among Asian Americans, particularly among subgroups of Asians. We aim to compare measures of disease status, including severity, damage, activity, and physical functioning, by race/ethnicity in a diverse SLE cohort.

Methods: Data were derived from the California Lupus Epidemiology Study (CLUES), a population based, multi-ethnic cohort of SLE patients in the San Francisco area begun in 2015. SLE was defined according to the 1997 ACR criteria. At baseline, participants had a physician exam that included the SELENA- SLE Disease Activity Index (SLEDAI) and SLICC/ACR Damage Index (SDI). The Lupus Severity Index (LSI) was computed based on the ACR criteria confirmed at the study visit. The LSI assigns a weighted value to each criterion and is scaled 0-10; it has been shown to correlate with disease activity and mortality. Patients completed the SF-36 Physical Functioning (PF) subscale; this scale has a potential range of 0-100, with higher values indicating better function. They also provided self-identified race/ethnicity and details of Asian origin. We compared SLE status measures by race/ethnicity and within subgroups of Asian origin, in regression models controlling for age, disease duration, income < 125% of the federal poverty limit, and gender. Tukey post hoc tests were used to compare the outcomes among Asian subgroups.

Results: Among 283 patients, 30% were white, 20% Latino, 11% African American, and 39% Asians. The 102 Asian Americans included 62 Chinese, 23 Filipino and 17 from all other subgroups. Nearly 90% of the cohort were women, with mean age 45±14 and mean disease duration of 16±10 years. Just over half the cohort had some damage (SDI> 0) at baseline. Overall means and distributions of the status measures are shown in the table, along with results from the regression models. Asian Americans in all subgroups had significantly higher LSI scores than whites, as did Latinos and African Americans. However, Asians did not differ from whites in SLICC, SLEDAI or SF-36 PF. Comparing outcomes among the Asian subgroups, the only significant differences were in the SF-36 PF scores, for which Chinese patients had less impairment (mean 48.0) compared to Filipinos (mean 42.1, p=0.02) or other Asians (mean 42.3, p=0.04).
Conclusion: In this multi-ethnic cohort, Asians had high disease severity, similar to African Americans and Latinos, but accumulated significantly less damage than these other racial/ethnic groups over time. The social, environmental, biological or health factors leading to this paradox among Asians requires further investigation. With the exception of physical functioning, there were few differences between the Asian subgroups, but this analysis was limited by small sample size and should be further explored as the cohort expands.

Table. SLE Disease Status Measures by Race/Ethnicity

<table>
<thead>
<tr>
<th>Race/ethnicity</th>
<th>Lupus Severity Index</th>
<th>SLICC Damage Index</th>
<th>SELENA-SLEDAI</th>
<th>SF36 Physical Functioning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total (n=238)</td>
<td>6.8 ± 1.6 (3.4-9.5)</td>
<td>1.2 ± 1.6 (0-7)</td>
<td>2.8 ± 2.9 (0-16)</td>
<td>44.1± 11.9 (15-57)</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td>adjusted mean (95% confidence interval) *</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>7.1 (6.8-7.4)**</td>
<td>1.2 (0.9-1.5)</td>
<td>2.8 (2.2-3.3)</td>
<td>46.3 (44.1-48.4)</td>
</tr>
<tr>
<td>African American</td>
<td>7.1 (6.6-7.6)**</td>
<td>1.8 (1.2-2.3)**</td>
<td>2.5 (1.5-3.5)</td>
<td>38.2 (34.3-42.1)**</td>
</tr>
<tr>
<td>Hispanic</td>
<td>7.2 (6.9-7.6)**</td>
<td>1.3 (1.0-1.7)</td>
<td>3.2 (2.5-3.9)</td>
<td>42.0 (39.4-44.7)</td>
</tr>
<tr>
<td>White</td>
<td>6.2 (5.9-6.5)</td>
<td>0.8 (0.5-1.2)</td>
<td>2.7 (2.1-3.3)</td>
<td>45.4 (43.0-47.8)</td>
</tr>
</tbody>
</table>

(diff by race/ethnicity) <0.001 0.02 0.67 0.001

* Adjusted for age, gender, disease duration, poverty level income (<125% federal poverty limit).

** Results significantly different from Whites for indicated measure.

Disclosure: L. Trupin, None; P. P. Katz, Bristol-Myers Squibb, 2; C. Lanata, None; L. A. Criswell, None; C. G. Helmick, None; M. Dall’Era, None; J. Yazdany, None.


Abstract Number: 230

The Impact of Limited Health Literacy on Patient-Reported Outcomes (PROs) in Systemic Lupus Erythematosus (SLE)

Patricia P. Katz1, Maria Dall’Era2, Laura Trupin3, Cristina Lanata2, Stephanie Rush4, Charles G. Helmick5, Lindsey A. Criswell4 and Jinoos Yazdany3, 1Medicine, University of California, San Francisco, San Francisco, CA, 2Medicine/Rheumatology, University of California, San Francisco, San Francisco, CA, 3Medicine/Rheumatology, University of California San Francisco, San Francisco, CA, 4University of California, San Francisco, San Francisco, CA, 5Centers for Disease Control and Prevention, Atlanta, GA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: ARHP Healthcare Disparities in Rheumatology Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: PROs play a prominent role in evaluating patient status in rheumatic diseases. PROs often reveal disparities in individuals with low education or income or among racial/ethnic minorities. Limited health literacy (LHL) may also be more prevalent in these groups. While some have acknowledged that LHL may create challenges in disease management, the impact of LHL on PROs has received little attention. We examined the impact of LHL on PROs in a diverse SLE cohort.

Methods: Data were from the California Lupus Epidemiology Study (CLUES), a population-based, multi-ethnic SLE cohort (n=281). Subjects participated in an in-person research clinic, in which study physicians completed the SLEDAI and SLICC Damage Index (SDI), and completed a structured interview administered by a trained interviewer, in which the following PROs were administered: SF-36, short forms of ten PROMIS domains, and self-reported measures of disease damage and activity (Table). Health literacy was assessed using a 3-item validated scale1. Individual education and household income were self-reported. Bivariate analyses examined differences in all PROs by education level (≤12 yrs vs. >12 yrs), income (≤125% of federal poverty level for household size vs. >125%), and LHL using t-tests. Multivariate linear regression analyses examined differences in PROs by LHL controlling for age, sex, race/ethnicity, disease duration,
SLEDAI, SDI, education, and income.

**Results:** The sample was 29% white (W), 23% Hispanic (H), 11% African American (AA), and 37% Asian (AS); 89% female; mean age 45 (±14) years; 22% with education ≤high school; 12% with poverty-level income; mean disease duration 16 (±10) years. 85% of interviews were completed in English. 35% had LHL, with significant differences by race/ethnicity (W 21%, AS 36%, AA 42%, H 46%, p<.01). Physician assessments of SLE activity and damage were not significantly different by health literacy (p>0.50). Bivariate analyses showed significant differences in all PROs by LHL and income, but few differences by education. In multivariate analyses, significant differences by LHL remained in all PROs except self-reported disease damage, even after controlling for all covariates including income and education (Table).

**Conclusion:** Individuals with SLE and LHL had worse status as measured by a wide range of PROs, even after accounting for physician-assessed disease, income, education, and race/ethnicity. Whether differences are due to unmeasured effects of LHL or to differential interpretation of PRO measures by individuals with LHL is unknown. However, findings suggest that attention to health literacy is crucial in the development and validation of PROs to ensure that variations in scores reflect actual differences in the underlying construct and not differential understanding or interpretation of the questions.


<table>
<thead>
<tr>
<th>Table. Adjusted means* of PROs for individuals with and without limited health literacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Limited health literacy</td>
</tr>
<tr>
<td>PROMIS</td>
</tr>
<tr>
<td>Physical Function</td>
</tr>
<tr>
<td>Pain Interference†</td>
</tr>
<tr>
<td>Fatigue†</td>
</tr>
<tr>
<td>Sleep Disturbance†</td>
</tr>
<tr>
<td>Sleep Impairment†</td>
</tr>
<tr>
<td>Cognitive Ability</td>
</tr>
<tr>
<td>Satisfaction with Social Roles</td>
</tr>
<tr>
<td>Participation in Social Roles</td>
</tr>
<tr>
<td>Social Isolation†</td>
</tr>
<tr>
<td>SF-36</td>
</tr>
<tr>
<td>Physical Function</td>
</tr>
<tr>
<td>Role Physical</td>
</tr>
<tr>
<td>Pain</td>
</tr>
<tr>
<td>General Health</td>
</tr>
<tr>
<td>Vitality</td>
</tr>
<tr>
<td>Social Functioning</td>
</tr>
<tr>
<td>Role Emotional</td>
</tr>
<tr>
<td>Mental Health</td>
</tr>
<tr>
<td>Disease-specific measures</td>
</tr>
<tr>
<td>BILD†</td>
</tr>
<tr>
<td>SLAQ†</td>
</tr>
<tr>
<td>SLE activity†</td>
</tr>
</tbody>
</table>

* Adjusted means calculated from multivariate linear regression analyses controlling for age, sex, race/ethnicity, disease duration SLEDAI, SLICC Damage Index, education, and income

† Lower scores reflect “better” status. For all other measures, higher scores are “better.”

Disclosure: P. P. Katz, Bristol-Myers Squibb, 2; M. Dall’Era, None; L. Trupin, None; C. Lanata, None; S. Rush, None; C. G. Helmick, None.
Long Term Survival of Biological Agents in Patients with Axial Spondyloarthritis. the Impact of Sociodemographic Factors in Latin-America

Magdalena Cavalieri1, Emilce E Schneeberger2, Fernando Dal Pra1, Rodrigo García Salinas3, Hernán Maldonado Ficco4 and Gustavo Citera1
1Section of Rheumatology, Instituto de Rehabilitación Psicofísica, Buenos Aires, Argentina, Buenos Aires, Argentina, 2Instituto de Rehabilitación Psicofísica, Buenos Aires, Argentina, Buenos Aires, Argentina, 3Section of Rheumatology, Hospital Italiano de La Plata, Buenos Aires, Argentina, La Plata, Argentina, 4Section of Rheumatology, Hospital San Antonio de Padua, Córdoba, Argentina, Córdoba, Argentina

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: ARHP Healthcare Disparities in Rheumatology Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The introduction of biological agents improved the prognosis of axial Spondyloarthritis (axSpA). The Lund Efficacy Index (LUNDEX) allows evaluation of both survival and efficacy of drugs. Our aims were to evaluate the long-term efficacy of biological disease modifying drugs (b-DMARD) in axSpA using the LUNDEX, compare them and to determine the variables associated to the discontinuation of these treatments. Methods: Patients ≥ 18 years old who met ASAS 2009 criteria for axSpA and who started b-DMARD for the first time between 01/2002 and 12/2016 were included. Sociodemographic variables, comorbidities, type of axSpA, disease duration and previous treatments were registered. Duration of therapy, causes of its suspension, efficacy and safety were evaluated. BASDAI was assessed at baseline and during the treatment and LUNDEX was calculated at 6 months and at 1 year of treatment using BASDAI cut-off <4 as efficacy endpoint. Cumulative drug survival was assessed by Kaplan Meier curves and comparisons using log Rank. Results: We included 101 patients. 80.2% were male, with a median age of 42 years (IQR 35-54.5), and median disease duration of 19.3 years (IQR 9.4-28.8). 26.7% of patients didn’t have health insurance. 63.4% had pure axSpA, 13.8% Psoriatic Arthritis, 3% Reactive Arthritis, 3% Inflammatory Bowel Disease and 16.8% Juvenile axSpA. The frequency of first b-DMARD was: 44.6% Etanercept (ETA), 41.6% Adalimumab (ADA), 7.9% Infliximab and 5.9% Certolizumab. 67.3% received b-DMARD monotherapy. BASDAI significantly improved over time. The mean (X) cumulative survival time was 66.2 months (95%CI: 51.8-80.5). ADA survival was longer than ETA one [ADA X 74.8 months (95%CI: 57.2-92.4) versus ETA X 53.2 (95%CI: 35.8-70.6) p = 0.02]. The causes of suspension were: lack of provision of the medication 41.1%, inefficacy 26.8%, adverse events 12.5% and other reasons 19.6%. Mean cumulative survival time was lower for ETA vs ADA (53.1±8.8 vs 74.8 ±8.9, Log Rank=0.02), being the main cause the lack of provision of the medication. In multivariate Cox regression analysis, after adjusting for other factors, having private health insurance was the only factor that influenced on the survival of the b-DMARD (HR 2.54, 95%CI 1.18-5.75). The global LUNDEX was 52.7% at 6 months and 46.9% at 12 months. The ADA LUNDEX was 50% at 6 months and 39.3% at 12 months, while ETA LUNDEX was 60.2% at 6 months and 52% at 12 months. Conclusion: In our cohort of patients with axSpA, survival time of b-DMARD was clearly affected by socio-economic factors. Patients who can afford a private health insurance are more likely to persist with medication.
Abstract Number: 232

The Charla De Lupus (Lupus Chat)® Program: Assessing the Needs of Teens and Young Adults with Lupus and Their Caregivers to Develop a Family Model Nutrition and Fitness Intervention

Melissa T. Flores1, Jillian Rose2, Priscilla Toral1, Lillian Mendez1, Dariana M. Pichardo1, Roberta Horton1 and Lisa F. Imundo3, 1Social Work Programs, Hospital for Special Surgery, New York, NY, 2Hospital for Special Surgery, New York, NY, 3Pediatrics, Columbia University Medical Center, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: ARHP Healthcare Disparities in Rheumatology Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Studies show Hispanics/Latinos are significantly impacted by health disparities, with higher rates of obesity & diabetes than Whites. Combined with SLE & higher risk for related health conditions, culturally tailored nutrition & fitness education efforts are warranted. A nutrition & fitness needs assessment was conducted for teens & young adults with SLE & their loved ones who participate in a bilingual hospital-based SLE support & education group. The program reported on a SLE specific nutrition intervention at ACR/ARHP in the past, & for the last 3 years, program evaluation data showed that nutrition was rated one of the top 5 topics.

Methods:

Two 72-item surveys with Likert scale, multiple choice & open-ended questions were conducted for teens/young adults (T/YAs) & parents/caregivers (Ps). Questions covered demographics, food intake, MyPlate food guide & food labels, exercise, & interest in a nutrition/fitness program. Separate analyses were conducted for T/YAs & Ps.
Results:

There were 147 surveys distributed electronically, 31% completed (55% T/YAs & 45% Ps). Over half (59%) were Hispanic, 30% White, 28% some other race, 25% Black/African American, 10% American Indian & 6% Asian. T/YAs mean age was 24 & 85% female. Most T/YAs (65%) were diagnosed < 10 years ago. Top reported lupus symptoms were joint pain (72%), fatigue (64%) & muscle weakness (56%). Top reported lupus medications were plaquenil (84%) & steroids (48%). Most T/YAs (54%) & Ps (90%) reported that their diet was “good,” but shared they would like to eat healthier (88% & 100%). T/YAs (30%) reported drinking ≤ 3 glasses of water a day & 22% reported consuming a sugary beverage daily.

While most T/YAs & Ps heard about MyPlate (87% & 72%), only 25% T/YAs & 46% Ps knew that it had 5 food groups. Ps (94%) reported ↑ desire to learn how to use food labels, while T/YAs (87%) had ↑ confidence in their ability to use food labels.

When asked about exercise, 74% T/YAs & 67% Ps reported that they exercised & 63% indicated that a MD suggested they do physical activity. However, 83% Ps & 61% T/YAs did not feel they were at ideal weight. Most respondents (94% Ps & 80% T/YAs) were interested in learning more about nutrition/exercise, & 88% Ps & 70% T/YAs expressed specific interest in a team nutrition/exercise program.

When asked about nutrition goals, Ps responses included “eating less fast foods” & “learn new ways to cook healthy,” T/YAs focused on “build bone mass due to osteoporosis” & “maintain a good weight.” When asked about fitness goals, Ps desired to exercise regularly & T/YAs indicated a desire to lose weight. When asked about motivation, the top 2 answers for both T/YAs & Ps were group activities (93% & 80%) & a coach/trainer (87% & 86%). Similarly, both groups reported that they would prefer to track their progress by cell phones (100% & 71%) & 52% preferred texting.

Conclusion:

Despite a small sample size, results show that nutrition & fitness are areas of concern for both T/YAs with SLE & Ps, with opportunities to increase nutrition/fitness knowledge & activity. Results reveal that participants were interested in a group-based nutrition/fitness program that is culturally tailored. Next steps are to organize focus groups with participants to discuss specific interventions.

Disclosure: M. T. Flores, None; J. Rose, None; P. Toral, None; L. Mendez, None; D. M. Pichardo, None; R. Horton, None; L. F. Imundo, None.

Engaging Community Stakeholders through a National Lupus Education Workshop

Karen Manzeca Cuevas1, Rosalind Ramsey-Goldman2, Sheryl McCalla3, Patricia Canessa4 and Zineb Aouhab1, 1Rheumatology, Northwestern University, Chicago, IL, 2FSM, Northwestern University, Chicago, IL, 3American College of Rheumatology, Atlanta, GA, 4Illinois Public Health Association, Springfield, IL

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: ARHP Healthcare Disparities in Rheumatology Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

The Popular Opinion Leader (POL) model based on health education theoretical foundations associated with Social Network Theory and Diffusion of Innovation was successfully piloted in several local Hispanic communities. The initial aim of the pilot problem was to develop and teach a core curriculum to address lupus health disparities and a second aim in conjunction, with the American College of Rheumatology and an Office of Minority Health funded grant, 1-CPIMP-151087-01-00 was to disseminate the program as a workshop in May 2016 to engage stakeholders in other targeted communities in the United States that served African American and Native American constituents. The target audience for the curriculum were POLs or Community Health Worker (CHW) equivalents.

Methods:

The multidisciplinary project team who provided training in the POL model included the Project Director who is a rheumatologist, a community Field Director who is a psychologist with cultural competency expertise, a rheumatology trainee, and the POL project manager.
The 14 stakeholders who are involved in ongoing lupus health disparities projects participated in the workshop training and they represented a wide range of institutions including community based organizations, academic centers and the ACR. The day long workshop included training of fundamental concepts, curriculum design, application exercises incorporating theory, community practice, and project dissemination adapting culturally-competent practices. Training was done in lecture format and interactive roundtable discussions. Participants completed a qualitative assessment of the workshop at the end of the training sessions.

Results:

Thirteen of fourteen participants responded questions covering workshop purpose and objectives, clarity and appropriateness of the workshop presentation, roundtable interactiveness, participant involvement, use of workshop time, and overall satisfaction. Additionally, open-ended questions were provided on expanding on the workshop strengths and weaknesses, and suggestions/additional comments on this workshop.

All respondents agreed that objectives were clearly stated and that all meeting participants were actively involved and satisfied with the workshop. The majority of respondents reported that the workshop was clear and relevant, that the round table discussions were interactive, and that there was shared decision-making in the workshop. The main shortcoming reported was that there were concerns about effective use of meeting time as some presentations during the workshop were longer than originally programmed.

Conclusion:

The major finding from the workshop is that participants were overall satisfied with their participation, programming of the event, particularly the roundtable discussion activities. Future directions include building on the initial workshop and based on future funding expand the learning experience to lupus-specific stakeholders. In future iterations of the workshop, it will be important to follow-up with program participants to assess program impact.

Disclosure: K. Mancera Cuevas, None; R. Ramsey-Goldman, None; S. McCalla, None; P. Canessa, None; Z. Aouhab, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/engaging-community-stakeholders-through-a-national-lupus-education-workshop

Abstract Number: 234

Impact of Arthritis Among Populations with Chronic Health Conditions in Rural Counties of the United States – 2015

Michael Boring1, Louise Murphy2, Jennifer M. Hootman3 and Yong Liu2, 1Arthritis Program, Centers for Disease Control and Prevention, Atlanta, GA, 2Division of Population Health, Centers for Disease Control and Prevention, Atlanta, GA, 3Centers for Disease Control and Prevention, Kennesaw, GA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: ARHP Healthcare Disparities in Rheumatology Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: US rural populations have well documented health disparities, including higher prevalence of chronic health conditions; however, arthritis prevalence among those with other chronic conditions is unknown. We estimated prevalence of arthritis and arthritis-attributable activity limitations (AAAL), among those with chronic health conditions in rural areas using 2015 Behavioral Risk Factor Surveillance System (BRFSS) data.

Methods: BRFSS is an ongoing, state-based, random-digit-dialed landline and cellphone survey of the noninstitutionalized adult population aged ≥18 years of the 50 states, the District of Columbia (DC), and the U.S. territories. Respondents had arthritis if they answered “yes” to “Have you ever been told by a doctor or other health professional that you have some form of arthritis, rheumatoid arthritis, gout, lupus, or fibromyalgia?” Among adults with arthritis, AAAL was identified by a “yes” to “Are you now limited in any way in any of your usual activities because of arthritis or joint symptoms?” Rural categories were created using the National Center for Health Statistics 2013 Urban-Rural Classification Scheme for Counties; we used 2 rural county classification categories: micropolitan (large rural [LR]) and noncore (small rural [SR]). Age-standardized prevalence of arthritis and AAAL were estimated by rural categories among those with each of 9 common chronic health conditions (hypertension, coronary artery disease [CAD], obesity, diabetes, chronic obstructive pulmonary disease [COPD], depression, asthma, cancer, and chronic kidney disease [CKD]). All analyses accounted for BRFSS’ complex sampling design.

Results: Overall, arthritis prevalence was high in rural populations with chronic health conditions (range = 36.0-56.0%). In SR areas,
arthritis prevalence was particularly high among those with CKD (53.6%), COPD (51.6%), stroke (49.5%), and CAD (49.5%). In LR areas, arthritis prevalence was highest among those with CAD (56.0%), COPD (54.8%), and CKD (50.7%). Overall, AAAL prevalence among those with arthritis and ≥ 1 chronic condition ranged from 58.4 to 76.5%. In SR areas, age-standardized AAAL prevalence was highest among those with arthritis and depression (71.2%), COPD (68.8%), CAD (65.8%), and stroke (65.5%). In LR areas, AAAL prevalence was highest among those with depression (66.1%), COPD (71.9%), CAD (69.9%), and stroke (76.3%).

**Conclusion:** In rural areas, arthritis commonly occurs with other chronic conditions; for some more than half had arthritis. Individuals with arthritis and chronic conditions in rural areas are significantly impacted by arthritis with roughly 2 in 3 reporting AAAL. Strategies that reduce arthritis impact include weight loss, routine physical activity and participation in self-management education courses (e.g., Chronic Disease Self-Management Program); these approaches also reduce adverse effects of co-occurring chronic conditions. By recommending these strategies to their patients, health care providers can simultaneously manage the impact of arthritis and other chronic conditions. Our results indicates the high need for these self-management strategies among rural adults.

**Disclosure:** M. Boring, None; L. Murphy, None; J. M. Hootman, None; Y. Liu, None.


**Abstract Number: 235**

**MRI in Rheumatoid Arthritis: Does Quantifying the Number of Erosive Lesions Improve Detection of Subtle Erosive Progression Compared to the Omeract RA MRI Scoring System?**

Ulfsundin1, Anna-Birgitte Ag2, Tore K Kvien3, Siri Lillegraven4 and Espen A. Haavardsholm4, 1Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, 2Department of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, 3Diakonhjemmet Hospital, Oslo, Norway, 4Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway

**First publication:** September 18, 2017

**Background/Purpose:** Early detection of erosive progression is an important application of MRI in RA. For research purposes the OMERACT Rheumatoid Arthritis MRI Scoring system (RAMRIS) is commonly applied, with semi-quantitative assessment of erosive volume. However, over time new erosive lesions can occur without sufficient increase in volume to result in a higher score. This could allow for subtle erosive progression to go undetected. We aimed to examine if quantifying the number of erosions in addition to erosive volume could provide improved sensitivity to change.

**Methods:** In a cohort consisting of 84 patients, all fulfilling the 1987 ACR criteria for RA, with disease duration of < 1 year, MRI of the dominant wrist was acquired at 0, 3, 6, and 12 months. A trained reader, blinded for patient data, scored the MRI images in known chronological order according to the RAMRIS method. In addition, we registered the number of erosive lesions at each site. The 78 patients who had completed at least the baseline and 6- or 12-month exams were by each method identified as either progressors or non-progressors, using an increase of 1 unit as cut-off value. The results were compared using cross tables and Spearman correlation.

**Results:** The median baseline age (25th, 75th percentile) was 58.1 (47.3, 66.4) years, disease duration was 107 (70, 186) days, 77% were female, and 55% were anti-CCP positive. Median baseline RAMRIS erosion score was 8 (5, 11) and the median number of MRI erosions was 10 (6, 14). Median 1 year change in RAMRIS erosion score was 1 (0, 2), and median change in number of erosions was 1 (0, 2). Both methods identified an equal number of patients as progressors, and agreement was observed in 82% of cases. Seven patients were progressors by the RAMRIS method only and 7 by the counting erosive lesions method only (table). The Spearman correlation coefficient of the two scores was 0.75, p<0.001 (figure).
**Conclusion:** The RAMRIS erosion score was generally low, both with respect to baseline level as well as progression rate. By supplementing the assessment with quantification of the number of erosive lesions, we could in this material identify a limited number of additional patients as progressors. Further longitudinal studies could show to what extent patients with this type of early minimal erosive lesions on MRI progress on conventional radiographs, and if this is clinically important.

**Disclosure:** U. Sundin, None; A. B. Aga, None; T. K. Kvien, AbbVie, Pfizer Inc, Roche Pharmaceuticals, UCB, BMS, MSD, 2, AbbVie, 5, Pfizer Inc, 5, BMS, 8, MSD, 8, Roche Pharmaceuticals, 8, UCB, 8, AbbVie, 8; S. Lillegaard, None; E. A. Haavardsholm, None.

**Abstract Number:** 236

**Are Magnetic Resonance Imaging Features of the Hand Associated with Patient Reported Physical Function, Global Assessment of Disease Activity, Pain and Health Related Quality of Life in Rheumatoid Arthritis in Clinical Remission? – Longitudinal Results from an Observational Cohort**

Daniel Glinatsi, Cecilie Heegaard Brahe, Merete Lund Hetland, Lykke Ørnbjerg, Simon Krabbe, Joshua Baker, Mikael Boesen, Zoreh Rastemadabadi, Lone Morsel-Carlsen, Henrik Rogind, Hanne Slott Jensen, Annette Hansen, Jesper Norregaard, Søren Jacobsen, Lene Terslev, Tuan Huynh, Natalia Manilo, Dorte Vendsel Jensen, Jakob M. Møller, Niels Steen Krogh, Mikkel Østergaard, 1 Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Rigshospitalet, Copenhagen, Denmark, 2 Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Rigshospitalet, Denmark, Glostrup, Denmark, 3 University of Copenhagen, Copenhagen, Denmark, 4 The DANBIO Registry, Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Rigshospitalet, Glostrup, Denmark, 5 Center for Rheumatology and Spine Diseases, Rigshospitalet, Copenhagen, Denmark, 6 Corporal Michael J. Crescenz VA Medical Center, Philadelphia, PA, 7 Department of Radiology and the Parker institute, Copenhagen University Hospital Frederiksberg, Copenhagen, Denmark, 8 Department of Radiology, Copenhagen University Hospital Frederiksberg, Copenhagen, Denmark, 9 Department of Radiology, Rigshospitalet, Copenhagen, Denmark, 10 Center for Rheumatology and Spine Diseases, Copenhagen University Hospital Frederiksberg, Denmark, 11 Department of Rheumatology, Copenhagen University Hospital Gentofte, Copenhagen, Denmark, 12 Center for Rheumatology and Spine Diseases, Nordsjællands Hospital, Hillerød, Denmark, 13 Center for Rheumatology and Spine

---

**Table**

<table>
<thead>
<tr>
<th>Progression in number of erosions</th>
<th>Yes</th>
<th>No</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>38</td>
<td>7</td>
<td>45</td>
</tr>
<tr>
<td>No</td>
<td>7</td>
<td>26</td>
<td>33</td>
</tr>
<tr>
<td>Total</td>
<td>45</td>
<td>45</td>
<td>75</td>
</tr>
</tbody>
</table>

**Figure**

Correlation between the 1-year change in RAMRIS erosion score and the number of erosive lesions.

---

**Abstract Number:** 236
SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: To assess whether magnetic resonance imaging (MRI) inflammation and damage in the wrist and hand of rheumatoid arthritis (RA) patients are associated with patient-reported outcomes (PROs) at clinical remission and relapse.

Methods: MRIs of the right wrist and hand were obtained in 114 patients with established RA in sustained clinical remission (>1 year), before tapering their biologic disease-modifying antirheumatic drug. MRIs were assessed according to the Outcome Measures in Rheumatology (OMERACT) RA MRI score (RAMRIS) for inflammation (synovitis/tenosynovitis/osteitis) and damage (bone erosions/joint space narrowing (JSN)) at baseline (i.e. remission, n=114) and in case of a relapse (n=70). Status and change MRI-scores were assessed for associations with patient-reported physical function (health assessment questionnaires (HAQ)), visual analogue scales for global disease activity and pain, EuroQol 5 dimensions and Short Form 36 physical and mental component summary (SF-36 PCS/MCS) using Spearman correlations, and in univariate/multivariable linear regression analyses including generalized estimating equations. C-reactive protein and swollen joint counts were forced into the models. MRI features were also assessed for trends against specific hand-related HAQ-items using Jonckheere trend tests.

Results: MRI-assessed bone erosion, JSN and combined damage score were associated with impaired PROs, mainly HAQ and SF-36 PCS at clinical remission and relapse (p<0.01), independent of clinical measures. The levels of bone erosions and JSN were associated with the level of the HAQ score in 4 of 5 hand-related HAQ-items (p<0.05). MRI-assessed inflammation was generally not associated with PROs at remission or relapse.

Conclusion: In patients with established RA MRI-assessed wrist and hand damage, but not inflammation is associated with patient-reported physical impairment at clinical remission and relapse, and the amount of damage in the wrist and hand is associated with reduced function of the hand.
<table>
<thead>
<tr>
<th></th>
<th>Univariate</th>
<th>HAQ</th>
<th>Multivariable</th>
<th>Univariate</th>
<th>VAS-PtGlobal</th>
<th>VAS-Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β (95% CI)</td>
<td>p</td>
<td>β (95% CI)</td>
<td>p</td>
<td>β (95% CI)</td>
<td>p</td>
</tr>
<tr>
<td>MRI Synovitis</td>
<td>0.00</td>
<td>0.97</td>
<td>-0.39</td>
<td>0.53</td>
<td>-0.39</td>
<td>0.57</td>
</tr>
<tr>
<td></td>
<td>0.03;0.03</td>
<td>1.63</td>
<td>0.58</td>
<td>0.84</td>
<td>1.37;0.76</td>
<td>0.67</td>
</tr>
<tr>
<td>MRI Tenosynovitis</td>
<td>0.00</td>
<td>0.77</td>
<td>-0.46</td>
<td>0.46</td>
<td>-0.46</td>
<td>0.31</td>
</tr>
<tr>
<td></td>
<td>0.03;0.03</td>
<td>0.95</td>
<td>0.51</td>
<td>0.26</td>
<td>0.63;1.96</td>
<td>0.21</td>
</tr>
<tr>
<td>MRI Osteitis</td>
<td>0.00</td>
<td>0.86</td>
<td>-0.25</td>
<td>0.25</td>
<td>-0.25</td>
<td>0.59</td>
</tr>
<tr>
<td></td>
<td>0.02;0.03</td>
<td>0.36</td>
<td>0.04</td>
<td>0.36</td>
<td>0.55;0.97</td>
<td>0.06</td>
</tr>
<tr>
<td>MRI Bone Erosion</td>
<td>0.01</td>
<td><strong>0.001</strong></td>
<td>0.01</td>
<td><strong>0.001</strong></td>
<td>0.01</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>0.01</td>
<td>0.08</td>
<td>0.09</td>
<td>0.08</td>
<td>0.06</td>
<td>0.12</td>
</tr>
<tr>
<td>MRI JSN</td>
<td>0.00</td>
<td>0.83</td>
<td>-0.52</td>
<td>0.77</td>
<td>-0.52</td>
<td>0.34</td>
</tr>
<tr>
<td></td>
<td>0.00;0.02</td>
<td>0.14</td>
<td>0.08</td>
<td>0.14</td>
<td>0.11</td>
<td>0.32</td>
</tr>
<tr>
<td>MRI Combined Inflammation</td>
<td>0.00</td>
<td>0.83</td>
<td>-0.77</td>
<td>0.77</td>
<td>-0.77</td>
<td>0.89</td>
</tr>
<tr>
<td></td>
<td>0.01;0.02</td>
<td>0.48</td>
<td>0.03</td>
<td>0.48</td>
<td>0.42</td>
<td>0.04</td>
</tr>
<tr>
<td>MRI Combined Damage*</td>
<td>0.00</td>
<td>0.00</td>
<td>-0.44</td>
<td>0.44</td>
<td>-0.44</td>
<td>0.33</td>
</tr>
<tr>
<td></td>
<td>0.000;0.001</td>
<td>0.05</td>
<td>0.04</td>
<td>0.05</td>
<td>0.04</td>
<td>0.11</td>
</tr>
<tr>
<td>SF-36 PCS</td>
<td>0.04</td>
<td>0.88</td>
<td>-0.55</td>
<td>0.88</td>
<td>-0.55</td>
<td>0.88</td>
</tr>
<tr>
<td></td>
<td>0.55;0.46</td>
<td>0.32</td>
<td>0.18</td>
<td>0.32</td>
<td>0.18</td>
<td>0.00</td>
</tr>
<tr>
<td>MRI Synovitis</td>
<td>0.00</td>
<td>0.91</td>
<td>-0.51</td>
<td>0.91</td>
<td>-0.51</td>
<td>0.78</td>
</tr>
<tr>
<td></td>
<td>0.68;0.60</td>
<td>0.34</td>
<td>0.05</td>
<td>0.34</td>
<td>0.05</td>
<td>0.00</td>
</tr>
<tr>
<td>MRI Tenosynovitis</td>
<td>0.00</td>
<td>0.67</td>
<td>-0.84</td>
<td>0.67</td>
<td>-0.84</td>
<td>0.43</td>
</tr>
<tr>
<td></td>
<td>0.46;0.30</td>
<td>0.52</td>
<td>0.01</td>
<td>0.52</td>
<td>0.01</td>
<td>0.00</td>
</tr>
<tr>
<td>MRI Osteitis</td>
<td>0.00</td>
<td>0.02</td>
<td>-0.03</td>
<td>0.02</td>
<td>-0.03</td>
<td>0.76</td>
</tr>
<tr>
<td></td>
<td>0.12;0.02</td>
<td>0.03</td>
<td>0.05;0.07</td>
<td>0.03</td>
<td>0.05</td>
<td>0.00</td>
</tr>
<tr>
<td>MRI Bone Erosion</td>
<td>0.00</td>
<td>0.04</td>
<td>-0.75</td>
<td>0.04</td>
<td>-0.75</td>
<td>0.57</td>
</tr>
<tr>
<td></td>
<td>0.004</td>
<td>0.03</td>
<td>0.05;0.07</td>
<td>0.03</td>
<td>0.05</td>
<td>0.00</td>
</tr>
<tr>
<td>MRI JSN</td>
<td>0.00</td>
<td>0.02</td>
<td>-0.78</td>
<td>0.02</td>
<td>-0.78</td>
<td>0.63</td>
</tr>
<tr>
<td></td>
<td>0.25;0.21</td>
<td>0.10</td>
<td>0.06</td>
<td>0.10</td>
<td>0.06</td>
<td>0.00</td>
</tr>
<tr>
<td>MRI Combined Inflammation</td>
<td>0.00</td>
<td>0.85</td>
<td>-0.63</td>
<td>0.85</td>
<td>-0.63</td>
<td>0.75</td>
</tr>
<tr>
<td></td>
<td>0.006</td>
<td>0.06</td>
<td>0.20;0.32</td>
<td>0.06</td>
<td>0.20</td>
<td>0.00</td>
</tr>
<tr>
<td>MRI Combined Damage*</td>
<td>0.00</td>
<td>0.02</td>
<td>-0.76</td>
<td>0.02</td>
<td>-0.76</td>
<td>0.59</td>
</tr>
<tr>
<td></td>
<td>0.08;0.02</td>
<td>0.03</td>
<td>0.03;0.04</td>
<td>0.03</td>
<td>0.03</td>
<td>0.00</td>
</tr>
</tbody>
</table>
Table 4. Univariate and multivariable general estimating equations (GEEs) for the association between MRI features and PROs. All analyses were adjusted for age and sex.

*If combined damage scores had a p-value ≤0.10 in univariate analyses, these were included in a separate multivariable model with CRP and SJC included in the model. **This parameter was included in a separate multivariable GEE model with SJC and CRP, due to co-linearity between bone erosion and JSN.


Disclosure: D. Glinatsi, None; C. H. Brahe, None; M. Lund Hetland, None; L. Ornbjerg, None; S. Krabbe, None; J. Baker, None; M. Boesen, None; Z. Rastie madabadi, None; L. Morsel-Carlsen, None; H. Rogind, None; H. S. Jensen, None; A. Hansen, Calgene, 5, Pfizer Inc, 5, Abbvie, 6; J. Norregaard, None; S. Jacobsen, None; L. Terslev, None; T. Huynh, None; N. Manilo, None; D. V. Jensen, None; J. M. Møller, None; N. S. Krogh, None; M. Østergaard, None.


Abstract Number: 237

The Discrepancy between the EULAR Response Criteria and Ultrasoundography Assessment for Monitoring Therapeutic Response in Rheumatoid Arthritis

Ryusuke Yoshimi1, Yuichiro Sato1, Natsuki Sakurai1, Takaaki Komiya1, Naoki Hamada1, Hideto Nagai1, Naomi Tsuchida2, Yumiko Sugiyama1, Yutaro Soejima1, Yoshike Kunishita1, Hiroto Nakano1, Daiga Kishimoto3, Reikou Kamiyama1, Kaoru Minegishi-Takase1, Yohei Kirino1, Shigeru Ohno4 and Hideaki Nakajima1,1 Department of Hematology and Clinical Immunology, Yokohama City University School of Medicine, Yokohama, Japan, 2Department of Hematology and Clinical Immunology, Yokohama City University Graduate School of Medicine, Yokohama, Japan, 3Center for Rheumatic Diseases, Yokohama City University Medical Center, Yokohama, Japan, 4Center for Rheumatic Disease, Yokohama City University Medical Center, Yokohama, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Although the European League Against Rheumatism (EULAR) response criteria based on the Disease Activity Score (DAS) 28 has been widely used for assessment of treatment response in clinical trials for rheumatoid arthritis (RA), it is still unclear whether it is indeed reflected by the change of synovitis severity. Musculoskeletal ultrasonography (US) is now one of the standard tools for the diagnosis and monitoring of active synovitis. Here, we investigated the association between the EULAR response criteria and the US assessment in monitoring RA activity.

Methods: Power Doppler (PD) US was performed in 24 joints, including all PIP, MCP, bilateral wrist and knee joints, as comprehensive evaluation in 23 RA patients treated with certolizumab pegol (CZP; n = 15) or tofacitinib (TOF; n = 8). Before and after treatment with CZP or TOF, PD signals and gray-scale (GS) images were scored semiquantitatively from 0 to 3 in each joint. Total PD score-24 and total PD score-8 were calculated by summing up PD scores of the 24 joints and the selected 8 joints (bilateral second and third MCP, wrist, and knee joints), respectively. Total GS score-24 and total GS score-8 were also calculated by summing up GS scores of the 24 joints and the selected 8 joints, respectively.

Results: Among the 23 patients, no response was shown in 5, moderate response was in 12, and good response was in 6 patients by EULAR response criteria. The change of total PD score-24 by treatment with CZP or TOF was significantly different between the patients with no response and moderate response (1[interquartile range (-2)-(2)] vs -5([-11]+(-1.75)), p = 0.012) or good response (1([-2]+(-2)) vs -8([-9.75]-)}
(-7), \ p = 0.0043). The change of total PD score-8 was also significantly different between the patients with no response and moderate response (1[-(2)-(2)] vs -3.5[-7.25]-(-1.75)), \ p = 0.012) or good response (1[-(2)-(2)] vs -6.5[-7.75]-(-5.25)), \ p = 0.0022). The change of total GS score-24 and total GS score-8 were significantly different between the patients with no response and good response (-2[-(2)-(1)] vs -9[-16.5]-(-4.5)), \ p = 0.011, and -1[-(1)-(1)] vs -6[(8)-(4)], 0.0022, respectively). Among the patients with no response, 2 (40%) showed decrease in total PD score-24 and total PD score-8, and 3 (60%) and 4 (80%) showed decrease in total GS score-24 and total GS score-8, respectively. Among the patients with moderate response, 2 (17%) showed no improvement in total PD score-24 and total PD score-8, and 3 (25%) and 5 (42%) showed no improvement or even increase in total GS score-24 and total GS score-8, respectively. Thus total 4 (17%) and 6 (26%) showed discrepancy between EULAR response criteria and 24-joint US assessment.

**Conclusion:** Although this study indicates the relationship between EULAR response criteria and US assessment as a whole, there are some cases showing discrepancy between these two assessment methods in monitoring RA activity. Thus the US assessment can be an essential method for monitoring response to treatment in RA patients.

**Disclosure:** R. Yoshihi, None; Y. Sato, None; N. Sakurai, None; T. Komiya, None; N. Hamada, None; H. Nagai, None; N. Tsuchida, None; Y. Sugiyama, None; Y. Soejima, None; Y. Kunishita, None; H. Nakano, None; D. Kishimoto, None; R. Kamiyama, None; K. Minegishi-Takase, None; Y. Kirino, None; S. Ohno, None; H. Nakagima, None.


**Abstract Number:** 238

**Power Doppler Ultrasonography Detects Superior Efficacy of Non-TNF Biologics Compared to Cycling of TNF Inhibitors in RA Patients Inadequate Response to First TNF Inhibitors**

Ayako Nishino1,2,3, Shinya Kawashiri2,3, Tamami Yoshitama2, Nobutaka Eiraku2, Naoki Matsuoka2, Yukitaka Ueki2, Akitomo Okada2, Hiroaki Hamada2, Yoshihiko Hidaka2, Shagi Nagano2, Tomomi Tsum2, Keita Fujikawa2, Yojirou Arinobu2, Yoshifumi Tada2, Yasuhiro Nagata1 and Atsushi Kawakami2,4, 1Center for Comprehensive Community Care Education, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, 2Kyushu multicenter rheumatoid arthritis ultrasound prospective observational cohort study group, Nagasaki, Japan, 3Department of Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, 4Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki City, Japan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Imaging of Rheumatic Diseases Poster I  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Efficacy of cycling of TNF inhibitors, judged by composite measures, is inferior to non-TNF biologics in patients with RA inadequate response to previous TNF inhibitors (TNF-IR patients). Ultrasonography (US) is a non-invasive imaging method to evaluate activity of synovitis more accurately than physical examinations, however, no previous reports have examined comparative efficacy of alternate TNF inhibitors or non-TNF biologics in RA patients inadequate response to previous TNF inhibitors by US. The aim of this study is to determine whether US find the difference of efficacy in switching to cycling TNF inhibitors compared to non-TNF biologics in TNF-IR patients.

**Methods:** We have investigated the above-mentioned comparison by the administrated RA patients in Kyushu multicenter rheumatoid arthritis ultrasound prospective observational cohort in which bilateral 22 wrists and finger joints were semi-quantitatively examined every 3 months by grey-scale (GS) and power Dopper (PD) from 0 to 3. US disease activity was determined as sum of GS or PD score (total GS score or PD score; 0-66, respectively). Among the 223 patients who registered and completed the first 12 months observation, thirty-nine patients were classified as switched to alternate TNF inhibitors (N = 11) or non-TNF biologics (N = 28) as second bDMARDs. We compared the efficacy of alternate TNF inhibitors group with non-TNF biologics group by US for 12 months using LOCF analysis.

**Results:** The characteristic of both groups at study entry was comparable including DAS28-ESR, duration of diseases, positivity of ACPA or RF and sum of GS and PD score. Drug retention rate at 12 months was superior in non-TNF biologics group compared to alternate TNF inhibitors group. Accordingly, sum of US score, especially PD score, clearly decreased in non-TNF biologics group whereas did poorly change in alternate TNF inhibitors group (Fig. 1). Change of DAS28-ESR was also more prominent in non-TNF biologics group compared to alternate TNF inhibitors group.
Conclusion: Our data confirm the previous clinical finding by US, especially PDUS, that switching to non-TNF biologics is more effective than cycling TNF inhibitors as a second choice of bDMARDs in TNF-IR patients.

Disclosure: A. Nishino, None; S. Kawashiri, None; T. Yoshitama, None; N. Eiraku, None; N. Matsuoka, None; Y. Ueki, None; A. Okada, None; H. Hamada, None; T. Hidaka, None; S. Nagano, None; T. Tsuru, None; K. Fujikawa, None; Y. Arinobu, None; Y. Tada, None; Y. Nagata, None; A. Kawakami, None.

Ultrasound Abnormalities Predict Arthritis Development in ACPA and/or RF Positive Arthralgia Patients

Annelies Blanken¹, Marian van Beers-Tas¹, Marlies Meursinge Reynders¹ and Dirkjan van Schaardenburg¹,², ¹Amsterdam Rheumatology and immunology Center | Reade, Amsterdam, Netherlands, ²Amsterdam Rheumatology and immunology Center | Academic Medical Center, Amsterdam, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Early diagnosis of rheumatoid arthritis (RA) is important for controlling disease activity and preventing joint damage. Individuals positive for anticitrullinated protein antibodies (ACPA) and/or rheumatoid factor (RF) are at risk of developing RA. In this study we investigated whether ultrasound (US) can predict development of arthritis in seropositive arthralgia patients.

Methods:
We included ACPA and/or RF positive patients with arthralgia, but without clinical arthritis. US was performed at baseline in 12 joints: bilateral MCP2-3,PIP2-3, wrist and MTP5. Images were scored semiquantitatively for synovitis and Power Doppler (PD) on a scale of 0-3. Grades 2 to 3 for synovitis and grades 1 to 3 for PD were regarded as abnormal. The association of ultrasound abnormalities with the development of arthritis was analyzed using Fisher’s exact test, expressed as odds ratios (OR) with 95% confidence interval (CI). Kaplan

Abstract Number: 239

Meier survival analysis with log-rank test and Cox regression analysis were used to assess the timing of arthritis development, expressed as median time to arthritis and hazard ratios (HR) with 95% CI.

**Results:**

In total, 169 seropositive arthralgia patients underwent US examination. Mean age was 51 (standard deviation (SD) 11) and 73% was female. Of these patients, 44 (22%) developed arthritis during a mean follow-up time of 27 (SD 19) months. Thirty seven (84%) patients developing arthritis satisfied the 2010 ACR/EULAR classification criteria for RA. Synovitis and PD signal in at least one joint was observed in 14 (8%) and 7 (4%) patients, respectively. The presence of synovitis was associated with arthritis development (OR 8.9, CI 2.6-30.2, \( p < 0.01 \), Table 1), whereas the presence of PD signal was not (OR 1.1, CI 0.2-6.1, \( p = 1.0 \)). Corresponding positive predictive values were 71% and 29%, respectively. Patients with synovitis or PD in at least one joint developed arthritis earlier than patients without US abnormalities (synovitis: median time to arthritis 11 versus 14 months, \( p < 0.01 \); PD: median time to arthritis 5 versus 12 months, \( p < 0.01 \); Fig 1) with corresponding HRs of 3.5 (CI 1.5-7.9, \( p < 0.01 \)) and 6.9 (CI 1.5-32.2, \( p < 0.02 \)) respectively.

**Conclusion:**

Synovitis on US predicted arthritis development in seropositive arthralgia patients. This association was not found for PD, however PD frequency was low and therefore the power to predict arthritis was low. However, when taking into account the time to arthritis development, both synovitis and PD were associated with an increased hazard on developing arthritis.

Table 1. Association of ultrasound abnormalities with arthritis development

<table>
<thead>
<tr>
<th>US abnormalities</th>
<th>Arthritis - n=125</th>
<th>Arthritis + n=44</th>
<th>OR (95% CI)</th>
<th>p-value</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synovitis*</td>
<td>4 (4%)</td>
<td>10 (23%)</td>
<td>8.9 (2.6-30.2)</td>
<td>( p &lt; 0.01 )</td>
<td>71%</td>
</tr>
<tr>
<td>Power Doppler*</td>
<td>2 (4%)</td>
<td>2 (5%)</td>
<td>3.1 (0.2-60.1)</td>
<td>( p = 1.0 )</td>
<td>29%</td>
</tr>
</tbody>
</table>

*Synovitis and Power Doppler in at least 1 Joint

OR, odds ratio; CI, confidence interval; PPV, positive predictive value

Figure 1. Kaplan-Meier survival curve for (A) synovitis and (B) Power Doppler (PD) and arthritis development

Disclosure: A. Blanken, None; M. van Beers-Tas, None; M. Meursinge Reynders, None; D. van Schaardenburg, None.


Abstract Number: 240

**Finger Joint Cartilage Thickness Evaluated By Semiquantitative Ultrasound Score in Patients with Rheumatoid Arthritis**

Takehisa Ogura¹, Ayako Hirata¹, Sayaka Takenaka², Hideki Ito², Yuki Inoue¹, Chihiro Imaizumi², Yuto Takakura², Kennosuke Mizushina¹, Takaharu Katagiri², Norihide Hayashi², Rie Kujime¹, Munetugu Imanura² and Hideto Kameda³, ¹Department of Rheumatology, Toho University Ohashi Medical Center, Tokyo, Japan, ²Toho University Ohashi Medical Center, Tokyo, Japan, ³Division of Rheumatology, Department of Internal Medicine, Toho University Ohashi Medical Center, Tokyo, Japan

First publication: September 18, 2017
Background/Purpose: Joint destruction in rheumatoid arthritis (RA) includes both bone and cartilage lesions. By X-ray examination, cartilage destruction is evaluated as the joint space narrowing (JSN). However, JSN is not a direct evaluation of cartilage. Previously we have confirmed the usefulness of the direct imaging of finger joint cartilage thickness (FJCT) by ultrasound (US). Then we aimed to evaluate the FJCT by semiquantitative US score and clarify its clinical significance in patients with RA.

Methods: We enrolled 53 RA patients in low disease activity or clinical remission (DAS28-CRP < 2.7) in this study. The FJCT of metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints of 2nd to 5th fingers was bilaterally visualized and measured at the middle portion of MCP and PIP joints from a longitudinal dorsal view, with approximately 90 degrees flexion. Furthermore, one US examiner performed the semiquantitative scoring of the recorded cartilage images in a blinded manner on a scale of 0–2 (0 = normal, 1 = minimal, and 2 = severe)\textsuperscript{1}. In addition, the JSN of fingers was scored by van der Heijde-modified Sharp method with a hand X-ray obtained within 2 months of US examination. The relationship among the total FJCT, the semiquantitative FJCT score and the JSN score were assessed by Spearman’s rank correlation coefficient.

Results: The total FJCT from 8 fingers ranged from 4.0 to 8.8 mm (median 6.7 mm), which was significantly correlated with the semiquantitative score (\(\rho=-0.681, p<0.001\)). And both total FJCT and semiquantitative score were significantly correlated with the total JSN score (\(\rho=-0.684, p<0.001\), and \(\rho=0.639, p<0.001\), respectively). The semiquantitative score was associated with disease duration (\(\rho=0.347, p=0.011\)), especially for MCP joints (\(\rho=0.453, p<0.001\)), but not for PIP joints (\(\rho=0.071, p=0.614\)). Age, height and seropositivity were not associated with semiquantitative FJCT score and JSN score.

Conclusion: A simplified and direct evaluation of cartilage damage by semiquantitative US score is valid and useful in patients with RA.


Disclosures: T. Ogura, None; A. Hirata, None; S. Takenaka, None; H. Ito, None; Y. Inoue, None; C. Inaizumi, None; Y. Takakura, None; K. Mizushima, None; T. Katagiri, None; N. Hayashi, None; R. Kujime, None; M. Imamura, None; H. Kameda, None.

Histological and Clinical Correlates of Ultrasound Measures of Joint Inflammation: Analysis of RA Tissue Obtained By Ultrasound Guided Biopsy in Phase I of the Accelerating Medicines Partnership RA Network

Andrew Filer\textsuperscript{1}, Arthur M. Mandelin II\textsuperscript{2}, Edward F. DiCarlo\textsuperscript{3}, Brendan Boyce\textsuperscript{4}, Darren Tabechian\textsuperscript{5}, Ralf G. Thiele\textsuperscript{6}, Stephan Kelly\textsuperscript{7}, Ellen M. Gravallese\textsuperscript{8}, Diane Horowitz\textsuperscript{9}, Kevin Wei\textsuperscript{10}, Deepak Rao\textsuperscript{11}, Vivian P. Bykerk\textsuperscript{12} and Jennifer H. Anolik\textsuperscript{13}, \textsuperscript{1}Institute of Inflammation and Ageing (IIA), University of Birmingham, Birmingham, United Kingdom, \textsuperscript{2}Rheumatology, Northwestern University, Chicago, IL, \textsuperscript{3}Laboratory Medicine, Hospital for Special Surgery, New York, NY, \textsuperscript{4}University of Rochester Medical Center, Rochester, Rochester, NY, \textsuperscript{5}Medicine, Division of Allergy, Immunology and Rheumatology, University of Rochester Medical Center, Rochester, NY, \textsuperscript{6}Medicine, University of Rochester Medical Center, Rochester, Rochester, NY, \textsuperscript{7}Queen Mary University of London, London, London, United Kingdom, \textsuperscript{8}Lazare Research Bldg, University of Massachusetts Medical School, Worcester, MA, \textsuperscript{9}Division of Rheumatology, North Shore - Long Island Jewish Health System, Woodbury, NY, \textsuperscript{10}Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, \textsuperscript{11}Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Spring, IN, \textsuperscript{12}2-005, Mt Sinai Hospital, Toronto, ON, Canada, \textsuperscript{13}Medicine- Allergy, Immunology and Rheumatology, University of Rochester Medical Center, Rochester, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM
The AMP-RA network applies cutting edge technologies to the study of tissue obtained by ultrasound guided synovial biopsy from patients with rheumatoid arthritis (RA). Ultrasound provides objective joint level measures of synovial inflammation, including hypertrophy (greyscale ultrasound, GSUS) and hyperaemia (Power Doppler ultrasound, PDUS). Furthermore, ultrasound joint count assessments enable higher sensitivity for measurement of systemic disease activity compared to clinical joint assessments alone. We examined the relationship between joint level ultrasound variables and synovial histology in Phase I patients with active RA. we also validated ultrasound measures against conventional measures of disease activity.

Methods:

During Phase I of AMP-RA we recruited patients fulfilling clinician RA diagnosis, 1987 or 2010 ACR/EULAR RA criteria with at least one joint amenable to biopsy. Patients were required to have a CDAI≥10; patients receiving i.a. steroids in the previous 4 weeks, i.m. in the last 8 weeks or oral steroids >10mg were excluded. 12 joint extended ultrasound assessments of 10 MCPs and 2 wrist joints using four point semiquantitative GSUS and PDUS scales were performed alongside collection of standard RA disease activity measures including DAS28CRP domains. 12 joint ultrasound indices were calculated by summing 0-3 grades for all joints. GSUS and PDUS measures were also assessed in the biopsied joint prior to the procedure. Retrieved tissue was fixed, stained and paraffin embedded prior to sectioning and staining by H&E. Tissues were assessed for quality: Where 50% or more tissue fragments out of a minimum of 4 contained lining layer histology, tissues were Krenn scored for lining layer and inflammatory infiltrate, and qualitative assessment of tissue pathotype by three histologists. In parallel, tissues were enzymatically disaggregated and cell yield determined using trypan dye exclusion.

Results:

In 15 tissue samples meeting QC taken from wrist (5), knee (9) and MCP (1) joints, Greyscale ultrasound (GSUS) grade correlated with the Krenn index of cellular inflammation (p<0.01, r=0.65) and the Krenn lining layer score (p<0.05, r=0.52). Power Doppler Ultrasound (PDUS) grade failed to correlate with either histological measure (p=0.34, p=0.48 respectively). Tissues with higher USGS, but not USPD scores, were more likely to show a lymphocyte predominant histological pathotype than other patterns (p<0.05). There was no consistent relationship between GSUS or PDUS measures of synovitis and cell yield at tissue disaggregation. GSUS extended joint indices correlated with DAS28CRP, 28 swollen joint and tender joint counts (p<0.05, r=0.70; p<0.01, r=0.78; p<0.05, r=0.65), while PDUS extended joint indices correlated with DAS28CRP and 28 swollen joint counts (p<0.05, r=0.66; p<0.05 r=0.76).

Conclusion:

Ultrasound measures of synovial hypertrophy correlate with the complexity of joint infiltrates and lining layer thickness. There was an association between synovial hypertrophy and a lymphocyte predominant pathotype. Extended joint indices demonstrate validity when compared to existing clinical domains.

Disclosure: A. Filer, None; A. M. Mandelin II, None; E. F. DiCarlo, None; B. Boyce, None; D. Tabechian, None; R. G. Thiele, Amgen, 8,AbbVie, 8,BioClinica, 5,Fujifilm SonoSite, 9; S. Kelly, None; E. M. Gravallese, Abbott Immunology Pharmaceuticals, 2,Lilly, Inc, 2,New England Journal of Medicine, 3,Up to Date, 7,Lilly Inc., 5,Sanofi/Genzyme, 5; D. Horowitz, None; K. Wei, None; D. Rao, None; V. P. Bykerk, None; J. H. Anolik, None.


Abstract Number: 242

Evaluation of Bone Erosions in Rheumatoid Arthritis Patients Using Cone Beam Computed Tomography, Magnetic Resonance Imaging, and Ultrasound

Jemima Alhayda1, Gaurav Thawaii2, Wojciech Zbijewski3, Alexander Martin3, Shadpour Demehri4, Jan Fritz4, John Yorkston2, Jeff Siewersden5 and Clifton O. Bingham III5, 1Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, 2Johns Hopkins University, Baltimore, MD, 3Biomedical Imaging Science, Johns Hopkins University, Baltimore, MD, 4Radiology, Johns Hopkins University, Baltimore, MD, 5Rheumatology, Johns Hopkins University, Baltimore, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM
Background/Purpose: This preliminary study was designed to determine the agreement and reproducibility of a novel cone beam CT (CBCT) extremity scanner, MRI and ultrasound (US) for detection of erosions in rheumatoid arthritis (RA). For this purpose, we compared the bone erosion scores for CBCT, MRI, and US in RA patients along with test-retest reproducibility of the CBCT data.

Methods: Ten patients (5 males, 5 females; mean age 58 years, age range 34 – 81 years) with a clinically confirmed diagnosis of RA were recruited for this institutional review board-approved study. All patients underwent an MRI, CBCT and US scan of the wrist and hand followed by a second CBCT scan one week later. The MRI was done using a 3T clinical MR scanner with dedicated hand coil; US using a state-of-the-art machine with an 18 Mhz hockey stick probe; while the CBCT was done using a prototype CBCT extremity scanner. US scans were performed and read by a rheumatologist with 5 years of experience in musculoskeletal ultrasound, scoring for the presence of absence of erosion in each joint. A radiologist with 7 years of musculoskeletal imaging evaluated MRI and CBCT images for erosions using RAMRIS like scoring between 1 to 10 (1 is 0-10% erosion, 2 is 11-20% erosion etc). The 2nd to 5th metacarpophalangeal joints, carpal bones and distal radius and ulna were assessed. Repeatability and agreement between methods were evaluated with Intraclass Correlation Coefficients (ICC) and Bland-Altman plots.

Results: Bland-Altman analysis showed agreement of 0.02±3.5, 3.5 to -3.5 (bias ± repeatability coefficient, 95% limits of agreement interval) with ICC score of 0.77 showing good correlation between MRI, US, and CBCT bone erosion scores. Correlation was higher for bone erosion scores of MCPs than for wrist joints. Test-retest reproducibility for the CBCT scans showed an excellent ICC score of 0.95.

Conclusion: Good correlation was seen for bone erosions as detected by CBCT, MRI and US, while the prototype extremity CBCT images showed high test-retest reproducibility. This study provides a good first approximation for evaluation of bone erosions across the three modalities.
Tracer Uptake from High Resolution Bone SPECT/CT is Linked to Response in Rheumatoid Arthritis Patients.

Background/Purpose:
To evaluate the association between response to TNF-α blockers and tracer uptake from dual-phase technetium-99m methylene diphosphonate (99mTc-MDP) bone scanning of the hands via a SPECT/CT system in patients with rheumatoid arthritis.

Methods:
Four patients with established rheumatoid arthritis (RA) were enrolled in this IRB-approved prospective pilot study. They were referred for performing bone scan prior to receiving TNF-α blockers. Early blood pool (15 minutes after tracer injection, marker of hypervascularity) and delayed osseous phase (3 hours after the same injection, marker of osteoblastic activity) scans of the hands using 99mTc-MDP were performed using high-resolution SPECT/CT scanner. A special hand positioning device was designed and used during the scans. Second- to 5th metacarpo-phalangeal joints (MCP) were assessed qualitatively (normal vs. abnormal uptake) and quantitatively (by measuring the maximum counts). All counts were corrected to the background (defined as the median count from all normal joints). Qualitative and quantitative data were assessed against response.

Results:
After a median follow-up of 7.8 months (range: 6.9-21.7), two patients were considered responders and two were non-responders. A total of 32 joints were assessed. Early and delayed uptake in the 2nd to 5th MCP joints were abnormal in 7 joints, all belong to non-responders; while it was normal in 25 joints, 16 of them were in responders & 9 in non-responders; P = 0.007.

The median corrected counts from delayed scans were 0.92 (range: 0.49-1.49) in responders vs. 1.14 (range: 0.81-2.93) in non-responders; P = 0.002.

The median corrected counts from blood pool scans were 0.95 (range: 0.6-1.67) in responders vs. 1.1 (range: 0.55-2.29) in non-responders; P = 0.2.

Conclusion:
Delayed osseous uptake in metacarpophalangeal joints of rheumatoid arthritis patients, measured from 99mTc-MDP SPECT/CT, performed prior to treatment with TNF-α blockers, was significantly higher in non-responders compared to responders, which might reflect higher baseline osteoblastic activity in non-responders.

Table 1: Ratio of the counts measured on 2nd to 4th metacarpophalangeal joints in responders and non-responders

<table>
<thead>
<tr>
<th>Baseline SPECT/CT</th>
<th>Responders</th>
<th>Non-Responders</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Pool</td>
<td>Median (Range)</td>
<td>0.95 (0.6-1.67)</td>
<td>1.1 (0.55-2.29)</td>
</tr>
<tr>
<td></td>
<td>Mean±SD</td>
<td>0.98±0.32</td>
<td>1.29±0.57</td>
</tr>
<tr>
<td>Delayed Phase</td>
<td>Median (Range)</td>
<td>0.92 (0.49-1.49)</td>
<td>1.38±0.61</td>
</tr>
<tr>
<td></td>
<td>Mean±SD</td>
<td>0.88±0.25</td>
<td>1.14 (0.81-2.93)</td>
</tr>
</tbody>
</table>

Figure 1:
Rheumatoid Arthritis Imaging on PET-CT Using a Novel Folate Receptor Ligand for Macrophage Targeting

Nicki Verweij1, Stefan Bruijnen1, Yoony Gent2, Marc Huisman3, Gerrit Jansen2, Carla Moltinho4, Qingshou Chen5, Philip Low5, Albert Windhorst3, Adriaan Lammertsma3, Otto Hoekstra3, Alexandre Voskuyl2 and Conny van der Laken2

1Dept. of Rheumatology, Amsterdam Rheumatology and immunology Center - location VU University Medical Center, Amsterdam, The Netherlands, Amsterdam, Netherlands, 2Department of Rheumatology, Amsterdam Rheumatology and immunology Center - location VU University Medical Center, Amsterdam, The Netherlands, Amsterdam, Netherlands, 3Department of Radiology & Nuclear Medicine, VU University Medical Center, Amsterdam, The Netherlands, Amsterdam, Netherlands, 4Department of Radiology & Nuclear Medicine, Amsterdam Rheumatology and immunology Center - location VU University Medical Center, Amsterdam, The Netherlands, Amsterdam, Netherlands, 5Department of Chemistry, Purdue University, West Lafayette, IN, USA, West Lafayette, IN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

PET imaging with macrophage tracers has been shown promising for detection of (sub)clinical synovitis, making it useful for both early diagnostics and therapy monitoring in rheumatoid arthritis (RA) patients (1,2). For detection of more subtle arthritis, a previously investigated macrophage tracer, \((R)-[^{11}\text{C}]\text{PK11195}\), was limited in use due to high background uptake in bone and bone marrow. \([^{18}\text{F}]\text{fluoro-PEG-folate}\) binds to the folate receptor \(\beta\), which is expressed on synovial macrophages (3). Preclinical research in arthritic rats has shown excellent targeting, making it a promising tracer for clinical testing in RA patients (4). In this study, we investigated the value of \([^{18}\text{F}]\text{fluoro-PEG-folate PET-CT}\) for imaging of inflamed joints in patients with clinically active RA.

Methods:

Nine RA patients with a minimal of two clinically inflamed hand joints were included. PET-CT scans were performed of the hands, after intravenous administration of either 185 MBq of \([^{18}\text{F}]\text{fluoro-PEG-folate}\) (n = 6) or 425 MBq of \((R)-[^{11}\text{C}]\text{PK11195}\) (n = 3) for comparison. Joints with visually marked uptake were further analyzed by calculation of Standardized Uptake Values (SUVs) in Volumes of Interest (VOI), drawn on top of the PET positive joints. We drew background VOIs on metacarpal bone in order to calculate Target-to-Background (T/B)
Results:

None of the patients showed adverse effects, establishing the safety of $[^{18}\text{F}]$fluoro-PEG-folate for use in humans. Arthritic joints were clearly visualized (Fig 1). In the patients injected with $[^{18}\text{F}]$fluoro-PEG-folate, 25 positive joints were observed, with a minimum of two joints per patient. In 10 of these 25 joints, clinical arthritis was confirmed. In the remaining 15 positive joints clinical inflammation was absent, suggesting the presence of subclinical inflammation. Whilst both $[^{18}\text{F}]$fluoro-PEG-folate and (R)-$[^{11}\text{C}]$PK11195 showed clear uptake in arthritic joints, $[^{18}\text{F}]$fluoro-PEG-folate demonstrated a significantly lower background uptake than (R)-$[^{11}\text{C}]$PK11195 (SUV of 0.18 vs 0.75; p < 0.001) respectively. T/B-ratios were significantly higher for $[^{18}\text{F}]$fluoro-PEG-folate (3.60 vs 1.72, p = 0.009).

Conclusion:

$[^{18}\text{F}]$fluoro-PEG-folate shows great potential as a macrophage tracer to image both clinical and presumably also subclinical arthritis in RA patients. The tracer shows improved characteristics compared to the established macrophage tracer (R)-$[^{11}\text{C}]$PK11195 for imaging arthritis, because of lower background signal.

References:


Disclosure: N. Verweij, None; S. Bruijnen, None; Y. Gent, None; M. Huisman, None; G. Jansen, None; C. Molthoff, None; Q. Chen, None; P. Low, None; A. Windhorst, None; A. Lammertsma, None; O. Hoekstra, None; A. Voskuyl, None; C. van der Laken, None.

Abstract Number: 245

The Clinical Utility of Splenic Fluorodeoxyglucose Uptake for Diagnosis and Prognosis in Patients with Macrophage Activation Syndrome

Sung Soo Ahn$^1$, Sang Hyun Hwang$^2$, Seung Min Jung$^1$, Sang-Won Lee$^1$, Yong-Beom Park$^3$, Mijin Yun$^2$ and Jason Jungsik Song$^1$, $^1$Division of Rheumatology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea, Republic of (South), $^2$Department of Nuclear Medicine, Yonsei University College of Medicine, Seoul, Korea, Republic of (South), $^3$Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea, Republic of (South)

First publication: September 18, 2017
Abstract

Background/Purpose: To evaluate splenic glucose metabolism in macrophage activation syndrome (MAS), characterised by overwhelming systemic inflammation. Splenic $^{18}$F-fluorodeoxyglucose (FDG) uptake was compared in patients with MAS and sepsis using positron emission tomography/computed tomography (PET/CT).

Methods: Clinical and FDG-PET/CT findings from patients with MAS and those with culture-proven sepsis were evaluated. Standardised uptake value (SUV) for the spleen and liver were measured. The maximum of the spleen to liver SUV ratio (SLR$_{\text{max}}$) was calculated as spleen SUV$_{\text{max}}$/liver SUV$_{\text{mean}}$. Radiological splenic volume was also measured, and splenic metabolic volume (MV) was defined as total splenic volume with an SLR$_{\text{mean}}$ $>$ 1.14. The association between clinical features, laboratory variables, and SLR$_{\text{max}}$ was analysed.

Results: The median SLR$_{\text{max}}$ and splenic MV were significantly higher in patients with MAS ($n = 38$) than they were in those with sepsis ($n = 15$) (SLR$_{\text{max}}$: 1.51 vs. 1.09, $p = 0.001$; MV: 346.0 vs. 154.0, $p = 0.015$) (Figure 1). Multivariate analyses revealed that SLR$_{\text{max}}$ $>$ 1.31 was useful for discriminating between MAS and sepsis (Table 1). SLR$_{\text{max}}$ positively correlated with ferritin and lactate dehydrogenase level in MAS. Furthermore, MAS patients with high splenic FDG uptake (SLR$_{\text{max}}$ $>$ 1.72) had higher in-hospital mortality compared to those with moderate to low splenic FDG uptake ($p = 0.013$).

Conclusion: This study was the first to demonstrate that splenic FDG uptake is significantly elevated in patients with MAS compared to those with sepsis. This may be useful to differentiate between MAS and sepsis, and to predict poor prognosis in patients with MAS.

References


Figure 1 Comparison of the standardised $^{18}$F-fluorodeoxyglucose uptake values (SUV) in patients with macrophage activation syndrome (MAS; $n = 38$), patients with sepsis ($n = 15$), and healthy controls ($n = 40$) (A) The SUV$_{\text{max}}$ of spleen to liver ratio. (B) The SUV$_{\text{max}}$ of bone marrow to liver ratio. (C) Spleen radiologic volume. (D) Spleen metabolic volume. (E) Representative $^{18}$F-FDG PET/CT images in patient with MAS (left), patient with sepsis (middle), and healthy control subject (right). ns, not significant. Data are expressed as the median; error bars indicate the interquartile range.
Disclosure: S. S. Ahn, None; S. H. Hwang, None; S. M. Jung, None; S. W. Lee, None; Y. B. Park, None; M. Yun, None; J. J. Song, None.


Abstract Number: 246

Development and Validation of a Flourescence Optical Imaging Rheumatoid Arthritis Scoring System for Synovitis in the Wrist and Hand

Mads Ammitzbøll-Danielsen1, Mikkel Østergaard1,2, Lene Terslev3, Sarah Ohrndorf4 and Daniel Glinatsi1, 1Center for Rheumatology and Spine Diseases, Rigshospitalet, Copenhagen Center for Arthritis Research, Copenhagen, Denmark, 2Center for Rheumatology and Spine Diseases, Copenhagen Center for Arthritis Research, Copenhagen, Denmark, 3Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Rigshospitalet, Copenhagen, Denmark, 4Rheumatology and Clinical Immunology, Charité-University Medicine Berlin, Berlin, Germany

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: To assess the intra- and inter-reader agreement and responsiveness of a novel scoring system for FOI-assessed synovitis.

Methods: FOI of were obtained of both wrists and hands of 46 RA patients inducing or escalating anti-rheumatic therapy and who had ≥1
clinically swollen joint in the hand at baseline, after 3 and 6 months’ follow-up. The hands were placed in the FOI-unit and the patient received a bolus of i.v. ICG-Pulsion (1mg/kg body weight) 10 seconds after starting the examination, which obtained 1 image/second over 6 minutes. The image-sets were anonymized and randomized and were assessed for synovial pathology at the wrist, 1st-5th metacarpophalangeal (MCP), 1st interphalangeal (IP) and 2nd-4th proximal interphalangeal (PIP) joint levels in both hands by two readers blinded to patient data but not chronology. The readers performed a calibration session before the exercise. The images of 23 patients were re-anonymized and were assessed as an intra-reader analysis. The scoring system for synovitis was based on the theory that inflamed tissue would demonstrate a more rapid enhancement than surrounding tissues. For each joint, the images were assessed sequentially from start of injection of ICG-Pulsion to peak enhancement. Synovial pathology was defined as a sharply margined enhancement with clear integrity from surrounding tissues and correct anatomical location lasting ≥ 3 seconds. The thickness of the pathology fulfilling these criteria were measured in the transverse plane of the hand at the 3rd second of enhancement and were scored as follows: 0: no enhancement, 1: <1/3, 2: ≥1/3 but <2/3, 3: ≥2/3 of joint thickness. Descriptive statistics and the Wilcoxon signed-rank test were used to assess change in score over time. Intra-/inter-reader for status and change scores were assessed using single measure intra-class correlation coefficients (ICC) and smallest detectable change (SDC, change scores only). Responsiveness was assessed using standardized response mean (SRM).

Results: The median (IQR) change in total synovitis score between baseline and 3/6 months’ follow-up were -5.0 (-10.0,-1.0)/-8.0 (-13.5,-3.0) (p<0.01). Intra- and inter-reader ICC were good to very good for status and change scores at all joint levels and for total scores (Table 1). The SDC were generally low and for the inter-reader SDC, 56%/60% of the patients had a change larger than the SDC between baseline and 3/6 months respectively. The mean SRM for total change scores between baseline and 3/6 months’ follow-up were moderate to good (0.7/0.8).

Conclusion: The novel FOI RA synovitis scoring system showed high reliability and moderate to good responsiveness in the hands. Future studies should focus on comparing the sensitivity and specificity of FOI with ultrasound and magnetic resonance imaging.

Table 1

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>3 months’ follow-up</th>
<th>6 months’ follow-up</th>
<th>Δ Baseline – 3 months</th>
<th>Δ Baseline – 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intra-reader ICC (SDC), reader 1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total scores</td>
<td>0.90</td>
<td>0.86</td>
<td>0.83</td>
<td>0.87 (6.2)</td>
<td>0.92 (4.9)</td>
</tr>
<tr>
<td>Wrist</td>
<td>0.82</td>
<td>0.92</td>
<td>0.62</td>
<td>0.88 (1.4)</td>
<td>0.91 (1.4)</td>
</tr>
<tr>
<td>MCP joints</td>
<td>0.86</td>
<td>0.72</td>
<td>0.93</td>
<td>0.76 (4.8)</td>
<td>0.85 (3.6)</td>
</tr>
<tr>
<td>PIP joints</td>
<td>0.95</td>
<td>0.96</td>
<td>0.86</td>
<td>0.90 (2.9)</td>
<td>0.90 (3.3)</td>
</tr>
<tr>
<td><strong>Intra-reader ICC (SDC), reader 2</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total scores</td>
<td>0.85</td>
<td>0.72</td>
<td>0.16</td>
<td>0.77</td>
<td>0.74</td>
</tr>
<tr>
<td>Wrist</td>
<td>0.84</td>
<td>0.77</td>
<td>0.71</td>
<td>0.80</td>
<td>0.78</td>
</tr>
<tr>
<td>MCP joints</td>
<td>0.84</td>
<td>0.67</td>
<td>0.47</td>
<td>0.87</td>
<td>0.84</td>
</tr>
<tr>
<td>PIP joints</td>
<td>0.94</td>
<td>0.73</td>
<td>0.24</td>
<td>0.73</td>
<td>0.68</td>
</tr>
<tr>
<td><strong>Inter-reader ICC (SDC)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total scores</td>
<td>0.88</td>
<td>0.84</td>
<td>0.60</td>
<td>0.80 (4.8)</td>
<td>0.70 (6.2)</td>
</tr>
<tr>
<td>Wrist</td>
<td>0.76</td>
<td>0.72</td>
<td>0.58</td>
<td>0.67 (1.1)</td>
<td>0.65 (1.3)</td>
</tr>
<tr>
<td>MCP joints</td>
<td>0.86</td>
<td>0.80</td>
<td>0.76</td>
<td>0.81 (3.1)</td>
<td>0.66 (3.7)</td>
</tr>
<tr>
<td>PIP joints</td>
<td>0.91</td>
<td>0.82</td>
<td>0.39</td>
<td>0.79 (2.6)</td>
<td>0.71 (3.6)</td>
</tr>
</tbody>
</table>

Disclosure: M. Ammitzbøll-Danielsen, None; M. Østergaard, AbbVie, BMS, Celgene, Crescendo Bioscience, Janssen, Merck, 2, Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Centocor, GSK, Hospira, Janssen, Merck, Novartis, Orion, Pfizer, Regeneron, Roche, Takeda, and UCB, 8; L. Terslev, None; S. Ohrndorf, None; D. Glinatsi, None.


Abstract Number: 247

Near Infrared Indocyanine Green Imaging Reveals Diminished Flow in Basilic Associated Lymphatic Vessels in the Hands of Rheumatoid Arthritis Patients during Flare

Richard Bell1, Alicia Lieberman2, Ronald Wood3, Cristy Bell4, Homaira Rahimi5, Edward Schwarz6 and Christopher T. Ritchlin7, 1Orthopedics, University of Rochester, Rochester, NY, 2Allergy, Immunology and Rheumatology, University of Rochester Medical Center, Rochester, NY, 3University of Rochester, Rochester, NY, 4Allergy, Immunology & Rheumatology, University of Rochester, Rochester, NY, 5Rheumatology, University of Rochester/Golisano Children's Hosp, Rochester, NY, 6Orthopediatrics, University of Rochester, Rochester,
Background/Purpose: Near infrared (NIR) imaging studies of subdermal indocyanine green (ICG) in murine models of inflammatory arthritis established the important contribution of lymphatic vessel (LV) function in joint homeostasis and flare. However, the role of lymphatic vessel function and altered joint drainage in rheumatoid arthritis (RA) flare is unknown.

Methods: The web spaces in both hands of 7 healthy controls (Ctl) and 2 subjects in RA flare were injected with 0.1ml of 100μM ICG on 2-4 separate occasions and the NIR fluorescence of the dorsal aspect imaged. Two independent graders counted the total number of fluorescent LVs crossing the mid-dorsal aspect of the hand, and the number of LVs associated with the basilic and cephalic veins and their tributaries. Differences between Ctl vs RA were evaluated using Fisher’s Exact Test, pooling left and right hand observations across all visits (n=32 Ctl, n=10 RA). The frequency of lymphatic contractions of these LVs were determined from graphs of region of interest intensity across time to calculate contractions per minute; differences evaluated using a Wilcoxon Rank Test.

Results: Representative raw images of Ctl and RA hands are presented in Fig 1A-B demonstrating the Mid-Dorsal region (Blue Box), Basilic (Dark Green Arrows) and Cephalic (Dark Red) associated clusters and their tributaries (Basilic = Light Green, Cephalic = Light Red). The number of basilic associated LVs crossing the mid dorsal region and the feeding tributaries were decreased in RA subjects compared to controls (Fig 1C and F, p<0.05). Contour plots generated by stabilizing and averaging all images during the 10min session show clear anatomic and bulk flow differences (Fig 1 D-E). Note the lack of Basilic LV filled with ICG in RA (circled region in E). Representative 3D plots of the ROI analysis are shown in Fig 2A and B with scored contractions (Black Arrows) revealing a significant increase in contraction frequency in the cephalic associated LVs in RA subjects (Fig 2C, p<0.05).

Conclusion: For the first time, we have characterized the lymphatic vessel anatomy of the hands of healthy subjects and RA subject using NIR ICG imaging. Furthermore, RA patients in flare show a reduced number of fluorescent LVs in the hands compared to Ctl. A decline in the number of LVs removing inflammatory cells and molecules from the joints and compensatory redirection of flow is likely to play a significant role in RA flare. Further studies to confirm these initial findings are underway.
Validation of Objective Quantification System for Disease Progression in Patients with Juvenile Idiopathic Arthritis

Olga Kubassova¹, N Tzaribachev², Romiesa Hagoug³ and Mikael Boesen⁴, ¹R&D, Image Analysis Group, London, England, ²University Medical Center Schleswig-Holstein, Bad Bramstedt, Germany, ³Imaging, Image Analysis Group, London, United Kingdom, ⁴Radiology, Copenhagen University Hospital, Bispebjerg and Frederiksberg, Frederiksborg, Denmark

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Imaging as outcome measure has been studied and extensively used in the assessment of treatment for adult patients with rheumatoid arthritis (RA)¹. In children with juvenile idiopathic arthritis (JIA) similar knowledge is very limited. This abstract presents a novel imaging based system for the assessment of treatment efficacy in JRA patients and its initial validation against clinical outcome measures.

Methods:
Patients with polyarticular JIA with insufficient (≥3 affected joints) response or intolerance to ≥3 months of Methotrexate, Etanercept were assessed by imaging. The MCP joints incClinically most affected hand were imaged with Dynamic Contrast Enhanced (DCE)-MRI at baseline (BL), month 3 and 6 of treatment using a 0.2T scanner. Clinical scores included active joint (AJ) counts. Clinical response was considered a state of ≤ 3 AJ. A region of interests (ROIs) were placed in DCE-MRI to quantify the synovium in MCPs 2-5. Output parameters included Dynamic Enhanced MRI Quantification scores (DEMRIQ-Vol) corresponding to the volume of enhancing voxels within the synovial ROIs alone or multiplied with the mean of the maximum enhancement (ME) or the initial rate of enhancement (IRE), DEMRIQ-ME and DEMRIQ-IRE. Differences in DEMRIQ-Vol scores between visits were analyzed using t-test (p<0.05* = statistically significant, p<0.25** = clinically meaningful). Correlation between clinical and DEMRIQ scores were described.

Results:
18 Caucasian patients (12 girls, median age 12.6 years, median disease duration 1.2 years) were included in the study. Two patients discontinued imaging after BL but continued treatment. In all but 3 of the remaining patients statistically significant and/or clinically meaningful changes were documented for DEMRIQ change (irrespective of the clinical scores) the outcome of the patient could be predicted:

- in 5 patients, improvement of DEMRIQ scores predicted response to treatment (within 2-6 months after last MRI examination)
- in 4 patients, an increase or persistence of a high DEMRIQ predicted non-response to treatment
- in 7 patients, increase in DEMRIQ (after initial decrease) or persistence of a high DEMRIQ predicted flare (in 3 of the patients flare occurred after treatment discontinuation)

In all patients, subclinical disease could be detected on MRI in clinically unaffected joints.

**Conclusion:**

DEMRIQ scores supported clinical examination by detecting subclinical inflammation. In most patients, the imaging scores were predictive of the patient outcomes such as response and non-response to treatment and flare, making it a useful outcome measure in clinical practice and research.


**Disclosure:** O. Kubassova, None; N. Tzaribachev, None; R. Hagoug, Image Analysis Group, 3; M. Boesen, None.


**Abstract Number:** 249

**Where to Look for Uric Acid Crystals? Results from a Norwegian Ultrasound Study**

Hilde B Hammer1, Lars Karoliussen2, Lene Terslev3, Espen A. Haavardsholm4, Tore K Kvien4 and Till Uhlig4, 1Rheumatology, Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, 2Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, 3Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Rigshospitalet, Denmark, Copenhagen, Denmark, 4Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, 5On behalf of the NOR-DMARD registry, Oslo, Norway

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017
**Session Title:** Imaging of Rheumatic Diseases Poster I
**Session Type:** ACR Poster Session A
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Ultrasound (US) has received an increasing attention in detecting uric monosodium urate (MSU) deposits, and is included in the ACR/EULAR classification criteria for gout. The OMERACT US group has developed definitions for US elementary lesions in gout including double contour (DC) sign (deposits of crystals on the surface of cartilage), tophus (larger hypo-echoic aggregation of crystals, usually well delineated), aggregates (small hyper-echoic deposits) and erosions. MSU deposits may be found in many different regions in an individual with gout but with some predilection sites. The present objective was to assess by US the presence of MSU deposits in a high number of locations known to be involved, and to identify areas to include when screening for gout by US.

**Methods:**

This includes baseline data from a prospective observational study where patients with crystal-proven gout who presented after a recent gout flare were included (117 patients (mean (SD) 56.9 (14.1) years old, 8.5 (7.3) years disease duration, 93.2% men), all with insufficiently treated serum uric acid level (>360 μmol/L/>6 mg/dl). We performed a systematic extensive assessment with US (GE E9 machine, grey scale 15MHz) to detect MSU deposits, using the OMERACT definitions for DC, tophi and aggregates. The following locations were assessed bilaterally; radiocarpal joint, MCP 2, insertion of triceps and quadriceps, the patellar tendon (divided into proximal and distal), cartilage of distal femur (maximal flexed knee) and the talar cartilage of the tibiotalar joint, the MTP 1 joint as well as the Achilles tendon. Sum of sites with deposits was calculated and correlations were performed by use of Spearman, and frequencies of deposits were calculated as percentages at each site.

**Results:**

The mean (SD) serum uric acid level was 488 (88) μmol/L. There was no significant correlation between number of sites with deposits and uric acid level (r=0.11), but with disease duration (r=0.25, p=0.007). The table shows that DC was primarily found in MTP1, followed by talar and femoral cartilage. Tophi and aggregates were primarily found in MTP1, followed by distal patellar and triceps tendons. There were no major differences between right and left side. In 21 patients (17.9%) DC was seen on femoral or talar cartilage, but not in the MTP1 joints.
Conclusion:

There is limited knowledge on the primary locations of MSU deposits, and the present study suggests US examinations of MTP1, distal patellar and triceps tendons as well as talar and femoral cartilage to be the most important sites to explore for presence of MSU deposits in patients examined for possible gout.

<table>
<thead>
<tr>
<th></th>
<th>Double contour</th>
<th>Tophus</th>
<th>Aggregates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Right</td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td>Wrist</td>
<td>1.7</td>
<td>0</td>
<td>7.7</td>
</tr>
<tr>
<td>MCP 2</td>
<td>0</td>
<td>0</td>
<td>3.5</td>
</tr>
<tr>
<td>Distal femur cartilage</td>
<td>15.3</td>
<td>16.1</td>
<td>NA</td>
</tr>
<tr>
<td>Talar cartilage</td>
<td>18.8</td>
<td>19.7</td>
<td>NA</td>
</tr>
<tr>
<td>MTP 1</td>
<td>36.2</td>
<td>32.5</td>
<td>44.0</td>
</tr>
<tr>
<td>Triceps</td>
<td>NA</td>
<td>NA</td>
<td>18.0</td>
</tr>
<tr>
<td>Quadriceps</td>
<td>NA</td>
<td>NA</td>
<td>6.0</td>
</tr>
<tr>
<td>Proximal patellar tendon</td>
<td>NA</td>
<td>NA</td>
<td>4.3</td>
</tr>
<tr>
<td>Distal patellar tendon</td>
<td>NA</td>
<td>NA</td>
<td>22.4</td>
</tr>
<tr>
<td>Achilles</td>
<td>NA</td>
<td>NA</td>
<td>8.7</td>
</tr>
</tbody>
</table>

Disclosure: H. B. Hammer, AbbVie Norway, 2,Abbvie, 8,Novartis Pharmaceutical Corporation, 5,Pfizer Inc, 8,Roche Pharmaceuticals, 8; L. Karoliussen, None; L. Terslev, None; E. A. Haavardsholm, None; T. K. Kvien, AbbVie, 2,Pfizer Inc, 2,Roche Pharmaceuticals, 2,UCB, 2,BMS, 2,MSD, 2,AbbVie, 5,Pfizer Inc, 5,BMS, 8,MSD, 8,Roche Pharmaceuticals, 8,UCB, 8,AbbVie, 8; T. Uhlig, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/where-to-look-for-uric-acid-crystals-results-from-a-norwegian-ultrasound-study

Abstract Number: 250

An Ultrasonographic Study for Investigating Relationships with the Signs of Uric Deposition and Bone Erosion in Patients with Hyperuricemia

Ikuko Tanaka1, Takashi Kato2, Motokazu Kai3, Kunikazu Ogawa3, Hisaji Oshima4 and Shigenori Tamaki5, 1NAGOYA Rheumatology Clinic, Nagoya, Japan, 2Department of Radiology, National Center for Geriatrics and Gerontology, Obu, Japan, 3Mie Rheumatology Clinic, Suzuki, Japan, 4Department of Connective Tissue Diseases, National Tokyo Medical Center, Tokyo, Japan, 5Nagoya Rheumatology Clinic, Nagoya, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Joint ultrasonography (US) is a noninvasive examination that can evaluate arthritis and uric acid deposition at gout attacks.

The purpose of this study was to investigate the progression of gouty arthritis using cross sectional data from the aspect of the joint sonographic features such as double contour sign (DCS), hyperechoic aggregate (HA), and bone erosion (BE). DCS and HA are signs showing uric acid deposition.

Methods:

The subjects were 644 consecutive male patients (Age: 45.7±10.7 y.o.) with hyperuricemia and/or gout attack. Seventy one patients (11%) had experienced neither any attacks nor diagnosis of gout (N group). One hundred eighty seven patients (29%) were diagnosed as the first
attack of gout (1st group), while 386 patients (60%) had their past history of the attacks (His group). They underwent joint US. Observed rates of DCS, HA, and BE (D: only DCS; H: only HA; B: both DCS and HA; A: DCS or HA; E: BE) in the first metatarsophalangeal (1st MTP) were compared.

**Results:**

In the N group, the observed rates of D, H, B, A, and E were 45%, 1%, 0%, 46%, and 1%, respectively. In the 1st group, arthritis on US was observed in the joints of the first metatarsophalangeal (1st MTP) (72%), ankle (18%), and knee (5%). In the 1st group, the patients of which attack was at 1st MTP represented that observe rates were D 29%, H 20%, B 38%, A 87%, and E 29%, while the patients of which attack was at other than 1st MTP were D 20%, H 4%, B 0%, A 24%, and E 0%. In His group, the observed rates were D 16%, H 18%, B 66%, A 100%, and E 57%. Observed frequency of DCS was highest in N group and was decreased along with articular destruction, respectively. In His group, 100% and more than 50% patients showed sonographic features of ureic acid deposition and bone erosion. Fisher’s exact tests demonstrated a significant relationship in HA and BE, but not in DCS and BE (p<0.05).

**Conclusion:**

The results suggested that DCS was the earliest sign of uric acid deposition that was observed in the asymptomatic stage in gount. Even at the first attack HA was frequently observed that was leading to BE.

**Disclosure:** I. Tanaka, None; T. Kato, None; M. Kai, None; K. Ogawa, None; H. Oshima, None; S. Tamaki, None.


**Abstract Number:** 251

**Articular Cartilage of Knee and First MTP Joint Are the Preferred Sites of Urate Crystal Deposition in Asymptomatic Hyperuricemic Individuals**

Danveer Bhadu1, Siddharth K. Das2, Urmila Dhakad3 and Archana Wakhlu4, 1Rheumatology, ALL INDIA INSTITUTE OF MEDICAL SCIENCES, NEW DELHI, NEW DELHI, India, 2Rheumatology, Prof. and Head, Rheumatology, K.G. Medical University, Lucknow, Lucknow, India, 3Rheumatology, Asst Professor, K.G. Medical University, Lucknow, India, Lucknow, India, 4Radiology, Senior Resident, Lucknow, India

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Imaging of Rheumatic Diseases Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The prevalence of hyperuricemia ranges from 2.6% to 47.2% in various populations [1,2]. Ultrasound evidence of urate crystal deposition in the form of double contour sign (DCS) and hyperechoic aggregates (HAGs) in asymptomatic hyperuricemic (AH) individuals has been documented in studies [3]. It has been reported that assessment of one joint (ie, radiocarpal) and two tendons (ie, patellar and triceps) for HAGs, and three articular cartilages (ie, first metatarsal (1st MTP), talar and second metacarpal/femoral) for DCS showed the best balance between sensitivity and specificity (84.6% and 83.3%, respectively) in diagnosing intercritical gout[4]. So we aimed to find the preferred sites of urate crystal deposition among these six sites in AH individuals.

**Methods:** 24 AH (serum uric acid (SUA) >7mg/dl) and fifty controls (SUA <7mg/dl) with age more than 18 years were included in this study. DCS was looked for at three articular cartilage sites (1st MTP, tibiotalar and femoral condyle) whereas HAGs were looked for at one joint site (radiocarpal joint) and two tendon sites (patellar tendon and triceps tendon). Ultrasound was done using multifrequency linear array transducer (8–13 MHz) of Logiq E; GE Medical Systems Ultrasound, on B mode gray scale (GS). Settings of machine were as follows: dynamic range of 40–50 dB, GS frequency of 11–13 MHz and GS gain of 60 dB.

**Results:** 8 out of 24 AH patients had ultrasound evidence of urate crystal deposition in 1st MTP joint area followed by knee joint area which was detected in 6 patients. The detection rate of ultrasound abnormalities in AH was 45.8% with two joint area (knee and 1st MTP) and 50% with six sites assessment. Amongst controls, 16% were found to have these abnormal ultrasound findings by both two joint area and six sites exams. (Figure: DCS at knee and 1st MTP joint)
Conclusion: The highest predilection of urate crystal deposition in AH patients is the articular cartilage of Knee and 1st MTP joints.

References:

Disclosure: D. Bhadu, None; S. K. Das, None; U. Dhakad, None; A. Wakhlu, None.


Abstract Number: 252

Correlations between Clinical and Ultrasound Scores of Peripheral Enthesitis and Disease Activity Scores in a Cohort of Spondyloarthritis

Assia Haddouche1, Sabrina Haid2, Siham Bencheikh3, Samy Slimani4, Amina Abdessened5, Nadjia Brahimi6, Aîcha Ladjouz Rezig6 and Fella Hamni6, 1of Medicine, Department of Medicine, University of Algiers 1, Algiers, Algeria, 2medicine, Department of Medicine, University of Algiers 1, Algiers, Algeria, 3EPH HADJOUT, Algiers, Algeria, 4Department of Medicine, University of Batna, Batna, Algeria, 5Medicine, Department of Medicine, University of Algiers 1, Algiers, Algeria, 6Department of Medicine, University of Algiers 1, Algiers, Algeria

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: To look correlations between clinical and ultrasound (US) scores of peripheral enthesitis (PE) and disease activity scores of SpA

Methods: A prospective study of 208 SpAs meeting SpA ASAS criteria. In the same consultation, 30 enthesitic sites per patient were examined clinically and 34 sites per patient were examined with US according to the US OMERACT 2014 definition of enthesitis. PE was assessed by the following clinical scores: Enthesitis Peripheral Score (PES= Sum of symptomatic peripheral entheses sites on clinical examination), Visual Analog Scale of peripheral enthesitis (VAS), Spondyloarthritis Research Consortium of Canada score (SPARCC) as well as the following US enthesitis scores: Acute Enthesitis score (Correlations between clinical scores and ultrasound scores and disease activity scores were calculated using SPSS software.

Results: A total of 208 patients were included, mainly men (63.5%). The mean age was 40.2 ± 11.7 years. The mean duration of the SpA was 11.8 ± 8.7 years. Axial radiographic SpA was the most frequent phenotype (69.2%). On examination 64.4% of SpA were NSAIDs and 88.9% had active disease (ASDAS-vs and / or ASDAS-crp> 1.3). Tables (1, 2) summarize the results of correlations between clinical
scores and US scores and disease activity scores. A weak correlation was found between: the acute enthesitis score and two clinical scores (peripheral enthesitis score, mean score of enthesitic VAS); the global enthesitis score and all clinical enthesitis scores and finally between the SES score and two clinical enthesitic scores (peripheral enthesitis score, mean score of enthesitic VAS).

A moderate correlation was observed between disease activity scores and all US scores of peripheral enthesitis except for the chronic enthesitis score for which the correlation was weak.

Table 1

<table>
<thead>
<tr>
<th>Scores</th>
<th>PES</th>
<th>VASm Enthesitis</th>
<th>SPARCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Enthesitis</td>
<td>r: 0.15</td>
<td>r: 0.15</td>
<td>r: 0.13</td>
</tr>
<tr>
<td></td>
<td>p: 0.03</td>
<td>p: 0.03</td>
<td>p: 0.06</td>
</tr>
<tr>
<td>Chronic Enthesitis</td>
<td>r: 0.10</td>
<td>r: 0.09</td>
<td>r: 0.09</td>
</tr>
<tr>
<td></td>
<td>p: 0.15</td>
<td>p: 0.17</td>
<td>p: 0.26</td>
</tr>
<tr>
<td>Global Enthesitis</td>
<td>r: 0.16</td>
<td>r: 0.16</td>
<td>r: 0.14</td>
</tr>
<tr>
<td></td>
<td>p: 0.02</td>
<td>p: 0.03</td>
<td>p: 0.04</td>
</tr>
<tr>
<td>Doppler Enthesitis</td>
<td>r: 0.06</td>
<td>r: 0.07</td>
<td>r: 0.06</td>
</tr>
<tr>
<td></td>
<td>p: 0.36</td>
<td>p: 0.32</td>
<td>p: 0.42</td>
</tr>
<tr>
<td>MASEI</td>
<td>r: 0.13</td>
<td>r: 0.13</td>
<td>r: 0.13</td>
</tr>
<tr>
<td></td>
<td>p: 0.06</td>
<td>p: 0.23</td>
<td>p: 0.07</td>
</tr>
<tr>
<td>SES</td>
<td>r: 0.13</td>
<td>r: 0.13</td>
<td>r: 0.13</td>
</tr>
<tr>
<td></td>
<td>p: 0.06</td>
<td>p: 0.04</td>
<td>p: 0.05</td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th></th>
<th>ASDAS-vs</th>
<th>ASDAS-crp</th>
</tr>
</thead>
<tbody>
<tr>
<td>PES</td>
<td>r: 0.41*</td>
<td>r: 0.39*</td>
</tr>
<tr>
<td></td>
<td>p &lt;0.0001</td>
<td>p &lt;0.0001</td>
</tr>
<tr>
<td>VASm Enthesitis</td>
<td>r: 0.43*</td>
<td>r: 0.40*</td>
</tr>
<tr>
<td></td>
<td>p &lt;0.0001</td>
<td>p &lt;0.0001</td>
</tr>
<tr>
<td>SPARCC</td>
<td>r: 0.39*</td>
<td>r: 0.38*</td>
</tr>
<tr>
<td></td>
<td>p &lt;0.0001</td>
<td>p &lt;0.0001</td>
</tr>
<tr>
<td>Acute Enthesitis</td>
<td>r: 0.33*</td>
<td>r: 0.46*</td>
</tr>
<tr>
<td></td>
<td>p &lt;0.0001</td>
<td>p &lt;0.0001</td>
</tr>
<tr>
<td>Chronic Enthesitis</td>
<td>r: 0.18</td>
<td>r: 0.23</td>
</tr>
<tr>
<td></td>
<td>p: 0.006</td>
<td>p: 0.002</td>
</tr>
<tr>
<td>Global Enthesitis</td>
<td>r: 0.35*</td>
<td>r: 0.46*</td>
</tr>
<tr>
<td></td>
<td>p &lt;0.0001</td>
<td>p &lt;0.0001</td>
</tr>
<tr>
<td>Doppler Enthesitis</td>
<td>r: 0.29*</td>
<td>r: 0.34*</td>
</tr>
<tr>
<td></td>
<td>p &lt;0.0001</td>
<td>p &lt;0.0001</td>
</tr>
<tr>
<td>MASEI</td>
<td>r: 0.38*</td>
<td>r: 0.48*</td>
</tr>
<tr>
<td></td>
<td>p &lt;0.0001</td>
<td>p &lt;0.0001</td>
</tr>
<tr>
<td>SES</td>
<td>r: 0.32*</td>
<td>r: 0.42*</td>
</tr>
<tr>
<td></td>
<td>p &lt;0.0001</td>
<td>p &lt;0.0001</td>
</tr>
</tbody>
</table>

**Conclusion:** All clinical and US scores, except for the chronic enthesitis score, would be of interest in assessing disease activity of SpA. US scores are weakly or even uncorrelated to the peripheral enthesitis clinical scores.
Disclosure: A. Haddouche, None; S. Haid, None; S. Bencheikh, None; S. Slimani, None; A. Abdessemed, None; N. Brahimi, None; A. Ladjouz Rezig, None; F. Hanni, None.


Abstract Number: 253

Presence of Bone Marrow Edema and Structural Lesions on Magnetic Resonance Imaging of the Sacroiliac Joints in Young Military Recruits before and after 6 Weeks of Intensive Physical Training

Gaëlle Varkas1, Manouk de Hooge2, Thomas Renson3, Sophie De Mits4, Philippe Carron5, Peggy Jacques4, Muriel Moris6, Geert Souverijns7, Lennart Jans8, Dirk Elewaut9 and Filip van Den Bosch10, 1Laboratory for Molecular Immunology and Inflammation, Department of Rheumatology, VIB, Ghent University and Ghent University Hospital, Ghent, Belgium, 2VIB, Ghent University and Ghent University Hospital, Leiden, Netherlands, 3Rheumatology, Ghent University Hospital, GENT, Belgium, 4Ghent University Hospital, Ghent, Belgium, 5Department of Rheumatology, Ghent University Hospital, Ghent, Belgium, 6Military Hospital Queen Astrid, Neder-Over-Heembeek, Belgium, 7Jessa Hospital Hasselt, Hasselt, Belgium, 8Department of Radiology, Ghent University Hospital, Ghent, Belgium, 9VIB Inflammation Research Center, University of Ghent, Ghent, Belgium, 10Rheumatology, Ghent University Hospital, Gent, Belgium

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
While MRI of the sacroiliac is a sensitive method for detection of bone marrow edema (BME) and structural lesions in axial spondyloarthritis (axSpA), there is only limited data regarding the specificity in a non-SpA population. Mechanical stress is considered to be an important factor in the pathogenesis of SpA. However, currently there are no data on the effect of intensive physical activity on the sacroiliac joints and how this could impact MRI findings of the sacroiliac joints (MRI-SIJ).

Methods:
Twenty-two military recruits underwent an MRI-SIJ before and after 6 weeks of intense and uniform physical training. Bone marrow edema (BME) and structural lesions were scored by 3 trained readers, blinded for time sequence and clinical findings. The Spondyloarthritis Research Consortium of Canada (SPARCC) score was used to assess BME and an adjusted method derived from the SPARCC scoring method was used to assess structural lesions: sclerosis, erosions, fatty lesions and ankylosis were scored per quadrant on 6 consecutive slices representing the cartilaginous part of the joint. Additionally, the agreement with the definition of a positive MRI defined by ASAS was evaluated.

Results:
At baseline, 40.9% (9/22) of recruits already presented with at least one BME lesion, whereas this number increased to 50.0% (11/22) at week 6 (p=0.625). In subjects displaying BME, the mean number of BME lesions was 2.4 (±0.4) at baseline, compared to 3.7 (±1.3) at week 6. Overall, the mean change in BME lesions over time in all 22 individuals was 0.9 (±0.6) (p=0.109). A positive MRI according to ASAS was present in 22.7% (5/22) of recruits at baseline, which increased to 36.4% at follow up (p=0.375). Structural lesions were present in 36.4% (8/22) of subjects at baseline, which increased to 50% subjects (11/22) after 6 weeks of intense physical training (p=0.453). There was a significant increase of MRI lesions over time when combining both structural and inflammatory lesions (p=0.038).

Conclusion:
We found a markedly high prevalence of BME and structural lesions in young, active, healthy volunteers, with almost 23% of them fulfilling the ASAS definition of a positive MRI. Overall, MRI lesions seem to increase after 6 weeks of intense physical training. Thus, our study underscores the necessity to interpret MRI findings of the sacroiliac joints in the appropriate clinical context, even in a young active population.

Disclosure: G. Varkas, None; M. de Hooge, None; T. Renson, None; S. De Mits, None; P. Carron, None; P. Jacques, None; M. Moris, None; G. Souverijns, None; L. Jans, None; D. Elewaut, Scientific Research Flanders; Research Council Ghent University; Interuniversity Attraction Pole., 2,Boehringer Ingelheim; Pfizer; UCB; Merck; Novartis; Janssen; Abbvie, 5; F. van Den Bosch, AbbVie Inc., Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer and UCB, 5,AbbVie Inc., Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer and UCB, 8.
Psoriatic Arthritis Sonographic Enthesitis Scores – Systematic Review of the Literature

Ofir Elalouf1, Sibel Bakirci2, Zahi Touma3, Melanie A Anderson4, Gurjit S. Kaeley5, Sibel Z. Aydin6 and Lihi Eder7,8, 1Rheumatology, Toronto Western Hospital, University of Toronto, Toronto, ON, Canada, 2Fellow in Rheumatology, Antalya, Turkey, 3Rheumatology, University of Toronto, Division of Rheumatology, Institute of Health Policy, Management and Evaluation, Toronto, ON, Canada, 4Toronto Western Hospital, University of Toronto, Toronto, ON, Canada, 5University of Florida, Ponte Vedra Beach, FL, 6University of Ottawa, Ottawa, ON, Canada, 7Medicine, University of Toronto, Toronto, ON, Canada, 8Women's College Research Institute, Women's College Hospital, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Enthesitis is a prominent feature of spondyloarthopathy (SpA), including psoriatic arthritis (PsA). The evaluation of enthesitis has conventionally been conducted by clinical exam, a method with significant limitations mainly its low sensitivity. Ultrasound can image entheses in high fidelity and may assist in the diagnosis and management of SpA patients. As part of the GRAPPA US sub-committee "Enthesitis Project" we performed a systematic review of the literature in order to assess the evidence and knowledge gaps in scoring systems of enthesitis in PsA.

Methods:

A systematic search of Pubmed, Embase and Cochrane was done. The search strategy was constructed to find original publications in English containing terms related to US, enthesitis, SpA or PsA. Two reviewers screened all abstracts for eligibility. Studies that reported used global sonographic scoring systems for assessment of enthesitis in patients with spondyloarthritis or their modifications were included. Data was extracted independently by 2 reviewers. Data extraction focused on the properties of the enthesitis scoring system used in each study. Specifically, we assessed the following component of the OMERACT filter: reliability of acquisition, feasibility, and construct validity as related to clinical assessment of enthesitis, biomarkers and imaging of enthesitis by other modalities, discriminative validity and responsiveness to treatment.

Results:

Fifty-one of 310 identified manuscripts were included. 13 studies used Glasgow Ultrasound Enthesitis Scoring System (GUESS) or its modifications, 9 used Madrid Sonographic Enthesitis Index Scoring System (MASEI), 6 used D'Agostino scoring system, 5 used Belgrade Ultrasound Enthesitis Score (BUSES), 3 used Sonographic Enthesitis Index (SEI), 1 used PsASon-Score, and 14 did not use a formal score. Only one of these scoring systems (PsASon) was developed and validated in patients with PsA. Only 18 (35%) of the studies involved patients with PsA, while the rest focused on SpA. Concerning the OMERACT filter, construct validity was assessed using biomarkers in 10 (19.6%) studies, only one study (2%) in PsA. Construct validity using clinical examination was assessed by 26 (51%), 11 (21.5%) were in PsA, only 6 (11.7%) compared US finding to imaging - none of them was performed on PsA. Responsiveness to treatment was assessed in 7 studies, none of them included PsA patients. Six (11.7%) studies evaluated discriminative validity two (4%) of them in PsA.

Conclusion:

Although sonographic indices have been developed for Spondyloarthritis, only a few have been validated for PsA. None of them fulfilled all the OMERACT filter criteria in patients with PsA. Additional research is needed to assess the validity or modification of existing scoring systems in patients with PsA.
Abstract Number: 255

Healing Time and Blood Perfusion By Laser Speckle Contrast Analysis in Patients with Systemic Sclerosis and Digital Ulcers

Simone Barsotti1,2, Anna d’Ascanio1, Valentina Venturini3, Laura Amanzi4, Silvia Bilia5, Marta Mosca1 and Alessandra Della Rossa6, 1Rheumatology Unit, University of Pisa, Pisa, Italy, 2Department of Medical Biotechnologies, University of Siena, Siena, Italy, 3Pisa University Hospital, Rheumatology unit, Pisa, Italy, 4Pisa University Hospital, Rheumatology Unit, Pisa, Italy, 5University of Pisa, Rheumatology Unit, Pisa, Italy, 6University of Pisa, Rheumatology Unit, Pisa, Italy

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Digital ulcers (DUs) are a major burden in patients with systemic sclerosis (SSc). Laser speckle contrast analysis (LASCA) is a novel technique that can analyse blood perfusion (BP) in the fingers and in DU areas. The objective of the present study was to evaluate BP in patients with SSc and DUs and correlate these values with the treatments and healing time.

Methods:
From February 2016 to March 2017, 23 consecutive Ssc patients presenting with DU at fingertips were enrolled: M:F=2:21; 15 lcSSc and 8 dcSSc; mean age 56±15.8 years. BP was assessed by LASCA in fingers affected by DUs, unaffected fingers, DU area, peri-ulcer area and the same area of unaffected fingers. DUs were defined infected if local signs of infection were present (swelling, severe pain, erythema, discharge). The treatment with major vasoactive drugs (iloprost, bosentan, sildenafil), the latency between the appearance of DU and first evaluation, and the time to DU healing under standard local treatment were collected.

Results:
BP was higher in peri-ulcer area with respect to the DUs area (84.1±21.0 vs 60.3±15.1 p<0.001), and no differences were observed between DUs area and similar area of unaffected fingers.

In patients without infection (n=17), healing time was negatively associated both to DUs BP (r=-0.618 p=0.011) and peri-ulcer BP (r=-0.488 p=0.011). The latency between appearance of DUs and first evaluation in our centre was also negatively correlated to mean healing time (r=0.36 p=0.036).

Patients with infection (n=6) presented a higher ulcer BP compared to non-infected pts (198.0±112.2 vs 103.3±66 p=0.023) and DUs needed a longer healing time (mean 130 vs 100 days).

The treatment with bosentan and iloprost was associated with higher BP in the unaffected fingers (respectively p=0.002 and p=0.001) but no BP changes at DU area or at fingers with DUs were observed. Sildenafil was not associated with significant differences in blood perfusion.

Conclusion: Our study suggests a potential usefulness of LASCA analysis of BP in the assessment of DUs in SSc patients. Although all DUs are ischaemic in nature (blood flow is lower than in unaffected area and periulcer area), BP values could help in identifying difficult to heal lesions, either due to a markedly reduced perfusion (low BP) or to the presence of an infection (higher than expected BP).

Additional data are needed to better define the role of BP as a guide to treatment, ulcer management and prevention in routine clinical practice.

Disclosure: S. Barsotti, None; A. d’Ascanio, None; V. Venturini, None; L. Amanzi, None; S. Bilia, None; M. Mosca, None; A. Della Rossa, None.

Abstract Number: 256

Tracking Digital Ulcers in Systemic Sclerosis: Feasibility Study Assessing Lesion Area from Patient-Recorded Smartphone Photographs

Graham Dinsdale1, Tonia Moore2, Joanne Manning2, Andrea Murray1, Ross Atkinson3, Karen Ousey4, Mark Dickinson5, Christopher Taylor6 and Ariane L. Herrick1,7, 1Division of Musculoskeletal & Dermatological Sciences, University of Manchester, Salford Royal Hospital NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, UK, Manchester, United Kingdom, 2Salford Royal Hospital NHS Foundation Trust, Salford, UK, Salford, United Kingdom, 3School of Health Sciences, Division of Nursing, Midwifery & Social Work, University of Manchester, Manchester, UK, Manchester, United Kingdom, 4Division of Podiatry and Clinical Sciences, University of Huddersfield, Huddersfield, UK, Huddersfield, United Kingdom, 5Photon Science Institute, School of Physics and Astronomy, University of Manchester, Manchester, UK, Manchester, United Kingdom, 6Centre for Imaging Sciences, Division of Informatics, Imaging & Data Sciences, University of Manchester, Manchester, UK, Manchester, United Kingdom, 7NIHR Manchester Musculoskeletal Biomedical Research Unit, Central Manchester NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, UK, Manchester, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Approximately 50% of patients with systemic sclerosis (SSc) will develop painful digital (finger) ulcers (DUs) at some point during their disease course. These lesions can be extremely disabling and are often refractory to treatment, requiring close monitoring of healing progression. Also, DUs are often the primary outcome measure in clinical trials of SSc-related digital vasculopathy. Our aims were to: (1) demonstrate the feasibility of patients with SSc taking smartphone photographs of their DUs, and (2) use software image analysis on collected images to track lesion area as a marker of wound status.

Methods: Patients with SSc and incident DUs were asked to photograph their lesion(s), using their own smartphone, once per day for a maximum period of 35 days. Patients received normal clinical wound care for the duration of the study, which in most cases was patient self-management. Image length scales were initially calibrated using a fixed (non-varying) object in each image sequence, allowing relative
length/area tracking throughout a sequence. Using digital planimetry software (developed and successfully tested in previous work on digital ulcer photographs [1]), lesion area was measured by fitting an elliptical shape to the wound image by a single observer. Areas from each image were then normalised to the area measured first in the time sequence.

**Results:** Image sequences describing 7 lesions were collected in-person at the end of the study period from 4 patients. The 7 image sequences cover median [range] duration of 29 [13-35] days. The relative area time course for each lesion is shown in Figure 1. At sequence end, relative lesion areas had, on average, reduced to 56% of the area measured on day 1, with 6 out of 7 lesions reducing in size over the time course.

**Conclusion:** We have demonstrated the feasibility of patients with SSc collecting images of digital ulcers using smartphone cameras. Images collected are of sufficient quality to allow software monitoring of wound progression (healing or worsening). Further work to build a smartphone app for lesion monitoring (for use in both clinical practice and as an outcome measure in clinical trials) is now required.

**References**


---

**Figure 1.** Normalised lesion area time course plots (blue squares) for each of seven digital ulcers. Red dashed line equals 100% relative area, i.e. equal to the value at the start of the sequence. Only lesion 3 showed an increase in area over the course of the study.

**Disclosure:** G. Dinsdale, None; T. Moore, None; J. Manning, None; A. Murray, None; R. Atkinson, None; K. Ousey, None; M. Dickinson, None; C. Taylor, None; A. L. Herrick, None.


**Abstract Number:** 257

**The Use of Positron Emission Tomography (PET)-Scan for the Quantitative Assessment of Interstitial Lung Disease in Systemic Sclerosis**

Daphne Peelen¹, Ben Zwezerijnen², Esther Nossem³, Lilian Meijboom¹, Otto Hoekstra³, Conny van der Laken⁴ and Alexandre Voskuyl⁴,

¹VUmc, Amsterdam, Netherlands, ²Nuclear Medicine, VUmc, Amsterdam, Netherlands, ³Department of Radiology & Nuclear Medicine, VU University Medical Center, Amsterdam, The Netherlands, ⁴Department of Rheumatology, Amsterdam Rheumatology and Immunology Center – Location VU University Medical Center, Amsterdam, The Netherlands

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Imaging of Rheumatic Diseases Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Interstitial lung disease (ILD) in systemic sclerosis is treated by immunosuppressive drugs (e.g. cyclophosphamide), aimed at reduction of inflammatory response. Differentiation between inflamed and non-inflamed fibrotic tissue might help to develop treatment stratification, with the aim of improving the prognosis of (subgroups of) SSc-ILD patients. ¹⁸F-Fluoro-Dexoxyglucose Positron
Emission Tomography ($^{18}$F-FDG PET) scan might be a promising tool to detect inflamed lung areas, as formerly shown in a semi-quantitative setting.[1, 2] This study aims to investigate the potential role of $^{18}$F-FDG PET–scan for the quantitative assessment of metabolically active SSc related ILD.

**Methods:** $^{18}$F-FDG PET–scans of 22 patients with systemic auto-immune disease, including 9 with SSc, 9 with systemic lupus erythematosus (SLE) and 4 with primary Sjögren’s syndrome (pSS), were retrospectively analyzed. FDG-uptake was quantitatively measured within 2cm-sized Regions of Interest (ROIs) at apical, medial and basal lung levels. A total of 22 ROI’s were drawn in each patient. SUVmean values of all ROI’s were corrected by the medial SUVmean bloodpool value. Subsequently, the average of 6 posterior basal SUVmean values was divided by the average of 6 posterior apical SUVmean values (basal/apical ratio). High Resolution Computed tomography (HRCT)-scans and Pulmonary Function Tests (PFT) were examined to confirm the diagnosis of ILD and to specify the pattern of fibrosis.

**Results:** Mean age of patients was 69.4 (SSc-ILD), 62.5 (SSc without ILD), 38.9 (SLE) and, 49.3 (pSS). In SSc patients, the mean disease duration was 5.0 (SSc-ILD) and 4.4 (SSc without ILD) years. Diffuse cutaneous sclerosis was present in 2 SSc-ILD and 1 SSc without ILD patients, while other SSc patients were diagnosed with limited cutaneous SSc. ILD was present in 5 out of 9 SSc patients as confirmed by HRCT and PFT. ILD was active in 3 out of 5 SSc-ILD patients. Posterior basal/apical SUVmean ratios of SSc-ILD patients were significantly increased compared to SSc patients without ILD (p=0.016), and compared to SLE and pSS patients without ILD (p=0.001 and p=0.016, respectively), which is shown in Figure 1.

**Conclusion:** Our findings demonstrate that $^{18}$F-FDG PET is potentially useful for the quantitative assessment of active ILD lesions in SSc patients. The technique may therefore provide opportunities to select the patients with inflammatory regions in ILD that are most likely to respond to immunosuppression.

**References:**


---

**Disclosure:** D. Peelen, None; B. Zwezerijnen, None; E. Nossent, None; L. Meijboom, None; O. Hoekstra, None; C. van der Laken, None; A. Voskuyl, None.

Prevalence of Echocardiographic Findings in Connective Tissue Diseases – a Retrospective Cohort Study

Valentin S. Schäfer1, Katharina Weiss2, Andreas Krause2 and Wolfgang A. Schmidt3, 1Immanuel Krankenhaus Berlin, Medical Center for Rheumatology Berlin-Buch, Berlin, Germany, 2Medical Centre for Rheumatology Berlin-Buch, Immanuel Krankenhaus Berlin, Berlin, Germany, 3Medical Center for Rheumatology and Clinical Immunology Berlin-Buch, Immanuel Krankenhaus Berlin, Berlin, Germany

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Echocardiography is frequently performed in patients with connective tissue diseases (CTD), mostly to evaluate cardiac involvement or development of pulmonary arterial hypertension (paH). Despite the application as part of routine clinical follow-up, there is incomplete data for the range and frequency of findings in different CTD.

Methods: We included all consecutive patients from a tertiary rheumatological referral center with CTD diagnosis and echocardiographic examination between January 1st 2006 and December 31st 2015 by retrospective chart review. For each echocardiographic finding, the proportion of patients per diagnosis with a pathological result in at least one examination was calculated. Further, each finding’s frequency in patients with and without previously documented inflammatory cardiac involvement was compared. For patients with more than one visit, we recorded how often findings developed or resolved over time.

Results: 1004 patients with different CTD and a total of 1660 performed echocardiographies were identified. Table 1 displays the frequency of findings in the whole cohort and for each CTD, respectively. The most common findings were mitral, aortic and tricuspid regurgitation, aortic valve sclerosis, left ventricular dysfunction, and left atrial dilatation. Table 2 shows which findings were significantly more common in patients with a history of inflammatory cardiac involvement (n=109). 314 patients had consecutive examinations; medium interval between first and last examination was 40 months (SD: 28, range: 0.9-115). Development and regression of findings during follow-up are given in table 3. Mitral (24%) or tricuspid regurgitation (21%), aortic valve sclerosis (18%) and left ventricular dysfunction (20%) most commonly developed.

Conclusion: This study is the first to report echocardiographic findings in a large cohort of different CTD. Abnormal findings are common in all disease entities. Some pathological findings are more common in patients having suffered from cardiac involvement, these seem to be disease-related. In follow-up, a change of findings was frequently observed. These results support the role of echocardiography for routine examination and in follow-up in patients with CTD.
Table 1: Frequency of echocardiographic findings in patients with CTDs

<table>
<thead>
<tr>
<th>CTD</th>
<th>All patients</th>
<th>ELS Primary Secondary</th>
<th>DMS Limited With/without</th>
<th>PM</th>
<th>SCD/MCTD/DM/MCTD</th>
<th>UCTD/MCTD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>100</td>
<td>190</td>
<td>200</td>
<td>115</td>
<td>84</td>
<td>145</td>
</tr>
<tr>
<td>Valvular regurgitation</td>
<td>50%</td>
<td>49%</td>
<td>54%</td>
<td>45%</td>
<td>51%</td>
<td>31%</td>
</tr>
<tr>
<td>Mitral</td>
<td>30%</td>
<td>33%</td>
<td>44%</td>
<td>50%</td>
<td>43%</td>
<td>33%</td>
</tr>
<tr>
<td>Aortic</td>
<td>17%</td>
<td>13%</td>
<td>26%</td>
<td>12%</td>
<td>15%</td>
<td>12%</td>
</tr>
<tr>
<td>Tricuspid</td>
<td>12%</td>
<td>12%</td>
<td>21%</td>
<td>12%</td>
<td>15%</td>
<td>12%</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>6%</td>
<td>6%</td>
<td>11%</td>
<td>6%</td>
<td>9%</td>
<td>6%</td>
</tr>
<tr>
<td>Valvular stenosis</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>Mitral</td>
<td>15%</td>
<td>15%</td>
<td>15%</td>
<td>15%</td>
<td>15%</td>
<td>15%</td>
</tr>
<tr>
<td>Aortic</td>
<td>20%</td>
<td>20%</td>
<td>20%</td>
<td>20%</td>
<td>20%</td>
<td>20%</td>
</tr>
<tr>
<td>Tricuspid</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Valvular disorders</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>Mitral</td>
<td>1%</td>
<td>1%</td>
<td>1%</td>
<td>1%</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Aortic</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>Tricuspid</td>
<td>1%</td>
<td>1%</td>
<td>1%</td>
<td>1%</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Conduction and motion</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>LV dyssynchrony</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>EF reduced (LVEF&lt;50%)</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>EF reduced (LVEF&lt;40%)</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>EF reduced (LVEF&lt;30%)</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>Global LV systolic function</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>Global LV systolic function (EF&lt;50%)</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>Other findings</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>Signs of pHT</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
</tr>
</tbody>
</table>

PM: Polymyocytitis, DM: Dermatomyositis, UCTD: Undifferentiated connective tissue disease, MCTD: Mixed connective tissue disease, pHT: Pulmonary arterial hypertension, EF: Ejection fraction

Table 2: Most frequent findings in patients with history of cardiac involvement

<table>
<thead>
<tr>
<th>Finding</th>
<th>Frequency in patients without history of cardiac involvement (n=896)</th>
<th>Frequency in patients with history of cardiac involvement (n=109)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valvular insufficiency</td>
<td>33.2%</td>
<td>45.0%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Tricuspid</td>
<td>n=206</td>
<td>n=49</td>
<td></td>
</tr>
<tr>
<td>Pulmonary</td>
<td>6.3%</td>
<td>15.6%</td>
<td>.001</td>
</tr>
<tr>
<td>Contraction</td>
<td>0.4%</td>
<td>3.7%</td>
<td>.007</td>
</tr>
<tr>
<td>Global hypokinesis</td>
<td>n=4</td>
<td>n=4</td>
<td></td>
</tr>
<tr>
<td>Cavity dilation</td>
<td>5.3%</td>
<td>11.0%</td>
<td>.025</td>
</tr>
<tr>
<td>LV dilation</td>
<td>n=45</td>
<td>n=12</td>
<td></td>
</tr>
<tr>
<td>LA dilation</td>
<td>17.5%</td>
<td>33.9%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>RA dilation</td>
<td>n=156</td>
<td>n=37</td>
<td></td>
</tr>
<tr>
<td>RV dilation</td>
<td>1.7%</td>
<td>15.6%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Other findings</td>
<td>Signs of pHT</td>
<td>5.3%</td>
<td>28.4%</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>6.5%</td>
<td>43.1%</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Disclosure: V. S. Schäfer, None; K. Weiss, None; A. Krause, None; W. A. Schmidt, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/prevalence-of-echocardiographic-findings-in-connective-tissue-diseases-a-retrospective-cohort-study

Abstract Number: 259

Imaging for Diagnosis, Monitoring and Outcome Prediction of Large Vessel Vasculitis: A Systematic Review of the Literature and Meta-Analysis Informing the EULAR Recommendations

Christina Duftner,1 Christian Dejaco2, Alexandre Sepriano3, Louise Falzon4, Wolfgang A. Schmidt5 and Sofia Ramiro6, 1Department of Internal Medicine, Clinical Division of Internal Medicine II, Medical University Innsbruck, Innsbruck, Austria, 2Rheumatology, Hospital of Bruneck, Bruneck, Italy, 3Rheumatology, Leiden University Medical Center, Leiden, Netherlands, 4Center for Behavioral Cardiovascular Health, Columbia University Medical Center, New York, NY, 5Medical Center for Rheumatology and Clinical Immunology Berlin-Buch, Immanuel Krankenhaus Berlin, Berlin, Germany, 6Rheumatology, Department of Rheumatology, LUMC, Leiden, Netherlands

First publication: September 18, 2017
Background/Purpose: Modern imaging techniques including ultrasound (US), magnetic resonance imaging (MRI), computed tomography (CT) and $^{18}$F-FDG positron emission tomography (PET) are increasingly studied in large vessel vasculitis (LVV); however, their role in daily clinical practice remains elusive so far. The aim of this study was to perform a systematic literature review (SLR) to inform the EULAR recommendations for imaging in LVV on the role of imaging methods on (1) diagnosis, (2) disease monitoring, (3) outcome prediction and (4) technical aspects in LVV.

Methods: A systematic literature search was conducted in the MEDLINE, EMBASE and Cochrane Library databases (untill 10th March 2017) without language restriction. Full research articles of prospective studies enrolling >20 patients and investigating the index test (US, MRI, CT, PET) in patients with suspicion of (diagnostic studies) and/or established (studies on monitoring or prediction) primary LVV were selected. The risk of bias for diagnostic accuracy and prognostic studies were evaluated by the QUADAS2 and QUIPS tools, respectively. Meta-analysis was conducted, whenever possible, to obtain pooled estimates for sensitivity, specificity, positive and negative likelihood ratios, by fitting random effects models.

Results: Forty-four studies were included [27 diagnosis giant cell arteritis (GCA), 6 outcome prediction GCA, 15 monitoring disease activity GCA, 2 diagnosis Takayasu arteritis (TAK), 2 monitoring disease activity TAK with some studies addressing more than one index test/key objective]. The “halo” sign at temporal arteries, as identified by US (8 studies, 605 patients), yielded a pooled sensitivity of 77% (95% CI: 62-87%) and a pooled specificity of 96% (95% CI: 85-99%) as compared to clinical diagnosis of GCA. MRI of extra-cranial arteries was found to have a pooled sensitivity of 73% (95% CI: 57-85) and a pooled specificity of 88% (95% CI: 81-92), when clinical diagnosis (6 studies, 509 patients) was used as gold standard. For both, US and MRI, similar diagnostic performances were observed when temporal artery biopsy was used as reference standard instead of clinical diagnosis. Only 2 studies (93 patients) addressed the diagnostic accuracy of PET in GCA reporting sensitivities of 67-77% and specificities of 66-100%. Studies addressing the role of imaging for outcome prediction, monitoring disease activity and technical aspects were very heterogenous. For TAK, 1 MRI (30 patients) and CT angiography study (25 patients) was identified revealing both a sensitivity of 98% and a specificity of 100% in comparison to conventional angiography. No study on isolated aortitis was identified.

Conclusion: The SLR confirms the good performance of US and MRI for the diagnosis of cranial GCA. Data on outcome prediction, monitoring and technical aspects of GCA, as well as imaging studies in TAK are limited.

Disclosure: C. Duftner, None; C. Dejaco, None; A. Sepriano, None; L. Falzon, None; W. A. Schmidt, None; S. Ramiro, None.

Use of Positron Emission Tomography for the Diagnosis of Aortitis. a Study of 170 Patients from a Single Center

Lucia C. Domínguez-Casas1, Javier Loricer1, Diana Prieto Peña1, Isabel Martínez-Rodriguez2, Jose Ignacio Banzo2, Monica Calderón Goercke1, Vanesa Calvo-Rio1, Nuria Vegas-Revenga1, MC Gonzalez-Vela3, Jesus Gonzalez- Vela4, José Luis Martín-Varillas1, Belén Atienza-Mateo1, Jose L. Hernández2, Miguel Angel González-Gay1 and Ricardo Blanco1, 1Rheumatology, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, 2Nuclear Medicine, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, 3Pathology Anatomy, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, 4Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, 5Internal Medicine, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain

First publication: September 18, 2017
Background/Purpose:

Aortitis is the inflammation of the aortic wall. This entity is often under-recognised because most of its manifestations are non-specific. PET/CT scan plays an important role in the diagnosis and management of aortitis; however this technique is expensive.

Our aim was to compare the baseline characteristics of patients with a suspicion of aortitis and positive results on PET/CT scan and those with a negative result in order to search for predictive factors that improve the clinical probability of diagnosis aortitis by this imaging technique.

Methods:

Retrospective study on 170 patients and PET/CT scans ordered by suspicion of aortitis from a referral center from January 2010 to December 2016. According to a pre-specified protocol, the baseline epidemiological and clinical variables of patients with positive and negative PET/CT scans results for aortitis were reviewed. Distributions of categorical variables were compared by the Pearson Chi² or Fisher exact test. Quantitative variables were analyzing using the Student t test or Mann-Whitney U test as appropriate.

Results:

In 170 patients, PET/CT scans were performed due to clinical suspicion of aortitis, being positive in 93 (54.7%) cases. Patients (113W/57M) had a mean age of 67.7±13.1 years (range, 20-90 years). One patient was excluded because missing clinical or laboratory data.

The underlying conditions at the moment of ordering the PET/CT scan were: giant cell arteritis (GCA) (n=28), spondiloarthropaties (n=7), connectivopaties (n=6), Takayasu arteritis (n=3), ulcerative colitis (n=3), other condition (n=11) The remaining 111 patients had not have any underlying condition suggestive of aortitis.

Characteristics of patients with positive and negative PET/CT scan were shown in the Table. Patients with GCA had a higher percentage of positive PET/CT scans, whereas were negative more frequently in patients who did not have any condition suggestive of underlying aortitis. Only inflammatory low back pain and polymyalgic syndrome were significantly more frequent in patients with positive PET/CT scans.

Conclusion:

In this study, we have found the presence of inflammatory low back pain and polymyalgic syndrome, especially in GCA patients, may have clinical relevance in ordering a PET/CT scan when aortitis was suspected.

TABLE
### Positive PET vs Negative PET

<table>
<thead>
<tr>
<th>Variable</th>
<th>Positive PET n= 92</th>
<th>Negative PET n= 77</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean±SD</td>
<td>67.4±11.1</td>
<td>68.1±15.2</td>
<td>0.73</td>
</tr>
<tr>
<td>Age ≥ 70 years, n (%)</td>
<td>39 (41.9)</td>
<td>41 (53.2)</td>
<td>0.14</td>
</tr>
<tr>
<td>Sex (women), n (%)</td>
<td>62 (67.4)</td>
<td>54 (70.1)</td>
<td>0.63</td>
</tr>
</tbody>
</table>

#### Underlying condition
- **Giant cell arteritis, n (%)**
  - Positive PET: 24 (26.1)
  - Negative PET: 4 (5.2)
  - p = 0.0002
- **Takayasu arteritis, n (%)**
  - Positive PET: 3 (3.3)
  - Negative PET: 0 (0)
  - p = 0.31
- **Ulcerative colitis, n (%)**
  - Positive PET: 2 (2.2)
  - Negative PET: 1 (1.3)
  - p = 0.87
- **Conectivopaties, n (%)**
  - Positive PET: 3 (3.3)
  - Negative PET: 3 (3.9)
  - p = 0.86
- **Spondiloarthropaties, n (%)**
  - Positive PET: 3 (3.3)
  - Negative PET: 4 (5.2)
  - p = 0.79
- **None, n (%)**
  - Positive PET: 54 (58.7)
  - Negative PET: 57 (74.0)
  - p = 0.03
- **Other, n (%)**
  - Positive PET: 3 (3.3)
  - Negative PET: 8 (10.4)
  - p = 0.11

#### Symptoms at the time of requesting PET
- **Constitutional syndrome, n (%)**
  - Positive PET: 30 (32.6)
  - Negative PET: 36 (46.8)
  - p = 0.06
- **Fever, n (%)**
  - Positive PET: 18 (19.6)
  - Negative PET: 15 (19.5)
  - p = 0.98
- **Inflammatory low back pain, n (%)**
  - Positive PET: 30 (32.6)
  - Negative PET: 14 (18.2)
  - p = 0.03
- **Diffuse lower limbs pain, n (%)**
  - Positive PET: 42 (45.7)
  - Negative PET: 28 (36.4)
  - p = 0.22
- **Atypical polymyalgia rheumatica, n (%)**
  - Positive PET: 30 (53.6)
  - Negative PET: 13 (38.2)
  - p = 0.15
- **Headache, n (%)**
  - Positive PET: 18 (19.6)
  - Negative PET: 9 (11.7)
  - p = 0.16
- **Polymialgic syndrome, n (%)**
  - Positive PET: 56 (60.9)
  - Negative PET: 34 (44.2)
  - p = 0.03

#### Laboratory markers at the time of requesting PET
- **Anaemia, n (%)**
  - Positive PET: 18 (20.2)
  - Negative PET: 22 (28.9)
  - p = 0.19
- **ESR (mm/1ªh), mean±SD**
  - Positive PET: 43.3±34.3
  - Negative PET: 43.5±31.1
  - p = 0.72
- **CRP (mg/dl), median [IQR]**
  - Positive PET: 0.9 [0.3-2.6]
  - Negative PET: 0.9 [0.3-2.5]
  - p = 0.54

#### Treatment at the time of requesting PET
- **Patients with corticosteroids, n (%)**
  - Positive PET: 48 (51.6)
  - Negative PET: 36 (46.8)
  - p = 0.48
- **Dosage of prednisone (mg), median [IQR]**
  - Positive PET: 10 [5-15]
  - Negative PET: 10 [7.5-15]
  - p = 0.80
- **Patients with traditional immunosuppressants, n (%)**
  - Positive PET: 11 (12.0)
  - Negative PET: 5 (6.5)
  - p = 0.21
Ultrasound CUT-Off in GIANT CELL Arteritis a Solution to Arteriosclerosis Pitfall in the Halo Sign

Eugenio De Miguel¹, Luis M Beltran², Irene Monjo², Francesco Deodati², Wolfgang A. Schmidt³ and Juan García-Puig², ¹Rheumatology, University Hospital La Paz, IdiPaz, Madrid, Spain, ²Internal Medicine, Hospital Universitario La Paz, MADRID, Spain, ³Immanuel Krankenhaus Berlin, Med Ctr for Rheumatology Berlin-Buch, Berlin, Germany

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: At the age of Giant Cell Arteritis (GCA) atherosclerosis is common. The ultrasonographic (US) appearance of athermanous plaque is usually easily differentiated from the hypoechoic halo of GCA. However, the US increase of the intima-media-thickness (IMT) in an atherosclerotic arteries may have a similar appearance as the halo sign (homogenous, hypoechoic wall thickening, well delineated towards the luminal side, visible in longitudinal and transverse planes). The new US high frequencies probes make possible not only to see the halo sign but also measure the increase of the intima-media-thickness (IMT), in this sense the aim of this study was to explore the better cut-off in the IMT of temporal arteries (TA) to minimise the number of false-positive GCA diagnosis caused by atherosclerosis.

Methods: Consecutive non selected patients, ≥50 years-old with high vascular risk according to European Guidelines on cardiovascular disease prevention, and without signs or symptoms of GCA, were included.

Ultrasonography of carotid artery: Carotid US examinations were performed on a Mylab Seven (Esaote Medical Systems, Italy) with a 4–13 MHz linear-array. The system employed dedicated software radiofrequency-tracking technology to obtain IMT (QIMT®).

Ultrasonography of temporal superficial artery: A color Doppler ultrasound (CDU) and grey scale measure of the IMT/halo sign in both TA and its branches was performed by a second experienced sonographer. A Mylab Twice equipment (Esaote, Geneve, Italy) was used, with a 22 MHz frequency for grey scale and a 12.5 MHz for CDU (color gain of 51, PRF of 2 kHz). The sonographer was blind to the clinical and carotid ultrasound IMT data.

Results: Forty patients were studied, 28 men (70%), with a mean age of 70.6 ± 6.9 years. Three patients were active smokers and 27 ex-smokers. Arterial hypertension was present in 39 (97.5%), dyslipidaemia in 34 (85%) and diabetes in 19 (47.5%). The mean erythrocyte sedimentation rate was 13.6 ± 11.0. Eighty carotids were studied, 50 had plaques and 30 did not with a IMT ranged from 0.528 to 1.480 mm. A increase in the carotid IMT is associated with an increase in the IMT of the TA with a weak Spearman correlation (parietal branches 0.282 p = 0.012 and frontal branches 0.228 p = 0.048). The table shows that an IMT > 0.30 mm (halo sign) was seen in at least 1 TA branch of 18 patients (45%) with 33 TA branches affected (20.6%). An IMT cut-off > 0.34 mm, was present in 4 patients (10 %). When at least two affected branches with this measure were required to make the US diagnosis (criteria recommended to improve specificity) only one patient (2.5%) produced a false-positive halo sign.
Conclusion: Carotid atherosclerosis increase the IMT in TA and is a potential cause of false-positive halo sign. We propose a cut-off of AT IMT > 0.34 mm in at least two branches to minimise the number of false positives in GCA diagnosis.

Disclosure: E. De Miguel, None; L. M. Beltran, None; I. Monjo, None; F. Deodati, None; W. A. Schmidt, Roche Pharmaceuticals, 8, Roche Pharmaceuticals, 5, Roche Pharmaceuticals, 2, GlaxoSmithKline, 2, GlaxoSmithKline, 5, Bristol-Myers Squibb, 5, Bristol-Myers Squibb, 8; J. García-Puig, None.

FDG PET/CT Visualization of Inflammation in Temporal and Maxillary Arteries in Treatment-Naive GCA Patients

Berit Dalsgaard Nielsen1,2, Ib Tønder Hansen3,4, Kresten Krarup Keller5, Philip Therkildsen6,7, Ellen-Margrete Hauge6,8 and Lars Christian Gormsen9, 1Rheumatology, Department of Rheumatology, Aarhus University Hospital, Århus C, Denmark, 2Clinical Medicine, Department of Clinical Medicine, Aarhus University Hospital, Århus N, Denmark, 3Clinical Medicine, Department of Clinical Medicine, Aarhus University Hospital, Århus C, Denmark, 4Department of Rheumatology, Aarhus University Hospital, Aarhus, Denmark, 5Rheumatology, Department of Rheumatology, Aarhus University Hospital, Aarhus, Denmark, 6Clinical medicine, Department of Clinical Medicine, Aarhus University Hospital, Århus N, Denmark, 7Department of Rheumatology, Aarhus University Hospital, Aarhus C, Denmark, 8Department of Rheumatology, Department of Rheumatology, Aarhus University Hospital, Aarhus, Denmark, 9Nuclear Medicine and PET Center, Department of Nuclear Medicine and PET Center, Aarhus University Hospital, Århus C, Denmark

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Fluorine-18-fluorodeoxyglucose (FDG) PET/CT is increasingly used to diagnose large vessel GCA (LV-GCA), but has previously been considered unable to reveal inflammation in temporal arteries due to limited spatial resolution. However, the arteritic pattern in GCA is heterogeneous and additionally may not always uniformly involve the entire vessel, rendering interpretation of the PET images difficult. An increased FDG uptake in branches of the external carotic artery, i.e. the temporal (TA) and maxillary arteries (MA), may therefore add to diagnostic specificity.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Carotid IMT</th>
<th>Right TA IMT</th>
<th>Right PA IMT</th>
<th>Left TA IMT</th>
<th>Left PA IMT</th>
<th>Number of Branches with Halo</th>
<th>Cut-off IMT &gt; 0.3mm</th>
<th>Cut-off IMT &gt; 0.34mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 4</td>
<td>1.185</td>
<td>0.37</td>
<td>0.31</td>
<td>0.31</td>
<td>0.31</td>
<td>4</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Patient 5</td>
<td>0.948</td>
<td>0.25</td>
<td>0.31</td>
<td>0.31</td>
<td>0.27</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patient 6</td>
<td>1.135</td>
<td>0.18</td>
<td>0.31</td>
<td>0.24</td>
<td>0.25</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patient 7</td>
<td>1.164</td>
<td>0.31</td>
<td>0.28</td>
<td>0.28</td>
<td>0.28</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patient 9</td>
<td>1.243</td>
<td>0.37</td>
<td>0.4</td>
<td>0.45</td>
<td>0.35</td>
<td>4</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Patient 10</td>
<td>1.196</td>
<td>0.28</td>
<td>0.28</td>
<td>0.34</td>
<td>0.28</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patient 11</td>
<td>1.21</td>
<td>0.31</td>
<td>0.25</td>
<td>0.28</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patient 12</td>
<td>1.165</td>
<td>0.29</td>
<td>0.28</td>
<td>0.28</td>
<td>0.21</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patient 14</td>
<td>1.37</td>
<td>0.29</td>
<td>0.22</td>
<td>0.31</td>
<td>0.31</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patient 16</td>
<td>1.039</td>
<td>0.25</td>
<td>0.28</td>
<td>0.23</td>
<td>0.35</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patient 17</td>
<td>1.027</td>
<td>0.28</td>
<td>0.52</td>
<td>0.57</td>
<td>0.34</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Patient 18</td>
<td>0.599</td>
<td>0.25</td>
<td>0.31</td>
<td>0.28</td>
<td>0.28</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patient 19</td>
<td>1.017</td>
<td>0.19</td>
<td>0.28</td>
<td>0.25</td>
<td>0.31</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patient 25</td>
<td>0.802</td>
<td>0.29</td>
<td>0.27</td>
<td>0.31</td>
<td>0.25</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patient 30</td>
<td>1.200</td>
<td>0.31</td>
<td>0.29</td>
<td>0.21</td>
<td>0.24</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patient 32</td>
<td>0.978</td>
<td>0.31</td>
<td>0.36</td>
<td>0.25</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Patient 35</td>
<td>0.766</td>
<td>0.23</td>
<td>0.28</td>
<td>0.33</td>
<td>0.29</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patient 37</td>
<td>1.048</td>
<td>0.34</td>
<td>0.33</td>
<td>0.27</td>
<td>0.31</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
Methods:

21 patients fulfilling the ACR criteria of GCA were identified from a LV-GCA cohort (table 1). Laboratory tests, temporal artery ultrasound (US) and FDG PET/CT (Siemens Biograph 64) were performed prior to treatment.

An experienced nuclear medicine physician performed blinded assessment of FDG uptake in TA and MA. FDG uptake was visually scored on a 4-point scale (a.m. Meller\textsuperscript{1}: 1; ≤ blood pool, 2; > blood pool, ≤ liver, 3; ≥ liver, 4; ≥ 2x liver), where score ≥2 was considered indicative of inflammation. In addition, mean and max standardized uptake values (SUV\textsubscript{mean}, SUV\textsubscript{max}; 20 hottest interconnected pixels) and target to background ratio (TBR=SUV\textsubscript{max}(artery)/SUV\textsubscript{mean}(venous blood)) were recorded for each vessel based on volumes of interest drawn on the PET images.

Correlations were calculated using Spearman’s test. Mann–Whitney U test or Student t test, when applicable, were used for quantitative data. Associations between two categorical variables were evaluated using Fisher’s exact test.

Results:

FDG uptake in cranial arteries was detectable in 20/21 patients; 12/21 TA and 20/21 MA. In 11 patients, at least one of the arteries was categorized with a Meller score≥2 indicating significant inflammation. SUVs and TBRs are shown in table 1. SUVs and TBR correlated with Meller scores.

In the 3 patients with negative TA US (n=2 biopsy positive) and in the 2 patients with negative TA biopsies (n=1 US positive), FDG uptake in TA and MA was either not detectable or with a Meller score of 1. Meller score in the TA correlated with the degree of inflammation (none, <transmural, transmural) in the TA biopsy (rho=0.64, p<0.01). Patients with a TA or MA Meller score≥2 were more likely to have severe cranial symptoms (p=0.02), jaw claudication (p<0.02), had a shorter disease duration prior to diagnosis (median 8 vs 17 weeks, p<0.02) and were younger (median 65 vs 69 years, p<0.01) than patients with Meller score<2. However, they did not differ in gender or CRP at time of diagnosis.

Conclusion:

Increased FDG uptake in the cranial arteries of GCA patients is frequent, correlated to histological inflammation and subjective symptoms and detectable by normal PET/CT systems. It may add to the diagnostic accuracy of 18F-FDG PET/CT in GCA and should not be overlooked by reading physicians.
Baseline characteristics of patients fulfilling ACR criteria for GCA

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. patients</td>
<td>21</td>
</tr>
<tr>
<td>Age, median (range)</td>
<td>68 (60-84)</td>
</tr>
<tr>
<td>Gender, females no.</td>
<td>13</td>
</tr>
<tr>
<td>CRP, mean (95% CI)</td>
<td>82 (65; 104)</td>
</tr>
<tr>
<td>Temporal artery biopsy positive, no</td>
<td>16/18</td>
</tr>
<tr>
<td>Temporal artery ultrasound positive</td>
<td>18/21</td>
</tr>
<tr>
<td>Temporal artery PET characteristics</td>
<td></td>
</tr>
<tr>
<td>$SUV_{\text{mean}}$</td>
<td>2.18 (1.69; 2.68)</td>
</tr>
<tr>
<td>$SUV_{\text{max}}$</td>
<td>3.10 (2.27; 3.94)</td>
</tr>
<tr>
<td>TBR</td>
<td>1.95 (1.47; 2.48)</td>
</tr>
<tr>
<td>Maxillary artery PET characteristics</td>
<td></td>
</tr>
<tr>
<td>$SUV_{\text{mean}}$</td>
<td>2.21 (1.77; 2.64)</td>
</tr>
<tr>
<td>$SUV_{\text{max}}$</td>
<td>2.86 (2.21; 3.71)</td>
</tr>
<tr>
<td>TBR</td>
<td>2.04 (1.49; 2.58)</td>
</tr>
</tbody>
</table>

Patients fulfilling ACR criteria for GCA were identified in a prospective cohort of 24 large-vessel GCA patients. Inclusion criteria in the cohort were: Age>50 years, CRP>15 or ESR>40, either cranial symptoms of GCA, abrupt new-onset of extremity claudication or weightloss>5kg or fever>38 for more than 3 weeks and PET proven large vessel involvement (FDG uptake higher than liver FDG uptake in aorta and/or supraaortic branches).

References

1. Stellingwerff MD et al. Medicine 2015

Quantitative Analysis of Vascular Calcification Using a Novel Semi-Automated Software

Shubhasree Banerjee1, Mohammadhadi Bagheri2, Veit Sandfort3, Ashkan Malayeri4, Mark Ahlman4, David A. Bluemke4, Jianhua Yao2 and Peter C. Grayson5, 1Fellowship and training branch, NIAMS/NIH, Bethesda, MD, 2Radiology and Imaging Sciences, NIH Clinical Center, Bethesda, MD, 3Clinical Center, Radiology and Imaging Sciences, NIH, Bethesda, MD, 4Radiology and Imaging Sciences, National Institutes of Health, Bethesda, MD, 5Research, National Institutes of Health, Bethesda, MD

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Calcification of the coronary arteries, aorta, and branch vessels can occur in both large vessel vasculitis (LVV) and atherosclerosis.
study objective was to determine 1) the location and amount of vascular calcification in LVV versus hyperlipidemia (HLD) and 2) risk factors associated with vascular calcification in LVV.

Methods:

Patients with giant cell arteritis (GCA), Takayasu’s arteritis (TAK), and HLD were recruited into an observational cohort. All subjects underwent computed tomography of the aorta and branch vessels. We developed a novel semi-automated software to compute vascular calcification in 14 specific arterial territories (ascending aorta, aortic arch, descending thoracic aorta, abdominal aorta, carotids, subclavians, innominate, iliacs, femorals and coronary arteries). Total amount of calcification throughout the large arteries was quantified by calculating a cumulative Agatston score. Multivariate linear regression analyses were performed in LVV to determine associations between total Agatston score and traditional or disease-specific risk factors. Traditional risk factors were age, gender, body mass index, smoking, statin use and hypertension. Disease-specific risk factors were disease duration, clinical activity status, glucocorticoid dose, inflammatory markers (ESR, CRP, fibrinogen) and vascular inflammation as measured by positron emission tomography (FDG-PET). Only variables with p<0.10 in univariate analyses were included in the multivariate models. Frequencies were compared by the chi-squared test. Agatston scores were compared by Kruskal-Wallis test with post-hoc Dunn’s test.

Results:

A total of 88 subjects, including GCA (n=29, median age=72, %female=79); TAK (n=22, median age=37, %female=73); and HLD (n=37, median age=66, %female=43), participated in the study. There were no differences in the location of vascular calcification in the aorta and branch vessels between LVV and HLD, except coronary artery calcification was more prevalent in HLD compared to both TAK and GCA (p<0.01). Total Agatston scores were higher in GCA (median 3260, range 25-18138) versus HLD (460.5, 19-17215) (p<0.01) but did not significantly differ between GCA and TAK (1944, 52-47520) (p=0.53). An Agatston score >1000, consistent with severe calcification burden, was observed in many patients with GCA (74%), TAK (56%), and HLD (42%). Factors associated with calcification in LVV are shown in the table.

Conclusion:

We have developed a novel software to quantify calcification in vascular territories. This software could be repurposed to calculate calcification burden in other regions of interest. Location of vascular calcification was found to be similar between LVV and HLD; however, the amount of calcification was higher in patients with LVV. Both traditional and disease-specific risk factors are associated with vascular calcification in LVV.

Table
<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariable</th>
<th></th>
<th>Multivariable</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimate</td>
<td>P Value</td>
<td>Estimate</td>
<td>P value</td>
</tr>
<tr>
<td>Age</td>
<td>0.06 (1.06)</td>
<td>0.01</td>
<td>0.14 (1.15)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Diagnosis (TAK vs GCA)</td>
<td>-0.96 (0.38)</td>
<td>0.30</td>
<td>4.02 (55.70)</td>
<td>0.03</td>
</tr>
<tr>
<td>Prednisone dose</td>
<td>0.05 (1.16)</td>
<td>0.08</td>
<td>0.05 (1.05)</td>
<td>0.04</td>
</tr>
<tr>
<td>Hypertensive Medication</td>
<td>2.43 (11.35)</td>
<td>&lt;0.01</td>
<td>1.16 (3.19)</td>
<td>0.19</td>
</tr>
<tr>
<td>Gender (Female vs Male)</td>
<td>0.85 (2.3)</td>
<td>0.04</td>
<td>0.12 (1.12)</td>
<td>0.90</td>
</tr>
<tr>
<td>C-reactive Protein</td>
<td>-0.03 (0.97)</td>
<td>0.11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FDG-PET interpretation</td>
<td>0.99 (2.69)</td>
<td>0.29</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statin Medication</td>
<td>1.49 (4.43)</td>
<td>0.17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment duration</td>
<td>0 (1)</td>
<td>0.53</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical Assessment</td>
<td>0.44 (1.55)</td>
<td>0.65</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease duration</td>
<td>0 (1)</td>
<td>0.74</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass index</td>
<td>0.02 (1.02)</td>
<td>0.77</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate</td>
<td>0.003 (1.0)</td>
<td>0.89</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Not included in multivariable model.

Disclosure: S. Banerjee, None; M. Bagheri, None; V. Sandfort, None; A. Malayeri, None; M. Ahlman, None; D. A. Bluemke, None; J. Yao, None; P. C. Grayson, None.


Abstract Number: 264

A Novel Method to Assess Subchondral Bone Formation Using Naf-PET in the Evaluation of Knee Osteoarthritis

Venkata S. Jonnakuti¹, William Y. Raynor¹, Elena G. Taratuta¹, Abass Alavi² and Joshua Baker³, ¹Radiology, University of Pennsylvania, Philadelphia, PA, ²Department of Radiology/Division of Nuclear Medicine, University of Pennsylvania, Philadelphia, PA, ³Rheumatology, University of Pennsylvania, Philadelphia, PA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM
Background/Purpose: Previous studies using $^{18}$F-sodium fluoride positron emission tomography (NaF-PET) have quantified the increase in bone formation associated with osteoarthritic (OA) abnormalities with the maximum standardized uptake value ($S_UV_{\text{max}}$) in user-defined regions of interest (ROIs). A limitation of this method of quantification is that it assumes that the voxel with the highest SUV within the ROI represents the overall activity of the affected tissue. To address this limitation, we developed a novel method of global joint analysis to assess regions of expected bone turnover in articulating joints using NaF-PET in a group of patients at high risk for OA.

Methods: The study population consisted of 18 patients with Rheumatoid Arthritis who underwent static NaF-PET 90 minutes after the intravenous administration of NaF tracer. The global knee activity was defined as the area-weighted average of the mean NaF tracer uptake within the ROI. These global assessments at the knee were subsequently adjusted for overall bone formation at a non-articular location by determining the ratio of tracer uptake at the knee over the uptake at the femoral neck. For comparison, the $S_UV_{\text{max}}$ for each ROI was calculated methods. Standard radiographs of the knee were also obtained from the medical record in 9 patients and scored by a radiologist using the Kellgren-Lawrence (K/L) grading system.

Results: The average $S_UV_{\text{mean}}$ score for the knees was 1.48 (SD = 0.68) with a range of 0.54 to 2.96. Patients with greater NaF uptake demonstrated greater deterioration of the medial and lateral intercondylar tubercles, as evidenced by the larger lesions in the corresponding NaF-PET/CT scans (Fig. 1). Greater NaF global joint activity was observed among individuals with higher K/L grading scores ($\rho = 0.69$, $p = 0.04$). K/L grading was also associated with $S_UV_{\text{max}}$ values ($\rho = 0.93$, $p = 0.0003$).

Conclusion: Both methods were strongly associated with K/L grading of knee OA. The potential advantage of the novel $S_UV_{\text{mean}}$ method is that it may be more sensitive at detecting changes in intra-ROI OA progression since new spatially distinct lesions with a lower SUV that develop within an ROI would not be detected by the $S_UV_{\text{max}}$ methodology. Furthermore, the adjustment for fluoride uptake in non-articular sites is likely important in order to adjust for age-related declines in overall bone turnover. Further study is needed to determine the utility of this methodology in longitudinal studies.

Disclosure: V. S. Jonnakuti, None; W. Y. Raynor, None; E. G. Taratuta, None; A. Alavi, None; J. Baker, None.


Abstract Number: 265

Reliability of an Omeract Semiquantitative Scoring System and Imaging Atlas for the Assessment of Cartilage in Hand Osteoarthritis

Alexander Mathiessen², Hilde B Hammer², Lene Terslev³, George A. W. Bruyn⁴, Maria Antonietta D'Agostino⁵, Emilio Filippucci⁶, Ida Kristin Haugen⁷, Marion Kortekaas⁸, Peter Mandl⁹, Ingrid Møller⁵, Esperanza Naredo¹¹, Ruth Wittoek¹², Annamaria Iagnocco¹³ and Karen Ellegaard¹⁴, ¹Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, ²Rheumatology, Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, ³Copenhagen University Hospital at Glostrup, Copenhagen, Denmark, ⁴Rheumatology, MC Groep, Loenga, Netherlands, ⁵Department of Rheumatology, Assistance publique-Hôpitaux de Paris Ambroise Paré Hospital, Boulogne-Billancourt,
SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Osteoarthritis (OA) is characterized by gradual loss of articular cartilage. Evaluation of cartilage in the small joints of the hands has shown that ultrasound may differentiate between normal and pathological joint cartilage, whereas semiquantitative scoring is not reliable. These studies have however assessed the dorsal aspects of the joint, in which osteophytes often limit the acoustic window.

The aim of the present study was to test the reliability of a semiquantitative scoring system for the assessment of palmar finger joint cartilage by ultrasound in a patient-based exercise of patients with hand OA.

Methods:

Six experienced sonographers participated in a patient-based reliability exercise. Bilateral proximal interphalangeal (PIP) joints of 12 patients with hand OA were assessed twice on the same day by all experts using ultrasound machines (GE Logiq E9) equipped with high-frequency transducers (18MHz) with presets calibrated for the appropriate assessment of cartilage. The palmar aspects of the joints were assessed in a transverse view with the fingers fully extended, and the participants had an imaging atlas available during the exercise (figure).

Intraclass correlation coefficient (ICC) values with 95% confidence intervals (CI) were calculated with average-measure for inter-reader and single-measure for intra-reader reliability. Reliability was defined as poor (<0.5), moderate (0.5–0.75), good (0.75–0.9) and excellent (>0.90).

Results:

A three-grade semiquantitative was applied: grade 0, normal cartilage (anechoic structure with visible margins of cartilage); grade 1, focal thinning of cartilage or loss of sharpness of at least one cartilage margin; grade 2, focal or complete loss of cartilage. In total 96 joints were assessed twice by every sonographer. The inter-reader reliability was excellent (ICC=0.90, 95% CI 0.77–0.97). Intra-reader reproducibility was excellent (0.95, 0.83–0.98) to moderate (0.56, 0.02–0.85), with a mean ICC value of 0.74.

Conclusion:

A semiquantitative scoring system for the assessment of joint cartilage in palmar aspects of PIP joints by ultrasound showed excellent inter- and moderate to excellent intra-reader reliability in a patient-based reliability study. Our study demonstrates that ultrasound with a high-frequency probe is a reliable tool for evaluating cartilage and supports the use of a new semiquantitative scoring system for assessment of finger cartilage in hand OA patients.

Figure

Disclosure: A. Mathiessen, None; H. B. Hammer, None; L. Terslev, None; G. A. W. Bruyn, None; M. A. D'Agostino, None; E.

Mario Giulini¹, Hasan Acar², Ralph Brinks³, Matthias Schneider², Benedikt Ostendorf⁴, Oliver Sander⁵ and Philipp Sewerin⁶. ¹Department for Rheumatology, Heinrich-Heine-University, Duesseldorf, Germany, ²Policlinic for Rheumatology & Hiller Research Centre for Rheumatology, Heinrich-Heine-University Duesseldorf, Duesseldorf, Germany, ³Department of Rheumatology & Hiller Research Unit, Heinrich-Heine University, Duesseldorf, Germany, ⁴Department of Rheumatology, Univ. Duesseldorf, Düsseldorf, Germany, ⁵Department of Rheumatology & Hiller Research Unit, Heinrich-Heine-University, Duesseldorf, Germany, ⁶Department and Hiller-Research-Unit for Rheumatology, Heinrich-Heine University, Düsseldorf, Germany

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The estimated prevalence of hand osteoarthritis (HOA) varies severely according to the selection of different diagnostic modalities, items of interest and subject samples. In most studies conventional radiography (CR) was used in this matter. Recently ultrasound (US) was considered reliable and reproducible, and even more sensitive in detecting HOA signs such as osteophytes. We assumed that the prevalence of HOA detected by US was higher as described in previous studies. The objectives of this study were to investigate the prevalence and precise pattern of HOA in a working population by US.

Methods: The study included 427 participants (15.7% women, 84.3% men, mean age 53.5 years). A total of 11,840 images were scored for synovitis 0-3, synovitis mm, erosions 0-3, osteophytes 0-3, joint space mm and cartilage thickness mm. US assessment was provided for both hands, scanning 26 finger joints of each participant (CMC 1, MCP 2-5, PIP 2-5 and DIP 2-5) using an Esaote Mylab 25Gold unit with an 18 MHz linear transducer. Gray-scale US was performed on the palmar side with all joints in neutral position. Static images were stored and evaluated afterwards using Esaote Mylab-Desk software. HOA was defined as present if one or more joints of the participant showed osteophytes.

Results: The overall prevalence for HOA was nearly 100%. Only one participant had no osteophytes. There is strong evidence to suggest that the number of osteophytes increase with age (p<0.001). With every additional year, a mean increase of 0.18 (standard error 0.03) osteophytes has been observed. We found no evidence for an association of the number of osteophytes with sex (p = 0.4, after adjustment of age p = 0.9). The prevalence rates of osteophytes in the following joints of the right hand were: 8.5% MCP 5, 38.2% PIP 5, 56.8% DIP 5, 18.1% MCP 4, 51.4% PIP 4, 65.6% DIP 4, 28.3% MCP 3, 58.7% PIP 3, 67.4% DIP 3, 19.8% MCP 2, 48.5% PIP 2, 66.7% DIP 2 and 37.5% CMC 1. The prevalence rates of osteophytes in the following joints of the left hand were: 7.3% MCP 5, 34% PIP 5, 47.5% DIP 5, 12.3% MCP 4, 51.5% PIP 4, 56.2% DIP 4, 19.7% MCP 3, 53.2% PIP 3, 67.3% DIP 3, 14.6% MCP 2, 45.8% PIP 2, 59.6% DIP 2 and 40.1% CMC 1. Overall, DIP 3 on the right-hand side was the most frequently affected joint, followed by DIP 3 on the left-hand side, then right-hand DIP 2 and DIP 4, then left-hand DIP 2.

Conclusion: US detected HOA shows a higher prevalence when compared to studies using CR. This supports prior studies emphasizing that US is more sensitive than CR in detecting HOA signs such as osteophytes. Nearly all participants showed HOA signs and on average more than 15% of the MCP joints were affected which could possibly be misinterpreted in the context of accompanying inflammatory joint diseases. Regarding that, HOA is an underestimated problem in sonographic assessments and has to be more carefully respected when interpreting US images of hand and finger joints.

Disclosure: M. Giulini, None; H. Acar, None; R. Brinks, None; M. Schneider, None; B. Ostendorf, None; O. Sander, None; P. Sewerin, None.
Musculoskeletal Ultrasound As a Diagnostic Tool for Eosinophilic Fasciitis and Correlation with MRI Findings

Florentina Berianu, Neha Narula and Andy Abril, 1Rheumatology, Mayo Clinic Florida, Jacksonville, FL, 2Division of Rheumatology, Mayo Clinic, Jacksonville, FL
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Imaging of Rheumatic Diseases Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Eosinophilic fasciitis (EF) presents with pain and induration of the skin. Currently the clinical diagnosis is based on typical physical findings along with MRI enhancement of the fascia, and the diagnosis is confirmed by documenting fascial thickening and inflammation on tissue histology, including eosinophilic infiltrates. A recent case report has suggested fascia thickness can be measured with use of MSK ultrasound. Changes in compressibility of subcutaneous tissue using a high-frequency probe have been shown to help distinguish it from scleroderma patients. Objective: To describe a cohort of 7 patients with MSK US finding supporting the diagnosis of eosinophilic fasciitis with corresponding MRIs findings compared with normal controls.

Methods: 7 patients with suspected EF seen in our rheumatology clinic underwent MSK US of upper or lower extremities that exhibited findings of induration suggestive of EF. An ultrasound was performed using a 12-18 MHZ linear array transducer to visualize muscle and fascia in the area of pain and induration. A measurement of fascial thickness was recorded in all patients. MSK US was also performed in 7 healthy controls. Patients subsequently underwent MRI of the same region. Full thickness skin to muscle biopsy to confirm the diagnosis was performed in 6 out of 7 cases (one patient refused biopsy). Initial labs with serum eosinophils were recorded. None of the patients had Raynaud’s or showed clinical or laboratory findings of scleroderma.

Results: 4 females and 3 males were included. Mean age: 43.5. Absolute eosinophil values ranged from 1051-4780/microL. The mean thickness of the fascia was 0.43 cm (ranges 0.21-0.7 cm) versus 0.14 cm in normal controls (ranges: 0.11-0. 19 cm). All patients had MRI with contrast with evidence of thickened and enhanced fascia of the same region. Diagnosis of EF was confirmed with tissue histology in all cases in which biopsy was performed.

Conclusion: MSK US may represent a quick, safe, inexpensive and reliable diagnostic method for patient with suspected EF. It can also help locate the best site for biopsy.

Disclosure: F. Berianu, None; N. Narula, None; A. Abril, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/musculoskeletal-ultrasound-as-a-diagnostic-tool-for-eosinophilic-fasciitis-and-correlation-with-mri-findings

Applications of Salivary Gland Ultrasonography in Sjögren Syndrome and Sicca Symptoms: A Single Center Experience

Yen-Po Tsao, Ming-Han Chen, Wei Sheng Chen, Chien Chih Lai and Chang Youh Tsai, 1National Yang-Ming University, Taipei, Taiwan, 2Division of Allergy-Immunology- Rheumatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, 3Division of Allergy-Immunology- Rheumatology, Department of Medicine, Division of Allergy-Immunology- Rheumatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, 4Faculty of Medicine, School of Medicine, National Yang-Ming University, Taipei, Taiwan, 5Department of medicine, division of allergy, immunology, rheumatology, Division of Allergy-Immunology-Rheumatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan
First publication: September 18, 2017

SESSION INFORMATION
Prevalence of Pneumococcal Vaccination in Rheumatologic Patients with Community Acquired Pneumonia. Biobadasar Registry

Gimena Gomez1, Alejandro Brigante Jr.2, Alejandro Benitez3, Osvaldo Cerda4, Soledad Retamozo5, Ignacio Javier Gandino6, Ana Quinteros7, Ida Exeni4, Belén Barrios8, Pablo Astesana9, Carolina Sanchez Andia4, María Victoria Collado10, Amelia Granel11, Ana Cappuccio6, Rosana Quintana12, Eduardo Mussano13, Andrea Smichowski2, Mercedes De La Sota14, Karin Kirmayr15, Edson Javier Velozo16, Maria Silvia Larroude17, Ana Bertoli18, Santiago Agueri19, Cristina Battagliotti20, Sidney Soares de Souza21, Emilia Cavillon9, Analía Bohr22, Oscar Luís Rillo2, Eugenia Bedoya23, Eduardo Kerzberg24, Boris Kisluk12, Ingrid Petkovic25, Dora Pereira26, Juan Carlos Barreira2, Luis Somma2, Ana Carolina Costi27, Belen Virasoro2, Fernando Melo28, Sergio Paira29, Luis Roa Perez2, Leandro Carlevaris Sr.30, Gustavo Casado4 and Maria Celina de La Vega4.

1Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 2Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 3Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 4Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 5Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 6Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 7Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 8Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 9Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 10Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 11Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 12Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 13Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 14Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 15Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 16Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 17Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 18Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 19Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 20Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 21Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 22Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 23Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 24Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 25Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 26Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 27Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 28Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 29Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, 30Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina.


Abstract Number:269
Disclosure: G. Gomez, None; A. Brigante Jr., None; A. Benítez, None; O. Cerda, None; S. Retamozo, None; I. J. Gandino, None; A. Quinteros, None; I. Exeni, None; B. Barrios, None; P. Astesana, None; C. Sanchez Andia, None; M. V. Collado, None; A. Granel, None; A. Cappuccio, None; R. Quintana, None; E. Mussano, None; A. Smichowski, None; M. De La Sota, None; K. Kirmayr, None; E. J. Velozo, None; M. S. Larroude, None; A. Bertoli, None; S. Aguero, None; C. Battagliotti, None; S. Soares de Souza, None; E. Cavillon, None;
HIV Infection and Avascular Necrosis in the Antiretroviral Era

Yasir Abdulqader¹, Muhsen Al-ani² and Konstantinos Parperis³, ¹Internal Medicine, Maricopa Integrated health system, Phoenix, AZ, ²Internal Medicine, Maricopa Integrated Health System and University of Arizona College of Medicine, Phoenix Campus, Phoenix, AZ, ³Rheumatology, Maricopa Integrated Health System and University of Arizona College of Medicine, Phoenix Campus, Phoenix, AZ

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Infection-related Rheumatic Disease Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Infection with the HIV has been associated with an increased risk of developing avascular necrosis (AVN), however there are only few studies in the US that analyzed the frequency and risk factors of the AVN in HIV patients on antiretroviral therapy (ART). The aim of this study was to determine the prevalence of AVN in well-controlled HIV-infected patients who were receiving antiretroviral treatment and evaluate potential risks factors including HIV medications.

Methods:
A retrospective review of our medical record database over a 6 year period was conducted using ICD-9 and ICD-10 codes. Three thousand patients with chronic HIV infection on ART that had more than 2 visits in the HIV clinic were identified. Individual electronic patient charts were reviewed and we identified patients diagnosed with AVN that was confirmed by magnetic resonance imaging studies. We collected data regarding patient’s demographic characteristics, co-morbidities, T-helper lymphocytes with CD4 cell surface marker count, HIV RNA viral load and antiretroviral regimen. Two hundred randomly selected HIV-infected patients on ART without a diagnosis of AVN were used as a control group. Group differences were statistically compared and presented using Mann-Whitney U and Fisher’s exact test.

Results:
Forty two out of 3000 HIV patients (1.4 %) with AVN were identified (mean age of 49.5 years, 87% male). The most commonly involved joint was the hip (80%, n=34), followed by the glenohumeral (7.5%, n=4), femoral condyle (4.7%, n=2) and ankle (4.7%, n=2). Associated co-morbidities in patients with AVN included hyperlipidemia (21%, n=9), hypertension (19%, n=8), COPD/asthma (12%,n=5), hepatitis C (12%,n=5). All the patients with COPD/asthma have been treated with corticosteroids. Ten patients underwent joint replacement (23%), 4 core decompression surgery (9%) and the rest non-operative management.

Compared with the 200 HIV control patients, the patients with AVN were older (mean age of 49.5 vs. 42.7 years; p<0.01), had a history of COPD treated with corticosteroids (p= 0.02) and had a longer duration of HIV infection (mean duration of 16.8 vs.10.3 years; p<0.01). Patients who developed AVN were more likely to be receiving integrase strand transfer inhibitors (66%) compare to those who never received integrase inhibitors (20%; p<0.01). No differences were found between AVN patients and controls with respect to CD4 cell counts or viral load.

Conclusion:
AVN remains one of the most frequent musculoskeletal complication in HIV patients. Potential risk factors associated with the development of AVN in HIV patients were older age, longer duration of HIV infection, history of COPD/asthma, corticosteroid use and the use of ART regimens containing integrase strand transfer inhibitors.

Disclosure: Y. Abdulqader, None; M. Al-ani, None; K. Parperis, None.
The Trend of Incidence Rate, Frequency and HLA Phenotype of Reactive Arthritis and Uveitis in Japanese Patients with Bladder Cancer Following Intravesical BCG Therapy: A 20-Year, Two-Center Retrospective Study

Yoshinori Taniguchi1, Satoshi Inotani2, Hirofumi Nishikawa2, Kosuke Inoue3, Taro Horino2, Takashi Karashima4, Yasuhiko Yoshinaga5 and Yoshio Terada3

1Endocrinology, Metabolism, Nephrology and Rheumatology, Kochi University, Kochi, Japan, 2Endocrinology, Metabolism, Nephrology and Rheumatology, Kochi Medical School, Nankoku, Japan, 3Kochi University, Nankoku, Japan, 4Urology, Kochi University, Nankoku, Japan, 5Kurashiki Medical Center, Kurashiki, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Infection-related Rheumatic Disease Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Intravesical instillation of Bacillus Calmette-Guerin (iBCG) is used as an effective immunotherapy of bladder cancer. However, it may have, as adverse event, a reactive arthritis (ReA) and the frequencies are known as about 0.5 to 1% in Western countries. Objective is to evaluate the trend of incidence rate, frequency and HLA phenotype of reactive arthritis (ReA), uveitis and other adverse events in Japanese patients with bladder cancer following iBCG therapy.

Methods: The clinical findings of Japanese patients who received iBCG (n = 555 [250 and 305 in Kochi Medical School Hospital and Kurashiki Medical Center, respectively]) for bladder cancer from March 1997 to February 2017 were retrospectively assessed, with specific attention to patients with ReA and uveitis. HLA phenotypes of patients with ReA were also looked. Moreover, iBCG-induced ReA diagnosed from 1997 to 2007 were compared with that from 2007 to 2017.

Results: Patients’ mean age was 72 ± 10 years and male/female ratio was 438/117. Fever, haematuria, and dysuria were presented in 91/555 (16.4%), 121/555 (21.8%), and 196/555 (35.3%), respectively of all enrolled patients. Of the 555 cases, ReA and uveitis were revealed in 11/555 (2.0%) and 4/555 (0.7%). The protocol of iBCG therapy was stable over the 20 years. Notably, HLA-B27, -B35, -B39 and -B51 positivity was more frequent in ReA patients (9.1%, 36.3%, 36.3% and 63.6%, respectively) (p<0.05) than in healthy subjects without ReA (0.3%, 8.3%, 4.0% and 9.1%, respectively). All 4 cases with uveitis had ReA, and showed positive HLA-B27 (25%), -B39 (50%) and –B51 (25%). Finally, the overall incidence of iBCG-ReA was not different between from 1997 to 2007 and 2007 to 2017.

Conclusion: The 2.0% iBCG-induced ReA frequency in Japanese patients exceeds that in Western countries, and its incidence has been stable over the last 20 years. HLA phenotype, especially HLA-B51 and -B39 alleles in addition to -B27, may be a risk factor in iBCG-induced ReA in Japanese patients.

Disclosure: Y. Taniguchi, None; S. Inotani, None; H. Nishikawa, None; K. Inoue, None; T. Horino, None; T. Karashima, None; Y. Yoshinaga, None; Y. Terada, None.

The Difference in the Clinical Characteristics between Cytomegalovirus Disease and Asymptomatic Cytomegalovirus Reactivation in Rheumatic Diseases

Shunya Kaneshita, Takashi Kida, Hidetake Nagahara, Yuko Kitagawa, Hideaki Sofue, Akiko Kasahara, Risa Sagawa, Takuya Inoue, Amane Nakabayashi, Yuji Kukida, Kazuki Fujikawa, Makoto Wada, Takahiro Seno, Masatake Kohno and Yutaka Kawaihito, Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan

First publication: September 18, 2017
Background/Purpose:

Cytomegalovirus (CMV) infection is one of the most common opportunistic infections in rheumatic diseases. A definite diagnosis of CMV infection usually requires histopathological confirmation, but performing biopsy is usually difficult in patients with poor general condition. The CMV antigenemia test, which detects the virus-specific protein pp65 antigen in polymorphonuclear leukocyte, is widely used to examine immunocompromised patients with rheumatic diseases and becomes positive (CMV reactivation) regardless of the symptoms. Anti-CMV agents should not be exclusively and needlessly used for asymptomatic patients with CMV reactivation to avoid side effects and social burden due to high medication cost. The aim of this study was to determine the difference in the clinical characteristics between patients with symptomatic and asymptomatic reactivation in rheumatic diseases.

Methods:

We retrospectively examined patients with CMV infection at our department, from January 2008 to December 2016. Patients positive for CMV reactivation were divided into two groups based on the symptoms they experienced, namely, CMV disease (with any symptoms) and asymptomatic CMV reactivation (without symptoms). The CMV antigenemia assay was used to assess the difference in the clinical characteristics between the two groups and their transitions 4 weeks prior to, and during, the first positive diagnosis.

Results:

In 80 patients with CMV reactivation, 31.2% were men and the mean age was 61.0±15.7 years. In the univariate analysis, patients with CMV disease were mostly men, with oral candidiasis, hypoalbuminemia, low lymphocyte count, and high titer CMV antigenemia count. In the multivariate analysis, the odds ratios (ORs) are 8.82 (95% confidence interval (CI) 1.64–47.30, P value=0.01), 0.81 (95% CI 0.69–0.95, P value<0.01), and 1.26 (95% CI 1.05–1.50, P value=0.01) for oral candidiasis, serum albumin, and CMV antigenemia count, respectively (Table 1). Moreover, the transition ORs 4 weeks prior to the first positive diagnosis using the CMV antigenemia are 1.96 (95% CI 1.09–3.54, P=0.025) and 2.02 (95% CI 1.07–3.8 P=0.03) for lymphocyte count and serum albumin, respectively (Table 2).

Conclusion:

Patients with CMV reactivation, who have a gradually decreasing serum albumin and lymphocyte count 4 weeks prior to the first positive diagnosis and who presented with hypoalbuminemia, oral candidiasis, and high CMV antigenemia count during the first positive diagnosis, are highly at risk for CMV disease in rheumatic diseases.

<table>
<thead>
<tr>
<th>Table 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>The difference in the clinical characteristics between CMV disease and asymptomatic CMV reactivation in Univariate and Multivariate analyses</td>
</tr>
<tr>
<td>CMV disease (n=27)</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>Age (yr)</td>
</tr>
<tr>
<td>Sex (male/female)</td>
</tr>
<tr>
<td>Oral candidiasis (%)</td>
</tr>
<tr>
<td>Serum albumin (g/l)</td>
</tr>
<tr>
<td>Serum CRP (mg/l)</td>
</tr>
<tr>
<td>Serum IgG (g/l)</td>
</tr>
<tr>
<td>Lymphocyte count (&lt;1000/mm³)</td>
</tr>
<tr>
<td>CMV antigenemia count (per 10⁶ PMN)</td>
</tr>
<tr>
<td>Prednisolone dose (mg/kg/day)</td>
</tr>
</tbody>
</table>

PMN=polymerorphonuclear leukocyte
Disclosure: S. Kaneshita, None; T. Kida, None; H. Nagahara, None; Y. Kitagawa, None; H. Sofue, None; A. Kasahara, None; R. Sagawa, None; T. Inoue, None; A. Nakabayashi, None; Y. Kukida, None; K. Fujioka, None; M. Wada, None; T. Seno, None; M. Kohno, None; Y. Kawahito, None.


Abstract Number: 273

The Risk Factors of Developing Adult T Cell Leukemia (ATL) in Human T Cell Leukemia Virus Type 1 (HTLV-1) Positive Patients with Rheumatoid Arthritis in Endemic Area, Japan; A Retrospective Cohort Study

Kunihiko Umekita1, Yayoi Hashiba2, Shunichi Miyauchi1, Kazuyoshi Kubo2, Toshikiko Hidaka2 and Akihiko Okayama1, 1Department of Rheumatology, Infectious Diseases and Laboratory Medicine, University of Miyazaki, Miyazaki, Japan, 2Institute of Rheumatology, Zenjinkai Shimin-no-Mori Hospital, Miyazaki, Japan
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Infection-related Rheumatic Disease Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Human T cell leukemia virus type 1 (HTLV-1) is the causative agent of adult T-cell leukemia (ATL). ATL is an aggressive T-cell malignancy caused by HTLV-1 infection and often occurs in HTLV-1-endemic areas, such as southwestern Japan, the Caribbean islands, Central and South America, Intertropical Africa, and Middle East. Recent study indicated that the estimated annual number of new HTLV-1 infection was 4,190 in nationwide blood donor surveillance in Japan. However, it is still not clear that the prevalence of HTLV-1 infection in patients with RA. Additionally, there are questions as to whether comorbidity of RA and its treatment in HTLV-1 carriers could increase the risk of developing ATL. The aim of this study is to clarify the prevalence of HTLV-1 infection in RA patients in HTLV-1 endemic area Miyazaki, Japan. In addition, we investigated the risk factors of developing ATL in HTLV-1 positive RA patients.

Methods: We established HTLV-1 positive RA cohort study in Miyazaki from 2012. Eight hundred sixty-one patients with RA were registered in this cohort until 2015. We evaluated blood levels in HTLV-1 proviral load (PVL) samples by real-time PCR, HTLV-1 antibody titer by particle agglutination assay, and the level of soluble IL-2 receptor (sIL-2R) by ELISA.

Results: The prevalence of HTLV-1 infection in RA patients was 6.0 % in this cohort. The age of HTLV-1 positive RA patients was higher than in HTLV-1 negative RA patients (p= 0.003). In the distribution of PVL, 20% of HTLV-1 positive RA patients showed highly PVL (> 4%), which was the known risk factor for ATL. The levels of sIL-2R in sera correlated to the levels of PVL, significantly (p=0.01).
Treatment of disease modifying anti-rheumatic drugs (DMARDs) including biologics were administrated in all patients. No effect to the levels of PVL and sIL-2R by the treatment with DMARDs was observed. A patient developed chronic type ATL, who were treated with MTX and anti-TNF inhibitor during 3-years observation periods (121 person-years) in this cohort.

**Conclusion:** The prevalence of HTLV-1 infection in RA patients in this cohort tended to be higher than that in nationwide surveillance in Japan. The incidence of ATL in HTLV-1 carriers was estimated to one per 1000 person-years. The incidence of ATL in HTLV-1 positive RA patients was higher than that in their study, although the sample size was small. A long-term follow-up of HTLV-1 positive RA patients is required to resolve whether the comorbidity of RA and its treatment increase the risk of developing ATL.

**Disclosure:** K. Umekita, None; Y. Hashiba, None; S. Miyachi, None; K. Kubo, None; T. Hidaka, None; A. Okayama, None.

**Abstract Number:** 274

**Frequency of Chronic Joint Pain Following Chikungunya Infection: A Colombian Cohort Study**

Aileen Chang1, Liliana Encinales2, Alexandra Porras3, Nelly Pacheco2, St. Patrick Reid4, Karen Martins5, Shamila Pacheco2, Eyda Bravo2, Marianda Navarno2, Alejandro Rico Mendoza3, Richard Amdur6, Priyanka Kamalapathy6, Gary S. Firestein7, Jeffrey Bethony6 and Gary Simon6

1Medicine, George Washington University, Washington, DC, 2Allied Research Society, Baranquilla, Colombia, 3Allied Research Society, Bogota, Colombia, 4University of Nebraska, Omaha, NE, 5United States Army Medical Research Institute of Infectious Disease, Frederick, MD, 6George Washington University, Washington, DC, 7Medicine, University of California San Diego, La Jolla, CA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Infection-related Rheumatic Disease Poster  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** To estimate the frequency of chronic joint pain after infection with chikungunya virus in a Latin American cohort.

**Methods:** A cross sectional follow-up of a prospective cohort of 500 Chikungunya patients from Atlántico Department, Colombia clinically diagnosed with chikungunya during the 2014-2015 Colombian epidemic. Baseline and follow-up (20-months) symptoms were evaluated in serologically confirmed cases.

**Results:** Among 500 patients enrolled, 485 cases were serologically confirmed with chikungunya. Patients were predominantly adults (age 49 ± 16 years), female, had a high school or less level of education and were of mestizo ethnicity. The most commonly affected joints were the small joints including the wrists, ankles and fingers. The initial joint pain lasted a median of 4 days (IQR 3-8). Sixteen percent of participants reported missing a median of 4 days (IQR 2-7) of school or work. After 20-months, one fourth of the participants had persistent joint pain. A multivariate analysis indicated that significant predictors of persistent joint pain included college graduate status, initial symptoms of headache or knee pain, missed work, normal activities affected, 4 or more days of initial symptoms, and 4 or more weeks of initial pain.

**Conclusion:** This is the first report to describe the frequency of chikungunya-related arthritis in the Americas after a 20-month follow-up. The high frequency of chronic disease highlights the importance of development of prevention and treatment interventions.

**Disclosure:** A. Chang, None; L. Encinales, None; A. Porras, None; N. Pacheco, None; S. P. Reid, None; K. Martins, None; S. Pacheco, None; E. Bravo, None; M. Navarro, None; A. Rico Mendoza, None; R. Amdur, None; P. Kamalapathy, None; G. S. Firestein, Janssen Pharmaceutica Product, L.P., 2; J. Bethony, None; G. Simon, None.

**Abstract Number:** 275

**Predictive Factors of Cytomegalovirus Infection in Patients with Connective Tissue**
Diseases Treated with Immunosuppressive Drugs

Yusuke Yoshida1, Hiroki Kohno2, Katsuhiro Oj3, Tadahiro Tokunaga3, Tatsuomi Kuranobu3, Takaki Nojima4, Shintaro Hirata3 and Eiji Sugiyama1,
1Department of Clinical Immunology and Rheumatology, Hiroshima University Hospital, Hiroshima, Japan, 2Hiroshima Prefectural Hospital, Hiroshima, Japan, 3Clinical Immunology and Rheumatology, Hiroshima University Hospital, Hiroshima, Japan, 4Clinical Immunology and Rheumatology, Graduate School of Medicine, Kyoto University, Kyoto, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Infection-related Rheumatic Disease Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Cytomegalovirus (CMV) infections occur frequently in immunocompromised patients. This disease will be fatal if proper treatment is not done. Therefore, in the treatment of connective tissue disease (CTDs), care should be taken while paying attention to the onset of cytomegalovirus infection. The purpose of this study is to clarify the predictors of CMV infection that developed in patients undergoing immunosuppressive treatment.

Methods: All CTD patients who were diagnosed as a CMV infection from January 2009 to March 2017 at our hospital were retrospectively reviewed. The diagnosis of CMV was made by clinical symptoms, radiological findings, the presence of CMV pp65 antigen in polymorphonuclear leukocyte (C7-HRP) and pathological findings of organ specimen. We compared the sequential changes in laboratory data between one month before diagnosis and at diagnosis. The differences in laboratory data between the survivors and non-survivors were also compared. Statistical analyses were performed using XLSTAT.

Results: A total of 20 patients were diagnosed with CMV infection (12 bone marrow suppression; 4 pneumonia; 2 enteritis; 1 genital ulcer; and 1 retinitis) and enrolled in this study. The mean age was 67.9 years old and 60% of patients was female. The CTDs of patients as follows: dermatomyositis (25%), adult-onset Still’s disease (15%), and microscopic polyangiitis (15%). All patients were positive for CMV pp65 (mean C7-HRP: 287.6 ± 510.0/50,000 WBC), who were treated with a moderate to high dose of glucocorticoids (mean prednisolone dose: 33.4 ± 15.9 mg/day). When compared laboratory data between one month before diagnosis and at diagnosis, reduction of leukocyte, lymphocytes, platelet counts and IgG levels were predictive for occurring CMV infection. Among them, lymphopenia was critical for distinguishing between survivors and non-survivors.

Conclusion: The decreased in the leukocyte, lymphocyte, platelet, and IgG levels are important predictive factors for CMV infection in CTDs. Among them, decreased lymphocytes counts is a critical predictive factor for life threatening condition.

Disclosure: Y. Yoshida, None; H. Kohno, None; K. Oi, None; T. Tokunaga, None; T. Kuranobu, None; T. Nojima, None; S. Hirata, None; E. Sugiyama, None.


Abstract Number: 276

Follow-up of Patients with Musculoskeletal Manifestations Related to Chikungunya Fever

Paula Murari-Nascimento1, Ana Beatriz Vargas-Santos2, Natalia Fortes1, Heruza Zoghi3, Otilia Santos3, Patricia Brasil3, Guilherme Calvet3, Rogério Valls3, Carlos Andrade3, Andre Siqueira3, Geraldo Castellar-Pinheiro2, Leticia Pereira1 and Rodrigo B. Chaves-Amorim4, 1State University of Rio de Janeiro, Rio de Janeiro, Brazil, 2Internal Medicine - Rheumatology, State University of Rio de Janeiro, Rio de Janeiro, Brazil, 3Evandro Chagas National Institute of Infectious Diseases, Oswaldo Cruz Foundation – FIOCRUZ, Rio de Janeiro, Brazil, 4Universidade do Estado do Rio de Janeiro - UERJ, Rio de Janeiro, Brazil

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Infection-related Rheumatic Disease Poster
Session Type: ACR Poster Session A
Background/Purpose:

Chikungunya fever (CHIK) has joint involvement as a striking characteristic, which may persist for months. This study aimed to better understand the clinical impact of this new disease, evaluating the patients of a reference center for infectious disease (Evandro Chagas National Institute of Infectious Diseases, Oswaldo Cruz Foundation – FIOCRUZ) in Brazil during the 2016 CHIK outbreak.

Methods:

From April 2016 to October 2016, patients who sought care at the FIOCRUZ’s Acute Febrile Disease Outpatient Clinic, with symptoms suggestive of CHIK (fever, musculoskeletal pain) were evaluated by a team of infectologists and rheumatologists through medical history, physical exam, clinical questionnaires and diagnostic lab tests. Patients were stratified by symptoms duration at first evaluation, classified as acute if symptoms present for ≤14 days and subacute/chronic if symptoms present for >14 days. After about 1 year from the initial visit, we contacted the patients by phone to obtain information about the current clinical status regarding joint pain, swelling and morning stiffness.

Results:

We evaluated 61 patients with suspected CHIK. Diagnosis was confirmed in 41 patients by serology or PCR; in 20 patients, lab results were not available. Demographic and clinical characteristics of patients with diagnostic confirmation were similar compared to those without lab results; thus, both groups were analyzed together. There were 36 women and 25 men; none had autoimmune disease. In 18 patients, extra-articular manifestations (bursitis, tenosynovitis and carpal tunnel syndrome) were described. Baseline characteristics are shown in Table.

At 1 year, we managed to contact 30 patients; 9 of them referred symptoms resolution and 11 presented partial improvement, while 10 patients reported pain level similar to the initial presentation. Most patients had peripheral involvement, mainly hands and feet. Pain was considered mild in 9 patients, moderate in 9 patients, and intense in 3 patients. Subjects who chronically persisted with similar symptoms had significantly higher mean HAQ-DI at baseline (HAQ-DI = 2.4, 95% confidence interval (CI) 2.0–2.8) than those who achieved partial improvement or symptoms resolution (HAQ-DI = 1.5, 95% CI 1.1–2.0, p=0.01).

Conclusion:

Our study showed that CHIK results in dramatic, and often chronic joint involvement, with severe pain, fatigue and functional disability. Furthermore, the baseline HAQ-DI may predict chronicity of symptoms, although our conclusions are limited by our sample size.

![Image](https://example.com/image1.png)

Table: Characteristics of patients with Chikungunya fever at first evaluation.

<table>
<thead>
<tr>
<th>Symptoms duration</th>
<th>Female, %</th>
<th>≥14 days</th>
<th>&gt;14 days</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=35</td>
<td>n=26</td>
<td>n=41</td>
<td></td>
</tr>
<tr>
<td>Age, years *</td>
<td>49.2 (23.7–67.1)</td>
<td>54.5 (24.0–70.3)</td>
<td>50.8 (23.6–70.3)</td>
<td></td>
</tr>
<tr>
<td>HAQ-DI*</td>
<td>1.8 (0–3)</td>
<td>2.0 (0–2.8)</td>
<td>1.8 (0–3)</td>
<td></td>
</tr>
<tr>
<td>Pain VAS*</td>
<td>70 (10–100)</td>
<td>75 (10–100)</td>
<td>70 (10–100)</td>
<td></td>
</tr>
<tr>
<td>Fatigue VAS*</td>
<td>60 (0–100)</td>
<td>70 (0–100)</td>
<td>70 (0–100)</td>
<td></td>
</tr>
<tr>
<td>MDGA VAS*</td>
<td>30 (10–70)</td>
<td>50 (0–80)</td>
<td>30 (0–80)</td>
<td></td>
</tr>
<tr>
<td>PGGA VAS*</td>
<td>60 (0–100)</td>
<td>80 (0–100)</td>
<td>70 (0–100)</td>
<td></td>
</tr>
<tr>
<td>Patient Global Health VAS *</td>
<td>60 (10–109)</td>
<td>70 (0–100)</td>
<td>60 (10–100)</td>
<td></td>
</tr>
<tr>
<td>Tender Joint Count (0-66)*</td>
<td>9 (0-58)</td>
<td>15 (0-18)</td>
<td>8 (0-58)</td>
<td></td>
</tr>
<tr>
<td>Swollen Joint Count (0-64)*</td>
<td>0 (0-3)</td>
<td>0 (0-15)</td>
<td>0 (0-15)</td>
<td></td>
</tr>
<tr>
<td>Morning Stiffness, minutes, %</td>
<td>46.6</td>
<td>15.2</td>
<td>28.3</td>
<td></td>
</tr>
<tr>
<td>≤30</td>
<td>44.4</td>
<td>30.2</td>
<td>36.7</td>
<td></td>
</tr>
<tr>
<td>&gt;30 – ≤60</td>
<td>7.4</td>
<td>33.3</td>
<td>20.0</td>
<td></td>
</tr>
<tr>
<td>&gt;60 – ≤120</td>
<td>7.4</td>
<td>15.2</td>
<td>6.7</td>
<td></td>
</tr>
<tr>
<td>&gt;120</td>
<td>0</td>
<td>6.1</td>
<td>8.3</td>
<td></td>
</tr>
</tbody>
</table>

*Median (range).

VAS (visual analog scale, 0-100mm); MDGA (medical global assessment of disease activity); PGGA (patient global assessment of disease activity).

Disclosure: P. Murari-Nascimento, None; A. B. Vargas-Santos, None; N. Fortes, None; H. Zogbi, None; O. Santos, None; P. Brasil, None; G. Calvet, None; R. Valls, None; C. Andrade, None; A. Siqueira, None; G. Castelan-Pinheiro, None; L. Pereira, None; R. B. Chaves-Amorim, None.


Abstract Number: 277

**Rheumatic Conditions Appearing De Novo after Infection with Chikungunya Virus in Venezuelan Patients**
Yurilis Fuentes-Silva1, Carlota Acosta2, Luisa Ortega3, Martin A Rodriguez4, Soham Al Snih5, Ivan Amaya6 and Irrama Maldonado3,

1Division of Rheumatology/Internal Medicine Department, 1Unidad de Reumatología adscrita al Centro Nacional de Enfermedades Reumáticas. Complejo Hospitalario Universitario Ruiz y Páez, Ciudad Bolívar, Venezuela (Bolivarian Republic of), 2Unidad de Reumatología adscrita al Centro Nacional de Enfermedades Reumáticas. Complejo Hospitalario Universitario Ruiz y Páez, Ciudad Bolívar, Venezuela (Bolivarian Republic of), 3Internal Medicine, 1Unidad de Reumatología adscrita al Centro Nacional de Enfermedades Reumáticas. Complejo Hospitalario Universitario Ruiz y Páez, Ciudad Bolívar, Venezuela (Bolivarian Republic of), 4Division of Rheumatology/Internal Medicine Department, Centro Nacional de Enfermedades Reumaticas. Hospital Universitario de Caracas, Caracas, Venezuela (Bolivarian Republic of), 5University of Texas Medical Branch, Galveston, TX, 6Facultad de Bioanálisis. Universidad de Oriente, Cuidad Bolivar, Venezuela (Bolivarian Republic of)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Infection-related Rheumatic Disease Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: It is well known that viral infections can trigger autoimmune rheumatic diseases. In 2014 there was an outbreak of Chikungunya (CHIK) virus infection in Venezuela. A majority of infected patients develop a flare of self-limited acute polyarthritis followed by complete remission. Some patients continue to experience subacute and chronic joint inflammatory symptoms. However, it is not well known how many of those patients evolve into a well-defined chronic rheumatic condition. The aim of this study was to examine how many patients with post-CHIK chronic inflammatory rheumatism (CHIK-CIR) evolve into a definite chronic rheumatic disease.

Methods: One hundred and sixty-eight patients seen during the period between 2,014 and 2,016 were included in this study. Post-CHIK CIR criteria were: 1. A triad of arthritis, fever and rash in presence of musculoskeletal manifestations (N=50, 29.76%) or 2. Musculoskeletal manifestations with or without the whole triad plus a positive IgM o IgG CHIK serology ELISA test (N=118, 70.23%). In both cases persistence of the symptoms for more than three months was required. The diagnosis for a definite rheumatic disease was done following the corresponding American College of Rheumatology (ACR) criteria. Statistical analysis was done by Chi-square and the Exact Fisher’s test. P-values of < 0.001 were considered statistically significant. All patients signed an informed consent.

Results: A positive CHIK serology test was tested and resulted positive in 70.23% of patients (IgM and IgG in 44 and 117 patients, respectively). Rheumatoid factor (RF) was positive in 24.13% and anti-citrullinated peptide antibodies (ACPA) in 25.66% of the patients. Of the total population (168 patients) with post-CHIK-CIR, 89.29% were female, mean age was 55.33 ± 12.72 years, and mean disease follow-up was 73.9±15.6 months. Forty patients (23.80%) had family history for autoimmunity. Thirty patients (17.85%) evolved into the following definite rheumatic diseases (P < 0.001 in each case). Other variables studied no related with development of de novo rheumatic disease were: IgM and IgG serology titers, presence of tenosynovitis and elevation of acute phase reagents.

Conclusion: CHIK virus infection can trigger a chronic autoimmune rheumatic disease, predominantly rheumatoid arthritis. Risk factors are the appearance of either RF or ACPA, or both.

Disclosure: Y. Fuentes-Silva, None; C. Acosta, None; L. Ortega, None; M. A. Rodriguez, None; S. Al Snih, None; I. Amaya, None; I. Maldonado, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/rheumatic-conditions-appearing-de-novo-after-infection-with-chikungunya-virus-in-venezuelan-patients

Abstract Number: 278

Corticosteroid Use, Biologic Therapy Switching, Smoking and Renal Failure Are Associated with Serious Infections in Rheumatoid Arthritis Patients Treated with Biologics: Data from Two Latin-American Registries

Maria de la Vega1, Gustavo Casado2, Gustavo Citerá2, Ieda Maria Magalhães Laurindo3, Georges Christopoulos3, Miguel Angel Descalzo4 and Roberto Ranza5, on behalf of BiobadaSar study group, Sociedad Argentina de Reumatología, Buenos aires, Argentina, 2on behalf of BiobadaSar study group, Sociedad Argentina de Reumatología, Buenos Aires, Argentina, 3on behalf of the BiobadaBrasil study group, Sociedade Brasileira de Reumatologia, São Paulo, Brazil, 4Unidad de Investigación Fundación Piel Sana Academia Española de
Background/Purpose: Infections are the most frequent and concerning serious adverse events related to rheumatoid arthritis (RA) treatment with biologic drugs (bDMARDs). Their safety profile might have substantial regional differences. In January 2009 started BiobadaAmerica, a common platform registry project open to all Latin American countries, focused on safety monitoring of bDMARDs. Purpose of this study is to present data on factors associated with serious infections (SI) in patients with RA exposed to bDMARDs in two Latin-American not mandatory registries.

Methods: Data from Argentinian Registry (BiobadaSar) and Brasilian Registry (BiobadaBrazil), both initiated in 2010, were downloaded on December 31, 2016, merged and analyzed. The same constant monitoring process guaranteed data quality. Patients with rheumatic diseases were included prospectively when started the first bDMARD. Time of exposure was set from start of the drug to the date of last administration or censorship. SI incidence rate was calculated per 1000 patient/years with 95%CI

Results: Data from 2591 RA patients were analyzed, for a total of 9300 p/y. Treatments were 3784, 64% aTNF (Adalimumab, Certolizumab, Etanercept, Golimumab, Infliximab), 36% non-aTNF (Abatacept, Rituximab, Tocilizumab) including Tofacitinib. Females 85%, at baseline mean age 53 (SD 12.8)yrs, mean disease duration 10(8.5)yrs, mean follow-up 2.7 (2) yrs. The overall incidence rate of SI was 30.54 (CI 27.18-34.30), Comparing patients with (191) and without (2400) SI, age, sex, disease duration, use of concomitants DMARD, presence of diabetes mellitus or pulmonary chronic disease and a positive history of previous câncer did not differ statistically. Exposition to more than one bDMARD (p<0.01), corticosteroid use (p=0.01), smoking (p=0.01) and presence of renal failure (p=0.03) were statistically associated with SI. Unexpectedly, basal DAS28 was higher in patients without SI (p=0.03).

Conclusion: Corticosteroid use, exposition to more than one biologic, smoking and renal failure are associated with serious infections in RA patients on bDMARDs.

Disclosure: M. de la Vega, None; G. Casado, None; G. Citera, AbbVie, Bristol-Myers Squibb, Janssen, Novartis, Pfizer Inc, 5,Novartis, Pfizer Inc, 2,AbbVie, Bristol-Myers Squibb, Janssen, Novartis, Pfizer Inc, 5; I. M. M. Laurindo, None; G. Christopoulos, None; M. A. Descalzo, None; R. Ranza, None.

Abstract Number: 279

the Usefulness of Cytomegalovirus Infection Strategy in Patients with Connective-Tissue Disease, Based on the Guidelines of the Japan Society for Hematopoietic Cell Transplantation 2011

Rika Suzuki¹, Yasuyoshi Kusanagi², Takashi Nakanishi², Hideyuki Horikoshi³, Fumihiko Kimura¹ and Kenji Itoh¹, ¹Department of Hematology and Rheumatology, Division of Internal medicine, National Defense Medical College, Saitama, Japan, ²Department of Hematology and Rheumatology, Division of Internal medicine, National Defence Medical College, Tokorozawa, Japan, ³National Defence Medical College, Tokorozawa, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Infection-related Rheumatic Disease Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM
**Background/Purpose:** Cytomegalovirus (CMV) infection is a life-threatening complication in immunocompromized hosts. There are no official guidelines for CMV infection management in patients with connective-tissue diseases (CTD) under immunosuppressive therapy. CMV infection management according to the guidelines of the Japan Society for Hematopoietic Cell Transplantation (JSHCT) 2011 was performed in CTD patients and its usefulness and safety were evaluated.

**Methods:** We retrospectively examined 98 CTD patients who were admitted to the National Defense Medical College Hospital from October 2012 to March 2017, and were receiving ≥20 mg/day of prednisolone. CMV infection was defined by the detection of CMV pp65 antigenemia. CMV disease was diagnosed by both detection of CMV pp65 antigenemia and the involvement of organs due to CMV reactivation. We managed the CMV infection according to the guidelines. The primary endpoint was mortality and major organ involvement due to CMV infection. We also evaluated the risk factors for CMV reactivation and intervention after scoring positive for CMV antigenemia.

**Results:** Sixty-six cases of positive CMV pp65 antigenemia occurred in the 98 patients. An antiviral drug was administered in accordance with the JSHCT guidelines in 36 cases (treatment group). The patients in the remaining 30 cases did not receive treatment (observation group). No patients died due to CMV disease. Four patients in the treatment group died due to renal failure, Pneumocystis pneumonia or deterioration of adult-onset Still’s Disease, in observation group none died. Persistent major organ involvement due to CMV infection did not occur in either groups. The risk factors for CMV reactivation were older age and steroid pulse therapy. The risk factor for CMV disease was CMV test positivity in the early period (<4 weeks) of steroid therapy. Thrombocytopenia is the most common manifestation of CMV disease.

**Conclusion:** This study demonstrates the usefulness of CMV infection management according to the JSHCT guidelines for CTD patients under immunosuppressive therapy.

**Disclosure:** R. Suzuki, None; Y. Kusanagi, None; T. Nakanishi, None; H. Horikoshi, None; F. Kimura, None; K. Itoh, None.

**Reasons Why Patients Failed Vaccinations Vs Influenza and Pneumococcus. Monocentric Cross-Sectional Study.**

Maria Chiara Ditto¹, Alberto Batticciotto¹, Maria Chiara Gerardi¹, Federica Rigamonti², Rossella Talotta¹ and Piercarlo Sarzi-Puttini¹,
¹Rheumatology Unit, ASST Fatebenefratelli - Sacco, L. Sacco University Hospital, Milano, Italy, ²Rheumatology Unit, ASST Fatebenefratelli - Sacco, L. Sacco University Hospital, Milan, Italy

First publication: September 18, 2017

**SESSION INFORMATION**
Session Date: Sunday, November 5, 2017
Session Title: Infection-related Rheumatic Disease Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM
**Background/Purpose:** Immunosuppressive therapies and bDMARDs especially increase the risk of infections. According to the EULAR guidelines, all patients affected by autoimmune/inflammatory diseases should receive vaccinations against influenza and pneumococcus. The primary aim of this work is to evaluate the prevalence of flu and pneumococcal vaccinations in a cohort of patients affected by inflammatory arthritides and SLE treated with biological drugs. The secondary aim was to explore the reason why patients do not receive vaccination.

**Methods:** We administered a self-reporting questionnaire about both flu and pneumococcal vaccination, to 274 consecutive patients from February to April 2017 treated with bDMARDs.

**Results:** The 65.3% of patients declared to have been informed from rheumatologist about the possibility to receive vaccinations during biological treatments but the 19.5% declared to have never been informed about them. The 46% of patients vaccination for influenza was performed after rheumatology suggestion and the 21% after their general practitioner suggestion, while the 30.1% has declared to have not performed it for several reasons: because concerned about adverse events (5.1%), because they don't see it as useful (17.4%) or for other reasons. The injection has been administered for free in the majority of patients (GPs 36.8%, local healthcare 33.5%). The 60.9% would have undergone vaccination even for a fee. The anti pneumococcal vaccination was administered to the 25.3%, while to the 50.3% has never been suggested to do it. The 4.4% has declared to have not performed it because concerned about adverse events and the 6.6% because they don't see it as useful. The injection has been administered for free at local healthcare facilities in the 84% of the patients. The 97.3% would have undergone vaccination even for a fee. At last the patients have declared to have always been well informed about vaccinations (48.9%), to have been well informed only about certain vaccinations (9.5%) or to have been informed only after asking (9.1%); The 19.1% was unsatisfied.

**Conclusion:** The acquired vaccine rate has been low for the influenza vaccination (<60%) and extremely low for the pneumococcal vaccination (26%). Even if the reasons of this results are partially attributable to a low patients' compliance (47.5% for the influenza vaccination, 11% for the anti pneumococcal vaccination), almost 20% has declared not to have ever been informed about vaccinations. So an additional effort to improve these results is mandatory.

**Disclosure:** M. C. Ditto, None; A. Batticciotto, None; M. C. Gerardi, None; F. Rigamonti, None; R. Talotta, None; P. Sarzi-Puttini, None.


**Abstract Number:** 281

**Direct Medical Costs Associated with the Extrahepatic Manifestations of Hepatitis C Virus Infection in France**

**Patrice Cacoub**¹, Mathieu vautier², Anne-Claire Desbois³, David Saadoun⁴ and Zobair Younossi⁵, ¹Department of Internal Medicine and Clinical Immunology, Groupe Hospitalier Pitié-Salpêtrière, Paris, France, ²Médecine Interne 1, Hôpital Pitié-Salpêtrière, Paris, France, ³Hôpital Pitié-Salpêtrière, Internal Medicine and Clinical Immunology, Paris, France, ⁴Sorbonne Universités, UPMC Univ Paris 06, UMR 7211, and Inflammation-Immunopathology-Biotherapy Department (DHU 12B), F-75005, Paris, France; INSERM, UMR_S 959, F-75013, Paris, France; CNRS, FRE3632, F-75005, Paris, France; AP-HP, Groupe Hospitalier, Paris, France, ⁵Medicine, Inova Fairfax Hospital, Falls Church, Falls Church, VT

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Infection-related Rheumatic Disease Poster

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The economic impact of the extrahepatic manifestations (EHM) of hepatitis C virus (HCV) infection remains unknown for France. To estimate the prevalence of HCV-EHM and the direct medical costs associated with HCV-EHM in France.

**Methods:** Estimates of thirteen EHM prevalence were obtained (i) from a retrospective data analysis of HCV-infected patients in specialized center in France, and the baseline prevalence in the general French population and (ii) from an international systematic review and meta-analysis. Per-patient-per-year (PPPY) inpatient, outpatient and medication costs to treat EHM in France were obtained from the literature, national databases, or expert opinion. The impact of achieving SVR after antiviral therapy was applied to the French healthcare costs.

**Results:** Using approach (i), increased EHM prevalence rates in HCV patients compared to the general population were observed for most
EHM, including cryoglobulinemia vasculitis (51.5% vs. 1.5%), rheumatoid-like arthritis (47.8% vs. 0.1%) and lymphoma (14.2% vs. 0.24%). The mean POPY cost of EHM in the French tertiary center was 3,296 € [95% CI 1,829; 5,540]. In France, HCV-EHM amounted to a total cost of 215 million (M) € per year [14; 299]. Using approach (ii), the mean POPY cost of EHM in France was estimated to be 1,117 €. The estimated total cost reduction in France associated with SVR was 13.9 M€ for diabetes, 8.6 M€ for cryoglobulinemia vasculitis, 6.7 M€ for myocardial infarction, 2.4 M€ for end-stage renal disease, and 1.4 M€ for stroke.

Conclusion: Extrahepatic manifestations of HCV infection substantially add to the overall economic burden of HCV infection in France. Sustained virological response after antiviral therapy is expected to significantly reduce the total costs of managing HCV-EHM in France.

Disclosure: P. Cacoub, None; M. vautier, None; A. C. Desbois, None; D. Saadoun, None; Z. Younossi, None.

Abstract Number: 282

The Value of Imaging As an Early Noninvasive Test for Prosthetic Joint Septic Arthritis

Kevin Byrne1, Mary Louise Fowler2, Sarah Lieber3, Robert Shmerling4 and Ziv Paz3, 1Boston University School of Medicine, Boston, MA, 2Boston University School of Medicine, Boston, MA, 3Beth Israel Deaconess Medical Center, Boston, MA, 4Rheumatology, Beth Israel Deaconess Medical Center, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Infection-related Rheumatic Disease Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Medical imaging is commonly obtained in evaluating patients with suspected prosthetic joint septic arthritis (PJSA); it may be helpful to detect other pathology in the joint (e.g., chondrocalcinosis), to establish a baseline, or to detect the presence of synovial fluid. Imaging may even help diagnose PJSA, but there is little data available to evaluate the value of various imaging modalities for the diagnosis of PJSA.

Objectives: To examine how the use of medical imaging for PJSA has changed over the 17 years of this study and to assess the value of different imaging modalities in differentiating patients with culture-positive PJSA from patients with culture-negative PJSA.

Methods: We conducted a retrospective study that included all patients ages 18 years and older who were diagnosed with monoarticular PJSA and underwent surgical intervention at a single, tertiary-care hospital between 1997 and 2014.

Results: Of the 280 patients with diagnosed PJSA, 214 (76.4%) had at least one imaging study during the index admission. Radiographs were performed in 167 patients (59.6%). The second most common imaging modality was CT scan (17 patients; 6.1%). The most common imaging findings were joint effusion in 91 (32.5%) patients and soft tissue swelling in 41 (14.6%) patients. Of the 280 patients assigned a diagnosis of PJSA, 190 (69.3%) were culture-positive. Patients with culture-positive PJSA were less likely to have normal findings in their plain radiographs (3.7 vs. 13.1%, p=0.007), more likely to have gas/free air (7.4 vs. 1.2%, p=0.043), but no more likely to have joint effusions (28.9 vs. 25.0%, p=0.56) or soft tissue swelling (13.2 vs. 8.3%, p=0.31). The percentage of patients receiving each imaging modality remained relatively constant over the course of the study (Figure 1).

Conclusion: Imaging studies—especially radiographs—are commonly ordered to evaluate patients with suspected PJSA. Our study demonstrates that patients with culture negative PJSA are more likely to have normal findings on imaging, including radiographs. Patients with culture-positive PJSA were significantly more likely to have radiographic findings of gas or free air. Imaging studies in general and radiographs in particular demonstrated joint effusions in patients at similar rates among PJSA patients with and without positive cultures. This study demonstrates that in most cases imaging studies have limited utility among patients with suspected PJSA and cannot be relied upon to demonstrate specific findings to suggest the diagnosis.
Metabolic Activity Sustains Macrophage Cytokine Production in Rheumatoid Arthritis and Coronary Artery Disease

Cornelia M. Weyand1, Markus Zeisbrich1, Lukas Brosig2, Barbara Wallis1, Niall Roche3, Janice Lin1 and Jorg Goronzy4, 1Medicine: Immunology and Rheumatology, Stanford University, Stanford, CA, 2Medicine: Immunology and Rheumatology, Stanford University, Stanfod, CA, 3The Arthritis Center, Pleasanton, CA, 4Medicine/Division of Immunology & Rheumatology, Stanford University School of Medicine, Stanford, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Innate Immunity and Rheumatic Disease Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Accelerated atherosclerosis has become increasingly recognized as a complication of chronic inflammatory disease, such as in patients with rheumatoid arthritis (RA). RA patients have a 2-fold increased risk of developing coronary artery disease (CAD) regardless of traditional risk factors and cardiovascular complications substantially contribute to their increased mortality. The inflammatory lesions in RA and CAD share the chronicity of tissue-destructive immune responses, with macrophages representing abundant effector cells.

Methods: Patients with RA who fulfilled 2010 ACR/EULAR RA Classification Criteria and patients with CAD (history of at least one myocardial infarction) were enrolled together with healthy age-matched controls. Monocytes were isolated from peripheral blood and differentiated into macrophages with macrophage colony-stimulating factor. Macrophages were polarized into M1 cells with IFN-γ and lipopolysaccharide. Mitochondrial reactive oxygen species (ROS) were quantified by MitoSOX staining and their production was inhibited with the ROS scavenger mitoTEMPO. Cellular ATP concentrations were quantified by fluorometric assay. Glycolytic rates and oxygen consumption were measured by Seahorse Flux Analyzer experiments. Relative gene expression was analyzed by quantitative RT-PCR and adjusted for β-actin transcripts.

Results: Seahorse experiments demonstrated increased glycolytic rates (ECAR) in RA and CAD macrophages compared to age-matched healthy controls. Key enzymes of glycolysis, HK-1 and PKM-2, were upregulated as well as GLUT-1, the main glucose uptake receptor in macrophages. The breakdown of glucose resulted in high mitochondrial activity characterized by an increase in mitochondrial membrane potential and by greater oxygen consumption, with mitochondria from CAD macrophages respiring even more than those from RA macrophages. Pharmaceutical uncoupling of the electron transport chain was used to measure maximal mitochondrial respiration. Notably, CAD mitochondria had explicitly more reserve capacity to work against imminent energy deficits and RA mitochondria still showed higher capacity than healthy ones. A byproduct of enhanced mitochondrial respiration is the generation of mitochondrial ROS, which was confirmed
Liver X Receptor-α (LXRα) Modulates Macrophage Phenotype and Disease Activity in SLE

Shuhong Han¹, Haoyang Zhuang¹, Pui Lee², Stepan Shumyak¹, Jingfan Wu¹, Chao Xie³, Hui Li³, Lijun Yang³ and Westley Reeves⁴, 
¹Medicine, University of Florida, Gainesville, FL, ²Harvard Medical School, Boston, MA, ³Pathology, Immunology and laboratory medicine, University of Florida, Gainesville, FL, ⁴Rheumatology & Clinical Immunology, University of Florida, Gainesville, FL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Innate Immunity and Rheumatic Disease Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: LXRα is an oxysterol-regulated transcription factor that plays a key role in reverse cholesterol transport by inducing the expression of ATP binding cassette A1 (ABCA1) and other genes. LXRα also promotes macrophage (Mφ) polarization away from proinflammatory (classically activated, M1) toward alternatively activated (M2) Mφ. M1 Mφ are metabolically dependent on glycolysis, whereas M2 Mφ require oxidative metabolism. Hypoxia-inducible factor 1-α (HIF1α), a key regulator of glycolysis, promotes M1 Mφ polarization. We have shown that Mφ depletion prevents diffuse alveolar hemorrhage (DAH) in mice with pristane-induced lupus. The present study explored the mechanisms involved.

Methods: Murine Mφ subsets were phenotyped by flow cytometry and the cell subsets were flow-sorted. Gene expression in SLE patients and mice with pristane-lupus was determined using RNA-Seq and real-time PCR. Cell metabolism was evaluated by extracellular flux analysis (Seahorse assay). Pristane-treated C57BL/6 mice received daily injections of the synthetic LXR agonist T0901317 (or vehicle) for 14-d after which we assessed DAH.

Results: Peritoneal Mφ from pristane-treated mice had an M1 phenotype with high CD274, Ym1, and IL-10 when cells were pretreated with mitoTempo, a ROS-scavenger that specifically targets mitochondria-derived superoxide. Production of pro-inflammatory key cytokines of the synovial joint and the atherosclerotic plaque was directly related to mitochondrial activity, as indicated by the effective inhibition of IL-6, IL-1b, IL-18, and IL-23 when cells were pretreated with mitoTempo, a ROS-scavenger that specifically targets mitochondria-derived superoxide.

Conclusion: Macrophages from RA and CAD patients share a distinct metabolic profile characterized by upregulated glycolysis and high mitochondrial activity; fueling excess production of ROS and cytokines. Metabolic activity directly regulates the macrophages’ inflammatory potential and might contribute to accelerated atherosclerosis in RA patients.

Disclosure: C. M. Weyand, None; M. Zeisbrich, None; L. Brosig, None; B. Wallis, None; N. Roche, None; J. Lin, None; J. Goronzy, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/liver-x-receptor-%e2%99%b1-lxr-%e2%99%b1-modulates-macrophage-phenotype-and-disease-activity-in-sle-

Abstract Number: 285

Liver X Receptor-α (LXRα) Modulates Macrophage Phenotype and Disease Activity in SLE

Disclosure: S. Han, None; H. Zhuang, None; P. Lee, None; S. Shumyak, None; J. Wu, None; C. Xie, None; H. Li, None; L. Yang, None; W. Reeves, None.
Serum Amyloid a Aggravates Rheumatoid Arthritis By Activating NFAT5-Mediated Migration of Macrophages

Yu-Mi Kim Sr.¹, Donghyun Kim Sr.¹, Seung-Ah Yoo Sr.², Jung Hee Koh Sr.², Jin-Sun Kong Sr.² and Wan-Uk Kim Sr.³, ¹Center for Integrative Rheumatoid Transcriptomics and Dynamics, The Catholic University of Korea, Seoul, Korea, Republic of (South), ²The Catholic University of Korea, Center for Integrative Rheumatoid Transcriptomics and Dynamics, seoul, Korea, Republic of (South), ³The Catholic University of Korea, Department of Internal Medicine, seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Innate Immunity and Rheumatic Disease Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Serum amyloid A (SAA) is an acute phase protein and its serum levels may increase up to 1000-fold over normal levels during inflammation, triggering perpetual inflammatory responses. The level of SAA has been reported to have a correlation with rheumatoid arthritis (RA) symptoms. However, the direct role of SAA in the RA pathogenesis remains unclear. In this study, we have identified that SAA contributes to the activation of macrophages through induction of nuclear factor of activated T cells 5 (NFAT5), resulting in the aggravation of arthritic symptoms.

Methods: Expression of NFAT5 was examined in the SAA-treated macrophages using Western blot analysis and immunofluochemistry. The transcriptional activation of NFAT5 was measured by luciferase reporter assay and Matrigel assay. To find the receptor and signaling pathway involved in the SAA-induced NFAT5 expression, chemical inhibitors and genetically deficient macrophages were used. The cell migrations were compared between wild type and NFAT5 knock-down or knock-out macrophages by using transwell migration assay, wound-healing assay and air-pouch mouse model. To confirm the importance of SAA-NFAT5 axis in vivo, we injected SAA into the arthritis mouse model induced by injection of methylated-bovine serum albumin/interlukin-1β (mBSA/IL-1β).

Results: SAA induced the expression and activation of NFAT5 in macrophages, which is mediated by TLR2 and TLR4 on their surface. MAPKs and PI3K signaling pathways, especially JNK1/2, were involved in the NFAT5 expression induced by SAA treatment. The induced NFAT5 contributed to the cytoskeletal rearrangement in macrophages, thereby leading to the cell migration in vitro and in vivo. Moreover, SAA injection aggravated disease severity, including increased macrophages, in the joints of mBSA/IL-1β-induced arthritis.

Conclusion: Our data show novel findings that SAA could induce the activation and migration of macrophages by stimulating the expression and activity of NFAT5 through TLR2/4 and MAPKs signaling pathways. Moreover, Increased SAA could contribute to the aggravation of arthritis symptoms in the mouse model. Thus, targeting SAA-NFAT5 axis may potentially be of therapeutic value in chronic inflammatory diseases accompanied by elevated SAA levels, such as rheumatoid arthritis.

Disclosure: Y. M. Kim Sr., None; D. Kim Sr., None; S. A. Yoo Sr., None; J. H. Koh Sr., None; J. S. Kong Sr., None; W. U. Kim Sr., the National Research Foundation of Korea, 2.


Abstract Number: 287

Anti-TNF Agents Induce Alternative Macrophages

Yannick Degboë¹, Benjamin Rauwel², Michel Baron², Jean Frédéric Boyer², Alain Cantagrel², Arnaud Constantin³ and Jean-Luc Davignon², ¹Centre de Physiopathologie Toulouse Purpan, INSERM UMR 1043, Toulouse, France, ²CPTP, INSERM UMR 1043, Toulouse, France, ³Department of Rheumatology, Purpan Hospital, Toulouse III University, Toulouse, France, Toulouse, France

First publication: September 18, 2017

SESSION INFORMATION
Macrophages contribute to the pathogenesis of rheumatoid arthritis (RA). They can display various states of activation or «polarization», characterized by distinct functions and plasticity. M1 polarization corresponds to the “classical”, pro-inflammatory activation as identified in RA. M2 “alternative” polarizations display immunoregulatory and wound-healing properties. Data concerning the effects of RA anti-cytokine biological drugs (bDMARDs) on macrophage polarization are scarce.

We aimed to assess in vitro modulation of macrophage polarization by RA bDMARDs.

Methods:

Blood monocytes from 15 healthy controls and 10 RA patients were positively sorted by CD14+ magnetic selection. Macrophages were derived from monocytes (MDM) by 5 days of culture in the presence of MCSF, and activated or not for 24h as M1 pro-inflammatory MDM (by LPS + IFNγ) or as M2 alternative MDM by IL10 or IL4, respectively M2(IL10) and M2(IL4). M1 MDM were cultured with or without bDMARDs.

We evaluated 2 anti-TNF agents (etanercept (ETA), adalimumab (ADA)), 1 anti-IL6R agent (tocilizumab (TCZ)), and 1 anti-CD20 agent (rituximab (RTX)) used as control monoclonal antibody. bDMARDs effects were assessed on M1 activation phase by flow cytometric analysis of membrane markers. Functional aspects of polarization were assessed by analysis of cytokine production in cell culture supernatants (cytometric bead array and ELISA) and phagocytosis (flow cytometry).

M1 MDM cultured in the presence of bDMARDs were compared to untreated M1 MDM by a Wilcoxon matched pairs test.

Results:

We validated membrane polarization markers in our culture model: CD40 and CD80 as M1 (LPS + IFNγ) markers; CD16, CD163, MerTK and CD64 as M2(IL10) markers, CD206 and CD200R as M2(IL4) markers.

When compared to MDM from healthy controls, MDM from RA patients displayed a biased plasticity: they significantly expressed higher levels of M1 markers after M1 activation and expressed lower levels of CD16 after differentiation or M1 and M2 activations.

Concerning the effect of bDMARDs on surface markers after M1 activation (M1 MDM): in RA patients and healthy controls, anti-TNF agents induced a significant decrease in M1 markers and a significant modulation in M2(IL10) markers. We observed (i) a decrease in CD40 and CD80, (ii) an increase in CD16, CD163, and MerTK, (iii) a decrease in CD64 with ETA and an increase with ADA. TCZ induced a slight but significant decrease in CD40 and an increase in CD64. RTX only increased CD64.

Anti-TNF agents led to a significant modulation of cytokines produced by M1 MDM from healthy controls: we observed a decrease in TNFα, IL6, IL12 and IL10 levels, and an increase in TGFβ. TCZ mainly affected IL6 and TNFα productions with a significant decrease. No significant effect was observed with RTX.

In healthy controls, phagocytosis was superior in M2(IL10) and M2(IL4) activated MDM than in M1 MDM. Anti-TNF agents, but neither TCZ nor RTX, induced an increase of phagocytosis in M1 MDM.

Conclusion:

Anti-TNF agents modulate the phenotype of MDM from healthy donors as well as from RA patients. They up-regulate M2 alternative properties and downregulate M1 inflammatory properties in macrophages.

Disclosure: Y. Degboé, Pfizer Inc, 2; B. Rauwel, None; M. Baron, None; J. F. Boyer, None; A. Cantagrel, None; A. Constantin, Pfizer Inc, 2; J. L. Davignon, Pfizer Inc, 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/anti-tnf-agents-induce-alternative-macrophages
Internalized By Human THP-1 Monocytes

HDL Modified with Malondialdehyde-Acetaldehyde (MAA) Is Bound and Rapidly Internalized By Human THP-1 Monocytes

Emma Dorris¹, Karen Creevey¹, John Moylett¹, Simon Tazzyman², Munitta Muthana² and Anthony G. Wilson¹, ¹UCD School of Medicine and Medical Science, Conway Institute, University College Dublin, Dublin, Ireland, ²University of Sheffield Medical School, Sheffield, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Innate Immunity and Rheumatic Disease Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: rs26232 in the first intron of C5orf30 has been associated with risk of developing rheumatoid arthritis (RA) and severity of tissue damage. C5orf30 is highly expressed by RA synovial fibroblasts (RASF) and macrophages. Inhibition of C5orf30 in RASF results in increased cellular invasiveness and migration in vitro and inhibition in the collagen-induced arthritis model accentuated joint inflammation and damage. There is no published data on the biological activities of C5orf30 in macrophages.

Methods: Monocyte cell line (THP1) and primary monocyte-derived macrophages (MDM) were used. C5orf30 mRNA was assessed by qPCR and protein via Western blot. Transcript and protein half-lives were assessed using actinomycin D and cyclohexamide. Polarization to M1 and M2a phenotypes and stimulation with TNF and LPS on C5orf30 expression were compared. C5orf30 levels were manipulated using siRNA and functional effects on macrophage biology was assessed using ELISAs, invasion assays, pathogen phagocytosis assays, reactive oxygen species assays, gene expression and intracellular signalling assays. In vivo, antisense morpholino oligonucleotides were used to knockdown C5orf30 in zebrafish. Confocal imaging was used to assess the number of invading macrophages.

Results: C5orf30 has a half-life of 3.13 hours, which does not significantly change with the addition of inflammatory (LPS +IFNγ) or anti-inflammatory (IL-4) stimuli. Protein half-life is 19.54 hours, rising to 22.05 hours when pretreated with LPS+ IFNγ (M1-like) and decreasing to 15.07 hours when pretreated with IL-4 (M2a-like). Polarization to M2a increased C5orf30 protein expression whereas polarization to M1 resulted in phosphorylation of C5orf30 protein and decreased expression of C5orf30 (p=0.01). Treatment with TNF or LPS reduced C5orf30 expression (TNF p=0.001, LPS p=0.02). LPS phosphorylates C5orf30. Pretreatment of cells with the JNK inhibitor SP600125 retarded the phosphorylation of C5orf30 in response to LPS in a dose-dependent manner and prevented downregulation of C5orf30 gene expression. Knockdown of C5orf30 reduced the invasive capacity of macrophages (p=0.003) with an associated decrease in MMP1 (p=0.01), MMP3 (p=0.01) and MMP9 (p=0.03). Decrease in invasion was intensified upon incubation with either TNF (p=0.02) or LPS (p=0.01). C5orf30 knockdown increased phagocytosis when co-stimulated with LPS (p=0.01). C5orf30 knockdown also increased activation of the JNK pathway. In vivo, tail amputations in zebrafish with C5orf30 deficient embryos showed an increased macrophage infiltration at the wound site (p=0.01).

Conclusion: Stimulation with inflammatory mediators induces phosphorylation of C5orf30 and downregulates C5orf30 gene expression, whereas treatment with anti-inflammatory signals increases C5orf30 protein expression. C5orf30 knockdown enhanced the proinflammatory macrophage phenotypes of phagocytosis and JNK activation whilst diminishing the tissue-clearing (M2-like) phenotype of macrophage invasion. This data indicates an important role for C5orf30 in the immunomodulatory regulation of macrophages and is consistent with our previous findings in RASF.

Disclosure: E. Dorris, None; K. Creevey, None; J. Moylett, None; S. Tazzyman, None; M. Muthana, None; A. G. Wilson, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-rheumatoid-arthritis-susceptibility-gene-c5orf30-is-an-immunomodulator-in-macrophages

Abstract Number: 289

HDL Modified with Malondialdehyde-Acetaldehyde (MAA) Is Bound and Rapidly Internalized By Human THP-1 Monocytes

Michael J. Duryee¹, Dahn L Clemens², Logan M. Duryee², Karen C. Easterling³, Carlos D. Hunter⁴, Lynell W. Klassen⁵, James R. O'Dell⁶, Daniel R. Anderson², Ted R. Mikuls⁵ and Geoffrey M. Thiele², ¹Research Services, Omaha VA Medical Center, Omaha, NE, ²University of Nebraska Medical Center, Omaha, NE, ³Internal Medicine, Division of Rheumatology, University of Nebraska Medical Center, Omaha, NE, ⁴Internal Medicine Division of Rheumatology, University of Nebraska Medical Center, Omaha, NE, ⁵Veteran Affairs Nebraska-Western Iowa Health Care System and University of Nebraska Medical Center, Omaha, NE, ⁶Department of Internal Medicine, University of Nebraska Medical Center, Omaha, NE

First publication: September 18, 2017
Background/Purpose: Rheumatoid arthritis (RA) is associated with an increased cardiovascular disease (CVD) burden, one that appears to be mitigated by increased concentrations of circulating HDL resulting from effective disease-modifying treatment. Our group has demonstrated that proteins modified with malondialdehyde-acetaldehyde (MAA), are present in the synovial tissues of RA patients and atherosclerotic lesions from non-RA patients with CVD. Previous data has also shown that MAA-modified proteins are bound and internalized by scavenger receptors (SRs) (SRA, SRBI, LOX-1, and CD36) present on immune cells. Therefore, in this study we evaluated whether HDL is modified by MAA and bound or internalized by monocytes.

Methods: Human HDL was labeled with 1,1'-diocadecyl-3,3,3',3'-tetramethylindocarbocyanine perchlorate (DIL-HDL). For MAA modification DIL-HDL (1 mg/ml) was incubated with 2mM malondialdehyde and 1mM acetaldehyde for 3 days and fluorescence of the dihydropyridine structure determined. To evaluate receptor mediated binding and internalization, PMA activated THP-1 cells (human monocytic) were incubated on ice at either 4°C or 37°C (respectively) for 90 minutes with 25 μg/ml of DIL-Albumin, DIL-HDL and DIL-HDL-MAA. Cells were washed, fixed in paraformaldehyde, and subjected to flow cytometry at 594 nm wavelength. Analysis was performed using FlowJo V10. Data are expressed as percent positive compared to the DIL-labeled human albumin.

Results: Human HDL was modified at 30,000 fluorescent units (FU), which was greater than the MAA modification observed for human serum albumin (22,000 FU). As shown in the Figure, THP-1 cells bound HDL (41.73%) at the cell surface significantly better than HDL-MAA (17.55%; P<0.001). Internalization studies revealed that HDL-MAA (48.9%) was taken up more by the cells than HDL (39.14%) alone, although this difference did not achieve statistical significance.

Conclusion: These data show that HDL can be modified with the MAA adduct and HDL-MAA is subsequently bound and internalized by human monocytes. THP-1 cells contain multiple scavenger receptors capable of binding and internalizing altered self-ligands as a normal clearance mechanism. These results demonstrate that HDL modified with MAA is bound at lower levels that HDL alone, but is internalized more efficiently by human monocytes. Taken together, these results suggest that MAA modification could impact cellular trafficking of HDL, thus influencing CVD pathogenesis in conditions characterized by oxidative stress and increased MAA adduct formation.

Disclosure: M. J. Duryee, None; D. L. Clemens, None; L. M. Duryee, None; K. C. Easterling, None; C. D. Hunter, None; L. W. Klassen, None; J. R. O'Dell, Medac, 5,Coherus, 5; D. R. Anderson, None; T. R. Mikuls, BMS, 2,Ironwood Pharm, 2,Pfizer Inc, 5,NIH, VA, 2; G. M. Thiele, None.

Abstract Number: 290

Characterization of Neutrophil Subsets and Neutrophil Extracellular Traps in Pyogenic Arthritis, Pyoderma Gangrenosum and Acne (PAPA) Syndrome

Pragnesh Mistry1, Carmelo Carmona-Rivera1, Nickie Seto1, Monica Purmalek1, Amanda Ombrello2, Ivona Aksentijevich2, Daniel L. Kastner2 and Mariana J. Kaplan1, 1Systemic Autoimmunity Branch, NIAMS/NIH, Bethesda, MD, 2Inflammatory Disease Section, NHGRI/NIH, Bethesda, MD

First publication: September 18, 2017
**Background/Purpose:** Pyogenic arthritis, pyoderma gangrenosum and acne (PAPA) syndrome is an autosomal dominant autoinflammatory disorder caused by mutations in the \textit{PSTPIP1}/\textit{CD2BP1} gene. PAPA syndrome is characterized by recurrent flares of sterile arthritis and severe skin inflammation in the absence of adaptive immune responses. Mutations in \textit{PSTPIP1} likely dysregulate the pyrin inflammasome leading to exuberant IL-1β production. PAPA patients respond to treatment with cytokine inhibitors, including IL-1 inhibitors. Neutrophils can undergo a form of cell death called NETosis where dying cells release a meshwork of decondensed DNA decorated with granule proteins called neutrophil extracellular traps (NETs). NETs have been shown to induce tissue damage in other systemic diseases. While previous studies have suggested that neutrophils may play critical roles in driving inflammation in PAPA syndrome, the mechanism by which it happens is still unclear. A subset of proinflammatory neutrophils called low-density granulocytes (LDGs) has been identified in other autoimmune/autoinflammatory conditions and these cells display an enhanced capacity to form NETs. Here, we aimed to elucidate the role of neutrophil subsets and NETs in the pathogenesis of PAPA syndrome.

**Methods:** Normal density neutrophils were isolated by dextran sedimentation from control and PAPA patients. LDGs were isolated by negative selection from the PBMC fraction. Immunofluorescence (IF) was used to assess the presence of NETs. To assess the effect of serum in NET formation, control neutrophils were incubated with 10% serum from control or PAPA patients in the presence or absence of the IL-1 receptor antagonist anakinra for 2 h. Circulating NET remnants were quantified by ELISA against citrullinated histone H3 (citH3)-DNA complexes. A skin biopsy from a PAPA patient was analyzed by IF, quantitative PCR, and western blot analysis for the presence of NETs and proinflammatory cytokines.

**Results:** LDGs were detected in PAPA patients. Neutrophils and LDGs from PAPA patients displayed an enhanced capacity to spontaneously form NETs when compared to control neutrophils. Serum from PAPA patients induced NET formation in control neutrophils and this process was inhibited in the presence of IL-1 inhibitor, anakinra. NET products, as measured by cit-H3-DNA complexes in plasma from PAPA patients, were significantly higher when compared to control plasma. We detected NETs in a skin biopsy from a PAPA patient, in association with upregulation of tissue IL-1β and IL-8 when compared to healthy skin biopsies. Furthermore, an immature granulocyte signature was detected in the skin biopsy tissue suggesting the presence of LDGs.

**Conclusion:** Taken together, neutrophils and LDGs in PAPA patients display dysregulated NET formation as assessed by \textit{in vitro} spontaneous NET formation and the presence of circulating NET remnants. Proinflammatory cytokines in serum and affected tissues of PAPA patients trigger the NET formation. Anakinra ameliorates serum-induced NETosis, suggesting a role of IL-1 signaling in NETosis. The identification of LDGs in skin tissue from PAPA patients point out a strong myeloid signature in this condition.

**Disclosure:** P. Mistry, None; C. Carmona-Rivera, None; N. Seto, None; M. Purmalek, None; A. Ombrello, None; I. Aksentijevich, None; D. L. Kastner, None; M. J. Kaplan, None.


**Abstract Number:** 291

**A Novel Real-Time Imaging Technique to Quantify Neutrophil Extracellular Traps and Distinguish Mechanisms of Cell Death in Neutrophils**

Sarthak Gupta\(^1\), Diana Chan\(^2\), Kristien Zaal\(^3\), Evelyn Ralston\(^4\) and Mariana J. Kaplan\(^2\), \(^1\)Systemic Autoimmunity Branch, National Institute of Arthritis, and Musculoskeletal and Skin Diseases/NIH, Bethesda, MD, \(^2\)Systemic Autoimmunity Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases/NIH, Bethesda, MD, \(^3\)Light Imaging Section, Office of Science and Technology, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, \(^4\)Light Imaging Section, Office of Science and Technology, National Institute of Arthritis and Musculoskeletal and Skin Diseases/NIH, Bethesda, MD

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Innate Immunity and Rheumatic Disease Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM
Background/Purpose: Neutrophils play a key role in host defenses and have recently been implicated in the pathogenesis of autoimmune diseases by several mechanisms including formation of neutrophil extracellular traps (NETs) through a distinct form of programmed cell death called NETosis. Techniques to assess and quantify NETosis in vitro in an unbiased, reproducible and efficient way are lacking, considerably limiting the advancement of this field. We optimized and validated a new method to automatically quantify the percentage of neutrophils undergoing NETosis in real time using IncuCyte ZOOM™, a two-color, live-content imaging platform, and the membrane permeability properties of two different DNA dyes. We also evaluated whether this technology would allow for the differentiation of various forms of neutrophil cell death.

Methods: Neutrophils were isolated from healthy controls and their nuclei were stained with the membrane permeable DNA binding NUCLEAR-ID red dye to count all cells. They were then seeded on a 96-well plate and incubated with various stimuli or inhibitors and a membrane-impermeable DNA dye, Sytox Green, that helped to assess cell death. Images were taken every 10 minutes and a processing definition was devised to automatically count all neutrophils at baseline and neutrophils undergoing cell death based on fluorescence intensity and stained nuclear area size.

Results: This imaging platform enabled efficient, real-time imaging and quantification of cells undergoing NETosis. Findings were confirmed with established method of immunofluorescence microscopy and the percentage counts of cells undergoing NETosis correlated well. The platform’s ability to rapidly measure NETosis and effects of drugs to modulate it was used to test various concentrations of an inhibitor of NETosis (Akt-inhibitor XI) which showed a dose dependent effect. This method was also able to distinguish between distinct neutrophil cell deaths. Neutrophils undergoing NETosis induced by phorbol-myristate acetate, bacterial toxin nigericin, calcium ionophore A23187 or platelet activating factor, exhibited a loss of multi-lobulated nuclei, nuclear decondensation and eventual membrane compromise. Necrosis induced by freeze-thaw resulted in instantaneous damage to membrane integrity with minimal change to nuclear morphology. In contrast, apoptotic cells induced by staurosporine showed nuclear condensation and cytoplasmic blebbing.

Conclusion: The IncuCyte ZOOM platform is a novel assay that quantifies NETosis in a rapid, automated and reproducible way, while retaining the ability to distinguish between different types of neutrophil cell death, and offers a significant advancement in the study of neutrophils. It is a powerful tool to assess neutrophil physiology and to swiftly develop novel neutrophil targets in autoimmune diseases.

Disclosure: S. Gupta, None; D. Chan, None; K. Zaal, None; E. Ralston, None; M. J. Kaplan, None.


Abstract Number: 292

Neutrophil Extracellular Traps Are Induced By Adenosine and Stimulate Release of TNF Alpha from Macrophages in Deficiency of Adenosine Deaminase 2 (DADA2)

Carmelo Carmona-Rivera1, Kyawt W. Shwin2, Jorge A. irizarry-Caro3, Sami S. Khaznadar4, Yudong Liu5, Kenneth A. Jacobson4, Amanda Ombrello5, Deborah L. Stone3, Wanxia Li Tsai3, Massimo G. Gadina4, Daniel L. Kastner5, Ivona Aksentijevich5, Mariana J. Kaplan3 and Peter C. Grayson7, 1Systemic Autoimmunity Branch, NIAMS/NIH, Bethesda, MD, 2Division of Rheumatic Diseases, Dallas VA Medical Center/ UT Southwestern Medical Center, Dallas, TX, 3NIAMS/NIH, Bethesda, MD, 4Molecular Recognition Section, NIDDK-NIH, Bethesda, MD, 5Inflammatory Disease Section, NHGRI/NIH, Bethesda, MD, 6Translational Immunology Section, Office of Science and Technology, NIAMS/NIH, Bethesda, MD, 7National Institute of Arthritis, Musculoskeletal and Skin Disease (NIAMS), Bethesda, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Innate Immunity and Rheumatic Disease Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Reduction of adenosine deaminase 2 (ADA2) activity due to autosomal recessive loss of function mutations in the CECR1 gene results in a systemic illness known as DADA2 characterized in part by early-onset stroke, vasculitis, and clinical response to TNF-inhibitors. Adenosine, which is extracellularly degraded by ADA2, modulates inflammation via four different adenosine receptors (ARs). Neutrophils and a subset of neutrophils known as low-density granulocytes (LDGs) have been implicated in the pathogenesis of small-vessel vasculitis through the formation of neutrophil extracellular traps (NETs). The study objective was to determine whether neutrophils and NETs play a pathogenic role in DADA2.

Methods: Neutrophils and LDGs were isolated from healthy volunteers, patients with DADA2, and their family members. NETs were quantified and visualized by fluorescence microscopy. Immunofluorescence was performed against citrullinated-histone H4 and macrophage
markers to detect NETs and macrophages in affected tissue from a patient with DADA2. Neutrophils were incubated with adenosine +/- ADA2 enzyme and resultant NET formation was quantified. Pharmacologic approaches were utilized to determine the specific receptor(s) and pathways that mediate NET formation by adenosine. ELISA quantified TNF-alpha release in supernatants from macrophages incubated with NETs.

**Results:** An abundance of circulating LDGs prone to spontaneous NET formation were observed during active disease in DADA2 and were significantly reduced after remission induction by anti-TNF therapies. Increased circulating LDGs were identified in unaffected heterozygous carriers of **CECR1** mutations. **In vivo** evidence demonstrated NETs and macrophages in affected gastrointestinal tissue in a patient with DADA2. Adenosine triggered NET formation by engaging A1 and A3 adenosine receptors and through ROS- and PAD4- dependent pathways. Adenosine-induced NETosis was inhibited in the presence of recombinant ADA2, A1/A3 AR antagonists, or an A2A agonist. M1 macrophages incubated with NETs from patients with DADA2 released significantly increased amounts of TNF-alpha. Treatment with IL-1Ra (anakinra) or an A2A AR agonist decreased nuclear translocation of NFkB and pro-inflammatory cytokines-induced by NETs in macrophages.

**Conclusion:** Neutrophils may play a pathogenic role in DADA2. LDGs and NETs are observed during active disease. Adenosine can trigger NET formation, and deficiency of ADA2 may enhance adenosine-mediated NETosis. M1 macrophages produce TNF-alpha when exposed to NETs from patients with DADA2, potentially explaining the efficacy of anti-TNF therapies in this disease. Modulation of adenosine-mediated NET formation may constitute a novel and directed therapeutic approach in the treatment of DADA2.

**Disclosure:** C. Carmona-Rivera, None; K. W. Shwin, None; J. A. irizarry-Caro, None; S. S. Khaznadar, None; Y. Liu, None; K. A. Jacobson, None; A. Ombrello, None; D. L. Stone, None; W. L. Tsai, None; M. G. Gadina, None; D. L. Kastner, None; I. Aksentijevich, None; M. J. Kaplan, None; P. C. Grayson, None.

**Abstract Number:** 293

**Expanded Therapeutic ACPA Utility for Different NET-Driven Human (Autoimmune) Diseases**

Renato G.S. Chirivi1,2, Jos W.G. van Rosmalen1, Kostantinos Kambas3, Gonny Schmets1, Hans Kalisvaart1, Galina S. Bogatkevich4, Tim Shaw2, Helmuth van Es2 and Jos M.H. Raats1,2, 1ModiQuest BV, Oss, Netherlands, 2Citryll BV, Nijmegen, Netherlands, 3Laboratory of Molecular Hematology, Democritus University of Thrace, Alexandroupolis, Greece, 4Division of Rheumatology and Immunology, Department of Medicine, Medical University of South Carolina, Charleston, SC

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Innate Immunity and Rheumatic Disease Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Aberrant Neutrophil Extracellular Trap (NET) formation contributes to the induction and propagation of inflammation and plays a key role in causing tissue damage in conditions like sepsis, SLE, RA and vasculitis. Citrullination of proteins is involved in the formation of NETs, autoimmunity, and the breaking of tolerance in NET-driven autoimmune diseases. In SLE and RA, neutrophils undergo enhanced NETosis, and NET components are observed in blood, inflamed tissues and joints.

Therapeutic ACPA (tACPA) are first in class NETosis-inhibiting antibodies targeting citrullinated histones 2A and 4, which are being developed for the treatment of human diseases in which aberrant NET formation adds to the severity of the pathology with an initial focus on autoimmune diseases.

Here, we demonstrate the utility of tACPA as a NETosis-inhibiting therapy for different NET-based diseases beyond RA, including SLE and Idiopathic pulmonary fibrosis (IPF).

**Methods:**

Previously, using two RA animal models, the therapeutic properties of tACPA have been demonstrated (Chirivi *et al*., 2013). In the current studies, neutrophils from RA and SLE donors, as well as biological NET-inducing stimuli, such as RA synovial fluid (SF), gout SF and...
activated platelets, have been used to demonstrate the NETosis-inhibiting properties of tACPA in different human disease contexts. We have further expanded tACPA’s therapeutic utility by testing it in a surrogate model for NET-mediated organ damage (sepsis) and idiopathic pulmonary fibrosis (IPF).

**Results:**

NETosis in human RA and SLE neutrophils have been induced with a calcium ionophore and could be inhibited by tACPA treatment (40-100% reduction). Similar results were obtained using RA and gout SF or activated platelets as NETosis inducers in combination with neutrophils from healthy donors. These observations have been confirmed with multiple NET readouts such as MPO activity, MPO/DNA ELISA, DNA quantification as well as imaging readouts. In addition, we demonstrated that in an LPS-induced sepsis model 30% of tACPA-treated mice survived (compared to 0% in placebo controls), showing protection against organ failure. In a bleomycin-induced IPF mouse model, tACPA protected mice from the development of lung fibrosis (compared to placebo controls). When determining neutrophil counts in bronchoalveolar lavage samples, we found that in tACPA-treated mice, neutrophil levels were normal, while levels in placebo-treated mice were elevated.

**Conclusion:**

In a sepsis and IPF mouse model, tACPA prevented NET-mediated organ damage, providing evidence that tACPA could be a promising therapeutic strategy for diseases where NET-mediated endothelial toxicity causes organ damage like SLE, vasculitis and IPF. Central to our strategy for generating a preclinical data package supporting clinical testing, is to demonstrate that patient NETosis can be significantly inhibited ex vivo. We will present data that confirm that tACPA can block human SLE NETosis as well as human NETosis induced by activated platelets or gout SF.

**Disclosure:**

R. G. S. Chirivi, Citryll, 3; J. W. G. van Rosmalen, None; K. Kambas, None; G. Schnets, None; H. Kalisvaart, None; G. S. Bogatkevich, None; T. Shaw, None; H. van Es, Citryll, 4; J. M. H. Raats, Citryll and ModiQuest, 4.

**View Abstract and Citation Information Online** - [http://acrabstracts.org/abstract/expanded-therapeutic-acpa-utility-for-different-net-driven-human-autoimmune-diseases](http://acrabstracts.org/abstract/expanded-therapeutic-acpa-utility-for-different-net-driven-human-autoimmune-diseases)

**Abstract Number:** 294

**DNA Area and Netosis Analysis (DANA): A High-Throughput Method to Quantify Neutrophil Extracellular Traps in Fluorescent Microscope Images**

Ryan Rebernick¹, Lauren Fahmy², Christopher Glover², Nicole Rademacher², Hemanth Potluri², Mandar Bawadekar¹, Christie M. Bartels³ and Miriam A. Shelef¹,⁴, ¹Department of Medicine, Division of Rheumatology, University of Wisconsin - Madison, Madison, WI, ²University of Wisconsin - Madison, Madison, WI, ³Rheumatology/Medicine, University of Wisconsin - Madison, Madison, WI, ⁴William S. Middleton Memorial Veterans Hospital, Madison, WI

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Innate Immunity and Rheumatic Disease Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Neutrophil extracellular traps (NETs), extracellular structures composed of decondensed chromatin, are released in a process called NETosis. NETs, which are part of normal host defense, have also been implicated in multiple rheumatologic diseases including rheumatoid arthritis, lupus, and vasculitis. Unfortunately, methods for quantifying NETs have limitations involving cost, speed, bias, and/or ease of use, which constrain the study of NETs in disease. The purpose of this project is to advance the methodology for NET quantification in order to maximize the ability of investigators to further elucidate the role of NETs in health and disease.

**Methods:** We created DNA Area and NETosis Analysis (DANA), a novel ImageJ/Java based program which provides a simple, semi-automated approach to quantify NET-like structures and DNA area for many fluorescent microscope images at once providing data on a per cell, per image, and per sample basis. To test DANA, 2 different individuals determined the frequency of NET-like structures for fluorescent microscope images of Sytox-stained human neutrophils by eye followed by running DANA on those images. DANA was then used to analyze images of neutrophils from rheumatoid arthritis subjects and control subjects. To test the ease of implementing DANA and applicability to other species and DNA stains, two individuals with no programming background installed DANA and repeated the above experiments using images of DAPI-stained unstimulated and stimulated murine bone marrow derived neutrophils.

**Results:** DANA quantified a similar frequency of NET-like structures to the frequency determined by eye, and in a fraction of the time, for
both human Sytox-stained neutrophil images and murine DAPI-stained neutrophil images. Also, as expected, DANA detected increased DNA area and frequency of NET-like structures in rheumatoid arthritis subjects compared to controls and in stimulated murine neutrophils compared to unstimulated.

**Conclusion:** DANA provides a means to quantify DNA decondensation and the frequency of NET-like structures in a reliable, simple, high-throughput, and cost-effective manner making it ideal to assess NETosis in a variety of conditions.

**Disclosure:** R. Rebernick, None; L. Fahmy, None; C. Glover, None; N. Rademacher, None; H. Potluri, None; M. Bawadekar, None; C. M. Bartels, Pfizer Inc, 2; M. A. Shelef, None.

**Ex Vivo Induced Neutrophil Extracellular Traps Are Intrinsically Different in ANCA-Associated Vasculitis and Systemic Lupus Erythematosus**

Laura van Dam¹, Tineke Kraaij¹, Sylvia Kamerling¹, Hans U. Scherer², Charles Pusey³, Ton Rabelink¹, Cees van Kooten¹ and Onno Teng¹,¹Nephrology, Leiden University Medical Center, Leiden, Netherlands, ²Rheumatology, Leiden University Medical Center, Leiden, Netherlands, ³Imperial College, London, United Kingdom

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Innate Immunity and Rheumatic Disease Poster I  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Neutrophil extracellular traps (NETs) are immunogenic, extracellular DNA structures that harness important autoantigens to be recognized by the adaptive immune system. NETs are thought to play a pivotal role in the pathogenesis of ANCA-associated vasculitis (AAV) and SLE. However it is still unclear how and if NETs can act as a common pathway in the pathophysiology of these clinically divergent autoimmune diseases. The aim of the present study is to characterize AAV- and SLE-induced NETs.

**Methods:** The present study involved 88 AAV patients according to the Chapel Hill consensus definitions of 2012, 59 SLE patients according to the ACR criteria 1997 and 10 healthy controls. Healthy neutrophils were stimulated with 10% serum of AAV or SLE patients to induce NETs. Ex vivo NET induction by serum and IgG-depleted serum was measured by a novel, highly-sensitive NET quantification assay using 3D-confocal microscopy¹. Qualitative characteristics of NETs were studied by immunofluorescence to detect NET-related auto-antigens. Additionally, the morphology and kinetics of AAV- and SLE-induced NETosis were visualized by live cell imaging and electron microscopy.

**Results:** Ex vivo NET induction by AAV sera was 19.36 [9.161 – 73.08], (median [Q1 – Q3]) fold higher than sera of healthy controls (n=10) and also significantly higher than NET induction by SLE sera 5.56 [2.34 – 14.33] (Figure 1). Depletion of IgG from serum did not reduce NET induction in AAV, but it decreased NET induction significantly in SLE, indicating that different triggers mediate the induction of neutrophil extracellular traps in these autoimmune diseases. Additionally, the colocalisation of NET-related auto-antigens was different: citrullinated histon-3 (CitH3) was predominantly found on AAV-induced NETs, whereas high mobility group box protein-1 (HMGB-1) was exclusively found on SLE-induced NETs. Moreover, live cell imaging demonstrated that the kinetics of SLE-induced NETs peaked at 60 minutes, while AAV-induced NETs peaked at 4 hours (Figure 2). Intriguingly, SLE sera induced immediate clustering of neutrophils surrounding NETs whereas AAV sera induced NETs composed of long, thin DNA-fibres through lytic expulsion.

**Conclusion:** We demonstrate intrinsically distinct features of AAV- and SLE-induced NETs, indicating that NET formation in AAV and SLE is based on different mechanisms. Future studies should be directed at unravelling how different NETs are involved in causing SLE- or AAV-associated glomerulonephritis.

Disclosure: L. van Dam, None; T. Kraaij, None; S. Kamerling, None; H. U. Scherer, None; C. Pusey, None; T. Rabelink, None; C. van Kooten, None; O. Teng, None.


Abstract Number: 296

A Module of Genes Describing Low Density Granulocytes Can be Identified and Followed in the Periphery of Lupus Patients

Brian Keggereis1, Michelle Catalina2, Nick Geraci1, Sarah Heuer2, Prathyusha Bachali2, Sushma Madamanchi2, Peter E. Lipsky2 and Amrie Grammer2, 1AMPELBioSolutions and RILITE Research Institute, Charlottesville, VA, 2AMPEL BioSolutions and RILITE Research Institute, Charlottesville, VA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Innate Immunity and Rheumatic Disease Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Lupus is an autoimmune disease characterized by a type I interferon signature thought to be initiated by granulocyte NETosis. The granulocyte population in the periphery of lupus patients contains abnormal LDGs (low-density granulocytes) that are correlated with SLEDAni and anti-
dsDNA antibodies. The current experiments were carried out to identify LDGs quantitatively by their genomic signature in peripheral and tissue datasets from lupus patients.

**Methods:**

Publicly available microarray or RNASeq gene expression profiles from lupus patients were identified in GEO, including those obtained from neutrophils, whole blood (WB), PBMC and skin, synovium, and kidney. The raw data were downloaded, normalized, curated and assessed for differentially expressed (DE) genes. Correlation with clinical or histologic features was carried out by WGCNA and variation in pathway activity was determined in individual samples and groups of samples by Gene Set Variation Analysis (GSVA). Curated STRING-based protein-protein interaction analysis was carried out using MCODE in Cytoscape. Functional categories were defined using the BIG-C clustering algorithm.

**Results:**

Analysis of control or lupus neutrophil RNA expression datasets as well as lupus LDGs resulted in three WGCNA modules that are consistent across patient samples. Specifically, modules were identified that were positively correlated with LDGs but negatively correlated with lupus and normal neutrophils (or vice-versa). Two WGCNA modules were identified in the LDG to neutrophil comparison that were positively correlated (A, 334 genes; B, 92 genes). “A” contains genes related to platelet activation and adhesion. “B” contains genes classic for neutrophils and granulocytes. One module was negatively correlated (C, 82 genes) and contains genes related to nuclear transport and translational machinery. The most informative module was “B”. 41/92 of “B” genes have been described to characterize neutrophils/granulocytes (M2.2)\(^1\). 30/92 genes fall under the Neutrophil Granulation GO term and 13 of the 30 genes described by the Neutrophil Granulation GO term are contained in M2.2. An end goal of this analysis was to identify a group of genes that could be used to query whole blood, PBMC and tissue datasets for the presence of neutrophils and LDGs. WGCNA modules for whole blood and PBMC were compared to the LDG modules described above and GSVA was utilized to examine the consistency across patients. Module B containing LDG genes was found in 3/3 PBMC and 3/3 WB datasets by three measurements (gene overlap LDG module to PBMC or WB module, eigengene correlation with module “B” and eigengene correlation with clinical traits).

Assessing correlation of the log\(_2\) fold change of DE genes in the WGCNA “B” module with the test sets (PBMCs or WB) gives an \(r\) range of 0.6-0.8 (p value < 0.05) regardless of disease activity. Genes within modules “A” and “C” were not significantly correlated. This observation was not found for lupus-affected tissues.

**Conclusion:**

These results indicate that a discrete LDG module can be identified in the periphery of lupus patients. However, the contribution of these cells to tissue pathology is uncertain.

**Disclosure:** B. Keggereis, None; M. Catalina, None; N. Geraci, None; S. Heuer, None; P. Bachali, None; S. Madamanchi, None; P. E. Lipsky, None; A. Grammer, None.


**Abstract Number:** 297

**Multiplexed Characterization of Circulating and Joint-Derived Human Neutrophils in Inflammatory Arthritis**

**Ricardo Grieshaber Bouyer\(^1\), Olha Halyabar\(^2\), Anais Levescot\(^1\), Kacie Hoy\(^2\), Lauren Henderson\(^2\) and Peter Nigrovic\(^1,2\), \(^1\)Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, \(^2\)Division of Immunology, Boston Children's Hospital, Harvard Medical School, Boston, MA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** In innate Immunity and Rheumatic Disease Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Neutrophils are innate immune cells that play a central role in the initiation of inflammatory arthritis as well as mediating tissue damage. We
sought to improve our understanding of the role of neutrophils in joint inflammation using two multiplex discovery modalities. We characterized simultaneous circulating and transmigrated, joint-derived neutrophils from patients with inflammatory arthritis and blood from healthy controls via mass cytometry (CyTOF) and RNA-Seq with the goal of gaining new insights into the biology of neutrophils in inflamed environments.

Methods:

We established a biospecimen pipeline that allowed for both immediate processing as well as cryopreservation of fresh samples. Synovial fluid and simultaneous peripheral blood samples were obtained from seven consented patients with inflammatory joint disease. Purified neutrophils were cryopreserved and stained with metal-conjugated antibodies directed against 30 surface proteins including lineage markers, adhesion molecules, chemokine receptors, Fc- and complement receptors and immune checkpoints. Gene expression of freshly isolated neutrophils from inflammatory arthritis patients and healthy controls was examined via Smart-seq2. Each gene was modeled as a linear-mixed combination of donor- and group-specific effects using DESeq2.

Results:

Circulating and transmigrated neutrophils demonstrated fundamentally distinct gene- and surface protein expression. Joint-derived neutrophils exhibited an activated phenotype reflected by increased surface expression of integrins, adhesion molecules and chemokine receptors and increased transcription of complement receptor, TNF and CD69 among many others. Intriguingly, joint neutrophils overexpressed the adaptive immunity regulatory gene PD-L1 – confirmed by CyTOF – suggesting that they might also act to restrain pathological inflammation by negatively regulating T-cell function. We further identified 11 significantly enriched Gene Sets in joint neutrophils compared to blood, including TNF-α signaling, IFN-α response, IL-2 and IL-6 signaling. Confirmation studies are ongoing.

Conclusion:

Using multiplex discovery modalities, this study examined both circulating and joint-derived neutrophils in the context of joint inflammation. The dysregulated pathways identified suggest that neutrophils not only serve as effectors of immunity but also provide feedback that could potentially regulate adaptive immune responses.

Disclosure: R. Grieshaber Bouyer, None; O. Halyabar, None; A. Levescot, None; K. Hoyt, None; L. Henderson, None; P. Nigrovic, None.
BID (n = 5), or prednisolone 15 mg OD (n = 5) for 4 days. On the 4th day, acute inflammation was triggered by intradermal injection of ultraviolet light-killed *E. coli* on both the forearms of healthy subjects. Local inflammatory exudate was acquired into a suction blister raised at 4 hr on one forearm (onset time point) and at 10 hr on the contralateral forearm (resolution time point). Inflammatory exudate was analyzed for soluble mediators and immune cells. Blood flow to the site of inflammation was monitored by laser doppler.

**Results:** Anabasum exerted a profound anti-inflammatory effect in this model by accelerating the resolution phase of the innate immune response. Anabasum: increased blood flow during the resolution phase at 10 hours; reduced IL-8 and neutrophils in blister exudate 10 hours post-challenge, as did prednisolone; reduced the proinflammatory lipid mediators LTB4, PGF₂α, TxB₂ and PGE₂; increased the SPMs lipoxins (LXA₄, LXB₄) and resolvins (RvD1, RvD3, RvD5); and hastened bacterial clearance, whereas prednisolone slowed bacterial clearance during the resolution phase (resolution toxic).

<table>
<thead>
<tr>
<th>Exudate content</th>
<th>Hours</th>
<th>Placebo</th>
<th>Anabasum 5 mg BID</th>
<th>Anabasum 20 mg BID</th>
<th>Prednisolone 15 mg QD</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-8, pg/ml</td>
<td>4</td>
<td>5931 (923)</td>
<td>3299 (773)</td>
<td>3024 (1235)</td>
<td>4289 (1375)</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>3241 (784)</td>
<td>1679 (602)</td>
<td>2007 (515)</td>
<td>2267 (543)</td>
</tr>
<tr>
<td>Neutrophils/ml x 10⁶</td>
<td>4</td>
<td>262 (71)</td>
<td>55 (17)</td>
<td>66 (16)</td>
<td>72 (25)</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>244 (101)</td>
<td>120 (52)</td>
<td>72 (21)</td>
<td>69 (16)</td>
</tr>
<tr>
<td>Macrophage CD163 intensity</td>
<td>4</td>
<td>705 (244)</td>
<td>1420 (460)</td>
<td>711 (277)</td>
<td>5233 (2145)</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>2383 (478)</td>
<td>3610 (968)</td>
<td>3338 (744)</td>
<td>5427 (1381)</td>
</tr>
<tr>
<td>Endotoxin, relative units</td>
<td>4</td>
<td>14.6 (4.2)</td>
<td>5.3 (2.0)</td>
<td>6.8 (4.3)</td>
<td>17.2 (5.3)</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>5.0 (3.3)</td>
<td>6.9 (4.5)</td>
<td>5.9 (2.7)</td>
<td>11.5 (3.2)</td>
</tr>
</tbody>
</table>

**Conclusion:** Anabasum has novel biologic effects on infection-induced innate immune responses as it exerts a striking anti-inflammatory effect greater than that of prednisone and leading to timely resolution of inflammation. This activity offers promise for anabasum in the treatment of SSc.

**Disclosure:** M. Motwani, None; F. Bennett, None; M. Tepper, Corbus Pharmaceuticals, I,Corbus Pharmaceuticals, 3; B. White, Corbus Pharmaceuticals, I,Corbus Pharmaceuticals, 3; P. Norris, None; R. MacAllister, None; C. Serhan, None; D. Gilroy, None.


**Abstract Number:** 299

**Bik Plays an Important Role of Cell Proliferation Caused By Nitric Oxide in Rheumatoid Arthritis Synovium**

Takeshi Ueha¹, Yoshitada Sakai¹, Kohjin Suzuki², Koji Fukuda³, Toshihisa Maeda³, Hanako Nishimoto³, Shinya Hayashi⁴, Yasushi Miura⁴, Ryosuke Kuroda³ and Akira Hashiramoto², ¹Division of Rehabilitation Medicine, Kobe University Graduate School of Medicine, Kobe, Japan, ²Department of Biophysics, Kobe University Graduate School of Health Sciences, Kobe, Japan, ³Department of Orthopaedic Surgery, Kobe University Graduate School of Medicine, Kobe, Japan, ⁴Orthpaedic Surgery, Kobe University Graduate School of Medicine, Kobe, Japan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Innate Immunity and Rheumatic Disease Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Nitric oxide (NO), a proinflammatory mediator responsible for various physiological processes, plays a central role in the pathogenesis of rheumatoid arthritis (RA). As a heme-based sensor for NO, a transcription factor neuronal PAS domain protein 2 (NPAS2) forms a heterodimer with clock gene BMAL1. Using RA fibroblast-like synoviocytes (-FLS), we previously reported the interaction of clock genes and Bcl-2-interacting killer (Bik) which was known to be an inducer of mitochondrial apoptosis, and the promoter site of Bik has the NPAS2/BMAL1 heterodimer binding enhanced box sites (E-box sites). In this study, we evaluated the role of NPAS2 in RA synovium in views of relationship between NO and Bik.
Methods: The synovium were obtained during total knee replacement surgery from patients. Immunohistochemistry was performed to determine NPAS2 expression in synovial tissue. Cell proliferation was assessed with WST-8 assay in RA-FLS, using varying concentrations of the NO donor, S-Nitroso-N-acetyl-DL-penicillamine (SNAP) (0-20 nM). To evaluate the relationship between NPAS2 and BIK, NPAS2-siRNA was used to measure BIK mRNA expression in the absence and presence (5, 20 nM) of SNAP in RA-FLS. Moreover, we cloned the three BIK promoters (see Figure1), made luciferase assay model, and measured the luciferase activity in the absence and presence of SNAP in RA-FLS.

Results: NPAS2 expression was observed in RA synovium. Cell proliferation was significantly increased by SNAP. In the presence of SNAP, BIK mRNA expression was significantly reduced in the control-siRNA group, but not in the NPAS2-siRNA group (Figure 2, *; P < 0.05). In the presence of SNAP, the luciferase activity was significantly reduced in the Bik-E2-promoter group, but not in the Bik-E0-promoter group (Figure 3, *; P < 0.05).

Conclusion: NPAS2 enhance Bik expression, and NO inhibited Bik expression by NPAS2. These results suggests that NO may inhibit NPAS2 to bind E-box of Bik promoter. We propose a novel action of NO that inhibits mitochondrial apoptosis of RA-FLS by preventing the binding between NPAS2 and BIK. Therefore, we suggested that the inhibition of NO and NPAS2 may clinically be potential of anti-hyperproliferation and anti-bone destruction in RA synovium.
The DNA-Binding Protein ARID3a Is Associated with Interferon Alpha Production in Lupus Patient Plasmacytoid Dendritic Cells and Neutrophils

Michelle Ratliff1, Joshua Garton1,2, Indra Adrianto3, Ambra Pastori4, Courtney Montgomery5, Patrick Gaffney4, Judith A. James3,6 and Carol Webb1,7,8,1 Medicine, University of Oklahoma Health Sciences Center, Oklahoma City, OK, 2Chemistry, University of Oklahoma, Oklahoma City, OK, 3Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 4Arthritis and Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, 5Arthritis & Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, 6Department of Pathology, University of Oklahoma Health Sciences Center, Oklahoma City, OK, 7Cell Biology, University of Oklahoma Health Sciences Center, Oklahoma City, OK, 8Microbiology and Immunology, University of Oklahoma Health Sciences Center, Oklahoma City, OK

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Innate Immunity and Rheumatic Disease Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: We previously demonstrated over-expression of the DNA-binding protein ARID3a in peripheral blood B lymphocytes from patients with systemic lupus erythematosus (SLE) compared to healthy controls. In addition, we found that ARID3a is induced in healthy control blood cells in response to toll receptor signaling, and specifically to CpG stimuli. Furthermore, ARID3a expression was associated with interferon alpha production in a subset of B lymphocytes from both CpG-stimulated healthy controls and SLE patients. Therefore we hypothesized that ARID3a might also be associated with interferon alpha production in other cell types that secrete interferons.

Methods: De-identified peripheral blood samples were obtained via our IRB approved protocol from SLE patients (classified via ACR criteria) and healthy age-matched control participants of the Oklahoma Rheumatic Diseases Core Center. Peripheral blood mononuclear cells were isolated over ficoll gradients and either subjected directly to immunofluorescence staining and flow cytometry analyses, or they were first subjected to magnetic bead enrichment for neutrophils or plasmacytoid dendritic cells (pDCs). Purified pDCs and neutrophils were subjected to RNA-seq and were evaluated for gene expression patterns in relation to ARID3a levels.
**Results:** Linear regression analyses demonstrated strong associations between ARID3a expression and interferon production in pDCs and neutrophils in SLE patients. In addition, ARID3a expression in those cell types was associated with increased SLE disease activity indices. Surprisingly, interferon subtypes were heterogeneous in neutrophils and pDCs. Gene expression data showed increased interferon-associated transcripts in patients with increased ARID3a protein expression.

**Conclusion:** Our data indicate co-expression of ARID3a and interferon in SLE patient blood cells may be linked to interferon signatures observed in SLE.

**Disclosure:** M. Rattliff, None; J. Garton, None; I. Adrianto, None; A. Pastori, None; C. Montgomery, None; P. Gaffney, None; J. A. James, None; C. Webb, None.


**Abstract Number:** 301

**MiR-221-3p Overexpression Impairs Anti-Inflammatory Activity of TLR4-Stimulated M2-Macrophages**

Lilian Quero1,2, Andre Tiaden1,2 and Diego Kyburz2,3, 1Department of Biomedicine, Experimental Rheumatology, University of Basel, Basel, Switzerland, 2Rheumatology, University Hospital Basel, Basel, Switzerland, 3Department of Biomedicine, Experimental Rheumatology, University of Basel, 4051 Basel, Switzerland

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Sunday, November 5, 2017
**Session Title:** Innate Immunity and Rheumatic Disease Poster I
**Session Type:** ACR Poster Session A
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** MicroRNAs (miRNAs) have been shown to contribute to the inflammatory response in rheumatoid arthritis (RA) and several of these miRNAs have been found to be dysregulated in synovial tissue, synovial fluid or plasma of RA patients. In addition, also inflammatory cells such as macrophages, which are infiltrating the synovium and promoting the pannus generation, exhibit an aberrant miRNA expression. As toll-like receptors (TLRs) play a pivotal role in RA, we conducted a study to explore the role of TLRs in regulating the expression of miRNAs in macrophages under conditions prone to RA. Based on a miRNA-screen in TLR-stimulated M1- and M2-macrophages we selected several potential candidates for further studies, among them miR-221-3p. We then compared the release of inflammatory versus anti-inflammatory cytokines upon miR-221-3p overexpression or inhibition in stimulated M1- and M2-macrophages.

**Methods:** Monocytes were isolated from buffy coats of 8 healthy donors by CD14 microbead separation and differentiated into M1 and M2 by culturing them in the presence of 50ng/ml GM-CSF and M-CSF, respectively, for 6 to 8 days. Subsequently, cells were stimulated for 8.5 or 24 hours with TLR2/3/4 ligands Pam3, PolyIC or LPS. Cytokine release was measured by ELISA and miRNA expression by qRT-PCR. For miRNA mimic and inhibition studies, cells were transfected with corresponding pre-miR or antagomir using lipofectamine for 72 hours prior to the stimulation of M1- and M2-macrophages with TLR ligands.

**Results:** The general outcome of the miRNA-screen showed that a higher proportion of the tested miRNAs were downregulated in M2 macrophages upon stimulation with TLR ligands Pam3 and LPS. The basal expression level of miR-221-3p was similar in M1- and M2-macrophages, however, stimulation with LPS and PolyIC resulted in a prominent downregulation of miR-221-3p only in M2-macrophages. In M1-macrophages LPS caused only a slight decrease of miR-221-3p expression. Since several recent studies detected higher miR-221-3p levels in serum of RA patients and also in synovium of an induced RA-mouse model, we checked how macrophages respond to aberrant miR-221-3p levels under inflammatory conditions. Overexpression or inhibition of miR-221-3p showed no effect in unchallenged M1- or M2-macrophages on the secretion of IL-6, IL-8 or IL-10. However, miR-221-3p overexpression in combination with LPS stimulation, but not Pam3 or PolyIC, significantly increased IL-6 and IL-8 cytokine secretion in M2 macrophages. In contrast, the same combinatorial treatment (LPS + miR-221-3p overexpression) significantly decreased the IL-10 secretion in M2 macrophages.

**Conclusion:** We herein demonstrate that aberrant miR-221-3p expression is significantly downregulating the anti-inflammatory activity of TLR4-stimulated M2-macrophages by decreasing the ratio of secreted IL-10/IL-6 and IL-10/IL-8. Thus, abundant miR-221-3p might contribute to promote and sustain the chronically inflammatory conditions apparent in disease settings such as RA synovial tissue by deregulating the pro-/anti-inflammatory cytokine profile of synovial macrophage subpopulations.

**Disclosure:** L. Quero, None; A. Tiaden, None; D. Kyburz, None.
Mir-221-3p overexpression impairs anti-inflammatory activity of TLR4-stimulated M2 macrophages.
From Monocytes to Macrophages: the Pathogeneses of Spontaneous Inflammatory Arthritis in CD11c-Flip-KO (HUPO) Mice

Qi Quan Huang1, Renee E. Doyle2, Philip J. Homan1, Harris Perlman3, Deborah R. WInter3 and Richard M. Pope2, 1Division of Rheumatology, Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, 2Medicine/Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL, 3Department of Medicine Division of Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Innate Immunity and Rheumatic Disease Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
We have generated a CD11c-Flip-KO mouse line (HUPO) that spontaneously develops erosive arthritis with incidence 70-80% at age ≥20 weeks. This study aimed at understanding the role of monocytes in HUPO arthritis and to define the molecular changes during differentiation to macrophages in the inflamed joint compared with controls.

Methods:
Arthritis was evaluated by clinical score. Cell types from blood and ankle joints are determined by flow cytometry. Cell proliferation are determined by BrdU incorporation and populations of cells were isolated for RNAseq.

Results:
Circulating monocytes, defined as CD45+CD11b+CD115+F4/80lo, were further characterized as classical (CM), Ly6C+CD62L+, or non-classical (NCM), Ly6C−CD62L−. CM were markedly increased in HUPO mice with arthritis and positively correlated with arthritis severity. 70-90% of CM are also CCR2+ in HUPO mice with arthritis, similar to that in control mice. In contrast, in the HUPO mice without arthritis, only 0-7% of these cells are CCR2+, and the CM numbers were normal. Monocytes recently recruited into synovium are defined as CD45+Ly6C+CD64+CD11b+F4/80intLy6C−MHCII−. This population demonstrated reduced CD115 and increase F4/80 compared with CMs. Within 24 hours after BrdU injection, in both HUPO and control mice, >60% of these Ly6C+MHCII− macrophages incorporated BrdU, comparable to CM and bone marrow monocytes. In contrast, < 1% in NCM incorporated BrdU. In HUPO mice during further differentiation the macrophages became Ly6C+MHCII+ and then Ly6C−MHCII+, with less BrdU incorporation in the more differentiated cells. A similar transition was observed in the control mice except the Ly6C+MHCII+ population was not identified. CMs and F4/80int macrophages were isolated for RNAseq. In the controls, clusters of differentially expressed genes were identified in CMs, and Ly6C+MHCII+ and Ly6C−MHCII+ joint macrophages. For example Immune response and leukocyte activation were increase in CMs while cell cycle and cell division were increased in Ly6C+MHCII+ macrophages. There were differences in these transcriptional profiles of the macrophages subset between HUPO and control mice, including those regulating cell cycle and differentiation as well as for monocyte differentiation and antigen processing.

Conclusion:
These observations demonstrate that during chronic inflammation, CMs enter the joints and undergo macrophage differentiation during homeostasis and chronic inflammation. The differences in transcriptional profiles between the control and HUPO mice will provide important insights into the mechanisms contributing to chronic inflammation.

Disclosure: Q. Q. Huang, None; R. E. Doyle, None; P. J. Homan, None; H. Perlman, None; D. R. WInter, None; R. M. Pope, None.

Outcomes after Hip Fracture in the Elderly: Does Social Isolation Matter?

Lisa A. Mandl¹, Omar Halawa², Jackie Szymonifka³, Kirsten Grueter⁴, and Joseph Lane⁵
¹Rheumatology, Hospital for Special Surgery Weill Cornell Medical College, New York, NY, ²Hospital for Special Surgery, New York, NY, ³Rheumatology, Hospital for Special Surgery, New York, NY, ⁴Orthopaedic Surgery, Hospital for Special Surgery, New York, NY, ⁵Orthopaedic Surgery, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY
First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Orthopedics, Low Back Pain and Rehabilitation Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Hip fractures are a serious public health issue with a significant population burden, especially among those over 65 years old. Social isolation—how integrated a patient is into his/her community—is a novel and potentially modifiable risk factor for poor health outcomes after low trauma hip fracture. This study evaluates the association of pre-operative social isolation with death, short-term complications and patient-reported functional recovery in elderly patients 3 months following surgical repair of low-trauma hip fracture.

Methods: The Lubben Social Networks Scale-18 (LSNS-18), a validated instrument specifically designed to measure social isolation in the elderly, PROMIS-29, which measures patient-reported outcomes, and the Lower Extremity Activity Scale (LEAS), which measures physical function, were administered to cognitively intact patients ≥ 65 years old with no active cancer, 2-4 days after surgical repair of hip fracture. Patients were specifically asked about their pre-fracture status. Patients were contacted 1 and 3 months after surgery and asked about adverse events and hospitalizations. The LSNS-18, PROMIS-29 and the LEAS were administered again at 3 months.

Results: 109 patients were enrolled, 72.5% female, 92.7% white, 78% college educated with a mean age of 80.7± 8.5 years. 45% of patients enrolled were socially isolated. Of the 109 patients enrolled, 19 had adverse events including pulmonary emboli, hypotension, hypoxia, urinary tract infection, peri-prosthetic fracture, CHF exacerbation, cholecystitis, lower extremity cellulitis, falls, wound dehiscence and duodenal ulcers. 5 patients died within the first 3 months. Of the 76 patients eligible for 3 month follow-up, 63 (83%) completed 3-month questionnaires. A higher proportion of socially isolated patients died by 3 months (8.2% vs. 1.7%), although this was not statistically significant (p=0.172). There was no statistically significant difference between socially isolated and non-socially isolated patients in short-term complications, or PROMIS-29 and LEAS scores 3 months after surgery.

Conclusion: There is a positive trend suggesting social isolation is associated with 3-month mortality in elderly patients undergoing surgical repair of low trauma hip fracture. There was no association between social isolation and short-term complications or self-reported short-term functional recovery. Whether social isolation is associated with longer term functional outcomes or mortality is unknown. Recruitment for this study is ongoing and all subjects will be studied for up to 1 year following surgery.

Disclosure: L. A. Mandl, None; O. Halawa, None; J. Szymonifka, None; K. Grueter, None; J. Lane, None.


Usefulness of Consecutive Doppler Ultrasound Examinations for Detecting Deep Venous Thrombosis during the Perioperative Period in Patients with Osteoporotic Fractures of the Proximal Femur

Ken Nakaseko and Norihiro Mayumi, Department of Orthopaedic Surgery and Rheumatology, Kuwana City Medical Center, Kuwana Mie, Japan
First publication: September 18, 2017

SESSION INFORMATION
Background/Purpose: Deep venous thrombosis (DVT) can lead to a venous thromboembolism and increase the risk of a pulmonary thromboembolism (PE). PE is one of the most common causes of death in hospitalized surgical patients. Although there have been some prospective studies regarding the prevalence of DVT on Doppler ultrasound examinations of the lower extremities, there have not been any prospective studies in which three consecutive Doppler ultrasound examinations were performed to detect DVT during the perioperative period. The purpose of the present study was to prospectively evaluate the occurrence of DVT in patients with osteoporotic fractures of the proximal femur, based on the results of examinations involving three consecutive ultrasound scans. In addition, the usefulness of the D-dimer level as a predictor of DVT was investigated.

Methods: This study was a single-center prospective study. Eighty-seven patients (14 males and 73 females) between the ages of 46 and 95 years with osteoporotic fractures of the proximal femur were enrolled. All patients were asymptomatic in terms of their clinical DVT findings. Three Doppler ultrasound examinations of the lower extremities were conducted in each case: on admission, one day before surgery, and one week after surgery. The period from admission to surgery ranged from 2 to 7 days (mean: 5.3 days). The D-dimer level was measured at one week after surgery and its relationship with the presence/absence of DVT was evaluated by calculating sensitivity, specificity, positive predictive, and negative predictive values.

Results: DVT was detected in 16 patients (2 patients on admission, 8 patients one day before surgery, and 6 patients one week after surgery). The overall prevalence of DVT in the perioperative period was 18.4% (16/87). As for the characteristics of the patients that did and did not develop DVT, there were no significant differences between the two groups. When the D-dimer cut-off level was set at 4.3 μg/ml, the sensitivity and negative predictive value reached 100%, while the specificity was 15.5%, and the positive predictive value was 21.1%. A receiver operating characteristic (ROC) curve was drawn, and the optimal D-dimer cut-off level was examined. The ROC curve was closest to the upper left corner when the D-dimer cut-off level was 12.2 μg/ml. At that point, the sensitivity, specificity, positive predictive value, and negative predictive value were 62.5%, 70.4%, 32.3%, and 89.3%, respectively.

Conclusion: In this prospective study, DVT was detected in 2 patients on admission, 8 patients one day before surgery, and 6 patients one week after surgery. As DVT can occur at any moment, performing repeated Doppler ultrasound examinations in the perioperative period is useful for quickly detecting DVT, which can cause PE. As for the D-dimer level, its sensitivity and negative predictive value reached 100% at a cut-off level of 4.3 μg/ml. Therefore, D-dimer assays could be a useful screening tool for DVT and might be a suitable substitute for Doppler ultrasound examinations.

Disclosure: K. Nakaseko, None; N. Mayumi, None.


Abstract Number: 305

Ultrasonographic Evaluation of the Femoral Cartilage, Achilles Tendon and Plantar Fascia in Young Women Wearing High-Heeled Shoes

Ayşen Akinci1, Kamal Mezian2, Ayşe Merve Ata1, Murat Kara1, Şule Şahin Onat3, Eda Gürçay4, Aslı Çalışkan1, Maria Ines Taboas Simoes5 and Levent Özşakar1, 1Hacettepe University Medical School Department of Physical Medicine and Rehabilitation, Ankara, Turkey, 2Czech Technical University in Prague, Faculty of Biomedical Engineering, Department of Health Care Disciplines and Population Protection, Kládno, Czech Republic, 3Ankara Physical Medicine and Rehabilitation Training and Research Hospital, Ankara, Turkey, 4Gaziler Physical Medicine and Rehabilitation Training and Research Hospital, Ankara, Turkey, 5PMR hospitalar assistant in Centro Hospitalar Entre Douro e Vouga, E.P.E, Portugal

First publication: September 18, 2017
Background/Purpose: Wearing high-heeled shoes (HHS) may include structural and functional abnormalities due to repetitive stress particularly in the knee and forefoot. The aim of this study was to investigate whether the distal femoral cartilage, Achilles tendon and plantar fascia were different between healthy young women wearing HHS and flat shoes.

Methods: A total of 91 healthy women (aged 20-45 years) participated in this cross-sectional study. Women wearing shoes with a heel height of >5cm were enrolled in the HHS group, and those wearing shoes with a heel height of <1.4 cm were included in the flat shoes group. Femoral cartilage from the lateral femoral condyle (LFC), intercondylar area and medial femoral condyle (MFC), and Achilles tendon and plantar fascia thicknesses were measured by using ultrasound.

Results: There were 34 women (mean age; 31.1±6.4 years, BMI; 21.6±2.3 kg/m^2) in the HHS group and 57 women (mean age; 29.5±7.3 years, BMI; 22.5±3.4 kg/m^2) in the control group (both p>0.05). In group comparisons, thicker right MFC and left Achilles tendon were obtained in the HHS group (both p<0.05). Between group comparisons yielded thicker left Achilles tendon in the HHS group than the flat shoes group (p<0.05). Plantar fascia thicknesses were similar both within and between group comparisons (both p>0.05). Right Achilles tendon thickness was positively correlated with right (r=0.469, p=0.005) and left (r=0.402, p=0.018) plantar fascia thicknesses only within the HHS group.

Conclusion: Wearing HHS resulted in thickening of the right MFC and left Achilles tendon in women wearing HHS which might definitely be interpreted as secondary to chronic overload. Our results may provide an understanding of the morphological changes with wearing HHS and recommend that this "social" issue that exists in women's lives be investigated further to reveal the musculoskeletal consequences.

Disclosure: A. Akinci, None; K. Mezian, None; A. M. Ata, None; M. Kara, None; Ş. Şahin Onat, None; E. Gürçay, None; A. Çalışkan, None; M. I. Taboas Simoes, None; L. Özçakar, None.


Abstract Number: 306

Relationship between Inflammatory Anterior or Posterior Arch MRI Abnormalities and Clinical Data in Low Back Pain Patients

Helene Braun1, Clement Geniez1, Yannick Degboe2, Arnaud Constantin3, Alain Cantagrel4, Delphine Nigon5, Marie Faruch-Bilfeldl and Adeline Ruyssen-Witrand4, 1Purpan Hospital, Toulouse, France, 2Department of Rheumatology, Purpan Hospital, Toulouse III University, Toulouse, France, 3Department of Rheumatology, Purpan Hospital, Toulouse III University, Toulouse, France, 4Rheumatology, Purpan Hospital, Toulouse III University, Toulouse, France, 5CHU Purpan, Toulouse, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Orthopedics, Low Back Pain and Rehabilitation Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: To compare demographic characteristics, characteristics of pain and functional status according to the presence of inflammatory anterior or posterior arch MRI abnormalities in low back pain (LBP) patients.

Methods: Design: Monocentric cross-sectional study. Patients: Chronic LBP patients with a lumbar spine MRI planned in the Toulouse Hospital Radiology Center were prospectively selected and filled a standardized questionnaire to get clinical data. MRI: STIR and T1 sagittal images from 3 and 1.5 Tesla MRI going up to T8-T9 stages were reviewed by two experienced rheumatologists, blinded from the diagnosis and clinical data. Inflammatory anterior arch abnormalities (IAAA: i.e.: MODIC I or II, inflammatory corner lesions) and inflammatory posterior arch abnormalities (IPAA: i.e.: pedicle edema, transverse and spinous process edema, interspinous process edema, costo-transverse or zygapophyseal joint arthropathy) were collected. Analyses: Clinical data (age, sex, disease duration, ODI, pain VAS, inflammatory pain, NSAIDs efficacy) were compared according to the presence/absence of IAAA or IPAA by Chi2 or Wilcoxon tests.

Results: Ninety-five patients were included in this study, 66 have IPAA. Inter and intra-observer agreement was excellent (κ=0.938). The most prevalent IPAA was zygapophyseal joint arthritis (62.5%), then 31.9% patients have interspinous process edema, 9.7% pedicle edema and 4.2% spinous process edema. Patients with IPAA had more frequently Modic I and/or II lesions than patients without
IPAA (39.2% versus 9.5%, p=0.01). There was no statistically significant association between IPAA presence and clinical data, including pain characteristics. IPAA seemed to be more prevalent in women (62.1% versus 41.4%, p=0.06), in patients with longer pain duration (6 years versus 4.75 years, p=0.22), with morning stiffness more than 30 minutes (42.4% versus 24.1%, p=0.2), and with better NSAID response (65.9% versus 55%, p=0.35). Furthermore, patients with Modic I had a better response to NSAIDs (90% versus 52%, p=0.04). Patients with Modic II seemed to be older than patients without Modic (66 years versus 43 years, p=0.0004). Modic I was often associated with IPAA at the same vertebral stage.

**Conclusion:** The most prevalent IPAA in patients with LBP was zygapophyseal joint arthritis. Modic I and/or II were more prevalent when patients have IPAA. There was no significant association between IPAA presence and clinical data. However, NSAIDs had a better efficacy in patients with Modic I, and Modic I was often associated with IPAA at the same vertebral stage.

**Disclosure:** H. Braun, None; C. Geniez, None; Y. Degboe, None; A. Constantin, None; A. Cantagrel, None; D. Nigon, None; M. Faruch-Bilfeld, None; A. Ruyssen-Witrand, None.


**Abstract Number:** 307

**Biochemical Intervertebral Disc Alterations in Patients with Low Back Pain and Radiculopathy**

Philipp Sewerin¹, Christoph Schleich², Ruben Sengewein³, Matthias Schneider⁴ and Benedikt Ostendorf⁴, ¹Department and Hiller Research-Unit for Rheumatology, Heinrich-Heine University, Düsseldorf, Germany, ²Dep. for diagnostic and interventional Radiology, Heinrich-Heine University, Duesseldorf, Germany, ³Department and Hiller Research Unit for Rheumatology, Heinrich-Heine University, Düsseldorf, Germany, ⁴Policlinic for Rheumatology & Hiller Research Centre for Rheumatology, Heinrich-Heine-University Duesseldorf, Duesseldorf, Germany

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Orthopedics, Low Back Pain and Rehabilitation Poster

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** To assess the glycosaminoglycan (GAG) content of lumbar intervertebral discs (IVD) in patients with low back pain (LBP) and radiculopathy using glycosaminoglycan chemical exchange saturation transfer imaging (gagCEST).

**Methods:** 258 lumbar IVDs of 53 participants, 21 healthy volunteers, 19 patients with LBP and 13 patients with radiculopathy (28 female; 25 male; mean age: 45.5 ± 16.7 years; range: 23 - 83 years), were examined with a 3T MRI scanner. Biochemical gagCEST imaging was used to determine the GAG content of each nucleus pulposus (NP) and annulus fibrosus (AF).

**Results:** Significantly reduced gagCEST values of NP were found in patients with LBP and/or radiculopathy (p < 0.0001) compared to healthy control group. NP gagCEST values were significantly lower in patients with LBP (p < 0.0001) and radiculopathy (p = 0.0005) compared to healthy volunteers, respectively. We saw an association between pain and GAG loss with significantly lower gagCEST values in participants with dorsal pain at examination day (p = 0.0004) and higher pain scores (p < 0.0001) compared to participants without LBP. Participants with body mass index ≥ 25 revealed lower gagCEST values compared to participants with BMI < 25 (p = 0.02).

**Conclusion:** GagCEST analysis indicated significantly lower GAG values of NP in patients with LBP or radiculopathy, in participants with elevated BMI, current pain at examination day and elevated pain scores.

**Disclosure:** P. Sewerin, None; C. Schleich, None; R. Sengewein, None; M. Schneider, None; B. Ostendorf, None.

Frequency, Morbidity and Healthcare Utilization of Diffuse Idiopathic Skeletal Hyperostosis (DISH) Patients at a University Hospital

Maanas Tripathi1, Divya Rajmohan2, Cody Quirk3, Brooke Beckett3, Donseok Choi4, Neha Rich-Garg5 and Atul A. Deodhar4,
1University of Miami, FL, Miami, FL, 2Oregon Health & Sciences University, Portland, OR, 3Radiology, Oregon Health & Science University, Portland, OR, 4Oregon Health & Science University, Portland, OR, 5Northwest Rheumatology Assoc., Portland, OR

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Orthopedics, Low Back Pain and Rehabilitation Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
DISH is a non-inflammatory condition affecting the spine, and characterized by ossification of paravertebral ligaments. DISH is traditionally considered asymptomatic, detected incidentally on spine radiographs. We investigated the frequency of DISH diagnosis, the associated morbidity and healthcare utilization by patients attending our university hospital.

Methods:
Our University’s radiology database was searched from years 2005 to 2015 for the words “DISH” or “diffuse idiopathic skeletal hyperostosis” in the recorded results of spinal radiographs. Patients from the year 2015 whose spinal radiographs mentioned these words were selected for further analysis. Their spinal radiographs were re-read by two authors. Patients were divided into those who fulfilled the Resnick Criteria for DISH (Group A), and those who did not fully meet the criteria but had radiographic features suggestive of DISH (Group B). Means and proportions were used to describe variables, for group comparisons, T-test and c2 were used. A p-value less than 0.05 was considered statistically significant. All computations were done in the R statistical program.

Results:
Between 2005-2015, 3439 radiology records had DISH mentioned as a diagnosis. Out of 196 patients diagnosed with DISH in 2015, 153 fulfilled the Resnick criteria (Group A), 41 didn’t fulfill the criteria but were diagnosed as DISH by the radiologists (Group B), and 2 had erroneous diagnoses. The Table shows the comparison between the two groups. Thoracic radiographs where DISH was mentioned were more likely to fulfill the Resnick criteria than not (35% vs 15%) compared to other radiographs (p < 0.03). Chronic back pain was very common in both groups, and more often reported in Group B than Group A (81% vs. 63%, p = 0.04). Back pain was the reason for performing the initial diagnostic radiograph in 45% of Group A and 61% of Group B. A substantial portion of patients required opioid medications for pain control (51%), spinal surgery (31%), and consultations with various specialists for regional pain (57%). Health care interventions were similar in both groups.

Conclusion:
DISH is a common diagnosis with significant morbidity, despite being commonly considered to be an asymptomatic condition. Majority of DISH patients had chronic back pain, required opioid medication, and a large proportion required spinal surgery. Future research is needed to systematically assess the healthcare utilization by DISH patients.

Table: Comparison of DISH patients: those fulfilling Resnick criteria vs. not fulfilling Resnick criteria but diagnosed by radiologists (ns = not significant)
<table>
<thead>
<tr>
<th>Variable</th>
<th>Group A: Resnick Criteria fulfilled (n = 153)</th>
<th>Group B: Resnick Criteria not fulfilled (n = 41)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years (mean)</td>
<td>70.6</td>
<td>62.4</td>
<td>(p &lt; 0.01)</td>
</tr>
<tr>
<td>Male Gender</td>
<td>110 (72%)</td>
<td>33 (28%)</td>
<td>(p = ns)</td>
</tr>
<tr>
<td>BMI</td>
<td>32.34</td>
<td>32.83</td>
<td>(p = ns)</td>
</tr>
<tr>
<td>Chronic Back Pain</td>
<td>96 (63%)</td>
<td>33 (81%)</td>
<td>(p = 0.04)</td>
</tr>
<tr>
<td>Type 2 Diabetes Mellitus</td>
<td>19 (12%)</td>
<td>3 (7%)</td>
<td>(p = ns)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>33 (22%)</td>
<td>8 (20%)</td>
<td>(p = ns)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>19 (12%)</td>
<td>5 (12%)</td>
<td>(p = ns)</td>
</tr>
<tr>
<td>Gout</td>
<td>10 (7%)</td>
<td>2 (5%)</td>
<td>(p = ns)</td>
</tr>
<tr>
<td>Type of Radiograph</td>
<td>2 (1%)</td>
<td>1 (3%)</td>
<td>(p = 0.03)</td>
</tr>
<tr>
<td>Spinal Survey</td>
<td>12 (8%)</td>
<td>6 (15%)</td>
<td></td>
</tr>
<tr>
<td>Cervical</td>
<td>11 (22%)</td>
<td>0 (NA)</td>
<td></td>
</tr>
<tr>
<td>Thoracolumbar</td>
<td>53 (35%)</td>
<td>6 (15%)</td>
<td></td>
</tr>
<tr>
<td>Thoracic</td>
<td>68 (45%)</td>
<td>26 (66%)</td>
<td></td>
</tr>
<tr>
<td>Lumbar</td>
<td>3 (2%)</td>
<td>0 (NA)</td>
<td></td>
</tr>
<tr>
<td>Sacroiliac</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reason for X-ray</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DISH</td>
<td>5 (3.3%)</td>
<td>0 (NA)</td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>69 (45%)</td>
<td>25 (61%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>78 (51%)</td>
<td>16 (39%)</td>
<td></td>
</tr>
<tr>
<td>Opioid Use</td>
<td>77 (54%)</td>
<td>22 (50%)</td>
<td>(p = ns)</td>
</tr>
<tr>
<td>Bisphosphonate Use</td>
<td>1 (1%)</td>
<td>0 (0%)</td>
<td>(p = ns)</td>
</tr>
<tr>
<td>Spinal Surgery</td>
<td>46 (31%)</td>
<td>14 (34%)</td>
<td>(p = ns)</td>
</tr>
<tr>
<td>Spinal Pumps</td>
<td>1 (1%)</td>
<td>0 (0%)</td>
<td>(p = ns)</td>
</tr>
<tr>
<td>Consultations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neurology</td>
<td>8 (6%)</td>
<td>3 (8%)</td>
<td>(p = ns)</td>
</tr>
<tr>
<td>Orthopedics</td>
<td>59 (42%)</td>
<td>23 (59%)</td>
<td></td>
</tr>
<tr>
<td>Rheumatology</td>
<td>7 (5%)</td>
<td>2 (5%)</td>
<td></td>
</tr>
<tr>
<td>Physical Medicine and Rehabilitation</td>
<td>5 (4%)</td>
<td>1 (3%)</td>
<td></td>
</tr>
</tbody>
</table>

Disclosure: M. Tripathi, None; D. Rajmohan, None; C. Quirk, None; B. Beckett, None; D. Choi, None; N. Rich-Garg, Pfizer Inc, 2; A. A. Deodhar, AbbVie, Amgen, Eli Lilly, GlaxoSmithKline, Janssen, Novartis, Pfizer, UCB Pharma, 2; Eli Lilly, Janssen, Novartis,
Compression Assisted Arthrocentesis and Intraarticular Injection

James Bennett1, Tej Bhavsar1, Romy Cabacungan2, Sabeen Yaqub1, Monthida Fangtham3, N. Suzanne Emil1, Roderick Fields4, Konstantin Konstantinov5, Arthur Bankhurst6, William Hayward7, and Wilmer Sibbitt Jr.3, 1Internal Medicine, Division of Rheumatology, University of New Mexico Health Sciences Center, Albuquerque, NM, 2Internal Medicine, Division of Rheumatology, University of New Mexico, Albuquerque, NM, 3Rheumatology, University of New Mexico, Albuquerque, NM, 4Internal Medicine/Rheumatology, University of New Mexico School of Medicine, Albuquerque, NM, 51 University Of New Mexico, University of New Mexico, Albuquerque, NM, 6Rheumatology, University of NM Medical Center, Albuquerque, NM, 7Exercise and Sport Sciences, New Mexico Highlands University, Las Vegas, NM

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Orthopedics, Low Back Pain and Rehabilitation Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

We hypothesized that compression assisted arthrocentesis of the knee would improve arthrocentesis fluid yields and intraarticular injection outcomes.

Methods:

We performed conventional arthrocentesis on 215 painful knees, both with and without effusions prior to injection. Subsequently a constant compression device (a commercially available elastomeric brace positioned or modified so classic arthrocentesis portals could be utilized) was placed and arthrocentesis was performed on 215 painful knees. In all cases, post arthrocentesis, 1mg/kg of triamcinolone acetonide (60-80 mg total, 80 mg maximum) was injected into each knee. Arthrocentesis fluid yield and time to the next flare were measured. The data were compared using Student's T-test.

Results:

The demographics of the study groups were similar. Fluid yield for complete arthrocentesis with constant compression was greater (by 230%) than the conventional technique: constant compression 5.3±11.2 ml, conventional 1.6±6.4 ml (difference 3.7 ml, CI of difference 1.9757 <3.7< 5.4243, p<0.00001). Fluid yield was also increased in the effusive knee subgroup (by 166%): constant compression (n = 38) 26.6±113.4 ml, conventional (n=37) 10.0±13.3 ml (p<0.00001)(Figure 1). Time to flare was 35% longer in the subjects treated with constant compression 6.9±3.5 months as opposed to conventional treatment 5.1±2.7 months (p<0.00001)(Figure 2). The prolonged effect of constant compression was present in both the effusive knee (30% longer, p<0.02) and the non-effusive knee (38% longer, p<0.01).

Figure 1:
Conclusion:

Constant compression of the knee results in greater arthrocentesis fluid yield and improved injection outcomes in both the effusive and non-effusive knee. We hypothesize that more accurate needle placement, forced extrusion of interstitial fluid and cytokines from compressed tissues, and more complete removal of fluid decrease inflammatory cells and cytokines and increase intraarticular drug concentrations, resulting in improved outcomes. Constant compression of the knee is a straightforward and effective quality improvement intervention for knee arthrocentesis and intraarticular injection.

Disclosure: J. Bennett, None; T. Bhavsar, None; R. Cabacungan, None; S. Yaqub, None; M. Fangtham, None; N. S. Emil, None; R. Fields, None; K. Konstantinov, None; A. Bankhurst, None; W. Hayward, None; W. Sibbitt Jr., None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/compression-assisted-arthrocentesis-and-intraarticular-injection

Abstract Number: 310

Comparison of Flexed and Extended Knee Arthrocentesis and the Role of Constant Compression
Sabeen Yaqub1, Tej Bhavsar1, Romy Cabacungan2, James Bennett1, Monthida Fangtham3, N. Suzanne Emil1, Roderick Fields4, Konstantin Konstantinov5, Arthur Bankhurst6, Luke Haseley7 and Wilmer Sibbitt Jr.3, 1Internal Medicine, Division of Rheumatology, University of New Mexico Health Sciences Center, Albuquerque, NM, 2Internal Medicine, Division of Rheumatology, University of New Mexico, Albuquerque, NM, 3Rheumatology, University of New Mexico, Albuquerque, NM, 4Internal Medicine/ Rheumatology, University of New Mexico School of Medicine, Albuquerque, NM, 51 University Of New Mexico, University of New Mexico, Albuquerque, NM, 6Rheumatology, University of NM Medical Center, Albuquerque, NM, 7Department of Physiotherapy and Exercise Physiology, Curtin University, Perth, Australia

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Orthopedics, Low Back Pain and Rehabilitation Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The objective of this study was to determine whether extended versus flexed knee position is superior for arthrocentesis.

Methods: 55 clinically effusive knees with osteoarthritis underwent arthrocentesis: 20 knees in the extended knee position using the lateral superior approach, and 35 knees in the flexed knee position using the inferolateral approach. Conventional arthrocentesis maneuvers including manual compression were used and fluid yield in milliliters measured. After fluid return ceased in the flexed knee, constant compression was applied using an elastomeric knee brace on the superior knee and additional fluid yield recorded. The measurement data were compared using the Student test.

Results: Fluid yield for arthrocentesis with the extended knee was greater (191% greater) than the flexed knee: extended knee: 16.9±15.7 ml, flexed knee 5.8±6.3 ml (difference 11.1 ml, CI 0.91 <8.8< 16.7, p<0.02). After constant compression to the flexed knee fluid yields were identical (1% different): extended knee: 16.9±15.7 ml, flexed knee 16.7±11.3ml (difference -0.2 ml, 95% CI 11.09 <-2.7< 5.6, p=0.73).

Conclusion: The extended knee lateral approach is superior to the flexed knee approach for conventional arthrocentesis. However, when constant compression is applied, the two approaches have identical fluid yields. This new flexed knee constant compression technique is particularly useful for patients who cannot get onto the examining table, who are in wheelchairs, have flexion contractures, or who cannot otherwise extend their knee.

![Figure 1: Fluid yields in extended and flexed knee positions](image-url)
Total Ankle Arthroplasty for Rheumatoid Arthritis Cases in This Biologics Era: Mid to Long-Term Follow-up

Makoto Hirao¹, Jun Hashimoto², Hideki Tsuboi³, Kosuke Ebina⁴ and Hideki Yoshikawa⁵, ¹Orthopaedic Surgery, Osaka University, Graduate School of Medicine,Suita, Japan, ²Rheumatology/Orthopaedics, Osaka-Minami Medical Ctr, Kawachinagano, Japan, ³Orthopaedics/Rheumatology, Osaka Rosai Hospital, Sakai, Japan, ⁴Orthopaedics, Osaka University Graduate School of Medicine, Suita, Japan, ⁵Department of Orthopedics, Osaka University Graduate School of Medicine, Suita Osaka, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Orthopedics, Low Back Pain and Rehabilitation Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

**Background/Purpose:** Outcomes after total ankle arthroplasty (TAA) combined with additive techniques (augmentation of bone strength, control of soft tissue balance, adjustment of the loading axis) for destructive rheumatoid arthritis (RA) cases were evaluated after mid to long-term follow-up. The influences of biologic treatment on the outcomes after TAA were also evaluated.

**Methods:** A retrospective observational study was completed involving 50 RA cases [mean follow-up period: 7.1 years] who underwent TAA. RA foot ankle scales were administered using the Japanese Society for Surgery of the Foot (JSSF) standard rating system, and a postoperative self-administered foot evaluation questionnaire (SAFE-Q) was also checked at final follow-up. Radiographic findings were also checked.

**Results:** This procedure significantly improved the clinical scores of the JSSF RA foot and ankle scales. Of 50 ankles, 48 had no revision TAA surgery. Prosthesis sinking at the talus side was seen in 8 ankles (6 ankles in biologics group, 2 ankles in non-biologics group); 2 required revision TAA. The social functioning score of the SAFE-Q scale at final follow-up was significantly higher in the biologic treatment group than in the non-biologic group. The biologic treatment group showed a significantly lower rate of prednisolone usage (12%) than the non-biologic treatment group (71%), and disease activity was significantly improved in the biologic treatment group at final follow-up.

**Conclusion:** TAA is recommended for RA cases, if disease control, augmentation of bone strength, control of soft tissue balance, and adjustment of loading axis are taken into account. Withdrawal of the steroid in biologics treatment might have a good effect on the durability of prostheses in long-term observation in the perspective of bone-mineral structure. Biologics treatment contributed to increase social activity after TAA in RA cases. So, prevention of talar component sinking for RA cases with such higher social activity should be further discussed and resolved in this biologics era.

**Disclosure:** M. Hirao, None; J. Hashimoto, None; H. Tsuboi, None; K. Ebina, Chugai Pharmaceutical, Eisai, Ono Pharmaceutical, Mitsubishi Tanabe Pharma, UCB Japan, 8; H. Yoshikawa, Chugai Pharmaceutical, Eisai, Ono Pharmaceutical, Mitsubishi Tanabe Pharma, Phizer, Astellas Pharma, 2.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/total-ankle-arthroplasty-for-rheumatoid-arthritis-cases-in-this-biologics-era-mid-to-long-term-follow-up](http://acrabstracts.org/abstract/total-ankle-arthroplasty-for-rheumatoid-arthritis-cases-in-this-biologics-era-mid-to-long-term-follow-up)

Abstract Number: 312

**Rates of Total Joint Replacement Utilization in the U.S.: Future Projections to 2020-2040 Using the National Inpatient Sample**

Jasvinder A. Singh and Shaohua Yu, University of Alabama at Birmingham, Birmingham, AL

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Sunday, November 5, 2017
Session Title: Orthopedics, Low Back Pain and Rehabilitation Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

**Background/Purpose:** To project the future utilization of total hip and knee joint arthroplasty (THA, TKA).

**Methods:** We used the 2000-2010 U.S. National Inpatient Sample combined with Census Bureau data to develop projections for primary and revision THA and TKA from 2020 to 2040 using negative binomial regression.

**Results:** Predicted total annual counts for THA and TKA utilization in the U.S. by 2020, 2025, 2030 and 2040 are (in thousands): primary THA, 527 (95% CI, 495, 561), 765 (95% CI, 712, 823), 1087 (95% CI, 999, 1184) and 2040 (95% CI, 1828, 2081); primary TKA, 1611 (95% CI, 1531, 1699), 2675 (95% CI, 2516, 2847); 4306 (95% CI, 4008, 4632) and 10314 (95% CI, 9391, 11343); revision THA 56 (95% CI, 51, 61), 68 (95% CI, 61, 76), 82 (95% CI, 72, 93) and 204 (95% CI, 183, 228); and revision TKA, 153 (95% CI, 140, 168), 250 (95% CI, 226, 279), 399 (95% CI, 353, 452) and 1031 ((95% CI, 939, 1134) (Figures 1 and 2). The utilization is projected to increase for both females and males (Figure 3), all age groups and all race/ethnicities (data not shown).

**Conclusion:** Significant increases in THA and TKA utilization are expected in the future. A policy change may be needed to meet increased demand.
FIGURES

Figure 1. The projected annual total utilization of primary total hip arthroplasty (THA) and total knee arthroplasty (TKA) procedures (in thousands) in the United States from 2020 to 2040

Figure 2. The projected annual total utilization of revision total hip arthroplasty (THA) and total knee arthroplasty (TKA) procedures (in thousands) in the United States from 2020 to 2040

Figure 3. The projected annual total utilization of primary total Knee arthroplasty (TKA) procedures in the United States from 2020 to 2040 by sex

Disclosure: J. A. Singh, Takeda and Savient, 2,Savient, Takeda, Regeneron, Merz, Iroko, Bioiberica, Crealta/Horizon and Allergan pharmaceuticals, WebMD, UBM LLC and the American College of Rheumatology., 5JAS serves as the principal investigator for an investigator-initiated study funded by Horizon pharmaceuticals through a grant to DINORA, Inc., a 501 (c)(3) entity., 9JAS is a member of the executive of OMERACT, an organization that develops outcome measures in rheumatology and receives arms-length funding from 36 companies., 9JAS is the editor and the Director of the UAB Cochrane Musculoskeletal Group Satellite Center on Network Meta-analysis., 9Jas is a member of the American College of Rheumatology's (ACR) Annual Meeting Planning Committee (AMPC); Chair of the ACR Meet-the-Professor, Workshop and Study Group Subcommittee., 9a member of the Veterans Affairs Rheumatology Field Advisory Committee, 9; S. Yu, None.
Abstract Number: 313

The Effect of Obesity on Walking; Comparison of the Spatiotemporal, Kinematic and Kinetic Parameters of Young Obese and Non-Obese Healthy Women

Erkan Kilic, Gamze Kilic and Fatma Inanici

Rheumatology Clinic, Afyonkarahisar State Hospital, Afyon, Turkey, Physical Medicine and Rehabilitation, Afyon Kocatepe University, Faculty of Medicine, Afyon, Turkey, Physical Medicine and Rehabilitation, Hacettepe University, Faculty of Medicine, Ankara, Turkey

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Orthopedics, Low Back Pain and Rehabilitation Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Obesity is a risk factor for development of knee osteoarthritis due to altered gait biomechanics. Gait analysis was performed mostly on older obese adults with knee osteoarthritis. Biomechanics of young obese individuals is unclear. The aim of this study was to investigate the effect of obesity on gait biomechanics in young women; and the relationship between obesity and occurrence of knee osteoarthritis.

Methods: 31 healthy normal-weighted and 31 obese women aged between 30-45 years and body mass indexes (BMI) between 30-40 kg/m2 were included in this study. Anthropometric measurements like body weight (BW), height, waist/hip ratios were measured. Skinfold thickness (SFT) was measured from right side of the body. Isokinetic quadriceps and hamstring muscle strengths were measured at 60°/s angular velocity and 0-90° joint range of motion. Body composition analyses were determined before breakfast. Gait analyses were performed by Vicon 612 gait analyses system with the subjects’ comfortable walking speed.

Results: Mean age of obese group was 39.4 years and control group was 35.8 years (p>0.05). Circumferences and SFT, body fat ratio, fat free mass (FFM) found higher in obese group (p<0.001) and there was a strong relation between fat ratio and circumferences (r =0.89), BMI (r=0.85) and SFT (r=0.83). When peak torque were normalized to BW, Isokinetic quadriceps and hamstring muscle strengths were significantly lower in obese individuals (p<0.001). Walking speed, single support time, step length and stride length were lower and stance phase, double support time and step width was higher in obese individuals (p<0.001). In obese group we found that total excursion of pelvic obliquity, hip rotation and knee flexion-extension angle was lower (p<0.001), knee varus moment (p<0.05) and second peak of vertical ground reaction force was higher in obese group (p<0.001).

Conclusion: In obese subjects, isokinetic quadriceps and hamstring muscles strengths were lower, knee and hip joint range of motion was diminished. Knee peak varus moment and vertical ground reaction force at the end of stance phase were significantly higher in obese group. These results suggest that obesity may contribute to knee osteoarthritis. Thus, prospective studies are needed to identify the influence of higher loading rates on knee osteoarthritis.

Disclosure: E. Kilic, None; G. Kilic, None; F. Inanici, None.

Abstract Number: 314

Effects of Exercise on Anxiety in Adults with Arthritis: A Systematic Review with Meta-Analysis

George Kelley, Kristi Kelley and Leigh F. Callahan

Biostatistics, West Virginia University, Morgantown, WV, Thurston Arthritis Research Center, University of North Carolina at Chapel Hill, Chapel Hill, NC

First publication: September 18, 2017
Background/Purpose: Previous randomized controlled trials have led to conflicting findings regarding the effects of exercise on anxiety in adults with arthritis and other rheumatic diseases (AORD). The purpose of this study was to use the meta-analytic approach to try and resolve these discrepancies.

Methods: The \textit{a priori} inclusion criteria were: (1) randomized controlled trials, (2) exercise (aerobic, strength training, or both) $\geq 4$ weeks, (3) comparative control group, (4) adults $\geq 18$ years of age with osteoarthritis, rheumatoid arthritis or fibromyalgia, (5) published and unpublished studies in any language since January 1, 1981, (6) anxiety as an outcome assessed. Studies were located by searching 8 electronic databases, cross-referencing and expert review. Dual selection of studies and data abstraction were performed. Hedge’s standardized effect size ($g$) was calculated for each result and pooled using the recently developed inverse-heterogeneity (IVhet) model. Non-overlapping 95% confidence intervals were considered statistically significant. Heterogeneity was estimated using $Q$ and $I^2$ with alpha values $< 0.10$ for $Q$ considered statistically significant. Small-study effects were examined using funnel plots and Egger’s regression test. In addition, the number-needed-to-treat (NNT), percentile improvement, and subgroup analyses were conducted. Risk of bias was assessed using the Cochrane Risk of Bias Assessment Instrument. Training program characteristics were reported as mean +/- standard deviation.

Results: Of the 639 citations screened, 14 studies representing 926 initially enrolled participants (539 exercise, 387 control) met the criteria for inclusion. Length of training averaged 15.8 +/- 6.7 weeks, frequency 3.3 +/- 1.3 times per week and duration 28.8 +/- 14.3 minutes per session. Overall, statistically significant exercise minus control reductions in anxiety were found ($g = -0.40$, 95% CI, $-0.65$, $-0.15$, $\tau^2 = 0.14$; $Q = 40.3$, $p = 0.0004$; $I^2 = 62.8\%$). The NNT was 6 with a percentile improvement of 15.5% and an estimated 5.3 million inactive US adults with AORD improving their anxiety if they started exercising regularly. Statistically significant small-study effects were observed ($p < 0.0001$). No between-group differences in anxiety were observed between type of arthritis and type of exercise. All studies were considered to be at high risk of bias with respect to blinding of participants to group assignment. Given the lack of information provided, greater than 50% of studies were at an unclear or high risk of bias with respect to (1) incomplete outcome reporting (78.6%), (2) allocation concealment (78.6%), and (3) blinding of outcome assessors (57.1%).

Conclusion: Exercise is associated with reductions in anxiety among adults with AORD. However, a need exists for additional, well-designed, randomized controlled trials on this topic.

Disclosure: G. Kelley, None; K. Kelley, None; L. F. Callahan, None.


Abstract Number: 315

Efficacy of a Wearable-Enabled Physical Activity Counselling Program for People with Knee Osteoarthritis

Linda Li\textsuperscript{1}, Eric C. Sayre\textsuperscript{2}, Navi Grewal\textsuperscript{2}, Juliane Chien\textsuperscript{2}, Greg Noonan\textsuperscript{3}, Ryan Falck\textsuperscript{1}, John Best\textsuperscript{4}, Teresa Lii-Ambrose\textsuperscript{1}, Alison Hoens\textsuperscript{5}, Valerie Gray\textsuperscript{6}, Karen Tsui\textsuperscript{7}, Wendy Watson\textsuperscript{6} and Lynne Feehan\textsuperscript{8}, \textsuperscript{1}Department of Physical Therapy, University of British Columbia, Vancouver, BC, Canada, \textsuperscript{2}Arthritis Research Canada, Richmond, BC, Canada, \textsuperscript{3}Mary Pack Arthritis Program, Vancouver General Hospital, Vancouver, BC, Canada, \textsuperscript{4}University of British Columbia, vancouver, BC, Canada, \textsuperscript{5}BC SUPPORT Unit, Vancouver, BC, Canada, \textsuperscript{6}OASIS Program, Vancouver Coastal Health Authority, Vancouver, BC, Canada, \textsuperscript{7}Fraser Health Authority, Surrey, BC, Canada, \textsuperscript{8}Rehabilitation Program, Fraser Health Authority, Surrey, BC, Canada

First publication: September 18, 2017
Background/Purpose: Current guidelines emphasize an active lifestyle in the management of knee osteoarthritis (OA), but up to 90% of OA patients are inactive. Several modifiable risk factors are associated with low physical activity participation, including lack of motivation, doubts about effectiveness of exercise, and lack of health professional advice regarding ways to adjust their activities based on symptoms. Our study aimed to assess the efficacy of a wearable-enabled physical activity counselling program for improving activity participation and disease status in people with knee OA.

Methods: Eligible participants had a self-reported knee OA diagnosis, or symptoms of knee OA based on a validated questionnaire. After baseline assessment and randomization, the Immediate Intervention Group (II) received group education, a Fitbit, and 4 biweekly phone calls by a physiotherapist to counsel activity goals over a 2-month period. The Delayed Intervention (DI) Group received the program 2 months later. Participants were assessed at baseline (T0) and the end of 2, 4 and 6 months (T1, 2, and 3). Outcome measures included: 1) mean moderate/vigorous physical activity (MVPA) time measured with a SenseWear® monitor; 2) mean daily step count; 3) mean sedentary behaviour time; 4) Knee Injury & OA Outcome Score (KOOS). Analysis of covariance (ANCOVA) was used to evaluate the effect of the group type on the outcome measures at T1, 2, and 3, after adjusting for T0. We assessed three planned contrasts of changes: 1) compared T0–T1 between the two groups to determine if II was superior to DI (the control); 2) compared T0–T2 in II against T0–T3 in DI; 3) compared T0–T2 in II against T1–T3 in the DI. The last 2 models assessed whether the two-month delay had an impact on the effect of the intervention.

Results: In 2015–2016, we recruited 61 participants (II: n=30, 73% women; DI: n=31, 90% women). Both groups were similar in age (II: 61.3 (9.4) years; DI: 62.1 (SD 8.5)) and body mass index [II: 29.2 (5.5); DI: 29.2 (4.8)]. Figure 1 summarizes the results. Pre-specified contrast analyses revealed a significant effect whereby the II group improved in the MVPA time at T0–T1 compared to the DI (contrast coefficient: 25.2; 95% CI 5.5, 44.9; p = 0.01). A significant effect was also found in the mean daily steps at T0–T1 (contrast coefficient: 1,519; 95% CI 256.2, 2,782.3; p = 0.02). We found no significant effect in any outcome measures in the other contrast analyses.

Table 1: Results of outcome measures

<table>
<thead>
<tr>
<th></th>
<th>Immediate Intervention Group</th>
<th>Delayed Intervention Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 30)</td>
<td>(n = 31)</td>
</tr>
<tr>
<td>Mean</td>
<td>T0 62.1</td>
<td>T0 65.3</td>
</tr>
<tr>
<td>MVPA time [mins]</td>
<td>T1 75.5</td>
<td>T1 49.6</td>
</tr>
<tr>
<td></td>
<td>T2 62.6</td>
<td>T2 60.1</td>
</tr>
<tr>
<td></td>
<td>T3 65.6</td>
<td>T3 70.7</td>
</tr>
<tr>
<td>daily steps [mins]</td>
<td>(54.6)</td>
<td>(77.4)</td>
</tr>
<tr>
<td></td>
<td>(54.3)</td>
<td>(46.8)</td>
</tr>
<tr>
<td></td>
<td>(56.3)</td>
<td>(76.8)</td>
</tr>
<tr>
<td></td>
<td>(48.5)</td>
<td>(71.9)</td>
</tr>
<tr>
<td>Mean</td>
<td>T0 7,069.2</td>
<td>T0 7,556.6</td>
</tr>
<tr>
<td>sedentary time [mins]</td>
<td>(3,375.3)</td>
<td>(6,713.6)</td>
</tr>
<tr>
<td></td>
<td>(3,095.5)</td>
<td>(7,631.9)</td>
</tr>
<tr>
<td></td>
<td>(3,420.7)</td>
<td>(7,573.6)</td>
</tr>
<tr>
<td></td>
<td>(3725.6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(5,054.1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(3,354.3)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(4,054.3)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(4,477.1)</td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>T0 66.2</td>
<td>T0 65.1</td>
</tr>
<tr>
<td></td>
<td>(16.1)</td>
<td>(14.5)</td>
</tr>
<tr>
<td></td>
<td>(15.6)</td>
<td>(14.7)</td>
</tr>
<tr>
<td></td>
<td>(14.7)</td>
<td>(15.3)</td>
</tr>
<tr>
<td></td>
<td>(17.2)</td>
<td>(14.5)</td>
</tr>
<tr>
<td></td>
<td>(19.1)</td>
<td>(19.8)</td>
</tr>
<tr>
<td>ADL</td>
<td>T0 67.5</td>
<td>T0 74.1</td>
</tr>
<tr>
<td></td>
<td>(17.5)</td>
<td>(17.2)</td>
</tr>
<tr>
<td></td>
<td>(17.5)</td>
<td>(17.9)</td>
</tr>
<tr>
<td></td>
<td>(15.8)</td>
<td>(16.4)</td>
</tr>
<tr>
<td>Sports &amp; recreation</td>
<td>T0 47.3</td>
<td>T0 47.0</td>
</tr>
<tr>
<td></td>
<td>(19.8)</td>
<td>(18.9)</td>
</tr>
<tr>
<td></td>
<td>(24.9)</td>
<td>(17.6)</td>
</tr>
<tr>
<td></td>
<td>(25.6)</td>
<td>(17.9)</td>
</tr>
<tr>
<td></td>
<td>(26.3)</td>
<td>(16.3)</td>
</tr>
<tr>
<td></td>
<td>(27.7)</td>
<td>(16.8)</td>
</tr>
<tr>
<td>Qol</td>
<td>T0 61.7</td>
<td>T0 63.4</td>
</tr>
<tr>
<td></td>
<td>(16.1)</td>
<td>(16.7)</td>
</tr>
<tr>
<td></td>
<td>(15.6)</td>
<td>(14.5)</td>
</tr>
<tr>
<td></td>
<td>(14.7)</td>
<td>(15.3)</td>
</tr>
<tr>
<td></td>
<td>(17.2)</td>
<td>(19.8)</td>
</tr>
<tr>
<td></td>
<td>(17.5)</td>
<td>(17.2)</td>
</tr>
<tr>
<td></td>
<td>(17.6)</td>
<td>(16.5)</td>
</tr>
<tr>
<td></td>
<td>(15.9)</td>
<td>(15.2)</td>
</tr>
<tr>
<td></td>
<td>(15.8)</td>
<td>(16.4)</td>
</tr>
</tbody>
</table>

Conclusion: Our wearable-enabled counselling program improved MVPA time and step counts in people with a diagnosis or symptoms of knee OA. The finding is important since an active lifestyle is recognized as an important component of successful self-management.

Disclosure: L. Li, None; E. C. Sayre, None; N. Grewal, None; J. Chien, None; G. Noonan, None; R. Falck, None; J. Best, None; T. Liu-Ambrose, None; A. Hoens, None; V. Gray, None; K. Tsui, None; W. Watson, None; L. Feehan, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/efficacy-of-a-wearable-enabled-physical-activity-counselling-program-for-people-with-knee-osteoarthritis
Pain, Fatigue and Function in Patients with Ehlers-Danlos Syndrome and Hypermobility Spectrum Disorder – Relationship with Perceived Benefits and Barriers to Exercise

Leslie Soever1, Laura Passalent2, Ahmed Omar3 and Medha Soowamber4, 1Toronto General Hospital, Toronto, ON, Canada, 2Allied Health, Toronto Western Hospital, Toronto, ON, Canada, 3Rheumatology, Toronto Western Hospital, University of Toronto, Toronto, ON, Canada, 4University Health Network, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: ARHP Orthopedics, Low Back Pain and Rehabilitation Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The Ehlers-Danlos Syndromes (EDS) are a heritable group of connective tissue disorders with predominant features including joint hypermobility, skin hyperextensibility and tissue fragility. Hypermobility Spectrum Disorders (HSD) include all phenotypes presenting with joint hypermobility plus one or more of its secondary manifestations but not satisfying the criteria for EDS (Castori, 2017). Common symptoms reported by patients with EDS and HSD include pain and fatigue, resulting in decreased function, including lack of exercise. It has been shown that patients with EDS and HSD overall improve with exercise interventions (Palmer, 2014). The purpose of this study was to explore relationships between self-reported pain, fatigue, and function; with perceived benefits and barriers to exercise.

Methods: A retrospective chart review was completed on 38 consecutive patients with either EDS or HSD to determine if there were any relationships between the scores for pain (high scores indicate greater pain), fatigue (high scores indicate greater fatigue), and function (low scores indicate greater function), as per the Multi-Dimensional Health Assessment Questionnaire (MD-HAQ); and the total score (high scores indicate more positive perception of exercise), benefits score (high scores indicate more positive perception of exercise), and barriers score (high scores indicate greater perception of barriers to exercise) on the Exercise Benefits and Barriers Scale (EBBS). These instruments were administered to patients as part of routine care to assist with treatment planning and recommendations. Descriptive statistics and univariate analysis (Pearson correlation coefficients) were used to determine if relationships existed between self-reported pain, fatigue, and function; and perceived benefits scores, barriers scores, and total EBBS scores reported by patients.

Results: The majority of the sample was female (96%); and the average age was 33.5 years. According to the 2017 International Classification for EDS, 23 patients had EDS (hypermobility type n=20; classical type n=1; vascular type n=1; kyphoscoliotic type n=1) and 15 patients had HSD. Overall, EBBS scores indicated high perceived value of exercise. There was no relationship between fatigue (r = -0.143; p = 0.39) nor pain (r = -0.192; p = 0.25) with total EBBS scores. However, the higher patients reported their level of function, the higher were their total EBBS scores (r = 0.392; p = 0.015). Similarly, higher function scores, correlated with higher total benefits scores (r = 0.383; p = 0.018); and patients who reported higher function reported fewer perceived barriers to exercise (r = -0.44; p = 0.006).

Conclusion: These results support previously reported importance of exercise in the management of patients with EDS and HSD; and further highlight the critical role of programs to educate patients, with EDS and HSD regarding the importance of exercise, who are experiencing difficulty with function.

Disclosure: L. Soever, None; L. Passalent, None; A. Omar, None; M. Soowamber, None.


Risk Factors for Blood Transfusions Following Total Joint Arthroplasty in Patients with Rheumatoid Arthritis
Elizabeth Salt, Andrew Johannemann, Amanda T. Wiggins, Mary Kay Rayens, Katelyn Brown, Kate Ekmann and Leslie Crofford, University of Kentucky, Lexington, KY, Nursing, University of Kentucky, Lexington, KY, College of Nursing, University of Kentucky, Lexington, KY, Rheumatology, Vanderbilt University School of Medicine, Nashville, TN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: ARHP Orthopedics, Low Back Pain and Rehabilitation Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Risk Factors for Blood Transfusions Following Total Joint Arthroplasty in Patients with Rheumatoid Arthritis

Abstract

Background/Purpose: Despite effective therapies, rheumatoid arthritis (RA) can result in joint destruction requiring total joint arthroplasty to maintain patient function. An estimated 16% to 70% of those undergoing total joint arthroplasty of the hip or knee will receive a blood transfusion. Few studies have described risk factors for blood transfusion following total joint arthroplasty in patients with RA. The purpose of this study is to identify demographic and clinical risk factors associated with receiving a blood transfusion following total joint arthroplasty among patients with RA.

Methods: A retrospective study ($N=3,270$) was conducted using de-identified patient health claims information from a commercially-insured, U.S. dataset (2007-2009). Data analysis included descriptive statistics and multivariate logistic regression.

Results: Females were more likely to receive a blood transfusion (Odds ratio [OR]=1.48; 95% Confidence Interval [CI]: 1.16-1.87; $p=.001$). When compared to those in the South, patients residing the Midwest were less likely to receive a blood transfusion following total joint arthroplasty (OR=0.56, 95% CI: 0.44-0.71). Relative to those receiving total knee arthroplasty, patients who underwent total hip arthroplasty were more likely to receive a blood transfusion (OR=1.39, 95% CI: 1.14-1.70), and patients who underwent a total shoulder arthroplasty were less likely to receive a blood transfusion (OR=0.14 and 95% CI: 0.05-0.38; $p<.001$). Patients with a history of anemia were more likely to receive a blood transfusion compared to those who did not have this diagnosis (OR=3.30, 95% CI: 2.62-4.14; $p<.001$).

Conclusion: Risk factors for the receipt of blood transfusions among RA patients who have undergone total joint arthroplasty were identified.

Disclosure: E. Salt, None; A. Johannemann, None; A. T. Wiggins, None; M. K. Rayens, None; K. Brown, None; K. Ekmann, None; L. Crofford, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/risk-factors-for-blood-transfusions-following-total-joint-arthroplasty-in-patients-with-rheumatoid-arthritis

Abstract Number: 318

A Randomized Alendronate-Controlled Trial of Romosozumab: Results of the Phase 3 Active-Controlled Fracture Study in Postmenopausal Women with Osteoporosis at High Risk

Kenneth Saag, Jeffrey Petersen, Maria Luisa Branci, Andrew Karaplis, Mattias Lorentzon, Thierry Thomas, Judy Maddox, Michelle Fan, Paul D. Meisner and Andreas Grauer, University of Alabama, Birmingham, AL, Amgen Inc., Thousand Oaks, CA, University of Florence, Florence, Italy, McGill University, Montreal, QC, Canada, University of Gothenburg and Sahlgrenska University Hospital, Mölndal, Sweden, CHU de Saint-Étienne, Saint-Étienne, France, UCB Pharma, Brussels, Belgium

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster I
Session Type: ACR Poster Session A
Background/Purpose: The bone forming agent romosozumab (Romo) was previously shown to reduce vertebral and clinical fractures in postmenopausal women with osteoporosis. Here we report the efficacy and safety results of the ARCH study (NCT01631214).

Methods: This multicenter double-blind study enrolled postmenopausal women age 55–90 years with osteoporosis and high fracture risk, defined as a BMD T-score ≤–2.5 at total hip [TH] or femoral neck [FN] and either ≥1 moderate/severe or ≥2 mild vertebral fractures, or a BMD T-score ≤–2.0 at TH or FN and either ≥2 moderate/severe vertebral fractures or a history of a recent hip fracture. Subjects were randomized 1:1 to 210mg Romo SC QM or 70mg alendronate (ALN) PO QW for 12 months, followed by open label 70mg ALN PO QW in both groups. Primary endpoints were subject incidence of new vertebral fracture through 24 months and clinical fracture through the primary analysis (PA). PA was performed when ≥330 clinical fractures had occurred and all subjects had completed the month 24 visit. Nonvertebral fracture at the PA was a secondary endpoint, as was BMD at the lumbar spine, TH, and FN at months 12 and 24. Hip fracture was evaluated as an additional secondary endpoint.

Results: 4093 women (mean age 74, mean TH T-score –2.8) were randomized to Romo or ALN. 12 months of Romo prior to ALN vs ALN alone significantly reduced new vertebral, clinical, nonvertebral, and hip fractures (Table). Treatment with Romo also significantly increased BMD at all sites measured, at months 12 and 24 vs ALN alone (Table). Overall adverse events were balanced between groups. During the open label ALN period, 6 subjects (2 Romo; 4 ALN) were positively adjudicated for AFF and 2 subjects (1 Romo; 1 ALN) for ONJ. Cardiovascular (CV) serious adverse events (SAEs) were independently adjudicated; at 12 months the subject incidence was 2.5% in the Romo group vs 1.9% in the ALN group with cardiac ischemic events at 0.8% vs 0.3% and cerebrovascular events at 0.8% vs 0.3%, respectively.

Conclusion: In postmenopausal women with osteoporosis, Romo 210mg QM followed by ALN significantly reduced new vertebral, clinical, nonvertebral, and hip fracture risk vs ALN alone, suggesting that in osteoporotic patients at high risk for fracture, a treatment regimen starting with Romo followed by ALN leads to superior fracture risk reduction over ALN alone. An observed imbalance in CV SAEs compared with ALN was not seen in the previous placebo-controlled 7180-patient FRAME study and is currently being evaluated.

Disclosure: K. Saag, Amgen, Merck, 2,Amgen, Merck, Radius, 5; J. Petersen, Amgen Inc., 1,Amgen Inc., 3; M. L. Brandi, Abiogen, Alexion, Amgen, Bruno Farmaceutici, Kyowa Kirin, Shire, SPA, 2,Abiogen, Alexion, Amgen, Bruno Farmaceutici, Kyowa Kirin, Shire, SPA, 5,Shire, 8; A. Karaplis, Amgen Canada, 2,Amgen Canada, 5,Amgen Canada, 8; M. Lorentzon, Consilient Health, Radius Health, 5,Amgen, Lilly, Meda, UCB, 9; T. Thomas, Amgen, Chugai/Roche, HAC-Pharma, LCA, MSD, Novartis, Pfizer, Servier, UCB, 2,Abbvie, Amgen, BMS, Chugai, HAC-Pharma, Expanscience, Gilead, Lilly, Medac, MSD, Pfizer, Teva, Thuasne, UCB, 5; J. Maddox, Amgen Inc., 1,Amgen Inc., 3; M. Fan, Amgen Inc., 1,Amgen Inc., 3; P. D. Meisner, UCB Pharma, 1; A. Grauer, Amgen Inc., 1,Amgen Inc., 3.

The Placebo-Controlled Fracture Study in Postmenopausal Women with Osteoporosis: The Foundation Effect of Rebuilding Bone with One Year of Romosozumab Leads to Continued Lower Fracture Risk after Transition to Denosumab

Felicia Cosman¹, Daria B Crittenden², Serge Ferrari³, Aliya Khan⁴, Nancy E Lane⁵, Kurt Lippuner⁶, Toshio Matsumoto⁷, Cassandra E Milmont², Cesar Libanati⁸ and Andreas Grauer², ¹Helen Hayes Hospital, West Haverstraw, and Columbia University, New York, NY, ²Amgen Inc., Thousand Oaks, CA, ³Geneva University Hospital, Geneva, Switzerland, ⁴McMaster University, Hamilton, ON, Canada, ⁵UC Davis Medical Center, Sacramento, CA, ⁶Osteoporosis Polyclinic, Inselspital, Bern University Hospital and University of Bern, Bern, Switzerland, ⁷University of Tokushima, Tokushima, Japan, ⁸UCB Pharma, Brussels, Belgium

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Romosozumab (Romo), a sclerostin antibody, has a dual effect of increasing bone formation and decreasing bone resorption. In the FRAME study, one year of Romo treatment resulted in large BMD increases at the lumbar spine and total hip versus placebo (PBO); the differences between groups remained after all subjects transitioned to denosumab (DMAb) during the second year of the study (Cosman NEJM 2016). Here, we further characterize the BMD gains during the FRAME study and the effect of building bone with Romo on fracture risk reduction upon transition to DMAb.

Methods: Subjects in FRAME (NCT01575834) were randomized to receive Romo 210 mg QM or PBO for 12 months, after which all subjects received DMAb 60 mg Q6M for an additional 12 months. Endpoints for the current analysis were mean change from baseline in BMD T-score, percent of subjects with a BMD gain, and subject incidence of fractures in the second year of the study, including new vertebral, clinical (nonvertebral plus symptomatic vertebral), and other fracture categories.

Results: There were 7180 subjects in the study (N=3589 Romo, N=3591 PBO). At month 12, mean change from baseline in lumbar spine BMD T-score was 0.88 for Romo and 0.03 for PBO; at month 24, after both treatment groups received DMAb in the second year, the mean change from baseline was 1.11 for Romo/DMAb and 0.38 for PBO/DMAb. At the total hip, the mean changes were 0.32 for Romo and 0.01 for PBO at month 12, with month-24 changes of 0.45 for Romo/DMAb and 0.17 for PBO/DMAb. 99% of subjects in the Romo group showed some increase in BMD at month 12, with 89% achieving ≥ 6% gains in lumbar spine BMD (Figure). Administration of Romo during the first year led to relative risk reductions in fractures between groups during the second year, despite both groups receiving DMAb in year two, with reductions of 81% for vertebral fractures (p < 0.001), 32% for clinical fractures (p = 0.052), and 39% for major osteoporotic fractures (p = 0.034).

Conclusion: Romo resulted in substantial T-score increases after one year; upon transition to DMAb, gains in both groups were similar, resulting in unprecedented BMD gains after treatment with Romo followed by DMAb. As a result of one year of Romo before transition to DMAb, fracture rates were substantially reduced during year two, when subjects in both groups received DMAb. The data support the clinical benefit of rebuilding the skeletal foundation with Romo treatment before transition to DMAb.
Teriparatide Compared with Risedronate and the Risk of Clinical Vertebral Fractures: 2-Year Results of a Randomized, Double-Dummy Clinical Trial

Cristiano A.F Zerbini¹, Piet Geusens², Eric Lespessailles³, Jean-Jacques Body⁴, Enrique Casado⁵, Jan Stepan⁶, David L Kendler⁷, Luis Russo⁸, Susan L. Greenspan⁹, Salvatore Minisola¹⁰, Alicia Bagur¹¹, Peter Lakatos¹², Astrid Fahrleitner-Pammer¹³, Rüdiger Möricke¹⁴, Pedro Lopez-Romero¹⁵ and Fernando Marin¹⁶, ¹Centro Paulista de Investigações Clinicas, São Paulo, Brazil, ²Maastricht University Hospital, Maastricht, Netherlands, ³Service de Rhumatologie, CHR d'Orléans, Orléans, France, ⁴CHU Brugmann, Free University Brussels, Brussels, Belgium, ⁵Rheumatology, University Hospital Parc Taulí, Sabadell, Spain, ⁶Institute of Rheumatology, Faculty of Medicine 1, Charles University, Prague, Czech Republic, ⁷University of British Columbia, Vancouver, BC, Canada, ⁸Centro de Analises e Pesquisas Clinicas LTDA., Rio de Janeiro, Brazil, ⁹University of Pittsburgh, Pittsburgh, PA, ¹⁰Internal Medicine, Policlinico Umberto I., Rome, Italy, ¹¹Centro de Osteopatías Comlit, Buenos Aires, Argentina, ¹²Department of Medicine, Semmelweis University, Budapest, Hungary, ¹³Division of Endocrinology, Medical University, Graz, Austria, ¹⁴Institut Präventive Medizin & Klinische Forschung, Magdeburg, Germany, ¹⁵Europe Research Center, Eli Lilly and Company, Madrid, Spain, ¹⁶Lilly Research Center Europe, Madrid, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster I  
Session Type: ACR Poster Session A  
Session Time: 9:00AM-11:00AM

Background/Purpose: The VERO trial was an active-controlled fracture endpoint clinical trial that recruited postmenopausal women with low bone mass and prevalent vertebral fractures (VFx). We have reported that the risk of new VFx and clinical fractures [a composite of clinical VFx and non-vertebral fragility fractures (NVFFx)] in patients treated with teriparatide (TPTD) compared with those treated with risedronate (RIS) was reduced by 56% and 52% respectively (p<.001 for each), with a non-significant reduction in NVFFx (34%, p=0.099). Here we present the pre-specified exploratory analysis of clinical vertebral fracture (ClinVFx) incidence over 24 months.

Methods: 1,360 postmenopausal women (680/arm; mean age: 72.1 years) with at least 2 moderate or 1 severe VFx and low bone mass (BMD T-score ≤ -1.5) were randomized to TPTD 20 µg sc/day or RIS (35 mg po/week) in a 2-year, double-blind, double-dummy trial. A ClinVFx was defined as an clinical episode associated with signs and symptoms suggestive of a VFx, such as acute onset of severe back pain, pain with little or no exertion or pain localised to a specific vertebra and associated with limited back mobility, confirmed with a new or worsened radiographic VFx (centrally adjudicated). A new vertebral fracture was radiologically defined as a loss of vertebral body height of at least 20% and 4 mm from the baseline radiograph by quantitative morphometry measurements, confirmed with a semiquantitative assessment (i.e.; the vertebral body also has an increase of 1 or more severity grade according to the Genant scale). Cumulative incidences of the first ClinVFx were obtained by Kaplan-Meier, and comparison was based on a stratified long-rank test. The stratified HR was computed from the log-rank test. Incidence rates, depicted as number of events per 100 patient-years, were also assessed.

Results: The mean (SD) number of prevalent VFx was 2.7 (2.1), 55.4% of the women had a BMD T-score <-2.5 (lowest value measured at the lumbar spine or hip), 36.5% a history of ClinVFx within the year before randomization, 27.9% were naïve to osteoporosis medications, and 57.9% were previously treated with bisphosphonates. A total of 31 women were diagnosed with an incident ClinVFx over the 24-month study duration: 7 women in the TPTD group (1.1%) compared to 24 women (3.9%) in the RIS group (hazard ratio: 0.29; 95% CI: 0.14-0.58; p=0.002) (Figure). The incidence rates (95% CI) were 0.58 (0.23-1.18) and 1.97 (1.27-2.91) events/patient-years in the TPTD and RIS treated subjects, respectively (p=0.004).

Conclusion: In postmenopausal women with severe osteoporosis, TPTD treatment for 24 months significantly reduced by 71% the risk of new clinical vertebral fractures compared with RIS.

Disclosure: C. A. F. Zerbini, Eli Lilly and Company, 2; P. Geusens, Pfizer, Abbott, Lilly, Amgen, MSD, Roche, UCB, BMS, Novartis, 5; E. Lespessailles, Abbvie, Amgen, Lilly, MSD, UCB, 2; J. J. Body, Eli Lilly and Company, 2; E. Casado, None; J. Stepan, None; D. L. Kendler, Amgen, Lilly, Astra-Zeneca, Astellas, UCB, 5; L. Russo, None; S. L. Greenspan, Eli Lilly and Company, 2; S. Minisola, Abiogen, Amgen, Diasorin, Lilly, Italfarmaco, Fujii, MSD, Takeda, 5; A. Bagur, None; P. Lakatos, None; A. Fahrleitner-Pammer, Amgen, Alexion, BMS, Lilly, Fresenius, 8; R. Möricle, None; P. Lopez-Romero, Eli Lilly and Company, 3; F. Marin, Eli Lilly and Company, 3.
A Meta-Analysis of 4 Clinical Trials of Denosumab Compared with Bisphosphonates in Postmenopausal Women Previously Treated with Oral Bisphosphonates

Paul D Miller¹, N Pannacciulli², J Malouf³, A Singer⁴, E Czerwinski⁵, HG Bone⁶, C Wang², Rachel B. Wagman² and JP Brown⁷,
¹Colorado Center for Bone Research, Lakewood, CO, ²Amgen Inc., Thousand Oaks, CA, ³Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, ⁴Georgetown University Medical Center, Washington, DC, ⁵Krakow Medical Center, Krakow, Poland, ⁶Michigan Bone and Mineral Clinic, Detroit, MI, ⁷CHU de Québec Research Centre and Laval University, Québec, QC, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Four clinical trials have separately shown greater BMD gains with transitioning to denosumab (DMAb) compared with continuing on bisphosphonates (BP) in subjects previously treated with oral BPs (Kendler JBMRI 2010; Recknor Obstet Gynecol 2013; Roux Bone 2014; Miller JCEM 2016). The aim of this meta-analysis was to improve estimates of effect size and provide an integrated assessment of safety/efficacy of DMAb vs BPs with different dosing regimens (weekly, monthly, yearly) and administration routes (oral, intravenous), over 12 months in postmenopausal women pretreated with oral BPs.

Methods: Data were pooled from 4 randomized studies in postmenopausal women with low bone mass or osteoporosis, aged ≥55 years, and pretreated with oral BPs, who were randomized 1:1 to DMAb (60mg every 6 months) or an oral (alendronate 70mg weekly, ibandronate 150mg monthly, risedronate 150mg monthly) or intravenous (zoledronic acid 5mg yearly) BP for 12 months. Percentage (%) change from baseline (BL) in BMD at the lumbar spine, total hip, femoral neck, and 1/3 radius (assessed in 2 studies) at month 12; % change from BL in serum C-terminal telopeptide of type I collagen (sCTX, in a subset of 1058 subjects) at 1, 6, and 12 months (in 2 of the studies); and safety were assessed. Fractures were collected as adverse events (AEs) and not adjudicated.

Results: A total of 2850 subjects were included (1426 DMAb; 1424 BP). Mean (SD) age was 68 (8) years, mean (SD) lumbar spine BMD T-score was −2.5 (1.0), and mean (SD) duration of prior oral BP use was 3.8 (3.6) years. BMD % change from BL at month 12 was significantly greater with DMAb vs BPs at all measured skeletal sites (Figure) and independent of length of prior BP use (<2 or ≥2 years) at all sites measured (except for 1/3 radius for those with <2 years of prior BP use). Median sCTX % decrease from BL was greater with DMAb than BPs at months 1 (~58% vs −12%), 6 (~36% vs −14%), and 12 (~26% vs 8%; all p<0.0001). Overall AEs/serious AEs were similar between groups. There were no cases of osteonecrosis of the jaw. Three events consistent with the definition of atypical femoral fracture were observed (2 DMAb; 1 BP). Osteoporosis-related fractures were reported in 47 (3.3%) DMAb and 43 (3.1%) BP subjects.

Conclusion: This integrated assessment shows greater clinical benefit with increases in BMD and reductions in bone turnover and similar safety profile in transitioning from oral BPs to DMAb, compared with continuing on or cycling through the same therapeutic class (from one BP to another).
**Safety of Denosumab in a Monocentric Cohort of Kidney Transplant Recipients**

Sonia Doddoli, Pierre Lafforgue and Thao Pham, Rheumatology, APHM, Aix Marseille Univ, Marseille, France

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Safety of denosumab, a fully human monoclonal antibody against RANKL developed for osteoporosis and prevention of fracture remains unclear in kidney transplanted patients.

A recent placebo-controlled trial has demonstrated its efficacy on bone mineral density (BMD) and bone turnover biomarkers (Bonani et al. Am J Transplant. 2016). Patients in the denosumab group experienced more episodes of cystitis and asymptomatic hypocalcemia than patients in the placebo group.

---

**Disclosure:** P. D. Miller, Amgen, Lilly, Merck, Radius Health, Ultradynex, 2,Amgen, Alexion, Lilly, Merck, Radius Health, Ultradynex, 5; N. Pannacciulli, Amgen, 1,Amgen, 3; J. Malouf, None; A. Singer, Amgen, Eli Lilly, Merck, Radius, UCB, 5,National Osteoporosis Foundation Board of Trustees, 6,Amgen, Eli Lilly, 8; E. Czerwinski, Amgen, 2; H. Bone, Amgen, Merck, Shire, 2,Amgen, Grünenthal, Merck, Radius, Shire, 5,Amgen, Radius, Shire, 8; C. Wang, Amgen, 1,Amgen, 3; R. B. Wagman, Amgen, 1,Amgen, Eli Lilly, 2,Amgen, Eli Lilly, Merck, 5,Amgen, Eli Lilly, 8.

Our aim was to assess the clinical and biological tolerance of denosumab in this specific population.

Methods:
Prospective observational monocentric cohort.

Inclusion criteria: kidney transplant recipient who received at least one subcutaneous injections of 60 mg denosumab; age ≥ 18 years.

Safety outcomes: The following variables were collected every 6 months: infection, reaction at the injection site, plasmatic parameters of renal function and mineral metabolism (estimated glomerular filtration rate, serum creatinine, calcium, 1–25 [OH], vitamin D, PTH).

Results:
Patients were recruited from April 2014 to September 2015. All patients received immunosuppression therapy including prednisolone ≥ 5 mg/d.

The main baseline characteristics of the 37 kidney transplant recipients were the following [mean]: male: 41%, age: 60.5 years, BMI: 24.1, transplantation duration: 7.1 years, osteopenia: 36%, osteoporosis: 64%, total lumbar spine T-score: -2.04 SD, total hip T-score: -2.7 SD, T-score femoral neck: 0.676 g/cm2, serum creatinine: 132.8 mmol/L, calcium: 2.33 mmol/L, 1–25 [OH] vitamin D: 93.5 nmol/L, PTH 95: ng/l. All patients were prescribed vitamin D and calcium supplementation.

During the mean 12-month follow-up period, there were no unexpected adverse event [AE] or severe adverse event, no graft failure and no deaths. No patient experienced fracture. Only one patient presented an infectious AE with recurrent cutaneous abscess. Renal function remained stable with no difference in serum creatinine between baseline and 12 months for the majority of the kidney transplant recipients. However, 9 recipients experienced a decrease in renal function with a mean increased in serum creatinine of 32.5 micromol/L between baseline and 12 months. Serum calcium was stable, no hypocalcaemia was observed. Among patients with normal baseline PTH, two presented hyperparathyroidism during the follow-up period. Among the 11 patients with baseline hyperparathyroidism, 7 had an increased PTH level between baseline and 12 months. None were initiated on cinacalcet. None of them experienced severe hypercalcaemia, nor hypocalcaemia.

Conclusion:
Our results suggest that denosumab is safe in kidney transplant recipients. We did not observe an increase in the infection rates, nor hypocalcaemia. However, several patients experienced a decrease in their renal function or an increased hyperparathyroidism.

Disclosure: S. Doddoli, None; P. Lafforgue, None; T. Pham, None.


Abstract Number: 323

Evaluation of Invasive Oral Procedures and Events in Women with Postmenopausal Osteoporosis Treated for up to 10 Years with Denosumab: Results from a Phase 3 Open-Label Extension Study

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Antiresorptive therapy use is associated with osteonecrosis of the jaw (ONJ), an infrequent but serious adverse event. Positively adjudicated ONJ in the denosumab (DMAb) clinical trial program is rare (between ≥1 and <10 per 10,000).
Completion of the 7-year FREEDOM Extension study (EXT) permitted an in-depth assessment of the risk factors and observed invasive oral procedures and events (OPEs; eg, dental implants, tooth extraction, natural tooth loss, scaling/root planing [extensive subgingival cleaning]) in the clinical trial setting. 

**Methods:** In the randomized, placebo-controlled FREEDOM study, women received DMAb 60mg or placebo SC every 6 months for 3 years. Patients who missed ≤1 dose of investigational product and completed the Year-3 visit were eligible to participate in the 7-year open-label EXT to receive DMAb, regardless of original treatment assignment in FREEDOM. Women who reached the EXT Year-3 visit were asked to chronicle their history of invasive OPEs since the start of the EXT through Year 2.5, as well as oral events (including jaw surgery) in the prior 6 months. The oral event questionnaire was then administered every 6 months through the end of the EXT.

**Results:** During the EXT, the overall ONJ rate was 5.2 per 10,000 patient-years. The majority of women (79%; 3591/4550 patients) participated in the survey. Over the EXT, 1621 (45.1%) reported at least one invasive OPE; the incidence of five individual OPEs were similar between groups (Table). There were 12 confirmed cases of ONJ among women who participated in the survey (11 had OPE and one did not) and one additional case in a woman who did not complete the survey. ONJ incidence was 0.7% (11/1621 patients) in women reporting invasive OPEs and 0.05% (1/1970 patients) in women reporting no invasive OPEs. Of the 12 ONJ cases with survey results, one outcome was unknown due to consent withdrawn, one was ongoing at the end of study, and 10 resolved with treatment. 

**Conclusion:** Nearly all cases of ONJ observed in this study occurred after a reported invasive OPE, yet while invasive OPEs were common in this group of DMAb-treated women with postmenopausal osteoporosis, ONJ incidence was low. The actual number of invasive OPEs may be underestimated due to limited capture of OPEs in medical charts and possible recall bias in patients with events that occurred in the first 2.5 years of the EXT. ONJ is an adverse event of interest that continues to be monitored in DMAb pharmacovigilance activities.

**Table:** Invasive OPEs during the EXT for patients who completed at least one oral event questionnaire

<table>
<thead>
<tr>
<th>7-year FREEDOM Extension</th>
<th>Cross-over (N = 1731)</th>
<th>Long-term (N = 1860)</th>
<th>All (N = 3591)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at EXT baseline in years, mean (SD)</td>
<td>74.3 (4.9)</td>
<td>74.4 (4.8)</td>
<td>74.3 (4.8)</td>
</tr>
<tr>
<td>Any invasive oral procedure or event, n (%)</td>
<td>795 (45.9)</td>
<td>826 (44.4)</td>
<td>1621 (45.1)</td>
</tr>
<tr>
<td>Scaling / root planing</td>
<td>503 (29.1)</td>
<td>531 (28.5)</td>
<td>1034 (28.8)</td>
</tr>
<tr>
<td>Tooth extraction</td>
<td>434 (25.1)</td>
<td>458 (24.6)</td>
<td>892 (24.8)</td>
</tr>
<tr>
<td>Dental implant</td>
<td>100 (5.8)</td>
<td>112 (6.0)</td>
<td>212 (5.9)</td>
</tr>
<tr>
<td>Natural tooth loss</td>
<td>72 (4.2)</td>
<td>75 (4.0)</td>
<td>147 (4.1)</td>
</tr>
<tr>
<td>Jaw surgery*</td>
<td>16 (0.9)</td>
<td>17 (0.9)</td>
<td>33 (0.9)</td>
</tr>
</tbody>
</table>

N = Number of patients who received ≥1 dose of investigational product in the EXT and responded to ≥1 oral event questionnaire related to the EXT 

n = Number of patients with an OPE

*Collected in the oral event questionnaire every 6 months; therefore, jaw surgery in the first 2.5 years of the EXT was not captured

**Disclosure:** N. B. Watts, AbbVie, Sanofi, 5,Amgen, Shire, 8; J. T. Grbic, None; N. Binkley, Amgen, GE Heathcare, Lilly, Merck, Novartis, Viking, 2,Amgen, Radius, 5; P. W. Butler, Amgen, 1,Amgen, 3; X. Yin, Amgen, 1,Amgen, 3; A. Tierney, Amgen, 1,Amgen, 3; R. B. Wagman, Amgen, 1,Amgen, 3; M. McClung, Amgen, Radius Health, 5,Amgen, Radius Health, 8.


**Abstract Number:** 324

**The Predictors of the Efficacy of Denosumab, a Monoclonal Antibody to RANK Ligand, on Osteoporosis in Rheumatoid Arthritis Patients from Japanese Multicenter Study**

Kyosuke Hattori¹, Yuji Hirano¹, Yasuhide Kanayama², Nobunori Takahashi³, Naoki Ishiguro³ and Toshihisa Kojima³, 
¹Rheumatology, Toyohashi Municipal Hospital, Toyohashi, Japan, ²Orthopaedic Surgery and Rheumatology, Toyota Kosei Hospital,
Background/Purpose: Although early intensive treatment has improved medication of rheumatoid arthritis (RA), treatment for osteoporosis (OP) in RA patient will be more important. Here, we report 2-year outcome of denosumab (DMB) on OP of RA patients. This was a multiple center, prospective study (TBCR-BONE) to investigate the efficacy of DMB for 2 years on OP of RA patients and the predictors for the efficacy in DMB treatment.

Methods: 74 females completed 24-month (m) DMB treatment and were used for the analysis. Bone mineral density (BMD) of lumbar spine (LS) and total hip (TH) by DEXA, and P1NP and TRACP-5b were measured every 6m.

Results: Mean age was 70.2 years old. Mean RA duration was 17.1 years. Oral PSL was used in 26 cases. Biological agents (BIO) were used in 17 cases. 33 cases had the past history of fractures. The rate of change in LS-BMD (%LS-BMD) significantly increased as 4.4% at 6m, 5.8% at 12m, 7.2% at 18m and 7.6% at 24m. %TH-BMD significantly increased as 2.7% at 6m, 3.3% at 12m, 4.6% at 18m and 4.6% at 24m. %P1NP at 24m was -28.1%. %TRACP-5b at 24m was -20.6%. To confirm the predictors for large increase of %LS-BMD at 24m and %TH-BMD at 24m, all cases were divided into two groups, good outcome group (LS-GO group: n=47, mean %BMD at 24m=11.4%) and no good outcome group (LS-NGO group: n=24, mean %BMD at 24m=0.18%) with the cutline of %LS-BMD at 24m (4.0%) and %TH-BMD at 24m (3.1%) made of each superior two thirds of all cases. We performed multivariate logistic regression analyses and confirmed large decrease of %TRACP-5b at 12m was associated with large increase of %LS-BMD at 24m (OR (%) 0.97, 95% CI 0.95-0.99), and concomitant use of BIO was associated with large increase of TH-BMD at 24m (OR 5.8, 95% CI 1.10-30.64). The cutoff value of %TRACP-5b at 12m for larger increase of %LS-BMD at 24m was -38.7% (AUC of ROC=0.766). We divided all cases into two groups, large decrease of %TRACP-5b at 12m for larger increase of %LS-BMD at 24m was -38.7% (AUC of ROC=0.766). We divided all cases into two groups, large decrease of %TRACP-5b at 12m for larger increase of %LS-BMD at 24m was -38.7% (AUC of ROC=0.766). We divided all cases into two groups, large decrease of %TRACP-5b at 12m for larger increase of %LS-BMD at 24m was -38.7% (AUC of ROC=0.766). We divided all cases into two groups, large decrease of %TRACP-5b at 12m for larger increase of %LS-BMD at 24m was -38.7% (AUC of ROC=0.766).

Conclusion: DMB was effective in OP of RA patients. Large decrease of %TRACP-5b at 12m was a predictor for large increase of %LS-BMD at 24m. Combination of BIO and DMB was a predictor for large increase of %TH-BMD at 24m. They might suggest that there are different mechanisms associated with increase of LS-BMD and TH-BMD in DMB treatment for OP of RA patients.

Disclosure: K. Hattori, None; Y. Hirano, None; Y. Kanayama, None; N. Takahashi, None; N. Ishiguro, None; T. Kojima, None.


Abstract Number: 325

Zoledronic Acid Did Not Impaired Renal Function in Patients with Osteoporosis
Background/Purpose:
Bisphosphonates are recommended for patients with osteoporosis, however concerns have been raised with regards to their effect on kidney function. The aim of this study was to investigate the safety of bisphosphonates on renal function in patients with magnetic resonance imaging-proven acute osteoporotic vertebral fractures after vertebroplasty.

Methods:
This retrospective study enrolled patients with osteoporosis and acute vertebral fractures who underwent vertebroplasty between January 2001 and December 2015. Their gender, age, body mass index, co-morbidities, and use of zoledronic acid were recorded. The patients with increased creatinine were defined as having worse renal function. Logistic regression was used to adjust for variables.

Results:
Of the 224 included patients (184 females; mean age, 72.91±9.26 years), 82 took zoledronic acid and the others received other anti-osteoporotic agents. Fifty-four (65.9%) of the patients who took zoledronic acid had an increased creatinine level, compared to 92 (64.8%) of those who received other anti-osteoporotic agents (p=0.885). After adjusting for confounding variables, zoledronic acid was not significantly associated with an increase in creatinine (p=0.815; OR: 0.926; 95% CI: 0.487-1.761).

Conclusion:
The use of zoledronic acid did not lead to an increase in creatinine compared to those who used did not use zoledronic acid. However, further studies are needed to confirm our findings.
Table 1. Risk of zoledronic acid treatment increasing creatinine after adjustments for covariates

<table>
<thead>
<tr>
<th></th>
<th>Regression coefficient</th>
<th>SE</th>
<th>P value</th>
<th>OR(95CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zoledronic acid</td>
<td>-0.076</td>
<td>0.328</td>
<td>0.815</td>
<td>0.926(0.487-1.761)</td>
</tr>
<tr>
<td>Age</td>
<td>0.057</td>
<td>0.023</td>
<td>0.012</td>
<td>1.059(1.013-1.107)</td>
</tr>
<tr>
<td>BMI</td>
<td>-0.023</td>
<td>0.034</td>
<td>0.499</td>
<td>0.977(0.914-1.045)</td>
</tr>
<tr>
<td>Gender</td>
<td>0.281</td>
<td>0.469</td>
<td>0.548</td>
<td>1.324(0.529-3.321)</td>
</tr>
<tr>
<td>Smoking</td>
<td>-0.867</td>
<td>0.859</td>
<td>0.313</td>
<td>0.420(0.078-2.263)</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>1.577</td>
<td>1.116</td>
<td>0.158</td>
<td>4.838(0.543-43.150)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>-0.324</td>
<td>0.334</td>
<td>0.333</td>
<td>0.723(0.376-1.393)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.285</td>
<td>0.317</td>
<td>0.369</td>
<td>1.329(0.715-2.473)</td>
</tr>
<tr>
<td>Neurologic disease</td>
<td>-1.235</td>
<td>0.499</td>
<td>0.013</td>
<td>0.290(0.109-0.773)</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>-0.091</td>
<td>0.430</td>
<td>0.832</td>
<td>0.913(0.393-2.120)</td>
</tr>
<tr>
<td>Pulmonary disease</td>
<td>0.147</td>
<td>0.399</td>
<td>0.713</td>
<td>1.158(0.530-2.532)</td>
</tr>
<tr>
<td>Gastrointestinal disease</td>
<td>-0.351</td>
<td>0.363</td>
<td>0.334</td>
<td>0.703(0.345-1.435)</td>
</tr>
<tr>
<td>Liver disease</td>
<td>0.524</td>
<td>0.465</td>
<td>0.260</td>
<td>1.688(0.679-4.201)</td>
</tr>
<tr>
<td>Renal disease</td>
<td>0.930</td>
<td>0.435</td>
<td>0.033</td>
<td>2.534(1.080-5.950)</td>
</tr>
</tbody>
</table>

Key: CI: confidence interval; OR: odds ratio; SE: standard error; BMI: body mass index

Disclosure: Y. C. Chen Sr., None;


Abstract Number: 326

**Osteoporosis and Vertebral Fractures Are Associated with Disease Activity, Low Vitamin D Levels and Spinal Radiographic Damage in Patients with Axial Spondyloarthritis**

Cintia Romera-López1, Cristina Fernández-Carballido2, Miguel Ángel García-Moreno3 and Teresa Pedraz4, 1Rheumatology, Hospital Universitario del Vinalopó, Elche, Spain, 2Hospital General Universitario de Elda, Elda, Spain, 3Hospital Universitario de Elda, Elda, Spain, 4Hospital Universitario de Elda, Elda, Spain

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Osteoporosis and vertebral fractures are comorbidities of Axial Spondyloarthritis (axSpA). We evaluated the relationship between disease activity and radiographic damage and bone mineral density (BMD) and vertebral fractures (VF) in patients with axSpA.
Methods: Cross-sectional study of patients with axSpA (ASAS Criteria). Disease activity variables: Bath AS Disease Activity Index (BASDAI), ESR, CRP, ASAS-endorsed disease activity scores (ASDAS). Lumbar spine and hip BMD by dual x-ray absorptiometry (DXA) (187(91%) patients). VF assessed by a semiquantitative method (Genant) in lateral thoracic and lumbar spine X-rays. Risk of fracture was assessed with FRAX tool. Bivariate analysis performed to investigate the associations with the presence of osteoporosis and/or VF. Then, binary and multiple logistic regression models applied. SPSS (v23); p-values significant if < 0.05.

Results: We included 206 patients (62 female and 144 male). Mean values: age 51.7±14.1; BASDAI 3.6±2.2; ASDAS-CRP 2.2±0.95; ASDAS-ESR 2.5±0.99; BASFI 3.3±2.78; mSASSS 20.46±19.14; CRP 4.97±8.97mg/L; ESR 18.2±14.8 mm; 25OHHvitD 19.83±9.25ng/mL. Vitamin D deficiency detected in 85.7% of the patients. Low lumbar BMD was detected in 25.7% (z score) and 28.9% (t score) of the patients and low femoral neck BMD in 45.2% (z score) and 59.7% (t score). Lumbar osteoporosis was present in 3.2%/6.9% and hip osteoporosis in 9.1%/13.4% (applying z/t scores respectively). VF were detected in 34% of the patients. Bivariate analysis: ESR, ASDAS-ESR, age, male sex, low 25OHHvitD and radiographic damage(mSASSS) were associated to low BMD. Multivariate models confirmed an association between disease activity (ASDAS-ESR) [OR 3.32 (IC 2.35–4.55) p=0.016] and 25OHHvitD [OR 0.95 (IC95 0.86–0.98) p=0.029] and low hip BMD(z score). Differences between patients with and without fractures shown in table 1. Multivariate models confirmed the association between CRP [OR2.34 (IC95 1.10-4.98) p=0.027], radiographic damage [mSASSS lumbar OR 1.06 (IC95 1.03-1.10) p=0.001], high lumbar BMD [OR 296 (IC95 5.07-12258)p=0.006] and low hip BMD (femoral neck t score) [OR 0.11 (IC95 0.03-0.12)p=0.000] and VF.

Conclusion: In patients with axSpA, low BMD is associated with disease activity and low 25OHHvitD. The presence of vertebral fractures is associated with CRP and low hip BMD (p=0.001). Radiographic damage “falsely” increases lumbar BMD results but is associated with the presence of fractures.

Table 1. Significative differences between patients without fractures versus patientes with vertebral fractures

<table>
<thead>
<tr>
<th>Variable</th>
<th>No fractures</th>
<th>Fractures</th>
<th>p value</th>
<th>t Student</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP (mg/L)</td>
<td>5.10</td>
<td>9.51</td>
<td>p = 0.003</td>
<td>t = -3.503</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>15.87</td>
<td>23.12</td>
<td>p = 0.002</td>
<td>t = -3.302</td>
</tr>
<tr>
<td>25OHHvitD (ng/mL)</td>
<td>20.80</td>
<td>18.043</td>
<td>p = 0.049</td>
<td>t = 1.979</td>
</tr>
<tr>
<td>mSASSS cervical</td>
<td>8.02</td>
<td>13.11</td>
<td>p = 0.002</td>
<td>t = -2.146</td>
</tr>
<tr>
<td>mSASSS lumbar</td>
<td>8.93</td>
<td>12.36</td>
<td>p = 0.000</td>
<td>t = -5.271</td>
</tr>
<tr>
<td>mSASSS total</td>
<td>17.66</td>
<td>27.13</td>
<td>p = 0.000</td>
<td>t = -3.873</td>
</tr>
<tr>
<td>BMD lumbar</td>
<td>1.090</td>
<td>1.191</td>
<td>p = 0.002</td>
<td>t = -3.068</td>
</tr>
<tr>
<td>BMD femoral neck</td>
<td>0.912</td>
<td>0.773</td>
<td>p = 0.000</td>
<td>t = 6.589</td>
</tr>
</tbody>
</table>

None: Has no relevant financial relationship to disclose

Disclosure: C. Romera-López, None; C. Fernández-Carballido, Gebro, 2; M. Á. García- Moreno, None; T. Pedraz, None.


Abstract Number: 327

Association of Anti-Cyclic Citrullinated Peptide Seropositivity and Lean Mass Index with Low Bone Mineral Density in Patients with Rheumatoid Arthritis

Katherine D. Wysham1, Dolores M. Shoback2, Kashif Jafri1, Sarah L. Patterson3, Gabriela Schmajuk4, John B. Imboden Jr.5 and Patricia P. Katz5, 1University of California, San Francisco, San Francisco, CA, 2Medicine, San Francisco VA Medical Center, University of California, San Francisco, San Francisco, CA, 3Division of Rheumatology, University of California, San Francisco, San Francisco, CA, 4San Francisco VA Medical Center, University of California San Francisco, San Francisco, CA, 5Medicine, University of California, San Francisco, San Francisco, CA

First publication: September 18, 2017
Background/Purpose: Osteoporotic fractures are associated with high morbidity and mortality. Persons with rheumatoid arthritis (RA) have twice the risk of osteoporosis-related fracture than age-matched controls. It is not known, however, which characteristics of RA or its treatments have the greatest impact on bone mineral density (BMD). We investigated associations of RA characteristics, medication use, and body composition to low BMD in patients with RA.

Methods: We performed a cross-sectional analysis of an existing longitudinal RA cohort study from years 2007-2009. All patients met ACR classification criteria for RA. Demographic, clinical, laboratory and functional variables were collected at study visits. Body composition (fat, lean muscle and BMD) was measured by dual x-ray absorptiometry. We used linear regression to evaluate the association between predictors and femoral neck BMD. To identify independent predictors of BMD, we performed multivariable linear regression analyses that included variables significant in the univariable analyses at p<0.10. To determine if there was a linear trend between anti-cyclic citrullinated peptide (CCP) level and BMD, we repeated the linear regression analysis restricted to anti-CCP positive participants.

Results: Of the 138 participants (82 women, 56 men), 70% were rheumatoid factor positive, and 55% were anti-CCP positive to a level 3 times the upper limit of normal. Mean disease duration was 19±10.9 years. 44% of participants reported taking prednisone and of those taking prednisone, the mean dose was 7.1±6.1 mg/day. The mean body mass index (BMI) was 27.2±6.0 kg/m², and mean appendicular lean mass index (ALMI) was 6.4±1.2 kg/m²; 59% of the participants were obese based on percent total body fat. 52% had low BMD based on a T or Z score <=-1 and 27% reported taking osteoporosis medications. Age and anti-CCP positivity were negatively associated with BMD, even after controlling for other variables (β=-0.003 and -0.055, respectively, p<0.05) (Table). ALMI had an independent positive association with BMD (β=0.053, p <0.0001). Among anti-CCP positive participants (n=61), higher anti-CCP level was associated with lower BMD (β for each 20-unit increase in anti-CCP=-0.011, p=0.026) when controlling for age, sex, disease duration, ALMI and knee flexion strength.

Conclusion: Anti-CCP positivity, ALMI and age were independently associated with BMD in patients with RA. The linear relationship of anti-CCP levels with lower BMD supports the hypothesis that processes specific to RA negatively impact BMD. In contrast, ALMI was positively associated with BMD, emphasizing the role of muscle mass as a potentially modifiable risk factor. Our findings highlight the complicated interplay of RA disease-specific and functional factors and their impact on bone mass.

Disclosure: K. D. Wysham, None; D. M. Shoback, None; K. Jafri, None; S. L. Patterson, None; G. Schmajuk, None; J. B. Imboden Jr., None; P. P. Katz, Bristol-Myers Squibb, 2.

Secular Trends in the Risk of Fragility Fracture Among Patients with Rheumatoid Arthritis: A General Population-Based Study

Sarah Keller1, Marcy B. Bolster2, Ammar Oza3, Sharan K. Rai4, Leo Lu3, Yuqing Zhang5 and Hyon K. Choi4, 1Rheumatology, Allergy and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, 2Division of Rheumatology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, 3Allergy, Immunology, and Rheumatology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, 4Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, 5Department of Rheumatology, Allergy and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA
Background/Purpose: The risk of osteoporotic (OP) fracture among patients with rheumatoid arthritis (RA) is higher than that of the general population. The worldwide incidence of OP fractures in high-risk individuals is expected to double over the next 40 years. It is unknown if improvements in the management of RA and OP has decreased the OP fracture risk in patients with RA. To address this knowledge gap, we compared the risk and incidence of OP fracture among patients with RA to the general population over two chronologic periods.

Methods: Using an electronic medical record database representative of the United Kingdom general population (The Health Improvement Network), we identified patients with incident RA and up to five individuals without RA matched for age, sex, and calendar year of diagnosis between 1999 and 2014. The RA cohort was divided in two sub-cohorts based on the year of RA diagnosis: the early cohort (1999-2006) and the late cohort (2007-2014). We identified incident OP fracture using physician diagnosis (READ) codes. Subjects with previously-diagnosed prevalent fractures were excluded from this analysis. We calculated the period-specific incidence rates of total OP fracture and hip fragility fracture for each cohort separately. We calculated the hazard ratio (HR) of incident fracture using a Cox proportional hazard model. In the multivariable model, we adjusted for age, body mass index, smoking status (non-smokers, ex-smokers, current smokers), alcohol use (non-drinkers, ex-drinkers, current drinkers), comorbidities, medication use, and the number of PCP visits.

Results: Both the early and late cohorts (N=54,291 and 59,915, respectively) had a similar mean age (60 and 59 years) and sex proportion (~70 and 69% female), and RA patients showed an increased risk of OP fracture compared with their corresponding comparison cohort (Table). In both cohorts, the incidence rate of total OP fracture slightly increased, and the corresponding relative risk (RR) was not significantly different between the two periods (corresponding multivariable HRs=1.23 [95% CI: 1.04 to 1.47] vs. 1.45 [95% CI: 1.26 to 1.68]; p for interaction = 0.21) (Table). Meanwhile, in both cohorts, the incidence rate of hip fragility fracture slightly declined and the corresponding RR was not significantly different between the two periods (corresponding multivariable HRs=1.68 [95% CI: 1.28 to 2.21] and 1.53 [95% CI: 1.16 to 2.03]; p for interaction = 0.24) (Table).

Conclusion: This general population-based cohort study indicates that RA patients still experience a higher risk of all OP and hip fragility fractures compared to non-RA patients, and that this difference has not improved over the past several decades despite advances in RA and OP therapy. This unclosing gap in increased fracture risk among RA patients calls for improved management of osteoporosis in RA.

Disclosure: S. Keller, None; M. B. Bolster, None; A. Oza, None; S. K. Rai, None; L. Lu, None; Y. Zhang, None; H. K. Choi, Selecta, Horizon, 5,AstraZeneca, 2.

Factors Associated with Worsening Serum Vitamin D Deficiencies in Japanese Patients with Rheumatoid Arthritis: Results from the IORRA Cohort Study

Masanori Nakayama¹, Takefumi Furuya¹, Eisuke Inoue², Eiichi Tanaka¹, Katsunori Ikari¹, Ayako Nakajima¹, Atsuo Taniguchi¹ and Hisashi Yamanaka¹, ¹Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan, ²Division of Medical Informatics, St. Marianna University School of Medicine, Kawasaki, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: In 2011, we evaluated serum vitamin D levels in Japanese patients with rheumatoid arthritis (RA) and reported the prevalence of, and factors associated with, vitamin D deficiency [1]. Limited data exist in the literature concerning factors that predispose patients with RA to a worsening vitamin D deficiency. The aim of this study was to investigate predictive factors for a worsening vitamin D deficiency using our Institute of Rheumatology Rheumatoid Arthritis (IORRA) cohort.

Methods: Established in the year 2000, the IORRA cohort is a single institute-based large cohort of Japanese RA patients. Over 120 publications have described various characteristics of Japanese patients with RA using this large cohort. In 2013, fresh serum from those patients who participated in our first vitamin D study in 2011 was evaluated for 25-hydroxyvitamin D [25(OH)D] levels via radioimmunoassay. A vitamin D deficiency was defined as serum 25(OH)D levels <20 ng/mL. To determine the predictive factors of a worsening vitamin D deficiency over a 2-year period, multivariate logistic regression analyses were used.

Results: Among the 2534 patients with RA who participated in our vitamin D studies in 2011 and 2013 (2179 women and 355 men; mean age 59.6 years), the mean (± standard deviation) serum 25(OH)D level was 18.0 (±5.8) ng/mL, and the prevalence of vitamin D deficiency was 68.2% in 2013. Via multivariate analysis, younger age, female gender, and a high score for the Japanese version of the Health Assessment Questionnaire disability index (J-HAQ-DI) were significantly associated with vitamin D deficiency (P<0.05). Serum vitamin D levels decreased by >5 ng/mL over the 2 years from 2011 to 2013 in 224 (8.8%) patients. For that subset of patients, a multivariate analysis revealed, younger age, female gender, bisphosphonate disuse, and higher baseline serum 25(OH)D levels were significantly associated with the decrease in vitamin D levels over the two years (P<0.05) (Table).

Conclusion: In Japanese patients with RA, younger age, female gender, bisphosphonate disuse, and a high baseline serum 25(OH)D level appear to be associated with serum vitamin D levels that worsen over time.

Table: Factors associated with a further decrease in serum 25(OH)D levels in Japanese patients with RA from 2011 to 2013.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Odds ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.981 (0.964-0.999)</td>
<td>0.0338</td>
</tr>
<tr>
<td>Female gender</td>
<td>2.190 (1.100-4.360)</td>
<td>0.0254</td>
</tr>
<tr>
<td>Bisphosphonate use</td>
<td>0.431 (0.201-0.925)</td>
<td>0.0308</td>
</tr>
<tr>
<td>Baseline serum vitamin D levels</td>
<td>1.310 (1.27-1.35)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>


Disclosure: M. Nakayama, Bristol-Myers Squibb, 8; T. Furuya, UCB, 8,Bristol-Myers Squibb, 8,Takeda, 8,Eisai, 8,Chugai, 8,Pfizer Inc, 8,Ono, 8,Asahi Kasei, 8; E. Inoue, Merck Serono Co., Ltd., 8; E. Tanaka, Abbvie, 8,Ayumi, 8,Bristol-Myers Squibb, 8,Chugai, 8,Eisai, 8,Nippon Kayaku, 8,Pfizer Inc, 8,Takeda, 8,UCB, 8; K. Ikari, Bristol-Myers Squibb, 8,Abbvie, 8,Eisai, 8,Asahi Kasei, 8,Astellas, 8,Chugai, 8,Hisamitsu, 8,Janssen Pharmaceutica Product, L.P., 8,TAISHO Toyama, 8,Takeda, 8,Santen, 8,Tanabe-Mitsubishi, 8,Kaken, 8; A. Nakajima, Nippon-Kayaku, 5,Bristol-Myers Squibb, 8,Chugai, 8,Novartis Pharmaceutical Corporation, 8,Pfizer Inc, 8,Siemens, 8,Tanabe-Mitsubishi, 8; A. Taniguchi, Pfizer Inc, 8; H. Yamanaka, MSD, 2,Astellas, 2,AbbVie, 2,BMS, 2,Kaken, 2,UCB,
Change in Bone Mineral Density in Patients with Rheumatoid Arthritis: Minimal 10-Year Follow-up

Hiraku Motomura, Isao Matsushita, Toshihito Hiraiwa and Tomoatsu Kimura, Department of Orthopaedic Surgery, Faculty of Medicine, University of Toyama, Toyama, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
To investigate the long-term change in bone mineral density (BMD) in patients with rheumatoid arthritis (RA).

Methods:
In a longitudinal study of 40 patients with RA, we collected clinical data and measured hip BMD by dual-energy X-ray absorptiometry at baseline and after at least 10 years. BMD of the total hip was measured as the percentage of young adult mean (YAM). We compared clinical characteristics between patients with osteopenia (BMD < 80% of YAM) and those without (normal group; BMD ≥ 80% of YAM) at baseline. We also analyzed factors associated with a decrease in YAM of >5% during the follow-up period using multivariate logistic regression analysis.

Results:
The mean patient age was 59.8 years, the mean disease duration was 11.5 years, and the mean follow-up period was 10.4 years. Most of the patients (90%) were women. At baseline, 22 patients (55%) were being treated with methotrexate (MTX, mean dose 5.4 mg/week), 26 patients (65%) with prednisolone (PSL, mean dose 6.7 mg/day), and one patient (2.5%) with a biologic disease-modifying antirheumatic drug (DMARD). The antiresorptive drug intervention rate at baseline was 20%. The mean serum C-reactive protein (CRP) and matrix metalloproteinase-3 (MMP-3) values at baseline were 2.21 mg/dL and 258.6 ng/mL, respectively. At follow-up, the mean dose of MTX had increased to 7.0 mg/week and the mean PSL dose had decreased to 2.9 mg/day. The antiresorptive drug intervention rate had increased to 77.5%, and treatment with biologic DMARDs had also increased to 55%. The mean CRP and MMP-3 values had decreased to 0.33 mg/dL and 105.4 ng/ml, respectively. Total hip BMD had decreased from 80.0% YAM at baseline to 76.8% YAM at follow-up. At baseline, 19 patients (47.5%) were classified as osteopenia (BMD < 80% of YAM). The total hip BMD in this group increased slightly from 67.2% YAM at baseline to 69.7% YAM at follow-up. By contrast, the normal group showed a significant decrease in BMD from 91.6% YAM at baseline to 83.1% YAM at follow-up. At both baseline and follow-up, the antiresorptive drug intervention rate was significantly higher in the osteopenia group than in the normal group. No significant differences were found in age, disease activity, use of MTX, PSL, or biological DMARDs between the osteopenia and normal groups. Multivariate logistic regression analysis was used to determine individual factors associated with a reduction in BMD (>5% decrease of YAM). Current use of antiresorptive drugs was strongly associated with a decreased risk for total hip bone loss (odds ratio: 0.04, 95% confidence intervals: 0.003–0.436, P = 0.009)

Conclusion:
Our findings suggest that osteoporosis treatment and tight control of RA disease activity are important for maintaining total hip BMD over a 10-year period. Even RA patients without osteopenia should be started on osteoporosis treatment to inhibit the progression of bone loss.

Disclosure: H. Motomura, None; I. Matsushita, None; T. Hiraiwa, None; T. Kimura, None.
Abstract Number: 331

Case Series: Comparison of Repository Corticotropin Injection (H.P. Acthar Gel) Versus Glucocorticoids on Bone Density in SLE Patients

Anny T. Wu¹ and Joshua June², ¹Rheumatology, Franciscan Alliance, Munster, IN, ²3394 E Jolly Rd Ste C, Great Lakes Center of Rheumatology, Lansing, MI
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Repository Corticotropin Injection (RCI) is an adrenocorticotropin hormone in 16% gelatin with a prolonged release after intramuscular (IM) or subcutaneous injection. Adverse effects of RCI are primarily related to its steroidogenic effects including decrease in BMD. However, there is recent renewed interest in RCI’s role as an alternative to high dose glucocorticoids and as last resort therapy for SLE.

Methods: This retrospective case series looks at the bone density changes of 5 adult female patients with mean age of 59 years on RCI vs. glucocorticoids at a Rheumatology practice. A list of 73 patients on RCI was populated using the EMR. Chart review was performed and patients were selected with the following criteria: on RCI for at least 6 months, history of SLE, verifiable DXA scan results from before and after starting RCI. Patients were then excluded if they had been on bone sparing agents during this time interval. The bone with the lowest density on the DXA report post-RCI is selected for comparison to the pre-RCI BMD. The lowest significant change of each BMD value is operator dependent and is within 95% confidence interval based on the certified technologist’s past DXAs. The same technologist performed all of the above DXAs. An example is as follows: for this particular technologist, her range of lowest significant change (at 95% confidence interval) in measurement of the femoral neck is plus or minus 0.010 gm/cm². If the difference in BMD of the femoral neck falls outside of this range on a latter DXA, then there is indeed a significant change.

Results: Two of the 5 patients had nonsignificant changes to their BMD before and after starting RCI. Two patients had a decrease in BMD that were significant but were noted to have been on higher doses of Prednisone (10mg and/or 20mg a day) and received more IM glucocorticoid injections. One patient had an increased BMD, although for her, RCI was started just 3 months prior to her latter DXA. Her third DXA scan 2 years later did show a significant decrease in BMD but she, too, had received more glucocorticoid IM injections.

Conclusion: These cases illustrate the possibility that RCI by itself does not contribute to significant BMD decrease. Rather, significant decrease in BMD is seen in those patients who have concurrently received more oral, IM or intra-articular glucocorticoids while on RCI. Although RCI may be understood to have similar side effects as glucocorticoids, we see a possible difference in side effects such as BMD decrease as compared to glucocorticoids.

Disclosure: A. T. Wu, None; J. June, Mallinckrodt, 8.

Abstract Number: 332

Serum 25-Hydroxyvitamin D, Acute Phase Reactants and Disease Activity in Rheumatologic Diseases

María Lorena Brance¹,², Lucas Ricardo Brun³, Maria Larroude⁴, Mónica Patricia Sacnun⁵, Carolina Aeschlimann⁵, Guillermo Berbotto⁶, Mariano Palatnik¹, Ignacio Chavero¹ and Ariel Sánchez⁷, ¹Centro de Reumatología, Rosario, Argentina, ²School of Medicine, Rosario National University, Bone Biology Laboratory, Rosario, Argentina, ³School of Medicine, Rosario National
SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Previous evidence indicates an association between vitamin D deficiency and autoimmune diseases. The aim of this study was to evaluate serum 25-hydroxyvitamin D (25OHD), acute phase reactants and disease activity in patients with rheumatologic diseases (RD).

Methods: This retrospective study evaluated 173 patients with RD (94 rheumatoid arthritis (RA), 18 spondyloarthopathies (SA), 61 collagenopathies (COL) (systemic lupus erythematosus, vasculitis, scleroderma, undifferentiated disease, superposition syndrome) and compared them with a control group (CG, n=121) matched by age (CG= 55.0±14.7 years; RD= 53.4±13.6, sex and body mass index (BMI). All patients were from Rosario (32°52´18´´S) and Buenos Aires (34°36´14´´S) cities. Exclusion criteria: supplementation with vitamin D, pregnancy, intestinal malabsorption, chronic liver or kidney disease, and cancer. Date are expressed as mean±SEM. Differences between groups were analyzed using the Mann-Whitney or Kruskal-Wallis tests. Correlations were performed with Spearman’s correlation test. Univariate linear regression and logistic regression analysis were performed. Contingency tables were evaluated with χ² test. The difference was considered significant if p<0.05.

Results: RD patients had significant lower 25OHD levels as a control group (CG= 26.8±1.1 ng/ml; RD= 19.8±0.6 ng/ml; p<0.0001). Furthermore, all subgroups had lower 25OHD (RA=20.7±0.7 ng/ml, SA= 15.4±1.3 ng/ml, COL= 19.7±1.1 ng/ml). The OR of patients with RD being vitamin D deficient (25OHD <20 ng/ml) was 2.7 (95%CI 1.6 to 4.4) with a probability of 73%. Consistent with 25OHD differences, significant lower serum calcium (CG= 9.33±0.04; RD= 9.14±0.08 mg/dl) and higher PTH (CG= 39.72±2.37; RD= 49.93±3.34 pg/ml) levels were found. No differences in serum phosphate, urinary calcium and urinary deoxipiridinoline were observed. 25OHD significantly correlated with erythrocyte sedimentation rate (ERS) \[r = -0.28; p=0.0017\] as acute phase reactants. No differences was found in reactive C-protein (RCP). Lower values of 25OHD were found at higher DAS-28 (<3.2= 22.9 ng/ml; 3.2-5.1= 19.8 ng/ml; >5.1= 19.9 ng/ml; p=0.23) and HAQ-DI (0-1= 22.9 ng/ml; 2= 19.8 ng/ml; 3= 19.9 ng/ml; p=0.001). Activity scores in other RD couldn’t be analyzed because of the small number of patients. Age, BMI, presence of RD, RCP and HAQ-DI were significantly and inversely associated with 25OHD levels. BMI, presence of RD, ERS and RCP were significantly associated with vitamin D deficiency.

Conclusion: Patients with RD have a high probability of being deficient in 25OHD. Low 25OHD levels are associated with high acute phase reactants in the whole group, and with high disease activity scores in RA patients.

Disclosure: M. L. Brance, None; L. R. Brun, None; M. Larroude, None; M. P. Sancun, None; C. Aeschlimann, None; G. Berbotto, None; M. Palatnik, None; I. Chavero, None; A. Sánchez, None.


Abstract Number: 333

Atypical Femoral Fracture in Patients of a Rheumatology Service: Clinical, Radiographic and Bone Histomorphometric Data

Mariana O Perez1, Diogo S Domiciano1, Vanda Jorgetti2 and Rosa M R Pereira1, 1Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, Brazil, 2Nephrology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, Brazil

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster I
Session Type: ACR Poster Session A
Background/Purpose: Atypical femoral fractures (AFF) are low energy femoral fractures with a specific radiographic pattern and subtrochanteric / diaphyseal localization that have been related to long-term bisphosphonate therapy. Glucocorticoid and rheumatic diseases, mainly rheumatoid arthritis has also been implicated in this comorbidity. Therefore, the aim of this study was to evaluate a cohort of patients with AFF from a Tertiary Rheumatology Center, including clinical presentation, radiographic data and findings of bone histomorphometry.

Methods: From January 2007 to May 2017, all patients from the Outpatient Clinic (Osteometabolic Disease) of a Tertiary Rheumatology Service, Clinics Hospital- School of Medicine who fulfilled the American Society of Bone Mineral Research (ASBMR, 2010) criteria for atypical fracture were included in this study. Clinical-epidemiological data were obtained from electronic chart review. Anteroposterior radiographs of bilateral hip were analyzed, according to ASBMR. Confirmation of bilateral AFF was performed by magnetic resonance imaging or scintigraphy. Serum markers of bone remodeling, C-terminal telopeptide of type 1 collagen (CTX) and alkaline phosphatase (AP) were also evaluated. Iliac crest bone biopsy and static and dynamic bone parameters (compared to reference values of healthy controls matched by sex and age) were performed by histomorphometric analysis (Osteomeasure® software).

Results: Eighteen patients presented AFF, mostly women (94.4%), Caucasian (72.2%), mean age of 64.9 ± 13.3 years and all had prodromal pain in the anterolateral region of the thigh before the clinical fracture. Seventeen used bisphosphonate (5.83 ± 2.74 years), mostly alendronate (83.3%) at the time of fracture. One patient was taking denosumab, but had previously received bisphosphonate for 6 years. Presence of any inflammatory rheumatic disease was observed in 9 (50%) patients: rheumatoid arthritis (n=4), systemic lupus erythematosus (n=1), Sjögren's syndrome (n=1), Behçet’s disease (n=1), inclusion body myositis (n=1) and adult-onset Still's disease (n=1). Eight patients (44.4%) were using oral glucocorticoid at a median dose of 5 mg/day (ranged 5-15mg/day). All fractures presented diaphyseal localization, 16 (88.8%) were complete fracture and 4 (22.2%) bilateral. Bone markers were in the normal range (CTX: 0.28±0.18ng/mL and AP: 76.11± 30.22 U/L). Bone biopsy performed in 6 patients revealed suppression of bone turnover (100%), with reduction of osteoid tissue, as well as decreasing of resorption, osteoclastic and osteoblastic surfaces and impairment of bone mineralization. Sixteen patients underwent surgical treatment and 2 only clinical treatment (teriparatide). In total, 14 patients received teriparatide, 1 strontium ranelate and 3 remained without medication.

Conclusion: Our study alerts the rheumatologist about the possibility of AFF in those patients with bisphosphonate above 5 years, mainly with inflammatory rheumatic diseases and glucocorticoid use. Bone biopsy revealed a bone turnover suppression. Attention should be aware of the prodromal thigh or groin pain and subclinical imaging changes in the lateral femur, both associated with AFF.

Disclosure: M. O. Perez, None; D. S. Domiciano, None; V. Jorgetti, None; R. M. R. Pereira, None.


Abstract Number: 334

Comparison of Outcomes in Osteoporosis in Patients on Denosumab between Standard and Non-Standard Dosing Intervals

Nouman A. Syed, Mohammed Wiqar, Douglas Einstadter and Marina N. Magrey, Case Western Reserve University at MetroHealth Medical Center, Cleveland, OH

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: ARHP Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Denosumab (Dmab) is an antiresorptive agent with an approximate half-life of 26 days and according to the prescribing information the recommended dose is 60 mg subcutaneous every 6 months. Although in real world clinical practice, strict adherence to this dosing regimen is frequently hampered due to delays in prior authorizations, follow up appointment scheduling and missed visits. We hypothesized that patients who did not adhere to the standard dosing regimen would have impaired efficacy of Dmab. The objective of this study is to determine whether there is difference in bone mineral density (BMD) after 2 years of therapy in patients who received Dmab at recommended 6 month intervals as compared with patients who did not.
Methods: All patients between 2009 and 2015 with a primary diagnosis of post-menopausal osteoporosis that had received 4 doses of Dmab in 2 consecutive years were identified from the electronic data base. Furthermore patients were required to have a baseline DXA within 2 years prior to Dmab initiation and a follow up DXA within 2-3 years thereafter done on the same GE Lunar machine (least significant change for hip 0.036 g/cm2). Patient records were reviewed to obtain information on demographics, weight, smoking history, baseline vitamin D level, Dmab administration and DXA results. Change in BMD at lowest T-score of hip or femoral neck for each patient was used as the outcome measure. Adherence to therapy was defined as receiving subsequent injections at 6 month ± 4 week intervals. Patients were divided into 3 groups with Group 1 being adherent with all injections. Patients in Group 2 were adherent with 2 of 3 subsequent injections whereas Group 3 patients received subsequent injections at 8-12 month intervals and were considered to be non-adherent. Descriptive analysis included continuous variables (means ± SD) and categorical variables (%). Data were compared by using ANOVA.

Results: 50 patients, all females, with mean age of 75 yrs (± 9.4), 74% were Caucasian, 12% African American, 6% Hispanic and 8% were of other ethnicities. 60% smokers and 56% had history of fragility fractures. Mean Vitamin D level was 39.3 ng/ml (± 21.5). The mean lowest BMD at the hip or femoral neck at baseline and follow up were 0.705 g/cm2 (± 0.130) and 0.726 g/cm2 (± 0.130), respectively. 14% of patients were adherent with all 3 injections whereas 40% were categorized as Group 2. 46% were non adherent. The mean change in BMD stratified by groups was 0.035 g/cm2 (± 0.061) for Group 1, 0.006 g/cm2 (± 0.035) for Group 2 and 0.031 g/cm2 (± 0.057) for Group 3. There was no significant difference in mean lowest BMD change at the hip or femoral neck between the 3 groups through ANOVA analysis (p=0.2073).

Conclusion: Despite low adherence to the standard dosing regimen for Dmab there was no significant difference in change of BMD in patients who were not adherent to the current prescribing information.

Disclosure: N. A. Syed, None; M. Wiqar, None; D. Einstadter, None; M. N. Magrey, Amgen, AbbVie, and UCB Pharma, 2,UCB and Janssen, 5.


Abstract Number: 335

Psoriatic Arthritis Patients Who Attain a Very Low Disease Activity State Have a Minimal Impact of the Disease on Their Lives

Rubén Queiro1, Juan D. Cañete2, Carlos Alberto Montilla-Morales3, Miguel A. Abad4, Susana Gomez Castro5 and Ana Cabez5,
1Rheumatology Department. Hospital Universitario Central de Asturias, Oviedo, Spain, 2Rheumatology Department, Arthritis Unit, Rheumatology Dpt, Hospital Clinic of Barcelona, Barcelona, Spain, 3Hospital Clínico Universitario de Salamanca, Salamanca, Spain, 4Rheumatology, HU. Virgen del Puerto., Plasencia, Spain, 5Pfizer, Madrid, Spain
First publication: September 18, 2017
Background/Purpose:

The target of treatment in psoriatic arthritis (PsA) should be remission or inactive disease. A potential definition that would fit with the Treat-to-Target Recommendations would be minimal disease activity (MDA) meeting all 7 criteria\(^1\), proposed as a definition of very low disease activity (VLDA) in PsA. Patient reported outcomes (PROs), such as those provided by the novel PsAID questionnaire \(^2\), are also important to evaluate healthcare interventions and to reflect the impact of PsA on patients’ lives. The aims of this study were to evaluate the prevalence of VLDA in patients with PsA and how much residual active disease is still present, so as to determine whether PsAID could be an additional useful tool to assess PsA interventions in clinical practice.

Methods:

This was a sub-analysis of the MAAPs study\(^3\). Patients were considered in VLDA when they met all the MDA criteria: tender joint count ≤1, swollen joint count ≤1, Psoriasis Area Severity index (PASI) score ≤1 or body surface area ≤3%, patient pain visual analog scale (VAS) score ≤15, patient global disease activity VAS score ≤20, Health Assessment Questionnaire (HAQ) score ≤0.5, and tender enthesal points ≤1. Patient acceptable symptoms state (PASS) is considered a PsAID value <4. Comparisons of qualitative variables have been made with the chi-square test or Fisher's exact test. Comparisons of quantitative variables were made with the Student's T test or with non-parametric tests if necessary.

Results: 227 patients from 25 Spanish rheumatology departments were included, and among them, 26 (11.5%) were in VLDA. The majority (96.2%) of VLDA patients had a PASS situation while 49.2% of non VLDA patients had a PASS, p<0.001.
<table>
<thead>
<tr>
<th>Variable</th>
<th>Non-VLDA (n: 201)</th>
<th>VLDA (n: 26)</th>
<th>p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>53.1 (12.1)</td>
<td>53.7 (14.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>52.7%</td>
<td>65.4%</td>
<td>NS</td>
</tr>
<tr>
<td>Disease duration (yr)</td>
<td>9.6 (7.6)</td>
<td>9.5 (9.1)</td>
<td>NS</td>
</tr>
<tr>
<td>Family history (PsA)</td>
<td>13.9%</td>
<td>0%</td>
<td>0.042</td>
</tr>
<tr>
<td>CHD</td>
<td>19.4%</td>
<td>34.6%</td>
<td>0.074</td>
</tr>
<tr>
<td>Obesity</td>
<td>3.8 (6.5)</td>
<td>1.9 (1.9)</td>
<td>0.002</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>35.8%</td>
<td>42.3%</td>
<td>NS</td>
</tr>
<tr>
<td>Hand erosive disease</td>
<td>29.4%</td>
<td>30.8%</td>
<td>NS</td>
</tr>
<tr>
<td>Foot erosive disease</td>
<td>52.2%</td>
<td>34.6%</td>
<td>0.091</td>
</tr>
<tr>
<td>NSAID</td>
<td>77.6%</td>
<td>57.7%</td>
<td>0.027</td>
</tr>
<tr>
<td>Corticoids</td>
<td>77.1 (72.2)</td>
<td>38.5 (38.6)</td>
<td>0.051</td>
</tr>
<tr>
<td>csDMARDs</td>
<td>47.3%</td>
<td>65.4%</td>
<td>0.082</td>
</tr>
<tr>
<td>Duration (months)</td>
<td>46.1 (35.5)</td>
<td>43.9 (30.9)</td>
<td>NS</td>
</tr>
<tr>
<td>Biologics</td>
<td>64.2%</td>
<td>94.2%</td>
<td>0.027</td>
</tr>
<tr>
<td>Duration (months)</td>
<td>0.6 (0.5)</td>
<td>0.06 (0.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ETA/ADA</td>
<td>5.4 (4.5)</td>
<td>1.1 (1.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HAQ</td>
<td>3.0 (2.3)</td>
<td>0.6 (0.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PsAID</td>
<td>3.4 (2.7)</td>
<td>0.6 (1.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BASDAI</td>
<td>3.5 (2.5)</td>
<td>0.5 (0.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pain VAS (0-10)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pt. disease activity</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


**Conclusion:**

11.5% of Spanish PsA patients achieved VLDA state in routine clinical practice. PsA patients who reached this state also had a minimal impact of disease according to PsAID. VLDA state could represent a situation of clinical remission in PsA.

**References**

Abstract Number: 336

**Patient–Reported Barriers to Achieving Rheumatoid Arthritis Disease Control**

**Maria I. Danila**, 1, Eric M. Ruderman², Leslie R Harrold³, Joshua A. Melnick¹, Ronan O'Beirne¹, Monika M. Safford⁴, Joel Kremer⁵ and Jeffrey R. Curtis⁶, ¹University of Alabama at Birmingham, Birmingham, AL, ²Northwestern University Feinberg School of Medicine, Chicago, IL, ³University of Massachusetts Medical School, Worcester, MA, ⁴Weill Cornell Medical College, New York, NY, ⁵Corrona, LLC, Southborough, MA, ⁶Rheumatology & Immunology, University of Alabama at Birmingham, Birmingham, AL

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Sunday, November 5, 2017
**Session Title:** Patient Outcomes, Preferences, and Attitudes Poster I
**Session Type:** ACR Poster Session A
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Many patients with RA do not achieve guideline-recommended treat-to-target (T2T) goals in clinical practice. There is a paucity of data regarding the challenges that patients face when attempting to achieve better control of their RA disease activity. In this study we sought to identify and prioritize patient-perceived barriers to achieving RA disease activity control.

**Methods:** Participants were recruited from the within the Consortium of Rheumatology Researchers of North America (Corrona) registry by email and invited to participate in 4 nominal groups. Each group generated a list of barriers that made it challenging for patients to control their RA disease activity. All generated items were combined in a single dataset and subjected to a card sort procedure to create common themes. A random sample of patients with RA enrolled in Corrona were invited by email to complete a compensated online survey and asked to rank their top 3 barriers. A weighted score was assigned for each barrier by considering the number of respondents who ranked it and the priority rank they assigned. The barriers were sorted into domains. The survey also included knowledge items about T2T strategy and attitudes about RA treatment.

**Results:** Four nominal groups with 37 RA patients identified 17 themes to achieving control of RA activity. We sent 1567 email invitations to complete the survey and 463 patients with RA responded within 3 weeks. Demographic and clinical data was available for 1331 persons, 383 of whom responded to the survey. There were no differences in age, sex, or disease duration between survey-respondents and non-respondents. A higher proportion of respondents were college-educated. A total of 289 (76%) respondents considered RA to be a high priority for their health, 193 (51%) reported being familiar with T2T as a treatment strategy, and 233 (75%) agreed that it is important to accept the risk of side effects now in order to improve the chance of being healthy in the future. Among the challenges to controlling RA disease activity, the domain that received the highest score was unpredictability of RA and its treatment, which comprised the following barriers: unpredictability of how RA may progress, medication risk aversion, effectiveness, and safety/tolerability concerns (Figure). Symptoms and illness burden domain received the second highest score, followed by the health system domain (Figure).

**Conclusion:** Important patient-perceived barriers to achieving RA disease control include unpredictability of how RA may progress, medication risk aversion, cost of RA care and RA physical limitations. Addressing these barriers, when possible, may improve goal-directed RA care.
Patient-Reported Flares Were Correctly Predicted By an Algorithm Using Machine-Learning Statistics on Activity Tracker Data on Steps, in a Longitudinal 3-Month Study of 170 Patients with Rheumatoid Arthritis (RA) or Axial Spondyloarthritis (axSpA)

Laure Gossec¹, Frédéric Guyard², Didier Leroy³, Thomas Lafargue², Michel Seiler³, Charlotte Jacquemin¹, Anna Molto⁴, Jeremie Sellam⁵, Violaine Foltz¹, Frédérique Gandjbakhch¹, Christophe Hudry⁶, Stéphane Mitrovic¹, Bruno Fautrel¹ and Herve Servy⁷,
¹UPMC University Paris 06, Pitié-Salpêtrière Hospital, Paris, France, ²IMT, Orange, Nice, France, ³Healthcare, Orange, Paris, France, ⁴Hôpital Cochin, Department of Rheumatology, Paris Descartes University, Paris, France, ⁵Rheumatology, Saint-Antoine Hospital, Paris, France, ⁶AP-HP Hôpital Cochin, Paris, France, ⁷e-health services, Sanoia, Gemenos, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The natural history of RA and axSpA comprises periods of low disease activity and flares. However, there are few data linking patient-reported flares to quantifiable outcomes. We previously indicated in the ActConnect study that flares were related to a moderate decrease in physical activity (1). Objective: to predict patient-reported flares based on activity-tracker-provided continuous flows of steps per minute.

Methods: This prospective multi-center observational study (ActConnect) included patients with definite RA (ACR/EULAR criteria) or axSpA (ASAS criteria), owning a smartphone. Over 3 months, physical activity was sampled continuously (each minute) using an activity tracker, and flares were self-assessed weekly using a specific flare question. In this reanalysis of the dataset, Machine Learning...
statistical methods were used. Physical activity data were first normalized at patient level using each patient’s mean and standard deviation of steps for a similar timeframe without flares. Then the data were analysed by multiclass Bayesian methods with a Machine Learning software belonging to Orange (2). The software was instructed to find the best predictive model of patient-reported flares. Sensitivities and specificities were calculated. Several sensitivity analyses were performed using different physical activity timeframes, different definitions of flares.

**Results:** In all, 170/178 patients (91 RA and 79 axSpA patients; 1228 weekly flare assessments and 24,972 1-hour physical activity assessment timeframes) were analyzed: mean age 45.5±12.4 years, mean disease duration 10.3±8.7 years; 60 (35.3%) were males and 90 (52.9%) received biologics. Disease was well-controlled (mean DAS28: 2.3±1.2; mean BASDAI: 3.3±2.1) but flares were frequent: reported in 24% of all the questionnaires. The Khiops generated model detected correctly both flares and absence of flare (Table) with a sensitivity of 96% and a specificity of 97%. The corresponding positive and negative predictive values were respectively 89% and 99%. Sensitivity analyses were confirmatory.

**Conclusion:** Machine Learning methods are useful to deal with repeated data in big datasets. The results confirm objectively the functional impact of patient-reported flares. Furthermore, the correct detection of flares by the activity tracker and adapted statistics opens the way for future studies of flares using connected devices with great precision and minimal patient burden.

1- Jacquemin C et al. Physical activity decreased significantly but moderately during weeks where patients reported flares: A 3-month study of 170 rheumatoid arthritis (RA) or axial spondyloarthritis (AXSPA) patients wearing an activity tracker, Ann Rheum Dis 2017 (suppl): EULAR congress, poster FRI0700.

2- Khiops software for data mining, PredicSis; accessed 06/01/2017: https://khiops.predicsis.com

**Disclosure:** L. Gossec, None; F. Guyard, Orange, 3; D. Leroy, Orange, 3; T. Lafargue, Orange, 3; M. Seiler, Orange, 3; C. Jacquemin, None; A. Molto, None; J. Sellam, None; V. Foltz, None; F. Gandjbakhch, None; C. Hudry, None; S. Mitrovic, None; B. Fautrel, AbbVie, Biogen, BMS, Celgene, Hospira, Janssen, Eli Lilly and Company, Novartis, Pfizer, Roche, SOBI Pharma, UCB, 5; H. Servy, None.


**Abstract Number:** 338

**Measurement Properties of Paindetect, a Neuropathic Pain Screening Tool, for Evaluating Pain Phenotype in Patients with Rheumatoid Arthritis: Developing Neuropathic Pain Scale As a Measure of Treatment Outcome By Applying Rasch Analysis**

Yong Gil Hwang1, Lei Zhu2, Ajay Wasan3 and Larry W. Moreland1, 1Rheumatology & Clinical Immunology, University of Pittsburgh, Pittsburgh, PA, 2University of Pittsburgh, Pittsburgh, PA, 3Departments of Anesthesiology and Psychiatry, University of Pittsburgh, Pittsburgh, PA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Patient Outcomes, Preferences, and Attitudes Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM
**Background/Purpose:** Ongoing pain state in rheumatoid arthritis (RA) often persists after the resolution of inflammation, indicating the transition between the acute inflammatory pain and post-inflammatory persistent pain phenotypes. PainDETECT (PDQ) was developed as a self-reported neuropathic pain screening tool. We conducted a Rasch analysis to investigate whether measurement properties of PDQ can be used as an outcome measure.

**Methods:** For RA subjects enrolled in the University of Pittsburgh Rheumatoid Arthritis Comparative Effectiveness Registry (RACER), Rasch analysis was conducted for all RACER patients who completed PDQ and PROMIS29 short form. Unidimensionality, reliability, item difficulty, category functioning, and differential item function were examined using the partial credit model for polytomous items (WINSTEPS ver. 3.93.2). Differential item function (DIF) analyses for gender and age groups (<60, 60-70, >70) were performed to examine item invariance for different groups.

**Results:** For the 302 subjects analyzed, age was 63.8 ± 12.4 (mean ± SD) years with disease duration of 18.4 ± 11.9 years. Given misfit and high fit residuals, time course and radiating pain items were removed. Remaining 7-item PDQ fit the Rasch model (Table 1). Item residuals showed high correlation between the burning and slight pressure items and these items were treated as a testlet. Cold-or-heat item exhibited marginally disordered threshold but the rescoring did not substantially affect fit (Table 2). DIF analyses for gender and age groups showed uniform DIF. Person-item distribution showed that PDQ was reasonably targeted (Figure).

**Conclusion:** Rasch analysis of 7-item PDQ suggests that PDQ may function as an outcome measure and may provide a useful tool to predict RA treatment outcome for neuropathic pain.

<table>
<thead>
<tr>
<th>PainDETECT items</th>
<th>9 items</th>
<th>8 items</th>
<th>7 items</th>
<th>7 items (testlet)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Global statistics</strong></td>
<td>Log-likelihood chi-squared*</td>
<td>5521.44</td>
<td>4863.36</td>
<td>4194.34</td>
</tr>
<tr>
<td>df</td>
<td>5553</td>
<td>4923</td>
<td>4257</td>
<td>3610</td>
</tr>
<tr>
<td>Probability**</td>
<td>0.62</td>
<td>0.72</td>
<td>0.75</td>
<td>0.811</td>
</tr>
<tr>
<td>Global RMSR with expected value</td>
<td>0.88 (0.89)</td>
<td>0.90 (0.89)</td>
<td>0.89 (0.88)</td>
<td>0.88 (0.87)</td>
</tr>
<tr>
<td><strong>Person</strong></td>
<td>Measure (location, logit)</td>
<td>-1.62</td>
<td>-1.66</td>
<td>-1.71</td>
</tr>
<tr>
<td>SE (logit)</td>
<td>0.54</td>
<td>0.61</td>
<td>0.67</td>
<td>0.73</td>
</tr>
<tr>
<td>Infit MNSQ</td>
<td>1.02</td>
<td>1.04</td>
<td>1.06</td>
<td>1.04</td>
</tr>
<tr>
<td>Outfit MNSQ</td>
<td>1.06</td>
<td>1.03</td>
<td>1.04</td>
<td>1.03</td>
</tr>
<tr>
<td>Separation</td>
<td>1.44</td>
<td>1.32</td>
<td>1.29</td>
<td>1.17</td>
</tr>
<tr>
<td>Reliability</td>
<td>0.68</td>
<td>0.63</td>
<td>0.63</td>
<td>0.58</td>
</tr>
<tr>
<td><strong>Item</strong></td>
<td>Measure (location, logit)</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>SE (logit)</td>
<td>0.07</td>
<td>0.07</td>
<td>0.07</td>
<td>0.07</td>
</tr>
<tr>
<td>Infit MNSQ</td>
<td>0.98</td>
<td>1.02</td>
<td>1.03</td>
<td>1.03</td>
</tr>
<tr>
<td>Outfit MNSQ</td>
<td>1.08</td>
<td>1.03</td>
<td>1.04</td>
<td>1.03</td>
</tr>
<tr>
<td>Separation</td>
<td>5.15</td>
<td>5.05</td>
<td>5.40</td>
<td>5.74</td>
</tr>
<tr>
<td>Reliability</td>
<td>0.96</td>
<td>0.96</td>
<td>0.97</td>
<td>0.97</td>
</tr>
<tr>
<td>Item</td>
<td>Difficulty (logit)</td>
<td>SE (logit)</td>
<td>Infit MNSQ</td>
<td>Outfit MNSQ</td>
</tr>
<tr>
<td>--------------------</td>
<td>--------------------</td>
<td>------------</td>
<td>------------</td>
<td>-------------</td>
</tr>
<tr>
<td>Burning</td>
<td>-0.21</td>
<td>0.06</td>
<td>0.92</td>
<td>0.90</td>
</tr>
<tr>
<td>Tingling</td>
<td>-0.08</td>
<td>0.06</td>
<td>0.88</td>
<td>0.89</td>
</tr>
<tr>
<td>Light touch</td>
<td>0.38</td>
<td>0.07</td>
<td>0.87</td>
<td>0.92</td>
</tr>
<tr>
<td>Sudden attack</td>
<td>-0.14</td>
<td>0.06</td>
<td>1.15</td>
<td>1.18</td>
</tr>
<tr>
<td>Cold or heat</td>
<td>0.53</td>
<td>0.08</td>
<td>1.19</td>
<td>1.23</td>
</tr>
<tr>
<td>Numbness</td>
<td>0.20</td>
<td>0.07</td>
<td>1.01</td>
<td>0.96</td>
</tr>
<tr>
<td>Slight pressure</td>
<td>-0.69</td>
<td>0.06</td>
<td>1.19</td>
<td>1.20</td>
</tr>
</tbody>
</table>

**Disclosure:** Y. G. Hwang, Pfizer Inc, 2; L. Zhu, None; A. Wasan, None; L. W. Moreland, None.


Abstract Number: 339

**Patients’ Attitudes and Experiences of Transitional Care in Paediatric Rheumatology: A Systematic Review of Qualitative Studies**

Ayano Kelly¹,²,³,⁴, Fiona Niddrie⁵, David Tunnicliffe⁴,⁶, Camilla Hanson⁴,⁷, Gabor Major⁸,⁹, Davinder Singh-Grewal¹⁰,¹¹,¹² and Allison Tong⁴,¹ Rheumatology, The Canberra Hospital, Canberra, Australia, ²School of Medicine, Australian National University, Canberra, Australia, ³Canberra Rheumatology, Canberra, Australia, ⁴Centre for Kidney Research, The Children's Hospital at Westmead, Sydney, Australia, ⁵Rheumatology, Bone and Joint Institute, John Hunter Hospital, Newcastle, Australia, ⁶Sydney School of Public Health, University of Sydney, Sydney, Australia, ⁷Sydney School of Public Health, University of Sydney, Sydney, Australia, ⁸Medicine, University of Newcastle, Newcastle, Australia, ⁹Rheumatology, Bone and Joint Institute, John Hunter Hospital NSW Australia, Newcastle, Australia, ¹⁰Faculty of Medicine, University of New South Wales, Sydney, Australia, ¹¹Department of Rheumatology, The Sydney Children's Hospital Network, Sydney, Australia, ¹²Sydney Medical School, University of Sydney, Sydney, Australia

First publication: September 18, 2017
Background/Purpose: Despite the increasing number of transition programs available for rheumatology patients moving from paediatric to adult care, transition continues to pose challenges for patients and leads to poorer health outcomes. We aimed to describe patients’ attitudes and experiences of transitional care in paediatric rheumatology to capture a deeper understanding of patients’ perspectives and inform the development of patient-centred transitional care programs.

Methods: MEDLINE, Embase, PsycINFO, CINAHL, dissertation databases and reference lists were searched to February 2017 and thematic synthesis was used to analyse the findings.

Results: We included 18 studies involving 267 patients with paediatric rheumatic conditions (juvenile idiopathic arthritis \(n=162\), systemic lupus erythematosus \(n=79\), mixed connective tissue disease \(n=5\)). We identified six themes (with subthemes): a sense of belonging (familial care and community, yearning for friends with shared experiences, comfort and reassurance in age appropriate care, communication to gain understanding and acceptance); trust in familiarity (emotionally preparing for a new environment, building connection with continuity, valuing privacy, a supportive point of contact); abandonment and fear of the unknown (abrupt and forced independence, ill-equipped to transfer medical information, shocking view of future self); depersonalised and discredited (like an object on a conveyor belt, unmet needs and disjointed priorities, sterile and uninviting environment, sudden loss of validation); quest for autonomy (refreshingly liberated, ready to leave the nest, freedom to disclose); and needing control of parental involvement (unintentionally undermined, the guilt of independence, reluctant solitude).

Conclusion: There are limited qualitative studies on transitional care in paediatric rheumatology which focus largely on patients with juvenile idiopathic arthritis. Available qualitative studies show that successful transition can be nurtured by building trust in familiarity, creating a sense of belonging and facilitating an adolescent’s quest for autonomy. However, some patients feel de-personalised, abandoned, ill prepared and out of control of the transition process. The findings of this review highlight important elements to include into transitional care programs and the need for further research into patients’ needs in transitional care.

Disclosure: A. Kelly, None; F. Niddrie, None; D. Tunnicliffe, None; C. Hanson, None; G. Major, None; D. Singh-Grewal, None; A. Tong, None.


Abstract Number: 340

**Accessing Positive (but Not Negative) Online Reviews Is Associated with Increased Willingness to Take Medication**

Changchuan Jiang¹, Ellen Peters² and Liana Fraenkel³, ¹Yale University, New Haven, CT, ²Decision Research, Eugene, OR, ³Rheumatology, Rheumatology, Yale University School of Medicine, New Haven, CT

First publication: September 18, 2017
The outcomes in the reviews were purposely composed to match the actual distribution of outcomes associated with a commonly used osteoporosis treatment. Each review was rated by actual patients on a 5-point scale (illustrated by stars). Willingness to take medication was measured on a 10-point scale before and after reading the description of the medication and reviews (in the two groups including testimonials). Reviews could be read by clicking on links. We examined whether ratings and number of online testimonials accessed influenced change in willingness to take the medication using linear mixed models adjusting for baseline willingness, age, sex, race, education, numeracy, osteoporosis/osteopenia and previous history of osteoporosis/fracture. Reviews rated above ‘3’ were defined as positive; the rest were defined negative. The influence of positive and negative reviews was examined in separate models due to their strong collinearity.

**Results:** 276 participants were randomized to one of the two groups including testimonials. The mean (SD) age was 59 (7), and the majority were female (61%), white (73%) and college graduates (67%). We found significantly positive associations between the number of accessed positive testimonials and willingness to take the medication (p=0.015). However, no significant association was found between the number of accessed negative testimonials and willingness. Education level and numeracy did not modify the association between reviews accessed and willingness to take the medication (data not shown).

**Conclusion:** In this study, we found that willingness to take a medication for osteoporosis was positively associated with the number of positive online testimonials accessed. These results support the need to examine the impact of evidenced-based narratives as decision support tools.

### Table. Association between Positive (Model 1) and Negative (Model2) reviews with willingness to take a medication for osteoporosis.

<table>
<thead>
<tr>
<th></th>
<th>Model1 β</th>
<th>p-value</th>
<th>Model2 β</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Willingness Before Reading the Description</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>-0.027</td>
<td>0.138</td>
<td>-0.025</td>
<td>0.170</td>
</tr>
<tr>
<td>Male vs. Female</td>
<td>0.401</td>
<td>0.130</td>
<td>0.376</td>
<td>0.159</td>
</tr>
<tr>
<td>White vs. Non-White</td>
<td>0.137</td>
<td>0.644</td>
<td>0.087</td>
<td>0.773</td>
</tr>
<tr>
<td>High Numeracy vs. Low</td>
<td>0.521</td>
<td>0.053</td>
<td>0.470</td>
<td>0.088</td>
</tr>
<tr>
<td>Education Level College Graduate vs. Less</td>
<td>0.276</td>
<td>0.294</td>
<td>0.340</td>
<td>0.196</td>
</tr>
<tr>
<td>History of Bone Fracture vs. None</td>
<td>0.194</td>
<td>0.615</td>
<td>0.174</td>
<td>0.655</td>
</tr>
<tr>
<td>Osteopenia/Osteoporosis vs. None</td>
<td>-0.019</td>
<td>0.949</td>
<td>-0.0284</td>
<td>0.927</td>
</tr>
<tr>
<td>Number of Positive Reviews Accessed</td>
<td>0.027</td>
<td>0.015</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Number of Negative Reviews Accessed</td>
<td>N/A</td>
<td>N/A</td>
<td>0.0563</td>
<td>0.218</td>
</tr>
</tbody>
</table>

**Disclosure:** C. Jiang, None; E. Peters, None; L. Fraenkel, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/accessing-positive-but-not-negative-online-reviews-is-associated-with-increased-willingness-to-take-medication](http://acrabstracts.org/abstract/accessing-positive-but-not-negative-online-reviews-is-associated-with-increased-willingness-to-take-medication)

**Abstract Number:** 341

**Understanding Perceptions and Experience of Gout through Linguistic Analysis of Online Search Activities**

Kayla Jordan¹, James Pennebaker¹, Keith Petrie² and Nicola Dalbeth², ¹University of Texas at Austin, Austin, TX, ²University of Auckland, Auckland, New Zealand

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017
Background/Purpose: Online search engines are widely used to seek information about disease and management strategies. The aim of this study was to understand what terms people seeking information about gout use most frequently in their online searches and to explore the psychological and emotional tone of these searches using a linguistic analysis of their search histories.

Methods: In cooperation with Microsoft Research, a large de-identified dataset of search histories from 200,000 consenting individuals was obtained from ComScore, a web analytics company, covering a two year period (2011 to 2013). Time-stamped search terms were logged from all major search engines (e.g., Google, Bing). From the larger dataset, three groups were identified: participants who searched for gout at least once (n = 1,388), participants who had searched for arthritis (arthritis control group, n = 2,289, matched to the gout group on age and sex), and a random set of participants matched on age and sex (general control group, n = 2,150). Meaning Extraction Helper (Boyd, 2016), a word frequency software, was used to calculate search term frequencies from the search history of each participant. Group membership was correlated with individual word frequencies. Search terms were further analyzed using Linguistic Inquiry and Word Count (LIWC; Pennebaker, Boyd, Jordan, & Blackburn, 2015), a text analysis software from which psychological processes can be inferred from the words people use.

Results: The most frequent unique searches in the gout group included gout-related and food-related terms (including uric, kidney, meats, purine, and atkins). Those who searched for gout were more likely to search for words related to eating or avoidance. In contrast, those who searched for arthritis were more likely to search for disease or health-related words. In the LIWC analysis, compared with the general control group, total word count was higher for the gout and arthritis groups, indicating higher information seeking by both groups. Both the gout and arthritis groups searched more for health (e.g., clinic, flu, pill) and ingest (e.g., dish, eat, pizza) words, and fewer social (e.g. family, talk, they), leisure (e.g., cook, chat, movie), and sexual (e.g. love, sex) words. Compared with the general control group, the searches of both the gout and arthritis groups were lower in positive emotion tone and higher in sadness words. There were very few differences between the gout and arthritis groups in the LIWC analysis, with the exception of higher use of health words by the arthritis group and higher use of insight words (e.g., know, learn, and means) by the gout group.

Conclusion: People searching about gout or arthritis have high levels of information seeking. The perception of gout as a condition managed by dietary strategies aligns with online information-seeking about the disease and its management. In contrast, people searching about arthritis are more focused on searching about medical strategies. Linguistic analysis reflects greater disability in social and leisure activities and lower positive emotion for those searching for medical conditions such as gout or arthritis.

Disclosure: K. Jordan, None; J. Pennebaker, LIWC, 4; K. Petrie, None; N. Dalbeth, Takeda, AstraZeneca, Abbvie, 9.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/understanding-perceptions-and-experience-of-gout-through-linguistic-analysis-of-online-search-activities

Abstract Number: 342

Health Related Quality of Life Is Comparable in Psoriatic Arthritis and Rheumatoid Arthritis Patients in Spite of Different Disease Activity. SF-36 Data from a Large Prospective Observational Multicentre Study

Brigitte Michelsen¹,², Till Uhlig¹, Eirik K Kristianslund¹, Joseph Sexton¹, Elisabeth Lie¹, Karen M Fagerli³, Hilde B Hammer⁴, Glenn Haugeberg⁵,⁶ and Tore K Kvien⁷, ¹Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, ²Dept. of Rheumatology, Hospital of Southern Norway Trust, Kristiansand, Norway, ³Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, ⁴Dept of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, ⁵Martina Hansens Hospital, Bærum, Norway, ⁶NTNU, Norwegian University of Science and Technology, Trondheim, Norway, ⁷Diakonhjemmet Hospital, Oslo, Norway

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM
It is well established that RA patients have lower health related quality of life (HRQoL) across several domains compared with the general population, whereas less is known about PsA patients.

The aim of this study was to compare the Medical Outcomes Survey Short Form-36 (SF-36) Physical and Mental Component Summaries (PCS, MCS) as well as domain scores between RA and PsA patients from a large prospective observational registry.

Methods:

We included first-time enrolled RA and PsA patients from the prospective observational multicenter NORwegian-Disease Modifying Anti-Rheumatic Drug (NOR-DMARD) study, starting synthetic and biologic DMARDs between year 2000 and 2012. Continuous variables were compared using independent t-test or Mann-Whitney U-test, as appropriate. Prespecified ANCOVA analyses adjusted for age, gender and disease duration were performed to compare the SF-36 domains between RA and PsA patients at baseline and after 3 months follow-up. Spyder diagram was made to visualize the differences in health domains (0 worst, 100 best) between the RA and PsA patients.

Results:

A total of 3903 RA and 1518 PsA patients were included (mean (SD) age 56.8 (31.6)/ 47.9 (12.6) years, median (25th-75th percentile) disease duration 1.9 (0.07-11.0)/ 2.0 (0.12-9.6) years, 71.2%/ 50.2% women). Mean (SD) 28-joint Disease Activity Score was higher in RA vs. PsA patients at baseline (4.9 (1.4)/ 4.2 (1.3)) and at 3 months (3.8 (1.5)/ (3.3 (1.4)) follow-up (p≤0.001). Unadjusted means and adjusted estimated marginal means of PCS, MCS and domain scores all improved during follow-up (table, figure). In adjusted analyses PCS and MCS were similar between the RA and PsA patients. However, RA patients had slightly worse physical function and role emotional domains and PsA patients had slightly worse general health and vitality domains both at baseline and at 3 months. Bodily pain was similar between RA and PsA patients at baseline, but slightly worse in the PsA patients at 3 months follow-up.

Conclusion:

Levels of HRQoL were comparable across all SF-36 domains and component summary scores between patients with RA and PsA, in spite of higher levels of joint inflammation in the RA patients.

### Table

<table>
<thead>
<tr>
<th>Summary score/ domain</th>
<th>Unadjusted analyses, mean (SD)</th>
<th>p-value</th>
<th>Estimated marginal means (95%CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RA</td>
<td>PsA</td>
<td></td>
<td>RA</td>
</tr>
<tr>
<td>Physical Component Summary</td>
<td>31.0 (9.9)</td>
<td>31.8 (9.5)</td>
<td>0.01</td>
<td>31.7 (31.3-32.0)</td>
</tr>
<tr>
<td>Mental Component Summary</td>
<td>46.0 (11.4)</td>
<td>46.3 (11.5)</td>
<td>0.31</td>
<td>46.4 (46.0-46.8)</td>
</tr>
<tr>
<td>Physical Function</td>
<td>49.7 (25.0)</td>
<td>54.5 (23.4)</td>
<td>&lt;0.001</td>
<td>51.6 (50.8-52.4)</td>
</tr>
<tr>
<td>Role Physical</td>
<td>20.0 (31.6)</td>
<td>23.7 (34.1)</td>
<td>&lt;0.001</td>
<td>21.4 (20.3-22.5)</td>
</tr>
<tr>
<td>Bodily Pain</td>
<td>34.5 (19.0)</td>
<td>34.7 (18.2)</td>
<td>0.77</td>
<td>35.4 (34.8-36.1)</td>
</tr>
<tr>
<td>General Health</td>
<td>51.1 (20.3)</td>
<td>49.4 (20.7)</td>
<td>0.006</td>
<td>51.7 (51.1-52.4)</td>
</tr>
<tr>
<td>Vitality</td>
<td>39.2 (20.5)</td>
<td>38.7 (20.9)</td>
<td>0.39</td>
<td>41.1 (40.4-41.8)</td>
</tr>
<tr>
<td>Social Functioning</td>
<td>63.9 (26.4)</td>
<td>64.8 (25.8)</td>
<td>0.28</td>
<td>65.5 (64.6-66.4)</td>
</tr>
<tr>
<td>Role Emotional</td>
<td>51.4 (42.9)</td>
<td>55.8 (42.9)</td>
<td>0.001</td>
<td>52.3 (50.9-53.8)</td>
</tr>
<tr>
<td>Mental Health</td>
<td>70.0 (18.3)</td>
<td>70.6 (17.7)</td>
<td>0.31</td>
<td>71.0 (70.3-71.6)</td>
</tr>
</tbody>
</table>

### 3 Months

<table>
<thead>
<tr>
<th>Summary score/ domain</th>
<th>Unadjusted analyses, mean (SD)</th>
<th>p-value</th>
<th>Estimated marginal means (95%CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RA</td>
<td>PsA</td>
<td></td>
<td>RA</td>
</tr>
<tr>
<td>Physical Component Summary</td>
<td>35.6 (11.1)</td>
<td>36.4 (19.0)</td>
<td>0.07</td>
<td>36.4 (36.0-36.8)</td>
</tr>
<tr>
<td>Mental Component Summary</td>
<td>48.1 (10.9)</td>
<td>48.1 (11.3)</td>
<td>0.98</td>
<td>48.2 (47.8-48.6)</td>
</tr>
<tr>
<td>Physical Function</td>
<td>57.6 (25.9)</td>
<td>62.1 (24.3)</td>
<td>&lt;0.001</td>
<td>59.6 (58.7-60.6)</td>
</tr>
<tr>
<td>Role Physical</td>
<td>34.5 (38.9)</td>
<td>38.3 (39.5)</td>
<td>0.003</td>
<td>35.9 (34.4-37.4)</td>
</tr>
<tr>
<td>Bodily Pain</td>
<td>49.0 (22.0)</td>
<td>47.9 (21.3)</td>
<td>0.12</td>
<td>49.8 (49.0-50.6)</td>
</tr>
<tr>
<td>General Health</td>
<td>54.2 (21.2)</td>
<td>53.1 (21.7)</td>
<td>0.14</td>
<td>54.8 (54.0-55.6)</td>
</tr>
<tr>
<td>Vitality</td>
<td>46.7 (21.5)</td>
<td>45.0 (21.1)</td>
<td>0.02</td>
<td>48.1 (47.3-48.9)</td>
</tr>
<tr>
<td>Social Functioning</td>
<td>71.8 (24.7)</td>
<td>72.2 (24.8)</td>
<td>0.68</td>
<td>73.0 (72.0-73.9)</td>
</tr>
<tr>
<td>Role Emotional</td>
<td>59.7 (41.4)</td>
<td>64.0 (40.9)</td>
<td>0.002</td>
<td>60.0 (58.4-61.5)</td>
</tr>
<tr>
<td>Mental Health</td>
<td>74.2 (17.3)</td>
<td>74.1 (17.1)</td>
<td>0.84</td>
<td>74.8 (74.2-75.5)</td>
</tr>
</tbody>
</table>
Independent t-test; ANCOVA adjusted for age, gender and disease duration

**Figure** Estimated marginal means adjusted for age, gender and disease duration of baseline and 3 months SF-36 domains

---

**Disclosure:** B. Michelsen, None; T. Uhlig, None; E. K. Kristianslund, None; J. Sexton, None; E. Lie, AbbVie, Celgene, Hospira and Pfizer, 8; K. M. Fagerli, None; H. B. Hammer, AbbVie Norway, 2, Abbvie, 8, Novartis Pharmaceutical Corporation, 5, Pfizer Inc, 8, Roche Pharmaceuticals, 8; G. Haugeberg, None; T. K. Kvien, AbbVie, 2, Pfizer Inc, 2, Roche Pharmaceuticals, 2, UCB, 2, BMS, 2, MSD, 2, AbbVie, 5, Pfizer Inc, 5, BMS, 8, MSD, 8, Roche Pharmaceuticals, 8, UCB, 8, AbbVie, 8.


**Abstract Number:** 343

**What Is the Impact of Functional Medicine on Patient Reported Outcomes in Inflammatory Arthritis?**

Nicole Droz¹, William Messner² and M. Elaine Husni³, ¹Rheumatology, Cleveland Clinic Foundation, Cleveland, OH, ²Quantitative Health Sciences, Cleveland Clinic, Cleveland, OH, ³Rheumatology, Cleveland Clinic, Cleveland, OH

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Patient Outcomes, Preferences, and Attitudes Poster I  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Both RA and PsA patients carry significant morbidity despite advances in treatment. Patients often do not achieve clinical remission which can be limited by patient’s global assessment of disease (PtGA). Currently utilized disease activity and functional status assessments do not address all treatment outcomes that are important to patients (such as fatigue, psychological distress and quality of life). These outcomes drive PtGA and represent important areas of focus to achieve remission in RA and PsA patients. The Patient Reported Outcome Measurement Information System (PROMIS®) developed by the National Institute of Health, is a set of patient centric measures evaluating physical, mental and social health and is a precise and reliable way to measure domains critical to PtGA.

Functional medicine utilizes a patient-centered approach, addressing sleep, exercise, nutrition, stress and other lifestyle factors. The desire for this approach has led more patients to turn to functional medicine for adjunctive care.
Methods: In this 12 week retrospective study, RA and PsA patients were identified by ICD 10 code. They were included if they were diagnosed by a board certified rheumatologist and participated in a 12 week functional medicine program adjunctive to their usual care. PROMIS global physical and mental health and pain scores were collected at baseline and after 12 weeks of enrollment and compared to patients with similar baseline characteristics who received usual care alone. Changes in PROMIS T score domains in global physical, global mental health and pain were compared between treatment groups using two-sample t-tests.

Results: 38 patients were identified for inclusion. Both functional medicine + usual care (n=19) and usual care alone (n=19) had similar baseline characteristics including age, gender, smoking status and seropositivity. Baseline global physical and mental health scores were similar, however, pain was significantly lower at baseline in the functional medicine group as compared to the usual care group. At 12 weeks, there was no statistically significant difference between groups in any primary outcome, however there was a trend towards improved physical health scores and pain in the functional medicine group at 12 weeks (Table 1).

Table 1: Change in primary outcome scores from baseline to week 12

<table>
<thead>
<tr>
<th>Factor</th>
<th>Total (N=38)</th>
<th>Usual Care (N=19)</th>
<th>Usual Care + Functional Medicine (N=19)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Health T-Score Change*</td>
<td>1.7±4.9</td>
<td>0.58±5.5</td>
<td>2.9±4.0</td>
<td>0.16</td>
</tr>
<tr>
<td>Mental Health T-Score Change*</td>
<td>1.2±3.8</td>
<td>0.99±4.0</td>
<td>1.5±3.7</td>
<td>0.70</td>
</tr>
<tr>
<td>Pain Change*</td>
<td>0.05±2.0</td>
<td>0.42±2.0</td>
<td>-0.33±1.9</td>
<td>0.25</td>
</tr>
</tbody>
</table>
*Data not available for all subjects. Statistics presented as Mean ± SD p-values computed via two-sample t-tests

Conclusion: Enrollment in an adjunctive functional medicine program did not demonstrate a statistically significant improvement in pain, functional or mental health scores after 12 weeks but did show trends toward improvement in pain and physical function. Larger, prospective studies of longer duration are needed to identify the subset of patients who would benefit from a functional medicine intervention.

Disclosure: N. Droz, None; W. Messner, None; M. E. Husni, Pfizer Inc, 6, Abbvie, 5, PASE questionnaire, 7, Novartis Pharmaceutical Corporation, 5, Lilly, 5, UCB, 5, Amgen, 5, Janssen Pharmaceutica Product, L.P., 5, Bristol Myers Squibb, 5, Regeneron, 5.


Abstract Number: 344

Real World Clinical Trial Comparing the Patient Reported Outcomes Measurement Information System Short Forms and Profiles to CDAI Disease Classification in Rheumatoid Arthritis Patients

Jeffrey R. Curtis1, Sergio Schwartzman2, Shelly Kafka3, Dennis Parenti3, Shawn Black3, Stephen Xu4, Wayne Langhoff4 and Clifton O. Bingham III5, 1Rheumatology & Immunology, University of Alabama at Birmingham, Birmingham, AL, 2Weill Cornell Medical College, New York, NY, 3Janssen Scientific Affairs, LLC, Horsham, PA, 4Janssen Research & Development, LLC, Spring House, PA, 5Rheumatology, Johns Hopkins University, Baltimore, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Patient (Pt) reported outcomes (PROs) play a role in overall disease evaluation, therapeutic response assessment and care of rheumatoid arthritis (RA) patients (Pts). The Pt Reported Outcomes Measurement Information System (PROMIS [P])
questionnaires developed by the NIH have been used in clinical practice and observational studies in RA (Bartlett 2015). AWARE (Comparative and Pragmatic Study of Golimumab Intravenous [IV] Versus Infliximab in RA) is a large, pragmatic multi-center United States-based, real-world evidence study of golimumab IV (GLM) vs. infliximab (IFX) in RA and will assess infusion reactions, disease activity, and multiple PROs as outcomes.

**Methods:** AWARE is a prospective, noninterventional, ongoing study in which 1200 adult Pts will be enrolled on initiation of treatment with GLM or IFX. Objectives include PRO assessments of Pt response to treatment using the PROMIS-29 Profile v2.0 (P29v2), P Pain Interference Short Form-6b (PISF) and P Fatigue Short Form-7a (FSF), 36-Item Short Form Health Survey (SF-36v2) and Clinical Disease Activity Index (CDAI). We report here an interim analysis of 747 pts’ baseline PROMIS questionnaire and CDAI scores, and their inter-relationships. PROMIS questionnaire results are normalized to the US population and reported as a “T-score” (mean of 50 and standard deviation (SD) of 10) with higher scores indicating more of the trait being measured. PROMIS T-scores were compared between HDA with MDA, LDA and remission, respectively. Data shown are mean ± SD. Statistical testing compared T-scores across CDAI categories using ANOVA for this IA of baseline data (before drug administration). Data from GLM and IFX pts are combined.

**Results:** Overall baseline CDAI score was 32.5 ± 15.4, with 71.7% of pts in high DA (HDA), 22.5% in moderate disease activity (MDA), 5.2% in low disease activity (LDA) and 0.7% in remission. All P29v2 domains, PISF and FSF scores were significantly worse in pts with CDAI>22 vs. CDAI≤22 (p < 0.05), as was true for the 8 SF-36 domains (data not shown). PROMIS T-scores (P29v2 domains, PISF and FSF) were compared to the 4 CDAI disease activity categories. As shown below, PROMIS T-scores correlated with CDAI disease category, with HDA Pt T-scores significantly (*, p<0.05) different from those of MDA, LDA and Remission pts (except between HDA and remission for Anxiety, Depression and Sleep Disturbance domains).

<table>
<thead>
<tr>
<th>Mean ± Standard Deviation of PROMIS T-Score of All Patients in Interim Analysis Dataset and a Comparison of T-Scores of PROMIS-29 Domains, Fatigue Short Form and Pain Interference Short Form to CDAI Disease Activity Category</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>P29-Physical Function</strong></td>
</tr>
<tr>
<td>All Patients (n=672-682)</td>
</tr>
<tr>
<td>Remission CDAI≤2.8 (n=5)</td>
</tr>
<tr>
<td>LDA 2.8&lt;CDAI≤10 (n=38)</td>
</tr>
<tr>
<td>MDA 10&lt;CDAI≤22 (n=165)</td>
</tr>
<tr>
<td>HDA CDAI&gt;22 (n=526)</td>
</tr>
<tr>
<td>37.9 ± 6.6</td>
</tr>
<tr>
<td>47.5 ± 5.7</td>
</tr>
<tr>
<td>45.0 ± 7.6</td>
</tr>
<tr>
<td>40.0 ± 6.7</td>
</tr>
<tr>
<td>36.6 ± 5.9*</td>
</tr>
<tr>
<td><strong>P29-Anxiety</strong></td>
</tr>
<tr>
<td>53.8 ± 10.4</td>
</tr>
<tr>
<td>45.2 ± 6.7#</td>
</tr>
<tr>
<td>47.7 ± 8.6</td>
</tr>
<tr>
<td>51.3 ± 10.0</td>
</tr>
<tr>
<td>55.2 ± 10.3*</td>
</tr>
<tr>
<td><strong>P29-Fatigue</strong></td>
</tr>
<tr>
<td>52.5 ± 10.3</td>
</tr>
<tr>
<td>42.6 ± 3.6*</td>
</tr>
<tr>
<td>45.9 ± 6.5</td>
</tr>
<tr>
<td>49.4 ± 9.8</td>
</tr>
<tr>
<td>54.0 ± 10.3*</td>
</tr>
<tr>
<td><strong>P29-Sleep Disturbance</strong></td>
</tr>
<tr>
<td>58.8 ± 9.9</td>
</tr>
<tr>
<td>42.3 ± 5.4</td>
</tr>
<tr>
<td>49.7 ± 9.7</td>
</tr>
<tr>
<td>55.6 ± 9.2</td>
</tr>
<tr>
<td>60.8 ± 9.4*</td>
</tr>
<tr>
<td><strong>P29 Ability to participate in Social Roles and Activities</strong></td>
</tr>
<tr>
<td>43.2 ± 8.6</td>
</tr>
<tr>
<td>57.3 ± 7.6</td>
</tr>
<tr>
<td>50.8 ± 8.5</td>
</tr>
<tr>
<td>45.9 ± 8.5</td>
</tr>
<tr>
<td>41.6 ± 8.0*</td>
</tr>
<tr>
<td><strong>P29 Pain Interference</strong></td>
</tr>
<tr>
<td>63.5 ± 7.7</td>
</tr>
<tr>
<td>46.9 ± 7.2</td>
</tr>
<tr>
<td>53.9 ± 8.4</td>
</tr>
<tr>
<td>60.1 ± 7.7</td>
</tr>
<tr>
<td>65.4 ± 6.5*</td>
</tr>
<tr>
<td><strong>Fatigue Short Form 7a</strong></td>
</tr>
<tr>
<td>59.3 ± 8.5</td>
</tr>
<tr>
<td>46.7 ± 8.8</td>
</tr>
<tr>
<td>51.6 ± 9.0</td>
</tr>
<tr>
<td>56.2 ± 7.5</td>
</tr>
<tr>
<td>61.0 ± 8.1*</td>
</tr>
<tr>
<td><strong>Pain Interference Short Form 6b</strong></td>
</tr>
<tr>
<td>62.5 ± 7.6</td>
</tr>
<tr>
<td>45.9 ± 7.5</td>
</tr>
<tr>
<td>53.9 ± 9.3</td>
</tr>
<tr>
<td>59.3 ± 5.6</td>
</tr>
<tr>
<td>64.3 ± 6.4*</td>
</tr>
<tr>
<td><strong>P29 Pain Intensity</strong></td>
</tr>
<tr>
<td>(scored 0-10 scale)</td>
</tr>
<tr>
<td>6.0 ± 2.2</td>
</tr>
<tr>
<td>1.6 ± 2.6</td>
</tr>
<tr>
<td>3.5 ± 2.3</td>
</tr>
<tr>
<td>5.1 ± 2.2</td>
</tr>
<tr>
<td>6.6 ± 1.9*</td>
</tr>
</tbody>
</table>

T-scores > 50 indicate worsening of the domain relative to the general population, except “Physical Function” and “Ability to participate in Social Roles and Activities”, where T-scores < 50 indicate worsening of these domains relative to the general population. *= p<0.05 vs respective scores in MDA, LDA and remission DA categories. # = not statistically different from HDA

**Conclusion:** Our interim findings demonstrate the feasibility of using PROMIS short forms and profiles to evaluate RA pts in clinical trials. These results confirm the domain validity of PROMIS measures according to CDAI disease category. PROMIS measures show the range of impact across multiple domains of physical, emotional, and social health experienced by RA pts. With a fully enrolled AWARE trial, evaluation of PROs, their responsiveness over time, and comparison with SF36 will provide important additional validation for their use in clinical trials.

**Disclosure:** J. R. Curtis, AbbVie, Roche/Genentech, BMS, UCB, Myraiden, Lilly, Amgen, Janssen, Pfizer, Corrona, 5,Amgen, Pfizer, Crescendo Bio, Corrona, 9; S. Schwartzman, AbbVie, Antares, Genentech, Janssen, Lilly, Novartis, Pfizer, Regeneron, Sanofi, UCB,
The Patient Experience of Musculoskeletal Imaging Tests for Investigation of Inflammatory Arthritis: A Mixed Methods Study

Sandra Bourke¹,², Nicola Dalbeth¹, William J. Taylor³, Anthony Doyle¹ and Merryn Gott¹, ¹University of Auckland, Auckland, New Zealand, ²Auckland district health board, Auckland, New Zealand, ³University of Otago, Wellington, New Zealand

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Musculoskeletal (MSK) imaging is widely used in rheumatology for diagnosis and management of arthritis. Although the technical and performance properties of MSK imaging tests are well recognised, few studies have examined the patient experience of undergoing these tests. The aim of this study was to understand the patient experience of MSK imaging tests for investigation of inflammatory arthritis, and factors that contribute to this experience.

Methods: In this mixed methods study, we conducted a thematic analysis of semi-structured interviews with 33 patients who had undergone a recent peripheral joint conventional radiograph, ultrasound, computed tomography or magnetic resonance imaging scan for investigation of inflammatory arthritis. Data from these interviews were used to generate an 18-item questionnaire about the experience of MSK imaging which was posted to rheumatology clinic patients within six weeks of peripheral joint imaging. Variables associated with the overall patient experience of the test were analysed using stepwise linear regression models.

Results: Analysis of the interviews identified six themes; knowledge about the test, the role of imaging in clinical care, awareness of potential harm, discomfort, experience of waiting, and ‘seeing is believing’. Patient understanding was informed by the information they received and previous experience of the test. Patients perceived imaging as part of clinical care and believed the benefits of having the test outweighed the potential risks. Discomfort was experienced by some patients, both emotional due to negative experiences of interactions with staff and claustrophobia, and physical due to positioning for the test. Some patients felt anxious about waiting times for the test and for receiving results. Viewing of the images (particularly during ultrasound) improved understanding of disease and gave a sense of personal involvement in their arthritis treatment. Completed questionnaires were available from 132 patients. In regression analysis (Table), a strong negative association was observed between the ‘Discomfort during the test’ item and the overall experience of the test (standardised beta 0.35, p<0.001). ‘Staff made the experience better’ (0.26, p<0.001) and ‘Information provided’ (0.28, p<0.001) were positively associated with the overall experience of the test. For those who viewed their images, ‘looking at the images with my doctor made me feel more involved in my care’ (0.24, p<0.019) was also associated positively with overall experience.

Conclusion: Factors before, during and after a musculoskeletal imaging test contribute to the patient experience. The overall experience is most influenced by patient discomfort, interactions with staff during the test, information provided, and viewing images to improve patient involvement in clinical care.
Table 1. Stepwise linear regression analysis of question items (excluding non-applicable questions) independently associated with overall experience of the test (all participants)

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Predictors</th>
<th>Standardized β</th>
<th>R² change</th>
<th>p</th>
<th>Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall experience</td>
<td>Discomfort during the test</td>
<td>-0.35</td>
<td>0.16</td>
<td>&lt;0.001</td>
<td>Adjusted R² = 0.32</td>
</tr>
<tr>
<td></td>
<td>Information provided</td>
<td>0.28</td>
<td>0.11</td>
<td>&lt;0.001</td>
<td>F = 20.0</td>
</tr>
<tr>
<td></td>
<td>Staff made the experience better</td>
<td>0.26</td>
<td>0.06</td>
<td>&lt;0.001</td>
<td>P &lt; 0.001</td>
</tr>
</tbody>
</table>

Items included in this analysis: imaging modality and all questionnaire items that did not include a not applicable response.

Disclosure: S. Bourke, None; N. Dalbeth, Takeda, AstraZeneca, Abbvie, 9; W. J. Taylor, Pfizer Inc, 5; A. Doyle, None; M. Gott, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-patient-experience-of-musculoskeletal-imaging-tests-for-investigation-of-inflammatory-arthritis-a-mixed-methods-study

Abstract Number: 346

What Are We Measuring? Influence of Contextual Factors on RAPID3 Scores in Psoriatic Arthritis

Alexis Ogdie¹, Christine Willinger², M. Elaine Husni³, Jose U. Scher⁴, Soumya M. Reddy⁵ and Jessica A. Walsh⁶,
¹Medicine/Rheumatology and Epidemiology, University of Pennsylvania, Philadelphia, PA, ²University of Pennsylvania, Philadelphia, PA, ³Cleveland Clinic, Cleveland, OH, ⁴New York University School of Medicine, New York, NY, ⁵Department of Medicine, Division of Rheumatology *contributed equally, New York University School of Medicine, New York, NY, ⁶Division of Rheumatology, University of Utah, Salt Lake City, UT

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Patient reported outcomes (PRO) provide valuable insights into patients’ perceptions of their disease and overall health and function, and these perceptions influence management of their disease. The objective of this study was to examine patient factors (also termed Òcontextual factorsÓ) that may be associated with the Routine Index of Patient Data (RAPID3) score among patients with psoriatic arthritis (PsA).

Methods: Patients with PsA were enrolled in the Psoriatic Arthritis Research Consortium (PARC) between 2015-2016. PARC is a longitudinal observational cohort study conducted at four institutions in the United States: University of Pennsylvania, Cleveland Clinic, New York University, and University of Utah. Only baseline data are included in this cross-sectional analysis. Potential contextual factors were defined prior to statistical testing. A contextual factor is defined by OMERACT as a Òvariable that is not an outcome of the study but needs to be recognized and measured in order to understand the study results.Ó We examined the association between potential contextual factors and RAPID3 scores using univariable linear regression models. Variables significant at the univariable stage (defined as p<0.05) were included in multivariable linear regression models. A final model to identify factors with an independent relationship with RAPID3 score after accounting for disease activity (e.g., swollen and tender joint counts, skin global assessment, enthesitis) was formed using backwards selection.

Results: Among the four centers, 401 patients were enrolled; 55% were female, mean age was 51.3, and 76% identified as Caucasian. Using RAPID3 cut-offs designed for RA, the mean disease activity (9.0, SD 6.7) would be categorized as Òmoderate.Ó Contextual factors significantly associated with RAPID3 score were female sex, current alcohol use, body mass index (BMI), depression, education level, and insurance status. In a multi-variable model insurance status, depression and BMI were most strongly associated with RAPID3 score, after accounting for PsA disease activity. These factors were similarly associated with the individual components of the RAPID3 (physical function, global assessment, and pain).
Conclusion: In PsA, the RAPID3 score is influenced by depression, insurance status, and obesity. These factors must be taken into account when using RAPID3 in clinical practice. Additionally, treating depression and improving obesity may be potential targets for improving the overall perception of disease in patients with PsA.
<table>
<thead>
<tr>
<th>Factor</th>
<th>Univariable</th>
<th></th>
<th>Multivariable*</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Beta-coefficient (95%CI)</td>
<td>p-value</td>
<td>Beta-coefficient (95%CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>Age</td>
<td>0.002 (-0.05-0.06)</td>
<td>NS</td>
<td>1.32 (-0.42-3.05)</td>
<td>0.14</td>
</tr>
<tr>
<td>Female vs Male</td>
<td>2.39 (0.92-3.86)</td>
<td>&lt;0.001</td>
<td>1.32 (-0.42-3.05)</td>
<td>0.14</td>
</tr>
<tr>
<td>Smoking (ever vs never)</td>
<td>1.22 (-0.42-2.86)</td>
<td>NS</td>
<td>1.32 (-0.42-3.05)</td>
<td>0.14</td>
</tr>
<tr>
<td>Alcohol (current use)</td>
<td>-2.12 (-3.66-0.58)</td>
<td>0.01</td>
<td>0.16 (0.04-0.29)</td>
<td>0.01</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>0.23 (0.12-0.34)</td>
<td>&lt;0.001</td>
<td>0.16 (0.04-0.29)</td>
<td>0.01</td>
</tr>
<tr>
<td>Depression</td>
<td>4.09 (2.36-5.82)</td>
<td>&lt;0.001</td>
<td>2.93 (0.94-4.92)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of Diabetes</td>
<td>0.89 (-1.34-3.12)</td>
<td>NS</td>
<td>0.16 (0.04-0.29)</td>
<td>0.01</td>
</tr>
<tr>
<td>History of Cardiovascular disease</td>
<td>1.85 (-0.01-3.71)</td>
<td>NS</td>
<td>0.16 (0.04-0.29)</td>
<td>0.01</td>
</tr>
<tr>
<td>Race</td>
<td>REF</td>
<td></td>
<td>REF</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>REF</td>
<td></td>
<td>REF</td>
<td></td>
</tr>
<tr>
<td>Black/African American</td>
<td>4.77 (-0.62-10.16)</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Native American</td>
<td>2.23 (-7.04-11.5)</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>-3.01 (-7.43-1.42)</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>3.45 (-2.44-9.34)</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>2.59 (-1.84-7.01)</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td>REF</td>
<td></td>
<td>REF</td>
<td></td>
</tr>
<tr>
<td>No college degree</td>
<td>REF</td>
<td></td>
<td>REF</td>
<td></td>
</tr>
<tr>
<td>College</td>
<td>-2.5 (-4.88-0.13)</td>
<td>0.04</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-graduate</td>
<td>-5.24 (-7.92-2.56)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insurance</td>
<td>REF</td>
<td></td>
<td>REF</td>
<td></td>
</tr>
<tr>
<td>Uninsured</td>
<td>REF</td>
<td></td>
<td>REF</td>
<td></td>
</tr>
<tr>
<td>Medicare/medicaid</td>
<td>-11.63 (-20.94-0.02)</td>
<td>0.02</td>
<td>-10.47 (-18.66-0.01)</td>
<td>0.01</td>
</tr>
<tr>
<td>Disease/Outcome factors</td>
<td>β-coefficients</td>
<td>95% Confidence Interval</td>
<td>p-value</td>
<td></td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>----------------</td>
<td>-------------------------</td>
<td>---------</td>
<td></td>
</tr>
<tr>
<td>Inflam Back Pain</td>
<td>-0.04</td>
<td>(-0.249-0.241)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>ASAS classification</td>
<td>0.68</td>
<td>(-0.205-3.41)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Skin Physician Global</td>
<td>0.72</td>
<td>(0.36-1.07)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Enthesitis Count</td>
<td>2.13</td>
<td>(1.09-3.17)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Total swollen joints</td>
<td>0.74</td>
<td>(0.5-0.97)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Total tender joints</td>
<td>0.39</td>
<td>(0.26-0.51)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Nail dystrophy</td>
<td>-1.06</td>
<td>(-3.53-1.41)</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

The β-coefficients can be interpreted as the difference in the mean PRO score between the two groups. The 95% confidence intervals do not include 0 (no
Prevalence of obesity was 42%, depression 19%, diabetes 10% and cardiovascular disease 18%.

Sex was specifically included in the previous model given others studies reporting an association between sex and patient reported outcome scores.

*All other items that were not significant in the multivariable models were removed.

Disclosure: A. Ogdie, Pfizer, Novartis, 2, Takeda, Pfizer, Novartis, 5; C. Willinger, None; M. E. Husni, Celgene, AbbVie, Genentech, Bristol-Myers Squibb, Pfizer, Novartis, and Janssen, 9; J. U. Scher, NIAMS-NIH, 2; S. M. Reddy, Eli Lilly and Company, 5; J. A. Walsh, Novartis, 5.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/what-are-we-measuring-influence-of-contextual-factors-on-rapid3-scores-in-psoriatic-arthritis

Abstract Number: 347

Disease Burden at One Academic Rheumatology Routine Care Setting Is Similar in Osteoarthritis (OA) and Rheumatoid Arthritis (RA) at First Visit but Significantly Greater in OA at a 6-Month Follow-up Visit

Jacquelin R. Chua1, Shakeel M. Jamal1, Isabel Castrejón1, Najia Shakoor1, Anne-Marie Malfait2, Joel A. Block2 and Theodore Pincus2, 1Division of Rheumatology, Rush University Medical Center, Chicago, IL, 2Rheumatology, Rush University Medical Center, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Osteoarthritis commonly is regarded as less severe and less debilitating than RA. However, limited data are available for direct comparison of OA versus RA, in large part because different measures traditionally have been used to assess patients, primarily a HAQ (Health Assessment Questionnaire) in RA and WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) in OA. RAPID3 (Routine Assessment of Patient Index Data) on an MDHAQ (Multi-Dimensional HAQ) is a composite of 3 patient self-report measures that was developed for RA, but is informative in many other rheumatic diseases, including OA. Recent observations from 4 settings indicate that RAPID3 and other MDHAQ scores were similar or higher in OA versus RA patients. Those findings were from a cross-sectional convenience sample, and likely were affected by treatment in most patients. We analyzed MDHAQ/RAPID3 scores in patients with a primary diagnosis of either OA or RA at their first visit to a rheumatology center and at 6 month follow-up.

Methods: At one academic center, all patients complete an MDHAQ/RAPID3 prior to seeing the rheumatologist. The 2-page MDHAQ/RAPID3 includes scores for physical function (FN) (0-3 converted to 0-10) and 0-10 visual analog scale (VAS) scores for pain (PN) and patient global assessment (PATGL), compiled into a 0-30 composite RAPID3. Patients with physician-diagnosed primary OA or RA were included in the study. Mean FN, PN, PATGL and RAPID3 scores in RA and OA at baseline and 6-month follow-up (range 3-9 months) were compared for differences between first and second visits using t-tests, as well as between OA and RA adjusted using MANOVA.

Results: At first visit, RAPID3 was 15.9 in OA vs 15.3 in RA - no meaningful differences in individual measures or index (Table). At 6-month follow-up, in OA, RAPID3 fell from 15.9 to 14.9 (-1.0, p=0.06) vs 15.3 to 11.1 (-4.2, p<0.001) in RA, indicating greater improvement in RA, resulting in significantly higher disease burden in OA vs RA. These differences remained significant after adjusting for age, sex, body mass index, and education level.
Mean and standard deviation (SD) at first visit and 6-month follow up visit MDHAQ/RAPID3 of patients with OA and RA seen in routine care

<table>
<thead>
<tr>
<th>Measures</th>
<th>OA (n=109)</th>
<th>RA (n=102)</th>
<th>OA vs RA p value</th>
<th>OA vs RA p adjusted*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Function (0-10)</td>
<td>3.15 (1.9)</td>
<td>2.89 (2.2)</td>
<td>0.34</td>
<td>0.60</td>
</tr>
<tr>
<td>Pain (0-10)</td>
<td>7.01 (2.3)</td>
<td>6.36 (2.9)</td>
<td>0.07</td>
<td>0.49</td>
</tr>
<tr>
<td>PATGL (0-10)</td>
<td>5.69 (2.8)</td>
<td>5.85 (3.0)</td>
<td>0.69</td>
<td>0.30</td>
</tr>
<tr>
<td>RAPID3 (0-30)</td>
<td>15.9 (5.9)</td>
<td>15.3 (7.0)</td>
<td>0.52</td>
<td>0.47</td>
</tr>
<tr>
<td>Function (0-10)</td>
<td>2.93 (1.9)</td>
<td>2.24 (2.2)</td>
<td>0.02</td>
<td>0.006</td>
</tr>
<tr>
<td>Pain (0-10)</td>
<td>6.36 (2.5)</td>
<td>4.60 (3.0)</td>
<td>&lt;0.001</td>
<td>0.03</td>
</tr>
<tr>
<td>PATGL (0-10)</td>
<td>5.62 (2.7)</td>
<td>4.10 (3.2)</td>
<td>&lt;0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>RAPID3 (0-30)</td>
<td>14.9 (6)</td>
<td>11.1 (7.6)</td>
<td>&lt;0.001</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*adjusted for age, sex, BMI and education

**Conclusion:** Patients with OA or RA have similar disease burdens at first visit, but OA patients have a considerably higher burden 6 months later, reflecting more effective treatments for RA than for OA. Nonetheless, OA is a severe disease at first visit, suggesting a need for further research in OA toward improved treatment and outcomes. MDHAQ/RAPID3 is feasible and useful to assess and monitor clinical status in routine care of patients with different rheumatic diseases.


**Disclosure:** J. R. Chua, None; S. M. Jamal, None; I. Castrejón, None; N. Shakoor, None; A. M. Malfait, Galapagos, Regeneron, Ferring, 5; J. A. Block, None; T. Pincus, Theodore Pincus, 7.


Abstract Number: 348

**The Impact of Rheumatoid Arthritis-Sustained Remission on Patient’s Reported Outcomes Differs Accordingly to Each Particular Outcome**

Irazú Contreras-Yáñez¹, Guillermo Guaracha², César Sifuentes-Cantú³ and Virginia Pascual-Ramos⁴, ¹Inmunología y Reumatología, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, ²Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, ³Department of Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, ⁴Instituto Nacional de Ciencias Médicas y Nutrición, Mexico City, Mexico

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Patient Outcomes, Preferences, and Attitudes Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM
**Background/Purpose:** Sustained remission (SR) is the most desirable status in patients with rheumatoid arthritis (RA). For adoption by patients, SR should reflect symptom’s resolution and impact patient-report-outcomes (PRO). The study was performed in an inception cohort of recent-onset RA, initiated in 2004. Objectives of the study were to describe PRO from patients who achieved SR for the first time, as well as the proportion of those patients who achieved PRO norms, and to describe the pattern of PRO’s normalization.

**Methods:** In November 2016, the cohort had 145 patients with ≥30 months of follow-up, with complete and regular rheumatic evaluations that additionally included a patient-pain visual analogue scale (PVAS), a patient-overall disease-VAS (OVAS), the health assessment questionnaire (HAQ), the Short-Form 36v2 Survey (SF-36) and fatigue assessment. First SR was defined according to DAS28 cut-offs (DAS28-SR) and to the ACR/EULAR 2011 Boolean definition (B-SR), if maintained for at least 12 months. The dependent t test and Mc Nemar’s tests were used. The study was approved by IRB and written informed consent was obtained from all the patients.

**Results:** At cohort inclusion, patients were primarily middle-aged female with a high frequency of auto-antibodies. Up to SR, 98% of the patients were on traditional DMARDs and 37-42% were receiving combined low doses of corticosteroids.

An increased number of patients achieved DAS28-SR compared to B-SR (78 vs. 63 patients, respectively). In addition, follow-up to DAS28-SR was shorter than to B-SR, and the duration of DAS28-SR was longer than the duration of B-SR (p≤0.03 for both).

In general, at SR (either DAS28-SR or B-SR) patients had PRO proxy to normal values (PRO-N); the percentage of patients with PRO-N varied from 97% for HAQ, but decreased to 50% for absence of fatigue.

In SR patients, we calculated (mean±SD) months of follow-up to achieve each particular PRO-N, and to achieve values within the normal range of erythrocyte sedimentation rate (ESR) and C reactive protein (CRP) and of overall-disease-physician-VAS. In DAS28-SR patients, normalization of ESR and CRP was detected at 1.5 and 2.9 months from baseline, respectively, followed by HAQ-N, PVAS-N, OVAS-N, SF-36-N (achieved between 6 and 7 months of follow-up); absence of fatigue was detected late, at 8.7 months of follow-up, similar to DAS28-SR, which was achieved at 9.8 months. A similar pattern was observed in B-SR patients (Figure. Pattern of outcome normalization).

**Conclusion:** At SR, RA patients achieved PRO proxy to normal values although the percentage of patients with PRO-N varied depending on each particular outcome. We identified a particular temporal pattern of outcome normalization. PRO provide unique information that cannot be collected from a physician and aid to complete the clinical picture of RA patients in SR.

**Disclosure:** I. Contreras-Yáñez, None; G. Guaracha, None; C. Sifuentes-Cantú, None; V. Pascual-Ramos, None.
Preferences and Satisfaction in a Pediatric Multidisciplinary Infusion Center

Catherine McDermott & 1, Brian Sohl1, Lisa M. McGregor2 and Lisabeth V. Scalzi3, 1Penn State Hershey Medical Center, Hershey, PA, 2Penn State Hershey Children’s Hospital, Hershey, PA, 3Department of Rheumatology, Penn State Hershey Children’s Hospital, Hershey, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Many pediatric rheumatology patients receive infusions in multi-specialty infusion centers (MSICs). There is little data about pediatric patient satisfaction and preferences within MSICs and no data about their physicians’ perceptions of these preferences. In order to better understand and improve the patient experience, we studied these concepts.

Methods:

We created and administered a survey containing free response and 5-point Likert scale questions to parents of children receiving infusion therapy and their respective physicians at our center. We compared means and sums of the scores using t-tests and ANOVA analyses.

Results:

We surveyed 21 physicians (8 oncologists, 13 non-oncologists) and 174 parents of patients with oncologic (n=66) and non-oncologic (n=108) diagnoses who were receiving infusions in our MSIC. Our results showed significant differences between family satisfaction/preference and physician perception (Fig 1).

For all 3 questions, families responded positively towards the multi-specialty nature of the infusion center, though oncology families to a lesser degree than non-oncology families (respectively, mean=4.5 ±0.07 vs. 4.8 ±0.05; p<0.009).

Rheumatologists had a greater discrepancy than oncologists did in their perceptions of their patients’ preferences, predicting their patients would be less satisfied receiving care in an MSIC than patients reported (Fig 2). In addition, rheumatologists believed their patients would prefer to receive infusions in a center specific for children without cancer, despite families not having this preference (mean = 1.3 ± 0.58 vs. 2.7±0.90; p<0.027, respectively).

Lastly, the majority of families surveyed reported they had increased awareness and empathy from exposure to children with other diagnoses, reflected in their comments (Table 1).

Conclusion:

Pediatric rheumatology patients are satisfied with their experiences in an MSIC. Patients are significantly more satisfied than their physicians perceive. As infusion therapy for rheumatologic conditions increases, it is important to understand patient preferences as a crucial aspect of patient-centered care. Patients are content to receive infusions in an MSIC and find value in their experiences with families of children with other diagnoses.
Patients with Gout Consider Zero Flares over the Previous Six or Twelve Months Necessary for a Remission State
William J. Taylor 1, Nicola Dalbath 2, Kenneth Saag 3, Jasvinder A. Singh 4, Elizabeth J. Rahn 5, Amy S. Mudano 6, Yi-Hsing Chen 7, Ching-Tsai Lin 8, Paul Tan 9, Worawit Louthrenoo 9, Janitzia Vazquez-Mellado 10, Hansel Hernández-Llinas 11, Tuhina Neogi 12, Ana Beatriz Vargas-Santos 12, Geraldo Castelan-Pinheiro 13, Rodrigo B. Chaves-Amorim 13, Till Uhlig 14, Hilde B Hammer 14, Maxim Eliseev 15, Fernando Perez-Ruiz 16, Lorenzo Cavagna 17, Geraldine M. McCarthy 18, Lisa K. Stamp 19, Martijin Gerritsen 20, Viktoria Fana 21, Francisca Sivera 22 and Angelo L. Gaffo 5, 1University of Otago, Wellington, New Zealand, 2University of Auckland, Auckland, New Zealand, 3Division Clinical Immunology & Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 4Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 5Department of Medicine, Division of Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 6University of Alabama at Birmingham, Birmingham, AL, 7Taichung Veterans General Hospital, Taichung, Taiwan, 8Division of Allergy, Immunology and Rheumatology, Taichung Veterans General Hospital, Taichung, Taiwan, 9Div of Rheumatology, Dept of Internal Medicine, Chiang Mai University, Chiang Mai, Thailand, 10Rheumatology, Hospital General de Mexico, Mexico City, Mexico, 11Hospital General de Mexico, Mexico City, Mexico, 12Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA, 13Universidade do Estado do Rio de Janeiro - UERJ, Rio de Janeiro, Brazil, 14Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, 15V. A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation, 16Servicio de Reumatología, Vizcaya, Spain, 17Division of Rheumatology, University and IRCCS Policlinico S. Matteo, Pavia, Italy, 18Div of Rheumatology, Mater Misericordiae University Hospital, Dublin, Ireland, 19University of Otago, Christchurch, New Zealand, 20Westfries Gasthuis, Hoorn, Netherlands, 21Center for Rheumatology and Spine Diseases, Rigshospitalet, Glostrup, Copenhagen Center for Arthritis Research (COPECARE), Copenhagen, Denmark, 22Sección de Reumatología, Hospital General Universitario de Elda., Elda, Spain

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Treatment targets for gout generally focus on serum urate, but patient-centred targets may be equally important. We seek to determine the relationship between gout flare rates and patient self-classification into 3 disease activity states: remission (no symptoms of disease), low disease activity (LDA, no symptoms of disease that require additional therapy), and patient acceptable symptom state (PASS, level of symptoms acceptable to the patient).

Methods: Patients with 2015 ACR/EULAR gout criteria attending rheumatology clinics in 17 countries were asked to recall the number of flares over the preceding 6 and 12 months. For each time horizon they were asked to consider whether they thought their gout had gone away (remission), didn’t require any additional or stronger therapy (LDA) or was controlled to their satisfaction (PASS). Multinomial logistic regression was used to determine the association between being in each disease state, flare count and self-reported current flare. A distribution-based approach and 3-state analysis of the volume under a ROC surface (VUS) with extended Youden index identified possible flare count thresholds for each state.

Results: 512 patients were recruited with mean (SD) age 58 (14) years, 89% were male, and disease duration of 12 (10) years. The states of LDA/PASS were combined since the distribution of recalled flares was very similar for these states. Each recalled flare reduced the likelihood of self-classified remission by 52% for 6 months and 23% for 12 months, and the likelihood of LDA/PASS by 15% and 5% for 6 and 12 months, respectively (Table). Not currently self-reporting a flare was strongly associated with self-classification into remission (OR 15.20 for 6 months and 15.13 for 12 months) or LDA/PASS (OR 5.74 for 6 months and 5.13 for 12 months) (Table). The VUS for 6-month flare count was 0.41 (95%CI 0.36 to 0.46) and the thresholds identified from the extended Youden index were 0 and 3.5; for 12-month flare count, the VUS was 0.38 (95%CI 0.33 to 0.43) and thresholds were 0 and 4.5. A threshold of 0 flares in preceding 6 and 12 months was associated with accurate classification of remission in 58% and 56% of cases, respectively.

Conclusion: Recalled flares are significantly associated with patient perceptions of disease activity in gout, supporting flare as an important target of therapy. Zero flares over prior 6 or 12 months were necessary for most patients to self-categorise as remission. Current flare is strongly associated with perception of disease activity, independently of the number of prior flares. However, recalled flare counts alone do not fully predict self-categorised states, suggesting that other factors may also contribute to perception of gout disease activity.
<table>
<thead>
<tr>
<th>Disease activity category*</th>
<th>OR (95% CI)‡</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Considering the previous 6 months</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Remission</td>
<td>No. of flares</td>
<td>0.48 (0.38 to 0.60)</td>
</tr>
<tr>
<td></td>
<td>Current flare absent†</td>
<td>15.20 (5.58 to 41.37)</td>
</tr>
<tr>
<td>LDA/Pass</td>
<td>No. of flares</td>
<td>0.85 (0.79 to 0.90)</td>
</tr>
<tr>
<td></td>
<td>Current flare absent</td>
<td>5.74 (3.51 to 9.37)</td>
</tr>
<tr>
<td><strong>Considering the previous 12 months</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Remission</td>
<td>No. of flares</td>
<td>0.77 (0.70 to 0.85)</td>
</tr>
<tr>
<td></td>
<td>Current flare absent†</td>
<td>15.13 (5.68 to 40.34)</td>
</tr>
<tr>
<td>LDA/Pass</td>
<td>No. of flares</td>
<td>0.95 (0.92 to 0.97)</td>
</tr>
<tr>
<td></td>
<td>Current flare absent</td>
<td>5.35 (3.33 to 8.60)</td>
</tr>
</tbody>
</table>

* The reference category is: Not in any of the 3 low disease activity states.
† The reference category is: Current flare present
‡ The OR are derived from a multinomial logistic regression model (separate models for 6 and 12 months), where the dependent variable was disease activity category and the independent variables were flare count and presence/absence of current flare

Disclosure: W. J. Taylor, AstraZeneca, Pfizer, Abbvie, Roche, 5; N. Dalbeth, AstraZeneca, 2,Takeda, Pfizer, AstraZeneca, Cymabay, Crealta, 5,Takeda, AstraZeneca, 9; K. Saag, AstraZeneca, Horizon, Ironwood, SOBI, Takeda, 5; J. A. Singh, Takeda, Savient, 2,Savient, Takeda, Regeneron, Merz, Bioiberica, Crealta, Allergan, WebMD, UBM LLC, American College of Rheumatology, 5; E. J. Rahn, None; A. S. Mudano, None; Y. H. Chen, None; C. T. Lin, None; P. Tan, None; W. Louthrenoo, None; J. Vazquez-Mellado, None; H. Hernández-Llinas, None; T. Neogi, None; A. B. Vargas-Santos, None; G. Castelar-Pinheiro, None; R. B. Chavez-Amorim, None; T. Uhlig, None; H. B. Hammer, None; M. Eliseev, None; F. Perez-Ruiz, Ardea Biosciences, AstraZeneca, Cymabay, Grunenthal, Menarini, 5; L. Cavagna, None; G. M. McCarthy, None; L. K. Stamp, None; M. Gerritsen, None; V. Fana, None; F. Sivera, AstraZeneca, 5; A. L. Gaffo, SOBI, 5,Amgen, 2.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/patients-with-gout-consider-zero-flares-over-the-previous-six-or-twelve-months-necessary-for-a-remission-state](http://acrabstracts.org/abstract/patients-with-gout-consider-zero-flares-over-the-previous-six-or-twelve-months-necessary-for-a-remission-state)

Abstract Number: 351

**Integration of Electronically Captured Patient-Reported Outcomes in a Pediatric Rheumatology Clinic Visit**

Alysha J. Taxter1 and Ajay Dharod2, 1Pediatrics, Brenner Children's Hospital, Wake Forest Baptist Medical Center, Winston-Salem, NC, 2Internal Medicine, Wake Forest Baptist Medical Center, Winston-Salem, NC

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Increasing emphasis has been placed on the use of patient reported outcomes (PROs) in both research and clinical practice. Capturing this data in clinical practice, however, is often challenging for providers and clinical staff: paper forms are easily lost and verbal questions may be rushed or skipped in busy clinics. Many electronic medical record systems (EMRs) have developed patient portal systems with the capacity to electronically administer questionnaires. This study aims to evaluate the use of a patient portal system for collecting PROs in a pediatric rheumatology clinic.

Methods: Response rates to patient reported outcome questionnaires were compared one month pre- and four months post-implementation of an electronic data capture system. Pre-implementation, verbal responses were manually entered into the chart by the physician. Post-implementation, data were captured electronically through our medical record patient portal. Questionnaires were completed on clinic computers or tablets in the waiting or exam room. Questions examined current physical symptoms, performed psychiatric screening, reported both patient pain and fatigue on 0-10 ordinal scales, and allowed entry of any concerns. English and Spanish versions were available. Patients and clinical staff were surveyed about their experiences.

Results:
There were 106 and 307 questionnaires completed pre- and post-implementation, respectively. Post-implementation, the majority of patients/parent-proxies entered their own data. Patient-portal activation increased from 53% to 88% (p<0.01). Higher response rates were seen in psychiatric symptoms after electronic questionnaire implementation. Identification of positive responses pre- and post-electronic questionnaire implementation respectively, are reported: depression increased from 3 to 14% (p<0.01), anxiety increased from 2 to 27% (p<0.01), and difficulty sleeping increased from 16 to 30% (p<0.01). Questionnaires also revealed themes in parental concerns, including “When can we reduce medication?” and “What can we do about her pain?” Physician satisfaction surveys estimated a time savings of 2-5 minutes per visit. Patients reported positive feedback to having portal access and state it allows more time to think about the questions. Furthermore, it introduces patients and their families to other functions within the portal, such as viewing labs and communicating with providers. There were 29 patient-portal correspondence messages prior to implementation and mean of 22 messages/month thereafter. Staff reported there was difficulty with activation of proxy accounts and password recovery workflow.

Conclusion: Integration of novel patient electronic data capture systems within pediatric clinics improve recognition and identification of psychiatric symptoms. It can also save valuable physician time. Improved discrete data capture is necessary to further improve clinical systems and patient care.

Disclosure: A. J. Taxter, None; A. Dharod, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/integration-of-electronically-captured-patient-reported-outcomes-in-a-pediatric-rheumatology-clinic-visit

Abstract Number: 352

Psychometric Features of a New Methotrexate (MTX)-Specific Adherence Tool for Use in the Management of Patients with Rheumatoid Arthritis (RA): Preliminary Results from an Online Patient Community

Elodie de Bock1, Corrado Bernasconi2, Tan P. Pham1, Ana Maria Rodriguez3, Khaled Sarsour4, J. Michael Nebesky2 and Christine de la Loge1, 1Mapi, Lyon, France, 2F. Hoffmann-La Roche, Basel, Switzerland, 3Patients Like Me (PLM), Cambridge, MA, 4Genentech, South San Francisco, CA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: F. Hoffmann-La Roche Ltd. and Mapi collaborated to develop a medication adherence measure among RA patients taking MTX—the Methotrexate Experience Questionnaire (MEQ). The MEQ aims to facilitate communication between patients and clinicians during consultation to help clinicians identify patients having difficulty with MTX adherence and specific issues
leading to nonadherence. The MEQ was developed in accordance with best psychometric practices, including patient interviews, and contains several domains providing a comprehensive picture of drivers and descriptors of adherence issues encountered by RA patients treated with MTX. An observational study was conducted with patients from the PatientsLikeMe (PLM) online community. The aims of the present analysis were to provide preliminary results regarding the MEQ psychometric features and identify drivers of poor adherence in a population of PLM online users treated with MTX for RA.

Methods: This was a cross-sectional study where PLM RA subjects treated with MTX (currently or within the past 6 months) were asked to complete the 4-item Morisky Medication Adherence Scale (MMAS-4) and the MEQ online. The MEQ includes 29 items with 4- or 6-point Likert scale answers. Key psychometric MEQ features were described: acceptability and appropriateness of items (quality of completion, distribution, floor and ceiling effects), construct validity (multi-trait correlation-based analyses), concurrent validity (description and comparison of MEQ scores across MMAS-defined adherence and clinical groups). Linear, logistic, and partial least squares regressions were used to identify drivers of poor adherence.

Results: The population included 217 patients (80.2% aged 40-65 years; 90.8% women) whose mean duration of RA was 9 years (SD ±10.5). The MEQ was well accepted (only 3.2% of completed questionnaires were missing ≥1 MEQ items). Some revisions to the theoretical structure were proposed in the process toward the development of the MEQ scoring algorithm (5 dimension scores were proposed: Perceived benefits of MTX, Convenience aspects of MTX, Drivers of nonadherence to MTX, Negative sides of MTX, Patient information). As expected, convenience and noncompliance scores were highly correlated to MMAS-4 (r=0.661 and 0.661, respectively), while Patient information and Perceived benefits did not show a significant association. Moreover, MEQ convenience, noncompliance, and Negative sides scores discriminated between low, moderate, and high adherence groups as defined by the MMAS-4 (p<0.0001). Multiple drivers of poor adherence were identified, including aspects related to convenience, symptom improvement, how sick the patient felt, patient activities, and patient travel plans.

Conclusion: These preliminary results related to psychometric features of MEQ look promising as the instrument appears to discriminate between low, moderate, and high adherence as defined from the generic MMAS-4 in an online community of patients with RA. Future research includes psychometric validation of the MEQ in patients with clinically diagnosed RA against an objective measure of adherence (prescription claims data).

Disclosure: E. de Bock, F. Hoffmann-La Roche, 5; C. Bernasconi, Roche, 5; T. P. Pham, F. Hoffmann-La Roche, 5; A. M. Rodriguez, None; K. Sarsour, Genentech, 3; J. M. Nebesky, F. Hoffmann-La Roche, 3; C. de la Loge, F. Hoffmann-La Roche, 5.


Abstract Number: 353

Patient Experiences of Rheumatoid Arthritis Models of Care: An International Survey

Cheryl L. Koehn1, Kelly Lendvoy1, Yue Ma2, Linda Li3, Alison Hoens4, Marion Souveton5 and John M. Esdaile4, 1Arthritis Consumer Experts, Vancouver, BC, Canada, 2Simon Fraser University, Burnaby, BC, Canada, 3Rheumatology, Arthritis Research Canada, Richmond, BC, Canada, 4Arthritis Research Canada, Richmond, BC, Canada, 5F. Hoffmann-La Roche Ltd, Basel, Switzerland

First publication: September 18, 2017

SESSON INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Despite the global prevalence of rheumatoid arthritis (RA), there is no single model of care (MoC) and little is known about the RA patient journey at the population level. 18 RA patient organizations launched a global survey to understand patient experiences of RA MoCs and identify common challenges, gaps, and opportunities for improvement.

Methods: A short online questionnaire of RA patients recruited by patient organizations from 25 countries in Europe, the Middle East, and North and South America was conducted by Kantar Health (March 15–June 9, 2017) in 16 languages. The survey include questions on the patient’s disease journey through 5 key elements of an RA MoC: 1) recognize symptoms/seek care, 2) access to specialist care, 3) medical management, 4) shared care, and 5) self-care. Countries with ≥30 respondents were included in this analysis. Data were
analyzed at the global and country levels; descriptive (means, medians, percentages) analyses were conducted using STAR ODEC version 2.9.13. Global results are presented.

**Results:** 2690 respondents from 14 countries were included in this analysis (Table 1): 90% women, 71.5% between 35-65 years of age, and 69.7% from urban communities. Most respondents first heard they had RA from a rheumatologist (66%) (Table 2) and classified their current RA severity as moderate (59%) or severe (24%). Respondents reported an average of 22 mo (median, 5 mo) to receive an RA diagnosis and 20 mo (median, 3 mo) for an initial rheumatologist visit after first experiencing RA symptoms. Although 47% waited <1 mo for their first rheumatologist appointment, 33% had to wait >3 mo. Half (49%) see a rheumatologist once every 3 mo for management, 32% less frequently, and 9% as needed or do not see a rheumatologist. The majority (92%) have been treated with methotrexate, hydroxychloroquine, or sulfasalazine; however, most have not taken or did not know whether they have received biologics (72%) or small molecule treatment (82%). One-third (30%) reported it took from 4 mo to “never” for a first medication effectiveness assessment. Many respondents (39%) are not completely confident when describing RA to other people (Table 2). Access to additional information about living with RA and self-care was noted as a need by half (49%).

**Conclusion:** This large international patient survey highlights self-reported gaps and delays in all 5 key elements of a standardized RA MoC, including significant delays to diagnosis and specialist access globally, delayed therapy effectiveness assessment, and additional education/information to increase the level of confidence to describe RA and improve effective self-care practice.

<table>
<thead>
<tr>
<th>Table 1. Respondent-reported sociodemographics</th>
<th>Patients, % N = 2690</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Country</strong></td>
<td></td>
</tr>
<tr>
<td>Brazil</td>
<td>40.0</td>
</tr>
<tr>
<td>France</td>
<td>27.4</td>
</tr>
<tr>
<td>Canada</td>
<td>5.7</td>
</tr>
<tr>
<td>Israel</td>
<td>4.4</td>
</tr>
<tr>
<td>Italy</td>
<td>3.3</td>
</tr>
<tr>
<td>Croatia</td>
<td>2.8</td>
</tr>
<tr>
<td>Serbia</td>
<td>2.5</td>
</tr>
<tr>
<td>Spain</td>
<td>2.4</td>
</tr>
<tr>
<td>Greece</td>
<td>2.3</td>
</tr>
<tr>
<td>Denmark</td>
<td>2.2</td>
</tr>
<tr>
<td>Bosnia and Herzegovina</td>
<td>2.1</td>
</tr>
<tr>
<td>Romania</td>
<td>2.0</td>
</tr>
<tr>
<td>Belgium</td>
<td>1.9</td>
</tr>
<tr>
<td>Slovenia</td>
<td>1.2</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>90</td>
</tr>
<tr>
<td>Male</td>
<td>10</td>
</tr>
<tr>
<td><strong>Age group, years</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;25</td>
<td>3.6</td>
</tr>
<tr>
<td>25-34</td>
<td>16.0</td>
</tr>
<tr>
<td>35-44</td>
<td>23.3</td>
</tr>
<tr>
<td>45-54</td>
<td>24.0</td>
</tr>
<tr>
<td>55-65</td>
<td>24.2</td>
</tr>
<tr>
<td>&gt;65</td>
<td>8.9</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>71.2</td>
</tr>
<tr>
<td>Hispanic Latino</td>
<td>8.8</td>
</tr>
<tr>
<td>Black or African American</td>
<td>5.2</td>
</tr>
<tr>
<td>Asian</td>
<td>0.9</td>
</tr>
<tr>
<td>Other</td>
<td>13.8</td>
</tr>
<tr>
<td><strong>Community</strong></td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>69.7</td>
</tr>
<tr>
<td>Suburban</td>
<td>18.3</td>
</tr>
<tr>
<td>Rural</td>
<td>12.0</td>
</tr>
<tr>
<td><strong>Healthcare coverage</strong></td>
<td></td>
</tr>
<tr>
<td>Public</td>
<td>65.4</td>
</tr>
<tr>
<td>Private</td>
<td>34.6</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2. Rheumatoid arthritis diagnosis, management, and respondent self-care</th>
<th>Patients, % N = 2690</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diagnosis</strong></td>
<td></td>
</tr>
<tr>
<td>Healthcare professional who informed the respondent of their diagnosis</td>
<td>Base from total: 100%</td>
</tr>
<tr>
<td>Rheumatologist</td>
<td>66</td>
</tr>
<tr>
<td>Family doctor/general practitioner</td>
<td>21</td>
</tr>
<tr>
<td>HCP other than the family doctor</td>
<td>7</td>
</tr>
<tr>
<td>Other</td>
<td>6</td>
</tr>
<tr>
<td><strong>Time from symptom onset to RA diagnosis</strong></td>
<td>Base from total: 93%</td>
</tr>
<tr>
<td>&lt;1 month</td>
<td>21</td>
</tr>
<tr>
<td>1-3 months</td>
<td>22</td>
</tr>
<tr>
<td>4-6 months</td>
<td>14</td>
</tr>
<tr>
<td>Time from symptom onset to first visit to a rheumatologist</td>
<td>Base from total: 66%</td>
</tr>
<tr>
<td>-----------------------------------------------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>-1 month</td>
<td>21</td>
</tr>
<tr>
<td>1-3 months</td>
<td>28</td>
</tr>
<tr>
<td>4-6 months</td>
<td>12</td>
</tr>
<tr>
<td>7-12 months</td>
<td>11</td>
</tr>
<tr>
<td>1-2 years</td>
<td>9</td>
</tr>
<tr>
<td>&gt;2 years</td>
<td>11</td>
</tr>
<tr>
<td>Waiting time until first appointment with rheumatologist</td>
<td>Base from total: 100%</td>
</tr>
<tr>
<td>-1 month</td>
<td>47</td>
</tr>
<tr>
<td>1-3 months</td>
<td>30</td>
</tr>
<tr>
<td>4-6 months</td>
<td>11</td>
</tr>
<tr>
<td>7-12 months</td>
<td>11</td>
</tr>
<tr>
<td>I am still waiting for my first visit</td>
<td>11</td>
</tr>
</tbody>
</table>

**Management**

<table>
<thead>
<tr>
<th>Frequency of respondent visits to a rheumatologist for disease management</th>
<th>Base from total: 100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Once a month</td>
<td>11</td>
</tr>
<tr>
<td>Once every 3 months</td>
<td>49</td>
</tr>
<tr>
<td>Once every 6 months</td>
<td>27</td>
</tr>
<tr>
<td>Once a year</td>
<td>5</td>
</tr>
<tr>
<td>I see them when I think I need to</td>
<td>8</td>
</tr>
<tr>
<td>Never</td>
<td>1</td>
</tr>
</tbody>
</table>

**Current treatment**

- Methotrexate: 58%
- Hydroxychloroquine: 16%
- Sulfasalazine: 7%
- None of the above: 33%

**Biologic treatment**

- My current treatment is a biologic: 24%
- I am no longer taking a biologic: 4%
- I have never taken a biologic: 23%
- I do not know: 49%

**Targeted small molecule treatment**

- My current treatment is a targeted small molecule: 13%
- I am no longer taking a targeted small molecule: 5%
- I have never taken a targeted small molecule: 46%
- I do not know: 36%

**Time since respondent started treatment until medication effectiveness assessed**

- 1-3 months: 69%
- 4-6 months: 22%
- 7-12 months: 6%
- Never since treatment started: 2%

**Respondent self-care**

- Respondent feels confident when describing RA to other people: 61%
- Yes, but not in great detail: 35%
- No: 4%

**Access to information about living with RA and self-care**

- Yes, I have access to enough information: 51%
- Yes, but the materials are not enough: 14%
- Yes, but I value more information from other patients: 23%
- Yes, but I value more information from my rheumatologist: 45%
- No: 6%

---

**Disclosure:** C. L. Koehn, F. Hoffmann-La Roche Ltd, 9; K. Lendvoy, F. Hoffmann-La Roche Ltd, 9; Y. Ma, None; L. Li, None; A. Hoen, None; M. Souveton, F. Hoffmann-La Roche Ltd, 3; J. M. Esaile, None.

Multidomain Functional Assessment in a Cohort of Patients with Systemic Lupus Erythematosus: A Pilot Study

Laura Plantinga¹, Benjamin Tift², C. Barrett Bowling³, Charmayne M. Dunlop-Thomas⁴, S. Sam Lim⁵ and Cristina Drenkard⁵, ¹Department of Medicine, Emory University School of Medicine, Atlanta, GA, ²Edward Via College of Osteopathic Medicine, Spartanburg, SC, ³Durham Veterans Affairs Medical Center, Durham, NC, ⁴Emory University School of Medicine, Atlanta, GA, ⁵Division of Rheumatology, Emory University School of Medicine, Atlanta, GA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic, complex disease with multiple comorbid conditions and non-disease-specific manifestations. Consequently, the impact of SLE on both physical and cognitive function may be analogous to what is seen in the general geriatric population. We used a multidomain functional assessment, commonly performed in geriatric patients but novel among SLE patients, to better understand the magnitude of the functional impairment in this population.

Methods: We recruited 60 adult (≥20 years old) SLE patients from an ongoing cohort study of Atlanta-area SLE patients for an in-person visit (10/16-4/17), in which we evaluated physical and cognitive function in several domains shown to be associated with poor outcomes in geriatric populations: physical performance (by the Short Physical Performance Battery; range on balance, gait speed, and lower body strength scores, 0-4; higher scores = better performance); cognitive performance (by NIH Toolbox measures of five fluid cognition domains; reported as adjusted t-scores); and self-reported measures including physical functioning (reported as t-scores), activities of daily living (ADLs), falls, and life-space mobility, which measures how far, how often, and how much help is needed as respondents move through their community (scale 0-120; higher scores = greater community mobility).

Results: Balance and gait speed scores were high, while mean lower body strength scores were low (Table). Cognitive performance was close to average (score=50) in the domains of episodic and working memory, but mean scores for cognitive flexibility, processing speed, and attention/inhibitory control were ~1 SD below average for healthy individuals of the same age, sex, race, ethnicity, and education level. Patients reported independence in most basic ADLs but dependence in several instrumental ADLs. Nearly half (45.0%) of patients reported falling in the prior year, and only 40.0% reported unlimited ability to travel without the help of another person. Overall, scores did not differ substantially by age, although older patients had slightly lower self-reported physical functioning and higher cognitive performance scores than younger patients in general.

<table>
<thead>
<tr>
<th>Functioning Measure</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD) physical performance (scale 0-4, higher=better)</td>
<td></td>
</tr>
<tr>
<td>Balance</td>
<td>3.65 (0.84)</td>
</tr>
<tr>
<td>Gait speed</td>
<td>3.37 (1.04)</td>
</tr>
<tr>
<td>Lower body strength</td>
<td>1.78 (1.34)</td>
</tr>
<tr>
<td>Mean (SD) cognitive performance (scale 0-100; higher=better)</td>
<td></td>
</tr>
<tr>
<td>Episodic memory</td>
<td>47.72 (9.24)</td>
</tr>
<tr>
<td>Working memory</td>
<td>48.58 (11.22)</td>
</tr>
<tr>
<td>Cognitive flexibility</td>
<td>43.72 (14.22)</td>
</tr>
<tr>
<td>Processing speed</td>
<td>42.55 (14.83)</td>
</tr>
<tr>
<td>Attention/inhibitory control</td>
<td>38.80 (8.38)</td>
</tr>
<tr>
<td>Mean (SD) self-reported physical functioning (scale 0-100, higher=better)</td>
<td>38.82 (10.92)</td>
</tr>
<tr>
<td>No. (%) reporting difficulty with ADLs (most common)</td>
<td></td>
</tr>
<tr>
<td>Shopping</td>
<td>25 (41.7%)</td>
</tr>
<tr>
<td>Food preparation</td>
<td>21 (35.0%)</td>
</tr>
<tr>
<td>Housework</td>
<td>8 (13.3%)</td>
</tr>
<tr>
<td>Bathing</td>
<td>8 (13.3%)</td>
</tr>
<tr>
<td>Dressing</td>
<td>9 (15.0%)</td>
</tr>
<tr>
<td>Incontinence</td>
<td>12 (20.0%)</td>
</tr>
<tr>
<td>No. (%) with falls in prior year</td>
<td>27 (45.0%)</td>
</tr>
<tr>
<td>Mean (SD) life-space mobility (scale 0-120, higher=better)</td>
<td>54.44 (34.35)</td>
</tr>
</tbody>
</table>

Conclusion: SLE patients of all ages report a substantial burden of functional impairment across multiple domains, similar to that among geriatric patients. Because impairment seems to be relatively independent of age in SLE and because greater levels of function may lead to better clinical and patient-centered outcomes, such as the ability to live independently, the value of functional assessment in the setting of SLE should be further explored. Further research could help inform potential interventions to improve or prevent further declines in functioning in this population.
Perceptions and Outcomes of Pregnancy and Lactation in Patients with Rheumatic Diseases

Brooke Mills¹, Kathryn H. Dao², Kristen Tecson², Emily Fishman³, Rachel Tate² and John J. Cush², ¹Internal Medicine, Baylor University Medical Center, Dallas, TX, ²Baylor Research Institute, Dallas, TX, ³Texas A&M HSC College of Medicine, Dallas, TX

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Once diagnosed with a rheumatic disease, women often defer or avoid pregnancy or lactation, fearing adverse outcomes for their offspring or for themselves. Scant data exist regarding the attitudes of women with these diseases toward pregnancy and lactation. Furthermore, there is an unclear relationship between breastfeeding and disease activity. Our study evaluates the perceptions of women with rheumatic diseases on pregnancy and lactation while analyzing their outcomes during this period.

Methods: We conducted a single center cohort study of women of childbearing age regarding their attitudes, concerns, and outcomes of pregnancy and lactation. Information was gathered from chart review, telephone interviews and surveys. Those who completed a pregnancy and breastfed were queried further regarding their use of disease modifying anti-rheumatic drugs (DMARD) or biologics while breastfeeding and if their infants had any adverse outcomes.

Results: 154 subjects were included. 51.6% of respondents indicated their diagnosis changed their views on pregnancy. Opinions differed significantly across the diagnoses of JIA (28.6%), AKS (45.5%), RA (43.1%), and SLE (69.4%) (P=0.04). 65.6% of women were concerned about medications affecting the baby. 33.6% indicated that their views on breastfeeding changed as a result of their disease diagnosis. Views on breastfeeding did not differ significantly between diagnoses. 29.7% of respondents said their diagnosis changed their minds about having children, a sentiment that differed significantly by diagnosis (AKS: 11.1%, JIA: 0.0%, Other: 30.0%, PSA: 33.3%, RA: 20.4%, SLE: 53.1%; P=0.01). The rates of breastfeeding did not differ significantly for babies born before or after the mothers’ diagnosis (before: 86.6%, after: 82.2%; P=0.50). Breastfeeding duration did not differ by diagnosis status (P=0.21). After diagnosis, more women stopped breastfeeding early to start a medication they believed to be contraindicated (before diagnosis: 2, 3.5%; after diagnosis: 12, 20%; P=0.005). Of the 46 who responded, breastfeeding positively, negatively, or did not affect the mother’s disease state in 21.7%, 43.5%, and 34.8%, respectively. There were 35.3% (12/34) instances of having to change medical therapy due to disease worsening while breastfeeding. 18 women breastfed 21 babies on a DMARD or biologic. None of these women reported a delay in their children’s developmental milestones.

Conclusion: After disease diagnosis, nearly half of women negatively changed their views on pregnancy, and a third of women negatively changed their views on lactation. Women were concerned that the use of a DMARD or biologic may affect their own health or their baby’s health. There was no difference in the rates or duration of breastfeeding between women before and after diagnosis, however after diagnosis, some respondents refrained from or curtailed breastfeeding due to concerns for medications or lack of information. Disease activity during lactation is variable based on our data; further studies are needed to fully evaluate this issue. This study highlights an unmet need in patients of childbearing potential for data and education regarding pregnancy and lactation.

Disclosure: B. Mills, None; K. H. Dao, None; K. Tecson, None; E. Fishman, None; R. Tate, None; J. J. Cush, None.
Abstract Number: 356

Preliminary Real World Data on Switching Patterns between Etanercept, Its Recently Marketed Biosimilar Counterpart and Its Competitor Adalimumab, Using Swedish Prescription Registry

Rieke Alten1, Petra Neregard2, Heather Jones3, Ena Singh4, Cinzia Curiale5, Thomas Meng6, Lara Lucchese7, Cristiana Miglio7 and Gudrun Jonasdottir Bergman8, 1Internal Medicine, Rheumatology & Clinical Immunology, Schloßpark-Klinik, University Medicine Berlin, Berlin, Germany, 2Pfizer, Stockholm, Sweden, 3Inflammation & Immunology Global Medical Affairs, Pfizer, Collegeville, PA, 4Pfizer, Collegeville, PA, 5Pfizer, Rome, Italy, 6Pfizer, Berlin, Germany, 7QuintilesIMS, London, United Kingdom, 8QuintilesIMS, Solna, Sweden

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The increasing availability of biologic treatments over the past 10 years has revolutionized the management of rheumatic diseases. In April 2016, the first etanercept biosimilar (EtnBS) was launched in Sweden, representing a cheaper option to its innovator counterpart and other anti-TNF agents. The objective of this study was to describe the position of etanercept innovator (EtnI) within the Swedish biologic market for rheumatic diseases, before and after the launch of its biosimilar. The study also provides early real-world data on the market penetration of EtnBS by evaluating switching dynamics to and from this drug since the date of launch.

Methods: The overall biologic market share across all type of rheumatic diseases was monthly tracked over the last year of available data in the Swedish Prescription Registry (100% coverage). The proportion of patients receiving a rheumatologists’ prescription for any biologic in each month, from November 2015 to March 2017, was recorded. In addition, switching dynamics of patients initiating EtnBS treatment between April 2016 and March 2017 were studied. The proportion of patients receiving no biologic treatment (naïve) and of those on treatment with EtnI, adalimumab and other biologic agents in the 12 months prior to initiate EtnBS was reported. Further, the proportion of patients who switched from EtnBS back to EtnI or adalimumab and the median time to this second switch were also evaluated.

Results: EtnI and adalimumab dominate the biologic market for rheumatic diseases in Sweden, holding the 40% and 28% of market share, respectively, up to April 2016. However, in the 11 months after EtnBS was launched, the share of EtnI decreased constantly, dropping to 22% in March 2017. Since April 2016, we identified in total 5,387 patients receiving first prescription of EtnBS by a rheumatologist. Of these, 1,845 (34%) were naïve to treatment, 2,938 (55%) had prior treatment with EtnI, 235 (4%) with adalimumab, 369 (7%) with other biologics. Among the patients who changed to EtnBS from prior EtnI, 11% switched back to EtnI after a median time of 55 days. Similarly, of those who were on previous adalimumab treatment, 5% switched back to adalimumab after, median time, 67 days.

Conclusion: Many patients changed from EtnI to its biosimilar treatment since its launch in Sweden. However, this study showed that 11% of these patients switch back to their original treatment after short time. Despite the change from a brand biologic to the biosimilar is very likely made for economic reasons, the reasons for switching back to the innovator are not clear and may imply patients’ preference or clinical reasons. Interestingly, the same pattern is observed for patients changing from adalimumab to EtnBS. Longer-term studies are required to confirm these early observations and investigate the reasons for switching back.

These results were presented at EULAR, Madrid 14-17 June 2017

Disclosure: R. Alten, None; P. Neregard, None; H. Jones, Pfizer Inc, 1,Pfizer Inc, 3; E. Singh, None; C. Curiale, None; T. Meng, None; L. Lucchese, None; C. Miglio, None; G. J. Bergman, None.


Abstract Number: 357
Determinants of Patient and Physician Disagreement on Presence of a Gout Flare

Aprejita Jagpal1, Nicola Dalbeth2, William J. Taylor3, Kenneth Saag1, Jasvinder A. Singh4, Amy S. Mudano5, Elizabeth J. Rahn6 and Angelo L. Gaffo6, 1Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 2University of Auckland, Auckland, New Zealand, 3University of Otago, Wellington, New Zealand, 4Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 5University of Alabama at Birmingham, Birmingham, AL, 6Department of Medicine, Division of Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Flare is a central feature of gout and patient self-report of flare was found to be an important element in a gout flare definition for research. However, patients may disagree with the clinicians on presence of a flare. In this study, we investigated factors impacting the concordance and discordance between investigators with expertise in gout and their patients, on presence of a gout flare.

Methods:

We used gout patient data collected at 21 international sites from a gout flare definition study published in 2012 and its ongoing validation study. Information on demographics, gout flares, and anatomical location of swelling and warmth during a flare were collected during routine clinic visits. We performed Chi-square and t-test comparisons of these variables in patients who agreed with the investigator on the presence of a flare (concordant) versus those who disagreed with the investigator on the presence of a flare (discordant). We also made comparisons within the discordant group (when investigator diagnosed a flare but patient disagreed versus when patient self-reported a flare and the investigator disagreed).

Results:

Concordant and discordant flares were noted in 187 and 81 cases, respectively. There were no differences between groups in age, sex, or disease duration. Compared to the discordant group, the concordant group had higher pain scores, increased patient global assessment of disease severity, greater proportions of patients with lower extremity joint (knee, ankle, or foot joints) involvement, and lower proportion of patients with tophi (Table). Fewer patients in the discordant group had either swollen or warm joint (patient reported) compared to the patients with concordant flares (76.5% vs 97.9%, p <0.0001). Within the discordant group, 70.4% of flares were patient determined and not endorsed by the investigators. All patients with an investigator-determined flare where patients disagreed had at least one swollen joint (100%) compared to only 57.9% in flares that were patient-determined but the investigator disagreed with (p<0.0001).

Conclusion:

We identified factors associated with agreement and disagreement among patients and investigators on the presence of a gout flare. Lower extremity involvement, higher patient global assessment of disease, less tophaceous disease, higher pain scores, and presence of at least one swollen or warm joint is associated with concordance. Having a swollen joint was a determinant in all the investigator-defined flares when patients disagreed, however it was much less important in patient-determined gout flares.

Table: comparison between patients in discordant flare group to concordant group
### Table 1: Comparison of Variable and P value

<table>
<thead>
<tr>
<th>Variable</th>
<th>Discordant flare</th>
<th>Concordant flare</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years; Mean (SD)</td>
<td>N=81</td>
<td>N=187</td>
<td></td>
</tr>
<tr>
<td>Male sex; n (%)</td>
<td>54.7 (13.8)</td>
<td>53.8 (14.0)</td>
<td>0.65</td>
</tr>
<tr>
<td>Disease duration in years; Mean (SD)</td>
<td>11.8 (8.1)</td>
<td>11.8 (10.3)</td>
<td>0.98</td>
</tr>
<tr>
<td>Presence of tophi; n (%)</td>
<td>50 (61.7)</td>
<td>87 (46.8)</td>
<td>0.0246</td>
</tr>
<tr>
<td>Lower extremity involvement in a flare; n (%)</td>
<td>48 (59.3)</td>
<td>157 (84.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PGA (0-10); Mean (SD)</td>
<td>4.3 (3.3)</td>
<td>6.6 (2.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pain at rest (0-10); Mean (SD)</td>
<td>4.1 (3.3)</td>
<td>6.9 (2.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Patient-reported</td>
<td>62 (76.5)</td>
<td>183 (97.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Any swollen or warm joint (%)</td>
<td>57 (70.4)</td>
<td>178 (95.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Any Swollen (%)</td>
<td>38 (46.9)</td>
<td>153 (81.8)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

SD= standard deviation, PGA = patient global assessment of disease severity

### Disclosure:

A. Jagpal, None; N. Dalbeth, AstraZeneca, 2,Takeda, Pfizer, AstraZeneca, Cymabay, Crealta, 5,Takeda, AstraZeneca, 9; W. J. Taylor, AstraZeneca, Pfizer, Abbvie, Roche, 5; K. Saag, AstraZeneca, Horizon, Ironwood, SOBI, Takeda, 5; J. A. Singh, Takeda, Savient, 2,Savient, Takeda, Regenron, Merz, Bioiberica, Crealta, Allergan, WebMD, UBM LLC, American College of Rheumatology, 5; A. S. Mudano, None; E. J. Rahn, None; A. L. Gaffo, SOBI, 5,Amgen, 2.


Abstract Number: 358

### Patients and Physicians Have Different Perceptions of the Relative Bother of the Symptoms and Impacts on Daily Activities in Psoriasis and Psoriatic Arthritis

M. Elaine Husni¹², Anthony Fernandez¹, Rakesh Singh³, Brett Hauber⁴, Jessie Sutphin⁴, Joshua Posner⁴ and Arijit Ganguli³, ¹Cleveland Clinic, Cleveland, OH, ²Rheumatology Dept A50, Cleveland Clinic Foundation, Cleveland, OH, ³AbbVie Inc., North Chicago, IL, ⁴RTI Health Solutions, Research Triangle Park, NC

First publication: September 18, 2017

### SESSION INFORMATION

Session Date: Sunday, November 5, 2017

Session Title: Patient Outcomes, Preferences, and Attitudes Poster I

Session Type: ACR Poster Session A

Session Time: 9:00AM-11:00AM

### Background/Purpose:
Psoriasis and psoriatic arthritis arise from the same immune system response but result in different symptoms and impacts on daily activities. A patient with both conditions may be treated by a dermatologist, rheumatologist, or both. Our objective was to assess patient, dermatologist, and rheumatologist perceptions of the bother of individual psoriatic outcomes in 3 separate areas: skin and joint symptoms and impacts on daily activities.

### Methods:
We developed a set of 7 skin symptoms, 7 joint symptoms, and 6 impacts on daily activities of psoriatic disease from existing validated measures. To measure perceived relative bother, we created an online best-worst scaling survey in which patients, dermatologists, and rheumatologists in the US, recruited through internet panels, indicated which of 5 items from the full set of 20 was most and least bothersome in each of 16 questions determined by an experimental design. We used these data to rank perceived relative bother in skin symptoms, joint symptoms, and daily activities for each respondent group.

### Results:
We surveyed 200 patients with self-reported physician diagnosis of both psoriasis and psoriatic arthritis with mean (SD) age of 42 (14) years. On a scale from 0 (none) to 10 (severe), patients had mean self-reported skin symptoms of 6.8 (2.5) and joint symptoms of 6.4 (2.6). Patients, dermatologists (n=150), and rheumatologists (n=150) differed on the most bothersome skin symptom (Table 1).
All respondent groups ranked joint pain, soreness, or tenderness as the most bothersome joint symptom and discomfort while doing everyday tasks as the most bothersome impact on daily activities. Among skin symptoms, embarrassment was ranked highest (most bothersome) by dermatologists, while painful skin was ranked higher than embarrassment by patients and rheumatologists. Among joint symptoms, patients and physicians ranked the relative burden of eye problems differently. Among daily activities, patients and physicians ranked the relative bother of difficulty sleeping differently.

**Conclusion:** The perception of the bother of psoriatic disease outcomes differs among patients, dermatologists, and rheumatologists. Greater communication among these groups is warranted and may help patients and physicians better address patient needs.

| Table 1. Item Rankings for Dermatologists, Rheumatologists, and Patients |
|-----------------------------|-----------------------------|-----------------------------|
| Ranking | Dermatologists | Rheumatologists | Patients |
| Skin Symptoms | | | |
| 1 | Embarrassment | Morning skin | Painful skin |
| 2 | Itching skin | Painful skin | Morning skin |
| 3 | Painful skin | Morning skin | Morning skin |
| 4 | Redness of skin | Embarrassment | Redness of skin |
| 5 | Difficulty choosing clothing | Difficulty choosing clothing | Difficulty choosing clothing |
| Joint Symptoms | | | |
| 1 | Joint pain, soreness, or tenderness | Joint pain, soreness, or tenderness | Joint pain, soreness, or tenderness |
| 2 | Swelling of fingers or toes | Swelling of fingers or toes | Difficulty walking |
| 3 | Difficulty walking | Difficulty walking | Difficulty walking |
| 4 | Morning stiffness | Morning stiffness | Morning stiffness |
| 5 | Fatigue | Fatigue | Morning stiffness |
| 6 | Difficulty dressing | Difficulty dressing | Difficulty dressing |
| 7 | Eye problems | Eye problems | Difficulty dressing |
| Impact on Daily Activities | | | |
| 1 | Difficulty while doing everyday tasks | Difficulty while doing everyday tasks | Difficulty while doing everyday tasks |
| 2 | Difficulty with work or school activities | Difficulty with work or school activities | Difficulty sleeping |
| 3 | Difficulty with social or leisure activities | Difficulty with social or leisure activities | Difficulty going shopping or doing housework or yard work |
| 4 | Difficulty going shopping or doing housework or yard work | Difficulty going shopping or doing housework or yard work | Difficulty with work or school activities |
| 5 | Problems with relationships | Problems with relationships | Difficulty with social or leisure activities |
| 6 | Difficulty sleeping | Difficulty sleeping | Problems with relationships |

**Disclosure:** M. E. Husni, AbbVie, Genentech, Bristol-Myers Squibb, Pfizer, Novartis, and Janssen, 9; A. Fernandez, Mallinkrodt, Roche, AbbVie, 2, AbbVie, 5, Celgene, AbbVie, 8; R. Singh, AbbVie, 3, AbbVie, 1; B. Hauber, RTI, which has received consulting fee from AbbVie to partner on this research, 3; J. Sutphin, RTI, which has received consulting fee from AbbVie to partner on this research, 3; J. Posner, RTI, which has received consulting fee from AbbVie to partner on this research, 3; A. Ganguli, AbbVie, 3, AbbVie, 1.

**Abstract Number:** 359

**Nurse Telephone Education for Promoting a Treat-to-Target Approach in Recently Diagnosed Rheumatoid Arthritis Patients – a Preliminary Review**

Bonita Libman1, Siobhan Farley1, Melinda Edwards1, Carl Possidente2 and Amanda Kennedy3, 1Medicine/Rheumatology, University of Vermont Medical Center, Burlington, VT, 2Medical Affairs, Pfizer, Inc., Jericho Center, VT, 3Internal Medicine, University of Vermont, Burlington, VT

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Patient Outcomes, Preferences, and Attitudes Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

---


---
**Background/Purpose:** A successful Treat-to-Target approach to managing Rheumatoid Arthritis (RA) requires shared decision making with patients and healthcare providers. However patients may not have the education they need around the time of a new diagnosis to effectively partner with their providers in their RA care. Educational efforts must focus on interventions that are feasible, sustainable, and available to all RA patients as part of their rheumatology care. The purpose of this project was to implement a pragmatic nurse telephone education program for patients with recently diagnosed RA that promotes shared decision making and a treat-to-target approach.

**Methods:** This was a pilot project of newly diagnosed adult RA patients between November 2015 and December 2016. Rheumatology clinic nurses telephoned patients to offer disease education, targeting no more than 20 minutes per call. A shared decision making toolkit was mailed to the patient. Demographic data included patient age, sex, and zip code. RA-specific data included date of RA diagnosis, prescribed RA medications, routine assessment data (RAPID3) scores if recorded, and date of next visit with the rheumatologist. Process measures included median call attempts, median call time, and a qualitative description of the free text notes. Outcome measures included the results from the satisfaction survey and proportion of patients who adhered to their next rheumatology visit. Data were analyzed descriptively and qualitatively.

**Results:** Twenty-six patients participated in the nurse calls. Most patients were female (65%), with a median age of 54 years (range 22-78). Median call length was 14.5 minutes with a range of 8-23 minutes. Qualitative notes indicate patients overwhelmingly support the nurse calls. Five patients returned the survey. All five patients indicated they would like calls from a nurse more than once per year. Twenty-three patients had follow-up visits at the time of this report. Sixteen patients (69.5%) were adherent to their follow-up visit.

**Conclusion:** This preliminary review successfully implemented an educational program that included a nurse-facilitated, RA-specific, telephone call and toolkit. The strength of our approach was designing our educational program with the goal of long-term sustainability and generalizability. This educational program could be a model for similar educational efforts by other rheumatology clinics.

**Disclosure:** B. Libman, Novartis Pharmaceutical Corporation, 2; Pfizer, Inc, 9; S. Farley, None; M. Edwards, None; C. Possidente, Pfizer, Inc., 1; full time employee Pfizer, Inc., 3; A. Kennedy, None.


**Abstract Number:** 360

**Evaluation of the Educational Needs in Argentinian Patients with Rheumatoid Arthritis Using the SpENAT Questionnaire**

**Silvana Karina Pérez**, 1, Maria Julia Santa Cruz, 1 María Alejandra Medina, 1 Diana Klajn, 2 Silvia Beatriz Papasidero, 1 Jose Angel Caracciolo, 1 Gisela Pendón, 3 Federico Giordano, 4 Dora Pereira, 5 Damaris Alvarez, 6 Valeria Astudillo, 6 Eduardo Kerzberg, 6 Adriana Perez Davila, 7 Analia Bohr, 7 Fernando Melo, 8 Nicolas Lloves, 8 Marta Mamaní, 9 Claudia Hartvig, 10 Gabriela Sanchez, 10 Monica Sacnun, 10 Yamila Chichotky, 11 José Velasco Zamora, 11 Mariana Benegas, 12 Javier Rosa, 13 María Victoria García, 14 Laura Raït, 15 Vanessa Cruzal, 15 Rosana Quintana, 16 Bernardo Pons-Estel, 17 Karin Kirmayr, 18 Andrea D’Orazio, 19 Cinthya Retamoza, 20 Olga Roman, 21 Rodolfo Perez-Alamino, 21 María de los Angeles Correa, 22 Gustavo Citera, 23 Oscar Rillo, 24, María Marta Zalar, 24 Ana Carolina Costri, 25 Mercedes Argentina García, 25 Graciela Gómez, 26 and Hernán Maldonado Fico, 27 1 Rheumatology Department, Hospital General de Agudos Dr. Enrique Tornú, Buenos Aires, Argentina, 2 Research Committee, Hospital General de Agudos Dr. Enrique Tornú, Buenos Aires, Argentina, 3 Hospital Ricardo Gutierrez, La Plata, Argentina, 4 Rheumatology Department, Hospital Ricardo Gutierrez, La Plata, Buenos Aires, Argentina, 5 Rheumatology Department, Hospital Ricardo Gutierrez, Buenos Aires, Argentina, 6 Rheumatology Department, Hospital Ramos Mejía, Buenos Aires, Argentina, 7 Rheumatology Department, Hospital de Rehabilitación Manuel Rocca, Buenos Aires, Argentina, 8 Rheumatology Department, Hospital Rivadavia, Buenos Aires, Argentina, 9 Rheumatology Department, Hospital Bernardino Rivadavia, Buenos Aires, Argentina, 10 Rheumatology Department, Hospital Provincial de Rosario, Santa Fe, Argentina, 11 Rheumatology Department, Reumatologia al sur, Buenos Aires, Argentina, 12 Rheumatology Department, Sanatorio de la Providencia, Buenos Aires, Argentina, 13 Rheumatology Unit, Internal Medicine Service, Hospital Italiano de Buenos Aires, CABA, Argentina, 14 Rheumatology Department, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina, 15 Rheumatology Department, Clínica Bessone, Buenos Aires, Argentina, 16 Rheumatology Department, Sanatorio Parque, Rosario, Santa Fe, Argentina, 17 GLADEL, Rosario, Santa Fe, Argentina, 18 Rheumatology Department, Sanatorio San Carlos, Bariloche, Argentina, 19 Rheumatology Department, Hospital Interzonal Dr. José Penna, Bahía Blanca, Buenos Aires, Argentina, 20 Rheumatology Department, Centro Especializado Diabetes y Reumatología, Salta, Argentina, 21 Rheumatology Department, Hospital de Clínicas Pte. Dr. Nicolás Avellaneda, Tucumán, Argentina, 22 Section Rheumatology, Instituto de Rehabilitación Psicofísica, Buenos Aires, Buenos Aires, Argentina, 23 Rheumatology Department, Instituto de Rehabilitación Psicofísica, Buenos Aires, Argentina.
Background/Purpose: The SpENAT, a Spanish version of the Educational Needs Assessment Tool, is a self-completed questionnaire that assesses educational needs (ENs) with the purpose of providing tailored and patient-centered information. It consists of 39 questions grouped into the 7 following domains: Pain management, Movement, Feelings, Arthritis process, Treatments, Self-help measures and Support system. The objective of the study was to describe the educational needs of RA patients using the SpENAT and to determine the main sources of information that these patients consult.

Methods: Multicenter, observational, cross-sectional study. We included consecutive patients ≥ 18 years with diagnosis of RA (ACR-EULAR 2010). Socio-demographic data, disease characteristics and clinimetric measurements were recorded. All patients completed the SpENAT and were asked about the sources employed to obtain information about their disease. Statistical analysis: Population characteristics were described. ENs were determined as percentages of the highest possible score for each domain. Needs for each domain according to sex, years of education, duration of disease, use of biologicals and functional capacity were analyzed by means of Anova test, and bivariate comparisons were made with Student's T test and Bonferroni correction. Correlation between domains was determined with Spearman's test. ENs were described by geographic region. We compared patients’ age by source of information with Student's t-test.

Results: We included 496 patients from 20 centers across the country. More ENs were observed in Movement, Feelings and Arthritis process domains (Table). Patients with higher educational level (> 7 years) reported more ENs in Arthritis process and Self-help measures domains. A higher functional impairment (HAQ-A ≥0.87) was associated with more ENs in every domain. Patients with high activity showed more ENs than those in remission in Managing Pain, Movement, Feelings, Treatments and Support system domains; and also than those with low activity in Self-help measures and Support system domains. Patients with moderate activity showed more ENs in Managing pain domain compared to patients in remission. All SpENAT domains showed positive correlations with each other (p <0.0001), being the most important Managing pain/ Movement and Treatments/ Arthritis process (r≥0.7). The most consulted source of information was the rheumatologist (93.95%); those who made use of internet were on average younger (p = 0.0004).

Conclusion: RA Patients were very interested in knowing more about their disease. ENs were higher in Movement, Arthritis process and Feelings domains. High functional impairment was associated with more ENs. Patients with high disease activity had higher EN levels in almost every domain. The rheumatologist was the main source of information of the patient with RA.

EN in RA patients according to the domain (N=496)

<table>
<thead>
<tr>
<th>Domain</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain management</td>
<td>79.17 (75.83-91.67)</td>
</tr>
<tr>
<td>Movement</td>
<td>90 (75-95)</td>
</tr>
<tr>
<td>Feelings</td>
<td>81.25 (75-100)</td>
</tr>
<tr>
<td>Arthritis process</td>
<td>89.29 (75-100)</td>
</tr>
<tr>
<td>Treatments</td>
<td>78.57 (71.43-100)</td>
</tr>
<tr>
<td>Self-help</td>
<td>75 (70.83-93.75)</td>
</tr>
<tr>
<td>Support system</td>
<td>75 (62.5-93.75)</td>
</tr>
</tbody>
</table>

Disclosure: S. K. Pérez, None; M. J. Santa Cruz, None; M. A. Medina, None; D. Klahn, None; S. B. Papasidero, None; J. A. Caracciolo, None; G. Pendón, None; F. Giordano, None; D. Pereira, None; D. Alvarez, None; V. Astudillo, None; E. Kerzberg, None; A. Perez Davila, None; A. Bohr, None; F. Melo, None; N. Lloves, None; M. Mamani, None; C. Hartvig, None; G. Sanchez, None; M. Sacnun, None; Y. Chichotky, None; J. Velasco Zamora, None; M. Benegas, None; J. Rosa, None; M. V. Garcia, None; L. Raiti, None; V. Cruzat, None; R. Quintana, None; B. Pons-Estel, None; K. Kirmayr, None; A. D'Orazio, None; C. Retamozo, None; O. Romano, None; R. Perez-Alamino, None; M. D. L. A. Correa, None; G. Citera, Novartis, Pfizer Inc, 2,AbbVie, Bristol-Myers Squibb, Janssen, Novartis, Pfizer Inc, 5; O. Rillo, None; M. M. Zalazar, None; A. C. Costi, None; M. A. García, None; G. Gómez, None; H. Maldonado Ficco, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/evaluation-of-the-educational-needs-in-argentinian-patients-with-rheumatoid-arthritis-using-the-spenat-questionnaire
Multi-National Observational Patient Diary Study to Assess Disease Burden of Periodic Fever Syndromes (PFS), Including Colchicine-Resistant Familial Mediterranean Fever (crFMF), TNF-Receptor Associated Periodic Syndrome (TRAPS) and Mevalonate Kinase Deficiency (MKD)


First publication: September 18, 2017
Severe PFS have a very broad impact on the lives of pts and their families, including work productivity and educational attainment. Therapeutic interventions that reduce the flare burden and long term complications of severe PFS, as well as psychosocial support for pts and caregivers, are needed.

Disclosure: J. B. Kuemmerle-Deschner, Novartis Pharmaceutical Corporation, 2,Novartis Pharmaceutical Corporation, 5; P. Quartier, Novartis Pharmaceutical Corporation, 2,Novartis Pharmaceutical Corporation, 6; S. Padeh, None; I. Koné-Paut, Chugai, 2,Navigant, Novartis, SOBI, PFIZER, Abbvie, Novimmune, LFB, Roche, 5; V. Hentgen, Novartis Pharmaceutical Corporation, 2,Novartis Pharmaceutical Corporation, 5; K. A. Marzan, Novartis Pharmaceutical Corporation, Abbvie, 2; F. Dedegolu, Novartis Pharmaceutical Corporation, 5; H. J. Lachmann, Novartis, GS K, SOBI, 5; T. Kallinich, None; N. Blank, None; S. Ozen, Novartis Pharmaceutical Corporation, R-Pharm, 5,Roche Pharmaceuticals, 8; Y. Bilginer, None; J. S. Hausmann, None; A. Diaz, None; R. Degun, Novartis Pharmaceutical Corporation, 5; N. Marinek, Novartis Pharmaceutical Corporation, 5; J. Gregson, Novartis Pharmaceutical Corporation, 3; K. G. Lomax, Novartis Pharmaceutical Corporation, 3,Novartis Pharmaceutical Corporation, 1; A. Livneh, None.


Abstract Number: 362

Patients’ Experiences and Attitudes about Non-Medical Switching of Biologics: Results from an Online Patient Survey

Amanda Teeple1, Lorie A. Ellis2, Laura Huff3, Chuck Reynolds3, Seth D. Ginsberg4, Leah McCormick Howard5, Danielle Wals6 and Jeffrey R. Curtis7, 1Janssen Scientific Affairs, LLC, Horsham, PA, 2Health Economics & Outcomes Research, Janssen Scientific Affairs, LLC, Horsham, PA, 3Benfield | Arthur J. Gallagher & Co., Webster Groves, MO, 4Global Healthy Living Foundation, CreakyJoints, Upper Nyack, NY, 5National Psoriasis Foundation, Portland, OR, 6BDJ Solutions, Melrose, MA, 7Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Health insurance plan designs often have benefits that result in highly prescriptive patient (pt) treatment options that can result in switching of patient’s medications for non-medical (economic) reasons.

Methods: An online pt survey was conducted in pts recruited from advocacy organizations (Global Healthy Living Foundation, National Psoriasis Foundation) and a research panel (Research Now). Pts were eligible if they were ≥18 years of age, resided in United States; had a diagnosis for one of the following: rheumatoid arthritis, Crohn’s disease, ulcerative colitis, psoriasis or psoriatic arthritis; were currently taking a biologic; and consented to participate. Pts who met these criteria answered follow up questions about their experiences related to a possible non-medical switch (NMS) of their biologic medication. Descriptive statistics (n%, mean, SD) were used to summarize responses.

Results: A total of 1,696 pts completed the 20-minute survey; 993 were from advocacy groups and 703 from a research panel. Of the 1,696 patients that were asked about their perceptions to a possible biologic NMS, 90% expressed that they wouldn’t want to switch biologics if their current medication was helping my disease. 71% indicated they would not risk switching to another biologic. Only 29% would switch if the new biologic was cheaper. 86% of patients expressed concern that switching may cause more side effects, and 81% worried that switching would increase their stress. 74% were concerned that switching would cause them to lose their copay support. 20% (n=337) of patients had received notification their biologic insurance coverage was changing and they should consider switching biologies to avoid paying a higher cost. Of these, 79% took at least one action to avoid a NMS, most often asking their doctors’ offices to appeal the switch; 56% did not make the switch. Of pts that agreed to a NMS (n= 150), 67% did so to avoid paying a higher cost for their current biologic medication; most often pts switched to a biologic with the same mode of administration. Additionally, of patients that reported a NMS, 67% indicated that the biologic they were previously taking worked well for them, and 70% didn’t want to switch to another biologic. More than half (56%) went without therapy for administrative reasons during the period of transition from the old biologic to the NMS treatment.
Conclusion: Pts reported multiple concerns about NMS that would impact treatment outcomes, and many of the pts who non-medically switched in this survey missed treatments. Future studies should be conducted on real world pt experience with NMS to understand the impact on treatment persistency and pt outcomes.

Disclosure: A. Teeple, Janssen, 3,Johnson & Johnson, LLC, 1; L. A. Ellis, Janssen, 3,Johnson & Johnson, LLC, 1; L. Huff, Janssen Scientific Affairs, LLC, 5; C. Reynolds, Janssen Scientific Affairs, LLC, 5; S. D. Ginsberg, None; L. McCormick Howard, Janssen Scientific Affairs, LLC, 5; J. R. Curtis, Janssen Scientific Affairs, LLC, 2.


Abstract Number: 363

Work Productivity Benefit in Patients with Rheumatoid Arthritis Initiating Etanercept in the United States

Mahdi Gharabeih1, Bradley S. Stolshek2, Alex Mutebi3, Amy M. Sainski-Nguyen4, David Collier5 and Emily Durden4, 1Amgen Inc., Thousand Oaks, CA, 2Amgen, Inc., Thousand Oaks, CA, 3Amgen, Thousand Oaks, CA, 4Truven Health Analytics, Ann Arbor, MI, 5Amgen, Inc, Terni, Italy

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Rheumatoid arthritis (RA) is a chronic inflammatory disease that can progress to joint destruction, functional impairment and disability that can lead to work productivity losses. Biologics are generally prescribed when conventional disease modifying agents are no longer effective or following disease progression. Treatment with etanercept (ETN), either as monotherapy or in combination with methotrexate (MTX), has been shown to improve functioning and work productivity in clinical and observational studies. The aim of this study was to assess the productivity benefit of treating RA patients with ETN compared to MTX.

Methods:
In this retrospective administrative claims analysis using the MarketScan Health and Productivity Management and the Commercial Claims and Encounters databases, adults diagnosed with RA who were treated with ETN, ETN+MTX, or MTX between January 1, 2007 and December 31, 2013 were identified. The index date was the date of the earliest qualifying ETN or MTX pharmacy or medical claim. Patients were continuously enrolled with medical and pharmacy benefits 12 months prior to and 12 months following the index date. Patients who switched to or added another biologic during the post-index period were excluded. Patients diagnosed with other autoimmune diseases or had evidence of pregnancy or childbirth at any time during the study period were excluded. The proportions of patients with any workplace absence (ABS) or short-term disability (STD) in the 12 months prior to and following the index date were evaluated. Multivariable logistic regression was used to compare the odds of work loss during follow-up for the ETN and ETN+MTX groups relative to the MTX group, adjusting for demographic and baseline clinical characteristics including but not limited to age, gender, additional RA-related medications, and baseline RA-related costs.

Results:
For the work loss due to ABS analysis, 34 patients on ETN monotherapy, 49 patients on ETN+MTX, and 308 patients on MTX monotherapy were identified. For the STD analysis, 207 patients on ETN, 274 patients on ETN+MTX, and 1,620 patients on MTX were identified. The proportions of patients with at least one event of ABS during the pre-index period for the ETN, ETN+MTX, and MTX cohorts were 82.4%, 73.5%, and 85.4%, respectively. In the post-index period, the proportions of patients with at least one event of ABS for the ETN, ETN+MTX and MTX cohorts were 83.3%, 75.5%, and 87.0%, respectively.

The proportion of patients with at least one event of STD during the pre-index period for the ETN, ETN+MTX and MTX cohorts were 8.7%, 13.9%, and 11.5%, respectively. In the post-index period, the proportion of patients with at least one event of STD for the ETN, ETN+MTX and MTX cohorts were 7.7%, 8.4%, and 11.7%, respectively. After adjusting for potential confounders, the odds (95%CI)
of losing a day due to ABS in the ETN and ETN+MTX groups relative to the MTX group were 0.61(0.19-1.98) and 0.33(0.13-0.85), respectively. The odds (95%CI) of having STD in the ETN and ETN+MTX groups relative to the MTX group were 0.61(0.35-1.07) and 0.50(0.30-0.84), respectively.

**Conclusion:**
Adding ETN to MTX reduces the probability of ABS from work by 67% and the probability of STD by 50% compared to those on MTX alone.

**Disclosure:** M. Gharaibeh, Amgen, 1,Amgen, 3; B. S. Stolshek, Amgen, 1,Amgen, 3; A. Mutebi, Amgen, 1; A. M. Sainski-Nguyen, Amgen, 5; D. Collier, Amgen, 1,Amgen, 3; E. Durden, Amgen, 5.


**Abstract Number: 364**

**Canakinumab First or Second Choice in Systemic Juvenile Idiopathic Arthritis – Experience from Clinical Practice**

Gerd Horneff1, Ivan Foeldvari2, Klaus Tenbrock3, K Minden4 and Jasmin B. Kuemmerle-Deschner5, 1Asklepios Clinic, Sankt Augustin, Germany, 2Kinder- und Jugendrheumatologie, Hamburger Zentrum Kinder-und Jugendrheumatologie, Hamburg, Germany, 3University Aachen, Aachen, Germany, 4Charité – University of Medicine Berlin, Berlin, Germany, 5Pediatrics, University Hospital Tübingen, Tübingen, Germany

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Sunday, November 5, 2017  
**Session Title:** Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster I: Autoinflammatory Disorders and Miscellaneous  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Canakinumab (CAN) has demonstrated its efficacy and safety in systemic juvenile idiopathic arthritis in clinical trials. We report on the experience with CAN in the clinical practice.

**Methods:** Surveillance of patients exposed to biologics is performed by the BIKER registry. Data on patients’ and disease characteristics, disease activity and safety reports until Dec. 2016 were analysed.

**Results:** Until June 2017, 39 JIA patients were registered in the German BIKER registry in whom CAN was started, representing 59.2 PY of exposure. In 14 patients CAN was used as first biologic agent. 25 patients were pretreated with other biologics, 14 received 1, 7 two, 3 three and 1 four biologics. 15 had been treated with Tocilizumab, 11 with Anakinra, 9 with Etanercept and 9 with Adalimumab. Of interest, 3 patients in the pre-exposed cohort had experienced a macrophage activation syndrome. Patient’s and disease characteristics comparison of biologics naïve and preexposed patients are given below.

Patients pretreated were older, had a longer disease duration and more comorbidities (Macrophage activation syndrome, pericarditis, pleuritic organomegaly and Cushing’s) than naïve patients. The proportion of patients with active arthritis, active systemic features and both were comparable.

Disease activity at baseline (number of active joints, Patient’s and physicians’ global, ESR, CRP and the JADAS) was higher in the biologic naïve cohort suggesting some clinical benefit from pretreatment in the exposed cohort. Dosing of CAN was comparable (3.9+/−0.4 vs. 3.5+/−0.7 mg/kg) as well as the median treatment duration.

Treatment efficacy at 6 month of treatment was stronger in the naïve cohort with more patients reaching a PedACR50/90 response, CRP normalisation, normal CHAQ, physician global indicating no activity (p=0.05) JADAS remission (p=0.02). Treatment with CAN was discontinued by 42% in the naïve cohort and 48% in the exposed cohort. Reasons for withdrawals were inefficacy (n=7; 19%), intolerance (n=2; 5%) and remission (n=7; 19%) of the disease and other (n=2;5%).

**Conclusion:** First experience with CAN for treatment of systemic JIA in clinical practice is presented. A high proportion of patients gained significant response to treatment. JADAS remission was reached in significantly more biologics naïve patients while few
patients discontinued treatment in remission so far. Intolerance was rare. The further long term surveillance of patients exposed to biologics is intended by the registry.

Table 1: Baseline characteristics in the comparison groups

<table>
<thead>
<tr>
<th></th>
<th>Biologics naive</th>
<th>Biologics pre-exposed</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (female gender)</td>
<td>14 (28%)</td>
<td>25 (52%)</td>
</tr>
<tr>
<td>Age at JIA onset (years); Median (IQR)</td>
<td>3.3 (2.7-5.2)</td>
<td>3.7 (2.6-7.1)</td>
</tr>
<tr>
<td>Disease duration (years); Median (IQR)</td>
<td>0.7 (0.2-5.6)</td>
<td>1.9 (0.6-8.7)</td>
</tr>
<tr>
<td>Concomitant treatment at baseline: NSAIDS</td>
<td>7 (50%)</td>
<td>10 (40%)</td>
</tr>
<tr>
<td>Steroids</td>
<td>6 (43%)</td>
<td>11 (44%)</td>
</tr>
<tr>
<td>MTX</td>
<td>3 (21%)</td>
<td>6 (24%)</td>
</tr>
<tr>
<td>Patients with active joints</td>
<td>8 (57%)</td>
<td>10 (40%)</td>
</tr>
<tr>
<td>Patients with active systemic features</td>
<td>9 (64%)</td>
<td>10 (40%)</td>
</tr>
<tr>
<td>Active joint count; Median (IQR)</td>
<td>2.5 (0-3)</td>
<td>0 (0-3)</td>
</tr>
<tr>
<td>Physician global VAS (0-10); Median (IQR)</td>
<td>5.2 +/-2.8</td>
<td>6.2 (3.2-7.2) 3.8 +/-3.4; 3.7 (0.7-6.3)</td>
</tr>
<tr>
<td>Patient Global VAS (0-10); Median (IQR)</td>
<td>4.8 +/-2.9</td>
<td>4.6 (2.7-7)</td>
</tr>
<tr>
<td>CHAQ-DI (0-3); Median (IQR)</td>
<td>0.5 (0.38-1.24)</td>
<td>0.65 +/-0.84; 0.25 (0-1.22)</td>
</tr>
<tr>
<td>ESR (mm/h); Median (IQR)</td>
<td>28 (10-55)</td>
<td>9 (4-18.5)</td>
</tr>
<tr>
<td>CRP (mg/l); Median (IQR)</td>
<td>43 (25-109)</td>
<td>3 (1-11)</td>
</tr>
<tr>
<td>JADAS10; Median (IQR)</td>
<td>15.2 (14-20.9)</td>
<td>9.5 (5.5-11.8)</td>
</tr>
</tbody>
</table>

Disclosure: G. Horneff, Pfizer Inc, 2; I. Foeldvari, None; K. Tenbrock, None; K. Minden, Pfizer, Abbvie, Roche, 2, Abbvie, Pfizer, Pharm-Allergan, Roche, 5; J. B. Kuemmerle-Deschner, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/canakinumab-first-or-second-choice-in-systemic-juvenile-idiopathic-arthritis-experience-from-clinical-practice

Abstract Number: 365
Canakinumab Treatment in Patients with Still’s Disease: A Pooled Analysis of Systemic Juvenile Idiopathic Arthritis Data By Age Groups

Eugen Feist¹, Pierre Quartier², Bruno Fautrel³, Rayfel Schneider⁴, Paolo Sfriso⁵, Petros Efthimiou⁶, Luca Cantarini⁷, Karine Lheritier⁸, Karolynn Leon⁹ and Antonio Speziale⁸

¹Department of Rheumatology and Clinical Immunology, Charité-Universitätsmedizin, Berlin, Germany, ²Necker-Enfants Malades Hospital, Paris, France, ³UPMC University Paris 06, Pitié-Salpêtrière Hospital, Paris, France, ⁴University of Toronto and The Hospital for Sick Children, Toronto, ON, Canada, ⁵University of Padova, Padova, Italy, ⁶Medicine/Rheumatology, New York University School of Medicine/NYU Langone Health, New York, NY, ⁷University of Siena, Siena, Italy, ⁸Novartis Pharma AG, Basel, Switzerland, ⁹Novartis Pharmaceuticals Corporation, East Hanover, NJ

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster I: Autoinflammatory Disorders and Miscellaneous
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Still’s disease presents in pediatric and adult patients as a disease continuum with similar symptoms and pathophysiology.¹,² The objective of this analysis was to evaluate the efficacy and safety of canakinumab, a selective human anti-IL1 β monoclonal antibody, in systemic juvenile idiopathic arthritis (SJIA) patients from pooled data across three age groups: children, adolescents and adults (the latter representing adult-onset Still’s disease [AOSD] population).

Methods: Data of canakinumab treated patients were pooled from 4 SJIA studies (NCT00426218, NCT00886769, NCT00889863, NCT00891046). Canakinumab was administered at 4 mg/kg every 4 weeks in majority of the patients. Efficacy parameters (adapted American College of Rheumatology [aACR] pediatric responses, juvenile idiopathic arthritis [JIA] ACR responses, patients with inactive disease), C-reactive protein (CRP) levels over 12 weeks and safety were assessed by age groups. One study (NCT00426218) was excluded for efficacy outcomes.

Results: 216 children (2–<12 years), 56 adolescents (12–<16 years) and 29 adults (≥16 years) were analyzed for efficacy outcomes. The efficacy parameters across the three age groups were comparable (Table 1). The safety profile of canakinumab was similar across age groups (Table 2). One patient from the adolescents group died because of pulmonary hypertension that was associated with macrophage activation syndrome. Clinical, laboratory and immunogenicity data showed no notable differences between the age groups.

Table 1. Efficacy: responses by age group and time point
<table>
<thead>
<tr>
<th>Age group</th>
<th>%</th>
<th>aACR pediatric; n/N (%)</th>
<th>JIA ACR; n/N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 15</td>
<td>Day 85</td>
<td>Day 15</td>
</tr>
<tr>
<td>Children</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥30</td>
<td>158/216 (73.1)</td>
<td>90/133 (67.7)</td>
<td>169/216 (78.2)</td>
</tr>
<tr>
<td>≥70</td>
<td>109/216 (50.5)</td>
<td>77/133 (57.9)</td>
<td>111/216 (51.4)</td>
</tr>
<tr>
<td>≥100</td>
<td>46/216 (21.3)</td>
<td>42/133 (31.6)</td>
<td>47/216 (21.8)</td>
</tr>
<tr>
<td>Adolescents</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥30</td>
<td>47/56 (83.9)</td>
<td>20/27 (74.1)</td>
<td>47/56 (83.9)</td>
</tr>
<tr>
<td>≥70</td>
<td>33/56 (58.9)</td>
<td>18/27 (66.7)</td>
<td>33/56 (58.9)</td>
</tr>
<tr>
<td>≥100</td>
<td>15/56 (26.8)</td>
<td>8/27 (29.6)</td>
<td>15/56 (26.8)</td>
</tr>
<tr>
<td>Adults</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥30</td>
<td>25/29 (86.2)</td>
<td>15/18 (83.3)</td>
<td>25/29 (86.2)</td>
</tr>
<tr>
<td>≥70</td>
<td>19/29 (65.5)</td>
<td>13/18 (72.2)</td>
<td>19/29 (65.5)</td>
</tr>
<tr>
<td>≥100</td>
<td>4/29 (13.8)</td>
<td>4/29 (13.8)</td>
<td>4/29 (13.8)</td>
</tr>
</tbody>
</table>

Inactive disease; n/N (%) CRP, median; mg/L (n/N)

<table>
<thead>
<tr>
<th>Age group</th>
<th>Day 15</th>
<th>Day 85</th>
<th>Day 15</th>
<th>Day 85</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children</td>
<td>40/216 (18.5)</td>
<td>32/133 (24.1)</td>
<td>12.00 (211/216)</td>
<td>9.75 (168/216)</td>
</tr>
<tr>
<td>Adolescents</td>
<td>18/56 (32.1)</td>
<td>10/27 (37.0)</td>
<td>10.00 (55/56)</td>
<td>8.40 (45/56)</td>
</tr>
<tr>
<td>Adults</td>
<td>6/29 (20.7)</td>
<td>8/18 (44.4)</td>
<td>4.50 (26/29)</td>
<td>7.80 (23/29)</td>
</tr>
</tbody>
</table>

Table 2. Safety: adverse events

<table>
<thead>
<tr>
<th></th>
<th>Children, n (%)</th>
<th>Adolescents, n (%)</th>
<th>Adults, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 233</td>
<td>N = 60</td>
<td>N = 31</td>
</tr>
<tr>
<td>AEs (at least one)</td>
<td>202 (86.7)</td>
<td>53 (88.3)</td>
<td>27 (87.1)</td>
</tr>
<tr>
<td>AEs leading to study drug discontinuation</td>
<td>26 (11.2)</td>
<td>10 (16.7)</td>
<td>6 (19.4)</td>
</tr>
<tr>
<td>AEs most common/special interest</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infections and infestations</td>
<td>176 (75.5)</td>
<td>42 (70.0)</td>
<td>23 (74.2)</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>122 (52.4)</td>
<td>32 (53.3)</td>
<td>18 (58.1)</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td>119 (51.1)</td>
<td>33 (55.0)</td>
<td>16 (51.6)</td>
</tr>
<tr>
<td>Opportunistic infections</td>
<td>3 (1.3)</td>
<td>4 (6.7)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>11 (4.7)</td>
<td>2 (3.3)</td>
<td>0</td>
</tr>
<tr>
<td>SAEs (at least one)</td>
<td>81 (34.8)</td>
<td>25 (41.7)</td>
<td>9 (29.0)</td>
</tr>
</tbody>
</table>

Conclusion: Pooled analyses indicate similar efficacy of canakinumab across all the age groups of children, adolescents and adult SJIA patients. There were no meaningful differences in safety profiles across the different age groups. These analyses suggest similar efficacy of canakinumab in AOSD patients as observed in the SJIA patients.


Disclosure: E. Feist, Novartis, 2,Novartis, 9; P. Quartier, AbbVie, Novartis, Pfizer, and Chugai-Roche, 2,AbbVie, Novartis, Sobi, and Roche, 8,AbbVie, Novartis, Pfizer, Sobi, Roche, Novimmune and Sanofi, 9; B. Fautrel, AbbVie, MSD, and Pfizer, 2,AbbVie, Biogen, BMS, Celgène, Hospira, Janssen, Lilly, MSD, Nordic Pharma, Pfizer, Roche, Sobi, and UCB, 9; R. Schneider, Novartis, 2,Novartis, Novimmune and Sobi, 9; P. Frisso, Novartis, 9; P. Efthimiou, Novartis, 9; L. Cantarini, Sobi, Novartis, and AbbVie, 9; K. Lheritier, Novartis, 3; K. Leon, Novartis, 3; A. Speziale, Novartis, 3.
Short-Term Outcomes in Patients with Systemic-Onset Juvenile Idiopathic Arthritis Treated with Either Tocilizumab or Anakinra in a Real-World Setting in the United Kingdom

Lianne Kearsley-Fleet1, Diederik De Cock1, Eileen Baildam2, Michael W. Beresford3, Helen E. Foster4, Taunton R. Southwood5, Wendy Thomson6,7 and Kimme L. Hyrich1,6, 1Arthritis Research UK Centre for Epidemiology, University of Manchester, Manchester Academic Health Science Centre, Manchester, United Kingdom, 2Clinical Academic Department of Paediatric Rheumatology, Alder Hey Children's NHS Foundation Trust, Liverpool, United Kingdom, 3Alder Hey Children's NHS Foundation Trust Hospital, Institute of Translational Medicine (Child Health), University of Liverpool, Liverpool, United Kingdom, 4Institute of Cellular Medicine and Paediatric Rheumatology, Newcastle University and Great North Children's Hospital, Newcastle Upon Tyne, United Kingdom, 5Institute of Child Health, University of Birmingham and Birmingham Children's Hospital, Birmingham, United Kingdom, 6National Institute of Health Research Manchester Musculoskeletal Biomedical Research Centre, Central Manchester NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, United Kingdom, 7Arthritis Research UK Centre for Genetics and Genomics, University of Manchester, Manchester Academic Health Science Centre, Manchester, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster I: Autoinflammatory Disorders and Miscellaneous
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Juvenile idiopathic arthritis (JIA) comprises 7 ILAR categories, but systemic-onset JIA (sJIA) appears to be distinct in genetic background and pathogenesis from the other categories of JIA. The aim of this study is to investigate real-world therapeutic short-term responses in patients with sJIA starting tocilizumab (TCZ) or anakinra (ANK), the 2 most common biologics used currently for this ILAR category.

Methods: This analysis included patients with sJIA enrolled in the UK Biologics for Children with Rheumatic Diseases (BCRD) study starting TCZ or ANK from 01/01/2010 (study start date), with data available at baseline, 6 months and 1 year by 31/12/2016. Disease activity was assessed at baseline, 6 months and 1 year, including outcomes; minimal disease activity (MDA), clinically inactive disease (CID) and ACRPedi90. Univariable logistic regression was used to identify baseline characteristics associated with the outcomes. Multiple imputation was used to account for missing data.

Results: A total of 78 sJIA patients were included (54 TCZ; 24 ANK) (Table); 55% were female and 70% received this drug as their first biologic. Patients starting ANK had a shorter disease duration (0 vs 2 years; p=0.003), and more had a history of macrophage activation syndrome (MAS) (38% vs 8%; p=0.002). Response rates between the 2 drugs were similar. In the whole group, at 1 year, 54% achieved ACRPedi90, 47% MDA and 33% CID (Table). Mean JADAS-71 change was -14 (p<0.001). No baseline characteristics were associated with achieving response. Nineteen (24%) patients stopped their biologic treatment by 1 year (Figure), for reasons including remission (N=1), inefficacy (N=6), adverse events (N=10, including one case of MAS in patient receiving TCZ) and unknown (N=2). Treatment survival was better with TCZ (87% at 1 year vs 50% ANK), with 4 children stopping for injection-related problems.

Conclusion: In this real-world cohort of children with sJIA receiving TCZ or ANK, approximately half the patients achieved a significant clinical short-term response, and one-third achieved inactive disease within 1 year. Although numbers in this analysis are low, reflecting the rarity of sJIA, it is important to report these reassuring real-world outcomes and similarities in response with other JIA categories. As this UK JIA study continues to develop, future analyses investigating longer term tolerability and safety will be possible.

Table: Baseline characteristics and one year outcomes of 78 systemic JIA patients; 54 tocilizumab and 24 anakinra.
<table>
<thead>
<tr>
<th></th>
<th>Anakinra (IL-1) N=24</th>
<th>Tocilizumab (IL-6) N=54</th>
<th>Total N=78</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%)</td>
<td>15 (63%)</td>
<td>28 (52%)</td>
<td>43 (55%)</td>
<td>P=0.4</td>
</tr>
<tr>
<td>First Biologic, n (%)</td>
<td>19 (86%) N=22</td>
<td>34 (63%)</td>
<td>53 (70%) N=76</td>
<td>P=0.04</td>
</tr>
<tr>
<td>Age (years), median (IQR)</td>
<td>6 (2, 13)</td>
<td>7 (4, 11)</td>
<td>7 (3, 12)</td>
<td>P=0.8</td>
</tr>
<tr>
<td>Disease Duration (years), median (IQR)</td>
<td>0 (0, 1) N=23</td>
<td>2 (1, 3)</td>
<td>1 (0, 2) N=77</td>
<td>P=0.003</td>
</tr>
<tr>
<td>Systemic Features Present, n (%)</td>
<td>13 (81%) N=16</td>
<td>24 (53%) N=45</td>
<td>37 (61%) N=61</td>
<td>P=0.05</td>
</tr>
<tr>
<td>History of Macrophage Activation Syndrome, n (%)</td>
<td>8 (38%) N=21</td>
<td>4 (8%) N=49</td>
<td>12 (17%) N=70</td>
<td>P=0.002</td>
</tr>
<tr>
<td>Concomitant Oral Steroids, n (%)</td>
<td>15 (63%)</td>
<td>36 (67%)</td>
<td>51 (65%)</td>
<td>P=0.7</td>
</tr>
<tr>
<td>Concomitant Methotrexate, n (%)</td>
<td>20 (83%)</td>
<td>44 (81%)</td>
<td>64 (82%)</td>
<td>P=0.8</td>
</tr>
<tr>
<td>Disease Activity, median (IQR)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active Joints (0-71)</td>
<td>4 (1, 11) N=19</td>
<td>4 (1, 8) N=48</td>
<td>4 (1, 9) N=67</td>
<td>P=0.9</td>
</tr>
<tr>
<td>Physician Global of Disease (0-10cm VAS)</td>
<td>3 (2, 6) N=16</td>
<td>4 (2, 6) N=34</td>
<td>3 (2, 6) N=50</td>
<td>P=0.8</td>
</tr>
<tr>
<td>Parent Global of Wellbeing (0-10cm VAS)</td>
<td>4 (1, 5) N=18</td>
<td>4 (2, 7) N=34</td>
<td>4 (1, 7) N=52</td>
<td>P=0.9</td>
</tr>
<tr>
<td>Childhood Health Assessment Questionnaire (0-3)</td>
<td>1.0 (0.4, 2.0) N=15</td>
<td>0.9 (0.4, 1.8) N=34</td>
<td>0.9 (0.4, 1.8) N=49</td>
<td>P=0.8</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate, mm/hr</td>
<td>55 (27, 86) N=19</td>
<td>26 (10, 58) N=49</td>
<td>35 (11, 67) N=68</td>
<td>P=0.1</td>
</tr>
<tr>
<td>JADAS-71</td>
<td>18 (6, 29) N=12</td>
<td>20 (11, 26) N=22</td>
<td>19 (7, 27) N=34</td>
<td>P=0.7</td>
</tr>
<tr>
<td>Six Month Outcomes*, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean JADAS-71 change</td>
<td>-10.4 (p=0.1)</td>
<td>-10.8 (p&lt;0.001)</td>
<td>-10.7 (p&lt;0.001)</td>
<td>P=0.9</td>
</tr>
<tr>
<td>ACR Pedi 90</td>
<td>51%</td>
<td>58%</td>
<td>56%</td>
<td>P=0.7</td>
</tr>
<tr>
<td>Minimal disease activity (MDA)</td>
<td>45%</td>
<td>50%</td>
<td>49%</td>
<td>P=0.7</td>
</tr>
<tr>
<td>Clinically inactive disease (CID)</td>
<td>15%</td>
<td>20%</td>
<td>19%</td>
<td>P=0.7</td>
</tr>
<tr>
<td>Twelve Month Outcomes*, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean JADAS-71 change</td>
<td>-13.3 (p&lt;0.001)</td>
<td>-13.7 (p&lt;0.001)</td>
<td>-13.6 (p&lt;0.001)</td>
<td>P=0.7</td>
</tr>
<tr>
<td>ACR Pedi 90</td>
<td>37%</td>
<td>62%</td>
<td>54%</td>
<td>P=0.7</td>
</tr>
<tr>
<td>Minimal disease activity (MDA)</td>
<td>41%</td>
<td>49%</td>
<td>47%</td>
<td>P=0.5</td>
</tr>
<tr>
<td>Clinically inactive disease (CID)</td>
<td>22%</td>
<td>38%</td>
<td>33%</td>
<td>P=0.2</td>
</tr>
</tbody>
</table>

*Using imputed data.

Interquartile range (IQR), visual analogue scale (VAS), 71-joint juvenile arthritis disease activity score (JADAS-71), American college of rheumatology paediatric criteria for 90% improvement (ACR Pedi 90).
Abstract Number: 367

Interleukin-1 Receptor Antagonist Is a Potential Treatment for Undifferentiated Autoinflammatory Syndromes

Ananta Subedi1, Daniella Schwartz2, Karyl Barron3, Daniel L. Kastner4 and Amanda Ombrello5, 1National Institute of Arthritis, Musculoskeletal and Skin Disease (NIAMS), Bethesda, MD, 2NIAMS - Rheumatology, National Institutes of Health, Bethesda, MD, 3National Institutes of Health, Inflammatory Disease Section, National Human Genome Research Institute, Bethesda, MD, 4Inflammatory Disease Section, National Human Genome Research Institute, National Institutes of Health, Bethesda, MD, 5Inflammatory Disease Section, NHGRI/NIH, Bethesda, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster I: Autoinflammatory Disorders and Miscellaneous
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The autoinflammatory diseases (AIDs) are a group of disorders of the innate immune system characterized by seemingly unprovoked inflammation1. A variety of genetic alterations are attributed to the clinical and pathological manifestations of these conditions; however, many of the patients presenting with clinical features of AIDs do not have a pathogenic mutation to be
classified under one of the monogenic AIDs\textsuperscript{2}. These patients are referred to as having an undifferentiated autoinflammatory syndrome. Blocking of the interleukin 1 (IL-1) pathway is defined as a treatment modality in some of the AIDs (FMF, CAPS, TRAPS and MVK); but, there is limited data on their use in undifferentiated autoinflammatory syndromes.

Aim: We aim to review the treatment effects of the IL-1 receptor antagonist, anakinra, in pediatric undifferentiated autoinflammatory syndrome patients.

**Methods:** We identified the pediatric patients enrolled in the protocol 94-HG-0105 “Genetics and Pathophysiology of Familial Mediterranean Fever and Related Disorders” who were prescribed Anakinra between October 2010 and October 2016. Patients who tested positive for known genetic mutation to cause periodic fever syndromes (FMF, CAPS, TRAPS, MKD, PAPA, DIRA, HA20 and DADA2) by commercially available methods were excluded. Medical records were reviewed to identify the response to treatment with Anakinra. Clinical response was determined based on the patient reported outcome. Laboratory data (White Blood Cell Count (WBC), ESR and CRP) were compared before and after the treatment. Statistical tests were done using RStudio (http://www.R-project.org). Clinical response to treatment were presented as frequency diagram. Laboratory data before and after the use of Anakinra was compared using the Wilcoxon signed rank test.

**Results:** We identified 75 patients who met the pre-specified criteria. Among the 75 patients, the majority of the patients were male (65%). The disease was predominantly seen among Caucasians (84%). Anakinra was prescribed as needed (PRN) for 56% of the patients, 44% required a daily dose. 59% of the patients were responders, 9% were partial responders and 17% did not have clinical response to the treatment. 13% of the patients were non-compliant, 1% could not tolerate and 1% of the patient did not have a follow up. Among the patients who had clinical response to treatment, we found a statistically significant decrease in ESR after treatment with anakinra (p-value = 0.01416, 95 percent confidence interval: 1.000085 8.999991).

**Conclusion:** The management of pediatric undifferentiated autoinflammatory syndromes is challenging. We found anakinra a very effective treatment option for use on both an intermittent and continuous basis. Anakinra has the potential to significantly improve the quality of life of such patients.

References:


Disclosure: A. Subedi, None; D. Schwartz, None; K. Barron, None; D. L. Kastner, None; A. Ombrello, None.

**Abstract Number:** 368

### Evaluation of Efficacy and Safety of Opocalcium Colchicine, and Anti-IL1 Treatment in Childhood Colchicine-Resistant Familial Mediterranean Fever

Kenan Barut, Amra Adrovic, Sezgin Sahin, Asli Kaplan and Ozgur Kasapcopur, Pediatric Rheumatology, Istanbul University, Cerrahpasa Medical School, Department of Pediatric Rheumatology, Istanbul, Turkey

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster I: Autoinflammatory Disorders and Miscellaneous  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

The colchicine-resistant FMF (crFMF) is defined as 6 or more polyserositis attacks in the last year despite the regular usage of colchicine in the highest tolerable dose. IL-1 receptor antagonists have been shown to be efficient in crFMF. We tried to define the efficacy of opocalcium colchicine (OC), anakinra and canakinumab by FMF50 scores, complete and partial clinical responses.

**Methods:**
Patients who were under OC, anakinra and canakinumab are considered to be resistant to standard colchicine treatment. The FMF50 score is used to define the response to treatment. Complete clinic and laboratory response is characterized by an absence of clinical features and normal laboratory findings. The partial clinical and laboratory response include 30 % improvement in clinical and laboratory features.

Results:

A total of 839 FMF patients has been assessed and 49/839 (5.8%) of them has been considered colchicine resistant. FMF50 response has been obtained in 4/49 (8.2%) patients under standard colchicine treatment; in 14/30 (46.7%) patients treated with OC, in 5/6 (83.3%) with anakinra and in 12/13 (92.3%) patients with canakinumab. The FMF50 response significantly differed according to treatment modality (p<0.005). Clinical remission has been achieved in 10/30 (33.3%), 5/6 (83.3%) and in 11/13 (84.6%) patients treated with OC, anakinra and canakinumab, respectively. Patients treated with OC significantly differed from those treated with anti IL-1 according to complete clinical remission (p<0.002). Laboratory remission has been obtained in 7/30 (23.3%), 4/6 (66.7%) and 11/13 (84.6%) patients treated with OC, anakinra and canakinumab, respectively. The laboratory remission was significantly different between patients treated with OC and with anti IL-1 (p<0.0001).

The most common adverse effect was diarrhea in 17/49 (34.6%), transaminases elevation in 3/49 (6%) patients and leukopenia in 1 patient. Diarrhea was seen in 3/30 (10%) patients under OC treatment. Local allergic reactions were seen in 3/6 (50%) anakinra patients. One patient developed pneumonia while on canakinumab treatment; upper respiratory tract infection has been registered in 3/13 (23%) patients and acute gastroenteritis in one patient. None of the patients developed severe adverse effect.

Conclusion:

The FMF50 response has not been achieved in majority of patients under OC treatment, although their drug compliance was better comparing to standard colchicine compound in our country. Complete clinical remission has been obtained in minority of patients treated with OC. In contrary, FMF50 response, complete clinical and laboratory response have been detected in most of patients treated with anakinra and canakinumab. Both of anti IL-1 agents were safe and effective in crFMF patients.

References


Disclosure: K. Barut, None; A. Adrovic, None; S. Sahin, None; A. Kaplan, None; O. Kasapcopur, Novartis Pharmaceutical Corporation, 8, Roche Pharmaceuticals, 8.

Hepatitis A Virus Vaccination in Juvenile-Onset Systemic Lupus Erythematosus

Sevinc Mertoglu¹, Sezgin Sahin¹, Omer Faruk Beser², Amra Adrovic¹, Kenan Barut¹, Pelin Yuksel³, Soner Sazak⁴, Bekir Kocazeybek⁵ and Ozgur Kasapcopur¹, ¹Pediatric Rheumatology, Istanbul University, Cerrahpasa Medical School, Department of Pediatric Rheumatology, Istanbul, Turkey, ²Pediatric Gastroenterology, Department of Pediatrics, Okmeydani Education and Training Hospital, Istanbul, Turkey, ³Microbiology, Istanbul University, Cerrahpasa Medical School, Department of Microbiology, Istanbul, Turkey, ⁴Pediatrics, Department of Pediatrics, Okmeydani Education and Training Hospital, Istanbul, Turkey, ⁵Istanbul University, Cerrahpasa Medical School, Department of Microbiology, Istanbul, Turkey

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster I: Autoinflammatory Disorders and Miscellaneous
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Various infections play significant roles in flares of systemic lupus erythematosus (SLE). Hepatitis A virus is one of these infectious agents that has high endemicity particularly in developing countries. Hence, immunization via vaccination against this infectious agent would provide a better management of the disease. However, both immunosuppressive drugs and the disease itself are believed to impair the normal functioning of immune system. Little is known regarding the safety and immunogenicity of vaccinations in SLE patients. Moreover, to the best of our knowledge safety and efficacy of hepatitis A vaccination were not studied in children with SLE.

In the present study, we aimed to compare the antibody titers and seropositivity rates in juvenile SLE and healthy subjects after hepatitis A vaccination. Besides, we examined the effect of immunosuppressive drugs and disease activity on antibody responses.

Methods:

Sixty-nine juvenile SLE patients were enrolled in the study. Initially, we evaluated anti-HAV IgM and anti-HAV IgG titers in juvenile SLE patients. Of the 69 subjects, 37 patients were seronegative and eligible for hepatitis A vaccination. Among them, 7 juvenile SLE patients refused to participate to the study. Finally, anti-HAV Ig G negative 30 patients and 39 healthy subjects were vaccinated with two doses of hepatitis A vaccine (at 0 months and at sixth months). After vaccinations, anti-HAV Ig G titers were measured and compared between two groups.

Results:

Anti-HAV Ig G concentrations were measured after vaccination in 30 patients with juvenile SLE and 39 control subjects. Anti-HAV Ig G titer of the juvenile SLE patients was significantly lower than that of the healthy controls (median 4.6 versus 11.9 IU/L, p=0.02). Although the rate of seropositivity was lower in juvenile SLE patients (n=24/30, 80%) compared to healthy controls (n=33/39, 84.6%); this was not statistically significant (p=0.6). No adverse reaction was reported after vaccination.

Conclusion:

Although anti-HAV Ig G antibody titers after vaccination have found to be somewhat lower than that of the healthy subjects, significant portion of juvenile SLE patients were seropositive. According to these results, we conclude that hepatitis A vaccine is adequately immunogenic and quite safe in juvenile SLE patients.

References:


Disclosure: S. Mertoglu, None; S. Sahin, None; O. F. Beser, None; A. Adriovic, None; K. Barut, None; P. Yuksel, None; S. Sazak, None; B. Kocayebek, None; O. Kasapcopur, Novartis Pharmaceutical Corporation, 8, Roche Pharmaceuticals, 8.
SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster I: Autoinflammatory Disorders and Miscellaneous
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: To validate the 2016 ACR/EULAR classification criteria of macrophage activation syndrome (MAS) complicating systemic juvenile idiopathic arthritis (s-JIA) in Japanese patients.

Methods: A combination of expert consensus and analysis of real patient data was conducted by a panel of 15 paediatric rheumatologists. Eighty-three profiles comprised 25 patients with s-JIA–associated MAS and 58 patients with active s-JIA without evidence of MAS. From these profiles, 19 points for full-blown MAS, 16 points for MAS onset and 58 points for acute s-JIA without MAS were evaluated.

Results: Evaluation of the classification criteria to discriminate full-blown MAS from acute s-JIA without MAS showed a sensitivity of 0.947 and specificity of 1.000 at the time of full-blown MAS. Sensitivity was 0.438 and specificity 1.000 at the time of MAS onset. The number of measurement items that fulfilled the criteria increased in full-blown MAS compared to that at MAS onset. At MAS onset, the positive rates of patients who met the criteria for platelet counts and triglycerides were low, whereas those for aspartate aminotransferase and fibrinogen were relatively high. At full-blown MAS, the number of patients who met the criteria for each measurement item increased.

Conclusion: The classification criteria for MAS complicating s-JIA had a very high diagnostic performance. However, the diagnostic sensitivity for MAS onset was relatively low. For the early diagnosis of MAS in s-JIA, the dynamics of laboratory values during the course of MAS should be further investigated.

Disclosure: M. Shimizu, None; M. Mizuta, None; T. Yasumi, None; N. Iwata, None; Y. Okura, None; N. Kinjo, None; H. Umebayashi, None; T. Kubota, None; Y. Nakagishi, None; K. Nishimura, None; M. Yashiro, None; J. Yasumura, None; K. Yamazaki, None; H. Wakiguchi, None; N. Okamoto, None; M. Mori, None.


Abstract Number: 371

Longer Term Outcomes of Chronic Relapsing Multifocal Osteomyelitis in a UK Tertiary Adolescent and Young Adult Rheumatology Centre

Kristina E.N. Clark1, Francesca Josephs2, Nicola Daly3, Claire Louise Murphy3 and Debjit Sen4, 1Rheumatology, University college London Hospitals, London, United Kingdom, 2Rheumatology, UCL, London, United Kingdom, 3Rheumatology, University College London Hospital, London, United Kingdom, 4Adolescent Rheumatology Department, University College London Hospital NHS Trust, London, United Kingdom
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster I: Autoinflammatory Disorders and Miscellaneous
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM
Background/Purpose:

Chronic relapsing multifocal osteomyelitis (CRMO) is a rare autoinflammatory bone condition presenting primarily in children & adolescents. It characteristically affects the epiphysis & metaphysis of long bones & presents with bony pain, local swelling & warmth.

The aim of this study was to collate our centre’s experience of managing patients with CRMO & establish their longer term outcomes.

Methods:

Our Centre provides a tertiary service for adolescents & young adults >13 years. We performed a retrospective case note review of all patients known to our service with a diagnosis of CRMO.

Results:

We identified 17 (10 female) patients with CRMO presenting between 1999 & 2015. The median age of initial symptoms & age of presentation was 12 years. Median follow up duration 4.75 years (range 1-16.5 years).

On review of long term outcomes, several patients evolved into a different disease phenotype: 3 SAPHO (synovitis, acne, pustolosis, hyperostosis, osteitis), 3 ERA (enthesitis related arthritis) & 2 oligoarticular juvenile idiopathic arthritis (OJIA). The clinical phenotype of patients with SAPHO was predominantly multifocal (involving wrists, jaw, ankle & ribs), with one patient having disease of only the sternoclavicular joints. Of the ERA patients, 2 had sacro-iliac & clavicle involvement, 1 had initial femur involvement which has progressed to ERA around the hips. All patients with OJIA had ankle involvement, with 1 developing knee synovitis as well & 1 wrist & shoulder inflammatory arthritis.

Unifocal osteomyelitis was seen in 35% of patients & 65% multifocal as confirmed by whole body MRI. 70.5% patients had recurrent episodes of inflammation, while 29.5% had only one flare & then remitted (either clinical or confirmed with MRI). 15 patients had their diagnosis confirmed with biopsy, 2 did not due to site of disease being close to the growth line (diagnosis based on clinic impression & typical radiographic findings).

Multiple sites of disease have been confirmed in our patients & include lower limbs (70%), upper limbs (35%), clavicle (29.4%), mandible (17.6%) & spine/pelvis (23.5%).

All patients were treated with NSAIDs. During the course of the disease at any point 76% have been on methotrexate; 47% had one pamidronate infusion & 23% more than 1. Other medications include sulfasalazine, azathioprine, risedronate &anti-TNFs.

On last clinic review, 35% of patients have evidence of ongoing active disease

Conclusion:

The perceived wisdom is that CRMO is a self-limiting disease which eventually goes into remission. However our Centre’s experience is that nearly 50% of our patients have a disease which evolves into another systemic autoimmune disease (SAPHO, OJIA or ERA). This is more frequent in those with multifocal CRMO. Previous case series have suggested only 0-30% of patients’ disease evolves. Our findings may be a reflection of our older cohort of patients.

The majority of patients have a recurrent and multifocal disease. The most common site of disease was in the lower limbs. All patients were treated with NSAIDS, a combination of DMARDs, bisphosphonates & biologic agents have been used, which has resulted in remission of disease in the majority of patients.

Disclosure: K. E. N. Clark, None; F. Josephs, None; N. Daly, None; C. L. Murphy, None; D. Sen, None.


Abstract Number: 372

Phenotype of Chronic Recurrent Multifocal Osteomyelitis in a Tertiary Referral Centre: The Great Ormond Street Hospital Experience

Kulsoom Riaz¹ and Sandrine Lacassagne², ¹Paediatric Rheumatology/Gastroenterology, Great Ormond Street Hospital, London, United Kingdom, ²Paediatric Rheumatology, Great Ormond Street Hospital, London, United Kingdom

First publication: September 18, 2017
Recruent Multifocal Osteomyelitis (CRMO) is an aseptic inflammatory bone disease that typically affects the metaphases of the long bones. It affects children, adolescents and young adults. The main presenting feature is local bone pain and/or swelling. It has a protracted course for years with exacerbations and improvement with treatment. The diagnosis of CRMO can be made on clinical presentation and confirmed by magnetic resonance imaging (MRI) and bone biopsy. On MRI examination there are mostly multifocal, and symmetrical lesions (especially in the metaphysis of tubular long bones, flat bones and spine). CRMO can be associated with skin, gut involvement and other rheumatological conditions.

Methods:

We reviewed reports of whole body MRI scans of 300 children, done in last 5 years between January 2012 and December 2016. Patients with MRI scan results consistent with CRMO were included in the study. Retrospective analysis of electronic clinical records of these patients was done and we recorded their clinical symptoms at presentation, any associated illnesses and Family history. Histopathological/ microbiological findings of bone biopsies were reviewed to rule out haematological, infectious or malignant causes.

Results:

Twenty three patients were included in the study. Five were male and eighteen female. These children were 8-18 years old with median age of 15 years. The clinical features of CRMO at first presentation are as under. All patients presented with musculoskeletal symptoms like backache, clavicular involvement, or joint pain. Five patients (21%) presented with abdominal pain and blood in stool. These patients were diagnosed as Inflammatory bowel disease (IBD) on the endoscopic and histopathological findings. Three patients presented with gut symptoms first and later on they developed joint pain and swelling. However one patient presented with joint pain to start with and diagnosed as CRMO. This patient later on developed gut symptoms. One patient presented with simultaneous onset of diarrhoea, blood in stool, abdominal pain and joint pain with swelling. There is significantly more raised inflammatory markers in the IBD/CRMO group than in the CRMO alone group. History of trauma was present in 13% of patients who presented with musculoskeletal symptoms. Hyper mobility was present in four patients. Juvenile idiopathic arthritis was an associated diagnosis in three patients. One patient was diagnosed as Enthesitis related arthritis (ERA) and CRMO overlap. Psoriasis, palmoplantar pustulosis, acne, atopic dermatitis, dermatitis artefacta were the skin conditions associated with CRMO but not in IBD/CRMO overlap group. There was family history of connective tissue disorders in six (26%) out of 23 patients, including systemic lupus erythematosus, ankylosing spondylitis, Crohn’s disease, rheumatoid arthritis, antiphospholipid syndrome and psoriasis. Only one patient (4%) out of 23 was HLAB27 positive.

Conclusion:

CRMO has a varied presentation. We identified that CRMO is associated with IBD in 21% of the patients. Further studies are needed to identify whether the CRMO/IBD overlap group has a separate phenotype.

Disclosure: K. Riaz, None; S. Lacassagne, None.


Abstract Number: 373

a Retrospective Study of Clinical Factors Influencing the Development of Overlapping Disease Features in Pediatric Patients with Chronic Recurrent Multifocal Osteomyelitis (CRMO) and Spondyloarthropathies (SpA)

Lillian Lim1, Jyoti Panwar2, Jennifer Stimec3, Shirley M.L. Tse4, Brian M. Feldman5 and Ronald M. Laxer6, 1 Paediatrics, The Hospital for Sick Children, Toronto, ON, Canada, 2 Christian Medical College, Vellore, India, Vellore, India, 3 The Hospital for Sick Children, Toronto, ON, Canada, 4 Rheumatology, The Hospital for Sick Children, University of Toronto, Toronto, ON, Canada, 5 Rheumatology, The Hospital for Sick Children, Toronto, ON, Canada, 6 Div of Rheumatology, The Hospital for Sick Children, Toronto, ON, Canada
Background/Purpose:

Some studies have suggested that chronic recurrent multifocal osteomyelitis (CRMO) and spondyloarthropathies (SpA) fall on a spectrum of disease, as they have been noted to share overlapping radiographic and clinical features. Most studies examining the link between inflammatory bone lesions and SpA have involved adult patients with SAPHO syndrome, with limited pediatric data. This study was done to test whether gender, HLA-B27 positivity, or age at onset of disease, influence whether and when pediatric CRMO and SpA patients develop overlapping features. Understanding of the clinical factors influencing overlap may have implications for earlier diagnosis, risk stratification, and treatment options.

Methods:

This was a retrospective inception cohort study of SickKids hospital charts. Eligible pediatric patients diagnosed with either CRMO or SpA between January 2000 and December 2016 were collected using the SickKids Rheumatology patient database. Using a secure web application (REDCap), we collected and compared the clinical, laboratory, and radiographic data of 40 randomly sampled patients from each of the CRMO and SpA groups. The MRIs were re-read by a radiologist. A patient was considered to have an overlap diagnosis if they had radiologic and clinical features of both CRMO and SpA.

Results:

7 patients (17.5%) and 8 patients (20.0%) from the CRMO and SpA groups, respectively, developed overlap. The median time to overlap was 36.0 months and 31.5 months, respectively. A survival (time-to-event) analysis, using the Kaplan-Meier approach, was used to show the proportion of patients without overlap features, since time of symptom onset. 28% of the entire sample population was HLA-B27 positive. Multivariable regression models using the Cox Proportional Hazards regression technique showed that the overall likelihood ratio test was not statistically significant (p=0.59), with hazard ratios of 1.11, 0.91, and 1.17 for each of male gender, HLA-B27 positivity, and age at symptom onset, respectively.

Conclusion:

Patient gender, HLA-B27 positivity, and age of symptom onset did not appear to increase the risk of developing overlap features of CRMO and SpA in our sample population. Nonetheless, overlap of clinical and radiologic features was found in approximately 20% of our patients. CRMO and SpA may represent two diseases on the same spectrum, though prospective studies with longer follow up are needed. Our study was limited by the small sample size and retrospective design, as it is unknown whether overlap may occur in the time exceeding clinical follow-up. Study of their clinical overlap is important to allow a better understanding of how to recognize and treat these rare diseases.

Disclosure: L. Lim, None; J. Panwar, None; J. Stimec, None; S. M. L. Tse, None; B. M. Feldman, None; R. M. Laxer, None.


Abstract Number: 374

A Pilot Study of Infrared Thermal Imaging to Detect Active Bone Lesions in Children with Chronic Nonbacterial Osteomyelitis

Yongdong Zhao¹, Ramesh Iyer², Lucas Reichley¹, Assaf Oron³, Averi Kitsch⁴, Seth Friedman⁵, Savannah Partridge⁴ and Carol A Wallace¹, ¹University of Washington, Department of Pediatrics, Seattle, WA, ²Division of Radiology, University of Washington, Seattle Children’s Hospital, Seattle, WA, ³Center for Clinical and Translational Research, Seattle Children’s Research Institute, Seattle, WA, ⁴Department of Radiology, University of Washington, Seattle, WA, ⁵Division of Radiology, University of Washington, Seattle Children's Hospital, Seattle, WA
Background/Purpose: Chronic nonbacterial osteomyelitis (CNO) is an autoinflammatory bone disease. For detection of active bone lesions, bone scintigraphy and magnetic resonance imaging (MRI) are much more sensitive than radiographs, but are more expensive and often require sedation for young children. A rapid and noninvasive imaging tool, infrared thermal imaging, was evaluated for its utility to detect active CNO lesions in extremities of children with CNO.

Methods: Children with suspected or established diagnosis of CNO in their lower extremities were enrolled. All subjects underwent infrared thermal imaging of both entire legs with four views each (anterior, posterior, medial, and lateral) and MRI examinations of their lower extremities. Relevant demographic, laboratory and clinical data were collected. Infrared thermal data were analyzed using custom software. Lower legs were divided equally into three segments longitudinally, and distal thigh was defined as the same length of proximal lower leg (Figure 1). Median and 95th percentile temperatures were recorded for each leg segment. MRI examinations were graded by a blinded pediatric musculoskeletal radiologist to determine the presence of bone edema as confirmation of inflammation within each segment. Temperature differences between inflamed and uninflamed extremities were evaluated using mixed-effects regression models.

Results: Nineteen children with MRI-confirmed CNO in their lower extremities were enrolled, Table 1. Overall, 26 distal, 2 mid (excluded from analysis), 18 proximal lower leg and 12 distal thigh lesions were detected on MRI. Inflamed distal lower leg segments had significantly higher median and 95th percentile temperatures than uninflamed counterparts (p<0.01 in all views). The mean difference between two groups ranged from 0.7°C to 1.7°C, with the greatest difference from medial view (Figure 2). Distal thigh and proximal lower leg temperatures did not differ between inflamed and uninflamed legs from any view.

Conclusion: Children with active CNO lesions in the distal lower leg exhibited higher regional temperatures versus healthy limbs. Further research is needed to evaluate infrared thermal imaging as a convenient and cost-effective tool to identify patients needing additional evaluation by MRI.

<table>
<thead>
<tr>
<th>Population</th>
<th>Children with CNO (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>10.2 (5.6-14.1)</td>
</tr>
<tr>
<td>Gender, F</td>
<td>9 (47%)</td>
</tr>
<tr>
<td>Race, Caucasian</td>
<td>17 (89%)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>136.6 (118.6-159.5)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>35.1 (21.3-46.5)</td>
</tr>
<tr>
<td>Number of CNO lesions</td>
<td>3 (1-6)</td>
</tr>
<tr>
<td>Current medications:</td>
<td>10 NSAIDs, 2 CS, 4 MTX, 4 Biologic, 1 PAM</td>
</tr>
<tr>
<td>Pain score</td>
<td>3 (0-7)</td>
</tr>
<tr>
<td>CHAQ score</td>
<td>0.4 (0-1.8)</td>
</tr>
<tr>
<td>Physician global assessment</td>
<td>2 (1-5)</td>
</tr>
<tr>
<td>ESR (mm/hr)</td>
<td>12 (5-34)</td>
</tr>
<tr>
<td>CRP (mg/dL)</td>
<td>0.8 (0.8-3.3)</td>
</tr>
</tbody>
</table>

*NSAID: non-steroidal anti-inflammatory drug, CS: corticosteroid, MTX: methotrexate, PAM: pamidronate*
Disclosure: Y. Zhao, None; R. Iyer, None; L. Reichley, None; A. Oron, None; A. Kitsch, None; S. Friedman, None; S. Partridge, None; C. A. Wallace, None.


Abstract Number: 375

Controlled Discontinuation of Colchicine Therapy in Familial Mediterranean Fever Patients with Single MEFV Mutation

Yonatan Butbul Aviel1, Shahe Fahoum2 and Riva Brik3, 1Department of Pediatrics B Pediatric Rheumatology Service, Ruth Rappaport Children's Hospital, Rambam Medical Center, Haifa, Israel, Haifa, Israel, 2Department of Pediatrics B., , Ruth Children's Hospital, Rambam Medical Center, Haifa, Israel, Pediatric Rheumatology Service, Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel, 3Pediatrics, Rambam Medical Center, Haifa, Israel

First publication: September 18, 2017

SESSION INFORMATION
Background/Purpose:

Familial Mediterranean fever (FMF) traditionally has been considered an autosomal recessive disease; however, the diagnosis remains predominantly clinical, since mutations cannot always be identified on both alleles.

The aim of our study was to evaluate cessation of colchicine therapy in selected group of patients with FMF who possess only 1 or none demonstrable MEFV mutation.

Methods:

We performed a prospective controlled study evaluated cessation of colchicines therapy in patients that were previously diagnosed and treated for FMF based on clinical features and did not carry any common MEFV mutation or were heterozygote for one of the mutations .

Patients were included in the study if they were between the age of 2-18 years and were treated with colchicine, had a normal level of serum amyloid A (SAA ) and had at least 6 months free of FMF attacks.

SAA levels were evaluated before colchicine cessation and at 3 and 6 months following cessation. Colchicine therapy was resumed in case of FMF attacks reappeared during this period.

Results:

thirteen patients ages 10.6±4 years enrolled in the study. Prior to entering the study patients were treated with colchicine for an average of 36.3 month ( 7-141 months median 31 months ). The average time with no FMF attacks before enrolment into the study was 12.8±8.6 months and the average follow up after stopping colchicine therapy was 16.3±6 months . Five patients were heterozygote for the M694V mutation four patients were heterozygote for E148Q two patients had other mutations and two patients had no mutations .

Five patients (41.6%) had an FMF attack during follow up and needed to renew colchicine therapy, the average time to renew colchicine therapy was 5.3 months (range 1.5-11.4 months) 3 of them (60%) carried the M694V mutation.

There were no differences between the groups of patients that did not relapse and the groups that needed to renew therapy regarding age (10.7±1.6 vs 10.6±6.3 p- 0.97) or levels of SAA at time of enrolment (4±3.6 vs 3.3±2.4 p-0.7). Length of colchicine therapy prior to enrolment showed tendency that didn't reach significance towards longer time in the patients needed to resume therapy (22.3±12.6 vs 53±51 months p-0.18).

Conclusion:

Cessation of colchicine therapy in selected group of patients who are not homozygous for the common MEFV mutation should be considered. Monitoring SAA levels every 3 months could not predict FMF attacks following cessation of colchicine therapy.

Disclosure: Y. Butbul Aviel, None; S. Fahoum, None; R. Brik, None.


Abstract Number: 376

Improvement of Disease Activity in Patients with Colchicine-Resistant FMF, Hids/Mkd and TRAPS Assessed By Autoinflammatory Disease Activity Index (AIDAI): Results from a Randomized Phase III Trial

Isabelle Koné-Paut1, Michaël Hofer2, Susanne Benseler3, Jasmin B. Kuemmerle-Deschner4, Annette Jansson5, Itzhak Rosner6, Raffaele Manna7, Sara Murias8, Omer Karadag9, Lori Tucker10, Ilonka Orban11, Vincent Tormey12, Maria Alessio13, Huri Ozdogan14, and Fabrizio De Benedetti15, 1Bicêtre Hospital, APHP, Univeristy Paris Sud, Paris, France, 2Unité romande d’immuno-rhumatologie pédiatrique, CHUV, University of Lausanne, Genova, Italy, 3Alberta Children's Hospital, Calgary, AB, Canada, 4University Hospital
SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster I: Autoinflammatory Disorders and Miscellaneous
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: AIDAI is a novel, validated tool for the assessment of disease activity across a wide spectrum of autoinflammatory diseases including recurrent fever syndromes such as familial Mediterranean fever (FMF), hyper-IgD syndrome/mevalonate kinase deficiency (HIDS/MKD) and TNF receptor-associated periodic syndrome (TRAPS). Canakinumab (CAN), a fully human anti-interleukin-1β monoclonal antibody, has demonstrated efficacy in resolving flares and preventing new flares in RFS patients (pts) through CLUSTER study (NCT02059291). Here we evaluate AIDAI scores over 16 weeks (wks) of CAN treatment in pts from CLUSTER study and assess correlation between AIDAI and disease/response characteristics.

Methods: CLUSTER study consisted of 3 cohorts (crFMF, HIDS/MKD and TRAPS). AIDAI was calculated as the sum of 12 items (Yes=1 or No=0) for 30 consecutive days. AIDAI score was calculated if the first score was recorded before ≥29 days. Missing AIDAI scores between first and last assessments were imputed with ‘No’. Missing items beyond last evaluable measurement were imputed by last observation carried forward (LOCF). Proportion of pts with inactive disease (ID; AIDAI score <9) was calculated at Wk 16. Correlation analysis of AIDAI with C-reactive protein (CRP), serum amyloid A (SAA), physician global assessment (PGA), Sheehan disability score (SDS), child health questionnaire–psychological/physical (CHQ–PsCS/PCS) and short form 12–physical/mental component summaries (SF12–PCS/MCS) were performed at baseline and Wk 16, with significance set at p<0.05.

Results: Overall, 181 (crFMF, N=63; HIDS/MKD, N=72; TRAPS, N=46) pts were randomized to CAN 150 mg or placebo every 4 wks. Median AIDAI scores in all 3 cohorts decreased from baseline to Wk 16 (Figure 1). The proportion of pts with ID at Wk 16 was 52% in crFMF, 40% in HIDS/MKD and 46% in TRAPS cohort. AIDAI at Wk 16 correlated significantly with: SDS in all 3 cohorts; PGA in HIDS/MKD and TRAPS; SF12–MCS in crFMF and HIDS/MKD (Table 1). CRP and SAA did not correlate with AIDAI.

Conclusion: Decrease in AIDAI scores over 16 weeks in crFMF, HIDS/MKD and TRAPS patients treated with canakinumab corroborates rapid and sustained disease control with canakinumab in CLUSTER study. At Week 16, approximately half of the crFMF and TRAPS patients, and 40% of the HIDS/MKD patients had inactive disease. AIDAI improvements at Week 16 correlated with patient and physician driven evaluations (PGA, SF12–MCS and SDS). CRP and SAA are indicators of response to treatment rather than a disease activity parameter.

Table 1. Correlation between AIDAI and disease activity/response variables at Week 16

<table>
<thead>
<tr>
<th></th>
<th>Correlation coefficient (95% CI)</th>
<th>crFMF N=63</th>
<th>HIDS/MKD N=72</th>
<th>TRAPS N=46</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CRP</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-0.12 (-0.36; 0.14)</td>
<td></td>
<td>0.23 (-0.01; 0.45)</td>
<td>0.12 (-0.19; 0.42)</td>
</tr>
<tr>
<td><strong>SAA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-0.01 (-0.27; 0.25)</td>
<td></td>
<td>-0.05 (-0.30; 0.21)</td>
<td>0.06 (-0.26; 0.37)</td>
</tr>
<tr>
<td><strong>PGA</strong></td>
<td></td>
<td>0.23 (-0.02; 0.46)</td>
<td>0.35§ (0.12; 0.55)</td>
<td>0.73* (-0.54; 0.85)</td>
</tr>
<tr>
<td><strong>CHQ–PsCS</strong></td>
<td></td>
<td>-0.18 (-0.56; 0.26)</td>
<td>-0.25 (-0.55; 0.11)</td>
<td>-0.33 (-0.72; 0.22)</td>
</tr>
<tr>
<td><strong>CHQ–PCS</strong></td>
<td></td>
<td>-0.33 (-0.66; 0.11)</td>
<td><strong>-0.46§ (-0.70; -0.14)</strong></td>
<td>-0.48 (-0.80; 0.04)</td>
</tr>
<tr>
<td><strong>SF12–PCS</strong></td>
<td></td>
<td>-0.26 (-0.57; 0.11)</td>
<td>-0.23 (-0.68; 0.35)</td>
<td><strong>-0.52† (-0.81; -0.03)</strong></td>
</tr>
<tr>
<td><strong>SF12–MCS</strong></td>
<td></td>
<td><strong>-0.45† (-0.70; -0.10)</strong></td>
<td><strong>-0.55† (-0.84; -0.03)</strong></td>
<td>0.09 (-0.43; 0.56)</td>
</tr>
<tr>
<td><strong>SDS</strong></td>
<td></td>
<td>0.47† (0.22; 0.67)</td>
<td>0.37§ (0.10; 0.59)</td>
<td>0.41‡ (0.06; 0.67)</td>
</tr>
</tbody>
</table>

* p<0.0001; † p<0.001; § p<0.01; ‡ p<0.05

Disclosure: I. Koné-Paut, Novartis, SOBI and Roche, 2; Novartis, SOBI, Pfizer, AbbVie and Roche, 5; M. Hofer, Novartis and AbbVie, 5; S. Benseler, Novartis, SOBI and AbbVie, 5; J. B. Kuenemmer-Deschner, Novartis, 2; Novartis, SOBI and Baxalta, 5; A. Jansson, Novartis, 2; I. Rosner, None; R. Manna, Novartis, 2; S. Murias, None; O. Karadag, None; L. Tucker, Novartis, 2; I. Orban, None; V. Tormey, None; M. Alessio, None; H. Ozdogan, Novartis, 5; F. De Benedetti, Novartis, Roche, Pfizer, SOBI, AbbVie, Novimmune, BMS, Sanofi, 2.


Abstract Number: 377

Novel Insights into Periodic Fever Syndromes

Tiffany Hoang1, Shreya Shrestha1 and Daniel Albert2, 1Dartmouth Medical School, Lebanon, NH, 2Medicine/Rheumatology, Dartmouth-Hitchcock Med Ctr, Lebanon, NH

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017

Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster I: Autoinflammatory Disorders and Miscellaneous

Session Type: ACR Poster Session A

Session Time: 9:00AM-11:00AM
The Periodic Fever Syndromes (PFS) are a rapidly expanding group of disorders primarily of the innate immune system that often affect the inflammasome. In our previous report (ACR 2014 Annual Meeting), we detailed 30 patients with about 1/3 with Periodic Fever, Aphthous Stomatitis, Pharyngitis and Adenopathy (PFAPA), 1/3 with a genetically defined PFS, and 1/3 unclassifiable. We now report with improved genetic testing (Medical Neurogenetics NextGen PFS Panel – 37 genes) novel phenotypic expressions of genetically determined PFS in 15 patients.

Methods: Case acquisition was performed by three methods: 1) review of ICD 9/10 coded records for Familial Mediterranean Fever (ICD 9 277.31); 2) laboratory test records for PFS genetic screening; and 3) clinic records between 1/1/2011 and 12/31/2017 after receiving approval from the Institutional Review Board for a de-identified retrospective case analysis.

Results: Twenty seven cases (12 female and 15 male) were obtained that underwent extensive clinical evaluation including PFS genetic screening. Clinical diagnoses included FMF (10), Muckle Wells (2), TRAPS (4), and HIDS (1). Other diagnoses included Crohn’s (1), SoJIA (1), FUO (1), PFAPA (6), and cold induced urticaria (1). Of these 27 cases, 15 were subsequently associated with a genetic cause. Seven of the 10 FMF cases were confirmed genetically, all of whom were either heterozygous or compound heterozygotes. Both cases of Muckle Wells had non classical genetics – one was a compound heterozygote for CIAS 1, and the other had a mutation in the NOD gene. Both TRAPS cases were atypical – one was asymptomatic, and the other developed SLE. Two patients had novel syndromes. One TRAPS patient had a mutation in the TNFRSF-1A gene who eventually remitted with IVIG after failing multiple drugs. The other had SoJIA with a mutation in the LPIN 2 gene but responded to colchicine. Only 1 of the 15 genetically proven cases had a classical presentation and classical genetics (HIDS secondary to a mutation in the MVK gene).

Conclusion: Most patients presented atypically both from a clinical and genetic standpoint, making treatment challenging and difficult. Genetic testing with PFS screen was helpful in over ½ of the cases to develop therapeutic treatment plans. Given the atypical clinical presentations seen with genetically determined PFS, extensive genetic testing is indicated for all patients presenting with a PFS except those with a classical PFAPA syndrome.

Disclosure: T. Hoang, None; S. Shrestha, None; D. Albert, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/novel-insights-into-periodic-fever-syndromes

Abstract Number: 378

Musculoskeletal Features in Copa Syndrome

William B. Lapin1, Monica Marcus2, Andrea A. Ramirez3, Marietta M. de Guzman3 and Levi B. Watkin4,5, 1Department of Pediatrics, Division of Immunology, Allergy and Rheumatology, Baylor College of Medicine, Texas Children's Hospital, Houston, TX, 2Pediatric Immunology, Allergy and Rheumatology, Texas Children's Hospital, Houston, TX, 3Immunology, Allergy and Rheumatology, Baylor College of Medicine, Texas Children's Hospital, Houston, TX, 4Department of Pediatrics, Division of Immunology, Allergy and Rheumatology, Baylor College of Medicine, Houston, TX, 5Texas Children's Hospital, Center for Human Immunobiology, Houston, TX

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster I: Autoinflammatory Disorders and Miscellaneous
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: COPA syndrome is a newly discovered primary immunodeficiency resulting in immune dysregulation showing autosomal dominant inheritance with incomplete penetrance. Its name is derived from the mutation of the gene encoding for the alpha subunit of the coatomer complex-I that is responsible for transportation of molecular cargo from the Golgi to the Endoplasmic Reticulum. Previously, studies have elucidated the molecular mechanisms responsible for the disease phenotype. Clinical features of COPA syndrome primarily included pulmonary disease (interstitial lung disease, pulmonary hemorrhage), musculoskeletal (MSK) manifestations, autoantibody formation and renal disease. Here we aim to review and describe the MSK features of this newly defined disorder.

Methods:

After IRB approval, we reviewed the MSK manifestations of patients with COPA mutation, as to characteristic nature, physical findings and diagnostic features. The clinical course of a family from this cohort, that was followed at our institution, was described.
Results:

The previously reported cohort included 21 patients with 62% female. The mean age at presentation was 3.5 years with a range of 6 months to 22 years. Joint pain was present in 24% of patients at initial presentation and joint complaints were mostly intermittent in nature. Findings of arthritis were described in 95% of patients involving both small and large joints along the clinical course, often with polyarticular disease. Most commonly affected joints included the knees, and the interphalangeal joints of the hands. Two patients had osteonecrosis along the femur, patella and tibiofibula. Fatty necrosis was noted in one patient. Notably, presence of autoantibodies was a prominent feature of this disorder: rheumatoid factor (43%), ANA (67%), and ANCA/MPO/PR-3 (71%).

The most common diagnosis included Rheumatoid Arthritis, Juvenile Idiopathic Arthritis and undifferentiated arthritis. Arthralgia exacerbation was found to mirror pulmonary disease flare. Joint manifestation had varying response to NSAID, steroids, methotrexate and anti-TNF therapy. Multimodal anti-inflammatory, immunolytic and immunomodulatory therapy indicated for the severe pulmonary and renal features did not provide prolonged remission of arthritis.

Table 1: COPA patients from single family carrying the R235H mutation

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age at disease onset (y)</th>
<th>Age at arthritis onset (y)</th>
<th>Ethnicity</th>
<th>MSK features at presentation</th>
<th>Type of arthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>2</td>
<td>4</td>
<td>Caucasian</td>
<td>Knee arthritis</td>
<td>Polyarticular</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>1.25</td>
<td>Unknown</td>
<td>Caucasian</td>
<td>Ankle, wrist arthritis</td>
<td>Polyarticular</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>12</td>
<td>12</td>
<td>Caucasian</td>
<td>Shoulder arthritis</td>
<td>Polyarticular</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>4</td>
<td>9</td>
<td>Caucasian</td>
<td>Wrist, ankle arthritis</td>
<td>Polyarticular</td>
</tr>
</tbody>
</table>

Conclusion:

Musculoskeletal manifestations are a prominent and important feature of COPA syndrome. Due to similarities in clinical features it is difficult to differentiate COPA arthritis from other inflammatory arthropathies of systemic immune mediated disorders.

Disclosure: W. B. Lapin, None; M. Marcus, None; A. A. Ramirez, None; M. M. de Guzman, None; L. B. Watkin, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/musculoskeletal-features-in-copa-syndrome](http://acrabstracts.org/abstract/musculoskeletal-features-in-copa-syndrome)

Abstract Number: 379

**H Syndrome: Five New Cases from the United States with Novel Features and Responses to Therapy**

Jessica Bloom¹, Clara Lin², Lisa F. Imundo³, Stephen Guthery⁴, Shelly Stepenskie⁵, Csaba Galambos⁶, Amy Lowichik⁷ and John F. Bohnsack⁸, ¹Pediatrics, Children's Hospital Colorado, Aurora, CO, ²Pediatric Rheumatology, Children's Hospital Colorado, Aurora, CO, ³Pediatrics, Columbia University Medical Center, New York, NY, ⁴Department of Pediatrics,, University of Utah, Salt Lake City, UT, ⁵Pathology and Dermatology, University of New Mexico, Albuquerque, NM, ⁶Pathology, Children's Hospital Colorado, Aurora, CO, ⁷Pathology, University of Utah, Salt Lake City, UT, ⁸Division of Allergy, Immunology and Pediatric Rheumatology, University of Utah, Salt Lake City, UT

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster I: Autoinflammatory Disorders and Miscellaneous
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM
**Background/Purpose:** H Syndrome is an autosomal recessive disorder characterized by cutaneous hyperpigmentation, hypertrichosis, and induration with numerous systemic manifestations. The syndrome is caused by mutations in *SLC29A3*, a gene located on chromosome 10q23, which encodes the human equilibrative transporter 3 (hENT3). Less than 100 patients with H syndrome have been described in the literature, with the majority being of Arab descent, and only a few from North America. Here we report five pediatric patients from three medical centers in the United States who were identified to have H syndrome by whole exome sequencing as well as their response to treatment.

**Methods:** All five patients presented to pediatric rheumatologists prior to diagnosis and include two of Northern European descent, bringing the total number of Caucasian patients described to three. Cases were discussed and compared in order to gather more data on H Syndrome and optimize treatment regimens.

**Results:** The patients were found to share many of the characteristics previously reported with H syndrome, including hyperpigmentation, hypertrichosis, short stature, insulin-dependent diabetes mellitus, arthritis and systemic inflammation, as well as some novel features, including selective IgG subclass deficiency and autoimmune hepatitis. They share genetic mutations previously described in patients of the same ethnic background, as well as a novel mutation. In two patients, treatment with prednisone improved inflammation, however both patients flared once prednisone was tapered. In one of these patients, treatment with tocilizumab alone resulted in marked improvement in systemic inflammation and growth. The other had partial response to prednisone, azathioprine, and TNF inhibition; thus, his anti-TNF biologic was recently switched to tocilizumab due to persistent polyarthritis. Another patient improved on Methotrexate, with further improvement after the addition of tocilizumab.

**Conclusion:** H syndrome is a rare autoinflammatory syndrome with pleiotropic manifestations that affect multiple organ systems and is often mistaken for other conditions. Rheumatologists should be aware of this syndrome and its association with arthritis. Some patients respond to treatment with biologics alone or in combination with other immune suppressants; in particular, treatment of systemic inflammation with IL-6 blockade appears to be promising. Overall, better identification and understanding of the pathophysiology may help devise earlier diagnosis and better treatment strategies.
Disclosure: J. Bloom, None; C. Lin, None; L. F. Imundo, None; S. Guthery, None; S. Stepenskia, None; C. Galambos, None; A. Lowichik, None; J. F. Bohnsack, Various, 2.


Abstract Number: 380

Treatment Outcomes of Down Syndrome Arthropathy

Jordan T. Jones¹, Leena Danawala², Nasreen Talib³ and Mara L Becker⁴, ¹Rheumatology Division, Children's Mercy Kansas City, Kansas City, MO, ²University of Missouri-Kansas City School of Medicine, Kansas City, MO, ³General Pediatrics, Children's Mercy Kansas City, Kansas City, MO, ⁴Rheumatology, Children's Mercy Kansas City, Kansas City, MO

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster I: Autoinflammatory Disorders and Miscellaneous

Table 1: Clinical Features

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Family 1</th>
<th>Family 2</th>
<th>Family 3</th>
<th>Family 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birthweight</td>
<td>5.2 lbs</td>
<td>6.2 lbs</td>
<td>4.5 lbs</td>
<td>5.5 lbs</td>
</tr>
<tr>
<td>Age at diagnosis</td>
<td>6 months</td>
<td>4 months</td>
<td>2 years</td>
<td>3 years</td>
</tr>
<tr>
<td>Current Age</td>
<td>18 months</td>
<td>18 months</td>
<td>2 years</td>
<td>2 years</td>
</tr>
</tbody>
</table>

Table 2: Laboratory Findings

<table>
<thead>
<tr>
<th>Laboratory Test</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid factor</td>
<td>Negative</td>
<td>Positive</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>ANA (1:100)</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>RF (1:100)</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Anti-Citrullinated Peptide Antibodies</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Anti-CCP</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Anti-PR3</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Anti-MPO</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Anti-Zymosan</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Anti-actin</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Anti-Collagen</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Anti-Collagen</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Anti-Collagen</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Anti-Collagen</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
</tbody>
</table>

Note: All values are normal unless otherwise specified.

Abstract: H. Syndrome: Five new cases from the United States with novel features and responses to therapy.
Background/Purpose: Crude prevalence estimates indicate Down syndrome arthropathy (DA) is 3-8 times more common than juvenile idiopathic arthritis (JIA), however, DA is still largely under recognized, and has a 2 year average delay from onset of symptoms to diagnosis. The majority of patients with DA present with greater than 5 affected joints, with small joints affected more predominantly. Additionally, treatment can be challenged by lack of efficacy and intolerance. Further, gaps in literature exist around optimal treatment approach and outcomes. The objective of this study was to investigate treatment approach and outcomes of DA at our institution.

Methods: In a retrospective chart review, potential DA patients were identified through electronic medical record system (EMR) from January 1, 1995 to December 31, 2015. ICD-9-CM codes were used to identify patients (less than 18 years of age) with both Down Syndrome (DS; 758.0) and JIA (714.3, 714.31, 714.32, 714.33). Individual charts were then manually reviewed to confirm diagnosis of DS and JIA. Chart review included analysis of all documents found in the EMR, including clinical visits and treatment data.

Results: Of 26 identified patients, (3 did not have DS and 2 had incomplete records) 21 met inclusion criteria and were analyzed. Patients were 62% female with polyarticular, RF negative presentation at diagnosis and had a mean (SD) follow-up of 4 (±4) years. There was a 19 month (±16) mean delay in diagnosis of arthritis from symptom onset, and at diagnosis of arthritis, 71% had morning stiffness with an average of 14 (±10) active joints, 12 (±10) limited joints, and mean physician global of disease activity (MD PGA) of 4.9 (±2). All patients were started on nonsteroidal anti-inflammatory drugs (NSAIDs) at diagnosis with 33% simultaneously starting a disease modifying antirheumatic drug (DMARD), and 5% a Biologic. Over the course of disease, 62% used a DMARD (57% MTX) and 48% used a biologic (90% etanercept). Six patients (29%) had at least one change in DMARD and another six patients had at least one change in biologic therapy (Table 1). Compared to diagnosis, at the last recorded visit there was a significant decrease in mean (SD) active joints: 3 (± 4), limited joints: 5 (± 6) and MD PGA: 1.7 (± 1.6) (p<0.01 respectively). Of those on DMARD therapy 54% had drug discontinuation due to side effects and 56% had an inadequate response to first-line biologic therapy.

Conclusion: Down syndrome arthropathy remains under recognized despite reports of higher prevalence compared with JIA. Although treatment approach is unclear, DA patients have significant improvement in the number of active and limited joints with NSAID, DMARD, and biologic therapies. Other barriers that inhibit optimal treatment and outcomes are DMARD toxicity and lack of anti-TNF effectiveness. More research is needed to determine the timing and choice of optimal therapy in patients with Down syndrome.

Disclosure: J. T. Jones, None; L. Danawala, None; N. Talib, None; M. L. Becker, Bristol Myers Squibb, 2,Sobi, 5.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/treatment-outcomes-of-down-syndrome-arthropathy

Abstract Number: 381

Down’s Arthritis (DA) – Clinical and Radiological Features of Arthritis in Children with Trisomy 21

Charlene Foley, Emma Jane Mac Dermott and Orla Killeen, National Centre for Paediatric Rheumatology, Our Lady's Children's Hospital Crumlin, Dublin, Ireland
**Down's Arthritis (DA) was first reported in the literature in 1984. Crude estimates suggest higher incidence and prevalence rates of DA compared with Juvenile Idiopathic Arthritis (JIA), (JIA prevalence 1/1000, estimated DA prevalence 8.7/1000). Despite this fact, there remains a paucity of data on this condition. DA is rarely recognised at onset, & remains under-diagnosed. As a direct consequence children with DA are presenting with significant joint damage and disability at diagnosis. Our aim was to perform a musculoskeletal examination on children with Trisomy 21 (T21) aged 0-20 years, looking specifically for features of undiagnosed arthritis. We also wanted to better define the disease in terms of it's clinical and radiological features.**

**Methods:** Children with T21 were invited to attend a screening clinic. Screening involved completion of a health questionnaire and a comprehensive musculoskeletal examination. DA cases detected were investigated & managed as per normal clinical practice. Data on a convenience sample of 33 newly diagnosed children with JIA was collected to create a comparison group.

**Results:** 503 children with T21 were screened for DA and 22 new cases identified. All of these children had poor language skills or were non-verbal. Only 11% of the parents suspected that their child may have arthritis prior to attending our screening clinics, and this was only after reading our recruitment literature. In total, we now have 33 children attending our centre with DA (combining cases attending pre-dating the start date of the study). This suggests the prevalence of DA in Ireland is 18-21/1000.

The majority of children presented with a polyarticular RF negative pattern of disease. No cases of uveitis have been observed to date. Small joint involvement of the hands was observed in 88% of the DA cohort, significantly higher than in the JIA comparison group (43%, p<0.01). Erosive changes were reported on X-ray in 29.2% of the DA cohort (9.5% in the JIA Cohort). Methotrexate-associated nausea was a significant barrier to treatment with this DMARD in DA. There was a significant delay in diagnosis of DA, 1.7 years (0.2-4.9yrs) versus 0.7 years (0.2-2.4yrs) in the JIA cohort.

**Conclusion:** Children with T21 are at increased risk of developing arthritis. There is a lack of awareness of this risk among health care professionals & the general public at large. This almost certainly contributes to poor recognition of the disease and a delay in diagnosis. The predominant pattern of disease is polyarticular small joint arthritis. Treatment with standard protocols used in JIA is complicated by drug-associated side effects in children with T21. However, a good response to treatment with steroid intra-articular joint injections and anti-TNF therapy has been observed. Our study has raised a number of questions. Our on-going research aims to accurately define this disease in terms of its immunological, histopathological and genetic basis, & identify best practice with regards to treatment. We advocate that all children with T21 should have an annual musculoskeletal examination as part of their health surveillance programme.

**Disclosure:** C. Foley, None; E. J. Mac Dermott, None; O. Killeen, None.

**Radiological Features Identified in the Hands of Children with Down Syndrome and Inflammatory Arthritis**

**Charlene Foley¹, Emma Jane Mac Dermott¹, Aisling Snow² and Orla G Killeen¹, ¹National Centre for Paediatric Rheumatology, Our Lady's Children's Hospital Crumlin, Dublin, Ireland, ²Radiology, Our Lady's Children's Hospital Crumlin, Dublin, Ireland**

**First publication:** September 18, 2017
Background/Purpose: Down’s Arthritis (DA) is an inflammatory joint condition affecting children with Down syndrome (DS). It is 18-21 times more common than JIA in the general paediatric population (JIA prevalence 1/1000). Children with DA usually present with a poly-articular, RF negative pattern of disease, with predominance in the small joints of the hands & wrists. Despite it’s higher prevalence, a significant delay in diagnosis is frequently observed. Joint laxity & hypotonia are almost universal in children with DS, contributing to an increased risk of a number of musculoskeletal disorders & degenerative joint disease. Clinical signs & symptoms may not always help differentiate between inflammatory joint disease & joint hypermobility. We aim to report the radiological features described by a Paediatric Musculoskeletal Radiologist (PMR) when reviewing hand & wrist radiographs in a cohort of children with DA.

Methods: A retrospective review of all hand & wrist radiographs in a convenience sample of 19 children with DA was undertaken by a PMR. Bone age, carpal & metacarpal bone abnormalities were documented, as were corresponding clinical findings following musculoskeletal examination by a Paediatric Rheumatologist. Wrist MRIs were performed on 4 of the 19 children. The results of these studies were also included in our report.

Results: 18/19 children (10/19 (53%) Female; Average Age 13yrs (0.8-19yrs); 100% Full Trisomy 21 genetics) had radiographs of their hands & wrists. Bone age was below chronological age in 5 (28%) of the cohort imaged. Time to DA diagnosis from symptom onset was known in 8/19 children & on average was 1.8 years (0.14-4.9 years). Over half (63%) of the cohort were detected through a musculoskeletal screening programme offered to children with DS & not from direct referral to the Tertiary Rheumatology Centre. On musculoskeletal examination the most commonly affected joints, 95% of cases, were the PIP joints, followed by the wrists (68%), knees (58%), toes (37%) & MCP joints (32%). The average joint hypermobility score using the Beighton system was 2 (0-6).

Radiograph & MRI review highlighted a range of carpal & metacarpal bone abnormalities. The most common abnormality was crowding of the carpal bones with associated degenerative disease (63%). The earliest sign of degenerative disease was observed in a child aged 10 months whose MRI with gadolinium contrast demonstrated synovial enhancement of the proximal carpal row. The second most common finding (42%) was scalloping of the base of the first metacarpal. Other less frequent features identified (5% of cohort) included carpal pits, tuft irregularity & dactylitis. Bone erosions were evident on plain film in 50% of the cohort.

Conclusion: Radiographic carpal & metacarpal bone changes appear to be prevalent in DA & do not always correspond to clinical signs & symptoms. Undetected, these features can have a significant functional impact. If detected & managed in a timely & appropriate manner, irreversible joint damage & long-term sequelae could be avoided. These results support the importance of access to a specialist PMR & MRI. Our plan now is to compare these results with two separate cohorts; children with JIA & children with DS with no evidence of inflammatory arthritis.

Disclosure: C. Foley, None; E. J. Mac Dermott, None; A. Snow, None; O. G. Killeen, None.

Immunogenicity of 13 Valent Pneumococcal Vaccine in Children with Lupus: Single Center Experience in South Texas

Elissa Gonzalez, Joe Cole and Mark Gorelik, Pediatrics, Baylor College of Medicine/Children's Hospital of San Antonio, San Antonio, TX

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster I: Autoinflammatory Disorders and Miscellaneous
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Pneumococcal vaccination is an important part of the care of pediatric and adult patients with systemic lupus erythematosus, and is recommended as a quality indicator for management of children with SLE. Literature on the immunogenicity of pneumococcal vaccines in children is scant. As part of a quality improvement project to increase the rates of pneumococcal vaccination in our center, we sought to evaluate immunogenicity to the 13-valent pneumococcal vaccine in our patients with lupus, and also to identify patients that may be at higher risk of infection due to non response.
**Methods:** Patients undergoing vaccination with 13-valent pneumococcal vaccine had pre-vaccination antibody levels to serotypes obtained when possible, and then post-vaccination antibody levels were obtained 4 weeks after vaccination. The percentage and number of patients with pre and post vaccination protective levels (defined as >70% serotypes >/= 1.3 mcg/dl) were evaluated. Medication status, disease activity and demographic information was obtained from these patients as well.

**Results:** 15 patients had pre and post pneumococcal antibody levels available for evaluation, and a further 5 had post pneumococcal antibody levels only. 5 of 15 patients had pre-vaccination protective levels of pneumococcal antibody despite no known previous vaccination. 8 of 10 patients with both pre and post pneumococcal antibody levels available demonstrated conversion to protective status, while 2 did not; a further 3 of the 5 patients who had post pneumococcal levels only available did not demonstrate achievement of protective levels. Thus in total, 15 of 20 patients achieved protected status. Patients not achieving protected status had a higher rate of recent rituximab or higher dose mycophenolate treatment, while patients with previous cytoxan exposure generally achieved protected status.

**Conclusion:** While the 13-valent pneumococcal vaccine achieves protective status for a majority of pediatric lupus patients, a significant number of these patients do not achieve this status after this vaccine. Further evaluation for responses after 23-valent vaccination is ongoing, but these results suggest that patient responses to vaccination may be important to evaluate in order to identify patients that are at higher risk of future infection.

**Disclosure:** E. Gonzalez, None; J. Cole, None; M. Gorelik, None.

**Abstract Number:** 384

**Protection Against Hepatitis B in Immunocompromised Pediatric Rheumatology and Gastroenterology Patients**

Najla Aljaberi¹, Emily A. Smitherman², Enas Ghulam³, Allen Watts², Dana MH Dykes⁴ and Jennifer L. Huggins⁵, ¹Pediatric Rheumatology, Pediatric Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, ²Pediatric Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, ³Environmental health and biostatistics, Department of Environmental Health, University of Cincinnati, Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, ⁴Gastroenterology, Hepatology, and Nutrition, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, ⁵Pediatrics, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster I: Autoinflammatory Disorders and Miscellaneous

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Hepatitis B infection remains a significant public health challenge, particularly for patients on chronic immunosuppressive therapy, due to a considerable mortality risk associated with hepatitis B reactivation. Serologic screening for immunocompromised patients should include hepatitis B surface antibodies (anti-HBsAb) to assess for immunity, hepatitis B core antibodies (anti-HBcAb) and hepatitis B surface antigen (HBsAg) to evaluate for acute or chronic infection. Our primary aim was to determine the burden of non-immunity against hepatitis B, provide insight into factors leading to lack of immunity against hepatitis B and establish the basis for the need for universal screening of these patients. Secondarily, we determined serologic response to a single hepatitis B vaccination booster.

**Methods:**

Subjects are patients seen at the rheumatology and inflammatory bowel disease (IBD) clinics who are immunocompromised. We use a clinical algorithm as part of standard practice to check hepatitis B serology in immunocompromised patients, offer a booster vaccination if needed, and then repeat serology to determine the response. The results of anti-HBsAb are reported as positive, negative or indeterminat. Immunity is defined as a positive result for anti-HBsAb. An indeterminate or negative result for anti-HBsAb is non-immune. A retrospective chart review was performed to collect demographic and clinical factors as well as serology results. Descriptive statistics were calculated for all variables. R software was used to perform all analyses. For continuous variables, mean and standard
deviation are reported, and comparisons were calculated using two-sample t-tests. For categorical variables, frequency and percentage are reported, and comparisons were calculated using chi-square tests.

Results:

A total of 502 patient charts of immunocompromised patients were reviewed, 280 rheumatology and 222 IBD. Out of the 502 patients, 70% were non-immune (anti-HBsAb negative/indeterminate) (see Table). The highest portion of non-immune patients were those between the ages of 16-20 years (p=0.005) There was no clinically significant difference between immune and non-immune patients with regards to diagnosis (p=0.69), age at the start of treatment (p=0.72) or type of medications. A total of 196 non-immune patients received a booster dose of hepatitis B vaccine and 61 (72%) of those re-screened developed a positive anti-HBsAb. Of note, one patient was identified with a previously unknown chronic hepatitis B infection (anti-HBcAb positive).

Conclusion:

A majority of patients had non-immune hepatitis B serology. Lack of serologic immunity is highest at 16-20 years. A majority of patients developed positive anti-HBsAb following booster vaccination. Results support serologic screening for hepatitis B in immunocompromised patients.

Table. Clinical characteristics by immune status

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Non-immune (anti-HBsAb -) (n=349)</th>
<th>Immune (anti-HBsAb +) (n=153)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>7-10 years</td>
<td>16.2 (3.9)</td>
<td>16.6 (4.5)</td>
<td>0.33</td>
</tr>
<tr>
<td>11-16 years</td>
<td>27 (8%)</td>
<td>21 (14%)</td>
<td>0.00</td>
</tr>
<tr>
<td>16-20 years</td>
<td>118 (34%)</td>
<td>39 (25%)</td>
<td></td>
</tr>
<tr>
<td>&gt; 20 years</td>
<td>158 (45%)</td>
<td>59 (30%)</td>
<td></td>
</tr>
<tr>
<td>Male (%)</td>
<td>151 (43%)</td>
<td>02 (41%)</td>
<td>0.64</td>
</tr>
<tr>
<td>Age at diagnosis (years)</td>
<td>11.4 (4.6)</td>
<td>10.6 (4.7)</td>
<td>0.36</td>
</tr>
<tr>
<td>Age at the start of treatment (years)</td>
<td>12.2 (4.1)</td>
<td>12.1 (4.6)</td>
<td>0.72</td>
</tr>
<tr>
<td>Age at screening (years)</td>
<td>15.4 (3.9)</td>
<td>15.8 (4.8)</td>
<td>0.37</td>
</tr>
<tr>
<td>Clinic Rheumatology</td>
<td>200 (57%)</td>
<td>80 (52%)</td>
<td>0.34</td>
</tr>
<tr>
<td>GI</td>
<td>140 (43%)</td>
<td>73 (48%)</td>
<td></td>
</tr>
<tr>
<td>Diagnosis Auto-immune arthritis</td>
<td>122 (35%)</td>
<td>46 (30%)</td>
<td>0.69</td>
</tr>
<tr>
<td>Connective tissue diseases</td>
<td>41 (12%)</td>
<td>20 (13%)</td>
<td></td>
</tr>
<tr>
<td>Other rheumatic diseases</td>
<td>37 (10%)</td>
<td>15 (10%)</td>
<td></td>
</tr>
<tr>
<td>IBD</td>
<td>140 (43%)</td>
<td>72 (47%)</td>
<td></td>
</tr>
<tr>
<td>Biologic* Anti TNF</td>
<td>278 (80%)</td>
<td>123 (80%)</td>
<td>0.94</td>
</tr>
<tr>
<td>Anti IL-1</td>
<td>39 (11%)</td>
<td>11 (7%)</td>
<td>0.94</td>
</tr>
<tr>
<td>Anti IL-6</td>
<td>10 (3%)</td>
<td>2 (1%)</td>
<td>0.26</td>
</tr>
<tr>
<td>Anti T-cell</td>
<td>28 (8%)</td>
<td>8 (5%)</td>
<td>0.36</td>
</tr>
<tr>
<td>Anti B-cell</td>
<td>11 (3%)</td>
<td>10 (7%)</td>
<td>0.13</td>
</tr>
<tr>
<td>History of non-biologic DMARDs use</td>
<td>247 (71%)</td>
<td>117 (76%)</td>
<td>0.22</td>
</tr>
</tbody>
</table>

Continuous variables reported as mean (standard deviation). Categorical variables reported as frequency (percentage). P-values in bold are statistically significant.

* This reflects the number of patients with history of medication use (% is reported out of total patients).

Disclosure: N. Aljaberi, None; E. A. Smitherman, None; E. Ghulam, None; A. Watts, None; D. M. Dykes, None; J. L. Huggins, None.


Abstract Number: 385

Reliable Implementation of a Hepatitis B Serology Screening and Vaccination Process for Immunocompromised Pediatric Rheumatology Patients

Emily A. Smitherman1, Adam Furnier2, Allen Watts1, Sandra Kramer1, Elizabeth Joy Baker1, Dana MH Dykes3, Rebecca Brady4 and Jennifer L. Huggins5, 1Pediatric Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 2James M. Anderson Center for Health Systems Excellence, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 3Gastroenterology, Hepatology,
SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster I: Autoinflammatory Disorders and Miscellaneous
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Vaccine-preventable infections, including reactivation of hepatitis B virus, are a leading cause of morbidity and mortality in immunocompromised patients. Guidelines recommend that all immunosuppressed patients should be screened with hepatitis B serologies for active or chronic infection as well as need for repeat vaccination. Previously at our center, we have implemented hepatitis B serology screenings for patients on intravenous biologics and pneumococcal vaccines for all immunocompromised patients. The aim of this intervention was to adapt these processes to hepatitis B serology screenings and vaccinations for all immunocompromised pediatric rheumatology patients.

Methods: The Model for Improvement was used to form a team, map the process, construct a key driver diagram, and develop an algorithm (Figure 1). Eligible patients included those over 7 years identified as immunocompromised using a validated algorithm in the electronic health record (EHR). A series of Plan-Do-Study-Act (PDSA) cycles were performed to test and implement the multi-step process. After building an electronic order-set in the EHR, we adopted the process of clinic staff pending needed orders during pre-visit planning. We also provided education and developed “talking points” for clinic staff and providers. Results were tracked on a statistical process control chart weekly, and failures were identified through Pareto analysis.

Results: The intervention began in December 2016 at a tertiary care pediatric rheumatology clinic. Prior to start, a subset of patients had previously received screenings and vaccines due to an initial process for patients on intravenous biologics. However, by systematically adopting interventions, we were able to rapidly and reliably achieve our goal performance (Figure 2). There were few failures for the serology screenings from orders not signed. Failures for vaccine administration included deferred, primary care preference, refusal, leaving before vaccine, and vaccine orders not signed. To date, we have screened 862 patients and administered 302 booster vaccines.

Conclusion: By adapting processes that were previously successful in our clinic setting, we were able to reliably implement a hepatitis B serology screening and vaccination program over a short time-frame. Next steps include sustainability planning and spread to other clinics with immunocompromised patients. The results of this project support the importance of adoption and spread of successful processes in order to expedite improvement in quality of care.
Figure 1. Hepatitis B serology screening and vaccine algorithm.
Analysis of the Effectiveness of Immunization with Pneumococcal Polysaccharide Vaccine in Children with Juvenile Idiopathic Arthritis

Ekaterina Alexeeva1,2, Tatiana Dvoryakovskaya1, Rina Denisova1, Olga Lomakina1, Ksenia Isaeva1, Margarita Soloshenko1, Anna Karaseva1, Nikolay Mayansky3, Irina Zubkova3, Darja Novikova4, Anna Gayvoronskaya4, Natalia Tkachenko4, Marika Ivardava4, Firuza Shakhtakhinskaya4 and Marina Fedoseenko4, 1Reumatology department, Federal State Autonomous Institution"National Scientific and Practical Center of Children's Health"Of the Ministry of Health of the Russian Federation, Moscow, Russian Federation, 2Pediatrics, The Federal State Autonomous Educational Institution of Higher Education The First Moscow State Medical University named after I.M. Sechenov Ministry of Health of the Russian Federation (Sechenov University), Moscow, Russian Federation, 3Clinical laboratory, Federal State Autonomous Institution"National Scientific and Practical Center of Children's Health"Of the Ministry of Health of the Russian Federation, Moscow, Russian Federation, 4Department of Vaccine Prevention, Federal State Autonomous Institution"National Scientific and Practical Center of Children's Health"Of the Ministry of Health of the Russian Federation, Moscow, Russian Federation

First publication: September 18, 2017
Background/Purpose: Juvenile idiopathic arthritis (JIA) is one of the most frequent and most disabling rheumatic diseases in childhood. Children suffering from JIA receiving immunosuppressive and genetically engineered biological agents belong to the high risk group for the development of bacterial and viral infections, including those managed by vaccine preventive means.

Objectives: To evaluate the effectiveness of vaccination of 13-valent pneumococcal polysaccharide vaccine (PPV) in children with JIA for the level of specific anti-pneumoconve antibodies (anti-SPP) IgG for Streptococcus pneumonia in the blood serum in patients with JIA before and after vaccination, as well as by recording the number of infections of the upper respiratory tract and pneumonia.

Methods: In a prospective, open comparative study, the effectiveness of vaccination was determined by the level of specific anti-pneumoconve antibodies (anti-SPP) IgG to Streptococcus pneumonia in serum in patients with JIA, as well as by the number of adverse events, the number of infections of the upper respiratory tract and pneumonia. An open prospective comparative study was conducted, which included 42 children with JIA: 21 children with JIA in the active stage of the disease, 21 - in remission of the disease. Vaccination with 13-valent conjugated PPV vaccine was carried out once in a dose (0.5 ml) subcutaneously, against the background of therapy of the underlying disease with methotrexate or etanercept, or 3 weeks before the appointment of methotrexate or etanercept.

Results:
The study included 42 children with JIA: 21 with JIA in the active stage of the disease, 21 - in remission of the disease. As a result of vaccination of all patients, an increase in the level of anti-pneumococcal antibodies (anti-SPP) IgG in children with JIA in the active stage was observed from 23.9 to 51.6 mg/l, with JIA in the remission phase from 26.1 to 73.0 mg/l (p = 0.005). Episodes flare of of JIA were not detected in any subject patient. Analysis of the frequency of ENT organs infections (otitis, rhinitis, sinusitis, tonsillitis, adenoiditis) and lower respiratory tract before and 12 months after vaccination showed a statistically significant decrease in the incidence rate. In the JIA group at the stage of remission of the disease, this index was 4 (3, 7) cases per year, after vaccination, it was reduced to 2 (1; 2) (p = 0.001). A similar situation was observed in the group of children with exacerbation of the disease: before vaccination, the median number of cases of infection with ENT organs was 4 (3; 4); within 12 months after the vaccination, the index decreased to 1 (1, 2) cases (p = 0.001). Pneumonia and/or bronchitis for 1 year after vaccination are not registered in any patient. Serious adverse events were not recorded during the study.

Conclusion: Thus, vaccination of 13-valent PPV of 13 PPV of children with JIA in the remission phase receiving MT or etanercept and children in the acute stage prior to the initiation of immunosuppressant or GIBP is highly effective, and is not accompanied by exacerbation/increase in the activity of the disease and the development of serious undesirable phenomena.

Disclosure: E. Alexeeva, Roche Pharmaceuticals, 2; T. Dvoryakovskaya, Roche Pharmaceuticals, 2; R. Denisova, None; O. Lomakina, None; K. Isaeva, None; M. Soloshenko, None; A. Karaseva, None; N. Mayansky, None; I. Zubkova, None; D. Novikova, None; A. Gayvoronskaya, None; N. Tkachenko, None; M. Ivardava, None; F. Shakhtakhtinskaya, None; M. Fedoseenko, None.


Abstract Number: 387

F4/80hi Synovial Macrophages in the Pathogeneses of Spontaneous Inflammatory Arthritis in CD11c-Flip-KO (HUPO) Mice

Qi Quan Huang1,2, Renee E. Doyle2, Philip J. Homan1, Harris Perlman3, Deborah R. Winter4 and Richard M. Pope2, 1Division of Rheumatology, Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, 2Medicine/Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL, 3Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, 4Department of Medicine Division of Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL

First publication: September 18, 2017
Synovial tissue macrophages (STMs) are critical in the pathogenesis of rheumatoid arthritis (RA). During homeostasis, the majority of murine synovial tissue resident macrophages (TRMs) are MHCII−Ly6C− and TRMs in other tissues are F4/80hi. In our novel CD11C-Flip-KO (HUPO) mouse model of RA, erosive, progressive arthritis develops spontaneously. This study examined the F4/80hi subsets of ankle macrophages from HUPO mice with arthritis and littermate controls.

Methods:
Arthritis was evaluated by clinical score. Cell types within the ankle joints were determined by flow cytometry. STMs were defined as CD45+CD11b+CD64+F4/80+, which were further grouped into subsets according to the expression of F4/80, MHCII and Ly6C. Subsets of F4/80hi STMs were isolated for RNAseq.

Results:
All STMs that are F4/80hi were also Ly6C− in both HUPO and control mice. In the controls mice, under homeostatic conditions, ~80% of the Ly6C−F4/80hi STMs were MHCII− and 20% MHCII+, and those that are MHCII− were considered TRMs. In contrast, in HUPO mice with arthritis the F4/80hiMHCII+ macrophages are greatly increased representing >90%, while the F4/80hi MHCII− macrophages were markedly reduced (<10%), and this reduction was inversely correlated with arthritis severity and duration. In HUPO mice, by flow cytometry, IL-6 expressing cells are increased in both MHCII+ and - subsets, while IL-10 expressing cells were reduced, compared with controls. The F4/80hi STM populations were further analyzed by RNAseq. From over 5,000 differentially expressed genes, a similarity analysis demonstrated limited correlation between HUPO and control F4/80hi STMs. Further, functionally distinct clusters were identified between HUPO and controls. For both MHCII+ and - subsets, cell differentiation and cell morphogenesis pathways were reduced, while pathways for innate immunity and inflammation were increased in the HUPO mice. In contrast, differences between the MHCII+ and the MHCII− subsets were observed for antigen processing and presentation and the regulation of hematopoiesis in the control mice, while metabolic processes and for tRNA and ntRNA regulation were differentially expressed in the HUPO mice.

Conclusion:
These observations demonstrate that F4/80hi STMs are markedly different under homeostatic and inflammatory conditions. The reduction of TRMs and an increase of inflammatory F4/80hiMHCII+ macrophages contribute to the pathogenesis of HUPO arthritis. Further studies on the regulation of macrophage biology under homeostatic and chronic inflammatory conditions will help inform the pathogenesis of RA.

Disclosure: Q. Q. Huang, None; R. E. Doyle, None; P. J. Homan, None; H. Perlman, None; D. R. Winter, None; R. M. Pope, None.


Abstract Number: 388

Induction of Anti-Citrullinated Protein Antibodies By Peptidyl Arginine Deiminase Immunization: A New Model for the Development of Anti-Citrullinated Protein Antibodies in Rheumatoid Arthritis

Fanny Arnoux1,2, Nathalie Lamber1,3, Nathalie Balandraud1,2,4, Jean Roudier1,3,5 and Isabelle Auger1,2, 1Aix Marseille University, Marseille, France, 2INSERM UMRs 1097, Marseille, France, 3Arthrites auto-immunes, INSERM UMRs 1097, Marseille, France, 4APHM, Marseille, France, 5Rheumatology dept, APHM, Marseille, France

First publication: September 18, 2017
Background/Purpose:

The most important immunological event in rheumatoid arthritis (RA) is the development of anti-citrullinated protein autoantibodies (ACPAs). ACPAs are present in 2/3 of patients. The mechanisms leading to the production of ACPAs are unknown. ACPAs are produced in the absence of identified T cell responses specific for each citrullinated protein. Peptidyl arginine deiminase 4 (PAD4), which binds numerous proteins and citrullinates them is the target of autoantibodies in early RA. This suggests a model for the emergence of ACPAs in the absence of T cells specific for each citrullinated antigen: anti-citrullinated protein autoantibodies could arise because PADs are recognized by T cells which help the production of autoantibodies to proteins being citrullinated by PADs, according to a “hapten/carrier” model. Here, we tested this model in mice.

Methods:

We used C3H mice which express a particular IEb\(^k\) whose third hypervariable region is highly homologous to that of RA-associated HLA-DRB1*04:01 allele and DBA/2 mice whose IEb\(^d\) is similar to that of non RA-associated HLA-DRB1*04:02. Mice were immunized subcutaneously with PADs or phosphate buffered saline (PBS) in Freund’s complete adjuvant (CFA). Three booster injections of PAD or PBS in Freund’ incomplete adjuvant (IFA) were given subcutaneously 15, 35 and 55 days later. Sera from primed mice were: 1) tested for anti-PAD antibodies by ELISA. 2) tested for T cell responses to native or citrullinated fibrinogen 65 days after PAD immunization. 3) tested for anti-citrullinated fibrinogen antibodies by ELISA using fibrinogen peptides under citrullinated and native form.

Results:

C3H mice immunized with human PAD2 or PAD4 developed antibodies and T cells to PADs and IgG antibodies to citrullinated peptides from fibrinogen, in the absence of T cell response to fibrinogen. To test whether the observed hapten carrier effect applies to immunization with self-proteins, we immunized C3H mice with murine PAD2 or PAD4 and looked for antibodies to peptides from fibrinogen under native or citrullinated form. The hapten carrier effect also occurred in the self-situation. Finally, to analyze the effect of the MHC background on hapten carrier immunization, we immunized DBA/2 mice whose IEb\(^d\) is similar to that of non RA-associated HLA-DRB1*04:02. DBA/2 mice failed to develop antibodies to citrullinated fibrinogen peptides.

Conclusion:

T cell immunization to PAD proteins triggers ACPAs through a hapten carrier mechanism in which the carrier is PAD which performs citrullination and the hapten any protein being citrullinated by PAD.

Disclosure: F. Arnoux, None; N. Lambert, None; N. Balandraud, None; J. Roudier, None; I. Auger, None.


Abstract Number: 389

S-110483 a New Potent EP4 Receptor Antagonist with Immunomodulatory and Analgesic Activities

Takashi Maeda\(^1\), Toshitaka Ochiai\(^2\), Toshie Nagayasu-Tanaka\(^1\), Yuta Morisaki\(^1\), Haruka Takizawa\(^1\), Seiji Ishihara\(^1\), Shigeo Kurokawa\(^1\), Kiyoharu Ukai\(^1\) and Masahiro Suda\(^1\), \(^1\)Pharmacology Department, Kaken Pharmaceutical Co., LTD, Kyoto, Japan, \(^2\)Kaken Pharmaceutical Co., LTD, Kyoto, Japan

First publication: September 18, 2017
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Prostaglandin (PG) E₂ is known to enhance the expansion of T helper 17 (Th17) cell population via EP4 receptor (EP4) in the early phase of rheumatoid arthritis (RA). Furthermore, EP4 signals are involved in inflammatory hyperalgesia. Therefore, EP4 antagonists would be useful disease modified anti-rheumatic drugs (DMARDs) with analgesic effect. On the basis of this concept, pharmacological characteristics of S-110483, our novel potent and selective EP4 antagonist, were compared with existing EP4 antagonists; in addition, evidence regarding the immunomodulatory/analgesic potential of S-110483 is provided using an RA model.

**Methods:** The antagonistic activities of S-110483 and existing EP4 antagonists were evaluated in mammalian cells overexpressing rat, mouse, or human EP4. The effects of S-110483 on the production of PGE₂ and PGI₂ were evaluated using human umbilical vein endothelial cells (HUVEC) stimulated with IL-1β. For estimating the effects on the Th17 expansion, inhibition of IL-23 release from mouse dendritic cells was measured. The anti-edema and analgesic effects of S-110483 were evaluated by using rat adjuvant-induced arthritis (AIA) models as follows. Rats received intradermal injections of adjuvant suspension on their left hind paw (day 0). S-110483 (0.003–3 mg/kg) or celecoxib (0.003–3 mg/kg) were orally administered once a day on days 9–20. On day 18, anti-hyperalgesia effects were evaluated by measuring the vocalization threshold. Anti-edema effects were evaluated by paw volume of day 8, day 14, and day 18.

**Results:** S-110483 showed potent antagonistic activities for the rat/mouse/human EP4 with IC₅₀ of 10.9/9.0/5.4 nmol/L, respectively. S-110483 (10–1000 nmol/L) did not inhibit PGE₂ and PGI₂ production from HUVEC. S-110483 dose-dependently inhibited IL-23 release from activated mouse dendritic cells. The in vitro evaluation including the EP4 antagonistic activity revealed that S-110483 is the most potent and effective antagonist among existing EP4 antagonists. In the AIA models, S-110483 (0.3 mg/kg) had considerable analgesic and anti-inflammatory effects. Compared to celecoxib, S-110483 showed the maximum anti-hyperalgesic effects starting at dose that was 10 times lower.

**Conclusion:** Our studies demonstrated that S-110483 is the best in class among EP4 receptor antagonists, and it shows not only immunomodulatory effects but also anti-inflammatory and analgesic effects without inhibiting PGE₂ and PGI₂ production. These findings suggested that S-110483 could become a superior therapeutic option in RA patients.

**Disclosure:** T. Maeda, None; T. Ochiai, None; T. Nagayasu-Tanaka, None; Y. Morisaki, None; H. Takizawa, None; S. Ishihara, None; S. Kurokawa, None; K. Ukai, None; M. Suda, None.

Methods: 1. Osteoclastogenesis: Mice bone-marrow cells were stimulated with M-CSF/RANKL and the numbers of differentiated osteoclasts were counted. 2. RANKL expression on osteoblasts: Mice preosteoblast cell line (MC3T3-E1) was stimulated with IL-1β and RANKL expression was evaluated. 3. The therapeutic effects of S-110483 and DMARDs on an adjuvant-induced arthritis (AIA) model: Rats were orally administered S-110483 or DMARDs for 25 days starting immediately after the adjuvant injection. Paw volumes were measured regularly. Twenty-five days after the adjuvant injection, rats were sacrificed and the wet weight of the thymus was measured. Furthermore, bone condition was evaluated by using X-ray and micro CT analysis. 4. Therapeutic effects of S-110483 and celecoxib on collagen-induced arthritis (CIA) model: DA rats were immunized with type-II collagen in CFA, and arthritis score and the paw volume were measured regularly. S-110483 or celecoxib was administered orally once a day from arthritis onset. Sixteen days after arthritis onset, bone condition was evaluated.

Results: 1. S-110483 (1–10 µmol/L) inhibited the osteoclastogenesis and its effect was more potent than tofacitinib and MTX. 2. S-110483 (1–10 µmol/L) also inhibited RANKL expression of osteoblast as well as DMARDs. 3. In the AIA model, anti-edema and anti-bone destruction effects of S-110483 were comparable with those of MTX (1 mg/kg), and were more potent than those of tofacitinib (10 mg/kg) and iguratimod (10 mg/kg). Furthermore, S-110483 showed the inhibitory effect on inflammation-related bone formation, unlike DMARDs, suggesting that S-110483 possessed excellent inhibitory effects on joint deformity. Interestingly, S-110483 improved thymus atrophy, an index of immunosuppression, unlike MTX and tofacitinib. 4. In the CIA model, while anti-edema effect of S-110483 was comparable to that of celecoxib (10 mg/kg), the anti-bone destruction effect of S-110483 was significantly more potent than that of celecoxib (10 mg/kg).

Conclusion: Our novel EP4 antagonist, S-110483, has not only anti-inflammatory effects but also has direct effects on osteoclasts and osteoblasts, similar to DMARDs. Furthermore, the anti-edema and anti-bone destruction effects of S-110483, without strong immunosuppressive effect, are comparable to those of DMARDs. These findings would support the excellent potential of S-110483 as a clinically useful DMARD.

Disclosure: T. Ochiai, None; T. Maeda, None; T. Nagayasu-Tanaka, None; J. Anzai, None; D. Kato, None; Y. Morisaki, None; K. Ukai, None; M. Suda, None.

Defective Glucose and Lipid Metabolism in Rheumatoid Arthritis Is Determined By Chronic Inflammation in Metabolic Tissues

Nuria Barbarroja1, Ivan Arias de la Rosa2, Sergio Rodriguez-Cuenca3, Yolanda Jiménez-Gómez1, Patricia Ruiz-Limon2, Carlos Perez-Sanchez1, Maria Carmen Abalos-Aguilera2, Irene Cecchi2, Rafaela Ortega-Castro1, Jerusalem Calvo-Gutierrez1, Rocio Guzman-Ruiz2, Maria del Mar Malagon5, Eduardo Collantes-Estévez1, Antonio Vidal-Puig3, Alejandro Escudero-Contreras2 and Chary Lopez-Pedrera1, 1Rheumatology service, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain, 2Rheumatology Service, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain, 3Metabolic Research Laboratories, Wellcome Trust-MRC Institute of Metabolic Science, Addenbrooke’s Hospital, University of Cambridge, Cambridge, United Kingdom, 4Department of Cell Biology, Physiology, and Immunology, IMIBIC/University of Córdoba/Reina Sofia University Hospital, Cordoba, Spain, 5Department of Cell Biology, Physiology, and Immunology, IMIBIC/University of Córdoba/Reina Sofia University Hospital, Cordoba, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Animal Models Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Rheumatoid arthritis (RA) patients are at higher risk for insulin resistance (IR). The association between RA and IR, and its role on the different characteristics of the disease, such as duration and activity have not been well defined. In addition, there is a gap of knowledge regarding the link between systemic/local inflammation and insulin sensitivity and lipid metabolism in RA patients. Objective: To explore the effects of the inflammation on the glucose and lipid metabolism in the RA context, following three strategies: RA patients, collagen induced arthritis (CIA) mouse model and in vitro treatment of 3T3L1 adipocytes.
**Methods: Human study:** 150 RA patients and 40 healthy donors were included. IR was quantified using the homeostatic model assessment of IR (HOMA-IR). **Mouse model:** 20 CB57J/BL mice were used; 5 mice were used as non-diseased group, and 15 were used in CIA modelling: sorted in low and high activity of the disease based on the number of inflamed digits depending on the duration of the disease. Plasma, leukocytes, skeletal muscle, liver and adipose tissue were collected. **Treatment of adipocytes with serum from RA patients:** 3T3L1 adipocytes were treated with serum 10% of RA patients and healthy donors for 24h. The expression of genes and proteins involved in inflammation, lipid metabolism and insulin signalling was analysed in all the tissues and cells.

**Results:** Percentages of obesity, hypertension, atherogenic risk, metabolic syndrome and IR were significantly increased in the RA group. Although mean time of evolution was 7 years, no association between IR and the duration of the disease was found. Levels of HOMA-IR significantly correlated with DAS28 and C-reactive protein levels, suggesting a link between the degree of systemic inflammation and the development of IR in these patients. These results were strengthened by observing that the induction of arthritis in mice resulted in a global inflammatory state characterized by defective carbohydrate and lipid metabolism in leukocytes, liver, muscle and adipose tissue, consistent with defects in insulin signaling. Adipose tissue was the organ most susceptible to the RA-induced metabolic alterations, which were observed from early stages of the disease. These metabolic effects were recapitulated in 3T3-L1 adipocytes treated with serum from RA patients.

**Conclusion:** 1) IR was closely associated with an increase in disease activity and systemic inflammation in RA patients. 2) Induction of arthritis in mice promoted an increase in inflammation in skeletal muscle, adipose tissue and leukocytes, accompanied by alterations in metabolic pathways favouring the development of insulin resistance on these tissues. 3) The inflammatory mediators in RA are the direct responsible for the metabolic alterations observed in adipose tissue. Altogether, our results show the direct effect of RA-associated chronic inflammation mediating the alterations occurred in glucose and lipid metabolism associated with this disorder. Thus, therapeutic strategies aimed to inhibit inflammation targeting proinflammatory cytokines might be an excellent option to normalize the metabolic alterations associated with RA. Funded by ISCIII-FIS (CP15/00158)

**Disclosure:** N. Barbarroja, None; I. Arias de la Rosa, None; S. Rodriguez-Cuenca, None; Y. Jiménez-Gómez, None; P. Ruiz-Limon, None; C. Perez-Sanchez, None; M. C. Abalos-Aguilera, None; I. Cecchi, None; R. Ortega-Castro, None; J. Calvo-Gutierrez, None; R. Guzman-Ruiz, None; M. D. M. Malagon, None; E. Collantes-Estévez, None; A. Vidal-Puig, None; A. Escudero-Contreras, None; C. Lopez-Pedrera, None.

**Abstract Number:** 392

**Effects of Synthetic Dmards on the Insulin Resistance and Obesity Associated with Rheumatoid Arthritis: An Obese Mouse Model of Arthritis**

Nuria Barbarroja1, Ivan Arias de la Rosa2, Miriam Ruiz-Ponce1, Sergio Rodriguez-Cuenca3, Maria Carmen Abalos-Aguilera2, Yolanda Jiménez-Gómez1, Patricia Ruiz-Limon2, Carlos Perez-Sanchez1, Eduardo Collantes-Estévez1, Antonio Vidal-Puig3, Alejandro Escudero-Contreras2 and Chary Lopez-Pedrera1, 1Rheumatology service, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain, 2Rheumatology Service, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain, 3Metabolic Research Laboratories, Wellcome Trust-MRC Institute of Metabolic Science, Addenbroke’s Hospital, University of Cambridge, Cambridge, United Kingdom

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Rheumatoid Arthritis – Animal Models Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Numerous studies have demonstrated the closely association between rheumatoid arthritis (RA) and metabolic complications such as obesity and insulin resistance (IR). Thus, there is an urgent need for the use of therapies targeting both the activity of the disease and such metabolic disorders. Yet, the beneficial/negative effect of conventional synthetic DMARDs (disease-modifying antirheumatic drugs) on the metabolic complications associated with cardiovascular disease prominent in RA patients is unknown yet. Objective: To analyze and compare the effects of methotrexate (MTX), leflunomide (LFN) and hydroxychloroquine (HDQ) on the obesity and IR in an obese collagen-induced arthritis (CIA) mouse model.

**Disclosure:** None
Methods: CIA was developed in obese-induced by high fat diet (HFD) and lean mice. 55 C57Bl/6 mice (4-5 weeks) were used. Groups of study: 5 non-diseased lean mice, 9 CIA lean mice, 5 non-diseased OB mice, 9 OB-CIA mice, 9 OB-CIA mice treated with LFN, 9 OB-CIA mice treated with MTx and 9 OB-CIA mice treated with HDQ for 15 days. Mice were weighted and the number of total swollen digits was recorded daily. After treatment, glucose tolerance test (GTT) was performed. HOMA-IR was calculated in all groups. Serum, plasma and adipose tissue were collected. Gene and protein expression of molecules involved in inflammation, insulin signaling and lipid metabolism.

Results: HFD promoted an early development of arthritis onset, however fat overloading did not affect the CIA effector phase. In contrast, the development of arthritis had not effect on body weight. Although the disease overcome was unaffected, obese CIA mice were more insulin resistant and display an elevated inflammatory state and an alteration of adipokines (at serum/plasma and adipose tissue levels) compared to lean CIA mice and non-arthritis obese mice. After 15 days of treatment, the therapies more effective on the disease progression were HDQ and MTX. Only the treatment with HDQ significantly reduced the body weight and improved insulin sensitivity at systemic level (HOMA-IR and area under the curve-GTT). Although systemic and adipose tissue high inflammatory status was reverted by the three DMARDs, MTX and HDQ, these were able to restore the metabolic alterations observed on adipose tissue. Thus, these DMARDs increased the expression of genes involved in insulin signaling (IRS-1 and 2, GLUT4 and AKT), lipid accumulation (DGAT, PLIN), and adipogenesis (PPARg, SREBP1 and INSIG1) and modulate the expression of leptin and adiponectin.

Conclusion: 1) Lipid overloading accelerates the disease onset in CIA mice. Although disease overcome was unaffected, the induction of arthritis in an obese state aggravates the metabolic alterations, suggesting that inflammation associated with RA strongly contributes to the development of metabolic complications. 2) MTX and HDQ can reduce the metabolic abnormalities induced by arthritis, modulating glucose and lipid metabolism and favoring the improvement of insulin sensitivity. Thus, they can be used as an excellent therapeutic strategy in patients with metabolic complications related to RA. Funded by ISCIII-FIS (CP15/00158) and Roche Pharma S.A

Disclosure: N. Barbarroja, None; I. Arias de la Rosa, None; M. Ruiz-Ponce, None; S. Rodriguez-Cuenca, None; M. C. Abalos-Aguilera, None; Y. Jiménez-Gómez, None; P. Ruiz-Limon, None; C. Perez-Sanchez, None; E. Collantes-Estèvez, None; A. Vidal-Puig, None; A. Escudero-Contreras, None; C. Lopez-Pedrera, None.

Abstract Number: 393

The Role of Follicular Helper 17 T Cells in Glucose-6-Phosphate Isomerase Induced Arthritis

Izumi Kurata, Isao Matsumoto, Atsumu Osada, Hiroshi Ebe, Hoshimi Kawaguchi, Yuya Kondo, Hiroto Tsuboi and Takayuki Sumida, Department of Internal Medicine, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Animal Models Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Follicular helper T (Tfh) cell is a novel T cell subset which promotes follicular B cell activation, differentiation to plasma cell and antibody production. Recently, circulating Tfh has been reported to be increased in RA and other autoimmune diseases. Some reports have showed the existence of Tfh subsets which share same characteristics as conventional Th subsets, but their function in RA has been still unclear. The aim of this study was to explore the role of Tfh subsets in glucose-6-phosphate isomerase (GPI) induced arthritis (GIA), which mouse model was dependent on CD4+ T cells, B cells and IL-17.

Methods:

1) The fluctuation in numbers of Tfh, the subsets and germinal center (GC) B cell in draining lymph nodes from GIA were analyzed by FACS during the course of arthritis.

2) The localization of Tfh and the subsets were analyzed by IF staining of the draining lymph nodes.
3) Anti-GPI antibody titers of sera from GIA were measured by ELISA. To assess Tfh function, Tfh and plasmablasts from GIA were co-cultured and the antibody titers of the culture supernatant were also measured.

**Results:**

1) Tfh cell population was increased after the immunization of GPI. The increase was peaked on day 7, just at the onset of the arthritis, then gradually subsided. The subset analysis revealed the specific increase of IL-17 producing Tfh (Tfh17) at the same phase. The increased population of GC B cells was also observed through the course of arthritis. Its increase started on day 7 in response to Tfh, and peaked on day 14.

2) The IF staining showed that Tfh17 cells were accumulated in the T cell zone of GC and physically contacted with GC B cells in the draining lymph nodes of GIA (Figure).

3) Anti-GPI antibody was detected from day 7 in the sera from GIA, and the titers were gradually elevated over time. The titers of anti-GPI antibody in the culture supernatant were significantly increased compared with those from non-Tfh CD4+ cells and plasmablasts co-culture.

**Conclusion:**

Tfh, particularly Tfh17, might have a crucial role in the development of arthritis via B cell activation and anti-GPI antibody production in GIA. We are now elucidating the function of Tfh17 in the generation of GIA.

**Disclosure:** I. Kurata, None; I. Matsumoto, None; A. Osada, None; H. Ebe, None; H. Kawaguchi, None; Y. Kondo, None; H. Tsuboi, None; T. Sumida, None.

**View Abstract and Citation Information Online** - [http://acrabstracts.org/abstract/the-role-of-follicular-helper-17-t-cells-in-glucose-6-phosphate-isomerase-induced-arthritis](http://acrabstracts.org/abstract/the-role-of-follicular-helper-17-t-cells-in-glucose-6-phosphate-isomerase-induced-arthritis)

**Abstract Number:** 394

**Female Tumor Necrosis Factor Transgenic Mice Have More Severe Arthritis Than Males and Suppressed Levels of Bifidobacterium Pseudolongum in Their Gut Microbiome**

Emily Wu1, Richard Bell2, Alex Grier3, Steven Gill4, Edward Schwarz5 and Homaira Rahimi6, 1Department of Immunology, Microbiology, and Virology, University of Rochester, Rochester, NY, 2Center for Musculoskeletal Research, University of Rochester,
SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Animal Models Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Rheumatoid arthritis (RA) has an increased prevalence and severity in women compared to men, yet the underlying etiology of this sexual dimorphism is unknown. Similar sex differences in the tumor necrosis factor-transgenic (TNF-Tg) mouse model of RA have been reported. Most notably, female TNF-Tg mice die earlier than males, with the majority dying between 6-7 months of age, while male mice die sporadically between 5-12 months of age. Recent studies have suggested that the gut microbiota significantly contribute to the pathogenesis of RA. This has been supported by the K/BxN mouse model of arthritis, which only develops arthritis when colonized with commensal bacteria. Based on this influence of microbiome on arthritis, we hypothesize that a sexually dimorphic microbiome exists in TNF-Tg mice, which is associated with disease severity.

Methods: An initial pilot study was performed to assess beta-diversity in male vs. female TNF-Tg mice (n=10), by 16S rRNA sequencing of fecal pellets. We also performed a principal coordinate analysis (PCoA) on these data. Based on significant findings, we collected samples from 4 separately housed cohorts of mice at 5.5 months of age, when TNF-Tg females have advanced disease and males have moderate disease. Cohorts were formed for the purpose of comparing TNF-Tg vs. WT and female vs male gut microbiome profiles (n=6 per cohort). 16S rRNA sequencing was performed on all samples.

Results: We found that female TNF-Tg mice had a significantly decreased beta-diversity (p<0.05) compared to their male counterparts. PCoA demonstrated a clear spatial separation between male and female samples, suggesting distinct gut microbiome profiles. Follow up studies demonstrated that female TNF-Tg mice had enriched levels of several Bacteroidetes and Firmicutes species, as well as suppressed levels of Bifidobacterium pseudolongum, a known commensal bacterium with noted immunosuppressive properties.

Conclusion: Here, we have shown for the first time that the TNF-Tg model of RA demonstrates both a disease-associated dysbiosis, as well as a sexually dimorphic microbiome profile within the TNF-Tg population. We have also shown that the female TNF-Tg microbiome was enriched in certain Bacteroidetes and Firmicutes species compared to the male cohort. The greatest disparity was with the bacterium Bifidobacterium pseudolongum, which multiple studies have suggested has an immunosuppressive phenotype and was greatly suppressed in female TNF-Tg mice. Further research is needed to investigate its role in inflammatory environments and whether active manipulation of the gut microbiome with probiotics may alter the disease state.

Disclosure: E. Wu, None; R. Bell, None; A. Grier, None; S. Gill, None; E. Schwarz, Janssen Pharmaceutica Product, L.P., 9,Lilly Inc., 9; H. Rahimi, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/female-tumor-necrosis-factor-transgenic-mice-have-more-severe-arthritis-than-males-and-supporessed-levels-of-bifidobacterium-pseudolongum-in-their-gut-microbiome

Abstract Number: 395

Pharmacological and Safety Profiles of Cyclin-Dependent Kinase 4/6 Inhibitor, Candidate for Development As Rheumatoid Arthritis Therapeutic Option

Johji Nomura1, Shunsuke Tsujimoto2, Kei Tamura2, Wataru Yamamoto2, Hiroshi Takahashi2, Kyohei Horie2, Toshiya Mashiko2, Naoki Hase2 and Tsunefumi Kobayashi2,1Teijin Institute for Bio-medical Research, TEIJIN PHARMA LIMITED, Tokyo, Japan, 2TEIJIN PHARMA LIMITED, Tokyo, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Animal Models Poster I
Session Type: ACR Poster Session A
**Background/Purpose:** The pathogenesis of rheumatoid arthritis (RA) is characterized by the infiltration of immune cells into the synovial tissues and the excessive proliferation of synovial fibroblasts, resulting in synovial hyperplasia (pannus formation) and subsequent destruction of the bones and joints. Therapeutic strategies to inhibit pro-inflammatory cytokines or immune cells with methotrexate and biologics are the mainstay in the current treatment of RA. However, they cannot induce complete clinical remission in all of the patients. Cyclin-dependent kinase (CDK) 4/6 are key regulators in cell cycle, and its inhibitors have been reported to attenuate the proliferation of synovial fibroblasts and the progression of arthritis without inhibiting acquired immune responses in mouse RA models. To provide novel therapeutic option to inhibit the synovial hyperplasia, we performed the screening for CDK4/6 inhibitors and found out Compound X with high potency and selectivity for CDK4/6. Here we show the pharmacological and safety profiles of Compound X.

**Methods:** In vitro activities of Compound X were examined in kinase assays to determine the inhibitory activity against CDK4/6 and the selectivity to other kinases. In vivo efficacies of Compound X were examined in collagen-induced arthritis (CIA) of mice. Combination efficacy of Compound X and etanercept was examined in anti-collagen antibody-induced arthritis (CAIA) of mice. Adjuvant-induced arthritis (AIA) in rats was performed to determine the safety margin of Compound X. Compound X was orally administrated twice daily for 19 days in mice and once daily for 3 weeks in rats, respectively. A toxicological profiling of Compound X was conducted with 4-week repeat dose studies in rats and monkeys. Telemetry study in monkeys and proarrhythmia study in human iPS cell-derived cardiomyocytes were conducted to evaluate the risk of the cardiovascular system.

**Results:** Compound X showed dose-dependent inhibition of the progression of arthritis and bone destruction in the CIA mice. The serum MMP-3 level was decreased by Compound X, which is consistent with the finding that inhibition of MMP-3 secretion by Compound X in synovial fibroblasts from RA patients. Furthermore, combination of Compound X with etanercept suppressed arthritic score and MMP-3 level more than monotherapy with Compound X or etanercept at the most effective dose. Whereas myelosuppression was observed at 120 mg/kg of Compound X in the AIA rats, the best efficacy in arthritic score was observed at 15 mg/kg. Four-week general toxicity studies in rats and monkeys demonstrated that Compound X is well-tolerated and has no critical concerns. In addition, telemetry study in monkeys and proarrhythmia study using human iPS-derived cardiomyocytes revealed a low risk of the cardiovascular system.

**Conclusion:** Compound X is an orally available CDK4/6 inhibitor and a promising candidate for development for RA treatment.

**Disclosure:** J. Nomura, TEIJIN PHARMA LIMITED, 3; S. Tsujimoto, TEIJIN PHARMA LIMITED, 3; K. Tamura, TEIJIN PHARMA LIMITED, 3; W. Yamamoto, TEIJIN PHARMA LIMITED, 3; H. Takahashi, TEIJIN PHARMA LIMITED, 3; K. Horie, Kyohei Horie, 3; T. Mashiko, TEIJIN PHARMA LIMITED, 3; N. Hase, TEIJIN PHARMA LIMITED, 3; T. Kobayashi, TEIJIN PHARMA LIMITED, 3.

---

**Phospho-STAT1 Inhibition Is the Initial Step after Tofacitinib Treatment in Rabbits with Severe Chronic Synovitis**

Sandra Pérez-Baos, Paula Gratal, Juan Ignacio Barrasa, Ana Lamuedra, Gabriel Herrero-Beaumont and Raquel Largo, Bone and Joint Research Unit, IIS-Fundación Jiménez Díaz UAM, Madrid, Spain

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Rheumatoid Arthritis – Animal Models Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Tofacitinib (TOFA) is a Janus Kinase (Jak) inhibitor approved for the treatment of rheumatoid arthritis (RA) \(^1\). It has recently been shown to selectively inhibit the expression of several chemokines in the synovium of RA patients that were treated over 28 days, without modifying the expression of various pro-inflammatory cytokines, nor the histopathological synovial inflammation, including macrophage infiltration \(^2\). Despite being the synovium the main articular tissue affected by RA, to date there are very limited data regarding the early modulation of synovial cytokines by this Jak inhibitor. In this sense, animal models may allow
a better understanding of the consequences of Jak inhibition in chronic arthritis (CA). Our aim was to develop a rabbit model of CA which mimicked severe human RA in early phases of treatment, in order to evaluate early tissue changes rather than the final therapeutic effect.

**Methods:** Twenty-four male, New Zealand white rabbits were randomly assigned to two groups: control (n=8) and CA (n=16). CA was induced over six weeks via intra-dermal ovalbumin sensitization and four subsequent intra-articular injections on a weekly basis. After the second intra-articular injection, eight CA rabbits were treated with TOFA (10mg/kg/day).

**Results:** CA animals showed reduced weight gain compared to controls, which TOFA tended to increase (weight gain, kg; Control: 0.8±0.05; CA: -0.09±0.06*; CA+TOFA: 0.18±0.1*; #p=0.07 vs CA). A substantial increase in serum C-reactive protein (CRP) was found both in CA and CA+TOFA animals. CA animals showed a severe synovitis that was partially prevented by TOFA (Krenn Score; Control: 0.9±0.3; CA: 7.6±0.2*; CA+TOFA: 6.6±0.2*; p<0.05 vs. control; # vs. CA), and exhibited an augmented macrophage infiltration which was not modified by this inhibitor. TOFA effectively reduced the synovial expression of matrix metalloproteinases MMP-1 (93% inhibition, p<0.05) and MMP-3 (83% inhibition p<0.05), the C-C Motif Chemokine Ligand 2 (CCL2, 74% inhibition, p<0.05) as well as the pro-inflammatory cytokines Interleukin-6 (IL-6, 42% inhibition, p<0.05) and Tumor Necrosis Factor-α (TNFa, 55% inhibition, p<0.05). However, IL-1β was not modified with this Jak inhibitor. Signal Transducer and Activator of Transcription (STAT) -1 and -3, and Nuclear Factor-κB (NF-κB) were activated during CA, but TOFA was only able to diminish STAT-1 phosphorylation.

**Conclusion:** In a synovial tissue with an intense inflammatory activity, TOFA treatment initially blocked STAT-1 phosphorylation, whereas phospho-STAT-3 levels remained unchanged. This Jak inhibitor induced a partial decrease in the synovitis score along with a marked reduction of the expression of MMPs and, to a lesser extent, other pro-inflammatory mediators. These data suggest a key role of STAT-1 in the initial changes occurring in the synovium after TOFA treatment.

**References:**

**Disclosure:** S. Pérez-Baos, None; P. Gratal, None; J. I. Barrasa, None; A. Lamuedra, None; G. Herrero-Beaumont, None; R. Largo, None.


**Abstract Number:** 397

**Anti-Fractalkine Monoclonal Antibody Ameliorates Joint Destruction in Collagen-Induced Arthritis Model through Suppression of Osteoclast Precursor Cell Survival and Migration**

Yoshikazu Kuboi¹, Kana Hoshino-Negishi¹, Masayoshi Ohkuro², Wataru Ikeda¹, Tomoya Nakatani¹, Naoto Ishii¹, Toshihiko Yamauchi¹, Nobuyuki Yasuda¹ and Toshio Imai³, ¹KAN Research Institute, Inc., Chuo-ku, Kobe-shi, Japan, ²Research Project Promotion Group, EA Pharma Co., Ltd., Kawasaki-ku, Kawasaki-shi, Japan, ³KAN Research Institute, Inc., Kobe, Japan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Rheumatoid Arthritis – Animal Models Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** In the Phase 1/2 clinical study, E6011, a novel humanized anti-fractalkine (FKN) mAb demonstrated a promising efficacy in active RA patients who were inadequately controlled by MTX and/or TNF-α inhibitors. In RA joint tissue, increased expression of FKN and abundant infiltration of CX3CR1-positive cells were observed. However, the precise mechanism(s) of FKN-CX3CR1 axis in RA, especially on joint destruction remains to be elucidated. FKN is expressed on endothelial cells and fibroblast-like synoviocytes in synovium and also expressed on osteoblasts. CX3CR1 is expressed on monocytes/macrophages and osteoclast precursor cells (OPCs). Therefore, FKN-CX3CR1 interaction could play pivotal roles in migration, differentiation and activation of those cells. Thus, we examined the roles of FKN-CX3CR1 axis in joint destruction, particularly focused on osteoclast precursor cells in *in vitro* and *in vivo* by using anti-mouse FKN mAb (anti-mFKN mAb).
Methods: DBA/1J mice were immunized with intradermal injections of bovine type II collagen to induce arthritis. Anti-mFKN mAb or control IgG were intraperitoneally injected twice a week. The clinical arthritis score was monitored, and joint destruction was evaluated by soft X-ray and histopathology. Blood parameters were measured using ELISA. In in vitro, effect of immobilized FKN on RANK ligand (RANKL)-induced osteoclast differentiation was examined. Cell survival of bone marrow-derived OPCs without or with immobilized FKN was also assessed by FACS. In in vivo, OPCs were labeled by fluorescein and transferred to CIA mice to evaluate migration of OPCs into inflamed synovium. Anti-mFKN mAb or control IgG were injected before the cell transfer. The number of fluorescein-labeled OPCs that migrated into the CIA joint tissue were counted.

Results: In both prophylactic and therapeutic treatments, anti-mFKN mAb clearly reduced the clinical arthritis score, soft x-ray score and histopathological changes (synovitis, bone erosion and cartilage destruction). The number of TRAP-positive cells in the joint was clearly decreased with anti-mFKN mAb treatment. Interestingly, anti-mFKN mAb suppressed plasma levels of COMP and MMP-3 without affecting those of IL-6, TNF-α and SAA. In in vitro, RANKL-induced osteoclast differentiation was enhanced by immobilized FKN, and anti-mFKN mAb suppressed FKN-dependent enhancement of osteoclast formation. FKN enhanced cell survival of OPCs and eventually increased the number of OPCs. In in vivo, fluorescein-labeled OPCs migrated into inflamed joint tissues, and anti-mFKN mAb clearly abrogated their migration into synovium.

Conclusion: Anti-mFKN mAb remarkably ameliorated the joint destruction with the marked reduction of osteoclasts by the inhibition of both OPC survival and OPC migration in inflamed joint tissues without affecting systemic inflammatory parameters. These results strongly indicate that inhibition of FKN-CX3CR1 axis by a humanized anti-FKN mAb, E6011, is an attractive and affected joints-selective therapeutic strategy for the treatment of both inflammatory synovitis and joint destruction in RA patients.

Disclosure: Y. Kuboi, None; K. Hoshino-Negishi, None; M. Ohkuro, None; W. Ikeda, None; T. Nakatani, None; N. Ishii, None; T. Yamauchi, None; N. Yasuda, None; T. Imai, KAN Research Institute, 3.

Abstract Number: 398

An on-Demand Drug Delivery System for the Treatment of Inflammatory Arthritis

Jing Yan1, Nitin Joshi2, Seth Levy2, Sachin Bhagchandani2, Kai Slaughter2, Nicholas Sherman1, Julian Amirault2, Xueyin He2, Tan Shi Rui2, Michael Valic2, Praveen Vemula3, Oscar Miranda2, Oren Levy2, Antonios Aliprantis4, Joerg Ermann1 and Jeffrey Karp2, 1Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA, 2Brigham and Women's Hospital, Boston, MA, 3Institute for Stem Cell Biology and Regenerative Medicine (inStem), Bangalore, India, 4Rheumatology/Immunology, Brigham and Women's Hospital, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Animal Models Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Many types of inflammatory arthritis (IA) are treated with systemic therapy. In situations where only one or a few joints are active, intra-articular drug administration may offer distinct advantages over starting or escalating systemic therapy by increasing drug bioavailability locally and reducing the potential for drug-induced systemic toxicity. However, local delivery of therapeutics is limited by short intra-articular half-lives. A drug delivery method that generates a local drug depot and titrates drug release to arthritis activity would represent an attractive solution to this problem. We investigated the utility of hydrogels generated from a generally recognized as safe (GRAS) compound for inflammation-responsive local drug delivery in a mouse model of IA.

Methods: Hydrogels were generated from triglycerol monostearate (TG-18) and loaded with triamcinolone acetonide (TA) or a fluorescent dye (DiR). TA-loaded hydrogels were incubated in vitro with defined enzymatic activities or human synovial fluid. TA release was measured using high performance liquid chromatography. IA was induced in C57BL/6 mice by two i.p. injections of K/BxN serum. DiR-loaded hydrogels were injected into the right hindpaw prior to disease induction and fluorescence signal decay was measured by IVIS imaging. To test therapeutic efficacy, TA-loaded hydrogel, blank hydrogel or free TA were injected into the right hindpaw immediately after disease induction, and disease severity was assessed by measuring paw thickness with calipers and clinical scoring.
**Results:** TG-18 hydrogels efficiently and stably encapsulate TA. In vitro, TA-loaded hydrogels released drug on-demand upon exposure to enzymes including matrix metalloproteases or synovial fluid from patients with rheumatoid arthritis. In mice with K/BxN serum transfer arthritis, locally injected DiR-hydrogels demonstrated loss of fluorescence over time due to hydrogel disassembly that correlated with arthritis severity. Moreover, a single dose of TA-loaded hydrogel but not the equivalent dose of locally injected free TA reduced arthritis activity in the injected paw.

**Conclusion:** Our results suggest that an inflammation-responsive hydrogel as self-titrating on-demand drug delivery system can offer improved therapeutic benefit in IA.

**Disclosure:** J. Yan, None; N. Joshi, None; S. Levy, None; S. Bhagchandani, None; K. Slaughter, None; N. Sherman, None; J. Amirault, None; X. He, None; T. S. Rui, None; M. Valic, None; P. Vemula, None; O. Miranda, None; O. Levy, None; A. Aliprantis, None; J. Ermann, Novartis Pharmaceutical Corporation, 5, UCB, 5, Takeda, 5, SPARTAN/GRAPPA, 9; J. Karp, Alivio Therapeutics, 1.


Abstract Number: 399

**Therapeutic Effect of Rosiglitazone-Mediated Dendritic Cells in Established Arthritis in Mice**

Jin Jung Choi¹, Sang-Yoon Jung², Kyung-Su Park³, Chong-Hyeon Yoon⁴ and Dae-Seog Lim⁵, ¹Rheumatology, CHA University Medical Center at Bundang, Sungnam, Korea, Republic of (South), ²Internal Medicine, Bundang CHA Medical Center, Seongnam, Korea, Republic of (South), ³Internal Medicine, St. Vincent's Hospital, The Catholic University of Korea, Suwon, Korea, Republic of (South), ⁴Rheumatology, The Catholic University of Korea, Uijeongbu St. Mary's Hospital, Uijeongbu, Korea, Republic of (South), ⁵Department of biotechnology, CHA University, Sungnam, Korea, Republic of (South)

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Animal Models Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

**Background/Purpose:**
Rosiglitazone is a selective ligand for peroxisome proliferator-activated receptor-gamma (PPAR-γ), which is expressed by antigen presenting cells (APCs) and plays a fundamental role in immune responses. Tolerogenic dendritic cells (tDCs) are professional APCs with antigen-specific immune regulation to induce autoimmune tolerance, suggesting the potential as antigen-specific immunotherapy for autoimmune diseases. The aim of this study was to investigate therapeutic effects of rosiglitazone-mediated DC (Rosi-DC) in a collagen-induced arthritis (CIA) mouse model.

**Methods:**
Rosi-DCs were generated by treating immature DCs with TNF-α, type II collagen, and rosiglitazone. CIA mice then received subcutaneously two injections of Rosi-DCs. The severity of arthritis was then assessed three times until Day 50 post-primary immunization. The phenotypes of the DC and regulatory T (Treg) cell populations in CIA mice were determined by flow cytometry and the effect of Rosi-DCs on the secretion of autoimmunity-inducing cytokines was examined by ELISA.

**Results:**
Rosi-DCs expressed lower levels of DC-related surface markers (CD80, CD86, CD40 and CD54) than mature DCs. Rosi-DCs produced lower levels of pro-inflammatory cytokines (IL-1β, IL-6, and IL-12p70) than mDCs. Upon the co-culture of DCs and T lymphocytes, Rosi-DCs markedly increased FoxP3+CD4+CD25+ Treg cell population and reduced the Th1/Th17 cell population.

Histopathological examination revealed that the degree of inflammation in the paws of Rosi-DC-treated mice was much lower than that in the paws of PBS-treated CIA mice. In vivo, the percentage of Treg cells in the spleens and inguinal lymph nodes of mice vaccinated with type II collagen-pulsed Rosi-DCs was markedly higher than that in mice injected with Ag-mismatched (myosin pulsed) or Ag-
unpulsed Rosi-DCs and PBS-treated CIA mice. Treatment with type II collagen-pulsed Rosi-DCs resulted in a reduction in the percentage of Th1 and Th17 cells within the splenocyte population.

Conclusion:

In this study, these results clearly show that rosiglitazone-mediated DCs ameliorate CIA, most likely via the induction of antigen-specific Treg cells.

Disclosure: J. J. Choi, None; S. Y. Jung, None; K. S. Park, None; C. H. Yoon, None; D. S. Lim, None.


Abstract Number: 400

Combination of the Collagen-Induced Arthritis and Organic Dust-Induced Airway Inflammation Models As a Model of Interstitial Lung Disease in Rheumatoid Arthritis

Katherine Janike1, Jill Poole1, Geoffrey M. Thiele2, Michael J. Duryee3, Lynell W. Klassen4, Amy Nelson5, Kristi Warren6, Benjamin Swanson7 and Ted R. Mikuls8, 1Medicine, University of Nebraska Medical Center, Omaha, NE, 2Int Med/Sec of Rheum/Immun, Univ of NE Medical Ctr, Omaha, NE, 3Internal Medicine Division of Rheumatology, University of Nebraska Medical Center, Omaha, NE, 4Department of Internal Medicine, University of Nebraska Medical Center, Omaha, NE, 5Department of Medicine, University of Nebraska Medical Center, Omaha, NE, 6Department of Medicine, University of Nebraska Medical Center, Omaha, NE, 7Department of Pathology, University of Nebraska Medical Center, Omaha, NE, 8Internal Medicine, Division of Rheumatology, University of Nebraska Medical Center, Omaha, NE

First publication: September 18, 2017
diffuse bone loss. However, data support a suppression of the lung inflammatory response in the setting of arthritis. Activation of the lung macrophage during arthritis induction may be responsible for this paradoxical finding. Finally, this co-exposure model could be exploited further and in other murine strains to better understand the pathogenesis and response to potential treatments for RA-ILD.

<table>
<thead>
<tr>
<th></th>
<th>Sham</th>
<th>CIA</th>
<th>ODE</th>
<th>CIA+ODE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Final Arthritis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammatory Score</td>
<td>0 (0)</td>
<td>1.33 (0.19)</td>
<td>0.70 (0.13)</td>
<td>1.60 (0.22)</td>
</tr>
<tr>
<td><strong>Bone mineral density</strong>, g/cm³</td>
<td>0.14 (0.006)</td>
<td>0.11 (0.008)</td>
<td>0.15 (0.009)</td>
<td>0.09 (0.01)</td>
</tr>
<tr>
<td>BALF neutrophil count, x 10³</td>
<td>8.2 (1.3)</td>
<td>9.0 (3.3)</td>
<td>524 (79)</td>
<td>246 (67)</td>
</tr>
<tr>
<td>BALF IL-6, pg/ml</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>246 (26)</td>
<td>130 (31)</td>
</tr>
<tr>
<td>BALF TNF-α, pg/ml</td>
<td>0.7 (0.7)</td>
<td>0 (0)</td>
<td>35 (7)</td>
<td>13 (5)</td>
</tr>
<tr>
<td>BALF CXCL2, pg/ml</td>
<td>59 (14)</td>
<td>52 (11)</td>
<td>142 (15)</td>
<td>69 (9)</td>
</tr>
<tr>
<td>BALF CXCL1, pg/ml</td>
<td>237 (142)</td>
<td>225 (53)</td>
<td>474 (54)</td>
<td>254 (41)</td>
</tr>
<tr>
<td>Lung tissue neutrophil count, x 10⁴</td>
<td>6.1 (2.0)</td>
<td>11.1 (2.0)</td>
<td>30.3 (7.5)</td>
<td>19.8 (1.2)</td>
</tr>
<tr>
<td>Lung tissue activated macrophage (CD11c⁺CD11bhi) count, x 10⁴</td>
<td>1.3 (0.4)</td>
<td>3.1 (0.7)</td>
<td>12.6 (3.1)</td>
<td>7.7 (0.9)</td>
</tr>
</tbody>
</table>

Statistical significance denoted as asterisks (*p<0.05; **p<0.01, ***p<0.001) vs. Sham. Statistical difference of ODE vs. CIA +ODE denoted as #p<0.05; ##p<0.01, ###p<0.001.

Disclosure: K. Janike, None; J. Poole, None; G. M. Thiele, None; M. J. Duryee, None; L. W. Klassen, None; A. Nelson, None; K. Warren, None; B. Swanson, None; T. R. Mikuls, BMS, 2, Ironwood Pharm, 2, Pfizer Inc, 5, NIH, VA, 2.


Abstract Number: 401

Cigarette Smoking Dose-Dependently Facilitates the Onset of Arthritis and Aggravates Arthritis in Female Experimental Arthritis Mice

Ji-Won Kim¹, Jennifer Lee², Yeon-Sik Hong³, Sung-Hwan Park² and Ji Hyeon Ju², ¹Medicine, Division of Rheumatology, Department of Internal Medicine, Seoul St. Mary’s Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea, Republic of (South), ²Division of Rheumatology, Department of Internal Medicine, Seoul St. Mary’s Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea, Republic of (South), ³Division of Rheumatology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Animal Models Poster I
**Background/Purpose:** Smoking is an important epidemiological factor for development of rheumatoid arthritis (RA). However, the mechanism of proarthritic role of smoking is not well understood. The purpose of this study is to precisely explore the arthritic role of smoking in two experimental arthritis models including collagen induced arthritis (CIA) and IL-1 receptor antagonist (Ra) knockout (KO) mice. Cigarette smoking was challenged by two routes of inhalation and drinking.

**Methods:** To deliver elaborate dosage of smoking, we utilized good laboratory product (GLP)-grade closed inhalation chamber system which is equipped in Korea Institute of Toxicology. Smoke was generated by routine analytic cigarette-smoking machine (ISO standard 3308). Tobacco produce-3R4F cigarette (9.4mg tar/0.7mg nicotine) was chosen by ISO standard 3402 for atmosphere conditioning and testing. This study was strictly followed by OECD guidelines for the testing of chemicals section 4 health effects test No.412 Subacute inhalation toxicity. CIA was induced in a total of 60 mice (negative control (n=10), CIA control (n=10), smoke control (n=10), and cigarette smoke (n=30)). After 1st collagen immunization, three different doses (T1~T3) of smoke were delivered to collagen induced mice (T1 dose 150 ug/L (n=10), T2 dose 300 ug/L (n=10), T3 dose 600 ug/L (n=10)). It is known that concentration of smoke exposure possibly ranges from 50 to 800 ug/L in real world. Cigarette smoke delivery was done 1 hour once a day, 5 days/week, for 4 weeks in close ventilation system. As a second smoking study, cigarette smoke extract (CSE) was delivered per oral to IL-1RaKO mice arthritis model.

**Results:** Cigarette smoking facilitated the onset arthritis. Twenty percent of mice in cigarette smoke group developed arthritis less than a week after 1st immunization, while control CIA mice showed 20% incidence of arthritis on four weeks after immunization. Time points of 60% arthritis incidence was on 3 weeks after 1st immunization, 4 weeks, and 6 weeks in high dose (T3), low dose (T1) and control CIA group, respectively (p<0.05). Higher dose of smoke challenge induced more lymphocyte infiltration in subpleural area of lung. Citrullination was dose dependently increased in smoking inhaled groups. Splenic Th17 population increased dose dependently in smoking groups. In contrary to smoking experiment, CSE drinking did not affect the arthritis development in experimental arthritis model. However, interestingly CSE aggravated arthritis score in female group as a subgroup analysis.

**Conclusion:** In this study, we revealed cigarette smoking facilitated the onset of arthritis and aggravated arthritis score in a dose-dependent manner. Smoking may play a role in advancing the onset of arthritis in those who are at risk of cigarette smoke exposure and contribute to developing RA. Female also can be more vulnerable to cigarette challenge. More precise, large scale epidemiological study may help to verify these observations.

**Disclosure:** J. W. Kim, None; J. Lee, None; Y. S. Hong, None; S. H. Park, None; J. H. Ju, None.


**Abstract Number:** 402

**Alteration of the Intestinal Microbiome in the Preclinical Phase of Experimental Arthritis and the Efficacy of Microbiota Modulation in Established Arthritis in Mice**

Rebecca Rogier¹, Heather Evans-Marin², Julia Manasson³, Peter M. van der Kraan⁴, Wim B. van den Berg⁵, Marije I. Koenders⁴, Jose U. Scher⁶ and Shahla Abdollahi-Roodsaz⁷,⁸,¹ Experimental Rheumatology, Radboud University Medical Center, Nijmegen, Netherlands, ²Division of Rheumatology, New York University School of Medicine, New York, NY, ³Department of Medicine, Division of Rheumatology, New York University School of Medicine, New York, NY, ⁴Experimental Rheumatology, Radboud university medical center, Nijmegen, Netherlands, ⁵Rheumatology Research and Advanced Therapeutics, Radboud University Medical Center, Nijmegen, Netherlands, ⁶New York University School of Medicine, New York, NY, ⁷Department of Medicine, Division of Rheumatology, New York University School of Medicine, New York, NY, ⁸Rheumatology, Radboud University Medical Center, Nijmegen, Netherlands

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017
**Session Title:** Rheumatoid Arthritis – Animal Models Poster I
**Session Type:** ACR Poster Session A
**Session Time:** 9:00AM-11:00AM
Background/Purpose:

The composition of intestinal microbiota is perturbed in patients with new-onset and chronic rheumatoid arthritis (RA). However, it is not known whether the changes in the intestinal microbiome precede the development of arthritis or are rather a consequence of the inflammatory processes. Furthermore, while both germ-free condition and administration of oral antibiotics prevent arthritis in mice, it is unclear whether modulation of the intestinal microbiota after the onset of arthritis may still suppress the disease. We aimed to identify alterations of the intestinal microbiome in the preclinical phase of inflammatory arthritis, and evaluate the efficacy of microbiota modulations in the treatment of established arthritis in mice.

Methods:

We sequenced fecal bacterial 16S rRNA genes of mice immunized for the induction of collagen-induced arthritis (CIA) prior to the onset of arthritis compared with naïve condition. To assess the efficacy of microbiota modulation during arthritis, mice with ongoing CIA were treated with oral antibiotics to partially eliminate the intestinal microbiota. T cell differentiation and production of cytokines in intestinal lamina propria and joint-draining lymph nodes were assessed by flow cytometry and Luminex. Arthritis was assessed macroscopically and by histology. K/BxN serum-transfer arthritis was used to assess the role of microbiota in T cell-independent arthritis.

Results:

The preclinical phase of arthritis in mice was characterized by marked changes in the intestinal microbiome, represented by a significant increase of the phylum Bacteroidetes and a decrease of Firmicutes and Proteobacteria. Among the most abundant bacterial families, S24-7 and Staphylococcaceae were expanded, whereas Lachnospiraceae were reduced during the early immune-priming phase of CIA. Several operational taxonomic units associated with S24-7 family increased, while those assigned to Lachnospiraceae and Ruminococcaceae decreased in the intestinal microbiota before the clinical onset of arthritis. The abundance of intestinal lamina propria Th17 cells significantly correlated with the severity of CIA; however, lamina propria Th1 cells were not correlated with arthritis. Elimination of intestinal microbiota during established arthritis specifically suppressed intestinal Th17 cell differentiation without affecting Th1 and regulatory T cells. Importantly, elimination of intestinal microbiota suppressed Th17 cell differentiation and IL-17 production in joint-draining lymph nodes, and reduced the severity of established CIA. In contrast, the T cell-independent serum-transfer arthritis was not affected by this strategy.

Conclusion:

These observations suggest that perturbations of the intestinal microbiome precede the development of inflammatory arthritis. Similar studies are warranted in human pre-RA or at-risk individuals to shed light on the potential relevance of the microbiome in the preclinical phase of RA. Our studies also suggest that modulation of the intestinal microbiota after the onset of arthritis may still provide opportunities to treat inflammatory arthritis.

Disclosure: R. Rogier, None; H. Evans-Marin, None; J. Manasson, None; P. M. van der Kraan, None; W. B. van den Berg, None; M. I. Koenders, None; J. U. Scher, NIAMS-NIH, 2; S. Abdollahi-Roodsaz, None.

Abstract Number: 403

Cardiac Immune Cells in SKG Mice with Inflammatory Arthritis before and after Myocardial Infarction

Christine Hsieh1, Isabella Imhof2, Luyi Li3, Erene Niemi1, Matthew Bell1, Joel Karliner4 and Mary Nakamura5, Medicine, SFVA/UCSF, San Francisco, CA, Medicine, SFVA/NCIRE, San Francisco, CA, SFVA/UCSF, San Francisco, CA, Medicine, SFVA/UCSF, San Francisco, CA, Department of Medicine, Division of Rheumatology, UCSF/SFVA, San Francisco, CA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Animal Models Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM
Background/Purpose:

Cardiovascular disease is a major cause of morbidity and mortality in patients with rheumatoid arthritis (RA). RA patients have an increased incidence of both myocardial infarction (MI) and congestive heart failure. Cardiac immune cells have been demonstrated to influence cardiac remodeling post infarction and our study examined the effect of inflammatory arthritis on cardiac immune cells using a mouse model of myocardial infarction in SKG mice, a model of inflammatory arthritis.

Methods:

Arthritis was induced in female SKG mice (BALB/c ZAP-70W163C-mutants) with a single injection of zymosan at 12 weeks age and were examined after development of arthritis at 4 weeks. Wild type Balb/c mice, SKG mice, and SKG mice with arthritis (4 weeks post-zymosan) with MI underwent permanent left anterior descending coronary artery ligation. Cardiac leukocytes were evaluated at day 1 and 6 post-infarction, following harvest with cardiac perfusion, disaggregation of the heart, collagenase digestion, cellular isolation and antibody staining for multicolor flow cytometry. Cells were analyzed using a FACS Aria and FlowJo software (hearts were analyzed individually, 5 mice per group) using lineage markers (CD90/CD19/NK1.1/Ly-6G) to evaluate T cells, B cells, NK cells, granulocytes and myeloid markers CD11b, F4/80, Ly-6C.

Results:

Hearts isolated from SKG mice without arthritis showed a slight increase in the number of cardiac neutrophils compared with wild type Balb/c, that was increased by 3-4 fold in SKG mice with arthritis. At baseline SKG mice with arthritis also had a 2-3 fold increase in inflammatory macrophages (Ly6C+) compared with either SKG or Balb/c mice. Hearts isolated from SKG mice with arthritis 1 day post MI, showed a 5-6 fold increase in Ly6G+ cells (neutrophils) and Ly6C+/CD11b (monocyte/macrophages) cells compared to the basal numbers seen in hearts isolated from wild-type Balb/c mice. At day 6, SKG mice and SKG mice with arthritis both showed a persistent increase in Ly-6C+ macrophages compared with the decrease in these cells observed in Bal/c mice at the same time point. Functional outcomes post-MI correlated with these changes are currently being evaluated.

Conclusion:

We found that inflammatory arthritis induces changes in the number and phenotype of cardiac immune cells in mice both before and after myocardial infarction which likely influences cardiac repair and ventricular remodeling post-MI contributing to detrimental cardiac outcomes with inflammatory arthritis.

Disclosure: C. Hsieh, None; I. Imhof, None; L. Li, None; E. Niemi, None; M. Bell, None; J. Karlner, None; M. Nakamura, None.

Gut Microbiota Modify Inflammatory Arthritis through Autoantibody Generation and Mucosal Cytokines Alteration

Widian Jubair1, Sumitra Adhikari2, Nirmal Banda2 and Kristine Kuhn3, 1Rheumatology, University of Colorado, Aurora, CO, 2Division of Rheumatology, UC Denver School of Medicine, Denver, CO, 3Division of Rheumatology, University of Colorado School of Medicine, Aurora, CO

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Animal Models Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

The pathogenesis of rheumatoid arthritis (RA) is thought to be influenced by a combination of genetic and environmental factors. Observations of microbial dysbiosis in patients with RA have raised interest in studying microbial-mucosal interactions as a potential trigger of RA. Using the murine collagen-induced arthritis (CIA) model, which is dependent upon generation of T and B cell reactivity
to CII as well as complement activation, we hypothesized that microbiota are required for the development of robust autoimmune arthritis.

**Methods:**

Male 6-week old DBA/1j mice were immunized with bovine type II collagen (CII) in Complete Freund’s Adjuvant (CFA) on days 0 and 21. Microbiota depletion was performed by continuous administration of broad spectrum antibiotics in drinking water early (7 days preceding and throughout the study) or late (starting after day 21 throughout the study) in the disease process. Microbial depletion was confirmed by quantifying bacterial 16S rRNA by qPCR in feces. Sera were collected every 7 days during the study for autoantibody and cytokine testing. Mice were euthanized on day 35 and intestinal tissues were harvested for cytokine analyses by ELISA. Disease severity starting at day 21 was assessed by assigning a score for the degree of paw swelling.

**Results:**

Depletion of the microbiota prior to the induction of CIA resulted in ~50% reduction in disease severity associated with significantly reduced serum inflammatory cytokines and anti-CII antibodies. In intestinal tissue, we observed delayed IL-17A and IL-22 responses. Unexpectedly, microbial depletion during the late, effector phase of CIA resulted in >90% decrease in disease severity and 50% reduction in prevalence. In these mice, anti-CII antibodies were mildly reduced, but were significantly impaired in their ability to activate complement. In addition to reduced systemic inflammatory cytokines and intestinal IL-17A and IL-22, IL-23 was significantly reduced, suggesting it may link mucosal immune responses with systemic autoantibody effectivity. Studies are now aimed at understanding this mechanism.

**Conclusion:**

While future studies are needed to solidify the role of the microbiota in driving CIA, our data supports a model in which intestinal dysbiosis triggers mucosal immune responses that stimulate systemic B cell activities that are key for the development of inflammatory arthritis. Understanding the pathway by which microbiota and mucosal immune responses modulate systemic autoantibody production is pivotal, as targeting the microbiota during the preclinical, seropositive phase of RA may have potential for disease prevention.

**Disclosure:** W. Jubair, None; S. Adhikari, None; N. Banda, None; K. Kuhn, None.


**Abstract Number:** 405

**Dynamics of Transcriptional Signatures from Purified Synovial Macrophage Subsets during Acute and Chronic Murine Models of Inflammatory Arthritis**

**Philip J. Homan, Salina Dominguez, Harris Perlman, Deborah R. WInter and Carla Cuda, Department of Medicine Division of Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL**

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Rheumatoid Arthritis – Animal Models Poster I  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Rheumatoid arthritis (RA) manifests in persistent synovial inflammation, cellular infiltration and pro-inflammatory cytokine production, resulting in progressive joint destruction. Macrophages have been implicated in RA progression and persistence through production of degradative enzymes, cytokines, and chemokines. However, the mechanisms underlying these activities are not fully elucidated. We previously demonstrated that naïve mouse joints contain both MHC II+ (monocyte-derived) and MHC II- (tissue-resident) macrophages. Interestingly, we have shown that the monocyte-derived macrophages drive inflammation, while the tissue-resident macrophages are involved in resolution based on an acute model of inflammatory arthritis. Thus, we have optimized a multi-parameter flow cytometry protocol to isolate synovial macrophage subsets to perform subset-specific transcriptomic analysis.
Methods: We used 3 mouse model of arthritis: the acute inducible K/BxN serum transfer-induced arthritis (STIA) model, and chronic inducible collagen induced arthritis (CIA) model, and the spontaneous KRN/Ag7 mice. STIA and CIA was induced in 10-12 week old female C57BL/6 mice. Flow cytometric analysis was employed to delineate macrophage subsets via expression of MHC II and CX3CR1 to obtain 4 distinct macrophage populations. These populations were sorted throughout the course of arthritis by FACS. RNA was extracted from sorted macrophage populations and processed for RNA-seq using Quantseq 3’ mRNA library preparation. The RNA-seq libraries were sequenced on an Illumina NextSeq 500 to an average depth of 5 million reads. The reads were aligned and mapped to genes using STAR and HTseq respectively.

Results: We observe by flow cytometry that the predominance of individual synovial macrophage subsets shift throughout the initiation, progression and resolution phases of arthritis and eventually return to their steady-state phenotype. PCA analysis of macrophage subsets in a naïve mouse show distinct transcriptional profiles. Analysis of the transcriptional profiles over the course of arthritis reveals that each macrophage subset responds differently at each phase of inflammation. K-means clustering of specific synovial macrophage subsets have identified distinct gene clusters and cellular processes that are differentially regulated to dictate their function during arthritis. Synovial macrophage populations from each arthritic model display a similar response to inflammation, suggesting that the transcriptional signatures and function of macrophages are consistent in inflammatory arthritis.

Conclusion: We conclude that fluctuations in the synovial macrophage populations over the course of arthritis coincide with the different phases of joint inflammation. These dynamics indicate that the specific macrophage subsets have different function during the course of disease as evidenced by their distinct transcriptional profiles. These high-throughput genomic approaches applied to macrophage subsets from models of both acute and chronic inflammatory arthritis allows us to comprehensively map their role in disease, thereby providing insight into potentially useful targets for therapy.

Disclosure: P. J. Homan, None; S. Dominguez, None; H. Perlman, None; D. R. WInter, None; C. Cuda, None.


Abstract Number: 406

Mapping Changes in Monocyte and Macrophage Populations in the Synovium: An Aging Study in Arthritic KRN Ag7 Mice

Anna B Montgomery1, Carla Cuda2, Philip J. Homan3, Harris Perlman2 and Deborah R. WInter2, 1Division of Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL, 2Department of Medicine Division of Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL, 3Division of Rheumatology, Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Animal Models Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is an autoimmune disease of the joints associated with accelerated aging and increased mortality. Further, RA is linked with a number of co-morbidities including cardiovascular disease, which accounts for 40% of RA mortality. Synovial macrophages are a key effector cell in joint inflammation, and a reduction in sublining synovial macrophages is the only current reproducible biomarker for successful response to therapy. Thus, characterization of synovial macrophages during disease could provide insight into progression of RA and increased mortality upon aging. To that end, the aim of this study was to use KRN Ag7 mice that develop spontaneous arthritis and atherosclerosis to monitor changes in the cellular composition of arthritic synovium in parallel with non-diseased C57Bl/6 controls.

Methods: KRN Ag7 and C57Bl/6 mice were bred in house and euthanized at desired timepoints (1, 3, 6, 9, 12, and 18 months) when ankles were collected for extraction of synovium. Single cell suspensions were prepared from synovial tissue and stained with an antibody cocktail designed to identify monocyte and macrophage populations, which were sorted from single cell suspensions using BD FACSaria 4-Laser. Statistical analysis was carried out in Flowjo v9 and Prism7. Statistical significance was defined P ≤ 0.05.
**Results:** KRN Ag\(^7\) mice displayed arthropathy from birth, and 20% increased mortality compared to C57Bl/6 at 12 months. Flow cytometry analysis of synovial tissue showed a trend towards an overall reduction in CD11b\(^+\) leukocytes in KRN Ag\(^7\) mice, which became statistically significant from 6 months. Further analysis of KRN Ag\(^7\) synovium identified two phases of disease, an inflammatory phase from months 1-3 and an attempted resolution phase from 6 months. The inflammatory phase was characterized by significant increases in eosinophils and neutrophils and a decrease in dendritic cells compared to C57Bl/6. During resolution phase levels of these three populations trended towards C57Bl/6 levels, but remained significantly different. Levels of neutrophils in KRN Ag\(^7\) mice also correlated with Ly6c\(^lo\) monocytes, which are required for neutrophil recruitment. Levels of CD11b\(^+\)CD64\(^+\)Ly6c\(^lo\) macrophages in KRN Ag\(^7\) synovium peaked in inflammation phase but remained lower than those of C57Bl/6 at all time points. Subdivision of macrophages into 4 populations based on expression of MHCII and CX3CR1 identified populations associated with both phases of disease. MHCII\(^+\)CX3CR1\(^+\) and MHCII\(^-\)CX3CR1\(^-\) macrophages were significantly higher and lower respectively than C57Bl/6 during inflammation, but during initial resolution at 6 months reached comparable levels to those of C57Bl/6. However this was not maintained, and levels of both populations returned to baselines by 18 months. Neither MHCII\(^+\)CX3CR1\(^+\) nor MHCII\(^-\)CX3CR1\(^-\) macrophages significantly changed.

**Conclusion:** Using KRN Ag\(^7\) mice, that best recapitulate human disease, we have characterized the cellular dynamics in arthritis upon aging, which are distinct from those observed in non-arthritic mice. By identifying the critical populations, and further characterization of their transcriptional profile, we can provide insight into RA progression with age.

**Disclosure:** A. B. Montgomery, None; C. Cuda, None; P. J. Homan, None; H. Perlman, None; D. R. Winter, None.

**Abstract Number:** 407

**Selective Inhibition of Tfh Cells By a Small Molecule Inhibitor Abrogates Progression of Experimental Inflammatory Arthritis**

**Frank Migliore**\(^1\), Sedrick Bradley\(^1\), Linh Hellmers\(^1\), Quretul Quresh\(^2\), Jerald M. Zakem\(^3\), William E. Davis\(^3\), Tamika Webb-Detiege\(^1\), Zongbing You\(^4\), Robert Quinet\(^2\) and Xin Zhang\(^5\), \(^1\)Ochsner Clinic Foundation, New Orleans, LA, \(^2\)Rheumatology, Ochsner Medical Center, New Orleans, LA, \(^3\)University of Queensland School of Medicine, Brisbane, Australia, \(^4\)Tulane University Health Science Center, New Orleans, LA, \(^5\)Laboratory of Cellular Immunology, Institution of Translational Research, Ochsner Medical Center, New Orleans, LA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Rheumatoid Arthritis – Animal Models Poster I  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**
Rheumatoid arthritis (RA) is a systemic inflammatory autoimmune disease characterized by progressive infiltration of the joints by T cells and other leukocytes, production of mediators of inflammation, and the eventual destruction of joints. T follicular helper (Tfh) cells are a unique subset of CD4\(^+\) T cells, predominantly located in B cell follicles, and regulate the survival of B cells and antibody production in germinal centers. Our previous studies have showed that circulating Tfh cells were significantly increased in active RA patients, correlating with the percentage of plasmablasts, anti-CCP antibody titer, and disease activity in active RA patients, indicating that Tfh cells may play an important role in RA pathogenesis. The purpose of this study is to investigate the therapeutic potential of a small molecule inhibitor targeting Tfh cells in mice with collagen-induced arthritis (CIA).

**Methods:**
CIA was induced in twenty-four DBA/1 mice by immunization with chicken type II collagen. Following the onset of clinical arthritis, mice were treated with a small molecule inhibitor (SMI-Tfh) selective blockage of Tfh cell signature transcription factor Bcl-6. Disease progression was monitored daily and recorded by arthritis severity scores weekly. Blood, spleen, and affected paws were collected at the end of the study. Tfh cells in spleen and blood were identified by their signature surface markers (CD4\(^+\)CXCR5\(^+\)ICOS\(^+\)) via flow
cytometry and analyzed using FlowJo software. The immune cells were further confirmed in mice spleen by immunohistochemistry staining. Statistical analysis was carried out using GraphPad Prism software and the significance was evaluated by t test.

Results:

Mice developed arthritis four weeks after immunization with type II collagen. Treatment with SMI-Tfh (50mg/kg) significantly reduced the disease progression/activity (as measured by paw swelling) in mice with CIA. SMI-Tfh significantly inhibited the frequency of Tfh cells in spleen ($P<0.01$), but not the frequency of circulating Tfh cells in CIA mice ($P>0.05$). In addition, SMI-Tfh also inhibited B cell proliferation induced by Tfh cells and antibody production in vitro.

Conclusion:

The small molecule inhibitor SMI-Tfh selectively inhibits Tfh cells and abrogates progression/activity of inflammatory arthritis in CIA mouse model. Treatment with our small molecule SMI-Tfh in CIA mice provides a potential strategy for joint protection and may be beneficial in RA patients. This is first report that a small molecule targeting Tfh cells in RA may be an approach worth further investigation in RA.

Disclosure: F. Migliore, None; S. Bradley, None; L. Hellmers, None; Q. Quresh, None; J. M. Zakem, None; W. E. Davis, None; T. Webb-Detiege, None; Z. You, None; R. Quinet, None; X. Zhang, None.


Abstract Number: 408

CR6086 Is Highly Effective and Improves Methotrexate Effect in a Mouse Model of Rheumatoid Arthritis

Gianfranco Caselli, Flora Ferrari, Eleonora Comi, Marco Perrella, Camilla Recordati, Adriana Grotti, Rosanna Cavagnoli, Marco Lanza and Lucio C. Rovati, Rottapharm Biotech, Monza, Italy, Milano, Italy, Milan, Italy, Milano, Italy, Milan, Italy, Milan, Italy

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Animal Models Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: CR6086, a selective EP4 antagonist, dose-dependently improves disease features in rheumatoid arthritis (RA) models in rodents. Indeed, recent studies highlight the role of the EP4 receptor in modulating autoimmunity and in counteracting bone erosion. Aim of the present study was to test CR6086 as an add-on medication with methotrexate (MTX).

Methods: DBA/1 male mice were immunized with bovine type II collagen (BCII) in CFA. On arthritis onset, animals were assigned to the following experimental groups: vehicle, oral CR6086 30 mg/kg/day, MTX 1 or 3 mg/kg/three times a week alone or in combination with daily CR6086 30 mg/kg. Edema measurement and clinical scores were blindly determined daily before drug administration. After 2 weeks of treatment, mice were sacrificed and serum BCII antibodies measured. Paw joints were blindly scored for histological features. Data were analyzed by ANOVA or by Kruskal-Wallis test followed by appropriate post-hoc comparison test.

Results: CR6086 strongly and significantly reduced score and edema within the first week of treatment compared to vehicle. MTX 3 mg/kg modestly reduced clinical signs over the second week of treatment, while MTX 1 mg/kg was inactive. CR6086/MTX combined treatments significantly reduced clinical score and edema within the first week of treatment. Figure 1 reports the AUC analysis of the whole treatment. Post-hoc pairwise comparisons showed that combined treatments were significantly superior to each single treatment ($P<0.05$ and $P<0.01$ vs. CR6086 and MTX alone, respectively).
Histological features showed a similar treatment pattern (Fig. 2), but the effects of CR6086 were so strong when given alone that we could not show a significant synergism with MTX but only a trend.

All treatments, but MTX 1 mg/kg, decreased BCII antibodies serum levels (Fig. 3).
Conclusion: In a widely used animal model for RA, CR6086 was effective on all parameters examined both alone and combined with MTX. The superior overall efficacy of CR6086 vs. a classical immunosuppressant as MTX, at equally effective doses on BCII antibodies, outlines that CR6086 independently controls various pathological RA pathways. Moreover, the fact that CR6086 improved MTX effect strengthens its use in early RA in DMARD naïve patients, as presently investigated in clinical trials.

Disclosure: G. Caselli, Rottapharm Biotech, 3; F. Ferrari, Rottapharm Biotech, 3; E. Comi, Rottapharm Biotech, 3; M. Perrella, Rottapharm Biotech, 3; C. Recordati, Rottapharm Biotech, 5; A. Grotti, Rottapharm Biotech, 3; R. Cavagnoli, Rottapharm Biotech, 3; M. Lanza, Rottapharm Biotech, 3; L. C. Rovati, Rottapharm Biotech, 3.

An Evaluation of Absolute Neutrophil Count As a Biomarker of Inflammatory and Clinical Disease Activity in Baricitinib-Treated Patients

Iain B. McInnes¹, Lee S. Simon², Robert J. Moots³, Vipin K. Arora⁴, John D. Bradley⁴ and David Muram⁴, ¹University of Glasgow, Glasgow, United Kingdom, ²SDG LLC, Cambridge, MA, ³University of Liverpool, Liverpool, UK, Liverpool, United Kingdom, ⁴Eli Lilly and Company, Indianapolis, IN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Rheumatoid arthritis (RA) patients (pts) tend to have higher absolute neutrophil count (ANC) values compared to healthy individuals.¹ Baricitinib (BARI), an oral, selective Janus kinase (JAK)1/JAK2 inhibitor,² reduced disease activity levels in RA pts with an inadequate response (IR) to methotrexate (MTX).³ BARI also reduced neutrophil counts in these pts.³ Herein we assessed the association between changes in ANC and the reduction in inflammation, as determined by high-sensitivity C-reactive protein (hsCRP) levels, and by inference clinical responses in pts receiving BARI 4-mg in the RA-BEAM trial.

Methods: RA-BEAM was a 52 week (wk) Phase 3 trial with RA pts randomized to placebo, BARI 4-mg once daily, or adalimumab 40-mg biweekly. Primary end-point of the trial was the proportion of pts achieving ACR20 at wk 12. This post hoc analysis evaluated the changes in observed ANC in BARI 4-mg treated pts with either ≤15% or ≥70% reduction in hsCRP from baseline to wk 12. Proportion of pts achieving low disease activity (LDA), as determined by Clinical Disease Activity Index (CDAI) ≤10, or DAS28-hsCRP <2.6 at 12 wks was evaluated as a function of percent change in ANC from baseline to wk 8, at which time a peak decline in ANC was observed (Figure 1).

Results: Of the 487 pts in the BARI 4-mg treatment arm of the RA-BEAM study, 78 pts demonstrated ≤15% reduction in hsCRP and 298 pts had ≥70% reduction in hsCRP at 12 wks. The mean neutrophil count at wk 8 in pts with ≤15% reduction in hsCRP was higher when compared to pts with ≥70% reduction (Figure 2), suggesting that the decline in ANC was associated with reduction in the inflammatory process. The reduction in ANC was associated with an improved clinical response as demonstrated by the proportion of pts achieving LDA (CDAI ≤10) or DAS28-hsCRP <2.6 at 12 wks. In contrast, a smaller proportion of pts achieved LDA when an increase in ANC was observed (Figure 3). These observations were similar regardless of the use of concomitant oral corticosteroids.

Conclusion: The decline in ANC is associated with a reduction in the overall inflammatory process and may also be associated with disease activity.

Figure 1. Least squares mean change from baseline in neutrophils (10^6 cells/L) in MTX-IR patients from the RA-BEAM trial

LS Mean Change from Baseline

P-value vs. Placebo

*** p<0.001

Time (weeks)

Placebo (N=488)
Barcinib 4-mg (N=487)
Adalimumab (N=330)

LS=least squares, N=number of patients

Figure 2. Mean neutrophil count in BARI 4-mg treated MTX-IR patients

Mean Neutrophil Count (SE)

Patients with ≤ 15% reduction in hsCRP, mLOCF (N=78)
Patients with ≥ 70% reduction in hsCRP, mLOCF (N=298)

mLOCF=modified last observation carried forward, N=number of patients in specific category at week 12, SE=standard error


Abstract Number: 410

Association between Anti-Citrullinated Protein Antibody Status and the Incidence of Erosive Disease in Patients with RA

Leslie R Harrold1, Heather J. Litman2, SE Connolly3, E Alemao3, Sabrina Rebello4, W Hua2 and Joel Kremer5, 1University of Massachusetts Medical School, Worcester, MA, 2Corrona, Southborough, MA, 3Bristol-Myers Squibb, Princeton, NJ, 4Corrona, LLC, Southborough, MA, 5Albany Medical College and The Center for Rheumatology, Albany, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Background/Purpose: RA is characterized by the production of autoantibodies including anti-citrullinated protein antibodies (ACPAs).\(^1\) ACPAs are considered a prognostic indicator for more severe RA and more rapid disease progression.\(^2,3\) Little is known regarding the incidence of erosions overall in a contemporary cohort of patients with access to biologics or the association with ACPA status. This analysis aimed to characterize the incidence of erosive disease and its association with ACPA serological status in patients with RA.

Methods: We identified patients aged ≥18 years with RA disease duration ≤2 years who were enrolled in the Corrona Registry (October 2001 to June 2016) with ACPA status available at or before their enrollment visit and no evidence of erosions on their first visit at which radiographic information was reported. To assess incidence of erosions, we followed patients until their first radiograph showed evidence of erosions or their last follow-up visit, whichever came first. The primary outcome was the incidence of erosions (calculated as the total number of first erosions divided by the total radiographic follow-up time), overall and by ACPA status (negative anti-cyclic citrullinated peptide [CCP] <20 vs positive anti-CCP ≥20), unadjusted and adjusted (for age and baseline disease activity using the CDAI). Cox proportional hazards modeling was used to assess the hazard ratio (HR) (with 95% CIs) of erosive disease.

Results: In total, 693 patients (452 ACPA positive and 241 ACPA negative) met the inclusion criteria. Most were women (70.6%), middle-aged (mean [SD] 55 [13.3] years), with moderate disease activity based on the CDAI (13.9 [13.0]). Prior use of ≥1 biologic/targeted synthetic DMARD had occurred in 29.3% of patients. In total, 187 first erosions over 1344.27 person-years of radiographic follow-up time were recorded with an incidence rate of 13.9 erosions/100 person-years of follow-up. The incidence of erosions among ACPA-positive patients was 14.8/100 person-years vs 12.2/100 person-years in those who were ACPA negative (unadjusted HR 1.21; 95% CI 0.88, 1.67; p=0.23; Table). In adjusted analyses, ACPA status was associated with the incidence of erosions (HR 1.30; 95% CI 0.94, 1.80; p=0.11), although the estimate included unity (Table).

Table. Incidence Rate Overall and by ACPA Status

<table>
<thead>
<tr>
<th>Total number of first erosions</th>
<th>Total number of person-years of radiographic follow-up time</th>
<th>Incidence rate of erosions (per 100 person-years)</th>
<th>Unadjusted HR (95% CI)</th>
<th>Adjusted* HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>187</td>
<td>1344.27</td>
<td>13.9</td>
<td>1.21 (0.88, 1.67)</td>
</tr>
<tr>
<td>ACPA+</td>
<td>132</td>
<td>893.60</td>
<td>14.8</td>
<td>1.21 (0.88, 1.67)</td>
</tr>
<tr>
<td>ACPA–</td>
<td>55</td>
<td>450.67</td>
<td>12.2</td>
<td>p=0.23 reference</td>
</tr>
</tbody>
</table>

*Adjusted for baseline CDAI score (0–10, >10–22, >22) and baseline age (18–<45, 45–<55, 55–<65, 65–90 years)

ACPA=anti-citrullinated protein antibody; HR=hazard ratio

Conclusion:

In this contemporary cohort of patients with early RA, incident erosions were common. Our findings suggest further exploration of the association of ACPAs and the incidence of erosions is needed, and whether medications including biologic/targeted synthetic DMARDs influence the relationship.


Disclosure: L. R. Harrold, Corrona, 1,Pfizer Inc, 2,Roche Pharmaceuticals, 5,Corrona, 3; H. J. Litman, Corrona, 3; S. Connolly, Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1; E. Alemao, Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1; S. Rebello, Corrona, 3; W. Hua, Corrona, 3; J. Kremer, Corrona, 1,AbbVie, BMS, Genentech, Lilly, Novartis, Pfizer, 2,Corrona, 3,Genentech and Biogen IDEC Inc., 8.

Factors That Drive Treatment Recommendation during Rheumatoid Arthritis Patient’s Follow-up, Differ According to Physician Experience

César Sifuentes-Cantú1, Irazu Contreras-Yañez2, Lina Saldarriaga Rivera3, Ana Cecilia Lozada4, Marwin Gutierrez5 and Virginia Pascual-Ramos1, 1Department of Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, 2Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico, Mexico, 3Instituto Nacional de Rehabilitación, Mexico, Mexico, 4Division of musculoskeletal and rheumatic diseases, Instituto Nacional de Rehabilitación, Mexico City, Mexico, 5Rheumatology, Instituto Nacional de Rehabilitación, Mexico City, Mexico

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

The management plan for rheumatoid arthritis (RA) might be a relatively simple task if only disease activity is considered but might become more complex when additional factors are considered.

Previously, in a real clinical setting of RA outpatients, we explored the impact of musculoskeletal ultrasound, added to clinical evaluations in the treatment decision; we found that ultrasound had a greater impact in the trainee (TR) than in the senior rheumatologist (SR).

The aim of the present study was to investigate which factors impact the treatment recommendation in RA outpatients and to detect potential differences among 2 rheumatologists categorized by their experience, TR vs. SR.

Methods:

Eighty-five consecutive and randomly selected RA outpatients underwent 170 assessments, 85 each by the SR and the TR. Initially, both physicians performed a complete rheumatic assessment which included disease activity as per DAS28 and recommended a treatment. Then, the patients underwent a musculoskeletal evaluation by an independent rheumatologist. In the final step, the TR and the SR integrated ultrasound findings with their previous evaluation and reviewed their recommendations. In addition, immediately after each patient encounter, both physicians were instructed to select and rate, which among the following factors were determinant in the final treatment proposal: clinical assessments, ultrasound findings, comorbidities, treatment related adverse events, costs/availability, patient’s preference and DMARD maximum dose. In all the instances, the SR and the TR were blinded to each other assessments. Data were obtained on standardized formats. Descriptive statistics were used. The study was approved by the local IRB and all the patients signed informed consent.

Results:

Patients were primary middle-aged (mean±SD: 45.1 ± 12.4 years) female (91.4%) and had disease duration of 7.5±3.9 years. The majority of the patients were in DAS28 remission (<2.6) and 24 (28.2%) showed some disease activity. All the patients were on DMARDs and 48% had additional low doses of oral corticosteroids.

Clinical assessments were rated as determinants in the totality of the clinical scenarios, followed by ultrasound findings in 84.7%, DMARD maximum dose in 41.2%, comorbidities in 23%, DMARD cost/availability in 21.2%, DMARD-related adverse events in 20% and finally, patient preference was rated as determinant in 14.1% of the clinical scenarios. Interestingly, the SR and the TR differed in the selection of the factors they considered determinant for the treatment proposal (Figure).

Conclusion:

Disease activity drives the treatment decision during RA patients follow-up, although additional factors may be considered. Considerable variation was observed in how doctors rated those factors and these variations depended on physician’s experience.

Figure
Disclosure: C. Sifuentes-Cantú, None; I. Contreras-Yañez, None; L. Saldarriaga Rivera, None; A. C. Lozada, None; M. Gutierrez, None; V. Pascual-Ramos, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/factors-that-drive-treatment-recommendation-during-rheumatoid-arthritis-patients-follow-up-differ-according-to-physician-experience

Abstract Number: 412

Baseline Values for Plantar Pressure and Background Characteristics As Indicators for the Limit of Conservative Treatment of Rheumatoid Forefoot Deformity

Hyunho Lee¹, Hajime Ishikawa¹, Asami Abe¹, Yumi Nomura¹, Eriko Hasegawa¹, Chinsu Takai¹, Daisuke Kobayashi¹, Hiroshi Otani¹, Satoshi Ito¹, Takanobu Sumino², Takao Ishii², Shu Saito³, Yasuaki Tokuhashi³, Kiyoshi Nakazono¹ and Akira Murasawa¹,

¹Department of Rheumatology, Niigata Rheumatic Center, Shibata, Japan, ²Department of Orthopaedic Surgery, Kawaguchi Municipal Medical Center, Kawaguchi, Japan, ³Department of Orthopaedic Surgery, Nihon University School of Medicine, Itabishi, Japan, ⁴Department of Orthopaedic Surgery, Nihon University School of Medicine, Itabashi, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Forefoot deformities are commonly seen in patients with RA. It has been reported that nearly 90% of the patients have foot problems.¹,² Patients with RA often suffer from callosity or metatarsalgia in the rheumatoid foot. Forefoot surgery is often necessitated in cases of painful forefoot deformities in which conservative treatment proves to be insufficient.³,⁴ The purpose of this study is to investigate the differences in plantar pressure and background characteristics between the patients without scheduled forefoot surgery (group N) and the patients with scheduled forefoot surgery (group S), and to identify those characteristics that might be useful as indicators for conservative treatment.

Methods: Patients with RA were divided into 2 groups: group N and group S. The former consisted of 250 feet in 141 patients, and the latter consisted of 125 feet in 72 patients. DAS28, hallux valgus angle (HVA), the angle between the first and the second metatarsal bone (M1/2), the angle between the first and the fifth metatarsal bone (M1/5) and distribution of the site of callosity were evaluated as background characteristics. Distribution of peak pressure as plantar pressure was measured in 9 sections, including the first interphalangeal joint, the first through the fifth metatarsophalangeal joints (MTPJ), the medial and lateral midfoot, and the hindfoot. In addition, maximum peak pressure (MAXPP), minimum peak pressure (MINPP) and the difference value between MAXPP and MINPP (Δ pressure) were also measured. The MAXPP and MINPP indicates the highest and lowest peak pressure value found among the peak pressure measurements of all 9 sections, respectively. Finally, cut-off values were calculated from the receiver operating characteristic curve for each item which differed significantly between the 2 groups.

Results: In groups N and S, the mean DAS was 3.7 and 3.0 (p<0.001), the mean HVA was 19.4° and 34.5° (P<0.001), the mean M1/2 was 11.5° and 14.1° (P<0.001), and the mean M1/5 was 30.3° and 33.1°, respectively. Callosities were seen at the second and third
MTPJ in half of all patients in group S. The mean peak pressure of group S at the first, second, third MTPJ, medial midfoot and hindfoot was significantly higher than that of group N \((P < 0.001, 0.05, 0.01,0.05 \text{ and } 0.01)\). Significant differences between the 2 groups were also seen in MAXPP, MINPP and \(\Delta\) pressure \((P < 0.001, 0.05 \text{ and } 0.001)\). The cut-off values were 24.9° for HVA, 4.81 kg/cm\(^2\) for MAXPP and 4.51 kg/cm\(^2\) for \(\Delta\) pressure. At the cut-off values, sensitivities were 76.0%, 69.6% and 67.4%, and specificities were 71.2%, 57.2% and 60.8%, respectively. Assessing HVA and MAXPP in combination, sensitivity was 46.4%, and specificity was 90.8%.

**Conclusion:** The combined assessment of HVA and MAXPP appeared to be useful as an indicator for conservative treatment of rheumatoid forefoot deformity. It is important to keep MAXPP under 4.81 kg/cm\(^2\) through drug treatment, orthotic treatment and physical treatment, in order to avoid forefoot surgery.

References:


Disclosure: H. Lee, None; H. Ishikawa, None; A. Abe, None; Y. Nomura, None; E. Hasegawa, None; C. Takai, None; D. Kobayashi, None; H. Otani, None; S. Ito, None; T. Sumino, None; T. Ishii, None; S. Saito, None; Y. Tokuhashi, None; K. Nakazono, None; A. Murasawa, None.


**Abstract Number: 413**

**Economic Burden Associated with Anti-Cyclic Citrullinated Peptide Antibody Positivity in Patients Newly Diagnosed with RA**

J An\(^1\), Z Bider\(^2\), J Kang\(^1\), E Alemao\(^3\), SE Connolly\(^3\) and TC Cheetham\(^1\), \(^1\)Western University of Health Sciences, Pomona, CA, \(^2\)Southern California Permanente Medical Group, Pasadena, CA, \(^3\)Bristol-Myers Squibb, Princeton, NJ

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

**Background/Purpose:** Anti-cyclic citrullinated peptide (anti-CCP) antibody positivity has been suggested as a strong predictor of joint erosion as well as a potential biomarker for guiding treatment decisions. There are limited data evaluating the economic burden of anti-CCP positivity. We investigated the association between anti-CCP positivity and healthcare expenditures in newly diagnosed patients (pts) with RA.

**Methods:** A retrospective cohort study was conducted in adult pts with RA in Kaiser Permanente Southern California (Jan 2007 to Dec 2014). Individuals were followed from their first RA diagnosis (index) for 12 months. Pts were required to have two International Classification of Diseases, Ninth Revision, RA diagnosis codes of 714.0–714.8, a DMARD prescription, and continuous eligibility for 12 months prior to and after index date. Pt demographics, anti-CCP status, co-morbidity and healthcare resource utilization during the study period were collected. Nationally recognized direct medical costs were assigned to healthcare utilizations to calculate healthcare costs in 2015 US dollars. Difference-in-difference (DID) propensity score analyses were conducted to determine the association between anti-CCP positivity and 12-month cost outcomes. A generalized linear regression model with recycled prediction methods was used to quantify the differences of changes in costs \((\delta_{\text{dd}})\) between the anti-CCP-positive (anti-CCP+) and anti-CCP-negative (anti-CCP−) groups.

**Results:** A total of 2448 newly diagnosed pts with RA were identified with a mean (SD) age of 55.5 (14.3) years; 75.7% were female. At baseline, 65.8% of pts were anti-CCP+ and 34.2% were anti-CCP−, where anti-CCP+ pts had fewer co-morbidities (median Elixhauser co-morbidity scores: 3 vs 4; \(p<0.001\)) versus anti-CCP− pts. During follow-up, more anti-CCP+ pts received ≥1 biologic DMARD (22.6 vs 12.9%; \(p<0.001\)) and had more frequent rheumatologist visits (median number: 5 vs 4; \(p<0.001\)) versus anti-CCP−.
During the 12-month follow-up, median (interquartile range) total healthcare expenditure for anti-CCP+ and anti-CCP– pts was $6200 ($3563–13,260) and $7022 ($3885–12,995), respectively. For the DID, when considering baseline costs, pt demographics and co-morbidities, anti-CCP positivity was significantly associated with higher prescription (δdd=$2499; p<0.001), laboratory testing (δdd=$183; p<0.001) and rheumatologist visit costs (δdd=$76; p<0.001). Total incremental cost associated with anti-CCP positivity was estimated as $2163 (p=0.001; Figure). No statistical differences were found in hospitalizations or emergency department-related costs.

Conclusion: In newly diagnosed pts with RA, the higher economic burden for anti-CCP+ pts was mainly driven by pharmacy costs. Future pt-reported outcomes and/or disease progression associated with the early economic burden may help guide treatment decisions.

Disclosure: J. An, Bristol-Myers Squibb, Pfizer, 2; Z. Bider, None; J. Kang, None; E. Alemao, Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1; S. Connolly, Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1; T. Cheetham, Bristol-Myers Squibb, 2.


Multi-Biomarker Disease Activity and Autoantibody Status Lead to Cost Effective Tapering Algorithms in Rheumatoid Arthritis Patients in Sustained Remission

Melanie Hagen1, Matthias Englbrecht2, Judith Haschka3, Michaela Reiser4, Arnd Kleyer5, Axel J. Hueber6, Bernhard Manger7, Camille Figueiredo8, Jayme Fogagnolo Cobra9, Hans-Peter Tony10, Stefanie Finzel11, Stefan Kleinert12, Joerg Wendler13, Florian Schuch13, Monika Ronneberger13, Martin Feuchtenberger14, Martin Fleck15,16, Karin Manger17, Matthias Schmitt-Haendle18, H.-M. Lorenz19, HG Nüßlein20, Rieke Alten21, Joerg C. Henes22, Klaus Krüger23, Georg Schett2 and Juergen Rech24, 1University of Erlangen-Nuremberg, Erlangen, Germany, 2Department of Internal Medicine 3, University of Erlangen-Nuremberg, Erlangen, Germany, 3Medical Department II, St. Vincent Hospital, the VINFORCE Study Group, Academic Teaching Hospital of Medical University of Vienna, Vienna, Austria, 4Department of Medicine 3, Rheumatology and Immunology, University of Erlangen-Nuremberg, Erlangen, Germany, 5Dept of Medicine 3, Rheumatology and Clinical Immunology, Department of Internal Medicine 3 – Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg, Erlangen, Germany, 6Department of Internal Medicine 3 and Institute for Clinical Immunology, University of Erlangen-Nuremberg, Erlangen, Germany, 7Dept of Medicine 3, Rheumatology and Clinical Immunology, University of Erlangen-Nuremberg, Erlangen, Germany, 8Institut de Rheumatologia, Sao Paolo, Brazil, 9Instituto de Reumatologia de Sao Paolo, Sao Paolo, Brazil, 10Rheumatology/Clinical Immunology, University of Würzburg, Würzburg, Germany, 11University of Freiburg, Freiburg, Germany, 12Rheumatologische Schwerpunktpraxis Erlangen, Erlangen, Germany, 13Schwerpunktpraxis Rheumatologie, Erlangen, Germany, 14Rheumatologie/Klinische Immunologie, Kreiskliniken Altötting-Burghausen, Burghausen, Germany, 15Department of Rheumatology and Clinical Immunology, Asklepios Medical Center Bad Abbach, Bad Abbach, Germany, 16Internal Medicine I, University Medical Center of Regensburg, Regensburg, Germany, 17Rheumatology Practice Bamberg, Bamberg, Germany, 18Rheumatology Practice, Bayreuth, Germany, Bayreuth, Germany, 19Rheumatologie, University Heidelberg, Heidelberg, Germany, 20Rheumatology Practice Nuremberg, Nuremberg, Germany, 21Schlosspark-Klinik, University Medicine Berlin, Berlin, Germany, 22Department of Internal Medicine II, Division of Rheumatology,
Background/Purpose:

Achieving remission is the ultimate treatment goal in patients with rheumatoid arthritis (RA). With the development and wider use of highly effective disease modifying anti-rheumatic drugs (DMARD) about half of RA patients reach the disease remission state (1), raising the question about tapering or stopping anti-rheumatic treatment and appropriate predictors (2). The purpose was to analyse the effect of a risk-stratified DMARD tapering algorithm based on multiple-biomarker disease activity (MBDA) score and anti-citrullinated protein (ACPA) status for successful DMARD tapering and treatment cost reduction in RA patients in sustained remission enrolled in the prospective randomized controlled RETRO study (3,4).

Methods: MBDA scores and ACPA status were determined in the baseline samples of 146. A patients in sustained remission. Patients either continued DMARDs (arm1), tapered dose by 50% (arm 2) or stopped DMARDs after tapering (arm 3) for one year according to the RETRO study protocol. Direct treatment costs (including testing costs at baseline) were evaluated every three months. MBDA and ACPA status were used as predictors creating a risk-stratified tapering algorithm based on relapse rates.

Results: RA patients with a low MBDA score (<30) and negative ACPA showed lowest relapse risk (19%). With either single positivity for ACPA or moderate/high MBDA scores (>30) relapse risk increased and was high in double-positive patients (61%). In MBDA negative (<30) and MBDA single-positive (>30) groups, DMARD tapering appears feasible. Considering only patients that did not flare, costs for synthetic and biologic DMARDs in the MBDA-negative and single-positive groups (n=41) would have been 123,751,29€ for full-dose treatment over one year. Tapering and stopping DMARDs in this low-risk relapse groups allowed a reduction of 92,821,50€ (-75%) of DMARD costs. Average reduction of DMARD costs per patient were 2,350,08€ in the double negative (MBDA- /ACPA-) and single negative (MBDA- /ACPA+) group and 1,761,43€ in the MBDA single positive (MBDA+ /ACPA-) group.

Conclusion: Combining MBDA score and ACPA status allows risk stratification for successful DMARD tapering and cost-effective use of biologic DMARD. Given that previous data of the RETRO have shown that patients relapsing after tapering their DMARDs respond well to their reintroduction, a stratified tapering and stopping of DMARDs is not only a cost economic but also clinically feasible strategy.

Disclosure: M. Hagen, None; M. Englbrecht, None; J. Haschka, None; M. Reiser, None; A. Kleyer, None; A. J. Hueber, None; B. Manger, None; C. Figueiredo, None; J. F. Cobra, None; H. P. Tony, None; S. Finzel, None; S. Kleinert, None; J. Wendler, None; F. Schuch, None; M. Ronneberger, None; M. Feuchtenberger, None; M. Fleck, None; K. Manger, None; M. Schmitt-Haendle, None; H. M. Lorenz, None; H. Nüßlein, None; R. Alten, None; J. C. Henes, None; K. Krüger, None; G. Schett, None; J. Rech, None.
Baricitinib Reduces GlycA Levels in Phase 2 and Phase 3 Clinical Trials in Patients with Moderate to Severe Rheumatoid Arthritis

Joel Kremer1, Paul Emery2, Margery A. Connelly3, James D. Otvos4, Steven H. Zuckerman5, Giacomo Ruotolo5, Lei Chen5, Maher Issa5, William L. Macias5 and Iain B. McInnes6, 1Albany Medical College, Albany, NY, 2Leeds MSK Biomed/Chapel Allerton Hospital, Leeds, United Kingdom, 3Laboratory Corporation of America Holdings (LabCorp), Morrisville, NC, 4Laboratory Corporation of America Holding (LabCorp), Morrisville, NC, 5Eli Lilly and Company, Indianapolis, IN, 6University of Glasgow, Glasgow, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Baricitinib (bari) is an oral selective inhibitor of Janus kinase (JAK) 1/JAK2. In the European Union, bari is approved for the treatment of moderate to severe RA in adults. GlycA, a measure of glycosylated acute phase proteins, is an emerging inflammatory marker that may be useful for assessment of disease activity and is associated with subclinical cardiovascular (CV) disease in patients with RA. The objective of this analysis was to assess GlycA levels in a Phase 2 and 3 (RA-BEAM) study in patients (pts) with RA treated with bari.

Methods: In the Phase 2 study, 301 pts were randomized 2:1:1:1:1 to placebo (PBO) or bari (1, 2, 4, or 8 mg) once daily (QD) for 12 weeks (wks). At Wk 12, pts initially assigned to PBO or bari 1 mg were rerandomized 1:1 to bari 2 mg twice daily or bari 4 mg QD; pts initially assigned to bari 2, 4, or 8 mg QD continued that treatment. In RA-BEAM, 1305 pts were randomized 3:3:2 to PBO, bari 4 mg QD, or adalimumab (ADA) 40 mg every 2 wks. GlycA levels were evaluated with nuclear magnetic resonance spectroscopy at baseline and Wks 12 and 24. In these post hoc analyses, change from baseline to week 12 in GlycA levels were compared between treatment groups without adjustment for multiple comparisons.

Results: Treatment with bari resulted in dose-dependent decreases in GlycA levels from baseline to Wk 12 in the Phase 2 study (-7.7% to -14.4% in the 1- and 8-mg treatment groups, respectively), with similar results at Wk 24 (Figure). In RA-BEAM at Wk 12, GlycA levels in pts treated with bari decreased significantly compared to PBO or ADA (Table 1). There were similar reductions in GlycA with bari regardless of baseline statin use (Table 2).

Conclusion: Bari decreases GlycA in a dose-dependent manner; reductions were seen regardless of baseline statin treatment. With recent studies suggesting GlycA as a marker for CV risk, these reductions in Phase 2 and 3 studies in an RA population may portend a reduction in overall CV risk. Further long-term data will be required to assess the possibility.

### Table 1. GlycA levels in the Phase 3 RA-BEAM study

<table>
<thead>
<tr>
<th></th>
<th>Placebo (N=488)</th>
<th>Baricitinib 4 mg (N=487)</th>
<th>Adalimumab (N=330)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline, µmol/L</strong></td>
<td>508.9 (104.6)</td>
<td>517.2 (114.4)</td>
<td>513.9 (106.4)</td>
</tr>
<tr>
<td><strong>Week 12, µmol/L</strong></td>
<td>496.9 (104.3)</td>
<td>404.3 (91.9)</td>
<td>416.3 (105.0)</td>
</tr>
<tr>
<td><strong>Change from baseline to Week 12</strong></td>
<td>-13.6 (3.8)</td>
<td>-110.9 (3.8)**†</td>
<td>-98.7 (4.7)**†</td>
</tr>
</tbody>
</table>

Absolute data are mean (standard deviation); change from baseline data are least-squares mean (standard error). **p≤0.001 vs placebo † p≤0.05 vs adalimumab

### Table 2. Change in lipid and GlycA levels from baseline to Week 12 according to baseline statin use in the Phase 3 RA-BEAM study

<table>
<thead>
<tr>
<th>Baseline Statin Use</th>
<th>Placebo (N=488)</th>
<th>Baricitinib 4 mg (N=487)</th>
<th>Adalimumab (N=330)</th>
<th>Baricitinib 4 mg vs Placebo</th>
<th>Adalimumab vs Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GlycA, µmol/L</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No (n=389)</td>
<td>-13.5 (4.0)</td>
<td>-109.5 (4.0)</td>
<td>-99.5 (4.9)</td>
<td>-96.0 (-107, -85)**</td>
<td>-86.0 (-98, -74)**†</td>
</tr>
<tr>
<td>Yes (n=37)</td>
<td>-14.3 (14.1)</td>
<td>-131.0 (14.3)</td>
<td>-94.2 (16.3)</td>
<td>-116.7 (-157, -77)**†</td>
<td>-79.9 (-123, -37)**†</td>
</tr>
<tr>
<td><strong>Total cholesterol, mg/dL</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No (n=412)</td>
<td>-1.3 (1.3)</td>
<td>25.5 (1.2)</td>
<td>11.6 (1.5)</td>
<td>26.8 (23.4, 30.3)**</td>
<td>12.9 (9.0, 16.8)**†</td>
</tr>
<tr>
<td>Yes (n=37)</td>
<td>-5.7 (6.7)</td>
<td>34.7 (6.4)</td>
<td>10.5 (7.6)</td>
<td>40.4 (22.0, 58.7)**†</td>
<td>16.2 (-3.9, 36.3)</td>
</tr>
<tr>
<td><strong>LDL cholesterol, mg/dL</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No (n=404)</td>
<td>-2.2 (1.1)</td>
<td>15.5 (1.0)</td>
<td>7.6 (1.3)</td>
<td>17.7 (14.8, 20.6)**</td>
<td>9.8 (6.5, 13.0)**</td>
</tr>
<tr>
<td>Yes (n=37)</td>
<td>-4.6 (5.4)</td>
<td>20.5 (5.2)</td>
<td>6.7 (6.2)</td>
<td>25.0 (10.1, 40.0)**</td>
<td>11.2 (-5.1, 27.6)</td>
</tr>
</tbody>
</table>

**p≤0.01, ***p≤0.001 vs placebo CI=confidence interval; LDL=low-density lipoprotein; LSM=least-squares mean; LSMD=least-squares mean difference, SE=standard error**
The Impact of Therapy on Anti-Carbamylated Protein Antibody Isotypes and Serostatus in Patients with Early RA Treated with Abatacept and MTX

LA Trouw¹, SE Connolly², A Johnsen², J Ye², MA Maldonado², REM Toes¹ and TWJ Huizinga¹, ²Leiden University Medical Center, Leiden, Netherlands, ³Bristol-Myers Squibb, Princeton, NJ

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Maturation of autoantibody responses has been suggested to be a proxy for disease maturation. Autoantibody responses against post-translationally modified antigens are present in autoimmune diseases and antibodies directed against carbamylated proteins (anti-CarP antibodies) are a marker of RA. Anti-CarP antibody analysis in patients (pts) with early RA offers the opportunity to estimate whether specific intervention during such early stages of autoantibody development may have an impact on the maturation of the anti-CarP antibody response. We assessed the relationship between changes in anti-CarP isotypes and rates of seroconversion to negative (–ve) in pts with early RA. Methods: In the AVERT study (NCT01142726), pts with early RA were treated with abatacept (ABA)+MTX, ABA monotherapy or MTX alone.¹ Pts were anti-cyclic citrullinated peptide-2 positive (+ve) at baseline for study entry.¹ In this post hoc analysis, concentrations of anti-CarP isotypes were measured using custom ELISAs. Anti-CarP ELISAs for immunoglobulin (Ig)G, IgM or IgA isotypes were performed in pt serum at baseline, and at Days 85 and 365 on treatment. Baseline levels of each anti-CarP antibody isotype and % seropositivity were comparable across treatment arms. Adjusted mean change from baseline was calculated using a longitudinal repeated measures model. Results: At baseline, 51.3, 42.5 and 29.3% of all pts with...
Improvement in Overall Work Productivity Among Biologic-Naïve Patients with Rheumatoid Arthritis Treated with Tocilizumab Subcutaneous Injection: A Prospective, Real World, Observational Study in Japan

Yoshiya Tanaka1, Hitoko Kameda2, Kazuyoshi Saito3, Yuko Kaneko4, Eiichi Tanaka5, Shinsuke Yasuda6, Naoto Tamura7, Keishi Fujio8, Takao Fujii9, Toshihisa Kojima10, Tatsuhiro Anzai11, Chikuma Hamada12, Yoshishisa Fujino13, Shinya Matsuda13 and Hitoshi Kohsaka14

1The First Department of Internal Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan, 2Division of Rheumatology, Department of Internal Medicine, Toho University Ohashi Medical Center, Tokyo, Japan, 3Tobata General Hospital, Fukuoka, Japan, 4Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, 5Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan, 6Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan, 7Department of Internal Medicine and Rheumatology, Juntendo University School of Medicine, Tokyo, Japan, 8Department of Allergy and Rheumatology, The University of Tokyo, Tokyo, Japan, 9Department of Rheumatism and Collagen Disease, Wakayama Medical University, Wakayama, Japan, 10Nagoya Univ. Grad. Schl. of Med., Nagoya, Japan, 11Data Science Division, Statistics Analysis Department 1, EPS Corporation, Tokyo, Japan, 12Department of Information and Computer Technology, Tokyo University of Science, Tokyo, Japan, 13Department of Preventive Medicine and Community Health, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, 14Department of Rheumatology, Tokyo Medical and Dental University (TMDU), Tokyo, Japan

First publication: September 18, 2017

Abstract Number: 417

Improvement in Overall Work Productivity Among Biologic-Naïve Patients with Rheumatoid Arthritis Treated with Tocilizumab Subcutaneous Injection: A Prospective, Real World, Observational Study in Japan
Background/Purpose: This is the first study assessing the effect of subcutaneous tocilizumab (TCZ-SC) and/or conventional synthetic DMARDs (csDMARDs) on work productivity and activity impairment (WPAI) in paid workers (PWs) and homeworkers (HWs) among Japanese patients with RA.

Methods: FIRST ACT-SC was a real-world, prospective, observational study (Jan 2014 to Sep 2015 at 82 centers). Biologic-naïve patients receiving ≥1 csDMARD, both PWs and HWs, and with moderate/high disease activity were enrolled and treated with TCZ-SC +/- csDMARDs or csDMARDs alone. The primary endpoint was the percentage change in overall work impairment (OWI; assessed using the WPAI questionnaire) from baseline to 52 weeks among PWs. Inverse probability of treatment weighting using propensity score was used to adjust for patient background to compare the 2 groups. Depending on the patients' symptoms during the observation period, change of dose, change to another csDMARD, or addition of another csDMARD was allowed.

Results: In total, 377 and 347 patients were enrolled in the TCZ-SC +/- csDMARD and csDMARD-alone groups, respectively, of which 321 (mean±SD age, 57.7±14.0 years; female, 81.6%) and 307 (60.1±12.8 years; 85.7%) patients, respectively, were included in the modified intent-to-treat population. Of these, 233 (72.6%) and 224 (73.0%) patients, respectively, completed 52 weeks of follow-up. The primary and secondary endpoint results are summarized in the Table 1. Although disease activity (DAS28, SDAI, CDAI, etc.) and HAQ-DI improvements were better in the TCZ-SC group compared to the csDMARD group, the weighted percentage change in OWI from baseline was only −0.189 in the TCZ-SC group at 52 weeks, and there was no difference between the 2 groups (weighted treatment difference, 0.003; 95% CI, −0.062 to 0.068; P = 0.929). In contrast, the improvement in percentage activity impairment in HWs and the overall group was significantly better in the TCZ-SC group compared to the csDMARD group at week 52 (P = 0.005 and P = 0.003, respectively). TCZ-SC-treated HWs also showed significant improvement in overall quality of life (QOL), including EQ-5D, J-HAQ, and K6.

Conclusion: There was no significant difference in OWI between the 2 treatment groups. However, activity impairment, disease activity, and QOL in HWs and the overall group were significantly improved with TCZ-SC than with csDMARDs alone. Taken together, improvement in work productivity/activity impairment is determined by differences in TCZ-SC +/- csDMARDs and differences in PWs and HWs at baseline.

Role of the Study Sponsor: This study was supported by funding from Chugai Pharmaceutical Co., Ltd.

Acknowledgments: Medical writing assistance was provided by Mami Hirano, M.S., of Cactus Communications. Support for study management was provided by EPS Corporation.
Exploratory Analysis to Identify Factors Associated with Risk of Structural Progression, Defined As Change from Baseline

Désirée van der Heijde1, Patrick Durez2, Georg Schett3, Esperanza Naredo4, Mikkel Østergaard5, Gabriella Meszaros6, Pedro Lopez-Romero7, Francesco de Leonardis6 and Roy Fleischmann8, 1Leiden University Medical Center, Leiden, Netherlands, 2UCL-Saint Luc, Bruxelles, Belgium, 3Department of Internal Medicine III, Institute for Clinical Immunology,, Friedrich-Alexander-University Erlangen-Nuremberg (FAU), Erlangen, Germany, 4Hospital Universitario Fundación Jimenez Diaz, Madrid, Spain, 5Glostrup Hospital, Rigshospitalet, Glostrup, Denmark, 6Eli Lilly and Company, Indianapolis, IN, 7Europe Research Center, Eli Lilly and Company, Madrid, Spain, 8University of Texas Southwestern Medical Center, Dallas, TX

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Baricitinib (BARI), an oral inhibitor of Janus kinase (JAK)1 and JAK2, is being developed for the treatment of RA. RA-BEGIN (NCT01711359) was a phase 3, double-blind, three-arm, multicenter study of BARI administered as monotherapy or in combination with methotrexate (MTX) to patients with early active RA who had no or limited treatment with MTX; MTX monotherapy was the active comparator. This analysis was conducted to identify factors associated with risk of radiographic progression in an early RA population after 52 weeks of treatment with BARI 4mg monotherapy, MTX monotherapy, or a combination of the two drugs.

Methods: Radiographic progression was defined as change from baseline (CFB) greater than the smallest detectable change (SDC) in van der Heijde-modified total Sharp score (mTSS) at week 52. The SDC in mTSS in the RA-BEGIN modified intent-to-treat population at week 52 was 1.4. Missing mTSS data at week 52 were imputed using linear extrapolation based on baseline data and the most recent radiographic data before the missed radiograph. Data for 39/584 patients with completely missing radiographic data were omitted from the analysis. The association of different baseline factors with radiographic progression was assessed using a multivariate logistic regression model including: treatment, age, gender, BMI, ACPA (≤10U/ml negative; >10U/ml positive), RF (≤14IU/ml negative; >14IU/ml positive), presence of joint erosions (yes/no), smoking habit (yes/no), hsCRP, HAQ-DI, mTSS, RA duration, CDAI, and geographic location.

Results: Radiographic progression at week 52 was seen in 21.9% (MTX), 14.9% (BARI 4mg) and 10.1% (BARI 4mg plus MTX) of patients. Female gender, smoking habit, higher hsCRP at baseline (Fig), higher CDAI at baseline (Fig) and lower BMI at baseline were significantly associated with an increased risk of radiographic progression (Tab).
Figure. Adjusted probability of radiographic progression as a function of A. baseline hsCRP and B. baseline CDAI, estimated with a multivariate logistic regression model

A.

Estimated odds ratio for baseline hsCRP is 1.018 (p=0.001). The odds of radiographic progression will increase by a factor of 1.018 when baseline hsCRP increases by one unit.

B.

Estimated odds ratio for baseline CDAI is 1.025 (p = 0.038). The odds of radiographic progression will increase by a factor of 1.025 when baseline CDAI increases by one unit.

CFB, change from baseline; CDAI, Clinical Disease Activity Index; hsCRP, high sensitivity C-reactive protein; Rd, radiographic; SDC, smallest detectable change.
Conclusion: In patients with early RA and no or limited previous use of MTX who were treated with MTX, Bari 4 mg, or Bari 4mg plus MTX, risk factors for radiographic progression can be identified. After multivariate adjustment, female gender, smoking, baseline hsCRP, CDAI and BMI showed a statistically significant association with radiographic progression.

Disclosure: D. van der Heijde, AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boeringer Ingelheim, Celgene,Daiichi, Eli-Lilly, Galapagos, Janssen, Merck, Novartis, Pfizer, Roche, Sanofi-Aventis, UCB, 5; P. Durez, Eli Lilly and Company, 5; G. Schett, None; E. Naredo, Abbvie, Roche, BMS, Pfizer, UCB, Novartis, Lilly, Janssen, 5; M. Östergaard, Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Centocor, GSK, Hospira, Janssen, Merck, Mundipharma, Novartis, Novo, Orion, Pfizer, Regeneron, Schering-Plough, Roche, Takeda, UCB, and Wyeth, 5; G. Meszaros, Eli Lilly and Company, 3; P. Lopez-Romero, Eli Lilly and Company, 3; F. de Leonardi, Eli Lilly and Company, 3; R. Fleischmann, AbbVie, Amgen, Astra Zeneca, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly and Company, Novartis, Roche, Sanofi-Aventis, Pfizer, UCB, 5.


Abstract Number: 419

Abatacept Initiation in Chilean Patients with Long Lasting Rheumatoid Arthritis. Hospital Padre Hurtado Experience

Omar Valenzuela1, María Paz Poblete2, Claudia Mardones2, Sebastián Ibáñez1, Katherine Mogollones2, Francisco Silva1 and María José Villar1, 1Rheumatology department, Hospital Padre Hurtado, Santiago, Chile, 2Hospital Padre Hurtado, Santiago, Chile

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Since the year 2016 Rheumatoid Arthritis (RA) patients in the Chilean public health system can access biologic treatment if they have active disease refractory to non biologic DMARDs (see inclusion criteria). At first only Abatacept was available
as first line biologic. The first patients that initiated biologic treatment in our center were those who had a long lasting active disease. Our main objective was to evaluate the response to treatment with Abatacept in the patients from our center.

Methods: RA patients (ACR 2010 criteria), 18 years old or older, that had a DAS28 ESR > 5.1 in two different occasions separated by at least one month despite the use of at least 3 DMARDs, including methotrexate or leflunomide, for at least 6 months, were included. Patients with any contraindication to use Abatacept were excluded. Information about work status, gender, age, years since diagnosis, comorbidities, and medications used was collected. The patients were followed for 6 months and the DAS28 ESR was measured at baseline and end of follow-up, and the EULAR response criteria was calculated. Changes from baseline to end of follow-up were analyzed using T-test for paired variables or Wilcoxon signed-rank sum test, and associations between variables were assessed using T-test, Mann-Whitney U test and Chi-Squared test or Fisher's exact test, as appropriate

Results: 44 patients were included. Baseline characteristics are described in table 1. Of note, 37.2% had a disability pension and the median years with disease were 13 (IQR 7-17). The improvement of DAS28 ESR and its variables was statistically significant (table 2). According to the EULAR response criteria 22.7% of the patients achieved a good response, 52.3% achieved a moderate response and 25% had no response to treatment with Abatacept. 4 of the 10 patients with good response achieved remission (DAS28 ESR <2.6). Gender, age, years since diagnosis, use of Metothrexate or other DMARDs, prenisone or NSAIDs use, comorbidities, tobacco use and basal DAS28 ESR did not influence the response to treatment. No adverse events were reported.

Conclusion: In our group of patients, with prolonged disease refractory to treatment with at least 3 DMARDs, 75% achieved at least a moderate response according to the EULAR response criteria without adverse events, but less than one quarter achieved a good response. This probably reflects that in these patients the window of opportunity to initiate a suitable treatment to achieve remission was lost. We believe that it is necessary to allow the inclusion of patients with lower DAS28 among the possible beneficiaries of biological therapy in the public health system of our country.
Table 1. Disease characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients</th>
<th>Age (mean, SD)</th>
<th>Female (%)</th>
<th>Years since diagnosis (median, IQR)</th>
<th>Metothrexate use (%)</th>
<th>Sulfasalazine use (%)</th>
<th>Hidroxicloroquine use (%)</th>
<th>Leflunomide use (%)</th>
<th>Prednisone use (%)</th>
<th>NSAIDs use (%)</th>
<th>Tramadol use (%)</th>
<th>Work:</th>
<th>Home activities (%)</th>
<th>Retirement (%)</th>
<th>Disability pension (%)</th>
<th>Comorbidities:</th>
<th>Diabetes (%)</th>
<th>Hypertension (%)</th>
<th>Dislipidemia (%)</th>
<th>Smokers (%)</th>
<th>Latent tuberculosis (%)</th>
<th>HIV, Hepatitis C or B (%)</th>
<th>Interstitial lung disease (%)</th>
<th>Months of follow-up (mean, SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>44</td>
<td>53.9 (10.29)</td>
<td>88.6%</td>
<td>13 (7-17)</td>
<td>77.3%</td>
<td>52.3%</td>
<td>65.9%</td>
<td>50%</td>
<td>95.5%</td>
<td>86.4%</td>
<td>50%</td>
<td>14%</td>
<td>7%</td>
<td>30.2%</td>
<td>11.6%</td>
<td>37.2%</td>
<td>29.5%</td>
<td>58.1%</td>
<td>15.9%</td>
<td>16.7%</td>
<td>0%</td>
<td>6.8%</td>
<td>6.4 (2.6)</td>
<td></td>
</tr>
<tr>
<td>Age (mean, SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Years since diagnosis (median, IQR)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metothrexate use (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sulfasalazine use (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hidroxicloroquine use (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leflunomide use (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prednisone use (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSAIDs use (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tramadol use (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Work:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With contract (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Independent (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home activities (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retirement (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disability pension (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comorbidities:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dislipidemia (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smokers (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latent tuberculosis (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV, Hepatitis C or B (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interstitial lung disease (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Months of follow-up (mean, SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Comparison from baseline to end of follow-up

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Basal (44 patients)</th>
<th>Follow-up (44 patients)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tender joints (median, IQR)</td>
<td>12 (10-17)</td>
<td>5 (3-10)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Swollen joints (median, IQR)</td>
<td>8 (5-9.5)</td>
<td>2.5 (1-4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VAS for pain (median, IQR)</td>
<td>80 (70-80)</td>
<td>40 (20-60)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ESR (median, IQR)</td>
<td>28 (18-40)</td>
<td>19.5 (13.5-28.5)</td>
<td>0.007</td>
</tr>
<tr>
<td>DAS28 ESR (mean, SD)</td>
<td>6.11 (0.66)</td>
<td>4.37 (1.25)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Abstract Number: 420

Machine Learning in Rheumatology: Development and Validation of a Predictive Model for Rheumatoid Arthritis Mortality Using Random Survival Forests

Luis Rodriguez-Rodriguez¹, José M Lezcano-Valverde², Fernando Salazar³, Leticia León², Esther Toledano⁴, Juan A Jover Jover⁵, Eduardo Soudah³, Benjamín Fernández-Gutiérrez⁵, Isidoro Gonzalez-Alvaro⁶ and Lydia A Alcazar¹, ¹Rheumatology Department and Heath Research Institute (IdISSC), Hospital Clínico San Carlos, Madrid, Spain, ²Rheumatology Department, Hospital Clinical San Carlos, Madrid, Spain, ³International Centre for Numerical Methods in Engineering (CIMNE), Madrid, Spain, ⁴Rheumatology, Hospital Clinical San Carlos, Madrid, Spain, ⁵Rheumatology, Hospital Clínico San Carlos, Madrid, Spain, ⁶Rheumatology Department, Hospital Universitario la Princesa, IIS-Princesa, Madrid, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is associated with increased mortality. Traditional survival techniques used to identify mortality risk factors, such as the Cox proportional hazards model (CPH), have several limitations, such as reliance on restrictive assumptions. To overcome these limitations, machine learning methods have been developed. Random survival forest (RSF), a non-parametric ensemble tree method, was proposed as an alternative approach to CPH. Our aim is to develop and validate (internally and externally) a predictive model for RA mortality using RSF.

Methods: Retrospective longitudinal study involving 2 independent RA cohorts from Madrid (Spain): the Hospital Clínico San Carlos RA Cohort (HCSC-RAC: 1,461 patients diagnosed between 2001 and 2011, followed-up until death or September 2013; used for model development), and the Hospital Universitario de La Princesa Early Arthritis Register Longitudinal study (PEARL: 280 patients diagnosed between 2001 and 2014, followed-up until death or January 2017; used for external validation). Demographic and clinical-related variables collected during the first two years after disease diagnosis were used. RSF models were developed with the \textit{randomForestSRC} R package, based on 1,000 trees. 100 iterations of each model were performed to measure the mean and standard deviation of the prediction error. Based on the predicted mortality estimated by the RSF model, mortality risk groups were established through a survival tree created with the R package \textit{rpart}.

Results: 148 and 21 patients from the HCSC-RAC and the PEARL died during a median follow-up time of 4.3 and 5.0 years, respectively. Age at diagnosis, median erythrocyte sedimentation rate, and number of hospital admissions in the first 2 years after RA diagnosis showed the higher predictive capacity. The prediction errors of our model in the training and in the validation cohorts were 0.187, and 0.233, respectively. The survival tree analysis identified 5 risk groups. After combining those three with intermediate risk, we observed that the intermediate and the high risk groups were significantly associated with higher mortality risk compared with the low risk, both in the HCSC-RAC and PEARL cohorts (Figures 1 and 2).

Conclusion: We developed and externally validated a clinical prediction model for RA mortality using RSF.

Figure 1: Kaplan Meier curves for the observed mortality of patients from the HCSC-RAC, grouped in mortality risk categories
Figure 2: Kaplan Meier curves for the observed mortality of patients from the PEARL, grouped in mortality risk categories.
Serum Calprotectin Is Not Predictive for Successful Dose Reduction or Discontinuation of TNF Inhibitors in RA Patients with Low Disease Activity

Nathan den Broeder¹, Lieke Tweehuysen¹, Noortje van Herwaarden¹, Thomas Vogl², F.H.J. van den Hoogen¹, Rogier Thurlings³ and Alfons A Den Broeder¹, ¹Rheumatology, Sint Maartenskliniek, Nijmegen, Netherlands, ²University of Muenster, Muenster, Germany, ³Rheumatology, Radboudumc, Nijmegen, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Dose reduction and discontinuation of TNF inhibitors (TNFi) have been shown feasible in a large proportion of RA patients with low disease activity.¹ To date, no predictors for successful dose reduction or discontinuation have been identified.² Calprotectin (a heterodimer of S100A8/S100A9) might be a promising biomarker in this context.³,4

Objectives: To investigate the predictive value of baseline serum calprotectin for successful TNFi dose reduction or discontinuation in RA patients with low disease activity.

Methods: Data was derived from the intervention arm of the DRESS (Dose REduction Strategies of Subcutaneous TNFi) study, which showed non-inferiority of a dose reduction strategy of adalimumab or etanercept compared to usual care.¹ TNFi dose interval was reduced stepwise every 3 months until flare (DAS28-CRP increase >1.2 or >0.6 if current DAS28-CRP ≥3.2) or discontinuation. Patients were classified at 18 months as being successfully dose reduced, discontinued or not able to reduce the TNFi dose. At baseline, quantification of calprotectin was carried out on serum samples using ELISA. Calprotectin levels were compared between each group and receiver-operator-characteristic (ROC) curves were created. In addition, calprotectin was correlated cross-sectionally with several clinical markers for disease activity.

Results: Calprotectin levels were available from 102 of 121 patients randomised to the intervention group; 61% were women, 63% received etanercept and 37% received adalimumab. Overall, 46% of patients successfully reduced the TNFi dose, 19% of patients successfully discontinued TNFi and 35% of patients could not reduce the TNFi dose. In these groups, median calprotectin levels were 599 ng/ml (p25-p75: 473-965), 629 ng/mL (p25-p75: 453-896) and 624 ng/mL (p25-p75: 514-931) (p=0.801) (Figure 1). The area under the ROC-curve was 0.52 (95% CI: 0.40-0.63) for predicting successful TNFi dose reduction, 0.53 (95% CI: 0.38-0.67) for successful TNFi discontinuation and 0.54 (95% CI: 0.42-0.66) for no dose reduction possible. Calprotectin levels were weakly correlated with C-reactive protein (CRP) levels with a Spearman ρ of 0.21 (p=0.03). No significant correlation was found between calprotectin and age, gender, DAS28-CRP, rheumatoid factor or ACPA positivity.

Conclusion: Serum calprotectin is not predictive for successful TNFi dose reduction or discontinuation in RA patients with low disease activity, and calprotectin was only weakly correlated to CRP levels. These results might be caused by the lack of variability in calprotectin levels at baseline as all patients were in low disease activity state.
No Added Predictive Value of Serum Calprotectin for Treatment Response to Adalimumab or Etanercept in RA Patients

Lieke Tweehuysen1, Nathan den Broeder1, Leo A.B. Joosten2, Thomas Vogl3, F.H.J. van den Hoogen4, Rogier Thurlings5 and Alfons A Den Broeder1, 1Rheumatology, Sint Maartenskliniek, Nijmegen, Netherlands, 2Internal Medicine, Radboud University Medical Center, Nijmegen, Netherlands, 3University of Muenster, Muenster, Germany, 4Rheumatology, Rheumatology Centre Sint Maartenskliniek and Radboud university medical center, Ubbergen (Nijmegen), Netherlands, 5Rheumatology, Radboudumc, Nijmegen, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: To date, no clinically useful baseline biomarkers have been found to predict response to TNF inhibitor (TNFi) treatment.1 Calprotectin was shown to be predictive for treatment response to adalimumab (ADA) while no difference in calprotectin

Abstract Number: 422

No Added Predictive Value of Serum Calprotectin for Treatment Response to Adalimumab or Etanercept in RA Patients

Lieke Tweehuysen1, Nathan den Broeder1, Leo A.B. Joosten2, Thomas Vogl3, F.H.J. van den Hoogen4, Rogier Thurlings5 and Alfons A Den Broeder1, 1Rheumatology, Sint Maartenskliniek, Nijmegen, Netherlands, 2Internal Medicine, Radboud University Medical Center, Nijmegen, Netherlands, 3University of Muenster, Muenster, Germany, 4Rheumatology, Rheumatology Centre Sint Maartenskliniek and Radboud university medical center, Ubbergen (Nijmegen), Netherlands, 5Rheumatology, Radboudumc, Nijmegen, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: To date, no clinically useful baseline biomarkers have been found to predict response to TNF inhibitor (TNFi) treatment.1 Calprotectin was shown to be predictive for treatment response to adalimumab (ADA) while no difference in calprotectin
levels was found between responders and non-responders in RA patients treated with etanercept (ETN) and methotrexate.2,3

**Objectives:** To assess the added predictive value of serum calprotectin for clinical response after 6 months treatment with ADA or ETN in RA patients.

**Methods:** RA patients starting treatment with ADA or ETN in the BIO-TOP study (a prospective cohort study) were included. Patients who discontinued TNFi treatment within 2 months were excluded from analysis. Serum calprotectin was measured at baseline using ELISA. EULAR response was measured at 6 months (good versus moderate/no response). Discontinuation of TNFi before 6 months was regarded as non-response (in case of lack of effect) and clinical response at 3 months was carried forward (when stopped for other reasons). First calprotectin levels were correlated cross-sectionally with several clinical baseline markers. Thereafter, receiver-operator-characteristic (ROC) curves were created for ADA and ETN separately. Finally logistic prediction models were created using backward selection, including baseline characteristics and calprotectin levels to examine the added predictive value of calprotectin.

**Results:** Calprotectin levels and EULAR response were available for 125 patients (ADA (n=50), ETN (n=75)), with 40% of patients achieving EULAR good response. Responders showed significantly higher baseline calprotectin levels: 985 ng/mL (p25-p75: 558-1417) versus 645 ng/mL (p25-p75: 415-973) (p=0.04). Calprotectin levels were significantly correlated to DAS28-CRP (Spearman ρ=0.32, p<0.01) and C-reactive protein (CRP) levels (Spearman ρ=0.57, p<0.01) and significantly higher in rheumatoid factor positive patients (p=0.03). No significant correlation was found between calprotectin and age, gender or ACPA positivity. The area under the curve (AUC) for calprotectin in the ADA and ETN group were 0.68 (95% CI: 0.49-0.88) and 0.49 (95% CI: 0.35-0.63), respectively. The basic model (selected variables: baseline DAS28-CRP and medication used (ADA vs ETN)) showed an AUC of 0.73 (95% CI: 0.64-0.82). The calprotectin added model performed similarly with an AUC of 0.76 (95% CI: 0.67-0.84) (p=0.27).

**Conclusion:** Serum calprotectin is modestly predictive for EULAR good response to ADA but not ETN treatment after 6 months in RA patients. However, calprotectin does not provide additional predictive value over a basic clinical prediction model.

**References**


**Disclosure:** L. Tweehuysen, None; N. den Broeder, None; L. A. B. Joosten, None; T. Vogl, None; F. H. J. van den Hoogen, Biogen Idec, 5,Celltrion, 5,Janssen Pharmaceutica Product, L.P., 5,Mundipharma, 5,Sandoz, 5; R. Thurlings, None; A. A. Den Broeder, None.
Abstract Number: 423

Refractory Pain in Spite of Inflammation Control after Start of Anti-TNF Therapy in RA: Observational Data from Southern Sweden

Tor Olofsson1, Johan K Wallman2, Maria EC Schelin3, Anna Jöud4 and Jon Lampa5,
1Lund University, Department of Clinical Sciences Lund, Rheumatology, Lund, Sweden, Lund, Sweden,
2Department of Clinical Sciences Lund, Rheumatology, Lund University, Lund, Sweden,
3Lund University, Department of Clinical Sciences Lund, Oncology, Lund, Sweden, Lund, Sweden,
4Lund University, Department of Laboratory Medicine Lund, Division of Occupational and Environmental Medicine, Lund, Sweden, Lund, Sweden,
5Karolinska Institute, Department of Medicine, Rheumatology Unit, Stockholm, Sweden, Stockholm, Sweden

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Pain is a dominant and debilitating feature of RA, but while a lot of focus has been put on the occurrence and management of inflammatory pain, less is reported on pain despite low inflammation. The aim of this study was therefore to investigate the prevalence of refractory pain in spite of inflammation control after start of a first anti-TNF therapy in RA patients and its relation to EULAR treatment response.

Methods: RA patients starting a first anti-TNF therapy 2004-2010 were identified in the prospective, observational South Swedish Arthritis Group register (n=1166; 76% women; >95% fulfillment of 1987 ACR criteria) with mean age 56 years and mean disease duration 10 years. Unacceptable pain (>40 mm on a Visual Analogue Scale, VAS; scale 0-100 mm)1 and unacceptable pain in spite of inflammation control (VAS pain>40 mm combined with CRP<10 mg/L,2 and ≤1 swollen joint) were assessed 1.5, 3, 6, and 12 months after treatment start. Furthermore, analyses were performed in relation to EULAR treatment response after 3 months (good response, moderate, no). Differences in pain measures between treatment response groups were estimated by logistic regression.

Results: At start of first anti-TNF therapy, 79.6% of the RA patients had unacceptable pain (VAS pain>40) which declined to 39.8% after 3 months, and then remained stable during the first treatment year, whereas the frequency of patients with unacceptable pain in spite of inflammation control increased from 4.0% at treatment start to 12.3% after 3 months, and then stabilized (Figure 1). Unacceptable pain at 3 months was strongly related to EULAR response (14.1% of good responders vs. 70.5% of non-responders; p<0.001). In contrast, the frequency of unacceptable pain in spite of inflammation control was largely similar in patients with good response and those with no response (10.9% vs. 14.4%; p=0.23). Among EULAR good responders, unacceptable pain despite inflammation control constituted 78% of all unacceptable pain at 3 months (Figure 2).

Conclusion: A substantial proportion of RA patients starting anti-TNF therapy have refractory, unacceptable pain in spite of good inflammation control during the first treatment year. In the present study, this pain status was as common in EULAR good responders as in non-responders. These data are in line with insufficient effects of biologics on a subgroup of patients with inflammation-independent pain, and strongly warrants alternative treatment strategies in these patients.
Re-Establishment of Efficacy of Tofacitinib, an Oral Janus Kinase Inhibitor, in Rheumatoid Arthritis Patients after Temporary Discontinuation

**Jeffrey Kaine**, John Tesser², Ryan DeMasi³, Liza Takiya³, Lisy Wang⁴, Mark Snyder³, Haiyun Fan⁴ and Jürgen Wollenhaupt⁵,

¹Sarasota Arthritis Research Center, Sarasota, FL, ²Arizona Arthritis & Rheumatology Associates, Glendale, AZ, ³Pfizer Inc, Collegeville, PA, ⁴Pfizer Inc, Groton, CT, ⁵Schön-Klinik Hamburg-Eilbek Teaching Hospital of the University of Hamburg, Hamburg, Germany

**First publication**: September 18, 2017

**SESSION INFORMATION**

**Session Date**: Sunday, November 5, 2017

**Session Title**: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response

**Session Type**: ACR Poster Session A

**Session Time**: 9:00AM-11:00AM
**Background/Purpose:** Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). We assessed tofacitinib efficacy and safety after temporary discontinuation and reinitiation of therapy in patients (pts) with RA.

**Methods:** Data were from a randomized, parallel-group (grp), controlled, open-label vaccine sub-study in pts with RA participating in a long-term extension study (NCT00413699). Pts were aged ≥18 years with active RA and had received tofacitinib 10 mg twice daily (BID) for ≥3 months. The sub-study included 2 treatment (tx) grps: ‘continuous tx’ (tofacitinib 10 mg BID ± methotrexate [MTX]) and ‘interrupted tx’ (tofacitinib withdrawn for 2 weeks post-randomization [Day 1–15; Visits 1–3], then tofacitinib 10 mg BID reinitiated ± MTX at Visit 3); randomization was stratified by MTX use. All pts received pneumococcal and influenza vaccines on Day 8 (Visit 2; vaccine titers reported previously\(^1\)). Blood samples were taken on Days 8, 15 (Visit 3), and 43 (Visit 4). Efficacy endpoints included change from baseline (CFB) in CRP, HAQ-DI, and DAS28-4(ESR) at each visit. A mixed-effects model with repeated measures was used to evaluate treatment effect at each visit. Efficacy analyses were exploratory, with no multiplicity adjustments. P<0.05 was considered as statistically significant.

**Results:** Of the 199 pts in this analysis (continuous, n=100; interrupted, n=99), 117 received concomitant MTX. At study baseline (BL) in the continuous and interrupted grps, respectively: 81.8/83.8% of total pts were white, 84.8/86.9% were female, and mean age was 55.0/53.9 years. CRP, HAQ-DI, and DAS28-4(ESR) BL values were generally similar between groups. At Day 8, mean CRP and DAS28-4(ESR) significantly increased from BL for pts receiving interrupted vs continuous tx; HAQ-DI values were similar between grps (Figure). At Day 15, mean CRP, HAQ-DI, and DAS28-4(ESR) significantly increased from BL for pts receiving interrupted vs continuous tx. After tofacitinib reinitiation for 28 days (Day 43), CFB in CRP, HAQ-DI, and DAS28-4(ESR) were similar between grps and approached BL levels. Adverse events (AEs) were experienced by 35.4% and 49.5% of pts receiving interrupted and continuous tx, respectively. The most frequent treatment-emergent AEs were bronchitis and upper respiratory tract infection (each AE: 6 pts) and vaccination-related immunisation reaction, myalgia, and rash (each AE: 5 pts). Serious AEs occurred in 3 pts (3%) in each grp. In total, 1 pt (1%) in the interrupted grp discontinued due to study drug-related AEs; no pts discontinued due to disease flare.

**Conclusion:** Efficacy of tofacitinib 10 mg BID can be re-established following a temporary (2 weeks) tx discontinuation in pts with RA. Pts receiving continuous tx maintained efficacy throughout the study. Further investigations are required.

**Reference:**


**Disclosure:** J. Kaine, Pfizer Inc, Bristol-Myers Squibb, 8; J. Tesser, Pfizer Inc, 2,Pfizer Inc, 5,Pfizer Inc, 8; R. DeMasi, Pfizer Inc, 1,Pfizer Inc, 3; L. Takiya, Pfizer Inc, 1,Pfizer Inc, 3; L. Wang, Pfizer Inc, 1,Pfizer Inc, 3; M. Snyder, Pfizer Inc, 1,Pfizer Inc, 3; H. Fan, Pfizer Inc, 1,Pfizer Inc, 3; J. Wollenhaupt, Pfizer Inc, 1,Pfizer Inc, 8.
Efficacy of Monotherapy of the Biologic Dmards in Patients with Rheumatoid Arthritis: Real Life Data from the Hong Kong Biologics Registry

Chi Chiu Mok, Ting Hung Wan and Lai Shan Fong, Medicine, Tuen Mun Hospital, Hong Kong, Hong Kong
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
To report the prevalence and efficacy of biologic DMARD (bDMARD) monotherapy in real life treatment of rheumatoid arthritis (RA).

Methods:
RA patients registered in the Hong Kong Biologics Registry who were receiving bDMARD monotherapy (without concomitant conventional synthetic DMARDs [csDMARDs] except low dose prednisolone) were identified. The efficacy (clinical response and drug retention rate) of bDMARD monotherapy was compared with bDMARD combination therapy (with csDMARDs) using statistical tests.

Results:
From December 2007 to April 2017, 2123 courses of bDMARDs/tsDMARDs were used in 1250 RA patients (83% women, mean age at therapy 53.8±12.7 years). Among 1881 courses of therapies with complete data, 164 (8.7%) was monotherapy at baseline. Low dose prednisolone (<10mg/day) was used in 56% of these courses. In the combination group, the commonest csDMARDs used in combination with bDMARDs were methotrexate (79%), sulphasalazine (27%), hydroxychloroquine (25%) and leflunomide (21%). The bDMARDs/tsDMARDs most frequently used as monotherapy were tofacitinib (14.3%), tocilizumab (11.6%) and abatacept (11.2%). Overall, the non-TNF was more commonly used as monotherapy (11.2%) than the anti-TNF bDMARDs (7.4%). At 6 months of bMDARD/tsDMARD therapy, the DAS remission rate was non-significantly higher in the combination than monotherapy group (11% vs 5%; p=0.42). The change in DAS28 score was also non-significantly greater in the combination group (-1.95±1.26 vs -1.68±1.56; p=0.30). The difference in 6-month efficacy between the combination and monotherapy groups was greater in anti-TNF users. The overall cumulative withdrawal rate of the bDMARDs/tsDMARDs due to either inefficacy or serious adverse events (SAEs) was 0.55 at 3 years and 0.47 at 5 years. The anti-TNF biologics had a significantly higher withdrawal rate than the non-TNF biologics (hazard ratio [HR] 1.83[1.56-3.14]; p<0.001). In Cox regression models, monotherapy of the bDMARDs was not significantly associated with drug withdrawal due to inefficacy (HR 0.95 [0.53-1.71]; p=0.87) or SAEs (HR 1.27 [0.51-3.19]; p=0.61) after adjustment for age, sex, anti-TNF (vs non-TNF) biologic use, previous use of bDMARDs (vs first time use) and DAS28 at baseline. Separate analyses of the anti-TNF and non-TNF biologics again did not reveal a significant relationship between monotherapy of the biologics with the drug withdrawal due to inefficacy or SAEs after adjustment for age, sex, previous use of bDMARDs and disease activity at baseline (HR 1.002 [0.56-1.80]; p=0.99 for anti-TNF and HR 1.20 [0.47-3.08]; p=0.70 for non-TNF biologics, respectively).

Conclusion:
Monotherapy of bDMARD/tsDMARD was used in 8.7% of our RA patients in real life practice, probably due to intolerance, inefficacy or non-compliance to the csDMARDs. Short-term efficacy tended to be better with bDMARDs/csDMARDs combination, especially in the anti-TNF biologics, but the long-term drug retention rate was similar between bDMARD monotherapy and combination therapy with the csDMARDs.

Disclosure: C. C. Mok, None; T. H. Wan, None; L. S. Fong, None.
Serum Levels of the Anti-TNF Biologics Correlate with Clinical Efficacy in Patients with Inflammatory Arthritis

Chi Chiu Mok\textsuperscript{1}, Lai Shan Fong\textsuperscript{1}, Ling Yin Ho\textsuperscript{2} and Chi Hung To\textsuperscript{3}, \textsuperscript{1}Medicine, Tuen Mun Hospital, Hong Kong, Hong Kong, \textsuperscript{2}Dept of Medicine, Tuen Mun Hospital, Hong Kong SAR, Hong Kong, \textsuperscript{3}Medicine, Pok Oi Hospital, Hong Kong, Hong Kong

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
To study the correlation between levels of the anti-TNF biologics and clinical efficacy in patients with inflammatory arthritis

Methods:
Adult patients who fulfilled the criteria for rheumatoid arthritis (RA), spondyloarthritis (SpA) and psoriatic arthritis (PSA) and were commenced on standard dosing regimens of the anti-TNF biologics were recruited. Stored serum samples at baseline, month 6 and 12 were assayed for the trough levels of the biologics (± anti-drug antibodies) retrospectively. Patients were followed longitudinally and efficacy analyses were conducted at 3-month intervals without the knowledge of the drug levels. Biologics would be discontinued from 6 months onwards according to protocol-based improvement criteria for each disease. Clinical efficacy of the anti-TNF biologics was compared among patients with different levels of the drug by statistical analyses.

Results:
112 patients were studied (58 RA, age 51.2±10.9 years, disease duration 72.9±67 months; 41 SpA, age 39.1±9.9 years, disease duration 74.3±81.6 months; 13 PSA, age 53.5±10.7 years, disease duration 44.3±35.4 years). The number of patients treated with infliximab (IFX), adalimumab (ADM), golimumab (GLM) and etanercept was 3, 31, 36 and 42, respectively. At month 12, neutralizing antibodies against IFX, ADM and GLM were present in 2 (67%), 14 (45%) and 1 (3%) of the patients, respectively. In ADM users, the drug level was significantly lower in those with antibodies than those without (1.81±2.63 vs 8.02±4.14 ug/ml; p<0.001). Antibody titer against ADM correlated negatively with the levels of ADM (Rho -0.72; p<0.001). Patients were stratified into 3 tertiles for each biologic according to the trough levels of the drugs. Low drug concentrations were defined as levels ≤1.30 ug/ml, 0.05 ug/ml and 0.60 ug/ml in ADM, ETN and GLM users, respectively. In patients with RA/PSA (N=71), patients with the lowest anti-TNF drug level group (N=30) had a trend of less improvement in DAS28, CDAI scores at month 12 when compared to others (N=41). However, significantly more patients withdrew treatment due to inefficacy at month 12 in this group compared to others (67% vs 7.3%, p<0.001). In patients with SpA (N=41), patients with lowest anti-TNF drug levels stratum (N=9) had significantly less improvement in ASDAS compared with others at month 12 (N=32) (-0.57±0.63 vs -1.93±1.28; p=0.003). The proportion of patients who achieved an ASAS20 response was also significantly lower in this group of patients (33% vs 75%; p=0.04). In all the 112 patients studied, the cumulative withdrawal rate of the anti-TNF biologics at month 12 (by Kaplan-Meier’s analysis) was significantly higher in those with low drug levels when compared to others with higher drug levels (26.1% vs 54.6%; p<0.001 log rank test).

Conclusion:
The presence of neutralizing antibodies to the anti-TNF monoclonals is associated with lower trough levels of the drugs. Trough level of the anti-TNF biologics is useful for optimizing the clinical efficacy of the drugs in patients with inflammatory arthritis.

Disclosure: C. C. Mok, None; L. S. Fong, None; L. Y. Ho, None; C. H. To, None.


Do We Treat Men and Women Differently, and Is This a Good Thing?
Sytske Anne Bergstra\textsuperscript{1}, Cornelia F Allaart\textsuperscript{1}, Sofia Ramiro\textsuperscript{2}, Arvind Chopra\textsuperscript{3}, Candida A. Silva\textsuperscript{4}, Nimmisha Govind\textsuperscript{5} and Robert B.M. Landewé\textsuperscript{6,7}, \textsuperscript{1}Department of Rheumatology, LUMC, Leiden, Netherlands, Leiden, Netherlands, \textsuperscript{2}Rheumatology, Department of Rheumatology, LUMC, Leiden, Netherlands, Leiden, Netherlands, \textsuperscript{3}Center for Rheumatic Diseases, Pune, India, Pune, India, \textsuperscript{4}Instituto Português de Reumatologia, Lisbon, Portugal, Lisbon, Portugal, \textsuperscript{5}Department of Rheumatology, University of the Witwatersrand, Johannesburg, South-Africa, Johannesburg, South Africa, \textsuperscript{6}Zuyderland Medical Center, Heerlen, Netherlands, Heerlen, Netherlands, \textsuperscript{7}Amsterdam Rheumatology & Immunology Center, Netherlands, Amsterdam, Netherlands

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Men seem to respond better to antirheumatic treatment than women with RA. In daily practice, expectations towards responsiveness may influence rheumatologists when making treatment choices. We investigated whether male and female RA patients are treated differently and whether they respond differently to treatment in daily clinical practice.

Methods: DMARD naive RA patients with symptom duration ≤5 years, ≥3 months follow-up, available data regarding medication use and baseline DAS≥1.6 were selected from the international observational METEOR database. Patients starting biologic DMARD treatment were excluded due to low numbers. Follow-up visits were selected until the first medication switch or the end of follow-up. Missing data were imputed using multiple imputation. Linear mixed model (LMM) analyses were performed to assess whether differences in treatment between men and women lead to differences in DAS or HAQ over time within each treatment group. If an added interaction between gender and treatment was statistically significant (p<0.05), models were stratified for treatment. Analyses were adjusted for potential confounders.

Results: Women (n 4393) more often started treatment with HCQ (HCQ monotherapy, MTX + HCQ and HCQ + glucocorticoid, but not more often with MTX + SSZ + HCQ), whereas men (n 1142) more often started treatment with SSZ and/or MTX (SSZ monotherapy, MTX + SSZ and MTX + glucocorticoid, table 1).

Mean (SD) baseline DAS and HAQ for women and men were DAS 3.7 (1.0) vs 3.5 (1.1) and HAQ 1.1 (0.7) vs 1.0 (0.7). LMM analyses showed that in general women improved less on initial treatment over time than men: DAS [β (95% CI) 0.16 (0.12; 0.20)] and HAQ [β (95% CI) 0.13 (0.10; 0.16)]. A statistically significant interaction was only found between female gender and initial HCQ [DAS β (95% CI) -0.17 (-0.33; -0.0045) and HAQ -0.12 (-0.23; -0.0047)] and between female gender and initial MTX + HCQ + SSZ for the outcome HAQ [β (95% CI) -0.19 (-0.38; -0.0048)]. Results were therefore stratified for individual DMARDs and for combination therapy with csDMARDs (table 2). It was found that women had a worse response than men to MTX monotherapy, MTX + HCQ and SSZ + HCQ (for DAS and HAQ) and for SSZ monotherapy and MTX + SSZ (for DAS). For patients using HCQ monotherapy or MTX + HCQ + SSZ there were no gender differences over time.

Conclusion: Women more often started treatment with HCQ, as monotherapy or in combination with MTX or a glucocorticoid, whereas men more often started treatment with MTX and/or SSZ. In general women had worse response to treatment than men, but we found no gender differences in response to HCQ monotherapy or to combination of MTX + HCQ + SSZ.
Disclosure: S. A. Bergstra, None; C. F. Allaart, Abb Vie, 5, UCB, 5, Schering-Plough, 5, Centocor, Inc., 5, MSD, 5, Roche Pharmaceuticals, 5, Mitsubishi Tanabe, 5, Pfizer Inc, 5; S. Ramiro, None; A. Chopra, None; C. A. Silva, None; N. Govind, None; R. B. M. Landewé, Abbott/Abb Vie, Ablynx, Amgen, Astra-Zeneca, Bristol Myers Squibb, Celgene, Janssen, Galapagos, Glaxo-Smith-Kline, Novartis, Novo-Nordisk, Merck, Pfizer, Roche, Schering-Plough, TiGenix, UCB, Wyeth, 5, Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, Wyeth, 2, Director of Rheumatology Consultancy BV, 4, Board Member Merit Foundation, 3.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/do-we-treat-men-and-women-differently-and-is-this-a-good-thing

Abstract Number: 428

Impact of Smoking Cessstion Advise in Patients with Rheumatoid Arthritis to Help Quit Smoking

Shama Khan1, Ahmad Butt1, Emmett Brennan2, Ausaf Mohammad1 and Killian O Rourke2, 1Rheumatology, Midlands Regional Hospital, Tullamore, Ireland, 2Tullamore, Midlands Regional Hospital, Tullamore, Ireland, 3Rheumatology, Midlands Regional Hospital, Tullamore, Co Offaly, Ireland

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Smoking is associated with an increased risk of comorbidities in rheumatoid arthritis (RA) and may reduce the efficacy of anti-rheumatic therapies. Smoking cessation is therefore critically important in RA management and may lead to a reduced comorbid burden (1,2). The aim of this pilot study was to investigate whether smoking cessation rates are increased following a smoking cessation advice for people with RA.

Methods:

We conducted a prospective study of one hundred and eighty RA patients fulfilling the 1987 American College of Rheumatology classification criteria, from October 2016 to March 2017, attending our rheumatology services. Ethics approval was obtained. Information on demographics and cigarette smoking status was collected through patients’ interviews and medical notes review. Current smokers were given advice on quitting smoking through face-to-face advice, handout, and nicotine replacement. Subjects were re-interviewed at 6-months to ascertain smoking status. The primary outcome was smoking cessation at 6 months.

Results:
180 current smokers with RA were included: mean age 56± 11.9 years and 76% were females. Overall, 64% of subjects stopped smoking at 6 months, and remainder RA smokers were thinking about quitting. More female subjects quit smoking as compared to males (74% vs. 26%). Those who quit smoking were younger (49 years vs. 57 years), had higher BMI (28.7 ± 3.6 vs. 26.7 ± 3.6), and had aggressive disease, DAS28-CRP (4.9 ± 0.9 vs. 2.9 ± 0.9) (P < .05). Subjects who stopped smoking stated “healthy life style” as motivation to quit.

Conclusion:

In our study significant proportion of RA patients stopped smoking when given advice on quitting. Smoking cessation advice was very beneficial in motivating them to quit smoking. There should be a structured plan in place to educate RA patients on smoking cessation, both in verbal and written form.

Disclosure: S. Khan, None; A. Butt, None; E. Brennan, None; A. Mohammad, None; K. O Rourke, None.

Repair of Joint Damage Is Rare in Newly Diagnosed Rheumatoid Arthritis Patients and Appears Not to Relate to Previous Suppression of Inflammation

Joy A. van der Pol1, Gulsah Akdemir1, Marianne van den Broek1, Linda Dirven1, Pit J.S.M. Kerstens2, Willem F. Lems3, Iris M. Markusse1, Cornelia F Allaart1 and Tom W.J. Huizinga1, 1Department of Rheumatology, LUMC, Leiden, Netherlands, Leiden, Netherlands, 2Department of Rheumatology, Reade, Amsterdam, Netherlands, 3Department of Rheumatology, VU Medical Center, Amsterdam, Netherlands

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Joint damage in RA is thought to be irreparable. We hypothesized that in patients in whom inflammation is persistently well suppressed, repair may be possible.

Objectives: To investigate whether reversal of erosions and joint space narrowing (JSN) in RA occurs and whether clinical variables predict repair.

Methods: In the BeSt study, patients with active early RA were randomized to 4 treatment strategies, each with the aim to induce and maintain suppression of disease activity by adjusting medication based on three-monthly calculations of the 44-joint Disease Activity Score (DAS), target ≤2.4. Radiographic joint damage was assessed yearly, using the Sharp/van der Heijde score (SHS). In this analysis, 8-years data of the study were used. Repair of erosions or JSN was defined at the individual joint level as a reduction of ≥1 SHS point compared to the previous available X-ray, present in ≥2 consecutive visits and with ≥3 out of 4 independent scorers agreeing. Radiographs were scored in random order per patient, blind for patient identity and treatment arm. Multiple logistic regressions were applied at the patient level for associations between achieving repair and maximum duration of previous remission, mean DAS until repair, previous prednisone use, previous infliximab use, ACPA, gender, age and randomization arm. All models were adjusted for mean joint damage over time in the group with repair. In the group without repair, the models were corrected for mean damage over time until mean time point of repair in the group with repair.

Results: Seven out of 508 patients did not have any X-ray images taken in the study. Of the remaining 501 patients, 320 had damage in at least 1 joint and thus could potentially show repair. In total, 2395 X-rays were available, on average 7.5 per patient (range 2-9). Median SHS after 8 years in these patients was 13 (IQR 4-21, range 0.67-255), and mean (SD) DAS from month 3 was 2.00 (0.67). Repair was seen in 17 out of 320 patients, 5.3%; 10 had reduction of JSN, 7 of erosions. In 14 patients repair was seen in 1 joint, in 3 patients repair was seen in 2 joints (same time point). Mean (SD) time to repair was 44.1 (20.1) months. Ten of 17 patients (59%) had previously achieved DAS-remission, compared to 100% of the patients who at a matching time point showed no repair. Adjusted for mean SHS until repair, we found a trend for less repair with longer baseline symptom duration and for less repair in the arm with initial
infliximab. There were no associations with repair for duration of remission, mean DAS until repair, gender, age, presence of ACPA, or previous exposure to prednisone or infliximab (table 1).

**Conclusion:** In this early RA cohort, during 8 years treated to target DAS ≤2.4, repair of JSN and erosions was seen in 17 patients (5.3%). Repair does not seem to relate to previous inflammation or other predictors in this cohort.

| Table 1. Multiple univariate logistic regression models to investigate associations with repair (n=17) |
|-------------------------|----------------|-----------------|--------------------------|
|                         | OR             | 95% CI          | P                        |
| Duration of previous remission* | -              | -               | -                        |
| Symptom duration at baseline (weeks) | 0.972 | 0.95 – 1.00 | 0.051                    |
| Mean DAS from month 3 to time of repair | 1.39 | 0.77 – 2.51 | 0.270                    |
| Previous prednisone | 1.09 | 0.385 – 3.09 | 0.871                    |
| Previous infliximab | 0.599 | 0.206 – 1.74 | 0.347                    |
| ACPA | 1.51 | 0.413 – 5.53 | 0.533                    |
| Gender | 1.13 | 0.401 – 3.16 | 0.822                    |
| Baseline age | 1.01 | 0.975 – 1.05 | 0.548                    |
| Randomization arm | -               | -               | -                        |
| Sequential monotherapy | ref | -               | -                        |
| Step-up combination therapy | 0.797 | 0.231 – 2.75 | 0.721                    |
| Initial combination with prednisone | 0.597 | 0.158 – 2.28 | 0.448                    |
| Initial combination with infliximab | 0.147 | 0.0173 – 1.25 | 0.680                    |

All models were adjusted for mean Sharp/van der Heijde score until repair.

DAS: disease activity score, ACPA: anti-citrullinated peptide antibody.

*No results due to 100% remission in non-repair comparator group.

**Disclosure:** J. A. van der Pol, None; G. Akdemir, None; M. van den Broek, None; L. Dirven, None; P. J. S. M. Kerstens, None; W. F. Lems, Pfizer, MSD, Eli Lilly, Abbvie, 8; I. M. Markusse, None; C. F. Allaart, Abb Vie, 5,UCB, 5,Schering-Plough, 5,Centocor, Inc., 5,MSD, 5,Roche Pharmaceuticals, 5,Mitsubishi Tanabe, 5,Pfizer Inc, 5; T. W. J. Huizinga, Janssen and Abbvie, 2,Merck, from UCB, from Bristol Myers Squibb, from Pfizer, from Novartis, from Roche, from Sanofi-Aventis, from Abbott, from Crescendo Bioscience, from Nycomed, from Boeringher, from Takeda, from Epirus and from Eli Lilly., 5.


**Abstract Number:** 430

**Implementation of a Treat-to-Target Remission Strategy for Rheumatoid Arthritis in Australian Public and Private Rheumatology Clinics – Identification of Clinician and Patient Barriers**

Helen Benham¹, Hedva Chiu², Joanne Tesiram³, Peter Landsberg⁴, Andrew A. Harrison⁵, Peter Nash⁶, Ranjeny Thomas⁷ and Mieke van Driel⁸, ¹The University of Queensland Faculty of Medicine, Brisbane, Australia, ²The University of Queensland Faculty of Medicine, Woolloongabba, Australia, ³Rheumatology, Princess Alexandra Hospital, Woolloongabba, Australia, ⁴Princess Alexandra Hospital, Woolloongabba, Australia, ⁵Department of Medicine, University of Otago Wellington, Wellington, New Zealand, ⁶University of Queensland, Brisbane, Australia, ⁷Diamantina Institute, Diamantina Institute University of Queensland, Brisbane, Australia, ⁸Primary Care Clinical Unit, The University of Queensland Faculty of Medicine, Herston, Australia

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Treat-to-target in rheumatoid arthritis (RA-T2T) improves outcomes for people living with RA. Implementing T2T in routine clinical practice however presents many challenges and an evidence practice gap has emerged.

**Methods:** Cross-sectional surveys were undertaken in parallel: A survey of RA patients and Australian rheumatologists. Agreement was measured using a 10-point Likert scale for RA-T2T recommendations and 5-point for use in daily practice. Questions related to
willingness to alter practice, education and patient perceptions were included with free-text comments and thematic analysis undertaken.

**Results:** 85 rheumatologists and 107 patients responded. Surveys show the majority of patients have no knowledge of RA-T2T (91%) but report high levels of agreement with the recommendations (8.61 to 9.51). Patients are willing to try a T2T approach (88%) and would be specifically willing to increase blood tests (96%), have joint counts performed (87%) and use a patient-reported-outcome tool (83%). They are less willing to have more frequent appointments (66%) and to spend additional time discussing RA-T2T (69%). 48% of patients feel their RA treatment could be improved and 28% would like to be more involved in treatment decision making. For rheumatologists the mean level of agreement scores ranged from 7.32 to 9.33. Lowest level of agreement was with the recommendation that a disease activity score is required to guide care in routine practice (7.32). 50% of rheumatologists reported they very often/often use a score in daily practice. 44% do not think RA-T2T is necessary for every RA patient. Rheumatologists are willing to schedule more visits (88%), perform joint counts (84%), use a PRO for shared decision-making (76%) and spend time discussing RA-T2T (85%). They are less willing to calculate a disease activity score (64%). Free text identified four thematic barriers to implementation of RA-T2T identified by rheumatologists: time, patient acceptance and adherence to medication change, lack of appointment availability and the lack of a rheumatology nurse in the clinic.

**Conclusion:** RA-T2T is an evidence-based intervention and is recommended for the management of RA. Agreement with some aspects of RA-T2T and uptake in routine clinical practice by Australian rheumatologists is low and the majority of patients are unaware of RA-T2T. Significant clinician and patient barriers exist and an implementation strategy utilizing an electronic and patient-driven knowledge-translation tool, for use at the point of care, is being created and tested for usability in Australian rheumatology clinics.

**Disclosure:** H. Benham, AbbVie, 2,AbbVie, 8; H. Chiu, None; J. Tesiram, None; P. Landsberg, None; A. A. Harrison, AbbVie, 8; P. Nash, None; R. Thomas, Janssen Pharmaceutica Product, L.P., 2,Janssen Pharmaceutica Product, L.P., 5; M. van Driel, None.

events /100 pt-years [pt-yrs]) for herpes zoster (HZ) and serious infection events (SIEs) during treatment +28 days, and for malignancies during the observational period.

**Results:** Overall, 2882 tofacitinib-treated pts were enrolled and included in the 6-month interim safety analysis: 79.9% were female, mean age 62.6 yrs, with 32.0% pts ≥70 yrs and 1241.4 pt-yrs of exposure. Of these, 686 pts (23.8%) discontinued treatment, mainly due to AEs (276 pts; 9.6%) or lack of effectiveness (260 pts; 9.0%; multiple reasons allowed). At least one AE was observed in 965 pts (33.5%); infections were observed in 367 pts (12.7%); the most frequent AEs were HZ (98 pts; 3.4%) and hepatic function abnormal (48 pts; 1.7%). SAEs occurred in 221 pts (7.7%); the most frequent SAEs were pneumonia (20 pts; 0.7%), HZ (16 pts; 0.6%), interstitial lung disease (14 pts; 0.5%) and condition aggravated (12 pts; 0.4%); serious infections occurred in 101 pts (3.5%). Malignancy (all causality) was reported in 21 pts (0.7%); ovarian cancer, pancreatic carcinoma, lung neoplasm, colon cancer, breast cancer, diffuse large B-cell lymphoma and lymphoproliferative disorder all occurred in 2 pts (0.07%) each. There were 16 deaths (0.6%) during the 6-month observed period; the most common causes of death (including pts with multiple causes listed) were infection (5 cases, all respiratory infections), malignancy (4 cases) and interstitial lung disease (3 cases). For AEs of special interest from all-period data during treatment +28 days, the IR of HZ (serious and non-serious) was 6.43/100 pt-yrs (160 pts; 2489.5 pt-yrs) and SIEs 5.96/100 pt-yrs (150 pts; 2517.0 pt-yrs), and during the observational period IR malignancy was 1.39/100 pt-yrs (42 pts; 3014.1 pt-yrs).

**Conclusion:** For this interim analysis, AEs during the initial 6-month treatment period from PMS reports of tofacitinib in Japanese pts did not reveal any new or unexpected safety signals vs the tofacitinib RA clinical program. Final results from this PMS study are awaited in order to make definitive conclusions on the safety profile of tofacitinib in these pts.

**Disclosure:** T. Mimori, Astellas, Ayumi, Chugai, Daiichi-Sankyo, Eisai, Mitsubishi Tanabe, MSD, Sanofi, Taisho Toyama, 2,Astellas, Bristol-Myers Squibb, Chugai, Eisai, Mitsubishi-Tanabe, 8; M. Harigai, Eisai, Takeda, Teijin, 2,Bristol-Myers Squibb, Chugai, Janssen, Pfizer Inc, 5; T. Atsumi, Alexion, Astellas, Bristol-Myers Squibb, Chugai, Eisai, Janssen, Mitsubishi-Tanabe, Sanofi, 2,AbbVie, Astellas, Chugai, Eisai, Mitsubishi-Tanabe, Pfizer Inc, Takeda, UCB Japan, 8,Bayer, Daiichi-Sankyo, Takeda, 9; M. Kuwana, Chugai, Eisai, Mitsubishi-Tanabe, Ono, Pfizer Inc, Santen, 2,Astellas, Chugai, Eisai, Janssen, Mitsubishi-Tanabe, Ono, Pfizer Inc, UCB, 8; S. Takei, Chugai, Eisai, Mitsubishi-Tanabe, Takeda, 2,Asahi-kasei, Ayumi, Chugai, Mitsubishi-Tanabe, Ono, 8; N. Tamura, AbbVie, Astellas, Bristol-Myers Squibb, Chugai, Eisai, Janssen, Mitsubishi-Tanabe, Takeda, 2,AbbVie, Astellas, Bristol-Myers Squibb, Eisai, Janssen, Mitsubishi-Tanabe, 8; T. Fujii, Daiichi-Sankyo, Eisai, Mitsubishi-Tanabe, Ono, Pfizer Japan Inc, 2,AbbVie, Mitsubishi-Tanabe, Ono, Pfizer Japan Inc, 8; H. Matsuno, Ayumi, Meiji Seika, Mochida, Nichi-Iko, 5; S. Momohara, AbbVie, Bristol-Myers Squibb, Eisai, Janssen, Mitsubishi-Tanabe, Ono, Pfizer Japan Inc, 2,AbbVie, Mitsubishi-Tanabe, Ono, Pfizer Japan Inc, 8; T. Fuji, Daiichi-Sankyo, Eisai, Mitsubishi-Tanabe, Ono, Pfizer Japan Inc, 2,AbbVie, Mitsubishi-Tanabe, Ono, Pfizer Japan Inc, 8; H. Matsuno, Ayumi, Meiji Seika, Mochida, Nichi-Iko, 5; S. Momohara, AbbVie, Bristol-Myers Squibb, Eisai, Janssen, Mitsubishi-Tanabe, Ono, Pfizer Japan Inc, 2,AbbVie, Mitsubishi-Tanabe, Ono, Pfizer Japan Inc, 8; K. Yamamoto, AbbVie, Astellas, Ayumi, Chugai, Eisai, Mitsubishi Tanabe, Nippon Kayaku, Pfizer, Taisho Toyama, Takeda, TEIJIN UCB, 2,Asahikasei, AstraZeneca, Ayumi, Boehringer Ingelheim, Bristol-Myers Squibb, Chugai, Eisai, Janssen, Mitsubishi-Tanabe, Pfizer Inc, Sanofi, Sumitomo Dainippon, Taisho Toyama, Takeda, TEIJIN, Toyama Chemical, UCB, 8; T. Kokubo, Pfizer Japan Inc, 3; Y. Endo, Pfizer Inc, 1,Pfizer Japan Inc, 3; N. Sugiyama, Pfizer Inc, 1,Pfizer Japan Inc, 3; T. Hirose, Pfizer Inc, 1,Pfizer Japan Inc, 3; Y. Morishima, Pfizer Inc, 1,Pfizer Japan Inc, 3; N. Yoshii, Pfizer Inc, 1,Pfizer Japan Inc, 3.


**Abstract Number:** 432

**ACPA and RF As Predictors of Sustained Clinical Remission in Rheumatoid Arthritis Patients: Data from a Rheumatoid Arthritis Cohort**

**Janet E. Pope** 1, Emmanouil Rampakakis 2, Mohammad Movahedi 3, Angela Cesta 3, John S. Sampalis 4 and Claire Bombardier 3

1Department of Medicine, Division of Rheumatology, University of Western Ontario, St Joseph's Health Care, London, ON, Canada, 2JSS Medical Research, Montreal, QC, Canada, 3Toronto General Hospital Research Institute, University Health Network, Toronto, ON, Canada, 4McGill University, Montreal, QC, Canada

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM
ACPA and RF as Predictors of Sustained Clinical Remission in Rheumatoid Arthritis Patients: Data From a Rheumatoid Arthritis Cohort

Background/Purpose: Positive serology for anti-citrullinated protein antibody (ACPA) and rheumatoid factor (RF) are included among the criteria for definitive RA diagnosis as per the 2010 ACR/EULAR classification criteria for rheumatoid arthritis (RA). Previous studies have shown that autoantibodies are positive predictors of response in rheumatoid arthritis (RA) patients treated with some biologics. The purpose of this study was to evaluate the interaction of RF and ACPA in predicting sustained clinical response in a large observational cohort of RA patients followed in routine clinical care. Methods: RA patients enrolled in the Ontario Best Practices Research Initiative (OBRI) registry, with active disease (≥1 swollen joint), available autoantibody information, and at least 1 follow-up assessment were included in the analysis. Sustained clinical remission was defined as CDAI ≤ 2.8 in at least 2 sequential visits separated by at least 3 and maximum of 12 months. Time to sustained remission was assessed with Kaplan-Meier survival analysis and multivariate cox regression. Results: A total of 970 patients were included in the analysis, of whom 262 (27%) were anti-CCP neg/RF neg, 60 (6.2%) anti-CCP pos/RF neg, 117 (12.1%) anti-CCP neg/RF pos, and 531 (54.7%) anti-CCP pos/RF pos. At baseline, significant differences were observed between groups in age (p=0.02), CDAI (p=0.03), tender joint count (p=0.02), and HAQ (p=0.002), with anti-CCP pos/RF pos and anti-CCP pos/RF neg patients being youngest and having the lowest disease activity and disability. No differences were observed in terms of biologic use which occurred in 15.9% of patients. Sustained remission was achieved by 43.5% of anti-CCP pos/RF pos patients, 43.3% of anti-CCP pos/RF neg patients, 31.6% of anti-CCP neg/RF pos patients and 32.4% of anti-CCP neg/RF neg patients (p=0.01). Significant (for RF, borderline non-significant) differences were observed in the time to achieving sustained clinical response based on anti-CCP status (p<0.001), RF status (p=0.06), and both (p=0.004) (Figure 1). Multivariate cox regression adjusting for baseline CDAI score, age and sex also showed differences between groups which reached statistical significance in anti-CCP pos/RF pos vs. anti-CCP neg/RF neg patients (HR [95%CI]: 1.30 [1.01-1.67]; p=0.03). Conclusion: These results suggest that anti-CCP but not RF positivity may be associated with improved response to anti-rheumatic medications in RA patients.

Figure 1: Time to Sustained Clinical Response by Autoantibody Status

Disclosure: J. E. Pope, AbbVie, Amgen, Bayer, BMS, Celtrion, Eli Lilly and Company, Merck, Novartis, Pfizer, Roche, UCB, 5,Amgen, Bayer, BMS, GSK, Merck, Novartis, Pfizer, Roche, UCB, 2; E. Rampakakis, Janssen Inc., 9; M. Movahedi, None; A. Cesta, None; J. S. Sampalis, None; C. Bombardier, Canada Research Chair in Knowledge Transfer for Musculoskeletal Care, 6,Pfizer Research Chair in Rheumatology, 6.


Abstract Number: 433

Predictors of Earlier Biologic Initiation Among Patients with Rheumatoid Arthritis Starting Methotrexate

Michael D. George1, Brian Sauer2, Chia-Chen Teng, MS2, Grant Cannon2, Bryant R. England3, Gail S. Kerr4, Ted R. Mikuls5 and Joshua Baker6, 1Division of Rheumatology, University of Pennsylvania, Philadelphia, PA, 2Salt Lake City VA Medical Center and University of Utah, Salt Lake City, UT, 3Division of Rheumatology & Immunology, Department of Internal Medicine, Nebraska-Western IA VA Health Care System & University of Nebraska Medical Center, Omaha, NE, 4VAMC, Georgetown University,
**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Biologic therapy for the treatment of RA has increased dramatically and has substantially increased costs of care. This study aimed to identify factors associated with initiation of biologic use, including previous methotrexate (MTX) adherence and dose.

**Methods:** We used U.S. Veteran’s Affairs administrative databases to identify RA patients receiving a first-ever prescription of MTX between 2005 and 2014 with at least 6 months of prior baseline data. Patients with prior biologic therapy use or those initiating biologic therapy within 30 days of starting MTX were excluded. Multivariable Cox analysis assessed factors associated with biologic therapy initiation within 2 years of MTX start, censoring at death. To assess impact of MTX adherence and dose on biologic use, we examined a subset of patients who received MTX continuously for at least 6 months with no biologic initiation during this time. In this population we evaluated associations between PDC (proportion of days covered) in the first 6 months and MTX dose at 6 months with subsequent biologic initiation.

**Results:** 17,634 patients met inclusion criteria contributing 29,350 person years of follow-up. 3,263 initiated biologic therapy within 2 years (incidence 11.1%/year). CCP positivity, later calendar year, and concurrent use of glucocorticoids, leflunomide, or sulfasalazine were associated with a greater likelihood of biologic initiation (Table 1). Factors associated with a lower rate of biologic initiation included advancing age, non-white race, greater comorbidity (Charlson score), congestive heart failure, and malignancy (Table 1, Figure 1). Among the smaller cohort of 9,851 patients remaining on methotrexate continuously for 6 months, methotrexate adherence (PDC ≥ 0.8) was not associated with likelihood of subsequent biologic initiation [aHR 1.00 (0.89-1.13), p = 0.94]. Higher methotrexate dose was associated with greater likelihood of initiating biologic therapy (Table 2).

**Conclusion:** Biologic therapy is initiated less frequently in elderly patients and those with comorbidities, possibly reflecting safety concerns. Future studies should evaluate whether these concerns lead to under-treatment of these populations. Surprisingly, low methotrexate adherence and dose were not associated with increased biologic use; the impact of reduced methotrexate effectiveness could be masked by differences in disease severity, follow-up, or medication preferences in these patients.
Table 1: Multivariable model evaluating factors associated with subsequent use of biologic therapy in patients starting methotrexate

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted HR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 50 Reference</td>
<td>1.00 (0.68, 1.39)</td>
<td></td>
</tr>
<tr>
<td>50-65</td>
<td>0.75 (0.42, 1.34)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>65-80</td>
<td>0.51 (0.30, 0.90)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>≥80</td>
<td>0.19 (0.15, 0.24)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Female</td>
<td>0.90 (0.50, 1.62)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>1.00 (0.73, 1.38)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Non-white</td>
<td>0.90 (0.57, 1.39)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>0.92 (0.32, 2.66)</td>
<td>0.89</td>
</tr>
<tr>
<td>Current smoking</td>
<td>0.98 (0.90, 1.08)</td>
<td>0.68</td>
</tr>
<tr>
<td>BMI (per 1 kg/m²)</td>
<td>0.93 (0.85, 1.01)</td>
<td>0.16</td>
</tr>
<tr>
<td>Ever current hypertension</td>
<td>1.23 (1.14, 1.33)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>CRP</td>
<td>0.99 (0.96, 1.02)</td>
<td>0.60</td>
</tr>
<tr>
<td>Depression</td>
<td>1.04 (0.96, 1.13)</td>
<td>0.35</td>
</tr>
<tr>
<td>Anxiety</td>
<td>0.95 (0.86, 1.05)</td>
<td>0.27</td>
</tr>
<tr>
<td>Post-traumatic stress disorder</td>
<td>1.00 (0.91, 1.11)</td>
<td>0.88</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>0.68 (0.52, 0.88)</td>
<td>0.001*</td>
</tr>
<tr>
<td>Cancer</td>
<td>0.82 (0.70, 0.97)</td>
<td>0.02</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>1.28 (1.00, 1.64)</td>
<td>0.05</td>
</tr>
<tr>
<td>Charlson score (per 1 unit)</td>
<td>0.94 (0.80, 1.10)</td>
<td>0.001*</td>
</tr>
<tr>
<td>Diuretics</td>
<td>1.36 (1.15, 1.61)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Current Hydroxychloroquine</td>
<td>1.04 (0.75, 1.44)</td>
<td>0.29</td>
</tr>
<tr>
<td>Current leflunomide</td>
<td>1.49 (1.11, 1.01)</td>
<td>0.01</td>
</tr>
<tr>
<td>Current Sulfasalazine</td>
<td>1.62 (1.21, 2.16)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Previous DMARD use</td>
<td>1.83 (0.73, 1.85)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Year 2011-2014 (vs. 2006-2010)</td>
<td>1.16 (0.68, 1.94)</td>
<td>&lt; 0.001*</td>
</tr>
</tbody>
</table>

* Statistically significant after Bonferroni correction for multiple comparisons (p < 0.0019). Included and not shown (p > 0.1): diabetes, chronic kidney disease, lung disease, interstitial lung disease. Missing data was not imputed.

1. Diuretics and leflunomide used in the 3 months prior to methotrexate initiation.
2. Hydroxychloroquine use within 1 month of methotrexate initiation.
3. Previous DMARD use with active prescription 30 days after methotrexate initiation.
4. DMARD prescription preceding MTX.
Table 2: Association between methotrexate adherence in the first 6 months and dose at 6 months with subsequent biologic initiation

<table>
<thead>
<tr>
<th>Dose (mg/week)</th>
<th>N (%)</th>
<th>Adjusted HR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDC ≥ 0.8*</td>
<td>6664 (69%)</td>
<td>1.00 (0.89-1.13)</td>
<td>0.94</td>
</tr>
<tr>
<td>MTX dose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10mg/week</td>
<td>1919 (19%)</td>
<td>1.00 (0.85-1.18)</td>
<td>0.82</td>
</tr>
<tr>
<td>&gt;10-15mg/week</td>
<td>3316 (32%)</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>&gt;15-20mg/week</td>
<td>3378 (34%)</td>
<td>1.30 (1.18-1.43)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt;20mg/week</td>
<td>3359 (35%)</td>
<td>1.40 (1.29-1.54)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Adjusted for age, sex, race, CRP, CCP-status, BMI, year, depression, anxiety, PTSD, smoking, congestive heart failure, diabetes, chronic kidney disease, coronary artery disease, cancer, interstitial lung disease, lung disease, Charlson score, glucocorticoid use, prior DMARD use, concurrent hydroxychloroquine, leflunomide, or sulfasalazine use. Missing COF, CRP, BMI, smoking values imputed. *PDC = proportion of days covered (pharmacy-based measure of adherence).

Disclosure: M. D. George, Bristol Myers Squibb, 2; B. Sauer, Amgen, 2; C. C. Teng, MS, Amgen, 2; G. Cannon, Amgen, 2; B. R. England, None; G. S. Kerr, Janssen, BMS, Genetech, Pfizer, 2; T. R. Mikuls, BMS, 2, Ironwood Pharm, 2, Pfizer Inc, 5, NIH, VA, 2; J. Baker, None.


Abstract Number: 434

Factors Associated with Treatment Adherence in Rheumatoid Arthritis: A Systematic Literature Review

Ee Teng Goh1, Alvin Jian Xiong Soo1, James Galloway2, Sam Norton3 and Elena Nikiphorou4, 1UCL Medical School, University College London, London, United Kingdom, 2King’s College, and King’s College Hospital, London, United Kingdom, 3Academic Rheumatology, King’s College London, London, United Kingdom, 4Academic Rheumatology Department, King’s College London, London, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM
Background/Purpose: Nonadherence to treatment in rheumatoid arthritis (RA) has been shown to negatively impact on treat to target goals and disease outcomes. Identifying and targeting potential factors influencing nonadherence is therefore crucial in optimising patient management. This review aims to determine factors associated with nonadherence in patients with RA.

Methods: An electronic search was performed by two independent reviewers using MEDLINE and focusing on articles published from inception to January 2017. The search strategy combined the thesaurus (MeSH) and expanded keyword searches of two concepts: RA and treatment adherence. Inclusion criteria included observational studies and clinical trials examining potential factors associated with nonadherence. Exclusion criteria included articles not in English or without online access and those with a focus on forms of therapy other than medication. Agreement between raters at the screening stage was high (94.6%, kappa=.88).

Results: The primary search yielded 1411 papers, from which 70 were eventually identified as suitable for full review (Figure). Of the 70 papers, 62 were based on observational studies and eight on clinical trials. Factors associated with nonadherence were broadly categorized into patient-related factors (demographics, socioeconomic factors, patient perceptions[beliefs/knowledge/attitudes]), disease-related factors (disease duration, disease activity, comorbidities, functional disability) and treatment-related factors (drug type, method of administration, concurrent treatment, side effects, cost). Many studies (74.3%) looking at beliefs, attitudes and patient knowledge reported significant associations between these factors and nonadherence. Adherence was found to be positively associated with stronger beliefs in the necessity of treatment, positive outlooks on disease control and medication, greater knowledge as well as greater self-efficacy. Studies reported greater comorbidities (n=8) including poorer mental health (n=5) to be implicated in nonadherence. Disease duration was largely non-significant in treatment adherence, although a few studies reported a negative correlation (n=3). The use of biologics was significantly associated with greater adherence. One study identified polypharmacy to be negatively associated with adherence. Drug side effects were associated with nonadherence (n=3).

Conclusion: Patient-related factors including personal perceptions were among key contributors to nonadherence to medication in RA patients. This highlights the need for addressing patient-driven perceptions, along with disease and treatment related factors as part of individualised patient care, to minimise the risk of nonadherence.
Characteristics of Rheumatoid Arthritis Patients Who Have a DMARD Interruption and the Impact of Using a Bridging Medication on Clinical and Patient Reported Outcomes

Christine Iannaccone1, Michelle Frits2, Taysir G. Mahmoud3, Gabriela Maica4, Jonathan Coblyn5, Michael Weinblatt2 and Nancy A. Shadick6

1Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA, 2Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 3Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 4Department of Rheumatology, Allergy, and Immunology, Brigham and Women's Hospital, Boston, MA, 5Department of Rheumatology, Brigham & Womens Hospital, Boston, MA, 6Rheumatology Immunology & Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: It is common for RA patients to interrupt their DMARD use due to events like infection, surgery, or pregnancy. Many RA patients may need to manage their symptoms during these times. Little is known about the characteristics of patients who have a break in their DMARD regimen and whether the use of a bridging medication produces better clinical and patient reported outcomes.

Methods: Clinical and patient reported data were collected from a prospective RA cohort. Data included whether patients reported DMARD interruption for any duration of time in the past 6 months and if they used a bridging medication (corticosteroid and/or NSAID) during the DMARD break. All data were collected at the time of survey. The outcomes (VAS Pain, fatigue, and patient global) were also collected at a study visit approximately 6 months prior and DAS28-CRP3 collected approximately 1 year prior. In univariate analyses, clinical and demographic characteristics of patients who had a DMARD interruption and used of a bridging medication were compared to patients who did not use of a bridging medication. The outcomes were evaluated in stepwise multiple linear regression models, adjusting for potential covariates of univariate significance (p<0.15) to assess the impact of a bridging medication (Figure).

Results: The study surveyed 503 RA patients, of which 112 (22%) reported a DMARD interruption in the last 6 months. Patients who reported a DMARD interruption had a median age of 59 (IQR 49.5, 68), were 85% female, and had median disease duration of 15 years (IQR 9, 25). Patients who used a bridging medication during a DMARD interruption (n=39) had higher disease activity (p=0.0002), fatigue (p=0.03), and pain (p=0.001) at the time of the survey compared to patients who did not use a bridging medication. In the final stepwise regression models evaluating the outcomes, comparing patients who did versus did not use a bridging medication, pain, fatigue, and patient global were no better with a bridging medication even after adjustment for baseline outcome severity (Figure). Use of a bridging medication was associated with a worse DAS28-CRP3 (p=0.008) after adjusting for covariates and baseline DAS28-CRP3 level (Figure).

Conclusion: In this study, nearly one quarter of RA patients reported an interruption of their DMARD regimen in the past 6 months and one third used an NSAID and/or corticosteroid to manage their symptoms during the break. Use of a bridging medication was not associated with better patient reported outcomes and patients had worse disease activity after the break. Better treatments for patients who need to manage symptoms during a DMARD interruption may be warranted.
Baseline Anemia As a Predictor of Radiographic Progression in Tofacitinib-Treated Rheumatoid Arthritis Patients: Post Hoc Analyses from Two Phase 3 Trials

Burkhard Moeller¹, Axel Finckh², Godehard Scholz¹, Harry Shi³, Carol A Connell⁴ and Sander Strengholt⁵,
¹Department for Rheumatology, Immunology and Allergology, University Hospital of Bern, Bern, Switzerland,
²University Hospital of Geneva, Geneva, Switzerland,
³Pfizer Inc, Collegeville, PA,
⁴Pfizer Inc, Groton, CT,
⁵Pfizer Inc, Capelle aan den IJssel, Netherlands
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Anemia in patients with rheumatoid arthritis (RA) can help to identify those with more rapid erosive disease.¹,² Tofacitinib is an oral Janus kinase inhibitor for the treatment of RA. In this post hoc analysis, we explored whether anemia was a predictor of radiographic progression in patients with RA who were treated with tofacitinib.

Methods: Data were from two 24-month, Phase 3 randomized controlled trials in methotrexate (MTX)-naïve (ORAL Start [NCT01039688]) or MTX-inadequate responder (IR) patients (ORAL Scan [NCT00847613]). Patients received either tofacitinib 5 or 10 mg twice daily (as monotherapy or with background MTX), placebo or MTX. Radiographic progression was evaluated by modified Total Sharp Score (mTSS) at baseline (BL), Month (M)6, M12, and M24. Anemia was defined as lower normal hemoglobin limits of 12 g/dL for women or 13 g/dL for men. We used a linear mixed model with repeated measure analysis to analyze the impact of BL anemia on change in radiographic joint damage (ΔmTSS), adjusting for treatment, age, gender, disease duration, and BL mTSS, autoantibody status, DAS28, corticosteroid, and non-steroidal anti-inflammatory drug (NSAID) use. Analyses were performed on observed data without linear extrapolation on missing data.
**Results:** Anemia was present at BL in 312/956 MTX-naïve patients (32.6%), RA duration ranged from 2.7–3.4 (mean) and from 0.7–0.8 (median) years, and in 321/797 MTX-IR patients (40.3%), RA duration ranged from 8.9–9.2 (mean) and from 6.0–7.7 (median) years. In MTX-naïve patients, anemia at BL was significantly associated with additional ΔmTSS from BL to M6 only (difference in ΔmTSS with and without BL anemia = 0.40; p<0.001) and increased ΔmTSS was also observed at M6 for patients receiving tofacitinib (0.25; p<0.05) or MTX monotherapy (0.95; p<0.005) (Figure 1A). There were no differences in ΔmTSS observed at M12 or M24 for either treatment group according to anemia status (data not shown). No associations between BL anemia and ΔmTSS were observed for MTX-IR patients overall or in either treatment group at M6 (Figure 1B), M12, or M24.

**Conclusion:** BL anemia was associated with radiographic progression at M6 in MTX-naïve patients, regardless of treatment received (tofacitinib or MTX monotherapy) but not at later time points (M12/M24). These data support the evidence that anemia at BL is a predictive parameter for joint damage progression in MTX-naïve patients, at least up to M6.

**References:**


**Figure 1.** Association between baseline anemia and change in radiographic progression at Month 6 in A) MTX-naïve and B) MTX-IR patients
Recruitment of RA Trials in the Modern Era: Are United States-Based Trials Still Feasible?

Carla Maldini¹-², Alfred Mahr³, David T. Felson⁴-⁵ and Michael P. LaValley⁶, ¹Internal Medicine, Hospital Saint-Louis, Paris, France, ²Rheumatology, Hospital Córdoba, Cordoba, Argentina, ³Internal Medicine, University Hospital Saint-Louis, Paris, France, ⁴Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA, ⁵Arthritis Research UK Centre for Epidemiology, Institute of Inflammation and Repair, University of Manchester, Manchester, United Kingdom, ⁶Biostatistics, Boston University School of Public Health, Boston, MA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Timely recruitment of patients into interventional trials is necessary for their successful completion. The aim of this study was to evaluate recruitment rates of interventional trials in RA with clinical centers in the United States (US).

Methods: We searched the ClinicalTrials.gov registry in May 2017 to identify trials in RA. Inclusion criteria were: phase 3 trials, starting enrollment in 2005 to 2016, adult RA patients, at least one center in the US, an intervention to modify RA activity, and a clinical evaluation (DAS28, ACR20, or other) as the primary endpoint. Exclusion factors were: if patients with other diseases were included, trials carried out only in specific RA subgroups, trials terminated early, trials which had not completed enrollment, and trials with insufficient data to calculate the recruitment rate. The recruitment rate was defined as the average number of patients enrolled per center per month during the recruitment period, with the recruitment period defined as the time between enrollment start date and date of enrollment of the last patient. As the registry only provides the “Primary Completion Date”, this was used as the proxy for date of enrollment of the last patient. Recruitment rate and other trial characteristics were compared in two calendar year periods (2005-2010 and 2011-2016) using the Wilcoxon rank sum test and chi-square test. Negative binomial regression was used to evaluate the relationship between the percent of US centers and recruitment rate.

Results: 179 trials were identified using our search strategy. 111 trials were excluded: 35 included other diseases, 24 did not complete recruitment (6 were terminated because low enrollment or sponsor decision), 40 did not use a clinical evaluation primary endpoint, and 12 started enrollment before 2005 or after 2016. Besides, 1 trial was excluded due to inconsistency on reported data. The ACR20 criteria was the most widely used outcome measure (70%). Most trials evaluated efficacy of biological therapies (97%), and only 2 evaluated efficacy of non-biological drugs. 8 trials (12%) assessed the efficacy of biosimilars. All trials but one were industry sponsored. Number of recruitment centers increased more than 25% in the second period (117 [77–154] vs 148 [111–186]; P = 0.058). Conversely, percent of US centers slightly decreased in the same period (35% vs 31%; P = 0.492). The recruitment rate per center per month was lower in the most recent time period (0.11 [0.08–0.16] vs 0.08 [0.05–0.11]; P = 0.02). Percentage of US centers was not related to recruitment rate (P = 0.295) in regression analysis.

Conclusion: The recruitment rate per center has decreased in recent years, accompanied by a non-significant rise in the number of centers per trial. While US-based trials remain feasible, understanding the reasons for declining enrollment trends is needed to improve the efficiency and performance of RA trials.
Table 1. Main characteristics of all 67 studies and by calendar year periods (2005-2010 and 2011-2016)

<table>
<thead>
<tr>
<th></th>
<th>Over period 2005-2016 n=67</th>
<th>Period 2005-2010 n=37</th>
<th>Period 2011-2016 n=30</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients enrolled per trial</td>
<td>637 (456–897)</td>
<td>643 (461–990)</td>
<td>590 (468–710)</td>
<td>0.194</td>
</tr>
<tr>
<td>No. of centers per trial</td>
<td>136 (88–180)</td>
<td>117 (77–154)</td>
<td>148 (111–186)</td>
<td>0.058</td>
</tr>
<tr>
<td>No. of U.S. centers per trial</td>
<td>45 (30–65)</td>
<td>41 (21–67)</td>
<td>46 (38–59)</td>
<td>0.492</td>
</tr>
<tr>
<td>ACR20 outcome measure, n (%)</td>
<td>47 (70.1)</td>
<td>28 (75.7)</td>
<td>19 (63.3)</td>
<td>0.272</td>
</tr>
<tr>
<td>Recruitment rate per month</td>
<td>12.9 (8.5–15.4)</td>
<td>12.9 (9.1–15.5)</td>
<td>12.2 (8.2–15.1)</td>
<td>0.512</td>
</tr>
<tr>
<td>Recruitment rate per center per month</td>
<td>0.10 (0.06–0.14)</td>
<td>0.11 (0.08–0.16)</td>
<td>0.08 (0.05–0.11)</td>
<td>0.020</td>
</tr>
</tbody>
</table>

Results are expressed as median and interquartile range unless otherwise noted.

Disclosure: C. Maldini, None; A. Mahr, None; D. T. Felson, None; M. P. LaValley, None.


Abstract Number: 438

High Multi-Biomarker Disease Activity Score Is Associated with High Risk of Radiographic Progression in Six Cohorts

Jeffrey R. Curtis1, Cecilie Heegaard Brahe2, Mikkel Østergaard3, Merete Lund Hetland2, Karen Hambardzumyan4, Saedis Saevardsdottir4, Xingbin Wang5, Eric H. Sasso5 and Tom W.J. Huizinga6, 1Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 2Copenhagen Center for Arthritis Research, Copenhagen, Denmark, 3Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Rigshospitalet, Denmark, Copenhagen, Denmark, 4Karolinska Institute and Karolinska University Hospital, Stockholm, Sweden, 5Crescendo Bioscience Inc., South San Francisco, CA, 6Rheumatology, Leiden University Medical Center, Leiden, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The multi-biomarker disease activity (MBDA) test uses a validated algorithm with 12 serum protein biomarkers to assess disease activity in patients with RA. The MBDA score has previously been found to be a predictor of risk for radiographic progression (RP). We evaluated data from 6 cohorts and performed a meta-analysis to collectively establish the relationship between the MBDA score and risk for RP.

Methods: Clinical, MBDA score and radiographic data were analyzed for 6 cohorts with N>100: Leiden, SWEFOT Year 1, SWEFOT Year 2, OPERA Year 1, and AMPLE Year 1 (abatacept and adalimumab arms). Analyses used data on file when published data were not available (ie, for Leiden and for OPERA CRP analyses). Frequency of RP over 1 year was determined by category of MBDA score (low, moderate, high on a scale of 1–100) at the start of the year, as reported for 4 cohorts and at the end of the year as reported for the 2 AMPLE cohorts. RP was defined using the threshold for change in modified total Sharp score (ΔmTSS) specific to each study (2 to >5 TSS units). Positive and negative predictive values (PPV and NPV) were determined for each study by comparing patients with high MBDA score (>44), DAS28-(ESR/CRP) (>5.1 or >4.09) or CRP (>3 mg/dL) vs those in a low/moderate category. Relative risk (RR)
for RP was determined for each study. RR values were integrated in a meta-analysis that included only the 3 non-overlapping cohorts that had reported radiographic analyses using MBDA scores at the start of the year. Results of published multivariate analyses and analyses that combined MBDA score with other risk factors for RP were summarized.

**Results:** The 6 study cohorts included patients receiving csDMARDs alone or with a biologic. Overall rates of RP were 10−26%. In each study, RP was most frequent among patients with a high vs low/medium MBDA score (≥44 vs ≤44). For high MBDA scores, NPVs were 93−97% and PPVs were 18−32%, with RR values of 3.6−9.5 (P=0.002 to <0.0001) (Figure). In a meta-analysis of the Leiden, SWEFOT Year 1 and OPERA Year 1 cohorts, RR was 5.1 (95% CI 3.8−6.7) for MBDA categories, and 1.4 (P=0.23) and 1.6 (P=0.01) for categories of DAS28-CRP or CRP, respectively. Published multivariate analyses in the Leiden and SWEFOT Year 1 cohorts showed MBDA score was an independent predictor of RP after accounting for the effect of other predictors. In the Leiden cohort, MBDA score was the strongest predictor and high MBDA score discriminated between high and low risk for RP among patients with high SJC (≥5) or high DAS28-CRP, with PPV as high as 57%.

**Conclusion:** High MBDA scores were associated with increased risk for RP in 6 study cohorts, including patients treated with csDMARDs, TNFi and abatacept. Based on high NPVs (≥93%), the MBDA score used alone had clinical value for identifying patients with little or no risk of RP. Combining the MBDA score with clinical measures yielded PPVs approaching 60%, suggesting that biomarkers can help stratify patients by their risk for RP.

### Table: Association between radiographic progression (RP) and high MBDA score (≥44) in 6 cohorts and a meta-analysis

<table>
<thead>
<tr>
<th>Cohort</th>
<th>N</th>
<th>RP cutoff</th>
<th>Overall % RP</th>
<th>PPV for MBDA≥44</th>
<th>NPV for MBDA≥44</th>
<th>Relative Risk* (95% CI)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leiden</td>
<td>163</td>
<td>&gt;44</td>
<td>17%</td>
<td>31%</td>
<td>93%</td>
<td>4.3 (1.9, 9.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>OPERA Year 1</td>
<td>164</td>
<td>&gt;44</td>
<td>26%</td>
<td>35%</td>
<td>92%</td>
<td>7.1 (4.1, 12.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>OPERA Year 1</td>
<td>164</td>
<td>&gt;44</td>
<td>26%</td>
<td>35%</td>
<td>92%</td>
<td>7.1 (4.1, 12.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>SWEFOT Year 1</td>
<td>425</td>
<td>&gt;44</td>
<td>18%</td>
<td>21%</td>
<td>97%</td>
<td>7.1 (1.9, 29.9)</td>
<td>0.008</td>
</tr>
<tr>
<td>Meta-analysis* (Leiden+SWEFOT Year 1+SWEFOT Year 1)</td>
<td>548</td>
<td>&gt;44</td>
<td>17%</td>
<td>32%</td>
<td>95%</td>
<td>6.2 (2.4, 16.5)</td>
<td>0.0001</td>
</tr>
<tr>
<td>AMPLIE Year 1</td>
<td>81</td>
<td>≥34</td>
<td>10%</td>
<td>18%</td>
<td>90%</td>
<td>4.5 (1.6, 13.3)</td>
<td>0.003</td>
</tr>
<tr>
<td>AMPLIE Year 1</td>
<td>81</td>
<td>≥34</td>
<td>10%</td>
<td>18%</td>
<td>90%</td>
<td>4.5 (1.6, 13.3)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

**Treatments referenced in abstract:**
- Leiden: csDMARDs, TNFi.
- OPERA: csDMARDs, TNFi.
- SWEFOT: csDMARDs, TNFi.
- AMPLIE: csDMARDs, TNFi.

**Disclosure:** J. R. Curtis, Crescendo Biosciences, 2; Crescendo Biosciences, 5; C. H. Brahe, None; M. Østergaard, AbbVie, BMS, Celgene, Crescendo Bioscience, Janssen, Merck, 2; Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Centocor, GSK, Hospira, Janssen, Merck, Novartis, Orinon, Pfzer, Regeneron, Roche, Takeda, and UCB, 5; M. Lund Hetland, AbbVie, Biogen, BMS, CelltrionRoche, Crescendo Biotechnology Inc., Eli Lilly, MSD, Pfizer, UCB, 2; Orinon, 8; K. Hambardzumyan, None; S. Saevardsdottir, None; X. Wang, Merck, Gnaic, Genetics, Inc., 1; Crescendo Biologicals Inc., 3; E. H. Sasso, Myriad Genetics, Inc., 1; Crescendo Bioscience Inc., 3; T. W. J. Huizinga, Merck, UCB, Bristol Myers Squibb, Biotest AG, Pfzer, GSK, Novartis, Roche, Sanofi-Aventis, Abbott, Crescendo Biotechnology Inc., Nycomed, Boeringher, Takeda, Zydus, Epirus, Eli Lilly, 5.


**Abstract Number:** 439

**Analysis of Rheumatoid Arthritis Patients That Did Not Achieve the Treatment Goal By the Treat-to-Target Strategy in Daily Practice**

Hideshi Yamazaki and Tetsuo Takanashi, Center for Rheumatic Disease, Marunouchi Hospital, Matsumoto, Japan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response

**Session Type:** ACR Poster Session A
Session Time: 9:00AM-11:00AM

**Background/Purpose:** Although the goal of rheumatoid arthritis (RA) treatment is to achieve remission or low disease activity with the treat-to-target (T2T) strategy, some patients do not achieve the goal in daily clinical practice. This study was performed to determine the reasons why these patients do not achieve the treatment goal.

**Methods:** A total of 504 patients with RA that were treated with the T2T strategy using electronic medical record system in 2014 – 2015 were investigated retrospectively. The patients had an average age of 63.7 years, and average disease duration of 15.9 years. A total of 144 patients were evaluated with moderate or high disease activity according to the simple disease activity index (SDAI) in 2014. After 1 year, 84 patients achieved the treatment goal, i.e., remission or low disease activity, while 60 patients still showed more than moderate disease activity and did not achieve the goal. In these patients, each item of SDAI, patient background, and treatment content were investigated.

**Results:**

In 2014, the patients that did not achieve the treatment goal in 2015 had significantly higher age, disease activity, tender joint count, patient global assessment, and HAQ-DI than the patients that did achieve the goal. In the patients that achieved the goal, all items of SDAI were significantly improved. In the patients that did not achieve the goal, swollen joint count and physician global assessment were significantly improved. As disease activity did not decrease, 21 patients were considered to have been treated insufficiently with the T2T strategy. Twenty-one patients had joint pain without arthritis. Eighteen patients were not treated sufficiently for complications, including six elderly patients, respiratory complications in eight patients, and others.

**Conclusion:**

Although the treatment goal of the T2T strategy in RA is remission or low disease activity, this goal is often not achieved in daily clinical practice. The patients that do not achieve the goal have higher disease activity or are not treated sufficiently with complications. It may be possible for these patients to achieve the goal by refining the treatment strategy or providing palliative treatment for pain. Additional T2T is necessary.

**Disclosure:** H. Yamazaki, None; T. Takanashi, None.


**Abstract Number:** 440

**Rheumatoid Arthritis Patient’s Journey: Delay in Diagnosis and Treatment**

Aurelia Luissi¹, Florencia Pierini¹, Maria Victoria Garcia¹, Mirtha Sabelli¹, Marina Scolnik¹, Santiago Ruta¹, Javier Rosa¹ and Enrique R Soriano²
¹Rheumatology Unit, Internal Medicine Service, Hospital Italiano de Buenos Aires, CABA, Argentina, ²Argentina, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** there is a wide variation in the time elapsed between first symptoms and diagnosis of RA, ranging from 1 month to 10 years in different studies; data from Latin America populations are scarce.

**Objective:** to establish the lag times between articular symptoms onset and first rheumatologist consultation, Rheumatoid Arthritis (RA) diagnosis and treatment with disease-modifying antirheumatic drugs (DMARDs), and to assess the impact of delay on radiologic structural damage.

**Methods:** electronic Medical Records of a cohort of RA adult patients, attending a Private Health Care System (PHCS) between 01/01/1996 and 31/12/2016, were retrospectively reviewed. Clinical and demographic data, and dates of first disease symptoms, diagnosis of RA and starting treatment with DMARDs were obtained. Physical function was assessed by Health Assessment
Questionnaire (HAQ). Radiologic structural damage was assessed by Sharp score modified by van der Heijde (SvdH score). For the logistic multivariable analysis, radiologic structural damage was defined as the presence of any value greater than 0 on SvdH score.

**Results:** 246 patients (81% female), with a mean age of 67.25 (SD:14.53) years, were included. Rheumatoid factor was positive in 82.5% and anti–citrullinated peptide antibodies in 91% of patients.

At the end of follow-up (mean: 7 years, SD: 3.8), median HAQ and SvdH were 0.125 (IQR: 0-0.87) and 15 (IQR: 6-33), respectively. Mean lag time between first disease symptom and rheumatologist consultation was 9.2 months [(SD:20) (median: 3 months)], mean lag time to RA diagnosis was 14.2 months [(SD: 24) (median: 4.8 months)] and was 16.9 months [(SD: 25.4) (median: 7 months)] for starting treatment with DMARDs (Table).

<table>
<thead>
<tr>
<th></th>
<th>Mean (SD)</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time elapsed from the beginning of symptoms to first health professional consultation (months)</td>
<td>8.5 (21.6)</td>
<td>1.8 (0.6-5.1)</td>
</tr>
<tr>
<td>Time elapsed from the beginning of symptoms to first rheumatologist consultation (months)</td>
<td>9.2 (20.5)</td>
<td>3 (1.2-7.1)</td>
</tr>
<tr>
<td>Time elapsed from the beginning of symptoms to RA diagnosis (months)</td>
<td>14.2 (24)</td>
<td>4.8 (2.4-13)</td>
</tr>
<tr>
<td>Time elapsed from the beginning of symptoms to starting DMARDs therapy (months)</td>
<td>16.9 (25.4)</td>
<td>7 (3-17)</td>
</tr>
</tbody>
</table>

More radiologic structural damage was observed in patients with more than 12 months delayed diagnosis of RA (mean SvdH score: 30.9 vs. 21.3, p = 0.0325). The presence of radiologic structural damage was associated with more than 12 months delayed diagnosis in logistic multivariable analysis (OR: 1.7 CI 95% 1.3-4.9, p=0.04).

**Conclusion:** in this cohort of RA patients from a PHCS there was a significant delay to achieve RA diagnosis and starting DMARDs therapy. A delay greater than 12 months was associated with radiologic structural damage during the follow-up period.

**Disclosure:** A. Luissi, None; F. Pierini, None; M. V. Garcia, None; M. Sabelli, None; M. Scolnik, None; S. Ruta, None; J. Rosa, None; E. R. Soriano, AbbVie, Janssen, Novartis, Pfizer Inc, UCB, 2;AbbVie, Janssen, Novartis, Pfizer Inc, UCB, 5;AbbVie, Bristol-Myers Squibb, Janssen, Novartis, Pfizer Inc, Roche, UCB, 8.


**Abstract Number: 441**

**Social Media Based, Direct-to-Patient Study Designed for Development of “from Home” Testing for Rheumatoid Arthritis Patients Is Feasible and Engaged Individuals with Distinct Clinical Characteristics**

Kristen Warren¹, Olga Derbeneva¹, Francisco Flores¹, Michelle Frits², James Healy¹, Christine Iannaccone³, Omar Khalid¹, Krishna Morampudi¹, Nancy Shadick⁴, Michael Weinblatt⁴, Hemani Wijesuriya¹ and **Robert Terbrueggen¹**, ¹DxTerity, Rancho Dominguez, CA, ²Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ³Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA, ⁴Brigham and Women's Hospital and Harvard Medical School, Boston, MA

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Background/Purpose:** Physicians equipped with low cost, patient-administered, “from home” genomic tests for monitoring disease activity and therapy response could revolutionize treatment for rheumatoid arthritis (RA) by enabling treat-to-target strategies, minimizing the use of ineffective therapies, and detecting changes in disease activity before a flare occurs. However, development of a “from home” strategy for patient care requires rigorous testing in the intended use cohort. In addition, the costs associated with recruiting and analyzing a patient cohort of sufficient size are formidable and further compounded by the possible confounding effects of concomitant RA therapies. Here, we investigated the feasibility of recruiting a patient cohort entirely through social media at minimal cost and cohort metrics were compared with clinical data of patients enrolled in a traditional, clinically managed study.

**Methods:** A cohort of self-reported RA participants were recruited under an IRB-approved, HIPAA compliant, Direct-to-Patient observational study entitled Baseline Rheumatoid Arthritis Verification and Outcomes (BRAVO; www.bravostudy.com). Participants were asked to complete 3 rounds of disease monitoring over a one month period, which included a short disease history questionnaire with RAPID3 ePRO and a self-collected 100 µL fingerstick blood sample returned through the US mail. Total RNA (50 ng) was isolated from the self-collected blood samples and sequenced using a custom 1200-gene pan-immunity Ampliseq panel on the Ion S5. Patient cohort metrics were compared with clinical data from the multi-center, longitudinal observational, 14-year, 1,400+ patient Brigham Women’s Rheumatoid Arthritis Sequential Study (BRASS; www.brassstudy.org).

**Results:** BRAVO participants (n = 109) were recruited over a 12-week period through social media platforms. Most participants (80%) enrolled and completed the questionnaires using a mobile device, and 84% of patient samples yield at least 100ng of isolated RNA with an average RIN of 7.1. Comparison of cohort attributes at baseline between BRAVO and BRASS individuals (Table) exhibited significant similarities between mean age, disease duration, and range of medications. However, the BRAVO cohort tended to have higher disease activity, lower use of biologic and non-biologic DMARDS, higher use of narcotic/opioid pain meds and increased ethnicity.

**Conclusion:** Social media and molecular analysis of patient-collected fingerstick samples are viable and cost-effective methods to examine efficacy of direct-to-patient testing for RA affected individuals. Cohorts however differed significantly on the basis of critical clinical parameters indicating that a direct-to-patient approach has the power to add depth to the complex RA patient population that can be effectively monitored.

**Disclosure:** K. Warren, DxTerity, 3; O. Derbeneva, DxTerity, 3; F. Flores, DxTerity, 3; M. Frits, None; J. Healy, DxTerity, 1,DxTerity, 3,DxTerity, 6; C. Iannaccone, None; O. Khalid, DxTerity, 3; K. Morampudi, DxTerity, 3; N. Shadick, None; M. Weinblatt, None; H. Wijesuriya, DxTerity, 3; R. Terbrueggen, DxTerity, 1,DxTerity, 3,DxTerity, 4,DxTerity, 6.

Early Treatment with Hydroxychloroquine Is Associated with Better Long-Term Outcomes in a Group of Hispanic Patients with Rheumatoid Arthritis

Franchesca Cruz-Pérez1, Mariangelí Arroyo-Ávila1, Ruth Fred-Jiménez2, Naydi Pérez-Ríos3, Noelia Rodríguez-Pérez1, Grissel Ríos4 and Luis M. Vílal5, 1Department of Medicine, Division of Rheumatology, University of Puerto Rico Medical Sciences Campus, San Juan, PR, 2Division of Rheumatology, University of Puerto Rico Medical Sciences Campus, San Juan, Puerto Rico, 3Puerto Rico Clinical and Translational Research Consortium, University of Puerto Rico Medical Sciences Campus, San Juan, PR, 4Rheumatology, University of Puerto Rico Medical Sciences Campus, San Juan, PR, 5Department of Medicine, Division of Rheumatology, University of Puerto Rico Medical Sciences Campus, San Juan, Puerto Rico

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Hydroxychloroquine (HCQ) has a disease-modifying effect in rheumatoid arthritis (RA) patients but also it is associated with improved lipid profile, and decreased risk for diabetes and cardiovascular events. However, the impact of early HCQ treatment in the long-term outcomes of RA is not well established. Therefore, we sought to determine the clinical manifestations, incident comorbidities, and functional status in a group of Hispanic patients with RA who received early therapy with HCQ.

Methods: A cross-sectional study was performed in a cohort of RA patients (per American College of Rheumatology classification criteria). Demographic features, health-related behaviors, cumulative RA manifestations, disease activity (per Disease Activity Score 28 [DAS-28]), functional status (per Health Assessment Questionnaire), incident comorbidities, and pharmacologic treatment were determined. Patients who received early treatment (within the first year from the onset RA symptoms), late treatment (>1 year from the onset of RA symptoms) or no treatment with HCQ were compared. All patients who were treated with HCQ received at least one year of therapy. Data were examined using bivariate and multivariate (logistic regression) analyses.

Results: A total of 419 patients were studied. The mean (SD) age of the study population was 56.0 (13.8) years and 87.3% were woman. The mean (SD) disease duration was 14.7 (9.1) years. Seventy-four (17.7%) patients received early treatment with HCQ, 131 (31.3%) late treatment with HCQ, and 214 (51.0%) patients did not receive therapy with HCQ. In the multivariate analysis adjusted for age and disease duration, those who received early treatment had lower HAQ scores (OR 0.59, 95% CI 0.41 – 0.85) and were less likely to have joint replacement surgeries (OR 0.15, 95% CI 0.03 – 0.67) than those who were not exposed to HCQ. These differences were not observed between patients who had late treatment and those who did not received HCQ treatment. No significant differences were observed between the three groups in terms of sex, lifestyle behaviors, joint deformities/contractures, extra-articular manifestations, current disease activity, incident comorbidities (arterial hypertension, diabetes mellitus, dyslipidemia, and cardiovascular events), and exposure to corticosteroids or other disease-modifying anti-rheumatic drugs (synthetic or biological).

Conclusion: In this group of Hispanic RA patients, those receiving early treatment with HCQ had better long-term outcomes, having less functional impairment and joint replacement surgeries than those who received late or no HCQ therapy. This study highlights the importance of early treatment with HCQ to prevent disease damage in RA.

Disclosure: F. Cruz-Pérez, None; M. Arroyo-Ávila, None; R. Fred-Jiménez, None; N. Pérez-Ríos, None; N. Rodríguez-Pérez, None; G. Ríos, None; L. M. Vílal, None.

Methotrexate Treatment Strategies in an Early Rheumatoid Arthritis Cohort

Sasha Bernatsky1, Orit Schieir2, Cristiano S. Moura3, Marie-France Valois4, Susan J. Bartlett5, Carol A Hitchon6, Janet E. Pope7, Gilles Boire8, Boulos Haraaou9, Edward C. Keystone10, Diane Tin11, Carter Thorne12 and Vivian P. Bykerk13, 1Divisions of Rheumatology and Clinical Epidemiology, Research Institute of the McGill University Health Centre, Montreal, QC, Canada, 2Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada, 31Division of Clinical Epidemiology, McGill University
Background/Purpose: Methotrexate (MTX) is recommended as part of initial therapy in early RA, but practices range widely. The objective of this analysis was to describe MTX treatment in an early RA cohort, beginning with initial therapy and assessing time to treatment failure across various treatment strategies.

Methods: We studied adult patients from a prospective multicenter early arthritis cohort (enrolled 2007-2017 within one year of symptom onset) who fulfilled ACR/EULAR RA criteria. RA patients were eligible for our analyses if they initiated MTX (+/- other DMARDs) within 90 days of cohort entry. The first analyses determined time until ‘failure’ of that initial MTX-based therapy, from the time of first initiation, left-censored at cohort entry. Treatment failure definition included: change of route for MTX monotherapy, adding or stopping a DMARD/biologic, and changing dose/frequency of a DMARD or biologic, due to inefficacy or a serious adverse event.

Results: We studied 1,484 early RA patients, the majority initiating either MTX monotherapy (oral or subcutaneous) or MTX plus a second agent (Table 1). At the time of entry into the early arthritis cohort, their mean (standard deviation, SD) age was 54 (15) years, their mean symptom duration was 5.6 months (2.8), their mean DAS28 scores were 5.3 (1.4), and one third (38%) were on oral steroids. Overall, 911/1464 (61%) had a treatment failure, primarily due to inefficacy (Table 1).

Table 1: Distribution of initial treatment and reasons for treatment failure

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Frequency</th>
<th>%</th>
<th>Length of time remaining on initial treatment (months)*</th>
<th>Any Failure</th>
<th>Drug stopped due to inefficacy</th>
<th>Serious adverse effect</th>
<th>Any side effect $</th>
<th>$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral MTX monotherapy</td>
<td>398</td>
<td>26.8</td>
<td>6.0 0.3 to 95.9</td>
<td>313 (79%)</td>
<td>13 (3.3%)</td>
<td>0 (0%)</td>
<td>70 (17.6%)</td>
<td></td>
</tr>
<tr>
<td>Subcutaneous MTX monotherapy</td>
<td>328</td>
<td>22.1</td>
<td>13.1 0.4 to 106.1</td>
<td>146 (45%)</td>
<td>1 (0.3%)</td>
<td>0 (0%)</td>
<td>61 (18.6%)</td>
<td></td>
</tr>
<tr>
<td>MTX plus a second DMARD</td>
<td>642</td>
<td>43.3</td>
<td>9.3 0.3 to 107.8</td>
<td>375 (58%)</td>
<td>23 (3.6%)</td>
<td>0 (0%)</td>
<td>168 (26.2%)</td>
<td></td>
</tr>
<tr>
<td>MTX-HQN-SSZ</td>
<td>116</td>
<td>7.8</td>
<td>9.8 0.3 to 96.8</td>
<td>77 (66%)</td>
<td>7 (6.0%)</td>
<td>1 (0.9%)</td>
<td>58 (50.0%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1484</td>
<td>100.0</td>
<td>9.0 0.3 to 107.8</td>
<td>911 (61%)</td>
<td>44 (3.0%)</td>
<td>1 (0.1%)</td>
<td>357 (24.1%)</td>
<td></td>
</tr>
</tbody>
</table>

$ The variable reason to stop, serious adverse events and any side effects are MD recorded.

The multivariate cox regression (Table 2) for the first analyses showed that, compared to oral MTX monotherapy, all MTX strategies had longer time to failure.

Table 2: Adjusted hazard ratios (HR) for drug changes after time zero* compared to oral MTX monotherapy (the reference)

<table>
<thead>
<tr>
<th>Treatment at time zero</th>
<th>Adjusted HR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTX subcutaneous monotherapy</td>
<td>0.91</td>
<td>0.61, 1.35</td>
</tr>
<tr>
<td>MTX + another DMARD</td>
<td>0.87</td>
<td>0.62, 1.22</td>
</tr>
<tr>
<td>MTX+SSZ+HCQ</td>
<td>0.64</td>
<td>0.44, 0.94</td>
</tr>
<tr>
<td>Biologics +/- DMARDs including MTX</td>
<td>0.31</td>
<td>0.20, 0.49</td>
</tr>
<tr>
<td>Non MTX DMARDs only</td>
<td>1.26</td>
<td>0.89, 1.77</td>
</tr>
</tbody>
</table>
Adjusting for baseline characteristics: age, sex, co-morbidities, symptom duration, race, education, smoking, erosions, DAS-28, disease activity, corticosteroids, NSAIDs, and COXIBs.

**Conclusion:** Our data in early RA patients initially exposed to MTX suggest that compared to oral MTX, all other MTX strategies had longer time to failure. These data do not confirm clear differences in outcomes with respect to methotrexate DMARD combinations, as the width of confidence intervals precludes definitive conclusions in this regard.

**Disclosure:** S. Bernatsky, None; O. Schieir, None; C. S. Moura, None; M. F. Valois, None; S. J. Bartlett, PROMIS, 6; Pfizer Inc, UCB, Lilly, 5; C. A. Hitchon, None; J. E. Pope, AbbVie, Amgen, Bayer, BMS, Celtrion, Eli Lilly and Company, Merck, Novartis, Pfizer, Roche, UCB, 5, Amgen, Bayer, BMS, GSK, Merck, Novartis, Pfizer, Roche, UCB, 2; G. Boire, None; B. Harauoi, AbbVie, Amgen, BMS, Celgene, Eli Lilly, Janssen, Merck, Pfizer, Roche, Sandoz, 6; AbbVie, Amgen, BMS, Janssen, Pfizer, Roche, and UCB; 2, Pfizer, and UCB; 8; E. C. Keystone, Abbott Laboratories, Amgen Inc., AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb, F. Hoffmann-La Roche Inc, Janssen Inc, Lilly Pharmaceuticals, Novartis Pharmaceuticals, Pfizer Pharmaceuticals, Sanofi-Aventis, UCB, 2, Abbott Laboratories, AstraZeneca Pharma, Biotest, Bristol-Myers Squibb Company, Crescendo Bioscience, F. Hoffmann-La Roche Inc, Genentech Inc, Janssen Inc, Lilly Pharmaceuticals, Merck, Pfizer Pharmaceuticals, UCB, 5, Amgen, Abbott Laboratories, AstraZeneca LP, Bristol-Myers Squibb Canada., 8; D. Tin, None; C. Thorne, AbbVie, Amgen, Celgene, Lilly, Novartis, Pfizer, Sanofi, and UCB; has served as a consultant for AbbVie, Amgen, Celgene, Centocor, Genzyme, Hospira, Janssen, Lilly, Medexus/Medac, Merck, Novartis, Pfizer, Sanofi, and UCB; 2, Medexus/Medac, 8; V. P. Bykerk, Amgen, Bristol-Myers Squibb Company, Gilead, Sanofi-Genzyme/Regeneron, Pfizer Pharmaceuticals, UCB, 5.

Table 1: Comparison between the concordant and discordant treatment decision groups. 3rd column shows details of 21 patients in whom PtGA > 50% of CDAI calculation. MSK = musculoskeletal co-morbidities, PtGA = Patient Global Assessment of Disease Activity, CDAI = Center For Disease Activity Index, T2T = Treat to Target, RF = Rheumatoid Factor, CCP = Cyclic Citrullinated Peptide, DMARD = Disease Modifying Anti Rheumatic Drugs.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Concordant decisions (71%, n=22)</th>
<th>Discordant decisions (29%, n=9)</th>
<th>PtGA &gt;50% of CDAI calculation (68%, n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean, years)</td>
<td>49</td>
<td>51</td>
<td>48</td>
</tr>
<tr>
<td>Sex (% females)</td>
<td>77</td>
<td>77</td>
<td>86</td>
</tr>
<tr>
<td>Ethnicity (% Caucasians)</td>
<td>86</td>
<td>89</td>
<td>86</td>
</tr>
<tr>
<td>&gt; College education (%)</td>
<td>63 (n=19)</td>
<td>50 (n=6)</td>
<td>66</td>
</tr>
<tr>
<td>&gt;1 MSK co-morbidity (%)</td>
<td>32</td>
<td>67</td>
<td>43</td>
</tr>
<tr>
<td>Duration of RA (median, years)</td>
<td>6.7</td>
<td>9.8</td>
<td>3</td>
</tr>
<tr>
<td>RF and/or CCP positive (%)</td>
<td>95</td>
<td>87.5</td>
<td>94</td>
</tr>
<tr>
<td>DMARD treatment (%)</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Glucocorticoid ≥ 5mg daily (%)</td>
<td>22.7</td>
<td>22.2</td>
<td>18</td>
</tr>
<tr>
<td>CDAI score (median)</td>
<td>8.5</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>PtGA score (median)</td>
<td>5</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>PtGA score ≥ 50% of CDAI calculation (%)</td>
<td>68</td>
<td>67</td>
<td>29% discordant decisions</td>
</tr>
<tr>
<td>T2T target remission (%)</td>
<td>86</td>
<td>100</td>
<td>90</td>
</tr>
</tbody>
</table>

Background/Purpose: The American College of Rheumatology strongly recommends using a treat-to-target (T2T) strategy because it has demonstrated improved outcomes compared to a non-targeted approach in RA. The crux of a T2T based strategy is accurate disease activity measurement using a composite disease activity tool like Clinical Disease Activity Index (CDAI) and then adapt therapy as necessary until the clinical target is met. The aim of our study is to measure concordance between usual care-treatment decisions and CDAI-based T2T treatment decisions and to identify reasons for discordance, if any. This is a crucial step in our internal validation of CDAI and development of a T2T-based treatment pathway.

Methods: Adult RA patients in our tertiary care rheumatology clinic during the period of 5/20/16 to 5/20/17 were prospectively identified. First, as part of the usual care treatment approach currently used at our clinic, a shared treatment decision was made after consideration of all patient, disease, and treatment related factors. Then a T2T based mutual disease target was established with the patient and a CDAI was scored to determine if the patient has met target or not. The ideal T2T strategy based treatment decision was recorded for study purposes to compare with the usual care decision. We measured concordance between the T2T and usual care treatment decisions, compared characteristics of concordant and discordant groups, and of those where the Patient Global Assessment of Disease Activity (PtGA) contributed to ≥ 50% of the total CDAI score. We recorded patient, disease and treatment related data at each visit.

Results: Patient demographic, RA disease and treatment related data can be found in Table 1. Of the total 40 patients, 9 patients were in remission and were excluded from the analysis as there was low likelihood of discordance. Of the remaining 31 patients, there were 9 instances (29%) of discordance between T2T and usual care treatment decisions. There were higher number of patients with ≥ 1 musculoskeletal comorbidity (osteoarthritis, bursitis, etc) -67% in the discordant group vs 32% in concordant group. There were slightly higher numbers of patients with ≥ college education in the concordant group (63%) than in the discordant group (50%). PtGA contributed to ≥ 50% of total CDAI score in 21 patients of the cohort (68%), and of these 43% had ≥ 1 musculoskeletal comorbidity.

Conclusion: In our small group of 40 RA patients, we found 29% discordance between the T2T and usual care treatment decisions, and the PtGA contributed to ≥ 50% of the total CDAI score in 68% patients. As accurate disease activity measurement is central in any T2T...
strategy, we believe that this deeper understanding of variation in CDAI, PtGA scores and T2T decisions is very useful. We have accordingly started using PtGA as a patient education opportunity and plan to repeat this study with a new amended CDAI questionnaire.

Disclosure: R. Gopalarathinam, None; M. Kimoto, None; T. S. Sharma, None.


Abstract Number: 445

FLARE-RA Instrument Detects RA Flares Independent of Disease Activity

Taysir G. Mahmoud1, Michelle Frits2, Christine Iannaccone3, Gabriela Maica4, Vivian P. Bykerk5, Michael Weinblatt6 and Nancy A. Shadick7, 1Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 2Brigham and Women's Hospital, Boston, MA, 3Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA, 4Department of Rheumatology, Allergy, and Immunology, Brigham and Women's Hospital, Boston, MA, 52-005, Mt Sinai Hospital, Toronto, ON, Canada, 6Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 7Rheumatology Immunology & Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Clinicians often associate the occurrence of a recent rheumatoid arthritis (RA) flare with an increase in overall disease activity. However, previous studies have shown that patients with RA in low disease states still report flares. The goal of this study is to examine if having a recent flare is independent from disease activity overall, using the FLARE-RA instrument.

Methods: Data were collected from a prospective RA registry including patient reported and clinical outcomes, such as flare frequency and the FLARE-RA instrument. FLARE-RA asks patients to rate 11 statements about their disease on a 0-10 scale (not true to absolutely true). The statements are about patient and physician identified flare features covering the following: morning stiffness, joint pain, joint swelling, sleep disturbance, pain killer or NSAID use, fatigue, decrease in physical activity, irritability, depression, withdrawal, and increased need for help. The score is the mean of all 11 items, where a higher score suggests a recent flare. Disease Activity Score 28 joint with CRP (DAS) was dichotomized into low/remission and moderate/high disease. Flare recency (presence of a flare in the past 6 months) was coded into 3 categories; no flare, at least 1 flare, and currently flaring. Nonparametric tests were performed to examine possible covariates in relation to the FLARE-RA score. A multiple regression model with FLARE-RA score as the outcome included covariates that had a p<0.15 in the univariate analyses.

Results: 503 participants were surveyed; 85% were female with a mean (SD) age of 61 (13), 75% had a college degree or higher, and the median disease duration was 16 (IQR 9, 26) years. The median DAS28-CRP3 was 2.1 (1.6, 2.8) and the median FLARE-RA score was 2 (0.5, 4.4). In univariate analyses, a linear trend between DAS category, flare recency, and FLARE-RA was seen (Figure). The regression model found that having a recent flare is associated with a higher FLARE-RA score independent of DAS category, while adjusting for gender, education, and disease duration. Additionally, flare recency had a higher effect size than DAS on total FLARE-RA score.

Conclusion: Having a current or recent flare drives the FLARE-RA score more than a patient’s current disease activity suggesting that this instrument is able to detect patients’ self report of flare. This instrument may be useful in detecting flares even in patients with low disease activity which could provide an additional rationale for treatment change.
Methotrexate Use and Fatigue in Rheumatoid Arthritis Patients: Results from a National Patient Registry

Huiyfeng Yun1, Shuo Yang2, W. Benjamin Nowell3, Cooper Filby1, Lang Chen1 and Jeffrey R. Curtis4, 1University of Alabama at Birmingham, Birmingham, AL, 2Division of Clinical Immunology & Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 3Global Healthy Living Foundation, Upper Nyack, NY, 4Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL

First publication: September 18, 2017
Background/Purpose: Methotrexate (MTX), a synthetic disease-modifying antirheumatic drug (DMARD), is the most commonly used medication for rheumatoid arthritis (RA). Considerable variations between patients taking MTX exist due to its potential adverse effects and tolerability issues. Although patient reported outcomes have been used for evaluating effectiveness of RA treatments in clinical trials, much less is understood from real-world settings. This study evaluated the association between MTX use and fatigue in the PCORI-funded Patient Powered Research Network for adult rheumatologic conditions, ArthritisPower.

Methods: Patients in the ArthritisPower registry were invited to provide medication information and PROs including the RAPID3 and 4 PROMIS instruments (pain interference, physical function, fatigue, and sleep disturbance) plus disease-specific information via a mobile application (App) on their smartphone or computer. Patients who used selected RA medications of interest (glucocorticoids, non-biologic DMARDs, biologics) and answered ≥ 1 instrument were eligible this study. We calculated the mean and standard deviation (SD) of RAPID3 and the 4 PROs across different RA treatments cross-sectionally. Multivariable regression analysis with repeated measures was used to evaluate the association between MTX use and fatigue.

Results: As of June 2017, ArthritisPower had recruited 5,830 patients; approximately 57% had RA. A total of 469 participants had RA medication use and answered relevant PROMIS instruments, with mean (SD) age of 48.3 (11.5) years; 32.0% used glucocorticoids, 83.2% used non biologic DMARDs, and 62.5% used biologics. The mean score for pain interference was 62.7 (SD: 7.3), physical function 38.0 (6.9), sleep disturbance 56.9 (8.4), fatigue 62.3 (8.5), and RAPID3 14.7 (5.7). Among different RA treatments, patients on biologic monotherapy had the highest scores for pain interference, sleep disturbance, fatigue, and RAPID3, whereas MTX monotherapy had the lowest. In contrast, MTX monotherapy had the highest physical function score whereas biologic monotherapy had the lowest (Table). Using fatigue as an example, MTX use is associated with 2.29 (95% confidence interval: -3.2, -1.4) units of lower fatigue score after adjusting for age, gender, race, insurance, employment and concurrent RA medications and medical conditions.

Conclusion: PROMIS measures are feasible to capture from patients with Smartphone and Web Apps. Despite potential concerns related to fatigue associated with use of MTX, these results suggest that on average, MTX is associated with lower fatigue scores. RA patients on MTX might be associated with better PROs, especially when it was combined with biologics use. More longitudinal data analyses are needed to better understand the relationship.

Table: Mean of PROMIS instruments on different RA medications

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Observations (patients)</th>
<th>Mean (SD) Pain interference</th>
<th>Mean (SD) Physical function</th>
<th>Mean (SD) Sleep disturbance</th>
<th>Mean (SD) Fatigue</th>
<th>Mean (SD) RAPID3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methotrexate monotherapy</td>
<td>196 (60)</td>
<td>59.3 (9.1)</td>
<td>41.3 (7.1)</td>
<td>54.9 (8.5)</td>
<td>59.3 (8.3)</td>
<td>11.7 (6.9)</td>
</tr>
<tr>
<td>Methotrexate + other non-biologic DMARDs</td>
<td>133 (51)</td>
<td>60.8 (7.9)</td>
<td>40.1 (7.7)</td>
<td>56.5 (8.9)</td>
<td>60.4 (9.6)</td>
<td>13.8 (6.1)</td>
</tr>
<tr>
<td>Biologic monotherapy</td>
<td>150 (69)</td>
<td>64.1 (6.4)</td>
<td>36.0 (6.7)</td>
<td>58.9 (8.6)</td>
<td>64.7 (8.8)</td>
<td>16.3 (5.8)</td>
</tr>
<tr>
<td>Biologic + methotrexate</td>
<td>703 (172)</td>
<td>63.0 (7.0)</td>
<td>37.5 (6.6)</td>
<td>57.8 (8.3)</td>
<td>63.0 (8.4)</td>
<td>15.2 (5.6)</td>
</tr>
<tr>
<td>Biologic + other non-biologic DMARDs</td>
<td>154 (42)</td>
<td>62.9 (7.7)</td>
<td>37.2 (8.4)</td>
<td>58.0 (8.6)</td>
<td>64.2 (10.6)</td>
<td>15.4 (6.1)</td>
</tr>
</tbody>
</table>

Disclosure: H. Yun, BMS, 2; S. Yang, None; W. B. Nowell, Global Healthy Living Foundation, 3; C. Filby, None; L. Chen, None; J. R. Curtis, UCB Pharma, Janssen-Cilag, Amgen, Roche, Myriad Genetics, Lilly, Novartis, BMS, Pfizer, 2; UCB Pharma, Janssen-Cilag, Amgen, Roche, Myriad Genetics, Lilly, Novartis, BMS, Pfizer, 5.


Abstract Number: 447

Tocilizumab Had Acceptable Retention Rate in Both Randomized Controlled Trials and Observational Studies: Systematic Review of Rheumatoid Arthritis
Levent Kilic1, Orhan Kucuksahin2, Zeynep Ozbalkan3, Cemal Bes4, Veli Yazisiz5, Ayten Yazici6, Dilek Solmaz7, Timucin Kasifoglu8 and Umut Kalyoncu9, 1Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Turkey, 2Rheumatology, Yıldırım Beyazıt University Faculty of Medicine, Ankara, Turkey, 3Rheumatology, Ankara Numune Education and Research Hospital, Ankara, Turkey, 4Rheumatology, Bakırköy Dr. Sadi Konuk Training and Research Hospital, İstanbul, Turkey, 5Rheumatology, Akdeniz University Faculty of Medicine, Ankara, Turkey, 6Department of Rheumatology, Kocaeli University, Faculty of Medicine, Kocaeli, Turkey, 7Rheumatology, Katip Çelebi University Faculty of Medicine, İzmir, Turkey, 8Rheumatology, Eskisehir Osmangazi University Faculty of Medicine, Eskisehir, Turkey, 9Department of Internal Medicine, Division of Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Turkey

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: In general, retention rate in biological DMARDs represent both efficacy and safety. Tocilizumab (TOC) is a humanized monoclonal antibody that binds to the interleukin-6 receptor. So far, TOC was used in randomized controlled trials (RCTs) and longitudinal observational studies (LOSs), as well. The aim of this study was to assess the retention rate of TOC for the treatment of RA patients in RCTs and LOS.

Methods: In January 2017, a systematic Review (SR) was performed in PUBMED MEDLINE. Publications were identified using the MeSH terms: (“rheumatoid arthritis and Tocilizumab”) with a limitation to “humans”, “all adults: 19+ years”, “English” and “clinical trials”. All available studies describing the retention rate of TOC were recruited to SR. Retention rate of TOC were calculated according to route (SC or IV), dosage (4 mg/kg vs 8 mg/kg), monotherapy or combination with methotrexate. Of the 662 publications identified by the literature search, 42 were recruited in the analysis. Retention rates of TOC at 12-16 weeks, 24-32 weeks, 48-52 weeks, 2. years, 3. years and 5. years were analyzed. Open label extension period of RCTs included to LOS. The causes of withdrawals of TOC were recorded as inefficacy, adverse event, and others.

Results: Of the 42 studies, 11 (26.2%) were RCTs and 31 (73.8%) were LOSs. Totally 20590 patients (15574 (75.6%) female) were pooled to analysis that 4817 patients (23.4%) were from RCTs. The mean age was 56.2 years and mean disease duration was 10.1 years. Seropositivity was 75.0% for rheumatoid factor and 76.5% for ACPA. Overall, 8934 (44.4%) of patients were biologic-naive. TOC was used as monotherapy (5111/16323, 31.3%), or concomitant with methotrexate (11976/19522, 61.4%). Available baseline DAS-28 score, CDAI, SDAI, and HAQ-DI score were 5.8, 30.4, 32.5, and 1.46 respectively. Retention rates of TOC intravenous 8 mg/kg at 48-52 weeks, 2. year, 3. year and 5. year were 75.5 - 85.2%, 48.4 - 76.1%, 69.9%, 66.2%, respectively. Retention rate and causes of withdrawal of TOC according to study type were shown in Table 1.

Conclusion: Both RCTs and LOSs, withdrawal of TOC was particularly well known in 24-32. weeks. TOC intravenous 8 mg/kg also had satisfactory retention rate in 48-52 weeks, 2. year, 3. year and 5. year. Moreover, retention rate of TOC in LOSs was comparable with other biologic DMARDs, as well.

Table 1: Retention Rate of Tocilizumab in Randomized Controlled Trials and Observational Studies
Predicting Remission at 6 Months in Early Rheumatoid Arthritis Treated with Conventional Synthetic Dmards

Michael D Wiese1, Robert Metcalf2, Mihir D Wechalekar3, Llew Spargo2, Leah McWilliams4, Michael James4,5, Catherine Hill6 and Susanna Proudman7, 1School of Pharmacy and Medical Sciences, University of South Australia, Adelaide, Australia, 2Rheumatology Unit, Royal Adelaide Hospital, South Australia, Adelaide, Australia, 3Royal Adelaide Hospital, Adelaide, Australia, 4Department of Rheumatology, Royal Adelaide Hospital, Adelaide, Australia, 5Department of Medicine, University of Adelaide, Adelaide, Australia, 6The Queen Elizabeth Hospital, Adelaide, Australia, 7University of Adelaide, Adelaide, Australia

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Initial treatment of RA with triple csDMARD therapy can achieve remission in a proportion of patients. Others respond poorly yet must wait at least 6 months to access publically funded bDMARDs in Australia, although they may benefit from earlier introduction of bDMARDs. The purpose of this study was to identify disease activity thresholds after 3 months of csDMARDs that were associated with ACR/EULAR remission after 6 months of therapy.

Methods: Consecutive patients >18 years with treatment-naïve RA (1987 ACR or 2010 ACR/EULAR criteria) and ≥ 6 months of follow up were included. Unless contraindicated, participants received triple DMARD therapy of methotrexate, sulfasalazine and hydroxychloroquine according to a treat-to-target approach, and if these failed, leflunomide was added. At baseline, 3 and 6-months, DAS28, SDAI and CDAI were determined. Remission after 6 months was defined by ACR/EULAR 2011 definition of SDAI ≤ 3.3 without initiation of leflunomide. The sensitivity and specificity of disease activity measures at 3 months to predict the 6 month remission rate were determined by a Receiver Operated Characteristics Curve, and the magnitude of association between the optimal
point on the curve and remission rate was determined. Both percentage and absolute reductions in disease activity scores were examined.

Results: Median baseline DAS28, CDAI and SDAI were 5.4, 27.7 and 30.0 respectively and 89% were initiated on triple DMARD therapy. Absolute rather than relative changes in disease activity metrics after 3 months of DMARDs were more strongly associated with RA remission after 6 months of treatment. Optimal SDAI and CDAI scores at 3 months had a stronger association with 6 month remission compared to DAS28 (Table).

<table>
<thead>
<tr>
<th>Disease Activity Cut-Off Point after 3-Months</th>
<th>n</th>
<th>Proportion Reaching cut-point</th>
<th>Remission Rate</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>45% Reduction in DAS28 from Baseline</td>
<td>259</td>
<td>0.24</td>
<td>0.19</td>
<td>8.8 (4.4-17.5)</td>
</tr>
<tr>
<td>65% Reduction in CDAI from Baseline</td>
<td>258</td>
<td>0.28</td>
<td>0.18</td>
<td>12.3 (5.9-25.6)</td>
</tr>
<tr>
<td>65% Reduction in SDAI from Baseline</td>
<td>250</td>
<td>0.26</td>
<td>0.18</td>
<td>8.5 (4.2-17.3)</td>
</tr>
<tr>
<td>DAS28 &lt;3.4</td>
<td>261</td>
<td>0.39</td>
<td>0.19</td>
<td>10.8 (4.9-23.5)</td>
</tr>
<tr>
<td>CDAI &lt;8.0</td>
<td>265</td>
<td>0.28</td>
<td>0.18</td>
<td>16.7 (7.8-35.7)</td>
</tr>
<tr>
<td>SDAI &lt;8.6</td>
<td>259</td>
<td>0.27</td>
<td>0.19</td>
<td>18.1 (8.4-39.1)</td>
</tr>
</tbody>
</table>

Conclusion: CDAI or SDAI scores at 3 months of csDMARD treatment in early RA are highly predictive of remission after 6 months and could be useful in predicting those who may ascertain long-term remission with conventional agents, and equally in identifying those who may benefit from early bDMARD initiation. In practical terms, CDAI has the advantage of providing an immediate score compared with SDAI where the results of CRP levels are required.

Disclosure: M. D. Wiese, None; R. Metcalf, None; M. D. Wechalekar, None; L. Spargo, None; L. McWilliams, None; M. James, None; C. Hill, None; S. Proudman, Actelion Pharmaceuticals US, 2, GlaxoSmithKline, 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/predicting-remission-at-6-months-in-early-rheumatoid-arthritis-treated-with-conventional-synthetic-dmards

Abstract Number: 449

Medical Bugs for Pain Relief in Patients with Rheumatoid Arthritis, a Systematic Review

Rongqiang Zhang¹, Puwei Yuan², Jia Li³, Bo Dong¹, Wulin Kang³, Stephanie Hyon⁴, Raveendhara R. Bannuru⁵, William F. Harvey⁴ and Chenchen Wang⁴, ¹Shaanxi University of Chinese Medicine, Xianyang 712046, China, Xianyang, China, ²Shaanxi University of Chinese Medicine, Xianyang 712046, China, XianYang, China, ³Shaanxi University of Chinese Medicine, Xianyang, China, ⁴Rheumatology, Center of Integrative Medicine and Division of Rheumatology, Tufts Medical Center, Boston, MA, Boston, MA, ⁵Center of Integrative Medicine and Division of Rheumatology, Tufts Medical Center, Boston, MA, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Medical bugs, a term used to describe insects and arthropods for medical treatment, have been widely used in the past centuries for pain relief. The treatment is believed to include biologically active substances that induce anti-inflammatory effects. Previous trials have shown that medical bugs may reduce the need for analgesic intake of people with rheumatoid arthritis (RA). However, few studies have been conducted to evaluate the effect of medical bugs on musculoskeletal disease. The aim of this systematic review was to evaluate the pain relief of commonly used medical bugs in RA patients to better understand its benefits and inform clinical practice.
Methods: A comprehensive search on PubMed and Chinese databases (CNKI, Wan Fang and VIP) and the Cochrane Library was conducted through May 1, 2017. Only randomized controlled trials (RCTs) using medical bug (including ant, centipedes, scorpions and others) therapy for adult RA patients who met diagnostic by the 1995 ACR criteria or 2002 Traditional Chinese Medicine criteria were included. The effects of medical bugs were evaluated with a tender joint count and pain score of joints. The differences between treatment groups were reported as mean difference (P-value) across the studies. The methodologic quality of the studies was assessed with the Jadad instrument. The heterogeneity of the studies, including varying comparison methods, and methodologic limitations, precluded a formal meta-analysis.

Results: Ten RCTs with a total of 1,176 RA patients (age range = 38-62 years, 59% female, disease duration range = 1 month-30 years) met the eligibility criteria. Studies were conducted between 2002 and 2015 in China. Outcomes included the Chinese pain score and Visual Analogue Scale (VAS). Medical bugs were either used singly or in combination with other Chinese herbs. The overall quality of trials was modest (mean Jadad score = 2). Table 1 summarizes the information from the included studies. All 10 studies utilizing medical bugs either alone or in combination with other Chinese herbs showed efficacy in pain relief for RA. No adverse events were reported in either treatment or control groups.

Conclusion: Medical bug therapy appears to relieve pain in patients with RA. These studies did not evaluate disease modifying effects, and the use of combination treatments makes it difficult to ascertain which ingredient may induce the effect. Still, the potential of medical bug treatment and its non-pharmacologic properties may have value and deserve further study. Rigorously designed and well-controlled multicenter RCTs of biological active compounds of medical bugs for RA symptom relief need to be conducted in future studies.

Table 1. Randomized Clinical Trials Evaluating Medical Bugs for Joint Pain in Rheumatoid Arthritis
<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>N</th>
<th>Age</th>
<th>Diagnostic Criteria</th>
<th>Medical bugs</th>
<th>Control</th>
<th>Duration (Weeks)</th>
<th>Effect on Tender Joint Score (mean changes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yang</td>
<td>2002</td>
<td>280</td>
<td>(ND)</td>
<td>Chinese criteria 2002</td>
<td>20 herbs including centipede and scorpion, 9g/day</td>
<td>Tripod, 2tablets*twice/day</td>
<td>12</td>
<td>#2.40 ^c (P&lt; 0.05)</td>
</tr>
<tr>
<td>Huang</td>
<td>2005</td>
<td>76</td>
<td>(38y)</td>
<td>ACR 1995 and Chinese criteria 2002</td>
<td>18 herbs including centipede 1g and Steleopha 5g, once/day; Methotrexate, 10mg/week; Penicillamine, 250mg*twice/day</td>
<td>Glucosidorum Tripterygil Totorum, 1mg/kg/day</td>
<td>8</td>
<td>#1.79 ^c (P&lt; 0.05)</td>
</tr>
<tr>
<td>Shen</td>
<td>2004</td>
<td>85</td>
<td>(39y)</td>
<td>ACR 1995</td>
<td>16 herbs including centipede 2g and scorpion 3g, 250ml*twice/day</td>
<td>Tripterygium polyglycoside tablets, 20mg*3 times/day</td>
<td>24</td>
<td>#1.80 ^d (P&lt; 0.01)</td>
</tr>
<tr>
<td>Huang</td>
<td>2014</td>
<td>82</td>
<td>(39y)</td>
<td>Chinese criteria 2002</td>
<td>14 herbs including centipede 0.35g, 6 Tablets<em>3times/day; Diclofenac Sodium Sustained Release Tablets, 75mg</em>twice/day</td>
<td>Diclofenac Sodium Sustained Release Tablets, 75mg*twice/day</td>
<td>8</td>
<td>#7.18 ^c (P&lt; 0.05)</td>
</tr>
<tr>
<td>Liu</td>
<td>2003</td>
<td>120</td>
<td>(ND)</td>
<td>ACR 1995</td>
<td>Prednisone adequate dose for 4 weeks; 14 herbs including scorpion 10g, 250ml*twice/day</td>
<td>Methotrexate, 10mg*once/week; Indometacin Tablets, 150mg/day; Prednisone, 30mg/day</td>
<td>14</td>
<td>#0.40 ^c (P&lt; 0.05)</td>
</tr>
<tr>
<td>Cheng</td>
<td>2003</td>
<td>79</td>
<td>(38y)</td>
<td>ACR 1995</td>
<td>10 herbs including scorpion, 2-3 times/day</td>
<td>Fenbid, 600mg *twice/day</td>
<td>8</td>
<td>#0.81 ^c (P&lt; 0.05)</td>
</tr>
<tr>
<td>Liu</td>
<td>2009</td>
<td>66</td>
<td>(49y)</td>
<td>ACR 1995</td>
<td>12 herbs including scorpion 3g, 250ml<em>twice/day; Methotrexate, 10mg/week; Meloxicam, 7.5mg</em>twice/day</td>
<td>Methotrexate, 10mg/week; Meloxicam, 7.5mg*twice/day</td>
<td>12</td>
<td>#1.10 ^d (P&lt; 0.05)</td>
</tr>
<tr>
<td>Liu</td>
<td>2011</td>
<td>80</td>
<td>(49y)</td>
<td>ACR 1995</td>
<td>3 herbs including scorpion 5g, 150 ml*3 times/day</td>
<td>2 herbs not including scorpion, 150ml*3 times/day</td>
<td>12</td>
<td>^0.25 (P&lt; 0.05)</td>
</tr>
<tr>
<td>Feng</td>
<td>2015</td>
<td>100</td>
<td>(62y)</td>
<td>Chinese criteria 2002</td>
<td>14 Herb including 1 centipede and 1 scorpions, 200g*twice/day; 6 herbs hot pack for 30-50 min, once or twice/day</td>
<td>Methotrexate, 5mg*3 times/day</td>
<td>3</td>
<td>#1.20 ^c (P&lt; 0.05)</td>
</tr>
<tr>
<td>Dai</td>
<td>2007</td>
<td>208</td>
<td>(39y)</td>
<td>ACR 1995</td>
<td>15 herbs including ant 30g, 150ml*twice/day</td>
<td>Ibuprofen, 300mg*3 times/day</td>
<td>5</td>
<td>#2.59 ^d (P&lt; 0.01)</td>
</tr>
</tbody>
</table>

^a N= number of patients included; ^b Age reported in years as a mean; ^c Mean difference was calculated between groups; ^d Severity of joint pain was scored 0, 1, 2, 3, respectively measured by physicians; ^e Chinese pain score: lower score = better outcome.

Chinese criteria: Guiding Principles of Clinical Research on Traditional Chinese Medicine, including main symptoms: joint swelling and pain and four of the following secondary symptoms: joint tenderness, limited flexion and extension, morning stiffness, joint cold, aggravated pain in nights, hand and foot cold, fatigue, aggravated pain in rainy days, pale tongue, heavy and soft pulse.

#: indicate decrease, ^: indicate increase.
Disease Duration and Withdrawal of Biologic Agents Predict Radiological Progression in a Cohort of Rheumatoid Arthritis Patients in Latin America. a Real World Study

Rocio V. Gamboa-Cardenas1,2, Manuel Ugarte-Gil3, Francisco Zevallos4, Mariela Medina4, Claudia Elera-Fitzcarrald4, Victor Pimentel-Quiroz4, Cristina Reategui-Sokolova4, Omar Sarmiento-Velasquez4, Zoila Rodriguez-Bellido4, José Alfaro4, Mariano Cucho-Venegas4, Cesar A. Pastor-Asurza4 and Risto Perich-Campos5, 1Rheumatology, Hospital Guillermo Almenara, EsSalud, Lima, Peru, 2Universidad Nacional Mayor de San Marcos, Lima, Peru, 3Peru, GLADEL, Lima, Peru, 4Rheumatology, Hospital Guillermo Almenara Irigoyen. EsSalud, Lima, Peru, 5Rheumatology, Hospital Guillermo Almenara Irigoyen, Lima, Peru

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Optimal management of Rheumatoid Arthritis (RA) based in identification of patients with risk factors for Joint Damage (JD) progression, is a main strategy, but there is scarce evidence regarding this aspect in Latin-America (LA). Objective: To determine factors associated with JD and predictors of radiographic progression (RP) in a RA cohort

Methods: Prospective analysis of Hospital Almenara RA cohort (Lima-Perú). JD and RP were determined with Sharp-VDH score. A single reader evaluated all X-ray films. Age, gender, ethnicity, socioeconomic level(Graffar), education, age at diagnosis, disease duration, diagnosis delay, tobacco, comorbidities(Charlson), current/past DMARDs, biologic and corticosteroids, biologic withdrawal ,DAS28, EULAR-remission, AntiCCP, JD (Sharp-VDH score) and disability (MHAQ) at baseline were analyzed as RP predictors. We applied a multivariate linear regression elimination model (p <0.05) and SPSS-21.0. Results: 313 patients from the 432 subjects of the hospital Almenara RA cohort were included , 91.4% women, 98.4% Mestizos, disease duration was 14.94 (12.79) and diagnosis delay 1.71 (2.59) years. Baseline Sharp-VDH was 94.53 (95.81). Most patient were using DMARDs (92%), but only 11.5% biologics. Current (B=42.86, CI: 6.49-79.24, p=0.021) or past (B=45.76, IC: 6.42-85.09, p=0.023) corticosteroids, current biologic (B=28.63, CI: 4.86-52.40, p=0.018) and longer disease duration (B=3.62, CI: 3.02-4.22, p<0.01) were associated with baseline JD. One hundred and eighty-four patients were prospectively followed, in this group the rate of RP total/erosion was 4.41(9.24) and 2.17(5.74)/year respectively, there was a DMARDs prescription delay of 6.56(8.02) years and 176 (95.7%) subjects without remission-EULAR criteria. Predictors of RP (erosions) were a longer disease duration (B=0.14, CI 0.01-0.27, p=0.04) and withdrawal of biologic (B=8.63 CI 2.28-14.98 p=0.008)

Conclusion: This cohort had a high disease duration and delay of DMARD introduction. Disease duration and biologic withdrawal predicted RP. Carefully biologic withdrawal in these patients could be a good strategy to prevent adverse results in our population

Disclosure: R. V. Gamboa-Cardenas, None; M. Ugarte-Gil, None; F. Zevallos, None; M. Medina, None; C. Elera-Fitzcarrald, None; V. Pimentel-Quiroz, None; C. Reategui-Sokolova, None; O. Sarmiento-Velasquez, None; Z. Rodriguez-Bellido, None; J. Alfaro, None; M. Cucho-Venegas, None; C. A. Pastor-Asurza, None; R. Perich-Campos, None.
A Matrix Risk Model for Prediction of Radiographic Progression in Early Rheumatoid Arthritis Based on Treatment Response at 3 Months

Pooneh S. Akhavan¹, Daming Li¹, Sahar Tabatabvakili¹ and Edward C. Keystone², ¹Mount Sinai Hospital, Toronto, ON, Canada, ²University of Toronto, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The present study aimed to develop a matrix to predict risk of radiographic progression in patients with early rheumatoid arthritis. The focus of this analysis was to identify a threshold for routine disease activity measures at 3 months i.e. response to initial treatment that is associated with the lower risk of future joint damage.

Methods: Using data from the PREMIER study, radiographic progression (RP) was defined as a change in modified Sharp/van der Heijde score (SHS) of ≥3.5 U/year. Patients enrolled into the control arm of the study who received methotrexate only were analyzed. Baseline characteristics and disease activity measures at 3 months were used to predict the risk of RP at 12 months. Logistic regression was used to identify the predictors and to calculate the probability of RP. Significant predictors were categorized in order to make the models more practical to use in daily practice. The results were combined into a matrix model including significant predictors of RP.

Results:

A total of 205 patients were included in this analysis with a mean (sd) baseline age 52.0 (13.1) years, disease duration 0.8 (0.8) year, 28 swollen joint count 14.7 (5.7), 28 tender joint count 17.1 (6.4), mean sharp score (MTSS) 21.4 (21.2) and CRP 4.0 (4.1). Logistic regression models identified month 3 SJC and CRP as significant predictors of radiographic damage progression at 1 year. These variables were categorized into three groups based on the variable distribution and clinical relevance. The matrix model showed that the SJC < 5 at 3 months was associated with a significantly lower damage progression rate at any given CRP category (Table-1).

<table>
<thead>
<tr>
<th>SJC at 3 months</th>
<th>CRP at 3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;1</td>
</tr>
<tr>
<td>&lt; 5</td>
<td>0.15 (0.08, 0.27)</td>
</tr>
<tr>
<td>5 - 10</td>
<td>0.50 (0.18, 0.46)</td>
</tr>
<tr>
<td>&gt; 10</td>
<td>0.35 (0.22, 0.52)</td>
</tr>
</tbody>
</table>

Conclusion: The disease activity state at 3 months has a significant impact on future radiographic damage. Patients with less than 5 swollen joints at this time point have lower risk of radiographic damage at 1 year. Further testing in other populations and with different therapies is needed to obtain a definitive risk model that will guide rheumatologists in making treatment decisions for early RA patients.

Disclosure: P. S. Akhavan, None; D. Li, None; S. Tabatabvakili, None; E. C. Keystone, Abbott Laboratories, Amgen Inc., AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb, F. Hoffmann-La Roche Inc, Janssen Inc, Lilly Pharmaceuticals, Novartis Pharmaceuticals, Pfizer Pharmaceuticals, Sanofi-Aventis, UCB, 2,Abbott Laboratories, AstraZeneca Pharma, Biotest, Bristol-Myers Squibb Company, Crescendo Bioscience, F. Hoffmann-La Roche Inc, Genentech Inc, Janssen Inc, Lilly Pharmaceuticals, Merck, Pfizer Pharmaceuticals, UCB, 5,Amgen, Abbott Laboratories, Astrazeneca LP, Bristol-Myers Squibb Canada,, 8.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/a-matrix-risk-model-for-prediction-of-radiographic-progression-in-early-rheumatoid-arthritis-based-on-treatment-response-at-3-months
Time to First Treatment Is Associated with a Refractory Course of Rheumatoid Arthritis

Manuel Bècède1, Farideh Alasti2, Lukas Hütter3, Lisa Hütter3, Andreas Kerschbaumer4, Uriel Landesmann1, Gabriela Supp4, Josef S. Smolen4,5 and Daniel Aletaha6, 1Department of Internal Medicine III, Division of Rheumatology, Medical University of Vienna, Vienna, Austria, 2Rheumatology, Medical University of Vienna, Vienna, Austria, 3Department of Medicine, Hietzing Hospital, Vienna, Austria, 4Medical University Vienna, Division of Rheumatology, Department of Internal Medicine III, Vienna, Austria, 5Department of Internal Medicine, Hietzing Hospital, Vienna, Austria, 6Department of Medicine III, Division of Rheumatology, Medical University of Vienna, Vienna, Austria

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
It is an ongoing matter of research, whether the course of rheumatoid arthritis (RA) can be altered by an early intervention, a concept historically referred to as the window of opportunity. So far, only short-term disease outcomes have been investigated, which are, however, inherently affected by the unknown rate of underlying rate of self-limiting disease. It is unclear, whether the disease course is really affected by the timing of initial treatment.

Methods:
Patients were identified from a clinical database at the Medical University of Vienna. We used stringent criteria to define refractory RA (reRA): >=3 treatment courses (>=1 biological) over >=18 months since diagnosis without reaching low disease activity (LDA) or remission (REM) defined by a Clinical Disease Activity Index (CDAI, >=10). In contrast, we defined treatment amenable RA (taRA) as patients reaching LDA, or REM within the first 2 treatment courses.

We first matched patients with reRA and taRA 1:1 for time of inception in our database to avoid bias by secular trends in management over time. Using the reRA or taRA status as the dependent variable, we performed logistic regression analysis. Furthermore, we performed the same analyses in an unselected group of all-comers at baseline regarding their probability of developing reRA.

Results:
We identified 412 patients who had their last clinic visit at or after July 1st, 2016: 70 reRA and 102 taRA patients were identified; 240 patients fulfilled neither definition. In the reRA group, female gender was more frequent, age of disease onset lower, and CDAI higher at first presentation. Remarkably, the time to first DMARD treatment was significantly delayed between reRA and taRA (table 1).

In the matched multivariate model, treatment delay (p=0.047), female gender (p=0.038) and higher disease activity (p<0.001) were significant. In the logistic regression analysis of the 412 patients treatment delay was significant univariately (p<0.001) and after adjustment for other significant predictors (p=0.007; table 2). We then conducted a matrix model based on this analysis with predicted probabilities of developing reRA (figure).

Conclusion:
Our data suggest that delay to initial treatment affects the long-term course of RA. Earlier treatment initiation thus may change the severity of RA.

Disclosure: M. Bécède, None; F. Alasti, None; L. Haupt, None; L. Hütter, None; A. Kerschbaumer, None; U. Landesmann, None; G. Supp, None; J. S. Smolen, None; D. Aletaha, None.

Table 1. Patient characteristics at first clinical visit. Data median, quartiles (Range 95% as available)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Male (n=44)</th>
<th>Female (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>55.0 (48.5-64.0)</td>
<td>45.0 (36.0-54.0)</td>
</tr>
<tr>
<td>SRI (mean)</td>
<td>21.5 (14.0-32.5)</td>
<td>17.0 (9.0-23.0)</td>
</tr>
<tr>
<td>RAP (mean)</td>
<td>22.0 (14.0-28.0)</td>
<td>14.5 (9.0-20.0)</td>
</tr>
</tbody>
</table>

Table 2. Main analysis comparing relapse rate in a case control study (adjusted logistic regression model) and relapse versus relapse in a cohort study (logistic regression model)

**P** matched for date of first clinical visit

**Figure 1.** Main risk model for the probability of relapse in a cohort of RA including all selected baseline risk factors

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Male (n=44)</th>
<th>Female (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>55.0 (48.5-64.0)</td>
<td>45.0 (36.0-54.0)</td>
</tr>
<tr>
<td>SRI (mean)</td>
<td>21.5 (14.0-32.5)</td>
<td>17.0 (9.0-23.0)</td>
</tr>
<tr>
<td>RAP (mean)</td>
<td>22.0 (14.0-28.0)</td>
<td>14.5 (9.0-20.0)</td>
</tr>
</tbody>
</table>

Table 3. Main analysis comparing relapse rate in a case control study (adjusted logistic regression model) and relapse versus relapse in a cohort study (logistic regression model)

**P** matched for date of first clinical visit

**Figure 1.** Main risk model for the probability of relapse in a cohort of RA including all selected baseline risk factors

Disclosure: M. Bécède, None; F. Alasti, None; L. Haupt, None; L. Hütter, None; A. Kerschbaumer, None; U. Landesmann, None; G. Supp, None; J. S. Smolen, None; D. Aletaha, None.

The Therapy with Tocilizumab Is Not Associated with Periarticular Demineralisation and Finger Joint Space Narrowing in Rheumatoid Arthritis

Alexander Pfeil1, Ottar Gadeholt2, Joachim Böttcher3, Diane Renz4, Peter Oelzner1 and Gunter Wolf1, 1Department of Internal Medicine III, Jena University Hospital, Jena, Germany, 2Rheumatology/Immunology, Medical Clinic II, University Clinic Wuerzburg, Wuerzburg, Germany, 3Institut of Interventional and Diagnostic Radiology, SRH Waldklinikum Gera, Gera, Germany, 4Institute of Diagnostic and Interventional Radiology, Jena University Hospital, Jena, Germany

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Digital X-ray Radiogrammetry (DXR) and Computer-Aided Joint Space Analysis (CAJSA) are established computer based techniques for the quantification of metacarpal bone mineral density and finger joint space width. Tocilizumab as humanized anti-interleukin-6 receptor antibody is a successful therapy strategy in rheumatoid arthritis (RA). The aim of this study was the evaluation metacarpal bone mineral density finger joint space width in RA-patients treated with tocilizumab or methotrexate.

Methods:
The multi-center study includes a retrospective analysis of 44 patients with RA in two matched groups which were treated with methotrexate or tocilizumab. All patients consist of radiographs at baseline and after 2.4 years in the follow-up. DXR was measured to quantify cortical thickness (CT), metacarpal index (MCI) and bone mineral density (BMD) of the metacarpal bones. The CAJSA-technique quantified joint space distance of the metacarpophalangeal joints (JSD-MCP) and proximal interphalangeal joints (JSD-PIP).

Results:
For the methotrexate group a significant change of BMD (-6.16%, p<0.05), CT (-7.05%, p<0.05), MCI (-4.74%, p<0.5), JSD-MCP (-4.51%, p<0.05) and JSD-PIP (-12.29%, p<0.05) was observed between baseline and follow-up. The tocilizumab group no significant difference was detected for BMD (-0.20%, p=n.s), CT (-0.70%, p=n.s.), MCI (-2.05%, p=n.s.), JSD-MCP (-0.76%, p=n.s.) and JSD-PIP (0%, p=n.s.).

Conclusion:
The study presented an absence of periarticular demineralisation and finger joint space narrowing in the treatment with tocilizumab, which highlights the effective treatment strategy of a biologic target in RA as well as the detailed computer based analysis of periarticular minerlisation and finger joint space width by DXR and CAJSA.

Disclosure: A. Pfeil, None; O. Gadeholt, None; J. Böttcher, None; D. Renz, None; P. Oelzner, None; G. Wolf, None.
Soluble Urokinase Plasminogen Activator Receptor (suPAR) Correlates with Disease Activity in Early Rheumatoid Arthritis and Reflects Joint Damage over Time

Helena Enocsson¹, Alf Kastbom¹, Tanja Lukic¹, Christopher Sjöwall², Thomas Skogh¹ and Jonas Wetterö¹,
¹Rheumatology, Division of Neuro and Inflammation Sciences, Department of Clinical and Experimental Medicine, Linköping University, Linköping, Sweden, Linköping, Sweden, ²Department of Clinical and Experimental Medicine, Linköping University, Sweden, Linköping, Sweden
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
The urokinase plasminogen activator receptor (uPAR) is expressed on various cell types and plays important roles in proteolysis, migration and adhesion. Receptor shedding yields a soluble form (suPAR) that has been intensively studied as a potential biomarker in several inflammatory diseases and malignancies. The previous few studies on suPAR in rheumatoid arthritis (RA) have shown an association with inflammation and swollen joints, but data on changes in suPAR levels in relation to early disease course are lacking. This study investigates whether suPAR levels predict or reflect disease activity and/or joint damage in early RA.

Methods:
Serum suPAR was measured by ELISA at disease onset (0 months), after 3 months and after 36 months in 252 RA patients from the Swedish early RA cohort TIRA-2. suPAR levels were compared with disease activity (defined by DAS28) and joint damage (Larsen score) at baseline and up to 36 months after disease onset. Healthy individuals (n=100) served as controls.

Results:
Circulating levels of suPAR were higher in RA patients at all three time points compared to healthy controls (mean suPAR = 3.62 ng/mL; p<0.001). The highest suPAR among patients was found at 3 months (mean = 8.47 ng/mL) and the lowest at 36 months (mean = 7.14 ng/mL). suPAR at inclusion correlated with baseline DAS28 (p<0.001, rho=0.25) whereas suPAR levels at 36 months correlated with Larsen score at 36 months (p=0.001, rho=0.24), and 24 months (p=0.002, rho=0.25), but not with DAS28 at any time point. No correlation was found between baseline suPAR and joint damage at any time point. Categorization of baseline DAS28 revealed higher baseline suPAR at high DAS28 (Fig. 1) whereas Larsen score at 36 month revealed higher suPAR (measured at 36 months) among patients with a high score (>5) compared to those with a low score (<2) (Fig. 2).

Conclusion:
suPAR levels associate with disease activity in early untreated RA, but at later stages rather reflect joint damage. Since suPAR levels seem to increase at or after damage accrual, we speculate that suPAR reflects active inflammation and ongoing processes in the joint, rather than being a causative agent.
Figure 1. Serum levels of suPAR and in different categories of disease activity (DAS28) at study inclusion. P-values are from One-way ANOVA with Tukey’s post hoc test. Error bars indicate 95% confidence interval.

Figure 2. Serum levels of suPAR and the degree of joint damage (Larsen score) 36 months after study inclusion. P-values are from One-way ANOVA with Tukey’s post hoc test. Error bars indicate 95% confidence interval.

Disclosure: H. Enocsson, None; A. Kastbom, None; T. Lukic, None; C. Sjöwall, None; T. Skogh, None; J. Wetterö, None.


Abstract Number: 455

Analysis of Real-World Treatment Patterns in a Matched Sample of Rheumatology Patients with Continuous Infliximab Therapy or Switched to Biosimilar Infliximab

Lorie A. Ellis1, Ismail Simsek2, Lin Xie3, Adesuwa Ogbomo3, Dennis Parenti4, Kavitha Goyal4 and Yusuf Yazici5, 1Janssen HECOR Immunology, Horsham, PA, 2Guven Hospital, Ankara, Turkey, 3STATinMED Research Inc., Ann Arbor, MI, 4Janssen Scientific Affairs, LLC, Horsham, PA, 5New York University School of Medicine, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Background/Purpose: Biosimilar infliximab (CT-P13) was first approved in Europe in 2013. This study compared treatment (tx) patterns of Turkish pts with a diagnosis of rheumatoid arthritis (RA) who initiated originator IFX (IFX) & either continued IFX or switched to CT-P13.

Methods: Adult pts with ≥1 RA diagnosis code & IFX claim were identified in a national Turkish healthcare database. Eligible pts initiated & continued IFX (Continuer cohort; CC) or initiated IFX & switched to CT-P13 (Switch cohort; SC) during the study period (01DEC2010-01JUN2016). The index date was defined as CT-P13 switch date for SC or a random IFX date during period of CT-P13 availability for CC. Cohorts were matched on age, sex, & number of IFX prescriptions during baseline (BL). Discontinuation (d/c) was defined as a switch to another biologic or no index biologic for ≥120 days without censoring. Pt demographics, d/c & switching were summarized with descriptive statistics.

Results: A total of 697 pts initiating IFX were studied; 87% (N=605) continued IFX throughout the study period; 13% (N=92) switched to CT-P13. BL & clinical characteristics are shown in Table. Mean duration of IFX therapy during BL period was 422 days (CC) & 438 days (SC). Average duration of post-index follow-up was 16 months (CC) & 15 months (SC). During the combined BL & post-index periods, median time on any IFX therapy was 1080 days (CC) & 540 days (SC) (Figure). D/c post-index occurred in 19% (CC) & 87% (SC); mean time from index to IFX d/c / censoring was 276 days (CC) while mean time from index to CT-P13 d/c / censoring was 132 days. While switching from IFX to CT-P13 occurred in 13% all IFX initiators on the index date; an additional 10% of the CC switched to a non-IFX anti-TNF post-index. The majority of SC (82%) switched again post-index (off CT-P13) & 88% of those re-initiated IFX. Regional variation in switching was noted. Switching from IFX to CT-P13 occurred most frequently in Central Anatolia (26% of 154 IFX initiators). Switching from CT-P13 occurred in >75% of SC pts in all regions except for Aegean (44% switched from CT-P13 to another biologic, predominantly IFX).

Conclusion: In Turkey, RA pts maintained on IFX had greater tx persistence than those who initiated IFX & switched to CT-P13. CT-P13 d/c resulted in IFX re-initiation in the majority of pts. Reasons for d/c are unknown, however regional differences in practice patterns were observed.
Table Demographics and Treatment Patterns for Continuer and Switcher Cohorts

<table>
<thead>
<tr>
<th></th>
<th>Continuers Cohort (N=605)</th>
<th>Switchers Cohort (N=92)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Mean) (years)</td>
<td>N/Mean %/SD</td>
<td>N/Mean %/SD</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>41 10.3</td>
<td>43 11.8</td>
</tr>
<tr>
<td>Baseline Concomitant Disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ankylosing Spondylitis</td>
<td>102 18%</td>
<td>27 13%</td>
</tr>
<tr>
<td>Psoriatic Arthritis</td>
<td>48 8%</td>
<td>11 5%</td>
</tr>
<tr>
<td>Crohn’s Disease</td>
<td>244 42%</td>
<td>114 56%</td>
</tr>
<tr>
<td>Ulcerative Colitis</td>
<td>42 7%</td>
<td>9 4%</td>
</tr>
<tr>
<td>Average Length of Follow-up Period (months)</td>
<td>16 2</td>
<td>15 2</td>
</tr>
<tr>
<td>Post-Index Concomitant Disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ankylosing Spondylitis</td>
<td>363 60%</td>
<td>58 63%</td>
</tr>
<tr>
<td>Psoriatic Arthritis</td>
<td>102 17%</td>
<td>13 14%</td>
</tr>
<tr>
<td>Crohn’s Disease</td>
<td>48 8%</td>
<td>3 3%</td>
</tr>
<tr>
<td>Ulcerative Colitis</td>
<td>33 5%</td>
<td>4 4%</td>
</tr>
<tr>
<td>Switching</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N and % of patients with ≥1 switch</td>
<td>115 19%</td>
<td>75 82%</td>
</tr>
<tr>
<td>N and % Primary Switches from CT-P13 to IFX</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Geographical Distribution of Patients with ≥1 switches (n=115 vs. 75)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>East Anatolia</td>
<td>6 5%</td>
<td>1 1%</td>
</tr>
<tr>
<td>South Eastern Anatolia</td>
<td>10 9%</td>
<td>9 12%</td>
</tr>
<tr>
<td>Marmara</td>
<td>39 34%</td>
<td>9 12%</td>
</tr>
<tr>
<td>Aegean</td>
<td>4 3%</td>
<td>4 5%</td>
</tr>
<tr>
<td>Mediterrane</td>
<td>19 17%</td>
<td>16 21%</td>
</tr>
<tr>
<td>Black sea</td>
<td>9 8%</td>
<td>1 1%</td>
</tr>
<tr>
<td>Central Anatolia</td>
<td>28 24%</td>
<td>35 47%</td>
</tr>
<tr>
<td>Discontinuation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N of Patients with Confirmed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discontinued</td>
<td>205 34%</td>
<td>80 87%</td>
</tr>
<tr>
<td>Time to confirmed discontinuation (days)</td>
<td>117 78</td>
<td>98 60</td>
</tr>
<tr>
<td>Time to any discontinuation or censoring (days)</td>
<td>276 124</td>
<td>132 104</td>
</tr>
</tbody>
</table>

N: Number; %: Percentage; IFX: Infliximab; SD: Standard Deviation; NA: Not available.

Figure Kaplan Meier (KM) curve for any Infliximab Use for the Switcher and Continuers Cohorts during the Baseline and Follow up Period.
Disclosure: L. A. Ellis, Janssen, 3; Johnson & Johnson, LLC, 1; I. Simsek, Janssen Scientific Affairs, LLC, 2; L. Xie, Janssen Scientific Affairs, LLC, 5; A. Ogbomo, Janssen Scientific Affairs, LLC, 5; D. Parenti, Janssen, 3; Johnson & Johnson, LLC, 1; K. Goyal, Janssen, 3; Johnson & Johnson, LLC, 1; Y. Yazici, Yusuf Yazici, 2.


Abstract Number: 456

Time from First Symptom Onset to First Advanced Therapy Amongst RA Patients in Latin America

Ivanio Pereira¹, Valderilio F Azevedo², Wilson Bautista-Molano³, Julio Casasola⁴, Generoso Guerra⁵, David Vega-Morales⁶, Enrique R Soriano⁷, Diana Rocio Gil⁸, José Antonio Maldonado-Cocco⁹, Leandro Aldunaté¹⁰ and Steve Lobosco¹¹, ¹Rheumatology, Universidade Federal de Santa Catarina, Hospital Universitário, Divisão de Reumatologia, Brazil, Florianopolis, Brazil, ²Adjunct Professor of Rheumatology, Federal University of Paraná; Brazil, Curitiba, Brazil, ³School of Medicine, Universidad Militar Nueva Granada and Rheumatology Department Hospital Militar. Colombia, Bogotá, Colombia, ⁴Rheumatology, Hospital General de Mexico, Mexico, Mexico, ⁵Centro Médico Paitilla Internal Medicine and Rheumatology Department. Panama, Panama City, Panama, ⁶Universidad Autónoma de Nuevo León. Rheumatology Service, Internal Medicine Department, Hospital Universitario "Dr. José Eleuterio González". Mexico, Montrerrey, Mexico, ⁷Argentina, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina, ⁸ART Medica - Hospital Universitario Mayor MEDERI Internal Medicine and Rheumatology. Colombia, Bogota, Colombia, ⁹Buenos Aires University, Consulting Professor of Rheumatology, Buenos Aires University. Argentina, Buenos Aires, Argentina, ¹⁰Immunology, Janssen Latin America, Buenos Aires, Argentina, ¹¹Adelphi, Immunology Director- Adelphi Group, Manchester, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
**Background/Purpose:** To understand the RA patient pathway in Latin America from first symptom onset; including time to diagnosis and to first advanced treatment.

**Methods:** Data from the 2015 RA Disease Specific Programme (DSP), a cross-sectional, multi-national survey of patients and rheumatologists conducted in Brazil, Argentina, Mexico, Colombia, Venezuela were analyzed against 2014 DSP data from the US and 5EU. Rheumatologists (n=188 Latin America, n=113 US, n=340 EU) completed forms containing patient demographics, age at first RA symptoms, age at RA diagnosis, age at csDMARD initiation and age at bDMARD initiation. Continuous data were tested using t tests.

**Results:** A total of 801 Latin America, 843 US and 2536 EU RA patients were included in this analysis. Current mean age across Latin America was 51.9 years and 82.8% female. Mean age of patients at RA symptom onset was 40.6 years, with age at diagnosis 42.6 years; resulting in a 2.2 year (3.9 SD) wait from first experiencing symptoms to receiving a confirmed diagnosis. Patients in Latin America waited 2.6 years (5.7 SD) from the point of RA diagnosis to initiation of first csDMARD vs. 1.0 years US (3.2 SD) and 1.1 years EU (3.0 SD) (both p<0.001), and 6.4 years (7.4 SD) from RA diagnosis to initiation of first bDMARD therapy vs. 3.9 years US (5.6 SD) and 5.2 years EU (5.7 SD) (both p<0.001).

**Conclusion:** RA patients in Latin America wait over 2 years from symptom onset to diagnosis and significantly longer than their US and EU counterparts to receive csDMARD and Biologic therapy. This highlights a clear need to shorten RA diagnosis times and time to treatment initiation.

**Disclosure:** I. Pereira, None; V. F. Azevedo, AbbVie, Eli Lilly, Genentech, GSK, Pfizer Inc, UCB, 2,AbbVie, Merck-Serono, Novartis, Pfizer Inc, 5,AbbVie, Janssen, Merck-Serono, Novartis, Pfizer Inc, Sanofi, 8; W. Bautista-Molano, None; J. Casasola, None; G. Guerra, None; D. Vega-Morales, None; E. R. Soriano, AbbVie, Janssen, Novartis, Pfizer Inc, UCB, 2,AbbVie, Janssen, Novartis, Pfizer Inc, UCB, 5,AbbVie, Bristol-Myers Squibb, Janssen, Novartis, Pfizer Inc, Roche, UCB, 8; D. Rocio Gil, None; J. A. Maldonado-Cocco, None; L. Aldunate, Janssen Pharmaceutica Product, L.P., 3; S. Lobosco, Adelphi, 3.

**View Abstract and Citation Information Online** - http://acrabstracts.org/abstract/time-from-first-symptom-onset-to-first-advanced-therapy-amongst-ra-patients-in-latin-america

**Abstract Number:** 457

**Levels of Satisfaction with RA Treatment and Associated Alignment between Rheumatologists and Their Patients across Latin America**

**Enrique R Soriano**¹, José Antonio Maldonado-Cocco², David Vega-Morales³, Diana Rocio Gil⁴, Ivanio Pereira⁵, Generoso Guerra⁶, Wilson Bautista-Molano⁷, Julio Casasola⁸, Valderilio F Azevedo⁹, Leandro Aldunate¹⁰ and Steve Lobosco¹¹, ¹Rheumatology Unit, Internal Medicine Service, Hospital Italiano de Buenos Aires, CABA, Argentina, ²Buenos Aires University, Consulting Professor of Rheumatology, Buenos Aires University, Argentina, Buenos Aires, Argentina, ³Universidad Autónoma de Nuevo León. Rheumatology Service, Internal Medicine Department, Hospital Universitario "Dr. José Eleuterio González”. Mexico, Monterrey, Mexico, ⁴ART Medica - Hospital Universitario Mayor MEDIERI Internal Medicine and Rheumatology. Colombia., Bogota, Colombia, ⁵Rheumatology, Universidade Federal de Santa Catarina, Hospital Universitário, Divisão de Reumatologia.Brazil, Florianopolis, Brazil, ⁶Centro Médico Paitilla Internal Medicine and Rheumatology Department. Panama, Panama City, Panama, ⁷School of Medicine, Universidad Militar Nueva Granada and Rheumatology Department Hospital Militar. Colombia, Bogotá, Colombia, ⁸Rheumatology, Hospital General de Mexico, Mexico, Mexico, ⁹Adjunct Professor of Rheumatology, Federal University of Paraná; Brazil, Curitiba, Brazil, ¹⁰Immunology, Janssen Latin America, Buenos Aires, Argentina, ¹¹Adelphi, Immunology Director-Adelphi Group, Manchester, United Kingdom

**First publication:** September 18, 2017
SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: To assess levels of rheumatologist and patient satisfaction with RA treatment across Latin America and any disconnects that may exist between the two in real world clinical practice.

Methods: Data from the 2015 RA Disease Specific Programme (DSP), a cross-sectional, multi-national survey of patients and rheumatologists conducted in Argentina, Mexico, Colombia and Venezuela were analyzed. Rheumatologists (n=141) completed forms containing patient demographics, patient disease severity and treatment satisfaction. Patients self-reported their level of treatment satisfaction and disease severity.

Results: A total of 555 RA patients from across Latin America were included in this analysis. Current mean age across Latin America was 51.9 years and 82.3% female. Proportions of rheumatologists and patients reporting satisfaction with treatment were statistically highly similar (79% and 83% respectively), however current disease severity reporting differed between rheumatologists and patients (mild 70% / moderate-severe 30% rheumatologists vs. 51% mild / 49% moderate-severe patients; p<0.001). When assessed for alignment, 21% of rheumatologists and patients disagreed on the level of satisfaction, driven mainly by rheumatologists over-stating dissatisfaction (13%) vs. their patient (8%) (p=0.031). For current disease severity, 36% of rheumatologists and patients disagreed, driven mainly by patients (28%) over-stating their severity vs. their rheumatologist (8%) (p<0.001). Of those patients for whom their rheumatologist was satisfied with treatment, 20% were classified as having moderate to severe RA by that same physician.

Conclusion: Despite many rheumatologists and their patients in Latin America reporting high levels of satisfaction with treatment, patients frequently remain moderate to severe and disconnected from their physician. There is a need to improve physician / patient engagement as a means to improving clinical control.

Disclosure: E. R. Soriano, AbbVie, Janssen, Novartis, Pfizer Inc, UCB, 2,AbbVie, Janssen, Novartis, Pfizer Inc, UCB, 5,AbbVie, Bristol-Myers Squibb, Janssen, Novartis, Pfizer Inc, Roche, UCB, 8; J. A. Maldonado-Cocco, None; D. Vega-Morales, None; D. Rocio Gil, None; I. Pereira, None; G. Guerra, None; W. Bautista-Molano, None; J. Casasola, None; V. F. Azevedo, AbbVie, Eli Lilly, Genentech, GSK, Pfizer Inc, UCB, 2,AbbVie, Merck-Serono, Novartis, Pfizer Inc, 5,AbbVie, Janssen, Merck-Serono, Novartis, Pfizer Inc, Sanofi, 8; L. Aldunate, Janssen Pharmaceutica Product, L.P., 3; S. Lobosco, Adelphi, 3.


Abstract Number: 458

Improving Knowledge of Rheumatoid Arthritis Clinical Trial Results Among Rheumatologists: Effect of an Online Educational Intervention

Edward Jackson and Piyali Chatterjee-Shin, Medscape Education, LLC, New York, NY
First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM
**Background/Purpose:** While major medical conferences provide the most up-to-date evidence regarding diseases and treatments, time demands and financial constraints are often cited as reasons for non-participation. A study was conducted to determine whether an online educational activity could effectively address a knowledge gap in awareness of emerging trial results as presented at a major rheumatology conference in the field of rheumatoid arthritis (RA).

**Methods:** An online educational intervention focusing on key abstracts in RA presented at the American College of Rheumatology Annual Meeting 2016 was developed and made available online. The education consisted of 3 video-based expert discussions covering both trial outcomes and associated clinical implications, for the intended audience of practicing rheumatologists. The educational impact was assessed by comparing participants’ responses to 3 identical paired pre- and post-assessment questions. Pairing of responses allows each learner to act as his/her own control. Data representing a statistical sampling of the overall learner population were collected from December 22, 2016 through January 31, 2017. Statistical analysis comprised a paired 2-tailed t-test comparing mean pre-assessment and post-assessment scores, McNemar’s $\chi^2$ statistic for measuring changes in responses to individual questions, and probability values ($P$ values) for both t-test and $\chi^2$ statistics. This analysis considers $P < .05$ as meeting statistical significance. Cramer’s $V$ was used to calculate the overall effect size of the intervention.

**Results:** For the rheumatologists who participated in the online activity, comparison of pre- and post-assessment responses demonstrated statistically significant improvements ($n = 59; P < .05$) in knowledge and a robust overall effect ($V = 0.307$). As a result of participating in this educational program, significant absolute percentage increases in correct responses were observed (all $P < .05$):

- 25% increase (44% vs 69%) in those who identified the trial design of an open-label extension of the MOBILITY trial regarding the 3-year efficacy of a specific IL-6 inhibitor
- 36% increase (10% vs 46%) in those who recognized the association between different types of disease flare and progression of joint damage as reported in a post hoc analysis of the PRESERVE trial
- 31% increase (44% vs 75%) in those who identified that tumor necrosis factor alpha therapy allowed patients to reduce or discontinue methotrexate or corticosteroid therapy as reported in a 10-year open-label extension of the PREMIER and DE019 trials

**Conclusion:** Participation in video-based expert discussions of clinical trial data from current and emerging agents resulted in significant improvement in knowledge of rheumatologists. A need for further education was also identified regarding the most up-to-date clinical information regarding management of RA as presented at major medical conferences.

**Disclosure:** E. Jackson, None; P. Chatterjee-Shin, None.


**Abstract Number:** 459

**Disease Course in Seronegative RA Patients Classified According to the 2010 ACR/EULAR Criteria**

Lena Bugge Nordberg$^1$, Siri Lillegraven$^2$, Anna-Birgitte Aga$^2$, Inge C Olsen$^3$, Elisabeth Lie$^4$, Hilde B Hammer$^2$, Till Uhlig$^2$, Désirée van der Heijde$^5$, Tore Kvien$^6$ and Espen A. Haavardsholm$^2$, $^1$Departement of Rheumatology, Diakonhjemmet hospital, oslo, Norway, $^2$Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, $^3$Department of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, $^4$Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, $^5$Rheumatology, Leiden University Medical Center, Leiden, Netherlands, $^6$Diakonhjemmet Hospital, Oslo, Norway

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Sunday, November 5, 2017
Background/Purpose:

The development of the 2010 classification criteria for rheumatoid arthritis (RA) has led to a redefinition of the patient population, including classification of seropositive versus seronegative patients (1). In our recently published study of early RA patients fulfilling the 2010 ACR/EULAR criteria, we found seronegative patients to have markedly higher disease activity at time of diagnosis, compared to seropositive patients (2). There is very limited information about the disease course of seronegative patients classified according to the new criteria. Our aim was to examine the disease course of seronegative RA patients fulfilling the 2010 ACR/EULAR criteria.

Methods:

In the treat-to-target ARCTIC trial, DMARD-naive RA patients classified according to the 2010 EULAR/ACR criteria were randomised 1:1 to follow-up with or without ultrasound. Patients in both arms were treated according to the same DMARD escalation strategy. Patients were assessed at 13 visits during two years of follow-up (3).

We stratified the patients as seropositive (rheumatoid factor (RF)+, anti-citrullinated peptide antibody (ACPA)+, or both) or seronegative (RF- and ACPA-). At baseline and 24-month follow-up, disease activity measures were compared across groups using independent t-test or Mann-Whitney U test as appropriate. We also compared the change in disease activity measures from 0-24 months across groups.

Results:

A total of 230 patients were included. Mean (SD) age was 51.4 (13.7) years and 61.3 % were female; 34 patients (14.8%) were seronegative. Mean age (SD) was 55.4 (2.7)/50.8 (0.9) years (p=0.07), mean (SD) disease duration was 7.7 (6.8)/7.0 (5.1) months (p=0.46), and 56/62 % were females (p=0.48) in the seronegative/seropositive groups.

At baseline disease activity measures and radiographic joint space narrowing were higher in seronegative compared to seropositive patients. At 24-month follow-up, measures of disease activity were similar between groups (table). There was a tendency towards more radiographic damage in terms of joint space narrowing in the seronegative patients.

Seronegative patients had a greater reduction (0-24 months) in disease activity measures in terms of DAS, swollen joints, physician global and ultrasound scores (table).
Conclusion:
In this study of early RA patients, seronegative patients had more inflammatory activity at baseline and a tendency to more radiographic damage, but disease activity after two years of treat-to-target therapy was similar to the seropositive patients. Our findings suggest that seronegative patients classified according to the new criteria respond to modern treatment strategies, with similar rates of patients reaching remission compared to seropositive patients.

2. Nordberg LB et al. ARD 2017;76:341-345
3. Haavardsholm EA et al., BMJ 2016;354:i4205

Disclosure: L. B. Nordberg, None; S. Lillegraven, None; A. B. Aga, None; I. C. Olsen, Pfizer Inc, 5; E. Lie, AbbVie, Celgene, Hospira and Pfizer, 8; H. B. Hammer, None; T. Uhlig, None; D. van der Heijde, None; T. Kvien, AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz, and UCB., 5,AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz, and UCB, 8; E. A. Haavardsholm, AbbVie, Pfizer, Roche, Eli Lilly, Celgene, UCB, 5,AbbVie, Pfizer, Roche, MSD, UCB, 2,AbbVie, Pfizer, Roche, Eli Lilly, Celgene, UCB, 8.

Usefullness of Serum Angiogenic and Proinflammatory Cytokines to Discriminate between 6 Sets of Remission Criteria and Biomarkers of Radiographic Progression and Clinical Flare in RA in Clinical Remission. Pre-Eliminary Results of a Study of 5 Years of Follow-up

Julio Ramírez1, Andrea Cuervo2, Raquel Celis3, Virginia Ruiz-Esquide1, M. Victoria Hernández4, Raimon Sanmarti5 and Juan D. Cañete6, 1Rheumatology Service, Hospital Clínic de Barcelona, Barcelona, Spain, 2Arthritis Unit. Rheumatology Dpt, Arthritis Unit, Rheumatology Dpt, Hospital Clinic of Barcelona and IDIBAPS, Barcelona, Spain, 3Rheumatology, Arthritis Unit, Barcelona, Spain, 4Hospital Clinic. Barcelona. Spain, Barcelona, Spain, 5Arthritis Unit, Rheumatology Dpt,
SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

The primary aim of this study was to analyse serum levels differences of angiogenic and inflammatory biomarkers between SDAI, CDAI, ACR, DAS28 and sonographic remission in patients with RA. As secondary objective, we tried to find clinical, serological or ultrasound biomarkers of radiographic progression and clinical flares in RA patients in clinical remission.

Methods:

We selected patients with RA in clinical remission (defined as DAS28-ESR<2.6 for > 6 months) tested by two independent rheumatologists. Clinical, epidemiological, demographic and serological data were analyzed. PDUS of knees and hands was performed by a sonographer with an ultrasound scanner with a linear probe of 8-12 MHz. Serum levels of biomarkers of inflammation/angiogenesis were determined by Quantibody® Human Array. Patients were classified according to 6 sets of remission criteria: SDAI (<3.3), CDAI (<2.8), ACR/EULAR, DAS28-ESR (<2.6), Doppler (score Doppler=0) and UdAS (ultrasound defined active synovitis: no joints with SH>2+PD). A clinical and radiographic follow-up of the patients was done along 5 years. Clinical flare was defined as the loss of remission (DAS28-ESR>2.6) and change on the baseline treatment for RA. Radiographic progression was defined as the new appearance of erosions in hands or feet.

Results:

60 patients with RA were collected. 76% female, aged (mean) 53 years; disease duration 110 months. Sixteen (26%) patients were taking oral prednisone (<5 mg/day), 47 (76%) conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs), and 27 (45%) biological therapies. At baseline, 67% of patients had PD signal and 48% fulfilled criteria for previously defined UdAS. Although patients in sonographic remission (both Doppler and UdAS) had lower levels of inflammatory biomarkers such as IL-6, IL-17 or IL-23, no significant differences were found between the 6 sets of remission criteria. Angiogenic biomarkers such as CXCL6 (0.039), ENA78 (0.007), SDF1 (0.047) and VEGF-R1 (0.025) were significantly lower in patients fulfilling CDAI remission. Patients with no PD signal (0.009) and no UdAS (0.006) had significantly lower levels of bFGF. After 5 years of follow-up, 12 patients (20%) flared and 14 (23.3%) had radiographic progression. No significant differences were found in flares or X-ray progression between the 6 sets of remission criteria. Patients fulfilling UdAS but not those with only PD, had more radiographic progression (p=0.014). Patients on biological therapy had less clinical flares along the 5 years of follow-up (p=0.049). Finally, patients with more CD20 + cells infiltrates in sinovial membrane had also more radiographic progression (p=0.033).

Conclusion:

RA patients in CDAI remission had significantly-lower levels of angiogenic cytokines. Remission according to DAS28-ESR did not show worse clinical or radiographic progression after 5 years of follow-up. Noteworthy, UdAS and CD20+ cells infiltrates were both significant factors of radiographic progression.

Disclosure: J. Ramírez, Gebro, 2; A. Cuervo, None; R. Celis, None; V. Ruiz-Esquide, None; M. V. Hernández, None; R. Sanmarti, None; J. D. Cañete, None.

Additions to Methotrexate with Conventional and Biologic DMARDs in Rheumatoid Arthritis: Are There Differences in Subsequent Time to Treatment Failure?

Sasha Bernatsky¹, Orit Schieir², Cristiano S. Moura³, Marie-France Valois⁴, Susan J. Bartlett⁵, Carol A Hitchon⁶, Janet E. Pope⁷, Gilles Boire⁸, Boulos Haraoui⁹, Edward C. Keystone¹⁰, Diane Tin¹¹, Carter Thorne¹² and Vivian P. Bykerk¹³

¹Divisions of Rheumatology and Clinical Epidemiology, Research Institute of the McGill University Health Centre, Montreal, QC, Canada, ²McGill University, Montreal, ON, Canada, ³Division of Clinical Epidemiology, McGill University Health Centre, Montreal, QC, Canada, ⁴McGill University, Montreal, QC, Canada, ⁵Department of Medicine, Division of ClinEpi, Rheumatology, Respirology, McGill University, Montreal, QC, Canada, ⁶University of Manitoba, Winnipeg, MB, Canada, ⁷Department of Medicine, Division of Rheumatology, University of Western Ontario, St Joseph's Health Care, London, ON, Canada, ⁸Rheumatology Division, Centre Hospitalier Universitaire de Sherbrooke and Université de Sherbrooke, Sherbrooke, QC, Canada, ⁹Institut de Rhumatologie de Montréal, Montreal, QC, Canada, ¹⁰University of Toronto, Toronto, ON, Canada, ¹¹The Arthritis Program, Southlake Regional Health Centre, Newmarket, ON, Canada, ¹²University of Toronto, Newmarket, ON, Canada, ¹³-005, Mt Sinai Hospital, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Our objective was to compare RA treatment strategies with conventional and biologic DMARDs after an initial MTX strategy was ineffective or associated with a severe adverse event.

Methods: We studied adults from a multicenter early arthritis cohort (enrolled from 2007-2017 within one year of symptom onset). RA patients were eligible for our analyses if they initiated MTX (+/- other DMARDs) within 90 days of cohort entry and subsequently changed therapy (changed MTX route, lowered or stopped MTX or other DMARD, or added another DMARD or biologic). For this analyses, the time of medication change formed the time zero for a survival analyses of the second treatment approach. Patients were followed from time zero to assess discontinuations of, or additions to, their therapy. Multivariable survival models were used to compare outcomes. We generated hazard ratios (HRs) and 95% confidence intervals (CI), comparing each of the treatment groups to oral methotrexate monotherapy.

Results: We included 911 RA patients initially exposed to MTX who had a first treatment failure. At time zero (time of initial failure), the most common second treatment strategies were MTX+ another DMARD (32.9%) and non MTX DMARDs (26.1%) (Table 1).

Table 1 Distribution of treatment approaches after a first MTX failure
The multivariable Cox regression analysis for the 911 RA patients suggested that those on biologics and those on triple therapy had a longer time to failure, compared to the group taking MTX oral monotherapy. (Table 2)

### Table 2 Adjusted hazard ratios (HR) for drug changes after time zero*

<table>
<thead>
<tr>
<th>Treatment at time zero</th>
<th>HR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTX subcutaneous monotherapy</td>
<td>0.91</td>
<td>0.61, 1.35</td>
</tr>
<tr>
<td>MTX + another DMARD</td>
<td>0.87</td>
<td>0.62, 1.22</td>
</tr>
<tr>
<td>MTX+SSZ+HCQ</td>
<td>0.64</td>
<td>0.44, 0.94</td>
</tr>
<tr>
<td>Biologics+/- DMARDs including MTX</td>
<td>0.31</td>
<td>0.20, 0.49</td>
</tr>
<tr>
<td>Non MTX DMARDs only</td>
<td>1.26</td>
<td>0.89, 1.77</td>
</tr>
</tbody>
</table>

*Adjusting for baseline characteristics: age, sex, co-morbidities, symptom duration, race, education, smoking, erosions, DAS-28, disease activity, corticosteroids, NSAIDs, and COXIBs

**Conclusion:** Our data suggest that, in those who fail initial MTX, RA patients given biologics or triple therapy remain on that treatment longer without further changes, versus those taking augmented MTX oral monotherapy. These data do not confirm clear differences in outcomes with respect to MTX (dual or triple) combinations, but width of confidence intervals precludes definitive conclusions in this regard.

**Disclosure:** S. Bernatsky, None; O. Schieir, None; C. S. Moura, None; M. F. Valois, None; S. J. Bartlett, PROMIS, 6, Pfizer, UCB, Lilly, 5; C. A. Hitchens, None; J. E. Pope, AbbVie, Amgen, Bayer, BMS, Celtrion, Eli Lilly and Company, Merck, Novartis, Pfizer, Roche, UCB, 5, Amgen, Bayer, BMS, GSK, Merck, Novartis, Pfizer, Roche, UCB, 2; G. Boire, None; B. Harouei, None; E. C. Keystone, Abbott Laboratories, Amgen Inc., AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb, F. Hoffmann-La Roche Inc, Janssen Inc, Lilly Pharmaceuticals, Novartis Pharmaceuticals, Pfizer Pharmaceuticals, Sanofi-Aventis, UCB, 2; Abbott Laboratories, AstraZeneca Pharma, Biotest, Bristol-Myers Squibb Company, Crescendo Bioscience, F. Hoffmann-La Roche Inc, Genentech Inc, Janssen Inc, Lilly Pharmaceuticals, Merck, Pfizer Pharmaceuticals, UCB, 5; Amgen, Abbott Laboratories, AstraZeneca LP, Bristol-Myers Squibb Canada, 8; D. Tin, None; C. Thorne, AbbVie, Amgen, Celgene, Lilly, Novartis, Pfizer, Sanofi, and UCB; has served as a consultant for AbbVie, Amgen, Celgene, Centocor, Genzyme, Hospira, Janssen, Lilly, Medexus/Medaç, Merck, Novartis, Pfizer, Sanofi, and UCB, 2; Medexus/Medaç, 8; V. P. Bykerk, None.

ABP 710: Matching Critical Biological Functions with Infliximab

Robert Sandrock1, Palanisamy Kanakaraj2 and Scott Kuhns1, 1Amgen, Inc., Thousand Oaks, CA, 2Amgen, Inc., Cambridge, MA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
ABP 710 is being developed as a biosimilar to infliximab, a recombinant chimeric monoclonal antibody that binds tumor necrosis factor alpha (TNFa) and inhibits the TNF receptor-mediated downstream pro-inflammatory signaling cascade. Although ABP 710 and infliximab reference product have the same primary amino acid sequence differences in production cell line and the manufacturing process can impact product quality attributes that may be critical for in vivo efficacy, pharmacokinetics and immunogenicity. To demonstrate that ABP 710 is similar to the reference product, we performed a comprehensive comparative biological characterization of ABP 710 with infliximab reference product.

Methods:
The functional similarity assessment of ABP 710 and infliximab reference product included: 1) binding to soluble (s) TNFa by ELISA, 2) binding to membrane-bound (mb) TNFa by a competitive imaging cytometry-based assay, 3) inhibition of sTNFa-induced apoptosis in the U937 cell line, and 4) reverse signaling via induction of apoptosis in mbTNFa-expressing Jurkat cells. To confirm similarity of Fc-mediated functions, antibody-dependent cell-mediated cytotoxicity (ADCC) was assessed using cells expressing mbTNFa as target cells and NK92-M1 cells expressing FcγRIIIa (158V) as effector cells. In addition, complement-dependent cytotoxicity (CDC) was assessed using rabbit complement and cells expressing mbTNFa. Data from at least three lots of ABP 710 and infliximab reference product sourced from the US (IFX-US) and infliximab reference product sourced from the EU (IFX-EU) were assessed as described.

Results:
Relative binding of ABP 710 to sTNFa (ABP 710 =93-105%; IFX-US =88-101%; IFX-EU =93-104%) and mbTNFa (ABP 710=101-109%; IFX-US =99-106%; IFX-EU =105-113%) were similar between ABP 710 and infliximab reference product. Relative inhibition of apoptosis in U937 cells (ABP 710 =87-112%; IFX-US =78-115%; IFX-EU =89-114%), and to induce apoptosis in Jurkat cells expressing mbTNFa (ABP 710 =99-105%; IFX-US =90-114%; IFX-EU =96-107%) were also similar between ABP 710 and infliximab reference product. Fc-mediated functions, ADCC (ABP 710=102-133%; IFX-US =91-169%; IFX-EU =100-166%) and CDC (ABP 710 =96-110%; IFX-US =93-136%; IFX-EU =98-135%) were similar as well between ABP 710 and infliximab reference product.

Conclusion:
As one aspect of the “totality of evidence” approach to support similarity, results from this assessment demonstrate that ABP 710 is functionally similar to infliximab reference product in multiple sensitive biological characterization assays.

Disclosure: R. Sandrock, Amgen, 1,Amgen, 3; P. Kanakaraj, Amgen, 1,Amgen, 3; S. Kuhns, Amgen, 1,Amgen, 3.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/abp-710-matching-critical-biological-functions-with-infliximab
Certolizumab Pegol for Fatigue in Chronic Inflammatory Rheumatic Diseases: A Meta-Analysis

Yesim Ozguler1, Sinem Nihal Esatoglu1, Guzin Karatemiz1, Ali Ugur Unal2, Gul Guzelant1, Elif Dinceses3, Mustafa Erdogan1, Sema Kaymaz Tahra2 and Gulen Hatemi1, 1Istanbul University, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey, 2Departement of Internal Medicine, Division of Rheumatology, Marmara University, Istanbul, Turkey, 3Istanbul University, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Fatigue is an important problem that impairs life quality in patients with rheumatic diseases. Although fatigue is often associated with disease activity, only a modest effect of anti-TNFs on fatigue was observed in patients with RA (1). We aimed to determine the efficacy of different doses of certolizumab pegol (CZP) in chronic inflammatory rheumatic diseases by a meta-analysis of randomized controlled trials.

Methods: A systematic literature search including patients with rheumatic diseases who received CZP was performed. We searched PubMed for all randomized controlled trials with CZP up to May 2017 without any restrictions. Studies that assessed fatigue in any rheumatic disease using the fatigue assessment scale (FAS) and reported the FAS score and/or the proportion of patients who met the minimum clinically important difference (MCID) for FAS score were included. The MCID for FAS is 1 over a scale of 0 to 10 where higher scores show increased severity of fatigue. The CZP 200 mg and CZP 400 mg arms of trials were pooled for comparison with the placebo arms.

Results: The literature search yielded 68 articles. 55 articles were excluded after evaluating the title and abstract, 5 were excluded after reading the full-text. Among the 8 RCTs that were selected-, the study population was RA in 6 RCTs, and psoriatic arthritis and axial spondyloarthritis in 1 RCT each. Overall, there were 2964 patients treated with CZP and 1056 with placebo. Table summarizes the included studies.

An improvement in the FAS score and an increase in the proportion of patients who met the MCID for FAS were observed in all the included trials regardless of the underlying disease (Figure-1, 2). The pooled results showed that CZP significantly improved fatigue compared to placebo (FAS: MD = -1.50, 95% CI: -1.71 - -1.29, p <0.0001, MCID: RR=2.53, 95% CI: 1.74-3.68).

Conclusion: This meta-analysis showed that CZP may be an effective treatment modality for fatigue in rheumatic diseases.

Reference:

## Table 1. Characteristics of randomized controlled studies included in the meta-analysis

<table>
<thead>
<tr>
<th>First author, year</th>
<th>Disease state</th>
<th>Inclusion criteria</th>
<th>Intervention arm</th>
<th>Comparator arm</th>
<th>Number of patients (M/W)</th>
<th>Study duration (weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fleischman, 2017</td>
<td>RA</td>
<td>Active disease despite ≥1 DMARD</td>
<td>CZP 400</td>
<td>Placebo every 4 weeks</td>
<td>111 (24/87)</td>
<td>NA (12/97)</td>
</tr>
<tr>
<td>Furst, 2015</td>
<td>RA</td>
<td>Active disease despite MTX</td>
<td>CZP 400</td>
<td>Placebo every 2 weeks</td>
<td>70 (12/58)</td>
<td>70 (23/49)</td>
</tr>
<tr>
<td>Pope, 2015</td>
<td>RA</td>
<td>Active disease despite ≥1 DMARD</td>
<td>CZP 200</td>
<td>Placebo every 2 weeks</td>
<td>NA</td>
<td>851 (NR)</td>
</tr>
<tr>
<td>Smolen, 2017</td>
<td>RA</td>
<td>Low/moderate active disease despite ≥1 DMARD</td>
<td>CZP 200</td>
<td>Placebo every 2 weeks</td>
<td>NA</td>
<td>96 (15/81)</td>
</tr>
<tr>
<td>Strand, 2009</td>
<td>RA</td>
<td>Active disease despite MTX</td>
<td>CZP 400</td>
<td>Placebo every 2 weeks</td>
<td>390 (64/326)</td>
<td>393 (69/324)</td>
</tr>
<tr>
<td>Strand, 2011</td>
<td>RA</td>
<td>Active disease despite MTX</td>
<td>CZP 400</td>
<td>Placebo every 2 weeks</td>
<td>246 (54/192)</td>
<td>246 (42/206)</td>
</tr>
<tr>
<td>Gladman, 2014</td>
<td>pSA</td>
<td>Active disease despite ≥1 DMARD*</td>
<td>CZP 400</td>
<td>Placebo every 2 weeks</td>
<td>135 (62/73)</td>
<td>138 (64/74)</td>
</tr>
<tr>
<td>Sieper, 2015</td>
<td>axial SpA</td>
<td>Active disease despite ≥1 NSAID*</td>
<td>CZP 400</td>
<td>Placebo every 2 weeks</td>
<td>107 (68/39)</td>
<td>111 (67/44)</td>
</tr>
</tbody>
</table>

*An history of an anti-TNF failure was not an exclusion criterion

DMARD: disease modifying anti-rheumatic drug; pSA: psoriatic arthritis; SpA: spondyloarthritis; MTX: methotrexate, NSAID: non-steroidal anti-inflammatory drugs; CZP: certolizumab pegol; NA: not applicable; NR: not reported
Disclosure: Y. Ozguler, None; S. N. Esatoglu, None; G. Karatemiz, None; A. U. Unal, None; G. Guzelant, None; E. Dincses, None; M. Erdogan, None; S. Kaymaz Tahra, None; G. Hatemi, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/certolizumab-pegol-for-fatigue-in-chronic-inflammatory-rheumatic-diseases-a-meta-analysis

Abstract Number: 464

Value of Matrix Metalloproteinase-3 Regarding Prediction for Joint Destruction at 1 Year Is Different between Sexes in Patients with Rheumatoid Arthritis

Yutaro Yamada1, Kentaro Inui2, Tadashi Okano3, Yuko Sugioka1, Kenji Mamoto4, Kazuki Orita5, Tatsuya Koike6, Masahiro Tada7 and Hiroaki Nakamura3. 1Orthopedic surgery, Osaka City University Graduate School of Medicine, Osaka, Japan, 2Orthopedic surgery, Osaka City University Graduate School of Medicine, Osaka, Japan, 3Orthopaedic Surgery, Osaka City University Graduate School of Medicine, Osaka, Japan, 4Orthopedic Surgery, Osaka City University Graduate School of Medicine, Osaka, Japan, 5Orthopedics, Shirahama hamayu Hospital, Shirahama, Japan, 6Center for Senile
SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Serum level of MMP-3 rises by synovial inflammation in patients with rheumatoid arthritis (RA). It destroys articular cartilage such as proteoglycans so that it has been used as a clinical biomarker of joint destruction. Also it has been reported as a predictor for radiographic progression. The purposes of this study are to confirm a relation between baseline MMP-3 and radiographic progression at 1 year and to examine the association of the MMP-3 level with ultrasonography (US) findings.

Methods: A total of 259 (213 women) consecutive patients with RA were enrolled in this study. Their baseline data including age, sex, disease duration, use of glucocorticoid (GC) or DMARDs, disease activity (DAS28), laboratory data (MMP-3, CRP, RF and ACPA), radiographic assessment (modified total Sharp score; mTSS) and the power doppler score (PD) in US assessment at digits and wrists were collected. Baseline MMP-3 level was analyzed in association with the baseline PD value and changes in mTSS (f_{mTSS}), erosion score (f_{ERN}), joint space narrowing (f_{JSN}) at 1 year from baseline using Pearson's correlation method. Correlations between f_{MMP-3} and f_{mTSS}, or f_{PD} were also analyzed. Multiple regression analysis was performed with f_{mTSS} as the outcome for baseline variables. Statistical analysis was performed separately by sex because the upper normal limits of MMP-3 is different between male and female.

Results: There was no correlation between baseline MMP-3 and disease duration, GC use, DAS28, RF, CRP and mTSS. There was moderate correlations between baseline MMP-3, f_{MMP-3}, f_{mTSS} and f_{JSN} at 1 year only in men. There was also a weak correlation between the baseline MMP-3 and baseline PD score only in men. However, MMP-3 could not predict joint destruction at 1 year in women. Multiple regression analysis revealed that the baseline MMP-3 level correlated independently with the f_{mTSS} only in men (p= 0.0031), whereas the baseline PD score was correlated independently with the f_{mTSS} in women (p= 0.0003).

Conclusion: The baseline MMP-3 level was a good predictor for deterioration of the mTSS at 1 year in male patients with RA, but not in female patients. On the other hand, the baseline PD score was a useful predictor of joint destruction in female patients with RA.
<table>
<thead>
<tr>
<th>variables</th>
<th>correlation coefficient</th>
<th>confidence interval</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline MMP-3</td>
<td>f_{\delta}mTSS</td>
<td>0.501&lt;sup&gt;a&lt;/sup&gt;</td>
<td>[0.246, 0.691]</td>
</tr>
<tr>
<td></td>
<td>f_{\delta}ERN</td>
<td>0.336&lt;sup&gt;b&lt;/sup&gt;</td>
<td>[0.051, 0.571]</td>
</tr>
<tr>
<td></td>
<td>f_{\delta}JSN</td>
<td>0.542&lt;sup&gt;a&lt;/sup&gt;</td>
<td>[0.299, 0.719]</td>
</tr>
<tr>
<td></td>
<td>baseline-PD</td>
<td>0.228&lt;sup&gt;b&lt;/sup&gt;</td>
<td>[-0.074, 0.492]</td>
</tr>
<tr>
<td>f_{\delta}MMP-3</td>
<td>f_{\delta}mTSS</td>
<td>-0.435&lt;sup&gt;a&lt;/sup&gt;</td>
<td>[-0.644, -0.165]</td>
</tr>
<tr>
<td></td>
<td>f_{\delta}ERN</td>
<td>-0.325&lt;sup&gt;b&lt;/sup&gt;</td>
<td>[-0.562, -0.038]</td>
</tr>
<tr>
<td></td>
<td>f_{\delta}JSN</td>
<td>-0.436&lt;sup&gt;a&lt;/sup&gt;</td>
<td>[-0.645, -0.167]</td>
</tr>
<tr>
<td></td>
<td>f_{\delta}PD</td>
<td>0.134</td>
<td>[-0.170, 0.414]</td>
</tr>
<tr>
<td>Female patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline MMP-3</td>
<td>f_{\delta}mTSS</td>
<td>0.0011</td>
<td>[-0.130, 0.132]</td>
</tr>
<tr>
<td></td>
<td>f_{\delta}ERN</td>
<td>0.0188</td>
<td>[-0.013, 0.150]</td>
</tr>
<tr>
<td></td>
<td>f_{\delta}JSN</td>
<td>-0.0148</td>
<td>[-0.146, 0.117]</td>
</tr>
<tr>
<td></td>
<td>baseline-PD</td>
<td>0.0985</td>
<td>[-0.040, 0.233]</td>
</tr>
<tr>
<td>f_{\delta}MMP-3</td>
<td>f_{\delta}mTSS</td>
<td>-0.0344</td>
<td>[-0.165, 0.098]</td>
</tr>
<tr>
<td></td>
<td>f_{\delta}ERN</td>
<td>-0.0485</td>
<td>[-0.179, 0.083]</td>
</tr>
<tr>
<td></td>
<td>f_{\delta}JSN</td>
<td>-0.0127</td>
<td>[-0.144, 0.119]</td>
</tr>
<tr>
<td></td>
<td>f_{\delta}PD</td>
<td>0.134</td>
<td>[-0.0058, 0.270]</td>
</tr>
</tbody>
</table>

<sup>a</sup>: Moderate correlation, <sup>b</sup>: Weak correlation. Statistical analysis was performed using Pearson’s correlation.

Disclosure: Y. Yamada, None; K. Inui, None; T. Okano, None; Y. Sugikawa, None; K. Mamoto, None; K. Orita, None; T. Koike, None; M. Tada, None; H. Nakamura, None.


Abstract Number: 465

**Basement Membrane Remodeling in Rheumatoid Arthritis Associates with Disease Activity, Response to IL-6 Inhibitor Treatment and Radiographic Progression: Analysis of Two Phase III Clinical Trials**

Natasja Stæhr Gudman<sup>1</sup>, Pernille Juhl<sup>1</sup>, Christian S. Thudium<sup>2</sup>, Peter Junker<sup>3</sup>, Anne Sofie Siebuhr<sup>4</sup>, Inger Byrjalsen<sup>1</sup>, Morten Karsdal<sup>5</sup> and Anne C. Bay-Jensen<sup>4</sup>,<sup>1</sup>Nordic Bioscience, Herlev, Denmark, <sup>2</sup>Biomarkers and Research, Nordic Bioscience, Herlev, Denmark, <sup>3</sup>Department of Rheumatology C, Odense University Hospital, Odense, Denmark, <sup>4</sup>Rheumatology, Nordic Bioscience, Herlev, Denmark, <sup>5</sup>Biomarkers and Research, Nordic Bioscience, Herlev, Denmark

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Sunday, November 5, 2017

Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Background/Purpose:
Rheumatoid arthritis (RA) is associated with neovascularization of the synovial membrane and increased risk of cardiovascular co-morbidity. The extra cellular matrix below the endothelial cells is referred to as the basement membrane, embedding and protecting the cells. Altered remodeling of basement membrane proteins, including type IV collagen is a core characteristic in persistent chronic inflammation. We aimed to investigate the association of type IV collagen turnover with RA disease activity, response to IL-6 inhibition and radiographic progression.

Methods:
The study was based on patients participating in LITHE (NCT00106522, n=687) and RADIATE (NCT00106535, n=217), phase III, double blinded, placebo controlled studies testing 4 and 8 mg/kg tocilizumab (TCZ) on top of methotrexate.

Baseline membrane turnover was assessed at baseline and subsequently for up to 52 weeks using ELISA for quantification of circulating C4M, an MMP generated collagen IV fragment in serum. We calculated correlations between C4M and disease activity measures, treatment response and imaging findings.

Results:
Baseline C4M was significantly correlated with clinical disease parameters in both study populations, including DAS28, HAQ score and VASpain (all p<0.00001). TCZ lowered C4M by 11%-40% in a dose dependent manner and the likelihood of achieving an ACR20 response by week 16 was associated with C4M suppression exceeding the median decrease at week 4 (p<0.0001). C4M at baseline correlated significantly with change in JSN (p=0.001) and Sharp score (p=0.00002) at 52 weeks.

Conclusion:
Basement membrane remodeling as assessed by C4M was associated with disease activity and radiographic progression in RA. This remodeling was persistently suppressed by TCZ in a dose dependent manner. These findings probably reflect that RA synovitis suppression and slowing of erosive progression are at least in part attributable to angiostatic effects by tocilizumab

Disclosure: N. S. Gudman, Nordic Bioscience Diagnostic, 3; P. Juhl, Nordic Bioscience Diagnostic, 3; C. S. Thudium, Nordic Bioscience Diagnostic, 3; P. Junker, None; A. S. Siebuhn, Nordic Bioscience Diagnostic, 3; I. Byrjalsen, Nordic Bioscience Diagnostic, 3; M. Karsdal, Symic Bio, 1; A. C. Bay-Jensen, Nordic Bioscience Diagnostic, 3.

Plasma Cytokines at Diagnosis May Predict Non-Response to Methotrexate in Patients with Early Rheumatoid Arthritis

Martin Pelletier¹, Paul R. Fortin¹,², Marie-Pier Longchamps¹, Geneviève Parent¹, Hadrien Benk-Fortin¹, Anne-Sophie Julien³, Nathalie Amiable¹, Emmanuelle Rollet-Labelle¹, Laetitia Michou², Louis Bessette² and Philippe A. Tessier¹,
¹Infectious Diseases and Immunity Research Division, CHU de Québec-Université Laval Research Center, Québec, QC, Canada, ²Division of Rheumatology, Department of Medicine, CHU de Québec-Université Laval, Québec, QC, Canada, ³Clinical Research Platform, CHU de Québec-Université Laval Research Center, Québec, QC, Canada
First publication: September 18, 2017
Background/Purpose: Methotrexate (MTX) is the first line treatment for patients with rheumatoid arthritis (RA). For over 30% of patients, MTX fails to diminish DAS28 score in a timely and satisfactory manner. The challenge is to find a way to identify these non-responders at the time of diagnosis. The aims of this study were to determine whether plasma cytokines could be used as biomarkers of early RA and of therapeutic response to MTX.

Methods: Thirty RA patients receiving MTX (mean age 58 ± 12 y.o. with symptom duration of 6 ± 3 mo.) from the Group for Early Arthritis Research (GEAR) / CHU de Québec SARD Biobank Data Repository (SBDR). Patients were evaluated clinically at baseline and 6 mo., and classified as responders to MTX or non-responders according to the DAS28CRP EULAR Classification (good response vs moderate/none). Plasma cytokines were measured at baseline by multiplex assay or ELISA and compared to age- and sex-matched healthy controls. Patients were Bivariate logistic regression was used to identify RA patients and non-responders based on cytokine concentration or detection, with Firth bias correction when needed. Optimal cut points were found using distance criteria and their predictive performance was assessed.

Results: Plasma concentrations of IL-1RA, CCL11/Eotaxin, CXCL10/IP-10, CCL2/MCP-1, CCL4/MIP-1β, CCL5/RANTES, CXCL12a/SDF-1α and calprotectin were significantly different in RA patients compared to controls. IL-21, IL-22, IL-1α, CXCL1/GROα were detected differently in RA plasma (Table 1). IL-1RA and CCL4/MIP-1β were good predictors of RA with sensitivity and specificity of approximately 95% when dichotomized with cut points of 280 and 124, respectively. Thirty-five percent of patients were non-responders to MTX. IL-1α, IL-18, IL-17A and IL-27 were less frequently detected in non-responders (Table 2).

Conclusion: Several cytokines differentially expressed in plasma are associated with early RA. Absence of detection of IL-1α, IL-17A and IL-27 and low concentration of IL-18 was associated with non-response to MTX. We propose that these cytokines could be used as predictors of MTX response in RA.

Acknowledgements: This work was partly funded by CIHR. We thank Pfizer, Amgen, BMS, Abbvie, Roche, Sanofi-Genzyme and Merck & Co. for unrestricted financial contribution to the SBDR.

Table 1: Plasma cytokine concentrations significantly different between RA patients and healthy controls at baseline.

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Controls (n=30)</th>
<th>RA (n=30)</th>
<th>Odds Ratios (95% CI)</th>
<th>Pvalue (Wald)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-1RA</td>
<td>92 (56-174)</td>
<td>1561 (1175-2607)</td>
<td>1.01(1.00-1.01)</td>
<td>0.0065</td>
</tr>
<tr>
<td>CCL11/Eotaxin</td>
<td>23 (17-33)</td>
<td>32 (25-38)</td>
<td>1.08(1.02-1.15)</td>
<td>0.0083</td>
</tr>
<tr>
<td>CXCL10/IP-10</td>
<td>10 (8-12)</td>
<td>30 (23-47)</td>
<td>1.30(1.16-1.52)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CCL2/MCP-1</td>
<td>19 (15-27)</td>
<td>37 (26-49)</td>
<td>1.07(1.03-1.13)</td>
<td>0.0034</td>
</tr>
<tr>
<td>CCL4/MIP-1β</td>
<td>22 (19-27)</td>
<td>180 (166-209)</td>
<td>1.03(1.02-1.05)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CCL5/RANTES</td>
<td>24 (20-27)</td>
<td>56 (42-67)</td>
<td>1.04(1.01-1.07)</td>
<td>0.0075</td>
</tr>
<tr>
<td>CXCL12a/SDF-1α</td>
<td>396 (349-423)</td>
<td>629 (482-754)</td>
<td>1.01(1.00-1.02)</td>
<td>0.0010</td>
</tr>
<tr>
<td>Calprotectin</td>
<td>1398 (1082-1915)</td>
<td>2675 (2171-3968)</td>
<td>1.00(1.00-1.00)</td>
<td>0.0006</td>
</tr>
<tr>
<td>IL-21</td>
<td>3 (10)</td>
<td>11(37)</td>
<td>5.21 (1.41-25.39)</td>
<td>0.0213</td>
</tr>
<tr>
<td>IL-22</td>
<td>14 (47)</td>
<td>1(3)</td>
<td>0.04(0.00-0.22)</td>
<td>0.0028</td>
</tr>
<tr>
<td>IL-1α</td>
<td>6(20)</td>
<td>16(53)</td>
<td>4.57(1.51-15.35)</td>
<td>0.0094</td>
</tr>
<tr>
<td>CXCL1/GRO-α</td>
<td>25(83)</td>
<td>4(13)</td>
<td>0.03 (0.01-0.12)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Values are presented as median in pg/ml (Quartile 1 – Quartile 3) or N(%)
<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Responders (N=19)</th>
<th>Non-responders (N=10)</th>
<th>Odds Ratios (95% CI)</th>
<th>P-value (Wald)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-18</td>
<td>24 (15-30)</td>
<td>16 (0-20)</td>
<td>0.93 (0.86-1.00)</td>
<td>0.0745</td>
</tr>
<tr>
<td>IL-1α</td>
<td>13 (68)</td>
<td>2 (20)</td>
<td>0.12 (0.01-0.63)</td>
<td>0.0205</td>
</tr>
<tr>
<td>IL-17A</td>
<td>7 (37)</td>
<td>0 (0)</td>
<td>0.08 (0.00-0.79)</td>
<td>0.12</td>
</tr>
<tr>
<td>IL-27</td>
<td>7 (37)</td>
<td>0 (0)</td>
<td>0.08 (0.00-0.79)</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Values are presented as median in pg/ml (Quartile 1 – Quartile 3) or N(%)

Disclosure: M. Pelletier, None; P. R. Fortin, None; M. P. Longchamps, None; G. Parent, None; H. Benk-Fortin, None; A. S. Julien, None; N. Amiable, None; E. Rollet-Labelle, None; L. Michou, None; L. Bessette, Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Lilly, Novartis, Sanofi; 8, Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Lilly, Novartis, Sanofi; 5, Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Lilly, Novartis, Sanofi; 2; P. A. Tessier, None.


Abstract Number: 467

Smoking and Opioid Use Is Associated with Symptom Severity in Rheumatoid Arthritis

Angela Karellis1,2, Emmanouil Rampakakis3, John S. Sampalis1,4, Martin Cohen5, Michael Starr5, Peter Ste-Marie6, Yoram Shir6, Mark Ware6 and MaryAnn FitzCharles6,7, 1JSS Medical Research, St-Laurent, QC, Canada, 2Department of Surgery, McGill University, Montreal, QC, Canada, 3JSS Medical Research, Montreal, QC, Canada, 4McGill University, Montreal, QC, Canada, 5Rheumatology, McGill University Health Centre, Montreal, QC, Canada, 6Alan Edwards Pain Management Unit, McGill University Health Centre, Montreal, QC, Canada, 7Rheumatology, McGill University, Montreal, QC, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Smoking and Opioid Use Is Associated with Symptom Severity in Rheumatoid Arthritis

Background/Purpose: Cigarette smoking, both current and past, is a risk for incident rheumatoid arthritis (RA), even for those with low exposure rates of 1-10 pack years. As smoking is associated with opioid use in patients with chronic pain, the aim of the current analysis was to examine disease status for RA patients and the relationship between current cigarette smoking and opioid use.
Methods: As part of a study to evaluate cigarette and marijuana smoking in rheumatic disease patients, 1000 consecutively attending rheumatology patients completed an anonymous self-administered questionnaire including: pain severity on visual analog scale (VAS), patient global assessment (PtGA) and cigarette or marijuana smoking status. Concomitant physician recorded information included: diagnosis, sociodemographics, co-morbidities, treatments for RA and physician global assessment (PGA). Patients were categorized according to current smoking status and opioid use. Patient characteristics were compared between groups with one-way ANOVA.

Results: 248 patients were diagnosed with RA [mean (SD) age = 62.4 (14.3) years and 77.4% female] stratified by smoking status and opioid use: 9 patients were current smokers and opioid users, 186 patients non-smokers and non-opioid users, and 53 patients current smokers or opioid users (Table 1). Unemployment/disability was statistically different between groups (current smokers & opioid users vs. non-smokers & non-opioid users vs. current smokers or opioid users: 11.1% vs. 3.3% vs. 13.5%; p = 0.015). Current smokers and opioid users reported significantly worse disease, including higher PGA (p < 0.001), PtGA (p = 0.021) and pain VAS (p = 0.001), followed by current smokers or opioid users. In regard to medication use, current smokers and opioid users took significantly more medications for disease management (p < 0.001), specifically NSAIDs (p = 0.019) and anti-epileptics (p = 0.020) with a trend towards more antidepressant use (p = 0.088).

Conclusion: Current smoking and opioid use is significantly associated with increased disease severity and other medication use, indicating that RA patients who smoke experience greater symptom severity and may use chemical coping methods to alleviate symptoms.
<table>
<thead>
<tr>
<th>Demographics</th>
<th>All patients (N=248)</th>
<th>Current smokers &amp; opioid users (n = 9)</th>
<th>Non-smokers &amp; non-opioid users (n = 186)</th>
<th>Current smokers or opioid users (n = 53)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean (SD)</td>
<td>62.4 (14.3)</td>
<td>59.6 (11.8)</td>
<td>62.9 (15.2)</td>
<td>61.3 (11.3)</td>
<td>0.656</td>
</tr>
<tr>
<td>Female gender, n (%)</td>
<td>192 (77.4%)</td>
<td>7 (77.8%)</td>
<td>147 (79.0%)</td>
<td>38 (71.7%)</td>
<td>0.530</td>
</tr>
<tr>
<td>Employment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.116</td>
</tr>
<tr>
<td>Full-time, n (%)</td>
<td>83 (33.9%)</td>
<td>3 (33.3%)</td>
<td>61 (33.2%)</td>
<td>19 (36.5%)</td>
<td></td>
</tr>
<tr>
<td>Part-time, n (%)</td>
<td>8 (3.3%)</td>
<td>0 (0.0%)</td>
<td>4 (2.2%)</td>
<td>4 (7.7%)</td>
<td></td>
</tr>
<tr>
<td>Student, n (%)</td>
<td>2 (0.8%)</td>
<td>0 (0.0%)</td>
<td>2 (1.1%)</td>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td>Unemployed, n (%)</td>
<td>3 (1.2%)</td>
<td>0 (0.0%)</td>
<td>2 (1.1%)</td>
<td>1 (1.9%)</td>
<td></td>
</tr>
<tr>
<td>Disabled, n (%)</td>
<td>11 (4.5%)</td>
<td>1 (11.1%)</td>
<td>4 (2.2%)</td>
<td>6 (11.5%)</td>
<td></td>
</tr>
<tr>
<td>Retired, n (%)</td>
<td>119 (48.6%)</td>
<td>4 (44.4%)</td>
<td>94 (51.1%)</td>
<td>21 (40.4%)</td>
<td></td>
</tr>
<tr>
<td>Homemaker, n (%)</td>
<td>19 (7.8%)</td>
<td>1 (11.1%)</td>
<td>17 (9.2%)</td>
<td>1 (1.9%)</td>
<td></td>
</tr>
<tr>
<td>Employment: unemployed/disabled</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.015</td>
</tr>
<tr>
<td>Yes, n (%)</td>
<td>14 (5.7%)</td>
<td>1 (11.1%)</td>
<td>6 (3.3%)</td>
<td>7 (13.5%)</td>
<td></td>
</tr>
<tr>
<td>No, n (%)</td>
<td>231 (94.3%)</td>
<td>8 (88.9%)</td>
<td>178 (96.7%)</td>
<td>45 (86.5%)</td>
<td></td>
</tr>
<tr>
<td>Comorbid conditions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular, n (%)</td>
<td>74 (29.8%)</td>
<td>3 (33.3%)</td>
<td>57 (30.6%)</td>
<td>14 (26.4%)</td>
<td>0.816</td>
</tr>
<tr>
<td>Pulmonary, n (%)</td>
<td>14 (5.6%)</td>
<td>1 (11.1%)</td>
<td>10 (5.4%)</td>
<td>3 (5.7%)</td>
<td>0.767</td>
</tr>
<tr>
<td>Gastrointestinal, n (%)</td>
<td>25 (10.1%)</td>
<td>0 (0.0%)</td>
<td>22 (11.8%)</td>
<td>3 (5.7%)</td>
<td>0.249</td>
</tr>
<tr>
<td>Neurological, n (%)</td>
<td>4 (1.6%)</td>
<td>0 (0.0%)</td>
<td>3 (1.6%)</td>
<td>1 (1.9%)</td>
<td>0.917</td>
</tr>
<tr>
<td>Endocrine, n (%)</td>
<td>50 (20.2%)</td>
<td>1 (11.1%)</td>
<td>38 (20.4%)</td>
<td>11 (20.8%)</td>
<td>0.787</td>
</tr>
<tr>
<td>Mood disorder, n (%)</td>
<td>26 (10.5%)</td>
<td>2 (22.2%)</td>
<td>18 (9.7%)</td>
<td>6 (11.3%)</td>
<td>0.475</td>
</tr>
<tr>
<td>Other psychiatric disorder, n (%)</td>
<td>1 (0.4%)</td>
<td>0 (0.0%)</td>
<td>1 (0.5%)</td>
<td>0 (0.0%)</td>
<td>0.846</td>
</tr>
<tr>
<td>Lipid disorder, n (%)</td>
<td>31 (12.5%)</td>
<td>2 (22.2%)</td>
<td>21 (11.3%)</td>
<td>8 (15.1%)</td>
<td>0.508</td>
</tr>
<tr>
<td>Other comorbid condition, n (%)</td>
<td>17 (6.9%)</td>
<td>1 (11.1%)</td>
<td>14 (7.5%)</td>
<td>2 (3.8%)</td>
<td>0.556</td>
</tr>
<tr>
<td>Medications for rheumatic diseases</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of medication types for rheumatic disease, mean (SD)</td>
<td>2.0 (1.1)</td>
<td>3.6 (1.3)</td>
<td>1.8 (1.0)</td>
<td>2.3 (1.1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Non-steroidal anti-inflammatory drug use, n (%)</td>
<td>110 (44.4%)</td>
<td>7 (77.8%)</td>
<td>74 (39.8%)</td>
<td>29 (54.7%)</td>
<td>0.019</td>
</tr>
<tr>
<td>Disease-modifying anti-rheumatic drug use, n (%)</td>
<td>184 (74.2%)</td>
<td>7 (77.8%)</td>
<td>134 (72.0%)</td>
<td>43 (81.1%)</td>
<td>0.398</td>
</tr>
<tr>
<td>Biologic use, n (%)</td>
<td>70 (28.2%)</td>
<td>2 (22.2%)</td>
<td>48 (25.8%)</td>
<td>20 (37.7%)</td>
<td>0.216</td>
</tr>
<tr>
<td>Opioids use, n (%)</td>
<td>23 (9.3%)</td>
<td>9 (100.0%)</td>
<td>0 (0.0%)</td>
<td>14 (26.4%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Tranquilizer use, n (%)</td>
<td>3 (1.2%)</td>
<td>0 (0.0%)</td>
<td>3 (1.6%)</td>
<td>0 (0.0%)</td>
<td>0.603</td>
</tr>
<tr>
<td>Antiepileptic use, n (%)</td>
<td>12 (4.8%)</td>
<td>2 (22.2%)</td>
<td>6 (3.2%)</td>
<td>4 (7.5%)</td>
<td>0.020</td>
</tr>
<tr>
<td>Antidepressant use, n (%)</td>
<td>14 (5.6%)</td>
<td>2 (22.2%)</td>
<td>9 (4.8%)</td>
<td>3 (5.7%)</td>
<td>0.088</td>
</tr>
<tr>
<td>Steroid use, n (%)</td>
<td>73 (29.4%)</td>
<td>3 (33.3%)</td>
<td>60 (32.3%)</td>
<td>10 (18.9%)</td>
<td>0.163</td>
</tr>
<tr>
<td>Disease assessment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Physician Global Assessment (PGA) (0-10), mean (SD)</td>
<td>2.7 (2.3)</td>
<td>4.4 (1.6)</td>
<td>2.3 (2.2)</td>
<td>3.8 (2.4)</td>
<td></td>
</tr>
<tr>
<td>Patient Global Assessment (PtGA) (0-10), mean (SD)</td>
<td>3.2 (2.7)</td>
<td>4.5 (2.5)</td>
<td>2.9 (2.6)</td>
<td>3.9 (2.8)</td>
<td>0.021</td>
</tr>
<tr>
<td>Pain, VAS cm, mean (SD)</td>
<td>4.0 (2.9)</td>
<td>6.6 (2.0)</td>
<td>3.7 (2.7)</td>
<td>4.9 (3.1)</td>
<td>0.001</td>
</tr>
<tr>
<td>Cigarette use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Past cigarette use n (%)</td>
<td>145 (58.5%)</td>
<td>9 (100.0%)</td>
<td>89 (47.8%)</td>
<td>47 (88.7%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Years, mean (SD)$^2$</td>
<td>26.5 (13.6)</td>
<td>40.0 (13.2)</td>
<td>21.9 (11.4)</td>
<td>32.5 (13.5)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Cigarettes/day, mean (SD)$^2$</td>
<td>15.3 (8.0)</td>
<td>21.1 (12.4)</td>
<td>15.6 (7.7)</td>
<td>13.6 (7.1)</td>
<td>0.042</td>
</tr>
<tr>
<td>Current cigarette use n (%)</td>
<td>46 (18.7%)</td>
<td>9 (100.0%)</td>
<td>0 (0.0%)</td>
<td>37 (72.5%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Cigarettes/day, mean (SD)$^2$</td>
<td>13.2 (9.7)</td>
<td>20.1 (12.9)</td>
<td>NA</td>
<td>11.5 (8.1)</td>
<td>0.015</td>
</tr>
<tr>
<td>Herbal cannabis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recreational herbal cannabis</td>
<td>Ever use, n (%)</td>
<td>35 (14.2%)</td>
<td>3 (33.3%)</td>
<td>22 (11.9%)</td>
<td>10 (19.2%)</td>
</tr>
</tbody>
</table>
Table 1. Patient Profile by Smoking Status and Opioid Use

<table>
<thead>
<tr>
<th>use</th>
<th>use</th>
<th>Current use, n (%)</th>
<th>All patients (N=248)</th>
<th>Current smokers &amp; opioid users (n = 9)</th>
<th>Non-smokers &amp; non-opioid users (n = 186)</th>
<th>Current smokers or opioid users (n = 53)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Current use, n (%)</td>
<td>3 (8.6%)</td>
<td>0 (0.0%)</td>
<td>3 (13.6%)</td>
<td>0 (0.0%)</td>
<td>0.379</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ever use, n (%)</td>
<td>4 (1.6%)</td>
<td>0 (0.0%)</td>
<td>2 (1.1%)</td>
<td>2 (3.8%)</td>
<td>0.363</td>
</tr>
<tr>
<td></td>
<td></td>
<td>More than 10 times, n (%)</td>
<td>2 (50.0%)</td>
<td>NA</td>
<td>1 (50.0%)</td>
<td>1 (50.0%)</td>
<td>&gt; 0.999</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Current medical use, n (%)</td>
<td>2 (50.0%)</td>
<td>NA</td>
<td>1 (50.0%)</td>
<td>1 (50.0%)</td>
<td>&gt; 0.999</td>
</tr>
<tr>
<td></td>
<td></td>
<td>If never used, consider medical herbal cannabis use, n (%)</td>
<td>75 (36.2%)</td>
<td>6 (75.0%)</td>
<td>52 (33.5%)</td>
<td>17 (38.6%)</td>
<td>0.055</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Current medical cannabis use</td>
<td>4 (11.1%)</td>
<td>0 (0.0%)</td>
<td>3 (13.6%)</td>
<td>1 (9.1%)</td>
<td>0.755</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Daily grams used, mean (SD)</td>
<td>2.0 (2.8)</td>
<td>NA</td>
<td>2.0 (2.8)</td>
<td>NA</td>
<td>0.667</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Monthly grams used, mean (SD)</td>
<td>38.0 (64.1)</td>
<td>NA</td>
<td>38.0 (64.1)</td>
<td>NA</td>
<td>0.667</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Method of herbal cannabis use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Smoke, n (%)</td>
<td>4 (100.0%)</td>
<td>NA</td>
<td>3 (100.0%)</td>
<td>1 (100.0%)</td>
<td>NC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vaporize, n (%)</td>
<td>1 (25.0%)</td>
<td>NA</td>
<td>1 (33.3%)</td>
<td>0 (0.0%)</td>
<td>&gt; 0.999</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Eat, n (%)</td>
<td>1 (25.0%)</td>
<td>NA</td>
<td>1 (33.3%)</td>
<td>0 (0.0%)</td>
<td>&gt; 0.999</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rub, n (%)</td>
<td>0 (0.0%)</td>
<td>NA</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>NC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Relief of symptoms, mean (0-10) (SD)</td>
<td>6.6 (1.6)</td>
<td>NA</td>
<td>7.7 (NC)</td>
<td>5.5 (NC)</td>
<td>NC</td>
</tr>
</tbody>
</table>

NA, not applicable; NC, non calculable.

Significant (p<0.05) p-values indicated in bold. Statistical trends (0.05 < p < 0.15) indicated in italics.

1Between unemployed/disabled and full-time/part-time/student/retired/homemaker patients.

2Among smokers.

3Patients may have used more than one method of herbal cannabis.

4Denominator of this proportion represents the total number of patients who have used herbal cannabis for medical reasons (n=2).

5Denominator of this proportion represents the total number of patients who have never used herbal cannabis for medical reasons (n=212).

6Patient reported no daily amount of herbal cannabis, though reported ‘1 gram’ as monthly usage. This was omitted from the description of the results.

7Proportions and p-values are based on the number of patients currently using herbal cannabis for any reason (All patients: n=4; Current smokers and opioid users: n=0; Non-smokers and non-opioid users: n=3; Current smokers or opioid users: n=1).

8Among patients using herbal cannabis for medical reasons. Minimum (0) represents ‘no relief’ and maximum (10) represents ‘maximum relief’.

Disclosure: A. Karellis, None; E. Rampakakis, None; J. S. Sampalis, None; M. Cohen, None; M. Starr, None; P. Ste-Marie, None; Y. Shir, None; M. Ware, None; M. FitzCharles, None.
Initiation of Biologic Disease Modifying Antirheumatic Drug Therapy and Associated Changes in Disease Activity Measures in Routine Clinical Practice: Findings from a Large Contemporaneous Real World Cohort

Zhaohui Su¹, Tom Brecht¹, Anna Lafontant¹, Costas Boussios¹, Francis O’Donovan², Charles Kekeh², Kathryn Starzyk¹, Richard Gliklich³ and Vandana Menon¹
¹Research, OM1, Inc, Cambridge, MA, ²Data Science, OM1, Inc, Cambridge, MA, ³OM1, Inc, Cambridge, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
While many clinical trials provide direct comparisons between biologic disease modifying antirheumatic drugs (bDMARD) and nonbiologic DMARD (nDMARD), there is a need for additional evidence on the effectiveness of these therapies in routine clinical practice. We evaluated changes in disease activity measures associated with bDMARD therapy, in a large cohort of patients with RA, under conditions of routine clinical practice.

Methods:
The OM1 platform collects, links, and leverages, structured and unstructured data from electronic medical records (EMR) and other sources in an ongoing and continuously updating manner. The OM1 RA Cohort includes data on >75,000 patients treated by rheumatologists. This analysis included patients who were treated with nDMARD between January 2013 and April 2017, had not received prior treatment with bDMARD, and either added or switched to another nDMARD or initiated bDMARD during the observation period (date of change in therapy is the index date). Established American College of Rheumatology cutpoints for standard disease activity measures (RAPID-3, CDAI, DAS28) were used to define remission. Advanced natural language processing was used to impute missing disease activity categories. Drug eras were defined using Observational Medical Outcomes Partnership (OMOP) definitions. Survival analyses were conducted to evaluate time to initial remission and confirmed remission defined as 2 consecutive scores denoting remission. To reduce the impact of subsequent treatment changes, data were censored at 12 months. Patients who switched or added nDMARD but subsequently initiated bDMARDs within 6 months after the index date were excluded in sensitivity analyses. To reduce the bias that more frequent disease activity measures may be associated with shorter time to remission, we matched the two groups on average number of disease activity measures per patient.

Results: The analysis cohort included 4,957 patients who met study inclusion criteria, none of whom were in remission at index date; 1,334 added or switched to another nDMARD and 3,623 added or switched to a bDMARD. There were an average of 4.2 disease activity measures per patient and a total of 20,605 disease activity measures during the 12 month study period. A larger proportion of patients in the bDMARD group achieved initial remission (18% versus 16%, p<0.05) and confirmed remission (13% versus 11%, p<0.05) compared to the nDMARD group. Time to remission was significantly shorter in the bDMARD group (mean±SD=5.2±3.4 months) compared to the nDMARD group (5.7±3.2 months, p<0.05). These results were unchanged in the sensitivity analysis.

Conclusion: Disease activity improved with changes in DMARD therapy; however, the addition of bDMARDs were associated with significantly shorter time to remission. This study uses novel data collection techniques to replicate
findings from prior observational studies in a much larger and contemporaneous cohort of patients under conditions of routine clinical practice.

Disclosure: Z. Su, None; T. Brecht, None; A. Lafontant, None; C. Boussios, None; F. O'Donovan, None; C. Kekeh, None; K. Starzyk, None; R. Gliklich, None; V. Menon, None.

Abstract Number: 469

Effect of Patient Involvement in Treatment Decision Making on Disease Outcomes in Rheumatoid Arthritis in the USA

Richard Hutchings¹, Shailja Panchal² and Elizabeth Baynton¹, ¹Ipsos Healthcare, London, United Kingdom, ²Ipsos Healthcare, New York, NY
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: ACR guidelines for treating Rheumatoid Arthritis (2015) suggest that treatment decisions should be made by physicians and patients through a shared decision-making process taking into account patients’ values, preferences, and comorbidities. Identifying the impact of patient involvement on disease outcomes in biologic patients would provide further evidence which could support ACR guideline recommendations and be used to inform optimal disease management.

Methods: A multi-center medical chart review study of patients with RA was conducted in Q4 2016 among physicians in hospitals and private practices to collect de-identified data on patients who were recently treated with a biologic as part of usual care in the USA. Physicians were screened for duration of practice (3-30yrs) and patient volume (≥2 RA biologic patients/week) and recruited from a large access panel to be geographically representative of the country. Eligible patient charts (≥5) were randomly selected from among the patients visiting each center/practice during the screening period. Physicians abstracted date of diagnosis, treatment patterns/dynamics, and symptomatology/disease status. Physicians identified the level of patient involvement in treatment decision making using a 7 point scale, and patient records were segmented into low-medium involvement (1-4/7) and high involvement (5-7/7). Sites waived local ethics review owing to collection of retrospective de-identified data. High involvement versus low involvement patients were compared using descriptive statistics.

Results: 517 biologic RA patients were assessed; overall, Highly involved: 409 (79%), Low-mid involved: 108 (21%). Patient characteristics (Highly involved/Low-mid involved) included: age (in years) 50/54; full time employment status 57%/42%; co-existing conditions: obesity (14%/28%), dyslipidemia (19%/33%), depression (19%/28%), none (45%/24%). Time since diagnosis (in months): 52.2/48.3. Among patients with available data, current lab measures included: ESR(mm/h) 20.3/24.0; CRP(mg/l) 2.8/3.8; rheumatoid factor(positive) 89%/84%; anti-CCP(positive) 80%/72%; measures of disease severity included: disease severity per physician judgment: mild (72%/53%), moderate (25%/40%), severe (3%/7%); disease under control 80%/69%; remission 63%/52%; mean DAS 28 2.7/3.2; mean tender joint count 3.4/3.6; mean swollen joint count 2.3/2.4.

Conclusion: In this cohort of RA patients in the USA, majority of patients with high involvement were seen to be younger, healthier patients who were full time employees. These patients were significantly more likely to be considered as mild disease severity (physician judgement) with a higher proportion in remission. Lab measures indicated lower disease burden
with low hematology scores for highly involved patients. Further investigation of the influence of socioeconomic status, insurance type, and other demographics on patient involvement in treatment may warrant further research.

Disclosure: R. Hutchings, None; S. Panchal, None; E. Baynton, None.


Abstract Number: 470

Clinical Response to the First Biologic in Rheumatoid Arthritis Patients with Moderate Disease in a Real World Clinical Cohort

Xiuying Li, Angela Cesta, Mohammad Movahedi and Claire Bombardier, Toronto General Hospital Research Institute, University Health Network, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

While most randomized trials assess the effectiveness of biologic DMARDs (bDMARDs) in rheumatoid arthritis (RA) patients with high disease activity, in the real world or routine care, patients with moderate disease activity are often treated with bDMARDs as well. This study aims to evaluate the effectiveness of the first biologic with or without conventional synthetic DMARD (csDMARDs) in patients with moderate disease activity.

Methods:

Biologic naïve patients enrolled in the Ontario Best Practices Initiative (OBRI), with moderate disease activity score (DAS28: >3.2-5.1), or high disease activity score (DAS28: >5.1) were included. Patients were also required to remain on the biologic for 6 months and to have complete follow up data during this time period. Clinical response to their first biologic was measured by the change in DAS28 and by the proportion of patients who reached low disease activity (LDA) during the first 6 months of treatment. The change in DAS28 was assessed using linear regression modelling, adjusted for potential confounders (age, gender, disease duration, and physician global assessment). Multivariate logistic regression was used to compare the proportion of patients who reached LDA in each group at 6 months, adjusting for the same potential confounders.

Results:

The analysis included 443 patients. At initiation of their first biologic, 238 patients had a moderate DAS28 and 205 had a high DAS28. Patient demographics for the two groups are shown in Table 1. At initiation of their first bDMARD, the two groups were similar with respect to age, gender, and disease duration. All of the DAS28 components, as well as the physician global were significantly different between the two groups. A significant change in DAS28 was found in both the moderate disease group [-0.89 (95% CI -1.12, -0.66)] and the high disease group [-1.86 (95% CI -2.10, -1.62)], with greater improvement seen in the high disease activity group. A comparison of the change in DAS28 between the two groups was also significant (0.97±0.16, p<0.0001). After 6 months of biologic treatment, a higher proportion of patients in the moderate DAS28 group reached LDA, when compared to the high DAS28 group (OR: 1.65; 95%CI: 1.03-2.65, p=0.04).

Table 1. Patient Characteristics at initiation of first bDMARD, by DAS28 group
<table>
<thead>
<tr>
<th>DAS28 group at bDMARDs start</th>
<th>Moderate DAS28 3.2-5.1</th>
<th>High DAS28 &gt;5.1</th>
<th>P - value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>238</td>
<td>205</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>55.3 (13.2)</td>
<td>57.1 (12.9)</td>
<td>0.14</td>
</tr>
<tr>
<td>Female n(%)</td>
<td>192 (80.7%)</td>
<td>169 (82.4%)</td>
<td>0.63</td>
</tr>
<tr>
<td>Disease duration, years</td>
<td>7.4 (8.8)</td>
<td>6.7 (7.6)</td>
<td>0.36</td>
</tr>
<tr>
<td>DAS28</td>
<td>4.18 (0.54)</td>
<td>5.98 (0.63)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>28 swollen joint count</td>
<td>5.4 (3.7)</td>
<td>9.1 (4.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>28 tender joint count</td>
<td>4.5 (3.5)</td>
<td>12.4 (5.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ESR, mm/h</td>
<td>19.1 (16.5)</td>
<td>34.3 (22.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CRP, mg/L</td>
<td>8.7 (15.4)</td>
<td>17.7 (24.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Patient global assessment (0-10)</td>
<td>5.0 (2.5)</td>
<td>6.7 (2.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Physician global assessment (0-10)</td>
<td>4.6 (2.0)</td>
<td>6.3 (1.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Rheumatoid factor positive n (%)</td>
<td>160 (72.7%)</td>
<td>143 (75.7%)</td>
<td>0.50</td>
</tr>
<tr>
<td>Previous CsDMARDs use ≥2 n(%)</td>
<td>213 (90%)</td>
<td>182 (89%)</td>
<td>0.81</td>
</tr>
<tr>
<td>Receiving oral steroid, n (%)</td>
<td>50 (21.0%)</td>
<td>37 (18.1%)</td>
<td>0.43</td>
</tr>
</tbody>
</table>

Values are given as mean (standard deviation) unless otherwise specified.

**Conclusion:**

**Conclusions:** Treatment with bDMARDs is effective in patients with moderate disease activity. While patients with high disease activity showed greater improvement after 6 months of biologic treatment, patients with moderate disease activity at initiation of a bDMARD were more likely to reach a LDA state.

**Disclosure:** X. Li, None; A. Cesta, None; M. Movahedi, None; C. Bombardier, Canada Research Chair in Knowledge Transfer for Musculoskeletal Care Non-remunerativePfizer Research Chair in Rheumatology, 6.


**Abstract Number:** 471

**Rheumatoid Arthritis Patients Resistant to Biologic Therapy, Are They Different?**

**Adeeba Al-Herz**1, Aqeel Ghanem2, Khulood Saleh3, Adel Al-Awadhi4, Waleed Al-Kandari3, Eman Hasan5, Mohammad Hussain5, Ibrahim Nahar2, Fatemah Abutiban6, Ahmad Alenizi6, Yaser Ali2, Ali Aldei1, Hebah Alhajeri2, Sawsan Hayat2, Ahmad Khadrawy3, Ammad Fazar3, Khaled Mokaddem1, Agaz Zamar2, Ghada Mazloum2, Youssef Bartella1, Sally Hamed1, Ramia Alsouk6 and Ahmed Al-Saber7, 1Rheumatology, Al-Amiri Hospital, Kuwait city, Kuwait, 2Rheumatology, Mubarak Al-Kabeer Hospital, Hawally, Kuwait, 3Rheumatology, Farwania Hospital, Farwania, Kuwait, 4Faculty of Medicine, Kuwait, Kuwait, 5Al-Amiri Hospital, Kuwait city, Kuwait, 6Rheumatology, Jahra Hospital, Jahra, Kuwait, 7Department of Mathematics, Kuwait Technical College, Kuwait city, Kuwait

**First publication:** September 18, 2017
Background/Purpose: Patients with rheumatoid arthritis (RA) may fail to respond to biologic therapy. We study patients who are resistant to different classes of biologic agents and compare their clinical and serological features to patients who are biologic respondents.

Methods: Patient from The Kuwait Registry for Rheumatic Diseases (KRRD) who satisfied the ACR classification criteria for RA from four major hospitals were studied from February 2013 through May 2017. Patients were divided into two main groups, biologic therapy resistant defined as patients previously switched from a biologic agent or who are currently not responding to biologic therapy (DAS28 > 3.2). The second group are patients who are biologic therapy respondents defined as patients who have been in remission or in low disease activity (DAS28 < 3.2) on biologics for at least three months with no previous history of any biologic resistance.

Biologic agents were then divided into anti-TNF and non-anti-TNF agents.

In addition, patients who were resistant to >3 biologics were further studied.

Results: Among 1,280 patients with RA, 318(24%) have been prescribed at least one anti-TNF agent sometime during their disease course. Among them, 194(61%) were resistant to one anti-TNF or more. 554(43%) were prescribed at least one non-anti-TNF. Among them, 313(56%) were resistant to one non-anti-TNF or more. Of the total resistant patient, 29/507(5.7%) have failed 3 or more biologics.

Comparing the anti-TNF resistant group with the anti-TNF respondents, there was a tendency toward a thyroid disease (15.5% vs 8.1%, p= 0.051) and a lower serum uric acid (means=263 vs 283 µmol/L, p=0.06). Patients who were resistant to non-anti-TNFs had more females than patients who responded to non-anti-TNFs (78% vs 68.5%, p= 0.012) and a lower uric acid (means=249 vs 267µmol/L, p=0.012). Comparing patients who were resistant to > 3 biologics with patients who are biologic respondents, resistant patients had more females (93.1% vs 69.4%, p=0.007), more hyperlipidemia (24.1% vs 9.5, p=0.014), more hypertension (41.4% vs 21.4%, p=0.014) and more osteoporosis (24.1 vs 10.4%, p=0.026).

Other factors such as age, age at RA diagnosis, body mass index, rheumatoid factor, anti-cyclic citrullinated peptide antibodies, ANA, extra-articular features, family history of a rheumatic disease and other co-morbidities including cardiovascular diseases were comparable between the groups.

Conclusion: RA patients resistant to biologic therapy have some features that are different from patients who are respondents. Further study of those patients may allow an early recognition aiming at a better planning of treatment and improving their outcome.

Disclosure: A. Al-Herz, None; A. Ghanem, None; K. Saleh, None; A. Al-Awadhi, None; W. Al-Kandari, None; E. Hasan, None; M. Hussain, None; I. Nahar, None; F. Abutiban, None; A. Alenizi, None; Y. Ali, None; A. Aldei, None; H. Alhajeri, None; S. Hayat, None; A. Khadrawy, None; A. Fazal, None; K. Mokaddem, None; A. Zaman, None; G. Mazloum, None; Y. Bartella, None; S. Hamed, None; R. Alsouk, None; A. Al-Saber, None.
Suraj Timilsina1, Harlan Sayles2, Bryant R. England3, James R. O'Dell4, Ted R. Mikuls5 and Kaleb Michaud2, 1Division of Rheumatology & Immunology, Department of Internal Medicine, University of Nebraska Medical Center, Omaha, NE, 2University of Nebraska Medical Center, Omaha, NE, 3Division of Rheumatology & Immunology, Department of Internal Medicine, Nebraska-Western IA VA Health Care System & University of Nebraska Medical Center, Omaha, NE, 4Department of Internal Medicine, University of Nebraska Medical Center, Omaha, NE, 5Internal Medicine, Division of Rheumatology, University of Nebraska Medical Center, Omaha, NE

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Viral hepatitis may complicate the treatment of RA since select DMARD have the potential to cause hepatotoxicity or reactivation of latent viral infections. Whether treatment patterns and RA outcomes are impacted by this comorbid condition is not well studied. Similarly, little is known about RA factors and the risk the developing of hepatitis. Thus, we assessed the associations of viral hepatitis with RA disease outcomes and DMARD use and determined the RA factors predictive of incident hepatitis.

Methods: We studied participants with RA within the National Data Bank for Rheumatic Diseases (NDB) from 2004 to 2017. Sociodemographic, health behaviors, comorbidities, RA measures, and medications were collected every 6 months via self-report. Additionally, participants were assessed for current or prior history of viral hepatitis. We used multivariable linear and logistic regression models to assess associations of prior viral hepatitis with RA outcome measures and treatments. We also assessed the associations of RA measures and DMARD with incident viral hepatitis using multivariable Cox proportional hazard regression models.

Results: Among 22,942 participants with RA, current or prior hepatitis was self-reported present in 207 (Hepatitis A), 165 (Hepatitis B), and 317 (Hepatitis C). Adjusting for age, sex, employment, education level, comorbidity index, smoking, alcohol and drug use, patients with prior hepatitis B and C had higher pain scores while patients with hepatitis C had higher patient activity scale (PAS) scores. Hepatitis C was also marginally associated with higher patient global assessment scores. MTX use was less frequent in those with hepatitis B and C while the use of NSAIDs and biologics did not differ between groups (Table 1). Over 90,952 patient-years of follow-up, 132 patients developed incident viral hepatitis. After multivariable adjustment, higher pain and PAS scores were independently associated with an increased risk of viral hepatitis (Table 2). Biologics were not associated with incident viral hepatitis while MTX was associated with a lower risk of incident hepatitis. To assess whether misclassification of prevalent hepatitis as incident hepatitis was occurring, we used a 6-month lag for viral hepatitis diagnosis, finding similar results.

Conclusion: History of viral hepatitis infection is associated with worse RA patient reported outcomes measures and lower use of MTX. Clinicians should be aware of the potential for viral hepatitis to influence patient reported outcomes measures in RA. Reassuringly, biologic DMARD do not appear to increase the risk of incident viral hepatitis.
### Table 1: Association of viral hepatitis with RA outcomes and treatment

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Hepatitis A</th>
<th>Hepatitis B</th>
<th>Hepatitis C</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Linear regression</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HAQ</td>
<td>0.01 (-0.09, 0.11)</td>
<td>0.02 (-0.84, 0.13)</td>
<td>0.05 (-0.03, 0.12)</td>
</tr>
<tr>
<td>Pain scale</td>
<td>-0.02 (-0.40, 0.36)</td>
<td>0.59 (0.18, 1.01)*</td>
<td>0.48 (0.18, 0.79)*</td>
</tr>
<tr>
<td>Patient global</td>
<td>0.01 (-0.31, 0.34)</td>
<td>0.26 (-0.12, 0.63)</td>
<td>0.28 (-0.05, 0.56)</td>
</tr>
<tr>
<td>Patient activity score</td>
<td>0.01 (-0.28, 0.29)</td>
<td>0.31 (-0.07, 0.62)</td>
<td>0.30 (0.06, 0.55)*</td>
</tr>
<tr>
<td>SF-36 Physical Summary</td>
<td>-0.17 (-1.60, 1.26)</td>
<td>-1.23 (-2.96, 0.49)</td>
<td>-0.58 (-1.88, 0.71)</td>
</tr>
<tr>
<td>SF-36 Mental Summary</td>
<td>-1.37 (-3.25, 0.51)</td>
<td>-0.92 (-3.03, 1.20)</td>
<td>-0.93 (-2.32, 0.47)</td>
</tr>
<tr>
<td><strong>Logistic regression</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methotrexate</td>
<td>0.83 (0.63, 1.10)</td>
<td>0.42 (0.30, 0.59)*</td>
<td>0.60 (0.47, 0.76)*</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>0.83 (0.51, 1.35)</td>
<td>0.64 (0.34, 1.81)</td>
<td>0.87 (0.59, 1.29)</td>
</tr>
<tr>
<td>Biologic</td>
<td>1.02 (0.77, 1.34)</td>
<td>0.90 (0.65, 1.23)</td>
<td>0.95 (0.75, 1.19)</td>
</tr>
<tr>
<td>Any NSAID</td>
<td>0.93 (0.70, 1.23)</td>
<td>0.84 (0.61, 1.16)</td>
<td>0.99 (0.79, 1.25)</td>
</tr>
<tr>
<td>Prednisone</td>
<td>1.11 (0.82, 1.50)</td>
<td>0.58 (0.40, 0.84)*</td>
<td>0.93 (0.72, 1.20)</td>
</tr>
</tbody>
</table>

Values β or Odds ratio (95%CI)

* p <0.05

Parameters assessed in separate models, each adjusted for age, sex, employment, education level, comorbidity index, smoking, alcohol and drug use
Table 2: Association of RA measures and treatments with incident viral hepatitis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard Ratio</th>
<th>95%CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA disease duration (years)</td>
<td>1.00</td>
<td>0.98, 1.01</td>
<td>0.578</td>
</tr>
<tr>
<td>HAQ</td>
<td>1.12</td>
<td>0.88, 1.41</td>
<td>0.356</td>
</tr>
<tr>
<td>Pain scale (0-10)</td>
<td>1.06</td>
<td>1.00, 1.13</td>
<td>0.039</td>
</tr>
<tr>
<td>Patient global (0-10)</td>
<td>1.05</td>
<td>0.98, 1.12</td>
<td>0.115</td>
</tr>
<tr>
<td>Patient activity score (0-10)</td>
<td>1.07</td>
<td>1.00, 1.15</td>
<td>0.046</td>
</tr>
<tr>
<td>SF-36 Physical summary</td>
<td>0.98</td>
<td>0.95, 0.99</td>
<td>0.022</td>
</tr>
<tr>
<td>SF-36 Mental summary</td>
<td>0.98</td>
<td>0.96, 0.99</td>
<td>0.040</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>0.58</td>
<td>0.40, 0.83</td>
<td>0.003</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>1.05</td>
<td>0.61, 1.79</td>
<td>0.728</td>
</tr>
<tr>
<td>Biologic</td>
<td>0.93</td>
<td>0.66, 1.31</td>
<td>0.693</td>
</tr>
<tr>
<td>Any NSAID</td>
<td>1.25</td>
<td>0.89, 1.77</td>
<td>0.193</td>
</tr>
<tr>
<td>Prednisone</td>
<td>1.34</td>
<td>0.93, 1.93</td>
<td>0.109</td>
</tr>
</tbody>
</table>

Parameters assessed in separate models, each adjusted for age, sex, employment, education level, comorbidity index, smoking, alcohol and drug use.

Disclosure: S. Timilsina, None; H. Sayles, None; B. R. England, None; J. R. O'Dell, Medac, 5,Coherus, 5; T. R. Mikuls, BMS, 2,Ironwood Pharm, 2,Pfizer Inc, 5,NIH, VA, 2; K. Michaud, None.


Abstract Number: 473

Medication Utilization Patterns of Rheumatoid Arthritis Patients Receiving Anti-TNF Infusion in Community Rheumatology Practices in the United States: Will Differences in Dosing and Administration Efficiencies between Intravenous Golimumab and Infliximab Have a Cost Impact for Payers?

Sergio Schwartzman¹, Lorie A. Ellis², Dennis Parenti³, Shawn Black³, Stephen Xu⁴, Wayne Langholf⁵ and Shelly Kafka³, ¹Weill Cornell Medical College, New York, NY, ²Janssen HECOR Immunology, Horsham, PA, ³Janssen Scientific Affairs, LLC, Horsham, PA, ⁴Janssen Research & Development, LLC, Spring House, PA
SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: AWARE (Comparative and Pragmatic Study of Golimumab IV Versus Infliximab in Rheumatoid Arthritis) is an ongoing Phase 4 comparator study designed to provide a real-world assessment of intravenous golimumab (GLM) and infliximab (IFX) in patients (pts) with rheumatoid arthritis (RA). Although the primary objective of AWARE is to compare the proportion of GLM and IFX pts with an infusion reaction, RA medication utilization patterns and biologic infusion times are collected for purposes of conducting dosing and cost analyses. Although cost and managed care coverage are frequently cited by practicing rheumatologists as variables involved in therapeutic choices, data is lacking in the published literature. Here we report on GLM and IFX drug utilization patterns from an interim analysis (IA) of the ongoing AWARE study.

Methods: AWARE is a prospective, noninterventional, observational, multicenter 3-year study conducted at 100 sites in the US. RA pts (1,200 adults) will be enrolled at the time of initiating treatment with either GLM or IFX. All treatment decisions including prescribed dose, administered drug amount and dosing interval are made at the discretion of the treating rheumatologist. Infusion duration was reported by the site. Data shown are mean ± standard deviation.

Results: 421 GLM pts and 326 IFX pts were included in the IA. GLM pts were 61.0 ±12.97 years and IFX pts were 57.2 ±13.02 years. Body weight of GLM pts was 85.3 ± 24.6 kg and body weight of IFX pts was 85.5 ± 23.3kg. BMI of GLM pts was 32.2 ± 13.4 kg/m² and BMI of IFX pts was 31.7 ± 9.5 kg/m². Of GLM pts, 34.7% were bionaïve and 49.7% of IFX pts were bionaïve. The % of GLM and IFX pts with prior exposure to 1 or 2 biologics was similar (data not shown), however exposure to ≥3 biologics was 19.2% of GLM pts compared to 9.8% of IFX pts. GLM and IFX were infused at a rheumatologist practice (95.0% and 96.3%, respectively). GLM pts received 1434 infusions at 2.00 ± 0.08 mg/kg, and IFX pts received 1328 infusions at 3.71 ± 1.21 mg/kg. The duration of GLM infusions was 0.65 ± 0.23 hours and IFX infusions was 2.0 ± 0.46 hours. There was a significant (p<0.0001) difference in the % of pts with a reported dose increase from baseline between GLM and IFX (2.6% vs 32.2%, respectively).

Conclusion: This IA of the AWARE study, reported on drug and administration utilization characteristics of GLM and IFX. While the dose of GLM was not reported to change over the course of the first 7 infusions, among pts with 7 infusions the mean dose of IFX increased by approximately 152% between the first and seventh dose. IFX dose escalation was evident at the third dose. These data provide evidence that in a real-world rheumatology practice setting, the dose of GLM remains
constant, whereas the dose of IFX is more variable and the mean infusion time of GLM was consistently shorter compared to IFX. The AWARE study will utilize these data to assess the relative cost effectiveness of GLM relative to IFX.

Disclosure: S. Schwartzman, AbbVie, Antares, Genentech, Janssen, Lilly, Novartis, Pfizer, Regeneron, Sanofi, UCB, 5,AbbVie, Janssen, Genentech, Pfizer, UCB, Crescendo, Novartis, 8,Crescendo Biosciences, Discus Analytics, National Psoriasis Foundation, 6; L. A. Ellis, Janssen, 3,Johnson & Johnson, LLC, 1; D. Parenti, Janssen, 3,Johnson & Johnson, LLC, 1; S. Black, Janssen, 3,Johnson & Johnson, LLC, 1; S. Xu, Janssen, 3,Johnson & Johnson, LLC, 1; W. Langhoff, Janssen, 3,Johnson & Johnson, LLC, 1; S. Kafka, Janssen, 3,Johnson & Johnson, LLC, 1.

Abstract Number: 474

Comparison of Tofacitinib Efficacy in Patients with Moderate Vs Severe Rheumatoid Arthritis: Pooled Analysis of Phase 3 Studies

Sergio Schwartzman1, Prashanth Sunkureddi2, Liza Takiya3, Mark Snyder3, Haiyun Fan4, Tatjana Lukic5, Jacqui Roberts6 and William F C Rigby7, 1Hospital for Special Surgery, New York, NY, 2Clear Lake Rheumatology, Nassau Bay, TX, 3Pfizer Inc, Collegeville, PA, 4Pfizer Inc, Groton, CT, 5Pfizer Inc, New York, NY, 6Pfizer Inc, Tadworth, United Kingdom, 7Geisel School of Medicine at Dartmouth, Lebanon, NH

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). We evaluated tofacitinib 5 and 10 mg twice daily (BID) efficacy in patients (pts) with moderate vs severe RA.

Methods: Tofacitinib 5 and 10 mg BID efficacy data were from 6 randomized, double-blind Phase 3 studies of 6–24 months’ (Mos) duration. Pts received tofacitinib as monotherapy (NCT00814307 ORAL Solo; NCT01039688 ORAL Start) or with csDMARDs, mainly MTX (NCT00960440 ORAL Step; NCT00847613 ORAL Scan; NCT00856544 ORAL Sync; NCT00853385 ORAL Standard). Pts receiving MTX monotherapy (ORAL Start) or placebo (PBO) (±csDMARDs) were combined as a single PBO group. Baseline (BL) disease severity was classified as moderate or severe using Disease Activity Score in 28 joints, erythrocyte sedimentation rate (DAS28: moderate 3.2–≤5.1; severe >5.1) and Clinical Disease Activity Index (CDAI; moderate 10–≤22; severe =22). Mo 3 efficacy outcomes included: pts (%) achieving low disease activity (LDA; DAS28≤3.2, CDAI ≤10), remission (REM; DAS28<2.6, CDAI ≤2.8), HAQ-DI <0.5 (normal physical functioning), HAQ-DI improvement >0.22, and mean change from BL (Δ) in DAS28, CDAI, and HAQ-DI. This post-hoc analysis had no multiplicity adjustments.

Results: More pts had severe disease at BL by DAS28 (91.8%) and CDAI (90.7%). Mo 3 efficacy outcomes for pts were classified by BL DAS28 disease severity (Table). BL characteristics were balanced between treatment groups in each disease severity category (Table). In general, Mo 3 efficacy was significantly greater for tofacitinib 5 and 10 mg BID vs PBO, regardless of BL disease severity. Larger proportions of tofacitinib-treated pts with moderate vs severe BL RA achieved LDA by either DAS28 (32.3–36.7% vs 13.8–19.1%) or CDAI (49.2–55.0% vs 26.0–31.7%). A higher proportion of pts achieved REM in the moderate vs severe BL groups by DAS28 (20.0–22.8% vs 6.2–9.0%) or CDAI (11.5–12.1% vs 5.1–6.7%). A greater proportion of pts achieved HAQ-DI <0.5 with moderate vs severe RA classified by BL DAS28 (45.0–
60.6% vs 24.5–30.0%) or BL CDAI (40.8–52.4% vs 24.7–30.4%). Pts with severe vs moderate RA had greater improvements from BL in disease activity and HAQ-DI when classified by BL DAS28 (Table), and by BL CDAI (tofacitinib 5/10 mg BID ΔCDAI: -21.1/-23.0 vs -8.1/-9.4; ΔHAQ-DI: -0.5/-0.6 vs -0.3/-0.4).

**Conclusion:** Tofacitinib 5 and 10 mg BID demonstrated efficacy in treating pts with moderate and severe RA with >7 years’ mean disease duration. By Mo 3, pts with severe vs moderate BL disease activity had greater improvements in disease activity and physical functioning; higher proportions of pts with moderate vs severe BL disease activity achieved REM, LDA, or normal physical functioning. This post-hoc analysis may be limited by the smaller sample size of the moderate disease group and the combining of mono- and combination-therapy results.

**Table. Baseline Disease Characteristics (A) and Month 3 Efficacy Outcomes (B) by Baseline Disease Severity Assessment using DAS28**

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Moderate (3.2 to ≤5.1)</th>
<th>Severe (&gt;5.1)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tofacitinib 5 mg BID</td>
<td>Tofacitinib 10 mg BID</td>
</tr>
<tr>
<td></td>
<td>N=120</td>
<td>N=127</td>
</tr>
<tr>
<td>Disease duration, years</td>
<td>7.1 (7.6)</td>
<td>7.7 (9.2)</td>
</tr>
<tr>
<td>CDAI</td>
<td>20.7 (6.2)</td>
<td>19.5 (5.4)</td>
</tr>
<tr>
<td>DAS28</td>
<td>4.6 (0.5)</td>
<td>4.7 (0.4)</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>1.0 (0.7)</td>
<td>0.8 (0.7)</td>
</tr>
</tbody>
</table>

**B) Month 3 efficacy outcomes**

- **Remission (DAS28=2.6), % (CI):**
  - Moderate: 20.0* (14.9, 31.5) vs 22.8** (18.3, 35.3)
  - Severe: 36.7*** (31.7, 51.1) vs 32.3*** (28.0, 46.6)
- **LDA (DAS28<3.2), % (CI):**
  - Moderate: 45.0 (35.9, 54.4) vs 60.6*** (51.6, 69.2)
  - Severe: 50.8* (41.6, 60.1) vs 55.9** (46.8, 64.7)
- **HAQ-DI improvement ≥0.22, % (CI):**
  - Moderate: 50.8* (41.6, 60.1) vs 55.9** (46.8, 64.7)
  - Severe: 50.7 (47.6, 54.8)
- **ΔDAS28, LSM (CI):**
  - Moderate: -1.1*** (-1.4, -0.9) vs -1.3*** (-1.6, -1.1)
  - Severe: -1.1*** (-1.4, -0.9) vs -1.3*** (-1.6, -1.1)
- **ΔHAQ-DI, LSM (CI):**
  - Moderate: -0.3*** (-0.4, -0.3) vs -0.4*** (-0.5, -0.3)
  - Severe: -0.3*** (-0.4, -0.3) vs -0.4*** (-0.5, -0.3)

* p<0.05; ** p<0.01; *** p<0.001 vs placebo

Disclosure: S. Schwartzman, AbbVie, Antares, Eli Lilly, Genentech, Janssen, Novartis, Pfizer Inc, Regeneron, Sanofi, UCB, 5,Crescendo Bioscience, Discus Analytics, National Psoriasis Foundation, 6,AbbVie, Crescendo Bioscience, Genentech, Janssen, Pfizer Inc, UCB, 8; P. Sunkureddi, Pfizer Inc, 5,Pfizer Inc, 8; L. Takiya, Pfizer Inc, 1,Pfizer Inc, 3; M. Snyder, Pfizer Inc, 1,Pfizer Inc, 3; H. Fan, Pfizer Inc, 1,Pfizer Inc, 3; T. Lukic, Pfizer Inc, 1,Pfizer Inc, 3; J. Roberts, Pfizer Inc, 1,Pfizer Inc, 3; W. F. C. Rigby, Amgen, Pfizer Inc, Roche, 2,Bristol-Myers Squibb, Eli Lilly, Pfizer Inc, Roche, 5.


**Abstract Number: 475**
Rheumatoid Arthritis Patient Characteristics Also Predict Response to Therapy with Biologic Agents: Results from the Corrona Certain Study

Dimitrios A. Pappas¹, James Murray², Carol J. Etzel¹, David R Nelson², Bernice Gershenson³, Katherine C. Saunders¹, Sabrina Rebello¹ and Joel Kremer⁴, ¹Corrona, LLC, Southborough, MA, ²Eli Lilly and Company, Indianapolis, IN, ³University of Massachusetts Medical School, Worcester, MA, ⁴Albany Medical College and The Center for Rheumatology, Albany, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster I: Treatment Patterns and Response
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Response to biologic agents approved for RA may be associated with patient reported factors that are not related to disease and usually not included in studies attempting to predict response to therapy. The objective was to evaluate whether such factors can influence the probability of response to biologic agents and persistency of therapy.

Methods: Patients with RA initiating a biologic agent while in moderate or high disease activity (based on CDAI levels) were eligible for participation in the Corrona-CERTAIN comparative effectiveness study and were included in the analysis. ENSEMBLE Minimum Data Set (MDS), which is comprised of 10 patient (pt) reported scales not specific to RA, (such as income levels, depression, perceived stress and depression, social support, education) was used to evaluate prediction of response to biologic agents in combination with factors collected in the Corrona registry (“traditional factors”). ENSEMBLE components were measured at time of initiation of biologic. Response to biologic therapy was evaluated at 6 months as achievement of low disease activity (LDA). Persistency was estimated using the Kaplan-Meier method. Associations of response to therapy and persistency with baseline values of ENSEMBLE components were assessed based on logistic and Cox regression, respectively. To determine whether ENSEMBLE components added value to “traditional” disease related factors in predicting response, Akaike information criterion (AIC) and Bayesian information criterion (BIC) were evaluated for the three models: mix of “traditional” and ENSEMBLE variables; traditional variables only; and emphasis of ENSEMBLE over traditional variables. The resulting response and persistency models with lowest AIC and BIC were identified and further evaluated for discriminatory power.

Results: Analysis included 2152 biologic initiations in moderate or high disease activity. At 6 months, 682 patients had achieved LDA (responders) and 1470 had not (non-responders). Of the responders, 58% were treated with a TNF inhibitor and 37% were biologic naïve prior to enrollment in CERTAIN, vs 49% and 30% of non-responders respectively. Of the three response models, the best AIC and BIC values corresponded to the logistic model that emphasized ENSEMBLE over traditional variables and the discriminatory power for this model was comparable (72.6%) to the other two models (72% and 72.5%).% in predicting response to therapy. For time to discontinuation of biologic, the emphasized ENSEMBLE model was again the best in terms of lowest AIC and BIC and discriminatory power (C-statistic) was comparable (60.8% to 59.7% and 61.7%).

Conclusion: The generic, non-disease specific set of scales of ENSEMBLE added value to models predicting response to therapy of RA with biologic agents. Such factors may allow a refined assessment of patient heterogeneity beyond traditionally used disease specific measures and have a similar performance in predicting therapy response and persistency with traditional factors.

Disclosure: D. A. Pappas, Corrona, LLC, 3,Novartis Pharmaceutical Corporation, 9; J. Murray, Eli Lilly and Company, 1,Eli Lilly and Company, 3; C. J. Etzel, Corrona, LLC, 3,Merck Human Health, 9; D. R. Nelson, Eli Lilly and Company, 1,Eli Lilly and Company, 3; B. Gershenson, None; K. C. Saunders, Corrona, LLC, 3; S. Rebello, Corrona, LLC, 3; J. Kremer, Corrona, LLC, 1,Corrona, LLC, 3,AbbVie, Amgen, BMS, Genentech, Lilly, Regeneron, Sanofi, Pfizer, 5,AbbVie, Genentech, Lilly, Novartis, Pfizer, 2.
Novel Interaction between Anti-Citrulline Monoclonal Antibodies and Apoptotic Cells Is Mediated through Citrullinated Nuclear Antigens

Katy A. Lloyd¹, Peter Sahlström², Johanna Steen¹, Philip J. Titcombe³,⁴, Diana Zhou¹, Christina Lundqvist⁵, Olov Ekwall⁶,⁷, Jimmy Ytterberg¹, Johan Rönnelid⁸, Daniel L. Mueller³, Lars Klareskog¹, Vivianne Malmström¹ and Caroline Grönwall⁹,¹¹,¹²
¹Dept. of Medicine, Rheumatology Unit, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, ²Dept. of Medicine, Rheumatology Unit, Karolinska Institutet, Stockholm, Sweden, ³Dept. of Medicine, University of Minnesota Medical School, Minneapolis, MN, ⁴Dept. of Medicine, Rheumatology Unit, Karolinska Institutet, Karolinska University Hospital, Sweden, Sweden, ⁵Dept. of Rheumatology and Inflammation Research, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Göteborg, Sweden, ⁶Dept. of Rheumatology and Inflammation Research, Institute of Medicine, Sahlgrenska Academy University of Gothenburg, Göteborg, Sweden, ⁷Dept of Pediatrics, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Göteborg, Sweden, ⁸Department of Immunology Genetics and Pathology, Uppsala University, Uppsala, Sweden, ⁹Dep. of Medicine, Rheumatology Unit, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden

First publication: September 18, 2017

session information
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Anti-citrullinated protein antibodies (ACPAs) display broad cross-reactivities and target proteins including a-enolase, filaggrin, vimentin, fibrinogen, and histones. However, every monoclonal ACPA has a distinct recognition pattern. Citrullination occurs during physiological processes such as NETosis and apoptosis, yet the interaction of ACPAs with nuclear antigens in apoptotic cells has not been previously investigated. Apoptotic cells, and especially defects in clearance of apoptotic and dead cells resulting in increased exposure to nuclear antigens, have been postulated to play a pivotal role in the pathogenesis of autoimmune disease.

Methods:

We screened a total of 12 recombinant monoclonal human ACPA-IgG, derived from synovial plasma cells or circulating memory B cells, and two control mAb for binding to full-length citrullinated histones by ELISA. Apoptotic cell binding was determined by flow cytometry and Western blotting, followed by mass spectrometry to identify key antigen targets. Fluorescent microscopy was performed to screen ACPA staining in anti-nuclear antibody (ANA)-Hep-2 tests and for binding to human thymus tissue. A total of 210 seropositive and 50 seronegative RA patients and 157 population controls from the EIRA case-control cohort, were screened for IgG reactivity against full-length native and citrullinated histone 2B (Cit-H2B) by ELISA. Reactivity to citrullinated peptides was determined by antigen microarray multiplex assay.

Results:

A distinct subset of ACPAs bound apoptotic cells of human and murine origin. We could also observe nuclear staining for these ACPAs in human thymus tissue, and ANA positivity with a nuclear dense fine speckled staining pattern. Mass spectrometry revealed that H2B was the pre-dominant target within apoptotic cells. The ANA-positive ACPAs had strong recognition of citrullinated histones (H2B, H4). Among CCP2-positive RA patients, 26% were positive for elevated anti-cit-H2B normalized for reactivity to native H2B, and the titer correlated the strongest with binding to citrullinated filaggrin
and fibrinogen peptides (R=0.4, p<0.0001). We also observed a weak correlation with disease activity in seropositive RA (R=0.20, p=0.02). Interestingly, 32% seronegative RA patients had autoreactivity to native H2B compared to 4.5% (p<0.0001) among controls, while there was no elevation in reactivity to cit-H2B normalized for native H2B (4% compared to 4.5% in controls).

Conclusion:

Interactions between ACPA and citrullinated histones facilitate apoptotic cell binding. We hypothesize that this may be a key functional feature in RA pathogenesis.

Disclosure: K. A. Lloyd, None; P. Sahlström, None; J. Steen, None; P. J. Titcombe, None; D. Zhou, None; C. Lundqvist, None; O. Ekwall, None; J. Ytterberg, None; J. Rönnelid, None; D. L. Mueller, None; L. Klareskog, None; V. Malmström, None; C. Grönwall, None.


Monoclonal ACPA-IgG Feature Extensive Fab Glycosylation

Katy A. Lloyd1, Johanna Steen1, Philip J. Titcombe2,3, Khaled Amara4, Diana Zhou1, Lena Israelsson5, Susanna L. Lundström6, Daniel L. Mueller3, Lars Klareskog1, Vivianne Malmström1 and Caroline Grönwall7, 1Dept. of Medicine, Rheumatology Unit, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, 2Dept. of Medicine, Rheumatology Unit, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, 3Dept. of Medicine, University of Minnesota Medical School, Minneapolis, MN, 4Department of Medicine, Rheumatology Unit, Karolinska Institutet, Stockholm, Sweden, 5Dept. of Medicine, Rheumatology Unit, Karolinska Institutet, Stockholm, Sweden, 6Dept. of Medical Biochemistry and Biophysics, Division of Physiological Chemistry, Karolinska Institutet, Stockholm, Sweden, 7Dept. of Medicine, Rheumatology Unit, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Fab-glycosylation is found in ~15-25% serum IgG and while its exact consequence remains unknown, it may alter IgG functionality. Recent data revealed elevated Fab-glycosylation in polyclonal anti-citrullinated protein autoantibodies (ACPA) from rheumatoid arthritis (RA) patients. Herein, we characterize the Fab-glycan profile of monoclonal ACPA.

Methods:

A total of 14 recombinant human ACPA, derived from RA synovial plasma cells or circulating memory, were evaluated for predicted N-linked glycosylation sites using the NetNGlyc server. Fab-glycosylation was verified with enzymatic digestion, Western blot, lectin-ELISA, and mass spectrometry. Antigen binding was investigated by CCP3 ELISA. VH-VL structure models were generated using the PIGS tool and the GlyProt server. The frequency of predicted VH-VL sites was compared to single-cell paired heavy and light chains from extensively mutated mAbs (>15 mutation in VH or VL): 51 expressed non-ACPA synovial B cells from seropos. RA, and 27 from seroneg. RA, and 198 bone marrow (BM) plasma cells, and 27 clones from healthy control circulating memory. These were compared to 19 highly-mutated broadly-neutralizing (bn) HIV
mAbs and 103 plasmodium faciparium (PF) specific mAbs from the literature. Fisher’s exact test or Kruskal-Wallis test was used in statistical analysis.

**Results:**

The majority of ACPA exhibited variable region N-linked motifs (85.7%), compared to 18.5% in control (p<0.0001), 21.2% in RA BM plasma cells (p<0.0001), 31.4% non-ACPA synovial RA mAbs (p=0.0005), 7.4% of clones from seroneg. RA (p<0.0001), 25.2% in PF mAbs (p<0.0001), and 63.2% of HIV bnAbs (p=0.24), featured in both framework and CDRs generated by somatic hypermutation (SHM). Indeed, ACPA displayed high level of SHM (average 30 VL and 52 VH), yet when adjusted for SHM, N-linked motifs were significantly elevated in ACPA compared to all groups including bnAbs. IgG mAb characterization revealed that N-linked motifs were indeed glycosylated, although preliminary data suggested that glycans had no striking effect on antigen-binding. Homology-based structures predicted glycans to be primarily positioned outside of the potential antigen-binding site. Lectin analysis and mass spectrometry suggested that ACPA mAb Fab-glycan composition was distinctly different from Fc-glycans, and could have high sialic acid content.

**Conclusion:**

The results support that Fab glycosylation is a key feature of ACPA. Significant increases in N-linked motifs in ACPA compared to other highly-mutated antibodies signifies that this is not solely associated to mutation frequency. Future studies are merited to further investigate the selection mechanisms and functional role of Fab-glycosylated autoantibodies.

**Disclosure:** K. A. Lloyd, None; J. Steen, None; P. J. Titcombe, None; K. Amara, None; D. Zhou, None; L. Israelsson, None; S. L. Lundström, None; D. L. Mueller, None; L. Klareskog, None; V. Malmström, None; C. Grönwall, None.

**View Abstract and Citation Information Online** - [http://acrabstracts.org/abstract/monoclonal-acpa-igg-feature-extensive-fab-glycosylation](http://acrabstracts.org/abstract/monoclonal-acpa-igg-feature-extensive-fab-glycosylation)

**Abstract Number: 478**

**Ectopic Lymphoid Tissue in the Lung Is Uniquely Associated with the ACPA IgA Isotype Even in Absence of Classifiable RA**

Lindsay B. Kelmenson¹, M. Kristen Demoruelle¹, Carlyne D. Cool² and Kevin D. Deane¹, ¹Rheumatology Division, University of Colorado Denver, Aurora, CO, ²Pathology, University of Colorado Denver, Aurora, CO

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Antibodies to citrullinated protein antigens (ACPA) precede the development of rheumatoid arthritis (RA) and may be generated in the lung of established and preclinical RA patients. An association has been demonstrated between serum ACPA and ectopic lymphoid tissue (ELT) in the lung of RA and non-RA patients with lung disease, suggesting that ELT may be a mechanism for ACPA generation in the lung (Rangel-Moreno 2016, Brown ACR 2015, Abstract #963). To further explore the mucosal basis of ACPA, we examined ACPA isotypes and lung histopathology in patients with and without RA.

**Methods:**

Using materials from the NIH’s Lung Tissue Resource Consortium (LTRC) we evaluated lung biopsies and serum samples from 10 RA patients with interstitial lung disease (RA-ILD), 30 non-RA patients with ILD (Non-RA ILD) and 35 non-RA
patients with emphysema or airway disease (Non-ILD). Serum was tested for IgA and IgG ACPA isotypes using the CCP3 antigen plate (Inova, research only). Lung tissue was evaluated by a pathologist blinded to patients’ clinical status to determine the presence of ELT defined as germinal centers (GCs) or lymphoid aggregates. Logistic regression was used to determine associations of isotype levels with ELT.

Results:

Patients' characteristics are presented in the Table. There were significantly higher mean IgG ACPA levels in RA cases compared to non-RA patients (Figure). Mean IgA ACPA levels were higher compared to IgG in non-RA ILD (83.2 vs. 26.6) and non-ILD patients (40.3 vs. 5.3), although in RA patients, there was no significant difference in isotype levels (Figure). There was an association between serum IgA ACPA levels and ELT in all subjects (p=0.01), but not IgG. Smoking, age, and gender were not significantly associated with ELT; however, RA was significantly associated with ELT (p=0.03). To evaluate the relationship between serum ACPA isotypes and ELT in absence of RA, an analysis of only non-RA subjects showed that IgA ACPA levels remained significantly associated with ELT (OR 1.14 for every 10-unit increase in IgA; 95% CI 1.01-1.28; p=0.02).

Conclusion:

Our findings support a link between serum ACPA and lung ELT. Given the strongest association was seen between ELT and IgA ACPA for non-RA subjects, it may be that IgA ACPA are related to ELT even in absence of articular disease. The strong association of IgG ACPA with RA may indicate that this isotype is a marker for RA-specific articular processes. Future studies should assess the mechanisms underlying these findings, and how differentiating IgA and IgG ACPA may help in the management of RA and non-RA patients with lung disease.

![Figure: Mean ACPA Isotype Levels by Lung Histopathology](image)

<table>
<thead>
<tr>
<th></th>
<th>RA-ILD n=10</th>
<th>Non-RA ILD n=30</th>
<th>Non-ILD n=35</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>55 (30.1)</td>
<td>63 (10.1)</td>
<td>61 (9.9)</td>
<td>0.24</td>
</tr>
<tr>
<td>Female, N (%)</td>
<td>8 (80%)</td>
<td>16 (53%)</td>
<td>19 (54%)</td>
<td>0.34</td>
</tr>
<tr>
<td>Non-Hispanic White, N (%)</td>
<td>9 (90%)</td>
<td>24 (80%)</td>
<td>25 (71%)</td>
<td>0.48</td>
</tr>
<tr>
<td>Past Smoker, N (%)</td>
<td>6 (60%)</td>
<td>23 (77%)</td>
<td>21 (60%)</td>
<td>0.35</td>
</tr>
<tr>
<td>Current Smoker, N (%)</td>
<td>1 (10%)</td>
<td>1 (3%)</td>
<td>3 (9%)</td>
<td>0.35</td>
</tr>
<tr>
<td>GC and/or lymphoid aggregate, N (%)</td>
<td>9 (90%)</td>
<td>21 (70%)</td>
<td>9 (26%)</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

Disclosure: L. B. Kelmenson, None; M. K. Demoruelle, None; C. D. Cool, None; K. D. Deane, Inova Diagnostics, Inc., 5.

Protein Carbamylation Is Induced By Activated Neutrophil: Ex Vivo Analysis

Shuichiro Nakabo¹, Koichiro Ohmura¹, Shuji Akizuki¹, Nobuo Kuramoto¹, Kosaku Murakami², Ran Nakashima², Motomu Hashimoto³, Hajime Yoshifuji¹, Masao Tanaka³ and Tsuneyo Mimori¹, ¹Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University, Kyoto, Japan, ²Clinical Immunology and Rheumatology, Graduate School of Medicine, Kyoto University, Kyoto, Japan, ³Department of Advanced Medicine for Rheumatic Diseases, Graduate School of Medicine, Kyoto University, Kyoto, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Protein carbamylation is induced by activated neutrophil: ex vivo analysis

Background/Purpose:
Anti-carbamylated protein (anti-CarP) antibodies were reported to be detected in 45% of rheumatoid arthritis (RA) patients [1]. We previously reported that carbamylated albumin (CarALB) was one of the target antigens of anti-CarP antibodies, and serum myeloperoxidase (MPO) level was elevated in rheumatoid arthritis patients with anti-CarALB antibody [2]. Protein carbamylation occurs by cyanate which MPO produces from thiocyanate (SCN⁻) and hydrogen peroxide (H₂O₂), and MPO abundantly exists in neutrophil. Therefore, neutrophil is a strong candidate for the production of carbamylated antigen. The purpose of this study is to demonstrate that activated neutrophil induces protein carbamylation.

Methods:
Human neutrophils were isolated from whole blood by ficoll-dextran methods. They were pre-treated for 30 min at 37°C in RPMI medium with or without 10⁻⁶M diphenyleneiodonium (DPI), which inhibits NADPH-dependent reactive oxygen species (ROS) production. Subsequently, they were incubated overnight at 37 °C in RPMI medium containing 0.01mg/mL ALB with or without 10⁻⁶M DPI, 20nM phorbol 12-myristate 13-acetate (PMA) and 100⁻⁶M potassium thiocyanate (KSCN). Then proteins in the medium were collected by trichloroacetic acid/acetone precipitation. The carbamylation of ALB was confirmed by Western blotting using anti-carbamyl-lysine (CBL) polyclonal antibody. MPO in the medium was detected by Western blotting using anti-MPO polyclonal antibody.

Results:
ALB was carbamylated only when both neutrophil and KSCN were present (Figure 1, lanes 4 and 5). Although the carbamylation occurred in the medium both with and without PMA, the level of the carbamylation was much higher in the medium with PMA (lane 5) than without PMA (lane 4). Carbamylation was inhibited by the presence of DPI, which diminishes ROS (lanes 7 and 8). MPO was released into the culture supernatant from the neutrophils (Figure 2, lane 2), and its release was accelerated by PMA (lanes 3 and 5), but attenuated by DPI (lanes 7 and 8).

Conclusion:
ALB in the culture medium was carbamylated by neutrophil. Given that PMA induces ROS production of neutrophil, and this reaction subsequently increases the MPO release, our data suggest that carbamylation is dependent on ROS and MPO from neutrophil. Addition of KSCN was necessary. This is the first report that showed direct relationship between neutrophil and protein carbamylation.

Reference:
Disclosure: S. Nakabo, None; K. Ohmura, None; S. Akizuki, None; N. Kuramoto, None; K. Murakami, None; R. Nakashima, None; M. Hashimoto, None; H. Yoshifuji, None; M. Tanaka, None; T. Mimori, None.

View Abstract and Citation Information Online - [Website URL]

Abstract Number: 480
ANTI-Carbamylated Protein Antibodies (CARP) in Palindromic Rheumatism: Prevalence and Clinical Significance

Raul Castellanos-Moreira Sr., Virginia Ruiz-Esquide, María José Gomara, Sonia Cabrera-Villalba, Sebastián C Rodriguez-García, Georgina Salvador, Andrea Cuervo, Julio Ramírez, M. Victoria Hernández, Juan Cañete, Isabel Haro and Raimon Sanmartí

1Rheumatology Service, Hospital Clínic de Barcelona, Barcelona, Spain, 2Unit of Synthesis and Biomedical Applications of Peptides, IQAC-CSIC, Barcelona, Spain, 3Hospital Universitario Mutua Terrassa, Barcelona, Spain

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis - Human Etiology and Pathogenesis Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Autoantibodies (RF or ACPA) are found in sera from patients with palindromic rheumatism (PR) but there are no studies analyzing the presence of Anti-carbamylated proteins antibodies (Anti-CarP) in patients with PR. The aim of this study was to analyse the prevalence of Anti-CarP in patients with PR and to evaluate their clinical significance and association with autoantibody status (RF and ACPA).

Methods: Patients with pure PR (not associated with any rheumatic disease at the time of serum measurement) with sera collected between June 2012 and June 2013 were included (Cabrera-Villalba S et al J Rheumatol 2014;41:1650-5). Anti-CarP were determined by a home-made ELISA test using a synthetic chimeric fibrin/filaggrin homocitrullinated peptide (CFFHP) as antigen. IgG, IgA and IgM isotype were measured using the corresponding secondary antibodies. Cut-off values were determined using ROC curves, with a specificity of 98% compared with a healthy population. ACPA, RF, progression toward persistent arthritis fulfilling ACR/EULAR RA criteria, and remission (no joint attacks in the last 6 months) was analyzed during the follow-up (until May 2017). Patients were treated according to physician criteria. A control group of established RA patients was also included.

Results: Anti-CarP antibodies were analyzed in 54 patients with pure PR and 53 patients with established RA controlled by age, gender and disease evolution. ACPA (CCP2) was positive in 64.8% of PR and 66.0% of RA patients. Anti-CarP were found in 9 out of 54 (16.7%) of PR patients. Patients with PR and Anti-CarP (+) were all ACPA positive and presented higher ACPA titers than Anti-CarP (-) patients (Table 1). In PR patients, IgG was the predominant isotype (100%) and only one patient presented IgA (11.1%) and none IgM. In the RA control group, the prevalence of Anti-CarP was 39.6% and the percentages of IgG, IgA and IgM were 57.1%, 47.6% and 38.1% of Anti-CarP (+) patients respectively. DMARDs were administered in 64.8% of patients (in all Anti-CarP (+) patients) at the last assessment, mainly antimalarials and methotrexate. More Anti-CarP (+) patients developed RA (33.3% vs. 16.3%) during follow up although the difference was not significant. Remission was more frequent in Anti-CarP negative patients (Table 1).

Conclusion:

Table 1. Clinical and serological characteristics of PR patients according to Anti-CarP status
<table>
<thead>
<tr>
<th></th>
<th>RP with Anti-CarP (+)</th>
<th>RP with Anti-CarP (-)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n: 9</td>
<td>n: 45</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>5 (55.6%)</td>
<td>29 (64.4%)</td>
<td>NS</td>
</tr>
<tr>
<td>Smoking Hx</td>
<td>5 (55.6%)</td>
<td>19 (44.4%)</td>
<td>NS</td>
</tr>
<tr>
<td>Age at onset (years)</td>
<td>42.9±8.9</td>
<td>39.1 ±11.8</td>
<td>NS</td>
</tr>
<tr>
<td>Mean disease duration (years)*</td>
<td>11.3± 7.6</td>
<td>12± 10.9</td>
<td>NS</td>
</tr>
<tr>
<td>Follow-up (years)**</td>
<td>3.8±1.23</td>
<td>3.9±1.07</td>
<td>NS</td>
</tr>
<tr>
<td>RF + (%)</td>
<td>7 (77.8%)</td>
<td>26 (57.8%)</td>
<td>NS</td>
</tr>
<tr>
<td>RF titer (UI)</td>
<td>286.7± 134.5</td>
<td>207.8± 325.6</td>
<td>NS</td>
</tr>
<tr>
<td>Anti-CCP2 + (%)</td>
<td>9 (100%)</td>
<td>26 (57.8%)</td>
<td>0.003</td>
</tr>
<tr>
<td>Anti-CCP2 titer UI</td>
<td>769.2± 638.4</td>
<td>381.1± 411.6</td>
<td>0.02</td>
</tr>
<tr>
<td>Progression to RA</td>
<td>3 (33%)</td>
<td>7 (15.5%)</td>
<td>NS</td>
</tr>
<tr>
<td>Remission at last follow-up</td>
<td>2 (22.2%)</td>
<td>26 (60.5%)</td>
<td>0.03</td>
</tr>
<tr>
<td>DMARDs</td>
<td>9 (100%)</td>
<td>26 (57.8%)</td>
<td>0.003</td>
</tr>
<tr>
<td>Antimalarials</td>
<td>5</td>
<td>18</td>
<td>NS</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>1</td>
<td>8</td>
<td>NS</td>
</tr>
</tbody>
</table>

* At the time of serum measurement

**: From sera measurement to last follow-up

Disclosure: R. Castellanos-Moreira Sr., None; V. Ruiz-Esquide, None; M. J. Gomara, None; S. Cabrera-Villalba, None; S. C. Rodriguez-Garcia, None; G. Salvador, None; A. Cuervo, None; J. Ramírez, Gebro, 2; M. V. Hernández, None; J. Cañete, None; I. Haro, None; R. Sanmartí, None.


Abstract Number: 481

**Immunocompetent Cells Expressing Citrullinated Proteins in Joint Synovium of Osteoarthritis and Rheumatoid Arthritis**

Kyoko Honne¹, Masahiro Iwamoto², Shunichiro Hanai¹, Satoshi Machida³, Hitoshi Sekiya⁴, Reina Tsuda⁵, Tatsuhiko Ozawa⁵, Tadayoshi Karasawa⁶, Atsushi Muraguchi⁵, Masafumi Takahashi⁶, Hiroyuki Kishi⁵ and Seiji Minota⁷, ¹Division of Rheumatology and Clinical Immunology, Jichi Medical University, Shimotsuke, Japan, ²Division of Rheumatology and Clinical Immunology, Jichi Medical University, Shimotsuke, Japan, ³Department of Orthopaedic Surgery, Orthopedics Clinic Medical Papas, Tochigi, Japan, ⁴Department of orthopedic surgery, Jichi Medical University, Shimotsuke, Japan, ⁵Department of Immunology, Graduate School of Medicine and Pharmaceutical Sciences, University of Toyama, Toyama,
SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Human monoclonal ACPA (Human-ACPA) is reported to strongly bind to synovium in RA patients [1]. The aims of our study were 1) To investigate whether Human-ACPA, which was generated from peripheral blood B cells from an RA patient by us, binds to synovium from OA and RA, and 2) To identify cell-type expressing citrullinated proteins in synovium from OA and RA patients.

Methods: Human-ACPA was produced by a method published earlier [2, 3]. Joint synovium from OA or RA patients (10 OA, 10 RA) were immunohistochemically stained with Human-ACPA. Double-label immunofluorescence staining with Human-ACPA/CD3, Human-ACPA/CD20 or Human-ACPA/CD68 (3 OA, 3 RA), and confocal laser scanning microscope (3 RA) were performed in the synovia for the images.

Results: Human-ACPA bound to all layers in synovium from RA patients. Human-ACPA positive cells were limited in the surface layer in 7 of 10 OA patients, while no Human-ACPA positive cells were found in the remaining 3 OA synovia. Human-ACPA positive cells in synovium of OA were not double-stained with CD3, CD20 or CD68 monoclonal antibody. On the other hand, there were Human-ACPA/CD3, Human-ACPA/CD20 or Human-ACPA/CD68 double positive cells in synovium of RA patients. Most of the ACPA positive cells were stained with CD68. Human-ACPA/CD3 and Human-ACPA/CD20 double positive cells also existed in deeper layers of synovium in RA patients.

Conclusion: All layers of synovium in RA patients were studded with cells which contained citrullinated proteins. Cells positive for citrullinated protein in RA were mainly macrophage-lineage (CD68+). Citrullinated protein was also expressed in T cells (CD3+) and B cells (CD20+) in RA. Citrullinated protein existed in the strip-shaped form only in the surface layer of OA synovia and may have been induced by mechanical stresses. No macrophages, T cells or B cells were positive for citrullinated protein in OA.


Disclosure: K. Honne, Takeda science foundation, 2; M. Iwamoto, None; S. Hanai, None; S. Machida, None; H. Sekiya, None; R. Tsuda, None; T. Ozawa, None; T. Karasawa, None; A. Muraguchi, None; M. Takahashi, None; H. Kishi, None; S. Minota, None.


Abstract Number: 482
The Link between ACPA and Erosion Development: Is ACPA Sufficient? an Association Study in Clinically Suspect Arthralgia

Robin M ten Brinck¹, REM Toes² and Annette H.M. van der Helm-van Mil¹, ¹Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, ²Rheumatology, Leiden University Medical Center, Leiden, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Anti-citrullinated protein antibodies (ACPA) associate with more severe joint erosions in rheumatoid arthritis (RA), but the underlying mechanism is unclear. Recent in vitro and murine studies indicate that ACPAs can directly activate osteoclasts leading to bone erosion and pain. This study sought evidence for this hypothesis on the human level and evaluated in arthralgia patients at risk for RA whether ACPA associated with erosions (detected by MRI) independent of inflammation, and also independent of the presence of other autoantibodies (Rheumatoid Factor, RF).

Methods:
225 patients with Clinically Suspect Arthralgia underwent ACPA- and RF-determination and 1.5T contrast-enhanced MRI of metacarpophalangeal, wrist and metatarsophalangeal joints at baseline. MRIs were scored for presence of local inflammation and erosions.

Results:
ACPA-positive patients had higher erosion-scores than ACPA-negative patients (p=0.02; Figure Panel A). ACPA-positive patients without subclinical inflammation did not have higher erosion-scores than ACPA-negative patients (p=0.45), in contrast to ACPA-positive patients with local inflammation (p=0.001, Figure Panel B). Mediation analyses suggested that local inflammation is in the causal path of ACPA leading to higher erosion-scores. Compared to autoantibody-negative patients, ACPA-positive/RF-negative patients did not differ (p=0.41), but ACPA-positive/RF-positive patients had higher erosion-scores (p=0.001 Figure Panel C).

Conclusion:
The effect of ACPA on erosions is mediated by inflammation and is not independent of RF.

Figure. Histograms showing median erosion-scores of patients with Clinically Suspect Arthralgia comparing ACPA-positive and ACPA-negative patients (A), ACPA-positivity and -negativity in relation to the concomitant presence of MRI-detected subclinical inflammation (B) or rheumatoid factor (C).
Anti-Peptidylarginine Deiminase-4 Antibodies Are Present in the Sputum of RA Patients and Can Activate Peptidylarginine Deiminase-4 Enzyme Activity

M. Kristen Demoruelle1, Hong Wang2, Ryan L. Davis2, A. Itzam Marin1, Jill M. Norris3, V. Michael Holers1, Kevin D. Deane1 and Erika Darrah2, 1Division of Rheumatology, University of Colorado School of Medicine, Aurora, CO, 2Division of Rheumatology, The Johns Hopkins University, Baltimore, MD, 3Department of Epidemiology, Colorado School of Public Health, Aurora, CO

First publication: September 18, 2017

Background/Purpose: Anti-peptidylarginine deiminase (PAD)-4 antibodies (Abs) are present in a portion of RA patients and associate with more severe joint disease, suggesting that they play a role in pathogenesis. A subset of anti-PAD4 Abs cross-react with PAD3, and these Abs are found to enhance PAD4 enzyme activity at physiologic calcium concentrations which can lead to increased citrullination. Anti-PAD3/4 cross-reactive Abs have also been associated with more severe lung disease in RA, suggesting they may have a direct effect in the lung. Because sputum anti-CCP Abs have been identified in RA, we sought to explore the presence and activity of anti-PAD4 Abs in the sputum of RA patients.

Methods: We studied 48 serum anti-CCP+ RA patients and 24 healthy controls. Induced sputum was tested for CCP using commercial ELISAs. Serum and sputum were tested for anti-PAD4 Abs using an established immunoprecipitation method. All anti-PAD4+ samples underwent testing for the presence of PAD3 cross-reactivity. To determine the effect of anti-PAD Abs on PAD4 enzymatic activity, Igs were purified from each anti-PAD+ sample and their effect on citrullination of the histone H3 substrate by PAD4 at increasing calcium concentrations (i.e. 0.2 and 2 mM) was measured by an anti-citrullinated histone H3 immunoblot.

Results: Serum anti-PAD4 Abs were detected in 6/48 (13%) of RA patients and 0/24 (0%) controls. Of the positive patients, 2/6 (33%) were also serum anti-PAD3+. Sputum anti-PAD4 Abs were detected in 3/48 (6%) of RA patients, and of those positive, 1/3 (33%) was also sputum anti-PAD3+. Serum anti-PAD4 Abs were more prevalent in RA patients with sputum anti-CCP Abs, with all anti-PAD4+ RA patients demonstrating sputum anti-CCP positivity (Table). In serum, anti-PAD4 Abs were predominately IgG, whereas in sputum, anti-PAD4 Abs were predominately IgA (Figure). Interestingly, all three samples (serum and sputum) with measurable anti-PAD3/4 Abs were able to increase PAD4 activity at 0.2 mM calcium (i.e. physiologic levels).

Conclusion: We identified serum anti-PAD4 Abs in a portion of RA patients, of which a subset was also anti-PAD3+. We demonstrate for the first time that anti-PAD4 Abs are also present in the sputum in a portion of RA patients, and
predominantly IgA. Importantly, we found that anti-PAD3/4 IgA present in the sputum was able to lower the calcium threshold required for PAD4 enzymatic activity. These findings suggest that anti-PAD4 Abs may have pathogenic activity directly in the lung, although larger studies are needed to understand the relationship between anti-PAD3/4 and underlying lung disease.

| Table. Characteristics associated with serum anti-PAD4 antibodies |
|-----------------------|-------------------|-------------------|------------------|
|                      | Serum anti-PAD4(+) | Serum anti-PAD4(-) | p-value*         |
| Age, median (IQR)    | 51 (29-64)        | 58 (45-62)        | 0.49             |
| % Female             | 83                | 79                | 0.24             |
| % Ever smoker        | 17                | 55                | 0.19             |
| % Current smoker     | 17                | 19                | 1.0              |
| % Shared epitope positive | 80            | 66                | 1.0              |
| % RA disease duration >1 year | 33          | 62                | 0.22             |
| % Any self-reported lung disease | 33    | 38                | 1.0              |
| % Sputum anti-CCP positivity** | 100 | 50 | 0.03 |

*P-value compares median levels (Mann-Whitney U) or prevalence of positivity (Chi-Square/Fishers) between groups as appropriate.

**Includes positivity for commercial assays CCP3 (IgG, Inova) and/or anti-CCP3.1(IgG/IgA, Inova). The cut-off level used to determine sputum anti-CCP positivity was established in a separate healthy control group.

Disclosure: M. K. Demoruelle, None; H. Wang, None; R. L. Davis, None; A. I. Marin, None; J. M. Norris, None; V. M. Holers, None; K. D. Deane, Inova Diagnostics, Inc., 5; E. Darrah, patent, 9.


Abstract Number: 484

**Sputum Neutrophils Demonstrate Increased Neutrophil Extracellular Trap Formation in RA-Free Subjects at-Risk of Future RA**

Yuko Okamoto¹, Michael P. Mohnning², Stacey M. Thomas², Ashley Visser¹, Lindsay B. Kelmenson³, Jill M. Norris⁴, Mariana J. Kaplan⁵, William J. Janssen², V. Michael Holers¹, Kevin D. Deane¹ and M. Kristen Demoruelle¹, ¹Division of Rheumatology, University of Colorado School of Medicine, Aurora, CO, ²Division of Pulmonary Disease and Critical Care Medicine, National Jewish Health, Denver, CO, ³Division of Rheumatology, University of Colorado School of Medicine,
SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Data support that ACPAs are generated in the lung in RA-free subjects At-Risk of future RA. Our group previously demonstrated a significant positive correlation between sputum ACPA levels and remnants of neutrophil extracellular traps (NETs) in At-Risk subjects (Demoruelle 2017). However, it is unknown if increased sputum NET levels in these subjects is due to aberrant neutrophil function or ineffective macrophage function (e.g. decreased macrophage efferocytosis that is a mechanism of apoptotic cell clearance). Herein, we sought to quantify ex vivo NET formation and macrophage efferocytosis in association with ACPA in the sputum of At-Risk subjects.

Methods: We collected serum and induced sputum from 24 subjects At-Risk for RA based on familial RA or serum ACPA positivity identified through community screenings [17 were serum ACPA- and 7 serum ACPA+ based on commercial CCP3.1 (IgG/IgA, Inova)], 3 healthy Controls and 3 serum ACPA+ classified RA patients. Sputum was tested for ACPA using CCP3.1 ELISA and the cut-off for positivity was determined in a separate healthy control group (N=70). Sputum plugs were processed and incubated for 1 hour without stimulation for NET measurements and a subset (N=15) were also incubated with apoptotic Jurkat cells for efferocytosis assays. The formation of NETs was assessed by fluorescence microscopy with staining for Hoechst 33342, neutrophil elastase and citrullinated histone-H3. Microscopy-based methods were used to quantify the percent of neutrophils demonstrating NET formation and the efferocytosis index for macrophages ingesting apoptotic Jurkats.

Results: NET formation in sputum neutrophils was significantly higher in serum ACPA+ At-Risk subjects compared to Controls (p=0.03) and serum ACPA- At-Risk subjects (p<0.01) (Figure Panel A), although a portion of serum ACPA- At-Risk subjects had elevated rates of sputum NET formation. There was a trend toward a higher prevalence of sputum ACPA positivity in At-Risk subjects with >60% NETosis [4/8 (50%) vs. 3/15 (20%), p=0.18]. There was no difference in NETosis based on smoking history. The efferocytosis index was lower in serum ACPA+ At-Risk subjects compared to Controls (p=0.03, Figure Panel B).

Conclusion: We found that sputum neutrophils in At-Risk subjects exhibit increased NET formation in serologically ACPA+ At-Risk individuals. Furthermore, in these subjects, sputum macrophages exhibited decreased efferocytosis. These findings suggest that enhanced neutrophil NET formation and ineffective macrophage efferocytosis in the lung may both play a role in the development of systemic and potentially local mucosal ACPA generation in subjects At-Risk for RA. Additional studies are needed to determine whether sputum NETs in At-Risk subjects contain unique citrullinated protein cargo as well as whether these processes are aberrant at other mucosal sites.

**Figure. Rates of Ex Vivo Neutrophil Extracellular Trap (NET) Formation and Macrophage Efferocytosis in Sputum.** The figure depicts the rates of NET formation in sputum neutrophils (Panel A) and the macrophage efferocytosis index (Panel B) in each group. The % NET formation is calculated by dividing the number of NETs formed by the total number of neutrophils in each subject. The efferocytosis index is calculated by multiplying the % of macrophages that phagocytosed an apoptotic Jurkat cell by the average number of apoptotic cells engulfed per macrophage. Open circles=sputum ACPA negative, close circles=sputum ACPA positive.

Abbreviations: HC=Healthy controls, Sp=Serum, ACPA=anti-citrullinated protein/peptide antibody, RA=Rheumatoid arthritis.
Different Citrullination Profiles in Spontaneous Versus Leukemia-Associated Rheumatoid Arthritis

Tal Gazitt¹, Son Hong Nguyen², Ari Salinger², Christian Lood³, Xizhang Sun¹, Lena M. Tanaka¹, David Feith⁴, Jeffrey Ledbetter⁵, Gordon Starkebaum⁶, Thomas Loughran Jr.⁷, Paul R. Thompson² and Keith B. Elkon⁸, ¹Division of Rheumatology, University of Washington, Seattle, WA, ²Biochemistry and Molecular Pharmacology, University of Massachusetts Medical School, Worcester, MA, ³Division of Rheumatology, Division of Rheumatology, Department of Medicine, University of Washington, Seattle, WA, ⁴Hematology and Oncology, University of Virginia, Charlottesville, VA, ⁵University of Washington, Seattle, WA, ⁶Department of Medicine, Division of Rheumatology, University of Washington, Seattle, WA, ⁷Hematology Oncology, University of Virginia, Charlottesville, VA, ⁸Division of Rheumatology, Department of Medicine, University of Washington, Seattle, WA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Protein citrullination, the post-translational conversion of arginine to citrulline, mediated by peptidylarginine deiminase (PAD) enzymes, is considered a likely mechanism for the stimulation of anti-citrullinated protein antibodies (ACPA) in patients with rheumatoid arthritis (RA). Hypercitrullination, the citrullination of multiple intracellular proteins, is seen in synovial fluid (SF) cells from RA patients. This unique form of citrullination is proposed to occur via immune-mediated, pore-forming membranolytic pathways such as perforin-granzyme activation. Indeed, perforin and granzyme-producing CD8⁺ T effector cells are found in the synovium of pre-clinical RA patients as well as in the peripheral blood (PB) and SF of active RA patients, persisting into disease remission.

Insight into the existence of potential cytotoxic mechanisms occurring in RA comes from the co-occurrence of RA in up to 36% of cases of T-cell Large Granular Lymphocyte (T-LGL) Leukemia, a clonal condition characterized by neutropenia attributed to the killing of neutrophils or their precursors by cytotoxic CD8⁺ T cells. We thus queried LGL leukemia as a model for neutrophil (PMN)-directed cytotoxicity contributing to hypercitrullination and disease propagation in inflamed joints of ACPA+ RA patients.

Methods:

The sera of 15 T-LGL leukemia patients (T-LGL), 19 T-LGL leukemia patients with co-existing RA (T-LGL/RA), and 4 healthy controls (HC) were analyzed for ACPA positivity by ELISA. ACPA titers of each group of patients were compared using unpaired two-tailed T tests. Neutrophils (PMN) from each of these groups were isolated from blood cells by density gradient centrifugation. Hypercitrullination of these cells (n=4/patient group) was compared with that of seropositive RA patients by proteomic analysis using Rhodamine-PG labeling, protein precipitation followed by Streptavidin enrichment, and sequent digestion. The resulting products were analyzed using LC-MS/MS on an LTQ-Orbitrap mass spectrometer. The
tandem MS data were searched using SEQUEST algorithm using a concatenated target/decoy variant of the human and mouse International Protein Index database.

Results:

T-LGL/RA patients had significantly higher serum ACPA positivity than T-LGL patients or HC (Fig. 1A). Surprisingly, however, the overall level of citrullinated proteins in PMN (Fig.1B) was not increased in T-LGL/RA compared to T-LGL patients, and was highest in PMN obtained from RA patients (Fig. 1B).

Conclusion:

These results reveal an interesting dichotomy between RA that occurs spontaneously versus that occurring in patients with LGL leukemia. Whereas both spontaneous and LGL-associated RA develop high titer ACPA, only RA patients show a high degree of citrullination of neutrophil proteins. Whether this suggests a different source of immunogenic proteins or relates to other biologic processes, remains to be determined.

Disclosure: T. Gazitt, None; S. H. Nguyen, None; A. Salinger, None; C. Lood, None; X. Sun, None; L. M. Tanaka, None; D. Feith, None; J. Ledbetter, None; G. Starkebaum, None; T. Loughran Jr., None; P. R. Thompson, None; K. B. Elkon, Celgene, 5,AstraZeneca, 5,Merck Human Health, 5,Resolve Therapeutic, 4,Amdax Therapeutics, 4.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/different-citrullination-profiles-in-spontaneous-versus-leukemia-associated-rheumatoid-arthritis

Abstract Number: 486

Anti-Citrullinated Protein Antibody Reactivities in Treatment NaïVe Early Rheumatoid Arthritis

Maria K. Jonsson1,2, Aase Hensvold3, Monika Hansson4, Linda Mathsson-Alm5, Anna-Birgitte Aga2, Joseph Sexton2, Bjørg-Tilde Frevang1,6, Siri Lillegravén2, Anca I. Catrina3 and Espen A. Haavardsholm2,7, 1Dept. of Rheumatology,
SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Anti-citrullinated protein antibody (ACPAs) can precede RA onset, and may be involved in the pathogenesis of the disease. We wanted to assess the prevalence of baseline ACPA reactivities in an inception cohort of early RA patients, including subgroups based on anti-CCP/RF status, and to compare the findings to healthy controls.

Methods: 217 DMARD-naïve early RA patients from the ARCTIC trial (1) were analyzed. Radiographs were scored according to van der Heijde Sharp (vdHS) score. Anti-CCP status was analyzed by FEIA (positive if ≥10 IU/mL) and RF by ELISA (positive if ≥25 IU/mL). ACPA titres (AU/ml) were considered positive if above the 98-percentile of values in 619 non-RA subjects. Analysis of 13 ACPA reactivities targeting citrullinated peptides from fibrinogen, alpha-1 enolase, vimentin, fillagrin and histone was performed at baseline in patients and 94 controls (blood donors matched for age/gender/smoking), using a multiplex chip-based assay (2). Positivity and median number of ACPA reactivities in the subgroups were compared using Chi-square test and Mann-Whitney U-test, respectively.

Results: Baseline characteristics are presented in the table. The median [IQR] number of antibody reactivities in all patients was 7[3,10], compared to 0[0,0] in controls (p<0.001, figure). The corresponding numbers were 8[5,10] and 0[0,1] for the anti-CCP+ vs. anti-CCP- patients (p=0.0001), 8[5,10] and 2[0,8] for the RF+ vs. RF- patients (p=0.001), and 8[6,10] and 0[0,1] for the anti-CCP+/RF+ vs. the anti-CCP-/RF- patients (p<0.001) (table, figure). Positivity for ACPA reactivities was seen mainly in the anti-CCP+, RF+ and anti-CCP+/RF+ patients, but also occurred more frequently in the anti-CCP-, RF- and anti-CCP-/RF- patients than in controls (anti-CCP- vs controls p=0.002, RF- vs controls p<0.001, and anti-CCP-/RF- vs. controls p=0.035) (table).

Table: Baseline characteristics
<table>
<thead>
<tr>
<th></th>
<th>Anti-CCP+</th>
<th>Anti-CCP-</th>
<th>RF+</th>
<th>RF-</th>
<th>Anti-CCP+/RF+</th>
<th>Anti-CCP-/RF-</th>
<th>All RA</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=178</td>
<td>50.8(13.2)</td>
<td>55.0(14.9)</td>
<td>51.9(13.3)</td>
<td>50.8(14.2)</td>
<td>51.7(13.6)</td>
<td>55.0(16.1)</td>
<td>51.5(13.6)</td>
<td>52(9.4)</td>
</tr>
<tr>
<td>n=39</td>
<td>109(61)</td>
<td>22(56)</td>
<td>91(59)</td>
<td>40(63)</td>
<td>86(59)</td>
<td>17(53)</td>
<td>131(60)</td>
<td>63(59)</td>
</tr>
<tr>
<td>n=154</td>
<td>122(69)</td>
<td>26(67)</td>
<td>109(71)</td>
<td>39(62)</td>
<td>103(70)</td>
<td>20(62)</td>
<td>148(68)</td>
<td>81(64)</td>
</tr>
<tr>
<td>n=63</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=147</td>
<td>3.4(1.1)</td>
<td>4.0(1.3)</td>
<td>3.5(1.2)</td>
<td>3.5(1.2)</td>
<td>3.42(1.13)</td>
<td>3.9(1.2)</td>
<td>3.5(1.2)</td>
<td>NA</td>
</tr>
<tr>
<td>n=32</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=217</td>
<td>51.9(13.3)</td>
<td>50.8(14.2)</td>
<td>51.7(13.6)</td>
<td>55.0(16.1)</td>
<td>51.5(13.6)</td>
<td>52(9.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=94</td>
<td>55.0(14.9)</td>
<td>50.8(14.2)</td>
<td>51.7(13.6)</td>
<td>55.0(16.1)</td>
<td>51.5(13.6)</td>
<td>52(9.4)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1Mean(SD), 2n(%), 3median[IQR], 4n positive(%)

**Figure:** Number of ACPA reactivities per patient
**Conclusion:** Prevalence of ACPA reactivities differed in subgroups of DMARD-naive early RA patients according to anti-CCP and RF status. In general, higher numbers of ACPA reactivities were seen in anti-CCP+ patients, but all RA subgroups, including anti-CCP-, RF- and anti-CCP-/RF- patients, had higher prevalence of ACPA reactivities compared to healthy controls.

**References:** 1) Haavardsholm et al BMJ 2016, 2) Hansson et al Arthr Res Ther 2012

**Disclosure:** M. K. Jonsson, None; A. Hensvold, None; M. Hansson, None; L. Mathsson-Alm, Thermo-Fisher Scientific, 3; A. B. Aga, None; J. Sexton, None; B. T. Fevang, Novartis Pharmaceutical Corporation, 2; S. Lillegraven, None; A. I. Catrina, None; E. A. Haavardsholm, AbbVie, Pfizer, Roche, Eli Lilly, Celgene, UCB, 5,AbbVie, Pfizer, Roche, MSD, UCB, 2,AbbVie, Pfizer, Roche, Eli Lilly, Celgene, UCB, 8.


Abstract Number: 487
ARE ANTI-Citrullinated Protein Antibody Levels Associated with Periodontal Disease in Rheumatoid Arthritis?

Jerián González Febles1, Fernando Sánchez-Alonso2, Jorge Luis Garnier Rodríguez3, Mariano Sanz Alonso1, Federico Díaz-González4 and Beatriz Rodriguez Lozano5,6

1Periodontology, Universidad Complutense de Madrid, Madrid, Spain, 2Unidad de Investigación, Spanish Society of Rheumatology, Madrid, Spain, 3Odontology, Dental Clinic Garnier, S/C Tenerife, Spain, 4Servicio de Reumatología. Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain, 5Rheumatology, Rheumatology Department. Hospital Universitario de Canarias, S/C TENERIFE, Spain, 6Rheumatology, Hospital de Canarias, S/C Tenerife, Spain

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Positivity of anti-citrullinated peptides antibodies (ACPA) indicates severity in Rheumatoid Arthritis (RA). There is evidence for chronic periodontitis (PD) in RA autoimmune response by periodontopathogenic bacteria, through protein citrullination. Thus, our objectives were: 1.To determine whether there is an association between PD and its severity with ACPA(+).2.To assess relationship between PD and ACPA titres.3.To identify association between certain periodontal parameters and ACPA titres and their possible cut-off points.

Methods: Cross-sectional study RA patients ≥18 yo with ≥4 teeth, no tooth cleaning, antibiotic intake 6 months before. Comorbidities, demographics, DAS-28(ESR), DAS-28(CRP) and SDAI were taken. Serum ACPA detection: Ab IgG against CCP2 (ELISA) Immunoscan CCPlus®test kit Euro Diagnostica: positive≥25 U/mL; ACPA titres stratification: Low (25–75), moderate (76–300) and high (>300). Periodontal parameters: plaque index (PI), bleeding on probing (Bop), probing pocket depth, clinical attachment level (CAL). CAL loss was categorized according to European Workshop 2005 (Tonetti):T level0 (absence), TL1 (mild), TL2 (severe). Statistical analysis: t-student, Kruskal Wallis, Chi- squared tests.

Results:

187 RA patients included (table 1), ACPA determined in 168 patients: 67.86% (+) with similar titres distribution: low 18%, moderate 26%, high 23%. PD:182 patients (97.3%): TL1 52.4%, TL2 44.9%. Although prevalence of severe PD/ACPA(+) was higher compared to PD/ACPA(-) (69.2% vs 30.7%), there was no association between PD and ACPA positivity/titres. Regarding the association with periodontal parameters, there was tendency of association between ACPA(+) and number of periodontal pockets ≥5mm, adjusted OR 1.02 (95% CI 0.9–1.04). However, there was a gradient effect, where number of pockets ≥ 5mm increased as ACPA titles increased, which was significant for high ACPA titres (p≤0.05, OR 1.03 95% CI 1.0–1.05). Moreover, RA patients who have 15 pockets ≥ 5mm showed 1.789-fold risk of having high ACPA titres (95% CI 0.9–1.04). However, there was a gradient effect, where number of pockets ≥ 5mm increased as ACPA titles increased, which was significant for high ACPA titres (p≤0.05, OR 1.03 95% CI 1.0–1.05). Moreover, RA patients who have 15 pockets ≥ 5mm showed 1.789-fold risk of having high ACPA titres (95% CI 0.9–1.04).

Conclusion: 1.Despite higher prevalence of severe PD in ACPA(+) patients, we found no association between the presence of PD and ACPA positivity nor with serum titres. 2. On analysis of ACPA titres in relation to the severity of the periodontal parameters, there was a “gradient” risk, where number of pockets ≥5mm increased as ACPA titres increased, which was significant for high ACPA titres.3. There was a lineal correlation between ACPA titres and number of pockets ≥5mm.

Disclosure: J. González Febles, None; F. Sánchez-Alonso, None; J. L. Garnier Rodríguez, None; M. Sanz Alonso, None; F. Díaz-González, None; B. Rodríguez Lozano, None.
Abstract Number: 488

**Increased Expression of TNF-α and PAD-2 in Human Monocytes Following Treatment with Protein Modified with Malondialdehyde-Acetaldehyde (MAA) and Citrulline**

Logan M. Duryee¹, Michael J. Duryee², Dahn L Clemens¹, Evan M. Ryan¹, Carlos D. Hunter², Lynell W. Klassen³, James R. O’Dell³, Daniel R. Anderson¹, Ted R. Mikuls⁴ and Geoffrey M. Thiele¹, ¹University of Nebraska Medical Center, Omaha, NE, ²Internal Medicine Division of Rheumatology, University of Nebraska Medical Center, Omaha, NE, ³Department of Internal Medicine, University of Nebraska Medical Center, Omaha, NE, ⁴Internal Medicine, Division of Rheumatology, University of Nebraska Medical Center, Omaha, NE

**First publication:** September 18, 2017

**SESSION INFORMATION**

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

**Background/Purpose:** We have previously shown that malondialdehyde-acetaldehyde (MAA) and citrullinated proteins are present together in the synovial tissues of rheumatoid arthritis (RA) patients. Macrophages are a major source of not only TNF-α, but also PAD enzymes and are both involved in the progression of RA. MAA adducts and citrullinated proteins alone have the ability to increase TNF-α release in many different cell types. Therefore, the objective of this study was to determine if proteins modified with both MAA and citrulline increase the expression and secretion of both PAD and TNF-α in a human monocytic cell line.

**Methods:** THP-1 cells were grown and activated with PMA. Following serum starvation the cells were incubated with either 50 µg/ml of human albumin (ALB), ALB-MAA, ALB-Citrulline (CIT) and ALB-MAA-CIT for 4 hours. Supernatants were collected and assayed for TNF-α protein by a commercial ELISA kit. RNA was extracted from the cells and subjected to RT-PCR for expression of PAD-2, PAD-4, and TNF-α.

**Results:** Human monocytic cells exposed to ALB-MAA significantly increased levels of TNF-α protein from 35.5 ± 0.75 pg/ml to 146.8 ± 33.55 pg/ml compared to ALB alone (P<0.01) (A). The addition of ALB-MAA-CIT significantly increased the secretion 435.5 ± 17.88 pg/ml (P<0.001) when compared to ALB-MAA (A). Cells incubated with ALB-MAA-CIT showed and increased expression of TNF-α mRNA by 6 fold (698.6 ± 96.62 RQ) compared to MAA-ALB (20.09 ± 6.48 RQ) (P<0.001) (B). PAD-2 mRNA was increased following exposure to both ALB-MAA (1.79 ± 0.96 RQ) and ALB-MAA-CIT (4.87 ± 1.71 RQ) (compared to each other (P<0.05), although only the latter achieved statistical significance compared to ALB alone (P<0.02) (C). No increase in PAD-4 mRNA was detected in any of the groups. Additionally, results from the stimulation by ALB-CIT were not different that ALB alone.

**Conclusion:** We and others have shown that MAA-modified proteins and citrullinated proteins alone can activate macrophages to release TNF-α. Until now, no studies have reported on the effects of these modified protein moieties commonly found in RA. The significantly increased expression of TNF-α and PAD-2 mRNA in human macrophages following exposure to ALB-MAA-CIT, supported by the clinical observation that these protein(s) are found together in synovial tissues strongly suggests a role in the pathogenesis of RA.
Disclosure: L. M. Duryee, None; M. J. Duryee, None; D. L. Clemens, None; E. M. Ryan, None; C. D. Hunter, None; L. W. Klassen, None; J. R. O'Dell, Medac, 5, Coherus, 5; D. R. Anderson, None; T. R. Mikuls, BMS, 2, Ironwood Pharm, 2, Pfizer Inc, 5, NIH, VA, 2; G. M. Thiele, None.


Abstract Number: 489

**Endotypic Clustering of Rheumatoid Arthritis Patients through the Use of Tissue Specific Serum Biomarkers Identifies Structural Progressors**

**Joseph Patrick Michele Blair**¹, Cecilie Liv Bager¹, Line Mærsk Staunstrup¹, Henning Bay Nielsen¹, Morten Karsdal² and Anne-C. Bay-Jensen³, ¹ProScion, Herlev, Denmark, ²Biomarkers and Reseacrh, Nordic Bioscience, Herlev, Denmark, ³Biomarkers and Reseach, Nordic Bioscience, Herlev, Denmark

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Treatment of RA patients is guided by measures of disease activity such as DAS28, best practice recommendation, and less often by a treat-to-target approach. This is due to a lack of diagnostic tools that can make an objective endotypic profile of the patient allowing for better targeted treatment. Another challenge is that traditionally used biomarkers reflect the level of systemic inflammation (e.g. cytokines) rather than the affected tissue. The aims were to test a novel combination of blood-based biomarkers reflecting tissue turnover and inflammation to identify patients with different forms of RA. In addition, we investigated whether such endotypes are associated with clinical disease activity and structural progression.

**Methods:**

Post-hoc analysis was conducted on a cohort of patients with active and moderate-severe RA from a biomarker sub-study of LITHE, a phase III clinical trial (N=741). Only patients from the placebo arm were considered, who had serological biomarkers measured at both baseline (BL) and week 4, as well as bone erosion (ERN) measured at BL and week 52 (n=69). Progression was defined as a positive absolute change in ERN from BL to week 52. The following biomarkers reflecting tissue metabolite were measured in BL samples: PIINP and C2M (cartilage formation/degradation); CTX-I, OC PINP and ICTP (bone resorption and formation); C1M and C3M (interstitial matrix degradation); C4M and C6M (basement membrane degradation; and CRPM and VICM (inflammation).
All serum measurements were log transformed and normalized to have values between zero and one. Unsupervised hierarchical clustering was then performed using serological biomarkers taken at BL and week 4. The significance of change in ERN of each group was tested using a Mann-Whitney U test.

**Results:**

Hierarchical clustering revealed two main clusters. Cluster A (see figure) is defined by low levels of collagen biomarkers and varying levels of other biomarkers. Cluster B displays high level of bone, connective tissue and basement membrane markers, and low levels of the cartilage markers. Ten of the 12 biomarkers were significantly lower in cluster A than in cluster B ($p < 0.5$). Cluster A can be divided into several subgroups characterised by high bone biomarkers and low bone biomarkers respectively. Due to the small population size in this study, the significance of these clusters was not investigated.

There is a trend showing that patients in cluster B have a higher DAS28 score at BL ($p = 0.08$). The change in ERN was significantly different between the clusters ($p = 0.04$) indicating group B (55% progressors) progresses faster than group A (29%).

**Conclusion:**
Using hierarchical clustering we were able to identify different endotypes of structural progression, including faster progressors in most need of treatment. Other likely endotypes were also identified, which shall be investigated further.

Disclosure: J. P. M. Blair, ProScion, 3; C. L. Bager, ProScion, 3; L. M. Staunstrup, ProScion, 3; H. B. Nielsen, ProScion, 3; M. Karsdal, Nordic Bioscience Diagnostic, 1; A. C. Bay-Jensen, Nordic Bioscience Diagnostic, 3.


Abstract Number: 490

Clinical and Biomarker Factors in the Prediction of Future Inflammatory Arthritis in ACPA Positive Subjects without Inflammatory Arthritis at Baseline

John P. Gerstenberger¹, Colin I. O'Donnell², Sarah L. Dill³, Randall Tagg⁴, Masoud Asadi-Zeydabadi⁴, M. Kristen Demoruelle⁵, V. Michael Holers⁶ and Kevin D. Deane⁷, ¹Department of Medicine, University of Colorado Denver School of Medicine, Aurora, CO, ²University of Colorado Denver School of Medicine, Aurora, CO, ³Division of Rheumatology, University of Colorado Denver School of Medicine, Aurora, CO, ⁴Department of Physics, University of Colorado Denver, Denver, CO, ⁵1775 Aurora Ct, ¹775 Aurora Ct, Aurora, CO, ⁶Rheumatology Division, University of Colorado School of Medicine, Aurora, CO, ⁷Division of Rheumatology, University of Colorado School of Medicine, Aurora, CO

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Antibodies to citrullinated protein antigens (ACPA) can identify individuals who may develop future inflammatory arthritis (IA) and classifiable rheumatoid arthritis (RA). Indeed, there are clinical trials underway where ACPA(+) individuals are treated to determine how IA/RA can be prevented or delayed. However, not all ACPA(+) subjects progress to IA/RA within the 2-3 years that is often duration for a clinical prevention trial. As such, identifying ways to predict which ACPA(+) subjects will most likely progress to IA/RA within defined time periods could improve selection of individuals for RA prevention trials as well as help to improve understanding of the biology of IA/RA development.

Methods:
21 ACPA(+) (CCP3, Inova) individuals without historical or current IA were identified at a Colorado-based health-fair. These individuals were followed prospectively for up to 24 months for incident IA/RA. Clinical and examination factors, and biomarkers including the shared epitope, CCP3, RF-IgM (Inova), and high sensitivity C-reactive protein (hsCRP), were evaluated to determine which factors predicted incident IA/RA. Specifically, optimal levels for association with IA/RA of autoantibodies and hsCRP were determined with machine learning techniques, and these optimal levels were then evaluated with other factors to identify the overall best models for discrimination of the development of IA/RA.

Results:
9 of 21 subjects (43%) developed IA/RA after a median of 11 months (Table 1). In univariate analyses of baseline factors, only self-reported joint stiffness was significantly associated with the development of IA/RA. Results from AUC analyses incorporating various variables are presented in Table 2. Overall, models using a combination of demographic and clinic factors, and optimized biomarker levels, had the highest discrimination (AUC 1.0) for the development of future IA/RA.

**Conclusion:**

Individuals at high risk for progression to IA/RA can be identified through health-fair evaluations for ACPA. Furthermore, clinically-obtainable factors including biomarkers that are optimized using machine learning techniques can be used to determine with high discrimination which serum ACPA(+) individuals will develop IA/RA within 24 months. Caveats include that this is a small sample set with potential overfitting of the models in regard to the optimized levels of biomarkers; therefore, these findings need additional validation. Nevertheless, this approach appears useful to better identify candidates for IA/RA preventive interventions.
Table 1. Descriptions and univariate analyses of baseline variables of subjects identified with anti-CCP3 positivity in absence of IA

<table>
<thead>
<tr>
<th></th>
<th>Incident IA/RA N=9</th>
<th>No IA/RA N=12</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Months to IA/RA or total follow-up, median (range)</td>
<td>11 (4-23)</td>
<td>10 (6-24)</td>
<td>1.00</td>
</tr>
<tr>
<td>Age, median (range)</td>
<td>55 (40-73)</td>
<td>48 (29-83)</td>
<td>0.31</td>
</tr>
<tr>
<td>Female, N (%)</td>
<td>4 (44%)</td>
<td>6 (50%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Non-Hispanic White, N (%)</td>
<td>8 (89%)</td>
<td>9 (75%)</td>
<td>0.60</td>
</tr>
<tr>
<td>Ever Smoker, N (%)</td>
<td>6 (67%)</td>
<td>5 (42%)</td>
<td>0.39</td>
</tr>
<tr>
<td>Current Smoker, N (%)</td>
<td>0 (0%)</td>
<td>1 (8%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Pack-Years, median (range)</td>
<td>4 (0-18)</td>
<td>0 (0-18)</td>
<td>0.35</td>
</tr>
<tr>
<td>Weekly alcohol intake &gt;=1 unit, N (%)</td>
<td>8 (89%)</td>
<td>10 (83%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Self-report FDR, N (%)</td>
<td>2 (22%)</td>
<td>1 (8%)</td>
<td>0.55</td>
</tr>
<tr>
<td>Shared Epitope Positive, N (%)</td>
<td>5 (56%)</td>
<td>3 (25%)</td>
<td>0.20</td>
</tr>
<tr>
<td>CCP3 Positive, N (%) (&gt;=20 units)</td>
<td>9 (100%)</td>
<td>12 (100%)</td>
<td>1.00</td>
</tr>
<tr>
<td>CCP3 Level, median (range)</td>
<td>78 (27-262)</td>
<td>55 (24-377)</td>
<td>0.60</td>
</tr>
<tr>
<td>RF-IgM Positive, N (%) (&gt;=13.6 units)</td>
<td>3 (33%)</td>
<td>3 (25%)</td>
<td>1.00</td>
</tr>
<tr>
<td>RF-IgM Level, median (range)</td>
<td>7 (1-120)</td>
<td>2 (0-44)</td>
<td>0.55</td>
</tr>
<tr>
<td>hsCRP positive, N (%) (&gt;10 mg/L)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>1.00</td>
</tr>
<tr>
<td>hsCRP Level, median (range)</td>
<td>1.4 (0.2-5.3)</td>
<td>0.8 (0.3-5.1)</td>
<td>0.38</td>
</tr>
<tr>
<td>Self-Report Joint Pain (Any Joint of 68), N (%)</td>
<td>6 (67%)</td>
<td>3 (25%)</td>
<td>0.09</td>
</tr>
<tr>
<td>Self-Report Morning Joint Stiffness (Any duration, any joint of 68)*</td>
<td>6 (67%)</td>
<td>2 (17%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Subjects with &gt;=1 tender joint on 68 joint examination, N (%)</td>
<td>3 (33%)</td>
<td>0 (0%)</td>
<td>0.06</td>
</tr>
<tr>
<td># of Tender Joints on 68 joint examination, median (range)</td>
<td>0 (0-1)</td>
<td>0 (0-0)</td>
<td>1.00</td>
</tr>
<tr>
<td>Subjects with &gt;=1 swollen joint consistent with RA-like synovitis on 66 joint examination</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Meeting 2010 ACR/EULAR Criteria at time of development of inflammatory arthritis, N (%)</td>
<td>7 (78%)</td>
<td>0 (0%)</td>
<td>-</td>
</tr>
</tbody>
</table>

*No subject reported a duration of morning joint stiffness of >60 minutes; for all subjects, the overall median (range) of duration of joint stiffness was 20 minutes (0-60).
Table 2. Discrimination of future IA/RA Variables in model | AUC
---|---
Core variables* plus CCP3, RF-IgM and hsCRP at optimized cut-off levels*** | 1.0
Core variables* plus CCP3 and RF-IgM at standard cut-off levels | 0.90
Core variables* alone | 0.76

*Core variables include age, gender, race, history of smoking (ever/never), presence of shared epitope (present/absent), self-reported joint pain (present/absent), self-reported joint stiffness (present/absent), and joint tenderness on examination (present/absent).

**Standard biomarker cut-off levels for positivity are: CCP3 >=20 units; RF-IgM >13.6 units; hsCRP >10 mg/L.

***Optimized biomarker levels are: CCP3 >42.61 units; RF-IgM 0.69 units; hsCRP 0.85 mg/L.

Disclosure: J. P. Gerstenberger, None; C. I. O'Donnell, None; S. L. Dill, None; R. Tagg, None; M. Asadi-Zeydabadi, None; M. K. Demoruelle, None; V. M. Holers, None; K. D. Deane, Inova Diagnostics, Inc., 5.


Abstract Number: 491

**Streptococcus Species Enriched in the Oral Cavity of RA Patients: A Persistent Source of Peptidoglycan-Polysaccharide Polymers Which Drive Disseminated Synovial Inflammation**

Rabia Moentadj¹, Linda Rehaume², Paraic O Cuiv³, Kate Ormerod⁴, Muralidhara Maradana³, Vanessa Anne Lakis³, Mark Morrison², Philip Hugenholtz⁴, Helen Benham⁵, Kim-Anh Lê Cao⁶ and Ranjeny Thomas¹, ¹University of Queensland Diamantina Institute, Brisbane, Australia, ²The University of Queensland Diamantina Institute, Translational Research Institute, Brisbane, Australia, ³The University of Queensland Diamantina Institute, Brisbane, Australia, ⁴Australian Centre for Ecogenomics, The University of Queensland, Brisbane, Australia, ⁵The University of Queensland Faculty of Medicine, Brisbane, Australia, ⁶School of Mathematics and Statistics, Centre for Systems Genomics, The University of Melbourne, Melbourne, Australia

First publication: September 18, 2017

SESSION INFORMATION
Background/Purpose:

In Rheumatoid Arthritis (RA), genetic predisposition and environmental risk factors promote dysbiosis of oral and fecal microbiota. We hypothesized that specific microbial taxa (operational taxonomic units, OTUs) from the oral microbiota differentiate between RA and HC and that bacteria enriched in RA subjects directly promote inflammatory arthritis.

Methods:

We characterized a prospective cohort of RA probands, FDR and HC. Probands met ACR 2010 criteria and/or had a confirmed RA diagnosis. FDRs included parents, full siblings or offspring of an RA proband; HC were drawn from the community. From all individuals, we obtained demographics, medical history, epidemiological questionnaires and tissue collections. After DNA extraction from tongue swabs, we undertook targeted 16S rRNA gene sequencing of all samples and next-generation sequencing of 18 samples. Statistical analysis used the mixOmics R package. Axenic *Streptococcus* isolates (n=3 per group, 16 isolates) were produced.

Results:

116 RA patients, 63 FDR and 43 HC matched for age and gender were recruited. 56% of RA, 4% of FDR and 0% of HCs were ACPA+. Oral microbiota were altered in RA relative to HC. The oral OTU profile of some FDRs segregated with the RA patients and some segregated with HC. The oral community profile in RA was enriched in *Streptococcus, Rothia, Bifidobacteria, Actinomyces and Prevotella* spp. Axenic *Streptococcus* isolates grown from oral swabs from 16 individuals were characterised as *Streptococcus Salivarius, Streptococcus Parasanguinis* or *Streptococcus Infantis* using 16S rRNA sequencing. The abundance of Streptococcal spp. was strongly associated with smoking history. Streptococcal cell walls (SCW) were generated from reference *Streptococcus pyogenes* and each of the oral isolates. After one i.p. injection of purified peptidoglycan-polysaccharide polymers (PG-PS 10S) from *Streptococcus pyogenes* to ZAP-70W163C-mutant BALB/c (SKG) mice, significant acute and chronic swelling occurred in wrist and ankle joints.

Conclusion:

We demonstrate distinct oral community profiles in RA patients and FDR relative to HC, which are influenced by smoking. Thus, compound genetic and environmental risks may create niches for opportunistic pathogens, such as *Streptococcus*, before and after the development of RA. The chronicity of SCW-induced arthritis in SKG mice suggests inability of a genetically predisposed host to effectively clear PG-PS 10S, which is resistant to degradation in vivo. Dissemination of persistently activated macrophages loaded with inflammatory bacterial remnants from the oral mucosa to lymphoid organs and peripheral joints may propagate the presentation of bacterial antigens and macrophage-driven inflammation in RA.

Disclosure: R. Moentadj, None; L. Rehaume, None; P. O Cuiv, None; K. Ormerod, None; M. Maradana, None; V. A. Lakis, None; M. Morrison, None; P. Hugenholtz, None; H. Benham, AbbVie, 2,AbbVie, 8; K. A. Lê Cao, None; R. Thomas, None.


Abstract Number: 492

Is Leukotoxin_A Produced By Aggregatibacter Actinomycetemcomitans Important for Initiating Autoimmune Responses Underlying Rheumatoid Arthritis?
Background/Purpose: In a recent publication in Science Translational Medicine, Konig et al. (2016) describe a potential explanation for the link between periodontal infection and RA. They identify a specific periodontitis-associated bacterium: *Aggregatibacter actinomycetemcomitans* (Aa), which via its pore-forming toxin (leukotoxin A: LtxA) can dysregulate the activity of citrullinating enzymes in neutrophils. Furthermore, the authors report that the risk conferred by the most important genetic risk factor for RA: the HLA-DRB1 shared epitope (HLA SE) alleles, was limited to RA patients who had been exposed to Aa as determined by seropositivity to LtxA. Aiming to replicate their findings, we focused on two main questions: 1) is the increased exposure to Aa as measured by the presence of anti-LtxA-antibodies specific for RA, or also present in other forms of inflammatory arthritis? 2) can we replicate the finding that the association between HLA SE alleles and ACPA-positive RA is limited to the anti-LtxA-positive subset?

Methods: We established an ELISA against purified LtxA (acquired from the same source as in the original article) and tested sera from 594 patients from the Leiden Early Arthritis Clinic with various diagnoses, including RA, OA, SpA, PsA, sarcoidosis, and gout. Serial dilutions of a mix of 3 strongly positive RA patients were used as a standard, and the lowest point of the linear part of the standard curve (2000 AU/ml) was defined as the cut-off.

Results: As shown in Figure 1, anti-LtxA antibodies could be found in a substantial proportion of RA patients, but also in patients with other forms of arthritis. Within RA patients, there was no association with the presence of HLA SE alleles and/or ACPA, in contrast to the previous findings.

Conclusion: Although microbial influences may well be important in the development of RA, our results do not support a key role of exposure to LtxA originating from the periodontal pathogen Aa in linking the effect of the HLA SE alleles and periodontal disease to anti-citrullinated protein autoimmunity in RA.

**Figure 1.**

Distribution of anti-LtxA antibodies in sera of 594 patients suffering from early arthritis. Levels of anti-LtxA antibodies in the serum of each individual are shown.

LtxA Leukotxin A, RA Rheumatoid arthritis, Aa *Aggregatibacter actinomycetemcomitans*, OA Inflammatory osteoarthritis, SpA Spondylarthritis with peripheral arthritis, PsA Psoriatic arthritis, Sarc Sarcoidosis, ACPA anti-citrullinated protein antibodies, SE shared epitope. Red lines indicate the median level per group. The dashed line indicates the cut-off. The number of patients per group and percentage of patients positive according to the cut-off are shown underneath.
Methotrexate Is an Antibacterial Drug Metabolized By Human Gut Bacteria

Renuka R. Nayak1, Kye Stapleton-Gray2, Colleen O'Loughlin3, Michael Fischbach4 and Peter J. Turnbaugh5,
1Department of Medicine, Division of Rheumatology, Rosalind Russell / Ephraim P. Engleman Rheumatology Research Center, San Francisco, CA, 2Carnegie Mellon University, Pittsburgh, PA, 3University of California, San Francisco, San Francisco, CA, 4Department of Bioengineering and Therapeutic Sciences., University of California, San Francisco, San Francisco, CA, 5Microbiology and Immunology, University of California, San Francisco, San Francisco, CA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Rheumatoid arthritis (RA) is an autoimmune disease of unknown etiology causing inflammation and irreversible damage in joints and other organs. Methotrexate (MTX) is first-line therapy used in the treatment of RA. However, not all patients respond to MTX -- about 50-60% of patients require additional therapy. Because MTX is a folic acid analogue that may...
affect evolutionarily conserved pathways found in bacteria, we hypothesized that the gut microbiome is altered by MTX and that gut bacteria metabolize the drug. Since gut bacteria have been shown previously to metabolize many pharmacologic drugs, we also sought to investigate the impact of the microbiome on inter-individual variations in MTX response. Here, we focus on the response of bacteria to MTX and ask whether bacteria can metabolize MTX.

Methods:

We tested the in vitro growth of 40 gut bacterial isolates in response to MTX. The minimal inhibitory concentration (MIC), or the concentration of MTX required to suppress bacterial growth >90%, was identified for each isolate. We asked if these in vitro findings were recapitulated in vivo by colonizing germ-free mice with human gut bacteria and treating with daily oral MTX at high (50 mg/kg) and low (1 mg/kg) doses. Next, we asked if bacteria metabolized MTX by examining either pure bacterial cultures in vitro or human stool sample ex vivo. Samples were incubated with MTX and metabolism was measured using HPLC. In select cases, we also used UPLC-MS-MS to learn the identity of MTX metabolites.

Results:

MTX inhibited the growth of 33 of the 40 isolates examined. MICs ranged from 2 ug/ml to >900 ug/ml in vitro. At the Phylum level, Bacteroidetes tended to be sensitive and Firmicutes tended to be resistant to the antimicrobial effects of MTX (Wilcoxon rank sum, p=0.005). In vivo studies showed that high-dose MTX altered the humanized gut microbiome of mice compared to those that were saline-treated (ANOSIM, p=0.001). The relative abundance of Bacteroidetes decreased while Firmicutes increased, recapitulating what was seen in vitro. Low-dose MTX also produced changes to the microbiome, but this effect was subtler. We next asked whether gut bacteria metabolize MTX, and found that 8 possessed this ability in vitro. At least two species metabolized MTX into polyglutamated MTX, which is a novel finding that has not been described previously in the literature. In ex vivo studies, human fecal slurries incubated with MTX produced known as well as novel MTX metabolites.

Conclusion:

We conclude that MTX is an antibacterial drug. Furthermore, we find that gut bacteria metabolize MTX. One metabolite found in our study was polyglutamated MTX, which prior studies have shown to be associated with patient response. Our ongoing and future studies will examine the in vivo implications of these findings in mice and examine whether bacterial metabolism of MTX is associated with clinical response in patients. Our findings support the hypothesis that a patient's response to MTX may be influenced by their gut microbiome. Thus, the microbiome may be an important factor in predicting patient response to MTX and perhaps other rheumatologic medications as well.

Disclosure: R. R. Nayak, None; K. Stapleton-Gray, None; C. O'Loughlin, None; M. Fischbach, None; P. J. Turnbaugh, None.
Background/Purpose:
The mouth is the second most abundantly colonized mucosal surface in the human body. Periodontitis, a polymicrobial infectious and inflammatory disease of tooth-supporting structures, is associated with rheumatoid arthritis (RA) and may be caused by oral microbial dysbiosis, with shift toward pathogenic commensal species. Particular pathogens such as Porphyromonas gingivalis (Pg), and Aggregatibacter actinomycetemcomitans (Aa) have been implicated, but few studies have analyzed oral microbiota composition in RA patients.

Methods: 73 subjects, 33 RA patients, the majority with new-onset RA, all meeting 2010 ACR/EULAR criteria, 20 age- and gender-matched healthy subjects (HS) without periodontitis or RA, and 20 patients with chronic periodontitis who lacked RA (non-RA CP) completed standardized periodontal examination. Subgingival plaque samples (2 per subject) were evaluated for the presence of 40 bacterial taxa associated with periodontitis biofilms by checkerboard DNA-DNA hybridization.

Results: Typical of RA cohorts, the 33 patients were mainly female (85%) with median age of 51; 23 had DMARD-naive early disease, 58% had rheumatoid factor (RF) or anti-citrullinated protein antibody (ACPA). Only one currently smoked. The majority (91%) received regular dental care with cleanings every 6 months.

Of the RA patients, 10 (30%) had periodontal health, 13 (39%) had gingivitis, and 10 (30%) had periodontitis. Pocket depth, clinical attachment loss, and bleeding on probing were all increased in the 33 patients compared with HS (P<0.002).

The RA patients had a significantly higher total bacterial load in dental plaque (111.8 x 10^5) compared with HS (58.9 x 10^5, P=0.01) and non-RA CP (70.5 x 10^5, P=0.03). RA patients with periodontal health had lower bacterial burden than those with gingivitis and periodontitis (P=0.03). Seropositive RA patients also tended to have a higher oral bacterial load than seronegative patients. By phylum, RA patients had particularly higher levels of Actinobacteria, Proteobacteria, and Firmicutes compared to both HS and non-RA CP (P≤0.03), whereas Fusobacteria, Spirochaetes, and Bacteroidetes were elevated compared to HS (P≤0.03) but similar to non-RA CP.

Accounting for multiple comparisons, 21 of 40 individual microbes had higher DNA probe counts (levels) in RA patients versus HS (P ≤0.01), this included only 1 red-complex classic pathogen, Tannerella forsythia. Notably, levels of Pg, detected in 5 RA patients, were not significantly different from HS. Aa was detected in only one RA patient who also had periodontitis.

While none of the 40 organisms correlated directly with ACPA, 4 correlated with RF levels, particularly Eubacterium saburreum (R=0.549, P≤0.001), and 9 organisms correlated with swollen joint counts, 6 of which were Actinobacteria species.

Conclusion: Despite routine dental care and lack of smoking, new-onset RA patients had an abundance of oral bacteria, with expansion of pathogenic species seen in non-RA CP. Thus dysbiosis is a feature of the oral, as well as gut microbiome, in RA. Besides pathogens such as Pg and Aa, other oral microbes here were associated with RA autoantibodies and will require further study.

Disclosure: S. Arvikar, None; H. Hasturk, None; K. Strle, None; D. Nguyen, None; M. B. Bolster, Johnson and Johnson, 1,Eli Lilly and Company, 2,Rheumatology Research Foundation Amgen Fellow Award, 9; D. Collier, None; A. Kantarci, None; A. Steere, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-oral-microbiome-is-altered-in-patients-with-rheumatoid-arthritis

Abstract Number: 495
Efficacy of Tofacitinib in Patients with Moderate to Severe Rheumatoid Arthritis By Baseline C-Reactive Protein Levels and Erythrocyte Sedimentation Rates

Sergio Schwartzman¹, Ronald F van Vollenhoven², Alan K Matsumoto³, Dana Orange⁴, Shweta Shah⁵, Ryan DeMasi⁵, Haiyun Fan⁵, Palle Dahl⁶, Ann Wouters⁷ and Edward C. Keystone⁸, ¹Hospital for Special Surgery, New York, NY, ²Karolinska Institute, Stockholm, Sweden, ³Arthritis & Rheumatism Associates, Wheaton, MD, ⁴Rockefeller University; Hospital for Special Surgery; and New York Genome Center, New York, NY, ⁵Pfizer Inc, Collegeville, PA, ⁶Pfizer Inc, Ballerup, Denmark, ⁷Pfizer Inc, New York, NY, ⁸University of Toronto, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor for the treatment of RA. This post-hoc analysis investigated the impact of inflammation severity at baseline (BL) – measured by BL CRP levels and ESR – on efficacy and safety of tofacitinib.

Methods: Data were analyzed from studies of tofacitinib in RA patients (pts) with prior inadequate response (IR) to conventional synthetic (cs) or biologic (b) DMARDs, who initiated tofacitinib 5 mg or 10 mg BID as monotherapy or in combination with csDMARDs, mainly methotrexate. Data were pooled from 4 Phase 2 trials (NCT00413660; NCT00550446; NCT00603512; NCT00687193) and 5 Phase 3 randomized, double-blind, placebo-controlled trials (ORAL Scan [NCT00847613]; ORAL Solo [NCT00814307]; ORAL Sync [NCT00856544]; ORAL Standard [NCT00853385]; ORAL Step [NCT00960440]). Analyses were stratified by tertiles, by BL CRP and BL ESR levels, separately. Efficacy variables analyzed at Month (M) 6 included ACR20/50/70 response rates, and changes from BL to M6 in Clinical Disease Activity Index (CDAI), DAS28-4 (ESR), and Simple Disease Activity Index (SDAI). Summary/descriptive statistics were provided. Adverse events (AEs) to M6 were summarized. The results were not adjusted for multiplicity.

Results: The pooled population included 2,161 pts in the csDMARD-IR group and 512 pts in the bDMARD-IR group. Pt characteristics at BL (Table) were generally similar between groups and across CRP and ESR tertiles, except for RA duration. In both dose groups, ACR20/50/70 response rates at M6 were generally numerically higher with higher BL CRP for both csDMARD-IR and bDMARD-IR pts (Figure). Generally, a trend for greater improvement from BL in disease activity at M6 was observed with higher BL CRP but not with higher BL ESR. Proportion of pts with AEs, serious AEs, serious infections, and discontinuations due to AEs to M6 were generally similar regardless of BL CRP or ESR.

Conclusion: While efficacy outcomes in csDMARD-IR and bDMARD-IR RA pts were improved after 6 months’ administration of tofacitinib 5 and 10 mg BID across BL CRP/ESR tertiles, this post-hoc analysis suggests that ACR response rates and disease activity improvements may be numerically greater with higher BL CRP, especially in bDMARD-IR RA pts. Of interest, this was not noted with higher BL ESR. This disproportionate potential predictive value needs further investigation. Analyses investigating the impact of inflammation severity at BL on tofacitinib efficacy in pts with RA are warranted and will include data based on both CRP/ESR tertiles as well as Tender Joint Count (TJC) and Swollen Joint Count (SJC) tertiles.
Table. Baseline demographic and disease characteristics by CRP concentration:

<table>
<thead>
<tr>
<th>CRP, mg/L</th>
<th>cDMARD-IR</th>
<th>tofacitinib 5 mg BID</th>
<th>tofacitinib 10 mg BID</th>
<th>BDMARD-IR</th>
<th>tofacitinib 5 mg BID</th>
<th>tofacitinib 10 mg BID</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4.46</td>
<td>4.46-15.2</td>
<td>&gt;15.2</td>
<td>&lt;4.46</td>
<td>&lt;4.46-15.2</td>
<td>&gt;15.2</td>
<td>&lt;4.46</td>
</tr>
<tr>
<td>&lt;4.46</td>
<td>4.46-15.2</td>
<td>&gt;15.2</td>
<td>&lt;4.46</td>
<td>&lt;4.46-15.2</td>
<td>&gt;15.2</td>
<td>&lt;4.46</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>5.12 (2.1)</td>
<td>5.12 (2.1)</td>
<td>5.12 (2.1)</td>
<td>5.12 (2.1)</td>
<td>5.12 (2.1)</td>
<td>5.12 (2.1)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>56 (56%)</td>
<td>56 (56%)</td>
<td>56 (56%)</td>
<td>56 (56%)</td>
<td>56 (56%)</td>
<td>56 (56%)</td>
</tr>
<tr>
<td>ERA, years</td>
<td>7.5 (2.2)</td>
<td>7.5 (2.2)</td>
<td>7.5 (2.2)</td>
<td>7.5 (2.2)</td>
<td>7.5 (2.2)</td>
<td>7.5 (2.2)</td>
</tr>
</tbody>
</table>

Figure. ACR20/50/70 responses at M6 for tofacitinib 5 and 10 mg BID by baseline CRP concentrations (mg/L) in A) cDMARD-IR and B) BDMARD-IR pts

Disclosure: S. Schwartzman, AbbVie, Antares, Eli Lilly, Genentech, Janssen, Novartis, Pfizer Inc, Regeneron, Sanofi, UCB, 5, Crescendo Bioscience, Discus Analytics, National Psoriasis Foundation, 6, AbbVie, Crescendo Bioscience, Genentech, Janssen, Pfizer Inc, UCB, 8; R. F. van Vollenhoven, AbbVie, Amgen, Bristol-Myers Squibb, GSK, Pfizer Inc, Roche, UCB, 2, AbbVie, AstraZeneca, Biotest, Bristol-Myers Squibb, Celgene, Crescendo, Eli Lilly, GSK, Janssen, Merck, Novartis, Pfizer Inc, Roche, UCB, Vertex, 5; A. K. Matsumoto, AbbVie, Amgen, Bristol-Myers Squibb, Pfizer Inc, 2, AbbVie, Amgen, Bristol-Myers Squibb, Pfizer Inc, 5; D. Orange, None; S. Shah, Pfizer Inc, 1, Pfizer Inc, 3; R. DeMasi, Pfizer Inc, 1, Pfizer Inc, 3; H. Fan, Pfizer Inc, 1, Pfizer Inc, 3; P. Dahl, Pfizer Inc, 1, Pfizer Inc, 3; A. Wouters, Pfizer Inc, 1, Pfizer Inc, 3; E. C. Keystone, Pfizer Inc, 2, Pfizer Inc, 5, Pfizer Inc, 8.

Repeated Rituximab Infusions for the Therapy of Rheumatoid Arthritis Is Not Associated with Increased Rates of Serious Infections

Dimitrios A. Pappas¹,², George W. Reed¹,³, Steve Zlotnick⁴, Jennie Best⁴, Robert Magner³, Gioia Persuitte¹ and Jeffrey D Greenberg¹,⁵, ¹Corrona, LLC, Southborough, MA, ²Department of Medicine, Division of Rheumatology, Columbia University, College of Physicians and Surgeons, New York, NY, ³University of Massachusetts Medical School, Worcester, MA, ⁴Genentech, Inc., South San Francisco, CA, ⁵NYU School of Medicine, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Extended observations in clinical trials have not demonstrated an increased risk of serious infection events (SIE) in patients with rheumatoid arthritis (RA) treated with rituximab.¹ However, continuous surveillance using large-scale observational data is of importance. Therefore, the objective of this study was to evaluate the rate of SIEs among patients with RA who received only an initial rituximab infusion vs those retreated with ≥ 1 rituximab infusion during the first year of therapy, and also to describe characteristics of rituximab-treated patients who experienced an SIE vs those who did not.

Methods: Patients with RA enrolled in the Corrona registry (NCT01402661) and treated with rituximab were followed until their most recent Corrona registry visit, first SIE, switch to another biologic or targeted synthetic disease-modifying antirheumatic drug, or 12 months after the most recent infusion with no further retreatment – whichever occurred first. The rate of SIEs was estimated in the overall population as well as in patients retreated with ≥ 1 infusion every 12 months after rituximab initiation and in those who did not receive a repeat infusion in the first 12 months. Patient characteristics were compared between those who experienced an SIE and those who did not.

Results: A total of 1361 patients with 1821 patient-years (PY) of follow-up were included; there were 59 SIEs for a rate of 3.24 SIE/100 PYs. 637 patients (46.8%) received ≥ 1 rituximab retreatment during the first 12 months and 724 (53.2%) received only the initial infusion. In the retreatment population there were 40 SIEs per 1312.8 PY for a rate (95% CI) of 3.05/100 PY (2.18-4.15), and in the no retreatment population there were 19 SIEs per 508.71 PY for a rate (95% CI) of 3.73/100 PY (2.25-5.83). The Kaplan-Meier curve depicting the occurrence of SIEs in the 2 cohorts during the first year of follow-up is shown (Figure). In the 59 patients (4.3%) who experienced an SIE, the mean (SD) number of rituximab infusions was 1.88 (1.18), compared with 2.07 (1.70) in the 1302 patients (95.7%) who did not experience an SIE. Patients who experienced an SIE vs those who did not were older (mean age [SD]: 62.9 [9.9] vs 58.1 [12.55] years), had longer disease duration (19.1 [13.1] vs 13.6 [10.4] years), were more frequently diabetic (16.9% vs 8.3%) and more frequently had cardiovascular disease (25.4% vs 12.8%), prior history of SIEs (18.6% vs 5.8%) and pulmonary disease (10.2% vs 4.8%). There were no differences in other clinical and medication history characteristics; steroid therapy was similar between the groups.

Conclusion: Retreatment with rituximab infusions did not result in a higher rate of SIEs in this study. Patients who experienced an SIE had a higher prevalence of risk factors for infections.

References:
The JAK1 Selective Inhibitor Filgotinib Regulates Both Enthesis and Colon Inflammation in a Mouse Model of Psoriatic Arthritis

Catherine Robin-Jagerschmidt¹, Stéphanie Lavazais¹, Florence Marsais¹, Maté Ongenaert², Alain Monjardet¹, Angélina Cauvin¹, Corinne Saccomani¹, Isabelle Parent¹, Didier Merciris¹, Emilie Chauvet¹, Roland Blanqué¹, Monica Borgonovi¹, Lién Lepescheux¹, Marielle Auberval¹, Sonia Dupont¹, Philippe Clément-Lacroix¹ and René Galien¹, ¹Galapagos SASU, Romainville, France, ²Galapagos NV, Mechelen, Belgium

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Because of their pleotropic role in cytokine signaling, Janus Kinases (JAKs) are key players in inflammatory diseases. Among the 4 members of the JAK family (JAK1, JAK2, JAK3, TYK2), JAK1 has been demonstrated as a validated target in inflammatory diseases with filgotinib (GLPG0634, GS-6034) displaying efficacy and safety in several phase 2 studies in rheumatoid arthritis (RA) patients. Psoriatic arthritis (PsA) is a heterogeneous chronic inflammatory disease characterized by the association of skeletal involvement and extra-skeletal symptoms such as psoriasis and Inflammatory Bowel Disease (IBD) with common findings including enthesitis and dactylitis. Current treatments include anti-TNFα, anti-IL-17 and anti-IL-12/IL-23 antibodies with varying success rates. The involvement of several pro-inflammatory cytokines suggests that therapies targeting JAKs may be effective. To gain insight in the potential of a JAK1-selective inhibitor in PsA, we evaluated filgotinib efficacy in a mouse model of PsA induced by the overexpression of IL-23.

Methods:

Overexpression of IL-23 was induced by hydrodynamic delivery of mIl23 enhanced Episomal Expression Vector (SBI) to male B10.RIII mice. Evolution of paw and finger inflammation was assessed by clinical scoring as well as by in vivo molecular imaging (Bruker In-Vivo Xtreme imaging system). Enthesis, colon and fingers were collected for transcriptomic analysis. Using immunohistochemistry, infiltration of immune inflammatory cells and pSTAT3 positive cells, were analyzed in Achilles’ enthesis, subcutaneous area and skin. Colon was also collected for histology and gene expression analysis.

Results:

High levels of IL-23 were maintained during the time-course of the study and were correlated with severity of finger and paw swelling and associated with inflammation of enthesis and finger as observed in PsA patients. Only moderate inflammation of the colon was observed. Filgotinib significantly improved clinical scoring and tended to prevent neutrophil/granulocyte infiltration in paw (notably at earlier time points) while strongly decreasing immune cell infiltration in the skin. Transcriptomic analysis of enthesis, fingers and colon showed that filgotinib reversed the effect of IL-23 for a consistent number of genes. Notably, expression of some upregulated inflammatory genes in enthesis and/or fingers (CCL20, CXCL1, IL-22, MMP9 and TNFα) as well as the target-related gene Mx2 were reduced. Filgotinib also significantly counteracted pSTAT3 induction in the subcutaneous area and in the epidermis (mainly concentrated in proliferating keratinocytes) further demonstrating target engagement in the diseased tissue.

Conclusion:

In a mouse model of PsA, filgotinib improved global clinical score and decreased signs of inflammation in hindlimbs. Target engagement both in hindlimbs and colon was also demonstrated. These data support the evaluation of filgotinib in patients with PsA.

References:


Disclosure: C. Robin-Jagerschmidt, Galapagos SASU, 3; S. Lavazais, Galapagos SASU, 3; F. Marsais, Galapagos SASU, 3; M. Ongenaert, Galapagos NV, 3; A. Monjardet, Galapagos SASU, 3; A. Cauvin, Galapagos SASU, 3; C. Sacconmani, Galapagos SASU, 3; I. Parent, Galapagos SASU, 3; D. Merciris, Galapagos SASU, 3; E. Chanudet, Galapagos SASU, 3; R. Blanqué, Galapagos SASU, 3; M. Borgonovi, Galapagos SASU, 3; L. Lepescheux, Galapagos SASU, 3; M. Auberval, Galapagos SASU, 3; S. Dupont, Galapagos SASU, 3; P. Clément-Lacroix, Galapagos SASU, 3; R. Galien, Galapagos SASU, 3.


Abstract Number: 498
Response to Abatacept of Different Patterns of Interstitial Lung Disease in Rheumatoid Arthritis. Multicenter Study of 63 Patients

Carlos Fernández-Díaz\textsuperscript{1}, Santos Castañeda\textsuperscript{2}, Clara Ojeda-Garcia\textsuperscript{3}, Alejandro Olivé\textsuperscript{4}, Patricia Carreira\textsuperscript{5}, Trinidad Perez Sandoval\textsuperscript{6}, Miriam Retuerto Guerrero\textsuperscript{7}, Evelin Cecilia Cervantes Pérez\textsuperscript{8}, Samantha Rodriguez\textsuperscript{9}, Bryan Josue Robles Flores\textsuperscript{10}, Blanca Hernández-Cruz\textsuperscript{11}, Ana Urruticoechea-Arana\textsuperscript{12}, Olga Maiz\textsuperscript{13}, Desiree Palma\textsuperscript{14}, Luis Arboleya\textsuperscript{15}, Gema Bonilla\textsuperscript{16}, Manuel Rodríguez-Gómez\textsuperscript{17}, Concepción Delgado\textsuperscript{18}, Rosa Expósito\textsuperscript{19}, Ana Ruibal Escribano\textsuperscript{20}, Luis Arboleya\textsuperscript{21}, Gema Bonilla\textsuperscript{22}, Manuel Rodríguez-Gómez\textsuperscript{23}, Concepción Delgado\textsuperscript{24}, Rosa Expósito\textsuperscript{25}, Ana Ruibal Escribano\textsuperscript{26}, Juan Blanco Madrigal\textsuperscript{27}, José Antonio Bernal\textsuperscript{28}, Paloma Vela\textsuperscript{29}, Belen Alvarez-Rodriguez\textsuperscript{30}, María Concepción Fito Manteca\textsuperscript{31}, Javier Narváez\textsuperscript{32}, Manuel Jose Moreno\textsuperscript{33}, Mireia López-Corbeto\textsuperscript{34}, Natalia Mena-Vazquez\textsuperscript{35}, S. Romero-Yuste\textsuperscript{36}, Clara Aguilera-Cros\textsuperscript{37}, Sergi Ordoñez\textsuperscript{38}, Ignacio Villa-Blanco\textsuperscript{39}, Nuria Vegas-Revenga\textsuperscript{40}, Victor Mora-Cuesta\textsuperscript{41}, Javier Lorícera\textsuperscript{42}, Miguel Angel González-Gay\textsuperscript{43}, José Luis Hernández\textsuperscript{44} and Ricardo Blanco\textsuperscript{45}, \textsuperscript{1}Rheumatology, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Spain, Santander, Spain, \textsuperscript{2}Hospital Universitario de la Princesa, Madrid. Spain, Madrid, Spain, \textsuperscript{3}Rheumatology, Hospital Virgen de la Macarena, Sevilla, Spain, \textsuperscript{4}Rheumatology, Hospital Germans Trias i Pujol, Badalona, Spain, \textsuperscript{5}Department of Rheumatology, Hospital Universitario 12 de Octubre, Madrid, Spain, \textsuperscript{6}Rheumatology, Hospital de León, LEÓN, Spain, \textsuperscript{7}Rheumatology, Hospital de León, Leon, Spain, \textsuperscript{8}Rheumatology, Hospital Santiago de Compostela, Santiago de Compostela, Spain, \textsuperscript{9}H. German Trias., Barcelona, Spain, \textsuperscript{10}Rheumatology, Hospital Universitario Puerta de Hierro Majadahonda, Madrid, Spain, \textsuperscript{11}Rheumatology, Hospital Universitario Virgen Macarena, Sevilla, Spain, \textsuperscript{12}Rheumatology Department. Hospital Can Misses, IBIZA, Spain, \textsuperscript{13}Hospital Donostia. Spain, San Sebastian, Spain, \textsuperscript{14}Rheumatology, Rafael Mendez Hospital, Spain., Lorca (Murcia), Spain, \textsuperscript{15}Rheumatology, Hospital Universitario Central de Asturias, Oviedo, Spain, \textsuperscript{16}Hospital Universitario La Paz, Madrid, Spain, \textsuperscript{17}Complejo Hospitalario Universitario de Ourense, Ourense, Spain, \textsuperscript{18}H. Clínico Universitario Lozano Blesa, Zaragoza, Spain, \textsuperscript{19}Rheumatology, Hospital Comarcal de Laredo. Spain, Laredo, Spain, \textsuperscript{20}Rheumatology, Hospital Universitario de Araba, Vitoria, Spain, \textsuperscript{21}Rheumatology, Hospital de Basurto, Bilbao, Spain, \textsuperscript{22}Reumatología, Hospital Universitario del Vinalopó, Elche, Spain, \textsuperscript{23}Reumatología, Hospital General Universitario de Alicante. Alicante. Spain, Alicante, Spain, \textsuperscript{24}Hospital Txagorritxu, Vitoria, Spain, \textsuperscript{25}Reumatología, Hospital de Navarra, Pamplona, Spain, \textsuperscript{26}Reumatología Department, Hospital de Bellvitge. Barcelona. Spain, L’Hospitalet de Llobregat, Spain, \textsuperscript{27}Rheumatology, Hospital Virgen de la Arrixaca, MURCIA, Spain, \textsuperscript{28}Hospital Universitario Vall d’Hebron, Barcelona, Spain, \textsuperscript{29}Rheumatology, Hospital Universitario de Malaga, Malaga, Spain, \textsuperscript{30}H. Pontevedra, Pontevedra, Spain, \textsuperscript{31}Rheumatology, Hospital Virgen del Rocío, Sevilla, Spain, \textsuperscript{32}Hospital Universitario Arnau de Vilanova, Vilanova, Spain, \textsuperscript{33}Hospital de Sierrañallana, Sierrañallana, Spain, \textsuperscript{34}Neumology, Hospital Universitario Marqués de Valdecilla, IDIVAL,, Santander, Spain, \textsuperscript{35}Division of Internal Medicine., Hospital Universitario Marqués de Valdecilla, IDIVAL,, Santander, Spain

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Disease modifying antirheumatic drugs (DMARD) such as methotrexate (MTX), ) or antiTNFα have been implicated in exacerbation of Interstitial lung disease (ILD) of rheumatoid arthritis (RA). Several radiological patterns of ILD have been described: i) usual interstitial pneumonia (UIP), ii) nonspecific interstitial pneumonia (NSIP), iii) obliterating bronchitis (OB), and iv) Organized pneumonia (OP)

Our aime was to assess the response to Abatacept (ABA) in these patterns of ILD
Methods: Retrospective multicenter study of RA-ILD treated with ABA. ILD was diagnosed by high-resolution CT scan (HRCT) and classified in radiological patterns (Travis et al). We consider 3 subgroups: a) UIP, b) NSIP and c) "other" (OB, OP or mixed). ABA was used at standard dose. We assessed: a) Dyspnea (Medical Research Council-modified scale; significant variations≥1); B) Respiratory function tests; significant changes≥10% in forced vital capacity (FVC) and DLCO≤10%, c) HRCT, d) DAS28. A comparative study was performed for the qualitative variables (Fisher test) between the baseline and 3, 6 and 12 months.

Results: We included 63 patients 29 UIP 17 NSIP 17 Others (27 women/36 men), mean age; 63.1±9.6 years. Patients with RA was seropositive in 85.7%. The ILD was related to DMARDs: MTX (4), etanercept (3), adalimumab (3), certolizumab (2), Infliximab (1). ABA was used in monotherapy (26) or combined with other DMARDs (37); LFN (15), Cyclosporin (1), sulfasalazine (4), MTX (6), hydroxychloroquine (10), azathioprine (4), chloroquine (1). Figure shows the evolution in the available cases. A significant improvement in dyspnea and HRCT. DLCO remained stable in most patients regardless of the radiological pattern. The activity of RA (DAS28) also improved.

![UIP EVOLUTION](image)

![EVOLUTION NSIP](image)

![EVOLUTION "OTHERS"](image)

Figure a), b) c): Evolution of different ILD patterns.

Conclusion: ABA appears to be effective in ILD associated-RA, including the pattern of poor prognosis (UIP).

Disclosure: C. Fernández-Díaz, None; S. Castañeda, None; C. Ojeda-Garcia, None; A. Olivé, None; P. Carreira, None; T. Perez Sandoval, None; M. Retuerto Guerrero, None; E. C. Cervantes Pérez, None; S. Rodriguez, None; B. J.
Assessment of Early Improvement in Pain and Other ACR Components As Predictors for Achieving Low Disease Activity or Remission in Three Phase 3 Trials of RA Patients Treated with Baricitinib

Michael Weinblatt¹, Mark C. Genovese², Joel Kremer³, Luna Sun⁴, Himanshu Patel⁴, Alisa Koch⁴, David Muram⁴, Jeffrey R. Curtis⁵, Cynthia J. Larmore⁴ and Baojin Zhu⁴, ¹Brigham and Women’s Hospital, Boston, MA, ²Stanford University Medical Center, Palo Alto, CA, ³The Center for Rheumatology, Albany Medical College, Albany, NY, ⁴Eli Lilly and Company, Indianapolis, IN, ⁵University of Alabama at Birmingham, Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
The purpose of this analysis was to assess whether early improvement in ACR components could act as predictors of low disease activity (LDA) or remission (REM) at Week 12 in Phase 3 trials of baricitinib (BARI). The patient’s assessment of pain, a patient-reported outcome measured by a 0-100 mm visual analog scale (VAS), was a focus for this analysis.

Methods:
In RA-BEAM¹, 487 patients with inadequate response (IR) to methotrexate (MTX) were randomized to BARI 4 mg once daily. In RA-BEACON², a trial of bDMARD-IR patients, 174 patients were randomized to BARI 2 mg and 177 to BARI 4 mg once daily. In RA-BUILD³, a trial with csDMARDs-IR patients, 229 patients were randomized to BARI 2 mg and 227 to BARI 4 mg once daily. LDA was defined as CDAI ≤10 or DAS28-ESR ≤3.2 and REM as CDAI ≤ 2.8 or DAS28-ESR<2.6 at Week 12. Early improvement, changes from baseline to Week 4, for each of the ACR components (pain VAS, PtGA, PGA, swollen joint count, tender joint count [TJC], HAQ-DI, hsCRP, and ESR) was evaluated on their respective predictability for LDA or REM at Week 12 using area under the curve (AUC) of receiver operating characteristic (ROC) curves. The optimum cutoff-point in percent improvement at Week 4 was evaluated based the Youden index and the negative predictive value (NPV).

Results:
Early improvement in pain VAS, TJC, PtGA, and PGA had among the highest predictability, whereas hsCRP and ESR had among the lowest, as measured by AUC of ROC (Figs. 1 and 2 for RA-BEAM data), for achieving both LDA and REM at Week 12. A threshold of 30-50% improvement in pain from baseline to Week 4 had the optimum range for predicting LDA
and REM at Week 12 (Table). Consistent results were observed for csDMARD-IR and bDMARD-IR patients, and these results were similar for both BARI 2 mg and BARI 4 mg doses.

**Conclusion:**

In these trials, patients with a lack of early response to BARI, as assessed by improvement in pain VAS at Week 4, tended to be less likely to achieve LDA or REM at Week 12 vs. patients with an early response. A minimum of 30% improvement in pain resulted in optimum NPV in this analysis.

**References:**

Figure 1. ROC curves for week 4 improvement in selected ACR components to predict week 12 CDAl-defined LDA for BARI patients in RA-BEAM

- Pain VAS
- SJIC28
- PhGA
- InaCRP

ACR Component | AUC (%)
--- | ---
Pain VAS | 72
Physician Global Assessment of Disease Activity (PGAs) | 75
Sjögren’s Joint Count-28 (SJIC28) | 75
Tender Joint Count-28 (TJC28) | 75
HAQ-DI* | 65
InaCRP | 54
ESR* | 56

* Curve not shown due to space constraints

Figure 2. ROC curves for week 4 improvement in selected ACR components to predict week 12 CDAl-defined remission for BARI patients in RA-BEAM

- Pain VAS
- SJIC28
- PhGA
- InaCRP

ACR Component | AUC (%)
Pain VAS | 81
Physician Global Assessment of Disease Activity (PGAs) | 80
Sjögren’s Joint Count-28 (SJIC28) | 80
Tender Joint Count-28 (TJC28) | 79
HAQ-DI* | 73
InaCRP | 51
ESR* | 52

* Curve not shown due to space constraints
Table. Negative Predictive Value (NPV) for improvement in pain VAS at Week 4 to predict low disease activity (LDA) and remission at Week 12

<table>
<thead>
<tr>
<th>Study</th>
<th>Pain Improvement at Week 4</th>
<th>DAS28-ESR</th>
<th>CDAI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>LDA Remission</td>
<td>LDA Remission</td>
</tr>
<tr>
<td>RA-BEAM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bari 4 mg</td>
<td>≥30%</td>
<td>93%</td>
<td>99%</td>
</tr>
<tr>
<td></td>
<td>≥40%</td>
<td>89%</td>
<td>95%</td>
</tr>
<tr>
<td></td>
<td>≥50%</td>
<td>88%</td>
<td>96%</td>
</tr>
<tr>
<td>RA-BEACON</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bari 2 mg</td>
<td>≥30%</td>
<td>94%</td>
<td>98%</td>
</tr>
<tr>
<td></td>
<td>≥40%</td>
<td>94%</td>
<td>98%</td>
</tr>
<tr>
<td></td>
<td>≥50%</td>
<td>94%</td>
<td>97%</td>
</tr>
<tr>
<td>Bari 4 mg</td>
<td>≥30%</td>
<td>96%</td>
<td>96%</td>
</tr>
<tr>
<td></td>
<td>≥40%</td>
<td>95%</td>
<td>97%</td>
</tr>
<tr>
<td></td>
<td>≥50%</td>
<td>94%</td>
<td>96%</td>
</tr>
<tr>
<td>RA-BUILD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bari 2 mg</td>
<td>≥30%</td>
<td>88%</td>
<td>95%</td>
</tr>
<tr>
<td></td>
<td>≥40%</td>
<td>89%</td>
<td>96%</td>
</tr>
<tr>
<td></td>
<td>≥50%</td>
<td>88%</td>
<td>95%</td>
</tr>
<tr>
<td>Bari 4 mg</td>
<td>≥30%</td>
<td>91%</td>
<td>96%</td>
</tr>
<tr>
<td></td>
<td>≥40%</td>
<td>90%</td>
<td>95%</td>
</tr>
<tr>
<td></td>
<td>≥50%</td>
<td>87%</td>
<td>94%</td>
</tr>
</tbody>
</table>

Disclosure: M. Weinblatt, Amgen, BMS, Crescendo Bioscience, UCB, Genzyme, 2,Amgen, Abbvie, BMS, Eli Lilly and Company, Gilead, Merck, Pfizer, Novartis, Roche, UCB, Crescendo Bioscience, Genzyme, Samsung, 5; M. C. Genovese, AbbVie, Eli Lilly and Company, Galapagos, Gilead, Pfizer, 5,AbbVie, Eli Lilly and Company, Galapagos, Gilead, Pfizer, 2; J. Kremer, Abbvie, Amgen, BMS, Genentech, GSK, Eli Lilly and Company, Novartis,Pfizer, 5,AbbVie, Genentech, Eli Lilly and Company, Novartis, Pfizer, 2,Corrona, 1,Corrona, 3; L. Sun, Eli Lilly and Company, 1,Eli Lilly and Company, 3; H. Patel, Eli Lilly and Company, 1,Eli Lilly and Company, 3; A. Koch, Eli Lilly and Company, 1,Eli Lilly and Company, 3; D. Muram, Eli Lilly and Company, 1,Eli Lilly and Company, 3; J. R. Curtis, AbbVie, Amgen, BMS, Janssen, Pfizer, Roche/Genentech, Corrona, UCB, 2,AbbVie, Amgen, BMS, Janssen, Pfizer, Roche/Genentech, Corrona, UCB, 5,University of Alabama at Birmingham, 3; C. J. Larmore, Eli Lilly and Company, 1,Eli Lilly and Company, 3; B. Zhu, Eli Lilly and Company, 1,Eli Lilly and Company, 3.


Abstract Number: 500

Low Patient Global Assessment Scores in Rheumatoid Arthritis Are Associated with Pain and Physical Function in Patients Treated with Tofacitinib: A Post-Hoc Analysis of Phase 3 Trials
Vibeke Strand1, Rieke Alten2, Jeffrey Kaine3, Arif Soonasra4, Christopher W Murray4, Haiyun Fan4, Christopher F Mojcik5 and Gene Wallenstein6, 1Stanford University, Palo Alto, CA, 2Schlosspark-Klinik, University Medicine Berlin, Berlin, Germany, 3Sarasota Arthritis Research Center, Sarasota, FL, 4Pfizer Inc, Collegeville, PA, 5Pfizer Inc, New York, NY, 6Pfizer Inc, Groton, CT

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). We examined associations of pain and physical function with Patient Global Assessment of disease activity (PtGA) in patients (pts) receiving tofacitinib 5 mg twice daily (BID) or placebo (PBO) with background conventional synthetic disease-modifying antirheumatic drugs (csDMARDs).

Methods: This was a post-hoc analysis of pooled data from three Phase 3 randomized controlled trials (ORAL Sync [NCT00856544]; ORAL Standard [NCT00853385]; ORAL Scan [NCT00847613]) in pts with inadequate responses to biologic or csDMARDs (ORAL Sync) or methotrexate (MTX) (ORAL Standard/Scan). Patient Assessment of Arthritis Pain (Pain; visual analog scale [VAS] 0–100 mm), Health Assessment Questionnaire-Disability Index (HAQ-DI), and PtGA (VAS 0–100 mm) scores were recorded at baseline (BL) and Month (M) 3. Associations between ‘low global assessment of disease’ (PtGA ≤20) and mild Pain (VAS score ≤30) or HAQ-DI response (score ≤0.5 or change from baseline ≥0.22) were independently evaluated. Relationships between PtGA and Pain or HAQ-DI were assessed using Spearman rank correlation coefficients at BL and M3 without adjustments for multiplicity.

Results: At M3 216/695 (31.1%) pts receiving tofacitinib 5 mg BID and 62/366 (16.9%) pts receiving PBO reported PtGA ≤20; 346/695 (49.8%) and 109/366 (29.8%) had Pain scores ≤30; 514/694 (74.1%) and 197/365 (54.0%) were HAQ-DI responders. Across treatment groups, of pts reporting PtGA ≤20 at M3, a larger proportion also reported Pain ≤30 vs Pain >30 (Table 1); of pts with PtGA >20, a high proportion had Pain scores >30. Of pts reporting PtGA ≤20 at M3, a larger proportion were HAQ-DI responders than HAQ-DI non-responders. Similar associations were noted between PtGA ≤20 and moderate or substantial improvements in Pain (data not shown). The proportions of pts reporting PtGA ≤20 and Pain ≤30 were numerically higher than those with PtGA ≤20 and HAQ-DI responses. Pain and HAQ-DI were significantly correlated with PtGA at BL and M3 (p<0.0001); correlation coefficients appeared numerically higher between PtGA and Pain than HAQ-DI (Table 2).

Conclusion: In this post-hoc analysis, reports of low PtGA scores were associated with low pain levels and improved physical function across treatment groups. Attainment of low PtGA levels appears more associated with improvements in pain than HAQ-DI responses.
Table 1. Summary of patients reporting low global assessment of disease (PtGA ≤20) according to Pain ≤30 and HAQ-DI response at Month 3

<table>
<thead>
<tr>
<th></th>
<th>PtGA ≤20</th>
<th></th>
<th>PtGA &gt;20</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N (%)</td>
<td>95% CI</td>
<td>n/N (%)</td>
<td>95% CI</td>
</tr>
<tr>
<td>Pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤30</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tofacitinib 5 mg BID</td>
<td>207/216 (95.8)</td>
<td>93.2, 98.5</td>
<td>139/479 (29.0)</td>
<td>25.0, 33.1</td>
</tr>
<tr>
<td>Placebo</td>
<td>57/62 (91.9)</td>
<td>85.2, 98.7</td>
<td>52/304 (17.1)</td>
<td>12.9, 21.3</td>
</tr>
<tr>
<td>&gt;30</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tofacitinib 5 mg BID</td>
<td>9/216 (4.2)</td>
<td>1.5, 6.8</td>
<td>340/479 (71.0)</td>
<td>66.9, 75.1</td>
</tr>
<tr>
<td>Placebo</td>
<td>5/62 (8.1)</td>
<td>1.3, 14.8</td>
<td>252/304 (82.9)</td>
<td>78.7, 87.1</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Responders³</td>
<td>Tofacitinib 5 mg BID</td>
<td>190/216 (88.0)</td>
<td>83.6, 92.3</td>
<td>324/478 (67.8)</td>
</tr>
<tr>
<td>Placebo</td>
<td>47/62 (75.8)</td>
<td>65.2, 86.5</td>
<td>150/303 (49.5)</td>
<td>43.9, 55.1</td>
</tr>
<tr>
<td>Non-responders</td>
<td>Tofacitinib 5 mg BID</td>
<td>26/216 (12.0)</td>
<td>7.7, 16.4</td>
<td>154/478 (32.5)</td>
</tr>
<tr>
<td>Placebo</td>
<td>15/62 (24.2)</td>
<td>13.5, 34.9</td>
<td>153/303 (50.5)</td>
<td>44.9, 56.1</td>
</tr>
</tbody>
</table>

³HAQ-DI score ≤0.5 or change from baseline ≥0.22
BID, twice daily; CI, confidence interval; HAQ-DI, Health Assessment Questionnaire-Disability Index; Pain, Patient Assessment of Arthritis Pain; PtGA, Patient Global Assessment of disease activity

Table 2. Spearman rank correlations of PtGA vs Pain and HAQ-DI at Baseline and Month 3 (absolute values)

<table>
<thead>
<tr>
<th>Correlation with PtGA</th>
<th>Baseline</th>
<th>Month 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Correlation coefficient</td>
</tr>
<tr>
<td>Pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tofacitinib 5 mg BID</td>
<td>695</td>
<td>0.74205 ≤0.0001</td>
</tr>
<tr>
<td>Placebo</td>
<td>365</td>
<td>0.77131 &lt;0.0001</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tofacitinib 5 mg BID</td>
<td>693</td>
<td>0.48120 &lt;0.0001</td>
</tr>
<tr>
<td>Placebo</td>
<td>364</td>
<td>0.46114 &lt;0.0001</td>
</tr>
</tbody>
</table>

BID, twice daily; HAQ-DI, Health Assessment Questionnaire-Disability Index; Pain, Patient Assessment of Arthritis Pain; PtGA, Patient Global Assessment of disease activity

Disclosure: V. Strand, AbbVie, Amgen, Bristol Myers Squibb, CORRONA, Eli Lilly, Janssen, Novartis, Pfizer Inc, UCB, 5; R. Alten, None; J. Kaine, Pfizer Inc, Bristol-Myers Squibb, 8; A. Soonasra, Pfizer Inc, 1,Pfizer Inc, 3; C. W. Murray,
Patient-Reported Outcomes of Long-Term Upadacitinib Use in Patients with Rheumatoid Arthritis: Interim Analysis Results of a Phase 2, Open-Label Extension Study

Vibeke Strand\textsuperscript{1}, Namita Tundia\textsuperscript{2}, and Alan Friedman\textsuperscript{2}, \textsuperscript{1}Stanford University, Palo Alto, CA, \textsuperscript{2}AbbVie Inc., North Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Janus kinase (JAK) inhibitors are being evaluated for treatment of active rheumatoid arthritis (RA). The efficacy of upadacitinib (UPA), a selective JAK inhibitor, in improving patient-reported outcomes (PROs) has been demonstrated.\textsuperscript{1} These analyses evaluated the long-term benefits of UPA on PROs in patients with active RA.

Methods: M13-538 (NCT02049138) is an ongoing, Phase 2 open-label extension study designed to assess long-term efficacy and safety of UPA in RA patients who completed BALANCE I and BALANCE II randomized controlled trials (RCTs) where doses of 3, 6, 12 and 18 mg BID were evaluated. All eligible patients received UPA 6 mg bid within 30 days of completing either RCT. At weeks 6 and 12, patients with <20\% improvement from baseline in tender (TJC) and swollen joint counts (SJC) received a dose increase to 12 mg bid UPA. After 6 weeks on 12 mg bid, patients failing to achieve ≥20\% improvement in TJC and SJC discontinued treatment. After week 6, at the discretion of the investigator, the dose could be titrated to 12 mg bid for patients who did not meet low disease activity as defined by the Clinical Disease Activity Index. Continuing patients were divided into 3 cohorts: those who remained on 6 mg bid (never titrated); who increased to and remained on 12 mg bid (titrated up); and who increased to 12 mg bid and subsequently reduced to 6 mg bid only for a safety concern or intolerability (titrated up and down). PROs included: Patient's Global Assessment of Disease Activity (PtGA), Pain by Visual Analog Scale (Pain VAS), Health Assessment Questionnaire – Disability Index (HAQ-DI), FACIT – Fatigue Scale (FACIT-F), Work Instability Score for Rheumatoid Arthritis (RA-WIS), and EuroQoL-5D (EQ-5D). For this interim analysis, data collected on or before January 13, 2017 were analyzed. Mean changes from baseline and 95\% confidence intervals (CI) were calculated for each PRO at week 48.

Results: 493 patients received UPA. Across cohorts, mean age was 53–56 years, 78\%–87\% were female, and mean duration of RA 8.6–9.5 years. The total patient population exposure to UPA was 725.1 patient-years; with 78\% of patients having exposure of ≥12 months and 72\% having exposure of ≥18 months. At week 48, patients within all cohorts reported improvements across all PROs (Table). The majority of patients who never titrated dose reported the largest improvements from baseline across PROs at week 48, followed by those who titrated up or up and down.

Conclusion: Patients treated with UPA maintained clinically meaningful improvements in disease activity, pain, physical functioning, fatigue, work functioning, and overall health status till week 48.

Reference
Table. Mean change in PRO scores from baseline to week 48.

<table>
<thead>
<tr>
<th>PRO</th>
<th>Never Titrated&lt;sup&gt;a&lt;/sup&gt;</th>
<th>N=328</th>
<th>Titrated Up and Not Down&lt;sup&gt;a&lt;/sup&gt;</th>
<th>N=150</th>
<th>Titrated Up and Down&lt;sup&gt;a&lt;/sup&gt;</th>
<th>N=15</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Week 48</td>
<td>Change</td>
<td>n</td>
<td>Week 48</td>
<td>Change</td>
</tr>
<tr>
<td>PtGA</td>
<td>250</td>
<td>23.4</td>
<td>−39.6</td>
<td>114</td>
<td>36.6</td>
<td>−31.2</td>
</tr>
<tr>
<td>Pain VAS</td>
<td>250</td>
<td>21.3</td>
<td>−42.7</td>
<td>114</td>
<td>35.5</td>
<td>−32.0</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>249</td>
<td>0.7</td>
<td>−0.8</td>
<td>114</td>
<td>1.0</td>
<td>−0.6</td>
</tr>
<tr>
<td>FACIT-F</td>
<td>249</td>
<td>40.6</td>
<td>10.8</td>
<td>114</td>
<td>36.3</td>
<td>10.5</td>
</tr>
<tr>
<td>RA-WIS&lt;sup&gt;b&lt;/sup&gt;</td>
<td>60</td>
<td>5.2</td>
<td>−7.3</td>
<td>41</td>
<td>9.3</td>
<td>−4.2</td>
</tr>
<tr>
<td>EQ-5D</td>
<td>249</td>
<td>77.4</td>
<td>26.5</td>
<td>114</td>
<td>70.5</td>
<td>19.8</td>
</tr>
</tbody>
</table>

<sup>a</sup>Titration status was determined based on dosing information up to the cutoff date for the interim analysis.

<sup>b</sup>Only included patients working at the time of questionnaire administration.

Disclosure: V. Strand, AbbVie, Amgen, AstraZeneca, BMS, Celgene, Genentech, GSK, Janssen, Lilly, Novartis, Pfizer, Regeneron, Sanofi, and UCB, 5,AbbVie, Amgen, AstraZeneca, BMS, Celgene, Genentech, GSK, Janssen, Lilly, Novartis, Pfizer, Regeneron, Sanofi, and UCB, 9; N. Tundia, AbbVie, 3; AbbVie, 1; A. Friedman, AbbVie, 3, AbbVie, 1.


Abstract Number: 502

Reduction in Disease Activity in Patients with RA and an Inadequate Response to MTX: Baricitinib Compared to Adalimumab and Placebo

Peter Nash<sup>1</sup>, Janet E. Pope<sup>2</sup>, Anabela Cardoso<sup>3</sup>, Marta Casillas<sup>3</sup>, Douglas E. Schlichting<sup>3</sup>, Baojin Zhu<sup>3</sup>, Scott D. Beattie<sup>3</sup> and Josef S. Smolen<sup>4</sup>,<sup>4</sup>University of Queensland, Brisbane, Australia, <sup>2</sup>St. Joseph's Health Care, London, ON, Canada, <sup>3</sup>Eli Lilly and Company, Indianapolis, IN, <sup>4</sup>Rheumatology, Medical University of Vienna, Vienna, Austria

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM
**Background/Purpose:** Baricitinib (BARI), is an oral Janus kinase (JAK)1/JAK2 selective inhibitor for treatment of patients with moderately to severely active RA. RA-BEAM was a phase 3 study in patients with RA and an inadequate response to MTX (MTX-IR) in which BARI demonstrated significant improvements in ACR20 response rates and DAS28-CRP compared to placebo (PBO) and adalimumab (ADA). This abstract examines the effects of baricitinib on disease activity scores and the improvement of disease activity compared to PBO and ADA utilizing CDAI, which does not include acute phase reactants and only uses clinical measures (adding physician and patient global assessments, to tender and swollen joint counts).

**Methods:** In RA-BEAM, 1305 patients were treated with PBO (N=488), ADA (N=330) or BARI 4 mg (N=487) and continued to receive background MTX. CDAI for the three treatment groups was determined at baseline (mean [SD] of 37.6 [12.8], 38.1 [12.0], 37.9 [13.0] for PBO, BARI and ADA, respectively) and at each visit post baseline for up to 24 weeks, and for the BARI and ADA groups for up to 52 weeks. In this analysis, CDAI and the improvement from baseline to Weeks 12 and 24 were compared between treatment groups using analysis of covariance (ANCOVA). The proportions of patients reaching a disease activity threshold and improvement threshold at Weeks 12 and 24 were compared between treatment groups using logistic models. Analyses were not adjusted for multiplicity. Missing values were imputed using modified last observation carried forward.

**Results:** At baseline, across all treatment arms, 91% of patients had high disease activity and 9% had moderate disease activity. Treatment with BARI resulted in significantly lower mean disease activity at Weeks 12 and 24 than PBO (p<0.001 at both Weeks 12 and 24) and ADA (p=0.008, Week 12; p=0.035, Week 24). Fewer patients treated with BARI (16.4%) remained in high disease activity at Week 24 compared to PBO (47.6%, p<0.001) and ADA (22.9%, p=0.017). Patients treated with BARI had significantly greater improvement in the mean disease activity compared to PBO (p<0.001) and ADA (p=0.023) at 24 weeks. A larger proportion of patients receiving BARI (86.2%) were able to achieve at least a 12-point reduction in CDAI, the minimal clinically important difference in disease activity improvement, by Week 24 compared to patients receiving PBO (52.4%, p<0.001) or ADA (77.5%, p=0.001) (Table and graphs).

**Conclusion:** In MTX-IR RA patients with moderate to severe disease activity, BARI significantly reduced the overall disease activity compared to PBO and ADA.
## CDAI: Disease Activity from Baseline to Weeks 12 and 24

<table>
<thead>
<tr>
<th></th>
<th>Week 12</th>
<th></th>
<th></th>
<th>Week 24</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo (N=488)</td>
<td>BARI 4-mg (N=487)</td>
<td>ADA (N=330)</td>
<td>Placebo (N=488)</td>
<td>BARI 4-mg (N=487)</td>
<td>ADA (N=330)</td>
</tr>
<tr>
<td><strong>CDAI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LS Mean (SE)</td>
<td>24.7 (0.6)</td>
<td>15.6 (0.7)***++</td>
<td>18.1 (0.8)***</td>
<td>23.9 (0.7)</td>
<td>13.4 (0.7)***++</td>
<td>15.5 (0.8)***</td>
</tr>
<tr>
<td>% Patients with HDA (CDAI &gt;22)</td>
<td>49.9</td>
<td>21.1***</td>
<td>26.2***</td>
<td>47.6</td>
<td>16.4***+</td>
<td>22.9***</td>
</tr>
<tr>
<td>% Patients with MDA (10&lt; CDAI ≤22)</td>
<td>32.8</td>
<td>37.5</td>
<td>39.6</td>
<td>31.3</td>
<td>31.3</td>
<td>28.4</td>
</tr>
<tr>
<td>% Patients with LDA§ (2.8&lt; CDAI ≤10)</td>
<td>15.5</td>
<td>32.9***+</td>
<td>27.4***</td>
<td>16.9</td>
<td>36.4***</td>
<td>36.9***</td>
</tr>
<tr>
<td>% Patients with remission (CDAI ≤2.8)</td>
<td>1.9</td>
<td>8.5***</td>
<td>6.7***</td>
<td>4.1</td>
<td>15.9***</td>
<td>11.9***</td>
</tr>
<tr>
<td><strong>Improvement in CDAI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LS Mean Change from baseline (SE)</td>
<td>-12.9 (0.6)</td>
<td>-22.0 (0.6)***++</td>
<td>-19.5 (0.7)***</td>
<td>-13.6 (0.6)</td>
<td>-24.2 (0.6)***++</td>
<td>-22.1 (0.7)***</td>
</tr>
<tr>
<td>LS Mean % Improvement (SE)</td>
<td>33.1 (1.5)</td>
<td>58.3 (1.5)***++</td>
<td>51.9 (1.8)***</td>
<td>35.1 (1.7)</td>
<td>64.1 (1.7)***++</td>
<td>58.9 (2.0)***</td>
</tr>
<tr>
<td>% Patients with CDAI improvement ≥6</td>
<td>71.1</td>
<td>91.8***</td>
<td>88.6***</td>
<td>71.5</td>
<td>92.9***</td>
<td>90.1***</td>
</tr>
<tr>
<td>% Patients with CDAI improvement ≥12</td>
<td>51.4</td>
<td>83.1*****</td>
<td>70.1***</td>
<td>52.4</td>
<td>86.2***++</td>
<td>77.5***</td>
</tr>
</tbody>
</table>

***p<0.001 vs. placebo; +p<0.05, ++p<0.01, +++p<0.001 vs. adalimumab using ANCOVA after adjusting for baseline value, region, and joint erosion status for the CDAI improvement outcome; adjusting for region and joint erosion status for the CDAI actual score; and using logistic regression models after adjusting for region and joint erosion status for the proportions of patients reaching a disease activity threshold and improvement threshold. §p-values for between treatment comparisons were based on CDAI ≤10. ANCOVA=Analysis of Covariance; ADA=adalimumab; BARI=baricitinib; CDAI=Clinical Disease Activity Index; HDA=high disease activity; LDA=low disease activity; LS=least squares; MDA=moderate disease activity; SE=standard error
Disclosure: P. Nash, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Hospira, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, 5, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Hospira, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, 8; J. E. Pope, AbbVie, Amgen, Bayer, BMS, Celtrion, Eli Lilly and Company, Merck, Novartis, Pfizer, Roche, UCB, 5; Amgen, Bayer, BMS, GSK, Merck, Novartis, Pfizer, Roche, UCB, 2; A. Cardoso, Eli Lilly and Company, 1; Eli Lilly and Company, 3; M. Casillas, Eli Lilly and Company, 1; Eli Lilly and Company, 3; D. E. Schlichting, Eli Lilly and Company, 1; Eli Lilly and Company, 3; B. Zhu, Eli Lilly and Company, 1; Eli Lilly and Company, 3; S. D. Beattie, Eli Lilly and Company, 1; Eli Lilly and Company, 3; J. S. Smolen, AbbVie, Amgen, Astra-Zeneca, Astro, BMS, Celgene, Celltrion, Chugai, Gilead, Glaxo, ILTOO, Janssen, Eli Lilly and Company, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi-Aventis, UCB, 5; AbbVie, Janssen, Eli Lilly and Company, MSD, Pfizer, Roche, 2; AbbVie, Amgen, Astra-Zeneca, Astro, BMS, Celgene, Celltrion, Chugai, Gilead, Glaxo, ILTOO, Janssen, Eli Lilly and Company, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi-Aventis, UCB, 8.


Abstract Number: 503
BMS-986195 Is a Highly Selective and Rapidly Acting Covalent Inhibitor of Bruton’s Tyrosine Kinase with Robust Efficacy at Low Doses in Preclinical Models of RA and Lupus Nephritis


First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: BMS-986195 is a potent, covalent, irreversible inhibitor of Bruton’s tyrosine kinase (BTK), a member of the Tec family of non-receptor tyrosine kinases essential in antigen-dependent B-cell signaling and function. BTK also plays a critical signaling role downstream of low-affinity activating Fcγ receptors (FcγR) in monocyctic cells, high-affinity immunoglobulin E receptors (FcεRI) in granulocytes, and the RANK receptor on osteoclasts. Pharmacologic inhibition of BTK, therefore, represents an intriguing approach for the treatment of autoimmune disorders such as RA and lupus. The present report details the cellular and in vivo pharmacology of BMS-986195.

Methods: The potency and selectivity of BMS-986195 were evaluated against a panel of 245 kinases. Cellular assays included antigen-dependent responses in B cells and immune complex-stimulated cytokine production in human peripheral blood mononuclear cells. BTK inactivation was determined using active-site probe-based measures of unmodified active sites, and these assays were used to determine the in vitro rate of inactivation in human whole blood, as well as the kinetics and dose relationships of in vivo inactivation of BTK in mice and cynomolgus monkeys after oral administration. The efficacy of BMS-986195 was evaluated in collagen-induced arthritis (CIA) and collagen antibody-induced arthritis (CAIA) models in mice, as well as against nephritis in NZB/W lupus-prone mice.

Results: BMS-986195 is a potent and highly selective inhibitor of BTK, which acts by covalently modifying an active-site cysteine residue. The compound is more than 5000-fold selective for BTK over all kinases outside of the Tec family, and selectivity ranges from 9- to 1010-fold within the Tec family. BMS-986195 inactivated BTK in human whole blood with a rapid rate of inactivation (3.5x10^{-4} nM^{-1} min^{-1}) and potently inhibited antigen-dependent interleukin-6 production, CD86 expression and proliferation in B cells (IC_{50} <1 nM) without effect on antigen-independent measures in the same cells. A similar potency was measured against FcγR-dependent TNF-α production in human cells. In mice, a dose as low as 0.5 mg/kg, taken orally (PO) daily (QD), resulted in peak BTK inactivation of 98% after only the second dose. BTK was inactivated to similar levels in whole blood, lymph nodes and spleen in a dose-dependent manner. BMS-986195 demonstrated robust efficacy in murine models of RA including CIA and CAIA, protecting against clinically evident disease, histologic joint damage and bone mineral density loss. In both models, maximal efficacy was observed at doses ≤0.5 mg/kg PO QD, which achieved ≥95% inactivation of BTK in vivo. At similar doses, the compound was also highly protective against nephritis in the NZB/W mouse model of lupus. To investigate the dynamics of BTK inactivation and resynthesis of BTK, cynomolgus monkeys were given single or multiple doses of BMS-986195. 100% peak inactivation of BTK was obtained with a single administration of BMS-986195 at 0.5 mg/kg PO.

Conclusion: The high selectivity, rapid rate of BTK inactivation and robust efficacy at low doses in preclinical models of RA and lupus support investigation of BMS-986195 in human autoimmune disorders.

Disclosure: J. Burke, Bristol-Myers Squibb, 3; K. Gillooly, Bristol-Myers Squibb, 3; M. Pattoli, Bristol-Myers Squibb, 3; L. Cheng, Bristol-Myers Squibb, 3; S. Skala, Bristol-Myers Squibb, 3; E. Heimrich, Bristol-Myers Squibb, 3; T. Taylor, Bristol-Myers Squibb, 3; C. Pulicicchio, Bristol-Myers Squibb, 3; D. Kukral, Bristol-Myers Squibb, 3; T. Petrone, Bristol-Myers Squibb, 3; I. Catlett, Bristol-Myers Squibb, 3; N. Zheng, Bristol-Myers Squibb, 3; W. Li, Bristol-Myers Squibb, 3; S. Watterson, Bristol-Myers Squibb, 3; J. Tino, Bristol-Myers Squibb, 3.
Abstract Number: 504

Monotherapy with Filgotinib, a JAK1-Selective Inhibitor, Reduces Disease-Related Biomarkers in Rheumatoid Arthritis Patients

Peter C. Taylor1, René Galien2, Annegret Van der Aa3, Corinne Jamoul3, Pille Harrison3, Chantal Tasset3, Yang Pan4, Lovely Goyal4, Wanying Li4 and Jacqueline Tarrant4, 1Kennedy Institute of Rheumatology, London, United Kingdom, 2Galapagos SASU, Romainville, France, 3Galapagos NV, Mechelen, Belgium, 4Gilead Sciences, Foster City, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The JAK1 selective inhibitor filgotinib (GLPG0634, GS-6034) has been evaluated in a 24-week phase 2B study (DARWIN 2) as monotherapy in active rheumatoid arthritis (RA) patients who were methotrexate inadequate responders and has shown a good safety and efficacy profile1. A broad range of serum biomarkers were measured to characterize the mode of action of filgotinib.

Methods: Serum samples from RA patients who received either placebo (PBO), or filgotinib monotherapy at 100mg or 200mg once daily (QD) were collected at baseline, weeks 4 and 12 and analyzed for 35 biomarkers by validated single- or multi-plex immunoassays. Median % changes from baseline for biomarkers are reported. Wilcoxon rank-sum test assessed the significance of the difference between filgotinib treated groups and PBO.

Results: Filgotinib monotherapy was associated with significant reductions in a broad panel of immune- and tissue-related biomarkers relevant to RA, compared to placebo (27/35 markers). The largest reductions were in the pro-inflammatory markers IL-6, SAA, and CRP (58-68% median reduction from baseline to week 12, p<0.01). Other top-ranked biomarkers by effect size were related to joint degradation (MMP1, 3, YKL-40), immune cell recruitment (CXCL10, CXCL13), and T\textsubscript{H1}/T\textsubscript{H17} cells (IL-23 and IL-10) (reductions of 28-31%, p<0.05 for all). These effects were present from week 4 and were maintained at week 12. Other biomarker changes also support down-modulation of T\textsubscript{H1} (IL-2, IFN-γ, IL-12), T\textsubscript{H2} (IL-4, IL-5, IL-13), B cell (CXCL13, IL-7, IL-21), and myeloid cells (GM-CSF, MIP-1α). Filgotinib monotherapy did not increase leptin above PBO-levels.

Table: Median percent change from baseline of biomarkers at week 12
<table>
<thead>
<tr>
<th></th>
<th>PBO (N=61)</th>
<th>FILGO 200mg QD (N=65)</th>
<th></th>
<th>PBO (N=61)</th>
<th>FILGO 200mg QD (N=65)</th>
<th></th>
<th>PBO (N=61)</th>
<th>FILGO 200mg QD (N=65)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BAFF</td>
<td>-3</td>
<td>-1 NS</td>
<td>IL-6</td>
<td>2</td>
<td>-58 **</td>
<td>MIP-1β</td>
<td>3</td>
<td>3 NS</td>
</tr>
<tr>
<td>CRP</td>
<td>-27</td>
<td>-68 **</td>
<td>IL-7</td>
<td>0</td>
<td>-21 **</td>
<td>MMP1</td>
<td>5</td>
<td>-28 *</td>
</tr>
<tr>
<td>CXCL10</td>
<td>-4</td>
<td>-31 *</td>
<td>IL-8</td>
<td>-7</td>
<td>-8 NS</td>
<td>MMP3</td>
<td>6</td>
<td>-31 ***</td>
</tr>
<tr>
<td>CXCL13</td>
<td>-4</td>
<td>-30 **</td>
<td>IL-10</td>
<td>13</td>
<td>-26 ***</td>
<td>RESISTIN</td>
<td>1</td>
<td>-16 **</td>
</tr>
<tr>
<td>EGF</td>
<td>11</td>
<td>21 NS</td>
<td>IL-12</td>
<td>6</td>
<td>-23 ***</td>
<td>SAA</td>
<td>0</td>
<td>-68 ***</td>
</tr>
<tr>
<td>GM-CSF</td>
<td>6</td>
<td>-21 ***</td>
<td>IL-13</td>
<td>13</td>
<td>-20 ***</td>
<td>sgp130</td>
<td>-2</td>
<td>0 NS</td>
</tr>
<tr>
<td>ICAM-1</td>
<td>-4</td>
<td>-8 NS</td>
<td>IL-17A</td>
<td>1</td>
<td>-16 **</td>
<td>TNFα</td>
<td>5</td>
<td>-14 **</td>
</tr>
<tr>
<td>IFN-γ</td>
<td>6</td>
<td>-23 ***</td>
<td>IL-21</td>
<td>4</td>
<td>-23 ***</td>
<td>TNF-RI</td>
<td>0</td>
<td>-18 ***</td>
</tr>
<tr>
<td>IL-1β</td>
<td>8</td>
<td>-16 ***</td>
<td>IL-23</td>
<td>-4</td>
<td>-31 ***</td>
<td>VCAM-1</td>
<td>0</td>
<td>-9 ***</td>
</tr>
<tr>
<td>IL-2</td>
<td>10</td>
<td>-21 ***</td>
<td>LEPTIN</td>
<td>20</td>
<td>26 NS</td>
<td>VEGF</td>
<td>0</td>
<td>-22 **</td>
</tr>
<tr>
<td>IL-4</td>
<td>21</td>
<td>-22 ***</td>
<td>MCP-1</td>
<td>-5</td>
<td>-13 NS</td>
<td>YKL-40</td>
<td>-4</td>
<td>-31 **</td>
</tr>
<tr>
<td>IL-5</td>
<td>3</td>
<td>-14 ***</td>
<td>MIP-1α</td>
<td>3</td>
<td>-6 **</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

p-values comparing % changes between filgotinib and PBO groups: NS, p>0.05; *p<0.05; **p<0.01; ***p<0.001

**Conclusion:** Filgotinib reduces the systemic levels of pro-inflammatory and RA-associated tissue-derived biomarkers. These effects on biomarkers in multiple disease processes and immune cell subsets provide insight into the efficacy shown by filgotinib evaluated as monotherapy in the Phase 2B study.


**Disclosure:** P. C. Taylor, UCB, 2,GlaxoSmithKline, 2,Galapagos NV, 2,Eli Lilly and Company, 2,UCB, 5,Eli Lilly and Company, 5,Pfizer Inc, 5,Galapagos NV, 5,Merck Pharmaceuticals, 5,GlaxoSmithKline, 5,Abbvie, 5,Bristol-Myers Squibb, 5,Janssen Pharmaceutica Product, L.P., 5,Novartis Pharmaceutical Corporation, 5,Sandoz, 5,Biogen Idec, 5; R. Galien, Galapagos SASU, 3; A. Van der Aa, Galapagos NV, 1,Galapagos NV, 3; C. Jamoul, Galapagos NV, 3; P. Harrison, Galapagos NV, 1,Galapagos NV, 3; C. Tasset, Galapagos NV, 1,Galapagos NV, 3; Y. Pan, Gilead Sciences, 3; L. Goyal, Gilead Sciences, 3; W. Li, Gilead Science, 3; J. Tarrant, Gilead Sciences, 3.


**Abstract Number:** 505

**Exposure-Response Analyses of the Effect of Upadacitinib on ACR Responses in the Phase 2b Rheumatoid Arthritis Trials in Patients with Inadequate Response to Methotrexate or to Anti-Tumor Necrosis Factor Therapy**

Ben Klünder¹, Mohamed-Eslam F. Mohamed², Heidi S. Camp² and Ahmed A. Othman², ¹AbbVie Deutschland GmbH & Co. KG, Ludwigshafen, Germany, ²AbbVie, North Chicago, IL

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017
Background/Purpose:

Upadacitinib, a selective JAK1 inhibitor, demonstrated favorable efficacy in two Phase 2 studies in subjects with moderate to severe rheumatoid arthritis (RA) who had inadequate response to prior treatment with anti-tumor necrosis factor (anti-TNF) therapy in BALANCE I or with methotrexate in BALANCE II. This work was done to characterize upadacitinib exposure-response relationships for effects on ACR responses in RA patients which supported dose selection for the ongoing Phase 3 RA trials.

Methods:

The analyses included data from 276 and 298 subjects in BALANCE I and BALANCE II, respectively. Subjects were randomized to receive 3, 6, 12, or 18 mg twice daily (BID) or matching placebo in BALANCE I and 3, 6, 12, 18 mg BID or 24 mg once daily or matching placebo in BALANCE II. Upadacitinib was administered in both studies as immediate-release formulation. Efficacy assessments and sparse blood samples for pharmacokinetic analyses were collected from over a 12-week period. ACR20, ACR50, and ACR70 responses as well as dropouts were collectively analyzed using a continuous-time Markov model, where upadacitinib enhanced transition of the status of patients to higher levels of response (e.g. no response to ACR20, ACR20 to ACR50, ACR50 to ACR70). The final model was used to predict the efficacy of different upadacitinib doses in both patient populations assuming 300 subjects for each dose. A separate model was utilized for simulation of placebo response in the anti-TNF inadequate responders population to better capture the lower placebo response in that population.

Results:

In the Markov analysis, point estimate for upadacitinib plasma concentrations associated with 50% of maximal effect on the transition rates to higher ACR responses was higher for anti-TNF inadequate responders compared with the methotrexate inadequate responders, however with overlapping confidence intervals between the populations. The predicted median (90% Prediction interval) ACR responses are shown in Table 1 compared to the observed ACR responses from BALANCE 1 and BALANCE II based on non-responder imputation.

Table 1. Predicted median (90% Prediction interval) ACR responses compared to the observed ACR responses based on non-responder imputation.
## Methotrexate Inadequate Responders

<table>
<thead>
<tr>
<th>Dose Group</th>
<th>Methotrexate Inadequate Responders</th>
<th>Anti-TNF Inadequate Responders</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ACR20</td>
<td>ACR50</td>
</tr>
<tr>
<td>Placebo</td>
<td>47 (38-57)</td>
<td>18 (13-27)</td>
</tr>
<tr>
<td>Observed</td>
<td>46</td>
<td>18</td>
</tr>
<tr>
<td>3 mg BID Model-Predicted</td>
<td>67 (60-72)</td>
<td>40 (33-47)</td>
</tr>
<tr>
<td>Observed</td>
<td>62</td>
<td>38</td>
</tr>
<tr>
<td>6 mg BID Model-Predicted</td>
<td>69 (63-74)</td>
<td>44 (36-51)</td>
</tr>
<tr>
<td>Observed</td>
<td>68</td>
<td>46</td>
</tr>
<tr>
<td>12 mg BID Model-Predicted</td>
<td>71 (65-76)</td>
<td>46 (38-54)</td>
</tr>
<tr>
<td>Observed</td>
<td>80</td>
<td>50</td>
</tr>
<tr>
<td>18 mg BID Model-Predicted</td>
<td>72 (65-78)</td>
<td>47 (39-55)</td>
</tr>
<tr>
<td>Observed</td>
<td>64</td>
<td>40</td>
</tr>
<tr>
<td>24 mg QD Model-Predicted</td>
<td>69 (63-75)</td>
<td>44 (37-52)</td>
</tr>
<tr>
<td>Observed</td>
<td>76</td>
<td>39</td>
</tr>
</tbody>
</table>

Simulated dropouts are imputed with non-response.

**Conclusion:**

The exposure-response models adequately described upadacitinib exposure-response relationships for ACR20, ACR50, and ACR70 in the BLANACE I and II studies. Using the immediate-release formulation, upadacitinib exposures associated with 6 mg BID dose are predicted to achieve near maximal efficacy in methotrexate inadequate-responders, while exposures associated with 12 mg BID dose may provide additional efficacy benefit in anti-TNF inadequate responders.

**Disclosure:** B. Klünder, AbbVie Inc, 1,AbbVie Inc, 3; M. E. F. Mohamed, AbbVie, 1,AbbVie, 3; H. S. Camp, AbbVie, 1,AbbVie, 3; A. A. Othman, AbbVie, 1,AbbVie, 3.


**Abstract Number:** 506

### The Selective JAK1 Inhibitor Upadacitinib Has No Effect on Pharmacokinetics of the Hormonal Contraceptives Levonorgestrel and Ethinylestradiol

Mohamed-Eslam F. Mohamed¹, Sheryl Trueman¹, Tian Feng², Alan Friedman³ and Ahmed A. Othman², ¹Clinical Pharmacology and Pharmacometrics, AbbVie, North Chicago, IL, ²AbbVie, North Chicago, IL, ³AbbVie Inc., North Chicago, IL

**First publication:** September 18, 2017
Background/Purpose:

Upadacitinib is a selective JAK1 inhibitor being developed for the treatment of several inflammatory diseases, including rheumatoid arthritis (RA). Upadacitinib showed favorable efficacy and acceptable safety profiles in two Phase 2 studies in subjects with RA. Currently, doses of 15 mg and 30 mg once daily (QD) are being evaluated in ongoing Phase 3 studies in RA. Oral contraceptives are expected to be commonly used with upadacitinib in patients with inflammatory diseases. This study evaluated the effect of multiple doses of upadacitinib on pharmacokinetics of ethinylestradiol and levonorgestrel.

Methods:

Healthy female subjects (N = 20) received single doses of a combined oral contraceptive tablet containing 30 μg ethinylestradiol and 150 μg levonorgestrel alone (Study Period 1) and on Day 12 of a 14-day regimen of upadacitinib 30 mg QD (Study Period 2). Upadacitinib was administered in the study using the extended-release tablet formulation being utilized in Phase 3 studies in RA. Blood samples for ethinylestradiol and levonorgestrel assays were collected by venipuncture prior to and for 96 hours after the oral contraceptive administration in each Study Period. Pharmacokinetic parameters for ethinylestradiol and levonorgestrel were calculated using non-compartmental analyses.

Results:

The ratios (90% confidence intervals) for Cmax and AUCinf following administration of the oral contraceptive with upadacitinib compared with administration of the oral contraceptive alone were 0.96 (0.89 to 1.02) and 1.11 (1.03 to 1.19), respectively, for ethinylestradiol and 0.96 (0.87 to 1.06) and 0.95 (0.85 to 1.07), respectively, for levonorgestrel.

Figure 1. Plasma Concentration versus Time Profiles for Ethinylestradiol and Levonorgestrel Following Administration of the Combined Oral Contraceptive Alone and with Upadacitinib 30 mg QD
Conclusion:

Upadacitinib has no effect on pharmacokinetics of ethinylestradiol and levonorgestrel; the 90% confidence intervals for the ratios of ethinylestradiol and levonorgestrel AUC and C_{max} when administered with upadacitinib relative to when administered alone were within the bioequivalence boundaries of 0.8 to 1.25. Therefore, oral contraceptives containing ethinylestradiol or levonorgestrel can be concomitantly administered with upadacitinib.

Disclosure: M. E. F. Mohamed, AbbVie, 1,AbbVie, 3; S. Trueman, AbbVie, 1,AbbVie, 3; T. Feng, AbbVie, 1,AbbVie, 3; A. Friedman, AbbVie, 3,AbbVie, 1; A. A. Othman, AbbVie, 1,AbbVie, 3.

Abstract Number: 507

Tofacitinib Monotherapy Improves Left Ventricular Mass and Cardiac Output in Patients with Rheumatoid Arthritis

Kensuke Kume^1, Kanzo Amano^2, Susumu Yamada^1, Toshikatsu Kanazawa^3 and Kazuhiko Hatta^4, ^1Rheumatology, Hiroshima Clinic, Hiroshima, Japan, ^2rheumatology., hiroshima clinic, Hiroshima, Japan, ^3rheumatology, hiroshima clinic, hiroshima, Japan, ^4Rheumatology, Hatta Clinic, Kure, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Rheumatologists need to develop primary prevention strategies for cardiovascular disease (CVD) in rheumatoid arthritis (RA) patients. We reported tofacitinib (Tofa) plus methotrexate improved left ventricular mass index (LVMI) in patients with rheumatoid arthritis. How about tofacitinib monotherapy? To study the effect of Tofa monotherapy (MTX) on LV morphology and function in conventional DMARDs resistant active RA patients, in a cohort study design.

Methods: RA patients were eligible if they had active disease despite treatment with conventional DMARDs. Consecutive 21 patients with moderate to severe active RA patients (DAS28>3.2) despite conventional DMARDs were received Tofa monotherapy. LV morphology and function was assessed with cardio-MRI at baseline and 24 weeks follow-up. Cardiovascular risk factors and clinical data were collected at regular visits.

Results: 19 patients completed 24 weeks. Left ventricular mass index (LVMI) was attenuated significantly by Tofa (week 0-week24, −10.02±4.8 g/m^2; p=0.02). Cardiac output (CO) was attenuated significantly by Tofa (week 0-week24, −0.65 ± 0.9/l/min), DAS28 and CRP improved significantly by Tofa (week 0-week24; DAS28: −2.16±0.95; CRP: 15.1±5.7 mg/l) (p<0.05). Surprisingly, the change of disease activity (DAS 28 and CRP) is no correlation with the change of LVMI or CO in this study. Observationally, 2 cases significantly improved right ventricular mass as well as left ventricular mass (20 % improved right ventricular mass index from baseline).

Conclusion: Tofa monotherapy improved LVMI and CO in active RA despite MTX. Tofa monotherapy improves LVMI and CO independently of its effects on disease activity. Tofa might be improved right ventricular mass. JAK-STAT pathway might be an important role of LV hypertrophy. Tofa, JAK-STAT pathway blocking, may prevent cardiovascular morbidity and mortality in RA.
References: 1) Tofacitinib improves left ventricular mass and cardiac output in patients with rheumatoid arthritis Kume K, et al. presentation at annual meeting of EULAR 2017


Disclosure: K. Kume, None; K. Amano, None; S. Yamada, None; T. Kanazawa, None; K. Hatta, None.

Improved Patient-Reported Outcomes in Patients with Rheumatoid Arthritis Who Failed Adalimumab or Placebo Treatment and Were Rescued with Baricitinib

Bruno Fautrel1, Peter C. Taylor2, Kaleb Michaud3, Himanshu Patel4, Baojin Zhu4, Carol L Gaich4, Jiaying Guo4, Amanda Quebe4 and Yoshiya Tanaka5, 1Paris VI Pierre et Marie Curie University, Paris, France, 2Botnar Research Centre, University of Oxford, Oxford, United Kingdom, 3Rheumatology, National Data Bank for Rheumatic Diseases & University of Nebraska Medical Center, Omaha, NE, 4Eli Lilly and Company, Indianapolis, IN, 5The First Department of Internal Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
In the Phase 3 RA-BEAM study, baricitinib (BARI) 4 mg once daily showed significant clinical improvements compared with placebo (PBO) and adalimumab (ADA).1 Switching from ADA to BARI, prompted by rescue or study design, without an ADA washout was associated with improved disease control during the initial 12 weeks after the switch.2 The objective of this analysis was to evaluate changes in patient-reported outcomes (PROs) from before and after rescue with BARI.

Methods:
1305 patients were randomized 3:3:2 to and treated with PBO for 24 weeks, BARI 4 mg once daily for 52 weeks, or ADA 40 mg every 2 weeks for 52 weeks. All patients received background methotrexate (MTX). Patients whose tender and swollen joint counts were reduced <20% from baseline at Week 16 were rescued to open-label BARI 4 mg once daily; after Week 16, rescue was at physician discretion. In this post hoc analysis, patients who were rescued between Weeks 16 and 24 were followed for 12 weeks after rescue. The pain visual analog scale (VAS, 0-100 mm), Health Assessment Questionnaire-Disability Index (HAQ-DI), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), SF-36 physical and mental component scores (PCS and MCS), and duration of morning joint stiffness (MJS) were assessed for patients rescued to BARI. Within group changes before and after rescue were assessed with sign tests for each of the evaluated PROs. The percentage of patients who met or exceeded clinically relevant thresholds at Week 12 after rescue, relative to the point of rescue, was also assessed. These analyses were not adjusted for multiplicity.

Results:
More patients randomized to PBO (26%, N=128) were rescued, than ADA (12%, N=40) or BARI (7%, N=35). Of the 203 patients rescued, 102 patients were rescued per protocol (Week 16) and 101 were rescued at the physician’s discretion. Patients who failed PBO or ADA and rescued to BARI showed significantly greater improvements in pain, HAQ-DI, FACIT-F, SF-36 PCS, and duration of MJS at 4 weeks after rescue which were sustained through 12 weeks (Table). A greater percentage of patients rescued from PBO to BARI, followed by ADA to BARI patients, tended to show clinically relevant improvements in pain, HAQ-DI, FACIT-F, and PCS compared to patients rescued from BARI to BARI (Figure).

Conclusion:

Upon treatment failure with either PBO or ADA, rescue with BARI 4 mg resulted in early, sustained, and clinically relevant improvements in PROs representing measures of quality of life and symptoms that are important to patients.

References:

2. Taylor et al., Arthritis Rheumatol 2016; 68 (suppl 10)
Long-Term Safety and Efficacy of Upadacitinib (ABT-494), an Oral JAK-1 Inhibitor in Patients with Rheumatoid Arthritis in an Open Label Extension Study

Mark C. Genovese1, Joel Kremer2, Sheng Zhong3 and Alan Friedman3, 1Stanford University Medical Center, Palo Alto, CA, 2Albany Medical College, Albany, NY, 3AbbVie Inc., North Chicago, IL
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
**Background/Purpose:** Upadacitinib (UPA, ABT-494) is a selective, oral JAK-1 inhibitor studied in two phase 2 randomized controlled trials (RCTs) in patients (pts) with rheumatoid arthritis (RA). We assessed UPA safety and efficacy in BALANCE-EXTEND, an ongoing, combined open-label extension (OLE) of the phase 2 RCTs.

**Methods:** Pts completing the two 12-week RCTs (in TNF-IR and MTX-IR pts)\(^1,2\) could enter the OLE. Pts switched to 6 mg UPA from their RCT dose of UPA 3, 6, 12, 18 mg twice daily (BID), 24 mg once daily (QD) or Placebo. A dose increase to 12 mg BID was required for pts with <20% improvement in both SJC and TJC on 6 mg BID (at wk 6 or 12), and permitted for pts not meeting CDAI LDA. Pts without 20% improvement in SJC and TJC 6 wks after escalation, or at any 2 consecutive visits, were discontinued. The dose was decreased to 6 mg BID only in pts with a safety concern or intolerability. Pts are grouped as: Never-titrated (on 6 mg BID throughout); Titrated-up (from 6 to 12 mg BID); Titrated-up and back down (to 6 mg BID). After Jan 2017, the 6 and 12 mg BID doses were replaced by 15 and 30 mg QD extended-release equivalents currently being studied in phase 3. Data up to Jan 13 2017 are reported. Adverse events (AE) per 100 yrs of pt exposure (PY) are summarized starting from day 1 of OLE. Efficacy is assessed by ACR20/50/70 and LDA (by DAS28-CRP and CDAI), and observed data are presented upto Wk 72 of OLE due to sample size consideration.

**Results:** Out of 516 pts who completed the 2 RCTs, 494 entered the OLE, 493 were dosed, 328 (66.5 %) were never-titrated, 150 (30.4%) were titrated-up, and 15 (3%) were titrated-up and back down; 150 pts (30.4%) were discontinued [42 (8.5%) withdrew consent, 37 (7.5%) due to AE and 24 (4.9%) due to lack of efficacy]. Mean exposure to UPA was 525.4 ± 221.4 days (range 1-961 days), and cumulative exposure was 725.1 PY (Table 1). The E/100PY for any AE in the OLE (170.5) was lower than for the RCTs in TNF-IR (697.9, 48 PY) and MTX-IR (408.4, 54.6 PY). The E/100PY was 2.3 for serious infection, 3.7 for herpes zoster, 0.8 for malignancies excluding non-melanoma skin cancer, and 1.0 for adjudicated cardiovascular events. There were 2 deaths. Changes from baseline in laboratory parameters were consistent with observations from phase 2 RCTs. For those pts completing Wk 72, efficacy was maintained in pts on 6 mg BID UPA from day 1 of OLE (never-titrated); 55% pts met ACR70 and 83% were in LDA by DAS28-CRP and CDAI based on as observed data (Table 2).

**Conclusion:** No unexpected safety signals were observed during this OLE. Efficacy responses were maintained upto 72 wks in pts on 6 mg BID UPA in the OLE.
<table>
<thead>
<tr>
<th>Event Category</th>
<th>Events (E/100PY)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE</td>
<td>1236 (170.5)</td>
</tr>
<tr>
<td>Serious AE</td>
<td>68 (9.4)</td>
</tr>
<tr>
<td>AE leading to discontinuation</td>
<td>42 (5.8)</td>
</tr>
<tr>
<td>AE leading to death&lt;sup&gt;#&lt;/sup&gt;</td>
<td>2 (0.3)</td>
</tr>
<tr>
<td>Infections</td>
<td>427 (58.9)</td>
</tr>
<tr>
<td>- Serious infections</td>
<td>17 (2.3)</td>
</tr>
<tr>
<td>- Opportunistic infections&lt;sup&gt;δ&lt;/sup&gt;</td>
<td>3 (0.4)</td>
</tr>
<tr>
<td>Anemia</td>
<td>19 (2.6)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>10 (1.4)</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>17 (2.3)</td>
</tr>
<tr>
<td>GI perforation</td>
<td>0</td>
</tr>
<tr>
<td>NMSC&lt;sup&gt;γ&lt;/sup&gt;</td>
<td>5 (0.7)</td>
</tr>
<tr>
<td>Malignancy other than NMSC&lt;sup&gt;‡&lt;/sup&gt;</td>
<td>6 (0.8)</td>
</tr>
<tr>
<td>Herpes Zoster</td>
<td>27 (3.7)</td>
</tr>
<tr>
<td>CPK elevation&lt;sup&gt;†&lt;/sup&gt;</td>
<td>36 (5.0)</td>
</tr>
<tr>
<td>Hepatic disorders&lt;sup&gt;§&lt;/sup&gt;</td>
<td>37 (5.1)</td>
</tr>
<tr>
<td>Adjudicated cardiovascular events</td>
<td>7 (1.0)</td>
</tr>
</tbody>
</table>

PY, patient years; E/100 PY, events/100 PY; AE, adverse events; NMSC, non-melanoma skin cancer; CPK, creatine phosphokinase

<sup>#</sup>1 sudden death, likely due to cardiac disease (undetermined or unknown cause of death); 1 death due to Hodgkin’s lymphoma (non-cardiovascular death).

<sup>δ</sup>1 pt with coccidiomycosis (from an endemic area); 2 pts with oral candidiasis

<sup>γ</sup>3 pts with basal cell carcinoma; 1 pt with 2 events of squamous cell carcinoma of skin

<sup>‡</sup>2 pts with breast cancer (1 pt had bilateral cancer); 2 pts with lymphoma; 1 pt with prostate cancer

<sup>†</sup>Not symptomatic

<sup>§</sup>All isolated elevations of ALT/AST or bilirubin; no Hy’s Law cases.
| Table 2. Efficacy Measures at Week 72 in Patients who Entered the OLE, n/N (%) |
|----------------------------------|------------------------------|----------------------------------|
|                                  | Never-titrated | Titrated-up | Overall efficacy in OLEδ |
| ACR20                           | 208/231 (90)   | 78/99 (79)  | 297/342 (87)           |
| ACR50                           | 172/230 (75)   | 44/100 (44) | 224/342 (65)           |
| ACR70                           | 127/232 (55)   | 22/101 (22) | 153/345 (44)           |
| DAS28-CRP LDA                   | 194/233 (83)   | 46/104 (44) | 250/349 (72)           |
| CDAI LDA                        | 191/230 (83)   | 42/104 (40) | 242/346 (70)           |

Observed data presented for pts completing Week 72. Efficacy data reflect attrition in the OLE.

δ Includes pts who were never-titrated, titrated-up, and titrated-up and back down.

ACR20/50/70: 20/50/70% improvement in American College of Rheumatology criteria; DAS28-LDA, 28-joint count disease activity score using C-reactive protein; CDAI, clinical disease activity index; LDA, low disease activity

Ref:


Disclosure: M. C. Genovese, AbbVie, Lilly, Astellas, Pfizer, Galapagos, Gilead, 5,AbbVie, Lilly, Astellas, Pfizer, Galapagos, Gilead, 2; J. Kremer, Corrona, 1,Corrona, 3,AbbVie, 2,BMS, Genentech, Gilead, GSK, Eli Lilly and Pfizer, 5; S. Zhong, AbbVie, 1,AbbVie, 3; A. Friedman, AbbVie, 3,AbbVie, 1.


Abstract Number: 510

**Association between Clinical Response and Normalization of Patient-Reported Outcome Measures in Rheumatoid Arthritis: Post-Hoc Analysis from Two Phase 2b Filgotinib Studies**

Mark C. Genovese1, Annegret Van der Aa2, Corinne Jamoul2, Chantal Tasset2, Pille Harrison2, René Westhovens3 and Arthur Kavanaugh4, 1Stanford University Medical Center, Palo Alto, CA, 2Galapagos NV, Mechelen, Belgium, 3University Hospitals Leuven on behalf of the CareRA Study Group, Leuven, Belgium, 4Medicine, University of California, San Diego, La Jolla, CA

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**
Filgotinib (GLPG0634, GS-6034) is an oral, selective JAK1 inhibitor that has demonstrated safety and efficacy data in two 24-week placebo-controlled phase 2B studies as add-on to methotrexate and as monotherapy in active rheumatoid arthritis (RA) patients with inadequate response to MTX (MTX-IR)\(^1,2\).

The objective is to evaluate the association between normalization of patient-reported outcome measures (PRO) and clinical response (ACR20) in MTX-IR RA patients treated with either filgotinib or placebo, as add-on to methotrexate (DARWIN 1), or as monotherapy (DARWIN 2).

**Methods:**

Patients with active RA were randomized in a double-blind manner to placebo (PBO) or one of 3 daily doses of filgotinib (FIL, 50mg, 100mg or 200mg) as once daily (DARWIN 1 and DARWIN 2) or twice daily regimen (DARWIN 1) for 24 weeks. This post-hoc analysis at week 12 (W12) included patients treated FIL 100mg and 200mg QD (selected Phase 3 doses), and PBO. PRO included SF-36 (mental and physical components: MCS and PCS respectively; cut-off 50), FACIT-F (cut-off 40), and HAQ-DI (cut-off 0.5).

**Results:**

594 and 283 patients with active RA were randomized in DARWIN 1 and 2 respectively. In DARWIN 1, 44%, 64%, and 69% of patients on PBO, FIL 100mg QD and FIL 200mg QD respectively achieved ACR20 response at W12; in DARWIN 2 the respective response was 29%, 66%, and 72%. For all PRO parameters (SF-36 MCS, SF-36 PCS, FACIT-F and HAQ-DI) and in both studies, a higher proportion of patients with normalized scores was achieved in ACR20 responders compared to non-responders at W12 across treatment groups (Table 1).

**Conclusion:**

This post-hoc analysis of two phase 2B studies in MTX-IR RA patients after 12 weeks of treatment suggests that normalization of PRO is associated with the ACR20 response, regardless of treatment with filgotinib and background MTX.

<table>
<thead>
<tr>
<th>% of patients</th>
<th>Placebo</th>
<th>100mg QD</th>
<th>200mg QD</th>
</tr>
</thead>
<tbody>
<tr>
<td>DARWIN 1 (MTX add-on), W12, ITT-LOCF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACR20 responders</td>
<td>N=38</td>
<td>ACR20 non-responders</td>
<td>N=48</td>
</tr>
<tr>
<td>SF-36 MCS ≥50</td>
<td>52.6</td>
<td>27.1</td>
<td></td>
</tr>
<tr>
<td>SF-36 PCS ≥50</td>
<td>7.9</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>FACIT-F ≥40</td>
<td>39.5</td>
<td>10.4</td>
<td></td>
</tr>
<tr>
<td>HAQ-DI ≤0.5</td>
<td>23.7</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>ACR20 responders</td>
<td>N=54</td>
<td>ACR20 non-responders</td>
<td>N=31</td>
</tr>
<tr>
<td>SF-36 MCS ≥50</td>
<td>59.3</td>
<td>35.5</td>
<td></td>
</tr>
<tr>
<td>SF-36 PCS ≥50</td>
<td>14.8</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>FACIT-F ≥40</td>
<td>57.4</td>
<td>25.8</td>
<td></td>
</tr>
<tr>
<td>HAQ-DI ≤0.5</td>
<td>31.5</td>
<td>19.4</td>
<td></td>
</tr>
<tr>
<td>ACR20 responders</td>
<td>N=59</td>
<td>ACR20 non-responders</td>
<td>N=27</td>
</tr>
<tr>
<td>SF-36 MCS ≥50</td>
<td>59.3</td>
<td>33.3</td>
<td></td>
</tr>
<tr>
<td>SF-36 PCS ≥50</td>
<td>16.9</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>FACIT-F ≥40</td>
<td>50.8</td>
<td>25.9</td>
<td></td>
</tr>
<tr>
<td>HAQ-DI ≤0.5</td>
<td>40.7</td>
<td>7.4</td>
<td></td>
</tr>
<tr>
<td>DARWIN 2 (monotherapy), W12, ITT-LOCF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACR20 responders</td>
<td>N=21</td>
<td>ACR20 non-responders</td>
<td>N=51</td>
</tr>
<tr>
<td>SF-36 MCS ≥50</td>
<td>42.9</td>
<td>23.5</td>
<td></td>
</tr>
<tr>
<td>SF-36 PCS ≥50</td>
<td>9.5</td>
<td>2.0</td>
<td></td>
</tr>
<tr>
<td>FACIT-F ≥40</td>
<td>38.1</td>
<td>7.8</td>
<td></td>
</tr>
<tr>
<td>HAQ-DI ≤0.5</td>
<td>19.0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>ACR20 responders</td>
<td>N=46</td>
<td>ACR20 non-responders</td>
<td>N=24</td>
</tr>
<tr>
<td>SF-36 MCS ≥50</td>
<td>54.3</td>
<td>33.3</td>
<td></td>
</tr>
<tr>
<td>SF-36 PCS ≥50</td>
<td>17.4</td>
<td>4.2</td>
<td></td>
</tr>
<tr>
<td>FACIT-F ≥40</td>
<td>52.2</td>
<td>8.3</td>
<td></td>
</tr>
<tr>
<td>HAQ-DI ≤0.5</td>
<td>32.6</td>
<td>4.2</td>
<td></td>
</tr>
<tr>
<td>ACR20 responders</td>
<td>N=50</td>
<td>ACR20 non-responders</td>
<td>N=19</td>
</tr>
<tr>
<td>SF-36 MCS ≥50</td>
<td>52.0</td>
<td>47.4</td>
<td></td>
</tr>
<tr>
<td>SF-36 PCS ≥50</td>
<td>14.0</td>
<td>10.5</td>
<td></td>
</tr>
<tr>
<td>FACIT-F ≥40</td>
<td>42.0</td>
<td>36.8</td>
<td></td>
</tr>
<tr>
<td>HAQ-DI ≤0.5</td>
<td>30.0</td>
<td>21.1</td>
<td></td>
</tr>
</tbody>
</table>
References


Disclosure: M. C. Genovese, Gilead, 5,Galapagos NV, 5,AbbVie, 5,Eli Lilly and Company, 5; A. Van der Aa, Galapagos NV, 1,Galapagos NV, 3; C. Jamoul, Galapagos NV, 3; C. Tasset, Galapagos NV, 1,Galapagos NV, 3; P. Harrison, Galapagos NV, 1,Galapagos NV, 3; R. Westhovens, Celltrion, 5,BMS Research Fund, 5,Roche Pharmaceuticals, 5,Galapagos NV, 5; A. Kavanaugh, Gilead Sciences, Inc, 5,Galapagos NV, 5,Pfizer Inc, 5,AbbVie, 5,Eli Lilly and Company, 5.


Abstract Number: 511

Safety Profile of Baricitinib for the Treatment of Rheumatoid Arthritis up to 5.5 Years: An Updated Integrated Safety Analysis

Mark C. Genovese1, Josef S. Smolen2, Tsutomu Takeuchi3, David Hyslop4, William L. Macias4, Terence P. Rooney4, Lei Chen4, Christina L. Dickson4, Jennifer Riddle Camp4, Tracy Cardillo4, Taeko Ishii5 and Kevin Winthrop6, 1Stanford University Medical Center, Palo Alto, CA, 2Rheumatology, Medical University of Vienna, Vienna, Austria, 3Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, 4Eli Lilly and Company, Indianapolis, IN, 5Eli Lilly and Company, Kobe, Japan, 6Oregon Health & Science University, Portland, OR

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Baricitinib (bari), an oral, selective inhibitor of Janus kinase (JAK) 1 and JAK 2, is approved in the EU for the treatment of moderately to severely active RA in adults. We further describe the drug’s safety profile with updated data from an on-going long-term extension (LTE) study.

Methods: Long-term safety of once-daily baricitinib was evaluated in the “all-bari-RA” dataset, which includes all patients (pts) with active RA exposed to any bari dose from 8 randomized trials (4 Ph3, 3 Ph2, 1 Ph1b) and 1 LTE study (data up to 01-Sept-2016). Previous all-bari-RA analyses1 are provided for comparison (data up to 10-Aug-2015). Placebo (PBO) comparisons were evaluated for up to Wk 24 in the “PBO-4mg” dataset from the 6 Ph2/3 trials in which pts were randomized to bari 4mg, with censoring at rescue or treatment switch. Dose responses were evaluated based on the 4 Ph2/3 trials in which pts were randomized to 2 or 4mg and includes data from the LTE (the “2mg-4mg-extended” dataset). Data were censored at rescue or dose change (as-treated analysis). Because of the latent period for malignancy, 2mg-4mg-extended was also analyzed without censoring for rescue or dose change (as-randomized analysis). Incidence rates (IR) per 100 patient-years (PY) were calculated.

Results: In the current analysis, 3492 pts received bari for 6637 total PY of exposure (an increase of over 2400 PY from previous analysis); maximum exposure was 5.5 yrs (Table 1). No differences were seen for bari 4mg vs PBO in adverse
events (AEs) leading to permanent study drug discontinuation, death, malignancy, serious infection, or major adverse cardiovascular event (MACE) (Table 1). Herpes zoster IR was significantly higher for bari 4mg vs PBO (IR 1.0 vs 4.3; PBO, 4mg, respectively). In 2mg-4mg-extended, no significant differences were observed comparing bari 2mg vs 4mg for the above mentioned events. Malignancy (excluding non-melanoma skin cancer (NMSC)) IR were 0.5 and 1.3 for 2mg and 4mg, respectively, with as-treated analysis and 0.7 and 0.9 with as-randomized analysis. For the above events, the current IRs in all-bari-RA are similar to those previously reported (Table 1). The following IRs were observed in the current all-bari-RA: lymphoma (0.09), gastrointestinal (GI) perforation (0.05), and tuberculosis (TB) (0.15, all in endemic areas). The IRs for these events are also similar to those previously reported (Table 1). Fewer than 1% of pts discontinued due to abnormal lab results.

**Conclusion:** In this updated integrated analysis of patients with moderately to severely active RA, including patients exposed for up to 5.5 years, baricitinib maintained a safety profile that was similar to that previously reported and acceptable in the context of demonstrated efficacy.\(^1\,^2\,^3\)

**References:**


### Table 1. Safety outcomes with up to 5.5 years of exposure to baricitinib

<table>
<thead>
<tr>
<th></th>
<th>PBO</th>
<th>bari 4 mg</th>
<th>bari 2 mg</th>
<th>bari 4 mg-extended</th>
<th>All-bari-RA 01-Sep-2016</th>
<th>All-bari-RA 10-Aug-2015</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Exposure</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of patients</td>
<td>1079</td>
<td>997</td>
<td>479</td>
<td>479</td>
<td>3492</td>
<td>3464</td>
</tr>
<tr>
<td>Patient-years of exposure</td>
<td>393.8</td>
<td>409.4</td>
<td>555.5</td>
<td>604</td>
<td>6657</td>
<td>4214</td>
</tr>
<tr>
<td>Median, days</td>
<td>166</td>
<td>169</td>
<td>257.0</td>
<td>342</td>
<td>760 (2.1 yrs)</td>
<td>2019 (5.5 yrs)</td>
</tr>
<tr>
<td>Longest exposure, days</td>
<td>235</td>
<td>211</td>
<td>127.6</td>
<td>1991</td>
<td>263 (3.8)</td>
<td>255 (6.1)</td>
</tr>
<tr>
<td>Permanent DC due to AE, n (IR)</td>
<td>33.5 (9.9)</td>
<td>47 (11.5)</td>
<td>37 (6.6)</td>
<td>55 (8.9)</td>
<td>393 (13.8)</td>
<td>255 (6.1)</td>
</tr>
<tr>
<td><strong>Mortality, n (IR), [95% CI]</strong></td>
<td>2 (0.5)</td>
<td>3 (0.7)</td>
<td>1 (0.3)</td>
<td>3 (0.9)</td>
<td>22 (0.3)</td>
<td>13 (0.3)</td>
</tr>
<tr>
<td>Lymphoma, n (IR), [95% CI]</td>
<td>0.1 (0.1-1.8)</td>
<td>0.1 (0.2-1.5)</td>
<td>0.0 (0.1-0.9)</td>
<td>0.0 (0.0-0.5)</td>
<td>0.0 (0.0-0.5)</td>
<td>0.0 (0.0-0.5)</td>
</tr>
<tr>
<td>Tuberculosis, n (IR), [95% CI]</td>
<td>0 (0.0-1.4)</td>
<td>0 (0.0-1.2)</td>
<td>0 (0.0-1.2)</td>
<td>0 (0.0-1.2)</td>
<td>0 (0.0-1.2)</td>
<td>0 (0.0-1.2)</td>
</tr>
<tr>
<td><strong>Infections, n (IR), [95% CI]</strong></td>
<td>17 (4.2)</td>
<td>16 (3.8)</td>
<td>18 (3.3)</td>
<td>29 (4.8)</td>
<td>394 (2.9)</td>
<td>133 (3.2)</td>
</tr>
<tr>
<td>Serious Infections</td>
<td>[0.3, 2.5]</td>
<td>[2.2, 6.2]</td>
<td>[1.5, 5.2]</td>
<td>[0.5, 1.6]</td>
<td>[3.2, 5.9]</td>
<td>[2.5, 3.4]</td>
</tr>
<tr>
<td>GI Perforation, n (IR), [95% CI]</td>
<td>2 (0.5)</td>
<td>3 (0.8)</td>
<td>1 (0.2)</td>
<td>2 (0.4)</td>
<td>31 (0.5)</td>
<td>16 (0.5)</td>
</tr>
<tr>
<td>MACE, n (IR), [95% CI]</td>
<td>0 (0.0-0.5)</td>
<td>0 (0.0-0.5)</td>
<td>0 (0.0-0.5)</td>
<td>0 (0.0-0.5)</td>
<td>0 (0.0-0.5)</td>
<td>0 (0.0-0.5)</td>
</tr>
</tbody>
</table>

95% CI for IR are based on Poisson distribution.
\(^a\)Data from treatment period up to Week 24, with data up to rescue/treatment switch.
\(^b\)All analysis based on as-treated method (data censored at rescue or dose change) unless otherwise specified.
\(^c\)In the “as-randomized” analysis for malignancy excluding NMSC, all data were attributed to the initial randomized treatment group disregarding rescue or dose changes. The patient-years of observation time with the as-randomized analysis were 1055 and 1064 years for 2 mg and 4 mg groups, respectively.
\(^d\)Potential cardiovascular (CV) adverse events from the PH 3 trials and LTE, identified by investigators or according to a predefined list of event terms, were adjudicated by an independent, external Clinical Endpoint Committee who remained blinded to treatment assignments.
\(^e\)No 0.05 for bari 4 mg vs placebo based on the proportion of patients with the event.

AE, adverse events; Bari, baricitinib; CI, confidence interval; DC, discontinuation; EAIR, exposure-adjusted incidence rates per 100 patient-years (exposure time not censored at event); IR, incidence rate per 100 patient-years (observation time censored at event); GI, gastrointestinal; MACE, major adverse cardiovascular event; NMSC, non-melanoma skin cancer; n, number of patients in a specified category; PBO, placebo; yrs, years.


Abstract Number: 512

Efficacy Response to Baricitinib Based on Baseline Characteristics in Patients Who Are Inadequate Responders to Conventional DMARD

Maxime Dougados1, Terence P. Rooney2, Li Xie2, Rena Klar3, Christina L. Dickson2, Ana Pinto Correia2, Yoshiya Tanaka4, Michael Schiff5 and Edward C. Keystone6, 1Department of Rheumatology, Rene Descartes University, Hôpital Cochin, Paris, France, 2Eli Lilly and Company, Indianapolis, IN, 3Quintiles IMS Holdings, Inc., Durham, NC, 4The First Department of Internal Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan, 5University of Colorado, Greenwood Village, CO, 6University of Toronto, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017

Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules

Session Type: ACR Poster Session A

Session Time: 9:00AM-11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic disease and some patients (pts) have an inadequate response (IR) to conventional DMARDs (csDMARDs). Baricitinib is an oral, selective inhibitor of Janus kinase (JAK) 1 and JAK 21 approved in the EU for the treatment of moderately to severely active RA in adults. We evaluated the effects of baseline characteristics, including prior csDMARD use, on the efficacy of bari in csDMARD-IR pts.

Methods: Eligible pts had active RA, were csDMARD-IR and biologic DMARD (bDMARD)-naïve, and were randomized to bari 4 mg or placebo in 5 global, randomized trials (2 Phase 3, 3 Phase 2). This analysis pooled data to evaluate efficacy outcomes (ACR50, DAS28-CRP ≤3.2, change from baseline in HAQ-DI) at Week (Wk) 12 in bari 4 mg vs placebo for potential subgroup interactions based on a variety of baseline characteristics including age, gender, weight, disease duration, etc. A logistic regression model was used to detect significant interactions; p-value ≤0.1 was considered significant, with significance in >1 measure given more weight.

Results: Overall samples were N=881 (4 mg) and N=803 (placebo). Pts were aged ~52 years, ~80% were female, and 44-49% had a history of 1 prior csDMARD (Table 1). In the overall pooled population at Wk 12, responses for ACR50, DAS28-CRP ≤3.2, and HAQ-DI change from baseline were significantly improved for bari 4 mg vs placebo (Tables 2, 3).
Across subgroups, odds ratios and least squares mean difference (LSMDs) predominately favored bari 4 mg over placebo at Wk 12 (Tables 2, 3) and were generally similar to the overall pooled population. Significant quantitative interactions were observed for bari 4 mg vs placebo for BMI in ACR50 and DAS28-CRP ≤3.2 (Table 2) and for race in ACR50 and DAS28-CRP ≤3.2. No significant interactions were observed for the number of prior cDMARDs. No qualitative interactions were observed.

**Conclusion:** Consistent with results in the overall pooled population of csDMARD-IR and bDMARD-naïve pts, at Wk 12 the point estimate for each endpoint favored baricitinib 4 mg vs placebo across subgroups. Thus, baricitinib demonstrated a consistent, beneficial treatment effect in subgroups, irrespective of baseline characteristics.


<table>
<thead>
<tr>
<th>Table 1. Baseline Demographics and Clinical Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Placebo</strong></td>
</tr>
<tr>
<td>N=881</td>
</tr>
<tr>
<td><strong>Age, mean (SD)</strong></td>
</tr>
<tr>
<td><strong>Female, n (%)</strong></td>
</tr>
<tr>
<td><strong>Race, n (%)</strong></td>
</tr>
<tr>
<td>White</td>
</tr>
<tr>
<td>Asian</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td><strong>Region, n (%)</strong></td>
</tr>
<tr>
<td>USA/Canada</td>
</tr>
<tr>
<td>Central/South America and Mexico</td>
</tr>
<tr>
<td>Asia (excluding Japan)</td>
</tr>
<tr>
<td>Japan</td>
</tr>
<tr>
<td>European Union</td>
</tr>
<tr>
<td>Rest of World</td>
</tr>
<tr>
<td><strong>Time for RA diagnosis, yrs, mean (SD)</strong></td>
</tr>
<tr>
<td><strong>No. of csDMARDS previously used, n (%)</strong></td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>≥3</td>
</tr>
</tbody>
</table>

csDMARDs, conventional DMARDs; n, number of patients in a specified category; SD, standard deviation; yrs, years
| Table 2. Efficacy Outcomes by Baseline Demographics/Characteristics at Week 12 |
|-----------------|-------------|-------------|-------------|-------------|
|                  | Placebo n (%) | Baricitinib 4 mg n (%) | Odds Ratio (95% CI) | Placebo n (%) | Baricitinib 4 mg n (%) | Odds Ratio (95% CI) |
| Overall study population | 127 (61.4) | 350 (86.9) | 4.1 (3.3, 5.2) | 146 (68.6) | 352 (86.8) | 4.2 (3.3, 5.5) |
| **Gender** |            |            |            |            |            |            |
| Female | 101 (69.4) | 296 (84.5) | 4.0 (3.0, 5.5) | 119 (79.6) | 272 (76.8) | 4.0 (3.0, 5.6) |
| Male | 26 (30.6) | 54 (15.5) | 6.4 (4.7, 8.5) | 27 (20.4) | 78 (23.2) | 3.8 (2.7, 5.5) |
| **Age Grouping (yrs)** |            |            |            |            |            |            |
| <50 | 179 (83.4) | 465 (86.4) | 0.9 (0.7, 1.1) | 195 (85.0) | 447 (87.8) | 0.9 (0.7, 1.1) |
| 50-64 | 19 (85.7) | 35 (80.4) | 1.3 (1.1, 1.5) | 21 (88.0) | 39 (88.4) | 1.0 (0.8, 1.3) |
| ≥65 | 20 (80.8) | 40 (80.8) | 1.0 (0.7, 1.4) | 22 (88.9) | 41 (88.7) | 1.0 (0.7, 1.4) |
| **Baseline weight (kg)** |            |            |            |            |            |            |
| <70 | 177 (69.8) | 317 (83.0) | 2.7 (2.1, 3.6) | 194 (70.6) | 337 (83.7) | 2.7 (2.1, 3.7) |
| 70-99 | 17 (86.1) | 29 (80.6) | 1.5 (1.1, 2.1) | 18 (88.9) | 28 (76.3) | 1.5 (1.1, 2.1) |
| ≥100 | 2 (100.0) | 2 (100.0) | 1.0 (0.0, 1.0) | 2 (100.0) | 2 (100.0) | 1.0 (0.0, 1.0) |
| **BMI (kg/m²)** |            |            |            |            |            |            |
| <18.5 | 16 (31.0) | 50 (95.1) | 2.9 (2.3, 3.7) | 21 (28.1) | 58 (76.3) | 2.9 (2.3, 3.7) |
| 18.5-24.9 | 11 (43.4) | 25 (96.2) | 2.2 (1.4, 3.3) | 14 (47.1) | 28 (93.5) | 2.2 (1.4, 3.3) |
| ≥25.0 | 10 (90.9) | 10 (90.9) | 1.0 (0.3, 3.2) | 11 (91.7) | 11 (91.7) | 1.0 (0.3, 3.2) |
| **Race (preferred)** |            |            |            |            |            |            |
| Asian | 32 (64.0) | 59 (70.6) | 1.2 (0.9, 1.7) | 39 (73.5) | 64 (77.3) | 1.2 (0.9, 1.7) |
| White | 105 (65.5) | 176 (84.1) | 2.7 (2.1, 3.5) | 115 (79.2) | 192 (83.1) | 2.7 (2.1, 3.5) |
| Other | 2 (90.9) | 2 (90.9) | 1.0 (0.0, 1.0) | 2 (90.9) | 2 (90.9) | 1.0 (0.0, 1.0) |
| **RA Diagnosis (yrs)** |            |            |            |            |            |            |
| <4 | 10 (80.0) | 25 (85.2) | 1.0 (0.7, 1.5) | 10 (80.0) | 25 (85.2) | 1.0 (0.7, 1.5) |
| 4-19 | 39 (68.9) | 57 (86.8) | 1.5 (1.1, 2.0) | 40 (69.0) | 57 (86.8) | 1.5 (1.1, 2.0) |
| ≥20 | 27 (75.7) | 36 (97.3) | 3.5 (2.9, 4.3) | 28 (75.7) | 36 (97.3) | 3.5 (2.9, 4.3) |
| **Baseline DAS28-4CRP** |            |            |            |            |            |            |
| ≤5.3 | 30 (75.0) | 46 (70.6) | 1.1 (0.8, 1.5) | 31 (75.0) | 47 (70.6) | 1.1 (0.8, 1.5) |
| >5.3 | 90 (49.3) | 232 (77.1) | 3.7 (3.0, 4.6) | 90 (49.3) | 232 (77.1) | 3.7 (3.0, 4.6) |
| **Serospositivity** |            |            |            |            |            |            |
| RF or ACR positive | 114 (74.8) | 155 (79.5) | 1.2 (1.0, 1.5) | 117 (74.4) | 157 (79.5) | 1.2 (1.0, 1.5) |
| RF and ACPA negative | 86 (70.5) | 105 (75.7) | 1.3 (1.0, 1.7) | 88 (72.2) | 107 (75.7) | 1.3 (1.0, 1.7) |
| No. of cDAS28 and ACPA previously used, n (%) |            |            |            |            |            |            |
| 0 | 2 (20.0) | 2 (20.0) | 1.0 (0.0, 1.0) | 2 (20.0) | 2 (20.0) | 1.0 (0.0, 1.0) |
| 1 | 55 (84.1) | 100 (80.6) | 0.9 (0.7, 1.1) | 56 (84.6) | 102 (81.6) | 0.9 (0.7, 1.1) |
| 2 | 48 (80.7) | 92 (84.0) | 1.0 (0.8, 1.3) | 47 (80.7) | 91 (84.0) | 1.0 (0.8, 1.3) |
| ≥3 | 29 (71.8) | 67 (79.2) | 1.2 (1.0, 1.5) | 29 (71.8) | 67 (79.2) | 1.2 (1.0, 1.5) |

*P<0.1, **P<0.001 for interaction terms in the logistic regression model, study treatment group, and subgroup treatment by subgroup.

When logistic regression sample size requirements are not met, odds ratio and 95% CI are not provided within a subgroup. P<0.1 was considered significant, with significance in 2-log measures given more weight.

Nonresponder imputation method was used.

*For determining seropositivity status, ACPA negative group includes patients with negative (≤7 U/mL) and indeterminate (7-19 U/mL) values. ACRP, auto-anti-citrullinated peptide antibody. cDAS28, American College of Rheumatology/Clinical Disease Activity Index. DAS28, Disease Activity Score 28 joints high sensitivity C-reactive protein. n, number of patients in a specified category. RF, rheumatoid factor; yr, years.
Table 3. Efficacy Outcomes by Baseline Demographics/Characteristics at Wk 12: Change from Baseline

<table>
<thead>
<tr>
<th>HAQ-DI Change from Baseline</th>
<th>Placebo</th>
<th>Baricitinib 4 mg</th>
<th>LSMD (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N-obs</td>
<td>LSM (SE)</td>
<td>N-obs</td>
<td>LSM (SE)</td>
</tr>
<tr>
<td>Gender (N-obs)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>698</td>
<td>-0.23 (0.03)</td>
<td>792</td>
</tr>
<tr>
<td>Male</td>
<td>170</td>
<td>-0.34 (0.06)</td>
<td>170</td>
</tr>
<tr>
<td>Age groupings (yrs)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65</td>
<td>739</td>
<td>-0.24 (0.03)</td>
<td>641</td>
</tr>
<tr>
<td>≥65</td>
<td>129</td>
<td>-0.23 (0.06)</td>
<td>151</td>
</tr>
<tr>
<td>&lt;75</td>
<td>854</td>
<td>-0.25 (0.03)</td>
<td>769</td>
</tr>
<tr>
<td>≥75</td>
<td>19</td>
<td>-0.19 (0.16)</td>
<td>23</td>
</tr>
<tr>
<td>Baseline weight group (kg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;60</td>
<td>269</td>
<td>-0.14 (0.06)</td>
<td>216</td>
</tr>
<tr>
<td>≥60 and ≤100</td>
<td>629</td>
<td>-0.30 (0.03)</td>
<td>507</td>
</tr>
<tr>
<td>≥100</td>
<td>70</td>
<td>-0.30 (0.08)</td>
<td>69</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;18.5</td>
<td>47</td>
<td>-0.07 (0.07)</td>
<td>34</td>
</tr>
<tr>
<td>≥18.5 and &lt;25</td>
<td>331</td>
<td>-0.15 (0.04)</td>
<td>369</td>
</tr>
<tr>
<td>≥25 and &lt;30</td>
<td>245</td>
<td>-0.28 (0.02)</td>
<td>247</td>
</tr>
<tr>
<td>≥30</td>
<td>245</td>
<td>-0.36 (0.07)</td>
<td>221</td>
</tr>
<tr>
<td>Race (pooled)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>266</td>
<td>0.16 (0.03)</td>
<td>226</td>
</tr>
<tr>
<td>White</td>
<td>534</td>
<td>-0.28 (0.03)</td>
<td>509</td>
</tr>
<tr>
<td>Other</td>
<td>67</td>
<td>-0.24 (0.10)</td>
<td>56</td>
</tr>
<tr>
<td>RA duration from diagnosis (yrs)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1</td>
<td>104</td>
<td>-0.37 (0.05)</td>
<td>111</td>
</tr>
<tr>
<td>≥1 and &lt;5</td>
<td>228</td>
<td>-0.33 (0.03)</td>
<td>229</td>
</tr>
<tr>
<td>≥5 and &lt;10</td>
<td>164</td>
<td>-0.21 (0.04)</td>
<td>163</td>
</tr>
<tr>
<td>≥10</td>
<td>207</td>
<td>-0.34 (0.04)</td>
<td>200</td>
</tr>
<tr>
<td>Baseline DAS28-hsCRP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤5.1</td>
<td>274</td>
<td>-0.15 (0.04)</td>
<td>217</td>
</tr>
<tr>
<td>&gt;5.1</td>
<td>593</td>
<td>-0.28 (0.03)</td>
<td>575</td>
</tr>
<tr>
<td>Seropositivity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RF or ACPA positive</td>
<td>737</td>
<td>-0.28 (0.03)</td>
<td>663</td>
</tr>
<tr>
<td>RF and ACPA negative</td>
<td>75</td>
<td>-0.22 (0.08)</td>
<td>70</td>
</tr>
<tr>
<td>No. of cDMARDS previously used, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>--</td>
<td>2</td>
</tr>
<tr>
<td>1</td>
<td>186</td>
<td>-0.27 (0.03)</td>
<td>188</td>
</tr>
<tr>
<td>2</td>
<td>306</td>
<td>-0.20 (0.03)</td>
<td>229</td>
</tr>
<tr>
<td>≥3</td>
<td>176</td>
<td>-0.18 (0.08)</td>
<td>173</td>
</tr>
</tbody>
</table>

*P < 0.001 for bar 4 mg vs placebo in overall pooled population.

No significant interactions were observed. The interaction p-values are based on the ANCOVA model:
Change = baseline*study+treatment*group+subgroup+treatment by subgroup. When any of the treatment group has <30 patients within a subgroup, only summary statistics are provided. Modified last observation carried forward method was used.

*For determining seropositivity status, ACPA negative group includes patients with negative (≤7 U/mL) and indeterminate (>7 and ≤30 U/mL) values.

ACPA, anti-citrullinated peptide antibody; ANCOVA, analysis of covariance; BMI, body mass index; cDMARDs, conventional DMARDs; DAS28-hsCRP, Disease Activity Score 28 joints high-sensitivity C-reactive protein; HAQ-DI, Health Assessment Questionnaire – Disability Index; LSMD, least squares mean difference; mLOCF, modified last observation carried; n, number of pts in a specified category; N-obs, number of patients in the analysis; RF, rheumatoid factor; SE, standard error; yrs, years.

Disclosure: M. Dougados, AbbVie, Pfizer, Eli Lilly and Company, Novartis, UCB, Merck, Roche, BMS, UCB, 2,AbbVie, Pfizer, Eli Lilly and Company, Novartis, UCB, Merck, Roche, BMS, UCB, 5; T. P. Rooney, Eli Lilly and Company, 1,Eli Lilly and Company, 3; L. Xie, Eli Lilly and Company, 1,Eli Lilly and Company, 3; R. Klar, Quintiles IMS Holdings, 3; C. L. Dickson, Eli Lilly and Company, 1,Eli Lilly and Company, 3; A. Pinto Correia, Eli Lilly and Company, 1,Eli Lilly and Company, 3; Y. Tanaka, Mitsubishi-Tanabe, Takeda, Bristol-Myers, Chugai, Astellas, AbbVie, MSD, Daiichi-Sankyo, Pfizer, Kyowa- Kirin, Eisai, Ono, 2,Daiichi-Sankyo, Astellas, Pfizer, Mitsubishi-Tanabe, Bristol-Myers, Chugai, YL Biologics, Eli Lilly and Company, Sanofi, Janssen, UCB, 8; M. Schiff, AbbVie, Amgen, Antares, BMS, Eli Lilly and Company, JJ, Novartis, Novo Nordisk, Pfizer, Roche, UCB, 5,Abbvie, BMS, 8; E. C. Keystone, Abbott Laboratories, Amgen, AstraZeneca, BMS, Hoffmann-LaRoche, Janssen, Eli Lilly and Company, Novartis, Pfizer, Sanofi-Aventis, UCB, 2,Abbott, AstraZeneca, Biotest, BMS, Crescendo Bioscience, Hoffmann-LaRoche, Genentech, Janssen, Eli Lilly and Company, Merck, Pfizer, UCB, 5,Abbott, Astra Zeneca, BMS Canada, Hoffmann-LaRoche, Janssen, Pfizer, UCB, Amgen, 8.


Abstract Number: 513
Time to Achieve Moderate/Low Disease Activity and Remission in RA Patients on Baricitinib Compared to Adalimumab, Methotrexate, and Placebo


1 University of Toronto, Toronto, ON, Canada, 2 Rene Descartes University, Cochin Hospital, Paris, France, 3 Northwestern University Feinberg School of Medicine, Chicago, IL, 4 Eli Lilly and Company, Indianapolis, IN, 5 Europe Research Center, Eli Lilly and Company, Madrid, Spain, 6 Eli Lilly Norge A.S., Oslo, Norway, 7 Diakonhjemmet Hospital, Oslo, Norway

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Baricitinib (BARI), an oral, selective Janus kinase (JAK)1/2 inhibitor, has shown efficacy in DMARD naïve RA patients (pts) and in pts with inadequate response to methotrexate (MTX-IR). In the EU, BARI is approved for treating moderate to severe active RA in adults. The objective of this analysis is to evaluate the time to achieve moderate disease activity (MDA), low disease activity (LDA), and remission in pts treated with BARI 4-mg compared to placebo (PBO) or active comparators, MTX and adalimumab (ADA) from the RA-BEGIN and RA-BEAM trials.

Methods: In RA-BEGIN, DMARD naïve pts were randomized to BARI 4-mg once daily (QD), MTX or BARI 4-mg+MTX for 52 weeks (wks). In RA-BEAM, MTX-IR pts were randomized to PBO, BARI 4-mg QD or ADA 40-mg biweekly for 52 wks (PBO switched to BARI 4-mg at 24 wks). This post hoc analysis estimated the time to achieve MDA (Clinical Disease Activity Index, CDAI ≤22), LDA (CDAI ≤10), and remission (CDAI ≤2.8) in modified intent-to-treat (mITT) pts and in the subset of pts with high baseline disease activity (HDA) defined as CDAI >22 from the two trials. Cumulative incidence of MDA, LDA, and remission over 52 wks for RA-BEGIN and 24 wks for RA-BEAM were estimated. Hazard ratios between treatments were obtained using Cox proportional hazards regression adjusting for region and baseline joint erosions (1-2 or ≥3 erosions) without control for multiple comparisons.

Results: In DMARD naïve population, BARI 4-mg monotherapy pts were 1.6 times more likely to achieve MDA and LDA and twice more likely to achieve remission compared to MTX (p<0.001) (Table). Median time to MDA and LDA with BARI 4-mg treatment (2 and 12 wks, respectively) was 2 and 8 wks shorter than with MTX (4 and 20 wks, respectively) (Figure). Bari 4-mg+MTX performed similar to BARI 4-mg monotherapy.

In MTX-IR population, BARI 4-mg treated pts were 1.7, 2.3, and 3.5 times more likely to achieve MDA, LDA, and remission than PBO (p<0.001) and 1.0, 1.1, 1.4 times more likely to achieve MDA (p=0.557), LDA (p=0.295), and remission (p=0.030) than ADA (Table). Median time to MDA was 5 wks shorter with BARI 4-mg treatment (2 wks) than PBO (7 wks) but similar to ADA (2 wks). Median time to LDA with BARI 4-mg (12 wks) was 2 wks shorter than ADA (14 wks) while PBO pts never reached the median time to LDA during the 24 wk study (Figure). Consistent results were obtained in pts with HDA.

Conclusion: DMARD naïve and MTX-IR pts were more likely to achieve LDA and remission, and at a faster pace, with BARI 4-mg than the comparator treatment groups.

Table: Hazard ratios and median times to achieving MDA, LDA, and remission in mTTR patients and patients with HDA at baseline from RA-BEGIN and RA-BEAM

<table>
<thead>
<tr>
<th>RA-BEGIN</th>
<th>RA-BEAM</th>
<th>HDA</th>
<th>ADA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>mTTR</strong></td>
<td><strong>mTTR</strong></td>
<td><strong>mTTR</strong></td>
<td><strong>mTTR</strong></td>
</tr>
<tr>
<td><strong>N = 210</strong></td>
<td><strong>N = 215</strong></td>
<td><strong>N = 159</strong></td>
<td><strong>N = 166</strong></td>
</tr>
<tr>
<td><strong>MDA</strong></td>
<td>4.1</td>
<td>2.3</td>
<td>1.8</td>
</tr>
<tr>
<td><strong>p-value</strong></td>
<td>&lt;0.001</td>
<td>0.166</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>LDA</strong></td>
<td>20.3</td>
<td>11.9</td>
<td>1.9</td>
</tr>
<tr>
<td><strong>p-value</strong></td>
<td>&lt;0.001</td>
<td>0.151</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Remission</strong></td>
<td>&gt;52</td>
<td>51.7</td>
<td>2.5</td>
</tr>
<tr>
<td><strong>p-value</strong></td>
<td>&lt;0.001</td>
<td>0.289</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>N = 488</strong></td>
<td><strong>N = 487</strong></td>
<td><strong>N = 330</strong></td>
<td><strong>N = 296</strong></td>
</tr>
<tr>
<td><strong>MDA</strong></td>
<td>7.4</td>
<td>2.1</td>
<td>1.7</td>
</tr>
<tr>
<td><strong>p-value</strong></td>
<td>&lt;0.001</td>
<td>0.557</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>LDA</strong></td>
<td>&gt;24</td>
<td>12.1</td>
<td>2.3</td>
</tr>
<tr>
<td><strong>p-value</strong></td>
<td>&lt;0.001</td>
<td>0.295</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Remission</strong></td>
<td>&gt;24</td>
<td>&gt;24</td>
<td>3.5</td>
</tr>
<tr>
<td><strong>p-value</strong></td>
<td>&lt;0.001</td>
<td>0.330</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CI: confidence interval, HDA: patients with high baseline disease activity (CDAI >22), HR: hazard ratio, LDA: low disease activity, CDAI <10, MDA: moderate disease activity, CDAI 22-32; Remission: CDAI ≤20; mTTR: modified intent-to-treat patients; wk: week; *DMARD naïve patients; **MTX-IR patients (on background csDMARDs)

Figure: Cumulative incidence of mTTR patients achieving LDA and remission from A. RA-BEGIN and B. RA-BEAM

A. RA-BEGIN (DMARD naïve patients)

B. RA-BEAM (MTX-IR patients)

*RA-BEAM patients were on background csDMARDs
Disclosure: E. C. Keystone, Abbott, Amgen, AstraZeneca, BMS, Hoffmann-LaRoche, Janssen, Eli Lilly and Company, Novartis, Pfizer, Sanofi-Aventis, UCB, 2,Abbott, AstraZeneca, Biotest, BMS, Crescendo Bioscience, Hoffmann-LaRoche, Genentech, Janssen, Eli Lilly and Company, Merck, Pfizer, UCB, 5,Abbott, AstraZeneca, BMS Canada, Hoffmann-LaRoche, Janssen, Pfizer, UCB, Amgen, 8; M. Dougdos, Abbvie, Pfizer, Eli Lilly and Company, Novartis, UCB, Merck, Roche, BMS UCB, 2,Abbvie, Pfizer, Eli Lilly and Company, Novartis, UCB, Merck, Roche, BMS, UCB, 5; E. M. Ruderman, AbbVie, Amgen, BMS, GSK, Janssen, Eli Lilly and Company, Novartis, Pfizer, Roche/Genentech, 5; B. Zhu, Eli Lilly and Company, 1,Eli Lilly and Company, 3; P. Lopez-Romero, Eli Lilly and Company, 1,Eli Lilly and Company, 3; H. Lund, Eli Lilly and Company, 1,Eli Lilly and Company, 3; A. Cardoso, Eli Lilly and Company, 1,Eli Lilly and Company, 3; D. E. Schlichting, Eli Lilly and Company, 1,Eli Lilly and Company, 3; P. Martinez Osuna, Eli Lilly and Company, 1,Eli Lilly and Company, 3; R. Ortmann, Eli Lilly and Company, 1,Eli Lilly and Company, 3; T. K. Kvien, AbbVie, Biogen, BMS, Celltrion, Eli Lilly and Company, Janssen, Merck-Serono, MSD, Novartis, Oktal, Orton Pharma, Hospira/Pfizer, Roche, Samsung, Sandoz, UCB, 5,AbbVie, Biogen, BMS, Celltrion, Eli Lilly and Company, Janssen, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Samsung, Sandoz, UCB, 8.


Abstract Number: 514

BMS-986195, a Novel, Rapidly Acting, Covalent Inhibitor of Bruton’s Tyrosine Kinase: Safety, Pharmacokinetic and Pharmacodynamic Profiles in Healthy Participants

IM Catlett, L Wei, N Zheng, A Liu, B He, I Girgis and M Nowak, Bristol-Myers Squibb, Princeton, NJ
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Bruton’s tyrosine kinase (BTK) is an attractive, novel therapeutic target for autoimmune disease, as it is required for signal transduction and activation via B-cell receptor, Fc receptor and RANKL pathways. Due to the relatively slow turnover of BTK, a covalently bound inhibitor with a short pharmacokinetic (PK) half-life can lead to prolonged pharmacodynamic (PD) effects. BMS-986195 is being developed for the treatment of autoimmune diseases. This study assessed the safety, tolerability, PK and PD of BMS-986195 following oral administration in healthy participants.

Methods: Healthy participants (18–50 years) were randomized in a 3:1 ratio to receive a single dose (0.3–30 mg BMS-986195 or placebo; n=30) or multiple doses (0.3–10 mg BMS-986195 or placebo once daily for 14 days; n=24). Safety and tolerability were assessed by physical examinations, vital sign measurements, 12-lead electrocardiograms and clinical laboratory evaluations. Plasma concentrations of BMS-986195 were measured using a validated liquid chromatography–tandem mass spectrometry (LC-MS/MS) assay at various time points. BTK occupied by BMS-986195 was measured using a novel LC-MS assay, as a PD and target engagement marker.

Results: BMS-986195 was well tolerated in the single- and multiple ascending dose study. No drug-related serious adverse events were observed. BMS-986195 was rapidly absorbed with peak concentrations occurring in <1 hour and eliminated with a half-life of <2 hours across all dose levels tested. Increases in the PK exposure (area under the curve and maximum serum concentration) were dose proportional. No time-dependent changes in PK were observed following the multiple-dose administration of BMS-986195. BTK occupancy increased in a dose-dependent manner following single-dose administration of BMS-986195. The mean (SD) peak BTK occupancy following a single dose was 19% (3%) at 0.3 mg, and 100% (0%) at ≥10 mg. 100% BTK occupancy was sustained for up to 24 hours. BTK occupancy returned towards baseline over the following 6 days (Figure). Total BTK levels did not vary over time or by dose group. With multiple-dose administration, 100% BTK occupancy was reached at ≥3 mg once daily, and drug-occupied BTK exhibited similar kinetics to that observed following a single-dose
administration. Additional PD and safety results from the multiple ascending dose study will be presented. **Conclusion:** BMS-986195 was well tolerated at the doses tested in healthy participants. It showed a favorable PK/PD profile with a rapid elimination of the compound and sustained PD activity, due to the relatively slow turnover of BTK and covalent binding of BMS-986195. 100% BTK occupancy over the entire daily dosing interval was observed. Overall results suggest that BMS-986195 is an attractive candidate for further clinical development. 1. Whang JA, et al. *Drug Discov Today* 2014;19:1200–4.

**Disclosure:** I. Catlett, Bristol-Myers Squibb, 3; L. Wei, Bristol-Myers Squibb, 3; N. Zheng, Bristol-Myers Squibb, 3; A. Liu, Bristol-Myers Squibb, 3; B. He, Bristol-Myers Squibb, 3; I. Girgis, Bristol-Myers Squibb, 3; M. Nowak, Bristol-Myers Squibb, 3.


**Abstract Number:** 515

**Leukopenia and Tumor Necrosis Factor Alpha Inhibitor Therapy**

Wenlu Xiong¹, Rochella A. Ostrowski², William Adams³ and Rodney Tehrani⁴, ¹Rheumatology, Vanderbilt University Medical Center, Nashville, TN, ²Rheumatology, Loyola University Medical Center, Maywood, IL, ³Clinical Research Office, Loyola University Medical Center, Maywood, IL, ⁴Rheumatology & Immunology, Loyola University Medical Center, Maywood, IL

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**- Background/Purpose:** Tumor necrosis factor (TNF) alpha, a key proinflammatory cytokine in rheumatoid arthritis (RA) and inflammatory bowel disease (IBD), has been a major target in the treatment of these conditions. Although the immunosuppressant side effects are well-known, recent studies suggest that TNF alpha inhibition is directly linked to the development of leukopenia and that serial complete blood cell (CBC) counts should be monitored. However, most studies investigating hematologic side effects of anti-TNF alpha therapy have been case studies. This study was designed to
identify the frequency of leukopenia in patients on anti-TNF alpha therapy at a tertiary care institution and whether certain demographics, baseline white blood cell (WBC) counts, or other factors correlate with the development of leukopenia.

- **Methods:** The chart review was performed for adult patients who received anti-TNF alpha therapy (adalimumab, etanercept, certolizumab, golimumab, or infliximab) at Loyola University Medical Center between 2007 and 2016 and who had a baseline WBC count in the year prior to therapy. Subjects with baseline leukopenia (WBC <4 K/uL) were excluded. Data analysis was performed using the chi-square test, analysis of variance, Student t-test, and a multivariable general linear model.

- **Results:** Of 89 patients who met the study criteria, 17 patients (19%) developed leukopenia during anti-TNF alpha therapy. Patients in the study were treated for RA, IBD, psoriasis, psoriatic arthritis, IBD with associated arthritis, inflammatory arthritis not otherwise specified, or other diagnoses. Patients who developed leukopenia had significantly lower mean WBC counts compared to those who did not develop leukopenia (p = 0.01) while all other factors including sex, race, age, type of TNF inhibitor, diagnosis, duration of therapy, and concomitant methotrexate use were comparable between the two groups (Table 1). After controlling for these variables, baseline WBC count was the only significant predictor of lowest WBC count. For every one unit (K/uL) decrease in baseline WBC, the lowest WBC on therapy decreased by 0.35 K/uL (p<0.001).

- **Conclusion:** In summary, leukopenia developed in a considerable proportion of patients on anti-TNF alpha therapy. This observation was not associated with several variables studied, including type of TNF inhibitor used, diagnosis, duration of therapy, and concomitant use of methotrexate. A lower baseline WBC count was the only significant predictor for both the development of leukopenia and of the greatest degree of leukopenia. These findings suggest that leukopenia should be screened periodically for all patients on TNF alpha inhibitor therapy regardless of baseline demographics and that those who have lower baseline WBC counts may warrant closer monitoring.

<table>
<thead>
<tr>
<th>Table 1: Demographics as a function of leukopenia status</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
</tr>
<tr>
<td>-----------</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Race</td>
</tr>
<tr>
<td>Caucasian</td>
</tr>
<tr>
<td>African American/Black</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>Diagnosis</td>
</tr>
<tr>
<td>RA</td>
</tr>
<tr>
<td>IBD</td>
</tr>
<tr>
<td>Psoriasis</td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
</tr>
<tr>
<td>IBD with arthritis</td>
</tr>
<tr>
<td>IBD not otherwise specified or Other</td>
</tr>
<tr>
<td>Type of Anti-TNF</td>
</tr>
<tr>
<td>Adalimumab</td>
</tr>
<tr>
<td>Etanercept</td>
</tr>
<tr>
<td>Infliximab</td>
</tr>
<tr>
<td>Certolizumab or Golimumab</td>
</tr>
<tr>
<td>Concomitant MTX Use</td>
</tr>
<tr>
<td>Yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>45.63 (15.72)</td>
<td>45.48 (14.36)</td>
<td>14.76 (15.40)</td>
</tr>
<tr>
<td>Duration of Anti-TNF (Months)</td>
<td>36.40 (28.52)</td>
<td>36.95 (23.44)</td>
<td>36.51 (27.84)</td>
</tr>
<tr>
<td>Baseline WBC</td>
<td>9.7 (5.2)</td>
<td>6.4 (2.8)</td>
<td>9.1 (5.0)</td>
</tr>
<tr>
<td>Lowest WBC on Anti-TNF</td>
<td>6.8 (2.4)</td>
<td>3.4 (0.5)</td>
<td>6.1 (2.5)</td>
</tr>
</tbody>
</table>

**Disclosure:** W. Xiong, None; R. A. Ostrowski, None; W. Adams, None; R. Tehrani, None.

**View Abstract and Citation Information Online** - [http://acrabstracts.org/abstract/leukopenia-and-tumor-necrosis-factor-alpha-inhibitor-therapy](http://acrabstracts.org/abstract/leukopenia-and-tumor-necrosis-factor-alpha-inhibitor-therapy)

**Abstract Number:** 516
Efficacy of Adding Iguratimod Therapy in Rheumatoid Arthritis Patients Who Had Inadequate Response to Biologic Dmards

Toshiaki Miyamoto, Rheumatology, SEIREI HAMAMATSU GENERAL HOSPITAL, Hamamatsu, Japan
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Iguratimod (IGU) was approved in June 2012 and recommended by JCR guideline 2014 in the treatment of rheumatoid arthritis (RA). Although there have been efficacy of monotherapy and concomitant MTX in clinical trials, however, there have been no reports of concomitant biologic DMARDs. Therefore, we investigated efficacy of concomitant IGU therapy in RA patients who had inadequate response to Bio at the author’s institution.

Methods: IGU were prescribed to 62 RA patients from August 2012 to June 2016, subjects were 57 patients adding IGU who had inadequate response to Bio. Previous treatment Bio was ADA. And concomitant MTX (mean 12 mg/week) of 54 patients (94%). Baseline characteristics were Mean age 53 years, mean duration of illness 5.5 years, corticosteroid use 14% (mean 2.9mg/day). The course of DAS28, SDAI, CDAI and remission rates were analyzed.

Results: Mean DAS28-ESR, DAS28-CRP, SDAI, CDAI were significantly decreased from the initiation of IGU treatment at 24 weeks (3.07→2.27, 2.55→1.63, 6.94→2.21, 6.23→1.95). Remission rates of DAS28-ESR, DAS28-CRP, SDAI, CDAI were 67%, 82%, 72%, 74% at 24 weeks. There were almost no side-effect after adding IGU.

Conclusion: IGU might be a new RA treatment option for aiming remission in patients who had inadequate response to Bio.

Disclosure: T. Miyamoto, None;

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/efficacy-of-adding-iguratimod-therapy-in-rheumatoid-arthritis%e3%80%80patients-who-had-inadequate-response-to-biologic-dmards

Abstract Number: 517

Evaluation of the Effectiveness of Injectable Methotrexate for the Treatment of Rheumatoid Arthritis

Jenny Wan1, Michele Spence2, Fang Niu3, Rita Hui3, Stephen Cheng1, Logan Saito4 and Antony Lin5, 1Kaiser Permanente Drug Information Services - California Regions, Downey, CA, 2Kaiser Permanente Pharmacy Outcomes Research Group, Downey, CA, 3Kaiser Permanente Pharmacy Outcomes Research Group, Oakland, CA, 4Kaiser Permanente Southern California Clinical Pharmacy Services, Downey, CA, 5Rheumatology, Kaiser Permanente Fontana Medical Center, Fontana, CA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A  
Session Time: 9:00AM-11:00AM

Background/Purpose:
Systemic methotrexate (MTX) is the first-line disease-modifying antirheumatic drug (DMARD) for treating early and established rheumatoid arthritis (RA). When compared to oral MTX, subcutaneous MTX enhances tolerability with a significant reduction in gastrointestinal side effects. Subcutaneous MTX has further demonstrated better clinical efficacy than oral MTX in patients who were both oral MTX-experienced and MTX-naïve. This study aimed to better quantify the role of subcutaneous MTX in delaying initiation of biologic DMARD (bioDMARD).

Methods:
In this retrospective cohort analysis, new users of oral MTX were identified between January 1, 2008 and December 31, 2014 (N=42,413). Patients aged 18 years or older with continuous health plan membership, drug benefit, and RA diagnosis (n=7,968) were included in this analysis. Patients who had at least one ≥2.5 mg increase in the weekly oral MTX dose (n=3,970) were compared to those who switched from oral MTX to subcutaneous MTX (n=421). The primary outcome was the likelihood of initiating a bioDMARD, which was analyzed using Cox proportional hazard model. Other outcomes measured were the timing of changes in treatment, and doses of oral or subcutaneous MTX at the time of switches or at the end of follow-up.

Results:
Comparing the two treatment strategies, the unadjusted and adjusted Cox regression analyses showed no significant difference in the likelihood of initiating bioDMARD. Factors associated with a reduced likelihood of initiation of bioDMARD included older age, African American, and the initiation of azathioprine. In contrast, the use of systemic prednisone at baseline and higher erythrocyte sedimentation rate (ESR) during follow-up were associated with an increased likelihood of initiation of bioDMARD. Among the patients who started bioDMARD, more than two-third of the patients never received MTX at doses >20 mg/week prior to initiating bioDMARD. Compared to patients who had a dose increase in oral MTX, patients who switched to subcutaneous MTX significantly delayed the use of bioDMARDs by 9 months (p<0.001).

Conclusion:
There is no significant difference in the likelihood of initiating bioDMARD between the two treatment strategies. Compared to oral MTX group, switching to subcutaneous MTX delayed the use of bioDMARD by 9 months. Given that bioDMARDs are costly and require injections, switching from oral MTX to subcutaneous MTX before using bioDMARD may be a reasonable alternative for patients who fail oral MTX.

Figure 1: Likelihood of BioDMARD Initiation

<table>
<thead>
<tr>
<th>Treatment Strategies</th>
<th>Unadjusted HR (95% CI, p-value) n = 4,391</th>
<th>Adjusted HR* (95% CI, p-value) n = 2,182</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased PO MTX Dose</td>
<td>1.00 (reference)</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>switched to SC MTX</td>
<td>1.10 (0.93-1.31, 0.280)</td>
<td>1.06 (0.82-1.38, 0.635)</td>
</tr>
</tbody>
</table>

95% CI = 95% confidence interval; PO = oral; HR = hazard ratio; SC = subcutaneous

*Adjusted for the following covariates:
- **Baseline covariates:** Age, sex, region, race, time since RA diagnosis, prednisone use, diabetes, Charlson’s comorbidity index, rheumatology visits, MTX dose, anti-citrullinated protein antibodies, rheumatoid factor
- **Follow-up covariates:** Initiation of azathioprine, hydroxychloroquine, leflunomide, sulfasalazine, tocainide, gold, cyclosporine, mycophenolate mofetil, cyclophosphamide, minocycline, penicillamine, erythrocyte sedimentation rate, C-reactive protein
Disclosure: J. Wan, None; M. Spence, None; F. Niu, None; R. Hui, None; S. Cheng, None; L. Saito, None; A. Lin, None.


Abstract Number: 518

The Occurrence of Shingles and the Effect of Zoster Vaccination with the Use of Methotrexate in Rheumatoid Arthritis Patients

Antony Lin1, Qiaowu Li2, Jiaxiao Shi2, Serena Lin3, Danielle Wang4, Jenny Wan5, Kevin Lee3, Hung-Fu Tseng2 and TC Cheetham6, 1Southern California Permanente Medical Group, Pasadena, CA, 2Department of Research and Evaluation, Kaiser Permanente, Pasadena, CA, 3Stanford University, Stanford, CA, 4UCI Medical Center, Irvine, CA, 5Kaiser Permanente Drug Information Services - California Regions, Downey, CA, 6Western University of Health Sciences, Pomona, CA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

To investigate the efficacy and safety of zoster vaccines administered in rheumatoid arthritis(RA) patients taking methotrexate(MTX).

Methods:

By reviewing data through the Kaiser Permanente electronic medical record (EMR) retrospectively, we identified 893 adult RA patients who received zoster vaccination between January 1, 2007 and December 31, 2012 and had at least 2 RA diagnoses documented within one year prior to the vaccination date. Patients treated with any biologic DMARDs within 6 months prior to the index dates were excluded. The cohort was followed until the occurrence of zoster infection, disenrollment, death or the end of study, whichever came first. The primary outcome, vaccination safety, was measured by time to occurrence of zoster infections within 42 days after zoster vaccines administered. The secondary outcome, vaccine efficacy, measured by time to occurrence of zoster infections (after day 42) until the end of follow-up period, was studied among those who maintain the treatment during follow-up period (n=762). Dosage effect was also analyzed among those taking MTX (n=342) by comparing patients taking $\geq 25$mg/week and those taking 22.5mg/week or less. Cox proportional model was used to analyze hazard ratios between groups.

Results:

Among 893 RA patients who were given zoster vaccines, 366 patients were taking MTX within 6 months prior to the zoster vaccination and 527 patients were not taking MTX. At baseline, 707(79%) patients were female with a mean age of 70.1 (SD: .5) and disease duration of 6.6 (3.9) years. The analysis showed that the rate of zoster infection was 0.13 per 1000-person day in the MTX group and the rate was 0.23 per 1000-person day in the non-MTX group. We found no significant statistical difference in the rate of zoster infections within the first 42 days of vaccination with adjusted hazard ratio of 0.50(95% CI 0.09-2.69, p-value=0.42). During the subsequent follow-up period, 742 patients continued their baseline treatment. The rate of zoster infection was 15.9 per 1000-person year in the MTX group and the rate was 18.6 per 1000-person year in the non-MTX group with the adjusted hazard ratio 0.79(95% CI 0.47-1.33, p-value=0.37). Among the 334 patients taking MTX, 292 patients were taking a dose of 22.5 mg or under while 42 were taking the dose of 25mg or more. The final analysis from the model showed no significant difference in dosage effect, the adjusted hazard ratio was 0.34(95% CI 0.04-2.54, p-value=0.29).

Conclusion:

Zoster vaccination is safe to be given to RA patients taking MTX regardless of the dosage. The vaccination is equally effective in RA patients taking MTX and not taking MTX.

Disclosure: A. Lin, None; Q. Li, None; J. Shi, None; S. Lin, None; D. Wang, None; J. Wan, None; K. Lee, None; H. F. Tseng, None; T. Cheetham, Bristol-Myers Squibb, 2.


Abstract Number: 519

Filgotinib, a Selective Janus Kinase 1 Inhibitor, Has No Effect on QT Interval in Healthy Subjects

Kacey Anderson¹, Hao Zheng², Chohee Yun³, Ellen Kwan⁴, Ann Qin¹, Florence Namour⁵, Brian P. Kearney¹ and Yan Xin¹, ¹Clinical Pharmacology, Gilead Sciences, Inc., Foster City, CA, ²Gilead Sciences, Inc., Foster City, CA, ³Clinical
Background/Purpose:

Filgotinib is a potent and selective Janus kinase 1 (JAK1) inhibitor being developed to treat inflammatory diseases. Safety pharmacology studies and Phase 1 studies indicate that there is a low risk of QT prolongation by filgotinib treatment. This dedicated Phase 1 study was conducted to evaluate the potential effect of filgotinib on the QT interval prolongation in healthy subjects per the International Conference on Harmonization (ICH) E14 guidance.

Methods:

52 healthy adults were randomized to receive a single dose of moxifloxacin 400 mg (positive control) or once daily doses of filgotinib 200 mg (top therapeutic dose), filgotinib 450 mg (supratherapeutic dose), or placebo for 7 days. There was a washout period of 9 days between each dosing period. Digital ECGs were collected in triplicates within 5 minutes at matched time points on the 1st day (predose) and 7th day (postdose) with 24 hours measurements for each treatment on the 7th day. QTc (QTcF and QTcI) were derived and average of triplicates provided time-matched QTc. Subjects with large QTc or QTc change from baseline were summarized. Changes from baseline in time-matched QTc were fit to a mixed effect model, and difference of QTc change between filgotinib treatments or moxifloxacin vs placebo were quantified. PK of filgotinib was evaluated, and safety was monitored throughout study. The 90% confidence intervals (CIs) were constructed for the ratios of geometric least squares means of filgotinib PK parameters (AUC$_{tau}$, C$_{max}$, and C$_{tau}$) for 450 mg vs. 200 mg daily dose. The association between QTc and plasma concentrations of filgotinib was explored.

Results:

46 (88.5%) subjects completed study drug treatments. The mean (range) age of subjects was 38 (20-55) years, 39 (75%) subjects were female, 28 (53.8%) were white and 15 (28.8%) were hispanic or latino.

Lack of QTcF prolongation has been demonstrated at both doses of filgotinib. The upper limits of the 2-sided 90% CI for mean difference in QTcF between 200 mg or 450 mg vs placebo were less than 10 msec (≤ 8.35 msec) at all time points. Similar results were observed with QTcI. Assay sensitivity was demonstrated using moxifloxacin at 400 mg, with the lower 96.7% CI for mean difference in QTcF above 5 msec (≥ 8.32 msec) at 2, 3, and 4 hours post dose. Filgotinib 450 mg provided 2.1-fold higher C$_{max}$ than 200 mg. There were no clinically relevant relationships between change from baseline (placebo-corrected) in QTcF/QTcI and plasma concentrations of filgotinib.

Overall, 8 (15.7%), 15 (30.0%), 0 (0.0%), and 5 (10.0%) subjects experienced treatment-related AEs during filgotinib 200 mg, filgotinib 450 mg, placebo, and moxifloxacin treatment periods, respectively. No serious or severe (≥ Grade 3) AEs occurred, and the majority of the AEs reported were Grade 1 (mild) in severity. No Grade 4 laboratory abnormalities occurred. There were no clinically significant trends in vital signs, or safety ECG recordings.

Conclusion:

Filgotinib does not affect QTc interval by definition of a negative thorough QT study per ICH E14 guidance at 200 mg (top therapeutic dose) and 450 mg (supratherapeutic dose; 2.1-fold higher C$_{max}$ than 200 mg).

Disclosure: K. Anderson, Gilead Sciences, Inc, 1,Gilead Sciences, Inc, 3; H. Zheng, Gilead Sciences, Inc, 1,Gilead Sciences, Inc, 3; C. Yun, Gilead Sciences, Inc, 1,Gilead Sciences, Inc, 3; E. Kwan, Gilead Sciences, Inc, 1,Gilead Sciences, Inc, 3;
Clinical and Structural Responses of Patients with Active Rheumatoid Arthritis (RA) Using Step-up Dosing of Tofacitinib in a Treat to Target Approach

Norman Gaylis¹, Joanne Sagliani¹ and Steven Needell², ¹Arthritis & Rheumatic Disease Specialties, Aventura, FL, ²Boca Radiology, Boca Raton, FL
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Tofacitinib has been shown to reduce the clinical signs and symptoms of some RA patients at an approved dose of 5 mg bid. Studies report that 10 mg bid is an effective dose. This is the first community practice trial to measure the clinical and structural benefits of stepping up the initial dose of 5 mg bid in non-responders to 10 mg bid in order to achieve a clinical response using a treat to target approach.

Objective: This study evaluates the optimal dose of tofacitinib (5 mg bid VS 10 mg bid) needed to reach treatment target in a cohort of patients with active RA while comparing the corresponding structural findings measured by low field MRI

Methods: 20 RA patients who were unresponsive to either methotrexate (10-25 mg weekly) or MTX plus up to 2 prior biologics with synovitis, osteitis or erosions on Baseline MRI (Esaote 0.3T) were treated with 5 mg bid tofacitinib with a treat to target goal of LDA or remission depending on the Clinical Activity Index (CDAI) score at Baseline. If the target was not met and sustained for 3 months, the dose of tofacitinib was increased to 10 mg bid in an attempt to reach target. MRIs of the hand/wrist were blindly read by a musculoskeletal radiologist using a RAMRIS score. A CDAI score of >10 was needed at study entry.

Results: Of the 20 enrolled patients, 6 remained at 5 mg bid and 14 were dose escalated to 10 mg bid most at the 12 week period. Of the 5 mg bid group, 3 completed the trial at target and 3 early termed (ET) for lack of efficacy, relocation and AE. Structurally, there was no change in erosions in all 3 patients; 2 showed regression of synovitis and 1 showed no change: 2 showed regression in osteitis and 1 no change. Of the 14 patients escalated to 10 mg bid, 11 completed the trial with 7 remissions, 2 at LDA, and 1 at MDA. 3 patients ET due to lack of efficacy. In the 10 mg bid group, 9 patients showed no change in erosions, 1 regression and 1 progression. 5 patients showed no change in synovitis and 6 showed regression, and 7 showed no change in osteitis, 3 showed regression and 1 showed progression. The CRP values correlated with the improvement of the clinical and structural results, in particular, the levels improved after the dose was increased to 10 mg bid.

Conclusion: Our results suggest that a significant number of patients treated with the standard dose of 5 mg bid may potentially have improved outcomes including LDA or remission when treated at a higher dose (10 mg bid). This is evidenced by the results of 11 of the 14 patients having significant improved response most after 3 months of treatment with 10 mg bid. Furthermore, the structural findings correlate in large part to the clinical findings showing stabilization or improvement in most patients. An extension trial is currently ongoing to determine if the positive outcome of LDA or remission at the higher dose (10 mg bid) can be sustained if the dose if reduced back down to 5 mg bid.
Update on the Clinical Phase 1 and Phase 2 Trials Investigating the Fully Human Immunocytokine Dekavil (F8IL10) in Patients with Rheumatoid Arthritis

Mauro Galeazzi\textsuperscript{1}, Gian Domenico Sebastiani\textsuperscript{2}, Jürgen Wollenhaupt\textsuperscript{3}, Jean Dudler\textsuperscript{4}, Christof Specker\textsuperscript{5}, Reinhard Voll\textsuperscript{6}, Pascal Zufferey\textsuperscript{7}, Piercarlo Sarzi Puttini\textsuperscript{8}, Ombretta Viapiana\textsuperscript{9} and Franziska Bootz\textsuperscript{10}, \textsuperscript{1}Rheumatology, University Hospital of Siena, Siena, Italy, \textsuperscript{2}Rheumatology, San Camillo Forlanini Hospital, Roma, Italy, \textsuperscript{3}Division of Reheumatology, Schoen-Klinik Hamburg-Eilbek Teaching Hospital of the University of Hamburg, Hamburg, Germany, \textsuperscript{4}Rheumatology, Cantonal Hospital Fribourg, Fribourg, Switzerland, \textsuperscript{5}Rheumatology, St. Josef Krankenhaus, Universitätsklinikum Essen, Essen, Germany, \textsuperscript{6}Clinic for Rheumatology and Clinical Immunology, Medical Center University of Freiburg, Freiburg, Germany, \textsuperscript{7}Department of Rheumatology, University Hospital Lausanne, Lausanne, Switzerland, \textsuperscript{8}Rheumatology, Luigi Sacco Hospital, Milan, Italy, \textsuperscript{9}University Hospital Verona, Verona, Italy, \textsuperscript{10}Clinical Department, Philochem AG (Philogen Group), Otelfingen, Switzerland

First publication: September 18, 2017
**Session Date:** Sunday, November 5, 2017  
**Session Title:** Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

The antibody-based targeted pharmacodelivery of cytokines by means of immunocytokines has the potential to enhance therapeutic activity at the site of disease while sparing healthy tissues. Dekavil (F8IL10) is a fully human immunocytokine consisting of the targeting antibody F8 (specific to EDA) fused to the anti-inflammatory payload interleukin-10. Dekavil is currently in phase 2 clinical development for the treatment of rheumatoid arthritis (RA).

**Methods:**

Patients diagnosed with RA according to ACR/EULAR classification criteria, who have active disease despite MTX therapy and who failed anti-TNF treatment are the target population.

In a recently completed phase 1b dose escalation study with the aim to explore safety, tolerability and the maximum tolerated dose (MTD), cohorts of 3-6 patients were treated with escalating doses of Dekavil (6-600 μg/kg + MTX). Patients received 4 weekly s.c. injections of Dekavil in combination with a fixed dose of MTX (10-15 mg). Patients willing to continue the treatment had the opportunity to receive 4 additional weekly injections of Dekavil.

The ongoing multicenter, double-blind, placebo-controlled phase 2 trial assesses therapeutic activity by measuring the mean change from baseline of DAS28-CRP. Patients are randomized into two treatment groups (Dekavil 30 or 160 μg/kg plus MTX) and one placebo group (placebo plus MTX). Study participants receive 8 weekly s.c. injections of Dekavil in combination with a fixed dose of MTX (10-15 mg).

**Results:**

In the phase 1 study, Dekavil was shown to be well tolerated up to the highest investigated dose (600 μg/kg) and an MTD was not reached. In 34 out of 35 patients treated in the phase 1 study, no DLTs, no SAEs and no SUSARs have been reported. One study subject in cohort 9 (450 μg/kg) experienced a DLT (G2 purpura), which was accompanied by a SAE (G2 dyspnea, not drug related). The patient fully recovered within one week after having received corticosteroid treatment. The most frequently observed adverse event was mild injection site reaction and occurred in 60% of the patients. Furthermore, two cases of drug related anemia (G3 and G2; 160 μg/kg and 450 μg/kg, respectively) were reported in this study. All adverse reactions resolved completely. At the first efficacy assessment after 4 cycles of treatment, 36.4% of patients (12/33) revealed ACR responses. The fraction of responding patients increased to 45.8% (11/24) after 8 cycles of treatment. Two patients benefited from a long lasting ACR70 responses for more than 12 months after the last drug administration.

As of May 2017, 23 out of 87 patients have been enrolled in the phase 2 clinical study. Neither SAE nor SUSARs nor treatment-related deaths were recorded so far. An interim analysis performed after 45 patients will allow for a more thorough understanding of the product.

**Conclusion:**

The currently available data suggest that the biologic agent Dekavil is a safe and well tolerated novel therapeutic approach for the treatment of RA.

**Disclosure:** M. Galeazzi, None; G. D. Sebastiani, None; J. Wollenhaupt, Abbott, BMS, MSD, Pfizer, UCB, 2; Abbott, BMS, MSD, Pfizer, UCB, 5; J. Dudler, None; C. Specker, None; R. Voll, None; P. Zufferey, None; P. Sarzi Puttini, None; O. Viapiana, None; F. Bootz, Philchem AG (Philogen group), 3.

Tofacitinib, an Oral Janus Kinase Inhibitor, in the Treatment of Rheumatoid Arthritis: Safety and Efficacy in Open-Label, Long-Term Extension Studies over 9 Years

Jürgen Wollenhaupt1, Joel Silverfield2, Eun Bong Lee3, Ketti Terry4, Kenneth Kwok5, Sander Strengholt6, Ryan DeMasi7 and Lisy Wang4, 1Schoen-Klinik Hamburg-Eilbek Teaching Hospital of the University of Hamburg, Hamburg, Germany, 2Healthpoint Medical Group, Tampa, FL, 3Division of Rheumatology, Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea, Republic of (South), 4Pfizer Inc, Groton, CT, 5Pfizer Inc, New York, NY, 6Pfizer Inc, Capelle aan den IJssel, Netherlands, 7Pfizer Inc, Collegeville, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). Here, we report tofacitinib safety and tolerability up to 114 months (Mos) and clinical efficacy up to 96 Mos in long-term extension (LTE) studies.

Methods: Data were pooled from 2 open-label studies (NCT00413699 [ongoing; database not locked at March 2017 data cut]; and NCT00661661) of patients (pts) with RA who had participated in Phase 1/2/3 studies of tofacitinib. Pts received tofacitinib 5 or 10 mg twice daily (BID) as monotherapy or with background DMARDs. As pts in the LTE studies were allowed to switch doses, they were assigned to the 5 mg BID group if the total daily dose was <15 mg/day, and to the 10 mg BID group if it was ≥15 mg/day. Primary endpoints were adverse events (AEs) and confirmed laboratory safety data. Secondary endpoints included clinical efficacy measures (ACR20/50/70 response rates, DAS28-4[ESR], HAQ-DI, and Clinical Disease Activity Index). Safety data were included up to Mo 114 and completer-analyzed efficacy data up to Mo 96 (n≤100 post-Mo 96).

Results: 4967 pts were treated (mean [max] duration: 3.5 [9.4] years). Total tofacitinib exposure was 17,738.5 pt-years (py); 76.4% of pts maintained their initial dose. In total, 2518 pts (50.7%) discontinued (AEs: 1189 [23.9%]; insufficient clinical response: 179 [3.6%]). Most common AE classes with highest AEs: infections and infestations (69.6%; exposure adjusted event rate [EAER; events per 100 py], 19.71) and musculoskeletal/connective tissue disorders (40.3%; EAER, 11.40). Most common AEs: nasopharyngitis (19.1%; EAER, 5.41), upper respiratory tract infection (17.9%; EAER, 5.07), bronchitis (12.6%; EAER, 3.58), and urinary tract infection (12.5%; EAER, 3.55). Serious AEs occurred in 29.4% of pts, and serious infections (SIEs) in 8.9% of pts. Malignancies, excluding non-melanoma skin cancer, were reported in 3.0% of pts. Incidence rates (IR; pts with events per 100 py) for AEs of interest, with 95% confidence intervals (CIs), are provided in Table 1. IRs for SAEs, SIEs and malignancies through Mo 114 did not increase vs reported data through Mo 105.1 Confirmed laboratory data are provided in Table 1. No new safety risks were identified. Clinical responses were sustained from Mo 1 to Mo 96 (Table 2).

Conclusion: In patients with RA who remained in the LTE studies, tofacitinib (5 or 10 mg BID), with or without background DMARDs, was associated with consistent safety through Mo 114 and sustained clinical efficacy through Mo 96.

Reference:

Table 1. Safety data (Mo 114) in LTE studies of tofacitinib in patients with RA

<table>
<thead>
<tr>
<th>IRs for AEs of interest, pts with events per 100 py (95% CI)</th>
<th>Tofacitinib (5 and 10 mg BID) ± background DMARDs</th>
<th>N=4967</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious adverse events</td>
<td>9.13 (8.67, 9.61)</td>
<td></td>
</tr>
<tr>
<td>Serious infections</td>
<td>2.46 (2.23, 2.70)</td>
<td></td>
</tr>
<tr>
<td>Malignancies (excluding NMSC)</td>
<td>0.83 (0.71, 0.98)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Confirmed laboratory abnormalities</th>
<th>n (%)</th>
<th>IR per 100 py (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased hemoglobin</td>
<td>104 (2.1)</td>
<td>0.59 (0.48, 0.71)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>0 (0.0)</td>
<td>0 (0.0, 0.0)</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>70 (1.4)</td>
<td>0.39 (0.30, 0.49)</td>
</tr>
<tr>
<td>Aminotransferases</td>
<td>285 (5.7)</td>
<td>1.62 (1.44, 1.82)</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>138 (2.8)</td>
<td>0.77 (0.65, 0.91)</td>
</tr>
</tbody>
</table>

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BID, twice daily; CI, confidence interval; BL, baseline; DMARDs, disease-modifying antirheumatic drugs; IR, incidence rate; LTE, long-term extension; Mo, Month; N, number of evaluable patients; NMSC, non-melanoma skin cancer; pt, patient; py, p-years; RA, rheumatoid arthritis; ULN, upper limit of normal

Table 2. Clinical efficacy outcomes (up to Mo 96) in LTE studies of tofacitinib in patients with RA (as observed)

<table>
<thead>
<tr>
<th>Tofacitinib (5 and 10 mg BID) ± background DMARDs</th>
<th>BL</th>
<th>Mo 1</th>
<th>Mo 96</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACR response rates, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACR20</td>
<td>NA</td>
<td>73.7</td>
<td>77.9</td>
</tr>
<tr>
<td>ACR50</td>
<td>NA</td>
<td>49.9</td>
<td>59.5</td>
</tr>
<tr>
<td>ACR70</td>
<td>NA</td>
<td>29.2</td>
<td>41.7</td>
</tr>
<tr>
<td>DAS28-4(ESR), mean (SE)</td>
<td>N=4782</td>
<td>6.32 (0.01)</td>
<td>3.75 (0.02)</td>
</tr>
<tr>
<td>HAQ-DI, mean (SE)</td>
<td>N=4924</td>
<td>1.42 (0.01)</td>
<td>0.82 (0.01)</td>
</tr>
<tr>
<td>CDAI, mean change from BL (SE)</td>
<td>N=4802</td>
<td>NA</td>
<td>-24.5 (0.21)</td>
</tr>
</tbody>
</table>

ACR20/50/70, American College of Rheumatology 20%/50%/70% improvement; BID, twice daily; BL, baseline; CDAL, Clinical Disease Activity Index; DAS28-4(ESR), Disease Activity Score in 28 joints; erythrocyte sedimentation rate; DMARDs, disease-modifying antirheumatic drugs; HAQ-DI, Health Assessment Questionnaire-Disability Index; LTE, long-term extension; Mo, Month; N, number of evaluable patients; NA, not applicable; RA, rheumatoid arthritis; SE, standard error

Disclosure: J. Wollenhaupt, Pfizer Inc, 1,Pfizer Inc, 8; J. Silverfield, Pfizer Inc, 2,Pfizer Inc, 8; E. B. Lee, Pfizer Inc, 5; K. Terry, Pfizer Inc, 1,Pfizer Inc, 3; K. Kwok, Pfizer Inc, 1,Pfizer Inc, 3; S. Strengholt, Pfizer Inc, 1,Pfizer Inc, 3; R. DeMasi, Pfizer Inc, 1,Pfizer Inc, 3; L. Wang, Pfizer Inc, 1,Pfizer Inc, 3.


Abstract Number: 523

Prevalence of Occult Hepatitis B Carrier Status and Its Associated Risk Factors in Patients with Rheumatic Diseases Undergoing Biological Therapies

Chi Chiu Mok¹, Ling Yin Ho², Kar Li Chan¹, Sau Mei Tse¹ and Chi Hung To³, ¹Medicine, Tuen Mun Hospital, Hong Kong, Hong Kong, ²Dept of Medicine, Tuen Mun Hospital, Hong Kong SAR, Hong Kong, ³Medicine, Pok Oi Hospital, Hong Kong, Hong Kong
Background/Purpose:
To study the prevalence of occult hepatitis B carrier status and its associated factors in patients with rheumatic diseases undergoing biological therapies

Methods:
Consecutive adult patients with various rheumatic diseases who were currently receiving biological therapies between November 2016 and April 2017 were recruited in this cross-sectional study. Blood was taken for evidence of hepatitis B infection (HBsAg, anti-HBs, anti-HBc-IgG). For patients tested positive for HBsAg or anti-HBc-IgG, assay of serum HBV-DNA level was also performed. Occult hepatitis B carrier was defined as patients who were HBsAg negative but anti-HBc-IgG positive. Logistic regression was performed to study factors independently associated with occult hepatitis B carrier status in these patients.

Results:
310 Chinese patients were studied (60% women, age at biological therapy 44.0±13.0 years). The underlying rheumatic diseases requiring biological therapies were rheumatoid arthritis (46%), spondyloarthritis (31%), psoriatic arthritis (12%) and systemic lupus erythematosus (8.1%). The biologics being used were the TNF inhibitors (66%), tocilizumab (16%), abatacept (2.9%), rituximab (7.7%), belimumab (5.8%) and tofacitinib (1.3%). Hepatitis B carrier (HBsAg+) status was detected in 11 (3.5%) patients and they were all put on preemptive anti-viral therapy (entecavir). A total of 105 patients (34%) were occult hepatitis B carriers (HBsAg- but anti-HBc-IgG+). Anti-HBs was present in 83/105 (79%) of these patients. Occult hepatitis B carriers were significantly older than the non-carriers (49.9±11.1 vs 40.9±13.3 years; p<0.001), and were more frequently identified in rheumatoid arthritis than other rheumatic diseases (45% vs 25%; p<0.001). However, there was no gender difference in the prevalence of the occult hepatitis B carrier status (37% in women vs 28% in men; p=0.10). Logistic regression revealed that older age (RR 1.05[1.03-1.08] per year; p<0.001) was the only independent factor significantly associated with occult hepatitis B infection. Rheumatoid arthritis was not significantly associated with occult hepatitis B carrier status after adjustment for age and sex. Of the occult hepatitis B carriers, 9 (8.6%) had detectable HBV-DNA levels but all were very low titers (<100IU/ml). Five (56%) patients with detectable HBV-DNA levels received entecavir treatment during biological therapies, while 19 (20%) patients without detectable HBV-DNA were put on preemptive entecavir treatment (including all patients who were receiving rituximab). None of the overt (HBsAg+) or occult hepatitis B (HBsAg- anti-HBc-IgG+) carrier patients developed clinical reactivation of hepatitis B during a mean of 5.0±3.7 years of biological therapies.

Conclusion:
Occult hepatitis B carrier status was present in one-third of Hong Kong Chinese patients with various rheumatic diseases undergoing biological therapies. Older age was the only independent factor associated with occult hepatitis B infection. Despite the relatively low rate of preemptive anti-viral treatment in these patients, clinical reactivation of hepatitis B was not reported over 5 years of biological therapies.

Disclosure: C. C. Mok, None; L. Y. Ho, None; K. L. Chan, None; S. M. Tse, None; C. H. To, None.


Abstract Number: 524
Predictors of Mortality in RA Patients before Biologic Therapy

Debora Cordeiro Rosario¹, Camila Nobre Bulhoes¹, Rodrigo Peres Toledo¹, Karina Bonfiglioli², Ana C.M. Ribeiro³, Julio C. B. Moraes², Carla G.S. Saad², Clovis A Silva⁴, Eloisa Bonfa⁵ and Nadia E Aikawa², ¹Rheumatology Division, Faculdade de Medicina da Universidade de São Paulo, Sao Paulo, Brazil, ²Rheumatology Division, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, ³Division of Rheumatology, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, ⁴Pediatric Rheumatology Unit, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, ⁵Rheumatology Division, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Several studies have evaluated mortality risk factors in rheumatoid arthritis (RA) but that are no data regarding baseline predictors of mortality in patients under biologic therapy. In fact, definition of these predictors is difficult due to many confounding variables such as age, gender, biologic drug itself and its duration. Therefore, the aim of this study was to identify clinical and laboratory baseline predictors of death in RA patients matched for all these parameters under biologic treatment.

Methods: This was a retrospective observational study that included all deceased RA patients (ACR classification criteria) regularly followed in the biologic therapy center of Rheumatology Division of a tertiary university hospital. All relevant parameters were evaluated using an electronic chart database established from 2007 to 2016. All biologic drugs, including subcutaneous and intravenous agents, are regularly administered in-hospital. A control group of RA patients under biologic treatment matched for gender, age, biologic drug and its duration was included. Demographic data, comorbidities, clinical and laboratorial findings and concomitant treatment were assessed at the baseline of last biologic drug and at the last visit before death.

Results: During the study, 22/436 (5%) RA patients died after biologic therapy start. Causes of death included infections in 18 (82%), complications of pulmonary fibrosis in 2 (9%), subarachnoid hemorrhage in 1 (4.5%) and hemorrhagic stroke in 1 (4.5%). Deceased and survivors patients were comparable with regard to current age (57 vs. 57 years, p=0.34), male gender (27% vs. 27%, p=1.0) and last biologic duration (12 vs. 10 months, p=0.51). Analysis of baseline therapeutic parameters of the last biologic drug in the deceased group compared to survival groups revealed similar median number of biologic agents (p=0.94), need of at least one switching to another biologic agent (68% vs. 63, P=0.79) and frequencies of other drugs [prednisone (p=0.25), methotrexate (p=0.8), leflunomide (p=0.79) or sulfasalazine (p=0.11)]. Likewise, clinical and laboratorial characteristics were alike in both groups [Disease Activity Score in 28 joints (DAS28) (4.75 vs 4.96, p=0.75), HAQ (1.75 vs. 1.185, p=0.37), RF (68% vs. 84%, p=0.2) and anti-CCP (18% vs. 21%, p=1.0)]. Concerning associated comorbidities, deceased patients had a significantly higher frequency of chronic renal failure (18% vs. 2%, p=0.041) and a trend for a higher frequency of osteoporosis (59% vs. 33%, p=0.062) compared to the control group. Further analysis of all parameters at last visit before death demonstrated that deceased group had a higher DAS28 (3.84 vs. 3.06, p=0.05) and Health Assessment Questionnaire (HAQ) (1.563 vs. 1.0, p=0.0054).

Conclusion: The present study design with rigorous control for confounding factors identified solely chronic renal failure and possibly osteoporosis (in non elderly population) as the most important baseline predictors of mortality in RA patients starting biologic therapy in a real life setting. High RA activity and severity at the last visit before death are short-term predictors of death in patients already under biologic treatment.

Disclosure: D. C. Rosario, None; C. N. Bulhoes, None; R. P. Toledo, None; K. Bonfiglioli, None; A. C. M. Ribeiro, None; J. C. B. Moraes, None; C. G. S. Saad, None; C. A. Silva, Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP #2014/14806-0 and 2015/03756-4 to CAS), Conselho Nacional de Desenvolvimento Científico e Tecnológico
Efficacy, Tolerability and Reasons for Changing Dmards, Biologics and Small Molecule Drugs in RA Patients without RA Lung Disease from a United States Tertiary Referral Center

Richard Meehan¹, Isabelle Amigues², David Muram³, Eric Hoffman⁴, Jim Crooks⁵, Tho Truong⁶ and Pearlanne Zelarney⁷, ¹MEDICINE, National Jewish Health, Denver, CO, ²Division of Rheumatology, Columbia University, College of Physicians & Surgeons, New York, NY, ³Eli Lilly and Company, Indianapolis, IN, ⁴Medicine/Rheumatology, National Jewish Health, Denver, CO, ⁵Biostatistics, National Jewish Health, Denver, CO, ⁶Rheumatology, National Jewish Health, Denver, CO, ⁷Bioinformatics, National Jewish Health, Denver, CO

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The goal of therapy of rheumatoid arthritis (RA) is to achieve a state of low disease activity (LDA) or remission and reduce joint damage and disability. When treatment with one agent is unsuccessful, an alternative DMARD, biologic or small molecule drug will be prescribed. This retrospective study reports the frequency and reasons for drug changes in RA patients in a tertiary US academic practice.

Methods: Records of 1300 RA patients were reviewed by 3 rheumatologists to select patients who received at least one biologic (b) DMARD, had no other rheumatic disease, no interstitial lung disease or chronic infections, and were followed for at least one year to be included in this report. The study cohort consists of 198 patients who fulfilled the inclusion criteria. Patient demographics, drugs used, duration of use, and reasons for change of therapy were recorded.

Results: Of the 198 patients, 75% were females, average age was 51, 65% were ACPA positive, and 31% of patients had erosions at first visit. Patient demographics are summarized in Table 1. These patients received an average of 2.5 drugs before their first visit. They changed to a new drug an average of 2.4 times during their average follow up visits of 6.2 years. The longest average duration of continuous use for any of the DMARDs was 6-24 months (Table 2). The main reasons for discontinuation of these medications were lack of efficacy and the occurrence of adverse events (AEs). The rate of AEs among patients receiving bDMARDs was similar to that in patients receiving conventional DMARDS. The reasons for discontinuation of specific medications are summarized in Table 3.

Conclusion: This retrospective review suggests that most patients with RA will require a change of therapy every 2-3 years, primarily due to perceived lack of efficacy or the occurrence of AEs. The frequent change of therapy in patients with chronic disease like RA suggests that patients will use many different drugs in the course of their illness. In the absence of an effective biomarker that predicts response to a specific medication, therapeutic agents selected may not be efficacious and require early recognition of lack of efficacy and subsequent change of therapy.
<table>
<thead>
<tr>
<th>Table 1. Patient Demographics and Clinical Features</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
</tr>
<tr>
<td><strong>Age at First Visit</strong></td>
</tr>
<tr>
<td><strong>Average BMI</strong></td>
</tr>
<tr>
<td><strong>Smoking Status</strong></td>
</tr>
<tr>
<td>Current</td>
</tr>
<tr>
<td>Never</td>
</tr>
<tr>
<td>Prior</td>
</tr>
<tr>
<td><strong>Disease Activity</strong></td>
</tr>
<tr>
<td>MDHAQ</td>
</tr>
<tr>
<td>RAPID3</td>
</tr>
<tr>
<td>CCP+</td>
</tr>
<tr>
<td>RF+</td>
</tr>
<tr>
<td>CRP normal &lt;0.4</td>
</tr>
<tr>
<td>ESR normal &lt;20</td>
</tr>
<tr>
<td><strong>Erosions</strong></td>
</tr>
<tr>
<td>Present</td>
</tr>
<tr>
<td>None</td>
</tr>
<tr>
<td>Unknown</td>
</tr>
<tr>
<td><strong>Deformities</strong></td>
</tr>
<tr>
<td>Present</td>
</tr>
<tr>
<td>None</td>
</tr>
<tr>
<td>Unknown</td>
</tr>
<tr>
<td><strong>Swollen Joints</strong></td>
</tr>
<tr>
<td>Patients with &gt;6 swollen joints</td>
</tr>
<tr>
<td>Patients with 1-5 swollen joints</td>
</tr>
<tr>
<td>No swollen joints</td>
</tr>
<tr>
<td><strong>Disease Duration</strong></td>
</tr>
<tr>
<td><strong>Deaths</strong></td>
</tr>
</tbody>
</table>

F=female; M=male; MDHAQ=Multi-Dimensional Health Assessment Questionnaire; RAPID3=Routine Assessment of Patient Index Data 3
Table 2. Longest Duration of Use (days)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tocilizumab</td>
<td>214.0 (162.6)</td>
</tr>
<tr>
<td>Certolizumab</td>
<td>699.5 (928.4)</td>
</tr>
<tr>
<td>Etanercept</td>
<td>463.0 (601.6)</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>513.0 (692.0)</td>
</tr>
<tr>
<td>Abatacept</td>
<td>535.7 (688.3)</td>
</tr>
<tr>
<td>Infliximab</td>
<td>551.7 (374.5)</td>
</tr>
<tr>
<td>Rituximab</td>
<td>231.0 (74.6)</td>
</tr>
<tr>
<td>Golimumab</td>
<td>201.8 (128.4)</td>
</tr>
<tr>
<td>Tofacitinib</td>
<td>114.3 (79.0)</td>
</tr>
</tbody>
</table>

SD=standard deviation

Table 3. Reasons for Discontinuation or Change of Medications (%)

<table>
<thead>
<tr>
<th>Biologics and Small Molecule Drugs</th>
<th>Lack of Efficacy</th>
<th>Adverse Event</th>
<th>New Medical Problem</th>
<th>Patient Preference</th>
<th>Insurance Issues</th>
<th>Patient Improved</th>
<th>Expense of Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tocilizumab</td>
<td>42.9</td>
<td>42.9</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>14.3</td>
<td>0</td>
</tr>
<tr>
<td>Certolizumab</td>
<td>42.9</td>
<td>28.6</td>
<td>14.3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Etanercept</td>
<td>32.4</td>
<td>25.7</td>
<td>20.3</td>
<td>6.8</td>
<td>5.4</td>
<td>2.7</td>
<td>4.1</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>54.9</td>
<td>14.1</td>
<td>11.3</td>
<td>5.6</td>
<td>7</td>
<td>2.8</td>
<td>2.8</td>
</tr>
<tr>
<td>Abatacept</td>
<td>54.8</td>
<td>16.1</td>
<td>9.7</td>
<td>3.2</td>
<td>12.9</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Infliximab</td>
<td>37.5</td>
<td>28.1</td>
<td>25</td>
<td>6.2</td>
<td>3.1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Rituximab</td>
<td>58.8</td>
<td>11.8</td>
<td>5.9</td>
<td>17.6</td>
<td>5.9</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Golimumab</td>
<td>50</td>
<td>12.5</td>
<td>25</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Tofacitinib</td>
<td>55.6</td>
<td>11.1</td>
<td>11.1</td>
<td>11.1</td>
<td>11.1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Average</td>
<td>47.76%</td>
<td>21.21%</td>
<td>13.62%</td>
<td>5.61%</td>
<td>5.64%</td>
<td>2.20%</td>
<td>0.77%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DMARDs</th>
<th>Lack of Efficacy</th>
<th>Adverse Event</th>
<th>New Medical Problem</th>
<th>Patient Preference</th>
<th>Insurance Issues</th>
<th>Patient Improved</th>
<th>Expense of Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydroxychloroquine</td>
<td>42.3</td>
<td>7.7</td>
<td>7.7</td>
<td>19.2</td>
<td>0</td>
<td>23.1</td>
<td>0</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>38.2</td>
<td>35.3</td>
<td>8.8</td>
<td>8.8</td>
<td>5.9</td>
<td>2.9</td>
<td>0</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>22</td>
<td>31.2</td>
<td>22</td>
<td>11.9</td>
<td>2.8</td>
<td>8.3</td>
<td>0</td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>34.5</td>
<td>37.9</td>
<td>10.3</td>
<td>13.8</td>
<td>0</td>
<td>3.4</td>
<td>0</td>
</tr>
<tr>
<td>Average</td>
<td>34.25%</td>
<td>28.03%</td>
<td>12.20%</td>
<td>13.43%</td>
<td>2.18%</td>
<td>9.43%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>
Abstract Number: 526

**Comparative Pulmonary Safety of Abatacept and Tumor Necrosis Factor Inhibitors in Patients with RA and Chronic Pulmonary Condition**

Eun Ha Kang¹, Yinzhu Jin², Sara Dejene³, Gregory Brill³, Rishi J. Desai², Jeffrey A. Sparks⁴ and Seoyoung C. Kim⁵, ¹Division of Rheumatology, Department of Internal Medicine, Division of Rheumatology, Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, Korea, Republic of (South), ²Division of Pharmacoepidemiology and Pharmacoeconomics, Brigham and Women’s Hospital, Boston, MA, ³Brigham and Women's Hospital, Boston, MA, ⁴Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ⁵Rheumatology, Immunology and Allergy; Pharmacoepidemiologyand Pharmacoeconomics, Brigham and Women's Hospital, Boston, MA

**First publication:** September 18, 2017

**SESSION INFORMATION**

Session Date: Sunday, November 5, 2017  
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules  
Session Type: ACR Poster Session A  
Session Time: 9:00AM-11:00AM

**Background/Purpose:** Patients with rheumatoid arthritis (RA) can have various pulmonary comorbidities including asthma, chronic obstructive pulmonary disease (COPD) and interstitial lung disease (ILD). Biologics can pose a potential risk for acute exacerbations (AE) of these pulmonary comorbidities by immunosuppression, drug-induced lung injury, or other mechanisms. We therefore compared the risk of pulmonary AE among RA patients initiating abatacept vs. TNF inhibitors (TNFi) with chronic pulmonary comorbidities at baseline.

**Methods:** We conducted a cohort study using claims data from Medicare (2008-2013) or a commercial health plan (MarketScan 2006-6/2015) in the US. Adults with RA and chronic pulmonary condition (i.e., asthma, COPD, or ILD) who initiated abatacept or TNFi were identified based on a combination of diagnosis codes and use of disease-specific medications. The cohort entry date was the 1st use of abatacept or TNFi after ≥12 month continuous enrollment. The primary outcome was a composite endpoint defined as any of: 1) inpatient stays or 2) ED visits for asthma, COPD, or ILD, or 3) outpatient visits for asthma, COPD or ILD plus dispensing of oral corticosteroids or antibiotics, or for respiratory complications such as pneumonitis and bronchitis. Secondary outcomes were individual components of the primary composite endpoint. Follow-up time started from the day after cohort entry to the earliest event of outcome occurrence, drug discontinuation, nursing home admission, disenrollment, end of study period, or death. To control for >50 potential confounders at baseline, abatacept initiators were matched to TNFi initiators on a propensity score (PS) with a 1:2 ratio in each of the three pulmonary condition subgroups. We estimated incidence rates (IR) and hazard ratios (HR) of the outcomes among abatacept initiators versus TNFi in the main cohort and the subgroups. PS-matched HRs from the two databases were then pooled using inverse variance-weighted fixed-effect method.
Results: After PS matching, we included 1,517 abatacept and 3,034 TNFi initiators with RA and chronic pulmonary condition from both databases. Mean (SD) age was 73.0 (6.1) years in Medicare and 61.2 (12.1) years in MarketScan. At baseline, 44% in MarketScan and 57% in Medicare used methotrexate. IR of the composite outcome per 100 person-years ranged from 47.6-49.6 in the abatacept group and from 51.8-53.5 in the TNFi group. For the primary composite outcome, the HR comparing abatacept to TNFi was 1.00 (95%CI 0.92-1.09) in Medicare and 1.00 (95%CI 0.89-1.12) in MarketScan with a pooled HR of 1.00 (95%CI 0.93-1.07). Secondary and subgroup analyses showed similar results (Figure).

Conclusion: Among patients with RA and chronic pulmonary condition, acute exacerbations of underlying asthma, COPD or ILD occurred frequently but we found no difference in the exacerbation risk between abatacept and TNFi initiators.

Disclosure: E. H. Kang, None; Y. Jin, None; S. Dejene, None; G. Brill, None; R. J. Desai, None; J. A. Sparks, None; S. C. Kim, BMS, 2,Roche Pharmaceuticals, 2,AstraZeneca, 2,Pfizer Inc, 2,Merck Pharmaceuticals, 2.

Cardiovascular Safety of Tocilizumab Versus Abatacept in Patients with Rheumatoid Arthritis: A Multi-Database Study

Seoyoung C. Kim1, Daniel H. Solomon1, James R. Rogers2, Sara Gale3, Micki Klearman3, Khaled Sarsour3 and Sebastian Schneeweiss2.

1Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA, 
2Brigham and Women's Hospital, Boston, MA, 3Genentech, South San Francisco, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM
**Background/Purpose:** While tocilizumab (TCZ) may increase serum lipid levels, recent studies do not suggest an increased cardiovascular (CV) risk associated with TCZ use compared to TNF inhibitors in patients with RA. The current study examined comparative CV safety of TCZ versus abatacept in RA patients.

**Methods:** We conducted a cohort study using data from 3 U.S. healthcare claims databases – Medicare Parts A/B/D (2010-13), ‘IMS’ PharMetrics Plus (2011-2014) or Truven ‘MarketScan’ (2011-6/2015). Adults aged ≥18 years with RA who newly started TCZ or abatacept entered the cohort on the day of their first use of TCZ or abatacept. All patients had ≥12 month continuous enrollment free of TCZ and abatacept use before cohort entry. The primary outcome was a composite CV endpoint of hospitalization of any length for myocardial infarction (MI) and stroke based on claims-based algorithms (PPV>94%). Secondary outcomes were hospitalization for MI, stroke, coronary revascularization, heart failure and all-cause mortality. For the primary as-treated analysis, follow-up time started the day after cohort entry and ended on treatment discontinuation, outcome occurrence, disenrollment, death, or the end of study period. We estimated a propensity score (PS) to control for >60 potential confounders including demographics, prior DMARD use, comorbidities, medications, and healthcare utilization. TCZ starters were PS-matched to abatacept starters with a variable ratio of 1:3 within each database. We estimated incidence rates (IR) of composite CV events in the TCZ group compared to the abatacept group separately in each database. Hazard ratios (HR) from the 3 PS-matched cohorts were combined by an inverse variance-weighted, fixed-effects model.

**Results:** We included a total of 6,237 TCZ starters PS-matched to 14,685 abatacept starters in all three databases. Mean age (in years) was 72 in Medicare, 51 in IMS and 53 in MarketScan. At baseline, 73% (Medicare), 70% (IMS) and 62% (MarketScan) of TCZ or abatacept patients used methotrexate. In the as-treated analysis, the median follow-up time varied between 175 days (MarketScan) to 183 days (IMS) in the TCZ group and 193 days (MarketScan) to 209 days (Medicare) in the abatacept group. A total of 32 CV events occurred in TCZ starters and 112 events in abatacept starters across the three databases. The IR of the primary composite CV events per 100 person-years ranged from 0.37 (IMS) to 1.64 (Medicare) in the TCZ group and from 0.59 (IMS) to 1.69 (Medicare) in the abatacept group. The risk of the primary composite CV events was similar between the two groups across all three databases (Table), with a combined HR of 0.82 (95%CI 0.55-1.22) in TCZ initiators versus abatacept initiators. Analyses on secondary outcomes showed similar results.

**Conclusion:** This large multi-database cohort study found no increase in the risk of CV events in patients with RA who newly start TCZ versus abatacept.

**Table.** Hazard ratios (95% confidence interval) for primary and secondary cardiovascular outcomes in tocilizumab starters versus abatacept: a 1:3 variable ratio propensity score-matched as-treated analysis

<table>
<thead>
<tr>
<th></th>
<th>Medicare</th>
<th>IMS</th>
<th>MarketScan</th>
<th>Combined *</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Composite CV endpoint</td>
<td>0.96</td>
<td>0.67</td>
<td>0.68</td>
<td>0.82</td>
</tr>
<tr>
<td>(0.56-1.83)</td>
<td>(0.25-1.84)</td>
<td>(0.32-1.42)</td>
<td>(0.55-1.22)</td>
<td></td>
</tr>
<tr>
<td><strong>Secondary:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalization for MI</td>
<td>1.38</td>
<td>1.05</td>
<td>0.83</td>
<td>1.11</td>
</tr>
<tr>
<td>(0.85-2.94)</td>
<td>(0.27-4.15)</td>
<td>(0.33-2.05)</td>
<td>(0.65-1.89)</td>
<td></td>
</tr>
<tr>
<td>Hospitalization for stroke</td>
<td>1.03</td>
<td>0.44</td>
<td>0.49</td>
<td>0.73</td>
</tr>
<tr>
<td>(0.44-2.42)</td>
<td>(0.10-2.01)</td>
<td>(0.14-1.74)</td>
<td>(0.39-1.39)</td>
<td></td>
</tr>
<tr>
<td>Coronary revascularization</td>
<td>0.63</td>
<td>1.43</td>
<td>1.22</td>
<td>0.97</td>
</tr>
<tr>
<td>(0.26-1.51)</td>
<td>(0.41-5.01)</td>
<td>(0.53-2.83)</td>
<td>(0.56-1.68)</td>
<td></td>
</tr>
<tr>
<td>Hospitalization for HF</td>
<td>0.86</td>
<td>1.80</td>
<td>1.28</td>
<td>1.18</td>
</tr>
<tr>
<td>(0.40-1.83)</td>
<td>(0.71-5.50)</td>
<td>(0.46-3.56)</td>
<td>(0.71-1.97)</td>
<td></td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>1.01</td>
<td>N/A</td>
<td>0.91</td>
<td>0.99</td>
</tr>
<tr>
<td>(0.80-1.70)</td>
<td></td>
<td>(0.28-3.01)</td>
<td>(0.62-1.60)</td>
<td></td>
</tr>
</tbody>
</table>

The abatacept group was the reference group. No death occurred in the IMS-TCZ group. Propensity score models included over 60 covariates including demographics, prior DMARD use, cardiovascular comorbidities, medications, and healthcare utilization.

* Hazard ratios were combined by an inverse variance-weighted, fixed-effects model.

**Disclosure:** S. C. Kim, AstraZeneca, Bristol-Meyers-Squibb, Genentech, Lilly, Pfizer, 2; D. H. Solomon, Amgen, AstraZeneca, Corrona, LLC, Genentech, Lilly, Pfizer, 2,Pfizer, 9; J. R. Rogers, None; S. Gale, Genentech, Inc., 3; M. Klearman, Genentech/Roche, 1,Genentech/Roche, 3; K. Sarsour, Genentech, Inc., 3; S. Schneeweiss, Boehringer Ingelheim, Genentech, Inc., 2,Aetion, Inc., WHISCON, LLC, 5,Aetion, Inc., 1.

Impact of Comorbidities on the Occurrence of Infections in Rheumatoid Arthritis Treated By Biologic Agents

Christopher Banse1, Nicolas Chrin2, Pascal Rottenberg3, Sophie Pouplin4, thierry Lequerre5 and Olivier Vittecoq3,
1Rheumatology, Rouen University Hospital, Rouen, France, 2Department of Biostatistics, Rouen University Hospital, 76031 Rouen, France, ROUEN, France, 3INSERM U905 & Normandy University, Institute for Research and Innovation in Biomedicine, Rouen, France, 4Rheumatology Department & Inserm 905, Department of Rheumatology, Rouen University Hospital & Inserm 905, Institute for Biomedical Research, University of Rouen, Rouen, France, 5Rheumatology Department, Rouen University Hospital, University of Rouen, 76031 Rouen, France., ROUEN, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: to investigate the potential relationship between the number of comorbidities at initiation of biotherapy and the occurrence of a severe infection or recurrent infections under biologic agent in rheumatoid arthritis (RA).

Methods: This was a monocentric and retrospective study conducted from 2001 to 2011. Population characteristics, number and nature of comorbidities and treatments were collected at baseline. The occurrence of severe infections leading to hospitalization or life threatening, as well as that of recurrent infections (> 4 per year) was collected during a 2 years-follow-up period after the introduction of an anti-TNF biologic agent or a non anti-TNF biotherapy in RA.

Results: 554 RA (70% women) were assessed during this 2 years follow up period. Mean age and RA duration were respectively at 64.1 (+/-13.8) years and at 15.2 (+/-10.4) years. 78% of patients were a rheumatoid factor or anti-CCP positive. The mean Disease Activity Score of C-Reactive protein (DAS 28 CRP) was 4.1. X-rays showed structural damage in 65.5% of cases. The mean dose of prednisone was 6.66 mg/l. 75.4% of patients received methorexate (mean dose: 10.5mg/week). Biological agents were prescribed as follows: abatacept (3.8%), adalimumab (20.6%), anakinra (7.8%), certolizumab (0.36%), etanercept (37.5%), infliximab (25.3%), rituximab (3.2%) and tocilizumab (1.6%). At 1 year, the therapeutic maintenance was 91.3%. In this population, 31.5% had no comorbidity, 27.4% had 1 comorbidity, 19.35% had 2 comorbidities and 21.7% had more than 2 comorbidities. The occurrence of recurrent infections during the 24th months was 5.6% whereas the occurrence of a severe infection was 3.8%. After adjustment (age, corticosteroid and DAS 28 CRP), there was a significant correlation between the number of comorbidities (more than 2 comorbidities) and the occurrence of severe infections. The number of comorbidities was not correlated with the occurrence of repeated infections. The Rabbit score predicted the risk of developing a severe infection of the order of 3.5%. Certain types of comorbidities were linked to the occurrence of severe or recurrent infections.

Conclusion: The presence of more than 2 comorbidities is significantly related to the occurrence of a severe infection during the 24 months following the initiation of a biological agent.

Disclosure: C. Banse, None; N. Chrin, None; P. Rottenberg, None; S. Pouplin, None; T. Lequerre, None; O. Vittecoq, None.


Abstract Number: 529
Pulmonary Involvement in Our Patients with Rheumatoid Arthritis Under Biological Therapy: A Tertiary Hospital Experience

Edurne Guerrero Basterretxea, Maria Luz Garcia Vivar, Itziar Calvo Zorrilla, Oihane Ibaruguengoitia, Eva Galindez Agirregoioka, Juan Maria Blanco Madrigal, Esther Ruiz Lucea, Ignacio Torre Salaberri, Olaia Begoña Fernandez Berrizbeitia, Clara Eugenia Perez, Ana Rosa Intxaurbe Pellejero, Natalia Rivera-Garcia and Iñigo Gorostiza Hormaetxe, 1 RHEUMATOLOGY, Rheumatology Department; Basurto University Hospital, Bilbao, Spain, 2 RHEUMATOLOGY, Rheumatology Department; Basurto University Hospital, BILBAO, Spain, 3 Rheumatology Department; Basurto University Hospital, Bilbao, Spain, 4 RESEARCH, Rheumatology Department; Basurto University Hospital, Bilbao, Spain, 5 RESEARCH, Research Department. Basurto University Hospital, BILBAO, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Use of biological therapy (BT) has dramatically improved Rheumatoid Arthritis (RA) management and outcomes for the last decade. Classic extraarticular manifestations are now uncommon, excepting for pulmonary involvement, which may be due to different factors and may itself affect also treatment election and patient prognosis. The aim of this study is to evaluate the presence of pulmonary complications in RA patients under BT in our hospital, assess its severity and related changes in treatment.

Methods: Review of clinical records of 208 RA patients receiving BT in the last 5 years (January 2012 to December 2016). 23 cases of preexisting lung disease for other causes (asthma, smoking) have been excluded. We collected demographic data, characteristics of RA, types of pulmonary involvement, followup and changes in treatment of 26 patients finally included. Statistical analysis were performed using SPSS v22.

Results:

73.1% were women, mean aged 59 years (31-80); 53.8% were never smokers. They suffered from longstanding RA yet (median 176.92 months, SD 199.34); only 2 patients were early arthritis (RA diagnose during the previous year). 85% were RF positive with positive CCP antibodies in 69.2%, and structural damage with erosions was present in 70%. Other extraarticular manifestations (3 patients with rheumatoid nodules, 4 with cardiac involvement) were present in 25%.

At the time of lung disease diagnosis, 1/2 patients were in remission or low activity (DAS 28), with a median CRP 0.52 mg/dL (SD 1.72). 90% had received methotrexate and almost half of them leflunomide; 30% had been previously treated with BT (50% TNF alpha inhibitors). Interstitial lung disease (ILD) was the most frequent pulmonary involvement (57.7%) and non-specific interstitial pneumonia (NSIP) the most prevalent pattern (> 60%). We also found obstructive pulmonary disease (11.5%) and vascular involvement (7.7%). Gold standard image diagnostic technique was high resolution CT (40% presented a normal X-ray).

Treatment was modified in 53.8% of the cases (synthetic DMARD was kept in 68% and BT in 64%).

The average followup of pulmonary involvement was 37.85 months (1-156). 80% of the patients kept stable or improved from their arthritis and also from respiratory disease. Only one patient received a lung trasplant and another one died.

We haven’t found association between different types of pulmonary involvement and the different variables analyzed in the study. We didn’t show significant differences in prognosis related to pulmonary disease distinct patterns; up to 80% of patients with ILD stabilize or improve.

Conclusion: Prevalence of pulmonary disease in our experience in RA patients under BT is similar to prevalence in other observational studies (10-20%), diagnosis here was made for a casual detection in a routine chest X-ray or for clinical
suspicions for respiratory symptoms (cough, dyspnea…). Pulmonary involvement evolution here has been good perhaps for the high prevalence of NSIP, which is also thought to require less therapeutic intervention. Protocols for search and management of lung disease in RA patients are an unmet need in clinical practice, and its pathogenesis and treatment are important fields for translational and clinical research.

Disclosure: E. Guerrero Basterretxea, None; M. L. García Vivar, None; I. Calvo Zorrilla, None; O. Ibarguengoitia, None; E. Galíndez Agirregaraioa, None; J. M. Blanco Madrigal, None; E. Ruiz Lucea, None; I. Torre Salaberrí, None; O. B. Fernandez Berribeita, None; C. E. Perez, None; A. R. Intxaurbe Pellejero, None; N. Rivera-García, None; I. Gorostiza Hormaetxe, None.

Abstract Number: 530

Efficacy and Safety of Baricitinib in Patients with Rheumatoid Arthritis: A Meta-Analysis of Randomized Controlled Trials

Sumit Kunwar1, Christopher E. Collins2 and Florina Constantinescu2, 1Rheumatology, MedStar Washington Hospital Center, Washington, DC, 2Rheumatology, MedStar Washington Hospital Center, Washington, DC
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Janus kinases (JAKs) play an important role in intracellular signaling for multiple cytokines in the pathogenesis of RA. Baricitinib is an oral, selective JAK 1 and 2 inhibitor which has been shown to be effective in the treatment of RA in several clinical trials. This meta-analysis aims to aggregate currently available data to assess the overall efficacy and safety of baricitinib in RA.

Methods:

We searched PubMed, EMBASE and Cochrane CENTRAL from inception through 05/25/17 without language restriction. Our eligibility criteria included human placebo-controlled RCTs in adults (≥ 18 years of age) that evaluated efficacy and safety outcomes of baricitinib in RA patients. We excluded meeting abstracts without full text publication. We used RevMan 5.3 to perform meta-analysis between groups on baricitinib 4mg per day and placebo using random effect model calculating odds ratio (OR) as well as 95% confidence interval (CI). I² statistic was used to identify heterogeneity between studies, and values of more than 50 was used to indicate significant heterogeneity. We measured efficacy using ACR20/50/70 and DAS28-CRP response criteria and safety with adverse events.

Results:
Five studies with a total of 2006 patients (967 on baricitinib and 1039 on placebo) were included for meta-analysis. The maximum study duration was 24 weeks. Baricitinib demonstrated greater efficacy in achieving ACR20/50/70 responses compared to placebo (66.7 vs 36.6%, OR 3.33, 95% CI 2.18-5.07, I² 75%, P<0.00001; 44.1 vs 17.8%, OR 3.56, 95% CI 2.77-4.58, I² 20%, P<0.0001 and 24.4 vs 6.5%, OR 4.62, 95% CI 2.96-7.19, I² 40%, P<0.00001 respectively). There was a small increase in any adverse events in the baricitinib group (70.4 vs 61.5%, OR 1.35, 95% CI 1.10-1.61, I² 47%, P=0.05), however, no increase in serious adverse events (5.5 vs 4.8%, OR 1.12, 95% CI 0.75-1.67, I² 0%, P=0.58) or serious infections (1.5 vs 1.5%, OR 0.94, 95% CI 0.46-1.92, I² 0%, P=0.86) when compared to placebo.

Conclusion:

Baricitinib is effective in treatment of RA, and did not appear to have significant safety concerns during the first six months of treatment. However, the long term safety profile of this drug should be evaluated by future clinical trials.

![Figure 1: Meta-analysis of efficacy outcomes.](image-url)
Comparative Effectiveness of Tofacitinib Versus Baricitinib in Rheumatoid Arthritis Using a Systematic Review and Network Meta-Analysis of
Randomized Trials

Natalia Zamora\textsuperscript{1,2,3}, Maria A. Lopez-Olivo\textsuperscript{1}, Jean Tayar\textsuperscript{1}, Robin Christensen\textsuperscript{2} and Maria Suarez-Almazor\textsuperscript{1}, \textsuperscript{1}Section of Rheumatology and Clinical Immunology, Department of General Internal Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA, Houston, TX, \textsuperscript{2}Musculoskeletal Statistics Unit, The Parker Institute, Bispebjerg and Frederiksberg Hospital, Copenhagen, Denmark, Copenhagen, Denmark, \textsuperscript{3}Reumatologia, Instituto de Rehabilitación Psicofísica, Buenos Aires, Argentina, Buenos Aires, Argentina

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: To explore the comparative effectiveness of tofacitinib or baricitinib in patients with rheumatoid arthritis (RA) following a systematic review of randomized trials, by performing a network meta-analysis inferring from both direct and indirect evidence.

Methods: We used the data of the Cochrane systematic reviews on tofacitinib and baricitinib for treating rheumatoid arthritis. For both reviews, the searches were performed in seven electronic databases and two trial registries. Retrieved records were screened independently by 2 investigators to include controlled trials comparing tofacitinib or baricitinib alone or in combination with methotrexate versus placebo, methotrexate or other traditional or biologic DMARDs. Published and unpublished trials were considered. Quality appraisal and data extraction from the included studies was done independently by 2 investigators. For the network meta-analysis the primary outcome was American College of Rheumatology (ACR) 50\% improvement criteria (ACR50) and secondary outcomes included remission according to the Disease Activity Score (DAS28), functional ability measured by the Health Assessment Questionnaire (HAQ), and serious adverse events as defined by the individual trials.

Results: Out of 2,673 unique citations, 21 trials met the inclusion criteria (9,839 patients). Most patients were female (74 to 96\%) with a mean age and disease duration ranging from 48-56 years and 2.7-13 years, respectively. For the tofacitinib trials, 2 out 14 trials were at high risk of reporting bias. For the baricitinib trials, selection bias could not be evaluated in 6 out 7 trials and for selection and performance bias in 7 out of 7. The network plot for the ACR50 included 12 nodes (i.e., daily doses: tofacitinib monotherapy 5 and 10 mgs, combined with methotrexate 5 and 10 mg, baricitinib monotherapy 4 mg, baricitinib combined with methotrexate 2, 4, and 8 mgs, adalimumab monotherapy, adalimumab combined with methotrexate, methotrexate and placebo). The relative effect achieving an ACR 50 at 12 weeks against placebo in descending order were: Bari8+MTX (13.5; 5.8-31.3), Tofa10+MTX (11.3; 5.9-21.4), Tofa5+MTX (10.5; 5.4-20.2), Bari2+MTX (9.6; 4.5-19.4), Bari4+MTX (9.5; 5.0-17.9), Bari4 (6.79; 3.2-14.3), ADA+MTX (6.8; 3.5-13.3), Tofa10 (6.2; 3.8-9.9), Tofa5 (5.1; 3.3-8.1), MTX (2.4; 1.4-4.4), and ADA (1.9; 0.8-4.7). When comparing indirectly, the only differences were observed in favor of baricitinib+MTX compared with tofacitinib alone. For DAS 28 there were 11 nodes and the order was (from most to least effective): Tofa10+MTX, ADA+MTX, Bari8+MTX, Bari4+MTX, Tofa5+MTX, Bari2+MTX, Tofa10, Bari4, Tofa5, and MTX. Serious adverse events were less likely to occur in the PBO, ADA, Tofa5+MTX, Tofa10+MTX, MTX, Bari8+MTX, Tofa10, Tofa5, Bari4+MTX, Bari4, and Ada+MTX.

Conclusion: All drug combinations were effective compared with placebo in reducing at least 50\% of symptoms or achieving remission at 12 weeks. Tofacitinib 10 mg and baricitinib 8 mg combined with methotrexate were among the most efficacious options. Serious adverse events were less likely with the tofacitinib groups, although the within-class differences were small and may not be clinically meaningful.

Disclosure: N. Zamora, None; M. A. Lopez-Olivo, None; J. Tayar, None; R. Christensen, None; M. Suarez-Almazor, Pfizer Inc, 5.

Genetic Predictors of Iguratimod Clinical Response and Toxicity in Patients with Rheumatoid Arthritis

Wenjing Xiao, Department of Rheumatology and Immunology, People’s Hospital, Peking University, Beijing, China

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Iguratimod (IGU) is a novel DMARD in rheumatoid arthritis (RA). The purpose of this study was to identify genetic predictors of response and adverse drug events (AEs) to IGU therapy in patients with RA.

Methods: Seven single nucleotide polymorphisms (SNPs) of enzyme and transporter proteins related to IGU, CYP1A2*1F (rs762551), CYP2C19*2 (rs4244285), NAT2 (rs1495741), ABCB1 (rs1045642, rs2032582C), ABCG2 (rs2231142) and SLCO1B1 (rs4149036), were determined by a genotyping approach in 272 IGU treated RA patients. SNPs were evaluated using real-time polymerase chain reaction. The efficacy of the IGU therapy was estimated using EULAR good response criteria based on the DAS-28. All AEs were recorded.

Results: 21.69% patients (59/272) were good responders and 36.40% patients (99/272) had AEs. Unvariant analyses and multivariate analyses demonstrated that the ABCG2 A allele was associated with good response to IGU (OR=2.084, 95% CI 1.147-3.786, P=0.015; OR=1.944, 95% CI 1.038-3.641, P=0.038). NAT2 G carrier was significantly associated with less favorable response to IGU (OR=0.476, 95% CI 0.256-0.884, P=0.017; OR=0.498, 95% CI 0.256-0.967, P=0.029). CYP2C19*2 A carriers had higher risk for IGU-induced toxicity than did the GG genotyping (OR=2.122, 95% CI 1.273-3.537, P=0.004; OR=2.368, 95% CI 1.395-4.019, P=0.001). No significant association was found between the genotypes of CYP1A2*1F, ABCB1 and SLCO1B1 SNP and the IGU response or AEs.

Conclusion: Our study suggests that ABCG2 (rs2231142), NAT2 (rs1495741) and CYP2C19*2 (rs4244285) genotyping may help to identify patients who will benefit from IGU treatment.

Disclosure: W. Xiao, None;


Assessment of Radiographic Progression in Patients with Rheumatoid Arthritis Treated with Tofacitinib: Data from an Open-Label Long-Term Extension Study over 3 Years
Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor for the treatment of RA. The long-term safety and clinical efficacy of tofacitinib 5 and 10 mg twice daily (BID) has been reported in patients (pts) with active RA up to 105 months.\textsuperscript{1-3} We evaluated the long-term effects of tofacitinib on progression of radiographic structural damage in pts with RA from a long-term extension (LTE) study.

Methods: Data were analyzed from an open-label LTE (NCT00413699 [ongoing; database not locked at Mar 2017 data-cut]) of pts with RA who participated in Phase 2 (NCT01164579, methotrexate [MTX] naïve, early RA) or Phase 3 (NCT00847613, MTX-IR; NCT01039688, MTX naïve) tofacitinib index studies. Baseline (BL) was defined as last visit in the index study prior to LTE entry. In the index studies pts received tofacitinib 5 or 10 mg BID as monotherapy (mono) or with conventional synthetic DMARDs (csDMARDs); at the physicians’ discretion pts could switch tofacitinib dose in the LTE, and were assigned to 5 mg BID if average total daily dose was <15 mg/day or to 10 mg BID if ≥15 mg/day. Outcomes to evaluate structural damage from BL to Month (M)36 included: mean and mean change (Δ) from BL in van der Heijde modified Total Sharp Score (mTSS), Erosion Score (ES), and Joint Space Narrowing Score (JSN); % of pts with no radiographic progression (ΔmTSS ≤0.5); and % of pts with no new erosions (ΔES≤0.5). Observed data were analyzed descriptively.

Results: A total of 1156 pts from the index studies were pooled in the LTE radiographic analysis; x-rays available in 88% (n=1019) of pts at M6; 497 pts received tofacitinib mono (5 mg BID, n=42; 10 mg BID, n=455) and 659 pts received tofacitinib with csDMARDs (5 mg BID, n=53; 10 mg BID, n=606). N at M12 was 86.8%, at M24 76.0%, and at M36 35.8% of the BL value. From LTE entry, mean duration of tofacitinib treatment in the total population was 1113 days (range 21–2396), and mean mTSS, ES, and JSN only slightly increased from BL to M36 (Figure). Mean (standard error [SE]) ΔmTSS was 0.25 (0.05) at M12 and 1.17 (0.28) at M36. Mean (SE) ΔES and ΔJSN were 0.21 (0.03) and 0.24 (0.02) at M12 and 0.68 (0.17) and 0.78 (0.13) at M36. The % (SE) of all tofacitinib-treated pts with radiographic non-progression (ΔmTSS ≤0.5); and % of pts with no new erosions (ΔES≤0.5). Observed data were analyzed descriptively.

Conclusion: Structural damage progression was limited during treatment with tofacitinib alone or with csDMARDs for up to 3 years in pts with RA.

References

1. Wollenhaupt J et al. Arthritis Rheumatol 2015; 67 Suppl 10; A1645
2. Wollenhaupt J et al. Arthritis Rheumatol 2016; 68 Suppl 10; A1647

Disclosure: D. van der Heijde, AbbVie, Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Daiichi, Eli Lilly, Galapagos, Gilead, GSK, Janssen, Merck, Novartis, Pfizer Inc, Regeneron, Roche, Sanofi, Takeda, UCB, 5,Director of Imaging Rheumatology bv., 9; J. Wollenhaupt, Pfizer Inc, 1, Pfizer Inc, 8; S. B. Cohen, AbbVie, Amgen, Boehringer Ingelheim, Gilead, Merck, Pfizer Inc, 5, AbbVie, Amgen, Boehringer Ingelheim, Gilead, Merck, Pfizer Inc, 9; S. Strengholt, Pfizer Inc, 1, Pfizer Inc, 3; K. Terry, Pfizer Inc, 1, Pfizer Inc, 3; R. DeMasi, Pfizer Inc, 1, Pfizer Inc, 3; K. Kwok, Pfizer Inc, 1, Pfizer Inc, 3; I. Lazariciu, Quintiles, 3, Pfizer Inc, 5; L. Wang, Pfizer Inc, 1, Pfizer Inc, 3.


Abstract Number: 534

Effect of Baseline MTX Dose on Clinical Efficacy and Safety in Rheumatoid Arthritis Patients Treated with Filgotinib: Post-Hoc Analysis from a Phase 2B Study

René Westhovens1, Annegret Van der Aa2, Corinne Jamoul2, Chantal Tasset2 and Pille Harrison2, 1KU Leuven Department of Development and Regeneration, Skeletal Biology and Engineering Research Center, Leuven, Belgium, 2Galapagos NV, Mechelen, Belgium

First publication: September 18, 2017
Background/Purpose:
Filgotinib (GLPG0634, GS-6034) is an oral, selective JAK1 inhibitor that has demonstrated safety and efficacy data in two 24-week placebo-controlled phase 2B studies as add-on to methotrexate and as monotherapy in active rheumatoid arthritis (RA) patients with inadequate response to MTX (MTX-IR)\textsuperscript{1,2}. The objective was to assess the effect of MTX dose on clinical efficacy and safety in MTX-IR RA patients treated with filgotinib as add-on to background MTX for 24 weeks.

Methods:
Patients with active RA on stable dose of MTX were randomized in a double-blinded manner to receive either placebo (PBO) or one of 3 daily doses of filgotinib (50mg, 100mg or 200mg) as once or twice daily regimen for 24 weeks\textsuperscript{1}. This post-hoc analysis includes patients treated with the selected Phase 3 filgotinib doses, 100mg and 200mg QD, and PBO for the efficacy parameters, and all dose groups for the safety analysis. MTX dose was categorized as low (\leq 12.5mg/wk), medium (>12.5 to <17.5 mg/wk) or high (\geq 17.5mg/wk).

Results:
Baseline disease activity was high and similar across the three MTX subgroups, with an overall mean DAS28(CRP) score of 6.10, mean HAQ-DI of 1.73, mean CDAI score of 42.10 and mean SDAI score of 44.57. Across all MTX subgroups, patients on filgotinib 100mg or 200mg QD for 24 weeks showed efficacy over PBO, as measured by change from baseline in DAS28(CRP), CDAI, SDAI, HAQ-DI, and ACR20 response. No pattern was observed to suggest that the baseline MTX dose had any effect on filgotinib efficacy. The incidences of TEAE and serious TEAE were comparable regardless of the MTX dose (Table 2).

Conclusion:
Post-hoc analysis of a phase 2B study in MTX-IR RA patients suggests that filgotinib treatment at 100mg and 200mg QD on the background of MTX is consistently associated with improved clinical outcomes compared to placebo, across all key efficacy parameters, irrespective of MTX dose. The safety profile was overall favorable and consistent with previous studies in RA with filgotinib, regardless of MTX dose.

Table 1. Mean (SE) change from baseline in key efficacy parameters at Week 24 by MTX subgroup.
<table>
<thead>
<tr>
<th>MTX Dose Range</th>
<th>PBO</th>
<th>Filgotinib 100mg QD</th>
<th>Filgotinib 200mg QD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low MTX dose (≤12.5mg/wk)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>14</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>DAS28(CRP)</td>
<td>-0.94 (0.28)</td>
<td>-1.96 (0.47)</td>
<td>-2.49 (0.43)</td>
</tr>
<tr>
<td>CDAI</td>
<td>-15.74 (4.67)</td>
<td>-23.32 (6.36)</td>
<td>-27.31 (5.27)</td>
</tr>
<tr>
<td>SDAI</td>
<td>-15.31 (4.68)</td>
<td>-24.87 (6.34)</td>
<td>-29.63 (5.70)</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>-0.30 (0.14)</td>
<td>-0.61 (0.26)</td>
<td>-0.73 (0.26)</td>
</tr>
<tr>
<td><strong>Medium MTX dose (&gt;12.5 to &lt;17.5mg/wk)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>43</td>
<td>48</td>
<td>44</td>
</tr>
<tr>
<td>DAS28(CRP)</td>
<td>-1.05 (0.23)</td>
<td>-2.77 (0.20)</td>
<td>-2.73 (0.21)</td>
</tr>
<tr>
<td>CDAI</td>
<td>-14.49 (2.81)</td>
<td>-29.73 (2.14)</td>
<td>-30.05 (2.04)</td>
</tr>
<tr>
<td>SDAI</td>
<td>-14.35 (2.92)</td>
<td>-31.49 (2.19)</td>
<td>-31.30 (2.23)</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>-0.36 (0.11)</td>
<td>-0.71 (0.09)</td>
<td>-0.79 (0.08)</td>
</tr>
<tr>
<td><strong>High MTX dose (≥17.5mg/wk)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>28</td>
<td>27</td>
<td>34</td>
</tr>
<tr>
<td>DAS28(CRP)</td>
<td>-1.51 (0.32)</td>
<td>-2.82 (0.30)</td>
<td>-2.97 (0.21)</td>
</tr>
<tr>
<td>CDAI</td>
<td>-18.67 (3.50)</td>
<td>-28.47 (2.76)</td>
<td>-29.18 (2.50)</td>
</tr>
<tr>
<td>SDAI</td>
<td>-18.36 (3.53)</td>
<td>-29.48 (2.86)</td>
<td>-30.95 (2.67)</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>-0.39 (0.10)</td>
<td>-0.94 (0.15)</td>
<td>-0.87 (0.13)</td>
</tr>
</tbody>
</table>

Table 2. Treatment-emergent adverse events (TEAE) and serious TEAEs at Week 24 by MTX subgroup.

<table>
<thead>
<tr>
<th>% of patients</th>
<th>PBO</th>
<th>Filgotinib</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low MTX dose (≤12.5mg/wk)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TEAE</td>
<td>57</td>
<td>55</td>
</tr>
<tr>
<td>Serious TEAE</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td><strong>Medium MTX dose (&gt;12.5 to &lt;17.5mg/wk)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TEAE</td>
<td>47</td>
<td>46</td>
</tr>
<tr>
<td>Serious TEAE</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td><strong>High MTX dose (≥17.5mg/wk)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TEAE</td>
<td>57</td>
<td>57</td>
</tr>
<tr>
<td>Serious TEAE</td>
<td>7</td>
<td>2</td>
</tr>
</tbody>
</table>

References


Disclosure: R. Westhovens, Bristol-Myers Squibb, 2,Roche Pharmaceuticals, 2,CellTrion, 5,Galapagos NV, 5; A. Van der Aa, Galapagos NV, 1,Galapagos NV, 3; C. Jamoul, Galapagos NV, 3; C. Tasset, Galapagos NV, 1,Galapagos NV, 3; P. Harrison, Galapagos NV, 1,Galapagos NV, 3.

Effect of a Step-up or Step-Down in Tofacitinib Dose on Efficacy and Safety in Long-Term Extension Studies

Ruediger Mueller¹, Hendrik Schulze-Koops², Daniel E Furst³, Stanley B Cohen⁴, Kenneth Kwok⁵, Anna Maniccia⁵, Lisy Wang⁶, Ernem Akylbekova⁷ and Johannes von Kempis¹, ¹Kantonsspital St. Gallen, St. Gallen, Switzerland, ²Klinikum der Universität München, Munich, Germany, ³UCLA, Los Angeles, CA, ⁴Metroplex Clinical Research Center and University of Texas Southwestern Medical Center, Dallas, TX, ⁵Pfizer Inc, New York, NY, ⁶Pfizer Inc, Groton, CT, ⁷QuintilesIMS, Durham, NC

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor for the treatment of RA. Efficacy and safety of tofacitinib 5 and 10 mg BID have been shown in long-term extension (LTE) studies up to 105 months. We assessed the impact of tofacitinib dose changes on efficacy and safety in patients (pts) who increased dose (step-up), and pts who decreased dose (step-down), vs pts who remained on the same dose when entering LTE studies.

Methods: In this exploratory, post-hoc analysis, data were pooled from 2 open-label LTE studies (NCT00413699 [ongoing; database not locked at January 2016 data-cut]; NCT00661661) of RA pts who had participated in Phase (P) 1/2/3 tofacitinib index studies and had ≥81 days of tofacitinib exposure (to allow ≥2 assessments) in each period (P1/2/3 index, LTE). Dose changes from index study dose were either mandated by protocol (upon LTE entry) or at the investigator’s discretion (during LTE). This analysis only included pts who remained on their initial/changed dose once in the LTE. Pts were analyzed in 4 groups: 5 mg BID [index]→10 mg BID [LTE] (Step-up; N=833); 5 mg BID [index]→5 mg BID [LTE] (Remain 5; N=248); 10 mg BID [index]→10 mg BID [LTE] (Remain 10; N=951); 10 mg BID [index]→5 mg BID [LTE] (Step-down; N=234). To determine whether initial efficacy (last index study assessment) may affect response following dose change on LTE entry, sub-groups for the Step-up and Remain 5 groups were defined based on initial ACR20 response, and sub-groups for the Step-down and Remain 10 groups were defined based on initial ACR50 response. Efficacy was assessed up to Month 12 in the LTE based on ΔDAS28-4(ESR). Exposure-adjusted event rates (pts with event/100 pt-yrs) are presented for the most common AEs for the entire LTE study exposure.

Results: No statistically significant differences in ΔDAS28-4(ESR) were observed between the Step-up and Remain 5 groups (Figure), whether or not they had an initial ACR20 response. In general, no significant differences in ΔDAS28-4(ESR) were observed between the Step-down and Remain 10 groups (Figure), whether or not they had an initial ACR50 response. The rates and types of adverse events (AEs) were similar across all groups (Table).

Conclusion: In RA pts, the safety profile was similar regardless of dose change. Step-up from tofacitinib 5 to 10 mg BID, or step-down from 10 to 5 mg BID did not affect efficacy over 12 months vs remaining on the same dose, and was not influenced by initial response. Conclusions are limited by small pt numbers in some groups, the open-label design, and inclusion of pts in the LTE who show tolerability for tofacitinib and drug retention.
**Table. Summary of AEs in the LTE study**

<table>
<thead>
<tr>
<th></th>
<th>Step-up: 5 to 10 mg BID</th>
<th>Remain on 5 mg BID</th>
<th>Step-down: 10 to 5 mg BID</th>
<th>Remain on 10 mg BID</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>833</td>
<td>248</td>
<td>234</td>
<td>951</td>
</tr>
<tr>
<td>Total years of exposure</td>
<td>2,729</td>
<td>907</td>
<td>822</td>
<td>3,030</td>
</tr>
<tr>
<td>Discontinued due to AEs, n</td>
<td>207</td>
<td>53</td>
<td>48</td>
<td>221</td>
</tr>
<tr>
<td><strong>Most common AE system organ classes, n (EAER): EAER &gt;10.00 in any group</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infections and infestations</td>
<td>578 (21.18)</td>
<td>171 (18.85)</td>
<td>141 (17.16)</td>
<td>663 (21.88)</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>257 (9.41)</td>
<td>93 (10.25)</td>
<td>83 (10.10)</td>
<td>266 (8.77)</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td>323 (11.83)</td>
<td>78 (8.59)</td>
<td>56 (6.81)</td>
<td>366 (12.08)</td>
</tr>
<tr>
<td><strong>Most common AE preferred terms, n (EAER): EAER &gt;3.00 in any group</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>101 (3.70)</td>
<td>70 (7.71)</td>
<td>63 (7.66)</td>
<td>146 (4.81)</td>
</tr>
<tr>
<td>Upper respiratory tract</td>
<td>139 (5.09)</td>
<td>37 (4.07)</td>
<td>33 (4.01)</td>
<td>179 (5.90)</td>
</tr>
</tbody>
</table>
Disclosure: R. Mueller, None; H. Schulze-Koops, None; D. E. Furst, Pfizer Inc, 5; S. B. Cohen, AbbVie, Amgen, Boehringer Ingelheim, Gilead, Merck, Pfizer Inc, 5, AbbVie, Amgen, Boehringer Ingelheim, Gilead, Merck, Pfizer Inc, 9; K. Kwok, Pfizer Inc, 1, Pfizer Inc, 3; A. Maniccia, Pfizer Inc, 1, Pfizer Inc, 3; L. Wang, Pfizer Inc, 1, Pfizer Inc, 3; E. Akylbekova, QuintilesIMS, 3, Pfizer Inc, 5; J. von Kempis, None.


Abstract Number: 536

Effectiveness, Tolerability, and Safety of Tofacitinib in Rheumatoid Arthritis: A Retrospective Analysis of Real-World Data from the St. Gallen Cohort

Ruediger Mueller¹, Frederik Mattow², Florian Popp³ and Johannes von Kempis⁴, ¹Division of Rheumatology, Cantonal Hospital, St. Gallen, Switzerland, ²Kantonsspital St. Gallen, St. Gallen, Switzerland, ³Rorschacherstrasse 95, Kantonsspital St. Gallen, St. Gallen, Switzerland, ⁴Rheumatology, Kantonsspital St. Gallen, St. Gallen, Switzerland

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Tofacitinib is an oral JAK inhibitor for the treatment of RA. Efficacy and safety of tofacitinib have been shown in several clinical studies. The study presented here aimed to assess the clinical effectiveness and tolerability of tofacitinib among patients with RA in real life.

Methods:

Consecutive patients between June 2013 and April 2017 with RA who fulfilled the American College of Rheumatology/EULAR 2010 criteria were analyzed in a prospectively designed analysis of retrospective data. Patients were initiated on tofacitinib 5mg bid. The primary objective was to analyze safety of tofacitinib in a real life cohort. Safety was assessed by the reasons to stop tofacitinib during follow up and changes of liver enzymes, hemoglobin, and creatinine. The secondary outcome was to analyze the frequency and time to achieve low disease activity (LDA) and remission as defined by DAS28.

Results:
Overall, 58 patients were treated with tofacitinib. 86% of the patients were pre-exposed to at least one biological agent. The average DAS 28 at initiation of tofacitinib was 4.5. 65% were rheumatoid factor and 52% ACPA positive. The mean follow up was 1.74 years after initiation of tofacitinib treatment. 32 (57%) patients remained on tofacitinib during follow up. The average time to stop tofacitinib was 112 days. Reasons to stop tofacitinib were: gastrointestinal (n=12), insufficient response (n=5), flare (n=3), pneumonia (n=2), blue toe syndrome (n=1), thoracic pain (n=1), and myalgia (n=1).

Increased of ALAT and ASAT were detected in 4 and 8 patients (>2x ULN: n=1 and n=2). These elevated transaminase levels were transient in 2 and 5 patients, respectively. The average hemoglobin level decreased by 2.6%. A decrease of more than 10% of the hemoglobin level was found in 7 patients during follow up. The average lymphocyte count increased by 6.6%. A decrease below 1000 Lymphocytes/mcl was detected in four patients. Three of them were transient. The mean creatinine level increased by 3.4%. An increase of more than 10% was detected in seven patients (n=1 with pathological creatinine level).

37 (63.8%) and 31(53.4%) of the patients achieved LDA or remission after 62.0 and 65.3 days respectively.

Conclusion:

Tofacitinib is a safe and effective treatment option for patients with RA. Tofacitinib may induce high rates of LDA and remission in patients with active disease, even after use of one or more biologics, over prolonged periods of time. Tofacitinib may be a valuable option in a treat to target approach because the time to determine its efficacy or adverse reaction leading to discontinuation is short, based on the data of our cohort.

Disclosure: R. Mueller, None; F. Mattow, None; F. Popp, None; J. von Kempis, None.


Abstract Number: 537

No Effect of Baseline Serum CRP Levels on Clinical Efficacy Parameters in Rheumatoid Arthritis Patients Treated with Filgotinib: Post Hoc Analysis from Two Phase 2B Studies

Arthur Kavanaugh¹, Annegret Van der Aa², Corinne Jamoul², Chantal Tasset², Pille Harrison² and René Westhovens³,
¹Medicine, University of California, San Diego, La Jolla, CA, ²Galapagos NV, Mechelen, Belgium, ³Department of Rheumatology, University Hospitals Leuven, Leuven, Belgium

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Filgotinib (GLPG0634, GS-6034) is an oral, selective JAK1 inhibitor that has demonstrated safety and efficacy data in two 24-week placebo-controlled phase 2B studies as add-on to methotrexate and as monotherapy in active rheumatoid arthritis (RA) patients with inadequate response to MTX (MTX-IR)⁴,⁵.

The objective was to evaluate the effect of baseline serum CRP levels on clinical efficacy after 12 weeks of treatment, as assessed by the ACR and DAS28(CRP) subcomponents in MTX-IR RA patients treated with filgotinib.
Methods:

Patients were randomized in a double-blind manner to placebo (PBO) or one of 3 daily doses of filgotinib (50mg, 100mg or 200mg) for 24 weeks. In the DARWIN 1 study, filgotinib on MTX background was evaluated as once (QD) or twice daily treatment. In the DARWIN 2 study once-daily filgotinib was assessed as monotherapy. The inclusion criterion for CRP was amended during the studies and was decreased from 13.5 mg/L to 6.3 mg/L. This post-hoc analysis included patients treated with the selected Phase 3 filgotinib doses, 100mg and 200mg QD, and PBO. Efficacy outcomes were analyzed by baseline CRP level (low: ≤9 mg/L and high: >9 mg/L, with 9mg/L as ULN).

Results:

Baseline disease activity was high and balanced across the different treatment groups. Comparable baseline values were shown between both CRP subgroups, except for the mean CRP levels (Table 1).

In both low and high CRP subgroups, patients on filgotinib at 100mg or 200mg QD for 12 weeks showed efficacy over PBO, as measured by change from baseline in different subcomponents of the ACR/DAS28(CRP) composite score (TJC68, SJC66, Pt pain, Pt GDA, Inv GDA, HAQ-DI and CRP) (Table 1). In both studies, there was no clear pattern suggesting that baseline CRP level had a consistent effect on filgotinib efficacy.

Conclusion:

This post-hoc analysis of two Phase 2B studies in MTX-IR RA patients suggests that filgotinib treatment once daily at 100mg and 200mg both on the background of MTX and as monotherapy was consistently associated with improved clinical outcomes compared to placebo at Week 12, regardless of baseline CRP levels, as measured by ACR and DAS28(CRP) subcomponents.

Table 1. Mean baseline and change from baseline (SE) values in key efficacy parameters at Week 12 by CRP subgroup
<table>
<thead>
<tr>
<th></th>
<th>PBO</th>
<th>DARWIN 1 filgotinib 100mg QD</th>
<th>filgotinib 200mg QD</th>
<th>PBO</th>
<th>DARWIN 2 filgotinib 100mg QD</th>
<th>filgotinib 200mg QD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low CRP subgroup (≤9 mg/L)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>33</td>
<td>25</td>
<td>15</td>
<td>11</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>TJC68</td>
<td>23.45</td>
<td>21.94</td>
<td>-9.42 (2.68)</td>
<td>-14.87</td>
<td>-3.55 (3.59)</td>
<td>-16.63 (2.71)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(2.82)</td>
<td></td>
<td></td>
<td>(2.90)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>17.00</td>
<td>14.18</td>
<td>19.50</td>
<td>13.21</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>15.52</td>
<td>14.30</td>
<td>-8.82 (1.62)</td>
<td>-12.07</td>
<td>-5.09 (3.11)</td>
<td>-10.75 (2.04)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(2.53)</td>
<td></td>
<td></td>
<td>-9.51 (1.30)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>64.94</td>
<td>61.24</td>
<td>-19.24 (6.41)</td>
<td>-27.27</td>
<td>-11.27 (7.63)</td>
<td>-36.05 (6.76)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(6.25)</td>
<td></td>
<td></td>
<td>(8.50)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>62.88</td>
<td>66.96</td>
<td>-17.82 (5.92)</td>
<td>-35.33</td>
<td>-13.36 (7.68)</td>
<td>-38.20 (5.74)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(5.74)</td>
<td></td>
<td></td>
<td>(7.35)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>65.27</td>
<td>65.84</td>
<td>-29.24 (5.84)</td>
<td>-41.40</td>
<td>-33.36 (9.51)</td>
<td>-50.50 (4.73)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(5.53)</td>
<td></td>
<td></td>
<td>(4.86)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.47</td>
<td>1.51</td>
<td>-0.21 (0.121)</td>
<td>-0.64</td>
<td>-0.12 (0.163)</td>
<td>-0.74 (0.172)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(0.133)</td>
<td></td>
<td></td>
<td>(0.158)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5.57</td>
<td>5.57</td>
<td>4.29</td>
<td>4.44</td>
<td>5.20</td>
<td>4.41</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>+5.97 (2.53)</td>
<td>+0.04</td>
<td>+1.56 (1.49)</td>
<td>-0.09 (0.99)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(1.96)</td>
<td></td>
<td></td>
<td>+0.89 (1.31)</td>
</tr>
<tr>
<td><strong>High CRP subgroup (&gt;9 mg/L)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>53</td>
<td>60</td>
<td>71</td>
<td>61</td>
<td>50</td>
<td>49</td>
</tr>
<tr>
<td>TJC68</td>
<td>25.94</td>
<td>26.73</td>
<td>-8.98 (1.44)</td>
<td>-18.22</td>
<td>-6.21 (1.62)</td>
<td>-15.29 (1.82)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(1.49)</td>
<td></td>
<td></td>
<td>(1.79)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>16.51</td>
<td>17.15</td>
<td>-6.87 (1.03)</td>
<td>-10.80</td>
<td>-3.89 (1.34)</td>
<td>-11.65 (1.48)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(1.22)</td>
<td></td>
<td></td>
<td>(1.48)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(1.27)</td>
</tr>
<tr>
<td></td>
<td>66.11</td>
<td>67.14</td>
<td>-15.49 (3.53)</td>
<td>-32.24</td>
<td>-13.70 (3.41)</td>
<td>-29.66 (4.02)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(3.72)</td>
<td></td>
<td></td>
<td>(3.82)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>65.00</td>
<td>67.83</td>
<td>-15.98 (3.39)</td>
<td>-33.94</td>
<td>-11.21 (3.19)</td>
<td>-26.78 (4.03)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(3.84)</td>
<td></td>
<td></td>
<td>(3.57)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>67.25</td>
<td>66.65</td>
<td>-25.77 (3.65)</td>
<td>-37.25</td>
<td>-21.87 (2.62)</td>
<td>-39.02 (3.15)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(3.10)</td>
<td></td>
<td></td>
<td>(3.30)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.83</td>
<td>1.78</td>
<td>-0.61 (0.087)</td>
<td>1.73</td>
<td>1.77</td>
<td>1.82</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(0.087)</td>
<td></td>
<td></td>
<td>(0.081)</td>
</tr>
<tr>
<td>CRP</td>
<td>-0.49 (0.080)</td>
<td>-0.78 (0.076)</td>
<td>-0.25 (0.074)</td>
<td>-0.74 (0.086)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-----------</td>
<td>---------------</td>
<td>---------------</td>
<td>---------------</td>
<td>---------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>22.89</td>
<td>31.91</td>
<td>40.82</td>
<td>33.70</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+0.61 (3.22)</td>
<td>-20.90 (3.88)</td>
<td>-10.56 (5.01)</td>
<td>-17.12 (6.19)</td>
<td>-21.27 (3.33)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### References


---

**Disclosure:** A. Kavanaugh, AbbVie, 5,Amgen, 5,Celgene, 5,Novartis Pharmaceutical Corporation, 5,Janssen Pharmaceutica Product, L.P., 5,Eli Lilly and Company, 5,Pfizer Inc, 5,UCB, 5,Galapagos NV, 5; A. Van der Aa, Galapagos NV, 1,Galapagos NV, 3; C. Jamoul, Galapagos NV, 3; C. Tasset, Galapagos NV, 1,Galapagos NV, 3; P. Harrison, Galapagos NV, 1,Galapagos NV, 3; R. Westhovens, Bristol-Myers Squibb, 2,Roche Pharmaceuticals, 2,CellTrion, 5,Galapagos NV, 5.


---

**Abstract Number: 538**

**Severe Adverse Drug Reactions Due to Disease Modifying Drugs in Patients with Incident Rheumatoid Arthritis**

**Lydia A Alcazar**1, Judit Font Urgelles2, Cynthia Milagros León Cárdenas2, Cristina Vadillo Font2, Dalifer Freites Núñez1, Leticia Leon1, Juan A Jover Jover2 and Zulema Rosales Rosado1,2, 1Instituto de Investigación Sanitaria San Carlos (IdISSC), Madrid, Spain, 2Rheumatology, Hospital Clínico San Carlos, Madrid, Spain

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** There is a well-known risk of developing adverse drug reactions (ADR) in rheumatology due, mainly, to the Disease Modifying Drugs (DMARD) used. It is mandatory to increase our knowledge of ADR; especially those that put the patient at risk. The purpose of our study was to describe the incidence and characteristics of severe ADR to DMARD in patients with incident RA as well as the factors associated to their development.

**Methods:** An observational longitudinal study was conducted. Patients: all recent onset RA patients diagnosed between April 15th 2007 and 31st June 2011 followed in outpatient clinic at Hospital Clinico San Carlos until December 31st 2016, which used any DMARD treatment (synthetic and biologic). Primary outcome: development of a severe ADR (discontinuation and hospitalization or death as a result of the ADR) due to DMARD treatment. Incidence rates of discontinuation (IR) per 100 patient-years were estimated using survival techniques with their respective 95% confidence limits.
interval [CI]. Comparisons between associated factors were run by Cox bivariate and multivariate regression models. Results were expressed by hazard ratio (HR) and [CI].

Results: We included 1054 courses of DMARD treatment in 405 patients (2277.9 patient-years). Of these, 78.27% were women with a mean age at diagnosis of 57 ± 15 years. The median time to the start of the first DMARD was 0.3 [± 0.6] days and the median value of ESR at diagnose was 40 [± 27] mm/h. 16.3% of patients were taking biological DMARD, 73.3% were using monotherapy and 89% were taking corticoids. There were 369 ADRs in 212 patients, 41 of them (11.1%) severe (IR: 1.8 [1.3-2.4]). Infection was the most frequent cause of severe ADR (n=26, 63.4%), followed by cancer (n=3, 7.3%); 6 patients died during follow up. Incidence rates are shown in table 1. In the multivariate analysis after adjusting by age: female sex (HR: 2.7 [1.2-5.9]), the use of biological DMARD compared to synthetic DMARD (HR: 3.6 [1.03-12.6]), higher ERS at the beginning of the DMARD (HR: 1.01 [1-1.02]) and the presence at baseline of congestive heart failure (HR: 4.3 [2-9.2]), periphery arteriopathy (HR: 3.1 [1.02-9.2]) and cancer (HR: 3.2 [1.6-6.5]) achieved statistically significant association with the development of a severe ADR. Whereas number of concomitant DMARD dropped from the model (HR: 1.23 [0.5-2.6]).

Conclusion: This study describes the incidence of severe ADR occurred in RA patients taking DMARD in real life conditions. The IR of severe ADR in our cohort was 1.8% patient-years, increasing to 3.6% in the population over 70 years old. Infection was the main cause of severe ADR followed by cancer. Caution might be taken regarding severe ADR in patients of female sex, those using biological DMARD, with higher ERS at the beginning of treatment or with certain comorbidities.
### TABLE 1

<table>
<thead>
<tr>
<th></th>
<th>patients-years</th>
<th>n</th>
<th>IR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Global</strong></td>
<td>2277.9</td>
<td>41</td>
<td>1.8</td>
<td>1.3-2.4</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td>1835.4</td>
<td>24</td>
<td>1.3</td>
<td>0.9-2</td>
</tr>
<tr>
<td><strong>Men</strong></td>
<td>442.5</td>
<td>17</td>
<td>3.8</td>
<td>2.4-6.2</td>
</tr>
<tr>
<td><strong>By age category</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-50 years</td>
<td>1065.5</td>
<td>11</td>
<td>0.6</td>
<td>0.6-1.9</td>
</tr>
<tr>
<td>51-70 years</td>
<td>716.9</td>
<td>12</td>
<td>0.9</td>
<td>0.9-2.9</td>
</tr>
<tr>
<td>&gt; 70 years</td>
<td>495.5</td>
<td>18</td>
<td>3.6</td>
<td>2.3-5.8</td>
</tr>
<tr>
<td><strong>By therapy regimen</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monotherapy</td>
<td>1609.5</td>
<td>25</td>
<td>1.6</td>
<td>1.1-2.3</td>
</tr>
<tr>
<td>Double therapy</td>
<td>568.9</td>
<td>12</td>
<td>2.1</td>
<td>1.2-3.7</td>
</tr>
<tr>
<td>Triple therapy</td>
<td>99.4</td>
<td>4</td>
<td>4</td>
<td>1.5-10.7</td>
</tr>
<tr>
<td><strong>By type of DMARD</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Synthetic</td>
<td>2048.3</td>
<td>31</td>
<td>1.5</td>
<td>1.1-2.2</td>
</tr>
<tr>
<td>Biological</td>
<td>229.5</td>
<td>10</td>
<td>4.4</td>
<td>2.3-8.1</td>
</tr>
<tr>
<td><strong>By corticoids use</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1997.2</td>
<td>39</td>
<td>1.9</td>
<td>1.4-2.7</td>
</tr>
<tr>
<td>No</td>
<td>278.3</td>
<td>2</td>
<td>0.7</td>
<td>0.2-2.9</td>
</tr>
<tr>
<td><strong>By drug</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abatacept</td>
<td>8.3</td>
<td>2</td>
<td>2.4</td>
<td>6.1-96.8</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>81.5</td>
<td>1</td>
<td>1.2</td>
<td>0.2-8.7</td>
</tr>
<tr>
<td>Antimalarials</td>
<td>749.7</td>
<td>6</td>
<td>0.8</td>
<td>0.4-1.8</td>
</tr>
<tr>
<td>Certolizumab</td>
<td>16</td>
<td>1</td>
<td>6.2</td>
<td>0.9-44.1</td>
</tr>
<tr>
<td>Etanercept</td>
<td>65.2</td>
<td>2</td>
<td>3.1</td>
<td>0.8-12.3</td>
</tr>
<tr>
<td>Golimumab</td>
<td>9.1</td>
<td>1</td>
<td>11</td>
<td>1.5-78</td>
</tr>
<tr>
<td>Infliximab</td>
<td>18.4</td>
<td>3</td>
<td>16</td>
<td>3.5-50.6</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>340.4</td>
<td>7</td>
<td>2.1</td>
<td>0.9-4.3</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>1463.5</td>
<td>24</td>
<td>1.6</td>
<td>1.1-2.4</td>
</tr>
<tr>
<td>Gold</td>
<td>83.6</td>
<td>7</td>
<td>8.4</td>
<td>4-17.6</td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>154</td>
<td>6</td>
<td>3.9</td>
<td>1.8-8.7</td>
</tr>
</tbody>
</table>

**Disclosure:** L. A. Alcazar, None; J. Font Urgelles, None; C. M. León Cárdenas, None; C. Vadillo Font, None; D. Freites Núñez, None; L. Leon, None; J. A. Jover Jover, None; Z. Rosales Rosado, None.

Comparison of Oral Versus Parenteral Methotrexate in Rheumatoid Arthritis: A Meta-Analysis

Sahar Janjua1, Andreea Bujor1, Michael P. LaValley2, Josefina Duran3, Jürgen Braun4 and David T. Felson5, 1Department of Rheumatology, Boston Medical Center, Boston, MA, 2Boston University School of Public Health, Boston, MA, 3Pontificia Universidad Católica de Chile, Santiago, Chile, 4Institut für angewandte Statistik Dr. Jörg Schnitker GmbH, Bielefeld, Germany, 5Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Methotrexate (MTX) is the mainstay first-line therapy for rheumatoid arthritis (RA), and it can be given orally or parenterally. Bioavailability of oral MTX may decrease at high doses, and parenteral administration could bypass this limitation. Practice guidelines recommend changing to biologics if response to MTX is suboptimal but these guidelines are based on studies comparing biologics to oral MTX. There is some evidence that parenteral MTX may be more efficacious than the oral form at equivalent doses. Also, studies suggest that the side effect profile of parenteral MTX may be better than oral MTX. We carried out a meta-analysis to compare the efficacy of oral versus parenteral MTX in RA.

Methods:
PubMed, Web of Science and Embase were systematically searched from inception to June 8th 2017 and reviewed following PRISMA 2009 guidelines. We also examined bibliographies of reviews and other articles. To be included, trials had to study adults with RA randomized to the same dose of either oral or parenteral MTX. Studies were selected and data extracted by two independent reviewers and at each stage the reviewers met to adjudicate discrepancies. The primary endpoint was ACR20 at 6 months. Other endpoints included ACR50, ACR70, SDAI, and DAS28 remission. One large trial allowed switching for poor response at 16 weeks and included only 24 week data, and trial authors reanalyzed data at 16 weeks. For another trial, data were reanalyzed to provide ACR20/50/70 rates. Intention-to-treat analyses were used when possible. Data from direct comparisons between oral and parenteral methotrexate were pooled and quantitatively analyzed using maximum likelihood random effects meta-analysis. Relative treatment effects were generated as odds ratio [OR] (OR>1 indicated a benefit for parenteral therapy). We also examined the mean difference in ACR20 rates between parenteral and oral MTX.

Results:
The search yielded 357 papers or abstracts. After review of titles or abstracts, we excluded 314. We then examined 43 full-text papers or abstracts and found 4 that met inclusion criteria with 703 patients randomized. Dose of MTX started at 15mg/week and increased to as high as 22.5mg/week. In each trial, ACR20 rates were higher for those randomized to parenteral than to oral MTX. The summary OR for achieving ACR20 using parenteral vs. oral MTX was 2.84 (95% CI 1.35, 5.98) (see figure). Those on parenteral had an 18.5% (95% CI 3.3%, 33.6%) greater absolute risk of attaining ACR20 than those on oral MTX. Similar results were seen for ACR50 and 70 and for SDAI and DAS.

Conclusion:
In this meta-analysis, parenteral MTX therapy had a significantly higher odds than oral MTX of achieving reduction in disease activity. We propose that parenteral MTX is more effective than oral MTX with a better safety profile; its widespread use may lead to better control of disease and a decrease in demand for biologic agents.
Disclosure: S. Janjua, None; A. Bujor, None; M. P. LaValley, None; J. Duran, None; J. Braun, Abbvie (Abbot), Amgen, Biogen, BMS, Boehringer, Celgene, Celltrion, centocor, Chugai, EBEWE Pharma, Epirus, Hikma, Hospira, Janssen, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis and UCB, 5; Abbvie (Abbot), Amgen, Biogen, BMS, Boehringer, Celgene, Celltrion, centocor, Chugai, EBEWE Pharma, Epirus, Hikma, Hospira, Janssen, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis and UCB, 2; Abbvie (Abbot), Amgen, Biogen, BMS, Boehringer, Celgene, Celltrion, centocor, Chugai, EBEWE Pharma, Epirus, Hikma, Hospira, Janssen, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis and UCB, 6; D. T. Felson, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/comparison-of-oral-versus-parenteral-methotrexate-in-rheumatoid-arthritis-a-meta-analysis

Abstract Number: 540

Being Elderly Is Not a Predictive Factor of Discontinuation of Abatacept Due to Adverse Events in Rheumatoid Arthritis Patients with Concomitant Methotrexate: A Retrospective Observational Study Based on Data from a Japanese Multicenter Registry Study

Nobunori Takahashi, Toshihisa Kojima, Shuji Asai, Tatsuo Watanabe, Takuya Matsumoto, Nobuyuki Asai, Yasumori Sobue and Naoki Ishiguro, Orthopaedic Surgery, Nagoya University Graduate School of Medicine, Nagoya, Japan
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM
Background/Purpose:

Abatacept is a new class of biologic agent for the treatment of rheumatoid arthritis (RA) that inhibits T cell activation by binding to CD80/86. Some evidences demonstrating that the abatacept may offer advantage on safety over the TNF inhibitors have been accumulated. Therefore, we sometimes tend to use abatacept in the elderly patients easily. We studied the clinical response and safety profile of abatacept in the real-world patients using the Japanese multicenter registry data.

Methods:

Participants were the consecutive 508 RA patients treated with abatacept who were registered in the Tsurumai Biologics Communication Registry (TBCR). We divided the patients into three groups according to the tertile value of age. As the efficacy endpoints, we compared mean and categorical distribution of DAS28-CRP score and EULAR response rate between the young (<62 years), middle (62-72 years), and elderly (>72 years) group at baseline, 4, 12, 24, and 52 weeks. As the safety endpoints, we studied the incidence rate (Kaplan-Meier method) and the predictive factors (multivariate Cox regression analysis) of the discontinuation of abatacept due to adverse events for up to 4 years. We studied the safety endpoints separately in the patients with and without concomitant methotrexate (MTX) treatment, since the MTX usually affects the safety profile.

Results:

There was significant difference between the young, middle, and elderly groups in age (52.7, 67.7, and 78.1 years; p<0.001), eGFR value (108.5, 91.1, and 79.6 ml/min/1.73m²; p<0.001), and MTX usage rate (57.7, 44.9, and 32.2 %; p<0.001). There was no significant difference between three groups in all of the clinical efficacy endpoints (data not shown). For the safety analysis, we divided the patients into two groups according to the cut-off value (69.5 years) from the ROC curve for age in the MTX (-) patients (Fig. A). The elderly group (>69.5 years) demonstrated higher incidence rate of discontinuation due to adverse events (1.0 vs 4.9% at 24 weeks, p=0.005) in the MTX (-) patients (Fig. B). The age of >69.5 years was identified as an independent predictor of incidence of discontinuation due to adverse events in the MTX (-) patients (Fig. C). However, there was no such difference in the incidence rate (Fig. B) and the being elderly (>69.5 years) was not a predictor in the MTX (+) patients (Fig. C).

Conclusion:

It was remarkable that abatacept therapy demonstrated the comparative efficacy in the elderly patients. Similar to a case of other biologics, we should pay attention to the incidence of severe adverse events in the elderly patients without concomitant MTX. However, especially in the patients being treated with MTX concomitantly, abatacept would be a good treatment option in the elderly from the view point of both efficacy and safety.
Disclosure: N. Takahashi, None; T. Kojima, None; S. Asai, None; T. Watanabe, None; T. Matsumoto, None; N. Asai, None; Y. Sobue, None; N. Ishiguro, Abbott, Astellas Pharma, Bristol-Myers, Chugai Pharmaceutical, DaiichiSankyo, Eisai, Hisamitsu, Janssen Pharmaceutical, Kaken Pharmaceutical, Mitsubishi Tanabe Pharma, Otsuka Pharmaceutical, Pfizer, Takeda Pharmaceutical, Taisho Toyama Pharmaceutical, UCB, 2, Abbott, Astellas Pharma, Bristol-Myers, Chugai Pharmaceutical, DaiichiSankyo, Eisai, Hisamitsu, Janssen Pharmaceutical, Mitsubishi Tanabe Pharma, Otsuka Pharmaceutical, Pfizer, Takeda Pharmaceutical, Taisho Toyama Pharmaceutical, UCB, 8.


Abstract Number: 541

Decreasing Trend of Serious Infections Incidence Rate Along Years in Rheumatoid Arthritis Patients Exposed to Biologics. Data from Two Latin America Registries
SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Infections are the most frequent and concerning serious adverse events related to rheumatoid arthritis (RA) treatment with biologic drugs (bDMARDs). Their safety profile might have substantial regional differences. Since January 2009, BiobadaAmerica, a common platform registry project open to all Latin America countries, was started with the goal of focusing on safety monitoring of bDMARDs. This study aims to present data on the serious infections (SI) incidence rate trend along years in patients with RA exposed to bDMARDs in two no-compulsory Latin America registries.

Methods: Data from Brazil (BiobadaBrasil) and Argentina (BiobadaSar) registries were downloaded on December 31, 2016 and merged. The same constant monitoring process granted data quality. Patients with rheumatic diseases were included prospectively when started on the first bDMARD. Time of exposure was set from starting of treatment to the date of last administration or censorship. SI incidence rate was calculated per 1000 patient/years with 95%CI

Results: Data from 2591 RA patients on bDMARDs were analyzed, for a total of 9300 p/y. There were 3784 treatment courses, 64% with aTNF (Adalimumab, Certolizumab, Etanercept, Golimumab, Infliximab), 36% non-aTNF (Abatacept, Rituximab, Tocilizumab) including Tofacitinib. Females 85%, mean age at baseline 53 yrs (SD 12.8), mean disease duration 10 yrs (8.5), mean follow-up 2.7 yrs (2). The overall incidence rate of SI (2010 – 2016) was 30.54 (CI 27.18-34.30), The trend along the years is reported in the following table.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>SI</td>
<td>26.57</td>
<td>26.03</td>
<td>36.59</td>
<td>35.85</td>
<td>18.3</td>
<td>16.18</td>
<td>7.27</td>
</tr>
</tbody>
</table>


Remarkable, the trend was the same in both registries when data were analyzed separately and reflected the general tendency seen for all serious side effects.

Conclusion: A decreasing trend of serious infections incidence rate has been observed along the years in patients with RA exposed to bDMARDs, in accordance with published data from other registries.

Disclosure: R. Ranza, None; I. M. M. Laurindo, None; G. Christopoulos, None; G. Gomez, None; E. R. Soriano, AbbVie, Janssen, Novartis, Pfizer Inc, UCB, 2; AbbVie, Janssen, Novartis, Pfizer Inc, UCB, 5; AbbVie, Bristol-Myers Squibb, Janssen, Novartis, Pfizer Inc, Roche, UCB, 8; M. A. Descalzo, None; M. de la Vega, None.


Abstract Number: 542
Is There Any Difference in RA Patients for Methotrexate Use Vs. Leflunomide Use As a Concomitant Treatment with Biological and Targeted Synthetic Dmards in Turkbio Registry?

Nevsun Inanc1, Gulsen Ozen2, Yasemin Yalçinkaya1, Ediz Dalkilic3, Suleyman Serdar Koca4, Gerçek Can5, Ahmet Karatas6, Yavuz Pehlivan7, Ayten Yazici8, Ayse Cefle9, Abdurrahman Tufan10, Servet Akar11, Soner Senel12, Burak Oz13, Nurullah Akkoc14 and Fatos Onen15. 1Departement of Internal Medicine, Division of Rheumatology, Marmara University, Istanbul, Turkey, 2Rheumatology, Marmara University, School of Medicine, Rheumatology, Istanbul, Turkey, 3Department of Internal Medicine, Division of Rheumatology, Uludag University, School of Medicine, Rheumatology, Bursa, Turkey, 4Department of Rheumatology, Firat University School of Medicine, Elazig, Turkey, 5Rheumatology, Dokuz Eylul University Faculty of Medicine, İzmir, Turkey, 6Department of Rheumatology, Firat University, School of Medicine, Rheumatology, Elazig, Turkey, 7Department of Rheumatology, Uludag University, Bursa, Turkey, 8Rheumatology, Kocaeli University, Kocaeli, Turkey, 9Rheumatology, Kocaeli University, School of Medicine, Rheumatology, Kocaeli, Turkey, 10Internal Medicine-Rheumatology, Gazi University Medical School, Rheumatology, Ankara, Turkey, 11Rheumatology, İzmir Katip Celebi University, School of Medicine, Rheumatology, İzmir, Turkey, 12Rheumatology, Kayseri Erciyes University, School of Medicine, Rheumatology, Kayseri, Turkey, 13Rheumatology, Firat University, School of Medicine, Rheumatology, Elazig, Turkey, 14Rheumatology, Private Practice, Rheumatology, İzmir, Turkey, 15Rheumatology, Dokuz Eylul University Faculty of Medicine, İzmir, Turkey

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: TURKBIO registry is the Turkish version of Danish DANBIO rheumatologic database which has been established in 2011. Demographic and clinical data including age, sex, disease type, disease duration, and previous or current treatment with conventional (csDMARD) and targeted synthetic (tsDMARD), and biological DMARDs (bDMARDs) were collected. In this study, we aimed to investigate the efficacy and safety status of methotrexate (MTX) vs. leflunomide (LEF) use as a concomitant treatment with bDMARDs and tsDMARD in this registry.

Methods: Frequencies of achievement of remission or remission+low disease activity (LDA) at the 6th month of bDMARD or tsDMARD treatment were compared between patients who were on these medications with MTX vs. LEF as a concomitant treatment. Similarly, patients who were on TNF inhibitors (TNFi), abatacept (ABA), rituximab (RTX), tocilizumab (TCZ), and tofacitibinib (TOFA) with MTX vs. LEF were also assessed separately for the achievement of remission and remission+LDA. Drug survival and switch rates of bDMARD and tsDMARD treatments either with MTX or LEF were compared. The adverse effects with MTX and LEF concomitant use were evaluated as well.

Results:

The study included 725 bDMARD or tsDMARD receiving RA patients from 8 participating centers of the TURKBIO registry. Of these patients, 462 (63.7%) were receiving concomitant MTX and 263 (36.3%) LEF. Demographic findings are given in the Table. Achievement of remission and remission+LDA at the 6th month of bDMARD or tsDMARD initiation was similar in concomitant MTX vs LEF groups (51.4% vs. 53%, P=0.683). When each bDMARD and tsDMARD was evaluated separately, achievement of remission were again similar in MTX and LEF concomitant users (TNFi: 53% vs. 54%; ABA: 50% vs. 59%; RTX: 53% vs. 61%; TCZ: 42% vs. 35%; P>0.05 for all). For TOFA, although remission+LDA rate was numerically higher in MTX concomitant group than LEF group (42% vs. 21%), the difference was not statistically significant due to the smaller sample size of TOFA (N=33). The results were similar for all DMARD groups when remission was evaluated alone. Drug survival (17±12 vs. 16±11 months, p>0.05 ) and drug discontinuation (42,2 vs 38,
Conclusions: Achievement of remission or remission + LDA was not different with the concomitant use of MTX vs. LEF with any bDMARD or tsDMARD treatment in RA patients with a similar safety profile. LEF might be an alternative as a concomitant DMARD in MTX-intolerant RA patients initiating bDMARDs or tsDMARD.

Table. Demographic findings of patients.

<table>
<thead>
<tr>
<th></th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, n (%)</td>
<td>596 (82,2)</td>
<td>129 (17,8)</td>
</tr>
<tr>
<td>Age, Median (Q1-Q3)</td>
<td>55 (45-62)</td>
<td>54±13</td>
</tr>
<tr>
<td>Age, Mean±SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease duration, Ortanca (Q1-Q3)</td>
<td>12 (8-17)</td>
<td>13±8</td>
</tr>
<tr>
<td>Disease duration, Ort±SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biological and targeted synthetic drugs, n (%)</td>
<td>354 (48,8)</td>
<td></td>
</tr>
<tr>
<td>TNFi*</td>
<td>144 (19,9)</td>
<td></td>
</tr>
<tr>
<td>RITUXIMAB</td>
<td>127 (17,5)</td>
<td></td>
</tr>
<tr>
<td>ABATACEPT</td>
<td>61 (8,4)</td>
<td></td>
</tr>
<tr>
<td>TOCILIZUMAB</td>
<td>36 (5,0)</td>
<td></td>
</tr>
<tr>
<td>TOFACITINIB</td>
<td>3 (0,4)</td>
<td></td>
</tr>
<tr>
<td>ANAKINRA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biological+MTX, n (%)</td>
<td>462 (63,7)</td>
<td></td>
</tr>
<tr>
<td>Biological+LEF, n (%)</td>
<td>263 (36,3)</td>
<td></td>
</tr>
</tbody>
</table>

*TNFi: ETANERCEPT, ADALIMUMAB, CERTOLIZUMAB, GOLIMUMAB, INFLIXIMAB, REMSIMA.

Disclosure: N. Inanc, None; G. Ozen, None; Y. Yalçınkaya, None; E. Dalkılıç, AbbVie, 2,AbbVie, MSD, Roche, UCB and Pfizer, 9; S. S. Koca, None; G. Can, None; A. Karatas, None; Y. Pehlivan, None; A. Yazici, None; A. Cefle, None; A. Tufan, None; S. Akar, None; S. Senel, None; B. Oz, None; N. Akkoc, None; F. Onen, None.


Abstract Number: 543

Adverse Events in Rheumatoid Arthritis Patients Treated with Disease Modifying Biological Drugs at Hospital Docente Padre Billini in Santo Domingo

I Mercedes-Núñez, E Tejada-Reyes, Y Cruz-Rojas, E Rodríguez-Bautista, R Munoz-Louis, V Rosario, R Peña-Blanco, T Valdez-Lorie and R Alba-Fériz, Rheumatology, Hospital Docente Padre Billini (HDPB), Santo Domingo, Dominican Republic

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Background/Purpose: Rheumatoid arthritis (RA) is a systemic inflammatory autoimmune chronic disease with disability and deforms joints. After the introduction of biological therapies the prognosis of patients has improved. Approximately one-third of patients do not respond to treatment with conventional disease modifying drugs (sDMARDs). There are registers about adverse events (AE) of biological drugs disease modifying (bDMARDs), BIOBADASAR registry in Argentina with a frequency of adverse events with the use of biologicals of 26%, with respiratory tract infections being the most frequent. According to the BIOBADASER record loss of efficacy is the most frequent cause with more than 42% of cases, infections 21%. Since we do not have reports of this type, our objective is to describe the AE in patients with RA treated with bDMARDs anti TNF and non anti TNF. The bDMARDs used were adalimumab (ADA), golimumab (GLM), Etanercept (ETN) as anti TNF, anti IL6 Tocilizumab (TCZ) and anti CD20 Rituximab (RTX).

Methods: A descriptive, ambispective cross-sectional study. Data were collected from the rheumatology service of Hospital Docente Padre Billini, which is a national reference hospital. Statistical analyses were performed using SPSS (V.23). We included all patients diagnosed with RA according to 2010 ACR/EULAR classification criteria treated with bDMARDs during the period January 2013 - April 2017. Patients who did not have continuous follow-up by rheumatology of at least 3 consecutive consultations in one year were excluded.

Results: We have 863 patients diagnosed with RA, 398 patients treated with bDMARDs, 220 patients met inclusion criteria. 93% were women, mean age 57.2 years old, time of disease 9.9 years. The bDMARDs distributions was 51.4% TCZ, 19.9% ADA, 12.3% ETN, 9.1% GLM, 7.7% RTX. 46.8% had AE: 37.2% treated with ADA, 48.1% ETN, 30% GLM, 23.5% RTX, 56.6% TCZ. In the follow-up we found a 5% therapeutic failure of which 45.5% were by ADA, 18.2% ETN, 18.2 TCZ%, 9.1% RTX, 9.1% GLM. 14.1% presented infections of which 16% were serious. 0.9% adverse event were due to pulmonary tuberculosis (TB). 8.6% dyslipidemia of these 73.7% were TCZ, 6.4% hypertransaminemia of these 71.4% TCZ. 6.4% (13) neutropenia. 1.4% was diagnosed with neoplasm.

Conclusion: We found 46.8% of AE of these only 4.8 were serious unlike other records that report a 13.1%. Patients had a good therapeutic response, in spite of the economic limitations of the population and the shortage of drugs occasionally. The majority of patients used in our cohort TCZ. Even though a tropical country with high TB prevalence of we only found two patients.

Disclosure: I. Mercedes-Núñez, None; E. Tejada-Reyes, None; Y. Cruz-Rojas, None; E. Rodríguez-Bautista, None; R. Munoz-Louis, None; V. Rosario, None; R. Peña-Blanco, None; T. Valdez-Lorie, None; R. Alba-Fériz, None.


Abstract Number: 544

Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of PF-06650833, a Novel, Potentially First-in-Class Inhibitor of Interleukin-1 Receptor Associated Kinase-4 (IRAK-4) in Healthy Subjects

Spencer Danto1, Negin Shojae1, Cheryl Li1, Steven A. Gilbert2, Ravi Shankar Singh1, Zorayr Manukyan1 and Iain Kilty1, 1Worldwide Research and Development, Pfizer, Inc., Cambridge, MA, 2Pfizer, Inc., Cambridge, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Background/Purpose: IRAK-4 is a key node in innate immune signaling and is activated by the interleukin (IL)-1 family receptors (IL-1R, IL-18R, and IL-33R), in addition to the Toll-like receptors (TLRs). Inhibition of IRAK-4 blocks the production of inflammatory cytokines such as type I interferons, IL-6, tumor necrosis factor (TNF), IL-1, and IL-12 that are key drivers of autoimmune and inflammatory diseases. Therefore, IRAK-4, would be an attractive therapeutic target for autoimmune diseases such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). PF-06650833 is a recently described, small molecule, reversible, highly potent and specific inhibitor of IRAK-4. Nonclinical studies of PF-06650833 have been conducted in rats and dogs that support studies up to 3 months in duration. The current abstract describes the results from the single and multiple ascending dose (SAD, MAD) studies of PF-06650833 in healthy subjects.

Methods: The SAD and MAD studies of PF-06650833 were conducted in male and female (of nonchildbearing potential) healthy subjects. The first-in-human study was a 5-way crossover SAD study that explored extemporaneously (extemp) prepared immediate (IR)- and modified release (MR) formulations of PF-06650833 from 1 – 6000 mg. The MAD study was a 14 day sequential ascending dose study of extemp IR and MR tablet formulations administered after a standard meal. Doses from 25 mg BID to 1000 mg QID of the IR formulation and 300 mg MR tablets were explored. Standard clinical, ECG, and laboratory safety monitoring were performed as well as exploratory biomarkers.

Results: PF-06650833 was generally safe and well tolerated after both SD and MD up to the maximal planned doses, with dose limiting toxicity. Safety profile in both the SAD and MAD studies were similar, with the most common adverse events (AEs) being headache, and gastrointestinal symptoms (mainly nausea and abdominal pain). There were no clinically significant changes in vital signs, ECGs, or any laboratory parameter (including LFTs). PK analyses showed a moderate absorption rate with median $T_{\text{max}}$ from ~2 h for IR doses and ~4 h for MR tablets after a standard meal at steady state. Exposures increased proportionally up to about 100 mg and somewhat less than proportionally > 100 mg. In the MAD study, $T_{1/2}$ ranged from ~25 – ~31 h across the top IR and MR doses after a standard meal.

Conclusion: PF-06650833, a highly selective and potent inhibitor of IRAK-4, is shown to be generally safe and well tolerated up to 6000 mg SD and 1000 mg QID in healthy subjects, with an MR PK profile sufficient to support QD dosing in patient populations. To the authors’ knowledge, PF-06650833 is the first IRAK-4 inhibitor to advance to Phase 2 clinical studies.

Disclosure: S. Danto, Pfizer, Inc., 3; N. Shojaee, Pfizer Inc, 3; C. Li, Pfizer Inc, 3; S. A. Gilbert, Pfizer Inc, 3; R. S. Singh, Pfizer Inc, 3; Z. Manukyan, Pfizer Inc, 3; I. Kilty, Pfizer Inc, 3.


Abstract Number: 545

Incidence of Infusion Reactions to Intravenous Golimumab: Results from a Prospective, Real-World Community Registry

Rafat Faraawi1, Andrew Chow2, Majed M M Khraishi3, Derek Haaland4, Milton F. Baker5, Cathy Tkaczyk6, Allen J Lehman7, Francois Nantel6 and Brendan Osborne6, 1McMaster University, Hamilton, ON, Canada, 2Credit Valley Rheumatology, Mississauga, ON, Canada, 3Faculty of Medicine, Memorial University of Newfoundland, St John's, NF, Canada, 4Rheumatology, Clinical Immunology & Allergy, McMaster University, Barrie, ON, Canada, 5VIHA, Victoria, BC, Canada, 6Medical Affairs, Janssen Inc., Toronto, ON, Canada

First publication: September 18, 2017
Background/Purpose: Golimumab (GLM) is a monoclonal antibody targeting TNF-alpha, indicated for the treatment of adults with rheumatoid arthritis in combination with methotrexate (MTX). GLM-IV is recommended to be administered at a dose of 2 mg/kg given as a 30-minute intravenous (IV) infusion at weeks 0, 4 and every 8 weeks thereafter. In two separate trials, GO-LIVE and GO-FURTHER, infusion reactions (IRs) were observed in a relatively small group of GLM-treated patients with 2.2% and 3.3% of patients having documented IRs, respectively. The GO-IV registry was initiated to evaluate the incidence and management of IRs with GLM-IV in a real-world Canadian practice setting.

Methods: GO-IV was a prospective, observational, non-interventional, multicenter study conducted at 11 Canadian sites from 2014-2016. GLM infusions were followed to document IRs and their management, pre-medication uses and adverse events (AE). An IR was defined as any AE occurring during the infusion or within 1 hour post-infusion. Patients had to be at least 18 years of age or older, a confirmed diagnosis of rheumatoid arthritis, provide written consent for data collection, be naïve to GLM (both subcutaneous and intravenous formulations) and be seen by a Canadian rheumatologist.

Results: The study was terminated early due to lack of public listing for the drug. At that time, a total of 79 patients were enrolled and 62 of them were still ongoing. Reasons for premature discontinuation included AEs (7), lack of response (4), geographic issues (3), mis-diagnosis, switch to subcutaneous GLM or withdrawal of consent (one each). A total of 77 patients were included in the primary analysis and 78 in the safety analysis. Only 4 patients (5.1%) documented an IR over 483 infusion visits (0.8%), none of which classified as serious or leading to discontinuation. Three of those IRs occurred at the first infusion and one at infusion number three. Infusion-related AEs included palpitations, nausea, fatigue, infusion site pain, dizziness and headache (one each). The impact of pre-medication could not be established since only four infusions were pre-medicated with diphenhydramine and one with steroids.

A total of 164 AEs were reported in 45 patients (57.7%); 2 patients (2.6%) reported a serious adverse event (acute myocardial infarction; multiple fractures, pneumothorax, concussion, traumatic haematoma and pneumothorax resulting from a fall). There was one incidence of a lipoma and no death. There were 30 infectious AEs reported in 24 patients.

Conclusion: The GO-IV registry shows that, in community-based infusion clinics, IRs to GLM are uncommon and predominantly mild in nature.
<table>
<thead>
<tr>
<th>Primary Analysis</th>
<th>(n=77)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean (SD)</td>
<td>55.5 (11.58)</td>
</tr>
<tr>
<td>Female Gender, n(%)</td>
<td>61 (79.2%)</td>
</tr>
<tr>
<td>Weight (Kg), mean (SD)</td>
<td>77.2 (19.55)</td>
</tr>
<tr>
<td>Any co-morbidity, n (%)</td>
<td>19 (24.6%)</td>
</tr>
<tr>
<td><strong>Concomitant Medication</strong></td>
<td></td>
</tr>
<tr>
<td>Any DMARD, n (%)</td>
<td>70 (90.9%)</td>
</tr>
<tr>
<td>Corticosteroids, n (%)</td>
<td>32 (41.6%)</td>
</tr>
<tr>
<td>MTX, n(%)</td>
<td>58 (75.3%)</td>
</tr>
<tr>
<td><strong>Number of infusions</strong></td>
<td></td>
</tr>
<tr>
<td>Mean per subject (SD)</td>
<td>6.1 (2.69)</td>
</tr>
<tr>
<td>Median per subject</td>
<td>6.0</td>
</tr>
<tr>
<td><strong>Mean IV Administration (minutes)</strong></td>
<td></td>
</tr>
<tr>
<td>Safety Analysis (n=78)</td>
<td></td>
</tr>
<tr>
<td>No. subjects with at least 1 infusion reaction, n (%)</td>
<td>4 (5.1%)</td>
</tr>
<tr>
<td>Subject with ≥1 AE, n (%)</td>
<td>45 (57.7%)</td>
</tr>
<tr>
<td>Subject with ≥1 SAE, n (%)</td>
<td>2 (2.6%)</td>
</tr>
</tbody>
</table>

Disclosure: R. Faraawi, None; A. Chow, None; M. M. M. Khraishi, None; D. Haaland, None; M. F. Baker, None; C. Tkaczyk, Janssen Inc, 3; A. J. Lehman, Janssen Inc., 3; F. Nantel, Janssen Inc., 3; B. Osborne, Janssen Inc., 3.


Abstract Number: 546

**Concomitant Hydroxychloroquine Impact on Anti-TNF Persistence in Patients with Rheumatoid Arthritis**

Ming Zhao¹, Harlan Sayles², James R. O'Dell¹ and Kaleb Michaud²,³ ¹Rheumatology, University of Nebraska Medical Center, Omaha, NE, ²University of Nebraska Medical Center, Omaha, NE, ³National Data Bank for Rheumatic Diseases, Wichita, KS

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Tumor necrosis factor-α inhibitors (TNFi) have been widely used in patients who failed conventional DMARDs in the treatment of rheumatoid arthritis (RA). While most patients respond well to TNFi, some patients experience loss of efficacy over time possibly due to forming TNFi antibodies. Studies have shown that concomitant use of methotrexate (MTX) with TNFi is associated with increased drug survival compared with TNFi monotherapy. However, whether hydroxychloroquine (HCQ) may also prolong TNFi persistence is unknown and was the purpose of this study.
**Methods:** We analyzed patients with RA and ≥1 year participation in the National Data Bank for Rheumatic Diseases (NDB), an ongoing US-wide longitudinal observational study with biannual questionnaires since 1998. Patients initiating 3 TNFi’s, infliximab, adalimumab, or etanercept, were categorized according to concomitant DMARD use: none (monotherapy), HCQ +/- other DMARDs but no MTX, MTX +/- other DMARDs but no HCQ, and HCQ and MTX +/- other DMARDs. Patients who have previously taken other biologics were also enrolled into our study. Patients were considered as continuing the TNFi if it was on hold for less than 12 months due to infection or surgery and the same TNFi was resumed after that. Baseline characteristics (including all prior therapies) were collected via self-report at enrollment while therapy continuation was collected on each follow-up questionnaire. We followed patients until TNFi discontinuation, censoring, or death. We compared the discontinuation rate and mean drug survival time between subgroups using Pearson chi-square tests and Kruskal-Wallis tests with Dunn’s tests.

**Results:** A total of 8611 patients were included with mean (SD) age of 59 (13) years, 81% female and RA duration 14 (11) years. Patients who received concomitant HCQ with TNFi initiation had similar therapy discontinuation rates compared to TNFi monotherapy. Concomitant HCQ use was associated with a longer drug survival compared to etanercept (p=0.007) or infliximab (p<0.001) monotherapy. Concomitant MTX use has the largest impact in infliximab comparing to monotherapy, associated with both lower discontinuation rate (p<0.001) and longer drug survival time (p<0.001). Concomitant MTX use is also associated with longer drug survival in adalimumab (p=0.001), while such association was not found with concomitant HCQ use (p=0.183). Otherwise, concomitant HCQ use has similar effect in prolonging TNFi survival comparing to concomitant MTX use.

<table>
<thead>
<tr>
<th></th>
<th>A Monotherapy</th>
<th>B +HCQ – MTX</th>
<th>C +MTX – HCQ</th>
<th>D +HCQ +MTX</th>
<th>P values ≤0.05</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Etanercept</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discontinued, %</td>
<td>53.7</td>
<td>58.6</td>
<td>53.2</td>
<td>59.3</td>
<td>C vs. D</td>
</tr>
<tr>
<td>Drug survival, months (SD)</td>
<td>32 (37)</td>
<td>41 (45)</td>
<td>36 (41)</td>
<td>39 (44)</td>
<td>A vs. B, C, &amp; D</td>
</tr>
<tr>
<td><strong>Infliximab</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discontinued, %</td>
<td>61.2</td>
<td>56.6</td>
<td>52.0</td>
<td>55.8</td>
<td>A vs. C</td>
</tr>
<tr>
<td>Drug survival, months (SD)</td>
<td>17 (21)</td>
<td>32 (38)</td>
<td>41 (42)</td>
<td>38 (42)</td>
<td>A vs. B, C, &amp; D</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>B vs. C &amp; D</td>
</tr>
<tr>
<td><strong>Adalimumab</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discontinued, %</td>
<td>58.1</td>
<td>62.0</td>
<td>56.5</td>
<td>56.6</td>
<td>None</td>
</tr>
<tr>
<td>Drug survival, months (SD)</td>
<td>25 (29)</td>
<td>28 (33)</td>
<td>30 (32)</td>
<td>30 (31)</td>
<td>A vs. C &amp; D</td>
</tr>
</tbody>
</table>

**Conclusion:** Concomitant use of HCQ with TNFi’s is associated with increased TNFi persistence. Our initial findings show promise for increased TNFi effectiveness with either HCQ or MTX, and followup studies examining TNFi-antibody levels may help explain this association.

**Disclosure:** M. Zhao, None; H. Sayles, None; J. R. O'Dell, Medac, 5,Coherus, 5; K. Michaud, None.


**Abstract Number:** 547
Long-Term Risk of Serious Infections in Patients with Rheumatoid Arthritis Treated with Rituximab: 5 Year Data from the British Society for Rheumatology Biologics Register for Rheumatoid Arthritis

Diederik De Cock1, Lianne Kearsley-Fleet1, Lucia Silva Fernández2, Mark Lunt1, Kath Watson1, Deborah P.M. Symmons1,3 and Kimme L. Hyrich1,3, 1Arthritis Research UK Centre for Epidemiology, University of Manchester, Manchester Academic Health Science Centre, Manchester, United Kingdom, 2Arthritis Research UK Centre for Epidemiology, Centre for Musculoskeletal Research, Manchester Academic Health Science Centre, The University of Manchester, Manchester, United Kingdom, 3National Institute of Health Research Manchester Musculoskeletal Biomedical Research Centre, Central Manchester NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: In the United Kingdom (UK), rituximab (RTX) or a second tumour necrosis factor inhibitor (TNFi) are both permitted treatment options for patients with rheumatoid arthritis (RA) who have failed a first TNFi. The risk of serious infection (SI) is similar between these 2 treatments during the first year. However, long-term data on risk of SI for RTX are scarce but required, in light of reports of reduction in IgG following repeated dosing. We compared the risk of SI over 5 years of treatment in patients with RA who had failed a first TNFi and then received either RTX or TNFi.

Methods: This study used patients with RA registered with the British Society for Rheumatology Biologics Register (BSRBR-RA) a large national prospective study established primarily to assess the long-term safety of exposure to biologic therapies in patients with RA. This analysis included patients treated with either a second TNFi or RTX after failing a first TNFi. Patients were followed until first SI, 90 days (TNFi) or 9 months (RTX) following last dose when treatment was discontinued, last recorded follow-up or the end of the 5th year after the switch, which ever came first. SI was defined as infection requiring intravenous antibiotics, hospitalisation or resulting in death. The risk of first SI was compared between TNFi and RTX using (i) unadjusted, (ii) adjusted for sex and age, and (iii) propensity score adjusted Cox proportional hazard models. A Nelson-Aalen (NA) plot was constructed to show the cumulative incidence of SI over 5 years.

Results: This analysis included 3419 TNFi-treated patients contributing 9527 person-years (pyrs), median (IQR) exposure time per person 2.0 (0.8-3.3) years; and 1396 RTX patients contributing 3570 pyrs, median (IQR) exposure time 2.9 (1.7-3.9) years. A total of 362 and 135 first SI were reported in TNFi and RTX patients respectively, giving a crude incidence rate (95% CI) of 38 (34-42) SI/1000 pyrs (TNFi) and 38 (32-45) SI/1000 pyrs (RTX). The unadjusted, adjusted for sex and age, and propensity score adjusted hazard ratios (95%CI) for SI were 0.9 (0.8-1.1), 0.9 (0.7-1.0) and 0.9 (0.7-1.1) respectively. The NA plot showed a similar cumulative incidence risk of SI between the two groups over 5 years of treatment (figure).

Conclusion: The risk of serious infections was comparable over 5 years of treatment between TNFi and RTX treatment in patients who had failed a single prior TNFi.
Disclosure: D. De Cock, None; L. Kearsley-Fleet, None; L. Silva Fernández, None; M. Lunt, None; K. Watson, None; D. P. M. Symmons, None; K. L. Hyrich, None.


Abstract Number: 548

**LDL and HDL Changes with Sirukumab Treatment Are Anti-Atherogenic: Results from Two Phase 3 Trials in Patients with Rheumatoid Arthritis**

Matthew Loza¹, Androniki Bili², Shruti Daga³, Kurt Brown⁴, Jennifer Gilbride⁵, Bidisha Dasgupta², Benjamin Hsu² and Iain B. McInnes⁶, ¹Janssen Research & Development, LLC, Springhouse, PA, ²Janssen Research & Development, LLC, Spring House, PA, ³GlaxoSmithKline, Uxbridge, United Kingdom, ⁴GlaxoSmithKline, Collegeville, PA, ⁵Sum of Squares Ltd, Hertfordshire, United Kingdom, ⁶University of Glasgow, Glasgow, United Kingdom

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Sunday, November 5, 2017

Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules

Session Type: ACR Poster Session A

Session Time: 9:00AM-11:00AM

Background/Purpose: Sirukumab (SIR), a human monoclonal antibody that selectively binds to the IL-6 cytokine with high affinity, has demonstrated efficacy in RA in the phase 3 SIRROUND studies. Lipid elevations have been observed with SIR, consistent with IL-6 pathway inhibition (Lancet 2017. 389:1206). A post hoc analysis evaluated the impact of SIR treatment on plasma lipids and lipid particle subtypes.
Methods: Lipids were analyzed in plasma samples obtained from RA patients in SIRROUND-H (active comparator monotherapy study; n=160, 159, and 162 for adalimumab (ADA) 40mg q2w, SIR 50mg q4w, and SIR 100mg q2w treatment groups) and SIRROUND-D (placebo(PBO)-controlled DMARD-inadequate responder (IR) study; n=293, 470, and 437 patients for PBO (excluding early escape patients), SIR 50mg q4w, and SIR 100mg q2w treatment groups). Plasma fasting levels of HDL, LDL, IDL, VLDL and their respective particle subtypes (LipoProfile® test), triglycerides, Apolipoproteins (Apo) A1 and B, and total cholesterol were measured centrally. LDL-receptor (LDL-R) levels on blood leukocytes were measured by flow cytometry in 15 (ADA 40mg q2w), 23 (SIR 50mg q4w), and 20 (SIR 100mg q2w) patients in SIRROUND-H. Significance of differences between baseline and week (Wk)24 sample data was tested using Wilcoxon signed-rank and Mann-Whitney tests (p<0.05 considered significant).

Results: Elevations in total cholesterol, LDL, HDL, IDL, VLDL and triglycerides from baseline to Wk24 were observed with SIR compared to PBO or ADA (p<0.05; Table 1 for the SIRROUND-H study). However, atherogenic indices increased slightly (total cholesterol:HDL) or remained unchanged (ApoB/ApoA1) with SIR. Increases in LDL levels with SIR were mainly due to increases in anti-atherogenic large particles, with decreases in smaller pro-atherogenic particle sizes. Increases in HDL were mainly due to increases in small anti-atherogenic particles, with decreases in medium particles. Increases in VLDL with SIR were associated with increases in all particle sizes. Results were similar for both SIR doses and both studies, with similar changes observed by Wk4 (SIRROUND-H). ADA was associated with smaller but significant decreases in very small, small, and medium LDL particles (Table 1). LDL-R levels were decreased (p=0.044) only in the SIR 100mg q2w group, but changes in LDL-R levels did not correlate to changes in lipids or lipid particles (p>0.05).

Conclusion: SIR treatment was associated with increased plasma lipid levels compared to placebo and ADA. However, atherogenic indices, which are considered more reliable lipid markers in RA (Mediators Inflamm 2012. 2012: 785946), remained unchanged or changed minimally with SIR. Changes in LDL and HDL levels with SIR were mainly due to a shift towards a more anti-atherogenic lipid profile. Despite the small sample size, modulation of LDL-R levels did not appear to be involved in the observed lipid changes.

Table 1. Week 24 changes from baseline in lipids, lipid particles, and LDL-Receptor in SIRROUND-H study.

<table>
<thead>
<tr>
<th>Lipid biomarker</th>
<th>ADA 40 q2w</th>
<th>SIR 50 q2w</th>
<th>SIR 100 q2w</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apolipoprotein A1 (g/l)</td>
<td>0.00 (0.1, 0.1)</td>
<td>0.00 (0.1, 0.1)</td>
<td>0.00 (0.1, 0.1)</td>
</tr>
<tr>
<td>Apolipoprotein B (g/l)</td>
<td>0.00 (0.1, 0.1)</td>
<td>0.00 (0.1, 0.1)</td>
<td>0.00 (0.1, 0.1)</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dl)</td>
<td>0.00 (0.1, 0.1)</td>
<td>0.00 (0.1, 0.1)</td>
<td>0.00 (0.1, 0.1)</td>
</tr>
<tr>
<td>HDL Cholesterol (mg/dl)</td>
<td>0.00 (0.1, 0.1)</td>
<td>0.00 (0.1, 0.1)</td>
<td>0.00 (0.1, 0.1)</td>
</tr>
<tr>
<td>LDL Cholesterol (mg/dl)</td>
<td>0.00 (0.1, 0.1)</td>
<td>0.00 (0.1, 0.1)</td>
<td>0.00 (0.1, 0.1)</td>
</tr>
<tr>
<td>VLDL Triglycerides (mg/dl)</td>
<td>0.00 (0.1, 0.1)</td>
<td>0.00 (0.1, 0.1)</td>
<td>0.00 (0.1, 0.1)</td>
</tr>
<tr>
<td>Small HDL Particles (umol/l)</td>
<td>0.00 (0.1, 0.1)</td>
<td>0.00 (0.1, 0.1)</td>
<td>0.00 (0.1, 0.1)</td>
</tr>
<tr>
<td>Large HDL Particles (umol/l)</td>
<td>0.00 (0.1, 0.1)</td>
<td>0.00 (0.1, 0.1)</td>
<td>0.00 (0.1, 0.1)</td>
</tr>
<tr>
<td>Very Small HDL Particles (umol/l)</td>
<td>0.00 (0.1, 0.1)</td>
<td>0.00 (0.1, 0.1)</td>
<td>0.00 (0.1, 0.1)</td>
</tr>
<tr>
<td>Large LDL Particles (umol/l)</td>
<td>0.00 (0.1, 0.1)</td>
<td>0.00 (0.1, 0.1)</td>
<td>0.00 (0.1, 0.1)</td>
</tr>
<tr>
<td>Medium Small LDL Particles (umol/l)</td>
<td>0.00 (0.1, 0.1)</td>
<td>0.00 (0.1, 0.1)</td>
<td>0.00 (0.1, 0.1)</td>
</tr>
<tr>
<td>Small LDL Particles (umol/l)</td>
<td>0.00 (0.1, 0.1)</td>
<td>0.00 (0.1, 0.1)</td>
<td>0.00 (0.1, 0.1)</td>
</tr>
<tr>
<td>LDL Receptor (MFI) % change</td>
<td>0.00 (0.1, 0.1)</td>
<td>0.00 (0.1, 0.1)</td>
<td>0.00 (0.1, 0.1)</td>
</tr>
</tbody>
</table>

*Absolute changes from baseline to week 24, summarized as median (IQR), stratified by treatment group, except when otherwise noted.

Conclusion: SIR treatment was associated with increased plasma lipid levels compared to placebo and ADA. However, atherogenic indices, which are considered more reliable lipid markers in RA (Mediators Inflamm 2012. 2012: 785946), remained unchanged or changed minimally with SIR. Changes in LDL and HDL levels with SIR were mainly due to a shift towards a more anti-atherogenic lipid profile. Despite the small sample size, modulation of LDL-R levels did not appear to be involved in the observed lipid changes.

Disclosure: M. Loza, Johnson & Johnson, 1,Johnson & Johnson, 1; A. Bili, Johnson & Johnson, 1,Johnson & Johnson, 3; S. Daga, GlaxoSmithKline, 3,GlaxoSmithKline, 1; K. Brown, GlaxoSmithKline, 3,GlaxoSmithKline, 1; J. Gilbride, Sum of Squares Ltd., 3,GlaxoSmithKline, 9; B. Dasgupta, Johnson & Johnson, 3; B. Hsu, Johnson & Johnson, 1,Johnson & Johnson, 3; I. B. McInnes, Janssen, Novartis, UCB, Pfizer, Abbvie, Lilly, and BMS, 9, Roche, UCB, BMS, 2.
Abstract Number: 549

Increases in Lipid Levels Following Sirukumab Treatment Are Associated with Suppression of Inflammation in Rheumatoid Arthritis: Results from Two Phase 3 Trials

Bidisha Dasgupta¹, Matthew Loza¹, Androniki Bili¹, Shruti Daga², Kurt Brown³, Jennifer Gilbride⁴, Benjamin Hsu¹ and Iain B. McInnes⁵, ¹Janssen Research & Development, LLC, Spring House, PA, ²GlaxoSmithKline, Uxbridge, United Kingdom, ³GlaxoSmithKline, Collegeville, PA, ⁴Sum of Squares Ltd, Hertfordshire, United Kingdom, ⁵University of Glasgow, Glasgow, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Understanding interactions of inflammatory cytokines and lipid metabolism in RA is of considerable interest. Blocking IL-6 receptor elevates lipid levels in RA while lowering inflammatory disease activity¹. Sirukumab (SIR), a human monoclonal antibody that selectively binds to the IL-6 cytokine with high affinity, demonstrated efficacy in RA in the phase 3 SIRROUND studies. This study evaluated the relationships between lipid levels and the suppression of inflammation and disease activity by SIR compared to adalimumab (ADA) in patients with moderate to severe RA.

Methods: Plasma from the SIRROUND-H (monotherapy) study was evaluated: 99 patients in SIR 50mg q4w group, 95 patients in SIR 100mg q2w group, and 140 patients in ADA 40mg q2w group (subcutaneous). Fasting HDL, LDL, IDL, VLDL levels and concentrations of specific particles (large, medium, small, and, for LDL, very small) plus triglycerides were measured using NMR. Apolipoproteins (Apo) A1 and B, total cholesterol, and cholesterol/HDL ratio were measured at Covance, LLC. CRP and SAA were measured using ELISA. Disease activity was measured using CDAI and DAS(CRP). Analyses were performed at baseline (BL), Wk 4, Wk 8 and Wk 24 timepoints. We compared changes from BL using non-parametric Wilcoxon signed-rank and Mann-Whitney tests (comparisons between treatment groups).

Results: SIR treatment significantly increased cholesterol, triglycerides, ApoA1, ApoB, HDL, IDL, LDL, and VLDL levels (p<0.0001 both SIR groups Wk 24 vs BL) while minimal changes were observed with ADA treatment. Increases in lipid biomarkers by SIR were observed by Wk 4 and sustained through Wk 24. Total cholesterol, LDL and large LDL particles were inversely correlated with CRP, and large and medium HDL and medium and small VLDL particles were inversely correlated with both CRP and SAA levels at BL (p<0.0001, -0.42<r<-0.30). Post-treatment increases in lipids were associated with reduced inflammation with SIR treatment: increases in HDL correlated with decreased SAA while increased ApoA1, cholesterol, LDL, and large LDL particles correlated with strong suppression of CRP and SAA at Wk 4 (p<0.0001 and -0.43<r<-0.31). In contrast, these trends were not observed with ADA as lipid levels post treatment remained similar to BL. BL values and changes from BL in lipid parameters did not correlate with disease activity. Results were similar for both doses of SIR. These results were confirmed in the placebo-controlled SIRROUND-D study.

Conclusion: Patients with higher BL inflammation have lower starting lipid levels. IL-6 inhibition by SIR results in significant increases in lipid levels that correlate to suppression of acute phase reactants. These findings were not observed with ADA where lipid levels were generally unchanged. The results suggest that the increase in lipid levels with SIR may be at least in part associated with improvement of underlying inflammation in RA.
Reference:


Disclosure: B. Dasgupta, Johnson & Johnson, 3; M. Loza, Johnson & Johnson, 1, Johnson & Johnson, 3; A. Bili, Johnson & Johnson, 1, Johnson & Johnson, 3; S. Daga, GlaxoSmithKline, 3, GlaxoSmithKline, 1; K. Brown, GlaxoSmithKline, 3, GlaxoSmithKline, 1; J. Gilbride, Sum of Squares Ltd, 3, GlaxoSmithKline, 9; B. Hsu, Johnson & Johnson, 1, Johnson & Johnson, 3; I. B. McInnes, Janssen, Novartis, UCB, Pfizer, Abbvie, Lilly, and BMS, 9, Roche, UCB, BMS, 2.


Abstract Number: 550

Long-Term Safety of Tocilizumab from Large Clinical Trial and Postmarketing Populations

Shalini Mohan¹, Margaret Michalska², Jeffrey Yourish², Jinglan Pei², Sara Gale¹, Christine Birchwood² and Erhan Berber², ¹Genentech, South San Francisco, CA, ²Genentech, Inc., South San Francisco, CA
First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Tocilizumab (TCZ) is a recombinant humanized monoclonal antibody targeted against the interleukin-6 receptor that was approved to treat rheumatoid arthritis (RA) in the EU in 2009 and in the US in 2010, and has now completed long-term extension (LTE) follow-ups in a number of intravenous and subcutaneous RA trials. The objective of this study was to provide an updated report on the incidence of safety events during TCZ treatment in patients with RA using data from multiple completed clinical trials and their LTEs, as well as an update from the global TCZ postmarketing safety database.

Methods: To provide an updated report on the incidence of safety events during TCZ treatment in patients with RA using data from multiple completed clinical trials and their LTEs, as well as an update from the global TCZ postmarketing safety database.

Results: The clinical trial all-exposure population consisted of 7647 TCZ-treated patients with RA (81.6% female; mean [SD] age, 52 [12.6] years), constituting 22,394 PY (mean follow-up: 2.93 years) of exposure. The overall rate (95% CI) of serious adverse events (SAE) in the clinical trial population was 14.16 (13.67-14.66) per 100 PY. Overall incidence rates for individual events for the clinical trial population were reported in the Table and were consistent in each 6-month period over the 5-year duration. The global postmarketing population included 606,937 patients. The overall spontaneous reporting rate (range) of adverse events of special interest in the postmarketing population was 9.37 (7.35-10.56) cases per 100 patients. Reporting rates of individual safety events of interest in the global postmarketing population are shown in the Table and were consistent in each 6-month period over the 7-year duration.

Conclusion: The safety profile of TCZ in the current analysis, which includes information about safety events from 12 clinical trials and their LTEs and across 7 years of real-world postmarketing reports encompassing ~ 600,000 patients, was consistent with previous safety reports. These findings are consistent with the previously reported profile of TCZ and indicate that there is no evidence of increased safety risk with increasing exposure to TCZ.
<table>
<thead>
<tr>
<th>Adverse event of special interest</th>
<th>RA Clinical Trial All-Exposure Population (N = 7,647; 22,394 PY)</th>
<th>Global Postmarketing Safety Database Population* (N = 606,937 Pts)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients With ≥ 1 AE (%)</td>
<td>Incidence Rate (95% CI), Events/100 PY</td>
</tr>
<tr>
<td>Serious infections</td>
<td>730 (9.5)</td>
<td>4.29 (4.02-4.57)</td>
</tr>
<tr>
<td>Malignancies†</td>
<td>242 (3.2)</td>
<td>1.18 (1.05-1.33)</td>
</tr>
<tr>
<td>Injection site reactions</td>
<td>444 (5.8)</td>
<td>6.51 (6.18-6.85)</td>
</tr>
<tr>
<td>Strokes / cerebrovascular disorders</td>
<td>130 (1.7)</td>
<td>0.67 (0.56-0.78)</td>
</tr>
<tr>
<td>Serious bleeding events</td>
<td>89 (1.2)</td>
<td>0.43 (0.35-0.52)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>72 (0.9)</td>
<td>0.33 (0.26-0.42)</td>
</tr>
<tr>
<td>Gastrointestinal perforations</td>
<td>39‡ (0.5)</td>
<td>0.20‡ (0.15-0.27)</td>
</tr>
<tr>
<td>Serious hypersensitivity reactions§</td>
<td>56 (0.7)</td>
<td>0.26 (0.20-0.33)</td>
</tr>
<tr>
<td>Anaphylaxis†</td>
<td>21 (0.3)</td>
<td>0.09 (0.06-0.14)</td>
</tr>
<tr>
<td>Serious hepatic events</td>
<td>9 (0.1)</td>
<td>0.04 (0.02-0.08)</td>
</tr>
<tr>
<td>Demyelination</td>
<td>8 (0.1)</td>
<td>0.04 (0.02-0.07)</td>
</tr>
</tbody>
</table>

AE, adverse event; N/A, not available; PY, patient year; RA, rheumatoid arthritis; TCZ, tocilizumab.

* Data are for multiple indications and from several sources (spontaneous reports, non-interventional programs, literature cases) reported following market authorization.

† Events of gastrointestinal perforations (Clinical Trial data set) and malignancies were medically confirmed.

‡ Includes both serious and non-serious cases.
Serious hypersensitivity was defined as a serious adverse event occurring during or within 24 hours of the injection or infusion, excluding injection site reactions, and not judged ‘unrelated’ to study treatment by the investigator.

Events of anaphylactic reactions meeting Sampson criteria (MedDRA SMQ (algorithmic) Anaphylactic reaction).


Abstract Number: 551

Comparison of Drug Tolerability and Discontinuation Reasons between 7 Biologics in Patients with Rheumatoid Arthritis -Results from Kansai Consortium for Well-Being of Rheumatic Disease Patients (ANSWER cohort)-

Kosuke Ebina¹, Makoto Hirao², Motomo Hashimoto³, Moritoshi Furu⁴, Wataru Yamamoto⁵, Ryota Hara⁶, Takanori Fujimura⁶, Toru Hirano⁷, Shuzo Yoshida⁸, Koji Nagai⁸, Hideki Amuro⁹, Yonsu Son⁹, Akira Onishi¹⁰, Kengo Akashi¹¹, Masaki Katayama¹², Keichi Yamamoto¹³ and Hideki Yoshikawa¹⁴, ¹Orthopaedic Surgery, Osaka University Graduate School of Medicine, Osaka, Japan, ²Orthopaedic Surgery, Osaka University, Graduate School of Medicine, Suita, Japan, ³Department of Advanced Medicine for Rheumatic Diseases, Graduate School of Medicine, Kyoto University, Kyoto, Japan, ⁴Graduate School of Medicine, Kyoto University, Kyoto, Japan, ⁵Kurashiki Sweet Hospital, Okayama, Japan, ⁶The Center for Rheumatic Diseases, Nara Medical University, Kashihara, Japan, ⁷Respiratory Medicine, Allergy and Rheumatic Diseases, Osaka University Graduate School of Medicine, Suita, Japan, ⁸Osaka Medical College, Osaka, Japan, ⁹Kansai Medical University, Osaka, Japan, ¹⁰Kobe University Graduate School of Medicine, Kobe, Japan, ¹¹Department of Rheumatology and Clinical Immnology, Kobe University Graduate School of Medicine, Kobe, Japan, ¹²Osaka Red Cross Hospital, Osaka, Japan, ¹³Osaka City University, Osaka, Japan, ¹⁴Department of Orthopedics, Osaka University Graduate School of Medicine, Suita Osaka, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster I: Comorbidities and Adverse Events; Efficacy and Safety of Small Molecules
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: More than 4 years have passed since 7 biologics became available for patients with rheumatoid arthritis (RA) in Japan, still lack reliable evidence in their differences of tolerability and discontinuation reasons.

Methods: A total of 1,037 biologics treatment courses of RA from 2009 to 2016 [female 81.8%, baseline age 59.6 y, disease duration 7.8y, bio continued duration 17.1 months, RF positivity 81.5%, ACPA positivity 86.7%, DAS28-ESR 4.4, CDAI 16.8, HAQ 1.1, Bio naïve 57.1% and switched 42.9%, methotrexate (MTX) 5.9 mg/week (limited to 16mg/week in Japan) (68.6%), prednisolone (PSL) 2.5 mg/day (43.5%), abatacept (ABT) 21.3%, tocilizumab (TCZ) 20.7%, golimumab
(GLM) 16.9%, etanercept (ETN) 13.6%, adalimumab (ADA) 11.1%, infliximab (IFX) 8.5%, certolizumab pegol (CZP) 7.9%] were included in this 7-center, retrospective study. The drug tolerability and discontinuation reasons at 36 months were estimated using Kaplan-Meier method, and adjusted by potent confounders [Sex / Age / Bio started date / Disease duration / ACPA positivity / RF positivity / bio naive or switched / combined csDMARDs (MTX, tacrolimus, bucillamine, salazosulfapyridine, iguratimod) and PSL / baseline DAS28-ESR / HAQ] which may affect biologics retention rates using a Cox proportional hazards model.

Results: There were no significant differences in the baseline disease activity (DAS28-ESR and CDAI). The major causes of 7 biologics treatment discontinuation were as follows. Drug inefficacy (47.7%), other nontoxic reasons (12.3%), remission (8.6%), infection (7.5%), patients’ preference (7.5%), other adverse events such as malignant, cardiovascular, pulmonary, renal, hematologic complications (6.2%), skin or systemic reaction (5.3%), and changing hospital (5.1%). Adjusted discontinuation reasons and ratio at 36 months in each drug were as follows. Drug inefficacy (TCZ 16.1%, ABT 23.7%, ETN 28.4%, CZP 32.9%, IFX 33.3%, ADA 42.3%, and GLM 46.1%; P=0.14), remission (IFX 11.4%, ADA 2.6%, ETN 1.4%, ABT 0.5%, TCZ 0.5%, GLM 0.0%, and CZP 0.0%; P<0.001), infection (ABT 1.4%, TCZ 1.5%, GLM 2.0%, ETN 2.3%, ADA 2.5%, IFX 4.0%, and CZP 5.5%; P=0.77), other adverse events (ABT 1.2%, ETN 2.0%, CZP 4.9%, GLM 5.6%, ADA 7.2%, TCZ 8.5%, and IFX 11.7%; P=0.03), and skin or systemic reaction (ABT 0.0%, TCZ 0.5%, GLM 1.1%, ADA 1.7%, ETN 2.1%, CZP 3.7%, and IFX 4.5%; P=0.02), respectively. Adjusted total retention rates at 36 months were as follows. TCZ 58.9%, ABT 55.1%, CZP 51.4%, ETN 50.2%, GLM 37.6%, ADA 32.7%, and IFX 21.7% (P=0.006).

Conclusion: When adjusted by potent confounders, TCZ showed lowest inefficacy and highest retention rate, ABT showed lowest infection, skin or systemic reaction, or other toxic adverse events rate, and IFX showed highest remission discontinuation rate at 36 months compared to other biologics in RA.

Disclosure: K. Ebina, Chugai Pharmaceutical, Eisai, Ono Pharmaceutical, Mitsubishi Tanabe Pharma, UCB Japan, 8; M. Hirao, None; M. Hashimoto, Astellas Pharma, 2, Tanabe-Mitsubishi, Chugai, Ayumi, UCB, Bristol-Meyers, 5; M. Furu, None; W. Yamamoto, None; R. Hara, None; T. Fujimura, None; T. Hirano, Mitsubishi Tanabe Pharma Corporation Chugai Pharmaceutical Co., Ltd. AbbVie, Ono Pharmaceutical, Astellas Pharma Inc., 5; S. Yoshida, None; K. Nagai, None; H. Amuro, None; Y. Son, None; A. Onishi, None; K. Akashi, None; M. Katayama, None; K. Yamamoto, None; H. Yoshikawa, Chugai Pharmaceutical, Eisai, Ono Pharmaceutical, Mitsubishi Tanabe Pharma, Phizer, Astellas Pharma, 2.

Mast Cells Are Involved in the Pathogenesis of Sjögren Syndrome By Inducing Tissue Fibrosis

Shinjiro Kaieda¹, Kyoko Fujimoto², Masaki Okamoto³, Masaki Tominaga², Tomoaki Hoshino⁴ and Hiroaki Ida⁵, ¹Department of Medicine, ²Division of Respirology, Neurology and Rheumatology, Kurume University School of Medicine, kurume, Japan, ³Kurume University School of Medicine, Kurume, Japan, ⁴Department of Medicine, Division of Respirology, Neurology and Rheumatology, Kurume University School of Medicine, Kurume, Japan, ⁵Respirology, Neurology and Rheumatology, Kurume University School of Medicine, Kurume, Japan. First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Sjögren's Syndrome Poster I: Translational Research
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM
Background/Purpose:
Mast cells have been implicated in many immune-inflammatory disorders. They mediate a variety of inflammatory and fibrotic conditions, but their role in sialadenitis and interstitial lung disease in patients with primary Sjögren syndrome is unclear. We examined whether mast cells play a critical role in the pathogenesis of Sjögren syndrome.

Methods:
Labial salivary glands and lung tissue were examined using histological and immunohistochemistry methods. Labial salivary gland samples were collected from 15 individuals with primary Sjögren syndrome and 7 with sicca syndrome (controls). Saliva production was evaluated by Saxon test.

Affected lung tissue from four patients with Sjögren syndrome-associated interstitial lung disease was obtained via biopsy. As control samples, we used 10 noncancerous lung sections from patients who had undergone surgery for lung cancer. We used immunohistochemistry to identify and quantify tryptase-positive mast cells and vimentin-positive fibroblasts. Fibrous tissue was identified by using EVG stain. Human mast cell line 1 (HMC-1) cells were co-cultured with pulmonary fibroblasts for 7 days using a transwell system, and IL-6, TGF-β, and VEGF expression in these cells was evaluated by RT-qPCR.

Results:
We found that the number of mast cells in labial salivary glands and lung tissues of patients with Sjögren syndrome was significantly increased compared to that in control subjects (p<0.001 and p<0.01, respectively). There was a significant negative correlation between the Saxon test results and the number of mast cells (r=0.81, P<0.01), suggesting the involvement of mast cells in decreased salivary secretion. The mast cells were usually present in close proximity to EVG-stained fibrous tissue in the labial salivary glands and lung tissues. Immunohistochemical analysis revealed that the mast cells were proximal to vimentin-positive fibroblasts. We hypothesized that mast cells were involved in the development of tissue fibrosis via modulation of fibroblast immune function, and conducted in vitro co-culture of HMC-1 cells and pulmonary fibroblasts. In these co-cultures, IL-6, TGF-β, and VEGF expression was significantly increased compared to in mast cell or fibroblast monoculture. These observations suggest that an amplification loop is generated between mast cells and fibroblasts, enhancing production of IL-6, TGF-β and VEGF.

Conclusion:
These results suggest a novel role for mast cells in the development of sialadenitis and interstitial lung disease in patients with Sjögren syndrome via induction of tissue fibrosis. An amplification loop between mast cells and fibroblasts enhances production of the pro-fibrotic factor, TGF-β, and angiogenic factor, VEGF, which may contribute to tissue fibrosis in sialadenitis and interstitial lung disease.

Disclosure: S. Kaieda, None; K. Fujimoto, None; M. Okamoto, None; M. Tominaga, None; T. Hoshino, None; H. Ida, None.


Abstract Number: 553

Decreased Circulating CXCR3+CCR9+ Th Cells Coincides with Elevated Levels of Their Ligands CXCL10 and CCL25 in the Salivary Gland of Sjögren’s Syndrome Patients Which Synergistically Facilitate Th Cell Migration

Sofie L.M. Blokland1,2, Maarten R. Hillen3,4, Stephan Meller5, Bernhard Homey5, Glennda Smithson6, Aike A. Kruize2, Timothy R.D.J. Radstake2,7 and Joel A.G. van Roon2,3, 1Rheumatology & Clinical Immunology/ Laboratory of Translational Immunology, University Medical Center Utrecht, Utrecht, Netherlands, 2Department of Rheumatology &
Primary Sjögren’s syndrome (pSS) is characterized by dryness and lymphocytic infiltration in the salivary glands. CXCR3+ T cells and ligands CXCL9/10/11 are known to be abundantly present in the salivary glands of pSS patients. In addition, both CXCR5+ T follicular helper (Tfh) cells and CCR9+ Tfh-like cells and their specific chemotactic ligands CXCL13 and CCL25 are present at increased levels in the salivary glands of pSS patients. Recently, we and others found that CCR9+ Th cells are elevated in pSS peripheral blood and co-express CXCR3 and other chemokine receptors, known to be differentially expressed by Th cell subsets. CCR9+ Th cells play an important role in mucosal immunity and have been shown to produce high levels of IFN-γ, like CXCR3+ Th1 cells. Since CXCL9/10/11 and CXCR3 are abundantly expressed in the salivary glands of pSS and CCR9+ Th cells have Th1 characteristics, the potential role in lymphocytic infiltration of the combination of the CXCL10-CXCR3 and CCL25-CCR9 interactions was studied in comparison with other chemokine receptors.

Methods:

CXCL10, CCL25, CXCL13, CCL17 and CCL20 mRNA and protein expression in the salivary gland of pSS and non-Sjögren’s sicca (nSS) patients was assessed (mRNA: n=9 vs n=9 and protein: n=24 vs n=33, respectively). Frequencies of CXCR3, CCR9, CXCR5, CCR4 and CCR6 expressing Th cells in blood of pSS patients and healthy controls were assessed by flow cytometry (n=11 vs n=11). Chemotaxis assays (n=6 HC, n=10 pSS) were performed to study migration induced by CXCL10 and CCL25.

Results:

CCL25, CXCL10 and CXCL13 expression were increased in pSS compared to nSS patients, both at mRNA and protein level in salivary gland supernatants (all p<0.05). CCL17 and CCL20 expression were low and detectable in only few patients. Protein levels of CXCL10 and CXCL13 correlated with lymphocytic focus scores and all 3 chemokines correlated with serum IgG levels in pSS (all p<0.05). CCL25 protein levels correlated with CXCL10 (p=0.01) but not with CXCL13. A relative decrease of CXCR3+ cells was found in the CCR9+ Th subset in the peripheral blood of pSS patients (p=0.04), which was most pronounced in the effector and effector memory subsets (64% vs 26%, p=0.03 and 51% vs 27% p=0.01, respectively). CCR4 or CCR6-expressing CCR9+ Th cells and CXCR3 or CCR6-expressing CXCR5+ Th cells were not decreased. To test the hypothesis that CXCR3 ligands and CCL25 facilitate migration, co-migration of lymphocytes in response to CXCL10 and CCL25 was studied. CXCL10 and CCL25 induced synergistic Th cell chemotaxis in vitro (both p<0.01 as compared to CCL25 or CXCL10 only).

Conclusion:

The decreased frequency of CXCR3+CCR9+ Th cells in blood of pSS patients may be facilitated by a concerted action of overexpressed ligands at the site of inflammation. Elevated expression of ligands CXCL10 and CCL25 in the salivary gland and the synergistic effect on chemotaxis in vitro indicate a potential role for these chemokines in formation of lymphocytic infiltrates in exocrine glands of pSS patients.

Disclosure: S. L. M. Blokland, None; M. R. Hillen, None; S. Meller, None; B. Homey, None; G. Smithson, Takeda, 3; A. A. Kruize, None; T. R. D. J. Radstake, Takeda, 5; J. A. G. van Roon, None.
Abstract Number: 554

Prognostic Significance of Double Positive Anti Ro/SS-a and La/SS-B Antibodies in Patients with Primary Sjogren’s Syndrome: Prospective Salivary Gland Ultrasound Study

Sang Heon Lee1, Kyung-Ann Lee2 and Hae-Rim Kim3, 1Division of Rheumatology, Department of Internal Medicine, Konkuk University School of Medicine, Seoul, Korea, Republic of (South), 2Department of Nuclear medicine, Konkuk University Medical center, seoul, Korea, Republic of (South), 3Division of Rheumatology, Department of Internal Medicine, Konkuk University Medical Center, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Sjögren's Syndrome Poster I: Translational Research
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The aim of the study was to assess the diagnostic value of salivary gland ultrasonography (SGUS) as a single test for the detection of primary sjogren’s syndrome (pSS) and to examine the prognostic factors for severe structural changes of major salivary glands based on SGUS scoring system.

Methods: Patients with pSS (n = 80) and idiopathic sicca syndrome (n = 42) were evaluated using a SGUS scoring system (0-48 scale) consisted of five SGUS parameters: parenchymal echogenicity, parenchymal homogeneity, number of hypoechoic areas, hyperechogenic reflections, and clearness of salivary gland posterior borders of both parotid and submandibular glands. The volumes and parenchymal power Doppler signal were also assessed. A multivariate regression was performed to determine factors associated with higher SCUS score.

Results: Patients with pSS revealed a significant higher SGUS score in comparison with controls (median (IQR): 25.0 (13.75) vs 6.5 (3.5), P < 0.001). The SGUS cut-off ≥ 12 showed a sensitivity of 82.5%, a specificity of 92.9%, a positive predictive value of 95.7%, and a negative predictive value of 73.6% for pSS diagnosis. There was no significant difference in the volumes between pSS and controls. Double positivity of anti Ro/SS-A and La/SS-B was independently associated with higher SGUS score (β = 5.45, p = 0.009). The SGUS score was also associated with unstimulated salivary flow test (USFR), rheumatoid factor, and IgG.

Conclusion: A new imaging modality, SGUS could be used as a highly specific diagnostic tool in pSS. Our study demonstrates double positivity of anti Ro/SS-A and La/SS-B could independently predict the severe structural damage of major salivary glands in pSS.

Disclosure: S. H. Lee, None; K. A. Lee, None; H. R. Kim, None.

Abstract Number: 555
The Corrected QT(QTc) Interval Is Associated with Myocardial Fibrosis in Primary Sjögren Syndrome, Assessed By a Cardiac Magnetic Resonance Approach: A Prospective Pilot Study at a Single Center

Atsuma Nishiwaki1, Hitomi Kobayashi1, Isamu Yokoe2, Yosuke Nagasawa3, Kaita Sugiyama3, Natsumi Ikumi4, Takamasa Nozaki3, Noboru Kitamura5 and Masami Takei5, 1Hematology and Rheumatology, Nihon University School of Medicine, Tokyo, Japan, 2Rheumatology, Kyoudo Hospital, Sasaki Institute, Tokyo, Japan, 3Nihon University School of Medicine, Tokyo, Japan, 4St. Vincent's University Hospital, Department of Rheumatology, Dublin, Ireland, 5Division of Hematology and Rheumatology, Nihon University School of Medicine, Tokyo, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Sjögren's Syndrome Poster I: Translational Research
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Congenital heart block in the fetus and neonate, which can cause acquired QT prolongation, may be associated with maternal anti-SS-A/anti-SS-B autoantibodies. However, there are increasing reports that primary Sjögren syndrome (pSS) is associated with an increased risk of cardiovascular disease and that disease-related clinical and immunological markers may promote cardiovascular disease. We hypothesized that myocardial abnormalities were associated with the corrected QT (QTc) interval in pSS. We used cardiac magnetic resonance imaging (CMR) to assess cardiac involvement and determine its association with the QTc interval in pSS patients without cardiac symptoms.

Methods:
Consecutive pSS patients, classified according to the 2012 ACR criteria with no history or clinical findings of hypertension, cardiovascular disease, diabetes, or dyslipidemia underwent contrast-enhanced CMR. Late gadolinium enhancement (LGE) was used to assess myocardial fibrosis. Myocardial inflammation was assessed using a black-blood T2-weighted image (T2-WI). The Sjögren syndrome disease activity index (ESSDAI) was determined. Eighty-six percent patients had documentation of a minor salivary gland biopsy. Salivary gland biopsy data were classified by focus score (FS). A QTc interval of 440 ms was considered as prolonged.

Results:
Fifty-five pSS patients were enrolled (mean age: 53.2±9.6 years). The mean ESSDAI was 2.5±2.7. Myocardial edema was seen in 3 patients (5%) on T2-WI. LGE was found in 9 (16%), 2 of whom demonstrated edema on T2-WI. Raynaud’s phenomenon was significantly associated with LGE-positive patients (p=0.0064). The greatest relative difference between LGE-positive and -negative patients was observed in FS ≥4, with an adjusted odds ratio of 4.0, although the FS was not associated with the QTc interval.

PSS patients had a longer mean QTc interval than did controls (432.5±24.9 vs. 420.5±14.4; p=0.003). Furthermore, there was significant difference in the QTc interval between the LGE-positive and LGE-negative group (447.7±15.7 vs 429.5±25.4; p=0.012). Other pSS characteristics, such as disease duration, anti-SS-A/anti-SS-B autoantibodies, ESSDAI, and cardiovascular risk factors, were not significantly associated with myocardial abnormalities and QTc interval.

A receiver operating characteristic analysis showed that the QTc interval reliably detected myocardial abnormalities (area under the curve, 0.77).

Conclusion:
Subclinical myocardial involvement, as detected by CMR, was frequent in pSS patients without cardiac symptoms. Abnormal CMR findings were associated with a QTc interval. To our knowledge, this was the first study to show that...
myocardial abnormalities in pSS were associated with the QTc interval.

Disclosure: A. Nishiwaki, None; H. Kobayashi, None; I. Yokoe, None; Y. Nagasawa, None; K. Sugiyama, None; N. Ikumi, None; T. Nozaki, None; N. Kitamura, None; M. Takei, None.


Abstract Number: 556

Identification and Validation of S100 Salivary Proteins As Putative Biomarkers for Different Subsets of Primary Sjögren’s Syndrome Patients

Chiara Baldini1, Francesco Ferro2, Nadia Ucciferri3, Enza Polizzi2, Silvia Rocchiccioli3, Marta Mosca2 and Antonella Cechettini3.1 Internal Medicine, Rheumatology Unit, University of Pisa, Pisa, Italy, 2Rheumatology Unit, University of Pisa, Pisa, Italy, 3IFC, CNR, Pisa, Italy
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Sjögren’s Syndrome Poster I: Translational Research
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: S100 A proteins are multifunctional proteins expressed predominantly by myeloid cells, with a regulatory role in a variety of cellular processes including inflammation. Recently, serum and salivary S100A proteins have been described as increased in patients with primary Sjögren’s syndrome (pSS) with respect to healthy volunteers. In this study, we aimed at investigating whether salivary expression of S100 proteins may reflect different pSS disease phenotypes stratified on the basis of the complexity of minor salivary gland biopsies (MSGB) and on the impairment of unstimulated salivary flow rate (USFR).

Methods: Patients with pSS (AECG 2002) were included in this study at the diagnosis of the disease. Demographic and clinical data were collected prospectively as well as their USFR and MSGBs. A focus score (FS) ≥3 was considered as high and an USFR<2.5 ml/15’ was considered as low. Saliva samples were collected on ice, centrifuged and stored at -80°C. After removal of Albumin and IgG, a nano-HPLC system coupled with a Triple TOFTM 5600 mass spectrometer was used for the analysis of saliva proteomes of pSS patients. For the validation phase of the study, S100A7/psoriasin levels were determined by CircuLex S100A7/psoriasin ELISA kit (MBL International Corporation), according to manufacturer’s instructions.

Results: Fifteen pSS women were enrolled for the proteomic analysis: 5 with high FS and normal USFR, 5 with high FS and reduced USFR and 5 with low FS and reduced USFR. Among differentially expressed proteins, we found that S100 A2, 7, 8, 9, 11 and 12 were significantly over-expressed in pSS with respect to controls. In details, S100 A7 levels were significantly increased in patients with higher FS and lower USFR with respect to the other two groups of patients; S100 A8 and A9 were increased in patients with higher FS and lower USFR only with respect to patients with high FS and normal USFR and S100 A 12 in patients with low FS and reduced USFR with respect to patients with high FS and normal USFR. We validated salivary expression of S100 A7 in 19 additional pSS patients and 8 controls confirming that S100A7 expression was significantly higher in patients with high FS and reduced USFR (305.6± 174 ng/ml vs 11±14 ng/ml vs 75.7±21.6 ng/ml, p=0.000).

Conclusion: Salivary S100 A proteins appeared as interesting novel potential biomarkers for the non-invasive stratification of homogenous subgroups of patients with pSS. ELISA results excellently mirrored proteomics and open the possibility to be clinically translated into routine diagnostic.
Enhanced Expression of NLRP3 Inflammasome-Related Inflammation in Peripheral Blood Mononuclear Cells in Sjögren’s Syndrome

Seong-Kyu Kim¹, Jung-Yoon Choe², Sung-Hoon Park³ and Hwajeong Lee², ¹Rheumatology, Catholic University of Daegu School of Medicine, Daegu, Korea, Republic of (South), ²Catholic University of Daegu School of Medicine, Daegu, Korea, Republic of (South), ³Internal Medicine, Catholic University of Daegu School of Medicine, Daegu, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Sjögren's Syndrome Poster I: Translational Research
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Sjögren's syndrome is a systemic autoimmune disease characterized by lymphocyte infiltration and subsequent dysfunction of exocrine glands, finally leading to dryness in the exocrine glands and dysfunction in the affected organs and tissues. The precise mechanism of Sjögren's syndrome remains unclear. Recently, novel insight into the NACHT, LRR and PYD domains-containing protein 3 (NLRP3) inflammasome that is responsible for innate immunity, has implicated it as a crucial regulator that plays a role in the pathogenesis of Sjögren's syndrome. The aim of this study was to identify the association of NLRP3 inflammasome-induced inflammation with disease activity and damage in Sjögren's syndrome.

Methods: A total of 33 female patients with Sjögren's syndrome and 34 sex- and age-matched, healthy controls were consecutively enrolled. The mRNA expression levels of NLRP3, ASC, caspase-1, interleukin-1β (IL-1β), and IL-18 in peripheral blood mononuclear cells (PBMCs) were measured, as well as serum IL-1β and IL-18 protein expression levels. The EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) and Sjögren's Syndrome Disease Damage Index (SSDDI) were also evaluated.

Results: Patients with Sjögren's syndrome group showed higher expression of mRNA IL-1β and IL-1β at the protein level than controls (p < 0.001 of both). The mRNA levels of caspase-1 and ASC were significantly increased in patients with Sjögren's syndrome compared to controls (p = 0.001 and p = 0.002, respectively). Based on the SSDDI scores, patients with damage (SSDDI ≥ 1) had higher IL-1β mRNA expression compared to patients without damage (SSDDI = 0) (p = 0.034). SSDDI scores were closely related with IL-18 protein levels (r = 0.357, p = 0.041). The levels of IL-1β mRNA and IL-1β protein were correlated with the mRNA level of NLRP3 (r = 0.597, p < 0.001 and r = 0.502, p = 0.003, respectively). IL-1β mRNA expression was responsible for the presence of damage for Sjögren's syndrome (p = 0.034).

Conclusion: This study confirmed that NLRP3 inflammasome-mediated inflammation might be implicated in the pathogenesis of Sjögren's syndrome.

Disclosure: S. K. Kim, None; J. Y. Choe, None; S. H. Park, None; H. Lee, None.
Salivary Syndecan-1 Levels Are Associated with Salivary Gland Dysfunction and Immune Dysregulation in Patients with Sjögren’s Syndrome

Eon Jeong Nam1, Jong Wan Kang1, Jung Su Eun1, Na Ri Kim1, Sang Jin Lee1, Keum Hee Sa2, Gi Bum Bae3 and Young Mo Kang4, 1Division of Rheumatology, Department of Internal Medicine, Kyungpook National University School of Medicine, Daegu, Korea, Republic of (South), 2Division of Rheumatology, Department of Internal Medicine, Kyungpook National University, Daegu, Korea, Republic of (South), 3Division of Rheumatology, Department of Internal Medicine, Daegu, Korea, Republic of (South), 4Division of Rheumatology, Department of Internal Medicine, Kyungpook National University School of Medicine, Daegu, Republic of Korea, Daegu, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Sjögren’s Syndrome Poster I: Translational Research
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Sjögren’s syndrome (SJS) is a chronic autoimmune disorder with lymphocytic infiltration of exocrine and non-exocrine epithelia, in which epithelial cells play a critical role in the initiation and amplification of inflammatory processes. Syndecan-1 (sdc-1), a transmembrane heparan sulfate proteoglycan, is predominantly expressed on epithelial cells and functions primarily as coreceptors through the binding of heparan sulfate chain to a wide range of ligands, such as extracellular matrix components, cytokines, and chemokines. Although ectodomain of sdc-1 is constitutively shed, ectodomain shedding is accelerated in response to diverse pathophysiological conditions and may be related with pathogenesis of SJS. In this study, we investigated the association of sdc-1 levels in plasma and saliva with functional parameters of salivary glands in SJS patients.

Methods: Unstimulated and stimulated salivary flow rates and sdc-1 levels of saliva and plasma were measured in 37 SJS patients and 34 normal controls (NC). We assessed the disease activity indexes, including ESSDAI and ESSPRI, and performed salivary gland scan and serologic markers in SJS patients.

Results: ESSDAI and ESSPRI scores of SJS patients were 3.78 ± 3.33 and 3.95 ± 1.50, respectively. Salivary flow rates in SJS patients and NC were 0.02 ± 0.04 and 0.31 ± 0.20, respectively (p<0.001). While unstimulated salivary flow rates were correlated with ejection fraction (EF) of submandibular glands (r=0.423, p=0.025) in salivary gland scan, stimulated salivary flow rates were associated with EF of parotid glands (r=0.531, p=0.04). Salivary flow rates were inversely associated with ESSPRI scores (r=-0.390, p=0.036) and dryness domain of ESSPRI (r=-0.622 p<0.001) in SJS patients. Plasma and salivary sdc-1 levels were significantly higher in SJS patients than NC (both p<0.001), and inversely correlated with salivary flow rate (plasma, r=-0.515, p=0.001; saliva, r=-0.472, p=0.003). Plasma sdc-1 levels were positively correlated with salivary sdc-1 levels in SJS patients (r=0.632, p<0.001) but not in NC (r=0.217, p=NS). Plasma and salivary sdc-1 levels were related with submandibular gland dysfunction in salivary gland scan. While plasma sdc-1 levels showed an inverse correlation with EF (r=-0.426, p=0.038), salivary sdc-1 levels were inversely correlated with both uptake ratio at 20 minutes (r=-0.526, p=0.017) and EF (r=-0.446, p=0.019). Furthermore, salivary sdc-1 levels were correlated with serum levels of anti-Ro (r=0.397, p=0.030) and -La antibodies (r=0.441, p=0.015) and IgG, although serum level of IgG showed a marginal statistical significance (r=0.331, p=0.074).

Conclusion: Plasma and salivary sdc-1 levels are increased in SJS patients, which is associated with salivary gland dysfunction. In addition, salivary sdc-1 levels may be related with immune dysregulation in pathogenesis of SJS.

Disclosure: E. J. Nam, None; J. W. Kang, None; J. S. Eun, None; N. R. Kim, None; S. J. Lee, None; K. H. Sa, None; G. B. Bae, None; Y. M. Kang, None.

Performance of Multiple Platforms for Autoantibody Testing in Sjögren’s Syndrome

Astrid Rasmussen1, Kiely Grundahl2, Lida Radfar3, C. Erick Kaufman4, David M. Lewis5, Barbara M. Segal6, Nelson L. Rhodus7, Harini Bagavant1, Umesh Deshmukh8, Christopher J Lessard8, R. Hal Scofield1 and Kathy L. Sivils1, 1Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 2Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation, Oklahoma CIty, OK, 3Department of Oral Diagnosis and Radiology, University of Oklahoma College of Dentistry, Oklahoma City, OK, 4College of Medicine, University of Oklahoma Health Sciences Center, Oklahoma City, OK, 5Department of Oral Pathology, University of Oklahoma College of Dentistry, Oklahoma City, OK, 6Rheumatology, Hennepin County Medical Center, Minneapolis, MN, 7Department of Diagnostic and Biological Sciences, University of Minnesota School of Dentistry, Minneapolis, MN, 8Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation, Oklahoma City, OK

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Sjögren's Syndrome Poster I: Translational Research
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The research classification and clinical diagnosis of Sjögren’s syndrome (SS) relies heavily on the detection of autoantibodies against Ro/SSA and La/SSB, particularly in the absence of salivary gland biopsy or when the histopathology of the minor salivary gland is normal. However, there is little consensus on the method or combination of methods that yield the best balance of sensitivity and specificity for SS.

Methods: We analyzed the results of multiple serology assessment platforms in 1530 subjects with SS or non-SS sicca evaluated at the OMRF Sjögren’s Research clinic. Our standard tests include ANA by indirect immunofluorescence on HEp-2 cells, Chrithidia luciliae for dsDNA, and double immunodiffusion (DID) for ENA. Anti-Ro/SSA and anti-La/SSB were determined by DID, a line assay (InnoLia ANA Update) and a bead-based assay (Bio-Rad BioPlex 2200) for anti-Ro52, Ro60 and La; and ELISA (Immunovision) for anti-Ro60. A subset of cases were also evaluated for anti-Ro52/TRIM21 by immunoprecipitation with human antigen and anti-La(+)Ro(-) cases were confirmed by DID on HEp-2000 cells and RT-PCR.

Results: We observed significant differences in the performance of the tests in the same individuals. The concordance rate (kappa statistic) is detailed in Fig. 1. The most significant discrepancies were between DID and Bioplex and InnoLia; in almost all discordant cases, DID results were negative while they were positive for at least one of the other tests (anti-Ro 353/1318, 26.8%; anti-La 145/1253, 11.5%). InnoLia and Bioplex were highly concordant or Ro52 and are likely interchangeable; anti-Ro60 also showed high concordance across the three platforms tested but the minor discrepancies would result in the loss of 1.1% of positive subjects. Another clinically relevant finding was that in 1% of Ro52(+)/Ro60(+) cases total anti-Ro was negative, an artifact that has previously been reported. All tests and analytes showed excellent specificity for classification as primary SS, albeit at the expense of low sensitivity (Table 1).

Conclusion: The very low sensitivity of anti-Ro and anti-La DID in SS patients may result in misclassification of up to 25% of cases. Algorithms for a tiered approach for additional testing are necessary in the clinical setting to optimize diagnosis at a reasonable cost. For research, in particular clinical trials that require high specificity, all the tested platforms perform very well.
Clinical Relevance of Serum Free Light Chain Level As Biomarker in Primary Sjögren’s Syndrome

Gwenny M. Verstappen¹, Johan Bijzet¹, Jolien F. van Nimwegen¹, Martha S. van Ginkel¹, Arjan Vissink², Hendrika Bootsma¹ and Frans G.M. Kroese¹, ¹Rheumatology and Clinical Immunology, University of Groningen, University
During immunoglobulin synthesis in B-cells, kappa and lambda light chains are produced in excess compared to heavy chains, and the surplus of light chains are secreted into serum as free light chains (FLC). Compared to healthy individuals, elevated serum levels of polyclonal FLCs are seen in autoimmune diseases associated with increased B-cell activation, including primary Sjögren’s syndrome (pSS). In pSS, serum FLC levels correlate with IgG, rheumatoid factor and systemic disease activity.\textsuperscript{1} However, the clinical relevance of serum FLC levels as biomarker in pSS remains unclear. The objective of this study is to assess if I) FLCs are already elevated at the time of diagnosis, II) FLC levels can discriminate non-SS sicca from pSS patients, and III) FLCs can be used to monitor treatment response.

Methods:

Serum samples of 102 consecutive patients referred to our expertise center for suspicion of pSS were included. Patients were classified by a panel of 3 clinical experts as non-SS sicca, incomplete pSS or pSS and fulfillment of ACR-EULAR criteria for pSS was assessed. Longitudinal serum samples of pSS patients treated with rituximab (n=20) or abatacept (n=15) were also included. Kappa (κ) and lambda (λ) FLCs were measured in serum by the Freelite assay (Binding Site, UK). Area under the ROC curve (AUC) was used to assess the ability of serum FLC levels to predict a pSS diagnosis. Generalized estimating equations were used to measure changes during treatment.

Results:

At the time of diagnosis, FLC\textsubscript{κ} and FLC\textsubscript{λ} serum levels were significantly higher in pSS patients compared to non-SS sicca patients (FLC\textsubscript{κ}: median (IQR)=29 (17-39) vs. 15 (11-17) mg/L, p<0.001; FLC\textsubscript{λ}: 27 (18-34) vs. 15 (13-18) mg/L, p<0.001). The κ/λ ratio was slightly increased in pSS compared to non-SS sicca patients (p=0.045). FLC\textsubscript{κ} and FLC\textsubscript{λ} both showed good accuracy to discriminate pSS from non-SS (FLC\textsubscript{κ}: AUC=0.806, 95% CI=0.708-0.904; FLC\textsubscript{λ}: AUC=0.802, 95% CI=0.705-0.899). However, the accuracy of serum IgG was higher (AUC=0.885, 95% CI=0.811-0.959). Interestingly, FLC\textsubscript{κ} was also elevated (>20 mg/L) in 4/9 incomplete pSS patients. In two of them, also FLC\textsubscript{λ} was elevated (>32 mg/L). In patients fulfilling ACR-EULAR criteria, FLC\textsubscript{κ} and FLC\textsubscript{λ} levels correlated with systemic disease activity, assessed by EULAR Sjögren’s syndrome disease activity index (FLC\textsubscript{κ}: Spearman’s ρ=0.282, p=0.004; FLC\textsubscript{λ}: ρ=0.321, p=0.001). Treatment with rituximab significantly lowered FLC\textsubscript{κ} and FLC\textsubscript{λ} levels (p<0.001 for both). Treatment with abatacept also reduced FLC\textsubscript{κ} and FLC\textsubscript{λ} levels, although to a smaller extent (p=0.006 and p=0.087, respectively).

Conclusion:

Serum FLCs are elevated in pSS patients at the time of diagnosis and can discriminate non-SS sicca from pSS. FLC\textsubscript{κ} is already elevated in a large part of the incomplete SS patients and may serve as an early diagnostic biomarker. Furthermore, serum FLC levels can be used to monitor the effect of treatment on B-cell activity and may be more sensitive to change than serum IgG, because of a shorter half-life.


Disclosure: G. M. Verstappen, None; J. Bijzet, None; J. F. van Nimwegen, None; M. S. van Ginkel, None; A. Vissink, None; H. Bootsma, None; F. G. M. Kroese, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/clinical-relevance-of-serum-free-light-chain-level-as-biomarker-in-primary-sjogren%e2%80%b2s-syndrome
Comprehensive Immuno-Phenotyping of Follicular Helper T Cell and B Cell Subpopulations in Primary Sjögren’s Syndrome

Nida Meednu1, Cécile Seifert2, Jennifer Barnard3, Madhu Ramaswamy4, Jeffrey Riggs5, Alex Rosenberg6, Jamie Biear7, Gianluca Carlesso8, Ralf G. Thiele8, Andreea Coca9, Fanny Monneaux2, Helene Dumortier2, Jacques-Eric Gottenberg2 and Jennifer H. Anolik1, 1Medicine- Allergy, Immunology and Rheumatology, University of Rochester Medical Center, Rochester, NY, 2CNRS, Immunopathologie et Chimie Thérapeutique/Laboratory of Excellence Medalis, Institut de Biologie Moléculaire et Cellulaire, Strasbourg, France, 3Medicine-Allergy, Immunology and Rheumatology, University of Rochester Medical Center, Rochester, NY, 4MedImmune LLC, Gaithersburg, MD, 5Respiratory, Inflammation and Autoimmunity (RIA), MedImmune LLC, Gaithersburg, MD, 6Department of Microbiology and Informatics Institute, University of Alabama at Birmingham, Birmingham, AL, 7Rheumatology, University of Rochester Medical Center, Rochester, NY, 8Medicine, University of Rochester Medical Center, Rochester, NY, 9University of Rochester Medical Center, Rochester, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Sjögren's Syndrome Poster I: Translational Research
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Primary Sjögren’s syndrome (pSS) is a systemic autoimmune disease characterized by immune cell infiltration in the salivary glands resulting in ocular and oral dryness. Abnormalities in B cell activation and skewing of T cell polarization toward Th2 and T follicular helper (TFH) associated with ectopic germinal center formation in the salivary gland are observed in pSS. However, the interplay between B and T cell subsets, and other immune abnormalities, as well as relationship to disease status, has yet to be fully elucidated. In this study, we evaluated changes in peripheral blood B and T cell populations in pSS compared to SLE and RA diseases and healthy controls.

Methods: Two cohorts of patients with pSS according to European-American Consensus and ACR criteria and age-matched healthy controls (HC) were recruited (Rochester, USA and Strasbourg, France) and disease activity assessed by ESSDAI and ESSPRI. The Rochester cohort also included RA (n=20) and SLE (n=15) classified based on ACR criteria. PBMCs were isolated by Ficoll-Hypaque and the frequencies of B and T subpopulations measured by multi-parameter flow cytometry. Data are reported as median [25th-75th quartile]. Correlation analysis was done by Pearson method, p < 0.05 was considered significant.

Results: We examined the expression of ICOS and PD-1, two important co-regulatory molecules of the B7-family, on memory T cells (CD4+CD45RA-) in pSS compared to HC, SLE and RA. pSS and SLE had higher frequency of memory T cells expressing both ICOS and PD-1 than HC while RA had higher frequency of PD-1+hi T cells. Accordingly, T follicular helper cells (TFH: CXCR5+ICOS+PD-1+) were found at higher frequency in pSS and SLE compared to HC (pSS (n=40): 5.96 [3.75-8.71]%; HC (n=58): 4.18 [2.51-4.91]%, p=0.0005; SLE (n=15): 4.61 [3.51-9.84]%, p=0.002). Further evaluation of TFH subsets (based on CXCR3 and CCR6), revealed higher frequency of TFH1 and lower TFH17 subset in pSS compare to HC and RA, also confirmed in the Strasbourg cohort. Characterization of B cells in pSS patients from Rochester cohort revealed significant contractions of switched memory (SM) and un-switched memory (USM) B cell compared to HC (pSS SM (n=39): 3.52 [1.65-7.28]%; HC SM (n=38): 7.57 [5.49-10.86]%, p=0.005; pSS USM (n=39): 10.07 [5.47-15.62]%; HC USM (n=38): 21.44 [15.16-31.27]%, p<0.0001). Furthermore, frequencies of ICOSL expressing SM and USM were lower in pSS than HC. There was a significant inverse correlation between ICOSL+ USM B cells and TFH1 in pSS patients (p= -0.55, p=0.0255). There were two distinct clusters of pSS based on T and B cell subsets, with one group distinct from HC and associated with higher disease activity and autoantibodies. In a subset of pSS (n=10), T and B cell frequencies were evaluated longitudinally at 6 months. Significant changes in frequency of ICOSL+ B cells were observed and negatively correlated with changes in CXCR5+ICOS+ T cells (p= -0.634, p=0.049).
Conclusion: Our data highlight the significant abnormalities in the peripheral TFH and B cell compartment in pSS and further suggest the critical role of TFH-B cell interactions. The decrease in ICOSL+ memory B cells suggests interaction with ICOS+ T cells in germinal center-like structures in salivary glands.

Disclosure: N. Meednu, None; C. Seifert, None; J. Barnard, None; M. Ramaswamy, MedImmune LLC, 3; J. Riggs, MedImmune, LLC, 3,AstraZeneca, 1; A. Rosenberg, None; J. Biear, None; G. Carlesso, MedImmune LLC, 3; R. G. Thiele, Amgen, 8,AbbVie, 8,BioClinica, 5,Fujifilm SonoSite, 9; A. Coca, None; H. Dumortier, None; J. E. Gottenberg, BMS, Gilead, Medimmune,Pfizer SanofiAventis, Ucb, 2; J. H. Anolik, None.


Abstract Number: 562

Anti-Muscarinic Receptor 3 Antibodies – a Cross Reactive Result of Ro60 Immunization

Syed M.S. Quadri1, Biji T Kurien2, Kristi A. Koelsch3 and R. Hal Scofield4, 1Medicine, University of Oklahoma Health Sciences Center, Oklahoma City, OK, 2Arthritis and Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, 3Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 4Oklahoma Medical Research Foundation, Oklahoma City, OK

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Sjögren's Syndrome Poster I: Translational Research
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Sjögren’s syndrome (SS) is a chronic autoimmune inflammatory disease characterized by impaired function of salivary and lacrimal glands leading to dry mouth and dry eyes. The hallmark of SS is the presence of autoantibodies against Ro and La antigens. High titers of anti-Ro60 autoantibodies have shown to correlate with severity of the disease. It is yet unclear how these antiRo60 antibodies correlate with severity. Autoantibodies against M3R are also prevalent in SS. Muscarinic receptor 3 abbr. as M3R is an end organ parasympathetic GPCR mainly present in lacrimal and salivary glands. The stimulation of M3R is well studied and is known to induce secretion in lacrimal and salivary glands and so an effect to M3R could possibly lead to a reduction in secretion. We immunized rabbits with Ro60 and found that immunization not only resulted in the formation of antibodies against Ro60 but also to 2nd and 3rd extracellular domains of the M3 receptor. The reactivity to Ro60 and M3R 2nd and 3rd extracellular domains has also shown a high correlation.

Methods: 

Immunization of rabbits: NZW rabbits were immunized with 500µg of either unmodified Ro60, Smith or RNP antigen) emulsified in 0.5 ml of complete Freund’s adjuvant given I/P with subsequent boosters at days 26, 53 and 99 with a final I/V boost on day 152. The sera were collected weekly in pre and post-immunized rabbits. Ro60 and M3R experiments: Reactivity of sera towards Ro60, MAPS of M3R 2nd or 3rd extracellular domains were tested using ELISA. Seral dilution ELISA was done using dilution 1:100 to 1: 100,000 and competition ELISA by preincubating sera with either Ro60 and MAPS of 2nd ECL was done to see the specificity of antibody binding.

Results: Rabbits immunized with Ro60 developed antibodies against Ro60, M3R 2nd and 3rd ECLs in a progressive way. A positive correlation was found between both Ro60 and M3R 2nd ECL (R² =0.66, p = <0.0001) and between Ro60 and M3R 3rd ECL(R² =0.789, p = <0.0001) . A positive correlation was also found between M3R 2nd and 3rd ECL ELISA (R² =0.56, p = 0.0001). Rabbits immunized with Smith and RNP antigen did not develop antibodies to any of the extracellular
domains of M3R to significant levels. Seral dilution ELISA showed a sequential decline in reactivity for both the 2nd and the 3rd ECL of M3R. Competition ELISA for 2nd ECL of M3R using sera preincubated with M3R 2nd ECL showed an inhibition of 48.2% to 58.99%, sera preincubated with Ro60 showed an inhibition of 54.5 to 89.03% verifying the specific binding.

**Conclusion:** Previously our studies found high reactivity for M3R and Ro60 antigen in fully human recombinant monoclonal antibodies produced from plasmablasts isolated from salivary glands of SS patients and was found to be inhibitory. The subsequent step, immunization of rabbits with Ro60 also supported the same hypothesis. The rabbits immunized with Ro60 developed antibodies to M3R extracellular domains supporting the concept of cross-reactivity. Our next step is to see whether the immunization of rabbits with M3R develops anti-Ro60 antibodies. Our future studies are also aimed at passive transfer of IgGs (from Ro60 immunized rabbit sera as well as human recombinant IgGs positive for M3R and Ro) to mice to see the *invivo* functional consequences of this cross-reactivity.

**Disclosure:** S. M. S. Quadri, None; B. T. Kurien, None; K. A. Koelsch, None; R. H. Scofield, None.

**View Abstract and Citation Information Online** - [http://acrabstracts.org/abstract/anti-muscarinic-receptor-3-antibodies-a-cross-reactive-result-of-ro60-immunization](http://acrabstracts.org/abstract/anti-muscarinic-receptor-3-antibodies-a-cross-reactive-result-of-ro60-immunization)

**Abstract Number:** 563

**The Effect of Non-Invasive Vagus Nerve Stimulation on Fatigue and Immune Responses in Patients with Primary Sjögren’s Syndrome**

Jessica Tarn⁠¹, Sarah Legg⁠², Sheryl Mitchell⁠², Bruce Simon⁠³ and Wan-Fai Ng⁴, ⁠¹Institute of Cellular Medicine, Musculoskeletal Research Group, Institute of Cellular Medicine, Newcastle University, Newcastle-Upon-Tyne, UK, Newcastle-Upon-Tyne, United Kingdom, ²Freeman Hospital, Newcastle upon Tyne, United Kingdom, ³electroCore Medical LLC, Basking Ridge, NJ, ⁴Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, United Kingdom

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Sjögren’s Syndrome Poster I: Translational Research

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Primary Sjögren's syndrome (pSS) sufferers have rated chronic fatigue as the most important symptom needing improvement and the main contributing factor to the loss of work productivity. Emerging data suggest cross-talk exists between the autonomic nervous system and the immune system via the vagus nerve in particular. The gammaCore device (electroCore), was developed to deliver stimulation of the cervical vagus nerve non-invasively, and has been CE marked for the treatment of epilepsy and migraine and has recently been FDA approved for the acute treatment of episodic cluster headache. In this study, we use the gammaCore device to dissect the relationship between the vagus nerve, fatigue and immune responses in pSS.

**Methods:** Fifteen female pSS subjects fulfilling the American European Consensus Group Classification criteria (2002) were included. At baseline, blood was drawn before and after non-invasive vagus nerve stimulation (nVNS). The subjects were then instructed to use the gammaCore device twice daily (2 min. over each carotid artery). The participants were followed up at day 7 and Day 28. At each visit, blood was drawn and patient reported outcome measures (PROMs) were collected including EULAR SjogrenOs syndrome Patient Reported Index (ESSPRI), Profile of fatigue (PRO-F), visual analogue scale (0-100 cm) of abnormal fatigue and Epworth Sleepiness Scale (daytime sleepiness). Whole blood samples were stimulated with 2ng/mL Lipopolysaccharides (LPS) or RPMI-1640 as control. After 24 hours, the levels of IFNγ, IL12-p70, TNFα , MIP1α, IFNa, IL-10, IL-1β, IL-6 and IP10 were measured in the supernatants by cytometric bead array (BD). In addition, whole blood cell subset proportions were profiled using flow cytometry.
Results: PRO-F, and Daytime sleepiness were significantly reduced across three visits. Trends of improvement were also observed in Abnormal fatigue VAS, ESSPRI-Dryness and ESSPRI-Physical fatigue subscales. Participants who appeared to have a sustained reduction in fatigue related PROMs over the study period concurrently had a significantly higher proportion of T-cells at most time points. Cytokine production, particularly TNFα by whole blood cells upon LPS stimulation was reduced over the period of device use. Additionally, TNFα and IL-1β levels were significantly reduced after the first device use compared with pre-VNS.

Conclusion: To our knowledge this is the first study into the effects of nVNS in pSS. These preliminary observations suggest that in some individuals, nVNS may reduce clinical symptoms of fatigue, which could be underpinned by biological changes detectable in the whole blood.

Disclosure: J. Tarn, None; S. Legg, None; S. Mitchell, None; B. Simon, electroCore, 3; W. F. Ng, None.


Abstract Number: 564

Molecular Identification of a Ro-Specific Salivary IgA Repertoire with Unique Clonal Signatures in Primary Sjogren’s Syndrome

Jing Jing Wang1, Alexander Colella1, Tim Chataway2, R. Hal Scofield3 and Tom Gordon1,4, 1Immunology, Flinders University, Adelaide, Australia, 2Proteomic Facility, Flinders University, Adelaide, Australia, 3Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 4Immunology, SA Pathology, Adelaide, Australia

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Sjögren's Syndrome Poster I: Translational Research
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Autoantibodies against 60-kD Ro (Ro60)/SSA have been detected in the saliva and serum of patients with primary Sjögren's syndrome (SS) by routine methods that are unable to resolve molecular characteristics of interacting antibodies. Accordingly, it is unknown whether the parallel glandular and systemic anti-Ro60 responses derive from related or independent antibody repertoires. In the present study, we have identified a Ro60-specific salivary IgA repertoire by analysing immunoglobulin variable region (IGV) subfamily composition and mutational profiles of matched salivary and serum proteomes.
Methods: Anti-Ro60 autoantibodies were purified and sequenced from Ro-specific precipitins prepared by electrophoresing native Ro60 protein against whole saliva or serum collected from 9 patients with seropositive primary SS. Microgram amounts of precipitating anti-Ro60 Igs were separated by SDS-PAGE, and in-gel chymotrypsin digests performed on heavy (H) and light (L) chain bands. VH/VL and constant-region peptides were subjected to nano-high performance liquid chromatography-mass spectrometry (nHPLC-MS/MS) followed by combined de novo amino acid sequencing and database matching using Peaks 8.0 software utilising ImMunoGeneTics (IMGT) and Uniprot databases.

Results: High-resolution MS sequencing of purified salivary anti-Ro60 H- and L-chains revealed a common (9/9 patients) oligoclonal IgA Ro60 repertoire dominated by IGHV3-23 and IGKV3-20 subfamily expression. Paired serum anti-Ro60 proteomes expressed a more diversified IgG1 repertoire with expression of additional IGHV1 and IGHV3 families in the systemic compartment. IGHV3-23-encoded H-chains were present in matched saliva and serum samples but were distinct in terms of their patterns of somatic mutations, suggesting independent pathways of affinity maturation. Three of 9 patients showed a less abundant IgG1 salivary anti-Ro60 proteome that was similar to the paired serum proteome.

Conclusion: Proteomic profiling of salivary and serum anti-Ro60 autoantibodies in primary SS reveals a unique salivary IgA repertoire with specific V-region peptide profiles, consistent with a parallel yet distinct salivary gland pathway of somatically selected anti-Ro60 autoantibodies. The novel proteomic workflow reported herein will allow analysis of clonal turnover of mucosal and systemic autoantibody repertoires in early versus established disease and provide molecular biomarkers to assess responses to therapy in the glandular and peripheral compartments.

Disclosure: J. J. Wang, None; A. Colella, None; T. Chataway, None; R. H. Scofield, None; T. Gordon, None.


Abstract Number: 565

Fatigue in Primary Sjögren’s Syndrome (pSS) Is Associated with Lower Levels of Proinflammatory Cytokines: A Validation Study

Kristen Davies1, Kamran Mirza1, Jessica Tarn2, Nadia Howard Tripp3, Robert J. Moots4, Nagui Gendi5, Michele Bombardieri6, Costantino Pitzalis6, Nurhan Sutcliffe6, Simon Bowman7, Neil J. McHugh8, John McLaren9, Devesh Mewar10, David Coady11, Kirsten MacKay12, Susan Knight13, Monica Gupta14, Marian Regan15, Cathy Lawson16, Jacqueline Andrews17, Peter Lanyon18, Mohammed Akil19, Elizabeth Price20, Annie Cooper21, Frances Hall22, Theodoros Dimitroula23, Gavin Clunie24, Saravanan Vadivelu25, Ian Giles26, Bhaskar Dasgupta27, Steve Young-Min28, Dennis Lendrem29,30 and Wan-Fai Ng2,31, 1Institute of Cellular Medicine, Musculoskeletal Research Group, Institute of Cellular Medicine, Newcastle University, Newcastle-Upon-Tyne, UK, Newcastle-Upon-Tyne, United Kingdom, 2Musculoskeletal Research Group, Institute of Cellular Medicine, Newcastle University, Newcastle-Upon-Tyne, UK, Newcastle-Upon-Tyne, United Kingdom, 3Newcastle-Upon-Tyne Hospitals NHS Foundation Trust, Newcastle-upon-Tyne, UK, Newcastle-upon-Tyne, United Kingdom, 4University of Liverpool, Liverpool, UK, Liverpool, United Kingdom, 5Basildon and Thurrock University Hospital, Basildon, UK, Basildon, United Kingdom, 6Barts Health NHS Trust & Barts and the London School of Medicine & Dentistry, London, UK, London, United Kingdom, 7Department of Rheumatology, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK, Birmingham, United Kingdom, 8Royal National Hospital for Rheumatic Diseases, Bath, UK, Bath, United Kingdom, 9NHS Fife, Kirkcaldy, UK, Kirkcaldy, United Kingdom, 10Royal Liverpool University Hospital, Liverpool, UK, Liverpool, United Kingdom, 11Sunderland Royal Hospital, Sunderland, UK, Sunderland, United Kingdom, 12Torbay Hospital, Torquay, UK, Torquay, United Kingdom, 13Macclesfield General Hospital, Macclesfield, UK, macclesfield, United Kingdom, 14Gartnavel General Hospital, Glasgow, UK, Glasgow, United Kingdom, 15Royal Derby Hospital, Derby, UK, Derby, United Kingdom, 16Harrogate District Hospital, Harrogate, UK, Harrogate, United Kingdom, 17Leeds Teaching Hospitals NHS Trust, Leeds, UK, Leeds, United Kingdom, 18Nottingham University Hospitals NHS Trust, Nottingham, UK, Nottingham, United Kingdom, 19Royal Hallamshire Hospital, Sheffield, UK, Sheffield, United Kingdom, 20Great Western Hospital, Swindon, UK, Swindon, United Kingdom, 21Royal Hampshire County Hospital, Winchester, UK, Winchester, United Kingdom, 22Addenbrooke’s Hospital, Cambridge, UK, Cambridge,
Background/Purpose: Primary Sjögren’s syndrome (pSS) is a chronic autoimmune rheumatic disease causing various symptoms including dryness, fatigue and pain. Previous work by our group has suggested that certain pro-inflammatory cytokines are inversely related to patient-reported levels of fatigue. This model in that study using pro-inflammatory cytokine levels, disease-specific and clinical parameters was able to predict fatigue with 67% accuracy. To date, these findings have not been validated. This study aims to validate this observation.

Methods: Blood levels of seven cytokines were measured in 120 patients with pSS from the United Kingdom Primary Sjögren’s Syndrome Registry and 30 age-matched healthy non-fatigued controls. Patient-reported scores for fatigue were classified according to severity and compared to cytokine levels using analysis of variance. The differences between cytokines in cases and controls were evaluated using Wilcoxon test. A logistic regression model was used to determine the most important predictors of fatigue.

Results: Three cytokines, interferon-γ-induced protein-10 (IP-10), tumour necrosis factor-α (TNFα) and interferon-α (IFNα) were significantly higher in patients with pSS (n=120) compared to non-fatigued controls (n=30). Levels of two pro-inflammatory cytokines, TNF-α (p=0.021) and lymphotoxin-α (p=0.043), were inversely related to patient-reported levels of fatigue. Based on the model previous used a regression model was created to predict fatigue in pSS. Cytokine levels, disease-specific and clinical parameters as well as pain, anxiety and depression were used as predictors in this validation model. The model correctly predicts fatigue levels with 85% accuracy.

Conclusion: Depression, pain and proinflammatory cytokines appear to be the most powerful predictors of fatigue in pSS, which is consistent with the original study. This data further challenges the notion that proinflammatory cytokines directly mediate fatigue in chronic immunological conditions. Validation in an independent international cohort would be necessary to further confirm these results.
Figure 1: Box plot showing median cytokine levels and IQR for a) IP-10, b) TNF-α, c) LT-α and d) IFN-γ in controls and pSS fatigue groups.

Figure 2: (A) Full ordinal logistic regression model with all parameters. All of these variables predict fatigue correct in 85% of cases. (B) shows that IFN-γ, IP-10, depression and pain alone predicted fatigue level with 80% accuracy.

Disclosure: K. Davies, None; K. Mirza, None; J. Tarn, None; N. Howard Tripp, None; R. J. Moots, None; N. Gendi, None; M. Bombardieri, GSK, Amgen/MedImmune and UCB, 5; C. Pitzalis, None; N. Sutcliffe, None; S. Bowman, I have consulted in the field of Sjogren's for: AstraZeneca/MedImmune, BMS, Celgene, Eli Lilly, Novartis, GSK, MTPharma, Novartis, Ono, Takeda, UCB, xtlbio). Roche provided Rituximab for the TRACTISS Study, 5; N. J. McHugh, None; J. McLaren, None; D. Mewar, None; K. MacKay, None; S. Knight, None; M. Gupta, None; M. Regan, None; C. Lawson, None; J. Andrews, None; P. Lanyon, None; M. Akil, None; E. Price, None; A. Cooper, None; F. Hall, None; T. Dimitroulas, None; G. Clunie, None; S. Vadivelu, None; I. Giles, None; B. Dasgupta, None; S. Young-Min, None; D. Lendrem, None; W. F. Ng, None.


Abstract Number: 566

Immune Response to Seasonal Flu Vaccination in Patients with Primary Sjogren’s Syndrome

Albin Björk1, Marika Kvarnström2, Gudny Ella Thorlacius2 and Marie Wahren-Herlenius2, 1Department of Medicine, Unit of Experimental Rheumatology, Department of Medicine, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, Stockholm, Sweden, 2Unit of Experimental Rheumatology, Department of Medicine, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, Stockholm, Sweden

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Sjögren's Syndrome Poster I: Translational Research
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM
**Background/Purpose:** Vaccination of rheumatic patients has been reported to induce lower antibody titers than in healthy individuals. However, studies have primarily included patients treated with immunomodulatory drugs. Previous data from our group revealed that untreated patients with primary Sjögren’s syndrome (pSS) respond with higher vaccine specific antibody titers than healthy controls (HC) following vaccination with a squalene adjuvanted H1N1 vaccine. Whether non-adjuvanted vaccines would also induce higher specific antibody responses in non-treated patients is not known. In the present study, we therefore monitored the vaccination response to the adjuvant-free vaccine for seasonal flu (Fluarix) in HC and untreated patients as well as that in patients receiving hydroxychloroquine (HCQ).

**Methods:** The study included 17 pSS patients without treatment, 8 pSS patients receiving HCQ, and 16 HC. All participants were women and all pSS patients were positive for SSA autoantibodies at the time of diagnosis. All individuals were vaccinated with the Fluarix 2015/2016 vaccine as part of the standard vaccination program. Clinical parameters were recorded using a questionnaire based on ESSPRI. Antibody titers were analysed by ELISA. RNA expression analysis was performed in CD14+ monocytes and CD19+ B cells using the Human Immunology v2 CodeSet (Nanostring).

**Results:** Untreated patients with pSS responded with significantly higher vaccine specific IgG titers than HC after immunization. Further, levels of anti-Ro52 autoantibodies increased in untreated patients, but not in HCQ-treated patients after vaccination. Nanostring RNA expression data confirmed the presence of an interferon (IFN)-signature in monocytes and in B cells from pSS patients and an IFN score calculated from B cell expression data could discriminate between high and low vaccine antibody response at day 29. No significant changes in self-reported clinical parameters were registered.

**Conclusion:** Untreated pSS patients display an increased serological responsiveness to the non-adjuvanted seasonal flu vaccine when compared to healthy controls. The increased response is however not mirrored by any clinical aggravation of the patients’ rheumatic disease.

**Disclosure:** A. Björk, None; M. Kvarnström, None; G. E. Thorlacius, None; M. Wahren-Herlenius, None.


**Abstract Number:** 567

**Minor Salivary Gland Histopathology, Major Salivary Gland Ultrasonography, and Secretory Function in Smoking Patients with Primary Sjögren’s Syndrome**

Daniel S. Hammenfors¹, Haris Causevic², Johan G. Brun³, Roland Jonsson¹ and Malin V. Jonsson⁴, ¹Department of Rheumatology, Haukeland University Hospital, University of Bergen, Bergen, Norway, ²Broegelmann Research Laboratory, Department of Clinical Science, University of Bergen, Bergen, Norway, ³Department of Rheumatology, Haukeland University Hospital, Bergen, Bergen, Norway, ⁴Department of Clinical Dentistry, Section for Oral and Maxillofacial Radiology, University of Bergen, Bergen, Norway

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Sjögren’s Syndrome Poster I: Translational Research

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Several studies have reported a protective effect of smoking with regard to risk for primary Sjögren’s syndrome (pSS) and minor salivary gland inflammation. To our knowledge, there are no studies investigating major salivary gland ultrasonography (SGUS) findings in smokers with pSS. The aim of this study was to investigate the frequency of smokers...
in a cohort of pSS, and to determine the possible impact of smoking on minor salivary gland histopathology, major salivary gland ultrasonography, and secretory function of the salivary and lacrimal glands.

Methods:

Patients with pSS (n=98) were recruited from the Department of Rheumatology, Haukeland University Hospital, Bergen, Norway. All patients had undergone clinical examination and SGUS using a simplified scoring system for glandular homogeneity and hypoechogenic areas. The parotid and submandibular salivary gland scans were graded 0-3; grades 0-1 considered corresponding to normal/non-specific changes and grades 2-3 to SS-like pathological changes. In addition, routine clinical and serological parameters, information regarding focus score, sicca symptoms, secretory function, fatigue, and smoking habits were available for retrospective analysis. All patients fulfilled the 2002 AECG criteria for pSS.

Results:

The majority of patients in this pSS cohort (n=59) were non-smokers, the remaining consisted of former smokers (n=27) and current smokers (n=12). Pathological SGUS findings were found in 38/59 (64 %) of the non-smokers, 13/27 (48 %) of the former smokers, and in 7/12 (58 %) of the current smokers.

Data on focus score (FS) was available in 83 patients, and correlated with SGUS score (p=0.010, r=0.283). Interestingly, 49/54 (91 %) non-smokers, 17/21 (81 %) former smokers and 3/8 (38 %) current smokers had FS≥1 (p<0.010, r=0.283). Mean focus score was 2.0 for non-smokers, 2.1 for former smokers, and 0.6 for current smokers; the difference between current and former smokers was significant (p=0.023).

Oral sicca symptoms correlated with SGUS score (p<0.001, r=0.378). Unstimulated salivary secretion was ≤1.5 ml/15 min in 42/57 (74 %) non-smokers, 18/26 (69 %) former smokers, and 7/12 (58 %) current smokers. Stimulated saliva was ≤3.5 ml/5 min in 27/57 (47 %) non-smokers, 12/26 (46 %) former smokers, and 4/12 (33 %) current smokers. Schirmer’s I-test levels (right and left eye, respectively) for current smokers were 9.3 and 11.3 mm, former smokers 4.9 and 3.8 mm, and non-smokers 7.7 and 7.9 mm. Differences were significant for the left eye when comparing current smokers and former smokers (p=0.021), and non-smokers and former smokers (p=0.048).

Interestingly, anti-Ro/SSA titers were elevated in 9/12 (75 %) current smokers and 20/27 (74 %) former smokers, compared to 35/58 (60 %) non-smokers. A similar trend was observed for anti-La/SSB titers in 6/12 (50 %) current smokers, 12/27 (44 %) former smokers, and 19/58 (33 %) non-smokers.

Conclusion:

In this cohort, smokers with pSS had a lower degree of minor salivary gland inflammation and pathological imaging findings in the major salivary glands. The sub-group also presented with better secretory function compared to non-smokers and former smokers.

Disclosure: D. S. Hammenfors, None; H. Causevic, None; J. G. Brun, None; R. Jonsson, None; M. V. Jonsson, None.


Abstract Number: 568

Complement Consumption As a Predictor of Pulmonary Manifestation in Patients with Primary Sjögren’s Syndrome: Results from a Unicentric Observational Study

Alisson Pugliesi1, RACHEL ZERBINI MARIANO2, Raquel Baldini Campos3, Simone Appenzeller4, Manoel Bertolo5 and ZORAIDA SACHETTO1, 1INTERNAL MEDICINE, DISCIPLINE OF RHEUMATOLOGY, Faculty of Medical Sciences, State University of Campinas (UNICAMP), CAMPINAS, Brazil, 2Radiology and Diagnostic Imaging, Faculty of Medical Sciences, State University of Campinas (UNICAMP), CAMPINAS, Brazil, 3Internal Medicine, Faculty of
Complement Consumption as a Predictor of Pulmonary Manifestation in Patients with Primary Sjögren’s Syndrome: Results from a Unicentric Observational Study

Background/Purpose: Primary Sjögren’s syndrome (pSS) may present with respiratory manifestations ranging from proximal and distal airways impairment to various forms of interstitial lung disease (pSS-ILD), which can affect up to 16% of patients. Studies on factors associated with pulmonary manifestations of pSS are few and of heterogeneous results. Our main objective was to identify clinical and laboratory elements related to pSS that may be predictors of lung disease.

Methods: Retrospective study of pSS patients in follow-up at a university hospital. Patients older than 18 years who met pSS classificatory criteria according to the American-European Consensus of 2002 were included. Patients with other CTD were excluded. Epidemiological, clinical, and laboratory data were extracted from medical records. Chest CT scans were reviewed by a radiologist without knowledge of the patients’ clinical data. Data from patients with pSS with and without pulmonary manifestations were compared and Fischer’s test was applied for statistical evaluation.

Results: Seventy patients with pSS were selected (68% female and mean age 45.8 ± 9.5). Fifteen (21.4%) had some form of pulmonary manifestation, 14 (20%) of ILD and 1 of bronchiolitis (1.4%). Among the analyzed variables, a statistically significant association was found between complement consumption (C3 or C4) and presence of pulmonary manifestation (38.4% versus 10.2%; p: 0.02). No association was found between autoantibodies such as ANA, RF, Ro/SSA and La/SSB or other forms of extraglandular manifestation (Table 1). No variables were correlated with the presence of pulmonary cysts or pSS-ILD. The radiological findings of patients with pulmonary manifestations are summarized in Table 2.

Conclusion: In our series of patients with pSS, we found a high frequency of individuals with pSS and pulmonary impairment. Complement consumption was a predictor of this form of manifestation, an association never seen before.
Disclosure: A. Pugliesi, None; R. Z. MARIANO, None; R. Baldini Campos, None; S. Appenzeller, None; M. Bertolo, None; Z. SACHETTO, None.


Abstract Number: 569

Is the Oral Microbiome Involved in the Pathogenesis of Sjogren’s Syndrome?

Taco A van der Meulen1, Frans G.M. Kroese2, S.C. Liefers2, Arnau Vich Vila3, Hermie J.M. Harmsen4, Hendrika Bootsma2, Fred K.L. Spijkervet1 and Arjan Vissink5, 1Oral and Maxillofacial Surgery, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, 2Rheumatology and Clinical Immunology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, 3Gastroenterology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, 4Medical Microbiology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, 5Department of Oral and Maxillofacial Surgery, University of Groningen, University Medical Center Groningen, Groningen, Netherlands

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Sjögren's Syndrome Poster I: Translational Research
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Environmental factors involved in the pathogenesis of primary Sjögren’s syndrome (pSS) are still largely unknown. The oral cavity is the microbial habitat closest to the salivary glands – the most affected tissue in pSS. Hypofunction of the salivary glands is the major cause underlying symptoms of a dry mouth (xerostomia), occurring in over 90% of the patients with pSS. The aim of our study was to explore whether the oral microbiome, in particular the bacterial composition and/or the presence of bacterial species, is specific for the oral microbiome of patients with pSS.

Methods: To assess whether changes in the oral microbiome of pSS patients are a cause of pSS or an effect of oral dryness, we included two control groups: patients with oral dryness not diagnosed as pSS (non-SS sicca patients) and population based controls. We collected a swab from the buccal mucosa of 82 patients with oral dryness referred to our outpatient

| BRONCHIOLITIS | 1 (6.6%) |
| GROUND GLASS | 8 (53.3%) |
| HONEYCOMBING | 2 (13.3%) |
| CYSTS | 10 (66.6%) |
| UIP PATTERN | 0 (0%) |
| NSIP PATTERN | 4 (30.7%) |
| LIP PATTERN | 9 (68.5%) |

UIP: USUAL INTERSTITIAL PNEUMONIA
NSIP: noneSPECIFIC INTERSTITIAL PNEUMONIA
LIP: LYMPHOCITIC INTERSTITIAL PNEUMONIA

Disclosure: A. Pugliesi, None; R. Z. MARIANO, None; R. Baldini Campos, None; S. Appenzeller, None; M. Bertolo, None; Z. SACHETTO, None.

Is the Oral Microbiome Involved in the Pathogenesis of Sjogren’s Syndrome?

Taco A van der Meulen1, Frans G.M. Kroese2, S.C. Liefers2, Arnau Vich Vila3, Hermie J.M. Harmsen4, Hendrika Bootsma2, Fred K.L. Spijkervet1 and Arjan Vissink5, 1Oral and Maxillofacial Surgery, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, 2Rheumatology and Clinical Immunology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, 3Gastroenterology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, 4Medical Microbiology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, 5Department of Oral and Maxillofacial Surgery, University of Groningen, University Medical Center Groningen, Groningen, Netherlands

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Sjögren's Syndrome Poster I: Translational Research
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Environmental factors involved in the pathogenesis of primary Sjögren’s syndrome (pSS) are still largely unknown. The oral cavity is the microbial habitat closest to the salivary glands – the most affected tissue in pSS. Hypofunction of the salivary glands is the major cause underlying symptoms of a dry mouth (xerostomia), occurring in over 90% of the patients with pSS. The aim of our study was to explore whether the oral microbiome, in particular the bacterial composition and/or the presence of bacterial species, is specific for the oral microbiome of patients with pSS.

Methods: To assess whether changes in the oral microbiome of pSS patients are a cause of pSS or an effect of oral dryness, we included two control groups: patients with oral dryness not diagnosed as pSS (non-SS sicca patients) and population based controls. We collected a swab from the buccal mucosa of 82 patients with oral dryness referred to our outpatient
clinic for a complete diagnostic work-up for pSS. After completing the diagnostic workup, 32 patients could be classified as pSS according to the 2002 AECG classification criteria and 50 patients as non-SS sicca. The bacterial composition of the buccal mucosa samples was determined with 16S rRNA sequencing. Buccal mucosa swab samples from a population based cohort study were used as population controls (n=118).

**Results:** Mean unstimulated whole salivary flow rates in pSS and non-SS sicca patients were 0.09 and 0.17 mL/min respectively. Significantly less 16S rRNA reads per sample were obtained from the buccal swab samples of patients with oral dryness (pSS and non-SS sicca together) compared to population controls (p<0.0001). Also the diversity of the bacterial composition from the buccal mucosa was significantly lower in pSS and non-SS sicca patients than in population controls (p=0.01 and p<0.001 respectively), but no difference was observed between pSS and non-SS sicca patients. Principal coordinate analysis showed no evident separation of the individual samples between the three different study groups, but the buccal mucosa bacterial communities from pSS patients were significantly more dissimilar to those from population controls than non-SS sicca patients from population controls (p=0.028). Multivariate analysis showed highly significant associations between oral dryness and the genera *Olsenella*, *Cryptobacterium* and *Fretibacterium* – all which have been associated with periodontal disease – since these genera were only detected in samples from the buccal mucosa of patients with oral dryness and not in population controls (p-value <0.005). However, no oral bacterial taxa were specifically associated with pSS.

**Conclusion:** Patients with pSS have a dysbiosis of the oral microbiome, viz. a reduced diversity and increase of pathogenic bacteria. We presume that dysbiosis in the oral microbiome of patients with pSS is largely an effect of oral dryness and not a causal factor in the pathogenesis of pSS. On top of this dysbiosis as a consequence of oral dryness, there might be a specific effect of pSS on the diversity of the oral microbiome.

**Disclosure:** T. A. van der Meulen, None; F. G. M. Kroese, None; S. C. Liefers, None; A. Vich Vila, None; H. J. M. Harmsen, None; H. Bootsma, None; F. K. L. Spijkervet, None; A. Vissink, None.


**Abstract Number:** 570

**Signalling Pathways Identified in Salivary Glands from Primary Sjögren’s Syndrome Patients Reveal Enhanced Adipose Tissue Development, As Demonstrated By Microarray Analysis, Real-Time PCR and Immunohistochemistry**

Lara A Aqrawi1, Janicke C Liaaen Jensen1, Gunnvor Øijordsbakken2, Ann-Kristin Ruus3, Ståle Nygård4,5, Marit Holden6, Roland Jonsson7,8, Hilde Kanli Galtung9 and Kathrine Skarstein10,11, 1Department of Oral Surgery and Oral Medicine, University of Oslo, Oslo, Norway, 2Department of Clinical Medicine, University of Bergen, Gade Laboratory for Pathology, Department of Clinical Medicine, University of Bergen, Bergen, Norway, 3Department of Oral Biology, University of Oslo, Oslo, Norway, 4Department of Informatics, University of Oslo, Oslo, Norway, 5Bioinformatics core facility, Institute for Cancer research, Oslo University Hospital, Oslo, Norway, 6Norwegian Computing Center, Oslo, Norway, 7Broegelmann Research laboratory, Department of Clinical Science, University of Bergen, Bergen, Norway, 8Department of Rheumatology, Haukeland University Hospital, Bergen, Bergen, Norway, 9Department of Oral Biology, University of Oslo, Oslo, Pakistan, 10Gade Laboratory for Pathology, Department of Clinical Medicine, University of Bergen, Bergen, Norway, 11Department of Pathology, Haukeland University Hospital, Bergen, Bergen, Norway

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Sunday, November 5, 2017
**Session Title:** Sjögren's Syndrome Poster I: Translational Research
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** A characteristic feature of Sjögren’s syndrome (SS) is the destruction of salivary and lacrimal glands mediated by mononuclear cell infiltration. Adipocytes can also occupy a large portion of the salivary gland (SG) tissue area, although little is known about their significance in SS. We have previously investigated adipose tissue infiltration in SG biopsies from SS patients and non-SS sicca controls. Our findings indicated distinct incidence of adipose tissue replacement in SS patients, where adipocytes were detected in IL6 rich regions. We now aimed to examine the development of adipocytes in the SG microenvironment, and delineate their possible involvement in immune reactions.

**Methods:** A microarray analysis was performed on SG from 6 SS patients and 6 non-SS controls, where the expression levels of genes involved in adipose tissue development were assessed. Real-time PCR was carried out on SG from 14 SS patients and 15 non-SS controls to account for interleukin (IL)-6, IL10 and IL17 mRNA levels. Immunohistochemical staining of frozen SG tissue using IL17 was also conducted.

**Results:** Upregulated signalling pathways identified in SG of SS patients show prominent adipose tissue development and mitochondrial fatty acid beta-oxidation, including the genes ARID5B, OXCT1, BDH1, SOX8, HMGCS2, FTO, ECHS1, PCCA, ACADL and ACADVL. Genes involved in interferon production and signalling were also detected (IRF1, IRF9, IRF7), in addition to IL6, IL10, and IL17 (Figure 1, Table 1). Higher mRNA levels of IL6, IL17 and IL10 were also observed in the SG of SS patients compared to controls. Moreover, IL17+ cells were observed mostly interstitially in the SG and around adipocytes, also within the focal infiltrates.

**Conclusion:** Adipocyte development seems to be more prominent in the SG of SS patients at the site of inflammation, where adipose tissue replacement is also evident. Detection of IL17 positive adipocytes in the target organ suggests their involvement in immune reactions.
Table 1. Genes identified in clusters A and B (Figure 1), and their function.

<table>
<thead>
<tr>
<th>Genes involved in adipose tissue development and fatty acid beta-oxidation</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARIDSB</td>
<td>Adipogenesis and expression of adipogenic genes</td>
</tr>
<tr>
<td>OXCT1</td>
<td>Key enzyme (CoA-transferase) involved in lipid formation</td>
</tr>
<tr>
<td>BDHH</td>
<td>Enzyme (dehydrogenase) involved in fatty acid production</td>
</tr>
<tr>
<td>SOX8</td>
<td>Transcription factor regulating adipose tissue development</td>
</tr>
<tr>
<td>HMGCS2</td>
<td>Enzyme regulating cholesterol metabolism and lipid biosynthesis</td>
</tr>
<tr>
<td>FTO</td>
<td>Control of adipocyte differentiation into brown or white fat cells</td>
</tr>
<tr>
<td>ECHS1</td>
<td>Fatty acid beta-oxidation (lipid metabolism)</td>
</tr>
<tr>
<td>PCCA</td>
<td>Fatty acid metabolism, biotin binding</td>
</tr>
<tr>
<td>ACADVL</td>
<td>Cellular lipid production, mitochondrial fatty acid beta-oxidation</td>
</tr>
<tr>
<td>ALDH5A1</td>
<td>Lipid metabolism, mitochondrial fatty acid beta-oxidation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genes involved in interferon production and signalling</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>IRF1</td>
<td>Type I interferon production, interferon signalling, apoptosis, CD8+ T cell differentiation, innate and adaptive immunity</td>
</tr>
<tr>
<td>IRF9</td>
<td>Type I interferon signalling, IFN-γ-mediated signalling pathway</td>
</tr>
<tr>
<td>IRF7</td>
<td>Type I interferon signalling, IFN-γ-mediated signalling pathway, IFN-β and IFN-γ production, innate and adaptive immunity</td>
</tr>
</tbody>
</table>

ARIDSB: AT-rich interactive domain-containing protein 5B
OXCT1: Oxaloacetate-CoA transferase 1 (mitochondrial)
BDHH: D-beta-hydroxybutyrate dehydrogenase (mitochondrial)
SOX8: Transcription factor SOX8
HMGCS2: HMG-CoA synthase (mitochondrial)
FTO: Alpha-ketoglutarate-dependent dioxygenase FTO
ECHS1: Enoyl-CoA hydratase (mitochondrial)
PCCA: Propionyl-CoA carboxylase alpha chain (mitochondrial)
ACADVL: Long-chain specific acyl-CoA dehydrogenase (mitochondrial)
ACADVL1: Very long-chain specific acyl-CoA dehydrogenase (mitochondrial)
IRF1: Interferon regulatory factor 1
IRF9: Interferon regulatory factor 9
IRF7: Interferon regulatory factor 7
**Disclosure:** L. A. Aqrawi, None; J. C. Liaaen Jensen, None; G. Øijordsbakken, None; A. K. Ruus, None; S. Nygård, None; M. Holden, None; R. Jonsson, None; H. K. Galtung, None; K. Skarstein, None.


Abstract Number: 571

**Anti-Modified Protein Antibody Response Pattern in Primary Sjögren’s Syndrome: Clinical and Prognostic Implications**

Alessia Alunno¹, Francesco Carubbi², Holger Bang⁴, Onelia Bistoni¹, Paul Studenic⁵, Günter Steiner⁵, Elena Bartoloni⁶, Josef S. Smolen⁵,⁷ and Roberto Gerli¹, ¹Department of Medicine, Rheumatology Unit, University of Perugia, Perugia, Italy, ²ASL1 Avezzano L'Aquila Sulmona, L'Aquila, Italy, ³Rheumatology Unit, University of L'Aquila, L'Aquila, Italy, ⁴Orgentec Diagnostika GmbH, Mainz, Germany, ⁵Division of Rheumatology, Department of Internal Medicine III, Medical University of Vienna, Vienna, Austria, ⁶Rheumatology Unit, University of Perugia, Perugia, Italy, ⁷Hietzing Hospital, Department of Internal Medicine, Vienna, Austria

First publication: September 18, 2017

SESSION INFORMATION

**Session Date:** Sunday, November 5, 2017

**Session Title:** Sjögren’s Syndrome Poster I: Translational Research

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Over the last decades, several post translationally modified proteins have been identified as autoantigens in rheumatoid arthritis (RA). No data regarding Abs against acetylated proteins (AAPA) and very few on Abs against carbamylated proteins (anti-CarP) are currently available in primary Sjögren’s syndrome (pSS). Acetylation of lysine/ornithin results from the addition of an acetyl group by the N-acetyltranferase enzyme, while carbamylation is the conversion of lysine residues into homocitrulline. In RA, carbamylation can be induced by cigarette smoke. The aim of our study was to investigate the prevalence and significance of AAPA and anti-CarP Abs in pSS.

**Methods:**

Eighty-seven pSS patients according to the 2002 American-European Consensus Criteria where enrolled. AAPA and anti-CarP were assessed by ELISA using mutated vimentin acetylated or carbamylated in position 7 as antigen. Acetylation could target either a lysin or an ornithin residue. To assess the possible effect of nearby antigens, acetylation and carbamylation were also alternatively included in position 2 (inverse peptide). Acetylated histone and non histone peptides were also employed as antigens. Clinical and serological records, including glandular and extraglandular manifestations, cardiovascular (CV) risk factors and CV events were retrospectively collected.

**Results:**

AAPA were identified in 20 pSS patients (23%). Seven patients displayed only one AAPA specificity while 13 displayed 2 or more AAPA specificities. Anti-CarP Abs have been identified in 4 pSS patients (5%) and in all cases the antigen was mutated vimentin carbamylated at position 7 but not the inverse peptide. AAPA+ patients did not display extra-glandular involvement including renal, pulmonary, gastrointestinal, central/peripheral nervous system manifestations or myositis.
Conversely, binary logistic regression revealed that AAPA positivity was associated with cardiac (namely pericarditis) and cardiovascular (CV) events (heart failure, pulmonary arterial hypertension, pulmonary embolism) (odds ratio=11; p<0.0001) but not with smoking or systemic arterial hypertension. pSS patients with anti-CarP Abs displayed more frequently leukopenia (p=0.01) and parotid gland swelling (p=0.03) but surprisingly none of the anti-CarP+ patients displayed articular involvement and none of them was a current or former smoker.

**Conclusion:**

Our study demonstrated for the first time that AAPA are detectable in pSS. Although preliminary, our results support the evidence of a possible association of AAPA and cardiac/CV manifestations. Likewise, specific anti-CarP Abs against mutated carbamylated vimentin are present in a small proportion of pSS patients and seem to be associated with leukopenia and parotid gland swelling but not with articular involvement and smoking. These results are of particular importance in light of the increased CV risk in pSS and will be assessed in a larger cohort of patients for validation purposes. Furthermore, it might be speculated that carbamylation in pSS may be induced by mechanisms other than cigarette smoking.

**Disclosure:** A. Alunno, None; F. Carubbi, None; H. Bang, None; O. Bistoni, None; P. Studenic, None; G. Steiner, None; E. Bartoloni, None; J. S. Smolen, None; R. Gerli, None.

**Biopsy Accuracy in Sjögren’s Syndrome: Analysis of 803 Patients Presenting with Sicca Syndrome Referred to Labial Salivary Gland Biopsy**

**Diego Baenas**¹, Soledad Retamozo², Juan Pablo Pirola³, Nadia Benzaquén⁴, María Flavia Ceballos⁵, Soledad Fiorentino³, María Jezabel Haye Salinas⁴, Nadia Riscanevo⁶, Janet Flores⁷, Ana C. Alvarez⁴, Verónica Saurit⁸, Alejandro Alvarellos⁸ and Francisco Caeiro⁹, ¹Reumatologia, Hospital Privado Universitario de Córdoba, Córdoba, Argentina, ²Rheumatology Unit, Hospital Privado Universitario de Córdoba, Institute University of Biomedical Sciences University of Córdoba (IUCBC), Córdoba, Argentina, ³Rheumatology, Rheumatology Unit, Hospital Privado Universitario de Córdoba., Cordoba, Argentina, ⁴Rheumatology, Rheumatology Unit, Hospital Privado Universitario de Córdoba, Córdoba, Argentina, ⁵Rheumatology, Rheumatology Unit, Hospital privado Universitario de Córdoba., Cordoba, Argentina, ⁶Rheumatology, Rheumatology Unit, Hospital privado Universitario de Córdoba, Cordoba, Argentina, ⁷Rheumatology Unit, Hospital privado Universitario de Córdoba, Cordoba, Argentina, ⁸Rheumatology, Rheumatology Unit, Hospital Privado Universitario de Córdoba, Córdoba, Argentina, ⁹Rheumatology, Hospital Privado Centro Médico de Córdoba, Córdoba, Argentina

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Sjögren's Syndrome Poster I: Translational Research

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Labial salivary gland biopsy (LSGB) is a minimally invasive procedure used in the diagnostic of Sjögren's Syndrome (SS). Objectives: to describe demographic, clinical and histological features of patients submitted to LSGB; to analyze the usefulness of LSGB in diagnosis of primary SS (pSS) and secondary SS (sSS); to assess the association between
histological findings and autoantibodies; to compare the sensitivity (Sn) and specificity (Sp) of the American-European 2002 (AE02) and ACR 2012 criteria.

Methods:

An observational, analytical, cross-sectional study was performed. A total of 803 patients were included between June 1996 and May 2016. A sub analysis of 674 patients was performed, excluding those with SSSs and others without antibodies.

Grades III and IV biopsy of the Chisholm and Mason’s (CM) classification were considered positive. Data was analyzed using STATA 17 software.

Results:

803 patients were included, 90% females. The mean age was 53 years (range 14-86). PSS was diagnosed in 238 (29.6%), and SS in 45 (5.6%), with female predominance in both groups (30.1% and 5.8%, respectively). Table 1 shows the clinical characteristics and complementary studies in patients with nonspecific dryness syndrome (NoSS) and SSP and SS.

Table 1.

<table>
<thead>
<tr>
<th>Parameters n (%)</th>
<th>NoSS n(%)</th>
<th>PSS n(%)</th>
<th>SSS n(%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xerostomía</td>
<td>399 (76.6)</td>
<td>200 (84)</td>
<td>39 (88.6)</td>
<td>0.019</td>
</tr>
<tr>
<td>Xerophthalmia</td>
<td>447 (85.8)</td>
<td>220 (92.4)</td>
<td>36 (81.8)</td>
<td>0.018</td>
</tr>
<tr>
<td>Abnormal ophtalmic test</td>
<td>209 (67.4)</td>
<td>175 (96.2)</td>
<td>28 (96.6)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Abnormal parotid sialography</td>
<td>31 (52.5)</td>
<td>24 (75)</td>
<td>-</td>
<td>0.036</td>
</tr>
<tr>
<td>Ro/SS-A</td>
<td>11 (2.4)</td>
<td>73 (32.7)</td>
<td>13 (32.5)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>La/SS-B</td>
<td>-</td>
<td>31 (14)</td>
<td>3 (7.5)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ANA</td>
<td>61 (12.4)</td>
<td>116 (49.6)</td>
<td>20 (48.8)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>RF</td>
<td>81 (16.4)</td>
<td>96 (41.6)</td>
<td>31 (73.8)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>LSGB G III-IV</td>
<td>8 (1.5)</td>
<td>217 (91.2)</td>
<td>26 (59.1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Pilocarpine</td>
<td>21 (4.04)</td>
<td>57 (24.1)</td>
<td>2 (4.6)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>43 (8.3)</td>
<td>206 (86.9)</td>
<td>26 (59)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Prednisone &lt;20mg</td>
<td>68 (65)</td>
<td>68 (29.5)</td>
<td>30 (5.5)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Prednisone &gt;20 mg</td>
<td>6 (1.5)</td>
<td>2 (0.9)</td>
<td>6 (13.6)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Rituximab</td>
<td>2 (0.4)</td>
<td>3 (1.5)</td>
<td>1 (2.3)</td>
<td>0.27</td>
</tr>
<tr>
<td>Other immunosuppressive drug</td>
<td>64 (15.7)</td>
<td>171 (72.8)</td>
<td>38 (86.4)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>
In the subanalysis of 674 patients, 33.1% were pSS, of which 204 (91.5%) were female. The mean age was 54 years (range 14-86). LSGB was 0, I or II grades in 8.5% patients with PSS, versus 91.5% patients with III-IV grades (p <0.01); Sn 91.5%, Sp 98.5%, positive predictive value (PPV) 96.7, negative predictive value (NPV) 95.9. Table 2 compares the serological characteristics of patients using LSGB as a "gold standard".

Table 2.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>LSGB (+)</th>
<th>LSGB (-)</th>
<th>p</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ro/SS-A</td>
<td>58 (27.5)</td>
<td>26 (31)</td>
<td>&lt;0.01</td>
<td>27.5</td>
<td>94.4</td>
<td>69.1</td>
<td>74.1</td>
<td>4.9</td>
</tr>
<tr>
<td>La/SS-B</td>
<td>24 (11.4)</td>
<td>7 (1.5)</td>
<td>&lt;0.01</td>
<td>11.4</td>
<td>98.5</td>
<td>77.4</td>
<td>70.9</td>
<td>7.5</td>
</tr>
<tr>
<td>ANA</td>
<td>97 (46.4)</td>
<td>71 (15.4)</td>
<td>&lt;0.01</td>
<td>46.4</td>
<td>84.6</td>
<td>57.7</td>
<td>77.6</td>
<td>3</td>
</tr>
<tr>
<td>RF</td>
<td>84 (40.8)</td>
<td>78 (48.2)</td>
<td>&lt;0.01</td>
<td>40.8</td>
<td>83</td>
<td>51.9</td>
<td>75.7</td>
<td>2.4</td>
</tr>
</tbody>
</table>

In multivariate analysis the significance for anti-Ro (OR: 2.0), ANA (OR: 2.9) and RF (OR: 2.5) was maintained.

The AE02 criteria had a Sn of 32.3%, Sp 97.3%, PPV 85.7% and NPV 74.4%.

The ACR 2012 had a Sn of 83.4%, Sp 98.5%, PPV 96.4% and NPV 92.3%.

**Conclusion:**

LSGB is a simple, safe, and useful tool for the diagnosis of Sjögren's syndrome. It exhibits an adequate balance between Sn, Sp, PPV and NPV.

Antibodies showed a significant association with a positive LSGB with low Sn for pSS screening but high Sp. The LSGB had a great value in "seronegatives patients".

**Disclosure:** D. Baenas, None; S. Retamozo, None; J. P. Pirola, None; N. Benzaquén, None; M. F. Ceballos, None; S. Fiorentino, None; M. J. Haye Salinas, None; N. Riscanevo, None; J. Flores, None; A. C. Alvarez, None; V. Saurit, None; A. Alvarellos, None; F. Caeiro, None.


**Abstract Number:** 573

**Subepithelial Infiltrate of the Vagina in Primary Sjogren’s Syndrome: The Cause of Vaginal Dryness?**

**Jolien F. van Nimwegen**¹, Karin van der Tuuk², Ellen R. Klinkert², Erlin A. Haacke³, Frans G.M. Kroese¹, Harry Hollema³, Marian J. Mourits² and Hendrika Bootsma¹, ¹Rheumatology and Clinical Immunology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, ²Obstetrics and Gynaecology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, ³Pathology and Medical Biology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands

**First publication:** September 18, 2017

**SESSION INFORMATION**

Session Date: Sunday, November 5, 2017
**Session Title:** Sjögren's Syndrome Poster I: Translational Research  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM  

**Background/Purpose:** Women with primary Sjögren’s syndrome (pSS) often experience vaginal dryness. The cause of this symptom is unknown. This study compared the vaginal and cervical health of women with pSS and controls, using clinical and histopathological parameters.

**Methods:** Consecutive premenopausal women with pSS according to the AECG and ACR-EULAR criteria, with symptoms of vaginal dryness, and age-matched controls planned for a risk-reducing salpingo-oophorectomy underwent a vaginal examination. Excluded were women with an inflammatory or infectious gynaecological disease, intra-uterine contraceptive device, or use of hormone therapy or DMARDs. Participants were screened for chlamydia, gonorrhea, and vaginal bacterial and fungal infections. The vaginal health index was recorded, which consists of 5 domains (elasticity, fluid secretion, pH, epithelial mucosa, moisture). Each domain was scored on a scale of 1-5, resulting in a score of 5-25. Low scores correspond to low vaginal health. In pSS patients, vaginal and endocervical biopsies were taken under local anesthesia. In controls, the investigation was performed under general anesthesia, prior to surgery. Formalin fixed and paraffin embedded tissue sections were stained for HE and CD45 (leucocytes) and examined by a dedicated gynaecopathologist. The percentage of area stained for CD45 was calculated with Aperio ImageScope v12.0. Groups were compared using Mann-Whitney U test.

**Results:** A total of 9 pSS patients and 5 controls were included so far. One pSS patient was excluded from the analysis due to presence of Chlamydia trachomatis. Median age was 35 years (IQR 30-46) in pSS patients and 37 years (IQR 36-42) in controls (p=0.62). Median vaginal health index was lower in pSS patients (18.5, range 14-23) compared to controls (23.0, range 20-23, p=0.019). In the HE staining of the vaginal tissue, a mild (n=6) or moderate (n=2) infiltrate was seen in all pSS patients. In controls, no infiltrate (n=3) or a mild infiltrate (n=2) was seen in the vaginal tissue. Infiltrates were mainly located in the subepithelial layer, with aggregates in dermal papillae (figure 1). The median percentage of area stained for CD45 in the vagina was higher in pSS patients (2.0%, range 1.0-5.0%) compared to controls (1.4%, range 0.4-1.4%, p=0.03). Endocervical tissue was obtained in 5 pSS patients and in 3 controls. In the HE staining of the endocervical tissue, moderate or severe infiltrates were seen in 3 pSS patients, and a moderate infiltrate in 1 control. The median percentage of area stained for CD45 in the endocervix did not differ between groups (patients 4.4%, range 1.1-28.3%; controls 3.2%, range 2.0-13.0%, p=1.00).

**Conclusion:** In this preliminary analysis, pSS patients show a lower vaginal health index and a higher percentage of subepithelial infiltrate in the vagina compared to controls, while endocervical histopathology did not differ. Detailed phenotypic evaluation of the infiltrate will follow.
Disclosure: J. F. van Nimwegen, None; K. van der Tuuk, None; E. R. Klinkert, None; E. A. Haacke, None; F. G. M. Kroese, None; H. Hollema, None; M. J. Mourits, None; H. Bootsma, None.


Abstract Number: 574

Is Elastography a New Tool to Differentiate Sjögren Syndrome to Sicca Syndrome?: Results of the Elsa (elastography of salivary glands) Study

Sandrine Jousse-Joulin1, luc Bressollette2, thibault depinoy3, guillermo carvajal Alegria3, Divi Cornec4, Thierry Marhadour5, Dewi Guellec6, Valérie Devauchelle-Pensec7 and Alain Saraux8, 1Rheumatology, CHu La cavle Blanche, Brest, France, 2Doppler unit, Cavale Blanche hospital, brest, France, 3rheumatology department, cavale blanche hospital, brest, France, 4CHU Brest, Brest, France, 5Rheumatology, CHU La Cavale Blanche, Brest, France, 6Rheumatology, CHU Brest, Brest, France, 7Rheumatology, Brest university medical school, EA 2216, Lab Ex, INSERM, IGO,UBO and CHU de la Cavale Blanche,, Brest, France, 8Rheumatology, Brest University Medical School Hospital, Brest, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Sjögren's Syndrome Poster I: Translational Research
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Ultrasonography (US) has been developed in salivary glands (SG) and particularly in primary Sjögren syndrome (pSS) for 10 years. However, the training curve is long and the reliability is not completely achieved (1). A new tool procedure has
been developed to study the elasticity of the tissue parenchyma using elastography and could be implemented in the evaluation of SGUS pSS patients. The objective was to evaluate SGUS using grey scale (GS) and the elasticity salivary glands parenchyma using elastography to differentiate pSS from sicca syndrome (SS) patients in a longitudinal consultation of sicca syndrome in Doppler Unit of Brest (France).

**Methods:** 63 patients complaining of sicca syndrome were enrolled in the ELSA study. At inclusion, all patients underwent a standardized workup including a clinical evaluation, laboratory tests, SG histology, SGUS and elastography. Immunological testing included: anti-nuclear antibodies, anti-SSA (recognizing both Ro 52 and 60 kDa), anti SSB, native anti-DNA, ANCA, rheumatoid factors and anti-CCP. A Toshiba Applio machine was used to evaluate in GS SGUS parenchyma and elastography -elastometry. The 6 main SG were examined in US according to previous scoring (2) elastography (with color map) and elastometry (in cm/sec) and left parotid gland (USLPG), left submandibular gland (USLSMG), left sublingual gland (USLSLG), right parotid gland, (USRPG) right submandibular gland (USRSMG), right sublingual gland (USRSLG).

**Results:** 15 patients fulfilled the AECG criteria. The clinical characteristics of the patients in terms of ocular dryness and shirmer test were not significant between pSS and Sicca patients. There was a significant difference (p= 0.04) concerning oral dryness (p=0.04), immunological datas: Antinuclear antibodies and anti SSA and minor salivary glands biopsy (p=0.007). We found significant differences between the 2 groups in GS for the USLPG (p=0.021) and USLSMG (p=0.05). Evaluation of sublingual glands using US in grey scale and elastometry of the 6 SG showed no significant differences between the two groups.

**Conclusion:** Grey scale SGUS seems to be more sensitive to differentiate pSS to Sicca patients compared to elastometry. US of sublingual glands showed no involvement in the echostructural damage in pSS patients and suggest not examining these glands in the USpSS evaluation. Elastometry has been described to be a new tool and might be added as a new imaging technique to ultrasonography in pSS patients (3). However, ELSA study results showed no differences between pSS and Sicca patients. We need to follow the evolution of the Sicca population with US in GS and elastometry to detect potential echostrural parenchymal damage which might not yet be present at inclusion.

**Disclosure:** S. Jousse-Joulin, None; L. Bressollette, None; T. depinoy, None; G. carvajal Alegria, None; D. Cornec, None; T. Marhadour, None; D. Guellec, None; V. Devauchelle-Pensec, None; A. Saraux, None.

**Abstract Number:** 575

**Distinct Clinical and Immunological Features of Anti-Centromere Antibody Positive Primary Sjögren’s Syndrome: A Single Center Cross-Sectional Cohort Study**

Masako Tsukamoto1,2, Katsuya Suzuki1, Noriyuki Seta2 and Tsutomu Takeuchi1, 1Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, 2Department of Internal Medicine, Tokyo Dental College Ichikawa General Hospital, Ichikawa, Japan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Sjögren's Syndrome Poster I: Translational Research

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Anti-centromere antibody (ACA) positive Sjögren’s syndrome (SS) is considered as a subtype in SS. Recent international collaborative large scale cohort study highlighted several clinical features such as Raynaud’s
phenomenon, sclerodactyly and extra glandular dysfunction (Arthritis Care Res. 2016). Assessment of ACA is potentially valuable for definitive diagnosis of this subtype and medical management in a certain number of patients uncovered by current 2015 ACR/EULAR classification criteria. However, enough information of clinical and immunological features of ACA positive SS has not been accumulated and clinical significance of ACA in SS may not be fully established. The aim of this study is to clarify clinical and immunological features of ACA positive SS.

Methods: All patients with primary SS (pSS) who visited to our Division of Rheumatology at Keio University Hospital in Tokyo between May 1995 and December 2016 were enrolled. Clinical information and immunological tests including immunoglobulin (Ig) and serum autoantibodies were collected and statistically analyzed.

Results: Five hundred and ninety nine patients were clinically classified as pSS (female: 93%, mean age: 55 ± 15). They were divided into 4 groups by serum ACA and anti-SS-A antibody status. Only discrete-speckled pattern in anti-nuclear antibody (ANA) test and/or anti-centromere antibody positive (ACA alone) were detected in 39 patients (6.5%), while only anti-SS-A antibody with no ACA (SS-A alone) were detected in 449 patients (75.0%). Number of patients with both ACA and SS-A (Double positive) was 40 (6.7%), while 67 patients had neither ANA nor SS-A (Seronegative). Then we statistically compared these 4 groups. The proportions of Raynaud’s phenomenon or sclerodactyly were higher in ACA alone and Double positive groups (p<0.01 or p<0.01). The proportion of dryness was no difference among 4 groups. The proportions of increase of serum IgG or IgA were 15% or 7% in ACA alone group, 61% or 20% in SS-A alone group, 50% or 28% in Double positive group and 22% or 4% in Seronegative group (p<0.01 or p<0.01). Existence of anti-SS-A antibody, not ACA associated to high concentration of IgG or IgA, while there was no difference between 4 groups as IgM (p=0.40). Regarding C3, C4 or CH50, there were no differences among 4 groups. Remarkably, the proportion of leukocytopenia in ACA alone group was significantly higher than the others (p=0.02). As compared with pulmonary, cardiac or articular involvements, no differences were found among 4 groups. Importantly the proportion of patients who had facial erythema was significantly lower in ACA positive SS (p<0.01).

Conclusion: Our large-scale study identified distinct characteristics of ACA-positive SS patients different from anti-SS-A/Ro antibody positive or seronegative SS patients in Japanese population.

Disclosure: M. Tsukamoto, None; K. Suzuki, None; N. Seta, None; T. Takeuchi, None.

Abstract Number: 576

Immunosignature-Based Diagnosis and Prediction of Therapeutic Response Enables Retrospective Patient Stratification in a Phase IIa Clinical Trial for VAY736 in Primary Sjögren’s Syndrome

Robert Gerwien1, Theodore M. Tarasow2, Jonathan Melnick2, Anna Lei3, Arvind Kinhikar4, Julie Doucet5, Remi Kazma5, Paul Maguire4, Irina Koroleva6, Giulio Macchiarella4, Alexandre Avrameas5, Marie-Anne Valentin5, Stephen Oliver5 and Alessandra Vitaliti5, 1HealthTell, Inc, san ramon, CA, 2HealthTell, Inc., San Ramon, CA, 3Health Tell, San Ramon, CA, 4Novartis, Cambridge, MA, 5Translational Medicine, Novartis Institutes for Biomedical Research, Basel, Switzerland, 6Novartis Institutes for BioMedical Research, Novartis Pharma AG, Cambridge, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Sjögren’s Syndrome Poster I: Translational Research
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM
**Background/Purpose:** Although patient stratification can improve the success rate of clinical trials, efforts to apply this strategy to autoimmune studies such as Sjögren’s syndrome are hindered by the nature of this disease area, intra-disease patient diversity, difficulties around diagnostic criteria and response metrics, as well as the lack of clear biological mechanisms to explain drug efficacy. In some of the diseases, the nexus of these variables is B-cell biology.

**Methods:** The ImmunoSignature Technology — the semi-quantitative profile of antibody binding specificity — is designed to enable patient stratification in autoimmune disease trials. HealthTell’s unique approach to peptide microarray fabrication, combining silicon wafer-based photolithographic synthesis with optimized peptide coupling chemistry and MALDI-based quality control, permits high-throughput ImmunoSignatureing with exceptional scalability, reproducibility and accuracy, making it broadly-applicable to diagnostic, clinical and discovery applications. In this study, HealthTell’s ImmunoSignature platform was applied to key steps in a clinical trial (NCT02149420) with VAY736, an anti-B cell activating factor (BAFF) receptor monoclonal antibody, in patients with primary Sjögren’s Syndrome.

**Results:** The ImmunoSignature distinguished Sjögren’s patients from healthy volunteers with an AUC of 0.84, with individual peptides showing a correlation to the EULAR Sjögren’s syndrome disease activity index (ESSDAI) of up to 0.74 (Pearson’s r). Using serum collected prior to treatment, the ImmunoSignature predicted which patients will respond to study drug with a drop in ESSDAI of ≥3, yielding an AUC of 0.75 from a small study (18 treated patients with 9 placebo). Response to therapy performance was also measured using sera drawn 12 weeks post treatment and resulted in an AUC of 0.84. Using the 12-week sample, principle component analysis correctly segregated drug-treated responders from drug-treated non-responders, placebo non-responders and the single placebo-responsive patient. Alignment of the peptides that comprise these contrasts to the human proteome yields not only known Sjögren’s autoantigens but also potential novel biomarkers.

**Conclusion:** The Immunosignature identified in this study is important for disease diagnosis and explanation of study drug response.

**Disclosure:** R. Gerwien, HealthTell, 3; T. M. Tarasow, HealthTell, 3, HealthTell, 1; J. Melnick, HealthTell, 3, HealthTell, 1; A. Lei, HealthTell, 3; A. Kinhikar, Novartis Pharmaceutical Corporation, 3; J. Doucet, Novartis Pharma AG, 3; R. Kazma, Novartis Pharma AG, 3; P. Maguire, Novartis Pharmaceutical Corporation, 3; I. Koroleva, Novartis Pharmaceutical Corporation, 3; G. Macchiarella, Novartis Pharmaceutical Corporation, 3; A. Avrameas, Novartis Pharma AG, 3; M. A. Valentia, Novartis Pharma AG, 3; S. Oliver, Novartis Pharma AG, 3; A. Vitaliti, Novartis Pharma AG, 3.

**Abstract Number:** 577

**The Value of C-Reactive Protein As a Predictor of Radiographic Spinal Progression Is Strongly Dependent on β-Fibrinogen and Factor XIII a-Subunit Genotypes in Patients with Axial Spondyloarthritis**

Denis Poddubnyy\(^1\),\(^2\), Christian Schwedler\(^2\), Hildrun Haibel\(^2\), Martin Rudwaleit\(^2\),\(^3\), Joachim Sieper\(^2\) and Berthold Hoppe\(^4\),

\(^1\)German Rheumatism Research Centre, Berlin, Germany, \(^2\)Charité Universitätsmedizin Berlin, Berlin, Germany, \(^3\)Klinikum Bielefeld Rosenhöhe, Bielefeld, Germany, \(^4\)Unfallkrankenhaus Berlin, Berlin, Germany

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM
Background/Purpose:

It has been shown in the past that inflammatory activity (i.e., elevated C-reactive protein) predicts radiographic spinal progression in patients with axial spondyloarthritis (axSpA). Fibrinogen and factor 13 genotypes have been recently identified as factors modifying inflammatory response due to differences in the properties of the fibrin network related to particular genotype constellations [1].

The objective of the current study was to investigate the association between α-fibrinogen (FGA), β-fibrinogen (FGB) and factor XIII A-subunit (F13A) genotypes with the level of CRP and radiographic spinal progression over 2 years in patients with early (up to 10 years symptom duration) axial SpA.

Methods:

Altogether 207 patients with early axial SpA from the German Spondyloarthritis Inception Cohort (GESPIC) were included. Clinical data and CRP level were collected at baseline and every 6 months thereafter. A time-averaged CRP level over 2 years (up to 5 time-points) was calculated. Structural damage in the spine was assessed on spinal radiographs at baseline and after two years according to the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). Significant radiographic spinal progression was defined as the worsening of the mSASSS by ≥2 points over two years. FGB −455G>A (rs1800790), FGA T312A (rs6050) and F13A V34L (rs5985) genotypes were determined with available samples using allele-specific primer pairs.

Results:

No clear association between studied genotypes and the time-averaged CRP or radiographic spinal progression could be found. However, the effect of CRP in the predictive model for radiographic spinal progression was strongly dependent on FGB genotype (table): the odds ratio (OR) for the elevated time-averaged CRP as a predictor of the mSASSS worsening by ≥2 points over two years was 5.47 (95%CI 1.51-19.79) in FGB −455GG (wild-type) carriers, while there was no such effect of CRP in carriers of the alternative (A) allele, OR=0.99 (95%CI 0.20-4.92). Interestingly, this effect modification was dependent also on F13A genotype: in carriers of the wild-type genotypes of both FGB (−455GG) and F13A (34VV), n=65, the OR for the elevated CRP as a predictor of radiographic spinal progression was 10.8 (95%CI 1.07-108.0), while alternative allele carriers (F13A 34L) showed a weak and non-significant association of CRP with radiographic spinal progression even in the presence of the wild-type FGB genotype (n=59): OR=2.01 (95%CI 0.34-12.04). F13A itself as well as FGA genotypes showed no effect-modifying effects on CRP.

Conclusion:

The predictive value of CRP regarding radiographic spinal progression seems to be dependent on FGB and F13A genotypes. This might also suggest that CRP is not a good indicator of inflammation in individuals with a specific genetic background.

References:

Table. The association between C-reactive protein and radiographic spinal progression in relation to β-fibrinogen genotype in patients with early axSpA.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Model 1, unstratified, n=207 OR (95% CI)</th>
<th>Model 2, FGB -455GG, n=124 OR (95% CI)</th>
<th>Model 3, FGB -455GA/AA, n=83 OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time-averaged CRP over 2 years, &gt;6 vs. ≤6 mg/l</td>
<td>2.52 (1.02-6.24)</td>
<td>5.47 (1.51-19.79)</td>
<td>0.99 (0.20-4.92)</td>
</tr>
<tr>
<td>Syndesmophytes, present vs. not present</td>
<td>4.78 (1.94-11.56)</td>
<td>3.36 (1.04-10.62)</td>
<td>12.12 (2.10-70.07)</td>
</tr>
<tr>
<td>Current smoking, present vs. not present</td>
<td>2.36 (1.00-5.69)</td>
<td>1.42 (0.46-4.39)</td>
<td>6.04 (1.17-31.07)</td>
</tr>
</tbody>
</table>

All models are adjusted for sex and for the presence of the definite radiographic sacroiliitis according to the modified New York criteria.

Disclosure: D. Poddubnyy, None; C. Schwedler, None; H. Haibel, None; M. Rudwaleit, None; J. Sieper, None; B. Hoppe, None.


Abstract Number: 578

**Added Value of Biomarkers Compared to Routine Clinical Parameters for the Prediction of Radiographic Spinal Progression in Axial Spondyloarthritis**

Lorraine Tietz\(^1\), Lien Le\(^2\), Agnes Hartl\(^1\), Martin Rudwaleit\(^1,3\), Joachim Sieper\(^1\), Ulrich Mansmann\(^2\) and **Denis Poddubnyy**\(^1,4\)
\(^1\)Charité Universitätsmedizin Berlin, Berlin, Germany, \(^2\)Ludwig-Maximilian University, Munich, Germany, \(^3\)Klinikum Bielefeld Rosenhöhe, Bielefeld, Germany, \(^4\)German Rheumatism Research Centre, Berlin, Germany

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthopathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Structural damage in the spine is an important determinant of the functional status and spinal mobility in axial spondyloarthritis (axSpA). Already present syndesmophytes, elevated C-reactive protein, cigarette smoking, and to a lesser extent male sex are routine clinical parameters predicting radiographic spinal progression in axSpA. In the last years, several biomarkers with a predictive value for radiographic spinal progression were identified. It is, however, not known, if biomarkers have a meaningful added value over clinical parameters in prediction of radiographic spinal progression in axSpA.

The objective of the study was to examine whether adding biomarkers to the routine clinical parameters would improve prediction of radiographic spinal progression in axSpA.

Methods:
Altogether 120 patients with radiographic axSpA who completed a 2-year clinical and radiographic follow-up in the ENRADAS trial were included. Structural damage in the spine was assessed on spinal radiographs at baseline and year 2 according to the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). Radiographic spinal progression was defined as a worsening of the mSASSS by ≥2 points after 2 years. Clinical predictors of radiographic spinal progression at baseline included syndesmophytes, elevated (>5mg/L) CRP, cigarette smoking, and sex. Serum biomarkers measured at baseline included: matrix metalloproteinase-3, vascular endothelial growth factor (VEGF), calprotectin, leptin, high molecular weight adiponectin (HMW-APN), osteoprotegerin, sclerostin, N-terminal telopeptide, procollagen type II N-terminal propeptide, and serum amyloid A (SAA).

**Results:** Repeated cross-validation analysis revealed two biomarker combinations: (1) Leptin + HWM-APN + VEGF + Sclerostin and (2) Leptin + HWM-APN + VEGF + SAA with added predictive value compared to the clinical model (syndesmophytes, smoking, elevated CRP, and sex). Adding these biomarker combinations to the clinical model resulted in improvement of the predictive value reflected by the Area Under the Curve (AUC): AUC_{Clinical+Biomarkers(1)}=0.765 (95%CI 0.646-0.876) and AUC_{Clinical+Biomarkers(2)}=0.775 (95%CI 0.674-0.876) vs. AUC_{Clinical}=0.656 (95%CI 0.546-0.766) – figure. The average prediction error (APE) of the Clinical+Biomarker(1) and Clinical + Biomarker(2) models were 0.227 and 0.229, respectively as compared to the APE for the pure clinical model (0.248). These findings were supported by the results of stability analyses.

**Conclusion:**

Biomarkers are able to improve prediction of radiographic spinal progression in axSpA if used in addition to the clinical parameters, but the added value seems to be rather small.

**Figure:** Receiver operator curve analyses of clinical vs. clinical + biomarker models for prediction of radiographic spinal progression (mSASSS worsening ≥2 points after 2 years) in axial SpA

---

**Disclosure:** L. Tietz, None; L. Le, None; A. Hartl, None; M. Rudwaleit, None; J. Sieper, None; U. Mansmann, None; D. Poddubnyy, None.


Abstract Number: 579

**Circulating MiR-145 As a Marker of Therapeutic Response to Anti-TNF Therapy in Patients with Ankylosing Spondylitis**
Klára Prajzlerová, Veronika Hruskova, Martin Komarc, Šárka Forejtová, Karel Pavelka, Jiri Vencovsky, Ladislav Senolt and Maria Filkova, 1Institute of Rheumatology and Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, Prague, Czech Republic, 2Department of Anthropometrics and Methodology, Faculty of Physical Education and Sport, Charles University, Prague, Czech Republic, Prague, Czech Republic, 3Institute of Rheumatology, Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, Prague, Czech Republic

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The altered expression of miRNAs contributes to the pathophysiology of inflammatory conditions. In addition, circulating miRNAs may serve as promising therapeutic and prognostic biomarkers. Our aim was to investigate the effect of anti-TNF therapy on the levels of circulating miRNAs in patients with ankylosing spondylitis (AS).

Methods: Our study included 19 AS patients. Disease activity scores (ASDAS-CRP, BASDAI) and laboratory parameters of disease activity were obtained at baseline (M0), month 3 (M3) and 12 (M12) after initiation of anti-TNF therapy. Total RNA was isolated from plasma using miRNeasy Serum/Plasma Kit (Qiagen). A comprehensive analysis of miRNAs was performed using TaqMan Low Density Array (TLDA) in 3 patients at M0, M3 and M12. dCt method was used for relative quantification: $dCt = C(t(miRNA)) - C(t(array average))$. Seventeen miRNAs with $\geq 1.5$-fold change in the expression prior and after the therapy initiation in all 3 samples were selected for next validation using single assays. The levels of miRNAs in validation measurements were normalized to an average of 3 spike-in controls of C. elegans origin: $dCt = C(t(spike-in average)) - C(t(miRNA))$. Data were analyzed using ANOVA with Bonferroni corrections and Spearman’s correlation coefficient.

Results: All AS patients had high disease activity (BASDAI 6.3±1.5, ASDAS 4.1±0.7, CRP 32.5±28.9mg/l, ESR 40.1±19.6mm/h) prior commencing anti-TNF therapy with a good therapeutic response at M3 (BASDAI 2.8±1.2, ASDAS 2.15±0.65, CRP 9.8±13.6mg/l, ESR 15.2±21.3mm/h, $p<0.001$ for all comparisons) and M12 (BASDAI 2.3±1.7, ASDAS 1.9±0.9, CRP 7.4±9.6mg/l, ESR 13.7±12.2mm/h, $p<0.001$ for all comparisons).

Out of all 380 miRNAs analyzed by TLDA, 125 miRNAs were detected in all samples, 148 miRNAs were detected at M0, 154 at M3 and 151 at M12. Validation of 17 selected miRNAs confirmed significant downregulation of miR-145 at M3 (TLDA 1.59-change; single assays 1.62-change, $p=0.024$), but the downregulation did not reach statistical significance at M12 (TLDA 1.46-change; single assays 1.11-change, $p>0.05$)

At baseline, miR-145 positively correlated with VAS ($r=0.450$, $p=0.048$). In addition, the decrease in miR-145 expression from M0 to M3 significantly correlated with disease activity improvement over time from M3 to M12 as per BASDAI ($\Delta$BASDAI M3/12=−0.50±1.93, $r=0.670$, $p=0.002$) and ASDAS scores ($\Delta$ASDAS M3/12=−0.28±0.70, $r=0.614$, $p=0.005$) and VAS at M12 ($r=0.528$, $p=0.020$). In line with this observation, high levels of miR-145 at M3 significantly correlated with disease activity worsening based on an increase in ASDAS from M3 to M12 ($r=0.595$, $p=0.007$) and higher ASDAS ($r=0.535$, $p=0.018$) and VAS ($r=0.564$, $p=0.012$) at M12.

Conclusion: We propose that an early change in miR-145 levels may be a predictor of future outcome of AS patients as it’s early decrease after anti-TNF initiation correlated with further disease activity improvement. These data, similarly to previous studies showing correlation of miR-145 with CRP and pro-inflammatory IL-6 (Cell Biochem Funct. 2015;33(5)), suggest potential use of circulating miRNAs as biomarkers of treatment response in AS.

Acknowledgement: Grant projects 17-33127A and SVV 260373.
Tenascin-C, a TLR 4 Endogenous Ligand Levels Are Increased in Ankylosing Spondylitis

Latika Gupta, Shruti Bhattacharya and Amita Aggarwal, Clinical Immunology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Monocytes of patients with Ankylosing Spondylitis (AS) over-express Toll-like receptor (TLR) 4 on their monocytes. Tenascin-C (TNC) is an extracellular-matrix-glycoprotein and acts as an endogenous TLR4 ligand. Thus we studied the serum and synovial fluid levels of TNC in adults with AS.

Methods:
TNC was measured in serum of 36 AS patients (ASAS 2009 criteria) and 10 healthy controls by ELISA. 22 patients were followed-up after 3 months of standard of care treatment. Five paired serum-synovial fluid samples were also analyzed. Disease activity was assessed by BASDAI, ASDAS, tender and swollen joint count; enthesitis score, ESR and CRP. All values are in median (IQR).

Results:
Median age was 30 (20-35) years and disease duration 5.5(1.3-10) years. 31 were male and 5 female. 25 cases had peripheral arthritis (69.5%). Median BASDAI was 5.3(3.3-6.7). HLA B27 was positive in 34 (94.5%) cases.

Median serum Tenascin C levels were higher in AS [554.6ng/ml] as compared to healthy controls [32.88 ng/ml, p<0.00001]. Serum TNC levels correlated with ASDAS ESR [r=0.367, p=0.028] and ESR [r=0.39, p=0.035]; but not with other disease activity measures. In patients with disease duration less than 5 years (early disease) serum levels had better correlation with ESR [r=0.59, p=0.009] and CRP [r=0.479, p=0.044]. On ROC analysis for active (PhGA≥6) vs. inactive (PhGA≤4) disease, TNC (AUC=0.60) performed as well as CRP (AUC=0.65) and ESR (AUC=0.73). The synovial fluid levels [11.61(5.99-176.9) ng/ml] were lower than in the serum [627.4 (488.5-779.1) ng/ml, p=0.008].

TNC levels fell with treatment [630.8 ng/ml to 376.4 ng/ml p=0.0006] in treatment responders (n=11) but not in non-responders (n=11) [562.3 to 445.6,p=0.33].

Conclusion:
Serum TNC levels are significantly raised in AS and can serve as marker of inflammation in early disease. Treatment reduces the TNC levels, probably due to control of disease activity.
Disclosure: L. Gupta, none; S. Bhattacharya, None; A. Aggarwal, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/tenascin-c-a-tlr-4-endogenous-ligand-levels-are-increased-in-ankylosing-spondylitis

Abstract Number: 581

**Diagnostic Value of Anti-CD74 Antibodies in Early Axial Spondyloarthritis: Data from the Spondyloarthritis Caught Early (SPACE) Cohort**

Janneke de Winter¹, Marleen van de Sande¹, Niklas Thomas Baerlecken², Inger Berg³, Roberta Ramonda⁴, Désirée van der Heijde⁵, Floris van Gaalen⁶, Torsten Witte⁷ and Dominique Baeten¹,⁸, ¹Clinical Immunology and Rheumatology, Amsterdam Rheumatology and immunology Center, Academic Medical Center/University of Amsterdam, Amsterdam, Netherlands, ²Rheumatology, Private Practice, Cologne, Germany, ³Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, ⁴Rheumatology Unit, Department of Medicine DIMED, University of Padova, Padova, Italy, ⁵Rheumatology, Leiden University Medical Center, Leiden, Netherlands, ⁶Leiden University Medical Center, Leiden, Netherlands, ⁷Clinical Immunology and Rheumatology, Medical University Hannover, Hanover, Germany, ⁸UCB Pharma, Slough, United Kingdom

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

**Background/Purpose:**

Anti-CD74 IgG antibodies are reported to be elevated in serum of patients with axial spondyloarthritis (axSpA). This study aimed to assess the diagnostic value of anti-CD74 antibodies to discriminate between early axSpA and non-SpA in early back pain patients.

**Methods:**

Using ELISA, we first confirmed the elevation of anti-CD74 IgG and IgA serum antibodies in patients with radiographic axSpA (ankylosing spondyloarthritis, (AS)) (n=138) when compared to healthy controls (n=57). Next, we tested their diagnostic value in patients with early axSpA (n=274) and non-SpA back pain controls (n=319) from the SPondyloArthritis Caught Early (SPACE) cohort.

**Results:**

Median anti-CD74 IgG antibodies (OD) were higher in AS patients than in healthy controls (0.70 vs. 0.51, p<.0001) and present in 79.7% of AS patients vs. 43.9% of healthy controls (p<0.0001). Anti-CD74 IgG antibody levels (OD) did not differ between axSpA patients and non-SpA back pain controls (0.50 vs. 0.52, p=0.152) and were present in 46.4% of the axSpA patients vs. 47.9% of the non-SpA back pain controls (p=0.713). Median anti-CD74 IgA antibodies (OD) were higher in AS patients than in healthy controls (0.31 vs. 0.20, p<0.0001) and present in 28.5% of AS patients vs. 5.3% of healthy controls (p=0.0001). In the SPACE cohort, anti-CD74 IgA antibodies (U/mL) were higher in axSpA patients than in non-SpA back pain controls (19.92 vs. 14.02, p<0.0001) and present in in 54.7% vs. 37.0% of the axSpA patients vs. non-SpA back pain controls (p=0.0001), respectively. This resulted in a PPV of 58.8% and a NPV of 59.1%. In a multivariate logistic regression model including anti-CD74 IgA and total serum IgA, total serum IgA was associated with a diagnosis of axSpA (Exp(B) 1.19, p<0.0001) whereas anti-CD74 IgA was not (Exp(B) 1.01, p=0.332).

**Conclusion:**
Anti-CD74 IgG and anti-CD74 IgA were elevated in AS versus healthy controls. Only anti-CD74 IgA is elevated in patients with early axSpA versus chronic back pain controls of the SPACE cohort. In the SPACE cohort, these differences disappear in a multivariate analysis with total IgA levels and have limited diagnostic value in these early back pain patients. Other biomarker or biological features of anti-CD74 IgA, including prediction/contribution to radiographic progression, should be investigated.

**Disclosure:** J. de Winter, None; M. van de Sande, Takeda, Tillots, MSD, Abbvie, novartis, boeringer ingelheim, 8, Takeda, Tillots, MSD, Abbvie, novartis, boeringer ingelheim, 2; N. T. Baerlecken, None; I. Berg, None; R. Ramonda, None; D. van der Heijde, None; F. van Gaalen, None; T. Witte, None; D. Baeten, UCB, 3.


**Abstract Number:** 582

**Low Dose Computed Tomography Detects More Progression of Bone Formation in Comparison to Conventional Radiography in Patients with Ankylosing Spondylitis**

Anoek de Koning¹, Freek de Bruin², Rosaline van den Berg³, Sofia Ramiro⁴, Xenofon Baraliakos⁵, Jürgen Braun⁵, Floris van Gaalen³, M. Reijnierse⁶ and Désirée van der Heijde⁷, ¹Rheumatology, Leiden University Medical Center, Leiden, Netherlands, ²LUMC, Leiden, Netherlands, ³Rheumatology, LUMC, Leiden, Netherlands, ⁴Rheumatology, Department of Rheumatology, LUMC, Leiden, Netherlands, ⁵Rheumazentrum Ruhrgebiet, Herne, Germany, ⁶Department of Radiology, Leiden University Medical Center, Leiden, Netherlands, ⁷Leiden University Medical Center, Leiden, Netherlands

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** A newly developed scoring method for low dose CT (ldCT) of the whole spine, CT Syndesmophyte Score (CTSS), has shown good inter-reader reliability and sensitivity to detect changes in bone formation over 2 years in Ankylosing Spondylitis (AS) patients¹. Next step in validation is the comparison of assessment of bone formation on ldCT with conventional radiographs (CR).

**Methods:** Patients from the Sensitive Imaging in Ankylosing Spondylitis cohort were analysed. Inclusion criteria: mNY-criteria+, ³1 syndesmophyte on cervical/lumbar spine CR and _1 inflammatory lesions on MRI-spine. Patients had baseline and two-year CR of the lateral cervical and lumbar spine and whole spine ldCT (approximately 4mSV). Two readers independently assessed CR and ldCT in separate sessions. Images were paired per patient, blinded to time order, patient information, and results of the other imaging technique. CR was assessed using mSASSS. On ldCT, syndesmophytes were scored in coronal and sagittal planes, assessing eight ÔquadrantsÕ per vertebral unit (VU). Scores for syndesmophytes according to the CTSS were: absent=0, <50% of intervertebral disc height (IVDH)=1, _50% of IVDH=2 or IVDH bridging=3. Formation of new syndesmophytes (CR score 0 ³ 2/3, CTSS 0 ³ 1/2/3) and growth of existing syndesmophytes (CR score 2³, CTSS 1 ³ 2/3, or 2³) and the combination of new or growing syndesmophytes was calculated per corner/quadrant. Consensus about each outcome was defined by agreement of readers on the same corner/quadrant. The number of syndesmophytes on CR and CT was compared by level. Level 1: upper four quadrants of a VU on ldCT and upper corner on CR. Level 2: lower four quadrants on ldCT and lower corner on CR. Data of CR and ldCT was compared per reader and for the consensus score.
Results: Fifty patients (mean age 50 years; 84% male; 86% HLA-B27+) were included in the analysis. In all comparisons, ldCT detected more patients with progression (table 1). This is especially apparent in case of growth and for cut-offs of a higher number of syndesmophytes per patient. E.g. using the consensus score, 30% of the patients showed bony proliferation (new or growing syndesmophytes) at ³3 sites on ldCT compared with only 6% on CR. ldCT detected more syndesmophytes in all sections of the spine, with most syndesmophytes occurring in the thoracic spine (figure 1).

Conclusion: Whole spine ldCT is more sensitive in assessing the formation and growth of syndesmophytes than CR, which is limited to cervical and lumbar spine and is a promising method of assessment for clinical research of AS.


Table 1. Comparison of CR and ldCT per reader and consensus* for the formation or growth of syndesmophytes in 50 patients with ankylosing spondylitis.

<table>
<thead>
<tr>
<th></th>
<th>Reader 1</th>
<th>Reader 2</th>
<th>Consensus</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CR</td>
<td>ldCT</td>
<td>CR</td>
</tr>
<tr>
<td></td>
<td>n(%)</td>
<td>n(%)</td>
<td>n(%)</td>
</tr>
<tr>
<td>New syndesmophytes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>³1</td>
<td>27 (54)</td>
<td>43 (86)</td>
<td>30 (60)</td>
</tr>
<tr>
<td>³2</td>
<td>14 (28)</td>
<td>38 (76)</td>
<td>14 (28)</td>
</tr>
<tr>
<td>³3</td>
<td>6 (12)</td>
<td>32 (64)</td>
<td>8 (16)</td>
</tr>
<tr>
<td>Growth of syndesmophytes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>³1</td>
<td>10 (20)</td>
<td>35 (70)</td>
<td>7 (14)</td>
</tr>
<tr>
<td>³2</td>
<td>8 (16)</td>
<td>36 (52)</td>
<td>6 (12)</td>
</tr>
<tr>
<td>³3</td>
<td>2 (4)</td>
<td>23 (46)</td>
<td>4 (8)</td>
</tr>
<tr>
<td>New syndesmophytes or growth of syndesmophytes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>³1</td>
<td>28 (56)</td>
<td>45 (90)</td>
<td>33 (66)</td>
</tr>
<tr>
<td>³2</td>
<td>18 (36)</td>
<td>42 (82)</td>
<td>19 (38)</td>
</tr>
<tr>
<td>³3</td>
<td>12 (24)</td>
<td>36 (72)</td>
<td>12 (24)</td>
</tr>
</tbody>
</table>

Results are presented as the number (%) of patients with ³1, ³2 and ³3 newly formed syndesmophytes and syndesmophytes that grew, as well as for the combination of new formation or growth. *Both readers agree about the formation or growth of a syndesmophyte at the same vertebral corner. CR: conventional radiography, ldCT: low-dose computed tomography.
Disclosure: A. de Koning, None; F. de Bruin, None; R. van den Berg, None; S. Ramiro, None; X. Baraliakos, None; J. Braun, None; F. van Gaalen, None; M. Reijnierse, None; D. van der Heijde, None.


Abstract Number: 583

**Associations of Changes of Radiographic Disease and Spinal Mobility Measures in Ankylosing Spondylitis**

Mark Hwang\textsuperscript{1,2,3}, Michael Weisman\textsuperscript{4}, MinJae Lee\textsuperscript{5}, Lianne S. Gensler\textsuperscript{6}, Matt Brown\textsuperscript{7}, Amirali Tahanan\textsuperscript{5}, Laura A. Diekman\textsuperscript{8}, Thomas Learch\textsuperscript{9}, Seth Eisen\textsuperscript{10}, Mohammad H. Rahbar\textsuperscript{5}, Michael Ward\textsuperscript{11} and John D. Reveille\textsuperscript{12}, \textsuperscript{1}Medicine, University of Texas-McGovern Medical School, Houston, TX, \textsuperscript{2}Internal Medicine-Rheumatology, University of Texas-McGovern Medical School, Saint Louis, MO, \textsuperscript{3}Washington University at Saint Louis School of Medicine, Saint Louis, MO, \textsuperscript{4}Cedars-Sinai Medical Center Division of Rheumatology, Los Angeles, CA, \textsuperscript{5}Biostatistics/Epidemiology/Research Design (BERD) Core | Center for Clinical and Translational Sciences, University of Texas-McGovern Medical School, Houston, TX, \textsuperscript{6}Medicine/Rheumatology, UCSF, San Francisco, CA, \textsuperscript{7}Translational Genomics Group, Institute of Health and Biomedical Innovation, Queensland University of Technology, Translational Research Institute, Brisbane, Australia,
Metrology indices aimed at assessing spinal mobility in ankylosing spondylitis (AS) patients are used in clinical trials and clinical practice to assess disease severity and progression. The purpose of this study was to examine the association between changes in spinal mobility and radiographic disease in AS patients enrolled in a longitudinal outcome study.

Methods:

AS patients meeting modified New York Criteria with at least 2 sets of radiographs for assessment of modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) spaced at least two years apart were included. Spinal mobility measurements conducted over the same interval as the sets of radiographs included occiput-to-wall distance, cervical rotation, cervical lateral bending, Schober's and lateral lumbar bending (mean number of sets of mobility measurements per patient, 2.7±0.9). Because some patients had cervical spine films not visualizing the lower segments, the cervical and lumbar spine assessments were analyzed separately. Visits were categorized into 3 groups based on changes of their metrology between visits: improving, worsening or no change in spinal mobility. Longitudinal multivariable negative binomial regression analyses using generalized estimating equation accounting for the correlation of repeated measures over time were conducted to assess associations between each of the respective spinal mobility indices and mSASSS progression. We adjusted each analysis for baseline mSASSS, study sites and clinical/demographic variables (gender, education, disease duration, current smoking status, longitudinal Bath Ankylosing Spondylitis Disease Activity scores, baseline CRP levels, and Patient Global Assessment).

Results:

523 patients met these criteria for the cervical spine analyses and 548 for the lumbar spine analyses. The median patient follow up time was 4.08 years (IQR= [2.17, 6.58]) for the cervical spinal and 4.17 years (IQR= [2.17, 6.67]) for the lumbar spinal measurements. Data summarized in Based on multivariable models, increases in occiput to wall distance were significantly associated with increased cervical mSASSS scores compared to no change (adjusted rate ratio (RR) =1.95; p=0.02) and no change in occiput to wall distance was negatively associated with increasing mSASSS compared to decreased occiput to wall distance (adjusted RR= 0.49; p<0.01). Despite a weak trend, no significant differences were noted when comparing positive vs. negative change in lateral cervical bending, cervical rotation, Schober or lateral lumbar bending assessments and changes in the mSASSS.

Conclusion:

Significant associations were observed between longitudinal changes in occiput to wall and mSASSS scores but not between cervical (lateral cervical bending, cervical rotation measures) or lumbar spinal mobility measures (Schober's, lateral lumbar bending). The occiput-to-wall analysis suggested any change of this measure, positive or negative, was associated with radiographic progression. This suggests that concomitant cervical and lumbar metrology and radiographic disease changes may be measuring different structural phenomena.

Disclosure: M. Hwang, None; M. Weisman, None; M. Lee, None; L. S. Gensler, Janssen Pharmaceutica Product, L.P., 5,Novartis Pharmaceutical Corporation, 5,Amgen, 2,UCB, 2,AbbVie, 2; M. Brown, None; A. Tahanan, None; L. A. Diekman, None; T. Learch, None; S. Eisen, None; M. H. Rahbar, None; M. Ward, None; J. D. Reveille, Janssen, Novartis, 5,UCB, Eli Lilly, 2.
Factors Associated with the “Bamboo Spine” Phenotype – Data from the Comospa Study

Koei Oh¹, Anna Molto², Corinne Miceli-Richard³, Soksay Singvongsa⁴, Adrien Etcheto⁴ and Maxime Dougados⁴,
¹Department of Rheumatology, Paris Descartes University, Hôpital Cochin, Paris, France, ²Hôpital Cochin, Department of
Rheumatology, Paris Descartes University, Paris, France, ³Department of Rheumatology, Paris Descartes University, Hôpital
Cochin, Paris, France, ⁴Department of Rheumatology, Paris Descartes University, Hôpital Cochin, Paris, France

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The factors associated with “Bamboo spine” occurrence, i.e. the most severe axial phenotype of
SpA patients, have been poorly assessed to date. The aim of this study was to clarify the factors associated with the severe
type of AS “Bamboo spine” by investigating associations with various demographics, clinical and functional outcomes.

Methods: 275 patients with Bamboo spine enrolled by ASAS-COMOSPA study (Cross-sectional international study
involving 22 countries and including 3984 SpA patients fulfilling the ASAS SpA criteria) were included in the analysis.
Demographic, Clinical, and biological characteristics were compared between Bamboo-spine and non-Bamboo spine
patients. Variables with significant difference in univariate analyses were used as dependent variables in multivariable
and logistic regression. A logistic regression was used for the analysis to clarify the parameters associated with the Bamboo
spine phenotype. Independent variables with a p value less than 0.2 in univariate linear/logistic regression analysis were
tested in multivariate regression models. Odds ratio (ORs) with 95% CIs were calculated.

Results: Results of the univariate analysis are provided in the table. Multivariate analysis showed that Bamboo spine
phenotype was independently associated with NSAIDs intake from first symptom (OR 4.29; 95% CI 1.45-12.71 P<0.02),
male gender (OR 4.09; 95% CI 2.37-7.05; P<0.02), HLA-B27 positivity (OR 2.26; 95% CI 1.34-3.83; P<0.02), increased
CRP (OR 1.76; 95% CI 1.20-2.60; P=0.02), osteoporosis (OR 1.52; 95% CI 0.99-2.34; P=0.05), with only a trend for
smoking (OR 1.38, 95% CI 0.97-1.98; P=0.07).

Conclusion: The results of this study confirm parameters that have been previously associated with axial structural severity
(longer disease duration, uveitis, smoking, HLA-B27 and male gender). NSAIDs have been reported to have a potential
protective effect on the structural progression of the disease. Nevertheless, in this cross sectional study, NSAIDs intake
from the first symptoms was associated with the Bamboo spine phenotype, suggesting that severe axial involvement leads
to a sustained NSAIDs intake for pain relief. This also suggest that patients evolving to a bamboo spine phenotype have not
been under-exposed to NSAIDs treatment and/or that NSAIDs sustained exposure is not sufficient to protect from Bamboo
spine phenotype.

Disclosure: K. Oh, None; A. Molto, None; C. Miceli-Richard, None; S. Singvongsa, None; A. Etcheto, None; M.
Dougados, None.
Frequencies of Ligament Ossification in Patients with Ankylosing Spondylitis According to Several Ligaments Around Spine By Whole Spine CT Scan

Ran Song1, Ji-Young Choi2, Yeon-Ah Lee2, Seung-Jae Hong2, Hyung-In Yang3 and Sang-Hoon Lee1, 1Rheumatology, Kyung Hee University Hospital at Gang dong, Seoul, Korea, Republic of (South), 2Rheumatology, Kyung Hee University Hospital, Seoul, Korea, Republic of (South), 3Kyung Hee University Hospital at Gang dong, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Ankylosing spondylitis is chronic inflammatory arthritis with ligament ossification in spine such as ant. longitudinal ligaments, post. longitudinal ligaments, or other several ligaments around spine joints. We generally use mSASSS to evaluate progression of ossification which method only calculate amount of ossification in ant. longitudinal ligament. But there has not been known which ligaments are ossified most commonly.

We performed whole spine CT scan in patients with ankylosing spondylitis to analyze the frequency of ligaments ossification according to the sites of spine.

Methods:
This is a retrospective chart review study. We enrolled the patients who were diagnosed as ankylosing spondylitis by modified NY criteria in our hospital. Among these patients, we analyzed the male patients who had been performed by whole spine CT scans in ages between 40 and 45. Total 119 patients were enrolled. We analyzed the frequency of ossification in ant. longitudinal ligaments, post. longitudinal ligaments, ligamentum flavum, ligaments around facet joints, interspinous ligaments, supraspinus ligaments and annulus fibrosus according to C, T and L spine.

Results:
The most frequent ossification site was lateral side of annulus fibrosus in T spine (68.9%). Even regardless of C, T, L spine, ossification of lateral side in annulus fibrosus was also the most frequent site (157 sites). Second common ligaments ossified were ant. longitudinal ligaments (142 sites) and third common ligaments were ligaments around facet joints (109 sites). According to spine, the ligaments of T spine were the most common ligaments ossified (252). The ligaments in L spine were second common ligaments ossified (177). Interestingly ossification in the ligaments around L spine did not developed, but developed in T spine in 27 patients (22.7%). This is very important finding because ossification in the ligaments around T spine is not included in mSASSS method which method is used to evaluate disease progression in ankylosing spondylitis at present. Ossification in ant. longitudinal ligaments was strongly statistically correlated with ossification in ligaments around facet joints in L spine strongly (p=0.00. r=0.547).

Conclusion:
Ligaments around T spine were most commonly ossified in ankylosing spondylitis and we need to find new method to evaluate of ossification in T spine.

Disclosure: R. Song, None; J. Y. Choi, None; Y. A. Lee, None; S. J. Hong, None; H. I. Yang, None; S. H. Lee, None.
Validation of Online Calibration Modules for the Spondyloarthritis Research Consortium of Canada MRI Scores Based on Real-Time Experiential Learning

Matthew Maksymowych1, Hanne Boutrup2, Jonathan Cheah3, Riccardo Guglielmi4, Eric Heffernan5, Jacob Jaremko1, Mats-Peter Johansson6, Simon Krabbe7, Georg Kroeber8, Fardina Malik9, Susanne Juhl Pedersen7, Sander Shafer6, Ulrich Weber10, Pam Weiss11, Brian Trinh12, Joel Paschke13 and Robert G. Lambert14, 1Radiology, University of Alberta, Edmonton, AB, Canada, 2University of Copenhagen, Copenhagen, Denmark, 3Medicine, Hospital for Special Surgery, New York, NY, 4Radiology, Ente Ospedaliero Cantonale, Lugano, Switzerland, 5Radiology, St. Vincent's University Hospital, Dublin, Ireland, 6Rheumatology, Gentofte Hospital, Copenhagen, Denmark, 7Center for Rheumatology and Spine Diseases, Copenhagen Center for Arthritis Research, Rigshospitalet, Copenhagen, Denmark, 8University of Southern Denmark, Odense, Denmark, 9Medicine- Rheumatology, Weill Cornell Medical College, New York, NY, 10Department of Research, King Christian 10th Hospital for Rheumatic Diseases, Graasten, Denmark, 11Pediatrics, Children's Hospital Philadelphia, Philadelphia, PA, 12CARE Arthritis, EDMONTON, AB, Canada, 13CARE Arthritis, Edmonton, AB, Canada, 14University of Alberta, Edmonton, AB, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The appropriate use of imaging-based scoring instruments is usually an ad hoc process based on passive learning from published manuscripts. Moreover, most instruments lack knowledge transfer tools that would facilitate attainment of pre-specified performance targets for reader reliability prior to use in clinical trials and research. We aimed to develop and validate online calibration modules for the SPARCC MRI Scores based on consensus scores from these instrument developers, experiential game psychology, and real-time iterative feedback built into a scoring schematic directly on the DICOM image.

Methods: The SPARCC BME inflammation calibration module is comprised of 50 DICOM cases, each with scans from baseline and 12 weeks after the start of tumor necrosis factor inhibitor therapy. The SPARCC structural score is comprised of 40 cases, each with scans from baseline and after 2 years follow-up. Scans are scored in pairs for status and change scores blinded-to-time-point. Continuous visual real-time feedback regarding concordance/discordance of scoring per SIJ quadrant with expert readers is provided by a color-coding scheme. Reliability is additionally assessed by real-time intra-class correlation coefficient with the first ICC data being provided after 20 cases per SIJ coronal slice (calibration-per-slice), and further ICC data after the entire case has been scored (calibration-per-case). Accreditation for SPARCC BME is achieved with a status score ICC of > 0.8 and a change score ICC of > 0.7, and for SPARCC structural, status score ICC of >0.7 is required for fat and ankylosis, >0.5 for erosion and backfill, and >0.5 for change score in all domains. 14 readers scored the SPARCC BME module and 11 the SPARCC structural module, only 2 having prior experience with these scores, and 9 being rheumatology fellows.

Results: For the SPARCC BME score and the calibration-per-slice method, all 14 readers completed the scoring and attained the required level of proficiency. For the SPARCC structural scores and the calibration-per-slice method, all 11 readers completed scoring, proficiency for status was attained by 10 for each lesion domain, and proficiency for change
was attained by 11, 5, 6, 8 for fat, erosion, backfill, ankylosis, respectively. All readers rated the modules as easy and intuitive with average time for reading each case for SPARCC BME and Structural being 9 min and 12 min, respectively.

Conclusion: Experiential online learning is an effective and feasible calibration tool in the scoring of MRI scans.

<table>
<thead>
<tr>
<th>SPARCC score</th>
<th>Calibration per SIJ Slice</th>
<th>Calibration per Case</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>12 weeks</td>
</tr>
<tr>
<td>SPARCC BME</td>
<td>0.97(0.96-0.97)</td>
<td>0.94(0.91-0.96)</td>
</tr>
<tr>
<td>SPARCC Fat</td>
<td>0.84(0.73-0.94)</td>
<td>0.89(0.83-0.96)</td>
</tr>
<tr>
<td>SPARCC Erosion</td>
<td>0.83(0.74-0.91)</td>
<td>0.81(0.73-0.89)</td>
</tr>
<tr>
<td>SPARCC Backfill</td>
<td>0.58(0.38-0.78)</td>
<td>0.79(0.70-0.88)</td>
</tr>
<tr>
<td>SPARCC Ankylosis</td>
<td>0.92(0.88-0.96)</td>
<td>0.96(0.92-1.00)</td>
</tr>
</tbody>
</table>

Disclosure: M. Maksymowych, None; H. Boutrup, None; J. Cheah, None; R. Guglielmi, None; E. Heffernan, None; J. Jaremko, None; M. P. Johansson, None; S. Krabbe, None; G. Kroeber, None; F. Malik, None; S. J. Pedersen, None; S. Shafer, None; U. Weber, None; P. Weiss, None; B. Trinh, None; J. Paschke, None; R. G. Lambert, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/validation-of-online-calibration-modules-for-the-spondyloarthritis-research-consortium-of-canada-mri-scores-based-on-real-time-experiential-learning

Abstract Number: 587

Detection of Structural Lesions on T1 Weighted MRI Versus Radiography of the Sacroiliac Joints in Early Axial SpA: 2-Year Data

Walter P. Maksymowych1, Pascal Claudepierre2, Manouk de Hooge3, Robert G. Lambert4, Robert B.M. Landewé5, Anna Molto6, Désirée van der Heijde3, Jack F Bukowskij7, Heather Jones8, Isabelle Logeart9, Lisa Marshall8, Ronald Pedersen10, Annette Szumski11, Bonnie Vlahos12 and Maxime Dougdados13, 1Radiology & Diagnostic Imaging, University of Alberta, Edmonton, AB, Canada, 2Université Paris Est Créteil, Paris, France, 3Leiden University Medical Center, Leiden, Netherlands, 4University of Alberta, Edmonton, AB, Canada, 5Amsterdam Rheumatology & Immunology Center, Amsterdam, Netherlands, 6Hôpital Cochin, Department of Rheumatology, Paris Descartes University, Paris, France, 7Clinical Affairs, Pfizer, Collegeville, PA, 8Inflammation & Immunology Global Medical Affairs, Pfizer, Collegeville, PA, 9Medical Affairs, Pfizer, France, Paris, France, 10Department of Biostatistics, Pfizer, Collegeville, PA, 11inVentiv Health, Princeton, NJ, 12Clinical Sciences, Pfizer, Collegeville, PA, 13Hopital Cochin, Paris Descartes University, Paris, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: At the SI joint (SIJ) level, several methods exist for evaluating structural damage, e.g., MRI, CT scan, radiographs. In EMBARK (NCT01258738) and DESIR (NCT01648907), MRI and radiographs were available at baseline and Week 104. We evaluated: (1) the association between presence/absence of erosion on MRI and presence/absence of erosion or sacroiliitis on radiographs at the SIJ at baseline and Week 104, and (2) the association
between decrease/increase in erosion on MRI and decrease/increase in erosion or sacroiliitis on radiographs at the SIJ between baseline and Week 104.

**Methods:** Patients in both studies had early axial SpA (axSpA). EMBARK included a 12-week double-blind placebo-controlled period, then open-label etanercept for 92 weeks. DESIR patients had no history of biologic therapy and did not receive biologics for 2 years. MRI and radiographs of the SIJ from DESIR and EMBARK were combined and anonymized; readers were unaware of film chronology and original patient cohort. Three experienced readers evaluated T1 weighted MRI images using the SpondyloArthritis Research Consortium of Canada (SPARCC) SIJ Structural Score (SSS), graded radiographic sacroiliitis using the modified New York grading system, and recorded the presence/absence of individual radiographic lesions (erosion, sclerosis, ankylosis) for each SIJ. Presence/absence of lesions at each time point and decrease/increase in lesions was identified for each patient based on agreement of 2 out of 3 readers. Statistical analyses included kappa coefficient of agreement and McNemar’s test for asymmetry.

**Results:** 224 patients had MRI and radiographs available. At baseline, concordance for presence or absence of erosion was observed in 162/224 (72.3%) (κ=0.42) (Table). In cases of discordance, erosion was more frequent on MRI (21.4%) than radiographs (6.3%; P<0.0001). Week 104 data were similar to baseline. Decrease in erosion from baseline to 104 weeks was more frequent than increase only when assessed by MRI, and was significantly more frequent on MRI than radiographs. Similarly, decrease in erosion on MRI was significantly more frequent than decrease in sacroiliitis grade.

**Conclusion:** In patients with early axSpA, erosion was present more often on MRI than on radiographs at baseline and Week 104. Decrease in erosion at Week 104 was noted more frequently on MRI than radiographs.

Table. Concordance between MRI and radiographs; baseline, Week 104, and change between baseline and Week 104

<table>
<thead>
<tr>
<th>Erosion on MRI / Erosion on x-ray at BL</th>
<th>N</th>
<th>Present / Present (%)</th>
<th>Absent / Absent (%)</th>
<th>Kappa (95% CI)</th>
<th>P-value for discordance asymmetry*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erosion on MRI / Erosion on x-ray at Week 104</td>
<td>222</td>
<td>44 (19.8%)</td>
<td>119 (53.6%)</td>
<td>0.41 (0.29, 0.53)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Erosion on MRI / sacroiliitis on x-ray at BL</td>
<td>224</td>
<td>56 (25.2%)</td>
<td>99 (44.6%)</td>
<td>0.37 (0.25, 0.50)</td>
<td>0.71</td>
</tr>
<tr>
<td>Erosion on MRI / sacroiliitis on x-ray at Week 104</td>
<td>222</td>
<td>56 (25.2%)</td>
<td>99 (44.6%)</td>
<td>0.37 (0.25, 0.50)</td>
<td>0.71</td>
</tr>
<tr>
<td>Erosion decrease on MRI / Erosion decrease on x-ray</td>
<td>221</td>
<td>4 (1.8%)</td>
<td>162 (73.3%)</td>
<td>0.06 (-0.05, 0.16)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Erosion increase on MRI / Erosion increase on x-ray</td>
<td>221</td>
<td>2 (0.9%)</td>
<td>187 (84.6%)</td>
<td>0.03 (-0.12, 0.18)</td>
<td>0.72</td>
</tr>
<tr>
<td>Erosion decrease on MRI / sacroiliitis grade decrease on x-ray</td>
<td>221</td>
<td>8 (3.6%)</td>
<td>154 (69.7%)</td>
<td>0.08 (-0.05, 0.21)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Erosion increase on MRI / sacroiliitis grade increase on x-ray</td>
<td>221</td>
<td>4 (1.8%)</td>
<td>180 (81.4%)</td>
<td>0.09 (-0.07, 0.25)</td>
<td>0.07</td>
</tr>
</tbody>
</table>

*McNemar’s test.

BL, baseline.
Disclosure: W. P. Maksymowych, Abbvie, Pfizer, 2, Abbvie, Janssen, Lilly, Merck, Novartis, Pfizer, UCB, 5; P. Claudepierre, None; M. de Hooge, MdH Research, 3; R. G. Lambert, BioClinica, 5, AbbVie, 8; R. B. M. Landewé, AbbVie/AbbVie, Ablynx, Amgen, AstraZeneca, Bristol Myers Squibb, Celgene, Janssen (formerly Centocor), Galapagos, GlaxoSmithKline, Novartis, Novo-Nordisk, Merck, Pfizer, Roche, Schering-Plough, TiGenix, UCB, and Wyeth, 5, AbbVie, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, and Wyeth, 2, AbbVie/AbbVie, Amgen, Bristol Myers Squibb, Janssen (formerly Centocor), Merck, Pfizer, Roche, Schering-Plough, UCB, and Wyeth, 8; A. Molto, None; D. van der Heijde, AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, Glaxo-Smith-Kline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB, AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer, 5, Director: Imaging Rheumatology bv; J. F. Bukowski, Pfizer Inc, 1, Pfizer Inc, 3; H. Jones, Pfizer Inc, 1, Pfizer Inc, 3; I. Logeart, Pfizer Inc, 1, Pfizer Inc, 3; L. Marshall, Pfizer Inc, 1, Pfizer Inc, 3; R. Pedersen, Pfizer Inc, 1, Pfizer Inc, 3; A. Szumski, inVentiv Health, 3; B. Vlahos, Pfizer Inc, 1, Pfizer Inc, 3; M. Dougdados, Pfizer, AbbVie, UCB, Merck and Lily, 2, Pfizer, AbbVie, UCB, Merck and Lily, 5.


Abstract Number: 588

Inflammatory Lesions of the Sacroiliac Joints, but Not of the Spine, Are of High Utility for Recent Onset Axial Spondyloarthritis Recognition

Anna Molto1, Laure Gossec2, Violaine Foltz2, Romain Beaufort3, Jean Denis Laredo4, Pascal Richette5, Philippe Dieude6, Philippe Goupille7, Antoine Feydy8 and Maxime Dougdados9, 1Hôpital Cochin, Department of Rheumatology, Paris Descartes University, Paris, France, 2UPMC University Paris 06, Pitié-Salpêtrière Hospital, Paris, France, 3Private Practice, Paris, France, 4Radiology Department, Lariboisière Hospital, Paris, France, 5Rheumatology Department, Université Paris Diderot, Paris, France, 6Université Paris-Diderot, Paris, France, 7Université François-Rabelais, Tours, France, 8Univ. Paris Descartes, PRES Sorbonne Paris Cité, Service de radiologie B, Hôpital Cochin, Assistance Publique - Hôpitaux de Paris, Paris, France, 9Department of Rheumatology, Paris Descartes University, Hôpital Cochin, Paris, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: only scarce data are available regarding the prevalence of MRI inflammatory lesions of the sacroiliac joints (SIJ) or the spine suggestive of axial Spondyloarthritis (axSpA) in patients with recent onset mechanical chronic back pain (CBP). The aim of this study was to evaluate the prevalence of MRI (SIJ,Spine) inflammatory lesions suggestive of axSpA in a non-axSpA CBP population and to compare its prevalence to an recent onset axSpA cohort.

Methods:

Patients: a) Recent onset axSpA patients: first, a sample of 100 patients representative in terms of imaging abnormalities of the global DESIR (1) recent onset axSpA cohort (> 3 months but <3 years), based on the results of the previously published central reading of baseline films of DESIR(2) were selected (e.g. 35% of patients fulfilling the ASAS definition of MRI sacroiliitis). b) Recent onset CBP patients: consecutive in- and outpatients consulting for recent (>3 months but <5 years) mechanical CBP, initiating before the age of 45y and with a maximum age of 50y, in four tertiary care Hospitals were included in the study. Imaging: MRI scans (T2-STIR and T1 sequences) of the SIJ and full spine were performed in both groups with identical protocol. Central reading: an experienced reader (AM) centrally read all MRI scans, blinded for
clinical diagnosis. Statistical analysis: prevalence of MRI inflammatory lesions suggestive of axSpA were compared in both groups. Sensitivity, specificity and positive likelihood ratio of each lesion were calculated.

**Results:**

A total of 98 patients with recent onset CBP were included, and compared to 100 recent onset axSpA patients. Age and gender were comparable (mean(SD) 36.2(9.9) vs. 32.2(8.7)y, and 41.8% and 45% males, in the CBP vs. axSpA groups, respectively). MRI inflammatory lesions of the SIJ were quite frequent in the CBP group (25% patients with at least one inflammatory lesion) but were significantly more frequently observed in the axSpA group (Table), with a mean SIJ - SPARCC score of 4.9 (8.8) vs. 0.6 (1.3), p<0.001. The ASAS definition of MRI sacroiliitis presented a high specificity and a good positive likelihood ratio. Conversely, prevalence of inflammatory lesions of the spine was very frequent in the CBP group and not significantly lower compared to the axSpA group (SPARCC spine 5.6 (13.5) vs. 3.3(5.8), in the axSpA vs. CBP groups, respectively). Regardless the definition of a positive MRI for the spine applied, performances were not good, with positive likelihoods ratios below 2.

<table>
<thead>
<tr>
<th></th>
<th>CBP</th>
<th>SpA</th>
<th>p</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR+</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SIJ-MRI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At least one inflammatory lesion of the SIJ</td>
<td>24 (25.3%)</td>
<td>40 (40.0%)</td>
<td>0.028</td>
<td>0.4 (0.3, 0.5)</td>
<td>0.8 (0.7, 0.8)</td>
<td>1.6 (1.0, 2.4)</td>
</tr>
<tr>
<td>n=95</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASAS definition of positive MRI sacroiliitis</td>
<td>8 (8.4%)</td>
<td>35 (35.0%)</td>
<td>&lt;0.001</td>
<td>0.4 (0.3, 0.5)</td>
<td>0.9 (0.8, 0.9)</td>
<td>4.2 (2.0, 8.5)</td>
</tr>
<tr>
<td>n=95</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At least one inflammatory lesions of the spine</td>
<td>44 (52.5%)</td>
<td>52 (52.5%)</td>
<td>NS</td>
<td>0.5 (0.4, 0.6)</td>
<td>0.6 (0.5, 0.7)</td>
<td>1.2 (0.9, 1.6)</td>
</tr>
<tr>
<td>n=99</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASAS definition of positive MRI spine ≥3 inflammatory lesions</td>
<td>33 (33.7%)</td>
<td>44 (44.4%)</td>
<td>NS</td>
<td>0.4 (0.3, 0.6)</td>
<td>0.7 (0.6, 0.8)</td>
<td>1.4 (0.9, 1.9)</td>
</tr>
<tr>
<td>n=99</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Spine-MRI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASAS definition of positive MRI spine ≥5 inflammatory lesions</td>
<td>25 (25.5%)</td>
<td>30 (30.3%)</td>
<td>NS</td>
<td>0.3 (0.2, 0.4)</td>
<td>0.7 (0.7, 0.8)</td>
<td>1.2 (0.8, 1.9)</td>
</tr>
<tr>
<td>n=99</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:**

ASAS definition of a positive MRI-sacroiliitis performed very well for axSpA recognition; however, definitions proposed for a positive MRI-spine suggestive of axSpA did not seem to perform adequately in this recent disease stage. This supports the idea of not including a positive MRI of the spine in the ASAS classification criteria.


**Disclosure:** A. Molto, None; L. Gossec, None; V. Foltz, None; R. Beaufort, None; J. D. Laredo, None; P. Richette, None; P. Dieude, None; P. Goupille, None; A. Feydy, None; M. Dougados, Abbvie, Pfizer, Eli Lilly and Company,
Erosions at the Sacroiliac Joints and Fatty Lesions at the Spine Are the Most Discriminant Lesions for Recent Onset Axial Spondyloarthritis Recognition

Anna Molto1, Laure Gossec2, Violaine Foltz2, Romain Beaufort3, Jean Denis Laredo4, Pascal Richette5, Philippe Dieude6, Philippe Goupille7, Antoine Feydy8 and Maxime Dougados9, 1Hôpital Cochin, Department of Rheumatology, Paris Descartes University, Paris, France, 2UPMC University Paris 06, Pitié-Salpêtrière Hospital, Paris, France, 3Private Practice., Paris, France, 4Radiology Department, Lariboisière Hospital, Paris, France, 5Rheumatology Department, Université Paris Diderot, Paris, France, 6Université Paris-Diderot, Paris, France, 7Department of Rheumatology, CHRU de Tours; and Université François-Rabelais de Tours, Tours, France, 8Univ. Paris Descartes, PRES Sorbonne Paris Cité, Service de radiologie B, Hôpital Cochin, Assistance Publique - Hôpitaux de Paris, Paris, France, Paris, France

First publication: September 18, 2017

Background/Purpose: only scarce data are available regarding the prevalence of MRI structural lesions of the sacroiliac joints (SIJ) or the spine suggestive of axial Spondyloarthritis (axSpA) in patients with recent onset mechanical chronic back pain (CBP). The aim was to evaluate the prevalence of MRI (SIJ and Spine) structural lesions suggestive of axSpA in a non-axSpA CBP population and to compare its prevalence to an recent onset axSpA cohort.

Methods:

Study design: Observational cross-sectional national multicentre study. Patients: a) Recent onset axSpA patients: first, a sample of 100 patients representative in terms of imaging abnormalities of the global DESIR (1) recent onset axSpA cohort (> 3 months but <3 years), based on the results of the previously published central reading of baseline films of DESIR(2) were selected (e.g. 21% of patients fulfilling the modified NY criteria (mNY)). b) Recent onset CBP patients: consecutive in- and outpatients consulting for recent (>3months but <5years) mechanical CBP, initiating before the age of 45y and with a maximum age of 50y, in four tertiary care Hospitals were included in the study. Imaging: MRI scans (T2-STIR and T1 sequences) of the SIJ and cervico-thoracic and thoraco-lumbar spine were performed in both groups with identical protocol. Central reading: an experienced reader (AM) centrally read all MRI scans, blinded for clinical diagnosis. Statistical analysis: prevalence of lesions and lesions combinations previously proposed(3) to be suggestive of axSpA was compared in both groups. Sensitivity, specificity and positive likelihood ratio (LR+) of each lesion were calculated.

Results: A total of 98 patients with recent onset CBP were included, and compared to 100 recent onset axSpA patients. Age and gender were comparable (mean (SD) 36.2 (9.9) vs. 32.2 (8.7)y, and 41.8% and 45% males, in the CBP vs. axSpA groups, respectively).Prevalence of chronic lesions of the SIJ was significantly greater in the axSpA group but up to 17% patients with CBP presented at least one chronic lesion of the SIJ (Table). The presence of at least 3 subchondral bone erosions at the SIJ performed the best for axSpA discrimination. Prevalence of chronic lesions of the spine was comparable
in the two groups, with high prevalence of fatty lesions across groups; erosions were rare in both groups. The presence of at least 5 fatty lesions was the most discriminant, with a high specificity. Performances of all other structural lesions of the spine were poor.
<table>
<thead>
<tr>
<th></th>
<th>CBP N=98</th>
<th>SpA N=100</th>
<th>p</th>
<th>Se</th>
<th>Spe</th>
<th>LR+</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI SIJ</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N(%) patients</td>
<td>16/95(16.8%)</td>
<td>24 (24%)</td>
<td>NS</td>
<td>0.2 (0.2, 0.3)</td>
<td>0.8 (0.7, 0.0)</td>
<td>1.4 (0.8, 2.5)</td>
</tr>
<tr>
<td>with at least</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>one structural</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>lesion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N(%) patients</td>
<td>10/95(10.5%)</td>
<td>32 (32%)</td>
<td>&lt;0.001</td>
<td>0.32 (0.2, 0.4)</td>
<td>0.9 (0.8, 1.0)</td>
<td>3.0 (1.6, 5.8)</td>
</tr>
<tr>
<td>with ≥3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>subchondral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bone erosions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N(%) patients</td>
<td>11/95(11.6%)</td>
<td>29 (29%)</td>
<td>0.004</td>
<td>0.29 (0.2, 0.4)</td>
<td>0.88 (0.8, 0.9)</td>
<td>2.5 (1.3, 4.7)</td>
</tr>
<tr>
<td>with ≥3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>subchondral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bone fatty</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>lesions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N(%) patients</td>
<td>13/95(13.7%)</td>
<td>33 (33%)</td>
<td>0.002</td>
<td>0.33 (0.2, 0.4)</td>
<td>0.9 (0.8, 0.9)</td>
<td>2.4 (1.4, 4.3)</td>
</tr>
<tr>
<td>with ≥5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>subchondral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bone erosions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>or fatty lesions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRI spine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N(%) patients</td>
<td>49/95(50.0%)</td>
<td>42/99(42.4%)</td>
<td>NS</td>
<td>0.4 (0.3, 0.5)</td>
<td>0.5 (0.4, 0.6)</td>
<td>0.8 (0.6, 1.2)</td>
</tr>
<tr>
<td>with at least</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>one structural</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>lesion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N(%) patients</td>
<td>6/99(6.1%)</td>
<td>7/99 (7.1%)</td>
<td>NS</td>
<td>0.1 (0.0, 0.1)</td>
<td>0.9 (0.9, 1.0)</td>
<td>1.2 (0.4, 3.3)</td>
</tr>
<tr>
<td>with ≥3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>subchondral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bone erosions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N(%) patients</td>
<td>21/99(21.4%)</td>
<td>15/99(15.2%)</td>
<td>NS</td>
<td>0.2 (0.1, 0.2)</td>
<td>0.8 (0.7, 0.9)</td>
<td>0.7 (0.4, 1.23)</td>
</tr>
<tr>
<td>with ≥3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>subchondral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bone fatty</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>lesions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N(%) patients</td>
<td>8/99(8.2%)</td>
<td>21/99 (21.2%)</td>
<td>0.02</td>
<td>0.2 (0.1,0.3)</td>
<td>0.9 (0.8, 0.9)</td>
<td>2.5 (1.2, 5.4)</td>
</tr>
<tr>
<td>with ≥5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>subchondral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bone fatty</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>lesions OR fatty</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N(%) patients</td>
<td>19/99(19.4%)</td>
<td>11/99(11.1%)</td>
<td>NS</td>
<td>0.1 (0.1, 0.2)</td>
<td>0.8 (0.7, 0.9)</td>
<td>0.6 (0.3, 1.1)</td>
</tr>
<tr>
<td>with ≥5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>subchondral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bone erosions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OR fatty lesions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** Presence of at least 3 erosions at the MRI-SIJ and at least 5 fatty lesions at the MRI-spine seemed to performed well for axSpA recognition. This suggests that these definitions might be considered (in the future) to be
**Disclosure:** A. Molto, None; L. Gossec, None; V. Foltz, None; R. Beaufort, None; J. D. Laredo, None; P. Richette, None; P. Dieude, None; P. Goupille, None; A. Feydy, None; M. Dougados, Abbvie, Pfizer, Eli Lilly and Company, Novartis, UCB, Merck, Roche, BMS UCB, 2, Abbvie, Pfizer, Eli Lilly and Company, Novartis, UCB, Merck, Roche, BMS, UCB, 5.


Abstract Number: 590

**X-Ray Spine Lesions Are Rare and Not Discriminant for Axial Spondyloarthritis Recognition in Patients with Recent Onset Chronic Back Pain**

Anna Molto1, Laure Gossec2, Violaine Foltz2, Romain Beaufort3, Jean Denis Laredo4, Pascal Richette5, Philippe Dieude6, Philippe Goupille7, Antoine Feydy8 and Maxime Dougados9, 1Hôpital Cochin, Department of Rheumatology, Paris Descartes University, Paris, France, 2UPMC University Paris 06, Pitié-Salpêtrière Hospital, Paris, France, 3Private Practice, Paris, France, 4Radiology Department, Lariboisière Hospital, Paris, France, 5Rheumatology Department, Université Paris Diderot, Paris, France, 6Université Paris-Diderot, Paris, France, 7Université François-Rabelais, Tours, France, 8Univ. Paris Descartes, PRES Sorbonne Paris Cité, Service de radiologie B, Hôpital Cochin, Assistance Publique - Hôpitaux de Paris, Paris, France, Paris, France, 9Department of Rheumatology, Paris Descartes University, Hôpital Cochin, Paris, France

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** only very scarce data is available regarding the prevalence of spine Xrays abnormalities suggestive of axial Spondyloarthritis (axSpA) in patients with recent onset mechanical chronic back pain (CBP).

**Objective:** To evaluate the frequency of spine X-ray abnormalities suggestive of axSpA in a non-axSpA CBP population and to compare its prevalence to an recent onset axSpA cohort.

**Methods:**

**Methods : Study design:** Observational cross-sectional national multicentre study. **Patients:** a) Recent onset axSpA patients: first, a sample of 100 patients representative in terms of imaging abnormalities of the global DESIR (1) recent onset axSpA cohort (> 3 months but <3 years), based on the results of the previously published central reading of baseline films of DESIR(2) were selected (e.g. 21% of patients fulfilling the modified NY criteria (mNY)). b) Recent onset CBP patients: consecutive in- and outpatients consulting for recent (>3months but <5years) mechanical CBP, initiating before the age of 45y and with a maximum age of 50y, in four tertiary care Hospitals were included in the study. **Imaging:** Full spine Xrays were performed in both groups with an identical protocol. **Central reading:** an experienced reader (AM) centrally read X-ray films, blinded for clinical diagnosis. **Statistical analysis:** Number of lesions suggestive of axSpA were compared in both groups.

**Results:** A total of 98 patients with recent onset CBP were included, and compared to 100 recent onset axSpA patients. Age and gender were comparable (mean (SD) 36.2 (9.9) vs. 32.2 (8.7)y, and 41.8% and 45% males, in the CBP vs. axSpA
Prevalence of spine lesions was globally very low, and only squaring was significantly more frequent in the axSpA group.

<table>
<thead>
<tr>
<th></th>
<th>CBP (N=95)</th>
<th>SpA (N=100)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of erosions</td>
<td>0.4 (0.8)</td>
<td>0.3 (0.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Number of sclerosis lesions</td>
<td>0.4 (1.6)</td>
<td>0.5 (1.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Number of squarring lesions</td>
<td>0.01 (0.1)</td>
<td>0.2 (0.8)</td>
<td>0.037</td>
</tr>
<tr>
<td>mSASSS*</td>
<td>2.0 (14.5)</td>
<td>2.2 (15.1)</td>
<td>NS</td>
</tr>
<tr>
<td>n=89</td>
<td>n=91</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of patients with at least one full bone bridge</td>
<td>2 (2.1%)</td>
<td>5 (5.0%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

*exclusion of patients with more than 75% missing corners per section (cervical and lumbar)

**Conclusion:** Lesions suggestive of axSpA in spine Xrays of patients with CBP are rare; however, even in this recent onset disease patients, squaring lesions were significantly more frequent in the recent onset axSpA patients.

Funding = ASAS grant


**Disclosure:** A. Molto, None; L. Gossec, None; V. Foltz, None; R. Beaufort, None; J. D. Laredo, None; P. Richette, None; P. Dieude, None; P. Goupille, None; A. Feydy, None; M. Dougados, Abbvie, Pfizer, Eli Lilly and Company, Novartis, UCB, Merck, Roche, BMS UCB, 2,Abbvie, Pfizer, Eli Lilly and Company, Novartis, UCB, Merck, Roche, BMS, UCB, 5.


**Abstract Number: 591**

**Inflammation on MRI of Spine and Sacroiliac Joints Is Highly Predictive of Structural Damage in Axial Spondyloarthritis: The 5 Years Data of the DESIR Cohort**

Alexandre Sepriano, Sofia Ramiro, Robert B.M. Landewé, Maxime Dougdos and Désirée van der Heijde, Leiden University Medical Center, Leiden, Netherlands, Rheumatology, Department of Rheumatology, LUMC, Leiden, Netherlands, Leiden, Netherlands, University of Amsterdam and Atrium Medical Center, Amsterdam, Netherlands, Paris-Descartes University,, Paris, France

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The effect of local inflammation on structural damage in patients (pts) with axial spondyloarthritis is not well known. We aimed to test the possible effect of inflammation on structural damage both assessed by MRI and at
the level of the spine and SIJ.

**Methods:** Pts with recent onset (≤3 years) axSpA (according to the treating rheumatologist) from the DESIR cohort were included. MRI of the SIJ (MRI-SIJ) and spine (MRI-spine) were obtained at baseline (BL), 2 and 5 years and scored by 3 trained central readers. Bone Marrow Edema (BME) at MRI-SIJ was assessed according to ASAS definition and at the MRI-spine by the presence of ≥ 3 lesions. Structural damage in the SIJ (MRI-SIJ-STR) and in the spine (MRI-spine-STR) was defined by ≥ 3 fatty lesions. The % of structural net progression (number of ‘progressors’ minus the number of ‘regressors’ divided by total number of pts) was assessed according to CRP and BME status at BL. The effect of BME on MRI-SIJ on MRI-SIJ-STR and of BME on MRI-spine on MRI-spine-STR was evaluated using two types of binomial generalized estimating equations (GEE) models: i. effect at BL on 5 years incorporating measurements from all readers (GEE adjusted for reader); ii. effect of BME over 5 years (longitudinal time-lagged models with auto-regression). The final models were adjusted for variables proved to confound the association of interest (variables tested: age, gender, HLA-B27, smoking status, CRP, BASDAI, ASDAS, treatment with NSAIDs and TNFi).

**Results:** In total, 151 and 145 pts had complete 5-year MRI-SIJ and MRI-spine data available from 3 readers, respectively. Of the 151 pts with complete MRI-SIJ data, the net % pts who switched from MRI-SIJ-STR negative to positive ranged from 3.8% to 24% according to the presence of objective signs of inflammation at BL (figure). Low number of pts did not allow for similar analysis in the spine. In the multivariable analysis, both the presence of BME at MRI-SIJ (OR=4.2 [95% CI: 2.4-7.3]), and BME at MRI-spine (OR=8.9 [95% CI: 2.1-38.7]) at baseline were highly predictive of MRI-SIJ and MRI-spine structural progression respectively 5 years later, adjusting for CRP (only factor found to confound the association of interest). Similar positive associations were found in the longitudinal models testing the effect of BME on MRI-SIJ-STR and MRI-spine-STR over 5 years (table).

**Conclusion:** Our results show that local inflammation is strongly associated with the development of structural damage over 5 years both in the SIJ and spine in early axSpA and that this effect is independent of systemic inflammation.

![Figure](image.png)

**Figure.** Net progression from MRI-SIJ-STR negative to MRI-SIJ-STR positive (≥ 3 fatty lesions) according to baseline objective inflammatory markers.

**Table.** Effect of inflammation on MRI (ASAS definition of sacroiliitis and BME in the spine) on binary MRI structural outcomes.

<table>
<thead>
<tr>
<th>Effect of BMI on:</th>
<th>≥ 3 fatty lesions on MRI-SIJ (OR [95% CI])</th>
<th>≥ 3 fatty lesions on MRI-Spine (OR [95% CI])</th>
</tr>
</thead>
<tbody>
<tr>
<td>By GEE adjusted for reader</td>
<td>4.2 (2.4; 7.3)*</td>
<td>8.9 (2.1; 38.7)*</td>
</tr>
<tr>
<td>By longitudinal GEE adjusted for reader and repeated measurements</td>
<td>5.1 (2.7; 9.6)£</td>
<td>15.6 (4.8; 50.3)£</td>
</tr>
</tbody>
</table>

* Adjusted for CRP at baseline; £ adjusted for time-varying lagged ASDAS-CRP.

**Disclosure:** A. Sepriano, None; S. Ramiro, None; R. B. M. Landewé, None; M. Dougados, None; D. van der Heijde, None.

Abstract Number: 592

Which Imaging Outcomes for AxSpA Are Most Sensitive to Change? a 5-Year Analysis of the DESIR Cohort

Alexandre Sepriano1, Sofia Ramiro2, Désirée van der Heijde1, Maxime Dougados3, Pascal Claudepierre4, Antoine Feydy5, M. Reijnierse6, Damien Loeuille7 and Robert B.M. Landewé8, 1Leiden University Medical Center, Leiden, Netherlands, 2Rheumatology, Department of Rheumatology, LUMC, Leiden, Netherlands, Leiden, Netherlands, 3Paris-Descartes University, Paris, France, 4Hôpital Henri Mondor, Créteil, France, 5Univ. Paris Descartes, PRES Sorbonne Paris Cité, Service de radiologie B, Hôpital Cochin, Assistance Publique - Hôpitaux de Paris, Paris, France, Paris, France, 6Department of Radiology, Leiden University Medical Center, Leiden, Netherlands, 7Rheumatology, CHRU Nancy, Vandoeuvre les Nancy, France, 8University of Amsterdam and Atrium Medical Center, Amsterdam, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Several imaging outcomes have become available to assess inflammation and structural damage over time in patients with axial spondyloarthritis (axSpA). However, no formal comparison of their sensitivity to change has been made in the early phases of the disease. We aimed to compare the sensitivity to change of different MRI and radiographic scoring methods in patients with early axSpA.

Methods: Patients from the DESIR cohort fulfilling the ASAS axSpA criteria were included. Radiographs and MRI of the sacroiliac joints and spine were obtained at baseline, 1 year, 2 years and 5 years. Each film was scored by 2 or 3 readers in 3 ‘reading-waves’ (wave 1: baseline; wave 2: baseline, 1 year, 2 years; wave 3: baseline, 2 years, 5 years). Outcomes measuring inflammation and structural damage both on MRI and radiographs in the spine and SIJ were assessed (Table). The analysis of change captured over time was performed using generalized estimating equations (GEE) longitudinal models separately for each outcome, taking into account data from all readers and waves (‘integrated analysis’). To allow comparisons across outcomes, these were standardized (difference between the individual score and the mean of all scores divided by the standard deviation, per reader, wave and time-point) before running the models. The higher the standardized coefficient the more change in inflammation/damage is captured.

Results: In total, 345 patients were included (mean (SD) symptom duration: 1.6 (0.9) years; 53% males; 89% HLA-B27 positive). Inflammation on MRI-SIJ (according to both the ASAS definition of sacroiliitis and the continuous SPARCC score) was more sensitive to change as compared to inflammation on the spine that remained essentially unchanged regardless of the outcome (Table). Structural damage on the SIJ was found to increase over time, but with a higher standardized yearly rate of change on MRI-SIJ (range: 0.015-0.274) as compared to X-SIJ (range: 0.043-0.126). Notably, ≥3 Fatty lesions on MRI-SIJ was the structural outcome in the SIJ with highest sensitive to change (0.274), while ≥3 erosions was the least sensitive (0.015). Spine structural damage slowly progressed over time but, in contrast to SIJ, radiographic outcomes (i.e. ≥ 1 syndesmophytes and mSASSS) were more sensitive to change than MRI structural outcomes.

Conclusion: Our data adds to the body of evidence showing that structural damage assessed in pelvic radiographs only has low sensitivity to change. MRI-SIJ is a promising alternative (especially fatty lesions) capturing more structural changes. In contrast, in detecting structural change in early axSpA radiographic outcomes outperform MRI outcomes.
Table. Standardized rate of change of imaging outcomes over 5 years of follow-up in early axSpA patients from the DESIR-cohort who fulfil the ASAS axSpA classification criteria.

<table>
<thead>
<tr>
<th>Imaging outcomes</th>
<th>Baseline score* (N=313-344)</th>
<th>Standardized rate of change/year†</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sacroiliac joints (MRI-SIJ)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammatory lesions (ASAS criteria)</td>
<td>134 (39.2%)</td>
<td>-0.278</td>
</tr>
<tr>
<td>SPARC SIJ score (0-72)</td>
<td>4.7 (7.9)</td>
<td>-0.441</td>
</tr>
<tr>
<td><strong>Structural lesions (MRI-SIJ)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 5 fatty lesions and/or erosions</td>
<td>66 (19.5%)</td>
<td>0.238††</td>
</tr>
<tr>
<td>≥ 3 erosions</td>
<td>60 (17.7%)</td>
<td>0.015</td>
</tr>
<tr>
<td>≥ 3 fatty lesions</td>
<td>56 (16.5%)</td>
<td>0.274</td>
</tr>
<tr>
<td>Number of fatty lesions and/or erosions (0-80)</td>
<td>2.9 (4.9)</td>
<td>0.111</td>
</tr>
<tr>
<td>Number of erosions (0-40)</td>
<td>1.3 (2.2)</td>
<td>0.030</td>
</tr>
<tr>
<td>Number of fatty lesions (0-40)</td>
<td>1.5 (3.5)</td>
<td>0.140</td>
</tr>
<tr>
<td>Total structural lesions (0-144)</td>
<td>3.4 (5.9)</td>
<td>0.115</td>
</tr>
<tr>
<td>Total structural lesions without sclerosis (0-104)</td>
<td>3.2 (5.8)</td>
<td>0.124</td>
</tr>
<tr>
<td><strong>Structural lesions (X-SIJ)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mNY dichotomous</td>
<td>73 (21.2%)</td>
<td>0.044</td>
</tr>
<tr>
<td>mNY 1-grade change</td>
<td>NA</td>
<td>0.126</td>
</tr>
<tr>
<td>mNY 1-grade change and value ≥ 2</td>
<td>NA</td>
<td>0.119</td>
</tr>
<tr>
<td>mNY continuous grade (0-8)</td>
<td>1.7 (1.8)</td>
<td>0.043</td>
</tr>
<tr>
<td><strong>Spine</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammatory lesions (MRI-Spine)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BME: ≥ 3 lesions</td>
<td>32 (9.4%)</td>
<td>-0.032</td>
</tr>
<tr>
<td>BME: ≥ 5 lesions</td>
<td>19 (5.6%)</td>
<td>-0.030</td>
</tr>
<tr>
<td>SPARC Spine score (0-414)</td>
<td>2.6 (7.7)</td>
<td>-0.050</td>
</tr>
<tr>
<td>Berlin Spine score (0-69)</td>
<td>0.9 (2.7)</td>
<td>-0.055</td>
</tr>
<tr>
<td><strong>Structural lesions (MRI-Spine)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 5 fatty lesions</td>
<td>5 (1.6%)</td>
<td>-0.013</td>
</tr>
<tr>
<td>Total structural lesions (0-322)</td>
<td>0.4 (1.0)</td>
<td>0.016</td>
</tr>
<tr>
<td>Number of fatty lesions (0-92)</td>
<td>0.3 (0.8)</td>
<td>0.008</td>
</tr>
<tr>
<td>Number of corner erosions (0-92)</td>
<td>0.1 (0.2)</td>
<td>0.012</td>
</tr>
<tr>
<td>Number of corner bone spurs (0-92)</td>
<td>0.1 (0.3)</td>
<td>0.027</td>
</tr>
<tr>
<td>Structural lesions (X-Spine)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 1 syndesmophyte</td>
<td>22 (6.6%)</td>
<td>0.036</td>
</tr>
<tr>
<td>mSASSS score (0-72)</td>
<td>0.4 (1.7)</td>
<td>0.041</td>
</tr>
</tbody>
</table>

* Agreement of ≥ 2 out of 3 readers for binary variables and mean (SD) of 3 readers for continuous variables from wave 3; † fatty lesions, erosions, sclerosis, partial ankylosis, total ankylosis; ‡ fatty lesions, erosions, bone spurs, ankylosis; NA, not applicable.

Disclosure: A. Sepriano, None; S. Ramiro, None; D. van der Heijde, None; M. Dougados, None; P. Claudepierre, None; A. Feydy, None; M. Reijnierse, None; D. Loeuille, None; R. B. M. Landewé, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/which-imaging-outcomes-for-axspa-are-most-sensitive-to-change-a-5-year-analysis-of-the-desir-cohort

Abstract Number: 593

Progression of Structural Damage on MRI in Patients with Axial Spondyloarthritis Is Limited: The 5 –Year Results in the DESIR Cohort

Alexandre Sepriano1, Sofía Ramiro2, Robert B.M. Landewé3, Maxime Dougados4 and Désirée van der Heijde1, 1Leiden University Medical Center, Leiden, Netherlands, 2Rheumatology, Department of Rheumatology, LUMC, Leiden, Netherlands, Leiden, Netherlands, 3University of Amsterdam and Atrium Medical Center, Amsterdam, Netherlands, 4Paris-Descartes University,, Paris, France

First publication: September 18, 2017
Background/Purpose: Reliably detecting radiographic structural change in patients with axial spondyloarthritis (axSpA), especially in the sacroiliac joints (SIJ), is notoriously difficult. Magnetic resonance imaging (MRI) is an alternative for radiographs to assess structural damage. However, so far the utility of MRI in capturing change in structural damage over time has been poorly studied. We aimed to evaluate the change over time of structural lesions on MRI of the SIJ and spine in patients with axSpA.

Methods: Patients with recent onset (≤3 years) axSpA (according to the treating rheumatologist) from the DESIR cohort were included. MRI of the SIJ (MRI-SIJ) and spine (MRI-spine) were obtained at baseline and 5 years and scored by 3 trained central readers unaware of their chronology. Structural damage in the SIJ (MRI-SIJ-STR) and in the spine (MRI-spine-STR) was defined according to 3 binary rules (A1: ≥ 5 fatty lesions and / or erosions; B1: ≥ 3 erosions; and C1: ≥ 3 fatty lesions) and 3 continuous scores (A2: number of fatty lesions /erosions; B2: number of erosions; and C2: number of fatty lesions). For binary outcomes, structural damage was defined by the agreement of at least 2 out of 3 readers and the % of net progression by subtracting the number of patients that ‘improved’ from those that ‘worsened’ divided by the total number of patients with complete baseline and 5-year data. For continuous outcomes, the mean of the 3 readers was used and the difference between year 5 and baseline was calculated.

Results: In total, 151 and 145 patients had complete MRI-SIJ and MRI-spine data available from 3 readers, respectively. The percentages of net progression at SIJ level are summarized in the figure. These were 6.6%, 0.7% and 7.9% for the binary outcomes A1, B1 and C1 respectively. Notably, the percentage of ‘improvement’ (4.6%) was almost as high as the percentage of ‘worsening’ (5.3%) for definition B1 (≥3 erosions); while no ‘improvements’ were seen by the 3 readers for definition C1 (≥3 fatty lesions). Similar differences were seen for the mean (standard deviation) change of the 3 MRI-SIJ-STR continuous outcomes (A2: 1.02 (2.60); B2: 0.20 (1.39); and C2: 0.83 (2.20); p<0.01 for all). MRI-spine-STR net change over time was almost absent (A1: -0.7%; B1: 0.0%; C1: 0.7%) considering the binary outcomes, and small (though statistically significant) considering definition A2 (0.18 (0.52); p<0.01) and C2 (0.14 (0.48); p<0.01) but absent for definition B2 (0.03 (0.24); p=0.109).

Conclusion: These results suggest that patients with early axSpA only show modest structural progression in the MRI of the SIJ and that fatty lesions are more sensitive to change compared to erosions. In this early axSpA population, MRI-detected structural progression in the spine is very limited/absent.

Figure. Changes in different binary MRI-SIJ-STR outcome measures. All outcomes are assessed according to the ‘2 out of 3’ definition in the completers population (N=151). MRI-SIJ-STR structural damage on magnetic resonance imaging of the sacroiliac joints.

Disclosure: A. Sepriano, None; S. Ramiro, None; R. B. M. Landewé, None; M. Dougados, None; D. van der Heijde, None.
Imaging Biomarkers in Crohn’s Associated Axial Spondyloarthritis

Fardina Malik1, John A. Carrino2, Madeline Epsten3, Ellen Scherl4, Stephanie Wichuk5, Ulrich Weber6, Susanne J Pedersen7, Joel Paschke8, Jackie Szymonifka3, Georg Kroebel9, Randy Longman4, Walter P. Maksymowych5 and Lisa A. Mandl1

1Rheumatology, Hospital For Special Surgery, New York, NY, 2Radiology, Hospital for Special Surgery, New York, NY, 3Rheumatology, Hospital for Special Surgery, New York, NY, 4Gastroenterology, Weill Cornell Medical College, New York, NY, 5Medicine, University of Alberta, Edmonton, AB, Canada, 6Institute of Regional Health Research, University of Southern Denmark, Odense, Denmark, 7Copenhagen Center for Arthritis Research, Glostrup Hospital, University of Copenhagen, Copenhagen, Denmark, 8CARE Arthritis, Edmonton, AB, Canada, 9University of Southern Denmark, Odense, Denmark

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Axial SpA has been reported in 4-16% of patients with Crohn's disease (CD). However, some plain radiograph or magnetic resonance imaging (MRI) studies in Crohn's population suggest presence of sacroiliitis in up to 40% patients. Whether axial SpA is underdiagnosed and hence undertreated is unclear, especially since it does not correlate with CD activity. This study utilizes standardized MRI SI joint (SJJ) imaging to determine prevalence of axial SpA in a cohort of CD patients and investigate its relationship with other clinical and serologic measures. In addition, we compare MRIs from our cohort of CD patients with separate cohorts of patients with known axial SpA with and without inflammatory bowel disease (IBD).

Methods: Adult consecutive patients meeting pathological, radiological and/or endoscopic criteria of CD and not currently on any biologic except vedolizumab, were prospectively enrolled from an IBD Clinic. Data collected included length of CD, history of joint/back pain, HLA-B27 status, BASMI, BASDAI, Harvey-Bradshaw Index (HBI) scores- a measure of CD activity, Ankylosing Spondylitis Disease Activity Score-C reactive protein (ASDAS-CRP). All patients underwent T1 and short tau inversion recovery (STIR) sequence MRI of SJJ. 3 expert readers, blinded to clinical history reviewed MRIs for presence of active and/or structural lesions globally indicative of SpA (bone marrow edema BME ≥ 2 and/or structural lesions) and 6 out of those were ASAS positive (presence of active inflammation/BME), including 2 asymptomatic patients. Older age (OR 1.4, 95% CI 1.04 - 1.90) and higher BASMI (OR 3.2 95% CI 1.1-9.6) were associated with MRI SpA findings. But presence of IBP, peripheral SpA, CD duration, BASDAI, ASDAS-CRP or HBI did not show association. Compared to historic cohort of AS patients with (n=23) and without (n=24) IBD, CD patients with IBP had similar BASDAI and ASDAS-CRP scores (p <0.05) but they had lower BME and structural lesions (p 0.02 and <0.001) compared to IBD with and without SpA.
**Conclusion:** MRI evidence of axial SpA was 35% and 16% in our cohort of CD patients with and without back pain respectively. MRI is a valuable tool to diagnose axial SpA in CD patients with back pain, especially those who are older and has evidence of restricted spinal mobility on exam. Presence of IBP did not show association, as previously suggested, although these patients experience similar morbidity as our comparator cohort with known AS with or without IBD.

**Disclosure:** F. Malik, None; J. A. Carrino, None; M. Epsten, None; E. Scherl, None; S. Wichuk, None; U. Weber, None; S. J. Pedersen, None; J. Paschke, None; J. Szymonifka, None; G. Kroeber, None; R. Longman, None; W. P. Maksymowych, None; L. A. Mandl, Boehringer Ingelheim, 2, American College of Physicians, 3, Up To Date, 7.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/imaging-biomarkers-in-crohns-associated-axial-spondyloarthritis](http://acrabstracts.org/abstract/imaging-biomarkers-in-crohns-associated-axial-spondyloarthritis)

**Abstract Number:** 595

**Improved Patient-Reported Outcomes in Psoriatic Arthritis Patients Treated with Abatacept: Results from a Phase III Trial**

**Vibeke Strand**1, E Alemao2, T Lehman2, A Johnsen2, S Banerjee2, HA Ahmad2 and Philip J Mease3, 1Stanford University, Palo Alto, CA, 2Bristol-Myers Squibb, Princeton, NJ, 3Swedish Medical Center and University of Washington, Seattle, WA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** In the Phase III ASTRAEA study (NCT01860976), abatacept (ABA) significantly increased ACR20 responses, alleviating musculoskeletal symptoms in patients (pts) with active psoriatic arthritis (PsA).1 Here we explore the effect of ABA on pt-reported outcomes (PROs) in ASTRAEA. **Methods:** Pts were randomized (1:1) to SC ABA 125 mg weekly or placebo (PBO) for 24 weeks (W). At W16, pts without ≥20% improvement in joint counts escaped to open-label ABA. Adjusted mean changes from baseline to W16 (all pts) and W24 (non-escape responder analysis) in Short Form-36 (SF-36; physical and mental component summary [PCS, MCS] and individual domain scores using spydergrams), HAQ-DI, Dermatology QoL Index (DLQI), and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scores were evaluated in total population (prespecified intent-to-treat analysis) and subgroups (post hoc) stratified by baseline CRP and prior TNF inhibitor (TNFi) use. Proportions of pts reporting improvements from baseline ≥minimal clinically important difference (MCID) in SF-36 summary (≥2.5) and domains (≥5.0), FACIT-F (≤−4.0), and HAQ-DI (≤−0.35), and scores ≥normative values in SF-36 summary (≥50) and individual domains, FACIT-F (<40), and HAQ-DI (<0.5) at W16 were analyzed in the total population. **Results:** In the total population, numerical improvements in most PROs were reported with ABA (n=213) vs PBO (n=211) at both time points (significant for SF-36 PCS at W16, HAQ-DI at W24, and DLQI at both time points; Table). At W16 before escape, improvements in all SF-36 domains were numerically greater with ABA (significant for physical function, bodily pain, and vitality). A higher proportion of pts receiving ABA vs PBO reported improvements ≥MCID in SF-36 PCS, SF-36 MCS, SF-36 domains, FACIT-F, HAQ-DI (Figure), and DLQI (not shown) at W16. Proportion of pts reporting scores ≥normative values at W16 was higher with ABA vs PBO for SF-36 PCS, SF-36 MCS, FACIT-F, and HAQ-DI. At W24, improvements in most SF-36 domain scores accrued in responders in both groups; numerical differences favored ABA. Improvements were observed in all PROs in the ABA vs PBO group for TNFi-naïve and -exposed subpopulations at W16. Improvements in all PROs were reported with ABA in baseline CRP > upper limit of normal (ULN) vs CRP ≤ ULN subpopulation at W16 (Table). Subgroup data at W24 were difficult to interpret due to lower number of pts assessed vs W16.

**Conclusion:** Abatacept treatment improved many PROs in pts with active PsA, with larger benefits in the elevated CRP subpopulation and regardless of prior TNFi exposure. 1. Mease PJ, et al. *Ann Rheum Dis* 2017 [Epub ahead of print]
<table>
<thead>
<tr>
<th>Table: Change from Baseline in PFO at 16 and 24 Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Week 16 (before escape)</strong></td>
</tr>
<tr>
<td><strong>Week 24 (responders only)</strong></td>
</tr>
<tr>
<td><strong>Total population</strong></td>
</tr>
<tr>
<td>ASA</td>
</tr>
<tr>
<td>PBO</td>
</tr>
<tr>
<td>Adjusted mean difference (95% CI)</td>
</tr>
<tr>
<td>ASA</td>
</tr>
<tr>
<td>PBO</td>
</tr>
<tr>
<td>Adjusted mean difference (95% CI)</td>
</tr>
<tr>
<td><strong>SF-36 PCS</strong></td>
</tr>
<tr>
<td>3.16 (0.28), n=320</td>
</tr>
<tr>
<td>2.92 (0.29), n=166</td>
</tr>
<tr>
<td>1.74 (0.32, 3.19)</td>
</tr>
<tr>
<td>1.70 (0.31, 3.19)</td>
</tr>
<tr>
<td>3.89 (0.31, 3.19)</td>
</tr>
<tr>
<td>1.42 (0.32, 3.19)</td>
</tr>
<tr>
<td><strong>SF-36 MCS</strong></td>
</tr>
<tr>
<td>2.62 (0.28), n=322</td>
</tr>
<tr>
<td>2.58 (0.28), n=166</td>
</tr>
<tr>
<td>1.56 (0.32, 3.19)</td>
</tr>
<tr>
<td>1.52 (0.31, 3.19)</td>
</tr>
<tr>
<td>3.59 (0.31, 3.19)</td>
</tr>
<tr>
<td>1.49 (0.31, 3.19)</td>
</tr>
<tr>
<td><strong>FACIT-F</strong></td>
</tr>
<tr>
<td>-2.67 (0.28), n=322</td>
</tr>
<tr>
<td>-2.61 (0.28), n=166</td>
</tr>
<tr>
<td>N/A</td>
</tr>
<tr>
<td>-4.65 (0.28), n=322</td>
</tr>
<tr>
<td>-4.19 (0.28), n=166</td>
</tr>
<tr>
<td>N/A</td>
</tr>
<tr>
<td>-4.19 (0.28), n=322</td>
</tr>
<tr>
<td>-4.19 (0.28), n=166</td>
</tr>
<tr>
<td><strong>EFGI</strong></td>
</tr>
<tr>
<td>-2.35 (0.28), n=322</td>
</tr>
<tr>
<td>-2.28 (0.28), n=166</td>
</tr>
<tr>
<td>-1.45 (0.28, 3.19)</td>
</tr>
<tr>
<td>-1.39 (0.28, 3.19)</td>
</tr>
<tr>
<td>-2.19 (0.28, 3.19)</td>
</tr>
<tr>
<td>-2.16 (0.28, 3.19)</td>
</tr>
<tr>
<td><strong>TNF-α nerve</strong></td>
</tr>
<tr>
<td>ASA</td>
</tr>
<tr>
<td>PBO</td>
</tr>
<tr>
<td>Adjusted mean difference (95% CI)</td>
</tr>
<tr>
<td>ASA</td>
</tr>
<tr>
<td>PBO</td>
</tr>
<tr>
<td>Adjusted mean difference (95% CI)</td>
</tr>
<tr>
<td><strong>SF-36 PCS</strong></td>
</tr>
<tr>
<td>3.83 (0.28), n=322</td>
</tr>
<tr>
<td>2.92 (0.29), n=166</td>
</tr>
<tr>
<td>1.56 (0.32, 3.19)</td>
</tr>
<tr>
<td>1.49 (0.31, 3.19)</td>
</tr>
<tr>
<td>3.79 (0.31, 3.19)</td>
</tr>
<tr>
<td>1.78 (0.31, 3.19)</td>
</tr>
<tr>
<td><strong>SF-36 MCS</strong></td>
</tr>
<tr>
<td>2.58 (0.28), n=322</td>
</tr>
<tr>
<td>2.54 (0.28), n=166</td>
</tr>
<tr>
<td>1.56 (0.32, 3.19)</td>
</tr>
<tr>
<td>1.52 (0.31, 3.19)</td>
</tr>
<tr>
<td>3.59 (0.31, 3.19)</td>
</tr>
<tr>
<td>1.49 (0.31, 3.19)</td>
</tr>
<tr>
<td><strong>FACIT-F</strong></td>
</tr>
<tr>
<td>-2.61 (0.28), n=322</td>
</tr>
<tr>
<td>-1.45 (0.28), n=166</td>
</tr>
<tr>
<td>1.56 (0.32, 3.19)</td>
</tr>
<tr>
<td>1.52 (0.31, 3.19)</td>
</tr>
<tr>
<td>3.59 (0.31, 3.19)</td>
</tr>
<tr>
<td>1.49 (0.31, 3.19)</td>
</tr>
<tr>
<td><strong>EFGI</strong></td>
</tr>
<tr>
<td>-2.35 (0.28), n=322</td>
</tr>
<tr>
<td>-1.45 (0.28), n=166</td>
</tr>
<tr>
<td>1.56 (0.32, 3.19)</td>
</tr>
<tr>
<td>1.52 (0.31, 3.19)</td>
</tr>
<tr>
<td>3.59 (0.31, 3.19)</td>
</tr>
<tr>
<td>1.49 (0.31, 3.19)</td>
</tr>
<tr>
<td><strong>TNF-α exposed</strong></td>
</tr>
<tr>
<td>ASA</td>
</tr>
<tr>
<td>PBO</td>
</tr>
<tr>
<td>Adjusted mean difference (95% CI)</td>
</tr>
<tr>
<td>ASA</td>
</tr>
<tr>
<td>PBO</td>
</tr>
<tr>
<td>Adjusted mean difference (95% CI)</td>
</tr>
<tr>
<td><strong>SF-36 PCS</strong></td>
</tr>
<tr>
<td>5.60 (0.70), n=320</td>
</tr>
<tr>
<td>5.60 (0.70), n=166</td>
</tr>
<tr>
<td>3.54 (0.32, 3.19)</td>
</tr>
<tr>
<td>2.78 (0.31, 3.19)</td>
</tr>
<tr>
<td>3.59 (0.31, 3.19)</td>
</tr>
<tr>
<td>3.59 (0.31, 3.19)</td>
</tr>
<tr>
<td><strong>SF-36 MCS</strong></td>
</tr>
<tr>
<td>2.69 (0.70), n=322</td>
</tr>
<tr>
<td>2.69 (0.70), n=166</td>
</tr>
<tr>
<td>3.54 (0.32, 3.19)</td>
</tr>
<tr>
<td>2.78 (0.31, 3.19)</td>
</tr>
<tr>
<td>3.59 (0.31, 3.19)</td>
</tr>
<tr>
<td>3.59 (0.31, 3.19)</td>
</tr>
<tr>
<td><strong>FACIT-F</strong></td>
</tr>
<tr>
<td>-3.34 (0.70), n=322</td>
</tr>
<tr>
<td>-3.34 (0.70), n=166</td>
</tr>
<tr>
<td>3.54 (0.32, 3.19)</td>
</tr>
<tr>
<td>2.78 (0.31, 3.19)</td>
</tr>
<tr>
<td>3.59 (0.31, 3.19)</td>
</tr>
<tr>
<td>3.59 (0.31, 3.19)</td>
</tr>
<tr>
<td><strong>EFGI</strong></td>
</tr>
<tr>
<td>-2.35 (0.70), n=322</td>
</tr>
<tr>
<td>-2.35 (0.70), n=166</td>
</tr>
<tr>
<td>3.54 (0.32, 3.19)</td>
</tr>
<tr>
<td>2.78 (0.31, 3.19)</td>
</tr>
<tr>
<td>3.59 (0.31, 3.19)</td>
</tr>
<tr>
<td>3.59 (0.31, 3.19)</td>
</tr>
<tr>
<td><strong>CRP (IL-6)</strong></td>
</tr>
<tr>
<td>1.33 (0.81), n=322</td>
</tr>
<tr>
<td>1.33 (0.81), n=166</td>
</tr>
<tr>
<td>0.33 (0.81, 3.19)</td>
</tr>
<tr>
<td>0.33 (0.81, 3.19)</td>
</tr>
<tr>
<td>0.33 (0.81, 3.19)</td>
</tr>
<tr>
<td>0.33 (0.81, 3.19)</td>
</tr>
<tr>
<td><strong>CRP (IL-10)</strong></td>
</tr>
<tr>
<td>3.83 (0.28), n=322</td>
</tr>
<tr>
<td>3.83 (0.28), n=166</td>
</tr>
<tr>
<td>5.02 (0.32, 3.19)</td>
</tr>
<tr>
<td>3.79 (0.31, 3.19)</td>
</tr>
<tr>
<td>3.79 (0.31, 3.19)</td>
</tr>
<tr>
<td>3.79 (0.31, 3.19)</td>
</tr>
<tr>
<td><strong>CRP (IL-12)</strong></td>
</tr>
<tr>
<td>1.97 (0.28), n=322</td>
</tr>
<tr>
<td>1.97 (0.28), n=166</td>
</tr>
<tr>
<td>1.97 (0.28, 3.19)</td>
</tr>
<tr>
<td>1.97 (0.28, 3.19)</td>
</tr>
<tr>
<td>1.97 (0.28, 3.19)</td>
</tr>
<tr>
<td>1.97 (0.28, 3.19)</td>
</tr>
<tr>
<td><strong>CRP (IL-6)</strong></td>
</tr>
<tr>
<td>0.89 (0.28), n=322</td>
</tr>
<tr>
<td>0.89 (0.28), n=166</td>
</tr>
<tr>
<td>2.00 (0.28, 3.19)</td>
</tr>
<tr>
<td>2.00 (0.28, 3.19)</td>
</tr>
<tr>
<td>2.00 (0.28, 3.19)</td>
</tr>
<tr>
<td>2.00 (0.28, 3.19)</td>
</tr>
<tr>
<td><strong>CRP (IL-10)</strong></td>
</tr>
<tr>
<td>2.69 (0.28), n=322</td>
</tr>
<tr>
<td>2.69 (0.28), n=166</td>
</tr>
<tr>
<td>2.69 (0.28, 3.19)</td>
</tr>
<tr>
<td>2.69 (0.28, 3.19)</td>
</tr>
<tr>
<td>2.69 (0.28, 3.19)</td>
</tr>
<tr>
<td>2.69 (0.28, 3.19)</td>
</tr>
<tr>
<td><strong>CRP (IL-12)</strong></td>
</tr>
<tr>
<td>1.04 (0.28), n=322</td>
</tr>
<tr>
<td>1.04 (0.28), n=166</td>
</tr>
<tr>
<td>1.04 (0.28, 3.19)</td>
</tr>
<tr>
<td>1.04 (0.28, 3.19)</td>
</tr>
<tr>
<td>1.04 (0.28, 3.19)</td>
</tr>
<tr>
<td>1.04 (0.28, 3.19)</td>
</tr>
</tbody>
</table>

Data are adjusted mean change (83), 95% CI of difference vs PBO within each 0. ASA=Astrazeneca; DLQI=Dermatology LifeQoL index; FACIT-F=Functional Assessment of Chronic Illness Therapy Fatigue scale; MCO=Motor component summary; PBO=Placebo; POC=physical component summary; SE=standard error; SF-36=Short Form-36; TNF=TNF inhibitor.
Figure. Percentage of Patients Reporting Improvements ≥MCID or ≥Normative Values on PROs at Week 16 (A) and SF-36 Domain Scores at Baseline, Week 16 and Week 24 for Abatacept (B) and Placebo (C) Groups Versus Age/Gender-Matched Normative Population

Disclosure: V. Strand, AbbVie, Amgen Corporation, AstraZeneca, Biogen, BMS, Boehringer Ingelheim, Celgene, Celltrion, Corrona, Crescendo / Myriad Genetic, EMD Serono, Genentech / Roche, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sandoz, Sano, 5; E. Alemao, Bristol-Myers Squibb, 1,Bristol-Myers Squibb, 3; T. Lehman, Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1, 9; A. Johnsen, Bristol-Myers Squibb, 1,Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1, 9; H. Ahmad, Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1, 9; H. Ahmad, Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1, 9; P. J. Mease, AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 2,AbbVie, Amgen, BMS, Celgene, Crescendo Bioscience, Corrona, Demira, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, Zynerba, Speaker Bureau: AbbVie, Amgen, BMS, Celgene, Crescendo Bioscience, Genentech, Janssen, Novartis, Pfizer, UCB, 5.


Abstract Number: 596
Effect of Tofacitinib on Patient-Reported Outcomes in Patients with Active Psoriatic Arthritis: Results from 2 Phase 3 Studies

Vibeke Strand¹, Kurt de Vlam², Jose A Covarrubias-Cobos³, Philip J Mease⁴, Dafna D Gladman⁵, Thijs Hendrikx⁶, Elizabeth Kudlacz⁷, Daniela Graham⁷, Joseph Wu⁷, Joseph C Cappelleri⁷ and Ming-Ann Hsu⁷, ¹Stanford University, Palo Alto, CA, ²UZ Leuven, Leuven, Belgium, ³Unidad Reumatologica Las Americas S.C.P, Yucatán, Mexico, ⁴Swedish Medical Center and University of Washington, Seattle, WA, ⁵Department of Medicine, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, ⁶Pfizer Inc, Collegeville, PA, ⁷Pfizer Inc, Groton, CT

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor under investigation for the treatment of psoriatic arthritis (PsA). Safety and efficacy were investigated in 2 Phase 3 randomized controlled trials (RCTs: OPAL Broaden [12 months; NCT01877668]; OPAL Beyond [6 months; NCT01882439]). This analysis evaluated patient-reported outcomes (PROs) in patients with active PsA in OPAL Broaden (N=422), with inadequate responses (IR) to ≥1 conventional synthetic DMARD, naïve to tumor necrosis factor inhibitors (TNFi); and in OPAL Beyond (N=394), IR to ≥1 TNFi.

Methods: Patients were randomized to tofacitinib 5 or 10 mg twice daily (BID) or placebo (PBO) advanced to either tofacitinib 5 or 10 mg BID at Month 3, and, in OPAL Broaden, to adalimumab 40 mg subcutaneously every 2 weeks. Based on a longitudinal model, least squares mean (LSM) changes from baseline were reported for the following: Patient Global Assessment of Disease Activity Visual Analog Scale (PtGA VAS), Pain VAS, Short Form-36 Health Survey Version 2 (SF-36v2), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), Dermatology Life Quality Index (DLQI), and Ankylosing Spondylitis Quality of Life (ASQOL). Findings were reported using nominal p values without adjustments for multiple comparisons.

Results: Improvements in PtGA and Pain were observed as early as Week 2 (first assessment), and exceeded PBO at Month 3 with both tofacitinib doses in both RCTs (p≤0.05 vs PBO) (Table). At Month 3, SF-36v2 Physical Component Summary (PCS), physical functioning (PF), bodily pain (BP), and vitality (VT) domains, and FACIT-F scores, exceeded PBO with both doses (p≤0.05) in both trials; improvements in PCS, PF, BP, and FACIT-F exceeded minimum clinically important differences (MCID). DLQI and ASQOL scores at Month 3 exceeded PBO with both doses in both RCTs (p≤0.05), and social functioning (SF) domain with both doses in OPAL Beyond and 5 mg BID in OPAL Broaden (p≤0.05). PRO improvements reported in OPAL Broaden with tofacitinib were similar to adalimumab. The percentages of patients receiving both tofacitinib doses reporting changes ≥MCID at Month 3 in SF-36v2 PCS, PF, and BP domains were statistically significant in both RCTs, as were general health (GH) and mental health (MH) domains with 10 mg BID and FACIT-F with both doses in OPAL Broaden, and SF domains with both doses in OPAL Beyond and role physical (RP) with 10 mg BID.

Conclusion: Patients with active PsA receiving tofacitinib reported statistically greater and clinically meaningful improvements in PROs compared with PBO at Month 3 in both RCTs.
Ixekizumab Improves Patient-Reported Outcomes through 52 Weeks in Patients with Active Psoriatic Arthritis and Previous Inadequate Response to Tumor Necrosis Factor-Inhibitors

Arthur Kavanaugh, 1, Helena Marzo-Ortega, 2, Ronald Vender, 3 Julie Birt, 4, David Adams, 4, Olivier Benichou, 4, Chen-Yen Lin, 4 and Peter Nash, 5, 1 Medicine, University of California, San Diego, La Jolla, CA, 2 Department of Rheumatology, Chapel Allerton Hospital, Leeds, United Kingdom, 3 Dermatrails Research, Inc., Hamilton, ON, Canada, 4 Eli Lilly and Company, Indianapolis, IN, 5 University of Queensland, Brisbane, Australia

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Background/Purpose: Ixekizumab (IXE) is a high affinity monoclonal antibody that selectively targets interleukin-17A. Up to 24 weeks, IXE was superior to placebo (PBO) in improving health related quality of life of patients with active psoriatic arthritis (PsA) and previous inadequate response to TNF inhibitors (TNFi) in a phase 3 trial (SPIRIT-P2; NCT02349295). Herein, we report the Week 52 interim patient-reported outcome (PROs) findings of IXE treatment during the Extension Period (EP) of SPIRIT-P2.

Methods: All 363 patients entering SPIRIT-P2 had an inadequate response to or were intolerant to TNFi. During the Double-Blind Treatment Period (DBTP; Weeks 0-24), patients were randomly assigned 1:1:1 to subcutaneous administration of either 80 mg IXE every 4 weeks (Q4W; N=122) or 2 weeks (Q2W; N=123) following a 160 mg starting dose at Week 0 or PBO (N=118). Of these, 310 patients completed the DBTP and entered the EP (Weeks 24-156). Patients randomized to IXE at Week 0 continued the same dose regimen in the EP. PBO patients were re-randomized (1:1) to IXE Q4W or Q2W at Week 16 (inadequate responders) or Week 24 and received a 160 mg starting dose. At baseline and Week 52, the following PROs were assessed: Short Form-36 Health Survey (SF-36) Physical Component Summary (PCS) and Mental Component Summary (MCS), European Quality of Life 5 Dimensions Visual Analog Scale (EQ-5D VAS; 0-100 scale), Work Productivity and Activity Impairment-Specific Health Problem (WPAI-SHP; absenteeism, presenteeism, work productivity, and activity impairment), fatigue Numeric Rating Scale (NRS; 0 [no fatigue]-10 [as bad as you can imagine] scale), and the itch NRS (0 [no itch]-10 [worst itch imaginable] scale). The fatigue NRS has not been validated. Itch NRS was assessed in patients with baseline psoriatic lesion involving ≥3% body surface area (BSA; N=175). All analyses were performed on the EP population. Change in PRO measures from baseline at Week 52 were summarized using descriptive statistics. Missing values were imputed by modified baseline observation carried forward.

Results: Mean baseline (Week 0) scores of PROs indicated that the EP population had impaired physical and mental function, quality of life, and work productivity (Table). Patients receiving IXE up to 52 weeks reported improvements in SF-36 (PCS and MCS), EQ-5D VAS, WPAI-SHP (presenteeism, work productivity, and activity impairment), and fatigue NRS (Table). For PsA patients with ≥3% BSA baseline psoriasis, improvements in itch NRS were observed for patients receiving IXE up to 52 weeks.

Conclusion: In patients with active PsA and previous inadequate response to TNF-i, IXE provided sustained improvement up to 52 weeks in all measured PROs, including physical and mental function, quality of life, work productivity, fatigue, and itch (≥3% BSA psoriasis).

1. Kavanaugh et al. EULAR. 2017 June 17; Madrid, Spain; [abstract SAT0446]
Disclosure: A. Kavanaugh, Eli Lilly and Company, 5; H. Marzo-Ortega, Janssen Pharmaceutica Product, L.P., 2,Abbvie, Celgene, Janssen, Eli Lilly and Company, MSD, Novartis, Pfizer, UCB, 5; R. Vender, AbbVie, Actelion, Amgen, Celgene, Cipher, Eli Lilly and Company, Galderma, GlaxoSmithKline, Janssen, Leo Pharma, Novartis, Palladin, Pfizer, and Valeant, 5,AbbVie, Amgen, Centocor, Dermira, Eli Lilly and Company, Galderma, GlaxoSmithKline,Leo Pharma, Merck, Novartis, Pfizer, Regeneron, and Takeda, 2,AbbVie, Actelion, Amgen, Celgene, Cipher, Eli Lilly and Company, Galderma, GlaxoSmithKline, Janssen, Leo Pharma, Novartis, Palladin, Pfizer, and Valeant, 8; J. Birt, Eli Lilly and Company, 3,Eli Lilly and Company, 1; D. Adams, Eli Lilly and Company, 1,Eli Lilly and Company, 3; O. Benichou, Eli Lilly and Company, 3,Eli Lilly and Company, 1; C. Y. Lin, Eli Lilly and Company, 1,Eli Lilly and Company, 3; P. Nash, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Hospira, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, 5,AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Hospira, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, 8,AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Hospira, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, 2.

Efficacy of Ustekinumab in Psoriatic Arthritis Patients By Prior Treatment Exposure and Disease Duration

Arthur Kavanaugh1, Soumya D. Chakravarty2,3, G. James Morgan4, M. Isabel Apaolaza5, Shelly Kafka2, Elizabeth C. Hsia6,7, Michael Song7, Yin You7 and Iain B. McInnes8,

1Medicine, University of California, San Diego, La Jolla, CA, 2Janssen Scientific Affairs, LLC, Horsham, PA, 3Drexel University College of Medicine, Philadelphia, PA, 4Janssen Scientific Affairs, LLC, Spring House, PA, 5Janssen Biologics BV, Leiden, Netherlands, 6University of Pennsylvania School of Medicine, Philadelphia, PA, 7Janssen Research & Development, LLC, Spring House, PA, 8University of Glasgow, Glasgow, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A  
Session Time: 9:00AM-11:00AM

Background/Purpose: To evaluate the efficacy of ustekinumab (UST) by prior treatment exposure and disease duration in adult PsA patients (pts) in the Phase 3 trials PSUMMIT 1 and PSUMMIT 2.

Methods: Pts had active PsA (≥5 swollen, ≥5 tender joints, CRP ≥ 3.0mg/L,) for ≥6 mos despite treatment with csDMARDs and/or NSAIDs (PSUMMIT 1) or csDMARDs, NSAIDs, and/or anti-tumor necrosis factor (TNF) agents (PSUMMIT 2). In both studies, pts were randomized to SC injections of placebo (PBO) or UST 45mg or 90mg at wks 0, 4 and every 12 wks. PBO pts crossed over to UST 45mg at wk 24. At wk 16, early escape (PBOàUST45mg; UST45mgàUST90mg; UST90mgàUST90mg) was possible. Stable doses of MTX were allowed. Pooled data from both PSUMMIT 1 and 2 were analyzed. Efficacy assessments included ACR response, DAS28-CRP response, DAS28-CRP remission (score <2.6), changes in enthesitis (modified MASES index) and dactylitis scores, and total van der Heijde-Sharp (vdH-S) score for radiographic progression. Pts who were anti-TNF-naïve, MTX- and anti-TNF-naïve, all csDMARD- and anti-TNF-naïve were evaluated. ACR response at wks 4 and 16 to assess for early efficacy was also evaluated for anti-TNF-naïve pts with PsA duration <1 year, ≥1 to <3 years, and ≥ 3 years.

Results: In the pooled data, 747 pts were anti-TNF-naïve (53.8% were male; mean age=47 years); 179 pts were MTX- and anti-TNF-naïve (63.7% were male; mean age =47 years); 146 pts were all csDMARD- and anti-TNF-naïve (61.0% male; mean age=46 years). In all three prior treatment populations, significantly greater proportions of pts in the combined UST group vs PBO achieved an ACR20, ACR50, or ACR70 at wk 24. (Table). Similarly, greater proportions of pts in the combined UST group had DAS28-CRP response or remission vs PBO across all three prior treatment populations. In anti-TNF-naïve pts, improvements in enthesitis and dactylitis were significantly greater in the combined UST group vs PBO, and mean change in total vdH-S score was significantly greater for pts in the PBO group than the combined UST group; comparable trends were observed for the MTX- and anti-TNF-naïve pts and all csDMARD- and anti-TNF-naïve pts, but did not reach statistical significance due to the smaller sample sizes in both subgroups. Among anti-TNF-naïve pts treated with UST, ACR20/50/70 response rates were similar across different PsA disease duration groups at early time-points (either wk 4 or wk 16).

Conclusion: UST-treated patients had greater improvements in signs and symptoms of PsA regardless of prior treatment exposure and disease duration.
<table>
<thead>
<tr>
<th>Table. Efficacy at week 24 in PSUMMIT 1 and PSUMMIT 2 combined.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-TNF-naive</td>
</tr>
<tr>
<td>Placebo</td>
</tr>
<tr>
<td>Randomized pts, n</td>
</tr>
<tr>
<td>ACR20</td>
</tr>
<tr>
<td>ACR50</td>
</tr>
<tr>
<td>ACR70</td>
</tr>
<tr>
<td>DAS28-CRP response</td>
</tr>
<tr>
<td>DAS28-CRP remission</td>
</tr>
<tr>
<td>Enthesitis (modified MASES index)</td>
</tr>
<tr>
<td>Pts with enthesitis at baseline, n</td>
</tr>
<tr>
<td>Percent of patients with resolution of enthesitis at week 24</td>
</tr>
<tr>
<td>Dactylitis (0-3)</td>
</tr>
<tr>
<td>Pts with dactylitis at baseline, n</td>
</tr>
<tr>
<td>Percent of patients with resolution of dactylitis at week 24</td>
</tr>
<tr>
<td>Change from baseline in total vDH-S score</td>
</tr>
</tbody>
</table>

Data presented as n (%) or mean ± SD unless otherwise noted.

ACR20/50/70, ≥20%/50%/70% improvement in American College of Rheumatology criteria; DAS28-CRP, 28-joint count disease activity score; MASES, Maastricht
Intravenous Golimumab in Adult Patients with Active Psoriatic Arthritis: Efficacy and Safety through Week 24

Arthur Kavanaugh¹, M. Elaine Husni², Diane D. Harrison³, Lilianne Kim³, Kim Hung Lo³ and Elizabeth C. Hsia⁴,
¹Medicine, University of California, San Diego, La Jolla, CA, ²Rheumatology, Cleveland Clinic, Cleveland, OH, ³Janssen Research & Development, LLC, Spring House, PA, ⁴Janssen Research & Development, LLC/University of Pennsylvania, Spring House/Philadelphia, PA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The GO-VIBRANT study was designed to evaluate the safety and efficacy of intravenous (IV) golimumab (GLM) in adult patients (pts) with active PsA (biologic-naïve).

Methods: GO-VIBRANT is a Phase 3, multicenter, randomized, double-blind, placebo (PBO)-controlled trial. Biologic-naïve active PsA pts were randomized (1:1) to IV GLM 2mg/kg at weeks (wk) 0, 4, and every 8 wks thereafter or PBO at wks 0, 4, 12, and 20 with crossover to GLM at wk24. The primary endpoint was ACR20 response at wk14. Multiplicity-controlled endpoints included ACR50, ACR70, PASI 75, change from baseline in HAQ-DI, enthesitis, dactylitis; and ACR50 and change from baseline in total modified vdH-S (structural damage) score at wk24. Efficacy analyses were based on randomized treatment. Adverse events (AE) through wk24 are reported here.

Results: 480 pts were randomized (PBO: 239; GLM: 241). The study met its primary and all controlled secondary endpoints. At wk14, significantly greater proportions of GLM pts vs PBO achieved ACR20 (75.1% vs. 21.8%). Also, GLM treatment resulted in significant change from baseline HAQ-DI score (-0.60 vs. -0.12), ACR50 (43.6% vs. 6.3%), PASI 75 (59.2% vs. 13.6%), ACR70 (24.5% vs. 2.1%), and change from baseline in enthesitis and dactylitis scores (-1.8 vs. -0.8 and -7.8 vs. -2.8, respectively) (all p<0.001) at wk14. At wk24, significantly greater proportions of GLM pts vs. PBO pts achieved ACR 50 (53.5% vs. 6.3%, p<0.001). At wk24, there was significantly less progression of structural damage for GLM pts vs PBO as measured by change from baseline in total modified vdH-S (structural damage) score (-0.36 vs. 1.95; p<0.001). ACR20 was significantly higher with GLM than PBO as early as wk2 (45.6% vs. 7.5%; p<0.001). 27.0% of GLM pts (vs. 4.2% PBO) achieved Minimal Disease Activity by wk14. In a post-hoc analysis, the number needed to treat for ACR20 at wk14 was 1.9 (Table). Through wk24, 46.3% of GLM pts and 40.6% of PBO pts had ≥1 AE; 2.9% vs. 3.3% of pts, respectively, had ≥1 serious AE. Two deaths and 2 malignancies, all in PBO pts and 1 demyelinating event in a GLM pt were reported. The most common type of AE was infection (20.0% of GLM pts vs. 13.8% of PBO pts). No opportunistic infection or
tuberculosis was reported through wk24. The rate of infusion reactions in GLM-treated pts was low at <2%; none was serious or severe.

**Conclusion:** In pts with active PsA, IV GLM demonstrated significant and clinically meaningful improvements of disease activity and physical function, skin psoriasis clearance, HRQoL, dactylitis and enthesitis, and inhibition of structural damage progression. GLM was well-tolerated through wk24; the safety profile was consistent with other anti-TNF therapies, including SC GLM.

**Table. Clinical Response**

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Golimumab 2 mg/kg</th>
<th>P-values</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients randomized, n</strong></td>
<td>239</td>
<td>241</td>
<td></td>
</tr>
<tr>
<td><strong>Clinical efficacy at wk14</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACR20, n (%)</td>
<td>52 (21.8%)</td>
<td>181 (75.1%)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>ACR50, n (%)</td>
<td>15 (6.3%)</td>
<td>105 (43.6%)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>ACR70, n (%)</td>
<td>5 (2.1%)</td>
<td>59 (24.5%)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>PASI 75, n (%)*</td>
<td>27/198 (13.6%)</td>
<td>116/196 (59.2%)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td><strong>Change from baseline in HAQ-DI (n)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>-0.12 (0.47)</td>
<td>-0.60 (0.53)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td><strong>Change from baseline in enthesitis</strong> (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>-0.8 (1.98)</td>
<td>-1.87 (1.75)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td><strong>Change from baseline in dactylitis</strong> (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>-2.8 (7.03)</td>
<td>-7.8 (8.57)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td><strong>Minimal Disease Activity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MDA n/N (%)</td>
<td>10/239 (4.2%)</td>
<td>65/241 (27.0%)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td><strong>Number Needed to Treat (ACR 20)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NNT (95% CI)</td>
<td>1.9 (1.64, 2.18)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Clinical efficacy at Week 24</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACR50, n (%)</td>
<td>15 (6.3%)</td>
<td>129 (53.5%)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td><strong>Imaging data at Week 24</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change from baseline in vdh-S score (N)</td>
<td>237</td>
<td>237</td>
<td></td>
</tr>
<tr>
<td>Mean (SE)</td>
<td>1.95 (0.264)</td>
<td>-0.36 (0.144)</td>
<td>p&lt;0.001</td>
</tr>
</tbody>
</table>

*Among pts with ≥3% BSA involvement at baseline
**Among pts with finding at baseline

ACR, American College of Rheumatology Criteria; PASI, Psoriasis Area Severity Index; HAQ-DI, Health assessment questionnaire disability index; CI, confidence interval; SD, standard deviation; SE, standard error; vdh-S, total modified van der Heijde-Sharp

**Disclosure:** A. Kavanaugh, Pfizer, AbbVie, Amgen, Janssen, UCB, Novartis, Eli Lilly, 5,AbbVie, Amgen, Janssen, UCB, Eli Lilly, Novartis, Pfizer, 2; M. E. Husni, AbbVie, Janssen, BMS, Novartis, Eli Lilly, 5; D. D. Harrison, Janssen Research & Development, LLC, 3,Johnson & Johnson, LLC, 1; L. Kim, Janssen Research & Development, LLC, 3,Johnson & Johnson, LLC, 1; K. H. Lo, Janssen Research & Development, LLC, 3,Johnson & Johnson, LLC, 1; E. C. Hsia, Janssen Research & Development, LLC, 3,Johnson & Johnson, LLC, 1.
Low Rates of Major Adverse Cardiac Events, Malignancies, and Serious Infections in Subjects with Psoriasis and Psoriatic Arthritis Treated with Apremilast for ≥156 Weeks: Pooled Analysis from the Esteem and Palace 1-3 Phase 3 Trials

Arthur Kavanaugh1, Matthias Augustin2, Eric Lespessailles3, Kim A. Papp4, Maria Paris5, Rongdean Chen5, Dafna D Gladman6, David M. Pariser7 and Ketty Peris8, 1University of California, San Diego, School of Medicine, La Jolla, CA, 2Institute for Health Care Research in Dermatology and Nursing (IVDP), University Medical Center Hamburg-Eppendorf, Hamburg, Germany, 3University of Orleans, Orleans, France, 4Probity Medical Research, Waterloo, ON, Canada, 5Celgene Corporation, Summit, NJ, 6Toronto Western Hospital, Toronto, ON, Canada, 7Eastern Virginia Medical School and Virginia Clinical Research, Inc., Norfolk, VA, 8Catholic University of Rome, Rome, Italy

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Apremilast (APR), an oral PDE4 inhibitor, was effective in phase 3, randomized, placebo (PBO)-controlled trials assessing treatment of moderate to severe plaque psoriasis (ESTEEM 1 and 2) and psoriatic arthritis (PsA; PALACE 1-3). We report MACE, malignancies, and serious infections (SIs; opportunistic and non-opportunistic) incidences in subjects receiving APR 30 mg BID (APR30) for ≥156 wks in a pooled analysis of these studies.

Methods: Incidence rates and exposure-adjusted incidence rates (EAIR)/100 subject-yrs of MACE, malignancies, SIs, and serious opportunistic infections (SOIs) are reported for 0 to 16 wks, 0 to ≤52 wks, and the APR-exposure period (0 to ≥156 wks) for subjects receiving APR30 any time during the studies, through February 2015; ~30% (n=575) of sbjs received >3 yrs (>156 wks) of APR exposure.

Results: 2,242 subjects were included in the safety analysis for 0 to 16 wks (PBO n=913, subject-yrs exposure [sy]=260.2; APR30 n=1,329, sy=377.8); 1,905 subjects received APR30 during the APR-exposure period, representing 3,527.5 sy. Exposure during 0 to ≤52 wks was 1,524.5 sy. At baseline, 64.2% of APR30 subjects with PsA (PALACE 1-3) were receiving concomitant DMARDs (including methotrexate). Incidence of MACE with APR30 was low and comparable to PBO during 0 to 16 wks. During 0 to ≤52 wks and the APR-exposure period, incidence of MACE (EAIR/100 subject-yrs) remained low (Table). Incidence rates (EAIR/100 subject-yrs) of hematologic malignancies, nonmelanoma skin cancers, and solid tumors were similar with PBO (0.0, 1.2, 0.4) and APR30 (0.0, 1.3, 0.3) during 0 to 16 wks; incidence rates remained low during 0 to ≤52 wks and the APR-exposure period (Table). During 0 to 16 wks, the overall rate of SIs and non-SIs was low and comparable between subjects receiving PBO (20.6%) and APR30 (24.8%). The overall rate of SIs and non-SIs was 42.2% during 0 to ≤52 wks and comparable to rates during the PBO-controlled period (0 to 16 wks); the majority of reported infections (upper respiratory tract infection, nasopharyngitis, sinusitis) were not serious. During the PBO-controlled period (0 to 16 wks), rates of SIs with APR30 were low and comparable to PBO; no SOIs were reported. During 0 to ≤52 wks, the overall rate of SIs was low (0.6%; EAIR/100 subject-yrs: 0.7). The rate of SIs remained low (1.8%; EAIR/100 subject-yrs: 1.0) during the long-term cumulative APR-exposure period (0 to ≥156 wks) (Table). No clustering of any particular event was noted with respect to SIs; most events occurred in only 1 subject. No clinical reactivation of tuberculosis was reported with long-term APR30 exposure (0 to ≥156 wks). The rate of marked hematologic abnormalities remained low with long-term APR exposure.
Conclusion: Incidence of MACE, malignancies, and SIs was low in subjects with psoriasis and PsA receiving APR30 for ≥156 wks. No new safety signals or SOIs were observed over time with APR30.

| Treatment Period | 0 to ≤52 Wks | APR-Exposure Period 0 to ≥156 Wks | Cumulative Events  
|------------------|--------------|----------------------------------|-----------------|
|                  | APR30  
|                  | n=1,905     | Subject-Yrs=1,524.5              | APR30  
|                  | n=1,905     | Subject-Yrs=5,527.5              | EAIR/100 Subject-Yrs | EAIR/100 Subject-Yrs  
| Major adverse cardiac events |  |  |  |
| Acute myocardial infarction | 0.1 | 0.1 |  |
| Myocardial infarction | 0.1 | 0.1 |  |
| Subarachnoid hemorrhage | 0.1 | 0.1 |  |
| Cardiac arrest | 0.0 | 0.1 |  |
| Cerebral infarction | 0.0 | 0.1 |  |
| Malignancies |  |  |  |
| Hematologic | 0.0 | 0.1 |  |
| Non-melanoma skin cancer | 0.0 | 0.5 |  |
| Solid tumors† | 0.3 | 0.4 |  |
| Serious infections | 0.7% | 1.0% |  |
| Pneumonia | 0.1 | 0.1 |  |
| Urinary tract infection | 0.1 | 0.1 |  |
| Appendicitis | 0.1 | 0.1 |  |
| Diverticulitis | 0.1 | 0.1 |  |
| Sepsis | 0.0 | 0.1 |  |
| Bronchitis | 0.0 | 0.1 |  |

*Each subject's total exposure is defined as the time interval between the date of the first and last dose of APR30, regardless of when treatment was initiated, through February 2015.

†No adjudication of major adverse cardiac events for the APR-exposure period.

‡Including malignant melanoma

§Serious infections occurring in subjects included pneumonia (n=2), urinary tract infection (n=2), appendicitis (n=1), and diverticulitis (n=1).

*Serious infections occurring in ≥2 subjects included pneumonia (n=5), appendicitis (n=3), bronchitis (n=3), diverticulitis (n=2), sepsis (n=2), and urinary tract infection (n=2).

APR30=apremilast 30 mg BID; EAIR=exposure-adjusted incidence rate; PBO=placebo.

Disclosure: A. Kavanaugh, Abbott, Amgen, AstraZeneca, BMS, Celgene Corporation, Centocor-Janssen, Pfizer, Roche, UCB, 2; M. Augustin, AbboVie, Almirall, Amgen, Biogen, Boehringer Ingelheim, Celgene Corporation, Centocor, Eli Lilly, GSK, Janssen-Cilag, LEO Pharma, Medac, Merck, MSD, Novartis, Pfizer, UCB, XenoPort, 5,AbboVie, Almirall, Amgen, Biogen, Boehringer Ingelheim, Celgene Corporation, Centocor, Eli Lilly, GSK, Janssen-Cilag, LEO Pharma, Medac, Merck, MSD, Novartis, Pfizer, UCB, XenoPort, 8; E. Lespessailles, Amgen, Eli Lilly, Novartis, Servier, 2,Amgen, Eli Lilly, Novartis, Servier, 8; K. A. Papp, AbbVie, Akros, Amgen, Astenas, AstraZeneca, Baxalta, Baxter, Boehringer Ingelheim, Bristol-Meyers Squibb, Can-Fite, Celgene, Dermira, Devonian, Dow Pharma, Eli Lilly, Galderma, Genentech, Janssen, Kyowa Hakko Kirin, Leo Pharma, Meiji Seika Pharma, 5,Merck MSD, Merck-Serono, Mitsubishi Pharma, Mylan, Novartis, Pfizer Inc, Regeneron, Roche, Sanofi-Aventis/Genzyme, Takeda, UCB, Valeant, 5,AbbVie, Amgen, Astenas, Celgene, Devonian, Eli Lilly, Galderma, Janssen, Kyowa Hakko Kirin, Leo Pharma, Merck MSD, Novartis, Pfizer Inc, Valeant, 8,Abbvie, Akros, Allergen, Amgen, Anacor, Astenas, Baxalta, Boehringer Ingelheim, Bristol-Meyers Squibb, Celgene, Dermira, Dow Pharma, Eli Lilly, Galderma, Genentech, GSK, Janssen, Kyowa Hakko Kirin, Leo Pharma, MedImmune, Merck MSD, Merck-Serono, Mylan, 2,Novartis, Pfizer Inc, Regeneron, Roche, Sanofi-Aventis/Genzyme, Stiefel, Takeda, UCB, Valeant, 2,AbbVie, Akros, Amgen, Baxter, Boehringer Ingelheim, Celgene, Eli Lilly, Galderma, Janssen, Kyowa Hakko Kirin, Merck MSD, Merck-Serono, Mitsubishi Pharma, Novartis, Pfizer Inc, Takeda, UCB, Valeant, 9,Akros, Anacor, Kyowa Hakko Kirin, 9,AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen, Kyowa Hakko Kirin, Merck MSD, Merck-Serono, Novartis, Pfizer Inc, Regeneron, Sanofi-Aventis/Genzyme, Valeant, 9,AbbVie, Amgen, Astenas, Baxter, Boehringer Ingelheim, Bristol-Meyers Squibb, Celgene, Dow Pharma, Eli Lilly, Galderma, Janssen, Merck MSD, Novartis, Pfizer Inc, Regeneron, Sanofi-Aventis/Genzyme, UCB, Valeant, 9; M. Paris, Celgene Corporation, 3; R. Chen, Celgene Corporation, 3; D. D. Gladman, Abbvie, 2,Amgen, 2,Celgene, 2,BMS, 2,Janssen Pharmaceutica Product, L.P., 2,Eli Lilly and Company, 5,Novartis Pharmaceutical Corporation, 2,Pfizer Inc, 2,UCB, 2; D. M. Pariser, Abbott Laboratories, Amgen, Astenas Pharma US, Asubio Pharmaceuticals, BaselGA Pharmaceutical, Celgene Corporation, Dow Pharmaceutical Sciences, Eli Lilly, Galderma Laboratories, Graceway
Long-Term (4-Year) Efficacy and Safety of Apremilast Monotherapy in DMARD-Naive Subjects with Active Psoriatic Arthritis

Alvin F. Wells1, Christopher J. Edwards2, Alan J. Kivitz3, Paul Bird4, Dianne Nguyen5, Maria Paris5, Lichen Teng5 and Jacob A. Aelion6, 1Rheumatology and Immunotherapy Center, Franklin, WI, 2University Hospital Southampton, Southampton, United Kingdom, 3Altoona Center for Clinical Research, Duncansville, PA, 4University Of New South Wales, Sydney, Australia, 5Celgene Corporation, Summit, NJ, 6West Tennessee Research Institute, Jackson, TN

First publication: September 18, 2017

Abstract Number: 601

**Long-Term (4-Year) Efficacy and Safety of Apremilast Monotherapy in DMARD-Naive Subjects with Active Psoriatic Arthritis**

**Background/Purpose:** Apremilast (APR) is an oral phosphodiesterase 4 inhibitor that helps regulate the immune responses that cause joint inflammation and other manifestations of psoriatic arthritis (PsA), including skin disease. The primary findings from the PALACE 4 study (NCT01307423) demonstrated greater efficacy with APR vs. placebo in disease-modifying anti-rheumatic drug (DMARD)-naïve subjects with active PsA.1 We describe the long-term efficacy and safety of APR monotherapy in DMARD-naïve subjects in PALACE 4 for up to 208 weeks.

**Methods:** Subjects were randomized (1:1:1) to placebo, APR 30 mg BID (APR30), or APR 20 mg BID (APR20). At Week 16, subjects were eligible for early escape. At Week 24, all subjects remaining on placebo were switched to APR. Double-blind treatment continued to Week 52, with open-label APR treatment for up to 4 additional years; subjects randomized to APR30 or APR20 continued with their assigned dose during open-label treatment.

**Results:** A total of 527 subjects were randomized and received ≥1 dose of placebo (n=176), APR30 (n=176), or APR20 (n=175). Of the subjects entering the fourth year of treatment, 92.6% (250/270) completed the Week 208 visit. At Week 52, 58.0% (119/205) of subjects receiving APR30 achieved a ≥20% improvement in modified American College of Rheumatology (ACR20) response. At Week 208, rates of improvement in PsA signs and symptoms and physical function were sustained (Table). Of the subjects still receiving study drug, 68.2%, 43.4%, and 23.1% achieved a modified ACR20, ACR50, and ACR70 response, respectively; 40.5% and 67.6% achieved ≥75% and ≥50% reduction from baseline Psoriasis Area and Severity Index (PASI-75 and PASI-50) responses, respectively (Table). During Weeks >156 to ≤208, the most common adverse events (AEs) among APR30-exposed subjects were upper respiratory tract infection (4.3%) and nasopharyngitis (6.5%); serious AEs occurred in 5.8% of APR30 subjects; serious infection was reported by 1 APR30 subject and no opportunistic infections were reported during Week >156 to ≤208. In general, no change in the types of AEs and no increase in the incidence and severity of AEs were seen with longer-term exposure. The APR20 safety profile was similar to that of APR30.

**Conclusion:** Over 208 weeks, APR monotherapy demonstrated sustained response and improvements in PsA signs and symptoms, including swollen and tender joint counts, enthesitis, dactylitis, physical function, and psoriasis. APR continued to demonstrate an acceptable safety profile and was generally well tolerated.

Disclosure: A. F. Wells, Celgene Corporation, 2; C. J. Edwards, Celgene Corporation, Pfizer, Roche, Samsung, 2, Celgene Corporation, Pfizer, Roche, Samsung, 5, AbbVie, GSK, Pfizer, Roche, 8; A. J. Kivitz, Cytori Therapeutics, 2; P. Bird, Celgene Corporation, 2; D. Nguyen, Celgene Corporation, 3; M. Paris, Celgene Corporation, 3; L. Teng, Celgene Corporation, 3; J. A. Aelion, AbbVie, Ardea Biosciences, AstraZeneca, BMS, Celgene Corporation, Centocor, Eli Lilly, Galapagos, Genencor, GSK, Human Genome Sciences, Janssen, Merck, Mesoblast, Novartis, Novo Nordisk, Pfizer, Roche, Sanofi-Aventis, Takeda, UCB, Vertex, 2.


Abstract Number: 602

Improvements in Work Productivity with up to 104 Weeks of Apremilast Monotherapy: Results from a Phase 3b, Randomized, Controlled Study in Biologic-Naïve Subjects with Active Psoriatic Arthritis

Philip J Mease1, Dafna D Gladman2, Eric K Davenport3, Xiaolei Zhou3, Benoit Guerette4, Lichen Teng4, Satyin Kaura4 and Peter Nash5, 1Swedish Medical Center and University of Washington School of Medicine, Seattle, WA, 2Krembil Research Institute, Toronto Western Hospital, Toronto, ON, Canada, 3RTI Health Solutions, Research Triangle Park, NC, 4Celgene Corporation, Summit, NJ, 5University of Queensland, Brisbane, Australia

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Patients with active psoriatic arthritis (PsA) may experience disease manifestations across multiple domains, as well as impaired functioning in daily activities at home and at work. ACTIVE, a phase 3b study, is evaluating the efficacy of apremilast (APR) monotherapy in biologic-naïve subjects with PsA who may have had exposure to 1 prior
conventional disease-modifying anti-rheumatic drug. The ACTIVE work productivity findings through Week 104 are reported.

Methods: Subjects were randomized (1:1) to receive APR 30 mg BID or placebo. Subjects who did not improve at least 10% in both swollen and tender joint counts at Week 16 were eligible for early escape. At Week 24, all remaining placebo subjects were switched to APR. Work productivity and activity impairment were assessed at baseline and Week 16 using the 6-item, self-administered Work Productivity and Activity Impairment Questionnaire: Psoriatic Arthritis (WPAI:PsA). The WPAI:PsA includes 4 subscale scores: Absenteeism, Presenteeism, Work Productivity Loss, and Activity Impairment; subscale scores each range from 0% to 100%, with higher scores indicating greater impairment. Work-related subscales were evaluated only among employed subjects, while activity impairment was evaluated among all subjects, regardless of employment. Correlations were examined at Week 16 between WPAI:PsA subscale scores and selected 36-item Short-Form Health Survey version 2 (SF-36v2) domain scores (i.e., Physical Functioning [PF], Bodily Pain [Pain], and Vitality [VIT]). Improvement in work productivity was assessed through Week 104.

Results: Baseline characteristics were similar between the APR and placebo subjects with WPAI:PsA scores included in the current analysis. At Week 16, APR significantly improved work productivity and the ability to carry out daily activities compared with placebo, with significantly greater mean improvements observed in the overall Work Productivity Loss score \((P=0.001)\) and Activity Impairment score \((P<0.001)\) (Table). Estimated mean change in the Absenteeism score was similar with APR vs. placebo \((P=0.679)\). By contrast, the Presenteeism score showed significant improvement with APR vs. worsening with placebo \((−10.8\% vs. 4.1\%; P=0.002)\). At Week 16, statistically significant correlations were observed between WPAI:PsA subscale scores (except Absenteeism) and SF-36v2 domain scores (i.e., PF, Pain, and VIT). Among subjects randomized to receive APR at baseline, Week 16 WPAI:PsA subscale score improvements were generally maintained through Week 104.

Conclusion: In biologic-naive subjects with active PsA, APR monotherapy contributed to an overall improvement in work productivity at Week 16, which correlated with SF-36v2 PF, Pain, and VIT scores; improvements in WPAI:PsA subscale scores were generally maintained to Week 104.

<table>
<thead>
<tr>
<th>Improvements in WPAI:PsA Subscale Scores (%) at Week 16</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WPAI:PsA Subscale</strong> Globle Period</td>
</tr>
<tr>
<td>Presenteeism</td>
</tr>
<tr>
<td>Apremilast LS Mean (95% CI) n=39</td>
</tr>
<tr>
<td>−10.8 (−17.8, −3.8)</td>
</tr>
<tr>
<td>Placebo LS Mean (95% CI) n=50</td>
</tr>
<tr>
<td>4.1 (−1.7, 9.9)</td>
</tr>
<tr>
<td>Treatment Difference (95% CI) P Value</td>
</tr>
<tr>
<td>−14.9 (−24.1, −5.8)</td>
</tr>
<tr>
<td>Work Productivity Loss</td>
</tr>
<tr>
<td>Apremilast LS Mean (95% CI) n=40</td>
</tr>
<tr>
<td>−1.9 (−18.8, −5.6)</td>
</tr>
<tr>
<td>Placebo LS Mean (95% CI) n=56</td>
</tr>
<tr>
<td>3.5 (−2.4, 9.4)</td>
</tr>
<tr>
<td>Treatment Difference (95% CI) P Value</td>
</tr>
<tr>
<td>15.4 (−2.5, 6.2)</td>
</tr>
<tr>
<td>Activity Impairment</td>
</tr>
<tr>
<td>Apremilast LS Mean (95% CI) n=87</td>
</tr>
<tr>
<td>−11.8 (−16.4, −7.1)</td>
</tr>
<tr>
<td>Placebo LS Mean (95% CI) n=103</td>
</tr>
<tr>
<td>−0.5 (−4.7, 3.8)</td>
</tr>
<tr>
<td>Treatment Difference (95% CI) P Value</td>
</tr>
<tr>
<td>−11.3 (−17.6, −5.0)</td>
</tr>
<tr>
<td>Absenteeism</td>
</tr>
<tr>
<td>Apremilast LS Mean (95% CI) n=40</td>
</tr>
<tr>
<td>−3.6 (−5.9, −1.3)</td>
</tr>
<tr>
<td>Placebo LS Mean (95% CI) n=55</td>
</tr>
<tr>
<td>−3.0 (−4.9, −1.0)</td>
</tr>
<tr>
<td>Treatment Difference (95% CI) P Value</td>
</tr>
<tr>
<td>−0.8 (−3.7, 2.4)</td>
</tr>
</tbody>
</table>

Results are from an analysis of covariance model, adjusted with baseline WPAI:PsA subscale score, baseline prednisone use (yes/no), and previous disease-modifying anti-rheumatic drug use (yes/no). LS mean is estimated using the observed margins of the covariates. WPAI:PsA scores were evaluated for subjects with values at both baseline and Week 16. Absenteeism, Presenteeism, and Work Productivity Loss were evaluated only among employed subjects. Activity Impairment scores were evaluated among all randomized subjects with scores of baseline and Week 16, regardless of employment status. CI=confidence interval; LS=least-square.

Disclosure: P. J. Mease, Celgene, Novartis, AbbVie, Amgen, BMS, Lilly, Pfizer and UCB, 2; Celgene, Corrona, Novartis, AbbVie, Amgen, BMS, Crescendo, Genentech, Janssen, Lilly, Merck, Pfizer and UCB, 5; AbbVie, Amgen, BMS, Crescendo, Celgene, Genentech, Janssen, Pfizer and UCB, 8; D. D. Gladman, Abbvie, 2; Amgen, 2; Celgene, 2; BMS, 2; Janssen Pharmaceutica Product, L.P., 2; Eli Lilly and Company, 5; Novartis Pharmaceutical Corporation, 2; Pfizer Inc, 2; UCB, 2; E. K. Davenport, None; X. Zhou, None; B. Guerette, Celgene Corporation, 3; L. Teng, Celgene Corporation, 3; S. Kaura, Celgene Corporation, 3; P. Nash, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Hospira, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, 5; AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Hospira, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, 8; AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Hospira, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, 2.
Abstract Number: 603

**Characterization of Clinical Benefits in Subjects Classified As ACR20 Non-Responders at Week 104 of Apremilast Treatment: Subanalysis of 3 Long-Term, Phase III Trials**

Philip J Mease1, Dafna D Gladman2, Arthur Kavanaugh3, Priscila Nakasato4, Benoit Guerette4, Lichen Teng4 and Peter Nash5, 1Swedish Medical Center and University of Washington School of Medicine, Seattle, WA, 2Krembil Research Institute, Toronto Western Hospital, Toronto, ON, Canada, 3University of California, San Diego, School of Medicine, La Jolla, CA, 4Celgene Corporation, Summit, NJ, 5University of Queensland, Brisbane, Australia

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

**Background/Purpose:** The PALACE 1, 2, and 3 trials evaluated the efficacy and safety of apremilast (APR) in subjects with active psoriatic arthritis (PsA) despite prior conventional disease-modifying anti-rheumatic drugs and/or biologics. The objective of this analysis is to further characterize the clinical benefits associated with long-term APR exposure in subjects who failed to achieve an ACR20 response at Week 104.

**Methods:** Subjects were randomized (1:1:1) at baseline to receive placebo (PBO), APR 30 mg BID (APR30), or APR 20 mg BID. Subjects who were randomized to APR30 at baseline and classified as ACR20 non-responders (ACR20NRs) at Week 104 were considered for this analysis. At Weeks 24, 52, and 104, ACR core components were examined as well as the proportions of subjects achieving a low disease activity (LDA) state (Clinical Disease Activity in Psoriatic Arthritis [cDAPSA] score ≤13), PASI-75/PASI-50 response among those with psoriasis involvement >3% of the body surface area at baseline, and dactylitis count and Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) of 0 among those with dactylitis or enthesitis at baseline. Safety is described for the overall PALACE 1-3 population.

**Results:** A total of 109 subjects randomized to APR30 treatment at baseline were ACR20NRs at Week 104. Lack of improvement in Patient's Global Assessment of Disease Activity, patient’s assessment of pain, HAQ-DI, and C-reactive protein outcomes most commonly had an impact on patients’ inability to achieve an ACR20 response. Baseline ACR core components were similar for ACR20NRs and ACR20 responders at Week 104. Among these ACR20NRs, several core components of ACR response, including swollen/tender joint counts and static Physician’s Global Assessment of Disease Activity (visual analog scale) scores, showed sustained improvements from baseline through Week 104 (Table). Importantly, of the 109 ACR20NRs at Week 104, 27.5% achieved cDAPSA LDA state and 50.0% achieved a PASI-50 response after continued treatment with APR30 through Week 104 (Table). Among ACR20NRs with baseline dactylitis (n=44) or enthesitis (n=74), 68.2% achieved a dactylitis count of 0 and 33.8% achieved a MASES of 0 at Week 104. In the overall subject population, no new safety concerns were identified through 104 weeks.

**Conclusion:** ACR20NRs receiving APR30 demonstrated significant improvements in core PsA domains. The data may explain why subjects who failed to achieve an ACR20 response remained on long-term APR treatment. These findings suggest that some subjects with PsA may experience meaningful clinical improvement that is not completely captured by the assessment of ACR20 response criteria. Outcome measures specifically designed for PsA patients may be more suitable for evaluating treatment response in PsA patients.
Abstract Number: 604

Consistent Safety Profile with up to 4 Years of Apremilast Treatment: Analysis of Data from 1,493 Subjects with Psoriatic Arthritis in 3 Large, Phase III, Long-Term Studies

Philip J Mease1, Dafna D Gladman2, Juan J. Gomez-Reino3, Stephen Hall4, Arthur Kavanaugh5, Eric Lespessailles6, Georg Schett7, Maria Paris8, Lichen Teng8 and Jürgen Wollenhaupt9, 1Swedish Medical Center and University of Washington School of Medicine, Seattle, WA, 2Toronto Western Research Institute, Toronto, ON, Canada, 3Hospital Clínico Universitario de Santiago, Santiago de Compostela, Spain, 4Monash University, CabriniHealth, Melbourne, Australia, 5University of California, San Diego, School of Medicine, La Jolla, CA, 6University of Orleans, Orleans, France, 7Friedrich Alexander University Erlangen-Nurnberg, Erlangen, Germany, 8Celgene Corporation, Summit, NJ, 9Schön Klinik Hamburg-Eilbek, Klinik für Rheumatologie, Hamburg, Germany

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Apremilast (APR), an oral phosphodiesterase 4 inhibitor, regulates immune activity in psoriatic arthritis (PsA) patients. We evaluated the long-term safety of APR treatment for up to 4 years in subjects with active PsA despite prior conventional disease-modifying anti-rheumatic drugs (DMARDs) and/or biologics. Safety data were pooled from the phase 3 PALACE 1, 2, and 3 studies.
Methods: Subjects were randomized at baseline (1:1:1) to receive placebo (PBO), APR 30 mg BID (APR30), or APR 20 mg BID (APR20). PBO subjects were re-randomized to APR30 or APR20 at Week 16 (early escape) or Week 24. Double-blind APR treatment continued to Week 52; subjects could continue APR during an open-label, long-term treatment phase for up to 5 years treatment. Visits in years 2, 3, and 4 were scheduled at 13-week intervals. Safety was assessed at each visit throughout the study, and results are summarized here by exposure.

Results: A total of 1,493 subjects were randomized and received ≥1 dose of study medication (PBO: n=495; APR30: n=497; APR20: n=501). At the 4-year data cut, the numbers of subjects receiving APR30 and APR20 in each exposure period were 1,441 in Weeks 0 to ≤52, 1,028 in Weeks >52 to ≤104, 865 in Weeks >104 to ≤156, and 767 in Weeks >156 to ≤208. During the 0- to ≤52-week APR-exposure period, adverse events (AEs) occurring in ≥5% of APR30-exposed subjects were diarrhea, nausea, headache, upper respiratory tract infection, and nasopharyngitis (Table). Most diarrhea and nausea AEs were reported within the first 2 weeks of treatment and usually resolved within 4 weeks; the frequency of gastrointestinal AEs decreased with longer APR30 exposure, and the frequency of other common AEs either decreased or remained stable with prolonged exposure (Table). Most AEs were mild or moderate in severity. During Weeks >156 to ≤208 of APR exposure, the discontinuation rate due to AEs was 1.7% with APR30, and the rate of serious AEs (SAEs) was 7.0%, consistent with earlier periods; most SAEs occurred in 1 subject each. Rates were very low for major cardiac events, malignant neoplasms, and serious opportunistic infections, comparable to the first year of treatment. Rates of depression remained very low in Weeks >156 to ≤208. Marked laboratory abnormalities were infrequent, and most returned to baseline values with continued treatment.

Conclusion: APR30 demonstrated a favorable and consistent safety profile and was well tolerated for up to 208 weeks, marked by the lack of an increase in infection rates or a need for specific laboratory monitoring. The incidence of AEs remained stable or decreased with long-term exposure to APR30.

![Table showing APR Exposure Periods and AEs](https://example.com/table.png)

<table>
<thead>
<tr>
<th>Subjects, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>21 AE</td>
</tr>
<tr>
<td>10 SAE</td>
</tr>
<tr>
<td>AEs leading to drug withdrawal</td>
</tr>
<tr>
<td>Death</td>
</tr>
</tbody>
</table>

A1 in 25% of subjects, n (%)

- Diarrhea: 112 (15.5)
- Nausea: 100 (13.0)
- Headache: 75 (10.4)
- Upper respiratory tract infection: 60 (8.3)
- Nasopharyngitis: 41 (5.7)

Select marked abnormalities in clinical laboratory parameters, n (%):

- Alanine aminotransferase >3x ULN: 2/753 (0.3)
- Creatinine >1.7x ULN: 372/753 (0.7)
- Leukocytes <1.6 x 10^9/L: 273/753 (0.4)
- Neutrophils >10x10^9/L: 372/753 (0.5)
- Platelets <150x10^9/L: 372/753 (0.7)
- Hemoglobin: male <10.5 g/dL, female <10 g/dL: 372/753 (0.7)

*Includes all subjects who received APR during the time interval relative to the start of APR treatment.*

Disclosure: P. J. Mease, Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Genentech, Janssen, Novartis, Pfizer, Roche, UCB, 2;Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Genentech, Janssen, Novartis, Pfizer, Roche, UCB, 5,Abbott, Amgen, Biogen Idec, BMS, Eli Lilly, Genentech, Janssen, Pfizer, UCB, 8; D. D. Gladman, Abbvie, 2,Amgen, 2,Celgene, 2,BMS, 2,Janssen Pharmaceutical Product, L.P., 2,Eli Lilly and Company, 5,Novartis Pharmaceutical Corporation, 2,Pfizer Inc, 2,UCB, 2; J. J. Gomez-Reino, Roche, Schering-Plough, 2,BMS,
Ixekizumab Exhibits a Favorable Safety Profile during 24 Weeks of Treatment in Subjects with Active Psoriatic Arthritis: Integrated Safety Analysis of Two Randomized, Placebo Controlled, Phase III Clinical Trials

Philip J Mease¹, Gerd R. Burmester², Susan Moriarty³, Olivier Benichou³, Wen Xu³ and Peter Nash⁴, ¹Swedish Medical Center and University of Washington, Seattle, WA, ²Department of Rheumatology and Clinical Immunology, Charité - University Medicine Berlin, Free University and Humboldt University Berlin, Berlin, Germany, ³Eli Lilly and Company, Indianapolis, IN, ⁴University of Queensland, Brisbane, Australia

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Ixekizumab (IXE) is a high affinity monoclonal antibody that selectively targets IL-17A. The objective of this analysis is to report the integrated safety of IXE in 2 pivotal trials in patients with active PsA.

Methods: The SPIRIT phase 3 trials consist of patients with active PsA who were bDMARD-naive (SPIRIT-P1, NCT01695239) or were inadequate responders to TNF-inhibitors (SPIRIT-P2; NCT02349295). Patients were randomized to 80 mg IXE every 4 weeks (Q4W, N=229) or 2 weeks (Q2W, N=225) after a 160 mg starting dose or PBO (N=224). Integrated safety data are presented from the PBO-controlled treatment periods (Weeks 0-24). Safety was assessed for patients who received at least 1 dose of study drug. At Week 16, patients deemed Inadequate Responders received rescue therapy and were included in this dataset only up to Week 16. Data was analyzed using a Cochran-Mantel-Haenszel test stratified by trial.

Results: The percentage of patients with ≥1 treatment emergent adverse event (TEAE) was significantly greater in the IXE compared to PBO treatment groups (Table 1). No clear difference was seen between groups for the percentage of patients with ≥1 serious adverse event (SAE) or discontinued early from study drug. Infection-related SAEs were reported in a significantly higher percentage of IXE Q2W than PBO patients. Treatment-emergent infections were numerically more frequent with IXE treatment compared to PBO (Table 2); upper respiratory tract infections, nasopharyngitis, and sinusitis were the most common infections. One PBO, 4 IXE Q4W, and 8 IXE Q2W-treated patients had ≥1 Candida infection. Injection site reactions were reported in a significantly higher percentage of patients in the IXE than the PBO treatment groups; most were of mild or moderate severity. Allergic reactions/hypersensitivity events were reported in a significantly higher percentage of IXE Q2W than PBO patients; no case of anaphylaxis was reported. Two cases of malignancy were reported (both IXE Q4W patients): prostate cancer and basal cell carcinoma. There were no major adverse cardiac events (MACE). While there were no reports of Crohn’s disease or ulcerative colitis, 1 IXE Q2W patient had SAEs of anal abscess...
and anal fistula, considered to represent inflammatory bowel disease; this patient continued study drug. There were no deaths or reports of suicide or suicidal ideation.

**Conclusion:** The safety profile of IXE during the placebo-controlled treatment period was consistent with published findings in patients receiving ixekizumab for moderate-to-severe plaque psoriasis.


<table>
<thead>
<tr>
<th>Event Type</th>
<th>PBO (N=224)</th>
<th>IXE Q4W (N=229)</th>
<th>IXE Q2W (N=225)</th>
<th>Total IXE (N=454)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with ≥1 TEAE</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>127 (57%)</td>
<td>153 (67%)*</td>
<td>156 (69%)*</td>
<td>309 (68%)*</td>
</tr>
<tr>
<td>Moderate</td>
<td>60 (27%)</td>
<td>91 (40%)</td>
<td>81 (36%)</td>
<td>172 (38%)</td>
</tr>
<tr>
<td>Severe</td>
<td>63 (28%)</td>
<td>54 (24%)</td>
<td>61 (27%)</td>
<td>115 (25%)</td>
</tr>
<tr>
<td>Patients with ≥1 SAE</td>
<td>6 (3%)</td>
<td>9 (4%)</td>
<td>11 (5%)</td>
<td>20 (4%)</td>
</tr>
<tr>
<td>Infection-related SAE</td>
<td>0</td>
<td>1 (&lt;1%)</td>
<td>5 (2%)*</td>
<td>6 (1%)</td>
</tr>
<tr>
<td>Discontinuation due to AE</td>
<td>8 (4%)</td>
<td>7 (3%)</td>
<td>12 (5%)</td>
<td>19 (4%)</td>
</tr>
</tbody>
</table>

Table 1. Overview of Adverse Events for the Integrated PBO-Controlled Treatment Period (Weeks 0-24).

Data depicted as n (%). Patients with multiple occurrences of the same event are categorized by the highest severity. *Statistically significant (p<0.05) compared with placebo.

<table>
<thead>
<tr>
<th>Event Type</th>
<th>PBO (N=224)</th>
<th>IXE Q4W (N=229)</th>
<th>IXE Q2W (N=225)</th>
<th>Total IXE (N=454)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>62 (28%)</td>
<td>77 (34%)</td>
<td>72 (32%)</td>
<td>149 (33%)</td>
</tr>
<tr>
<td>Candida</td>
<td>1 (&lt;1%)</td>
<td>4 (2%)</td>
<td>8 (4%)*</td>
<td>12 (3%)</td>
</tr>
<tr>
<td>Cytophenias</td>
<td>2 (1%)</td>
<td>2 (1%)</td>
<td>4 (2%)</td>
<td>6 (1%)</td>
</tr>
<tr>
<td>Grade 3 or 4 Neutropenia</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Injection-site reactions</td>
<td>10 (4%)</td>
<td>40 (17%)*</td>
<td>57 (25%)*</td>
<td>97 (21%)*</td>
</tr>
<tr>
<td>Allergic reactions/</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hypersensitivities</td>
<td>4 (2%)</td>
<td>10 (4%)</td>
<td>14 (6%)*</td>
<td>24 (5%)*</td>
</tr>
<tr>
<td>Malignancies</td>
<td>0</td>
<td>2 (1%)</td>
<td>0</td>
<td>2 (&lt;1%)</td>
</tr>
<tr>
<td>MACE</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Depression</td>
<td>3 (1%)</td>
<td>4 (2%)</td>
<td>4 (2%)</td>
<td>8 (2%)</td>
</tr>
<tr>
<td>Interstitial Lung Disease</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hepatic Events</td>
<td>10 (4%)</td>
<td>7 (3%)</td>
<td>11 (5%)</td>
<td>18 (4%)</td>
</tr>
<tr>
<td>Crohn’s Disease</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ulcerative Colitis</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 2. Adverse Events of Special Interest for the Integrated PBO-Controlled Treatment Period (Weeks 0-24).

Data depicted as n (%). Reported as adverse events according to the high level term in MedDRA (Medical Dictionary for Regulatory Activities) *Statistically significant (p<0.05) compared with placebo.

**Disclosure:** P. J. Mease. None; G. R. Burmester, AbbVie, 5,AbbVie, 9,Celgene, 5,Celgene, 9,Gilead, 5,Gilead, 9,Eli Lilly and Company, 5,Eli Lilly and Company, 9,Pfizer Inc, 5,Pfizer Inc, 9; S. Moriarty, Eli Lilly and Company, 1,Eli Lilly and Company, 3,O. Benichou, Eli Lilly and Company, 3,Eli Lilly and Company, 1; W. Xu, Eli Lilly and Company, 1,Eli Lilly and Company, 3; P. Nash, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Hospira, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, 5,AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Hospira, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, 8,AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Hospira, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, 2.


**Abstract Number:** 606

**Secukinumab Demonstrates Consistent Safety over Long-Term Exposure in Patients with Psoriatic Arthritis and Moderate to Severe Plaque Psoriasis: Updated Pooled Safety Analyses**
SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Pooled safety data from secukinumab psoriasis (PSO) and psoriatic arthritis (PsA) clinical trial programs after ~1 year of exposure have been reported previously.1, 2 Here, we report updated longer-term safety data of secukinumab exposure from PSO and PsA studies.

Methods: The PSO data pool consisted of 9 Phase III studies in moderate-to-severe plaque PSO and PsA pool consisted of 3 Phase III studies in active PsA. Secukinumab doses differed in the studies and included intravenous (up to 10 mg/kg) or subcutaneous (s.c.; 75–300 mg) loading, followed by s.c. maintenance dosing (300, 150 or 75 mg). Placebo patients were re-randomized to secukinumab at 12–24 weeks depending on study design. Exposure adjusted incident rates (EAIR) were used to adjust for differences in treatment exposure and analyses included all patients who received ≥1 dose of secukinumab.

Results: A total of 3893 and 1380 patients from PSO and PsA studies representing an exposure of 7769.0 and 2841.3 patient years, respectively, were included in this pooled safety analysis. In both PsO and PsA, the most frequently reported adverse events (AEs) with secukinumab were nasopharyngitis, headache, non-serious infections of the upper respiratory tract and arthralgia (Table). The EAIRs of AEs of special interest with secukinumab including serious infections, Candida infections, inflammatory bowel disease, and major adverse cardiac events (Table) were similar in both PSO and PsA indications, and comparable to those reported previously.1,2 No cases of tuberculosis were reported.

Conclusion: Secukinumab demonstrated a favorable safety profile during long term treatment (up to 7769 patient-years of exposure) in patients with moderate-to-severe plaque PSO or PsA consistent with previous reports. Safety was comparable across psoriasis and PsA patients supporting long-term use in these chronic conditions.

## Table: Summary of Secukinumab Safety across PSO and PsA studies: Entire Safety Period

<table>
<thead>
<tr>
<th></th>
<th>PSO Any secukinumab</th>
<th>PsA Any secukinumab</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 3893</td>
<td>N = 1380</td>
</tr>
<tr>
<td>Total exposure, patient-years</td>
<td>7769.0</td>
<td>2841.3</td>
</tr>
<tr>
<td>Min–max exposure (days)</td>
<td>1–1526</td>
<td>8–1464</td>
</tr>
<tr>
<td>Exposure (days), mean (SD)</td>
<td>728.9 (421.9)</td>
<td>752.0 (379.8)</td>
</tr>
<tr>
<td>Death, n (%)</td>
<td>7 (0.2)</td>
<td>7 (0.5)</td>
</tr>
</tbody>
</table>

**EAIR per 100 Patient-years (95% CI)**

<table>
<thead>
<tr>
<th></th>
<th>Any AE</th>
<th>Any serious AE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>196.9 (190.3, 203.6)</td>
<td>162.0 (152.9,171.5)</td>
</tr>
<tr>
<td>Frequent AEs(^{\dagger})</td>
<td>7.2 (6.6, 7.8)</td>
<td>7.9 (6.8, 9.0)</td>
</tr>
</tbody>
</table>

**AEs of special interest**

<table>
<thead>
<tr>
<th></th>
<th>PSO</th>
<th>PsA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious infections</td>
<td>1.4 (1.2, 1.7)</td>
<td>1.7 (1.2, 2.2)</td>
</tr>
<tr>
<td><em>Candida</em> infections</td>
<td>2.1 (1.8, 2.4)</td>
<td>1.7 (1.3, 2.3)</td>
</tr>
<tr>
<td>Inflammatory Bowel Disease</td>
<td>0.3 (0.2, 0.4)</td>
<td>0.4 (0.2, 0.7)</td>
</tr>
<tr>
<td>Crohn's disease</td>
<td>0.1 (0.0, 0.1)</td>
<td>0.1 (0.0, 0.3)</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>0.2 (0.1, 0.3)</td>
<td>0.1 (0.0, 0.3)</td>
</tr>
<tr>
<td>MACE</td>
<td>0.3 (0.2, 0.5)</td>
<td>0.4 (0.2, 0.7)</td>
</tr>
</tbody>
</table>

\(^{\dagger}\)Adverse events in the secukinumab group that occurred with an EAIR of ≥5 during the entire safety period in either of the pooled groups. AE, adverse event; EAIR, exposure adjusted incidence rate per 100 patient-years; MACE, major adverse cardiac event; N, number of patients in the analysis; SD, standard deviation.

**Disclosure:** P. J. Mease, AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Merck, Novartis, Pfizer, SUN, and UCB, 2,AbbVie, Amgen, BMS, Celgene, Crescendo Bioscience, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, SUN, and UCB, 5,AbbVie, Amgen, BMS, Celgene, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, and UCB, 8; I. B. McInnes, Novartis, Amgen, Janssen, BMS, Pfizer, UCB, AbbVie, Celgene, Lilly, 5; K. Reich, AbbVie, Amgen, Biogen, Boehringer Ingelheim Pharma, Celgene, Centocor, Covagen, Forward Pharma, GlaxoSmithKline, Janssen-Cliag, Leo, Lilly, Medac, Merck Sharp and Dohme Corp., Novartis, Ocean Pharma, Pfizer, Regeneron, Takeda, UCB Pharma, Xenoprot, 2,AbbVie, Amgen, Biogen, Boehringer Ingelheim Pharma, Celgene, Centocor, Covagen, Forward Pharma, GlaxoSmithKline, Janssen-Cliag, Leo, Lilly, Medac, Merck Sharp and Dohme Corp., Novartis, Ocean Pharma, Pfizer, Regeneron, Takeda, UCB Pharma, Xenoprot, 8; P. Nash, Novartis, AbbVie, Roche, Pfizer, BMS, Janssen, and Celgene, 2,Novartis, AbbVie, Roche, Pfizer, BMS, Janssen, and Celgene, 5,Novartis, AbbVie, Roche, Pfizer, BMS, Janssen, and Celgene, 8; M. Andersson, Novartis Pharma AG, 3; K. Abrams, Novartis Pharmaceutical Corporation, 3,Novartis Pharmaceutical Corporation, 1; L. Pricop, Novartis Pharmaceutical Corporation, 1,Novartis Pharmaceutical Corporation, 3; T. Fox, Novartis Pharma AG, 1,Novartis Pharma AG, 3.


**Abstract Number:** 607

**Secukinumab Treatment of Psoriatic Arthritis and Moderate to Severe Psoriasis Relieves Anxiety/Depression up to 52 Weeks: An Overview from**
Secukinumab Phase 3 Clinical Trials

Philip J Mease1, Mark Lebwohl2, Isabelle Gilloteau3, Todd Fox3, Jaime Oliver3, Steffen Jugl3 and Alice B Gottlieb4;
1University of Washington School of Medicine and Swedish Medical Center, Seattle, WA, 2Icahn School of Medicine at Mount Sinai, New York, NY, 3Novartis Pharma AG, Basel, Switzerland, 4Department of Dermatology, New York Medical College, Vallhalla, NY

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Secukinumab (SEC), a fully human monoclonal antibody selectively neutralizing interleukin-17A, exhibits significant efficacy, with a favorable safety profile, in the treatment of psoriatic arthritis (PsA) and moderate to severe psoriasis. SEC has a rapid onset of action and demonstrates sustained responses. PsA and psoriasis patients are at greater risk for psychological distress, including depression and suicidality. Previous analysis, using pooled data from phase 3 studies FIXTURE and ERASURE, reported high and sustained relief from anxiety/depression in psoriasis patients treated with SEC 300 mg up to Week (Wk) 52 (~80% of patients reported not being anxious/depressed) from the EuroQol 5-dimensional (Mobility, Self-Care, Usual Activities, Pain/Discomfort, and Anxiety/Depression) and 3-level questionnaire (EQ-5D-3L). Here, we aim to confirm these results in additional phase 3 SEC trials in patients with PsA and psoriasis.

Methods: Results of the ‘Anxiety/Depression’ dimension ("not anxious/depressed", "moderately anxious/depressed", or "extremely anxious/depressed") of EQ-5D-3L were derived from three phase 3 studies using an approved SEC dose: FUTURE 1 and FUTURE 2, two randomized, double-blind clinical trials, comparing SEC 150 mg to placebo in active PsA; and CLEAR, a multicenter, double-blind, parallel-group study comparing SEC 300 mg to ustekinumab in moderate to severe psoriasis. The proportions of patients reporting as not being anxious/depressed are described as observed for each individual study up to Wk 52.

Results: In FUTURE 1, 76/200 (38.0%) of PsA patients treated with SEC 150 mg reported being not anxious/depressed at baseline, increasing to 99/192 (51.6%) at Wk 4 and 109/184 (59.2%) at Wk 52 (Fig. 1). Similarly, in FUTURE 2, 32/100 (32.0%) and 41/99 (41.4%) of PsA patients treated with SEC 150 mg or 300 mg, respectively reported being not anxious/depressed at baseline, increasing to 51/99 (51.5%) and 52/95 (54.7%) at Wk 4 and 49/89 (55.1%) and 55/95 (57.9%) at Wk 52 (Fig. 1). In the CLEAR study, 154/326 (47.2%) psoriasis patients treated SEC 300 mg reported being not anxious/depressed at baseline, and this increased to 238/322 (73.9%) at Wk 4, 263/326 (80.7%) at Wk 16, and was sustained up to Wk 52 (237/292, 81.2%) (Fig. 1).

Conclusion: This analysis of the patient-reported EQ-5D-3L anxiety/depression measure from three phase 3 SEC trials showed consistently higher anxiety/depression burden among patients with PsA than among those with moderate to severe psoriasis; however, it also indicates that SEC treatment improves and provides sustained relief from anxiety/depression among all treated patients, regardless of their disease, up to 1 year.
Figure 1. Percentages of patients with psoriatic arthritis or psoriasis reporting not being anxious/depressed on EQ-5D following treatment with secukinumab in three phase 3 clinical trials (as observed).

Disclosure: **P. J. Mease**, AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Merck, Novartis, Pfizer, SUN, and UCB, 2,AbbVie, Amgen, BMS, Celgene, Crescendo Bioscience, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, SUN, and UCB, 5,AbbVie, Amgen, BMS, Celgene, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, and UCB, 8; **M. Lebwohl**, Mount Sinai Medical Center, 3,AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen Research & Development, LLC, Kadmon, LEO Pharma, Novartis, Pfizer and ViDac, 2; **I. Gilloteau**, Novartis Pharma AG, 3; **T. Fox**, Novartis Pharma AG, 1,Novartis Pharma AG, 3; **J. Oliver**, Novartis Pharma AG, 3; **S. Jugl**, Novartis Pharma AG, 1,Novartis Pharma AG, 3; **A. B. Gottlieb**, Amgen Inc, Astellas, Akros, Centocot Janssen), Inc; Celgene Corp, Bristol Myers Squibb Co, Beiersdorf Inc, Abbott Labs Abbvie), TEVA, Actelion, UCB, Novo Nordisk, Novartis, Dempipsor Ltd., Incyle, Pfizer, Canfite, Eli Lilly and Company, Coronado, Vertex., 5,Janssen Incyte, 2.


Abstract Number: 608

**Presence of Poor Prognostic Factors May Predict Response to Abatacept in Patients with Active Psoriatic Arthritis: Results from a Post Hoc Analysis from a Phase III Study**

**Philip J Mease**1, Iain B. McInnes2, Vibeke Strand3, O FitzGerald4, H Ahmad5, A Johnsen5, J Ye5 and S Banerjee5, 1Swedish Medical Center and University of Washington, Seattle, WA, 2University of Glasgow, Glasgow, Great Britain, 3Stanford University, Palo Alto, CA, 4Department of Rheumatology, St Vincent’s University Hospital and University College Dublin, Dublin, Ireland, 5Bristol-Myers Squibb, Princeton, NJ

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthopathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM
Background/Purpose: Abatacept, a selective T-cell co-stimulation modulator, significantly increased ACR20 response and had an overall beneficial effect on musculoskeletal symptoms in patients with active psoriatic arthritis (PsA) in the Phase III Active pSoriaTic athRitis rAndomizEd triAl (ASTRAEA, NCT01860976). Factors that may predict responses to abatacept were explored in this post hoc analysis. The aim of this study was to evaluate the relationship between baseline characteristics and abatacept response in a post hoc analysis of ASTRAEA. Methods: Patients were randomized (1:1) to SC abatacept 125 mg weekly or placebo for 24 weeks in this trial. Patients without >20% improvement in joint counts at Week 16 were switched to open-label abatacept (early escape). ACR20 response rate in patients stratified by baseline variables was investigated in a multivariate analysis and odds ratios (ORs) generated to identify differences in response. Using a cut-off of OR 1.2, indicating patient subgroups in whom abatacept appeared to have a meaningful treatment benefit, baseline variables were further investigated in a univariate analysis and estimated differences calculated.

Results: Of 424 patients enrolled, 213 received abatacept and 211 placebo. In abatacept-treated patients, the multivariate model showed a difference in ACR20 response (OR >1.2) for baseline CRP (>upper limit of normal [ULN] vs ≤ULN; OR 1.346 [95% CI 0.668, 2.712]), DAS28 (CRP) (>5.1 vs ≤5.1; 1.489 [0.782, 2.836]), dactylitis (>0 vs 0; 1.372 [0.708, 2.659]), and median baseline erosions (≥3 vs <3; 1.924 [1.032, 3.587]). In placebo-treated patients, the OR was >1.2 for dactylitis only (1.406 [0.619, 3.193]). These factors, which have been identified previously as indicating poor prognosis in PsA, were balanced between treatment arms at baseline. In the univariate model by poor prognostic factors, the differences in ACR20 response rates with abatacept treatment vs placebo in distinct subgroups were numerically greater in patients who were positive for these prognostic factors at baseline than in those who were not (Figure).

Conclusion: These findings identified subgroups of patients with PsA with certain baseline characteristics in whom abatacept is most likely to be effective. The predictive factors identified are aligned with poor prognostic factors in the EULAR and Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) guidelines, and may indicate patients with the highest unmet medical need.


Disclosure: P. J. Mease, AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 2,AbbVie, Amgen, BMS, Celgene, Crescendo Bioscience, Corrona, Demira, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, Zynerba, 5,AbbVie, Amgen, BMS, Celgene, Crescendo Bioscience, Genentech, Janssen, Novartis, Pfizer, UCB, 8; I. B. McInnes, BMS,
Body Mass Index Does Not Influence the Efficacy of Subcutaneous Abatacept in Patients with PsA: Results from a Phase III Trial

Iain B. McInnes, Gianfranco Ferraccioli, MA D'Agostino, M Le Bars, S Banerjee, H Ahmad, Y Elbez, J Ye and Philip J Mease

1University of Glasgow, Glasgow, Great Britain, 2Division of Rheumatology - Institute of Rheumatology and Affine Sciences, Catholic University of the Sacred Heart, Rome, Italy, 3Hôpital Ambroise Paré, Boulogne-Billancourt, France, 4Bristol-Myers Squibb, Rueil-Malmaison, France, 5Bristol-Myers Squibb, Princeton, NJ, 6Excelya, Boulogne-Billancourt, France, 7Swedish Medical Center and University of Washington, Seattle, WA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Obesity is a risk factor for the development and severity of psoriatic arthritis (PsA). Patients (pts) with increased BMI (overweight/obese) are less likely to achieve sustained minimal disease activity (MDA) vs those with normal BMI, independent of biologic and non-biologic DMARD use. Moreover, obese pts with PsA respond less favourably to TNFα inhibitors vs normal BMI pts. In the Phase III ASTRAEA study (NCT01860976), abatacept (ABA) significantly improved disease activity and was well tolerated; the primary endpoint of ACR20 at 24 weeks (W) was met. We evaluated the relationship between BMI and ABA response in a post hoc analysis of ASTRAEA.

Methods: Pts were randomized (1:1) to weekly SC ABA 125 mg or placebo (PBO) for 24W. Pts without ≥20% improvement in joint counts at W16 were switched to open-label ABA (early escape; EE). Pts designated as EE or with missing data were imputed as non-responders. ACR20/50/70 responses and % of pts with DAS28 (CRP) ≤3.2 or <2.6, MDA, HAQ-DI response (change from baseline [CFB] ≥0.35) and radiographic non-progression (PsA-modified total Sharp/van der Heijde score, CFB ≤0) at W24 were compared for ABA vs PBO between three BMI subgroups (underweight/normal: <25 kg/m²; overweight: 25–30 kg/m²; obese: >30 kg/m²) using univariate and multivariate analyses. BMI <25 kg/m² subgroup was the reference and key potential confounding factors for treatment efficacy were included in the multivariate model. Odds ratios (ORs), 95% CIs and p values were calculated for each BMI subgroup comparison.

Results: Overall, 212 ABA- and 210 PBO-treated pts had available baseline BMI status. For ABA vs PBO, respectively, 31 (14.6%) vs 39 (18.6%) were underweight/normal, 77 (36.3%) vs 57 (27.1%) were overweight and 104 (49.1%) vs 114 (54.3%) were obese. In the ABA and PBO groups, neither overweight nor obese pts had a significantly lower ACR20 response vs underweight/normal pts in the univariate model. This was confirmed in the multivariate models in overweight and obese pts, respectively, vs underweight/normal pts: ABA: OR (95% CI) 1.215 (0.437, 3.378), p=0.7087 and 0.446 (0.162, 1.228), p=0.1181; PBO: OR (95% CI) 0.554 (0.189, 1.621), p=0.2811 and 0.460 (0.166, 1.271), p=0.1343. Similar results were observed for all other outcomes tested (Figure).

Conclusion: As in RA, BMI does not appear to affect the
efficacy of abatacept in PsA; this is consistent across both objective and pt-reported outcome measures. Given that 1 in 3 pts with PsA are overweight/obese, these data strongly suggest an advantage of abatacept therapy in this debilitating disease.


**Figure.** Adjusted Comparisons of Various Efficacy Outcomes Between BMI Groups in Abatacept (A) and Placebo (B) Patients

<table>
<thead>
<tr>
<th>BMI &lt;25 kg/m²</th>
<th>BMI 25–30 kg/m²</th>
<th>BMI &gt;30 kg/m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR (95% CI)</td>
<td>p value</td>
<td></td>
</tr>
<tr>
<td>A) AC20 response</td>
<td>Reference</td>
<td>0.7087</td>
</tr>
<tr>
<td>MDA response</td>
<td>Reference</td>
<td>0.6390</td>
</tr>
<tr>
<td>DAS28 (CRP) &lt;2.6</td>
<td>Reference</td>
<td>0.5460</td>
</tr>
<tr>
<td>SRI non-progression &lt;10</td>
<td>Reference</td>
<td>0.4680</td>
</tr>
<tr>
<td>B) AC20 response</td>
<td>Reference</td>
<td>0.2811</td>
</tr>
<tr>
<td>MDA response</td>
<td>Reference</td>
<td>0.3290</td>
</tr>
<tr>
<td>DAS28 (CRP) &lt;2.6</td>
<td>Reference</td>
<td>0.0647</td>
</tr>
<tr>
<td>SRI non-progression &lt;10</td>
<td>Reference</td>
<td>0.0740</td>
</tr>
</tbody>
</table>

MDA=minimal disease activity; OR=odds ratio; SRI=Sharp/Van der Heijde score.

Disclosure: I. B. McInnes, BMS, Celgene, Janssen, UCB, Roche, 2,BMS, Celgene, Janssen, Novartis, Pfizer, AbbVie, UCB, Lilly, 5; G. Ferraccioli, Roche, BMS, Pfizer, 2,MSD, UCB, Pfizer, AbbVie, Lilly, Cellgene, Novartis, Roche, 8; M. D'Agostino, BMS, AbbVie, Novartis, 8; M. Le Bars, Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1, 9; S. Banerjee, Bristol-Myers Squibb, 1,Bristol-Myers Squibb, 3, H. Ahmad, Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1, 9; Y. Elbez, None; J. Ye, Bristol-Myers Squibb, 1,Bristol-Myers Squibb, 3, P. J. Mease, AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 2,AbbVie, Amgen, BMS, Celgene, Crescendo Bioscience, Corrona, Demira, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, Zynerba, 5,AbbVie, Amgen, BMS, Celgene, Crescendo Bioscience, Genentech, Janssen, Novartis, Pfizer, UCB, 8.
Abstract Number: 610

Baseline Structural Damage Predicts Response to Abatacept in Patients with Psoriatic Arthritis: A Post Hoc Analysis from a Phase III Study

Georg Schett1, T Lehman2, HA Ahmad2, A Johnsen2, S Banerjee2 and Philip J Mease3, 1University of Erlangen-Nuremberg, Erlangen, Germany, 2Bristol-Myers Squibb, Princeton, NJ, 3Swedish Medical Center and University of Washington, Seattle, WA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is a heterogeneous disease in which treatment selection and patient stratification based on clinical domains have recently been proposed.1 The efficacy and safety of the co-stimulation modulator abatacept in patients with PsA was investigated in the Phase III ASTRAEA study (NCT01860976).2 The aim of this analysis was to identify baseline factors that predict response to abatacept treatment in patients with PsA in ASTRAEA.

Methods: Baseline disease and demographic characteristics of patients treated with abatacept (n=213) or placebo (n=211) in the Phase III ASTRAEA study achieving high-level response (ACR50: abatacept n=41, placebo n=26; ACR70: abatacept n=22, placebo n=14) at Day 169 (Week 24) were compared with those of patients not achieving an ACR20 response (abatacept n=129, placebo n=164). Due to the inclusion of an early escape (EE) at Day 114 (Week 16), patients who entered the EE were imputed as non-responders at Day 169 and included in the ACR20 non-responders group.

Results: For both the abatacept and placebo groups, most baseline demographic and disease characteristics, including age, BMI, disease duration and disease activity at baseline, were similar among ACR50 and ACR70 responders and ACR20 non-responders (Table, abatacept group). Joint-space narrowing, erosion, total PsA-modified Sharp/van der Heijde scores, and the swollen joint count, however, were higher in abatacept ACR50 and ACR70 responders than in ACR20 non-responders. Conversely, placebo ACR 20 non-responders show a higher degree of baseline structural damage than ACR50 and ACR70 responders. Baseline CRP was higher in both abatacept and placebo ACR50 and ACR70 responders than in ACR20 non-responders.

Conclusion: These data show that a higher degree of baseline structural joint damage and higher swollen joint count is associated with a greater response to abatacept therapy in PsA. These observations suggest that PsA patients with signs of synovitis-driven osteoclast formation and disease activity including swollen joints and structural damage may be good candidates for abatacept treatment. These results are in accordance with recent data showing that CTLA-4 controls osteoclast differentiation and bone resorption3 and the known mechanism of abatacept on T-cell co-stimulation mediated inflammation2. 1. Coates L, et al. Arthritis Rheumatol 2016;68:1060–71. 2. Mease P, et al. Ann Rheum Dis 2017 May 4; Epub ahead of print. 3. Bozec A, et al. Sci Transl Med 2014;6:235ra60.
<table>
<thead>
<tr>
<th></th>
<th>ACR20 non-responders (n=129)</th>
<th>ACR50 responders (n=41)</th>
<th>ACR70 responders (n=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>51.5 (10.3)</td>
<td>50.2 (11.7)</td>
<td>49.1 (10.9)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>31.7 (7.1)</td>
<td>28.4 (4.0)</td>
<td>29 (4.4)</td>
</tr>
<tr>
<td>Duration of PsA (years)</td>
<td>8.7 (8.8)</td>
<td>7.6 (6.9)</td>
<td>7.0 (6.2)</td>
</tr>
<tr>
<td>Tender joints</td>
<td>20.1 (12.8)</td>
<td>20.1 (12.8)</td>
<td>22.5 (12.7)</td>
</tr>
<tr>
<td>Swollen joints</td>
<td>10.8 (7.0)</td>
<td>14.1 (8.5)</td>
<td>15.5 (8.0)</td>
</tr>
<tr>
<td>DAS28 (CRP)</td>
<td>4.9 (1.0)</td>
<td>5.0 (1.1)</td>
<td>5.3 (0.8)</td>
</tr>
<tr>
<td>Joint-space narrowing score</td>
<td>6.7 (16.4)</td>
<td>16.6 (36.3)</td>
<td>10.5 (34.9)</td>
</tr>
<tr>
<td>Erosion score</td>
<td>9.5 (20.7)</td>
<td>21.8 (48.1)</td>
<td>14.3 (41.1)</td>
</tr>
<tr>
<td>Total SHS score</td>
<td>16.2 (36.6)</td>
<td>38.4 (84.0)</td>
<td>24.8 (75.8)</td>
</tr>
<tr>
<td>Baseline CRP (mg/L)</td>
<td>13 (21.8)</td>
<td>15.5 (18.0)</td>
<td>14.7 (18.5)</td>
</tr>
</tbody>
</table>

Data are expressed as mean (SD)

PsA=psoriatic arthritis; SHS=Sharp/van der Heijde score

Disclosure: G. Schett, None; T. Lehman, Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1, 9; H. Ahmad, Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1, 9; A. Johnsen, Bristol-Myers Squibb, 1,Bristol-Myers Squibb, 3; S. Banerjee, Bristol-Myers Squibb, 1,Bristol-Myers Squibb, 3; P. J. Mease, AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 2,AbbVie, Amgen, BMS, Celgene, Crescendo Bioscience, Corrona, Demira, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, Zynerba, 5,Amgen, BMS, Celgene, Crescendo Bioscience, Genentech, Janssen, Novartis, Pfizer, UCB, 8.

Abstract Number: 611

Effectiveness of Early Adalimumab Therapy in Psoriatic Arthritis Patients from Reuma.Pt

Helena Santos¹, Mónica Eusébio², Joana Borges³, Diana Gonçalves⁴, Pedro Ávila-Ribeiro⁵, Daniela Santos Faria⁶, Carina Lopes⁷, João Rovisco⁸, Ana Águeda⁹, Patrícia Nero¹⁰, Paula Valente¹¹, Ana Rita Cravo¹² and Maria José Santos¹³,

¹Instituto Português de Reumatologia, Lisbon, Portugal, ²Sociedade Portuguesa de Reumatologia, Lisboa, Portugal, ³Instituto Português de Reumatologia, Lisboa, Portugal, ⁴Centro Hospitalar de São João, Coimbra, Portugal, ⁵Centro Hospitalar Lisboa Norte, Lisboa, Portugal, ⁶ULSAM, Ponte de Lima, Portugal, ⁷Hospital de Egas Moniz-CHLO, Lisboa, Portugal, ⁸Centro Hospitalar e Universitário de Coimbra, Lisboa, Portugal, ⁹Centro Hospitalar do Baixo Vouga, Aveiro, Portugal, ¹⁰Hospital CUF Descobertas, Lisboa, Portugal, ¹¹Centro Hospitalar Entre o Douro e Vouga, Lisboa, Portugal, ¹²Medical, AbbVie, Lisboa, Portugal, ¹³Reuma.pt, Almada, Portugal, Almada, Portugal

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017

Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I

Session Type: ACR Poster Session A

Session Time: 9:00AM-11:00AM
**Background/Purpose:** There is a lack of evidence on the effect of biologics in early treatment of psoriatic arthritis (PsA) patients (Pts). Benefit of concomitant use of DMARDs remains controversial in this indication.

**Methods:** To compare clinical outcomes in patients with PsA starting adalimumab (ADA), with short and long disease duration and evaluate the potential effect of concomitant use of DMARDs or corticosteroids (CS), both on PsARC response and persistence on ADA. The analyses included adult PsA Pts who have been registered on Reuma.pt between June 2008 - June 2016 and have received ADA therapy for at least 3 months. PsARC, DAS28, tender and swollen joint count, ESR, CRP, PtGA, PhGA evaluated on a 10 cm VAS, and HAQ were compared between Pts <5 years of disease (early PsA) and those with ≥5 years of disease duration (late PsA) when starting ADA. Time to achieve PsARC response was estimated using Kaplan-Meier method, adjusted with Cox Regression with Efron method for ties with robust estimates of variance for baseline characteristics. Same analyses were repeated to compare patients with and without concomitant use of DMARDs or CS.

**Results:** We included 135 PsA patients who started ADA, 41 of them with early PsA. Pts with early PsA were younger, more frequently males, smokers, had significantly more hypertension. Overall, PsARC response was achieved by 72.9% of the Pts (88% early PsA vs 62.2% late PsA; p=0.022) at 3 months, by 85.4% of Pts at 24 months (100% early PsA vs 75.9% late PsA; p=0.044) after starting ADA. Patients with early PsA, achieved significantly less painful joints (2.7 vs 6.7; p=0.006), lower mean CRP (0.5 mg/dl vs 1.3 mg/dl; p=0.011) and PhGA (18.3 vs 28.1; p=0.020) at 3 months. In the long term, early PsA Pts showed less swollen joints (0.3 vs 1.7; p=0.030), lower PhGA (6.3 vs 21.9; p<0.001), CRP (0.4 mg/dl vs 1.0 mg/dl; p=0.026) and disease activity evaluated by DAS28 (2.2 vs 3.2; p=0.030). Early PsA Pts obtained PsARC response more rapidly than those with late PsA (3.8 and 7.4 months, respectively; p=0.008). Concomitant DMARDs, in the long term, showed clinical benefit (PsARC response at 2 years 88.3% vs 60.0%; p=0.044). Concomitant CS had no noticeable effect on PsARC response, over 2 years of follow-up. Survival on treatment with ADA was similar in the 2 groups and was not influenced by DMARD or CS therapy.

**Conclusion:** Patients with early PsA had greater chance of improvement after starting ADA, better functional outcome and achieved PsARC response more rapidly than patients with longer disease duration. Our results suggest that comedication with DMARDs may improve PsARC response in the long term.

<table>
<thead>
<tr>
<th>Disease duration</th>
<th>Baseline</th>
<th>3 months</th>
<th>2 years</th>
<th>p value</th>
<th>Adjusted p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=38</td>
<td>n=50</td>
<td>n=38</td>
<td>n=50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DAS28, mean (SD)</td>
<td>4.5 (0.9)</td>
<td>3.0 (0.7)</td>
<td>2.2 (0.6)</td>
<td>0.010</td>
<td>0.301</td>
</tr>
<tr>
<td>Painful joints, mean (SD)</td>
<td>10.2 (6.3)</td>
<td>6.7 (2.7)</td>
<td>2.2 (1.0)</td>
<td>0.013</td>
<td>0.007</td>
</tr>
<tr>
<td>Swollen joints, mean (SD)</td>
<td>6.1 (3.6)</td>
<td>4.5 (2.3)</td>
<td>1.5 (1.4)</td>
<td>0.037</td>
<td>0.004</td>
</tr>
<tr>
<td>PtGA, mean (SD)</td>
<td>0.3 (0.3)</td>
<td>0.3 (0.1)</td>
<td>0.3 (0.1)</td>
<td>0.002</td>
<td>0.055</td>
</tr>
<tr>
<td>PtGA, mean (SD)</td>
<td>0.3 (0.3)</td>
<td>0.3 (0.1)</td>
<td>0.3 (0.1)</td>
<td>0.002</td>
<td>0.055</td>
</tr>
<tr>
<td>CRP, mg/dl</td>
<td>0.7 (0.5)</td>
<td>0.3 (0.3)</td>
<td>0.3 (0.3)</td>
<td>0.800</td>
<td>0.212</td>
</tr>
<tr>
<td>ESR, mm/h</td>
<td>31.8 (10.2)</td>
<td>22.9 (8.2)</td>
<td>21.1 (8.1)</td>
<td>0.019</td>
<td>0.179</td>
</tr>
<tr>
<td>PsARC yes, n (%)</td>
<td>NA (NA)</td>
<td>33 (28)</td>
<td>21 (19)</td>
<td>0.044</td>
<td>0.044</td>
</tr>
</tbody>
</table>

**Table 1:** Disease characteristics by PsA disease duration and response to Adalimumab. Adjusted for age of beginning of treatment with biologic agents, gender, smoking habits, and BMI.
Disclosure: H. Santos, None; M. Eusébio, None; J. Borges, None; D. Gonçalves, None; P. Ávila-Ribeiro, None; D. Santos Faria, None; C. Lopes, None; J. Rovisco, None; A. Águeda, None; P. Nero, None; P. Valente, None; A. R. Cravo, AbbVie, 3,AbbVie, 1; M. J. Santos, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/effectiveness-of-early-adalimumab-therapy-in-psoriatic-arthritis-patients-from-reuma-pt

Abstract Number: 612

Safety and Effectiveness of Ustekinumab for the Treatment of Psoriatic Arthritis over a 6 Month Period

Regan Arendse¹, Anna Jaroszynska², Derek Haaland³, Pauline Boulos⁴, Isabelle Fortin⁵, Raheem Kherani⁶, Ariel Masetto⁷, Jonathan Chan⁸, Eliofotisti Psaradellis⁹, Melissa Stutz⁹, Brendan Osborne¹⁰, Francois Nantel¹⁰ and Allen J Lehman¹¹, ¹University of Saskatchewan, Saskatoon, SK, Canada, ²Private practice, Burlington, ON, Canada, ³Rheumatology, Clinical Immunology & Allergy, McMaster University, Barrie, ON, Canada, ⁴Rheumatology, McMaster University, Hamilton, ON, Canada, ⁵Centre de Rhumatologie De l’Est du Quebec, Rimouski, QC, Canada, ⁶University of British Columbia, Richmond, BC, Canada, ⁷Centre Hospitalier Universitaire de Sherbrooke, Sherbrooke, QC, Canada, ⁸Rheumatology, University of British Columbia, Vancouver, BC, Canada, ⁹JSS Medical Research, Montreal, QC, Canada, ¹⁰Medical Affairs, Janssen Inc., Toronto, ON, Canada, ¹¹Janssen Inc., Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Ustekinumab (UST) is a fully human immunoglobulin monoclonal antibody against interleukin-12 (IL-12) and interleukin-23 (IL-23) that has been proven safe and efficacious for the treatment of PsA in randomized clinical
trials. The aim of the current analysis was to assess the safety and effectiveness of UST among PsA patients treated under Canadian routine clinical care.

**Methods:** BioTRAC is an ongoing, prospective registry of patients initiating treatment with infliximab or golimumab for rheumatoid arthritis, ankylosing spondylitis, or PsA, or with UST for PsA. Eligible participants for this analysis included UST-treated PsA patients enrolled between 2014-2016. Clinical outcomes assessed at Baseline and the Month 6 visit were: SJC, TJC, pain (100mm visual analogue scale; VAS), PtGA and MDGA (100mm VAS), PASI, HAQ-DI, DAS-28, and joint counts for dactylitis and enthesitis. Safety was ascertained by the incidence of adverse events (AEs), reported per 100 patient years (PY) of follow-up. Descriptive statistics were produced for all variables, and between-visit changes in outcomes were assessed for statistical significance with the paired-samples t-test.

**Results:** A total of 63 UST-treated PsA patients were identified. Mean (SD) age and disease duration at Baseline was 52.8 (11.2) and 5.5 (8.1) years, respectively. A majority of patients were female (63.5 %), and 100.0% were biologic naïve. Changes from Baseline to Month 6 were statistically significant for all clinical outcomes (p < 0.05), except for the PtGA (Table 1). With respect to enthesitis and dactylitis, missing data did not permit assessment of improvement from baseline to Month 6. At baseline, 50.9% of patients had some dactylitis and 34.9% had some enthesitis.

Overall, 36 AEs were reported by 21 patients from Baseline to the Month 6 visit. The majority were mild in nature (n=26/36; 72.2%); "probable" and "very likely" relation to the study drug was determined for 11.1% (n=4/36) and 8.3% (n=3/36) of AEs, respectively. The most common AEs included General Disorders and Administration Site Conditions (n=7/21; 33.3%) and Infections and Infestations (n=8/21; 38.1%). No serious AEs were reported.

**Table 1. Clinical outcome parameters over time, and changes from Baseline to Month 6**

<table>
<thead>
<tr>
<th>Parameter, mean (SD)</th>
<th>Baseline</th>
<th>Month 6</th>
<th>Change</th>
<th>p-value$</th>
</tr>
</thead>
<tbody>
<tr>
<td>SJC-28</td>
<td>3.8 (3.8)</td>
<td>1.6 (2.1)</td>
<td>-2.7 (6.0)</td>
<td>0.014</td>
</tr>
<tr>
<td>TJC-28</td>
<td>6.5 (5.6)</td>
<td>3.4 (5.7)</td>
<td>-3.6 (3.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pain, mm*</td>
<td>55.1 (22.2)</td>
<td>44.6 (27.7)</td>
<td>-11.3 (22.5)</td>
<td>0.008</td>
</tr>
<tr>
<td>PtGA, mm*</td>
<td>58.2 (22.4)</td>
<td>49.1 (28.3)</td>
<td>-9.7 (33.0)</td>
<td>0.101</td>
</tr>
<tr>
<td>MDGA, mm*</td>
<td>51.8 (22.9)</td>
<td>23.4 (19.7)</td>
<td>-28.3 (25.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PASI</td>
<td>4.4 (7.2)</td>
<td>0.7 (1.1)</td>
<td>-3.7 (4.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>1.1 (0.6)</td>
<td>0.8 (0.6)</td>
<td>-0.3 (0.7)</td>
<td>0.019</td>
</tr>
<tr>
<td>DAS-28</td>
<td>4.0 (1.2)</td>
<td>3.5 (1.2)</td>
<td>-0.5 (0.9)</td>
<td>0.026</td>
</tr>
</tbody>
</table>

* 100 mm VAS; † Based on patients with available Baseline and Month 6 data; § P-value derived from the paired samples t-test

**Conclusion:** The results of this analysis demonstrate that UST, administered to PsA patients in a routine clinical care setting, is safe and effective in improving clinical outcomes over 6 months of treatment.

**Disclosure:** R. Arendse, None; A. Jaroszynska, None; D. Haaland, None; P. Boulos, None; I. Fortin, None; R. Kherani, None; A. Masetto, None; J. Chan, None; E. Psaradellis, Janssen Inc., 9; M. Stutz, None; B. Osborne, Janssen Inc., 3; F. Nantel, Janssen Inc., 3; A. J. Lehman, Janssen Inc., 3.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/safety-and-effectiveness-of-ustekinumab-for-the-treatment-of-psoriatic-arthritis-over-a-6-month-period

**Abstract Number:** 613

**Effect of Tofacitinib on Efficacy and Patient-Reported Outcomes in Psoriasis Patients with Baseline Psoriatic Arthritis: A Pooled Analysis of 2 Phase 3 Studies**
Tofacitinib is an oral Janus kinase inhibitor under investigation for the treatment of psoriatic arthritis (PsA). Up to 42% of patients (pts) with psoriasis also have PsA. We examined tofacitinib efficacy and patient-reported outcomes (PROs) in pts with psoriasis and concomitant PsA.

Methods: Data were pooled from identical 52-week, randomized, controlled studies: OPT Pivotal 1 (NCT01276639) and OPT Pivotal 2 (NCT01309737). Both studies enrolled pts with moderate to severe psoriasis. This analysis included only those with a medical history of PsA at baseline (prior diagnosis by a rheumatologist). Pts were randomized 2:2:1 to receive tofacitinib 5 or 10 mg twice daily (BID), or placebo (PBO). Pts receiving PBO advanced to tofacitinib at Week 16. The co-primary efficacy endpoints at Week 16 were the proportion of pts achieving a 75% improvement in the Psoriasis Area and Severity Index score (PASI75) and the proportion of pts achieving Physician’s Global Assessment (PGA) of “clear” or “almost clear”. Secondary endpoints included the proportion of pts achieving Patient’s Global Assessment (PtGA) of “clear” or “almost clear” and changes from baseline in Joint Pain Assessment (ΔJPA), Nail Psoriasis Severity Index (ΔNAPSI), and Short Form-36 Health Survey (ΔSF-36) physical component summary (PCS) score, mental component summary (MCS) score, and 8 domain scores.

Results: The analysis included 430 psoriasis pts with PsA at baseline; 172, 168, and 90 pts received tofacitinib 5 mg BID, tofacitinib 10 mg BID, and PBO, respectively. At Week 16 a greater proportion of pts achieved PASI75, PGA, and PtGA responses with tofacitinib 5 and 10 mg BID vs PBO (all p<0.0001 vs PBO; Table). Improvements were observed with tofacitinib 5 and 10 mg BID vs PBO in ΔJPA and ΔNAPSI (all p<0.0001 vs PBO; Table). Tofacitinib 5 mg BID significantly improved SF-36 PCS (p≤0.05) and 5 of 8 domain scores (physical functioning, role limitations: physical, bodily pain, vitality, social functioning [all p≤0.05]). Tofacitinib 10 mg BID significantly improved SF-36 PCS (p<0.001), MCS (p<0.001), and all 8 domain scores (all p≤0.05). A dose-response was observed across all endpoints following tofacitinib treatment (Table).

Conclusion: Tofacitinib significantly improved clinical endpoints and PROs vs PBO at Week 16 in pts who had concomitant psoriasis and PsA. Details of safety endpoints in pts with psoriasis and PsA in the OPT Pivotal studies will be included in the final presentation.
<table>
<thead>
<tr>
<th>Table: Efficacy endpoints at Week 16</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>(N=1272)</td>
</tr>
<tr>
<td>PASI75 response, n (%)a</td>
</tr>
<tr>
<td>PGA response, n (%)b</td>
</tr>
<tr>
<td>PGA response, n (%)c</td>
</tr>
<tr>
<td>ΔPASI, LS mean (SE)d</td>
</tr>
<tr>
<td>ΔNAPSI, LS mean (SE)d</td>
</tr>
</tbody>
</table>

*Nominal p≤0.05, **p<0.001, ***p<0.0001 vs placebo; aNon-responder imputation; bObserved cases; cΔ change from baseline; DIB: twice daily; JPA: Joint Pain Assessment; LS, least squares; MCS, mental component summary; N: number of patients included in the analysis; n, number of patients achieving a response; NAPSI, Nails Psoriasis Severity Index; PASI75, 75% improvement in the Psoriasis Area and Severity Index score; PBO, placebo; PCS, physical component summary; PGA, Physician’s Global Assessment; PGT, Patient’s Global Assessment; SE, standard error; SF-36, Short Form-36 Health Survey

Disclosure: H. Bachelez, Pfizer Inc, 2,AbbVie, Amgen, Boehringer Ingelheim, Baxalta, Celgene, Eli Lilly, Janssen, Leo Pharma, Novartis, Pfizer Inc, Sun Pharmaceuticals, UCB, 5,AbbVie, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen, Leo Pharma, Novartis, Pfizer Inc, Sun Pharmaceuticals, 8; C. E. Griffiths, AbbVie, Celgene, Eli Lilly, GSK, Janssen, Leo Pharma, Pfizer Inc, Novartis, Sandoz, 2,AbbVie, Almirall, Celgene, Eli Lilly, GSK, Janssen, Leo Pharma, Novartis, Pfizer Inc, Sun Pharmaceuticals, UCB, 5,AbbVie, Almirall, Celgene, Eli Lilly, GSK, Janssen, Leo Pharma, Novartis, Pfizer Inc, Sun Pharmaceuticals, UCB, 8; K. Papp, AbbVie, Akros, Allergen, Amgen, Anacor, Astellas, Baxalta, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Dermira, Dow Pharma, Eli Lilly, Galdema, Genentech, GSK, Janssen, Kyowa Hakko Kirin, Leo Pharma, MedImmune, Merck MSD, Merck-Serono, Mylan, 2,Novartis, Pfizer Inc, Regeneron, Roche, Sanofi-Aventis/Genzyme, Stiefel, Takeda, UCB, Valeant, 2,AbbVie, Akros, Amgen, Astellas, AstraZeneca, Baxalta, Baxter, Boehringer Ingelheim, Bristol-Myers Squibb, Can-Fite, Celgene, Dermira, Devonian, Dow Pharma, Eli Lilly, Galdema, Genentech, Janssen, Kyowa Hakko Kirin, Leo Pharma, Meiji Seika Pharma, 5,Merck MSD, Merck-Serono, Mitsubishi Pharma, Mylan, Novartis, Pfizer Inc, Regeneron, Roche, Sanofi-Aventis/Genzyme, Takeda, UCB, Valeant, 5,AbbVie, Amgen, Astellas, Celgene, Devonian, Eli Lilly, Galdema, Janssen, Kyowa Hakko Kirin, Leo Pharma, Merck MSD, Novartis, Pfizer Inc, Valeant, 8,Akros, Anacor, Kyowa Hakko Kirin, 9,AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen, Kyowa Hakko Kirin, Merck MSD, Merck-Serono, Novartis, Pfizer Inc, Regeneron, Sanofi-Aventis/Genzyme, Valeant, 9,AbbVie, Amgen, Astellas, Baxter, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Dow Pharma, Eli Lilly, Galdema, Janssen, Merck MSD, Novartis, Pfizer Inc, Regeneron, Sanofi-Aventis/Genzyme, UCB, Valeant, 9; S. Hall, AbbVie, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, Roche, UCB, 5; J. F. Merola, AbbVie, Amgen, Biogen Idec, Eli Lilly, Janssen, Kiniksa, Momenta, Mallinckrodt, Novartis, Pfizer Inc, Sunnumed, UCB, 5,AbbVie, 8,Biogen Idec, Novartis, Pfizer Inc, 9; S. R. Feldman, Eli Lilly, Janssen, Novartis, Pfizer Inc, 2,AbbVie, Celgene, Eli Lilly, Janssen, Novartis, Leo Pharma, Pfizer Inc, 5,AbbVie, Eli Lilly, Celgene, Janssen, Novartis, 8; M. Khraishi, Pfizer Inc, 5; A. Tallman, Pfizer Inc, 1; H. Tan, Pfizer Inc, 1; Pfizer Inc, 3; M. A. Hsu, Pfizer Inc, 1; Pfizer Inc, 3.

Effect of Tofacitinib on Reducing Pain in Patients with Rheumatoid Arthritis, Psoriatic Arthritis and Ankylosing Spondylitis

Alexis Ogdie1, Kurt de Vlam2, Iain B. McInnes3, Philip J Mease4, Philip Baer5, Tatjana Lukic6, Kenneth Kwok6, Cunshan Wang7, Ming-Ann Hsu7 and Anna Maniccia6, 1Division of Rheumatology, Department of Medicine, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, 2UZ Leuven, Leuven, Belgium, 3Glasgow Biomedical Research Centre, University of Glasgow, Glasgow, United Kingdom, 4Swedish Medical Center and University of Washington, Seattle, WA, 5Baer Weinberg MPC, Scarborough, ON, Canada, 6Pfizer Inc, New York, NY, 7Pfizer Inc, Groton, CT

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA), which has also been evaluated in other inflammatory rheumatic diseases (IRD) including psoriatic arthritis (PsA) and ankylosing spondylitis (AS). Pain contributes substantial morbidity in patients (pts) with IRD and directly impacts treatment adherence, assessment of disease improvement, and health-related quality of life. We evaluated the effectiveness of tofacitinib in reducing pain in randomized controlled clinical trials in pts with RA, PsA, and AS.

Methods: Five pt populations treated with tofacitinib 5 mg twice daily (BID), 10 mg BID, or placebo (PBO) were evaluated: [1] conventional synthetic disease-modifying antirheumatic drug (csDMARD)-inadequate response (IR) RA pts pooled from ORAL Scan (NCT00847613), ORAL Sync (NCT00856544), and ORAL Standard (NCT00853385), [2] tumor necrosis factor inhibitor (TNFi)-IR RA pts from ORAL Step (NCT00960440), [3] csDMARD-IR PsA pts from OPAL Broaden (NCT01877668), [4] TNFi-IR PsA pts from OPAL Beyond (NCT01882439), and [5] AS pts from a Phase 2 study (NCT01786668). Pain outcomes evaluated from baseline to Month (M)6 (Week [W]12 in the AS population) included Pt’s Assessment of Arthritis Pain (PAAP) (RA and PsA populations only), Short-Form Health Survey (SF)-36v2 Q7 (bodily pain in the past week), SF-36v2 Bodily Pain Domain (BP), EuroQol Five Dimensions Questionnaire Pain/Discomfort Domain (EQ-5D PD; all populations), and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) Q2 (level of AS neck, back, or hip pain) and Q3 (other pain) score (PsA and AS populations only; PsA pts had presence of spondylitis at screening and baseline BASDAI total score >0 in the full analysis set [FAS]). Data were analyzed descriptively.

Results: The csDMARD-IR RA, TNFi-IR RA, csDMARD-IR PsA, TNFi-IR PsA, and AS populations comprised a total of 2066, 399, 316, 394, and 155 pts in the FAS, respectively. In each RA or PsA csDMARD-IR and TNFi-IR population treated with tofacitinib, mean PAAP at baseline (5 mg BID, range 55.7–65.7 mm; 10 mg BID, 54.4–60.1 mm) decreased as early as W2 (1st post-baseline assessment; 45.8–49.8 mm; 38.9–44.8 mm) and continued to decrease through M6 (30.9–34.4 mm; 28.2–36.7 mm); decreases were numerically greater vs PBO and the magnitude of change in RA and PsA populations was similar (Table). Improvements in SF-36v2 Q7 (Table), SF-36v2 BP (Table), and EQ-5D PD were observed in all 4 RA and PsA csDMARD-IR and TNFi-IR populations, and in BASDAI Q2 and Q3 in the csDMARD-IR PsA and TNFi-IR PsA populations. In the AS population, improvements from baseline in mean SF-36v2 Q7 (Table), SF-36v2 BP (Table), EQ-5D PD, and BASDAI Q2 and Q3 were reported at W12 and were numerically greater vs PBO.

Conclusion: Treatment with tofacitinib is associated with a rapid improvement and sustained reduction of pain in pts with RA and PsA who are csDMARD-IR or TNFi-IR, and in pts with AS.
Disclosure: A. Ogdie, Novartis, University of Pennsylvania, 2,Novartis, Pfizer Inc, Takeda, 5; K. de Vlam, Eli Lilly, Pfizer Inc, 5,Galapagos, 9; I. B. McInnes, Celgene, Janssen, Novartis, Pfizer Inc, Roche, UCB, 2,AbbVie, Celgene, Janssen, Novartis, UCB, 5; P. J. Mease, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, Sun Pharmaceutical, UCB, 2,AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, Sun Pharmaceutical, UCB, 5,AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Genentech, Janssen, Novartis, Pfizer Inc, UCB, 8; P. Baer, AbbVie, Amgen, Eli Lilly, Johnson and Johnson, Novartis, Paladin, Sanofi-Genzyme, Takeda, 5,Amgen, Janssen, Lifelabs, Pfizer Inc, 8; T. Lukic, Pfizer Inc, 1,Pfizer Inc, 3; K. Kwok, Pfizer Inc, 1,Pfizer Inc, 3; C. Wang, Pfizer Inc, 1,Pfizer Inc, 3; M. A. Hsu, Pfizer Inc, 1,Pfizer Inc, 3; A. Maniccia, Pfizer Inc, 1,Pfizer Inc, 3.


Abstract Number: 615

Efficacy of Tofacitinib By Background Methotrexate Dose in Patients with Psoriatic Arthritis: A Post Hoc Analysis of Pooled Data from 2 Phase 3 Trials

Alan J. Kivitz1, Oliver FitzGerald2, Peter Nash3, Shirley Pang4, Valeridilio F Azevedo5, Elizabeth Kudlace6, Cunshan Wang6, Daniela Graham6 and Liza Takiya7, 1Department of Rheumatology, Altoona Center for Clinical Research, Duncansville, PA, 2Department of Rheumatology, St Vincent's University Hospital, Dublin, Ireland, 3Department of Medicine, University of Queensland, St Lucia, Brisbane, Australia, 4St. Jude Medical Center, Fullerton, CA, 5Universidade Federal do Paraná, Curitiba, Brazil, 6Pfizer Inc, Groton, CT, 7Pfizer Inc, Collegeville, PA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: November 5, 2017

Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I

Session Type: ACR Poster Session A

Session Time: 9:00AM-11:00AM

Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor under investigation for psoriatic arthritis (PsA). The efficacy of tofacitinib has been evaluated in 2 Phase 3 studies in patients (pts) with PsA. In this analysis, we describe the efficacy of tofacitinib by background methotrexate (MTX) dose in pts with PsA.

Methods: This post hoc analysis utilized efficacy data pooled from 2 Phase 3, randomized, double-blind, placebo-controlled studies (OPAL Broaden [12 months; NCT01877668] and OPAL Beyond [6 months; NCT01882439]) in pts with a diagnosis (≥6 months) of active PsA (≥3 swollen and ≥3 tender joints). Pts in OPAL Broaden were tumor necrosis factor
inhibitor (TNFi)-naïve and had an inadequate response (IR) to ≥1 conventional synthetic disease-modifying antirheumatic drug (csDMARD). Pts in OPAL Beyond had an IR to ≥1 TNFi. Pts were randomized to tofacitinib 5 or 10 mg twice daily (BID), placebo, or adalimumab 40 mg subcutaneous every 2 weeks (OPAL Broaden; adalimumab data not shown). All pts received a stable dose of 1 csDMARD (eg MTX, leflunomide, or sulfasalazine) as background therapy. The maximum dose of MTX allowed per protocol was 20 mg/week. Efficacy outcomes for tofacitinib at Month 3 were evaluated by background MTX dose (≤15 vs >15 mg/week) and included: ACR20/50/70 response rates (≥20/50/70% improvement from baseline, respectively), Health Assessment Questionnaire-Disability Index (HAQ-DI) response rate (reduction from baseline ≥0.35 points), and mean change from baseline in HAQ-DI score. Analyses were based on the full analysis set for pts receiving MTX on Day 1; pts with missing data were considered as having a non-response for binary endpoints. No statistical testing was performed.

**Results:** In total, data from 556 pts who received tofacitinib plus MTX only or placebo plus MTX only (tofacitinib 5 mg BID, n=186; tofacitinib 10 mg BID, n=178; placebo, n=192) were included in this analysis. Most pts were treated with background MTX at doses ≤15 mg/week (n=371, 66.7%; mean [SD] dose, 12.6 [3.1] mg/week) vs >15 mg/week (n=185, 33.3%; mean [SD] dose, 19.8 [0.8] mg/week). Baseline demographics and disease characteristics were generally similar between arms in MTX dose groups (Table). At Month 3, tofacitinib 5 and 10 mg BID were generally associated with numerically greater ACR and HAQ-DI response rates and greater changes from baseline in HAQ-DI score compared with placebo. The magnitude of tofacitinib effects on efficacy outcomes appeared broadly similar between background MTX dose groups (Table).

**Conclusion:** The results of this pooled analysis suggest that the efficacy of tofacitinib in pts with PsA was greater than placebo and does not differ when evaluated by background MTX dose (≤15 vs >15 mg/week), although small pt numbers in some groups may limit the conclusions that can be made. These results are consistent with findings from similar analyses of tofacitinib in pts with rheumatoid arthritis.

**Table:** Patient demographics and disease characteristics at baseline, and efficacy outcomes in March 3 by MTX dose

<table>
<thead>
<tr>
<th>MTX dose (mg/week)</th>
<th>Tofacitinib 5 mg BID (N=154)</th>
<th>Tofacitinib 10 mg BID (N=152)</th>
<th>Placebo (N=168)</th>
<th>Tofacitinib 5 mg BID (N=172)</th>
<th>Tofacitinib 10 mg BID (N=164)</th>
<th>Placebo (N=182)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>54.9 (12.6)</td>
<td>54.8 (12.4)</td>
<td>54.9 (12.3)</td>
<td>54.9 (12.1)</td>
<td>54.8 (12.3)</td>
<td>54.9 (12.3)</td>
</tr>
<tr>
<td>Sex: female (%)</td>
<td>51.0 (51.0)</td>
<td>51.0 (51.0)</td>
<td>51.0 (51.0)</td>
<td>51.0 (51.0)</td>
<td>51.0 (51.0)</td>
<td>51.0 (51.0)</td>
</tr>
<tr>
<td>Number of swollen joints, mean (mm)</td>
<td>20.0 (48.0)</td>
<td>20.5 (48.0)</td>
<td>20.0 (48.0)</td>
<td>20.0 (48.0)</td>
<td>20.5 (48.0)</td>
<td>20.5 (48.0)</td>
</tr>
<tr>
<td>Number of tender joints, mean (mm)</td>
<td>20.0 (48.0)</td>
<td>20.5 (48.0)</td>
<td>20.0 (48.0)</td>
<td>20.0 (48.0)</td>
<td>20.5 (48.0)</td>
<td>20.5 (48.0)</td>
</tr>
<tr>
<td>Number of tender muscles, mean (mm)</td>
<td>20.0 (48.0)</td>
<td>20.5 (48.0)</td>
<td>20.0 (48.0)</td>
<td>20.0 (48.0)</td>
<td>20.5 (48.0)</td>
<td>20.5 (48.0)</td>
</tr>
</tbody>
</table>

**Disclosure:** A. J. Kivitz, AbbVie, Genentech, Genzyme, Janssen, Novartis, Pfizer Inc, Sanofi, UCB, 5,Celgene, Genentech, Genzyme, Novartis, Pfizer Inc, Sanofi, 8; O. FitzGerald, AbbVie, Bristol-Myers Squibb, Novartis, Pfizer Inc, 2,Amgen, Celgene, Eli Lilly, Janssen, 5; P. Nash, None; S. Pang, None; V. F. Azevedo, AbbVie, Eli Lilly, Genentech, GSK, Pfizer Inc, UCB, 2,AbbVie, Merck-Serono, Novartis, Pfizer Inc, 5,AbbVie, Janssen, Merck-Serono, Novartis, Pfizer Inc, Sanofi, 8; E. Kudlacz, Pfizer Inc, 1,Pfizer Inc, 3; C. Wang, Pfizer Inc, 1,Pfizer Inc, 3; D. Graham, Pfizer Inc, 1,Pfizer Inc, 3; L. Takiya, Pfizer Inc, 1,Pfizer Inc, 3.

Integrated Safety Summary of Tofacitinib in Psoriatic Arthritis Clinical Studies

Gerd R. Burmester¹, Oliver FitzGerald², Kevin Winthrop³, Valerilio F Azevedo⁴, William F C Rigby⁵, Keith S Kanik⁶, Cunshan Wang⁶, Pinaki Biswas⁷, Thomas Jones⁸, Sujatha Menon⁶, Niki Palmetto⁷ and Ricardo Rojo⁶, ¹Charité - University Medicine Berlin, Berlin, Germany, ²Department of Rheumatology, St Vincent's University Hospital, Dublin, Ireland, ³Oregon Health & Science University, Portland, OR, ⁴Universidade Federal do Paraná, Curitiba, Brazil, ⁵Geisel School of Medicine at Dartmouth, Lebanon, NH, ⁶Pfizer Inc, Groton, CT, ⁷Pfizer Inc, New York, NY, ⁸Pfizer Inc, Collegeville, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor under investigation for psoriatic arthritis (PsA). We describe the safety profile of tofacitinib from integrated Phase (P)3 and long-term extension (LTE) studies.

Methods: Data were analyzed for patients (pts) who received ≥1 dose of tofacitinib 5 or 10 mg twice daily (BID) or placebo (PBO), integrated across 2 P3 studies (OPAL Broaden [12 months; NCT01877668]; OPAL Beyond [6 months; NCT01882439]) and 1 LTE study (OPAL Balance [ongoing, database not locked; NCT01976364]). Common adverse events (AEs; occurring in ≥2% of tofacitinib pts in any group) were analyzed in the PBO-controlled portion (Months 0–3) of the P3 studies (Cohort 1 [C1]). Serious AEs (SAEs) and discontinuations due to AEs were analyzed over 12 months in pts randomized to tofacitinib 5 or 10 mg BID in P3 studies (Cohort 2a [C2a]); pts randomized to PBO were excluded from this analysis. Deaths and AEs of special interest (serious infections [SI], herpes zoster [HZ], opportunistic infections [OI] including HZ, major adverse cardiovascular events [MACE], malignancies, non-melanoma skin cancer [NMSC]) were evaluated in all tofacitinib-treated pts in the P3 and LTE studies (Cohort 3 [C3]). Incidence rates (IR; pts with events/100 pt-years [PY] and 95% confidence intervals) are reported. Laboratory results will be reported in future publications.

Results: C1 included 474 tofacitinib- and 236 PBO-treated pts; C2a included 474 tofacitinib-treated pts; and C3 included 783 tofacitinib-treated pts (exposure: 776 PY). Nasopharyngitis (5.9%) and headache (8.5%) were the most commonly reported AEs at Month 3 in pts receiving tofacitinib 5 and 10 mg BID, respectively (Table). In pts randomized to tofacitinib 5 or 10 mg BID, over 12 months (C2a), the IRs for SAEs were 7.92 (4.09, 13.84) and 8.11 (4.19, 14.17), respectively. Discontinuation due to AEs occurred in 11 (4.6%) and 11 (4.7%) pts randomized to tofacitinib 5 and 10 mg BID, respectively, with IRs of 7.16 (3.58, 12.82) and 7.31 (3.65, 13.08), respectively, over 12 months (C2a). Across all tofacitinib-treated pts in the P3 and LTE studies (C3), SIs occurred in 11 pts (1.4%; IR 1.40 [0.70, 2.50]). HZ was reported in 16 pts (2.0%; IR 2.05 [1.17, 3.33]) receiving tofacitinib. All 3 cases of multidermatomal HZ were adjudicated as OIs; these were the only OIs (0.4%; IR 0.38 [0.08, 1.11]). In C3, 2 deaths occurred (0.3%; IR 0.25 [0.03, 0.91]); all were considered unrelated to the study drug. MACE were reported in 3 pts (0.4%; IR 0.38 [0.08, 1.11]), malignancies (excluding NMSC) in 5 pts (0.6%; IR 0.63 [0.21, 1.48]), and NMSC in 4 pts (0.5%; IR 0.51 [0.14, 1.30]) in C3.

Conclusion: Tofacitinib in active PsA demonstrated a safety profile consistent to that seen with tofacitinib in RA; no new risks were identified. Longer-term follow-up and larger pt populations will provide further information on the safety profile of tofacitinib in pts with PsA.
Table: Common adverse events (>2% occurrence in any group, all causalities) at Month 3 in patients receiving tofacitinib 5 or 10 mg BID or placebo (Cohort 1)

<table>
<thead>
<tr>
<th>Common adverse events, n (%)</th>
<th>Tofacitinib 5 mg BID</th>
<th>Tofacitinib 10 mg BID</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N=238)</td>
<td>(N=236)</td>
<td>(N=236)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>6 (3.4)</td>
<td>9 (3.8)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>5 (2.1)</td>
<td>2 (0.8)</td>
<td>2 (0.8)</td>
</tr>
<tr>
<td>Nausea</td>
<td>6 (2.5)</td>
<td>5 (2.1)</td>
<td>7 (3.0)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>0</td>
<td>7 (3.0)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>6 (2.5)</td>
<td>4 (1.7)</td>
<td>0</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>14 (5.9)</td>
<td>13 (5.5)</td>
<td>6 (2.5)</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>1 (0.4)</td>
<td>7 (3.0)</td>
<td>3 (1.3)</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>12 (5.0)</td>
<td>11 (4.7)</td>
<td>11 (4.7)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>3 (1.3)</td>
<td>6 (2.5)</td>
<td>5 (2.1)</td>
</tr>
<tr>
<td>Headache</td>
<td>9 (3.8)</td>
<td>20 (8.5)</td>
<td>11 (4.7)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>6 (2.5)</td>
<td>1 (0.4)</td>
<td>3 (1.3)</td>
</tr>
<tr>
<td>Acne</td>
<td>3 (1.3)</td>
<td>5 (2.1)</td>
<td>0</td>
</tr>
<tr>
<td>Hypertension</td>
<td>4 (1.7)</td>
<td>5 (2.1)</td>
<td>3 (1.3)</td>
</tr>
</tbody>
</table>

BID, twice daily; N, number of patients evaluable

Disclosure: G. R. Burmester, Pfizer Inc, 2, Pfizer Inc, 5; O. FitzGerald, AbbVie, Bristol-Myers Squibb, Novartis, Pfizer Inc, 2, Amgen, Celgene, Eli Lilly, Janssen, 5; K. Winthrop, Bristol-Myers Squibb, 2, AbbVie, Bristol-Myers Squibb, Eli Lilly, Galapagos, Pfizer Inc, UCB, 5; V. F. Azevedo, AbbVie, Eli Lilly, Genentech, GSK, Pfizer Inc, UCB, 2, AbbVie, Merck-Serono, Novartis, Pfizer Inc, 5, AbbVie, Janssen, Merck-Serono, Novartis, Pfizer Inc, Sanofi, 8; W. F. C. Rigby, Roche, 5; K. S. Kanik, Pfizer Inc, 1, Pfizer Inc, 3; C. Wang, Pfizer Inc, 1, Pfizer Inc, 3; P. Biswas, Pfizer Inc, 1, Pfizer Inc, 3; T. Jones, Pfizer Inc, 1, Pfizer Inc, 3; S. Menon, Pfizer Inc, 1, Pfizer Inc, 3; N. Palmetto, Pfizer Inc, 1, Pfizer Inc, 3; R. Rojo, Pfizer Inc, 1, Pfizer Inc, 3.


Abstract Number: 617

Comparing Tofacitinib Safety Profile in Patients with Psoriatic Arthritis in Clinical Studies with Real-World Data

Jeffrey R. Curtis¹, Huifeng Yun¹, Oliver FitzGerald², Kevin Winthrop³, Valderilio F Azevedo⁴, Gerd R. Burmester⁵, William F C Rigby⁶, Keith S Kanik⁷, Ricardo Rojo⁷, Sujatha Menon⁷, Cunshun Wang⁷, Pinaki Biswas⁸, Thijs Hendrikx⁹ and Niki Palmetto⁸, ¹University of Alabama at Birmingham, Birmingham, AL, ²Department of Rheumatology, St Vincent’s University Hospital, Dublin, Ireland, ³Oregon Health & Science University, Portland, OR, ⁴Universidade Federal do Paraná, Curitiba, Brazil, ⁵Rheumatology and Clinical Immunology, Charité - University Medicine Berlin, Free University and Humboldt University Berlin, Berlin, Germany, ⁶Geisel School of Medicine at Dartmouth, Lebanon, NH, ⁷Pfizer Inc, Groton, CT, ⁸Pfizer Inc, New York, NY, ⁹Pfizer Inc, Collegeville, PA

First publication: September 18, 2017

SESSION INFORMATION
Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor under investigation for the treatment of psoriatic arthritis (PsA). Two Phase 3 studies have been completed (NCT01877668; NCT01882439) and a long-term extension (LTE) study is ongoing (database not locked; NCT01976364). This analysis compares incidence rates (IR) for adverse events (AEs) of special interest in a tofacitinib cohort from the Phase 3 PsA trials with real-world experience in a comparison cohort from the US Truven MarketScan database.

Methods: The tofacitinib cohort included adult patients (pts) from 2 Phase 3 studies with ≥6 months’ PsA diagnosis who met CASPAR criteria, had active plaque psoriasis, and active arthritis (≥3 swollen and ≥3 tender/painful joints). Pts were grouped by those who received tofacitinib 5 (N=238) or 10 mg (N=236) twice daily (BID) in the Phase 3 studies, and all pts who received ≥1 dose of tofacitinib in the Phase 3 studies or the LTE (tofacitinib all doses, N=783). The comparison cohort (N=5,799) comprised pts with moderate to severe PsA, defined by ≥1 inpatient or ≥2 outpatient 696.0 diagnosis codes on 2 unique calendar days (≥1 by a rheumatologist) between Oct 2010 and Sep 2015, or initiated therapy with a systemic agent for PsA. Key Phase 3 study exclusion criteria were applied to the comparison cohort. IRs for serious infection events (SIEs), herpes zoster (HZ), malignancies (excluding non-melanoma skin cancer [NMSC]), NMSC, and major adverse cardiovascular events (MACE) were compared.

Results: Mean age, gender, and diabetes history were generally similar between the tofacitinib and comparison cohorts (48.7–49.5 years, 42.4–49.2% male, 12.2–15.7% history of diabetes). Overall, more tofacitinib-treated pts had prior experience with corticosteroids (15.7–28.2%), csDMARDs (100%), and tumor necrosis factor inhibitors (48.1–55.9%) vs the comparison cohort (11.9%, 46.6%, and 36.6%, respectively). IRs per 100 PY (95% CI) for SIEs requiring parenteral antibiotics in an outpatient/emergency setting, or resulting in hospitalization were 1.30 (0.16, 4.69) and 2.00 (0.41, 5.83) in the tofacitinib 5 and 10 mg BID groups, respectively (Table). IRs were generally similar between the tofacitinib and comparison cohorts for SIEs resulting in hospitalization only, and for SIEs requiring parenteral antibiotics in emergency settings or resulting in hospitalization (data not shown). In general, the tofacitinib cohort had a higher rate of HZ vs the comparison cohort, and similar IRs for malignancies and MACE between cohorts (Table).

Conclusion: IRs of AEs of special interest reported in tofacitinib PsA Phase 3 studies were generally comparable to those in a general PsA population comprising pts receiving a range of biologic agents, except HZ, which was higher for tofacitinib-treated pts but similar to the incidence observed with tofacitinib treatment in other indications.
Table. Incidence rates (95% CI) of adverse events of special interest

<table>
<thead>
<tr>
<th>Tofacitinib cohort⁴</th>
<th>SEIr⁵</th>
<th>BZ</th>
<th>Malignancies⁵</th>
<th>NMSC</th>
<th>MACE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tofacitinib 5 mg BID (N=238)</td>
<td>1.39 (0.16, 4.69)</td>
<td>1.96 (0.41, 5.74)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Tofacitinib 10 mg BID (N=236)</td>
<td>2.09 (0.41, 5.83)</td>
<td>2.66 (0.73, 8.61)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Tofacitinib all doses (N=783)</td>
<td>NR</td>
<td>NR</td>
<td>0.63 (0.21, 1.48)</td>
<td>0.51 (0.14, 1.30)</td>
<td>0.38 (0.08, 1.11)</td>
</tr>
</tbody>
</table>

Comparison cohort

| Any bDMARD | 5.82 (4.19, 9.57) | 1.26 (0.91, 1.70) | 0.50 (0.34, 0.74) | 1.40 (1.01, 1.75) | 0.38 (0.22, 0.66) |
| Any bDMARD + csDMARD | 5.10 (3.83, 6.66) | 1.53 (0.94, 2.37) | 0.40 (0.16, 0.82) | 1.79 (1.21, 2.53) | 0.25 (0.07, 0.64) |
| Any TNFi | 5.13 (4.26, 6.11) | 1.26 (0.90, 1.71) | 0.51 (0.33, 0.74) | 1.39 (1.00, 1.97) | 0.41 (0.24, 0.65) |
| Any TNFi + csDMARD | 5.12 (3.83, 6.72) | 1.51 (0.91, 2.36) | 0.42 (0.17, 0.86) | 1.75 (1.17, 2.52) | 0.26 (0.07, 0.67) |
| Adalimumab (N=1,034) | 4.16 (3.00, 5.63) | 1.16 (0.65, 1.95) | 0.48 (0.23, 0.88) | 1.00 (0.94, 2.01) | 0.41 (0.16, 0.84) |
| Etanercept (N=1,044) | 4.82 (3.37, 6.67) | 1.10 (0.55, 1.97) | 0.41 (0.16, 0.84) | 1.45 (0.90, 2.24) | 0.30 (0.08, 0.76) |
| Infliximab (N=1,412) | 7.47 | 1.00 | 1.20 | 1.70 | 1.34 |
| Golimumab (N=1,615) | 3.99 (1.90, 7.19) | 1.16 (0.24, 3.59) | 0.00 (0.00, 0.90) | 0.99 (0.57, 1.75) | 0.19 (0.09, 0.47) |
| Certolizumab (N=267) | 6.80 (2.74, 14.62) | 1.91 (0.62, 5.06) | 0.00 (0.00, 0.24) | 1.72 (0.83, 3.52) | 0.00 (0.00, 0.44) |
| Adalimumab (N=477) | 5.04 (2.56, 9.82) | 2.62 (0.85, 5.13) | 1.14 (0.24, 5.35) | 3.45 (1.58, 7.56) | 0.00 (0.00, 0.44) |

| Patients with event per 100 PY, SEIr: any infection requiring parenteral antimicrobial therapy or hospitalization if the infection met criteria for a serious adverse event in the tofacitinib cohort, infections requiring parenteral antimicrobial treatment and hospitalization in the comparison cohort; 'All malignancies excluding non-melanoma skin cancer, †Tofacitinib 5 and 10 mg BID new include patients randomized to these doses, respectively, in the 2 Phase 3 studies (12 or 6 months’ duration), tofacitinib all doses row includes patients who received ≥1 dose of tofacitinib in the 2 Phase 3 studies or the LTE. IR estimates include events occurring ≥28 days after last dose of study drug (or to data cut-off in the LTE). Exposure (PY) is the total follow-up-time to the day of the first event within the event-counting period for patients with events, or the last dose date plus a risk period of 28 days after the last dose (or to data cut-off for LTE) for patients without events. For IR estimates of SEIr, the follow-up time of the comparison cohort was truncated at 1 year for each treatment episode, so mimicking the average follow-up time of the in clinical trials. bDMARD, biologic disease-modifying antirheumatic drug; BZ, biologic zoster; IR, incidence rates; LTE, long-term extension study; MACE, major adverse cardiovascular event; NMSC, non-melanoma skin cancer; NR, not reported; PY, patient-years; SEIr, serious infection event; TNFi, tumor necrosis factor inhibitor.

Disclosure: J. R. Curtis, Amgen, Corona, Crescendo Bio, Pfizer Inc, 2,AbbVie, Amgen, Bristol-Myers Squibb, Corona, Eli Lilly, Janssen, Myriad, Pfizer Inc Roche/Genevantech, UCB, 5; H. Yun, Bristol-Myers Squibb, 2; O. FitzGerald, AbbVie, Bristol-Myers Squibb, Novartis, Pfizer Inc, 2,Amgen, Celgene, Eli Lilly, Janssen, 5; K. Winthrop, Bristol-Myers Squibb, 2,AbbVie, Bristol-Myers Squibb, Eli Lilly, Galapagos, Pfizer Inc, UCB, 5; V. F. Azevedo, AbbVie, Eli Lilly, Genentech, GSK, Pfizer Inc, UCB, 2,AbbVie, Merck-Serono, Novartis, Pfizer Inc, 5,AbbVie, Janssen, Merck-Serono, Novartis, Pfizer Inc Sanofi, 8; G. R. Burmester, Pfizer Inc, 2,Pfizer Inc, 5; W. F. C. Rigby, Roche, 5; K. S. Kanik, Pfizer Inc, 1,Pfizer Inc, 3; R. Rojo, Pfizer Inc, 1,Pfizer Inc, 3; S. Menon, Pfizer Inc, 1,Pfizer Inc, 3; C. Wang, Pfizer Inc, 1,Pfizer Inc, 3; P. Biswas, Pfizer Inc, 1,Pfizer Inc, 3; T. Hendriks, Pfizer Inc, 1,Pfizer Inc, 3; N. Palmetto, Pfizer Inc, 1,Pfizer Inc, 3.


Abstract Number: 618

Secukinumab Sustains Individual Clinical Responses over Time in Patients with Psoriatic Arthritis: 2-Year Results from a Phase 3 Trial

Paul Emery¹, Iain B. McInnes², Philip J Mease³, Michael Schiff⁴, Luminita Pricop⁵, Steven Shen⁶, Zailong Wang⁷ and Corine Gaillée⁶, ¹NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom, ²University of Glasgow, Glasgow, United Kingdom, ³Swedish Medical Center and University of Washington, Seattle, WA. ⁴University of Colorado, Denver, CO, ⁵Novartis Pharmaceuticals Corporation, East Hanover, NJ, ⁶Novartis Pharma AG, Basel, Switzerland

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
**Background/Purpose:** Achieving, sustaining, and improving clinical responses to biologics in PsA are important parts of EULAR and GRAPPA recommendations aimed to optimize treatment goals.\(^1,2\) Here we present patient (pt)-level secukinumab data and report the likelihood of improving, sustaining, or worsening an ACR response and disease status (28-joint disease activity score using CRP [DAS28-CRP]) from Week (Wk) 24 to 104 in pts with active PsA from the FUTURE 2 trial.\(^3,4\)

**Methods:** Data from FUTURE 2 trial through Wk 104 have been previously reported.\(^4\) This *post-hoc* shift analysis was performed on ACR responses (ACR non-responders [NR], ACR20, 50, or 70) between Wks 24 and 104 for subgroups of secukinumab-treated pts categorized by their highest ACR response criteria at the earlier time point, by evaluating whether this response was improved, sustained or worsened at the later time point, using mutually exclusive ACR response categories and as observed analyses. Similar shift analyses on DAS28-CRP derived criteria were performed in 4 exclusive categories: high, moderate, and low disease activity (HDA, MDA, and LDA), and remission (REM) only.\(^5\)

**Results:** In total, 86/100 (86\%) and 76/100 (76\%) pts in the secukinumab 300 and 150 mg groups, respectively, completed the 104-wk treatment. Of which, 73/70 and 81/75 pts in secukinumab 300/150 mg were eligible for ACR and DAS28-CRP shift analysis, respectively, from Wk 24 to 104. Baseline demographics and clinical characteristics were balanced across treatment groups.\(^3,4\) Most secukinumab-treated pts who achieved at least an ACR20, 50, or 70 response at Wk 24, improved or sustained their response at Wk 104 (Figure). Similarly, a majority of pts who were in the MDA, LDA, or REM status at Wk 24 sustained or improved their disease status related to DAS28-CRP score at Wk 104 (Figure). In secukinumab 300 mg group, 53\% of pts with LDA improved to REM and a majority (76\%) of pts with REM maintained their status from Wk 24 to 104, whereas, in 150 mg group, a majority of pts (75\% and 72\% with LDA and REM, respectively) improved or maintained their status by Wk 104.

**Conclusion:** In this *post-hoc* analysis, a majority of secukinumab-treated pts who achieved at least ACR20 response or at least MDA at Wk 24 sustained or improved their ACR response or disease status at Wk 104. Numerically higher sustained ACR response and LDA or REM rate was observed for secukinumab 300 mg, thereby extending the sustainability of ACR response and lowering the disease activity that has been previously reported at group level.\(^2,3\)

Disclosure: P. Emery, AbbVie, BMS, Merck, Novartis, Pfizer, Roche, UCB, 5; I. B. McInnes, Novartis, Amgen, Janssen, BMS, Pfizer, UCB, AbbVie, Celgene, Lilly, 5; P. J. Mease, AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Merck, Novartis, Pfizer, SUN, and UCB, 2,: AbbVie, Amgen, BMS, Celgene, Crescendo Bioscience, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, SUN, and UCB, 5,AbbVie, Amgen, BMS, Celgene, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer and UCB, 8; M. Schiff, AbbVie, BMS, Lilly, J&J, 5,AbbVie, 8; L. Pricop, Novartis Pharmaceutical Corporation, 1,Novartis Pharmaceutical Corporation, 3; S. Shen, Novartis Pharmaceutical Corporation, 3; Z. Wang, Novartis Pharmaceutical Corporation, 3; C. Gaillez, Novartis Pharma AG, BMS, 1,Novartis Pharma AG, 3.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/secukinumab-sustains-individual-clinical-responses-over-time-in-patients-with-psoriatic-arthritis-2-year-results-from-a-phase-3-trial

Abstract Number: 619

Integrated Efficacy Analysis of Tofacitinib, an Oral Janus Kinase Inhibitor, in Patients with Active Psoriatic Arthritis

Peter Nash1, Laura C Coates2, Roy Fleischmann3, Kim Papp4, Juan J. Gomez-Reino5, Keith S Kanik6, Cunshan Wang6, Joseph Wu6, Thijs Hendrikx7 and William C Ports8, 1Department of Medicine, University of Queensland, St Lucia, Brisbane, Australia, 2Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom, 3Metroplex Institute of Rheumatic and Musculoskeletal Medicine, University of Texas Southwestern Medical Center, Dallas, TX, 4Probiot Medical Research and K. Papp Clinical Research Inc, Waterloo, ON, Canada, 5Fundacion Ramon Dominguez, Hospital Clinico Universitario, Santiago de Compostela, Spain, 6Pfizer Inc, Groton, CT, 7Pfizer Inc, Collegeville, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor under investigation for treatment of psoriatic arthritis (PsA). We examined tofacitinib efficacy in patients (pts) with active PsA.

Methods: Data were pooled from 2 placebo (PBO)-controlled, double-blind, multicenter, global Phase 3 studies (OPAL Broaden [N=422; 12 months; NCT01877668]; OPAL Beyond [N=394; 6 months; NCT01882439]). Pts had active PsA and either inadequate response (IR) to ≥1 conventional synthetic disease-modifying antirheumatic drug (csDMARD) and were tumor necrosis factor inhibitor (TNFi)-naïve (OPAL Broaden), or had IR to ≥1 TNFi (OPAL Beyond). Pts were randomized to tofacitinib 5 mg twice daily (BID), 10 mg BID, adalimumab 40 mg subcutaneous injection once every 2 weeks (OPAL Broaden only), or PBO, and a single, stable csDMARD. PBO pts moved to tofacitinib 5 mg or 10 mg BID at Month (M)3. Endpoints included ACR20/50/70 response rates (≥20%/≥50%/≥70% improvement), change from baseline (D) in Health Assessment Questionnaire-Disability Index (HAQ-DI), HAQ-DI response (decrease from baseline [BL] of ≥0.35), ≥75% improvement from BL in Psoriasis Area and Severity Index (PASI75), Δ Leeds Enthesitis Index (LEI) and enthesitis absence, Δ Dactylitis Severity Score (DSS) and dactylitis absence, and Δ Dermatology Life Quality Index (DLQI). Tofacitinib 5 mg and 10 mg BID data (to M6) and PBO data (to M3), were pooled. Significance was declared at p≤0.05 without correction for multiplicity.

Results: In total, 238, 236 and 236 pts received tofacitinib 5 mg BID, 10 mg BID, or placebo, respectively. Pts were white (94.2%) and female (55.4%) with ≥5 peripheral swollen or tender joints (98.0%), enthesitis (LEI>0; 67.5%), dactylitis (DSS>0; 52.5%), psoriatic body surface area ≥3% (67.7%), and C-reactive protein levels >2.87 mg/L (62.5%) at BL. Mean age was 49.1 years; mean PsA duration was 8.0 years. Significant improvements vs PBO at M3 were seen for peripheral arthritis and physical function endpoints for tofacitinib 5 mg and 10 mg BID: ACR20, ACR50, ACR70, ΔHAQ-DI, and HAQ-DI response (Table 1). Significant improvements in psoriasis, enthesitis, and dactylitis endpoints vs PBO were seen for tofacitinib 5 mg and 10 mg BID at M3: PASI75, ΔLEI, enthesitis absence (using LEI), ΔDSS, dactylitis absence (using DSS), and ΔDLQI (Table 1). Efficacy was maintained or further improved at M6.

Conclusion: In a pooled analysis of csDMARD-IR/TNFi-naïve and TNFi-IR pts, tofacitinib 5 mg and 10 mg BID improved peripheral arthritis and physical function, psoriasis, enthesitis, and dactylitis vs PBO at M3.
Table 1. Efficacy endpoints at Month 3 and Month 6: pooled data from OPAL Broden and OPAL Beyond (Full Analysis Set)  

<table>
<thead>
<tr>
<th>Month 3</th>
<th>Tofacitinib 5 mg BID (N=238)</th>
<th>Tofacitinib 10 mg BID (N=238)</th>
<th>Placebo (N=238)</th>
<th>Tofacitinib 5 mg BID (N=238)</th>
<th>Tofacitinib 10 mg BID (N=238)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACR70, a (%):</td>
<td>119 (50.0)***</td>
<td>125 (53.0)***</td>
<td>66 (28.0)</td>
<td>141 (59.7)</td>
<td>135 (57.2)</td>
</tr>
<tr>
<td>ACR50, a (%):</td>
<td>69 (29.0)***</td>
<td>79 (33.5)***</td>
<td>29 (12.3)</td>
<td>91 (38.2)</td>
<td>87 (36.9)</td>
</tr>
<tr>
<td>ACR20, a (%):</td>
<td>40 (16.8)***</td>
<td>34 (14.4)*</td>
<td>18 (7.6)</td>
<td>47 (19.8)</td>
<td>52 (22.0)</td>
</tr>
<tr>
<td>△HAQ-DI* (SE) (N=113)</td>
<td>-0.38 (0.03)***</td>
<td>-0.38 (0.03)***</td>
<td>-0.16 (0.03)</td>
<td>-0.45 (0.03)***</td>
<td>-0.41 (0.04)***</td>
</tr>
<tr>
<td>HAQ-DI response, d</td>
<td>109/212*** (51.4)</td>
<td>101/215*** (47.0)</td>
<td>61/210 (29.1)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PASI75* (N=132)</td>
<td>52/162 (32.1)***</td>
<td>66/161 (43.7)***</td>
<td>24/168 (14.5)</td>
<td>65/162 (40.1)</td>
<td>79/151 (52.3)</td>
</tr>
<tr>
<td>Enthesitis absence rate (LED), e</td>
<td>58/158 (36.7)</td>
<td>58/163 (35.6)</td>
<td>34/158 (21.5)</td>
<td>75/158 (47.5)</td>
<td>71/163 (46.3)</td>
</tr>
<tr>
<td>△DSSL (SE) (N=132)</td>
<td>-4.6 (0.6)*</td>
<td>-5.8 (0.6)***</td>
<td>-2.5 (0.7)</td>
<td>-6.0 (0.7)</td>
<td>-6.4 (0.7)***</td>
</tr>
<tr>
<td>Dactylitis absence rate (DSSL, e) (N=132)</td>
<td>55/127 (43.3)</td>
<td>69/125 (55.2)</td>
<td>37/121 (30.6)</td>
<td>71/127 (55.9)</td>
<td>76/125 (60.8)</td>
</tr>
<tr>
<td>△DLQI (SE) (N=132)</td>
<td>-4.1 (0.3)***</td>
<td>-5.3 (0.3)***</td>
<td>-2.1 (0.3)</td>
<td>-4.4 (0.3)***</td>
<td>-5.7 (0.4)***</td>
</tr>
</tbody>
</table>

Nominal p<0.05; **p<0.01; ***p<0.001 vs placebo at M3  
*All randomized patients who received ≥1 dose of study medication; †values not calculated at M6 as the placebo-controlled period ended at M3; ‡primary endpoint in each individual study at M3; §among patients with baseline HAQ-DI ≥0.35 (analysis at M6 not performed); ‖among patients with baseline BSA ≥3% and baseline PASI >0;  §among patients with baseline score >0  
Large sample approximation to the difference in binomial proportions was used to analyse ACR20/50/70, HAQ-DI response, enthesitis absence, dactylitis absence and PASI75; missing response considered as non-response. △HAQ-DI, △LeI, △DSS, and △DLQI were analysed with a mixed model for repeated measures without imputation for missing values.  
△ change from baseline, ACR20/50/70, American College of Rheumatology ≥20/50/70% improvement; BID twice daily, BSA body surface area, DLQI Dermatology Life Quality Index, DSS Dactylitis Severity Score, HAQ-DI Health Assessment Questionnaire-Disability Index, LEI Leeds Enthesitis Index, LSS least squares mean; M, Month; N, number of patients in the Full Analysis Set; n, number of patients with response; N1, number of patients available at a visit; N2, number of patients included in the model; N3, number of patients evaluable at a visit (denominator); PASI, Psoriasis Area and Severity Index; PASI75, 75% improvement from baseline PASI; SE, standard error.

Disclosure: P. Nash, None; L. C. Coates, AbbVie, Janssen, 2,AbbVie, Amgen, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer Inc, Sun Pharma, UCB, 5; R. Fleischmann, AbbVie, Pfizer Inc, UCB, 2,AbbVie, Pfizer Inc, UCB, 5; K. Papp, AbbVie, Akros, Allergan, Amgen, Anacor, Astellas, Baxalta, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Derma, Dow Pharma, Eli Lilly, Galderma, Genentech, GSK, Janssen, Kyowa Hakko Kirin, Leo Pharma, Medimmune, Merck MSD, Merck-Serono, Miylan, 2,Novartis, Pfizer Inc, Regeneron, Roche, Sanofi-Aventis/Genzyme, Stiefel, Takeda, UCB, Valeant, 2,AbbVie, Akros, Amgen, Astellas, AstraZeneca, Baxalta, Baxter, Boehringer Ingelheim, Bristol-Myers Squibb, Can-Fite, Celgene, Dermo, Devionan, Dow Pharma, Eli Lilly, Galderma, Genentech, Janssen, Kyowa Hakko Kirin, Leo Pharma, Meiji Seika Pharma, 5,Merck MSD, Merck-Serono, Mitsubishi Pharma, Miylan, Novartis, Pfizer Inc, Regeneron, Roche, Sanofi-Aventis/Genzyme, Takeda, UCB, Valeant, 5,AbbVie, Amgen, Astellas, Celgene, Devionan, Eli Lilly, Galderma, Janssen, Kyowa Hakko Kirin, Leo Pharma, Merck MSD, Merck-Serono, Novartis, Pfizer Inc, Regeneron, Sanofi-Aventis/Genzyme, Valeant, 9,AbbVie, Amgen, Astellas, Baxter, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Dow Pharma, Eli Lilly, Galderma, Janssen, Merck MSD, Novartis, Pfizer Inc, Regeneron, Sanofi-Aventis/Genzyme, UCB, Valeant, 9; J. J. Gomez-Reino, AbbVie, MSD, Pfizer Inc, Roche, 2,Pfizer Inc, 5,AbbVie, Biogen, Bristol-Myers Squibb, Janssen, MSD, Pfizer Inc, Roche, 8; K. S. Kanik, Pfizer Inc, 1,Pfizer Inc, 3; C. Wang, Pfizer Inc, 1,Pfizer Inc, 3; J. Wu, Pfizer Inc, 1,Pfizer Inc, 3; T. Hendrikx, Pfizer Inc, 1,Pfizer Inc, 3; W. C. Ports, Pfizer Inc, 1,Pfizer Inc, 3.

Safety and Efficacy of Tofacitinib, an Oral Janus Kinase Inhibitor, up to 36 Months in Patients with Active Psoriatic Arthritis: Data from the Second Interim Analysis of OPAL Balance, an Open-Label, Long-Term Extension Study

Peter Nash\textsuperscript{1}, Laura C Coates\textsuperscript{2}, Alan J. Kivitz\textsuperscript{3}, Philip J Mease\textsuperscript{4}, Dafna D Gladman\textsuperscript{5}, Jose A Covarrubias-Cobos\textsuperscript{6}, Dona Fleishaker\textsuperscript{7}, Cunshan Wang\textsuperscript{7}, Elizabeth Kudlacz\textsuperscript{7}, Sujatha Menon\textsuperscript{7}, Thijs Hendrikx\textsuperscript{8} and Keith S Kanik\textsuperscript{7}, \textsuperscript{1}Department of Medicine, University of Queensland, St Lucia, Brisbane, Australia, \textsuperscript{2}Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom, \textsuperscript{3}Department of Rheumatology, Altoona Center for Clinical Research, Duncansville, PA, \textsuperscript{4}Swedish Medical Center and University of Washington, Seattle, WA, \textsuperscript{5}Department of Medicine, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, \textsuperscript{6}Unidad Reumatologica Las Americas S.C.P, Yucatán, Mexico, \textsuperscript{7}Pfizer Inc, Groton, CT, \textsuperscript{8}Pfizer Inc, Collegeville, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor under investigation for psoriatic arthritis (PsA). Interim data up to January 2017 (database not locked) report the safety, tolerability and efficacy of tofacitinib for patients (pts) with active PsA from ≤36 months’ participation in an ongoing open-label, long-term extension study (LTE; NCT01976364 OPAL Balance).

Methods: Eligible pts from 2 pivotal Phase (P)3 tofacitinib PsA studies (NCT01877668 OPAL Broaden, NCT01882439 OPAL Beyond) could enter a 3-year LTE ≤3 months after completing the qualifying study or discontinuing for reasons unrelated to the study drug. Pts received tofacitinib 5 mg twice daily (BID) for 1 month, after which an increase to 10 mg BID for efficacy reasons or a reduction back to 5 mg BID for safety reasons was permitted. All pts entered on a background of a csDMARD, as was mandated by the qualifying studies. Primary endpoints were incidence and severity of adverse events (AEs) and change from baseline in laboratory values. Efficacy was a secondary endpoint.

Results: 686 pts were enrolled and treated in OPAL Balance and 530 pts (77.3%) remained at data cut-off. Mean (range) duration of tofacitinib exposure in the LTE was 448 (1–1,015) days. On Day 1, 676 (98.5%) pts received a csDMARD, of which 56 (8.3%) later discontinued. To Month 36, 1,685 AEs were reported in 502 (73.2%) pts, 72 (10.5%) pts had serious AEs, and 52 (7.6%) discontinued due to AEs. AEs of special interest included 11 serious infections (1.6%), 19 herpes zoster events (2.8%) including 1 serious event of facial herpes zoster, 2 major adverse cardiovascular events (0.3%), and 13 (1.9%) malignancies. No AEs of gastrointestinal perforation or inflammatory bowel disease were reported. One AE of uveitis was reported. There were 4 deaths (not attributed to treatment, as assessed by the investigator) due to metastatic pancreatic carcinoma, acute cardiac failure/hypertensive heart disease, chronic obstructive pulmonary disease, and pulmonary embolism. Four AEs of latent tuberculosis were reported in pts whose previously negative Quantiferon response became positive. Few pts experienced elevated liver enzyme levels; ALT was elevated ≥3 x ULN in 20 (2.9%) pts, AST ≥3 x ULN in 11 (1.6%) pts. Four (0.6%) pts met discontinuation criteria for laboratory values due to 2 sequential hemoglobin values <8.0 g/dL or decreases >30% from baseline value, 2 sequential platelet counts <75 x10\textsuperscript{9}/L, 2 sequential AST or ALT elevations ≥5 x ULN regardless of total bilirubin or accompanying signs or symptoms, and 2 sequential increases in serum creatinine >50% and an increase >0.5 mg/dL over average of screening and baseline. Efficacy was maintained in the LTE (Table).

Conclusion: Over 36 months in the LTE, the safety profile of tofacitinib in pts with active PsA was generally similar to that of the pivotal P3 studies. No new safety signals were identified. Efficacy across various PsA disease domains was maintained over time.
Disclosures: P. Nash, None; L. C. Coates, AbbVie, Janssen, 2,AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer Inc, Sun Pharma, UCB, 5; A. J. Kivitz, AbbVie, Genentech, Genzyme, Janssen, Novartis, Pfizer Inc, Sanofi, UCB, 5,Celgene, Genentech, Genzyme, Novartis, Pfizer Inc, Sanofi, 8; P. J. Mease, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, Sun Pharmaceutical, UCB, 2,AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Novartis, Pfizer Inc, Sun Pharmaceutical, UCB, 5,AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Genentech, Janssen, Novartis, Pfizer Inc, UCB, 8; D. D. Gladman, AbbVie, Amgen, BMS, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, UCB, 2,AbbVie, Amgen, BMS, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, UCB, 5; J. A. Covarrubias-Cobos, Bristol-Myers Squibb, Eli Lilly, Janssen, Novartis, Pfizer Inc, 2; D. Fleishaker, Pfizer Inc, 1,Pfizer Inc, 3; C. Wang, Pfizer Inc, 1,Pfizer Inc, 3; E. Kudlacz, Pfizer Inc, 1,Pfizer Inc, 3; S. Menon, Pfizer Inc, 1,Pfizer Inc, 3; T. Hendrikx, Pfizer Inc, 1,Pfizer Inc, 3; K. S. Kanik, Pfizer Inc, 1,Pfizer Inc, 3.


Abstract Number: 621

Secukinumab Provides Sustained Improvement in Major and Moderate Response of Disease Activity Index for Psoriatic Arthritis (DAPSA): 2-Year Results from a Phase 3 Study

Josef S. Smolen1, Philip J Mease2, Christopher T. Ritchlin3, Tore K Kvien4, Luminita Pricop5, Todd Fox6, Lawrence Rasoullyan7, Steffen Jugl6 and Corine Gaillez6, 1Medical University of Vienna, Vienna, Austria, 2Swedish Medical Center and University of Washington, Seattle, WA, 3Division of Allergy, Immunology and Rheumatology, School of Medicine and Dentistry, Division of Allergy, Immunology and Rheumatology, School of Medicine and Dentistry, University of Rochester, Rochester, New York, USA, Rochester, NY, 4Diakonhjemmet Hospital, Oslo, Norway, 5Novartis Pharmaceuticals Corporation, East Hanover, NJ, 6Novartis Pharma AG, Basel, Switzerland, 7RTI Health Solutions, Barcelona, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM
Background/Purpose: DAPSA score is a validated tool to measure disease activity states and response criteria, focusing on peripheral joint involvement in patients (pts) with PsA. Secukinumab, a fully human anti–IL-17A mAb, significantly improved signs and symptoms vs placebo (PBO) at Week (Wk) 24, with sustained ACR responses through Wk 104 from the FUTURE 2 study. This post-hoc analysis assessed DAPSA responses through Wk 104 from FUTURE 2 study.

Methods: FUTURE 2 study design has been previously reported. DAPSA score was derived as the sum of five variables: tender and swollen joint counts (TJC 68 and SJC 66), pt global and pt pain assessed on a 10 cm visual analog scale, and CRP level (mg/dL). DAPSA responses are presented for secukinumab 300 and 150 mg (approved doses) in overall population and in pts stratified by prior anti-TNF therapy use (anti–TNF-naïve vs inadequate response/intolerance to these agents [anti–TNF-IR]) and time since first PsA diagnosis (≤2 vs >2 years) using observed data.

Results: Baseline demographics and clinical characteristics were similar across treatment groups. A total of 96,100, and 87 pts treated with secukinumab 300, 150 mg, and PBO, respectively, were available for the evaluation of DAPSA response at Wk 16. DAPSA response in overall population showed moderate/major response in 16%/14% and 22%/12% vs 2%/5%; minor response in 28% and 23% vs 15%; no response in 43% and 43% vs 78% in secukinumab 300 and 150 mg vs PBO, respectively. DAPSA response rates were higher and sustained at Wk 104 in secukinumab-treated pts. A higher proportion (35% and 23%) of pts showed major response, with moderate response observed in 12% and 14% of pts treated with secukinumab 300 and 150 mg, respectively, at Wk 104. The proportion of pts achieving DAPSA response at Wks 16 and 104 by anti-TNF use and time since first PsA diagnosis is shown in the figure. The proportion of pts in overall population meeting DAPSA core components thresholds and other components of PsA among pts with DAPSA moderate/major response at Wks 16 and 104 is shown in the table.

Conclusion: In the overall population, around 30% of secukinumab-treated pts at Wk 16 achieved DAPSA moderate/major response vs <5% in PBO group, with numerical increase in the major response at Wk 104. Moderate/major response at Wk 16 was observed in pts regardless of prior anti-TNF use or time since first PsA diagnosis. Majority of the pts who achieved major response met all core components criteria, in contrast to the pts with moderate response.

## Table: Proportion of Patients Meeting the Selected Variable Thresholds

<table>
<thead>
<tr>
<th>Criterion, n/M (%)</th>
<th>Week</th>
<th>DAPSA moderate response</th>
<th>DAPSA major response</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Secukinumab 300 mg</td>
<td>Secukinumab 150 mg</td>
</tr>
<tr>
<td>PtGA &lt;1 cm</td>
<td>16</td>
<td>3/15 (20.0)</td>
<td>5/22 (22.7)</td>
</tr>
<tr>
<td></td>
<td>104</td>
<td>1/10 (10.0)</td>
<td>1/11 (9.1)</td>
</tr>
<tr>
<td>CRP &lt;5 mg/dL</td>
<td>16</td>
<td>15/15 (100.0)</td>
<td>22/22 (100.0)</td>
</tr>
<tr>
<td></td>
<td>104</td>
<td>10/10 (100.0)</td>
<td>11/11 (100.0)</td>
</tr>
<tr>
<td>SJC 66 ≤1</td>
<td>16</td>
<td>7/15 (46.7)</td>
<td>14/22 (63.6)</td>
</tr>
<tr>
<td></td>
<td>104</td>
<td>8/10 (80.0)</td>
<td>7/11 (63.6)</td>
</tr>
<tr>
<td>TJC 68 ≤1</td>
<td>16</td>
<td>5/15 (33.3)</td>
<td>13/22 (59.1)</td>
</tr>
<tr>
<td></td>
<td>104</td>
<td>7/10 (70.0)</td>
<td>4/11 (36.4)</td>
</tr>
<tr>
<td>HAQ-DI ≤0.5</td>
<td>16</td>
<td>13/15 (86.7)</td>
<td>12/22 (54.5)</td>
</tr>
<tr>
<td></td>
<td>104</td>
<td>8/10 (80.0)</td>
<td>6/11 (54.5)</td>
</tr>
<tr>
<td>Enthesitis resolution</td>
<td>16</td>
<td>13/15 (86.7)</td>
<td>21/22 (95.5)</td>
</tr>
<tr>
<td></td>
<td>104</td>
<td>9/10 (90.0)</td>
<td>9/11 (81.8)</td>
</tr>
<tr>
<td>Dactylitic resolution</td>
<td>16</td>
<td>12/15 (80.0)</td>
<td>20/22 (90.9)</td>
</tr>
<tr>
<td></td>
<td>104</td>
<td>9/10 (90.0)</td>
<td>11/11 (100.0)</td>
</tr>
<tr>
<td>PASI Score ≤1</td>
<td>16</td>
<td>14/15 (93.3)</td>
<td>14/22 (63.6)</td>
</tr>
<tr>
<td></td>
<td>104</td>
<td>8/10 (80.0)</td>
<td>7/11 (63.6)</td>
</tr>
</tbody>
</table>

CRP, C-reactive protein; DAPSA, Disease Activity Index for Psoriatic Arthritis; HAQ-DI, Health Assessment Questionnaire - Disability Index; M, the number of evaluable patients; n, number of patients who met the threshold criterion; PASI, Psoriasis Area and Severity Index; PtGA, Patient Global Assessment; SJC, swollen joint count; TJC, tender joint count

---

**Disclosure:** J. S. Smolen, AbbVie, Janssen, Eli Lilly, MSD, Pfizer, Roche, Amgen, AstraZeneca, Astro, Celgene, Celltrion, GSK, ILTOO, Medimmune, Novartis-Sandoz, Pfizer, Samsung, Sanofi and UCB, 2, AbbVie, Janssen, Eli Lilly, MSD, Pfizer, Roche, Amgen, AstraZeneca, Astro, Celgene, Celltrion, GSK, ILTOO, Medimmune, Novartis-Sandoz, Pfizer, Samsung, Sanofi and UCB, 5; P. J. Mease, AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Merck, Novartis, Pfizer, SUN, and UCB, 2; AbbVie, Amgen, BMS, Celgene, Crescendo Bioscience, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, SUN, and UCB, 5; AbbVie, Amgen, BMS, Celgene, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer and UCB, 8; C. T. Ritchlin, Amgen, UCB, Abbvie, Novartis, and Janssen, Amgen, UCB, Abbvie, Novartis, and Janssen, 2, Amgen, UCB, Abbvie, Novartis, and Janssen, Amgen, UCB, Abbvie, Novartis, and Janssen, 5, Amgen, UCB, Abbvie, Novartis, and Janssen, Amgen, UCB, Abbvie, Novartis, and Janssen, 8; T. K. Kvien, AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz, UCB, 5; AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz, UCB, 8; L. Pricop, Novartis Pharmaceutical Corporation, 1, Novartis Pharmaceutical Corporation, 3; T. Fox, Novartis Pharma AG, 1, Novartis Pharma
Secukinumab Provides Sustained Minimal Disease Activity (MDA) and Remission Related to Disease Activity Index for Psoriatic Arthritis (DAPSA): 2-Year Results from a Phase 3 Study

Laura C Coates¹, Peter Nash², Tore Kvien³, Laure Gossec⁴, Philip J Mease⁵, Lawrence Rasouliyan⁶, Luminita Pricop⁷, Steffen Jugl⁸, Kunal Gandhi⁷, Corine Gaillez⁸ and Josef S. Smolen⁹, ¹University of Oxford, Leeds, Great Britain, ²University of Queensland, Brisbane, Australia, ³Diakonhjemmet Hospital, Oslo, Norway, ⁴UPMC, University Paris 06, Pitié-Salpêtrière Hospital, Paris, France, ⁵Swedish Medical Center and University of Washington, Seattle, WA, ⁶RTI Health Solutions, Barcelona, Spain, ⁷Novartis Pharmaceuticals Corporation, East Hanover, NJ, ⁸Novartis Pharma AG, Basel, Switzerland, ⁹Medical University Vienna, Division of Rheumatology, Department of Internal Medicine III, Vienna, Austria

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Very low disease activity (VLDA) or remission (REM) and alternatively, minimal disease activity (MDA) or low disease activity (LDA) are optimal targets to be achieved by psoriatic arthritis (PsA) patients (pts).¹,² DAPSA and MDA are validated composite indices used in PsA to measure disease activity states.³ This exploratory analysis assessed the proportion of pts treated with secukinumab reaching DAPSA REM or LDA and those who reached either MDA or VLDA at Weeks (wks) 16 and 104 in the FUTURE 2 study.

Methods: Data through 2 years for the FUTURE 2 study have been reported.⁴ DAPSA cut-offs included: REM (≤4) and LDA (>4 and ≤14).⁵ MDA and VLDA are defined as having achieved at least 5 (≥5/7) or all (7/7) of the 7 pre-specified criteria, respectively.⁶ DAPSA-REM, DAPSA-REM/LDA, MDA, and VLDA and their core components were assessed in the overall population and in pts stratified by prior anti-tumor necrosis factor use and time since first PsA diagnosis using as observed data. Only data for secukinumab 300 and 150 mg (approved doses) and placebo are reported.

Results: Baseline characteristics were similar across treatment groups.⁴ At Wk 16, in the overall population, the proportion of pts treated with secukinumab 300/150 mg achieving remission was 14%/10% (DAPSA-REM) and 8%/6% (VLDA) and achieving low disease activity was 42%/44% (DAPSA-REM/LDA) and 28%/23% (MDA). DAPSA and MDA responses by prior TNF-inhibitor status and time since diagnosis are presented in figure. DAPSA and MDA responses with secukinumab were sustained through Wk 104. Secukinumab treated pts who achieved either DAPSA-REM or VLDA at Wk 16 had complete resolution of TJC, SJC, enthesitis and PtGA. Numerically somewhat higher proportion of pts achieved skin clearance, HAQ-DI and PGA with VLDA than DAPSA-REM at Wk 16 and sustained to Wk 104 (Table).

Conclusion: In the overall population, a higher proportion of secukinumab treated pts at Wk 16 achieved DAPSA-REM, VLDA, DAPSA-REM/LDA, and MDA than those treated with placebo with a greater number of pts achieving DAPSA-REM or LDA than VLDA or MDA, respectively. These responses were sustained through Wk 104. At Wk 16, a higher proportion of anti–TNF-naïve pts and pts with early diagnosis (≤2 years) treated with secukinumab achieved and sustained DAPSA-REM, MDA and VLDA than in the overall population.

**Disclosure:** L. C. Coates, Abbvie, BMS, Celgene, Pfizer, UCB, MSD, Boehringer Ingelheim, Novartis, Lilly, Janssen, 5,Abbvie, Janssen, 2; P. Nash, Novartis, Abbvie, Roche, Pfizer, BMS, Janssen, and Celgene, 2,Novartis, Abbvie, Roche, Pfizer, BMS, Janssen, and Celgene, 5,Novartis, Abbvie, Roche, Pfizer, BMS, Janssen, and Celgene, 8; T. Kvien, AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz, and UCB, 5,AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz, and UCB, 8; L. Gossec, UCB, Eli Lilly, and Pfizer, 2,AbbVie, BMS, Celgene, Janssen, Eli Lilly, Novartis, Pfizer, Roche, and UCB, 5; P. J. Mease, AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Merck, Novartis, Pfizer, SUN, and UCB, 2,AbbVie, Amgen, BMS, Celgene, Crescendo Bioscience, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, SUN, and UCB, 5,AbbVie, Amgen, BMS, Celgene, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, and UCB, 8; L. Rasouliyan, Novartis, 5,RTI Health Solutions, 3; L. Pricop, Novartis Pharmaceutical Corporation, 1,Novartis Pharmaceutical Corporation, 3; S. Jugl, Novartis Pharma AG, 1,Novartis Pharma AG, 3; K. Gandhi, Novartis Pharmaceutical Corporation, 1,Novartis Pharmaceutical Corporation, 3; C. Gailez, Novartis Pharma AG, BMS, 1,Novartis Pharma AG, 3; J. S. Smolen, AbbVie, Janssen, Eli Lilly, MSD, Pfizer, Roche, Amgen, AstraZeneca, Astro, Celgene, Celltrion, GSK, ILTOO, Medimmune, Novartis-Sandoz, Pfizer, Samsung, Sanofi and UCB, 2,AbbVie, Janssen, Eli Lilly, MSD, Pfizer, Roche, Amgen, AstraZeneca, Astro, Celgene, Celltrion, GSK, ILTOO, Medimmune, Novartis-Sandoz, Pfizer, Samsung, Sanofi and UCB, 5.
**Tofacitinib Improves Composite Endpoint Measures of Disease in Patients with Psoriatic Arthritis**

Philip S. Helliwell¹, Laura C Coates¹, Oliver FitzGerald², Peter Nash³, Enrique R Soriano⁴, M. Elaine Husni⁵, Ming-Ann Hsu⁶, Keith S Kanik⁶, Thijs Hendrikx⁷, Joseph Wu⁶ and Elizabeth Kudlacek¹, ¹Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom, ²ASRI, Dublin, Ireland, Dublin, Ireland, ³Department of Medicine, University of Queensland, St Lucia, Brisbane, Australia, ⁴Hospital Italiano de Buenos Aires, Buenos Aires, Argentina, ⁵Cleveland Clinic Lerner Research Institute, Cleveland, OH, ⁶Pfizer Inc, Groton, CT, ⁷Pfizer Inc, Collegeville, PA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM  

**Background/Purpose:** Tofacitinib is an oral Janus kinase inhibitor under investigation for the treatment of psoriatic arthritis (PsA). PsA is a heterogeneous disease and composite endpoints allow assessment of multiple clinical outcomes in one instrument. We examined the effects of tofacitinib treatment on several composite endpoints in patients (pts) with PsA.

**Methods:** In 2 placebo (PBO)-controlled, double-blind, multicenter, global Phase 3 studies, pts had active PsA and either had an inadequate response (IR) to ≥1 conventional synthetic disease-modifying antirheumatic drug (csDMARD) and were tumor necrosis factor inhibitor (TNFi)-naïve (OPAL Broaden [N=422; 12 months; NCT01877668]), or had an IR to ≥1 TNFi (OPAL Beyond [N=394; 6 months; NCT01882439]). Pts were randomized to receive tofacitinib 5 mg BID, tofacitinib 10 mg BID, adalimumab 40 mg subcutaneous injection once every 2 weeks (OPAL Broaden only), or PBO (advancing to tofacitinib 5 or 10 mg BID at Month 3, OPAL Broaden and OPAL Beyond), in addition to continuing on a single, stable csDMARD. Composite endpoints assessed: Psoriatic Arthritis Disease Activity Score (PASDAS), Disease Activity Score using 28 joints with C-reactive protein, Disease Activity Index for Reactive Arthritis/Psoriatic Arthritis (DAREA/DAPSA), and Composite Psoriatic Disease Activity Index score.

**Results:** Demographics and baseline disease characteristics were generally similar between treatment groups within the 2 studies, except for duration of PsA disease (longer in OPAL Beyond) and geographic distribution (OPAL Broaden having more Eastern EU pts). Baseline values for composite endpoints were generally similar across treatment groups and studies (Table). Both doses of tofacitinib showed improvements in composite endpoints vs PBO at Month 3 in both studies (Table). In OPAL Broaden, the effects of adalimumab were similar to both doses of tofacitinib across composite endpoints. Effect size for the composite endpoints (using a subpopulation of pts who had all available data for all endpoints) was highest for PASDAS and typically lowest for DAREA/DAPSA; this rank order of effect size was similar across treatment arms and studies. At Month 3, effect sizes in pts receiving active treatment ranged from 0.90 (DAREA/DAPSA for tofacitinib 5 mg BID) to 2.40 (PASDAS for tofacitinib 10 mg BID) in OPAL Broaden, and 0.81 (DAREA/DAPSA for tofacitinib 5 mg BID) to 1.84 (PASDAS for tofacitinib 10 mg BID) in OPAL Beyond (Table). Standardized response means generally followed the same pattern as effect size across studies with both doses of tofacitinib (Table).

**Conclusion:** In 2 Phase 3 studies, tofacitinib 5 mg and 10 mg BID improved composite endpoint scores vs PBO over 3 months in pts with PsA. The largest effect size and standardized response means were observed for PASDAS. Effect sizes and standardized response means varied across endpoints but were consistent across studies.
Table. Summary of mean at baseline, LS mean change from baseline, effect size, and standardized response mean at Month 3 for composite endpoints (PASDAS, DAS28-3CRP, DAREA/DAPSA, CFDAS) in OPAL Broaden and OPAL Beyond studies

<table>
<thead>
<tr>
<th>Study</th>
<th>OPAL Broaden</th>
<th>OPAL Beyond</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PASDAS</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Baseline mean (SD)</strong></td>
<td><strong>Baseline mean (SD)</strong></td>
</tr>
<tr>
<td></td>
<td>Tofacitinib</td>
<td>Tofacitinib</td>
</tr>
<tr>
<td><strong>NS</strong></td>
<td>105</td>
<td>104</td>
</tr>
<tr>
<td><strong>NS</strong></td>
<td>6.00</td>
<td>6.01</td>
</tr>
<tr>
<td><strong>NS</strong></td>
<td>[1.15]</td>
<td>[1.06]</td>
</tr>
<tr>
<td><strong>NS</strong></td>
<td>4.56</td>
<td>4.48</td>
</tr>
<tr>
<td><strong>NS</strong></td>
<td>[0.02]</td>
<td>[0.97]</td>
</tr>
<tr>
<td><strong>NS</strong></td>
<td>45.55</td>
<td>43.69</td>
</tr>
<tr>
<td><strong>NS</strong></td>
<td>[20.33]</td>
<td>[19.51]</td>
</tr>
<tr>
<td><strong>NS</strong></td>
<td>9.9</td>
<td>10.0</td>
</tr>
<tr>
<td><strong>NS</strong></td>
<td>[2.59]</td>
<td>[2.76]</td>
</tr>
</tbody>
</table>

LS mean change from baseline at Month 3 (NS)*

<table>
<thead>
<tr>
<th>Study</th>
<th>PASDAS</th>
<th>DAS28-3 (CRP)</th>
<th>DAREA/DAPSA</th>
<th>CFDAS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NS</strong></td>
<td><strong>Baseline mean (SD)</strong></td>
<td><strong>Baseline mean (SD)</strong></td>
<td><strong>Baseline mean (SD)</strong></td>
<td><strong>Baseline mean (SD)</strong></td>
</tr>
<tr>
<td><strong>NS</strong></td>
<td>1.99***</td>
<td>-0.39***</td>
<td>-1.27***</td>
<td>-1.21</td>
</tr>
<tr>
<td><strong>NS</strong></td>
<td>[0.14]</td>
<td>[0.14]</td>
<td>[0.14]</td>
<td>[0.15]</td>
</tr>
<tr>
<td><strong>NS</strong></td>
<td>[0.10]</td>
<td>[0.10]</td>
<td>[0.10]</td>
<td>[0.11]</td>
</tr>
<tr>
<td><strong>NS</strong></td>
<td>[1.72]</td>
<td>[1.73]</td>
<td>[1.77]</td>
<td>[1.82]</td>
</tr>
<tr>
<td><strong>NS</strong></td>
<td>[0.34]</td>
<td>[0.36]</td>
<td>[0.36]</td>
<td>[0.36]</td>
</tr>
<tr>
<td><strong>NS</strong></td>
<td>[81]</td>
<td>[68]</td>
<td>[77]</td>
<td>[81]</td>
</tr>
</tbody>
</table>

Effect size at Month 3

<table>
<thead>
<tr>
<th>Study</th>
<th>PASDAS</th>
<th>DAS28-3 (CRP)</th>
<th>DAREA/DAPSA</th>
<th>CFDAS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N3=68</td>
<td>N3=62</td>
<td>N3=66</td>
<td>N3=77</td>
</tr>
<tr>
<td></td>
<td>N3=64</td>
<td>N3=62</td>
<td>N3=72</td>
<td>N3=72</td>
</tr>
<tr>
<td><strong>NS</strong></td>
<td>1.75</td>
<td>2.40</td>
<td>1.69</td>
<td>1.01</td>
</tr>
<tr>
<td><strong>NS</strong></td>
<td>1.27</td>
<td>1.77</td>
<td>1.37</td>
<td>0.73</td>
</tr>
<tr>
<td><strong>NS</strong></td>
<td>1.66</td>
<td>2.29</td>
<td>1.89</td>
<td>0.92</td>
</tr>
<tr>
<td><strong>NS</strong></td>
<td>0.89</td>
<td>1.27</td>
<td>1.11</td>
<td>0.80</td>
</tr>
</tbody>
</table>

Standardized response mean at Month 3

<table>
<thead>
<tr>
<th>Study</th>
<th>PASDAS</th>
<th>DAS28-3 (CRP)</th>
<th>DAREA/DAPSA</th>
<th>CFDAS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NS</strong></td>
<td>1.42</td>
<td>1.79</td>
<td>1.73</td>
<td>1.19</td>
</tr>
<tr>
<td><strong>NS</strong></td>
<td>1.25</td>
<td>1.46</td>
<td>1.40</td>
<td>0.79</td>
</tr>
<tr>
<td><strong>NS</strong></td>
<td>1.65</td>
<td>2.29</td>
<td>1.89</td>
<td>0.92</td>
</tr>
<tr>
<td><strong>NS</strong></td>
<td>0.89</td>
<td>1.27</td>
<td>1.11</td>
<td>0.80</td>
</tr>
</tbody>
</table>

*P<0.05; **P<0.01; ***P<0.001 vs placebo at Month 3.
For CFDAS, only patients with IL, DSA ≥2% were included.
Based on MMDM model including data from baseline up to Month 3 without imputation.
Number of patients at Month 3 was defined as (mean at baseline – mean at Month 3)/SD of change from baseline at Month 3, standardized response mean at Month 3 was defined as (mean at baseline – mean at Month 3)/SD of change from baseline at Month 3.

Disclosure: P. S. Helliwell, AbbVie, Janssen, Pfizer Inc, 2,AbbVie, Amgen, Janssen, Pfizer Inc, UCB, 8,AbbVie, Janssen, UCB, 9; L. C. Coates, AbbVie, Janssen, 2,AbbVie, Amgen, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer Inc, Sun Pharma, UCB, 5; O. FitzGerald, AbbVie, Bristol-Myers Squibb, Novartis, Pfizer Inc, 2,Amgen, Celgene, Eli Lilly, Janssen, 5; P. Nash, None; E. R. Soriano, AbbVie, Janssen, Novartis, Pfizer Inc, UCB, 2,AbbVie, Janssen, Novartis, Pfizer Inc, UCB, 5,AbbVie, Bristol-Myers Squibb, Janssen, Novartis, Pfizer Inc, Roche, UCB, 8; M. E. Husni, AbbVie, Amgen, Bristol-Myers Squibb, Eli Lilly, Janssen, Novartis, Regeneron, UCB, 5,Pfizer Inc, 6,PASE Questionnaire, 7; M. A. Hsu, Pfizer Inc, 1,Pfizer Inc, 3; K. S. Kanik, Pfizer Inc, 1,Pfizer Inc, 3; T. Hendrikx, Pfizer Inc, 1,Pfizer Inc, 3; J. Wu, Pfizer Inc, 1,Pfizer Inc, 3; E. Kudlacz, Pfizer Inc, 1,Pfizer Inc, 3.


Abstract Number: 624
Ixekizumab Provides Sustained Improvement in Signs and Symptoms in Patients with Active Psoriatic Arthritis: Two Year Results from a Phase 3 Trial

Philip S. Helliwell1, Eric Lespessailles2, Catherine Shuler3, Lotus Mallbris3, Janelle Erickson3 and Roy Fleischmann4, 1St. Luke's Hospital and University of Leeds, Bradford, United Kingdom, 2University Orleans, Orleans, France, 3Eli Lilly and Company, Indianapolis, IN, 4Metroplex Clinical Research Center, Dallas, TX

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Ixekizumab (IXE) is a high affinity monoclonal antibody that selectively targets IL-17A. In the SPIRIT-P1 phase 3 study (NCT01695239), IXE was superior to placebo (PBO) in achieving ACR20 response at Week 24 in biologic DMARD (bDMARD)-naïve patients with active psoriatic arthritis (PsA). Here, the efficacy and safety of IXE over 2 years in SPIRIT-P1 is evaluated.

Methods: During the SPIRIT-P1 double-blind treatment period (DBTP; Weeks 0-24), 417 bDMARD-naïve patients with active PsA were randomized 1:1:1:1 to 80 mg subcutaneous IXE (160 mg starting dose at Week 0) every 4 weeks (Q4W), every 2 weeks (Q2W), 40 mg adalimumab every 2 weeks (ADA, active reference arm), or PBO. Of these, 381 patients entered the extension period (Weeks 24-52), followed by the long-term extension period (Weeks 52-156). Data presented here are for the combined extension periods (CEP; Weeks 24-108) in patients who completed the initial 24 weeks of treatment and received ≥1 dose of study drug during the CEP (CEP population). IXE-randomized patients continued on IXE throughout the CEP. PBO and ADA patients were re-randomized (1:1) to IXE Q4W or Q2W at Week 16 (inadequate responders) or Week 24; ADA patients had an 8-week washout period before receiving IXE. Patients failing to demonstrate ≥20% improvement in both tender joint count and swollen joint count at Week 32, or any subsequent visit, were discontinued from the study. Efficacy measures included ACR20/50/70 responses, HAQ-Disability Index (DI) Score, DAS 28 based on C-reactive protein (DAS 28-CRP), 75%, 90%, and 100% improvement in the Psoriasis Area and Severity Index (PASI 75/90/100), Leeds Enthesitis Index (LEI), and Leeds Dactylitis Index-Basic (LDI-B). Missing values were imputed by nonresponder imputation for categorical data and modified baseline observation carried forward for continuous data.

Results: Efficacy and safety results for the CEP population are summarized in Table 1. Improvements in ACR and PASI responses, resolution in enthesitis and dactylitis, and improvements from baseline in HAQ-DI, DAS 28-CRP, enthesitis, and dactylitis were observed at Week 108. Frequency of treatment-emergent adverse events (AEs) were similar across treatment arms and the majority were mild or moderate in severity; serious AEs occurred in 46 patients. One death occurred in the CEP population: an ADA/IXE Q4W patient with a history of dyslipidemia, diabetes mellitus, hypertension, and a previous transient ischemic attack, suffered a cerebrovascular accident at Week 108.

Conclusion: For patients naïve to biologic treatment, IXE demonstrated clinically significant improvement in the signs and symptoms of PsA across treatment groups up to 2 years of treatment. The safety profile of IXE observed during the CEP was similar to that observed in the DBTP of SPIRIT-P1 and SPIRIT-P2, as well as other phase 3 studies of IXE in patients with plaque psoriasis.

Abstract Number: 625

Rapid Onset of Efficacy in Patients with Active Psoriatic Arthritis Treated with Ixekizumab: A Pooled Analysis of Data from Two Phase III Clinical Trials

Atul A. Deodhar, Kim A. Papp, Catherine Shuler, So Young Park and Tore K. Kvien, Oregon Health & Science University, Portland, OR, K Papp Clinical Research and Proibity Medical Research Inc, Waterloo, ON, Canada, Eli Lilly and Company, Indianapolis, IN, Diakonhjemmet Hospital, Oslo, Norway

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM
Background/Purpose: Rapid onset of clinical improvement is an important attribute of treatment success for patients with PsA. These analyses evaluate the speed of onset of clinical improvement in patients with active PsA treated with the IL-17A selective monoclonal antibody ixekizumab (IXE) compared with placebo (PBO) and include populations naïve to biologic treatment or with a previous inadequate response to TNF inhibitors.

Methods: Data were integrated from two Phase III, multicenter, double-blind, PBO- controlled trials. Patients with active PsA either naïve to biologic disease modifying anti-rheumatic drugs (SPIRIT-P1) or with prior lack of efficacy or intolerance to TNF-inhibitor(s) (SPIRIT-P2) were randomized to placebo (PBO, N=224), 80 mg IXE every 4 weeks (IXE Q4W, N=229) or every 2 weeks (IXE Q2W, N=226), after a 160 mg starting dose. Continuous data were analyzed using mixed-effects model for repeated measures; categorical data, using a logistic regression model with missing values imputed by nonresponder imputation.

Results: ACR20 response rates were significantly greater for both IXE doses (p<.001) at week 1 (Fig 1). ACR50 response rates were significantly greater by week 2 for IXE Q4W (p=.013) and week 1 for IXE Q2W (p=.030). ACR70 response rates were significantly greater by week 4 (IXE Q4W, p=.039) or week 2 (IXE Q2W, p=.002). With the exception of the IXE Q2W ACR70 response rate at week 4 (p=.176), response rates for ACR20, ACR50, and ACR70 remained statistically significant compared to PBO through the 24-week, double-blind study period. In patients with plaque psoriasis (≥3% body surface area) at baseline, both IXE dosing regimens achieved significant improvements in psoriasis area and severity index total score compared to PBO by week 1 (Fig 2). Patients with HAQ-DI ≥ 0.35 at baseline demonstrated significantly improved physical function by week 1, as measured by HAQ-DI minimal clinically important difference (≥0.35) response rates (p<.001) for both doses of IXE (Fig 3).

Conclusion: Patients achieved significantly greater improvements in PsA, skin conditions, and physical function with both IXE dose regimens compared to PBO. Statistically significant improvements in multiple clinical measures occurred as early as week 1 and remained statistically significant through 24-weeks.
Figure 1. ACR20 Response Rate by Treatment, NRI
Double-Blind Treatment Period ITT Population, PBO-Controlled Integrated Analysis Set

![Graph showing ACR20 Response Rate by treatment over time.]

*p < .001 vs. PBO; ACR20 = at least 20% improvement in the American College of Rheumatology response criteria; ITT = Intent-to-Treat; IXE =Ixekizumab; NRI = Nonresponder Imputation; PBO = Placebo; Q2W = Every 2 Weeks; Q4W = Every 4 Weeks

Figure 2. PASI Total Score Percent Improvement From Baseline, ITT Population with ≥3% BSA at baseline, Double-Blind Treatment Period ITT, PBO-Controlled Integrated Analysis Set

![Graph showing PASI Total Score Percent Improvement over time.]

*p < .001 vs. PBO; BSA = body surface area; ITT = Intent-to-Treat; IXE =Ixekizumab; MMRM = Mixed-Effects Model for Repeated Measures; PASI = Psoriasis Area and Severity Index; PBO = Placebo; Q2W = Every 2 Weeks; Q4W = Every 4 Weeks
Disclosure: A. A. Deodhar, Eli Lilly and Company, GSK, Janssen, Novartis, Sun Pharma, UCB, 2, Abbvie, Eli Llilly and Company, Janssen, Novartis, UCB, 5; K. A. Papp, Amgen, Anacor, AbbVie, Akros, Allergan, Astellas, Astra-Zenica, Baxalta, Baxter, BMS, Boehringer-Ingelhein, Can-Fite, Celgene, Coherus, Dermira, Dow Pharma, Eli Lilly and Company, Forward Pharma, Galderma, Genentech, GSK, Janssen, Kyowa Hakko Kirin, Leo P, 9; C. Shuler, Eli Lilly and Company, 3; S. Y. Park, Eli Lilly and Company, 1, Eli Lilly and Company, 3; T. K. Kvien, AbbVie, Biogen, BMS, Celltrion, Eli Lilly, Janssen, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Samsung, Sandoz and UCB, 5, AbbVie, Biogen, BMS, Celltrion, Eli Lilly, Janssen, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Samsung, Sandoz and UCB, 9.


Abstract Number: 626

Radiographic Progression of Structural Joint Damage in Patients with Active Psoriatic Arthritis Treated with Ixekizumab over 52 Weeks

Désirée van der Heijde¹, Masato Okada², Chin H. Lee³, Catherine Shuler², Suchitrita Rathmann³, Chen-Yen Lin³ and Philip J Mease⁴, ¹Leiden University Medical Center, Leiden, Netherlands, ²Immuno-Rheumatology Center, St. Luke's International Hospital, Tokyo, Japan, ³Eli Lilly and Company, Indianapolis, IN, ⁴Swedish Medical Center and University of Washington, Seattle, WA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Background/Purpose: Ixekizumab (IXE), an anti-interleukin-17A monoclonal antibody, was shown to be superior to placebo (PBO) in clinical responses and inhibiting the progression of structural joint damage in patients with PsA treated for 24 weeks (wks). The objective was to assess the progression of structural joint damage in PsA pts with IXE for up to 52 wks.

Methods: Biologic DMARD-naïve pts with active PsA (N=417) entered into SPIRIT-P1 (NCT01695239), a double-blind phase 3 trial. Pts must have had ≥1 joint erosion on the hand and foot x-rays confirmed by central reading or had a C-reactive protein level ≥6 mg/L at screening. 417 pts were randomized to IXE 80 mg every 2 wks (Q2W; N=103) or 4 wks (Q4W; N=107) following a 160 mg initial dose, PBO (N=106), or adalimumab 40 mg every 2 wks (ADA; active reference arm; N=101) for 24 wks. In the Extension period (EXT: Wks 24-52), PBO and ADA pts were re-randomized (1:1) to IXEQ2W or IXEQ4W at Wk 16 (inadequate responders) or Wk 24; ADA pts underwent a washout prior to IXE treatment. All pts were assessed for structural joint damage using the van der Heijde-modified PsA Total Sharp Score (mTSS, 0-528 scale). X-rays at Wks 0, 24, and 52 were scored independently by 2 readers blinded to time point and clinical data (average of readers). mTSS was excluded from the pre-specified analysis if the radiograph was taken after the scheduled visit date. In a post hoc analysis, mTSS from a radiograph taken after the scheduled visit date was interpolated and considered as observed data. Any missing data at Wk 52, in either presentation, were imputed using a linear extrapolation if they had at least 1 post-baseline value.

Results: Pts had active PsA at Wk 0 (Table). 381 pts (91.3%) entered the EXT, with 374 (98.2%) having radiographs collected during the EXT. Wk 52 mean (SD) mTSS change from baseline were 0.54 (2.11) and 0.09 (1.0) for pts randomized to IXEQ4W and IXEQ2W at baseline, respectively. Similar changes at Wk 52 were obtained with the post hoc analysis (Table). The majority of IXEQ2W or IXEQ4W pts exhibited no structural progression through 1 year of IXE treatment (Figure). In pts who switched from PBO or ADA to IXE, Wk 52 mean change from baseline mTSS values scores ranged from -0.03 to 0.41 (Table).

Conclusion: Over a 52-wk period, minimal changes in mTSS were observed in PsA pts entering the EXT and treated with IXEQ2W or IXEQ4W.


| Table. Radiographic Progression of Structural Joint Damage for EXT Pts |
|-----------------|----------------|----------------|----------------|----------------|
|                 | PBO/IXEQ4W (N=45) | PBO/IXEQ2W (N=46) | ADA/IXEQ4W (N=49) | ADA/IXEQ2W (N=48) |
| **Baseline (Week 0)** Disease Characteristics, Mean (SD) |                   |                   |                   |                   |
| mTSS            | 11.5 (15.5)     | 24.5 (17.3)      | 15.6 (24.3)      | 15.4 (30.2)      |
| Tender Joint Count | 18.5 (11.0)    | 19.2 (14.0)      | 18.8 (11.9)      | 18.8 (12.8)      |
| Swollen Joint Count | 9.6 (6.2)      | 10.7 (7.1)       | 10.1 (7.4)       | 9.6 (5.5)        |
| **mTSS, Pre-specified, Mean (SD)** |                 |                   |                   |                   |
| Week 52 Change from Baseline | n=31 | n=37 | n=36 | n=34 |
| mTSS             | 0.27 (0.8)      | 0.41 (0.8)       | 0.32 (1.0)       | -0.03 (0.4)      |
| **mTSS, Post Hoc, Mean (SD)** |                 |                   |                   |                   |
| Week 52 Change from Baseline | n=44 | n=45 | n=47 | n=45 |
| mTSS             | 0.25 (0.8)      | 0.51 (1.1)       | 0.24 (0.9)       | 0.06 (0.5)       |

N=EXT pts; n=pts with baseline and ≥1 post-baseline radiograph assessments
Efficacy and Safety of Apremilast through 104 Weeks in Subjects with Moderate to Severe Psoriasis Randomized to Placebo, Apremilast, or Etanercept Who Continued on or Switched to Apremilast after Week 16 in a Phase 3b Study

Kristian Reich1, Mark Goodfield2, Lawrence Green3, Kristine Nograles4, Rongdean Chen4, Eugenia Levi4 and Richard G.B. Langley5, 1Dermatologikum Hamburg, Hamburg, Germany, 2Leeds General Infirmary, Leeds, United Kingdom, 3George Washington University School of Medicine, Washington, DC, WA, 4Celgene Corporation, Summit, NJ, 5Dalhousie University, Halifax, NS, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Many subjects (sbj) with chronic plaque psoriasis exhibit nail and scalp involvement that can markedly affect quality of life and be difficult to treat. The phase 3b LIBERATE study evaluated efficacy and safety of apremilast or etanercept vs. placebo in biologic-naive sbj with moderate to severe plaque psoriasis. Efficacy assessments included effects on preexisting nail and scalp disease and skin lesions.
**Methods:** In this double-blind, double-dummy study, sbj were randomized (1:1:1) to placebo (PBO), apremilast 30 mg BID (APR), or etanercept 50 mg QW (ETN) through Wk 16; thereafter, all sbj switched to or continued APR (PBO/APR, ETN/APR, APR/APR) through Wk 104. The primary endpoint was achievement of a PASI-75 response at Wk 16 with APR vs. PBO; the secondary endpoint was PASI-75 achievement at Wk 16 with ETN vs. PBO. Physician assessments were conducted for overall psoriatic activity (static Physician’s Global Assessment [sPGA]); scalp disease activity (Scalp Physician Global Assessment [ScPGA], limited to sbj with score ≥3 at baseline [BL], indicating moderate to very severe scalp disease); and nail disease (Nail Psoriasis Severity Index [NAPSI], limited to sbj with active disease [NAPSI ≥1] in the target nail at BL). Responses were assessed through Wk 104 using last-observation-carried-forward methodology.

**Results:** The APR extension phase (Wks 16 to 104) included 226 sbj (PBO/APR n=73; APR/APR n=74; ETN/APR n=79). At Wk 16, PASI-75 response vs. PBO was significant for both APR and ETN; long-term treatment with APR maintained both PASI-75 and sPGA 0 or 1 response levels (Table). Improvements were seen in nail and scalp disease at Wk 16, and the proportion of responders continued to increase with APR treatment over 104 wks and in sbj who switched from ETN to APR (Table). ScPGA 0 or 1 was achieved by 50.0% to 59.2% of sbjs across treatment arms, and mean percent improvement from BL NAPSI score ranged from −48.1% to −51.1% (Table); the proportion of sbj achieving NAPSI-50 response ranged from 48.6% to 65.2%. Adverse events (AEs) occurring in ≥5% of sbj during Wks 0 to 16 were diarrhea, nausea, nasopharyngitis, upper respiratory tract infection, headache, and tension headache; long-term assessment by exposure-adjusted incidence rates (EAIR)/100 sbj-yrs showed no increase with longer-term APR exposure. No increase in EAIR/100 sbj-yrs of serious AEs occurred during the APR extension phase (4.01 to 5.49, across groups) vs. Wks 0 to 16 (PBO 0.0; APR 12.57; ETN 7.91). Changes in laboratory parameters were infrequent and transient; EAIR/100 sbj-yrs remained low across groups through 104 wks.

**Conclusion:** APR demonstrated efficacy through Wk 104 in sbj who continued APR and sbj who switched from PBO or ETN to APR at Wk 16. The AE profile remained consistent with prolonged APR exposure; no new safety or tolerability issues were observed through Wk 104 in sbj with moderate to severe plaque psoriasis.

**Disclosure:** K. Reich, AbbVie, Amgen, Biogen, Boehringer Ingelheim, Celgene Corporation, Centocor, Covagen, Eli Lilly, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, LEO Pharma, Medac, Merck Sharp and Dohme, Novartis, Ocean Pharma, Pfizer Wyeth, Regeneron, Takeda, UCB Pharma., 5;AbbVie, Amgen, Biogen, Boehringer Ingelheim, Celgene Corporation, Centocor, Covagen, Eli Lilly, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, LEO Pharma, Medac, Merck Sharp and Dohme, Novartis, Ocean Pharma, Pfizer Wyeth, Regeneron, Takeda, UCB Pharma., 5; M. Goodfield,
Integrated Efficacy Results from Two Phase 3 Trials of Ixekizumab for the Treatment of Psoriatic Arthritis

Bernard Combe¹, Peter Nash², David Adams³, Lisa Kerr³ and Olivier Benichou³, ¹Rheumatology, CHU Lapeyronie and Montpellier University, Montpellier, France, ²University of Queensland, Brisbane, Australia, ³Eli Lilly and Company, Indianapolis, IN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Ixekizumab (IXE) is a high-affinity monoclonal antibody that selectively targets interleukin-17A. Here, we present integrated efficacy data at Week 24 from two phase 3 trials of IXE for the treatment of psoriatic arthritis (PsA).

Methods: Patients with active PsA (SPIRIT-P1) and with prior lack of efficacy or intolerance to TNF-inhibitor(s) (SPIRIT-P2) were randomized to placebo (PBO, N=224), 80 mg IXE every 4 weeks (IXEQ4W, N=229) or every 2 weeks (IXEQ2W, N=226), after a 160 mg starting dose. All patients considered as inadequate responders at Week 16 received rescue therapy (changes in background therapy), while inadequate responders to PBO were also re-randomized to IXEQ4W or IXEQ2W. Continuous data were analyzed using mixed-effects model for repeated measures; categorical data, using a logistic regression model with missing values imputed by non-responder imputation.

Results: At Week 24, significantly more patients treated with either dose of IXE (p<.001) compared to PBO achieved the primary endpoint of ACR 20, as well as ACR 50, ACR 70, and HAQ-DI change from baseline. Treatment with either dose of IXE resulted in significantly more patients achieving resolution of enthesitis (LEI; p<.05) and dactylitis (LDI-B; p<.001) compared to PBO. LDI-B improvements from baseline were also significantly greater (p<.05) for IXE-treated patients versus PBO. Finally, greater skin clearance (via PASI improvement) was significantly higher for IXE-treated patients (p<.001).

Conclusion: Patients treated with either dose regimen of IXE achieved significantly greater improvements in arthritis, physical function, and skin lesions compared to PBO at Week 24.
Is Earlier Golimumab Treatment Initiation in Psa and As Patients Associated with Improved Outcomes?

Suneil Kapur1, Proton Rahman2, Michelle Teo3, Jodie Reis4, Rajwinder Dhillon5, Pauline Boulos6, Raman Rai7, Regan Arendse8, Julie Vaillancourt9, Emmanouil Rampakakis9, Allen J Lehman10, Francois Nantel11 and Brendan Osborne11, 1University of Ottawa, 139 Greenbank Rd, Suite 203, ON, Canada, 2Rheumatology, St Cllaires Mercy Hospital, St Johns, NF, Canada, 3Balfour Medical Clinic, Penticton, BC, Canada, 4University of Saskatchewan, Saskatoon, SK, Canada.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/integrated-efficacy-results-from-two-phase-3-trials-of-ixekizumab-for-the-treatment-of-psoriatic-arthritis

Abstract Number: 629
5Private Practice, Niagara Falls, ON, Canada, 6Private Practice, Dundas, ON, Canada, 7Private Practice, Hamilton, ON, Canada, 8University of Saskatchewan, Saskatoon, ON, Canada, 9JSS Medical Research, Montreal, QC, Canada, 10Janssen Inc., Toronto, ON, Canada, 11Medical Affairs, Janssen Inc., Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Previous studies have suggested that treating patients earlier with biologics could improve disease outcomes. The aim of this analysis was to assess the impact of disease duration on clinical and patient-reported outcomes in patients with psoriatic arthritis (PsA) or ankylosing spondylitis (AS) treated with subcutaneous golimumab (GLM) in Canadian routine practice.

Methods: BioTRAC is an ongoing, prospective registry of patients initiating treatment with infliximab or GLM for rheumatoid arthritis, AS, or PsA, or with ustekinumab for PsA. Eligible patients for this analysis included PsA and AS patients initiating GLM treatment since 2010. Disease duration at entry in the registry was categorized by tertiles as early (PsA: <2 years; AS: <1 year), mid (PsA: 2-5 years; AS: 1-2 years) and long-term (PsA: ≥6 years; AS: ≥3 years) duration. Standard outcomes were assessed; key outcomes of interest were low disease activity (LDA), remission (based on DAS28-ESR <2.6 and CDAI≤2.8), and minimal disease activity (MDA) achievement for PsA patients, and inactive disease (ASDAS <1.3) for AS patients. In order to determine the impact of disease duration on disease activity at 12 and 24 months, multivariate logistic regression and general linear models adjusted for age, gender, prior biologic treatment, and baseline disease parameters were utilized.

Results: A total of 253 PsA patients (54.4% female) and 376 AS patients (58.6% male) were included with a mean (SD) age of 52.7 (13.2) and 44.7 (13.3) years, respectively. Most patients were biologic naïve (PsA: 95.3%; AS: 95.5%). The mean (SD) duration of PsA and AS at baseline was 5.7 (7.7) and of 5.4 (9.8) years, respectively.

In the PsA patient group, significantly greater improvements in MD global assessment (MDGA) and pain from baseline to month 24 were observed amongst patients treated at early term (Table 1). Based on multivariate logistic regression analyses, patients treated at later stage disease were significantly less likely than patients treated early to achieve MDA (OR: 0.10; p=0.025) and CDAI LDAS (OR: 0.06; p=0.002) at 24-month. There was no association between PsA duration and LDA, remission and MDA achievement at 12 months.

Among AS patients treated at early term, significantly greater improvements in BASFI from baseline to month 24 were observed (Table 1). Based on multivariate logistic regression analyses, AS patients treated at mid- and long-term were significantly less likely than patients treated at early term to achieve inactive disease based on ASDAS at 12 months, with odds ratios of 0.21 (p=0.028) and 0.12 (p=0.003), respectively. Disease duration was not associated with AS inactivity at 24-month.

Conclusion: The results of this analysis demonstrate that earlier treatment of PsA and AS with GLM in real-world is associated with improved outcomes, particularly in selected patient-reported outcomes at 12 and 24 months.
Table 1. Adjusted changes in clinical and patient-reported outcomes from baseline to 24 months by disease duration among PsA and AS patients

<table>
<thead>
<tr>
<th>Outcomes, LSM (95% CI)</th>
<th>PsA Patients</th>
<th>AS Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Early Term (N=103)</td>
<td>Mid Term (N=62)</td>
</tr>
<tr>
<td>ΔSJC</td>
<td>-4.5 (-5.4; -3.6)</td>
<td>-4.7 (-5.6; -3.7)</td>
</tr>
<tr>
<td>ΔTJC</td>
<td>-6.5 (-7.8; -5.1)</td>
<td>-6.5 (-7.9; -5.0)</td>
</tr>
<tr>
<td>ΔMDGA</td>
<td>-4.0 (-4.9; -3.1)</td>
<td>-3.1 (-4.1; -2.1)</td>
</tr>
<tr>
<td>ΔPtGA</td>
<td>-33.0 (-47.2; -18.9)</td>
<td>-16.7 (-32.2; -1.2)</td>
</tr>
<tr>
<td>ΔPain</td>
<td>-32.5 (-45.0; -19.9)</td>
<td>-10.9 (-24.1; 2.3)</td>
</tr>
<tr>
<td>ΔHAQ</td>
<td>0.0 (-0.2; 0.3)</td>
<td>-0.2 (-0.4; 0.0)</td>
</tr>
<tr>
<td>ΔDAS28-ESR</td>
<td>-2.1 (-2.9; -1.4)</td>
<td>-1.4 (-2.0; -0.8)</td>
</tr>
<tr>
<td>ΔSDAI</td>
<td>-19.2 (-23.0; -15.4)</td>
<td>-17.3 (-21.7; -13.0)</td>
</tr>
<tr>
<td>ΔCDAI</td>
<td>-17.6 (-20.6; -14.7)</td>
<td>-16.1 (-19.2; -12.9)</td>
</tr>
<tr>
<td>ΔPASI</td>
<td>-2.5 (-3.7; -1.3)</td>
<td>-1.7 (-3.1; -0.3)</td>
</tr>
</tbody>
</table>

LSM: Least Square Mean
p-value reflects the comparison of early vs. mid vs. long term.

Disclosure: S. Kapur, None; P. Rahman, None; M. Teo, None; J. Reis, None; R. Dhillon, None; P. Boulos, None; R. Rai, None; R. Arendse, None; J. Vaillancourt, Janssen Inc., 9; E. Rampakakis, Janssen Inc., 9; A. J. Lehman, Janssen Inc., 3; F. Nantel, Janssen Inc., 3; B. Osborne, Janssen Inc., 3.


Abstract Number: 630

**Effects of Intravenous Golimumab, an Anti-Tnfa Monoclonal Antibody, on Mental and Physical Functioning and Health-Related Quality of Life in Active Psoriatic Arthritis: 24-Week Results of a Phase 3 Trial**

M. Elaine Husni¹, Arthur Kavanaugh², Eric K. H. Chan³, Nan Li⁴, Steven Peterson⁴, Elizabeth C. Hsia⁵, Lilianne Kim⁴, Kim Hung Lo⁴ and Diane D. Harrison⁴, ¹Rheumatology, Cleveland Clinic, Cleveland, OH, ²Medicine, University of
SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: To evaluate physical and mental health functioning, health state, and health-related quality of life (HRQoL) in patients with active psoriatic arthritis (PsA) treated with intravenously administered (IV) golimumab (GLM), an anti-TNFα monoclonal antibody.

Methods: In this Phase 3, multicenter, randomized, double-blind, placebo-controlled trial, adult patients (N=480) with active PsA naïve to anti-TNFα therapy (mean age=46 yr) received IV GLM 2 mg/kg (N=241) at Weeks 0 and 4 and every 8 weeks thereafter or placebo (N=239) at Weeks 0, 4, 12, and 20 with crossover to IV GLM at Week 24. Three self-report instruments were included: 1) Short Form Health Survey (SF-36), a generic instrument of physical and mental health functioning: scores for its Physical (PCS) and Mental Component Summary (MCS) and 8 subscales (physical functioning, role-physical, body pain, general health, vitality, social functioning, role-emotional, and mental health) each range from 0 to 100 with higher scores indicating better function; 2) EuroQol visual analog scale (EQ-VAS), a generic measure of current health state (0=worst health you can imagine to 100=best health you can imagine); 3) Dermatology Life Quality Index (DLQI), a disease-specific HRQoL instrument measuring impact of skin disorders on daily living (scores range from 0-30 with lower scores indicating lesser impact). SF-36 PCS and MCS at Week 14 were controlled secondary endpoints. Least square mean differences between the treatment groups were estimated using analysis of covariance controlling for methotrexate use and baseline score.

Results: Mean improvements from baseline with IV GLM vs placebo occurred as early as Week 8 in SF-36 PCS (8.0 vs 1.7) and MCS (5.0 vs 1.2) scores (Table 1). Greater mean improvements from baseline in PCS (p<0.001) and MCS (p<0.001) scores were seen with IV GLM vs placebo at Weeks 14 and 24. Greater mean improvements in all 8 SF-36 subscales at Weeks 14 and 24 were also observed with IV GLM vs placebo (p<0.001 for all). The percentages of patients achieving clinically meaningful change (5 points or greater) in PCS and MCS scores were higher in IV GLM vs placebo at Weeks 14 and 24 (PCS: 67.6% vs 29.7%, 69.7% vs 29.3%; MCS: 51.5% vs 26.4%, 46.9% vs 29.3%; p<0.001 for all). Mean EQ-VAS improvements were observed as early as Week 8 with IV GLM vs placebo (17.2 vs 3.7) and remained greater with IV GLM vs placebo at Weeks 14 and 24 (both p<0.001; Table 1). Mean changes in DLQI were observed with IV GLM as early as Week 8 (-7.2 vs -1.7; Table 1). Higher percentages of patients in the IV GLM cohort achieved DLQI scores of 0 or 1 at Weeks 14 (35.3% vs 9.8%; p<0.001) and 24 (40.7% vs 9.8%; p<0.001) vs placebo.

Conclusion: Adult patients with active PsA treated with IV GLM showed marked improvements from baseline vs. placebo in physical and mental health function, health state, and HRQoL as early as Week 8; improvements were maintained through Weeks 14 and 24.
Table 1: Summary of mean (standard deviation) changes in SF-36, EQ-VAS, and DLQI

<table>
<thead>
<tr>
<th></th>
<th>Golimumab 2 mg/kg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient self-report instruments</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mean (SD) change from baseline in SF-36</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PCS:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 8</td>
<td>8.0 (7.30)</td>
<td>1.7 (5.40)</td>
</tr>
<tr>
<td>(n=237)</td>
<td>(n=236)</td>
<td></td>
</tr>
<tr>
<td>Week 14</td>
<td>8.6 (7.59)</td>
<td>2.6 (5.84)</td>
</tr>
<tr>
<td>(p&lt;0.001)</td>
<td>(n=237)</td>
<td>(n=236)</td>
</tr>
<tr>
<td>Week 24</td>
<td>9.4 (8.07)</td>
<td>2.4 (6.07)</td>
</tr>
<tr>
<td>(n=237)</td>
<td>(n=236)</td>
<td></td>
</tr>
<tr>
<td><strong>MCS:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 8</td>
<td>5.0 (9.85)</td>
<td>1.2 (7.60)</td>
</tr>
<tr>
<td>(n=237)</td>
<td>(n=236)</td>
<td></td>
</tr>
<tr>
<td>Week 14</td>
<td>5.3 (9.88)</td>
<td>0.9 (7.58)</td>
</tr>
<tr>
<td>(p&lt;0.001)</td>
<td>(n=237)</td>
<td>(n=236)</td>
</tr>
<tr>
<td>Week 24</td>
<td>5.3 (10.20)</td>
<td>0.8 (7.45)</td>
</tr>
<tr>
<td>(n=237)</td>
<td>(n=236)</td>
<td></td>
</tr>
<tr>
<td><strong>Mean (SD) change from baseline in EQ-VAS:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Week 8</strong></td>
<td>17.2 (22.70)</td>
<td>3.7 (21.81)</td>
</tr>
<tr>
<td>(n=232)</td>
<td>(n=225)</td>
<td></td>
</tr>
<tr>
<td><strong>Week 14</strong></td>
<td>18.7 (24.29)</td>
<td>5.3 (21.02)</td>
</tr>
<tr>
<td>(p&lt;0.001*)</td>
<td>(n=233)</td>
<td>(n=222)</td>
</tr>
<tr>
<td><strong>Week 24</strong></td>
<td>20.2 (24.23)</td>
<td>5.5 (23.09)</td>
</tr>
<tr>
<td>(n=231)</td>
<td>(n=221)</td>
<td></td>
</tr>
<tr>
<td><strong>Mean (SD) change from baseline in DLQI:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Week 8</strong></td>
<td>-7.2 (7.24)</td>
<td>-1.7 (4.91)</td>
</tr>
<tr>
<td>(n=194)</td>
<td>(n=195)</td>
<td></td>
</tr>
<tr>
<td><strong>Week 14</strong></td>
<td>-7.7 (7.18)</td>
<td>-1.8 (5.70)</td>
</tr>
<tr>
<td>(p&lt;0.001*)</td>
<td>(n=194)</td>
<td>(n=195)</td>
</tr>
<tr>
<td><strong>Week 24</strong></td>
<td>-8.1 (7.72)</td>
<td>-1.9 (5.90)</td>
</tr>
<tr>
<td>(n=194)</td>
<td>(n=195)</td>
<td></td>
</tr>
</tbody>
</table>
Abstract Number: 631

Predictors of Long-Term Retention of Methotrexate and Other Dmards with Golimumab in Rheumatoid Arthritis and Psoriatic Arthritis: An Analysis from a Prospective, Observational Registry

Derek Haaland¹, Anna Jaroszynska², B Haraoui³, Suneil Kapur⁴, Jacqueline Stewart⁵, Wojciech Olsynzynski⁶, Keltie Anderson⁷, Raman Rai⁸, Michael Starr⁹, Alexander Tsoukas¹⁰, Eliofotisti Psaradellis¹¹, Emmanouil Rampakakis¹¹, Cathy Tkaczyk¹², Allen J Lehman¹³, Francois Nantel¹² and Brendan Osborne¹², ¹Rheumatology, Clinical Immunology & Allergy, McMaster University, Barrie, ON, Canada, ²Private practice, Burlington, ON, Canada, ³Institut de Recherche en Rhumatologie de Montréal (IRRM), Montreal, QC, Canada, ⁴University of Ottawa, 139 Greenbank Rd, Suite 203, ON, Canada, ⁵Penticton Regional Hospital, Penticton, BC, Canada, ⁶University of Saskatchewan, Saskatoon, ON, Canada, ⁷University of Saskatchewan, Saskatoon, SK, Canada, ⁸Private Practice, Hamilton, ON, Canada, ⁹Rheumatology, McGill University, Pointe-Claire,, QC, Canada, ¹⁰McGill University, Montreal, QC, Canada, ¹¹JSS Medical Research, Montreal, QC, Canada, ¹²Medical Affairs, Janssen Inc., Toronto, ON, Canada, ¹³Janssen Inc., Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Previous studies have suggested that concomitant methotrexate therapy may increase the efficacy of biologic treatments. A scarcity of data exists on the benefits of combination therapy with golimumab (GLM) and MTX as well as other DMARDs (oDMARDs). The aim of this analysis was to compare the long-term retention of GLM monotherapy vs. combination therapy with MTX and/or oDMARDs and to explore independent predictors of retention in patients with rheumatoid arthritis (RA) and psoriatic arthritis followed in Canadian routine practice.

Methods: BioTRAC is an ongoing, prospective registry of patients initiating treatment with infliximab or GLM for RA, ankylosing spondylitis, or PsA, or with ustekinumab for PsA. Eligible participants for this analysis included RA and PsA patients treated with GLM. Patients were excluded if they had follow-up <24 months and were not discontinued. Treatment durability was assessed with the Kaplan Meier (KM) estimator of the survival function and Cox regression.

Results: A total of 336 RA patients were included; baseline characteristics and disease parameters are summarized by treatment group in Table 1. There were 195 (58.0%) patients who discontinued with a KM-based mean (SE) time to discontinuation of 36.2 (1.7) months. Between group differences were observed with higher treatment durability for
MTX+GLM+oDMARDs [39.8 (2.3)] months, followed by MTX+GLM [37.4 (3.4)], GLM+oDMARDs [27.2 (4.8)] and GLM monotherapy with [25.2 (3.0)] (p=0.025). Upon adjusting for potential confounders, higher durability was observed for the MTX+GLM+oDMARDs group vs. GLM monotherapy [hazard ratio -HR- (95% CI): 0.59 (0.36-0.96), p=0.032]. Moreover, increased baseline DAS28 [HR (95% CI): 1.17 (1.03-1.32), p=0.014] and previous use of MTX [HR (95% CI): 1.73 (1.00-3.00), p=0.052], were independently associated with premature treatment termination.

A total of 167 PsA patients were included; baseline characteristics and disease parameters are described by treatment group in Table 1. There were 96 (57.5%) patients who discontinued with a KM-based mean (SE) time to discontinuation of 34.7 (2.3) months. No between group differences were observed for treatment durability. However, upon adjusting for potential confounders, increased baseline MDGA [HR (95% CI): 1.12 (1.01-1.25), p=0.038], previous use of MTX [HR (95% CI): 3.54 (1.09-11.45), p=0.035], and female gender [HR (95% CI): 1.96 (1.19-3.21), p=0.008] were independently associated with premature treatment termination.

**Conclusion:** The results of this analysis have shown that combination therapy with GLM, MTX and other DMARDs is significantly associated with higher treatment durability compared to GLM monotherapy among RA patients. Although gender and MDGA were identified as significant independent predictors of long-term retention among PsA patients, treatment durability was not affected by concomitant MTX and DMARD use.
<table>
<thead>
<tr>
<th>Cohort</th>
<th>Baseline Parameter</th>
<th>GLM Monotherapy (n=41)</th>
<th>MTX+GLM (n=89)</th>
<th>MTX+GLM+oDMARDs (n=175)</th>
<th>GLM+oDMARDs (n=31)</th>
<th>p-value&lt;sup&gt;€&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA</td>
<td>Age, years</td>
<td>58.5 (16.2)</td>
<td>57.5 (13.1)</td>
<td>57.4 (13.1)</td>
<td>54.8 (11.9)</td>
<td>0.477</td>
</tr>
<tr>
<td></td>
<td>Disease Duration, years</td>
<td>8.4 (9.5)</td>
<td>8.2 (9.0)</td>
<td>7.4 (7.8)</td>
<td>10.2 (11.5)</td>
<td>0.773</td>
</tr>
<tr>
<td></td>
<td>Females, n(%)</td>
<td>29 (70.7)</td>
<td>68 (76.4)</td>
<td>109 (62.3)</td>
<td>25 (80.6)</td>
<td>0.071</td>
</tr>
<tr>
<td></td>
<td>Bio-naïve, n(%)</td>
<td>39 (95.1)</td>
<td>84 (94.4)</td>
<td>166 (94.9)</td>
<td>26 (83.9)</td>
<td>0.126</td>
</tr>
<tr>
<td></td>
<td>MTX dose, mg/week</td>
<td>NA</td>
<td>20.5 (12.9)</td>
<td>19.9 (4.5)</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sulfasalazine&lt;sup&gt;¥&lt;/sup&gt;, n(%)</td>
<td>NA</td>
<td>NA</td>
<td>31 (17.7)</td>
<td>0 (0.0)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Hydroxychloroquine&lt;sup&gt;¥&lt;/sup&gt;, n(%)</td>
<td>NA</td>
<td>NA</td>
<td>119 (68.0)</td>
<td>13 (41.9)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Leflunomide&lt;sup&gt;¥&lt;/sup&gt;, n(%)</td>
<td>NA</td>
<td>NA</td>
<td>81 (46.3)</td>
<td>18 (58.1)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Cyclosporine&lt;sup&gt;¥&lt;/sup&gt;, n(%)</td>
<td>NA</td>
<td>NA</td>
<td>1 (0.6)</td>
<td>0 (0.0)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Previous DMARD use, n(%)</td>
<td>38 (92.7)</td>
<td>87 (97.8)</td>
<td>169 (96.6)</td>
<td>30 (96.8)</td>
<td>0.543</td>
</tr>
<tr>
<td></td>
<td>Previous MTX use, n(%)</td>
<td>34 (82.9)</td>
<td>79 (88.8)</td>
<td>154 (88.0)</td>
<td>23 (74.2)</td>
<td>0.163</td>
</tr>
<tr>
<td></td>
<td>SJC</td>
<td>7.5 (5.0)</td>
<td>7.7 (5.9)</td>
<td>8.5 (6.0)</td>
<td>7.7 (5.4)</td>
<td>0.630</td>
</tr>
<tr>
<td></td>
<td>TJC</td>
<td>9.7 (6.7)</td>
<td>9.8 (7.4)</td>
<td>9.0 (6.8)</td>
<td>8.6 (6.7)</td>
<td>0.763</td>
</tr>
<tr>
<td></td>
<td>Pain, mm*</td>
<td>49.0 (25.5)</td>
<td>55.7 (27.5)</td>
<td>54.6 (25.9)</td>
<td>50.3 (27.7)</td>
<td>0.498</td>
</tr>
<tr>
<td></td>
<td>PtGA, mm*</td>
<td>53.2 (26.4)</td>
<td>56.8 (26.8)</td>
<td>56.7 (26.1)</td>
<td>48.2 (28.4)</td>
<td>0.536</td>
</tr>
<tr>
<td></td>
<td>MDGA, mm*</td>
<td>58.8 (18.9)</td>
<td>56.6 (24.7)</td>
<td>57.4 (21.3)</td>
<td>56.8 (24.8)</td>
<td>0.983</td>
</tr>
<tr>
<td></td>
<td>Morning stiffness, min</td>
<td>42.0 (41.9)</td>
<td>36.3 (41.8)</td>
<td>46.6 (45.3)</td>
<td>36.5 (41.3)</td>
<td>0.240</td>
</tr>
<tr>
<td></td>
<td>DAS28</td>
<td>5.5 (1.3)</td>
<td>5.0 (1.7)</td>
<td>5.1 (1.5)</td>
<td>5.0 (1.3)</td>
<td>0.540</td>
</tr>
<tr>
<td>PsA</td>
<td>Age, years</td>
<td>50.9 (12.8)</td>
<td>51.6 (13.4)</td>
<td>51.3 (13.0)</td>
<td>56.0 (12.0)</td>
<td>0.575</td>
</tr>
<tr>
<td></td>
<td>Disease Duration, years</td>
<td>5.6 (9.0)</td>
<td>4.8 (5.6)</td>
<td>4.4 (6.3)</td>
<td>5.4 (6.3)</td>
<td>0.586</td>
</tr>
<tr>
<td></td>
<td>Females, n(%)</td>
<td>14 (46.7)</td>
<td>36 (51.4)</td>
<td>21 (47.7)</td>
<td>10 (43.5)</td>
<td>0.853</td>
</tr>
<tr>
<td></td>
<td>Bio-naïve, n(%)</td>
<td>27 (90.0)</td>
<td>64 (91.4)</td>
<td>43 (97.7)</td>
<td>21 (91.3)</td>
<td>0.526</td>
</tr>
<tr>
<td></td>
<td>MTX dose, mg/week</td>
<td>NA</td>
<td>19.8 (5.8)</td>
<td>20.1 (4.9)</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sulfasalazine&lt;sup&gt;¥&lt;/sup&gt;, n(%)</td>
<td>NA</td>
<td>NA</td>
<td>23 (52.3)</td>
<td>5 (21.7)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Hydroxychloroquine&lt;sup&gt;¥&lt;/sup&gt;, n(%)</td>
<td>NA</td>
<td>NA</td>
<td>17 (38.6)</td>
<td>2 (8.7)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Leflunomide&lt;sup&gt;¥&lt;/sup&gt;, n(%)</td>
<td>NA</td>
<td>NA</td>
<td>11 (25.0)</td>
<td>16 (69.6)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Previous DMARD use, n(%)</td>
<td>26 (86.7)</td>
<td>68 (97.1)</td>
<td>41 (93.2)</td>
<td>23 (100.0)</td>
<td>0.108</td>
</tr>
<tr>
<td></td>
<td>Previous MTX use, n(%)</td>
<td>24 (80.0)</td>
<td>66 (94.3)</td>
<td>39 (88.6)</td>
<td>18 (78.3)</td>
<td>0.088</td>
</tr>
<tr>
<td></td>
<td>SJC</td>
<td>5.4 (4.0)</td>
<td>4.5 (4.0)</td>
<td>5.5 (4.1)</td>
<td>5.2 (5.2)</td>
<td>0.552</td>
</tr>
<tr>
<td></td>
<td>TJC</td>
<td>6.0 (5.7)</td>
<td>6.7 (6.8)</td>
<td>7.8 (6.8)</td>
<td>7.4 (7.4)</td>
<td>0.697</td>
</tr>
<tr>
<td></td>
<td>Pain, mm*</td>
<td>47.4 (23.2)</td>
<td>49.3 (25.5)</td>
<td>58.1 (23.8)</td>
<td>47.3 (27.3)</td>
<td>0.213</td>
</tr>
<tr>
<td></td>
<td>PtGA, mm*</td>
<td>44.5 (25.6)</td>
<td>50.1 (26.6)</td>
<td>58.9 (22.9)</td>
<td>53.8 (25.2)</td>
<td>0.179</td>
</tr>
<tr>
<td></td>
<td>MDGA, mm*</td>
<td>51.8 (17.9)</td>
<td>47.4 (23.5)</td>
<td>55.1 (18.8)</td>
<td>53.3 (21.1)</td>
<td>0.412</td>
</tr>
<tr>
<td></td>
<td>Morning stiffness, min</td>
<td>44.1 (47.9)</td>
<td>31.0 (35.0)</td>
<td>47.5 (44.5)</td>
<td>45.7 (43.8)</td>
<td>0.253</td>
</tr>
</tbody>
</table>
Concomitant DMARD use

P-value derived from non-parametric Kruskal Wallis test for continuous variables and from Pearson Chi-Square for categorical variables. No statistically significant between group differences were observed among RA and PsA patients. NA=not applicable

Disclosure: D. Haaland, None; A. Jaroszynska, Janssen Pharmaceutica Product, L.P., 9; B. Haraoui, None; S. Kapur, None; J. Stewart, None; W. Olszynska, None; K. Anderson, None; R. Rai, None; M. Starr, None; A. Tsoukas, None; E. Psaradellis, Janssen Inc., 9; E. Rampakakis, Janssen Inc., 9; C. Tkaczyk, Janssen Inc, 3; A. J. Lehman, Janssen Inc., 3; F. Nantel, Janssen Inc., 3; B. Osborne, Janssen Inc., 3.

Abstract Number: 632

**Long-Term Golimumab Retention Rate in Patients with Psoriatic Arthritis. Is Concomitant DMARD Important?**

Belen Serrano¹, Carlos M Gonzalez², Roberto González³, Juan Gabriel Ovalles-Bonilla⁴, Juan Carlos Nieto², Julia Martínez-Barrio⁵, Justina Janta², Larissa Valor³, Indalecio Monteagudo² and Francisco Javier López Longó⁶,

¹Rheumatology, Hospital General Universitario Gregorio Marañón, Genoa, Italy, ²Rheumatology, Hospital General Universitario Gregorio Marañón, Madrid, Spain, ³Rheumatology, Hospital general Universitario Gregorio Marañón, Madrid, Spain, ⁴Instituto de Investigación Sanitaria Gregorio Marañón, Madrid, Spain, ⁵Servicio de Reumatologia, Hospital General Universitario Gregorio Marañón, Madrid, Spain, ⁶Facultad de Medicina, Universidad Complutense de Madrid, Madrid, Spain

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The efficacy of Golimumab (GLM) treatment in psoriatic arthritis (PsA) patients has been widely documented. The aim of this study was to analyze the long-term retention of GLM and to identify independent predictors of drug retention in patients with PsA including concomitant DMARD.

Methods: Prospective monocentric cohort of PsA patients treated with GLM according to clinical practice. Study was approved by local Ethics Committee. Demographic and clinical variables were analyzed with Cox proportional hazard regression model.

Results: 48 patients were included, 20/48 (41.7%) oligoarticular, 19/48 (39.6%) polyarticular and 9/48 (18.7%) with peripheral and axial PsA. The baseline characteristics of the patients are shown in Table 1. Mean follow-up time was 22.3 months (SD 19.0). Mean survival time was 40.3 months (95% CI: 32.0-48.5). Age, mean evolution time and previous biological use were significant in the univariate analysis. Concomitant DMARD had no influence on GLM retention rate (HR: 1.3; 95% CI: 0.5-3.2; p: 0.6). Figure 1. Patients with PsA treated with GLM as first or second biological tended to
have a better retention rate of the drug, but did not reach statistical significance. Fig 2. 18/48 (37.5\%) withdraw GLM treatment. 13/18 (72.2\%) due to lack of efficacy, 1/18 (0.6\%) due to adverse events and 4/18 (22.2\%) due to other reasons.

Table 1. Baseline demographic and clinical characteristics of the patients.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean (SD)-years)</td>
<td>48.3 (11.1)</td>
</tr>
<tr>
<td>Female gender %</td>
<td>52.1%</td>
</tr>
<tr>
<td>Mean evolution time (SD) years</td>
<td>8.4 (7.9)</td>
</tr>
<tr>
<td>TJC</td>
<td>4.1 (4.1)</td>
</tr>
<tr>
<td>SJC</td>
<td>2.9 (2.7)</td>
</tr>
<tr>
<td>CRP mg/dl Mean (SD)</td>
<td>0.6 (0.7)</td>
</tr>
<tr>
<td>DAS28-CRP</td>
<td>3.7 (1.5)</td>
</tr>
<tr>
<td>Concomitant DMARD %</td>
<td>50%</td>
</tr>
<tr>
<td>Biological Therapy naïve %</td>
<td>52.1%</td>
</tr>
</tbody>
</table>
**Conclusion:** Real-world Golimumab retention rate in patients with PsA was good and did not depend on concomitant treatment with DMARD. When used as first or second biologic, Golimumab retention rate tend to be better.

**Disclosure:** B. Serrano, None; C. M. Gonzalez, MSD, Celgene, Novartis, Abbvie, Janssen, 5, MSD, Celgene, Novartis, Janssen, UCB Pharma, 8; R. González, None; J. G. Ovalles-Bonilla, Pfizer, Roche, BMS, Asacpharma, Nordic Pharma, 8, Sanofi-Aventis Pharmaceutical, 5; J. C. Nieto, Roche Pharmaceuticals, MSD, Abbvie, Novartis, Celgene, BMS, 8; J. Martínez-Barrio, None; I. Janta, None; L. Valor, Roche, Novartis, Celgene, Janssen; Sanofi, 8; I. Monteagudo, None; F. J. López Longo, None.


**Abstract Number:** 633

**Improvement of Joint Inflammation As Assessed By MRI and Power Doppler Ultrasound (PDUS) in an Open Label Study in Patients with Active Psoriatic Arthritis Treated with Secukinumab.**

Eleni Kampylafka¹, Isabelle Oliveira¹, Christina Linz², Veronika Lerchen¹, Matthias Englbrecht¹, Michael Sticherling³, Arnd Kleyer¹, Juergen Rech¹, Georg Schett¹ and Axel J. Hueber¹, ¹Department of Internal Medicine 3 – Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg, Erlangen, Germany, ²Department of Internal Medicine 3 – Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg, e, Germany, ³Department of Dermatology, Friedrich-Alexander-University Erlangen-Nürnberg, Erlangen, Germany

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Secukinumab, an anti-interleukin 17A monoclonal antibody, showed significant improvement of signs and symptoms of psoriatic arthritis (PsA) in phase 3 studies. Available studies used conventional radiography, not allowing a deeper imaging analysis of the inflammatory changes during application. The aim of this study was to assess short term efficacy of secukinumab on inflammation and structural damage according to change in OMERACT-EULAR ultrasound score, the MRI PsAMRIS score, and HRpQCT scans of the MCP and PIP joints in PsA patients.

**Methods:**

PsA patients with active disease (TJC and SJC ≥ 3), were included in the 24 week open label prospective PSARTROS study and treated with subcutaneous secukinumab 300 mg once weekly over 4 weeks, then once every 4 weeks. Baseline 1,5T MRI hand scans, HRpQCT scans of the MCP and PIP joints, and ultrasound imaging of 28 joints were performed at baseline and after 24 weeks of treatment. MRI was scored according to PsAMRIS. HRpQCT scans were evaluated for erosions and osteo-proliferation. Ultrasound was assessed for synovial hypertrophy and Doppler activity according to OMERACT scores. Statistical significance was set at p≤0.05.

**Results:** 20 patients, mean age 52 ± 9.9 years, 60% female, mean disease duration 6.7 ± 5.9 years, 50% naive for biological therapy, were included in the study. Three patients were early discontinued (recurrent pharyngitis, lack of efficacy, withdrawal of consent), and were not included into the longitudinal analysis. Baseline DAS28 was 5.03±0.96, baseline
DAPSA was 32.2±12.1. On baseline MRI, all patients had at least one inflammatory sign (synovitis: 90%, osteitis: 20%, periarticular inflammation: 25%, flexor tenosynovitis: 35%, bone proliferation: 30%, erosions: 60%). Baseline composite PsAMRIS score was 11.6±12.8 and baseline PsAMRIS synovitis score was 3.7±3.3. Baseline ultrasound synovial hypertrophy and Doppler activity were 6.2±4.5 and 3.5±4.0, respectively. Specific MRI and ultrasound scores were significantly correlated with DAS28 and DAPSA at baseline. Clinical disease activity parameters significantly improved at follow up (DAS28: 2.9±0.95, p<0.001; DAPSA: 8.8±5.8, p<0.001). PsAMRIS synovitis score (2.5±2.4) as well as composite PsAMRIS score (8.8±10.0) decreased longitudinally with secukinumab treatment (p=0.034 and p=0.039, respectively). There was no progression in erosion or proliferation scores between baseline and follow-up through MRI and HRpQCT imaging. Synovial hypertrophy and Doppler activity in ultrasound also significantly improved with secukinumab treatment (2.3±3.5; p=0.009 and 1.8±2.7; p=0.003, respectively). A significant percentage of patients reaching minimal disease activity showed residual signs of synovitis in the MRI and US (66% and 50%, respectively).

Conclusion:

Secukinumab significantly improves MRI and ultrasound signs of joint inflammation in patients with PsA. No progression in articular damage or osteo-proliferation was observed.

Disclosure: E. Kampylafka, None; I. Oliveira, None; C. Linz, None; V. Lerchen, None; M. Englbrecht, None; M. Sticherling, None; A. Kleyer, None; J. Rech, None; G. Schett, None; A. J. Hueber, None.

Abstract Number: 634

International League of Associations for Rheumatology. Systematic Review of the Literature to Inform Treatment Recommendations for Psoriatic Arthritis in Resource-Poor Countries

Musaab Elmamoun1, Maria Eraso2, Laura C Coates3, Ajesh Maharaj4, Vinod Chandran5, Ahmed Abogamal6, Valerilio F Azevedo7, Wilson Bautista-Molano8, Alex G. Ortega9, Jorge Medina-Rosas10,11, Fabian Hernandez12,13, Adma Lima14, Uyi Ima-Edomwonyi15, Adeola Ajibade16, Tarun Narang17, Olusola Ayanlowo18, Claudia Goldenstein-Schainberg19, Roberto Ranza20,21,22,23,24,25, Girish M Mody26, Sueli Carneiro27,28, Aman Sharma29, Oscar Vega-Hinojosa30, Luis E. Vega31, Adewale O Adebayo32 and Sergio Toloza33. 1Rheumatology, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, 2University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, 3Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences., Oxford, United Kingdom, 4Nelson R. Mandela School of Medicine, University of KwaZulu Natal, Durban, South Africa, 5Medicine, Krembil Research Institute, Toronto Western Hospital, University of Toronto, Toronto, ON, Canada, 6Al-Azhar University, Cairo, Egypt, 7Adjunct Professor of Rheumatology, Federal University of Paraná; Brazil, Curitiba, Brazil, 8School of Medicine, Universidad Militar Nueva Granada and Rheumatology Department Hospital Militar. Colombia, Bogotá, Colombia, 9Virginia Commonwealth University, Richmond, VA, 10Rheumatology, Universidad de la Sabana, Bogota, Colombia, 11Universidad del Valle, Cali, Colombia, 12Universidad del Cauca, Popayan, Colombia, 13Universidad de Caldas, Pereira, Colombia, 14Federação Universidade Regional de Blumenau, Blumenau, Brazil, 15Internal Medicine, Lagos University Teaching Hospital, Surulere, Nigeria, 16Obafemi Awolowo University Teaching Hospitals Complex Osun state, Nigeria., Osogbo, Nigeria, 17Postgraduate Institute of Medical Education and Research, Chandigarh, India, 18Lagos University Teaching Hospital, Lagos, Nigeria, 19Universidade de São Paulo, São Paulo, Brazil, 20on behalf of the Biobadabrasil study group, Sociedade Brasileira de Reumatologia, Uberlandia, Brazil, 21Rua Otavio Rodrigues DaCunha, Uberlandia MG, Brazil, 22Servicio de Reumatologia, Universidade Federal de Uberlandia, Uberlandia, Brazil, 23Reumatologia, Reumatologia, Universidade Federal de Uberlandia, Uberlandia, Brazil, 24Matematica, Matematica, Universidade Federal de Uberlandia, Uberlandia, Brazil, 25Universidade Federal de Uberlandia, Uberlandia MG, Brazil, 26Dept of Rheumatology, University of Kwa Zulu-Natal, Durban, South Africa, 27Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil, 28University of São Paulo,
Psoriatic Arthritis (PsA) is a heterogeneous disease which makes management of PsA a challenge. European League Against Rheumatism (EULAR) and the Group for Research and Assessment of Psoriasis and PsA (GRAPPA) updated their respective recommendations for the management of PsA in 2015. However, these recommendations are primarily based on studies conducted in resource replete countries of Europe and North America; they may not necessarily be applicable to PsA patients in countries in Central and South America, Africa and the Asia-Pacific region. Therefore there is a need to adapt the EULAR and GRAPPA recommendations for each of these regions under the auspices of ILAR.

Methods:

1) The ADAPTE process for guideline adaptation was used to assess and adapt the EULAR and GRAPPA treatment recommendations for PsA. Guideline quality was assessed using the 23 criteria of the Appraisal of Guidelines for Research and Evaluation (AGREE) instrument.

2) A literature search included three databases Medline, Embase, LILACS to identify studies that addressed additional treatment issues in Central and South America, Africa and the Asia-Pacific region.

Results:

The setup phase of the ADAPTE process was completed. Key health professionals in Pan-American League of Associations for Rheumatology (PANLAR) and The African League of Associations in Rheumatology (AFLAR) as well as patient research-partners identified key health issues faced. The adaptation phase of the ADAPTE process was carried out with both EULAR and GRAPPA recommendations assessed for quality and relevance to ILAR regions. Three different categories were assessed in the two guidelines; a) efficacy and safety of pharmacotherapy, b) recommendation for physicians with limited access to other specialists, c) screening and management of tuberculosis (TB), hepatitis B/C, human immunodeficiency virus (HIV), Chagas’ disease, leishmaniasis, and leprosy. The consensus (> 75% of votes) was to adapt the GRAPPA guidelines in terms of recommendations regarding efficacy and safety of pharmacotherapy, however, recommendations for combination therapy with conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) and biologic (b)DMARDs was not stated and evidence needed to be synthesized from literature review. Similarly, recommendation for biosimilars, biomimics; physicians with limited access to specialists; screening and management of TB, HB/C, HIV, Chagas’ disease, leishmaniasis, was lacking and referred to literature review.

The literature search retrieved a total of 634 articles; following exclusion of duplicates and off-topic items and after title and abstract review 26 articles were included for full text review. Results from the literature review suggests lack of recommendation/evidence around use of biosimilars/biomimics, skin treatment in the absence of dermatologist, and issues around screening and management of certain diseases relevant to resource-poor countries.

Conclusion:

New ILAR recommendations have been devised using adaptation from the GRAPPA recommendations where appropriate and additional SLR data to answer specific issues for resource poor settings and devise a research agenda for these regions.

Disclosure: M. Elmamoun, None; M. Eraso, None; L. C. Coates, None; A. Maharaj, None; V. Chandran, None; A. Abogamal, None; V. F. Azevedo, None; W. Bautista-Molano, None; A. G. Ortega, None; J. Medina-Rosas, None; F.
Short-Term Efficacy and Safety of New Biological Agents Targeting the IL-6, IL-12/23 and IL-17 Pathways for Active Psoriatic Arthritis: A Network Meta-Analysis of Randomised Controlled Trials

Dongze Wu, Jiang Yue and Lai-Shan Tam, Department of Medicine & Therapeutics, The Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong, Hong Kong

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
According to EULAR recommendations, in patients with peripheral arthritis and an inadequate response to at least one conventional synthetic DMARD, biologic DMARDs targeting IL-12/23, IL-17 pathways may be used in patients for whom TNF inhibitors are inappropriate. The objective of this study was to investigate comparative efficacy, safety and tolerability of IL-6, IL-12/23 or IL-17 inhibitors for patients with active psoriatic arthritis (PsA).

Methods:
Randomized controlled trials (RCTs) evaluating the efficacy, safety and tolerability of IL-6, IL-12/23 or IL-17 inhibitors were identified by a comprehensive systematic literature review. Pair-wise meta-analyses and Bayesian network meta-analyses using the random-effects model were performed to estimate pooled odds ratios (ORs) and 95% credible interval (CrI) of attaining a 20% improvement according to American College of Rheumatology criteria (ACR20) and ACR 50 response across trials.

Results:
Six trials were identified which included 2,411 participants and 11 treatments. Pair-wise meta-analysis showed that secukinumab, ustekinumab and ixekizumab demonstrated superior efficacy over placebo in achieving ACR 20 and ACR50 response. However, Ixekizumab has a higher incidence of adverse events (AE) than placebo. In contrast, ustekinumab has a higher tolerability (less likely to be discontinued due to AE) than placebo. Network meta-analysis showed that secukinumab (300mg monthly) had the highest efficacy in achieving ACR20 and ACR50; whereas clazakizumab (200mg monthly), ustekinumab (45mg 12 weekly), secukinumab (150mg monthly) had the lowest probability of having AE, serious AE, and intolerability respectively. Considering overall risk-benefit profile, secukinumab (150mg monthly) may offer an optimal balance for active PsA patients.

Conclusion:
From available evidence, secukinumab was found to be the safest and most efficacious short-term treatments for active PsA amongst all the new biologics targeting the IL-6, IL-12/23 and IL-17 pathways.
**Disclosures**: This study has partly presented at EULAR2017.

**Disclosure**: D. Wu, None; J. Yue, None; L. S. Tam, None.


**Abstract Number**: 636

**Effect of Adding MTX to TNF Inhibitors on Joint Severity Indices and Skin Scores in Psoriatic Arthritis: A Post-Hoc Meta-Analysis of Randomized, Controlled Trials**

Rochelle Castillo¹, Khushboo Sheth² and Santhanam Lakshminarayanan³, ¹University of Connecticut, Farmington, CT, ²Rheumatology, Stanford University, Palo Alto, CA, ³Division of Rheumatology, University of Connecticut Health Center, Farmington, CT

**First publication**: September 18, 2017

**SESSION INFORMATION**

**Session Date**: Sunday, November 5, 2017
Background/Purpose:

Co-medication of MTX with TNF inhibitors (TNFi) has proven superior to TNFi monotherapy in improving clinical outcomes in patients with RA. Whether this holds true in psoriatic arthritis (PsA) remains unclear. We undertook this study to summarize the post-hoc data from randomized, controlled trials (RCTs) on PsA to determine the effect of adding MTX to TNFi on joint severity indices and skin scores.

Methods:

We performed a systematic search of PubMed, Medline, Scopus, and the reference lists of relevant articles for studies published up to April 2017. RCTs containing data on the effect of combination MTX and TNFi versus TNFi monotherapy were included. A random effects model was used to pool extracted data. Heterogeneity was evaluated with I²; p-values < 0.05 were considered significant. Relative benefit, the equivalent of relative risk in studies that aim to improve outcomes, was used to measure the effect size of dichotomous variables.

Results:

Eight clinical trials consisting of 1,055 subjects were included. Responses were grouped into categories based on duration of treatment (12±4 weeks, 24±4 weeks, 48±4 weeks) and outcome measured. Meta-analysis was performed when at least two studies provided data for the same outcome during the same time frame. In studies measuring ACR 20/50/70 at Week 12, there was no statistically significant difference between combining TNFi with MTX vs. TNFi alone (Figure 1). The same trend of no added benefit to combination therapy was observed in ACR 20/50/70 at Week 24 and ACR 20 at Week 48. In studies that measured PASI 75, there was a non-significant trend toward increased response at Weeks 24 and 48 with combination therapy compared to TNFi monotherapy (Figure 2).

Conclusion:

In contrast to RA, the post-hoc data gleaned from PsA trials has not suggested a benefit to adding MTX to TNFi in improving joint severity indices. This may be attributed to the fact that MTX monotherapy is generally considered less effective in PsA than in RA. However, the non-significant trend toward increase in PASI 75 suggests that combination therapy may be beneficial in the subset of PsA patients with significant skin involvement. An inherent limitation of the included studies is that subjects in the MTX+TNFi group were already on stable MTX doses prior to initiating TNFi therapy. Thus, studies directly comparing TNFi monotherapy with combination therapy with MTX in MTX-naive patients are needed to arrive at definitive conclusions.

Figure 1. ACR 20/50/70 at Week 12 with adalimumab (ADA) and infliximab (IFX)
Figure 2. PASI 75 at Weeks 24/48 with ADA, etanercept (ETN), and IFX.

Disclosure: R. Castillo, None; K. Sheth, None; S. Lakshminarayanan, None.


Abstract Number: 637

The Effect of Biologic Therapies on the Gut Microbial Composition in Psoriatic Arthritis

Julia Manasson1, Carles Ubeda2, Lu Yang3, Melania Fanok4, Gary E. Solomon1, Soumya M. Reddy5, Sergei Koralov6, Jose C. Clemente7 and Jose U. Scher1,4, 1Department of Medicine, Division of Rheumatology, New York University School of Medicine, New York, NY, 2Institute for Research in Public Health, Valencia, Spain, 3New York University School of Medicine, New York, NY, 4New York University School of Medicine, New York, NY, 5Department of Medicine, Division of Rheumatology *contributed equally, New York University School of Medicine, New York, NY, 6Pathology, New York University School of Medicine, New York, NY, 7Department of Genetics and Genomic Sciences, Icahn Institute for Genomics and Multiscale Biology, Icahn School of Medicine at Mount Sinai, New York, NY

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is a heterogeneous inflammatory arthritis affecting multiple clinical domains. If left untreated, it has the potential for significant morbidity and disability. Prior to the introduction of TNF-alpha inhibitors (TNFi), therapeutic options were limited. Agents that block the IL-17 pathway (IL-17i) were recently FDA-approved, showing remarkable improvement in psoriasis, as well as similar efficacy to TNFi in PsA. Surprisingly, IL-17i are not effective for all autoimmune conditions, and appear to exacerbate Crohn’s disease, even leading to de novo intestinal inflammation. Because IL-17 plays a physiologic role in maintaining gut epithelial health and fighting extracellular bacteria and fungi, we propose that intestinal inflammation occurs as a result of microbial dysbiosis. The goal of this study was to better understand the interaction between IL-17i and the microbiome in humans and mice.

Methods: Fecal samples were collected from subjects with PsA pre- and post-treatment with secukinumab (n=9), an anti-IL-17A monoclonal antibody, and adalimumab (n=10), a TNFi, which served as the control. In parallel, fecal pellets were collected from wild type mice pre- and post-exposure to anti-IL-17 or MOPC isotype control antibodies. Samples underwent DNA extraction, amplification, and 16S rRNA gene sequencing with Illumina MiSeq. Analysis was performed
with Quantitative Insights into Microbial Ecology (QIIME) and R. Additionally, short and medium chain fatty acids (SCFA/MCFA) were measured utilizing liquid chromatography coupled with mass spectrometry (LC-MS/MS).

**Results:** PsA subjects treated with IL-17i did not show differences in overall microbial alpha or beta diversity pre- and post-treatment. However, there was a significant shift in the Firmicutes to Bacteroidetes ratio after just five weeks of therapy. Subjects clustered into two well-defined groups based on expansion or contraction of the Clostridiales taxa. Relative abundance of Clostridiales correlated with levels of the SCFA acetate (r=0.4, p=0.09) and the MCFA hexanoate (r=0.4, p=0.09). These differences were absent in TNFi-treated controls. Similarly, mice exposed to anti-IL-17 antibody showed parallel perturbations in microbiota composition as demonstrated by alpha (p<0.05) and beta diversity (p<0.05), with expansion of Clostridia and related taxa (p<0.05).

**Conclusion:** We characterized the effects of biologic therapies on gut microbiota composition and metabolites in human PsA and in mice. Treatment with IL-17i leads to a gut microbial dysbiosis not seen with TNFi. Further studies to understand the downstream effects of these perturbations may allow for the development of precision medicine approaches to PsA.

**Disclosure:** J. Manasson, None; C. Ubeda, None; L. Yang, None; M. Fanok, None; G. E. Solomon, Abvie, 9; S. M. Reddy, None; S. Koralov, None; J. C. Clemente, None; J. U. Scher, NIAMS-NIH, 2.


**Abstract Number:** 638

Are There Clinical Demographic or Subclinical Ultrasonographic Data That Can Predict Flare in Psoriatic Arthritis Patients during a Phase of Minimal Disease Activity after Spacing of Anti-TNF Blockers Injections?

**Pierluigi Macchioni**1, Giovanni Ciancio2, Gilda Sandri3, Alen Zabotti4, Luca Montaguti5, Gentiana Vukatana6, Fabio Mascella7, Donatella Chessa8, Elisa Verduci9, Marcello Govoni10, Amelia Spinella3, Francesca Zuliani11, Marco Bruschi5, Nazzarena Malavolta12 and Mariacristina Focherini7,

1Rheumatology Unit, Arcispedale S Maria Nuova, IRCCS, Reggio Emilia, Italy, 2Rheumatology Unit, Department of Medical Sciences, University of Ferrara and Azienda Ospedaliera-Universitaria Sant’Anna - Ferrara (Italy), ferrara, Italy, 3Rheumatology Unit, University fo Modena & Reggio, Modena, Italy, 4Rheumatology Clinic, Department of Medical and Biological Sciences, Santa Maria della Misericordia" University Hospital, Udine, Italy, 5Dipartimento Internistico SS di Reumatologia, AUSL Romagna Ospedale Bufalini, Cesena, Italy, 6Rheumatology Unit, Department CardioThoracic Vascular, S.Orsola- Malpighi Hospital, Alma Mater Studiorum, Bologna, Bologna, Italy, 7Internal Medicine and Rheumatology, Ospedale Infermi Rimini, Rimini, Italy, 8Internal Medicine, Ospedale Paolo Dettori, Tempio Pausania, Italy, 9Rheumatology Unit, Arcispedale S. Maria Nuova, Reggio Emilia, Italy, 10Rheumatology Clinic, Department of Medical and Biological Sciences, University of Ferrara and Azienda Ospedaliera-Universitariana Sant’Anna - Ferrara (Italy), ferrara, Italy, 11Rheumatology Unit, Department of Medical Sciences, Santa Maria della Misericordia" University Hospital, Udine, Italy, 12Policlinico S.Orsola-Malpighi, Azienda Ospedaliero-Universitariana of Bologna, Bologna, Italy

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**
Tumour necrosis factor (TNF)-blocker tapering has been proposed for patients with psoriatic arthritis (PA) in clinical remission. To evaluate if there are clinical, demographic and ultrasound (US) data predictive of disease recurrence after spacing of anti-TNF therapy in PA patient during a phase of minimal disease activity (MDA).

**Methods:**

Patients treated with anti-TNF for at least 12 months and with at least 6 months duration of MDA were consecutively recruited at 6 Italian centers.

In every center, the local rheumatologists provided PA pts to be examined by US. Personal history, demographic and clinical data were recorded. Each patient underwent the following US examinations: metacarpophalangeal (MCP), knee and tibio-tarsal (TT) joint, flexor and extensor tendon of hand digit, flexor and extensor tendon at carpal area, flexor and extensor tendon of foot, and enthesis of common extensor tendon insertion on the lateral epicondyle of the humerus, quadriceps tendon, patellar tendon, Achilles tendon and plantar fascia insertions on the calcaneus. Each examination was performed by rheumatologists expert in US, to assess synovitis (joint effusion, synovial proliferation, and power Doppler (PD) signal), and bone erosions, flexor tendon tensynovitis, ext tendon tenonitis, and enthesel involvement using an Esaote MyLabClass with a 5-13 or 6-18 MHz linear probe. US examinators were blind of clinical data of the pts. After the clinical and US examination patients increased the interval between the anti-TNF administration according to a common protocol. The patients were clinically evaluated at three month interval for the maintenance of a state of MDA. Baseline clinical and US data were compared between the group of patients still in MDA at the end of a minimum follow-up period of 6 month vs the group of patient with disease recurrence.

**Results:**

Sixty-three pts were recruited (mean age 53+13y, mean PA duration 13+8y, mean MDA duration 21+11m). At the end of follow-up period 5 patient were lost, 47 (81%) maintained a state of MDA and 11 (19%) had recurrence. At baseline US examination 66.7 % of pts had at least one peripheral joint involved (17.5 % had peripheral active synovitis), 47.6% had acute enthesitis and 95.2% chronic enthesopathy. US bursitis was present in 22.2% of pts, 3.7% had hand extensor finger tendon involvement. No significant difference in any US and demographic data were present between the group in persistent MDA vs the recurred group. Patients with baseline Maastricht enthesis index (MEI) > 0 had higher risk of recurrences as compared with the group with MEI = 0 (36% vs 10%, p = 0.034).

**Conclusion:**

The presence of joint, entheseal and tendon abnormalities at US examination are not predictive of disease recurrence after anti-TNF spacing in PA patients in MDA. Only a value of MEI > 0 is significantly correlated to recurrence.

**Disclosure:** P. Macchioni, None; G. Ciancio, None; G. Sandri, None; A. Zabotti, None; L. Montaguti, None; G. Vukatana, None; F. Mascella, None; D. Chessa, None; E. Verduci, None; M. Govoni, None; A. Spinella, None; F. Zuliani, None; M. Bruschi, None; N. Malavolta, None; M. Focherini, None.


**Abstract Number:** 639

### Clinical and Sonographic Analysis of Patients with Psoriasis without Musculoskeletal Complaints. Preliminary Results of a Prospective Study: The PRE-Psa Cohort

**Andrea Cuervo**¹, Julio Ramírez², Merce Alsina³, Raimon Sanmartí⁴ and Juan D. Cañete⁵, ¹Arthritis Unit. Rheumatology Dpt, Arthritis Unit, Rheumatology Dpt, Hospital Clinic of Barcelona and IDIBAPS, Barcelona, Spain, ²Rheumatology
SESSION INFORMATION

**Session Date:** Sunday, November 5, 2017

**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Early diagnosis in psoriatic arthritis (PsA) is mandatory in order to initiate early therapy and prevent disability. Around 20% of patients with Psoriasis (PsO) routinely visited in Dermatology departments have PsA previously undiagnosed. The aim of this study is to evaluate the presence of inflammation by clinical examination and ultrasound in joints and enthesis of patients with PsO without musculoskeletal symptoms.

**Methods:** Patients with PsO under topic or PUVA therapy without musculoskeletal symptoms were referred to our Arthritis Unit. Clinical and demographic data were collected. The patients were evaluated for Body Surface Area (BSA), Swollen Joint Count (SJC) (66 joints), Tender Joint Count (TJC) (68 joints) and enthesis (MASES). Psoriatic Arthritis Impact of Disease tool questionnaire (PsAID) and Psoriasis Epidemiology Screening tool questionnaire (PEST) were used to assess the impact of the disease. A comprehensive ultrasound evaluation of 46 joints and 12 enthesis was made (ESAOTE MylabTwice, 12-18 Mhz probe). Enthesis score was calculated using the Madrid Sonographic Enthesis Index (MASEI) and a total score for synovitis (synovial hypertrophy and Power Doppler) was also calculated.

**Results:** 32 patients were included. 18 patients were female (56.3%), mean age (SD) was 48.3 years (14.6) and disease duration was 17.9 years (15.9). Mean BMI was 24.6 (5.2) and BSA 6.69 (8.7). 8 out of 32 (25%) had severe PsO (systemic treatment or BSA>10% at any time of evolution). 4 patients (12.5%) had Power Doppler signal and 2 (6.3%) fulfilled criteria for ultrasound-defined active synovitis (SH>2+PD) despite no signs or symptoms of musculoskeletal disease. However, although structural alterations such as calcifications and enthesophytes were frequent, no PD was found at any enthesis. In the univariate analysis, higher BMI (p=0.013), weight (p=0.010), waist (p=0.033) and hip (p=0.014) circumferences were significantly associated with severe PsO. In the same way, CRP serum levels were also significantly higher in patients with severe PsO (p=0.027).

**Conclusion:** Patients with severe PsO had significantly higher CRP serum levels, BMI, weight, waist and hip circumferences. Of note, 12.5% of PsO patients had subclinical synovitis defined as PD. These patients should be followed in order to confirm if they develop Psoriatic Arthritis.

**Disclosure:** A. Cuervo, None; J. Ramírez, Gebro, 2; M. Alsina, None; R. Sanmartí, None; J. D. Cañete, None.


**Abstract Number:** 640

**Is There a Relationship between Spondyloarthritis and Periodontitis? a Case-Control Study**

Wilson Bautista-Molano1, Désirée van der Heijde2, Robert B.M. Landewe2,3, Gloria Lafaurie4, Julieth De Avila4, Rafael Valle-Oñate5 and Consuelo Romero-Sanchez6, 1School of Medicine, Universidad Militar Nueva Granada and Rheumatology Department Hospital Militar, Colombia, Bogotá, Colombia, 2Leiden University Medical Center, Leiden, Netherlands, 3University of Amsterdam and Atrium Medical Center, Amsterdam, Netherlands, 4Unit of Oral Basic Investigation-UIBO, School of Dentistry, Universidad El Bosque, Colombia, Bogotá, Colombia, 5School of Medicine,
SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Knowledge of the existence of an epidemiological association between SpA and periodontitis may fuel pathophysiological thinking about SpA and if established, have clinical implications. Currently, it is unclear whether SpA patients have a higher frequency of periodontitis and data in the literature reporting a possible association is limited. Therefore, the aim of the present study was to compare the frequency and severity of periodontitis in SpA-patients with healthy-control individuals, through the evaluation of clinical, serological and microbiological periodontal condition.

Methods: Patients with a diagnosis of SpA (n=78) and bDMARD-naive fulfilling the ASAS classification criteria as well as 156 healthy-controls matched for age/gender, were included. Two trained and calibrated periodontologists performed the periodontal clinical assessment. The presence of periodontitis and its severity were determined according to the criteria established by the Center for Disease Control and Prevention-American Academy of Periodontology (CDC-AAP). The clinical periodontal variables, IgG1/IgG2 antibodies against *P. gingivalis* and periodontopathic bacterial identification, were also established. Comparisons of periodontal characteristics between the SpA-patients and the control-group were performed using univariable analyses. A logistic regression analyses was performed to calculate the odds ratio (95% CI) for diagnosis of periodontitis in SpA-patients and matched-controls.

Results: A diagnosis of periodontitis was established in 56% in SpA patients vs. 69% of healthy-controls (p=<0.001). Severe periodontitis was found in 3% vs 12% in SpA vs healthy-controls respectively (p=<0.001). There was no significant increase of frequency of any periodontal variable, IgG1/IgG2 antibodies against *P. gingivalis* or the presence of periodontopathic bacteria between SpA patients and control-group. Periodontitis was not positively associated with a diagnosis of SpA (OR: 0.57 95% CI 0.32-1.00, p=0.05) in the logistic regression analyses.

Conclusion:

Our results suggest that –unlike the situation in RA- there is not a positive association between SpA and periodontitis in Colombian patients. We even found a lower prevalence of periodontitis and less severe periodontitis in comparison to healthy controls. Moreover, all periodontal characteristics evaluated including clinical parameters, antibodies anti *P. gingivalis* and bacterial identification were not increased in SpA patients as compared to controls.

Table 1 Characteristics and periodontal variables in patients with spondyloarthritis (SpA) and healthy controls
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>SpA (n=78)</th>
<th>Controls (n=156)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>39.6 (11.0)</td>
<td>39.5 (11.1)</td>
<td>†</td>
</tr>
<tr>
<td>Male gender N (%)</td>
<td>47 (60.3)</td>
<td>94 (60.3)</td>
<td>†</td>
</tr>
<tr>
<td>Smoking (currently) N (%)</td>
<td>11 (14.1)</td>
<td>14 (9.0)</td>
<td>0.14</td>
</tr>
<tr>
<td>Obesity (BMI ≥30) N (%)</td>
<td>6 (7.6)</td>
<td>16 (10.2)</td>
<td>0.43</td>
</tr>
<tr>
<td>Periodontitis (positive)* N (%)</td>
<td>44 (56.4)</td>
<td>108 (69.2)</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Severity of Periodontitis</strong> N (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>34 (43.6)</td>
<td>48 (30.8)</td>
<td>0.01</td>
</tr>
<tr>
<td>Mild</td>
<td>11 (14.1)</td>
<td>20 (12.8)</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>31 (39.7)</td>
<td>69 (44.2)</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>2 (2.6)</td>
<td>19 (12.2)</td>
<td></td>
</tr>
<tr>
<td>Insertion level total mouth (mm)</td>
<td>2.4 (0.5)</td>
<td>2.9 (0.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CAL average interproximal (mm)</td>
<td>1.9 (0.6)</td>
<td>2.3 (0.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total pocket depth mouth (mm)</td>
<td>3.3 (1.7)</td>
<td>3.2 (1.9)</td>
<td>0.29</td>
</tr>
<tr>
<td>Plaque Index (%)</td>
<td>0.4 (0.2)</td>
<td>0.5 (0.2)</td>
<td>0.12</td>
</tr>
<tr>
<td>Gingival index (%)</td>
<td>0.3 (0.2)</td>
<td>0.4 (0.5)</td>
<td>0.33</td>
</tr>
<tr>
<td>Number of teeth present</td>
<td>26.1 (4.1)</td>
<td>25.5 (5.4)</td>
<td>0.79</td>
</tr>
<tr>
<td><em>P. gingivalis</em> (presence) N (%)</td>
<td>23 (29.4)</td>
<td>71 (45.5)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><em>T. denticola</em> (presence) N (%)</td>
<td>13 (16.6)</td>
<td>84 (53.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><em>T. forsythia</em> (presence) N (%)</td>
<td>6 (7.6)</td>
<td>75 (48.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IgG1 anti <em>P. gingivalis</em> (positive) N (%)</td>
<td>40 (51.2)</td>
<td>80 (51.2)</td>
<td>1</td>
</tr>
<tr>
<td>IgG2 anti <em>P. gingivalis</em> (positive) N (%)</td>
<td>41 (52.5)</td>
<td>74 (47.4)</td>
<td>0.32</td>
</tr>
</tbody>
</table>

All values given as mean (SD) unless specified;

† Age and gender were matching criteria

*Criteria and severity definition according to the Center for Disease Control and Prevention-American Academy of Periodontology (CDC-AAP)

BMI, body mass index; CAL, clinical attachment loss

**Disclosure:** W. Bautista-Molano, None; D. van der Heijde, None; R. B. M. Landewé, None; G. Lafaurie, None; J. De Avila, None; R. Valle-Oñate, None; C. Romero-Sanchez, None.

**View Abstract and Citation Information Online** - [http://acrabstracts.org/abstract/is-there-a-relationship-between-spondyloarthritis-and-periodontitis-a-case-control-study](http://acrabstracts.org/abstract/is-there-a-relationship-between-spondyloarthritis-and-periodontitis-a-case-control-study)

**Abstract Number:** 641
Children with Treatment-Naive Enthesitis-Related Arthritis Have Decreased Fecal Abundance of Faecalibacterium Prausnitzii A2-165 and Bacteroides Fragilis: A Multi-Center Collaborative Study

Matthew L. Stoll1, Pamela F. Weiss2, Jennifer E. Weiss3, Peter Nigrovic4, Barbara Edelheit5, S. Louis Bridges Jr.6, Maria I. Danila7, Charles Spencer8, Marilyn Punaro9, Kenneth Schikler10, Andreas Reiff11, Ranjit Kumar12, Randy Q. Cron1, Casey D Morrow13 and Elliot J. Lefkowitz14

1Pediatric Rheumatology, University of Alabama at Birmingham, Birmingham, AL; 2Division of Rheumatology, Center for Pediatric Clinical Effectiveness, Children's Hospital of Philadelphia, Philadelphia, PA; 3Hackensack University Medical Center, Hackensack, NJ; 4Division of Rheumatology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA; 5Pediatric Rheumatology, Connecticut Childrens Medical Center, Hartford, CT; 6Clinical Immunology & Rheum, Univ of Alabama, Birmingham, AL; 7University of Alabama at Birmingham, Birmingham, AL; 8Rheumatology, Nationwide Childrens Hospital/OSU, Columbus, OH; 9Children's Health, Dallas, TX; 10University of Louisville Medical School, Louisville, KY; 11Children’s Hospital of Los Angeles, Los Angeles, CA; 12Center for Clinical and Translational Sciences, University of Alabama at Birmingham, Birmingham, AL; 13Cell, Developmental, and Integrative Biology, University of Alabama at Birmingham, Birmingham, AL; 14Microbiology, University of Alabama at Birmingham, Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthopathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Prior studies have demonstrated abnormalities in the composition of the gastrointestinal microbiota in pediatric and adult patients with spondyloarthritis (SpA). In particular, diminished fecal abundance of Faecalibacterium prausnitzii and abnormalities in both directions in the abundance of the Bacteroides genus have been identified, mirroring results in studies of patients with inflammatory bowel disease.

Methods: We obtained fecal specimens from children with treatment-naive enthesitis-related arthritis (ERA) and healthy controls from multiple geographic locations, as well as specimens from adult patients with long-standing SpA. All of the samples underwent sequencing of the 16S ribosomal DNA (rDNA). A subset of the ERA and healthy pediatric fecal samples were also subjected to shotgun metagenomics sequencing.

Results: Children with ERA (n = 30) and healthy controls (n = 19) underwent 16S rDNA sequencing. Clustering of the microbiota based upon diagnosis (p = 0.046) was observed, while among ERA patients, there was no clustering by geographic location. In contrast to previous studies, fecal abundance of F. prausnitzii was slightly higher in the patients versus controls (10.0% vs 7.8%, p = 0.192); however strain-level differences were observed, with patients having relatively decreased abundance of the anti-inflammatory A2-165 strain (41% versus 54%, p = 0.084) and an increased abundance of the control L2/6 strain (28% versus 15%, p = 0.038). Similar trends were observed in adults with long-standing SpA (n = 11) and controls (n = 10): total F. prausnitzii 10% in patients versus 6.9% in controls (p = 0.427), while A2-165 as percentage of F. prausnitzii was 25% in patients versus 41% in controls (p = 0.175).

With respect to B. fragilis, opposite trends were seen among the pediatric versus the adult subjects. Specifically, pediatric patients with ERA demonstrated increased abundance of B. fragilis compared to controls (2.0% versus 0.45%, p = 0.045), yet adult subjects demonstrated decreased abundance of the Bacteroides genus (11% versus 26%, p = 0.036) and specifically of B. fragilis (0.2% versus 1%, p = 0.106).

Shotgun metagenomics sequencing of the fecal DNA in the pediatric subjects did not demonstrate any global pathway differences. However, it did reveal diminished coverage of the butanoate pathway (abundance normalized to controls of 1 versus 0.72 in ERA, p = 0.037).
Conclusion: Our study supports previous work indicating that decreased fecal abundance of a regulatory strain of *F. prausnitzii* may be at least partly responsible for the pathogenesis of SpA, possibly due to decreased production of butyrate, and suggests that efforts to replenish it in patients with SpA may be a potential therapeutic avenue. In contrast, the mechanism by which *Bacteroides* impacts arthritis may differ in pediatric and adult patients, possibly reflecting altered immunologic development in the former rather than direct pathogenicity or the organism. If this is the case, then enthusiasm for microbial-based interventions to address this organism may be tempered. Instead, our findings may underscore the necessity of prevention efforts, such as avoiding unnecessary use of antibiotics in healthy children.

Disclosure: M. L. Stoll, None; P. F. Weiss, None; J. E. Weiss, None; P. Nigrovic, Novartis Pharmaceutical Corporation, 2, Novartis Pharmaceutical Corporation, 5, Sobi, 2, Sobi, 5, UCB, 5, Pfizer Inc, 5, Casebia, 5, UpToDate, 7, American Academy of Pediatrics, 7; B. Edelheit, None; S. L. Bridges Jr., None; M. I. Danila, None; C. Spencer, None; M. Punaro, None; K. Schikler, None; A. Reiff, None; R. Kumar, None; R. Q. Cron, SOBI, 5, MedacPHARMA, 5; C. D. Morrow, None; E. J. Lefkowitz, None.


Abstract Number: 642

**Downstream Effects of Apremilast in Human Arthritic Ex Vivo Models**

**Tue Wenzel Kragstrup**¹,², Søren Lomholt², Morten Aagaard Nielsen², Line Dam Heftdal², Peter H. Schafer³ and Bent Deleuran²,⁴ ¹Randers Regional Hospital, Randers, Denmark, ²Department of Biomedicine, Aarhus University, Aarhus, Denmark, ³Department of Translational Development, Celgene Corporation, Summit, NJ, ⁴Department of Rheumatology, Aarhus University Hospital, Aarhus, Denmark

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Sunday, November 5, 2017

Session Title: Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster I

Session Type: ACR Poster Session A

Session Time: 9:00AM-11:00AM

**Background/Purpose:**

Apremilast (Otezla) is a PDE4 inhibitor approved for the treatment of psoriasis and psoriatic arthritis, but the mechanisms of action of apremilast are not fully described. The objective of this study was to study the downstream effects of apremilast on cells of the inflamed joint in ex vivo models of immune mediated inflammatory arthritis. Therefore, we tested the ex vivo effect of apremilast on the secretion of several cytokines, chemokines and growth factors by synovial fluid mononuclear cells (SFMCs), fibroblast-like synovial cells (FLSs), osteoclasts, synovial macrophages, and osteoblasts.

**Methods:**

SFMCs and FLSs were obtained from a study population consisting of patients with active RA, or peripheral SpA with at least one swollen joint (for obtaining synovial fluid) (n=14). Peripheral blood mononuclear cells (PBMCs) were obtained from healthy controls and osteoblasts were purchased. SFMCs were cultured for 48 hours with and without addition of apremilast measuring the secretion of a large panel of cytokines, chemokines and growth factors by the Olink proseek multiplex interferon panel and commercially available ELISA assays. These effects were compared with the effects of the TNFα inhibitor adalimumab. Further, FLS-PBMC co-cultures were used to study the secretion of metalloproteinases, SFMCs cultured for 21 days were used to study inflammatory osteoclastogenesis and macrophage differentiation, and a mineralization assay was used to study new bone formation.

**Results:**
In SFMCs cultured for 48 hours, apremilast decreased the production of IL-12B (P<0.00001) CSF1 (P=0.009), sCD6 (P=0.03), sCD40 (P=0.04), and MCP-1 (P=0.02), and increased the production of CXCL5 (P=0.003) dose-dependently. In sub-analyses, the apremilast induced decrease in cytokine production was greater in cultures with a high lymphocyte count and in cultures from patients with a low C-reactive protein level. Further, apremilast had a very different response signature compared with adalimumab, e.g. with a more robust inhibition of IL-12B (P=0.01) and less inhibition of IL-8 (P=0.0001) (see figure). In FLS-PBMC co-cultures, apremilast decreased MMP3 production (P=0.009). In SFMCs cultured for 21 days, apremilast did not significantly decrease inflammatory osteoclastogenesis (P=0.2). However, apremilast increased the secretion of IL-10 (P=0.04) without affecting the secretion of MCP-1 (P=0.5). Finally, apremilast did not significantly decrease mineralization by human osteoblasts (P=0.2).

Conclusion:

This study reveals the downstream effects of apremilast in ex vivo models of arthritis with a strong inhibition of IL-12B. Further, apremilast induced IL-10 production in synovial macrophages and decreased MMP3 in FLS-PBMC co-cultures. Our findings could explain some of the efficacy of apremilast seen in IL-12/IL-23 driven immune mediated inflammatory diseases such as psoriasis and psoriatic arthritis.

Disclosure: T. W. Kragstrup, None; S. Lomholt, None; M. A. Nielsen, None; L. D. Heftdal, None; P. H. Schafer, Otezla, 1, 9,Otezla, 3; B. Deleuran, Otezla, 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/downstream-effects-of-apremilast-in-human-arthritic-ex-vivo-models

Abstract Number: 643

Mir-10b-5p Is a IL-22 Regulator in CD4+T Cells from Ankylosing Spondylitis

Tae-Jong Kim1, So-Hee Jin2, Liye Chen3, Mohammad Hussein Al-Mossawi3, Anna Ridley3, Takuya Sekine3, Davide Simone3, Hui Shi3, Frank Penkava3 and Paul Bowness3, 1Rheumatology, Chonnam National University Medical School and Hospital, Gwangju, Korea, Republic of (South), 2Chonnam National University Medical School and Hospital, Gwangju, Korea, Republic of (South), 3Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Emerging data suggest that a single microRNA (miR) can profoundly alter the phenotype and outcome of immune responses, offering the prospect of therapeutic use. We recently reported a novel Th17 regulator miR-10b-5p that is present in Th17 cells from patients with Ankylosing Spondylitis (AS). IL-22 is closely related to Th17 cells and also regulated by IL-23, a key cytokine for IL-17A production. Moreover, IL-22 has been implicated in the regulation of new bone formation in experimental models. Therefore, we wonder whether miR-10b-5p affects IL-22 production in AS.

Methods:

Primary CD4+ T cells were negatively isolated from PBMCs from AS patients (Miltenyi Biotec). Transfection was performed with the Neon transfection system (Thermo Fisher Scientific, Germany) according to manufacturer’s instructions.

The transfection efficiency was evaluated by monitoring FAM (Fluorescein) positive cells using flow cytometry, and qPCR at 24 h after transfection. miR-10b-5p function was determined by overexpression of miR mimic in CD4+ T cells followed by intracellular cytokine staining, cytokine measurement, and qPCR. Statistical analysis was performed using Prism 5.0 Software (GraphPad Software, San Diego, USA). A p < 0.05 was considered statistically significant.

Results:

Overexpression of miR-10b-5p reduced both IL-22+CD4+ T cell frequencies and IL-22 production in CD4+ T cells from patients with AS. To identify the cellular targets of miR-10b-5p, we previously performed RNA-sequencing of CD4+ T cells transfected with miR-10b-5p together with in silico Target Scan analysis. MAP3K7 was selected as a target gene because of its known role in cytokine regulation. We then silenced MAP3K7 in CD4+ T cells using siRNA and found the suppression of IL-22 response, mimicking the effect of miR-10b-5p overexpression.

Conclusion:

Our data suggest that miR-10b-5p suppress IL-22 production by targeting MAP3K7. miR-10b-5p might be a potential therapeutic candidate for regulation of new bone formation in patients with AS.

Disclosure: T. J. Kim, None; S. H. Jin, None; L. Chen, None; M. H. Al-Mossawi, None; A. Ridley, None; T. Sekine, None; D. Simone, None; H. Shi, None; F. Penkava, None; P. Bowness, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/mir-10b-5p-is-a-il-22-regulator-in-cd4t-cells-from-ankylosing-spondylitis

Abstract Number: 644

Association of Osteonectin, Osteopontin and Osteocalcin with Inflammation and Cardiovascular Risk in Patients with Axial Spondyloarthritis

Fernanda Genre1, Javier Rueda-Gotor2, Juan Irure-Ventura3, Sara Remuzgo-Martínez1, Alfonso Corrales1, Begoña Ubilla1, Veronica Mijares1, Carlos Fernández-Díaz1, Virginia Portilla1, Ricardo Blanco1, Javier Llorca4, J. Gonzalo Ocejo-Vinyals3, Raquel López-Mejías1 and Miguel Angel González-Gay5 1Epidemiology, Genetics and Atherosclerosis Research Group on Systemic Inflammatory Diseases, IDIVAL, Santander, Spain, 2Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, 3Immunology Division, Hospital Universitario Marqués de Valdecilla, Santander, Spain, 4Department of Epidemiology and Computational Biology, School of Medicine, University of Cantabria, and CIBER Epidemiologia y Salud Pública (CIBERESP), Santander, Spain, 5Epidemiology, Genetics and Atherosclerosis Research Group on Systemic Inflammatory Diseases, IDIVAL and School of Medicine, University of Cantabria, Santander, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Background/Purpose: A higher incidence of cardiovascular (CV) risk factors and atherosclerosis has been reported in axial spondyloarthritis (axSpA) patients\(^1\). Since axSpA (particularly AS) is an inflammatory disease characterized by changes in the osteoproliferative process, a dysregulation in the molecules involved in bone remodeling is highly plausible in these patients, also affecting vascular calcification in the context of atherosclerosis. Therefore, we aimed to assess the role of osteonectin (ON), osteopontin (OPN) and osteocalcin (OC), implicated in bone metabolism\(^2\), in the development of subclinical atherosclerosis and its association with CV risk factors in a large cohort of axSpA patients.

Methods: Serum ON, OPN and OC levels were measured by multiplex assays in 171 Spanish axSpA patients (including both non-radiographic axSpA [nr-axSpA] and AS), recruited from Hospital Universitario Marqués de Valdecilla and Hospital de Laredo (Spain) who fulfilled the Assessment of SpondyloArthritis international Society (ASAS) classification criteria (for nr-axSpA)\(^3\) and also the 1984 modified New York criteria (for AS)\(^4\). Patients with history of CV disease, diabetes mellitus, chronic kidney disease, IBD or psoriasis were excluded. Carotid US was performed to evaluate the presence of subclinical atherosclerosis. The association of these molecules with the different variables of study were assessed by ANOVA, partial correlation or Student’s t test, where appropriate, using STATA® v. 11.1. The results were adjusted by potential confounding factors.

Results: ON and OPN positively associated with ESR at study (p=0.01 and 0.02). Higher ON levels were observed in men and axSpA patients who smoked (p=0.01), and also correlated with CRP levels at study (p=0.02). In addition, patients with CRP at diagnosis >3 mg/L showed higher OPN levels. Regarding OC, hypertensive patients displayed higher levels of this molecule (p=0.02). No association was found between these molecules and markers of subclinical atherosclerosis.

Conclusion: We disclosed an association of ON, OPN and OC with inflammation and CV risk factors, supporting an implication of these molecules in the development and progression of atherosclerotic disease in axSpA.


FG is a recipient of a Sara Borrell post-doctoral fellowship from the Instituto de Salud Carlos III (ISCIII)(Spain) (CD15/00095). SR-M is supported by the RETICS Program (RIER) (ISCIII, Spain)(RD16/0012/0009). RL-M is supported by a Miguel Servet type I programme (ISCIII, Spain)(CP16/00033). This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Disclosure: F. Genre, None; J. Rueda-Gotor, None; J. Irure-Ventura, None; S. Remuzgo-Martínez, None; A. Corrales, None; B. Ubilla, None; V. Mijares, None; C. Fernández-Diaz, None; V. Portilla, None; R. Blanco, None; J. Llorca, None; J. G. Ocejo-Vinyals, None; R. López-Mejías, None; M. A. González-Gay, None.


Abstract Number: 645

An Oral Tyk2 Inhibitor Effectively Suppresses the Development of Murine Th17 Cells In Vivo and Prevents Joint Damage in Experimental Ankylosing Spondylitis

Eric Gracey\(^1,2\), Melissa Lim\(^2\), Zoya Qaiyum\(^1\), Yuriy Baglaenko\(^1,2\), Wenyen Miao\(^3\), Craig Masse\(^3\), William Westlin\(^3\) and Robert D Inman\(^1,4\), \(^1\)Department of Immunology, University of Toronto, Toronto, ON, Canada, \(^2\)Toronto Western Hospital, University Health Network, Toronto, ON, Canada, \(^3\)Nimbus Therapeutics, Cambridge, MA, \(^4\)Toronto Western Hospital, University Health Network, toronto, ON, Canada
Th17 cells play an important role in the pathogenesis of ankylosing spondylitis (AS). Tyk2, a member of the Janus Kinase (JAK) family of signaling molecules, was the first JAK to be associated with AS in genome-wide association studies. Tyk2 plays a crucial role in Th17 cell function through mediating IL-23 intracellular signaling, making Tyk2 an attractive target for the treatment of AS. Here we examine the expression of Tyk2 at the cellular level in human peripheral blood mononuclear cells (PBMCs) for evidence of SNP-mediated changes in expression. We further tested a novel, potent and selective Tyk2 inhibitor, NDI-031407, for therapeutic effect in the SKG mouse model of AS.

Methods:

Flow cytometry on PBMC was carried out on 76 AS patients, 47 healthy controls and 21 RA patients. Tyk2 mRNA was assessed in unstimulated cells using PrimeFlow and cytokines were assessed in PMA/ionomycin-stimulated cells. SKG mice were gavaged twice daily with NDI-031407 or methylcellulose vehicle from weeks 1 to 8 post-disease induction. Mice were scored weekly for clinical presence of peripheral and axial arthritis, dermatitis and blepharitis. Sacroiliitis was assessed by T1- and T2-weighted MRI. Histology was assessed by H&E staining. Th17 frequency and phenotype were assessed by flow cytometry in popliteal, mesenteric and sciatic lymph nodes.

Results:

Tyk2 mRNA expression in PBMCs by flow cytometry did not demonstrate significant differences between AS and controls. Tyk2 expression levels did not stratify by candidate SNPs (rs12720356, rs35164067) and did not correlate with Th17 frequency. NDI-031407 is a small molecule Tyk2 inhibitor that inhibits Tyk2 with a Ki of 0.2 nM, and is 218-, 148-, and 20-fold selective against JAK1, JAK2, and JAK3, respectively. In SKG mice, therapeutic dosing with NDI-031407 significantly reduced the clinical scores of joint and skin inflammation to normal levels (see figure). MRI of the sacroiliac joint (SIJ) showed joint space narrowing and edema with disease progression and NDI-031407 protected against these SIJ changes. Enthesitis and bone erosion in the ankle and tail were prevented by Tyk2 inhibition. FACS showed that NDI-031407 suppressed the expansion of IL-17A+ Th17 cells (vehicle vs NDI-031407; 6.04% vs 2.73% of CD4+ T cells, p<0.001) in addition to reducing IL-17F, IL-22, ICOS and Ki67 expression.

Conclusion:

AS-associated Tyk2 SNPs do not impart a difference in Tyk2 expression and likely contribute to AS through promoting Th17 cell function. Our findings indicate that Tyk2 inhibition can prevent disease progression in SKG mice by reducing Th17 cells and associated inflammatory cytokines. Future studies aim to unravel the role of Tyk2 in Th17 cell development to better understand the mechanism behind Tyk2 inhibition. This work provides the first evidence that Tyk2 inhibition presents as a viable therapeutic target in AS.
Endoplasmic Reticulum Aminopeptidase 1 (ERAP1) Is a Susceptibility Factor for Early Axial Spa Meeting the ASAS Classification Criteria: Results from the Spondyloarthritis Caught Early and DEvenir des Spondyloarthrites Indifférenciées Récentes Cohorts

Anoek de Koning1, Marjolijn Hameetman2, Corinne Miceli-Richard3, Maxime Dougados4, Désirée van der Heijde5, Fina Kurreeman6 and Floris van Gaalen7, 1Rheumatology, Leiden University Medical Center, Leiden, Netherlands, 2Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, 3Department of Rheumatology, Hôpital Bicêtre, Paris, France, 4Department of Rheumatology, Rene Descartes University, Hôpital Cochin, Paris, France, 5Leiden University Medical Center, Leiden, Netherlands, 6Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, 7Rheumatology, LUMC, Leiden, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Genetic research in axSpA is performed in patients with longstanding ankylosing spondylitis (AS). Early axial spondyloarthritis (axSpA) is a diverse patient group in which a minority of the patients have AS. Therefore, it is
not known if recently identified genetic risk factors for AS are also risk factors for early axSpA. The aim is to evaluate if ERAP1 and HLA-B*4001 are susceptibility factors for early axSpA.

Methods: Patients with early axSpA meeting the ASAS classification criteria from the SPondyloArthritis Caught Early (SPACE) cohort (inclusion criteria: back pain for ≥3 months, ≤2 years, onset <45 years) and the DEvenir des Spondyloarthrites Indifférenciées Récentes (DESIR) cohort (inclusion criteria: inflammatory back pain for ≥3 months, ≤3 years, age <50) were typed for two well established AS genetic risk factors: ERAP1 SNPs (rs30187 (susceptibility), rs17482078 (protective) and rs10050860 (neutral)) and HLA-B*4001. Subsequently, for ERAP1 SNPs sub analyses were performed for AS and non-radiographic axSpA (nr-axSpA) patients. Analysis of weaker AS risk factors was limited by sample size. For ERAP1, genotyped Dutch healthy controls (n=1085) (data kindly provided by C. Wijmenga and A. Zhernakova (UMCG)) and published French subjects were used as controls. For HLA-B*4001 healthy blood bank donors from the Netherlands (n=5584) and France (n=10177) were used as controls.

Results: In 486 DESIR patients (mean age 32.5 (SD 8.6); 50% male; 84% HLA-B27+; 18% X-SI+) and 144 SPACE patients (mean age 29.5 (SD 8); 51% male; 88% HLA-B27+; 24% X-SI+) ERAP1 SNP rs30187 was more common than in controls (OR 1.2, p=0.01 in meta-analysis; table 1). rs17482078 and rs10050860 were negatively associated with early axSpA (both OR 0.7 (0.6-0.9) p<0.01 in meta-analysis). Minor allele frequencies were similar for AS patients and nr-axSpA patients (table 2). Although both cohorts were sufficiently powered, HLA-B*4001 was not positively associated with early axSpA (OR 0.6 (0.4-0.9) in meta-analysis).

Conclusion: ERAP1 rs30187 is a genetic risk factor for early axSpA patients with and without radiographic sacroiliitis. To our knowledge this is the first report of genetic risk factor research in early axSpA patients meeting the ASAS criteria. Larger cohorts are needed to study additional AS risk factors.


Table 1. Minor allele frequency and odds ratio of ERAP1 SNPs in axSpA patients in SPACE and DESIR compared with Dutch and French controls respectively.

<table>
<thead>
<tr>
<th>SNP</th>
<th>Minor allele</th>
<th>SPACE n=144</th>
<th>Dutch controls n=1086</th>
<th>OR (95% CI)</th>
<th>DESIR n=588</th>
<th>French controls* n=354</th>
<th>OR (95% CI)</th>
<th>Meta-analysis OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs30187</td>
<td>T</td>
<td>0.36</td>
<td>0.32</td>
<td>1.2 (1.0-1.5)</td>
<td>0.37</td>
<td>1.2 (0.9-1.6)</td>
<td>1.2 (1.0-1.4)</td>
<td>p&lt;0.04</td>
</tr>
<tr>
<td>rs17482078</td>
<td>T</td>
<td>0.14</td>
<td>0.21</td>
<td>0.6 (0.4-1.1)</td>
<td>0.19</td>
<td>0.6 (0.4-1.0)</td>
<td>0.7 (0.6-0.9)</td>
<td>p&lt;0.004</td>
</tr>
<tr>
<td>rs10050860</td>
<td>T</td>
<td>0.15</td>
<td>0.22</td>
<td>0.6 (0.4-0.9)</td>
<td>0.15</td>
<td>0.6 (0.5-1.1)</td>
<td>0.7 (0.6-0.9)</td>
<td>p=0.022</td>
</tr>
</tbody>
</table>

*From published data

Table 2. Minor allele frequency and odds ratio of ERAP1 SNPs in AS and nr-axSpA patients in SPACE and DESIR compared with Dutch and French controls respectively.

<table>
<thead>
<tr>
<th>SNP</th>
<th>Minor allele</th>
<th>SPACE n=103</th>
<th>nr-axSpA n=65</th>
<th>Dutch controls n=1086</th>
<th>OR (95% CI)</th>
<th>DESIR n=354</th>
<th>nr-axSpA vs control OR (95% CI)</th>
<th>French controls* n=354</th>
<th>OR (95% CI)</th>
<th>nr-axSpA vs control OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs30187</td>
<td>T</td>
<td>0.38</td>
<td>0.21</td>
<td>0.5 (0.3-0.8)</td>
<td>0.42</td>
<td>0.6 (0.4-0.9)</td>
<td>0.7 (0.6-0.9)</td>
<td>0.7 (0.6-0.9)</td>
<td>p&lt;0.03</td>
<td></td>
</tr>
<tr>
<td>rs17482078</td>
<td>T</td>
<td>0.14</td>
<td>0.22</td>
<td>0.6 (0.4-1.1)</td>
<td>0.19</td>
<td>0.6 (0.4-1.1)</td>
<td>0.7 (0.6-0.9)</td>
<td>0.7 (0.6-0.9)</td>
<td>p&lt;0.03</td>
<td></td>
</tr>
</tbody>
</table>

*From published data

Disclosure: A. de Koning, None; M. Hameetman, None; C. Miceli-Richard, None; M. Dougados, None; D. van der Heijde, None; F. Kurreeman, None; F. van Gaalen, None.


Abstract Number: 647

Gene Expression in Cellular Subsets in Psoriatic Disease

Anastasiya Muntyanu1, Fatima Abji2, Remy Pollock1, Vinod Chandran2 and Dafna D Gladman2, 1University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, 2Rheumatology, University of Toronto, Toronto Western Hospital,
Background/Purpose: Psoriatic arthritis is an inflammatory musculoskeletal disease which develops in 30% of patients with psoriasis. Our previous peripheral blood microarray study identified CXCL10, NOTCH2NL, HAT1, and SETD2 as differentially expressed between PsA and psoriasis patients without arthritis (PsC). This study aimed to determine gene expression in leukocyte subsets to elucidate their functions in psoriatic disease.

Methods: Peripheral blood mononuclear cells were isolated using Ficoll paque separation from PsA and PsC patients not receiving biologic therapy and healthy controls (HC). T cells (CD3+), monocytes (CD14+), and NK cells (CD56+) were separated by positive selection. mRNA was extracted using RNeasy miniprep kits and qPCR performed with 75ng mRNA to determine CXCL10, CXCR3, NOTCH2NL, IL-17A, HAT1, and SETD2 gene expression. A two-way ANOVA with Bonferroni’s post-hoc test was used to determine significant differences (p<0.05).

Results: Gene expression was measured in 15 PsA (mean age 59, 60% males), 15 PsC (mean age 57, 67% males), and HC (mean age 54, 60% males). Expression of IL-17A in monocytes was 18.42-fold greater in PsA patients than PsC (p<0.0001) and 31.36-fold greater in PsA than HCs (p<0.0001). There were no other significant differences in gene expression between disease groups in each given cell type. However, in T cells, CXCL10 was elevated in PsA compared to PsC (1.42-fold) and HC (2.47-fold). A similar trend was found for the receptor, CXCR3, where expression was higher in PsA than PsC (1.18-fold) and HC (1.13-fold). Finally, SETD2 expression in PsA was higher than PsC (1.65-fold) and HC (1.28-fold) in T cells. CXCL10 expression in monocytes (p<0.0001; 11.1-fold) and NK cells (p<0.0001; 2.04-fold) was higher than in T cells. Expression of CXCR3 was higher in T cells compared to monocytes (p<0.0001; 208.17-fold) and NK cells (p<0.0001; 1.3-fold). HAT1 was more highly expressed in T cells as compared to monocytes (p=0.0003; 3.4-fold) and NK cells (p=0.0082; 1.22-fold). NOTCH2NL expression was elevated in T cells compared to monocytes (p=0.0154; 2.43-fold).

Conclusion: Genes of interest were differentially expressed in leukocyte subsets. The higher expression of these genes in PsA compared to PsC and HCs could provide insight into their role in driving the development of PsA. Knowing which cell types are predominantly involved with expression of certain biomarkers will aid in developing targeted treatments.

Disclosure: A. Muntyanu, None; F. Abji, None; R. Pollock, None; V. Chandran, None; D. D. Gladman, None.


Abstract Number: 648

Are Choline Metabolites Associated with Inflammation in Psoriatic Arthritis?

Roxana Coras1,2, Arthur Kavanaugh2, Doquyen Huynh3, Mohit Jain2 and Monica Guma2, 1Medicine, Autonomous University of Barcelona, Barcelona, Spain, 2Medicine, University of California, San Diego, La Jolla, CA, 3Medicine, University of California, San Diego, San Diego, CA

First publication: September 18, 2017
Psoriatic arthritis (PsA) is an inflammatory disease affecting the joints and connective tissue and is associated with psoriasis of the skin and nails. In our daily clinical routine, patients often report changes in their disease activity with certain foods, despite the ongoing treatment. Choline metabolism has been recently strongly related to inflammation. Dietary intake of choline, through two circulating metabolites, trimethylamine (TMA), and trimethylamine N-oxide (TMAO), are mechanistically linked to cardiovascular inflammation. The objective of this study was to explore the link between choline metabolites and inflammation in PsA.

Methods: Patients with PsA, diagnosed based on the CASPAR criteria, were recruited from the Rheumatology Outpatient Clinic at the University of California, San Diego. A thorough clinical examination, including joint and skin disease evaluations, was conducted. Patients completed a health assessment questionnaire. DAS28, Clinical Disease Index (CDAI) and Simple Disease Index (SDAI) scores and body surface area (BSA) of psoriasis were calculated. Serum concentration of choline metabolites: choline, TMA, TMAO, and betaine were determined by Mass Spectrometry. Inflammatory biomarkers in serum were determined by ELISA. Statistical analysis included means, standard deviation, t-test and Pearson correlation.

Results: 38 patients (average age 47.45 years, standard deviation [SD] 10.29) were recruited. The mean (SDs) of DAS28PCR was 2.24 (1.29). 27 patients (71.05%) had active skin disease, with an average BSA of 4.73 (SD, 14.5). 23.68% of patients had enthesitis, 5.26% had dactylitis and 47.36% had nail involvement. 65.11% received biological therapy (46.42% of them in association with a synthetic disease modifying drug DMARD), 13.95% received sDMARD in monotherapy and 20.9% received symptomatic treatment. We found that TMAO, a choline metabolite, correlated with parameters of disease activity for both skin (BSA) and joint (DAS28, CDAI, SDAI) (Table 1). Choline, TMA and TMAO also correlated with inflammatory markers (Table 2). TMAO was higher in patients with active joint disease (CDAI>2.8) versus patients in remission (CDAI<2.8; p = 0.01) and in patients with higher severity of skin disease (BSA >5%) versus low severity (BSA <5%; p = 0.03).

Conclusion: In our cohort, choline metabolism was associated with inflammation in PsA patients. Since diet is the main source of choline, modulating choline food intake might help to better control disease activity in these patients. Further studies are needed to explore the mechanistic links between choline and TMAO and inflammation.

Disclosure: R. Coras, None; A. Kavanaugh, None; D. Huynh, None; M. Jain, None; M. Guma, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/are-choline-metabolites-associated-with-inflammation-in-psoriatic-arthritis

Abstract Number: 649
Role of Eicosanoids As Biomarkers in Psoriatic Arthritis

Roxana Coras¹,², Arthur Kavanaugh¹, Doquyen H. Huynh¹, Aladdin Shadyab³, Sara Marsal⁴, Oswald Quehenberger⁵ and Monica Guma¹, ¹Medicine, University of California, San Diego, La Jolla, CA, ²Medicine, Autonomous University of Barcelona, Barcelona, Spain, ³Family Medicine and Public Health, University of California, San Diego, La Jolla, CA, ⁴Rheumatology Research Unit, Vall d'Hebron Hospital, Barcelona, Spain, ⁵Pharmacology, Medicine, University of California, San Diego, La Jolla, CA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is an inflammatory disease affecting the joints and connective tissue and is associated with psoriasis of the skin and nails. There is no reliable biomarker to identify psoriatic patients at risk of joint disease or disease progression. Eicosanoids, including prostaglandins and leukotrienes, are biological lipids that are implicated in various pathological processes including inflammation. We hypothesized that by defining more precisely the eicosanoid profile in PsA patients, we might identify novel diagnostic or prognostic biomarkers for disease activity and PsA pathogenesis.

Methods: Patients with PsA, diagnosed based on the CASPAR criteria, were recruited from the Rheumatology Outpatient Clinic at the University of California, San Diego. A thorough clinical examination, including joint and skin disease evaluations, was conducted. Patients completed a health assessment questionnaire. DAS28, Clinical Disease Activity Index (CDAI) and Simple Disease Activity Index (SDAI) scores and body surface area (BSA) of psoriasis were calculated. Serum eicosanoids were determined by mass spectrometry and were classified in groups according to the enzyme that participates in synthesis: cyclooxygenase (COX), 5-, 12- or 15-lipoxygenase (LOX), cytochrome P450, or non-enzymatic pathway. Inflammation markers were determined by ELISA. Statistical analysis included mean, standard deviation and Spearman correlation.

Results: 43 patients (average age 49.8, standard deviation 10.88) were recruited. Thirty-two (74.41%) had active skin disease with an average BSA of 4.25 (SD, 13.67). The means (SDs) of DAS28PCR was 2.25 (1.25) and CDAI was 10.69 (11.87). 48.83% of patients had nail disease, 20.93% had enthesitis, and 4.65% had dactylitis. Further, 65.11% received biological therapy (46.42% of them in association with a synthetic disease modifying drug, such as DMARD), 13.95% received sDMARD in monotherapy, and 20.9% had symptomatic treatment. Several eicosanoids, especially those in the 12-15-LOX pathway, significantly correlated with joint disease activity, but not with skin disease activity (Table 1). Several eicosanoids correlated with serum markers of (IL6, Resistin, EGF, IL1β and IL8), but not with CRP (Table 1). Of note, there was a weak correlation between CRP and SDAI that didn’t reach statistical significance (p=0.06).
Table 1. Correlation of Eicosanoids with clinical and serum parameters of inflammation

<table>
<thead>
<tr>
<th>Eicosanoid</th>
<th>CDAI</th>
<th>SDAI</th>
<th>DAS28</th>
<th>BSA</th>
<th>CRP</th>
<th>IL6</th>
<th>EGF</th>
<th>Resistin</th>
<th>IL1β</th>
<th>IL8</th>
</tr>
</thead>
<tbody>
<tr>
<td>COX</td>
<td>PGE2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15-LOX</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15-HETE</td>
<td>0.259*</td>
<td>0.382***</td>
<td>0.333**</td>
<td></td>
<td>0.392**</td>
<td>0.499***</td>
<td>0.428***</td>
<td>0.399***</td>
<td>0.533***</td>
<td></td>
</tr>
<tr>
<td>15-HEPE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15HETrE</td>
<td>0.317**</td>
<td>0.489***</td>
<td>0.379**</td>
<td></td>
<td>0.496***</td>
<td>0.579**</td>
<td>0.638***</td>
<td>0.310**</td>
<td>0.603***</td>
<td></td>
</tr>
<tr>
<td>13HODE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13HOTrE</td>
<td>0.453***</td>
<td>0.471***</td>
<td>0.432***</td>
<td></td>
<td>0.276*</td>
<td>0.290*</td>
<td>0.342**</td>
<td>0.441***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12-LOX</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12-HETE</td>
<td>0.260*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.383**</td>
<td>0.391**</td>
<td></td>
<td>0.472***</td>
<td></td>
</tr>
<tr>
<td>12-HEPE</td>
<td>0.266*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.317**</td>
<td>0.539***</td>
<td>0.501***</td>
<td></td>
<td>0.512***</td>
</tr>
<tr>
<td>Tetrano12-HETE</td>
<td>0.399***</td>
<td>0.365**</td>
<td></td>
<td></td>
<td>0.373**</td>
<td>0.386**</td>
<td>0.530***</td>
<td></td>
<td>0.547***</td>
<td></td>
</tr>
<tr>
<td>HXB3</td>
<td>0.350**</td>
<td>0.284*</td>
<td></td>
<td></td>
<td>0.366**</td>
<td>0.440***</td>
<td>0.485***</td>
<td>0.290*</td>
<td>0.552***</td>
<td></td>
</tr>
</tbody>
</table>

PGE2-Prostaglandin E; HETE- hydroxyeicosatetraenoic acid; HETrE- hydroxyeicosatrienoic acid; HODE- Hydroxyoctadecadienoic acid; HOTrE- hydroperoxyoctadecatrienoic acid; HXB3-Hepoxilin B3.* p<0.1, ** p<0.05, *** p<0.01

**Conclusion:** Eicosanoids, especially in the 12- and 15-LOX pathways, correlated with joint disease activity better than the CRP, but not with skin disease, suggesting that they may be potential biomarkers of joint activity in psoriatic and PsA patients. Further studies are needed to determine whether 12- and 15-LOX pathways also play a role in the pathogenesis of joint inflammation in PsA.

**Disclosure:** R. Coras, None; A. Kavanaugh, None; D. H. Huynh, None; A. Shadyab, None; S. Marsal, None; O. Quehenberger, None; M. Guma, None.


**Abstract Number:** 650

**Genome-Wide DNA Methylation, Transcriptomics, and Proteomics of Psoriasis and Psoriatic Arthritis in Monozygotic Twins**

Angela Ceribelli1, Elvezia Maria Paraboschi2, Natasa Isailovic1, Elena Generali1, Michela Robusto2, Maria De Santis1, Giulia Cardamone2, Francesco Sacrini3, Antonio Costanzo3, Stefano Duga2 and Carlo Selmi1, 1Rheumatology and Clinical Immunology, Humanitas Research Hospital, Rozzano (MI), Italy, 2Laboratory of Medical genetics and RNA biology, Humanitas Research Hospital, Rozzano, Italy, 3Dermatology Unit, Humanitas Research Hospital, Rozzano, Italy

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM
Background/Purpose: Psoriatic disease is a chronic inflammatory disorder spanning from skin disease (PsO) to psoriatic arthritis (PsA) without known serum biomarkers. The genetic background is insufficient to explain disease onset as illustrated by monozygotic (MZ) twins and epigenetics may contribute to disease susceptibility modulating gene expression. We analyzed the DNA methylation, transcriptome, and proteomic profile in MZ twins discordant for PsO/PsA.

Methods: MZ twin couples discordant and concordant for PsO/PsA were investigated for (1) genome-wide DNA methylation (Infinium MethylationEPIC BeadChip), (2) RNA and transcriptome (Illumina TruSeq Stranded mRNA kit), and (3) proteomics using aptamers (SOMAlogic). Results observed with aptamers were further validated by ELISA.

Results: The epigenetic analysis identified 19 genes consistently differentially methylated and mostly involved in the pathway of TGF-β and IFN response. Pathway analysis of integrated DNA methylation and transcriptome demonstrated an enrichment in “transcription regulation”, “innate immunity”, “ATP-binding” and, “Srp-dependent co-translational proteins”, that may be involved in the psoriatic condition. Serum proteomics reported a significant up- and downregulation of 10 and 3 proteins, respectively, largely involved in the innate and adaptive immune response, DNA repair and DNA damage sensors. Validation results showed a significant correlation between the SOMAlogic and ELISA tests for 2 proteins (respectively r=0.70, p=0.02, and r=0.50, p=0.04) and we confirmed that levels of 3 proteins involved in the regulation of UV radiation-induced apoptosis and in the cutaneous inflammatory response were elevated in sera from psoriatic disease patients, albeit not significantly, and one protein involved in hematopoietic and dendritic cell differentiation and apoptosis was significantly more expressed in both Pso and PsA compared to controls (HC n=2, 20%, Pso+PsA n=18, 60%, p=0.028; Pso n=10, 66.7%, p=0.02).

Conclusion: We report the first -omics approach in MZ twins discordant for psoriatic disease and suggest that the observed changes may constitute disease biomarkers and point to biological pathways with a potential pathogenic role.

Disclosure: A. Ceribelli, None; E. M. Paraboschi, None; N. Isailovic, None; E. Generali, None; M. Robusto, None; M. De Santis, None; G. Cardamone, None; F. Sacrini, None; A. Costanzo, None; S. Duga, None; C. Selmi, None.

Role of Mir-21-5p As a Potential Biomarker of Psoriatic Arthritis and Response to Treatment

Rohan Machhar1, Justine (Yang) Ye1, Vinod Chandran2 and Dafna D Gladman3, 1University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, 2Rheumatology, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, 3Rheumatology, Toronto Western Hospital, University of Toronto, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is an inflammatory arthritis occurring in patients with psoriasis. miRNA’s are small non coding RNAs whose main function, at a post transcriptional level, is to modulate the expression of target genes via translation inhibition or mRNA degradation. A recent study identified miR-215p to be upregulated in early PsA and early rheumatoid arthritis (RA) and found down regulation post 12 weeks of methotrexate (MTX) treatment. Mir-21-5p was also found to be upregulated in several inflammatory and autoimmune diseases such as systemic sclerosis, systemic lupus erythematosus, RA, type 1diabetes, and psoriasis. We aimed to determine the role of miR-21-5p as a biomarker for PsA and response to methotrexate.
Methods: Whole blood RNA samples collected in Tempus tubes from 40 patients with early PsA (<2 years disease duration and not receiving biologic therapy), 40 patients with PsC who have been confirmed by rheumatologist not to have PsA (>10 years psoriasis duration, not receiving biologic therapy, and matched to PsA patients on age, sex, psoriasis duration, and age of psoriasis onset), and 42 HC (matched to patients based on age, sex). RNA was extracted using the Tempus Spin RNA Isolation Kit with a genomic DNA removal step. miR-21-5p was validated using droplet digital PCR (ddPCR), a novel and sensitive technology for miRNA quantification. miR-21-5p expression was also measured in 10 PsA patients before and after 24 weeks of MTX treatment.

Results: The clinical, laboratory and miRNA expression data are presented in Table 1. Significant up regulation of miR-21-5p was seen in both early PsA and in PsC in comparison to HC (p<0.001). There was more upregulation in early PsA compared with PsC (p< 0.001), miR-21-5p was significantly down regulated 24 weeks post treatment in 10 patients (p< 0.008) (figure 1).

Conclusion: We have determined the role of miR21-5p as a biomarker for early PsA and response to methotrexate. Our results support previous work suggesting the potential role of miR21-5P in response to treatment biomarker in early PsA and as in inflammatory disorder marker.

Table 1: Demographic, clinical and relative expression data

<table>
<thead>
<tr>
<th>Variable</th>
<th>PsA (N=40)</th>
<th>PsC (N=40)</th>
<th>CTL (N=42)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>miR-21-5p*</td>
<td>122.7 (93.1)</td>
<td>58.5 (36.0)</td>
<td>11.5 (9.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gender - Male</td>
<td>16 (40%)</td>
<td>15 (38%)</td>
<td>15 (38%)</td>
<td>0.97</td>
</tr>
<tr>
<td>Gender - Female</td>
<td>24 (60%)</td>
<td>25 (63%)</td>
<td>25 (63%)</td>
<td></td>
</tr>
<tr>
<td>Age*</td>
<td>40.7 (11.0)</td>
<td>41.9 (11.0)</td>
<td>43.8 (12.0)</td>
<td>0.002</td>
</tr>
<tr>
<td>PASI*</td>
<td>7.1 (10.8)</td>
<td>6.2 (4.4)</td>
<td>N/A</td>
<td>0.61</td>
</tr>
<tr>
<td>Actively inflamed joints*</td>
<td>6.4 (7.0)</td>
<td>NA</td>
<td>N/A</td>
<td>NA</td>
</tr>
<tr>
<td>CRP (positive), n (%)</td>
<td>6 (15%)</td>
<td>1 (3%)</td>
<td>N/A</td>
<td>0.048</td>
</tr>
</tbody>
</table>

*mean±SD; PASI-psoriasis area severity index, actively inflamed joints tender and/or swollen joints; CRP- C reactive protein.

Fig 1: miR 21-5p expression in PsA patients at baseline and after 24 weeks of therapy (p <0.008).

Disclosure: R. Machhar, None; J. Ye, None; V. Chandran, None; D. D. Gladman, None.


Abstract Number: 652
Investigating the Role of Mechanical Stress in Spondyloarthritis Pathogenesis

Breanna Nguyen¹, Robert Colbert² and Gerlinde Layh-Schmitt¹, ¹National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, ²NIAMS/NIH, Bethesda, MD

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Mechanotransduction is a cell’s ability to translate mechanical stimuli into biochemical signals and has been implicated in signaling pathways involving differentiation and proliferation. Mechanical stress at entheses and adjacent tissues has additionally been implicated in the pathogenesis of spondyloarthropathies, such as ankylosing spondylitis and psoriatic arthritis, by triggering inflammation. However, the mechanisms underlying these processes remain unclear. This project aims to establish an in vitro system to study the effects of mechanical stress on mesenchymal stem cells and osteoblasts, specifically examining mineralization and cytokine production.

Methods: Mechanical stress was applied to rat calvarial mesenchymal stem cells (MSCs) using the Flexcell FX-5000 Tension System. This instrument uses a computer-controlled vacuum pump to apply uniform axial strain to cells plated on silicone bottomed Bioflex plates. For osteogenic differentiation, 3% uniform axial strain was applied to the cells. After applying strain for 5 days, cells were cultured in osteogenic medium (OS+) to induce differentiation. Mineralization was measured with Alizarin red stain after 28 days. For measuring cytokine secretion upon stress, MSCs were subjected to 24 hours of 10% strain. ELISA was used to quantify cytokine secretion into cell culture supernatants at 24, 48, and 72h after stimulation. For all experiments, non-stretched cells were used as controls.

Results: For MSCs cultured in OS+ for 28d, overall mineralization was 2 to 3-fold higher than MSCs cultured in OS-, as expected. In OS+ conditions, stress resulted in a 12% decrease in mineralization for stretched cells compared to non-treated controls (p < 0.05). In addition, stress increased secretion of RANTES and IL-6 from MSCs, as determined by ELISA. For RANTES, stretch led to a 130% increase in production at 24h, a 56% increase at 48h, and a 43% increase 72h after stimulation (p = 0.06; p < 0.001; p < 0.01, respectively). For IL-6, stretch led to a 324% increase in production at 24h, an 85% increase 48h, and a 55% increase 72h after stimulation (p < 0.01; p < 0.05; p < 0.05, respectively).

Conclusion: These results suggest that mechanical stress can alter osteogenic ability and cytokine secretion from MSCs. RANTES and IL-6 have been previously shown to play a positive role in bone formation, so further studies are needed to determine whether these mediators have a biological effect during osteogenesis in this system. Future studies will focus on optimizing the system and then using it to study the role of ankylosing spondylitis risk genes in MSC and osteoblast function.

Disclosure: B. Nguyen, None; R. Colbert, None; G. Layh-Schmitt, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/investigating-the-role-of-mechanical-stress-in-spondyloarthritis-pathogenesis

Abstract Number: 653

Reduced Ubiquitination of Misfolded HLA-B27 Is Associated with Inefficient Degradation By ERAD and Autophagy

Fatemeh Navid¹, Gerlinde Layh-Schmitt¹, Keith A. Sikora² and Robert Colbert¹, ¹National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, ²Pediatric Translational Research Branch,
SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
The HLA class I allele, HLA-B27, is associated with spondyloarthritis (SpA), an immune-mediated inflammatory disease affecting the axial skeletal, skin, gut and eyes. HLA-B27 has a tendency to misfold, and accumulate in the endoplasmic reticulum (ER) and on the cell surface as disulfide-linked dimers. ER accumulation can generate stress resulting in an unfolded protein response (UPR). The UPR upregulates several pathways that promote folding and secretion and/or ER-associated degradation (ERAD) of accumulated proteins, which involves retrotranslocation and ubiquitination of target proteins in the cytosol where they are degraded by proteasomes. Our recent studies suggest that autophagy as well as ERAD contributes to the disposal of misfolded HLA-B27, yet these pathways are still not sufficient to prevent misfolded HLA-B27 from accumulating. Since these pathways of protein degradation require substrate ubiquitination, we asked whether HLA-B27 heavy chains were ubiquitinated using HLA-B7 for comparison.

Methods: Bone marrow derived macrophages from HLA-B27 and human β2m (hβ2m) transgenic rats were examined with and without IFNγ and proteasome or autophagy inhibitors. Immunoprecipitation, western blotting, and immunofluorescence were used to measure HLA-B27 heavy chains and ubiquitination mount. Autophagy was activated using rapamycin, or blocked with bafilomycin. ERAD was inhibited by inhibiting proteasome function with bortezomib. HLA-B7/hβ2m transgenic rat macrophages were used as controls.

Results: Blocking autophagic flux with bafilomycin resulted in the accumulation of misfolded HLA-B27 dimers and oligomers as well as monomers, comparable to blocking ERAD with the proteasome inhibitor bortezomib. HLA-B7 monomers also accumulated after blocking each degradation pathway. The proportion of ubiquitinated heavy chains was ~3-fold lower for HLA-B27 compared to HLA-B7. Immunoprecipitation experiments using anti-ubiquitin antibody followed by blotting for HLA class I heavy chains, further confirmed that HLA-B7 is significantly more ubiquitinated than HLA-B27. Activation of autophagy with rapamycin rapidly eliminated ~50% of misfolded HLA-B27, while folded HLA-B27 or HLA-B7 monomeric heavy chains were minimally affected.

Conclusion: These results demonstrate for the first time that both autophagy and ERAD play a role in the elimination of excess HLA class I heavy chains expressed in transgenic rats. Our results suggest that impaired ubiquitination of HLA-B27 may play a role in the accumulation of misfolded disulfide-linked dimers, whose elimination can be enhanced by activation of autophagy. Manipulation of the autophagy pathway should be further investigated as a potential therapeutic avenue in experimental spondyloarthritis.

Disclosure: F. Navid, None; G. Layh-Schmitt, None; K. A. Sikora, None; R. Colbert, None.


Abstract Number: 654

Effect of Anti Tnfa Drugs on the Frequency of Circulating CD19+CD24hiCD38hi Breg Cells in Ankylosing Spondylitis

M. Belén Bautista-Caro¹, Eugenio De Miguel¹, Diana Peiteado¹, Alejandro Villalba¹, Irene Monjo¹, Amaya Puig-Kröger², Paloma Sanchez-Mateos³, Emilio Martín-Mola¹ and Maria Eugenia Miranda-Carus¹, ¹Rheumatology, Hospital La Paz-
CD19+CD24hiCD38hi B cells demonstrate a regulatory capacity and their frequency is altered in the peripheral blood of patients with various autoimmune diseases. The pathogenic implication of autoinflammatory and/or autoimmune mechanisms has been reported in spondyloarthritis (SpA), and an increased frequency of circulating B cells expressing a regulatory phenotype has been described in SpA (Cantaert T. et al, Arthritis Rheumatol 2012). Therefore our objective was to study the frequency of CD19+CD24hi CD38hi B cells (Breg) in patients with Ankylosing Spondylitis (AS) naïve for TNF blockers, and the effect of anti-TNFα drugs on this B cell subset in AS.

**Methods:**

Peripheral blood was drawn from AS patients naïve for TNFα blockers (AS/nb) (n=42), AS patients who were already receiving treatment with anti-TNFα drugs (AS/b) (n=59: 37 infliximab, 10 adalimumab, 10 golimumab, 2 certolizumab) and healthy controls (HC) matched for age and gender (n=101). In addition, six AS/nb patients who were started on anti-TNFα drugs (2 infliximab, 1 adalimumab, 2 golimumab, 1 certolizumab) donated blood at two time points: right before the first dose of anti-TNFα was administered and 6 months thereafter. For each of these 6 patients, the same healthy donor acted as a control on both occasions. After isolation by Ficoll-Hypaque, PBMCs were stained with antibodies to CD3, CD4, CD19, CD24, and CD38, and examined by cytometry.

**Results:**

When compared with HC, AS/nb patients demonstrated a significantly increased frequency of Breg cells, which did not correlate with ASDAS-CRP, serum calprotectin, CRP or ESR values. In contrast, in AS/b patients, the frequency of circulating Breg cells was not different from HC. The 6 AS/nb patients who started treatment with anti-TNFα drugs demonstrated a significant reduction of circulating Breg numbers, which were no longer elevated after six months of treatment. At the same time, a significant decrease of CRP, serum calprotectin and ASDAS-CRP was observed in all 6 patients; in 4 of them, the ΔASDAS-CRP was > 2.0.

**Conclusion:**

An increased frequency of circulating CD19+CD24hiCD38hi B cells is observed in AS/nb patients, that does not correlate not related with disease activity parameters. Treatment with anti-TNFα drugs is able to downmodulate circulating Breg numbers in AS.
Background/Purpose: Innate lymphoid cells (ILCs) produce disease-related cytokines including IL-17 and IL-22 and are therefore of substantial interest in PsA. Spreading the disease from the skin to the joints most likely requires trafficking of cells through the circulation. Upon perturbation of immune homeostasis, the pool of resident ILCs is replenished by migration of ILCs into the peripheral blood. Tackling their potential contribution to immunopathology of PsA we quantified circulating ILC subsets in PsA patients in correlation to disease activity and structural tissue damage.

Methods: 124 patients satisfying the Classification Criteria for Psoriatic Arthritis (CASPAR) and 26 healthy volunteers were enrolled in the study. Information regarding the tender and swollen joint count of 68 joints, the visual analogue scala (VAS) of pain and global assessment, presence of plaque psoriasis, psoriatic nail dystrophy, enthesitis, history of uveitis/iritis, CRP levels, erythrocyte sedimentation rate, imaging results (MRI and high-resolution peripheral quantitative CT) were collected and disease activity score 28 (DAS28), disease activity in psoriatic arthritis (DAPSA), minimal disease activity score (MDA) were calculated. MRI and high-resolution peripheral CT were taken and PsA MRI score (PsAMRIS) was assessed. Flow cytometric analysis was performed and IFNγ-producing ILC1s, IL-4/IL-5-producing ILC2s and IL-17/IL-22-producing ILC3s were identified among ILCs. Multivariate linear regression and Receiver-Operating Characteristic (ROC) Curve analysis was performed using the IBM SPSS Statistics software.

Results: Total number of circulating ILCs were increased in PsA patients compared to healthy controls (p<0.001). Linear regression analyses of the relationship between disease activity and circulating ILC counts showed that ILC2 negatively (R = -0.3732; p < 0.0001) and ILC1 and ILC3 positively correlated with DAPSA score (R = 0.2622, p = 0.0057; R = 0.4092, p < 0.0001 respectively). The strongest correlation was observed when the ratio of ILC2 to ILC3 was analyzed (R = -0.5709; p < 0.0001). ILC2/3 ratio was also reduced in patients with active psoriatic skin disease, presence of enthesitis or a history of concomitant uveitis. Extend of synovitis or tenosynovitis or presence of bone erosions or osteophytes on MRI was inversely correlated with the ILC2/3 ratio (R = -0.6753; p < 0.0001, R = -0.5828; p = 0.0011 and p < 0.001 respectively). Consistently, presence of erosions and/or osteoproliferation assessed by HR-pQCT was correlated with a significant lower ILC2/3 ratio. Furthermore, ROC Curve was used to test the performance of the ILC2/3 ratio as marker in differentiating between remission and disease activity of PsA. Indeed, a cut-off 0.57 exhibited highest sensitivity (92.9%) and a 84.7% specificity in identifying remission.

Conclusion: We show that perturbed ILC homeostasis is correlated with both composite clinical disease activity scores and with imaging signs of inflammation and structural damage suggesting pathogenic impact of ILCs in PsA. Further studies are necessary to validate ILC2/ILC3 ratio as biomarker for immunological disease activity in PsA.
Prostaglandin E2 and Its Receptor Subtype EP4 Are Involved in Ankylosing Spondylitis Disease Progression

Archita Srinath1,2,3, Giuliana Guggino4, Ismail Sari5, Fanxing Zeng6, Francesco Ciccia4 and Nigil Haroon5, 1Institute of Medical Sciences, University of Toronto, Toronto, ON, Canada, 2Genes and Development, University Health Network, Toronto, ON, Canada, 3Krembil Discovery Tower, Toronto, ON, Canada, 4Rheumatology Unit, University of Palermo, Palermo, Italy, 5Rheumatology, Toronto Western Hospital, University of Toronto, Spondylitis Clinic, Toronto, ON, Canada, 6University Health Network, Toronto, ON, Canada

First publication: September 18, 2017

Background/Purpose: Single Nucleotide Polymorphisms (SNPs) in PTGER4 were found to be associated with Ankylosing spondylitis (AS) in GWAS. PTGER4 codes for the prostaglandin-E2 receptor EP4. PGE2/EP4 interaction can affect bone formation and inflammation. We studied serum PGE2 levels and SNPs in PTGER4 in relation to spinal fusion in AS patients. We further evaluated the interaction of smoking, PGE2 and EP4 in driving IL23 production.

Methods: Patients diagnosed with AS using the modified New York criteria and followed prospectively using a standardized protocol, were included in this study. Biological samples including serum, gut, synovial and bone marrow (BM) samples, DNA and RNA were stored and radiographs of the spine obtained every two year to assess progression. ELISA for Serum PGE2 and immunohistochemistry tissue expression of Prostaglandin-Endoperoxide Synthase 1 (PTGS1), EP4 and pCREB were performed. Radiographs were scored by modified Stoke Ankylosing Spondylitis Spine Score(mSASSS). Patients with an increase of ≥ 1 mSASSS unit/year on follow up were deemed progressors. Five PTGER4 single nucleotide polymorphisms (SNPs) satisfying inclusion criteria (associated with AS or related diseases, call rate above 90%, MAF > 0.1 and not in LD above 0.8) were studied. Immune cell subsets from peripheral blood mononuclear cells (PBMCs) were analyzed for surface expression of the EP4 receptor. Additionally, PBMCs were incubated with nicotine, PGE2, or EP4 agonist to determine cytokine expression by flow cytometry and RT-PCR.

Results: Serum PGE2 levels were significantly higher in AS progressors (n=88) than in non-progressors (n = 101) (p<0.001). In multivariable regression analysis, there was significantly more progression in patients with higher baseline mSASSS (B =0.02; p = 0.01) and serum PGE2 (B = 0.001; p = 0.002), but lower progression with longer TNF inhibitor use (B = -0.01; p = 0.03). There was a trend towards higher progression with higher baseline ESR (B = 0.012; p = 0.08). 3) A total of 172 AS patients had DNA and X-ray data for analysis. Patients with CC genotype of PTGER4 SNP rs6896969 were significantly more likely to progress compared to AA/AC (OR: 2.45, 95% CI: 1.3 to 4.6; p=0.006). Progressors tended to more likely be homozygous for the major allele G of the rs4957341 SNP (OR 2.1; 25% CI; 0.98-4.35; p = 0.058). Increased expression of EP4, PTGS1 and pCREB were observed in the inflamed gut, BM and synovial samples in AS patients. EP4 expression was upregulated in AS monocytes, especially smokers, and the percentage of EP4+ monocytes correlated with the disease activity evaluated by BASDAI. Sorted EP4+CD14+ cells showed a higher expression of CREB and IL-23

**Conclusion:** PGE2 and its receptor EP4 are significant players in AS driving both inflammation and spinal fusion. The complex interaction of smoking, prostaglandin pathway upregulation and Th17 activation via CREB can contribute to the pathogenesis of AS.

**Disclosure:** A. Srinath, None; G. Guggino, None; I. Sari, None; F. Zeng, None; F. Ciccia, None; N. Haroon, None.

**View Abstract and Citation Information Online** - [http://acrabstracts.org/abstract/prostaglandin-e2-and-its-receptor-subtype-ep4-are-involved-in-ankylosing-spondylitis-disease-progression](http://acrabstracts.org/abstract/prostaglandin-e2-and-its-receptor-subtype-ep4-are-involved-in-ankylosing-spondylitis-disease-progression)

**Abstract Number:** 657

**Dyslipidemia Management Is Insufficient in Psoriatic Arthritis Despite Increased Cardiovascular Morbidity and Mortality**

**Richard Koch**¹, JEAN BERNARD RUIDAVETS Sr.², Yannick Degboe³, Alain Cantagrel³, Adeline Ruyssen-Witrand⁴, JEAN FERRIERES⁵ and Arnaud Constantin³, ¹Department of Rheumatology, Purpan Hospital, Toulouse III University, Toulouse, France, TOULOUSE, France, ²DEPARTMENT OF EPIDEMIOLOGY, URM 1027 INSERM, TOULOISE UNIVERSITY HOSPITAL, TOULOISE, France, ³Department of Rheumatology, Purpan Hospital, Toulouse III University, Toulouse, France, ⁴Rheumatology, Purpan Hospital, Toulouse III University, Toulouse, France, ⁵DEPARTMENT OF CARDIOLOGY, URM 1027 INSERM, TOULOISE UNIVERSITY HOSPITAL, TOULOUSE, France

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017
**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster I
**Session Type:** ACR Poster Session A
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Psoriatic arthritis (PsA) is associated with increased cardiovascular (CV) morbidity and mortality. Assessing individual CV risk and achieving the recommended LDL-cholesterol (LDL-C) target could contribute to reduce the burden of CV disease in PsA. Aims: To compare the prevalence of CV risk factors (CVRFs) and history of CV disease (CVD) among French PsA patients and age- and sex-matched controls; to quantify individual CV risk using SCORE, QRISK2 and REYNOLDS risk scores; to assess the proportion of PsA patients or controls achieving the recommended LDL-C target according to their individual CV risk.

**Methods:** Observational case-control single-site study. PsA patients (CASPAR criteria), consulting a rheumatologist or hospitalized in the Rheumatology Department of a French University Hospital between March 2016 and January 2017, were included in the study after informed consent was obtained. Age- and sex-matched controls (2:1) were extracted from the Mona Lisa, general population study. CVRF and history of CVD were collected and compared between PsA patients and controls. Individual CV risk was quantified, using SCORE (with or without using a 1.5 multiplication factor), QRISK2 (with or without including PsA as a CVRF) and REYNOLDS risk scores and compared between PsA patients and controls. The proportion of PsA patients or controls achieving the recommended LDL-C target according to their individual CV risk was assessed.

**Results:** 207 PsA patients and 414 controls were included in this study. CVRF and history of CVD were significantly increased in PsA patients in comparison with controls (Table1). Individual CV risk was higher in PsA patients in comparison with controls using SCORE (p=0.002), QRISK2 (p=0.001) and REYNOLDS (p=0.003) risk scores (data not shown). The proportion of PsA patients or controls achieving the recommended LDL-C target according to their individual...
CV risk, quantified using SCORE, was low in both groups (Table 2). Among PsA patients or controls with an individual risk score \(^3\) 10%, quantified using QRISK2, only 22.9% or 35.8% were respectively treated with a statin.

**Conclusion:** Our study confirms that the prevalence of CVRF and history of CVD is higher in PsA patients than in controls. It shows that individual CV risk is higher in PsA patients than in controls, whatever risk score is used for its quantification. It highlights that a low proportion of PsA patients achieve LDL-C target (SCORE) or initiate a treatment with a statin (QRISK2) in spite of high individual CV risk.

Table 1. CVRF and history of CVD in PsA patients and controls

<table>
<thead>
<tr>
<th></th>
<th>PsA patients (n=207)</th>
<th>Controls (n=414)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean or % SD</td>
<td>Mean or % SD</td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>134 15</td>
<td>129 22</td>
<td>0.001</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>79 11</td>
<td>80 12</td>
<td>0.27</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.6 4.9</td>
<td>25.2 4.0</td>
<td>0.001</td>
</tr>
<tr>
<td>Triglycerides (g/l)</td>
<td>1.24 0.72</td>
<td>1.06 0.63</td>
<td>0.001</td>
</tr>
<tr>
<td>LDL (g/l)</td>
<td>1.26 0.38</td>
<td>1.43 0.35</td>
<td>0.001</td>
</tr>
<tr>
<td>HDL (g/l)</td>
<td>0.54 0.14</td>
<td>0.59 0.14</td>
<td>0.001</td>
</tr>
<tr>
<td>Total cholesterol (g/l)</td>
<td>2.04 0.43</td>
<td>2.23 0.38</td>
<td>0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>34.4</td>
<td>26.3</td>
<td>0.03</td>
</tr>
<tr>
<td>Diabetes 1 and 2</td>
<td>12.1</td>
<td>7.7</td>
<td>0.09</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>25.1</td>
<td>42.0</td>
<td>0.001</td>
</tr>
<tr>
<td>Smoking</td>
<td>0.04</td>
<td>0.04</td>
<td>0.04</td>
</tr>
<tr>
<td>Never</td>
<td>42.0</td>
<td>48.1</td>
<td>0.04</td>
</tr>
<tr>
<td>Current</td>
<td>24.2</td>
<td>15.9</td>
<td>0.04</td>
</tr>
<tr>
<td>Former</td>
<td>33.8</td>
<td>36.0</td>
<td>0.04</td>
</tr>
<tr>
<td>Metabolic syndrome (NCEP2)</td>
<td>28.4 11.6</td>
<td>28.4 11.6</td>
<td>0.001</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>5.8 2.9</td>
<td>2.9 2.9</td>
<td>0.08</td>
</tr>
<tr>
<td>Cerebrovascular stroke</td>
<td>2.4 1.0</td>
<td>2.4 1.0</td>
<td>0.18</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>1.5 0.5</td>
<td>1.5 0.5</td>
<td>0.23</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>8.7 4.1</td>
<td>8.7 4.1</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Table 2: Proportion of PsA patients or controls achieving LDL-C target (SCORE)
<table>
<thead>
<tr>
<th>SCORE LDL-C Target</th>
<th>Controls n</th>
<th>Controls %</th>
<th>p</th>
<th>PsA n</th>
<th>PsA %</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCORE &lt; 5 %</td>
<td>286</td>
<td>22</td>
<td>0.002</td>
<td>122</td>
<td>41</td>
</tr>
<tr>
<td>LDL-C &lt;1.15 g/l</td>
<td>63</td>
<td>4.4</td>
<td>0.81</td>
<td>50</td>
<td>3.6</td>
</tr>
<tr>
<td>SCORE 5-9 %</td>
<td>68</td>
<td>3.6</td>
<td>0.27</td>
<td>28</td>
<td>13.7</td>
</tr>
<tr>
<td>LDL-C &lt;1 g/l</td>
<td>56</td>
<td>3</td>
<td></td>
<td>1</td>
<td>13.7</td>
</tr>
<tr>
<td>SCORE ³10 %</td>
<td>2</td>
<td>2</td>
<td></td>
<td>7</td>
<td>13.7</td>
</tr>
<tr>
<td>LDL-C &lt;0.7 g/l</td>
<td>56</td>
<td>3</td>
<td></td>
<td>7</td>
<td>13.7</td>
</tr>
</tbody>
</table>

Disclosure: R. Koch, None; J. B. RUIDAVETS Sr., None; Y. Degboe, None; A. Cantagrel, None; A. Ruyssen-Witrand, None; J. FERRIERES, None; A. Constantin, None.

Abstract Number: 658

Functionally Active MAIT Cells in Psoriatic Arthritis: A New Member of the IL-23/IL-17 Cytokine Network

Siba P. Raychaudhuri¹ and Smriti K. Raychaudhuri², ¹Rheumatology Section, Sacramento Veterans Affairs Medical Center, Sacramento, CA, ²Rheumatology/Immunology, VA Sacramento Medical Center, Davis, CA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthopathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The mucosal-associated invariant T (MAIT) cells recently have been implicated in autoimmune diseases. Murine model experiments also suggest that MAIT cells are capable of inducing or exacerbating arthritis. However, their gut origin, effector phenotype and lineage towards IL-23/IL-17 cytokine signatures make them more relevant for spondyloarthritis rather than RA. More so these cells are predominantly CD8+; thus altogether this subpopulation of T cells likely to have all the potentials to have a contributing role in the pathogenesis of psoriatic arthritis (PsA). Here we have explored relevance and functional significance of the MAIT cell in PsA.

Methods: We collected PBMC and synovial fluid mononuclear cells (SFMC) from age/sex matched active untreated PsA patients (n=10) and normal individuals (n=10). We used two methods to culture and enrich the MAIT cells: (i) the
established method for enrichment of IL-17+ T cell by culturing these cells with rIL-23 for 6 days and (ii) the standard protocol for MAIT cell culture with PMA/Inomycin. Hi-D FACS studies were done to identify the activated memory effector CD11a+CD45RO+IL-17+ T cells. MAIT cells were identified as CD3+Vα7.2TCR+CD161^{high}. The percentages of each cell population and the mean fluorescence intensity (MFI) were analyzed using FlowJo software.

**Results:** MAIT cells were identified in PBMC and SFMC. In both PsA and controls CD3+IL+17 MAIT cells were identified in PBMC (<2%). Where as in SFMC it varied between 4%-8% (5.182 ± 0.251%, SD). However we have made several important observations- (i) Among the IL-17 producing T cells only the MAIT cells were predominantly CD8+ (~90%), (ii) IL-23R was strongly expressed (~ 20%), and IL-23R was functionally active (iii) rIL-23 induced significant proliferation of the IL-17+ MAIT cells (Fig 1).

**Conclusion:** MAIT cells produce multiple inflammatory cytokines (IL-17, IFNγ, and TNFα) thus relevant for several T cell mediated autoimmune diseases. However Tc17 CD8+ /MAIT cells obviously are more relevant for PsA because of its MHC class-1 association. Moreover our observation that these cells express functionally active IL-23R brings a new dimension that once these cells migrates to joint tissue IL-23 can independently regulate these critical Tc17 CD8+ MAIT cells and thus these cells likely to become a part of the IL-23/IL-17 cytokine network; and there may not be a need for the MR1 associated presentation of bacterially derived vitamin B metabolites to active these MAIT cells.

**Fig 1-** A representative FACS plot of rIL-23 induced marked proliferation of the CD3+Vα7.2TCR+CD161^{high}IL-17+ T cells

---

**Disclosure:** S. P. Raychaudhuri, None; S. K. Raychaudhuri, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/functionally-active-mait-cells-in-psoriatic-arthritis-a-new-member-of-the-il-23il-17-cytokine-network](http://acrabstracts.org/abstract/functionally-active-mait-cells-in-psoriatic-arthritis-a-new-member-of-the-il-23il-17-cytokine-network)

**Abstract Number:** 659

**IL-17 Producing T Cells and Its Dichotomy: A Mixed Response of the Innate and Acquired Immune System in Psoriatic Arthritis**

Siba P. Raychaudhuri1 and Smriti K. Raychaudhuri2, 1Rheumatology Section, Sacramento Veterans Affairs Medical Center, Sacramento, CA, 2Rheumatology/Immunology, VA Sacramento Medical Center, Davis, CA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster I
**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Source of IL-17 in human has been mainly attributed to ab T cells, more specifically to the Th17 cells. However, some reports suggest that cells of the innate immune system: γδ T cells and NKT cells may be the major contributing IL-17 producing cells in psoriatic arthritis (PsA). To have a definite answer; here we have studied arrays of IL-17 producing T cell phenotypes in PsA including the Mucosal associated invariant T (MAIT) cells.

**Methods:**

- PBMC and synovial fluid mononuclear cells (SFMC) from age/sex matched active PsA patients (n=15) and normal individuals (n=15) were collected
- Patients were not on DMARDS or biologics
- rIL-23 induced activated IL-17+ T cells were generated and stained as per our earlier reports (Raychaudhuri SP, et al. Mol Cell Biochem. 2012;359:419-29).
- Hi-D FACS studies were done to identify the activated memory effector CD11a+CD45RO+IL-17+ T cells. MAIT cells were CD3+Vα7.2TCR+CD161high, γδ T cells were CD3+γδTCR+, ab T cells were CD3+abTCR+, invariant CD1d-restricted natural killer (NK) T cells were CD1d/PBS-57 tetramer+CD3+. The percentages of each cell population and the mean fluorescence intensity (MFI) were analyzed using FlowJo software.

**Results:**

The percentage of IL-17+ CD3+ T cells was far higher in both PBMC (20.5 ± 0.5%) and SFMC (43± 0.7%) in PsA patients compared to 3± 0.5% in PBMC of healthy persons (p<0.001).

Both PBMC and SFMC in PsA patients demonstrated IL-17+ effector memory T cells (TEM) in the following T cell phenotypes: ab T cells, γδ T cells, NKT cells and MAIT cells. The frequency of these CD3+IL-17+ T cells in the PBMC and SFMC in PsA patients are described in the Table-1 (Table 1). An important observation we noticed that IL-17+ MAIT cell in SFMC were enriched (5%) compared to 1 % in PBMC and they were predominantly CD8+ (~ 90%).

**Conclusion:**

- In PsA, pathologic CD11a+CD45RO+IL-17+ T cells are comprised of cells of both the innate and acquired immune response: ab T cells, γδ T cells, MAIT cells and NKT cells.
- However, compared to the other phenotypes, the dominant (~ 80%) IL-17+T cells in PsA (both in PBMC and SFMC) were conventional T-helper 17 (Th17) CD4+CD11a+CD45RO+abTCR+ T cells (p<0.001%) (Table 1).
- MHC class-1 association, subclinical colitis and enrichment of Tc17 CD8+/MAIT cells in SFMC in PsA could be of additional pathological significance and needs further evaluation.

**Table 1.** IL-17 expression (%) in gated CD3+CD11a+CD45RO+ T cells in different T cell phenotypes in SFMC and PBMC of PsA. αβ TCR IL-17+ cells are significantly more than NKT, MAIT and γδ TCR, p<0.001.

<table>
<thead>
<tr>
<th></th>
<th>PBMC (% ± SD)</th>
<th>SFMC (%± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NKT</td>
<td>15.155 ± 1.275</td>
<td>17.012 ± 2.362</td>
</tr>
<tr>
<td>MAIT</td>
<td>1.995 ± 0.089</td>
<td>5.182 ± 0.251</td>
</tr>
<tr>
<td>dgTCR</td>
<td>2.907 ± 0.469</td>
<td>1.391 ± 0.229</td>
</tr>
<tr>
<td>baTCR</td>
<td>79.943 ± 1.112</td>
<td>76.496 ± 0.224</td>
</tr>
</tbody>
</table>
Strain-Dependent IL-17A Secretion By CD4-CD8- DN αβ T Cells Correlates with Disease Susceptibility in Murine Spondyloarthritis

Imtiyaz Hossain, Mederbek Matmusaev and Joerg Ermann, Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Hydrodynamic injection of IL-23 minicircles into adult B10.RIII mice induces an inflammatory disease with phenotypic features of human spondyloarthritis. Tissue-resident CD4-CD8- double negative (DN) T cells secreting IL-17A in response to stimulation with IL-23 are thought to be critical in this model. To further dissect disease pathogenesis, IL-23 minicircle injection into genetically modified mice would be informative. C57BL/6, the background strain for most genetically engineered mice, has been shown to be less permissive than B10.RIII in several autoimmune or inflammatory disease models. Here, we tested the susceptibility of C57BL/6 mice to IL-23 minicircle-induced spondyloarthritis and compared number and function of DN T cells between C57BL/6 and B10.RIII mice.

Methods: Adult C57BL/6 and B10.RIII mice were injected with IL-23 minicircles and monitored clinically for disease development. IL-23 induction was measured by quantitative PCR (liver tissue) and ELISA (serum). Single cells suspensions were prepared from blood, liver, spleen, skin and the Achilles tendon enthesis. Cells were analyzed by multicolor flow cytometry. IL-17A production was measured by intracellular staining after stimulation with IL-23/IL-1β or PMA/ionomycin in the presence of Golgi-Stop for 4 hours.

Results: In contrast to B10.RIII mice, C57BL/6 mice were resistant to induction of IL-23 minicircle-induced spondyloarthritis. While IL-23 expression did not differ between the two strains, C57BL/6 mice failed to develop paw swelling or psoriasis-like skin changes over the observation period of up to 4 weeks. Frequency and number of DN αβ and γδ T cells were not different in the five tissues analyzed. However, upon in vitro stimulation, we observed a statistically significantly higher frequency of IL-17A positive DN αβ T cells in susceptible B10.RIII mice compared with resistant C57BL/6 animals.

Conclusion: C57BL/6 mice in our animal facility are resistant to IL-23 minicircle-induced spondyloarthritis, which limits the utility of this model for mechanistic studies. IL-17A secretion by DN αβ T cell but not γδ T cells correlated with strain-dependent disease susceptibility.
Normal Human Enthesis Contains a Resident Population of γδT-Cells

Richard Cuthbert1, Evangelos M. Fragkakis1, Robert Dunsmuir2, Peter Giannoudis3, Elena Jones1, Darren Newton4 and Dennis McGonagle1, 1Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom, 2Department of Spinal Surgery, National Health Service, Leeds, United Kingdom, 3Academic Department of Trauma and Orthopaedics, University of Leeds, Leeds, United Kingdom, 4Leeds Institute of Cancer and Pathology, University of Leeds, Leeds, United Kingdom
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Recent animal studies have suggested that γδT-cells accumulate at enthesis, secrete IL-17 and are responsible for driving the spondyloarthritis (SpA) phenotype resulting from IL-23 overexpression in mice (1, 2). In humans examination of the immunological profile of enthesis has been hampered by lack of tissue. Recently, we used a novel strategy to show that group 3 innate lymphoid cells are present at the human enthesis (3). Here we extend our methodology to examine the broader immunological profile of human enthesis and to determine if γδT-cells are also present.

Methods:
Human etheseal soft tissue (EST) and peri-entheseal bone (PEB) was harvested from normal spinous process in patients undergoing elective spinal orthopaedic procedures. Interspinous EST was dissected from PEB and enzymatically digested, followed by isolation of mononuclear cells. Flow cytometry was then used to determine the proportion of B-cells (CD45+, CD19+) NK cells (CD45+, CD3-, CD56+) and T-cells (CD45+, CD3+). T-cells were then sub divided based on expression of CD4 (T-helper cells), CD8 (Cytotoxic T-cells) and T-cell receptor (TCR) γδ (γδT-cells). For analysis of TCRγδ isoform cDNA was isolated from peripheral blood, EST and PEB and probed with TCRγδ isoform specific oligonucleotides. Entheseal data was compared to age-matched peripheral blood from healthy controls.

Results:
Entheseal digests contained on average a lower proportion of T-cells compared to peripheral blood (p=0.018). However, the proportion of T-cells not expressing either CD4 or CD8 was greater in enthesal tissues (p=0.021). As a proportion of T-cells, γδT-cells were 6-fold more numerous in EST compared to peripheral blood (p=0.024), and PEB had 3-fold more. 37% of EST γδT-cells expressed CCR6, this compared to 26% and 34% in PEB and peripheral blood respectively. 46% of EST and 54% PEB enthesal γδT-cells expressed the Vδ1 isoform of the TCR, and clear differences in TCR isoform expression could be observed between peripheral blood, EST and PEB γδT-cell cDNA.

Conclusion:
γδT-cells are present in normal human enthesis and constitute a greater proportion of the T-cell pool compared to peripheral blood. A very similar proportion γδT-cells that expressed CCR6, a functional marker for IL-17 production, as was observed
as reported in mice (2). Flow cytometry and transcript analysis indicate a high proportion of γδT-cells expressing the Vδ1 isoform of the TCR, which is also associated with homing to the gut and skin. This is the first description of γδT-cells at the human enthesis and offers tentative confirmation of findings in mouse models where these cells play a key role in SpA pathogenesis.


Disclosure: R. Cuthbert, None; E. M. Fragkakis, None; R. Dunsmuir, None; P. Giannoudis, None; E. Jones, None; D. Newton, None; D. McGonagle, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/normal-human-enthesis-contains-a-resident-population-of-%ce%b3%ce%b4t-cells

Abstract Number: 662

Clinical Significance of Non-Albumin Proteinuria for Severity Assessment of Tubulointerstitial Inflammation in Lupus Nephritis

Oh Chan Kwon1, Seokchan Hong1, Jung Sun Lee2, Byeongzu Ghang1, Doo-Ho Lim3, Wook Jang Seo4, Yong-Gil Kim1, Chang Keun Lee1 and Bin Yoo1, 1Division of Rheumatology, Department of Internal Medicine, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea, Republic of (South), 2Internal medicine, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea, Republic of (South), 3Division of Rheumatology, Department of Internal Medicine, University of Ulsan College of Medicine, Ulsan University Hospital, Ulsan, Korea, Republic of (South), 4Seoul Veterans Hospital, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Tubulointerstitial inflammation (TI) has been shown to have prognostic significance in renal outcome of lupus nephritis. Considering that the type of protein excreted in urine is different between glomerular disease and tubulointerstitial disease, we aimed to determine whether non-albumin proteinuria is associated with severity of TI in lupus nephritis.

Methods: We included patients with biopsy-confirmed lupus nephritis at a tertiary medical center in Korea from January 2000 to February 2017. Patients were included if their urine protein/creatinine ratio (uPCR) and urine albumin/creatinine ratio (uACR) were simultaneously measured. All included patients met the ACR criteria for classification of systemic lupus erythematosus. Clinical and laboratory variables including C3 and C4 levels as well as anti-double strand DNA (anti-dsDNA) antibody titers were collected. Non-albumin proteinuria was calculated by subtracting uACR from uPCR (uPCR –
Renal pathology including International Society of Nephrology/Renal Pathology Society (ISN/RPS) classification 2003, activity and chronicity indices, and severity of TI was reviewed. Logistic regression analysis was performed to identify the clinical and laboratory parameters associated with TI severity.

**Results:** Of the total 36 patients, 27 (75%) had no-to-mild TI and 9 (25%) had moderate-to-severe TI. 31 (86.1%) had proliferative type glomerulonephritis (class III \(\frac{3}{4}\) V and IV \(\frac{3}{4}\) V) and 5 (13.9%) had non-proliferative type glomerulonephritis (class II and V). In logistic regression analysis, the following factors were significantly associated with moderate-to-severe TI: uPCR (odds ratio [OR] 1.599, 95% confidence interval [CI] 1.025-2.494, p = 0.039) and non-albumin proteinuria (uPCR – uACR) (OR 3.558, 95% CI 1.147-11.038, p = 0.028).

**Conclusion:** In lupus nephritis, non-albumin proteinuria, as assessed by the difference between uPCR and uACR, was associated with severity of TI, to a more relevant degree than uPCR alone. Thus, measuring non-albumin proteinuria can be a valuable non-invasive method for assessing the severity of TI in lupus nephritis.

<table>
<thead>
<tr>
<th>Table 1. Factors associated with TI severity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Odds ratio</strong></td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>uACR</td>
</tr>
<tr>
<td>uPCR</td>
</tr>
<tr>
<td>uAPR</td>
</tr>
<tr>
<td>uPCR – uACR</td>
</tr>
<tr>
<td>Cr</td>
</tr>
<tr>
<td>C3</td>
</tr>
<tr>
<td>C4</td>
</tr>
<tr>
<td>Anti-dsDNA</td>
</tr>
<tr>
<td>GN activity index</td>
</tr>
<tr>
<td>GN chronicity index</td>
</tr>
<tr>
<td>ISN/RPS class (proliferative GN)</td>
</tr>
</tbody>
</table>

**Disclosure:** O. C. Kwon, None; S. Hong, None; J. S. Lee, None; B. Ghang, None; D. H. Lim, None; W. J. Seo, None; Y. G. Kim, None; C. K. Lee, None; B. Yoo, None.


**Abstract Number:** 663

**Urinary Tumor-Necrosis Factor-like Weak Inducer of Apoptosis Is an Important Biomarker for Renal Lupus**

Michelle Petri¹, Daniel Goldman², Linda Burkly³, Nicolas Wisniacki⁴, Chris Stebbins⁵ and Laurence S Magder⁵,

¹Medicine (Rheumatology), Division of Rheumatology, Johns Hopkins University School of Medicine, MD, USA, Baltimore, MD, ²Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, ³Biogen, Cambridge, MA, ⁴GlaxoSmithKline, London, United Kingdom, ⁵Epidemiology and Public health, University of Maryland School of Medicine, Baltimore, MD

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A  
Session Time: 9:00AM-11:00AM

Background/Purpose: Tumor-necrosis factor (TNF)-like weak inducer of apoptosis (TWEAK) drives release of proinflammatory mediators from renal tubular and mesangial cells, and has been implicated in the pathogenesis of lupus nephritis, angiogenesis and fibrosis. We examined the utility of urinary levels of TWEAK (uTWEAK) as a biomarker for lupus nephritis activity in patients with systemic lupus erythematosus (SLE).

Methods: 296 SLE patients in a longitudinal cohort had urine collected at baseline and analyzed by an ELISA for TWEAK developed by Biogen. Urine TWEAK (uTWEAK) concentration was normalized by dividing by urine creatinine concentration. Patients were subsequently seen at regular intervals of three months. At every visit, assessment of disease activity was recorded using SELENA-SLEDAI, BILAG-2004 and the Physician’s Global Assessment (PGA). Standard of care laboratory tests were also performed at each visit.

Results: uTWEAK was associated with ethnicity (highest in Asians) and strongly associated with prednisone dose. Table 1 shows the relationship of uTWEAK with organ specific SLE activity. uTWEAK was only associated with renal activity. It was negatively associated with serum creatinine ($r = -0.25$, $p < 0.00001$). The association of uTWEAK with urine protein/creatinine ratio was mainly seen after uTWEAK/creatinine ratio of approximately 0.12.

Table 1: Risk of specific types of SLE disease activity by urinary TWEAK levels at the same visit.

<table>
<thead>
<tr>
<th>SLE Disease Activity (SLEDAI descriptors)</th>
<th>Urinary TWEAK / Creatinine Ratio</th>
<th>P-value (trend)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1st Quartile (n=74)</td>
<td>2nd Quartile (n=74)</td>
</tr>
<tr>
<td>Renal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>--Proteinuria &gt; 500 mg</td>
<td>7 (9%)</td>
<td>5 (7%)</td>
</tr>
<tr>
<td>--Hematuria</td>
<td>5 (7%)</td>
<td>5 (7%)</td>
</tr>
<tr>
<td>--Pyuria</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Skin</td>
<td>24 (32%)</td>
<td>23 (31%)</td>
</tr>
<tr>
<td>Hematologic</td>
<td>1 (1%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>1 (1%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Immunologic</td>
<td>22 (30%)</td>
<td>21 (28%)</td>
</tr>
</tbody>
</table>

uTWEAK at baseline was predictive of renal activity over the next year (Table 2).

Table 2: Risk of specific types of SLE disease activity in visits made in the next year by urinary TWEAK levels.
### Urinary TWEAK / Creatinine Ratio

<table>
<thead>
<tr>
<th>SLE Disease Activity</th>
<th>1&lt;sup&gt;st&lt;/sup&gt; Quartile (n=240)</th>
<th>2&lt;sup&gt;nd&lt;/sup&gt; Quartile (n=224)</th>
<th>3&lt;sup&gt;rd&lt;/sup&gt; Quartile (n=228)</th>
<th>4&lt;sup&gt;th&lt;/sup&gt; Quartile (n=239)</th>
<th>P-value&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.016</td>
</tr>
<tr>
<td>--Proteinuria</td>
<td>11 (5%)</td>
<td>18 (8%)</td>
<td>36 (16%)</td>
<td>43 (18%)</td>
<td>0.011</td>
</tr>
<tr>
<td>--Hematuria</td>
<td>10 (4%)</td>
<td>12 (6%)</td>
<td>36 (16%)</td>
<td>40 (17%)</td>
<td>0.011</td>
</tr>
<tr>
<td>--Pyuria</td>
<td>1 (1%)</td>
<td>1 (&lt;1%)</td>
<td>15 (7%)</td>
<td>11 (5%)</td>
<td>0.28</td>
</tr>
<tr>
<td>Skin</td>
<td>74 (31%)</td>
<td>69 (31%)</td>
<td>65 (29%)</td>
<td>51 (21%)</td>
<td>0.16</td>
</tr>
<tr>
<td>Hematologic</td>
<td>9 (4%)</td>
<td>10 (4%)</td>
<td>10 (4%)</td>
<td>10 (4%)</td>
<td>0.84</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>8 (3%)</td>
<td>7 (3%)</td>
<td>3 (1%)</td>
<td>15 (6%)</td>
<td>0.35</td>
</tr>
<tr>
<td>Immunological</td>
<td>71 (30%)</td>
<td>53 (24%)</td>
<td>72 (32%)</td>
<td>72 (30%)</td>
<td>0.80</td>
</tr>
</tbody>
</table>

<sup>1</sup> Based on a test for trend, imputing scores of 0,1,2,3 for the consecutive quartiles, accounting for repeated measures on the same patient using GEE.

**Conclusion:** In a clinical trial, blocking TWEAK did not improve renal lupus. However, our results show that uTWEAK still has great utility as a lupus nephritis marker, as uTWEAK is only associated with renal activity and does not correlate with non-renal activity. In addition, it predicts renal activity over the next year.

**Disclosure:** M. Petri, Anthera Inc, 5,GlaxoSmithKline, 5,EMD Serono, 5,Eli Lilly and Company, 5,Bristol Meyer Squibb, 5,Amgen, 5,United Rheumatology, 5,Global Academy, 5,Exagen, 2; D. Goldman, None; L. Burkly, Biogen Idec, 3; N. Wisniacki, GlaxoSmithKline, 3; C. Stebbins, Biogen, 3; L. S. Magder, None.


**Abstract Number:** 664

### Low Vitamin D Is Associated with Thrombosis in Systemic Lupus Erythematosus

**Michelle Petri**<sup>1</sup>, Wei Fu<sup>2</sup> and Daniel Goldman<sup>2</sup>, <sup>1</sup>Medicine (Rheumatology), Division of Rheumatology, Johns Hopkins University School of Medicine, MD, USA, Baltimore, MD, <sup>2</sup>Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Low vitamin D is common in systemic lupus erythematosus (SLE). It is also found in antiphospholipid syndrome. Vitamin D has effects on tissue factor, PAI-1, thrombomodulin and platelet aggregation that suggest it has an anti-thrombotic role. We asked whether low vitamin D was associated with thrombosis in SLE, adjusting for lupus anticoagulant.
**Methods:** A total of 1,392 SLE patients were included in the analysis. At the first visit when vitamin D was measured, 76.7% had levels of 25-hydroxyvitamin D <40 ng/mL. The SLE patients were: 92% female, mean age 42.9 years, and ethnicity 50% Caucasian, 41% African American. 27% patients had a history of thrombosis; 7% stroke, 4% MI and 14% DVT.

**Results:** Vitamin D, measured either as a continuous variable or as “low” (<40 ng/mL) vs. normal, was associated with any thrombosis and with DVT.

Table 1: Associations of First Vitamin D Measurement with Thrombosis

<table>
<thead>
<tr>
<th></th>
<th>Positive for Thrombotic Event</th>
<th>No Thrombotic Event</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Any Thrombotic Event</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin D (ng/ml)</td>
<td>27.6(15.1)</td>
<td>30.6(14.6)</td>
<td>0.0008</td>
</tr>
<tr>
<td>Vitamin D &lt; 40 ng/ml</td>
<td>299(80.4)</td>
<td>759(75.4)</td>
<td>0.064</td>
</tr>
<tr>
<td><strong>Stroke</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin D (ng/ml)</td>
<td>28.9(15.2)</td>
<td>29.9(14.7)</td>
<td>0.5408</td>
</tr>
<tr>
<td>Vitamin D &lt; 40 ng/ml</td>
<td>79(75.2)</td>
<td>988(76.9)</td>
<td>0.7914</td>
</tr>
<tr>
<td><strong>Myocardial Infarction (MI)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin D (ng/ml)</td>
<td>30.2(16.9)</td>
<td>29.8(14.7)</td>
<td>0.883</td>
</tr>
<tr>
<td>Vitamin D &lt; 40 ng/ml</td>
<td>35(70)</td>
<td>1032(77)</td>
<td>0.3258</td>
</tr>
<tr>
<td><strong>DVT</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin D (ng/ml)</td>
<td>25.9(13.4)</td>
<td>30.4(14.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Vitamin D &lt; 40 ng/ml</td>
<td>171(87.2)</td>
<td>895(75)</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

We next adjusted for race, age, sex and lupus anticoagulant. Low vitamin D remained associated with DVT.

Table 2 Summary of Adjusted Odds Ratio for Low Vitamin D (< 40 ng/ml)

<table>
<thead>
<tr>
<th>Dependent Variables</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Thrombosis</td>
<td>1.33 (0.99,1.79)</td>
<td>1.36 (0.99,1.86)</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.91 (0.58,1.45)</td>
<td>0.92 (0.57,1.48)</td>
</tr>
<tr>
<td>MI</td>
<td>0.7 (0.38,1.29)</td>
<td>0.8 (0.42,1.53)</td>
</tr>
<tr>
<td>DVT</td>
<td>2.28 (1.47,3.54)</td>
<td>2.31 (1.47,3.65)</td>
</tr>
</tbody>
</table>

We next looked prospectively: this analysis excluded thrombotic events before the first vitamin D measurement. It allowed for vitamin D to be a time-varying variable, as replacement therapy was given if it was low. After adjustment for race, age and sex, the adjusted hazard ratio remained significant for any thrombosis: 1.75 (1.04,2.92).
**Conclusion:** Low vitamin D was significantly associated with any thrombosis and with DVT (even after adjustment for lupus anticoagulant). In prospective models it remained significantly associated with any thrombosis. As supplementation with vitamin D was proven to reduce thrombosis in an oncology randomized clinical trial, vitamin D replacement should become routine in SLE patients at risk for thrombosis.

**Disclosure:** M. Petri, Anthera Inc, 5,GlaxoSmithKline, 5,EMD Serono, 5,Eli Lilly and Company, 5,Bristol Meyer Squibb, 5,Amgen, 5,United Rheumatology, 5,Global Academy, 5,Exagen, 2; W. Fu, None; D. Goldman, None.

**Disclosure:** M. Petri, Anthera Inc, 5,GlaxoSmithKline, 5,EMD Serono, 5,Eli Lilly and Company, 5,Bristol Meyer Squibb, 5,Amgen, 5,United Rheumatology, 5,Global Academy, 5,Exagen, 2; W. Fu, None; D. Goldman, None.


**Abstract Number:** 665

**Low Vitamin D Is Associated with End Stage Renal Disease in Systemic Lupus Erythematosus**

Michelle Petri¹, Wei Fu² and Daniel Goldman², ¹Medicine (Rheumatology), Division of Rheumatology, Johns Hopkins University School of Medicine, MD, USA, Baltimore, MD, ²Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Vitamin D insufficiency/deficiency is common in SLE. Replacement therapy may help renal disease activity. We asked whether low vitamin D predicted later organ damage.

**Methods:** We considered all follow-up after a patient’s first measure of vitamin D. The first measure of vitamin D usually occurred in late 2009 or 2010 for existing patients and at the first visit of new patients after that. The patients were categorized based on their first measure of vitamin D as <20 ng/mL versus 20+ ng/mL. A total of 1,392 SLE patients were included in the analysis. At the first visit when vitamin D was measured, 27.3% had levels of 25-hydroxy vitamin D <20 ng/ml. The SLE patients were: 92% female, mean age 47.3 years and ethnicity 50% Caucasian, 41% African American.

**Results:** Risk of lifetime organ damage was calculated, using SLICC/ACR Damage Index.

Table 1: Risk of organ damage adjusted for age, gender and ethnicity.
<table>
<thead>
<tr>
<th>Categorical Vitamin D (≤ 20 ng/ml as abnormal)</th>
<th>RR (95% CI)</th>
<th>P-Value</th>
<th>Adjusted RR (95% CI)</th>
<th>Adj. P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ocular Damage</td>
<td>0.97 (0.76,1.25)</td>
<td>0.83</td>
<td>1.10 (0.86,1.4)</td>
<td>0.4388</td>
</tr>
<tr>
<td>Neuropsychiatric Damage</td>
<td>0.95 (0.73,1.24)</td>
<td>0.7222</td>
<td>1.04 (0.79,1.36)</td>
<td>0.7979</td>
</tr>
<tr>
<td>Renal Damage</td>
<td>1.87 (1.23,2.84)</td>
<td><strong>0.0033</strong></td>
<td><strong>1.66 (1.08,2.54)</strong></td>
<td><strong>0.0206</strong></td>
</tr>
<tr>
<td>Pulmonary Damage</td>
<td>1.01 (0.74,1.38)</td>
<td>0.9321</td>
<td>1.04 (0.77,1.41)</td>
<td>0.7888</td>
</tr>
<tr>
<td>Cardiovascular Damage</td>
<td>1.11 (0.77,1.59)</td>
<td>0.5882</td>
<td>1.20 (0.83,1.74)</td>
<td>0.3396</td>
</tr>
<tr>
<td>Peripheral Vascular Damage</td>
<td>1.18 (0.7,2)</td>
<td>0.5346</td>
<td>1.23 (0.75,2)</td>
<td>0.4134</td>
</tr>
<tr>
<td>Gastrointestinal Damage</td>
<td>0.91 (0.65,1.26)</td>
<td>0.553</td>
<td>1.04 (0.74,1.46)</td>
<td>0.8093</td>
</tr>
<tr>
<td>Musculoskeletal Damage</td>
<td>1.03 (0.82,1.28)</td>
<td>0.8208</td>
<td>1.09 (0.86,1.37)</td>
<td>0.4706</td>
</tr>
<tr>
<td>Skin Damage</td>
<td>1.69 (1.11,2.57)</td>
<td><strong>0.0145</strong></td>
<td>1.22 (0.81,1.84)</td>
<td>0.3561</td>
</tr>
<tr>
<td>Total Damage</td>
<td>1.11 (0.97,1.28)</td>
<td>0.1246</td>
<td><strong>1.17 (1.02,1.33)</strong></td>
<td><strong>0.0245</strong></td>
</tr>
</tbody>
</table>

**Conclusion:** Low vitamin D associated with total damage and with End Stage Renal Disease. As vitamin D supplementation reduces proteinuria, this further suggests that vitamin D supplementation should be part of treatment of lupus nephritis. Surprisingly, low vitamin D did not associate with musculoskeletal damage (including with the subtype of osteoporotic fractures).

**Disclosure:** M. Petri, Anthera Inc, 5,GlaxoSmithKline, 5,EMD Serono, 5,Eli Lilly and Company, 5,Bristol Meyer Squibb, 5,Amen, 5,United Rheumatology, 5,Global Academy, 5,Exagen, 2; W. Fu, None; D. Goldman, None.

**Abstract Number:** 666

**Vitamin D Deficiency Is Associated with Increased Serum Cholesterol Among Patients with Systemic Lupus Erythematosus**

Michelle Petri1, Daniel Goldman2 and Laurence S Magder3, 1Medicine (Rheumatology), Division of Rheumatology, Johns Hopkins University School of Medicine, MD, USA, Baltimore, MD, 2Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, 3Epidemiology and Public health, University of Maryland School of Medicine, Baltimore, MD

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Sunday, November 5, 2017
**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
**Session Type:** ACR Poster Session A
**Background/Purpose:** Vitamin D insufficiency/deficiency is common in SLE. In other populations, vitamin D has been associated with cardiovascular risk factors such as blood pressure and serum cholesterol. We assessed whether there was an association between serum vitamin D and total serum cholesterol in a large SLE cohort.

**Methods:** Serum 25-hydroxy vitamin D [25(OH)D] was measured at quarterly clinic visits in a large SLE cohort. 1358 different patients were observed from 1 to 40 visits (the median was 11). The patients were 92% female, 50% Caucasian, 41% African American. Age ranged from 17 to 89 years. When the 25(OH)D level was below 40 mg/ml, the patient was prescribed supplemental vitamin D, usually 50,000 IU weekly. We explored the association between serum vitamin D levels and serum cholesterol using longitudinal regression models.

**Results:** Levels of 25(OH)D below 50 ng/ml were associated with a higher mean cholesterol. There was a significantly negative linear relationship between vitamin D and mean cholesterol when 25(OH)D was below 50 ng/ml.

<table>
<thead>
<tr>
<th>Range of 25(OH) Vitamin D</th>
<th>Estimated slope (95% Confidence Interval)</th>
<th>Unadjusted</th>
<th>P-value</th>
<th>Adjusted</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-50 ng/ml</td>
<td>-0.37 (-0.42, -0.32)</td>
<td>&lt;0.0001</td>
<td>-0.30 (-0.35, -0.24)</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>50+ ng/ml</td>
<td>-0.09 (-0.15, -0.02)</td>
<td>0.014</td>
<td>-0.11 (-0.18, -0.03)</td>
<td>0.0037</td>
<td></td>
</tr>
</tbody>
</table>

1 Adjusted for age, age-squared, sex, race, proportion of time on hydroxychloroquine use, corticosteroid use, BMI and systolic blood pressure.

**Conclusion:** We observed a decline in total cholesterol as vitamin D increased to the normal range. Vitamin D supplementation significantly reduced cholesterol, even after adjustment for hydroxychloroquine. Vitamin D, like hydroxychloroquine, has benefit beyond immunomodulation, in that it reduces multiple cardiovascular risk factors.

**Disclosure:** M. Petri, Anthera Inc, 5,GlaxoSmithKline, 5,EMD Serono, 5,Eli Lilly and Company, 5,Bristol Meyer Squibb, 5,Amgen, 5,United Rheumatology, 5,Global Academy, 5,Exagen, 2; D. Goldman, None; L. S. Magder, None.

Background/Purpose: Lupus nephritis (LN) represents the main prognostic factor in systemic lupus erythematosus (SLE) [1]. The clinical significant classes of LN –due to the need of treatment- are the proliferative (III, IV), membranous (V) and mixed classes (III or IV/V). The aim of the study was to find a urinary metabolomic fingerprint to diagnose classes III, IV and/or V of LN.

Methods: Cross-sectional study. Inclusion criteria: lupus patients with and without clinical significant lupus nephritis (classes III, IV, V and mixed classes). Urine samples were screened for metabolites using gas chromatography mass spectrometry (coupled with electronic nose) and principal component analysis for metabolite selection.

Results: We included 29 lupus patients, 11 with LN and 18 without LN. Age between groups were 26 years (IQR 14.5) in patients with LN and 33 (IQR 22.3) in patients without LN (p 0.48). The median SLEDAI score in LN patients was of 13 and 3 in those without NL (p <0.0001). Class IV nephritis was present in 45% of LN patients, mixed class in 36%, and class V in 18%. The median proteinuria of patients with NL was 1g/L, (IQR 2.7). We observed differences in metabolic fingerprint in patients with and without LN, with an AUC 90%. Metabolic pathway analysis was conducted, and we found several pathways involved, like methane, glycolysis, pyruvate and glycerophospholipid pathways. The most significant metabolites of the PCA that discriminated LN, were 2-nonanone with a sensitivity of 0.87 and specificity of 0.93. Obtaining the ratio of 2-bromopropane with 2-nonanone, the diagnostic accuracy improved, with a positive likelihood ratio (LR) of 14 and a negative LR of 0.1.

Conclusion: We identified a urinary metabolomic fingerprint that involved several metabolic pathways; 2-nonanone and the ratio of 2-bromopropane/2-nonanone had the best diagnostic accuracy in our study.

Is Uric Acid Level a Predictor of Long-Term Renal Outcome in Lupus Nephritis?

Michelle Lopes¹, Samara Gavinier², Elaine Leon², Vilma Viana², Eduardo Ferreira Borba¹ and Eloisa Bonfa³,

¹Rheumatology, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, ²Rheumatology, Hospital das Clínicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, BR, São Paulo, Brazil, ³Rheumatology Division, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Hyperuricemia has been reported to be associated with chronic kidney disease (CKD) in several clinical conditions, and recent studies also observed an association between increased uric acid (UA) serum levels and renal damage in lupus. However, the predictive value of UA for the development of long-term renal dysfunction in lupus nephritis is unknown. The purpose of this study was to evaluate if the UA level may be considered a predictor of long-term renal outcome in patients with lupus nephritis.

Methods: 75 biopsy-proven lupus nephritis patients with more than 7 years follow-up were consecutively selected for this study. Clinical and laboratorial data were obtained using a standardized electronic chart database protocol carried out at 1-6 months interval. UA levels were measured in sera stored at -70°C for all SLE patients at biopsy during nephritis flare and in 31 patients, for whom sera were available, at 6 and 12 months post-biopsy. The renal outcome was addressed after 7 years of follow-up to determine if UA was a predictor of good long-term renal outcome (Cr<1.5mg/dL in 7 years). SLE patients were divided in two groups according to the renal outcome [good outcome (Cr<1.5mg/dL in 7 years) and poor outcome (Cr≥1.5mg/dL in 7 years)] to assess whether UA levels at different time-points of follow-up were able to differentiate such groups. ROC curves were plotted to assess UA accuracy.
**Results:** At baseline, patients had mean SCr of 1.7±1.3 mg/dl, proteinuria of 5.7±4.7 g/24h, albumin of 2.4±0.8 g/dl, and SLEDAI scores of 9.5±5.0. Almost two thirds of the patients (66%) patients had positive anti-dsDNA and 28 patients (35%) had SCr≥1.5mg/dl. The distribution of histological classes among studied patients was: class II (6%), class III / IV (53%) and pure class V (36%). Serum UA levels were not able to differentiate good from poor long-term renal outcomes in patients with lupus nephritis at any of the time points analyzed: baseline, 6, 12 months (respectively p = 0.96, p = 0.76, p = 0.77). As expected, the ROC curve with higher AUC (12 months) showed a low accuracy (AUC=0.59). The cut-off for UA was 5.46mg/dL (Sensitivity=0.63, Specificity= 0.65, Positive Predictive Value=0.38, Negative Predictive Value=0.16, 95% CI=0.2-0.7, p<0.05). The AU was only associated with the current creatinine levels: at baseline (p=0.01), 6 months (p=0.03) and 12 months (p=0.01).

**Conclusion:** This study demonstrated that serum uric acid levels in lupus patients reflect solely the current renal function and it is not a good predictor of long-term renal outcome in lupus nephritis.

**Disclosure:** M. Lopes, None; S. Gavinier, None; E. Leon, None; V. Viana, None; E. F. Borba, None; E. Bonfa, None, 2.

**Abstract Number:** 669

**Unbiased Screening of Urinary Protein Biomarkers for Glomerular Filtration Rate Normalization**

**Sanam Soomro**¹, Samantha Stanley², Ramesh Saxena³, Michelle Petri⁴ and Chandra Mohan¹, ¹Biomedical Engineering, University of Houston, Houston, TX, ²Biomedical Engineering Department, University of Houston, Houston, TX, ³Internal Medicine/Division of Nephrology, University of Texas Southwestern Medical Center, Dallas, TX, ⁴Medicine (Rheumatology), Division of Rheumatology, Johns Hopkins University School of Medicine, MD, USA, Baltimore, MD

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** To account for glomerular filtration rate, urinary creatinine is routinely used for the normalization of urine biomarkers related to disease. Because of the small size of this metabolite, antibodies are difficult and expensive to develop, limiting the applications of disease-specific urine protein biomarkers for antibody-based point of care applications. **Methods:** An aptamer-based screening of 1129 proteins in 24 human urine samples (8 active lupus nephritis (LN), 8 inactive LN, 8 healthy controls (HC)) was carried out to identify urine proteins that correlated well with urine creatinine but not disease. **Results:** The screen uncovered 18 proteins that correlated well with urinary creatinine but were similar in patients with or without nephritis. Further validation in an independent cohort of 48 subjects (16 active LN, 16 inactive LN, 16 HC) showed a significant positive correlation of urine HVEM, RELT, and Dectin-1 to urinary creatinine. The most promising marker, urine HVEM, was significantly correlated to urinary creatinine in both white (Pearson r = 0.7229, P = 0.0001) and black subjects (Pearson r = 0.6111, P = 0.0009). Finally, normalization of other urinary biomarker proteins against urine HVEM showed comparable fold change and statistical significance as normalization to urinary creatinine. **Conclusion:** Instead of the metabolite creatinine, proteins such as HVEM, RELT and Dectin-1 can be used for normalization of urine biomarkers. The use of proteins instead of metabolites for normalization paves the way towards novel diagnostic approaches.
Urine HVEM, RELT, and Dectin-1 were validated by ELISA and found to be significantly correlated with urinary creatinine. HVEM, the most promising marker for GFR normalization, was also used to normalize ALCAM, a biomarker for SLE, to have comparable fold change and statistical significance as normalization to urinary creatinine.

Disclosure: S. Soomro, None; S. Stanley, None; R. Saxena, None; M. Petri, None; C. Mohan, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/unbiased-screening-of-urinary-protein-biomarkers-for-glomerular-filtration-rate-normalization

Abstract Number: 670

Membrane Attack Complex (MAC) Deposition in Lupus Nephritis Is Associated with Hypertension and Poor Clinical Response to Treatment

Shudan Wang1, Ming Wu2, Luis Chiriboga3, Briana Zeck4 and H. Michael Belmont5, 1Department of Medicine, Division of Rheumatology, New York University School Medicine, New York City, NY, 2New York University School of Medicine, New York, NY, 3Pathology, New York University School Medicine, New York, NY, 4Pathology, New York University School Medicine, New York City, NY, 5Medicine, New York University School of Medicine, New York, NY
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
LN is characterized by deposition of immune complexes in the kidney. Activation of the classical complement pathway by dsDNA is believed to play a role in its pathogenesis. The relative importance of C5a generation versus MAC involvement in tissue injury remains uncertain. We study immunohistochemistry staining for C9 in renal biopsies as a marker for intensity of kidney damage and clinical response to therapy.

Methods:
Chromogenic immunohistochemistry was performed on formalin-fixed, paraffin-embedded, 4-µm human renal biopsy sections using unconjugated, murine anti-human Complement C9 (Hycult Biotech, clone X197) from SLE patients who fulfill 4 ACR or SLICC criteria. Positive control is C3 glomerulopathy and negative control is normal kidney. Clinical parameters assessed at time of biopsy and 6 months. Student t-test, Fisher’s exact test, and logistic regression were performed in SAS.
**Results:**

30 renal biopsies were obtained from SLE patients with LN Class II (2), III (5), IV (8), V (5), III+V (8) and IV+V (2) This study included 24 women and 6 men, mean age 32.9 ± 12.1 years, with 4 Asians, 9 Blacks, 11 Hispanics and 6 Caucasians. 13/30 (43.3%) biopsies stained positive for glomerular C9 (Figure 1). Patients with +C9 have significantly higher systolic/diastolic BP, trend towards lower C3, and male gender; known predictors of poor renal outcomes (Table 1). There was no significant difference for ISN/RPN class, activity or chronicity indices between +C9 vs. –C9 groups. Five (45.5%) of 11 patients with +C9 did not respond to therapy at 6 months (defined as <50% reduction in proteinuria), compared with 2/15 (13.3%) patients with –C9. No difference in induction or maintenance therapy and compliance to therapy was found between +C9 and –C9 groups. +C9 patients were significantly more likely to be a non-responder at 6 months (OR=5.3, 95% CI 0.8, 36.4) compared to –C9 patients. After adjusting for systolic BP, compliance to treatment and proteinuria at time of biopsy in a multivariate logistic model, +C9 patients remain more likely to be non-responders (OR=4.3, 95% CI 0.3, 65.2).

**Conclusion:**

This study demonstrates that MAC deposition is a biomarker for more intense disease and that targeting C5a may be insufficient for controlling inflammation and damage in LN. MAC staining may be useful in routine IF studies of suspected or known lupus renal biopsies to identify patients at risk for aggressive and refractory disease and who may be candidates for novel therapies targeting terminal complement pathway.
<table>
<thead>
<tr>
<th>Demographics and Clinical</th>
<th>Positive for Glomerular C9 (n = 13)</th>
<th>Negative for Glomerular C9 (n = 17)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (µ ± SD years)</td>
<td>34.3 ± 12.5</td>
<td>31.8 ± 12.0</td>
<td>0.577</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>5 (38.5%)</td>
<td>1 (5.9%)</td>
<td>0.061</td>
</tr>
<tr>
<td>Ethnicity, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>2 (15.4%)</td>
<td>2 (11.8%)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>3 (23.1%)</td>
<td>6 (35.3%)</td>
<td>0.806</td>
</tr>
<tr>
<td>Hispanic</td>
<td>6 (46.1%)</td>
<td>5 (29.4%)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>2 (15.4%)</td>
<td>4 (23.5%)</td>
<td></td>
</tr>
<tr>
<td>Taking Plaquenil, n (%)</td>
<td>9 (69.2%)</td>
<td>14 (82.4%)</td>
<td>0.666</td>
</tr>
<tr>
<td>Taking Prednisone, n (%)</td>
<td>8 (61.5%)</td>
<td>11 (64.7%)</td>
<td>1.000</td>
</tr>
<tr>
<td>SLEDAI (µ ± SD)</td>
<td>10.7 ± 3.5</td>
<td>10.3 ± 4.2</td>
<td>0.784</td>
</tr>
<tr>
<td>Systolic BP (µ ± SD mm/Hg)</td>
<td>133.1 ± 15.3</td>
<td>116.6 ± 12.4</td>
<td>0.003</td>
</tr>
<tr>
<td>Diastolic BP (µ ± SD mm/Hg)</td>
<td>82.3 ± 9.5</td>
<td>70.1 ± 15.4</td>
<td>0.018</td>
</tr>
<tr>
<td>Laboratory</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum Creatinine (µ ± SD mg/dL)</td>
<td>1.2 ± 1.2</td>
<td>1.0 ± 1.2</td>
<td>0.690</td>
</tr>
<tr>
<td>Serum Albumin (µ ± SD g/dL)</td>
<td>2.8 ± 0.9</td>
<td>3.0 ± 0.4</td>
<td>0.425</td>
</tr>
<tr>
<td>Urine protein (µ ± SD g/24hr)</td>
<td>4.1 ± 3.3</td>
<td>4.2 ± 4.3</td>
<td>0.891</td>
</tr>
<tr>
<td>Serum C3, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C3 ≥ 80 mg/dL</td>
<td>1 (7.7%)</td>
<td>6 (35.3%)</td>
<td>0.104</td>
</tr>
<tr>
<td>C3 &lt; 80 mg/dL</td>
<td>12 (92.3%)</td>
<td>11 (64.7%)</td>
<td></td>
</tr>
<tr>
<td>Serum C4, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C4 ≥ 14 mg/dL</td>
<td>3 (23.1%)</td>
<td>7 (41.2%)</td>
<td>0.440</td>
</tr>
<tr>
<td>C4 &lt; 14 mg/dL</td>
<td>10 (76.9%)</td>
<td>10 (58.8%)</td>
<td></td>
</tr>
<tr>
<td>DsDNA, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low (0-75 IU/mL)</td>
<td>6 (46.1%)</td>
<td>7 (41.2%)</td>
<td></td>
</tr>
<tr>
<td>Borderline High (76-300 IU/mL)</td>
<td>5 (38.5%)</td>
<td>5 (29.4%)</td>
<td>0.721</td>
</tr>
<tr>
<td>High (&gt;300 IU/mL)</td>
<td>2 (15.4%)</td>
<td>5 (29.4%)</td>
<td></td>
</tr>
</tbody>
</table>
A New Histological Index for Predicting a Decline in Kidney Function in Patients with Lupus Nephritis. a Mexican Cohort Study of 186 Patients with a Kidney Biopsy

Marco Ulises Martinez-Martinez1, Cesar Eduardo Vallin Orozco2, David Martinez-Galla3 and Carlos Abud-Mendoza4,  
1Unidad de Investigaciones Reumatológicas, Faculty of Medicine, Universidad Autónoma de San Luis Potosí and Hospital Central, San Luis Potosí, Mexico, 2Rheumatology, Hospital Central "Dr. Ignacio Morones Prieto", San Luis Potosí, Mexico, 3Pathology, Hospital Central "Dr. Ignacio Morones Prieto", San Luis Potosí, Mexico, 4Unidad de Investigaciones Reumatológicas y Osteoporosis, Faculty of Medicine, Universidad Autónoma de San Luis Potosí and Hospital Central, San Luis Potosí, Mexico
**Background/Purpose:** The NIH indexes (of activity and chronicity) were proposed by Austin et al., in 1984. At the moment, there are therapies which can modify the histology of lupus nephritis; therefore, the markers of prognosis in the kidney biopsy may have different hazard ratios to the described by Austin et al.

**Methods:** We evaluated all the patients in whom a kidney biopsy was performed. DKF was defined as a glomerular filtration rate (GFR) of ≤ 60 ml/min/m² in two determinations in the follow-up. Histology was graded from 0-3 for glomerular or tubular abnormalities weighted by the intensity of damage. Factors associated with the development of DKF according to the different factors were evaluated through Kaplan-Meier curves and multivariate Cox regression analysis. Cox regression analysis was used to evaluate independent factors associated with the development of DKF. Independent factors in the multivariate analysis were used to construct the new index using the hazard ratio of each variable. ROC curves for survival (Heagerty et al, 2000) were used to evaluate the performance of the new index in comparison with the activity and chronicity indexes.

**Results:** We have followed 186 patients with LN and kidney biopsy, 143 (76.9%) women, mean age at kidney biopsy was 29.7 ± 12.9 years; classes of LN were: 78 patients (41.3%) class IV, 31 (16.4%) class V, 23 (12.2%) class III/V, 23 (12.2%) class IV/V, 19 (10.1%) class III, and other classes 12 patients; 135 patients (79.5%) have a minimum follow-up of 12 months. Table 1 shows the results of the univariate and the final multivariate model that was used to develop the new index. ROC curves showed AUC for detecting DKF at 12 moths for activity, chronicity and our new index of 0.59, 0.70 and 0.74 respectively. Figure 1 shows the survival according two groups: low index (new index lower than the median) and high index.

**Table1.**
<table>
<thead>
<tr>
<th>Histological feature</th>
<th>Univariate HR (CI)</th>
<th>Univariate p-value</th>
<th>Multivariate HR (CI)</th>
<th>Multivariate p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Glomerular abnormalities</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cellular proliferation</td>
<td>1.06 (0.88-1.28)</td>
<td>0.547</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Karyorrhexis</td>
<td>0.94 (0.72-1.13)</td>
<td>0.364</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Cellular crescents</td>
<td>1.09 (0.96-1.22)</td>
<td>0.364</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Hyaline thrombi</td>
<td>0.91 (0.70-1.17)</td>
<td>0.453</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Leukocyte infiltration</td>
<td>1.23 (0.97-1.57)</td>
<td>0.059</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Glomerular sclerosis</td>
<td>1.64 (1.33-2.03)</td>
<td>&lt; 0.001</td>
<td>1.48 (1.14-1.91)</td>
<td>0.003</td>
</tr>
<tr>
<td>Fibrous crescents</td>
<td>1.68 (1.27-2.21)</td>
<td>&lt; 0.001</td>
<td>1.35 (0.99-1.82)</td>
<td>0.051</td>
</tr>
<tr>
<td><strong>Tubulointerstitial abnormalities</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interstitial cell infiltration</td>
<td>1.34 (1.17-1.55)</td>
<td>&lt; 0.001</td>
<td>1.41 (1.02-1.94)</td>
<td>0.038</td>
</tr>
<tr>
<td>Interstitial fibrosis</td>
<td>1.30 (0.97-1.75)</td>
<td>0.162</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Tubular atrophy</td>
<td>1.35 (1.05-1.74)</td>
<td>0.025</td>
<td>NA*</td>
<td>NA*</td>
</tr>
</tbody>
</table>

* Tubular atrophy was no included in the final model.

**Conclusion:** We suggest predicting the risk of DKF with glomerular sclerosis, fibrous crescents, and interstitial cell infiltration. Maybe the other histological characteristics could be modified by the new therapies.

Figure 1.
Baseline Hyperuricemia As a Predictive Value for Development of Lupus Nephritis in Premenopausal SLE Patients

Doo-Ho Lim¹, Seokchan Hong², Ji Seon Oh³, Yong-Gil Kim², Chang Keun Lee², Seung Won Choi¹ and Bin Yoo²,
¹Division of Rheumatology, Department of Internal Medicine, University of Ulsan College of Medicine, Ulsan University Hospital, Ulsan, Korea, Republic of (South), ²Division of Rheumatology, Department of Internal Medicine, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea, Republic of (South), ³Division of Rheumatology, Department of Internal Medicine, National Medical Center, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Although lupus nephritis is a common and serious manifestation of SLE, there have been few predictive markers for development of lupus nephritis in SLE patients. Serum uric acid level is affected by decreased renal function, besides several factors such as old age, male, menopause, and drugs. However, it is not yet well known whether hyperuricemia is independently associated with lupus nephritis in SLE patients with normal glomerular filtration rate (GFR). The aim of this study was to evaluate the association of baseline serum uric acid level and development of lupus nephritis.

Methods: We retrospectively reviewed electronic medical records of 101 female SLE patients whose ages at the time of diagnosis (baseline) were 45 years old or below in a tertiary medical center from January 2000 to March 2015. SLE with renal involvement was diagnosed when patients met the 2015 ACR/SLICC revised criteria for diagnosis of SLE. We compared baseline serum uric acid levels of the SLE patients who had nephritis at the time of diagnosis or later (nephritis group) with the patients who had not developed nephritis (non-nephritis group) during follow-up period.

Results: Among 101 patients, 22 (22%) had hyperuricemia at baseline and 45 (45%) had developed lupus nephritis during follow-up period (median 6.1 years). There were significant differences in baseline serum uric acid level, GFR, anti-dsDNA antibody and complement level between non-nephritis group and nephritis group (Table). Interestingly, among 59 patients with normal renal function (baseline GFR > 90 mL/min/1.73m²), baseline serum uric acid level was also significantly higher in the nephritis group than non-nephritis group (Figure 1). Moreover, the patients with hyperuricemia (uric acid > 6 mg/dL) at baseline were more likely to develop lupus nephritis than those without hyperuricemia during follow-up period (64% vs. 39%, p = 0.042) (Figure 2).

Conclusion: These findings suggest that high serum uric acid level at the time of diagnosis may be independently associated with lupus nephritis even in SLE patients with normal GFR. More careful evaluation would be required for development of lupus nephritis in hyperuricemic patients.
| Table. Baseline Characteristics of Study Patients with Systemic Lupus Erythematosus. |
|----------------------------------|-------------------------------|-----------------|--------|
|                                  | Non-nephritic group | Lupus nephritic group | $p$   |
| All patients (%)                 | 56 (55)              | 45 (45)            |        |
| Sex: Female (%)                  | 56 (100)             | 45 (100)           |        |
| Age, years                       | 28.2 ± 6.3           | 28.9 ± 7.6         | 0.660  |
| Body Mass Index, kg/m$^2$        | 21.2 ± 3.8           | 22.0 ± 3.0         | 0.105  |
| Follow-up, years                 | 6.0 ± 4.3            | 7.5 ± 4.3          | 0.068  |
| Serum Uric Acid, mg/dL          | 4.5 ± 1.6            | 5.5 ± 1.5          | 0.003  |
| eGFR, mL/min/1.73m$^2$           | 103.1 ± 24.9         | 85.6 ± 27.0        | 0.001  |
| anti-dsDNA, IU/mL                | 56.4 ± 107.9         | 141.8 ± 163.4      | 0.001  |
| C3, mg/dL                        | 80.1 ± 32.3          | 48.6 ± 30.2        | 0.000  |
| C4, mg/dL                        | 14.0 ± 6.3           | 9.6 ± 6.2          | 0.005  |
| Drugs that may increase serum uric acid level$^1$(%) | 5 (6.9)            | 2 (4.4)            | 0.626  |
| Drugs that may decrease serum uric acid level$^2$(%) | 1 (1.8)            | 0 (0.0)            | 1.000  |

<table>
<thead>
<tr>
<th>Patients with normal renal function (baseline GFR&gt;90%) (%)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Uric Acid, mg/dL</td>
<td>4.3 ± 1.4</td>
</tr>
<tr>
<td>eGFR, mL/min/1.73m$^2$</td>
<td>113.0 ± 15.6</td>
</tr>
<tr>
<td>anti-dsDNA, IU/mL</td>
<td>56.2 ± 111.0</td>
</tr>
<tr>
<td>C3, mg/dL</td>
<td>75.3 ± 35.0</td>
</tr>
<tr>
<td>C4, mg/dL</td>
<td>13.3 ± 7.8</td>
</tr>
</tbody>
</table>

Values are mean ± SD or number (%).

BMI = body mass index, GFR = glomerular filtration rate

1) Diuretics, aspirin, pyrazinamids, or cyclospoine
2) Allopurinol, febuxostat, benzbrumarone, losartan, fenofibrate, or atorvastatin.

**Figure 1.** Comparison of baseline serum uric acid levels between patients with normal renal function (GFR>90%) who had developed nephritis and who had not developed nephritis.
Disclosure: D. H. Lim, None; S. Hong, None; J. S. Oh, None; Y. G. Kim, None; C. K. Lee, None; S. W. Choi, None; B. Yoo, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/baseline-hyperuricemia-as-a-predictive-value-for-development-of-lupus-nephritis-in-premenopausal-sle-patients

Abstract Number: 673

Cell Bound Complement Activation Products Distinguish Systemic Lupus Erythematosus from Other Diseases Among Patients with High Antinuclear Antibody Titer and Normal Complement

Daniel J. Wallace1, Elena Massarotti2, Rosalind Ramsey-Goldman3, Christopher E. Collins4, Anca Askanase5, Jill P. Buyon6, Richard Furie7, Sonali Narain7, Amit Saxena8, Kenneth C. Kalunian9, Cristina Arriens10, Chaim Putterman11, John Conklin12, Roberta Alexander12, Claudia Ibarra12, Tyler O'Malley13, Tarun Chandra14, Joseph Ahearn15, Susan Manzi16, Arthur Weinstein17 and Thierry Dervieux12,

1Cedars-Sinai Medical Center, UCLA, Los Angeles, CA,
2Brigham and Women's Hospital, Boston, MA, 3FSM, Northwestern University, Chicago, IL, 4Rheumatology, MedStar Washington Hospital Center, Washington, DC, 5Department of Medicine, Rheumatology, Columbia University College of Physicians & Surgeons, New York, NY, 6Rheumatology, NYU Langone Medical Center, New York, NY, 7Northwell Health, Great Neck, NY, 8NYU Langone Medical Center, New York, NY, 9Division of Rheumatology, Allergy and Immunology, UCSD School of Medicine, La Jolla, CA, 10Arthritis & Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, 11Division of Rheumatology, Albert Einstein College of Medicine, Bronx, NY, USA, Bronx, NY, 12Exagen Diagnostics, Inc., Vista, CA, 13Research and Development, Exagen Diagnostics, Inc., Vista, CA, 14Empiriqua LLC, Long Grove, IL, 15Lupus Center of Excellence, West Penn Allegheny Health System, Pittsburgh, PA, 16Medicine, Allegheny Health Network, Pittsburgh, PA, 17Rheumatology, MedStar Washington Hospital Center/Georgetown University Medical Center, Washington, DC

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Background/Purpose: Patients are often referred to the rheumatologist because of elevated anti-nuclear antibody (ANA) titers. We sought to evaluate the association of cell bound complement activation products (CB-CAPs), low complement (C3 or C4), and anti-double stranded (ds) DNA with systemic lupus erythematosus (SLE) and ANA titers.

Methods: The cohort (n=1155 adults) consisted of 498 patients with SLE with established disease (all fulfilling the 1997 ACR criteria, 91% females, mean age 41 years) pooled from prior studies of complement activation products, and a control group of 657 subjects (86% females; mean age 56 years; 314 with rheumatoid arthritis and 343 with other diseases). Abnormal CB-CAPs consisted of C4d bound to erythrocyte or B-lymphocyte levels above the 99th percentile of normal healthy. Low complement (C3 or C4) and anti-dsDNA (all confirmed using Crithidia luciliae) were determined using immunoassays. ANA titers were determined by indirect immunofluorescence, with subjects classified as having negative (<1:80), intermediate (1:80 to 1:320) or high (≥1:640) ANA status. The sensitivity, specificity, and Youden’s index (J), a measure of diagnostic effectiveness that combines sensitivity and specificity (J = sensitivity + specificity - 1) of various markers in distinguishing SLE from non-SLE, were evaluated. J differences were tested using t-tests.

Results: The diagnostic effectiveness of abnormal CB-CAPs, low complement, and anti-dsDNA in distinguishing SLE from non-SLE is presented in the Table. Overall, abnormal CB-CAPs had a significantly greater association with SLE (J=0.51) than low complement (J=0.32) and anti-dsDNA (J=0.31) (p<0.01; n=1155). The greater association of abnormal CB-CAPs in comparison to low complement and anti-dsDNA was statistically significant in the group of subjects with high ANA (p<0.03), intermediate ANA (p<0.01), and negative ANA (p<0.02). This association was also seen among subjects with high ANA (J=0.60) compared to intermediate (J=0.45) and negative ANA (J=0.17) (p<0.01). Similar results were observed for low complement and anti-dsDNA (p<0.01). In the group of subjects with normal complement (309 SLE and 619 non SLE), abnormal CB-CAPs was 50% sensitive and 89% specific while anti-dsDNA was 20% sensitive and 99% specific (J=0.39 vs 0.19; p<0.01). In the subset of subjects with high ANA and normal complement (117 SLE and 106 non SLE), abnormal CB-CAPs was 68% sensitive and 82% specific and yielded higher diagnostic value than anti-dsDNA (40% sensitive and 93% specific) (J=0.50 vs 0.34; p<0.01).

Conclusion: Abnormal CB-CAPs has higher diagnostic performances for SLE than low complement and anti-dsDNA and is a sensitive and specific measure for SLE in patients with high ANA titers and normal complement levels.

<table>
<thead>
<tr>
<th></th>
<th>Negative ANA</th>
<th>Intermediate ANA</th>
<th>High ANA</th>
<th>All ANA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-dsDNA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Se</td>
<td>64.2%</td>
<td>84.3%</td>
<td>51.4%</td>
<td>54.4%</td>
</tr>
<tr>
<td>Sp</td>
<td>99.0%</td>
<td>100.0%</td>
<td>44.7%</td>
<td>99.0%</td>
</tr>
<tr>
<td>J</td>
<td>0.02±0.02</td>
<td>0.17±0.03</td>
<td>0.46±0.04</td>
<td>0.21±0.02</td>
</tr>
<tr>
<td>Low complement</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Se</td>
<td>68.3%</td>
<td>74.1%</td>
<td>51.3%</td>
<td>58.2%</td>
</tr>
<tr>
<td>Sp</td>
<td>95.1%</td>
<td>94.2%</td>
<td>94.2%</td>
<td>94.1%</td>
</tr>
<tr>
<td>J</td>
<td>0.02±0.03</td>
<td>0.28±0.04</td>
<td>0.45±0.04</td>
<td>0.32±0.02</td>
</tr>
<tr>
<td>Abnormal CB-CAPs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Se</td>
<td>62.5%</td>
<td>50.4%</td>
<td>77.3%</td>
<td>62.2%</td>
</tr>
<tr>
<td>Sp</td>
<td>86.2%</td>
<td>82.4%</td>
<td>89.1%</td>
<td>89.1%</td>
</tr>
<tr>
<td>J</td>
<td>0.11±0.03</td>
<td>0.52±0.06</td>
<td>0.60±0.05</td>
<td>0.31±0.02</td>
</tr>
</tbody>
</table>

Table: Performance characteristics (Sensitivity [Se], Specificity [Sp], Youden’s Index [J]) by ANA status.

Disclosure: D. J. Wallace, Exagen, 2,Exagen, 5; E. Massarotti, Exagen, 2; R. Ramsey-Goldman, Exagen, 2; C. E. Collins, Exagen, 2,Exagen, 8; A. Askarane, Exagen, 2, J. P. Buyon, Exagen, 2; R. Furie, Exagen, 2; S. Narain, Exagen, 2; A. Saxena, Exagen, 2; K. C. Kalunian, Exagen, 2; C. Arriens, Exagen, 2; C. Putterman, Exagen, 2; J. Conklin, Exagen, 3; R. Alexander, Exagen, 3; C. Ibarra, Exagen Diagnostics, Inc., 3; T. O’Malley, Exagen Diagnostics, 3; T. Chandra, Exagen, 5; J. Ahearn, Exagen, 2,Exagen, 5,Exagen, 7; S. Manzi, Exagen, 2,Exagen, 7,Exagen, 5; A. Weinstein, Exagen, 2,Exagen, 5,Exagen, 9; T. Dervieux, Exagen, 3.

Identification of IRAK4-Dependent Gene Signature As a Biomarker Candidate for IRAK4 Small-Molecule Inhibitor in Systemic Lupus Erythematosus

Abstract Number: 674
Background/Purpose: Systemic Lupus Erythematosus (SLE) is a heterogeneous disease. Interleukin-1 receptor-associated kinase 4 (IRAK4) activity is predicted to affect multiple pathogenic pathways in SLE\(^1\). We hypothesized that coordinated expression of IRAK4-regulated genes reflective of toll-like receptor (TLR) and other upstream stimulation will reflect activity of the pathway. We aimed to identify a TLR7/8-induced gene signature to identify SLE patients who are more likely to respond to the inhibition of the IRAK4 pathway.

Methods: To determine candidate genes, we first identified those with impaired response to TLR7 or 8 stimulation by R848 in patients carrying loss-of-function mutations in IRAK4 (analyzed from GEO: GSE 25742)\(^2\). We then selected differentially-expressed genes that also showed elevated baseline expression in SLE blood vs. healthy controls in 2 datasets: PBMC microarray data from an extra-renal SLE cohort (SLE n=61, HC=20) and whole blood (WB) RNA sequencing data from a second extra-renal cohort (SLE n=103; HC= 19)\(^3\). We then confirmed these genes underwent dose-dependent down-regulation in response to R848 in healthy human WBs treated with selective IRAK4 small molecule inhibitor (SMI) compounds.

Results: Our analysis of the GSE 25742 microarray dataset showed 285 genes that displayed significantly lower induction by R848 in the whole blood from IRAK4-deficient patients vs. healthy controls (FDR<0.05; FC>1.25). The IRAK4-deficient patients did not upregulate type I interferons (IFNs) in response to R848. Baseline levels of 44 differentially-expressed genes were up-regulated in blood from SLE vs. healthy controls in both SLE cohorts analyzed. We further observed that 9 genes were down-regulated in a dose-dependent manner by 2 distinct IRAK4 SMI compounds in the human whole blood assay. These genes formed an inter-correlating signature in SLE patient blood, and partially overlapped with the interferon signature. Significant positive correlations were observed between top candidate genes and ISM status, anti-dsDNA status, and levels of BAFF, anti-RNP and anti-Sm, while significant negative correlations were observed between the candidate genes and levels of C3 and C4 in both SLE datasets.

Conclusion: We have identified a set of IRAK4-dependent genes with an inter-correlating signature and partial overlap with the interferon signature, that could potentially serve as biomarkers of the IRAK4 pathway in SLE patient blood samples.

Disclosure: A. F. Setiadi, Roche Pharmaceuticals, 3, Roche Pharmaceuticals, 1; K. Senger, Roche Pharmaceuticals, 3, Roche Pharmaceuticals, 1; J. Hackney, Roche Pharmaceuticals, 3, Roche Pharmaceuticals, 1; N. Zuckerman, Roche Pharmaceuticals, 3, Roche Pharmaceuticals, 1; S. Sujatha-Bhaskar, Roche Pharmaceuticals, 3, Roche Pharmaceuticals, 1; G. Francis, Roche Pharmaceuticals, 3, Roche Pharmaceuticals, 1; M. Bryan, Roche Pharmaceuticals, 3, Roche Pharmaceuticals, 1; H. Brightbill, Roche Pharmaceuticals, 3, Roche Pharmaceuticals, 1; A. A. Zarrin, Roche Pharmaceuticals, 3, Roche Pharmaceuticals, 1; M. J. Townsend, Roche Pharmaceuticals, 1, Roche Pharmaceuticals, 3.

Tissue-Based Biomarkers in Cutaneous Lupus Erythematosus: Type I IFN Responsive Protein Mxa and a Marker for Lymphocytic Inflammation
(CD45) Correlate with CLASI Cross-Sectionally and Longitudinally

Taylor L. Reynolds1, Carrie Wager1, Stefan Hamann1, Xueli Zhang1, Galina Marsh1, Cristina Musselli1, Nathalie Franchimont1, Agnes Gardet1, Robert Dunstan2, Dania Rabah1 and Victoria P Werth3, 1Biogen, Cambridge, MA, 2Abbvie, Worcester, MA, 3University of Pennsylvania and the VA Medical Center, Philadelphia, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Cutaneous lupus erythematosus (CLE) is the cutaneous manifestation of SLE, affecting 85% of patients1. CLE is subdivided into acute, subacute and chronic/discard forms. Discoid lupus erythematosus (DLE) can present in the absence of SLE, but up to 28% of DLE subjects will progress to SLE2. CLE lesions are characterized by interface dermatitis and a dermal perivascular immune infiltrate consisting largely of lymphocytes and histiocytes, with relatively large numbers of plasmacytoid dendritic cells (pDCs), with or without fibrosis. As robust producers of type I interferon, pDCs may play a central role in the pathogenesis of CLE lesions. To monitor the effect of therapeutic pDC-specific inhibition, we aimed to develop quantitative interlesional measures of immune infiltrate and Type I IFN pathway related proteins.

Methods: Patients with lesions consistent with a diagnosis of CLE and treated according to standard of care were recruited by the Perelman Center for Advanced Medicine at the University of Pennsylvania. Enrolled patients presented with subacute, chronic (other than discoid) or discoid forms of CLE with or without systemic lupus erythematosus as defined by ≥4 out of 11 classification criteria (n=10 subjects who met SLE criteria out of a total of n=19, mean CLASI = 14.21 (range=1-29). At baseline and week 12, 3-5 mm punch biopsies from active CLE lesions were collected and used for immunohistochemistry with anti-MxA (MX dynamin-like GTPase), CD45 (hematopoietic cells) and CD303 (BDCA-2) antibodies. Glass slides were examined, then digitized. Using custom-designed algorithms in Visiopharm (Denmark) software, percent areas were quantified as the portion of immunoreactive area / total tissue area for epidermis, papillary dermis and reticular dermis. R and p represent Pearson correlation and p-values.

Results: At baseline (n=19 subjects), CLASI correlated with relative area of epidermal (but not dermal) CD45 (r=0.72, p=0.0005) and MxA (r=0.61, p=0.0056). Also at baseline, relative area of CD303 correlated with MxA in all skin regions. Compared with papillary and reticular dermis, MxA was enriched in epidermis. In contrast, CD45+ and CD303+ cells were most plentiful in papillary and reticular dermis. Biopsies from the second visit (week 12) were available for 14 subjects. When all skin regions were combined, longitudinal change in CLASI correlated with change in CD45+ (r=0.59, p=0.0255) and MxA+ relative areas (r=0.61, p=0.0218).

Conclusion:

At a single time point and as indicators of longitudinal change, relative areas of MxA and CD45 are useful tissue-based biomarkers. They can be used to complement CLASI in the setting of a clinical trial. These findings warrant investigation of tissue-based quantification of CD45 and MxA for stratification of CLE patients and to augment biopsy evaluation in the diagnostic setting.


Disclosure: T. L. Reynolds, Biogen Idec, 3, Biogen Idec, 1; C. Wager, Biogen Idec, 3, Biogen Idec, 1; S. Hamann, Biogen Idec, 3, Biogen Idec, 1; X. Zhang, Biogen Idec, 3, Biogen Idec, 1; G. Marsh, Biogen Idec, 3, Biogen Idec, 1; C. Musselli,
Immunosignature Autoantibody Profiles Provide Mechanistic Insight into Systemic Lupus Erythematosus and Differentiation from Symptomatically Overlapping Diseases

Theodore M. Tarasow¹, Robert Gerwien¹, Jonathan Melnick¹, Scott A. Melville¹ and Chaim Putterman², ¹HealthTell, Inc., San Ramon, CA, ²Division of Rheumatology, Albert Einstein College of Medicine, Bronx, NY, USA, Bronx, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Diagnosis and monitoring of patients with SLE usually requires careful evaluation by a rheumatologist. However, difficulties in accurately quantifying disease and treatment response can make patient care subjective and inconsistent. A quantitative and reproducible test that facilitates SLE differential diagnosis and disease stratification may help decrease time to definitive diagnosis and improve treatment outcomes.

The Immunosignature (IS) technology uses a high-density array of 126,000 unique peptides designed to survey an individual’s antibody repertoire. For autoimmune diseases, differential antibody binding profiles have the potential to provide accurate differential diagnosis, disease activity, and progression measures as well as provide more comprehensive autoantigen profiles.

The objective of this study was to use the IS technology to differentiate and characterize the autoantibody profiles in subjects with SLE from healthy controls and subjects with inflammatory and non-inflammatory diseases that share symptoms with SLE patients.

Methods:
A well-annotated cohort of 371 serum samples was prospectively collected and included patients with SLE (n=75), RA (n=95), SS (n=20), OA (n=24), FM (n=22), other disease (OD) (n=76) and healthy controls (HC) (n=59). Subjects with rheumatological diseases were diagnosed based on ACR criteria. There were no significant differences in gender, race or ethnicity across all groups. Antibody (IgG)-peptide binding with significant intensity differences between contrasting groups was identified by Bonferroni adjusted t-test. Support vector machine classifiers were trained using the most distinguishing peptides. Classifier performance was evaluated by a cross-validation routine that included feature selection, model training and testing. Distinguishing peptides were mapped to putative autoantigens using a BLAST routine modified for array amino acid composition.

Results:
The number of peptides significantly different between SLE contrasts and the cross validated classification performance as measured by the area under the curve (AUC) are shown in the Table. Significant peptides associated with SLE were
mapped to known and novel putative autoantigens, including a known immunogenic epitope of SS-B.

<table>
<thead>
<tr>
<th>Contrast</th>
<th># Samples</th>
<th>Significant Peptides</th>
<th>cvAUC (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLE vs. HC</td>
<td>134</td>
<td>5,121</td>
<td>0.90 (0.88-0.92)</td>
</tr>
<tr>
<td>SLE vs. All Disease*</td>
<td>312</td>
<td>684</td>
<td>0.79 (0.77-0.81)</td>
</tr>
<tr>
<td>SLE vs. RA</td>
<td>170</td>
<td>201</td>
<td>0.80 (0.76-0.85)</td>
</tr>
<tr>
<td>SLE vs. OA</td>
<td>99</td>
<td>455</td>
<td>0.88 (0.86-0.91)</td>
</tr>
<tr>
<td>SLE vs. FM</td>
<td>97</td>
<td>464</td>
<td>0.83 (0.78-0.87)</td>
</tr>
<tr>
<td>SLE vs. SS</td>
<td>95</td>
<td>0</td>
<td>0.65 (0.60-0.70)</td>
</tr>
</tbody>
</table>

*All Disease = SLE, SS, OA, FM, and OD (PsA (11), gout (9), scleroderma (7), DM (6), PM (5), other connective tissue disorders (38 total, <5 each)).

**Conclusion:**

Based on these observations, the IS technology can be used to classify subjects with SLE from healthy controls or subjects with diseases that have common symptoms or are similarly characterized by underlying immunological dysregulation. The ability to broadly survey the antibody repertoire within and between diseases allows for the identification of putative autoantigens and may provide additional approaches to subsetting patients. These results need verification in cohorts from other sites and validation in blinded studies.

**Disclosure:** T. M. Tarasow, HealthTell, 3, HealthTell, 1; R. Gerwien, HealthTell, 3, HealthTell, 1; J. Melnick, HealthTell, 3, HealthTell, 1; S. A. Melville, HealthTell, 3, HealthTell, 1; C. Putterman, HealthTell, 2, HealthTell, 5.

**Abstract Number:** 677

**Soluble Urokinase Plasminogen Activator Receptor (suPAR) Predicts the Development of Organ Damage over 5 Years in Systemic Lupus Erythematosus: Results from the Systemic Lupus International Collaborating Clinics (SLICC) Inception Cohort**

Helena Enoesson1, Lina Wiresam1, Jonas Wetterö1, Thomas Skogh1, Ian N. Bruce2,3, and Christopher Sjöwall4,
1Rheumatology, Division of Neuro and Inflammation Sciences, Department of Clinical and Experimental Medicine, Linköping University, Linköping, Sweden, Linköping, Sweden, 2Central Manchester University Hospital NHS Foundation Trust and Manchester Academic Health Science Centre, Arthritis Research UK Epidemiology Unit, The University of Manchester, Manchester Academic Health Sciences Centre, Manchester, United Kingdom, 3NIHR Manchester Musculoskeletal Biomedical Research Centre, Central Manchester University Hospitals NHS Foundation Trust, Manchester, United Kingdom, 4Department of Clinical and Experimental Medicine, Linköping University, Sweden, Linköping, Sweden

**First publication:** September 18, 2017
Background/Purpose:

The urokinase plasminogen activator receptor (uPAR) is expressed on various cell types and plays important roles in proteolysis, migration and adhesion. Receptor shedding yields a soluble form (suPAR) that has emerged as a promising severity biomarker in malignancies, inflammatory and infectious diseases. Previously, suPAR was shown to reflect accumulated organ damage in systemic lupus erythematosus (SLE). Our aim was to investigate suPAR as a potential predictor of future organ damage in well-characterized patients with recent-onset SLE.

Methods:

A total of 345 patients with SLE (≥4 ACR criteria) were included in this study. All patients originated from the SLICC inception cohort and were selected based on a minimum of 5-years follow-up and absence of organ damage (SLICC/ACR damage index; SDI>0) at inclusion. The patients were enrolled within 15 months of SLE diagnosis. Plasma creatinine was available for 180 patients and estimated glomerular filtration rate (eGFR) was calculated according to the MDRD 4-Variable Equation. Serum suPAR levels were measured by ELISA (Virogates, Birkerod, Denmark) at inclusion only, and levels at inclusion were related to SDI after 5-years of follow-up. Age- and sex-matched controls (1:1) were from the Swedish population.

Results:

Baseline suPAR levels were higher in patients who acquired damage (SDI >1) over a 5-year period (n=33) compared to patients without damage development (n=246; p<0.001) and controls (n=345; p=0.007) (Fig. 1). There were no significant differences in suPAR levels with regard to ethnicity (Caucasians vs. non-Caucasians) or sex in patients and controls, but there was a weak correlation between age and suPAR among controls (p<0.001, r=0.23). No correlations (r>0.2) were found between suPAR and disease activity (SLEDAI-2K), corticosteroid dose or eGFR in patients. Logistic regression revealed significant impact of baseline suPAR on future damage (SDI>1) (p=0.014; area under curve, AUC=0.64) and the predictive value became stronger after adjustment for age, sex, ethnicity and corticosteroid dose (p=0.008; AUC=0.74). Examining the components of the SDI individually revealed significant impact of suPAR on damage in the musculoskeletal domain (SDI≥1) (p=0.018; AUC=0.66) also when adjusting for covariates (p=0.020; AUC=0.68).

Conclusion:

Prognostic biomarkers of disease severity in SLE could identify patients in need of tight control and improved treatment strategies. suPAR has become an interesting option for patient triaging and prognostication in various diseases, and here, for the first time, it is shown to have predictive potential of damage accrual in SLE. Continued follow-up of patients could elucidate the association between suPAR and damage in specific organ domains. Furthermore, the possible role of suPAR as a causative agent in SLE organ damage remains to be investigated.
Disclosure: H. Enocsson, None; L. Wirestam, None; J. Wetterö, None; T. Skogh, None; I. N. Bruce, None; C. Sjöwall, None.


Abstract Number: 678

Systemic Hypertension Is Associated with Presence of Vascular Injury on Lupus Nephritis Renal Biopsies: A Retrospective Cohort Study

Cianna Leatherwood, Brigham and Women's Hospital, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Vascular injury in lupus nephritis is often described on renal biopsy, but its clinical correlates are not well understood. Recent evidence suggests it may be associated with poorer prognosis. We retrospectively investigated clinical and laboratory characteristics associated with vascular injury on renal biopsy among patients diagnosed with lupus nephritis.

Methods: We reviewed initial renal biopsy reports performed at a single academic medical center between 1996 and 2015 showing Class II-VI lupus nephritis. Experienced pathologists interpreted the histologic findings. Vascular injury was defined as arterial or arteriolar thickening of the intima without thrombosis, necrosis or proliferation. The extent of vascular injury was described as absent, mild, moderate, or severe. Clinical variables including i) hypertension (systolic blood pressure ≥ 140mmHg or diastolic blood pressure ≥90mmHg), ii) demographics, iii) serum laboratories at the time of biopsy and iv) medications for 30 days prior to the biopsy were obtained from the medical records. We used univariable analyses and multivariable logistic regression to model risk of vascular injury on biopsy.
**Results:** Among 155 initial lupus nephritis biopsies 103 exhibited vascular injury. The average age was 39 years, 84% were female, 42% were African American and dsDNA was positive in 84%. ISSN lupus nephritis biopsy classes overall were 14% II, 26% III, 33% IV and 26% V, and class was not statistically associated with presence of vascular injury. There were no statistically significant differences in duration of SLE at biopsy or prior medications between biopsies with or without vascular injury (Table). Vascular injury was associated with older age [39 (±13) vs. 34 years (±11), p 0.02], elevated creatinine [1.8 vs 0.97 mg/dL, p 0.0006] and hypertension (36% vs. 19%, p 0.03) in univariable analyses. Presence of antiphospholipid antibodies and treatment with high dose glucocorticoids, immunosuppressants and ACE inhibitors at the time of biopsy did not differ between groups. Hypertension remained a strong correlate of vascular injury in a multivariable model controlling for age, race, sex and creatinine [OR 1.32 (95% CI 1.08, 1.62)].

**Conclusion:** Systemic hypertension was associated with vascular injury on lupus nephritis renal biopsy in this study. Further work in characterizing any differences in vascular lesions among patients with and without lupus nephritis is necessary as understanding the pathogenesis of these lesions may give insight into novel treatment pathways. These findings may support the importance of aggressive blood pressure management in patients with lupus nephritis.
Table. Univariable Analyses of Clinical Factors Potentially Associated with Vascular Injury on 155 Initial Lupus Nephritis Biopsies

<table>
<thead>
<tr>
<th></th>
<th>Vascular Injury (n=103)</th>
<th>No Vascular Injury (n=52)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean</td>
<td>39 (±13)</td>
<td>34 (±11)</td>
<td>0.02</td>
</tr>
<tr>
<td>Duration of SLE at biopsy (years), mean</td>
<td>7.8 (±8)</td>
<td>5.5 (7)</td>
<td>0.16</td>
</tr>
<tr>
<td>Female</td>
<td>87 (84%)</td>
<td>45 (87%)</td>
<td>0.73</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td>0.11</td>
</tr>
<tr>
<td>White</td>
<td>32 (33%)</td>
<td>18 (35%)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>41 (42%)</td>
<td>12 (24%)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>9 (9%)</td>
<td>9 (18%)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>15 (15%)</td>
<td>10 (20%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1 (1%)</td>
<td>2 (4%)</td>
<td></td>
</tr>
<tr>
<td>Laboratory Values</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin (g/dL), mean</td>
<td>10.7 (2)</td>
<td>10.7 (2)</td>
<td>0.96</td>
</tr>
<tr>
<td>Anti-dsDNA (IU/mL), median</td>
<td>141 [43, 454]</td>
<td>254 [50, 1000]</td>
<td>0.14</td>
</tr>
<tr>
<td>Anti-RNP positive</td>
<td>39 (42%)</td>
<td>23 (49%)</td>
<td>0.4</td>
</tr>
<tr>
<td>Antiphospholipid Antibodies**</td>
<td>22 (28%)</td>
<td>13 (28%)</td>
<td>0.98</td>
</tr>
<tr>
<td>C4 (mg/dL), mean</td>
<td>14 (12)</td>
<td>11 (8)</td>
<td>0.26</td>
</tr>
<tr>
<td>Creatinine (mg/dL), mean</td>
<td>1.8 (±2)</td>
<td>0.97 (±1)</td>
<td>0.0006</td>
</tr>
<tr>
<td>Clinical Data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior high dose glucocorticoids***</td>
<td>28 (31%)</td>
<td>17 (35%)</td>
<td>0.61</td>
</tr>
<tr>
<td>Prior immunosuppression****</td>
<td>21 (23%)</td>
<td>10 (21%)</td>
<td>0.73</td>
</tr>
<tr>
<td>Prior ACE Inhibitor</td>
<td>29 (32%)</td>
<td>18 (38%)</td>
<td>0.53</td>
</tr>
<tr>
<td>SBP ≥140mmHg or DBP≥ 90mmHg</td>
<td>38 (36%)</td>
<td>10 (19%)</td>
<td>0.03</td>
</tr>
<tr>
<td>SLICC score, median</td>
<td>3 [1, 6]</td>
<td>2.5 [1,6]</td>
<td>0.14</td>
</tr>
</tbody>
</table>

*Continuous variables evaluated with t-test or Wilcoxon and binary and categorical variables were assessed using chi-squared tests or Fisher’s exact as appropriate.

** positive vs. negative or not tested

*** glucocorticoid ≥20mg/day for past 30 days

**** receiving azathioprine, cyclophosphamide, mycophenolate mofetil, rituximab, cyclosporine or tacrolimus at the time of biopsy

Disclosure: C. Leatherwood, None;


Abstract Number: 679
Distinct Interferon Scores Are Separately Associated with Activity and Long Term Sequelae in SLE

Katherine Dutton1, Antonios Psarras2, Md Yuzaiful Md Yusof2, Paul Emery3, Yasser M El-Sherbiny4 and Edward M Vital1, 1University of Leeds, Leeds, United Kingdom, 2Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom, 3NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom, 4NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals, NHS Trust, Leeds, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Type I interferon (IFN-I) has a crucial role in the pathogenesis and activity of Systemic Lupus Erythematosus (SLE). IFN-I targeted therapies are currently in phase III clinical trials. Early findings suggest that anti-INF-I therapy responses are superior in individuals with high INF-I signature. In established SLE, the level of IFN-I activity can be measured using an interferon gene expression score. We previously described two independent interferon gene expression scores that we called Score A and B. We also previously described a memory B cell flow cytometric marker (Tetherin) that can be used to measure IFN-I response in B cells. We aimed to describe the clinical phenotype of IFN-high SLE patients and to correlate this with Score A, Score B and Tetherin levels.

Methods: IFN gene expression Scores A and B as well as memory B cell tetherin were measured in 156 consecutive SLE patients attending the Leeds SLE clinic. For this preliminary analysis, we selected 59 patients across a spectrum of levels of IFN assays for detailed retrospective notes review.

Results:
**Characteristic** | **Internal organ involvement** | **Previous cyclophosphamide** | **Cardiovascular Disease** | **Objective flare 3 months before or after test** | **Increased glucocorticoid dose 3 months before or after test**
---|---|---|---|---|---
Number of patients | 21 | 13 | 5 | 18 | 15

**Objective** flare 3 months before or after test

**Increased glucocorticoid dose 3 months before or after test**

**Number of patients**

<table>
<thead>
<tr>
<th></th>
<th>Yes (n=)</th>
<th>No</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFN Score A median (IQR)</td>
<td>0.02 (0.40)</td>
<td>0.124</td>
<td>0.913</td>
</tr>
<tr>
<td>INF Score B median (IQR)</td>
<td>0.12 (0.33)</td>
<td>0.12 (0.33)</td>
<td>0.17 (0.30)</td>
</tr>
<tr>
<td>Memory B cell tetherin median (IQR)</td>
<td>1318 (2176)</td>
<td>1714 (2866)</td>
<td>1537 (2787)</td>
</tr>
</tbody>
</table>

* numerically there was a stepwise increase in score B comparing 0, 1 and 2 internal organs affected but not statistically significant.

**There were also significant correlations between average dose of prednisolone in over 3 months before and after the sample date and IFN Score A (Rho = 0.402, p=0.014) and memory B cell tetherin (Rho = 0.537, p<0.001)

There was no substantive relationship between interferon assays and number of previous oral immunosuppressants. There was a trend to higher tetherin levels in patients with exposure to 1 or more antimalarials (p=0.068).

**Conclusion:** High interferon is associated with more severe disease. We observed a stronger relationship between Score A and tetherin with parameters that reflect current disease activity, while long term sequelae were more clearly associated with Score B. Interferon assays may allow clinicians to better stratify SLE patients for therapy and severity prediction.

**Disclosure:** K. Dutton, AstraZeneca, 2; A. Psarras, None; M. Y. Md Yusof, None; P. Emery, AstraZeneca, 2, Roche Pharmaceuticals, 2; Y. M. El-Sherbiny, None; E. M. Vital, Roche, GSK and AstraZeneca, 2.


**Abstract Number:** 680

**Abnormalities in Complement System Are Related to Disease Severity in Systemic Lupus Erythematosus (SLE)**

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: We sought to evaluate the relationships between low complement C3 and C4 proteins, abnormal complement activation (cell-bound complement activation products [CB-CAPs]), and a Lupus Severity Index (LSI) instrument recently developed.

Methods: The study was multi-centered and enrolled 500 SLE subjects (mean age 41.0±0.6 [SEM] years; 91% female; mean disease duration 10.9±0.4 years), all fulfilling the 1982 American College of Rheumatology (ACR) criteria revised in 1997. LSI was determined using the ACR criteria and sub-criteria elements collected from medical records as described (Bello et al., Lupus Science & Medicine 2016;3:e000136). Serum C3 and C4 levels were determined using standard immunochemistry techniques. Complement activation was assessed by quantitative flow cytometry, and abnormal activation was defined as levels of C4d bound to erythrocyte (EC4d) or B-lymphocytes (BC4d) above the 99th percentile of a control group of normal healthy individuals (>14 and >60 net mean fluorescence intensity [MFI], respectively). Multivariate linear regression analysis was used to evaluate the contributions of low complement and abnormal CB-CAPs to LSI, with age and disease duration as covariates. Pearson's Chi-Square and Kruskal Wallis ANOVA tests were used as appropriate for group comparisons.

Results: In this cohort, median LSI score was 0.596 points (range 0.327-0.938 points, first tertile: 0.544; second tertile: 0.792). Multivariate linear regression analysis revealed that higher LSI scores were associated with abnormal CB-CAPs (estimate=0.063±0.015 points; p<0.01), low complement (estimate=0.030±0.015; p=0.048), younger age (estimate=−0.026±0.001 per 10-years increment; p<0.01), and longer disease duration (estimate=0.027±0.003 per 10-years increment, p<0.01) (Global R²=0.13). Altogether, subjects presenting with both low complement and abnormal CB-CAPs had higher LSI (median [IQ range]: 0.785 [0.558-0.839]) than those presenting with either abnormality (median [IQ range]: 0.591 [0.526-0.817]) or those presenting with normal complement and normal CB-CAPs (median [IQ range]: 0.546 [0.481-0.703]) (p<0.001). Figure 1 illustrates the higher frequencies of low complement (p<0.01) and abnormal CB-CAPS (p<0.01) by LSI tertiles and shows that abnormal CB-CAPs is more prevalent than low complement at all LSI levels (p<0.01).

Conclusion: These data indicate that abnormalities in the complement system are associated with increased LSI.

Figure 1: Lupus Severity Index (LSI) and complement abnormalities

Disclosure: C. Arriens, Exagen, 9; S. Narain, Exagen, 2; A. Saxena, Exagen, 2; C. E. Collins, Exagen, 2, Exagen, 8; D. J. Wallace, Exagen, 2, Exagen, 5; E. Massarotti, Exagen, 2; J. Conklin, Exagen, 3; R. Alexander, Exagen, 3; K. C. Kalunian, Exagen, 2; C. Putterman, Exagen, 2; R. Ramsey-Goldman, Exagen, 2; J. P. Buyon, Exagen, 2; A. Askanase,
Abstract Number: 681

A Panel of Lupus Biomarkers for the Monitoring of Systemic Lupus Erythematosus: Performance Characteristics in Distinct SLE Cohorts

Joan T. Merrill¹, Thierry Dervieux², Jill P. Buyon³, Rosalind Ramsey-Goldman⁴, Kenneth C. Kalunian⁵, Chaim Putterman⁶, John Conklin² and Michelle Petri⁸, ¹Oklahoma Medical Research Foundation, Oklahoma City, OK, ²Exagen Diagnostics, Inc., Vista, CA, ³Medicine, New York University School of Medicine, New York, NY, ⁴FSM, Northwestern University, Chicago, IL, ⁵Division of Rheumatology, Allergy and Immunology, UCSD School of Medicine, La Jolla, CA, ⁶Division of Rheumatology, Albert Einstein College of Medicine, Bronx, NY, USA, Bronx, NY, ⁷Northwell Health, Great Neck, NY, ⁸Medicine (Rheumatology), Division of Rheumatology, Johns Hopkins University School of Medicine, MD, USA, Baltimore, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Antibody titers to double stranded DNA (anti-dsDNA) and complement C3 and C4 proteins have clinical utility in the routine monitoring of systemic lupus erythematosus (SLE). We evaluated the performance characteristics of antibody titers to C1q (anti-C1q), and C4d bound to erythrocytes (EC4d) as additional biomarker candidates in the monitoring of SLE disease activity.

Methods: SLE patients (total 124 patients, mean age 42 years, 97% females) were enrolled from three different cohorts. The first cohort enrolled 37 subjects, all selected for active disease in the presence of complement activation. The second and third cohorts enrolled 64 and 24 SLE subjects, respectively. Disease activity was assessed longitudinally using the Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA) SLE disease activity index (SLEDAI) without anti-dsDNA and complement components; this modification is referred to as the clinical SELENA-SLEDAI. Also, the Physician’s Global Assessment of disease activity (PGA: 0-3-point scale) was collected. Antibody titers, serum C3 and C4 levels were determined using standard immunoassays (low C3/C4 was defined as either C3 or C4 below normal range). EC4d levels were determined using quantitative flow cytometry and expressed as net mean fluorescence intensity (MFI). The relationships between fluctuations in SLE disease activity and biomarkers were analyzed using Spearman rank test and linear mixed effect models with the clinical SELENA-SLEDAI and PGA as the dependent variables and biomarkers as independent predictor of disease activity fluctuations (autoantibody titers and EC4d levels were log normalized for the analysis). Marginal $R^2$ were calculated to evaluate the proportion of variance explained by independent variables.

Results: Overall, a total of 624 study visits were collected in the 124 patients. At baseline, both clinical SELENA-SLEDAI (average 6.0 points) and PGA scores (average 1.0 point) correlated with EC4d levels C3/C4 status, anti-dsDNA and anti-C1q titers (p<0.01). Linear mixed effect models revealed that changes in EC4d, C3/C4 anti-dsDNA and anti-C1q titers were all significantly associated with fluctuations in disease activity (p<0.01)(Table I). Of the 124 subjects, 97 of them presented with either chronically low C3/C4 (n=40) or normal C3/C4 status at all visits (n=57). In this subset, changes in EC4d levels were associated with fluctuations in clinical SELENA-SLEDAI (estimate 1.2±0.3, marginal $R^2$=8%) and PGA (estimate 0.2±0.1, marginal $R^2$=9%).

Conclusion: These data indicate that anti-dsDNA, anti-C1q, low complement and EC4d are associated with disease fluctuations in SLE. EC4d correlates with disease activity among subjects with chronically low or normal complement.
Complement Activation in Peripheral Blood in Relation to Lupus, Antiphospholipid and Rheumatoid Arthritis Autoantibodies: Insights from Clinical Laboratory Evaluations

Thierry Dervieux¹, John Conklin¹, JoAnne Ligayon¹, Rowena Lafon², Armida Sace³, Tyler O'Malley⁴, Roberta Alexander¹ and Claudia Ibarra¹, ¹Exagen Diagnostics, Inc., Vista, CA, ²Immunochemistry, Exagen Diagnostics, Inc., Vista, CA, ³Automated Chemistry, Exagen Diagnostics, Inc., Vista, CA, ⁴Research and Development, Exagen Diagnostics, Inc., Vista, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Abnormal activation of the complement system is emerging as a useful biomarker in the evaluation of patients presenting symptoms of autoimmune rheumatic diseases. We sought to evaluate the relationships between complement activation and autoantibodies associated with systemic lupus erythematosus (SLE), anti-phospholipid Syndrome (APS) and rheumatoid arthritis (RA).

Methods: From May 2014 to November 2016, a cohort of 32,404 patients within the United States (mean 51±15 [SD] years, 86% females) was tested. EDTA whole blood and serum were collected within 48 hours of patient examination and processed in a CLIA certified/CAP accredited clinical laboratory. C4d bound to erythrocyte or B lymphocyte above the 99th percentile of normal healthy group were defined as abnormal. The panel of 16 autoantibodies (all determined by solid phase immunoassays) consisted of 6 SLE autoantibodies (high ANA, anti-dsDNA confirmed using Crithidia, anti-U1 RNP, anti-C1q, anti-ribosomal P, anti-Smith, all IgGs), 6 APS autoantibodies (anti-cardiolipin, anti-β2 glycoprotein 1, anti-phosphatidylserine/prothrombin complex, IgM and IgG) and 4 RA autoantibodies (anti-CCP, anti-MCV, IgM RF, IgA RF). The relationships between abnormal complement activation and the presence of the autoantibodies were analyzed on de-identified patient data using multivariate logistic regression with abnormal complement activation as the dependent variable and the presence of autoantibodies as predictors. Adjusted odds ratio were calculated for each autoantibody.

Results: Of the 32,404 patients tested 12% of them presented with abnormal complement activation. The overall incidence of autoantibodies ranged from 1% (anti-Sm) to 22% (ANA). The presence of SLE and APS antibodies were all associated with abnormal complement activation with adjusted OR ranging from 1.40 for anti-C1q (CI95%: 1.24-1.58) to 4.52 for anti-dsDNA (CI95%: 3.95-5.17), and from 1.47 for anti-cardiolipin IgG (CI95%: 1.22-1.77) to 3.2 for anti-PS/PT IgM (CI95%: 3.20-2.92), respectively (p<0.02). Of the 4 RA-associated antibodies, only anti-CCP (adjusted OR=1.25, CI95%:
1.02-1.54) and IgM RF (adjusted OR=1.17, CI95%: 1.04-1.32) were significantly associated with complement activation (p<0.05). Figure 1 illustrates the relationship between the cumulative presence of lupus, APS and RA autoantibodies, and abnormal complement activation. Across the cumulative range of SLE and APS associated antibodies, we detected a 319-fold (CI95%: 240-424), and 120-fold (CI95%: 94-153) increased likelihood of abnormal complement. In contrast, the cumulative presence of RA autoantibodies yielded minimum impact of the likelihood of abnormal complement activation (adjusted OR=2.3; CI95%: 2.0-2.7)

**Conclusion:** These diagnostic immunology data suggest that complement activation in peripheral blood is intimately related to SLE and APS antibodies.

Figure 1: SLE, APS and RA autoantibodies in relation to abnormal complement activation

![Graph illustrating complement activation](image)

Cumulative presence of autoantibodies

**Disclosure:** T. Dervieux, Exagen, 3; J. Conklin, Exagen, 3; J. Ligayon, Exagen Diagnostics, Inc., 3; R. Lafon, Exagen Diagnostics, Inc., 3; A. Sace, Exagen Diagnostics, Inc., 3; T. O'Malley, Exagen Diagnostics, 3; R. Alexander, Exagen, 3; C. Ibarra, Exagen Diagnostics, Inc., 3.


Abstract Number: 683

**The Presence of Anti-Ro and Anti-La Antibodies Is Associated with Tubulointerstitial Damage in Lupus Nephritis**

Alejandra Londono Jimenez¹, Wenzhu Mowrey² and Anna R. Broder², ¹Internal Medicine, Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, NY, ²Albert Einstein College of Medicine/Montefiore Medical Center, New York, NY

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Moderate-to-severe tubulointerstitial damage (TID) is associated with poor renal outcomes in lupus-related kidney disease, independent of glomerular pathology¹. Unlike glomerular damage, TID is not associated with anti-dsDNA or complement levels and no serologic parameters associated with TID in SLE have been identified to date ². The presence of anti-Ro/La antibodies in Sjögren's syndrome is associated with extraglandular manifestations, including...
tubulointerstitial nephritis\textsuperscript{3}. Whether anti-Ro/La antibodies are associated with TID in lupus-related kidney disease has not been studied.

**Objective:** To study an association between anti-Ro/La antibodies and TID in lupus nephritis (LN).

**Methods:** We identified all patients who fulfilled ACR and/or SLICC criteria for SLE at a large urban tertiary care center. Medical history, demographic and laboratory data were ascertained from chart review. Patients were included if they had an index renal biopsy consistent with LN between January 2005 and July 2015 and had complete data on TID and anti-Ro/La. All biopsies were reviewed by 2 experienced renal pathologists and TID was classified as mild, moderate or severe when tubular atrophy and/or interstitial fibrosis involved <25%, 25-50% or >50% of the interstitium, respectively\textsuperscript{1}.

**Results:** Of the 157 LN patients, 39 (25%) had moderate/severe TID (Table). Moderate/severe TID was associated with older age, proliferative LN (class III/IV±V) and lower estimated glomerular filtration rate (eGFR) at biopsy. Anti-Ro/La were present in 11/118 (9%) with none/mild TID vs 11/39 (28%) with moderate/severe TID (p=0.003), and in 13/114 (11%) with none/mild TII vs. 8/37 (22%) with moderate/severe TII (p=0.12). In the logistic regression model adjusted for age, eGFR and LN class, dual positivity for anti-Ro/La antibodies was associated with a 3-fold increase in the odds of TID, OR 3.1, 95% CI (1.1-9.1), \( p=0.04 \).

**Conclusion:** Dual anti-Ro/La positivity is associated with moderate/severe TID in patients with biopsy proven LN after adjusting for age, LN class and eGFR. The presence of only anti-Ro antibodies is not associated with moderate/severe TID. Understanding the role of anti-Ro/La in the mechanisms underlying TID in LN may lead to novel preventive and therapeutic strategies.

**References:**


Baseline characteristics by TID (none/mild vs. moderate/severe)

<table>
<thead>
<tr>
<th></th>
<th>None/Mild TID (n=118)</th>
<th>Moderate/Severe TID (n=39)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (IQR), years</td>
<td>26 (17, 37)</td>
<td>41 (25, 53)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Men, n(%)</td>
<td>21 (18)</td>
<td>10 (26)</td>
<td>0.29</td>
</tr>
<tr>
<td>Black Race, n(%)</td>
<td>55 (47)</td>
<td>22 (56)</td>
<td>0.29</td>
</tr>
<tr>
<td>Charlson comorbidity index, median (IQR)</td>
<td>3 (1, 4)</td>
<td>3 (1, 4)</td>
<td>0.09</td>
</tr>
<tr>
<td>Creatinine (mg/dL), median (IQR)</td>
<td>0.8 (0.6, 1.2)</td>
<td>1.6 (1, 2.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>eGFR mL/min/1.73m2, median (IQR)</td>
<td>91 (61, 127)</td>
<td>42 (26, 75)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Protein/Creatinine ratio (mg/mg), median (IQR)</td>
<td>2.2 (1.0, 4.9)</td>
<td>2.1 (1.5, 5.5)</td>
<td>0.68</td>
</tr>
<tr>
<td>LN class n(%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I/II</td>
<td>10 (9)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>III/IV ± V</td>
<td>71 (61)</td>
<td>34 (87)</td>
<td>0.008</td>
</tr>
<tr>
<td>V</td>
<td>35 (30)</td>
<td>5 (13)</td>
<td></td>
</tr>
<tr>
<td>Low C3, n(%)</td>
<td>83 (75)</td>
<td>23 (70)</td>
<td>0.51</td>
</tr>
<tr>
<td>Low C4, n(%)</td>
<td>76 (70)</td>
<td>22 (67)</td>
<td>0.69</td>
</tr>
<tr>
<td>Elevated dsDNA, n(%)</td>
<td>70 (68)</td>
<td>21 (66)</td>
<td>0.81</td>
</tr>
<tr>
<td>Anti-Ro, n(%)</td>
<td>55 (47)</td>
<td>17 (44)</td>
<td>0.74</td>
</tr>
<tr>
<td>Anti-Ro and anti-La, n(%)</td>
<td>11 (9)</td>
<td>11 (28)</td>
<td>0.003</td>
</tr>
<tr>
<td>Tubulointerstitial inflammation (TII), n(%)</td>
<td>19 (17)</td>
<td>18 (49)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Disclosure: A. Londono Jimenez, None; W. Mowrey, None; A. R. Broder, None.


Abstract Number: 684

ANTI-RO52 KDa and ANTI-RO60 KDa Analysis in Systemic LUPUS Erythematous Patients to Detect ANTI-RO False-Negatives

Elena Grau Garcia, Inmaculada Chalmeta Verdejo, David Gimenez-Romero, Eztizen Labrador Sanchez, Merixell Fernandez Matilla, Francisco Miguel Ortiz-Sanjuán, Carlos Feced Olmos, Nagore Fernandez-Llanio Cornella, Karla Arevalo Ruales, Rosa Negueroles Albuixech, Jose Ivorra Cortes, Jorge Juan Fragio Gil, Isabel Martinez Cordellat, Roxana Gonzalez Mazzario, Luis Gonzalez Puig, Cristina Alcainiz Escandell, Carmen Najera Herranz, Ines Canovas Olmos, Elvira Vicens Bernabeu, Jose Eloy Oller Rodriguez, Jose Antonio Castellano Cuesta, Victoria Fornes Ferrer, David Hervás Marin, Marta De la Rubia Navarro and Jose Andres Roman Ivorra, Rheumatology Department. Hospital Universitario y Politecnico La Fe, Valencia, Spain, Physical-Chemistry Department, UV, Valencia, Spain, Rheumatology Section. Hospital Arnau de Vilanova, Valencia, Spain, Biostatistics Unit. IIS La Fe, Valencia, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A  
Session Time: 9:00AM-11:00AM  

Background/Purpose:

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by immune system disruption with autoantibodies production. One of the upregulated autoantibodies is the specific to the Ro antigen, a ribonucleoprotein associated to a small RNA, constituted by the 52KDa and 60 KDa polypeptides, whose epitopes are mainly conformational. The routine detection method for anti-Ro is an enzyme immunoassay, however, is possible to obtain false-negatives for anti-Ro and this could be avoided by analyzing both subunits separately. The aim of the present study is to identify false-negatives for anti-Ro by analyzing both 52KDa and 60 KDa subunits separately, as well as to characterize if there are clinical or molecular differences in this subgroup of patients compared to anti-Ro negative cases.

Methods:

A cross-sectional, observational study of patients diagnosed of SLE according to SLICC 2012 criteria was performed. In these patients a complete blood-test was made, and clinical data by personal interview was collected. INF1A, Anti-Ro, anti-Ro52KDa and anti-Ro60KDa levels where measured by colorimetric methods. Biostatistical analysis was performed with R 3.3.2.

Results:

We selected 69 SLE patients with negative results for anti-Ro (2.34±4.17 U/mL) out of 142 total SLE patients. A total of 51 patients were negative for both anti-Ro subunits and 18 cases presented positive results (up to 20 pg/mL) for at least one of them.

<table>
<thead>
<tr>
<th></th>
<th>NEGATIVES N=51</th>
<th>Anti-RO52KDa POSITIVES N=8</th>
<th>Anti-RO60KDa POSITIVES N=2</th>
<th>Anti-RO52KDa / Anti-RO60KDa POSITIVES N=8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-RO [U/mL] Mean (DS)</td>
<td>1.92 (3.11)</td>
<td>1.65 (3.2)</td>
<td>0.5 (0.71)</td>
<td>6.15 (8.37)</td>
</tr>
<tr>
<td>Anti-RO52 KDa [pg/mL] Mean (DS)</td>
<td>1.26 (1.89)</td>
<td>147.24 (74.25)</td>
<td>1.05 (0.89)</td>
<td>196.82 (50.06)</td>
</tr>
<tr>
<td>Anti-RO60 KDa [pg/mL] Mean (DS)</td>
<td>1.73 (2.71)</td>
<td>6.3 (7.01)</td>
<td>120.96 (111.78)</td>
<td>145.22 (76.69)</td>
</tr>
</tbody>
</table>

The subgroup of patients that exhibit simultaneously high levels of anti-Ro52KDa and anti-Ro60KDa have higher clinical activity compared to negative anti-Ro cases (75% of active patients against 41.2% in anti-Ro negative patients). However, no differences in the accumulated damage evaluated by SLICC score between negative anti-Ro cases and patients with at least one positive subunit were observed.

We analyze serum levels of INF1A cytokine in the four groups of patients, and anti-Ro and subunits negative cases showed significant lower INF1A levels than the other patients (8.26±14.87 pg/mL and 26.62±40.71 pg/mL respectively; P=0.04). In addition, patients with high levels of anti-Ro52KDa subunit are those with the highest INF1A levels (anti-Ro 52+/anti-Ro60- 23.5±47.6pg/mL of INF1A; anti-Ro 52+/anti-Ro60+ 36.4±37.9pg/mL of INF1A).

Conclusion:

In our anti-Ro seronegative patients, a 26% of false-negative cases were detected. These cases with high levels of almost one anti-Ro subunit showed significantly higher levels of INF1A in contrast to negative cases, supporting the fact that they are indeed a different group from the negative cases. Moreover, the high INF1A levels could be the reason of the observed differences in the clinical activity measured by SLEDAI score in both groups.

Disclosure: E. Grau Garcia, None; I. Chalmeta Verdejo, None; D. Gimenez-Romero, None; E. Labrador Sanchez, None; M. Fernandez Matilla, None; F. M. Ortiz-Sanjuán, None; C. Feced Olmos, None; N. Fernandez-Llanio Cornella, None; K. Arevalo Ruales, None; R. Negueroles Albuixech, None; J. Ivorra Cortes, None; J. J. Fragio Gil, None; I. Martinez Cordellat, None; R. Gonzalez Mazario, None; L. Gonzalez Puig, None; C. Alcañiz Escandell, None;
Abstract Number: 685

**Anti-C1q Antibodies and Disease Activity in a Multi-Ethnic Lupus Cohort**

Sameer Bahal\(^1\), **Debasish Pyne**\(^1\), Ravindra Rajakariar\(^1\), Myles Lewis\(^1\), Angela Pakozdi\(^1\), Sofia Grigoriadou\(^2\) and Andrea Cove-Smith\(^1\), \(^1\)Barts Lupus Centre, Barts Health NHS Trust, London, United Kingdom, \(^2\)Immunology Department, Barts Health NHS Trust, London, United Kingdom

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Anti-C1q antibodies (C1Q Ab) are observed in 30-60% of patients with Systemic Lupus Erythematosus (SLE). A number of studies have shown that the presence of C1Q Ab correlates with disease activity. In particular C1Q Ab is reported to strongly correlate with active renal disease with some studies reporting antibody absence having a negative predictive value of close to 100% for active lupus nephritis (LN) (1). However specificity for active lupus remains controversial and variations may be due to timing of samples, assay used, cut off values and population studied.

Here we undertook a point-in-time measurement of C1Q Ab in a multi ethnic cohort of SLE patients and investigated correlations between this and clinical and serologic parameters of SLE.

**Methods:**

SLE patients attending an inner city Lupus Clinic were involved in the study. Disease activity was calculated using the SLE Disease Activity Index (SLEDAI 2K); erythrocyte sedimentation rate (ESR), dsDNA Ab, complement levels (C3, C4), and urine protein creatinine ratio (uPCR) were measured. For patients with biopsy proven LN renal inactivity was defined as a PCR < 50 mg/mmol. C1Q Ab was quantified by ELISA (Orgentec Diagnostika GmbH). A positive test defined by the manufacturer is a level above 10 U/ml. Correlation of C1Q Ab levels with disease activity markers was measured using Pearson’s correlation.

**Results:**

116 patients were included in the study. All fulfilled the 2012 SLICC criteria for SLE. 103 (89%) were female. There were 38 (32.8%) South Asians (SA), 48 (41.3%) Afro Caribbean (AC) and 25 (21.6%) White Caucasians (WC). C1Q Ab positivity was present in 29% SA patients, 13% AC patients and 28% WC patients (p=0.06).

There was a positive correlation between C1Q Ab levels and dsDNA levels (r=0.358, p<0.01); whilst a negative correlation was observed with C3 levels (r=-0.406, p<0.01). No correlation was found with SLEDAI scores(r=0.18, p=0.053), uPCR (r=0.13, p=0.16) and ESR (r=0.045, p=0.63). Positive C1Q Ab was more common in patients with a history of biopsy proven LN (32.7%); of these patients, 43% (n=12/28) had inactive LN at the time of sampling with a positive C1q Ab. In addition, C1Q Ab was present in 15.5% (n=9) of patients with minimally active disease (SLEDAI≤ 4).

**Conclusion:**
The overall prevalence of C1Q Ab was 23.3% in our lupus cohort, and was present in all ethnic groups. Its presence was correlated with dsDNA but not with SLEDAI score, ESR and PCR. There was a negative correlation with C3 level. C1Q Ab was found more commonly in renal than in non-renal patients. Importantly a positive C1Q Ab level was found in 15.5% of patients with inactive disease defined as SLEDAI≤ 4 and in 43% of LN patients with inactive renal disease (defined as PCR<50). We would therefore caution against use of C1Q Ab as a stand-alone biomarker for active lupus.

References


Disclosure: S. Bahal, None; D. Pyne, None; R. Rajakariar, None; M. Lewis, None; A. Pakozdi, None; S. Grigoriadou, None; A. Cove-Smith, None.


Abstract Number: 686

**Endothelial Dysfunction in Systemic Lupus Erythematosus Patients without Cardiovascular events and Risk Factors: Correlation with Microvascular Alterations and angiogenic T Cells**

Ilaria Cavazzana¹, Mara Taraborelli², Silvia Piantoni³, Ivano Bonadei⁴, Edoardo Sciatti⁵, Micaela Fredi⁶, Marco Metra⁴, Angela Tincani⁷, Franco Franceschini¹ and Enrico Vizzardi⁴, ¹Rheumatology and Clinical Immunology, Spedali Civili of Brescia, Brescia, Italy, ²Internal Medicine; Ospedale Mellini, Chiari (Brescia), Italy, ³Rheumatology and Clinical Immunology Unit, Spedali Civili, University of Brescia, Brescia, Italy, ⁴Cardiology Unit, Spedali Civili, University of Brescia, Brescia, Italy, ⁵Cardiology Unit, Spedali Civili, University of Brescia, Brescia, Italy, ⁶Department of Rheumatology and Clinical Immunology, Rheumatology and Clinical Immunology, Rheumatology and Clinical Immunology, Spedali Civili and University of Brescia, Brescia, Italy

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** early identification of subclinical cardiovascular disease (CVD) in systemic lupus erythematosus (SLE) patients is mandatory to reduce morbidity and mortality. Endothelial dysfunction (ED) is one of the first steps of the process leading to atherosclerosis and has been associated with further CVD development. Aim of the study was to assess the prevalence of ED by a non invasive procedure in SLE patients with early disease without CVD and risk factors, and correlate ED with nailfold capillary morphology and angiogenic T (angT) cells. AngT cells are a T cell subpopulation, involved in repair mechanisms of the endothelium, cooperating with endothelial progenitors cells.

**Methods:** all the consecutive SLE patients, according to SLICC Classification Criteria, with a disease duration less than 5 years, evaluated from december 2014 to march 2016 were proposed to participate to the study. Exclusion criteria were represented by history of CVD, diabetes, chronic renal disease (creatinine clearance<60 ml/min), not controlled systemic arterial hypertension, current or past smoking (in the last 3 years), hypercholesterolemia (total cholesterol>240 mg/dl), obesity (body mass index > or =30), statin or beta-blocker use. Each patient underwent a clinical and serological evaluation, a transthoracic doppler echocardiogram, endothelial function study by endoPAT technique, nailfold
videocapillaroscopy (NVC) and T cell subpopulation study. Characteristics of patients with ED (ED+), defined as reactive hyperemic index $\leq 2$, were compared to those of patients without ED (ED-) and normal controls, matched for age, sex and CV exclusion criteria, by Fisher, T student or Mann-Whitney tests as appropriate.

**Results:** Among 46 screened SLE patients, 20 patients were enrolled (100% female, 80% caucasian) with a median disease duration of 14 months (0-68), a mean age of 42 years ($\pm 15$), and a mean age at diagnosis of 40 years ($\pm 16$). Arthritis, cutaneous and hematological features were found in 70%, 55% and 65% of cases, respectively. ANA, antidsDNA and anti-ENA were found in 100%, 50% and 50% of cases. Anti-cardiolipin and antibeta2glycoprotien I antibodies in 20% and 10%. ED was found in 8 patients (40%). ED didn't correlate with any demographic-clinical-serological-echocardiographic features. A significantly higher prevalence of ED (p:0.003), vascular stiffness (p:0.02), left ventricular concentric remodelling (p:0.003), grade I diastolic dysfunction (p:0.04) were found in SLE patients compared to controls. ED+ patients more frequently showed minor NVC abnormalities (i.e. tortuous/crossed/enlarged) (p: 0,007), lower capillary number/mm (p: 0,01) and wider intercapillary distance (p: 0,06) compared to controls. AngT cells were significantly reduced in SLE patients compared to controls (p: 0,045), but they were increased in ED+ SLE compared to ED- (p: 0,04).

**Conclusion:** A significant proportion of SLE patients showed signs of ED despite a recent disease and the absence of cardiovascular risk factors. ED correlates with microvascular alterations by videocapillaroscopy and increased ang T cells, as marker of endothelium repair.

**Disclosure:** I. Cavazzana, None; M. Taraborelli, None; S. Piantoni, None; I. Bonadei, None; E. Sciatti, None; M. Fredi, None; M. Metra, None; A. Tincani, None; F. Franceschini, None; E. Vizzardi, None.


**Abstract Number:** 687

**Homocysteine Levels Are Independently Associated with Damage Accrual in Systemic Lupus Erythematosus Patients (SLE)**

**Paola Zeña-Huancas**¹, Manuel Ugarte-Gil², Rocio Gamboa-Cárdenas¹, Francisco Zevallos¹, Mariela Medina¹, Victor Pimentel-Quiroz², Claudia Elera-Fitzcarrald¹, Omar Sarmiento-Velasquez¹, Cristina Reategui-Sokolova¹, Mariano Cucho-Venegas¹, José Alfaro-Lozano¹, Zoila Rodriguez-Bellido¹, Cesar A. Pastor-Asurza¹, Graciela S. Alarcón³ and Risto Perich-Campos⁴,⁶ ¹Rheumatology, Hospital Guillermo Almenara Irigoyen. EsSalud, Lima, Peru, ²Peru, GLADEL, Lima, Peru, ³Universidad Cientifica del Sur, Lima, Peru, ⁴Universidad Nacional Mayor de San Marcos, Lima, Peru, ⁵University of Alabama at Birmingham, Birmingham, AL, ⁶Rheumatology, Hospital Guillermo Almenara Irigoyen, Lima, Peru

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Homocysteine level is a predictor of the occurrence of cardiovascular diseases, however, its role as a predictor of damage in SLE has not been studied. The aim of this study is to determine the impact of homocysteine levels on damage accrual in SLE patients.

**Methods:**
These analyses were conducted in 145 SLE patient, 136 females and 9 males, followed longitudinally at a single center. Evaluations were done every six months and included interview, medical records review, physical examination and laboratory tests. Disease activity was measured with the SLEDAI (Systemic Lupus Erythematosus Disease Activity Index). Damage accrual was ascertained with the SLICC/ACR damage index (SDI). Univariable and multivariable Cox regression models were performed to determine if homocysteine levels were associated with damage accrual. The multivariable model was adjusted for variables known to be associated with this outcome [age at diagnosis, gender, socioeconomic status, disease duration, SLEDAI, antimalarials and immunosuppressive drugs use, average daily dose and time of exposure to prednisone (PDN)].

Results:

The patients mean (SD) age at diagnosis was 43.70 (12.09) years, nearly all were Mestizo. At baseline, disease duration was 7.55 (6.73) years. The SLEDAI was 5.60 (4.34) and the SDI 0.97 (1.35). The average daily dose of PDN was 7.30 (5.78) mg/d and the time of exposure to PDN was 7.36 (6.73) years. Mean homocysteine levels was 10.07 (3.71) µmoles/liter. Patients were followed for 3.54 (1.27) years, and 75 (51.7%) increased at least one point in the SDI. Homocysteine level predicted new damage accrual in the univariable and multivariable models [HR 1.08 (CI95%: 1.03-1.14); p=0.002 and HR: 1.09 (CI95%: 1.02-1.16); p=0.008 respectively.]
<table>
<thead>
<tr>
<th>Variables</th>
<th>HR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homocysteine</td>
<td>1.090</td>
<td>[1.023-1.162]</td>
<td>0.008</td>
</tr>
<tr>
<td>Age at diagnosis, years</td>
<td>1.025</td>
<td>[1.001-1.050]</td>
<td>0.045</td>
</tr>
<tr>
<td>Disease duration, years</td>
<td>1.058</td>
<td>[0.999-1.121]</td>
<td>0.054</td>
</tr>
<tr>
<td>Gender (female)</td>
<td>0.834</td>
<td>[0.292-2.380]</td>
<td>0.734</td>
</tr>
<tr>
<td>Socioeconomic status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>Ref.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medium status</td>
<td>1.196</td>
<td>[0.602-2.378]</td>
<td>0.609</td>
</tr>
<tr>
<td>Low status</td>
<td>1.129</td>
<td>[0.634-2.011]</td>
<td>0.681</td>
</tr>
<tr>
<td>SLEDAI, median</td>
<td>1.026</td>
<td>[0.969-1.086]</td>
<td>0.379</td>
</tr>
<tr>
<td>Immunosuppressive drugs use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>Ref.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Past</td>
<td>0.949</td>
<td>[0.456-1.975]</td>
<td>0.888</td>
</tr>
<tr>
<td>Current</td>
<td>1.474</td>
<td>[0.838-2.593]</td>
<td>0.178</td>
</tr>
<tr>
<td>Hydroxychloroquine use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>Ref.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Past</td>
<td>0.782</td>
<td>[0.294-2.080]</td>
<td>0.622</td>
</tr>
<tr>
<td>Current</td>
<td>0.558</td>
<td>[0.266-1.172]</td>
<td>0.124</td>
</tr>
<tr>
<td>Prednisone current dose (mg/d)</td>
<td>0.995</td>
<td>[0.955-1.037]</td>
<td>0.821</td>
</tr>
<tr>
<td>Time of exposure to prednisone, years</td>
<td>1.000</td>
<td>[0.945-1.059]</td>
<td>0.998</td>
</tr>
<tr>
<td>SDI</td>
<td>0.867</td>
<td>[0.688-1.094]</td>
<td>0.229</td>
</tr>
</tbody>
</table>

SDI SLICC/ACR damage index, SLEDAI systemic lupus erythematosus disease activity index

**Conclusion:**

Homocysteine levels in SLE patients predicted damage accrual independently of other well-known risk factors of damage.

**Disclosure:** P. Zeña-Huancas, None; M. Ugarte-Gil, None; R. Gamboa-Cárdenas, None; F. Zevallos, None; M. Medina, None; V. Pimentel-Quiroz, None; C. Elera-Fitzcarrald, None; O. Sarmiento-Velasquez, None; C. Reategui-Sokolova, None; M. Cucho-Venegas, None; J. Alfaro-Lozano, None; Z. Rodriguez-Bellido, None; C. A. Pastor-Asurza, None; G. S. Alarcón, None; R. Perich-Campos, None.
Associations between Standard Serological Markers and Different Clinical Phenotypes in Systemic Lupus Erythematosus

Ilana Abeles\(^1\) and Vasileios C. Kyttaris\(^2\), \(^1\)Division of Internal Medicine, Beth Israel Deaconess Medical Center, Boston, MA, \(^2\)Rheumatology, Beth Israel Deaconess Medical Center, Boston, MA

First publication: September 18, 2017

Background/Purpose:
Systemic lupus erythematosus (SLE) affects various body organs making its clinical presentation highly variable. While previous studies have demonstrated associations between lab abnormalities and individual clinical manifestations of disease, our study aimed to be more specific and categorized patients into sub-groups based on their unique presentations. We then investigated associations between immunological/serological abnormalities and exclusive clinical phenotypes of SLE.

Methods:
Information regarding SLE related clinical symptoms and serological data were collected from 201 patients diagnosed with SLE. Laboratory abnormalities included: anti-nuclear antibody (Ab), anti-Ro Ab, anti-La Ab, anti-Smith Ab, anti-U1-ribonucleoprotein Ab, anti-rheumatoid factor Ab, anti-dsDNA Ab, low C3, low C4, anti-cardiolipin Ab, lupus anticoagulant and beta2-glycoprotein. Patients were classified into clinical subgroups based on manifestation(s) of disease: arthritis alone (A); mucocutaneous disease alone (B); nephritis alone (C); arthritis + mucocutaneous disease (D); arthritis + nephritis (E); nephritis + mucocutaneous disease (F); or all 3 (G). Omnibus chi-square tests evaluated associations between individual lab abnormalities and phenotype with subsequent post-hoc evaluation for significant omnibus tests. Positive and negative predictive values (PPV, NPV) were also investigated.

Results:
Analyses revealed that anti-Smith, anti-dsDNA antibodies and low levels of C3 and C4 were associated with phenotype G (p=0.001, Chi-square ($\chi^2$)=11.3; p=0.004, $\chi^2$=8.3; p=0.0001, $\chi^2$=21.4; p=0.0001, $\chi^2$=22.5 respectively) with a PPV of 59.4%, 85.3%, 91.2% and 85.3% respectively, and anti-Sm Ab had a NPV of 71.3%. Anti-dsDNA Ab, low C3 and C4 levels were additionally significantly associated with phenotype F (p=0.01, $\chi^2$= 6.25; 0.01, $\chi^2$=6.48; p=0.01, $\chi^2$=6.54 respectively). PPV of anti-dsDNA Ab, low C3 and C4 for F was 93.3%, 91.2%, and 80% respectively and 73.3% combined. Further, anti-ds-DNA Ab, low C3 and C4 for F was 93.3%, 91.2%, and 80% respectively and 73.3% combined. Anti-dsDNA Ab, low C3 and C4 were negatively associated with phenotype B (p<.001, $\chi^2$= 15.3; p<.001, $\chi^2$=12.48; p=.014, $\chi^2$=6.1, respectively). Low complement levels were also negatively associated with phenotype D (C3: p=.038, $\chi^2$=4.3; C4: p=.011, $\chi^2$= 6.54). While nephritis alone was not significantly associated with any markers, anti-dsDNA Ab, and low complement levels combined had an 80.8% NPV for renal disease.

Conclusion:
Our results suggest that an expanded epitope including anti-dsDNA and anti-Smith antibodies, along with low complement levels are associated with a broader phenotype in SLE which includes arthritis, nephritis and mucocutaneous involvement.
Anti-dsDNA Ab and low complement levels were also associated with the mucocutaneous disease and nephritis combined but not nephritis or mucocutaneous disease alone. In fact, these serological markers were negatively associated with mucocutaneous involvement. These findings suggest that immunological profiles may reflect unique phenotypes of SLE. Future genetic models that target particular phenotypes of SLE and associated immunologic abnormalities may be useful in developing new drug therapies.

Disclosure: I. Abeles, None; V. C. Kyttaris, None.


Abstract Number: 689

Apolipoprotein L1 Risk Variants Associate with Hypertension and Nephritis Progression Despite Lower dsDNA Titers in Ghanaian Systemic Lupus Erythematosus Patients

Ashira Blazer1, Ida Dzifa Dey2, Sara Rasmussen3, Robert M. Clancy4 and Jill P. Buyon5, 1Internal Medicine Division of Rheumatology, NYU School of Medicine, New York, NY, 2Internal Medicine, Rheumatology, The University of Ghana, Accra, Ghana, 3Department of Medicine, Division of Rheumatology, NYU School of Medicine, New York, NY, 4NYU School of Medicine, New York, NY, 5Rheumatology, New York University School of Medicine, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Two Apolipoprotein L1 (APOL1) risk variants (RV), G1 and G2 are enriched in African populations due to a conferred resistance to Trypanosoma brucei. This comes with the cost of progressive renal disease by multiple causes including SLE. Despite the high regional allelic frequencies, APOL1 variant phenotypes have never been described in a Sub-Saharan African SLE cohort. Further, it is unclear if SLE nephritis progression in RV carriers is driven by inflammation or intrinsic nephropathy. Accordingly, this prospective longitudinal cohort study evaluated APOL1 genotype-phenotype traits in the context of SLE activity in 72 Ghanaian patients seeking care at Korle bu Teaching Hospital in Accra, Ghana.

Methods: All 72 patients met 4 ACR criteria for SLE and were stratified by APOL1 genotype using PCR/sequencing as follows: ancestral (G0/G0), RV heterozygotes (RV/G0), and RV homozygotes (RV/RV). DNA was extracted from saliva, and ancestry informative markers were performed on a subset of 20 patients to confirm heritage. ANAs were confirmed in the NYU clinical lab by multiplex analysis. Endpoints collected at three, 6 month intervals included demographics, ACR criteria, SLEDAI score, vital signs, and lab values as available. To measure SLE serologic activity, dsDNA titers were completed and in 15 subjects (5 per genotype), interferon (IFN) signature was measured by the WISH cell assay.

Results: The frequencies of the G0, G1, and G2 alleles were 60%, 25%, and 14.5% respectively (meeting Hardy Weinberg Equilibrium) and principal component analysis confirmed ancestry. Subjects were all female, average age of 32.1 years with SLE duration of 2.3 years. Data were collected on at least one, two, or three time points on 72, 56, and 30 subjects respectively. There were no differences in history of nephritis, diabetes, or age across the genotypes. The RV associated with higher average BPs; 109.9/75.7, 111.3/75.2, and 125.2/85.6 mmHg in the G0/G0, RV/G0, and RV/RV groups respectively (p: 0.04 systolic; 0.02 diastolic). Only 13% of the cohort took anti-hypertensives regardless of genotype. Among those with nephritis, RV/RV had increased creatinine: 0.9, 1.1, and 2.5 mg/dL in the G0/G0, RV/G0, and RV/RV groups respectively (p: 0.03). RV/RV carriers took higher doses of prednisolone (17.2mg) compared to G0/G0 or RV/G0
(11.2mg; 11.8mg respectively), however this did not reach statistical significance and there was no difference in SLEDAI scores. Despite higher creatinine, RV/RV carriers were less likely to ever have had anti-DNA positivity (11% positive) and had lower dsDNA titers (10.7 IU/mL) than G0/G0 (41% positive; 57.1 IU/mL) and RV/G0 (43% positive; 95.6 IU/mL) carriers (p: 0.03). IFN signatures in both G0/G0 and RV/G0 patients were higher than in RV/RV (245.7, 81.3, and 24.3 respectively). G0/G0 or RV/G0 carriers were more likely to have IFN scores above the average value of 109.9 (LR: 4.3; p: 0.04).

Conclusion:
Taken together, RVs associated with higher BP and creatinine in this Ghanaian SLE cohort. Despite having poorer renal function, RV homozygotes exhibited lower dsDNA titers and lower IFN signatures than G0/G0 or RV/G0 patients potentially suggesting intrinsic renal disease independent of SLE activity in RV homozygotes.

Disclosure: A. Blazer, None; I. D. Dey, None; S. Rasmussen, None; R. M. Clancy, None; J. P. Buyon, None.


Abstract Number: 690

SSA Antibodies Are Associated with Valvular Abnormalities in SLE Patients without Clinical Cardiovascular Disease

Elizabeth George1, Thania Perez2, Anca Askanase3 and Laura Geraldino-Pardilla4, 1Rheumatology, Columbia University College of Physicians and Surgeons, New york, NY, 2Columbia University College of Physicians & Surgeons, New York, NY, 3Rheumatology, Columbia University College of Physicians & Surgeons, New York, NY, 4Columbia University, New york, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Cardiovascular involvement including pericardium, conduction system, coronary arteries and valvular abnormalities are frequent manifestations of SLE. It is estimated to occur in more than 50% of SLE patients and the prevalence is increasing in the setting of imaging modalities like echocardiogram. Studies have shown approximately 11 times higher risk of any valvular abnormalities in SLE, with mitral valve regurgitation being the most common among them. The mechanism of injury and risk factors are still not completely understood. While association of antiphospholipid antibodies and SLE related valve disease is well known, role of other antibodies like SSA and Anti-Smith remains poorly defined. Recent studies have shown the increased incidence of SSA antibodies in SLE and their positive association with severe mitral valve regurgitation. Though the detection of the early or minor changes by using echocardiography may be limited, these parameters are reliable for all-cause mortality and cardiac morbidity. We sought to test the association between valvular abnormalities and SSA antibodies in SLE patients without clinical cardiovascular disease (CVD).

Methods: Adult SLE patients without clinical CVD continuously seen at a University Lupus Center between April 2016 and March 2017, meeting 1997 ACR classification criteria for SLE were studied. Patient characteristics including demographics, SLE-specific features, medication use, traditional CVD risk factors, 12-lead electrocardiogram (EKG) were ascertained. Trans Thoracic Echocardiogram (TTE) was obtained mainly retrospectively from within one year of the date of
enrolment. Univariable and multivariable linear regression models were constructed to test the association of SSA antibodies with valvular abnormalities.

Results: Sixty-four SLE patients (baseline characteristics in table 1) were studied. In univariable analyses, presence of SSA antibodies was significantly associated with a higher incidence of any valvular abnormality (OR= 5.8, P = 0.042), mitral valve regurgitation (OR = 3.08, p=0.05) and tricuspid valve regurgitation (TVR) (OR = 4.95, p= 0.018). Multivariable regression models showed the absence of any confounders. There were a total of 54 (84%) valvular abnormalities with TVR being the most common at 49 (77%).

Conclusion: SSA Antibodies are associated with valvular abnormalities with TVR being most common in SLE patients without clinical cardiovascular disease

Disclosure: E. George, None; T. Perez, None; A. Askanase, Exagen, 2; L. Geraldino-Pardilla, None.

Abstract Number: 691

Serum Anti-NR2 Has a Better Specificity Than Sensitivity in Diagnosing Neuropsychiatric Systemic Lupus Erythematosus (NPSLE)

Seyed-Foad Ahmadi1, Golara Zahmatkesh2, Masoud Majed3 and Sheetal Desai4, 1Department of Medicine, University of California Irvine, Orange, CA, 2Department of Psychiatry, Charles Drew University of Medicine and Science/UCLA, Los Angeles, CA, 3Division of Neuroimmunology, Mayo Clinic, Rochester, MN, 4Medicine/Rheumatology, University of California, Irvine, Orange, CA

First publication: September 18, 2017
Background/Purpose: Anti-NR2, a subclass of anti-NMDA receptor antibodies, is reportedly associated with NPSLE syndromes. However, its diagnostic accuracy is inconsistent across prior studies. Hence, we aimed to quantitatively synthesize the data regarding the sensitivity and specificity of anti-NR2 in diagnosing NPSLE.

Methods: We searched PubMed, Embase, CINAHL and the Web of Knowledge. We included the studies of the diagnostic test accuracy of anti-NR2 for diagnosing NPSLE among patients with SLE, in which they used the ACR case definitions or other validated tools as their reference standards. Two investigators (SFA, GZ) independently replicated data extraction by using a standard form, which included an assessment of study quality as well as participant-level data to populate 2×2 contingency tables. For meta-analysis, we used the Hierarchical Summary Receiver Operating Characteristic (HSROC) model by Rutter & Gatsonis (2001) in Stata 13.0.

Results: We screened 1583 records and eventually included the data from 8 studies with a collective sample of 984 patients (Figure 1). The pooled data represented a wide range of NPSLE manifestations including acute confusional state, seizure disorders, cerebrovascular disease, aseptic meningitis, headaches, cognitive dysfunction, psychoses, mood disorders, movement disorders (chorea), myasthenia gravis, demyelinating syndromes, myelopathy, plexopathy, and mono, poly, and cranial neuropathies. The reported sensitivities fell within a wider range (5% to 100%) compared to the specificities range (64% to 92%) (Figure 2). Meta-analysis of the results yielded the following pooled results with their 95% confidence intervals: Sensitivity 53% (24-80%), Specificity 77% (69-83%), -Likelihood ratio (LR) 0.61 (0.30-1.25), and +LR 2.26 (1.07-4.76) (Figure 3).

Conclusion: Serum anti-NR2 Ab has non-significant sensitivity and -LR, but it has statistically significant specificity and +LR in diagnosing NPSLE. Thus, patients with suspected NPSLE may benefit from checking their anti-NR2 levels. Nevertheless, further analyses are needed before recommending anti-NR2 for routine clinical use.
High Plasma Factor XIII Transglutaminase Activity Inversely Correlates with SLE Disease Activity Yet Associates with Higher Carotid Artery IMT and Low CD14+CD16+ Monocyte Levels

Brian Skaggs1, Isao Matsuura2, Elaine Lourenco1, Eloise Olmos3, Jennifer M. Grossman1 and Maureen A. McMahon1, 1University of California-Los Angeles, David Geffen School of Medicine, Division of Rheumatology, Los Angeles, CA, 2Department of Rheumatology, Tokyo Women’s Medical University Yachiyo Medical Center, Chiba, Japan, 3Division of Rheumatology, UCLA David Geffen School of Medicine, Los Angeles, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The transglutaminase Factor XIII (FXIII) stabilizes blood clots through crosslinking fibrin lysine and glutamine residues at the end of the complement cascade. Enzymatic activity and plasma levels of FXIII appear to be tightly controlled, as excess FXIII can lead to increased arterial plaque, yet low or absent FXIII leads to fibrin instability. In addition, recent data suggest that tissue macrophages could be the main source of plasma FXIII. Anti-FXIII antibodies have been observed in SLE and correlate with brain hemorrhage, although other clinical correlations between plasma FXIII and SLE remain unexplored.

Methods: 120 SLE patients were recruited from a pre-existing longitudinal cohort developed to study atherosclerosis in SLE. Anti-dsDNA, C3 and C4 levels were analyzed in the clinical lab of our university hospital. Carotid ultrasound was performed to determine the presence or absence of subclinical atherosclerosis and intima-media thickness (IMT). The Technochrom FXIII kit (Diapharma, West Chester, OH) was utilized to determine plasma FXIII transglutaminase activity. Plasma monocyte subpopulations were identified by flow cytometry using anti-CD14 and –CD16 fluorescent antibodies (Biolegend).

Results: 66/120 SLE patients had high plasma FXIII transglutaminase activity (>143% of the mean of the standard curve). SLEDAI was significantly lower in the high FXIII activity group compared to patients with normal FXIII activity (2.08±3.9 versus 4.2±3.1, p=0.006). In addition, anti-dsDNA antibody levels were significantly lower in the high FXIII activity group (87.5±255.7 versus 274.7±323.8, p=0.041). Significantly higher levels of plasma C3 and C4 levels were also observed in the high FXIII activity group. Taken together, these results show that higher FXIII activity might be a biomarker for lower SLE disease activity.

In contrast, percentages of CD14+CD16int and CD14+CD16hi plasma monocytes (considered precursors to anti-inflammatory ‘M2’ macrophages) were inversely proportional to FXIII activity (r=-0.54, p=0.008; r=-0.64, p=0.005, respectively), although there was no correlation between classical plasma monocyte levels (CD14+CD16, ‘M1’ macrophage precursors) and FXIII enzymatic activity. In addition, IMT positively correlated with FXIII activity (r=0.40, p=0.01). No correlations between carotid plaque presence and FXIII activity were noted.

Conclusion: High plasma FXIII transglutaminase activity correlates with multiple measures of low disease activity in SLE patients. Conversely, high FXIII activity inversely correlated with low numbers of anti-inflammatory monocytes. Higher
IMT was also observed in patients with high FXIII activity. Careful regulation of FXIII enzymatic activity, and, by extension, its crucial role in fibrin crosslinking and plaque stabilization, could be dysregulated in a subset of SLE patients at risk for accelerated atherosclerosis.

Disclosure: B. Skaggs, None; I. Matsuura, None; E. Lourenco, None; E. Olmos, None; J. M. Grossman, Medimmune, 2,AstraZeneca, 2,Aurinia, 2,Genentech and Biogen IDEC Inc., 2; M. A. McMahon, None.


Abstract Number: 693

The Utility of a Rise in Anti – Double Stranded DNA Antibodies for Predicting Disease Flares in Systemic Lupus Erythematosus. a Meta-Analysis

Margrét Arna Viktorsdóttir¹, Sæmundur Rögnvaldsson¹, Þórunn Jónsdóttir² and Gunnar Tomasson³, ¹University of Iceland, Faculty of Medicine, Reykjavík, Iceland, ²Landspítali University Hospital, Reykjavík, Iceland, ³University of Iceland, Faculty of Medicine, Reykjavík, IS

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The ability of predicting disease flares in systemic lupus erythematosus (SLE) by serial measurements of antibodies to double stranded DNA (anti-dsDNA) remains uncertain. Previous studies have found inconsistent results and clinical guidelines provide vague recommendations regarding this aspect of disease management. The objective of this study is to assess the diagnostic value of rise in anti-dsDNA for prediction of a disease flare in SLE.

Methods: A MEDLINE search without language restrictions was conducted to identify papers on anti-dsDNA and disease flares in SLE. Papers that could not be excluded by a review of titles and abstracts were subject to a detailed review. The primary inclusion criteria were 1) availability of the data to extract the sensitivity and specificity of a rise in anti-dsDNA for a disease flare and 2) the rise in anti-dsDNA preceded the flare. For each study, the positive and negative likelihood ratios were calculated and information extracted on disease manifestations and laboratory methods of anti-dsDNA measurements. Summary estimates with 95% confidence intervals (CI) were calculated with a random effects model and results expressed with forest plots. Between-study heterogeneity was assessed with $I^2$, which takes a value from 0 to 1 and refers to the part of the total variability in the meta-analysis that is due to heterogeneity. Meta-regression was used to assess the impact of the i)publication year, ii)gender proportions, iii)proportion of patients who had renal manifestations, iv)method- and v)frequency of anti-dsDNA measurements on summary estimates and heterogeneity. Egger's test was used to assess for publication bias using p-value of $<0.05$ as cut-off. The trim-and-fill method was used to adjust the summary estimates for publication bias.

Results:

Literature search identified 1690 papers of which 58 underwent full-text review. Nine studies with a total of 922 patients were included, of them 256 patients had a rise in anti-dsDNA and 243 had flares. Summary estimates for positive and negative likelihood ratios for anti-dsDNA rise and subsequent disease flare were 4.15 (95% CI 2.03-8.47) and 0.47 (95% CI 0.31-0.72) respectively (Figure). There was substantial between-study heterogeneity $I^2=0.89$. Neither disease manifestations nor the methods anti-dsDNA measurements affected the summary estimates or explained heterogeneity. Findings were consistent with presence of publication bias (p=0.021). Adjustment for publication bias substantially
attenuated the summary estimates resulting in positive and negative likelihood ratios of 1.90 (95% CI 0.84-4.33) and 0.72 (95% CI 0.46-1.14), respectively.

Conclusion:

A rise in anti-dsDNA has a limited ability for predicting flares in SLE and publication bias may have exaggerated the utility of serial anti-dsDNA measurements. These findings have direct implications for clinical management of SLE.

Disclosure: M. A. Viktorsdóttir, None; S. Rögnvaldsson, None; Þ. Jónsdóttir, None; G. Tomasson, None.


Abstract Number: 694

**Serum Wisteria Floribunda Agglutinin-Positive Mac-2-Binding Protein Can Reflect Systemic Lupus Erythematosus Activity**

Sung Soo Ahn¹, Younhee Park², Seung Min Jung¹, Jason Jungsik Song¹, Yong-Beom Park¹ and Sang-Won Lee¹,
¹Division of Rheumatology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea, Republic of (South), ²Department of Laboratory Medicine, Yonsei University College of Medicine, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Abstract Background/Purpose: Serum Mac-2-binding protein (M2BP) is elevated in various chronic inflammatory diseases. Recently, the Wisteria floribunda agglutinin positive-M2BP (WFA+-M2BP) immunoassay has shown promise in detection of highly glycosylated M2BP. We aimed to evaluate the clinical utility of serum M2BP for assessing disease activity of systemic lupus erythematosus (SLE), using the WFA+-M2BP immunoassay. **Methods**: Serum M2BP was measured in 203 patients with SLE. The associations between SLEDAI-2K and variables was assessed using multivariate
linear regression analysis. The relationship between serum M2BP and laboratory variables related to the SLE disease activity index (SLEDAI)-2K and inflammatory burdens was evaluated by Pearson’s correlation analysis. Multivariate logistic regression analysis was used to compare the odds ratios (ORs) of laboratory variables in predicting active SLE. Results: Eighty patients were classified as having active SLE (SLEDAI-2K ≥ 5) and 123 patients as having inactive SLE. The median serum M2BP was higher in patients with active SLE than those with inactive SLE (2.1 vs. 0.9, p < 0.001) (Table 1). In multivariate linear regression analysis, serum M2BP, anti-ds DNA, C3, and erythrocyte sedimentation rate were associated with SLEDAI-2K (Table 2). Serum M2BP was strongly correlated with laboratory variables related to SLEDAI-2K and inflammatory burdens, compared to other significant variables. Multivariate logistic regression analysis demonstrated that serum M2BP was more useful in predicting active SLE than other laboratory variables. Conclusion: Serum M2BP can reflect SLE activity and furthermore, it can predict active SLE. We suggest that serum M2BP may be a convenient complementary laboratory tool to SLEDAI-2K in the clinical setting. References 1. Nielsen CT, et al. Plasma levels of galectin-3-binding protein reflect type I interferon activity and are increased in patients with systemic lupus erythematosus. Lupus Sci Med 2014;1(1):e000026.
Disclosure: S. S. Ahn, None; Y. Park, None; S. M. Jung, None; J. J. Song, None; Y. B. Park, None; S. W. Lee, None.


Abstract Number: 695

Development of a Multimarker Model for the Detection of Systemic Lupus Erythematosus Based on New and Traditional Autoantibodies

Petra Budde1, Hans-Dieter Zucht1, Johannes Schulte-Pelkm1, Daniel Wirtz1, Torsten Witte2, Matthias Schneider3 and Peter Schulz-Knappe1, 1Protagen AG, Dortmund, Germany, 2Clinical Immunology and Rheumatology, Hannover Medical School, Hannover, Germany, 3Policlinic for Rheumatology & Hiller Research Centre for Rheumatology, Heinrich-Heine-University Duesseldorf, Duesseldorf, Germany

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Given the heterogeneity of clinical presentations, the diagnosis of Systemic Lupus Erythematosus (SLE) can be challenging, in particular in those patients presenting with early or incomplete disease, or with overlapping or atypical features. Autoantibodies (AABs) are important in aiding the clinical diagnosis of SLE, with some few AABs, anti-double-stranded DNA (dsDNA), anti-Smith (Sm), and anti-ribosomal P (riboP) being highly associated with SLE. As none of the traditional AABs has sufficient sensitivity to achieve diagnosis of SLE, current testing is based on measuring multiple AAB assays either in parallel or serial. We have recently identified novel AABs in SLE, which hold promise for improving diagnostic testing of SLE (1). We have developed quantitative ELISA-prototypes for five new AABs, which were tested in combination with traditional AABs. The objectives of this study were to evaluate the diagnostic value of novel AABs and to screen for an optimized combination of novel and traditional AABs using logistic regression to increase the diagnostic accuracy of SLE testing.

Methods: Serum samples were obtained from 156 SLE patients with European ancestry at the rheumatology department of the Heinrich-Heine University (Düsseldorf, Germany), and Hannover Medical School (Hannover, Germany). SLE samples were compared against 126 samples from autoimmune diseases (AID; myositis: n=20; Sjögren’s syndrome (SjS): n=31; rheumatoid arthritis (RA) n=36; systemic sclerosis (SSc): n=39), and 77 healthy control samples. Prototype bead based ELISAs were developed for 5recently identified novel antigens. Traditional diagnostic AABs were measured using IVD ELISAs and included: SSA/Ro60, SSA/Ro52, La/SSB, Sm, RNP, dsDNA, Scl70, CENPB, Jo-1, CCP, phospholipid and dsDNA. Optimized marker combinations of new and traditional markers were tested using logistic regression and receiver operating curve analysis (ROC).

Results: When comparing 156 SLE patients with 203 control samples, the area under the curve (AUC) of the five novel SLE ELISAs ranged from 0.63 to 0.75. A cut-off was set at a specificity of 95% and yielded a sensitivity ranging from
13.5% to 21.2% for the five novel assays. The sensitivity and specificity of new ELISAs was comparable to traditional ELISAs, which was in this cohort for anti-dsDNA 35% and 97%, anti-Sm 15% and 97%, and anti-RiboP 26% and 97%. A logistic regression model was used to combine the results of multiple tests. Compared to a logistic regression with traditional assays, a logistic regression with novel markers achieved higher sensitivity by pertaining high specificity. The logistic regression model based on a multimarker IVD assay with ten extracted nuclear antigens (ENA) yielded an AUC of 0.87 and a sensitivity of 58% at a specificity of 95%. By contrast, the optimal combination of traditional and novel ELISAs reached an AUC of 0.92 and a sensitivity of 75% at a specificity of 95%.

**Conclusion:** This study demonstrates the feasibility of combining test results of novel and traditional AABs using logistic regression to increase the diagnostic accuracy for SLE. Further studies are required to assess the impact of different ethnicities on marker selection and algorithm performance.

**Disclosure:** P. Budde, ProtagenAG, 3; H. D. Zucht, Protagen AG, 3; J. Schulte-Pelkum, ProtageAG, 3; D. Wirtz, Protagen AG, 3; T. Witte, None; M. Schneider, Protagen AG, 5; P. Schulz-Knappe, ProtagenAG, 3.


**Abstract Number:** 696

**An ANA Screening Assay Containing Multiple Antigens Increases the Sensitivity and Specificity of ANA Testing By Indirect Immunofluorescence**

Thomas Karonitsch, Hans Peter Kiener and Günter Steiner, Rheumatology, Medical University of Vienna, Vienna, Austria

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Indirect immunofluorescence (IIF) on Hep-2 cells is still considered the gold standard for screening of antinuclear antibodies (ANA), the serological hallmark of connective tissue diseases (CTD). While this method is sensitive it lacks specificity. Moreover, low-titer ANA subspecificities may escape detection by IIF. It was therefore the aim of this study to investigate the diagnostic usefulness of an ANA screening assay containing 13 diagnostically relevant antigens.

**Methods:**

Sera from 265 consecutive patients presenting with symptoms characteristic of connective tissue diseases (but without a clear diagnosis yet) were analysed by both IIF and the EliA® CTD Screen (Thermo Fisher Scientific) containing the following antigens: dsDNA, U1-snRNP, Sm, Ro60/SSA, Ro52/TRIM21, La/SSB, ribosomal protein P (ribP), topoisomerase I (Scl-70), centromere B, RNA polymerase III, fibrillarin, Jo-1, Mi-2, Pm/Scl.

**Results:**

Among the 265 patients, 90 were positive in IIF and 78 in the CTD Screen; 61 sera were positive in both systems, 17 only in the CTD Screen and 29 only in the IIF assay. Thus, the CTD Screen increased diagnostic sensitivity of ANA testing by approximately 6%. In all double positive patients at least one diagnostically relevant antibody was detected, with anti-Ro/SSA (n=32), anti-Ro52/TRIM21 (n=21) and anti-dsDNA (n=15) antibodies being the most frequently detected ones. In addition to the antibodies determined by standard routine diagnostics (dsDNA, U1-snRNP, Sm, Ro60/SSA, Ro52/TRIM 21, La/SSB, topoisomerase I, centromere B, Jo-1) antibodies to ribP, RNA polymerase III and Pm/Scl were detected in one
Importantly, antibodies were also detected in 15 of the 17 patients exclusively positive in the CTD Screen: anti-dsDNA (n=7), anti-Ro60/SSA (n=4), anti-U1snRNP (n=2), anti-La/SSB (n=1) and anti-Jo-1 (n=1). In contrast, among the 29 sera exclusively positive in IIF only two contained a diagnostically relevant antibody (low titre anti-DNA and anti-Sm). Clinical evaluation suggested that the majority of CTD Screen pos/IIF negative patients were at high risk for developing a CTD, particularly primary Sjogren’s syndrome. Most common symptoms were arthralgia (n=13), sicca syndrome (n=12) and Raynaud’s phenomenon (n=5). These patients require careful monitoring during clinical follow-up and might have escaped early diagnostic detection due the negative IIF result.

**Conclusion:** CTD screening assays containing multiple antigens seem to be useful and highly specific diagnostic tools that increase sensitivity of ANA testing enabling the detection of disease-associated ANA subspecificities in IIF-negative sera. This may reduce the number of false negative diagnoses enabling the physician to diagnose and treat “ANA negative” connective tissue diseases at an earlier stage.

**Disclosure:** T. Karonitsch, None; H. P. Kiener, None; G. Steiner, Thermo Fisher Scientific (Phadia GmbH), 2.

**Abstract Number:** 697

**Does Erythrocyte Sedimentation Rate Reflect and Discriminate Flare from Infection in Systemic Lupus Erythematosus? Correlation with Clinical and Laboratory Parameters of Disease Activity**

Valentin S. Schäfer¹, Katharina Weiss², Andreas Krause² and Wolfgang A. Schmidt³, ¹Immanuel Krankenhaus Berlin, Medical Center for Rheumatology Berlin-Buch, Berlin, Germany, ²Medical Centre for Rheumatology Berlin-Buch, Immanuel Krankenhaus Berlin, Berlin, Germany, ³Medical Center for Rheumatology and Clinical Immunology Berlin-Buch, Immanuel Krankenhaus Berlin, Berlin, Germany

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** ESR is applied for monitoring disease activity in SLE. It is known to be influenced by age and infections. We aimed at evaluating how ESR correlates with commonly applied disease activity parameters and how infections influence these results.

**Methods:** Retrospective analysis of laboratory parameters, clinical activity, infection and serositis in consecutive SLE patients between 2006 and 2015. Based on the treating physician’s judgement on disease activity and presence of infection, patients were separated into four groups: flare, infection, both and neither. ESR was correlated to CRP, ferritin, anti-dsDNA antibodies, C3, serositis and erythrocyturia with proteinuria. For age, ESR, CRP, ferritin and age- and gender-adapted ESR (ESRp), mean values between groups were compared. ESRp was calculated as the percentage of an ESR cut-off considering age and gender.

**Results:** We identified 203 SLE patients with 371 visits, flare n=147, infection n=48, both n=23 and neither flare nor infection n=153. Correlation coefficients of ESR and other parameters are given in table 1; there was moderate correlation with CRP (r=0.47-0.58) and weak correlation with other parameters (r<0.2). As shown in figure 1, ESR and CRP levels were normal in patients in remission, but did not differ between flare, infection or both. ESRp was higher in patients with flare versus with infection (p=0.01). ESR and CRP lost association to activity in infected patients and, conversely, to
infection in patients with flare. ESRp, serositis and anti-dsDNA antibodies were related to disease activity regardless of infections (table 2).

**Conclusion:** ESR is raised in flares, but also in infected and older patients. CRP levels do not enable discrimination between flare and infection. Both parameters argue against flare and infection when normal. ESRp can help to differentiate between flare, infection or even both.

Table 1: Correlation coefficients of ESR with other laboratory and clinical parameters

<table>
<thead>
<tr>
<th></th>
<th>CRP</th>
<th>Ferritin</th>
<th>C3-reduction</th>
<th>Raised anti-dsDNA-antibodies</th>
<th>erythrocyturia + proteinuria</th>
<th>Serositis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All visits</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=371)</td>
<td>0.498*</td>
<td>0.256*</td>
<td>0.165*</td>
<td>0.134*</td>
<td>0.186*</td>
<td>0.079</td>
</tr>
<tr>
<td><strong>Flare only</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=147)</td>
<td>0.549*</td>
<td>0.268*</td>
<td>0.064</td>
<td>0.101</td>
<td>0.141</td>
<td>0.094</td>
</tr>
<tr>
<td><strong>Infection only</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=48)</td>
<td>0.468*</td>
<td>0.109</td>
<td>0.172</td>
<td>0.12</td>
<td>0.214</td>
<td>-0.338*</td>
</tr>
<tr>
<td><strong>Both</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=23)</td>
<td>0.575*</td>
<td>0.266</td>
<td>0.037</td>
<td>0.205</td>
<td>0.091</td>
<td>-0.09</td>
</tr>
<tr>
<td><strong>Silent</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=153)</td>
<td>0.556*</td>
<td>0.25</td>
<td>0.032</td>
<td>0.082</td>
<td>0.137</td>
<td>-0.016</td>
</tr>
</tbody>
</table>

(Pearson’s r); significant correlation is marked with *.

Table 2: Association of laboratory and clinical parameters with SLE flare and infection
<table>
<thead>
<tr>
<th></th>
<th>ESR</th>
<th>ESRp</th>
<th>CRP</th>
<th>Ferritin</th>
<th>C3-reduction</th>
<th>Raised anti-dsDNA-antibodies</th>
<th>Erythrocyturia + Proteinuria</th>
<th>Se</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>P-value for the association with disease activity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>all visits</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=371)</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>0.692</td>
<td>0.405</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>0.002*</td>
<td></td>
</tr>
<tr>
<td>without infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=300)</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>0.318</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>0.01*</td>
<td></td>
</tr>
<tr>
<td>with infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=71)</td>
<td>0.186</td>
<td>&lt;0.001*</td>
<td>0.321</td>
<td>0.713</td>
<td>0.268</td>
<td>&lt;0.001*</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>P-value for the association with infections</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>all visits</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=371)</td>
<td>&lt;0.001*</td>
<td>0.053</td>
<td>&lt;0.001*</td>
<td>0.797</td>
<td>0.384</td>
<td>0.023*</td>
<td>0.831</td>
<td></td>
</tr>
<tr>
<td>without activity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=201)</td>
<td>&lt;0.001*</td>
<td>0.001*</td>
<td>&lt;0.001*</td>
<td>0.642</td>
<td>0.281</td>
<td>0.068</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>with activity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=170)</td>
<td>0.039</td>
<td>0.052</td>
<td>0.213</td>
<td>0.576</td>
<td>0.255</td>
<td>1</td>
<td>0.506</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1: 95% confidence interval of mean values of age, ESR, ESRp, CRP, and ferritin in SLE groups
Disclosure: V. S. Schäfer, None; K. Weiss, None; A. Krause, None; W. A. Schmidt, None.


Abstract Number: 698

Selected Nailfold Videocapillaroscopy Changes Are Linked to SLE Onset in a Cohort of Uctd Subjects

Marianna Meroni1, Carmen Pizzorni2, Alberto Sulli1, Paola Rossi3, Paolo Stobbione3 and Maurizio Cutolo4, 1Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, IRCCS A.O.U. San Martino-IST, University of Genova, Genoa, Italy, Genova, Italy, 2Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, IRCCS San Martino, Genoa, Italy, Genoa, Italy, 3Rheumatology Unit, Internal Medicine Department - A.O. S.S. Antonio e Biagio e Cesare Arrigo, Alessandria, Italy,
Background/Purpose: Nailfold capillaroscopy (NVC) is a useful, non-invasive, reproducible and cost-effective diagnostic tool, able to assess the shape of capillaries in the nailfold bed. According to the presence of peculiar abnormalities, it is essential in the early differential diagnosis of connective tissue diseases (CTDs), mainly “scleroderma-spectrum disorders” (SSD). Despite its large diffusion, no univocal NVC patterns have been ascribed to undifferentiated connective tissue disease (UCTD) as well as to systemic lupus erythematosus (SLE). The aim of the study was to evaluate the most common NVC pictures in a population of UCTD patients and if selected NVC pictures might be linked to SLE onset in these patients.

Methods: We evaluated a cohort of 42 UCTD-affected women, diagnosed according to 2014 criteria proposed by Mosca et al. (age, 38 years±46 months; duration of disease, 71±54 months) presenting Raynaud's phenomenon. During the observational period (3 years), all of the UCTD patients were evaluated every 6 months. We considered the following NVC parameters/pictures: presence of ectasic capillary loops (diameter ≥20 µm); giant capillaries (diameter ≥50 µm); hemosiderin deposits; capillary number reduction; meandering capillaries (tortuosity); elongated capillaries; ramified/bushy capillaries; micro-vascular array disorganization. SLE diagnosis was posed according to the 2012 SLICC/ACR criteria. Qualitative variables were expressed in frequencies; their association, by non-parametric tests; quantitative variables, by analysis of co-variance.

Results: Non-specific NVC alterations (for instance, not suggestive of SDD) were detected in 40 (98%) of the UCTD patients during the observational period. On the other hands, the presence of hemosiderin deposits, ectasic loops, elongated and ramified capillaries was found associated to the clinical subgroup of UCTD patients that later developed SLE (4/42 subjects, 10%; OR=10.5).

In particular, the independent variables “hemosiderin deposits” (OR=8.32) and “elongated capillaries” (OR 6.28), were found significantly linked to the SLE onset (p<0.05), whereas the independent variables “tortuosity” (OR=12.16) and “ramified/bushy capillaries” (OR 9.47) were, at the opposite, predictive for the prosecution of the status of UCTD patient (p<0.05).

Conclusion: The present study reports NVC pictures that can be more frequently observed in UCTD patients. In addition, the NVC analysis suggests that the presence of typical capillaroscopic microvascular abnormalities seems more frequently observed in those UCTD patients that move to SLE.

Disclosure: M. Meroni, None; C. Pizzorni, None; A. Sulli, None; P. Rossi, None; P. Stobbione, None; M. Cutolo, None.
Impact of Anti-RBP Antibodies on Disease Activity and Quality-of-Life in Immunosuppressant Naive Systemic Lupus Erythematosus

Rene Bermea¹, Tammy Utset² and Kichul Ko³, ¹Medicine, University of Chicago, Chicago, IL, ²Medicine, Section of Rheumatology, University of Chicago, Chicago, IL, ³Medicine, Section of Rheumatology and Gwen Knapp Center for Lupus and Immunology Research, University of Chicago, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: There is a lack of phenotypic data on SLE patients who have never been on immunosuppressive therapy. Anti-RNA binding protein (anti-RBP) antibodies (anti-Smith, anti-RNP, anti-SSA, anti-SSB) in SLE have been linked to an upregulation in transcriptional patterns, some thought to contribute to disease. This study sought to characterize the impact of these autoantibodies on disease activity and quality-of-life in immunosuppressant naïve SLE patients.

Methods: Retrospective cross-sectional analysis of subjects meeting ACR Classification Criteria for SLE was performed. Subjects were anti-RBP positive (RBP+) if at least one titer was ≥ 20 (units, ELISA); others were classified as anti-RBP negative (RBP-). Subjects ever on non-corticosteroid immunosuppression or currently on corticosteroids were excluded. Baseline characteristics included age, sex, disease duration, anti-dsDNA, C3, C4, and ethnicity (African-American [AA] or European-American [EA]). A measure of all four anti-RBP titers and most baseline characteristics were necessary for inclusion. Disease activity was measured using the SLEDAI and quality-of-life indices included the Beck Depression Inventory (BDI), Fatigue Severity Scale (FSS), Numerical Rating Scale for Pain (NRS-Pain Scale), and the Medical Outcomes Study Sleep Scale (MOS-SS). Both groups were compared using Mann-Whitney U, two-tailed Fisher’s Exact tests, and multivariate linear regression.

Results: Forty-one subjects met criteria for inclusion, 29 of which were identified as RBP+ and 12 RBP-. There was no difference in age, sex, disease duration, anti-dsDNA, C3, or C4 between groups. There were significantly more AA in the RBP+ group (65.5% vs 16.7%, p <0.01) and EA in the RBP- group (34.5% vs 75.0%, p=0.037). Disease activity and quality-of-life indices between groups is demonstrated in Figure 1. SLEDAI was significantly worse in RBP+ vs RBP- subjects (3 vs. 0, p=0.009), a relationship confirmed with multivariate regression (standardized beta coefficient = 0.515, p = 0.017). Similarly, BDI scores were worse in the RBP+ cohort (10 vs. 4, p=0.050). RBP+ subjects trended towards worse fatigue by FSS (4.67 vs. 2.72, p=0.139) and pain by NRS-Pain Scale (21 vs. 4, p=0.087). MOS-SS sleep indices were also worse among RBP+ subjects. To account for the difference in ethnicity between groups, a subgroup analysis of EA patients was conducted and found similar trends in RBP+ patients.

Conclusion: Anti-RBP positive SLE subjects showed worse measures of disease activity and quality-of-life. RBP+ subjects were more likely to be African-American, although similar outcomes were seen in a European-American sub-analysis. Our study was limited by sample size given our exclusion of immunosuppressed subjects. Further study is needed to measure these antibodies’ impact on clinical outcomes and response to treatment prospectively.
Disclosure: R. Bermea, None; T. Utset, None; K. Ko, None.


Abstract Number: 700

Variability in Method of Testing for Antinuclear Antibodies (ANA): A Survey of Participants in the College of American Pathologist’s (CAP) Proficiency Testing Program

Stanley J. Naides¹, Jonathan Genzen², Gyorgy Abel³, Christine Bashleben⁴ and Mohammad Qasim Ansari⁵, ¹Immunology, Quest Diagnostics Nichols Institute, San Juan Capistrano, CA, ²ARUP Laboratories Inc, Salt Lake City, UT, ³Department of Pathology and Laboratory Medicine, Lahey Clinic Burlington, Burlington, VT, ⁴College of American Pathologists, Northfield, IL, ⁵Department of Pathology and Laboratory Medicine, Louis Stokes VAMC, Cleveland, OH

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: A 2010 American College of Rheumatology position paper designated indirect immunofluorescence assay (IFA) on HEp-2 cells the “gold standard” for ANA testing and that laboratories performing other methods should state the method used and describe its performance parameters. This study was performed to determine laboratory practices in ANA testing.

Methods: Supplemental questions were sent to laboratories participating in the College of American Pathologist’s proficiency testing program for ANA as part of the Special Immunology S-A Survey 2016 to determine the practice of ANA testing. Of 5847 kits distributed, 1206 (21%) responded to the questionnaire; 942 were in the United States and 264 were international.

Results: ANA screening method varied: 56% IFA, 21% ELISA, 12% multi-bead immunoassay, and 18% “other” methods. Ordering test name indicated method used in only 32%; only 39% stated method used on the report. Of 644 laboratories, 80% used HEp-2 substrate, 18% HEp-2000 (HEp-2 cell line engineered to overexpress SSA), and 2% “other.” Slides were prepared manually (67%) or on an automated platform (33%), and examined by direct microscopy (84%) or images.
captured by an automated platform (16%). IFA patterns were interpreted by personnel in 95% of laboratories; <1% used automated image capture and analysis solely; 4% interpreted images both by personnel and an automated platform. 97% of 641 laboratories reporting ANA by IFA provided a titer. Only 51% reported a positive result at the traditional 1:40 dilution. Titer was reported to endpoint routinely by 43%, only upon request by 23%, or never by 35%. 8% did not report dual patterns. Of those reporting multiple patterns, 24% did not report a titer with each pattern.

**Conclusion:** Only slightly more than half of testing laboratories utilize the ACR “gold standard” IFA method with HEp-2 cell substrate.

**Disclosure:** S. J. Naides, Quest Diagnostics, 3; J. Genzen, None; G. Abel, None; C. Bashleben, None; M. Q. Ansari, None.


**Abstract Number: 701**

**Variability in ICAP (International Consensus on ANA Patterns) Pattern Reporting in Testing for Antinuclear Antibodies (ANA) By Indirect Immunofluorescence Assay (IFA)**

**Stanley J. Naides**¹, Jonathan Genzen², Gyorgy Abel³, Christine Bashleben⁴ and Mohammad Qasim Ansari⁵,

¹Immunology, Quest Diagnostics Nichols Institute, San Juan Capistrano, CA, ²ARUP Laboratories Inc, Salt Lake City, UT, ³Department of Pathology and Laboratory Medicine, Lahey Clinic Burlington, Burlington, VT, ⁴College of American Pathologists, Northfield, IL, ⁵Department of Pathology and Laboratory Medicine, Louis Stokes VAMC, Cleveland, OH

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** ANA IFA pattern may guide clinical evaluation by directing specific antibody testing. ICAP has defined consensus ANA IFA patterns and the level of competency required to identify and interpret them. This study was performed to determine laboratory practices in interpreting and reporting ANA IFA patterns.

**Methods:** Supplemental questions were sent to laboratories participating in the College of American Pathologist’s proficiency testing program for ANA as part of the Special Immunology S-A Survey 2016 to determine the practice of ANA testing. Of 5847 kits distributed, 1206 (21%) responded to the questionnaire; 942 were in the United States and 264 were international.

**Results:** Of 638 performing ANA by IFA and reporting a pattern, nearly 100% reported nucleolar, 99% homogeneous and speckled, and 96% centromere, all competent-level ICAP patterns. Only 42% reported nuclear dots (competent-level). 53% reporting nucleolar pattern further described expert-level subpatterns. Of 519 reporting speckled patterns, only 29% reported dense fine speckles, a competent-level pattern reportedly found in normals. “Other” speckled was reported by 44%. 4% did not report speckled pattern at all. Of those reporting nuclear dots, 86% differentiated many nuclear dots and 84% few nuclear dots. Nuclear envelope (expert-level) was reported by 18%. Competent-level cytoplasmic patterns were reported: golgi 69%, mitochondrial 65%, speckles 30%, 17% rods and rings, reticular 12% and polar 10%. Expert-level cytoplasmic patterns were reported: spindle apparatus 59%, centriole 55%, mid body 45%, and lysosomal 32%. Only 54% used an internal fluorescence intensity standard.
**Conclusion:** Pattern reporting practice is variable. Cytoplasmic pattern reporting is limited, possibly reflecting a lack of consensus that cytoplasmic patterns should be reported in an “antinuclear” antibody test. Failure to use an internal fluorescence intensity standard by nearly half of the laboratories may increase inter-assay and inter-observer variation in the threshold for staining positivity and in titer determination.

**Disclosure:** S. J. Naides, Quest Diagnostics, 3; J. Genzen, None; G. Abel, None; C. Bashleben, None; M. Q. Ansari, None.


**Abstract Number:** 702

**Positive Direct Coombs’ Test in the Absence of Hemolytic Anemia Predicts High Disease Activity and Poor Renal Response in Systemic Lupus Erythematosus**

**Hironari Hanaoka,** Harunobu Iida, Tomofumi Kiyokawa, Yukiko Takakuwa and Kimito Kawahata, Division of Rheumatology and Allergology, Department of Internal Medicine, St. Marianna University School of Medicine, Kawasaki, Japan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Direct Coombs' test in the absence of hemolytic anemia was newly included in the immunologic criterion of the SLICC/ACR 2012 criteria for SLE. Since erythrocyte complement receptor contributes to the clearance of circulating immunocomplex, the direct Coombs' test in the absence of hemolytic anemia may indicate excessive immunocomplex production. In this study, we determined its clinical significance in Japanese SLE population.

**Methods:** Patients who fulfilled SLICC/ACR classification criteria of SLE and visited St. Marianna University Hospital during Jan to Nov 2016 were prospectively evaluated with direct Coombs' test. Hemolysis was defined as lower haptoglobin concentration than the normal limit. Clinical features including SLEDAI, treatment, and laboratory findings were examined. For patients with lupus nephritis class III or IV, we additionally compared renal pathological features and cumulative complete renal response (CR) rate between patients with positive result for direct Coombs' test in the absence of hemolytic anemia and those with negative.

**Results:** Among 186 patients enrolled, 10 (5.4%) patients were positive with direct Coombs' test in the absence of hemolytic anemia. They had higher SLEDAI (p<0.01), lower CH50 (p<0.01), higher anti-DNA titer (p<0.01) and lower cumulative CR rate (p=0.03) (Figure 1) comparing to those who were negative. In the renal pathological analysis, a significantly higher percentage of subendothelial deposit was determined in patients who were positive comparing to those who were negative (p=0.02). Multivariate analysis indicated that SLEDAI was the independent factor strongly correlated with the direct Coombs' test (OR 2.44, 95%CI 1.66-4.98, p<0.01) (Table 1).

**Conclusion:** Direct Coombs' test in the absence of hemolytic anemia might be correlated with high disease activity and poor renal response in SLE.
Clinical Value of Autoantibodies for Lupus Myelitis and Its Subtypes: A Systematic Review

Hiroshi Oiwa¹, Akira Kuriyama², Tomoyasu Matsubara³ and Eiji Sugiyama⁴, ¹Rheumatology, Hiroshima City Hiroshima Citizens Hospital, Hiroshima, Japan, ²General Medicine, Kurashiki Central Hospital, Kurashiki, Japan, ³Neurology, Hiroshima University Hospital, Hiroshima, Japan, ⁴Department of Clinical Immunology and Rheumatology, Hiroshima University Hospital, Hiroshima, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: We conducted a systematic review to investigate the clinical value of clinical characteristics and autoantibodies, especially lupus-specific antibodies, for lupus myelitis and its subtypes.

Methods: We searched PubMed, EMBASE, and ICHUSHI without language restrictions for case reports or series of lupus myelitis. We focused on cases reported since 1997, when the revised classification criteria for systemic lupus erythematosus were published. Associations between patient characteristics including autoantibodies and functional...
outcome, survival, and subtypes of myelitis (grey and white matter myelitis) were examined. We attempted to contact authors to supplement missing information for analysis.

**Results:** Our search identified 224 cases from 105 articles. White matter myelitis predicted favorable function (odds ratio, 15.18; 99% confidence interval, 3.09 to 151.31; p<0.0001). Anti-nuclear antibody also predicted favorable function (p=0.007). Age ≥50 years was associated with poor survival outcomes (p=0.007). Grey matter myelitis was associated with longitudinally extensive transverse myelitis (p<0.001) and anti-double-stranded DNA (p=0.003), and tended to be associated with anti-β2-glycoprotein I (p=0.011). White matter myelitis tended to be associated with optic neuritis and anti-neuromyelitis optica antibodies. Although our study might be susceptible to under-reporting of original cases and selection bias, we aimed to provide a conservative interpretation by setting the statistical significance threshold at p<0.01.

**Conclusion:** This systematic review confirmed that grey matter myelitis predicted poor functional outcome, and was associated with longitudinally extensive transverse myelitis and anti-double-stranded DNA antibodies. White matter myelitis was associated with favorable functional outcomes and may partially represent a complication of neuromyelitis optica.

Disclosure: H. Oiwa, None; A. Kuriyama, None; T. Matsubara, None; E. Sugiyama, None.

**Abstract Number:** 704

**Detection of dsDNA Antibodies By New Fluoroimmunoassay with Comparable Diagnostic Sensitivity and Specificity to Farr-Ria**

Katja Lakota1,2, Tanja Kveder2, Tinka Svec2, Polona Žigon2, Ales Ambrožić3, Borut Božič2,4, Matija Tomšič2,5, Saša Čučnik2,4 and Snezna Sodin Semrl2,1, 1Faculty of Mathematics, Natural Science and Information Technology, University of Primorska, Koper, Slovenia, 2Department of Rheumatology, University Medical Centre Ljubljana, Ljubljana, Slovenia, 3Department of Rheumatology, University Medical Centre Ljubljana, 1000 Ljubljana, Slovenia, 4Faculty of Pharmacy, University of Ljubljana, Ljubljana, Slovenia, 5University of Ljubljana, Faculty of Medicine, Ljubljana, Slovenia

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Antibodies against double-stranded deoxyribonucleic acid (anti-dsDNA) are a useful and valuable serological marker for diagnosis of systemic lupus erythematosus (SLE). Studies suggest strong correlation between increasing levels of anti-dsDNA and subsequent flares, particularly renal disease. The radioactive immunoassay (RIA) by FARR (FARR-RIA) has been utilized as the gold standard in the past for anti-dsDNA determination, detecting mostly high avidity antibodies. Additionally, enzyme-linked immunoassay (ELISA) and immunofluorescence (Cithidia luciliae) (CLIF) both recognize also low avidity anti-dsDNA and ELISA also detects antibodies against ssDNA. There is a need for replacing FARR-RIA with a safer and more environmentally friendly immunoassay. To modify the detection of anti-dsDNA by FARR-RIA, by replacing the radioactive isotope 14C and other toxic reagents and evaluate the newly developed, environmentally-friendly fluoroimmunoassay (FIA) for daily laboratory and clinical practice.

**Methods:** We tested 759 sequentially collected samples for anti-dsDNA testing, with FARR-RIA and FIA (using Picogreen® as intercalating dye). The group consisted of 146 blood donors, 70 SLE, 25 antiphospholipid syndrome, 28
rheumatoid arthritis, 25 Sjögren’s syndrome and 465 patients with unknown diagnoses. Final results of both methods were calculated from difference of signal measured between supernatant (S) and precipitate (P) divided by the sum of signals in S and P.

**Results:** At cut-off value of 0.35, both diagnostic specificity and sensitivity were comparable using FARR-RIA and FIA. Diagnostic specificity in both methods was 100%, while diagnostic sensitivity for FARR-RIA and FIA were 50% and 53%, respectively. Diagnostic accuracy for FIA was slightly lower compared to FARR-RIA, 0.781 vs. 0.887. There was comparable inter-accuracy of both methods in high positive results (CV$_{\text{FARR-RIA}}$ = 11%, CV$_{\text{FIA}}$ = 12%), while low positive results (CV$_{\text{FARR-RIA}}$ = 29%, CV$_{\text{FIA}}$ = 18%) showed greater variation. We confirmed comparable intra-repeatability in high positive results (CV = 2% for both methods) and low positive results (CV$_{\text{FARR-RIA}}$ = 33%, CV$_{\text{FIA}}$ = 28%). At high and low positive results comparable analytical accuracy was observed, while analytical sensitivity was higher in FIA. Neither ssDNA nor RNA affected the detection of anti-dsDNA. A correlation of 0.626 (p<0.01) was found between FARR-RIA and FIA positive results.

**Conclusion:** FIA and FARR-RIA showed comparable diagnostic specificity and sensitivity. Therefore, FARR-RIA could be replaced with FIA in daily laboratory routine practice for the detection of anti-dsDNA.

**Disclosure:** K. Lakota, None; T. Kveder, None; T. Svec, None; P. Žigon, None; A. Ambrozic, None; B. Božič, None; M. Tomšič, None; S. Čučnik, None; S. Sodin Semrl, None.

**Optimization of a Cost-Effective Diagnostic ANA Algorithm**

Mathieu Cauchie$^1$, Bert Vander Cruyssen$^2$, Stefanie Van den Bremt$^3$, Muriel Stubbe$^4$, Xavier Bossuyt$^5$ and Lieve Van Hoove$^{3}$, $^1$OLV Hospital, Aalst, Belgium, $^2$Rheumatology, OLV hospital, Aalst, Belgium, $^3$Laboratory medicine, OLV Hospital, Aalst, Belgium, $^4$Rheumatology, OLV Hospital, Aalst, Belgium, $^5$Laboratory medicine, University Hospital Leuven, Leuven, Belgium

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Due to the poor specificity of the anti-nuclear antibodies (ANA) indirect immunofluorescence (IIF) assay, enhanced by the huge increase in ANA requests by non-rheumatologists, second line identification of specific anti-double stranded DNA (dsDNA) and anti- extractable nuclear antigen (ENA) is necessary.

Our study aims to objectify a cost-effective diagnostic ANA algorithm, standardizing the work-out of positive ANA IIF tests in a routine, secondary care setting.

**Methods:**

The ANA test results reported in our laboratory were retrospectively reviewed over a 9-month period. Positive ANA IIF test results on NOVA View® (Inova, USA) at 1:80 screening dilution (cut off = 49 Light Intensity Units (LIU)) were further analysed by dsDNA- (dsDNA-NcX IgG ELISA, Euroimmun, Germany) and ENA-screen (ANA screen 11 IgG
ELISA, Euroimmun). For positive ENA-screen samples, ANA identification was performed with EUROLINE ANA profile 3 (Euroimmun). Based on ROC-curve analysis of LIU versus ENA/dsDNA identification, the LIU cut off at 95% sensitivity was determined.

Results:

3276 samples of 2916 patients were tested for ANA, of which 49.8% were from the rheumatology ward. 279 (9.6%) patients had repeated ANA requests. None of the repeated ANA IIF, dsDNA/ENA screen tests had a clinically significant result. 45.9% patients tested ANA IIF positive, with identification of a specific Ab (dsDNA/ENA) in 11.6% of the patients. ROC analysis of LIU in function of ENA/dsDNA identification revealed a specificity of 3.0% (2.1-4.3) for the 49 LIU cut off. A global ANA IIF sensitivity of 94.8% for ENA/dsDNA identification was obtained at a cut off of 88 LIU, with a specificity of 36.1% (33.6-39.5%) (Table 1). ROC curve analysis for isolated homogeneous, speckled, centromere and speckled metaphase positive IIF patterns confirmed an acceptable analytical performance and LR’s of ENA/dsDNA positivity at LIU of 88 (Table 2), in concordance with earlier published LR’s for ANA associated rheumatic disease positivity. Using this 88 LIU cut off for second line testing, can result in a yearly cost reduction of 5.060€. Introducing a limitation of the ANA workout to once yearly, if ANA IIF titer and pattern are stable, implies a supplementary cost reduction of 4.290€.

Conclusion:

Analytical performance analysis reveals a clinical and cost effective cut off for ANA IIF of 88 LIU for the initiation of second-level testing. If the patient is clinically stable and ANA IIF pattern and titer has not significantly changed, a yearly repetition of the diagnostic ANA workout is more than clinically sufficient.

### Table 1

<table>
<thead>
<tr>
<th>ANA IIF pattern</th>
<th>ENA/dsDNA+/ENA/dsDNA-</th>
<th>LIU interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-87</td>
<td>88-300</td>
</tr>
<tr>
<td></td>
<td>301-1000</td>
<td>&gt;1000</td>
</tr>
<tr>
<td>Likelihood ratio of AARD*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>97/467</td>
<td>0.28</td>
</tr>
<tr>
<td></td>
<td>0.65</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.14</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8.53</td>
<td></td>
</tr>
</tbody>
</table>

### Table 2

<table>
<thead>
<tr>
<th>ANA IIF pattern</th>
<th>Cut off 49 LIU</th>
<th>Cut off 88 LIU</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sensitivity</td>
<td>Specificity</td>
</tr>
<tr>
<td>All</td>
<td>100.0%</td>
<td>2.6%</td>
</tr>
<tr>
<td>(97.6-100)</td>
<td>(1.7-3.7)</td>
<td></td>
</tr>
<tr>
<td>Homogeneous</td>
<td>100.0%</td>
<td>1.0%</td>
</tr>
<tr>
<td>(92.6-100)</td>
<td>(0.03-5.4)</td>
<td></td>
</tr>
<tr>
<td>Specified</td>
<td>100.0%</td>
<td>0.7%</td>
</tr>
<tr>
<td>(95.5-100)</td>
<td>(0.1-2.0)</td>
<td></td>
</tr>
<tr>
<td>Specified metaphase</td>
<td>100.0%</td>
<td>1.4%</td>
</tr>
<tr>
<td>Centromere</td>
<td>(89.7-100)</td>
<td>(0.5-3.0)</td>
</tr>
<tr>
<td></td>
<td>(1.7-3.7)</td>
<td></td>
</tr>
</tbody>
</table>

Disclosure: M. Cauchie, None; B. Vander Cruyssen, None; S. Van den Bremt, None; M. Stubbe, None; X. Bossuyt, None; L. Van Hoovels, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/optimization-of-a-cost-effective-diagnostic-ana-algorithm](http://acrabstracts.org/abstract/optimization-of-a-cost-effective-diagnostic-ana-algorithm)

Abstract Number: 706
Elevated Erythrocyte Sedimentation Rate Among Obese Patients with SLE—Not Always a Marker of Disease Activity

George Stojan$^1$, Erik Barr$^2$ and Michelle Petri$^3$, $^1$Medicine, Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, $^2$Epidemiology and Public Health, University of Maryland School of Medicine, Baltimore, MD, $^3$Medicine (Rheumatology), Division of Rheumatology, Johns Hopkins University School of Medicine, MD, USA, Baltimore, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Obesity is more common in patients with SLE compared to the general population. The prevalence of obesity among SLE patients is between 28 and 50 percent. We hypothesized that a higher body mass index was associated with elevated ESR after adjusting for disease activity, prednisone and immunosuppressive use.

Methods:
Our analysis is based on 2246 different patients who were observed from 1 to 137 visits. The median number of visits per patient was 15.

The “between-person” association addresses the question of whether those who tend to have high BMI also tend to have high ESR. To assess this, we calculated the person-specific mean ERS values and plotted them against the person-specific mean BMIs. We fit crude and adjusted models to estimate the slope in the expectation of mean ESR per unit difference in mean BMI. The results are shown in Table 1.

The within-person analysis addresses the question of whether a person tends to have higher ESR when his/her BMI is lower than his average BMI. To assess this, for each visit, we calculated the difference between the BMI level at that visit and the person’s average of BMI. Then we modelled the relationship between these differences in BMI and the difference between the person’s ESR at each visit and the person’s average ESR.

Results:
Table 1: Difference in person-specific mean ESR per 1 unit difference in person-specific mean BMI
Table 2: Difference in ESR at each visit per 1 unit difference in between the person’s BMI at that visit and the person’s average BMI.

<table>
<thead>
<tr>
<th>Model</th>
<th>Effect</th>
<th>Unadjusted</th>
<th>Adjusted&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Estimated difference in mean ESR per 1 unit difference in mean BMI (95%)</td>
<td>Estimated difference in mean ESR per 1 unit difference in mean BMI (95%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CI)</td>
<td>P-value</td>
</tr>
<tr>
<td>Model 1</td>
<td>BMI</td>
<td>0.6 (0.4, 0.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pooling across Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 2</td>
<td>BMI</td>
<td>0.6 (0.5, 0.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Allowing different association by sex</td>
<td>Female</td>
<td>5.0 (-12.2, 22.2)</td>
<td>0.57</td>
</tr>
<tr>
<td></td>
<td>BMI*Sex</td>
<td>-0.5 (-1.1, 0.2)</td>
<td>0.14</td>
</tr>
</tbody>
</table>

<sup>1</sup> Adjusted for age, age-squared, race, mean disease activity, mean prednisone dose, proportion of time on immunosuppressant medication.

Conclusion:

Patients whose mean BMI is 10 points higher have a mean ESR that is 6mm/hour higher (p<0.0001). The association between BMI and ESR does not vary by sex and is not affected by adjusting for covariates.

We also found a significant within person association between ESR and BMI: a 1 unit increase in BMI increases the expected ESR by 0.09mm/hour (p=0.004).
Careful interpretation of clinical data is necessary in obese patients—an elevated ESR may not be a manifestation of disease activity.

Disclosure: G. Stojan, None; E. Barr, None; M. Petri, Anthera Inc, 5, GlaxoSmithKline, 5, EMD Serono, 5, Eli Lilly and Company, 5, Bristol Meyer Squibb, 5, Amgen, 5, United Rheumatology, 5, Global Academy, 5, Exagen, 2.

Abstract Number: 707

**Distinctive Features of Positive Anti-Cell Antibody Tests on HEp-2 Cells (HEp-2-ANA) in Patients with Non-Autoimmune Diseases**

Renan Agustinelli¹, Silvia H. Rodrigues², Monica Prado³, Henrique Mariz⁴ and Luis Eduardo C. Andrade⁵,⁶

¹Rheumatology Division, Escola Paulista de Medicina, Universidade Federal de Sao Paulo, Sao Paulo, Brazil, ²Rheumatology Division, Escola Paulista de Medicina, Universidade Federal de Sao Paulo, Sao Paulo, Brazil, ³Rheumatology Division, Escola Paulista de Medicina - Universidade Federal de Sao Paulo, Sao Paulo, Brazil, ⁴Internal Medicine Department, Hospital das Clinicas - Universidade Federal de Pernambuco, Recife, Brazil, ⁵Rheumatology Division, Universidade Federal de Sao Paulo, Sao Paulo, Brazil, ⁶Immunology Division, Fleury Medicine and Health, Sao Paulo, Brazil

First publication: September 18, 2017

SESSION INFORMATION

**Session Date:** Sunday, November 5, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The indirect immunofluorescence (IIF) test for anti-cell or antinuclear (ANA) antibodies on HEp-2 cells (HEp-2-ANA) is considered the gold standard method for ANA detection. However, this is a very sensitive test and detects autoantibodies also in some healthy individuals and patients with non-autoimmune diseases. The establishment of distinctive HEp-2-ANA features in SARD patients and in healthy individuals has proven to be helpful in the daily medical practice. However, the HEp-2-ANA test is not expected to be requested for healthy individuals, but rather for those seeking medical care due to some health disorder. Therefore, we aimed to determine the frequency and characteristics of positive HEp-2-ANA tests in individuals affected by a variety of non-autoimmune diseases.

**Methods:** This is a cross-sectional observational study comparing HEp-2-ANA results in 588 non-autoimmune disease (NAD) patients, 194 patients with systemic autoimmune rheumatic diseases (SARD) and 1,217 healthy individuals. NAD group comprised 4 subgroups: 95 patients with malignancy, 148 with infectious diseases, 163 with psychiatric diseases and 152 with multiple co-morbidities (diabetes mellitus, arterial hypertension, and metabolic syndrome). Sera were tested at 1:80 dilution and diluted to the end titer. Slides were analyzed by two independent blinded examiners at x400 magnification. We followed the anti-cell (AC) pattern nomenclature according to the ICAP (International Consensus on ANA Patterns) recommendations.

**Results:** A positive HEp-2-ANA result occurred in 102 (18.3%) NAD patients, 170 (87.6%) SARD patients and 150 (12.3%) healthy individuals. The four subgroups of NAD patients did not differ regarding HEp-2-ANA titer or pattern. HEp-2-ANA titer in NAD patients was higher than in healthy individuals and these two groups had lower titer than SARD patients. The nuclear dense fine speckled pattern (AC-2) was more frequent in healthy individuals than in NAD patients (p = 0.029) and was not observed in the SARD group. The nuclear homogeneous (AC-1) and nuclear coarse speckled (AC-5) patterns were more frequent in SARD patients than in the other groups (p < 0.001). The most common pattern in all groups was the nuclear fine speckled (AC-4) pattern, which presented a gradient in titer across the three groups (p < 0.001):
healthy individuals and NAD patients had predominantly low and intermediate titer, respectively, and SARD patients had predominantly high titer.

**Conclusion:** The pattern and titer of HEp-2-ANA positive tests in NAD patients clearly differ from SARD patients. In addition, when compared to healthy individuals, NAD patients present positive HEp-2-ANA tests with slightly higher titer and with lower frequency of the nuclear dense fine speckled (AC-2) pattern.

**Disclosure:** R. Agustinelli, None; S. H. Rodrigues, None; M. Prado, None; H. Mariz, None; L. E. C. Andrade, None.


**Abstract Number:** 708

**Anti-RNP/Sm Antibodies Plus Lupus Anticoagulant As Risk Factor for Thrombosis in Patients with Systemic Lupus Erythematosus**

Mari Carmen Zamora-Medina1, Andrea Hinojosa-Azaola2, Carlos Núñez-Álvarez3 and Juana Romero-Diaz4,

1Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutricion S.Z., Mexico City, Mexico, 2Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutricion Salvador Zubirán, Mexico City, Mexico, 3Immunology and Rheumatology, Instituto Nacional de Ciencias Medicas y Nutricion S.Z., Mexico city, Mexico,

4Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutricion Salvador Zubirán, Mexico city, Mexico

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** In a previous study, we identify a potential role of anti-RNP/Sm in combination with LA as risk factor for thrombosis. We aimed to validate this association

**Methods:** Case-control study of patients with SLE who presented thrombosis after SLE diagnosis and controls with SLE without thrombosis. All patients fulfilled 4 American College of Rheumatology revised and updated classification criteria for SLE. Comorbidities, traditional risk factors, clinical variables, disease activity and treatment were evaluated. Also, a blood sample was drawn to determine antiphospholipid (aPL) and anti-RNP/Sm antibodies. **Statistical analysis:** Differences between groups were evaluated with the Student t-test or Mann-Whitney U test for continuous variables; Chi-square or Fisher’s exact test for categorical variables. Univariate logistic regression analyses and multivariate analyses were performed. Odds-ratio (OR) and 95% confidence intervals (95% CI) were calculated

**Results:** 63 cases and 63 controls were studied, 88% women, median age of 40 years and disease duration of 135 months at study inclusion. No differences were found between groups regarding age, comorbidities, or clinical characteristics at SLE diagnosis. Patients with thrombosis were more frequently positive for anti-RNP/Sm (83% vs 62%, p=0.001); IgG aCL (29% vs 11%, p=0.02); IgG anti-B2GPI (21% vs 13%, p=0.02); IgM anti-B2GPI (p=0.02); LA (62% vs 19%, p<0.001); the combination of anti-RNP/Sm + LA (52% vs 14%, p<0.001), and aPL triple marker (17% vs 2%, p=0.002), compared to controls. The combination of anti-RNP/Sm + LA (OR 5.98, 95% CI 2.17-16.47, p=0.001); SLEDAI-2K (OR 1.18, 95% CI 1.04-1.32, p=0.007), and prednisone dose (OR 1.08, 95% CI 1.03-1.12, p<0.001) were independently associated with thrombosis.

**Conclusion:** This study confirmed an independent association between the combination of anti-RNP/Sm antibodies and LA with thrombosis. Further studies to identify potential pathogenesis mechanisms of the presence of anti-RNP/Sm and
thrombosis are needed

Disclosure: M. C. Zamora-Medina, None; A. Hinojosa-Azaola, None; C. Núñez-Álvarez, None; J. Romero-Diaz, None.


Abstract Number: 709

Characteristics of Cardiac Diseases in Systemic Lupus Erythematosus and Risk Factors of Different Echocardiographic Features

Nevin Hammam1,2, Mona H EL zohri3 and Alaa A A Mohamed1, 1Rheumatology, Rehabilitation and Physical medicine, Assiut University, Faculty of Medicine, Assiut, Egypt, 2Department of Physical therapy, University of Alberta, Edmonton, AB, Canada, 3Internal medicine department, Assiut University, Faculty of Medicine, Assiut, Egypt
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by involvement of different organs in the body. The cardiovascular (CVD) involvement in SLE is responsible for high morbidity and is often the leading cause of death. Despite that, little is known about the risks of development of different CVDs in SLE. We aimed to determine the rate of different echocardiographic findings and their risks and clinical correlates in SLE patients.

Methods:
SLE patients (n=59), fulfilling 4 or more ACR criteria for SLE, attending outpatient Rheumatology clinics, were recruited. Demographic data, disease characteristics and current medication use were gathered from the patients. Clinical evaluation with SLE Disease Activity Index (SLEDAI), echocardiography, anthropometric measurements and routine laboratory tests were done. Mann-Whitney U test, Chi-square test, Fisher exact test and logistic regression analysis were used for statistical analysis as appropriated.

Results:
The mean age of the patients was 31.4±10.5, and 86.4% of the patients were females. The rate of different echocardiographic findings was as follow: overall valve lesions (47.5%), pulmonary hypertension (PHT) (18.6%), pericardial effusion (13.6%) and pericardial thickening (6.8%). The most common valve abnormalities were: mitral regurge (33.9%), tricuspid regurge (32.2%), mitral thickening (18.6%), and aortic thickening (18.6%) but less common were aortic regurge (6.8%) and pulmonary regurge (5.1%). The least common were pulmonary stenosis, mitral stenosis, and tricuspid and pulmonary thickening representing only (1.7%) each. The frequency of occurrence of different echocardiographic findings with different SLE features is shown in fig1. Univariate and multivariate analyses revealed a significant association of PHT with age (OR=1.095, p=0.023, CI=1.013 - 1.184), mucocutaneous disease was a negative predictor of mitral regurge (OR=0.227, p=0.03, CI=0.059 - 0.868) and mitral thickening, (OR=0.046, p=0.032, CI=0.003 - 0.765), unlike Raynaud phenomenon which is a positive predictor of mitral thickening (OR=14.614, p=0.036, CI=1.199 - 178.1). Levels of HDL were associated with aortic thickening (OR= 0.907, p=0.05, CI =0.823 - 1.0). The use of prednisolone reduced the risk of developing aortic thickening (OR= 0.054, p=0.012, CI=0.006 - 0.53). Pericardial effusion was
associated with metabolic syndrome (OR=12.4, p=0.025, CI=1.367 - 112.5) and high triglycerides levels (OR=1.012, p=0.028, CI=1.001 - 1.023). The echocardiographic findings showed no association with SLEDAI scores.

Conclusion:

Different laboratory and clinical correlates with different echocardiographic findings reflect the complexity of CVD mechanisms and warrant further studies to unravel disease pathogenesis.

Fig.1 The frequency of different echocardiographic findings in different SLE features

Disclosure: N. Hammam, None; M. H. EL zohri, None; A. A. A. Mohamed, None.


Abstract Number: 710

D-Dimer As an Early Marker in Patients with Lupus Mesenteric Vasculitis

Xiaolei Ma¹, Bingzhu Hua¹, Hong Wang¹, Yun Zhu¹, Zhiyong Chen¹ and Lingyun Sun², ¹Department of Rheumatology and Immunology, the Affiliated Drum Tower Hospital, Nanjing University Medical School, Nanjing, China, ²Department of Rheumatology and Immunology, the Affiliated Drum Tower Hospital, Nanjing University Medical School, nanjing, China

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A  
Session Time: 9:00AM-11:00AM

Background/Purpose: No early serum marker of accurate diagnosis of lupus mesenteric vasculitis (LMV) contributes to the treatment decision-making process. The study was undertaken to evaluate clinical significance of serum D-dimer level as an early diagnosis marker of LMV patients.

Methods: Thirty-eight systemic lupus erythematosus (SLE) patients who presented with acute and subacute abdominal pain were retrospectively analyzed and classified into LMV group (n=15) and Non-LMV group (n=23) between January 2006 and January 2016. The patients were evaluated by serum D-dimer level on the first day after admission, abdominal CT, other laboratory-testing parameters, as well as SLE disease activity index (SLEDAI) during the same period.

Results: No significance difference of the SLEDAI, autoantibodies and laboratory profiles at admission was detected between two groups. The D-dimer value on the first day of admission was significantly higher in patients with LMV than those with other causes ($P<0.05$, $P=0.04$). In addition, serum D-dimer level was also significantly higher in patients with long-term ($\geq 7d$) gut resting and high-dose steroid therapy ($P<0.01$, $P=0.003$). All LMV patients showed good response to high-dose intravenous steroids and there was no patient required immunosuppressive and surgical therapy.

Conclusion: D-dimer level could be an effective and early serum marker indicating the clinical evolution of LMV. D-dimer may also assist the treatment determination and prognostic evaluation.

Disclosure: X. Ma, None; B. Hua, None; H. Wang, None; Y. Zhu, None; Z. Chen, None; L. Sun, None.


Abstract Number: 711

Prevalence and Risk Factors of Depressive Disorders in Chinese Patients with Systemic Lupus Erythematosus (SLE)

Chi Chiu Mok$^1$, Yan Tung Lilian Lo$^2$, Chi Wai Cheng$^2$ and Kam Shan Poon$^2$, $^1$Medicine, Tuen Mun Hospital, Hong Kong, Hong Kong, $^2$Psychiatry, Castle Peak Hospital, Hong Kong, Hong Kong

First publication: September 18, 2017

SESSON INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Depression is common in SLE but most previous studies utilized self-rated scales for evaluation. Formal diagnosis of depression was not established by psychiatric interviews. This study was conducted to determine the prevalence of depressive disorders, severity of depressive symptoms and the associated risk factors in Chinese patients with SLE.

Methods: Adult patients who fulfilled $\geq 4$ ACR criteria for SLE were randomly recruited from the rheumatology out-patient clinics and hospital admissions in a 6-month period. Psychiatric disorders were diagnosed through a direct interview by a designated psychiatrist using the Chinese-bilingual Structural Clinical Interview for DSM-IV Axis I disorders, patient research version (CB-SCID-I/P). The severity of depressive symptoms was assessed by the Hamilton Depressive Rating Scale.
Results:

175 SLE patients were studied (95% women, age 39.2±12.4 years, SLE duration 10.3±6.7 years). Twenty-seven (15.4%) and 37 (21.1%) patients were diagnosed as having a current depressive (52% major depressive disorder, 22% dysthymia) and anxiety (35% generalized anxiety, 14% panic, 14% phobia, 8% adjustment disorder) disorder, respectively. Patients with depressive disorders, as compared to those without any psychiatric disorders, had higher SLE activity (p=0.03), were more likely to have a history of psychiatric diagnosis (p<0.001) and receive financial assistance from the Government (p=0.04). Independent factors associated with a current depressive disorder were SLEDAI score (1.13[1.02-1.24] per point; p=0.02), perceived poor social support (p=0.03) and a past history of psychiatric disorders (p=0.003). On the other hand, being separated/divorced (β=0.19; p=0.02), higher SLEDAI score (β=0.16; p=0.02), shorter SLE duration (β= -0.18; p=0.02) and a history of psychiatric disorders (β=0.18; p=0.01) were independently associated with higher HAM-D scores, which reflected the severity of depression. Depressive disorders and severity of depression were associated with poorer quality of life. ROC analysis showed a cut-off of 14 points of the self-rated BDI had a sensitivity of 89% and a specificity of 83% for providing good psychometric property for differentiating a current depressive disorder from those without.

Conclusion:

Depressive disorder is prevalent in Chinese patients with SLE. Independent risk factors include more active disease, perceived poor social support and a past history of psychiatric disorders. Patients with more active SLE, shorter disease duration, a past history of psychiatric disorders and being separated are associated with more serious depressive symptoms. The self-rated BDI provides a good screening tool for identifying depressive disorders in SLE patients.

Disclosure: C. C. Mok, None; Y. T. L. Lo, None; C. W. Cheng, None; K. S. Poon, None.


Abstract Number: 712

Novel Electronic Health Record Method Reveals That dsDNA Antibody-Negative Systemic Lupus Erythematosus Is Associated with Pain, Sleep, and Mood Disorders

April Barnado¹, Robert Carroll², Carolyn Casey³, Joshua C. Denny² and Leslie Crofford¹, ¹Medicine, Vanderbilt University Medical Center, Nashville, TN, ²Biomedical Informatics, Vanderbilt University Medical Center, Nashville, TN, ³Lehigh Valley Health Network, Allentown, PA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic lupus is a heterogeneous disease with diverse presentations. Studies have shown that dsDNA antibodies associate with renal disease. However, less is known about comorbidities in SLE patients without dsDNA antibodies. Using a large, novel electronic health record (EHR) cohort of SLE patients with a long duration of follow-up, we sought to identify not only ACR SLE criteria that associate with dsDNA antibody status but also other...
comorbidities that might not be assessed in cohort studies. We used a technique that scans across EHR billing codes called phenome-wide association study (PheWAS) to compare comorbidities in SLE patients with and without dsDNA antibodies.

**Methods:** We used our validated SLE algorithm of ≥ 4 counts of the SLE ICD-9 code (710.0) and ANA positive ≥ 1:160 while excluding dermatomyositis and systemic sclerosis ICD-9 codes with an internally validated positive predictive value of 94% and a sensitivity of 86%. We identified SLE cases in a de-identified EHR called the Synthetic Derivative (SD) that contains over 2.8 million subjects with longitudinal data. SLE subjects have on average 9 years of follow-up. dsDNA status was defined as positive if ever positive, negative if there was at least 1 assay and all were negative, and measured via enzyme-linked immunosorbent assays with manufacturer values to determine positivity. Demographics of dsDNA positive vs. negative subjects were compared using chi-square and Mann-Whitney U tests. PheWAS was performed in dsDNA positive vs. negative SLE patients using logistic regression adjusting for current age and race and correcting for multiple testing using Bonferroni (p < 1.35 x 10^{-4}).

**Results:** Of 1097 SLE subjects, 521 had a positive dsDNA, 503 negative dsDNA, and 73 with missing data. dsDNA positive subjects were more likely to be African American vs. Caucasian (61% vs. 45%, p < 0.001) and younger at age of first SLE ICD-9 code (37 ± 17 vs. 43 ± 15, p < 0.001) with no difference in sex (female 51% vs. male 52%, p = 0.58). As expected, dsDNA positive subjects, compared to dsDNA negative, were more likely to have renal codes including nephritis, renal failure, and end stage renal disease (Table 1). dsDNA positive subjects were also more likely to have codes for hematologic and serositis criteria. dsDNA negative subjects were more likely to have codes for sleep, pain, and mood disorders.

**Conclusion:** Using a novel EHR technique in a large SLE cohort with longitudinal follow-up, dsDNA positive subjects were more likely to have codes for renal, serositis, and hematologic involvement. In contrast, dsDNA negative subjects were more likely to have codes related to neuropsychiatric symptoms. Our results demonstrate that PheWAS can expand our understanding of SLE disease heterogeneity by uncovering important clinical differences in subgroups of SLE patients.

| Table 1. |

**Table 1.**
<table>
<thead>
<tr>
<th>PheWAS codes</th>
<th>Phenotype present*</th>
<th>Phenotype absent*</th>
<th>Adjusted Odds Ratio for age and race (95% Confidence Interval)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codes favoring dsDNA positive subjects</td>
<td></td>
<td></td>
<td>dsDNA positive: 4.66 (3.00 – 7.22)</td>
<td>5.95 x 10^-12</td>
</tr>
<tr>
<td>Nephritis and nephropathy in diseases classified elsewhere</td>
<td>162</td>
<td>614</td>
<td>dsDNA negative: 1.00 (ref)</td>
<td></td>
</tr>
<tr>
<td>Renal failure</td>
<td>261</td>
<td>614</td>
<td>2.33 (1.71 – 3.19)</td>
<td>1.15 x 10^-7</td>
</tr>
<tr>
<td>Other anemias</td>
<td>275</td>
<td>585</td>
<td>1.87 (1.37 – 2.55)</td>
<td>7.67 x 10^-5</td>
</tr>
<tr>
<td>End stage renal disease</td>
<td>77</td>
<td>614</td>
<td>2.71 (1.55 – 4.71)</td>
<td>4.31 x 10^-4</td>
</tr>
<tr>
<td>Pleurisy; pleural effusion</td>
<td>130</td>
<td>739</td>
<td>2.00 (1.33 – 3.03)</td>
<td>9.75 x 10^-4</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>94</td>
<td>616</td>
<td>2.19 (1.36 – 3.53)</td>
<td>1.31 x 10^-3</td>
</tr>
<tr>
<td>Codes favoring dsDNA negative subjects</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep disorders</td>
<td>124</td>
<td>820</td>
<td>0.48 (0.32 – 0.72)</td>
<td>3.94 x 10^-4</td>
</tr>
<tr>
<td>Obstructive sleep apnea</td>
<td>41</td>
<td>820</td>
<td>0.30 (0.14 – 0.63)</td>
<td>1.48 x 10^-3</td>
</tr>
<tr>
<td>Back pain</td>
<td>196</td>
<td>699</td>
<td>0.59 (0.42 – 0.82)</td>
<td>2.00 x 10^-3</td>
</tr>
<tr>
<td>Myalgia and myositis unspecified</td>
<td>243</td>
<td>682</td>
<td>0.65 (0.48 – 0.88)</td>
<td>5.55 x 10^-3</td>
</tr>
<tr>
<td>Major depressive disorder</td>
<td>57</td>
<td>820</td>
<td>0.44 (0.21 – 0.85)</td>
<td>5.75 x 10^-3</td>
</tr>
</tbody>
</table>

*Subjects with 1 instance of a code are excluded, so total number for each PheWAS code does not add up to the 1097 subjects.

Disclosure: A. Barnado, None; R. Carroll, None; C. Casey, None; J. C. Denny, None; L. Crofford, None.
Long-Term Outcomes in Prolonged Low Disease Activity Are Comparable to Complete Clinical Remission in Systemic Lupus Erythematosus

Konstantinos Tselios¹, Dafna D Gladman², Zahi Touma³, Jiandong Su⁴, Nicole Anderson² and Murray Urowitz⁵,
¹Medicine, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, ²Rheumatology, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, ³Rheumatology, University of Toronto, Division of Rheumatology, Institute of Health Policy, Management and Evaluation, Toronto, ON, Canada, ⁴University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, ⁵Centre for Prognosis Studies in the Rheumatic Diseases, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Prolonged clinical remission is a desirable, though rare outcome in systemic lupus erythematosus (SLE). We recently showed that low disease activity (LDA) state confers the same risk as complete remission with regard to damage accumulation and flare rate at two years. The aim of the present study was to assess the impact of prolonged LDA (for 10 years) on such outcomes as compared to patients who achieved complete remission.

Methods: The inception cohort of a large lupus clinic (patients enrolled within 18 months of diagnosis) was investigated. Patients selected had a minimum follow-up of 10 years and no interval greater than 18 months between consecutive visits. Prolonged clinical remission was defined based on SLEDAI-2K=0 (serology excluded), achieved within the first five years since diagnosis and maintained for ≥10 years. Prolonged LDA was defined as SLEDAI-2K ≤ 2 (serology excluded) for the same period. Statistical analysis was performed with SAS 9.0 software; p<0.05 was considered significant.

Results: Of the 883 inception patients, 382 fulfilled the inclusion criteria. Twenty-seven patients (7.1%) achieved prolonged clinical remission and 48 (12.6%) prolonged LDA. There were no differences regarding demographic, clinical, and immunological variables at diagnosis and at 10 years. Mean prednisone dose at diagnosis was higher in the patients who achieved remission. Antimalarial usage was higher in patients with LDA both at diagnosis and at 10 years. The two groups had comparable cumulative damage over 10 years, flare rate after 10 years, and mortality throughout follow-up. Details are given in Table 1.
Table 1. Comparison between patients with prolonged remission and LDA

<table>
<thead>
<tr>
<th>Variable</th>
<th>At diagnosis</th>
<th></th>
<th>At 10 years</th>
<th></th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis (y)</td>
<td>39±14.1</td>
<td>39.1±14.9</td>
<td>0.976</td>
<td>39±14.1</td>
<td>39.1±14.9</td>
</tr>
<tr>
<td>ACR criteria (mean±SD)</td>
<td>4.4±1.4</td>
<td>4.9±1.7</td>
<td>0.199</td>
<td>4.4±1.4</td>
<td>4.9±1.7</td>
</tr>
<tr>
<td>Time to remission or LDA (y)</td>
<td>1.6±1.3</td>
<td>1.8±1.6</td>
<td>0.656</td>
<td>1.6±1.3</td>
<td>1.8±1.6</td>
</tr>
<tr>
<td>SLEDAI-2K (mean±SD)</td>
<td>10.7±11.6</td>
<td>9.5±10</td>
<td>0.642</td>
<td>1.2±1.6</td>
<td>1.6±1.7</td>
</tr>
<tr>
<td>Low complement (n, %)</td>
<td>9 (33.3%)</td>
<td>16 (33.3%)</td>
<td>1.000</td>
<td>8 (29.6%)</td>
<td>13 (27.1%)</td>
</tr>
<tr>
<td>Anti-dsDNA (n, %)</td>
<td>13 (48.1%)</td>
<td>16 (33.3%)</td>
<td>0.206</td>
<td>6 (22.2%)</td>
<td>12 (25.0%)</td>
</tr>
<tr>
<td>Glucocorticosteroids (n, %)</td>
<td>17 (63.0%)</td>
<td>33 (68.8%)</td>
<td>0.61</td>
<td>6 (22.2%)</td>
<td>10 (20.8%)</td>
</tr>
<tr>
<td>Mean prednisone dose (mg/d)</td>
<td>16.8±9.5</td>
<td>10.7±8.4</td>
<td>0.028</td>
<td>5.3±3.2</td>
<td>4.6±1.4</td>
</tr>
<tr>
<td>Cumulative prednisone dose (g)</td>
<td>18.1 ± 12.4</td>
<td>13.4 ± 9.1</td>
<td>0.129</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antimalarials (n, %)</td>
<td>16 (59.3%)</td>
<td>38 (79.2%)</td>
<td>0.065</td>
<td>11 (40.7%)</td>
<td>32 (66.7%)</td>
</tr>
<tr>
<td>Immunosuppressives (n, %)</td>
<td>9 (33.3%)</td>
<td>16 (33.3%)</td>
<td>1.000</td>
<td>3 (11.1%)</td>
<td>8 (16.7%)</td>
</tr>
<tr>
<td>No Medications (n, %)</td>
<td>12 (44.4%)</td>
<td>19 (39.6%)</td>
<td>0.682</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLICC/DI (mean±SD)</td>
<td>0.26±0.53*</td>
<td>0.33±1.04*</td>
<td>0.73</td>
<td>0.96 ± 1.06</td>
<td>1.10 ± 1.32</td>
</tr>
<tr>
<td>Disease flare after 10 years</td>
<td>7 (25.9%)</td>
<td>15 (31.3%)</td>
<td>0.627</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time to flare (median in years)</td>
<td>12 (11-15)</td>
<td>11 (10-13)</td>
<td>0.217</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deceased (n, %)</td>
<td>3 (11.1%)</td>
<td>5 (10.4%)</td>
<td>0.925</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*At one year after diagnosis, CR: complete remission, LDA: low disease activity, SLICC/DI: Systemic Lupus International Collaborating Clinics/Damage Index

**Conclusion:** Patients with prolonged (>10 years) LDA achieved comparable outcomes as those with complete remission in the long term. Differences regarding therapeutic approach were observed but did not affect damage accumulation. Approximately 40% of these patients were able to discontinue all medications 10 years after diagnosis. Prolonged LDA status is an acceptable treat to target outcome in SLE.

**Disclosure:** K. Tselios, None; D. D. Gladman, None; Z. Touma, None; J. Su, None; N. Anderson, None; M. Urowitz, GlaxoSmithKline, 5.


**Abstract Number:** 714

**Prolonged Antimalarial Treatment Is Associated with Increased Risk for Elevated Myocardial Biomarkers in Systemic Lupus Erythematosus**
**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Antimalarial (AM)-induced cardiomyopathy (AMIC) has been rarely reported in systemic lupus erythematosus (SLE). However, given the large number of patients treated, it seems possible that AMIC is under-recognized and may run undiagnosed as an ill-defined heart failure syndrome. Specific cardiac biomarkers may identify patients at risk. We sought to investigate the prevalence and associated factors for such biomarkers in systemic lupus erythematosus (SLE).

**Methods:** One hundred sixty eight consecutive patients (153 females) attending a large lupus clinic, without past history of cardiac disease (heart failure, coronary artery disease, valvulopathy etc.) and/or pulmonary hypertension, were enrolled. None had chest pain or electrocardiographic (ECG) abnormalities suggestive of acute coronary syndrome. High-sensitivity cardiac troponin I (cTnI) and B-natriuretic peptide (BNP) were measured simultaneously in serum and plasma samples, respectively. Patients were categorized according to normal or abnormal BNP and/or cTnI. For the assessment of the impact of AM duration on abnormal cardiac biomarkers, patients were divided in two groups according to the median duration of use, which was calculated at 5.6 years in the current cohort. Statistical analysis was performed with SAS 9.0 software; \( p<0.05 \) was considered significant.

**Results:** Sixteen patients (9.5%) had elevated BNP and/or cTnI. Compared to subjects with normal biomarkers, they were older, had longer disease and AM use duration and more frequently persistent creatine phosphokinase (CPK) elevation. Details are shown in Table 1.
Table 1. Comparison between BNP/cTnI abnormal and BNP/cTnI normal patients

<table>
<thead>
<tr>
<th>VARIABLE (At assessment)</th>
<th>BNP/cTnI abnormal (no history of heart disease or PAH) (n=16)</th>
<th>BNP/cTnI normal (n=152)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>54.7 ±15.1</td>
<td>47.83 ± 12.15</td>
<td>0.037</td>
</tr>
<tr>
<td>SLE duration (y)</td>
<td>22.54 ± 10.44</td>
<td>15.45 ± 10.05</td>
<td>0.008</td>
</tr>
<tr>
<td>SLEDAI-2K</td>
<td>1.88 ± 2.47</td>
<td>2.79 ± 3.64</td>
<td>0.329</td>
</tr>
<tr>
<td>Adjusted Mean SLEDAI-2K for 2 years prior</td>
<td>2.52±2.96</td>
<td>3.02±3.18</td>
<td>0.549</td>
</tr>
<tr>
<td>eGFR &lt; 30ml/min</td>
<td>0 (0%)</td>
<td>3 (2%)</td>
<td>0.571</td>
</tr>
<tr>
<td>Hypertension</td>
<td>10 (62.5%)</td>
<td>54 (35.5%)</td>
<td>0.035</td>
</tr>
<tr>
<td>Diuretics treatment</td>
<td>5 (31.3%)</td>
<td>8 (5.3%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic BP at test (mmHg)</td>
<td>118.4 ± 21.7</td>
<td>113.5 ± 16.9</td>
<td>0.28</td>
</tr>
<tr>
<td>Diastolic BP at test (mmHg)</td>
<td>71.9 ± 10.1</td>
<td>69.5 ± 11.8</td>
<td>0.444</td>
</tr>
<tr>
<td>Abnormal CPK ⬇️</td>
<td>7 (43.8%)</td>
<td>24 (15.8%)</td>
<td>0.008</td>
</tr>
<tr>
<td>Cumulative years on AM</td>
<td>13.66 ± 9.14</td>
<td>7.88 ± 8.02</td>
<td>0.008</td>
</tr>
<tr>
<td>AM duration&gt;5.6 years</td>
<td>14 (87.5%)</td>
<td>69 (45.4%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>8 (50%)</td>
<td>70 (46.1%)</td>
<td>0.763</td>
</tr>
<tr>
<td>Mean prednisone (mg/day)</td>
<td>9.4 ± 4.2</td>
<td>7.53 ± 5.1</td>
<td>0.326</td>
</tr>
<tr>
<td>Immunosuppressives</td>
<td>10 (62.5%)</td>
<td>87 (57.2%)</td>
<td>0.685</td>
</tr>
</tbody>
</table>

eGFR: estimated glomerular filtration rate, PAH: pulmonary arterial hypertension, BP: blood pressure, CPK: creatine phosphokinase, AM: antimalarials, CQ: chloroquine, HCQ: hydroxychloroquine, ⬇️ Three abnormal measurements during the last two years

Multivariable regression analysis showed prolonged AM treatment (>5.6 years) and persistent CPK elevation to be important predictors for elevated cardiac biomarkers [HR=5.43, 95%CI=1.14-25.9, p=0.034 and HR=4.62, 95%CI=1.22-17.51, p=0.024, respectively]. Two patients were diagnosed with AMIC on endomyocardial biopsy; both had CPK and BNP/cTnI elevation.

**Conclusion:** Approximately 9% of SLE patients had elevated myocardial biomarkers, in the absence of prior cardiac disease or pulmonary arterial hypertension. Prolonged AM therapy and persistent CPK elevation conferred an increased risk for abnormal BNP and cTnI, which might predict AMIC.

**Disclosure:** K. Tselios, None; D. D. Gladman, None; P. Harvey, None; S. Akhtari, None; J. Su, None; M. Urowitz, None.


**Abstract Number:** 715

**Long-Term Outcome of Demyelinating Syndrome in Systemic Lupus Erythematosus: A Longitudinal Study**
Background/Purpose: Demyelinating syndromes (DS) in systemic lupus erythematosus (SLE) are characterized by inflammation, demyelination and neurodegeneration. Little is known, however, about the tenet of dissemination in time or space of DS in SLE. The aim of this study is to evaluate the long-term outcomes in SLE patients with DS in a large SLE cohort.

Methods: Data of patients with DS were obtained from the SLE cohort at the University of Maryland, between 1996 and 2016. Demographic, clinical features, serological studies, SLE-related treatment, and DS treatment-related exposures, Expanded Disability Status Scale (EDSS) score at baseline, were included. SLE patients with DS were classified as Clinically Isolated Syndrome (CIS), [those presenting with optic neuritis, partial myelitis or a brain stem syndrome], and Radiologically Isolated Syndrome (RIS), [those exhibiting radiological disease with T2/fluid attenuated inversion recovery or enhancing magnetic resonance imaging (MRI) typical of demyelination as a biomarker of acute inflammatory activity].The primary outcomes were DS progression, overall survival, cognitive dysfunction and residual disability. The predictors of DS progression were calculated using multivariable Cox proportional hazards regression analysis models. To avoid bias, patients were included in the analysis regardless of their duration of follow-up.

Results: 25 SLE cases with DS were identified [mean age; 41.9 ± 12.3 years, 80 % African America, 84% women, with a mean follow up of 6.9 ± 1.8 years]. The median baseline EDSS score was 4.5 (range, 1.5-6.5). CIS was observed in 15 cases (60 %) [Optic neuritis n=6 (24%), acute transverse myelitis n=9 (36%)]. Ten patients (40%) had RIS. Two patients (8 %) had neuromyelitis optica syndrome.

Nine patients (36%) had progressive forms of DS, 8 (32 %) had cognitive dysfunction and 9 (36 %) had worsening disability. Three deaths at follow up, were observed and were considered SLE-related mortality.

Factors associated with progression of DS included, SSA antibody [Odds ratio, 10.5 (95% CI: 1.5-72, p < 0.005)], and presence of oligoclonal bands on spinal fluid analysis. There were lack of association with INF gene expression, DS modifying therapy, phospholipid syndrome, or use of hydroxychloroquine.

Worsening disability overtime was associated with spinal cord lesions {OR 34 (95 % CI: 3.5-93.2, p < 0.001)}, and CIS [OR 10.3 (95 % CI 1.0-102, p < 0.008)]. The use of DS modifying therapy tended to be protective, (OR 0.8, 95% CI, 0.6-0.9, p < 0.051).

Older age (> 40 years) [OR 3.6 (95% CI: 1.7- 67, p < 0.03] and midbrain lesion (OR 2.7, 95 % CI: 1.1-6.5, p < 0.05]) were associated with cognitive impairment.

Conclusion: More than half of SLE patient with DS remained free from neurological progression for 5 years after DS diagnosis. Younger age, relapsing form of DS, prior immunotherapies, and lower baseline EDSS score were factors associated with better outcomes. Identifying novel biomarkers of DS progression in SLE will help develop therapeutic options and engender mechanisms of neurodegeneration.

Disclosure: J. A. Mikdashi, None; I. Ramadan, None.


Abstract Number: 716
Prolonged Exposure to Antiphospholipid Antibodies Is Associated with Endothelial Dysfunction in Patients with Systemic Lupus Erythematosus

In-Woon Baek¹, Yune-Jung Park², Ki-Jo Kim³, Wan-Uk Kim Sr.⁴ and Chul-Soo Cho¹, ¹Internal Medicine, Yeouido St. Mary's Hospital, The Catholic University of Korea, Seoul, Korea, Republic of (South), ²Internal Medicine, St. Vincent's Hospital, The Catholic University of Korea, Suwon, Gyeonggido, Korea, Republic of (South), ³Internal Medicine, St. Vincent's Hospital, The Catholic University of Korea, Suwon, Korea, Republic of (South), ⁴The Catholic University of Korea, Department of Internal Medicine, seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Antiphospholipid syndrome has been shown to be associated with increased cardiovascular mortality, but the role of antiphospholipid antibodies (aPL) on endothelial dysfunction remains elusive. We investigated the association between endothelial dysfunction and aPL in systemic lupus erythematosus (SLE) patients.

Methods: 185 SLE patients and 62 controls were enrolled. Endothelial function was measured by flow-mediated dilatation (FMD). Cardiovascular risk factors were assessed and quarterly measurement of anti-cardiolipin (aCL) and anti-β₂ glycoprotein I Ab were used to calculate time-integrated values throughout disease duration. Circulating endothelial progenitor cell (EPC), defined by CD34+/KDR+ mononuclear cells, was quantified by flow cytometry.

Results: Median FMD was significantly lower in SLE patient than in controls (6.9 versus 9.3%, P<0.001). In univariate analysis, older age, hypertension, and persistent positive lupus anticoagulant (LAC) were associated with decreased FMD in SLE patients (P=0.034, P=0.020, and P=0.028). Time-integrated aCL value (TI-aCL), but not a single value, was correlated with decreased FMD (P=0.003). Multivariate analysis showed that hypertension and TI-aCL were independent factors for decreased FMD (P=0.012, P=0.011); addition of positive LAC increased the adjusted probability of decreased FMD (P=0.003). FMD was correlated with EPC number (r=0.342, P=0.005) and TI-aCL was also an independent factor of reduced EPC after multiple adjustment (P=0.024). The predicted probability of endothelial dysfunction at median EPC level was higher in group with high TI-aCL than in group with low TI-aCL (P=0.004).

Conclusion: Cumulative burden of aPL was closely associated with endothelial dysfunction in SLE patients, which was mediated in part by reduction of EPC.

Disclosure: I. W. Baek, None; Y. J. Park, None; K. J. Kim, None; W. U. Kim Sr., the National Research Foundation of Korea, 2; C. S. Cho, None.


Abstract Number: 717

Risk Factors for Neuropsychiatric Systemic Lupus Erythematosus and Its Recurrence

Ryusuke Anan, Yuko Kaneko, Jun Kikuchi and Tsutomu Takeuchi, Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan

First publication: September 18, 2017
Background/Purpose: Neuropsychiatric involvement in systemic lupus erythematosus (NPSLE) is the leading cause of morbidity and mortality in patients with SLE but not well understood. The aim of this study was to identify risk factors for NPSLE and its recurrence.

Methods: We enrolled consecutive patients with SLE who had visited Keio University Hospital between 2013 and 2015. The patients were divided according to the presence or absence of NPSLE, and their clinical characteristics, manifestations, findings of cerebrospinal, electroencephalographic and neuroimaging examination, treatment and prognosis were compared. Patients with NPSLE were further divided by the recurrence of NPSLE, and its risk factors were examined.

Results: A total of 302 patients with SLE were enrolled. Two hundred seventy (89%) were female, and the mean age was 49.2 years. Forty-two (14%) patients were diagnosed with NPSLE during the course of SLE according to the ACR case definitions. The patients with NPSLE had a history of serositis more frequently than those without (37% vs 20%, p=0.03). Anti-Ro/SSA antibody (76% vs 54%, p=0.02) and anti-phospholipid antibody (55% vs 35%, p=0.03) were more frequently detected in patients with NPSLE while no difference was found in other autoantibodies including anti-DNA, anti-Sm, anti-RNP, and lupus anticoagulant. Among NPSLE patients, 22 (52%) had recurrent central nervous involvement. Serologically, the recurrent group had higher positivity of anti-Ro/SSA antibody than the non-recurrent group (88% vs 59%, p=0.02). Patients with focal hypoperfusion in single photon emission computed tomography (SPECT) at the first NPSLE had significantly higher relapse rate than those with diffuse hypoperfusion (86% vs 36%, p=0.02). Patients treated with intravenous cyclophosphamide at the first NPSLE were at a lower risk of recurrence (12% vs 46%, p=0.01).

Conclusion: Anti-Ro/SSA antibody was a risk for recurrent NPSLE. Patients with focal hypoperfusion of SPECT at the first NPSLE had significantly higher risk for NPSLE recurrence. Cyclophosphamide is important for preventing the recurrence of NPSLE.


View Abstract and Citation Information Online - http://acrabstracts.org/abstract/risk-factors-for-neuropsychiatric-systemic-lupus-erythematosus-and-its-recurrence
Atherosclerotic Vascular Events in a Multinational SLE Inception Cohort: Description and Predictive Risk Factors over a 17 Year Period

Murray Urowitz, Dafna D Gladman, Nicole Anderson and Jiandong Su,

Centre for Prognosis Studies in the Rheumatic Diseases, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, Rheumatology, Toronto Western Hospital, University of Toronto, Toronto, ON, Canada, Rheumatology, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: A large multicentre multinational inception cohort was established to study risk factors for atherosclerosis (AS) in SLE. We aim to describe all vascular events (VE) and determine the predictors of atherosclerotic vascular events (AVE) in this cohort over a 17 year period.

Methods: Patients enter the cohort within 15 months of SLE diagnosis (≥4 ACR criteria). Clinical and laboratory features of SLE are collected annually in a standardized protocol from 2000-2017. Patients with <3 years of follow-up or VEs attributed to other causes were excluded. VEs recorded include myocardial infarction (MI), angina, congestive heart failure (CHF), intermittent claudication (PVD), transient ischemic attack (TIA), pacemaker insertion and stroke. Diagnosis of a VE is confirmed using standard clinical criteria, relevant laboratory data and imaging where appropriate. Attribution to AS was made on the basis of lupus disease being inactive at the time of VE, and/or the presence of typical AS changes on imaging or pathology and/or evidence of AS elsewhere. Factors associated with AVE were analyzed on patients with AVEs that occurred after study enrollment using time to event analysis with time dependent covariates and cox proportional hazard model.

Results: 1848 patients entered the cohort (88.7%F; age at SLE 34.7 ± 13.4 years, disease duration 5.6 ± 4.2 months, mean follow-up of 7.3 ± 4.5 years). Thus far, there have been 231 VEs in 159 patients. These include: MI (24), angina (31), CHF (52), pacemaker insertion (9), PVD (20), TIA (29) and stroke (66). 106 VEs were attributed to active lupus and 42 to other causes. 83 VE in 57 patients were attributed to AS including: MI (17), angina (26), CHF (12), pacemaker (5), PVD (9), TIA (7), and stroke (7). 14 patients in the AS group had >1 AVE. SLE duration at first AVE was 3.7 ± 3.5 years. Of the 57 AVE patients, 47 had an AVE that occurred after study enrollment.
Table 1. Cohort Characteristics at Enrolment

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patient that had a AVE (N=47)</th>
<th>Patients that did not have a VE (N=1364)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>13 (27.7%)</td>
<td>133 (9.8%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Caucasian</td>
<td>34 (72.3%)</td>
<td>663 (48.6%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Age at SLE diagnosis (Mean ± SD)</td>
<td>51.82 ± 14.89</td>
<td>33.99 ± 12.93</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Smoking</td>
<td>25 (53.2%)</td>
<td>466 (34.2%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>26 (55.3%)</td>
<td>446 (32.7%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3 (6.7%)</td>
<td>46 (3.4%)</td>
<td>0.241</td>
</tr>
<tr>
<td>Obese</td>
<td>23 (51.1%)</td>
<td>381 (28.9%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>21 (44.7%)</td>
<td>475 (34.8%)</td>
<td>0.165</td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>21 (45.7%)</td>
<td>300 (22.5%)</td>
<td>0.001</td>
</tr>
<tr>
<td>SLEDAI-2K (Mean ± SD)</td>
<td>4.13 ± 4.83</td>
<td>5.38 ± 5.33</td>
<td>0.112</td>
</tr>
<tr>
<td>Total ACR Criteria (Mean ± SD)</td>
<td>4.96 ± 1.21</td>
<td>4.91 ± 1.05</td>
<td>0.683</td>
</tr>
<tr>
<td>Serositis</td>
<td>21 (44.7%)</td>
<td>367 (26.9%)</td>
<td>0.007</td>
</tr>
<tr>
<td>Renal Disorder</td>
<td>12 (25.5%)</td>
<td>389 (28.5%)</td>
<td>0.655</td>
</tr>
<tr>
<td>Neurologic Disorder</td>
<td>3 (6.4%)</td>
<td>55 (4.0%)</td>
<td>0.425</td>
</tr>
<tr>
<td>Immunologic Disorder</td>
<td>39 (83.0%)</td>
<td>1,044 (76.5%)</td>
<td>0.304</td>
</tr>
<tr>
<td>Anticardiolipin</td>
<td>7/35 (20.0%)</td>
<td>116/894 (14.5%)</td>
<td>0.198</td>
</tr>
<tr>
<td>Lupus Anticoagulant</td>
<td>13/35 (37.1%)</td>
<td>187/926 (20.2%)</td>
<td>0.026</td>
</tr>
<tr>
<td>Treated with oral steroids</td>
<td>32 (68.1%)</td>
<td>928 (69.7%)</td>
<td>0.802</td>
</tr>
<tr>
<td>Average daily corticosteroid dose (Mean ± SD)</td>
<td>14.20 ± 17.58</td>
<td>16.73 ± 17.39</td>
<td>0.327</td>
</tr>
<tr>
<td>Treated with antimalarials</td>
<td>26 (55.3%)</td>
<td>936 (68.6%)</td>
<td>0.251</td>
</tr>
<tr>
<td>Treated with immunosuppressives</td>
<td>18 (38.3%)</td>
<td>542 (39.7%)</td>
<td>0.926</td>
</tr>
</tbody>
</table>

Table 2. Predictive Risk Factors – Multivariable Analysis

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Hazard Ratio</th>
<th>95% Confidence Interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at SLE diagnosis</td>
<td>1.08</td>
<td>1.06, 1.10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ACR Criteria – Serositis</td>
<td>2.47</td>
<td>1.34, 4.54</td>
<td>0.003</td>
</tr>
<tr>
<td>Antimalarial treatment</td>
<td>0.52</td>
<td>0.28, 0.95</td>
<td>0.033</td>
</tr>
</tbody>
</table>

The classic risk factors at inception were not predictive, but they do increase over time (Figure 1).
Conclusion: Over the follow-up of an inception cohort with SLE there were 83 AVEs in 57 patients of which 47 occurred after enrollment. Only older age and serositis are significant risk factors for AVE and antimalarials were protective. However, traditional risk factors increase over time and may have an impact on the development of AVE in the future.

Disclosure: M. Urowitz, None; D. D. Gladman, None; N. Anderson, None; J. Su, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/atherosclerotic-vascular-events-in-a-multinational-sle-inception-cohort-description-and-predictive-risk-factors-over-a-17-year-period

Abstract Number: 719

Lupus Nephritis in Isolation or Accompanied By Extra-Renal Manifestations: Early Lessons from the Accelerating Medicines Partnership

Judith A. James1, Michelle Petri2, Chaim Puterman3, Betty Diamond4, David Wofsy5, Chun Hao Lee6, Derek Fine6, Anna R. Broder7, Robert M. Clancy8, Peter M. Izmirly9, Michael Belmont10, Nicole Bornkamp11, Anne Davidson12, Patti Tosta13, Kenneth C. Kalunian14, Meyeon Park15, Maria Dall'Era16, Richard Furie17, Elena Massarotti18, German T. Hernandez19, Fernanda Payan-Schober20, Sean M. Connery19, Diane L. Kamen21, Iris Lee22, William Pendergraft III23, Jennifer H. Anolik24, Ummara Shah25, Soumya Raychaudhuri26, Yvonne C. Lee27, Joel M. Guthridge28, V. Michael Holers29, Paul J. Utz30, Mina Pichavant31, Rohit Gupta31, Holden T. Maecker32, Michael Weisman33 and Jill P. Buyon34, 1Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 2Medicine (Rheumatology), Division of Rheumatology, Johns Hopkins University School of Medicine, MD, USA, Baltimore, MD, 3Division of Rheumatology, Albert Einstein College of Medicine, Bronx, NY, USA, Bronx, NY, 4Autoimmune and Musculoskeletal Diseases, The Feinstein Institute for Medical Research, Manhasset, NY, 5Rheumatology, UCSF, San Francisco, CA, 6Johns Hopkins University, Baltimore, MD, 7Albert Einstein College of Medicine, Bronx, NY, 8NYU School of Medicine, New York, NY, 9New York University School of Medicine, New York, NY, 10New York University, NYC, NY, 11Medicine, New York University School of Medicine, New York, NY, 12Autoimmunity and Musculoskeletal Diseases, Feinstein Institute for Medical Research, Manhasset, NY, 13Immune Tolerance Network, San Francisco, CA, 14Division of Rheumatology, Allergy & Immunology, UCSD School of Medicine Center for Innovative Therapy, La Jolla, CA, 15University of California San Francisco, San Francisco, CA, 16Medicine/Rheumatology, University of California, San Francisco, San Francisco, CA, 17Hofstra Northwell, Manhasset, NY, 18Brigham and Women's Hospital, Boston, MA, 19Texas Tech University HSC El Paso, El Paso, TX, 20Texas Tech University HSC El Paso, El Paso, TX, 21Medicine/Rheumatology & Immunology, Medical University of South Carolina, Charleston, SC, 22Temple University
Background/Purpose: Lupus nephritis (LN) remains one of the most serious complications of SLE, occurring in up to 50% of patients. Current LN treatments are not sufficiently efficacious, are accompanied by significant off-target toxicities and result in a high percent of patients progressing to end stage renal disease. Thus, additional efforts are needed to understand LN at the molecular level, and to identify clinical responsiveness with specific molecular pathways.

Methods: SLE patients with proteinuria and suspected LN (n=105) were enrolled over 15 months by 12 US-based lupus centers to the RA/Lupus Accelerated Medicines Partnership Phase I program. Demographic, clinical, and therapeutic information was gathered using standard case report forms and entered into a study-specific database. ACR and SLICC SLE classification criteria, biopsy information, modified SELENA-SLEDAI, laboratory values and patient reported outcomes (PROMIS29) were collected. Serum, plasma, PBMCs, total blood leukocytes, urine, urine cells, and renal biopsy tissue were collected, with non-lesional, non-sun exposed skin biopsies in 25%. Complete renal response was considered improvement of urine protein to <500mg (or UPCR <0.5) and normal serum creatinine (or up to 125% of baseline) with prednisone taper, while partial response required improvement of urine protein by ≥50%.

Results: Of the 105 SLE patients recruited, 93 (89%) were female and most were non-Caucasian (n=84; 80%), including 28% Hispanic, 39% African-American, 11% Asian, 2% mixed ethnicity/not reported. Of the SLE renal biopsies (n=105), 75% were ISN Class III, IV, V or mixed. LN patients were on average 33.7 years of age (range: 14-58) with a baseline urine protein:creatinine ratio of 3.3 (with 34% > 3; n=21), 70% anti-dsDNA positive (n=48), 84% with low complement levels (n=59) and 39% with Hg < 10 g/dL (n=28). The average SLEDAI was 12.3, with 56% of this group presenting with global disease activity (e.g. 2 organ systems active in addition to renal, e.g. arthritis, skin, serositis). Analysis of 30 LN patients with longitudinal information revealed that 33% achieved complete response and 17% partial response to standard of care (SOC) therapy at 6 months. LN patients with extra renal disease activity were twice as likely to be renal non-responders to SOC (n=10 NR; n=5 CR/PR) than those LN patients whose disease activity was limited to renal and immunologic features only (n=6 NR; n=9 CR/PR).

Conclusion: These preliminary findings suggest that renal response to current SOC may occur more often in patients without other active manifestations of lupus. Significant clinical heterogeneity exists between LN patients emphasizing a need for deeper molecular phenotyping.

Disclosure: J. A. James, None; M. Petri, Anthera Inc, 5,GlaxoSmithKline, 5,EMD Serono, 5,Eli Lilly and Company, 5,Bristol Meyer Squibb, 5,Amgen, 5,United Rheumatology, 5,Global Academy, 5,Exagen, 2; C. Putterman, None; B. Diamond, None; D. Wofsy, None; C. H. Lee, None; D. Fine, None; A. R. Broder, None; R. M. Clancy, None; P. M. Izmirly, None; M. Belmont, None; N. Bornkamp, None; A. Davidson, None; P. Tosta, None; K. C. Kalunian, Pfizer Inc, Gilead, UCB, Amgen, 2; M. Park, None; M. Dall’Era, None; R. Furie, None; E. Massarotti, Exagen, 5,BMS, 2,Springer Publishing, 7; G. T. Hernandez, None; F. Payan-Schober, None; S. M. Connery, None; D. L. Kamen, None; I. Lee, None; W. Pendergraft III, None; J. H. Anolik, None; U. Shah, None; S. Raychaudhuri, Pfizer Inc, 2,Roche
Ambulatory Blood Pressure and Skin Sodium Concentrations in Patients with Systemic Lupus Erythematosus

Daniel Carranza Leon¹, Cecilia P. Chung¹, Michelle J. Ormseth², Annette M. Oeser³, Ping Wang⁴, Adriana Marton¹, Jens Titze³ and C. Michael Stein¹, ¹Medicine, Vanderbilt University Medical Center, Nashville, TN, ²Rheumatology, Vanderbilt Medical Center, Nashville, TN, ³Vanderbilt University Medical Center, Nashville, TN, ⁴Radiology, Vanderbilt University Medical Center, Nashville, TN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Ambulatory 24-hour blood pressure and nocturnal blood pressure measurements are better predictors of cardiovascular risk than office blood pressure. Patients with systemic lupus erythematosus (SLE) have a high prevalence of hypertension and cardiovascular events. Recent findings indicate that sodium stored in the skin can be measured with $^{23}$Na$^+$ magnetic resonance imaging (MRI) and plays an important role in both blood pressure and immune regulation. Little is known about ambulatory blood pressure in SLE and its relationship to skin Na$^+$ is not known.

Methods:
Office blood pressure was measured at study enrollment using standard procedures and ambulatory 24-hour blood pressure measurements were recorded (Meditech, Budapest, Hungary) in 23 patients with SLE and 23 controls frequency-matched for age, race, and sex. Skin Na$^+$ content in the lower leg was measured with a 3T $^{23}$Na$^+$ knee-coil with a magnetic resonance imaging scanner (Philips Achieva 3T) in 13 patients with SLE. Phantoms containing aqueous solutions with 10, 20, 30, and 40 mmol/L NaCl were included for calibration. Blood pressure measurements in patients and control subjects were compared using Wilcoxon-rank sum tests and adjusted for age, race, and sex using a linear regression model. Spearman correlations were used to assess the correlation between blood pressure measurements and skin sodium in SLE patients.

Results:

Results: Office blood pressure was not significantly different in patients with SLE and controls (Table). However, ambulatory blood pressure measurements, particularly nocturnal measurements, were higher in patients with SLE. In patients with SLE (n=13), skin Na$^+$ concentrations were 15.0 (IQR 13.3 – 18.4) mmol/L and were significantly correlated with both office (rho= 0.67, P=0.023) and mean 24-hour systolic blood pressure (rho= 0.62, P= 0.04).
<table>
<thead>
<tr>
<th></th>
<th>SLE (N=23)</th>
<th>Controls (N=23)</th>
<th>p-value</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>35 (31-52)</td>
<td>35 (26-50)</td>
<td>0.73</td>
<td></td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>25.9 (22.7-33.8)</td>
<td>24.3 (22.7-26.8)</td>
<td>0.22</td>
<td></td>
</tr>
<tr>
<td>Sex female</td>
<td>19 (82.61%)</td>
<td>20 (87.0%)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Race white</td>
<td>15 (65.2%)</td>
<td>19 (82.6%)</td>
<td>0.31</td>
<td></td>
</tr>
<tr>
<td>Smoker never</td>
<td>17 (73.9%)</td>
<td>17 (73.9%)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>24 hr Mean SBP, mmHg</td>
<td>128.5 (113-139.1)</td>
<td>115 (110.6-121)</td>
<td>0.05</td>
<td>0.04</td>
</tr>
<tr>
<td>24 hr Mean DBP, mmHg</td>
<td>78 (68.9-85.2)</td>
<td>72.4 (66.8-74.9)</td>
<td>0.02</td>
<td>0.04</td>
</tr>
<tr>
<td>Awake Mean SBP, mmHg</td>
<td>130.2 (115-139.3)</td>
<td>118.5 (114.7-124.7)</td>
<td>0.07</td>
<td>0.07</td>
</tr>
<tr>
<td>Awake Mean DBP, mmHg</td>
<td>82 (70.6-89)</td>
<td>76.1 (70.2-78.6)</td>
<td>0.07</td>
<td>0.07</td>
</tr>
<tr>
<td>Sleep Mean SBP, mmHg</td>
<td>115 (104.7-129)</td>
<td>107 (97.8-112.6)</td>
<td>0.02</td>
<td>0.03</td>
</tr>
<tr>
<td>Sleep Mean DBP, mmHg</td>
<td>68 (58-80)</td>
<td>60.8 (53.6-66)</td>
<td>0.008</td>
<td>0.02</td>
</tr>
<tr>
<td>Office SBP, mmHg</td>
<td>126 (114-140)</td>
<td>121 (115-127)</td>
<td>0.37</td>
<td>0.43</td>
</tr>
<tr>
<td>Office DBP, mmHg</td>
<td>83 (68-90)</td>
<td>82 (73-90)</td>
<td>0.76</td>
<td>0.84</td>
</tr>
<tr>
<td>Hypertension, Yes</td>
<td>11 (47.8)</td>
<td>2 (8.7)</td>
<td>0.007</td>
<td></td>
</tr>
</tbody>
</table>

BMI= body mass index, SBP = systolic blood pressure, DBP = diastolic blood pressure, *Adjusted for age, sex, and race
** Continuous and categorical data expressed as median (interquartile range) and counts (percent) respectively

**Conclusion:**

Despite similar office blood pressure measurements, ambulatory blood pressure, particularly nocturnal blood pressure, was higher in patients with SLE than controls. Skin Na⁺ levels were correlated with systolic blood pressure in SLE. Studies to further assess the relationship between skin Na⁺ and disease activity, blood pressure, and cardiovascular disease in patients with SLE are needed.

**Disclosure:** D. Carranza Leon, None; C. P. Chung, None; M. J. Ormseth, None; A. M. Oeser, None; P. Wang, None; A. Marton, None; J. Titze, None; C. M. Stein, Lupus Research Alliance, 2.


**Abstract Number:** 721

**Improving the Quality of Care in Systemic Lupus Erythematosis (SLE) through Time-Structured, Information Technology-Enhanced, Quality Improvement Indicator-Driven Patient Management**

**Frank Migliore**¹, Robert Quinet², William E. Davis³, Daniel Wray⁴, Timothy Hilbun⁵ and Magdelena Budziakowska¹, ¹Ochsner Clinic Foundation, New Orleans, LA, ²Rheumatology, Ochsner Medical Center, New Orleans, LA, ³University of Queensland School of Medicine, Brisbane, Australia, ⁴Twine Clinical Consulting LLC, Park City, UT, ⁵IS ANALYTICS NOM, Ochsner Medical Center, New Orleans, LA
SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster I: Biomarkers and Outcomes
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Gaps exist in SLE patient care in monitoring and management of comorbidities, treatment related toxicities, and disease activity, suggesting a lack of well-defined systems of care in SLE. Our hypothesis was that a more time structured, IT enhanced, and QI indicator-driven approach to SLE management would translate to more frequent, comprehensive, and guideline adherent interactions with the lupus patient (“tight” management) that would lead to improved outcomes.

Methods:
To prompt “tight” management of SLE patients at Ochsner main campus (687 patients - 2014 baseline; 644 patients - 2015 interventional; 581 patients – 2016 post-interventional), the following interventions were implemented:

• Lupus Management Module: SLE specific dashboard embedded into Epic EHR. Dashboard incorporates automated SLE management specific reminders, alerts (and facilitates ordering appropriate testing/management), test result tracking, and customized assessments (SELENA-SLEDAI, SLICC- SDI). SLICC-DI assessment is prompted 1x annually. SLEDAI assessment prompted every office visit. The occurrence of flare is prompted tabulated and based on change in SELENA- SLEDAI assessment. Clinicians have the ability to override or confirm the tabulated occurrence of flare. Also, clinicians could manually designate the occurrence of flare independently of the automated tracking system.

• Patient Campaigning: Identification of patients due for SLE specific testing or management activities. Of primary importance were to prompt an office visit at least 1x/6 months and prompt pre office visit lab testing to enable completion of the SELENA- SLEDAI tabulation at the point of care, thereby enabling and facilitating fully informed management decision making at the point of care.

Results:
These interventions prompted improvement in rate of SELENA-SLEDAI application 1x/6 months (26.35% - 2014 baseline period, 43.79% - 2015 interventional period, 39.93% - 2016 post-interventional period; p < 0.0001), rate of SLICC-SDI application 1x/12 months (22.83% - 2015 interventional period, 34.25% - 2016 post-interventional period; p < 0.0001), rate of performance of ALL appropriate labs 1x/6 months (28.38% - 2014 baseline period, 44.57% - 2015 interventional period, 43.37% - 2016 post-interventional period; p < 0.0001), rate of cardiovascular assessment 1x/12 months (35.95% - 2014 baseline period, 51.71% - 2015 interventional period, 46.30% - 2016 post-interventional period; p < 0.0001), rate of influenza vaccination 1x/12 months (18.78% - 2014 baseline period, 29.50% - 2015 interventional period, 37.18% - 2016 post-interventional period; p < 0.0001), rate of lupus flare (16.30% - 2015 interventional period, 12.05% - 2016 post-interventional period; p = 0.0338), and rate of hospitalization (8.59% - 2014 baseline period, 6.68% - 2015 interventional period, 5.68% - 2016 post-interventional period; p = 0.0466).

Conclusion:
Time structured, IT enhanced, and QI indicator driven interventional modalities prompted more frequent, more comprehensive, guideline adherent point of care interaction with SLE patients. “Tighter" management resulted in the improved outcomes of both rate of lupus flare and rate of hospitalization in SLE patients.

Disclosure: F. Migliore, None; R. Quinet, None; W. E. Davis, None; D. Wray, None; T. Hilbun, None; M. Budziakowska, None.


Abstract Number: 722

Differential Diagnosis of Autoimmune Diseases, Outlier Detection Plus Subgrouping in Clinical Trials By High Content Autoantibody Profiling
Background/Purpose: Early diagnosis as well as initiation of successful treatment are two big challenges in the management of patients with autoimmune diseases (AID). Overlap of a plethora of clinical symptoms, ranging from multi-organ involvement, fatigue, inflammation to CNS-involvement make differential diagnosis quite challenging. Especially in early disease these signs are difficult to quantify, hence the lag time from start of disease until clinical diagnosis may be delayed, sometimes for years. With the growing interest in conducting clinical trials in AID, there is a need for new biomarkers that can be used to diagnose individual AIDs to reduce the inclusion of patients not carrying the intended disease, and identify clinical subsets, predict treatment outcome and assess disease activity.

Methods: The autoantibody reactivity pattern in serum of AID patients was analyzed using a Luminex bead-based antigen array (SeroTag) and 1,600 – 8,000 selected human protein antigens. We screened over 3,000 serum samples from Sjögren’s Syndrome (n= 350), SLE (n= >1000), SSc (n= >250), RA (n= >1000), and several other AIDs and over 1,000 healthy individuals to confirm known and to discover novel autoantibodies, create reduced autoantibody panels for differential diagnosis and disease subgrouping.

Results: Apart from clear confirmation of the known benchmark autoantigens known for many years we have discovered over 80 novel autoantibodies, which were detected in frequencies of 10 to >25% in selected AIDs. Some novel autoantibodies are specific for certain diseases, such as the major vault protein in SLE or BICD2 in SSc. Others are present in several diseases, indicating overlap syndromes. Multiplex panels of 50-100 AABs were generated and tested to allow for a subgroup definition of Sjögren’s, SLE, and for clear segregation of SjS/SLE overlap syndrome patients. As well, subgrouping of SSc and early RA patients was achieved.

Conclusion: A set of 100-150 autoantigens, half of them well established, the other half novel, succeed in differential diagnosis of AID, in some diseases already at early disease stage. This panel has been used in several drug trials to subgroup SLE, Sjögrens or RA into subgroups. Especially in SLE, outliers in the range of 10-15% of the trial population were seen which can be used to curate a trial population, eventually to arrive at a more precise assessment of trials primary objectives.

Disclosure: P. Schulz-Knappe, ProtagenAG, 3; P. Budde, Protagen, 3; H. D. Zucht, Protagen AG, 3.
### Background/Purpose
To evaluate the incidence and variability of traditional coronary artery disease (CAD) risk factors in a cohort of systemic lupus erythematosus (SLE) patients.

### Methods
174 women were included (T0) in this prospective study on SLE atherosclerosis. The following traditional CAD risk factors were analyzed: hypertension (blood pressure \( \geq 140/90 \) mmHg or antihypertensive medication), diabetes mellitus (DM) (fasting glucose \( \geq 126 \) mg/dl on at least two occasions or use of oral hypoglycemic agents or insulin), dyslipidemia (total-cholesterol \( \geq 200 \) mg/dl or HDL \( < 40 \) mg/dl or LDL \( \geq 130 \) mg/dl or use of oral lipid-lowering agents), hypertriglyceridemia (triglycerides \( \geq 150 \) mg/dl), obesity (body mass index \( \geq 30 \) kg/m\(^2\)), abdominal obesity (waist circumference \( \geq 88 \) cm), smoking, positive family history for coronary event. Metabolic syndrome (MetS), according to Third Report of the NCEP/ATP III criteria, and Framingham risk score (FRS) were computed. The cumulative incidence between T0 and T1 for all risk factors was investigated. The incidence rate (person-years) for hypertension, DM, dyslipidemia and hypertriglyceridemia, with a CI95%, were calculated based in the data collected from the medical records. The frequency of risk factor disappearance at T1 (including the absence of treatment in the definition of disappearance), among patients with the risk factor at T0, was also described.

### Results
The mean (SD) age at T0 of 151 patients reevaluated after 39 (36.5-42.0) months (T1) was 37.8 (11.1) years old, 75.5% non-white. The cumulative incidence, the incidence rate and the disappearance of some risk factors for CAD are presented in Table 1. The cumulative incidence during follow up were zero for smoking, 3.8% for positive family history for premature CAD, 16.5% for obesity, 18.8% for MetS and 39.1% for abdominal obesity. Eleven (11.7%) of 143 patients with low FRS in T0 were classified in high risk category in T1. Considering the risk factors disappearance, 26.0% with MetS at T0, 16.7% with obesity and 6.3% with abdominal obesity presented without the risk factor at T1. Only 1 (12.5%) patient within the higher risk of coronary event in 10 years (FRS\(>10\%\)) at T0 “reduced” the risk to \(<10\%\) in T1.

### Conclusion
The authors identified a significant increase in the incidence of CAD risk factors in lupus patients with a follow-up of approximately 3 years. Conditions such as hypertension, obesity and DM presented less fluctuation than dyslipidemia between T0 and T1, raising considerations about the importance of statins use in lupus patients over time.

### Table 1. Coronary artery disease risk factors cumulative incidence, incidence rate and disappearance after 39 (37-42) months, in lupus patients

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Cumulative incidence*</th>
<th>Incidence rate 1000 person-years (CI 95%)</th>
<th>Disappearance of risk factor**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>18/79 (22.8%)</td>
<td>72.1 (38.8-105.4)</td>
<td>6/72 (8.3%)</td>
</tr>
<tr>
<td>DM</td>
<td>5/143 (3.5%)</td>
<td>10.4 (1.3-19.5)</td>
<td>0</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>33/89 (37.1%)</td>
<td>133.2 (87.8-178.6)</td>
<td>27/62 (43.5%)</td>
</tr>
<tr>
<td>LDL-c(&gt;130)mg/dl</td>
<td>20/126 (15.9%)</td>
<td>49.9 (28.1-71.8)</td>
<td>9/25 (36.0%)</td>
</tr>
<tr>
<td>Total Chol(&gt;200)</td>
<td>27/122 (22.1%)</td>
<td>71.9 (44.8-99.0)</td>
<td>11/29 (37.9%)</td>
</tr>
<tr>
<td>HDL-c(&lt;40)mg/dl</td>
<td>15/111 (13.5%)</td>
<td>44.2 (21.8-66.5)</td>
<td>27/40 (43.5%)</td>
</tr>
<tr>
<td>TGL(&gt;150)mg/dl</td>
<td>16/108 (14.8%)</td>
<td>49.1 (25.0-73.1)</td>
<td>18/30 (41.9%)</td>
</tr>
</tbody>
</table>
Antibodies Against the Chemokine Receptors CXCR3 and CXCR4 Predict Progressive Lung Fibrosis in Systemic Sclerosis (SSc)

Gabriela Riemekasten1, Elise Siegert2 and Harald Heidecke3, 1Department of Rheumatology, Universitätsklinikum Schleswig-Holstein, Lubeck, Germany, 2Rheumatology and Clinical Immunology, University Hospital Charité, Berlin, Germany, 3CellTrend GmbH Luckenwalde, Luckenwalde, Germany

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Chemokine receptors CXCR3 and CXCR4 are involved in immune cell migration and in the pathogenesis of inflammatory fibrosis, a key feature of systemic sclerosis (SSc). It is hypothesized that IgG antibodies (ab) against these two receptors are present in patients with SSc and associated with clinical findings.

Methods: Anti-CXCR3 and anti-CXCR4 ab levels were measured in 449 sera from 327 SSc patients and in 234 sera from healthy donors (HD) by ELISA. In SSc, ab levels were compared with clinical data in a cross-sectional and longitudinal setting. Protein expression of CXCR3 and CXCR4 on PBMC was analyzed in 17 SSc patients and 8 HD by flow cytometry.

Results: Anti-CXCR3 and anti-CXCR4 ab levels were different among SSc subgroups compared to HD and were highest in diffuse SSc patients. The ab levels strongly correlate with each other (r = 0.85). Patients with SSc-related interstitial lung disease (SSc-ILD) exhibited higher ab levels, which negatively correlated with lung function parameters (e.g. r = -0.5 and r = -0.43 for predicted vital capacity, respectively). However, patients with deterioration of lung function showed lower anti-CXCR3/4 ab levels compared to those with stable disease. Frequencies and median fluorescence intensities (MFI) of CXCR3+ and CXCR4+ PBMC were lower in SSc patients compared to HD. They correlated with the severity of skin and lung fibrosis (Fig. 1).

![Image of CXCR3 and CXCR4 expression](image_url)

Fig. 1: Frequency of CXCR3-positive CD14+ monocytes among CD14+ monocytes (a) as well as CXCR3 density (b) on CD14+ monocytes negatively correlated with the predicted percentages of forced vital capacity (FVC). (c) CXCR4 density on CD4+ T cells correlated with modified Rodnan skin score (mRSS).
Conclusion: Anti-CXCR3/4 ab and their corresponding receptors are linked with severity of lung fibrosis. High ab levels could serve as marker for SSc-ILD stability suggesting a protective role of these ab in SSc-ILD.

Disclosure: G. Riemekasten, CellTrend, 4; E. Siegert, None; H. Heidecke, Heidecke, 4,Riemekasten, 4.


Abstract Number: 725

Safety and Efficacy of Anabasum (JBT-101) in Diffuse Cutaneous Systemic Sclerosis (dcSSc) Subjects Treated in an Open-Label Extension of Trial JBT101-SSc-001

Robert F. Spiera1, Laura K. Hummers2, Lorinda Chung3, Tracy M. Frech4, Robyn T. Domsic5, Vivien Hsu6, Daniel E. Furst7, Jessica K. Gordon1, Maureen D. Mayes8, Robert W. Simms9, Scott Constantine10 and Barbara White10, 1Rheumatology, Hospital for Special Surgery, New York, NY, 2Medical and Rheumatology, Johns Hopkins University, Baltimore, MD, 3Rheumatology, Stanford University Medical Center, Palo Alto, CA, 4Division of Rheumatology, University of Utah, Salt Lake City, UT, 5Medicine - Rheumatology, University of Pittsburgh, Pittsburgh, PA, 6Rheumatology, Robert Wood Johnson University Scleroderma Program, New Brunswick, NJ, 7David Geffen School of Medicine at UCLA, Los Angeles, CA, 8Internal Medicine/Rheumatology, University of Texas Health Science Center at Houston, Houston, TX, 9Rheumatology, Boston University School of Medicine, Boston, MA, 10Corbus Pharmaceuticals, Inc., Norwood, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Anabasum (JBT-101) is a selective cannabinoid receptor type 2 agonist that activates resolution of innate immune responses and limits fibrosis in animal models of SSC. It is a synthetic, oral, non-immunosuppressive small molecule. Anabasum had acceptable safety and tolerability and showed evidence of clinical benefit in diffuse cutaneous SSC (dcSSc) in Phase 2 trial JBT101-SSc-001 (NCT02465437). The objective of this study was to provide long-term open-label safety and efficacy data in dcSSc subjects who received anabasum in that trial.

Methods: Subjects who completed the double-blind placebo-controlled (DBPC) part of JBT101-SSc-001 were eligible to receive anabasum 20 mg BID in an open-label extension (OLE).

Results: 36/38 (95%) eligible subjects enrolled in the OLE and 34/36 (94%) were on baseline immunosuppressive drugs. At the time of data cut-off, 1 subject had discontinued from the OLE, the duration of OLE dosing was median 194 days (range 25, 207 days) and total duration of DBPC + OLE dosing with anabasum was median 234 days (range 28, 295 days). All 36 subjects had at least one OLE visit ≥ 28 days post baseline. Adverse events (AEs, n = 88) occurred in 28/36 (78%) subjects in the OLE. Most AEs were mild (55/88, 62%) or moderate (30/88, 34%) in severity and unrelated to anabasum (75/88, 85%). The AEs that occurred in ≥ 10% of subjects (n, % of subjects) were mild fatigue (5, 14%) and mild/moderate upper respiratory tract infection (4, 11%). Dizziness occurred in 2 (6%) subjects. Only one subject had more than mild or moderate AEs. That subject developed renal crisis 7 days after starting 60 mg/day prednisone prescribed by a non-study physician for suspected temporal arteritis and had 2 severe and 1 life-threatening/serious AEs related to the renal crisis and deemed unrelated to anabasum. In the period between DBPC and OLE off study product (median 50 days, range 5 - 360 days), the modified Rodnan skin score (mRSS) was stable in all subjects, subjects treated with anabasum and
subjects treated with placebo during DBPC dosing (Table 1). After 10 weeks of anabasum treatment in OLE (Visit 3 in OLE), mRSS declined from baseline in these same groups of subjects.

Table 1. Changes in mRSS before and after 10 weeks dosing in OLE

<table>
<thead>
<tr>
<th>Period</th>
<th>Group</th>
<th>mRSS change from baseline</th>
<th>P, 2-sided paired t test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Off study drug between DBCP and OLE dosing</td>
<td>All subjects, N = 36</td>
<td>0.1 (4.1)</td>
<td>0.9372</td>
</tr>
<tr>
<td></td>
<td>Subjects previously treated with anabasum, N = 23</td>
<td>0.6 (4.4)</td>
<td>0.5459</td>
</tr>
<tr>
<td></td>
<td>Subjects previously treated with placebo, N = 13</td>
<td>-0.8 (3.6)</td>
<td>0.4106</td>
</tr>
<tr>
<td>On anabasum Visit 1 to Visit 3 (10 weeks)</td>
<td>All subjects, N = 29</td>
<td>-3.2 (3.9)</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td>Subjects previously treated with anabasum, N = 20</td>
<td>-2.5 (3.5)</td>
<td>0.0049</td>
</tr>
<tr>
<td></td>
<td>Subjects previously treated with placebo, N = 9</td>
<td>-4.8 (4.5)</td>
<td>0.0128</td>
</tr>
</tbody>
</table>

**Conclusion:** In OLE of Phase 2 trial JBT101-SSc-001, anabasum continues to have acceptable safety and tolerability in dcSSc with no severe or serious AEs or study discontinuations related to anabasum. The mRSS improved, although open-label nature of dosing with anabasum is acknowledged. These data support further testing of anabasum for treatment of dcSSc.

**Disclosure:** R. F. Spiera, Roche-Genetech, 2,GSK, 2,BMS, 2,Boehringer Ingelheim, 2,Cytori, 2,Chemocentryx, 2,Corbus Pharmaceuticals, 2,Prism, 2,Boehringer Ingelheim, 5,GSK, 5,Boehringer Ingelheim, 5; L. K. Hummers, None; L. Chung, Cytori, Actelion, Reata, 5; T. M. Frech, None; R. T. Domsic, None; V. Hsu, None; D. E. Furst, Grant/Research Support: Amgen,BMS Novartis, Pfizer, Roche/Genentech,Corbus. Consultant:AbbVie, Amgen, BMS, Corbus, Cytori, , Novartis, Pfizer, Roche/Genentech,. Speakers Bureau(CME or non-promotional only): BMS, Abbvie NO stocks, royalties, direct fina, 2,see above, 5,see above, 8; J. K. Gordon, Corbus Pharmaceuticals, 2,Cumberland Pharmaceuticals, 2,Bayer Pharmaceuticals, 2; M. D. Mayes, None; R. W. Simms, None; S. Constantine, Corbus Pharmaceuticals, Inc., 1,Corbus Pharmaceuticals, Inc., 3; B. White, Corbus Pharmaceuticals, 1,Corbus Pharmaceuticals, 3.


Abstract Number: 726

**Performance of the American College of Rheumatology Provisional Composite Response Index in Systemic Sclerosis (CRISS) in the Scleroderma Lung Study-I**

Dinesh Khanna1, Donald P. Tashkin2, Holly Wilhalme2 and Chi-hong Tseng3, 1University of Michigan, Ann Arbor, MI, 2University of California, Los Angeles, David Geffen School of Medicine, Los Angeles, CA, 3Medicine, University of California, Los Angeles, David Geffen School of Medicine, Los Angeles, CA

**First publication:** September 18, 2017
Background/Purpose: The CRISS has been proposed as a composite outcome measure for trials in systemic sclerosis. CRISS is a 2-step process that assigns a probability of improvement for each individual patient on 0.00 [no improvement] to 1.00. Step 1 assesses clinically meaningful decline in cardio-pulmonary-renal involvement (based on consensus expert opinion) and assigns a probability of 0.00. For remaining subjects who do not experience a clinically meaningful decline, 5 variables are used over 12 months to calculate probability of improvement. These are: FVC%, mRSS, patient and physician global assessments (MD GA), and HAQ-DI. Scleroderma Lung Study-I compared oral daily cyclophosphamide (CYC) vs. placebo (PLA) in subjects with SSc-ILD, which showed modest efficacy favoring CYC at 12-month but greater improvements in patient-reported outcomes. Our objective was to assess if CRISS index can discriminate CYC from PLA in the SLS-I over 12 months.

Methods: We used patient-level data for this analysis. For Step 2, MD GA was not assessed in the SLS-I. Therefore, linear regression model was developed to predict MD GA from variables which were similar between the original CRISS cohort and SLS-I. Stepwise regression (using maximum $R^2$ method) was used to identify the best prediction model for MD GA and applied to the SLS-I data. We compared the CYC vs. PLA for the whole population and for the diffuse cutaneous SSc using the Wilcoxon rank-sum test for CRISS and Student’s t-test for individual variables. In addition, we explored the proportion of subjects who had a probability score ≥ 0.60 and compared the 2 groups using Chi-square.

Results: The mean (SD) baseline disease duration was 3.2 (2.1) years; 59% had diffuse cutaneous SSc. The prediction model for MD GA included the FVC (at baseline and 12 month change), mRSS (at baseline and 12 month change), gender, disease duration, and joint contractures ($R^2$ of 0.44).

For Step 1, the definition of worsened cardio-pulmonary-renal involvement was met by 9 in CYC vs. 13 in PLA and were given a CRISS score of 0.0. For the remaining subjects, [60 in CYC and 52 in PLA], we applied Step 2. Using the CRISS as a continuous measure, CYC was statistically superior to PLA for the whole group (p=0.007) and diffuse SSc (p=0.0.02; Table). Lack of administration of MD GA in the trial is a limitation of this analysis.

Conclusion: In this post-hoc analysis using individual data from SLS-I, CRISS is able to discriminate CYC from PLA, supporting its validity in an independent cohort.


Table: Performance of individual components of Step 2 in CRISS and overall CRISS in SLS-I
<table>
<thead>
<tr>
<th></th>
<th>CYC (N=67)</th>
<th>Placebo (N=65)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Changed Score</td>
<td>N</td>
<td>Changed Score</td>
<td>P-value</td>
</tr>
<tr>
<td><strong>Overall</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Δ MRSS, mean</td>
<td>68</td>
<td>-3.65</td>
<td>63</td>
<td>-0.94</td>
<td>0.01</td>
</tr>
<tr>
<td>Δ FVC% predicted, mean</td>
<td>72</td>
<td>-1.39</td>
<td>70</td>
<td>-3.23</td>
<td>0.19</td>
</tr>
<tr>
<td>Δ Patient Global, mean</td>
<td>68</td>
<td>-0.43</td>
<td>63</td>
<td>0.12</td>
<td>0.22</td>
</tr>
<tr>
<td>Δ HAQ -DI, mean</td>
<td>68</td>
<td>-0.11</td>
<td>63</td>
<td>0.15</td>
<td>0.001</td>
</tr>
<tr>
<td>Δ MD Global, mean</td>
<td>67</td>
<td>0.07</td>
<td>63</td>
<td>0.79</td>
<td>0.01</td>
</tr>
<tr>
<td>CRISS Index Score (median, IQR)*</td>
<td>69</td>
<td>0.09 (0.00, 0.71)</td>
<td>65</td>
<td>0.002 (0.00, 0.19)</td>
<td>0.007</td>
</tr>
<tr>
<td>CRISS index ≥ 0.60</td>
<td>19</td>
<td>28%</td>
<td>10</td>
<td>15%</td>
<td>0.09</td>
</tr>
<tr>
<td><strong>Diffuse SSc</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Δ MRSS, mean</td>
<td>43</td>
<td>-5.30</td>
<td>37</td>
<td>-1.70</td>
<td>0.03</td>
</tr>
<tr>
<td>Δ FVC% predicted, mean</td>
<td>46</td>
<td>-1.23</td>
<td>41</td>
<td>-2.81</td>
<td>0.4</td>
</tr>
<tr>
<td>Δ Patient Global, mean</td>
<td>44</td>
<td>-0.42</td>
<td>37</td>
<td>-0.21</td>
<td>0.73</td>
</tr>
<tr>
<td>Δ HAQ -DI, mean</td>
<td>44</td>
<td>-0.13</td>
<td>37</td>
<td>0.15</td>
<td>0.007</td>
</tr>
<tr>
<td>Δ MD Global, mean</td>
<td>43</td>
<td>0.04</td>
<td>37</td>
<td>1.03</td>
<td>0.02</td>
</tr>
<tr>
<td>CRISS Index Score (median, IQR)*</td>
<td>45</td>
<td>0.24 (0.001, 0.96)</td>
<td>39</td>
<td>0.005 (0.00, 0.32)</td>
<td>0.02</td>
</tr>
<tr>
<td>CRISS index ≥ 0.60</td>
<td>18</td>
<td>40%</td>
<td>9</td>
<td>23%</td>
<td>0.10</td>
</tr>
</tbody>
</table>

*includes Step 1 and Step 2 probability scores

Negative score is improvement in MRSS, Patient Global, HAQ-DI, and Physician Global assessments and worsening in FVC% predicted

**Disclosure: D. Khanna**, Actelion, Bayer, BoehringerIngelheim, Chemomab, Corbus, Covis, Cytori,Eicos, EMD Serono, Genentech/Roche, Gilead, GSK, Sanofi-Aventis,UCB Pharma, 5,NIH/NIAMS, NIH/NIAID,Bayer, BMS, Genentech/Roche, Pfizer, 2,Eicos, 4; **D. P. Tashkin**, None; **H. Wilhalme**, None; **C. H. Tseng**, None.


**Abstract Number: 727**

**Survival and Clinical-Capillaroscopic Characteristics of French Canadian Systemic Sclerosis Patients: Analysis Based on Systemic Sclerosis Autoantibodies and the Novel Anti-BICD2 Autoantibody**

**Boyang Zheng**¹, Michael Mahler², Jean-Luc Senécal³, France Joyal⁴ and Martial Koenig⁵, ¹Division of Internal Medicine, Centre Hospitalier de l'Université de Montréal (CHUM), Montreal, QC, Canada, ²Research and Development, Inova Diagnostics, San Diego, CA, ³Rheumatology, Centre Hospitalier de l'Université de Montréal (CHUM), Montréal, QC,
Background/Purpose:

Systemic sclerosis (SSc) autoantibodies (aAbs) are invaluable for SSc diagnosis and prognosis. Anti-centromere (ACA), anti-topoisomerase I (ATA) and anti-RNA polymerase III (RNAP) have been incorporated into SSc classification criteria, whereas anti-Th/To is much less commonly tested. Meanwhile, newly discovered anti-BICD2 seems particularly interesting in predicting milder SSc.

Our goal was to characterize the aAb profile in French Canadian SSc patients and its correlation with clinical features, nailfold capillaroscopy (NCM) findings and survival rates.

Methods:

Biobanked sera obtained at first visit from 303 SSc patients were tested for SSc aAbs by indirect immunofluorescence, ELISA and immunoblotting. Clinical data and NCM findings at first visit were compared by aAb subsets. Survival status and causes of death were extracted from a previous study (1). Survival was estimated by Kaplan Meier analysis and additional predictors for mortality were identified.

Results:

In the 303 patients, aAb prevalence was: ACA 35% (n=145), ATA 10% (31), anti-Th/To 7% (21), anti-RNAP 4% (12) and anti-BICD2 8.9% (27). All anti-BICD2+ patients were also ACA+ and 96% had limited cutaneous SSc (lcSSc). Only the presence of puffy fingers was more prevalent in anti-BICD2+ patients compared to other ACA+ patients (37% vs 19% respectively, p=0.04). Diffuse cutaneous SSc (dcSSc) was most prevalent in ATA+ (20%) and anti-RNAP+ (68%) patients. Pulmonary fibrosis was more strongly associated with ATA than other aAbs (26% vs 9%, p=0.01). On NCM, anti-RNAP+ patients presented earlier capillary dilations after disease onset than other SSc patients (median interval 0.8 years vs 2 years, p=0.03).

Overall, 32 SSc related deaths occurred after a mean (± SD) of 9.8 (± 4.5) years following diagnosis. Risk factors associated with mortality were dcSSc (OR 2.6, CI 1.3-6.7), lung fibrosis (OR 5.5, CI 2.2-13.6), and anti-SSA/Ro presence (OR 2.5, CI 1.1-5.8). Kaplan Meier analysis of SSc related deaths showed that only ATA+ patients had a significantly lower cumulative 15 year survival rate (58%) (Fig. 1, log rank p=0.03), whereas survival was similar between other aAb subsets, including anti-BICD2.

Conclusion:

These data reaffirm and expand the importance of SSc related aAbs as prognostic markers. ATA are associated with dcSSc, lung fibrosis and worst survival in comparison to other SSc aAbs. Anti-BICD2 was always associated with ACA. The latter were both strongly associated with lcSSc and had similar survival rates. The only difference was an increased prevalence of puffy fingers in anti-BICD2+ patients.

Abstract Number: 728

Symptoms of Autonomic Dysfunction in Systemic Sclerosis Assessed By the Compass-31 Questionnaire

Brittany Adler¹, James Russell², Laura K. Hummers³ and Zsuzsanna McMahan⁴, ¹Rheumatology, Johns Hopkins University, Baltimore, MD, ²Neurology, Anatomy and Neurobiology, University of Maryland School of Medicine, Baltimore, MD, ³Medical and Rheumatology, Johns Hopkins University, Baltimore, MD, ⁴Department of Internal Medicine, Johns Hopkins University, Baltimore, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Autonomic dysfunction is a known complication of systemic sclerosis (SSc) and can affect vascular tone, gastrointestinal (GI) motility, and heart rate and blood pressure control. We sought to quantify autonomic symptom burden in a large cohort of patients with SSc and to determine clinical and serologic risk factors that associate with autonomic symptom burden.

Methods:
Patients with SSc were recruited from the Johns Hopkins Scleroderma Center and completed the Composite Autonomic Symptom Score (COMPASS)-31 questionnaire, which is a validated tool to measure autonomic symptom burden. The COMPASS-31 scores and subdomain scores in orthostatic, secretomotor, vasomotor, gastrointestinal, urinary, and pupillomotor dysfunction were quantified for each patient. Demographic information, clinical and serologic data, and Medsger disease severity scores were obtained from the longitudinal Johns Hopkins Scleroderma Center database. We analyzed the relationship between various features of systemic sclerosis and the total COMPASS-31 scores and subdomain scores using the student’s t-test for dichotomous variables and linear regression analysis for continuous variables.

Results:

104 patients with SSc completed the COMPASS-31 questionnaire. The average COMPASS-31 score among our SSc cohort was 24.9 ± 15.5, which was comparable to previously published scores in other diseases known to affect the autonomic nervous system such as small-fiber polyneuropathy. There was no relationship between the COMPASS-31 score and SSc subtype or autoantibody status. Patients with severe GI disease reported higher scores in multiple subdomains of the COMPASS-31, including orthostatic intolerance (p=0.006) and secretomotor dysfunction (p=0.03), compared to patients with mild or absent GI disease. There was also a dose-response relationship between GI disease severity and autonomic symptom burden (see Figure).

Conclusion:

We determined that patients with SSc have a significant burden of autonomic symptoms across multiple domains of autonomic function. All patients with SSc are at risk for autonomic symptoms regardless of SSc subtype or autoantibody status. We also determined that patients with severe GI disease have more symptoms of dysautonomia, which suggests that some of the GI disease in systemic sclerosis may be a cause or consequence of autonomic dysfunction.

Disclosure: B. Adler, None; J. Russell, None; L. K. Hummers, None; Z. McMahan, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/symptoms-of-autonomic-dysfunction-in-systemic-sclerosis-assessed-by-the-compass-31-questionnaire

Abstract Number: 729

Clinically Relevant Serum Proteins in Patients with Early Diffuse Cutaneous Systemic Sclerosis

Guoshuai Cai1, Kelsey S. Flood2, Shervin Assassi3, Elana J. Bernstein4, Robyn T. Domsic5, Jessica K. Gordon6, Faye Hant7, Elena Schiopu8, Virginia D. Steen9, Tracy M. Frech10, Dinesh Khanna11, Ami A. Shah12, Victoria K.
SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The Prospective Registry of Early Systemic Sclerosis (PRESS), an 11 center US cohort study of early diffuse cutaneous systemic sclerosis (dcSSc) patients, was designed to study dcSSc pathogenesis and patient response to treatments. Modified Rodnan skin score (mRSS), used to quantify skin severity, correlates with mortality. The study purpose was to identify a serum signature associated with dcSSc and correlated with mRSS.

Methods: Baseline serum samples and clinical data were collected from PRESS subjects at enrollment and healthy matched controls. Subjects met SSc ACR criteria, had early dcSSc (defined as < 2 years duration since first non-Raynaud symptom attributed to SSc; swollen hands or sclerodactyly; PLUS 1 or more of the following: present anti-topoisomerase I or anti-RNA polymerase III serum autoantibodies; proximal skin involvement; tendon friction rubs). Samples were subjected to a custom Multi-Analyte Profiles (MAP) that uses multiplexed ELISA for serum protein quantification. Analytes with >40% missing values were excluded. The fold-change in protein expression between early dcSSc versus control samples was calculated. A t-test was used to test for statistical significance with correction for multiple hypothesis testing using the Benjamini-Hochberg method. mRSS was fitted to a linear model to assess for correlation with protein expression.

Results: Characteristics of dcSSc patients and controls were summarized (Table 1). Of 109 analytes, 28 analytes with missing values were excluded, leaving 81 analytes for analysis. 45 proteins were differentially expressed between early dcSSc patients and controls at baseline (q-value <0.05, Table 2). ANG-2, IGFBP-2, MIP-3 beta, TNFR2 and myoglobin had >2 fold-change in dcSSc patients vs. controls (Fig 1). 106 out of 112 (95%) dcSSc patients had baseline mRSS values. C-reactive protein correlated with mRSS (Fig 1).

Conclusion: We identified 45 proteins with variable expression between early dcSSc patients and healthy controls. Further, we identified that C-reactive protein expression correlates with mRSS severity, which has also been shown to be associated with lung disease progression. Future work includes developing a mRSS-predictive model by studying changes in protein expression in patients with longitudinal mRSS.
<table>
<thead>
<tr>
<th>Table 1: Discovery cohort clinical characteristics.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean (SD) as indicated</strong></td>
</tr>
<tr>
<td><strong>Age, years</strong></td>
</tr>
<tr>
<td><strong>Sex (% female)</strong></td>
</tr>
<tr>
<td><strong>Ethnicity (% Caucasian)</strong></td>
</tr>
<tr>
<td><strong>SSc disease duration (from first non-Raynaud)</strong></td>
</tr>
<tr>
<td><strong>Anti-U1 RNP antibody</strong></td>
</tr>
<tr>
<td><strong>Anti-RNA polymerase III, n (%) positive</strong></td>
</tr>
<tr>
<td><strong>Baseline mRSS</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Protein analyses</strong></th>
<th><strong>Fold Change</strong></th>
<th><strong>p-value</strong></th>
<th><strong>q-value</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Up-regulated</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angiopoietin-2 (ANG-2)</td>
<td>2.92</td>
<td>6.49E-18</td>
<td>5.26E-16</td>
</tr>
<tr>
<td>B cell-activating factor (BAFF)</td>
<td>1.96</td>
<td>3.15E-13</td>
<td>8.51E-12</td>
</tr>
<tr>
<td>Insulin-like Growth Factor-Binding Protein 2 (IGFBP-2)</td>
<td>2.59</td>
<td>3.84E-12</td>
<td>6.22E-11</td>
</tr>
<tr>
<td>Tumor necrosis factor ligand superfamily member 13 (APRIL)</td>
<td>1.86</td>
<td>4.26E-11</td>
<td>5.95E-10</td>
</tr>
<tr>
<td>Tumor necrosis factor receptor 2 (TNFR2)</td>
<td>2.06</td>
<td>4.79E-11</td>
<td>5.94E-10</td>
</tr>
<tr>
<td>Matrix Metalloproteinase-7 (MMP-7)</td>
<td>1.87</td>
<td>2.16E-10</td>
<td>2.18E-09</td>
</tr>
<tr>
<td>Macrophage inflammatory protein 3 beta (MIP-3 beta)</td>
<td>2.39</td>
<td>9.89E-10</td>
<td>8.90E-09</td>
</tr>
<tr>
<td>Myoglobin</td>
<td>2.03</td>
<td>1.38E-09</td>
<td>1.28E-08</td>
</tr>
<tr>
<td>Monocyte Chemotactic Protein 1 (MCP-1)</td>
<td>1.96</td>
<td>1.15E-07</td>
<td>5.47E-07</td>
</tr>
<tr>
<td>Interferon gamma Induced Protein 10 (IP-10)</td>
<td>1.89</td>
<td>4.35E-05</td>
<td>1.41E-04</td>
</tr>
<tr>
<td><strong>Down-regulated</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adiponectin</td>
<td>0.67</td>
<td>1.12E-03</td>
<td>2.75E-03</td>
</tr>
<tr>
<td>Brain-Derived Neurotrophic Factor (BDNF)</td>
<td>0.78</td>
<td>7.20E-04</td>
<td>1.88E-03</td>
</tr>
<tr>
<td>Myeloperoxidase (MPO)</td>
<td>0.72</td>
<td>8.63E-03</td>
<td>1.63E-02</td>
</tr>
<tr>
<td>Thrombospondin-1</td>
<td>0.71</td>
<td>8.99E-03</td>
<td>3.90E-03</td>
</tr>
<tr>
<td>Vitronectin</td>
<td>0.73</td>
<td>4.71E-04</td>
<td>3.11E-03</td>
</tr>
</tbody>
</table>

Table 2: Proteins with differential expression in early dcSSc patients vs. healthy controls. 45 proteins were differentially expressed between early dcSSc patients and controls at baseline (q-value < 0.05); included are the top 10 upregulated and 5 downregulated proteins. Differential protein expression is expressed in terms of fold-change; for example, a fold-change of 2 correlates to protein expression that is two times greater in early dcSSc patients vs. controls whereas a fold-change of 0.5 correlates to protein expression in early dcSSc patients that is half as much as compared to controls.
Disclosure: G. Cai, None; K. S. Flood, None; S. Assassi, Bayer Healthcare, 2,Biogen Idec, 2,Reata, 5,Boehringer Ingelheim, 5; E. J. Bernstein, None; R. T. Domsic, None; J. K. Gordon, Corbus Pharmaceuticals, 2,Cumberland Pharmaceuticals, 2,Bayer Pharmaceuticals, 2; F. Hant, None; E. Schiopu, None; V. D. Steen, None; T. M. Frech, None; D. Khanna, Actelion Pharmaceuticals Ltd, Bayer, Bristol-Myers Squibb, Covis, Cytori, EMD Serono, Genentech/Roche, Gilead, GSK, Sanofi-Aventis, 5,NIH K24AR063120, 2; A. A. Shah, None; V. K. Shanmugam, Multiple, 9; F. V. Castelino, None; M. Hinchcliff, None.


Abstract Number: 730

The Association of Pulmonary Hypertension with Isolated Nucleolar Serum Autoantibodies in Systemic Sclerosis

Kathleen Aren1, Mary A. Carns1, Michael Cuttica2, Julia (Jungwha) Lee3, Virginia D. Steen4 and Monique Hinchcliff5, 1Northwestern University, Feinberg School of Medicine Scleroderma Program, Chicago, IL, 2Northwestern University, Feinberg School of Medicine, Division of Pulmonary and Critical Care, Chicago, IL, 3Preventive Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, 4Division of Rheumatology, Department of Medicine, MedStar Georgetown University Hospital, Washington, DC, 5Department of Medicine Division of Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM
**Background/Purpose:** Serum antibodies are used to identify SSc patients who may be at higher risk for SSc-PH. The Pulmonary Hypertension Assessment and Recognition of Outcomes in Scleroderma (PHAROS) Registry cohort followed SSc-PH patients. We assessed the validity of prior reports of association between serum antibodies and PH using data from PHAROS and the Northwestern Scleroderma Registry (NW).

**Methods:** Antibody data were compared between PHAROS and NW subjects (mPAP ≥25 mmHg on right heart catheterization). World Health Organization PH group (pulmonary arterial hypertension/PAH=Group 1, pulmonary venous hypertension/PVH=Group 2, and PH-interstitial lung disease/PH-ILD=Group 3) was determined. The association between antibodies and PH was studied using two approaches: 1) antibody distribution was compared between PHAROS and NW PH subjects; 2) antibody distribution was compared between combined PHAROS and NW PH (in total and by WHO group) and NW subjects without PH. Chi-square or Fisher’s exact tests were used for comparisons.

**Results:** Clinical characteristics were similar for 326 PHAROS subjects and 768 NW Registry subjects, 84 with PH (Table 1). There were significant differences in antibodies between PHAROS and NW subjects, p=0.005 (Table 1). When the PH groups were combined (n=410) and compared to NW subjects without PH (n=684), the antibodies between the groups were significantly different, p<0.0001 (Table 2). Subjects in the PH group had a higher percentage of isolated nucleolar antibodies (21%) compared to the NW subjects (8%). Similar percentages of ACA were found in both groups (28% for the PH group and 27% for the NW subjects without PH). When the subclassifications of PH groups were examined, the percentage of isolated nucleolar antibodies remained high in all 3 groups.

**Conclusion:** Isolated nucleolar serum antibodies were more prevalent in PH subjects compared to non-PH NW subjects. When the PH groups were examined separately, higher percentages of isolated nucleolar antibodies remained in all 3 groups. Similar percentages of ACA were found in both the PH group and NW subjects without PH, suggesting that isolated nucleolar antibodies may be a more specific marker for PH than ACA. Screening for isolated nucleolar antibodies may help to identify patients with SSc who are at higher risk for developing PH.
<table>
<thead>
<tr>
<th>Mean (SD) or n, %</th>
<th>PHAROS (All WHO groups) n=326</th>
<th>NW PH (All WHO groups) n=84</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>58 (11)</td>
<td>52 (13)</td>
<td>0.003</td>
</tr>
<tr>
<td>Sex, women</td>
<td>262, 80%</td>
<td>70, 83%</td>
<td>0.83</td>
</tr>
<tr>
<td>Race/Ethnicity, Caucasian</td>
<td>236, 72%</td>
<td>54, 64%</td>
<td>0.15</td>
</tr>
<tr>
<td>SSc Subtype, lcSSc</td>
<td>198, 61%</td>
<td>54, 64%</td>
<td>0.55</td>
</tr>
<tr>
<td>mRSS</td>
<td>9 (9)</td>
<td>8 (7)</td>
<td>0.42</td>
</tr>
<tr>
<td>SSc disease duration, years</td>
<td>10 (9)</td>
<td>9 (9)</td>
<td>0.54</td>
</tr>
<tr>
<td><strong>Serum autoantibodies</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>19, 6%</td>
<td>2, 2%</td>
<td>0.005</td>
</tr>
<tr>
<td>Anticentromere (ACA)</td>
<td>95, 29%</td>
<td>20, 24%</td>
<td></td>
</tr>
<tr>
<td>RNA Polymerase III</td>
<td>14, 4%</td>
<td>9, 11%</td>
<td></td>
</tr>
<tr>
<td>Anti-topoisomerase I (Scl-70)</td>
<td>44, 14%</td>
<td>18, 21%</td>
<td></td>
</tr>
<tr>
<td>U1 RNP</td>
<td>13, 4%</td>
<td>2, 2%</td>
<td></td>
</tr>
<tr>
<td>Isolated nucleolar antinuclear</td>
<td>78, 24%</td>
<td>9, 11%</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>63, 19%</td>
<td>24, 29%</td>
<td></td>
</tr>
</tbody>
</table>

Other=multiple antibodies, +ANA (homogenous, speckled, or multiple patterns)
Table 2: Distribution of autoantibodies in PHAROS and Northwestern PH (combined, all WHO groups) compared to Northwestern no PH

<table>
<thead>
<tr>
<th>Autoantibodies</th>
<th>PHAROS and NW PH (all WHO groups) n=410</th>
<th>NW no PH n=684</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>21, 5%</td>
<td>19, 3%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Anticentromere (ACA)</td>
<td>115, 28%</td>
<td>188, 27%</td>
<td></td>
</tr>
<tr>
<td>RNA Polymerase III</td>
<td>23, 6%</td>
<td>130, 19%</td>
<td></td>
</tr>
<tr>
<td>Anti-topoisomerase I (Scl-70)</td>
<td>62, 15%</td>
<td>151, 22%</td>
<td></td>
</tr>
<tr>
<td>U1RNP</td>
<td>15, 4%</td>
<td>29, 4%</td>
<td></td>
</tr>
<tr>
<td>Isolated nucleolar pattern</td>
<td>87, 21%</td>
<td>54, 8%</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>87, 21%</td>
<td>113, 17%</td>
<td></td>
</tr>
</tbody>
</table>

Other=includes multiple antibodies, +ANA (homogenous, speckled, or multiple patterns)

Table 3: Autoantibodies in the Northwestern no PH group compared to PHAROS and Northwestern PH (combined), by WHO group

<table>
<thead>
<tr>
<th>Autoantibodies</th>
<th>NW no PH N=684</th>
<th>PHAROS and NW PH (Group 1) n=266</th>
<th>PHAROS and NW PVH (Group 2) n=74</th>
<th>PHAROS and NW PH-ILD (Group 3) N=70</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>19, 3%</td>
<td>11, 4%</td>
<td>6, 8%</td>
<td>4, 6%</td>
</tr>
<tr>
<td>Anticentromere (ACA)</td>
<td>188, 27%</td>
<td>99, 37%</td>
<td>12, 16%</td>
<td>4, 6%</td>
</tr>
<tr>
<td>RNA Polymerase III</td>
<td>130, 19%</td>
<td>16, 6%</td>
<td>6, 8%</td>
<td>1, 1%</td>
</tr>
<tr>
<td>Anti-topoisomerase I (Scl-70)</td>
<td>151, 22%</td>
<td>22, 8%</td>
<td>13, 18%</td>
<td>27, 39%</td>
</tr>
<tr>
<td>U1RNP</td>
<td>29, 4%</td>
<td>9, 3%</td>
<td>3, 4%</td>
<td>3, 4%</td>
</tr>
<tr>
<td>Isolated nucleolar pattern</td>
<td>54, 8%</td>
<td>55, 21%</td>
<td>19, 26%</td>
<td>13, 19%</td>
</tr>
<tr>
<td>Other</td>
<td>113, 17%</td>
<td>54, 20%</td>
<td>15, 20%</td>
<td>18, 26%</td>
</tr>
</tbody>
</table>

Other= includes multiple antibodies, +ANA (homogenous, speckled, or multiple patterns)

When comparing distribution of autoantibodies between NW no PH and each PH group, p<0.0001.

Disclosure: K. Aren, None; M. A. Carns, None; M. Cuttica, None; J. Lee, None; V. D. Steen, None; M. Hinchcliff, None.


Abstract Number: 731
Prediction of Progression of Interstitial Lung Disease in Patients with Systemic Sclerosis

Wanlong Wu¹, Suzana Jordan², Mike Oliver Becker³, Rucsandra Dobrota³, Shuang Ye⁴, Britta Maurer⁵ and Oliver Distler²

¹Department of Rheumatology, Center of Experimental Rheumatology, University Hospital Zurich; Department of Rheumatology, Renji Hospital South Campus, Shanghai Jiao Tong University School of Medicine, Zurich, Switzerland, ²Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland, ³Department of Rheumatology, Center of Experimental Rheumatology, University Hospital Zurich, Zurich, Switzerland, ⁴Department of Rheumatology, Renji Hospital South Campus, School of Medicine, Shanghai Jiao Tong University, Shanghai, China, ⁵Department of Rheumatology, Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

No data are available to distinguish between progressive and stable patients when mild lung fibrosis is diagnosed in systemic sclerosis (SSc) patients. This study aimed to identify clinical and laboratory parameters that can predict the progression of interstitial lung disease (ILD) within 1 year in patients with mild SSc-ILD.

Methods:

Data prospectively collected in our local SSc cohort were analyzed in this observational study. Inclusion criteria were: diagnosis of SSc fulfilling ACR/EULAR 2013 criteria, diagnosis of ILD by HRCT, < 20% lung involvement extent on HRCT at the first visit (baseline), available HRCT and pulmonary function tests at baseline and annual follow-up visits (12±3 months), no concomitant with PAH.

The primary endpoint, progression of ILD was defined if any of the following parameters was fulfilled: > 20% extent of lung involvement on HRCT at any follow-up visit, decrease in FVC ≥15% within 1 year, or decrease in FVC ≥ 10% and DLCO ≥ 15% within 1 year.

Candidate predictors for logistic regression were selected by expert opinion based on clinical consideration. Receiver Operating Characteristic (ROC) curve analysis was performed to determine the optimal cut-off value for each significant continuous parameter.

Results:

From the 81 patients included, 25 (30.9%) had progression of ILD. Differences of parameters between progressors and non-progressors were analyzed by univariate analysis (Table 1).

Three candidate predictors reflecting the overall disease severity including worst SpO₂ during 6-minute walk test (6MWT), arthritis ever and modified Rodnan skin score (mRSS) were selected for logistic regression by expert opinion. The final regression model identified worst SpO₂ (p=0.011, OR: 0.78, 95% CI 0.64 to 0.94) and arthritis ever (p=0.002, OR: 7.15, 95% CI 2.01 to 25.48) as independent predictors. The ROC curve analysis identified the best cut-off value for worst SpO₂ as 94% (area under the curve: 0.78, sensitivity 0.667, specificity 0.857).

By employing combination of both predictors, the prediction model increased the prediction success rate from 30.9% in the whole cohort to 100% in the optimized enrichment cohort (Table 2).

Conclusion:
Our study identified exercise-induced SpO2 decline and arthritis ever as independent predictor of progression of mild SSc-ILD within 1 year. The derived evidence-based prediction model might be helpful for the risk stratification of this subgroup in clinical practice and cohort enrichment for future clinical trial design.

Table 1. Univariate analysis of parameters between non-progressors and progressors

<table>
<thead>
<tr>
<th>Parameter / mean value ± SD</th>
<th>Non-progressor (n=56)</th>
<th>Progressor (n=25)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>54.6±12.5</td>
<td>59.8±13.8</td>
<td>0.062</td>
</tr>
<tr>
<td>Disease duration (month)</td>
<td>76.2±62.5</td>
<td>69.4±67.21</td>
<td>0.540</td>
</tr>
<tr>
<td>mRSS (unit)</td>
<td>6.91±0.08</td>
<td>10.88±8.78</td>
<td>0.012</td>
</tr>
<tr>
<td>FVC (%)</td>
<td>100.3±19.2</td>
<td>102.2±18.9</td>
<td>0.402</td>
</tr>
<tr>
<td>TLC (%)</td>
<td>100.9±17.1</td>
<td>94.8±14.9</td>
<td>0.127</td>
</tr>
<tr>
<td>DICO/SSR (%)</td>
<td>77.8±17.7</td>
<td>70.8±15.8</td>
<td>0.064</td>
</tr>
<tr>
<td>6-minute walk distance (m)</td>
<td>557.2±82.3</td>
<td>505.2±105.6</td>
<td>0.019</td>
</tr>
<tr>
<td>Real SpO2 during 6MWT(%)</td>
<td>97.1±1.1</td>
<td>98.3±2.2</td>
<td>0.153</td>
</tr>
<tr>
<td>Worst SpO2 during 6MWT (%)</td>
<td>95.6±3.1</td>
<td>92.5±3.6(n=24)</td>
<td>0.000</td>
</tr>
<tr>
<td>ESR (mm/hr)</td>
<td>16.8±16.3(n=55)</td>
<td>21.8±16.7</td>
<td>0.059</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>3.50±4.83</td>
<td>6.46±13.4</td>
<td>0.221</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parameter in (frequency)</th>
<th>Non-progressor (n=56)</th>
<th>Progressor (n=25)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea NYHA 2-4</td>
<td>19(33.9%)</td>
<td>15(60.0%)</td>
<td>0.028</td>
</tr>
<tr>
<td>Tractions on HRCT</td>
<td>12(21.4%)</td>
<td>11(44.0%)</td>
<td>0.057</td>
</tr>
<tr>
<td>Arthritis ever</td>
<td>6(10.7%)</td>
<td>12(48.0%)</td>
<td>0.000</td>
</tr>
<tr>
<td>Joint Contractures</td>
<td>20(35.7%)</td>
<td>16(64.0%)</td>
<td>0.018</td>
</tr>
</tbody>
</table>

Table 2. Prediction models of progression of mild SSc-ILD

<table>
<thead>
<tr>
<th>Model</th>
<th>Included prediction markers</th>
<th>Prediction success (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>worst SpO2 during 6MWT ≤84%</td>
<td>16/24 (66.7)</td>
</tr>
<tr>
<td>2</td>
<td>arthritis ever</td>
<td>12/18 (66.7)</td>
</tr>
<tr>
<td>3</td>
<td>worst SpO2 during 6MWT ≤84% AND arthritis ever</td>
<td>9/9 (100.0)</td>
</tr>
<tr>
<td>4</td>
<td>worst SpO2 during 6MWT ≤84% OR arthritis ever</td>
<td>19/33 (57.6)</td>
</tr>
</tbody>
</table>

Disclosure: W. Wu, None; S. Jordan, None; M. O. Becker, None; R. Dobrota, None; S. Ye, Continent Pharmaceutical Company (China), 2; B. Maurer, AbbVie, Protagen, EMDO, Novartis, German SSc Society, Pfizer, Roche, Actelion, MSD, 5,mir-29 for the treatment of systemic sclerosis, 9; O. Distler, 4 D Science, Actelion, Active Biotec, Bayer, Biogen Idec, Boehringer Ingelheim Pharma, BMS, ChemomAb, EpiPharm, Ergonex, espeRare foundation, GSK,Roche-Genentech, Inventiva, Lilly, medac, MedImmune, Mitsubishi Tanabe, Pharmacycles, Pfizer, Sanofi, Seroda, 2.


Abstract Number: 732

Progression of Skin Fibrosis Is Associated with Decline in Lung Function in Patients with Diffuse Cutaneous Systemic Sclerosis: A European Scleroderma Trials and Research (EUSTAR) Analysis

Wanlong Wu¹, Suzana Jordan², Nicole Graf³, Janethe Pena⁴, John Curram⁵, Yannick Allanore⁶, Marco Maturri-Cerinic⁷, Janet E. Pope⁸, Christopher Denton⁹, Dinesh Khanna¹⁰ and Oliver Distler¹, ¹Department of Rheumatology, Center of
Previously, we have identified short disease duration (≤15 months) and low baseline modified Rodnan skin score (mRSS) (≤22/51) as independent predictors of progressive skin fibrosis (>5 mRSS units and ≥25% increment within 1 year) in patients with diffuse cutaneous systemic sclerosis (dcSSc). While this strategy has resulted in recruitment of more patients with progression of skin fibrosis in clinical trials, it might lead to recruitment of patients with less severe internal organ disease. This study was designed to determine whether progression of skin fibrosis is associated with progression of internal organ disease on longitudinal follow-up of patients with dcSSc.

Methods:

This study analyzed prospectively collected data from the EUSTAR cohort. Inclusion criteria were: diagnosis of SSc fulfilling ACR criteria, diffuse cutaneous involvement, mRSS ≥7 at baseline visit in 2009 or later, valid mRSS with a time interval of 12±3 months after baseline visit, and at least one available annual follow-up visit.

Progression of skin fibrosis was defined as an increase in mRSS >5 units and ≥25% from baseline to 12±3 months later. The outcome was defined as one of the following new events occurring at any follow-up visit based on expert group consensus: 1) renal crisis; 2) decrease in forced vital capacity (FVC) ≥10%; 3) left ventricular ejection fraction (LVEF) <45% or decrease in LVEF by >10% for patients with baseline LVEF <50%; 4) pulmonary hypertension (PH) on echocardiography as judged by the investigator; 5) death.

Kaplan–Meier analyses and log-rank tests were used to compare disease progression between progressors and non-progressors for up to 6 years of follow-up.

Results:

A total of 871 dcSSc patients were eligible. The median follow-up period was 3.26 years (IQR: 1.49−5.14). Sixty-seven (7.7%) patients had worsening of skin fibrosis within 1 year (defined as progressors). Cumulatively, 235/666 (35.3%) patients had a decrease in FVC ≥10%, 96/593 (16.2%) had new PH, 22/564 (3.9%) had worsening LVEF, 16/844 (1.9%) had a new renal crisis, and 58/871 (6.7%) died. Mean FVC% at baseline was 87.2% ± 20.4%, while 134 (20.1%) patients had baseline FVC% <70%.

Log-rank tests indicated the probability for a decrease in FVC ≥10% was significantly higher for progressors than non-progressors (53.2% vs. 33.9%, p=0.004) (Figure). There were non-significant differences in probabilities for new PH (9.5% vs. 16.7%), worsening LVEF (7.3% vs. 3.6%), new renal crisis (0.0% vs. 2.1%) and death (7.5% vs. 6.6%) between progressors and non-progressors.

Conclusion:

Progression of skin fibrosis is associated with a decline in lung function in dcSSc patients over follow-up. Our data indicate that evidence-based criteria for cohort enrichment of progressive skin fibrosis might also be appropriate to recruit more
dcSSc patients at higher risk of lung function decline in future clinical trials.

**Disclosure:** W. Wu, None; S. Jordan, None; N. Graf, Biotronik AG, 5; J. Pena, Bayer Healthcare Pharmaceuticals Inc, 3; J. Curram, Bayer Plc, 1, Bayer Plc, 3; Y. Allanore, Actelion Pharmaceuticals US, 2, Bayer AG, 2, Bristol-Myers Squibb, 2, Inventiva, 2, Medac, 2, Pfizer Inc, 2, Roche Pharmaceuticals, 2, Genentech and Biogen IDEC Inc., 2, Sanofi-Aventis Pharmaceutical, 2, Servier, 2, Actelion Pharmaceuticals US, 5, Bayer AG, 5, Bristol-Myers Squibb, 5, Inventiva, 5, Medac, 5, Pfizer Inc, 5, Roche Pharmaceuticals, 5, Genentech and Biogen IDEC Inc., 5, Sanofi-Aventis Pharmaceutical, 5; M. Matucci-Cerinic, None; J. E. Pope, Actelion, 2, Bayer AG, 2, Bristol-Myers Squibb, 2, Merck, 2, Pfizer Inc, 2, Roche, 2, Actelion, 5, Bayer AG, 5, Bristol-Myers Squibb, 5, Merck, 5, Pfizer Inc, 5, Roche, 5; C. Denton, Actelion Pharmaceuticals US, 5, Bayer AG, 5, GlaxoSmithKline, 5, CSL Behring, 5, Merck-Serono, 5, Roche Pharmaceuticals, 5, Genentech and Biogen IDEC Inc., 5, Inventiva, 5, Sanofi-Aventis Pharmaceutical, 5, Boehringer Ingelheim, 5, Actelion Pharmaceuticals US, 8, Bayer AG, 8, GlaxoSmithKline, 8, CSL Behring, 8, Merck-Serono, 8, Roche Pharmaceuticals, 8, Genentech and Biogen IDEC Inc., 8, Inventiva, 8, Sanofi-Aventis Pharmaceutical, 8, Boehringer Ingelheim, 8; D. Khanna, Bristol-Myers Squibb, 2, GlaxoSmithKline, 2, NIH/NIAMS, 2, NIH/NIAID, 2, Patient-Centered Outcomes Research Institute, 2, Scleroderma Foundation, 2, Actelion Pharmaceuticals US, 5, Bayer AG, 5, Cytori, 5, EMD Serono, 5, Genkyotex, 5, Gilead, 5, GlaxoSmithKline, 5, Genentech/Roche, 5, Sanofi-Aventis Pharmaceutical, 5, Seattle Genetics, 5; O. Distler, Actelion, 5, Bayer, 5, Biogen Idec, 5, Boehringer Ingelheim, 5, ChemomAb, 5, espeRare Foundation, 5, Genentech/Roche, 5, GlaxoSmithKline, 5, Inventiva, 5, Lilly, 5, Medac, 5, MedImmune, 5, Mitsubishi Tanabe Pharma, 5, Pharmacyclics, 5, Novartis Pharmaceutical Corporation, 5, Pfizer Inc, 5, Sanofi, 5, Sinoxa, 5, UCB in the area of potential treatments of scleroderma and its complications, 5, Patent mir-29 for the treatment of systemic sclerosis licensed, 5, Actelion, 2, Bayer, 2, Biogen Idec, 2, Boehringer Ingelheim, 2, ChemomAb, 2, espeRare Foundation, 2, Genentech/Roche, 2, GlaxoSmithKline, 2, Inventiva, 2, Lilly, 2, Medac, 2, MedImmune, 2, Mitsubishi Tanabe Pharma, 2, Pharmacyclics, 2, Novartis, 2, Pfizer Inc, 2, Sanofi, 2, Sinoxa, 2, UCB in the area of potential treatments of scleroderma and its complications, 2, Patent mir-29 for the treatment of systemic sclerosis licensed, 2.


**Abstract Number:** 733

**Ethnic Variation in Systemic Sclerosis Morbidity and Mortality**
Sindhu Johnson, Zareen Ahmad and Haifa Al Sheikh, Division of Rheumatology, Toronto Western Hospital, Mount Sinai Hospital, Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, ON, Canada, Toronto Scleroderma Program, Division of Rheumatology, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada, Division of Rheumatology, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic sclerosis (SSc) is an uncommon connective tissue disease characterized by pathological skin thickening and can involve multiple internal organs. Ethnic variations in SSc have been reported in clinical manifestations, severity of the disease as well as survival. Our aim was to compare the survival and disease manifestations across ethnicity among SSc patients.

Methods: The Toronto Scleroderma Program is the largest single-center, multiethnic, longitudinal SSc cohort in Canada. Patients are followed every 6 to 12 months using a standardized protocol. Patients who fulfilled the American College of Rheumatology-European League Against Rheumatism classification criteria for SSc and are 16 years of age or older were included in our retrospective cohort study. The study period was 1970–2017. Ethnicity was self-reported and was categorized as: Caucasian, African-American, Hispanic, Arab, East-Asian, First Nations or Persian. The primary outcome was the time from diagnosis to death from all causes. Secondary outcomes were differences in disease duration, SSc subtype, clinical manifestations, and serology. Survival probabilities and median survival times were determined using Kaplan-Meier survival curves. Cox proportional hazard models were used to estimate adjusted survival.

Results: 1005 subjects were evaluated, the majority of whom were Caucasian (n=745 (74%), African-American n=58 (6%), South Asian (n=69 (7%)), and East Asian (n=80 (8%)). Compared to Caucasians, East Asians less frequently had calcinosis (29% versus 9%, p=0.002), and esophageal dysmotility (88% versus 69%, p=0.002); African-Americans more frequently had interstitial lung disease (31% versus 53%, p=0.007); and First Nation subjects more frequently had diffuse cutaneous disease (35% versus 56%, p=0.02) and diabetes (5% versus 33%, p=0.03). There were no differences across ethnicities in the prevalence of pulmonary hypertension, renal crisis, or digital ulcers.

We found no difference in the short-term survival across ethnicities. However, in the long-term, there was trend for Hispanic subject to have better survival (81.3% (95%CI 63, 100), while First Nations (58.3% (95%CI 25, 100) and South Asian subjects (52.6% (95%CI 32, 87) had worst survival at 15 years and 20 years, respectively. East Asians appear to have the longest median survival time 43.3 years.

Conclusion: Ethnic variations in disease SSc disease manifestations are observed. However, in the setting of a universal health care system, this does not result in significant differences in survival.
Correlation of the American College of Rheumatology Provisional Composite Response Index in Systemic Sclerosis with Serum Biomarkers of Fibrogenesis in an Observational Cohort

Giuseppina Abignano¹, Sookhoe Eng², Maya H. Buch³, Paul Emery⁴, Dinesh Khanna⁵ and Francesco Del Galdo²,
¹Rheumatology Department of Lucania,, Rheumatology Institute of Lucania (IReL), San Carlo Hospital of Potenza and Madonna delle Grazie Hospital of Matera,, Potenza, Italy, ²Leeds Musculoskeletal Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom, ³NIHR-Leeds Musculoskeletal Biomedical Research Unit, Leeds, United Kingdom, ⁴NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom, ⁵University of Michigan, Ann Arbor, MI
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The CRISS is a composite index of response in diffuse cutaneous systemic sclerosis (dCSSC). It is a 2-step process for the probability of improvement ranging from 0.0 (no improvement) to 1.0. Patients with decline in cardio-pulmonary-renal involvement are assigned score 0.0 in step 1. All remaining subjects are scored for improvement in FVC, mRSS, patient (PT GA) and physician globals (MD GA), and HAQ-DI.

Two independent studies including in total 464 patients from 6 different centres have shown that skin, lung and overall fibrosis correlate with three serum biomarkers (Procollagen III N terminal pro-peptides (PIIINP), Tissue inhibitor of Metalloproteinase I (TIMP-1) and Hyaluronic Acid (HA)), either singularly or combined in the ELF Test algorithm. Here we aimed to determine whether CRISS correlated with the serum concentration of one or more of the ELF biomarkers and explore the scope to build a combined score with better performance in measuring the probability of clinical response in dCSSC.

Methods: 31 Consecutive dCSSc patients were included in the study at a single centre. Clinical data and serum were collected at baseline, at 12 and 24 months. CRISS and ELF score were calculated at the same time points. CRISS scores were calculated using the published formula and we assessed correlation coefficients between CRISS scores and biomarkers. Comparison between two groups and correlation were performed using Mann-Whitney and Spearman’s tests, respectively. P<0.05 was considered statistically significant. Statistical analysis was carried out using GraphPad Prism Version 7.

Results: Thirty-one dCSSc patients were enrolled (12 M; mean age=50.3 ±11.5). CRISS at 12 months was 0% in 19 patients, whereas in the remaining 12 patients it ranged from 0.1 to 1.0 (median=0.35). Five out of the 12 CRISS “responders” had a CRISS 24-12 >0.0, the remaining 7 had no further response (CRISS=0). Overall CRISS 24-0 was >0.0 in 16 patients (median=0.065, range=0.01-0.93). No clinical features at baseline were significantly different in the responders vs non responders at 12 or 24 months, including mRSS, FVC%, DLCO%, autoantibody profile, age, disease duration, Medsger Severity Score and CRP (P>0.05 for all). TIMP-1 concentration at baseline was significantly lower in patients with CRISS>0 vs. CRISS=0 (218.5 vs 265.9 respectively, p= 0.03), similar trend was observed for TIMP-1 at 12 months and CRISS 24 months. Accordingly TIMP-1 at baseline or 12 months statistically significant correlation with CRISS 24 months ( R=–0.389 and -0.374, respectively; p < 0.05 for both).
**Conclusion:** This is the first evaluation of CRISS in an observational setting. Although limited by single centre setting and low number, we show that in any 12 months interval a proportion between 38 and 51% of patients show a CRISS >0. Whereas only 6 to 22.5% of patients showed a CRISS>0.10. None of the routinely used clinical parameters can predict CRISS at 12 months whereas TIMP-1 concentration at baseline is significantly lower in the responders. This needs to be explored in additional cohorts and opens the possibility to include serum biomarkers of fibrogenesis within a combined response index for Systemic Sclerosis.

**Disclosure:** G. Abignano, None; S. Eng, None; M. H. Buch, Pfizer Ltd, 2,Roche Pharmaceuticals, 2,Abbott Immunology Pharmaceuticals, 5,Sandoz, 5; P. Emery, Pfizer,MSD,Abbvie,BMS,UCB,Roche,Novartis,Samsung, Sandoz, Eli Lilly and Company, 5; D. Khanna, Actelion, Bayer, BoehringerIngelheim, Chemomab, Corbus, Covis, Cytori,Eicos, EMD Serono, Genentech/Roche, Gilead, GSK, Sanofi-Aventis,UCB Pharma, 5,NIH/NIAMS, NIH/NIAID,Bayer, BMS, Genentech/Roche, Pfizer, 2,Eicos, 4; F. Del Galdo, None.


**Abstract Number:** 735

**Cardiopulmonary Exercise Testing to “Detect” Pulmonary Arterial Hypertension in Systemic Sclerosis**

Rosa Casella¹, Alessandro Santaniello²,³, Marco Vicenzi¹ and Lorenzo Beretta², ¹Cardiovascular Unit, Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Milan, Italy, ²Scleroderma Unit, Referral Center for Systemic Autoimmune Diseases, Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico di Milano, Milan, Italy, ³VIA FRANCESCO SFORZA 28, OSPEDALE MAGGIORE POLICLINICO, MILANO, Italy

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster I  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Pulmonary arterial hypertension (PAH) is one of the leading death causes in SSc patients. To gain a better prognosis, screening methods are needed to provide an early diagnosis and intervention. The DETECT algorithm is a highly sensitive tool, however it presents a very low positive predictive value. To reduce the number of unnecessary right heart catheterizations (RHC), we evaluated the predictive performance of cardiopulmonary exercise testing (CPET) in a DETECT positive SSc population.

**Methods:**

Two-hundred-fifty-eight adult SSc consecutive patients attending our Scleroderma Unit were considered. Among those, the DETECT algorithm was applied to the subjects responding to the application criteria (ACR criteria for SSc, DLco < 60%, disease duration ≥ 3 years). DETECT positive patients underwent CPET and RHC. CPET was performed on a COSMED Quark-B2 equipment, on a cycle ergometer with an incremental work rate between 5 and 15 watts per minute up to the patients’ maximum tolerance.

Pearson’s correlation was used to evaluate linear associations between CPET parameters and mean pulmonary pressure (mPAP); the difference between PAH vs non-PAH patients for the best parameter was assessed by means of Student’s t-test. Finally, the sensitivity/specificity trade-off of this parameter was evaluated by ROC analysis.
Results:

The enrolment flow chart is reported in Figure 1. Overall 81 patients were eligible for DETECT screening, 39 were positive and underwent CPET and RHC (Figure 1). The patients’ clinical characteristics are reported in Table 1. RHC found 12 cases of PAH (30.7%), 1 case of PH due to left heart disease (2.6%) and non-PH in 26 subjects (66.7%).

We found the following significant correlation:

- $mPAP-PetCO_2@lt$ (r 0.74, p $0.7\times10^{-7}$)

- $mPAP-VE/VCO_2@lt$ (r 0.8, p $0.1\times10^{-8}$)

- $mPAP-VE/VCO_2$ slope (r 0.85, p $0.7\times10^{-11}$)

The VE/VCO$_2$ slope was selected for further investigation.

VE/VCO$_2$ slope statistically differed between PAH and non-PAH patients (mean ± DS: 45.5 ± 4.95 vs 35.11 ± 5.04; p $0.5\times10^{-5}$). ROC analysis showed a remarkable performance of the VE/VCO$_2$ slope in detecting PAH in the DETECT population (AUC 0.955, p $0.7\times10^{-5}$). A single cut-point value equal to 38.5 of the VE/VCO$_2$ slope was capable of discriminating PAH and non-PAH patients with a 100% sensitivity and 82% specificity.

Conclusion:

This study shows that CPET can fruitfully be applied to patients screened with the DETECT improve its specificity. The VE/VCO$_2$ slope determination allows to significantly reduce the number of useless invasive RHC (from 39 to 17), without increasing missed diagnosis rate.
FIGURE 1 – DETECT screening

SSC patients
n = 258

SSC according to ACR criteria
n = 154

• DLco < 60%
• Duration > 3 years
n = 81

n = 6 excluded cause to:
- missed informed consent
- impossibility to perform CPET

STEP 1 +
n = 57

n = 2 lost follow-up

STEP 1 -
n = 18

STEP 2 -
n = 16

n = 1 PH due to left heart disease

STEP 2 +
n = 39

PAH +
n = 12

PAH -
n = 26
TABLE 1

<table>
<thead>
<tr>
<th></th>
<th>PAH</th>
<th>non-PAH</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE (years), mean ± sd</td>
<td>67.5 ± 7.9</td>
<td>63.2 ± 12.1</td>
<td>NS</td>
</tr>
<tr>
<td>SEX, f/m</td>
<td>12/0</td>
<td>25/2</td>
<td>NS</td>
</tr>
<tr>
<td>SUBSET, lcSSc/dcSSc</td>
<td>10/2</td>
<td>23/4</td>
<td>NS</td>
</tr>
<tr>
<td>FVC (%pred), mean ± sd</td>
<td>95.5 ± 21.6</td>
<td>103.9 ± 24.8</td>
<td>NS</td>
</tr>
<tr>
<td>DLco (%pred), mean ± sd</td>
<td>39.8 ± 10.7</td>
<td>47.7 ± 8.4</td>
<td>NS</td>
</tr>
<tr>
<td>ANTI-CENTROMERE, +/-</td>
<td>9/3</td>
<td>20/7</td>
<td>NS</td>
</tr>
<tr>
<td>TELEANGECTASIAS, +/-</td>
<td>10/2</td>
<td>25/1</td>
<td>NS</td>
</tr>
<tr>
<td>NTproBNP (pg/ml), mean ± sd</td>
<td>615.6 ± 727.2</td>
<td>151.1 ± 105.6</td>
<td>0.05</td>
</tr>
<tr>
<td>URIC ACID (mg/dl), mean ± sd</td>
<td>5.5 ± 1.8</td>
<td>4.8 ± 1.2</td>
<td>NS</td>
</tr>
<tr>
<td>RIGHT AXIS DEVIATION, +/-</td>
<td>11/1</td>
<td>0/27</td>
<td>NS</td>
</tr>
<tr>
<td>STEPL score, mean ± sd</td>
<td>338 ± 16.7</td>
<td>330 ± 11.4</td>
<td>NS</td>
</tr>
<tr>
<td>RIGHT ATRIUM AREA (cm²), mean ± sd</td>
<td>15.8 ± 5.0</td>
<td>15.7 ± 2.9</td>
<td>NS</td>
</tr>
<tr>
<td>TRICUSPID JET VELOCITY (cm/s), mean ± sd</td>
<td>3.32 ± 0.64</td>
<td>2.6 ± 0.42</td>
<td>0.3*10²</td>
</tr>
<tr>
<td>STEP2 score, mean ± sd</td>
<td>54.7 ± 9.3</td>
<td>42.9 ± 4.8</td>
<td>0.1*10¹</td>
</tr>
<tr>
<td>mPAP (mmHg), mean ± sd</td>
<td>28.9 ± 2.4</td>
<td>19.5 ± 3.4</td>
<td>0.7*10²</td>
</tr>
<tr>
<td>sPAP (mmHg), mean ± sd</td>
<td>47.0 ± 5.7</td>
<td>31.1 ± 5.1</td>
<td>0.9*10⁸</td>
</tr>
<tr>
<td>dPAP (mmHg), mean ± sd</td>
<td>18.8 ± 2.5</td>
<td>12.6 ± 2.7</td>
<td>0.5*10⁷</td>
</tr>
<tr>
<td>PCWP (mmHg), mean ± sd</td>
<td>9.1 ± 3.3</td>
<td>7.9 ± 3.8</td>
<td>NS</td>
</tr>
<tr>
<td>RAP (mmHg), mean ± sd</td>
<td>4.5 ± 1.8</td>
<td>4.2 ± 2.8</td>
<td>NS</td>
</tr>
<tr>
<td>CI (/min/m²), mean ± sd</td>
<td>2.9 ± 0.7</td>
<td>3.2 ± 0.8</td>
<td>NS</td>
</tr>
<tr>
<td>PVR (UW), mean ± sd</td>
<td>4.9 ± 1.6</td>
<td>2.4 ± 0.7</td>
<td>0.2*10³</td>
</tr>
</tbody>
</table>

Disclosure: R. Casella, None; A. Santaniello, None; M. Vicenzi, None; L. Beretta, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/cardiopulmonary-exercise-testing-to-detect-pulmonary-arterial-hypertension-in-systemic-sclerosis

Abstract Number: 736

N-Terminal Pro-Brain Natriuretic Peptide Is Disproportionately Elevated in Scleroderma Associated Pulmonary Arterial Hypertension Compared to Idiopathic Pulmonary Arterial Hypertension

Alexander Hannan¹, Raed Dweik², Kristin B. Highland³, Gustavo Heresi⁴, Adriano Tonelli⁵, William Messner⁶ and Soumya Chatterjee¹,⁷ ¹Rheumatic and Immunologic Diseases, Cleveland Clinic, Cleveland, OH, ²Respiratory Institute, Cleveland Clinic, Cleveland, OH, ³Rheumatology.org, Cleveland Clinic, Cleveland, OH, ⁴Respiratory Institute - Pulmonary Medicine, Cleveland Clinic, Cleveland, OH, ⁵Pulmonary Medicine - Respiratory Institute, Cleveland Clinic, Cleveland, OH, ⁶Quantitative Health Sciences, Cleveland Clinic, Cleveland, OH, ⁷Rheumatic and Immunologic Ds, Cleveland Clinic, Cleveland, OH

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: N-Terminal pro-brain natriuretic peptide (NT-proBNP) level tends to correlate with myocardial wall stress and/or myocardial damage (fibrosis). Hence, it has been promoted as a potential biomarker to support the diagnosis of pulmonary arterial hypertension (PAH) and help monitor its severity, progression, and response to therapy. A
previous study has noted disproportionately elevated serum NT-proBNP levels among patients with scleroderma associated PAH (SSc-PAH) compared to similar patients with idiopathic PAH (iPAH).\(^1\) Our goal was to (1) verify the above results using a much larger cohort of SSc-PAH and iPAH patients, and (2) to identify possible explanations for this phenomenon.

**Methods:** A retrospective chart-review was conducted comparing demographic, laboratory, and hemodynamic [echocardiographic and right heart catheterization (RHC)] data from a total of 862 patients (686 with iPAH and 176 with SSc-PAH) enrolled in the Cleveland Clinic Pulmonary Hypertension Database. The diagnosis of PAH was confirmed by RHC, and the diagnosis of SSc was confirmed by a rheumatologist. NT-proBNP levels were measured at the time of the patient’s first RHC, which was also considered to be the time of PAH diagnosis. Mean pulmonary artery pressure (mPAP) and pulmonary vascular resistance (PVR) [data from RHC] and estimated right ventricular systolic pressure [data from transthoracic echocardiogram] were collected in both SSc-PAH and iPAH patients. A multivariate linear regression with a disease x log(NT-proBNP) interaction term was performed.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Total (N=862)</th>
<th>Idiopathic PAH (N=686)</th>
<th>Scleroderma Associated (N=176)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary Vascular Resistance (Wood unit)*</td>
<td>9.3±16.1</td>
<td>9.7±16.3</td>
<td>8.0±15.2</td>
<td>0.002(^a)</td>
</tr>
<tr>
<td>Mean Pulmonary Artery Pressure (RHC)*</td>
<td>49.1±14.7</td>
<td>50.9±14.8</td>
<td>42.3±11.8</td>
<td>&lt;0.001(^a)</td>
</tr>
<tr>
<td>Right Ventricular Systolic Pressure*</td>
<td>75.3±24.6</td>
<td>76.5±24.9</td>
<td>71.1±23.2</td>
<td>0.012(^a)</td>
</tr>
<tr>
<td>NT-proBNP Level*</td>
<td>680.0</td>
<td>619.0</td>
<td>1079.5</td>
<td>0.013(^d)</td>
</tr>
<tr>
<td></td>
<td>[232.0,2621.0]</td>
<td>[202.0,2513.0]</td>
<td>[381.0,4099.0]</td>
<td></td>
</tr>
<tr>
<td>log(NT-proBNP)*</td>
<td>6.6±1.7</td>
<td>6.5±1.6</td>
<td>7.1±1.6</td>
<td>0.010(^d)</td>
</tr>
</tbody>
</table>

*Data not available for all subjects. Missing values: Pulmonary Vascular Resistance = 89, Mean Pulmonary Artery Pressure = 5, Right Ventricular Systolic Pressure, TTE = 93, log(NT-proBNP) = 557, NT-proBNP Level = 557. Statistics presented as Mean ± SD, Median (P25, P75), Median (min, max) or N (column %). p-values: a=ANOVA, b=Kruskal-Wallis test, c=Pearson's chi-square test, d=Fisher's Exact test.
**Results:** In our cohort, at the time of first RHC, SSc-PAH patients were noted to have significantly higher NT-proBNP levels, yet much lower PVR and mPAP readings compared to similar iPAH patients. Also, there was a significant, positive correlation between NT-proBNP levels, mPAP, and PVR only in SSc-PAH patients, but not in iPAH patients.

**Conclusion:** One plausible explanation for higher NT-proBNP levels in SSc-PAH patients is intrinsic subclinical myocardial damage from SSc-induced fibrosis (which does not occur in early iPAH), in addition to right ventricular wall stress resulting from the occlusive pulmonary vasculopathy.


**Disclosure:** A. Hannan, None; R. Dweik, None; K. B. Highland, None; G. Heresi, None; A. Tonelli, None; W. Messner, None; S. Chatterjee, None.


Abstract Number: 737

**Dynamic Prediction of Pulmonary Hypertension Development in Systemic Sclerosis Patients Using Landmark Analysis – Comparison of Two Models**

**Svetlana I. Nihtyanova**¹, Voon H. Ong², Emma C. Derrett-Smith³, Benjamin Schreiber⁴, J. Gerry Coghlan⁴, Bianca DeStavola⁵ and Christopher Denton⁶, ¹Division of Medicine, Centre for Rheumatology and Connective Tissue Diseases, University College London, London, United Kingdom, ²Rheumatology, UCL Division of Medicine, London, United Kingdom, ³Centre for Rheumatology and Connective Tissue Diseases, UCL Division of Medicine, London, United Kingdom, ⁴National Pulmonary Hypertension Service, Royal Free Hospital, London, United Kingdom, ⁵Faculty of Population Health Sciences, UCL Institute of Child Health, London, United Kingdom, ⁶Department of Rheumatology, University College London, Royal Free Hospital, London, United Kingdom

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017
Background/Purpose:

Pulmonary hypertension (PH) contributes substantially to systemic sclerosis (SSc)-related morbidity and mortality. It tends to develop later in the disease, creating an opportunity for early risk stratification.

Previously published prediction models for PH have been based on cross-sectional data.

We set out to develop a model predicting PH development within 12 months, accounting for disease duration and utilising time-updated clinical characteristics, including serial measurements of lung function. We compare the use of most recent lung function results and serial changes in lung function over the preceding 4 years.

Methods:

We used data from a large unselected longitudinal cohort of SSc patients.

Sequential survival analyses with origins set at 6 consecutive landmark (LM) time-points, 12 months apart, starting at 60 months from disease onset were performed. The predictor variables included time-invariant characteristics (sex, subset and autoantibodies) and LM-specific information (age, presence of organ disease, FVC and DLCO, % predicted). Time to PH from the LMs was calculated with censoring at 12 months. Analyses were combined using a stratified Cox proportional hazards model, with each LM representing a stratum.

Results:

The study cohort consisted of 652 SSc patients. Of those 41.3% had diffuse SSc, 14.9% were male and the average age at disease onset was 48 years. Most patients (96%) either died during follow-up or were followed for over 10 years from disease onset. At the end of follow-up 13.3% of the subjects had developed PH.

The two final multivariable models both included the values at LM of age, presence of pulmonary fibrosis (PF) and antibody specificities (anti-U3RNP and anti-RNA polymerase (ARA)). Model 1 used most recent DLCO values, while Model 2 incorporated patient-specific intercept and slope of DLCO change over the 4 years prior to the LM (Table 1).

Both models were very similar, demonstrating that older age, ARA and anti-U3RNP positivity increase the hazard for PH development. Lower DLCO, both included as most recent measurement and as intercept and slope for the serial change in DLCO over the 4 years prior to LM, predicted increased hazard for PH. This effect was attenuated by presence of clinically-significant PF. None of the estimated effects varied between LM strata.

The two models had very similar fit and discrimination performance with C-index=0.88 for the model with most recent DLCO and C-index=0.87 for the one using intercept and slope for the linear change in DLCO.

Conclusion:

Our results show that comparatively simple models, using only information on age, autoantibodies and serial DLCO assessments could be used for risk stratification and prediction of PH development with good discriminating ability. After validation, this model could be used in clinical practice or for cohort enrichment in clinical trials.

Table 1. Comparison of the two prediction models for PH development
<table>
<thead>
<tr>
<th></th>
<th><strong>Model 1</strong></th>
<th><strong>Model 2</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>HR (95% CI)</strong></td>
<td><strong>HR (95% CI)</strong></td>
</tr>
<tr>
<td>Anti-RNA polymerase antibody</td>
<td>4.9 (1.91, 12.56)</td>
<td>4.81 (1.87, 12.35)</td>
</tr>
<tr>
<td>Anti-U3RNP antibody</td>
<td>5.97 (1.73, 20.69)</td>
<td>5.7 (1.62, 20.11)</td>
</tr>
<tr>
<td>Age at landmark, years</td>
<td>1.03 (1.00, 1.06)</td>
<td>1.03 (1.00, 1.07)</td>
</tr>
<tr>
<td>DLCO last assessment, %</td>
<td>0.9 (0.87, 0.92)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DLCO last assessment, % x Pulmonary fibrosis</td>
<td>1.05 (1.03, 1.07)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DLCO intercept, %</td>
<td></td>
<td>0.91 (0.88, 0.94)</td>
</tr>
<tr>
<td>DLCO intercept, % x Pulmonary fibrosis</td>
<td>1.05 (1.03, 1.08)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DLCO slope, % (standardised)</td>
<td>0.57 (0.42, 0.79)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

**Model performance**

<table>
<thead>
<tr>
<th></th>
<th><strong>Model 1</strong></th>
<th><strong>Model 2</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Akaike information criterion</td>
<td>320.023</td>
<td>325.192</td>
</tr>
<tr>
<td>Bayesian information criterion</td>
<td>348.283</td>
<td>359.105</td>
</tr>
<tr>
<td>Concordance Index (Harrell's C)</td>
<td>0.8826</td>
<td>0.8724</td>
</tr>
</tbody>
</table>

Disclosure: S. I. Nihtyanova, None; V. H. Ong, None; E. C. Derrett-Smith, None; B. Schreiber, None; J. G. Coghlan, None; B. DeStavola, None; C. Denton, None.


Abstract Number: 738

**Prospective Validation of the Systemic Sclerosis Skin Symptoms Patient-Reported Outcome (SSPRO) in a Phase 2 Trial of Anabasum (JBT-101) in Diffuse Cutaneous Systemic Sclerosis (dcSSc)**

Ada Man¹, Nancy Dgetluck² and Barbara White³, ¹Rheumatology, University of Manitoba, Winnipeg, MB, Canada, ²Biostatistics, Corbus Pharmaceuticals, Norwood, MA, ³Corbus Pharmaceuticals, Inc., Norwood, MA

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster I  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Skin thickening is the defining manifestation of dcSSc. A dcSSc patient’s assessment of their skin involvement can provide information about how that patient feels and functions in response to treatment. No skin-specific patient-reported outcome (PRO) measure has been prospectively validated in dcSSc in a clinical trial.

**Methods:** SSPRO is a validated PRO measure that assesses health-related quality of life (HRQOL) related to skin involvement in SSC. It has 18 items representing 4 HRQOL scales: physical effects, emotional effects, physical function, and social effects. All items are scored from 0 (better) to 6 (worse). Anabasum is a preferential cannabinoid receptor type 2 agonist that was tested for safety and efficacy in dcSSc in a double-blind randomized placebo-controlled Phase 2 trial (JBT101-SSc-001). Efficacy outcomes included the SSPRO, Patient Global Assessment (PtGA), HAQ-DI, Physician Global Assessment (MDGA), modified Rodnan Skin Score (mRSS), and FVC % predicted. SSPRO baseline scores were correlated with other baseline outcome scores using Pearson’s Correlation Coefficient. Internal consistency was estimated using Cronbach’s α. Effect size (ES, ratio of mean change in SSPRO total score from baseline to 12 weeks, to the standard deviation of the total score at baseline) was calculated to assess the SSPRO’s responsiveness to change.
Results: SSPRO was administered to 41 subjects with dcSSc. Internal consistency was high for the total (0.87) and for all scale scores (0.92). The SSPRO total and scale scores correlated strongly with PtGA, and moderately with HAQ-DI (except for the emotion scale) showing convergent validity. SSPRO also correlated moderately with MDGA and weakly with mRSS. As expected, SSPRO total and scale scores did not correlate with FVC % predicted, showing divergent validity. The SSPRO total mean score showed a significant difference in anabasum-treated (N = 26) compared to placebo-treated subjects (N = 15) at 12 weeks, LS means difference (SE) = -16.9 (6.0), P = 0.004 ANCOVA. The ES (n = 41) was moderate at -0.51, also demonstrating the SSPRO’s responsiveness to change.

Table 1. Correlations of SSPRO with other efficacy outcomes at baseline in a Phase 2 trial of anabasum in dcSSc

<table>
<thead>
<tr>
<th>Efficacy Outcome</th>
<th>Total Score</th>
<th>Physical Effects</th>
<th>Emotional Effects</th>
<th>Physical Function</th>
<th>Social Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>PtGA</td>
<td>0.626(^4)</td>
<td>0.506(^3)</td>
<td>0.482(^3)</td>
<td>0.646(^3)</td>
<td>0.573(^4)</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>0.521(^3)</td>
<td>0.500(^3)</td>
<td>0.264</td>
<td>0.592(^4)</td>
<td>0.581(^4)</td>
</tr>
<tr>
<td>MDGA</td>
<td>0.514(^3)</td>
<td>0.371(^1)</td>
<td>0.372(^1)</td>
<td>0.543(^3)</td>
<td>0.551(^3)</td>
</tr>
<tr>
<td>mRSS</td>
<td>0.445(^3)</td>
<td>0.378(^1)</td>
<td>0.387(^1)</td>
<td>0.338(^1)</td>
<td>0.433(^3)</td>
</tr>
<tr>
<td>FVC</td>
<td>-0.315</td>
<td>-0.115</td>
<td>-0.242</td>
<td>-0.165</td>
<td>-0.211</td>
</tr>
</tbody>
</table>

\(^1\) P ≤ 0.05; \(^2\) P ≤ 0.01; \(^3\)P ≤ 0.005; \(^4\)P ≤ 0.0001

Conclusion: In this clinical trial dcSSc population, SSPRO showed high internal consistency, construct validity, and responsiveness to change. Moderate and significant correlations of SSPRO scores with PtGA and HAQ-DI scores validate the usefulness of SSPRO as an outcome measure of how the patient with dcSSc feels and functions. Its weaker but still significant and directionally concordant correlations with mRSS shows that the SSPRO may provide additional information on the patient’s experience of their skin involvement that the mRSS does not assess. This is the first prospective validation of the SSPRO in a clinical trial.

Disclosure: A. Man, None; N. Dgetluck, Corbus Pharmaceuticals, 3; B. White, Corbus Pharmaceuticals, 1, Corbus Pharmaceuticals, 3.


Abstract Number: 739

How Effective Is the Home Exercise Program for Hands in Patients with Systemic Sclerosis: Preliminary Results from a Randomized Controlled, Single-Blind, Clinical Trial

Neslihan Gokcen\(^1\), Suade Ozlem Badak\(^2\), Tunay Sarpe\(^3\), Yasar Sertdemir\(^4\) and Eren Erken\(^2\), \(^1\)Physical Medicine and Rehabilitation, Division of Rheumatology, Cukurova University School of Medicine, Adana, Turkey, \(^2\)Internal Medicine, Division of Rheumatology, Cukurova University School of Medicine, Adana, Turkey, \(^3\)Physical Medicine and Rehabilitation, Cukurova University School of Medicine, Adana, Turkey, \(^4\)Department of Biostatistics and Medical Informatics, Cukurova University School of Medicine, Adana, Turkey

First publication: September 18, 2017
Background/Purpose: Systemic sclerosis (SSc) represents a heterogeneous autoimmune disease characterized by fibrosis of skin and internal organs. In particular, thickening of the skin, puffy hands, digital ulcers, calcinosis and joint contractures has contributed to disease prognosis by decreasing function of the hand and quality of life. The present study aims to investigate the effectiveness of the hand exercise program and demonstrate its influence on quality of life, as well as anxiety and depression in SSc patients.

Methods: Thirty female patients with SSc who fulfilled the 2013 ACR/EULAR classification criteria for systemic sclerosis were included in the study. Patients with neurological disorders, arthritis, myositis, amputation of fingers, serious contracture resisting hand grip and history of undergoing hand surgery were excluded. Patients were randomized into an exercise (n=16) and a control (n=14) group. Each group were informed of their disease and given recommended advice such as avoiding cold and trauma. The exercise group participated in a single hand exercise training applied by a medical doctor. Hereafter, they were given instructions for the home exercise program. The 8-week intervention consisted of isometric hand exercise and self-administered stretching repeated 10 times/2 set of training exercises per a day. Each group’s hand functions were assessed by Hand Mobility in Scleroderma (HAMIS) and Duruöz Hand Index (DHI). Additionally, all patients were estimated by Short Form 36 (SF-36), The Health Assessment Questionnaire (HAQ), Beck Anxiety and Beck Depression Inventory. Each group were evaluated at baseline and reassessed after 4 (V1) and 8 (V2) weeks.

Results: The baseline demographics and disease characteristics between the groups were similar. When comparing V1 and V2, we established a statistically significant amelioration from baseline measurement of handgrip strength in the exercise group (p<0.001). Accordingly, values of HAMIS, DHI, HAQ and Beck Depression Inventory were also significantly improved at V2 (p=0.002, 0.001, 0.001, 0.071, respectively) (Table). The assessment between the two groups at V1 and V2 indicated significant improvement in the exercise group with respect to the controls.

Conclusion: Exercise therapy showed a greater amelioration in the patients’ measurements of handgrip strength, quality of life and depression in SSc patients, indicating improvement in their hand function when compared to the control group.

Table: Outcome measurement changes in between the two groups at baseline, after 4 week and 8 week.
<table>
<thead>
<tr>
<th>Outcome</th>
<th></th>
<th>Baseline mean±SD median (min-max)</th>
<th>Week 4 mean±SD median (min-max)</th>
<th>Week 8 mean±SD median (min-max)</th>
<th>P&lt;sub&gt;time&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modified Rodnan Skin Score</td>
<td></td>
<td>E 15.4±8.1 14 (4-33)</td>
<td>C 15.1±8.8 13.5 (3-34)</td>
<td>E 14.3±7.2 12.0 (5-32)</td>
<td>0.026*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>C 14.7±8.0 13.5 (3-30)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HAMIS</td>
<td></td>
<td>E 5.3±6.0 4.5 (0-18)</td>
<td>C 4.0±5.2 3.0 (0-19)</td>
<td>E 2.5±4.8 0 (0-14)</td>
<td>0.002*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>C 4.0±4.6 2.5 (0-13)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DHI</td>
<td></td>
<td>E 8.0±6.0 5.0 (0-29)</td>
<td>C 13.7±13.4 7.0 (0-35)</td>
<td>E 5.3±6.8 3.5 (0-22)</td>
<td>&lt;0.001§</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>C 14.9±13.3 15.0 (0-32)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valentini activity score</td>
<td></td>
<td>E 2.4±1.4 2.0 (0.5-5)</td>
<td>C 3.4±1.5 3.3 (1-6)</td>
<td>E 1.5±1.4 1.0 (0-4.5)</td>
<td>&lt;0.001§</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>C 2.3±0.9 2.0 (0.5-4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beck Depression Inventory</td>
<td></td>
<td>E 19.8±11.6 18.0 (2-46)</td>
<td>C 23.1±10.3 22.5 (3-40)</td>
<td>E 18.0±11.3 18.5 (3-39)</td>
<td>0.035*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>C 23.0±11.6 24.5 (4-50)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beck Anxiety Inventory</td>
<td></td>
<td>E 16.3±9.2 15.0 (3-36)</td>
<td>C 9.5 (1-40)</td>
<td>E 17.0±10.1 14.5 (6-41)</td>
<td>0.071</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>C 13.4±10.2 9.5 (1-41)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>E</td>
<td>C</td>
<td>P&lt;sub&gt;group&lt;/sub&gt;</td>
<td>p group</td>
<td></td>
</tr>
<tr>
<td>------------------</td>
<td>------------------</td>
<td>------------------</td>
<td>------------------</td>
<td>---------</td>
<td></td>
</tr>
<tr>
<td><strong>Dominant handgrip strength (kg)</strong></td>
<td>18.6±6.7 (10-32)</td>
<td>15.5±6.4 (11-30)</td>
<td>0.984</td>
<td>0.093</td>
<td></td>
</tr>
<tr>
<td></td>
<td>18.0 (10-32)</td>
<td>18.0 (11-30)</td>
<td>0.013*</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>22.3±7.1 (14-36)</td>
<td>18.7±6.8 (9-30)</td>
<td>0.034*</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>24.6±6.8 (14-38)</td>
<td>18.4±6.4 (9-30)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HAQ</strong></td>
<td>10.5±7.7 (0-26)</td>
<td>13.6±13.3 (0-40)</td>
<td>0.843</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>6.3±7.8 (0-23)</td>
<td>7.0±7.8 (0-35)</td>
<td>0.992</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.1±6.2 (0-18)</td>
<td>8.5±6.2 (0-32)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SF-36 Physical function</strong></td>
<td>43.8±25.0 (5-90)</td>
<td>46.8±31.4 (0-100)</td>
<td>0.438</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>53.4±21.9 (20-100)</td>
<td>39.6±34.5 (0-100)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>67.8±17.1 (30-100)</td>
<td>37.9±30.8 (0-100)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Role physical</strong></td>
<td>20.3±32.0 (0-100)</td>
<td>14.3±27.2 (0-100)</td>
<td>0.759</td>
<td>0.077</td>
<td></td>
</tr>
<tr>
<td></td>
<td>40.6±38.6 (0-100)</td>
<td>17.9±28.5 (0-100)</td>
<td>0.343</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>55.0±38.1 (0-100)</td>
<td>25.0±39.2 (0-100)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Body pain</strong></td>
<td>56.8±32.3 (0-100)</td>
<td>52.7±29.6 (0-90)</td>
<td>0.728</td>
<td>0.822</td>
<td></td>
</tr>
<tr>
<td></td>
<td>60.5±30.84 (0-100)</td>
<td>50.5±26.0 (10-90)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>60.0±21.0 (22-90)</td>
<td>60.0±26.0 (0-100)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>General health</strong></td>
<td>44.7±20.5 (0-67)</td>
<td>44.4±24.5 (0-75)</td>
<td>0.233</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>45.1±17.0 (10-70)</td>
<td>39.7±23.9 (10-70)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>46.1±18.3 (15-75)</td>
<td>34.8±22.7 (10-70)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>E</td>
<td>C</td>
<td>P&lt;sub&gt;group&lt;/sub&gt;</td>
<td>0.224</td>
<td></td>
</tr>
<tr>
<td>----------</td>
<td>-------------</td>
<td>-------------</td>
<td>-------------------</td>
<td>-------</td>
<td></td>
</tr>
<tr>
<td>Vitality</td>
<td>45.9±17.7</td>
<td>43.4±17.5</td>
<td>0.488</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>50.0 (10-70)</td>
<td>40.0 (15-75)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>34.3±18.6</td>
<td>39.6±18.1</td>
<td>0.281</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>37.5 (0-60)</td>
<td>42.5 (5-65)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social</td>
<td>44.5±20.9</td>
<td>42.9±14.6</td>
<td>0.842</td>
<td></td>
<td></td>
</tr>
<tr>
<td>functioning</td>
<td></td>
<td>50.0 (12-63)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>37.4±22.5</td>
<td>43.0±19.5</td>
<td>0.524</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>37.5 (0-75)</td>
<td>50.0 (0-75)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Role</td>
<td>33.2±36.5</td>
<td>43.7±20.3</td>
<td>0.214</td>
<td></td>
<td></td>
</tr>
<tr>
<td>emotional</td>
<td>33.0 (0-100)</td>
<td>33.0 (0-67)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>33.1±34.5</td>
<td>30.7±27.5</td>
<td>0.426</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>33.0 (0-100)</td>
<td>33.0 (0-100)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mental</td>
<td>54.5±16.8</td>
<td>51.3±18.1</td>
<td>0.256</td>
<td></td>
<td></td>
</tr>
<tr>
<td>health</td>
<td>54.0 (16-80)</td>
<td>50.0 (28-96)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>47.4±16.3</td>
<td>49.4±8.7</td>
<td>0.905</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>46.0 (16-72)</td>
<td>50.0 (36-68)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P&lt;sub&gt;group&lt;/sub&gt;</td>
<td>0.240</td>
<td>0.886</td>
<td>0.208</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*p<0.05, *p<0.01, §p<0.001

E: Exercise group, C: Control group, HAMIS: Hand Mobility in Scleroderma, DHI: Duruöz Hand Index, HAQ: The Health Assessment Questionnaire, SF-36: Short Form 36.

Disclosure: N. Gokcen, None; S. O. Badak, None; T. Sarpel, None; Y. Sertdemir, None; E. Erken, None.


Abstract Number: 740
Prediction of Fibrosis Progression in Systemic Sclerosis By Collagen Biomarkers

Rucsandra Dobrota¹, Suzana Jordan², Pernille Juhl³, Britta Maurer⁴, Lukas Wildi⁴, Anne-C. Bay-Jensen⁵, Morten Karsdal⁶, Anne Sofie Siebuhr⁷ and Oliver Distler², ¹Department of Rheumatology, Center of Experimental Rheumatology, University Hospital Zurich, Zurich, Switzerland, ²Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland, ³Nordic Bioscience, Herlev, Denmark, ⁴Department of Rheumatology, Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland, ⁵Biomarkers and Research, Nordic Bioscience, Herlev, Denmark, ⁶Biomarkers and Research, Nordic Bioscience, Herlev, Denmark, ⁷Biomarkers and Research, Nordic Bioscience, Herlev, Denmark

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Altered extracellular matrix (ECM) remodeling leading to fibrosis is a key pathogenic process in systemic sclerosis (SSc). We previously showed that collagen formation and degradation metabolites are deregulated in SSc and that type III collagen turnover could identify progressive patients (1). Here, we report additional longitudinal analysis exploring serological collagen biomarkers potential for diagnosis and prediction of progression of skin and lung fibrosis in SSc.

Methods:
Patients (n=174) meeting the 2013 ACR/EULAR classification criteria for SSc and age and sex matched healthy controls (HC; n=29) were analyzed. 10% decrease in FVC% predicted or increase in mRSS ≥25% and 5 points at 1 year follow up defined progression. “Stable” were patients not meeting these criteria. Longitudinal clinical assessment and data, and baseline sera collection were conducted by EUSTAR quality standards. Collagen degradation (C3M, C4M2), BGM (MMP-degraded biglycan) and collagen formation markers (P1NP, P4NP7S, PRO-C3, PRO-C5, Pro-C6) were measured in serum by ELISA. Statistical analysis included Mann-Whitney U, Kruskal-Wallis tests, ROC analysis, and binary logistic regression.

Results:
174 patients with SSc as well as 29 HC were analysed. There were 25 (14%) SSc patients who progressed during 1 year. Baseline levels of most collagen biomarkers were higher in SSc compared to HC. C3M, C4M2 and PRO-C3 distinguished well between HC and SSc patients: C3M (AUC 0.90, p<0.001, 95%CI 0.85-0.95), C4M2 (AUC 0.90, p<0.001, 95%CI 0.85-0.94), PRO-C3 (AUC 0.75, p<0.001, 95%CI 0.67-0.83) (Figure 1). In addition to the previously reported ratio of PRO-C3/C3M (1), C3M and C4M2 predicted 1-year progression: C3M (AUC 0.87, p<0.001, 95%CI [0.79-0.95]), C4M2 (AUC 0.78, p<0.001, 95%CI [0.68-0.88]). A cut-off for PRO-C3/C3M at >1.2 showed a sensitivity of 84% with a specificity of 78% to predict progressive patients. In logistic regression adjusted for age and sex, PRO-C3M/C3M could predict decrease of FVC≥10% (OR 3.8, 95%CI [1.5-9.2], p=0.004) and increase of mRSS≥25% and 5 points (OR=2.1, 95%CI [1.0-4.2], p=0.04). Further, PRO-C3/C3M (OR 2.87, 95%CI [1.8-4.5], p<0.001) and C3M (OR 0.69, 95%CI [0.6-0.8], p<0.001) were identified as significant predictors of progression of skin and lung fibrosis.

Conclusion:
The dysbalance of collagen turnover suggests decreased collagen degradation in progressive vs. stable patients. Markers of collagen III and IV particularly arise hereby as potential new diagnostic and prognostic biomarkers in SSc.

Figure 1. Levels of biomarkers in healthy controls (HC) and patients with systemic sclerosis (SSc)

Disclosure: R. Dobrota, None; S. Jordan, None; P. Juhl, Nordic Bioscience Diagnostic, 3; B. Maurer, AbbVie, Protagen, EMDO, Novartis, German SSc Society, 2, Pfizer, Roche, Actelion, MSD, 9, mir-29 for the treatment of systemic sclerosis, 9; L. Wildi, None; A. C. Bay-Jensen, Nordic Bioscience Diagnostic, 3; M. Karsdal, Symic Bio, 1; A. S. Siebuhr, Nordic Bioscience Diagnostic, 3; O. Distler, 4D Science, Actelion, Active Biotec, Bayer, Biogen Idec, Boehringer Ingelheim Pharma, BMS, ChemomAb, EpiPharm, Ergonex, espeRare foundation, GSK, Roche-Genentech, Inventiva, Lilly, medac, MedImmune, Mitsubishi Tanabe, Pharmacyclics, Pfizer, Sanofi, Seroda, 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/prediction-of-fibrosis-progression-in-systemic-sclerosis-by-collagen-biomarkers

Abstract Number: 741

**Cardiac MRI in Systemic Sclerosis As Prognostic Tool of Cardiac Mortality in Symptomatic Patients**

Silvia Bosello\(^1\), Giovanni Canestrari\(^1\), Enrico De Lorenzis\(^1\), Gerlando Natalello\(^2\), Federico Parisi\(^1\), Agostino Meduri\(^3\), Riccardo Marano\(^3\), Gianfranco Ferraccioli\(^4\) and Elisa Gremsen\(^5\), 1Division of Rheumatology, Università Cattolica - Fondazione Policlinico Universitario A.Gemelli, Rome, Italy, 2Division of Rheumatology, Università Cattolica - Fondazione Policlinico Universitario A.Gemelli, Rome, Italy, 3Università Cattolica - Fondazione Policlinico Universitario A.Gemelli, Rome, Italy, 4Institute of Rheumatology, Università Cattolica - Fondazione Policlinico Universitario A.Gemelli, Rome, Italy, 5Division of Rheumatology - Institute of Rheumatology and Affine Sciences, Università Cattolica - Fondazione Policlinico Universitario A.Gemelli, Rome, Italy

First publication: September 18, 2017

SESSION INFORMATION
Background/Purpose:

Cardiac involvement is a relevant prognostic determinant of outcome in Systemic Sclerosis (SSc). Since the role of cardiac MRI (CMR) is still uncertain, we examined the cardiac involvement in symptomatic SSc patients through CMR, and defined its prognostic role value and its modification over the time.

Methods:

Sixty-two SSc-patients with symptoms of cardiac involvement (dyspnea, palpitations) and/or signs of cardiac failure and elevation of cardiac enzymes (MB-CK and/or troponin T) underwent C-MRI. Patients were followed for 51.0±27.2 months and 23 patients underwent a serial C-MRI studies because of modification and/or a worsening of their symptoms and signs.

Results:

CMR demonstrated abnormalities in 67.7% of patients, in particular T2 hyperintensity in 6 (9.7%) patients, while none of the patients presented early gadolinium enhancement and 20 (32.2%) patients presented late gadolinium enhancement (LGE). We identified 3 different patterns of distribution of LGE: subepicardial, midwall and subendocardial. Fourteen patients presented a single pattern of distribution (22.6%), while 6 patients (9.7%) presented more than one: 20.9% of patients presented a midwall distribution of LGE, 8.1% of patients presented a subepicardial LGE with a linear distribution pattern and 9.7% presented a subendocardial LGE distribution. Twelve patients (19.4%) showed one hypokinetic area and three patients akinetic areas. After a mean follow-up of 51.0±27.2 months, 4 patients (6.0%) died for arrhythmias or heart failure and 75% presented a subendocardial DE distribution pattern (p=0.003).

During the follow-up, 23 SSc patients presented a modification and/or a worsening of their cardiac symptoms and signs and they repeated the CMR assessment; CMR abnormalities were partially confirmed in 12 in the subsequent evaluation, 5 CMR demonstrated the development of new areas of T2 hyperintensity, subepicardic and subendocardic DE and ipo/akinesia; finally 7 CMR previously negative remained negative despite new symptoms. Furthermore a statistical significant reduction of the ejection fraction (EF) of left (59.4±10.6 vs 56.1±11.3, p<0.001) and right ventricles (54.6±12.0 vs 52.1±12.3, p<0.001) was noticed over the time.

Conclusion:

CMR represents a useful tool to assess the cardiac involvement in systemic sclerosis patients with cardiac signs and symptoms. Yet clear-cut links between each CMR finding and cardiac symptoms needs to be better defined Our data suggest that CMR offers the most comprehensive assessment of the extension of myocardial damage and identifies patients with a poor cardiac outcome especially when a subendocardial DE is present. Serial CMR evaluations allow to identify the new cardiac damage and to follow reduction of EF of both ventricles.

Disclosure: S. Bosello, None; G. Canestrari, None; E. De Lorenzis, None; G. Natalello, None; F. Parisi, None; A. Meduri, None; R. Marano, None; G. Ferraccioli, None; E. Gremese, None.


Abstract Number: 742

Quantitative CT Evalutation in Diffuse Interstitial Lung Involvement in Systemic Sclerosis: Usefulness of Lung Texture Analysis to Predict the Functional Change over Time
Background/Purpose:

The prognosis of patients with scleroderma and interstitial lung involvement (SSc-ILD) can be evaluated by combining data of pulmonary function tests (PFTs) and high-resolution computed tomography (HRCT), but both methods have intrinsic limitations. An automated system able to define the extent and pattern of lung parenchyma involvement could be very useful in clinical practice.

We aimed to evaluate the performance of such an automated system (CALIPER, Imbio LLC, MN) (1-2) in patients with SSc-ILD together with PFTs parameters and visual scoring of HRCT scans according to Goh’s visual reader based score (3). Moreover, we aimed to evaluate the prognostic value of CALIPER with respect to PFTs changes over time.

Methods:

Thirty-five scleroderma patients with ILD-SSc were consecutively enrolled. PFTs as well as lung HRCT were performed at both baseline and at latest follow-up. Quantitative analysis of parenchymal involvement on HRCT was performed by using CALIPER, which provided data on the relative volume of 5 different parenchymal patterns: normal, ground-glass, reticular, hyperlucent and honeycombing. Semi-quantitative analysis of the CT scans was performed by two radiologists according to the Goh’s visual reader based score.

Results:

Quantitative evaluation by CALIPER was successful in 31/35 patients (88.57%), requiring 20 m’ to 30 m’ per patient for the software. The two most common patterns were ground-glass (16.64%) and reticular (4.48%), with a mean disease extent of 18.8% and a prevalent distribution at middle and lower zones and in peripheral areas.

The correlations between PFTs and the relative volume of ground-glass were good (FVC: r=-0.72, p<0.001; TLC: r=-0.74, p<0.001; DLCO: r=-0.40, p=0.001), whereas PFTs and the relative volume of reticular pattern showed weaker correlations (FVC: r=-0.38, p=0.003; TLC: r=-0.42, p=0.02; DLCO: r=-0.31, p=0.02). The relative volume of normal lung had good correlations with FVC (r=0.63, p<0.001) and TLC (r=0.42, p=0.02).

The concordance between analysis performed by CALIPER and the Goh’s visual score was weak either in the ground-glass pattern (ICC:0.67, CI95%: 0.50-0.78) or in the reticular pattern (ICC:0.27, CI95%: 0.03-0.48).

Patients were followed-up for 26.0±15.6 months. Considering as clinically relevant a decrease in FVC greater than 10% or a decrease in FVC between 5-10% together with a decrease in DLco greater than 15%, reductions of lung volumes higher than -7.2 could predict a functional worsening with a sensitivity of 81% and a specificity of 70% (ROC curve analysis: AUC: 0.74, 0.54-0.93, p=0.035).

Conclusion:
Quantitative analysis performed by CALIPER arose as a useful tool to determine the extent and disease pattern in patients with SSc-ILD, correlating with PFT. The discriminatory performance of such an automated program to identify patients who presented a worsening of lung function suggests that quantitative analysis can help in evaluating response to therapy in scleroderma patients with ILD.

2. Bartholmai Brian J. J Thorac Imaging. 2013 September ; 28(5)

Disclosure: S. Bosello, None; M. E. Occhipinti, None; G. Canestrari, None; E. De Lorenzis, None; F. Parisi, None; G. Natalello, None; G. Leucone, None; A. R. larici, None; C. De Waure, None; G. Ferraccioli, None; E. Gremese, None.

Impact of Detect on Right Heart Catheterization Referral and Results; Data from a Prospective, Unselected, Systemic Sclerosis Cohort

Anna-Maria Hoffmann-Vold1, Håvard Fretheim2, Anders Heiervang Tennøe2, Oyvind Midtedt2, Torhild Garen2, Einar Gude2, Arne K Andreassen2 and Øyvind Molberg2, 1Division of Rheumatology, Oslo University Hospital, Oslo, Norway, 2Oslo University Hospital, Oslo, Norway

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The DETECT calculator has been freely available as a tool for earlier detection and diagnosis of pulmonary arterial hypertension (PAH) in systemic sclerosis (SSc) since 2014. Here, we aimed to evaluate its impact on PAH incidence rates, risk profile and functional class (FC) of patients at time of PAH diagnosis.

Methods: The study cohort included all patients in the prospective Oslo University Hospital (OUH) SSc cohort who performed an incident right heart catheterization (RHC) from 2009 and onwards. We grouped the patients in an early cohort with RHC conducted in 2009-2013, and a DETECT cohort with RHC from 2014-17. PH diagnosis was made by an experienced cardiologist according to the updated ESC guidelines with mean (m) PAP ≥ 25 mmHg measured by RHC and borderline PH with a mPAP >19mmHg. Pre and post capillary PHT was defined by PCW above or below 15 mmHg. Risk stratification at time of diagnosis was done using the low, intermediate and high risk grouping system suggested by ESC in 2016. Patients with ≥ 1 parameter of poor prognosis were considered at high risk and with ≥ 1 parameter of intermediate prognosis, at intermediate risk.

Results: An incident RHC was available in 161 patients, 77 from the early cohort and 84 from the DETECT cohort. Clinical and demographic characteristics are shown in Table 1. Absolute numbers of RHC, PAH and borderline PH cases in the years 2009-2017 are shown in Figure 1. At the time of PAH diagnosis, 27% of the DETECT cohort were in the low risk group compared to 19% in the early cohort, while 27% and 47% respectively belonged in the high risk groups (p-value 0.219) (Figure 2). We also observed a trend towards lower functional class in the DETECT cohort (Figure 2).

Conclusion: We show that the number of new PAH cases per year has been stable since 2009, with no apparent change following the introduction of the DETECT algorithm. From 2014 and onwards, we observed a, not significant, increase in
amount of newly diagnosed PAH cases with low risk group, and better functional class status. The total number of RHC increased from 2014 and onwards, with a concomitant increase in the number of borderline PH cases.

### Table 1: Demographics and clinical characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total cohort (n=161)</th>
<th>2009-13 (n=77)</th>
<th>2014-17 (n=84)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at RHC, yrs (SD)</td>
<td>61 (11.8)</td>
<td>59.6 (12.2)</td>
<td>62.4 (11.3)</td>
<td>0.137</td>
</tr>
<tr>
<td>Time onset to RHC, yrs (SD)</td>
<td>6.6 (8.2)</td>
<td>6.3 (8.3)</td>
<td>6.9 (8.1)</td>
<td>0.634</td>
</tr>
<tr>
<td>Follow-up, yrs (SD)</td>
<td>2.9 (2.4)</td>
<td>4.6 (2.2)</td>
<td>1.2 (0.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Females, no (%)</td>
<td>126 (78.8)</td>
<td>60 (77.9)</td>
<td>66 (78.6)</td>
<td>0.582</td>
</tr>
<tr>
<td>Ever smoker, no (%)</td>
<td>67 (41.9)</td>
<td>28 (36.4)</td>
<td>39 (46.4)</td>
<td>0.064</td>
</tr>
<tr>
<td>Limited cutaneous SSc, no (%)</td>
<td>125 (78.1)</td>
<td>63 (81.8)</td>
<td>63 (75)</td>
<td>0.502</td>
</tr>
<tr>
<td>Anti-centromere Ab, no (%)</td>
<td>78 (48.8)</td>
<td>37 (48.1)</td>
<td>34 (40.5)</td>
<td>0.848</td>
</tr>
<tr>
<td>Digital ulcers, n (%)</td>
<td>61 (38.1)</td>
<td>31 (40.3)</td>
<td>30 (35.7)</td>
<td>0.911</td>
</tr>
<tr>
<td>Scleroderma renal crisis, n (%)</td>
<td>7 (4.4)</td>
<td>4 (5.2)</td>
<td>3 (3.6)</td>
<td>0.562</td>
</tr>
<tr>
<td>Baseline modified Rodnan skin score</td>
<td>9.9 (8.8)</td>
<td>9.8 (10.5)</td>
<td>9.9 (9.8)</td>
<td>0.934</td>
</tr>
<tr>
<td>Pulmonary hypertension, n (%)</td>
<td>65 (40.6)</td>
<td>35 (45.5)</td>
<td>30 (35.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PAH total, n (%)</td>
<td>31 (19.4)</td>
<td>16 (20.8)</td>
<td>15 (17.9)</td>
<td></td>
</tr>
<tr>
<td>PH-ILD, n (%)</td>
<td>20 (12.5)</td>
<td>14 (18.2)</td>
<td>6 (7.1)</td>
<td></td>
</tr>
<tr>
<td>Post capillary PH, n (%)</td>
<td>14 (8.8)</td>
<td>5 (6.5)</td>
<td>9 (10.7)</td>
<td></td>
</tr>
<tr>
<td>Borderline PH, n (%)</td>
<td>38 (23.8)</td>
<td>19 (24.7)</td>
<td>27 (32.1)</td>
<td></td>
</tr>
<tr>
<td>No PH, n (%)</td>
<td>57 (35.6)</td>
<td>23 (29.9)</td>
<td>27 (32.1)</td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction, n (%)</td>
<td>14 (8.8)</td>
<td>8 (10.4)</td>
<td>6 (7.1)</td>
<td>0.557</td>
</tr>
<tr>
<td>Angina pectoris, n (%)</td>
<td>14 (10.1)</td>
<td>9 (11.7)</td>
<td>5 (6)</td>
<td>0.414</td>
</tr>
</tbody>
</table>

**Figure 1:** Frequency of conducted incident RHC, PAH, borderline PH and no PH

**Figure 2:** Risk stratification and functional class

Disclosure: A. M. Hoffmann-Vold, None; H. Fretheim, None; A. Heiervang Tennøe, None; O. Midtvedt, None; T. Garen, None; E. Gude, None; A. K. Andreassen, None; Ø. Molberg, None.
Prediction of All-Cause Mortality and Pulmonary Arterial Hypertension (PAH) Progression in Systemic Sclerosis (SSc), an Echocardiography Study

Anders Heiervang Tønne1, Anna-Maria Hoffmann-Vold1, Øyvind Molberg1, Håvard Fretheim1, Torhild Garen1, Einar Gude1, Arne K Andreassen1, Klaus Murbræch2, Svend Aakhus3, Johanna Andreassen2 and Oyvind Midtvedt1, 1Oslo University Hospital, Oslo, Norway, 2Cardiology, Oslo University Hospital, Oslo, Norway, 3Circulation and Medical Imaging, Norwegian University of Science and Technology, Trondheim, Norway

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Pulmonary arterial hypertension (PAH) is one of the leading causes of death in systemic sclerosis (SSc). Annual echocardiograms (echo) are recommended to detect PAH at an early stage, potentially improving outcome. We aimed to evaluate the potential of baseline echo parameters to predict PAH progression and all-cause mortality.

Methods: The study cohort included all SSc patients from the prospective Oslo University Hospital (OUH) cohort who had an evaluable baseline protocol echo performed between 2003 and 2016. This echo was analyzed regarding left- and right-sided systolic and diastolic function. Right heart catheterization (RHC) was performed in patients suspected of PH. PAH diagnosis was made by an experienced cardiologist with mean pulmonary artery pressure ≥ 25 mmHg, pulmonary capillary wedge pressure <15mmHg, stable forced vital capacity >70% and <10% lung fibrosis on HRCT. Vital status was available for all patients and PAH progression, defined by occurrence of new PAH related events were calculated. Cox regression analyses were conducted.

Results: In total, 337 SSc patients with baseline echo were included. RHC was conducted in 149 (44.2%) patients and 48 (14.2%) were diagnosed with PAH; of those, 34 patients showed PAH progression. Demographic and clinical characteristics are summarized in Table 1. Significant results from univariable and multivariable cox analyses of death are shown in Table 2, and for PAH progression in Table 3. In the final cox regression model for death, age (HR 1.06, 1.03-1.10 95%CI , p<0.001), DLCO (HR 0.97, 0.96-0.98 95%CI , p=0.001), pericardial effusion (HR 2.24, 1.37-3.63 95%CI , p<0.001), left atrium area (HR 1.07, 1.01-1.14 95% CI, p=0.024) and tricuspid annular plane systolic excursion (TAPSE) (HR 0.38, 0.19-0.74 95% CI, p=0.004) were associated (c-index 0.82). PAH progression was associated with age (HR 1.06, 1.02-1.11 95% CI, p=0.005), DLCO (HR 0.97, 0.95-0.99 95% CI, p=0.002), and right atrium area (HR 1.17, 1.10-1.25 95% CI, p<0.001) (c-index 0.86).

Conclusion: In our large and unselected SSc cohort, impaired baseline right heart function, but not left ventricular systolic or diastolic parameters, was predictive for both death and PAH progression. Echo may serve as a tool to stratify patients at risk for PAH and death.
Table 1: Demographic and clinical characteristics of all SSc patients, SSc-PAH patients and deceased patients.

<table>
<thead>
<tr>
<th></th>
<th>All cases (n=337)</th>
<th>Deceased patients (n=101)</th>
<th>PAH (n=48)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, no (%)</td>
<td>57 (17)</td>
<td>25 (25)</td>
<td>8 (17)</td>
</tr>
<tr>
<td>ACA, no (%)</td>
<td>172 (55)</td>
<td>39 (39)</td>
<td>38 (83)</td>
</tr>
<tr>
<td>lcSSc, no (%)</td>
<td>224 (68)</td>
<td>65 (64)</td>
<td>44 (92)</td>
</tr>
<tr>
<td>Death, no (%)</td>
<td>101 (30)</td>
<td>-</td>
<td>25 (52)</td>
</tr>
<tr>
<td>Age at echo, mean (SD)</td>
<td>58 (14)</td>
<td>64 (12)</td>
<td>64 (11)</td>
</tr>
<tr>
<td>Observation period, years, median (min,max)</td>
<td>5.1 (0-14)</td>
<td>3.0 (0-12)</td>
<td>5.3 (0.1-12.3)</td>
</tr>
<tr>
<td>TAPSE, cm (SD)</td>
<td>2.3 (0.5)</td>
<td>2.0 (0.6)</td>
<td>2.0 (0.6)</td>
</tr>
<tr>
<td>Right ventricular strain % (SD)</td>
<td>23.0 (6.1)</td>
<td>20.3 (7.1)</td>
<td>19.3 (7.3)</td>
</tr>
<tr>
<td>Left atrium area, cm2 (SD)</td>
<td>18 (5)</td>
<td>19 (5)</td>
<td>17 (4)</td>
</tr>
<tr>
<td>LV Global longitudinal strain, % (SD)</td>
<td>18.4 (3.0)</td>
<td>17.6 (3.5)</td>
<td>18.4 (2.2)</td>
</tr>
<tr>
<td>LVEF, % (SD)</td>
<td>58 (8)</td>
<td>56 (10)</td>
<td>59 (7)</td>
</tr>
<tr>
<td>E-wave, m/s (SD)</td>
<td>0.72 (0.21)</td>
<td>0.72 (0.29)</td>
<td>0.67(0.24)</td>
</tr>
<tr>
<td>A-wave, m/s (SD)</td>
<td>0.70 (0.22)</td>
<td>0.77 (0.26)</td>
<td>0.72(0.21)</td>
</tr>
<tr>
<td>e’ septal, cm/s (SD)</td>
<td>7.5 (2.6)</td>
<td>5.9 (2.1)</td>
<td>5.7 (2.1)</td>
</tr>
<tr>
<td>E/e’ ratio (SD)</td>
<td>10.6 (4.5)</td>
<td>13.0 (6.3)</td>
<td>12.7 (6.1)</td>
</tr>
<tr>
<td>Tricuspid regurgitant pressure (TRp), mmHg (SD)</td>
<td>34 (21)</td>
<td>44 (25)</td>
<td>50 (26)</td>
</tr>
<tr>
<td>Right atrium, area, cm2 (SD)</td>
<td>17 (6)</td>
<td>19 (7)</td>
<td>21 (8)</td>
</tr>
<tr>
<td>Fractional area change (FAC), % (SD)</td>
<td>39 (10)</td>
<td>35 (10)</td>
<td>32 (11)</td>
</tr>
<tr>
<td>Pericardial effusion, no (%)</td>
<td>42 (13)</td>
<td>22 (22)</td>
<td>9 (19)</td>
</tr>
</tbody>
</table>

Table 2: Univariable and multivariable cox regression analyses associated with death

<table>
<thead>
<tr>
<th></th>
<th>Univariable</th>
<th>Multivariable</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>2.09</td>
<td>1.49-2.94</td>
</tr>
<tr>
<td>Left atrium, area</td>
<td>1.05</td>
<td>1.01-1.05</td>
</tr>
<tr>
<td>TAPSE</td>
<td>0.29</td>
<td>0.19-0.45</td>
</tr>
<tr>
<td>Right ventricular strain</td>
<td>0.93</td>
<td>0.89-0.98</td>
</tr>
<tr>
<td>Right atrium, area</td>
<td>1.08</td>
<td>1.05-1.12</td>
</tr>
<tr>
<td>TRp</td>
<td>1.02</td>
<td>1.01-1.03</td>
</tr>
</tbody>
</table>
Table 3: Univariable and multivariable cox regression analyses (adjusted for age and gender) associated with PAH progression

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariable</th>
<th></th>
<th></th>
<th></th>
<th>Multivariable</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR</td>
<td>95% CI</td>
<td>p-value</td>
<td>HR</td>
<td>95% CI</td>
<td>p-value</td>
<td>HR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>2.9</td>
<td>1.76-4.69</td>
<td>&lt;0.001</td>
<td>3.2</td>
<td>1.83-5.55</td>
<td>&lt;0.001</td>
<td>3.2</td>
<td>1.83-5.55</td>
</tr>
<tr>
<td>TAPSE</td>
<td>0.17</td>
<td>0.09-0.34</td>
<td>&lt;0.001</td>
<td>0.24</td>
<td>0.12-0.47</td>
<td>&lt;0.001</td>
<td>0.24</td>
<td>0.12-0.47</td>
</tr>
<tr>
<td>Right ventricular strain</td>
<td>0.89</td>
<td>0.85-0.95</td>
<td>0.001</td>
<td>0.89</td>
<td>0.84-0.95</td>
<td>&lt;0.001</td>
<td>0.90</td>
<td>0.85-0.95</td>
</tr>
<tr>
<td>Right atrium, area</td>
<td>1.17</td>
<td>1.11-1.22</td>
<td>&lt;0.001</td>
<td>1.14</td>
<td>1.08-1.20</td>
<td>&lt;0.001</td>
<td>1.14</td>
<td>1.08-1.20</td>
</tr>
<tr>
<td>FAC</td>
<td>0.93</td>
<td>0.89-0.96</td>
<td>&lt;0.001</td>
<td>0.94</td>
<td>0.90-0.97</td>
<td>0.001</td>
<td>0.94</td>
<td>0.90-0.97</td>
</tr>
</tbody>
</table>

Disclosure: A. Heiervang Tennøe, None; A. M. Hoffmann-Vold, None; O. Molberg, None; H. Fretheim, None; T. Garen, None; E. Gude, None; A. K. Andreassen, None; K. Murbræch, None; S. Aakhus, None; J. Andreassen, None; O. Midtvedt, None.


Abstract Number: 745

An International Qualitative Research Study Exploring the Patient Experience of Raynaud’s Phenomenon in Systemic Sclerosis

John D. Pauling1,2, Robyn T. Domsic3, Lesley Ann Saketkoo4, Celia Almeida5, Tracy M. Frech6, Francesca Ingegnoli7, Jane Withey8, Hilary Jay8, Emma Dures9, Joanna Robson10, Neil J. McHugh11,12, Ariane L. Herrick13,14, Marco Maucci-Cerinic15, Dinesh Khanna16 and Sarah Hewlett17, 1Department of Pharmacy and Pharmacology, University of Bath, Bath, United Kingdom, 2Department of Rheumatology, Royal National Hospital for Rheumatic Diseases, Bath, United Kingdom, 3Medicine - Rheumatology, University of Pittsburgh, Pittsburgh, PA, 4Tulane, New Orleans, LA, 5HAS - Nursing and Midwifery, University of the West of England, Bristol, United Kingdom, 6Division of Rheumatology, University of Utah, Salt Lake City, UT, 7Dept. of clinical and community science, Rheumatology, Istituto G. Pini, University of Milan, Milano, Italy, 8Patient Research Partner, Bath, United Kingdom, 9Academic Rheumatology, Bristol, University of the West of England, Bristol, Bristol, United Kingdom, 10Rheumatology, University of the West of England (UWE Bristol), Bristol, United Kingdom, 11Rheumatology, Royal National Hospital for Rheumatic Diseases, Bath, United Kingdom, 12Department of Pharmacy and Pharmacology, The University of Bath, Bath, United Kingdom, 13Centre for Musculoskeletal Research, University of Manchester, MAHSC, Salford Royal Hospital, Manchester, United Kingdom, 14School of Translational Medicine, University of Manchester, Manchester Academic Health Science Centre, Manchester, United Kingdom, 15Dept of Medicine/Div of Rheum, University of Florence, Florence, Italy, 16Department of Medicine, University of Michigan Scleroderma Program, Ann Arbor, MI, 17UWE Academic Rheumatology, University of West of England, Bristol, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster I
Background/Purpose:

Raynaud’s phenomenon (RP) is consistently ranked highest in patient surveys exploring the frequency and impact of disease related manifestations of systemic sclerosis (SSc). SSc-RP is an episodic phenomenon and not easily assessed in the clinical setting. A thorough understanding of the patient experience of SSc-RP is essential if severity and impact are to be captured using patient-reported outcome (PRO) instruments. We report the findings of an international qualitative research study to investigate the patient experience of SSc-RP.

Methods:

Focus groups (FGs) comprising patients with SSc-RP (fulfilling 2013 ACR/EULAR classification criteria) were conducted across 3 scleroderma centers in the United States and United Kingdom, using a topic guide devised by a steering committee comprising qualitative researchers, SSc patients and SSc experts. Participants were enrolled according to an a priori purposive sampling framework ensuring we sought the views of a diverse (geographic, cultural and ethnic) and representative (disease subtype, disease duration, gender and history of digital ulcer disease) cohort of SSc patients. FGs were audio recorded, transcribed, anonymised and analysed using inductive thematic analysis. Additional FGs were conducted until thematic saturation was achieved.

Results:

Forty SSc patients participated in 6 focus groups conducted in Bath (n=2), New Orleans (n=3) and Pittsburgh (n=1). The participant demographics are presented (Table). The patient experience of SSc-RP can be described according to 7 major inter-related themes comprising; physical symptoms, emotional impact, triggers & exacerbating factors, constant vigilance & self-management, impact on daily life, uncertainty and adaptation. A conceptual map demonstrating the inter-relationship of the 7 themes is presented (Figure).

Conclusion:

This is the first qualitative study to explore the patient experience of SSc-RP. The multi-center design and purposive sampling framework ensured experiences were obtained from a diverse and representative SSc cohort. SSc-RP comprises a complex interplay of experiences that result in significant physical/emotional distress, disability and altered social participation which adversely affects health-related quality of life. The themes (and subthemes) identified herein are not captured using existing PRO instruments for assessing SSc-RP. Work to develop a novel PRO instrument for assessing the severity and impact of SSc-RP, comprising domains/items grounded in the patient experience of SSc-RP identified in this work is now underway.
**Demographics and clinical feature of enrolled patients presented according to purposive sampling framework**

<table>
<thead>
<tr>
<th>Total number of participants:</th>
<th>40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease subtype:</td>
<td></td>
</tr>
<tr>
<td>limited</td>
<td>24</td>
</tr>
<tr>
<td>diffuse</td>
<td>16</td>
</tr>
<tr>
<td>Sex:</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>34</td>
</tr>
<tr>
<td>Male</td>
<td>6</td>
</tr>
<tr>
<td>Ethnicity:</td>
<td></td>
</tr>
<tr>
<td>White/Caucasian</td>
<td>26</td>
</tr>
<tr>
<td>Black/African-American</td>
<td>12</td>
</tr>
<tr>
<td>Hispanic</td>
<td>2</td>
</tr>
<tr>
<td>Disease duration (time since 1st non-Raynaud’s symptom)</td>
<td></td>
</tr>
<tr>
<td>≥3 years</td>
<td>34</td>
</tr>
<tr>
<td>&lt;3 years</td>
<td>6</td>
</tr>
<tr>
<td>History of DU disease:</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>23</td>
</tr>
<tr>
<td>No</td>
<td>17</td>
</tr>
</tbody>
</table>

**Disclosure:** J. D. Pauling, Actelion Pharmaceuticals UK, 2; Actelion Pharmaceuticals UK, 5; R. T. Domsic, None; L. A. Saketkoo, None; C. Almeida, None; T. M. Frech, None; F. Ingegnoli, None; J. Withey, None; H. Jay, None; E. Dures, None; J. Robson, None; N. J. McHugh, None; A. L. Herrick, None; M. Matucci-Cerinic, None; D. Khanna, Actelion, Bayer, BoehringerIngelheim, Chemomab, Corbus, Covis, Cytori, Eicos, EMD Serono, Genentech/Roche, Gilead, GSK, Sanofi-Aventis, UCB Pharma, 5; NIH/NIAMS, NIH/NIAID, Bayer, BMS, Genentech/Roche, Pfizer, 2; Eicos, 4; S. Hewlett, None.


**Abstract Number:** 746
Comparison of Disease Characteristics in Patients with Juvenile-Onset and Adult-Onset Progressive Systemic Sclerosis

Guzin Karatemiz1, Amra Adrovic2, Sinem Nihal Esatoglu1, Sezgin Sahin2, Kenan Barut2, Gulen Hatemi1, Vedat Hamuryuden1, Ozgur Kasapcoper2 and Emire Seyahi1, 1Istanbul University, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey, 2Pediatric Rheumatology, Istanbul University, Cerrahpasa Medical School, Department of Pediatric Rheumatology, Istanbul, Turkey

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Progressive systemic sclerosis (PSSc) has been known to affect mainly adults of 30-50 years of age. Juvenile-onset has been reported to be rare and studies comparing clinical differences between juvenile-onset and adult onset form have been limited (1). One study from North America revealed that there is more skeletal muscle involvement, more severe cardiac disease, whereas improved survival compared with adult onset pSSc cases (1). Recently, one multicenter European study revealed that juvenile-onset PSSc showed scleroderma pattern on the capilleroscopy more frequently than that observed in adult-onset pSSc (2). As there would be also effects of ethnic differences, we aimed to assess clinical differences between the two forms of pSSc of pediatric and adult rheumatology centers of a tertiary center, in Turkey.

Methods: Adult onset patients were defined as those who were registered and followed as ‘scleroderma’ at the departments of adult and pediatric rheumatology at Cerrahpasa Medical Faculty, Istanbul, between 2005 and 2017. Only those with at least 2 follow-up visits were included in the study. Patients’s charts were re-evaluated retrospectively for demographic and clinic characteristics.

Results: There were 140 patients with scleroderma diagnosis in the adult outpatient clinic records, and 51 in the pediatric clinic records. Of these patients, 3 adults and 25 (49 %) pediatric patients had localized scleroderma (p<0.001). We studied the remaining patients (adults: n=137, juvenile: n =26) who had systemic pattern.

As shown in Table, male/female ratio, median follow-up duration, familial history of chronic inflammatory diseases and the frequency of sclerodactyly, digital ulcers, Raynaud phenomenon, arrhythmia/heart failure and gastrointestinal involvement were similar between juvenile and adult onset groups. The frequency of interstitial lung disease, pulmonary artery hypertension, and serum ANA positivity were significantly more common in the adult onset group. Whereas, joint and muscle involvements were significantly more common among juvenile onset patients. DMARD use was significantly more common in the juvenile group, on the other hand, the use of vasodilators was more frequent among adults.

Conclusion: Our results are online with previous reports: juvenile onset patients seem to have a milder form of disease. Major organ involvement as defined interstitial lung disease and pulmonary artery hypertension was more common among adult onset patients. On the other hand, as expected, joint involvement and myopathy were major causes of morbidity in the juvenile group. Contrary to that previously reported, cardiac involvement was not common in the juvenile group.

References:

Table. Demographic and clinic characteristics of the patients
<table>
<thead>
<tr>
<th></th>
<th>Adult onset (n= 137)</th>
<th>Juvenile onset (n = 26)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at disease onset, mean± SD</td>
<td>38.6 ± 13.4</td>
<td>10.1 ± 4.3</td>
<td>-</td>
</tr>
<tr>
<td>Age at diagnosis, mean± SD</td>
<td>43.6 ± 14.0</td>
<td>11.4 ± 3.2</td>
<td>-</td>
</tr>
<tr>
<td>Follow-up duration, med. [IQR], years</td>
<td>5 [2.0-7.0]</td>
<td>4 [2.5-6.0]</td>
<td>NS</td>
</tr>
<tr>
<td>Male/Female</td>
<td>20/117</td>
<td>2/24</td>
<td>NS</td>
</tr>
<tr>
<td>Familial history of chronic inflammatory diseases, n (%)</td>
<td>20 (14.6)</td>
<td>4 (15.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Sclerodactyly, n (%)</td>
<td>128 (93.4)</td>
<td>25 (96.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Raynaud phenomenon, n (%)</td>
<td>135 (98.5)</td>
<td>24 (92.3)</td>
<td>NS</td>
</tr>
<tr>
<td>Digital ulcers, n (%)</td>
<td>55 (41.4)</td>
<td>14 (54.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>Interstitial lung disease, n (%)</td>
<td>71 (52.2)</td>
<td>6 (24.0)</td>
<td>0.009</td>
</tr>
<tr>
<td>PAH, n (%)</td>
<td>20 (14.9)</td>
<td>0</td>
<td>0.045</td>
</tr>
<tr>
<td>Arrhythmia/heart failure, n (%)</td>
<td>14 (10.4)</td>
<td>1 (4.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Joint involvement, n (%)</td>
<td>20 (14.9)</td>
<td>13 (50.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Skeletal muscle involvement/myopathy n (%)</td>
<td>10 (7.5)</td>
<td>7 (28.0)</td>
<td>0.002</td>
</tr>
<tr>
<td>Gastrointestinal system involvement, n (%)</td>
<td>42 (31.8)</td>
<td>8 (32.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Arterial hypertension, n (%)</td>
<td>24 (18.2)</td>
<td>0</td>
<td>0.015</td>
</tr>
<tr>
<td>ANA positivity, n (%)</td>
<td>119 (93.0)</td>
<td>18 (75.0)</td>
<td>0.007</td>
</tr>
<tr>
<td>DMARD use, n (%)</td>
<td>90 (65.7)</td>
<td>25 (96.2)</td>
<td>0.002</td>
</tr>
<tr>
<td>Vasodilators, n (%)</td>
<td>113 (82.5)</td>
<td>13 (50.0)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Disclosure:** G. Karatemiz, None; A. Adrovic, None; S. N. Esatoglu, None; S. Sahin, None; K. Barut, None; G. Hatemi, None; V. Hamuryudan, None; O. Kasapcopur, None; E. Seyahi, None.


**Abstract Number:** 747

**Autoantibodies to Rpp25 (Th/To) Are Specific Markers for Systemic Sclerosis and Are Associated with Limited Cutaneous Disease and Young Age at Disease Onset**

Boyang Zheng¹, Martial Koenig², Marychel Tiongson³, Andrea Seaman³, Danilo Villalta⁴, Gabriella Morozzi⁵, Nicola Bizzaro⁶, Gabriella Pucci⁷, Michaelin Richards³ and Michael Mahler³, ¹Division of Internal Medicine, Centre Hospitalier de l'Université de Montréal (CHUM), Montreal, QC, Canada, ²Internal Medicine, Hôpital Notre-Dame du CHUM, Montréal, QC, Canada, ³Research and Development, Inova Diagnostics, San Diego, CA, ⁴Allergologia e Immunologia Clinica, AO S. Maria degli Angeli, Pordenone, Pordenone, Italy, ⁵Chirurgiche e Neuroscienze, Sezione di Reumatologia, Università di Siena, Dipartimento Scienze Mediche, Siena, Italy, ⁶Ospedale San Antonio, Tolmezzo, Italy, ⁷Chirurgiche e Neuroscienze, Sezione di Reumatologia, Università di Siena, Siena, Italy

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster I

**Session Type:** ACR Poster Session A
Autoantibodies to Rpp25 (Th/To) are specific markers for systemic sclerosis and are associated with limited cutaneous disease and young age at disease onset [MM1]

Boyang Zheng⁴, Martial Koenig⁴, Michael Mahler¹,

¹ Inova Diagnostics, INC.  San Diego, CA, USA;
² Department of Medicine, McGill University, Montreal, Quebec, Canada

Background/Purpose:
Antinuclear antibodies (ANA), present in 80-90% of systemic sclerosis (SSc) patients, are important for disease diagnosis. Of particular utility are those with SSc-specific and SSc-associated antibodies, including anti Th/To amongst others (i.e. antibodies to centromere, Scl-70, RNA Pol-III, PM/Scl, Ro52/TRIM21 and U1RNP). However, in a significant minority of ANA positive SSc patients, no fine specificities are detected using conventional diagnostic protocols. Recently, it was found that anti-Rpp25 antibodies are an important autoantigenic component of the Th/To complex. However, no FDA cleared assay is available for the detection of anti-Th/To antibodies. Consequently, the present study aimed to analyze a large well characterized Canadian SSc patient cohort in comparison to other disease control groups for antibodies to Rpp25 in a standardized assay.

Methods:
Sera from 320 Canadian SSc patients [48 diffuse cutaneous (dc) SSc, 223 limited cutaneous (lc) SSc and 49 sine SSc] and various disease controls (n=889) were tested for anti-Rpp25 antibodies by a bead based immunoassay (research use only, Inova Diagnostics, US).

Results:
Anti-Th/To antibodies were significantly more common and present in higher titers in SSc patients compared to all controls (p<0.05). The prevalence in SSc and in the different control groups is summarized in the figure below.

![Receiver operating characteristic (ROC) analysis showed an area under the curve of 0.70 (95% Confidence interval 0.67-0.73). The sensitivity and specificity for SSc was 9.7% (95% CI 6.9-13.4%) and 99.0% (95% CI 98.1-99.5%), respectively. The odds ratio for SSc was 10.6 (95% CI 5.1-22.3). Anti-Rpp25 antibodies were present in 0/48 dcSSc (0.0%), in 27/223 lcSSc (12.1%) and in 4/49 (8.2%) sine SSc patients. The difference between lcSSc and dcSSc was significant (p=0.01). In addition, anti-Rpp25 antibodies were associated with a younger age at SSc disease onset (34.3 vs. 39.8 years; p=0.048).](attachment:figure.png)

Conclusion:
Autoantibodies to Rpp25 as part of the Th/To autoantigen show high specificity for SSc and define a subset of SSc with lcSSc and younger age of disease onset.
Abstract Number: 748

Scleromyxedema Phenotype Pre- and Post-Treatment with Intravenous Immunoglobulin

Christopher A. Mecoli¹, Andrea Fava², Francesco Boin³ and Laura K. Hummers⁴, ¹Rheumatology, Johns Hopkins University, Baltimore, MD, ²Johns Hopkins University, Baltimore, MD, ³Rheumatology, University California, San Francisco, San Francisco, CA, ⁴Medical and Rheumatology, Johns Hopkins University, Baltimore, MD

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Scleromyxedema is a rare scleroderma mimic that often responds to intravenous immunoglobulin therapy (IVIG). The clinical and biochemical changes in response to treatment have not been well-characterized.

Methods: 15 patients with scleromyxedema were recruited for the study. Clinical information and blood samples were obtained immediately before and again 2-3 weeks after receiving IVIG therapy. Clinical information included the modified modified Rodnan Skin Score (MMRSS) which includes assessing the patients’ back and ears, and visual analog scales to assess patients’ pain, itch, flexibility, and softness of their skin. In addition, Health Assessment Questionnaire Disability Index (HAQ-DI) and percent body surface area involved were recorded.

Results: Demographic data and disease characteristics can be found in Table 1. Twelve of the 15 patients were receiving maintenance IVIG, and three were treatment-naïve. All patients except for one had a monoclonal gammopathy of undetermined significance (MGUS), 12 of which were IgG lambda, and two were IgG kappa.

Post-treatment, the average MMRSS decreased from 13.6 to 10.3 (p=0.003). Skin flexibility, skin softening and skin global all improved as assessed using visual analog scales, and were statistically significant (Table 2). Correlation studies demonstrated that the MMRSS correlated with the Health Assessment Questionnaire-Disability Index (HAQ-DI) R=0.47, p=0.009). The three treatment-naïve patients had a larger improvement (mean MMRSS 20 ± 5.1 to 13.3 ± 4.7 compared to patients receiving maintenance IVIG, 11.9 ± 10 to 9.5 ± 8).

The two patients with a history of neurologic complications relating to scleromyxedema had a markedly lower MMRSS of 1 ± 0.8 compared to patients without neurologic complications, 13.6 ± 8.3, p=0.006. Patients with lambda IgG MGUS had a higher MMRSS compared to those with kappa IgG or no MGUS, 13.3 ± 9.8 compared to 7.8 ± 5.2, p=0.22.

Conclusion: Patients with scleromyxedema have clinical improvement to IVIG in several domains, and the extent of skin involvement correlates with their HAQ-DI. Patients with a history of neurologic complications of scleromyxedema or non-IgG lambda MGUS have lower skin scores.
Demographic Data

<table>
<thead>
<tr>
<th></th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>12 (80)</td>
</tr>
<tr>
<td>Age (mean ± SD)</td>
<td>53 ± 11</td>
</tr>
<tr>
<td>Caucasian</td>
<td>14 (93)</td>
</tr>
<tr>
<td>Neurologic involvement</td>
<td>2 (13)</td>
</tr>
<tr>
<td>IgG MGUS</td>
<td>14 (93)</td>
</tr>
<tr>
<td>Lambda</td>
<td>12</td>
</tr>
<tr>
<td>Kappa</td>
<td>2</td>
</tr>
<tr>
<td>Treatment naïve</td>
<td>3 (20)</td>
</tr>
</tbody>
</table>

Table 1

<table>
<thead>
<tr>
<th>Clinical Parameters</th>
<th>Pre-IVIG (mean)</th>
<th>Post-IVIG (mean)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician Global Assessment</td>
<td>1.40</td>
<td>1.10</td>
<td>0.100</td>
</tr>
<tr>
<td>Body Surface Area (%)</td>
<td>36.20</td>
<td>25.40</td>
<td>0.090</td>
</tr>
<tr>
<td>MMRRSS (0-60)</td>
<td>13.60</td>
<td>10.30</td>
<td><strong>0.003</strong></td>
</tr>
<tr>
<td>Skin scale pain (0-100)</td>
<td>17.70</td>
<td>13.70</td>
<td>0.250</td>
</tr>
<tr>
<td>Skin scale itch (0-100)</td>
<td>2.10</td>
<td>2.10</td>
<td>1.000</td>
</tr>
<tr>
<td>Skin scale flexibility (0-100), 0=Best</td>
<td>54.00</td>
<td>32.00</td>
<td><strong>0.013</strong></td>
</tr>
<tr>
<td>Skin scale softening (0-100), 0=Best</td>
<td>46.00</td>
<td>26.00</td>
<td><strong>0.022</strong></td>
</tr>
<tr>
<td>Skin scale global (0-100)</td>
<td>45.00</td>
<td>27.00</td>
<td><strong>0.029</strong></td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>0.62</td>
<td>0.54</td>
<td>0.400</td>
</tr>
</tbody>
</table>

Table 2

Disclosure: C. A. Mecoli, None; A. Fava, None; F. Boin, None; L. K. Hummers, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/scleromyxedema-phenotype-pre-and-post-treatment-with-intravenous-immunoglobulin

Abstract Number: 749

Treatment with Cyclophosphamide for Systemic Sclerosis-Interstitial Lung Disease Does Not Lead to a Sustained Improvement in Lung Function in Two Independent Cohorts

Elizabeth R. Volkmann1, Donald P. Tashkin1, Myung Sim1, Ning Li2, Dinesh Khanna3, Michael Roth4, Philip J. Clements4, Anna-Maria Hoffmann-Vold5, Daniel E. Furst1, Grace Kim6, Jonathan Goldin1 and Robert Elashoff7,

1University of California, Los Angeles, David Geffen School of Medicine, Los Angeles, CA, 2Biomathematics, University of California, Los Angeles, Los Angeles, CA, 3University of Michigan, Ann Arbor, MI, 4Medicine, University of California, Los Angeles, Los Angeles, CA, 5Oslo University Hospital, Oslo, Norway,
Radiology, University of California, Los Angeles, David Geffen School of Medicine, Los Angeles, CA, University of California, Los Angeles, Los Angeles, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Compared with placebo, treatment with cyclophosphamide (CYC) improved lung function in patients with systemic sclerosis-related interstitial lung disease (SSc-ILD) after 1 year in Scleroderma Lung Study (SLS) I. However, the effects of CYC waned after monitoring patients for an additional year off therapy. In SLS II (comparing CYC and mycophenolate [MMF]), treatment with 1-year of CYC appeared to have a more sustained effect on lung function over 2-years, although SLS II used a different analysis approach than SLS I. To further understand the effects of CYC on SSc-ILD outcomes, the present analysis directly compared outcomes between the CYC arms of SLS I and II.

Methods: Participants enrolled in the CYC arms of SLS I (N=79) and II (N=73) were included. SLS I and II randomized participants to oral CYC for 1 year and followed patients for an additional year off therapy (In SLS II, patients received placebo in the second year). Eligibility criteria for SLS I and II were nearly identical. Outcomes included the FVC%-predicted and DLCO%-predicted (measured every 3 months) and quantitative radiographic extent of ILD (QILD) (measured at 1 and 2 years for SLS I and SLS II, respectively). Joint models were created to evaluate the treatment effect on the course of the FVC/DLCO over 2-years while controlling for baseline disease severity.

Results: SLS II-CYC participants had similar baseline characteristics compared with SLS I-CYC participants in terms of gender (75% vs. 77% female), disease duration (mean [SD] years: 2.6 [1.8] vs. 3.1 [2.3]), and FVC%-predicted (mean [SD]: 66.9 [9.9] vs. 67.6 [11.4]), respectively. SLS II-CYC patients were slightly older (mean [SD] years: 52.2 [9.6] vs. 48.4 [12.2]; P=0.037) and had a higher DLCO%-predicted (mean [SD]: 54.5 [14.6] vs. 47.2 [13.9]; P=0.0002) than SLS I-CYC participants. After adjusting for baseline QILD and FVC%-predicted, there was no difference in the course of the FVC%-predicted between the CYC arms of SLS I and II (P=0.555), nor the DLCO%-predicted (P=0.172). In both groups, treatment with CYC led to a significant improvement in the FVC%-predicted from 3-12 months, but no significant improvement beyond this point (Figure 1). Treatment with CYC had no effect on the DLCO for either group.

Conclusion: Although there are limitations in comparing participants from two trials, the baseline characteristics of the SLS I and SLS II participants were relatively similar. Treatment with 1 year of oral CYC led to similar improvements in lung function in both SLS I and II, although the effects were not sustained following CYC cessation. There results suggest that increasing the duration of ILD therapy may improve outcomes for SSc-ILD patients.

References:
Disclosure: E. R. Volkmann, None; D. P. Tashkin, None; M. Sim, None; N. Li, None; D. Khanna, Actelion, Bayer, BoehringerIngelheim, Chemomab, Corbus, Covis, Cytori,Eicos, EMD Serono, Genentech/Roche, Gilead, GSK, Sanofi-Aventis,UCB Pharma, 5,NIH/NIAMS, NIH/NIAID,Bayer, BMS, Genentech/Roche, Pfizer, 2,Eicos, 4; M. Roth, None; P. J. Clements, None; A. M. Hoffmann-Vold, None; D. E. Furst, None; G. Kim, None; J. Goldin, None; R. Elashoff, None.


Abstract Number: 750

Diltiazem Gel As a New Local Treatment for Scleroderma Digital Ulcers

Mohammad Ali Nazarinia1, Elmira Esmaeilzadeh2 and Saeedeh Shenavandeh2, 1Shiraz Geriatric Research Center, Shiraz University of Medical Sciences, Shiraz, Iran, Shiraz, Iran (Islamic Republic of), 2Department of Internal Medicine, Division of Rheumatology, Shiraz University of Medical Sciences, Shiraz, Iran., Shiraz, Iran (Islamic Republic of)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Assessing the effect of Diltiazem gel on healing process of scleroderma digital ulcers and comparing its effect with Nitroglycerin ointment and placebo.

Methods: Ninety scleroderma patients divided to three groups underwent a single blind randomized clinical trial. Experimental group 1 received Diltazem gel 2%, experimental group 2 received Nitroglycerin ointment 2% and control group received Vaseline as placebo. All interventions were applied 2 times per day for 8 weeks. The mean of maximum diameters of the ulcers was measured for each patient at the beginning and at the end of the study. The site of the ulcers and the number of new ones were, also, determined for each patient.

Results:
The mean diameter of the ulcers at the end of the study was significantly lower in three studied groups compared to the beginning of the study (Diltiazem P<0.001, Nitroglycerin P= 0.002 and Control P= 0.027). However, the difference in size of the ulcers was significantly higher in diltiazem group compared to nitroglycerin and placebo (P= 0.04), especially, in ulcers at distal part of digits (P=0.32). In addition, number of new ulcers did not differ significantly between three groups. Moreover, nitroglycerin ointment (42%) was found to induce more complications for patients compared to Diltiazem gel (28%) and placebo (28%).

**Conclusion:** Diltiazem gel can be an effective topical therapy with lower complications for treating scleroderma digital ulcers compared to nitroglycerin ointment and placebo.

**Disclosure:** M. A. Nazarinia, None; E. Esmaeilzadeh, None; S. Shenavandeh, None.

**Abstract Number: 751**

**Effect of Probiotics on the Gastrointestinal Symptoms and Immune Parameters in Patients with Systemic Sclerosis: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial**

Thais Marighela1, Maria Izabel Arismendi1, Milena Brunialti2 and Cristiane Kayser1, 1Rheumatology Division, Universidade Federal de São Paulo, São Paulo, Brazil, 2Division of Infectious Diseases, Universidade Federal de São Paulo, São Paulo, Brazil

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Abnormalities in the intestinal microbiota have been associated with several autoimmune diseases, including systemic sclerosis (SSc). Recent studies have demonstrated the potential of probiotics in modulating the microbioma and the immune responses in several autoimmune diseases. T cell abnormalities including a predominant T helper type 2 (Th2) profile and increased levels of Th17 cells have been implicated in the pathogenesis of SSc. The objective of this study was to evaluate the effects of probiotics on the gastrointestinal (GI) symptoms and immune parameters in patients with SSc.

**Methods:**

In this double-blind, placebo-controlled, randomized clinical trial 73 patients with SSc (EULAR/ACR criteria from 2013) with a moderate-to-severe total score (0.5–3.00) on the University of California Los Angeles Scleroderma Clinical Trial Consortium Gastrointestinal Tract Instrument 2.0 (UCLA GIT 2.0) were randomized to receive probiotics (1 capsule/day of *Lactobacillus paracasei, L. rhamnosus, L. acidophilus* and *Bifidobacterium lactis*, 10^9 colony-forming units per capsule) or placebo (identical capsules containing maltodextrin) for 8 weeks. The primary outcome measurement was improvement in the UCLA GIT 2.0 total score after 8 weeks of treatment. Secondary outcomes included changes in Th1, Th2, Th17 and regulatory T cells serum levels, immunoglobulin A (IgA), scleroderma Health Assessment Questionnaire (SHAQ) score, anthropometric parameters, and dietary intake. The frequencies of Th1 (CD3^+CD8^-IFN-γ^+), Th2 (CD3^+CD8^-IL4^+), Th17 (CD3^+CD8^-IL17^+) and regulatory T (CD3^+CD4^+CD25^+Foxp3^+) cells in peripheral blood were measured using flow
cytometry. Clinical and immune parameters were assessed at baseline (T0), after four (T4) and eight weeks (T8) of treatment. The trial was registered on ClinicalTrials.com under the identifier NCT 02302352.

Results:

Thirty-seven patients were randomized to probiotics (mean age 47.7 years) and 36 (mean age 46.1 years) to the placebo group. After 8 weeks, there was a significant improvement in UCLA GIT 2.0 total score in both groups (p<0.001), but changes were not different between the two groups (p=0.934). The probiotic group presented a significant decrease in the serum percentage of Th2 (from 2.2% in T0 to 1.5% in T8) and Th17 (from 2.0% in T0 to 1.4% in T8) cells compared with the placebo group (from 2.3% in T0 to 2.5% in T8 for Th2; from 1.9% in T0 to 1.9% in T8 for Th17 cells) (p=0.038, p=0.04; respectively). No significant changes were observed in percentages of Th1 and Treg cells, IgA serum levels, SHAQ score, anthropometric parameters, and dietary intake after treatment between the two groups. No serious adverse events were reported.

Conclusion:

In this first randomized, double-blind trial evaluating the effects of probiotics in SSc, there was no reduction in the GI symptoms with probiotic supplementation compared with placebo. Nonetheless, probiotics showed to reduced the peripheral percentages of Th2 and Th17 cells in patients with SSc. These results indicate that probiotics have immunomodulatory effects and anti-inflammatory properties and might represent an innovative therapeutic approach to SSc patients.

Disclosure: T. Marighela, None; M. I. Arismendi, None; M. Brunialti, None; C. Kayser, None.

Role of the Six-Minute Walk Test in Systemic Sclerosis: Five Years Evolution

Els Vandecasteele1, Karin Melsens2, Filip De Keyser3, Michel De Pauw4, Ellen Deschepper5, Saskia Decuman6, Yves Piette2, Kristof Thevissen7, Guy Brusselle8 and Vanessa Smith3, 1Dep of Cardiology, University Hospital Ghent, Ghent, Belgium, 2Ghent University Hospital, Department of Rheumatology, Ghent, Belgium, Ghent, Belgium, 3Ghent University, Department of Internal Medicine, Ghent, Belgium, Ghent, Belgium, 4Dep of cardiology, University Hospital Ghent, Ghent, Belgium, 5Biostatistics Unit, UGent, Ghent, Belgium, 6Department of Internal Medicine, Ghent University, Ghent, Belgium, 7University Hospital Ghent, Ghent, Belgium, 8Gent University, Gent, Belgium

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Title
Role of the Six-Minute Walk Test in Systemic Sclerosis: five years evolution.

Background/Purpose: Interstitial lung disease (ILD) and pulmonary arterial hypertension (PAH) are the leading causes of death in Systemic Sclerosis (SSc) patients. Although the six-minute walk test (6MWT) is used for evaluating ILD and PAH in clinical practice, no data are available on the natural evolution of the six-minute walk distance (6MWD) in SSc patients without ILD and PAH.

Methods: Prospectively collected data of the first 6MWT (at baseline or at 6-month follow-up) and the 6MWTs at 18-, 30-, 42-, 54-, and 66-month visit of 165 consecutive SSc patients without ILD and PAH, included in the Ghent University Systemic Sclerosis Cohort between May 2006 and December 2016 were analysed.

Results: The mean 6MWD during the baseline 6MWT of 165 SSc patients without ILD and PAH (35% limited SSc, 56% limited cutaneous SSc, 9% diffuse cutaneous SSc) was 484.20+/-92.65m with no significant difference in the distance walked at different follow-up visits as compared to baseline. 96-100% of the SSc patients without ILD and PAH performed a 6MWT during the different follow-up visits.

Conclusion: In SSc without ILD and PAH, the 6MWT is feasible and the 6MWD is clinically stable over a 66 months period. A 6MWT performed at the time of SSc diagnosis may be used as a reference 6MWD for those SSc patients who develop ILD or PAH during follow-up.

Table 1. Baseline characteristics of 165 SSc without ILD and PAH.
Characteristic       N  
Age (years) °       165 48.02±13.19
♀/♂ *              165 124/41 (75.2/24.8)
Raynaud *           165 162 (98.2)
Disease duration since first Raynaud (months)#       162 60 (20-176)
Disease duration since first non-Raynaud (months)#       137 26 (10-74)
LSSc/LcSSc/DcSSc *           165 58/92/15 (35.2/55.8/9.1)
mRSS #               165 3 (0-7)
DAS #                162 0.5 (0-1.5)
HAQ #                141 0.25 (0.00-0.63)
AntiScl70 AB *       165 16 (9.7)
ACA *                165 100 (60.6)
FVC (%pred) #        165 113 (99-126)
DLCO (%pred) #       165 77 (69-88)
Peak TVR (m/s) #     131 2.3 (2.1-2.4)
6MWD (m) °          165 484.20±92.65

Table 2. Evolution of the 6MWD from baseline to the different follow-up visits

<table>
<thead>
<tr>
<th></th>
<th>6MWT</th>
<th>N</th>
<th>N Tx</th>
<th>6MWD T0 (m)</th>
<th>6MWD Tx(m)</th>
<th>Pearson’s correlation(95%CI) (m)</th>
<th>Mean Difference (95%CI) (m)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0 vs</td>
<td>130</td>
<td>130</td>
<td>487.13±94.41487.95±96.30</td>
<td>0.817</td>
<td>0.82 (-9.19; 10.83)</td>
<td>0.871</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T18</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0 vs</td>
<td>98</td>
<td>101</td>
<td>490.62±90.31488.07±85.98</td>
<td>0.745</td>
<td>-2.55 (-15.20; 10.10)</td>
<td>0.690</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T30</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0 vs</td>
<td>77</td>
<td>80</td>
<td>481.56±95.56466.52±105.490.694</td>
<td>-15.04 (-33.01; 2.93)</td>
<td>0.100</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T42</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0 vs</td>
<td>65</td>
<td>68</td>
<td>480.79±97.47480.86±102.530.765</td>
<td>0.08 (-16.96; 17.12)</td>
<td>0.993</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T54</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0 vsT6646</td>
<td>46</td>
<td></td>
<td>480.37±90.25483.74±95.85</td>
<td>0.564</td>
<td>3.37 (-22.49; 29.23)</td>
<td>0.794</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

N 6MWT: number of patients performing a six-minute walk test, N Tx visit: number of patients having a follow-up visit at month x, 6MWD: six-minute walk distance, T0: baseline visit, Tx: x-month visit, m: meter, SD: standard deviation, CI: confidence interval

Disclosure: E. Vandecasteele, None; K. Melsens, None; F. De Keyser, None; M. De Pauw, None; E. Deschepper, None; S. Decuman, None; Y. Piette, None; K. Thevissen, None; G. Brusselle, None; V. Smith, Fund for Scientific Research Flanders, 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/role-of-the-six-minute-walk-test-in-systemic-sclerosis-five-years-evolution

Abstract Number: 753
The Histone Demethylase Jumonji Domain-Containing Protein 3 (JMJD3) As Central Mediator of Fibroblast Activation

Christina Bergmann¹, Amelie Brandt¹, Clara Dees², Yun Zhang³, Chih-Wei Chen⁴, Tatjana Mallano⁵, Thomas Wohlfahrt⁶, Ruifang Liang⁷, Rosebeth Kagwiria¹, Aline Bozec⁸, Ralf Rieker⁹, David Abraham¹⁰, Andreas Ramming¹¹, Oliver Distler¹², Georg Schett¹³ and Jörg Distler¹⁴, ¹Department of Internal Medicine 3 and Institute for Clinical Immunology, Friedrich-Alexander-University of Erlangen-Nuremberg and University Hospital Erlangen, Erlangen, Germany, ²Department of Internal Medicine 3 and Institute for Clinical Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Erlangen, Germany, ³Department of Internal Medicine 3 and Institute for Clinical Immunology, Department of Internal Medicine 3 and Institute for Clinical Immunology, Friedrich-Alexander-University of Erlangen-Nuremberg and University Hospital Erlangen, Erlangen, Germany, ⁴Department of Internal Medicine 3 – Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Erlangen, Germany, ⁵Department of Internal Medicine 3 – Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Erlangen, Germany, ⁶Department of Internal Medicine 3, Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Erlangen, Germany, ⁷Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, Department of Internal Medicine 3 and Institute for Clinical Immunology, Friedrich-Alexander-University Erlangen-Nuremberg and University Hospital Erlangen, Erlangen, Germany, ⁸Department Clinic of Medicine 3 - Immunology und Rheumatology, University of Erlangen-Nürnberg, Department Clinic of Medicine 3 - Immunology and Rheumatology, Erlangen, Germany, ⁹Department of Pathology, University Clinic Erlangen, Erlangen, Germany, ¹⁰Centre for Rheumatology and Connective Tissue, UCL School of Life and Medical Sciences, London, London, United Kingdom, ¹¹Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Erlangen, Germany, ¹²Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland, ¹³Department of Internal Medicine 3 – Rheumatology and Immunology, Department of Internal Medicine 3 and Institute for Clinical Immunology, Friedrich-Alexander-University of Erlangen-Nuremberg and University Hospital Erlangen, Erlangen, Germany, ¹⁴Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Erlangen, Germany

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster 1
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Epigenetic modifications are key drivers of chronic fibroblast activation. Trimethylation of histone 3 at lysine residue K27 (H3K27me3) is a repressive modification, that is implicated in fibroblasts activation. Inhibition of H3K27 trimethylation promotes fibroblast activation. However, the role of H3K27me3 demethylases in fibrosing disorders has not been characterized. The aim of this study is to characterize the role of JMJD3 in as potential drug target in fibrotic disease.

Methods:

siRNA mediated knockdown and GSKJ4 were used to target JMJD3 in vitro and in vivo. Fibroblast activation was analyzed by quantifying collagen synthesis and release, stress fiber formation and by scratch assays. The effects of GSKJ4 on experimental fibrosis were assessed in the Topoisomerase I-mouse model of skin and lung fibrosis and in Bleomycin-induced skin fibrosis. Inflammatory infiltrates in the skin were assessed by immunofluorescence staining. H3K27me3 of target genes was analyzed by ChIP.

Results: We demonstrated increased expression of JMJD3 in fibrotic diseases with increased expression of JMJD3 in the skin of SSc patients and in tissue from patients with liver fibrosis and idiopathic pulmonary fibrosis compared to healthy
controls. The overexpression was particularly pronounced in fibroblasts. JMJD3 was also overexpressed in dermal and pulmonary fibrosis in Topol-induced fibrosis and in bleomycin-induced skin fibrosis. Targeting JMJD3 in vitro ameliorated the activated fibroblast phenotype with decreased collagen release and reduced expression of myofibroblast markers. By screening for several profibrotic pathways, we identified FRA2 as central downstream mediator of JMJD3 mediated fibroblast activation. H3K27me3 at the FRA2 promoter was reduced by TGFβ stimulation, which resulted in increased expression of FRA2. Treatment with GSKJ4 prevented the TGFβ-induced downregulation of H3K27me3 at the FRA2 promoter. The functional importance of FRA2 for JMJD3 regulated fibroblast activation was further highlighted by knockdown studies: Upon knockdown of FRA2, GSKJ4 loses its inhibitory function on collagen secretion. In vivo, we observed potent antifibrotic effects of JMJD3 inhibition on dermal and pulmonary fibrosis with reduced fibrotic tissue remodeling, decreased collagen content and impaired differentiation of resting fibroblasts into myofibroblasts. As GSKJ4 treatment had no effect on B-cell counts in experimental fibrosis. However, GSKJ4 treatment resulted in a slight reduction of T-cell counts.

Conclusion:

We present first evidence for a dysregulation of JMJD3 in SSc. JMJD3 regulates fibroblast activation by modulating the levels of H3K27me3 at the FRA2 promoter. Targeted inhibition of JMJD3 reduces the aberrant activation of SSc fibroblasts and has strong antifibrotic effects in murine models of SSc.

Disclosure: C. Bergmann, None; A. Brandt, None; C. Dees, None; Y. Zhang, None; C. W. Chen, None; T. Mallano, None; T. Wohlfahrt, None; R. Liang, None; R. Kagwiria, None; A. Bozec, None; R. Rieker, None; D. Abraham, None; A. Ramming, None; O. Distler, 4D Science, Actelion, Active Biotec, Bayer, Biogen Idec, Boehringer Ingelheim Pharma, BMS, ChemomAb, EpiPharm, Ergonex, espeRare foundation, GSK, Roche-Genentech, Inventiva, Lilly, medac, MedImmune, Mitsubishi Tanabe, Pharmacyclics, Pfizer, Sanofi, Seroda, 2; G. Schett, None; J. Distler, 4D Science, 1, Anamar Medical, Active Biotec, Array Biopma, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, GSK, Novartis, Sanofi-Aventis, UCB, 2, Actelion Pharmaceuticals US, Active Biotech, Anamar, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi, UCB, 5.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-histone-demethylase-jumonji-domain-containing-protein-3-jmjd3-as-central-mediator-of-fibroblast-activation

Abstract Number: 754

**Interferon Siganture in Systemic Sclerosis Lung Microvascular Endothelial Cells**

Fabian A Mendoza\(^1\), Sonsoles Piera-Velazquez\(^2\), Peter J. Wermuth\(^3\), Sankar Addya\(^4\), Carol A. Feghali-Bostwick\(^5\) and Sergio A. Jimenez\(^6\), \(^1\)Rheumatology Division, Department of Medicine, Thomas Jefferson University, Jefferson Institute of Molecular Medicine and Scleroderma Center, Thomas Jefferson University, Philadelphia, PA, \(^2\)Jefferson Institute of Molecular Medicine and Scleroderma Center, Thomas Jefferson University, Philadelphia, PA, \(^3\)Jefferson Institute of Molecular Medicine, Division of Connective Tissue Diseases and Scleroderma Center, Thomas Jefferson University, Philadelphia, PA, \(^4\)Kimmel Cancer Center, Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, PA, \(^5\)Division of Rheumatology and Immunology, Medical University of South Carolina, Charleston, SC, \(^6\)Scleroderma Center and Jefferson Institute of Molecular Medicine, Thomas Jefferson Univ, Philadelphia, PA

First publication: September 18, 2017

SESSION INFORMATION

**Session Date:** Sunday, November 5, 2017

**Session Title:** Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster 1

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM
Background/Purpose:

Systemic Sclerosis (SSc) is characterized by severe fibroproliferative vasculopathy, exaggerated deposition of extracellular matrix molecules (ECM) in skin and multiple internal organs, and alterations of humoral, cellular and innate immunity. Vascular changes are responsible for the earliest SSc clinical manifestations; however the mechanisms responsible have not been elucidated.

The goal of this study was to analyze the gene expression differences between normal and SSc lung microvascular endothelial cells (EC) to improve the understanding of SSc vasculopathy pathophysiology.

Methods:

Pulmonary microvascular EC were isolated employing immunomagnetic procedures from lungs from patients with SSc undergoing lung transplantation. Control EC were isolated from autopsies of individuals who died from non-related pulmonary causes. Following isolation, microarrays were performed in EC from each group. Expression of genes with the highest differential expression was validated with RT-PCR, Western blots and confocal laser microscopy.

Results:

Interferon-stimulated genes (ISGs) including IFI44L, IFI44, IFI6, IFIH1, IFIT1, displayed the highest differential expression; being overexpressed in EC obtained from SSc donors. Others genes such as those encoding ECM production related proteins, genes associated with post-translational methylation and genes for numerous chemokines were also differentially overexpressed in SSc EC. Increased gene expression and increased protein levels of selected ISGs were confirmed by Western blots and confocal laser microscopy.

Conclusion:

Numerous ISGs are differentially overexpressed in SSc pulmonary microvascular EC in comparison with normal control EC. These results suggest that events leading to an interferon response in these cells may play a role in the pathogenesis of SSc lung vasculopathy.

References


Disclosure: F. A. Mendoza, None; S. Piera-Velazquez, None; P. J. Wermuth, None; S. Addya, None; C. A. Feghali-Bostwick, None; S. A. Jimenez, None.


Abstract Number: 755

Genome-Wide DNA Methylation Pattern in Systemic Sclerosis Microvascular Endothelial Cells: Identification of Epigenetically Affected Key Genes and Pathways

Shadia Nada1, Ibtissam Gad2, Ali Alqahtani3, Ahmad Assaly2, Sadik Khuder4, Yongqing Wang5, Bashar Kahaleh1 and Nezam Altorok1, 1Medicine/Rheumatology, University of Toledo, Toledo, OH, 2University of Toledo, Toledo, OH, 3Internal Medicine, University of Toledo, Toledo, OH, 4Department of Medicine, University of Toledo, Toledo, OH, 5Medicine, University of Toledo, Toledo, OH

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The etiology of systemic sclerosis (SSc) is not clear, but there is evidence suggesting a critical role for epigenetic alterations in disease pathogenesis and clinical expression. We sought in this study to characterize the genome-wide DNA methylation signature in SSc Microvascular Endothelial Cells (MVECs).

Methods: We performed a genome-wide DNA methylation study in MVECs derived from 7 diffuse cutaneous SSc (dSSc) patients compared to 7 age, sex, and ethnicity-matched healthy controls. Cytosine methylation was quantified across the genome. We divided samples from patients and controls in two groups of matched SSc subjects and controls. Differentially methylated CpG sites between patients and controls were identified by fold difference in methylation level ≥ 1.2, and false discovery rate (FDR) adjusted P value <0.01. Moreover, quantitative real-time RT-PCR was performed to assess the correlation between DNA methylation and gene expression levels in selected genes.

Results: We identified 71,353 differentially methylated CpG sites in SSc-MVECs using Infinium MethylationEPIC microarray in the first group (0.081% of representative probes), and 33,170 CpG sites in the second group using HumanMethylation 450 microarray (0.073% of representative probes) in dSSc-MVEC. Among the two groups of subjects, we identified differential methylation of 2,455 CpG sites, representing 1,301 genes. Most of the differentially methylated CpG sites were hypermethylated (1,625 CpG), corresponding to 910 genes. There were 830 hypomethylated CpG sites, representing 485 genes. Common Hypermethylated genes in SSc MVECs include NOS1, which encodes for nitric oxide synthase -1, DNMT3A, DNMT3B, HDAC4 and ANGPT2. We also identified hypomethylation of IL17RA, CTNNA3, ICAM2 and SDK1 in SSc MVECs. Furthermore, we demonstrate significant inverse correlation between DNA methylation status and gene expression in the majority of genes evaluated.

Gene ontology analysis of hypermethylated genes demonstrated enrichment of genes involved in homophilic cell adhesion via plasma membrane adhesion molecules (P= 2.10E-07) and angiogenesis (P= 0.0006). Pathway analysis of hypomethylated genes includes genes involved in Wnt signaling pathway (P= 0.001), vascular smooth muscle contraction (P= 0.014) and adherens junctions (P 0.013).

Conclusion: Our data suggest the presence of significant genome-wide DNA methylation aberrancies in SSc-MVEC, and identify novel affected genes and pathways in SSc MVECs.
Novel Machine Learning Classifier Accurately Predicts Intrinsic Molecular Subsets for Patients with Systemic Sclerosis

Jennifer Franks¹, Viktor Martyanov¹, Guoshuai Cai¹ and Michael L. Whitfield², ¹Department of Molecular and Systems Biology, Geisel School of Medicine at Dartmouth, Hanover, NH, ²Molecular and Systems Biology, Geisel School of Medicine at Dartmouth, Hanover, NH

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: High-throughput gene expression profiling of skin biopsies from patients with systemic sclerosis (SSc) has identified four “intrinsic” gene expression subsets conserved across multiple cohorts and tissues. These are the inflammatory, fibroproliferative, normal-like, and limited subsets. In order to classify patients in clinical trials or for diagnostic purposes, supervised methods that can assign a single sample to a molecular subset are required. Here, we introduce a novel machine learning classifier which is a robust predictor of intrinsic subset and test it on multiple independent patient cohorts.

Methods: Three independent SSc cohorts (Milano et al. 2008, Pendergrass et al. 2012, Hinchcliff et al. 2013) with gene expression data and intrinsic subset assignments were carefully curated and merged to create a training dataset covering a broad set of 297 skin biopsies representing 97 unique patients. Supervised machine learning algorithms were rigorously trained and evaluated using repeated three-fold cross-validation. We performed external validation using two independent SSc datasets: Chakravarty et al. 2015, which contains 16 samples/8 patients and Gordon et al. 2015, which contains 12 samples/6 patients. Additionally, we validated the classifier on a cohort of SSc patients with gene expression data independently generated by Assassi et al. 2015 (102 samples/97 patients). We used weighted gene co-expression network analysis and g:Profiler to identify and functionally characterize gene modules associated with the intrinsic subsets.

Results: Repeated cross-fold validation identified gene expression features using multinomial elastic net and incorporated them into the final model which achieved an average classification accuracy of 88%. All molecular subsets were classified with high average sensitivity and specificity, particularly inflammatory (83.3% sensitivity, 95.8% specificity) and fibroproliferative (89.7% sensitivity, 94.1% specificity). Through multiple rounds of external validation, the classifier maintained an accuracy ranging from 70% to 85%. In a re-analysis of gene expression data from Assassi et al. study, we identified subsets of patients that represent the canonical inflammatory, fibroproliferative, and normal-like subsets. The inflammatory subset showed upregulated gene modules enriched in biological processes such as inflammatory response, lymphocyte activation, and stress response. Similarly, gene modules enriched for cell cycle processes were increased in the fibroproliferative subset.

Conclusion: We have developed a highly accurate and reliable classifier for SSc molecular subsets for single samples trained and tested on diverse cohorts comprised of 427 skin biopsies from 208 independent patients. These analyses show that the intrinsic gene expression subsets are a common feature of SSc found across multiple internal and external validation cohorts. Machine learning methods provide a robust and accurate mechanism for stratifying intrinsic gene expression subsets and can be used to aid clinical decision-making and interpretation for SSc patients and in clinical trials.
Disclosure: J. Franks, None; V. Martyanov, None; G. Cai, None; M. L. Whitfield, Corbus, UCB, glaxosmithkline, 5; Celdara medical llc, 9.


Abstract Number: 757

Plasmacytoid Dendritic Cells Activated through TLR8 Promote Systemic Sclerosis

Marie-Dominique Ah Kioon1, Claudio Tripodo2, Alexandra Morquette3, Robert F. Spiera3, Jessica K. Gordon3 and Franck J. Barrat1, 1Autoimmunity and Inflammation Program, Hospital for Special Surgery, New York, NY, 2Department of Health Science, Human Pathology, tumor immunology unit, Palermo, Italy, 3Rheumatology, Hospital for Special Surgery, New York, NY
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Plasmacytoid Dendritic Cells (PDCs) are the key cell type mediating TLR-induced inflammation in several autoimmune diseases such as lupus, dermatomyositis, lichen sclerosus and cutaneous GVHD. In these diseases, PDC infiltrate the skin and produce IFNα, contributing to cutaneous lesions. In lupus, IFNα production was due to TLR7 and -9 recognition of endogenous RNA and DNA respectively. PDCs may also be part of the pathogenesis of systemic sclerosis (SSc). PDCs traffic to the skin in a mouse model of stiff skin syndrome. Moreover PDCs from SSc patients secrete CXCL4 and their levels in the serum correlated with skin and pulmonary disease. Although it is well described that PDC infiltrate the skin following injury or in diseases, little is known about what is controlling PDC trafficking and subsequent activation in the skin or whether PDCs can play a role in promoting/sustaining inflammation-related fibrosis. The aim of our study was to identify the nature of PDC activation in SSc patients, the role of TLRs or the impact of CXCL4 on PDC response.

Methods:
For the human studies, blood was obtained from 87 SSc patients and 23 healthy volunteers (HV), and PBMCs were isolated by density gradient. PDC were then isolated from PBMC by positive selection with BDCA4 magnetic beads or by cell sorting. In mice, fibrosis was induced by sub-cutaneous injection of bleomycin (BLM) in WT and transgenic mice expressing human TLR8 (Tg8).

Results: Aberrant expression of TLR8 was observed on SSc PDCs while absent on HV. TLR8 activation in SSc PDCs significantly induced CXCL4 secretion (p=0.003) compared to unstimulated PDC while TLR9 induction had no effect (p=0.5). TLR8 activation led to an increase secretion of IFNα and pro-inflammatory IL-6 and TNF. CXCL4 further increased TLR8-induced IFNα production by PDC (3-fold) (1393±153pg/ml for TLR8-induced PDC vs 503±747pg/ml for CXCL4+TLR8-induced PDC) while it had no effect on IL-6 (1390±129pg/ml vs 1365±100pg/ml) and TNF production (3404±241pg/ml vs 3251±207pg/ml). In mice, following BLM treatment, a significant increase in skin thickness was observed in WT mice (200±6mm vs 357±3mm, p<0.0001) and further increased in Tg8 mice (396±5mm, p=0.04 vs WT BLM). Moreover, PDCs accumulation was observed in the skin of WT BLM mice as compared to WT PBS as assessed by in situ analysis of SiglecH positive cells. PDCs infiltration were further enhanced in the skin of Tg8 mice (p=0.0008) as well as enhanced expression of IFN related genes, IP10 (p=0.006), IFIT2 and IFI35 (p=0.03).
Conclusion: Taken together our data demonstrate that the secretion of CXCL4 is due to the aberrant presence of TLR8 on PDCs of SSc patients, and that CXCL4 contributes to excessive IFNα response by TLRs. In mice, TLR8 exacerbates fibrosis due to an increased PDC infiltration in the skin.

Disclosure: M. D. Ah Kioon, None; C. Tripodo, None; A. Morquette, None; R. F. Spiera, None; J. K. Gordon, None; F. J. Barrat, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/plasmacytoid-dendritic-cells-activated-through-tlr8-promote-systemic-sclerosis

Abstract Number: 758

Identification of Biomarkers Predictive of Pulmonary Arterial Hypertension in Systemic Sclerosis

Kathleen D. Kolstad1, Tyson Holmes2, Yael Rosenberg-Hasson2, Andrew Sweatt3, Roham T. Zamanian4, Shufeng Li5, Virginia D. Steen6, Paul J. Utz7 and Lorinda Chung8, 1Rheumatology, Stanford University Medical Center, Stanford, CA, 2Stanford University Medical Center, Stanford, CA, 3Medicine, Division of Pulmonary and Critical Care, Stanford University Medical Center, Stanford, CA, 4Stanford University Medical Center, Palo Alto, CA, 5Dermatology, Stanford University School of Medicine, Stanford, CA, 6Rheumatology, MedStar Georgetown University Hospital, Washington, DC, 7Medicine, Stanford University School of Medicine, Stanford, CA, 8Rheumatology, Stanford University Medical Center, Palo Alto, CA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic sclerosis (SSc) is an autoimmune disease characterized by vascular abnormalities, immune system dysregulation, and fibrosis. Pulmonary arterial hypertension (PAH) affects approximately 10% of SSc patients and is a leading cause of death. We sought to identify cytokines predictive of progression to PAH in SSc.

Methods: Pulmonary Hypertension Assessment and Recognition of Outcomes in Scleroderma (PHAROS) is a prospective registry that includes SSc patients at high risk for PAH based on pulmonary function test and echocardiographic parameters. Serum was available from 38 high-risk patients for this study. Baseline characteristics were assessed at the time of serum acquisition. Kaplan-Meier estimates were generated for time to PAH from first non-Raynaud Os Phenomenon (RP) symptom. The Luminex (eBioscience) immunoassay (Human 62-plex) was used for serum cytokine profiling. Missing data were multiply imputed to generate 60 complete datasets. Using multivariable Cox regression, time to PAH was regressed on a candidate predictor set consisting of all cytokines' preprocessed median fluorescence intensities and four clinical covariates which had previously been shown to be associated with progression to PAH in the PHAROS cohort (exercise induced O2 saturation, % predicted diffusing capacity for carbon monoxide (DLCO), forced vital capacity/DLCO, systolic pulmonary artery pressure on echocardiogram) (1). Regression coefficients were estimated by five-fold cross-validated, likelihood-based boosting.

Results: Baseline characteristics are shown in Table 1. At 1, 5,10, 15, and 20 years after first non-RP symptoms, the rate of progression to PAH in this high-risk population was 3%, 5%, 15%, 18%, and 31% respectively. Elevated levels of IL-1Beta (Figure 1) and IL-15 (not shown) correlated with an increased risk of progression to PAH.

Conclusion: These preliminary results identified IL-1Beta and IL-15 as potential biomarkers associated with progression to PAH in SSc. These may be useful in identifying high-risk patients who warrant early referral to right heart catheterization,
and may provide further insight into the mechanism of disease. We plan to validate our findings in an independent cohort.


Disclosure: K. D. Kolstad, None; T. Holmes, None; Y. Rosenberg-Hasson, None; A. Sweatt, None; R. T. Zamanian, None; S. Li, None; V. D. Steen, None; P. J. Utz, None; L. Chung, Cytori, Actelion, Reata, 5.


Abstract Number: 759
Multi Dimensional Analysis of the Immunome in Systemic Sclerosis Reveals Functionally Related Abnormalities in MAIT and B Cell Compartments

Bhairav Paleja¹, Pavanish Kumar¹, Suzan Saidin¹, Ahmad Lajam², Camillus Chua¹, Liyun Lai¹, Andrea Hsiu Ling Low² and Salvatore Albani¹, ¹SingHealth Translational Immunology and Inflammation Centre (STIIC), Duke-NUS Medical School, Singapore, Singapore, ²Singapore General Hospital, Singapore, Singapore

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Systemic sclerosis (SSc) is an autoimmune disease characterised by excessive fibrosis of skin and internal organs, and vascular dysfunction. Association of T and B cell subsets have been reported in SSc, however there is lack of systematic studies of functional relations between immune cell subsets in this disease. This lack of mechanistic knowledge hampers targeted intervention. In the current study we sought to determine differential immune cell composition and heterogeneity in peripheral blood of SSc patients compared to healthy controls.

Methods:
SSc patients fulfilling ACR 2013 criteria (n=20, of whom 10 were of diffuse cutaneous subtype; 10 had interstitial lung disease) and healthy controls (n=10) were included. Mononuclear cells from blood were analysed by mass cytometry using a 36 marker (cell-surface and intracellular) panel to aid in identification of major PBMC lineages including T cells, B cells, monocytes and NK cells and their subsets. Unsupervised clustering of mass cytometry data was performed using in-house developed analysis software MARVIS. This software combines dimension reduction and clustering steps to identify all possible cellular subsets. Further, custom R scripts helped in identifying nodes that were differentially expressed between the study groups and also phenotype of these nodes.

Results:
Unsupervised clustering performed revealed significant differences in the frequencies of T cell and B cell subsets. Most strikingly we identify a 3 fold decrease in frequencies of Va7.2+ CD161+ mucosal associated invariant T cells (MAIT) in SSc patients and 2 fold increase in total B cells, particularly CD19+ CD27- naive cells. A subset of memory CD8+ T cell, expressing CXCR3 was found to be increased in SSc patients as compared to healthy controls. Transcriptome analysis of sorted B cell and T cell subsets showed decrease in genes related to survival and increased expression of apoptotic genes in CD4,CD8 T and MAIT cells from SSc patients. Interestingly, high expression of CXCR3 gene was observed in transcriptome analysis of CD8+ T cells from SSc patients.

Conclusion:
This study provides an in depth analysis of systemic immune composition in SSc with the potential to delineate mechanisms of pathogenesis and identify diagnostic and/or therapeutic targets. This is the first demonstration of dysfunction of MAIT cells in SSc and further characterisation of their function in this context is required.

Disclosure: B. Paleja, None; P. Kumar, None; S. Saidin, None; A. Lajam, None; C. Chua, None; L. Lai, None; A. H. L. Low, None; S. Albani, None.

Abstract Number: 760

Antisense Long Noncoding RNA HAND2-AS1 and OTUD6B-AS1 Have Important Roles in the Pathogenesis of Systemic Sclerosis

Miki Takata1, Elena Pachera1, Anastasiia Kozlova1, Astrid Jüngel1, Tobias Messemaker2, Jeska de Vries-Bouwstra2, Tom W.J. Huizinga3, Fina Kurreeman2 and Oliver Distler4, 1Department of Rheumatology, Center of Experimental Rheumatology, University Hospital Zurich, Zurich, Switzerland, Zurich, Switzerland, 2Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, Leiden, Netherlands, 3Department of Rheumatology, LUMC, Leiden, Netherlands, Leiden, Netherlands, 4Department of Rheumatology, Center of Experimental Rheumatology, University Hospital Zurich, Zurich, Switzerland

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster 1
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Long noncoding RNAs (lncRNAs) represent a class of transcripts longer than 200 nucleotides that are not translated into proteins. In recent years, antisense (AS) lncRNAs have increasingly been recognized as important regulators of their sense genes and they have been found to play key roles in the pathogenesis of several diseases. However, the role of AS lncRNAs in SSc is still unknown. Our previous study identified two AS lncRNAs in SSc skin biopsies namely HAND2-AS1 and OTUD6B-AS1. Here we aim to characterize the functional relevance of these AS lncRNAs.

Methods: Sense and AS gene expression was analyzed by qPCR in RNA samples of HC and SSc dermal fibroblasts (Fb). Dermal Fb were stimulated with different profibrotic cytokines and growth factors like TGFβ, PDGF and IL-4 at physiological concentrations. Function of AS lncRNAs was analyzed by qPCR and Western Blot (WB) in HC dermal Fb and human pulmonary artery smooth muscle cells (HPASMC) transfected with locked nucleic acid antisense oligonucleotides (LNA GapmeRs).

Results: RNA sequencing analysis of skin biopsy revealed consistent and significant downregulation of HAND2-AS1 and OTUD6B-AS1 expression. In SSc and HC dermal Fb, no difference was recorded in the basal level of HAND2-AS1, HAND2, OTUD6B-AS1 and OTUD6B expression. However, HAND2 and HAND2-AS1 expression in SSc dermal Fb was significantly downregulated after TGFβ and IL-4 stimulation (n=4-5, \(p<0.05\), up to 0.09 fold reduction). HAND2-AS1 expression was also significantly downregulated after PDGF stimulation (n=4, \(p<0.05\), up to 0.12 fold reduction) and HAND2 expression had the same trend. OTUD6B expression in SSc dermal Fb was significantly downregulated after PDGF stimulation (n=7, \(p<0.05\), up to 0.16 fold reduction) and OTUD6B-AS1 expression was also decreased. OTUD6B-AS1 expression was significantly downregulated after IL-4 stimulation (n=4, \(p<0.05\), up to 0.52 fold reduction). Importantly, HAND2-AS1 knockdown significantly reduced collagen 1A1, fibronectin and \(\alpha\)-smooth muscle actin (\(\alpha\)SMA) mRNA in dermal Fb (\(p<0.05\)). Downregulation of fibronectin expression was also confirmed after HAND2-AS1 knockdown by WB analysis (n=4). In contrast to HAND2-AS1, OTUD6B-AS1 knockdown did not affect extracellular matrix production. However, we observed effects on cell cycle regulation after OTUD6B-AS1 knockdown. OTUD6B-AS1 knockdown in Fb and HPASMC significantly increased OTUD6B, and cell cycle regulators c-MYC, Cyclin D1 and Cyclin D2 mRNA (n=6, \(p<0.05\)). Upregulation of OTUD6B, c-MYC and Cyclin D1 in HPASMC was also confirmed after OTUD6B-AS1 knockdown by WB analysis (n=2).

Conclusion: This is the first report analyzing the functional role of AS lncRNAs in SSc. These results point to an important role of HAND2-AS1 in extracellular matrix production and of OTUD6B-AS1 in cell cycle progression.

Disclosure: M. Takata, None; E. Pachera, None; A. Kozlova, None; A. Jüngel, None; T. Messemaker, None; J. de Vries-Bouwstra, None; T. W. J. Huizinga, None; F. Kurreeman, None; O. Distler, Actelion, 5,Bayer, 5,Biogen Idec, 5,Boehringer Ingelheim, 5,ChemomAb, 5,espeRare Foundation, 5,Genentech/Roche, 5,GlaxoSmithKline, 5,Inventiva,
Increased Expression of the TNF Superfamily Member LIGHT/TNFSF14 and Its Receptor (TNFRSF14) in Patients with Systemic Sclerosis

Otylia Kowal-Bielecka¹, Ewa Gindzienska-Sieskiewicz¹, Oliver Distler², Joanna Reszec³, Suzana Jordan², Pawel Bielecki⁴, Andrzej Sieskiewicz⁴, Agnieszka Sulik¹ and Krzysztof Kowal⁵,⁶, ¹Department of Rheumatology and Internal Medicine, Medical University of Bialystok, Bialystok, Poland, ²Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland, ³Department of Medical Pathomorphology, Department of Medical Pathomorphology, Medical University of Bialystok, Bialystok, Poland, ⁴Department of Otolaryngology, Medical University of Bialystok, Bialystok, Poland, ⁵Department of Allergology and Internal Medicine, Medical University of Bialystok, Bialystok, Poland, ⁶Department of Experimental Allergology and Immunology, Medical University of Bialystok, Bialystok, Poland

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster 1
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The TNF Superfamily member LIGHT (TNFSF14) regulates immune response and angiogenesis. Moreover, recent studies indicate that interactions of LIGHT with its receptor, TNFRSF14, might also play a role in regulation of tissue remodeling. Since autoimmunity, vascular injury and fibrosis are key elements of the pathogenesis of systemic sclerosis (SSc) we hypothesized that LIGHT might be involved in development of SSc. This study was aimed to assess potential role of LIGHT in SSc through evaluation of: 1) expression of LIGHT and its receptor, TNFRSF14, in skin biopsies and 2) associations between serum concentration of LIGHT and clinical features in SSc patients.

Methods: Expression of LIGHT and its receptor, TNFRSF14, was investigated by means of immunohistochemistry, and evaluated semiquantitatively (score from 0 to 3), in skin biopsies from 18 SSc patients and 9 healthy controls. Serum levels of LIGHT were measured using commercially available ELISA kits in 320 patients with SSc and 50 control subjects.

Results: Expression of both, LIGHT and TNFRSF14 was significantly higher in skin biopsies from SSc patients as compared with healthy controls (p<0.05). Patients with early SSc (<= 3 years from the first non-Raynaud’s phenomenon, n=13) showed significantly higher skin expression of TNFRSF14 (p<0.05) and tended to have greater skin expression of LIGHT (p=0.06) as compared with SSc patients with longer disease (n=5).

The mean serum concentration of LIGHT was significantly higher in SSc patients as compared with the controls (p<0.05). Moreover, mean serum concentration of LIGHT was significantly higher in SSc patients with digital ulcers (DUs) as compared with SSc patients without DUs, patients without anti-centromere antibodies (ACA) as compared with those with ACA, patients with muscle involvement (defined by elevated serum CK levels) compared with patients without CK elevation and in patients receiving steroids, as compared with those without steroid therapy (p<0.05 for all comparisons).
addition, the mean concentration of LIGHT was significantly higher in male patients as compared with female SSc patients (p<0.05). There were also statistically significant (p<0.05) although very weak correlations between serum concentration of LIGHT and skin involvement (modified Rodnan skin score (mRSS); R-Spearman = 0.13), erythrocyte sedimentation rate (ESR; R-Spearman = 0.15), and, inverse, with diffusing capacity of the lungs for CO (DLCO; R-Spearman = -0.22). We could not find any significant associations between serum LIGHT concentrations and other SSc features, including subtype of SSc, disease duration, presence of interstitial lung disease, pulmonary hypertension, or other antibodies. In multivariate regression analysis including, as predictors, DUs, ACA, serum CK elevation, steroid therapy, mRSS, DLCO, ESR, and sex, only presence of DUs and DLCO were independently associated with serum concentration of LIGHT (p<0.05 for both).

Conclusion: These data provide the first evidence of overexpression of LIGHT and its receptor in SSc and suggest that LIGHT-TNFRSF14 axis might contribute to the pathogenesis of SSc. Increased serum concentrations of LIGHT seem to reflect vascular injury in SSc.

Disclosure: O. Kowal-Bielecka, None; E. Gindzienska-Sieszkiewicz, None; O. Distler, 4 D Science, Actelion, Active Biotec, Bayer, Biogen Idec, Boehringer Ingelheim Pharma, BMS, ChemomAb, EpiPharm, Ergonex, espeRare foundation, GSK,Roche-Genentech, Inventiva, Lilly, medac, MedImmune, Mitsubishi Tanabe, Pharmacyclics, Pfizer, Sanofi, Seroda, 2; J. Reszec, None; S. Jordan, None; P. Bielecki, None; A. Sieszkiewicz, None; A. Sulik, None; K. Kowal, None.


Abstract Number: 762

M10, a Caspase Cleavage Product of the Hepatocyte Growth Factor Receptor, Downregulates Bone Morphogenetic Protein-9-Induced Smad1/5/8 Phosphorylation and Collagen Production in Human Lung Fibroblasts

Atsushi Noguchi, Ilia Atanelishvili, Tanjina Akter, Richard M. Silver and Galina S. Bogatkevich, Division of Rheumatology and Immunology, Department of Medicine, Medical University of South Carolina, Charleston, SC

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster 1
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: We recently identified M10, a caspase cleavage product of the hepatocyte growth factor receptor, as an anti-fibrotic peptide that interacts with Smad2 and inhibits TGFβ-induced Smad2 phosphorylation and collagen production in human lung fibroblasts [1]. While Smad2/3 signaling pathway is mainly activated by TGFβ1 through type I receptor activin receptor-like kinase (ALK) 5, Smad1/5 signaling pathway is mainly activated by bone morphogenetic proteins (BMPs), which are other members of TGFβ superfamily, through ALK1/2/3/6 receptors. Recently, BMP9 has been identified as a pro-fibrotic ligand in mouse embryo fibroblasts [2]. In SSc fibroblasts, ALK1/Smad1/5 pathway is suggested to play a pivotal role in the regulation of fibrosis [3]. The aims of this study are to investigate the role of BMP9 in SSc lung fibroblasts and to examine the additional anti-fibrotic mechanisms of M10.

Methods: Fibroblasts were derived from lung tissues obtained at autopsy from SSc patients and from age- race-, and sex-matched normal subjects. MRC5 human fetal lung fibroblasts were purchased from Sigma. Potential peptide-protein interactions were modeled in-silico using PepSite [4]. Smad phosphorylation, type I collagen, and smooth muscle α-actin (α-SMA) expression were determined by immunoblotting and RT-PCR.

Results: Using a computational modulation approach available from PepSite, we found a statistically significant (p < 0.0001) potential interaction of M10 with the BMP9/ALK1/activin receptor type II B (ActRIIB) complex. The most
probable binding sites are located at β-turn motifs in BMP9. We demonstrate that when recombinant BMP9 is added to the medium, phosphorylation of Smad1/5/8 is rapidly induced in MRC5 cells and SSc lung fibroblasts in a dose-dependent manner. The expression of type I collagen is upregulated after 48 hours treatment with BMP9 in MRC5 cells and SSc lung fibroblasts as well as normal lung fibroblasts. The expression of α-SMA is increased in normal lung fibroblasts in a dose dependent manner. Intriguingly, the anti-fibrotic peptide M10 significantly downregulated BMP9-induced type I collagen expression and α-SMA expression as well as Smad1/5/8 phosphorylation in lung fibroblasts.

**Conclusion:** We demonstrate that BMP9 shows pro-fibrotic effects in human fetal lung fibroblasts and in adult lung fibroblasts obtained from SSc patients and matched normal subjects. M10 peptide has a potential to bind to BMP9 and to inhibit BMP9-induced collagen production and epithelial-mesenchymal transition through the Smad1/5/8 signaling pathway.

References:


**Disclosure:** A. Noguchi, None; I. Atanelishvili, None; T. Akter, None; R. M. Silver, NIH/NIAMS P60 AR062755, 2,SC SmartState®, 2; G. S. Bogatkevich, NIH/NIAMS P60 AR062755, 2,Scleroderma Foundation, 2.

**Abstract Number:** 763

**Mechanisms of Insulin-like Growth Factor-II-Mediated Fibrosis**

Sara Garrett1, Justin Thomas2, Eileen Hsu3 and Carol A. Feghali-Bostwick4, 1Medicine/Rheumatology & Immunology, Medical University of South Carolina, Charleston, SC, 2Eisenhower Medical Center, Rancho Mirage, CA, 3Kaiser Permanente Medical Group, Mclean, VT, 4Division of Rheumatology and Immunology, Division of Rheumatology and Immunology, Medical University of South Carolina, Charleston, SC, United States, Charleston, SC

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Previous work has shown that insulin-like growth factor (IGF)-II is increased in fibrosing lung diseases, including idiopathic pulmonary fibrosis (IPF) and scleroderma/systemic sclerosis (SSc)-associated pulmonary fibrosis. Our goal was to identify the mechanism by which upregulated IGF-II expression contributes to fibrosis in these conditions.

**Methods:** Fibroblasts derived from lung tissues of normal donors (NL), patients with IPF, and patients with SSc-associated pulmonary fibrosis were used. Gene expression, protein expression, phosphorylation, and secretion were analyzed with qRT-PCR, immunoprecipitation, immunoblotting, and ELISA, respectively, in early passage primary fibroblasts. Antibody, siRNA, and inhibitors were used to neutralize, knockdown, or block endogenous IGF-II and the IGF-II receptors: IGF-1 receptor (IGF1R), IGF2R, and/or insulin receptor (IR).
**Results:** The IGF1R, IGF2R, and IR receptors showed lower basal gene expression in SSc fibroblasts. Extracellular matrix (ECM) transcripts, though unchanged in NL, were dramatically increased in IPF and SSc with IGF-II (200 ng/mL) stimulation. Activation of IGF1R, assessed via receptor phosphorylation, occurred 5 min following IGF-II. Phosphorylation decreased by 10 min in NL, but persisted through 10 min in SSc fibroblasts. Phosphorylation was abrogated by antibody-mediated neutralization of endogenous IGF-II. Dual siRNA knockdown of IGF1R and IR decreased ECM components collagen and fibronectin in NL and SSc fibroblasts, as did treatment with an IGF1R tyrosine kinase inhibitor. IGF-II decreased IGF1R and IR transcripts at 6 hr in NL, IPF, and SSc and decreased IGF2R in NL from 1-48 hr. MMP3 transcript was decreased with IGF-II stimulation in IPF and SSc, whereas TIMP1 transcript and secretion were increased.

**Conclusion:** Decreased basal receptor pools, ECM component upregulation, and longer receptor activation render fibroblasts from pathologic lung more sensitive to IGF-II-stimulated fibrosis. Inhibitor studies indicate IGF-II signaling is mediated by IGF1R and IR, which can form a hybrid receptor. IGF-II causes disruption of steady-state ECM deposition and breakdown through altered MMP:TIMP levels, promoting a pro-fibrotic milieu in IPF and SSc.

**Disclosure:** S. Garrett, None; J. Thomas, None; E. Hsu, None; C. A. Feghali-Bostwick, None.

**Abstract Number:** 764

**Application of a Novel Computational Approach to Identify New Targets and Pathways for Therapeutic Intervention in Scleroderma**

Elma Kurtagic, Joel Pradines, Anthony Manning and **Ishan Capila**, Research, Momenta Pharmaceuticals, Inc., Cambridge, MA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster I

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Systemic Sclerosis (SSc) is a complex autoimmune disease with chronic progressive course and high interpatient variability. It is characterized by inflammation, vascular dysfunction and fibrosis. Fibrosis of the skin and visceral organs results in irreversible scarring and ultimately organ failure, accounting for high mortality. There is no approved targeted therapy with disease-modifying potential. Several translational studies were published, which focused on transcriptional analysis of samples from SSc patients in order to understand the heterogeneity of underlying disease. We interrogated these datasets using a novel data analysis methodology that leverages the knowledge of protein interaction networks (STRING) for deriving biological insights and identifying intervention points into this heterogeneous disease.

**Methods:**

Publically available datasets composed of gene expression analysis of patient skin biopsies were identified. Datasets were subjected to sample size and quality assessment. Selected high-quality datasets were analyzed using a novel computational and statistical method. Namely, each gene was scored for both its differential expression and its known protein interactions with top differentially expressed genes (DEGs). This approach led to identification of Well-Associated Proteins (WAPs); gene products that have a significantly large number of known associations to top DEGs, without choosing a threshold for differential expression. The scoring method corrects for the total number of interactions of each gene and is optimally fast,
enabling false discovery rate (FDR) estimates for each WAP via permutation testing, thus taking into account gene co-expression. Furthermore, permutation testing was utilized to identify WAPs that correlated with measurable clinical factors.

**Results:**

Four publically available datasets were analyzed. Key biology pathways associated with SSc were identified. More importantly, > 100 potential targets/WAPs were identified with FDR score < 0.01%. ~75% of the significant WAPs were not perturbed at the mRNA level and would have been missed via standard statistical methods. Their significant connectedness to top DEGs in the datasets suggests biologically relevant role in SSc. Robustness analysis revealed that WAP scores were ~40% reproducible across pairs of datasets, as compared to only ~10% for DEG scores. Of the top 100 WAPs obtained by combining the two largest data sets, 59 were previously targeted providing drug-repurposing opportunities and 41 were novel targets for drug discovery. Additional analysis identified WAPs (e.g. OSM) that significantly correlated with measurable clinical factors such as MRSS (global skin score), diffuse disease and some auto-antibodies.

**Conclusion:**

A novel data analysis methodology was developed, leveraging protein interaction networks to identify WAPs that represent potentially unique targets for therapeutic intervention in SSc. WAPs are unique as they were reproducibly detected across multiple publicly available SSc datasets. Additionally, patient sub-populations that may benefit from targeted therapeutics against selected WAPs were identified.

**Disclosure:** E. Kurtagic, Momenta Pharmaceuticals Inc., 1,Momenta Pharmaceuticals Inc., 3; J. Pradines, Momenta Pharmaceuticals Inc., 1,Momenta Pharmaceuticals Inc., 3; A. Manning, Momenta Pharmaceuticals Inc., 1,Momenta Pharmaceuticals Inc., 3; I. Capila, Momenta Pharmaceuticals Inc, 3,Momenta Pharmaceuticals Inc, 1.


**Abstract Number: 765**

**Proteomic Analysis of Scleroderma Associated Joint Disease**

Chan Kim¹, Julio Mantero², Robert A. Lafyatis³ and Robert W. Simms⁴, ¹Rheumatology and Clinical Epidemiology, Boston University School of Medicine, Boston, MA, ²Arthritis Center, Boston University School of Medicine, Boston, MA, ³Division of Rheumatology and Clinical Immunology, University of Pittsburgh School of Medicine, Pittsburgh, PA, ⁴Rheumatology, Boston University School of Medicine, Boston, MA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster 1 
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

The pathophysiology of joint disease in scleroderma, a heterogeneous multisystem disease mostly characterized by fibrosis, is unknown. We performed proteomic analysis of serum in patients with scleroderma and joint tenderness. Understanding systemic protein expression in scleroderma may help us understand joint disease in scleroderma. Our goal was to characterize protein expression differences between scleroderma patients with joint tenderness and scleroderma patients without joint tenderness.
Methods:

Patients with scleroderma were recruited from the registry at Boston University Medical Center’s Scleroderma Center. Serum (blood) samples were drawn and were analyzed with SOMAscan for 1129 protein biomarkers. As part of the routine examination performed by a senior rheumatologist on all registry participants, tender joint count (0-18) was assessed on physical exam. If a subject had a tender joint count of 2 or more, then that subject had joint disease. If a subject had a tender joint count of 0, then that subject did not have joint disease. For this study, 40 scleroderma subjects had both SOMAscan data and tender joint count assessment. One subject with only 1 tender joint count was excluded, so 39 subjects were analyzed. For analysis, the biomarkers were log2 transformed, and differential expression analyses were performed using the “limma” package using the R statistical software.

Results:

Among the 39 scleroderma subjects, 9 participants had joint pain (average tender joint count 4.9), and protein expression was compared between scleroderma participants with joint disease and scleroderma participants without joint disease. The top 20 most significant biomarkers are shown in table 1. In previous analyses (not shown), similar biomarkers (such as MMP (matrix metalloproteinase), fibrinogen, tumor necrosis factor), were seen elevated in all scleroderma participants (compared to normal subjects without scleroderma). Notably, IL-6, cadherin-2 (involved in bone and cartilage formation), BRF1 (RNA Polymerase III transcription initiation factor subunit) were expressed higher in scleroderma subjects with joint disease compared to those without joint disease. VEGF-121 (vascular endothelial growth factor) was expressed lower in scleroderma subjects with joint pain compared to those without joint disease.

Conclusion:

Although scleroderma participants had many protein expression changes due to fibrosis, autoimmunity and vasculopathy, several biomarkers such as IL-6, cadherin-2, BRF1, VEGF-121 were differentially expressed in scleroderma participants with joint disease and could provide insight into the pathophysiology of joint disease in scleroderma.

Table 1: Joint disease vs no joint disease

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Log Fold Change</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MK12</td>
<td>0.375414</td>
<td>0.000385</td>
</tr>
<tr>
<td>IL-6</td>
<td>0.425859</td>
<td>0.002113</td>
</tr>
<tr>
<td>VEGF121</td>
<td>-0.69485</td>
<td>0.002898</td>
</tr>
<tr>
<td>MBL</td>
<td>0.697418</td>
<td>0.003867</td>
</tr>
<tr>
<td>ADAM 9</td>
<td>0.920928</td>
<td>0.008789</td>
</tr>
<tr>
<td>a1-Antitrypsin</td>
<td>0.459117</td>
<td>0.00907</td>
</tr>
<tr>
<td>CDC37</td>
<td>0.173549</td>
<td>0.009931</td>
</tr>
<tr>
<td>TSP4</td>
<td>0.472696</td>
<td>0.012891</td>
</tr>
<tr>
<td>LDH-H 1</td>
<td>0.32681</td>
<td>0.013691</td>
</tr>
<tr>
<td>BRF-1</td>
<td>0.29382</td>
<td>0.014471</td>
</tr>
<tr>
<td>MMP-14</td>
<td>0.379094</td>
<td>0.016855</td>
</tr>
<tr>
<td>PDGF-BB</td>
<td>-0.44877</td>
<td>0.017505</td>
</tr>
<tr>
<td>iC3b</td>
<td>-0.46833</td>
<td>0.017607</td>
</tr>
<tr>
<td>Siglec-9</td>
<td>1.04874</td>
<td>0.020749</td>
</tr>
<tr>
<td>Carbonic Anhydrase IV</td>
<td>-0.30158</td>
<td>0.023048</td>
</tr>
<tr>
<td>Cadherin-2</td>
<td>0.285673</td>
<td>0.024096</td>
</tr>
<tr>
<td>MK11</td>
<td>0.265757</td>
<td>0.025145</td>
</tr>
<tr>
<td>Thrombospondin-1</td>
<td>-0.34304</td>
<td>0.025595</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>0.429274</td>
<td>0.027908</td>
</tr>
<tr>
<td>Macrophage mannose receptor</td>
<td>0.269891</td>
<td>0.029517</td>
</tr>
</tbody>
</table>

Disclosure: C. Kim, None; J. Mantero, None; R. A. Lafyatis, None; R. W. Simms, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/proteomic-analysis-of-scleroderma-associated-joint-disease
Increased Plasma Levels of Hsp90 Are Associated with More Severe Organ Involvement in Patients with Systemic Sclerosis

Hana Storkanova¹, Sabina Oreska¹, Maja Spiritovic¹,², Karel Pavelka¹, Jiri Vencovsky¹, Jörg Distler³, Ladislav Senolt¹, Radim Becvar¹ and Michal Tomcik¹, ¹Institute of Rheumatology, Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, Prague, Czech Republic, ²Faculty of Physical Education and Sport, Charles University, Prague, Czech Republic, Prague, Czech Republic, ³Department of Internal Medicine III and Institute for Clinical Immunology, University of Erlangen-Nuremberg, Erlangen, Germany, Erlangen, Germany

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Our previous study demonstrated that Heat shock protein 90 (Hsp90) is overexpressed in the skin of patients with systemic sclerosis (SSc), in cultured SSc fibroblasts and preclinical models of SSc in a TGF-β dependent manner. We showed that Hsp90 is a new regulator of canonical TGF-β signalling and its inhibition prevents the stimulatory effects of TGF-β on collagen synthesis and dermal fibrosis in three preclinical models of SSc¹. The aim of this study was to evaluate Hsp90 in the circulation of SSc patients and characterize its potential association with skin changes and SSc-related features.

Methods: A total of 91 patients (78 females; mean age 52.7; disease duration 6.0 years; diffuse cutaneous (dc)SSc / limited cutaneous (lc)SSc = 38/53) who met the ACR/EULAR 2013 classification criteria for SSc and 85 age- and sex- matched healthy individuals were included. Plasma Hsp90 levels were measured by ELISA (eBioscience, Vienna, Austria). SSc-related manifestations were obtained from the Czech Registry of SSc patients. Skin changes were assessed using the modified Rodnan skin score (mRSS) and EUSTAR SSc activity score was determined. Data are presented as median (IQR, 25. – 75. percentile).

Results: Plasma Hsp90 levels were increased in SSc patients compared to healthy controls [12.5 (9.6–17.9) vs. 9.9 (7.9–12.6) ng/mL, p = 0.001], but no difference between (lc)SSc and (dc)SSc were detected [13.1 (9.4–18.1) vs. 11.5 (9.5–17.5) ng/mL, p = 0.316]. Hsp90 levels in all patients positively correlated with CRP (r = 0.313, p = 0.006). Furthermore, Hsp90 concentrations were increased in patients with interstitial lung disease (ILD) compared to those without ILD [12.8 (10.2–17.9) vs. 10.3 (8.6–16.6) ng/mL, p = 0.045] and were negatively associated with functional parameters of ILD: FVC (r = -0.299, p = 0.011), FEV1 (r = -0.256, p = 0.031), DLCO (r = -0.303, p = 0.009) and SpO₂ (r = -0.317, p = 0.038). In addition, only in patients with dcSSc, Hsp90 levels positively correlated with the mRSS (r = 0.437, p = 0.006). Concentrations of extracellular Hsp90 were not significantly affected by other main clinical parameters of SSc.

Conclusion: We demonstrated higher plasma levels of Hsp90 in SSc patients compared to healthy controls. Concentrations of extracellular Hsp90 increase with higher inflammatory activity, with deteriorated lung functions in ILD and also with the extent and severity of the skin involvement in patients with diffuse cutaneous SSc. These data further highlight the role of Hsp90 as a significant regulator of fibroblast activation and tissue fibrosis in SSc.


Acknowledgement: Supported by AZV – 16-33542A and SVV – 260373.

Disclosure: H. Storkanova, None; S. Oreska, None; M. Spiritovic, None; K. Pavelka, None; J. Vencovsky, Samsung Bioepis Co., Ltd., Biogen, 5; J. Distler, 4D Science, 1,Anamar Medical, Active Biotech, Array Biopma, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, GSK, Novartis, Sanofi-Aventis, UCB, 2,Actelion Pharmaceuticals US, Active
Elevated MeCP2 Expression in Diffuse Cutaneous Systemic Sclerosis Dermal Fibroblasts Is Associated with Anti-Fibrotic Effects

Ye He¹, Pei-Suen Tsou², Dinesh Khanna³ and Amr H Sawalha², ¹Rheumatology, University of Michigan, Ann Arbor, MI, ²Division of Rheumatology, University of Michigan, Ann Arbor, MI, ³University of Michigan, Ann Arbor, MI

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic Sclerosis (SSc) is a multisystem autoimmune connective tissue disorder characterized by vascular injury and fibrosis of the skin and internal organs. Methyl-CpG-binding protein 2 (MeCP2) is a transcription activator or repressor depending on its interacting complexes. Increasing evidence shows that MeCP2 is closely involved in lung, liver, and kidney fibrosis. In this study, we aim to elucidate the role of MeCP2 in dermal fibroblasts from patients with SSc.

Methods: Dermal fibroblasts were isolated from healthy controls or patients with diffuse cutaneous SSc (dcSSc). MeCP2 expression was analyzed by qRT-PCR and western blotting. A scratch wound healing assay was used to evaluate fibroblast migration. MeCP2 overexpression was achieved by transfecting fibroblasts with MeCP2 DNA plasmids, while transfection with empty vectors was used as control. MeCP2 knockdown was done using MeCP2 siRNA. RNA isolated from dcSSc fibroblasts after 48hrs of MeCP2 knockdown was sequenced by Ilumina HiSeq2500. Gene pathway analysis was performed using GeneMANIA and by searching literatures and GeneCards database.

Results: MeCP2 expression was increased by 1.8-fold (p=0.02) in dcSSc fibroblasts (n=6) compared to normal fibroblasts (n=7) at the protein level. However, no change was observed at the mRNA level, suggesting that dysregulation of MeCP2 in dcSSc occurs at the post-transcriptional level. Overexpression of MeCP2 in normal fibroblasts inhibited cell migration (n=4, p=0.02) while MeCP2 knocked down dcSSc fibroblasts showed higher wound repair ability than controls (n=5, p<0.01). In addition, the mRNA levels of pro-fibrotic genes such as α-SMA and COL1A1 were significantly downregulated in MeCP2 overexpressing normal fibroblasts (n=6, p=0.03) while anti-fibrotic PPAR-γ was upregulated (n=6, p<0.01). Using RNA-seq we identified 51 differentially expressed genes after MeCP2 knockdown in dcSSc fibroblasts (n=5, ≥1.2 fold or ≤0.8 fold, adjusted p-value<0.05). 14 out of 51 differentially expressed genes appeared to be involved in fibrosis, among which 5 downregulated genes including ITGB1 and NID2 were shown to be related to COL1A1, and 4 genes, including ITGB1, PLAU, ADA, and TNFPIA1, were involved in cell migration/adhesion. None of the 14 screened genes were differentially expressed between normal and dcSSc fibroblasts, suggesting that MeCP2 might suppress fibrosis via balancing the expression of some of these candidate genes. Moreover, we further confirmed that 9 downregulated fibrosis-related genes identified by RNA-seq were indeed MeCP2-regulated genes, as they were upregulated when MeCP2 was overexpressed in normal fibroblasts.

Conclusion: MeCP2 exerts anti-fibrotic effects in dcSSc fibroblasts by reducing cell migration and myofibroblast differentiation. Whole transcriptome profiling reveals that MeCP2 is involved in cell adhesion and controls extracellular matrix (ECM)-related genes. Importantly, MeCP2 overexpression in dcSSc fibroblasts appears to be a defense mechanism to counteract the pro-fibrotic nature of the disease. MeCP2 might be a novel target to restore normal skin function in SSc.
A Positive Feedback Loop between Estrogen and IL-6 Leads to Fibrosis in Human Skin

DeAnna Baker Frost¹ and Carol A. Feghali-Bostwick², ¹Medicine, Division of Rheumatology and Immunology, Medical University of South Carolina, Charleston, SC, ²Division of Rheumatology and Immunology, Division of Rheumatology and Immunology, Medical University of South Carolina, Charleston, SC, United States, Charleston, SC

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic Sclerosis (SSc) is a disease characterized by an increase in the synthesis of extracellular matrix (ECM) components in various organs, including the skin, resulting in increased morbidity. Like most autoimmune diseases, SSc has a female predominance that increases during childbearing years. Interestingly, post-menopausal SSc patients have higher circulating estradiol (E2) levels compared to age-matched controls. E2 exerts pro-fibrotic and pro-inflammatory activity, increasing ECM components and IL-6, both of which are also increased in SSc patients. Aromatase (CYP19) is a cytochrome p450 enzyme active in extra-gonadal tissues, including the skin. It is responsible for the aromatization of androgens into estrogens. Increased activity of aromatase may underlie the increase E2 levels in SSc patients. Since SSc dermal fibroblasts secrete increased levels of IL-6, and increased E2 levels are reported in SSc patients, we hypothesized that there is an interplay between E2 and IL-6 contributing to the pro-fibrotic phenotype.

Methods: Human skin in organ culture was stimulated with E2 or IL-6 and its soluble receptor, sIL6R, for 24 or 48 hours. Transcript levels of aromatase, IL-6, and collagen 1A1 were measured using real-time PCR. Aromatase activity was measured using an ELISA-based testosterone conversion assay. Statistical significance was determined using ANOVA, with significance defined as p≤0.05.

Results: Human skin stimulated with E2 or IL-6 + sIL-6R ex vivo showed increased levels of collagen. E2 stimulation also resulted in increased IL-6 transcript and protein levels. Stimulation of human skin with IL-6 and sIL-6R led to increases in the levels of aromatase mRNA. Skin samples stimulated with IL-6 and sIL-6R also had increased aromatase activity, translating into increased conversion of testosterone into estradiol. The aromatase activity decreased significantly after treatment with anastrozole, an aromatase inhibitor.

Conclusion: Our data show that both E2 and IL-6 exert pro-fibrotic effects in human skin. Our findings further establish the existence of a positive feedback loop between E2 and IL-6, supporting a pro-fibrotic cycle that leads to increased ECM production and fibrosis. Our results implicate E2 and IL-6 in dermal fibrosis in SSc. Our results also suggest that effective therapies for SSc may require concomitant inhibition of E2 and IL-6.
Proteomic Analysis of Human Fibroblasts in Systemic Sclerosis Reinforces the Role of Transforming Growth Factor-ß and Points Toward Epidermal Growth Factor Receptor / Phosphatidylinositol 3 Kinase Pathway Inhibition

Benjamin Chaigne1, Guilhem Clary2, Morgane Le Gall3, Nicolas Dumoitier4, Sebastien Lofek5, Philippe Chafey2, Pia Moinzadeh6, Thomas Krieg7, Christopher Denton8 and Luc Mouthon9
1Service de Médecine Interne, Centre de Référence Maladies Systémiques Autoimmunes Rares d’Île de France, hôpital Cochin, DHU Authors, Assistance Publique-Hôpitaux de Paris, Paris, France, 2INSERM U1016, Institut Cochin,, Paris, France, 3INSERM U1016 Institut Cochin, Paris, France, 4INSERM U1016, Institut Cochin, Equipe Neutrophiles et Vascularites, Paris, France, 5INSERM U1016, paris, France, 6Department of Rheumatology, UCL Division of Medicine, London, United Kingdom, 7Universität zu Köln, Köln, Germany, 8Department of Rheumatology, University College London, Royal Free Hospital, London, United Kingdom, 9Service de Médecine Interne, Hôpital Cochin, Centre de référence national pour les maladies systémiques autoimmunes rares d’Île de France, DHU Authors, Assistance Publique-Hôpitaux de Paris (AP-HP), Paris, France ;Université Paris Descartes Sorbonne Paris, Paris, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Systemic sclerosis (SSc) is a rare autoimmune connective tissue disorder characterized by autoimmunity, vasculopathy and fibrosis. Fibrosis is due to an exaggerated activation of fibroblasts by the transforming growth factor-ß (TGF-ß). In this study we investigated the proteomic response of skin fibroblasts to TGF-ß in patients with SSc.

Methods:
Skin fibroblasts from 4 patients with SSc and 3 healthy controls (HC) were cultured in the presence or in the absence of TGF-ß. Two-dimensional gel electrophoresis and mass spectrometry (MS) were used to identify proteins differentially expressed between groups. Ingenuity Pathway analysis (IPA) and Panther softwares were used to analyse identified proteins. Finally real-time cell analyser (RTCA) was used to assess fibroblast proliferation and viability in order to validate proteins of interest.

Results:
We identified 687 protein spots differentially expressed between groups. 297 protein spots were analysed by MS. Principal component analysis revealed significant differences between fibroblasts of patients with SSc and HC when cultured in the presence or in the absence of TGF-ß. IPA revealed specific process networks such as actin cytoskeleton signalling, integrin signalling, and remodelling of epithelial adherens junctions. Panther revealed predominant biological processes such as cellular process, metabolic process and cellular component organization. TGF-ß enhanced the synthesis of fibroblasts’ proteins involved in actin cytoskeleton signalling and integrin signalling. Using IPA and RTCA we identified and validated the involvement of epidermal growth factor receptor (EGFR) and phosphatidylinositol 3 kinase (Pi3K) in the proliferation and the viability of fibroblasts from patients with SSc.
Conclusion:

In conclusion, we confirmed that the proteome profile of fibroblasts differs between patients with SSc and HC and demonstrated that fibroblasts enhance their proteomic phenotype upon stimulation with TGF-β. We finally highlighted that EGFR and Pi3K are proteins of interest in fibroblasts from patients with SSc and should be considered as potential targets to inhibit fibrosis in SSc.

Disclosure: B. Chaigne, None; G. Clary, None; M. Le Gall, None; N. Dumoitier, None; S. Lofek, None; P. Chafey, None; P. Moinzadeh, None; T. Krieg, None; C. Denton, Actelion, Pfizer, GlaxoSmithKline, Bayer, Sanofi-Aventis, Boehringer Ingelheim, Genentech-Roche, CSL Behring, Biogen, 5,Actelion, GlaxoSmithKline, Bayer, Genentech-Roche, CSL Behring, 2; L. Mouthon, None.


Abstract Number: 770

Integrating Analysis of Skin RNA in Situ Hybridization Using Rnascope and Whole Skin Gene Expression in Systemic Sclerosis Skin to Localize Key Pathogenic Drivers of Skin Fibrosis

Corrado Campochiaro1, Emma C. Derrett-Smith1, Voon H. Ong2, Gail Pearse3, Katherine Nevin3, Shaun Flint3, Mary Morse3, Nicolas Wisniacki4 and Christopher Denton5, 1Centre for Rheumatology and Connective Tissue Diseases, UCL Division of Medicine, London, United Kingdom, 2Rheumatology, UCL Division of Medicine, London, United Kingdom, 3GlaxoSmithKline, Stevenage, United Kingdom, 4ImmunoImflammation, GlaxoSmithKline, Stevenage, United Kingdom, 5Department of Rheumatology, University College London, Royal Free Hospital, London, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Skin gene expression profiling can distinguish SSc from normal skin and can detect different subsets of disease. Previous studies have reported a cross-sectional relationship between the expression of genes in whole skin and the modified Rodnan skin score (mRSS). We aim to compare gene expression in early versus late dcSSc and define cells responsible for the upregulation of candidate genes.

Methods: Total RNA was extracted from forearm skin biopsies of 3 early dcSSc anti-RNA polymerase III positive (ARA+) patients and 3 late dcSSc ARA+ patients. COMP, chemokine ligand 2 (CCL2), PDGF-A, collagen type I a 1 chain (COL1A1), interferon Induced Protein 44 (IFI44), IL-6, MMP3, SERPINE, TGF-b and thrombospondin 1 (THBS1) was measured using quantitative PCR analysis. mRSS was assessed in all patients and correlated with normalized gene expression. RNA in situ hybridization for a-actin-2 (ACTA2), CCL2, COL1A1, COL3A1, COMP, SERPINE and THBS1 mRNA was performed using RNAScope¨ 2.5 LS Reagent Kit in early dcSSc ARA+ patients (n=2) and healthy controls (HC) (n=3). Semi-quantitative scoring criteria were applied (score from 0 to 4).

Results: Whole skin relative normalized gene expression of COMP, CCL2, IL-6, SERPINE and THBS1 was significantly (p < 0.05) higher in early compared to late SSc skin (COMP mean 25049.15 ± 10862.16 vs 5256.47 ± 2380.53; CCL2 mean 1722.04 ± 598.93 vs 638.25 ± 279.96; IL-6 mean 43.98 ± 40.76 vs 11.91 ± 5.44; SERPINE mean 1770.32 ± 704.46 vs 184.48 ± 61.37; THBS1 mean 7190.75 ± 309.89 vs 1176.81 ± 235.35) [Figure 1]. There was a positive correlation between
SERPINE and THBS1 and mRSS (SERPINE $r^2 = 0.493$, $p = 0.09$; THBS1 $r^2 = 0.91$, $p = 0.02$). Whole skin relative normalized gene expression of all the remaining genes, except for IFI44, was also higher in early compared to late patients although not significantly. RNAscope analysis revealed positive SERPINE staining in subsets of fibroblast-like cells located in the mid-dermis in early dcSSc only (score 3 and 4 in early dcSSc vs score 0 in HCs). An increased number of THBS1+ and COMP+ fibroblast-like cells (α-smooth muscle actin +) were found in the deep dermis of early dcSSc (score 4 in early dcSSc pts vs score 0, 2 and 3 in HCs).

**Conclusion:** SERPINE, THBS1, COMP, CCL2 and IL-6 are upregulated in early compared to late dcSSc patients. THBS1 and COMP are key genes associated with skin involvement and both are TGF-b regulated. RNAscope technology not only confirmed the upregulation of SERPINE, COMP and THBS1 in early dcSSc, but detected the expression of these genes in the dermis of patients in subsets of cells. These findings highlight how specific cells may be responsible for the pro-fibrotic and inflammatory changes typical of the early stages of the disease. Upregulation of fundamental pro-fibrotic and inflammatory genes could be crucial in the early stages of SSc and specific subsets of cells in the dermis could be the responsible for this.

**Disclosure:** C. Campochiaro, None; E. C. Derrett-Smith, None; V. H. Ong, None; G. Pearse, GlaxoSmithKline, 3,GlaxoSmithKline, 1; K. Nevin, GlaxoSmithKline, 3,GlaxoSmithKline, 1; S. Flint, GlaxoSmithKline, 3,GlaxoSmithKline, 1; M. Morse, GlaxoSmithKline, 3,GlaxoSmithKline, 1; N. Wisniacki, GlaxoSmithKline, 3,GlaxoSmithKline, 1; C. Denton, Actelion, Pfizer, GlaxoSmithKline, Bayer, Sanofi-Aventis, Boehringer Ingelheim, Genentech-Roche, CSL Behring, Biogen, 5,Actelion, GlaxoSmithKline, Bayer, Genentech-Roche, CSL Behring, 2.


**Abstract Number:** 771

**Serological Biomarkers of Collagen Formation Is Increased in Systemic Sclerosis**

Pernille Juhl, Mette Mogensen, Line Iversen, Tonny Karlsmark, Morten Karsdal, Anne-C. Bay-Jensen and Anne Sofie Siebuhr, Nordic Bioscience, Herlev, Denmark, Department of Dermatology, Bispebjerg Hospital, Copenhagen, Denmark, Biomarkers and Research, Nordic Bioscience, Herlev, Denmark, Biomarkers and Research, Nordic Bioscience, Herlev, Denmark, Biomarkers and Research, Nordic Bioscience, Herlev, Denmark, Biomarkers and Research, Nordic Bioscience, Herlev, Denmark, Biomarkers and Research, Nordic Bioscience, Herlev, Denmark

**First publication:** September 18, 2017
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a multisystem, autoimmune disease characterized by immune dysregulation, vasculopathy and excessive fibrosis of the skin and internal organs. Fibrosis is the pathological state where the unbalance in ECM turnover is shifted towards increased formation. The main family of ECM protein is collagen and the excessive fibrosis results in release of ECM fragments to circulation, where they may be quantified as biomarkers. Skin is rich in type I and III collagen, while type IV, V, VI and VII collagen is present to a lesser amount. The objective is to investigate if the level of collagen turnover could aid in describing skin fibrosis in SSc.

Methods: SSc patients (n=121) from a cross-sectional study fulfilling the 2013 ACR/EULAR SSc criteria were included together with non-symptomatic controls (n=9). The study included both limited SSc (n=79) and diffuse SSC (n=42). The mean age of the population was 57.4 (SD 11.6) years, 84% were female, mean disease duration was 11.7 (8.9) years and mean skin score was 11.2 (8.6). Biomarkers of type I, III, IV, V and VI collagen formation (PINP, PRO-C3, P4NP7S, PRO-C5 and PRO-C6, respectively) and type III, IV, V, VI and VII collagen degradation (C3M, C4M, C5M, C6M and C7M, respectively) were assessed in serum by competitive ELISAs. Furthermore, a biomarker of a degraded and citrullinated form of vimentin (VICM) was measured in serum. Statistical differences between non-symptomatic controls and SSc patients was tested by t-test (Mann-Whitney).

Results: In SSc patients formations biomarkers of type I, VI and VII collagen was significantly increased compared to non-symptomatic controls (PINP: P=0.02, PRO-C5: P=0.01, PRO-C6: P=0.03) (Figure 1). Formation biomarkers of type III and VI collagen were not significantly increased. The degradation biomarkers of type III, IV and V collagen were not significantly increased in SSc patients (Figure 2). However, degradation of type VI and VII collagen (C6M: P=0.02 C7M: P=0.05) were significantly increased in SSc patients. Furthermore, VICM was also significantly elevated in SSc patients compared to non-symptomatic controls (P<0.0001).

Conclusion: This pilot study showed that collagen turnover appears to be significantly different between SSc patients and non-symptomatic controls. Even if the collagen formation is increased, the degradation of all collagens are not. These data suggest that serological assessment of ECM turnover could be relevant in SSc, and offers area of investigation of disease pathogenesis.

![Figure 1: Mean level of collagen formation biomarkers in SSc patients and non-symptomatic controls. Mann-Whitney T-test was used to test difference between the two groups. Statistical significance was considered when P<0.05. Data is shown as mean ± SEM](image-url)
Molecular Mechanism for the Therapeutic Effect of Extracorporeal Shock Wave Therapy on Digital Ulcers of Systemic Sclerosis

Yukiko Kamogawa1, Hiroshi Fujii1, Tsuyoshi Shirai1, Tomonori Ishii2 and Hideo Harigae1, 1Department of Hematology and Rheumatology, Tohoku University Graduate School of Medicine, Sendai, Japan, 2Clinical Research, Innovation and Education Center, Tohoku University Hospital, Sendai, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster I
Session Type: ACR Poster Session A
**Background/Purpose:** Digital ulcers (DUs) are the most common skin manifestations in systemic sclerosis (SSc). DUs in SSc are not usually caused by vasculitis and are often refractory to conventional immunosuppressive therapies. Extracorporeal shock wave therapy (ESWT) has been used to treat urinary stones since 1980s. The therapy has also been applied to treat various diseases such as chronic tendinopathy, ischemic heart disease, and wound healing disorders. Previously, we reported that the low energy ESWT dramatically improved refractory DUs in SSc (Saito et al. Tohoku J. Exp. Med. 238:19, 2016). Because ESWT was applied on palms and forearms distant from DUs, we considered that the healing effect of ESWT on DUs may be due to enhanced angiogenesis via some angiogenic factors rather than a direct physical stimulus on ulcers. However, the precise molecular mechanism remains unknown. In this study, we tried to clarify the molecular basis of shock wave (SW) treatment on dermal endothelial cells using *in vitro* SW treatment system. We found that FBJ murine osteosarcoma viral oncogene homolog B (FOSB), which is a component of multipotent transcriptional factor AP-1, was prominently increased after SW treatment. We also examined the functional consequence of FOSB on angiogenesis.

**Methods:** (1) Human Dermal Microvascular Endothelial Cells (HDMECs) were cultured on a cover glass with 2.5% agarose gel (Fig-1) and treated with SW. RNA was extracted from HDMECs 2 h after SW treatment, and gene expression profiling was analyzed using microarray (Agilent). (2) FOSB expression after SW treatment was measured using RT-PCR. (3) FOSB-expressing HDMECs were stimulated with serum, and vascular growth factor A (VEGFA) induction was evaluated using RT-PCR.

**Results:** In the culture system shown in Fig-1, HDMECs were stable without any significant detachment or death of cells after SW treatment. The microarray analysis revealed that FOSB gene expression level was significantly elevated (>10-fold, p < 0.05) after SW treatment in three independent experiments. In RT-PCR analysis, FOSB gene expression level was also increased in proportion to SW energy at 1 h after the treatment. Aberrant expression of FOSB in HDMECs increased VEGFA induction by stimulation with serum (Fig-2).

**Conclusion:** SW treatment elevated FOSB gene expression in HDMECs, which directly led to increased sensitivity for VEGFA induction, suggesting that FOSB may be a master regulator responsible for the angiogenic effect of ESWT. This finding may help in the development of more effective strategies using ESWT for DUs in SSc.
The Immunophenotyping of Peripheral Blood Associates with Nailfold Microvascular Changes in Patients with Systemic Sclerosis

Satoshi Kubo1, Shingo Nakayamada2, Maiko Yoshikawa1, Yusuke Miyazaki1, Hiroko Yoshinari3, Yurie Satoh3, Yasuyuki Todoroki3, Kazuhide Nakano2, Shigeru Iwata4, Kentaro Hanami1, Shunsuke Fukuyo5, Minoru Satoh6 and Yoshiya Tanaka7, 1The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, 2First Department of Internal Medicine, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, 3University of Occupational and Environmental Health, Japan, Fukuoka, Japan, 4First Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, 5University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, 6Department of Clinical Nursing, School of Health Sciences, University of Occupational and Environmental Health, Kitakyushu, Japan, 7The First Department of Internal Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster 1
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

The immunophenotyping of peripheral blood associates with nailfold microvascular changes in patients with systemic sclerosis

Background/Purpose: Systemic sclerosis (SSc) is a complex disease with autoimmunity and vasculopathy, leading to subsequent fibrosis. However, little is known about the relationship between immunological abnormality and microvascular changes. Here, we stratified SSc patients based on peripheral immunophenotyping and investigated the association between immunophenotyping and vasculopathy in SSc.
**Methods:** Ninety patients with SSc were enrolled in this study. Nailfold videocapillaroscopy was performed for qualitative assessment of morphological microvascular. Peripheral blood mononuclear cells were obtained and the phenotype of circulating B, T, NK and dendritic cells was defined based on flow cytometric analysis for human immune system termed "the Human Immunology Project". Based on these results, SSc patients were classified into subgroups by cluster analysis.

**Results:** The proportion of effector T cell was higher in SSc than the healthy control. The proportion of activated Th1 (2.0% vs 1.3%) and activated Th17 (1.2% vs 0.8%), but not Treg and Tfh, was higher in SSc. On the other hand, the abnormalities of B cell differentiation in SSc patients were mild. The proportion of plasmablast was comparable and that of naïve B cell was higher in SSc. However, cluster analysis stratified SSc patients into three subgroups (Figure): patients who showed almost normal immunophenotype (without abnormality group), patients with high percentage of effector T cell and Th17 cells (T cell-dominant group), and patients with high proportion of plasmablast and effector B cell (B cell-dominant group). The majority (81%) of SSc patients belonged to the without abnormality group. In contrast, the percentage of patients who had severe microvascular changes was highest among the T cell-dominant group and the B cell-dominant group.

**Conclusion:** Immune abnormality in peripheral blood was not necessarily found in all cases of SSc. However, our data indicated that there are two types of immunological abnormalities associated with the risk of vasculopathy in patients with SSc. Accumulation of further evidence will not only contribute to elucidate the pathogenesis of SSc but also help the development of targeted therapy.

**Figure.** Immune cell characteristics based on statistical cluster analysis in patients with systemic sclerosis: Immunophenotypes of the three groups. P values by one-way analysis of variance.

**Disclosure:** S. Kubo, Bristol-Myers Squibb, 8,Pfizer Inc, 8,Takeda Pharmaceutical Company Ltd, 8; S. Nakayamada, Bristol-Myers Squibb, 8; M. Yoshikawa, None; Y. Miyazaki, None; H. Yoshinari, None; Y. Satoh, None; Y. Todoroki, None; K. Nakano, None; S. Iwata, None; K. Hanami, None; S. Fukuyo, None; I. Miyagawa, None; M. Satoh, None; Y. Tanaka, Mitsubishi-Tanabe, Takeda, Bristol-Myers, Chugai, Astellas, Abbvie, MSD, Daiichi-Sankyo, Pfizer, Kyowa-Kirin,
The αV Integrin Inhibitor Abituzumab Inhibits Myofibroblast Differentiation

Eileen Samy, Yin Wu, Georgianna Higginbotham, Roland Grenningloh and Daigen Xu
1TIP Immunology, EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA, 2EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster 1
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Scleroderma is a progressive fibrotic multi-organ disease characterized by the hardening and tightening of the skin and connective tissues. TGF-β1 is a potent mediator of fibroblast to myofibroblast transition (FMT), which contributes to increased extracellular matrix deposition and is the main driver of disease. There is substantial evidence for crosstalk between αV integrins and TGF-β during these processes. TGF-β is secreted in a latent form which contains a Latency Associated Peptide (LAP) region. The LAP of TGF-β1 contains an Arg-Gly-Asp (RGD) motif, which interacts with the integrins αVβ1, αVβ3, αVβ5, αVβ6 and αVβ8 resulting in activation of TGF-β1. Abituzumab is a human antibody specific for αV and therefore inhibits ligand binding of these five integrins. The goal of this study was to determine if abituzumab can block TGF-β activation and FMT in vitro and thus have potential as a scleroderma therapeutic.

Methods: Expression of integrins and myofibroblast markers in human lung fibroblasts was analyzed by RT-PCR in the presence and absence of abituzumab. In addition, we examined the ability of abituzumab to block FMT in an epithelial cell (NCI-H358 or Calu3)/fibroblast co-culture, mimicking the potential interaction of epithelial cells and fibroblasts in tissues undergoing fibrosis.

Results: Analysis of integrin expression showed that human lung fibroblasts express ITGB1>ITGB5>ITGB8>ITGB3. TGF-β-induced FMT caused an increase in the expression of ITGB5, and to a lesser extent ITGB1 and ITGB3. TGF-β treatment increased myofibroblast marker genes in lung fibroblasts, and immunofluorescence staining revealed increased αVβ5 and α-SMA expression. Abituzumab treatment of fibroblast cultures showed a reduction in the increased αSMA expression, as well as production of IL-6 and collagen gel contraction, demonstrating an ability for abituzumab to block TGF-β-induced FMT. Co-culture of epithelial cells with fibroblasts resulted in induction of αSMA and multiple mRNA transcripts that are markers for FMT, as well as increased IL-6 production. In this system, these markers were reduced by abituzumab treatment, demonstrating that αV integrins play a role in FMT.

Conclusion: Results reported here indicate abituzumab has the potential to block TGF-β-induced FMT and thus development of fibrosis. It may potentially be an efficacious drug for treatment of scleroderma.

Disclosure: E. Samy, EMD Serono, Inc, 3; Y. Wu, EMD Serono, Inc, 3; G. Higginbotham, EMD Serono, Inc, 3; R. Grenningloh, EMD Serono, Inc, 3; D. Xu, EMD Serono, Inc, 3.
Abstract Number: 775

Transcriptome Sequencing Reveals Genetic Polymorphisms Associated with Ssc Gene Expression Subtypes

Guoshuai Cai1, Bhaven K. Mehta2, Mengqi Huang2, Jennifer Franks1, Tammara A. Wood1, Kathleen D. Kolstad3, Marianna Stark4, Antonia Valenzuela5, David Fiorentino6, Robert W. Simms7, Nicole Orzechowski8, Lorinda Chung9 and Michael L. Whitfield2, 1Department of Molecular and Systems Biology, Geisel School of Medicine at Dartmouth, Hanover, NH, 2Molecular and Systems Biology, Geisel School of Medicine at Dartmouth, Hanover, NH, 3Rheumatology, Stanford University Medical Center, Stanford, CA, 4Stanford University, Stanford, CA, 5Immunology and Rheumatology, Stanford University, Palo Alto, CA, 6Department of Dermatology, Stanford University School of Medicine, Palo Alto, CA, 7Rheumatology, Boston University School of Medicine, Boston, MA, 8Dartmouth-Hitchcock Medical Center, Lebanon, NH, 9Rheumatology, Stanford University Medical Center, Palo Alto, CA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a complex disease characterized by substantial genotypic and phenotypic heterogeneity. Four molecular gene expression subsets have been identified from SSc skin, including inflammatory, fibroproliferative, normal-like, and limited. Genome-wide association studies have identified genetic variants associated with disease risk. However, these studies were not designed to interrogate genetic changes underlying specific gene expression subtypes. Here, our objective was, by RNA-seq in SSc skin, to identify potential genetic variants associated with specific gene expression subtypes and disease phenotypes.

Methods: We generated RNA-seq data from skin biopsies of 42 patients with SSc and 14 healthy controls. Variants were detected and filtered by quality, sequencing depth, minor allele frequency, and potential deleterious effects on gene function. Gene burden tests were used to identify susceptibility loci in cases compared to healthy controls, as well as in healthy controls of a European population from the phase III 1000 Genomes Project (N=503). We further quantitated gene expression and used an additive genetic model to identify gene expression associated variants. Variants enriched in each of the SSc molecular subsets were detected by Fisher's exact test.

Results: We identified 267 potentially deleterious variants in 253 genes in patients with SSc, including 30 genes (e.g. IRF6, NCF2, IL37) enriched in immunological processes and 10 genes (e.g. ITGB4, COL5A1, LAMA3) significantly enriched in extracellular matrix-related pathways. We found variants enriched in each of the inflammatory (35 variants), fibroproliferative (7 variants), and normal-like (45 variants) subsets. Potentially deleterious variants in IL37 were enriched in patients with diffuse skin involvement and were significantly correlated with increased gene expression of IL6 and STAT3 in patient samples. Consistently, HapMap B cell lines harboring deleterious IL37 variants showed increased expression of IL6 upon immune stimulation.

Conclusion: This study demonstrates the value of RNA-seq for identifying genetic variants associated with SSc gene expression subtypes. Results indicate genetic variants can be associated with each of the intrinsic gene expression subset and may influence innate immune responses and ECM deposition. The identified IL37 variant may modulate SSc pathogenesis by increasing expression of the IL-6 pathway.

Disclosure: G. Cai, None; B. K. Mehta, None; M. Huang, None; J. Franks, None; T. A. Wood, Celdara Medical, LLC, 5; K. D. Kolstad, None; M. Stark, None; A. Valenzuela, None; D. Fiorentino, None; R. W. Simms, None; N. Orzechowski, None; L. Chung, Cytori, Actelion, Reata, 5; M. L. Whitfield, Corbus, UCB, glaxosmithkline, 5,Celdara medical llc, 9.
Circulating Fibrocytes in Systemic Sclerosis Patients and Healthy Subjects: An in Vitro Study

Maurizio Cutolo¹, Paola Montagna², Stefano Soldano², Amelia Chiara Trombetta³, Paola Contini⁴, Vanessa Smith⁵, Barbara Ruoaro², Alberto Sulli³ and Renata Brizzolara², ¹Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, IRCCS A.O.U. San Martino-IST, University of Genova, Genoa, Italy, Genoa, Italy, ²Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, IRCCS San Martino, Genoa, Italy, Genoa, Italy, ³Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, IRCCS A.O.U. San Martino-IST, University of Genova, Genoa, Italy, Genova, Italy, ⁴Division of Clinical Immunology, Department of Internal Medicine, University of Genova, Genoa, Italy, Genova, Italy, ⁵Faculty of Internal Medicine, Ghent University, Ghent, Belgium

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster I
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Circulating fibrocytes seem to exert immunomodulatory effects, expressing class II major histocompatibility complex molecules (HLA-DP, -DQ, and -DR) and could have a role in fibrosing diseases (i.e. systemic sclerosis, SSc), due to the capacity of such cells to migrate into affected tissues (through CXCR4/CXCL12 interaction) and to differentiate into fibroblasts/myofibroblasts, then inducing matrix protein deposition and fibrosis [1-4].

The aim of this study was to isolate fibrocytes from peripheral blood mononuclear cells (PBMCs) of SSc patients and healthy subjects (CNTs) and comparing both after having identified them by fluorescence-activated cell sorter analysis (FACS) (using their specific markers: the leukocyte common antigen CD45, collagen I (COL I), the chemokine receptor CXCR4 and HLA-DR [2]).

Methods:
Blood samples were collected, after signed informed consent, at basal time (T0), from 11 SSc patients (treated only with different vasodilator drugs) and 5 CNTs. In addition, PBMCs, isolated from 9 SSc patients and 5 CNTs, were cultured on fibronectin-coated plates [5]. The non-adherent cells were removed and after 8 days (T8) of culture (standardized time) the adherent spindle shaped cells were lifted through incubation in 0.05% EDTA (ice-cold). Fibrocyte identification was performed by FACS, using anti-CD45, anti-COL I, anti-CXCR4 and anti-HLA-DR monoclonal antibodies.

Results:
FACS analysis revealed that, at T0, among the CD45+ cells, the percentage of fibrocytes, identified as CD45+, COL I+, CXCR4+ was 1.0±1.2 % in SSc patients and 0.5±0.2 % in healthy subjects (CNTs). In addition, the HLA-DR expression on fibrocytes in both CNTs and SSc patients showed low values (22.1±21.1 % and 13.1±4.7 %, respectively).

After 8 days (T8) of culture, fibrocytes presented adherent and spindle shaped morphology and FACS analysis demonstrated that the percentage of fibrocytes CD45+, COL I+, CXCR4+ increased up to 52.8±27.1% in SSc patients and up to 61.9±24.4 in CNTs, compared to T0.
Therefore, at T8 of culture, the HLA-DR+ expression on fibrocytes in SSc patients and CNTs strongly increased (90.1±22.7 \% and 97.9±1.9, respectively), compared to T0.

Conclusion:

Circulating fibrocytes, identified as CD45, COL I and CXCR4 positive cells, resulted in very low percentage in peripheral blood at basal time, but after 8 days of culture in proper conditions, the percentage of differentiated fibrocytes increased up to 50 times in SSc (and CNTs), whereas the HLA-DR expression increased up to 68\% in SSc and 85\% in CNTs. Data suggest that circulating fibrocytes might be an early cellular targets in presence of fibrosing diseases.

References:


Disclosure: M. Cutolo, None; P. Montagna, None; S. Soldano, None; A. C. Trombetta, None; P. Contini, None; V. Smith, None; B. Ruaro, None; A. Sulli, None; R. Brizzolara, None.


Abstract Number: 777

Differences between Temporal Artery Biopsy-Positive and Biopsy-Negative Giant Cell Arteritis: A Comparative Cohort Study

Matthew J. Koster\textsuperscript{1}, Karthik Yeruva\textsuperscript{1}, Cynthia S. Crowson\textsuperscript{2} and Kenneth J. Warrington\textsuperscript{1}, \textsuperscript{1}Rheumatology, Mayo Clinic, Rochester, MN, \textsuperscript{2}Health Sciences Research, Mayo Clinic College of Medicine and Science, Rochester, MN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Giant cell arteritis (GCA) is the most common systemic vasculitis in patients aged 50 years or older. The presence of cranial features and an abnormal temporal artery biopsy have historically been the primary focus for diagnosis of this condition. A notable percentage of patients with GCA have negative temporal artery biopsies. Few cohort studies exist comparing the presentation and outcome of patients based on biopsy positivity.

Methods: Patients with temporal artery biopsy-negative GCA diagnosed between 1/1/1998 and 12/31/2013 were identified retrospectively. Final diagnosis was confirmed by consensus among two rheumatologists and a physician abstractor. Clinical characteristics, treatment course and outcomes were compared to a cohort of biopsy-positive patients with GCA (n=286) from the same institution.

Results:

110 patients with temporal artery biopsy-negative GCA were identified. Unilateral biopsies were performed in 73, bilateral-sequential in 10, and bilateral same day in 27 cases. Median duration between steroid initiation and biopsy was 3 days. Median length of first biopsy was 14mm and second biopsy (if performed) was 22mm. Among biopsy-negative patients with advanced imaging within 6-months of diagnosis, 67\% (41/61) had evidence of large vessel vasculitis.
Patients with biopsy-negative GCA were younger (72.0±9.0 vs 75.0±7.6; p=0.001), met fewer ACR criteria (≥3 criteria 64% vs 95%; p<0.001) and had a shorter time from symptom onset to diagnosis (median 1.1 vs 2.1 months; p<0.001). Vascular risk factors evaluated at diagnosis showed a higher rate of pre-existing hypertension and obesity among patient with biopsy-negative GCA but similar rates of smoking and diabetes mellitus. Frequency of headache and vision loss at time of presentation were similar between groups. However, biopsy-negative GCA patients had more temporal artery tenderness (35% vs 16%; p<0.001) and arm claudication (13% vs 2%; p<0.001) but less frequent jaw claudication (19% vs 52%; p<0.001). Anorexia, fatigue, and arthralgia were also more commonly noted in biopsy-negative patients. Baseline CRP was lower among patients with negative biopsies (44.3±53.6 vs 70.4±63.9 mg/L; p<0.001).

Initial prednisone dose was similar among both cohorts. Although cumulative glucocorticoid (GC) was lower in biopsy-negative patients at 1 year (6.3±2.6 vs 7.2±2.7 g; p=0.004), cumulative GC doses at 2-years and 5-years were equivalent. Biopsy-positive patients (5-years, 56±3%) were able to discontinue GC sooner than biopsy-negative patients (5-years, 30±5%; p<0.001). The number of relapses, time-to-first relapse, annual relapse rate and mortality did not differ based on biopsy positivity.

**Conclusion:** While similarities are present, there are notable differences in clinical presentation between biopsy-positive and -negative GCA. Although current ACR criteria underperform in patients with biopsy-negative GCA, imaging studies are often useful for confirmation of diagnosis. Further studies are needed to confirm and understand the observed variability in GC duration.

**Disclosure:** M. J. Koster, None; K. Yeruva, None; C. S. Crowson, None; K. J. Warrington, None.


**Safety Number:** 778

**Safety Events in Giant Cell Arteritis and Rheumatoid Arthritis Patient Populations**

**Sara Gale**¹, Sophie Dimonaco², Huong Trinh¹, Katie Tuckwell², Neil Collinson², John H. Stone³, Khaled Sarsour¹, Jinglan Pei⁴, Jennifer H. Best¹, Christine Birchwood⁴ and Shalini Mohan¹, ¹Genentech, South San Francisco, CA, ²Roche Products, Ltd., Welwyn Garden City, United Kingdom, ³Massachusetts General Hospital Rheumatology Unit, Harvard Medical School, Boston, MA, ⁴Genentech, Inc., South San Francisco, CA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Vasculitis Poster I: Large Vessel Vasculitis  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Recent clinical trial findings have shown efficacy for tocilizumab (TCZ) in treating giant cell arteritis (GCA).¹² TCZ was approved for the treatment of GCA in the US in 2017 and of rheumatoid arthritis (RA) in the EU in 2009 and in the US in 2010, and it has a well-characterized safety profile in RA patients (pts). However, the safety profile of TCZ in GCA pts may differ from that observed in RA pts due to differences in the underlying disease and the higher dosing of glucocorticoids (GCs) used to treat GCA. This study describes the incidence rates (IRs) of safety events in GCA pts or RA pts in a general healthcare claims database and in the TCZ clinical development program to contextualize the observed safety profile of TCZ in GCA.
Methods: Adverse events of special interest (AESI) IRs for TCZ in adult GCA and RA pts were estimated from a US-based MarketScan administrative healthcare claims database. GCA pts were ≥50 years and received ≥2 prescriptions for oral GCs (the first within 6 months of diagnosis); for comparability, only RA pts who were ≥50 years were included. AESI included infections, hepatic events, gastrointestinal (GI) perforation, demyelination, cardiovascular events, bleeding events, and malignancies. AESI IRs were also calculated for a pooled population of RA pts who received TCZ in clinical trials and for GCA pts who received TCZ in the GiACTA clinical trial.1-3 Risks for AESI among GCA pts vs RA pts in the claims database, adjusted for age and oral GC use, were estimated with Poisson regression.

Results: The healthcare claims database included 4804 GCA pts (mean [SD] age, 73.4 [9.8] years; follow-up, 3.89 [3.12] years) and 15,164 RA pts (mean [SD] age, 60.3 [8.17] years; follow-up, 4.52 [3.78] years). IRs of myocardial infarction, stroke, GI perforation, and hepatic events in TCZ-naive GCA pts from the healthcare claims database (Table) exceeded IRs in TCZ-naive RA pts from healthcare insurance claims. Consistent with this, AESI IRs in TCZ-treated GCA pts (n = 149, ~138 PY) in the GiACTA clinical trial were different from those in TCZ-treated RA pts (n = 7647; mean [SD] age, 52 [12.6] years; ~22,394 PY) in the pooled clinical trial population. GCA pts were at higher risk than RA pts for all AESI in the US claims database after adjusting for age and oral GC use.

Conclusion: TCZ-naive GCA pts from the healthcare claims analysis had higher AESI IRs than TCZ-naive RA pts. Clinical trial data for TCZ in RA pts and GCA pts reflect these findings and suggest differences in the underlying disease burdens associated with RA and GCA. The higher doses and longer courses of GCs used in GCA may also influence the incidence of AESI. Future analyses are needed to determine how differences in patient demographics may further differentiate the safety profile of TCZ between RA pts and GCA pts. References: 1Stone H et al. Arthritis Rheumatol. 2016;68:S10 abstr. 2Stone JH et al. N Engl J Med. In press. 3Villiger PM et al. Lancet. 387(10031):1921.

<table>
<thead>
<tr>
<th>Table</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data Source</td>
</tr>
<tr>
<td>---------</td>
</tr>
<tr>
<td>TCZ exposure</td>
</tr>
<tr>
<td>Patient population</td>
</tr>
<tr>
<td>n = 149 [*138 PY]</td>
</tr>
<tr>
<td>AESI Events per 100 PY</td>
</tr>
<tr>
<td>(95% CI)</td>
</tr>
<tr>
<td>AESI Events per 100 PY</td>
</tr>
<tr>
<td>(95% CI)</td>
</tr>
<tr>
<td>Risk Ratio (95% CI)</td>
</tr>
<tr>
<td>GCA Risk/RA Risk Ref*</td>
</tr>
</tbody>
</table>

Disclosure: S. Gale, Genentech/Roche, 1, Genentech/Roche, 3; S. Dimonaco, Roche Products Ltd., 1, Roche Products Ltd., 3; H. Trinh, Genentech, 3; K. Tuckwell, Roche, 1, Genentech, 3; N. Collinson, Roche Products Ltd., 1, Roche Products Ltd., 3; J. H. Stone, Roche, 2, Roche, 5; K. Sarsour, Genentech, 3; J. Pei, Roche, 1, Genentech, 3; J. H. Best, Roche, 1, Genentech, 3; C. Birchwood, Genentech, 3; S. Mohan, Genentech, 3.
Abstract Number: 779

Assessment of Treatment Response By 18f-Fludeoxyglucose Positron Emission Tomography (FDG-PET) in Patients with Large Vessel Vasculitis (LVV)

Shubhasree Banerjee1, Sara Alehashemi2, Ali Cahid Civelek3, Elaine Novakovich4, Armin Bagheri5, Ashkan Malayeri3, Mark Ahlman3 and Peter C. Grayson6,
1Fellowship and training branch, NIAMS/NIH, Bethesda, MD, 2Rheumatology, National Institutes of Health, Bethesda, MD, 3Radiology and Imaging Sciences, National Institutes of Health, Bethesda, MD, 4Systemic Autoimmunity Branch, NIAMS, National Institutes of Health, Bethesda, MD, 5Vasculitis Translational Research Program, NIAMS, NIH, Bethesda, MD, 6Research, National Institutes of Health, Bethesda, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
Disease activity in large vessel vasculitis (LVV) is traditionally assessed by clinical and serological (ESR, CRP) parameters. Imaging assessment, including FDG-PET, may also be useful to monitor LVV. The study objective was to determine if currently available therapies for LVV impact disease activity as assessed by clinical, serologic, and imaging-based parameters.

Methods:
Patients with giant cell arteritis (GCA) or Takayasu’s arteritis (TAK) were recruited into a prospective, observational cohort. All subjects in this study underwent ≥2 FDG-PET/CT scans at 6-month intervals. Serologic assessment (ESR, CRP), clinical assessment [physician global assessment (PGA)] and imaging assessment (PETVAS) was determined at each visit. PETVAS is a global summary score of arterial FDG uptake assessed qualitatively relative to liver activity in 9 vascular beds with higher scores indicating more vascular inflammation. Clinical and imaging assessments were performed blinded to each other. Treatment status between visits was categorized as increased, decreased, or unchanged. Treatment change was defined as change in daily prednisone by ≥5mg or addition/50% dose change of a DMARD or biologic therapy. Paired Wilcoxon test was used to compare changes in PETVAS, ESR, CRP and PGA with change in overall therapy and with addition/increase in specific medications.

Results:
FDG-PET/CT was performed in 33 patients with LVV (GCA=21; TAK=12) over 98 visits. Interval treatment changes involved glucocorticoids (n=32), methotrexate (n=13), tocilizumab (n=7), TNF inhibitors (n=7), or another DMARD/biologic (n=6). Increased, decreased, or unchanged therapy was recorded over 27, 13, and 23 visit intervals respectively. There was simultaneous glucocorticoid reduction with DMARD increase over 2 intervals, which were excluded from analysis. In the increased treatment group, a significant reduction in PETVAS score (p<0.01), inflammatory markers (p<0.01) and PGA (p=0.01) was noted. In the decreased treatment group, PETVAS scores increased (p=0.05) but there was no change in ESR (p=0.3), CRP (p=0.2), or PGA (p=0.28). In the unchanged treatment group, PETVAS (p=0.88), ESR (p=0.8), CRP (p=0.6) and PGA (p=0.48) remained unchanged. In terms of specific therapies, addition of tocilizumab, resulted in significant reduction in PETVAS (p=0.01), acute phase reactants (p=0.01) and PGA (p=0.03), whereas TNF inhibitors and methotrexate addition/dose increase had variable effects on clinical, serological, and imaging parameters.

Conclusion:
Similar to clinical and serologic assessment, vascular inflammation assessed by FDG-PET improves with increased treatment and is stable without change in therapy. Unlike clinical and serological assessment, which did not change with reduction in treatment over a 6 month interval, vascular inflammation assessed by FDG-PET worsens with decreased therapy. Specific medications may affect vascular FDG uptake differently. These findings suggest that FDG-PET is useful to monitor treatment response and may be a more sensitive biomarker to detect disease recurrence in the setting of treatment reduction compared to clinical and serologic assessment.

Disclosure: S. Banerjee, None; S. Alehashemi, None; A. C. Civelek, None; E. Novakovich, None; A. Bagheri, None; A. Malayeri, None; M. Ahlman, None; P. C. Grayson, None.


Abstract Number: 780

Short and Long-Term Follow-up with Tocilizumab in Giant Cell Arteritis. National Multicenter Study of 49 Patients of Clinical Practice

Lucia C. Domínguez-Casas1, Javier Loricera1, Jose L. Hernández2, Santos Castañeda3, Vicente Aldasoro4, María Varela-García5, Rosario Ibañez-Bosh5, Antonio Mera6, Eva Pérez-Pampin6, Alicia Humbría7, Jaime Calvo-Alén8, Elena Aurrecoechea9, Javier Narváez10, Amalia Sánchez-Andrade11, Paloma Vela12, Elvira Diez Alvarez13, Clara Moriano14, Cristina Mata15, Pau Lluch16, Concepción Moll17, Íñigo Hernández-Rodriguez18, Vanesa Calvo-Rio1, José Andrés Román-Ivorra19, Carlos Vazquez20, Alfonso Corrales1, MC Gonzalez-Vela21, Francisco Ortiz-Sanjuán22, Belén Atienza-Mateo1, José Luis Martín-Varillas1, Miguel Angel González-Gay23 and Ricardo Blanco1.

1Rheumatology, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, 2Internal Medicine, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, 3Hospital Universitario La Princesa. IIS-IP. Madrid. Spain, Madrid, Spain, 4Hospital Alto Deba. Mondragón. Spain, Mondragon, Spain, 5Rheumatology, Complejo Hospitalario de Navarra. Navarra. Spain, Navarra, Spain, 6Rheumatology, Complejo Hospitalario Universitario de Santiago. Galicia. Spain, Santiago de Compostela, Spain, 7Rheumatology, Hospital Universitario La Princesa. IIS-IP. Madrid. Spain, Madrid, Spain, 8Rheumatology, Hospital de Sierallana. Torrelavega. Cantabria. Spain, Alava, Spain, 9Rheumatology, Hospital de Sierallana, Torrelavega. Cantabria. Spain, Torrelavega, Spain, 10Rheumatology Department, Hospital de Bellvitge. Barcelona. Spain, L’Hospitalet de Llobregat, Spain, 11Hospital Universitario Lucus Augusti. Lugo. Spain, Lugo, Spain, 12Reumatología, Hospital General Universitario de Alicante. Alicante. Spain, Alicante, Spain, 13Complejo Asistencial Universitario de León. León. Spain, León, Spain, 14Rheumatology, Complejo Asistencial Universitario de León. León. Spain, León, Spain, 15Rheumatology, Hospital de Laredo. Laredo. Spain, 16Rheumatology, Hospital Mateu Orfila. Menorca. Spain, Menorca, Spain, 17Rheumatology., Hospital Mateu Orfila. Menorca. Spain, Menorca, Spain, 18Rheumatology, CHUVI Vigo. Galicia. Spain, Vigo, Spain, 19Rheumatology, Hospital Universitario La Fe. Valencia. Spain, Valencia, Spain, 20Rheumatology, Hospital Miguel Servet. Zaragoza. Spain, Zaragoza, Spain, 21Pathology Anatomy, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, 22Rheumatology., Hospital Universitario La Fe. Valencia. Spain, Valencia, Spain, 23Rheumatology, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Johannesburg, South Africa

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM
Background/Purpose: Randomized clinical trial has shown the efficacy of tocilizumab (TCZ) in Giant cell arteritis (GCA). However this data are of selected cases of clinical trial and only a short follow-up have been published. Our aim was to assess the short and long-term efficacy/side effects in clinical practice.

Methods: Multicenter open-label study on 49 GCA patients treated with TCZ [iv; 8 mg/kg/monthly (n=45), and subcutaneously; 162 mg/week (n=4)]. We assessed the short and long-term efficacy/safety and the optimization of TCZ dose.

Results: We included 49 patients (39 women/10 men), mean age 73±9 years. The main clinical features at TCZ onset were: polymyalgia rheumatica (n=31), headache (25), asthenia (17), constitutional syndrome (15), jaw claudication (5), and visual loss (6). Besides corticosteroids and before TCZ, 43 patients had also received several conventional immunosuppressive and/or biologic drugs. 45 of 49 patients achieved a rapid and maintained clinical improvement after TCZ (Table). After a median follow-up of 18 [IQR, 7-28] months we observe a reduction of the median of: a) C-reactive protein; b) ESR; and c) prednisone dose. In this follow-up period, the outcome of patients was as follows: a) discontinuation of TCZ due to sustained remission(n=8); b) dose reduction due to improvement (8) or side effects (4); c) withdrawal of TCZ because of side effects (9); and d) the same dose that at onset (19). TCZ was discontinued due to: severe neutropenia; colon adenocarcinoma; cytomegalovirus infection; Alzheimer’s disease and atrioventricular blockade; hypertensive crisis during infusion; myelodysplastic syndrome; colon neoplasm and overall health deterioration. The latter patient died because of stroke. Another patient also died after the second TCZ infusion due to stroke in the context of an infective endocarditis. In another one, the dose had to be reduced by recurrent urinary tract infection. In other two patients TCZ was reduced because of moderate neutropenia (one of them also developed cellulitis) and another patient developed diverticulitis.

Conclusion: TCZ therapy leads to a rapid and maintained improvement in patients with refractory GCA and/or with unacceptable side effects related to corticosteroids. However, the risk of neutropenia and infection should be kept in mind when using this biologic agent in patients with GCA.

TABLE

<table>
<thead>
<tr>
<th>Clinical improvement, % (n)</th>
<th>Baseline</th>
<th>Month 6</th>
<th>Month 12</th>
<th>Month 18</th>
<th>Month 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laboratory markers, median [IQR]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESR (mm/1st/h)</td>
<td>43 [18-66] (46)</td>
<td>16 [2-5]** (38)</td>
<td>5 [2-8.5]** (28)</td>
<td>2 [2-15.5]** (20)</td>
<td>6 [2-12.5]** (16)</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>1.9 [1.1-3.2] (49)</td>
<td>0.1 [0.1-0.2]** (41)</td>
<td>0.1 [0.1-0.3]** (29)</td>
<td>0.1 [0.1-0.6]* (18)</td>
<td>0.2 [0.1-0.3]** (16)</td>
</tr>
<tr>
<td>Dose of corticosteroids, median [IQR]</td>
<td>15 [10-30] (49)</td>
<td>5 [2.5-7.5] (47)</td>
<td>2.5 [0-5] (33)</td>
<td>2.5 [0-5] (23)</td>
<td>2.5 [0-5.6] (17)</td>
</tr>
</tbody>
</table>

The number of patients with available data is shown in parentheses

* p <0.05 ** p < 0.01 vs. baseline (Wilcoxon test)

Disclosure: L. C. Domínguez-Casas, None; J. Lorícera, None; J. L. Hernández, None; S. Castañeda, None; V. Aldasoro, None; M. Varela-García, None; R. Ibáñez-Bosch, None; A. Mera, None; E. Pérez-Pampin, None; A. Humbria, None; J. Calvo-Alén, None; E. Aurrecoechea, None; J. Narváez, None; A. Sánchez-Andrade, None; P. Vela, None; E. Diez Alvarez, None; C. Moriano, None; C. Mata, None; P. Lluch, None; C. Moll, None; I. Hernández-Rodríguez, None; V. Calvo-Río, None; J. A. Román-Ivorra, None; C. Vazquez, None; A. Corrales, None; M. Gonzalez-Vela, None; F. Ortiz-Sanjuán, None; B. Atienza-Mateo, None; J. L. Martin-Varillas, None; M. A. González-Gay, None; R. Blanco, None.

A Patient Based Reliability Exercise of Omeract Ultrasound Definitions in Giant Cell Arteritis

Valentin S. Schäfer1, Stavros Chrysidis2, Christian Dejaco3, Christina Duftner4, Annamaria Iagnocco5, George A. W. Bruyn6, Greta Carrara7, MA D'Agostino8, Eugenio De Miguel9, Andreas P Diamantopoulos10, Ulrich Fredberg11, Wolfgang Hartung12, Alojzija Hočevar13, Tanaz A. Kermani14, Matthew J. Koster15, Tove Lorenzen16, Pierluigi Macchioni17, Marcin Milchert18, Uffe Møller Døhn19, Chetan Mukhtyar20, Cristina Ponte21, Sofia Ramiro22, Carlo Alberto Scirè23, Lene Terslev24, Kenneth J. Warrington15, Bhaskar Dasgupta25 and Wolfgang A. Schmidt26, 1Immanuel Krankenhaus Berlin, Medical Center for Rheumatology Berlin-Buch, Berlin, Germany, 2Department of Rheumatology, Hospital of Southwest Denmark, Esbjerg, Denmark, 3Rheumatology and Immunology, Medical University Graz, Graz, Austria, 4Department of Internal Medicine, Clinical Division of Internal Medicine II, Medical University Innsbruck, Innsbruck, Austria, 5Academic Rheumatology Unit, Università degli Studi di Torino, Torino, Italy, 6Rheumatology, MC Groep, Loenga, Netherlands, 7Epidemiology Unit, Italian Society for Rheumatology, Milano, Italy, 8Rheumatology, Versailles-Saint Quentin en Yvelines University, Boulogne-Billancourt, France, 9Medicine, Universidad Autonoma Madrid, MADRID, Spain, 10Martina Hansens Hospital, Bærum, Oslo, Norway, 11Diagnostic Centre, Silkeborg Regional Hospital, 8600 Silkeborg, Denmark, 12Department of Rheumatology/Clinical Immunology, Asklepios Medical Center, 93077 Bad Abbach, Germany, 13Department of Rheumatology, University Medical Centre Ljubljana, Ljubljana, Slovenia, 14Rheumatology, University of California Los Angeles, Los Angeles, CA, 15Rheumatology, Mayo Clinic, Rochester, MN, 16Diagnostic Centre, Region Hospital Silkeborg, Silkeborg, Denmark, 17Arcispedale Santa Maria Nuova, Reggio Emilia, Italy, 18Pomeranian Medical University, Szczecin, Szczecin, Poland, 19Center for Rheumatology and Spine Diseases, Rigshospitalet, Glostrup, Copenhagen Center for Arthritis Research (COPECARE), Glostrup, Denmark, 20Norfolk and Norwich University Hospital, Norwich, United Kingdom, 21Rheumatology Department, Hospital de Santa Maria - Centro Hospital Lisboa Norte, Lisbon, Portugal, 22Rheumatology, Department of Rheumatology, LUMC, Leiden, Netherlands, Leiden, Netherlands, 23Italian Society for Rheumatology, Milan, Italy, 24Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Rigshospitalet, Copenhagen, Denmark, 25Rheumatology, Southend University Hospital NHS Foundation Trust, Southend, UK, Westcliff-on-Sea, United Kingdom, 26Medical Center for Rheumatology and Clinical Immunology Berlin-Buch, Immanuel Krankenhaus Berlin, Berlin, Germany

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: To test the reliability of recently established consensus-based ultrasound definitions for normal and vasculitic temporal and axillary arteries in patients with giant cell arteritis (GCA) and in controls.

Methods: A preliminary one-day meeting was held in Southend, United Kingdom. One year later, a full three-day meeting according to OMERACT ultrasound group guidelines for patient based reliability testing was conducted in Berlin, Germany. This meeting included a 6-hour training session for standardization of examination technique and ultrasound machine settings. In both exercises 6-18 MHz linear ultrasound transducers of high quality ultrasound machines were used. Bilateral common superficial temporal arteries with frontal and parietal branches as well as axillary arteries were examined at two time points by 12 sonographers for normal findings, halo sign and compression sign using consensus-based definitions. In the preliminary meeting, 4 patients had longstanding established GCA, 1 patient had severe arteriosclerosis; and 1 normal control was included. In the second meeting, 4 GCA patients with more recent diagnosis and 2 healthy controls were examined. Inter- and intra-observer reliability was calculated.

Results: In the preliminary exercise, inter-reader reliabilities were fair to moderate for the overall diagnosis of GCA (Light’s kappa, 0.29-0.51) and poor to fair for identifying vasculitis in the respective anatomical segments (Light’s kappa, 0.02-0.46).
Intra-reader reliabilities were moderate (Cohen’s kappa, 0.32-0.64). In the main exercise, inter-reader reliability was good to excellent (Light’s kappa, 0.76-0.86) for the overall diagnosis of GCA and moderate to good (Light’s kappa, 0.46-0.71) for identifying vasculitis in the respective anatomical segments. Intra-reader reliability was excellent for diagnosis of GCA (Cohen’s kappa, 0.91) and good (Cohen’s kappa, 0.71-0.80) for the anatomical segments.

**Conclusion:** The patient based reliability for ultrasound definitions of halo and compression sign of temporal and for halo sign of axillary artery is good to excellent in recent onset GCA. Training of a standardized examination protocol is crucial for achieving specific results and good inter- and intra-observer reliabilities. The reliability in established disease requires further study.

**Disclosure:** V. S. Schäfer, None; S. Chrysidis, None; C. Dejaco, Merck Sharp and Dohme GmbH, 5, Merck Sharp and Dohme GmbH, 7; C. Duftner, None; A. Iagnocco, None; G. A. W. Bruyn, None; G. Carrara, None; M. D’Agostino, BMS, AbbVie, Novartis, 8; E. De Miguel, None; A. P. Diamantopoulos, Roche Pharmaceuticals, 8, BMS, 8; U. Fredberg, None; W. Hartung, None; A. Hočevar, None; T. A. Kermani, None; M. J. Koster, None; T. Lorenzen, None; P. Macchioni, None; M. Milchert, None; U. M. Dohn, None; C. Mukhtyar, None; C. Ponte, None; S. Ramiro, None; C. A. Scirè, None; L. Terslev, None; K. J. Warrington, None; B. Dasgupta, None; W. A. Schmidt, None.


**Abstract Number:** 782

**Serum IL-6, SAA and Calprotectin As Biomarkers in Giant Cell Arteritis and Polymyalgia Rheumatica**

**Yannick van Sleen**, Marjolein Hoekstra, Johan Bijzet, Wayel H. Abdullahad, Annemieke M.H. Boots and Elisabeth Brouwer, Rheumatology and Clinical Immunology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Vasculitis Poster I: Large Vessel Vasculitis

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** GCA and PMR are closely related inflammatory diseases. The diagnostic criteria of both disorders depend on a combination of clinical features and elevated ESR or CRP levels. ESR and CRP are also used to monitor disease activity. These biomarkers, however, are not disease specific and not consistently elevated in all GCA and PMR patients. Previously, serum levels of IL-6, SAA and calprotectin were found to be increased in small scale cross-sectional GCA and PMR studies. Calprotectin expression was also found in neutrophils and macrophages in temporal artery biopsies (TABs) of GCA patients. The aim of this study was to identify and compare the values of IL-6, SAA and calprotectin as biomarkers for diagnosing GCA and PMR, monitoring disease activity and predicting disease course.

**Methods:** Serum concentrations of IL-6, SAA and calprotectin were determined by ELISA in 36 newly diagnosed GCA patients (C-GCA (TAB+) or LV-GCA (PET/CT+)) and 27 newly diagnosed PMR patients (fulfilling the Chuang-Hunder criteria), before start of glucocorticoid treatment. Thirty age- and sex matched healthy controls were included as well. Follow-up sera from patients were tested again 3 months (n= 21 for GCA and n= 21 for PMR) and 1 year (n= 23 for GCA and n= 16 for PMR) after the start of treatment. TABs (n=17) from GCA patients were stained with anti-calprotectin and anti-CD15 by immunohistochemistry.

**Results:** Baseline levels of IL-6, SAA and calprotectin in GCA and PMR patients were higher compared to healthy controls. Treatment decreased the levels of IL-6 and SAA in both GCA patients and PMR patients, but serum levels of calprotectin
decreased in PMR patients only. Relapse free survival between the groups with relatively low and high levels of the serum markers did not differ. IL-6 correlated with CRP, and SAA correlated with both CRP and ESR. Calprotectin did not correlate with IL-6, SAA, CRP or ESR, suggesting an IL-6 independent pathway. Interestingly, calprotectin levels were also elevated in GCA and PMR patients with normal ESR or CRP levels. Immunohistochemical staining of TABs showed calprotectin expression in all TABs (Fig. 1). Only a minority of calprotectin positive cells were CD15+ neutrophils.

**Conclusion:** Serum levels of IL-6, SAA and calprotectin discriminate GCA and PMR patients from healthy controls at the group level. In addition, serum levels of IL-6 and SAA decrease with treatment induced remission in GCA and PMR patients. None of the biomarkers tested at baseline predicted future relapse. Serum calprotectin could be a potential marker for silent ongoing vascular inflammation in GCA patients. The diagnostic value of serum IL-6, SAA and especially calprotectin as biomarkers should be further examined and validated.

**Disclosure:** Y. van Sleen, None; M. Hoekstra, None; J. Bijzet, None; W. H. Abdulahad, None; A. M. H. Boots, None; E. Brouwer, None.


Abstract Number: 783

**European League Against Rheumatisms Recommendations for the Use of Imaging in Large Vessel Vasculitis in Clinical Practice**

Christian Dejaco¹, Sofia Ramiro², Christina Duffner³, Florent L. Besson⁴, Thorsten Bley⁵, Daniel Blockmans⁶, Elisabeth Brouwer⁷, Marco A. Cimmino⁸, Eric Clark⁹, Bhaskar Dasgupta¹⁰, Andreas P Diamantopoulos¹¹, Haner Direskeneli¹², Annamaria Iagnocco¹³, Thorsten Klink⁴, Lorna Neill¹⁴, Cristina Ponte¹⁵, Carlo Salvarani¹⁶, Riemer Slart¹⁷, Madeline Whitlock¹⁸ and Wolfgang A. Schmidt¹⁹, ¹Rheumatology, Hospital of Bruneck, Bruneck, Italy, ²Rheumatology, Department of Rheumatology, LUMC, Leiden, Netherlands, ³Department of Internal Medicine, Clinical Division of Internal Medicine II, Medical University Innsbruck, Innsbruck, Austria, ⁴Department of Nuclear Medicine, CHU Bicêtre, AP-HP, Université Paris-Sud, Paris, France, ⁵University of Würzburg, Würzburg, Germany, ⁶General Internal Medicine, University Hospital Gasthuisberg, Leuven, Belgium, ⁷Rheumatology and Clinical Immunology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, ⁸Research Laboratory and Academic Unit of Clinical Rheumatology, Department of Internal Medicine, University of Genova, Genova, Italy, ⁹PMRGCAuk, London, United Kingdom, ¹⁰Rheumatology, Southend University Hospital NHS Foundation Trust, Southend, UK, Westcliff-on-Sea, United Kingdom, ¹¹Rheumatology, Martina Hansens Hospital, Bærum, Oslo, Norway, ¹²Department of Internal Medicine, Division of Rheumatology, Marmara University, Istanbul, Turkey, ¹³Academic Rheumatology Unit, Università degli Studi di
SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Modern imaging modalities including ultrasound, magnetic resonance imaging (MRI), computed tomography (CT) and 18F-FDG positron emission tomography (PET/CT) have been increasingly used in primary large vessel vasculitis (LVV) including giant cell arteritis (GCA) and Takayasu arteritis (TAK). However, there is still significant controversy and uncertainty about when to use which imaging technique, and whether imaging might be helpful during follow-up to assess disease activity and damage. We aimed to develop EULAR recommendations for the use of imaging modalities in LVV in clinical practice.

Methods: The EULAR Standardised Operating Procedures have been followed. A systematic literature review was conducted to retrieve data on the role of imaging in LVV. Based on evidence and expert opinion, the task force consisting of 20 experts (physicians, a health care professional and patients) from 12 EULAR countries developed recommendations, with consensus obtained through informal voting. The final level of agreement was voted anonymously.

Results: A total of 12 recommendations have been formulated (Table). The task force recommends an early imaging test in patients with suspected LVV, assuming high expertise and prompt availability of the imaging technique. Ultrasound has been suggested as the first choice imaging modality in GCA, because of a good performance of the test, easy access, absence of radiation and other procedural risks, and low resource use. MRI, and in case of predominant large vessel (LV)-GCA, PET and CT, might be alternatives to ultrasound. For TAK, MRI is the preferred imaging modality, because of the absence of radiation exposure and the possibility to assess simultaneously the vessel wall and luminal changes of the aorta and its proximal branches. PET, CT and ultrasound can be used as alternatives.

In patients with a suspected flare of LVV, imaging might be helpful to assess disease activity. The frequency and choice of imaging modalities for long-term monitoring of structural damage remains an individual based decision. All imaging should be performed by a trained specialist using appropriate equipment, operational procedures and settings.

Conclusion: These are the first EULAR recommendations providing up-to-date guidance on the role of imaging in the diagnosis and monitoring of patients with (suspected) LVV.
1. In patients with suspected GCA, an early imaging test is recommended to complement the clinical criteria for diagnosing GCA, assuming high expertise and prompt availability of the imaging technique. Imaging should not delay initiation of treatment.

2. In patients in whom there is a high clinical suspicion of GCA and a positive imaging test, the diagnosis of GCA may be made without an additional test (biopsy or further imaging). In patients with a low clinical probability and a negative imaging result, the diagnosis of GCA can be considered unlikely. In all other situations, additional efforts towards a diagnosis are necessary.

3. US of temporal ± axillary arteries is recommended as the first imaging modality in patients with suspected predominantly cranial GCA*. A non-compressible 'halo' sign is the US finding most suggestive of GCA.

4. High resolution MRI of cranial arteries† to investigate mural inflammation may be used as an alternative for GCA diagnosis if US is not available or inconclusive.

5. CT and PET are not recommended for the assessment of inflammation of cranial arteries.

6. US, PET, MRI and/or CT may be used for detection of mural inflammation and/or luminal changes in extracranial arteries to support the diagnosis of LV-GCA. US is of limited value for assessment of aortitis.

7. In patients with suspected TAK, MRI to investigate mural inflammation and/or luminal changes should be used as the first imaging test to make a diagnosis of TAK, assuming high expertise and prompt availability of the technique.

8. PET, CT and/or US may be used as alternative imaging modalities in patients with suspected TAK. US is of limited value for assessment of the thoracic aorta.

9. Conventional angiography is not recommended for the diagnosis of GCA or TAK as it has been superseded by the previously mentioned imaging modalities.

10. In patients with LVV (GCA or TAK) in whom a flare is suspected, imaging might be helpful to confirm or exclude it. Imaging is not routinely recommended for patients in clinical and biochemical remission.

11. In patients with LVV (GCA or TAK), MRA, CTA and/or US may be used for long-term monitoring of structural damage, particularly to detect stenosis, occlusion, dilatation and/or aneurysms. The frequency of screening as well as the imaging method applied should be decided on an individual basis.

12. Imaging examination should be done by a trained specialist using appropriate equipment, operational
procedures and settings. The reliability of imaging, which has often been a concern, can be improved by specific training. Suggestions for technical and operational parameters are depicted in Box 1.

LoA, level of agreement; CT, computed tomography; GCA, giant cell arteritis; LV-GCA, large vessel GCA; LoE, Level of evidence according to the Oxford Centre for Evidence Based Medicine; LVV, large vessel vasculitis; MRI, magnetic resonance imaging; PET, 18F-FDG positron emission tomography; TAK, Takayasu arteritis; US, ultrasound

*cranial symptoms of GCA include headache, visual symptoms, jaw claudication, swelling and/or tenderness of temporal arteries; †cranial arteries: superficial temporal, occipital and facial, usually all visible in one examination in MRI.

Disclosure: C. Dejaco, None; S. Ramiro, None; C. Duftner, None; F. L. Besson, None; T. Bley, None; D. Blockmans, None; E. Brouwer, None; M. A. Cimmino, None; E. Clark, None; B. Dasgupta, None; A. P. Diamantopoulos, Roche Pharmaceuticals, 8, Bristol-Myers Squibb, 8; H. Direskeneli, None; A. Iagnocco, None; T. Klink, None; L. Neill, None; C. Ponte, None; C. Salvarani, None; R. Start, None; M. Whitlock, None; W. A. Schmidt, None.


Abstract Number: 784

Damage and Predictors of Damage in Takayasu’s Arteritis

Antoine G. Sreih1, Tanaz A. Kermani2, David Cuthbertson3, Simon Carette4, Nader A. Khalidi5, Curry L. Koeing6, Carol A. Langford7, Carol A. McAlear8, Paul A. Monach9, Larry W. Moreland10, Christian Pagnoux11, Philip Seo12, Kenneth J. Warrington13, Steven R. Ytterberg13 and Peter A. Merkel1,14, 1Division of Rheumatology, University of Pennsylvania, Philadelphia, PA, 2Division of Rheumatology, University of California, Los Angeles, CA, 3Biostatistics and Informatics, Department of Pediatrics, University of South Florida, Tampa, FL, 4Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada, 5Rheumatology, McMaster University, Hamilton, ON, Canada, 6Rheumatology, University of Utah, Salt Lake City, UT, 7Rheumatic and Immunologic Diseases, Cleveland Clinic, Cleveland, OH, 8University of Pennsylvania, Philadelphia, PA, 9Boston University School of Medicine, Boston, MA, 10Rheumatology & Clinical Immunology, University of Pittsburgh, Pittsburgh, PA, 11Rheumatology-Vasculitis clinic, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada, 12Medicine, Johns Hopkins University, Baltimore, MD, 13Rheumatology, Mayo Clinic, Rochester, MN, 14Biostatistics, Epidemiology, and Bioinformatics, University of Pennsylvania, Philadelphia, PA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Information regarding the degree and the predictors of damage in patients with Takayasu’s arteritis (TAK) is limited. This study aimed to characterize damage and identify predictors of damage in patients with TAK.

Methods: Patients with TAK enrolled in a multicenter, longitudinal study were included. Measures of disease damage, including the Vasculitis Damage Index (VDI) and the Large-Vessel Vasculitis Index of Damage (LVVID), were assessed at baseline and follow-up visits. Results from patients with a diagnosis of TAK made within 6 months prior to entry to the cohort were also separately analyzed. Kaplan-Meier survival curves were used to analyze development of new damage.
Univariate statistics and multivariate Cox regression modeling was used to analyze clinically-relevant baseline predictors of new damage.

**Results:** The study included 128 patients with TAK: 94% female, 89% Caucasian, and median duration of follow-up 3.5 years (1.9, 6.2). At entry into the cohort, 113 patients (88%) had at least one damage item recorded on VDI and LVVID [VDI median score 3 (IQR: 1-5)] and [LVVID median score: 2 (1-4)]. 31/128 (24%) of patients had a diagnosis of TAK made within 6 months prior to study entry, 81% of whom had at least 1 item documented on VDI and LVVID. During the follow-up period 96 patients (75%) accrued at least one new damage item, most of which occurred in the first year of follow-up (**Figure 1**). The cardiac and peripheral arterial systems accounted for most of the damage captured at baseline and follow-up. Results of univariate and multivariate analysis of clinically-relevant baseline predictors are shown in **Table 1**. Patients with new-onset disease (diagnosed ≤ 6 months within study entry) had a higher risk of new damage than patients with longer disease duration. The use of glucocorticoids was not associated with development of new damage.

**Conclusion:** Damage predominantly related to disease rather than treatment is present in the majority of patients with TAK, even within 6 months of diagnosis. Although damage accrues more commonly early in the disease course, the majority of patients with TAK continue to accrue new damage, mostly related to disease, even after several years of follow-up. Future research should address the question of whether treatment of TAK during the early stages of the disease reduces accumulation of disease-related damage.

**Figure 1.** Time to development of new damage on the Vasculitis Damage Index or the Large Vessel Vasculitis Index of Damage in 128 patients with Takayasu’s arteritis
Table 1. Baseline predictors of new damage during follow-up for patients with Takayasu’s arteritis

<table>
<thead>
<tr>
<th>Predictors of damage</th>
<th>Univariate analysis</th>
<th></th>
<th></th>
<th></th>
<th>Multivariate analysis</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hazard Ratio</td>
<td>95% CI</td>
<td>p value</td>
<td>Hazard Ratio</td>
<td>95% CI</td>
<td>p value</td>
<td></td>
</tr>
<tr>
<td>Age &gt; 35 at baseline</td>
<td>0.940</td>
<td>0.592-1.494</td>
<td>0.794</td>
<td>0.861</td>
<td>0.526-1.411</td>
<td>0.553</td>
<td></td>
</tr>
<tr>
<td>Duration of the disease (≤6 months)</td>
<td>2.343</td>
<td>1.397-3.930</td>
<td>0.001</td>
<td>1.957</td>
<td>1.025-3.738</td>
<td>0.041</td>
<td></td>
</tr>
<tr>
<td>Presence of damage at baseline</td>
<td>1.943</td>
<td>0.888-4.252</td>
<td>0.096</td>
<td>1.512</td>
<td>0.636-3.595</td>
<td>0.349</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>0.698</td>
<td>0.698-0.280</td>
<td>0.439</td>
<td>1.060</td>
<td>0.396-2.835</td>
<td>0.907</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td>1.129</td>
<td>0.540-2.360</td>
<td>0.747</td>
<td>1.381</td>
<td>0.638-2.992</td>
<td>0.412</td>
<td></td>
</tr>
<tr>
<td>No disease activity Physician Global Assessment=0</td>
<td>0.629</td>
<td>0.395-1.001</td>
<td>0.050</td>
<td>0.747</td>
<td>0.448-1.246</td>
<td>0.263</td>
<td></td>
</tr>
<tr>
<td>No glucocorticoids at baseline</td>
<td>0.729</td>
<td>0.456-1.164</td>
<td>0.185</td>
<td>0.681</td>
<td>0.418-1.109</td>
<td>0.122</td>
<td></td>
</tr>
<tr>
<td>No immunosuppressive therapy at baseline</td>
<td>1.579</td>
<td>0.994-2.508</td>
<td>0.053</td>
<td>1.239</td>
<td>0.709-2.164</td>
<td>0.451</td>
<td></td>
</tr>
<tr>
<td>No previous flare at baseline</td>
<td>1.471</td>
<td>0.925-2.339</td>
<td>0.102</td>
<td>1.200</td>
<td>0.678-2.124</td>
<td>0.531</td>
<td></td>
</tr>
</tbody>
</table>

Disclosure: A. G. Sreih, None; T. A. Kermani, None; D. Cuthbertson, None; S. Carette, None; N. A. Khalidi, None; C. L. Koening, None; C. A. Langford, None; C. A. McAlear, None; P. A. Monach, None; L. W. Moreland, None; C. Pagnoux, None; P. Seo, GlaxoSmithKline, 5; K. J. Warrington, None; S. R. Ytterberg, None; P. A. Merkel, None.


Abstract Number: 785

Longitudinal Angiographic Findings in Patients with Takayasu’s Arteritis

Antoine G. Sreih1, Tanaz A. Kermani2, David Cuthbertson3, Simon Carette4, Lindsey J. Forbes5, Nader A. Khalidi6, Curry L. Koening7, Carol A. McAlear8, Paul A. Monach9, Larry W. Moreland10, Christian Pagnoux11, Philip Seo12, Robert F. Spiera13, Kenneth J. Warrington14, Steven R. Ytterberg14, Carol A. Langford15 and Peter A. Merkel16,17, 1Rheumatology, University of Pennsylvania, Philadelphia, PA, 2Division of Rheumatology, University of California, Los Angeles, CA, 3Biostatistics and Informatics, Department of Pediatrics, University of South Florida, Tampa, FL, 4Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada, 5Medicine, Division of Rheumatology, Cedars-Sinai Medical Center, Los Angeles, CA, 6Rheumatology, McMaster University, Hamilton, ON, Canada, 7Rheumatology, University of Utah, Salt Lake City, UT, 8University of Pennsylvania, Philadelphia, PA, 9Boston University School of Medicine, Boston, MA, 10Rheumatology & Clinical Immunology, University of Pittsburgh, Pittsburgh, PA, 11Rheumatology-Vasculitis clinic, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada, 12Medicine, Johns Hopkins University, Baltimore, MD, 13Rheumatology, Hospital for Special Surgery, New York, NY, 14Rheumatology, Mayo Clinic, Rochester, MN, 15Rheumatic
SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Longitudinal data on the type, progression, and predictors of arterial lesions in patients with Takayasu’s arteritis (TAK) is limited. This study aimed to characterize lesions of large arteries in patients with TAK and identify predictors of new lesions.

Methods: Clinical, laboratory, and imaging data from patients with TAK enrolled in a prospective, multicenter, longitudinal study and/or a randomized clinical trial were included in this study. Lesions were defined as “new or worse” or “improved” arterial aneurysm, stenosis, or occlusion as determined by angiography (83% Magnetic Resonance Angiogram, 23% Computerized Tomography Angiogram, and 4% Conventional Angiogram). Clinical features were defined as the presence of any symptom or sign attributed to vasculitis. Logistic regression was used to analyze the association of baseline (visit 1) variables with new/worse or improved lesions.

Results: The study included 175 patients with TAK: 93% female, 85% Caucasian, mean (±SD) age at diagnosis = 34.4±13.4 years, and mean (±SD) follow-up = 3.8±3.1 years. At baseline, the most frequently affected arteries were subclavian (73% of patients), abdominal aorta (44%), thoracic aorta (42%), and common carotid (37%) (Figure 1). In 123 patients with serial imaging, new or worse arterial lesions were noted in 35 patients (28%) predominantly in the subclavian, common carotid, renal, and iliac territories. 96% of patients with new lesions were either on prednisone and/or other immunosuppressive agents. Improved stenotic lesions, mostly of the subclavian and common carotid arteries, were noted in 16 patients (13%) at follow-up. Clinical features of active disease were absent in 40% of visits at which a new lesion was detected. The mean levels of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) did not differ between the immediate prior visit versus the visit at which a new lesion was detected (ESR mean ± SD= 24.6 ± 4.0 and mean CRP ± SD =12.2 ± 2.8 mg/L at prior visit vs. ESR= 23.5 ± 3.9 and CRP= 9.5 ± 2.8 mg/L at lesion visit, p= 0.63 and 0.12 for ESR and CRP respectively). There were no differences in age, sex, ethnicity, presence of a flare prior to the onset of new lesion, or disease duration in patients with or without new/worse lesions and with or without improved lesions.

Conclusion: Among patients with TAK, large arterial abnormalities are common both at presentation and follow-up. One in 3 patients will continue to develop new or worsening arterial lesions while on treatment with 40% exhibiting no clinical or laboratory changes. Lesions involving the subclavian and carotids are more likely to improve during follow-up. These findings raise concerns about the current definition of active disease in TAK and have implications for the management of patients with TAK and the design and conduct of clinical trials in TAK.

![Arterial Territories with Lesions at Baseline and Follow-up](Image)

Figure 1. Distribution of arterial lesions at baseline and follow-up visits for patients with Takayasu’s arteritis.
Smoking As a Risk Factor for Giant Cell Arteritis: A Systematic Review and Meta-Analysis

David Brennan1, Patompong Ungprasert2, Kenneth J. Warrington2 and Matthew J. Koster2,
1Internal Medicine, Mayo Clinic, Rochester, MN, 2Rheumatology, Mayo Clinic, Rochester, MN
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Tobacco smoking is a well-established risk factor for the development of several autoimmune diseases such as rheumatoid arthritis and systemic lupus erythematosus. A similar association between smoking and giant cell arteritis (GCA) has been suspected but remains unclear due to limited study size and conflicting epidemiologic data. In order to further investigate the association between smoking and the development of GCA we conducted a systematic review and meta-analysis.

Methods: Two investigators (D.B. and M.K.) independently searched published studies indexed in MEDLINE and EMBASE from inception to February 2017 using the terms “giant cell arteritis,” “temporal arteritis,” “cranial arteritis,” and “Horton disease.” Recent conference abstracts available online were also reviewed. The following inclusion criteria were used: 1) original observational study comparing patients with GCA to healthy controls; 2) inclusion of smoking history; 3) provision of absolute numbers and/or statistical comparisons with 95% confidence intervals. Study eligibility was independently determined by the two investigators, with disagreements reviewed by a third investigator (P.U.) and resolved by consensus. RevMan 5.3 software was used for the data analysis. Point estimates and standard errors were extracted from individual studies and were combined by the generic inverse variance method of DerSimonian and Laird. Given the high likelihood of between-study variance, we used a random-effect model rather than a fixed-effect model. Statistical heterogeneity was assessed using the Cochran's Q test.

Results: The initial search yielded 3312 articles. Of these, thirteen studies (8 prospective and, 5 retrospective case-control studies) with unique cohorts were identified and included in the primary analysis (ever vs. never smoking history). Patients in the GCA cohort were more likely to have a history of smoking with an odds ratio of 1.19 (95% CI, 1.01 – 1.39) [Figure 1A]. Considerable heterogeneity was present (I^2 = 85%). Five of these studies included information on current smoking status. One additional study, which only reported current smoking status, was also included. The GCA cohort showed an association with current tobacco use with an odds ratio of 1.18 (95% CI, 1.01 – 1.38) [Figure 1B].

Conclusion: Our study demonstrated a statistically significant increased risk of GCA among smokers compared to non-smokers.
**Prevalence of Relapses of Giant Cell Arteritis in Patients Treated with Corticosteroids: A Meta-Analysis**

Alexandra Addario¹, Quitterie Reynaud²,³, Maxime Samson⁴, Mathilde Francois³, Stéphane Durupt³, Francois Gueyffier¹, Michel Cucherat¹, Isabelle Durieu²,⁵ and Jean-Christophe Lega³,⁶ ¹Equipe Evaluation et Modélisation des Effets thérapeutiques, Lyon 1 University, Lyon, France, ²HESPER group, Lyon 1 University, Lyon, France, ³Department of Internal and Vascular Medicine, Lyon Sud Hospital, Hospices Civils de Lyon, Lyon, France, ⁴Department of Internal Medicine and Clinical Immunology, Hôpital François Mitterrand, CHU de Dijon, Dijon, France, ⁵Department of Internal and Vascular, Lyon Sud Hospital, Hospices Civils de Lyon, Lyon, France, ⁶Equipe Evaluation et Modélisation des Effets thérapeutiques, UMR CNR 5558, Lyon 1 University, Lyon, France

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Vasculitis Poster I: Large Vessel Vasculitis

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The relapse rate of giant cell arteritis (GCA) in the patients treated by corticosteroids (CS) varied widely in observational series and randomized trials. The purpose of this systematic review was to (i) estimate the prevalence of relapse and (ii) explain the heterogeneity of relapse rate in patients receiving CS alone.

**Methods:** We searched from PubMed up to April 2017. Two investigators independently extracted data. The prevalence of relapse was pooled by random effect model. Heterogeneity ($I^2 > 50\%$) was explored by meta-regression.
**Results:** A total of 37 cohorts (6 trials) totaling 16839 patients were selected. The overall prevalence of relapse was 43% (95% confidence interval [CI] 0.37-0.50) with a high heterogeneity ($I^2 = 90\%$). The year of publication was positively associated with relapse (37 studies, rate increase of 6.1% for one decade, $p = 0.02$) (Figure 1). The length of CS administration was negatively correlated with the relapse rate (15 studies, rate decrease of 1.1% for one additional month, $p = 0.04$) (Figure 2), but not with the initial CS dose at diagnosis ($P = 0.46$) or time of follow-up ($p = 0.12$). The patients included in the control arms of randomized trials testing immunosuppressive drugs relapsed more frequently (62%, CI 47-75) compared to those in observational studies (40%, CI 33-47) ($p = 0.006$).

**Conclusion:** The relapse rate of GCA remains high without improvement across decades. The relapse rate might be related to the duration of CS administration rather than initial dose at induction. Our results challenged the schedules of CS administration used in randomized trials as standard of care and questioned the size of estimated efficacy of methotrexate and tocilizumab.

**Figure 1**

![Figure 1](image1.png)

**Figure 2**

![Figure 2](image2.png)
Mast Cell Mediated Inhibition of Systemic IL-6 in candida Albicans Water-Soluble Fraction (CAWS) Induced Model of Large Vessel Vasculitis

Mingcai Zhang\(^1\), Mehrdad Maz\(^2\), Don Smith\(^3\), Noriko Miura\(^4\), Naohito Ohno\(^5\), Kottarappat Dileepan\(^6\) and Jason Springer\(^7\), 
\(^1\)Department of Orthopedics, University of Kansas Medical Center, Kansas City, KS, \(^2\)Allergy, Clinical Immunology, and Rheumatology, Division of Allergy, Clinical Immunology and Rheumatology, Department of Internal Medicine, University of Kansas Medical Center, Kansas City, KS, \(^3\)University of Kansas Medical Center, Kansas City, KS, \(^4\)School of Pharmacy, Tokyo University of Pharmacy and Life Sciences, Tokyo, Japan, \(^5\)Tokyo University of Pharmacy and Lift Sciences, Tokyo, Japan, \(^6\)Department of Medicine, University of Kansas Medical Center, Kansas, KS, \(^7\)Department of Internal Medicine, Division of Allergy, Clinical Immunology, & Rheumatology, Kansas University Medical Center, Kansas City, KS

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: In forms of large vessel vasculitis (LVV) systemic IL-6 has been shown to follow disease activity. Furthermore, IL-6 inhibition is an effective treatment for giant cell arteritis, a form of LVV. Our group has demonstrated that systemic mast cell degranulation results in inhibition of LPS-induced systemic IL-6 production. Further studies...
demonstrated that this effect may be mediated through stimulation of histamine-1 receptor (H1R). The purpose of this study was to determine if mast cell degranulation could inhibit systemic production of IL-6 in a mouse model of vasculitis (Candida albicans water-soluble fraction induced model or CAWS).

Methods: Two month old male C57Bl6/J mice were randomized to 4 groups (n=4/group). Mice were given intraperitoneal injections of either: a) normal saline (controls), b) CAWS extract, c) compound 48/80 (C48/80, systemic mast cell degranulation agent), or d) CAWS + C48/80. Injections were given on five consecutive days. Animals were sacrificed at 30 days for measurements of systemic TNF-α, INF-γ and IL-6 by ELISA as well as aortic expression of messenger RNAs coding for IL-6, suppressor of cytokine signaling-1 (SOCS1), INF-γ, IL-10 and TNF-α. Two tailed student’s T-test were used for comparisons with p<0.05 considered significant.

Results: CAWS mice had significantly higher systemic IL-6 levels compared to controls (345.2 pg/ml±132.9 vs 56.4pg/ml±19.3,p<0.001). Mice injected with C48/80 + CAWS had significantly lower IL-6 compared to CAWS alone (177.3pg/ml±113.6 vs 345.2pg/ml±132.9, p=0.02). There was significantly higher systemic INF-γ in both the CAWS and CAWS+C48/80 compared to controls. No difference in TNFα was observed between the groups. No significant differences were observed in aortic IL-6 expression between groups. Comparing CAWS+C48/80 to CAWS alone, there was significantly higher aortic expression of both SOCS1 (p<0.001) and TNF-α (p=0.03).

Conclusion: The results demonstrate that systemic mast cell degranulation inhibits systemic IL-6 levels in a mouse model of LVV. This was not accompanied by reduced aortic expression of IL-6 suggesting that this effect is occurring in other tissues, possibly the liver. Mast cell degranulation was also associated with increased aortic expression of SOCS-1, a negative inhibitor of IL-6 signaling, suggesting that mast cells may play a direct role in IL-6 signaling as well. Since our prior studies suggest mast cells mediate IL-6 production through H1R stimulation, future research will be devoted to determining if H1R inhibition can inhibit the formation of LVV in a mouse model.

Acknowledgements: Endowment from Division of Allergy, Clinical Immunology and Rheumatology and Basic Science Research Development Award from Department of Medicine, University of Kansas Medical Center

Disclosure: M. Zhang, None; M. Maz, None; D. Smith, None; N. Miura, None; N. Ohno, None; K. Dileepan, None; J. Springer, None.


Abstract Number: 789

Markers of Inflammation and Patient-Reported Measures As Predictors of Relapse in Giant Cell Arteritis

Tanaz A. Kermani1, Antoine G. Sreih2, Gunnar Tomasson3, David Cuthbertson4, Renee Borchin5, Simon Carette6, Lindsy J. Forbes7, Nader A. Khalidi8, Curry L. Koening9, Carol A. McAlear10, Paul A. Monach11, Larry W. Moreland12, Christian Pagnoux6, Philip Seo13, Robert F. Spiera14, Kenneth J. Warrington15, Steven R. Ytterberg15, Carol A. Langford16 and Peter A. Merkel17,18

1Rheumatology, University of California Los Angeles, Los Angeles, CA, 2Rheumatology, University of Pennsylvania, Philadelphia, PA, 3University of Iceland, Faculty of Medicine, Reykjavik, IS, 4Biostatistics and Informatics, Department of Pediatrics, University of South Florida, Tampa, FL, 5University of South Florida, Tampa, FL, 6Division of Rheumatology, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada, 7Medicine, Division of Rheumatology, Cedars-Sinai Medical Center, Los Angeles, CA, 8Rheumatology, McMaster University, Hamilton, ON, Canada, 9Rheumatology, University of Utah, Salt Lake City, UT, 10University of Pennsylvania, Philadelphia, PA, 11Boston University School of Medicine, Boston, MA, 12Rheumatology & Clinical Immunology, University of Pittsburgh, Pittsburgh, PA, 13Medicine, Johns Hopkins University, Baltimore, MD, 14Rheumatology, Hospital for Special Surgery, New York, NY, 15Rheumatology, Mayo Clinic, Rochester, MN, 16Rheumatic and Immunologic Diseases, Cleveland Clinic, Cleveland, OH, 17Division of Rheumatology, University of Pennsylvania, Philadelphia, PA, 18Biostatistics, Epidemiology, and Bioinformatics, University of Pennsylvania, Philadelphia, PA

First publication: September 18, 2017
Background/Purpose: The significance of increasing erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) in clinically asymptomatic individuals with giant cell arteritis (GCA) is controversial. Patient-reported outcomes may be useful in distinguishing disease states but have not been well studied in GCA. This study evaluated the association of changes in ESR, CRP, and patient-reported measures as predictors of subsequent relapse in patients with GCA.

Methods: Data from patients with GCA enrolled in a multicenter, longitudinal cohort and/or a clinical trial were included. Subjects were followed with standardized clinical assessments including symptoms attributed to vasculitis, patient global assessment (PtGA) on an 11 point numerical scale (0-10) and The Short Form Health Survey (SF-36). Physical component scores (PCS) and mental component scores (MCS) were calculated from SF-36 and normalized to the general population (mean ± SD=50 ± 10) with lower scores indicating poorer outcomes. Relapse was defined as presence since the last visit of any symptom attributable to vasculitis by the treating physician. Robust generalized estimating equations in logistic regression models were used to evaluate the association between change in PtGA, PCS, MCS, ESR, CRP from the visit prior to relapse with subsequent relapse.

Results: The study included 202 patients; 149 (74%) women; mean age at diagnosis = 71.6±8.3 years. All subjects met ACR classification criteria modified to include subjects with angiographic evidence of large-vessel vasculitis. Temporal artery biopsy was positive in 135/163 (82%) in whom it was performed. In the multivariable model, increase in PtGA (OR 1.18, 95% CI 1.08, 1.28), decrease in PCS (OR 1.05; 95% CI 1.02, 1.08), and increase in ESR (OR 1.03, 95% CI 1.00, 1.05) were all associated with relapse (Table 1). Change in MCS or CRP were not associated with relapse (Table 1). Increase in ESR or CRP was not associated with relapse in subjects when there was no change in PtGA from prior visit (change in PtGA <1) (Table 1).

Conclusion: In GCA increases in ESR are not associated with relapse if PtGA is unchanged. Where patient-reported measures worsen compared to a prior visit, a change in ESR is significant and is associated with an increased risk of relapse. Changes in PtGA are more strongly associated with relapse than ESR or PCS. Changes in CRP are not associated with relapses, regardless of patient-reported measures. Patients’ self-reports are important in the clinical assessment of disease activity in GCA and in predicting relapse as currently defined. These results support the incorporation of patient-reported outcomes into disease assessment in clinical trials and practice for GCA.
Table 1. Multivariate analysis evaluating predictors of relapse in 202 patients with giant cell arteritis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Model 1 with all variables OR (95%CI)</th>
<th>Model 2 with no change in PtGA OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>1.0 (1.0, 1.0)</td>
<td>1.0 (1.0, 1.0)</td>
</tr>
<tr>
<td>Male sex</td>
<td>0.45 (0.25, 0.81)</td>
<td>0.44 (0.19, 1.02)</td>
</tr>
<tr>
<td>Caucasian ethnicity</td>
<td>1.34 (0.47, 3.82)</td>
<td>1.07 (0.29, 3.90)</td>
</tr>
<tr>
<td>Unit increase ESR, mm/hour</td>
<td>1.03 (1.00, 1.05)</td>
<td>N/A</td>
</tr>
<tr>
<td>Unit increase CRP, mg/L</td>
<td>1.01 (0.98, 1.04)</td>
<td>1.00 (0.95, 1.05)</td>
</tr>
<tr>
<td>Unit increase PtGA</td>
<td>1.18 (1.08, 1.28)</td>
<td>N/A</td>
</tr>
<tr>
<td>Unit decrease MCS</td>
<td>1.02 (0.99, 1.04)</td>
<td>N/A</td>
</tr>
<tr>
<td>Unit decrease PCS</td>
<td>1.05 (1.02, 1.08)</td>
<td>N/A</td>
</tr>
</tbody>
</table>

OR = odds ratio; CI = confidence interval; PtGA = patient global assessment; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; MCS = mental component score; PCS = physical component score; N/A = not applicable

Disclosure: T. A. Kermani, None; A. G. Sreih, None; G. Tomasson, None; D. Cuthbertson, None; R. Borchin, None; S. Carette, None; L. J. Forbes, None; N. A. Khalidi, None; C. L. Koening, None; C. A. McAlear, None; P. A. Monach, None; L. W. Moreland, None; C. Pagnoux, None; P. Seo, None; R. F. Spiera, None; K. J. Warrington, None; S. R. Ytterberg, None; C. A. Langford, None; P. A. Merkel, None.

Pre-Clinical Evidences of Immunomodulatory Activities of Tuftsin-Phosphorylcholine on Samples from Patients with Giant Cell Arteritis in Comparison to Corticosteroids

Stefania Croci¹, Martina Bonacini¹, Francesco Muratore²,³, Andrea Caruso³, Antonio Fontana⁴, Luigi Boiardi³, Alessandra Soriano³,⁵, Alberto Cavazza⁶, Luca Cimino⁷, Lucia Belloni¹, Maria Parmeggiani¹, Miri Blank⁸,⁹, Yehuda Shoenfeld⁸,⁹ and Carlo Salvarani²,³, ¹Unit of Clinical Immunology, Allergy and Advanced Biotechnologies, Arcispedale Santa Maria Nuova-IRCCS, Reggio Emilia, Italy, Reggio Emilia, Italy, ²University of Modena and Reggio Emilia, Italy, Modena, Italy, ³Unit of Rheumatology, Arcispedale Santa Maria Nuova-IRCCS, Reggio Emilia, Italy, Reggio Emilia, Italy, ⁴Unit of Vascular Surgery, Arcispedale Santa Maria Nuova-IRCCS, Reggio Emilia, Italy, Reggio Emilia, Italy, ⁵Campus Bio-Medico, University of Rome, Italy, Roma, Italy, ⁶Unit of Pathology, Arcispedale Santa Maria Nuova-IRCCS, Reggio Emilia, Italy, Reggio Emilia, Italy, ⁷Unit of Ocular Immunology, Arcispedale Santa Maria Nuova-IRCCS, Reggio Emilia, Italy, Reggio Emilia, Italy, ⁸Zabludowicz Center for Autoimmune Diseases, Sheba Medical Center, Tel-Hashomer, Israel, Ramat-Gan, Israel, ⁹Sackler Faculty of Medicine, Tel-Aviv University, Israel, Tel-Aviv, Israel

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Background/Purpose: Tuftsin-PhosphorylCholine (TPC) is a novel bi-specific molecule which has shown immunomodulatory effects in experimental mouse models of lupus, colitis and arthritis but data in human autoimmune diseases are lacking. The present study aimed to investigate the effects of TPC in vitro on samples from patients with a suspicion of giant cell arteritis (GCA), an inflammatory disease of large- and medium-sized arteries.

Methods: Effects of TPC were determined in vitro on peripheral blood mononuclear cells (PBMCs) and temporal artery biopsies (TABs) obtained from six patients who underwent TABs because of a suspicion of GCA. Patients were naïve from therapy. 3 patients had inflamed TABs (GCA). 3 patients had normal TABs and received a different diagnosis (controls). GCA patients satisfied the ACR criteria for GCA. TPC was provided by TPCera (Jerusalem, Israel). Treatment with dexamethasone was included as standard of care. To model in vitro the inflammatory state, PBMCs were activated with CD3/CD28 beads for 48 hours and with phorbol 12-myristate 13-acetate (PMA) plus ionomycin for 4 hours in presence of different doses of TPC or dexamethasone. T helper (Th) cell subsets were analyzed by intracellular flow-cytometry. Cell viability was assessed by the WST-1 assay. To analyze the effects at tissue level, TABs were cut in fragments, placed in culture medium with TPC or dexamethasone in matrigel drops for 5 days. Levels of 18 cytokines in supernatants of TABs and CD3/CD28 activated PBMCs were quantified with the Procarta Plex Th1, Th2, Th9, Th17, Th22, Treg cytokine panel. Data were calculated relative to untreated cells. Column statistics, one-sample t test with an hypothetical value of 100 was used.

Results: Supernatants of PBMCs activated through CD3/CD28 and treated with TPC showed significant lower concentrations of IL-1beta, IL-9, IL-12(p70), IL-13 (>80% decrease), IL-2, IL-5, IL-6, IL-17A, IL-21, IL-23, IFNgamma, TNFalpha, GM-CSF (60-75% decrease) and to a lesser degree of IL-18, IL-22, IL-27. Treatment with TPC had no significant effects on IL-10. It had similar effects on PBMCs from GCA and control patients with the exception of IL-17A which was down-regulated only in PBMCs from GCA patients. IL-1beta, IL-13, IL-17A, IL-18 were detected only in supernatants from inflamed TABs and were significantly down-regulated by TPC treatment. IL-2, IL-5, IL-6, IL-10, TNFalpha were detected in supernatants both from inflamed and normal TABs: IL-6 was down-regulated by TPC treatment while no differences were found in IL-2, IL-5, IL-10 and TNFalpha. TPC and dexamethasone treatments had similar effects on cytokine production by CD3/CD28 activated PBMCs and TABs. Neither TPC nor dexamethasone treatments modified the percentage of Th1, Th17 and Th22 cell subsets induced by PMA plus ionomycin. Both TPC and dexamethasone treatments slightly reduced viability in unstimulated PBMCs while did not have any effects on viability of CD3/CD28 activated PBMCs.

Conclusion: TPC treatment in vitro remarkably down-regulated the production of several cytokines by CD3/CD28 activated PBMCs and TABs, similarly to dexamethasone, supporting further studies to validate the potential use of TPC in autoimmune diseases.

Disclosure: S. Croci, None; M. Bonacini, None; F. Muratore, None; A. Caruso, None; A. Fontana, None; L. Boiardi, None; A. Soriani, None; A. Cavazza, None; L. Cimino, None; L. Belloni, None; M. Parmeggiani, None; M. Blank, TPCera, 9; Y. Shoenfeld, TPCera, 9; C. Salvareani, None.


Abstract Number: 791

Aortic Dilatation in Patients with Large Vessel Vasculitis: A Longitudinal Case Control Study Using Positron Emission Tomography/Computed Tomography

Filippo Crescentini1, Francesco Muratore2, Lucia Spaggiari3, Giulia Pazzola1, Luigi Boiardi1, Nicolò Pipitone1 and Carlo Salvareani4, 1Rheumatology Unit, Arcispedale Santa Maria Nuova - IRCCS, Reggio Emilia, Italy, 2Rheumatology Unit, Arcispedale Santa Maria Nuova - IRCCS; Università di Modena e Reggio Emilia, Reggio Emilia, Italy, 3Radiology Unit,
SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: To evaluate aortic diameter and predictors of aortic dilatation using FDG-PET/CT in a longitudinally followed cohort of patients with large vessel vasculitis (LVV) compared with controls.

Methods: All consecutive patients with LVV who underwent at least 2 PET/CT scans between January 2008 and May 2015 were included. The first and last PET/CT study of each patient was independently evaluated by a radiologist and a nuclear medicine physician. The diameter of the aorta was measured at 3 different levels: ascending, descending thoracic and infrarenal aorta. Aortic dilation was defined as a diameter of >4 cm in the ascending, ≥4 cm in the descending thoracic and ≥3 cm in the infrarenal aorta. Aortic FDG uptake was graded at the same levels using a 0-3 semiquantitative scale and was reported as negative (score 0 or 1) or positive (score 2 and 3). Patients younger than 50 years at symptoms’ onset were classified as Takayasu arteritis (TAK), while those older than 50 years as giant cell arteritis (GCA). 29 age- and sex-matched patients with lymphoma who underwent at least 2 PET/CT in the same time interval without evidence of aortic FDG uptake were selected as controls.

Results: 93 patients with LVV were included in the study. 53% of patients were newly-diagnosed; the remaining 47% had a median disease duration of 34 months. At first PET/CT, the mean (SD) diameter of descending thoracic aorta was significantly higher in LVV patients compared with controls [28.07 (4.40) vs 25.60 (3.59) mm, p=0.012]. At last PET/CT, after a median time of 31 months, patients with LVV compared with controls had higher diameter of ascending [35.41 (5.54) vs 32.97 (4.11) mm, p=0.029] and descending thoracic aorta [28.42 (4.82) vs 25.72 (3.55) mm, p=0.007] and more frequently had aortic dilatation [19% vs 3%, p=0.023]. Significant predictors of aortic dilatation were male sex [OR 7.27, p=0.001], and the diameter of ascending [OR 2.03, p<0.001], descending thoracic [OR 1.57, p<0.001] and infrarenal [OR 1.25, p=0.005] aorta at first PET/CT study. Positive aortic FDG uptake, disease activity and elevated inflammatory markers at first PET/CT were not associated with an increased risk of aortic dilatation. Results remained unchanged when the analysis were restricted to the 48 newly-diagnosed LVV patients.

According to age at symptoms onset, 56% of patients were classified as GCA and 44% as TAK. At first PET/CT, GCA compared with TAK patients had shorter disease duration, more frequent positive aortic FDG uptake and higher level of inflammatory markers. Compared with TAK, GCA patients had higher aortic diameter at all 3 levels evaluated in both first and last PET/CT study. However there were no differences in the proportion of patients with aortic dilatation (at last PET/CT 23% in GCA vs 15% in TAK, p=0.306). Results remained unchanged when the analysis were restricted to the newly-diagnosed patients.

Conclusion: Patients with large vessel vasculitis are at increased risk of aortic dilatation compared with age- and sex-matched controls. Significant predictors of aortic dilatation are male sex and aortic diameter at first imaging study. Positive aortic FDG uptake at first PET/CT is not associated with increased risk of aortic dilatation.

Disclosure: F. Crescentini, None; F. Muratore, None; L. Spaggiari, None; G. Pazzola, None; L. Boiardi, None; N. Pipitone, None; C. Salvarani, None.


Abstract Number: 792
Glucocorticoid Use and Adverse Events in Patients with Polymyalgia Rheumatica in a Contemporary Population-Based Cohort

Izzat Shbeeb¹, Divya Challa¹, Shafay Raheel², Cynthia S. Crowson³ and Eric L. Matteson⁴, ¹Division of Rheumatology, Mayo Clinic, Rochester, MN, ²Rheumatology, Mayo Clinic, Rochester, MN, ³Division of Biomedical Statistics and Informatics, Department of Health Sciences Research, Mayo Clinic, Rochester, MN, ⁴Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, MN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:
To investigate the use of glucocorticoids (GC) and related adverse events (AE) in a long-term, geographically-defined cohort of patients with polymyalgia rheumatica (PMR).

Methods:
Using a population-based inception cohort, details of GC therapy were abstracted from medical records of all patients diagnosed with PMR in 2000-2014. Age- and sex-matched comparators without PMR were identified from the same underlying population. Cumulative and daily dosage of GC, rate of disease relapse, occurrence of GC-related AE, and rate of GC discontinuation were analyzed.

Results:
The study included 359 patients with PMR and 359 comparators. The median time to taper below 5mg/day for 6 months was 1.44 years (95% confidence interval [CI]:1.36-1.62), while the median time to permanent discontinuation was 5.95 years (95%CI:3.37-8.88). GC dosage permanent discontinuation (solid line), reaching <5 mg/day for 6 months (dashed line), and reaching <10 mg/day for 6 months (dotted line are depicted in Figure 1, top panel. Relapse rates according to time after PMR diagnosis are shown in Figure 1, bottom panel. The mean cumulative dose of GC at 2 and 5 years was 4.0 grams (g) (standard deviation [SD] 3.5g) and 6.3g (SD 9.8g), respectively. The mean daily dose of GC at 2 and 5 years was 6.1 mg/day (SD 7.6) and 7.2 mg/day (SD 9.5), respectively. There were no differences in rates of AE between patients with PMR and comparators for diabetes mellitus, hypertension, hyperlipidemia, or hip, vertebral or Colles fractures (p>0.2 for all). Cataracts were more common in patients with PMR than comparators (hazard ratio:1.72; 95%CI:1.23-2.41).

Conclusion:
The duration of GC therapy in patients with PMR is often protracted. Relapse rates are highest in the early stages of therapy. GC-related AE are not more common in PMR than comparators, except for cataracts.
Metotrexate in the Treatment of Giant Cell Arteritis: To be or Not to be

Ignacio Castaño¹, Irene Monjo², Alejandro Balsa³, Diana Peiteado², Sara García-Carazo⁴ and Eugenio De Miguel¹,
¹Medicine, Universidad Autonoma Madrid, MADRID, Spain, ²Rheumatology, Hospital Universitario La Paz, MADRID, Spain, ³Rheumatology, Hospital La Paz-IdiPAZ, Madrid, Spain, ⁴Rheumatology, La Paz University Hospital, Madrid, Spain
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

The high-dose glucocorticoids (GCs) are the mainstay of treatment in Giant Cell Arteritis (GCA). Patients treated with greater GC dosages are at the greatest risk of morbidity. Immunosuppressive agents have been trialled in an effort to reduce toxicity from GCs and to improve efficacy of treatment. The results of one meta-analysis with the three trials that included methotrexate (MTX) showed a weak benefit in those patients receiving MT), but the results were heterogeneous, with one trial showing significant benefit, while the other two did not (1). In this sense, our main objective was to study the efficacy and safety of MTX adjunct to GCs in the treatment of GCA.

Methods:

New-onset giant-cell arteritis initiating treatment of the disease was included in a retrospective observational study to compare treatment efficacy and safety. According to the treatment received the patients were divided two groups: a) GCs alone and b) MTX and GCs. To avoid bias, in group b, only patients who started MTX in the first trimester of treatment were included. As efficacy outcome the number of relapses and the cumulative dose of GCs at 6, 12 and 24 months were collected. For safety, the number of emergency room visits, hospitalization admissions and treatment related side adverse events were investigated in the follow-up.

Results:

Among the 147 patients included in the study, 64 (43.5%) received GCs alone (mean age 78.6±7.5 years) and 83 (56.5%) received GCs and MTX as an adjuvant treatment at some time during follow-up. 52 of these 83 patients (mean age 78.5±8.0 years) received MTX in the first trimester after diagnosis (group b). In the MTX group 43 patients received a dose of 7.5-15mg/week and 9 patients received a dose ≥15mg/week. Compared with only GCs treatment, MTX introduced in the first three months therapy did not reduce the rate of relapses, 51% in MTX group vs. 37.7% in the GCs group (p<0.09). The mean cumulative dose of prednisone was higher in the MTX group than in prednisone alone group (table). Patients in the MTX group, at any dose, presented a higher incidence of hospital admissions and hospital admissions by infections (p<0.05).

Conclusion:

Whilst MTX have been used in an effort to reduce toxicity from GCs and to improve efficacy of treatment our observational study shows that there is no benefit from adjunct MTX in GCA either in terms of efficacy or toxicity.


Disclosure: I. Castaño, None; I. Monjo, None; A. Balsa, None; D. Peiteado, None; S. García-Carazo, None; E. De Miguel, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/metotrexate-in-the-treatment-of-giant-cell-arteritis-to-be-or-not-to-be
Negative Temporal Artery Biopsies: Comparison between Biopsy-Negative GCA and Non-GCA Patients

Karthik Yeruva¹, Kenneth J. Warrington¹, Cynthia S. Crowson² and Matthew J. Koster¹, ¹Rheumatology, Mayo Clinic, Rochester, MN, ²Health Sciences Research, Mayo Clinic College of Medicine and Science, Rochester, MN

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Temporal artery biopsy (TAB) plays a key role in diagnosis of giant cell arteritis (GCA). However, approximately 15-20% of patients ultimately diagnosed with GCA have negative biopsies. Among patients with negative TAB, it is often challenging to identify patients with GCA from those with an alternate (non-GCA) diagnosis. Therefore, we sought to compare TAB-negative GCA with patients receiving a non-GCA alternate diagnosis.

Methods: Two cohorts were retrospectively identified through direct medical record review. The first cohort consisted of patients with TAB-negative GCA diagnosed between 1/1/1998 and 12/31/2013. The second cohort included all patients with a negative TAB performed between 1/1/2009 and 12/31/2010 in which a non-GCA alternate diagnosis was provided after a minimum of 6 months of follow up. Final diagnoses were confirmed by consensus among two rheumatologists and a physician abstractor. Baseline characteristics were compared between the two cohorts using chi-square and rank sum tests.

Results: 110 patients with TAB-negative GCA and 195 non-GCA patients with a negative TAB were identified. Alternate diagnoses for non-GCA patients are listed in Table 1. Age, sex, number of days on glucocorticoids prior to biopsy, and biopsy length were similar in both groups. Time from first symptom to diagnosis was longer in non-GCA patients [mean (SD); 2.6 (2.5) vs 1.5 (2.1) months; p<0.001] and fewer non-GCA patients fulfilled ≥3 ACR criteria for GCA (27% vs 64%; p<0.001). Although headache was the primary symptom in both cohorts (66% TAB-negative GCA; 68% non-GCA), patients with biopsy-negative GCA had more frequent anorexia, fatigue, fever, polymyalgia rheumatica, temporal artery tenderness and claudication (jaw, arm, or leg). Baseline transient (5% TAB-negative GCA; 6% non-GCA; p=0.58) and permanent (3% TAB-negative GCA; 3% non-GCA; p=0.86) vision loss were infrequently observed. ESR was higher in TAB-negative GCA patients [64.0 (35.1) vs 55.2 (67.4) mm/hr; p=0.002] compared to non-GCA patients but CRP did not differ [44.3 (53.6) vs 43.8 (61.9) mg/L; p=0.39].

Conclusion: In this cohort, neither headache nor vision loss at presentation were associated with an ability to discriminate between diagnosis of TAB-negative GCA compared to patients without GCA. ACR criteria may be helpful in identifying

Table 1: Alternate diagnoses among patients with negative temporal artery biopsies

<table>
<thead>
<tr>
<th>Alternate diagnosis, n (%)</th>
<th>Negative biopsy with alternate diagnosis (N=195)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurologic condition</td>
<td>75 (38%)</td>
</tr>
<tr>
<td>Isolated PMR</td>
<td>38 (19%)</td>
</tr>
<tr>
<td>Rheumatic disease other than PMR or GCA</td>
<td>26 (13%)</td>
</tr>
<tr>
<td>Non-articritic AION</td>
<td>10 (5%)</td>
</tr>
<tr>
<td>Fever of unknown origin</td>
<td>9 (5%)</td>
</tr>
<tr>
<td>Infectious disease</td>
<td>7 (4%)</td>
</tr>
<tr>
<td>Non-malignant hematologic condition</td>
<td>7 (4%)</td>
</tr>
<tr>
<td>Malignant disease</td>
<td>6 (3%)</td>
</tr>
<tr>
<td>Other vasculitis</td>
<td>6 (3%)</td>
</tr>
<tr>
<td>Cervical arthritis</td>
<td>5 (3%)</td>
</tr>
<tr>
<td>Systemic disease of unknown etiology</td>
<td>5 (3%)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (1%)</td>
</tr>
</tbody>
</table>

AION: anterior ischemic optic neuropathy; GCA: giant cell arteritis; PMR: polymyalgia rheumatica
patients with TAB-negative GCA. Among patients with negative TAB, constitutional symptoms and claudication (jaw/limb) were more frequently associated with an ultimate diagnosis of TAB-negative GCA.

Disclosure: K. Yeruva, None; K. J. Warrington, None; C. S. Crowson, None; M. J. Koster, None.


Abstract Number: 795

Characteristics and Treatment Outcomes of Giant Cell Arteritis with Large-Vessel Lesions in a Nationwide, Retrospective Cohort Study in Japan

Takahiko Sugihara1, Hitoshi Hasegawa2, Haruhito Uchida3, Hajime Yoshifuji4, Yoshikazu Nakaoka5, Yoshiko Watanabe6, Eisuke Amiya7, Masanori Konishi8, Yasuhiro Katsumata9, Yoshinori Komagata10, Taio Naniwa11,12, Takahiro Okazaki13, Yoshiya Tanaka14, Tsutomu Takeuchi15, Masayoshi Harigai16, Yoshihiro Arimura17 and Mitsuaki Isebe8,18, 1Department of Medicine and Rheumatology, Tokyo Metropolitan Geriatric Hospital, Tokyo, Japan, 2Department of Hematology, Clinical Immunology and Infectious Diseases, Ehime University Graduate School of Medicine, Ehime, Japan, 3Department of Chronic Kidney Disease and Cardiovascular Disease, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan, 4Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University, Kyoto, Japan, 5Osaka University Graduate School of Medicine, Osaka, Japan, 6First Department of Physiology, Kawasaki Medical School, Kurashiki, Japan, 7Department of Cardiovascular Medicine, University of Tokyo Graduate School of Medicine, Tokyo, Japan, 8Department of Cardiovascular Medicine, Tokyo Medical and Dental University, Tokyo, Japan, 9Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan, 10First Dept. of Internal Medicine, Kyorin University School of Medicine, Tokyo, Japan, 11Division of Rheumatology, Dept of Internal Medicine., Nagoya City University Hospital, Nagoya, Japan, 12Department of Respiratory Medicine, Allergy and Clinical Immunology, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan, 13Internal Medicine, St. Marianna University School of Medicine, Kawasaki, Japan, 14The First Department of Internal Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan, 15Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, 16Division of Epidemiology and Pharmacoepidemiology of Rheumatic Diseases, Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan, 17First Department of Internal Medicine, Kyorin University School of Medicine, Tokyo, Japan, 18Sakakibara Heart Institute, Tokyo, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Giant cell arteritis (GCA) often affects aorta or its branches, but it is unclear whether the large-vessel (LV) lesions are associated with treatment outcomes. The objective of this study was to evaluate clinical features of GCA with LV lesions and their associations with treatment outcomes in Japanese patients with GCA.

Methods: From a retrospective, multi-center, nationwide registry of GCA and Takayasu arteritis (TAK), we selected 137 newly diagnosed GCA patients who were treated with glucocorticoids (GCs) and 4 relapsed patients who were treated with GCs between 2007 and 2014. Differential diagnosis of GCA and elderly-onset TAK was made by the discretion of the site
investigators, while 110 out of the 141 patients satisfied the ACR classification criteria for GCA. The primary outcomes were achievement of remission (disappearance of clinical symptoms with normal C-reactive protein) and remission at low dose GCs (prednisolone (PSL) ≤7.5mg/day).

**Results:** Imaging examinations were performed in 100 of the 141 GCA, and 69 of them had LV lesions. Stenosis and aneurysm of the aorta or its branches were detected in 18 (26%) and 9 (13%) of the 69 GCA patients, respectively. On the other hand, inflammatory lesion of arterial wall was detected in 51 (74%) patients with enhanced CT, MRI or PET-CT. Of the 69 GCA patients with LV lesions, 34 had inflammatory lesions in left subclavian artery (a.), 29 in right subclavian a., 29 in left carotid a., 23 in right carotid a., 21 in ascending thoracic aorta, 31 in aortic arch, 32 in descending thoracic aorta, and 35 in abdominal aorta. We compared GCA patients with LV lesions by imaging (LVL group, n=69) and the others (non-LVL group, n=72) for clinical features and treatment response. Headache, abnormal temporal artery, jaw claudication, visual disturbance, and musculoskeletal manifestations were observed in 39%, 39%, 25%, 12% and 52% of the LVL group and in 81%, 75%, 47%, 38% and 65% of the non-LVL group. Initial PSL doses (mean ± standard deviation) were 0.78 ± 0.21 and 0.75 ± 0.25 mg/kg/day, and concomitant immunosuppressive drugs were used in 48% and 33% throughout observational period of two years, for the LVL group and the non-LVL group, respectively. Remission was achieved in 94% and 96% of the LVL group and the non-LVL group, and relapse-free survival rates were not significantly different between the two groups. The log-rank test showed cumulative rate of remission at low dose GCs was significantly lower in the LVL group compared to the non-LVL group.

**Conclusion:** LV lesions in Japanese patients with GCA were mostly limited to inflammation of arterial wall without stenosis or aneurysm formation, but were associated with poorer treatment outcomes.


**Abstract Number:** 796

**Presentation and Outcome of Large-Vessel Vasculitis Diagnosed between 50 and 60 Years: Case-Control Study Based on 183 Cases**

Laure Delaval1,2, Aurélie Daumais3, Maxime Samson4, Mikael Ebbo5, Hubert de Boysson6, Eric Liozon7, Henry Dupuy8, Alexis Regent9, Mathieu Puyade10, Daniel Blockmans11, Estibaliz Lazarro12, Ygal Benhamou13, Karim Sacre14, Alice Bérezen15, Loïc Guilleven8,9,16 and Benjamin Terrier17,18,19, 1National Referral Center for Rare Systemic Autoimmune Diseases, Hôpital Cochin, AP–HP, Université Paris Descartes, paris, France, 2Internal medicine, Cochin University Hospital, Paris, France, 3Department of Internal Medicine, Aix-Marseille Université, La Timone University Hospital, AP-HM, Marseille, France, 4Department of Internal Medicine and Clinical Immunology, Hôpital François Mitterrand, CHU de Dijon, Dijon, France, 5Internal medicine, Aix-Marseille Université, La Timone University Hospital, AP-HM, Paris, France, 6Department of Internal Medicine, Caen University Hospital, Caen, France, 7Department of Internal Medicine, Limoges
University Hospital, Limoges, France, 8Department of Internal Medicine, Haut-Lévêque Hospital, Pessac, France, 9National Referral Center for Rare Systemic Autoimmune Diseases, Hôpital Cochin, AP–HP, Université Paris Descartes, Paris, France, 10Department of Internal Medicine, University Hospital of Poitiers, Poitiers, France, 11General Internal Medicine, University Hospital Gasthuisberg, Leuven, Belgium, 12Department of Internal Medicine and Clinical Immunology, Bordeaux University Hospital, Pessac, France, 13Department of internal medicine, University Hospital of Rouen, Rouen, France, 14Department of Internal Medicine, Bichat Hospital, Paris, France, 15Department of internal medicine, CHR Annecy-Genevois, Metz-Tessy, France, 16French Vasculitis Study Group (FVSG), Paris, France, 17Service de Médecine Interne, Hôpital Cochin, Centre de référence national pour les maladies systémiques autoimmunes rares d’Île de France, DHU Authors, Assistance Publique-Hôpitaux de Paris (AP-HP), Paris, France, 18Internal Medicine, Cochin University Hospital, Paris, France, 19French Vasculitis Study Group (FVSG), Paris, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Primary large-vessel vasculitis (LVV) include giant cell arteritis (GCA) and Takayasu arteritis (TA). Age at onset is commonly used to distinguish GCA and TA. TA usually occurs before 50 years, whereas GCA occurs after age 50. However, GCA onset before age 60 remains very rare, reason why LVV between age 50 and 60 could be difficult to classify.

Methods: We conducted a national, retrospective study including patients with LVV, defined by histological (temporal artery biopsy) and/or imaging (circumferential thickening and/or hypermetabolism on FDG PET/CT) evidence of inflammatory vascular disease, and aged between 50 and 60 years at onset (LVV50-60). Cases were compared to controls with GCA aged over 60 years (LVV>60), and matched on gender with a ratio of 1:1.

Results:

We included 183 patients (136 women). Initial symptoms of LVV were: constitutional symptoms in 144 (79%) cases, cephalic symptoms in 133 (73%), polymyalgia rheumatica in 55 cases (30%), peripheral limb ischemic manifestations in 42 (23%), ocular signs in 32 (17%), stroke in 4 cases (2%) and mesenteric ischemia in 2 cases (1%). Temporal artery biopsy showed evidence of vasculitis in 78 (43%) cases.

Computed tomography (CT) angiography was performed in 102 (56%) cases and was abnormal in 74%, involving aorta in 83% (thoracic 29%, abdominal 8% and both 63%), subclavian artery in 26%, iliofemoral artery in 18% and carotid artery in 14%. Isolated aortitis was observed in 38%.

FDG PET/CT scan was performed in 105 (57%) cases, showing hypermetabolism in 90%. Overall, aortitis was noted on CT angiography and/or FDG-PET/CT in 113 (78%) cases, without any cephalic symptoms in 22%.

All patients received glucocorticoids. After a median follow-up of 43.8 months, 78 (31%) patients required second-line therapy, 27 (18%) three-line, and 14 (9%) more lines. Overall, 35% received methotrexate and 12% biological agent (anti-TNFa and/or IL-6 blockade). Fifteen patients required surgery (bypass surgery or angioplasty). At the end of follow-up, only 45% had discontinued glucocorticoids.

Case-control comparison showed that LVV50-60 had more frequent peripheral limb ischemic manifestations (23 vs 5%, P<0.0001), and less frequent cephalic symptoms (72 vs 90%, P<0.0001) and ocular signs (17 vs 27%, P=0.04). CT angiography and FDG PET/CT scan were more frequently abnormal in LVV50-60 (41 vs 23%, P<0.0001; and 51 vs 27%, P=0.007, respectively), with aorta being more frequently involved (78 vs 47%, P<0.0001). LVV50-60 received a median of 2 lines of treatment compared to one in LVV>60 (P=0.0002). LVV50-60 had more frequent surgery (10 vs 0%, P<0.0001), received more frequent biological agents (12 vs 3%, P=0.003), and had at last follow-up higher median prednisone dose (8.8
Conclusion: Primary LVV onset between 50 and 60 years identifies a subset of patients with more frequent aorta and peripheral limb vascular involvement compared to patients with LVV onset after 60. LVV between 50 and 60 were also characterized by more refractory disease requiring more methotrexate and/or biological agent.

Disclosure: L. Delaval, None; A. Daumas, None; M. Samson, None; M. Ebbo, None; H. de Boysson, None; E. Liozon, None; H. Dupuy, None; A. Regent, None; M. Puyade, None; D. Blockmans, None; E. Lazaro, None; Y. Benhamou, None; K. Sacre, None; A. Bérezné, None; L. Guillevin, None; B. Terrier, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/presentation-and-outcome-of-large-vessel-vasculitis-diagnosed-between-50-and-60-years-case-control-study-based-on-183-cases

Abstract Number: 797

Temporal Arteritis Revealing Antineutrophil Cytoplasmic Antibody–Associated Vasculitides: A Retrospective Study of 50 Cases

Laure Delaval1,2, Maxime Samson3, Flora Schein4, Christian Agard5, Olivier Aumaître6, Alban Deroux7, Henry Dupuy8, Cyril Garrouste9, cedric landron10, Francois Maurier11, Pascal Cathebras12, Loïc Guillevin2,13,14 and Benjamin Terrier15,16,17, 1National Referral Center for Rare Systemic Autoimmune Diseases, Hôpital Cochin, AP–HP, Université Paris Descartes, paris, France, 2Internal medicine, Cochin University Hospital, paris, France, 3Department of Internal Medicine and Clinical Immunology, Hôpital François Mitterrand, CHU de Dijon, Dijon, France, 4Internal medicine, University Hospital St Etienne, Saint Etienne, France, 5Internal Medicine Department, Nantes University Hospital, Nantes, France, 6CHU Pitié-Salpêtrière - Department of Internal Medicine 2. Referal center for SLE/APS, Paris, France, 7Internal Medicine, CHU de Grenoble, Grenoble, France, 8Department of Internal Medicine, Haut-Lévêque Hospital, Pessac, France, 9Nephrology, CHU, Clermont-Ferrand, France, 10service de médecine interne, CH Poitiers, CHU Poitiers, poitiers, France, 11Internal Medicine, Sainte-Blandine de Metz Hospital, Metz, France, 12Internal Medicine, University Hospital St Etienne, St Etienne, France, 13French Vasculitis Study Group (FVSG), Paris, France, 14National Referral Center for Rare Systemic Autoimmune Diseases, Hôpital Cochin, AP–HP, Université Paris Descartes, Paris, France, 15Service de Médecine Interne, Hôpital Cochin, Centre de référence national pour les maladies systémiques autoimmunes rares d’Ile de France, DHU Authors, Assistance Publique-Hôpitaux de Paris (AP-HP), Paris, France, 16French Vasculitis Study Group (FVSG), paris, France, 17Internal Medicine, Cochin University Hospital, Paris, France

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Giant cell arteritis (GCA) is a non-necrotizing granulomatous arteritis involving large vessels, whereas antineutrophil cytoplasmic antibodies (ANCA)-associated vasculitides (AAV) are a group of necrotizing vasculitis involvement small and medium-size vessels. AAV can be revealed by temporal arteritis (TA) leading to cephalic symptoms and misdiagnosis of GCA, whereas therapeutic management and prognosis strongly differ between these two entities.

Methods: We conducted a retrospective multicenter study including patients with symptomatology of TA revealing AAV. We compared these cases (TA-AAV) to controls with GCA randomly selected with a ratio of 1:2.

Results:
Fifty patients (26 women, mean age 70 years) were included. Initial symptoms of TA were: cephalic symptoms suggesting GCA in 44 (88%) cases, polymyalgia rheumatica symptoms and cough in 15 (30%) each, and ocular manifestations in 8 (16%). All patients without cephalic symptoms had inflammation on TAB consistent with GCA. However, 33 (66%) patients presented at initial presentation atypical symptoms for GCA: ENT involvement in 16 (32%), renal involvement (haematuria, proteinuria or acute renal failure) in 13 (26%), pulmonary involvement (nodule, alveolar condensation or alveolar hemorrhage) in 9 (18%), peripheral neuropathy in 8 (16%), abdominal pain and cutaneous manifestations in 5 (10%) each, episcleritis in 3 and cardiac involvement in 2. ANCA were screened at initial presentation in 33 cases, and were found in 88%, targeting MPO in 62% and PR3 in 38%.

Overall, diagnosis of AAV was made after a median time of 15.2 months (range 1.1-201), after initial flare in 20 (40%), after refractory disease in 13 (26%) and after vasculitis relapse in 17 (34%). AAV diagnoses were GPA, PAM and EGPA in 31, 16 and 3 cases, respectively. Manifestations leading to AAV diagnoses by physicians were common, including pachymeningitis in 4 cases. Once AAV diagnosis was made, all patients received glucocorticoids, in combination with immunosuppressive agents in 84% (cyclophosphamide, rituximab, azathioprine or methotrexate). After median follow-up of 43.2 months, 14 patients presented a relapse of the AAV and 5 patients died.

To identify AAV in patients with TA manifestations, we compared TA-AAV with GCA patients. AAV patients were slightly younger than GCA (70 vs. 74 years, P=0.01), and had more frequently: peripheral neuropathy (16 vs. 0%, P<0.001), lung involvement (40 vs. 16%, P=0.002), ENT (34 vs. 0%, P<0.001) and renal involvement (37 vs 0%, P<0.001). Histologically, TAB from AAV had significantly more fibrinoid necrosis (23 vs. 0%, P<0.001) and adventitial vasculitis (23 vs. 0%, P<0.001) and less frequently granulomatous inflammation (13 vs. 40%, P=0.01), disruption of the internal elastic membrane (45 vs. 69%, P=0.04) and giant cells (29 vs. 60%, P=0.01)).

Conclusion: Diagnosis of AAV should be considered in patients presenting with cephalic symptoms, especially in case of unusual manifestations and in case of necrosis or adventitial vasculitis on TAB. ANCA testing should also be performed in all patients with TA manifestations before retaining GCA diagnosis.

Disclosure: L. Delaval, None; M. Samson, None; F. Schein, None; C. Agard, None; O. Aumaître, None; A. Deroux, None; H. Dupuy, None; C. Garrouste, None; C. landron, None; F. Maurier, None; P. Cathebras, None; L. Guillevin, None; B. Terrier, None.

Altered Phenotype of Platelets and Neutrophils Toward Neutrophil-Platelet Interaction in Circulation of Small and Large Vessel Vasculitis

Kotaro Matsumoto¹, Hidekata Yasuoka², Komei Sakata¹, Keiko Yoshimoto¹,³, Katsuya Suzuki¹,⁴, Kunihiro Yamaoka¹ and Tsutomu Takeuchi¹,¹Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, ²³³Shinanomachi, Shinjuku, Keio University School of Medicine, Tokyo, Japan, ³Keio University School of Medicine, Clinical and Translational Research Center, Tokyo, Japan, ⁴Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Neutrophils play an important role in the pathogenesis of necrotizing vasculitis, and activation of neutrophil is one of important triggers of the disease process. Recent reports suggest that platelets can stimulate neutrophils
directly via aggregation by these cells or indirectly via chemokines produced by platelets. Thus, we hypothesized that activation of neutrophils by platelets may contribute to the progression of vasculitis. Our aim of this study is to clarify the phenotype alteration of circulating platelets and neutrophils toward aggregation in patients with vasculitis.

**Methods:** Untreated patients with antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) and large vessel vasculitis (LVV) who visited Keio University Hospital between 2015 and 2017 were consecutively involved and compared with 33 healthy controls (HC). Patients with AAV and LVV fulfilled 2012 Revisited International Chapel Hill Consensus Normencature or American College of Rheumatology 1990 criteria. Platelet-rich plasma and neutrophils were isolated from heparinized whole blood using gradient centrifugation. Expression levels of CD62P on platelets and CD41a on neutrophils which involved in platelet-neutrophil interaction were analyzed by FACS. The correlation between expression levels of CD62P and CD41a on these cells and clinical parameters of the patients were also analyzed.

**Results:** Four microscopic polyangitis (MPA), 2 granulomatosis with polyangitis (GPA) as AAV, and 5 giant cell arteritis (GCA), 3 Takayasu arteritis (TAK) as LVV were involved. As of AAV, mean age was 67 ± 8 years, 62% male, mean BVAS 15 ± 2, mean neutrophil counts 6,654 ± 1,262 /μL, and mean platelet counts 34 ± 6 × 10^4 /μL. As of LVV, mean age 66 ± 4 years, 53% male, mean neutrophil counts 5,507 ± 600 /μL, and mean platelet counts 36 ± 5 × 10^4 /μL. The treatment was started with 1 mg/kg/day of prednisolone for all patients. Proportion of CD62P^+ platelets was remarkably higher in AAV (2.5 ± 0.09 versus 1.7 ± 1.0, p = 0.05) and LVV (3.2 ± 1.1 versus 1.7 ± 1.0, p = 0.005) compared with HC. Moreover, proportion of CD62P^+ platelets was tended to be decreased by immunosuppressive treatment (2.6 ± 0.7 versus 2.0 ± 0.6, p = 0.1) along with improvement of disease activity. In addition, proportion of CD41a^+ neutrophils also tended to be higher in AAV and LVV compared with HC (27 ± 8.8 versus 20 ± 5.8, p = 0.07), and decreased by the treatment (29 ± 9.2 versus 18 ± 6.8, p = 0.07). Interestingly, proportion of CD41a^+ neutrophils was significantly and positively correlated with CD62P^+ platelets (r^2 = 0.8, p = 0.04) and ANCA titer (r^2 = 0.9, p = 0.003) in AAV patients.

**Conclusion:** Phenotype of circulating platelets and neutrophils are altered toward cell to cell contact and associate with disease activity. These results suggest that platelet-neutrophil interaction is involved in the disease process of vasculitis.

**Disclosure:** K. Matsumoto, None; H. Yasuoka, None; K. Sakata, None; K. Yoshimoto, None; K. Suzuki, None; K. Yamaoka, None; T. Takeuchi, None.

[View Abstract and Citation Information Online](http://acrabstracts.org/abstract/altered-phenotype-of-platelets-and-neutrophils-toward-neutrophil-platelet-interaction-in-circulation-of-small-and-large-vessel-vasculitis)

**Abstract Number:** 799

**Acetylcholinesterase Is Highly Expressed in the Inflamed Vessel Wall of Patients with Giant Cell Arteritis**

**Philip Therkildsen**¹, Berit Dalsgaard Nielsen¹, Kresten Krarup Keller², Torben Steiniche³, Lars Christian Gormsen⁴, Ib Tender Hansen⁵ and Ellen-Margrete Hauge⁶, ¹Department of Rheumatology, Aarhus University Hospital, Aarhus C, Denmark, ²Rheumatology, Department of Rheumatology, Aarhus University Hospital, Aarhus, Denmark, ³Department of Histopathology, Aarhus University Hospital, Aarhus C, Denmark, ⁴Nuclear Medicine and PET Center, Department of Nuclear Medicine and PET Center, Aarhus University Hospital, Århus C, Denmark, ⁵Department of Rheumatology, Aarhus University Hospital, Aarhus, Denmark, ⁶Department of Rheumatology, Department of Rheumatology, Aarhus University Hospital, Aarhus, Denmark

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Vasculitis Poster I: Large Vessel Vasculitis

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM
**Background/Purpose:** The temporal artery biopsy (TAB) remains the gold standard in the diagnosis of giant cell arteritis (GCA). However, TABs are false-negative in 40% of cases. Cellular studies have shown that activated immune cells upregulate the expression of acetylcholinesterase (AChE). If AChE is upregulated in the active GCA vessel wall, it may potentially improve the TAB as a diagnostic tool. The purpose was to investigate the *in-situ* expression of AChE in the vessel wall of patients with TAB-positive GCA and compare to non-GCA patients. **Methods:** In this histological case-control study, TABs from a total of 24 TAB-positive GCA and 44 TAB-negative non-GCA patients were retrospectively included from the period 2012-2015. Only positive TABs showing clear transmural inflammation were included. Clinical data were obtained from electronic patient records to confirm or dismiss clinical diagnosis. Immunohistochemical methods were used to determine the AChE expression and verified using positive/negative controls. The histological inflammation and AChE expression were assessed and graded on 0-1-2 scale by a pathologist, blinded to clinical data. Solitary AChE staining of the media was not included in the assessment. **Results:** All positive TABs showed AChE expression, 10/24 showed high AChE expression (grade 2) and 14/24 showed moderate AChE expression (grade 1). No non-specific AChE expression was observed outside the media in any of the negative TABs from non-GCA patients (i.e. grade 0). The AChE expression was in 79% agreement with the histological inflammation. Prednisolone treatment did not suppress the AChE expression. Neither the AChE expression, nor the histological inflammation showed correlation with any clinical findings. Clinical characteristics of included patients are shown in table 1. **Conclusion:** High to moderate AChE expression was observed in all 24 biopsies from TAB-positive GCA patients, and the AChE expression was in good agreement with the histological inflammation. No false positive staining was observed in any of the 44 TABs from TAB-negative non-GCA patients. This indicates that AChE could be a potential biomarker in GCA and may play a significant role in the inflammatory process in GCA.

Table 1: Baseline characteristics
<table>
<thead>
<tr>
<th>Variables</th>
<th>Positive biopsy diagnosed with GCA N=24</th>
<th>Negative biopsy diagnosed with PMR N=21</th>
<th>Negative biopsy diagnosed with other disease(^1) N=23</th>
<th>(p) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean (95% CI), years)</td>
<td>70.1 (67.5-72.8)</td>
<td>71.6 (67.5-75.6)</td>
<td>68.7 (64.1-73.3)</td>
<td>0.565</td>
</tr>
<tr>
<td>Females - no. (%)</td>
<td>16/24 (67)</td>
<td>11/21 (52)</td>
<td>13/23 (57)</td>
<td>0.613</td>
</tr>
<tr>
<td>Time from symptoms to hospital admission (median (95% CI), days)</td>
<td>41 (27-63)</td>
<td>70 (37-132)</td>
<td>83 (40-170)</td>
<td>0.198</td>
</tr>
<tr>
<td>Cumulative prednisolone dose before biopsy (median (95% CI), mg)</td>
<td>204 (136-308)</td>
<td>136 (81-231)</td>
<td>197 (73-535)</td>
<td>0.672</td>
</tr>
<tr>
<td>Fulfilled ACR criteria for GCA - no. (%)</td>
<td>23/24 (96)</td>
<td>2/21 (10)</td>
<td>7/23 (30)</td>
<td>0.000*</td>
</tr>
<tr>
<td>Localized headache(^2) - no. (%)</td>
<td>17/22 (77)</td>
<td>2/18 (11)</td>
<td>9/20 (45)</td>
<td>0.000*</td>
</tr>
<tr>
<td>Abnormal temporal artery(^3) - no. (%)</td>
<td>14/23 (61)</td>
<td>4/18 (22)</td>
<td>9/19 (47)</td>
<td>0.047*</td>
</tr>
<tr>
<td>ESR (mean (95% CI), mm/hour)</td>
<td>73.9 (62.2-85.5)</td>
<td>39.1 (25.6-52.6)</td>
<td>40.3(25.0-55.6)</td>
<td>0.000*</td>
</tr>
<tr>
<td>CRP (median (95% CI), mg/l)</td>
<td>65.8 (44.8-96.5)</td>
<td>33.3 (20.9-53.0)</td>
<td>8.0 (3.8-16.6)</td>
<td>0.000*</td>
</tr>
</tbody>
</table>

Continuous variables are expressed as mean (95% CI); in cases of logarithmic transformation, data are expressed as median (95% CI). Binomial variables are expressed as number (percentage). * Statistical significant

\(^1\) Cancer, osteo arthritis, infection, or ischemic vascular disease.

\(^2\) New unilateral headaches localized in either the occipital, frontal or temporal region.

\(^3\) Tenderness, thickening or decreased pulse of the temporal artery.

Disclosure: P. Therkildsen, None; B. D. Nielsen, None; K. K. Keller, None; T. Steiniche, None; L. C. Gormsen, None; I. Tønder Hansen, None; E. M. Hauge, None.

Measurement of Serum Cytokines during the Apparent Remission State of Takayasu Arteritis – What Do Cytokines Tell Us?

Bruna Savioli¹, Bruno Salu², Marlon Vilela², Maria Luiza Vilela Oliva² and Alexandre W.S. Souza³,⁴ ¹Internal Medicine - Rheumatology Division, Universidade Federal de São Paulo - Escola Paulista de Medicina, São Paulo, Brazil, ²Biochemistry, Universidade Federal de São Paulo - Escola Paulista de Medicina, São Paulo, Brazil, ³Rheumatology Div/Dept of Med, Escola Paulista de Medicina - Universidade Federal de São Paulo, Sao Paulo, Brazil, ⁴Internal Medicine, Universidade Federal de São Paulo, São Paulo, Brazil

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The definition of remission in Takayasu arteritis (TA) is a challenge in clinical practice, since smoldering arterial inflammation may occur without overt signs and symptoms of disease activity in TA. There is an unmet need for biomarkers in TA to predict disease progression in patients considered in remission. Thus, this study aims to evaluate serum cytokines in TA patients and to analyze associations with disease phenotypes and therapy during the remission state.

Methods: Thirty-four consecutive TA patients with stable disease during the last 6 months were evaluated for serum levels of pro-inflammatory (TNFα, IL-1β, IL-6), anti-inflammatory (IL-2, IL-10), Th1 (IL-12, IFNγ), Th2 (IL-4, IL-5, IL-13), Th9 (IL-9), Th17 (IL-17A, IL-17E, IL-17F, IL-21, IL-23) and Th22 (IL-22) cytokines by the multiplex technique.

Results: Serum TNFα, IL-17F, IL-21 and IL-23 were significantly higher in patients with stable disease presenting angiographic type V compared with other angiographic types while serum IL-17E, IL-17F, IL-22 and IL-23 were higher in TA patients with previous ischemic events. Similar levels of cytokines were observed in TA patients with and without aortic aneurysmal disease, and in TA patients with and without therapy with prednisone, immunosuppressive or biological agents. However, by multivariate linear regression analysis, serum IL-4 (β = 0.064; p = 0.004), IL-6 (β = 14.12; p = 0.006), IL-17A (β = 11.09; p = 0.012), IL-17E (β = 0.064; p = 0.003), IL-17F (β = 0.028; p = 0.016), IL-21 (β = 26.16; p = 0.007), IL-22 (β = 0.062; p = 0.012) and IL-23 (β = 1.86; p = 0.002) levels were independently associated with angiographic type V. Moreover, an independent association was also found between ischemic events and serum IL-17E (β = 0.044; p = 0.005), IL-22 (β = 0.039; p = 0.029) and IL-23 (β = 1.16; p = 0.006). Daily prednisone dose was associated with lower serum IL-4 (β = -0.002; p = 0.002), IL-6 (β = -0.28; p = 0.010), IL-17A (β = -0.22; p = 0.021), IL-17E (β = -0.001; p = 0.003), IL-22 (β = -0.001; p = 0.011) and IL-23 levels (β = -0.03; p = 0.005), whereas the use of an immunosuppressive simultaneously with a biological agent led to lower serum IL-4 (β = -0.044; p = 0.024), IL-17E (β = -0.046; p = 0.017) and IL-23 (β = -0.98; p = 0.048) levels.

Conclusion: A predominant Th17 response seems to be ongoing in TA patients with extensive arterial involvement (i.e. angiographic type V) or previous ischemic events, despite the remission state. Therapy has a significant impact on serum levels of several cytokines in TA. These findings highlight the potential role of Th17 response in the pathophysiology of TA.

Disclosure: B. Savioli, None; B. Salu, None; M. Vilela, None; M. L. Vilela Oliva, None; A. W. S. Souza, None.

PET-CT Findings and Clinical Outcomes in Takayasu Arteritis – Does 18F-Fluorodeoxyglucose Uptake in Arteries Predict Relapses?
Background/Purpose: PET-CT scan with 18F-Fluorodeoxyglucose (18F-FDG) has been frequently used as a tool to assess disease activity in Takayasu arteritis (TA) and increased 18F-FDG uptake in arteries is considered a surrogate marker of ongoing arterial inflammation. A previous cross-sectional study showed an association between the maximal standardized uptake value (SUVmax) in TA and disease activity in TA. To date, it is not known whether 18F-FDG uptake in arteries is associated with disease progression in TA with the development of new angiographic lesions. This study aims to evaluate associations between 18F-FDG uptake in arteries from TA and the risk to develop relapses, ischemic events, sustained remission (i.e. absence of disease activity and complete withdrawal of glucocorticoids for at least 6 months), new angiographic lesions and the need to change therapy in TA patients.

Methods: TA patients underwent PET-CT scan with 18F-FDG with arterial uptake measured by the SUV and SUVmax in arterial walls to assess disease activity and were longitudinally assessed for disease activity using Kerr’s criteria and for the development of new angiographic lesions by magnetic resonance angiography and/or by computerized tomography angiography.

Results: Amongst 36 TA patients initially evaluated by 18F-FDG PET-CT scan, 32 were longitudinally followed for a median of 83.5 months. The median SUVmax value in arteries was 1.57 (1.16-2.23). At baseline, 20 TA patients (62.5%) had SUVmax ≥ 1.3, whereas 11 TA patients (34.4%) had active disease by Kerr’s criteria. At follow-up, 23 (71.9%) patients had at least one disease relapse at a median of 17.0 months and new arterial lesions were observed in 14 (43.8%) cases. There were no differences regarding the baseline SUV value in arteries that developed and arteries that did not develop new angiographic lesions in TA patients. A higher frequency of disease relapses (85.0% vs. 50.0%, p = 0.049) and the need for changing immunosuppressive therapy (85.0% vs. 41.7%, p = 0.018) was observed in TA patients with SUVmax ≥1.3 at baseline compared with those with SUVmax <1.3. No differences regarding SUVmax ≥1.3 in arteries and the development of ischemic events, sustained remission and new angiographic lesions were found in TA patients. Using the Kaplan-Meier curve, a trend for a higher frequency of relapses was observed in TA patients with SUVmax ≥1.3 (p = 0.056) by the log rank test. No independent associations were found between baseline SUVmax ≥1.3 and the risk of relapses (HR = 1.07; 95CI: 0.39-2.92; p = 0.892) or between baseline SUVmax ≥1.3 and the risk of developing new angiographic lesions in (HR = 0.24; 95CI: 0.02-2.57; p = 0.239) by the multivariate Cox’s proportional hazard analysis.

Conclusion: There is no association between arterial SUV and development of new arterial lesion in TA, but arterial SUVmax in TA patients is marginally associated with a higher frequency of disease relapses and with the need for changing immunosuppressive therapy.


Disclosure: A. L. Faria Janes, None; M. Fang Castro, None; B. Savioli, None; A. E. Diniz Arraes, None; E. Sato, None; A. W. S. Souza, None.


Abstract Number: 802
Sensorineural Hearing Loss in Takayasu’s Arteritis

Ugur Kimyon¹, Sinem Nihal Esatoglu¹, Ebru Kara², Ahmet Atas², Elif Emel Gunay², Emine Deniz Gozen², Emin Karaman², Vedat Hamuryudan¹, Hasan Yazici¹ and Emire Seyahi¹, ¹Istanbul University, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey, ²Istanbul University, Cerrahpasa Medical Faculty, Department of Otorhinolaryngology, Istanbul, Turkey

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Sensorineural hearing loss has been reported to be increased in several chronic autoimmune and non-autoimmune diseases such as systemic lupus erythematosus (SLE), progressive systemic sclerosis, rheumatoid arthritis, small vessel vasculitides, ankylosing spondylitis and Behçet’s syndrome. We had sporadically noted several degrees of sensorineural hearing loss among our Takayasu’s arteritis (TA) patients. While, some revealed this in their past history, others had relapsing attacks of hearing loss independent of or associated with vascular relapses. We formally investigated the frequency and type of hearing loss among TA patients and suitable controls.

Methods: The study was done in two parts. In the first part, consecutive TA and SLE patients seen at outpatient clinic along with apparently healthy controls were administered a standardized questionnaire that assessed hearing loss, tinnitus and episodic vertigo. In the second part previously registered TA and SLE patients for another study (1-2), were called to specifically for otological examination and audiometry tests that included pure-tone air and bone conduction, speech audiometry and acoustic reflex threshold test.

Results: In the first part, 73 patients with TA, 107 patients with SLE and 133 healthy controls were studied as shown in Table 1. The frequency of those with hearing deficit/loss, tinnitus and vertigo were significantly more common among both TA and SLE patients (Table 1). While the frequency of those with hearing deficit/loss was similar in TA and SLE, those with tinnitus and vertigo were significantly most common in TA.

Audiometry tests revealed that, several degrees of hearing loss were present in 36.6 % of the patients with TA and 25.0 % of the patients with SLE (Table 2). This was mostly due to sensorineural hearing loss in both groups (TA: 31.7 %; SLE: 20.0 %) and high –frequency type was the most common pattern. Moreover, those TA patients with sensorineural hearing loss did not show any specific vascular pattern.

Conclusion: We are unaware of previous surveys of sensorineural hearing loss in TA. Our study shows that audiovestibular system is considerably affected in TA, similar to that observed in SLE. The fact that there was no clear vascular pattern among patients with hearing loss, suggest that small vessel vasculitis was probably the cause of this hearing loss.
<table>
<thead>
<tr>
<th>Table 1. Results of the questionnaire survey</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Takayasu’s arteritis (n = 73)</td>
</tr>
<tr>
<td>SLE (n = 107)</td>
</tr>
<tr>
<td>Healthy controls (n= 133)</td>
</tr>
<tr>
<td><strong>p value</strong></td>
</tr>
<tr>
<td>Mean age</td>
</tr>
<tr>
<td>43.7 ± 11.0</td>
</tr>
<tr>
<td>44.0 ± 10.3</td>
</tr>
<tr>
<td>42.5 ± 8.3</td>
</tr>
<tr>
<td>NS</td>
</tr>
<tr>
<td>Disease duration, med [IQR]</td>
</tr>
<tr>
<td>7 [3-12]</td>
</tr>
<tr>
<td>8 [3-11]</td>
</tr>
<tr>
<td>NA</td>
</tr>
<tr>
<td>NS</td>
</tr>
<tr>
<td>Hearing deficit/loss, n (%)</td>
</tr>
<tr>
<td>20 (27.4)</td>
</tr>
<tr>
<td>21 (19.6)</td>
</tr>
<tr>
<td>4 (3.0)</td>
</tr>
<tr>
<td>0.001</td>
</tr>
<tr>
<td>Tinnitus, n (%)</td>
</tr>
<tr>
<td>37 (50.7)</td>
</tr>
<tr>
<td>34 (31.8)</td>
</tr>
<tr>
<td>16 (12.0)</td>
</tr>
<tr>
<td>0.001</td>
</tr>
<tr>
<td>Vertigo, n (%)</td>
</tr>
<tr>
<td>39 (53.4)</td>
</tr>
<tr>
<td>38 (35.5)</td>
</tr>
<tr>
<td>19 (14.3)</td>
</tr>
<tr>
<td>0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2. Results of the audiometry tests</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Takayasu’s arteritis,</td>
</tr>
<tr>
<td>SLE</td>
</tr>
<tr>
<td><strong>p value</strong></td>
</tr>
<tr>
<td>(n = 41)</td>
</tr>
<tr>
<td>(n = 20)</td>
</tr>
<tr>
<td>Mean age</td>
</tr>
<tr>
<td>41.3 ± 8.9</td>
</tr>
<tr>
<td>42.1 ± 10.3</td>
</tr>
<tr>
<td>NS</td>
</tr>
<tr>
<td>Disease duration, med [IQR]</td>
</tr>
<tr>
<td>6 [4-11]</td>
</tr>
<tr>
<td>7 [3-11]</td>
</tr>
<tr>
<td>NS</td>
</tr>
<tr>
<td>Hearing loss, n (%)</td>
</tr>
<tr>
<td>15 (36.6)</td>
</tr>
<tr>
<td>5 (25.0)</td>
</tr>
<tr>
<td>NS</td>
</tr>
<tr>
<td>Sensorineural type, n (%)</td>
</tr>
<tr>
<td>12 (29.3)</td>
</tr>
<tr>
<td>4 (20.0)</td>
</tr>
<tr>
<td>NS</td>
</tr>
<tr>
<td>Conductive type, n (%)</td>
</tr>
<tr>
<td>3 (7.3)</td>
</tr>
<tr>
<td>1 (5.0)</td>
</tr>
</tbody>
</table>

Disclosure: U. Kimyon, None; S. N. Esatoglu, None; E. Kara, None; A. Atas, None; E. E. Gunay, None; E. D. Gozen, None; E. Karaman, None; V. Hamuryudan, None; H. Yazici, None; E. Seyahi, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/sensorineural-hearing-loss-in-takayasus-arteritis](http://acrabstracts.org/abstract/sensorineural-hearing-loss-in-takayasus-arteritis)

Abstract Number: 803

**Cardiovascular Risk Factors and Comorbid Diseases in Takayasu’s Arteritis**

Helin Masyan, Sinem Nihal Esatoglu, Ayse Merve Celik, Vedat Hamuryudan, Hasan Yazici and Emire Seyahi, Istanbul University, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

**Background/Purpose:** In addition to the occlusive vasculitis, hypertension and accelerated atherosclerosis are probably risk factors of the cardiovascular complications in Takayasu arteritis (TA). Although, management of traditional cardiovascular risk factors is recommended to diminish these cardiovascular complications, we still do not know whether traditional risk factors and other comorbid conditions are increased or operative. We looked at the frequency of traditional atherosclerotic risk factors and comorbid conditions among pts with TA.
Methods: Between March and December 2016, we studied consecutive 88 TA pts and 81 systemic lupus erythematosus (SLE) pts. In addition, 111 hospital workers were studied as healthy controls. Participants were interviewed with the help of a standardized questionnaire that assesses the presence of traditional atherosclerotic risk factors. The presence of atherosclerosis was not separately assessed. The presence of comorbid conditions was also assessed with the help of the Charlson comorbidity index. Additionally, Framingham coronary heart disease risk score was calculated; however, this was done only for women, because there were only a few male patients in the study cohort and male gender is an independent risk factor in this calculation.

Results: As shown in Table 1, among the Framingham components, only hypertension was significantly more frequent in TA. When only females were analyzed, Framingham risk score was more likely to be higher only in TA. Framingham score of SLE pts was found to be similar to that of the healthy controls, despite an increased frequency of hypertension observed among SLE pts. Additionally, familial history of cardiovascular diseases and sudden death were significantly more common among the TA pts compared to the SLE pts and healthy controls. Pericardial/pleural and renal diseases were more frequently observed among the SLE pts, (Table 2). On the other hand, cardiovascular and chronic pulmonary diseases were more common in TA pts. The frequency of inflammatory upper/lower back pain and rheumatologic diseases were increased in both TA and SLE. However, inflammatory bowel diseases (IBD) were only observed among the TA pts.

Conclusion: Among the traditional atherosclerotic risk factors, only hypertension appears to be increased among the TA pts. The frequencies of IBD and inflammatory upper/lower back pain are substantially high and deserves further scrutiny. Moreover, the increased incidence of cardiovascular and rheumatologic diseases among the first-degree relatives of TA pts suggest that genetic mechanisms may play role in TA.

Table 1. The demographic features and cardiovascular risk factors among females

<table>
<thead>
<tr>
<th></th>
<th>Takayasu arteritis (n = 77)</th>
<th>SLE (n = 77)</th>
<th>Healthy controls (n = 87)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD</td>
<td>44.5 ± 12.6</td>
<td>42.5 ± 12.4</td>
<td>44.6 ± 11.4</td>
<td>0.454</td>
</tr>
<tr>
<td>Smoking (current and past), n (%)</td>
<td>24 (31)</td>
<td>33 (45)</td>
<td>37 (42)</td>
<td>0.160</td>
</tr>
<tr>
<td>Body mass index, mean ± SD</td>
<td>26 ± 5</td>
<td>26 ± 6</td>
<td>26 ± 5</td>
<td>0.987</td>
</tr>
<tr>
<td>Total cholesterol, mg/dl</td>
<td>192 ± 47</td>
<td>186 ± 44</td>
<td>193 ± 36</td>
<td>0.580</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dl</td>
<td>56 ± 14</td>
<td>59.5 ± 19</td>
<td>57 ± 15</td>
<td>0.470</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>44 (57)</td>
<td>24 (31)</td>
<td>19 (22)</td>
<td>&lt;0.001&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>7 (9)</td>
<td>8 (10)</td>
<td>12 (14)</td>
<td>0.612</td>
</tr>
<tr>
<td>Familial history of cardiovascular diseases, n (%)</td>
<td>36 (47)</td>
<td>16 (21)</td>
<td>22 (25)</td>
<td>0.001&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Familial history of sudden death, n (%)</td>
<td>20 (26) ††</td>
<td>11 (14)</td>
<td>10 (11.5)</td>
<td>0.036&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td>Framingham risk score, median [IQR]</td>
<td>4.1 [1.8-9.4]</td>
<td>3.3 [1.3-5.8]</td>
<td>3.2 [1.1-5.9]</td>
<td>0.056</td>
</tr>
</tbody>
</table>

<sup>1</sup>TA–Healthy controls and SLE-Healthy controls, p <0.05; <sup>2</sup>TA –SLE and TA-Healthy controls, p <0.05; <sup>3</sup>TA-SLE and TA-Healthy controls, p <0.05
Table 2. Comorbid diseases and accompanying rheumatologic diseases across the groups

<table>
<thead>
<tr>
<th></th>
<th>Takayasu arteritis (n = 88)</th>
<th>SLE (n = 81)</th>
<th>Healthy controls (n=111)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female/male</td>
<td>77/11</td>
<td>77/4</td>
<td>87/24</td>
<td>0.0041^1</td>
</tr>
<tr>
<td>Age, mean ± SD</td>
<td>44.0 ± 12.3</td>
<td>42.3 ± 12.3</td>
<td>44.3 ± 11.7</td>
<td>0.482</td>
</tr>
<tr>
<td>Disease duration, median (IQR)</td>
<td>7 [3-12.8]</td>
<td>7 [4-14]</td>
<td>-</td>
<td>0.213</td>
</tr>
<tr>
<td>Chronic pulmonary diseases, n (%)</td>
<td>11 (12.5)</td>
<td>2 (2.5)</td>
<td>5 (4.5)</td>
<td>0.0172^2</td>
</tr>
<tr>
<td>Cardiovascular diseases, n (%)</td>
<td>38 (43.2)</td>
<td>18 (22.2)</td>
<td>10 (9.0)</td>
<td>&lt;0.0013^3</td>
</tr>
<tr>
<td>Renal diseases, n (%)</td>
<td>12 (13.6)</td>
<td>21 (25.9)</td>
<td>8 (7.2)</td>
<td>0.0014^4</td>
</tr>
<tr>
<td>Neurologic diseases, n (%)</td>
<td>14 (15.9)</td>
<td>9 (11.1)</td>
<td>4 (3.6)</td>
<td>0.0125^5</td>
</tr>
<tr>
<td>Thyroid diseases, n (%)</td>
<td>12 (13.6)</td>
<td>20 (24.7)</td>
<td>24 (21.6)</td>
<td>0.172</td>
</tr>
<tr>
<td>Antidepressant drug use, n (%)</td>
<td>26 (29.5)</td>
<td>30 (37.0)</td>
<td>19 (17.1)</td>
<td>0.0076^6</td>
</tr>
<tr>
<td>Rheumatologic diseases</td>
<td>19 (21.6)</td>
<td>16 (19.8)</td>
<td>1</td>
<td>0.768</td>
</tr>
<tr>
<td>Crohn’s disease/Ulcerative colitis</td>
<td>9 (10.2)</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Ankylosing spondylitis</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Behcet’s syndrome</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Takayasu’s arteritis</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Psoriasis</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Anti-phospholipid syndrome</td>
<td>0</td>
<td>7</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Sjögren’s syndrome</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Inflammatory upper/lower back pain</td>
<td>21 (23.9)</td>
<td>23 (28.4)</td>
<td>6 (5.4)</td>
<td>&lt;0.001^7</td>
</tr>
<tr>
<td>Pericarditis/pleuritis</td>
<td>7 (8.0)</td>
<td>13 (16.0)</td>
<td>0</td>
<td>0.001^8</td>
</tr>
<tr>
<td>Family history of rheumatologic diseases</td>
<td>26 (29.5)</td>
<td>23 (28.4)</td>
<td>5 (4.5)</td>
<td>&lt;0.001^9</td>
</tr>
</tbody>
</table>

^1: TA-Healthy controls and SLE-Healthy controls, p<0.05; 2: TA-SLE and TA-Healthy controls, p<0.05; 3: TA-Healthy controls and SLE-Healthy controls, p<0.05; 4: SLE-TA and SLE-Healthy controls, p<0.05; 5: TA-Healthy controls and SLE-Healthy controls, p<0.05; 6: TA-SLE and TA-Healthy controls, p<0.05; 7: TA-Healthy controls and SLE-Healthy controls, p<0.05; 8: TA-SLE and TA-Healthy controls, p<0.05; 9: TA-Healthy controls and SLE-Healthy controls, p<0.05

Disclosure: H. Masyan, None; S. N. Esatoglu, None; A. M. Celik, None; V. Hamuryudan, None; H. Yazici, None; E. Seyahi, None.


Abstract Number: 804

The Efficacy and Safety of the Anti-IL-6 Receptor Antibody Tocilizumab for Polymyalgia Rheumatica Patients with Resistance or Intolerance to Glucocorticoids and Methotrexate

Manami Hirata1, Akiko Ueno2, kazuyuki fujita2, Nobuyuki Shibutou2 and Masahiro Yamamura3, 1Center for Rheumatology, Okayama Saiseikai General Hospital, Okayama, Japan, 2Center for Rheumatology, Okayama Saiseikai General Hospital, Okayama, Japan, 3Okayama Saiseikai General Hospital, Okayama, Japan
**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Vasculitis Poster I: Large Vessel Vasculitis  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Some patients show inadequate responses to initial glucocorticoids (GC) doses or relapses during GC tapering and develop side effects of GCs. The 2015 EULAR/ACR recommendations for the management of PMR has been proposed, in which early introduction of methotrexate (MTX) in addition to GCs was recommended for such GC-resistance or GC-intolerance. A recent trial of tocilizumab (TCZ) in patients with newly diagnosed PMR, conducted in Europe and the United States, has shown its efficacy and safety. To determine the efficacy and safety of TCZ for patients with resistance or intolerance to GCs and/or MTX.

**Methods:** Sixty patients had been diagnosed with having PMR since 2011. The patients are all compatible with the 2012 EULAR/ACR provisional classification criteria for PMR, and had been treated first with GC and then, if they were resistant or intolerant to GC, were added MTX, similarly to the 2015 EULAR/ACR recommendations for the management of PMR. In GCs and MTX resistant patients we assessed the effects of tocilizumab plus GCs and MTX. The disease activity were measured by PMR-AS.

**Results:** There were 16 patients with GC/MTX resistant or intolerant PMR (26.7%). Of them, 8 patients with PMR agreed to the proposal of TCZ addition, and their therapeutic responses to TCZ and its safety were determined. They were at the age of 69.1 ± 11.3, including two males and six females. Before TCZ addition, the patients were treated with prednisolone (PSL) at 6.9 ± 2.4 mg/day plus MTX at 6.0 ± 4.1 mg/week, and serum CRP were at 1.0 ± 1.1 mg/dL. After 9.3 ± 6.6 months of TCZ treatment, PSL and MTX had been reduced to 0.9 ± 1.2 mg/day and 2.3 ± 3.3 mg/week, respectively, with CRP at 0.02 ± 0 mg/dL. GCs were able to be withdrawn in 5 patients, and MTX were additionally withdrawn in 2 patients. Two patients reached drug-free remission, as judged from MR-AS (< 1.5). During TCZ therapy, each one patient showed the worsening of depression and occlusion of the central retinal vein.

**Conclusion:** These results indicate that TCZ may provide a therapeutic option for patients with severe PMR who were resistant or intolerant to GC and additional MTX.

**Disclosure:** M. Hirata, None; A. Ueno, None; K. Fujita, None; N. Shibutou, None; M. Yamamura, None.


**Abstract Number:** 805

**Serological Immune-Inflammatory Markers of the First RCT about Tocilizumab to Treat Giant Cell Arteritis**

**Andrea Gloor**, Daniel Yerly, Stefan Kuchen, Sabine Adler, Stephan Reichenbach, Michael Seitz and Peter M. Villiger, Rheumatology, University hospital, Bern, Switzerland, Department of Rheumatology, Immunology and Allergology, University Hospital Bern, Bern, MD, Switzerland, Rheumatology, University Hospital Bern, Bern, Switzerland, Rheumatology, Clinical Immunology & Allergology, University Hospital Bern, Bern, Switzerland, Rheumatology, Immunology and Allergology, University Hospital Bern, Bern, Switzerland  

**First publication:** September 18, 2017
Background/Purpose: As published in The Lancet online, March 4, 2016, the first randomized, placebo-controlled trial (RCT) about tocilizumab (TCZ) in giant cell arteritis (GCA) showed clinical efficacy of the anti-IL-6R biologic agent in the induction and maintenance of remission for 52 weeks (ClinicalTrials.gov registration number: NCT01450137). So far nothing is known about the profile of biomarkers in complete remission controlled by TCZ. In this study we compared a large variety of biomarkers in complete remission induced by TCZ plus glucocorticoids (GC; early phase of the study) versus complete remission induced by TCZ monotherapy (late phase of the study), and we compared the data with age-matched healthy controls.

Methods:
Serum levels of 18 biomarkers were quantified using Multiplex technology (R&DSystems and Invitrogen) at weeks 0, 4, 12 and 52 of the RCT. TCZ concentrations were determined by QPS, Groningen, The Netherlands. Sex and age matched healthy individuals were included as controls (CTRL).

Results: TCZ plasma concentrations reached a plateau by week 20. Several molecules did not display a discrete pattern over time (sCD25, adiponectin, resistin, leptin, BAFF, IFNa, YKL-40, TNF-R2, hsCRP, sICAM-1, CD163) or remained undetectable (IL17a, IL28A, II-11, IL-20, VCAM-1). MMP-3 and Pentraxin-3 showed a decline over time and reached almost normal values at the end of the study. Their concentrations correlated with TCZ plasma levels and inversely with GC dose. None of the parameters predicted flare after study end.

Conclusion: The analysis of a wide variety of immune-inflammatory markers documents a persistent subclinical disease activity during co-medication of TCZ and GC, but a near normalization of most values under TCZ monotherapy. In conclusion the results corroborate the advantage of anti-IL-6R therapy over GCs.

Disclosure: A. Gloor, None; D. Yerly, None; S. Kuchen, None; S. Adler, None; S. Reichenbach, None; M. Seitz, None; P. M. Villiger, None.


Abstract Number: 806

Epidemiological Study of Giant Cell Arteritis Using a Japanese Administrative Database

Eishi Uechi and Kiyohide Fushimi, Department of Health Policy and Informatics, Tokyo Medical and Dental University Graduate School, Tokyo, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The giant cell arteritis (GCA) management requires the administration of high-dose glucocorticoid (GC) at the introduction remission and the gradual reduction of the dosage. However, the long-term usage of GC can cause several side effects such as diabetes, osteoporosis and infections. Since patients with GCA are mainly elderly, the risk of side effects due to high doses or long-term administration of GC is greater. However, in clinical practice, the protocol of tapering
GC depends on the judgment of an individual clinician. There is no research describing the clinical practice of GCA and GC tapering. Therefore, this study describes the background of patients with GCA and its management using the nationwide clinical database in Japan.

**Methods:** This was a retrospective cohort study using the Diagnosis Procedure Combination (DPC) database, a nationwide inpatient database of Japan. We identified patients who received treatment for GCA (ICD10 code: M316) between 2010 and 2013 and tracked patient data up to 180 days after hospitalization and confirmed the treatment situation of GCA.

**Results:** 875 patients were hospitalized for GCA treatment from 2010 to 2013. 135 patients with age less than 50 years or no GC administration were excluded from the study and 740 patients were analyzed. 354 patients were followed until 90 days after admission and 220 patients were followed until 180 days after admission (Figure 1). The average patient age was 75 years, the mean body weight was 52 kg, and the complications were 27.6% (204/740) of diabetes, 10.4% (77/740) of gastrointestinal ulcers, and 6.8% (50/740) of malignancy. The GC dosage at the start of the treatment was 36.4 mg of prednisolone. The usage of pulse GC and immunosuppressant was 14.2% (105/740) and 11.6% (86/740), respectively. Of all, 69.7% (516/740) were prevented from osteoporosis. Although the mean GC dosage at the beginning was less than the key study protocol average and the recommended guideline, the dosage of GC after 90 days of admission was high (17.6 vs. 7.8 vs. 15 mg; Figure 2). The patients' age (>74 years) significantly affected the GC dosage reduction after 90 days of admission (P < 0.045). However, none of the hospital type (university hospital or an educational institution approved by the Japan College of Rheumatology), immunosuppressant combination, patient comorbidity affected the GC tapering at 90 days.

**Conclusion:** Many patients with GCA present with comorbidities. However, the tapering of GC dosage was slower than the main study protocol. Prophylaxis of complications due to GCs was not sufficiently undertaken.

---

**Disclosure:** E. Uechi, None; K. Fushimi, None.

B Cells in Giant Cell Arteritis: a Novel Target for Treatment?

Jacoba C. Graver¹, Maria Sandovici², Wayel H. Abdulahad², Erlin A. Haacke³, Annemieke M.H. Boots² and Elisabeth Brouwer⁴, ¹Rheumatology and Clinical Immunology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, ²Rheumatology and Clinical Immunology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, ³Pathology and Medical Biology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, ⁴Department of Rheumatology and Clinical Immunology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Giant cell arteritis (GCA) is the most common type of systemic vasculitis. Currently, two forms of GCA are described: a cranial(C)-GCA (temporal arteritis) and a systemic, large-vessel (LV)-GCA. Late complications of LV-GCA are aortic aneurysms or aortic rupture. Based on the analysis of temporal artery tissue, GCA is postulated to start at the adventitial site and to be T cell-mediated. In the temporal artery infiltrates, T cells clearly outnumber B cells. However, our report on a disturbed homeostasis of B cells in newly diagnosed C-GCA patients shows evidence for a putative role of B cells in GCA. Recently, the presence of B cells organized in artery tertiary lymphoid organs (ATLOs) has been described in C-GCA. The immunopathological role of B cells in both forms of GCA is underexplored and it is unknown whether B cells are present in the vessel wall of patients with LV-GCA. The objective of this study was to assess the presence and organization of B cells in the aorta of patients with LV-GCA.

Methods: Aorta tissue samples of 11 histologically-proven LV-GCA patients who underwent surgery due to an aortic aneurysm were studied by immunohistochemistry. Staining was performed with antibodies against CD20 (B cells), CD3 (T cells), CD21 (follicular dendritic cells (FDC)), PNAd (high endothelial venules (HEV)), bcl6 (germinal centers), and CD138 (plasma cells). None of the patients was receiving immunosuppressive treatment at the time of surgery. For comparison 22 aorta samples from age- and sex-matched atherosclerosis patients with an aortic aneurysm were included.

Results: Aorta tissues of LV-GCA patients showed massive infiltration of B cells (see fig. 1). The infiltrating B cells were mainly found in the adventitia and were organized into high density B cell areas. In contrast to the temporal artery, B cells outnumbered T cells in the aorta. Besides the presence of T cells, FDC, germinal centers, plasma cells, and HEV were documented at the areas of B cell infiltrates, which are typical for organized ATLOs.

Conclusion: Aorta tissues from patients with histologically-proven LV-GCA showed massive and organized B cell infiltrates mostly located in the adventitia. The mere presence of B cells at the site of inflammation prompts further investigation into the role of B cells in the pathogenesis of GCA.


Fig. 1. Aorta from a LV-GCA patient with organized high density CD20+ B cells areas in the adventitia (DAB/brown).

Disclosure: J. C. Graver, None; M. Sandovici, None; W. H. Abdulahad, None; E. A. Haacke, None; A. M. H. Boots, None; E. Brouwer, None.


Abstract Number: 808

Assessing the Possible Link between Varicella Zoster Virus and Giant Cell Arteritis Using Clinical Assessment, Serology and Biopsy Antigen Detection – Interim Results from the Giant Cell Arteritis and PET Scan (GAPS) Cohort

Anthony Sammel1, Katherine Nguyen2, Susan Smith3, Christopher Little3, Janice Brewer2 and Rodger Laurent2,
1Rheumatology, Royal North Shore Hospital, St Leonards, Sydney, Australia, 2Royal North Shore Hospital, St Leonards, Sydney, Australia, 3Raymond Purves Bone and Joint Research Laboratories, Kolling Institute, Sydney, Australia
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Recent studies have suggested that giant cell arteritis (GCA) may be triggered by reactivation of varicella zoster virus (VZV) based on high rates of VZV antigen detected in temporal artery specimens. We attempted to replicate these findings and further validate the possible link between VZV and GCA by assessing clinical and serological markers of acute infection.

Methods: 24 patients suspected of having GCA were recruited prior to temporal artery biopsy (TAB) between July 2016 and April 2017. Patients were clinically evaluated for active and past VZV infection and had serum tested for VZV IgM and IgG. All were treated with high dose corticosteroids for at least one week while awaiting TAB and were followed clinically for at least one month. Formalin fixed biopsies were cut into a minimum of four sections and were stained using a mouse derived antibody against VZV antigen and reported by two experienced, blinded immunohistochemistry researchers.

Results: Mean age was 68 and 17 (71%) were female. 23 (96%) reported headache, 15 (63%) scalp tenderness and nine (38%) visual disturbance. Inflammatory changes were seen on seven (29%) biopsies; four had mural inflammation and three
had limited periadventitial small vessel vasculitis (SVV). 16 (67%) met ACR criteria for GCA and 11 (46%) were assessed by the treating clinician as having definite or probable (≥ 50% chance) GCA at two-week follow-up. No patients had clinical features of herpes zoster (shingles) at the time of enrolment. Six (25%) reported a history of zoster, 22 (92%) chickenpox and none had received the adult zoster vaccine. A single patient developed zoster ophthalmicus one week after commencing corticosteroids with subsequent ipsilateral biopsy showing SVV. All 24 biopsies stained negative for VZV antigen by immunohistochemistry. Of the 23 who had VZV serology, all were IgM negative. 21/23 (91%) were VZV IgG positive consistent with past exposure.

**Conclusion:** VZV antigen was not detected in biopsy specimens. IgM serology was negative in all 23 tested patients. Only one patient developed herpes zoster on follow-up. These interim results do not support a link between VZV and GCA.

**Disclosure:** A. Sammel, Arthritis Australia, 2; K. Nguyen, None; S. Smith, None; C. Little, None; J. Brewer, None; R. Laurent, None.

**Abstract Number:** 809

**Prevalence and Distribution of Vascular FDG Uptake on Positron Emission Tomography (PET)-CT in Patients Suspected of Having Giant Cell Arteritis – Interim Results from the Giant Cell Arteritis and PET Scan (GAPS) Study**

Anthony Sammel1, Edward Hsiao2, Katherine Nguyen3, Geoffrey Schembri2, Leslie Schrieber3, Peter Youssef4, Beatrice Janssen3 and Rodger Laurent3, 1Rheumatology, Royal North Shore Hospital, St Leonards, Sydney, Australia, 2Royal North Shore Hospital, St Leonards, Australia, 3Royal North Shore Hospital, St Leonards, Sydney, Australia, 4Royal Prince Alfred Hospital, Camperdown, Sydney, Australia

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Vasculitis Poster I: Large Vessel Vasculitis  
**Session Type:** ACR Poster Session A  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Positron emission tomography (PET)-CT scan can assess large vessel vasculitis in giant cell arteritis (GCA). It has a reported sensitivity of 80% for biopsy positive disease but the superficial temporal, occipital and vertebral arteries have not previously been assessed due to difficulties with spatial resolution.

**Methods:** 41 patients suspected of having GCA between May 2016 and April 2017 underwent fluorine-18 fluoro-2-deoxyglucose (FDG) time-of-flight PET-CT scan within 72 hours of commencing corticosteroids and before clinically guided temporal artery biopsy (TAB). Patients were imaged from the vertex of the head to the diaphragm with 1mm CT slice...
reconstruction. FDG uptake was graded at 16 vascular sites using a semi-quantitative scale defined as zero (less than or equal to blood pool), one (minimally increased), two (clearly increased) or three (very marked uptake) by one of two blinded, experienced nuclear medicine physicians. Arterial calcification, shoulder region FDG uptake, infection and cancer were also reported.

**Results:** Mean age was 70 and 29 (71%) were female. Headache (88%), jaw claudication (34%), PMR (32%) and visual disturbance (29%) were common reported symptoms. Median CRP was 16 mg/L (range 1 – 299) and ESR was 36 mm/hr (range 5 – 130). Eight (20%) patients had mural inflammation on biopsy, four (10%) had limited periadventitial small vessel vasculitis and one had unequivocal thoracic aortitis on CT scan and did not undergo TAB. 28 (68%) had negative biopsies. 30 (73%) met the 1990 ACR criteria for GCA and 18 (44%) were assessed by the treating clinician as having definite or probable (>= 50% chance) GCA at two-week follow-up. 28 (68%) had at least grade one uptake in one or more vascular territory and 14 (34%) had at least grade two uptake. The carotid (44%), vertebral (32%) and superficial temporal (27%) arteries were the most affected. 6 (15%) patients had increased uptake isolated to the vertebral, temporal or occipital arteries. Shoulder region uptake was detected in 23 (56%) of patients, infection in three (two sinusitis, one pneumonia) and lung cancer in three. Vascular calcification did not globally correlate with increased FDG uptake (Spearman’s correlation coefficient = 0.05).

**Conclusion:** 68% of patients initially suspected of having GCA had at least mild increased FDG uptake on PET-CT scan. This compared with only 30% with inflammatory changes on biopsy. Increased uptake was commonly seen in the vertebral and temporal arteries which have not previously been assessed in PET-CT studies. Long-term follow-up will determine the clinical role of this protocol in GCA.

**Disclosure:** A. Sammel, Arthritis Australia, 2; E. Hsiao, None; K. Nguyen, None; G. Schembri, None; L. Schrieber, None; P. Youssef, None; B. Janssen, None; R. Laurent, None.
Abstract Number: 810

Sensitivity of Temporal Artery Biopsy in Giant Cell Arteritis: Systematic Literature Review and Meta-Analysis of Clinical Data

Emma Rubenstein¹, Carla Maldini², Solange Gonzalez-Chiappe³, Sylvie Chevret⁴ and Alfred Mahr³, ¹Internal medicine, University Hospital Saint-Louis, Paris, France, ²Rheumatology, Hospital Córdoba, Cordoba, Argentina, ³Internal Medicine, University Hospital Saint-Louis, Paris, France, ⁴Biostatistics, University Hospital Saint-Louis, Paris, France
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: Temporal artery biopsy (TAB) is a reference test for establishing a diagnosis of giant cell arteritis (GCA). A subset of patients with a clinical diagnosis of GCA does not show the characteristic histopathological signs, possibly because of technical artifacts or true phenotypic differences. The proportion of TAB-positive GCA cases varies across studies, and the lack of consensus on the sensitivity of TAB hampers comparisons with the performance of non-invasive diagnostic tests. In addition, the patient or study characteristics potentially influencing the sensitivity of TAB are not known. We performed a systematic literature review and meta-analysis to estimate the sensitivity of a positive TAB in GCA and identify factors involved in its variations.

Methods: We searched MEDLINE, EMBASE and CENTRAL databases for articles reporting TAB in GCA that were published from 1990 to 2016, with no language restriction. Eligibility criteria included studies with at least 30 GCA cases fulfilling the 1990 ACR criteria. From eligible publications, two independent researchers extracted the main demographic, clinical and study design characteristics and the number of TAB-positive cases among all cases with interpretable results for TAB. By meta-analysis, we computed the pooled proportion of TAB-positive GCA cases by a random-effects model with logit transformation. The extent of variability between studies was assessed by the I² statistic. Subgroup and meta-regression analyses were used to examine the effect of covariates (e.g., clinical, geographic, temporal and study descriptors) on TAB positivity.

Results: Among 3642 screened publications, 108 met the eligibility criteria. After publications with overlapping patient populations were removed, 43 studies (3836 GCA patients in total) were used for analysis. The pooled proportions of TAB positivity in GCA for all studies combined and within subgroups are shown in the Table. The proportion of TAB-positive GCA did not notably differ by patient or study characteristics on subgroup or meta-regression analysis.

Conclusion: The estimated proportion of 70% TAB-positive GCA provides a reference for the sensitivity of TAB in GCA. The unexplained high between-study heterogeneity could result from differences in TAB sampling and processing methods or histopathologic criteria applied or varying propensities to diagnose TAB-negative GCA.
**Disclosure:** E. Rubenstein, None; C. Maldini, None; S. Gonzalez-Chiappe, None; S. Chevret, None; A. Mahr, None.


**Abstract Number:** 811

**The Presence of Giant Cells in the Temporal Artery Biopsy Is Associated with Reduced Risk of Future Large Vessel Involvement in Patients with Biopsy-Proven Giant Cell Arteritis**

Nazanin Naderi1,2, Aladdin Mohammad3,4,5, Minna Willim4,6, Jan-Åke Nilsson1,6, and Carl Turesson1,6, 1Rheumatology, Department of Clinical Sciences, Malmö, Lund University, Malmö, Sweden, 2Department of Rheumatology, Danderyd Hospital, Stockholm, Sweden, 3Department of Renal Medicine, Vasculitis and Lupus Clinic, Addenbrooke's Hospital, Cambridge, United Kingdom, 4Rheumatology, Department of Clinical Sciences, Lund, Lund University, Lund, Sweden, 5Department of Rheumatology, Skåne University Hospital, Lund, Sweden, 6Department of Rheumatology, Skåne University Hospital, Malmö, Sweden  

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Vasculitis Poster I: Large Vessel Vasculitis  
**Session Type:** ACR Poster Session A

<table>
<thead>
<tr>
<th>Study and pt. characteristics</th>
<th>No. of studies (pt.)</th>
<th>TAB sensitivity (%) (95% CI)</th>
<th>( I^2 ) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All studies</td>
<td>43 (3836)</td>
<td>70.4 (63.5–76.5)</td>
<td>93.9</td>
</tr>
<tr>
<td>Females</td>
<td>&lt;70% of pt.</td>
<td>75.9 (65.5–84.0)</td>
<td>91.5</td>
</tr>
<tr>
<td>Age of pt., mean</td>
<td>&gt;70% of pt.</td>
<td>75.5 (64.0–84.2)</td>
<td>92.6</td>
</tr>
<tr>
<td>Ophthalmological signs</td>
<td>&lt;74 yr-old</td>
<td>80.9 (70.5–88.3)</td>
<td>86.2</td>
</tr>
<tr>
<td>Polymyalgia</td>
<td>&gt;74 yr-old</td>
<td>68.1 (56.2–78.0)</td>
<td>90.8</td>
</tr>
<tr>
<td>signs</td>
<td>&lt;20% of pt.</td>
<td>65.9 (48.4–80.0)</td>
<td>85.4</td>
</tr>
<tr>
<td>Polymyalgia</td>
<td>&gt;20% of pt.</td>
<td>79.4 (59.9–90.9)</td>
<td>96.7</td>
</tr>
<tr>
<td>rheumatica</td>
<td>&lt;32% of pt.</td>
<td>76.9 (67.3–84.4)</td>
<td>76.5</td>
</tr>
<tr>
<td>Polymyalgia</td>
<td>&gt;32% of pt.</td>
<td>70.2 (55.3–81.7)</td>
<td>94.7</td>
</tr>
<tr>
<td>Large-vessel</td>
<td>&gt;15% of pt.</td>
<td>66.5 (55.7–75.9)</td>
<td>77.1</td>
</tr>
<tr>
<td>involvement</td>
<td>3 (454)</td>
<td>63.4 (57.6–68.9)</td>
<td>0</td>
</tr>
<tr>
<td>Study area</td>
<td>North Europe</td>
<td>72.0 (54.0–84.9)</td>
<td>94.8</td>
</tr>
<tr>
<td>South Europe</td>
<td>69.4 (61.0–76.7)</td>
<td>91.9</td>
<td></td>
</tr>
<tr>
<td>North America</td>
<td>64.1 (43.6–80.5)</td>
<td>95.2</td>
<td></td>
</tr>
<tr>
<td>M. East/Asia</td>
<td>78.6 (68.6–86.0)</td>
<td>68.1</td>
<td></td>
</tr>
<tr>
<td>Study period</td>
<td>&lt;1990</td>
<td>75.5 (63.2–84.8)</td>
<td>94.8</td>
</tr>
<tr>
<td>1990–1999</td>
<td>69.4 (56.4–80.0)</td>
<td>94.1</td>
<td></td>
</tr>
<tr>
<td>2000–2009</td>
<td>65.1 (52.3–76.0)</td>
<td>92.7</td>
<td></td>
</tr>
<tr>
<td>&gt;2010</td>
<td>80.4 (73.0–86.2)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Study purpose</td>
<td>Diagnose</td>
<td>69.0 (51.2–82.5)</td>
<td>92.7</td>
</tr>
<tr>
<td>Other</td>
<td>70.8 (63.2–77.4)</td>
<td>94.1</td>
<td></td>
</tr>
<tr>
<td>Study design 1</td>
<td>Retrospective</td>
<td>67.7 (59.3–75.1)</td>
<td>94.8</td>
</tr>
<tr>
<td>Prospective</td>
<td>78.4 (66.0–87.2)</td>
<td>88.3</td>
<td></td>
</tr>
<tr>
<td>Study design 2</td>
<td>Monocentric</td>
<td>67.6 (57.8–76.0)</td>
<td>94.4</td>
</tr>
<tr>
<td>Multicentric</td>
<td>75.7 (67.8–82.1)</td>
<td>89.1</td>
<td></td>
</tr>
</tbody>
</table>

Pt.: patient
**Background/Purpose:** Giant cell arteritis (GCA) is a systemic disease with extensive vascular involvement. The mechanisms underlying the diversity of GCA phenotypes are incompletely understood. The purpose of this study was to investigate predictors of large vessel involvement (LVI) in a population based cohort of patients with GCA.

**Methods:** Patients with biopsy-proven GCA were identified using a regional pathology register. Patients with positive temporal artery biopsies (TAB) performed between 1997 and 2010 who were diagnosed with GCA in two defined areas of the region were included. A structured review of histopathology reports and case records through July 2016 of all the identified patients was performed. Reports of all relevant radiological and clinico-physiological studies were reviewed, and cases with LVI were identified according to a pre-specified protocol. LVI was defined as aneurysm, ectasia or stenosis of the aorta or its main branches. Patients were censored at the date of first LVI, death, migration from the area or July 29, 2016. Event free survival was estimated using the Kaplan-Meier method. Potential predictors of LVI were also examined using Cox regression models.

**Results:** A total of 274 patients with biopsy-proven GCA (77% women) were included. The mean age at GCA onset was 75.7 years (standard deviation (SD) 8.1). Fifty-one patients (19%) had documented LVI during the follow-up. The median time from diagnosis of GCA to detection of LVI was 4.5 years (interquartile range 0.6-7.4). There were 32 patients with aortic involvement (63% of those with LVI; 12% of all GCA cases). LVI occurred to a similar extent in women and men (75th percentile of LVI-free survival 12.9 and 13.1 years, respectively; p=0.96). Survival free of LVI was significantly longer in patients with giant cells present in the TAB (75th percentile 13.7 vs 6.7 years; p=0.014). There was a trend towards reduced risk of LVI with increasing age at GCA diagnosis (hazard ratio (HR) 0.81 per SD; 95% confidence interval 0.61-1.08). Other histopathology features, visual symptoms, platelet count, CRP, ESR or symptoms of polymyalgia rheumatica had no significant impact on the risk of LVI. In age-adjusted analysis, the presence of giant cells in the TAB was associated with a reduced risk of LVI (HR 0.48; 95% CI 0.27-0.86).

**Conclusion:**

Clinical features of GCA had no major impact on the risk of LVI. However, the negative association with giant cells in the biopsy suggests that patients with LVI constitute a subset of GCA with particular disease mechanisms.

---

**Disclosure:** N. Naderi, None; A. Mohammad, None; M. Willim, None; J. Á. Nilsson, None; C. Turesson, None.

**Background/Purpose:** To determine mortality risk in polymyalgia rheumatic (PMR) and compare cause-specific mortality rates among patients with PMR to age- and sex-matched comparators from the same population.

**Methods:** The study cohorts included all incident cases of PMR in a geographically-defined area diagnosed between 1970 and 2014 and non-PMR subjects from the same underlying population with similar age, sex and calendar year of index. Patients were followed until death, migration, last contact or December 31, 2014. Risk factors obtained by retrospective chart review among patients diagnosed in 2000-2014 included: morning stiffness, shoulder, hip and neck ache, anorexia, fatigue, weight loss, fever, erythrocyte sedimentation rate, C-reactive protein, rheumatoid factor positivity, smoking status and education. The underlying cause of death was coded from national mortality statistics and grouped according to ICD 9/10 chapters. Cox models were used for analysis.

**Results:** A total of 760 PMR and 760 non-PMR subjects (66% female; mean age 73.7 years for both) were followed for medians of 9.3 and 7.6 years, respectively, during which 444 PMR and 460 non-PMR subjects died. The overall standardized mortality ratio (SMR) in PMR patients was 0.81 (95% confidence interval [CI]: 0.74-0.89; Figure 1). The SMR remained consistent over the time period (Figure 2). Among patients with PMR there were fewer deaths from cancer (70 vs 88; hazard ratio [HR]: 0.67; 95% CI: 0.49-0.92), and neurological causes (16 vs 38; HR: 0.35; 95% CI: 0.20-0.63) than those without PMR. Risk factor analyses among 377 patients (with 109 deaths) diagnosed in 2000-2014 showed age (HR: 1.14 per 10 year increase; 95% CI: 1.11, 1.18) and male sex (HR: 1.82; 95% CI: 1.23, 2.71) were associated with higher mortality. No other significant risk factors were identified.

**Conclusion:** Survival among patients with PMR is not worse than the general population. Further research needs to be done in order to determine factors associated with improved survival in these patients.
Incidence of Herpes Zoster in Patients with Polymyalgia Rheumatica: A Population-Based Cohort Study

Shafay Raheel¹, Cynthia S. Crowson² and Eric L. Matteson³, ¹Rheumatology, Mayo Clinic, Rochester, MN, ²Health Sciences Research, Mayo Clinic College of Medicine and Science, Rochester, MN, ³Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, MN
**Background/Purpose:** To determine the incidence, time trends and, severity of herpes zoster in a population-based incidence cohort of patients with polymyalgia rheumatic (PMR) compared to individuals without PMR from the same population.

**Methods:** All incident cases of PMR in a geographically-defined area diagnosed between 1990 and 2014 were identified. Patients were followed by retrospective chart review until death, migration, last contact or December 31, 2015. The medical records of all patients with codes for herpes zoster (HZ) were reviewed to confirm the diagnosis, to ascertain the extent of skin disease (single or multidermatomal lesions) and to determine the outcome of HZ infection (extent of organ involvement/ complications and hospitalizations).

**Results:** The study included 541 patients with PMR and 541 subjects without PMR. The average age at PMR incidence (index date for the non-PMR cohort) was 74 years, and 349 (65%) subjects were female in each cohort. The median follow up was 8.5 years in PMR group and 7.3 years in non-PMR groups. During follow-up, 67 patients with PMR and 41 patients without PMR developed HZ. The cumulative incidence of HZ was higher in PMR patients compared to non-PMR subjects (14.3±1.8 at 10 years in PMR vs. 10.4±1.8 at 10 years in non-PMR; p<0.05; Figure 1). Therefore, patients with PMR were more likely to develop HZ than those without PMR (hazard ratio: 1.51; 95 % confidence interval: 1.03 – 2.23). HZ rates by decade among patients with PMR were 1.0, 2.0 and 1.2 per 100 person-years [py] compared to 0.6, 1.6 and 0.9 per 100 py among non-PMR in 1990-1999, 2000-2009 and 2010-2016, respectively. The decline in HZ incidence after year 2006 likely reflects the introduction and use of zoster vaccine in this time period (Figure 2). Complications of HZ occurred at a similar rate in both cohorts. Rate of vision impairment and multidermatomal involvement was higher in PMR group but this did not reach statistical significance.

**Conclusion:** The incidence of HZ in PMR is increased compared to the general population. Patients with PMR should be evaluated for shingles vaccination. Further research needs to be done in order to understand the determinants of increased incidence of HZ in PMR patients.
Disclosure: S. Raheel, None; C. S. Crowson, None; E. L. Matteson, None.


Abstract Number: 814

Clinical Presentation and Outcome of Orbital Mass in Antineutrophil Cytoplasmic Antibody-Associated Vasculitides

Orbital mass is a rare ophthalmologic manifestation of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV) that remains a therapeutic challenge. This study aimed to describe clinical presentation, therapeutic management and outcome of orbital mass in the setting of AAV.

Methods: We conducted a nationwide retrospective study including 59 patients with AAV fulfilling the American College of Rheumatology criteria or Chapel Hill Consensus Conference definitions and orbital mass based on clinical and radiological features. Clinical, biological, radiological and histological characteristics, treatment use and efficacy, and outcome, were analyzed.

Results: Fifty-nine patients (33 women) were included. Fifty-six (95%) patients had granulomatosis with polyangiitis (GPA), two cosinophilic granulomatosis with polyangiitis, and one microscopic polyangiitis, with histological evidence of vasculitis found in 52 (90%) patients. Fifty-one (86%) patients were ANCA-positive, with a specificity against PR3 in 71%.

First publication: September 18, 2017
antagonist in one (2%). Complete response was noted in 15 (27%) cases, partial response in 27 (48%), stabilization in 10 (18%) cases, and worsening in 4 (7%) cases. Among patients with complete response, seven (47%) were MPO-ANCA positive. Twenty seven patients (47%) required a second line of treatment because of relapse in 16 patients (59%) after a median delay of 13 months and refractory course in 11 cases (41%). Six of these 27 patients (22%) received corticosteroids alone as first line. All patients were treated with corticosteroids and one or combined immunosuppressive agent(s). After a median follow-up of 68 months after orbital mass diagnosis, ophthalmologic sequelae included visual impairment in 28% with blindness in 17%, orbital muscular extension on MRI with diplopia in 36%, and naso-sinusal bone defect on MRI in 22%.

Conclusion: Orbital mass represents a therapeutic challenge during AAV, especially during GPA. This rare manifestation is associated with refractory course and high-frequency of sequelae, in particular blindness. Histological findings could help physicians to manage orbital mass.

Disclosure: C. A. Durel, None; A. Hot, None; L. Trefond, None; O. Aumaître, None; G. Pugnet, None; M. Samson, None; S. Abad, None; A. Belot, None; C. Blanchard-Delaunay, None; P. Cathebras, None; P. Cohen, None; F. Cohen, None; V. Cottin, None; B. Crestani, None; S. Dumonteil, None; C. de Morcuil, None; S. Durupt, None; J. G. Fuzibet, None; M. Garzaro-regard, None; N. Girszyn, None; B. Godeau, None; E. Hachulla, None; Y. Jamilloux, None; P. Jego, None; E. Lazaro, None; T. Le Gallou, None; E. Liozon, None; T. Martin, None; T. Papo, None; A. Perlat, None; P. Pillet, None; K. Sacre, None; P. Sève, None; L. Guillevin for the French Vasculitis Study Group, None; B. Terrier, None.

Incidence in Large Vessel GCA in Northern Italy during a 11-Year Period

Luigi Boiardi1, Giovanna Restuccia2, Pierluigi Macchioni3, Pamela Mancuso4, Mariagrazia Catanoso5, Francesco Muratore6, Filippo Crescentini1, Giulia Pazzola1, Nicolò Pipitone1 and Carlo Salvarani7, 1Rheumatology Unit, Arcispedale Santa Maria Nuova - IRCCS, Reggio Emilia, Italy, 2Rheumatology Unitn, Arcispedale S Maria Nuova, IRCCS, 42100, Italy, 3Rheumatology, Arcispedale Santa Maria Nuova, Reggio Emilia, Italy, 4Interinstitutional Epidemiology Unit, Azienda USL di Reggio Emilia (Local Health Authority) and Azienda Ospedaliera IRCCS di Reggio Emilia,, Reggio Emilia, Italy, 5Rheumatology Service, Arcispedale S Maria Nuova-IRCCS, Reggio Emilia, Italy, 6Rheumatology Unit, Arcispedale Santa Maria Nuova - IRCCS; Università di Modena e Reggio Emilia, Reggio Emilia, Italy, 7Rheumatology Unit, Arcispedale Santa Maria Nuova - IRCCS; Università di Modena e Reggio Emilia, Reggio-Emilia, Italy

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: there are few studies regarding the incidence of large vessel GCA (LV GCA). Purpose: to investigate the incidence in patients diagnosed with large vessel GCA in the Reggio Emilia Area from 2005 through to 2016.

Methods: All patients with incident large vessel GCA diagnosed between 1 January 2005 and 31 December 2016 and living in the Reggio Emilia area, were identified by capture and re-capture checking of computerized discharge diagnosis codes (ICD10) and using outpatients databases from rheumatology, internal medicine, surgery, pathology, imaging departments of Reggio Emilia Hospital as well as by examining the Reggio Emilia district database for rare diseases. To be included in the study, patients must satisfy the following 2 criteria: Age at disease onset ≥ 50 years; evidence of large-vessel vasculitis by angiography, MRA, CTA, PET/CT and/or ultrasonography; we included in the study also patients associating biopsy proven gca to evidence of LVV at the imaging.
Results: There were 81 incident cases of LV GCA (57 women) during the 11-year study period; Mean ± SD age at diagnosis was 70 ± 9 years. Incidence per 100,000 persons aged ≥50 years was 3.38 (95% confidence interval [95% CI 2.69, 4.20]). Incidence was significantly higher in women (4.39 [95% CI 3.25, 5.53]) than in men (2.19 [95% CI 1.31, 3.07]) (p <0.0036). Incidence rates significantly increased by 11.1% every 3 years from 2.86 (2005-2007) to 4.06 (2014-2016). The highest incidence in women and in men was observed in the 70–79 years age group (women 3.55 [95% CI 2.17,5.48]; men 2.48 [95% CI 1.24,4.43]).

Conclusion: The incidence of LV GCA in the Reggio Emilia area was 3.38 and it was lower than that of patients with biopsy proven GCA (5.8) (1); the incidence of LV GCA was significantly higher in women as in biopsy proven GCA and increase during the follow-up period.

References


Disclosure: L. Boiardi, None; G. Restuccia, None; P. Macchioni, None; P. Mancuso, None; M. Catanoso, None; F. Muratore, None; F. Crescentini, None; G. Pazzola, None; N. Pipitone, None; C. Salvarani, None.

Comparison between Giacta Trial and a Multicenter Series of Giant Cell Arteritis Patients from Clinical Practice with Tocilizumab

Nuria Vegas-Revenga1, Javier Loricera1, Antonio Mera2, Eva Pérez- Pampín2, Santos Castañeda3, Lucia C. Domínguez-Casas1, José Luis Martín-Varillas4, Belén Atienza-Mateo4, MC Gonzalez-Vela1, Jose L. Hernández5, Miguel Angel González-Gay4 and Ricardo Blanco4, 1Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, 2Rheumatology, Complejo Hospitalario Universitario de Santiago. Galicia. Spain, Santiago de Compostela, Spain, 3Hospital Universitario de La Princesa, Madrid. Spain, Madrid, Spain, 4Rheumatology, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, 5Internal Medicine, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: GiACTA study is a randomized, phase III controlled clinical trial of tocilizumab (TCZ) in giant cell arteritis (GCA) (1,2). Our aim was to compare GiACTA trial data from those of a national multicenter series of patients with GCA from the clinical practice, focusing on the baseline characteristics of the patients.

Methods: Differences between the GiACTA study and clinical practice series were assessed. In the latter, the diagnosis of GCA was established by the ACR-1990 criteria and in the GiACTA trial by the ACR modified criteria. In the clinical practice study TCZ was used at standard IV dose (8 mg/kg/month) while in the GiACTA trial it was given subcutaneously (162 mg every 1 or 2 weeks). Quantitative variables were expressed as mean±SD and they were compared by the Student’s t-test. Dichotomous variables were expressed as percentages and compared using the chi-square test.
Results: At TCZ onset, in the clinical practice series there were a significantly greater (TABLE): a) duration of GCA, b) polymyalgia rheumatica frequency, c) ESR, and d) previous conventional immunosuppressants (mainly MTX). There was also a non-statistically significant lower sustained remission. The mean dose of prednisone at the TCZ onset was lower in patients from the clinical practice. In comparing only GiACTA patients with relapsing-GCA versus those of the clinical practice these differences remained unchanged, except for the GCA duration. PET/CT was performed more frequently in the series of the clinical practice.

Conclusion: Patients receiving TCZ in the clinical practice study have several baseline clinical and laboratory differences when compared to those included in the GiACTA trial.

TABLE
<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>GIACTA overall (n=251)</th>
<th>GIACTA (only relapsing- GCA; n=132)</th>
<th>Clinical Practice (n=49)</th>
<th>GIACTA (overall) vs Clinical Practice p</th>
<th>GIACTA (relapsing) vs Clinical Practice p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women / men</td>
<td>188/63</td>
<td>99/33</td>
<td>39/10</td>
<td>0.60</td>
<td>0.65</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>69 (8.2)</td>
<td>69.1 (8)</td>
<td>73 (9)</td>
<td>0.002</td>
<td>0.005</td>
</tr>
<tr>
<td>Inclusion criteria</td>
<td>ACR 1990 modified</td>
<td>ACR 1990 modified</td>
<td>ACR 1990</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Newly diagnosed GCA/ recurrent GCA</td>
<td>119/132</td>
<td>0/132</td>
<td>0/49</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Time (months) from GCA diagnosis, mean (SD)</td>
<td>9.1 (16.8)</td>
<td>16.9 (20.3)</td>
<td>26.4 (30.9)</td>
<td>0.0004</td>
<td>0.05</td>
</tr>
<tr>
<td>Signs/symptoms of GCA at TCZ onset#</td>
<td>98 (39)</td>
<td>59 (44.7)</td>
<td>31 (63.3)</td>
<td>0.003</td>
<td>0.04</td>
</tr>
<tr>
<td>PMR, n (%)</td>
<td>49 (19.5)</td>
<td>40 (30.3)</td>
<td>31 (63.3)</td>
<td>&lt;0.0001</td>
<td>0.0001</td>
</tr>
<tr>
<td>Unilateral blindness, n (%)</td>
<td>4 (1.6)</td>
<td>4 (3)</td>
<td>1 (4.5)</td>
<td>0.69</td>
<td>0.88</td>
</tr>
<tr>
<td>Bilateral blindness, n (%)</td>
<td>1 (0.4)</td>
<td>1 (0.8)</td>
<td>1 (4.5)</td>
<td>0.74</td>
<td>0.95</td>
</tr>
<tr>
<td>Amaurosis fugax, n (%)</td>
<td>2 (0.8)</td>
<td>1 (0.8)</td>
<td>1 (2.0)</td>
<td>0.98</td>
<td>0.95</td>
</tr>
<tr>
<td>Blurred vision, n (%)</td>
<td>14 (5.6)</td>
<td>10 (7.6)</td>
<td>0 (0)</td>
<td>0.19</td>
<td>0.11</td>
</tr>
<tr>
<td>ESR, mean (SD)</td>
<td>24 (19.4); n=246</td>
<td>26.8 (19.6)</td>
<td>44.3 (33.8)</td>
<td>0.0002</td>
<td>0.001</td>
</tr>
<tr>
<td>CRP, mean (SD)</td>
<td>7.5 (13.4); n=250</td>
<td>8.4 (15.4)</td>
<td>4.2 (6.8)</td>
<td>0.01</td>
<td>0.01</td>
</tr>
<tr>
<td>Positive TAB, n (%)</td>
<td>156 (62.1)</td>
<td>82 (62.1)</td>
<td>32 (65.3)</td>
<td>0.78</td>
<td>0.82</td>
</tr>
<tr>
<td>Imaging techniques, n (%)</td>
<td>138 (55)</td>
<td>70 (53)</td>
<td>29 (59.2)</td>
<td>0.70</td>
<td>0.57</td>
</tr>
<tr>
<td>Positive MRA, n (%)</td>
<td>8 (3.2)</td>
<td>4 (3)</td>
<td>3 (6.1)</td>
<td>0.56</td>
<td>0.60</td>
</tr>
<tr>
<td>Positive CT scan, n (%)</td>
<td>13 (5.2)</td>
<td>7 (5.3)</td>
<td>1 (2.0)</td>
<td>0.98</td>
<td>0.59</td>
</tr>
<tr>
<td>Positive PET/CT scan, n (%)</td>
<td>97 (38.7)</td>
<td>42 (31.8)</td>
<td>26 (53.1)</td>
<td>0.08</td>
<td>0.01</td>
</tr>
<tr>
<td>Patients on corticosteroids at study onset, n (%)</td>
<td>251 (100)</td>
<td>132 (100)</td>
<td>48 (98.0)</td>
<td>0.36</td>
<td>0.60</td>
</tr>
<tr>
<td>Dosage of prednisone at TCZ onset, mean (SD)</td>
<td>recent GCA: 40 (13.1)</td>
<td>30.2 (12)</td>
<td>22.8 (17.6)</td>
<td>&lt;0.0001</td>
<td>0.008</td>
</tr>
<tr>
<td>Patients who had received traditional immunosuppressant agents, n (%)</td>
<td>27 (10.8)</td>
<td>23 (17)</td>
<td>43 (87.7)</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Patients who had received biologic therapy, n (%)</td>
<td>-</td>
<td>-</td>
<td>2 (4.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TCZ route</td>
<td>SC</td>
<td>SC</td>
<td>IV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sustained remission, n (%)§</td>
<td>82 (54.6)</td>
<td>-</td>
<td>19 (38.8)</td>
<td>0.51</td>
<td></td>
</tr>
<tr>
<td>Severe infection, n (%)§</td>
<td>9/150 (6)</td>
<td>-</td>
<td>5 (10.2)</td>
<td>0.49</td>
<td></td>
</tr>
</tbody>
</table>
# includes localized headache, TA, or scalp tenderness, jaw claudication, new or worsened extremity claudication.

§ In RCT patients with active TCZ therapy were only considered

*p<0.05

References:


Disclosure: N. Vegas-Revenga, None; J. Loricera, None; A. Mera, None; E. Pérez- Pampín, None; S. Castañeda, None; L. C. Domínguez-Casas, None; J. L. Martín-Varillas, None; B. Atienza-Mateo, None; M. Gonzalez-Vela, None; J. L. Hernández, None; M. A. González-Gay, None; R. Blanco, None.


Abstract Number: 817

**Extension of Affected Vascular Territories in Secondary Aortitis Is Associated to Different Clinical Subtypes?**

Nuria Vegas-Revenga¹, Javier Loricera¹, Diana Prieto Peña¹, Isabel Martinez-Rodriguez¹, Jose Ignacio Banzo², Monica Calderón Goercke³, Jesús Gonzalez- Vela¹, Jose L. Hernández¹, Vanessa Calvo-Rio¹, L. C. Domínguez-Casas¹, José Luis Martín-Varillas³, Belén Atienza-Mateo³, MC Gonzalez-Vela¹, Miguel Angel González-Gay¹ and Ricardo Blanco³,

¹Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain,
²Nuclear Medicine, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain,
³Rheumatology, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

**Background/Purpose:**

Aortitis is characterized by inflammation of the aortic wall. Aortitis may be associated with different conditions.

Our aim was to assess if the different vascular territories affected in aortitis is associated to different underlying diseases or to different clinical subtypes.

**Methods:**

Retrospective study of 38 patients with non-infectious aortitis diagnosed by PET/CT. Whole-body FDG-PET uptake was assessed 180 minutes after injection of 7 MBq/Kg of 18F-FDG. Images were visually evaluated according to the intensity of the 18F-FDG uptake by the vessel wall at the supraaortic trunks (ST), thoracic aorta (TA), abdominal aorta (AA), iliac arteries (IA) and arteries of lower limbs (LL).
Results:

Thirty-eight patients (28 women/10 men) with a mean age of 68±11 years were assessed. The underlying conditions were: giant cell arteritis (n=24), Takayasu arteritis (n=3), spondiloarthropathie (n=3), Sjögren syndrome (n=3), ulcerative colitis (n=2), sarcoidosis (n=1), rheumatoid arthritis (n=1), and polyarteritis nodosa (n=1).

A total of 190 vascular territories were evaluated, observing FDG-uptake in 122 (64.2%): ST (n=28, 22.3%), TA (n=38, 31.1%), AA (n=26, 21.3%), IA (n=13, 10.7%), and LL (n=17, 13.9%).

Four out of 38 patients (10.5%) had FDG-uptake in a single vascular territory (TA), 10 (26.3%) in 2 territories, 6 (15.8%) in 3, 10 (26.3%) in 4, and 8 (21.1%) in the 5 territories. The most common affection was observed in the 5 territories (n=8), ST/AA (n=6), ST/TA/AA/LL (n=5), ST/TA/AA (n=4) and ST/TA/AA/IA (n=4). Significative differences were observed between the extension of the affection (≤2 vs >2 territories) and the number of months from the symptoms onset to the diagnosis (79.1±59.9 vs 24.5±33.4 months; p=0.003). Differences regarding age, sex underlying disease, C-reactive protein, ESR, or treatment were not observed.

Conclusion:

In patients with secondary non-infectious aortitis, the PET/CT demonstrated a frequent involvement of several vascular territories in addition to aorta, mainly ST. The extension of the vascular affection did not relate to the severity of the clinical syndrome.

Disclosure: N. Vegas-Revenga, None; J. Loricer, None; D. Prieto Peña, None; I. Martínez-Rodríguez, None; J. I. Banzo, None; M. Calderón Goerke, None; J. Gonzalez- Vela, None; J. L. Hernández, None; V. Calvo-Rio, None; L. C. Dominguez-Casas, None; J. L. Martín-Varillas, None; B. Atienza-Mateo, None; M. Gonzalez-Vela, None; M. A. González-Gay, None; R. Blanco, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/extension-of-affected-vascular-territories-in-secondary-aortitis-is-associated-to-different-clinical-subtypes

Correlation between the Routine Assessment of Patient Index Data (RAPID3) and Inflammatory Markers in Patients with PMR

Tiffany Kolniak1, Joshua Baker2, Abhijeet Danve3 and Shiv Tej Sehra4, 1Internal Medicine, Mount Auburn Hospital, Harvard Medical School, Cambridge, MA, 2Rheumatology, University of Pennsylvania, Philadelphia, PA, 3Yale University, New Haven, CT, 4Rheumatology, Mount Auburn Hospital, Harvard Medical School, Cambridge, MA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: The routine assessment of patient index data (RAPID3) was developed for monitoring and prognosis of patients with Rheumatoid Arthritis and has since been extended for use in other rheumatologic disorders including ankylosing spondylitis, psoriatic arthritis and Sjogren’s disease. The purpose of this study was to evaluate the correlation between the RAPID3 and inflammatory markers as well as the physician global assessment of disease (PGA) in patients with polymyalgia rheumatica (PMR).
Methods: Twenty-one patients, including four new cases and seventeen previously diagnosed cases of PMR, were enrolled in the study over a one year period. Each patient completed a RAPID3 questionnaire, had a clinical examination by a rheumatologist and had routine laboratory testing for sedimentation rate (ESR) and C-reactive protein (CRP) as part of routine care at each clinical visit. PGA was collected as active v. inactive disease. The rheumatologist was blinded to the results of the RAPID3 at the time of the visit. The independent associations between RAPID3 and other clinical variables were determined by multivariable linear regression models incorporating generalized estimating equations.

Results: Data was gathered for a total of 53 visits. The patients included in the study were all Caucasian and majority were female (66.7%). The average age was 76 ± 12. The average daily prednisone dose over the course of the year was 5.6 ± 5.1 mg. 43.6% of visits were considered in remission according to the scores on the RAPID3. Nineteen percent of visits had normal ESR and CRP and 75% were felt to be inactive by the treating rheumatologist. In univariate analysis, higher scores on the RAPID3 were correlated with higher ESR [B 0.095 (0.026, 0.17) p=0.008], female sex [B: 4.03 (0.70, 7.37) p=0.02] and physician global scores [B: 7.75 (4.45, 11.1) p<0.001]. In multivariable models, only female sex and physician global were independently associated with RAPID3 score. PGA strongly associated with ESR [B: 11.8 (3.21, 20.36) p<0.001].

Conclusion: The RAPID3 is modestly correlated with inflammatory markers and is strongly associated with physician global assessment of disease activity in PMR. Female sex was also independently associated with higher RAPID3 scores in this population. Further study of the use of RAPID3 in the assessment of disease activity in PMR is of value to determine its potential use as a rapid and easily accessible screening tool for active disease.

<table>
<thead>
<tr>
<th>Association with RAPID3</th>
<th>(N=21, Obs=53)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.024 (-0.19, 0.24)</td>
<td>0.83</td>
</tr>
<tr>
<td>Female</td>
<td>3.94 (0.35, 7.53)</td>
<td>0.03</td>
</tr>
<tr>
<td>Physician Global</td>
<td>7.47 (3.85, 11.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ESR</td>
<td>-0.036 (-0.16, 0.087)</td>
<td>0.57</td>
</tr>
</tbody>
</table>

Disclosure: T. Kolniak, None; J. Baker, None; A. Danve, None; S. T. Sehra, None.


Abstract Number: 819

Risks of Non-Cardiovascular Corticosteroid Related Adverse Events and Cancer in Giant Cell Arteritis: A French Population-Based Cohort Study

Minh Phuong Do¹, Grégory Pugnet², Guillaume Moulis³, Gregory Guernec⁴, Maryse Lapeyre-Mestre⁵ and Laurent Sailler⁶, ¹Faculté de Médecine, Toulouse University, Laboratoire de Pharmacopédiologie, Equipe émergente, UMR INSERM 1027, Toulouse, France, ²Department of Internal Medicine, Toulouse University Hospital, University of Toulouse, INSERM UMR 1027, Toulouse, France, ³Internal Medicine, Toulouse University Hospital, Toulouse, France, ⁴Faculté de Médecine, Toulouse University, UMR INSERM 1027, Toulouse, France, ⁵UMR 1027, INSERM-University of Toulouse, Toulouse, France, ⁶Medecine Interne, CHU Toulouse, Toulouse, France

First publication: September 18, 2017
Background/Purpose:

Corticosteroid related adverse events are a main concern in patients suffering from giant cell arteritis. Conflicting results are reported on this topic, recurrent events are usually not taken into account and direct comparisons with the general population are scarce. We investigated non-cardiovascular corticosteroid related adverse events and cancer risks in an incident GCA patients cohort, the Midi-Pyrénées (southwest France) APOGEE cohort.

Methods:

APOGEE is an administrative database cohort of 103 incident GCA patients (median age : 77 [51-91] years ) and 606 age- and sex-matched controls included between January 2005 and December 2008. The risk of events was compared between patients and controls during the first 36 months of follow-up using Cox models for single events and a linear negative binomial regression model for multiple events (infections and hospitalizations). Generalized estimating equations were used to compare the risk of occurrence across 6-months time periods.

Results:

More than 1 Charlson comorbidity was present before diagnosis in 35% and 46.6% of GCA and control patients, respectively (p=0.03). The hazard ratios (HR) and incidence rate ratios (IRR) of main events are reported in table 1. The risk of any corticosteroid-related events was increased by 49.6% in GCA patients, but it was significant only during the 24 months following diagnosis of GCA. Recurrent (≥2) infections occurred in 61.2% of GCA patients versus 46.7% (p<0.001). The rate ratio of infections was increased and stable throughout the follow-up. Age over 75 years and sex were not significantly associated with the risk of infection but suffering ≥1 comorbidity was (IRR = 1.187, p<0.01). Infection was the main cause of hospitalization in GCA patients. The risk of hospitalization for any cause (excluding the first hospitalization corresponding to GCA diagnosis) was increased (50.5% vs 35.5%, p<0.001) and repeated hospitalizations were more frequent (p<0.001) in GCA patients. Presence of comorbidities was the sole independent predictor of the risk of hospitalization. The initial prednisone dose (<60 mg prednisone vs ≥ 60 mg/d) was not associated with the occurrence of any adverse event.

Conclusion:

Muskuloskeletal events were rare in the setting of osteoporosis prevention. Overall, the risk of serious (leading to hospitalization) or repeated infections is a concern. The increased risk of cancer was unexpected.

Table 1 : risk of new corticosteroid related events and cancer in GCA patients (compared to age and sex matched controls).

<table>
<thead>
<tr>
<th>De novo events</th>
<th>p-value</th>
<th>HR, IC 95%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>&lt;0.05</td>
<td>2.33 [1.03-5.22]</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>&lt;0.01</td>
<td>2.60 [1.35-5.03]</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>&lt;0.001</td>
<td>2.41 [1.45-4.03]</td>
</tr>
<tr>
<td>Cataract (after 1 year)</td>
<td>&lt;0.05</td>
<td>2.14 [1.08-4.23]</td>
</tr>
<tr>
<td>Cutaneous</td>
<td>&lt;0.05</td>
<td>1.28 [1.01-1.63]</td>
</tr>
<tr>
<td>Neuropsychiatric</td>
<td>&lt;0.01</td>
<td>1.48 [1.11-1.95]</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>0.28</td>
<td>IRR , IC 95%</td>
</tr>
</tbody>
</table>

| Infections           | <0.05   | 1.27 [1.07-1.50]|
| Hospitalizations     | <0.05   | 1.79 [1.26-2.53]|

Disclosure: M. P. Do, None; G. Pugnet, None; G. Moulis, None; G. Guernec, None; M. Lapeyre-Mestre, None; L. Sailler, None.
Prognostic Value of Positron Emission Tomography in a Prospective, Longitudinal Cohort of Patients with Large Vessel Vasculitis

Peter C. Grayson¹, Sara Alehashemi², Armin Bagheri³, Ali Cahid Civelek⁴, Thomas Cupps⁵, Mariana J. Kaplan⁶, Ashkan Malayeri⁴, Peter A. Merkel⁷, Elaine Novakovich⁸, David A. Bluemke⁴ and Mark Ahlman⁴, ¹National Institute of Arthritis, Musculoskeletal and Skin Disease (NIAMS), Bethesda, MD, ²Rheumatology, National Institutes of Health, Bethesda, MD, ³Vasculitis Translational Research Program, NIAMS, NIH, Bethesda, MD, ⁴Radiology and Imaging Sciences, National Institutes of Health, Bethesda, MD, ⁵Rheumatology, Georgetown University, Bethesda, MD, ⁶NIAMS/NIH, Bethesda, MD, ⁷University of Pennsylvania, Philadelphia, MN, ⁸Systemic Autoimmunity Branch, NIAMS, National Institutes of Health, Bethesda, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: While several studies have examined the potential of ¹⁸F-fluorodeoxyglucose (FDG) positron emission tomography (PET) to help establish a diagnosis of large vessel vasculitis (LVV), the role of FDG-PET to monitor disease activity over time and predict clinical outcomes remains unclear. The study objective was to assess the clinical value of FDG-PET in a prospective cohort of patients with large-vessel vasculitis (LVV) and disease comparators.

Methods: Patients with Takayasu’s arteritis (TAK) and giant cell arteritis (GCA) were studied, along with a comparator group consisting of patients with hyperlipidemia, diseases that mimic LVV, and healthy controls. All participants underwent clinical evaluation and FDG-PET imaging, and patients with LVV underwent serial imaging at six-month intervals. Performance characteristics of FDG-PET interpretation were calculated to differentiate clinically active LVV from disease comparators and from clinical remission. Multivariable logistic regression in a mixed effects model was used to identify clinical factors associated with FDG-PET scan activity. A qualitative summary score based on global arterial FDG uptake in specific arterial territories was developed (the PET Vascular Activity Score – PETVAS). PETVAS was used to study associations between FDG-PET activity and clinical characteristics and to predict relapse.

Results: 170 FDG-PET scans were performed in 115 patients (LVV=56; comparators=59). FDG-PET differentiated patients with clinically active LVV and disease comparators with a sensitivity=85% (95%CI: 69-94%) and specificity=83% (95%CI: 71-91%). FDG-PET scans were interpreted as active vasculitis in the majority of patients with LVV in clinical remission (41 of 71, 58%). Clinical disease activity status, disease duration, body mass index, and glucocorticoid use were independently associated with FDG-PET remission activity. Among 39 patients who underwent FDG-PET during remission, clinical relapse requiring a change in medical management was more common in patients with a high versus low PETVAS (45% versus 11%, p=0.03) over a median follow-up of 15 months.

Conclusion: FDG-PET provides information about vascular inflammation that is complimentary to, and unique from, clinical assessment in LVV. Use of FDG-PET to detect subclinical vascular inflammation in LVV during remission has prognostic value.

Disclosure: P. C. Grayson, None; S. Alehashemi, None; A. Bagheri, None; A. C. Civelek, None; T. Cupps, None; M. J. Kaplan, None; A. Malayeri, None; P. A. Merkel, None; E. Novakovich, None; D. A. Bluemke, None; M. Ahlman, None.
Discrepancies between Clinical- and Imaging-Based Assessments of Disease Activity in Takayasu’s Arteritis

Peter C. Grayson¹, Mark Ahlman², Kathleen Marinelli³, Renee Borchin⁴, Simon Carette⁵, Nader A. Khalidi⁶, Carol A. Langford⁷, Carol A. McAlear⁸, Paul A. Monach⁹, Christian Pagnoux⁵, Kenneth J. Warrington¹⁰, Steven R. Ytterberg¹⁰ and Peter A. Merkel¹¹

¹National Institute of Arthritis, Musculoskeletal and Skin Disease (NIAMS), Bethesda, MD, ²Radiology and Imaging Sciences, National Institutes of Health, Bethesda, MD, ³NIAMS, National Institutes of Health, Bethesda, MD, ⁴University of South Florida, Tampa, FL, ⁵Division of Rheumatology, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada, ⁶Rheumatology, McMaster University, Hamilton, ON, Canada, ⁷Rheumatic and Immunologic Diseases, Cleveland Clinic, Cleveland, OH, ⁸University of Pennsylvania, Philadelphia, PA, ⁹Boston University School of Medicine, Boston, MA, ¹⁰Rheumatology, Mayo Clinic, Rochester, MN, ¹¹Biostatistics, Epidemiology, and Informatics, University of Pennsylvania, Philadelphia, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose: To study the relationship between clinically-determined disease activity and vascular inflammation assessed by positron emission tomography (PET) in patients with Takayasu’s arteritis (TAK).

Methods: Patients with new or relapsing TAK were evaluated at 5 centers. Whole body ¹⁸F-fluorodeoxyglucose (FDG)PET-CT imaging was performed during a period of clinical disease activity. Clinical assessments were performed blinded to PET scan findings. A single nuclear medicine physician interpreted all of the PET scans, blinded to clinical data, to determine presence of active vasculitis based on degree of arterial FDG uptake. Classification and regression tree analysis (CART) defined predictors of PET scan activity. Elevated acute phase reactants (ESR>30mm/hr, CRP>10mg/L), prednisone dose at time of imaging, ongoing use of other immunosuppressive agents for >1 month at time of clinical assessment, interval between clinical and imaging assessments, and clinical features of disease activity (vascular vs nonspecific) were studied within the CART models. Vascular features included asymptomatic disease progression by angiography. Non-specific features of disease activity were defined as constitutional symptoms accompanied by elevated acute phase reactants in the absence of signs or symptoms of vascular involvement.

Results: Clinical assessments were performed in 25 patients with TAK, and PET scans were performed a mean of 7 days later. FDG-PET findings were suggestive of active vasculitis in 13 of 25 patients (52%). Interval increase in glucocorticoid therapy between clinical assessment and imaging occurred in 4/13 (31%) patients with an active scan and 5/12 (42%) patients with an inactive scan (p=0.69). CART analysis predicted FDG-PET scan activity with 84% accuracy based upon 3 variables: clinical features of disease activity, prednisone dose at the time of imaging, and use of a non-glucocorticoid immunosuppressive agent (Figure). Acute phase reactants and time interval delay between clinical and imaging assessments were not predictive within the model. Clinical features of disease were the strongest determinant of vascular activity on FDG-PET. Among patients with vascular symptoms of disease activity, use of <10mg daily prednisone at the time of imaging assessment and treatment with glucocorticoid monotherapy were associated with increased probability of active vasculitis on FDG-PET.

Conclusion: Clinical features of disease and treatment status are associated with different findings on vascular FDG-PET scan in TAK. Clinical studies that incorporate imaging-based assessment of disease activity in TAK should ideally obtain
baseline imaging studies prior to the initiation of glucocorticoid therapy and should consider exclusion of patients with exclusively non-specific symptoms of disease activity.

![Diagram of Takayasu's Arteritis Assessment](image)

**Disclosure:** P. C. Grayson, None; M. Ahlman, None; K. Marinelli, None; R. Borchin, None; S. Carette, None; N. A. Khalidi, None; C. A. Langford, None; C. A. McAlear, None; P. A. Monach, None; C. Pagnoux, None; K. J. Warrington, None; S. R. Ytterberg, None; P. A. Merkel, None.


**Abstract Number:** 822

**The Incidence Rate of Deep Vein Thrombosis and/or Pulmonary Embolism in Patients with Giant Cell Arteritis – Single Center Observational Study**

**Rok Jese**¹, Alenka Mavri², Ziga Rotar¹, Natasa Kejzar³, Sonja Praprotnik¹, Matija Tomsic¹ and Alojzija Hočevar¹,

¹Department of Rheumatology, University Medical Centre Ljubljana, Ljubljana, Slovenia, ²University Medical Centre Ljubljana, Ljubljana, Slovenia, ³Faculty of Medicine, Institute for Biostatistics and Medical Informatics, University of Ljubljana, Ljubljana, Slovenia

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017
**Session Title:** Vasculitis Poster I: Large Vessel Vasculitis
**Session Type:** ACR Poster Session A
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Recent studies have indicated a higher incidence of deep vein thrombosis (DVT) and pulmonary embolism (PE) in patients with giant cell arteritis (GCA)¹,². Our objective was to determine the incidence rate of concurrent DVT and PE in our prospectively followed GCA patient cohort.

**Methods:** We performed an analysis of our prospectively collected incipient cohort of patients with GCA from December 1st 2011 to December 1st 2016 at a single secondary/tertiary rheumatology center. The proportion of patients who were
diagnosed with concurrent DVT or PE was determined based on patients’ reports and electronic or paper medical records, in addition to clinical and laboratory features of each patient. The DVT and/or PE were defined as concurrent when diagnosed within a time frame extending from 6 months prior until 6 months after the diagnosis of GCA. The cumulative incidence rate of DVT and PE in population aged 50 years and above from the same well defined geographical region in years 2012 to 2015 was acquired from the local electronic DVT/PE registry. Ultimately, standardized incidence ratios (SIR) for DVT and PE with respective 95% confidence intervals (CI) were calculated using Fisher’s exact test.

**Results:** During the 5-year observation period, we identified 83 new GCA cases (median age 73.8 (IQR 66.6–78.8) years, 70% female, 47% ever smokers). Sixty-eight (82%) patients fulfilled the 1990 ACR classification criteria for GCA; the remaining 18% had imaging evidence of large vessel vasculitis. We identified a single patient with PE and no patients with DVT within the prespecified one-year time frame. The 79-year-old non-smoking female was diagnosed with PE 1 week after GCA diagnosis and had a history of arterial hypertension, diabetes and hypercholesterolemia. She had no traditional antiphospholipid antibodies, however we detected IgA subtype antibodies against antiprothrombin/phosphatidilserine complex. No patients were diagnosed with DVT or a PE more than 6 months prior to the diagnosis of GCA. The average incidence rate for concurrent DVT/PE in our GCA cohort was 12.0 per 1000 patient-years, whereas the average incidence rate for DVT/PE in the general population aged 50 years and above, residing in the same region, was 2.4 per 1000 patient-years (565 cases/235,800 residents per year). The SIR was 5.0 (95% CI 0.13–27.86; p=0.362).

**Conclusion:** Contrary to the recent reports, the incidence rate of DVT and PE was not significantly different in our GCA cohort than in the general population of comparable age and residence. Because of the small patient number and only one thrombotic event in our cohort, further monitoring is warranted to confirm or exclude the association between GCA and DVT/PE.

References:

Disclosure: R. Jese, None; A. Mavri, None; Z. Rotar, None; N. Kejzar, None; S. Praprotnik, None; M. Tomsic, None; A. Hočevar, None.


Abstract Number: 823

**Seasonal Variation in Giant Cell Arteritis and Polymyalgia Rheumatica Hospitalizations: Data from Nationwide Inpatient Sample**

Paras Karmacharya1, Dilli Poudel2, Pragya Shrestha3, Rashmi Dhital4 and Raju Khanal4, 1Division of Rheumatology, Mayo Clinic, Rochester, MN, 2Internal Medicine, Reading Health System, WEST READING, PA, 3Internal medicine, Reading Health System, West Reading, PA, 4Internal Medicine, Reading Health System, West Reading, PA

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Sunday, November 5, 2017
**Session Title:** Vasculitis Poster I: Large Vessel Vasculitis
**Session Type:** ACR Poster Session A
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Most studies looking at seasonal variations in giant cell arteritis (GCA) note a seasonal trend, but show disparity on timing. Concurrent peaks of GCA and polymyalgia rheumatica (PMR) have been described by some studies questioning a common precipitating agent. We aimed to analyze the seasonal variation of GCA and PMR in the US using a large inpatient database.
Methods: We used Nationwide Inpatient Sample (NIS) database to identify patients aged ≥ 18 years from 2009-11 with a diagnosis of GCA and PMR with ICD-9-CM codes 446.5 and 725 in the first 3 positions. We used the Edwards’ recognition and estimation of cyclic trend method to study the seasonal patterns of GCA and PMR hospitalizations stratified by age. Z-test was used to compare seasonal incidences.

Results:

A total of 57728 and 242862 hospitalizations with a diagnosis of GCA and PMR respectively were reported from 2009-11. A significant seasonal variation was observed with highest number of GCA hospitalizations in summer (peak/low ratio 1.092, 95% CI 1.067-1.118, p<0.0001) and most significant peaks seen in age group 65-69 (peak/low ratio 1.092, 95% CI 1.067-1.118, p<0.0001) (Figure 1). No significant seasonal variation was seen with PMR hospitalizations.

Conclusion:

Our study found peak GCA hospitalizations in summer months which is concurrent with trends seen in Israel and England but differ from other studies showing peaks in late winter and autumn. Interestingly, no similar pattern was observed in closely related disorder, PMR. A better understanding of these patterns could lead to identification and possibly control of potential environmental triggers in the genetically predisposed population.

Disclosure: P. Karmacharya, None; D. Poudel, None; P. Shrestha, None; R. Dhital, None; R. Khanal, None.


Abstract Number: 824

Long Term Efficacy and Safety of Intravenous and Subcutaneous Biologics in Large Vessels Vasculitis: 21 Patients Belonging to a Single Italian Center from 2011 to 2017

Paola Toniati¹ and Angela Tincani², ¹RHEUMATOLOGY, SPEDALI CIVILI, BRESCIA, Italy, ²University and Spedali Civili of Brescia, Brescia, Italy

First publication: September 18, 2017
SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Vasculitis Poster I: Large Vessel Vasculitis
Session Type: ACR Poster Session A
Session Time: 9:00AM-11:00AM

Background/Purpose:

Large vessels vasculitis (LVV) is the most common form of primary vasculitis comprising giant cell arteritis (GCA) and Takayasu arteritis (TAK) and aortitis.

Methods:

We collect retrospectively 21 patients affected by LVV, resistant to conventional therapy and treated with intravenous or subcutaneous biologics. Four patients were affected by GCA, with positive temporal artery biopsy; nine patients were affected by TAK according to 1990 ACR criteria and eight patients were affected by aortitis (two with associated retroperitoneal fibrosis), diagnosed with a positive 18F-FDG-PET scan, indicating active LVV with aortic involvement. Data from 18F-FDG PET and CT or MRI associated with improvement of clinical and inflammatory index (ESR and PCR) were used as a criteria of response to treatment. Our aim is to demonstrate the long term efficacy and safety of biologics in LVV.

Results:

The mean age of 21 patients were 57 year (18-87). Five patients were men with mean age of 65 year (32-79), 16 were women with mean age of 55.3 year (18-87). The mean follow-up time of patients was 29 months (2-79). Eighteen patients out of 21 (86%), suffered an aortic involvement at diagnosis discovered with 18F-FDG-PET scan. These patients were checked yearly with imaging using 18F-FDG-PET with a semiquantitative analysis. 18F-FDG-PET scan follow-up data were available in 12 patients. Tocilizumab (TCZ) was used in 19 patients for a medium period of follow-up period of 25 months (2-60). All patients started with EV TCZ (8 mg/kg/4w), then five patients passed to subcutaneous TCZ reducing the dose to 162 mg/2w. Seventeen patients demonstrated a good response with clinical improvement, reduction of inflammatory index and sparing of steroid dose. Two TAK patients experienced a failure treatment (new stenosis) one after one and the other after 4 year of treatment each. Infliximab was used in 3 patients and suspended in all three patients for infusive reactions, after three (one patient) and six month (2 patients) of treatment. Adalimumab (ADA) was used in 2 patients: one patient responded well with a negative PCR and a negative 18F-FDG-PET scan after one year of treatment and maintain stable remission without steroid, lasting 79 months; the other patient started the treatment three month ago. Golimumab 100 mg/m was used in one TAK patient, resistant to TCZ, with achieving a stable clinical and imaging remission (no new stenosis) during the last year. This patient refused steroid assumption. The side effects were bronchitis affecting two patients with TCZ and one patient with ADA and golimumab each. One patient with aortitis retroperitoneal fibrosis suspended TCZ after two infusions for acute cholecystitis. Mean steroid dose at the beginning of biologics treatment were 30 mg/day (50-0). Mean steroid dose at the last follow-up was 7 mg/day (32-0).

Conclusion:

In these group of 21 patients biological treatments demonstrated longterm efficacy and acceptable safety profile and important steroid sparing effect.

Disclosure: P. Toniati, None; A. Tincani, None.


Abstract Number: 825

Radiological Disease Activity Is the Major Determinant for Physicians While Deciding Active Disease in Takayasu Arteritis
Gokce Kenar¹, Sedanur Karaman², Pinar Cetin³, Handan Yarkan⁴, Berrin Zengin¹, Gercek Can¹, Merih Birlik⁵ and Fatos Onen¹, ¹Rheumatology, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey, ²Internal Medicine, Dokuz Eylul University, izmir, Turkey, ³Rheumatology, Dumlupınar University School of Medicine, Kutahya, Turkey, ⁴Rheumatology, Dokuz Eylul University Faculty of Medicine, İzmir, Turkey, ⁵Rheumatology, Dokuz Eylul University Faculty of Medicine, İzmir, Turkey

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Vasculitis Poster I: Large Vessel Vasculitis

**Session Type:** ACR Poster Session A

**Session Time:** 9:00AM-11:00AM

Background/Purpose: There are no valid followup parameters in the assessment of disease activity in Takayasu arteritis (TA). We investigated the impact of incorporation of vascular imaging into ITAS in the assessment of disease activity in TA.

**Methods:** 52 patients who fulfilled the ACR criteria were included. Physician global assessment (PGA), Kerr, et al's criteria (K, eC) and ITAS2010/ITAS-A scores were evaluated in all patients (1,2). All the patients were followed using 3-6 monthly USG and 6-12 monthly MR angiography (MRA). Radiological activity (Rad) was defined based on the presence of any of the 3 parameters including new vessel involvement by any imaging technique (5 points), the increase in vessel wall thickness USG (3 points) and vessel wall edema on MRA (3 points). Then we incorporated these scores with ITAS-A to obtain a composite disease activity index (ITAS-A-Rad)(table1).

**Results:** Total 410 visits of 52 TA patients (mean age 50.7, F:92.3%, mean followup duration: 6.4 ± 2.9 yrs) were evaluated. Radiological assessment was done in 359 visits. Patients were categorized as having active disease in 194 visits (47.4%) according to PGA and 72 visits (17.5%) according to K, eC. The agreement between them was fair (66%, :0.29). Rad parameters were determined in 105 out of 359 visits. The total agreement was found to be 83% (:0.58) between the radiological disease activity and K, eC and 76% (:0.52) between the RAD and PGA. Mean ITAS-A-Rad scores were significantly higher in visits with active disease compared to visits with inactive disease according to both PGA and K, eC (table2). The ITAS-A-Rad was significantly correlated with all the other activity parameters including ITAS2010, ITAS-A, and APRs. There were 43 visits with new vessel involvement by any of the two imaging techniques; all visits included patients with active disease based on both PGA and Kerr et al criteria. The agreement between ITAS2010 and PGA was fair (69%, :0.38). When acute phase reactant was added (ITAS-A), it did not improve (68%, :0.34). But the agreement between ITAS-A-Rad and PGA (72%, :0.50) and also K, eC (82%,:0.56) was found to be moderate. When only ITAS-A-USG or only ITAS-A-MRA was used, the agreement with PGA remained unchanged (73%,:0.45 and 76%,:0.52 respectively). When responsiveness to change of ITAS-A-Rad score was evaluated by serial visits of patients, it was found that the mean value of the score was discriminative for disease activity according to PGA in 9 of 11 visits (Figure1).

**Conclusion:** This study suggest that ITAS A Rad, a modified ITAS2010 score may be used to be a valuable follow-up parameter in the assessment of disease activity in TA.
TGF-β-Induced Epigenetic Silencing of SOCS3 Facilitates STAT3 Signaling to Promote Fibroblast Activation and Tissue Fibrosis in Systemic Sclerosis
Clara Dees\textsuperscript{1}, Yun Zhang\textsuperscript{2}, Sebastian Poetter\textsuperscript{1}, Christina Bergmann\textsuperscript{3}, Andreas Ramming\textsuperscript{4}, Oliver Distler\textsuperscript{5}, Georg Schett\textsuperscript{6} and Jörg Distler\textsuperscript{7}, \textsuperscript{1}Department of Internal Medicine 3 and Institute for Clinical Immunology, University of Erlangen-Nuremberg, Erlangen, Germany, \textsuperscript{2}Department of Internal Medicine 3 and Institute for Clinical Immunology, Department of Internal Medicine 3 and Institute for Clinical Immunology, Friedrich-Alexander-University of Erlangen-Nuremberg and University Hospital Erlangen, Erlangen, Germany, \textsuperscript{3}Department of Internal Medicine 3 and Institute for Clinical Immunology, Friedrich-Alexander-University Erlangen-Nuremberg and University Hospital Erlangen, Erlangen, Germany, \textsuperscript{4}Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Erlangen, Germany, \textsuperscript{5}Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland, \textsuperscript{6}Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, Erlangen, Germany., Erlangen, Germany, \textsuperscript{7}Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Erlangen, Germany

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Plenary Session I
Session Type: ACR Plenary Session
Session Time: 11:00AM-12:30PM

Background/Purpose: Tissue fibrosis caused by pathological activation of fibroblasts is a major hallmark of systemic sclerosis (SSc). Although fibroblast activation is initially driven by external factors, prolonged activation can render fibroblasts independent of external stimuli. Accumulating evidence suggests that epigenetic alterations play a central role to establish the persistently activated phenotype of fibroblasts. In the present study, we tested the hypothesis that epigenetic silencing of SOCS expression may contribute to the aberrant activation of JAK2 / STAT3 signaling in SSc, and that re-establishment of the endogenous, SOCS-dependent control of JAK / STAT signaling may prevent aberrant fibroblast activation and ameliorate tissue fibrosis.

Methods: DNA methylation was evaluated by methylation-specific PCR and MeDIP assays. 5-aza-2’-deoxycytidine (5-aza) was used to inhibit DNA methyltransferases (DNMTs). Knockdown analyses were done by nucleofection of siRNA \textit{in vitro} and by fibroblast-specific knockout mice \textit{in vivo}.

Results: SOCS3 was strongly downregulated in skin of SSc patients compared to healthy individuals. Chronically increased levels of TGF\(\beta\) induced an SSc-like phenotype and reduced the levels of SOCS3 in normal fibroblasts to a level comparable with SSc fibroblasts. These findings suggested that epigenetic mechanisms may account for the reduced expression of SOCS3. Indeed, methylation analyses demonstrated a prominent promoter hypermethylation of SOCS3 in SSc fibroblasts and in normal fibroblasts exposed to persistently high levels of TGF\(\beta\). Mechanistically, chronically increased levels of TGF\(\beta\) promoter hypermethylation of the SOCS3 promoter by induction of DNMT3A. Pharmacological inhibition of DNMTs or selective knockdown of DNMT3A restored the normal expression of SOCS3 and reduced fibroblast activation and collagen release. Knockdown of SOCS3 in normal dermal fibroblasts induced an SSc-like phenotype with increased activation of JAK2-STAT3 signaling, enhanced expression of myofibroblast markers and increased collagen release. Fibroblast-specific knockout of SOCS3 promoted JAK2-STAT3 signaling and aggravated tissue fibrosis in bleomycin- and TGF\(\beta\)RI\textsuperscript{act}-induced dermal fibrosis. Vice versa, forced overexpression of SOCS3 inhibited TGF\(\beta\)-induced JAK2-STAT3 signaling and reduced TGF\(\beta\)-mediated fibroblast activation. Overexpression of SOCS3 also ameliorated the endogenous activation of SSc fibroblasts. Moreover, treatment with DNMT inhibitors or fibroblast-specific knockdown of DNMT3A re-activated the expression of SOCS3, reduced JAK2-STAT3 signaling and exerted potent antifibrotic effects in bleomycin- and TGF\(\beta\)RI\textsuperscript{act}-induced dermal fibrosis.

Conclusion: We demonstrate that chronic activation of TGF\(\beta\) signaling perturbs the epigenetic control of STAT signaling by DNMT3A-induced silencing of SOCS3 expression in SSc. Re-establishment of the endogenous regulation of STAT signaling, either by forced expression of SOCS3 or by pharmacologic inhibition of DNMTs, prevents aberrant STAT3 signaling, inhibits TGF\(\beta\)-induced fibroblast activation and collagen release and ameliorates experimental fibrosis.

Disclosure: C. Dees, None; Y. Zhang, None; S. Poetter, None; C. Bergmann, None; A. Ramming, None; O. Distler, 4 D Science, Actelion, Active Biotec, Bayer, Biogen Idec, Boehringer Ingelheim Pharma, BMS, ChemomAb, EpiPharm,
Temporary Methotrexate Discontinuation for 2 Weeks Improves Immunogenicity of Seasonal Influenza Vaccination in Patients with Rheumatoid Arthritis: A Randomized Clinical Trial

Jin Kyun Park¹, Kichul Shin², You-Jung Ha³, Yun Jong Lee⁴, Eun Young Lee⁵, Yeong Wook Song⁶, Yunhee Choi⁷, Kevin Winthrop⁸ and Eun Bong Lee⁹

¹Division of Rheumatology, Seoul National University Hospital, Seoul, Korea, Republic of (South), ²Kyungnam villa #102, Division of Rheumatology, Department of Internal Medicine, SMG-SNU Boramae Medical Center, Seoul, Korea, Republic of (South), ³Yonsei University College of Medicine, Seoul, Korea, Republic of (South), ⁴Division of Rheumatology, Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, Korea, Republic of (South), ⁵Division of Rheumatology, Department of Internal Medicine, Seoul National University, Seoul, Korea, Republic of (South), ⁶Department of Molecular Medicine and Biopharmaceutical Sciences, Graduate School of Convergence Science and Technology, and College of Medicine, Seoul National University, Seoul, Korea, The Republic of, Seoul, Korea, Republic of (South), ⁷Division of Rheumatology, Department of Medical Statistics, Medical Research Collaborating Center, Seoul National University College of Medicine, Seoul, Korea, Republic of (South), ⁸Oregon Health & Science University, Portland, OR, ⁹Division of Rheumatology, Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Plenary Session I

**Session Type:** ACR Plenary Session

**Session Time:** 11:00AM-12:30PM

**Background/Purpose:** Methotrexate (MTX), a widely used immune-suppressive agent, decreases vaccine response in patients with rheumatoid arthritis (RA). We investigated whether a temporary MTX discontinuation for 2 weeks after vaccination improves the efficacy of seasonal influenza vaccination in RA patients.

**Methods:** In this prospective, multicenter, randomized, parallel-group trial, RA patients taking stable dose of MTX were randomly assigned at a ratio of 1:1 to continue MTX (MTX-continue group) or to suspend MTX for 2 weeks after vaccination (MTX-hold group). All participants were vaccinated with seasonal quadrivalent influenza vaccine containing H1N1, H3N2, B-Yamagata, and B-Victoria. The primary outcome was frequency of satisfactory vaccine response, defined as ≥4-fold increase in hemaglutination inhibition (HI) antibody titer at 4 weeks after vaccination against ≥2 of 4 vaccine strains. Secondary endpoints included seroprotection rate, fold-change in antibody titers relative to baseline in geometric mean titer (GMT).

**Results:** We enrolled 320 patients between Oct 7, 2016 and Jan 9, 2017. The modified intention-to-treat population consisted of 316 patients (156 in the MTX-continue group and 160 in the MTX-hold group). Higher proportion of patients in MTX-hold group achieved satisfactory vaccine response compared to MTX-continue group (75.5% vs. 54.5%, p < 0.001) (Figure). Post-vaccination seroprotection rate was higher for all 4 antigens in the MTX-hold group than the MTX-continue group (H1N1: 75.6% vs. 86.3%, p=0.016; H3N2: 62.2% vs.78.1%, p=0.002; B-Yamagata: 74.4% vs. 88.1%, p=0.002; B-
Victoria: 60.9% vs. 75.6%, p = 0.005). Similarly, the MTX-hold group achieved higher fold increase of post-vaccination HI antibody titer in GMT [95% CI] for each antigen (H1N1: 4.6 [3.7 - 5.7] vs. 6.7 [5.4 - 8.3], p = 0.017; H3N2: 4.3 [3.5 - 5.3] vs. 8.0 [6.4 - 9.9], p < 0.001; B-Yamagata: 3.1 [2.6 - 3.8] vs. 5.6 [4.7 - 6.6], p < 0.001; B-Victoria: 2.9 [2.4 - 3.4] vs. 5.7 [4.9 - 6.7], p < 0.001). Vaccine was well tolerated. Disease activity after vaccination did not differ between both groups.

Conclusion:

Temporary MTX discontinuation for 2 weeks after vaccination improves the immunogenicity of seasonal influenza vaccination in RA patients without increasing RA disease activity.

Trial registration: [www.clinicaltrials.gov, protocol number NCT02897011].

**Figure. Frequency of satisfactory vaccine response to 4 influenza antigen strains.** Numbers in the bars (95% confidence interval) indicate the percentage of satisfactory responses. MTX, methotrexate.

Disclosure: J. K. Park, None; K. Shin, None; Y. J. Ha, None; Y. J. Lee, None; E. Y. Lee, None; Y. W. Song, None; Y. Choi, None; K. Winthrop, Pfizer, UCB, Abbvie, Eli Lilly and Company, Amgen, BMS, 5, Pfizer, BMS, 2; E. B. Lee, Green Cross Corp, 2, Pfizer Inc, 5.


Abstract Number: 828

**The Impact of the Duration of Bisphosphonate Drug Holidays on Hip Fracture Rates**

Jeffrey R. Curtis¹, Rui Chen², Zixu (Eric) Li², Tarun Arora², Kenneth Saag³, Nicole C. Wright⁴, Shanette Daigle², Meredith Kilgore⁵ and Elizabeth Delzell⁶, ¹Rheumatology & Immunology, University of Alabama at Birmingham, Birmingham, AL, ²University of Alabama at Birmingham, Birmingham, AL, ³Department of Medicine, Veterans Administration San Diego Healthcare System/UC San Diego, San Diego, CA, ⁴Epidemiology, University of Alabama at Birmingham, Birmingham, AL, ⁵Health Care Organization & Policy, University of Alabama at Birmingham, Birmingham, AL, ⁶Retired - University of Alabama at Birmingham, Birmingham, AL

First publication: September 18, 2017
Background/Purpose: Given FDA warnings, drug holidays (temporary or permanent discontinuation) of bisphosphonates (BPs) after long-term (3-5 years) continuous therapy is becoming increasingly common in the United States (US). However, the benefits and risks of stopping BPs, and the optimal timing to restart, remain unclear. We conducted a population-based cohort study of women on long term BP therapy to evaluate the rate of hip fracture following a drug holiday.

Methods: We used Medicare data (2006-2014) to identify all women with medical and pharmacy coverage who initiated a BP and were at least 80% adherent for ≥3 years (‘baseline’), at which follow-up time began. Patients using other bone therapies (e.g. denosumab, estrogen, teriparatide, calcitonin) were excluded or censored if they started after follow-up began. We calculated crude rates of hip fracture for continuing BP therapy and among those who discontinued, for categories of time since discontinuing (i.e., length of drug holiday), extending up to 3 years. We used Cox proportional hazards models to evaluate the risk of discontinuing per the length of the drug holiday, using age as the time axis and controlling for potentially confounding factors, with and without adjusting for death as a competing risk.

Results: We identified 156,236 women who were highly adherent, long-term BP users. The mean (SD) age was 78.5 (7.5) years. The most commonly used BPs were alendronate (71.7% ever use, 52% exclusive use) and zoledronic acid (16.2% ever use, 8.9% exclusive use). During a median (IQR) follow up of 2.1 (1.0, 3.3) years, 62,676 (40.1%) of women stopped BP therapy for at least 6 months or more. Among these women, 7,947 (12.7%) subsequently restarted any BP. Overall, 16,904 (10.8 %) died.

A total of 3,745 hip fractures occurred during follow-up. Hip fracture rates were lowest among women who were current users, and gradually increased as the length of the drug holiday increased, achieving their maximum with a drug holiday >2 years (Table).

Conclusion: In a large cohort of U.S. women, a BP drug holiday greater than 2 years was associated with a significantly increased risk for hip fracture of up to 39% compared to continued BP use.

<table>
<thead>
<tr>
<th>Time since Bisphosphonate Discontinuation (yrs)</th>
<th>Number of hip fractures, n</th>
<th>Crude Incidence Rate per 1,000 person-years</th>
<th>Adjusted* Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (i.e. current use)</td>
<td>1958</td>
<td>9.6 (9.2, 10.1)</td>
<td>1.0 (reference)</td>
</tr>
<tr>
<td>&gt;0 to &lt;= 3 months</td>
<td>530</td>
<td>13.1 (12.0, 14.3)</td>
<td>1.29 (1.17, 1.42)</td>
</tr>
<tr>
<td>&gt;3 months &lt;=1 year</td>
<td>539</td>
<td>12.0 (11.0, 13.1)</td>
<td>1.12 (1.02, 1.24)</td>
</tr>
<tr>
<td>&gt;1 to &lt;=2 years</td>
<td>422</td>
<td>13.3 (12.0, 14.6)</td>
<td>1.21 (1.09, 1.35)</td>
</tr>
<tr>
<td>&gt;2 to &lt;=3 years</td>
<td>235</td>
<td>15.7 (13.7, 17.8)</td>
<td>1.39 (1.21, 1.59)</td>
</tr>
</tbody>
</table>

*adjusted for age, region, race, rural or urban, median income, calendar year, comorbidity(fragility fracture, charlson comorbidity index score), DXA, number of physician visits, care by a rheumatologist or endocrinologist, long term care residence, vitamin D deficiency, glucocorticoids, and proton pump inhibitors

Disclosure: J. R. Curtis, AbbVie, Roche/Genentech, BMS, UCB, Myriad, Lilly, Amgen, Janssen, Pfizer, Corrona, 5,Amgen, Pfizer, Crescendo Bio, Corrona, 9; R. Chen, Amgen, 2; Z. Li, Amgen, 2; T. Arora, Amgen, 2; K. Saag, Amgen, Merck and Radius, 5,Amgen, Merck, 2; N. C. Wright, None; S. Daigle, None; M. Kilgore, Amgen, 2; E. Delzell, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-impact-of-the-duration-of-bisphosphonate-drug-holidays-on-hip-fracture-rates

Abstract Number: 829
Unraveling Race and Social Context in Understanding Disparities in Lupus Mortality in the United States

Titilola Falasinnu, Yashaar Chaichian, Latha Palaniappan and Julia F Simard, Health Research and Policy, Stanford University, Stanford, CA; Medicine, Immunology & Rheumatology Division, Stanford School of Medicine, Stanford, CA; Stanford University Medical Center, General Medical Disciplines, Stanford, CA; Division of Epidemiology, Health Research and Policy Department, Stanford School of Medicine, Stanford, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Plenary Session I
Session Type: ACR Plenary Session
Session Time: 11:00AM-12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that is a source of significantly decreased life expectancy in the United States. Women and racial/ethnic minorities account for an increasingly disproportionate number of cases, with genetic factors regarded as potentially causative. The role of social and environment contexts has received little attention. We examined SLE mortality rates across eight groups of race-county combinations of the US population, developed by Murray et al in 2006, that are referred to as the “Eight Americas”. We examined SLE mortality in the Eight Americas over time to assess whether the impact of race is attenuated when the social and geographic context is also considered. We also examined whether age at death in SLE decedents differs across the Eight Americas, and explicated patterns of disease comorbidities among SLE decedents in the Eight Americas.

Methods: Using death certificate data from the National Center for Health Statistics Multiple Cause of Death (MCOD) database, SLE-related deaths were identified via International Classification of Diseases, 10th revision (ICD-10) codes: M32.1, M32.9, and M32.8. Annual SLE-related mortality rates and mortality rate ratios were calculated for each of the Eight Americas using America 3 as the reference category. Average Annual Percent Change (AAPC) in mortality rates summarized trends over a fixed predetermined interval. To examine trends in associated causes of death listed in the death certificates of SLE decedents, we calculated Proportionate Mortality Ratios (PMRs) for the top causes of death (derived from the literature) among SLE patients. Statistical analyses were performed using SAS version 9.4.

Results: There were 24,773 SLE-related deaths between 2003 and 2014. Mortality was highest among blacks in three race-geographical contexts (Americas 6, 7, & 8). Age at death was lowest (~48 years) for blacks and Asians, regardless of geographical context, and highest among low-income rural whites (~65 years). Blacks and Asians were also more likely to have infectious diseases listed as associated causes of death, a finding consistent across geographical contexts, while whites were more likely to have cardiovascular diseases and neoplasms reported as associated causes of death.

Conclusion: Blacks sharing the same social and geographical contexts as whites were disproportionately more likely to die young and exhibit severe patterns of mortality. Although blacks inhabited three vastly different geographical and social contexts, SLE mortality parameters did not vary among socially advantaged and disadvantaged blacks. Together, these findings suggest that race may transcend social and geographical parameters as a key determinant of SLE mortality.

Disclosure: T. Falasinnu, None; Y. Chaichian, None; L. Palaniappan, None; J. F. Simard, None.


Abstract Number: 830

Performance on Quality Measures in the RISE Registry and the Merit-Based Incentive Payment System (MIPS)
SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Plenary Session I
Session Type: ACR Plenary Session
Session Time: 11:00AM-12:30PM

Background/Purpose: Under the new Medicare Access and CHIP Reauthorization Act (MACRA), the quality of care rheumatologists provide will have financial repercussions through the Merit Based Incentive Program (MIPS). MIPS will score providers across four domains: Quality, Clinical Practice Improvement, Advancing Care Information and Cost. In this study, we sought to evaluate performance on quality measures for practices participating in the Rheumatology Informatics System for Effectiveness (RISE) registry in the first quarter of 2017 and to develop a prototype dashboard for RISE to assist clinicians in understanding their MIPS performance.

Methods: The RISE informatics platform continuously collects data from the electronic health records (EHRs) of participating practices, allowing centralized aggregation and analysis of quality measures. Measures in the areas of rheumatoid arthritis, drug safety, preventive care and gout were examined. For the first quarter of 2017 (the initial period eligible for MIPS reporting), we calculated performance on quality measures, defined as the percentage of eligible patients receiving recommended care. We also developed a prototype dashboard for RISE that will display scores across the four MIPS domains to help clinicians track their performance over time.

Results: Data from 548,990 patients across 491 clinicians and 109 practices was examined. Most rheumatologists were in a group practice (72%); 26% were in solo practice and 2% part of a larger health system. Mean (SD) patient age was 59 (16) years, 75% were female, 21% were racial/ethnic minorities. Performance on measures varied significantly across practices (Table). For 2 of 5 measures for which the Medicare program has set national benchmarks, average performance of RISE practices exceeded targets in the first quarter of 2017. Quality measures that make up the MIPS quality domain were combined with simulated information for other MIPS domains to develop a MIPS dashboard prototype for RISE, displayed in the Figure.

Conclusion: We found significant variation in performance on quality measures in the first quarter of 2017 across RISE practices, with some practices having already achieved a very high level of performance. We anticipate that the MIPS dashboard prototype will go-live on the RISE user interface in late 2017 and will aid rheumatologists in proactively monitoring their MIPS score.

Table. Performance on Quality Measures in the RISE Registry in 2017.
<table>
<thead>
<tr>
<th>Measure</th>
<th>Measure</th>
<th>Average</th>
<th>Practice-level</th>
<th>CMS benchmark</th>
</tr>
</thead>
<tbody>
<tr>
<td>eCQM</td>
<td>denominator</td>
<td>performance</td>
<td>percentile</td>
<td>(N)</td>
</tr>
<tr>
<td>Rheumatoid arthritis: Assessment of Disease Activity</td>
<td>95,662</td>
<td>46.2</td>
<td>43.6</td>
<td>83.8</td>
</tr>
<tr>
<td>Functional Status Assessment</td>
<td>95,662</td>
<td>45.6</td>
<td>42.6</td>
<td>85.9</td>
</tr>
<tr>
<td>DMARD Drug Safety</td>
<td>9,684</td>
<td>57.9</td>
<td>65.9</td>
<td>78.6</td>
</tr>
<tr>
<td>TB screening pre-biologic</td>
<td>159,370</td>
<td>5.7</td>
<td>2.8</td>
<td>0</td>
</tr>
<tr>
<td>1+ High-Risk Medication in Elderly*</td>
<td>159,370</td>
<td>0.1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2+ High-Risk Medications in Elderly* Preventive Care</td>
<td>280,725</td>
<td>77.9</td>
<td>87.4</td>
<td>92.3</td>
</tr>
<tr>
<td>Tobacco screening and counseling</td>
<td>231,846</td>
<td>41.7</td>
<td>34.3</td>
<td>59.0</td>
</tr>
<tr>
<td>BMI documentation, follow-up plan</td>
<td>58,594</td>
<td>62.9</td>
<td>62.4</td>
<td>74.8</td>
</tr>
<tr>
<td>Blood pressure management</td>
<td>2,487</td>
<td>32.1</td>
<td>36.4</td>
<td>47.1</td>
</tr>
<tr>
<td>Gout</td>
<td>3,251</td>
<td>30.0</td>
<td>26.5</td>
<td>47.5</td>
</tr>
<tr>
<td>Serum urate monitoring</td>
<td>1,098</td>
<td>64.2</td>
<td>80</td>
<td>95.7</td>
</tr>
<tr>
<td>Serum urate target &lt;6.8 mg/dL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum urate lowering therapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Interferon-Alpha Disrupts Tolerance in a Mouse Model of B Cell Anergy

Dario Ferri\textsuperscript{1}, Yuriy Baglaenko\textsuperscript{2}, Kieran Manion\textsuperscript{2}, Nan-Hua Chang\textsuperscript{2} and Joan E. Wither\textsuperscript{3}, \textsuperscript{1}Immunology, University of Toronto, Toronto, ON, Canada, \textsuperscript{2}Genetics and Development, Krembil Research Institute, University Health Network, Toronto, ON, Canada, \textsuperscript{3}Rheumatology, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: B Cell Biology and Targets in Autoimmune Disease
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is characterized by the production of anti-nuclear antibodies that deposit within tissues leading to organ damage. A central mediator of SLE pathogenesis is interferon-alpha (IFN\textalpha), which is elevated in the serum of SLE patients. IFN\textalpha has been shown to enhance B cell signaling and promote the survival of B cells. It also plays a major role in the induction of B cell activating factor (BAFF). While past studies have explored the indirect effects of IFN\textalpha through BAFF on B cell tolerance, little work has focused on how IFN\textalpha itself directly affects this process. We hypothesize that elevated levels of IFN\textalpha directly contribute to the breach of B cell tolerance in SLE. To address this question, we have obtained an adenoviral vector encoding mouse IFN\textalpha (mDEF201), which we are using to induce sustained elevations of serum IFN\textalpha in several well characterized mouse models of B cell tolerance.

Methods: IgHEL/sHEL double transgenic mice, with transgenes encoding anti-hen egg white lysozyme (HEL) Ig and soluble HEL were injected IV with $10^7$ PFU of Ad-mIFN\textalpha (mDEF201) or Ad-dl70-3 (empty control vector). At 2 weeks post-treatment immune cell populations in the spleen and bone marrow were examined by flow cytometry, and anti-HEL antibody production was measured by ELISA. Serum levels of IFN\textalpha were quantified by ELISA and tissue-specific IFN-induced gene expression was assessed by qRT-PCR.

Results: 6-8 week old C57BL/6 mice administered with mDEF201, but not Ad-dl70-3, showed robust elevations of serum IFN\textalpha from 48h to 2 weeks post infection. At 2 weeks post injection expression of several IFN-inducible genes (2-5’ Oas, Pkr, Mx1, Ifit1, Irf7, Lsg15), but not Baff, was elevated in the liver, bone marrow and spleen of infected mice. B cell homeostasis and activation were altered in IgHEL/sHEL mice following administration of mDEF201. At 2 weeks post
infection mice displayed increased proportions of total splenic B cells (B220⁺CD19⁺). Infected mice also displayed an increase in the proportion of mature B cells (B220⁺CD93⁺) and decreased proportions of immature transitional 1 and 2 B cells (CD24⁺CD21⁻/int). Upregulation of the B cell activation marker B7.2 (CD86⁺) and down regulation of surface IgM was observed on mature B cells in infected mice suggestive of enhanced B cell signalling. At 2 weeks post infection mice also displayed increased proportions of germinal center B cells (B220⁺GL7⁺CD95⁺). Upregulation of CD86 and enhanced maturation of the B cell compartment was not seen following infection of mice with Ad-dI70-3. Anti-HEL IgM antibody production was increased 2 weeks post infection signifying a breach of B cell tolerance in IgHEL/shHEL mice. No differences in T cell populations or activation state were seen suggesting that the observed effects on B cells occurred largely from altered B and not T cell function.

**Conclusion:** IFNα may be playing an important role in breaching B cell tolerance in SLE not only through the induction of BAFF but also through its direct actions on B cells. Further research into the effects of IFNα on these processes may prove IFNα to be a more effective therapeutic target than BAFF for SLE patients.

**Disclosure:** D. Ferri, None; Y. Baglaenko, None; K. Manion, None; N. H. Chang, None; J. E. Wither, None.


**Abstract Number:** 832

**Single Cell Analysis Reveals Heterogeneity of Type I IFN Gene Expression in Developing Autoreactive B Cells**

**Jennie Hamilton**, PingAr Yang, Qi Wu, Bao Luo, Shanrun Liu, Jun Li, Mark Walter, Eleanor Fish, Hui-Chen Hsu and John D. Mountz, 
1Medicine/Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 2Department of Medicine, Clinical Immunology & Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 3Department of Medicine, University of Alabama at Birmingham, Birmingham, AL, 4Division of Clinical Immunology and Rheumatology, Department of Medicine, University of Alabama at Birmingham, Birmingham, AL, 5Biochemistry & Molecular Genetics, University of Alabama at Birmingham, Birmingham, AL, 6Medicine, University of Alabama at Birmingham, Birmingham, AL, 7Microbiology, University of Alabama at Birmingham, Birmingham, AL, 8University Health Network & Department of Immunology, University of Toronto, Toronto General Research Institute, Toronto, ON, Canada, 9University of Alabama at Birmingham, Department of Medicine, Birmingham, AL

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** B Cell Biology and Targets in Autoimmune Disease

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 2:30PM-4:00PM

**Background/Purpose:** B cell development involves passage through a formative transitional B cell stage in the spleen. In SLE, self-nucleic acid reactive B cells fail to be deleted at the transitional B cell stage but the factors promoting specific expansion of these autoreactive cells are unknown. Transitional B cells have been shown to exhibit dysregulated type I interferon (IFN) in SLE, and a sub-population of transitional and naïve B cells from SLE patients were recently shown to express high levels of IFNα. The purpose of these studies was to investigate if B cell endogenous type I IFN can act in an autocrine manner to promote survival and development of autoreactive transitional B cells.

**Methods:** Wild type C57BL/6 (B6), B6-CD45.1, CD45.2 B6-<sup>Rag1</sup>⁻/⁻, and BXD2 were obtained from Jackson Lab. B6-IFNβ⁻/⁻ mice were provided by Dr. Fish. A 1:1 ratio of bone-marrow cells was used to reconstitution. Type1 interferon-α or
IFNβ stimulation or blockade was carried out using validated sources. Single-cell QRT-PCR was carried out using a Fluidigm-BioMark system on FACS-sorted T1 B cells. Hierarchical clustering was carried out using ClustVis.

**Results:** Examination of all B cells subsets in B6 and BXD2 mouse spleen revealed that transitional stage 1 (T1) B cells expressed high levels of type I IFNα genes and IFNβ in both strains. T1 B cells from BXD2 lupus-prone mice overexpressed IFNβ relative to B6 mice, and intriguingly, T1 B cells expressed IFNβ at levels comparable to pDCs. T1 B cells from both B6 and BXD2 mice also exhibited higher expression of IFNαR1 and expressed CD86 and CD69 upon IFNβ stimulation. TLR7 responses following stimulation with CL264 was highly dependent upon this endogenous IFN-β in T1 B cells, but not in other B cell subpopulations. Single-cell examination of Ifnb-/- vs. Ifnb+/+ T1 B cells revealed heterogeneous expression of IFNβ in WT T1 B cells and distinct gene expression signatures that required endogenous IFNβ. IFNβ-/- T1 B cells exhibited significantly lower expression of CD86, TLR7, and PKR, and type I IFN genes. Single cell analysis of autoimmune BXD2 T1 B cells that overexpressed IFNβ revealed that IFNβ is expressed in early T1 B cell development with subsequent upregulation of TLR7 and IFNαs. Functional analysis of Ifnb+/+ and Ifnb-/- B cells derived from double chimeric mice revealed that IFNβ was required for development of germinal center, autoreactive, and IgG class switched anti-DNA, anti-La and anti-Histone autoAb producing B cells.

**Conclusion:** Together, these data highlight the role of IFNβ in shaping T1 B cell responses in the mouse spleen, including their survival and responses to TLR7. Notably, they indicate that these effects are mediated through the endogenous expression of IFNβ in T1 B cells. This mechanism suggests that endogenous IFNβ-expressing T1 B cells are initially autonomous and that their expression of IFNβ plays a key role in regulating their responsiveness to external factors, including externally-derived type 1 IFNs and TLR7. In lupus, overexpression of IFNβ in T1 B cells may promote the development of autoreactive mature B cells leading to the generation of polyreactive self-antigen-reactive mature B cells.

**Disclosure:** J. Hamilton, None; P. Yang, None; Q. Wu, None; B. Luo, None; S. Liu, None; M. Walter, None; E. Fish, None; H. C. Hsu, None; J. D. Mountz, None.

Abstract Number: 833

**Chronic Cutaneous Lupus Erythematosus Patients Have a Breakdown in Autoreactive VH4.34 Antibody Tolerance While Maintaining Tolerance to dsDNA and Chromatin**

Scott Jenks1, Regina Bugrovsky1, Xiaqian Wang1,2, Aisha Hill3, Chungwen Wei4, S. Sam Lim5, Ignacio Sanz6 and Cristina Drenkard5, 1Emory University School of Medicine and Lowance Center for Human Immunology, Atlanta, GA, 2Division of Rheumatology and Lowance Center for Human Immunology, Emory University School of Medicine, Atlanta, GA, 3Medicine, Emory University School of Medicine, atlanta, GA, 4Medicine, Emory University School of Medicine, Atlanta, GA, 5Division of Rheumatology, Emory University School of Medicine, Atlanta, GA, 6Rheumatology and Lowance Center for Human Immunology, Emory University School of Medicine and Lowance Center for Human Immunology, Atlanta, GA

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Sunday, November 5, 2017

Session Title: B Cell Biology and Targets in Autoimmune Disease

Session Type: ACR Concurrent Abstract Session

Session Time: 2:30PM-4:00PM

**Background/Purpose:** While the contribution of humoral immunity to SLE is well established, the role it plays in chronic cutaneous lupus erythematosus (CCLE) is less clear. One characteristic of SLE is a breakdown of tolerance in autoreactive VH4.34 antibodies that are recognized by the rat anti-human idiotypic antibody 9G4 (9G4+). 9G4+ antibodies have germ...
line encoded autoreactive specificity for glycolipids found on red blood cells and B cells. Despite a high frequency of naive 9G4+ B cells, healthy control donors (HC) have low amounts of serum 9G4+ IgG. In contrast, many SLE patients have high levels of serum 9G4+ IgG that is associated with higher disease activity and highly correlated with anti-dsDNA and a substantial proportion of anti-dsDNA antibodies are 9G4+. The purpose of this study was to compare 9G4+ IgG and associated SLE auto-antibodies between CCLE patients and SLE patients.

Methods: We analyzed samples from 36 HC and 52 patients with primary CCLE, 44 SLE with CCLE, and 303 SLE without CCLE. Cases with a validated diagnosis of either discoid, panniculitis, tumidus or chilblain lupus were included as CCLE. The ACR criteria and attending rheumatologist/dermatologist judgement were used to classify CCLE cases as primary or associated with SLE. We used ELISA to measure 9G4 with the rat monoclonal 9G4, and goat anti-human IgG. Anti-dsDNA and anti-chromatin IgG were measured using commercial ELISA kits. B cell binding 9G4+ was evaluated ex-vivo by flow cytometry.

Results: 41% of SLE patients were positive for 9G4 IgG and had significantly higher serum concentration than HC (p<0.001) Surprisingly, CCLE patients also had high levels of 9G4+ IgG, 38% were positive and serum concentrations were significantly higher than HC (p<0.001) and did not statistically differ from SLE patients. In contrast, while many SLE patients had anti-dsDNA (48%) and anti-chromatin (52%), few CCLE patients were positive for these specificities (12% and 21%) and the concentration was significantly lower for both (p<0.001). Consequently, 9G4+ IgG concentration was highly correlated with both anti-dsDNA (p<0.001, r=0.48) and anti-chromatin (p<0.001, r=0.45) concentration in SLE patients but not in CCLE patients. CCLE patients, however, did have auto-reactive 9G4+, as B cell binding antibodies were similar between SLE and CCLE patients.

Conclusion: Our study confirms the correlation between 9G4+ IgG and anti-dsDNA in SLE and extends this to anti-chromatin. Surprisingly, CCLE patients had high levels of 9G4+ IgG but not anti-dsDNA. This suggests a two-step model of 9G4 tolerance in SLE, the breakdown of general tolerance of germline encoded autoreactive VH4.34 antibodies and a subsequent development of 9G4+ specific for dsDNA. CCLE patients clearly have a defect in the first step and the mechanism of this defect is potentially shared between CCLE and SLE. However, the second step is not shared, as CCLE patients with 9G4+ IgG do not have high levels of anti-dsDNA. Regulation of this step may help determine if otherwise immunologically similar patients may develop SLE or CCLE. Because the specificity of 9G4+ in CCLE is unknown, it remains to be determined whether these antibodies contribute directly to CCLE disease.

Disclosure: S. Jenks, None; R. Bugrovsky, None; X. Wang, None; A. Hill, None; C. Wei, None; S. S. Lim, None; I. Sanz, None; C. Drenkard, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/chronic-cutaneous-lupus-erythematosus-patients-have-a-breakdown-in-autoreactive-vh4-34-antibody-tolerance-while-maintaining-tolerance-to-dsdna-and-chromatin

Abstract Number: 834

Citrulline-Polyspecific B Cell Antigen Receptors Arising from Somatic Hypermutation within Clades Demonstrate Pathogenicity in Rheumatoid Arthritis

Philip J. Titcombe1,2, Gustaf Wigerblad3, Natalie Sippl3, Na Zhang1, Anna K. Shmagel4, Peter Sahlström5, Yue Jack Zhang1, Laura Barsness Motschenbacher1, Yogita Ghodke-Puranik6, Monika Hansson7, Lena Israelsson5, Timothy B. Niewold8, Lars Klareskog9, Camilla Svensson10, Khaled Amara7, Vivianne Malmström11 and Daniel L. Mueller1,
1Medicine/Rheumatic and Autoimmune Diseases, University of Minnesota Medical School, Minneapolis, MN,
2Rheumatology Unit, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden,
3Department of Medicine, Solna, Karolinska Institutet, Stockholm, Sweden,
4Rheumatic & Autoimmune Diseases, University of Minnesota Medical School, Minneapolis, MN,
5Dept. of Medicine, Rheumatology Unit, Karolinska Institutet, Stockholm, Sweden,
6Colton Center for Autoimmunity, New York University, New York, NY,
7Department of Medicine, Rheumatology Unit, Karolinska Institutet, Stockholm, Sweden,
8Rheumatology and Immunology, Mayo Clinic, Rochester, MN,
9Rheumatology unit,
Background/Purpose: Citrulline–modified proteins arising from the post-translational modification of arginine residues are recognized as primary rheumatoid arthritis (RA) autoantigen targets based on the strong association of anti-citrullinated protein antibodies (ACPA) with RA disease development. Nevertheless, the repertoire of citrullinated protein–specific B cell antigen receptors (BCRs) has not previously been directly assessed.

Methods: 89 subjects from the IRB-approved University of Minnesota ACPA+ RA cohort who met the 2010 ACR/EULAR criteria for RA provided blood samples and clinical data for use in this study. Citrullinated filaggrin peptide CFC1 and citrullinated α-enolase peptide CEP-1 were used in the construction of tetramer sets designed to specifically capture and characterize autoreactive citrullinated protein–specific B cells in the unaltered, polyclonal repertoire of RA patients. Citrullinated peptide tetramer–bound B cells were subjected to flow cytometric cell sorting and single cell IGH, IGK, and IGL gene sequencing for B cell lineage determinations. BCR gene sequences were also expressed as recombinant human monoclonal antibodies, and tested for their ability to bind to citrullinated peptides and proteins. Finally, select human V-(D)-J sequences were expressed as recombinant mouse monoclonal antibodies to test their ability to prolong endotoxin-induced arthritis.

Results: Tetramer–binding CFC1– and CEP-1–specific IgD+ CD27+ switched-memory B cells were found in increased numbers in the blood of RA subjects who also demonstrated high titers of anti-CFC1 and/or –CEP-1 serum antibodies, respectively (5.7-fold increase for CFC1, P value < 0.01; 5.3-fold increase for CEP-1; P value = 0.01). The frequency of CFC1–specific switched-memory B cells was also positively associated with the duration of disease (p = 0.02), the presence of subcutaneous nodules (p = 0.02), and the DAS28-ESR disease activity index (p = 0.01). Citrullinated peptide tetramer–specific BCRs had highly mutated immunoglobulin (Ig) heavy and light chain complementarity determining region (CDR) sequences, biased V-region gene usage, and conserved CDR3 junction lengths. Parsimonious clustering of related IGH, IGK, and IGL nucleotide sequences demonstrated that the clonal expansion of rare individual B cell lineages occurs in association with progressive amino acid sequence divergence. Recombinant human monoclonal antibodies generated from citrullinated peptide tetramer–sorted B cells within extended clades confirmed target peptide antigen–binding for most clones, yet citrulline–dependent cross-reactivity to a broad set of distinct citrullinated peptides and proteins implicated in RA was also observed. Finally, a pair of citrullinated protein–specific recombinant monoclonal antibodies with cross-reactive autoantigen–binding profiles promoted arthritis in mice.

Conclusion: Broad anti-citrullinated protein antibody specificities in RA may arise from a restricted repertoire of B cell clades with evolving and divergent citrulline–polyspecific BCRs.

Disclosure: P. J. Titcombe, None; G. Wigerblad, None; N. Sippl, None; N. Zhang, None; A. K. Shmagel, None; P. Sahlström, None; Y. J. Zhang, None; L. Barsness Motschenbacher, None; Y. Ghodke-Puranik, None; M. Hansson, None; L. Israelsson, None; T. B. Niewold, EMD Serono and Janssen, Inc, 2; L. Klareskog, None; C. Svensson, None; K. Amara, None; V. Malmström, None; D. L. Mueller, None.


Abstract Number: 835

Generation of an Efficient CRISPR-Cas9 Editing Technique in Human Primary B Cells for the Targeted Study of Autoimmune Susceptibility Genes
Yuriy Baglaenko¹, Dario Ferri², Juan Carlos Zuniga-Pflucker³ and Joan E. Wither²,⁴,⁵, ¹Genetics and Development, Krembil Research Institute, University Health Network, Toronto, ON, Canada, ²Immunology, University of Toronto, Toronto, ON, Canada, ³Biological Sciences, Sunnybrook Research Institute, Toronto, ON, Canada, ⁴Krembil Research Institute, University Health Network, Toronto, ON, Canada, ⁵Genetics and Development, Toronto Western Research Institute, Toronto Western Hospital, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: B Cell Biology and Targets in Autoimmune Disease
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:
Autoimmunity is a complex, poly-genic disorder that culminates in multi-organ damage. In systemic lupus erythematosus (SLE), the prototypic autoimmune disorder, a breakdown of tolerance leads to erroneous immune cell activation and the production of disease-causing autoantibodies. B cell functional abnormalities appear to be central to this process and many of the lupus susceptibility genes identified by genome wide association studies (GWAS) are predicted to impact B cell selection, differentiation, signaling, and proliferation. However, their precise mechanisms of action in human B cells remain to be defined. A major challenge preventing the application of GWAS data to therapeutic potential is that animal models often do not recapitulate human phenotypes. In fact, a number of identified autoimmune disease-related genes are known to have differential expression in mice and humans. For this reason, it is important to investigate gene function directly in primary human B cells. To date, the methods for investigating gene function in human B cells has been limited by the relative rarity of many susceptibility alleles and ineffective or transient RNA silencing approaches. CRISPR-Cas9 technology, which uses customizable guide RNAs (gRNA) to direct the cutting of DNA by Cas9 enzymes, presents an unexplored opportunity for studying gene function directly in primary human lymphocytes. The aim of this study was to develop a robust CRISPR-Cas9 method for studying gene function directly in peripheral human B cells isolated from PBMCs.

Methods:
Primary human B cells were isolated from healthy donors using Ficoll-Paque gradients followed by negative magnetic sorting of B cells. Isolated B cells were nucleofected with CRISPR-Cas9 ribonuclear protein complexes and cultured on BAFF and CD40L expressing OP9 stroma for 7 days. Function was assessed by calcium flux assays and phoshosignaling using a flow cytometer.

Results:
Taking advantage of recent advances in genome editing technologies, we were able to successfully and robustly knockout CD22 in primary human B cells from healthy donors, achieving an average efficiency of 35% as measured by loss of cell surface expression. Using this highly adaptable system, we show that gRNA selection can have a profound impact on knockout efficiency and that B cell lines are not an effective proxy for this process. Consistent with the literature, knockout of CD22 in primary B cells resulted in the generation of activated/memory B cells with significantly increased expression of CD86. Furthermore, knockout of CD22 resulted in increased basal activation and as a consequence, total B cells had a reduced capacity for pSyk and pPLCγ signaling. Supporting this observation, IgD⁺ B cells were hyperresponsive to IgM stimulation with an increased capacity for calcium fluxing.

Conclusion: These findings demonstrate, for the first time, the ability to robustly knockout genes directly in primary human B cells. Using this approach, the role of CD22 in maintaining naïve B cells was confirmed in healthy donors. This methodology allows for the targeted study of autoimmune-related genes and their impact on B cell function.

Disclosure: Y. Baglaenko, None; D. Ferri, None; J. C. Zuniga-Pflucker, None; J. E. Wither, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/generation-of-an-efficient-crispr-cas9-editing-technique-in-human-primary-b-cells-for-the-targeted-study-of-autoimmune-susceptibility-genes
**B Cell Receptor Sequencing of Anti-Citrullinated Protein Antibody Expressing B Cells Indicates a Selective Advantage for the Introduction of N-Glycosylation Sites during Somatic Hypermutation**

Rochelle D. Vergroesen\(^1\), Linda Slot\(^1\), Lise Hafkenscheid\(^1\), Marvyn T. Koning\(^2\), Ellen I.H. van der Voort\(^3\), Christine A. Grooff\(^1\), George Zervakis\(^2\), Tom W.J. Huizinga\(^1\), Theo Rispens\(^2\), Rene E.M. Toes\(^1\) and Hans U. Scherer\(^3\), \(^1\)Rheumatology, Leiden University Medical Center, Leiden, Netherlands, \(^2\)Hematology, Leiden University Medical Center, Leiden, Netherlands, \(^3\)Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, \(^4\)Immunopathology, Sanquin Research, Amsterdam, Netherlands

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** B Cell Biology and Targets in Autoimmune Disease  
**Session Type:** ACR Concurrent Abstract Session  
**Session Time:** 2:30PM-4:00PM

**Background/Purpose:**

The vast majority (>90%) of anti-citrullinated protein antibodies (ACPAs) of the IgG isotype in serum and synovial fluid of patients with rheumatoid arthritis carry N-linked glycans in the antibody variable region. This remarkable degree of Fab-glycosylation is absent from ACPA-depleted control IgG and from autoantibodies in other diseases. N-glycosylation requires a specific amino acid consensus sequence in the protein backbone (termed an N-glycosylation site), which is very rare in germline-encoded variable region genes. Here, we analysed the B cell receptor (BCR) repertoire of ACPA-expressing B cells to understand the molecular basis for this remarkable glycosylation.

**Methods:**

We used anchoring reverse transcription of immunoglobulin (Ig) sequences and amplification by nested PCR (ARTISAN) to obtain full-length rearrangements of ACPA-expressing B cells. ACPA-expressing B cells and non citrulline-reactive control B cells were obtained from peripheral blood of patients with established RA by antigen-specific tetramer staining and fluorescence activated cell sorting. Cells were either sorted in pools, or sorted as single cells. Somatic mutations and N-glycosylation sites were identified in the sequence reads using IMGT (High)V-QUEST. Paired heavy and light chain sequences (HC/LC) were used to model the spatial positioning of N-glycosylation sites.

**Results:**

Sequence analysis of pools of cells identified 97 unique ACPA-IgG clones derived from n=8 donors. 87 unique ACPA-IgG clones were retrieved from single cell analysis (n=6 donors). In both datasets, over 80% of ACPA-IgG clones contained N-glycosylation sites in both HC and LC. All sites were created by somatic mutations. The mutation rate did not correlate with the number of N-glycosylation sites, and their distribution across the variable region and their preference differed from the pattern seen in controls. Structural modelling predicted N-glycosylation sites on the exterior of the antibody molecule.

**Conclusion:**

ACPAs-expressing B cells generate BCRs with a high frequency of N-glycosylation sites. Frequency and localization of sites suggest that ACPA-expressing B cells gain a selective survival advantage by acquiring glycans in the variable domain, thereby escaping from putative checkpoints in B cell selection.

**Disclosure:** R. D. Vergroesen, None; L. Slot, None; L. Hafkenscheid, None; M. T. Koning, None; E. I. H. van der Voort, None; C. A. Grooff, None; G. Zervakis, None; T. W. J. Huizinga, None; T. Rispens, None; H. Veelken, None; R. E. M. Toes, None; H. U. Scherer, None.
Rheumatoid Arthritis and Risk for Chronic Obstructive Pulmonary Disease or Asthma Among Women during 38 Years of Prospective Follow-up

Jeffrey A. Sparks¹, Tzu-Chieh Lin², Carlos Camargo³, Medha Barbhaiya⁴, Sara K. Tedeschi⁵, Karen H. Costenbader², Benjamin Raby⁶, Hyon K. Choi⁷ and Elizabeth Karlson⁴, ¹Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ²Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ³Emergency Medicine, Massachusetts General Hospital and Harvard Medical School, Boston, MA, ⁴Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ⁵Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ⁶Pulmonary Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ⁷Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Epidemiology and Public Health I: Lung, Bone, and Infection Outcomes
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose : Rheumatoid arthritis (RA) has been associated with increased risk for chronic obstructive pulmonary disease (COPD) and asthma, but these findings may have been confounded by smoking behaviors occurring before and after RA diagnosis. Citrullination of proteins in the airways is important in both RA and COPD etiology so may link these diseases beyond smoking. Marginal structural modeling (MSM) is a statistical method to control for factors, such as smoking, on the causal pathway for an outcome, such as COPD or asthma. We investigated whether RA increases risk for COPD or asthma using MSM to adjust for smoking occurring before RA onset or mediating these respiratory morbidities after RA diagnosis.

Methods : Within the prospective NursesÕ Health Study (n=121,701 women; 1976-2014), we identified an incident RA cohort and matched each woman with RA to 10 non-RA comparators by age and year of RA diagnosis (index date). All RA cases met the 1987 ACR classification criteria. We excluded women with prevalent COPD or asthma at baseline. Data were obtained through biennial questionnaires and medical records. We used MSM to determine the independent effect of RA on incident self-reported COPD or asthma, adjusting for time-varying covariates by inverse probability weighting. Smoking was categorized as fixed pre-index intensity/duration (0, >0 to 10, 10.1 to 20, or >20 pack-years) and time-varying post-index status (never, past, or current). In subgroup analyses, we separately investigated seropositive RA and seronegative RA for risk of COPD or asthma.

Results : We identified 843 women with incident RA during 38 years of follow-up in the NHS, matched to 8,399 comparators without RA. Mean age was 59.8 years and mean follow-up after index date was 18.6 years (SD 9.0) for RA and 18.8 years (SD 9.5) for comparators. During 173,484 person-years of follow-up after index date, we identified 68 (8.1%) incident COPD and 40 (4.7%) asthma cases among women with RA, and 459 (5.5%) COPD and 268 (3.2%) asthma cases among comparators. RA was associated with increased risk of COPD (HR 1.52, 95%CI 1.17-1.97, Table) and asthma (HR 1.55, 95%CI 1.11-2.16) compared to comparators matched to age and year at index date. After adjustment for time-varying covariates, including smoking before and after index date, RA was significantly associated with COPD (HR 1.68, 95%CI 1.36-2.07), but not asthma (HR 1.11, 95%CI 0.59-2.09), compared to non-RA. Women with seropositive RA (HR 1.74, 95%CI 1.36-2.23) and seronegative RA (HR 1.62, 95%CI 1.09-2.40) had similar increased risk for COPD compared to comparators.
**Conclusion**: In this large prospective cohort study with time-varying measures throughout long-term follow-up, RA was associated with increased risk for incident COPD, but not asthma, independent of smoking and other lifestyle factors. These results provide rationale to investigate the effect of RA-specific factors beyond smoking on COPD risk.

<table>
<thead>
<tr>
<th>COPD</th>
<th>Asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (95% CI)</td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td>All RA (n=943 RA; n=8,399 comparators)</td>
<td></td>
</tr>
<tr>
<td>Age-adjusted</td>
<td>1.52 (1.17-1.97)</td>
</tr>
<tr>
<td>Smoking-adjusted</td>
<td>1.43 (1.09-1.87)</td>
</tr>
<tr>
<td>Multivariable-adjusted</td>
<td>1.68 (1.36-2.07)</td>
</tr>
<tr>
<td>Seropositive RA (n=518 RA; n=5,163 comparators)</td>
<td></td>
</tr>
<tr>
<td>Age-adjusted</td>
<td>1.60 (1.17-2.19)</td>
</tr>
<tr>
<td>Smoking-adjusted</td>
<td>1.44 (1.04-2.00)</td>
</tr>
<tr>
<td>Multivariable-adjusted</td>
<td>1.74 (1.30-2.33)</td>
</tr>
<tr>
<td>Seronegative RA (n=325 RA; n=4,236 comparators)</td>
<td></td>
</tr>
<tr>
<td>Age-adjusted</td>
<td>1.41 (0.89-2.23)</td>
</tr>
<tr>
<td>Smoking-adjusted</td>
<td>1.47 (0.91-2.39)</td>
</tr>
<tr>
<td>Multivariable-adjusted</td>
<td>1.62 (1.05-2.49)</td>
</tr>
</tbody>
</table>

1. Adjusted for matching factors (age and calendar year) at index date.
2. Adjusted for matching factors (age and calendar year) at index date, pre-index smoking pack-years (0, 0-10, 10-20, ≥20), and time-varying smoking status (never, past, current) using marginal structural models.
3. Adjusted for matching factors (age and calendar year) at index date as well as baseline factors of annual family income (<$40,000, ≥$40,000) and pre-index smoking pack-years (0, 0-10, 10-20, ≥20) as well as time-varying factors of smoking status (never, past, current), body mass index (continuous, kg/m²), Alternate Healthy Eating Index (quartiles), menopausal status and current PMI use (prenatal/puerperal and nonzero current PMI use, postmenopausal and current PMI use, postmenopausal and current PMI use, physical activity continuous, METs/week), and aspirin use (yes/no) using marginal structural models.

**Disclosure**: J. A. Sparks, None; T. C. Lin, None; C. Camargo, None; M. Barbhaiya, None; S. K. Tedeschi, None; K. H. Costenbader, None; B. Raby, None; H. K. Choi, None; E. Karlson, None.

**View Abstract and Citation Information Online** - http://acrabstracts.org/abstract/rheumatoid-arthritis-and-risk-for-chronic-obstructive-pulmonary-disease-or-asthma-among-women-during-38-years-of-prospective-follow-up

**Abstract Number**: 838

**Rates of New-Onset Pulmonary Disease Among Patients with Systemic Lupus Erythematosus in Sweden**

Lindsy J. Forbes¹, Michael Weisman² and Julia F Simard³, ¹Medicine, Division of Rheumatology, Cedars-Sinai Medical Center, Los Angeles, CA, ²Cedars-Sinai Medical Center Division of Rheumatology, Los Angeles, CA, ³Division of Epidemiology, Health Research and Policy Department, Stanford School of Medicine, Stanford, CA

**First publication**: September 18, 2017

**SESSION INFORMATION**

**Session Date**: Sunday, November 5, 2017

**Session Title**: Epidemiology and Public Health I: Lung, Bone, and Infection Outcomes

**Session Type**: ACR Concurrent Abstract Session

**Session Time**: 2:30PM-4:00PM

**Background/Purpose**: Our goal was to examine lung disease and types of pulmonary manifestations observed in patients with SLE. We studied population-based register data from Sweden to determine the incidence of pulmonary diagnoses among incident and prevalent SLE patients compared to the general population.

**Methods**: Using data from a linkage of Swedish registers we identified patients with SLE (at least 2 SLE coded discharge diagnoses and at least 1 SLE-specific discharge diagnosis by a specialist who manages SLE) and matched them to individuals from the general population on age, sex, and county of residence when the SLE index case first presented with SLE. Pulmonary diagnoses were identified using ICD codes from the National Patient Register’s (NPR) discharge diagnoses for inpatient and outpatient visit data. Those with a history of pulmonary disease were excluded. Individuals were followed until they had their first pulmonary diagnosis, died, emigrated, or reached the study end. We calculated incidence rates and corresponding 95% confidence intervals (95% CI) overall and by type of pulmonary disease, for incident (2003-2013) and prevalent SLE (2001-2013). To be classified as incident SLE, an individual’s first SLE diagnosis code had to occur in 2003
or later. Cox proportional hazards models estimated hazard ratios (HR) and 95% CIs for the association between SLE and pulmonary disease in age and sex adjusted models. Sensitivity analyses assessed the robustness of results using semi-automated approach to quantitative probabilistic bias analysis to account for potential bias due to unmeasured confounding by smoking.

**Results:** 3,209 incident SLE cases were identified using NPR data in Sweden contributing a median 4.8 person-years of follow-up time (vs. 5.1 among non-SLE comparators). We also identified a contemporary cohort of 6,908 individuals with prevalent SLE. The incidence rate for new onset pulmonary disease (about 14 cases per 1000 person-years) was similar in prevalent and incident SLE. Those with incident SLE had a nearly six-times higher rate of new onset pulmonary disease compared to the non-SLE comparator (HR=5.80 (4.84,6.95)) and were comparable in male and female patients. Incident and prevalent SLE was associated with an increased rate of interstitial lung disease (ILD), (HR=19.0 (10.7, 34.0) and 14.3 (10.8-18.8), respectively). Bias due to unmeasured confounding by smoking was unlikely to explain our findings in sensitivity analyses.

**Conclusion:** Lung disease is common among SLE patients, and particularly increased when compared to the general population. Clinicians caring for SLE patients should have a heightened suspicion for lung disease, including ILD, even early within the disease course.

**Table.** Relative risk of pulmonary disease among SLE compared to non-SLE general population comparators overall and by type of pulmonary disease, presented as age- and sex-adjusted hazard ratios and 95% confidence intervals.

<table>
<thead>
<tr>
<th></th>
<th>Prevalent SLE</th>
<th>Incident SLE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6908 SLE</td>
<td>3209 SLE</td>
</tr>
<tr>
<td>Any pulmonary disease</td>
<td>37046 non-SLE</td>
<td>17658 non-SLE</td>
</tr>
<tr>
<td></td>
<td>5.42 (4.90-5.99)</td>
<td>5.80 (4.84-6.95)</td>
</tr>
<tr>
<td>By specific pulmonary disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interstitial lung disease</td>
<td>14.27 (10.84-18.78)</td>
<td>19.04 (10.66-34.00)</td>
</tr>
<tr>
<td>ARDS and hemorrhage</td>
<td>5.78 (3.94-8.48)</td>
<td>5.34 (2.72-10.49)</td>
</tr>
<tr>
<td>Pleural disorders</td>
<td>4.64 (3.92-5.49)</td>
<td>5.91 (4.43-7.89)</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>6.75 (4.74-9.61)</td>
<td>6.14 (3.19-11.82)</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>3.77 (3.12-4.55)</td>
<td>3.78 (2.64-5.40)</td>
</tr>
<tr>
<td>Diseases of the upper airway</td>
<td>4.19 (3.04-5.79)</td>
<td>3.10 (1.66-5.79)</td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>4.32 (2.80-6.65)</td>
<td>3.30 (1.40-7.80)</td>
</tr>
</tbody>
</table>

**Disclosure:** L. J. Forbess, None; M. Weisman, None; J. F. Simard, None.


Abstract Number: 839

**Use of Bisphosphonate and Risk of Incident Atrial Fibrillation in a Population-Based Study**
**Background/Purpose:**

Bisphosphonates remain the first-line agent prescribed medication for the prevention and treatment of osteoporosis. Apart from concern about atypical fractures, another concern about risk of atrial fibrillation has been raised. However, data regarding the relation of specific types of bisphosphonate use to risk of atrial fibrillation has been conflicting, and this has been reflected in contradicting conclusions from different meta-analyses. We sought to evaluate this risk using more contemporary data in a population-based cohort in which data on use of different types of bisphosphonates were available.

**Methods:**

We conducted a propensity score matched cohort study based on a UK population-based general practitioner database (The Health Improvement Network (THIN) database). From Jan 1, 1998 until Dec 31, 2014, we included 107,282 women who were age 50-89 years, who were free of atrial fibrillation or atrial flutter, and with no prior use of bisphosphonate within 2 years prior to study entry. Incident bisphosphonate users were defined as women with first bisphosphonate prescription. Comparators were women without bisphosphonate use prior to the 1-year cohort accrual block, with the index date randomly assigned within the 1-year accrual block. Incident atrial fibrillation was defined using READ codes. We performed an intent to treat analysis using Cox proportional hazards model, stratified by the 1 year cohort accrual blocks.

**Results:**

During a median of 4.5 years of follow up, we identified 53,641 pairs of bisphosphonate initiators and PS-matched comparators, whose mean age was 70. The crude incident rate of atrial fibrillation was 8.63 per 1000 person years for bisphosphonate initiators, and 8.7 per 1000 person years for comparators, with an adjusted hazard ratio of 1.01 (95%CI: 0.95-1.08). When restricted only to the commonly used bisphosphonates alendronate, ibandronate, and risedronate, the hazard ratio comparing initiators vs. comparators was 1.05 (95%CI: 0.99-1.11). Results were similar when current vs. past bisphosphonate users were compared, and when further stratified by calendar year to account for secular trends.

**Conclusion:**

In this large UK general population, use of bisphosphonate was not associated with risk of atrial fibrillation.

**Disclosure:** S. Sheehy, None; C. Peloquin, None; T. Neogi, None.
Background/Purpose: In prior work, we found a higher incidence of hip fractures in RA than age and sex matched general population controls (4.1 vs. 2.9 per 1000 PY). To assess burden of disease, we compared age- and sex-adjusted all-cause mortality post hip fracture in RA and general population controls.

Methods: We conducted a retrospective study of a population-based incident RA cohort, using administrative health data. Using physician billing data, we identified all people with RA onset between 1997 and 2009 in a Canadian province. Controls (with no diagnosis of RA or other inflammatory arthritis) were randomly selected from the general population, matched 2:1 to RA cases on birth yr, gender and index yr. RA patients and controls with prior hip fractures, pathological fractures or Paget’s disease were excluded. Hip fractures were identified using hospitalization data (ICD9-CM codes 820.0, 820.2; ICD10-CA codes S72.0, S72.1, S72.2), from ≤25 codes defining reason for admission or complications during hospitalization. RA individuals and controls were followed from incident hip fracture to death, last health care use, or study end (Dec. 2014). Mortality data was obtained from Vital Statistics. Cox-proportional hazard models, adjusted for age and sex, compared mortality risk in RA vs. controls with a hip fracture.

Results: The cohort included 60,101 incident RA cases and 120,462 controls, of whom 2463 (4.1%) RA individuals and 3566 (3.0%) controls sustained an incident hip fracture and make up the study sample (78% females in RA and 81% in controls; mean (SD) age at time of fracture: 78.9(10.9) yrs for RA and 82.1(9.0) yrs for controls). Crude all-cause mortality rate post hip fracture was 5.9% (n=143) and 8.2% (n=288) at 30 days; and 19.9% (n=481) and 24.5% (n=854) at 1-yr, for RA and controls, respectively. After age and sex adjustment, RA persons with hip fractures had a 17.5% lower risk of death than persons without RA at 30-days and 10.2% lower risk at 1-yr. The mean age at death for 30-day mortality was 83.9 yrs for RA and 86.1 yrs for controls.

<table>
<thead>
<tr>
<th>Subset</th>
<th>30 Day Mortality</th>
<th>1 Year Mortality</th>
<th>5 Year Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>aHR</td>
<td>95% CI</td>
<td>aHR</td>
</tr>
<tr>
<td>Overall</td>
<td>0.825</td>
<td>(0.675, 1.010)</td>
<td>0.888</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>0.884</td>
<td>(0.669, 1.126)</td>
<td>0.863</td>
</tr>
<tr>
<td>Male</td>
<td>0.697</td>
<td>(0.475, 1.027)</td>
<td>0.993</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤69</td>
<td>0.771</td>
<td>(0.557, 1.056)</td>
<td>1.538</td>
</tr>
<tr>
<td>70-89</td>
<td>0.820</td>
<td>(0.646, 1.063)</td>
<td>0.800</td>
</tr>
<tr>
<td>≥90</td>
<td>0.812</td>
<td>(0.565, 1.169)</td>
<td>0.845</td>
</tr>
<tr>
<td>Age &amp; Sex Stratified</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F ≤69</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F 70-89</td>
<td>0.943</td>
<td>(0.702, 1.266)</td>
<td>0.863</td>
</tr>
<tr>
<td>F 90+</td>
<td>0.777</td>
<td>(0.510, 1.184)</td>
<td>0.821</td>
</tr>
<tr>
<td>M ≤69</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M 70-89</td>
<td>0.614</td>
<td>(0.384, 0.982)</td>
<td>0.960</td>
</tr>
<tr>
<td>M 90+</td>
<td>0.905</td>
<td>(0.434, 1.887)</td>
<td>0.941</td>
</tr>
</tbody>
</table>

Table 1: Risk of mortality in RA relative to general population controls, adjusted for age and sex.
*Results not provided for cells with data <8 patients to protect patient confidentiality.

Conclusion: Despite a higher incidence of hip fractures in RA, the 30-day and 1-year post hip fracture all-cause mortality was lower in RA than controls, after adjusting for sex and age at time of fracture. Further research is needed to understand
whether mortality differences are related to co-morbidities, differences in post-op care, or other characteristics influencing post-fracture mortality risk.

Disclosure: C. A. Jones, None; P. Guy, None; H. Xie, None; E. C. Sayre, None; D. Lacaille, None.


Abstract Number: 841

Optimal Regimens of Sulfamethoxazole-Trimethoprim for Chemoprophylaxis of Pneumocystis Pneumonia in Patients with Systemic Rheumatic Diseases: 52-Week Follow-up of a Non-Blinded, Randomized Controlled Trial

Masayoshi Harigai1,2, Masako Utsunomiya2,3,4, Hiroaki Dobashi5, Toshio Odani6,7, Kazuyoshi Saito8,9, Naoto Yokogawa10, Kenji Nagasaka11,12, Kenchi Takenaka3,11, Makoto Soejima11,13, Takahiko Sugihara14, Hiroyuki Hagiya15, Shinya Hirata16, Kazuo Matsui17,18, Yoshinori Nonomura19, Masahiro Kondo20, Fumihito Suzuki13,21, Makoto Tomita22, Mari Kihara23, Waka Yokoyama3, Fumio Hirano24, Hayato Yamazaki3, Ryoko Sakai2,25, Toshihiro Nanki2,26, Ryuji Koike2,3, Hitoshi Kohsaka2 and Nobuyuki Miyasaka3, 1Division of Epidemiology and Pharmacoepidemiology of Rheumatic Diseases, Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan, 2Department of Pharmacovigilance, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan, 3Department of Rheumatology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan, 4Department of Rheumatology, Musashino Red Cross Hospital, Tokyo, Japan, 5Internal Medicine Division of Hematology, Rheumatology, and Respiratory Medicine, Kagawa University, Kagawa, Japan, 6Third Department of Internal Medicine, Obihiro-Kosei General Hospital, Hokkaido, Japan, 7Molecular Physiology and Therapeutics Branch/Adeno-Associated Virus Biology Section, National Institute of Dental and Craniofacial Research (NIDCR)/ National Institutes of Health (NIH), Bethesda, MD, 8Tobata General Hospital, Fukuoka, Japan, 9The First Department of Internal Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan, 10Department of Rheumatic Diseases, Tokyo Metropolitan Tama Medical Center, Tokyo, Japan, 11Department of Rheumatology, Ome Municipal General Hospital, Tokyo, Japan, 12Department of Pharmacovigilance, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan, 13Department of Rheumatology, Soka Municipal Hospital, Saitama, Japan, 14Department of Medicine and Rheumatology, Tokyo Metropolitan Geriatric Hospital, Tokyo, Japan, 15Department of Rheumatology, Yokohama City Minato Red Cross Hospital, Kanagawa, Japan, 16Department of Hematology, Rheumatology, and Infectious Disease, Kumamoto University, Kumamoto, Japan, 17Department of Rheumatology, Kameda Medical Center, Chiba, Japan, 18Department of Internal Medicine, Takikawa Municipal Hospital, Hokkaido, Japan, 19Department of Rheumatology, Tokyo Kyosai Hospital, Tokyo, Japan, 20Department of Rheumatology, Faculty of Medicine, Shimane University, Shimane, Japan, 21Department of Rheumatology, JA Toride Medical Center, Ibaraki, Japan, 22Clinical Research Center, Tokyo Medical and Dental University, Tokyo, Japan, 23Department of Rheumatology and Pharmacoepidemiology of Rheumatic Diseases, Institute of Rheumatology, Tokyo Women’s Medical University, Tokyo, Japan, 24Departments of Rheumatology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan, 25Division of Epidemiology and Pharmacoepidemiology of Rheumatic Diseases, Institute of Rheumatology, Tokyo Women’s Medical University, Tokyo, Japan, 26Division of Rheumatology, Department of Internal Medicine, Toho University School of Medicine, Tokyo, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017

Session Title: Epidemiology and Public Health I: Lung, Bone, and Infection Outcomes
Session Type: ACR Concurrent Abstract Session  
Session Time: 2:30PM-4:00PM

Background/Purpose: Sulfamethoxazole-trimethoprim (SMX/TMP) is a standard drug for the prophylaxis of *Pneumocystis* pneumonia (PCP), but is sometimes discontinued due to adverse events (AEs). We have previously reported the results of this non-blinded, randomized, non-inferiority trial up to week 24 to explore an effective SMX/TMP regimen for PCP with a low drug discontinuation (d/c) rate. We here report the results at week 52.

Methods: Adult patients with systemic rheumatic diseases who started prednisolone >0.6 mg/kg/day were randomized into three groups and treated up to week 24: a single-strength group (SS, SMX/TMP of 400/80 mg daily), half-strength group (HS, 200/40 mg daily), and escalation group (ES, started with 40/8 mg daily, raising incrementally to 200/40 mg daily). After week 24, attending physicians determined the use of SMX/TMP including doses, intervals, and treatment duration. The observation period was up to week 52 irrespective of the use of SMX/TMP. The primary endpoint was non-incidence rates (non-IR) of PCP at week 24. Secondary endpoints were PCP non-incidence rate at week 52, treatment d/c rate, and AEs. We estimated the non-incidence rates of PCP using the exact confidence interval as a post-hoc analysis and analyzed treatment d/c rates using the Kaplan-Meier method and log-rank test.

Results: Of 183 patients randomly allocated at a 1:1:1 ratio into the three groups, 58 patients in SS, 59 in HS, and 55 in ES started SMX/TMP and were analyzed. Of the 172 patients who started SMX/TMP, 32, 46, and 38 at week 24, and 29, 43, and 34 at week 52 were receiving SMX/TMP as allocated. No cases of PCP were reported up to week 52. Estimated non-IR of PCP in patients who received daily SMX/TMP of 200/40 mg, either starting at this dose or increasing incrementally, was 96.8–100%. From week 0 to 52, the overall d/c rate was significantly lower in HS compared to that in SS (22.7% vs 47.2%, p = 0.004) (Figure). The d/c rates due to AEs were significantly lower in HS (19.1%, p = 0.007) and ES (20.3%, p = 0.007) compared to that in SS (41.8%). The IR of AEs requiring dose reduction of SMX/TMP (p = 0.007) and AEs of special interest (p = 0.001) at week 52 were different among the three groups with significantly higher IR in SS compared to HS and ES. Almost all AEs requiring dose reduction of SMX/TMP and AEs of special interest were reported by week 24.

Conclusion: The combined group of HS and ES had an excellent estimated non-IR of PCP at week 52 and both were superior in safety to SS. From the perspective of feasibility and drug d/c rates, the daily half-strength regimen is suggested to be optimal for prophylaxis of PCP in patients with systemic rheumatic diseases.

*Disclosure: M. Harigai, Eisai Ltd, Takeda Ltd, Teijin, 2,Eli Lilly and Company, BMS, Chugai, Janssen, 5; M. Utsunomiya, None; H. Dobashi, None; T. Odani, None; K. Saito, None; N. Yokogawa, None; K. Sagasaka, Chugai Pharmaceutical Co., Ltd., 5; K. Takenaka, None; M. Soejima, None; T. Sugihara, Takeda Pharmaceutical Co. Ltd., Mitsubishi-Tanabe Pharma Co., Chugai Pharmaceutical Co., Ltd., Ayumi Pharmaceutical Co., Ltd., UCB Japan Co. Ltd, Astellas Pharma Inc., Janssen Pharmaceutical K.K., Pfizer Japan Inc., and Bristol Myers Squibb K.K, 5; H. Hagiyama, None; S. Hirata, None; K. Matsui, None; Y. Nonomura, None; M. Kondo, None; F. Suzuki, None; M. Tomita, None; M. Kihara, None; W.*


**Abstract Number: 842**

**Risk of Serious Infection in Patients with Rheumatoid Arthritis Treated with Biologic Vs. Non-Biologic Dmards**

**Gulsen Ozen**¹, **Sofia Pedro**², **Bryant R. England**³, **Bella Mehta**⁴, **Frederick Wolfe**² and **Kaleb Michaud**¹, ¹Rheumatology, University of Nebraska Medical Center, Omaha, NE, ²National Data Bank for Rheumatic Diseases, Wichita, KS, ³Division of Rheumatology & Immunology, Department of Internal Medicine, Nebraska-Western IA VA Health Care System & University of Nebraska Medical Center, Omaha, NE, ⁴Rheumatology, Hospital for Special Surgery/Weill Cornell Medical College, New York, NY

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Epidemiology and Public Health I: Lung, Bone, and Infection Outcomes  
**Session Type:** ACR Concurrent Abstract Session  
**Session Time:** 2:30PM-4:00PM

**Background/Purpose:** Serious infections (SIs) are a major concern in RA patients, significantly contributing to increased mortality. We examined the SI risk associated with bDMARDs compared to csDMARDs in a US-wide observational RA cohort.

**Methods:** RA patients initiating bDMARDs or csDMARDs from 2001 through 2016 in the National Data Bank for Rheumatic Diseases (NDB) were assessed for SIs (infection + intravenous antibiotics, hospitalization or death). DMARDs were categorized into 3 groups: (1) csDMARDs-reference (bDMARD naive) (2) TNF inhibitors (TNFi) (3) Non-TNFi biologics (abatacept, rituximab, tocilizumab, and anakinra). Each patient contributed to the last DMARD reached. Followup continued until the first SI, DMARD discontinuation, death, or end of study period. SIs were attributed to the corresponding DMARD group when the treatment was ongoing or discontinued ≤3 months before SI. Propensity scores (PS) reflecting the probability of receiving a specific DMARD were calculated using multinomial logistic regression models with characteristics at treatment initiation. PS was added to the Cox models as a continuous variable along with time-varying confounders (age, disease duration, comorbidities, HAQ, pain and patient global scores, weighted cumulative exposure [WCE] of glucocorticoids [GC], prior sDMARDs and bDMARDs counts) of which changes over time might alter the SI risk.

**Results:** 694 (5.9%) first SIs were identified in 11,623 RA patients during a 27,552 patient-years of follow-up. TNFi and non-TNFi biologics-initiators had significantly higher disease activity, disability, and comorbidity scores than csDMARDs initiators. Crude incidence rate (95% CI) in TNFi group was non-significantly higher than csDMARD and non-TNFi biologic initiators (Figure). The PS-only adjusted model showed a non-significant SI risk increase with TNFi (HR 1.11 [0.91-1.34], P = 0.309) and non-TNFi biologics (HR 1.26 [0.95-1.68], P = 0.102) whereas further adjustment for time-varying confounders revealed significantly increased risk of SI with both TNFi (HR 1.33 [1.05-1.68], P = 0.019) and non-TNFi (HR 1.48 [1.02-2.16], P = 0.041) compared to csDMARDs. Other factors associated with SI are presented in Table.
Conclusion: TNFi and non-TNFi biologics were associated with an increased SI risk in RA compared to csDMARDs. In addition to DMARDs, older age, comorbidity burden, pulmonary disease, higher disability, disease activity, and cumulative GC exposure were predictive of SI. Assessment and modification of these factors should be completed before and during bDMARD treatment to minimize SI risk.

Figure. Cumulative incidence of serious infections by DMARD groups during the first 2 years of treatment
### Table. Risk of serious infections in rheumatoid arthritis by treatment: results from the Cox proportional hazard models with propensity scores* and time-varying confounders

<table>
<thead>
<tr>
<th></th>
<th>Adjusted HR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;50</td>
<td>Reference</td>
<td>-</td>
</tr>
<tr>
<td>50-64</td>
<td>1.39 (1.03-1.89)</td>
<td>0.034</td>
</tr>
<tr>
<td>≥65</td>
<td>2.31 (1.70-3.12)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Annual income &gt; $45,000</strong></td>
<td>0.70 (0.57-0.84)</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Rheumatic disease comorbidity index</strong></td>
<td>1.20 (1.13-1.26)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Selected comorbidities</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.15 (0.94-1.41)</td>
<td>0.174</td>
</tr>
<tr>
<td>Pulmonary disease</td>
<td>1.46 (1.21-1.77)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Disease duration, years</td>
<td>1.00 (0.99-1.01)</td>
<td>0.852</td>
</tr>
<tr>
<td>HAQ disability</td>
<td>1.27 (1.10-1.47)</td>
<td>0.001</td>
</tr>
<tr>
<td>Pain scale</td>
<td>1.04 (1.00-1.08)</td>
<td>0.050</td>
</tr>
<tr>
<td>Patient global scale</td>
<td>1.06 (1.02-1.11)</td>
<td>0.008</td>
</tr>
<tr>
<td>WCE-prednisone</td>
<td>1.33 (1.22-1.45)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Count of prior csDMARDs</td>
<td>1.11 (1.05-1.17)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Count of prior bDMARDs</td>
<td>0.90 (0.80-1.02)</td>
<td>0.095</td>
</tr>
<tr>
<td><strong>DMARD groups</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>csDMARDs</td>
<td>Reference</td>
<td>-</td>
</tr>
<tr>
<td>TNFi</td>
<td>1.33 (1.05-1.68)</td>
<td>0.019</td>
</tr>
<tr>
<td>Non-TNFi biologics</td>
<td>1.48 (1.02-2.16)</td>
<td>0.041</td>
</tr>
</tbody>
</table>

*Propensity score was estimated based on the following characteristics at the time of treatment initiation: age, gender, ethnicity, insurance, annual income, RA disease duration, smoking status, rheumatic diseases comorbidity index, HAQ, pain and patient global scores, GC use, prior csDMARDs and bDMARDs counts, prior serious infection, and calendar year.

WCE=Weighted cumulative exposure of glucocorticoid as prednisone equivalent doses: The weights assigned to past doses were estimated using a flexible cubic spline-based method.

**Disclosure:** G. Ozen, None; S. Pedro, None; B. R. England, None; B. Mehta, None; F. Wolfe, None; K. Michaud, None.


**Abstract Number:** 843

**The Role of Personality in Patients with Fibromyalgia**

Andrew Seto\(^1\), Teresa Wu\(^1\), Lori Lyn Price\(^2,3,4,5\), Xingyi Han\(^6\), William F. Harvey\(^1\) and Chenchen Wang\(^7\), \(^1\)Tufts Medical Center, Boston, MA, \(^2\)Institute for Clinical Research and Health Policy Studies, Tufts Medical Center, Boston, MA, \(^3\)Clinical Care Research, Tufts Medical Center, Boston, MA, \(^4\)Biostatistics Research Center, Institute for Clinical Research and Health Policy Studies, Tufts Medical Center, Boston, MA, \(^5\)Tufts Clinical and Translational Science Institute, Tufts
SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: ARHP Psychosocial Impact on Rheumatic Disease
Session Type: ARHP Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:

Previous studies investigating the potential associations between personality and clinical symptoms in fibromyalgia (FM) patients have found mixed results. The purpose of this study was to clarify whether personality dimensions are associated with clinical symptoms, mindfulness, self-efficacy, social support, and outcome expectations among adult patients with FM.

Methods:

We performed a secondary analysis using baseline data from a randomized controlled comparative effectiveness trial between Tai Chi and aerobic exercise for FM. Personality was assessed using the NEO-Five Factor Inventory, a validated measure of 5 basic personality factors: agreeableness, conscientiousness, extraversion, neuroticism, and openness. Fibromyalgia syndrome was evaluated using the validated revised Fibromyalgia Impact Questionnaire (FIQR). Other measures included symptom severity, anxiety, depression, stress, health-related quality of life, social support, self-efficacy, mindfulness, and outcome expectations for exercise. Multivariable linear regression was performed to assess the associations between personality dimensions and measures of health and FM impact, while controlling for age, gender, body mass index (BMI), and living situation.

Results:

The sample consisted of 92 participants, with 95% female, mean age 52 years (SD 12), BMI 30 kg/m² (6), 52% white, 94% had a high school degree, and mean duration of body pain 14 years (11). After adjusting for covariates using multivariable linear regression, neuroticism was significantly associated with FIQR and symptom severity (Table 1). Higher neuroticism was also associated with higher levels of anxiety, depression, and stress, and worse mental component quality of life, lower self-efficacy, mindfulness, and social support. Higher conscientiousness and extraversion were associated with better mental component quality of life and mindfulness, and lower symptom severity, anxiety, depression, and stress. Higher conscientiousness was associated with better self-efficacy and outcome expectations. Higher extraversion was associated with better social support. More openness was associated with better self-efficacy and outcome expectations. Higher extraversion was associated with better social support. More openness was associated with better outcome expectations, mindfulness, and lower levels of depression. Agreeableness was not significantly associated with any outcome. None of the 5 personality dimensions were associated with physical component of quality of life.

Conclusion:

Personality was significantly correlated with FM impact, a variety of health outcomes, and strongly associated with self-efficacy and mindfulness. Higher neuroticism was associated with worse psychosocial factors, suggesting this subset of patients may benefit from individualized treatment that takes personality into consideration. Results further elucidate characteristics of FM patients and highlight the importance of personality in the management of FM.
<table>
<thead>
<tr>
<th>Dependent Variable</th>
<th>Personality Dimension</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Agreeableness</td>
</tr>
<tr>
<td><strong>FIQR†</strong></td>
<td>-0.04 (0.91)</td>
</tr>
<tr>
<td><strong>Symptom Severity†</strong></td>
<td>0.04 (0.27)</td>
</tr>
<tr>
<td><strong>HADS-Anxiety†</strong></td>
<td>-0.09 (0.19)</td>
</tr>
<tr>
<td><strong>HADS-Depression†</strong></td>
<td>-0.03 (0.75)</td>
</tr>
<tr>
<td><strong>Perceived Stress †</strong></td>
<td>-0.18 (0.22)</td>
</tr>
<tr>
<td><strong>SF-36 Mental Component Score</strong></td>
<td>0.42 (0.06)</td>
</tr>
<tr>
<td><strong>SF-36 Physical Component Score</strong></td>
<td>-0.28 (0.07)</td>
</tr>
<tr>
<td><strong>Medical Outcomes Study Social Support Survey</strong></td>
<td>0.03 (0.11)</td>
</tr>
<tr>
<td><strong>Chronic Pain Self-Efficacy</strong></td>
<td>-0.046 (0.26)</td>
</tr>
<tr>
<td><strong>Outcome Expectations for Exercise</strong></td>
<td>0.02 (0.12)</td>
</tr>
<tr>
<td><strong>Five Facet Mindfulness Questionnaire -Total</strong></td>
<td>0.64 (0.10)</td>
</tr>
</tbody>
</table>

Note: FIQR = Revised Fibromyalgia Impact Questionnaire; HADS = Hospital Anxiety and Depression Scale; SF-36 = Short Form-36, a measure of quality of life

Bolded p-values indicate statistical significance (p-value < 0.05)

*All models were adjusted for age, gender, BMI, and living situation

†Higher scores indicate worse health

Disclosure: A. Seto, None; T. Wu, None; L. L. Price, None; X. Han, None; W. F. Harvey, None; C. Wang, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/the-role-of-personality-in-patients-with-fibromyalgia](http://acrabstracts.org/abstract/the-role-of-personality-in-patients-with-fibromyalgia)

Abstract Number: 844

Social Support, Stress and Health Outcomes in Systemic Lupus Erythematosus: Georgians Organized Against Lupus (GOAL) Cohort

Charmayne M. Dunlop-Thomas, S. Sam Lim, Gaobin Bao and Cristina Drenkard, Division of Rheumatology, Emory University School of Medicine, Atlanta, GA

First publication: September 18, 2017
Background/Purpose: Stress can influence immune and neuroendocrine processes, and may lead to poor outcomes in people with systemic lupus erythematosus (SLE). Social support can potentially reduce the negative influences of stress on disease outcomes. We examined the relationships between stress and disease outcomes and whether social support mitigates those relationships in SLE.

Methods: We examined cross-sectional data from GOAL, a large population-based cohort of patients with validated SLE from Atlanta, Georgia. Since 2011, participants respond annually to validate self-administered health outcome surveys. Social Support was assessed with the Patient-Reported Outcomes Measurement Information System Social Support Short Form 4a (Emotional, Informational and Instrumental). We used Cohen’s Perceived Stress Scale 4 (PSS-4), Systemic Lupus Activity Questionnaire (SLAQ) and the Patient Health Questionnaire-9 (PHQ) for depression severity. Analysis of covariance (ANCOVA) was used to examine the effect of social support (categorical) on the linear relation between perceived stress and disease outcomes.

Results: Among 670 participants (93.9% women, 80.0% Black; mean age 48.4), mean(SD) scores were 7.20(2.55) for PSS-4, 15.18(8.66) for SLAQ, and 7.18(5.92) for PHQ-9. Mean(SD) social support scores were 52.03(9.28) for instrumental, 52.80(10.73) for informational, and 55.45(9.33) for emotional support. Stress was significantly associated with disease activity and depression. Instrumental support was the only social support construct that modified the effect of stress on disease activity. Neither emotional, informational nor instrumental support influenced the association between stress and depression. However, at a given stress level, participants with low social support have significantly worse disease activity and depression.

Conclusion: In a population-based SLE cohort with large numbers of Blacks, there was an elevated level of perceived stress and moderate to severe disease activity, with 30% endorsing moderate to severe depression. Instrumental social support may buffer the association between disease activity and stress. Recognizing the importance of developing more instrumental resources, such as transportation and home care services may contribute significantly to improving SLE health outcomes.

Table 1. ANCOVA analysis of disease activity or depression and perceived stress score by social support categories

<table>
<thead>
<tr>
<th>Relation</th>
<th>Categorical group (Social Support)</th>
<th>Low Support (Score&lt;=50)</th>
<th>High Support (Score&gt;50)</th>
<th>Intercept difference</th>
<th>P</th>
<th>Slope difference</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intercept</td>
<td>Slope</td>
<td>Intercept</td>
<td>Slope</td>
<td>Difference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease Activity</td>
<td>Emotional</td>
<td>7.76</td>
<td>1.19</td>
<td>5.54</td>
<td>1.19</td>
<td>2.12</td>
<td>0.0010</td>
</tr>
<tr>
<td></td>
<td>Instrumental</td>
<td>11.21</td>
<td>0.86</td>
<td>4.20</td>
<td>1.37</td>
<td>7.02</td>
<td>0.0004</td>
</tr>
<tr>
<td>vs. Perceived Stress</td>
<td>Informational</td>
<td>8.84</td>
<td>1.13</td>
<td>5.91</td>
<td>1.13</td>
<td>2.93</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Depression</td>
<td>Emotional</td>
<td>-0.10</td>
<td>1.12</td>
<td>-1.62</td>
<td>1.12</td>
<td>1.53</td>
<td>0.0002</td>
</tr>
<tr>
<td>vs. Perceived Stress</td>
<td>Informational</td>
<td>0.04</td>
<td>1.11</td>
<td>-1.27</td>
<td>1.11</td>
<td>1.40</td>
<td>0.0009</td>
</tr>
<tr>
<td></td>
<td>Instrumental</td>
<td>-0.08</td>
<td>1.13</td>
<td>-1.43</td>
<td>1.13</td>
<td>1.35</td>
<td>0.0013</td>
</tr>
</tbody>
</table>

Disclosure: C. M. Dunlop-Thomas, None; S. S. Lim, None; G. Bao, None; C. Drenkard, No commercial interest, 2.
Effectiveness of Brief Group Psychoanalytic Psychotherapy in Patients with Systemic Lupus Erythematosus and Follow-up

Emilia Sato¹,², Céu Conceiçao³, Ivone Meinão⁴ and Sergio Blay⁵, ¹Rheumatology Division. Escola Paulista de Medicina, Universidade Federal de Sao Paulo, Sao Paulo, Brazil, ²Rheumatology Div/Dept of Med, Escola Paulista de Medicina - Universidade Federal de Sao Paulo, Sao Paulo, Brazil, ³Medicine, Escola Paulista de Medicina, Universidade Federal de São Paulo, Sao Paulo, Brazil, ⁴Medicine, Universidade Federal de São Paulo, Sao Paulo, Brazil, ⁵Psychiatry, Escola Paulista de Medicina, Universidade Federal de Sao Paulo, Sao Paulo, Brazil

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: ARHP Psychosocial Impact on Rheumatic Disease
Session Type: ARHP Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: There are few studies evaluating the effectiveness of psychotherapy in Systemic Lupus Erythematosus (SLE) patients.

Objectives: To evaluate the effectiveness of brief group psychoanalytic psychotherapy (BGPP) in improving quality of life, anxiety and depression levels and coping strategies in SLE. Methods: Prospective, randomized clinical trial (number NCT01840709), including 80 SLE patients in a tertiary hospital. Patients were randomized into two groups: therapy (TG n=37) and control (CG n=43). Both groups received standard clinical treatment. TG received BGPP, weekly for 20 consecutive weeks performed by a specialized psychologist. CG remained in the waiting list. Assessments: at baseline (T1), after 20th weeks (T2), and 24 months after the end of the study (T3). Damage and disease activity were assessed by SLICC/ACR-DI score and SLEDAI-2k score, respectively. Self-administered questionnaires supervised by a blind evaluator were used to evaluate symptoms (SLE-SSC), quality of life (SLEQOL), anxiety and depression (HAD) and coping strategies (CIS). Inclusion criteria: female gender; SLE (ACR-1997 classification criteria), age ≥ 18 years, minimum follow-up of six months and signing consent form approved by Institutional Ethic Committee. Exclusion criteria: illiterate patients, physical and mental comorbidities that preclude the attendance, and external psychological treatment. Statistical analysis: intent to treat analysis. Comparisons of variance between groups over time (ANOVA repeated measures). SPSS version 17. p <0.05 was considered significant.

Results: At baseline, TG and CG were homogeneous in all variables, including medication. In T2, TG showed significant improvement in the majority of domains of SLEQOL (Table 1), all domains of HAD (Table 2) and several domains of CIS (Table 3). Some of benefits were maintained at the 24-month follow-up after the end of the therapy, including the most appropriate coping strategies to face the disease. No significant differences were observed in medication and clinical variables.

Conclusion: This study showed effectiveness of BGPP in improving quality of life, depression, anxiety and coping strategies to deal with stress in SLE patients, and some of the benefits were maintained in a long follow-up.
Table 1. SLEQOL scores in SLE patients’ assessments

<table>
<thead>
<tr>
<th>DOMAIN</th>
<th>TIME</th>
<th>CONTROL</th>
<th>THERAPY</th>
<th>intgroup p</th>
<th>interation p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Function</td>
<td>T1</td>
<td>15.2 (9.5)</td>
<td>14.4 (8.8)</td>
<td>0.099</td>
<td>0.096</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>16.9 (9.3)</td>
<td>13.6 (7.6)</td>
<td>0.099</td>
<td>0.096</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>16.9 (8.9)</td>
<td>13.1 (7.4)</td>
<td>0.099</td>
<td>0.096</td>
</tr>
<tr>
<td></td>
<td>Intrgroup p</td>
<td>0.889</td>
<td>0.889</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>28.1 (16.9)</td>
<td>27.3 (13.0)</td>
<td>0.812</td>
<td>0.812</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>33.1 (15.8)</td>
<td>20.8 (10.4)</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>35.5 (14.6)</td>
<td>20.8 (9.7)</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Intrgroup p</td>
<td>0.053</td>
<td>&lt; 0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptoms</td>
<td>T1</td>
<td>22.3 (9.7)</td>
<td>23.9 (12.1)</td>
<td>0.516</td>
<td>0.516</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>25.2 (9.6)</td>
<td>17.7 (8.6)</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>25.6 (9.2)</td>
<td>18.7 (8.1)</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Intrgroup p</td>
<td>0.008</td>
<td>0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td>T1</td>
<td>11.0 (5.0)</td>
<td>10.6 (4.2)</td>
<td>0.648</td>
<td>0.648</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>11.8 (5.7)</td>
<td>8.1 (4.2)</td>
<td>0.002</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>12.3 (5.3)</td>
<td>8.7 (4.4)</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Intrgroup p</td>
<td>0.230</td>
<td>0.009</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Humor</td>
<td>T1</td>
<td>13.9 (7.7)</td>
<td>15.4 (7.5)</td>
<td>0.561</td>
<td>0.561</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>14.6 (7.3)</td>
<td>10.1 (5.8)</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>14.7 (6.9)</td>
<td>10.4 (6.0)</td>
<td>0.004</td>
<td>0.004</td>
</tr>
<tr>
<td></td>
<td>Intrgroup p</td>
<td>0.816</td>
<td>&lt; 0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self-image</td>
<td>T1</td>
<td>22.4 (10.7)</td>
<td>25.2 (10.5)</td>
<td>0.247</td>
<td>0.247</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>23.0 (10.7)</td>
<td>16.5 (7.0)</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>24.6 (10.8)</td>
<td>17.1 (7.1)</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Intrgroup p</td>
<td>0.260</td>
<td>&lt; 0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Score</td>
<td>T1</td>
<td>112.6 (46.3)</td>
<td>117.2 (42.3)</td>
<td>0.649</td>
<td>0.649</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>122.1 (45.9)</td>
<td>85.1 (34.4)</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>128.2 (53.9)</td>
<td>88.5 (53.7)</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Intrgroup p</td>
<td>0.004</td>
<td>&lt; 0.001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SLEQOL - Systemic Lupus Erythematosus Quality of Life (Range 0-95)  
Intergroup p, interation p - ANOVA (Analysis of Variance)  
p < 0.05 - significant  
Mean (Standard deviation)

Table 2. HAD scores in SLE patients’ assessments

<table>
<thead>
<tr>
<th>DOMAIN</th>
<th>TIME</th>
<th>CONTROL</th>
<th>THERAPY</th>
<th>intgroup p</th>
<th>interation p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>T1</td>
<td>7.81 (4.37)</td>
<td>8.08 (4.13)</td>
<td>0.370</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>8.66 (4.72)</td>
<td>6.38 (3.50)</td>
<td>0.010</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>8.53 (4.22)</td>
<td>6.81 (3.78)</td>
<td>0.060</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Intrgroup p</td>
<td>0.285</td>
<td>&lt; 0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>T1</td>
<td>6.23 (4.44)</td>
<td>7.24 (4.94)</td>
<td>0.300</td>
<td>0.300</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>7.33 (4.15)</td>
<td>5.22 (3.82)</td>
<td>0.021</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>6.95 (3.99)</td>
<td>5.09 (2.02)</td>
<td>0.106</td>
<td>0.106</td>
</tr>
<tr>
<td></td>
<td>Intrgroup p</td>
<td>0.145</td>
<td>&lt; 0.001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

HAD - Hospital Anxiety and Depression Scale (Range 0-21 per domain)  
Intergroup p, interation p - ANOVA (Analysis of Variance)  
p < 0.05 - significant  
Mean (Standard deviation)
Disclosure: E. Sato, None; C. Conceiçao, None; I. Meinão, None; S. Blay, None.


Abstract Number: 846

Social Support in Couples-Focused Physical Activity Interventions for People with Hip or Knee Osteoarthritis: What Kinds of Partner Support Are Associated with Increases in Physical Activity and Reductions in Sedentary Behavior?

Christine Rini1, Liubov Arbeeva2, Stephanie Bahorski2, Cynthia Khan3, Rebekah Layton2, Derek Hales2, Julie Upchurch2, Shelby Rimmler2, Ida Griesemer2, Mary Altpeter2, Dana Carthron4, Todd Schwartz2 and Leigh F. Callahan5, 1Biomedical Research, Hackensack University Medical Center, Hackensack, NJ, 2University of North Carolina at Chapel Hill, Chapel Hill, NC, 3Econometrica, Inc., Bethesda, MD, 4Michigan State University, East Lansing, MI, 5Thurston Arthritis Research Center, University of North Carolina at Chapel Hill, Chapel Hill, NC

First publication: September 18, 2017
Background/Purpose: Physical activity (PA) reduces joint symptoms in people with osteoarthritis (PWOA), but most PWOA get insufficient PA. They would benefit from small but sustained increases in PA, but PA interventions usually elicit short-lived increases. Social support is a reliable predictor of PA, and partners (e.g., a spouse) can provide support that helps PWOAs make lasting increases in PA (e.g., by providing encouragement or joining in PA). Yet, partner support may also fail to provide intended resources (i.e., PWOAs may appraise it as “ineffective”—a poor match for their need for a certain quality and quantity of support). Partners may also provide solicitous support that hinders behavior change (e.g., well-intentioned discouragement of activity in favor of rest). The purpose of this dyadic study was to examine these aspects of partner support for PA, as reported by PWOA (“support received”) and their partner (“support provided”).

Methods: 173 couples, with PWOAs who had hip or knee OA and were insufficiently active, completed a couples-focused PA intervention with 3-hours of in-person education and 12-weeks of workbook activities. They also completed questionnaires and wore accelerometers at baseline and at 1-week and 3-, 6-, and 12-months post-intervention. We used multilevel modeling to examine support received and provided as predictors of PWOAs’ moderate to vigorous PA (MVPA) and sedentary behavior across these timepoints.

Results: Models adjusted for sociodemographic covariates revealed that PWOAs’ MVPA at each timepoint was higher for PWOAs who reported receiving more encouragement for PA from their partner \((p<.01)\) and those who reported that their partner joined in their PA \((p=.02)\). PWOAs’ MPVA was also higher when partners reported joining in their PA \((p=.03)\). PWOAs’ appraised effectiveness of this support did not moderate its association with MVPA, nor were partners’ solicitous behaviors (as reported by PWOAs or partners) associated with MVPA. In addition, an interaction showed a negative association between partner-reported solicitous support and PWOA sedentary behavior when PWOAs appraised this support as relatively ineffective (i.e., a poor match for their needs). This association was attenuated among PWOAs who appraised the effectiveness of their partner’s solicitous support more favorably (i.e., a better match for their needs; \(p=.02)\). A similar interaction occurred for partner-provided joining in PA \((p=.048)\).

Conclusion: These findings highlight different pathways by which to change MVPA and sedentary behavior and have implications for designing couples-based PA interventions that elicit lasting behavior change that thus ensure that PWOAs get the health benefits of PA.

Disclosure: C. Rini, None; L. Arbeeva, None; S. Bahorski, None; C. Khan, None; R. Layton, None; D. Hales, None; J. Upchurch, None; S. Rimmler, None; I. Griesemer, None; M. Altpeter, None; D. Carthron, None; T. Schwartz, None; L. F. Callahan, None.


Abstract Number: 847

The Mediational Role of Helplessness in Psychological Outcomes in Systemic Lupus Erythematosus

Desiree R Azizoddin1, Sarah D. Mills2, Perry M. Nicassio3, Geraldine Zamora Racaza4 and Michael Weisman5, 1611 W Harrison, 1611 W Harrison, Chicago, IL, 2SDSU/UC San Diego Joint Doctoral Program in Clinical Psychology, San Diego, CA, 3Cousins Center for PNI, UCLA, LA, CA, 4Division of Rheumatology, Cedars-Sinai Medical Center, Los Angeles, CA, 5Cedars-Sinai Medical Center Division of Rheumatology, Los Angeles, CA

First publication: September 18, 2017
Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic, autoimmune disease affecting multiple organs, leading to a significant impact on health-related quality of life. Theoretical models are critical to understanding the mechanisms behind the relationships between pain and psychosocial variables and can be used to help guide future research and treatment among patients with SLE. Thus, the present study examined whether helplessness is a mediator of the relationship between pain and three types of psychological distress among patients with SLE; specifically anxiety, depression, and perceived stress.

Methods: A convenience sample was obtained of patients aged 18 years and above diagnosed with SLE according to ACR 1982 guidelines at a large medical center in Southern California. Assessment included the Lupus Patient-Reported Outcome tool, Arthritis Helplessness Index, Perceived Stress Scale-10, and Hospital Anxiety and Depression Scale. Multiple mediation analysis was completing using an SPSS macro called “PROCESS.”

Results: The cohort of 136 patients had a mean age of 48.6 years (SD = 13.87), and was mostly female (92.6%) and Caucasian (44.9%). The direct effect of pain vitality on anxiety symptoms was $-0.074$, $p < .001$; the relationship between pain vitality and anxiety symptoms was significantly decreased when helplessness was included in our model, $ab = -.041$, BCa 95% CI [-0.073, -0.015]. The direct effect of pain vitality on depressive symptoms was $-0.069$, $p < .001$; the relationship between pain vitality and depressive symptoms was significantly decreased when helplessness was included in our model, $ab = -.035$, BCa 95% CI [-0.502, -.212]. The direct effect of pain vitality on stress was $-0.038$, $p < .01$; the relationship between pain vitality and stress was significantly decreased when helplessness was included in our model, $ab = -.041$, BCa 95% CI [-0.063, -.027].

Conclusion: Consistent with studies conducted in other autoimmune populations, findings suggested that helplessness fully mediated the relationship between pain and measures of anxiety, depression, and perceived stress. These results provide a theoretical model to better understand mechanisms that may help explain the relationship between pain and psychological distress in this population. Despite the moderate to low reports of perceived stress, the high reports of perceived helplessness, anxiety and depressive symptoms suggest a need for intervention to improve self-efficacy and reduce psychological distress.
Table 1. Demographic Characteristics of sample (n = 136) and results of multiple mediation analysis assessing relationship between LupusPRO-Pain Vitality

<table>
<thead>
<tr>
<th>Demographics</th>
<th>M (SD)</th>
<th>N (%)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>48.6 (13.8)</td>
<td>18-81</td>
<td></td>
</tr>
<tr>
<td>Education in years</td>
<td>15.2 (2.8)</td>
<td>8-24</td>
<td></td>
</tr>
<tr>
<td>Annual Income ($)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;15K</td>
<td>11 (8.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15-25K</td>
<td>16 (11.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25-39K</td>
<td>12 (8.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40-60K</td>
<td>13 (9.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>60-75K</td>
<td>13 (9.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>75-100K</td>
<td>21 (15.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;100K</td>
<td>49 (36.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>126 (92.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>61 (44.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>25 (18.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>19 (14.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>29 (15.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other Mixed Race/Ethnicity</td>
<td>11 (8.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marital Status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married/Lives with partner</td>
<td>76 (55.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single/Never married</td>
<td>54 (25.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Divorced/Separated/Widowed</td>
<td>22 (16.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease Activity: Active</td>
<td>62 (45.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease Duration</td>
<td>16.9 (11.9)</td>
<td>0-55</td>
<td></td>
</tr>
<tr>
<td>Anxiolytic Use</td>
<td>35 (25.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antidepressant Use</td>
<td>34 (25.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medication Use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prednisone Use</td>
<td>59 (43.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immunosuppressant Use</td>
<td>87 (64.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cytotoxic</td>
<td>24 (17.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biologic</td>
<td>62 (45.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HADS-Depression</td>
<td>5.4 (4.0)</td>
<td>43 (23.1%)</td>
<td>0-21</td>
</tr>
<tr>
<td>HADS-Anxiety</td>
<td>7.7 (4.1)</td>
<td>61 (41%)</td>
<td>0-21</td>
</tr>
<tr>
<td>PSS</td>
<td>17.8(6.3)</td>
<td>0-40</td>
<td></td>
</tr>
<tr>
<td>LupusPRO-Pain Vitality</td>
<td>56.6(27.3)</td>
<td>0-100</td>
<td></td>
</tr>
<tr>
<td>AHI-Helplessness</td>
<td>14.5(5.4)</td>
<td>5-30</td>
<td></td>
</tr>
</tbody>
</table>

Mediational Analysis

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Direct Effect without mediator</th>
<th>Indirect Effect with Helplessness Mediator</th>
<th>Boot SE</th>
<th>BCa 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>-.069 (.011)</td>
<td>-.035 (.007)</td>
<td>-.050, -.021</td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>-.074 (.021)</td>
<td>-.041 (.015)</td>
<td>-.073, -.015</td>
<td></td>
</tr>
<tr>
<td>PSS</td>
<td>-.038 (.013)</td>
<td>-.043 (.009)</td>
<td>-.063, -.027</td>
<td></td>
</tr>
</tbody>
</table>

Note. HADS N% pertains to participants reporting a score of 8 or above for depression and anxiety subscale. SE: Standard Error of the
“Suddenly You Are a Person at Risk of Developing Rheumatoid Arthritis!”
Different Perspectives of Individuals on Predictive Testing – Results of an International Qualitative Interview Study

Erika Mosor\textsuperscript{1}, Michaela Stoffer\textsuperscript{2}, Günter Steiner\textsuperscript{3}, Karim Raza\textsuperscript{4}, Rebecca J Stack\textsuperscript{4}, Gwenda Simons\textsuperscript{4}, Marie Falahhee\textsuperscript{4}, Georg Schett\textsuperscript{5}, Matthias Englbrecht\textsuperscript{6}, Josef S. Smolen\textsuperscript{2}, Axel J. Hueber\textsuperscript{6} and Tanja Stamm\textsuperscript{7}, \textsuperscript{1}Section for Outcomes Research, Center for Medical Statistics, Informatics, and Intelligent Systems, Medical University of Vienna, Vienna, Austria, \textsuperscript{2}Division of Rheumatology, Department of Internal Medicine III, Medical University of Vienna, Vienna, Austria, \textsuperscript{3}Rheumatology, Medical University of Vienna, Vienna, Austria, \textsuperscript{4}Department of Rheumatology, University of Birmingham and Sandwell & West Birmingham Hospitals NHS Trust, Birmingham, UK, Birmingham, United Kingdom, \textsuperscript{5}Rheumatology and Immunology, Department of Internal Medicine 3, Universitätsklinikum Erlangen, Erlangen, Germany, Erlangen, Germany, \textsuperscript{6}Department of Medicine 3, Rheumatology and Immunology, University of Erlangen-Nuremberg, Erlangen, Germany, \textsuperscript{7}Section for Outcomes Research, Center for Medical Statistics, Informatics, and Intelligent Systems, Medical University of Vienna, Vienna, Vienna, Austria

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: ARHP Psychosocial Impact on Rheumatic Disease
Session Type: ARHP Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: People at risk of developing rheumatoid arthritis (RA) may be candidates for interventions aimed at preventing RA development \cite{1}. The identification of such at risk populations includes testing for genetic and other (e.g. autoantibody) biomarkers. However, little is known about the perspectives of at risk individuals on these tests, how they react and cope when identified as having an elevated risk status and what support they need. This study was undertaken to address this gap in the current knowledge.

Methods: A qualitative interview study with people who were informed of being at risk of developing RA was conducted. People either took part in a predictive test for RA as part of an extended health examination, or were patients with clinically suspect arthralgia. The interview schedule explored perceptions of RA risk and different types of predictive tests. All interviews were audio-recorded, transcribed verbatim and analyzed using thematic analysis.

Results: A total of 34 individuals (rheumatoid factor and/or ACPA positive) from three different European countries, who previously had been informed that they had an elevated risk of developing RA participated in the study. Analysis of the interview data revealed five overarching themes related to predictive testing in the context of RA (Figure).
There were differences between the perceptions of arthralgia patients and asymptomatic individuals. People suffering from pain were much more frightened and worried when informed of being at risk of developing RA. As a consequence, they reported that they modified their lives to a larger extent and had greater knowledge about RA than those without any symptoms who were surprised, but kept calm and did not envisage changing their lifestyle as a consequence of being tested positive. Almost all participants in this study preferred precise predictive tests in the context of RA. However, more than half of them reported that they would refuse synovial biopsy or preventive medication. Recommendations for predictive testing in the field of RA were given, which could promote uptake of preventive strategies.

**Conclusion:** Participants showed a variety of views about predictive testing in the context of RA risk and offered specific suggestions that should be incorporated into service design and delivery in the context of future predictive testing programmes. These findings may also be relevant to prediction and prevention in the context of other diseases where multiple genetic risk factors interact with environmental risk factors to drive disease development.

Iago Pinal-Fernandez1, Berta Ferrer-Fabregas2, Ernesto Trallero-Araguas1, Eva Balada1, Maria Angeles Martinez3, Jose Cesar Milisenda4, Gloria Aparicio-Españoł5, Moises Labrador-Horrillo1, Vicente Garcia-Patos1, Josep Maria Grau-Junyent4 and Albert Selva O'Callaghan6, 1Internal Medicine, Autoimmune Diseases Unit. Vall d’Hebron Hospital, Barcelona, Spain, 2Pathology, Vall d’Hebron, Barcelona, Spain, 3Immunology, Immunology Department, Barcelona, Spain, 4Muscle Research Group and Ciberer, Hospital Clinic Provincial, Barcelona, Spain, 5Dermatology, Vall d’Hebron Hospital, Barcelona, Spain, 6Internal Medicine, Hospital Universitari General Vall d'Hebron, Barcelona, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Muscle Biology, Myositis and Myopathies
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: To analyze the influence of genetic alterations and differential expression of the TIF1 genes in the pathophysiology of cancer-associated myositis (CAM).

Methods: Whole exome sequencing of paired blood and tumor DNA samples from anti-TIF1g positive CAM patients and controls were analyzed for the presence of somatic mutations and copy number changes in the TIF1 genes. To better understand the genesis and maintenance of the autoimmune process we also studied the expression of TIF1g in the different tissues involved in CAM (skin, muscle, and tumor) calculating the immunohistochemical H-score.

Results: Six out of 7 tumors from anti-TIF1g positive patients showed somatic mutations or loss of heterozygosity in one or more of the 4 TIF1 genes compared with just one myositis control tumor (86% vs. 17%, p=0.03). Compared with control tumors from non-myositis patients, tumors from both anti-TIF1g positive (H-score 255 vs. 196, p=0.01) and anti-TIF1g negative CAM patients (H-score 251 vs. 152, p=0.03) showed more intense TIF1g staining, without significant differences between anti-TIF1g positive and negative patients. Compared with anti-TIF1g negative patients, TIF1g muscle staining was more intense in anti-TIF1g positive patients (H-score 22 vs. 5, p=0.03), while the skin of both myositis and control patients showed intense TIF1g staining.

Conclusion: Mutations of TIF1 genes in tumors with high expression of TIFg may trigger myositis. We hypothesize that an intense antineoplastic immune response may cause a rapid depletion of tumor neo-antigen shifting the target of immune cells experiencing affinity maturation towards the wild-type form of the antigen, abundantly expressed in the skin and muscle of these patients.

Disclosure: I. Pinal-Fernandez, None; B. Ferrer-Fabregas, None; E. Trallero-Araguas, None; E. Balada, None; M. A. Martinez, None; J. C. Milisenda, None; G. Aparicio-Españoł, None; M. Labrador-Horrillo, None; V. Garcia-Patos, None; J. M. Grau-Junyent, None; A. Selva O'Callaghan, None.


Abstract Number: 850

Immune Checkpoint Inhibitors and Inflammatory Myopathies: Data from the US Food and Drug Administration Adverse Event Reporting System

Xerxes Pundole, Mohsin Shah, Noha Abdel-Wahab and Maria Suarez-Almazor, Section of Rheumatology and Clinical Immunology, Department of General Internal Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA, Houston, TX

First publication: September 18, 2017

SESSION INFORMATION
Background/Purpose:

Immune checkpoint inhibitors have become standard of care for many malignancies. Although these therapies are effective, they can activate the immune system resulting in adverse consequences. Inflammatory myopathies are increasingly being appreciated as one of the adverse phenotypes stemming from immune checkpoint inhibitor therapy, but few reports have been described in the literature. We aimed to analyze rates and disproportionality using drugs from the US Food and Drug Administration (FDA) Adverse Events Reporting System (FAERS).

Methods:

We ran a query on AERSMine, an open access web based application designed to mine the FAERS database from the first quarter (Q1) of 2004 to the fourth quarter (Q4) of 2016, in a total of 8,864,346 reports. We ran queries to obtain the number of cases and to calculate the rates and measures of disproportionality; proportional reporting ratios [PRRs] and safety signals [information components (IC)]. Search terms included immune checkpoint inhibitors, namely ipilimumab, nivolumab and pembrolizumab. Inflammatory myopathy terms searched were myositis, dermatomyositis and polymyositis. We used Evans 2001 criteria to detect a signal which includes a PRR of 2 or greater, a $x^2$ of 4 or more and at least 3 reports.

Results:

The FAERS files from 2004 Q1 to 2016 Q 4 contain 42, 94 and 24 inflammatory myopathy reports for ipilimumab, nivolumab and pembrolizumab respectively. Myositis (n=28; $x^2=71.4$; PRR=4.5; IC=2.2), dermatomyositis (n=9; $x^2=33.8$; PRR=6.2; IC=2.6) and polymyositis (n=5; $x^2=5.5$; PRR=3.2; IC=1.7) showed disproportionality signals in relation with ipilimumab. Reports with nivolumab showed similar results with myositis (n=78; $x^2=847.2$; PRR=13.1; IC=3.7), dermatomyositis (n=5; $x^2=6.8$; PRR=3.6; IC=1.8) and polymyositis (n=11; $x^2=54.1$; PRR=7.4; IC=2.9). There were 3 reports of Nivolumab and necrotizing myositis with a $x^2$ of 88.7 and a PRR of 47.3. Pembrolizumab demonstrated a disproportionality signal with myositis (n=24; $x^2=177.3$; PRR=9.7; IC=3.3). There were 2 reports of necrotizing myositis with pembrolizumab and no reports of dermatomyositis or polymyositis with pembrolizumab.

Conclusion:

Inflammatory myopathies are disproportionally related with immune checkpoint inhibitors. To the best of our knowledge this is the first study to evaluate adverse events in relation with immune checkpoint inhibitors using the FDA FAERS data. All results are hypothesis generating and usual caveats and limitations of pharmacovigilance data mining should be applied while interpreting the results.

Disclosure: X. Pundole, None; M. Shah, None; N. Abdel-Wahab, None; M. Suarez-Almazor, Bristol-Myers Squibb, 5.


Abstract Number: 851

Autoantibodies Predict Long Term Survival in Myositis Associated Interstitial Lung Disease

Silvia Martinez1, Rohit Aggarwal2,3 and Chester V. Oddis4, 1Internal Medicine, UPMC, Pittsburgh, PA, 2Department of Medicine / Rheumtology, University of Pittsburgh Medical Center, Pittsburgh, PA, 3Rheumatology, University of Pittsburgh, Pittsburgh, PA, 4Rheumatology/Clinical Immunology, University of Pittsburgh/University of Pittsburgh Medical Center, Pittsburgh, PA
Background/Purpose: Interstitial lung disease (ILD) significantly contributes to morbidity and mortality in adult polymyositis (PM) and dermatomyositis (DM). Myositis associated autoantibodies (MAA) are associated with unique clinical phenotypes and patient outcomes. In particular, the anti-tRNA synthetase autoantibodies (anti-synAbs) are associated with high rates of ILD. Our aim was to determine predictors of survival in myositis associated ILD (MA-ILD) and to evaluate differences related to autoantibody (autoAb) subsets.

Methods: PM and DM subjects with ILD or with the antisynthetase (anti-syn) syndrome with ILD were consecutively identified from the University of Pittsburgh (UPITT) CTD registry which encompasses more than three decades of prospective data linked to a sample repository collected on outpatients and inpatients with various autoimmune diseases. PM and DM patients met probable or definite Bohan and Peter criteria and the anti-syn patients possessed one of the 8 known anti-syn autoAbs (i.e. anti-Jo-1, PL-7, PL-12, EJ, OJ, KS, Zo and Tyr). ILD was radiographically defined by characteristic xray or high-resolution computerized tomography findings. Death or transplant was determined from the registry or electronic medical record. Kaplan Meier and log rank tests were used to determine survival rates and differences between autoAb groups. Cox proportional hazards model was used to determine survival differences after controlling for co-variates including age at diagnosis, gender, ethnicity and baseline FVC%.

Results: 369 patients met criteria for MA-ILD and 306 (83%) had positive autoAbs. Overall, 63% (231/369) had MAAs and 54% (198/369) had a positive the anti-syn autoAb. The most common autoAb subset in the entire autoAb (+) cohort was anti-Jo-1 (124/306; 41%). The overall 5 and 10 year survival of MA-ILD was 80% at 5 years and 72% at 10 years. Patients with an MAA had better survival compared to MAA (-) subjects (5 and 10 year survival 80% vs. 72%; 72% vs. 58%, p=0.003). Among MAA (+) patients, those with anti-syn autoAbs had better survival compared to those with non-anti-syn autoAbs (5 and 10 years survival 80% vs. 73%; 73% vs. 61%, p=0.004). Among the entire anti-syn autoAb (+) subjects, those with anti-Jo-1 had a better survival than those patients with 1 of the 7 other anti-syn autoAbs (5 and 10 year survival 86% vs. 72%; 77% vs. 65%, p=0.04).

Conclusion: Myositis patients with MAA, particularly anti-syn autoAbs have better survival rates compared to those without autoAbs. Among anti-syn autoAb (+) patient’s Jo-1 positivity confers a better survival. Myositis-associated autoAbs predict survival and long-term prognosis in myositis.
Abstract Number: 852

RNAseq Detection of Gene Dysregulation in PBMCs from Juvenile Dermatomyositis, Positive for p155/140 Myositis Specific Antibody

Chiang-Ching Huang1, Victoria Hans2, Dong Xu3, Megan L. Curran4,5, Gabrielle A. Morgan6, Elisha D.O. Roberson7 and Lauren M. Pachman8,9, 1Biostatistics, Joseph J. Zilber School of Public Health, Milwaukee, WI, 2CureJM Center of Excellence, Stanly Manne Research Center, Chicago, IL, 3Pediatric Rheumatology, Stanley Manne Research Center, Chicago, IL, 4Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, IL, 5Division of Rheumatology, Ann and Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, 6Cure JM Program of Excellence in Myositis Research, Chicago, IL, 7Depts. of Medicine and Genetics, Division of Rheumatology, Washington University, St. Louis, MO, 8Cure JM Program of Excellence in Juvenile Myositis Research, Stanley Manne Children’s Research Institute, affiliated with Ann & Robert H. Lurie Children’s Hospital of Chicago, Chicago, IL, 9Pediatric Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Muscle Biology, Myositis and Myopathies
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Children with Juvenile Dermatomyositis (JDM) have variable responses to the available immunosuppressive drugs, with less than optimal outcomes, making it essential to characterize their variable inflammatory response. It is recognized that Myositis Specific Antibodies (MSA) are each associated with different clinical features and disease course, but scarce information is available comparing the differences in genetic regulation among these MSAs. The purpose of this study was to compare RNASeq data from PBMCs obtained from untreated children with new onset JDM positive for p155/140 — the most common MSA — with the RNASeq data from age related controls, as well as JDM who were either positive for MJ or who did not have a recognized MSA. Clinically, children with p155/140 often follow a more variable and recurrent disease course than those patients with other MSA’s.

Methods: Newly diagnosed, untreated children with JDM were recruited for this IRB approved study (2008-13457), after obtaining age-appropriate informed consent: there were 75% girls, mean age 7.2 ±4.1; Mean DAS=12/20, while the controls had 80% girls, but were slightly older, 16.9±2.9. JDM disease activity was assessed using the Disease Activity Scores (DAS) which range from 0-20. MSA were determined by immunoblot and immunoprecipitation, (Oklahoma Research Laboratory): 4 of the JDM were positive for p155/140, 2 were MJ+, and 2 were negative for MSA, compared with 5 healthy pediatric controls. RNASeq libraries were generated from PBMC RNA using the Clontech stranded high input ribosomal depletion total RNA kits. The samples were sequenced on either an Illumina HiSeq2500 or HiSeq300 in paired-end mode. Serum levels of antibody to specific cytokines were determined by Mesoscale.

Results: The untreated JDM had active disease with a mean DAS-total=12.1. The RNASeq data identify 96 genes (adjusted p-value < 0.05) differentially expressed between JDM who were p155/140+ and JDM who either had anti-MJ antibody or were negative for MSA. The overall expression pattern of these genes is also different from the healthy controls. Pathway and gene ontology analysis reveals significant enrichment of this gene list in immune response, especially the interferon signaling (P=2*10^-15). We identified among this gene list, OSA1,2,3, TNF, MX1,2, TRIM 14, 22, 25, IFNG, TNFαA1P3, TNFSF-10, TGFBPI3, IL-2RB, and others, clearly indicating enhanced immune activation in the children positive for p155/140. Determination of some of the many cytokines involved in the JDM inflammatory pathway showed significant increases in p155/140 sera vs controls: Interferon- γ: p= 0.013, IL-10:p= 0.0056, IL-6: p=0.026; IL-8: p=0.011; TNF-α p=0.003892.

Conclusion: We have shown, for the first time, using RNASeq, that the MSA, p155/140 not only identifies children with JDM who will have a difficult diseases course — but that this MSA is also associated with specific enhanced immune activation. Speculation: Further definition of the specific differences in gene activation associated with the individual
MSA's may lead to more targeted therapeutic interventions, and may provide a means of assessing the child’s response to therapy.

Disclosure: C. C. Huang, None; V. Hans, None; D. Xu, None; M. L. Curran, None; G. A. Morgan, None; E. D. O. Roberson, None; L. M. Pachman, None.


Abstract Number: 853

Anti-TIF-1 Antibody Positivity Is Associated with a Five-Fold Increase in Cancer Risk in the Idiopathic Inflammatory Myopathies

Alexander Oldroyd1,2, Jamie C Sergeant1,3, Paul New4, Neil J. McHugh5,6, Zoe Betteridge5, Janine Lamb7, William Ollier7, Robert Cooper4,7,8 and Hector Chinoy2,9, 1Arthritis Research UK Centre for Epidemiology, Centre for Musculoskeletal Research, Manchester Academic Health Science Centre, University of Manchester, Manchester, United Kingdom, 2NIHR Manchester Biomedical Research Centre, Central Manchester NHS Foundation Trust, Manchester, United Kingdom, 3Centre for Biostatistics, University of Manchester, Manchester Academic Health Science Centre, Manchester, United Kingdom, 4MRC/ARUK Centre for Integrated Research into Musculoskeletal Ageing, University of Liverpool, Liverpool, United Kingdom, 5Department of Pharmacy and Pharmacology, The University of Bath, Bath, United Kingdom, 6Royal National Hospital for Rheumatic Diseases, Bath, UK, Bath, United Kingdom, 7Division of Population Health, Health Services Research and Primary Care, University of Manchester, Manchester Academic Health Science Centre, Manchester, United Kingdom, 8Department of Rheumatology, Aintree University Hospital, Liverpool, United Kingdom, 9Department of Rheumatology, Salford Royal NHS Foundation Trust, Manchester Academic Health Science Centre, Salford, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Muscle Biology, Myositis and Myopathies
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:
There is an increased cancer risk associated with the idiopathic inflammatory myopathies (IIM). Studies have identified that positivity for the autoantibody against transcriptional intermediary factor 1 (anti-TIF-1 Ab) confers an even greater cancer risk in the IIMs. Investigating the temporal relationship between anti-TIF-1 Ab positivity and cancer onset in a large longitudinal IIM cohort will inform future cancer screening practice. This study aimed to characterise the temporal relationship between anti-TIF-1 Ab positivity and cancer onset in a large UK-based adult IIM cohort.

Methods:
Data from adults with a Bohan & Peter-verified diagnosis of IIM from the UKMYONET study were analysed. Anti-TIF-1 Ab (alpha and gamma serosubtype) positive and negative patients were included. Each patient was followed up until they either developed cancer or were censored due to death. UKMYONET recruitment began in 1999, and cancer occurrence linkage was carried out up until December 2016 through the UK Health and Social Care Information Centre. Cancer associated myositis (CAM) was defined as an incident cancer occurring three years either side of the onset of IIM. The cumulative incidence of cancer after IIM onset was estimated according to Kaplan-Meier methods for the anti-TIF-1 Ab positive and negative cohorts. Hazard ratios for the time to cancer diagnosis by anti-TIF-1 Ab positivity were calculated using a Cox-regression model adjusted for age, gender and smoking status.
Results:

Data from 711 IIM cases were analysed, with a total of 8009 person-years follow up (Table 1); 55 (8%) of the IIM cases were anti-TIF-1 Ab positive, and all had dermatomyositis. A higher proportion of the anti-TIF-1 Ab positive cohort developed CAM, compared to the anti-TIF-1 Ab negative cohort: 38% vs 8%. Even after only one year of follow up, the proportion of the anti-TIF-1 Ab positive patients developing cancer (27%) exceeded the three year proportion of the anti-TIF-1 Ab negative cohort (8%). Cox proportional modelling revealed that anti-TIF-1 Ab positivity was significantly associated with an increased hazard of an associated cancer following IIM onset: HR 3.4 (95% CI 2.2, 5.4). Breast (33%), ovarian (19%) and lymphoma (14%) were the three most common cancers in the anti-TIF-1 Ab positive patients, whereas breast (20%), bowel (14%), lung (6%) and cervix (6%) were the most common sites in anti-TIF-1 Ab negative patients.

Conclusion:

This study has helped to characterise the temporal relationship between anti-TIF-1 Ab positivity and cancer onset. The findings that earlier cancer onset is associated with anti-TIF-1 Ab positivity, and that associated cancer types differ, are potentially of clinical significance, and appear to suggest a specific cancer screening approach in anti-TIF-1 Ab positive patients.

Table 1 – Baseline demographics and time to cancer confirmation in anti-TIF-1 Ab positive and negative cohorts
<table>
<thead>
<tr>
<th></th>
<th>Total cohort n = 711</th>
<th>Anti-TIF-1 Ab positive, n = 55</th>
<th>Anti-TIF-1 negative, n = 656</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female (%)</td>
<td>438 (61.6)</td>
<td>44 (80.0)</td>
<td>394 (60.1)</td>
</tr>
<tr>
<td>Smokers (%)</td>
<td>237 (33.3)</td>
<td>17 (30.9)</td>
<td>220 (33.5)</td>
</tr>
<tr>
<td>CAM* (%)</td>
<td>72 (10.1)</td>
<td>21 (38.2)</td>
<td>51 (7.8)</td>
</tr>
<tr>
<td>Proportion of patients with cancer preceding IIM onset** (%)</td>
<td>36 (5.1)</td>
<td>7 (12.7)</td>
<td>29 (4.4)</td>
</tr>
<tr>
<td>Proportion of patients with cancer following IIM onset*** (%)</td>
<td>36 (5.1)</td>
<td>14 (25.5)</td>
<td>22 (3.4)</td>
</tr>
<tr>
<td>Median age at IIM onset (years, IQR)</td>
<td>61.8 (51.9, 69.1)</td>
<td>62.3 (55.2, 65.9)</td>
<td>53.2 (42.6, 63.9)</td>
</tr>
<tr>
<td>Median age at cancer onset (years, IQR)</td>
<td>60.9 (50.4, 68.6)</td>
<td>60.3 (52.2, 67.2)</td>
<td>61.0 (50.4, 69.5)</td>
</tr>
<tr>
<td>Median time to cancer onset (years, IQR)</td>
<td>1.9 (0.0, 8.0)</td>
<td>0.8 (0.0, 2.2)</td>
<td>1.7 (0.0, 5.1)</td>
</tr>
<tr>
<td>Cumulative proportion with cancer onset in years after IIM onset (%), 95% CI:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.5 year after IIM onset</td>
<td>6.2 (4.4, 7.9)</td>
<td>14.5 (4.7, 23.4)</td>
<td>5.5 (3.7, 7.2)</td>
</tr>
<tr>
<td>1 year after IIM onset</td>
<td>7.5 (5.5, 9.4)</td>
<td>27.3 (14.5, 38.1)</td>
<td>5.8 (4.0, 7.6)</td>
</tr>
<tr>
<td>2 years after IIM onset</td>
<td>9.0 (6.9, 11.1)</td>
<td>34.5 (20.7, 46.0)</td>
<td>6.9 (4.9, 8.8)</td>
</tr>
<tr>
<td>3 years after IIM onset</td>
<td>10.1 (7.9, 12.3)</td>
<td>38.2 (23.9, 49.8)</td>
<td>7.8 (5.7, 9.8)</td>
</tr>
</tbody>
</table>

*CAM = cancer associated myositis – cancer occurring within 3 years either side of an IIM onset

** Defined as cancer occurring less than 3 years prior to IIM onset

*** Defined as cancer occurring less than 3 years after IIM onset

IIM = idiopathic inflammatory myopathy

IQR = interquartile range

CI = confidence interval

Disclosure: A. Oldroyd, None; J. C. Sergeant, None; P. New, None; N. J. McHugh, None; Z. Betteridge, None; J. Lamb, None; W. Ollier, None; R. Cooper, None; H. Chinoy, Novartis Pharmaceutical Corporation, 5, Novartis Pharmaceutical Corporation, 2.


Abstract Number: 854
Predictive Modeling of Mortality in Polymyositis/Dermatomyositis Patients with Interstitial Lung Disease Based on Combination of Serum Myositis-Specific Autoantibodies and Conventional Biomarkers

Takahisa Gono1, Kenichi Masui2, Yasushi Kawaguchi3, Kei Ikeda4, Atsushi Kawakami5, Maasa Tamura6, Yoshinori Tanino7, Takahiro Nunokawa8, Yuko Kaneko9, Shinji Sato10, Katsuaki Asakawa11, Naoshi Nishina9 and Masataka Kuwana1, 1Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan, 2Department of Anesthesiology, National Defense Medical College School of Medicine, Tokorozawa, Japan, 3Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan, 4Department of Allergy and Clinical Immunology, Chiba University Hospital, Chiba, Japan, 5Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki City, Japan, 6Department of Stem Cell and Immune Regulation, Yokohama City University Graduate School of Medicine, Yokohama, Japan, 7Department of Pulmonary Medicine, Fukushima Medical University School of Medicine, Fukushima, Japan, 8Department of Rheumatic Diseases, Tokyo Metropolitan Tama Medical Center, Tokyo, Japan, 9Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, 10Division of Rheumatology, Department of Internal Medicine, Tokai University School of Medicine, Isehara, Japan, 11Division of Respiratory Medicine, Niigata University Medical and Dental Hospital, Niigata, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Muscle Biology, Myositis and Myopathies
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Interstitial lung disease (ILD) is one of the leading causes of mortality in patients with polymyositis or dermatomyositis (PM/DM). Since clinical courses and outcomes of ILD are highly variable among PM/DM patients with ILD, disease subsetting is essential in deciding management regimens, by offering opportunity to identify patients who have a greater risk of mortality, especially early in the disease course. In this regard, myositis-specific autoantibodies (MSAs) correlate with unique subsets of PM/DM-associated ILD, but potential utility of other serum biomarkers routinely measured in clinical practice, such as CRP and ferritin, in predicting prognosis is also reported. The aim of this study is to establish predictive modeling of mortality in patients with PM/DM-associated ILD using a large cohort data.

Methods: This study was conducted using a database of a multicenter retrospective cohort of patients with PM/DM-ILD (JAMI cohort), which involved 44 institutions across Japan. We enrolled 487 patients based on adult-onset definite or probable PM/DM including clinically amyopathic DM (CADM), ILD confirmed by imaging study, and availability of serum samples at diagnosis. Anti-melanoma differentiation-associated gene 5 (MDA5) and anti-amyloplac tRNA synthetase (ARS) antibodies were detected by enzyme linked immunosorbent assay and RNA immunoprecipitation, respectively. CRP, ferritin, KL-6 and surfactant protein-D (SP-D) were chosen as serum biomarkers for PM/DM-ILD. Independent risk factors for all-cause mortality were identified by Cox regression analysis using MSAs and serum biomarkers, including CRP, ferritin, KL-6 and surfactant protein-D (SP-D) as explanatory variables. The backward selection method was applied; explanatory variables were eliminated when p value was > 0.10.

Results: The overall survival rate was 83% at 1 year. The survival rate was significantly lower in patients with anti-MDA5 than in those without (P<0.0001). The cut-off values of individual serum biomarkers for predicting mortality determined by the receiver operating characteristic curve were CRP ≥1 mg/dl, ferritin ≥500 ng/ml, KL-6 ≥1000 mg/dl and SP-D <100 ng/ml. The presence of anti-MDA5 (hazard ratio [HR] = 3.0, 95% confidence interval 1.6-5.7), CRP ≥1 mg/dl (HR = 2.4, 1.4-4.0), KL-6 ≥1000 mg/dl (HR = 2.0, 1.3-3.3) and ferritin ≥500 ng/ml (HR = 1.8, 1.0-3.2) were identified as risk factors for poor prognosis. Our modeling showed that the predicted mortality rates were 1.8%, 8%, 22%, 44% and 54% in patients with zero, one, two, three and all four risk factor score, respectively (Figure 1).

Conclusion: We successfully generated predictive modeling of mortality in patients with PM/DM-associated ILD using convenient serum biomarkers. This model is potentially useful in identifying the patients with high mortality risk, which
apparently require intensive treatment

Disclosure: T. Gono, Astellas, Japan Blood Products Organization, 8; K. Masui, None; Y. Kawaguchi, None; K. Ikeda, None; A. Kawakami, None; M. Tamura, None; Y. Tanino, None; T. Nunokawa, None; Y. Kaneko, AbbVie, Eisai, Daiichi Sankyo, Sanofi, 2,Bristol-Myers Squibb, Eli Lilly, Janssen, 5,AbbVie, Eisai, Astellas, Chugai Pharmaceutical, UCB, Pfizer, Bristol-Myers Squibb, Janssen, Tanabe-Mitsubishi, Ayumi Pharmaceutical, and Taisho-Ttoyama, 8; S. Sato, Medical & Biological Laboratories, Co., Ltd, 8; K. Asakawa, None; N. Nishina, None; M. Kuwana, Astellas, 2,Medical & Biological Laboratories, Co., Ltd, 7,Astellas, Medical & Biological Laboratories, Co., Ltd, Japan Blood Products Organization, 8.

Abstract Number: 855

Rapid and Sustained Pain Improvement in Rheumatoid Arthritis Patients Treated with Baricitinib Compared to Adalimumab or Placebo

Peter C. Taylor1, Roy Fleischmann2, Elizabeth Perkins3, Jeffrey Lisse4, Baojin Zhu4, Carol L Gaich4, Xiang Zhang4, Douglas E. Schlichting4, Christina L. Dickson4 and Tsutomu Takeuchi5, 1NDORMS, University of Oxford, Oxford, United Kingdom, 2University of Texas Southwestern Medical Center, Dallas, TX, 3Rheumatology, Rheumatology Care Center, Birmingham, AL, 4Eli Lilly and Company, Indianapolis, IN, 5Keio University School of Medicine, Tokyo, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Pain – Basic and Clinical Aspects Oral
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:
Assessment of pain improvement during treatment for rheumatoid arthritis (RA) may help frame patient expectations and may be useful to clinical decision-making and discussions between providers and their patients. Baricitinib (BARI) 4 mg once daily was associated with significant clinical improvements in the Phase 3 study, RA-BEAM, in active RA patients with an inadequate response to methotrexate (MTX) compared with adalimumab (ADA) and placebo (PBO). The objective of this post hoc analysis was to evaluate the time and likelihood of achieving different levels of pain control with BARI relative to ADA and PBO.

Methods:
1305 patients on stable background MTX were randomized 3:3:2 to PBO, BARI 4 mg, or ADA 40 mg. The patient’s assessment of pain was assessed with a 0-100 mm visual analog scale (VAS) at each study visit. The likelihood of achieving ≥30%, ≥50%, and ≥70% pain VAS improvement through Week 24 and the median time when 50% of patients achieved these pain improvement thresholds were assessed with Cox proportional hazards models and the cumulative incidence estimate. Pain improvement was analyzed by baseline pain VAS subgroup (≤median, >median). Analyses were not adjusted for multiplicity.

Results:

BARI-treated patients were more likely to achieve at least 30%, 50%, and 70% pain improvement than PBO and ADA with HR of 1.7, 1.9, and 2.5, respectively (p<0.001) compared to PBO, and 1.1 (p=0.145), 1.2 (p=0.032), and 1.3 (p=0.003) compared to ADA. The median time for 50% of patients to achieve at least 30%, 50%, and 70% pain improvement, respectively, was 1.9, 4.0, and 12.4 weeks for BARI, 2.0, 7.9, and 20.0 weeks for ADA, and 4.6, 14.0, and >24 weeks for PBO (Table). The cumulative incidence for achieving 50% pain improvement is presented (Figure). The effects of BARI on pain improvement were consistent regardless of baseline pain severity. In contrast, pain improvement for patients treated with ADA or PBO varied by baseline pain severity (Table).

Conclusion:

BARI demonstrated faster and greater pain improvement than ADA or PBO through Week 24. In addition, unlike ADA and PBO, BARI showed consistent improvement regardless of baseline pain severity.

References:


2Gooley TA Statist Med 1999

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/rapid-and-sustained-pain-improvement-in-rheumatoid-arthritis-patients-treated-with-baricitinib-compared-to-adalimumab-or-placebo

Abstract Number: 856

Trends and Predictors of Chronic Opioid Use in Individuals with RA

Yvonne C. Lee1, Joel Kremer2, Hongshu Guan3, Jeffrey D Greenberg4 and Daniel H. Solomon5, 1Rheumatology Immunology & Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 2The Center for Rheumatology, Albany Medical College, Albany, NY, 3Rheumatology, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 4NYU School of Medicine, New York, NY, 5Brigham and Women's Hospital and Harvard Medical School, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Pain – Basic and Clinical Aspects Oral
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM
**Background/Purpose**: The opioid epidemic is a major public health concern, requiring urgent action. However, little is known about chronic opioid use among individuals with RA. We examined trends in chronic opioid use in RA patients from 2002-2015 and identified clinical factors predicting chronic opioid use.

**Methods**: RA patients were identified from a large multicenter US registry. Opioid use was ascertained from surveys obtained at routine clinical visits, as often as once every 3 months. The primary outcome was chronic opioid use, defined as any opioid use reported during at least 2 consecutive study visits. Cox Proportional Hazards regression models were performed to identify associations between patient characteristics and incident chronic opioid use. Subgroup analyses were performed among RA patients with no pain at study entry and RA patients with at least 1 documentation of opioid use from 2002-2015.

**Results**: Among 31,993 individuals with data on opioid use from at least 2 visits, chronic opioid use increased from 7.4% in 2002 to 15.5% in 2014 and decreased to 11.3% in 2015 (Figure). Among the 25,054 individuals who were not taking opioids at baseline, longer disease duration, higher RA disease activity, worse disability, more pain, biologic DMARD use, corticosteroid use and antidepressant use were significantly associated with increased risk of chronic opioid use (Table). Asian race and a greater number of past DMARDs were associated with lower risk of chronic opioid use. Similar results were observed in a sensitivity analysis with chronic opioid use defined as at least 3 consecutive reports of opioid use. In a subgroup analysis of RA patients with no pain at baseline (N = 6,580), being female (HR 1.37, 95% CI 1.07-1.75) and being on both Medicare and Medicaid (HR 2.03, 95% CI 1.00-4.12) were associated with chronic opioid use, whereas RA disease duration and disability were no longer associated with chronic opioid use. In a subgroup analysis of RA patients with at least 1 report of opioid use during the study period (N = 6,758), the risk of progression to chronic opioid use was most strongly predicted by high disease activity (HR 2.56, 95% CI 2.02-3.24) and high pain (HR 1.36, 95% CI 1.14-1.64).

**Conclusion**: Among individuals with RA, chronic opioid use doubled from 2002 to 2014 but did not increase in 2015. Worse RA disease characteristics predicted increased risk of chronic opioid use, whereas a higher number of past DMARDs was associated with a lower risk of chronic opioid use. Future studies are needed to determine whether aggressive treatment of inflammatory disease leads to a decrease in chronic opioid use.
Table. Multivariable, time-updated, adjusted hazards ratios for the association between patient characteristics and incident chronic opioid use among individuals with RA, from 2002-2015 (N = 25,054).

<table>
<thead>
<tr>
<th>Patient Characteristic</th>
<th>Multivariable Adjusted Hazards Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.00 (0.99-1.00)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>Ref</td>
</tr>
<tr>
<td>Female</td>
<td>1.04 (0.96-1.13)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>Ref</td>
</tr>
<tr>
<td>Hispanic</td>
<td>0.97 (0.79-1.18)</td>
</tr>
<tr>
<td>Black</td>
<td>1.01 (0.84-1.21)</td>
</tr>
<tr>
<td>Asian</td>
<td>0.46 (0.33-0.66)</td>
</tr>
<tr>
<td>Other</td>
<td>0.99 (0.79-1.25)</td>
</tr>
<tr>
<td>Insurance</td>
<td></td>
</tr>
<tr>
<td>Private</td>
<td>Ref</td>
</tr>
<tr>
<td>Medicaid</td>
<td>1.16 (0.98-1.37)</td>
</tr>
<tr>
<td>Medicare</td>
<td>1.14 (1.00-1.30)</td>
</tr>
<tr>
<td>Both Medicaid and Medicare</td>
<td>1.14 (0.87-1.49)</td>
</tr>
<tr>
<td>None</td>
<td>0.92 (0.65-1.29)</td>
</tr>
<tr>
<td>RA duration</td>
<td></td>
</tr>
<tr>
<td>&lt;5 years</td>
<td>Ref</td>
</tr>
<tr>
<td>5-10 years</td>
<td>0.98 (0.88-1.10)</td>
</tr>
<tr>
<td>&gt;10 years</td>
<td>1.15 (1.04-1.28)</td>
</tr>
<tr>
<td>CDAI category</td>
<td></td>
</tr>
<tr>
<td>Remission (less than or equal to 2.8)</td>
<td>Ref</td>
</tr>
<tr>
<td>Low (&gt;2.8-10)</td>
<td>1.75 (1.51-2.02)</td>
</tr>
<tr>
<td>Moderate (&gt;10-22)</td>
<td>2.73 (2.30-3.24)</td>
</tr>
<tr>
<td>High (&gt;22)</td>
<td>3.79 (3.13-4.59)</td>
</tr>
<tr>
<td>HAQ Disability Index</td>
<td></td>
</tr>
<tr>
<td>Less than or equal to 0.5</td>
<td>Ref</td>
</tr>
<tr>
<td>0.5-1.0</td>
<td>1.27 (1.15-1.40)</td>
</tr>
<tr>
<td>&gt; 1.0</td>
<td>1.18 (1.03-1.36)</td>
</tr>
<tr>
<td>Pain</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>Ref</td>
</tr>
<tr>
<td>Low</td>
<td>1.73 (1.50-1.99)</td>
</tr>
<tr>
<td>Moderate</td>
<td>2.10 (1.76-2.51)</td>
</tr>
<tr>
<td>High</td>
<td>2.40 (2.01-2.88)</td>
</tr>
<tr>
<td>Number of previous DMARDs used</td>
<td>0.85 (0.82-0.88)</td>
</tr>
<tr>
<td>Biologic DMARD use</td>
<td>1.45 (1.32-1.59)</td>
</tr>
<tr>
<td>Corticosteroid use</td>
<td>1.28 (1.17-1.39)</td>
</tr>
<tr>
<td>Antidepressant use</td>
<td>1.66 (1.53-1.81)</td>
</tr>
</tbody>
</table>

Disclosure: Y. C. Lee, Express Scripts, 1,Pfizer Inc, 2; J. Kremer, Abbvie, Amgen, BMS, Genentech, GSK, Eli Lilly and Company, Novartis,Pfizer, 5,Abbvie, Genentech, Eli Lilly and Company, Novartis, Pfizer, 2,Genentech and Biogen IDEC Inc., 8,Corrona, 1,Corrona, 3; H. Guan, None; J. D. Greenberg, corrona, LLC, 1,Corrona, LLC, 3,Genentech, Janssen, Novartis, Pfizer, Eli Lilly, 5; D. H. Solomon, Amgen, 2,Lilly, 2,AstraZeneca, 2,Abbvie, 2,Genentech, 2,Pfizer, 2.
Relation of Pain Sensitization to Low Physical Function: The Multicenter Osteoarthritis Study

Joshua Stefanik1,2, Daniel White3, Carrie Brown4, Laura Frey-Law5, Michael Nevitt6, Cora E. Lewis7 and Tuhina Neogi2,
1Physical Therapy, Northeastern University, Boston, MA, 2Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA, 3Department of Physical Therapy, University of Delaware, Newark, DE, 4Boston University School of Public Health, Boston, MA, 5University of Iowa, Iowa City, IA, 6Department of Epidemiology & Biostatistics, University of California San Francisco School of Medicine, San Francisco, CA, 7University of Alabama Birmingham, Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Pain – Basic and Clinical Aspects Oral
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Peripheral and central sensitization (alterations in pain signaling) are related to heightened pain severity and can be present in knee osteoarthritis (OA). Sensory input plays an integral role in motor function, and the pain adaptation theory recognizes the impact of pain on motor function. However, it is unknown if sensitization independently contributes to alterations in physical function beyond the effect of pain severity. We examined the relation of sensitization to low physical function in older individuals with or at risk for knee OA independent of pain severity.

Methods: The MOST Study is a NIH-funded cohort of persons with or at risk of knee OA. Two sensitization measures were assessed: 1) Temporal summation (a marker of central sensitization) was defined as being present when, after touching the skin of the right wrist with a 60g monofilament repeatedly at 1Hz for 30s, the participant reported new or increased pain at the wrist. 2) Pressure pain threshold (PPT) is a marker of peripheral +/- central sensitization at sites of disease/inflammation, or of central sensitization when assessed at an otherwise normal area. PPT was assessed with an algometer (1 centimeter (cm)² tip) as the point at which the participants indicated that the pressure first changed to slight pain. Three trials (0.5 kilograms (kg)/s) at each anatomic site were averaged. PPT was assessed at the right wrist and index patella (i.e., knee with the worst knee pain). PPT was divided into sex-specific tertiles. Low physical function was assessed by gait speed and WOMAC function (0-68 scale). Gait speed was calculated from the 20-meter walk test (meters (m)/second(s)). Gait speed and WOMAC function were dichotomized at 1.0 m/s and >28/68, respectively, which are standard definitions of low physical function. Logistic regression models were used to determine the relation of temporal summation and PPT to physical function while adjusting for age, sex, BMI, clinic site, depressive symptoms, catastrophizing, and knee pain severity.

Results:
2171 participants were included: mean±SD age and BMI were 67.9±7.8 and 30.7±5.9, respectively; 60% were female. Temporal summation was present at the wrist in 42.2% of participants. The mean PPT at the wrist and index patella were 3.4±1.5 and 5.0±2.2 kg/cm², respectively. 53.3% and 10.9% of participants had low physical function as defined by slow walking and WOMAC, respectively. In general, participants with temporal summation at the wrist and low PPTs at the wrist and index patella were more likely to have slow walking (Table). Participants with low PPTs at the patella were more likely to have low WOMAC physical function.

Conclusion: Measures of pain sensitization are related to physical function. The relation is independent of knee pain severity and provides support that peripheral and central nervous system alterations may not only affect pain severity, but
also physical function.

<table>
<thead>
<tr>
<th>Sensitization Measure</th>
<th>Adjusted* OR (95% CI) for Gait Speed (Outcome)</th>
<th>WOMAC Function &gt;28</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of Temporal Summation: Wrist</td>
<td>1.5 (1.2, 2.0)</td>
<td>1.1 (0.8, 1.6)</td>
</tr>
<tr>
<td>PPT Wrist (kg/cm²):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lowest Tertile</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle Tertile</td>
<td>1.4 (1.0-2.0)</td>
<td>1.4 (0.9-2.1)</td>
</tr>
<tr>
<td>Highest Tertile</td>
<td>1.3 (0.9-1.8) 1.0 (ref)</td>
<td>1.3 (0.8-2.0) 1.0 (ref)</td>
</tr>
<tr>
<td>PPT Index Patella (kg/cm²):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lowest Tertile</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle Tertile</td>
<td>1.6 (1.1-2.3)</td>
<td>1.8 (1.1-2.8)</td>
</tr>
<tr>
<td>Highest Tertile</td>
<td>1.1 (0.8-1.7) 1.0 (ref)</td>
<td>1.3 (0.8-2.1) 1.0 (ref)</td>
</tr>
</tbody>
</table>

*Adjusted for age, sex, BMI, clinic site, depressive symptoms, catastrophizing, and knee pain severity

Disclosure: J. Stefanik, None; D. White, None; C. Brown, None; L. Frey-Law, None; M. Nevitt, None; C. E. Lewis, None; T. Neogi, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/relation-of-pain-sensitization-to-low-physical-function-the-multicenter-osteoarthritis-study

Abstract Number: 858

Identification of Clinically Relevant Pain Profiles in Individuals with Active RA

Alyssa Wohlfahrt¹, Zhi Zhang¹, Bing Lu², Clifton O. Bingham III³, Marcy B. Bolster⁴, Wendy Marder⁵, Larry W. Moreland⁶, Kristine Phillips⁷, Tuhina Neogi⁸ and Yvonne C. Lee⁹, ¹Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA, ²Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ³Rheumatology, Johns Hopkins University, Baltimore, MD, ⁴Division of Rheumatology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, ⁵Internal Medicine-Rheumatology, University of Michigan, Ann Arbor, MI, ⁶Rheumatology & Clinical Immunology, University of Pittsburgh, Pittsburgh, PA, ⁷Rheumatology, Vanderbilt University Medical Center, Nashville, TN, ⁸Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA, ⁹Rheumatology Immunology & Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Pain – Basic and Clinical Aspects Oral
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM
**Background/Purpose:** Despite DMARD treatment, many RA patients continue to suffer from pain. Defining distinct pain phenotypes may advance the use of therapies targeted at specific pain mechanisms. This study identified pain profiles among RA patients with active disease, with the goal of informing treatment decisions to improve pain outcomes.

**Methods:** 146 RA patients with active disease were identified from 5 academic medical centers. Trained assessors performed joint and tender point counts. Patient-reported measures of pain, fatigue, sleep and psychological distress were assessed. Quantitative sensory testing was done to evaluate pain sensitivity (pressure pain thresholds), central pain sensitization (temporal summation) and descending pain inhibition (conditioned pain modulation). A principle components analysis (PCA) was performed to identify variables explaining the most variance. These variables were used in a hierarchical cluster analysis to identify pain phenotypes. General linear and logistic regression models were used to identify differences in clinical characteristics.

**Results:** Based on PCA, 20 variables were included in the cluster analysis, which identified 3 pain profiles (Figure): 1) low pain and temporal summation with low psychological distress, fatigue, and sleep problems (N = 48, 32.9%); 2) moderate pain and high temporal summation with moderate psychological distress, fatigue, and sleep problems (N = 44, 30.1%) and 3) moderate pain and temporal summation with high psychological distress, fatigue and sleep problems (N = 54, 37.0%). Catastrophizing and patient global differed across groups, with the low pain group (cluster 1) having the lowest levels of both (Table). NSAID use differed across groups, with the highest frequency of use in the high temporal summation group (cluster 2). Disease duration, CRP and swollen joint count did not differ across groups.

**Conclusion:** Among RA patients with active disease, 3 pain phenotypes emerged that may inform treatment decisions. Patients with moderate pain and high temporal summation (cluster 2) may benefit from strategies to reduce central sensitization, whereas patients with moderate pain and high psychological distress/fatigue/sleep problems (cluster 3) may benefit from treatments to improve mood and sleep. The finding that NSAID use was highest in the group with high temporal summation is interesting, given a study showing that COX-2 inhibition decreases temporal summation and improves pain (Arendt-Nielsen 2016). Future studies are needed to determine the role of pain phenotypes in directing pain management.
Identifying Pain Susceptibility Phenotypes in Those Free of Knee Pain with or at Risk for Knee Osteoarthritis and Their Relation to Developing Knee Pain

Lisa Carlesso1, Neil Segal2, Laura Frey-Law3, Yuqing Zhang4, Na Lu5, Cora E. Lewis6, Michael C. Nevitt7 and Tuhina Neogi5, 1School of Rehabilitation, Université de Montréal, Montreal, QC, Canada, 2University of Kansas, Shawnee, KS, 3UIowa, Iowa City, IA, 4Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA, 5Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA, 6University of Alabama Birmingham, Birmingham, AL, 7Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Pain – Basic and Clinical Aspects Oral
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: It is well recognized that factors beyond structural features contribute to the pain experience in people with knee osteoarthritis (OA). Independent of structural pathology, characteristics such as psychological factors, sleep, and sensitization may increase the risk of developing pain. We examined the relation of pain susceptibility phenotypes to incident pain in people free of pain, but with or at risk of knee OA using indicators of psychological and neurophysiological aspects of pain.

Methods: We used data from the Multicenter Osteoarthritis (MOST) Study, a NIH-funded longitudinal prospective cohort of 3026 older adults with or at risk of knee OA. We identified subjects who were free of frequent knee pain (FKP) (pain on most days during the past month) at both the clinic visit and a telephone screen ~1 month before the clinic visit. We excluded subjects who had a total knee replacement or possible peripheral neuropathy. We used latent class analysis to determine groupings (phenotypes) of baseline psychological and neurophysiological characteristics likely to influence pain (widespread pain, sleep, pain catastrophizing, positive affect, depressive symptoms and quantitative sensory testing (pressure pain thresholds (PPT), temporal summation (TS))). We assessed the relation of these phenotypes to incident consistent FKP (CFKP) (i.e., pain at both the clinic visit and telephone screen ~30 days prior) 2 years later using logistic regression, and examined predictors of class membership (age, sex, education, race, BMI, comorbidities, radiographic knee OA).
Results: 852 participants met inclusion criteria (mean age; 67.1; mean BMI 29.5 kg/m^2, 55% women); 87 (11%) developed incident CFKP over 2 years. We identified 3 classes (phenotypes) that we labeled as “low”, “moderate” and “high” risk phenotypes based on prevalence of pain risk factors. PPT was a distinguishing characteristic of the high-risk group, while psychological factors were not (Figure 1A). Those in the moderate and low risk groups had significantly lower incidence of CFKP over 2 years OR (95% CI) 0.53 (0.21, 0.86) and OR 0.62 (0.27, 0.96) respectively, compared with the high-risk group. Women were more likely to be in the moderate and high risk groups compared to the low, while those with older age were more likely to be in the high-risk group only (Figure 1B).

Conclusion: In this cohort free of frequent knee pain with or at risk of knee OA, 3 pain susceptibility phenotypes were identified based on psychological and neurophysiological indicators that were associated with differential risk of developing knee pain, irrespective of structural disease. The high-risk pain susceptibility group was predominated by neurophysiological evidence of sensitization. Women were more likely to have higher risk pain susceptibility phenotypes suggesting that sex specific pain phenotypes may be an avenue for future study.

Disclosure: L. Carlesso, None; N. Segal, None; L. Frey-Law, None; Y. Zhang, None; N. Lu, None; C. E. Lewis, None; M. C. Nevitt, None; T. Neogi, None.


Abstract Number: 860

Effective Treatment of Persistent Arthritis Pain Requires Co-Modulation of TNF and Type I Interferon

Sarah Woller¹, Tony Yaksh² and Maripat Corr³, ¹Anesthesiology, UCSD, La Jolla, CA, ²Anesthesiology 0818, UCSD, La Jolla, CA, ³Division of Rheumatology, Allergy, and Immunology, UCSD, La Jolla, CA

First publication: September 18, 2017
**Background/Purpose:** Pain persisting beyond the resolution or control of clinical signs of rheumatoid arthritis (RA) decreases quality of life for millions of people. Unfortunately, this pain does not respond well to typical analgesics, and, while tumor necrosis factor (TNF) is a pivotal cytokine in RA, the persistence of pain in the face of anti-TNF treatment indicates that control of this cytokine alone is insufficient to treat this pain. We have shown that in the K/BxN serum transfer model male C57Bl/6 (WT) mice develop transient inflammation and a corresponding tactile allodynia (TA), which persists beyond the resolution of inflammation. Here, we aimed to understand the role of TLR4 associated spinal cytokines, specifically TNF and interferon (IFN) β in the development of this persistent, post-inflammatory pain state, which is mediated through Toll-like receptor (TLR) 4 signaling.

**Methods:** K/BxN sera (100μl) was injected into male WT, Tnf<sup>−/−</sup>, Tlr4<sup>−/−</sup>, and Ifnar1<sup>−/−</sup> mice on Days 0 and 2. Ankle width and withdrawal thresholds were examined over 28 days. Separate groups of mice were injected intrathecally (IT) with anti-TNF antibody or with IFNβ.

**Results:** In male mice, there is a pivotal time (~2 weeks) beyond which administration of a TNF inhibitor or a TLR4 antagonist can no longer abrogate the neuropathic pain state in this animal model. Hence, we examined spinal cords from arthritic mice on day 10 for differences in gene expression of key inflammatory cytokines associated with allodynia in male Tlr4<sup>−/−</sup> and WT mice, as the WT male mice develop persistent pain, but the Tlr4<sup>−/−</sup> do not. We found IFNβ transcripts decreased in WT mice (average fold change (AFC): 0.41) and were increased in Tlr4<sup>−/−</sup> mice (AFC: 18.84). In contrast, TNF transcripts increased in WT mice (AFC 1.33), and remained unchanged in Tlr4<sup>−/−</sup> mice (AFC 0.96). The levels of mRNA expression for IL-1β and IL-6 were equivalent between the two strains.

To further understand the roles of TNF and IFNβ in K/BxN-induced arthritis and pain, we assessed male Ifnar1<sup>−/−</sup> and Tnf<sup>−/−</sup> mice. The inflammatory phase TA was attenuated in Ifnar1<sup>−/−</sup> mice (1.18g relative to 0.5g in WT males, ρ <0.05); however, these mice developed persistent TA while the late phase TA was reduced in Tnf<sup>−/−</sup> mice (1.29g relative to 0.74g in WT males, ρ <0.05), suggesting neither TNF nor IFNβ is completely responsible for the persistent pain state. Next, male WT mice were injected IT with anti-TNF antibody or with IFNβ. Neither pharmacologic treatment alone affected TA (ρ >0.05). However, when Tnf<sup>−/−</sup> male mice were given IT IFNβ, we saw a persistent reversal in TA. Finally, WT male mice were treated with the combination of both anti-TNF and IFNβ and showed a reversal in their persistent pain state, with a day 28 threshold of 1.4g relative to 0.27g in vehicle treated controls (ρ <0.05).

**Conclusion:** These results suggest that the pharmacological co-modulation of TNF and IFNβ is necessary for the treatment of persistent arthritis-related pain.

**Disclosure:** S. Woller, None; T. Yaksh, None; M. Corr, NIH, 2.


**Abstract Number:** 861

**CD11b+Gr1dim tolerogenic Dendritic Cell-like Cells Suppress the Progression of Interstitial Lung Disease in SKG Mice**

Sho Sendo<sup>1</sup>, Jun Saegusa<sup>1</sup>, Hirotaka Yamada<sup>2</sup>, Yoshihide Ichise<sup>2</sup>, Ikuko Naka<sup>3</sup>, Yo Ueda<sup>2</sup>, Takaichi Okano<sup>2</sup>, Soshi Takahashi<sup>4</sup>, Kengo Akashi<sup>5</sup>, Akira Onishi<sup>6</sup> and Akio Morinobu<sup>4</sup>, 1Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, Kobe, Japan, 2Department of Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, Kobe, Japan, 3Department of Clinical Pathology and Immunology, Kobe University Graduate School of Medicine, Kobe, Japan, 4Department of Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, Kobe, Japan, 5Department of Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, Kobe, Japan, 6Department for Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, Kobe, Japan

**First publication:** September 18, 2017
CD11b+Gr1\textsuperscript{dim} tolerogenic Dendritic Cell-like Cells Suppress the Progression of Interstitial Lung Disease in SKG Mice

**Background/Purpose:** SKG mice develop interstitial lung disease (ILD) resembling rheumatoid arthritis-associated ILD (RA-ILD) in human. We identified a new cell population, CD11b\textsuperscript{+}Gr1\textsuperscript{dim} cells, in the lung of zymosan A (ZyA)-treated SKG mice. The purpose of this study is to elucidate the origin and the function of CD11b\textsuperscript{+}Gr1\textsuperscript{dim} cells, in the pathogenesis of ILD in SKG mice.

**Methods:** We assessed the severity of ZyA-induced ILD in SKG mice histologically, and examined lung-infiltrating cells by flow cytometry. Total lung cells and isolated monocytic myeloid-derived suppressor cells (M-MDSCs) were cultured in vitro with GM-CSF (and IL-4). The proliferation of CSFE-labeled naïve T cells co-cultured with isolated CD11b\textsuperscript{+}Gr1\textsuperscript{dim} cells and MDSCs was evaluated by flow cytometry. In vitro-generated CD11b\textsuperscript{+}Gr1\textsuperscript{dim} cells were transferred to ZyA-treated SKG mice.

**Results:** Histological analysis revealed that ZyA-treated mice developed various severity of ILD; HS1: 25%, HS2: 50% and HS3: 25%. MDSCs, Th17 cells, and group 1 and 3 innate lymphoid cells (ILC1s and ILC3s) were increased in the lungs; the proportion of these cells varied with ILD severity. In this process, we found that a unique cell population, CD11b\textsuperscript{+}Gr1\textsuperscript{dim} cells, was expanded in the lungs with diffusely affected area greater than 60%. About half of the CD11b\textsuperscript{+}Gr1\textsuperscript{dim} cells expressed CD11c, and the cells were morphologically DC-like. The CD11b\textsuperscript{+}Gr1\textsuperscript{dim} cells were induced from M-MDSCs with GM-CSF in vitro and were considered tolerogenic because they suppressed T-cell proliferation and expressed high levels of PD-L1. The regulatory function of CD11b\textsuperscript{+}Gr1\textsuperscript{dim} cells was partially canceled by addition of Anti-TGF-beta neutralizing antibody when generating them. The CD11b\textsuperscript{+}Gr1\textsuperscript{dim} cells have never described previously and termed CD11b\textsuperscript{+}Gr1\textsuperscript{dim} tolerogenic dendritic cell-like cells (CD11b\textsuperscript{+}Gr1\textsuperscript{dim} toDC-LCs). Furthermore, adoptive transfer of CD11b\textsuperscript{+}Gr1\textsuperscript{dim} toDC-LCs significantly suppressed the progression of ILD in SKG mice.

**Conclusion:** CD11b\textsuperscript{+}Gr1\textsuperscript{dim} toDC-LCs were differentiated from M-MDSCs, and could suppress the progression of ILD in SKG mice.

**Disclosure:** S. Sendo, None; J. Saegusa, None; H. Yamada, None; Y. Ichise, None; I. Naka, None; Y. Ueda, None; T. Okano, None; S. Takahashi, None; K. Akashi, None; A. Onishi, None; A. Morinobu, None.
Abstract Number: 862

iNKT Mediated Immunoregulatory Feedback Control Development of Autoimmune Arthritis in Mice

Mattias N. D. Svensson1,2, Meng Zhao3, Mitchell Kronenberg3 and Nunzio Bottini1,2, 1Department of Medicine, University of California San Diego, La Jolla, CA, 2Cellular Biology, La Jolla Institute for Allergy and Immunology, La Jolla, CA, 3Developmental Immunology, La Jolla Institute for Allergy and Immunology, La Jolla, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Animal Models
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Invariant Natural Killer T cells (iNKT) express an invariant T cell receptor (TCR) alpha chain and recognize lipid antigens – such as alpha-GalCer (aGC), presented by CD1d. iNKT cells differentiate in the thymus into one of three distinct populations: iNKT1, iNKT2 and iNKT17, which are analogous to Th1, Th2 and Th17. In arthritis iNKT cells have been found to either promote or suppress disease, an effect that could be attributed to involvement of distinct populations of iNKT cells. However, the differentiation and function of iNKT subsets during arthritis have not been explored. We use the Zap70-mutant BALB/c SKG mouse, which develops autoimmune arthritis due to defective thymic CD4 T cell selection, to explore iNKT cell subsets during arthritis development.

Methods: Arthritis induced by mannan injection was evaluated in NKT deficient (CD1d−/−) and NKT sufficient (CD1d+/+) SKG mice. Also, iNKT cells were depleted in SKG mice by injection of an NKT cell-depleting antibody two days before arthritis onset. CD4 SKG T cells were adoptively transferred into RAG2-KO mice, alone or in combination with thymic iNKT cells. aGC was injected once on the day of arthritis onset in WT and IFNy−/− SKG mice. Flow cytometry was used to evaluate iNKT cells in arthritic joints and the development of iNKT cells in the thymus of SKG and WT BALB/c mice.

Results: In SKG mice disease severity correlated with a reduced frequency of iNKT1 (r=-0.7914, P=0.0003) and an expansion of iNKT17 (r=0.7938, P=0.0003) in arthritic joints. Furthermore, in SKG mice deficient for iNKT cells, either following genetic deletion of CD1d or by antibody mediated depletion, severity of arthritis was exacerbated (P=0.009 and P=0.03 respectively). In line with these results, adoptive transfer of SKG iNKT cells ameliorated development of arthritis in RAG2-KO mice in co-transfer of CD4 SKG T cell (P=0.01). SKG mice showed an altered thymic development of iNKT subsets, with an increased frequency of iNKT1 (P<0.0001) and reduced frequencies of iNKT2 (P=0.0002) and iNKT17 (P=0.0016). Activation of iNKT cells in vivo using aGC ameliorated arthritis in SKG mice (P=0.05) through an IFNγ dependent mechanism.

Conclusion: We identify an immune regulatory mechanism by which arthritogenic abnormalities of CD4 T cell selection are associated with enhanced development of arthritis-protective iNKT1 and propose that activation of iNKT1 could be a beneficial therapeutic intervention in rheumatoid arthritis.

Disclosure: M. N. D. Svensson, None; M. Zhao, None; M. Kronenberg, None; N. Bottini, None.

Abstract Number: 863
Functionally Distinct Pathogenic Subsets of Fibroblasts Exist within the Inflamed Synovial Membrane and Mediate Specific Aspects of Inflammatory Disease Pathology

Adam Paul Croft¹, Joana Campos², Loriane Savary², Emma Bishop², Jason Turner¹, Guillaume Desanti², Francesca Barone³, Andrew Filer³ and Chris Buckley², ¹Institute of Inflammation and Ageing, University of Birmingham, Birmingham, United Kingdom, ²University of Birmingham, Birmingham, United Kingdom, ³Institute of Inflammation and Ageing (IIA), University of Birmingham, Birmingham, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Animal Models
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Fibroblasts are key effector cells in the persistence of synovial inflammation and joint damage. It is not yet known whether specific subsets of synovial fibroblasts exist, and if so, if they are responsible for the distinct fibroblast mediated features observed in inflammatory arthritis such as invasion of cartilage, bone damage, and persistence of inflammation. Using selective cell deletion strategies and adoptive cellular transfer we demonstrate the presence of functionally distinct subsets of synovial fibroblasts that mediate specific aspects of joint pathology.

Methods: Flow cytometry of digested synovial tissue was performed to determine the expression of fibroblast subsets using a cassette of distinct cell surface makers. Bulk transcriptomics was performed using ultra-low input RNAseq. We utilized a transgenic mouse in which FAP expressing cells were conditionally ablated (FAP-DTR) by administration of diphtheria toxin. Poly-arthritis was performed using either the KRN serum transfer model. Mice were scored for clinical signs of arthritis and MicroCT was performed to evaluate inflammatory bone changes.

Results:

We identified distinct populations of fibroblasts defined by their expression of a cassette of cell surface markers including: podoplanin (PDPN), fibroblast activation protein (FAP), VCAM-1, Cadherin-11 and Thy1.2. Bulk transcriptomic analysis of these targeted subpopulations of cells revealed distinct transcriptional signatures which associated with whether the fibroblast subsets were located in the lining or sub-lining layers of the synovium. Synovial inflammation was associated with activation and selective expansion of these cell subsets with distinct compartments of the synovial membrane. Within the intimal layer of the synovium FAP+ PDPN+ Thy1- fibroblasts highly express MMPs, proteases and were found within pannus tissue invading articular cartilage and bone. In contrast, PDPN+ FAP+ Thy1+, cells rapidly expand within the sub-intimal layer and express pro-inflammatory cytokines, chemokine and survival factors associated with the recruitment and retention of leucocytes.

Utilising their shared expression of FAP we selectively deleted these cells using the FAP-DTR mouse. The deletion of these cells in vivo lead to attenuation of synovial inflammation, inhibited leucocyte accumulation and protected against inflammatory bone damage and remodelling. Consistent with these findings the adoptive transfer of FAP+, PDPN+ Thy1+ cells into arthritic mouse joints lead to a more severe and persistent inflammatory arthritis, whereas injection of FAP+ PDPN+ Thy1- cells did not.

Conclusion: Synovial inflammation is associated with the expansion, activation and differentiation of fibroblasts into pathogenic distinct functional subsets of cells that regulate those specific aspects of inflammatory joint pathology. Direct targeting of specific pathogenic subsets of synovial fibroblasts may provide a novel, non-immunosuppressive approach to the treatment of inflammatory arthritis.

Disclosure: A. P. Croft, None; J. Campos, None; L. Savary, None; E. Bishop, None; J. Turner, None; G. Desanti, None; F. Barone, None; A. Filer, None; C. Buckley, None.
Abstract Number: 864

IL-9-Producing Innate Lymphoid Cells – Keyplayers That Orchestrate Resolution of Chronic Inflammation in Arthritis

Simon Rauber¹, Markus Luber¹, Stefanie Weber¹, Lisa Maul², Alina Soare³, Thomas Wohlfahrt¹, Aline Bozec⁴, Martin Herrmann⁵, Mario Zaiss², Ursula Fearon⁶, Douglas J. Veale⁷, Juan Canete⁸, Oliver Distler⁹, Felice Rivellesi¹⁰, Costantino Pitzalis¹⁰, Georg Schett¹¹, Jörg Distler³ and Andreas Ramming¹², ¹Department of Internal Medicine 3, Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Erlangen, Germany, ²Department of Internal Medicine 3 – Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Erlangen, Germany, ³Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Erlangen, Germany, ⁴Department Clinic of Medicine 3 - Immunology und Rheumatology, University of Erlangen-Nürnberg, Department Clinic of Medicine 3 - Immunology and Rheumatology, Erlangen, Germany, Erlangen, Germany, ⁵Medicine III, Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Osterreich, Germany, ⁶Trinity College Dublin, Department of Molecular Rheumatology, Trinity College Dublin, Dublin, Ireland, ⁷Rheumatology, St. Vincent's University Hospital, Dublin 4, Ireland, ⁸Rheumatology, Hospital Clinic and IDIBAPS, Barcelona, Spain, ⁹Department of Rheumatology, Center of Experimental Rheumatology, University Hospital Zurich, Zurich, Switzerland, ¹⁰Centre for Experimental Medicine and Rheumatology, William Harvey Research Institute, Barts and The London, School of Medicine and Dentistry, Queen Mary University of London, London, United Kingdom, ¹¹Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, Erlangen, Germany., Erlangen, Germany, ¹²Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Erlangen, Germany

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Animal Models
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Transition from acute to chronic inflammation is a key step in the pathogenesis of inflammatory disease but incompletely characterized to date. Similar to the onset phase of inflammation, resolution of inflammation is actively regulated but coordinated by mediators diverse as those that initiate inflammation. Here we identified IL-9-producing Type 2 Innate lymphoid cells (ILC2s) as key regulators in the interaction between innate and adaptive immune responses that orchestrate resolution of inflammation in arthritis.

Methods: Wild-type and Il9 deficient mice were analyzed in three different models of arthritis, namely antigen induced arthritis (AIA), serum induced arthritis (SIA) and monosodium urate crystal (MSU) induced arthritis model, followed by histomorphometric analyses of inflammation, cartilage damage, bone damage, and micro-computed tomographies. For synovial tissue analyses (ILC2, IL-9-expressing cells) samples from untreated active RA patients (N=19) and RA patients in remission receiving treatment with DMARDS (methotrexate N=15, TNF inhibitors: N=5) were analyzed (N=19). In addition, a longitudinal biopsy cohort of 10 early (<12 months disease duration) RA patients receiving synovial biopsies at baseline and 6 months after start of anti-rheumatic therapy was analyzed. For the analysis of circulating ILC2s a cohort of 111 RA patients was analyzed. 63 of these 111 patients received a follow-up assessment of circulating ILC2s 6 to 12 months after baseline assessment.
Results: In the absence of IL-9, ILC2s did not proliferate and arthritis transformed into a chronic disease with persistent joint swelling, chronic synovial inflammation, excessive cartilage destruction and bone loss. Treatment with recombinant IL-9 led to proliferation and activation of ILC2s and promoted ILC2-dependent activation of regulatory T cells (Treg). This cell/cell contact dependent interaction between ILC2s and Tregs via GITR and ICOS resulted in suppression of Th17 driven inflammation and thereby also crucially influenced tissue damage and bone loss. The course of acute inflammation in response to MSU crystals was not affected by IL-9. IL-9-producing ILC2s increase during resolution of RA both in the synovial membrane as well as in the peripheral blood. IL-9+ ILC2 counts were very low in the synovium of active RA patients, in whom IL-9 production was mostly confined to lineage (Lin) positive cells. In contrast, RA patients in remission (DAS28 < 2.6) showed a strong upregulation of Lin- IL-9+ ILC2s. Also the longitudinal analysis of synovial tissue of RA patients showed a switch of the cellular source of IL-9 from Lin+ IL-9+ cells during active disease to Lin- IL-9+ ILC2s after successful treatment with anti-rheumatic drugs over 6 months.

Conclusion: IL-9 driven activation of ILC2s might thus provide a novel therapeutic anchor to induce resolution of chronic inflammatory disease such as arthritis and to restore immune homeostasis. Current cytokine-targeting strategies exclusively suppress the activation pathways rather than fostering resolution of disease, our data provide evidence for a new concept in inflammatory medicine by modifying cytokine pathways relevant for resolution of inflammation.

Disclosure: S. Rauber, None; M. Luber, None; S. Weber, None; L. Maul, None; A. Soare, None; T. Wohlfahrt, None; A. Bozec, None; M. Herrmann, None; M. Zaiss, None; U. Fearon, None; D. J. Veale, AbbVie, Actelion, Bristol-Myers Squibb, Janssen, MSD, Novartis, Pfizer Inc, Roche, UCB, 2,AbbVie, Actelion, Bristol-Myers Squibb, Janssen, MSD, Novartis, Pfizer Inc, Roche, UCB, 5; J. Canete, Gebro, 2; O. Distler, 4 D Science, Actelion, Active Biotech, Bayer, Biogen Idec, Boehringer Ingelheim Pharma, BMS, ChemomAb, EpiPharm, Ergonex, espeRare foundation, GSK, Roche-Genentech, Inventiva, Lilly, medac, MedImmune, Mitsubishi Tanabe, Pharmacies, Pfizer, Sanofi, Seroda, 2; F. Rivellese, None; C. Pitzalis, None; G. Schett, None; J. Distler, 4D Science, 1,Anamar Medical, Active Biotech, Array Biopma, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, GSK, Novartis, Sanofi-Aventis, UCB, 2,Actelion Pharmaceuticals US, Active Biotech, Anamar, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi, UCB, 5; A. Ramming, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/il-9-producing-innate-lymphoid-cells-keyplayers-that-orchestrate-resolution-of-chronic-inflammation-in-arthritis

Abstract Number: 865

Lasp-1 Regulates Cell-Matrix and Cell-Cell Contacts in Arthritic Mouse Models

Denise Beckmann\textsuperscript{1}, Annika Krause\textsuperscript{2}, Uwe Hansen\textsuperscript{1}, Hans Peter Kiener\textsuperscript{3}, Thomas Kamradt\textsuperscript{4}, Catherine S. Chew\textsuperscript{5}, Thomas Pap\textsuperscript{2} and Adelheid Korb-Pap\textsuperscript{1}, \textsuperscript{1}Institute of Musculoskeletal Medicine, University Hospital Muenster, Muenster, Germany, \textsuperscript{2}Institute for Musculoskeletal Medicine, University Hospital Muenster, Muenster, Germany, \textsuperscript{3}Rheumatology, Medical University of Vienna, Vienna, Austria, \textsuperscript{4}Institute of Immunology, University Hospital Jena, Jena, Germany, \textsuperscript{5}Institute of Molecular Medicine and Genetics, Medical College of GA, GA, GA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Animal Models
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: In rheumatoid arthritis (RA) the attachment of synovial fibroblasts (SF) to articular cartilage is an important prerequisite in the process of cartilage degradation. The actin-associated protein Lasp-1 is involved in processes of actin organization and polymerization and focal adhesion turnover, respectively. Therefore, we investigated its role in regulating cell-cell contacts and ECM interactions of synovial fibroblasts in RA.
Methods: Lasp-1 expression was analysed in tissue from RA patients, in hind paws of arthritic mouse models such as the hTNFtg and G6PI mouse model by using WB and immunohistochemistry. Furthermore, Lasp-1−/− mice were interbred with hTNFtg mice and offsprings were analysed for the progression of joint destruction by clinical evaluation and histopathology. Cell spreading as well as migration characteristics of SF derived from wild type (wt), Lasp-1−/−, hTNFtg and Lasp1−/−hTNFtg mice were analysed by live cell imaging and TEM. Cell-matrix interactions as well as cell-cell contacts of isolated SF from all different genotypes were investigated in an electrical cell/substrate impedance sensing assay (ECIS). Additionally, we used an in vitro 3D organ culture system for functional analyses.

Results: Lasp-1 expression levels were significantly increased in human and murine RA tissue as well as in arthritic SF in comparison to healthy controls. Evaluation of Lasp-1−/−hTNFtg mice revealed a milder arthritis score, less cartilage degradation and reduced SF attachment to articular cartilage compared to hTNFtg mice. Results of cell spreading and migration analyses demonstrated alterations in spreading morphology and cell-cell contacts and a significantly reduced migration rate of Lasp-1−/− SF and Lasp-1−/−hTNFtg SF compared to healthy controls. Immunofluorescence showed an unstructured and irregular cytoskeleton in cells with Lasp-1 deletion compared to other cells, confirmed by TEM. ECIS analysis demonstrated increased cell-cell contact formation in Lasp-1−/− compared to wt SF (+22% vs wt SF) and prolonged cell-cell interactions of Lasp-1−/−hTNFtg SF in comparison to hTNFtg SF. Histological sections of the 3D matrices demonstrated that wt SF formed an organised synovial structure comparable with healthy synovial tissue in vivo whereas in matrices with hTNFtg SF, this synovial architecture was not seen. Interestingly, Lasp-1 deletion in the hTNFtg background resulted in an organised cellular lining layer comparable with wt SF matrices.

Conclusion: Lasp-1 regulates the migratory behaviour of synovial fibroblasts and their invasion into cartilage matrix in rheumatoid arthritis by controlling the dynamics of cell-matrix and cell-cell contacts.

Disclosure: D. Beckmann, None; A. Krause, None; U. Hansen, None; H. P. Kiener, None; T. Kamradt, None; C. S. Chew, None; T. Pap, Orthogen, 5; A. Korb-Pap, None.

Abstract Number: 866

Interferon-Alpha Overexpression Triggers an Expansion of Highly Suppressive Regulatory T Lymphocytes Protecting Against Experimental Arthritis

Matthieu Ribon1,2, Katarzyna Matyja2,3, Roxane Hervé2,3, Delphine Lemeiter2,3, François Santinon2,3, Ken Tsuniyama4, Shunichi Shiozawa4, Marie-Christophe Boissier3,5,6, Natacha Bessis2,3 and Patrice Decker2,3, 1Li2P, University of Paris 13, Sorbonne Paris Cité, Bobigny, France, 2UMR 1125, INSERM, Bobigny, France, 3Li2P, University of Paris 13, Sorbonne Paris Cité, Bobigny, France, 4Department of Medicine, Rheumatic Diseases Unit, Kyushu University Beppu Hospital, Beppu, Japan, 5Rheumatology Department, Assistance Publique – Hôpitaux de Paris (AP-HP), Avicenne Hospital, Bobigny, France, 674 rue Marcel Cachin, INSERM, Bobigny, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Animal Models
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Type I interferons (IFN-I) can be both anti- and pro-inflammatory. Among them, IFN-α inhibits normal Th17 differentiation, whereas it is pathogenic in lupus. The role of IFN-I is controversial in rheumatoid arthritis (RA) and experimental models. An IFN-I signature has been reported in RA patients, the signification of which is unclear. In
mice, IFN-I enhance or inhibit arthritis development according to IFN subtype, arthritis model and kinetics. We have evaluated the therapeutic effect of early IFN-α production in collagen-induced arthritis (CIA).

**Methods:** CIA was induced by 2 immunizations with collagen/CFA. Disease development was studied in conditional transgenic mice over-expressing mouse IFN-α1 after cessation of doxycyclin (Dox) administration (Tet-off system). IFN-α1-negative littermates were used as controls. All mice express endogenous IFN-α. All mice received Dox. Arthritis was followed by clinical evaluation. Inflammation/bone destruction were estimated by histology. Pain was followed by stance and Von Frey tests. Plasma cytokines/anti-collagen antibodies were measured by Luminex/ELISA. Leukocytes subpopulations and Th1/Th2/Th17 polarization were analyzed by flow cytometry. Bone marrow cells were cultured with M-CSF/RANKL to evaluate osteoclast differentiation and activity. CD4+CD25+ regulatory T cells (Treg) and CD4+CD25+ effector T cells (Teff) were purified by magnetic sorting. Treg ATPase activity was determined in vitro by a luminescent assay. Treg inhibition of Teff activation was measured by flow cytometry/ELISA in co-cultures. The in vivo therapeutic capacity of purified Treg was estimated by adoptive transfer.

**Results:** Induction of mouse IFN-α1 production before the first or even before the second immunization resulted in CIA protection and lower pain parameters. Anti-collagen antibody production was lower in IFN-α1+ mice. Likewise, IFN-α1+ mice produced less IL-6 but more IL-5. Protection was associated with decreased polarization to Th17 and lower IL-17 secretion capacity and increased polarization to Th2 and IFN-γ-positive Th1 and NK cells. On the contrary, osteoclastogenesis and osteoclast activity were decreased in IFN-α1+ mice. CIA protection in IFN-α1-overexpressing mice was associated with impaired B cells while increased CD86+ PMN in the bone marrow and particularly with an expansion of Treg with a higher CD39/CTLA-4 expression, higher ATPase activity and a higher capacity to inhibit Teff proliferation and cytokine secretion. Most importantly, adoptive transfer of those highly suppressive Treg from CIA IFN-α1+ mice impaired CIA development in recipients in comparison to adoptive transfer of Treg purified from CIA IFN-α1- mice.

**Conclusion:** This is the first study analyzing the impact of IFN-α on CIA development. Early induction of IFN-α1 production and even after the first immunization (i.e., seropositive mice) nearly completely protects against arthritis, highlighting a therapeutic window. Protection is associated with an expansion of more suppressive Treg able to confer protection upon adoptive transfer. This work better defines the role of IFN-α and shows its potent modulatory effect in inflammatory arthritis.

**Disclosure:** M. Ribon, None; K. Matyja, None; R. Hervé, None; D. Lemeiter, None; F. Santinon, None; K. Tsumiyama, None; S. Shiozawa, None; M. C. Boissier, None; N. Bessis, None; P. Decker, None.


**Abstract Number:** 867

**Highly Sensitive Cardiac Troponin-I in Peripheral Blood Predicts Cardiovascular Events in Patients with Rheumatoid Arthritis**

George Karpouzas1, Joel Estis2, Long Pham3, John Todd2 and Matthew Budoff4, 1Division of Rheumatology, Harbor-UCLA Medical Center, Torrance, CA, 2Singulex, Alameda, California, Alameda, CA, 3Rheumatology, Harbor-UCLA Medical Center, Torrance, CA, 4Cardiology, Harbor-UCLA Medical Center, Torrance, CA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Rheumatoid Arthritis – Clinical Aspects I: Cardiac Comorbidities

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 2:30PM-4:00PM
Background/Purpose: Cardiac troponins (cTn) are specific biomarkers of myocardial injury; their measurement with highly-sensitive assays and at subthreshold levels for myocardial infarction (MI) diagnosis, predicts greater risk of both fatal and non-fatal coronary heart disease, heart failure hospitalization, and overall mortality in the general population. We previously reported that highly-sensitive cardiac troponin-I (cTnI>1.5pg/ml), independently predicted occult coronary plaque burden and composition on coronary computed tomography angiography (CTA) in patients with established rheumatoid arthritis (RA). We now explore whether high cTnI predicts cardiovascular events in the same cohort after five years of follow-up.

Methods: One hundred and fifty RA patients without prior diagnosis of cardiovascular disease (CVD) underwent a baseline 64-slice CTA for plaque evaluation between 3/2010-3/2011. Blood was collected for cTnI and other biomarker assessments at the time of the CTA. Subjects were followed for a mean of 60±26 months for incident CV events. Composite rates of ischemic [cardiac death, non-fatal MI, ischemic stroke, peripheral arterial ischemia] as well as non-ischemic [new onset heart failure hospitalization] CV events were the study end-points. Cox regression analysis evaluated the association between high cTnI (>1.5pg/ml) and CV events in raw and several adjusted models; hazards ratios (HR) were calculated as an estimate of CV event risk associated with high cTnI.

Results: Eleven patients suffered incident events (1.54/100PY): 8 were ischemic, including 1 cardiac death, 3 MI, 2 strokes, and 2 peripheral arterial ischemic events requiring emergent revascularizations; the 3 non-ischemic events were new onset, hospitalized, systolic heart failure. cTnI was higher in patients with events compared to those without [2.6 (2.1-4.4) vs. 1.5 (1.0-2.4) pg/ml, p=0.006]. High cTnI predicted risk of incident CV events (Figure 1, p=0.03) independently of demographic and traditional cardiac risk factors (Table 1). Additionally, patients with low cTnI (=<1.5pg/ml) were 82% less likely to suffer a CV event. No events occurred in patients with both low cTnI and low interleukin-6 (=<2.85pg/ml).

Conclusion: Highly-sensitive cTnI may provide prognostic information on long-term CV event risk assessment in RA patients without symptoms or known history of CV disease.

Figure 1. Kaplan-Meier curves in RA patients with high and low cTnI

Table 1. cTnI>1.5pg/ml portends higher risk of cardiovascular events

<table>
<thead>
<tr>
<th>Model</th>
<th>HR (Hazard Ratio)</th>
<th>CI (Confidence Interval)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted</td>
<td>4.7</td>
<td>1.0-21.7</td>
<td>0.048</td>
</tr>
<tr>
<td>Adjusted for age and gender</td>
<td>4.6</td>
<td>1.0-23.1</td>
<td>0.052</td>
</tr>
<tr>
<td>Fully adjusted</td>
<td>5.4</td>
<td>1.1-25.9</td>
<td>0.037</td>
</tr>
<tr>
<td>Adjusted for Framingham D’Agostino score</td>
<td>4.3</td>
<td>0.9-19.7</td>
<td>0.084</td>
</tr>
</tbody>
</table>

*adjusted for age, gender, hypertension, diabetes, dyslipidemia, smoking, BMI, and prednisone use

Disclosure: G. Karpouzas, None; J. Estis, Singulex, 3; L. Pham, None; J. Todd, Singulex, 3; M. Budoff, None.

Baseline Troponin Levels Are Associated with Mortality in a Cohort of Patients with Inflammatory Polyarthritis: Results from the Norfolk Arthritis Register

Sarah Skeoch,1,2 Paul Welsh3, James M Gwinnutt4,5, Jennifer Humphreys4, Jacqueline Chipping6, Alex J Macgregor7, Suzanne M Verstappen4,5, Deborah P.M. Symmons8, Naveed Sattar9 and Ian N. Bruce4,10

1Arthritis Research UK Centre for Epidemiology, Centre for Musculoskeletal and Dermatology Research, Faculty of Medicine, Biology and Health, University of Manchester, Manchester, United Kingdom, 2NIHR Manchester Musculoskeletal Biomedical Research Centre, Central Manchester Hospitals NHS Foundation Trust, Manchester, United Kingdom, 3Institute of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, United Kingdom, 4Arthritis Research UK Centre for Epidemiology, Centre for Musculoskeletal and Dermatology Research, Faculty of Medicine, Biology and Health, University of Manchester, Manchester, United Kingdom, 5Manchester Academic Health Science Centre, Manchester, United Kingdom, 6Norwich Medical School, University of East Anglia, Norwich, United Kingdom, 7Rheumatology, Norfolk and Norwich University Hospital, Norwich, United Kingdom, 8Centre for Musculoskeletal Research, Faculty of Biology, Medicine and Health, Manchester Academic Health Science Centre, The University of Manchester, Arthritis Research UK Centre for Epidemiology, Manchester, United Kingdom, 9Institute of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, United Kingdom, 10NIHR Manchester Musculoskeletal Biomedical Research Centre, Central Manchester University Hospitals NHS Foundation Trust, Manchester, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects I: Cardiac Comorbidities
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Serum troponin is used in clinical practice in the diagnosis of acute myocardial infarction. Recent studies have found that high sensitivity assays can predict cardiovascular (CV) events in the general population. We sought to evaluate the association of troponin and mortality in a cohort of inflammatory polyarthritis (IP) patients.

Methods: Patients recruited between 2000 and 2009 to the Norfolk Arthritis Register, an IP inception cohort (inclusion criteria: 2 or more swollen joint for 4 or more weeks, aged over 16 years) had CV risk factors and IP characteristics recorded at inclusion and blood samples stored. High sensitivity troponin I (Tn-I) was measured on baseline samples, using an automated clinical assay (Abbott, UK). Patients were flagged with the national death register and cause of death classified using ICD10 codes. Patients were followed until death or December 2016. Tn-I was log transformed for analysis. Association with all-cause and CV mortality was tested using Cox regression. Further Cox regression models were performed for CV mortality, with adjustment for CV then IP factors. Subgroup analyses were performed in those with no prior CV events and in those who met ACR/EULAR 2010 criteria for rheumatoid arthritis. The cohort was split into tertiles based on Tn-I levels and Kaplan Meier curves were used to explore differences in CV mortality.

Results: 1022 patients were evaluated. Baseline characteristics are seen in Table 1. 158 deaths occurred during 11,237 person years follow up, 37 were CV deaths. Tn-I levels were associated with all-cause and CV mortality (HR[95%CI]: 1.71[1.46, 2.00] and 2.03[1.58, 2.61] per 1 unit increase in log Tn-I ). Results from adjusted regression models are seen in Table 2. The association with CV mortality remained on adjustment for CV and IP factors. In both subgroup analyses, a significant association between Tn-I and CV mortality was found. Survival curves are seen in Figure 1. Patients in the highest tertile had a 7.7 fold increased risk of CV death compared to those in the lower tertiles (HR [CI 95%]: 7.78[3.56, 17.0]).

Conclusion: Tn-I levels are associated with CV mortality in IP, independent of CV risk factors and the association is not explained by baseline IP disease characteristics or inflammation. The role of Tn-I in CV risk prediction warrants further investigation.
Table 1. Baseline characteristics (median[IQR] or frequency[%]) where*  

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>56 (44, 68)</td>
</tr>
<tr>
<td>Female*</td>
<td>657 (61.4%)</td>
</tr>
<tr>
<td>Symptom duration (months)</td>
<td>10.6 (5.6, 26.5)</td>
</tr>
<tr>
<td>Serositivity (RF and/or ACPA)*</td>
<td>512 (50.5%)</td>
</tr>
<tr>
<td>3 component disease activity index (DAI)</td>
<td>3.73 (2.86, 4.60)</td>
</tr>
<tr>
<td>Health Assessment Questionnaire (HAQ) score</td>
<td>1 (0.375, 1.625)</td>
</tr>
<tr>
<td>ACR/EULAR 2010 criteria for rheumatoid arthritis (RA)*</td>
<td>628 (64.4%)</td>
</tr>
<tr>
<td>Prior CV event*</td>
<td>39 (3.9%)</td>
</tr>
<tr>
<td>Diabetes*</td>
<td>72 (7%)</td>
</tr>
<tr>
<td>Current smoker*</td>
<td>214 (20.8%)</td>
</tr>
<tr>
<td>Hypertension*</td>
<td>186 (17.8%)</td>
</tr>
<tr>
<td>Total cholesterol to HDL ratio (TC:HDL)</td>
<td>4.13 (3.77, 5.38)</td>
</tr>
<tr>
<td>CRP (mg/l)</td>
<td>11.4 (5.5, 21)</td>
</tr>
<tr>
<td>Creatinine (mmol/l)</td>
<td>60.41 (27)</td>
</tr>
<tr>
<td>Troponin I (pg/ml)</td>
<td>0.16 (0.0, 8.7)</td>
</tr>
<tr>
<td>Detectable Tn I levels*</td>
<td>1022 (100%)</td>
</tr>
</tbody>
</table>

Table 2. Association of baseline Tn I levels with subsequent CV mortality (per 1 unit increase in log Tn-I)  

<table>
<thead>
<tr>
<th>Model</th>
<th>Whole cohort (n=1022) HR (95% CI)</th>
<th>Subjects no prior CVD (n=984) HR (95% CI)</th>
<th>RA patients (n=628) HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1: Unadjusted model</td>
<td>2.03 (1.58, 2.61)</td>
<td>1.98 (1.49, 2.63)</td>
<td>1.91 (1.41, 2.60)</td>
</tr>
<tr>
<td>Model 2: Age and gender adjusted</td>
<td>1.74 (1.10, 2.76)</td>
<td>2.37 (1.20, 2.99)</td>
<td>1.74 (1.13, 2.67)</td>
</tr>
<tr>
<td>Model 3: CV risk factors adjusted</td>
<td>1.71 (1.14, 2.59)</td>
<td>1.58 (0.99, 2.56)</td>
<td>1.61 (0.99, 2.53)</td>
</tr>
<tr>
<td>Model 4: IP Factors</td>
<td>1.64 (1.05, 2.49)</td>
<td>1.50 (0.91, 2.43)</td>
<td>1.73 (1.09, 2.72)</td>
</tr>
<tr>
<td>Model 5: Full adjusted</td>
<td>1.61 (1.04, 2.52)</td>
<td>1.59 (0.91, 2.42)</td>
<td>1.61 (0.98, 2.70)</td>
</tr>
</tbody>
</table>

Model 1: age, gender, prior CV events, current smoking, diabetes, hypertension, TC:HDL, creatinine  
Model 2: age and gender adjusted  
Model 3: CV risk factors adjusted  
Model 4: IP factors  
Model 5: full adjusted  
Model 3: age, gender, prior CV events, current smoking, diabetes, hypertension, TC:HDL, creatinine, CRP, 3 component DAS28, HAQ score, serositivity, symptom duration.
Disclosure: S. Skeoch, None; P. Welsh, None; J. M. Gwinnutt, None; J. Humphreys, None; J. Chipping, None; A. J. Macgregor, None; S. M. Verstappen, None; D. P. M. Symmons, None; N. Sattar, Novartis Pharmaceutical Corporation, 5, Roche Pharmaceuticals, 2; I. N. Bruce, None.


Abstract Number: 869

Utility of Carotid Ultrasound Compared to Framingham Risk Score in Predicting Cardiovascular Mortality in Rheumatoid Arthritis

Pankhuri Gupta1, Agustin Escalante2, Daniel F. Battafarano3, Jose Felix Restrepo2 and Inmaculada del Rincon2,
1Rheumatology, University of Texas Health Science Center at San Antonio, SAN ANTONIO, TX, 2Internal Medicine-Rheumatology, University of Texas Health Science Center at San Antonio, San Antonio, TX, 3Medicine, San Antonio Military Medical Center, San Antonio, TX
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects I: Cardiac Comorbidities
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Rheumatoid arthritis (RA) patients have a greater risk of cardiovascular (CV) mortality compared to general population. Traditional CV risk factors may be less accurate in predicting CV mortality in RA patients. We examined the performance of the CV risk factors compared to carotid ultrasound measures of intima-media thickness (IMT) in predicting CV mortality in a RA cohort.

Methods: We recruited patients who met the 1987 ACR criteria for RA from private, public and military rheumatology practices. We measured carotid IMT using high resolution ultrasound. Baseline data on traditional CV risk factors which included systolic blood pressure, diabetes, smoking, high density lipoprotein and total cholesterol were collected. For Framingham CV risk, we used published tables to calculate the predicted 10-year risk of coronary heart disease, based on
the above risk factors. We then divided Framingham risk score into three categories defined as low (<10%), intermediate (10-20%) and high (>20%) risk of CV mortality. We also divided IMT into risk groups of low (IMT < 1.0 mm), intermediate (IMT 1.0-1.5 mm) and high (IMT > 1.5 mm). Patients were followed prospectively until they either died or reached the censoring date of Nov 12, 2015. Certificates were obtained for all deaths, and cause of death classified as CV according to established criteria. We then plotted area receiver operator characteristic (ROC) curves, calculated the area under the curve (AUC) and compared curves using Stata 8.2. We also computed the Net Reclassification Index (NRI).

**Results:** We followed 1,194 RA patients for 7,062 patient years. During this time, 113 CV related deaths occurred, for a CV mortality rate of 1.6 per 100 patient-years. Both the Framingham risk score and the carotid IMT were significantly associated with CV mortality. Patients in the high Framingham risk group had a CV mortality rate of 5.7 per 100 patient years, while those in the lower risk group had a CV mortality rate of 0.8 per 100 patient years. Patients in high IMT category had a CV mortality rate of 5.8 per 100 patient years, while those in the low IMT category had a CV mortality rate of 0.6 per 100 patient years. The ROC area for the Framingham risk score was 0.7695 and while that of carotid IMT was 0.7760 (P=ns). When combined the Framingham risk score with the carotid IMT, the ROC curve area increased to 0.8096 (P < 0.0001, Figure). The carotid IMT added to the Framingham risk score, correctly reclassified 12.6% of the patients (NRI of 0.126, p=0.01).

**Conclusion:** Our findings suggest that carotid ultrasound measures of IMT significantly increase accuracy of CV mortality predictions in RA patients over Framingham risk score.

---

**Disclosure:** P. Gupta, None; A. Escalante, None; D. F. Battafarano, None; J. F. Restrepo, None; I. del Rincon, None.


Abstract Number: 870

**Detection of Left Ventricular Regional Function in Rheumatoid Arthritis Patients without Cardiac Symptoms, As Assessed By Feature Tracking Cardiac Magnetic Resonance Imaging**

Hitomi Kobayashi¹, Yasuyuki Kobayashi², Isamu Yokoe³, Akiyuki Kotoku⁴, Atsuma Nishiwaki⁵, Kaita Sugiyama⁶, Noboru Kitamura⁵ and Masami Takei⁵, ¹Division of Heamatology and Rheumatology, Nihon University School of Medicine, Tokyo, Japan, ²Advanced Biomedical Imaging Informatics, St.Marianna University School of Medicine, Kawasaki, Japan, ³Rheumatology, Kyoundo Hospital, Sasaki Institute, Tokyo, Japan, ⁴Advanced Biomedical Imaging Informatics, St. Marianna University School of Medicine, Kawasaki, Japan, ⁵Division of Hematology and Rheumatology, Nihon University School of Medicine, Tokyo, Japan, ⁶Nihon University School of Medicine, Tokyo, Japan
SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects I: Cardiac Comorbidities
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Cardiac involvements cause of morbidity and mortality globally in rheumatoid arthritis (RA). Myocardial disease is typically clinically silent, only manifesting as myocardial dysfunction after an extended preclinical phase. Feature tracking (FT) cardiac magnetic resonance (CMR) imaging could reliably be used to assess myocardial function in patients with early dysfunction. Left ventricular (LV) global longitudinal peak systolic strain (GLS) is prognostic of adverse cardiovascular outcomes in various patient populations. Global circumferential peak systolic strain (GCS) is a predictor of congestive heart failure. We sought to measure GLS and GCS by using FT-CMR approach in RA patients without cardiac symptoms. Furthermore, we aimed to evaluate the association of GLS and GCS with RA status and severity.

Methods: RA patients and controls without cardiac symptoms were enrolled. RA patients and control subjects with no history and/or clinical findings of systemic and pulmonary hypertension, coronary artery disease, valvular heart disease, atrial fibrillation, diabetes mellitus, and dyslipidemia underwent a non-contrast CMR. Patients with RA were administered non-biologic disease-modifying antirheumatic drugs (nbDMARDs) or biologic DMARDs (bDMARDs). All subjects underwent evaluation of LV regional function, as measured by FT-CMR. GLS and GCS were calculated in the sixteen segments of the whole LV. Group comparisons were made using the Wilcoxon rank sum test, Fisher’s exact test and Steel test where appropriate.

Results: We compared 90 patients with RA (95% women; mean age, 59.5±9.0 years) with 30 healthy controls (100% women; mean age, 55.7±4.5 years). No statistically significant differences were observed in the characteristics between the patients and the healthy controls in cardiovascular risk (CV) factors. GCS was significantly reduced by 31% in the RA group compared to controls (p=0.011). Furthermore, GCS was significantly lower in the nbDMARD than in the bDMARD group (p=0.04). GCS in the RA group was associated with the Simplified Disease Activity Index (SDAI) and levels of matrix metalloprotease 3 (MMP3) (p=0.03, p=0.02, respectively). GCS in the RA group was not associated with CV risk factors or other RA status. GLS in the RA group was significantly reduced by 21% compared to the control group (p=0.05). GCS in the RA group was not associated with CV risk factors or RA status. GLS tended to be lower in the bDMARD group than in the nbDMARD group. GLS tended to be associated with only the SDAI.

Conclusion: This prospective study is among the largest studies of LV regional dysfunction in RA, assessed by FT-CMR, and the only study to explore the multivariable associations of RA characteristics with CMR-assessed GSC and GLS. Subclinical LV regional dysfunction was prominent in the RA patients without cardiac symptoms. We demonstrated the association of GCS with disease activity and MMP3. Longitudinal studies are required to track whether the regional dysfunction we observed predict those destined to develop clinical cardiac involvements.

Disclosure: H. Kobayashi, None; Y. Kobayashi, None; I. Yokoe, None; A. Kotoku, None; A. Nishiwaki, None; K. Sugiyama, None; N. Kitamura, None; M. Takei, None.


Abstract Number: 871

Coronary Microvascular Dysfunction in Rheumatoid Arthritis Compared to Diabetes Mellitus in Patients without Obstructive Coronary Artery Disease

Katherine P. Liao¹, Gabrielle Cremone², Ethan Lam², Zhi Yu¹, Jon M. Hainer², Victoria Morgan³, Courtney Bibbo³ and Marcelo Di Carli³, ¹Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard
Background/Purpose:

Patients with DM have increased coronary microvascular dysfunction (CMD) compared to the general population, leading to higher rates of cardiac death despite normal perfusion scans. While CMD is also thought to play a role in excess cardiovascular (CV) risk in RA, studies are limited. CMD can be detected using coronary flow reserve (CFR), calculated using data from clinically available stress myocardial perfusion PET scans. A pathognomonic sign of CMD is a patient with normal perfusion on a stress test, but impaired CFR. The objective of this study was to compare the frequency of CMD in RA compared to DM among subjects with normal perfusion scans.

Methods:

We performed a retrospective study within a tertiary care hospital registry of patients who received stress myocardial perfusion PET scans as part of routine clinical care between 1/1/2006-1/1/2016. The registry contains data on demographics, CV risk factors, stress test results (normal vs abnormal perfusion), CFR, and adjudicated mortality outcomes. RA patients were identified using a validated algorithm and their medical records were reviewed to confirm prevalent RA at the time of the stress test. We created a DM comparison group, matching to RA by age, gender, race, and year of stress test. Among patients with normal perfusion scans, we compared the distribution of CFR in RA compared to DM, and their mean CFRs using the student’s t-test. We performed chi-square tests to determine whether an impaired CFR (CFR<2) was associated with a higher proportion of all-cause mortality in the RA and DM groups.

Results:

We studied 49 RA and 163 DM patients with normal perfusion scans. The RA patients had a mean age of 64.4 years at the time of their scan, 59.2% white, 51% seropositive. There was no significant difference between the age, gender, hypertension, dyslipidemia, family history of CVD, or smoking status between the RA and DM groups. The mean CFR was 2.02 for RA and DM, with a similar distribution of CFR between the two groups (p=0.98) (Figure). During a median follow-up of 5.4 years, DM with impaired CFR had a significantly higher all-cause mortality than those with normal CFR (p=0.02); a similar trend was observed in RA (p=0.29) (Table).

Conclusion:

In patients undergoing clinically indicated stress tests with normal perfusion scans, we observed a similar distribution of CMD in RA compared to DM. These data suggest that CMD may contribute to the excess CV risk in RA as in DM. CFR, calculated from clinically available stress myocardial perfusion PET scans is a promising imaging biomarker to guide CV risk assessment in RA.
Figure. Distribution of CFR in RA compared to DM among subjects with a normal perfusion scan.

Table. All-cause mortality in RA compared to DM among patients with a normal perfusion scan stratified by coronary flow reserve (CFR)*.

<table>
<thead>
<tr>
<th>Coronary Flow Reserve (CFR)</th>
<th>RA, mortality (%)</th>
<th>DM, mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CFR &gt; 2, normal</td>
<td>13.6</td>
<td>2.9</td>
</tr>
<tr>
<td>CFR &lt; 2, coronary microvascular dysfunction</td>
<td>25.9</td>
<td>13.7</td>
</tr>
<tr>
<td>p-value</td>
<td>0.29</td>
<td>0.02</td>
</tr>
</tbody>
</table>

*Median follow-up time: 5.2 years

Disclosure: K. P. Liao, None; G. Cremone, None; E. Lam, None; Z. Yu, None; J. M. Hainer, None; V. Morgan, None; C. Bibbo, None; M. Di Carli, None.


Abstract Number: 872

Myocardial Abnormalities Improve in RA Patients Treated Actively – a Cardiac MRI Follow-up Study

Riitta Koivuniemi1,2, Mia Holmström3, Antti Kuuliala2, Sari Kivistö3 and Marjatta Leirisalo-Repo1,2, 1Rheumatology, University of Helsinki, Helsinki, Finland, 2Rheumatology, Helsinki University Hospital, Helsinki, Finland, 3Radiology, HUS Medical Imaging Center, University of Helsinki and Helsinki University Hospital, Helsinki, Finland

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects I: Cardiac Comorbidities
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:
Patients with RA are prone to develop myocardial dysfunction, in which chronic inflammation is suggested to play an important role. We have previously shown myocardial abnormalities on cardiac MRI (cMRI) in active RA.

**Methods:**

We collected 2 RA groups: a) patients with untreated active early RA (ERA; n=30) starting conventional synthetic DMARDs (csDMARDs, n=28) or biological DMARDs (bDMARDs, n=2) and b) patients with CRA (n=28) with active RA and were candidates for bDMARDs. Patients with coronary artery disease, diabetes or smoking, and aged >70 years were excluded. Before and after one-year DMARD therapy, the patients (n=58) underwent cMRI. Sex and age-matched 22 FM patients and 35 healthy volunteers underwent cMRI once. cMRI (1.5T or 3T) included analyses of T1 relaxation times, late gadolinium enhancement (LGE), and cardiac functions.

**Results:**

Of ERA patients, 77% used csDMARDs combinations (60% used MTX-SSZ-HCQ combination). Of CRA patients, 86% used anti-TNF therapy. In RA patients, LGE was detected as frequently at baseline as at follow-up (67%). None of FM patients had LGE. Over time, DAS28-crp (mean+SD) declined in ERA (3.7+1.0 vs 2.0+1.0; p<0.001) and in CRA (3.3+1.1 vs 2.6+0.9; p=0.002). At baseline, cardiac function was impaired in RA patients compared with FM patients or healthy volunteers. In RA patients, cardiac function improved over study-period (Table 1). ERA patients experienced improvement in LV TPFR (496+96 mms vs 445+126; p=0.010) and in RV ESV (36+8 ml/m² vs 34+7; p=0.043). In CRA, no significant improvement was observed in cardiac functions. T1 time did not improve in ERA patients, but it improved in nine CRA patients who underwent 3.0 T cMRI (1168+21 ms vs 1125+67; p=0.044).

<table>
<thead>
<tr>
<th>Table1. Cardiac MRI in RA patients (n=58) over study-period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>LV EF %</td>
</tr>
<tr>
<td>LV ESV, ml/m²</td>
</tr>
<tr>
<td>LV EDV, ml/m²</td>
</tr>
<tr>
<td>LV TPRF, ms</td>
</tr>
<tr>
<td>LV mass (mg/m²)</td>
</tr>
<tr>
<td>SV index, ml/m²</td>
</tr>
<tr>
<td>RV EF %</td>
</tr>
<tr>
<td>RV ESV, ml/m²</td>
</tr>
<tr>
<td>RV EDV, ml/m²</td>
</tr>
<tr>
<td>T1 relaxation time (1.5T cMRI)</td>
</tr>
<tr>
<td>T1 relaxation time (3.0T cMRI)</td>
</tr>
</tbody>
</table>

(n=22)

LV= left ventricle, RV=right ventricle, ESV = end-systolic volume, EDV=end-diastolic volume, SV=stroke volume, EF = ejection fraction, TPRF = time to peak filling rate

**Conclusion:**

Patients with active RA show myocardial abnormality on cMRI at baseline: prolonged myocardial T1 relaxation times suggesting diffuse inflammation or fibrosis, LGE indicating local myocardial scars, and impairments of myocardial functions. After 1-year treatment, targeting to remission, myocardial functions improved in early RA patients in parallel with decreasing RA activity. In some CRA patients, T1 time improved. Active rheumatological inflammation seems to be deleterious to the myocardium.

**Disclosure:** R. Koivuniemi, None; M. Holmström, None; A. Kuuliala, None; S. Kivistö, None; M. Leirisalo-Repo, None.
Type I High-IFN Gene Signature in Associated with Higher Essdai at Enrollment and Follow-up in the Prospective Multicenter Assess Cohort of 395 Patients


First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Sjögren's Syndrome I: Clinical Assessment and Trial Outcomes
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:

The type I interferon (IFN) signature is a hallmark of the pathogenesis of primary Sjögren’s syndrome (pSS). However, little is known regarding the clinical utility of assessing this signature in a large cohort of patients prospectively followed up.

Methods:

395 patients with pSS were enrolled in the « ASSessment and Evolution of Systemic complications in primary Sjögren’s syndrome ». Patients have been followed up every year ever since and completed their 5-year follow-up. At baseline, along evaluation of clinical disease activity using international scores, ESSDAI and ESSPRI, serum B-cell activation biomarkers, and whole blood RNA were collected in all enrolled patients. The type I IFN signature was evaluated using the gene expression of IFI27, IFI44 et OAS3 (ref1).
IFN-high signature is associated with an earlier onset of the disease and a higher systemic disease activity at enrollment.

The type I interferon signature was assessed in 366 patients at enrollment. 187 patients (51.1%) had a high IFN signature and 179 had a low IFN signature (49.9%). Patients with a high IFN signature had a significantly earlier onset of symptoms (median age at first symptoms: 44 [34 ;54] years versus 50 [42 ;58] years in patients with low IFN signature, p< 0.0001). ESSDAI was significantly higher in high-IFN patients (4 [2 ;8] versus 2 [1 ;7] in low-IFN patients, p=0.01). ESSPRI tended to be lower in high IFN patients (5.3 [3.3 ; 6.7] vs 5.7 [4.2 ;7.3], p= 0.07. IFN-high patients had significantly more frequently active hematological and biological domains of ESSDAI (71.9% and 72.1%, respectively) than IFN-low patients (47.6 and 34.5%, respectively, p<0.0001 for both comparisons) and tended to have more frequently active lymphadenopathy (80 vs 52.8%, p= 0.1), glandular (66.7 vs 50%, p= 0.2) and muscle (80 vs 53%, p= 0.37) domains of ESSDAI.

IFN high signature is associated with a higher systemic disease activity during the prospective follow-up.

Median ESSDAI during the 5-year follow-up was significantly higher in IFN-high than IFN-low patients (3.6 [2 ;7.33] vs 2.8[1 ;6], p=0.003).

Among the 5 patients who developed a lymphoma during the prospective follow-up, 4 out of 5 (80%) were IFN-high at enrollment (versus 50.6% in patients without lymphoma and 43.8% in patients with a history of lymphoma).

Immunological correlates:

High IFN signature was highly associated with anti-SSA and anti-SSB antibodies (9.4% in anti-SSA/SSB negative patients, 66.7% in anti-SSA-positive only patients and 87.5% in anti-SSA and anti-SSB-positive patients, p< 0.0001).

IFN score was inversely correlated with components of the hematological domain and C3, C4 and was significantly correlated with IgG (r= 0.53, p< 0.0001), kappa and lambda free light chains of 1g (r=0.46 and 0.48, p< 0.0001 for both), RF (r= 0.45,p< 0.0001), beta-2 microglobulin (r= 0.61, p<0.0001), and BAFF(r=0.36, p< 0.0001).

Conclusion:

IFN gene signature is associated with a more active and systemic disease in a 5-year multicenter prospective cohort and with increased serum markers of B-cell activation. This reinforces the rationale to target type I IFN in pSS-related systemic complications.

Ref 1 Petri M, Behrens T et al Lupus 2009

Disclosure: J. E. Gottenberg, BMS, Gilead, Medimmune,Pfizer SanofiAventis, Ucb, 2; P. E. BOST, None; B. Schwikowski, None; R. Seror, None; V. Devauchelle-Pensec, Roche-Chugai provided me tocilizumab for the SEMAPHORER study, 2; P. Dieudé, None; J. J. Dubost, None; A. L. Fauchais, None; V. Goeb, Roche SAS, 5,Chugai Pharma France, 5; E. Hachulla, None; P. Y. Hatron, None; C. Larroche, None; V. Le-Guern, None; J. Morel, None; A. Perdriger, None; E. Dernis, None; S. Rist Bouillon, None; A. Saraux, None; D. Sène, None; J. Sibilia, None; O. Vittecoq, None; G. Nocturne, None; S. TUBIANA, None; P. Ravaud, None; X. Mariette, None;


Abstract Number: 874

Effect of Rituximab on a Salivary Gland Ultrasound Score in Primary Sjögren’s Syndrome: Results of Multicentre Double-Blind Randomised Controlled Trial Sub-Study

Benjamin Fisher, Colin Everett, John Rout, John O'Dwyer, Paul Emery, Costantino Pitzalis, Wan-Fai Ng, Andrew Carr, Colin Pease, Elizabeth Price, Nurhan Sutcliffe, Jimmy Makdissi, Anwar Tappuni, Nagui Gendi, Frances Hall, Sharon Roodoo, Catherine Fernandez, Claire Hulme, Kevin Davies, Christopher J. Edwards, Peter Lanyon, Robert J. Moots, Euthalia Roussou, Linda Sharples, Michele Bombardieri and Simon Bowman,
Background/Purpose: B lymphocytes are important in the pathogenesis of primary Sjögren’s syndrome (PSS), but two phase III trials (TEARS and TRACTISS) of the B cell depleting agent rituximab (RTX) failed to show an effect on their primary endpoints in PSS. It is possible that RTX may lack efficacy in a non-stratified PSS population, but other explanations for these negative results include the choice and timing of primary outcome. In a small single-site salivary gland ultrasound (SGUS) substudy in TEARS, more subjects in the RTX arm demonstrated improvement in parotid gland echostructure. Importantly, SGUS is an operator-dependent technique and we sought to compare the effects of RTX versus placebo on SGUS in PSS, in a multicentre, multiobserver randomised double-blind substudy of TRACTISS.

Methods: All subjects fulfilled 2002 American-European Consensus Group Criteria for PSS, were anti-Ro antibody positive, had symptomatic oral dryness and fatigue, some residual salivary flow, and evidence of systemic disease if disease duration was greater than 10 years. Subjects also consenting to SGUS were randomised to 1000mg RTX or placebo given at weeks 0, 2, 24 and 26, and scanned at baseline and weeks 16 and 48. Sonographers completed a 0-11 total ultrasound score (TUS) comprising domains of echogenicity, homogeneity, glandular definition, glands involved, and size of hypoechoic foci. Baseline-adjusted values of TUS were analysed over time, modelling change from baseline at each time point. For each TUS domain we fitted a repeated measures logistic regression model to model the odds of a response in the RTX arm (defined as a 1 point improvement) as a function of the baseline score, age category, disease duration and time point.

Results: 66 patients (49.6% of the total study population) consented to SGUS, and 52 (39.1%; n=26 RTX and n=26 placebo) completed the baseline and at least one follow-up visit. Estimated baseline-adjusted TUS at week 16 was 6.2 (95% CI 5.4-7.0) for placebo and 5.0 (95% CI 4.4-5.6) for RTX, and at week 48, 6.1 (95% CI 5.5-6.6) and 4.8 (95% CI 4.2-5.4) respectively. Estimated between group differences (RTX-placebo) in baseline adjusted TUS were -1.2 (95% CI -2.1 to -0.3; p=0.0099) and -1.2 (95% CI -2.0 to –0.5; p=0.0023) at weeks 16 and 48. Glandular definition was the only domain to show statistically significant improvement with an OR of 6.8 (95% CI 1.1-43.0; p=0.043) at week 16 and 10.3 (95% CI 1.0-105.9; p=0.050) at week 48. Improvement of ≥1 point in TUS was associated with improvement in oral dryness VAS at week 16 (diff=15.9; CI 1.5 to 30.3; p=0.030) but not week 48.

Conclusion: TUS differed between study arms, favouring RTX. This encourages further research into both B cell depletion therapies in PSS and SGUS as an imaging biomarker in PSS clinical trials.
Serum Autoantibody Profiling of Primary Sjögren’s Syndrome Patients Reveals Novel Biomarkers Associated with the Disease, Disease Activity, and Clinical Response to VAY736

Petra Budde¹, Julie Doucet², Hans-Dieter Zucht¹, Remi Kazma², Paul Maguire², Alexandre Avrameas², Marie-Anne Valentin², Stephen Oliver², Peter Schulz-Knape¹ and Alessandra Vitaliti², ¹Protagen AG, Dortmund, Germany, ²Translational Medicine, Novartis Institutes for Biomedical Research, Basel, Switzerland

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Sjögren’s Syndrome I: Clinical Assessment and Trial Outcomes
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:

Overexpression of B cell activating factor (BAFF) in salivary glands contributes to the pathogenesis of primary Sjögren’s syndrome (pSS) by promoting autoantibody (AAB) production. Treatment of pSS patients with VAY736, an anti-BAFF receptor mAb, appears promising and was associated with a depletion of circulating B cells and a positive therapeutic effect [1]. In addition to the classical anti-SS-A/Ro and anti-SS-B/La, a broader set of AABs may reflect B cell disturbances in pSS and could serve as markers during clinical development of novel pSS therapeutics. In this study, we explored novel AABs in pSS patients and healthy controls (HCs) and we tested their associations with the disease, disease activity, and clinical response to VAY736.

Methods: Reactivity of AABs to 1,596 antigens was measured in serum samples from 27 pSS patients from a placebo-controlled trial at baseline and post-treatment week 12 and from 50 age and gender-matched HCs. Patients were treated at baseline with a single dose of VAY736 at 10 mg/kg (n=12), 3 mg/kg (n=6), or placebo (n=9). First, to identify AABs associated with pSS, 3 different methods compared AAB levels at baseline between pSS patients and HCs: Wilcoxon rank sum test, significance analysis of microarrays, and comparison of the 90th quantiles between groups. Second, to identify AABs associated with pSS activity, Pearson correlation of AABs with EULAR Sjögren’s Syndrome Disease Activity Index, secondary outcomes, and salivary and serum BAFF were tested, using baseline and week 12 levels as well as relative changes. Third, VAY736 treatment-specific changes in AAB levels were investigated using linear mixed-effects models adjusting for dosage, age, and gender effects.

Results:

Of 1,596 antigens, 36 were significantly different between pSS patients and HCs for at least one of the 3 tests, including the known SS-A/Ro and SS-B/La (significant for all 3 tests) as well as novel antigens. SS-A/Ro and SS-B/La AABs were not associated with disease activity or response to treatment. However, 48 AABs were significantly correlated with pSS activity combining all treatment arms, and 12 AABs had baseline values that correlated with change in pSS activity upon VAY736 treatment (unadjusted p<0.05). Interestingly, 51 serum AABs correlated with BAFF saliva levels (|r| > 0.55), but not with...
BAFF serum levels. The genes encoding novel antigens are involved in apoptotic, anti-viral, metabolic, inflammatory, blood coagulation and B-cell processes, suggesting a possible link to the disease pathology. Finally, there was no reduction in AABs levels in response to VAY736.

Conclusion: In conclusion, we identified new AABs in pSS patients that have the potential to serve as markers of diagnosis, pSS activity, or as predictors of clinical outcome measures. Further large-scale studies are needed to confirm the value of these markers.


Disclosure: P. Budde, Protagen AG, 3; J. Doucet, Novartis Pharma AG, 3; H. D. Zucht, Protagen AG, 3; R. Kazma, Novartis Pharma AG, 3; P. Maguire, Novartis Pharma AG, 3; A. Avrameas, Novartis Pharma AG, 3; M. A. Valentin, Novartis Pharma AG, 3; S. Oliver, Novartis Pharma AG, 3; P. Schulz-Knapp, ProtagenAG, 3; A. Vitaliti, Novartis Pharma AG, 3.


Abstract Number: 876

Epidemiologic Subsets Drive a Differentiated Clinical and Immunological Presentation of Primary Sjögren Syndrome: Analysis of 9302 Patients from the Big Data International Sjögren Cohort

Soledad Retamazo1,2,3, Pilar Brito-Zerón3,4, Margit Zeher5, Kathy L. Sivils6, Raphaele Seror7, Thomas Mandl8, Xiaomei Li9, Chiara Baldini10, Jacques-Eric Gottenberg11, Debashish Danda12, Roberta Priori13, Luca Quartuccio14, Gabriela Hernandez-Molina15, Aike A. Kruize16, Seung-Ki Kwok17, Marie Wahren-Herlenius18, Sonja Propratnik19, Damien Sene20, Roberto Gerti21, Roser Solans22, Yasunori Suzuki23, David A. Izenberg24, Maureen Rischmueller25, Gunnel Nordmark26, Guadalupe Fraile27, Piotr Wiland28, Hendrika Bootsma29, Takashi Nakamura30, Valeria Valim31, Roberto Giacomelli32, Valérie Devauchelle-Pensec33, Benedikt Hofauer34, Michele Bombardieri35, Virginia Fernandes Moça Trevisani36, Daniel S. Hammenfor37, Steven E. Carsons38, Sandra Gofinet Pasto39, Jacques Morei40, Tamer Gheita41, Fabiola Atzen42, Cristina F. Vollenweider43, Belchin Kostov44, Xavier Mariette45 and Manuel Ramos-Casals46, 1Rheumatology Unit, Hospital Privado Universitario de Córdoba, Instituto University of Biomedical Sciences University of Córdoba (IUCBC), Cordoba, Argentina, 2Instituto de Investigaciones en Ciencias de la Salud, Universidad Nacional de Córdoba, Consejo Nacional de Investigaciones Científicas y Técnicas (INICSA-UNC-CONICET), Cordoba, Argentina, 3Laboratory of Systemic Autoimmune Diseases “Josep Font”, CELLEX, Institut d’Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Department of Systemic Autoimmune Diseases, ICMID, Hospital Clinic, Barcelona, Barcelona, Spain, 4Autoimmune Diseases Unit, Department of Medicine, Hospital CIMA- Sanitas, Barcelona., Barcelona, Spain, 5Division of Clinical Immunology, Faculty of Medicine, University of Debrecen, Debrecen, Hungary., Debrecen, Hungary, 6Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 7Center for Immunology of Viral Infections and Autoimmune Diseases, Assistance Publique – Hôpitaux de Paris, Hôpitaux Universitaires Paris-Sud, Le Kremlin-Bicêtre, Université Paris Sud, INSERM, Paris, France, Paris, France, 8Department of Rheumatology, Skåne University Hospital, Malmö, Sweden, Lund, Sweden, 9Department of Rheumatology and Immunology, Anhui Medical University Affiliated Provincial Hospital, China, HeFei, Anhui, China, 10Internal Medicine, Rheumatology Unit, University of Pisa, Pisa, Italy, 11Department of Rheumatology, Strasbourg University Hospital, Université de Strasbourg, CNRS, Strasbourg, France, Strasbourg, France, 12Clinical Immunology & Rheumatology, Christian Medical College, Vellore, India, Vellore, India, 13UO Complessa Reumatologia, Policlinico Umberto I Università Sapienza di Roma, Rome, Italy, 14Rheumatology Clinic, DSMB, University of Udine, Udine, Italy, Udine, Italy, 15Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición SЗ, mexico city, Mexico, 16Rheumatology & Clinical Immunology, University Medical Center Utrecht, Utrecht, Netherlands, 17seungki73@catholic.ac.kr, Division of Rheumatology, Department of
Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea, Republic of (South), 18Unit of Experimental Rheumatology, Department of Medicine, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, Stockholm, Sweden, 19Department of Rheumatology, University Medical Centre Ljubljana, Ljubljana, Slovenia, 20Service de Médecine Interne 2, Hôpital Lariboisière, Université Paris VII, Assistance Publique-Hôpitaux de Paris, 2, Paris, France, Paris, France, 21University and Azienda Ospedaliera di Perugia, Perugia, Italy, 22Autoimmune Systemic Diseases Unit, Department of Internal Medicine, Hospital Vall d'Hebron, Autonomous University of Barcelona, Spain, Barcelona, Spain, 23Division of Rheumatology, Kanazawa University Graduate School of Medicine, Ishikawa, Japan, Kanazawa, Japan, 24Centre for Rheumatology Research, Division of Medicine, University College London, London, United Kingdom, 25Rheumatology, The Queen Elizabeth Hospital, South Australia, Adelaide, Australia, 26Department of Medical Sciences, Section of Rheumatology, Uppsala University, Uppsala, Sweden, Uppsala, Sweden, 27Autoimmune Diseases Department, Hospital Ramón y Cajal, Madrid, Spain, 28Department and Clinic of Rheumatology and Internal Medicine, Medical University, Wroclaw, Poland, 29Rheumatology and Clinical Immunology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, 30Department of Radiology and Cancer Biology, Nagasaki University School of Dentistry, Nagasaki, Japan, 31Rheumatology, Department of Medicine, Universidade Federal do Espírito Santo, Vitória, Brazil, Vitória, Brazil, 32University of L'Aquila, L'Aquila, Italy, 33Department of Rheumatology, Brest University Hospital, Brest, France, 34Hals-Nasen-Ohrenklinik und Poliklinik, Technische Universität München, München, Germany, 35Centre for Experimental Medicine and Rheumatology, William Harvey Research Institute, Queen Mary University of London, UK, London, United Kingdom, 36UNIFESP, Sao Paulo, Brazil, San Paulo, Brazil, 37Department of Rheumatology, Haukeland University Hospital, University of Bergen, Bergen, Norway, 38NYU Winthrop University Hospital, Department of Medicine, Mineola, NY, 39Internal Medicine, Division of Rheumatology - Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, São Paulo, Brazil, 40Department of Rheumatology, Teaching hospital and University of Montpellier, France, Montpellier, France, 41Rheumatology, Rheumatology Department, Faculty of Medicine, Cairo University, Egypt, Cairo, Egypt, 42Rheumatology Unit, ASST Fatebenefratelli - Sacco, L. Sacco University Hospital, Milano, Italy, 43Rheumatology, German Hospital, Buenos Aires, Argentina, Buenos Aires, Argentina, 44Primary Care Research Group, Institut d’Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Primary Care Centre Les Corts, CAPSBE, Barcelona, Spain, 45Université Paris-Sud, AP-HP, Hôpitaux Universitaires Paris-Sud, Paris, France, 46Laboratory of Systemic Autoimmune Diseases “Josep Font”, CELLEX, Institut d’Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Department of Systemic Autoimmune Diseases, ICMID, Hospital Clinic, Barcelona, Spain, Barcelona, Spain

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Sjögren's Syndrome I: Clinical Assessment and Trial Outcomes
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: To analyse whether epidemiologic factors (such as gender or age at diagnosis of the disease) are associated with particular disease expressions and define some specific subsets in patients with primary Sjögren syndrome (SS).

Methods: The Big Data Sjögren project is an international, multicentre registry formed in 2014 to take a “high-definition” picture of the main features of primary SS at diagnosis by merging international SS databases using a Data-Sharing methodological approach. By January 2017, the database included 9302 consecutive patients recruited from 21 countries of the five continents. The main features at diagnosis (time of criteria fulfilment) or at recruitment were collected and analysed.

Results: Of the 9032 patients, 8680 (93%) were women and 622 (7%) were men with a mean age at diagnosis of primary SS of 50 years; 76% were Caucasian. The frequency of fulfilment of the 2002 criteria was: 92% for dry eye, 93% for dry mouth, 88% for positive salivary gland biopsy, 93% for positive ocular tests, 85% for positive oral tests and 71% for positive Ro/La autoantibodies. Other immunological tests included positive ANA (81%), RF (49%), low C4 levels (13%), low C3 levels (14%) and cryoglobulins (7%). Men with primary SS presented a higher frequency of White ethnicity (83% vs 76% in women, p < 0.001) and rheumatoid factor (54% vs 49%, p = 0.017), and a lower frequency of dry eyes (89% vs 92%, p = 0.011) and dry mouth (90% vs 94%, p = 0.026) in the multivariate model analysis. Patients with a younger onset (< 35 years) showed a lower frequency of White ethnicity (69% vs 77% in aged > 35 yrs, p < 0.001), dry eyes (86% vs 93%, p <
Modification of the Classification Criteria for Primary Sjögren Syndrome: An International Vignette Survey

Sandrine Jousse-Joulin1, Florence Gatteau2, Chiara Baldini3, Alan N. Baer4, Francesca Barone5, Hendrika Bootsma6, Simon Bowman7, Pilar Brito Zerón8, Divi Corne9, Thomas Doerner10, Salvatore De Vita11, Benjamin Fisher12, Daniel S. Hammenfors13, Malin V. Jonsson14, Xavier Mariette15, Vera Milic16, Hideki Nakamura17, Wan-Fai Ng18, Emmanuel Nowak2, Manuel Rasos-Casals19, Astrid Rasmussen20, Raphaelé Seror21, Caroline Shiboski22, Takashi Nakamura23, Arjan Vissink24, Alain Saraux25 and Valérie Devauchelle-Pensec1, 1Rheumatology, Brest university medical school, EA 2216, UBO and CHU de la Cavale Blanche, Brest, France, 2INSERM CIC 1412, Brest Medical University Hospital, Brest, France, 3Internal Medicine, Rheumatology Unit, University of Pisa, Pisa, Italy, 4Medicine (Rheumatology), Johns Hopkins University School of Medicine, Baltimore, MD, 5Institute of Inflammation and Ageing (IIA), University of Birmingham, Birmingham, United Kingdom, 6Department of Rheumatology and Clinical Immunology, University of Groningen, University Medical Centre Groningen, Groningen, Netherlands, 7Department of Rheumatology, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK, Birmingham, United Kingdom, 8Autoimmune Diseases Unit, Department of Internal Medicine, Hospital CIMA-Sanitas, Barcelona, Spain, 9CHU Brest, Brest, France, 10Charité Universitätsmedizin Berlin and DRFZ, Berlin, Germany, 11Rheumatology Clinic, Academic Hospital S. M. della Misericordia, Medical Area Department, University of Udine, Italy, Udine, Italy, 12Rheumatology Research Group, University of Birmingham, Birmingham, United Kingdom, 13Broegelmann Research Laboratory, Department of Clinical Science, University of Bergen, Bergen, Norway, Bergen, Norway, 14Section for Oral and Maxillofacial Radiology, Department of Clinical Dentistry, University of Bergen, Bergen, Norway, Bergen, Norway, 15Université Paris Sud, Paris, France, 16Institute of Rheumatology, School of Medicine, University of Belgrade, Belgrade, Serbia, 17Department of Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, 18Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, United Kingdom, 19Department of Medicine, University of Barcelona, Barcelona, Spain, 20Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 21Assistance Publique-Hôpitaux de Paris (APHP), Hôpitaux universitaires Paris Sud, Université Paris...
SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Sjögren's Syndrome I: Clinical Assessment and Trial Outcomes
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:

The common classification criteria sets of primary Sjogren syndrome, did not considered the ultrasonography (US) of the major salivary glands as a useful item. However, it is well known that US can increase the performance of these two sets.

UTOPIA study (ultrasonography to diagnose and classify pSS) was an international vignette survey undertaken to determine the accuracy of salivary gland ultrasonography (SGUS) and to add it as a new item in the AECG-2002 and new ACR/EULAR-2017 classification criteria.

Methods: Twenty four experts in primary Sjogren, from 20 countries participated in the study (22 Europeans from 13 countries, two North Americans and two Japanese). They evaluated on an internet-secure relational database, 512 realistics vignettes, randomly assigned, abstracted from 150 patients of an Italian cohort (CB). Each vignettes contained items of the classification criteria and sections on ‘history’ (duration of the symptoms, gender, age), clinical symptoms (dry mouth or eyes and systemic manifestations) and results of the SGUS evaluation. Each expert has to consider the diagnosis of pSS as absent, unlikely, likely or present for 64 vignettes. Each vignette was evaluated by 3 experts. The diagnosis of pSS (the gold standard) was obtained when 2/3 considered it as likely or present. Univariate and multivariate analysis were performed to evaluate the association of US to the diagnosis of pSS. Data were secondly verified on an independent French cohort (DiapSS cohort).

Results: The univariate and multivariate analysis confirmed that both classification criteria and SGUS were independently associated with the diagnosis of pSS (p<0.001). Disease duration, OSS and ocular dryness were not associated with the diagnosis of pSS. When adding US to the AECG-2002 criteria, the sensitivity (Se) and specificity (Sp) were respectively of 91 % and 83 % and of 98% and 80% if we add US. For the ACR/EULAR 2017 criteria, (with a global score of 4), the Se and Sp were respectively of 90 % and 84 % and of 95% and 82% if we add US. Results were quite similar in the independent French DiapSS. The SE of the ACR/EULAR 2017 were 87.5 and 84.5% and of 92.5 and 82 % with US. If we considered each items of the vignettes separately to build a new weighted score, only 6 variables were selected by logistic regression analysis: presence of anti-SSA (weight:4), focus score (weight:4), SGUS (weight:2), Schirmer’s test (weight:1), dry eye (weight:1) and salivary flow rate (weight:1). According to ROC curve analysis, a score of ≥5 had 96% Se and 84% Sp, compared with 90% Se and 84% Sp for the ACR/EULAR 2017 Criteria. The corrected C statistic (AUC) for the new weighted score was 0.98.

Conclusion:

Adding US item to both AECG and ACR/EULAR 2017 classification criteria increased Se but did not change Sp. The modified scores are easy to use especially the ACR/EULAR 2017.

Disclosure: S. Jousse-Joulin, None; F. Gatineau, None; C. Baldini, None; A. N. Baer, None; F. Barone, None; H. Bootsma, None; S. Bowman, I have consulted in the field of Sjogren's for: AstraZeneca/ Meddimmune, BMS, Celgene, Eli Lilly, Glenmark, GSK, MTPharma, Novartis, Ono, Takeda, UCB, xtlbio). Roche provided Rituximab for the TRACTISS Study, 5; P. Brito Zeron, None; D. Corne, None; T. Doernner, None; S. De Vita, None; B. Fisher, Novartis, Roche, Virtualscopics, 5; D. S. Hammenfors, None; M. V. Jonsson, None; X. Mariette, None; V. Milic, None; H. Nakamura, None; W. F. Ng, None; E. Nowak, None; M. Ralos-Casals, None; A. Rasmussen, None; R. Seror, None; C. Shiboski, None;
Diagnosis of Salivary Gland Lymphoma in Sjogren’s Syndrome Utilizing Ultrasound-Guided Core Needle Biopsies

Alan N. Baer¹, Thomas Grader-Beck¹, Brendan Antiochos¹, Julius Birnbaum¹, Qing Kay Li², Deborah Belchis² and Joel Fradin³, ¹Medicine (Rheumatology), Johns Hopkins University School of Medicine, Baltimore, MD, ²Pathology, Johns Hopkins University School of Medicine, Baltimore, MD, ³Radiology, Johns Hopkins University School of Medicine, Baltimore, MD

First publication: September 18, 2017

Background/Purpose:
Ultrasound (US)-guided core needle biopsy (CNB) with or without concomitant fine needle aspiration (FNA) is a standard method for pre-operative evaluation of salivary gland tumors. Its application to the diagnosis of salivary gland lymphoma in patients with Sjogren’s syndrome (SS) has not been evaluated extensively. We sought to review our experience with these diagnostic techniques in SS patients with suspected salivary gland lymphoma.

Methods:
All patients of the Hopkins Sjogren’s Syndrome Center who underwent an US-guided CNB of a major salivary gland between 7/1/2009 and 5/30/2017 were identified through a computer database search. Twenty-six such patients had documented SS at the time of the biopsy and 25 underwent the procedure for evaluation of possible salivary gland lymphoma. All US-guided procedures were performed by radiologists with extensive experience in these techniques. CNB and FNA were done under real-time US guidance, using an 18 or 12 MHz linear transducer. The procedures included FNA at the discretion of the radiologist. FNA was generally done first with cellular material assessed for adequacy by a cytotechnologist present in the procedure room. The CNBs were obtained with an 18 gauge InRad needle. Patients were contacted one day after the procedure to assess for complications.

Results:
The indications for CNB included bilateral parotid gland enlargement (n=15), unilateral parotid (n=1) or submandibular gland (n=1) enlargement, discrete masses in the parotid (n=5) or submandibular (n=2) glands, and a sonographically abnormal intraparotid lymph node (n=1). The US-guided procedures included CNB in all 25 patients [mean number of CNB per gland = 2.15 (range, 1-4)], and FNA in 20 patients. Samples were sent for flow cytometry in 24 patients, using material obtained from CNB alone in 4, CNB and FNA in 18, and FNA alone in 2. Immunohistochemistry (IHC) was performed on 9 CNB samples with a prominent lymphocytic infiltrate. Final pathologic diagnoses were marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT; n=8), benign lymphocytic infiltrate (n=10), salivary gland tissue without an inflammatory infiltrate (n=6), and lymphoepithelial cyst (n=1). Flow cytometry revealed a clonally restricted cell population in 10/24 patients (B cell in 9, plasma cell in 1), of whom 7 were diagnosed with MALT lymphoma based on histopathology, IHC, and IgH gene rearrangement phenotyping of the B-cells. Flow cytometric samples were comprised of largely debris
and thus without diagnostic utility in 4 patients (despite inclusion of tissue cores in 3); none of these 4 had MALT lymphoma on final diagnosis. No complications ensued from the procedures.

Conclusion:

US-guided CNB, coupled with flow cytometric analysis from one of the CNB samples and/or FNA, is a safe and effective method for differentiating benign from malignant lymphoid proliferation of the salivary gland in patients with SS. A clonally restricted B cell population on flow cytometry is not always indicative of lymphoma and must be corroborated by IHC and routine histopathologic analysis of CNB samples.

Disclosure: A. N. Baer, None; T. Grader-Beck, None; B. Antiochos, None; J. Birnbaum, None; Q. K. Li, None; D. Belchis, None; J. Fradin, None.

Association of Venous Thromboembolism with Spondyloarthopathies Among Hospitalized Patients – Data from National Inpatient Sample

Dilli Poudel1, Rashmi Dhital2, Raju Khanal2, Pragya Shrestha3, Sijan Basnet2, Sushil Ghimire2 and Paras Karmacharya4, 
1Internal Medicine, Reading Health System, WEST READING, PA, 2Internal Medicine, Reading Health System, West Reading, PA, 3Internal medicine, Reading Health System, West Reading, PA, 4Division of Rheumatology, Mayo Clinic, Rochester, MN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthopathies and Psoriatic Arthritis – Clinical Aspects and Treatment I
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Venous thromboembolism (VTE) encompassing deep venous thrombosis (DVT) and pulmonary embolism (PE) is the third most common cause of death related to cardiovascular disease following stroke and heart attack. Studies in the past have shown an increased association with the common inflammatory rheumatological disorders, however they still remain under-recognized as risk factors for VTE. We examined the risk of VTE among hospitalized spondyloarthritis patients in a large inpatient US database.

Methods: Using the National Inpatient Sample (NIS) data from 2006-2011, we identified VTE related hospitalizations (DVT or PE as primary diagnosis) and selected patients with spondyloarthritis, malignancy and osteoarthritis based ICD-9 codes. NIS is the largest publicly available all-payer inpatient care database in US. Discrete cohorts of patients with spondyloarthopathies (SpA), osteoarthritis (OA), malignancy and control group were created after excluding all hospitalizations with other common rheumatological diseases such as (RA, SLE, myositis, APS, vasculitis). Univariate and multivariate logistic regressions (adjusted for age, sex, race, obesity, from nursing home, long bone fractures, prior malignancy, post-surgery status, DM, CHF, respiratory failure, spinal cord injury, prior VTE, hypercoagulability, smoking, length of stay ≥ 3 days, calendar year, venous catheterizations and infections) were used to derive odds ratio for measures of association. SVY function was used in STATA version 13.0 to make weighted estimation for the whole US population.

Results:

Our study included 29,116 hospitalizations (weighted N = 143,650) with spondyloarthritis from 2006-2011. The rates of VTE related hospitalizations was comparable between SpA and malignancy (1.50 % vs 1.54 %). Adjusted OR of VTE among
patients with SpA was close to that of malignancy (1.30 (1.17-1.4) vs 1.31 (1.29-1.33)), while that of osteoarthritis was 0.81 (0.79-0.83) (Table 1).

**Conclusion:**

It has been shown that inflammation drives thrombosis with imbalance between innate pro-coagulants, anti-coagulants and fibrinolysis. Alarmingly elevated risk of VTE among inflammatory rheumatological diseases are reported and our study is in line with the same. We found a relatively high risk of VTE among patients hospitalized with SpA, which was comparable with that of malignancy (Table 1). This raises an argument as to whether an inflammatory rheumatological disease like SpA should be considered as an independent risk factor for VTE among hospitalized patients. Given the large, rising burden of rheumatological diseases and its proven associations with VTE, it appears prudent to include these in the pre-test probability calculators such as Well’s or other validated scores for VTE. The weightage or score to be given should be guided by future large, prospective trials.

<table>
<thead>
<tr>
<th>Disease Groups</th>
<th>Total</th>
<th>Cases without Vte</th>
<th>Cases with VTE</th>
<th>Rate of VTE (%)</th>
<th>OR Unadjusted</th>
<th>CI</th>
<th>p-value</th>
<th>OR adjusted</th>
<th>CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>136028746</td>
<td>134542591</td>
<td>1486155</td>
<td>1.09</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spondyloarthritis</td>
<td>143,651</td>
<td>141,491</td>
<td>2,159</td>
<td>1.50</td>
<td>1.38</td>
<td>1.25 - 1.52</td>
<td>&lt;0.001</td>
<td>1.25</td>
<td>1.13 - 1.39</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Psoriatic</td>
<td>82,145</td>
<td>80,856</td>
<td>1,289</td>
<td>1.57</td>
<td>1.44</td>
<td>1.27 - 1.64</td>
<td>&lt;0.001</td>
<td>1.30</td>
<td>1.14 - 1.49</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Reactive</td>
<td>2,073</td>
<td>2,050</td>
<td>24</td>
<td>1.13</td>
<td>1.04</td>
<td>0.43 - 2.52</td>
<td>0.94</td>
<td>1.68</td>
<td>0.68 - 4.14</td>
<td>0.26</td>
</tr>
<tr>
<td>Enteropathic</td>
<td>3,674</td>
<td>3,637</td>
<td>38</td>
<td>1.02</td>
<td>0.93</td>
<td>0.44 - 1.98</td>
<td>0.86</td>
<td>0.71</td>
<td>0.34 - 1.5</td>
<td>0.38</td>
</tr>
<tr>
<td>AS</td>
<td>55,759</td>
<td>54,949</td>
<td>810</td>
<td>1.45</td>
<td>1.33</td>
<td>1.14 - 1.56</td>
<td>&lt;0.001</td>
<td>1.21</td>
<td>1.03 - 1.41</td>
<td>0.018</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>15260121</td>
<td>15103916</td>
<td>156,205</td>
<td>1.02</td>
<td>0.94</td>
<td>0.92 - 0.96</td>
<td>&lt;0.001</td>
<td>0.78</td>
<td>0.76 - 0.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cancer</td>
<td>12059300</td>
<td>11873868</td>
<td>185,432</td>
<td>1.54</td>
<td>1.41</td>
<td>1.39 - 1.44</td>
<td>&lt;0.001</td>
<td>1.39</td>
<td>1.37 - 1.41</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total</td>
<td>166534017</td>
<td>164658376</td>
<td>1875641</td>
<td>1.13</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 1: Proportion and odds of association of Spondyloarthritides with VTE

**Disclosure:** D. Poudel, None; R. Dhital, None; R. Khanal, None; P. Shrestha, None; S. Basnet, None; S. Ghimire, None; P. Karmacharya, None.


Abstract Number: 880

**Tofacitinib Treatment in Patients with Psoriatic Arthritis and Rates of Radiologic Progression According to Baseline CRP Levels: Results from a Phase 3 Clinical Study**
Désirée van der Heijde, Dafna D Gladman, Oliver FitzGerald, Arthur Kavanaugh, Daniela Graham, Cunshan Wang and Lara Fallon, Leiden University Medical Center, Leiden, Netherlands, Department of Medicine, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, Department of Rheumatology, St Vincent's University Hospital, Dublin, Ireland, University of California San Diego School of Medicine, La Jolla, San Diego, CA, Pfizer Inc, Groton, CT, Pfizer Canada, Montreal, QC, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment I
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor under investigation for the treatment of psoriatic arthritis (PsA). Here, we evaluate radiographic progression in PsA patients (pts) treated with tofacitinib, using data from a global, 12-month, placebo- and active-controlled, parallel-group Phase 3 study. Pts had an inadequate response to ≥1 conventional synthetic disease-modifying antirheumatic drug, and were tumor necrosis factor inhibitor-naïve (OPAL Broaden; NCT01877668).

Methods: Pts were randomized to receive oral tofacitinib 5 mg twice daily (BID), tofacitinib 10 mg BID, adalimumab (ADA) 40 mg subcutaneous once every 2 weeks, or placebo (PBO). Pts who initially received PBO advanced to tofacitinib 5 or 10 mg BID at Month (M)3. Radiographs of the hands and feet at baseline (BL) and M12 were scored independently by 2 assessors using the van der Heijde-modified Total Sharp Score for PsA (mTSS; range 0–528); average scores were used. For radiographs missing at M12, mTSS was calculated by linear extrapolation from an earlier mTSS. Change from BL in mTSS, erosion and joint space narrowing (JSN) was reported for all pts and pts grouped by BL C-reactive protein (CRP) >2.87 mg/L or ≤2.87 mg/L. The proportion of pts with radiographic non-progression (defined as either an increase from BL in mTSS ≤0.5 or ≤0 and less than the smallest detectable change [SDC; ≤0.66 derived from this trial]) at M12 are reported for all pts.

Results: Treatment groups were comparable for demographics and BL characteristics (Table 1). Pts in all groups demonstrated minimal changes from BL in mTSS, erosion, and JSN at M12 (Table 2). Change from BL was similar in pts with CRP >2.87 mg/L or ≤2.87 mg/L. Radiographic non-progression at M12 using any threshold was observed in >90% of pts in all groups. At M12, 95.9%, 94.9%, and 97.9% of pts receiving tofacitinib 5 mg BID, tofacitinib 10 mg BID, and ADA, respectively, were non-progressors based on radiographic changes less than the SDC in mTSS.

Conclusion: Pts with PsA receiving tofacitinib showed minimal mean changes in mTSS at M12, regardless of whether BL CRP level was >2.87 mg/L or ≤2.87 mg/L. At M12, >90% of pts who received tofacitinib or ADA met all radiographic non-progression criteria.

Disclosure: D. van der Heijde, AbbVie, Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Daiichi, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer Inc, Regeneron, Roche, Sanofi, Takeda, UCY, 5, Imaging Rheumatology bv., 9; D. D. Gladman, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, UCY, 2, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, UCY, 5, O. FitzGerald, AbbVie, Bristol-Myers Squibb, Novartis, Pfizer Inc, 2, Amgen, Celgene, Janssen, Lilly, 5; A. Kavanaugh, Pfizer Inc, 9; D. Graham, Pfizer Inc, 1, Pfizer Inc, 3; C. Wang, Pfizer Inc, 1, Pfizer Inc, 3; L. Fallon, Pfizer Inc, 1, Pfizer Inc, 3.


Abstract Number: 881
Ustekinumab Is Superior to TNF Inhibitor Treatment in Resolving Enthesitis in PsA Patients with Active Enthesitis- Results from the Enthesial Clearance in Psoriatic Arthritis Study

Elizabeth G. Araujo1, Matthias Englbrecht2, Sabrina Hoepken1, Stephanie Finzel3, Axel J. Hueber2, Juergen Rech4 and Georg Schett1
1Rheumatology and Immunology, Department of Internal Medicine 3, Universitätsklinikum Erlangen, Erlangen, Germany; Erlangen, Germany, 2Department of Medicine 3, Rheumatology and Immunology, University of Erlangen-Nuremberg, Erlangen, Germany, 3Rheumatology and Clinical Immunology, University Medical Center Freiburg, Freiburg, Germany, and 4Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, Erlangen, Germany.

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment I
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: IL-23 is considered to play an important role in the development of enthesitis. Ustekinumab (UST), a combined inhibitor of IL-12/IL-23 shows efficacy in psoriatic arthritis (PsA), while it has no therapeutic role in diseases driven by synovitis only such as rheumatoid arthritis. We therefore speculated that inhibition of IL-23 is particularly effective in enthesitis-driven PsA patients. To compare the efficacy of UST with tumor necrosis factor inhibitor (TNFi) treatment in clearing enthesitis in PsA patients.

Methods: ECLIPSA is a prospective, observational, open study. Patients with PsA with active enthesitis (at least one painful enthesis on SPARCC or MASES sites), were consecutively enrolled 1:1, receiving either standard doses of UST (arm 1) or TNFi (arm 2). At baseline the following parameters were assessed: age, gender, BMI, disease duration, previous DMARDs, use of corticosteroids, use of non-steroidal anti-inflammatories (NSAIDs), swollen and tender joint count, VAS-pain, VAS-global, NAPSI, PASI, MASES, SPARCC, LDI, BASDAI, BASFI, HAQ-DI, SF-36, FACIT-F, ESR and CRP. Primary endpoint was a SPARCC of 0 after 6 months. Patients were seen every 3 months and followed for a total of 6 months. In order to investigate the effects of study treatment over time we used 2x3 mixed design ANOVA models for both physician’s and patient’s reported outcomes. Furthermore, exploratory logistic regression was used to predict a SPARCC of 0 at month 6 from baseline PASI, tender joint count, swollen joint count, and FACIT while additionally accounting for age, gender, PsA duration and study treatment.

Results: 51 patients (UST=25; TNFi= 26) were screened and 47 patients (UST=23; TNFi= 24) were enrolled with 4 patients not presenting with active enthesitis at baseline. Mean ± SD age was 59.11 ± 12.16 years and mean ± SD disease duration was 6.4 ± 7.79 years. Mean± SD SPARCC at baseline was 4.9±2.7 in the UST group and 3.8±2.5 in the TNFi group. Other baseline characteristics were similar between both groups with exception of gender and mental component of the SF-36. In regards to the effect of study treatment (TNFi vs. UST) and time, the corresponding ANOVAs suggested an important interaction of both factors for measures of enthesitis (MASES and SPARCC), patient-reported disease activity (HAQ-DI), and skin activity (PASI), all p≤0.03 with superiority of UST. After 6 months, 17 out of 24 UST patients (70.8%) and 10 out of 26 TNFi patients (38.4%) reached the primary endpoint defined as clearance of enthesitis (SPARCC=0). Logistic regression predicting enthesitis-free state of disease according to SPARCC was significantly related to study treatment, with patients receiving UST being more likely to show no signs of enthesitis at month 6 (OR=0.034; p=0.005). Higher FACIT scores at baseline were also predictive of an enthesitis free-state (OR=0.864; p=0.024).

Conclusion: These results show that UST is superior to TNFi in resolving the enthesitis component of disease in a population of PsA patients characterized by active enthesial disease. Based on these data more stratified treatment approaches can be designed in PsA patients, where enthesitis-driven patients are targeted by IL-23/IL-17 pathway inhibitors.

Disclosure: E. G. Araujo, None; M. Englbrecht, None; S. Hoepken, None; S. Finzel, None; A. J. Hueber, None; J. Rech, None; G. Schett, None.
A New Model of Care for Improving Early Rheumatology Access of Psoriatic Arthritis Patients

Keith Colaco1,2, Dana Jerome3, Jensen Yeung4,5, Noah Ivers6,7,8, Carol Kitai7, Chandra Farrer3 and Lihi Eder1,9,
1Women's College Research Institute, Women's College Hospital, Toronto, ON, Canada, 2Institute of Medical Science, University of Toronto, Toronto, ON, Canada, 3Rheumatology, Women's College Hospital, Toronto, ON, Canada, 4Dermatology, Women's College Hospital, Toronto, ON, Canada, 5University of Toronto, Toronto, ON, Canada, 6Institute for Clinical Evaluative Sciences, Toronto, ON, Canada, 7Women's College Hospital, Toronto, ON, Canada, 8Family and Community Medicine, University of Toronto, Toronto, ON, Canada, 9Medicine, University of Toronto, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment I
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: The prevalence of undiagnosed psoriatic arthritis (PsA) in psoriasis patients is high, with delays in diagnosis contributing to poor patient outcomes. We aimed to describe a novel model of care involving a self-referral system and central triage clinic for psoriasis patients with musculoskeletal (MSK) symptoms and to compare the efficacy of several triage methods for PsA.

Methods: Patients with psoriasis were identified by searching the institutional electronic medical records. These patients received a letter inviting them to contact the research team if they were experiencing any MSK symptoms. Participants were assessed in a central triage clinic to determine their likelihood of having PsA. The following triage methods were used: 1) three PsA screening questionnaires (TOPAS-2, PEST, PASE); 2) MSK ultrasound assessment of symptomatic joints and entheses; 3) clinical assessment by an advanced practice physiotherapist and 4) levels of CRP and ESR. Each patient was then assessed by a rheumatologist to determine whether they have PsA. Patients were classified by the rheumatologist to “Not PsA”, “Possible PsA” or “PsA”. The rheumatologist was blinded to the results of the triage methods. The performance of each triage method to identify PsA was assessed by calculating its sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and area under the ROC curve (AUC).

Results: Of the 1159 patients invited to participate, 300 responded (26%) and 152 (13%) agreed to participate. Of the 94 patients assessed thus far in the clinic, 69 (73%) did not have PsA, 17 (18%) had possible PsA, and 8 (9%) had PsA. The performance of triage methods is presented in Table 1. The advanced practice physiotherapist’s assessment in detecting clinical PsA was highly sensitive (100%) with good specificity (71%). The screening questionnaires varied by their sensitivity and specificity with TOPAS-2 showing highest sensitivity (88%) and PASE with highest specificity (87%). The prevalence of positive MSK inflammation by ultrasound (at least 1 joint or enthesis with positive power Doppler signal) was 39.4%. The sensitivity of positive MSK ultrasound was high (88%) but its specificity was moderate (65%). 22% of the study participants who had positive MSK ultrasound findings were not classified by the rheumatologist as having PsA. The performance of CRP and ESR as triage methods was poor.

Conclusion: MSK ultrasound, advanced practice physiotherapist and TOPAS-2 were highly sensitive in identifying patients with PsA among psoriasis patients with MSK symptoms. A significant proportion of patients with positive MSK inflammation by ultrasound were not identified as having PsA by the clinician.
Table 1 – Properties of various triage methods in detecting clinical PsA among patients with psoriasis and musculoskeletal symptoms

<table>
<thead>
<tr>
<th>Triage Method</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive MSK ultrasound (Definition 1)</td>
<td>88%</td>
<td>65%</td>
<td>19%</td>
<td>98%</td>
<td>0.76</td>
</tr>
<tr>
<td>at least 1 joint or entheseal sites with positive power Doppler signal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive MSK ultrasound (Definition 2)</td>
<td>75%</td>
<td>78%</td>
<td>24%</td>
<td>97%</td>
<td>0.77</td>
</tr>
<tr>
<td>at least 2 joint or entheseal sites with positive power Doppler signal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Advanced Practice Physiotherapist: Positive assessment</td>
<td>100%</td>
<td>71%</td>
<td>24.2%</td>
<td>100%</td>
<td>0.86</td>
</tr>
<tr>
<td>Positive TOPAS-2 questionnaire</td>
<td>88%</td>
<td>65%</td>
<td>19%</td>
<td>98%</td>
<td>0.76</td>
</tr>
<tr>
<td>Positive PEST questionnaire</td>
<td>75%</td>
<td>72%</td>
<td>21%</td>
<td>97%</td>
<td>0.74</td>
</tr>
<tr>
<td>Positive PASE questionnaire</td>
<td>63%</td>
<td>87%</td>
<td>31%</td>
<td>96%</td>
<td>0.75</td>
</tr>
<tr>
<td>Elevated CRP (&gt;5 mg/dL)</td>
<td>43%</td>
<td>84%</td>
<td>19%</td>
<td>94%</td>
<td>0.63</td>
</tr>
<tr>
<td>Elevated ESR (Men: &gt;15 mm/hr, Women: &gt;20 mm/hr)</td>
<td>43%</td>
<td>78%</td>
<td>15%</td>
<td>94%</td>
<td>0.61</td>
</tr>
</tbody>
</table>

MSK – Musculoskeletal, TOPAS – Toronto Psoriatic Arthritis Screening, PEST – Psoriasis Epidemiology Screening Tool, PASE – Psoriatic Arthritis Screening and Evaluation, CRP – C-Reactive Protein, ESR – Erythrocyte Sedimentation Rate

Disclosure: K. Colaco, None; D. Jerome, None; J. Yeung, None; N. Ivers, None; C. Kitai, None; C. Farrer, None; L. Eder, None.


Abstract Number: 883

The Risk of Deep Venous Thrombosis and Pulmonary Embolism in Ankylosing Spondylitis: A General Population-Based Study

Jonathan Chan¹, Anthony So², Eric C. Sayre³ and J. Antonio Avina-Zubieta⁴, ¹Rheumatology, University of British Columbia, Vancouver, BC, Canada, ²University of British Columbia, Vancouver, BC, Canada, ³Arthritis Research Canada, Richmond, BC, Canada, ⁴Division of Rheumatology, Department of Medicine, University of British Columbia, Vancouver, BC, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment I
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:

Venous thromboembolism (VTE) (pulmonary embolism [PE] and deep vein thrombosis [DVT]) is a potentially life threatening disease. Previous hospital-based studies have shown an increased risk of VTE in patients with ankylosing spondylitis (AS) but limited population-based data are available. We estimated the population-based risk of newly recorded PE and DVT among incident cases with AS compared with controls from the general population using physician-billing and hospitalization databases that cover the entire population of the province of British Columbia, Canada (~5 million).

Methods:

Our data includes all visits to health professionals and all hospital admissions from Jan 1, 1996 to Dec 31, 2012 and all dispensed medications from Sept 1, 1996 to Dec 31, 2012 for all individuals. We conducted a retrospective matched cohort study of all patients >18 years of age satisfying the following criteria: 1) two ICD-9 or 10 codes (720.0 or M45) for AS at least two months apart and within a 2-year period by any physician or hospitalization; 2) all AS cases had at least a 7-year run-in period before the 1st ICD code for AS in order to consider the case as incident. Each AS patient was matched with up to 10 controls by birth year, sex, and entry cohort time. We excluded cases that were diagnosed with other inflammatory conditions such as rheumatoid arthritis, vasculitis, myositis, and systemic lupus erythematosus on at least two visits. Ten non-AS controls matched by birth year, sex, and calendar year of follow-up were selected from the general population for each case.

Our outcomes were incident PE and DVT events that were recorded from outpatient visits, hospitalizations, or death certificates. For non-fatal events, we required the use of anticoagulation medications within six-months as part of all outcome definitions. We estimated relative risks (RRs) by comparing those with AS to age, sex, and entry time matched comparison cohorts, adjusting for potential known risk factors for VTE.

Results:

Among 7,190 incident cases of AS (51% male, mean age of 46yrs [SD 15.6]), 35, 47, and 69 developed PE, DVT, or both, respectively (incidence rates = 0.79, 1.06, and 1.56 per 1000 person years, respective) (see table). Compared with age, sex, and entry time matched controls, the RRs were 1.95 (95% CI; 1.36-2.81), 2.19 (95% CI; 1.60-3.00), and 2.06 (95% CI; 1.59-2.68) for PE, DVT, and both, respectively. After adjusting for covariates, the results remained similar (see table 1).

Conclusion:

This large population-based study indicates an increased risk of PE and DVT in patients with AS. Our results support the increased need for awareness and potential monitoring of these complications in AS patients.

Table 1. Relative Risk of Incident PE and DVT according to AS Status
<table>
<thead>
<tr>
<th></th>
<th>AS</th>
<th>Non-AS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=7,190</td>
<td>N=71,900</td>
</tr>
<tr>
<td><strong>PE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases, N</td>
<td>7,165</td>
<td>71,775</td>
</tr>
<tr>
<td>Incidence Rate/1000 Person-Years</td>
<td>0.79</td>
<td>0.40</td>
</tr>
<tr>
<td>Age-, Sex-, Entry Time-Matched Cox HR (95% CI)</td>
<td>1.95 (1.36, 2.81)</td>
<td>1.00</td>
</tr>
<tr>
<td>Glucocorticoid-Adjusted Age-, Sex-, Entry Time-Matched Cox HR (95% CI)</td>
<td>1.60 (1.09, 2.34)</td>
<td>1.00</td>
</tr>
<tr>
<td>Number of Outpatient Visit-Adjusted Age-, Sex-, Entry Time-Matched Cox HR (95% CI)</td>
<td>1.56 (1.08, 2.26)</td>
<td>1.00</td>
</tr>
<tr>
<td>*Fully-Adjusted Age-, Sex-, Entry Time-Matched Cox HR (95% CI)</td>
<td>1.36 (0.92, 1.99)</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>DVT</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases, N</td>
<td>47</td>
<td>218</td>
</tr>
<tr>
<td>Incidence Rate/1000 Person-Years</td>
<td>1.06</td>
<td>0.50</td>
</tr>
<tr>
<td>Age-, Sex-, Entry Time-Matched Cox HR (95% CI)</td>
<td>2.19 (1.60, 3.00)</td>
<td>1.00</td>
</tr>
<tr>
<td>Glucocorticoid-Adjusted Age-, Sex-, Entry Time-Matched Cox HR (95% CI)</td>
<td>2.00 (1.44, 2.78)</td>
<td>1.00</td>
</tr>
<tr>
<td>Number of Outpatient Visit-Adjusted Age-, Sex-, Entry Time-Matched Cox HR (95% CI)</td>
<td>1.71 (1.23, 2.36)</td>
<td>1.00</td>
</tr>
<tr>
<td>*Fully-Adjusted Age-, Sex-, Entry Time-Matched Cox HR (95% CI)</td>
<td>1.62 (1.16, 2.26)</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>VTE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases, N</td>
<td>69</td>
<td>336</td>
</tr>
<tr>
<td>Incidence Rate/1000 Person-Years</td>
<td>1.56</td>
<td>0.78</td>
</tr>
<tr>
<td>Age-, Sex-, Entry Time-Matched Cox HR (95% CI)</td>
<td>2.06 (1.59, 2.68)</td>
<td>1.00</td>
</tr>
<tr>
<td>Glucocorticoid-Adjusted Age-, Sex-, Entry Time-Matched Cox HR (95% CI)</td>
<td>1.83 (1.39, 2.40)</td>
<td>1.00</td>
</tr>
<tr>
<td>Number of Outpatient Visit-Adjusted Age-, Sex-, Entry Time-Matched Cox HR (95% CI)</td>
<td>1.66 (1.27, 2.16)</td>
<td>1.00</td>
</tr>
<tr>
<td>*Fully-Adjusted Age-, Sex-, Entry Time-Matched Cox HR (95% CI)</td>
<td>1.53 (1.16, 2.01)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

* Fully-adjusted models include the following selected covariates: Glucocorticoid use and number of outpatient visits.

**Disclosure:** J. Chan, None; A. So, None; E. C. Sayre, None; J. A. Avina-Zubieta, None.


Abstract Number: 884

**Changes in Lipid Levels and Incidence of Cardiovascular Events Following Tofacitinib Treatment in Patients with Psoriatic Arthritis: An Integrated Analysis across Phase 3 and Long-Term Extension Studies**
Dafna D Gladman¹, Christina Charles-Schoeman², Iain B. McInnes³, Douglas J. Veale⁴, Bruce Thiers⁵, Daniela Graham⁶, Cunshan Wang⁶, Thomas Jones⁷, Robert Wolk⁶ and Ryan DeMasi⁷, ¹Department of Medicine, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, ²University of California, Los Angeles, Los Angeles, CA, ³Glasgow Biomedical Research Centre, University of Glasgow, Glasgow, United Kingdom, ⁴St. Vincent’s University Hospital and University College Dublin, Dublin, Ireland, ⁵Medical University of South Carolina, Charleston, SC, ⁶Pfizer Inc, Groton, CT, ⁷Pfizer Inc, Collegeville, PA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment I
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Cardiovascular (CV) disease and cardiometabolic syndrome are common comorbidities/causes of mortality in patients (pts) with psoriatic arthritis (PsA). Tofacitinib is an oral Janus kinase inhibitor under investigation for PsA. We investigated changes in lipid levels and incidence of CV events in pts with PsA treated with tofacitinib in Phase (P) 3 and long-term extension (LTE) studies.

Methods: Data were analyzed for pts who received ≥1 dose of tofacitinib 5 or 10 mg BID or placebo (PBO), integrated across 2 P3 studies (OPAL Broaden [12 months (mo); NCT01877668, including adalimumab control]; OPAL Beyond [6 mo; NCT01882439]) and 1 LTE study (OPAL Balance [data cut-off May 2016; ongoing, database not locked; NCT01976364]). lipid levels were assessed throughout P3 and LTE studies; this analysis included data from the PBO-controlled period (Mo 0–3) of P3 studies. Blood pressure, hypertension events (standardized MedDRA query [narrow]), and adjudicated (independent/blinded to treatment) major adverse cardiovascular events (MACE) are reported for all pts who received ≥1 dose of tofacitinib, pooled across doses. Incidence rates (IR; pts with events/100 pt-years [PY]) and 95% CI are reported.

Results: Overall, 783 pts (776 PY of tofacitinib exposure) were included in P3 and LTE studies; treatment duration was 1–927 days. After 3 mo of tofacitinib treatment in P3 studies, dose-dependent increases in lipid levels were observed with tofacitinib; minimal changes were observed with PBO, except for triglycerides (Fig). Concurrent increases in high-density and low-density lipoprotein (HDL/LDL) and no change in the total cholesterol/HDL ratio were shown. Across P3 and LTE studies, no clinically significant changes in systolic or diastolic blood pressure were seen to 24 mo. Hypertension events were reported in 38 (4.9%) pts: IR 4.93 (95% CI 3.49, 6.77). Of these events, 4 led to pt discontinuation, and 2 were serious adverse events. MACE were reported for 3 (0.4%) pts receiving tofacitinib (IR 0.38; 95% CI 0.08, 1.11), and included sudden cardiac death (57 days of exposure at time of event), myocardial infarction (197 days), and ischemic stroke (80 days). This is within the range reported in tofacitinib studies in pts with psoriasis (IR 0.24 [0.15, 0.37]; 8,759 PY of exposure) and rheumatoid arthritis (RA) (IR 0.38 [0.30, 0.47]; 21,886 PY of exposure). No dose-dependent effects on blood pressure, hypertension, or MACE were apparent.

Conclusion: In pts with PsA, the magnitude and dose dependency of increases in lipid levels to Mo 3 were consistent with findings in tofacitinib studies in pts with psoriasis and RA. In P3 and LTE studies, no clinically significant changes were seen in blood pressure or incidence of hypertension. Incidence of MACE was within the range reported in prior tofacitinib studies in psoriasis and RA; however, the long latency of MACE requires longer-term observation.
Disclosure: D. D. Gladman, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, UCB, 2; AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, UCB, 5; C. Charles-Schoeman, AbbVie, Bristol-Myers Squibb, Pfizer Inc, 2; Amgen, Pfizer Inc, Regeneron-Sanofi, 3; I. B. McInnes, Celgene, Janssen, Novartis, Pfizer Inc, Roche, UCB, 2; AbbVie, Celgene, Janssen, Novartis, UCB, 5; D. J. Veale, AbbVie, Actelion, Bristol-Myers Squibb, Janssen, MSD, Novartis, Pfizer Inc, Roche, UCB, 2; AbbVie, Actelion, Bristol-Myers Squibb, Janssen, MSD, Novartis, Pfizer Inc, Roche, UCB, 8; B. Thiers, Pfizer Inc, Valeant Pharmaceuticals, 5; D. Graham, Pfizer Inc, 1; Pfizer Inc, 3; C. Wang, Pfizer Inc, 1; Pfizer Inc, 3; T. Jones, Pfizer Inc, 1; Pfizer Inc, 3; R. Wolk, Pfizer Inc, 1; Pfizer Inc, 3; R. DeMasi, Pfizer Inc, 1; Pfizer Inc, 3.


Abstract Number: 885

48-Week Complete Remission By Ethnic, Sex and Age Subgroups in Patients with Active Lupus Nephritis Treated with Voclosporin

David Wofsy1, David A. Isenberg2, Frédéric A. Houssiau3, Mary Anne Dooley4, Neil Solomons5 and Simrat Randhawa6, 1Rheumatology, UCSF, San Francisco, CA, 2Centre for Rheumatology Research, Division of Medicine, University College London, London, United Kingdom, 3Rheumatology, Pôle de Maladies Rhumatismales, Université catholique de Louvain, Brussels, Belgium, 4UNC Kidney Centre, Chapel Hill, NC, 5Aurinia Pharmaceuticals Inc., Victoria, BC, Canada, 6Medical Affairs, Aurinia Pharmaceuticals, Victoria, BC, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment I: Novel and Current Therapies
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:
Voclosporin (VCS) is a novel CNI with a favorable metabolic profile, no observed effect on electrolytes, and a predictable dose response potentially eliminating the need for therapeutic drug monitoring.

VCS has completed testing in a global phase II trial, AURA, in patients with active lupus nephritis (LN). In AURA, two doses of VCS (23.7mg BID, 39.5mg BID) were evaluated vs placebo in a double blind RCT when added on top of MMF (2g/ day) and a stringent steroid taper.

Methods:

The primary endpoint was 24-week complete remission (CR). However, blinding and randomization were maintained through 48 weeks permitting further efficacy assessments at 48 weeks. CR required a confirmed UPCR of <0.5 mg/mg, eGFR >60 ml/min without a decrease of >20% from baseline, low-dose steroids for at least 8 weeks prior to the endpoint assessment and no administration of rescue medications.

Results:

Previously reported 24-week data showed a statistically significant CR improvement in patients receiving low dose VCS vs control (32.6% vs. 19.3%; OR: 2.03, p=0.045) and 27.3% in high dose VCS (p=NS). Furthermore, at 24 weeks both doses of VCS demonstrated statistical superiority over control in partial response (PR, 50% reduction in proteinuria from baseline) time to CR and time to PR. VCS treatment effect increased at 48 weeks with 49.4% low-dose (OR 3.21, p<.001) and 39.8% high dose (OR 2.1, p=.026) VCS patients achieving CR vs 29.6% of control patients. Additionally, all low dose VCS patients in CR at 24 weeks remained in CR at 48 weeks. More AEs (84% control, 96% high, 91% low) and SAEs (19% control, 25% high, 28% low) were observed in both VCS arms compared to control. There were 13 deaths (low dose 10, high dose 2, control 1). All deaths were considered unrelated to VCS treatment by investigators and were consistent with cause seen in other LN studies. Eleven of thirteen deaths were clustered in sites with compromised access to standard of care and which disproportionately recruited to the low dose VCS arm. Following completion of study treatment, 3 control arm patients died while one developed a malignancy. No additional deaths were reported in the low dose VCS arm following 24 weeks.

We now present a 48-week CR subgroup analysis based on ethnicity, sex and age.

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Low dose CR% (OR)</th>
<th>High dose CR% (OR)</th>
<th>Control CR %</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>56.7 (3.64)</td>
<td>50 (2.82)</td>
<td>26.2</td>
<td>108</td>
</tr>
<tr>
<td>Asian Indian subcontinent</td>
<td>59.1 (2.95)</td>
<td>40 (1.35)</td>
<td>33.3</td>
<td>60</td>
</tr>
<tr>
<td>Asian other</td>
<td>40 (2.43)</td>
<td>29.2 (1.47)</td>
<td>22.2</td>
<td>72</td>
</tr>
<tr>
<td>Other</td>
<td>28.6 (&gt;99)</td>
<td>25 (&gt;99)</td>
<td>0</td>
<td>25</td>
</tr>
<tr>
<td>Female</td>
<td>51.3 (3.87)</td>
<td>38.3 (2.2)</td>
<td>21.9</td>
<td>230</td>
</tr>
<tr>
<td>Male</td>
<td>38.5 (1.19)</td>
<td>57.1 (2.63)</td>
<td>33.3</td>
<td>35</td>
</tr>
<tr>
<td>Age ≤30</td>
<td>44.2 (2.17)</td>
<td>39.2 (1.7)</td>
<td>27</td>
<td>140</td>
</tr>
<tr>
<td>Age ≥30</td>
<td>56.8 (4.82)</td>
<td>40.5 (2.5)</td>
<td>21.6</td>
<td>125</td>
</tr>
</tbody>
</table>

Conclusion:

48-week subgroup analysis demonstrates sustained VCS treatment effect that was consistent across subgroups. AURA was not powered to show statistical significance in these subgroups; however, odds ratios strongly favored low and high dose VCS across these 8 subgroups. Further data regarding VCS treatment effect in subgroups of patients with active LN will is currently being generated in the phase III AURORA trial.

Disclosure: D. Wofsy, None; D. A. Isenberg, EMD Serono, Inc, 5; F. A. Houssiau, None; M. A. Dooley, None; N. Solomons, Aurinia Pharmaceutical, 3; S. Randhawa, Aurinia Pharmaceuticals, 3.
CC-220 Decreases B-Cell Subsets and Plasmacytoid Dendritic Cells in Systemic Lupus Erythematosus (SLE) Patients and Is Associated with Skin Improvement: Pharmacodynamic Results from a Phase IIa Proof of Concept Study

Victoria P Werth¹, Richard Furie², Allison Gaudy³, Ying Ye³, Shimon Korish³, Nikolay Delev³, Douglas Hough³, Michael Weiswasser³, Suktae Choi³ and Peter Schafer³, ¹University of Pennsylvania and the VA Medical Center, Philadelphia, PA, ²Northwell Health, Great Neck, NY, ³Celgene Corporation, Summit, NJ

First publication: September 18, 2017

BACKGROUND/PURPOSE:
CC-220 is a high affinity ligand for cereblon with immunomodulatory properties, currently in development for the treatment of Systemic Lupus Erythematosus as well as other autoimmune conditions and multiple myeloma. CC-220 administration results in significant reductions in ikaros (IKZF1) and aiolos (IKZF3), transcription factors which are genetically linked to SLE risk, and are overexpressed in the peripheral blood of SLE patients compared to healthy controls.

METHODS:
CC-220-SLE-001 is a randomized, double-blinded, placebo-controlled, phase 2a dose escalation study to investigate the safety, PK, PD, and efficacy of CC-220 in patients with SLE. Forty-two (42) adult SLE subjects fulfilling SLE ACR criteria, having a history of SLE for ≥6 months and a baseline Safety of Estrogens in Lupus Erythematosus National Assessment–Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) score ≥4. Subjects were randomized to placebo or 1 of 4 escalating doses of CC-220 (0.3 mg QOD, 0.3 mg QD, 0.6/0.3 mg alternating QD, or 0.6 mg QD). Efficacy endpoints were exploratory and included Cutaneous Lupus Area and Severity Index (CLASI) skin scores.

RESULTS:
CC-220 significantly reduced total CD20+ B cells, immature B cells, unswitched memory B cells, switched memory B cells, BAFFR+ B cells, and plasmacytoid dendritic cells (pDC) by as much as 96%, 91.2%, 59%, 81.4%, 67.5%, and 86.5% (Day 85 median percent change from baseline), respectively. CD4+ and CD8+ T cell counts were not significantly affected, but trended upward, paralleling an increase in plasma cells in those subjects who received the highest dose (0.6 mg). Mean CLASI activity score at baseline was 9.8 with mean reductions in the CLASI activity score at day 85 ranging from 4.3 to 7.8 in the CC-220 treatment groups compared to an increase of 0.4 in the placebo group. The reductions in CLASI activity score were even more significant among subjects who had moderate-to-severe skin involvement (CLASI score ≥10 at baseline). Strong correlations between CLASI improvement and pDC reductions, rather than B cell depletion, were observed in the overall population and in subjects with a baseline CLASI score ≥10.

CONCLUSION:
CC-220 reduces B-Cell subset populations and pDCs in SLE subjects. Treatment with CC-220 resulted in improvement on CLASI score in all treatment groups compared to placebo with strong correlation with pDC depletion. These results support further development of CC-220 in SLE patient population with skin involvement.
A Randomized, Placebo-Controlled, Double-Blind, Ascending-Dose, Safety, and Pharmacokinetics Study of CC-220 in Subjects with Systemic LUPUS Erythematosus

Richard Furie¹, Victoria P. Werth², Allison Gaudy³, Ying Ye³, Shimon Korish³, Ada Azaryan³, Nikolay Delev³, Douglas Hough³, Michael Weiswasser³, Suktae Choi³ and Peter Schafer³, ¹Northwell Health, Great Neck, NY, ²University of Pennsylvania and the VA Medical Center, Philadelphia, PA, ³Celgene Corporation, Summit, NJ

First publication: September 18, 2017

Background/Purpose: CC-220 is a CUL4CRBN E3 ubiquitin ligase modulator that binds to cereblon and leads to potent and deep reduction of the transcription factors Ikaros (IKZF1) and Aiolos (IKZF3), which are overexpressed in the peripheral blood of Systemic Lupus Erythematosus (SLE) subjects. CC-220 is currently in development for the treatment of SLE as well as other autoimmune conditions and multiple myeloma. This study evaluated the safety, tolerability and pharmacokinetics of CC-220 in subjects with SLE. Exploratory efficacy assessments were included.

Methods: Subjects with history of SLE ≥6 months and a baseline of hybrid SELENA-SLEDAI (hSS) score ≥4 were randomized to 1 of 4 escalating doses of CC-220 or matching placebo (PBO). The 4 active treatments were CC-220 0.3 mg QOD, 0.3 mg QD, 0.3 mg alternating with 0.6 mg QD, and 0.6 mg QD; subjects were randomized 4:1 active to PBO in each group for 12 weeks of treatment, followed by 12 weeks of observational follow-up and/or long-term extension. Stable doses of corticosteroids (≤10 mg prednisone or equivalent daily), non-steroidal anti-inflammatory drugs, and antimalarials were permitted. Safety assessments included clinical evaluation of adverse events (AEs), laboratory parameters, electrocardiograms, physical examinations, and overall tolerability. Exploratory efficacy assessments included hSS, Cutaneous Lupus Area and Severity Index (CLASI) skin scores, Physician Global Assessment (PGA), swollen joint counts (SJC), and tender joint counts (TJC).

Results: A total of 42 adult subjects were randomized; 39 subjects were female (93%); Mean age was 47.2 years; 64% were White and 31% were Black or African-American. Mean SLE duration was 9.4 years, with a mean baseline hSS score of 6.6, CLASI activity score of 9.8, and PGA score of 1.3. Seventy-nine percent of subjects completed the study; 9 of 42 subjects discontinued, of which 6 subjects discontinued due to an adverse event (AE): 1 in the placebo group and 5 in the 2 highest CC-220 groups combined. No discontinuations were due to lack of efficacy. Four subjects had serious AEs (highest CC-220 doses: n=2 [pneumonia]; PBO: n=2). Three subjects had neutropenia (grade 3: n=2; grade 1: n=1); 2 subjects in the highest CC-220 dose group had dermatitis, and 1 subject in the 0.3 mg QD and 1 in the 0.6 mg QD dose groups had urticaria. Pharmacokinetic evaluation demonstrated dose proportional exposure between cohorts, with moderate accumulation in the
Phase 3 Trial Results with Blisibimod, a Selective Inhibitor of B-Cell Activating Factor, in Subjects with Moderate-to-Severe Systemic Lupus Erythematosus

Joan T. Merrill¹, Renee S. Martin², William Shanahan², Morton Scheinberg³, Kenneth C. Kalunian⁴ and David Wofsy⁵,
¹Oklahoma Medical Research Foundation, Oklahoma City, OK, ²Anthera, Hayward, CA, ³Department of Immunology, Center for Clinical Immunology, Sao Paulo SP, Brazil, ⁴Division of Rheumatology, Allergy and Immunology, UCSD School of Medicine, La Jolla, CA, ⁵Rheumatology, UCSF, San Francisco, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment I: Novel and Current Therapies
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: The Phase 3 CHABLIS-SC1 trial (NCT01395745) evaluated blisibimod, an inhibitor of B-cell activating factor (BAFF), in SLE. Prior SLE trials suggested that treatments are better distinguished from placebo in patients with higher disease activity, greater corticosteroid use, anti-double-stranded DNA (dsDNA), low complement. The population in this study was enriched for these factors.

Methods: 442 SLE patients on corticosteroids (≤ 0.5 mg/kg or 40 mg) with anti-nuclear antibodies and/or anti-dsDNA and SELENA-SLEDAI score ≥10 on standard of care medications were randomized to weekly subcutaneous blisibimod (200 mg) or placebo. Patients with renal activity were eligible unless proteinuria exceeded 6 g/24hour or disease severity required escalation of immunosuppressive therapy. Corticosteroid taper was encouraged from Week 8 with the goal to reach ≤7.5 mg prednisone/day. The primary endpoint was the Week 52 SLE Responder Index-6 (SRI-6) in the absence of new/increased immunosuppressives or antimalarials: ≥6-point improvement in SELENA-SLEDAI, no new BILAG 1A or 2B domain scores, and <0.3-point increase in Physician’s Global Assessment.

Results: At enrollment, the mean SELENA-SLEDAI score and corticosteroid dose was 13.5±4.2 and 15.6±9.1mg, respectively. The SRI-6 primary endpoint at Week 52 was not met (Figure), and placebo response was greater than reported in previous studies. More blisibimod-treated subjects achieved corticosteroid taper to prednisone ≤ 7.5 mg/day during Weeks 40-52 and better blisibimod effect was observed under the secondary endpoint which, in addition to meeting SRI-6 criteria at Week 52, required corticosteroid dose in Weeks 40-52 to be lower than baseline (Figure). Reductions in anti-dsDNA, non-alternating dose cohort. An exposure-response analysis demonstrated decreasing B cells, pDCs with increased exposure to CC-220.

Conclusion: CC-220 was generally well tolerated in this SLE population over 12 weeks of treatment, with neutropenia and dermatitis observed at the highest doses studied. Treatment with CC-220 resulted in a trend toward greater improvement in multiple measures of SLE disease activity compared with PBO. These results support further development of CC-220 in SLE patient population.

Disclosure: R. Furie, Celgene, 5; V. P. Werth, Celgene Corporation, 2; A. Gaudy, Celgene, 3; Y. Ye, Celgene, 3; S. Korish, Celgene, 3; A. Azaryan, Celgene Corporation, 3; N. Delev, Celgene Corporation, 3; D. Hough, Celgene Corporation, 3; M. Weiswasser, Celgene, 3; S. Choi, Celgene, 3; P. Schafer, Celgene, 3.


Abstract Number: 888
significant reductions in peripheral B cell lineages, anti-phospholipid antibodies, and immunoglobulins, and significant increases in complement C3 and C4 were observed with blisibimod.

In a subgroup of subjects with baseline urinary protein:creatinine ratio (UPCR) ≥0.5 mg/mg, greater decreases in UPCR from baseline were observed in the blisibimod arm (Figure). At week 52, significantly more subjects who received blisibimod achieved >50% reduction in UPCR from baseline (59.7 vs 30.8%, p=0.006), and/or UPCR <0.5 (53.2 vs 30.8%, p=0.02).

Adverse events were balanced between treatment arms except injection/application site reactions which were more common with blisibimod. None were serious or severe.

**Conclusion:** This study did not meet its primary endpoint. Blisibimod treatment was associated with successful steroid reduction, decreased UPCR, and biomarker responses.

**References:** (1) van Vollenhoven Ann Rheum Dis 2012;71:1343

**Disclosure:** J. T. Merrill, Anthera, Amgen, EMD Serono, GSK, 5; R. S. Martin, Anthera, 1,Anthera, 3; W. Shanahan, Anthera Pharmaceuticals Inc, 1,Anthera Pharmaceuticals Inc, 3; M. Scheinberg, Anthera, 5; K. C. Kalunian, Anthera Pharmaceuticals, 5; D. Wofsy, Anthera, Celgene, GSK, Coherus, 5.


**Abstract Number:** 889

**Attainment of Low Disease Activity By Patients with Systemic Lupus Erythematosus Starting with High Disease Activity in a 24-Week,**
Randomized, Placebo-Controlled, Phase IIb Study of Atacicept (ADDRESS II)

Eric F. Morand¹, Joan T. Merrill², Amy H. Kao³, Cristina Vazquez-Mateo³, Stephen Wax⁴, Peter Chang⁴, Kishore Pudota³ and David A. Isenberg⁵,¹Monash University, Melbourne, Australia, ²Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, ³EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA, ⁴EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA, ⁵Centre for Rheumatology, Division of Medicine, University College London, London, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment I: Novel and Current Therapies
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Low disease activity (LDA) in lupus patients is increasingly a goal of treatment. For instance, Lupus Low Disease Activity State (LLDAS) attainment is associated with reduced damage accrual in patients with SLE (Franklyn et al Ann Rheum Dis 2016). Atacicept targets the B-cell stimulating factors, BLyS and APRIL, and was associated with reduction of disease activity in SLE patients (pts) starting with high disease activity (HDA; SLEDAI-2K ≥10 at Screening) in the Phase IIb ADDRESS II study. We present a post-hoc analysis of LDA attainment by ADDRESS II pts who started with HDA.

Methods: In ADDRESS II (NCT01972568), pts received weekly atacicept (75 or 150 mg SC injection) or placebo (PBO) for 24 weeks (1:1:1 randomization). 3 LDA definitions were used: LDA-1 (SLEDAI-2K ≤ 2); LDA-2 (SLEDAI-2K ≤ 2 and prednisone-equivalent ≤7.5 mg/day); and LLDAS (SLEDAI–2K ≤ 4 without major organ activity, no new disease activity vs previous visit, Physician’s Global Assessment ≤1, prednisone-equivalent ≤7.5 mg/day, and stable maintenance doses of immunosuppressants). Each LDA definition was assessed at each post-baseline study visit. The association of LDA attainment with SLE responder index (SRI)-6 was explored using descriptive statistics, and differences in LDA attainment between HDA pts treated with atacicept vs PBO at Week 24 were analyzed using odds ratio (OR) of LDA attainment estimated from logistic regression.

Results: Of the 306 pts in ADDRESS II, 158 (52%) had HDA at Screening (52 PBO; 55 atacicept 75 mg; 51 atacicept 150 mg). Fig 1 shows the attainment of LDA and SRI-6 response at Week 24: 37 pts (23.4%) achieved LDA-1, 19 (12.0%) LDA-2, 25 (15.8%) LLDAS and 67 (42.4%) SRI-6 response, irrespective of treatment. Each LDA definition identified a similar subset of pts, with LDA-2 the most stringent. Of the SRI-6 responders, 64.2% also attained LDA; all except 2 pts who attained LDA were SRI-6 responders. LDA attainment increased with atacicept dose. Pts who received atacicept 150 mg were more likely to attain LDA at Week 24 vs those who received PBO (LDA-1: OR 3.82 [95% CI 1.44, 10.15], p=0.007; LDA-2: OR 3.30 [95% CI 0.98, 11.17], p=0.055; LLDAS: OR 5.03 [95% CI 1.32, 19.06], p=0.018; Fig 2).

Conclusion: For pts in the ADDRESS II study starting with high disease activity, LDA attainment was associated with SRI-6 response. Treatment with atacicept 150 mg vs PBO was associated with a 3- to 5-fold relative increase in the odds of LDA attainment. These results warrant further evaluation of atacicept in SLE, and suggest that LDA endpoints, including LLDAS, which has been validated against damage accrual, can be robust outcome measures in future SLE clinical trials.
Figure 1. Overlap of Groups Achieving SRI-6 and each of the 3 LDA Definitions at Week 24 for Patients Starting with HDA

LDA-1: SLEDAI-2K ≤2
LDA-2: SLEDAI-2K ≤2 and Prednisone-equivalent ≤7.5 mg/day
LLDAS: SLEDAI-2K ≤4 without major organ activity, no new disease activity compared with previous visit, Physician’s Global Assessment (0–3) ≤1, prednisone-equivalent ≤7.5 mg/day, and stable maintenance doses of immunosuppressants
SRI-6: SLE Responder Index with at least 6-point reduction in SLEDAI-2K

*One patient with LDA-1, LDA-2 and LLDAS was not an SRI-6 responder
Figure 2. Time Course of LDA Attainment in Patients Starting with HDA on Treatment with Atacicept or Placebo

LDA-1: SLEDAI-2K ≤2
LDA-2: SLEDAI-2K ≤2 and Prednisone-equivalent ≤7.5 mg/day
LLDAS: SLEDAI–2K ≤ 4 without major organ activity, no new disease activity compared with previous visit, Physician’s Global Assessment (0–3) ≤1, prednisone-equivalent ≤7.5 mg/day, and stable maintenance doses of immunosuppressants
OR, odds ratio; *p-value < 0.05; **p-value < 0.01

Disclosure: E. F. Morand, None; J. T. Merrill, Anthera Pharmaceuticals, Lilly, EMD Serono, GlaxoSmithKline and Biogen, 5; A. H. Kao, EMD Serono, Inc, 3; C. Vazquez-Mateo, EMD Serono, Inc, 3; S. Wax, EMD Serono, Inc., 3; P. Chang, EMD Serono, Inc, 3; K. Pudota, EMD Serono Research & Development Institute, 3; D. A. Isenberg, EMD Serono, Inc, 5.

Synergetic B-Cell Immunomodulation with Rituximab and Belimumab Combination Treatment in Severe, Refractory SLE

Tineke Kraaij1, Sylvia W.A. Kamerling1, Esther N.M. de Rooij1, Paul L. van Daele2, O.W. Bredewold1, Jaap A. Bakker3, Ingeborg Bajema4, Hans U. Scherer5, Rene E.M. Toes5, Tom W.J. Huizinga5, Ton Rabelink1, Cees van Kooten1 and Y.K. Onno Teng1, 1Nephrology, Leiden University Medical Center, Leiden, Netherlands, 2Immunology, Erasmus Medical Center, Rotterdam, Netherlands, 3Clinical Chemistry and Laboratory Medicine, Leiden University Medical Center, Leiden, Netherlands, 4Pathology, Leiden University Medical Center, Leiden, Netherlands, 5Rheumatology, Leiden University Medical Center, Leiden, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment I: Novel and Current Therapies
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:
Neutrophil extracellular traps (NETs) are auto-antigenic DNA strands and potentially give rise to SLE-specific autoantibodies that can deposit in glomeruli. It has been shown that autoantibodies can induce NETs, contributing to the vicious circle of immune activation in SLE. We hypothesized that eliminating autoantibodies can lead to decreased NET induction and thereby ameliorating disease in SLE. Therefore, we designed a proof-of-concept study to eliminate autoantibodies and NET formation through synergetic B-cell immunomodulation (SynBiose) with rituximab and belimumab (RTX+BLM) in severe, refractory SLE.

Methods:
We treated patients with severe, refractory SLE in a phase 2 study with RTX+BLM. The primary endpoint assessed reduction of pathogenic autoantibodies and NET induction at 24 weeks. Anti-dsDNA autoantibodies were measured and high sensitivity FACS was performed to assess B-cell subsets. NET induction was measured with 3D confocal immunofluorescence microscopy.

Results:
We included 14 patients with severe, refractory SLE of whom 11 had a renal flare. At 24 weeks we observed significant reductions in anti-dsDNA autoantibodies (p=0.0015). CD19+ B-cells were depleted throughout the study (p=0.0005) while plasma cells (PCs) temporarily decreased but returned at week 24 despite persistent depletion of transitional B-cells. Taken together with the observed reductions of autoantibodies and stable total IgG, there is no reconstitution of autoreactive PCs. We also observed significant decrease in NET reduction (p=0.0017). In vitro studies elucidated this resulted in reduction of immune complexes by RTX+BLM. Importantly, the beneficial immunological effects translated to amelioration of clinical disease activity: SLEDAI decreased from a median of 18 to 2 (p=0.0002). Ten out of 11 LN patients showed a response (4 complete renal responders). The response was achieved while tapering immunosuppressive medication. Treatment was generally well-tolerated.

Conclusion:
The SynBiose study is the first to demonstrate that RTX+BLM ameliorated disease in severe SLE in association with the reduction of pathogenic autoantibodies and immune complex-mediated NET induction. Therefore, RTX+BLM represents a novel treatment concept in SLE.

Disclosure: T. Kraaij, None; S. W. A. Kamerling, None; E. N. M. de Rooij, None; P. L. V. Daele, None; O. W. Bredewold, None; J. A. Bakker, None; I. Bajema, None; H. U. Scherer, None; R. E. M. Toes, None; T. W. J. Huizinga,
Long-Term Efficacy and Safety of Tocilizumab in Patients with Refractory Takayasu Arteritis Treated Continuously over 52 Weeks: Results from Phase 3, Randomized, Double-Blind, Placebo-Controlled Trial and Open-Label Extension in Japan

Yoshikazu Nakaoka1, Mitsuaki Isobe2, Syuji Takei3, Yoshiya Tanaka4, Tomonori Ishii5, Shumpei Yokota6, Akira Nomura7, Seitaro Yoshida7 and Norihiro Nishimoto8, 1Department of Vascular Physiology, National Cerebral and Cardiovascular Center Research Institute, Osaka, Japan, 2Sakakibara Heart Institute, Tokyo, Japan, 3Pediatrics of Developmental Medicine, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima, Japan, 4The First Department of Internal Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan, 5Clinical Research, Innovation and Education Center, Tohoku University Hospital, Sendai, Japan, 6Laboratory of Pediatric Research, Institute of Medical Science, Tokyo Medical University, Tokyo, Japan, 7Chugai Pharmaceutical Co., Ltd., Tokyo, Japan, 8Department of Molecular Regulation for Intractable Disease, Institute of Medical Science, Tokyo Medical University, Tokyo, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Vasculitis I: Clinical Trials and Outcomes
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Tocilizumab (TCZ), a humanized anti–IL-6 receptor antibody, showed a favorable trend toward relapse suppression in patients (pts) with refractory Takayasu arteritis (TAK) in a randomized, double-blind (DB), placebo-controlled, multicenter trial in Japan (TAKT Study; Arthritis Rheumatol. 2016;68:suppl 10). However, little is known about the long-term efficacy and safety of TCZ in pts with TAK. Here we present the efficacy and safety of TCZ treatment over 52 weeks (wks) in the DB period and open-label extension (OLE) of the ongoing TAKT Study.

Methods: Pts ≥12 years old with TAK diagnosed according to the Japanese Circulation Society guideline (Circ J. 2011;75:474-503), who had relapsed while receiving oral glucocorticoid (GC; ≥0.2 mg/kg/day prednisolone equivalent) within the prior 12 wks, were randomly assigned 1:1 to weekly subcutaneous TCZ 162 mg or placebo (PBO) after achieving remission with oral GC therapy. During the DB period, background GC was tapered by 10%/wk from Wk 4 to a minimum of 0.1 mg/kg/day. Pts who experienced protocol-defined relapse during the DB period could enter the OLE period to receive weekly TCZ 162 mg. The DB period ended when relapse of TAK occurred in 19 pts and all pts were eligible to move on to the OLE period. During the OLE period, background GC doses were adjusted at the investigator’s discretion. All pts were evaluated for reduction of GC dose and protocol-defined relapse of TAK in long-term treatment of TCZ.

Results: Thirty-six pts were randomized to receive study treatment (18 pts received TCZ and 18 pts received PBO) in the DB period and all pts entered the OLE period. As of the November 2016 data cut-off, 7 pts had withdrawn from the study during the OLE period. The median (min–max) total duration of TCZ treatment was 70.4 (8.1–108.0) wks and 31 pts were treated with TCZ over 52 wks. The median GC dose decreased from 0.22 mg/kg/day at relapse before participation in the study to 0.13 mg/kg/day at Wk 52 (Figure). Twelve of the 31 pts achieved at least 50% reduction of GC dose and 2 pts were weaned off GC at Wk 52. Protocol-defined relapse was observed in 8 pts during the OLE period. The exposure-adjusted relapse rate was 23.6 events per 100 patient-years (PYs) in the OLE period while they were 203.1 events per 100 PYs in the PBO group and 101.1 events per 100 PYs in the TCZ group in the DB period. In total, 34 (94.4%) pts experienced at least 1 adverse event (AE) while receiving TCZ. The exposure-adjusted AE rate did not increase after the DB period. Serious AEs...
were reported in 6 pts (16.7%). Infections were the most frequent AEs (31 pts; 86.1%) and SAEs (2 pts; 5.6%). No new safety concerns were observed with TCZ throughout the study. No pts died in this study.

**Conclusion:** Over 52 wks, TCZ exhibited sustained, clinically meaningful, steroid-sparing effects in pts with refractory TAK. TCZ continued to show a safety profile consistent with that observed with RA/JIA.

**Disclosure:** Y. Nakaoka, Chugai, Takeda, 2,Chugai, Daiichi Sankyo, MSD, Kowa, 8,Chugai, 5; M. Isobe, None; S. Takei, Chugai, Eisai, Takeda, Bristol-Myers Squibb, 2,Chugai, Mitsubishi-Tanabe, Pfizer, Ayumi, 8; Y. Tanaka, Mitsubishi-Tanabe, Takeda, Daiichi-Sankyo, Chugai, Bristol-Myers, MSD, Astellas, Abbvie, Eisai, 2,Abbvie, Chugai, Daiichi-Sankyo, Bristol-Myers, Mitsubishi-Tanabe, Astellas, Takeda, Pfizer, Teijin, Asahi-kasei, YL Biologics, Sanofi, Janssen, Eli Lilly, GlaxoSmithKline, 8; T. Ishii, Chugai, Ono, Pfizer, Mitsubishi-Tanabe, Astellas, 8; S. Yokota, Chugai, 5,Chugai, 7; A. Nomura, Chugai, 3; S. Yoshida, Chugai, 3; N. Nishimoto, Chugai, 2,Chugai, 5,Chugai, 7.


**Abstract Number:** 892

**Health-Related Quality of Life in Patients with Giant Cell Arteritis Treated with Tocilizumab in a Randomized Controlled Phase 3 Trial**

Vibeke Strand, Sophie Dimonaco, Katie Tuckwell, Micki Klearman, Neil Collinson and John H. Stone, 1 Division of Immunology/Rheumatology, Stanford University, Stanford, CA, 2Roche Products, Ltd., Welwyn Garden City, United Kingdom, 3Genentech, South San Francisco, CA, 4Massachusetts General Hospital Rheumatology Unit, Harvard Medical School, Boston, MA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Vasculitis I: Clinical Trials and Outcomes

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 2:30PM-4:00PM

**Background/Purpose:** Superior rates of sustained glucocorticoid (GC)–free remission were shown in patients with giant cell arteritis (GCA) treated with weekly (QW) or every-other-week (Q2W) subcutaneous (SC) tocilizumab (TCZ) 162 mg + 26-week GC taper (TCZ+26) for 52 weeks compared with placebo + 26-week or 52-week GC taper (PBO+26 or PBO+52) in a phase 3 randomized controlled trial (GiACTA). Improvements in patient-reported SF-36 Physical Component Summary (PCS) score and Patient Global Assessment (PtGA) of disease activity were also reported for TCZ vs PBO+52 (Stone JH et al, *N Engl J Med*, in press). QW TCZ was recently approved for the treatment of patients with GCA.
Methods: Exploratory analysis of patient-reported outcomes (PROs) was performed in patients treated with QW TCZ+26 \((n = 100)\) vs PBO+52 \((n = 51)\) for 52 weeks based on observed data. Analyses included mean PROs based on a repeated-measures model that included all patients and post-escape data. Post hoc exploratory analyses were based on proportions of patients, and those who withdrew were classified as nonresponders at week 52.

Results: Improvements in SF-36 Physical Component Summary (PCS) and Mental Component Summary (MCS) scores, 6 of 8 domains, and Functional Assessment of Chronic Illness Therapy (FACIT)–Fatigue at week 52 were statistically greater with QW TCZ+26 than PBO+52 (descriptive \(p < 0.01\); Table, Figure); similar trends were observed vs PBO+26 (not shown). At week 52, mean scores exceeded age and gender (A/G)–matched normative scores with QW TCZ+26; higher proportions of patients reported scores \(\geq\)A/G norms in SF-36, PCS, MCS, all domains, and FACIT-Fatigue scores (Table). The median cumulative prednisone dose over 52 weeks was lower with QW TCZ+26 (1862.0 mg) than with PBO+52 (3817.5 mg) \((p < 0.0001)\).

Conclusion: Patients with GCA treated with weekly TCZ 162 mg and a 26-week taper reported greater improvements in health-related quality of life and fatigue than those treated with a 52-week prednisone taper alone, in part ascribed to lower prednisone doses.

<table>
<thead>
<tr>
<th>Table</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>PBO+52</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 51</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Baseline</td>
</tr>
<tr>
<td>PCGA Mean score</td>
<td>47.78</td>
</tr>
<tr>
<td>FACIT-Fatigue Mean score</td>
<td>31.42</td>
</tr>
<tr>
<td>≥A/G norms (40.0)</td>
<td>32.7%</td>
</tr>
<tr>
<td>SF-36 PCS Mean score</td>
<td>41.12</td>
</tr>
<tr>
<td>≥A/G norms (50.0)</td>
<td>20.4%</td>
</tr>
<tr>
<td>SF-36 MCS Mean score</td>
<td>40.45</td>
</tr>
<tr>
<td>≥A/G norms (50.0)</td>
<td>34.7%</td>
</tr>
<tr>
<td>SF-36 domain scores</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical function</td>
<td></td>
</tr>
<tr>
<td>Mean score</td>
<td>59.40</td>
</tr>
<tr>
<td>≥A/G norms (67.56)</td>
<td>42.0%</td>
</tr>
<tr>
<td>Role physical</td>
<td></td>
</tr>
<tr>
<td>Mean score</td>
<td>45.38</td>
</tr>
<tr>
<td>≥A/G norms (69.44)</td>
<td>28.0%</td>
</tr>
<tr>
<td>Bodily pain</td>
<td></td>
</tr>
<tr>
<td>Mean score</td>
<td>55.67</td>
</tr>
<tr>
<td>≥A/G norms (64.52)</td>
<td>34.7%</td>
</tr>
<tr>
<td>General health</td>
<td></td>
</tr>
<tr>
<td>Mean score</td>
<td>55.69</td>
</tr>
<tr>
<td>≥A/G norms (66.49)</td>
<td>36.0%</td>
</tr>
<tr>
<td>Vitality</td>
<td></td>
</tr>
<tr>
<td>Mean score</td>
<td>42.38</td>
</tr>
<tr>
<td>≥A/G norms (58.65)</td>
<td>28.0%</td>
</tr>
<tr>
<td>Social function</td>
<td></td>
</tr>
<tr>
<td>Mean score</td>
<td>63.00</td>
</tr>
<tr>
<td>≥A/G norms (81.49)</td>
<td>40.0%</td>
</tr>
<tr>
<td>Role emotional</td>
<td></td>
</tr>
<tr>
<td>Mean score</td>
<td>60.33</td>
</tr>
<tr>
<td>≥A/G norms (82.08)</td>
<td>36.0%</td>
</tr>
<tr>
<td>Mental health</td>
<td></td>
</tr>
<tr>
<td>Mean score</td>
<td>59.10</td>
</tr>
<tr>
<td>≥A/G norms (77.16)</td>
<td>24.0%</td>
</tr>
</tbody>
</table>

A/G norms, age- and gender-matched normative values; LSMA, least squares mean change from baseline to wk 52.

All analyses are based on observed data (post-escape data are included). Mean scores are based on a repeated-measures model. A/G norm values are shown in parentheses.

\(p < 0.01\) vs PBO+52.
**Disclosure:** V. Strand, AbbVie, Amgen, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Celltrion, CORRONA, Crescendo, EMD Serono, Genentech/Roche, GSK, Janssen, Lilly, Merck, Novartis, Pfizer, Protagen, Regeneron, Samsung, Sandoz, Sanofi, UCB, 5; S. Dimonaco, Roche Products Ltd., 1, Roche Products Ltd., 3; K. Tuckwell, Roche, 1, Genentech, 3; M. Klearman, Genentech/Roche, 1, Genentech/Roche, 3; N. Collinson, Roche Products Ltd., 1, Roche Products Ltd., 3; J. H. Stone, Roche, 2, Roche, 5.

**Efficacy and Safety of Belimumab in Combination with Azathioprine for Remission Maintenance in Granulomatosis with Polyangiitis and Microscopic Polyangiitis: A Multicenter Randomized, Placebo-Controlled Study**

David Jayne¹, Daniel Blockmans², Raashid Luqmani³, Beulah Ji⁴, Yulia Green⁵, Leanne Hall⁶, David Roth⁷ and Peter A. Merkel⁸, ¹Vasculitis and Lupus Clinic, Department of Medicine, University of Cambridge, Cambridge, United Kingdom, ²General Internal Medicine, University Hospital Gasthuisberg, Leuven, Belgium, ³Botnar Research Centre, University of Oxford, Oxford, United Kingdom, ⁴GSK Stockley Park, Uxbridge, United Kingdom, ⁵GSK Stockley Park, Stockley Park, United Kingdom, ⁶GSK Stevenage, Stevenage, United Kingdom, ⁷GSK Collegeville, Collegeville, PA, ⁸Division of Rheumatology, University of Pennsylvania, Philadelphia, MN

**First publication:** September 18, 2017

**SESSION INFORMATION**
Background/Purpose: GPA (Wegener’s) and MPA are organ- and life-threatening systemic vasculitides characterized by the presence of ANCA-associated vasculitis (AAV), implicating B cells in disease pathogenesis. This study investigated the efficacy and safety of belimumab (BEL), a monoclonal antibody that inhibits B lymphocyte stimulator, in addition to standard of care, for the maintenance of remission in AAV following a standard induction regimen.

Methods: This multicenter, double-blind study (BEL115466/NCT01663623) randomized (1:1) patients (≥18 years) with GPA or MPA in remission (Birmingham Vasculitis Activity Score [BVASv3] = 0 plus prednisolone ≤10 mg/day or equivalent) following prior induction with CYC or RTX for new or relapsing disease. Patients received azathioprine (AZA) 2 mg/kg/day, and oral glucocorticoids, plus either intravenous BEL 10 mg/kg or placebo (PBO) (Days 0, 14, 28, and every 28 days thereafter until study completion [12 months after last patient randomized]). The primary endpoint was time to first relapse, defined as ≥1 major BVAS item, total BVAS score ≥6, or receipt of prohibited medications resulting in treatment failure. Adverse events (AE) were monitored. The study was truncated from 300 to 105 patients due to changes in conventional treatment practice.

Results: When the study stopped, of 105 patients in the intent-to-treat population, 76 continued for ≥1 year, 21 for ≥2 years, and 2 for ≥3 years. Baseline data:

<table>
<thead>
<tr>
<th>Table 1. Baseline demographics and disease characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Age, years</td>
</tr>
<tr>
<td>Sex, female</td>
</tr>
<tr>
<td>Disease duration, years</td>
</tr>
<tr>
<td>Disease stage pre-induction</td>
</tr>
<tr>
<td>Initial diagnosis</td>
</tr>
<tr>
<td>Relapsing disease</td>
</tr>
<tr>
<td>GPA</td>
</tr>
<tr>
<td>MPA</td>
</tr>
<tr>
<td>ANCA type (historical diagnosis)</td>
</tr>
<tr>
<td>Anti-PR3</td>
</tr>
<tr>
<td>Anti-MPO</td>
</tr>
<tr>
<td>Induction regimen</td>
</tr>
<tr>
<td>Intravenous CYC</td>
</tr>
<tr>
<td>Oral CYC</td>
</tr>
<tr>
<td>Rituximab</td>
</tr>
</tbody>
</table>

There was no significant difference in time to first relapse between treatment groups: adjusted hazard ratio (95% confidence interval), 1.07 [0.44, 2.59]; p=0.884. Among patients who relapsed (BEL, 10 [19%]; PBO, 11 [21%]), median (range) time to first relapse was 162 (1–371) days for BEL and 95 (15–789) days for PBO. For patients induced with RTX there were 0/1 relapses classified as vasculitis related in the BEL group versus 3/4 in the PBO group. In CYC-induced patients there were 6/9 versus 5/7 vasculitis relapses, respectively. At the final visit (double-blind) most patients were in remission (BEL, 40 [82%]; PBO, 40 [87%]).

AEs were reported in 49 (93%) BEL and 43 (83%) PBO patients post baseline. The most common AE category was infection (BEL, 30 [57%]; PBO, 30 [58%]). Serious AEs (SAEs) occurred in 18 (34%) BEL and 16 (31%) PBO patients; the most common category was infection (BEL, 4 [8%]; PBO, 4 [8%]).

Conclusion: In patients with AAV who were in remission, the addition of BEL to maintenance therapy with AZA and oral glucocorticoids did not reduce risk of relapse. RTX-induced patients exhibited numerically fewer relapses of vasculitis with
treatment with belimumab compared with placebo, warranting further investigation. Overall relapse rate was low (21/105 [20%]). No new safety signals were identified for BEL in the overall population.

Study funded/conducted by GSK. Editorial assistance: Sam Halliwell, PhD, Fishawack Indicia Ltd, funded by GSK

**Disclosure:** D. Jayne, None; D. Blockmans, None; R. Luqmani, Arthritis Research UK, GSK, MRC, UCSF/OIF, Canadian Institutes of Health Research, The Vasculitis Foundation, 2, Roche, GSK, Medpace, MedImmune, 5; B. Ji, GSK, 1, GSK, 3; Y. Green, GSK, 1, GSK, 3; L. Hall, GSK, 1, GSK, 3; D. Roth, GSK, 1, GSK, 3; P. A. Merkel, Actelion, Alexion, Boston Pharm., Bristol-Myers Squibb, ChemoCentryx, Genzyme/Sanofi, GlaxoSmithKline, Genentech/Roche, InflaRx, PrincipioBio, Proteon, Seattle Genetics, 5, Actelion, Bristol-Myers Squibb, CardianBCT, Celgene, ChemoCentryx, Genentech/Roche, GlaxoSmithKline, Kypha, MedImmune/AstraZeneca, 2, American College of Rheumatology, European League Against Rheumatism, National Institutes of Health: NHLBI, NIAMS, NIAID, NCATS, ORDR, US Food and Drug Administration, The Patient-Centered Outcomes Research Institute, The Vasculitis Foundation, 2.


**Abstract Number:** 894

**All Oral Interferon-Free Antivirals for Hepatitis C Virus Cryoglobulinemia Vasculitis: A Long Term Follow up Multicenter International Study**

Patrice Cacoub1, Si Nafa Si Ahmed2, Yasmina FerFar3, SN Pol4, Dominique Thabut5, Christophe Hezode6, Laurent Albic7, Cloé Comarmond8,9,10, Gaafar Ragab11, Luca Quartuccio12, Mohamed Hegazy13, Thierry Poynard5, Mathieu Resche-Rigon14 and David Saadoun15, 1Department of Internal Medicine and Clinical Immunology, Groupe Hospitalier Pitié-Salpêtrière, Paris, France, 2Hôpital Orléans, Orléans, France, 3Internal Medicine, Hopital Pitié-Salpetrière, Paris, France, 4Department of Hepatology, APHP, Hôpital Cochin, Paris, paris, France, 5Groupe Hospitalier Pitié-Salpêtrière, Paris, France, 6Hôpital Henri Mondor, Creteil, France, 7Centre hospitalier universitaire Purpan, Purpan, France, 8Internal Medicine and Clinical Immunology, Referral Center for Autoimmune diseases, Internal Medicine and Clinical Immunology, Hôpital Pitié Salpêtrière, Paris, France, 9DHU 2iB Internal Medicine Referral Center for Autoimmune diseases Pitie Hospital, Paris, France, 10Internal Medicine, Hôpital Pitié Salpêtrière, Paris, France, 11 Cairo University, Cairo, Egypt, 12University Hospital "Santa Maria della Misericordia, Udine, Italy, 13Faculty of Medicine – Cairo University, Cairo, El Salvador, 14Hôpital Saint-Louis, Paris, France, 15Sorbonne Universités, UPMC Univ Paris 06, UMR 7211, and Inflammation-Immunopathology-Biotherapy Department (DHU i2B), F-75005, Paris, France; INSERM, UMR_S 959, F-75013, Paris, France; CNRS, FRE3632, F-75005, Paris, France; AP-HP, Groupe Hospitalier, Paris, France

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Vasculitis I: Clinical Trials and Outcomes

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 2:30PM-4:00PM

**Background/Purpose:** Interferon (IFN) containing regimens used for hepatitis C virus (HCV)-cryoglobulinemia vasculitis (CryoVas) are poorly effective and associated with important side effects. In small-size and short term studies, direct antiviral agents (DAAs) have been reported to have a better response rate and tolerance. To evaluate effectiveness and
Methods: 145 patients (57 years, 55% F) presenting symptomatic HCV-CryoVas who received DAAs, i.e. Sofosbuvir (SOF) plus Ribavirin (n=50), SOF plus Daclatasvir (n=49), SOF plus Ledipasvir (n=23), SOF plus Simeprevir (n=18), or other DAAs (n=5), for 12 or 24 weeks. Primary efficacy end point was a complete clinical response of CryoVas 12 weeks after stopping antivirals. Secondary endpoints: (i) sustained virological response (SVR12), (ii) tolerance of antivirals, and (iii) complete clinical response of CryoVas at the end of follow up.

Results: Baseline HCV-CryoVas features included arthralgia (64%), purpura (57%), neuropathy (58%), and glomerulonephritis (17%). Forty six (36%) patients had cirrhosis and 70 (48.3%) were naïve of antivirals. At 12 weeks post-DAAs, 103 (72%) showed a complete clinical response, 33 (23.1%) a partial response and 7 (4.9%) no response of CryoVas symptoms. Cryoglobulinemia disappeared in 53.1%. SVR12 was obtained in 97.1%. Premature DAAs withdrawal due to side effects was noted in 6 (4.1%). Main differences between patients with a complete response of the vasculitis (n=103) vs. partial/no response (n=40) were a severe form of CryoVas (65.1% vs 85%), arterial hypertension (22.3% vs. 45%), type 3 mixed cryoglobulinemia (31.3% vs. 9.1%), and use of immunosuppressant/plasma exchange (36.1% vs. 13.7%). The only factor that remained independently associated with a poor response was a severe form of CryoVas [OR 0.26, CI95% 0.07-0.98; P=0.04]. After a median follow-up of 15.3 months, 4 (2.8%) patients died. The 12-months survival rate was 97% [CI95% 94,100]. At the end of follow up, rates of CryoVas manifestations clearance were skin ulcers (98%), purpura (98%), renal involvement (92%), arthralgia (87%), neuropathy (78%) and cryoglobulinemia (54%). Rates of CryoVas complete remission at week12 post-treatment and at the end of follow up were for SOF plus Ribavirin 62% and 70%, SOF plus Simeprevir 67% and 72%, SOF plus Daclatasvir 78% and 88%, and SOF plus Ledipasvir 87% and 87%, respectively.

Conclusion: Sofosbuvir-based IFN-free DAAs combinations are highly effective in HCV-CryoVas patients in short term and long term, with a very good tolerance profile.

Disclosure: P. Cacoub, None; S. N. Si Ahmed, None; Y. FerFar, None; S. Pol, None; D. Thabut, None; C. Hezode, None; L. Albric, None; C. Comarmond, None; G. Ragab, None; L. Quartuccio, None; M. Hegazy, None; T. Poynard, None; M. Resche-Rigon, None; D. Saadoun, None.

Abstract Number: 895

Temporal Trends in Incidence and Outcomes of End-Stage Renal Disease Due to Granulomatosis with Polyangiitis in the US from 1995-2014

Zachary S. Wallace1, Yuqing Zhang2, Leo Lu3, John H. Stone4 and Hyon K. Choi5, 1Division of Rheumatology, Allergy and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, 2Department of Rheumatology, Allergy and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, 3Allergy, Immunology, and Rheumatology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, 4Massachusetts General Hospital Rheumatology Unit, Harvard Medical School, Boston, MA, 5Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Vasculitis I: Clinical Trials and Outcomes
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM
Temporal Trends in Incidence and Outcomes of End-Stage Renal Disease due to Granulomatosis with Polyangiitis in the US from 1995-2014

Background/Purpose:

Granulomatosis with polyangiitis (GPA) often affects the kidneys, frequently leading to end-stage renal disease (ESRD). The national trends in the frequency and outcomes of ESRD due to GPA are largely unknown, although these data would provide important benchmarks in assessing GPA disease burden and care. Our objective was to examine temporal trends in the incidence and outcomes of ESRD due to GPA.

Methods:

We identified ESRD due to GPA in the US Renal Data System (USRDS) between 1995 and 2014, using nephrologists’ ICD-9 coding (446.4) for the ESRD etiology. The cohort was divided into four five-year subcohorts based on year of ESRD onset. Overall and sociodemographic group trends in incidence rates (IRs) were assessed. Changes in rates for mortality, waitlisting, and transplantation were assessed using Cox-proportional hazards models. We conducted analyses taking into account the competing risk of death in analyses for the outcomes of waitlisting and transplantation.

Results:

Between 1995 and 2014, there were 5,929 incident cases. The annual incidence rate increased over the study period (P-for-trend <0.0001). The incidence rate of death (per 1,000 patient-years) declined from 19.0 (17.2-21.1) to 15.3 (14.0-16.7, P<0.0001) with a corresponding adjusted HR of 0.77 (95% CI, 0.67-0.89). The log-rank test also showed significant improvement in survival during the study period (P=0.03) (Figure 1). Adjusted HRs for death were 1.0, 0.90, 0.82, and 0.77 for the 1995-1999, 2000-2004, 2005-2009, and 2010-2014 sub-cohorts, respectively (P-for-trend = 0.005). Accounting for competing risk, there was a 70% increase in the risk of being waitlisted for transplant (adjusted HR for 2010-2014, vs 1995-1999 = 1.7, 95% CI, 1.38-2.11), whereas the risk for transplantation decreased by 30% (corresponding adjusted HR = 0.70, 95% CI, 0.53-0.93).

Conclusion:

The burden of ESRD due to GPA has increased in the US over the past two decades, which is likely related to overall improvements in GPA survival. During the same period, survival of patients with GPA ESRD has improved, although the likelihood for being waitlisted for a transplant is rising with access to renal transplantation becoming more limited. With 5,929 GPA ESRD patients included, this is the largest AAV study to date in the literature.

Figure 1: Kaplan-Meier Curve of Overall Survival in ESRD due to GPA (1995-2014)
Disclosure: Z. S. Wallace, None; Y. Zhang, None; L. Lu, None; J. H. Stone, Xencor, 2; H. K. Choi, None.


Abstract Number: 896

**The Steroid Tapering in ANCA Vasculitis Evaluation Study (STAVE) 2: A Systematic Review and Meta-Analysis**

Jennifer Rodrigues¹, David Collister¹, Amy Archer², Kim Cheema³, Paul Alexander⁴, Christian Pagnoux⁵, Lehana Thabane⁶, Peter A. Merkel⁶, David Jayne⁷ and Michael Walsh¹;

¹Nephrology, McMaster University, Hamilton, ON, Canada, ²Rheumatology, Northwestern University, Chicago, IL, ³Nephrology, University of Calgary, Calgary, AB, Canada, ⁴Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, ON, Canada, ⁵Division of Rheumatology, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada, ⁶Division of Rheumatology, University of Pennsylvania; Perelman School of Medicine, Philadelphia, PA, ⁷Vasculitis and Lupus Clinic, Department of Medicine, University of Cambridge, Cambridge, United Kingdom

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Sunday, November 5, 2017
Session Title: Vasculitis I: Clinical Trials and Outcomes
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM
Background/Purpose: Relapses of ANCA-associated vasculitis (AAV) are associated with death, decreased renal function, and end-stage renal disease. Whether longer-term treatment with glucocorticoids (GC) reduces the risk of relapse is unclear. The objective of this study was to determine the association between dosages of GC and relapse in patients with AAV and update a previous meta-analysis with long-term follow-up and trials with rituximab.

Methods: MEDLINE, EMBASE, Cochrane Clinical Trials, and the Grey Literature were searched from January 1, 2008 until May 26, 2016 without language restriction for studies with patients with AAV. Studies were included if duration of GC use was specified a priori and patients were followed for a minimum of 18 months. Both randomized controlled trials (RCT) and prospective cohort studies were included. Quality of evidence was assessed using modified Newcastle-Ottawa criteria. Meta-analysis was completed using a random-effects model of DerSimonian and Laird.

Results: Twenty-four studies met inclusion criteria consisting of 2272 patients. Thirteen (54%) discontinued GC in less than one year. All patients received additional non-GC immunotherapy for induction of remission and 3 studies (<10% of patients) included patients receiving only GC as maintenance therapy. The pooled relapse rate was 14.3 per 100 patient years (95% CI 4.5, 24.0). Relapse was more frequent when discontinuation of GC at any time was compared to long-term, low-dose GC (20.7 per 100 patient years, 95% CI 6.8,34.5 as compared to 8.0 per 100 patient years, 95% CI 5.7,21.7). Multivariable linear meta-regression confirmed that long-term, low-dose GC was associated with lower relapse rates (b = -0.16, 95% CI -0.26,0.07, P = 0.001) and overall follow up time was associated with increased relapse rates (b = 0.003, 95% CI 0.001,0.006, P = 0.002). Time to discontinuation of non-GC immunotherapy, time to GC discontinuation, study type, renal function, presence of relapsing disease at baseline, and immunotherapy that included oral cyclophosphamide did not demonstrate any significant association with relapse rates.

Conclusion: Long-term, low-dose GC is associated with decreased relapse rates in patients with AAV. The clinical severity and consequences of the excess relapses are not well studied. Characterization and reporting of adverse events limited analysis. These data have implications for both clinical care and trial design. RCTs are needed to determine optimal GC administration in patients with AAV.

Figure Legend: Random effects meta-analysis of long-term, low dose GC as compared to GC discontinuation on relapse per patient year. CYC = cyclophosphamide, MTX = methotrexate, IV = intravenous, PO = oral, MMF = mycophenolate mofetil, AZA = azathioprine, LEF = leflunomide, RTX = rituximab, PLEX = plasma exchange, C = continuation arm, WD = withdrawal arm.

Disclosure: J. Rodrigues, None; D. Collister, None; A. Archer, None; K. Cheema, None; P. Alexander, None; C. Pagnoux, None; L. Thabane, None; P. A. Merkel, Actelion Pharmaceuticals US, Bristol-Myers Squibb, CaridianBCT, Celgene, ChemoCentryx, Genentech/Roche, GlaxoSmithKline, Kypha, MedImmune/AZ, 2,American College of Rheumatology, European League Against Rheumatism, National Institutes of Health, US Food and Drug Administration,
Cutaneous Lupus Is Driven By an Exaggerated Interferon Kappa Loop Which Primes for Interferon Alpha Responses

Johann Gudjonsson¹, Mrinal Sarkar¹, Alex Tsoi², Celine C. Berthier³, Grace Hile⁴, Yun Liang⁴, Jianhua Liu⁵, Paul Harms⁶ and J. Michelle Kahlenberg⁷, ¹Dermatology, University of Michigan, Ann Arbor, MI, ²Departments of Dermatology and Computational Medicine and Bioinformatics, University of Michigan, Ann Arbor, MI, ³Nephrology, Division of Nephrology, University of Michigan Medical Center, Ann Arbor, MI, ⁴University of Michigan, Ann Arbor, MI, ⁵Internal Medicine, Division of Rheumatology, University of Michigan, Ann Arbor, MI, ⁶Pathology, University of Michigan, Ann Arbor, MI, ⁷Internal Medicine, Division of Rheumatology, University of Michigan Medical Center, Ann Arbor, MI

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: 2017 Rheumatology Research Foundation Edmond L. Dubois, MD Memorial Lecture
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Cutaneous inflammation is a common and disfiguring manifestation for 70% of patients with systemic lupus erythematosus, yet our understanding of the pathogenesis of cutaneous lupus erythematosus (CLE) has lagged. Type I IFN signatures are elevated in CLE lesions and contribute to pathology. However, the source of type I IFN production and the function of type I IFNs in CLE has not been examined. We thus investigated the sources of type I IFN in CLE and examined the role of keratinocyte-produced IFN kappa to prime for type I IFN responses in keratinocytes.

Methods: 90 biopsy-proven CLE patients were examined for type I IFN expression using Affymetrix ST2.1 microarray. Tissue expression of IFNs was confirmed with immunofluorescence microscopy. Primary keratinocytes were grown from biopsies of non-lesional, non-sun exposed skin from healthy controls and patients meeting >4 ACR SLE criteria with a history of documented CLE. IFN activation was examined using real-time PCR and Western blot. IFN kappa knockout keratinocyte lines were made using CRISPR/cas9-mediated deletion.

Results: Analysis of CLE lesions confirmed heightened type I IFN responses and demonstrated IFNK as one of only two increased type I IFN transcripts in CLE lesions vs. control skin. IFN kappa was expressed predominantly in the basal keratinocyte layer in both healthy skin and lesional CLE, but its expression was increased in CLE lesions and in non-lesional SLE keratinocytes. Importantly, IFN kappa was required for basal type I IFN responses in keratinocytes. Indeed, absence of IFNK resulted in minimal type I IFN gene expression and a delayed response to exogenous type I IFN stimulation. In contrast, IFN kappa overexpression accelerated and amplified responses to exogenous IFN alpha in a IFN kappa dependent manner.

Conclusion: IFN kappa is a key regulator of IFN responses in keratinocytes. In SLE and CLE, keratinocytes are primed by an abundance of IFN kappa to generate robust responses to exogenous type I IFNs, setting up a feed forward loop which promotes exaggerated IFN responses and subsequent activation of the immune system. Thus, IFN kappa may serve as an excellent and specific target for treatment and prevention of cutaneous inflammation in SLE patients.

Disclosure: J. Gudjonsson, None; M. Sarkar, None; A. Tsoi, None; C. C. Berthier, None; G. Hile, None; Y. Liang, None; J. Liu, None; P. Harms, None; J. M. Kahlenberg, Idera Pharmaceuticals, Celgene, 5.
B Cell Specific TLR9 Suppresses Disease in Murine Lupus

**Jeremy Tilstra**1, Rachael Gordon2, Shinu John3, Brady Marburger2, Sheldon Bastacky4, Kevin Nickerson2 and Mark Shlomchik5, 1Rheumatology, Univ of Pittsburgh Medical Center, Pittsburgh, PA, 2University of Pittsburgh, Pittsburgh, PA, 3Modern Therapeutics, Cambridge, MA, 4Pathology, University of Pittsburgh Medical Center, Pittsburgh, PA, 5Immunology, University of Pittsburgh, Pittsburgh, PA

**First publication:** September 18, 2017

**SESSION INFORMATION**
- **Session Date:** Sunday, November 5, 2017
- **Session Title:** 2017 Rheumatology Research Foundation Edmond L. Dubois, MD Memorial Lecture
- **Session Type:** ACR Concurrent Abstract Session
- **Session Time:** 4:30PM-6:00PM

**Background/Purpose:**
Toll-like receptor (TLR) signaling is a central to lupus pathogenesis. GWAS studies have repeatedly identified components of TLR signaling pathway in SLE patients. Furthermore, the endosomal TLRs, 7 and 9, have been implicated in numerous murine models of SLE. Despite being a “pro-inflammatory” innate immune receptor, TLR9 deficiency in lupus prone MRL.Fas1pr mice exacerbates clinical manifestations including reduced lifespan and more severe nephritis, despite lacking anti-nucleosome (anti-DNA) antibodies; while TLR7 deficiency dominantly ameliorates disease. Similar regulatory roles for TLR9 have been identified in multiple other lupus models. The mechanisms by which TLR9 suppresses rather than promotes autoimmunity are unclear. We hypothesized that TLR9 has cell-specific functions.

**Methods:**
We created two novel murine strains: a conditional TLR9 knock-out (Tlr9flox) and a conditional TLR9 overexpression allele (rosa26-flox-stop-Tlr9). These strains were both fully backcrossed onto lupus prone backgrounds MRL.Fas1pr (MRL/lpr) and B6.Yaa.Fcgr2b-/-Yaa. The Tlr9flox allele was crossed several different cre alleles; including CD19-cre (B cell specific), CD11c-cre (DC specific), MRP8-cre (neutrophil specific), and LysM-cre (macrophage and neutrophil targeting) to assess for cell specific roles of TLR9. Cell specific deletion was assessed using cell sorting and qPCR of genomic DNA. These cohorts were analyzed for disease pathology including proteinuria, renal histology, dermatitis, ANA, and immune cell activation.

**Results:**
Strikingly, of all the strains tested only B-cell specific deletion of TLR9 exacerbated disease, similar to what was observed in the complete knockout, exhibiting increased proteinuria (p<0.05) and nephritis (p<0.05) with loss of anti-DNA antibodies (p<0.001). DC, macrophage and neutrophil cell specific deletion of TLR9 did not result in alteration of pathology. Given the positive results in the B cell specific deletion. We then performed the reciprocal experiment using the TLR9 overexpression allele which results in a 2 fold overexpression of TLR9 in B cells with a concomitant increase in function. When TLR9 was overexpressed only in B cells, we found that disease was ameliorated in two models of SLE, MRL.Fas1pr and B6.Fcgr2b-/-Yaa. In both models, there was reduced renal disease including proteinuria (p<0.05) and glomerulonephritis (p<0.05); however, there were minimal alterations in tested anti-RNA and anti-DNA autoantibodies.

**Conclusion:**
These data, in which we manipulate TLR9 expression in both directions, indicate B cell expression of TLR9 accounts for a substantial proportion of the known TLR9 regulatory effect. Additionally we have effectively ruled out a role for TLR9 in numerous other hematopoietic cell types. The data further suggests that anti-DNA antibodies either play no role or are
protective in SLE pathogenesis in these murine models, thus going against the conventional wisdom in the field. To our knowledge this is the first data to show that TLR9 overexpression can be protective, and given its significant ameliorative effect, TLR9 overexpression in B cells alone may represent a potential therapeutic strategy.

Disclosure: J. Tilstra, None; R. Gordon, None; S. John, None; B. Marburger, None; S. Bastacky, None; K. Nickerson, None; M. Shlomchik, None.

Abstract Number: 899

Neutrophil Gene Signature and Low Density Granulocyte Subsets Associate with Coronary Plaque Burden and Vascular Inflammation in Systemic Lupus Erythematosus

Philip Carlucci1, Monica Purmalek1, Simantini Sakhardande1, Yenealem Temesgen-Oyelakin1, Amit K. Dey2, Aditya A. Joshi2, Joseph B. Lerman3, Alice Fike1, Michael Davis4, Hong-Wei Sun1, Jonathan H. Chung2, Martin P. Playford2, Pragnesh Mistry1, Gustavo Gutierrez-Cruz1, Stefania Dell'Orso1, Faiza Naz1, Heather Teague2, Zerai G. Manna5, Peter C. Grayson1, Mohammad Naqi1, Marcus Chen2, Sarfaraz A. Hashi1, Nehal N. Mehta2 and Mariana J. Kaplan1, 1NIH/NIAMS, Bethesda, MD, 2NIH/NHLBI, Bethesda, MD, 3NIH/CC, Bethesda, MD, 4NIH/NIAMS, Bethesda, IA, 5NIH/NIAMS, Bethesda, MD, Afghanistan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: 2017 Rheumatology Research Foundation Edmond L. Dubois, MD Memorial Lecture
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Systemic lupus erythematosus (SLE) increases a young woman’s risk of myocardial infarction by up to 50-fold. This marked increase in cardiovascular disease (CVD) risk is not explained by Framingham risk and is not well understood. It has been suggested that innate immune responses associated with aberrant neutrophils, known as low density granulocytes (LDGs), enhance CVD risk by promoting vascular damage due to their proinflammatory properties. LDGs may represent a heterogeneous population of neutrophils and the pathogenicity of various LDG subsets has not been characterized. In this study, we sought to explore the association of these cells with subclinical vascular disease.

Methods: SLE patients fulfilling ACR criteria and healthy controls underwent FDG-PET/CT scans to assess vascular inflammation as target-to-background ratio (TBR) and coronary CT angiogram for coronary plaque characterization. Total and non-calcified plaque burden were quantified using QAngio. Circulating LDGs and cholesterol efflux were measured by previously validated methods. RNA sequencing of whole blood was used to analyze the transcriptional profile of both patients and controls. A neutrophil gene signature was created by calculating a z-score for the most upregulated primary granule neutrophil genes (AZU1, MPO, CTSG, PRTN3, ELANE, DEFA3) found in patients with cardiovascular involvement.

Results: Compared to controls, SLE patients had significantly elevated aortic TBR (1.68±0.16 vs.1.59±0.14, p=0.007) and coronary non-calcified plaque burden (NCB) (0.86±0.33 vs. 0.76±0.19, p=0.022). We identified diverse subsets of LDGs based on maturation. The percentage of an immature subset of LDGs was significantly elevated in peripheral blood mononuclear cells in patients compared to controls (1.6 (3.2-0.47) vs. 0.35 (0.96-0.13), p<0.001). This immature subset associated with the primary granule neutrophil gene signature (β=0.844, p<0.001), TBR (β=0.34 p=0.015), and with NCB (β=0.31, p=0.001) in unadjusted analyses. The neutrophil gene signature also associated with NCB (β = 0.44, p<0.001). In addition, a mature subset of LDGs was present in SLE, which associated with TBR (β=0.23, p=0.02), NCB (β=0.31, p=0.002), and HDL efflux (β=-0.29, p=0.024), supporting previous work that suggests the enhanced neutrophil extracellular
trap formation in mature LDGs impairs HDL efflux. These associations persisted after adjusting for traditional risk factors in multivariate analyses.

**Conclusion:** Patients with SLE have an increase in both aortic vascular inflammation and coronary plaque burden compared to controls. The associations of aberrant neutrophil subsets with this atherosclerotic phenotype support studies suggesting a pathogenic role for these cells in assaulting the vasculature and that targeting responses triggered by these cells may have potential therapeutic benefits.

**Disclosure:** P. Carlucci, None; M. Purmalek, None; S. Sakhardande, None; Y. Temesgen-Oyelakin, None; A. K. Dey, None; A. A. Joshi, None; J. B. Lerman, None; A. Fike, None; M. Davis, None; H. W. Sun, None; J. H. Chung, None; M. P. Playford, None; P. Mistry, None; G. Gutierrez-Cruz, None; S. Dell’Orso, None; F. Naz, None; H. Teague, None; Z. G. Manna, None; P. C. Grayson, None; M. Naqi, None; M. Chen, None; S. A. Hasni, None; N. N. Mehta, None; M. J. Kaplan, None.


**Choroid Plexus Tertiary Lymphoid Structures in Lupus: A Novel Neuro-Immune Interface**

**Ariel Stock**, 1, Evan Der, 2, Sivan Gelb, 3, Ayal Ben-Zvi, 3 and Chaim Putterman, 4, 1Microbiology and Immunology, Albert Einstein College of Medicine, Bronx, NY, 2Albert Einstein College of Medicine, Bronx, NY, 3Hebrew University, Jerusalem, Israel, 4Division of Rheumatology, Albert Einstein College of Medicine, Bronx, NY, USA, Bronx, NY

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** 2017 Rheumatology Research Foundation Edmond L. Dubois, MD Memorial Lecture

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 4:30PM-6:00PM

**Background/Purpose:** The central nervous system (CNS) manifestations of SLE remain poorly understood. Although potentially neuropathic autoantibodies have been identified in the serum, lupus patients show inconsistent correlations between these and neuropsychiatric SLE (NPSLE). This is likely due to the highly restrictive nature of the blood brain barrier and the variability between patients in barrier dysfunction and humoral immune transmission into the CNS.

**Methods:** We used the MRL/MpJ-Fas<sup>lpr/lpr</sup> mouse, a well-established model of lupus associated neuropsychiatric deficits, to evaluate the immune effectors responsible for CNS disease. We performed RNA sequencing, immunofluorescent phenotyping, and light and electron microscopy of brain tissue to identify signaling pathways and cellular contributors to NPSLE.

**Results:** We found extensive cellular infiltrates in the MRL/MpJ-Fas<sup>lpr/lpr</sup> choroid plexus by 16 weeks of age, when these mice display profound cognitive deficits and depression like behavior (Figure 1). Transcriptome analysis of the choroid plexus revealed an expression signature driving tertiary lymphoid structure (TLS) formation, including elevated Cxcl13, Lta/β (lymphotoxin α/β), Ccl19, and a host of other cytokines and chemokines related to lymphoid organization. Additionally, gene ontology assessment revealed transcriptional profiles closely related to various stages of lymphocyte activation and germinal center formation. Immunofluorescent evaluation of the choroid plexus defined the cellular infiltrate in NPSLE mice to include locally proliferating B and T cells, extensive T-cell activation, and evidence of in-situ somatic hypermutation and class switch recombination and IgG+ plasma cells. Finally, the choroid plexus was found to be important
in trafficking lymphocytes into the CNS, as evidenced by the routine presence of intra-epithelial lymphocytes on transmission electron microscopy. Evaluation of human lupus choroid plexus tissue is in progress.

**Conclusion:** Collectively, we not only determined a potential new pathway underlying neuropsychiatric lupus, we identified TLS formation in the choroid plexus as a novel mechanism through which the immune system may bypass the blood brain barrier.

![Image](imageurl)

Figure 1: Representative H&E staining and scanning electronic microscopy of the choroid plexus in 16 week old female mice reveals extensive cellular infiltration with dramatically expanded stroma in the choroid plexus in MRL/lpr mice, whereas control MRL/+ mice appear normal. Arrows= choroid plexus epithelium; asterisks= mixed cellular infiltrate.

**Disclosure:** A. Stock, None; E. Der, None; S. Gelb, None; A. Ben-Zvi, None; C. Putterman, None.


**Abstract Number:** 901

**Role of Epstein Barr Virus Serologic Reactivation in Transitioning to Systemic Lupus Erythematosus in at Risk Individuals**

Neelakshi R. Jog¹, Kendra A. Young², Melissa E. Munroe¹, Michael T Harmon³, Joel M. Guthridge⁴, Diane L. Kamen⁵, Gary S. Gilkeson⁶, Michael Weisman⁷, David Karp⁸, John B. Harley⁹,¹⁰, Daniel J. Wallace¹¹, Jill M. Norris¹² and Judith A. James¹³,¹⁴, ¹Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, ²Epidemiology, Colorado School of Public Health, Aurora, CO, ³Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, ⁴Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, OKC, OK, ⁵Medicine/Rheumatology & Immunology, Medical University of South Carolina, Charleston, SC, ⁶Department of Medicine, Medical University of South Carolina, Charleston, SC, ⁷Rheumatology, Cedars-Sinai Medical Center, Los Angeles, CA, ⁸Rheumatology, UT Southwestern Med Ctr, Dallas, TX, ⁹US Department of Veterans Affairs Medical Center, Cincinnati, OH, ¹⁰Cincinnati Children's Hospital Medical Center, Cincinnati, OH, ¹¹Division of Rheumatology, Cedars-Sinai Medical Center, Los Angeles, CA, ¹²Department of Epidemiology, Colorado School of Public Health, Aurora, CO, ¹³Arthritis & Clinical Immunology Program, Oklahoma Medical Research
Systemic Lupus Erythematosus (SLE) is a systemic autoimmune disease characterized by autoantibody production and periods of elevated and suppressed disease activity. Various genetic and environmental factors likely contribute to disease pathogenesis. Epstein Barr Virus (EBV) is an environmental factor consistently associated with SLE. EBV maintains latency in B cells and shows frequent reactivation, which can be measured indirectly in terms of antibodies to EBV antigens. In this study we determined whether antibody measures of viral reactivation and single nucleotide polymorphisms (SNPs) in EBV associated genes were associated with transitioning to SLE in at risk individuals.

Methods: Blood relatives (n=436) of SLE patients who did not meet ACR SLE classification criteria at baseline were evaluated an average of 6.3 (± 3.9) years later. At both baseline and follow-up, detailed demographic, environmental, clinical information, and blood samples were obtained. 56 individuals (13%) transitioned to SLE (> 4 cumulative ACR criteria) as verified by protocolled medical record review. Healthy, matched, unrelated individuals (n=122) were recruited at local health fairs. To assess evidence of viral exposure/reactivation, antibody responses against the EBV antigens Viral Capsid Antigen (VCA) and early antigen (EA) and Cytomegalovirus (CMV) were measured by ELISA. 5 SNPs in IL10, 1 in complement receptor 2 (CR2) and 3 in CD40 gene were typed by Immunochip. Generalized estimating equations (GEE), accounting for correlation within families, were used to test associations between the viral antibody variables and the categorical outcome of transitioning to SLE. Associations between SNPs, seroconversion and disease transition were examined in an additive model. Interactions between SNPs and antibody titers were examined.

Results: Higher proportion of individuals who transitioned to SLE were positive for anti EA IgG at baseline compared to healthy controls (37.5% vs 12.7%, \( p = 0.0005 \)). Mean baseline anti VCA and EA IgG levels were significantly different between those family members who transitioned to SLE and those who did not (4.88±1.80 vs 4.18±2.83; \( p = 0.007 \); 1.19±1.11 vs 0.88±0.76; \( p = 0.008 \) respectively). Increased levels of VCA IgG and EA IgG were associated with transitioning to SLE when compared to healthy controls (OR 1.05, 95%CI 1.01-1.10; OR 1.18, 95%CI 1.09-1.26 respectively). VCA IgG, EA IgG and CMV IgG positively correlated with number of autoantibody specificities and ACR scores at both baseline and follow-up visits. Significant interaction was observed between SNPs in CD40 and VCA IgG and between SNPs in IL10 and VCA IgA in transitioning to SLE.

Conclusion: Elevated EA IgG and VCA IgG were associated with transitioning to SLE in unaffected SLE relatives, suggesting that viral reactivation may contribute to development or worsening of SLE autoimmune responses. To our knowledge, this is the first prospective study examining the pre-clinical association between serologic measures of EBV reactivation and SLE disease transition.

Disclosure: N. R. Jog, None; K. A. Young, None; M. E. Munroe, None; M. T. Harmon, None; J. M. Guthridge, None; D. L. Kamen, None; G. S. Gilkeson, None; M. Weisman, None; D. Karp, None; J. B. Harley, None; D. J. Wallace, None; J. M. Norris, None; J. A. James, None.


Abstract Number: 902

Evidence for Inhibition of Osteoclastogenesis By Cytomegalovirus Infection: Implication in RA Bone Erosion and Identification of a Cellular Protein As a Therapeutic Target
Exacerbated differentiation of monocytes into osteoclasts (OC) contributes to the pathogenesis of rheumatoid arthritis (RA) resulting in severe bone erosion and functional damage. Osteoclastogenesis is initiated by M-CSF and RANKL signalization through their respective receptor CSF-1R and RANK. In vitro, it has been demonstrated that Human Cytomegalovirus (HCMV) infection inhibits macrophage differentiation through a down regulation of numerous receptor, including CSF-1R [Frascaroli et al., J. Immunol., (2009)]. As CSF-1R signaling is essential to induce RANK expression, the key receptor for osteoclast differentiation, we studied the effect of HCMV infection on osteoclastogenesis and evaluated the consequences of HCMV seropositivity on bone erosion evolution in a RA cohort.

Methods: Blood monocytes from healthy donors were purified by adherence selection and differentiated in osteoclast by recombinant M-CSF and RANKL (both at 50 ng/ml) during 12 days. After 24 hours of differentiation, pre-osteoclasts were infected with a HCMV clinical strain (VHL/E) at the m.o.i. of 3. Expression of cellular proteins CSF-1R, RANK, and “X-protein” (patent being filed) and viral protein (IE) expressions were studied by RT-qPCR, Western Blot, Flow Cytometry and fluorescence microscopy. OC differentiation was evaluated by manual counting after TRAP staining. Lentiviral transduction and Amaza transfections were performed to over-express or inhibit the expression of “X-protein” and confirm its role.

We then analyzed patients from the French « ESPOIR » cohort, fulfilling the 2010 ACR/EULAR criteria for RA. We evaluated the correlation between HCMV serology status and structural involvement assessed by the modified Sharp score, at baseline and 1 year.

Results: We demonstrated for the first time that HCMV infection inhibits osteoclastogenesis. No osteoclast was observed in HCMV infected wells in vitro. We observed that HCMV infection inhibits CSF-1R and RANK mRNA and proteins expression in a viral replication dependent manner. We found that viral IE protein expression was followed by an increase of expression of the cellular “X-protein”. To confirm these observations, we over-expressed the “X protein” in monocytes and observed that CSF-1R, RANK and, as a result, osteoclastogenesis were completely inhibited. Knock-down experiment of “X protein” with shRNA lentiviral vectors blocked the inhibitory effect of HCMV on CSF-1R and RANK expression.

Analysis of the ESPOIR cohort, including 273 HCMV+ and 214 HCMV- RA patients, demonstrated that, although there was no difference at inclusion, HCMV seropositive patients displayed less severe bone erosion score in comparison with HCMV negative ones after one year (p=0.0151), thus providing a pathophysiological counterpart of our in vitro observations.

Conclusion: HCMV infection inhibits osteoclastogenesis through a mechanism involving “X-protein” and results in a protective effect on bone erosion during RA. Over expression of this “X-protein” inhibited OC differentiation and could be a new therapeutic target to limit bone erosion during chronic inflammatory disease such as RA and in osteoporosis.

Disclosure: B. Rauwel, None; M. Baron, None; A. Ruyssen-Witrant, None; D. Nigon, None; Y. Degboé, None; J. Izopet, None; A. Cantagrel, None; J. L. Davignon, None.


Abstract Number: 903
Increased Expression of CCN4/WISP1 in Osteoarthritic Articular Cartilage Is Epigenetically Regulated and Disrupts Cartilage Homeostasis

Martijn H. van den Bosch,1 Yolande F. Ramos,2 Wouter den Hollander,2 Nils Bömer,2 Rob G. Nelissen,3 Judith V. Bovée,1 Peter L. van Lent1, Arjen B. Blom1, Peter M. van der Kraan1 and Ingrid Meulenbelt2,
1Experimental Rheumatology, Radboud university medical center, Nijmegen, Netherlands, 2Department of Molecular Epidemiology, Leiden University Medical Center, Leiden, Netherlands, 3Department of Orthopedics, Leiden University Medical Center, Leiden, Netherlands, 4Department of Pathology, Leiden University Medical Center, Leiden, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Biology and Pathology of Bone and Joint
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Previously, we described increased expression of Wnt-1-induced signaling protein 1 (Wisp1) in murine synovium and cartilage after induction of experimental osteoarthritis (OA) models. WISP1 is a downstream target of canonical Wnt signaling, which has been shown to play a pivotal role in the etiopathology of OA. In agreement with this, we have observed increased breakdown of the articular cartilage after overexpression of Wisp1 in naïve mouse knee joints, whereas Wisp1−/− mice revealed decreased cartilage degeneration in three independent experimental OA models compared to wild type controls. Together, these data indicate a direct correlation between Wisp1 and OA in mice. In the current study we set out to characterize the relation between expression of WISP1 and human OA.

Methods: Articular cartilage from preserved and degenerated OA areas was collected from 39 Caucasian end-stage OA patients. Cartilage from non-OA-diagnosed individuals was collected after femoral neck fractures. Cartilage degeneration was classified according to the Mankin scoring system. DNA was isolated to determine correlation between WISP1 expression and methylation profiles using Generalized Linear Mixed Model (GLMM). RNA expression levels were determined with microarray analysis and RNA sequencing analysis. Immunohistochemical staining was used to determine WISP1 protein expression. Recombinant WISP1 was added to human chondrocyte microparticles, and cartilage extracellular matrix deposition was determined by measuring cartilage microparticle size and Safranin O/Fast Green staining.

Results:

We observed increased WISP1 expression in cartilage of OA patients compared to non-OA-diagnosed controls. Moreover, within OA patients, both WISP1 mRNA and protein expression were significantly increased in OA-affected cartilage compared to preserved regions of the same joint, and WISP1 expression significantly correlated with Mankin score. Interestingly, we found that positional CpG dinucleotides were hypomethylated in cartilage of OA-affected areas as compared to unaffected areas from the same joint, which correlated with increased RNA expression as determined with both microarray analysis and RNA sequencing analysis. Of note, methylation levels of a CpG affecting WISP1 transcription were found to highly significantly correlate to a single nucleotide polymorphism (SNP) at the WISP1 locus. Next, to investigate effects of increased WISP1 levels on chondrocyte microparticles, we added human recombinant WISP1. This resulted in a significantly decreased deposition of cartilage extracellular matrix as reflected by decreased microparticle circumference, and a strongly decreased proteoglycan content, suggesting that increased WISP1 levels are detrimental to cartilage.

Conclusion:

The expression of WISP1 is increased in OA-affected as compared to preserved articular cartilage. This increased expression is inversely correlated with methylation levels of a positional CpG, which was found to be under the influence of a SNP at the WISP1 locus. Together, our results suggest that tight regulation of WISP1 expression via methylation is essential to maintain cartilage homeostasis.

Disclosure: M. H. van den Bosch, None; Y. F. Ramos, None; W. den Hollander, None; N. Bömer, None; R. G. Nelissen, None; J. V. Bovée, None; P. L. van Lent, None; A. B. Blom, None; P. M. van der Kraan, Contract research UCB, 2; I. Meulenbelt, None.
Deficient Autophagy Induces Lamin a/C Accumulation in Aging and Osteoarthritis

Paloma Lopez de Figueroa1, Uxia Nogueira-Recalde2, Fernando Osorio3, Martin Lotz4, Carlos Lopez-Otin3, Francisco J Blanco2 and Beatriz Carames1, 1Cartilage Biology Group. Rheumatology Division, INIBIC-CHUAC, A Coruña, Spain, A Coruña, Spain, 2Cartilage Biology Group. Rheumatology Division, INIBIC-CHUAC, A Coruña, A Coruña, Spain, 3Degradome Lab, Universidad de Oviedo, Oviedo, Spain, 4Department of Molecular & Experience Medicine, Scripps Research Institute, LaJolla, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Biology and Pathology of Bone and Joint
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Autophagy, an essential chondrocyte homeostasis mechanism, is defective in Aging and Osteoarthritis (OA). However, the targets regulating this mechanism are still unknown. Here, we aimed to identify targets regulating autophagy in human chondrocytes.

Methods: We performed quantitative proteomic analysis of Atg5 knockdown primary human chondrocytes using iTRAQ (isobaric tags for relative and absolute quantitation) labeling coupled with on-line 2D LC/MS/MS. Protein identification and quantification were performed using Protein Pilot Software v 4.0. Each MS/MS spectrum was searched in the Uniprot/Swissprot database for Homo sapiens. Human chondrocytes and human cartilage from healthy, aged and OA patients were employed to confirm the role of the identified target by Western Blot (WB), Immunofluorescence (IF) and Immunohistochemistry (IHC). Importantly, CRISPR/Cas9 genome editing technology and mutant mice were used for mechanism of action studies.

Results: 24 out of 487 proteins were significantly altered (p<0.05) in response to defective autophagy. Cytoskeleton organization, collagen catabolism, oxidative stress, and aging pathways were affected. Interestingly, Lamin A/C, a nuclear protein implicated in cell senescence, was found upregulated under defective autophagy. Increased Lamin A/C expression was found in human chondrocytes with reduced autophagy. Furthermore, aging and OA human cartilage showed increased Lamin A/C expression. Induction of chondrocyte aging by genetic deletion of Zinc Metalloproteinase STE24 (Zmpste24) via CRISPR-Cas9, lead to Lamin A/C accumulation, accompanied by a reduction of LC3 and increased chondrocyte death and mitochondrial dysfunction. Importantly, Zmpste24 KO mice showed bone damage and intervertebral disc degeneration (IDD), suggesting that deficient autophagy is correlated with aging and OA phenotype.

Conclusion: Lamin A/C, a nuclear protein contributing to structural integrity to the nucleus and matrix was identified as candidate target for regulating cartilage function under defective autophagy, such as aging and OA. These results support the hypothesis that autophagy is decreased with aging. Therefore, targeting autophagy might be a promising strategy to find novel therapeutics for cartilage aging and OA.

Disclosure: P. Lopez de Figueroa, None; U. Nogueira-Recalde, None; F. Osorio, None; M. Lotz, None; C. Lopez-Otin, None; F. J. Blanco, None; B. Carames, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/deficient-autophagy-induces-lamin-ac-accumulation-in-aging-and-osteoarthritis
Regenerating Cartilage and Reversing Osteoarthritis (OA) Stimulation of Adenosine A2A Receptors (A2AR) Increases Cartilage Volume and Matrix in Vitro and In Vivo

Carmen Corciulo1, Cristina Castro2, Thomas Coughlin3, Tuere Wilder1, Oran Kennedy4 and Bruce Cronstein5,
1Department of Medicine, Division of Rheumatology, NYU School of Medicine, New York, NY, 2Medicine, NYU School of Medicine, New York, NY, 3Orthopaedic Surgery, NYU School of Medicine, New York, NY, 4Department of Anatomy, Royal College of Surgeons, Dublin, Ireland, 5Rheumatology, New York University School of Medicine, Division of Rheumatology, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Biology and Pathology of Bone and Joint
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: We have recently reported that endogenously produced adenosine, interacting with A2AR, is a critical autocrine factor for maintenance of chondrocyte and cartilage homeostasis and intra-articular injections of liposomal preparations of adenosine inhibit progression of OA in a post-traumatic OA (PTOA) model in rats. We therefore determined whether intra-articular injection of a more selective A2AR agonist could also prevent progression and possibly reverse OA in this model and in the obesity related OA model in mice.

Methods:
PTOA was induced in SD rats following rupture of the anterior cruciate ligament (ACL) by application of external force to the knee. Starting 4 weeks after injury, when OA has already progressed, knees were injected with 100ul of saline, empty liposomes (LIPO) or liposomes containing CGS21680 (LIPO-CGS) every 10 days (6 injections) before sacrifice. The cartilage volume in OA and normal knees was measured by microCT after staining with hexabrix (40%). Chondrocytes were isolated from neonatal mice and cultured, only first passage chondrocytes were studied.

For the obesity-OA model, C57Bl6 mice (3/group, 12 weeks old) were fed a 60% fat diet (HFF mice). After 3 months, when OA was present, mice received intrarticular knee injection (10 µl) of LIPO, LIPO-CGS or liposomal adenosine (LIPO-Ado) every 10 days for 4 injections before sacrifice.

Results: Injection of LIPO-CGS but not saline or LIPO, significantly reduced swelling of affected rat knees (p<0.001). Surprisingly, there was an increase in tibial and femoral cartilage volume in normal knees treated with intra-articular injections of LIPO-CGS but not LIPO or saline (47% increase in tibia and 22% in femur). More importantly, intra-articular injections of LIPO-CGS, but not LIPO or saline, increased tibial and femoral cartilage volume in OA knees, as compared to normal knees and completely abrogated the histologic evidence of OA as well (OARSI score for CGS21680 0.66±0.33 vs 4.55±0.82 in the vehicle group and 3.90±0.89 in the saline group). There was marked chondrocyte proliferation in the deep cartilage of knees of rats treated with LIPO-CGS (Ki67 immunofluorescence).

Similarly, LIPO-CGS reversed the OA changes in the obesity related OA model. HFF mice had an OARSI score of 4.7±1.2. Treatments with LIPO-Ado and lipo-CGS decreased OA severity (OARSI score 1.3±0.3 and 0.7±0.6, respectively, p<0.001 vs untreated). A2AR stimulation increased TGF-β immunostaining in LIPO-CGS-injected joints and increased TGF-b production by cultured neonatal murine chondrocytes with increased SMAD2/3 phosphorylation and diminished RUNX2 expression.

Conclusion: These results demonstrate that intra-articular injection of a long-acting A2AR agonist stimulates chondrocyte and cartilage regeneration, likely by a TGF-β-dependent mechanism. More importantly, these results indicate that treatment with an A2AR agonist can reverse OA in both traumatic and obesity-related OA.
Anp32a Is a Critical Regulator of Oxidative Stress in Cartilage and Protects Against Osteoarthritis

Frederique Cornelis¹, Silvia Monteagudo¹, Wouter den Hollander², Tine Peeters³, Laura-An Guns¹, Lies Storms¹, Ingrid Meuilenbelt² and Rik Lories¹, ¹Skeletal Biology and Engineering Research Center, KU Leuven, Leuven, Belgium, ²Department of Molecular Epidemiology, Leiden University Medical Center, Leiden, Netherlands, ³Skeletal Biology and Engineering Research Center, KU Leuven, 3000, Belgium

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Biology and Pathology of Bone and Joint
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: We described an association between polymorphisms in the ANP32a gene and osteoarthritis. Osteoarthritis is one of the most common chronic musculoskeletal disorders and a cause of serious morbidity and disability, particularly in the elderly population. Progressive damage to the articular cartilage and bone leads to pain and loss of joint function. The development of osteoarthritis is very complex and is influenced by both genetic and acquired or environmental risk factors. Anp32a (acidic leucine-rich nuclear phosphoprotein 32 family member a) functions as a tumor suppressor gene and as a regulator of gene transcription, stabilization of RNA, intracellular transport and apoptosis. Moreover, Anp32a associates with Axin-1 and Phosphatase 2A, molecules that exert a regulating role in the Wingless-type signaling (Wnt) pathway, a signaling cascade with important roles in skeletal development, homeostasis and disease, including in osteoarthritis. But it remains unknown how Anp32a affects cartilage health and osteoarthritis.

Methods: ANP32A expression levels were determined in preserved and damaged areas of articular cartilage of patients with osteoarthritis (OA) by RNA sequencing. Different established mouse models for OA were induced in Anp32a−/− mice. Genome-wide transcriptome analysis of the articular cartilage, comparing Anp32a−/− mice to C57Bl/6 wild-type (WT) mice, was performed to understand how loss of Anp32a affects cartilage homeostasis at the molecular level. Chromatin immunoprecipitation-quantitative PCR (CHIP-qPCR) and siRNA-mediated silencing were performed in primary human articular chondrocytes. Detection of Atm and ROS was performed using immunohistochemical staining on mice knee sections of Anp32a−/− and C57Bl/6 WT mice.

Results: We observed a significant decrease in ANP32A expression, in damaged areas of the cartilage of patients with OA, compared to non-damaged areas in the same patients. In the different OA mouse models, absence of Anp32a resulted in increased cartilage damage as compared to control animals. Transcriptome analysis identified Ataxia-telangiectasia-mutated (Atm) as a potential Anp32a effector gene. Indeed, Atm was highly downregulated in Anp32a−/− mice. Atm is a suppressor of reactive oxygen species (ROS), which are known to induce chondrocyte hypertrophy during endochondral ossification and in the onset of osteoarthritis. It is reported that the detrimental effects of Atm depletion on cartilage homeostasis can be reversed by inhibiting ROS with N-acetyl-cysteine (NAC). We treated our Anp32a−/− mice in the DMM-induced OA model with NAC, via the drinking water. Effectively, this treatment ameliorated the cartilage damage observed in our Anp32a−/− mice. CHIP-qPCR demonstrated that Anp32a binds to the Atm gene promoter and influences the recruitment of the RNA polymerase II transcription machinery.
Conclusion: We have demonstrated that Anp32a plays a relevant role in osteoarthritis, and identified Anp32a as an essential regulator of Atm and oxidative stress in cartilage. Our insights have therapeutic implications, as pharmacological blockade of ROS ameliorates osteoarthritis induced in Anp32a−/− mice.

Disclosure: F. Cornelis, None; S. Monteagudo, None; W. den Hollander, None; T. Peeters, None; L. A. Guns, None; L. Storms, None; I. Meulenbelt, None; R. Lories, None.

Abstract Number: 907

Five-Year Evolution of the Center of Excellence in Musculoskeletal Care and Education: A National Resource for the Continuum of Health Professions Education and Scholarship

Andrea Barker1, J. Peter Beck2, Grant Cannon3, Marissa Grotzke4, Scott Swasey5,6, Curry L. Koening7, Dorota Lebiedz-Odrobina6, Yasuharu Okuda8 and Michael J. Battistone1,1, Veterans Affairs Salt Lake City Health Care System and University of Utah School of Medicine, Salt Lake City, UT, 2Orthopaedics, Salt Lake City VA Medical Center and University of Utah, Salt Lake City, UT, 3Salt Lake City VA Medical Center and University of Utah, Salt Lake City, UT, 4Division of Endocrinology, Veterans Affairs Salt Lake City Health Care System and University of Utah School of Medicine, Salt Lake City, UT, 5Salt Lake City VA Medical Center, Salt Lake City, UT, 6University of Utah, Salt Lake City, UT, 7Rheumatology, University of Utah, Salt Lake City, UT, 8VHA SimLEARN National Center, Orlando, FL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Education
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: In 2011, the Veterans Affairs (VA) Office of Academic Affiliations funded the creation of the Center of Excellence (COE) in Musculoskeletal (MSK) Care and Education at the Salt Lake City (SLC) VA. This report reviews the growth of the COE from a local training program to a national resource supporting multicenter projects in health professions education and scholarship.

Methods: Data was collected from program faculty on activities of the COE over the last five years.

Results: Four educational programs, two clinical experiences and 44 scholarly projects were identified.

Educational programs (offerings and participants listed in Figure 1):

1. MSK Education Week—an intensive week-long rotation for students and trainees
2. SLC Mini-Residency—a 3-day accredited continuing professional education (CPE) program for primary care providers (PCPs)
3. National Mini-Residency—an accredited CPE program presented jointly as an educational partnership between faculty from the SLC VA and 12 VA medical centers
4. National Simulation, Learning, Education, and Research Network (SimLEARN)—two programs: MSK Master Educator (designed for educational leaders) and MSK Clinician (for PCPs seeking to expand their MSK skills)
Clinical experiences offering hands-on application of skills following educational programs (Figure 2):

1. A new-model MSK clinic embedded in primary care (PC MSK) and staffed by rheumatologists and a physician assistant with orthopedic experience

2. A multidisciplinary MSK clinic (MD MSK), with rheumatology, endocrinology, orthopedics, physiatry and primary care

Scholarship (summarized in Figure 3) has included published descriptions of educational programs, evidence of validity of novel assessment tools, impact on learners’ clinical behaviors, and the durability of change.

Conclusion: The COE in MSK Care and Education has evolved from a local experience for students and trainees to a national repository for a range of programs serving the continuum of health professions education that fulfils the three-fold mission of academic health centers: clinical care, education, and scholarship. In addition to creating resources for educators, the COE is now developing a shared database to support collaborative projects initiated by leaders at other sites participating in this program through dissemination of their own innovations.

Disclosure: A. Barker, None; J. P. Beck, None; G. Cannon, Amgen, 2; M. Grotzke, None; S. Swasey, None; C. L. Koenig, None; D. Lebiedz-Odrobina, None; Y. Okuda, None; M. J. Battistone, None.

Impact of a National Training Program on Primary Care Providers Utilization of Knee MRI

Erica Jaffe1, Andrea Barker2, J. Peter Beck3, Grant Cannon4 and Michael J. Battistone2, 1Internal Medicine, Veterans Affairs Salt Lake City Health Care System and University of Utah School of Medicine, Salt Lake City, UT, 2Veterans Affairs Salt Lake City Health Care System and University of Utah School of Medicine, Salt Lake City, UT, 3Orthopaedics, Salt Lake City VA Medical Center and University of Utah, Salt Lake City, UT, 4Salt Lake City VA Medical Center and University of Utah, Salt Lake City, UT

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Education
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose:
The US Department of Veterans Affairs (VA) has developed a national continuing professional development program to train primary care providers (PCPs) in the care of patients with common musculoskeletal (MSK) conditions. Utilization of advanced imaging technology (e.g., magnetic resonance imaging (MRI)) in evaluating knee pain is an important concern because inappropriate ordering of MRI adds to costs in health care systems without increasing benefits, and limits access to this technology for other patients who may have greater need. Several recent reports suggest that PCPs overuse MRI in evaluating knee pain, and have called for the creation of educational programs and establishment of performance measures to address this issue. The aim of this study was to investigate the impact of this educational program on providers’ utilization of MRI in the evaluation of knee pain.

Methods:
Two hundred twenty seven providers from 13 VA medical centers participated in the MSK ÒMini-ResidencyÓ between April 2012 and October 2014. All orders for knee MRIs submitted by these providers over the 12-months prior to their participation in the mini-residency (pre-training) were reviewed, as well as all orders submitted over the 12-months following their participation (post-training). MRIs were categorized as follows:

ÓInappropriateÓ: No prior weight-bearing x-rays done within the 12 months preceding the MRI order

ÓProbably InappropriateÓ: Findings of osteoarthritis (OA) described on x-ray report

ÓPossibly AppropriateÓ: No findings of OA described on x-ray report.

The number of MRIs in each category was recorded for the pre-training and post-training period specific to each provider, and the number of MRIs in each category was tallied. Differences in the numbers of MRIs that were ordered post-training as compared to pre-training for each of the three categories were evaluated using paired StudentÕs t-test (2-tailed).

Results:
Numbers of MRIs ordered in the 12 months preceding training and following training for each of the categories described above are presented in the Table:
### Table

<table>
<thead>
<tr>
<th>Category</th>
<th>Pre-training</th>
<th>Post-training</th>
<th>Change</th>
<th>Change (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inappropriate</td>
<td>255 (76%)</td>
<td>180 (73%)</td>
<td>-75 (-29%)</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Probably Inappropriate</td>
<td>59 (18%)</td>
<td>34 (14%)</td>
<td>-25 (-42%)</td>
<td>0.09</td>
</tr>
<tr>
<td>Possibly Appropriate</td>
<td>22 (7%)</td>
<td>31 (13%)</td>
<td>9 (41%)</td>
<td>0.23</td>
</tr>
<tr>
<td>Total</td>
<td>336 (100%)</td>
<td>245 (100%)</td>
<td>-91 (-27%)</td>
<td>&lt;0.005</td>
</tr>
</tbody>
</table>

### Conclusion:

Following the MSK Mini-Residency program, the total number of MRIs ordered by participants decreased by 27%. This reduction was greatest in the number of studies classified as inappropriate. The total number of knee MRI orders that were categorized as either inappropriate or probably inappropriate decreased by 100 (32%), while the number of those that were possibly appropriate were not significantly changed. These findings provide further evidence that the VA MSK Mini-Residency program is effective in changing provider behavior and improving access to appropriate care for patients, though the high percentage of MRI scans classified as inappropriate indicate that additional work is needed in this area.

### Disclosure:

E. Jaffe, None; A. Barker, None; J. P. Beck, None; G. Cannon, Amgen, 2; M. J. Battistone, None.


Abstract Number: 909

### Two-Year Impact of a Continuing Professional Education Program to Train Primary Care Providers to Perform Arthrocentesis

Michael J. Battistone, Andrea Barker, J. Peter Beck, Phillip Lawrence and Grant Cannon, Veterans Affairs Salt Lake City Health Care System and University of Utah School of Medicine, Salt Lake City, UT, Orthopaedics, Salt Lake City VA Medical Center and University of Utah, Salt Lake City, UT, Salt Lake City VA Medical Center and Roseman University of Health Sciences, Salt Lake City, UT, Salt Lake City VA Medical Center and University of Utah, Salt Lake City, UT

First publication: September 18, 2017

### Session Information

Session Date: Sunday, November 5, 2017
Session Title: Education
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Initial reports of a local continuing professional education (CPE) program designed for primary care providers (PCPs) described an increase in the number of joint injections performed by those who had participated in the training.(1) The aim of this study was to examine the magnitude and durability of this behavioral change in a larger, geographically diverse impact of cohort of primary care providers. Methods: Thirty-eight primary care providers (PCPs) from 28 VA clinics representing 15 states participated in the week-long MSK “Mini-Residency” which was held at the Salt Lake City VA periodically between April 2012 and October 2013. The number of de-identified procedure codes performed by participants over the 24-months prior to their matriculation in the mini-residency (pre-training) were reviewed, and
compared to those performed 24-months following their participation (post-training). Differences in the numbers of procedure codes that were documented post-training as compared to pre-training were evaluated using paired Student’s t-test (2-tailed). **Results:** Thirty-four PCPs (25 MDs/Dos, 9 PAs/NPs—89% of the total number of trainees) were clinically active in primary care following the program. The mean number of injection codes per provider, as well as the ranges and standard deviations for the physician and non-physician provider groups at 2-years and 1-year prior to the training, as well as at 1- and 2-years post-training are presented in the Table below. Differences in these numbers, as well as the percent change from the preceding period of observation, are also shown:

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>2 Years Pre-Training Mean Injections/yr [Range, s.d.]</th>
<th>1 Year Pre-Training</th>
<th>1 Year Post-Training</th>
<th>2 Years Post-Training</th>
</tr>
</thead>
<tbody>
<tr>
<td>MD/DO</td>
<td>25</td>
<td>12 [0-75, 20]</td>
<td>12 (0%; 0.92) [0-75, 18]</td>
<td>34 (183%; 0.02) [0-248, 54]</td>
<td>43 (26%; 0.26) [0-309, 81]</td>
</tr>
<tr>
<td>ARNP/PA</td>
<td>9</td>
<td>3 [0-12, 4]</td>
<td>3 (0%; 0.86) [0-12, 4]</td>
<td>16 (464%; 0.07) [2-54, 16]</td>
<td>43 (40%; 0.18) [2-74, 35]</td>
</tr>
<tr>
<td>Overall</td>
<td>34</td>
<td>10 [0-75, 17]</td>
<td>10 (0%; 0.96) [0-75, 16]</td>
<td>29 (205%; 0.004) [0-248, 48]</td>
<td>37 (28%; 0.17) [0-309, 71]</td>
</tr>
</tbody>
</table>

**Conclusion:** Results from the pilot program are confirmed at 2 years, showing sustained changes in clinical behavior, for both physician and non-physician provider groups. Substantial variance in the number of joint injections was observed across the participants, suggesting that after the training some providers expanded their clinical repertoire more than did others. These findings should inform decisions made by clinic managers and clinical leadership in selecting participants for a training opportunity designed to increase proficiency in joint injections. Additional investigation of the sources of variance in provider behavior following the mini-residency program is needed to better understand these results.

**Reference List**


**Disclosure:** M. J. Battistone, None; A. Barker, None; J. P. Beck, None; P. Lawrence, None; G. Cannon, Amgen, 2.


**Abstract Number:** 910

**Training Adult Rheumatology Fellows in Young Adult Transition and Transfer Skills**

Rebecca Sadun\(^1\), Gary Maslow\(^2\), Richard Chung\(^3\) and Lisa Criscione-Schreiber\(^4\), \(^1\)Rheumatology Adult and Pediatric, Duke University Medical Center, Durham, NC, \(^2\)Psychiatry and Pediatrics, Duke University Medical Center, Durham, NC, \(^3\)Internal Medicine and Pediatrics, Duke University Medical Center, Durham, NC, \(^4\)Internal Medicine, Duke University Medical Center, Durham, NC

**First publication:** September 18, 2017
Background/Purpose: The transition from pediatric to adult healthcare is a vulnerable time for adolescents and young adults (AYA) with chronic conditions. EULAR and the Pediatric Rheumatology European Society jointly published expert opinions regarding transition care of AYA with juvenile-onset rheumatic diseases, and the ACR recently developed a transition toolkit. However, there are no published curricula for teaching transition guidelines, skills, or utilization of existing tools. We therefore designed and evaluated a workshop to help adult rheumatology fellows learn key skills for providing effective transition care to transferring young adult patients.

Methods: A 1-hour skills-based workshop on transition and transfer best practices was developed alongside an objective standardized clinical examination (OSCE) station in which trainees welcomed a young adult with lupus – and her parent – to a first visit in an adult clinic. Adult rheumatology fellows (n=19) from 5 institutions were asked to self-asses their ability to perform 10 transition/transfer skills pre- and post-workshop on a Likert scale from 1-4, with 1 being “not at all prepared” and 5 being “completely prepared.” The OSCE evaluation rubric assessed 5 transition/transfer skills on a Likert scale of 1-5, with 5 being the best performance. Twelve fellows were tested with the OSCE de novo, whereas 7 were tested with the OSCE after participating in the workshop. Aggregated pre- and post-workshop survey responses were compared using Fisher’s exact test, and OSCE scores were compared using an unpaired t-test.

Results: After participating in the workshop, fellows felt significantly more prepared with regards to 8 of the 10 transition/transfer skills (table 1). In addition, OSCE performance (table 2) was significantly better among the fellows who participated in the OSCE after the workshop than among those who took the OSCE de novo (p=0.01).

Conclusion: This brief educational intervention successfully increased adult rheumatology fellows’ confidence with many transition/transfer skills as well as increasing fellows’ ability to employ transition best practices in an OSCE setting. Making this curriculum available to all rheumatologists-in-training would likely improve the care young adult rheumatology patients receive when transferring from pediatric to adult rheumatology. Further exploration is needed to determine optimal teaching strategies to enhance communication between pediatric and adult rheumatologist and to equip adult rheumatologists with rapport-building skills for working with young adults.

<table>
<thead>
<tr>
<th>Self-Assessed Preparedness Increased</th>
<th>Self-Assessed Preparedness Not Increased</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orient young adult to adult rheumatology care (p&lt;0.01)</td>
<td>Establish rapport and trust with young adult patients (p=0.13)</td>
</tr>
<tr>
<td>Provide expectations of the young adult patient (p&lt;0.01)</td>
<td>Speak w/ pediatric providers re transferring patients (p=0.07)</td>
</tr>
<tr>
<td>Explain differences between pediatric &amp; adult care (p&lt;0.01)</td>
<td></td>
</tr>
<tr>
<td>Assess young adult self-management skills (p&lt;0.0001)</td>
<td></td>
</tr>
<tr>
<td>Assure young adult of confidentiality (p&lt;0.001)</td>
<td></td>
</tr>
<tr>
<td>Ask parent to leave the room for social history (p=0.01)</td>
<td></td>
</tr>
<tr>
<td>Take a transition-focused adolescent social history (p&lt;0.01)</td>
<td></td>
</tr>
<tr>
<td>Identify barriers to transition and adherence (p&lt;0.05)</td>
<td></td>
</tr>
</tbody>
</table>
Explaining differences between pediatric and adult care
Placing the AYA patient in the primary role (parent for corroboration)
Assessing self-management skills
Performing a confidential adolescent social history
Assessing barriers to transition & adherence
Total score / Average score

Pre-workshop (n=12)
3.5 4.3 3.8 2.8 2.3 16.7/3.3
Post-workshop (n=7)
4.6 5.0 4.4 4.7 2.6 21.3/4.3
p-value <0.01 <0.05 0.18 0.01 0.86 0.01

Disclosure: R. Sadun, None; G. Maslow, None; R. Chung, None; L. Criscione-Schreiber, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/training-adult-rheumatology-fellows-in-young-adult-transition-and-transfer-skills

Abstract Number: 911

How Well Do Rheumatology Fellows Manage Acute Infusion Reactions? a Pilot Curricular Intervention

Jason Weiner¹, Amanda M. Eudy² and Lisa Criscione-Schreiber³, ¹Department of Medicine, Division of Rheumatology and Immunology, Duke University Medical Center, Durham, NC, ²Duke University Medical Center, Chapel Hill, NC, ³Internal Medicine, Duke University Medical Center, Durham, NC
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Education
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose:
Infusible DMARDs are commonly prescribed in rheumatology and other fields. There are no published formal educational curricula rheumatology fellowship programs can use to teach infusion reaction management skills to fellows. We aimed to better understand this educational gap, and implement and assess the effectiveness of an experiential curriculum on acute infusion reaction management.

Methods:
We included current rheumatology fellows and recent graduates from five fellowship programs. Using a novel behavioral checklist, we assessed fellows' performance managing an infusion reaction in a simulation, followed by a didactic focused on infusion reactions. Pre and post-surveys assessed experiences to determine relevance, as well as attitudes and knowledge.

Results:
Despite ubiquitous prescribing of infusible biologic DMARDs, >50% of fellows were uncomfortable managing infusion reactions and 11% preferred prescribing injections because of these concerns. Only 11% of fellows reported infusion reaction training during fellowship, but 56% reported managing actual patient infusion reactions. Graduates reported similar experiences with 67% currently utilizing infusion services within their immediate clinic areas and 50% having managed
actual patient infusion reactions. Furthermore, all graduates reported no specific training requirements prior to prescribing infusible DMARDs in their current practice. In the simulated infusion reaction, fellows managed grade 1 reactions appropriately, but grade 4 reactions poorly, meeting <50% of objectives. All fellows discontinued the infusion in the setting of anaphylaxis, but only 56% administered epinephrine. There was no difference in performance or written knowledge by training year. All fellows felt more prepared to manage infusion reactions post-curriculum and were satisfied with the experience. All graduates recommended fellows receive education on this topic.

Conclusion:

We confirmed an education gap in rheumatology fellowship training regarding infusion reactions, both in knowledge and performance. We developed and implemented a brief experiential curriculum including simulation of a high-risk patient care scenario. This curriculum was well received and is easily exportable to other programs and fields of medicine.
Disclosure: J. Weiner, None; A. M. Eudy, None; L. Criscione-Schreiber, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/how-well-do-rheumatology-fellows-manage-acute-infusion-reactions-a-pilot-curricular-intervention

Abstract Number: 912

Has the Attractiveness of a Career in Rheumatology Changed for the Better? Comparison of Trends in the Rheumatology Fellowship Match from 2014 to 2017 with 2008 to 2013

Huyhn Tran1 and Richard Panush2, 1Special Project Manager, University of Southern California, Los Angeles, CA, 2Rheumatology, Program Director, University of Southern California, Los Angeles, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Education
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM
Background/Purpose:
Rheumatology has been a less attractive career choice than most other medical subspecialties for many years. The 2015 American College of Rheumatology (ACR) workforce study, derived largely from rheumatology fellowship matching data from 2008 to 2013, projected a shortage of up to 4,729 full-time equivalent rheumatologists by 2030. However the attractiveness of rheumatology seems to have changed since 2014.

<>Goals/Objectives:
We therefore compared more recent trends in application and match rates in rheumatology with other popular medical subspecialties.

Methods:
We reviewed data from the National Resident Matching Program from 2008 to 2017, the ACR Rheumatology workforce study of 2015, and Medscape physician salaries from 2008 to 2017. We examined the numbers of applicants, numbers of fellowship positions, ratios of applicants-to-fellowship positions, percentages of offered positions filled, percentages of applicants who matched, percentages of US graduates in fellowships, and salary trends in rheumatology. We compared data for rheumatology with that for non-procedure-oriented medical subspecialties (endocrinology, hematology/oncology, infectious disease, and nephrology) and procedure-oriented medical subspecialties (cardiology, gastroenterology, and pulmonology/critical care medicine) and trends for 2008-2013 with those from 2014-2017.

<>Results:
For rheumatology, the total number of applicants from 2008 to 2013 decreased from 251 to 230 (-8%) with an average annual percentage change of -3.32 ± 2.8% (mean ± SEM) but from 2014 to 2017 increased from 230 to 332 (+44%) with an average annual percentage change of 21 ± 10.5% (p = 0.02) (Figure). For non-procedural medical subspecialties the total number of applicants from 2008 to 2013 decreased from 1,940 to 1,594 applicants (-18%) with an average annual percentage change of -5.42 ± 3.4% but from 2014 to 2017 increased from 1,594 to 1,714, (+8%) with an average annual percentage change of 0.9 ± 2.3%. For procedural medical subspecialties the total number of applicants from 2008 to 2013 increased from 2,455 to 2,562 (+4%) with an average annual percentage change of 0.6 ± 1.4% while from 2014 to 2017 the number of total applicants continued to increase from 2,562 to 2,631 (+3%) with an average annual percentage of 1 ± 1.1%. The increase for rheumatology from 2014-2017 was significantly greater than changes in non-procedural specialties (p < 0.05) (Figure). Trends for the other parameters examined generally supported the increased attractiveness and competitiveness of rheumatology.

<>Conclusion:
Our observations complement and extend the 2015 ACR workforce report. While a few years and perhaps relatively small quantitative changes may not constitute a lasting tendency, analysis of recent trends suggests that rheumatology has become a more attractive career choice since 2014.
High Erythrocyte Levels of the n-6 Polyunsaturated Fatty Acid Linoleic Acid Are Associated with Lower Risk of Subsequent Rheumatoid Arthritis in a Southern European Nested Case-Control Study

Paola de Pablo1, Dora Romaguera2,3, Helena Fisk4, Philip Calder4, Anne-Marie Quirke5, Alison Cartwright5, Salvatore Panico6, Amalia Mattiello6, Diana Gavrila7, Carmen Navarro7, Carlotta Sacerdote8, Paolo Vincis2,9, Rosario Tumino10, William Ollier11, Dominique Michaud2,12, Elio Riboli2, Patrick Venables5 and Benjamin Fisher13,1 University of Birmingham, Birmingham, United Kingdom, 2Imperial College London, London, United Kingdom, 3CIBER-OBN (Fisiopatología de la Obesidad y Nutrición), University Hospital Son Espases, Palma, Spain, 4University of Southampton, Southampton, United Kingdom, 5Kennedy Institute of Rheumatology, University of Oxford, Oxford, United Kingdom, 6 Federico II University of Naples, Naples, Italy, 7Murcia Regional Health Council, Murcia, Spain, 8Città della Salute e della Scienza University-Hospital, Turin, Italy, 9Human Genetics Foundation, Turin, Italy, 10“Civic - M.P.Arezzo” Hospital, Ragusa, Italy, 11Division of Population Health, Health Services Research and Primary Care, University of Manchester, Manchester Academic Health Science Centre, Manchester, United Kingdom, 12Tufts University Medical School, Boston, MA, 13Rheumatology Research Group, University of Birmingham, Birmingham, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Epidemiology and Public Health II: Non-Genetic Risk Factors for Incident Disease
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM
**Background/Purpose:**

Long-chain n-3 (also known as omega-3) polyunsaturated fatty acids (PUFA), especially eicosapentaenoic acid (EPA; 20:5n-3) and docosahexaenoic acid (DHA; 22:6n-3), have long-been considered to have anti-inflammatory and immunomodulatory actions. Both n-3 and n-6 series PUFA (determined by the number of carbon atoms between the methyl end of the fatty acyl chain and the first double-bond) cannot be synthesized de novo by animals. Findings relating to the dietary intake of n-3 PUFA and risk of rheumatoid arthritis (RA) are mixed. We compared erythrocyte membrane PUFA, as an accurate biomarker of PUFA status, between pre-RA individuals and matched controls from a population-based sample.

**Methods:**

EPIC is a multicentre, pan-European prospective cohort study of apparently healthy populations. We undertook a nested case-control study, by identifying RA cases with onset after enrolment (pre-RA) in four EPIC cohorts: Naples, Turin and Ragusa in Italy, and Murcia in Spain. Identification and case validation has been previously described [1]. Confirmed pre-RA cases were matched with controls by age, sex, centre, and date, time and fasting status at blood collection. Total erythrocyte lipids were extracted and dissolved in toluene. Fatty acid methyl esters were synthesised and resolved in a BPX-70 fused silica capillary column using an Agilent 6890 gas chromatograph equipped with flame ionisation detection. We also measured the following serum cytokines: TNFα, IL-1β, IL-2, IL-4, IL-5, IL-6, IL-10, IL-12p70, IL-13 and IFNγ (Meso Scale Diagnostics). Conditional logistic regression (CLR) analysis of data was adjusted for potential confounders including body mass index (BMI), waist circumference, education level, physical activity, smoking status, and alcohol intake. Negative binomial regression was used to test the relationship between PUFA and serum cytokine level, stratified by incident RA, and adjusting for age, sex, country of origin, BMI, and smoking status.

**Results:**

The study analysed pre-symptomatic samples from 354 individuals of which 96 individuals went on to subsequently develop RA. In this analysis, time to diagnosis (defined as time between date of blood sample and date of diagnosis), was 6.71 years (SD 3.43).

No association was observed for any individual n-3 PUFA, or with total n-3 PUFA or total long chain n-3 PUFA, or with total n-3/n-6 ratio, and risk of RA. However a significant inverse association was observed with the n-6 PUFA linoleic acid (LA) level and pre-RA in the fully adjusted model (highest tertile : OR 0.29; 95% CI 0.12 to 0.75; p for trend 0.01).

Among the controls, LA was positively associated with serum levels of TNFα and IL-6 and negatively with IL-4, IL-5, IL-10, IL-12, IL-13 and IFNγ in fully adjusted models. In the pre-RA population, LA was positively associated with TNFα and IL-1, and negatively with IL-6, IL-5, IL-12 and IL-13 levels.

**Conclusion:**

In this nested case-control study within southern European prospective cohorts, high erythrocyte levels of the n-6 PUFA LA are associated with lower levels of T cell related cytokines and with lower risk of subsequent RA.


**Disclosure:** P. de Pablo, None; D. Romaguera, None; H. Fisk, None; P. Calder, None; A. M. Quirke, None; A. Cartwright, None; S. Panico, None; A. Mattiello, None; D. Gavrila, None; C. Navarro, None; C. Sacerdote, None; P. Vineis, None; R. Tumino, None; W. Ollier, None; D. Michaud, None; E. Riboli, None; P. Venables, None; B. Fisher, None.


**Abstract Number:** 914
Occupational Exposure to Combustion Products and Risk of Developing Rheumatoid Arthritis

Anna Ilar1, Pernilla Wiebert1,2, Saedis Saevarsdottir3, Johan Askling4,5, Per Gustavsson1,2 and Lars Alfredsson1,2, 1The Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden, 2Stockholm County Council, Centre for Occupational and Environmental Medicine, Stockholm, Sweden, 3Rheumatology Unit, Department of Medicine, Karolinska University Hospital and Karolinska Institutet, Stockholm, Sweden, 4Rheumatology unit, Department of Medicine, Karolinska University Hospital and Karolinska Institutet, Stockholm, Sweden, 5Unit of Clinical Epidemiology, Department of Medicine, Karolinska University Hospital and Karolinska Institutet, Stockholm, Sweden

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Epidemiology and Public Health II: Non-Genetic Risk Factors for Incident Disease
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose:
Studies have suggested a potential association between traffic pollutants and rheumatoid arthritis (RA), but findings have been inconclusive. We therefore assessed the risk of RA from occupational exposure to combustion products in a large population-based case-control study.

Methods:
We included participants living in Sweden from 2006 to 2013. Incident cases of RA were enrolled from the Swedish Rheumatology Quality Register. Ten controls per case, matched on sex, age and county, were enrolled from the total population register. Work histories were available through population and housing censuses. We estimated exposure to asphalt fumes, diesel engine exhaust and polycyclic aromatic hydrocarbons from 1955 to 1995 with job-exposure matrices. Conditional logistic regression was used to estimate the risks of two histological subtypes of RA (seropositive or seronegative RA) from exposure to either of the combustion products taken separately or all of them combined. All main exposures were adjusted for potential confounding from each other as well as from respirable crystalline silica dust and household disposable income. The results are presented for men and women separately.

Results:
We analyzed 9 180 cases and 81 367 controls. Ever exposure to diesel engine exhaust in men was associated with a marginally higher risk of seropositive RA (OR: 1.11, 95 % CI: 1.00-1.23), which was slightly higher among workers with at least 20 years of exposure (OR: 1.22, 95 % CI: 1.00-1.49). More than 20 years of asphalt fumes exposure was also associated with a higher risk estimate for seropositive RA among men (OR: 1.87, 95 % CI: 1.05-3.31). Being exposed to asphalt fumes, diesel engine exhaust or polycyclic aromatic hydrocarbons combined for more than 20 years resulted in an OR of 1.22 (95 % CI: 1.03-1.45) among men for seropositive RA and 0.91 (95 % CI: 0.77-1.23) for RA overall.

Women were less likely than men to have been exposed to combustion products during work and few female workers had been exposed for a longer period of time. Ever exposure to polycyclic aromatic hydrocarbons in women was associated with a potentially higher risk of seropositive RA (OR: 1.22, 95 % CI: 1.00-1.48). Women exposed to asphalt fumes, diesel engine exhaust or polycyclic aromatic hydrocarbons combined for more than 20 years had an OR of 0.91 (95 % CI: 0.36-2.29) for RA overall.

Conclusion:
Long-term exposure to combustion products may increase the risk of seropositive RA among men after adjustments for potential confounders.
Disclosure: A. Ilar, None; P. Wiebert, None; S. Saevarsdottir, None; J. Askling, AbbVie, Eli Lilly, Janssen, Merck, Pfizer, Roche, UCB, Samsung, 2; P. Gustavsson, None; L. Alfredsson, None.

Abstract Number: 915


Jessica Williams,1 Shun-Chiao Chang,1 Corine Sinnette,1 Susan Malspeis,2 Christine G. Parks,3 Elizabeth Karlson,1 Patricia Fraser,1 and Karen H. Costenbader,1,1 Brigham and Women's Hospital, Harvard Medical School, Boston, MA, 2 Division of Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 3 Epidemiology Branch, National Institute of Environmental Health Sciences, NIH, Durham, NC

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Epidemiology and Public Health II: Non-Genetic Risk Factors for Incident Disease
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose:

Several studies have reported an association between exposure to pesticides and the risk of systemic lupus erythematosus (SLE). However, this association has not yet been examined in an urban population, where residential pesticide exposure is more common than agricultural exposure. The purpose of this study was to assess the risk of SLE associated with residential exposure to pesticides in an urban population of predominantly African-American females.

Methods:

Female patients with SLE were identified via 6 hospital databases and community screening in 3 predominantly African-American neighborhoods in Boston, Massachusetts. Each SLE patient was reviewed by a rheumatologist and confirmed to have ≥4 ACR criteria for SLE. Subjects without SLE were female volunteers from the same neighborhoods, screened for the absence of connective tissue disease by questionnaire and finger stick anti-nuclear antibody. In-person interviews from April 2002 to August 2003 determined type and frequency of pesticide exposure prior to SLE diagnosis or corresponding reference age in subjects without SLE. Subjects were considered exposed to pesticides if they had ever required an exterminator for an ant, cockroach, or termite problem. The risks associated with exposure to pesticides were analyzed using multivariable logistic regression models, adjusted for age, race, parity, employment status, educational attainment, smoking status, and place of birth.

Results:

93 SLE patients and 170 subjects without SLE were matched by age and race, with similar baseline characteristics (see table). Patients with SLE were more likely to have had exposure to pesticides than subjects without SLE (65% vs. 51%, p=0.03). Pesticide exposure was associated with SLE, even after controlling for potential confounders (OR 2.24, 95% CI 1.28-3.93). A dose-response effect for increased frequency of exterminator service use was not statistically significant (p for trend=0.21).

Conclusion:

Residential exposure to pesticides in an urban community of predominantly African-American women was associated with an increased risk of SLE, even after controlling for potential confounders. Our findings demonstrate that previous reports of
an association between pesticide exposure and SLE may be applicable to urban African-American women, a population at increased risk for SLE. As our results may be limited by recall bias and/or residual confounding, additional research is needed to determine whether pesticide exposure is implicated in SLE pathogenesis, or is instead serving as a surrogate for a related exposure such as pest burden or poor living conditions.

Table. Characteristics of subjects with and without SLE*

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>SLE</th>
<th>No SLE</th>
<th>p-value†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=93</td>
<td>n=170</td>
<td></td>
</tr>
<tr>
<td>Exposed to pesticides‡</td>
<td>60 (65)</td>
<td>86 (51)</td>
<td>0.03</td>
</tr>
<tr>
<td>Age, mean ± SD years</td>
<td>44 ± 13</td>
<td>47 ± 15</td>
<td>0.11</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td>0.10</td>
</tr>
<tr>
<td>African-American non-Hispanic</td>
<td>71 (76)</td>
<td>147 (86)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>7 (8)</td>
<td>7 (4)</td>
<td></td>
</tr>
<tr>
<td>Caucasian non-Hispanic</td>
<td>6 (6)</td>
<td>3 (2)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>9 (10)</td>
<td>13 (8)</td>
<td></td>
</tr>
<tr>
<td>Parity, ever</td>
<td>71 (76)</td>
<td>134 (79)</td>
<td>0.64</td>
</tr>
<tr>
<td>Working full-time or part-time</td>
<td>44 (47)</td>
<td>90 (53)</td>
<td>0.38</td>
</tr>
<tr>
<td>Completed high school</td>
<td>71 (76)</td>
<td>122 (72)</td>
<td>0.42</td>
</tr>
<tr>
<td>Smoking status (≥100 cigarettes per lifetime)‡</td>
<td></td>
<td></td>
<td>0.33</td>
</tr>
<tr>
<td>Current (past 30 days smoked ≥1 cigarette)</td>
<td>16 (17)</td>
<td>35 (21)</td>
<td></td>
</tr>
<tr>
<td>Past</td>
<td>20 (22)</td>
<td>47 (28)</td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>57 (61)</td>
<td>88 (52)</td>
<td></td>
</tr>
<tr>
<td>Born in Boston</td>
<td>36 (39)</td>
<td>81 (48)</td>
<td>0.16</td>
</tr>
</tbody>
</table>

*Unless indicated otherwise, values are the number (%).

†By chi-square test. Wilcoxon rank-sum test was used for age.

‡Before age at diagnosis or corresponding reference age.

Disclosure: J. Williams, None; S. C. Chang, None; C. Sinnette, None; S. Malspeis, None; C. G. Parks, None; E. Karlson, None; P. Fraser, None; K. H. Costenbader, None.


Abstract Number: 916

**Long Term Effects of Early Childhood Thymectomy: A Population-Based Cohort Study of Association with Autoimmune Disease, Cancer, Infectious and Atopic Diseases**

Judith Gudmundsdottir1,2, Jonas Söderling3, Håkan Berggren4, Sólveig Óskarsdóttir5, Martin Neovius6, Olof Stephansson3 and Olov Ekwall7,8, 1Dept of Rheumatology and Inflammation Research, The Institute of Medicine, The Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, 2Children's Medical Center, Landspitali University Hospital, Reykjavik, Iceland, 3Clinical Epidemiology Unit, Dept of Medicine, Karolinska Institute, Stockholm, Sweden, 4Dept of Molecular and Clinical Medicine, Institute of Medicine, The Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, 5Dept of Pediatrics, Institute of Clinical Sciences, The Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, 6Department of Medicine, Clinical Epidemiology Unit, Karolinska Institutet, Stockholm, Sweden, 7Dept. of Rheumatology and Inflammation Research, Institute of Medicine, Sahlgrenska Academy University of
Gothenburg, Göteborg, Sweden, Dept of Pediatrics, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Göteborg, Sweden

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Epidemiology and Public Health II: Non-Genetic Risk Factors for Incident Disease
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose:

The thymus is the site of T cell maturation and selection and thus of vital importance for the development of immunological tolerance. Early thymectomy is routinely performed in infants undergoing surgical correction of congenital heart defects. Various immunological changes have been described after early thymectomy but the long-term clinical consequences are unknown. The aim of this study was to investigate the association between early thymectomy and risks of autoimmune disease, cancer, infectious and atopic diseases.

Methods:

The study is a nationwide population-based cohort study using the Medical Birth, Cause of Death and National Patient Registers in Sweden. We identified 5664 individuals born in 1973-2009 thymectomized before five years of age. For each individual, ten age and sex matched general population controls as well as 2276 surgery controls who had undergone early cardiac surgery, not involving thymectomy, were included. The main outcomes were incidence rates and hazard ratios for selected autoimmune diseases, cancer, infectious and atopic diseases.

Results:

Compared to the surgery controls, thymectomized individuals were at increased risk for hypothyroidism (HR 3.03; 95%CI 1.17-7.83), type 1 diabetes (HR 3.16; 95%CI 1.08-9.21) and both viral (HR 1.40; 95%CI 1.30-1.50) and bacterial (HR 1.26; 95%CI 1.11-1.43) infections. The HR for asthma was reduced (HR 0.69; 95%CI 0.58-0.83). Compared to the general population, increased risks were detected for hypothyroidism (HR 4.94; 95%CI 3.27-7.46), juvenile idiopathic arthritis (HR 1.85; 95%CI 1.11-3.09), rheumatic diseases (HR 1.89; 95%CI 1.00-3.57), celiac disease (HR 1.96; 95%CI 1.42-2.72), cancer (HR 1.61; 95%CI 1.07-2.43), infections (HR 3.18; 95%CI 3.07-3.30) and asthma (HR 1.84; 95%CI 1.64-2.07) in thymectomized individuals.

Conclusion:

In conclusion, early thymectomy is associated with increased risks of autoimmune disease, cancer as well as infectious disease. The study implicates important roles for the post-natal human thymus for the preservation of immunological tolerance as well as for immune effector functions. The results also indicate that avoidance of total thymectomy during early cardiac surgery may be advisable.

Disclosure: J. Gudmundsdottir, None; J. Söderling, None; H. Berggren, None; S. Óskarsdóttir, None; M. Neovius, Pfizer Inc, 2,AstraZeneca, 2,Pfizer Inc, 5; O. Stephansson, None; O. Ekwall, None.


Abstract Number: 917

Prospective Association of Metabolic Syndrome with Incident Symptomatic Interphalangeal Osteoarthritis but Not Thumb Based or Erosive Hand
Osteoarthritis

Charles Eaton1, Lena Franziska Schaefer2, Ida K. Haugen3, Mary Roberts4, Bing Lu5, Stacy Smith6, Jeffrey Durylea2, Jeffrey B. Driban7 and Timothy E. McAlindon8, 1Family Medicine and Epidemiology, Warren Alpert Medical School, School of Public Health, Brown University, Providence, RI, 2Radiology, Brigham & Women's Hospital/ Harvard Medical School, Boston, MA, 3Diakonhjemmet Hospital, Oslo, Norway, 4Center for Primary Care and Prevention, Memorial Hospital of Rhode Island, Pawtucket, RI, 5Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 6Radiology/Division of Musculoskeletal Imaging & Intervention, Brigham & Women's Hospital/ Harvard Medical School, Boston, MA, 7Rheumatology, Tufts Medical Center, Boston, MA, 8Division of Rheumatology, Tufts Medical Center, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Epidemiology and Public Health II: Non-Genetic Risk Factors for Incident Disease
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Symptomatic Hand Osteoarthritis (SxHOA) is a painful, destructive and deforming polyarticular disorder that is highly prevalent. The epidemiology of incident SxHOA and its association with metabolic processes is unclear with limited studies and conflicting results. We aimed to characterize individuals who develop symptomatic interphalangeal, thumb-based and erosive hand osteoarthritis and compare them to those who did not.

Methods: We evaluated 3604 participants in the Osteoarthritis Initiative (OAI) with complete data for baseline and 48-month radiographic hand OA. We defined interphalangeal OA as a hand with at least two joints with KL grade ≥2 on at least two fingers (digits 2 to 5), thumb-base OA using same KL criteria of either the CMC or STT joints, and erosive hand OA if one erosion was also present on any interphalangeal joint.

SxHOA required both presence of radiographic OA and symptoms (pain, aching, stiffness) on most days for the past 30 days. A metabolic syndrome score (MetS) was defined by summing presence of abdominal obesity (defined by gender-specific waist circumference), hypertension, diabetes, and dyslipidemia (range 0-4). Logistic regression was performed adjusting for age, sex and race for all models and other confounders (knee OA, smoking) depending on the outcome examined using a backward selection process to define the most parsimonious model.

Results: The overall 4-year incidence of symptomatic interphalangeal OA (SxIPOA), thumb-based OA(SxTBOA) and erosive hand OA(SxeHOA) were: SxIPOA n=536 (14.9%) ; SxTBOA n=551(15.3%); SxeHOA n=150 (4.2%). Older age, female sex, and knee OA were associated with SxIPOA, SxTBOA, while SxeHOA was not associated with knee OA. Black race compared to whites was inversely associated with all three symptomatic hand OA sub-types. (Table 1) A monotonically increasing risk of SxIPOA was found related to MetS compared to no metabolic risk factors (1 component OR=1.36; 2 components OR=1.50; 3 or 4 components OR=1.59, P for trend <0.01). Of the MetS risk factors dyslipidemia was significantly associated an increased risk of SxIPOA (OR=1.34, 95% CI 1.09,1.65 and SxTBOA(OR=1.34, 95% CI 1.09,1.64) while hypertension was associated with incident SeHOA(OR=1.52, 95% CI 1.06,2.18). MetS was not associated with sxTBOA or SxeHOA nor with incident radiographic defined IPOA, TBOA and eHOA unrelated to symptoms.

Conclusion: Metabolic syndrome risk factors demonstrate a monotonically increased risk for SxIPOA but not with radiographically defined IPOA. Further research into the metabolic pathways, sex and race differences in the progression of symptomatic hand OA appear warranted.
<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>SxIPOA</th>
<th>SxTBOA</th>
<th>SxeHOA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per SD)</td>
<td>1.81 (1.63, 2.00)</td>
<td>1.51 (1.37, 1.66)</td>
<td>1.86 (1.55, 2.24)</td>
</tr>
<tr>
<td>Sex</td>
<td>1.63 (1.34, 2.00)</td>
<td>1.68 (1.38, 2.05)</td>
<td>2.60 (1.78, 3.84)</td>
</tr>
<tr>
<td>Female vs Male</td>
<td>0.67 (0.50, 0.89)</td>
<td>0.62 (0.46, 0.82)</td>
<td>0.23 (0.10, 0.54)</td>
</tr>
<tr>
<td>Race</td>
<td>1.36 (1.05, 1.77)</td>
<td>1.14 (0.89, 1.46)</td>
<td>1.34 (0.86, 1.55)</td>
</tr>
<tr>
<td>Black vs White</td>
<td>1.50 (1.13, 1.98)</td>
<td>1.31 (1.01, 1.71)</td>
<td>1.31 (0.80, 2.12)</td>
</tr>
<tr>
<td>MetS 1 vs None</td>
<td>1.59 (1.13, 2.22)</td>
<td>1.34 (0.96, 1.86)</td>
<td>1.24 (0.68, 2.28)</td>
</tr>
<tr>
<td>MetS 2 vs None</td>
<td>1.24 (1.02, 1.52)</td>
<td>1.29 (1.06, 1.57)</td>
<td>N/A</td>
</tr>
<tr>
<td>MetS 3-4 vs None</td>
<td>1.39 (0.99, 1.95)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Knee OA</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Smoking Past vs Never</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Smoking Current vs Never</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Disclosure: C. Eaton, None; L. F. Schaefer, None; I. K. Haugen, None; M. Roberts, None; B. Lu, None; S. Smith, None; J. Duryea, None; J. B. Driban, None; T. E. McAlindon, None.


Abstract Number: 918

**Development and Validation of a Clinical Rule to Facilitate Recognition of Clinical Arthritis By General Practitioners**

Robin M ten Brinck¹, Bastiaan T van Dijk², Hanna W van Steenbergen¹, Saskia le Cessie³, Mattijs E Numans⁴ and Annette H.M. van der Helm-van Mil¹, ¹Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, ²Rheumatology, Leiden University Medical Center, Leiden, Netherlands, ³Medical statistics and Epidemiology, Department of Medical Statistics and Epidemiology, Leiden University Medical Center, Leiden, Netherlands, ⁴Public Health and Primary Care, Leiden University Medical Center, Leiden, Netherlands

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Sunday, November 5, 2017

Session Title: Epidemiology and Public Health II: Non-Genetic Risk Factors for Incident Disease

Session Type: ACR Concurrent Abstract Session

Session Time: 4:30PM-6:00PM

**Background/Purpose:**

Early treatment of rheumatoid arthritis requires the early detection of arthritis. This is generally done by joint examination and difficult for general practitioners (GPs). To promote early recognition of arthritis, the Leiden Early Arthritis Recognition Clinic (EARC) was initiated, where GPs can send patients if in doubt about arthritis (instead of ‘wait-and-see’). Although the EARC importantly improved the early identification, this approach may not be easily implemented at other places. This study determined the discriminative value of a combination of symptoms and other signs for clinical arthritis.

**Methods:**
1,288 patients visited the EARC between 2010 and 2015. Symptoms and signs were studied with the presence of synovitis (joint examination by experienced rheumatologist) as outcome. Parameters were identified using multivariable logistic regression in 644 patients and validated in another 644 patients. A simplified rule was derived to facilitate application in clinical practice.

**Results:**

41% had arthritis at examination. Male sex, age ≥60 years, a short symptom duration, morning stiffness >60 minutes, a low number of tender joints, the presence patient-reported swollen swelling and difficulties with making a fist were significantly associated with the presence of arthritis in the derivation cohort. A simplified rule, consisting of these 7 items, was generated (Figure); it had an AUC of 0.74 (95%CI 0.78-0.70). When a sensitive rule is preferred, a cut-off of ≥4 yields a sensitivity of 94%; when a specific rule is preferred the cut-off ≥6 has a specificity of 92%. Risks of arthritis were determined, and also estimated for a setting in which the prevalence of clinical arthritis in patients with suspected arthritis was half of that observed here.

**Conclusion:**

A rule composed of clinical parameters had a reasonable discriminative ability for clinical arthritis. Ultimately this could assist GPs in decision-making in patients with suspected inflammatory arthritis.

**Figure.** The Clinical Arthritis Rule (CARE) and corresponding risks of the presence of inflammatory arthritis per score.

**Disclosure:** R. M. ten Brinck, None; B. T. van Dijk, None; H. W. van Steenbergen, None; S. le Cessie, None; M. E. Numans, None; A. H. M. van der Helm-van Mil, None.


**Abstract Number:** 919

**HLA Type Imputation in the Genome Research in African American Scleroderma Patients (GRASP) Cohort Reveals Strong Associations of African Ancestry MHC Class II Types with Scleroderma and Lack of Class I HLA Type Associations**

Elaine F. Remmers¹, Pravitt Gourh², Steven Boyd³, Nadia D. Morgan⁴, Ami A. Shah⁴, Adebowale Adeyemo¹, Amy Bentley¹, Mary A. Carns⁵, Settara C. Chandrasekharappa¹, Lorinda Chung⁶, Lindsey A. Criswell⁷, Chris T. Derk⁸, Robyn T. Domsic⁹, Ayo Doumatey¹, Heather Gladue¹⁰, Avram Goldberg¹¹, Jessica K. Gordon¹², Vivien M Hsu¹³, Reem Jan¹⁴, Dinesh Khanna¹⁵, Maureen D. Mayes¹⁶, Thomas A. Medsger Jr.¹⁷, Paula S. Ramos¹⁸, Marcin A. Trojanowski¹⁹, Lesley A.
anti-topoisomerase antibody-positive cases carry revealed a strong disease risk conferred by either contributors to disease risk, but no association was found for MHC class I alleles (Figure 1). 34.6% of GRASP cases carry identified another African DRB1 allele, with odds ratio 2.95, 95%CI 2.26-3.85 (Figure 1). Regression analysis conditioning on the disease-associated alleles were performed after recoding the genotype data to 0 or 1 using a dominant model and the top 10 principal components were included as covariates.

**Methods:** SNP genotyping of 934 scleroderma cases and 946 controls was performed on the Illumina Multi-Ethnic Global SNP genotyping array. We extracted the genotypes of 25,256 markers from 20 Mb encompassing the greater MHC region and used the Michigan Imputation Server with 1000G Phase 3 v5 reference and Eagle phasing algorithm to obtain input data for submission to the HLA*IMP:03 web server. HLA types were converted to presence or absence genotypes (PP/PA/AA) for each typed allele and disease association was determined using a dominant model. Regression and conditional analyses were performed after recoding the genotype data to 0 or 1 using a dominant model and the top 10 principal components were included as covariates.

**Results:** The most significantly scleroderma-associated HLA type was a predominantly African allele, HLA-DRB1*08:04, with odds ratio 2.95, 95%CI 2.26-3.85 (Figure 1). Regression analysis conditioning on the disease-associated alleles identified another African DRB1 allele, *I*1:02, as well as HLA-DPB1*13:01, and HLA-DRB4*01:01 as independent contributors to disease risk, but no association was found for MHC class I alleles (Figure 1). 34.6% of GRASP cases carry either DRB1*08:04 or *I*1:02 compared with 16.3% of controls. Analysis of 246 anti-topoisomerase antibody positive cases revealed a strong disease risk conferred by HLA-DPB1*13:01 (P=4.93x10^-17, OR=4.10, 2.90-5.79). Remarkably, 30.49% of anti-topoisomerase antibody-positive cases carry HLA-DPB1*13:01, compared with 9.7% of controls.
Conclusion: The scleroderma risk-associated HLA-DRB1 types identified in the GRASP cohort differ from those reported in individuals of European ancestry. These HLA types are found at a higher population frequency than the European scleroderma risk types and therefore could contribute to the increased disease incidence or severity observed in African American patients.

Disclosure: E. F. Remmers, None; P. Gourh, None; S. Boyden, None; N. D. Morgan, None; A. A. Shah, None; A. Adeyemo, None; A. Bentley, None; M. A. Carns, None; S. C. Chandrasekharappa, None; L. Chung, Cytori, Actelion, Reata, 5; L. A. Criswell, None; C. T. Derk, None; R. T. Domsic, None; A. Doumaty, None; H. Gladue, None; A. Goldberg, None; J. K. Gordon, Corbus Pharmaceuticals, 2, Cumberland Pharmaceuticals, 2, Bayer Pharmaceuticals, 2; V. M. Hsu, None; R. Jan, None; D. Khanna, Actelion, Bayer, BoehringerIngelheim, Chemomab, Corbus, Covy, Cytori, Eicos, EMD Serono, Genentech/Roche, Gilead, GSK, Sanofi-Aventis, UCB Pharma, 5, NIH/NIAMS, NIH/NIAID, Bayer, BMS, Genentech/Roche, Pfizer, 2, Eicos, 4; M. D. Mayes, None; T. A. Medsger Jr., None; P. S. Ramos, None; M. A. Trojanowski, None; L. A. Saketkoo, None; E. Schiopu, None; V. K. Shanmugam, Multiple, 9; D. Shriner, None; R. M. Silver, None; V. D. Steen, None; A. Valenzuela, None; J. Varga, BMS, 2, Pfizer Inc, 2; C. Rotimi, None; F. M. Wigley, None; F. Boin, None; D. L. Kastner, None.


Abstract Number: 920

Area-Level Predictors of Medication Nonadherence Among U.S. Medicaid Beneficiaries with Lupus: A Multilevel Study

Candace H. Feldman1, Karen H. Costenbader2, Daniel H. Solomon3, S.V. Subramanian4 and Ichiro Kawachi5, 1Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA, 2Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 3Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 4Social and Behavioral Sciences, Harvard T.H. Chan School of Public Health, Boston, MA, 5Social and Behavioral Sciences, Harvard T. H. Chan School of Public Health, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Healthcare Disparities in Rheumatology
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM
Background/Purpose: Among lupus patients, adherence to hydroxychloroquine (HCQ), the backbone of therapy, remains suboptimal. Individual-level factors, including younger age, poverty, and black race, have been associated with HCQ nonadherence. However, contextual factors including neighborhood poverty and concentration of healthcare resources have not been examined. We constructed multilevel models to investigate whether zip code, county and state-level characteristics were associated with HCQ nonadherence.

Methods: We identified individuals with SLE enrolled in Medicaid (2000-2010) from 28 U.S. states using a previously defined algorithm. We included new users of HCQ (no use in ≥6 months) with ≥12 months of continuous enrollment with complete drug dispensing data following HCQ initiation. Adherence was measured over this 12-month period using the proportion of days covered (PDC) and defined as ≥80%. We identified individual-level characteristics (demographics, medications, comorbidities) from Medicaid data. We obtained zip code, county and state-level characteristics (percent of the population below the Federal poverty level (FPL), educational attainment and percent black population) from the American Community Survey. Health resource data (per capita hospitals, physicians, pharmacies and health professional shortage areas) were obtained from Area Health Resources Files. We used four-level hierarchical multivariable logistic regression models with Markov Chain Monte Carlo procedures to examine odds (OR [95% credible interval]) of adherence vs. nonadherence.

Results: Among 10,268 HCQ initiators with SLE residing within 4,930 zip codes in 1,414 counties in 28 states, 15% were adherent. After adjusting for individual-level characteristics, we observed lower odds of adherence across zip codes with higher percentages of black residents (highest tertile OR 0.81 [0.68-0.96] vs. lowest) (Table). The association remained after controlling for zip code percent below FPL and educational attainment. Odds of adherence were higher in counties with the greatest number of hospitals vs. the fewest (OR 1.32 [1.08-1.60]), and lower in health professional shortage areas (OR 0.86 [0.75-1.00]). There was no association with county-level per capita number of physicians or pharmacists. There was minimal variation in adherence by geographic area; the greatest was between states (1.4%).

Conclusion: Among Medicaid beneficiaries with lupus, after accounting for individual-level factors, we observed reduced odds of HCQ adherence in areas with higher percentages of black residents, fewer hospitals, and shortages of health professionals. Further studies are needed to assess whether racial residential segregation and poorer availability of high-quality medical care may contribute to racial differences in HCQ nonadherence and in turn, to disparities in lupus outcomes.
Table: Multilevel hierarchical logistic regression models examining the odds (OR with 95% credible interval) of adherence (PDC≥80%) vs. nonadherence among 10,268 individuals with lupus within 4,930 zip codes in 1,414 counties in 28 states

<table>
<thead>
<tr>
<th>Zip code-level fixed effect variables</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
<th>Model 4</th>
<th>Model 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Black Population</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tertile 2</td>
<td>0.84 (0.73-0.98)</td>
<td>0.85 (0.73-0.97)</td>
<td>0.87 (0.74-1.02)</td>
<td>0.84 (0.74-1.00)</td>
<td>0.85 (0.74-0.98)</td>
</tr>
<tr>
<td>Tertile 3</td>
<td>0.81 (0.68-0.96)</td>
<td>0.79 (0.66-0.94)</td>
<td>0.83 (0.69-1.00)</td>
<td>0.81 (0.68-0.98)</td>
<td>0.82 (0.70-0.96)</td>
</tr>
<tr>
<td>% Below Federal Poverty Level</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tertile 2</td>
<td>1.02 (0.87-1.19)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tertile 3</td>
<td>1.09 (0.93-1.28)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| County-level fixed effect variables   |         |         |         |         |         |
| Hospitals per capita                  |         |         |         |         |         |
| Tertile 2                             |         |         |         |         |         |
| Tertile 3                             |         |         |         |         |         |
| Health Professional Shortage Area     |         |         |         |         |         |
| Partial                               |         |         |         |         |         |
| Whole                                 |         |         |         |         |         |
| Rheumatologists per capita            |         |         |         |         |         |
| Tertile 2                             |         |         |         |         |         |
| Tertile 3                             |         |         |         |         |         |

In all models, tertile 1 is the reference. All models are adjusted for individual-level age, sex, race/ethnicity, SLE risk-adjustment index, lupus nephritis, diabetes mellitus, antidepressant use, corticosteroid use, immunosuppressive medication use, number of lupus-related lab tests, number of medications, healthcare utilization, obesity, smoking and calendar year. All models account for zip code, county and state-level random effects. County and state-level models are adjusted for all individual-level characteristics as well as zip code-level percent black (Model 1). Model 1 was chosen from Models 1-2, and an additional model including educational attainment, because it had the lowest deviance information criterion (DIC). Models 3-5 included healthcare resource variables separately due to collinearity.

Disclosure: C. H. Feldman, None; K. H. Costenbader, None; D. H. Solomon, None; S. V. Subramanian, None; I. Kawachi, None.


Abstract Number: 921

Discordant Patient-Physician Assessments of Disease Activity and Its Persistence Adversely Impact Quality of Life and Work Productivity in
United States Hispanics with Rheumatoid Arthritis

George Karpouzas1, Sera Ramadan2, Chelsie Cost3, Taylor Draper4, Elizabeth Hernandez3 and Sarah Ormseth3, 1Division of Rheumatology, Harbor-UCLA Medical Center, Torrance, CA, 2Internal Medicine, Dignity Health St. Mary Medical Center, Long Beach, CA, 3Rheumatology, Harbor-UCLA Medical Center, Torrance, CA, 4Psychology, Loma Linda University, Loma Linda, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Healthcare Disparities in Rheumatology
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: The impact of discordant patient-physician assessments of rheumatoid arthritis (RA) activity on quality of life is largely unknown. We examined the prevalence and stability of discordance on serial visits, over two years, in a large cohort of Hispanics from a single center in the US; we further explored the influence of discordance -at any point- and its persistence on health-related quality of life (HRQoL) and work productivity upon final visit.

Methods: We evaluated 308 patients with established RA. Patient (PGA) and physician/evaluator (EGA) global assessments were measured annually on 10-cm visual analogue scales; discordance was defined as a difference ≥ 3 cm between them. HRQoL was quantified using the SF-12 physical (PCS) and mental (MCS) component summary scores (higher scores indicate better HRQoL). Activity impairment, work productivity loss, presenteeism and absenteeism were calculated based on the Work Productivity and Activity Impairment Questionnaire. The impact of discordance and its persistence on HRQoL, activity impairment and employment-related outcomes at two years was assessed using analysis of covariance, adjusting for baseline values of those outcomes.

Results: Positive discordance (PD, or higher patient ratings) was more prevalent and stable over time (k range 0.32-0.36); 85 (27.6%) subjects had PD once, 49 (15.9%) twice, and 45 (14.6%) at all three time points. Negative discordance (ND, or lower patient ratings) was less common and unstable; 45 (14.6%) patients had ND once, 10 (3.3%) twice, and 1 (0.3%) at all three time points. Any PD throughout the study adversely impacted HRQoL upon last visit; persistence of PD yielded progressively lower SF-12 PCS (Fig 1A, p<0.001), and SF-12 MCS was lower among patients with any PD compared to those without (Fig 1B, p<0.001). Presence and persistence of PD yielded progressively greater activity impairment at final visit (Fig 1C, p<0.001). PD was negatively associated with employment (p<0.025); moreover, higher presenteeism (p=0.001) and work productivity loss (p=0.014) were seen with any PD (Fig 1D). PD appeared to be a patient-specific rather than a visit-specific feature; those with baseline PD had higher prevalence of fibromyalgia and irreversible articular damage (both p<0.01), and were 5-times more likely to have future PD.

Conclusion: Positive discordance is common and generally stable over time. Its presence at any time- and persistence adversely and incrementally impact clinical outcomes, including health related quality of life, work productivity, and activity impairment upon final visit.
Disclosure: G. Karpouzas, None; S. Ramadan, None; C. Cost, None; T. Draper, None; E. Hernandez, None; S. Ormseth, None.


Abstract Number: 922

Biologic DMARD Prescribing Patterns in Elderly Patients with Rheumatoid Arthritis

Britney Jones¹, Imran Hassan², Walter P. Maksymowycz³ and Elaine Yacyshyn⁴, ¹University of Alberta, Edmonton, AB, Canada, ²EPICORE Centre, University of Alberta, Edmonton, AB, Canada, ³Department of Rheumatology, University of Alberta, Edmonton, AB, Canada, ⁴Medicine, University of Alberta, Edmonton, AB, Canada

First publication: September 18, 2017
Rheumatoid arthritis is a chronic inflammatory process involving progressive destruction of joints.

Currently, 30% of rheumatoid arthritis (RA) patients are over the age of 65. As the population ages, shifts in epidemiology and disease patterns will require an appropriate response from the healthcare system. Elderly patients frequently have more active disease; however, inequalities in prescribing patterns may favor more aggressive treatment in younger patients. There are myriad different reasons why this may be the case; elderly patients tend to have a higher number of comorbidities, more medications, and a greater degree of frailty.

Elderly patients with RA benefit from tight disease control and use of biologic Disease Modifying Anti-rheumatic Drugs (boDMARDs) minimizes the need for other medications. There is a growing body of evidence suggesting that patient outcomes do not significantly decline with age. The reluctance to use boDMARDs in the elderly from concerns around side effects paradoxically means these patients may be exposed to much more deleterious drugs such as glucocorticoids, narcotics, and NSAIDs that may be less desirable in the elderly population.

This study identified differences in biologic prescribing patterns between young (<65 years old) and elderly (> 65 years old) patients with RA. Secondary outcomes examined demographic variation and disease activity between patient age groups.

**Methods:**

A retrospective cohort study of 1581 patients was conducted using information collected from the Rheumatoid Arthritis Pharmacovigilance Program and Outcomes Research in Therapeutics (RAPPORT) Database. This database encompasses an inception cohort of all RA patients in Northern Alberta starting treatment with biologics.

Fisher’s exact test was used to determine the age of RA patients at first boDMARD prescription using the cutoff of young (<65 years old) and elderly (> 65 years old).

Wilcoxon-Mann-Whitney test was used to stratify disease activity in different age groups using the Health Assessment Questionnaire (HAQ) and Disease Activity Score (DAS28).

**Results:**

A significantly larger proportion of young RA patients were prescribed boDMARDs compared with elderly RA patients (96.8% vs 90.0%; \( p = 0.006 \)). Elderly patients prescribed boDMARDs had significantly higher HAQ (mean 1.69 +/- 0.66; \( p = 0.001 \)) and DAS28 (mean 6.0 +/- 1.68; \( p = 0.002 \)) scores compared to younger patients (mean 1.41 +/- 0.72 and mean 5.29 +/- 1.7, respectively)

There was no statistically significant difference in other demographic information including sex, ethnicity, and years of schooling.

**Conclusion:**

Despite current guidelines recommending early, aggressive disease control including the timely introduction of boDMARDs, this study suggests that a prescribing bias remains. Younger patients with lower levels of disease activity are more likely to receive biologic therapies than their elderly counterparts. While there was no statistically significant difference between the basic demographics of each cohort, patient’s level of frailty and comorbid conditions were not accounted for in this study.

**Disclosure:** B. Jones, None; I. Hassan, None; W. P. Maksymowych, None; E. Yacyshyn, None.

Can Education Mitigate the Effect of Poverty on Total Knee Replacement (TKR) Outcomes?

Susan M. Goodman1, Bella Y. Mehta2, Meng Zhang3, Jackie Szymonifka4, Iris Navarro-Millán5, Joseph T. Nguyen3, Yu-Yu Lee3, Mark P. Figgie6, Michael L. Parks6, Shirin A. Dey4, Daisy Crego4, Linda A. Russell1, Lisa A. Mandl1 and Anne R. Bass1

1Rheumatology, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, 2Hospital for Special Surgery/Columbia University Mailman School of Public Health, New York, NY, 3Epidemiology and Biostatistics, Hospital for Special Surgery, New York, NY, 4Rheumatology, Hospital for Special Surgery, New York, NY, 5Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, 6Orthopaedic Surgery, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Healthcare Disparities in Rheumatology
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Health outcomes after total knee replacement (TKR) are generally worse for patients from high poverty neighborhoods. Whether education mitigates the effect of poverty is not known. We assessed the interaction between education and poverty on pain and function 2 years after TKR.

Methods: Patient-level variables - demographics, baseline and 2-year WOMAC pain and function scores, and geocodable US addresses - were obtained from an institutional TKR registry (5/07 - 2/11). Individual patient data were linked to US Census Bureau data at the census tract level. Statistical models including both patient-level and census tract-level variables were constructed within multilevel frameworks. Linear mixed effects models with separate random intercepts for each census tract were used to assess the effect of the interaction between education at the individual and census tract level and census tract poverty level on WOMAC scores at 2 years.

Results: Of 3970 TKR cases, 2438 (61%) were college-educated or above (Table 1, Figure 1). In the univariable analysis, race, sex, BMI, baseline WOMAC, and Medicaid were significantly associated with worse WOMAC scores at 2 years. In a linear mixed effects model, living in neighborhoods where <15% are college-educated and living in neighborhoods where ≥15% are below poverty were significantly associated with worse WOMAC pain (p=0.02) and function (p=0.006) at 2 years. There was little interaction between individual education and census tract education in our models, but when we assessed the interaction between individual education and community poverty, we found a significant interaction between them and WOMAC pain or function at 2 years. Comparing patients without college in high vs low poverty communities, WOMAC pain at 2 years was predicted to be 10 points lower (83.36 versus 72.75) and decreased in a linear fashion as community poverty increased, whereas patients with college had a difference in predicted WOMAC pain scores of only 1 point (87.10 vs. 86.09) (Figure 2); results for WOMAC function were similar.

Conclusion: In poorer communities, those without college education attain WOMAC scores 10 points lower than those with college education, a clinically meaningful difference. Education has no effect in wealthier communities. The reason education appears protective in poorer communities needs further study.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total</th>
<th>College or above</th>
<th>Non-college</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>3970 (100%)</td>
<td>2438 (61%)</td>
<td>1532 (39%)</td>
<td></td>
</tr>
<tr>
<td>Age at surgery (years), mean (SD)</td>
<td>67.13 (9.58)</td>
<td>66.86 (9.35)</td>
<td>67.55 (9.92)</td>
<td>0.014</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>2437 (61.39%)</td>
<td>1397 (57.30%)</td>
<td>1040 (67.89%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BMI (kg/m²), mean (SD)</td>
<td>29.99 (5.92)</td>
<td>29.29 (5.53)</td>
<td>31.10 (6.34)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hispanic, n (%)</td>
<td>81 (2.30%)</td>
<td>39 (1.78%)</td>
<td>42 (3.15%)</td>
<td>0.008</td>
</tr>
<tr>
<td>One or more comorbidities, n (%)</td>
<td>1120 (28.21%)</td>
<td>634 (26.00%)</td>
<td>486 (31.72%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>White, n (%)</td>
<td>3780 (95.21%)</td>
<td>2352 (96.47%)</td>
<td>1428 (93.21%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Insurance payer, n (%)</td>
<td>58 (1.46%)</td>
<td>13 (0.53%)</td>
<td>45 (2.94%)</td>
<td></td>
</tr>
<tr>
<td>Medicaid</td>
<td>2492 (62.77%)</td>
<td>1499 (61.48%)</td>
<td>993 (64.82%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Medicare</td>
<td>1420 (35.77%)</td>
<td>926 (37.98%)</td>
<td>494 (32.25%)</td>
<td></td>
</tr>
<tr>
<td>Other insurance</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASA Class, n (%)</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>3162 (79.69%)</td>
<td>1963 (80.55%)</td>
<td>1199 (78.31%)</td>
<td>0.09</td>
</tr>
<tr>
<td>I-II</td>
<td>806 (20.31%)</td>
<td>474 (19.45%)</td>
<td>332 (21.69%)</td>
<td></td>
</tr>
<tr>
<td>III-IV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital for Special Surgery Expectations Score, mean (SD)</td>
<td>78.50 (17.99)</td>
<td>79.03 (17.56)</td>
<td>77.59 (18.68)</td>
<td>0.087</td>
</tr>
<tr>
<td>WOMAC pain at baseline, mean (SD)</td>
<td>54.32 (17.65)</td>
<td>57.23 (16.92)</td>
<td>49.63 (17.81)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>WOMAC pain at 2 Years, mean (SD)</td>
<td>87.42 (16.05)</td>
<td>89.21 (14.01)</td>
<td>84.54 (18.52)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Delta WOMAC pain, mean (SD)</td>
<td>33.13 (20.30)</td>
<td>32.08 (19.36)</td>
<td>34.85 (21.65)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>WOMAC function at baseline, mean (SD)</td>
<td>53.45 (17.76)</td>
<td>56.95 (17.07)</td>
<td>47.85 (17.39)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>WOMAC function at 2 Years, mean (SD)</td>
<td>85.08 (16.49)</td>
<td>86.94 (14.52)</td>
<td>82.09 (18.86)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Delta WOMAC function, mean (SD)</td>
<td>31.58 (19.73)</td>
<td>30.00 (18.87)</td>
<td>34.11 (20.80)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Census Tract Percent Below Poverty Level, n (%)</td>
<td>3174 (79.97%)</td>
<td>2021 (82.93%)</td>
<td>1153 (75.26%)</td>
<td></td>
</tr>
<tr>
<td>&lt;10%</td>
<td>594 (14.97%)</td>
<td>318 (13.05%)</td>
<td>276 (18.02%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>10%-20%</td>
<td>201 (5.06%)</td>
<td>98 (4.02%)</td>
<td>103 (6.72%)</td>
<td></td>
</tr>
<tr>
<td>&gt;20%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Census Tract Percent Below Poverty Level, n (%)</td>
<td>3174 (79.97%)</td>
<td>2247 (92.20%)</td>
<td>1346 (87.86%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Low poverty &lt;15%</td>
<td>594 (14.97%)</td>
<td>190 (7.80%)</td>
<td>186 (12.14%)</td>
<td></td>
</tr>
<tr>
<td>Middle to high poverty &gt;=15%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Census Tract Percent of 25 or older with Bachelor’s degree or above, n (%)</td>
<td>81 (2.04%)</td>
<td>18 (0.74%)</td>
<td>63 (4.11%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Low Education &lt;15%</td>
<td>1194 (30.08%)</td>
<td>537 (22.03%)</td>
<td>657 (42.89%)</td>
<td></td>
</tr>
<tr>
<td>Middle Education 15%-39.9%</td>
<td>2695 (67.88%)</td>
<td>1883 (77.24%)</td>
<td>812 (53.00%)</td>
<td></td>
</tr>
</tbody>
</table>
Prevalence of Juvenile Idiopathic Arthritis in the Alaska Native Population
SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Healthcare Disparities in Rheumatology
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: High rates of rheumatoid arthritis and systemic lupus erythematosus have been described in indigenous North American (INA) populations. Few studies have investigated the prevalence or clinical patterns of juvenile idiopathic arthritis (JIA) in INA populations, but two studies have suggested high rates in specific regions of the US and Canada. The purpose of this project was to determine the prevalence of JIA overall and its subtypes in Alaska Native children statewide and to describe the clinical characteristics and treatment patterns of JIA in this population.

Methods: Potential cases of JIA were identified by a query of administrative data from the electronic health record of the Alaska Native Medical Center for codes possibly identifying JIA and from adult and pediatric rheumatology clinic databases. Cases were required to be under age 18 as of 9/30/2015 and to have a diagnosis of JIA confirmed by medical record abstraction. The denominator for prevalence was the 2015 Alaska Area Indian Health Service user population under the age of 18. Medical record abstraction was used to confirm the criteria met for JIA, subtype diagnosed, demographic features, other clinical characteristics, and medications ever used for treatment.

Results: The unadjusted prevalence of JIA in Alaska Native children was 67.5 per 100,000 (age-adjusted 71.7 per 100,000). JIA was more common in females than males (unadjusted prevalence 91.2 vs. 45.5 per 100,000). Oligoarthritis was the most common subtype (32% of cases), but enthesitis-related arthritis was also common (26.3% of cases). The mean age at diagnosis was 9 years and the prevalence was highest in children aged 16-18. During the one year study period, cases had a mean of 2.2 visits to a rheumatologist. Of the combined cohort, 53% had a positive ANA, 26% had positive rheumatoid factor, 24% had positive anti-CCP antibody, and 26% had the presence of HLA B27. Uveitis had been diagnosed in 26% of cases. Methotrexate was the most commonly prescribed non-biologic DMARD (ever prescribed in 66% of cases) and adalimumab was the most commonly prescribed biologic (in 32%).

Conclusion: The prevalence of JIA in Alaska Native children may be slightly higher than the general US population. Enthesitis-related arthritis makes up a higher proportion of cases than in other populations described, likely because of the high prevalence of HLA B27 in this population.

Disclosure: B. Khodra, None; A. Stevens, None; E. Ferucci, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/prevalence-of-juvenile-idiopathic-arthritis-in-the-alaska-native-population

Abstract Number: 925

Open-Source Consensus-Based Models to Improve the Cost-Effectiveness of Rheumatology Care

Devin Incerti¹, Jeffrey R. Curtis², Maria Lorenzi¹ and Jeroen Jansen¹, ¹Innovation and Value Initiative, Oakland, CA, ²Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL

First publication: September 18, 2017
Background/Purpose: The treatment and prognosis of moderate to severe rheumatoid arthritis has improved considerably due to the advent of biological therapies. But at the same time, the high costs of treatment are a threat to affordability and access to patients, and highlight the need for cost-effectiveness models that can help align prices with value. Unfortunately, there is no consensus in the literature on the proper mathematical structure for these models and estimates of value vary widely. Moreover, new evidence on the efficacy of biologics is rapidly evolving, so estimates of value must be updated as the evidence base evolves. Transparent, flexible, and accessible cost-effectiveness models that shed light on the implications of different modeling approaches are needed.

Methods: We developed an open-source “family” of cost-effectiveness models that reflects a number of scientifically defensible approaches and variation in the perspectives of decision makers. The code is publicly available on GitHub, a version control repository, and the model has been released as an R package. We also created a user-friendly web application where users can modify parameter values or structural assumptions and run the model online. We used the models to compare the cost-effectiveness of a standard sequence of 6 biologics treatments to conventional disease-modifying antirheumatic drugs (cDMARDs) using a number of different modeling assumptions.

Results: Under various plausible assumptions, incremental cost-effectiveness ratios (ICERs) ranged from less than $100,000 to around $300,000. Biologics were predicted to be more cost-effective when they had a larger effect on the Health Assessment Questionnaire (HAQ) Disability Index score at 6 months, increases in the HAQ score were assumed to lead to larger increases in mortality, the drop in clinical efficacy after each treatment failure was smaller, the HAQ score on cDMARDs progressed more quickly over time, biologics were assumed to be discounted more from their wholesale acquisition cost, and productivity losses were larger. For example, under our baseline assumptions, the ICER was approximately $120,000 when the effect of treatment on HAQ did not decline after the first treatment failure and over $200,000 when we assumed no clinical efficacy after 1st line treatment. In addition, subgroup analyses conducted using our baseline assumptions indicated that biologics were more cost-effective in younger patients, with ICERs ranging from $100,000 at age 35 to $165,000 at age 70.

Conclusion: Estimates of value vary considerably across different modeling assumptions, suggesting that steps must be taken to shrink diversity in modeling approaches and evidence considered to the greatest extent possible. These include new research studies and processes to encourage collaboration.

Disclosure: D. Incerti, Amgen, 5; J. R. Curtis, Crescendo Biosciences, 2, Crescendo Biosciences, 5; M. Lorenzi, None; J. Jansen, Amgen, 5.


Abstract Number: 926

Relationship of Traumatic Knee Injuries to Early-Onset Knee Osteoarthritis in Young Military Officers

Yvonne M. Golightly¹, Maryalice Nocera², John Cantrell², Jordan B. Renner³ and Stephen W. Marshall⁴, ¹Epidemiology, University of North Carolina at Chapel Hill, Chapel Hill, NC, ²Injury Prevention Research Center, University of North Carolina at Chapel Hill, Chapel Hill, NC, ³UNC School of Medicine, University of North Carolina, Chapel Hill, NC, ⁴Epidemiology, University of North Carolina, Chapel Hill, NC

First publication: September 18, 2017
Background/Purpose: Traumatic knee injuries, such as tears and ruptures of the anterior cruciate ligament (ACL) and/or menisci, are associated with osteoarthritis (OA). Surprisingly little is known, however, about the etiology and pathology underlying this association. Large epidemiologic studies of populations with high rates of knee injury are needed to enhance our understanding of the onset and progression of injury-mediated OA. We investigated radiographic OA, symptoms, and patient-reported outcomes in military officers with and without a history of traumatic knee injury.

Methods:

Participants were 439 military officers who either had a history of ACL and/or meniscal injuries (knee injury group) or were injury-free (uninjured group). Participants were recruited from an existing cohort of 6452 military officers originally enrolled between 2004 and 2008 as matriculating cadets at the U.S. Air Force Academy, U.S. Military Academy, or U.S. Naval Academy. The knee injury group (n=167) experienced ACL/meniscal injuries prior to, during, or after their 4-year academy career. The uninjured group (n=272) was site-matched from the same source cohort but had no history of ACL/meniscal injuries. Injury status was established using a self-reported injury history questionnaire, confirmed by clinical record review. Knee OA was assessed using 1) a single-item measure of knee pain, aching, or stiffness in the past 30 days, 2) a patient-reported knee outcome measure (Knee injury and OA Outcome Score [KOOS]; 0 [extreme] - 100 [no problems]), and 3) standardized weight-bearing posteroanterior radiographs of the tibiofemoral joint obtained using a fixed-flexion knee positioning frame. Radiographic knee OA was defined as Kellgren-Lawrence grade ≥2. Knee-injured and non-injured groups were compared using descriptive statistics and prevalence ratios (PR) with 95% confidence intervals (95%CI).

Results: Enrollment was completed on March 31, 2017, and collection of survey and radiographic data is on-going. Currently available data are presented. Among 403 participants with survey data, mean age was 28 years and mean body mass index was 25 kg/m². Per the parent cohort, 40% were women. Mean time from first ACL/meniscal injury to follow-up assessment was 8.6 years. Among participants with available knee radiographic data, 19.0% (16/84) of knee-injured had radiographic knee OA, compared to 0% (0/104) of the uninjured (PR=40, p<0.001). Nearly 38% (51/136) of participants with knee injury reported moderate-severe symptoms vs. 13% (20/156) of the uninjured (PR=2.9, 95%CI: 1.8, 4.7, p<0.001). Among 292 participants with available KOOS data, the knee-injured had clinically-relevant deficits on KOOS symptoms, sports/recreation, and quality of life scales (mean differences: -7.7, -8.1 and -11.0, respectively vs. non-injured, all p<0.001).

Conclusion: Traumatic knee injuries are strongly linked to early-onset knee OA, which greatly impacts quality of life and knee function during physically-vigorous activities. At a mean age of <30 years, young officers with a history of knee trauma experience substantial limitations from OA that impede their military performance.

Disclosure: Y. M. Golightly, None; M. Nocera, None; J. Cantrell, None; J. B. Renner, None; S. W. Marshall, None.


Abstract Number: 927

Do Familiarity with Centers for Disease Control Guidelines, Continuing Education, and Provider Characteristics Influence Adherence to Chronic Pain Management Practices and Opioid Prescribing?

Kim Jones¹, Ronald Friend², Robert M. Bennett¹ and Jean McCalmon³, ¹Schools of Nursing and Medicine, Oregon Health & Science University, Portland, OR, ²School of Nursing, Oregon Health & Science University, Portland, OR, ³Nursing, Oregon Health & Science University, Portland, OR

First publication: September 18, 2017
SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: ARHP Clinical Practice/Patient Care/Health Services Research
Session Type: ARHP Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: 1) To evaluate providers’ experience and knowledge with chronic pain management and opioid use with actual utilization of the Centers for Disease Control’s 2016 Guidelines for Prescribing Opioids for Chronic Pain. 2) To evaluate the specific influence of continuing education (CME), familiarity with CDC guidelines, and provider profession and region on confidence and best practice adherence in chronic pain management.

Methods:

A cross-sectional, web-based survey conducted between January and April of 2017 with a convenience sample of 417 Oregon prescribing providers consisting of 210 MD and 207 NP participants (Urban/Rural= 64/36%; Age= 49.7 sd=12.2, Female=32%, Years of Practice= 15.7, sd =12.3). Measures included CME hours in past 2 years (minimal, 0-3; moderate, 4-10; high, 11 or more) and CDC familiarity (not read or read not applied vs. read and applied). Primary outcome variables included provider confidence in pain management (0-9), opioid conversion confidence (0-9), and adherence to best practices (opioid risk tool, urine drug screening, opioid treatment agreement, Oregon Prescription Drug Monitoring Program; all Likert, 0-5). Multivariate analysis of variance (MANOVA) and Chi-Square were used to analyze the influence of CME, CDC familiarity, provider profession and regional medical setting on provider best practices and confidence ratings.

Results: CME hours was significantly associated with increased use of opioid best practices (2.6, 3.2, 3.8; p <.001; scale 0-5), opioid conversion confidence (5.5, 6.5, 7.4; p <.001; scale 0-9) and confidence in pain management (5.5, 5.9, 6.9; p <.001, scale 0-9). Providers familiar with CDC guidelines were only slightly more likely to apply best practices than were not (57% vs 43%), while increases in CME were more strongly associated with CDC best practices use (42% vs 57% vs 72%; p <.001). Neither providers professional status (MD vs NP) nor regional setting (urban vs. rural) showed differences in opioid best practices or general confidence in pain management with the exception of opioid conversion confidence where NPs reported slightly less than MDs (5.9 vs. 6.9; p < .001, scale 0-9) and rural slightly more than urban providers (6.8 vs 6.2; p< .05; scale 0-9).

Conclusion: Results demonstrate that recent CME in chronic non-cancer pain positively benefits provider confidence in pain management and application of best practices, as defined by the CDC guidelines. Nurse Practitioners and rural providers were found to provide equivalent adherence to best practices and confidence levels to their MD and urban counterparts, with minor exceptions.

Disclosure: K. Jones, None; R. Friend, None; R. M. Bennett, None; J. McCalmont, None.


Abstract Number: 928

Online Consultation for Chinese Patients with Rheumatic Diseases Based on Smart System of Disease Management (SSDM) Mobile Tool: A Study of Medical Economics

Fei Xiao1, Rui Wu2, Zhenchun Zhang3, Weiqi Min4, Yanchun Tang5, Xinwang Duan6, Lingfei Mo7, Zhaojun Guo8, Yanping Zhao9, Henglian Wu10, Xia Xu11, Feng Jiang12, Jing Yu13, Jianhong Qiang14, Yan Wang9, Ruijie Wu15, Anbing Zhang16, Limei Gu17, Hui Xiao1, Yuhua Jia1, Yuan Liu1, Bing Wu1, Chunhui Shi1 and Fengchun Zhang18, 1Gothic Internet Technology Corporation, Shanghai, China, 2The First Affiliated Hospital of Nanchang University, Nanchang, China, 3People's Hospital of Linyi, Shandong, Linyi, China, 4Heze Municiple Hospital, Heze, China, 5Yantai YuHuangDing Hospital, Yantai, China, 6Department of rheumatology, The Second Affiliated Hospital of Nanchang University, Nanchang,
Background/Purpose: China doesn’t have efficient primary medical care and referral system. Patients can choose any hospitals or any doctors they like to seek medical care. As a result, most patients with rheumatic diseases rushed to a few large cities. Surveys showed that more than 40% of the rheumatic disease patients were unnecessary to go to hospital and they only need advices from specialist. Smart System of Disease Management (SSDM) is a series of applications for chronic diseases management, which strengthens the interaction between doctors and patients based on valuable clinical data. Our previous study showed that rheumatoid arthritis (RA) patients can master the SSDM and perform self-management after training, including disease activity score with 28 joints (DAS28) and health assessment questionnaire (HAQ) evaluations, as well as medication and lab test data entries. The purpose of this study is to evaluate the feasibility and benefit of the medical economics of online consultation based on SSDM by rheumatologist.

Methods: The rheumatologists implemented the education and training programs on patients in using SSDM and assist the patients in downloading SSDM mobile application. The SSDM includes doctors’ and patients’ interfaces. The patient’s terminal system includes self-assessment (DAS28, HAQ), medication management, adverse events management and laboratory records. After data entry, patients can synchronize data to the authorized doctor. On the basis of these data, the rheumatologists can accept the request from their follow-up patients and practice consultation through SSDM in the form of text or voice.

Results: From February 2015 to June 2017, 403 rheumatologists supplied 4,002 patients (RA 42%, systemic lupus erythematosus 21%, ankylosing spondylitis 11%, gout 10%, osteoarthritis 5%, Sjogren syndrome 3% and other rheumatic diseases 7%) with 293 free and 3,709 paid consultations. Paid consulting included 3,983 times text Q&A and 19 voice consultations. The consulting fee ranged from RMB 10 to 500 yuan (UDS: RMB =1: 6.81) each in average of 96.06 ± 38.61 yuan, which match the registration fee in hospital. The total collection of fee for consultations was 477,960 yuan RMB. 35.3% patients receiving online consultation lived in different city with the rheumatologists. If patients seek medical care in hospital, in addition to the registration fees and medical expenses, the mean cost of transportation, accommodation, meals and lost wages was 565.17 ± 510.49 (200 - 2,800) yuan. The total of cost for all patients would have been 3,157,220 yuan RMB, which is 6.61 times higher compared with the cost of online. Online consultations through the SSDM can save 84.86% of the cost for patients. Survey shows that all patients were satisfied and 66.35% of them were "very satisfied" with the consultations.

Conclusion: Through online consultations using SSDM system, Chinese patients with rheumatic diseases can enjoy reduced cost with high satisfaction. In the era lack of primary care system in China, SSDM may serve as a complimentary platform to control medical care cost, as well as develop a new partnership between physicians and patients.

Disclosure: F. Xiao, None; R. Wu, None; Z. Zhang, None; W. Min, None; Y. Tang, None; X. Duan, None; L. Mo, None; Z. Guo, None; Y. Zhao, None; H. Wu, None; X. Xu, None; F. Jiang, None; J. Yu, None; J. Qiang, None; Y. Wang, None; R. Wu, None; A. Zhang, None; L. Gu, None; H. Xiao, None; Y. Jia, None; Y. Liu, None; B. Wu, None; C. Shi, None; F. Zhang, Xian Janssen, 8.

Variation in SLE-Related Pain – a Seven Year Follow-up Study

Eva Waldheim1, Sofia Ajeganova2, Stefan Bergman3, Johan Frostegård4 and Elisabet Welin Henriksson5,6,1 Karolinska Institutet, Stockholm, Sweden,2 Rheumatology unit, Department of Medicine, Karolinska Institutet at Karolinska University Hospital Huddinge, Stockholm, Sweden,3 University of Gothenburg, Gothenburg, Sweden,4 Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden,5 Department of Medical and Health Sciences, Linköping University, Linköping, Sweden,6 Neurobiology, Care Sciences and Society, Karolinska Institutet, Stockholm, Sweden

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: ARHP Clinical Practice/Patient Care/Health Services Research
Session Type: ARHP Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: We have previously shown that 24% of the patients in a SLE-cohort study (n=84) reported high levels of SLE-related pain (VAS≥40 mm), and also impaired HRQoL, more fatigue, higher levels of symptoms regarding anxiety and depression. In contrast, the patients reporting ≤39 mm on VAS did not differ from the controls regarding patient reported outcomes. We have now investigated the variation in SLE-related pain and its association with chronic widespread pain (CWP) and patient-related outcomes after seven years of follow-up.

Methods: 64 of 84 patients agreed to participate in the 7-year follow-up and answered questionnaires on pain (VAS/mm), fatigue (MAF), HRQoL (SF-36), anxiety and depression (HADS) and, in case of remaining pain > three months, marked painful body regions on a pain-drawing. Disease activity and damage (SLAM, SLEDAI, SLICC) were also captured. Nonparametric statistics were used, and difference in measures (diff) between inclusion and follow-up was calculated.

Results: For the patients with low levels of SLE-related pain the previous week (≤39 mm on VAS) at inclusion, n=50, there were no significant difference at 7 years follow-up in pain, fatigue, anxiety, depression and most dimensions of SF-36. Of these patients with low level of pain, 26% indicated chronic widespread pain on the pain drawing.

Among patients with high degree of pain (≥40 mm VAS) at inclusion, n=14, half of the patients reported significantly decreased pain, diff (IQR) 45 (35 to 65), p=0.021, fatigue, 8 (8 to 17), p=0.018, anxiety, 4 (1 to 4), p=0.035 and depression, 4 (2 to 5), p=0.018 and improvements in most dimensions of SF-36.

However, half of the patients with high degree of pain at inclusion reported no significant changes at follow up regarding pain, median diff (IQR) -13 (-20 to 28), fatigue, 5 (-0.3 to 6), anxiety, 2 (-1 to 3) and depression, 0 (-3 to 2). These patients reported significant deterioration in vitality in SF-36 but no significant changes in the other dimensions of SF-36. All patients with high remaining pain indicated chronic widespread pain on the pain drawing. These patients with remaining pain had significantly higher SLAM at follow-up compared to the patients with decreased pain at follow-up, p=0.017 and the patients with low levels of pain at inclusion, p=0.006. No significant differences were found in SLEDAI and disease damage.

Conclusion: For most patients, pain and other patient reported outcomes remained low or improved after seven years. However, a minority of the patients reported remaining high levels of pain after seven years, and were characterized by a heavy symptom burden with widespread pain more than three months, high levels of pain-related problems, impaired health-related quality of life and remaining high levels of fatigue. The results highlight the heterogeneous nature of SLE and stresses the needs of special attention to vulnerable sub-groups of patients with SLE.

Disclosure: E. Waldheim, None; S. Ajeganova, None; S. Bergman, None; J. Frostegård, None; E. Welin Henriksson, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/variation-in-sle-related-pain-a-seven-year-follow-up-study
Efficacy and Safety of Modified-Release Prednisone in Managing Moderate Activity SLE during Pregnancy: An Implemented Case-Control Study

Marianna Meroni1, Véronique Laure Ramoni2, Massimiliano Parodi3, Paolo Stobbione3 and Maurizio Cutolo4, 1Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, IRCCS A.O.U. San Martino-IST, University of Genova, Genoa, Italy, Genova, Italy, 2Division of Rheumatology, IRCCS San Matteo Hospital Foundation, University of Pavia, Pavia, Italy, Pavia, Italy, 3Rheumatology Unit, Internal Medicine Department, A.O. S.S. Antonio e Biagio e Cesare Arrigo, Alessandria, Italy, Alessandria, Italy, 4Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, IRCCS A.O.U. San Martino-IST, University of Genova, Genoa, Italy, Genoa, Italy

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: ARHP Clinical Practice/Patient Care/Health Services Research
Session Type: ARHP Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Systemic lupus erythematosus (SLE) can affect young women and pregnancy still represents a challenge. Prednisone is safely used, at low doses (<7.5 mg daily), during pregnancy. Modified-release prednisone (MRP) optimize corticosteroid treatment strategy in rheumatic diseases, thanks to its capability of respecting the physiological cortisol circadian secretion. MRP has been approved from FDA in SLE treatment, but no data are available regarding its administration during pregnancy.

We aimed to investigate whether this drug is safe and effective as the immediate release prednisone (IRP) in SLE pregnant patients.

Methods: We retrospectively evaluated 9 female patients, fulfilling the ACR criteria for SLE, consulting our centers in a 4-years observational range. All of them, thanks to a stable disease (not requiring treatment regimen modifications within 12 months), experienced a successful pregnancy during the observation. All the cases were taking low-dose MRP (5 to 7.5 mg/daily) as a baseline treatment, from at least 6 months. They were matched to 9 controls, defined as SLE patients with the same age and duration of disease, taking the same prednisone dose, from at least 6 months, in the IR formulation. Age of patients and disease duration (months); overall pregnancy outcome features; SLE disease activity (calculated at least once during pregnancy, SLEPDAI) and at baseline/post-partum (SLEDAI) score; patient’s global assessment (VAS) at baseline, during pregnancy and in postpartum (mm); need of treatment changes throughout pregnancy and at postpartum (%) were assessed. Homogeneity tests, percentages and scores comparison were run out by non-parametric statistical analysis.

Results: Mean MRP age group was 312±52 months; disease duration, 48±96 months; IR one, respectively, 336±43 and 36±108 (both, p=ns). SLEDAI at baseline was 1±0.1 among MPR and 1±0.3 among IR women; SLEPDAI, 1±0.9 and 2±0.2 (both, p=ns). No major perinatal complications were detected. Preterm births, caesarean section rates, newborn’s weight and APGAR scores, assessed 5 minutes after delivery, did not differ between the two subpopulations (all, p=ns). SLEDAI assessed at postpartum was 2.8±0.6 in MRP subjects and 3.4±0.4 in IR (p<0.05). Patients VAS (MRP vs IR) was 3±0.4 and 2±09 at baseline (p=ns); 2±0.6 and 4±0.7 during pregnancy (p<0.05) and 3±0.3 and 4±0.9 at postpartum (p<0.05).

Regarding treatment regimen changes (add-on strategy), the observed rates involved 1/9 (MRP) and 5/9 (IR) women during the observational gap (pregnancy+postpartum) (p<0.001).

Conclusion: Activity (SLEDAI) score was significantly higher at postpartum and treatment had to be increased in IR patients, in comparison to the MRP, to manage SLE. VAS, conversely, was significantly higher among IR, both during pregnancy and postpartum. No major perinatal side effects were observed during the study; minor and expected complications rates did not differ between the two subpopulations. Despite the limited number of subjects, MRP treatment seems to be as safe, but more effective, in comparison to the standard IR one, during pregnancy of SLE-affected women.

Disclosure: M. Meroni, None; V. L. Ramoni, None; M. Parodi, None; P. Stobbione, None; M. Cutolo, None.
Dose-Response Effects of Tai Chi and Physical Therapy Exercise Interventions in Symptomatic Knee Osteoarthritis

Augustine Lee¹, William F. Harvey², Lori Lyn Price³,4, Xingyi Han¹, Jeffrey B. Driban¹, Maura D. Iversen⁵,6, Raveendhara R. Bannuru¹ and Chenchen Wang², ¹Rheumatology, Tufts Medical Center, Boston, MA, ²Rheumatology, Center of Integrative Medicine and Division of Rheumatology, Tufts Medical Center, Boston, MA, Boston, MA, ³Tufts Clinical and Translational Science Institute, Tufts University, Boston, MA, ⁴Institute for Clinical Research and Health Policy Studies, Tufts Medical Center, Boston, MA, ⁵Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ⁶Department of Physical Therapy, Movement & Rehabilitation Sciences, Northeastern University, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Osteoarthritis – Clinical Aspects I: Pain and Functional Outcomes
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Therapeutic exercise is the recommended non-pharmacological treatment for knee osteoarthritis (OA). However, the optimal treatment dose and clinically meaningful treatment durations remain unclear. Our purpose was to examine dose-response relationships, the minimum effective dose, and baseline factors associated with the timing of response from two exercise interventions among adults with symptomatic knee OA.

Methods: Secondary analysis of a single-blind, randomized trial comparing 12-week Tai Chi and Physical Therapy exercise programs among adults with symptomatic knee OA (ACR Criteria). WOMAC pain (0-500) and function (0-1700) scores were completed each week of intervention. We defined dose as attendance-weeks (i.e. total treatment weeks attended), and treatment response as ≥20% and ≥50% improvement in pain and function. Using log-rank tests, we compared time-to-response between interventions, and used Cox regression to examine baseline factors associated with the timing of response (≥50% improvement only).

Results: We examined 182 participants (mean age 61 years, BMI 32 kg/m², 70% female, 55% white). Both interventions had linear dose-response effect resulting in a 9 to 11-point reduction in WOMAC pain and a 32 to 41-point improvement in function per week. There was no significant difference in overall time-to-response for pain and function between treatment groups (Figure). Median time-to-response for ≥20% improvement in pain and function was 2 attendance-weeks and 4 to 5 attendance-weeks for ≥50% improvement. On unadjusted models, we found a general pattern wherein physical health factors, self-efficacy, and outcome expectations tended to be significantly associated with treatment response rather than psychosocial or biomechanical factors (Table). On multivariable models, outcome expectations were independently associated with incident function response (Hazard Ratio: 1.47; 95% CI: 1.004 to 2.14).

Conclusion: Both interventions had linear dose-dependent effects on pain and function, their minimum effective doses ranged from 2 (≥20% improvement) to 5 weeks (≥50% improvement), and patient-perceived benefits of exercise independently influenced the timing of response among adults with symptomatic knee OA. These results may help clinicians optimize patient-centered exercise treatments and better manage patient expectations.
Figure (A-D). Time-to-Response from Tai Chi and Physical Therapy Interventions in Knee OA: PT=Physical Therapy; TC=Tai Chi. Kaplan-Meier curves for ≥20% improvement in pain (Panel A) and physical function (Panel B) and for ≥50% improvement in pain (Panel C) and physical function (Panel D) by attendance-week. P-values refer to log-rank tests comparing overall time-to-response between interventions. The number “at risk” (i.e. participants not responded) is listed at each cumulative attendance-week by treatment group.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Hazard Ratio (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pain</td>
</tr>
<tr>
<td>Age, years</td>
<td>1.01 (0.99, 1.03)</td>
</tr>
<tr>
<td>Female Sex, n (%)</td>
<td>1.32 (0.87, 2.01)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
</tr>
<tr>
<td>White reference</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>0.71 (0.47, 1.07)</td>
</tr>
<tr>
<td>Asian/Other</td>
<td>0.94 (0.53, 1.67)</td>
</tr>
<tr>
<td>Body Mass Index, kg/m²</td>
<td>0.98 (0.96, 1.01)</td>
</tr>
<tr>
<td>Duration of knee pain, years</td>
<td>1.01 (1.00, 1.03)</td>
</tr>
<tr>
<td>Highest Level of Education, n (%)</td>
<td></td>
</tr>
<tr>
<td>High school graduate or less</td>
<td></td>
</tr>
<tr>
<td>Some college or more</td>
<td>1.69 (0.97, 2.94)</td>
</tr>
<tr>
<td>WOMAC Pain (Range: 0-500); (50-point units)</td>
<td>n/a</td>
</tr>
<tr>
<td>WOMAC Physical Function (Range: 0-1700); (100-point units)</td>
<td>0.96 (0.91, 1.004)</td>
</tr>
<tr>
<td>Patient Global Assessment (Range: 0-10cm)</td>
<td><strong>0.87 (0.80, 0.94)</strong></td>
</tr>
<tr>
<td>SF-36 Physical Component Summary (Range: 0-100); (10-point units)</td>
<td><strong>1.35 (1.10, 1.65)</strong></td>
</tr>
<tr>
<td>PROMIS Sleep disturbance (Range, T-Score: 28.9-76.5); (10-point units)</td>
<td>0.88 (0.74, 1.05)</td>
</tr>
<tr>
<td>SF-36 Energy and Vitality (Range: 0-100); (10-point units)</td>
<td>1.06 (0.96, 1.17)</td>
</tr>
<tr>
<td>CHAMPS Physical Activity (500-calories/week)</td>
<td><strong>1.05 (1.003, 1.10)</strong></td>
</tr>
<tr>
<td>6-Minute Walk Test (50-meter units)</td>
<td><strong>1.12 (1.01, 1.25)</strong></td>
</tr>
<tr>
<td>Arthritis Self-Efficacy Scale-8 (Range: 0-10)</td>
<td><strong>1.11 (1.01, 1.21)</strong></td>
</tr>
<tr>
<td>Outcome Expectations (Range: 1.0-5.0)</td>
<td>1.14 (0.82, 1.57)</td>
</tr>
</tbody>
</table>

CHAMPS= Community Healthy Activities Model Program for Seniors; PROMIS= Patient-Reported Outcomes Measurement Information Systems; SF-36= Short Form-36; WOMAC= Western Ontario and McMasters Osteoarthritis Index. *Normal range reported for the general population. #Higher score indicates greater health.
Disclosure: A. Lee, None; W. F. Harvey, None; L. L. Price, None; X. Han, None; J. B. Driban, None; M. D. Iversen, NIAMS-NIH, PZifer, Fulbright, 2; R. R. Bannuru, None; C. Wang, None.


Abstract Number: 932

**Association of Varus Knee Thrust during Walking to Worsening Knee Pain over Two Years**

Alexandra Wink¹, K. Douglas Gross², Carrie Brown³, Michael C. Nevitt⁴, Cora E. Lewis⁵, James Torner⁶, Leena Sharma⁰ and David T. Felson⁸, ¹Anatomy and Neurobiology, Boston University School of Medicine, Boston, MA, ²Clinical Epidemiology Research, Boston University School of Medicine, Boston, MA, ³Boston University School of Public Health, Boston, MA, ⁴Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, CA, ⁵University of Alabama Birmingham, Birmingham, AL, ⁶University of Iowa, Iowa City, IA, ⁷Division of Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL, ⁸Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Sunday, November 5, 2017
Session Title: Osteoarthritis – Clinical Aspects I: Pain and Functional Outcomes
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

**Background/Purpose:** Varus knee thrust is an abrupt change in frontal plane tibiofemoral alignment observed during gait. Thrust has been linked to radiographic knee OA progression and worsening cartilage and bone marrow lesions. In addition, thrust has been cross-sectionally linked to knee pain presence during weight-bearing. *Our objective was to determine the longitudinal effect of knee thrust on worsening knee pain over 2 years in older adults with or at risk for OA.*

**Methods:** The Multicenter Osteoarthritis Study (MOST) is a prospective cohort study of older Americans with or at risk for knee OA. At the 60-month clinic exam, 60 Hz frontal plane videos recorded participants completing two self-paced walking trials over a 4.9 meter walkway. A trained reader, blinded to disease status, assessed the presence of varus thrust on a majority of steps (intra-rater κ = 0.73). Pain in each knee while walking, using stairs, standing upright, sitting, and in bed was assessed using the WOMAC questionnaire at 60 and 84 months. Among knees with submaximal WOMAC scores at 60 months, worsening pain at 84 months was defined as any increase in WOMAC score, and clinically important worsening was defined as an increase of ≥ 1.28 in WOMAC score. To assess the relation of thrust to worsening knee pain, we used logistic regression with generalized estimating equations to account for non-independent limbs from a subject, adjusting for age, sex, race, BMI, and gait speed. We repeated the analysis on a subset of knees with baseline WOMAC scores of 0 to assess the relation of thrust to incident WOMAC knee pain. We also assessed the relation of thrust to worsening knee pain in a subset of knees without baseline radiographic OA (Kellgren-Lawrence (KL) Grade < 2).

**Results:** 1623 participants (mean age 67.2 ± 7.6 years, mean BMI 30.4 ± 5.9, 59.9% female, 88.7% White) contributed 3204 knees. Varus thrust was observed in 31.5% of knees. At baseline, mean total WOMAC pain was 2.40, and 41% of knees had radiographic knee OA (KL ≥ 2). Knees with a varus thrust had 1.45 (95% CI: 1.22, 1.72) and 1.46 (95% CI: 1.20, 1.77) times the odds of any worsening and clinically important worsening total WOMAC pain, respectively, compared to knees.
without thrust; this increased pain was consistent across all WOMAC listed activities (see Table) and among the subset of knees without radiographic knee OA at baseline (OR = 1.39; 95% CI: 1.06, 1.82). Among knees with no WOMAC pain at baseline, knees with thrust had 1.81 times the odds (95% CI: 1.35, 2.41) of incident pain at two years compared to knees without thrust.

**Conclusion:** Varus knee thrust observed during walking is associated with increased odds of worsening knee pain during both weight-bearing and non-weight-bearing activities in older adults with or at risk for OA. Given that thrust is potentially modifiable using non-invasive therapies, detecting thrust provides an opportunity to prevent worsening knee pain in these populations.

<table>
<thead>
<tr>
<th>WOMAC Pain</th>
<th>Varus Thrust Status</th>
<th>n/N*</th>
<th>Adjusted** Odds Ratio (95% C.I.)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total WOMAC Pain Score</strong></td>
<td>Present</td>
<td>355/1010</td>
<td>1.45 (1.22, 1.72)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>625/2194</td>
<td>1.00 (ref)</td>
<td></td>
</tr>
<tr>
<td><strong>Clinically Important Worsening (≥ 1.28†)</strong></td>
<td>Present</td>
<td>221/1010</td>
<td>1.46 (1.20, 1.77)</td>
<td>0.0002</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>375/2194</td>
<td>1.00 (ref)</td>
<td></td>
</tr>
<tr>
<td><strong>Individual WOMAC Pain Questions</strong></td>
<td>Present</td>
<td>185/1010</td>
<td>1.32 (1.08, 1.62)</td>
<td>0.008</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>325/2194</td>
<td>1.00 (ref)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Present</td>
<td>230/1010</td>
<td>1.38 (1.14, 1.67)</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>412/2194</td>
<td>1.00 (ref)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Present</td>
<td>202/1010</td>
<td>1.44 (1.16, 1.79)</td>
<td>0.0009</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>328/2194</td>
<td>1.00 (ref)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Present</td>
<td>163/1010</td>
<td>1.40 (1.12, 1.76)</td>
<td>0.003</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>293/2194</td>
<td>1.00 (ref)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Present</td>
<td>145/1010</td>
<td>1.33 (1.06, 1.68)</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>268/2194</td>
<td>1.00 (ref)</td>
<td></td>
</tr>
</tbody>
</table>

*Number of knees with worsening pain/Total knees

**Adjusted for age, sex, race, BMI, and gait speed

†Based on the Minimum Clinically Important Difference for WOMAC Pain from Angst et al. (2002)

**Disclosure:** A. Wink, None; K. D. Gross, None; C. Brown, None; M. C. Nevitt, None; C. E. Lewis, None; J. Torner, None; L. Sharma, None; D. T. Felson, None.


**Abstract Number:** 933
Longitudinal Association between Sleep Quality and Knee Pain in the Multicenter Osteoarthritis Study

Zhaoli (Joy) Dai1, Carrie Brown2, Tuhina Neogi3 and David T. Felson3, 1Boston University School of Medicine, Boston, MA, 2Boston University School of Public Health, Boston, MA, 3Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Osteoarthritis – Clinical Aspects I: Pain and Functional Outcomes
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Sleep and pain have been shown to be reciprocally related. Studies have suggested a stronger effect of sleep impairment on chronic pain such as fibromyalgia and widespread pain than pain effects on sleep quality. In this study, we attempted to disentangle the longitudinal association of sleep quality with knee pain development and worsening related to knee OA from chronic widespread pain.

Methods: In the Multicenter Osteoarthritis Study of participants with or at risk of knee OA, sleep quality was assessed at the 60-month study visit (baseline) using a single questionnaire item on a four-point Likert scale from the Pittsburgh Sleep Quality Index, i.e. the overall quality of sleep in the past 7 days and 2) in the Center for Epidemiologic Studies Depression Scale Revised (CESD) for frequency of restless sleep. We categorized sleep quality as ‘fairly good’ and ‘very good’ for the upper two category responses, and ‘bad’ (referent group) for the lower two category responses combined together. Chronic widespread pain (WSP) was defined as having pain above and below the waist, on both sides of the body, and in the axial region. We defined our outcomes as follows: 1) knee pain worsening as relative change ≥ 14% or absolute change ≥ 2 in WOMAC pain score; and 2) incident consistent frequent knee pain (CFKP, knee pain on most days in past month at both the clinic visit and telephone screen ~30 days prior to the clinic visit and not present at baseline). We examined the relation of sleep quality to each knee pain outcome over a 2-year period stratified by baseline WSP status using logistic regression with Generalized Estimating Equations to account for correlations between two knees within an individual, and adjusted for potential confounders (see Table).

Results: We included 2329 participants (4658 knees) with valid values for sleep quality [mean (SD) age: 62.1 (7.9), BMI: 30.9 (6.1), 60.5% female, 84.3% White, 41% with WSP]. The spearman correlation for sleep quality and restless sleep was 0.69 (p<0.001). There was a significant interaction between sleep quality and baseline WSP for both outcome measures (p<0.01). In those who had knee pain at baseline, better sleep quality was associated with a lower risk of knee pain worsening regardless of baseline WSP (p for trend <0.04), with an effect that appeared to be stronger among those with WSP. No significant association was found for risk of incident CFKP in either stratum of WSP (see Table). Similar results were observed using restless sleep in CESD.

Conclusion: Although better sleep quality was associated with a lower risk of worsening knee pain regardless of chronic widespread pain, sleep quality did not affect the risk of developing new knee pain. Objective measures of sleep quality and knee pain are warranted to study the role of sleep in knee pain in OA. Nonetheless, these data suggest that for those with knee pain, sleep quality improvement should be considered for knee pain management.
Table Odds ratio (OR) [95% confidence interval (CI)] for relation of sleep quality from the Pittsburgh Sleep Quality Index to knee pain worsening and joint pain stratified by baseline widespread pain status in the Multicenter Osteoarthritis Study

<table>
<thead>
<tr>
<th>Knee pain outcomes</th>
<th>Sleep quality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0,1=Bad (Referent group)</td>
</tr>
<tr>
<td><strong>Knee pain worsening</strong></td>
<td></td>
</tr>
<tr>
<td>Widespread pain absence (N=2746)</td>
<td></td>
</tr>
<tr>
<td>Knee # (n/N)</td>
<td>71/358</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>1.0</td>
</tr>
<tr>
<td>Widespread pain presence (N=1912)</td>
<td></td>
</tr>
<tr>
<td>Knee # (n/N)</td>
<td>176/470</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>1.0</td>
</tr>
<tr>
<td><strong>Incident consistent frequent joint pain</strong></td>
<td></td>
</tr>
<tr>
<td>Widespread pain absence (N=2398)</td>
<td></td>
</tr>
<tr>
<td>knee # (n/N)</td>
<td>80/318</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>1.0</td>
</tr>
<tr>
<td>Widespread pain presence (N=1656)</td>
<td></td>
</tr>
<tr>
<td>Knee # (n/N)</td>
<td>203/392</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

1 Number of knees: n (knees with pain worsening or incident joint pain) / N (total number of knees)

2 Model adjusted for age (years), sex (men vs. women), race (white vs. non-white), study site, BMI (kg/m²), education level (college and above vs. below college), current work for pay (yes, no), tobacco packyears, Charlson’s comorbidity index, fatigue (10-point scale), CESD (without the sleep question), and use of NSAIDs.

Disclosure: Z. Dai, None; C. Brown, None; T. Neogi, None; D. T. Felson, None.


Abstract Number: 934

Effectiveness of FX006 Intra-Articular Injection in Patients with Knee Osteoarthritis Who Present with and without Clinical Inflammation at Baseline: A Pooled Analysis of Data from 3 Double-Blind, Randomized, Parallel-Group Clinical Trials

Herbert S. B. Bara¹, Christian Lattermann², Deryk G. Jones³, Philip G. Conaghan⁴, Joelle Lufkin⁵, James Johnson⁶, Scott Kelley⁷ and Neil Bodick⁵, ¹Center for Rheumatology and Bone Research, Wheaton, MD, ²University of Kentucky, Orthopaedic Surgery and Sports Medicine, Lexington, KY, ³Ochsner Sports Medicine Institute, New Orleans, LA, ⁴Leeds
Background/Purpose: Inflammation is a key contributor to osteoarthritis (OA).\(^1\) OA pain is mediated by interactions between inflammatory cytokines and other features including local tissue damage, synovitis and cellular response mechanisms.\(^1\) Synovitis is integral to OA, and is associated with symptom severity, joint dysfunction and cartilage loss.\(^2\) FX006, an extended-release formulation of triamcinolone acetonide (TA) for intra-articular (IA) injection, provided statistically and clinically significant, sustained improvements in pain/stiffness/function of knee OA vs placebo in clinical trials.\(^3\) We compared FX006 efficacy in patients with and without baseline inflammation determined by clinical assessment.

Methods: A pooled subgroup analysis of 3 double-blind, randomized, placebo-controlled trials (NCT01487161/NCT02116972/NCT02357459) was conducted. Patients with Kellgren-Lawrence grade 2/3 knee OA and Average Daily Pain (ADP)-intensity score $\geq 5$–$\leq 9$ (0–10 Numerical Rating Scale) received a single IA injection of FX006 40 mg or saline-placebo. Investigators assessed index knees for clinical indicators of inflammation (effusion, Baker’s cyst, tenderness, swelling, and/or redness/heat). ADP-intensity was assessed daily for 24 weeks. Western Ontario and McMaster University Arthritis Index for OA (WOMAC; 0–4 Likert scale) pain (A), stiffness (B), and physical function (C) were assessed at baseline and Weeks 4/8/12.

Results: 349/586 patients (60%) had baseline clinical inflammation (Table). Changes from baseline in weekly mean ADP-intensity and WOMAC-A, B, C consistently favored FX006 vs saline-placebo (Figure). FX006 effect was enhanced, generally $\geq 2$-fold, in patients with vs without baseline clinical inflammation: least squares mean differences for ADP and WOMAC-A, B, C, respectively, was $-1.84$ vs $-0.74$, $-0.71$ vs $-0.27$, $-0.82$ vs $-0.41$, and $-0.69$ vs $-0.26$ at Week 8, and $-1.35$ vs $-0.37$, $-0.44$ vs $-0.16$, $-0.50$ vs $-0.27$, and $-0.44$ vs $-0.16$ at Week 12.

Conclusion: FX006 provided sustained clinical improvement in knee OA vs saline-placebo irrespective of baseline clinical inflammation. Enhanced FX006 effect in patients with baseline clinical inflammation is consistent with the role of inflammation in OA pathogenesis and known anti-inflammatory action of TA. A drawback of this study is the lack of standardized measures of inflammation. Longer-term evaluations with objective inflammation measures (e.g., ultrasound, biomarkers) are needed.


Table. Baseline characteristics among individuals with and without evidence of index-knee OA* inflammation at baseline

| Parameter/Statistics | Inflammation | | | | | |
|----------------------|--------------|--------------|--------------|--------------|--------------|
|                      | FX006 40 mg  | Saline-placebo | FX006 40 mg  | Saline-placebo |
|                      | (N=211)      | (N=138)      | (N=211)      | (N=124)      |
| Male - n (%)         | 86 (40.8)    | 56 (40.6)    | 53 (46.9)    | 49 (39.5)    |
| Age at consent (years) - mean (SD) | 60.6 (8.87) | 62.2 (8.63) | 60.2 (9.71) | 60.4 (8.78) |
| BMI (kg/m²) - mean (SD) | 30.6 (4.75) | 30.5 (4.76) | 30.5 (4.84) | 30.7 (5.01) |
| Years since diagnosis - mean (SD) | 7.0 (6.50) | 6.5 (5.85) | 7.1 (6.46) | 6.0 (5.70) |
| Kellgren-Lawrence grade - n (%) | 2 | 82 (38.9) | 52 (37.7) | 45 (39.8) | 54 (43.5) |
|                      | 3 | 129 (61.1) | 86 (62.3) | 68 (60.2) | 70 (56.5) |
| ADP-intensity (0–10), score category - n (%) | 5–5.9 | 75 (35.5) | 49 (35.5) | 43 (38.1) | 50 (40.3) |
|                      | 6–6.9 | 74 (35.1) | 42 (30.4) | 39 (29.2) | 36 (29.0) |
|                      | ≥7    | 62 (29.4) | 47 (34.1) | 37 (32.7) | 38 (30.6) |
| ADP-intensity (0–10) - mean (SD) | 6.4 (0.92) | 6.5 (1.02) | 6.4 (1.06) | 6.4 (1.06) |
| WOMAC-A Pain (0–4) - mean (SD) | 2.1 (0.53) | 2.2 (0.57) | 2.0 (0.57) | 2.0 (0.58) |
| WOMAC-B Stiffness (0–4) - mean (SD) | 2.4 (0.73) | 2.5 (0.67) | 2.2 (0.91) | 2.3 (0.81) |
| WOMAC-C Physical function (0–4) - mean (SD) | 2.2 (0.55) | 2.2 (0.57) | 2.1 (0.54) | 2.1 (0.58) |

* Designated as the most painful knee by those with bilateral knee OA; diagnosis confirmed by ACR criteria.
ADP = Average Daily Pain, SD = standard deviation, WOMAC = Western Ontario and McMaster University Arthritis Index for OA.

Figure. Changes from baseline to Weeks 4, 8, and 12 in weekly mean ADP-intensity scores (A) and WOMAC-A, B, and C scores (B) among individuals with and without clinical evidence of index-knee inflammation (pooled analyses, full analysis set).

Disclosure: H. S. B. Baraf, Flexion Therapeutics, 2,F. Pfizer Inc, 2,AbbVie, 8,Horizon, 8; C. Lattermann, Cartiheal, 5,Cartilage, 9,Sports Physiology, 9,The Knee, 9,Orthopaedic Journal of Sports Medicine, 9,Cocoon, 1,International Cartilage Repair Society, 6,German-speaking Arthroscopy Society AGA, 6,Novartis Pharmaceutical Corporation, 5,Samumed, 5,Smith & Nephew, Inc., 2,Vericel, 5; D. G. Jones, Genzyme Corporation, 5,Mitek, 5,Musculoskeletal
Results from a 52 Week Randomized, Double-Blind, Placebo-Controlled, Phase 2 Study of a Novel, Intra-Articular, Wnt Pathway Inhibitor (SM04690) for the Treatment of Knee Osteoarthritis

Yusuf Yazici1, Timothy E. McAlindon2, Allan Gibofsky3, Nancy E. Lane4, Daniel J. Clauw5, Eddie Armas6, Nebojsa Skrepnik7, Christopher J. Swearingen1, Anita DiFrancesco1, Jeymi Tambiah1 and Marc Hochberg8, 1Samumed, LLC, San Diego, CA, 2Division of Rheumatology, Tufts Medical Center, Boston, MA, 3Rheumatology, Weill Cornell Medicine, and Hospital for Special Surgery, New York, NY, 4Center for Musculoskeletal Health, University of California at Davis, Hillsborough, CA, 5Chronic Pain & Fatigue Research Center, University of Michigan, Ann Arbor, MI, 6Well Pharma Medical Research, Miami, FL, 7Tuscon Orthopedics Institute, Tuscon, AZ, 8Head, Division of Rheumatology & Clinical Immunology; Vice Chair, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Osteoarthritis – Clinical Aspects I: Pain and Functional Outcomes
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Knee osteoarthritis (OA) is characterized by pain, disability and joint deformity due to articular cartilage degradation and bone remodeling. Wnt signaling is involved in these cellular processes and inflammation. SM04690, a small molecule Wnt pathway inhibitor, is in development as a potential disease modifying drug for knee OA. A phase 2, multicenter, 52-week, randomized, double-blind, placebo-controlled (PBO) trial was conducted to determine the safety and efficacy of SM04690.

Methods: Knee OA subjects with Kellgren-Lawrence (KL) grades 2-3, received a single 2 mL injection of 0.03 mg, 0.07 mg, 0.23 mg SM04690 or PBO in target (most painful) knees. Western Ontario and McMaster Universities Arthritis Index Outcome (WOMAC) Pain [0-50] and Function [0-170] were assessed at Weeks 0, 4, 13, 26, 39 and 52, and radiographs were taken at Weeks 0, 26 and 52 for medial joint space width (mJSW). Analysis of covariance adjusted for baseline in the intention-to-treat (ITT) population was conducted with multiple imputation. Two subgroups were explored: 1) unilateral symptomatic knee OA subjects as determined by investigator through history and examination (pre-specified), and 2) unilateral symptomatic knee OA subjects without widespread pain (Widespread Pain Index ≤4 and Symptom Severity ≤2 [WP], post-hoc).

Results: 455 subjects (mean age 60.3 [±8.7], BMI 29.9 [±4.6] kg/m², female 58.9%, KL 3 [64.4%], unilateral symptomatic OA [36.0%]) were enrolled. Serious adverse events, all deemed unrelated to SM04690, were reported in 17 (3.7%) subjects (4.5% [0.03 mg], 3.5% [0.07 mg], 3.8% [0.23 mg], 2.8% [PBO]).

In the ITT population, clinically meaningful outcomes improvements (>10% full range) compared to baseline were seen in all groups at all timepoints. Unilateral symptomatic subjects treated with 0.07 mg SM04690 had significant improvements in...
WOMAC Pain with clinically meaningful and significant improvements in WOMAC Function compared to PBO at Week 52. Unilateral symptomatic subjects without WP treated with 0.07 mg SM04690 had clinically meaningful and significant improvements in WOMAC Pain and Function compared to PBO at Weeks 26, 39, and 52 (Figure). At Week 52 in the ITT population, mean changes in mJSW were -0.14 mm in PBO, 0.10 mm in 0.03 mg (NS), 0.06 mm in 0.07 mg (NS), and -0.02 mm 0.23 mg (NS).

**Conclusion:** In this phase 2 study, improvements compared to PBO in WOMAC Pain and Function were seen in study subgroups of unilateral symptomatic and unilateral symptomatic without WP subjects. SM04690 maintained or improved mJSW over 52 weeks. Radiographic and clinical outcomes suggested SM04690 has potential as a DMOAD for knee OA treatment.

**Disclosure:** Y. Yazici, Samumed, LLC, 3, Samumed, LLC, 1; T. E. McAlindon, None; A. Gibofsky, Pfizer Inc, 1, AbbVie, 1, Amgen, 1, Bristol-Myers Squibb, 1, Johnson & Johnson, 1, Regeneron, 1, AbbVie, 5, AbbVie, 8, Pfizer Inc, 5, Pfizer Inc, 8, Celgene, 8, Novartis Pharmaceutical Corporation, 8, Takeda, 5, Horizon, 5, Relbun, 5, Samumed, 5; N. E. Lane, Pfizer Inc, 5, Eli Lilly and Company, 5, Regeneron, 5, Amgen, 5, Samumed, LLC, 5; D. J. Clauw, Abbott Pharmaceutical, 5, Aptinyx, 5, Astellas Pharmaceutical, 5, Cerephex, 5, Daiichi Sankyo, 5, Pfizer Inc, 5, Pierre Fabre, 8, Samumed, 5, Theravance, 5, Tonix, 5; E. Armas, Samumed, LLC, 2; N. Skrepnik, Orthofix, 5, Regeneron, 5, Sanofi-Aventis Pharmaceutical, 5; C. J. Swearingen, Samumed, LLC, 3, Samumed, LLC, 1; A. DiFrancesco, Samumed, LLC, 3, Samumed, LLC, 1; J. Tambiah, Samumed, LLC, 3, Samumed, LLC, 1; M. Hochberg, Bioiberica SA, 5, Bristol-Myers Squibb, 5, EMD Serono, 5, Galapagos, 5, IBSA

**Figure.** Ladder plots depicting change from baseline in WOMAC Pain and Function between treatment groups to placebo adjusting for baseline. The x-axis represents change in WOMAC score of treatment vs. PBO, where 0 equals no effect. Error bars represent 95% confidence interval.
Knee Confidence Trajectories over 8 Years and Factors Associated with Poor Trajectories: Data from the Osteoarthritis Initiative

Alison H. Chang, Julia (Jungwha) Lee, Orit Almagor, Joan S. Chmiel, Kirsten C. Moisio, Karen W. Hayes, Julie Szymbaszek and Leena Sharma, Northwestern University, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Osteoarthritis – Clinical Aspects I: Pain and Functional Outcomes
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Lack of knee confidence, a frequent complaint, has been associated with function decline in knee OA. Given its key role in weight-bearing activities, a better understanding of how confidence changes over time and modifiable factors associated with poor trajectories will inform strategies to help to prevent function decline. Our objectives were to identify, in persons with or at higher risk for knee OA, distinct trajectories of knee confidence over 8 years and baseline factors associated with poor trajectories.

Methods: The OAI is a prospective longitudinal cohort study of persons with or at higher risk for knee OA aged 45-79 yrs. Knee confidence was self-reported annually from baseline to 96m in the KOOS (Knee Injury and Osteoarthritis Score), as how much an individual is troubled by lack of confidence in their knees: 0, not at all; 1, mildly, 2, moderately, 3, severely, and 4, extremely. Confidence trajectories for % with score 2-4 were modeled using 4515 OAI participants who had ≥3 time points for confidence. Latent class models identified groups with a similar underlying trajectory, and, in 4105 persons with complete baseline data, logistic regression was used to model associations of baseline predictors with poor (vs. good) trajectories.

Results: We identified 4 distinct knee confidence trajectories (Figure), persistently good, declining, improving, and persistently poor, with estimated probabilities to each trajectory of 62.9%, 11.0%, 14.7%, and 11.3%, respectively. The 4105 persons had a mean age 61.4 years (SD 9.2), BMI 28.6 kg/m² (4.8), and 2381 (58.0%) were women. As shown in the Table, baseline factors associated with both persistently poor and declining confidence were BMI, depressive symptoms, disease severity, and worse function; with persistently poor only were younger age, male sex, extensor weakness, injury, and knee and ankle pain; with declining only were comorbidity, falls, and hip pain.

Conclusion: Four distinct 8-year knee confidence trajectories were identified in persons with or at higher risk for knee OA. Targeting BMI, depressive symptoms, function, extensor weakness, and knee, ankle, and hip pain may help to prevent poor or declining confidence trajectories.
Table: Associations of Baseline Predictors with Persistently Poor and Declining vs. Persistently Good Knee Confidence Trajectory (Dependent Variable)

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Persistently Poor Knee Confidence vs. Persistently Good</th>
<th>Declining Knee Confidence vs. Persistently Good</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>0.05 (0.94, 0.97)</td>
<td>0.99 (0.97, 1.01)</td>
</tr>
<tr>
<td>Sex (reference: male)</td>
<td>0.63 (0.46, 0.89)</td>
<td>0.90 (0.68, 1.21)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>0.66 (0.33, 1.39)</td>
<td>1.84 (0.84, 4.07)</td>
</tr>
<tr>
<td>Other Races (reference: white)</td>
<td>0.73 (0.32, 1.69)</td>
<td>0.78 (0.36, 1.70)</td>
</tr>
<tr>
<td>Co-morbidities (number)</td>
<td>1.06 (0.91, 1.25)</td>
<td>1.20 (1.03, 1.41)</td>
</tr>
<tr>
<td>Depression symptoms (CESD)</td>
<td>0.95 (1.04, 1.07)</td>
<td>1.04 (1.02, 1.06)</td>
</tr>
<tr>
<td>Fall (yes vs. no)</td>
<td>1.19 (1.06, 1.37)</td>
<td>1.20 (1.06, 1.54)</td>
</tr>
<tr>
<td>Self-reported physical activity (PASE)</td>
<td>1.00 (0.90, 1.02)</td>
<td>1.00 (0.90, 1.02)</td>
</tr>
<tr>
<td>KL grade 1 (reference: KL 0)</td>
<td>0.91 (0.54, 1.55)</td>
<td>1.13 (0.76, 1.69)</td>
</tr>
<tr>
<td>KL grade 2 (reference: KL 0)</td>
<td>1.93 (1.29, 2.87)</td>
<td>1.85 (1.19, 2.90)</td>
</tr>
<tr>
<td>KL grade 3 (reference: KL 0)</td>
<td>3.16 (2.04, 4.81)</td>
<td>3.23 (1.94, 5.36)</td>
</tr>
<tr>
<td>KL grade 4 (reference: KL 0)</td>
<td>6.44 (2.61, 13.99)</td>
<td>3.94 (1.31, 10.59)</td>
</tr>
<tr>
<td>WOMAC pain</td>
<td>1.67 (1.05, 2.65)</td>
<td>1.95 (1.06, 3.57)</td>
</tr>
<tr>
<td>WOMAC function</td>
<td>1.19 (1.06, 1.35)</td>
<td>1.95 (1.06, 3.57)</td>
</tr>
<tr>
<td>Knee extensor strength (Newton)</td>
<td>0.95 (0.99, 0.99)</td>
<td>1.00 (0.99, 1.00)</td>
</tr>
<tr>
<td>History of knee injury (yes vs. no)</td>
<td>1.47 (0.90, 2.39)</td>
<td>1.25 (0.97, 1.60)</td>
</tr>
<tr>
<td>History of knee surgery (yes vs. no)</td>
<td>1.17 (0.66, 2.05)</td>
<td>1.11 (0.63, 1.90)</td>
</tr>
<tr>
<td>Hip pain (yes vs. no)</td>
<td>1.23 (0.91, 1.67)</td>
<td>1.40 (1.12, 1.72)</td>
</tr>
<tr>
<td>Arthral pain (yes vs. no)</td>
<td>2.40 (1.69, 3.39)</td>
<td>1.36 (0.87, 2.10)</td>
</tr>
<tr>
<td>Foot pain (yes vs. no)</td>
<td>0.68 (0.36, 1.37)</td>
<td>1.68 (0.71, 3.98)</td>
</tr>
</tbody>
</table>

Results from two logistic regression models are shown. Values are adjusted for all other predictors. Significant findings are bolded.

Disclosure: A. H. Chang, None; J. Lee, None; O. Almagor, None; J. S. Chmiel, None; K. C. Moisio, None; K. W. Hayes, None; J. Szymaszek, None; L. Sharma, None.


Abstract Number: 937

Treatment Response in Polyarticular JIA Is Associated with Transcriptional Changes and Chromatin Reorganization in CD4+ T Cells

Evan Tarbell1, Kaiyu Jiang2, Yanmin Chen2, Tao Liu3 and James Jarvis4, 1Biochemistry, University at Buffalo, Buffalo, NY, 2Pediatrics, University at Buffalo, Buffalo, NY, 3Biochemistry, University at Buffalo Jacobs School of Medicine,
**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** Pediatric Rheumatology – Pathogenesis and Genetics  
**Session Type:** ACR Concurrent Abstract Session  
**Session Time:** 4:30PM-6:00PM

**Background/Purpose:** To identify transcriptional changes in CD4+ T cells as children with polyarticular JIA transition from active disease to remission, and to identify underlying changes in chromatin architecture that account for these changes.

**Methods:** We isolated RNA from CD4+ T cells of children with 3 phenotypes: active, treated polyarticular JIA (ADT, n=12), children on medication who fit criteria for clinical remission (CRM, n=10), and 10 healthy children (HC). RNA sequencing was performed using the Illumina HiSeq 2500 platform. We used the assay for transposase-accessible chromatin-sequencing (ATACseq) to survey open chromatin in a subset of these same patients (6 HC, and 5 ADT and CRM). We investigated whether regions of open chromatin that were unique to any of the 3 phenotypes (ADT, CRM, or HC) might show enrichment for specific transcriptional regulators, using standard computational approaches to determine whether unique peaks were associated with up-regulated genes, as determined by phenotype-to-phenotype comparisons of RNAseq data. We divided peaks into central and flanking regions then calculated the best match to each of 700+ motifs for each sub-region within each peak, and calculated enrichment by comparing the score of the best central match to the score of the best flanking matches.

**Results:** Each of the 3 phenotypes was associated with its own its own chromatin accessibility signature as identified by ATACseq and its own transcriptional signature. We identified 16,039 accessible sites that were unique to HC, 38,451 that were unique to ADT, and 58,289 sites that were unique to CRM. Further analyses of the open regions unique to the HC cells showed that these regions were highly enriched (compared to genome background) for CCCTC-binding factor (CTCF) binding sites. These CTCF binding sites were absent in JIA CD4+ T cells. Differential CTCF accessibility was identified within 2 of the known JIA risk haplotypes, those identified by the SNPs rs147992 (upstream of the IL2 gene) and rs2266959, an intronic region of the UBE2LR gene that also features H3K27ac+ enhancer marks in CD4+ T cells. This finding suggests that aberrant 3D chromatin architecture (which is regulated by CTCF) may be a primary driver of the transcriptional aberrations observed in JIA. Analysis of the combined RNAseq and ATACseq using BETA software demonstrated that the differences in chromatin accessibility had high regulatory potential for the differentially expressed genes, providing strong evidence that the chromatin changes and gene expression changes are causally linked. The CRM state was not associated with normalization of either the chromatin or transcriptional signatures of CD4+ T cells in children with JIA.

**Conclusion:** Treatment response in JIA is associated with significant re-organization of chromatin and is accompanied by significant changes in transcription that can be attributed to the chromatin re-organization. Patterns of chromatin accessibility suggest important roles for chromatin regulators (e.g., CTCF) in JIA and possible genetic determinants governing CTCF accessibility. The achievement of CRM does not result in a normalization of either the transcriptome or the epigenome of CD4+ T cells.

**Disclosure:** E. Tarbell, None; K. Jiang, None; Y. Chen, None; T. Liu, None; J. Jarvis, None.


**Abstract Number:** 938

**A Germline Macrophage Activation Syndrome-Associated Nlrc4 Mutation Causes Chronic, Systemic, Non-Hematopoietic IL-18 Elevation and Intestinal MHC-II Upregulation**
Eric Weiss¹, Corinne Schneider², and Scott Canna³, ¹RK Mellon Institute, Children’s Hospital of Pittsburgh, Pittsburgh, PA, ²Pediatrics, Children's Hospital Pittsburgh, Pittsburgh, PA, ³NIAMS, National Institutes of Health, Bethesda, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Pediatric Rheumatology – Pathogenesis and Genetics
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Patients prone to the development of Macrophage Activation Syndrome (MAS) can have extreme and often chronic elevation in the pro-inflammatory cytokine interleukin-18 (IL-18). In particular, those with gain-of-function mutations in the inflammasome-nucleating protein NLRC4 provided the first mechanistic link between the inflammasome, IL-18, and MAS. Other inflammasome-associated disorders lack such extreme and persistent IL-18 elevation (Fig. 1). In order to dissect the mechanisms associated with NLRC4 hyperactivity, we generated a mouse with an MAS-associated germline missense mutation (T337S) in Nlrc4 (N4-TS mice).

Methods: N4-TS mice were generated by Crispr-Cas9 genome engineering and bred to WT for at least four generations. IL-18 was measured by bead-based immunoassay (Luminex or BD Cytometric Bead Array). RNA-sequencing was performed on duodenal epithelial mucosal tissue scrapings placed into Trizol. MHC-II upregulation was assessed by flow cytometry.

Results: N4-TS mice overproduced IL-18 in an allele-dependent manner. We found that IL-18 elevation was present as early as 3 weeks of age, and was unaffected by co-housing or antibiotic treatment. Using bone-marrow chimeras, we determined that IL-18 elevation in N4-TS mice was non-hematopoietic. Upon review of publicly available transcriptional datasets, we discovered that barrier epithelia, and in particular intestinal epithelial cells (IECs), are a rich source of colonization-independent Il18 and expressed high levels of Nlrc4 compared to other inflammasome nucleators. RNA-seq of duodenal epithelium showed upregulation of pathways associated with antigen presentation and epithelial turnover in N4-TS mice. Though we saw no increase in Dextran Sodium Sulfate-Induced colitis in N4-TS mice, increased baseline IEC proliferation was confirmed by EdU incorporation. MHC-II was upregulated in N4-TS intestinal epithelial cells as well intraepithelial and αβ- and γδ-T-cells, but not in splenic or liver lymphocytes. By contrast, mice with transgenic expression of Il18 (Il18tg) had MHC-II upregulation in intestines, liver, and spleen. (Fig. 2)

Conclusion: Like NLRC4-MAS patients, N4-TS mice spontaneously overproduce IL-18. Barrier epithelia may be an important site for NLRC4-dependent IL-18 maturation. MHC-II upregulation is tissue-specific in Nlrc4-T337S mice and
may be an anti-inflammatory response. These data suggest a role for barrier epithelial dysfunction as a contributor to systemic inflammatory diseases, particularly those associated with chronic IL-18 elevation and MAS.

Disclosure: E. Weiss, None; C. Schneider, None; S. Canna, AB2Bio Ltd, 5.


Abstract Number: 939

Stimulator of Interferon Genes (STING)-Induced Endothelial-Mesenchymal Transition (EndMT) Contributes to Interstitial Lung Disease in Sting-Associated Vasculopathy with Onset in Infancy (SAVI) Patients

Louise Malle1, Dan Yang2, Adriana Almeida de Jesus1, Guibin Chen2, Bernadette Marrero1, Gina A. Montealegre Sanchez1, Yin Liu3, Gregor Dueckers4, Suzanne Ramsey5, Joseph Fontana6, Rachel VanTries1, Yan Huang1, Laisa Santiago7, Benito Gonzalez8, Paul Brogan9, Juergen Brunner10, Ebun Omoyinmi11, Athimalaipet V. Ramanan12, Amy Paller13, Olcay J. Jones14, Seza Ozen15, Stephen R. Brooks16, Manfred Boehm17 and Raphaela Goldbach-Mansky1,

1Translational Autoinflammatory Disease Studies (TADS), Laboratory of Clinical Investigation and Microbiology (LCIM), NIAID/NIH, Bethesda, MD, 2Center for Molecular Medicine, NHLBI/NIH, Bethesda, MD, 3Scientific Review Branch, NIAMS/NIH, Bethesda, MD, 4Helios Kliniken - Kinderklinik, HELIOS Klinikum Krefeld, Krefeld, Germany, 5Pediatric Rheumatology, IWK Health Centre, Dalhousie University, Halifax, NS, Canada, 6Cardiovascular and Pulmonary Branch, NHLBI/NIH, Bethesda, MD, 7Johns Hopkins All Children's Hospital Rheumatology, Saint Petersburg, FL, 8Luis Calvo Mackenna Hospital, Santiago, Chile, 9Infection Inflammation and Rheumatology, UCL Institute of Child Health, and Great Ormond Street Hospital NHS Foundation Trust, London, United Kingdom, 10Division of Pediatric Rheumatology, Medical University Innsbruck, Innsbruck, Austria, 11University College London Institute of Child Health, London, United Kingdom, 12Bristol Royal Hospital for Children, Bristol, United Kingdom, 13Department of Dermatology, Northwestern University Feinberg School of Medicine, Chicago, IN, 14Department of Pediatrics, Walter Reed National Military Medical Center, Bethesda, MD, 15Department of Pediatrics, Division of Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Turkey, 16Biodata Mining and Discovery Section, Office of Science and Technology, NIAMS/NIH, Bethesda, MD, 17Center for Molecular Medicine, NHLBI/NIH, Bethesda, MD

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Pediatric Rheumatology – Pathogenesis and Genetics
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Pulmonary fibrosis, is a life-threatening complication of the monogenic autoinflammatory interferonopathy, STING-Associated Vasculopathy with onset in Infancy (SAVI) that is caused by gain-of-function mutations in the viral sensor/adaptor TMEM173/STING. Pathogenic mechanisms causing fibrosis and factors modifying the onset and severity of lung fibrosis in SAVI patients (pts.) are unknown. Here we show that STING-mediated endothelial cell activation induces an endothelial-mesenchymal transition (EndMT)-like differentiation program that causes lung fibrosis in SAVI pts.

Methods: To understand the role of STING signaling in pulmonary fibrosis, we assessed chest computed tomography (CT), pulmonary function tests (PFTs) in 13 SAVI patients (pts.), and lung histopathology was available from 4 pts. We conducted pts. and control fibroblast, human lung and umbilical vein endothelial cell (EC) lines (HMVEC-L and HUVECs, respectively) and pts. and control induced pluripotent stem cell (iPSC)-derived EC stimulations with endogenous and microbial cGAMP plus/minus IFNb. Gene expression (q-RT-PCR, RNA-seq), cytokine production, and EndMT (by cell
morphology and gene expression studies), were assessed. Pts. were genotyped for a common STING SNP (R232H, rs1131769) and the modifying effect of the variant was examined in transfection studies in HEK293T cells.

**Results:** Of 13 SAVI pts., 10 had severe lung disease, 4 succumbed to pulmonary complications. Pulmonary findings included hilar lymphadenopathy, diffuse ground glass opacities and cystic emphysematous changes on chest CT, and reduced diffusing lung capacity for carbon monoxide (DLCO) and abnormal 6-minute walk test on PFTs. In contrast to control lung biopsies (n=5), pts.' biopsies (n=4) displayed perivascular fibrosis on Masson’s trichrome-stain around medium-sized and small alveolar vessels. In pts., endothelial lining co-expressed mesenchymal (α-SMA) and stromal fibroblast (FSP-1) markers within the subendothelial compartment. cGAMP stimulation in pt. and control fibroblasts showed no expression of myofibroblast and extracellular matrix (ECM) markers by RNA-seq and q-RT-PCR. *Endogenous* cGAMP stimulation on HMVEC-L induced morphologic transition to fibroblasts with a decreased expression of EC markers CDH5 (V-cadherin), VWF and PECAM1 (CD31), and an increased expression of the mesenchymal markers ACTA2 (α-SMA) and FAP and of the stromal fibroblast marker S100A4 (FSP-1). IFNβ and cGAMP stimulation synergize and addition of a JAK inhibitor attenuated the mesenchymal transformation. IPSC-derived EC (iEC) from 4 SAVI pts. but not HCs spontaneously differentiated into myofibroblasts in culture. Differentiation was attenuated by JAK inhibition and in shRNA STING knock down iEC. Homozygosity for R232/R232, a STING SNP associated with increased IFNβ production, in addition to the SAVI STING mutation led to a more severe clinical lung phenotype in SAVI patients.

**Conclusion:** We suggest a novel pathway of STING-mediated ECs activation to induce EndMT-like mesenchymal transformation as cause for lung fibrosis in SAVI pts.

**Disclosure:** L. Malle, None; D. Yang, None; A. Almeida de Jesus, None; G. Chen, None; B. Marrero, None; G. A. Montealegre Sanchez, Eli Lilly and Company, 9; Y. Liu, None; G. Dueckers, None; S. Ramsey, None; J. Fontana, None; R. VanVries, None; Y. Huang, None; L. Santiago, None; B. Gonzalez, None; P. Brogan, None; J. Brunner, None; E. Omoynimni, None; A. V. Ramanan, None; A. Paller, None; O. Y. Jones, None; S. Ozen, None; S. R. Brooks, None; M. Boehm, None; R. Goldbach-Mansky, Eli Lilly and Company, 9;SOBI, 9,Regeneron, 9,Novartis Pharmaceutical Corporation, 9.


**Abstract Number:** 940

**IL1RN Variation Is Associated with Systemic Juvenile Idiopathic Arthritis and Predicts Non-Response to Anakinra Treatment**

Emily Shuldiner¹, Victoria Arthur¹, Anne Hinks², Patricia Woo³, Wendy Thomson², Elaine F. Remmers⁴ and Michael J. Ombrello¹, ¹Translational Genetics and Genomics Unit, NIAMS, NIH, Bethesda, MD, ²Arthritis Research UK Centre for Genetics and Genomics, Centre for Musculoskeletal Research, Manchester Academic Health Sciences Centre, The University of Manchester, Manchester, United Kingdom, ³University College London, London, United Kingdom, ⁴Genetics and Genomics Branch, NIH, NIAMS, Bethesda, MD

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Pediatric Rheumatology – Pathogenesis and Genetics

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 4:30PM-6:00PM

**Background/Purpose:** Systemic juvenile idiopathic arthritis (sJIA) is a childhood inflammatory disease whose pathophysiology is poorly understood. sJIA is phenotypically heterogeneous with variable manifestations and responses to treatment. Until recently genetic investigations of sJIA have consisted of candidate gene studies in small patient collections. These studies found only modest associations, yet these associations are regularly included in discussions of sJIA
Methods: Single nucleotide polymorphism (SNP) genotypes were extracted from the INCHARGE dataset, (771 sJIA, 6947 controls). Logistic regression was performed in each case-control stratum and association results were meta-analyzed. The effect of sJIA associated SNPs on gene expression was evaluated in silico in paired whole genome (WGS) and RNA sequencing (RNAseq) data from lymphoblastoid cell lines (LCL) of 373 European 1000 Genomes Project subjects. The relationship between sJIA associated SNPs and response to recombinant interleukin-1 (IL-1) receptor antagonist (anakinra) treatment was evaluated in 38 US patients for whom treatment response data were available.

Results: None of the 26 SNPs with previously reported sJIA associations demonstrated even nominal (p<0.05) association with sJIA in our study. We expanded the analysis to determine whether the 11 loci containing the 26 SNPs harbored any sJIA risk SNPs. We examined 5479 SNPs from the 11 candidate regions, among which 500 SNPs were independent (r^2<0.5), defining the study’s significance threshold as p<1E-4. Association meta-analysis revealed only one significant association among the 11 candidate loci, the promoter region of IL1RN, where 3 SNPs in strong linkage disequilibrium showed a significant association with sJIA. Analysis of LCL data showed that the sJIA associated SNPs correlated with IL1RN expression, with an inverse correlation between sJIA risk and IL1RN expression. Importantly, the presence of homozygous IL1RN high expression alleles correlated strongly with non-response to anakinra (p=9.8E-4, OR 17.3 [2.8, 108.1]).

Conclusion: IL1RN was the only candidate locus associated with sJIA in our study. The sJIA associated SNPs are among the strongest known determinants of IL1RN and IL1RA levels, linking low expression with increased sJIA risk. Although high expression alleles were protective against sJIA, patients with 2 high expression alleles were significantly less likely to respond to anakinra treatment than those with 1 or 2 low expression alleles. Even though anakinra is well known to ameliorate or reduce inflammation in some sJIA patients, this is the first report to link sJIA risk and response to anakinra treatment with genetically determined capacity to produce IL1RN or IL1RA. These SNPs are the first potential biomarker(s) capable of prospectively guiding therapeutic decision making in sJIA.

Disclosure: E. Shuldiner, None; V. Arthur, None; A. Hinks, None; P. Woo, None; W. Thomson, None; E. F. Remmers, None; M. J. Ombrello, None.

Abstract Number: 941

Ro/SSA Autoantibody Exposed Neonates Have an Expansion of NK Cells and a Discernible Type II IFN Signature with High IFNγ in Peripheral Blood

Margarita Ivanchenko¹, Malin Hedlund¹, Gudny Ella Thorlacius¹, Vijole Ottosson¹, Karine Chemin², Sven-Erik Sonesson³ and Marie Wahren-Herlenius¹, ¹Unit of Experimental Rheumatology, Department of Medicine, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, Stockholm, Sweden, ²Department of Medicine, Center for Molecular Medicine, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, Stockholm, Sweden, ³Pediatric Cardiology Unit, Department of Women’s and Children’s Health, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, Stockholm, Sweden

First publication: September 18, 2017
**Background/Purpose:** Congenital heart block (CHB) may develop in the fetus of women with Ro/SSA autoantibodies. The mothers are commonly diagnosed with Sjögren’s syndrome or SLE. During pregnancy, the antibodies are transported across placenta and bind to the fetal heart where inflammation develops, leading to the fibrosis and calcification that cause the permanent disruption of impulse propagation. The mechanism by which the antibodies initiate inflammation is however not understood. In the mother, Ro/SSA antibodies may induce type I IFN production, and we recently described an upregulation of type I IFN-regulated genes in PBMC as well as an increase in circulating IFN-alpha also in the Ro/SSA exposed newborns. IFN-alpha is known to influence leukocytes, expand and activate NK cells, and in this study, we, therefore, analyzed the immune cell populations in cord blood of anti-Ro/SSA exposed neonates and evaluated the influence of IFN-alpha on fetal cardiac cells.

**Methods:** Maternal and cord blood was sampled at birth from healthy controls (HC) (n=9) and Ro/SSA positive pregnancies (n=13). PMBC were prepared and used for microarray analysis and for flow cytometry to define CD19^+ B cell (CD27^-IgD^+ naive, CD27^+IgD^- memory, CD27^+IgD^+ marginal zone), CD3^+ T cell (CD8^+, CD4^+) subpopulations and CD16^+CD56^+ NK cells. Cardiomyocyte cultures were established from human fetal tissues (n=5) and stimulated by medium with or without IFN-alpha for 6 hours before mRNA preparation and microarray analysis.

**Results:** In the Ro/SSA positive mothers, an increase in naïve B cells, but decrease in memory and marginal zone cells was observed, confirming previous reports for non-pregnant Sjögren’s syndrome and SLE. Surprisingly, Ro/SSA exposed neonates presented an expanded population of NK cells (p=0.02), the presence of which was influenced by immunomodulatory treatment of the mother (neonates of non-treated mothers p=0.002, neonates of treated mothers p=ns compared to HC). No other differences in the T or B cell subsets analyzed were observed. Microarray analysis of PBMC revealed a type II IFN signature with high IFNγ, the prototype cytokine produced by activated NK cells, in Ro/SSA exposed neonates compared to HC. Finally, stimulation of fetal cardiomyocytes with IFN-alpha induced upregulation of MICA and MICB (major histocompatibility complex (MHC) class I chain related sequence A and B), which are ligands for activating NK cell receptors.

**Conclusion:** Our data demonstrate an expansion of NK cells and their activity markers in Ro/SSA exposed neonates, as well as an upregulation of activating NK cell receptors in fetal cardiac cells after IFN-alpha exposure, indicating that NK cell related effector mechanisms such as antibody-dependent cell cytotoxicity (ADCC) may be a central mechanism by which the inflammation is initiated in CHB. The expansion of NK cells in neonates at risk for CHB is a novel observation, and implicates fetal innate immune mechanisms in the pathogenesis.

**Disclosure:** M. Ivanchenko, None; M. Hedlund, None; G. E. Thorlacius, None; V. Ottosson, None; K. Chemin, None; S. E. Sonesson, None; M. Wahren-Herlenius, None.


**Abstract Number:** 942

**Role of the Pyrin Inflammasome in Resistance to Yersinia Pestis: A Possible Selective Advantage for Carriers of MEFV Mutations**

Yong Hwan Park^1, Wonyong Lee^1, Lawton Chung^2, James Bliska^2, Daniel L. Kastner^1 and Jae Jin Chae^3, ^1Inflammatory Disease Section, National Human Genome Research Institute, National Institutes of Health, Bethesda, MD, ^2Department of Molecular Genetics and Microbiology, School of Medicine, Stony Brook University, Stony Brook, NY, ^3Inflammatory disease section, National Human Genome Research Institute, National Institutes of Health, Bethesda, MD

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017

**Session Title:** Pediatric Rheumatology – Pathogenesis and Genetics

**Session Type:** ACR Concurrent Abstract Session
Background/Purpose: Mutations in MEFV, encoding pyrin, cause the prototypic autoinflammatory disease, familial Mediterranean fever (FMF). The carrier frequency of FMF-associated MEFV mutations is extraordinarily high in Mediterranean and Middle Eastern populations, suggesting that heterozygous FMF mutations may confer a selective advantage against some pathogenic microbes. Inactivation of the RhoA GTPase is a common bacterial virulence mechanism, because RhoA activation is required for actin polymerization and leukocyte migration, phagocytosis, and degranulation. The pyrin inflammasome senses RhoA inactivation and activates IL-1β as part of the host defense against these bacteria. Pathogenic Yersinia, including Y. pestis, the agent of plague in humans, deliver virulence effectors, termed Yersinia outer proteins (Yops), into host cells; some of these Yops are known to inactivate RhoA. In the current study, we utilized pyrin knockin (KI) and knockout (KO) mice to examine the role of pyrin in host defense against Yersinia infection.

Methods: Pyrin-KO and FMF-KI mice harboring the FMF-associated M680I or V726A mutations were examined for susceptibility to Y. pestis by infection studies. We measured IL-1β production by ELISA in immune cells from wild type and from FMF-KI mouse strains, in response to wild type (WT) Y. pseudotuberculosis or Y. pestis, or to mutant Yersinia strains with deletions of specific Yops. Protein interactions were studied by immunoprecipitation.

Results: In Yersinia-infected macrophages, the pyrin inflammasome was activated by the RhoA-inactivating enzymatic activities of YopE and YopT. On the other hand, YopM specifically inhibited pyrin to promote virulence by activating the host protein kinases (PKN1 and PKN2) that phosphorylate pyrin to block pyrin inflammasome activation. Pyrin-KO mice were highly susceptible to Yersinia yopM mutant infection, while WT mice were not susceptible. However, bone marrow-derived macrophages (BMDMs) from both homozygous and heterozygous FMF-KI mice released significantly higher levels of IL-1β in comparison with WT BMDMs in response to Yersinia infection. These results suggest that the FMF-associated mutant pyrin is not suppressed by YopM, thereby providing survival advantage of FMF-KI mice against Yersinia infection. Indeed, FMF-KI mice, both homozygotes and heterozygotes, showed significant resistance to Y. pestis infection in comparison with WT mice.

Conclusion: These findings, taken together with the historical record of high-mortality epidemics throughout human history, suggest that Yersinia pestis played an important role in selecting for the high frequency of FMF-associated MEFV mutations in Mediterranean and Middle Eastern populations.

Disclosure: Y. H. Park, None; W. Lee, None; L. Chung, None; J. Bliska, None; D. L. Kastner, None; J. J. Chae, None.


Abstract Number: 943

The Course of the Forced Vital Capacity during Treatment for Systemic Sclerosis-Related Interstitial Lung Disease Predicts Long-Term Survival in 2 Independent Cohorts

Elizabeth R. Volkmann1, Donald P. Tashkin1, Myung Sim1, Dinesh Khanna2, Michael Roth3, Philip J. Clements3, Daniel E. Furst1, Lynette Keyes-Elstein4, Ashley Pinckney4, Ellen Goldmanz5, Robert Elashoff6 and Keith Sullivan7, 1University of California, Los Angeles, David Geffen School of Medicine, Los Angeles, CA, 2University of Michigan, Ann Arbor, MI, 3Medicine, University of California, Los Angeles, David Geffen School of Medicine, Los Angeles, CA, 4Rho Federal Systems, Inc., Chapel Hill, NC, 5NIAID, NIH, Bethesda, MD, 6University of California, Los Angeles, Los Angeles, CA, 7Duke University, Durham, NC

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017

Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics I
Background/Purpose: While prior observational studies have identified predictors of mortality in systemic sclerosis-interstitial lung disease (SSc-ILD), no studies have evaluated predictors of long-term mortality in a clinical trial, in which all patients receive standard care. The objective of this study was to identify predictors of mortality in patients who participated in the Scleroderma Lung Study (SLS) I\(^1\) and II\(^2\).

Methods: SLS I randomized 158 SSc-ILD patients to 1 year of oral cyclophosphamide (CYC) versus placebo. SLS II randomized 142 patients to 1 year of oral CYC followed by 1 year of placebo versus 2 years of mycophenolate (MMF). The FVC%-predicted and DLCO%-predicted were measured every 3 months for 2 years in both trials. 12 years after SLS I commenced, each study center contacted enrolled patients/designated surrogates to assess morbidity and mortality outcomes. Counting process Cox proportional hazard modeling identified variables associated with mortality. A joint model of longitudinal FVC and survival data was used to internally validate the model. We externally validated the model using long-term mortality data from SLS II (up to 5 years of follow-up).

Results: Among SLS I patients, 43% died during the follow-up period (median follow-up: 8 years), and only 24% remained alive without organ failure. Where known, the cause of death was attributable most often to SSc. The most common type of organ failure was respiratory failure (N=31 of 33 organ failures) defined as the need for supplemental oxygen therapy (N=29) and/or lung transplantation (N=3). There was no significant difference in the time to death between patients randomized to CYC versus placebo (Figure 1). The Cox model identified the following mortality predictor variables: baseline skin score (HR 1.03; \(P=0.004\)), age (HR 1.06; \(P<0.0001\)), and the course of the FVC from baseline to 24 months (HR 0.98; \(P=0.022\)). The course of the FVC was a better predictor than the baseline FVC. The joint model identified the same variables associated with mortality. Using the SLS II data, the Cox model identified the same mortality predictor variables: baseline skin score (HR 2.08; \(P=0.021\)), age at randomization (HR 1.08; \(P=0.011\)), and the course of the FVC from baseline to 24 months (HR 0.79; \(P=0.020\)).

Conclusion: Treatment with 1-year of oral CYC for SSc-ILD did not significantly decrease long-term mortality compared with placebo. In addition to identifying traditional mortality risk factors in SSc (i.e. increased skin score and advanced age), this study found that a decline in FVC over 2 years was a better predictor of mortality than the baseline FVC. These findings suggest that early changes in surrogate measures of SSc-ILD progression may have important effects on long-term outcomes.

\(^1\) Tashkin et al. *NEJM* 2006.


![Figure 1. Time to death in patients randomized to CYC (solid line) and placebo (dotted line).](image-url)
Abstract Number: 944

Long-Term Survival and Follow-up of Anti-Th/to Antibody Positive Systemic Sclerosis Patients

Devon Charlton¹, Maureen Laffoon², Thomas A. Medsger Jr.³ and Robyn T. Domsic⁴, ¹Division of Rheumatology and Clinical Immunology, University of Pittsburgh Medical Center, Pittsburgh, PA, ²Rheumatology, University of Pittsburgh Medical Center, Pittsburgh, PA, ³Department of Medicine/Rheumatology, University of Pittsburgh, Pittsburgh, PA, ⁴Medicine - Rheumatology, University of Pittsburgh, Pittsburgh, PA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics I
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose:

Anti-Th/To antibody is an autoantibody associated with systemic sclerosis (SSc), occurring in 5-10% of patients. To date, only relatively small case series have described the clinical associations of this autoantibody, as commercial testing has not been readily available. Thus, the long-term clinical features and outcomes of patients with anti-Th/To antibody is not known. The objective of this study was to further characterize the clinical associations and mortality risk of SSc patients who are anti-Th/To positive.

Methods:

We performed a case-control study. Eligible patients were identified from consecutive new SSc patients seen at a large US SSc Center between 1980-2015. Cases were found to be anti-Th/To antibody positive by immunoprecipitation. Each case was matched to the next two consecutive SSc patients seen in clinic (2:1 match). Descriptive statistics, Kaplan-Meier and Cox proportional hazards was performed using SAS 9.4.

Results:

199 Th/To-positive SSc patients were identified and matched to 398 controls. The mean age of the entire population was 51.6 ± 14.1 years, 78% female and 92% Caucasian. Th/To positive patients were more frequently Caucasian, had long disease duration at evaluation and more often presented with SSC sine scleroderma (see Table 1). At baseline Th/To patients were more frequently found to have pulmonary hypertension, but less frequent joint involvement. There was no difference in rate of interstitial lung disease (ILD) found on radiographic imaging (Table 1).

As of last follow-up 41 (21%) of Th/To positive patients had developed PAH compared to 43 (11%; p=0.001). Twenty-five (13%) Th/To positive patients had developed PH secondary to ILD compared to 33 (8%) controls (p= 0.10), with no difference in frequency of ILD. Despite the greater frequency of PH in cases, 5-year cumulative survival was not any different between Th/To positive patients (29%) and controls (28%; p=0.90), even after adjustment for age and gender.

Conclusion:
This is the largest cohort of Th/To antibody positive SSc patients for which there is long-term follow-up for clinical features and survival data available. Compared to other SSc patients, anti-Th/To patients develop higher rates of PAH. Cumulative 5-year survival is not reduced in Th/To patients, likely reflecting advances in PAH management. SSc patients should be routinely screened for the Th/To antibody, with consideration of appropriate screening for PAH.

Table 1: Characteristics of Anti-Th/To Positive Patients and Controls at First SSc Center Visit

<table>
<thead>
<tr>
<th></th>
<th>Anti-Th/To n=199</th>
<th>Controls n=398</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age in years at first visit* (SD)</td>
<td>52.4 (12.2)</td>
<td>51.2 (15.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Female</td>
<td>156 (78%)</td>
<td>312 (78%)</td>
<td>NS</td>
</tr>
<tr>
<td>Caucasian</td>
<td>189 (95%)</td>
<td>356 (90%)</td>
<td>0.04</td>
</tr>
<tr>
<td><strong>SSc Disease Characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median disease duration in years (IQR)</td>
<td>7.8 (2.5, 15.0)</td>
<td>5.4 (1.8, 13.0)</td>
<td>0.01</td>
</tr>
<tr>
<td>Median modified Rodnan skin score† (IQR)</td>
<td>2 (1,4)</td>
<td>4 (2,14)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Limited skin thickening</td>
<td>197 (99%)</td>
<td>364 (95%)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Systemic sclerosis sine scleroderma</td>
<td>45 (23%)</td>
<td>62 (16%)</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>Overlap</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overlap</td>
<td>0 (0%)</td>
<td>7 (3.5%)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>SSc Internal Organ Involvement at 1st Visit</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary Arterial Hypertension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibrosis by imaging</td>
<td>36 (18%)</td>
<td>74 (19%)</td>
<td>NS</td>
</tr>
<tr>
<td>Cardiac</td>
<td>24 (12%)</td>
<td>41 (10%)</td>
<td>NS</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>26 (14%)</td>
<td>77 (19%)</td>
<td>NS</td>
</tr>
<tr>
<td>Joint</td>
<td>62 (32%)</td>
<td>223 (58%)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Renal Crisis</td>
<td>3 (2%)</td>
<td>15 (4%)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>WHO Group Pulmonary Hypertension</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary arterial hypertension (Group 1)</td>
<td>35</td>
<td>29</td>
<td>0.02</td>
</tr>
<tr>
<td>Related to cardiac disease (Group 2)</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Related to lung disease (Group 3)</td>
<td>14</td>
<td>20</td>
<td></td>
</tr>
</tbody>
</table>

*Disease onset defined as first symptom attributable to SSc; SD = standard deviation; IQR = interquartile range

Disclosure: D. Charlton, None; M. Laffoon, None; T. A. Medsger Jr., None; R. T. Domsic, None.


Abstract Number: 945
Autoantibodies to the hPOP1 and Rpp25/38 Components of the Th/to Complex Identify a Subgroup of Systemic Sclerosis (SSc) Associated Interstitial Lung Disease (ILD) and Antibodies to hPOP1 Are Associated with Reduced Survival

Jennifer G Walker1, Mandana Nikpour2, Molla Huq3, Karen Patterson1, Peter Roberts-Thomson4, Susanna Proudman5, Wendy Stevens6, Susan Lester7, Maureen Rischmueller8, Jane Zochling9, Joanne Sahhar10, Peter Nash11, Janet Roddy12, Catherine Hill13, Marie Hudson14, Murray Baron15, Janet E. Pope16, Maureen D. Mayes17, Shervin Assassi18, Michael Mahler19 and Marvin J. Fritzler20, 1Flinders University of South Australia, Adelaide, Australia, 2Melbourne University, Melbourne, Australia, 3Department of Medicine (Rheumatology), Melbourne University, Melbourne, Australia, 4Immunology, Flinders University of South Australia, Adelaide, Australia, 5University of Adelaide, Adelaide, Australia, 6Rheumatology, St. Vincent’s Hospital, Melbourne, Australia, 7Queen Elizabeth Hospital, Adelaide, Australia, 8Medicine, University of Adelaide, Adelaide, Australia, 9Menzies Institute for Medical Research, Tasmania, Hobart, Australia, 10Department of Rheumatology, Monash Medical Centre, Melbourne, Australia, 11University of Queensland, Brisbane, Australia, 12Royal Perth Hospital, Perth, Australia, 13Medicine, The University of Adelaide, Adelaide, Australia, 14Division of Rheumatology, Jewish General Hospital, Lady David Institute for Medical Research, Montreal, QC, Canada, 15Medicine, McGill University, Quebec, Montreal, QC, Canada, 16Department of Medicine, Division of Rheumatology, University of Western Ontario, St Joseph's Health Care, London, ON, Canada, 17Internal Medicine/Rheumatology, University of Texas Health Science Center at Houston, Houston, TX, 18University of Texas McGovern Medical School, Houston, TX, 19Research and Development, Inova Diagnostics, San Diego, CA, 20Medicine, University of Calgary, Calgary, AB, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics I
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: The clinical associations of anti-Th/To antibodies (Abs) are not fully established, and until recently immunoprecipitation (IP) was the only reliable assay. Using IP, anti-Th/To Abs are mostly detected in SSc but other reported associations include ILD. Our objective was to examine clinical correlates of anti-Th/To Abs targeted against three different proteins associated with the Th/To autoantigen complex in SSc. We used a commercially available hPOP1 immunoblot and a recently described Rpp25 and Rpp38 chemiluminescence assay in a multinational cohort of SSc.

Methods: Cross sectional retrospective study including 1312 patients from the Australian Scleroderma Cohort study (ASCS), Canadian Scleroderma Research Group (CSRG) and the Genetics versus Environment in Scleroderma Outcome Study (GENISOS). Demographic and clinical variables were harmonized and sera tested for anti-Th/To Abs using hPOP1 (EUROLINE, Eurimmun, Lubeck, Germany) and Rpp25/38 (QUANTA Flash Assay, Inova Diagnostics Inc, San Diego, CA). Rpp25/38 was defined as positive if either one or both autoantibodies were present. ILD was determined by high resolution CT chest (HRCT) or a published algorithm [1] which allows diagnosis of ILD by chest X-ray showing increased interstitial markings or fibrosis and/or physician reported “velcro-like crackles” when HRCT is not available. Descriptive statistics summarise baseline demographic and clinical variables and Kaplan Meier analyses were used to assess survival.

Results:

Patients had median (interquartile range) age at disease onset 46.3y (18.6) and disease duration 5.1y (11.4) at recruitment. hPOP1 was positive in 2.4% and Rpp25/38 was positive in 4.5% patients. Notably hPOP1 and Rpp25/38 identified overlapping patient populations (p=0.001). Median age of disease onset for hPOP1 patients was 48.9y (23.3) and for Rpp25/38 patients was 48.8y (17.3).

hPOP1 was associated with ILD on HRCT chest (OR:5.16; p=0.02) but not ILD by algorithm (OR:1.19; p= 0.642). hPOP1 was negatively associated with centromere Abs (CENP) (OR:0.24, p=0.018) and positively associated with PM75/100 (OR:
3.07, p=0.01), and Ro52/TRIM21 (OR: 3.18, p=0.002). hPOP1 was not associated with Scl-70 (p=0.089).

Fifty patients (4.0%) were Rpp25 positive and 14 patients (1.1%) Rpp38 positive with strong correlation between the two (p <0.001; rho=0.72). Rpp25/38 was associated with ILD detected by HRCT (OR:3.04; p=0.009) and by algorithm (OR: 2.01 p=0.01). Rpp25/38 was negatively associated with CENP (OR: 0.08, p<0.001) and Scl-70 (OR: 0.19, p=0.020).

Survival was reduced in hPOP1 positive patients (p<0.001), especially when ILD was present. Rpp25/38 and hPOP1 positivity was not associated with pulmonary hypertension nor other disease manifestations.

**Conclusion:**

In a large multinational SSc cohort autoantibodies to the hPOP1 and Rpp25/38 components of Th/To were found infrequently and appeared to identify two ILD populations. hPOP1 positivity was associated with ILD on HRCT chest and reduced survival while Rpp25/38 positivity was associated with ILD on HRCT and by clinical algorithm and testing may therefore identify those with differing lung involvement.


**Disclosure:**

J. G. Walker, None; M. Nikpour, I have received, either directly, or indirectly through close research collaborations, research support from the following companies: Actelion, GSK, Pfizer, BMS, UCB, Astra Zeneca, Janssen., 2,I have presented for UCB as a speaker. I have consulted for Eli Lilly., 5; M. Huq, None; K. Patterson, None; P. Roberts-Thomson, None; S. Proudman, Actelion Pharmaceuticals US, 2,GlaxoSmithKline, 2; W. Stevens, None; S. Lester, None; M. Rischmueller, None; J. Zochling, None; J. Sahhar, None; P. Nash, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Hospira, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, 5,AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Hospira, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, 8,AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Hospira, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, 2; J. Roddy, None; C. Hill, None; M. Hudson, None; M. Baron, None; J. E. Pope, AbbVie, Amgen, Bayer, BMS, Celtrion, Eli Lilly and Company, Merck, Novartis, Pfizer, Roche, UCB, 5,Amgen, Bayer, BMS, GSK, Merck, Novartis, Pfizer, Roche, UCB, 2; M. D. Mayes, None; S. Assassi, Bayer Healthcare, 2,Biogen Idec, 2,Reata, 5,Boehringer Ingelheim, 5; M. Mahler, Inova Diagnostics, Inc., 3; M. J. Fritzler, Inova Diagnostics, Inc., 5.


**Abstract Number: 946**

**Clinical and Serological Features of Systemic Sclerosis in a Multicenter African American Cohort: Analysis of the Genome Research in African American Scleroderma Patients Clinical Database**

Nadia D. Morgan1, Ami A. Shah1, Maureen D. Mayes2, Robyn T. Domsic3, Thomas A. Medsger Jr.4, Virginia D. Steen5, John Varga6, Mary A. Carns7, Paula S. Ramos8, Richard M. Silver9, Elena Schiopu10, Dinesh Khanna10, Vivien Hsu11, Jessica K. Gordon12, Heather Gladue13, Lesley A. Saketko14, Lindsey A. Criswell15, Chris T. Derk16, Marcin A. Trojanowski17, Victoria K. Shanmugam18, Lorinda Chung19, Antonia Valenzuela20, Reem Jan21, Avram Goldberg22, Elaine F. Remmers23, Daniel L. Kastner23, Fredrick M. Wigley24, Pravitt Gourh25 and Francesco Boin26, 1Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, 2Rheumatology, University of Texas Health Science Center at Houston, Houston, TX, 3Medicine - Rheumatology, University of Pittsburgh, Pittsburgh, PA, 4Department of Medicine/Rheumatology, University of Pittsburgh, Pittsburgh, PA, 5Division of Rheumatology, Department of Medicine, MedStar Georgetown University Hospital, Washington, DC, 6Rheumatology and Dermatology, Northwestern University, Feinberg School of Medicine Scleroderma Program, Chicago, IL, 7Northwestern University, Feinberg School of Medicine Scleroderma Program, Chicago, IL, 8Division of Rheumatology and Immunology, Medical University of South Carolina, Charleston, SC, 9Division of Rheumatology and Immunology, Department of Medicine, Medical University of South
Racial differences exist in the severity of systemic sclerosis (SSc). To enhance our knowledge about SSc in African Americans, we established a comprehensive clinical database from the largest multicenter cohort of African American SSc patients assembled to date (the Genome Research in African American Scleroderma Patients (GRASP) cohort). We compared the phenotypic manifestations of SSc in the GRASP cohort to that reported in the European League Against Rheumatism Scleroderma Trials and Research (EUSTAR) cohort 1.

Methods:

African American SSc patients were enrolled retrospectively and prospectively over a 30-year period (1987 to 2016), from 18 academic centers throughout the United States. 945 (94%) patients met the 2013 ACR/EULAR classification criteria for SSc, with the remaining 64 (6%) meeting the 1980 ACR orCREST criteria. The cross-sectional prevalence of sociodemographic, clinical and serological features was evaluated using data obtained at the time of study enrollment. Factors associated with clinically significant manifestations of SSc were assessed using multivariate logistic regression analyses.

Results:

The study population included a total of 1009 African American SSc patients comprised of 84% women. While 43% were actively employed, 33% required disability support. The majority (57%) had the more severe diffuse subtype and a young age at symptom onset (39.1±13.7 years), in marked contrast to that reported in the EUSTAR cohort. 11% of patients had a severe Medsger cardiac score2 of 4 (Figure 1). Pulmonary fibrosis evident on computed tomography (CT) chest was present in 43% of patients, and was significantly associated with anti-topoisomerase I positivity (Table 1). 38% of patients with CT evidence of pulmonary fibrosis had a severe restrictive ventilator defect with forced vital capacity (FVC) £50% predicted. 16% of patients in the GRASP cohort required oxygen therapy compared to 3% in the EUSTAR cohort. A significant association was noted between longer disease duration and higher odds of pulmonary hypertension (Table 1). The prevalence of potentially fatal scleroderma renal crisis was 7%, 3.5 times higher than that reported in the EUSTAR cohort.

Conclusion:

Our study emphasizes the unique and severe disease burden of SSc in African Americans compared to those of European ancestry.


**TABLE 1. Factors associated with Clinical Manifestations of Systemic Sclerosis, adjusted odds ratio (95% confidence interval)**

<table>
<thead>
<tr>
<th></th>
<th>Diffuse Sclerodema</th>
<th>Digital Tip\textsuperscript{a} Ulcers or Gangrene</th>
<th>Severe\textsuperscript{a} Muscle weakness</th>
<th>Pulmonary\textsuperscript{b} Fibrosis</th>
<th>Pulmonary\textsuperscript{b} Hypertension</th>
<th>Scleroderma Renal Crisis</th>
<th>Severe Gl\textsuperscript{b} Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at onset (per year)</td>
<td>0.99</td>
<td>0.97</td>
<td>0.98</td>
<td>1.00</td>
<td>1.00</td>
<td>0.99</td>
<td>0.99</td>
</tr>
<tr>
<td>Disease duration (per year)</td>
<td>0.93</td>
<td>1.00</td>
<td>1.04</td>
<td>1.02</td>
<td>1.06</td>
<td>1.01</td>
<td>1.00</td>
</tr>
<tr>
<td>Male Sex</td>
<td>1.51</td>
<td>0.98</td>
<td>3.56</td>
<td>0.80</td>
<td>1.53</td>
<td>1.81</td>
<td>0.93</td>
</tr>
<tr>
<td>Diffuse SSc subtype</td>
<td>–</td>
<td>3.28</td>
<td>2.03</td>
<td>0.63</td>
<td>0.93</td>
<td>2.45</td>
<td>2.11</td>
</tr>
<tr>
<td>ACA</td>
<td>0.14</td>
<td>1.47</td>
<td>( \neq )</td>
<td>0.45</td>
<td>1.52</td>
<td>( \neq )</td>
<td>0.79</td>
</tr>
<tr>
<td>Topo I</td>
<td>1.67</td>
<td>1.10</td>
<td>0.87</td>
<td>2.14</td>
<td>1.29</td>
<td>0.53</td>
<td>1.21</td>
</tr>
<tr>
<td>TOPOL III</td>
<td>(1.08-2.58)</td>
<td>(0.93-2.05)</td>
<td>(1.51-3.13)</td>
<td>(1.38-3.31)</td>
<td>(0.79-2.10)</td>
<td>(0.19-4.49)</td>
<td>(0.68-2.13)</td>
</tr>
<tr>
<td>Smoking status</td>
<td>2.56</td>
<td>0.54</td>
<td>3.95</td>
<td>1.00</td>
<td>1.22</td>
<td>2.88</td>
<td>0.74</td>
</tr>
</tbody>
</table>
| NIH/NIAMS, NIH/NIAID, Bayer, BMS, Genentech/Roche, Pfizer, Eicos, 4; V. Hsu, None; J. K. Gordon, None; H. Gladue, None; L. A. Saketkoo, None; L. A. Criswell, None; C. T. Derk, None; M. A. Trojanowski, None; V. K. Shamugam, Multiple, 9; L. Chung, Cytori, Actelion, Reata, 5; A. Valenzuela, None; R. Jan, None; A. Goldberg, None; E. F. Remmers, None; D. L. Kastner, None; F. M. Wigley, None; P. Gourh, None; F. Boin, None.

Norway As a National Reference Population for Systemic Sclerosis; Preliminary Results from a Complete, Nationwide Cohort

Anna-Maria Hoffmann-Vold, Håvard Fretheim, Anne Kristine Halse, Marit Seip, Marianne Wallenius, Helle Bitter, Torhild Garen, Oyvind Midtvedt and Øyvind Molberg, Oslo University Hospital, Oslo, Norway, Haukeland University Hospital, Bergen, Norway, University Hospital of North Norway, Tromso, Norway, St. Olav's University Hospital, Trondheim, Norway, Hospital of Southern Norway, Kristiansand, Norway

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics I
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: To fully understand the impact of Systemic sclerosis (SSc) there is a need to complement existing multi-center registry data with novel, unbiased, high resolution results from large population based cohorts, such as complete, nationwide cohorts. The Norwegian health system is organized so that all SSc patients are followed by specialists at public hospitals; making it possible to identify every single patient resident in the country within a defined time period. Here, we took advantage of this possibility; and aimed to determine incidence, prevalence, mortality and organ involvement of SSc in Norway (denominator population 5.0 million).

Methods: The Norwegian, nationwide SSc (Nor-SSc) study cohort included all adult patients in Norway who were; (A) resident in Norway from 2000-12, (B) first time registered with an ICD-10 code M34 (SSc) in a public hospital database, (C) had a clinical SSc diagnosis verified by rheumatologist and (D) met the 1980 ACR and/or 2013 ACR/EULAR classification criteria for SSc. Detailed electronic patient journal review was performed in all cohort patients to assess disease features from SSc onset and to the end of the defined observation period (January 2013).

Results: The Nor-SSc cohort included 885 patients, of whom 666 (75.3%) were alive by January 2013. Point prevalence of SSc in Norway was estimated to 13/100.000. Number of new SSc cases per year is shown in Figure 1. Mean age at onset was 49 years, 70% were female and 70% had limited cutaneous SSc (Figure 2). Preliminary analyses of echocardiography data (available in 705 patients; 80%), lung HRCT (from 637 pts; 72%) and right heart catheterization (performed in 290 pts; 33%) indicate frequencies of cardiopulmonary involvement that are comparable to multi-centre registry data (Figure 3). Upper GI involvement appears to be highly prevalent (Figure 3).

Conclusion: In this population based, nationwide study, we found a comparable SSc prevalence to regional studies from other northern European countries. We found that a large proportion of the patients had severe organ involvement; reinforcing the view that SSc truly has a very high burden of disease.

Figure 1:
Application of a Diagnostic Algorithm to Identify Inflammatory Myopathy in Systemic Sclerosis

Vandana Bhushan\textsuperscript{1,2}, Adam Maundrell\textsuperscript{1}, Charlotte Proudman\textsuperscript{1,2}, Leah McWilliams\textsuperscript{1}, Llew Spargo\textsuperscript{1}, Robert Metcalf\textsuperscript{3}, Jennifer Walker\textsuperscript{3}, Mandana Nikpour\textsuperscript{4,5}, Wendy Stevens\textsuperscript{4}, Vidya Limaye\textsuperscript{1,2} and Susanna Proudman\textsuperscript{1,2},\textsuperscript{1}Rheumatology Unit, Royal Adelaide Hospital, South Australia, Adelaide, Australia,\textsuperscript{2}Discipline of Medicine, University of Adelaide, South Australia, Adelaide, Australia,\textsuperscript{3}Flinders University of South Australia, Adelaide, Australia,\textsuperscript{4}St Vincent's Hospital, Melbourne, Victoria, Melbourne, Australia,\textsuperscript{5}Department of Medicine, University of Melbourne, Victoria, Melbourne, Australia

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics I
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose:
Muscle involvement in systemic sclerosis (SSc) is under-recognised and poorly understood. Reported prevalence varies up to 15%, reflecting lack of consistent definition, the heterogeneous spectrum of muscle involvement, ranging from non-specific myopathic changes to idiopathic inflammatory myopathies such as polymyositis, but also lack of a standardised approach to detection. Early diagnosis of inflammatory myopathy by muscle biopsy is important to guide immunosuppressive therapy to minimise irreversible loss of muscle power and function. We sought to determine the prevalence of inflammatory myopathy in patients with SSc assessed annually for features of muscle involvement according to a standardised algorithm.

Methods:

Consecutive patients with SSc, according to the 1980 ACR or LeRoy and Medsger criteria, enrolled in the Australian Scleroderma Cohort Study (ASCS) since 2007, are assessed annually for features of myopathy: proximal muscle weakness based on the Medical Research Centre scale and elevated creatine kinase (CK) > 150 U/L. No specific guidelines for further investigation are followed. In a subset of patients from a single ASCS centre, if proximal weakness and/or elevated CK were present, myositis immunoblot for myositis specific antibodies (MSA) and/or MRI of upper or lower limbs for increased T2 signal or fatty infiltration and atrophy were performed; positive findings prompted a muscle biopsy. Features of patients with and without histopathological features of inflammation on biopsy were compared.

Results:

Among 1197 patients enrolled in the ASCS, 176 (14.7%) had elevated CK with or without weakness at any time during follow up, 128 (10.7%) had weakness with a normal CK, and 18 (1.5%) patients had biopsy-proven inflammatory myopathy. In a separate ASCS cohort of 333 patients in South Australia, 89 of 323 (27.6%) had elevated CK, 83 of 326 (25.5%) had proximal weakness and 34 (10.2%) were selected for muscle biopsy. Abnormalities were present in all 34 biopsies, with inflammatory myopathy (polymyositis, 10; dermatomyositis, 4; inclusion body myositis, 3; necrotising, 1; other, 2) confirmed in 20 (58.8%) and nonspecific features of myopathy reported in 14.

Among the biopsied patients, incidence of diffuse cutaneous subtype and levels of CK were significantly higher in those with inflammatory compared with non-inflammatory myopathy (Table 1). Immunosuppressive use at time of biopsy was similar in the two groups.

Table 1: Characteristics of SSc patients selected for muscle biopsy
<table>
<thead>
<tr>
<th></th>
<th>Inflammatory myopathy</th>
<th>Non-inflammatory myopathy</th>
<th>P value&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 20</td>
<td>n = 14</td>
<td></td>
</tr>
<tr>
<td>Diffuse SSc</td>
<td>6</td>
<td>0</td>
<td>0.031</td>
</tr>
<tr>
<td>SSc antibodies:</td>
<td>10/20</td>
<td>9/14</td>
<td>0.500</td>
</tr>
<tr>
<td>ACA</td>
<td>3</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Scl70</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>RNA polymerase III</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>RNP</td>
<td>4</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Immunosuppressive therapy at time of biopsy</td>
<td>9</td>
<td>9</td>
<td>0.147</td>
</tr>
<tr>
<td>Elevated CK</td>
<td>14</td>
<td>7</td>
<td>0.238</td>
</tr>
<tr>
<td>CK level U/L (median, IQR)</td>
<td>436 (243-571)</td>
<td>132 (63-383)</td>
<td>0.023&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Proximal weakness</td>
<td>15</td>
<td>11</td>
<td>1.000</td>
</tr>
<tr>
<td>Myositis immunoblot +ve:</td>
<td>10/17</td>
<td>4/10</td>
<td>0.440</td>
</tr>
<tr>
<td>Ro52</td>
<td>7</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Mi-2</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Ku</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>PM-Scl75</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Jo-1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>SRP</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>PL7</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>PL12</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Increased T2 signal on MRI muscle</td>
<td>6/7</td>
<td>2/7</td>
<td>0.103</td>
</tr>
</tbody>
</table>

IQR, interquartile range

<sup>1</sup>Fisher’s exact test except where indicated. <sup>2</sup>Mann Whitney U.

**Conclusion:**

A diagnostic algorithm including MSA and MRI, detected biopsy-proven muscle involvement in 10.2% of patients with SSc and increased the detection of inflammatory myopathy to 6% of patients compared with 1.5% in the whole ASCS cohort.

**Disclosure:** V. Bhushan, None; A. Maundrell, None; C. Proudman, None; L. McWilliams, None; L. Spargo, None; R. Metcalf, None; J. Walker, Actelion Australia, Bayer, CSL Biotherapies, GlaxoSmithKline Australia and Pfizer, 2; M. Nikpour, Actelion Australia, Bayer, CSL Biotherapies, GlaxoSmithKline Australia and Pfizer, 2; W. Stevens, Actelion Australia, Bayer, CSL Biotherapies, GlaxoSmithKline Australia and Pfizer, 2; V. Limaye, None; S. Proudman, Actelion Australia, Bayer, CSL Biotherapies, GlaxoSmithKline Australia and Pfizer, 2,Actelion Australia, 8.
Sequence Homology and Immune Reactivity between T Cell Epitopes of Related Gut Microbes and Two Novel Autoantigens Provide a Link between Microbial and Host Immunity in Patients with Rheumatoid Arthritis

Annalisa Pianta¹, Sheila Arvikar², Klemen Strle³, Elise E. Drouin¹, Qi Wang⁴, Catherine E. Costello⁴ and Allen C. Steere⁵, ¹Center for Immunology and Inflammatory Diseases, Massachusetts General Hospital, Harvard Medical School, Boston, MA, ²Center for Immunology and Inflammatory Diseases, Massachusetts General Hospital, BOSTON, MA, ³Department of Immunology and Inflammatory Diseases, Massachusetts General Hospital, BOSTON, MA, ⁴Center for Biomedical Mass Spectrometry, Boston University School of Medicine, Boston, MA, ⁵Center for Immunology and Inflammatory Diseases, Massachusetts General Hospital, Harvard Medical School, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: T Cell Biology and Targets in Autoimmune Disease
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: It has been proposed that immunological triggers at mucosal sites, such as the gut microbiota, may promote autoimmunity affecting joints in patients with rheumatoid arthritis (RA). We recently reported evidence for immune relevance of Prevotella copri, a gut microbe, in a subgroup of new-onset and chronic RA patients. However, it has been unclear how immune responses to gut microbes may be linked to autoimmune joint pathology.

Methods: To identify disease-relevant microbial and self antigens involved in the pathogenesis of RA, we used a novel proteomic approach to identify HLA-DR-presented peptides (T cell epitopes) in patients’ samples by tandem mass spectrometry. Immunoreactive peptides or their source proteins were then tested for T cell reactivity by IFN-γ ELISpot assay and for antibody responses by ELISA in our large cohort of RA patients or control subjects. Serum samples were also analyzed for innate, Th1, and Th17 mediators by Luminex. Immunoreactive epitopes were searched for microbial sequence homology using BLASTp, and homologous peptides were tested for T cell reactivity. All RA patients met the 2010 ACR/EULAR criteria for RA.

Results: From proteomic analyses, we identified two novel autoantigens, N-acetylglucosamine-6-sulfatase (GNS) and filamin A (FLNA), as targets of T and B cell responses in about half of RA patients. These autoantibody responses were found primarily in patients with antibodies to P. copri, and both IgG and IgA responses to P. copri correlated with the autoantibody levels. These microbial and self immune responses occurred specifically in RA patients, and not in those with other rheumatic diseases or in healthy subjects. Both self proteins were highly expressed in synovia. GNS (but not FLNA) appeared to be citrullinated, and antibody to the citrullinated GNS correlated with anti-citrullinated-protein antibody levels. Anti-GNS and anti-FLNA autoantibodies also correlated with inflammatory cytokines IFN-γ, IL-12, IL17-F, and IL-22, indicative of Th1 and Th17 adaptive immune responses. In a search for T cell epitope mimicry, the HLA-DR-presented GNS peptide was found to have marked sequence homology with epitopes from sulfatase proteins of the gut microbes of the Prevotella and Parabacteroides sp., whereas the HLA-DR-presented FLNA peptide had homology with epitopes from proteins of Prevotella and Butyricimonas sp., another gut commensal. Patients with T cell reactivity with each self-peptide had responses to the corresponding microbial peptides, and the levels correlated directly. These responses were more common in patients with shared-epitope alleles.

Conclusion: These findings provide evidence for immune relevance of a related order of gut commensals in a subgroup of RA patients, and suggest that gut dysbiosis may compromise the mucosal barrier resulting in leakage of microbes. Moreover, the identification of T cell epitope mimicry between microbial and self epitopes as well as significant correlations
in patients’ immune responses to these antigens provide a mechanism linking mucosal immunity and joint autoimmunity in these patients. Finally, the specificity of these responses may advance diagnostic testing in RA.

**Disclosure:** A. Pianta, None; S. Arvikar, None; K. Strle, None; E. E. Drouin, None; Q. Wang, None; C. E. Costello, None; A. C. Steere, None.


**Abstract Number:** 950

**Identification of Naturally Processed Immunodominant Topoisomerase I Epitopes in Patients with Systemic Sclerosis**

Eleni Tiniakou¹, Andrea Fava², Tara Guhr³, Francesco Boin⁴ and Erika Darrah⁵, ¹Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, ²Johns Hopkins University, Baltimore, MD, ³University of North Carolina, Chapel Hill, NC, ⁴Rheumatology, University California, San Francisco, San Francisco, CA, ⁵Department of Medicine/Division of Rheumatology, The Johns Hopkins University School of Medicine, Baltimore, MD

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017  
**Session Title:** T Cell Biology and Targets in Autoimmune Disease  
**Session Type:** ACR Concurrent Abstract Session  
**Session Time:** 4:30PM-6:00PM

**Background/Purpose:**

Identification of immunodominant T cell epitopes of autoantigens is crucial to understanding the pathogenesis of autoimmune diseases and developing disease-specific diagnostic and therapeutic tools. A subset of patients with systemic sclerosis (SSc) exhibit autoantibodies and CD4+ T cells specific for topoisomerase-I (Topo-I), which are quantitatively associated with the presence and severity of lung fibrosis. Mapping of immunodominant Topo-I T cell epitopes has been difficult due to poor sensitivity, high cost of current protocols, and has mainly been based on in silico prediction or overlapping peptide libraries. Existing data are limited by the low precision of these approaches and the poor sensitivity of detection assays. We present a new method for mapping immunodominant Topo-I T cell epitopes using the natural processing and presentation of HLA-DR-restricted Topo-I peptides by monocyte derived dendritic cells (MoDCs) from SSc patients.

**Methods:**

MoDCs from 6 anti-Topo-I positive SSc patients were pulsed with whole Topo-I protein. Following overnight exposure, immunoprecipitation was performed to isolate HLA-DR/peptide complexes. Peptides were identified by mass spectrometry, and matched to the Topo-I sequence. The peptides were then synthesized and used to stimulate peripheral blood mononuclear cells (PBMCs) from these patients in the presence of anti-CD40 antibody. Topo-I-reactive CD4+ T cells were identified by flow cytometry based on activation status (CD40L/CD154 upregulation). PBMCs from 8 additional randomly selected anti-Topo-I + patients and 6 anti-Topo-I negative controls (anti-centromere or anti-RNA-Polymerase-III) were stimulated using the same protocol.

**Results:**

Ten different naturally processed Topo-I peptides were identified. The peptides detected were located mainly in the core region of the molecule. The median number of distinct peptides presented by each individual patient was 4 (range 1-8). Peptide overlap among patients existed despite differences in their HLA-DR haplotype, with 8 out of 10 epitopes being
presented by two or more subjects. All Topo-I peptides were able to stimulate CD154 upregulation by CD4+ T cells from at least one of the 14 anti-Topo-I positive patients tested. These T cell responses were significantly higher than that of 6 randomly selected anti-Topo-I negative SSc controls (p<0.001).

Conclusion:

Through characterization of naturally processed peptides, we have identified immunodominant Topo-I epitopes capable of stimulating CD4+ T cells from anti-Topo-I positive patients with SSc. Additionally, our approach showed that a restricted set of immunodominant Topo-I epitopes is presented by SSc patients carrying diverse HLA-DR alleles. This method represents a cost-effective and dependable way to identify immunodominant epitopes and can provide novel targets for disease monitoring and eventually, designing peptide-targeted immunotherapy.

Disclosure: E. Tiniakou, None; A. Fava, None; T. Guhr, None; F. Boin, None; E. Darrah, None.


Abstract Number: 951

Cross Sectional Analysis of Citrullinated-Synovial Antigen-Specific CD4+ T Cells in an RA Cohort Demonstrates Antigen Based Differences in T Cell Frequency, Phenotype and the Influence of Immunotherapy

Cliff Rims¹, Sylvia Posso¹, Bernard Ng², Jeffrey Carlin³, Eddie James⁴ and Jane H. Buckner⁴, ¹Translational Research, Benaroya Research Institute at Virginia Mason, Seattle, WA, ²Rheumatology, VA Puget Sound Healthcare System, Seattle, WA, ³Rheumatology, Virginia Mason Medical Center, Seattle, WA, ⁴Benaroya Research Institute at Virginia Mason, Seattle, WA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: T Cell Biology and Targets in Autoimmune Disease
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose:
The presence of ACPA in RA indicates that an immune response directed toward citrullinated synovial antigens participates in disease development or persistence. Research from our group have identified T cell targets derived from the auto-antigens aggrecan, vimentin, fibrinogen, alpha-enolase, and cartilage intermediate layer protein (CILP). In this study, we visualized peripheral antigen-specific CD4+ T cells using a multiplexed flow-cytometry based HLA class II tetramer assay in a cross-sectional cohort of 80 RA and 30 matched healthy control subjects to understand their relevance to RA disease progression and response to therapy.

Methods:
All subjects were DRB1*04:01. RA subjects were CCP positive and represented a range of characteristics including time from diagnosis, disease activity and treatment at the time of blood draw. Antigen-specific T cells were visualized by directly staining peripheral blood mononuclear cells (PBMC) with multiple tetramers corresponding to different antigens. Frequencies and phenotypic features of antigen-specific CD4+ T cells were assessed for correlation with clinical characteristics.

Results:
Ex-vivo analysis of PBMC revealed an increase in synovial targeted CD4 T cells when compared to matched healthy DRB1*04:01 subjects. When analyzed by individual antigen CD4 T cells, aggrecan, vimentin and fibrinogen were increased in RA, and by contrast cartilage-intermediate-layer-protein (CILP) and enolase specific T cells were reduced in comparison to healthy subjects, suggesting that the characteristics of the CD4+ T cells response to synovial epitopes may be unique to antigen specificity.

Within this patient cohort we found a lower frequency of synovial specific T cells in individuals on TNF therapies sampled within 5 years of diagnosis. These differences were most pronounced in the CD4 T cells specific for aggrecan, vimentin and fibrinogen, and showed alterations in chemokine receptor and activation marker expression in the treated group.

Ongoing studies will determine if frequency, phenotype and specificity of synovial specific CD4 T cells correlate directly with disease duration, therapeutic duration, and clinical diagnostic values such as level of RF, CCP, CRP, and disease severity.

Conclusion:

We have shown that a multiplexed tetramer assay can define the breadth and character of the T cell response to synovial antigens. Characterizing a relatively large cohort of subjects, we demonstrate differences in the phenotype and frequency of the T cells that respond to a diverse set of synovial antigens thought to be important targets in RA. In particular, we show that synovial specific T cell frequency is influenced by therapeutic interventions. Better understanding the interplay of antigen specificities and phenotypes in RA is vital to understanding disease pathogenesis, response to therapy and ultimately developing antigen specific therapies.

Disclosure: C. Rims, None; S. Posso, None; B. Ng, None; J. Carlin, None; E. James, None; J. H. Buckner, None.


Abstract Number: 952

Serine Arginine-Rich Splicing Factor 1 (SRSF1) Is a Novel Regulator of T Lymphocyte Homeostasis In Vivo and Its Deficiency Associates with Lymphopenia in SLE Patients

Takayuki Katsuyama1, Michael W. Mosho1, Andrew R. Gillooly2, George C. Tsokos1 and Vaishali R. Moulton3, 1Division of Rheumatology, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, 2Medicine/ Rheumatology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, 3Rheumatology, Beth Israel Deaconess Medical Center, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: T Cell Biology and Targets in Autoimmune Disease
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Lymphopenia is a common clinical feature in patients with systemic lupus erythematosus (SLE), and associates with high disease activity and comorbidities including infections. However, the mechanisms of lymphopenia in SLE patients are not fully understood. SLE T cells exhibit increased susceptibility to apoptosis and display altered expression of apoptosis/survival related genes such as the Bel-2 family genes, many of which have pro- and anti-apoptotic isoforms. Using discovery approaches we previously identified the serine arginine-rich splicing factor 1 (SRSF1) in human T cells, and showed that it regulates normal expression of the CD3zeta chain and is required for IL-2 production. We showed that SRSF1 expression levels are decreased in T cells from SLE patients, and this decrease associates with severe disease.
Because it is reported that SRSF1 regulates alternative splicing of the apoptosis-related gene BcL-x to promote the anti-apoptotic long (L) isoform over the pro-apoptotic short (s) isoform, we hypothesized that SRSF1 is important for T lymphocyte homeostasis, and its deficiency leads to apoptosis and lymphopenia in mice and in SLE patients.

**Methods:** 42 SLE patients, and age-, race- and gender-matched healthy individuals were enrolled, and clinical and laboratory parameters recorded. Peripheral blood T cells were isolated by negative selection and SRSF1 protein levels assessed by western blot. SLE patients were divided into lymphopenic (<1000/μL) and non-lymphopenic groups, and correlations were assessed with relative SRSF1 expression levels, and compared to gender- and age-matched healthy controls. To generate T cell-specific Srsf1 conditional knockout (Srsf1-cko) mice, Srsf1-flox mice were crossed with d.Lck.Cre transgenic mice. Mice were euthanized at 10-20 weeks of age or aged to ≥1 year, and lymphoid tissues (spleen and lymph nodes) were analyzed. Immune cell phenotype was assessed by flow cytometry. Apoptosis was assessed in splenocytes ex vivo or after induction by anti-CD95 (Fas) crosslinking, by flow cytometry staining for 7AAD and Annexin V.

**Results:** SLE patients with lymphopenia presented significantly lower expression levels of SRSF1 (0.65 vs. 1.05, p=0.0074), whereas there was no correlation of SRSF1 with hemoglobin, platelet counts, or serum complement levels. In parallel, peripheral T cell lymphopenia was observed in Srsf1-cko mice. Lymphopenia was more evident in younger mice, and was more profound in the CD8 than CD4 T cells. Crosslinking with anti-CD95 (Fas) antibody led to increased apoptosis in T cells from Srsf1-cko mice. The expression levels of anti-apoptotic gene Bcl-xL were decreased in spleen cells from the Srsf1-cko mice both ex vivo and after anti-CD95 (Fas) crosslinking. These results indicate that a deficiency of SRSF1 induces apoptosis in T cells through decreased expression of Bcl-xL.

**Conclusion:** SRSF1 controls the expression of the anti-apoptotic gene Bcl-xL and is an important regulator of T lymphocyte homeostasis in vivo and its reduced expression levels associate with lymphopenia in SLE patients. Therefore, deficiency of SRSF1 may represent a molecular defect that contributes to the pathophysiology of systemic autoimmune disease.

**Disclosure:** T. Katsuyama, None; M. W. Mosho, None; A. R. Gillooly, None; G. C. Tsokos, GSK, 5; V. R. Moulton, None.

**Abstract Number:** 953

**Persistence of Pathogenic CD4 Memory T Cells Revealed through Cytometry Time of Flight in Juvenile Idiopathic Arthritic Patients with Disease Resurgence upon Withdrawal of Anti-TNFA Biologics**

**Jing Yao Leong**1, Joo Guan Yeo2, Phyllis Chen3, Liyun Lai4, Fauziah Ally5, Loshinidevi D/O Thana Bathi3, Justin Hung Tiong Tan2, Thaschawee Arkachaisri2, Femke van Wijk6, Salvatore Albani4, Daniel J Lovell7 and Gerdien Mijnheer8,

1SingHealth Translational Immunology and Inflammation Centre, Singapore Health Services Pte Ltd, Singapore, Singapore, 2Rheumatology and Immunology Service, KK Women's and Children's Hospital, Singapore, Singapore, 3Singhealth Translational Immunology and Inflammation Centre (STIIC), Duke-NUS Medical School, Singapore, Singapore, 4SingHealth Translational Immunology and Inflammation Centre (STIIC), Duke-NUS Medical School, Singapore, Singapore, 5STIIC, SingHealth Translational Immunology and Inflammation Centre (STIIC), Singapore, Singapore, 6University Medical Center Utrecht, Utrecht, Netherlands, 7Rheumatology, PRCSG - Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 8Laboratory of Translational Immunology, Department of Paediatric Immunology, , The Netherlands, University Medical Centre Utrecht, Wilhelmina Children’s Hospital, Utrecht, Netherlands

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Sunday, November 5, 2017
Session Title: T Cell Biology and Targets in Autoimmune Disease
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Treatment of polyarticular JIA with anti-TNFA biologics has experienced significant success, with up to 80% of patients demonstrating clinically meaningful efficacy. Yet concerns regarding medium/long term toxicities and costs, have driven the clinical need to locate predictors for successful drug discontinuation. Compelling evidence indicate that T cells play a paramount role in disease progression. Identification of these pathogenic subsets within the T cell immunome will likely help stratify patients in terms of clinical fate. JIA patients previously treated with anti-TNFA were recruited through the Understanding TNFA trial and segregated into flare, active and inactive arms after drug discontinuation. Utilising a high dimensional platform, CyToF, that is capable of phenotyping up to 41 markers at single cell resolution, we aim to identify the pathogenic subsets responsible for clinical relapse and signatures capable of distinguishing therapeutic outcomes.

Methods: Patients treated with anti-TNF-alpha were recruited into the study (Improved Understanding of the Biology and Use of TNF inhibition in Children with JIA Trial) with clinically inactive disease on treatment (Wallace criteria) and initiated with therapy discontinuation. The patients were followed and evaluated as flare, inactive and active based on 6 JIA core set parameters; number of joints with active arthritis and/or loss of motion, MD global assessment of current disease activity, patient/parent global assessment of overall disease severity in prior week, a validated measure of physical function and ESR.

Results: PBMCs from 47 JIA patients (Flare= 18, Active= 11, Inactive= 18) and 10 healthy controls were stained and interrogated with CyToF. Patients destined to flare (vs inactive/healthy) prior to therapy withdrawal, displayed significant dysregulation in the CD4 Memory compartment (p< 0.05), enriched particularly in (a) CD4 CD45RA^-TNFA^+, (b) CD4 CD45RA^-CXCR5^+, and were skewed towards (c) CD152^-PD1^- . When contrasting against healthy controls, patients destined to flare additionally upregulated CD4 CD45RA^-TNFA^-IL-6^+, possibly a sub-clinical disease subset. Intriguingly we noted a migratory subset, CD4 CD45RA^-CXCR3^+CCR6^+ that was present in patients destined to develop active disease (vs inactive/healthy). Upon flaring, the sub-clinical subset CD4 CD45RA^-TNFA^-IL-6^+ surfaces and CD4 memory subsets are now upregulating expression of CD152/PD1 (vs inactive) in response to ongoing inflammation, but when compared to healthy controls are still inadequate. Parallel pathogenic subsets were also detected in the synovial microenvironment, reflecting targeting towards the joints.

Conclusion: For some patients (Flare), anti-TNFA therapy is merely suppressing disease activity and not curative. The persistence of CD4 memory cells are likely to play a pivotal role in disease relapse, that may be partially explained by a weaker control through immune checkpoints (CD152/PD1). These results suggest that clinical fate is immunologically predetermined and patients who will develop different clinical fates can be identified from prior biologic sampling.

Disclosure: J. Y. Leong, None; J. G. Yeo, None; P. Chen, None; L. Lai, None; F. Ally, None; L. D. T. Bathi, None; J. H. T. Tan, None; T. Arkachaisri, None; F. van Wijk, None; S. Albani, None; D. J. Lovell, None; G. Mijnheer, None.


Abstract Number: 954

**Microrna-21 Is a Critical Regulator of Autoimmunity through Promoting Effector and Metabolic Function of Pathogenic TH17 Cells**

Xiang Yu1 and Nan Shen1,2,3, 1Shanghai Institute of Rheumatology, Renji Hospital, School of Medicine, and Shanghai Jiao Tong University, Shanghai, China, 2Institute of Health Sciences, Shanghai Jiao Tong University School of Medicine and Shanghai Institutes for Biological Sciences, University of Chinese Academy of Sciences, Chinese Academy of Sciences, Shanghai, China, 3Center for Autoimmune Genomics and Etiology, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH
SESSION INFORMATION
Session Date: Sunday, November 5, 2017
Session Title: T Cell Biology and Targets in Autoimmune Disease
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose:
Systemic lupus erythematosus (SLE) is a prototypical autoimmune disease that causes mortality and morbidity worldwide. Recent studies suggest proinflammatory TH17 cells are key pathogenic factors that contribute to lupus nephritis. Our group previously demonstrate that microRNA-21 was highly upregulated in effector CD4\(^+\) T cells from both lupus patients and lupus-prone mice. However, the role of microRNA-21 in pathogenic TH17 cells and TH17 cell-mediated autoimmune diseases is still unclear. In this study, we systemically dissect the role of microRNA-21 in the differentiation and effector function of pathogenic TH17 cells and they-mediated autoimmune diseases.

Methods:
MicroRNA-21 knockout and conditional knockout mice (CD11c-cre, Lyz2-cre, and CD4-cre) were generated for studying the role of microRNA-21 in the differentiation and effector function of TH17 cells. Experimental autoimmune encephalomyelitis (EAE) was induced to study the role of microRNA-21 in pathogenic TH17 cell-mediated autoimmune diseases. RNA-seq and DAVID bioinformatic analysis were conducted to find key microRNA-21 regulated pathway and molecular targets in pathogenic TH17 cells. Metabolomics study and metabolic assays were done to study the glycolytic activity of microRNA-21-deficient pathogenic TH17 cells.

Results:
In this study, we demonstrate that microRNA-21 induced by IL-6-STAT3 signaling targets the E3 ubiquitin ligase Peli1-c-Rel axis to promote effector and metabolic function of pathogenic TH17 cells. We demonstrate that microRNA-21 is not required for the development of intestinal homeostatic TH17 cells, but is essential for the maintenance of pathogenic TH17 cells in vivo. MicroRNA-21-deficient TH17 cells express less pathogenic TH17 signature genes and show less glycolytic activity. Many of the genes involved in glycolytic and related metabolic pathways are significantly downregulated in microRNA-21-deficient pathogenic TH17 cells, which include key transporters for glucose intake, Slc2a1/3 (Glut1/3), and rate-limiting enzymes, Hk1/2, Pfkl, Pgm2, Ldha and Pdk1. Interestingly, we find that non-pathogenic and pathogenic TH17 cells have greatly distinct metabolic states, with pathogenic TH17 cells highly glycolytic. We further show that conditional deletion of microRNA-21 in CD4\(^+\) T cells protects mice from EAE while loss of microRNA-21 expression by dendritic cells and myeloid cells do not.

Conclusion:
To our knowledge, our study identifies the first evidence that by targeting the E3 ubiquitin ligase Peli1 microRNA-21 promotes the effector and metabolic function of pathogenic TH17 cells. Furthermore, the selective dependence of pathogenic TH17 cells on microRNA-21-mediated metabolic reprogramming has provided novel targets for therapeutic intervention of autoimmune and inflammatory diseases elicited by pathogenic TH17 cells.

Disclosure: X. Yu, None; N. Shen, None.


Abstract Number: 955

**In Vitro Effects of CR6086, a Potent ProstaglandinE2 Subtype 4 Receptor Antagonist, on Bone Erosive Pathways**
Background/Purpose: CR6086 is a selective EP4 receptor antagonist immunomodulator in clinical development for rheumatoid arthritis (RA). In animal models of RA, it demonstrated a superior efficacy vs. conventional, biologic, or targeted synthetic DMARDs in both early and late disease paradigms. In vitro on human immunocompetent cells, we previously showed that CR6086 counteracts the immunological unbalance characteristic of RA. This partly explains its efficacy in vivo, but does not completely account for its superior efficacy vs. DMARDs. Bone erosion contributes even to very early phases of RA and EP4 receptors have a key role in bone resorption. Acting on this receptor, PGE2 stimulates different cell types (including macrophages, chondrocytes, and osteoblasts) to release mediators causing bone erosion. Among them, IL-6, RANK ligand (RANKL), the major inducer of osteoclastogenesis, and VEGF that has angiogenic, pro-inflammatory and bone destructive roles in RA. Aim of this study was to assess the effects of CR6086 on the expression and release of these mediators by human macrophagic cells, chondrocytes and osteoblasts.

Methods: Human THP-1 cells were differentiated to macrophages with PMA. Chondrocytes and osteoblasts were purified from material obtained from patients undergoing knee replacement. Gene expression and release of IL-6, RANKL with its endogenous inhibitor osteoprotegerin (OPG), and VEGF were analysed by Real Time PCR and ELISA assay.

Results: CR6086 dose-dependently inhibited gene expression of IL-6, RANKL and VEGF in human macrophages and/or chondrocytes. Conversely, it had no effect on gene expression of OPG, maintaining the balance RANKL/OPG in favor of a reduction of bone erosion. In particular, in macrophages stimulated with LPS 10ng/ml + PGE2 10nM, CR6086 dose dependently inhibited gene expression of VEGF (fig. 1), reduced IL-6 gene expression (up to 44%) and IL-6 release (up to 53%).

In chondrocytes stimulated with PGE2 or IL-1β + PGE2, CR6086 dose-dependently suppressed RANKL and IL-6 gene expression (Table 1). Similar results were obtained in osteoblasts.
Conclusion: The new potent EP4 receptor antagonist immunomodulator CR6086 directly affects bone resorption by inhibiting the expression of different mediators that induce bone erosions in RA (RANKL, IL-6 and VEGF). These results support the in vivo findings and confirm that CR6086 may potentially act as a novel DMARD. CR6086 is in Phase II clinical development in DMARD-naïve early RA patients.

Disclosure: T. Piepoli, Rottapharm Biotech, 3; M. Montagna, Rottapharm Biotech, 3; D. Maggioni, Rottapharm Biotech, 3; S. Zerbi, Rottapharm Biotech, 3; L. Mennuni, Rottapharm Biotech, 3; M. Lanza, Rottapharm Biotech, 3; G. Caselli, Rottapharm Biotech, 3; L. C. Rovati, Rottapharm Biotech, 3.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/in-vitro-effects-of-cr6086-a-potent-prostaglandine2-subtype-4-receptor-antagonist-on-bone-erosive-pathways](http://acrabstracts.org/abstract/in-vitro-effects-of-cr6086-a-potent-prostaglandine2-subtype-4-receptor-antagonist-on-bone-erosive-pathways)

Abstract Number: 956

**Inhibition of Fucosylation in Endothelial Cells Reduces Rheumatoid Arthritis Angiogenesis**

Takeo Isozaki, Airi Nishimi, Shinichiro Nishimi, Sho Ishii, Takahiro Tokunaga, Hidekazu Furuya, Kuninobu Wakabayashi and Tsuyoshi Kasama, Div of Rheumatology, Showa University School of Med, Shinagawa-ku Tokyo, Japan

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017

Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster II: Mesenchymal Cells Do React - But How?

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM

**Background/Purpose:** Glycosylation has been reported to associate with tumor invasion and metastasis. Fucosylation is involved the biological functions of adhesion molecules and growth factor receptors. In regards to arthritis, we have previously reported that fucosylated proteins were expressed on rheumatoid arthritis (RA) synovial tissues. Here, we examined the expression of fucosylated proteins in RA and mediates angiogenesis.

**Methods:** Total glycans were determined in serum from normal (NL) subjects and RA patients using mass spectrometry. To determine whether fucosylated proteins involved with RA inflammation, the correlation with disease activity score (DAS) 28 (ESR) was measured. 2-deoxy-D-galactose (2-dGal) is an analog of hexose that inhibits fucosylation. In order to confirm the role of fucosylation in RA angiogenesis, we did Matrigel assays *in vitro*. To block the expression of fucosylated proteins, human umbilical vein endothelial cells (HUVECs) were treated with 2-dGal (15 mM) for 5 days. After treatment with 2-dGal, HUVECs were plated on Matrigel and were incubated with phosphate buffered saline (PBS) or RA synovial fluids. Finally, expression of proangiogenic cytokines such as fractalkine/CX3CL1, CXCL16, interleukin (IL)-8/CXCL8, monocyte chemotactic protein 1 (MCP-1)/CCL2, epithelial neutrophil-activating protein 78 (ENA-78)/CXCL5 and vascular endothelial growth factor (VEGF) in 2-dGal treated HUVEC conditioned medium were measured by ELISA.

**Results:** Total glycans in RA serum were significantly higher than in NL serum [mean ± SEM; 477 ± 24 pmol/μl (n=10) and 339 ± 14 pmol/μl (n=10), p<0.05, respectively]. In addition, total glycans in RA serum were significantly decreased with tocilizumab treatment at 24 weeks. Total glycans in RA serum were also correlated with DAS28 (ESR). Percent of fucosylated proteins in total glycans were decreased with TCZ treatment at 24 weeks. 2-d Gal treated HUVEC tube formed
towards RA synovial fluids (n=6 patients) were decreased compared with nontreated HUVEC tube formed (number of tube formed; 7 ± 1 and 25 ± 2, p<0.05, respectively). Fractalkine/CX3CL1, CXCL16, or IL-8/CXCL8 in 2-d Gal treated HUVEC conditioned medium were decreased compared with in non-treated HUVEC conditioned medium but not MCP-1/CCL2, ENA-78, or VEGF.

Conclusion: These data indicate that glycoproteins are involved with RA, and play a role in angiogenesis in RA and suggest that targeting glycosylation especially fucosylation may provide a method by which to decrease inflammation and potentially treat other inflammatory diseases.

Disclosure: T. Isozaki, None; A. Nishimi, None; S. Nishimi, None; S. Ishii, None; T. Tokunaga, None; H. Furuya, None; K. Wakabayashi, None; T. Kasama, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/inhibition-of-fucosylation-in-endothelial-cells-reduces-rheumatoid-arthritic-angiogenesis

Abstract Number: 957

A Disintegrin and Metalloprotease 15 Is Expressed on Rheumatoid Arthritis Synovial Tissue Endothelial Cells and Mediates Angiogenesis

Shinichiro Nishimi, Takeo Isozaki, Airi Nishimi, Sho Ishii, Takahiro Tokunaga, Hidekazu Furuya, Kuninobu Wakabayashi and Tsuyoshi Kasama, Div of Rheumatology, Showa University School of Med, Shinagawa-ku Tokyo, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017

Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster II: Mesenchymal Cells Do React - But How?

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM

Background/Purpose: A disintegrin and metalloproteases (ADAMs) are reported that membrane-anchored glycoproteins composed of multiple distinct protein modules. ADAM-15 is one of them and is reported in several malignancies such as breast cancer and prostate cancer. However, the role of ADAM-15 in autoimmune diseases is unclear. Here, we have shown the role of ADAM-15 in rheumatoid arthritis (RA) angiogenesis.

Methods: RA and osteoarthritis (OA) synovial fluids (SFs) were obtained from patients. RA and normal (NL) serum were also obtained. ADAM-15 expression was measured in serum and SFs using enzyme-linked immuno sorbent assay (ELISA). To clarify the differences of ADAM-15 in RA treatment, the level of ADAM-15 at pre, 12, 24 and 54 weeks with tocilizumab treatment was measured. To determine ADAM-15 expression on RA synovial tissues, immunohistochemistry was performed. In order to examine the role of ADAM-15 in RA angiogenesis, we used human umbilical vein endothelial cells (HUVECs). To examine whether ADAM-15 was expressed on HUVECs, immunohistochemistry was also performed. To block the expression of ADAM-15, HUVECs were transfected with small interfering (si) RNA against ADAM-15. In order to confirm the role of angiogenesis, we did Matrigel assays in vitro. Finally, proangiogenic cytokines in ADAM-15 siRNA transfected HUVEC conditioned medium were measured.

Results: ADAM-15 in RA serum was significantly higher compared with NL (500 ± 21 pg/ml and 390 ± 29 pg/ml, respectively, p<0.05). The levels of ADAM-15 in RA SFs were also higher compared with OA SFs (619 ± 53 pg/ml and 328 ± 39 pg/ml, respectively, p<0.05). After treatment with tocilizumab, ADAM-15 in serum was significantly decreased between pre and 24 weeks (500 ± 21 pg/ml and 432 ± 21 pg/ml, respectively, p<0.05), pre and 54weeks (500 ± 21 pg/ml and 434 ± 22 pg/ml, respectively, p<0.05). We found that ADAM-15 was expressed on RA synovial tissue ECs and HUVECs. ADAM-15 siRNA treated HUVECs had decreased EC line and tube formed in Matrigel in response to RA SFs compared with non-treated HUVECs (number of EC lines 14 ± 2 and 7 ± 1, respectively, p<0.05) (number of EC tube formed 4 ± 1 and 1 ± 0, respectively, p<0.05). Epithelial neutrophil-activating protein 78 (ENA-78)/CXCL5 and intercellular adhesion
molecule (ICAM-1) in tumor necrosis factor (TNF-α) stimulated ADAM-15 siRNA transfected HUVEC conditioned medium were decreased compared with in TNF-α stimulated control siRNA transfected HUVEC conditioned medium.

**Conclusion:** These data show that ADAM-15 is expressed on RA synovial tissue ECs and may play a role in RA angiogenesis. ADAM-15 may be a potential target in inflammatory disease such as RA.

**Disclosure:** S. Nishimi, None; T. Isozaki, None; A. Nishimi, None; S. Ishii, None; T. Tokunaga, None; H. Furuya, None; K. Wakabayashi, None; T. Kasama, None.


Abstract Number: 958

**Tumor Necrosis Factor-α Induces Production of Eotaxin-1/CCL11 from Fibroblast-like Synoviocyte in Rheumatoid Arthritis**

**Kuninobu Wakabayashi,** Takeo Isozaki, Airi Nishimi, Shinichiro Nishimi, Sho Ishii, Takahiro Tokunaga, Hidekazu Furuya and Tsuyoshi Kasama, Div of Rheumatology, Showa University School of Med, Shinagawa-ku Tokyo, Japan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster II: Mesenchymal Cells Do React - But How?

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Chemokine C-C motif ligand 11 (CCL11) also known as eotaxin-1 is a member of the CC chemokine family, which acts as a major chemotactrant of eosinophils and a stimulator of basophils. Eotaxin-1/CCL11 is produced by lymphocytes, eosinophils and monocytes/macrophages and interacts with C-C chemokine receptor 3 (CCR3). CCR3 is associated with numerous inflammatory conditions and a recent study has also suggested expression of CCR3 on fibroblast-like synoviocyte (FLS) in rheumatoid arthritis (RA). In this study, we investigate the expression and the role of eotaxin-1/CCL11 and CCR3 in RA.

**Methods:** The levels of eotaxin-1/CCL11 were determined in serum from healthy control (HC) and the patients with RA using enzyme-linked immunosorbent assay (ELISA). We also measured the levels of eotaxin-1/CCL11 and tumor necrosis factor α (TNF-α) in synovial fluids (SFs) from the patients with RA and osteoarthritis (OA) using ELISA. To investigate the expression of eotaxin-1/CCL11 on RA FLS, cells were left unstimulated or were stimulated for 12-, 24- and 48-hours with 50 ng/mL of TNF-α. After stimulation, the protein expression levels of eotaxin-1/CCL11 in TNF-α treated RA FLS conditioned medium were measured by ELISA and the messenger RNA (mRNA) expression of eotaxin-1/CCL11 and CCR3 in RA FLS were measured by quantitative polymerase chain reaction (qPCR) analysis. The expression of eotaxin-1/CCL11 on RA FLS was demonstrated by immunohistochemistry.

**Results:** The levels of eotaxin-1/CCL11 in the serum from RA were higher than those in the serum from HC [mean ± SEM; 76 ± 6 pg/mL (n=48) and 52 ± 9 pg/mL (n=31), p<0.05, respectively]. The levels of eotaxin-1/CCL11 in SFs from the patients with RA were higher than those in SFs from the patients with OA [mean ± SEM; 61 ± 24 pg/mL (n=43) and 9 ± 2 pg/mL (n=20), p<0.05, respectively] and were positively correlated with the levels of TNF-α (r=0.35, p<0.05). The expression of eotaxin-1/CCL11 mRNA and the secretion of eotaxin-1/CCL11 in RA FLS were time-dependently increased by TNF-α stimulation following 12-, 24- and 48-hours (p<0.05). The expression of CCR3 mRNA was also induced time-dependently by TNF-α stimulation (p<0.05). Furthermore, it was observed that the eotaxin-1/CCL11 mRNA expression was positively correlated with the CCR3 mRNA expression (r=0.89, p <0.01). In addition, we confirmed that the expression of eotaxin-1/CCL11 on RA FLS was increased with TNF-α stimulation using immunohistochemistry.
Conclusion: These data indicate that TNF-α induced production of eotaxin-1/CCL11 from RA FLS, suggesting that eotaxin-1/CCL11 and CCR3 may play an important role of inflammation in RA.

Disclosure: K. Wakabayashi, None; T. Isozaki, None; A. Nishimi, None; S. Nishimi, None; S. Ishii, None; T. Tokunaga, None; H. Furuya, None; T. Kasama, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/tumor-necrosis-factor-%ce%b1-induces-production-of-eotaxin-1ccl11-from-fibroblast-like-synoviocyte-in-rheumatoid-arthritis

Abstract Number: 959

A Disintegrin and Metalloprotease -17 Is Overexpressed on Rheumatoid Arthritis Osteoblasts and Is Regulated with TNF-α Stimulation

Hidekazu Furuya, Takeo Isozaki, Shinichiro Nishimi, Airi Nishimi, Takahiro Tokunaga, Kuninobu Wakabayashi and Tsuyoshi Kasama, Div of Rheumatology, Showa University School of Med, Shinagawa-ku Tokyo, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster II: Mesenchymal Cells Do React - But How?
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: A disintegrin and metalloprotease family proteins (ADAMs) have been reported to be involved in a number of inflammatory conditions. We have previously reported a disintegrin and metalloprotease-17 (ADAM-17) is expressed in rheumatoid arthritis (RA) synovial fluids and synovial tissues, and is increased compared to osteoarthritis (OA) synovial fluids. Cells involved in bone formation express a variety of cytokines and osteoblasts appear to be major regulators of bone remodeling in RA. The association between ADAM-17 expression and osteoblasts is unclear. Here, we examine the expression of ADAM-17 in RA osteoblasts.

Methods: RA human osteoblasts (HOB) isolated from femora of RA patients were incubated. RA-HOB were stimulated with 25 ng/ml tumor necrosis factor (TNF)-α at 4 hours, and messenger RNA (mRNA) was collected. ADAM-17 mRNA expression was examined using quantitative polymerase chain reaction (qPCR). To examine the expression of ADAM-17 in TNF-α stimulated RA-HOB conditioned medium, RA-HOB were stimulated with 0.25 ng/ml, 2.5 ng/ml and 25 ng/ml TNF-α at 24 hours and measured using enzyme linked immunosorbent assay (ELISA). To determine ADAM-17 expression in RA-HOB lysate, western blotting (WB) was also performed. Finally, to confirm the presence of ADAM-17 on RA osteoblasts, immunostaining was performed.

Results: ADAM-17 was expressed in TNF-α stimulated RA-HOB conditioned medium which was significantly higher compared to non-stimulated (NS) RA-HOB conditioned medium (mean ± SEM; 171 ± 4 pg/ml and 310 ± 21 pg/ml, respectively, p<0.05). Furthermore TNF-α was induced dose-dependent secretion of ADAM-17 levels from RA-HOB (mean±SEM; NS: 171 ± 4 pg/ml, TNF-α 0.25 ng/ml: 255 ± 15 pg/ml, TNF-α 2.5 ng/ml: 234 ± 7 pg/ml, TNF-α 25 ng/ml: 310 ± 21 pg/ml, p<0.05). We found that ADAM-17 mRNA in TNF-α stimulated RA-HOB was 70 times elevated compared with non-stimulated RA-HOB (p<0.05). Additionally, we also found that ADAM-17 expression on RA-HOB was inducible by TNF-α by using immunostaining and WB.

Conclusion: We have reported that ADAM-17 is involved in angiogenesis in synovial tissue of RA. In this study, we showed the expression of ADAM-17 in RA osteoblasts, suggesting the possibility that it plays an important role in bone destruction in inflammatory disease such as RA.

Disclosure: H. Furuya, None; T. Isozaki, None; S. Nishimi, None; A. Nishimi, None; T. Tokunaga, None; K. Wakabayashi, None; T. Kasama, None.
ADAM-17 Is Expressed on Rheumatoid Arthritis Synovial Fibroblasts and Mediates Monocyte Migration and Adhesion

Sho Ishii, Takeo Isozaki, Airi Nishimi, Shinichiro Nishimi, Takahiro Tokunaga, Hidekazu Furuya, Kuninobu Wakabayashi and Tsuyoshi Kasama, Div of Rheumatology, Showa University School of Med, Shinagawa-ku Tokyo, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster II: Mesenchymal Cells Do React - But How?
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: A disintegrin and metalloproteinase 17 (ADAM-17), also known as tumor necrosis factor-α converting enzyme (TACE), have been reported to be involved in a number of inflammatory conditions. We examined the expression of ADAM-17 in rheumatoid arthritis (RA) biological fluids and the role it plays in monocyte migration and adhesion to RA synovial fibroblasts.

Methods: ADAM-17 expression was measured by enzyme-linked immunosorbent assay in serum and synovial fluids from normal (NL) subjects, osteoarthritis (OA) patients and RA patients. We also analyzed relativity with ADAM-17 and disease activity score 28 (DAS28) in RA. To determine expression of ADAM-17 on RA synovial tissues (STs) and RA fibroblast like synoviocyte (FLS), immunofluorescence was performed. To determine the role of ADAM-17 in RA, RA FLSs or THP-1(human acute monocyctic leukemia cell line) were transfected with small interfering RNA (siRNA) against of ADAM-17. THP-1 adhesion to ADAM-17 siRNA transfected RA FLSs was measured. THP-1 chemotaxis assay was performed towards RA synovial fluids or monocyte chemotactic protein-1 (MCP-1)/CCL2.

Results: The levels of ADAM-17 in RA serum was significantly higher compared with NL serum [mean ± SE; 2093 ± 359 pg/ml (n=23) and 0 ± 0 pg/ml (n=7), respectively, p<0.05] . ADAM-17 in RA synovial fluids was higher compared with OA synovial fluids [1644 ± 952 pg/ml (n=10) and 4.6 ± 4.3 pg/ml (n=7), respectively, p<0.05] .The level of ADAM-17 in RA serum was also correlated with DAS28 (n=58, r=0.64, p<0.05). ADAM-17 was expresssed on RA ST lining cells. On the other hand, ADAM-17 was not expresssed on OA STs. ADAM-17 was also expressed on RA FLS. THP-1 adhesion to ADAM-17 siRNA transfected RA FLS had decreased compared with that to control siRNA transfected RA FLS [adhesion index; 0.61 ± 0.10 (n=12) and 0.93 ± 0.05 (n=12), respectively, p<0.05]. We found ADAM-17 siRNA transfected THP-1 cells had decreased migration compared with control siRNA transfected THP-1 cells towards RA synovial fluids [number of THP-1 migrated 6 ± 2 (n=6) and 33 ± 12 (n=6), respectively, p<0.05]. Furthermore, ADAM-17 siRNA transfected THP-1 cells also had decreased migration compared with control siRNA transfected THP-1 cells towards MCP-1/CCL2 [number of THP-1 migrated 27 ± 4 (n=3) and 146 ± 18 (n=3), respectively, p<0.05].

Conclusion: These data indicate that ADAM-17 may play a role in RA inflammation by regulating monocyte migration and adhesion to RA synovial fibroblasts. ADAM-17 may be a potential target in inflammatory disease like RA.

Disclosure: S. Ishii, None; T. Isozaki, None; A. Nishimi, None; S. Nishimi, None; T. Tokunaga, None; H. Furuya, None; K. Wakabayashi, None; T. Kasama, None.
Adalimumab Reduces CXCR4 Expression during Inflammatory Arthritis and in Fibroblast-like Synoviocytes and Osteoclasts Under Chronic TNF Exposure

Bohdan P. Harvey¹, Li Li¹, Mark Konrad¹, Heather Knight¹, Susan Westmoreland², Melanie Ruzek¹ and Zehra Kaymakcalan¹, ¹AbbVie Bioresearch Center, Worcester, MA, ²AbbVie Inc, AbbVie Bioresearch Center, Worcester, MA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster II: Mesenchymal Cells Do React - But How?
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The CXCL12/CXCR4 chemokine axis has been implicated in the pathogenesis of RA. The expression of this chemokine and receptor has been shown to be increased in RA synovium, and moreover, CXCR4 levels in synovium have been correlated with joint destruction in RA patients. Given that high levels of CXCR4 are associated with RA pathogenesis, we sought to determine whether CXCR4 levels are altered by adalimumab (ADA) both in vivo in RA patients and in the human TNF transgenic mouse model (huTNF Tg197) of arthritis, as well as in vitro with RA fibroblast-like synoviocytes (RA-FLS) and human osteoclast precursors (OCP) following TNF exposure. In addition, we investigated the role of CXCR4 in human osteoclastogenesis (OCgenesis) under chronic TNF exposure.

Methods: Public DNA microarray data of synovial tissue from ADA treated RA patients was analyzed for changes in the expression level of various chemokines and their cognate receptors. PBMC populations from ADA treated RA patients taken at baseline, wks. 4 & 12 were assessed by CyTOF for CXCR4. IHC staining was performed on formalin paw sections from wk. 13 placebo control and ADA treated (1 mg/kg i.p.) huTNF Tg197 mice to evaluate CXCR4 expression in various pannus-associated cells. To assess the role of TNF and concomitant ADA treatment on human cultures in vitro, CXCR4 RNA expression was evaluated in RA-FLS treated with conditioned media from PBMCs +/-ADA for 6 hrs., and CXCR4 protein on OCP by flow cytometry in response to 72 hr. M-CSF+RANKL+/+-TNF+/+-ADA. To demonstrate the role of CXCR4 in OCgenesis, OCP were cultured for 6 d. in M-CSF+RANKL+/+-TNF following 30 min. pretreatment with CXCR4 neutralizing antibody. OC maturation and activity were assessed by measuring TRAcP 5b activity and CTX-I release, respectively.

Results: Preliminary microarray data analysis of RA synovial tissue demonstrated that active RA patients over-expressed CXCR4 while CXCR4 was significantly normalized (two-fold reduction) in the responders to Ada therapy. In addition, CyTOF analysis of PBMC from ADA treated RA patients indicated a significant reduction from baseline in CXCR4 expression on B cells and CD4+ T cells by wk. 4. In huTNF Tg197 mice, CXCR4 expression in the inflamed pannus (most notably in FLS, lymphocytes and OC) was also decreased by ADA therapy. In vitro human cultures of similar cell types including RA-FLS and OCP were subjected to conditioned media or TNF, respectively, and found to express higher levels of CXCR4 that was reduced with concomitant ADA treatment. Finally, antibody-mediated blockade of CXCR4 on human OCP decreased both TNF-enhanced OC maturation and activity.

Conclusion: Our findings demonstrate that ADA therapy reduces CXCR4 expression in vivo both in RA patient PBMCs and in the pannus of huTNF Tg mice with inflammatory arthritis especially in lymphocytes, FLS and OC. Similar results were also observed with our in vitro human cultures of equivalent cell types. More importantly, we’ve shown that inhibition of CXCR4 can reduce TNF-enhanced OCgenesis in vitro, suggesting that CXCR4 may be a contributing factor to TNF-mediated osteolysis in RA.

Role of Syndecans in Cytokine Mediated Inflammation in Rheumatoid Arthritis Synovial Fibroblasts

Solomon Agere¹, Nahid Akhtar¹, David Fox² and Salahuddin Ahmed¹, ¹Department of Pharmaceutical Sciences, Washington State University, College of Pharmacy, Spokane, WA, ²Department of Medicine [Division of Rheumatology], University of Michigan Medical System, Ann Arbor, MI
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster II: Mesenchymal Cells Do React - But How?
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Syndecans (SDCs) are type-I transmembrane proteoglycans that prominently interact with heparan sulfate, extracellular matrix (ECM) components and glycoproteins. The present study was carried out to determine the role of syndecans in promoting tissue destruction mediated using human rheumatoid arthritis synovial fibroblasts (RASFs) and a rat adjuvant-induced arthritis (AIA) model of RA

Methods: Human RASFs and healthy (NL) SFs were isolated from de-identified RA and NL synovial tissues, respectively, under an IRB approved protocol. RASF and NLSF lysates were prepared to study the expression of SDC-1, SDC-2, SDC-3, and SDC-4 using qRT-PCR and Western immunoblotting. Knockdown of SDCs using siRNA approach was conducted to study its effect on IL-1β (10 ng/ml) or TNF-α (20 ng/ml) induced signaling pathways and downstream inflammatory mediators in RASFs. Ankle, heart, spleen and liver homogenates from naïve and AIA rats were analyzed for differences in the expression levels of SDCs. Serum levels of SDC-2 and SDC-4 were also analyzed in RA patients and in AIA rats. p<0.05 was considered significant.

Results: Our qRT-PCR results showed that the expression of SDC-2 (~320%) and SDC-4 (~80%) was significantly higher in RASFs when compared to NLSFs, which was also confirmed in protein levels using Western blotting method. No significant changes were observed in SDC-1 and SDC-3 expression in RASFs compared to NLSFs. Stimulation of RASFs with IL-1β or TNF-α-induced SDC-2 and SDC-4, but not SDC-1 or SDC-3, expression compared to the un-stimulated controls. Knockdown of SDC-2 and SDC-4 significantly inhibited IL-1β-induced matrix metalloproteinase-1 (MMP-1) and MMP-13 production, which could partly be due to the decrease in ERK and PKCδ activation in RASFs. In addition, we also observed a statistically significant decrease in IL-1β-induced IL-6 production with the knockdown of SDC-2 or SDC-4. Evaluation of the tissue homogenates from naïve and early (day 8) and established (day 18) AIA in rats for SDC expression showed a marked increase in SDC-2 and -4 expression in serum, ankles, liver, and spleen in AIA group at day 8 and at day 18 compared with naïve group. Treatment of methotrexate (MTX) significantly decreased both SDC-2 and -4 expression compared to the AIA alone group. However, human RA serum samples showed a consistent increase only in SDC-4 expression compared to the serum from healthy donors.

Conclusion: These findings suggest SDC-4 may be a potential therapeutic target in regulating the role of cytokines and MMPs in mediating tissue destruction in RA.

Disclosure: S. Agere, None; N. Akhtar, None; D. Fox, None; S. Ahmed, None.

Artesunate Inhabits Migration and Invasion of Fibroblast-like Synoviocytes and Matrix Metalloproteinases Expression Via Suppression of PI3K/Akt Pathway in Rheumatoid Arthritis

Jian-Da Ma¹, Jun Jing¹, Tao Yan², Ying-Qian Mo¹ and Lie Dai¹, ¹Department of Rheumatology, Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Guangzhou, China, ²Zhongshan School of Medicine, Sun Yat-Sen University, Guangzhou, China

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster II: Mesenchymal Cells Do React - But How?
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Fibroblast-like synoviocytes (FLS) play major roles on joint destruction in rheumatoid arthritis (RA) through migrating and invading cartilage and bone by secreting proteases such as matrix metalloproteinases (MMPs). Recent studies show that artesunate, an important artemisinin derivative, may inhibit proinflammatory cytokines secretion of RA-FLS. We aim to investigate the effect of artesunate on migration and invasion of RA-FLS and its underlying mechanism

Methods: FLS isolated from knee synovium of active RA patients were cultured in vitro. The effects of artesunate, methotrexate (MTX) or hydroxychloroquine (HCQ) on cell viability and anti-proliferation were measured by CCK-8 assay. Effects on migration and invasion capacity were detected by wound healing and transwell assays. Differential expression of MMPs were analyzed by Proteome profiler human protease array (R&D Systems) and furtherly verified by quantitative real-time PCR, western blot (WB) and ELISA. The expression of PI3K, PIP2, PIP3, PDK1 and Akt in PI3K/Akt signal pathway was measured by WB.

Results: The IC₅₀ value of artesunate, MTX and HCQ on RA-FLS were 6891μM, 181.4nM and 5433μM respectively. Compared with untreated group, IC₁-20μM, IC₃-40μM, IC₅-60μM of artesunate, IC₅-10nM of MTX and IC₅-20μM of HCQ showed no significant change in proliferation even after 72h. Wound healing and migration assays for 12h and invasion assay for 24h showed artesunate inhibits the migration and invasion of RA-FLS in a dose-dependent manner. MTX also has inhibition effect on the migration and invasion of RA-FLS, but HCQ not (Fig. A). Proteome profiler human protease array of culture supernatant showed that 60μM artesunate markedly inhibited MMP-2/9 expression (Fig. B). Further verification showed that RA-FLS pretreated with 60μM artesunate attenuated MMP-2/9 mRNA and protein expression, and ELISA results showed 60μM artesunate decreased MMP-2 and MMP-9 concentration of 5.82±0.45 and 11.74±1.30ng/mL respectively (Fig. C). Further pre-treatment with recombination human MMP-2 (6 ng/ml) or MMP-9 (12 ng/ml) for 24h could reverse inhibitory effect of 60μM artesunate on invasion, but not migration (Fig. D). Quantitative real-time PCR and WB analysis showed that PDK1 expression and Akt activity (phophso-Akt/Akt) in 60μM artesunate treatment group was significantly lower than that in untreated group which indicated that artesunate suppressed generation of PDK1-induced activation of Akt (Fig. E).

Conclusion: Artesunate could inhibit migration and invasion of RA-FLS and MMP-2/9 expression through suppressing PDK1-induced activation of Akt.
Disclosure: J. D. Ma, National Natural Science Foundation of China (no. 81471597 and 81671612), 2,Guangdong Natural Science Foundation (no.2014A030313074), 2,Scientific Program of Traditional Chinese Medicine Bureau of Guangdong Province (no. 20161058), 2,Medical Science Research Grant of Guangdong Province, China (no. A2017109), 2; J. Jing, National Natural Science Foundation of China (no. 81471597 and 81671612), 2,Guangdong Natural Science Foundation (no.2014A030313074), 2,Scientific Program of Traditional Chinese Medicine Bureau of Guangdong Province (no. 20161058), 2; T. Yan, National Natural Science Foundation of China (no. 81471597 and 81671612), 2,Guangdong Natural Science Foundation (no.2014A030313074), 2,Scientific Program of Traditional Chinese Medicine Bureau of Guangdong Province (no. 20161058), 2; Y. Q. Mo, National Natural Science Foundation of China (no. 81471597 and 81671612), 2,Guangdong Natural Science Foundation (no.2014A030313074), 2,Scientific Program of Traditional Chinese Medicine Bureau of Guangdong Province (no. 20161058), 2; L. Dai, National Natural Science Foundation of China (no. 81471597 and 81671612), 2,Guangdong Natural Science Foundation (no.2014A030313074), 2,Scientific Program of Traditional Chinese Medicine Bureau of Guangdong Province (no. 20161058), 2.


Abstract Number: 964

Atherogenic Potency of Plasma from Persons with Autoimmune Rheumatic Disorders: Comparative Effects on Cholesterol Flux in Human Macrophages

Andrew Maidhof1, Allison B. Reiss1,2, Lora J. Kasselman2, Elise Belilos1, Kristina Belostocki1, Gary Rosenblum1, Lois Bonnetti1, Melissa Fazzari2, Joshua DeLeon1 and Steven E. Carsons1,2, 1NYU Winthrop University Hospital, Department of Medicine, Mineola, NY, 2NYU Winthrop University Hospital, Winthrop Research Institute, Mineola, NY

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster II: Mesenchymal Cells Do React - But How?
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM
Background/Purpose:

Although the risk of atherosclerotic cardiovascular disease and abnormalities in cholesterol transport have been demonstrated in rheumatoid arthritis (RA), lupus (SLE) and, to a lesser extent, in psoriatic arthritis (PsA), the degree of cholesterol transport abnormalities is not known. This study examines the effect of RA, PsA, and SLE versus healthy control (HC) plasma on cholesterol transport genes. Particular genes affect atherosclerotic processes by modulating cholesterol influx, catabolism, and efflux. Dysfunctional cholesterol handling underlies mechanisms that promote atherosclerosis.

Methods:

THP-1 human macrophages \( (10^6/\text{ml}) \) were incubated (18h-24h, RPMI1640 media) in the presence of 10% plasma from patients diagnosed as follows: 8 RA females; 12 SLE (9 female, 3 male), 22 PsA (7 female, 15 male); 21 HC (21 female). Cholesterol transport mRNA was quantified by real-time RT-PCR using specific primers for each gene. Statistical analysis was performed using Graphpad Prism. All data were analyzed by one-way analysis of variance, and pairwise multiple comparisons were made between control and treatment conditions using Bonferroni correction. RA patients fulfilled the 2010 revised criteria of the American College of Rheumatology for classification of RA. SLE patients fulfilled the Systemic Lupus International Collaborating Clinics Classification Criteria of 2012. PsA patients fulfilled the Classification Criteria for Psoriatic Arthritis of 2006. Patients with previous documentation of a diagnosis of a connective tissue disorder other than RA, PsA or SLE were excluded.

Results:

**SLE:** 10% SLE plasma increased cholesterol influx gene expression. CD36 mRNA increased by 220±56% (P<0.001), LOX-1 by 202±22% (P<0.001), and SR-A1 increased to 122.0±45.0% versus HC plasma (set at 100%). Efflux genes were suppressed. ABCA1 mRNA decreased to 77.0±47.0%, ABCG1 to 89.0±33.0%, and 27-hydroxylase (27-OH) mRNA to 20.0±48.0% versus HC.

**RA:** 10% RA plasma increased CD36 by 157.4±111.0%, SR-A1 to 124±19.0%, and LOX-1 to 102.0±53.0% versus HC. Mean ABCA1 mRNA decreased to 65.7±28.4 (P<0.001), ABCG1 to 65.0±47.0% (P<0.05), and 27-OH to 32.5±14.2% (P<0.01) in RA treated plasma versus HC plasma.

**PsA:** 10% PsA plasma didn’t alter message level of influx nor efflux genes. However, levels of SR-A1 decreased to 80.0±30.0%.

Conclusion:

Consistent with clinic evidence, cholesterol transport abnormalities are most deranged in SLE. RA and SLE plasma induced a consistent pro-atherogenic profile of cholesterol flux genes. PsA plasma was less atherogenic, reflecting their lesser disease-related cardiovascular risk. These results identify cholesterol transport genes as a potential new therapeutic target for atherosclerosis prevention in the setting of autoimmunity.

Disclosure: A. Maidhof, None; A. B. Reiss, None; L. J. Kasselman, None; E. Belilos, None; K. Belostocki, None; G. Rosenblum, None; L. Bonnetti, None; M. Fazzari, None; J. DeLeon, None; S. E. Carsons, None.


Abstract Number: 965

**Decoy Receptor 3 up-Regulates Cadherin 2 in Rheumatoid Synovial Fibroblasts**

Koji Fukuda\(^1\), Yasushi Miura\(^2,3\), Shinya Hayashi\(^2\), Toshihisa Maeda\(^1,4\) and Ryosuke Kuroda\(^1\), \(^1\)Department of Orthopaedic Surgery, Kobe University Graduate School of Medicine, Kobe, Japan, \(^2\)Orthopaedic Surgery, Kobe University Graduate School of Medicine, Kobe, Japan, \(^3\)Department of Rehabilitation Science, Kobe University Graduate School of Health Sciences, Kobe, Japan, \(^4\)Department of Immunology and Rheumatology, Stanford University, Stanford, CA
Background/Purpose: Decoy receptor 3 (DcR3) is a secreted decoy tumor necrosis factor receptor and competitively binds and inhibits the TNF family including Fas-ligand, LIGHT, and TL1A. We previously reported that DcR3 overexpressed in rheumatoid synovial fibroblasts (RA-FLS) stimulated by TNFα protects the cells from Fas-induced apoptosis [1]. We recently reported that DcR3 binds to TL1A expressed on RA-FLS resulting in the negative regulation of cell proliferation induced by inflammatory cytokines [2]. Further, we newly revealed the gene expression profiles in RA-FLS regulated by DcR3 by using microarray data analysis [3] and the possible involvement of tryptophan hydroxylase 1 down-regulated [4], interleukin 12B up-regulated by DcR3 [5] and centrosomal protein 70kDa [6] in the pathogenesis of RA. The profiles indicated that Cadherin 2/type 1/N-cadherin (CDH2) was up-regulated by DcR3 (fold change 1.93) [3]. CDH2 has been reported to be associated with cell attachment and migration [7], osteoblast differentiation [8], and the proliferation of RA-FLS [9]. The hemophilic interaction of CDH2 suppresses the proliferation of RA-FLS through increasing the P27Kip1 that inhibit cell-cycle progression [9]. In this study, we investigated the significance of DcR3 regulation of CDH2 for RA-FLS.

Methods: Before the quantification of relative expression levels of CDH2 mRNA by real-time polymerase chain reaction (real-time PCR), RA-FLS were stimulated with various concentration of DcR3-Fc or 1,000 ng/ml IgG1 as a control, or left untreated in serum-free Opti-MEM® for 12 h. Anti-CDH2 antibody was applied to frozen sections of synovial tissues from patients with RA or OA for overnight. After that, the expression of CDH2 protein was evaluated by immunohistochemical analysis.

Results: Real-time PCR demonstrated that DcR3-Fc significantly increased the expression of CDH2 mRNA in RA-FLS. Immunohistochemistry revealed that CDH2 was expressed more in the sublining layer of rheumatoid synovium than OA synovium.

Conclusion: In the gene expression profiles, we focused on CDH2 as the gene was highly up-regulated and belonged to major functional clustering categories; protein complex assembly, cell motility, regulation of transcription, cell membrane and glycosylation. In this study, we showed that the expression of CDH2 mRNA in RA-FLS was induced by DcR3 and that CDH2 was increased in the sublining layer of rheumatoid synovium. Considering the fact that CDH2 inhibits RA-FLS proliferation, the induction in CDH2 expression by DcR3 signaling may control the hyperplasia of RA synovium.

References: 1. Hayashi S. et al., Arthritis Rheum. 2007;56:1067-1074,
6. Fukuda K. et al., Mod Rheumatol. in press

Disclosure: K. Fukuda, None; Y. Miura, None; S. Hayashi, None; T. Maeda, None; R. Kuroda, None.
Abstract Number: 966

**In Search of Mechanisms Underlying Fibroblast-like Synoviocyte Cell-to-Cell Cargo Transfer**

**Ruth Byrne**\(^1\), Isabel Olmos Calvo\(^2\), Felix Kartnig\(^3\), Uwe Hansen\(^4\), Denise Beckmann\(^4\), Adelheid Korb-Pap\(^4\), Bernhard Brandtättler\(^1\), Thomas Karonitsch\(^1\), Günter Steiner\(^1\), Johannes Holinka\(^5\), Peter Ertl\(^6\), Thomas Pap\(^4\), Josef S. Smolen\(^7\) and Hans Peter Kiener\(^1\), \(^1\)Rheumatology, Medical University of Vienna, Vienna, Austria, \(^2\)Department of Chemical Technologies and Analytics, Vienna University of Technology, Vienna, Austria, \(^3\)CeMM, Research Center for Molecular Medicine of the Austrian Academy of Sciences, Vienna, Austria, \(^4\)Institute of Musculoskeletal Medicine, University Hospital Muenster, Muenster, Germany, \(^5\)Orthopaedics, Medical University of Vienna, Vienna, Austria, \(^6\)Vienna University of Technology, Vienna, Austria, \(^7\)Medical University Vienna, Division of Rheumatology, Department of Internal Medicine III, Vienna, Austria

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster II: Mesenchymal Cells Do React - But How?

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The synovium is primarily built by fibroblast-like-synoviocytes (FLS). These cells form a complex tissue network via long-distance connections (nanotubes) and wide intercellular matrix spaces. FLS coordinate and transfer information between each other to carry out tissue functions that are critical to joint homeostasis. For this, they exchange cargo, i.e. organelles like mitochondria either via transfer through interconnecting nanotubes or vesicles. Here we search for the underlying mechanisms of cell-to-cell cargo transfer. As targets, we selected actin and tubulin, both part of the cytoskeleton of nanotube structures, as well as the clathrin pathway for endocytosis.

**Methods:** Human FLS were taken from joint synovectomies. Passaged FLS were used to generate micromass cell cultures using Matrigel (BD®). Within just a few days these cells build a 3D structure that strongly resembles the in-vivo situation of the synovium. Cells were dyed with Celltracker and Mitotracker dyes (TF®) and challenged with various blocking agents. Analyses of the 3D confocal and multiphoton imaging data were done with Imaris Bitplane® software.

**Results:** By extracting the actin skeleton from the cells body, we show the triangular arrangement of actin filaments connected by the Arp2/3 complex at the basis of nanotubes as well as their linear arrangement in building nanotubes using electron microscopy. To block actin filament construction via the Arp2/3 complex we used CK666. This not only changed the architecture of the tissue but also significantly lowered the mitochondrial transfer rate between cells.

While thin nanotubes only consist of actin filaments, thick nanotubes may also contain microtubules. Additionally, kinesins use microtubules to shuttle cargo through the cytoplasm. To block tubulin synthesis, we used nocodazole. This treatment changed the structure of FLS micromasses, however, did not significantly lower the mitochondrial transfer rate. Moreover, we determined the mitochondrial travelling speed through nanotubes at 45,4 μm/h. This contrasts kinesin-mediated shuttling which amounts to 0,005 μm/h.

Clathrin mediated endocytosis, and thus the transfer of vesicles between cells, can be blocked by sucrose. Intriguingly, this treatment does not only affect vesicle transfer but also the formation of nanotubes, as it hinders the cell to build curvatures into its membrane. Sucrose treatment resulted in both a change in tissue architecture and significantly lowered the mitochondrial transfer rate.
**Conclusion:** Since the mitochondrial transfer rate was not affected by blocking the synthesis of microtubules and the traveling speed of mitochondria in our experiments was very different from that of kinesin shuttling, we conclude that microtubules are not involved in cell-to-cell cargo transfer. However, by blocking actin synthesis as well as clathrin mediated endocytosis, mitochondrial transfer was significantly lowered. Thus, cell-to-cell cargo transfer is likely an important feature of synovial tissue function that operates using distinct cellular pathways. Further studies will demonstrate its significance in the normal as well as the diseased synovium.

**Disclosure:** R. Byrne, None; I. Olmos Calvo, None; F. Kartnig, None; U. Hansen, None; D. Beckmann, None; A. Korb-Pap, None; B. Brandstätter, None; T. Karonitsch, None; G. Steiner, None; J. Holinka, None; P. Ertl, None; T. Pap, Orthogen, 5; J. S. Smolen, AbbVie, Amgen, Astra-Zeneca, Astro, BMS, Celgene, Celltrion, Chugai, Gilead, Glaxo, ILTOO, Janssen, Eli Lilly and Company, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi-Aventis, UCB, 5,AbbVie, Janssen, Eli Lilly and Company, MSD, Pfizer, Roche, 2,AbbVie, Amgen, Astra-Zeneca, Astro, BMS, Celgene, Celltrion, Chugai, Gilead, Glaxo, ILTOO, Janssen, Eli Lilly and Company, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi-Aventis, UCB, 8; H. P. Kiener, None.


**Abstract Number:** 967

**NF-κb-Inducing Kinase Regulates LTβR-Driven NF-κb Signaling and Inflammatory Activation of Endothelium**

Paulina Kucharzewska1, Chrisita Maracle2, Jan Piet van Hamburg2, **Kim Jeucken**2, Henric Olsson1 and Sander W. Tas3, 1Bioscience, AstraZeneca, Göteborg, Sweden, 2Department of Clinical Immunology & Rheumatology and Laboratory for Experimental Immunology, Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands, 3Department of Clinical Immunology & Rheumatology and Laboratory for Experimental Immunology, ARC | Academic Medical Center/University of Amsterdam, Amsterdam, Netherlands

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster II: Mesenchymal Cells Do React - But How?

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Sites of chronic inflammation, such as rheumatoid arthritis synovial tissue, are characterized by neovascularization and often contain tertiary lymphoid structures with characteristic features of lymphoid organs such as endothelial venules (HEV), and sometimes true germinal centers. Ligation of the lymphotoxin-β receptor (LTβR) results in activation of both canonical and NF-κB-Inducing Kinase (NIK)-dependent non-canonical NF-κB signaling in endothelial cells (ECs) and plays a crucial role in lymphoid neogenesis. Non-canonical NF-κB signaling in ECs promotes inflammation-induced angiogenesis and triggers the development of the cuboidal HEV appearance. However, the relative contribution of the individual pathways to the acquisition of leukocyte traffic-regulating properties by ECs is less well understood.

Goal of the current study is to identify molecular pathways by which LTβR drives inflammatory activation of ECs to promote interactions with leukocytes.

**Methods:** Primary human ECs were treated with LTβ or LIGHT to activate LTβR. Induction of downstream signaling pathways was assessed by western blot and NF-κB transcription factor ELISA. The expression of adhesion molecules, inflammatory cytokines and chemokines in ECs was measured by RT-qPCR and cytokine antibody arrays. EC interactions with leukocytes were determined by adhesion assay, and EC barrier integrity was assessed by permeability assay. To repress canonical NF-κB signaling pathway, a small molecule inhibitor of IKKβ was used, and inactivation of non-canonical NF-κB
signaling was achieved with siRNAs targeting NFκB2. The role of NIK in LTβR signaling was investigated using small molecule inhibitors of NIK, siRNAs targeting NIK and adenoviral vectors encoding wild type and kinase-deficient NIK.

**Results:** LTβR triggering in ECs resulted in activation of both canonical and non-canonical NF-κB signaling pathways and induced the expression of inflammatory cytokines and chemokines (CXCL1, CXCL5, CXCL8, MCP-1, GM-CSF, CCL5). Consistent with inflammatory activation of ECs, LTβR ligation also induced adhesion of immune cells to activated endothelium and increased permeability across EC monolayers. IKKβ inhibition completely repressed LTβR-induced inflammatory activation of ECs, indicating that this process was mediated through canonical NF-κB signaling. Interestingly, inactivation of NIK with small molecule inhibitors and siRNAs significantly decreased LTβR-induced expression of inflammatory cytokines and adhesion of immune cells to endothelium, whereas silencing of NFκB2 had no effect. This suggests that the non-canonical pathway is dispensable for NIK-dependent activation of endothelial cells through the canonical NF-κB pathway. Further analyses, including silencing of NIK and NIK overexpression, demonstrated a role for NIK in activation of the canonical NF-κB pathway by amplifying IKK complex activity.

**Conclusion:** These findings suggest that in addition to its pivotal role in the non-canonical pathway, NIK can serve as an amplifier of the canonical NF-κB pathway and associated inflammatory responses in ECs mediated by LTβR ligation, which may play a role in development and maintenance of chronic inflammation.

**Disclosure:** P. Kucharzewska, AstraZeneca, 3; C. Maracle, None; J. P. van Hamburg, None; K. Jeucken, None; H. Olsson, AstraZeneca, 3; S. W. Tas, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/nf-%ce%bab-inducing-kinase-regulates-lt%ce%b2r-driven-nf-%ce%bab-signaling-and-inflammatory-activation-of-endothelium](http://acrabstracts.org/abstract/nf-%ce%bab-inducing-kinase-regulates-lt%ce%b2r-driven-nf-%ce%bab-signaling-and-inflammatory-activation-of-endothelium)

**Abstract Number:** 968

**Mononuclear Phagocytes Mediate Systemic Autoimmune Disease-Related Valvular Heart Disease Via Inflammatory Cytokine Production and Recruitment of Tissue-Reparative macrophages**

**Lee Meier**¹, Jennifer L. Auger², Brianna J. Engelson³, Hannah Cowan³, Elise Breed⁴, Mayra Gonzalez-Torres⁵, Joshua Boyer⁶ and Bryce A. Binstadt⁷, ¹Pediatrics, University of Minnesota, Minneapolis, MN, ²Center for Immunology and Department of Pediatrics, University of Minnesota, Minneapolis, MN, ³Pediatrics, University of Minnesota, Minneapolis, MN, ⁴University of Minnesota Medical School, Minneapolis, MN, ⁵University of Puerto Rico, Ponce, Puerto Rico, ⁶University of California, San Diego, San Diego, CA, ⁷remove this, remove this, remove this, MN

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Monday, November 6, 2017
**Session Title:** Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster II: Mesenchymal Cells Do React - But How?
**Session Type:** ACR Poster Session B
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**
Cardiovascular comorbidity is significant in patients with systemic autoimmune diseases including rheumatoid arthritis and systemic lupus erythematosus. T cell receptor transgenic K/B.g7 mice develop autoimmune arthritis and concomitant inflammatory and fibrotic valvular heart disease (VHD) with complete penetrance. This model allows dissection of the molecular and cellular pathways that drive accelerated cardiovascular disease in the setting of systemic autoimmunity. We have previously demonstrated that VHD in K/B.g7 mice is orchestrated by discrete mononuclear phagocyte populations with CD301b⁺ tissue-reparative macrophages comprising the dominant valve-infiltrating population. We have also demonstrated
that a TNF/IL6-VCAM1-VLA4 axis drives disease. Here we sought to assess the specific contribution of mononuclear phagocytes (MNPs) in this disease process, using a conditional gene knockout approach.

**Methods:**

To test the hypothesis that MNPs responding to circulating autoantibodies provide the source of TNF and IL6 during mitral valve disease (MVD) initiation, we first generated a $\text{Cx3cr1-Cre}:\text{Syk}^{\text{fl}}/\text{fl}$ K/B.g7 line to prevent FcyR-mediated MNP activation. Histological assessment of valve disease severity and flow-cytometric assessment of TNF and IL6 production from valve-infiltrating and lymphoid MNPs were employed. Secondly, to test the hypothesis that recruitment of circulating MNPs drives MVD progression through VLA4-VCAM1 interactions, we generated a $\text{Cx3cr1-Cre}:\text{Itga4}^{\text{fl}}/\text{fl}$ K/B.g7 line to disrupt this interaction. Valve inflammation and fibrosis were quantified histologically. Cre-negative littermates were employed as controls in all cases.

**Results:**

Deletion of Syk in from MNPs ameliorated MVD severity and was accompanied by impaired TNF and IL6 production by valve infiltrating macrophages. Interestingly, lymphoid-resident MNP cytokine production was unaffected. Impairing MNP recruitment through deletion of VLA4 ($\text{Itga4}$) significantly attenuated the severity of K/B.g7 cardiac valve inflammation and fibrosis.

**Conclusion:**

These studies define the critical molecular pathways used by MNPs to promote cardiovascular pathology in the setting of systemic autoimmunity. We have defined multiple therapeutic targets (TNF, IL6, Syk, VLA4, VCAM1) that could be exploited for the treatment of the cardiovascular comorbidity that accompanies human rheumatic diseases. Ongoing studies are aimed at clarifying the molecular pathways governing MNP-mediated matrix production following their infiltration to the valve stroma.

**Disclosure:** L. Meier, None; J. L. Auger, None; B. J. Engelson, None; H. Cowan, None; E. Breed, None; M. Gonzalez-Torres, None; J. Boyer, None; B. A. Binstadt, None.


**Abstract Number: 969**

**Modulation of Cartilage Degradation Biomarkers Reflect the Activation and Inhibition of Pro-Inflammatory Cytokine Signaling in an Ex Vivo Model of Bovine Cartilage**

Cecilie F. Kjelgaard-Petersen$^{1,2}$, Neha Sharma$^{1,3}$, Ashref Kayed$^{4,5}$, Britt Christensen$^1$, Morten Karsdal$^6$, Anne-C. Bay-Jensen$^7$ and Christian S. Thudium$^1$, $^1$Biomarkers and Research, Nordic Bioscience, Herlev, Denmark, $^2$Bioengineering, Technical University of Denmark, Kgs. Lyngby, Denmark, $^3$Biomedical Sciences, University of Copenhagen, Copenhagen, Denmark, $^4$Research and Biomarkers, Nordic Bioscience, Herlev, Denmark, $^5$Biomolecular Sciences, University of Copenhagen, Copenhagen, Denmark, $^6$Biomarkers and Research, Nordic Bioscience, Herlev, Denmark, $^7$Biomarkers and Research, Nordic Bioscience, Herlev, Denmark

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster II: Mesenchymal Cells Do React - But How?
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Several inflammatory cytokines and intracellular signaling pathways have been targeted in drug development with varying clinical results. Improved understanding of the intracellular signaling’s modulation of the extracellular matrix turnover could aid in selecting novel anti-inflammatory treatments for inflammatory arthritis. The aim of this study was to investigate the effect of small molecule inhibitors targeting 4 main pro-inflammatory signaling pathways (p38, Syk, IκBα, and STAT) on Oncostatin M (OSM) and Tumor Necrosis Factor α (TNFα) stimulated cartilage.

Methods:

Full depth cartilage explants (FDC) were isolated from bovine knees. The FDCs were cultured for 21 days without (WO) treatment, OSM [10ng/mL]+TNFα [2ng/mL] or OSM+TNFα together with SB203580, R406, TPCA-1 or Tofacitinib (Tofa) at 3 µM, 1 µM, 0.3 µM, or 0.1µM. DMSO was included in WO and OSM+TNFα. The inhibitors were given at start of the experiment (preventive) or after 10 days of OSM+TNFα stimuli (interventive). Activation of the p38, JNK, ERK, IκBα, and STAT3 signaling pathways were assessed at time 0, 15’, 30’, 1h, 2h, 4h, 8h, and 24h of OSM+TNFα stimuli by western blot. The effect of the OSM+TNFα induced cartilage turnover was assessed by the biomarkers AGNx1, C2M, and FFGV by ELISA in the conditioned medium.

Results:

Western blot verified activation of p38, JNK, ERK, IκBα, and STAT3 signaling within 24h of OSM+TNFα stimuli. OSM+TNFα significantly increased the biomarkers AGNx1 ($P<0.001$), FFGV ($P<0.001$) (Fig. 1), and C2M ($P<0.001$). Preventive SB203580 treatment had no effect on OSM+TNFα induced AGNx1 release, while R406 (3µM: $P=0.034$), TPCA-1 (3µM: $P<0.001$) and Tofa (3µM: $P<0.001$) significantly decreased AGNx1 in a dose-dependent manner. All inhibitors given preventive inhibited the release of C2M and FFGV (Fig.1a-d). SB203508 in a dose-dependent manner (3µM: $P=0.001$), while all concentrations of R406, TPCA-1, and Tofa significantly inhibited the release ($P<0.05$). Interventive treatment with SB203580 tended to decrease C2M and FFGV (Fig. 1e) release 4 days after addition. R406, TPCA-1, and Tofa had no effect on C2M or FFGV after 4 days of interventive treatment, but tended to decrease C2M and significantly decreased FFGV (Fig. 1f-h) release after seven days of treatment in a dose-dependent manner (C2M: 3 µM, $P≤0.055$, FFGV).

Conclusion:

In summary, we verified that OSM+TNFα stimulation activates a series of signaling pathways in our FDC culture. Using small molecule inhibitors targeting these individual pathways we found that they modulate the release of extracellular matrix degradation fragments in a spatial and temporal manner. This is both dependent on the target signaling pathway and whether the treatment is preventive or interventive.
ACPA Activate Challenged Synovial Fibroblasts through a PAD Dependent Mechanism: A Potential Explanation of the “Second Hit Model” in RA
Meng Sun1, Vijay Joshua1, Akilan Krishnamurthy1, Aase Hensvold1, Yanying Liu2, Sergiu-Bogdan Catrina3, Caroline Ospelt4, Vivianne Malmström1, Johanna Steen1, Marianne Engström1, Heidi Wähämaa1, Bence Rethi1 and Anca I. Catrina1,
1Rheumatology Unit, Department of Medicine, Karolinska Institute, Karolinska University Hospital, Stockholm, Sweden, 2Rheumatology Unit, Department of Medicine, Peking University People's Hospital, Beijing, China, 3Molecular Medicine and Surgery, Molecular Medicine and Surgery, Stockholm, Sweden, 4Center of Experimental Rheumatology, University Hospital Zürich, Zurich, Switzerland

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster II: Mesenchymal Cells Do React - But How?
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Anti-citrullinated proteins antibodies (ACPAs) injected in mice induce IL-8 dependent bone loss and arthralgia, but no synovial changes. We hypothesized that additional stimulus, sensitizing the synovial compartment to ACPA effects, is needed for the transition from bone to synovial pathology.

Methods:
Synovial biopsies were obtained from healthy volunteers and RA patients by arthroscopy. Synovial fibroblasts (SFs) were isolated from synovial tissue of RA patients by enzymatic digestion. Polyclonal ACPA and other non-ACPA IgGs were separated from peripheral blood of RA patients by affinity purification on a cyclic citrullinated peptide (CCP)-2 column. Monoclonal ACPAs were generated from synovial fluid single B-cells. SFs migration capacity was tested by scratch-assays in starved and non-starved cultures treated with ACPAs, with or without presence of IL-8. The results were evaluated by NIH ImageJ software. SF adhesion was analyzed by xCELLigence System Real-Time Cell Analyzer (ACEA bioscience). Peptidylarginine deiminases (PAD) expression and protein citrullination were evaluated by immunohistochemistry and immunofluorescence on SFs. Citrullination level of synovial biopsies were evaluated by biotinylated monoclonal ACPAs. The role of signaling pathways in the ACPA-mediated SF modulation was analyzed by using specific signal inhibitors and by monitoring protein phosphorylation using western blot.

Results:
Serum starvation of SFs increased citrullinated proteins and PAD expression. Starved but not non-starved SFs showed an increased mobility index following polyclonal ACPA stimulation to a mean±SD fold increase of 2.6±0.5. Similar effects were observed with monoclonal B09 but not C03, with a fold increase of the migration index of 1.8±0.4 for B09 antibody and 1.0±0.5 for C03 antibody. This effect was abolished by PAD inhibition as well as ACPA blocking with citrullinated but not native fibrinogen. Exogenous pro-inflammatory cytokines IL-8 and TNF induced PAD expression in SF and synergistically increased their mobility when added together with ACPA. Phosphorylation and inhibition studies of intracellular signaling pathways in starved SFs indicated an important role for PI3K-mediated signals in the ACPA-induced increase of SF mobility. Neither B09 nor C03 were binding to the non-inflammed healthy synovial tissues, while both B09 and C03 showed various degrees of binding to the inflammed RA synovial biopsies, with only B09 bidning the fibroblast cell population.

Conclusion:
We demonstrated that some but not all ACPAs fail to activate SFs in basal conditions but have a pronoucne effect on cellular stressed SF. Our findings offer a novel scenario on how a synovial insult (in this case the in vitro induced cellular stress) that will normally resolve unobserved, might be essential for the transition towards chronic synovial changes in the presence of ACPA.

Disclosure: M. Sun, None; V. Joshua, None; A. Krishnamurthy, None; A. Hensvold, None; Y. Liu, None; S. B. Catrina, None; C. Ospelt, None; V. Malmström, None; J. Steen, None; M. Engström, None; H. Wähämaa, None; B. Rethi, None;
Synovial Fibroblast CD318 Expression Mediates T Cell Adhesion and Migration in Rheumatoid Arthritis

Ray A. Ohara¹, Stephanie M. Rasmussen¹, W. Alexander Stinson¹, Huadong Cui¹, Yuxuan Du¹, Daniel P. Weber¹, M. Asif Amin¹, Phillip L. Campbell², Nora Singer³, Feng Lin⁴, David A. Fox¹ and Jeffrey H. Ruth⁵, ¹Division of Rheumatology and Clinical Autoimmune Center of Excellence, University of Michigan, Ann Arbor, MI, Ann Arbor, MI, ²Ann Arbor, MI, ³Division of Rheumatology, MetroHealth Medical Center, Cleveland, OH, Cleveland, OH, ⁴Department of Immunology, Lerner Research Institute, Cleveland Clinic, Cleveland, OH, Cleveland, OH, ⁵Internal Medicine, Division of Rheumatology and Clinical Autoimmune Center of Excellence, University of Michigan, Ann Arbor, MI, Ann Arbor, MI

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster II: Mesenchymal Cells Do React - But How?
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: CD6 is an important marker and regulator of T cells and interacts with its known ligand, CD166. Our group has previously shown that interferon gamma (IFNγ)-inducible antigen recognized by monoclonal antibody 3A11 is a new CD6 ligand distinct from CD166. And, it has recently been discovered that CD318 is the new CD6 ligand recognized by 3A11. CD318 is a cell surface protein widely expressed on epithelial tissues and tumor cells as an important regulator of cell adhesion through phosphorylation of its intracellular tyrosine domain. We currently examined CD318 expression on synovial tissues (STs) and soluble CD318 concentrations in synovial fluids (SFs) of rheumatoid arthritis (RA) patients. In addition, we investigated its potential roles in recruitment and retention of T cells in the RA joints. We hypothesize that CD6 on T cells interacts with CD318 on synovial fibroblasts and may lead to activation of either or both cellular subsets to induce proinflammatory responses in RA.

Methods: To determine the localization of CD318 in the RA joints, normal (NL), RA, and osteoarthritis (OA) ST sections were stained via both chromogenic and fluorescent immunohistochemistry using 3A11. To quantify the CD318 levels, STs were homogenized and measured for CD318 using ELISA. Additionally, to examine whether CD318 is shed in a soluble form, NL and RA peripheral blood sera and RA, OA, and juvenile idiopathic arthritis (JIA) SFs were measured for CD318 using ELISA. To confirm the expression of CD318 in vitro, synovial fibroblasts were treated with or without IFNγ and stained for CD318 for flow cytometric analysis. To investigate the role of CD318 in the interaction between synovial fibroblasts and T cells, adhesion assays were performed on synovial fibroblasts stimulated with or without IFNγ in the presence or absence of neutralizing antibodies to CD318 and CD166. T cell migration assay was performed in a modified 48-well Boyden chamber system.

Results: Immunohistochemistry revealed robust staining in the RA STs, specifically on the synovial fibroblasts and endothelial cells, greater in RA than in NL and OA STs. ELISA showed elevated levels of CD318 in the RA ST homogenates compared to that of NL and OA ST homogenates. ELISA for SFs also showed that soluble CD318 is selectively and significantly elevated in the SF from patients with RA and JIA. Flow cytometry showed upregulation of CD318 on synovial fibroblast lines upon IFNγ treatment. In adhesion assays, without IFNγ treatment, only CD166 was functionally involved, consistent with low expression of CD318 on these cells. In contrast, with IFNγ treatment, both CD318 and CD166 were functionally involved, and adhesion was substantially diminished only by antibodies to both CD166 and CD318. T cell migration assay confirmed CD318 as a chemoattractant at concentrations corresponding to the levels seen in RA sera and SFs.
Conclusion: CD318 is highly elevated in the RA joints and involved in T cell adhesion to synovial fibroblasts. Soluble CD318 is a T cell chemoattractant and its levels are similarly elevated in the SFs of RA and JIA patients. CD318 is a potential new biomarker or target for the diagnosis and treatment of RA and other inflammatory arthritides.

Disclosure: R. A. Ohara, None; S. M. Rasmussen, None; W. A. Stinson, None; H. Cui, None; Y. Du, None; D. P. Weber, None; M. A. Amin, None; P. L. Campbell, None; N. Singer, None; F. Lin, None; D. A. Fox, None; J. H. Ruth, None.


Abstract Number: 972

JAK/STAT Mediated Inhibition of Mir-23a~24-2~27a Cluster Potentiates Activation of CD14+ Monocytes in Treatment-Resistant RA

Marina Frleta-Gilchrist, Donna McIntyre, Aziza Elmesmari, Lynn Stewart, Derek Baxter, Mariola Kurowska-Stolarska, Derek Gilchrist and Iain B. McInnes, Institute of Infection, Immunity and Inflammation, University of Glasgow, Glasgow, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster II: Mesenchymal Cells Do React - But How?
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

While emerging and existing treatments of RA allow better options and clinical outcomes for patients, studies informing drug resistant states and further clinical therapeutic choices are lagging. We sought herein to compare a cross-sectional cohort of patients with maintained low disease activity on conventional DMARDs (cDMARDs) and patients failing multiple modes of both conventional or biologic treatments. A broad insight into the treatment resistant state was obtained by selecting blood derived CD14+ cells as precursors of many pathogenic cell types in RA. From these, we profiled the expression of microRNAs (miR), which as post-transcriptional regulators have the ability to control entire pathways giving an informative ‘snapshot’ of cell state. The resulting data identified regulatory miRs and associated pro-inflammatory pathways underpinning treatment resistance in RA, highlighting how they could be utilized to inform future treatment choices.

Methods:

RA patients meeting ACR 2010 diagnostic criteria were selected for this study. Two control groups included 21 healthy matched controls and 16 patients with established disease, well controlled by conventional DMARDs (cDMARDs); while treatment resistant groups contained 22 patients with high disease activity with cDMARDs and 41 patients with active disease after multiple biologic agents. Peripheral blood CD14+ cells were isolated using Miltenyi isolation kit. MiR expression was determined using the Affymetrix 3.0 miR Array. Predicted miR targets were identified using TargetScan. Direct miR-target interactions were confirmed by luciferase reporter assay. CD14+ cells isolated from buffy coats were stimulated with IL-6, IFNg or GM-CSF. THP-1 cell lines lacking the activities of miR-23a, miR-27a singly or together were created by the stable introduction of miR sponge transgenes.

Results:

Microarray profiling of CD14+ cells from patient cohort showed that the expression of miR-23a~24-2~27a cluster was significantly repressed in both treatment resistant RA groups. Specifically, miR-23a and miR-27a were found to mediate a
novel regulatory feedback loop of the IL-6 pathway. IL-6 stimulation of primary monocytes suppressed the expression of these miRs. In turn, this alleviated the repression of their direct targets, both soluble and membrane bound IL-6R, further sensitizing the cells to IL-6 signaling. Additionally, miR-23a and miR-27a expression was repressed by other cytokines utilizing JAK/STAT signaling cascade, such as viral mediator IFNγ, but also monocyte maturation factor GM-CSF, suggesting a potential mechanism for their activation upon migration into tissues. Moreover, cells lacking miR-23a and miR-27a expressed higher levels of the pro-inflammatory cytokines TNFα and IL-6 upon LPS stimulation.

Conclusion:

Collectively, these data provide evidence of how the multifactorial induction of intracellular JAK/STAT signaling inhibits miR-23a cluster expression leading to increased production of IL-6R, further potentiating the role of this novel pro-inflammatory circuit in treatment resistant RA.

Disclosure: M. Frleta-Gilchrist, None; D. McIntyre, None; A. Elmesmari, None; L. Stewart, None; D. Baxter, None; M. Kurowska-Stolarska, None; D. Gilchrist, None; I. B. McInnes, None.


Abstract Number: 973

**IL-6 and TNF-a Cooperate to Modulate the Cell Cycle of RA-Fibroblast-like Synoviocytes Via Cyclin Dependent Kinase Inhibitors**

Kenta Kaneshiro1, Kohsuke Yoshida1, Ayako Nakai1, Kohjin Suzuki1, Koto Uchida1, Teppei Hashimoto2, Yoshiko Kawasaki3, Natsuko Nakagawa4, Koji Tateishi5, Nao Shibanuma6, Yoshitada Sakai7 and Akira Hashiramoto1, 1Department of Biophysics, Kobe University Graduate School of Health Sciences, Kobe, Japan, 2Department of Rheumatology, Kobe Kaisei Hospital, Kobe, Japan, 3The Center of Rheumatic Diseases, Department of Rheumatology, Kobe Kaisei Hospital, Kobe, Japan, 4Department of Orthopaedic Surgery, Konan-Kakogawa Hospital, Kakogawa, Japan, 5Orthpaedic Surgery, Kobe University Graduate School of Medicine, Kobe, Japan, 6Department of Orthopaedic Surgery, Kobe Kaisei Hospital, Kobe, Japan, 7Division of Rehabilitation Medicine, Kobe University Graduate School of Medicine, Kobe, Japan

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017

Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster II: Mesenchymal Cells Do React - But How?

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM

Background/Purpose:

IL-6 and TNF-α play an important role in the pathogenesis of RA, and the proliferation of RA-synoviocytes (FLS) is controlled by cell cycle regulators including Cyclins, Cyclin dependent kinases (CDK), CDK inhibitors (CKDs) and retinoblastoma protein (RB). To reveal actions of proinflammatory cytokines on the cell cycle of RA-FLS, we examined the expressions of the cell cycle regulators and the cellular viability under stimulations of IL-6 and TNF-α.

Methods:

RA-FLS were cultured with or without IL-6/soluble IL-6 receptor (sIL-6R) (100ng/ml) or TNF-α (10ng/ml). The expressions of CDKIs (p16INK4a, p21Cip1, p27Kip1) and Cyclin E1/2 mRNA were measured by Real-time PCR, CYCLIN D and CYCLIN E protein were measured by Western blot, the expression of CYCLIN D and the phosphorylation of RB were observed by immunofluorescence, and the cellular viabilities were measured by WST-8. In addition, siRNA/p27Kip1 was...
introduced into RA-FLS to analyze the expression of Cyclin E1 mRNA by Real-time PCR, under stimulations with or without IL-6/sIL-6R or TNF-α.

**Results:**

IL-6/sIL-6R decreased the expression of p16\(^{INK4a}\), whereas increased CYCLIN D and the phosphorylation of RB. TNF-α increased the expressions of p27\(^{Kip1}\), Cyclin E1/2 mRNA, CYCLIN D, and the phosphorylation of RB. The expression of CYCLIN D and the phosphorylation of RB were synergistically increased by IL-6 and TNF-α. The expression of Cyclin E1 mRNA was decreased by siRNA/p27\(^{Kip1}\).

**Conclusion:**

Results clearly indicate that IL-6 and TNF-α interact with each other in regulating the cell cycle of RA-FLS.

---

**Disclosure:** K. Kaneshiro, None; K. Yoshida, None; A. Nakai, None; K. Suzuki, None; K. Uchida, None; T. Hashimoto, None; Y. Kawasaki, None; N. Nakagawa, None; K. Tateishi, None; N. Shibanuma, None; Y. Sakai, None; A. Hashiramoto, None.


**Abstract Number:** 974

**Leucine-Rich α-2 Glycoprotein Promotes Lung Fibrosis By Modulating TGF-β Signaling in Fibroblasts**

Hiromi Honda, Minoru Fujimoto, Satoshi Serada, Hyun Lee, Tomoharu Ohkawara and Tetsuji Naka, Center for Intractable Immune Disease, Kochi University, Nankoku, Japan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster II: Mesenchymal Cells Do React - But How?

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Interstitial lung disease (ILD) is one of the most common extraarticular manifestation of rheumatoid arthritis. ILD is characterized by progressive fibrosis of the lung parenchyma and is associated with increased morbidity and mortality. Since TGF-β is thought to play an important role in tissue fibrosis, understanding the molecular details of TGF-β signaling will provide us a novel therapeutic target for fibrotic disorders. Recently, leucine-rich α-2 glycoprotein (LRG) was reported to function as a modulator of TGF-β signaling in angiogenesis in retinal disease and cardiac remodeling. However, the role of LRG in fibrotic diseases including lung fibrosis has not yet been investigated. In this study, we aimed to investigate the involvement of LRG in lung fibrosis using an animal model of lung fibrosis.

**Methods:** Bleomycin was intratracheally administered to C57BL/6 (WT) mice and LRG knockout (KO) mice, and lung fibrosis was evaluated by Masson’s trichrome staining and hydroxyproline quantification in the lung. TGF-β signaling in the lung was examined by analyzing phosphorylation of Smad proteins and expression of TGF-β downstream genes. Furthermore, in vitro analysis using L929 mouse fibroblast cell line was performed to assess the effect of LRG on TGF-β signaling in fibroblasts.

**Results:** The amount of LRG in BALF of WT mice was increased after bleomycin treatment. Immunohistochemistry of the lung section showed that LRG was expressed in alveolar epithelial cells, bronchial epithelial cells and infiltrated immune cells in bleomycin-treated WT mouse lung. In LRG KO mice, fibrosis in the lung was less severe as indicated by attenuated
Masson’s trichrome staining and lower collagen content in the lung compared with WT mice. In addition, expression of α-SMA was decreased and phosphorylation of Smad2 was reduced in the lung of LRG KO mice compared with WT mice, suggesting that fibroblast activation was inhibited in the absence of LRG. In vitro experiments indicated that LRG enhanced TGF-β-induced phosphorylation of Smad2 and expression of PAI-1 and α-SMA in fibroblasts. On the other hand, Smad1/5/8 signaling was not enhanced by LRG. Although endoglin, an accessory TGF-β receptor, is known to be essential for LRG to modulate TGF-β signaling in endothelial cells, we found that endoglin was not involved in the process of enhancing Smad2 phosphorylation in fibroblasts.

**Conclusion:** LRG promotes lung fibrosis by enhancing TGF-β-induced phosphorylation of Smad2 in fibroblasts and by accelerating fibroblast differentiation into myofibroblasts.

**Disclosure:** H. Honda, None; M. Fujimoto, None; S. Serada, None; H. Lee, None; T. Ohkawara, None; T. Naka, Practical Project for Rare/Intractable Diseases from Japan Agency for Medical Research and development (15ek0109045h0003), 2,Research collaboration with SEKISUI MEDICAL, 2.

**Abstract Number:** 975

**IL-17A Induced Autophagy That the Proliferation of Rheumatoid Arthritis Fibroblast-like Synoviocytes through Down-Regulation of PI3K/AKT/mTOR Signaling Pathway**

_Sang-Hyon Kim_1, Jihye Bang2, Ji-Min Kim1, Chang-Nam Son1, Jin-Nyeong Chae1 and Hye-Jin Jeong3, 1Division of Rheumatology, Department of Internal Medicine, Keimyung University Dongsan Medical Center, Keimyung University School of Medicine, Daegu, Republic of Korea, Daegu, Korea, Republic of (South), 2Division of Rheumatology, Department of Internal Medicine, Dongsan Medical Center, Keimyung University School of Medicine, Daegu, Korea, Republic of (South), 3Department of Rheumatology, Keimyung University Dongsan Medical Center, Daegu, Korea, Republic of (South)

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster II: Mesenchymal Cells Do React - But How?

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Autophagy is generally thought of as a survival mechanism, although its deregulation has been linked to non-apoptotic cell death. Fibroblast-like synoviocytes (FLS) resistance to apoptosis is a major characteristic of rheumatoid arthritis (RA). We hypothesized that interleukin (IL)-17A might have an impact on autophagic flux and that modulation of autophagy might be involved in migration and proliferation of synovial fibroblasts in the patients with RA under inflammatory condition.

**Methods:** Synovial tissue was obtained from clinically involved knee joints of patients with RA or osteoarthritis (OA) patients. The autophagosome of FLS isolated from RA and OA patients displayed different morphological and physiological features by using transmission electron microscopy. The effects of IL-17 on the relationship between autophagy and cell migration were evaluated with co-treatment of autophagy inhibitor using bafilomycin A1 and transfection of si-Atg5.

**Results:** IL-17 induced autophagosome formation and autolysosome accumulation in RA FLS, suggesting that they were resistant to apoptosis. IL-17A increased autophagy of RA FLS by causing up-regulation of LC3II, Atg5 and Beclin1. Migration and proliferation of FLS stimulated by IL-17A was suppressed by bafilomycin A1 and si-Atg5 which knocked
down of autophagy. And, autophagy inhibitor regulated signaling pathway which decreased IL-17A-induced expression of phosphorylation-Akt and increased mTOR signaling pathway.

**Conclusion:** Taken together, our findings demonstrated that IL-17A could induce activate autophagy, induce inflammatory response, and eventually lead to proliferation of synoviocytes. We suggest that autophagy can be one of the therapeutic target for the RA management.

**Disclosure:** S. H. Kim, None; J. Bang, None; J. M. Kim, None; C. N. Son, None; J. N. Chae, None; H. J. Jeong, None.


**Abstract Number:** 976

**Cannabinoid Receptor 2 Agonist (JWH-015) Inhibits Interleukin-1β-Induced Inflammation in Rheumatoid Arthritis Synovial Fibroblasts**

Sabrina Fechtner and Salahuddin Ahmed, Department of Pharmaceutical Sciences, Washington State University, College of Pharmacy, Spokane, WA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster II: Mesenchymal Cells Do React - But How?

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by activated synovial fibroblasts in which pro-inflammatory cytokine interleukin-1β (IL-1β) mediates inflammation. The endocannabinoid system (ECS) is comprised of two evolutionarily conserved cannabinoid receptors 1 and 2 (CB1 and CB2) which elicit their effects through Gi/o mediated signaling. However, the mechanism through which ECS activation can modulate inflammatory signaling in RA is poorly understood.

**Methods:** Human RASFs were obtained from patients diagnosed with RA according to the ACR guidelines (7 female, 2 male, average age 50 ± 43 years). RASFs were pre-treated with 10 or 20 µM of JWH-015 for 10 minutes prior to the addition of IL-1β (10 ng/mL). Stimulation duration was for 30 minutes for signaling studies or 24 hours to evaluate the production of IL-6, IL-8, PGE₂, and cyclooxygenase (Cox) enzymes. Conditioned media was used for the quantification of IL-6, IL-8, and PGE₂ by ELISA and cell lysates were prepared for the analysis of IL-1β signaling proteins like p-P38, p-JNK, p-ERK, and p-TAK-1 Thr184/187 using Western immunoblotting. To understand the role of CB2, knockdown studies were performed using CB2 siRNA for 48 hours prior to the addition of JWH-015 and IL-1β.

**Results:** Pretreatment of JWH-015 inhibited IL-1β-induced IL-6 (39 and 50% at 10 and 20 µM, respectively) and IL-8 (20 and 47% at 10 and 20 µM, respectively) production in human RASFs (p<0.05; n=3). Evaluation of the signaling pathways using Western immunoblotting showed JWH-015 reduced the expression of phosphorylated TAK-1 Thr184/187 by 12% and 27% at 10 and 20 µM concentration, respectively. Phosphorylated JNK1 was also inhibited by 11% and 22% at 10 and 20 µM and JNK2 by 18% and 64% at 10 and 20 µM, respectively (p<0.05; n=3). Knockdown of CB2 expression using siRNA approach showed almost 40% reduction in the production of IL-β-induced IL-6 and IL-8 and also abrogated the protective effect of JWH-015 (p< 0.05; n=3), suggesting CB2 as a receptor central to JWH-015’s anti-inflammatory action. We also observed CB2 knockdown resulted in a significant decrease of IL-1β-induced Cox-2 expression by ~58%, which resulted in a marked inhibition of PGE₂ production by ~80% (p<0.05; n=3).
Conclusion: Our study provides novel evidence that CB2 activation is anti-inflammatory in response to IL-1β stimulation in RASFs, and JWH-015 elicits anti-inflammatory effects through CB2, not CB1, in human RASFs. These findings suggest that JWH-015 may be tested as an adjunct therapy option to reduce inflammation and the perception of local pain through the ECS.

Disclosure: S. Fechtner, None; S. Ahmed, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/cannabinoid-receptor-2-agonist-jwh-015-inhibits-interleukin-1%ce%b2-induced-inflammation-in-rheumatoid-arthritis-synovial-fibroblasts

Abstract Number: 977

Association of Leisure-Time Physical Activity with Late-Life Mobility Limitation Among Women with Total Joint Replacement for Hip or Knee Osteoarthritis

Aladdin Shadyab¹, Wenjun Li², Charles Eaton³ and Andrea LaCroix⁴, ¹Family Medicine and Public Health, University of California, San Diego, La Jolla, CA, ²Medicine, University of Massachusetts Medical School, Worcester, MA, ³Family Medicine and Epidemiology, Warren Alpert Medical School, School of Public Health, Brown University, Providence, RI, ⁴Family Medicine and Public Health, University of California, San Diego School of Medicine, La Jolla, CA

First publication: September 18, 2017

SEsson INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Epidemiology and Public Health Poster II: Rheumatic Diseases Other than Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Maintaining mobility in old age is an important public health goal for patients with hip or knee osteoarthritis (OA), who are vulnerable to functional decline and disability. Previous studies have observed that physical activity (PA) may improve physical function among OA patients and before undergoing total joint replacement (TJR) surgery for hip or knee OA. However, the association of PA with long-term functional outcomes after total hip (THR) or total knee (TKR) replacement for OA is less clear. We examined associations of leisure-time PA with late-life mobility limitation and death among women who underwent THR or TKR for OA.

Methods: The Women’s Health Initiative recruited women aged 65-79 years from 1993-1998 and followed them through 2012. Medicare claims data were used to determine THR (n=904) and TKR (n=1867) for OA. Women were followed for up to 18 years after receiving a TJR to determine mobility status at age 85. If women reported that their health limited their ability to walk one block or climb one flight of stairs in annual follow-up, they were classified as having mobility limitation. Women completed a questionnaire at baseline to determine engagement in activities of light, moderate, and vigorous intensities. PA variables were analyzed in metabolic equivalent-hours/week (MET-h/wk). Multinomial logistic regression analyses were performed to determine associations of PA variables with mobility limitation at age 85 and death before age 85 (reference category=mobility intact at age 85). Total PA, moderate-to-vigorous physical activity (MVPA), walking, and walking speed were analyzed in separate regression models adjusted for demographic, lifestyle, and health-related characteristics.

Results: Relative to women with the highest level of total PA (>17.42 MET-h/wk), women with THR (odds ratio [OR]=2.41; 95% confidence interval [CI]=1.29-4.51) or TKR (OR=1.56; 95% CI=1.04-2.34) who reported no PA had the highest risk of developing mobility limitation at age 85. Compared with women with the highest amount of MVPA (≥15 MET-h/wk), women with THR (OR=1.96; 95% CI=1.18-3.24) or TKR (OR=1.48; 95% CI=1.05-2.07) who reported no MVPA had increased risk of mobility limitation; the risk was also increased among women who did not meet federal guidelines of ≥7.5 MET-h/wk of MVPA. Women with THR (OR=2.03; 95% CI=1.16-3.58) or TKR (OR=1.54; 95% CI=1.05-2.27) who reported casual compared with fast walking speed were more likely to experience mobility limitation.
Among women with THR, there were significant dose-response associations of total PA, MVPA, walking, and walking speed with mobility limitation and death. Among women with TKR, there were significant dose-response associations of total PA, MVPA, and walking speed with mobility limitation and death.

**Conclusion:** Among older women with hip or knee OA, higher levels of total PA and MVPA, as well as faster walking speed, before TJR were associated with better mobility in late life and decreased risk of death. Further studies are needed to determine whether physical activity before TJR is associated with better mobility later in life among women with hip or knee OA.

**Disclosure:** A. Shadyab, None; W. Li, None; C. Eaton, None; A. LaCroix, None.

**Abstract Number:** 978

**Dietary Patterns and Risk of Developing Knee Osteoarthritis: Data from the Osteoarthritis Initiative**

**Bing Lu**, Jeffrey B. Driban, Timothy E. McAlindon and Charles Eaton, 1Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 2Rheumatology, Tufts Medical Center, Boston, MA, 3Division of Rheumatology, Tufts Medical Center, Boston, MA, 4Family Medicine and Epidemiology, Warren Alpert Medical School, School of Public Health, Brown University, Providence, RI

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017
**Session Title:** Epidemiology and Public Health Poster II: Rheumatic Diseases Other than Rheumatoid Arthritis
**Session Type:** ACR Poster Session B
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Few studies have examined the effect of diet on future risk of knee OA development. The association between overall dietary patterns and risk of OA is unknown. We aimed to examine the prospective association of major dietary patterns by principal component analysis (PCA) with risk of developing radiographic knee OA.

**Methods:** In the Osteoarthritis Initiative (OAI), 2835 participants (4570 knees) without knee OA in at least one knee [Kellgren and Lawrence (KL) grade of 0 or 1] who had dietary data at baseline were followed up to 48 months. We defined knee OA incidence as KL grade ≥ 2. Dietary intake was assessed with a Block Brief Food Frequency Questionnaire completed at baseline. We identified two major underlying patterns of food consumption by PCA: “Western” pattern, characterized by high intakes of red / processed meats, refined grains, french fries, desserts, and sweets, and the “Prudent” pattern characterized by high intakes of fruit/vegetables, legumes, poultry, and fish. Each subject receives a score for each dietary pattern, with a higher score indicating a higher adherence to the respective pattern. The derived patterns are statistically uncorrelated with each other. We grouped the dietary pattern scores using quartiles. We developed a Cox proportional hazards model (with discrete time) to assess the association between dietary patterns and incident knee OA. The robust covariance estimates were used to account for intra-subject correction.

**Results:** Among our sample, 414 knees developed knee OA within 48 months. In multivariable models after controlling for age, sex, race, injury/surgery, and other covariates, adherence to the Western pattern was associated with an increased risk of knee OA (HRQ4 vs Q1: 1.60, 95% CI: 1.03 to 2.51, p trend: 0.03), while adherence to the Prudent pattern tended to be associated with a reduced risk of knee OA (HRQ4 vs Q1: 0.72, 95% CI: 0.52 to 1.00, p trend: 0.11) (Table). The observed associations were attenuated after additionally adjusting for body mass index (BMI).
**Conclusion:** Following a Western diet may increase the future risk of knee OA, whereas following a Prudent pattern may be associated with a reduced risk of knee OA. The associations may be partially mediated through BMI. Replication of these novel findings in other prospective studies demonstrating that improvement of dietary quality leads to delay in knee OA development are needed.

**Key words:** Western dietary pattern, Prudent dietary pattern, osteoarthritis.

| Table. Dietary patterns and risk of knee OA (Hazard ratio, 95% CI) |
|---------------------|-----------------|-----------------|-----------------|-----------------|
| Quartiles           | Western pattern | Prudent pattern |                |                |
|                     | HR (95% CI)     | HR (95% CI)     | P trend         | P trend         |
| Q1                   | 1.00 (Ref)      | 1.00 (Ref)      | 0.03            | 0.14            |
| Q2                   | 1.60(1.19,2.16) | 1.50(1.11,2.04) | 1.50(1.11,2.04) | 0.14            |
| Q3                   | 1.55(1.11,2.17) | 1.42(1.01,1.99) | 1.38(0.88,2.19) | 0.14            |
| Q4                   | 1.60(1.03,2.51) | 0.87(0.65,1.17) | 0.76(0.55,1.07) | 0.22            |
|                     | 0.85(0.63,1.15) | 0.97(0.72,1.30) | 0.76(0.55,1.07) | 0.22            |
|                     | 0.93(0.69,1.24) |                 |                |                |
|                     | 0.72(0.52,1.00) |                 |                |                |

* Cox proportional hazards model with the discrete likelihood method handling ties in failure times, adjusting for age, sex, race, physical activity, NSAIDs use, injury/surgery, and total energy intake.

† Additionally adjusting for BMI.

**Disclosure:** B. Lu, None; J. B. Driban, NIAMS-NIH, 2,AXSOME Therapeutics, Inc., 5; T. E. McAlindon, None; C. Eaton, None.


**Abstract Number:** 979

**What Have We Learned from Trajectory Analysis of Clinical Outcomes in Osteoarthritis?**

Maud Wieczorek¹, Anne-Christine Rat¹,²,³, Francis Guillemin¹,² and Christine Rotonda¹, ¹Université de Lorraine, EA4360, APEMAC, Nancy, France, ²Inserm, CIC-1433 Epidémiologie Clinique, Vandoeuvre-lès-Nancy, France, ³Rheumatology Department, CHRU Nancy, Vandoeuvre-lès-Nancy, France

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Epidemiology and Public Health Poster II: Rheumatic Diseases Other than Rheumatoid Arthritis

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The aims of this review were to summarize the literature on the trajectories of clinical outcomes in knee and hip OA, to describe the distinct trajectories for each outcome and to collect the predictive factors associated with these trajectories.

**Methods:** The Medline database was searched for relevant studies. Selection criteria were: i) patients >= 18 years old, ii) patients at high risk of, or diagnosed with, knee or hip OA, iii) studies aiming to identify homogeneous subgroups with distinct trajectories of clinical outcomes, iv) methodology and analysis designed to identify trajectories (longitudinal design...
Results: Of the 3867 abstracts retrieved, 37 studies met inclusion criteria among which 15 other studies analyzed trajectories before surgery. The other 22 studies focused specifically on the course of clinical outcomes after hip or knee arthroplasty. The most frequent outcome reported in the papers was pain (28 studies) while 19 studies reported results on function, 5 on mental health, 1 on stiffness, 3 on social participation and 1 on activity limitation. In the cohort studies without surgery, hip pain trajectories were divided in stable mild, moderate and severe pain. 3 additional subgroups included patients who underwent a moderate pain regression, oscillated between moderate and severe pain levels or highly progressed over time (Fig). A low educational level, high body mass index (BMI), an impaired physical function WOMAC score, high Kellgren (KL) grade for the hip, a limited flexion and internal rotation of the hip and concurrent back and trochanteric pain were associated with the membership in the severe pain trajectory. For the knee joint, the number of trajectories identified in the literature was between 1 and 6. A “no pain”, a mild pain, a moderate pain and a severe pain trajectories were identified as well as pain progression (moderate or severe worsening) or regression (major or moderate improvement) trajectories. Patients belonging to the severe pain trajectory were more likely to be male, have a younger age, a low educational level, a low social class, a high BMI, a high number of comorbidities, a high WOMAC physical function score, a high KL grade, higher levels of anxiety and depression, and a poorer general health.

Conclusion: This review highlighted the high heterogeneity across studies in terms of numbers of trajectories retrieved, especially for the pain outcomes. Nonetheless, some predictive factors of membership in a severe pain trajectory have been identified and these findings could be an aid to an early identification of patients with a high risk of clinical worsening.

Disclosure: M. Wieczorek, None; A. C. Rat, None; F. Guillemin, None; C. Rotonda, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/what-have-we-learned-from-trajectory-analysis-of-clinical-outcomes-in-osteoarthritis

Is Intra-Articular Injection of Synvisc Associated with a Delay to Knee Arthroplasty in Knee OA Patients?

Kevin Ong1, Maria Runa1, Edmund Lau2 and Roy Altman3, 1Exponent, Inc., Philadelphia, PA, 2Exponent, Inc., Menlo Park, CA, 3UCLA Medical Center, Los Angeles, CA

First publication: September 18, 2017
SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Epidemiology and Public Health Poster II: Rheumatic Diseases Other than Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Knee OA patients may undergo intra-articular (IA) hyaluronic acid (HA) injection treatment, but there is debate about its effectiveness. We asked: (1) What is the epidemiology of IA HA use in knee arthroplasty (KA) patients? (2) Is hylan G-F 20 associated with a delay to KA? (3) Is there a difference in the delay to KA with the number of HA courses?

Methods: A retrospective, observational dataset (Optum Clinformatics; 2006 to June 2016) was used to identify knee OA patients. Three different cohorts were identified: (1) No HA cohort who did not receive any IA HA; (2) Non-hylan G-F 20 cohort who received multiple HA types or only one type of non-hylan G-F 20 HA; and (3) hylan G-F 20 cohort who received only hylan G-F 20. Patients who subsequently received a KA were further identified. A quantile regression model was used, adjusting for clinical confounding factors and with propensity score weighting, to evaluate the effect of the covariates on the median duration from knee OA to KA. The trend in time to KA with each additional course of HA was also evaluated.

Results: From the initial cohort of 4,027,848 knee OA patients, 141,305 KA patients were identified. Overall median time from knee OA diagnosis to KA was 1.2 years (average: 1.9 ± 1.9 years) with a corresponding interquartile range of 0.4 to 2.8 years. After propensity score adjustment, HA patients had significantly longer median time to KA by at least 5 months (p<0.001; Table 1). When the HA cohort was compared after adjusting for the time to HA and number of injections, no significant differences in the time to KA between multiple-shot hylan G-F 20 and non-hylan G-F 20 HA patients were observed (p≥0.620), but a longer time was observed for one-shot hylan G-F 20 patients by about 3 months and patients who received both one- and multiple- shot hylan G-F 20 (“One+multiple-shot hylan G-F 20”) by about 15 to 16 months. There was a trend toward longer time to KA the more HA courses the patient underwent (Figure 1). For example, the average time to KA increased from 2.3 years to 5.1 years as the hylan G-F 20 patients increased their treatment courses from one to five or more. There was disparity between states in terms of KA patients who used HA. The three states with the lowest percent of KA patients who used HA were HI (14.5%), IN (16.3%), and AK (16.7%), while the three states with the highest percent of KA patients who used HA were NJ (39.1%), LA (33.9%), and MS (31.8%).

Conclusion: Most KA patients did not use HA (73.7%) and the ones who received it were associated with a longer median time to KA by 5 to 22 months, depending on the HA cohort. The time to KA was shown to increase with more HA courses.


Abstract Number: 981

The Common Risk Factors for Hyperuricemia and Gout Do Not Predict Incident Gout Once Hyperuricemia Is Established

Richard J. Reynolds¹ and Jasvinder A. Singh², ¹Medicine, University of Alabama at Birmingham, Birmingham, AL, ²Rheumatology, University of Alabama at Birmingham, Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Epidemiology and Public Health Poster II: Rheumatic Diseases Other than Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Metabolic syndrome, chronic kidney disease and hypertension are known to be associated with hyperuricemia and gout. Hypertension is associated with incident gout. The Normative Aging Study indicates five times the number of people with gout have asymptomatic hyperuricemia, and it is not understood what factors can explain this difference. Using data from two prospective cohorts, the Framingham Heart Study (FHS) and the Atherosclerosis Risk in Communities Study (ARIC), we tested the hypothesis that traits representing the comorbid conditions of hyperuricemia and gout, given hyperuricemia at baseline, could discriminate those that subsequently develop gout from those that do not during the follow-up period.

Methods: A total of 3,415 and 1,040 participants from ARIC and FHS, respectively met the inclusion criterion in which serum urate concentration was greater than 7.0 mg/dL at the 1st exam in ARIC or exam 1, 2, or 8 of the offspring cohort in FHS. Prevalent gout cases were excluded. With ARIC, incident gout was defined only if self report gout was reported at the fourth exam (ARIC). With FHS, incident gout was defined only if clinical diagnostic impression of gout was reported at any exam subsequent to the exam with serum urate concentration greater than 7.0. We extracted the following variables at the exam where hyperuricemia was recorded: Age, sex, race (ARIC), systolic blood pressure, glomerular filtration rate (ARIC),
BMI, triglycerides, low-density lipoprotein-LDL, WaistHipRatio (ARIC), glucose and serum urate level (7-8, > 8 mg/dL). Logistic regression was used to model incident gout with a linear predictor comprising the explanatory variables.

**Results:** A total (proportion) of 167 (0.05) and 99 (0.095) incident gout cases occurred during follow-up. The mean (SD) age at baseline was 55 (5.8) and 39.5 (11.5) with 10 and 16 years of follow-up for ARIC and FHS, respectively. Age at first exam (P-value=0.047-ARIC; 0.033-FHS), with odds ratio-OR (95% confidence interval [CI]), 0.97 (0.94, 1.0)-ARIC, 0.98 (0.96, 0.999)-FHS, and serum urate level (P-value=<0.0001-ARIC, 0.056-FHS), with OR 3.42 (2.38, 4.93)-ARIC, 1.53 (0.985, 2.38)-FHS, were the only consistent explanatory variables for incident gout between the two data sets. Increased LDL was associated with incident gout in FHS (P-value=0.02, mean (SD) in gout vs no gout 145.2 (33.9) vs 138.2 (36.1), with OR = 1.01 (1.001,1.014)). The model $R^2$ was 6.3% and 2.8% for the ARIC and FHS datasets respectively.

**Conclusion:** The traditional risk factors for hyperuricemia and gout do not differentiate people with hyperuricemia that develop incident gout from those that do not during the follow-up period. A possible explanation is that most of the risk factors predict the development of hyperuricemia but not gout. Individuals presenting with serum urate levels > 8 mg/dL had the highest risk for developing gout in the future. The low explanatory ability of these models indicates that additional features, possibly molecular (e.g., genomic, metabolomic), behavioral (e.g. exercise, smoking, alcohol use) and use of medications (diuretics, aspirin, ACE inhibitors), may be important predictors of gout given the state of hyperuricemia.

**Disclosure:** R. J. Reynolds, None; J. A. Singh, Takeda, Savient, 2,consultant fees from Savient, Takeda, Regeneron, Merz, Iroko, Bioiberica, Crealta and Allergan pharmaceuticals, WebMD, UBM LLC and the American College of Rheumatology, 5,. JAS serves as the principal investigator for an investigator-initiated study funded by Horizon pharmaceuticals through a grant to DINORA, Inc., a 501 (c)(3) entity. JAS is a member of the executive of OMERACT, an organization that develops outcome mea, 9.


**Abstract Number:** 982

**Epidemiology and Mortality in Systemic Sclerosis in South Korea: A Nationwide Population-Based Study**

**Kyong-Hee Jung**¹, Seong-Ryul Kwon¹, Joo-Hyun Lee², Hyeong Sik Ahn³, Hyun Jung Kim³ and Gil Won Kang⁴,
¹Rheumatology, Inha University, Incheon, Korea, Republic of (South), ²Rheumatology, Inje University Ilsan Paik Hospital, Goyang, Korea, Republic of (South), ³Korea University, Seoul, Korea, Republic of (South), ⁴Chungbuk University, Cheongju, Korea, Republic of (South)

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017
**Session Title:** Epidemiology and Public Health Poster II: Rheumatic Diseases Other than Rheumatoid Arthritis
**Session Type:** ACR Poster Session B
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Systemic sclerosis (SSc) is an autoimmune connective tissue disease characterized by small vessel vasculopathy, autoantibody production, and excessive collagen deposition in the skin and internal organs. Its clinical manifestations and progressions are chronic and diverse. Studies on epidemiology and mortality of systemic sclerosis (SSc) at the national level are scarce. To investigate incidence, prevalence, mortality, and causes of death in SSc patients using nationwide population based data in Korea.

**Methods:**
We used data from the Rare Intractable Disease (RID) registry and Health Insurance Review and Assessment (HIRA) service, which include information on all SSc patients diagnosed based on uniform criteria between 2008 and 2013. The RID’s diagnostic criteria for SSc adopt the 1980 criteria of American College of Rheumatology. We linked the data from Statistics Korea to the HIRA-RID database to confirm the causes of death.

Results:

The mean annual incidence of SSc in Korea was 8.0 per 10^6 population, with a female-to-male ratio of 3.9:1. The prevalence in 2013 was 77.7 per 10^6 population. The average annual mortality was 1.40 per 10^6 people, and the standardized mortality ratio was 4.34. The 5-year survival rates were 88.5%, which was significantly lower than the age-gender matched general population. SSc was the most common cause of death (36.5% of total death), followed by malignancy (18.2%), cardiovascular diseases and respiratory diseases (10.7%, each).

Conclusion:

Incidence and prevalence of SSc in East Asian countries is considered to be lower than in North America and Australia, but higher than in Northern European countries. The higher mortality of SSc patients compared to the general population is attributable to SSc related diseases, lung cancer and respiratory diseases. Post-diagnosis survival of SSc patients was better than previous studies, which may represents a recent improvement in patient management.

Figure 1. Incidence of Systemic sclerosis by sex and age in Korea, 2008–2013. The vertical axis shows incidence rates per 10^5 population; the horizontal axis shows age in 5-year increments until the age of 80.

Disclosure: K. H. Jung, None; S. R. Kwon, None; J. H. Lee, None; H. S. Ahn, None; H. J. Kim, None; G. W. Kang, None.


Abstract Number: 983

Identifying Exposures to Chemicals in Patients with SLE – a Non-Targeted Exposome Approach Reveals Enrichment for Phthalates

Cristina Lanata¹, Thomas Lin², Maria Dall’Era¹, Jinoos Yazdany³, Patricia P. Katz¹, Laura Trupin³, Charles G. Helmick⁴, Roy Gerona⁵ and Lindsey A. Criswell¹, ¹Medicine/Rheumatology, University of California, San Francisco, San Francisco, CA, ²Univeristy of California, San Francisco, SAN FRANCISCO, CA, ³Medicine/Rheumatology, University of California
Environmental exposures may play a substantial role in the pathogenesis of SLE. The goal of this study is to characterize the serum levels of multiple chemicals in a cohort of SLE patients and controls.

Methods:
Patients from the California Lupus Epidemiology Study and healthy controls were studied. Banked serum was analyzed by Liquid Chromatography Quadruple Time-of-Flight Mass Spectrometry (LC-QTOF/MS). The results of the LC-QTOF/MS analysis were matched into a database of 740 potentially detected environmental organic chemicals. Detection frequencies of chemicals were calculated. Univariate and multivariate analyses were performed, adjusting for potential confounders. Association testing between chemical classes, chemicals and specific lupus phenotypes and disease activity was performed.

Results:
58 females with SLE and 78 healthy females were studied. The number of unique chemicals detected was 309, with an average of 60 chemical-hit matches per subject (range 32-150). SLE patients had a higher detection frequency of phthalates whereas healthy controls had a higher detection frequency of pesticides and phenols (table 1). A higher phthalate detection frequency was associated lupus nephritis, but did not correlate with disease activity (SLEDAI score), hypocomplementemia or anti ds-DNA status. In patients with SLE, a per count increase in detection frequency of a phthalate was associated with an OR of 1.4 for history of lupus nephritis, adjusting for age, disease duration, race, education and income (p=0.002, CI[1.1-1.7]). Chemicals detected at a higher frequency in SLE were enriched for specific phthalates such as metabolites of DHEP (table 2). Among SLE patients, 2 specific phthalates, mono2ethyl5oxohexylphthalate (p=0.00002) and mono2ethyl5oxohexylphthalate (p=0.00015) were associated with lupus nephritis.

Conclusion:
LC-QTOF/MS can identify a wider range of potential chemical exposures in SLE, and may aid in prioritizing chemicals for further research and intervention. We found that patients with SLE had significantly increased exposure to phthalates compared to healthy controls, with further enrichment among patients with lupus nephritis. Exposure to Mono-(2-carboxymethylhexyl) phthalate has been associated with dsDNA production and lupus nephritis in NZB/W F1 mice.
Disclosure: C. Lanata, None; T. Lin, None; M. Dall'Era, None; J. Yazdany, None; P. P. Katz, Bristol-Myers Squibb, 2; L. Trupin, None; C. G. Helmick, None; R. Gerona, None; L. A. Criswell, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/identifying-exposures-to-chemicals-in-patients-with-sle-a-non-targeted-exposome-approach-reveals-enrichment-for-phthalates

Abstract Number: 984

Identification of Key Screening Characteristics for Systemic Lupus Erythematosus Natural History

Kendra A. Young1, Melissa E. Munroe2, Joel M. Guthridge3, Diane L. Kamen4, Gary S. Gilkeson5, Michael Weisman6, David Karp7, John B. Harley8, Daniel J. Wallace6, Judith A. James9, and Jill M. Norris10, 1Epidemiology, University of Colorado Denver, Aurora, CO, 2Arthritis and Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, 3Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, OKC, OK, 4Medicine/Rheumatology & Immunology, Medical University of South Carolina, Charleston, SC, 5Department of Medicine, Medical University of South Carolina, Charleston, SC, 6Cedars-Sinai Medical Center Division of Rheumatology, Los Angeles, CA, 7Rheumatology, UT Southwestern Med Ctr, Dallas, TX, 8Center for Autoimmune Genomics and Etiology (CAGE), Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 9Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 10Department of Epidemiology, Colorado School of Public Health, Aurora, CO

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Epidemiology and Public Health Poster II: Rheumatic Diseases Other than Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: A prospective study of preclinical SLE disease evolution is needed to help elucidate critical aspects of disease etiology and early pathogenesis, and to identify early directed therapeutic targets. However, designing the most informative study of this complex heterogeneous disease is unclear without better definition of high-risk populations. Our objective was to determine screening characteristics to identify individuals for follow-up in a prospective study.

Methods: We sent letters to 3823 individuals who reported having a family member with SLE and who did not meet ≥ 4 ACR criteria for SLE at their baseline visit to enroll in a follow-up study to gather information regarding interim development of signs and symptoms consistent with SLE; 436 enrolled. Fifty-six individuals had transitioned to SLE (≥ 4 cumulative ACR criteria, verified by medical record review) by the time of follow-up. Generalized estimating equations, accounting for correlation within families, assessed associations between our dichotomous outcome of transitioning to SLE with baseline characteristics, including age, sex, race, ANA positivity (ANA+), Connective Tissue Disease Screening Questionnaire (CSQ) SLE score, and number of ACR criteria. Predictive accuracy of characteristics on transitioning were analyzed using positive predictive value (PPV), negative predictive value (NPV), sensitivity, and specificity. Characteristics

| Table 2. Environmental chemicals detected at higher frequency among patients with SLE |
|--------------------------------------|------------------|------------------|-------|
| Environmental Organic Chemical      | Class | SLE (%) | Healthy (%) | p value |
| 1-cyclohexylphthalate                | phthalate | 35 (25.3) | 2 (2.6) | 9.43E-15 |
| Saepphyphthalate                     | phthalate | 39 (67.2) | 6 (7.7) | 1.17E-13 |
| Mono-4-methyl-7-carboxylophthalate   | phthalate | 45 (77.6) | 13 (15.7) | 5.61E-13 |
| Mono-3-carboxylophthalate            | phthalate | 47 (31) | 23 (29.5) | 1.89E-09 |
| Monocrolophthalate                   | phthalate | 25 (42.1) | 5 (6.4) | 4.59E-07 |
| Mono-2-carboxymethylphthalate        | phthalate | 52 (87.5) | 40 (51.3) | 6.02E-06 |
| Butyloxylhydroxyacetic               | phthalate | 36 (62) | 22 (28) | 4.22E-03 |
| Methylbenzothiol                    | phthalate | 10 (17.2) | 0.002±00 | 0.0001 |

The table above lists the environmental chemicals detected at higher frequency among patients with SLE. The table provides the number of occurrences, frequency, and statistical significance for each chemical.
Results: Age (47.2 vs 47.2 years), sex (87.5% vs 83.2%), and race (76.8% vs 73.4% European American (EA)) were similar between those who transitioned and those who did not transition. Sisters of a SLE proband were just as likely to transition as other first-degree relatives (OR=1.5, 95% CI 0.8-2.8), as were those <30 years of versus those ≥ 30 years old (OR=1.3, 95% CI 0.5-3.2), and non-EAs versus EA (OR=1.3, 95% 0.5-3.5). ANA+, CSQ classification of possible or probable SLE (CSQ-SLE+), and greater number of ACR criteria were each associated with transitioning to SLE. Being ANA+ and having photosensitivity by confirmed ACR criteria had the highest PPV and specificity for transitioning to SLE (Table 1). CSQ-SLE+ had a better PPV, NPV, sensitivity and specificity than ANA+ alone. Combining ANA+ and CSQ-SLE+ increased the PPV and specificity of transitioning to SLE; additionally limiting to females did not increase the predictive accuracy.

Conclusion: Limiting follow-up to females or to a specific race/ethnic group does not appear to be needed. Confirmed ACR criteria provided the best predictive accuracy. Given limited resources, identifying subjects based on the SLE portion of the CSQ questionnaire could be most efficient for follow-up.

Table 1. Predictive Accuracy of Baseline Characteristics for Transitioning to SLE.
<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>N (%) with Characteristic(s)</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Using Questionnaire Data alone</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CSQ-SLE+*</td>
<td>183 (42.0%)</td>
<td>27.9%</td>
<td>98.0%</td>
<td>91.1%</td>
<td>65.3%</td>
</tr>
<tr>
<td>Female</td>
<td>365 (83.7%)</td>
<td>13.4%</td>
<td>90.1%</td>
<td>87.5%</td>
<td>16.8%</td>
</tr>
<tr>
<td>CSQ-SLE+* and Female</td>
<td>166 (38.1%)</td>
<td>27.7%</td>
<td>96.3%</td>
<td>82.1%</td>
<td>68.4%</td>
</tr>
<tr>
<td><strong>Using Questionnaire Data and Blood Draw for Measurement of ANA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANA+</td>
<td>226 (51.8%)</td>
<td>19.0%</td>
<td>93.8%</td>
<td>76.8%</td>
<td>51.8%</td>
</tr>
<tr>
<td>ANA+ and CSQ-SLE+*</td>
<td>122 (28.0%)</td>
<td>32.8%</td>
<td>94.9%</td>
<td>71.4%</td>
<td>78.4%</td>
</tr>
<tr>
<td>ANA+ and Female</td>
<td>200 (45.9%)</td>
<td>19.5%</td>
<td>92.8%</td>
<td>69.6%</td>
<td>57.6%</td>
</tr>
<tr>
<td>ANA+, CSQ-SLE+*, and Female</td>
<td>113 (25.9%)</td>
<td>32.7%</td>
<td>94.1%</td>
<td>66.1%</td>
<td>80.0%</td>
</tr>
<tr>
<td>ANA+ and Positive Photosensitivity from CSQ</td>
<td>80 (18.4%)</td>
<td>33.8%</td>
<td>91.9%</td>
<td>48.2%</td>
<td>86.1%</td>
</tr>
<tr>
<td>ANA+ and Positive Raynaud from CSQ</td>
<td>112 (25.7%)</td>
<td>28.6%</td>
<td>92.6%</td>
<td>57.1%</td>
<td>78.9%</td>
</tr>
<tr>
<td><strong>Using Blood Draw for Measurement of ANA and Medical Records to confirm ACR Criteria</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANA+ and Immunologic Disorder by Confirmed ACR Criteria</td>
<td>21 (4.8%)</td>
<td>52.4%</td>
<td>89.2%</td>
<td>19.6%</td>
<td>97.4%</td>
</tr>
<tr>
<td>ANA+ and Positive Photosensitivity by Confirmed ACR Criteria</td>
<td>24 (5.5%)</td>
<td>62.5%</td>
<td>90.0%</td>
<td>26.8%</td>
<td>97.6%</td>
</tr>
<tr>
<td>ANA+ and Positive Clinical† ACR Criteria</td>
<td>60 (13.8%)</td>
<td>58.3%</td>
<td>94.4%</td>
<td>62.5%</td>
<td>93.4%</td>
</tr>
</tbody>
</table>

Disclosure: K. A. Young, None; M. E. Munroe, None; J. M. Guthridge, None; D. L. Kamen, None; G. S. Gilkeson, None; M. Weisman, None; D. Karp, None; J. B. Harley, None; D. J. Wallace, None; J. A. James, None; J. M. Norris, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/identification-of-key-screening-characteristics-for-systemic-lupus-erythematosus-natural-history](http://acrabstracts.org/abstract/identification-of-key-screening-characteristics-for-systemic-lupus-erythematosus-natural-history)

Abstract Number: 985

Heart Failure Hospitalizations Among SLE and Diabetes Mellitus Patients Compared to the General U.S. Medicaid Population
Background/Purpose: Cardiovascular disease (CVD) risk is increased in SLE patients, compared to the general population and age- and sex-matched diabetes mellitus (DM) patients. Heart failure (HF) is the leading cause of hospitalizations in the U.S., and HF risk is elevated among DM patients compared to those without DM. Given the elevated CVD risk in SLE patients, we investigated rates and risks of HF hospitalization among SLE patients and age- and sex-matched DM and general Medicaid patients.

Methods: We used Medicaid Analytic eXtract (MAX) data, containing billing claims for Medicaid patients from the 29 most populated US states, 2007-2010. We identified both SLE and DM patients, ages 18-65, using >3 ICD-9 codes for SLE or DM, each separated by >30 days. Index date was the date of the 3rd diagnosis code. We matched each SLE patient at index date to 2 DM patients and 4 general Medicaid patients without SLE or DM, by age at index date and sex. (The general Medicaid cohort had non-SLE, non-DM ICD-9 codes on date of SLE index date.) We required a baseline period of 6 months of continuous Medicaid enrollment prior to the index date for all patients. Subjects were followed from index date until death, disenrollment or end of follow-up. We used ICD-9 codes to identify HF as primary or secondary hospital discharge diagnosis and calculated rates of first HF hospitalization event per 1,000 person-years for each cohort. We used Cox proportional hazard models to calculate hazard ratios (HR) for first HF hospitalization events. In a secondary analysis, we excluded those with baseline HF.

Results: 40,212 SLE patients were matched to 80,424 DM and 160,848 general patients. In all cohorts, 92% were female, and mean age was 40.3 (+12.1) years. Mean follow up was 1.8 (+1.1) years for SLE, 1.8 (+1.1) years for DM, and 1.6 (+1.2) years for general patients. Baseline CVD was prevalent in 18% of SLE, 13% of DM and 1% of non-SLE, non-DM cohorts, and baseline HF was prevalent in 6% of SLE, 5% of DM and <1% of non-SLE, non-DM patients. HF hospitalization rates per 1,000-person years were similar in SLE and DM, but lower in the general population (Table). Adjusted HRs for first HF hospitalizations were higher among DM (HR 4.0, 95% CI 3.6-4.3) and SLE (HR 2.4, 95% CI 2.2-2.7) patients compared to non-SLE, non-DM patients. When patients with baseline HF were excluded, the HR for first HF hospitalizations were similar between SLE (HR 2.5, 95% CI 2.3-2.8) and DM (HR 2.7, 95% CI 2.4-2.9).

Conclusion: SLE and age- and sex-matched DM patients had significantly higher rates of HF hospitalization than age- and sex-matched general (non-SLE, non-DM) Medicaid patients. The adjusted risk of first HF hospitalization was also over twice as high in both SLE and DM patients than in patients without either condition, which has important implications for improving clinical care for SLE patients.
Table. Rates and Multivariable Hazard Ratios for Hospitalizations for HF* among SLE Patients and Age- and Sex-Matched DM Patients, compared to the General (non-SLE, non-DM) Medicaid population, 2007-2010

<table>
<thead>
<tr>
<th>Cohort†</th>
<th>Events</th>
<th>Person-years</th>
<th>Rate‡ (95% CI)</th>
<th>HR§ (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>General Medicaid</td>
<td>620</td>
<td>250,281</td>
<td>2.5 (2.3-2.7)</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>SLE</td>
<td>837</td>
<td>73,299</td>
<td>11.4 (10.7-12.2)</td>
<td>2.4 (2.2-2.7)</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>1,675</td>
<td>145,692</td>
<td>11.5 (11.0-12.1)</td>
<td>4.0 (3.6-4.3)</td>
</tr>
</tbody>
</table>

*HF: Heart failure events by hospitalization ICD-9 diagnosis codes 402.01, 402.11, 402.91, 404.01, 404.11, 404.91, 404.03, 404.13, 404.93, and 428.xx, but excluding 398.91 rheumatic heart disease (Chen J, Circulation, 2013).
†Cohort: SLE cohort defined as >3 SLE ICD-9 codes (710.0), each separated by >30 days; DM cohort defined as >3 ICD-9 codes (249.XX, 250.XX, 357.2, 362.01-362.06, 366.41), 1:2 matched by age, sex to SLE cohort; General Medicaid cohort defined as any non-SLE, non-DM ICD-9 code on same date as SLE index date, 1:4 matched by age, and sex to SLE cohort
‡Rate: Rate of first HF hospitalization events per 1000 person-years of follow up
§HR: Hazard ratio for first HF hospitalization event adjusted for age, sex, race/ethnicity, US region of residence, zip-code level socioeconomic status, Charlson comorbidity index; Two separate Cox proportional hazard models: 1) including all patients, 2) excluding patients who had baseline HF diagnosis

Disclosure: S. Chen, None; M. Barbhaiya, None; M. A. Fischer, None; H. Guan, None; C. H. Feldman, None; B. M. Everett, None; K. H. Costenbader, None.


Abstract Number: 986

**Do Death Certificates Underestimate the Burden of Rare Diseases: The Example of Systemic Lupus Erythematosus Mortality in Sweden**

Titilola Falasinnu¹, Marios Rossides², Yashaar Chaichian³ and Julia F Simard⁴, ¹Health Research and Policy, Stanford University, Stanford, CA, ²Medicine Solna, Clinical Epidemiology Unit, Karolinska Institutet, Stockholm, Sweden, ³Medicine, Immunology & Rheumatology Division, Stanford School of Medicine, Stanford, CA, ⁴Division of Epidemiology, Health Research and Policy Department, Stanford School of Medicine, Stanford, CA

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017

Session Title: Epidemiology and Public Health Poster II: Rheumatic Diseases Other than Rheumatoid Arthritis

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM

Background/Purpose: Routine data sources such as death certificates are used to estimate the burden or cost of disease in a population. However, mortality due to rare diseases, e.g., systemic lupus erythematosus (SLE), that are significant sources of
Death Certificates Do Not Accurately Identify SLE Patients

Kelly Kaysen, Cristina Drenkard, Gaobin Bao and S. Sam Lim, Division of Rheumatology, Emory University School of Medicine, Atlanta, GA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Epidemiology and Public Health Poster II: Rheumatic Diseases Other than Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Mortality rates are higher in SLE patients compared to the general population, and research on SLE mortality is ongoing. The majority of mortality studies have relied on death certificates to identify SLE patients. However, this approach may misclassify cases and include both false positives and negatives. The rate of misclassification on death certificates is unclear. Using a large population-based registry of validated SLE patients, we sought to ascertain the accuracy of death certificates in identifying SLE patients.

Methods: The Georgia Lupus Registry (GLR) is a population-based registry of validated SLE patients living in Atlanta, GA from 2002-04. The state HIPAA exemption for surveillance allowed health care providers and facilities to provide access to protected health information without written patient consent. Patients were validated by meeting ≥4 ACR criteria or 3 ACR criteria with a final diagnosis of SLE by a board-certified rheumatologist. These patients were matched to the Georgia Office of Vital Records death certificates through 2013. The primary, secondary, tertiary, and contributing causes of death were identified on the death certificates using ICD-10 codes.
**Results:** State death certificates matched with 321 SLE patients from the GLR through 2013. Only 24.6% (79/321) of patients had SLE listed on the death certificate. Characteristics of the deceased SLE patients are listed in the below table. While there were no significant differences with race and sex, SLE patients captured in death certificates were much younger at SLE diagnosis and died at a younger age.

**Conclusion:** In a population-based registry with many high-risk black SLE patients, SLE was recorded on the death certificates of only 24.6% of deaths. SLE was listed more often on the death certificates of those who were younger at SLE diagnosis and death, perhaps indicating more severe disease or increased awareness by the caring providers. Death certificates do not accurately capture the full spectrum of SLE patients. Reliance on death certificates to obtain SLE mortality data will underestimate the burden of the disease.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Category</th>
<th>Overall (n=321)</th>
<th>SLE captured in death certificate</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, n (%)</td>
<td>Male</td>
<td>44 (13.7)</td>
<td>37 (84.1)</td>
<td>0.15</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>277 (86.3)</td>
<td>205 (74.0)</td>
<td></td>
</tr>
<tr>
<td>Race, n (%)</td>
<td>White</td>
<td>58 (18.1)</td>
<td>47 (81.0)</td>
<td>0.27</td>
</tr>
<tr>
<td></td>
<td>Black</td>
<td>263 (81.9)</td>
<td>195 (74.1)</td>
<td></td>
</tr>
<tr>
<td>Age at diagnosis (years)</td>
<td>Mean ± SD</td>
<td>39.1 ± 17.6</td>
<td>41.0 ± 17.5</td>
<td>33.4 ± 16.6</td>
</tr>
<tr>
<td>Age at death (years)</td>
<td>Mean ± SD</td>
<td>52.7 ± 17.3</td>
<td>55.5 ± 16.4</td>
<td>44.4 ± 17.6</td>
</tr>
</tbody>
</table>

**Disclosure:** K. Kaysen, None; C. Drenkard, None; G. Bao, None; S. S. Lim, None.

**View Abstract and Citation Information Online** - [http://acrabstracts.org/abstract/death-certificates-do-not-accurately-identify-sle-patients](http://acrabstracts.org/abstract/death-certificates-do-not-accurately-identify-sle-patients)

Abstract Number: 988

**Association of Ultraviolet-B Radiation and Risk of SLE Among Women in the Nurses’ Health Studies**

Medha Barbhaiya¹, Jaime Hart²,³, Susan Malspeis⁴, Sara K. Tedeschi⁵, David J. Kreps⁵, Trang VoPham⁶, Jeffrey A. Sparks⁷, Elizabeth Karlson⁵, Francine Laden²,³,⁸ and Karen H. Costenbader⁵, ¹Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ²Department of Environmental Health, Harvard T.H. Chan School of Public Health, Boston, MA, ³Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ⁴Division of Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ⁵Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ⁶Department of Epidemiology, Harvard T. H. Chan School of Public Health, Boston, MA, ⁷Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ⁸Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Epidemiology and Public Health Poster II: Rheumatic Diseases Other than Rheumatoid Arthritis
Background/Purpose: Ultraviolet-B radiation (UV-B) exposure may lead to worsened photosensitivity, rashes, and systemic flares among SLE patients. Although UV-B radiation damages keratinocytes and may result in production of novel forms of autoantigens, it remains unknown whether UV-B exposure increases the risk of developing SLE. We aimed to examine the association of UV-B exposure with risk of incident SLE in a large prospective cohort of women, examining SLE risk overall and by subtypes defined by presence of anti-Ro/La antibodies (+anti-Ro/La) and/or cutaneous manifestations most associated with UV exposure in SLE patients.

Methods: The Nurses’ Health Study (NHS) enrolled 121,701 U.S. female nurses in 1976; NHSII enrolled 116,430 in 1989. Biennial questionnaires collected lifestyle, environmental, and medical data. Residential addresses were geocoded. Incident SLE was confirmed by medical record review. National Aeronautics and Space Administration Total Ozone Mapping Spectrometer and Ozone Monitoring Instrument gridded remote sensing images scaled to a 1 km spatial resolution predicted average July noon-time erythemal UV-B (mW/m²) annually starting in 1980. Participants without UV-B data at baseline were excluded. Hazard ratios (HR) and 95% confidence intervals (CI) were estimated using Cox regression models across tertiles of cohort-specific, time-varying cumulative average UV-B through one cycle prior to SLE onset. We examined SLE risk overall and stratified by presence of anti-Ro/La or cutaneous manifestations (malar rash and/or photosensitivity) at diagnosis through 2014 (NHS) or 2013 (NHSII), controlling for potential confounders. We also conducted a ‘lagged’ analysis by ending the exposure window two cycles prior to SLE diagnosis, as SLE symptoms may develop insidiously pre-diagnosis.

Results: Mean age at SLE diagnosis was 49.3 (10.4) years among 286 SLE cases in NHS/NHSII. At SLE diagnosis, 13% of women had +anti-Ro/La whereas 80% had either +anti-Ro/La or at least one cutaneous manifestation. Compared to the lowest tertile of UV-B exposure, risk of overall SLE, SLE with +anti-Ro/La, or SLE with photosensitivity in the highest UV-B tertile were increased, but not statistically significant in the main analysis (Table) or in lagged analyses. However, women in the highest UV-B tertile had statistically significantly increased risks of SLE with malar rash (HR 1.68 [95% CI 1.08-2.62]) (Table), but this was no longer significant in the lagged analysis (HR 1.41 [95% CI 0.88-2.25]).

Conclusion: Increasing cumulative UV-B exposure was not associated with risk of developing overall SLE. However, among women at risk for SLE, living in areas with higher UV-B exposure was associated with increased risk of developing SLE presenting with malar rash. Further studies are warranted to determine whether high UV-B exposure may play a role in triggering SLE onset with malar rash.
Disclosure: M. Barbhaiya, None; J. Hart, None; S. Malspeis, None; S. K. Tedeschi, None; D. J. Kreps, None; T. VoPham, None; J. A. Sparks, None; E. Karlson, None; F. Laden, None; K. H. Costenbader, None.


Abstract Number: 989

**Impact of DMARD Treatment on Risk of Repeat Cardiovascular Events Among Patients with Rheumatoid Arthritis, Psoriatic Arthritis, or Psoriasis**

Jeffrey A. Sparks¹, Tamara Lesperance², Neil A. Accortt³ and Daniel H. Solomon⁴, ¹Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ²DOCS Global, Inc., North Wales, PA, ³Center for Observational Research, Amgen, Inc., Thousand Oaks, CA, ⁴Brigham and Women's Hospital and Harvard Medical School, Boston, MA

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017

Session Title: Epidemiology and Public Health Poster II: Rheumatic Diseases Other than Rheumatoid Arthritis

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM

Background/Purpose: Chronic inflammatory diseases such as rheumatoid arthritis (RA), psoriatic arthritis (PsA), and psoriasis (PsO) increase the risk of cardiovascular (CV) disease. However, it is unclear what factors, including DMARD treatment, after a first CV event may affect risk of subsequent CV events. We estimated and compared the incidence of subsequent CV events among patients with RA, PsA, or PsO who were being treated with DMARDs prior to the initial CV event.

Methods: Patients with RA, PsA, or PsO, who experienced a major non-fatal CV event (acute myocardial infarction, stroke, or cardiac revascularization) between 1/1/2006 and 6/30/2015 were identified in an administrative claims database. Index date was defined as the hospital discharge date for the first non-fatal CV event during the study period. Eligible patients were: continuously enrolled for 12 months prior to index date; had ≥1 DMARD claim (categorized as TNF inhibitor (TNFi), conventional synthetic [csDMARD], or a non-TNFi biologic DMARD including tofacitinib) within 12 months prior to the index date; and had ≥30 days of follow-up after index date. The primary outcome was the occurrence of any CV event.
during the follow-up period. Incidence rates (IR) per 1,000 person-years with 95% confidence intervals (CI) were calculated and age and sex standardized to the general population. The hazard ratio (HR) and 95% CI for a subsequent CV event was estimated using Cox proportional hazard models. Patients who were not treated with any DMARD after initial CV event were not included in the analyses.

**Results:** We identified 8,610 patients with RA, PsA, or PsO eligible for study. After the index date, 2,924 (34.0%) patients used a TNFi, 4,813 (55.9%) used a csDMARD as monotherapy or combination, and 873 (10.1%) used a non-TNFi biologic DMARD. Median follow-up time after initial CV event was 1.6 years. Patients using non-TNFi biologic DMARDs had higher crude incidence rates of repeat CV events than those who used TNFi or csDMARDs (Table 1). The multivariate adjusted hazard ratios for subsequent CV events were 0.98 (95% CI, 0.82-1.17) for csDMARDs, and 1.16 (0.86-1.57) for other biologic DMARDs compared to TNFi (Table 2). RA diagnosis (as compared to PsO diagnosis) and heart failure diagnosis in baseline were risk factors independently associated with increased risk of subsequent CV event.

**Conclusion:** In this large nationwide database reflecting typical clinical care, we found that type of DMARD use after initial non-fatal CV event was not associated with risk for subsequent CV event among RA, PsA, and PsO patients. Predictors of subsequent CV event included having RA and heart failure prior to initial CV event.

<p>| Table 1. Incidence of Subsequent CV Events among RA, PsA, PsO Patients (n=9,529) |
|-----------------------------------------------|-----------------|-----------------|-----------------|
| Subsequent CV events (stroke, AMI, revascularization), n | 230 (TNF Inhibitors n=2,924) | 288 (csDMARDs n=4,813) | 53 (Other (non-TNFi) Biologics n=873) |
| Follow-up, person-years | 2744.4 (1,800.8-3,587.6) | 2984.7 (1,614.5-3,355.0) | 482.0 (1,381.4-2,292.2) |
| Median follow-up per patient, years (IQR) | 1.8 (1.0-3.5) | 1.6 (1.0-3.1) | 1.4 (1.0-2.6) |
| Age- and sex-standardized Incidence Rate (95% CI) per 1,000 person-years | 75.2 (54.4-96.0) | 83.6 (53.3-113.9) | 122.4 (60.6-184.3) |</p>
<table>
<thead>
<tr>
<th>Covariate</th>
<th>Adjusted HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1a</td>
<td></td>
</tr>
<tr>
<td>csDMARD vs. TNFi</td>
<td>1.03 (0.86-1.23)</td>
</tr>
<tr>
<td>Non-TNFi biologics vs. TNFi</td>
<td>1.23 (0.91-1.66)</td>
</tr>
<tr>
<td>Model 2b</td>
<td></td>
</tr>
<tr>
<td>csDMARD vs. TNFi</td>
<td>0.97 (0.80-1.18)</td>
</tr>
<tr>
<td>Non-TNFi biologics vs. TNFi</td>
<td>1.17 (0.86-1.58)</td>
</tr>
<tr>
<td>Model 3c</td>
<td></td>
</tr>
<tr>
<td>csDMARD vs. TNFi</td>
<td>0.98 (0.82-1.17)</td>
</tr>
<tr>
<td>Non-TNFi biologics vs. TNFi</td>
<td>1.16 (0.86-1.57)</td>
</tr>
<tr>
<td>Age, per 10 years</td>
<td>1.02 (0.94-1.10)</td>
</tr>
<tr>
<td>Male sex</td>
<td>1.13 (0.96-1.34)</td>
</tr>
<tr>
<td>RA vs. PsO</td>
<td>1.55 (1.00-2.39)</td>
</tr>
<tr>
<td>PsA vs. PsO</td>
<td>1.43 (0.85-2.40)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>1.39 (1.13-1.72)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.16 (0.97-1.39)</td>
</tr>
<tr>
<td>Renal disease</td>
<td>1.27 (0.96-1.67)</td>
</tr>
<tr>
<td>Pre-index oral glucocorticoid use‡</td>
<td>1.14 (0.96-1.35)</td>
</tr>
</tbody>
</table>

*Model 1 was adjusted for age and sex.

*Model 2 was adjusted as model 1 plus disease indication, index CV event, pre-index comorbidities (heart failure, chronic pulmonary disease, diabetes mellitus, hyperlipidemia, hypertension, obesity, unstable angina, renal disease), number of pre-index unique DMARDs used, and baseline medication exposures (statins, oral glucocorticoids, ACE inhibitors, beta blockers).

*Model 3 adjusted model 2 via backwards elimination and the following covariates were retained: age, sex, disease indication, pre-index comorbidities (heart failure, diabetes mellitus, renal disease), and pre-index oral glucocorticoid use.

‡Defined as use in the 12 months prior to index CV event.

Disclosure: J. A. Sparks, Amgen, 2; T. Lesperance, Amgen, 5; N. A. Accortt, Amgen, 3, Amgen, 1; D. H. Solomon, Amgen, 2.


Abstract Number: 990

Higher Omega-6 to Omega-3 Fatty Acid Ratio Is Associated with Increased Odds of Inflammatory Arthritis in a Health Fair Population Positive for Anti-Citrullinated Protein Antibodies (ACPA)
Kristen J. Polinski¹, Ryan W. Gan², Elizabeth A. Bemis¹, M. Kristen Demoruelle³, Michael J. Clare-Salzler⁴, V. Michael Holers⁵, Kevin D. Deane⁶ and Jill M. Norris⁷, ¹Epidemiology, Colorado School of Public Health, Aurora, CO, ²Colorado School of Public Health, University of Colorado Denver, Aurora, CO, ³1775 Aurora Ct, 1775 Aurora Ct, Aurora, CO, ⁴Experimental Pathology, University of Florida, College of Medicine, Gainesville, FL, ⁵Rheumatology Division, University of Colorado School of Medicine, Aurora, CO, ⁶Division of Rheumatology, University of Colorado School of Medicine, Aurora, CO, ⁷Department of Epidemiology, Colorado School of Public Health, Aurora, CO

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Epidemiology and Public Health Poster II: Rheumatic Diseases Other than Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: We previously found that lower levels of omega-3 fatty acids (n-3 FA) were associated with the presence of inflammatory arthritis (IA) as well as risk of developing incident IA in ACPA+ individuals without IA at baseline. Omega-6 fatty acids (n-6 FA) compete with n-3 FA for elongation and desaturation enzymes in the body that help determine the pro- and anti-inflammatory potential of these FA and their derivatives. Western diets tend to have a high n-6 to n-3 ratio that may promote the pathogenesis of inflammatory and autoimmune diseases. We examined the association between n-6 FA levels and the presence of IA/rheumatoid arthritis (RA) in ACPA+ individuals.

Methods: At Colorado-based health fairs from 2008-2014, 47 subjects without a previous diagnosis of RA tested positive for the ACPA, anti-cyclic citrullinated peptide (CCP3, Inova), and were recruited into a follow-up research study. At their immediate post-health fair research visit (baseline), 10 of these ACPA+ subjects were identified as having disease-modifying anti-rheumatic drug (DMARD)-naive IA. Of the 10 ACPA+ subjects with prevalent IA at baseline, 8 were classified as RA by 2010 ACR/EULAR Criteria. Findings in those subjects with IA were compared to those without IA. Specifically, n-3 and n-6 as percent of total lipids in red blood cell membranes (RBC) were measured. Logistic regression assessed the associations between baseline IA and RBC n-6 FA%, as well as the n-6 to n-3 ratio.

Results: Subjects with IA at baseline were more likely to be ever smokers and test positive for rheumatoid factor and C-reactive protein than those without IA (Table 1). In addition, we found that subjects with higher n-6 FA and linoleic acid levels had higher odds of IA (Table 2). Furthermore, analysis of the n-6 to n-3 ratio demonstrated that higher total n-6 FA % relative to total n-3 FA % in RBCs significantly increased the odds of IA by almost 3-fold (Table 2).

Conclusion: We found that a higher n-6 to n-3 ratio was associated with prevalent IA in this ACPA+ population. Building off our previous work, this suggests a potential beneficial role of n-3 FAs in decreasing the risk of transitioning from ACPA positivity to IA. Specifically, our findings herein suggest that decreasing the n-6 to n-3 FA ratio in the body, perhaps either via n-3 FA supplementation or diet may play a role in decreasing the transition from an ACPA+ state to IA, findings that warrant further investigation.
Table 1: Descriptive Characteristics by IA status at Baseline, Colorado Health Fair Population, 2008-2014

<table>
<thead>
<tr>
<th>Variable</th>
<th>Prevalent IA at Baseline (n=10)</th>
<th>No IA at Baseline (n=37)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs (mean ± SD)</td>
<td>55.9 (10.3)</td>
<td>55.9 (10.4)</td>
<td>0.996</td>
</tr>
<tr>
<td>Age ≥ 50 yrs</td>
<td>8 (80.0)</td>
<td>26 (70.3)</td>
<td>0.703</td>
</tr>
<tr>
<td>Sex: Female</td>
<td>8 (80.0)</td>
<td>21 (56.8)</td>
<td>0.277</td>
</tr>
<tr>
<td>Race/Ethnicity: non-Hispanic White</td>
<td>7 (70.0)</td>
<td>29 (78.4)</td>
<td>0.679</td>
</tr>
<tr>
<td>Education: &gt; High school</td>
<td>8 (80.0)</td>
<td>32 (86.5)</td>
<td>0.630</td>
</tr>
<tr>
<td>Income: &gt; $40,000</td>
<td>7 (77.8)</td>
<td>25 (71.4)</td>
<td>1</td>
</tr>
<tr>
<td>Smoking: Ever</td>
<td>9 (90.0)</td>
<td>16 (43.2)</td>
<td>0.012</td>
</tr>
<tr>
<td>Shared Epitope (SE)+</td>
<td>7 (70.0)</td>
<td>16 (43.2)</td>
<td>0.168</td>
</tr>
<tr>
<td>Omega 3 supplement use</td>
<td>8 (80.0)</td>
<td>19 (51.3)</td>
<td>0.154</td>
</tr>
<tr>
<td>Rheumatoid Factor (RF)+</td>
<td>6 (60.0)</td>
<td>5 (13.5)</td>
<td>0.006</td>
</tr>
<tr>
<td>C-Reactive Protein (CRP)+</td>
<td>6 (60.0)</td>
<td>7 (18.9)</td>
<td>0.017</td>
</tr>
<tr>
<td>n-6 : n-3 ratio (mean ± SD)</td>
<td>4.00 (1.41)</td>
<td>3.14 (0.81)</td>
<td>0.093</td>
</tr>
</tbody>
</table>

All values reported as n(%) unless otherwise stated. Fisher Exact p-values presented for categorical variables. Satterthwaite p-values reported for continuous variables.

Table 2: Adjusted analyses evaluating the relationship between omega-6 fatty acid % and IA at Baseline (N=47)

<table>
<thead>
<tr>
<th>FA% in RBC</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n-6 : n-3 FA ratio</td>
<td>2.99 (1.11, 8.05)</td>
<td>0.030</td>
</tr>
<tr>
<td>Total n-6 FA</td>
<td>2.96 (1.12, 7.79)</td>
<td>0.028</td>
</tr>
<tr>
<td>Linoleic acid</td>
<td>2.63 (1.10, 6.29)</td>
<td>0.030</td>
</tr>
<tr>
<td>Gamma linolenic acid</td>
<td>4.91 (0.85, 28.35)</td>
<td>0.075</td>
</tr>
<tr>
<td>Arachidonic acid</td>
<td>0.81 (0.21, 3.22)</td>
<td>0.768</td>
</tr>
</tbody>
</table>

The n-6:n-3 FA ratio model adjusted for ever smoking status, SE, RF+, and CRP+; and the OR represents the odds of IA for each unit difference in the n-6:n-3 ratio. The n-6 models adjusted for ever smoking status, n-3 FA supplement use, SE+, RF+, and CRP+; and the ORs represent the odds of IA for a one standard deviation (SD) difference in the n-6 FA% in RBC. The SD for these variables are as follows: Linoleic acid: 1.72, Gamma linolenic acid: 0.06, Arachidonic acid: 1.37, Total n-6: 1.97.

Disclosure: K. J. Polinski, None; R. W. Gan, None; E. A. Bemis, None; M. K. Demoruelle, None; M. J. Clare-Salzler, None; V. M. Holers, None; K. D. Deane, Inova Diagnostics, Inc., 5; J. M. Norris, None.


Abstract Number: 991

Publication Timeliness of the Randomized Controlled Trials of Drug Therapy for Inflammatory Arthritis

Vyjayanthi Ganga¹, Mohan Edupuganti² and Nasim A. Khan³, ¹St. Vincent Healthcare System, Little Rock, AR, ²Internal Medicine, University of Arkansas for Medical Sciences, Little Rock, AR, ³Rheumatology, University of Arkansas for Medical Sciences and Central Arkansas Veterans Healthcare System, Little Rock, AR

First publication: September 18, 2017
Background/Purpose: Timely publication of randomized controlled trials (RCTs) is crucial for their potential impact on patient care. We assessed the publication timeliness of drug therapy RCTs of inflammatory arthritis.

Methods: The print issues (or online issues for online-only journal) of the 10 highest impact factor (IF) rheumatology journals publishing original research and 5 highest IF internal medicine journals for the years 2013-2014 were searched using Medline. Original parallel-design, non-phase-1 RCTs reports of drug therapy for inflammatory arthritis with clinical primary outcome(s) were eligible. RCT completion dates were retrieved either from the manuscript or the respective trial registry information in the manuscript. The dates of manuscript submission, acceptance, first online publication, and publication in a print issue were used to calculate the intervals in the publication process of study RCTs. RCT characteristics associated of with the time from trial completion to first (online or print) and final (typically print) available version were assessed.

Results: Eligibility criteria were met by 67 RCTs. The study conditions were rheumatoid arthritis (68.7%), spondyloarthropathy (20.9%), gout (6%) and others (4.5%). Experimental drug manufacturer fully or partially funded 56 (83.6%) RCTs. All RCTs had trial registry information (ClinicalTrials.gov for (58[86.6%]) RCTs). The experimental interventions included biologics (73.1%), small molecule (14.9%), traditional disease modifying agent [(10.4%), and other (1.5%). Most trials were multicenter (92.5%) and multinational (56.7%). RCT completion date was obtained from the manuscript for 16 (23.8%) and trial registry record for 49 (73.1%) RCTs. Some dates such as manuscript submission and acceptance were unreported for nearly 45% RCTs. Table shows the different time intervals in the publication process. The first available version was published within a year of completion for 8 (12%) and within 2 years for 39 (58%) RCTs. Final available version of RCTs with positive results (statistically significant result favoring the experimental intervention) was available earlier [median (IQR): 25.5 (21.7-35) months for positive vs 32.5 (26.6-44.5) months, p = 0.04]. No significant differences were noted in the time from RCT completion to first or final publication according to study condition, funding source, experimental intervention type, and whether the RCT was multicenter or multinational.

Conclusion: There is a considerable time lag between the completion and publication of RCTs. Several crucial dates needed to assess the publication timeliness were unavailable in the manuscripts. Clinical trial registries enabled publication timeliness assessment. Advance online publication helps in early availability of trial results.

<table>
<thead>
<tr>
<th>Time interval</th>
<th>N*</th>
<th>Median (IQR)**</th>
<th>Range**</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCT completion to manuscript submission</td>
<td>35</td>
<td>20 (13-30)</td>
<td>14-100</td>
</tr>
<tr>
<td>Manuscript submission to acceptance</td>
<td>36</td>
<td>4 (3.5-6)</td>
<td>1.5-12</td>
</tr>
<tr>
<td>Manuscript acceptance to first published version</td>
<td>56</td>
<td>1 (0.7-1.4)</td>
<td>0-3.5</td>
</tr>
<tr>
<td>First version to final published version</td>
<td>67</td>
<td>4.6 (1.5-9)</td>
<td>0-15</td>
</tr>
<tr>
<td>RCT completion to first version</td>
<td>65</td>
<td>21.7 (18-32.9)</td>
<td>4.6-98.5</td>
</tr>
<tr>
<td>RCT completion to final version</td>
<td>65</td>
<td>27.5 (22.5-39.6)</td>
<td>13.8-99.5</td>
</tr>
</tbody>
</table>

*RCTs with available data, **months

Disclosure: V. Ganga, None; M. Edupuganti, None; N. A. Khan, None.
The Effect of Anti-TNF Therapy on Work Productivity and Activity Impairment in Patients with Rheumatoid Arthritis, Ankylosing Spondylitis and Psoriatic Arthritis over One Year – Real Life Data from the Czech Biologics Registry Attra

Jakub Zavada¹, Lenka Szczukova², Karel Pavelka³ and Jiri Vencovsky³, ¹Institute of Rheumatology, Prague, Czech Republic, ²Institute of Biostatistics and Analyses. Faculty of Medicine, Masaryk University, Brno, Czech Republic, ³Institute of Rheumatology and Department of Rheumatology, First Faculty of Medicine, Charles University, Prague, Czech Republic

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Epidemiology and Public Health Poster II: Rheumatic Diseases Other than Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The ATTRA registry captures more than 95% of patients with RA, PSA or AS treated with biologics in the Czech Republic (CZ). In CZ, anti-TNF-therapy is reimbursed for RA if DAS28>5.1 despite therapy with csDMARDs, for PSA if disease is not Òadequately controlledÓ with csDMARDs and for AS if BASDAI>4 and CRP/ESR elevated above normal. To assess the effect of anti-TNF therapy on work productivity using the Work Productivity and Activity Impairment-Specific Health Problem (WPAI-SHP) questionnaire in patients with RA, PSA and AS in the real life setting using the data from ATTRA.

Methods: WPAI-SHP scores were collected for all patients enrolled in ATTRA since 2012 at baseline and after 12 months of anti-TNF exposure. BionŠive patients with RA (n=352), AS (n=442) and PSA (n=133) starting anti-TNF therapy with available baseline data on demography, disease duration and physical function, and WPAI-SHP at baseline and at 12 months were included in this analysis. Patients older than 60 years, on maternity leave or students were excluded. Only patients working for pay at baseline were assessed for WPAI-SHP summary scores: absenteeism (mean % work time missed), presenteeism (mean % productivity loss at work), overall work impairment (mean % overall work productivity loss), and activity impairment (mean % productivity loss in regular activities). Regression analyses were performed to analyse the predictors of improvement in WD overall work impairment one year.

Results: Baseline characteristics were significantly different between diagnoses (Table 1). Working status changed significantly only in patients with RA (employed 69→64%, p=0.013), but not in AS (77→78%) or PSA (77→73%). In patients employed for pay at baseline and assessed for WPAI-SHP summary scores: absenteeism (mean % work time missed), presenteeism (mean % productivity loss at work), overall work impairment (mean % overall work productivity loss), and activity impairment (mean % productivity loss in regular activities). Regression analyses were performed to analyse the predictors of improvement in WD overall work impairment one year.

Conclusion: In the real life setting of the CZ, anti-TNF therapy effectively reduced absenteeism, presenteeism, activity impairment and work impairment over one year in employed patients with RA, AS and PSA.

Acknowledgements: Supported by project 00023728 of Ministry of Health, CZ.
Table 1. Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>RA (n = 352)</th>
<th>AS (n = 442)</th>
<th>PSA (n = 133)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>257 (73.0%)</td>
<td>104 (23.5%)</td>
<td>58 (43.6%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Disease duration</td>
<td>7.1 ± 5.7</td>
<td>7.0 ± 6.7</td>
<td>7.5 ± 7.2</td>
<td>0.245</td>
</tr>
<tr>
<td>Age at start of anti-TNF therapy</td>
<td>47.2 ± 8.9</td>
<td>39.5 ± 8.6</td>
<td>44.4 ± 9.1</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>HAQ</td>
<td>1.5 ± 0.5</td>
<td>1.2 ± 0.5</td>
<td>1.2 ± 0.6</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Post-hoc analysis (with Bonferroni correction): statistically significant difference btw groups A) RA vs. AS, B) RA vs. PSA, C) AS vs. PSA. Values or N (%) or mean (SD).

Table 2. The effect of one year of anti-TNF therapy on WPAI-SHP components across diagnoses.

<table>
<thead>
<tr>
<th>Dg.</th>
<th>WPAI –SHP component</th>
<th>Baseline</th>
<th>12 months</th>
<th>Mean change after 12 months</th>
<th>Number of assessed patients</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA</td>
<td>Absenteeism</td>
<td>12.8 (27.9)</td>
<td>5.1 (18.5)</td>
<td>7.7 (30.3)</td>
<td>203</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Presenteeism</td>
<td>52.1 (21.9)</td>
<td>27.6 (20.9)</td>
<td>24.5 (26.3)</td>
<td>183</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Overall work impairment</td>
<td>53.9 (22.8)</td>
<td>28.7 (22.0)</td>
<td>25.2 (26.9)</td>
<td>183</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Activity impairment</td>
<td>62.4 (21.4)</td>
<td>36.0 (23.0)</td>
<td>26.4 (27.7)</td>
<td>352</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>AS</td>
<td>Absenteeism</td>
<td>10.6 (25.6)</td>
<td>3.5 (15.8)</td>
<td>7.1 (28.0)</td>
<td>307</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Presenteeism</td>
<td>53.1 (22.2)</td>
<td>21.1 (18.0)</td>
<td>32.0 (24.9)</td>
<td>282</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Overall work impairment</td>
<td>54.8 (22.6)</td>
<td>21.8 (18.8)</td>
<td>33.0 (25.5)</td>
<td>281</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Activity impairment</td>
<td>60.7 (22.1)</td>
<td>27.3 (21.4)</td>
<td>33.5 (26.4)</td>
<td>442</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>PSA</td>
<td>Absenteeism</td>
<td>5.7 (17.3)</td>
<td>4.2 (18.4)</td>
<td>1.5 (24.6)</td>
<td>90</td>
<td>0.135</td>
</tr>
<tr>
<td></td>
<td>Presenteeism</td>
<td>43.9 (24.0)</td>
<td>15.3 (16.2)</td>
<td>28.6 (24.5)</td>
<td>84</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Overall work impairment</td>
<td>45.2 (25.0)</td>
<td>15.9 (16.8)</td>
<td>29.3 (25.1)</td>
<td>84</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Activity impairment</td>
<td>57.4 (24.6)</td>
<td>26.2 (21.3)</td>
<td>31.2 (26.5)</td>
<td>133</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Values are mean %(SD). * Wilcoxon paired test for difference between baseline and 12 months within each WPAI score.
Table 3 Prediction of improvement in overall work impairment

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td></td>
<td>β (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>Diagnosis: RA reference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis: AS</td>
<td>7.83 (3.01; 12.65)</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>6.67 (1.12; 12.23)</td>
<td>0.019</td>
</tr>
<tr>
<td>Diagnosis: PSA</td>
<td>4.128 (-2.555; 10.812)</td>
<td>0.226</td>
</tr>
<tr>
<td></td>
<td>5.85 (-0.79; 12.50)</td>
<td>0.084</td>
</tr>
<tr>
<td>Gender (male) reference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender (female)</td>
<td>-5.10 (-9.52; -0.67)</td>
<td>0.024</td>
</tr>
<tr>
<td></td>
<td>-2.87 (-7.65; 1.90)</td>
<td>0.238</td>
</tr>
<tr>
<td>Age at start of anti-TNF</td>
<td>-0.41 (-0.65; -0.17)</td>
<td>0.001</td>
</tr>
<tr>
<td>therapy</td>
<td>-0.35 (-0.61; -0.10)</td>
<td>0.006</td>
</tr>
<tr>
<td>Disease duration</td>
<td>-0.25 (-0.59; 0.09)</td>
<td>0.151</td>
</tr>
<tr>
<td>Ln (CRP)</td>
<td>3.64 (1.62; 5.67)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>1.90 (-0.10; 3.90)</td>
<td>0.062</td>
</tr>
<tr>
<td>HAQ</td>
<td>11.49 (7.33; 15.64)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>14.21 (9.99; 18.43)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Disclosure: J. Zavada, None; L. Szczukova, None; K. Pavelka, None; J. Vencovsky, Samsung Bioepis Co., Ltd., Biogen, 5.


Abstract Number: 993

Increase in Prevalence of Psoriasis Arthritis over Time: Analysis of Claims Data from 65 Million People in Germany from 2009 to 2012

Philipp Sewerin1, Matthias Schneider2, Benedikt Ostendorf1 and Ralph Brinks3, 1Department and Hiller-Research-Unit for Rheumatology, Heinrich-Heine University, Düsseldorf, Germany, 2Policlinic for Rheumatology & Hiller Research Centre for Rheumatology, Heinrich-Heine-University Duesseldorf, Duesseldorf, Germany, 3Department and Hiller-Research-Unit for Rheumatology, Heinrich-Heine University, Duesseldorf, Germany

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017

Session Title: Epidemiology and Public Health Poster II: Rheumatic Diseases Other than Rheumatoid Arthritis

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM

Background/Purpose: Epidemiological studies are important contributors for our understanding of psoriatic arthritis (PsA). Currently, there are no data about temporal trends of prevalence of PsA on the population level. The aim of this study is to estimate the annual age- and sex-specific prevalence of diagnosed PsA in Germany during 2009 to 2012.
Methods: Complete diagnosis data from about 80% of the overall German population from 2009 to 2012 were screened for physician diagnosed and ascertained PsA. Diagnoses are based on claims data from all insurances of the German statutory health insurance (SHI) system. Quality checked claims data were provided by a governmental data trustee. After determining the age- and sex-specific prevalence of PsA for each of the years from 2009 to 2012, trend tests for age-standardized and age-specific prevalence in men and women were applied.

Results: In 2009, a total of 127 thousand patients with diagnosed and ascertained PsA were identified in 64.6 million people from the German SHI. In the following years 2010 to 2012, 138, 146, and 156 thousand people with diagnosed PsA have been observed, respectively. The age-standardized prevalence increases from 1.8 to 2.1 per mil in men (p-trend = 0.009), and from 2.1 to 2.5 per mil in women (p-trend = 0.01). The age-specific prevalence of PsA for men and women increases linearly from age group <20 to a peak of about 60 years of age. After age 60, the age-specific prevalence is steeply decreasing. In virtually all age groups, there is evidence for an increase of the age-specific prevalence with time in men and women. The highest increases are in the age groups 60+.

Conclusion: These data from about 65 million people insured in the German SHI for the first time indicate that there is an increasing prevalence of PsA on the population level. A selection bias is likely to be present, because the roughly 20% of the overall German population not included in our analysis is known to have other health risks (mainly privately insured people). However, our results refer to the vast majority of the German population and the 127 to 156 thousand people with diagnosed PsA. The analysis cannot be adjusted for potential confounders other than age and sex (e.g., socio-economic position or presence of co-morbidities).

Disclosure: P. Sewerin, None; M. Schneider, None; B. Ostendorf, None; R. Brinks, None.


Abstract Number: 994

Increasing Population Burden of Psoriatic Disease in Ontario, Canada – a Longitudinal Cohort Study

Lihi Eder1,2, Jessica Widdifield3, Cheryl F. Rosen4, Dafna D Gladman2,5, Raed Alhusayen6, Michael Paterson7, Stephanie Cheng7, Shirin Jabbari7, Willemina Campbell8, Sasha Bernatsky9 and Karen Tu7, 1Women's College Research Institute, Women's College Hospital, Toronto, ON, Canada, 2Medicine, University of Toronto, Toronto, ON, Canada, 3University Health Network, Toronto, ON, Canada, 4Dermatology, Toronto Western Hospital, University of Toronto, Toronto, ON, Canada, 5Rheumatology, University Health Network, Toronto, ON, Canada, 6Sunnybrook Research Institute, Sunnybrook Health Sciences Centre, Toronto, ON, Canada, 7Institute for Clinical Evaluative Sciences, Toronto, ON, Canada, 8Rheumatology, Toronto Western Hospital, Toronto, ON, Canada, 9Divisions of Rheumatology and Clinical Epidemiology, Research Institute of the McGill University Health Centre, Montreal, QC, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Epidemiology and Public Health Poster II: Rheumatic Diseases Other than Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: There is limited information on the epidemiology of psoriasis and psoriatic arthritis (PsA) in North America. The aims of this study were to estimate the prevalence and incidence rates of psoriasis and PsA and their temporal trends in Ontario, Canada.

Methods: A retrospective cohort analysis was performed in Ontario health administrative databases. The following validated algorithms were used for case definition: 1) Psoriasis: diagnosis in hospitalization records or at least 2 psoriasis
diagnostic codes assigned by any physician (specificity 99%, sensitivity 52%, PPV 62%); 2) PsA: diagnosis in hospitalization records or a combination of: [1 psoriasis code by any physician or 1 prescription of topical anti-psoriatic treatment] and 2 diagnostic codes of spondyloarthritis at least 1 by a rheumatologist (specificity 100%, sensitivity 52%, PPV 66%). The crude and age and sex-standardized prevalence and incidence rates of psoriasis were calculated from 2000 to 2015 in the general population. For PsA, results are reported from 2008 onwards due to a change in billing code in 2006.

**Results:** Among the 10,757,627 individuals aged 20 years and older living in Ontario in 2015, we identified 263,586 and 16,144 patients with psoriasis, and PsA, respectively, resulting in overall crude psoriasis and PsA cumulative prevalence of 2.25% and 0.14%, respectively. For psoriasis, the age and sex-standardized prevalence increased from 1.43% in 2000 to 2.24% in 2015 (Figure 1). For PsA, the age and sex-standardized prevalence increased from 0.07% in 2008 to 0.13% in 2015 (Figure 2). In contrast, the incidence rates of both diseases remained relatively stable.

**Conclusion:** These findings enhance our understanding of the Canadian epidemiology of psoriatic disease and burden for healthcare resources planning. Although our previous validation work showed that administrative data under captures psoriatic disease the prevalence and incidence rates of psoriasis and PsA in Ontario were comparable to European populations. The steady increase in the prevalence of psoriasis and PsA over the past decade may be attributable to population growth, an aging demographic, and increase in patients seeking medical care.
Figure 1 – Temporal trends in the Prevalence (1A) and Incidence (1B) of psoriasis in Ontario from 2000 to 2015
Figure 2 – Temporal trends in the Prevalence (2A) and Incidence (2B) of psoriatic arthritis in Ontario from 2008 to 2015

Disclosure: L. Eder, None; J. Widdifield, None; C. F. Rosen, None; D. D. Gladman, None; R. Alhusayen, None; M. Paterson, None; S. Cheng, None; S. Jabbari, None; W. Campbell, None; S. Bernatsky, None; K. Tu, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/increasing-population-burden-of-psoriatic-disease-in-ontario-canada-a-longitudinal-cohort-study

Abstract Number: 995
The Epidemiology of Psoriatic Arthritis in Israel – a Population-Based Study

Lihi Eder¹,², Arnon Dov Cohen³, Ilan Feldhamer⁴, Sari Greenberg-Dotan⁴, Eraz Batat⁴ and Devy Zisman⁵, ¹Women's College Research Institute, Women's College Hospital, Toronto, ON, Canada, ²Medicine, University of Toronto, Toronto, ON, Canada, ³Chief Physician's Office, Central Headquarters, Clalit Health Services, Tel Aviv, Israel, ⁴Chief Physician’s Office, Central Headquarters, Clalit Health Services, Tel Aviv, Israel, ⁵The Ruth and Bruce Rappaport Faculty of Medicine, Technion, Haifa, Israel

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Epidemiology and Public Health Poster II: Rheumatic Diseases Other than Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: There is limited information on the epidemiology of Psoriatic Arthritis (PsA) in general and in Middle Eastern populations in particular. The aims of this study were to estimate the prevalence and incidence rates of PsA and their temporal trends in the general population in Israel.

Methods: In this study, we derived a cohort of adult patients with PsA from the database of Clalit Health Services (CHS), Israel’s largest health fund, with over 4.4 million members (52% of Israel’s population). PsA cases were identified if they fulfilled one of the following conditions: 1) PsA diagnosis assigned at least once by a rheumatologist; 2) permanent diagnosis code assigned by a family physician combined with use of synthetic or biologic disease modifying antirheumatic drugs; 3) PsA code listed in a hospitalization discharge summary. This algorithm had positive predictive value, sensitivity and specificity of 90.5%, 88.7% and 88.1%, respectively.

We calculated crude and age- and sex-standardized prevalence and incidence rates of PsA from 2006 to 2015 in the general population. The variation in PsA prevalence was assessed in relation to several demographic factors.

Results: Among the 2,931,199 individuals aged 18 years and older registered in the CHS database in 2015, 4490 patients had a diagnosis of PsA (322 incident cases), resulting in overall crude prevalence and incidence rates of 0.153% (95% CI 0.149%, 0.158%) and 10.9 (95% CI% 9.8, 12.3) per 100,000 population, respectively. The prevalence of PsA in Israel doubled between 2006 and 2015 (0.073% to 0.153%). In contrast, the global incidence rate remained stable, with a gradual increase in the incidence among individuals aged 51 to 70 years (Figure 1). PsA is associated with Jewish ethnicity, high socioeconomic status, rural residency and higher body mass index (Table 1).

Conclusion: The prevalence and incidence of PsA in Israel are within the range of previous estimates from Southern European populations. An increase in the prevalence of PsA was observed over the past decade in the general population in Israel.
<table>
<thead>
<tr>
<th>Demographic Characteristic</th>
<th>Prevalence (%)</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>0.147</td>
<td>0.93</td>
<td>0.87, 0.98</td>
</tr>
<tr>
<td>Female</td>
<td>0.159</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Socioeconomic status</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>0.204</td>
<td>1.76</td>
<td>1.63, 1.90</td>
</tr>
<tr>
<td>Middle</td>
<td>0.167</td>
<td>1.44</td>
<td>1.35, 1.55</td>
</tr>
<tr>
<td>Low</td>
<td>0.116</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jewish</td>
<td>0.175</td>
<td>2.13</td>
<td>1.95, 2.33</td>
</tr>
<tr>
<td>Arab</td>
<td>0.082</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Residential Area</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>0.151</td>
<td>0.82</td>
<td>0.73, 0.92</td>
</tr>
<tr>
<td>Rural</td>
<td>0.184</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;30</td>
<td>0.266</td>
<td>2.57</td>
<td>2.37, 2.80</td>
</tr>
<tr>
<td>25-30</td>
<td>0.200</td>
<td>1.94</td>
<td>1.78, 2.10</td>
</tr>
</tbody>
</table>

Figure 1 – Sex standardized prevalence (1A) and incidence (1B) of PsA in Israel by age groups from 2006 to 2015

Disclosure: L. Eder, None; A. D. Cohen, None; I. Feldhamer, None; S. Greenberg-Dotan, None; E. Batat, None; D. Zisman, None.


Abstract Number: 996

**Accuracy of Canadian Administrative Health Data in Identifying Patients with Psoriasis and Psoriatic Arthritis Using Primary Care Medical Records As the Reference Standard**

Lihi Eder1,2, Jessica Widdifield3, Cheryl F. Rosen4, Dafna D Gladman2, Raed Alhusayen5, Michael Paterson6, Stephanie Cheng6, Shirin Jabbari6, Willemina Campbell7, Sasha Bernatsky8 and Karen Tu6, 1Women's College Research Institute, Women's College Hospital, Toronto, ON, Canada, 2Medicine, University of Toronto, Toronto, ON, Canada, 3University
Health Network, Toronto, ON, Canada, 4Dermatology, Toronto Western Hospital, University of Toronto, Toronto, ON, Canada, 5Sunnybrook Research Institute, Sunnybrook Health Sciences Centre, Toronto, ON, Canada, 6Institute for Clinical Evaluative Sciences, Toronto, ON, Canada, 7Rheumatology, Toronto Western Hospital, Toronto, ON, Canada, 8Divisions of Rheumatology and Clinical Epidemiology, Research Institute of the McGill University Health Centre, Montreal, QC, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017

Session Title: Epidemiology and Public Health Poster II: Rheumatic Diseases Other than Rheumatoid Arthritis

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM

Background/Purpose: We assessed the accuracy of algorithms to identify patients with psoriasis and psoriatic arthritis (PsA) in administrative health data in a validation set derived from primary care electronic medical records (EMRs), and contrasted the effect of different algorithms on the population-based prevalence of psoriasis and PsA in Ontario, Canada.

Methods: We developed a validation set using a sample of 2210 adult patients with suspected psoriasis and PsA. This sample was identified through a targeted search for psoriatic disease-related terms in the EMRs of a random sample of 30,424 patients in the primary care Electronic Administrative data Linked Database (EMRALD) in Ontario, Canada. The reference standard for classifying patients with physician-recorded psoriasis or PsA, was confirmed using a retrospective chart abstraction. All patients were then linked to health administrative data to assess the performance of the different algorithms combining physician billing and hospitalization diagnostic codes, medications and procedures for identification of patients with psoriatic disease. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of each algorithm were computed. Estimated population prevalence of psoriasis and PsA were then calculated for each algorithm.

Results: Based on our reference standard we identified 1028 patients with psoriasis and 90 patients with PsA which resulted in overall psoriasis and PsA prevalence of 3.4% and 0.29%, respectively. The majority of the patients with PsA (67%) had a documented diagnosis by a rheumatologist, while only 29% of the psoriasis patients had a documented diagnosis by a dermatologist. The accuracy of selected psoriasis and PsA case definition algorithms are presented in Table 1. All algorithms had excellent specificity (97-100%). However, the sensitivity and PPV of the algorithms were low to modest, ranging from 28% to 72% for sensitivity and 43% to 72% for PPV. The population prevalence of psoriasis (1.07-2.4%) and PsA (0.12-0.14%) ranged depending on the algorithm used for case definition.

Conclusion: The accuracy of identifying patients with psoriasis and PsA in Ontario health administrative databases varies widely, however when we applied these algorithms to the entire Ontario population, we observed similar patterns and a steady increase in prevalence, irrespective of the algorithm used. We recommend that PsA receives a distinct outpatient diagnostic code to improve case ascertainment.
**Table 1 – The accuracy of selected psoriasis case definition algorithms**

<table>
<thead>
<tr>
<th>Algorithm</th>
<th>Sensitivity (%</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Prevalence (per 100 population)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 H or 1 P ever</td>
<td>71%</td>
<td>97%</td>
<td>43%</td>
<td>99%</td>
<td>2.40%</td>
</tr>
<tr>
<td>1 H or 1 P ever by a specialist</td>
<td>50%</td>
<td>98%</td>
<td>48%</td>
<td>98%</td>
<td>1.69%</td>
</tr>
<tr>
<td>1 H or 2 P ever</td>
<td>52%</td>
<td>99%</td>
<td>62%</td>
<td>98%</td>
<td>1.76%</td>
</tr>
<tr>
<td>1 H or 2 P ever at least 1 by a specialist</td>
<td>43%</td>
<td>99%</td>
<td>63%</td>
<td>98%</td>
<td>1.46%</td>
</tr>
<tr>
<td>1 H or 2 P in 1 years</td>
<td>44%</td>
<td>99%</td>
<td>63%</td>
<td>98%</td>
<td>1.49%</td>
</tr>
<tr>
<td>1 H or 2 P in 2 years</td>
<td>47%</td>
<td>99%</td>
<td>63%</td>
<td>98%</td>
<td>1.58%</td>
</tr>
<tr>
<td>1 H or 2 P in 3 years</td>
<td>48%</td>
<td>99%</td>
<td>63%</td>
<td>98%</td>
<td>1.61%</td>
</tr>
<tr>
<td>1 H or 3 P ever</td>
<td>41%</td>
<td>99%</td>
<td>71%</td>
<td>98%</td>
<td>1.38%</td>
</tr>
<tr>
<td>1 H or 3 P in 2 years</td>
<td>28%</td>
<td>100%</td>
<td>72%</td>
<td>98%</td>
<td>1.07%</td>
</tr>
<tr>
<td>1 H or 3 P in 3 years</td>
<td>32%</td>
<td>100%</td>
<td>72%</td>
<td>98%</td>
<td>1.14%</td>
</tr>
<tr>
<td>1 H or 1 P ever or 1 prescription of anti-psoriatic treatment</td>
<td>72%</td>
<td>97%</td>
<td>42%</td>
<td>99%</td>
<td>2.42%</td>
</tr>
<tr>
<td>1 H or 2 P ever or 1 prescription of anti-psoriatic treatment</td>
<td>55%</td>
<td>99%</td>
<td>60%</td>
<td>98%</td>
<td>1.86%</td>
</tr>
<tr>
<td>1 H or 2 P ever or 2 prescription of anti-psoriatic treatment</td>
<td>54%</td>
<td>99%</td>
<td>61%</td>
<td>98%</td>
<td>1.82%</td>
</tr>
</tbody>
</table>

H: Hospitalization psoriasis code; P: physician psoriasis diagnostic code; Specialist = dermatologist; anti-psoriatic medications = tar, topical or oral retinoids, topical vitamin D derivate, IL-17 inhibitor, PDE4 inhibitor, IL-12/23 inhibitor

**Table 2 – The accuracy of selected PsA case definition algorithms**

<table>
<thead>
<tr>
<th>Algorithm</th>
<th>Sensitivity (%</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Prevalence (per 100 population)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 H or (1 P(Ps) and 1 P(SpA)) ever</td>
<td>53%</td>
<td>100%</td>
<td>53%</td>
<td>100%</td>
<td>0.13%</td>
</tr>
<tr>
<td>1 H or (1 P(Ps) and 2 P(SpA)) ever</td>
<td>51%</td>
<td>100%</td>
<td>64%</td>
<td>100%</td>
<td>0.13%</td>
</tr>
<tr>
<td>1 H or (1 P(Ps) and 3 P(SpA)) ever</td>
<td>48%</td>
<td>100%</td>
<td>66%</td>
<td>100%</td>
<td>0.12%</td>
</tr>
<tr>
<td>1 H or ((1 P(Ps) ever or 1 prescription of topical anti-psoriatic treatment) and 1 P(SpA) ever)</td>
<td>55%</td>
<td>100%</td>
<td>54%</td>
<td>100%</td>
<td>0.14%</td>
</tr>
<tr>
<td>1 H or ((1 P(Ps) ever or 1 prescription of topical anti-psoriatic treatment) and 2 P(SpA) ever)</td>
<td>52%</td>
<td>100%</td>
<td>65%</td>
<td>100%</td>
<td>0.13%</td>
</tr>
<tr>
<td>1 H or ((1 P(Ps) ever or 1 prescription of topical anti-psoriatic treatment) and 2 P(SpA) ever at least 1 by a specialist)</td>
<td>52%</td>
<td>100%</td>
<td>66%</td>
<td>100%</td>
<td>0.13%</td>
</tr>
<tr>
<td>1 H or ((1 P(Ps) ever or 1 prescription of topical anti-psoriatic treatment) and 3 P(SpA) ever at least 1 by a specialist)</td>
<td>49%</td>
<td>100%</td>
<td>68%</td>
<td>100%</td>
<td>0.12%</td>
</tr>
</tbody>
</table>

H: Hospitalization PsA code; P(Ps)=physician psoriasis diagnostic code; P(SpA)=physician spondyloarthritis diagnostic code; Specialist = rheumatologist; topical anti-psoriatic treatment = tar, retinoids or vitamin D derivate
Incidence and Clinical Characteristics of Active Tuberculosis in a Cohort of Patients with Inflammatory Arthritis Treated with TNF-Inhibitors

Ana Maria Gheorghiu¹, Alexandru Garaiman², Alexandra Radu², Alina Soare³, Victoria Arama⁴, Dragos Bumbacea⁵, Rucsandra Dobrota⁶, Raida Oneata⁷, Simona Pintilie², Mihaela Milicescu⁷, Ioan Ancuta⁷, Andrei Martin², Mariana Sasu¹, Claudia Ciofu¹, Liviu Macovei¹, Victor Stoica⁷, Mihai Bojinca⁷ and Carina Mihai⁸, ¹Carol Davila University of Medicine and Pharmacy, Internal Medicine and Rheumatology Department „Dr.I.Cantacuzino” Clinical Hospital, Bucharest, Romania, ²Internal Medicine and Rheumatology, CANTACUZINO HOSPITAL, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania, ³Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Erlangen, Germany, ⁴Infectious Diseases 1 Department, Matei Bals National Institute for Infectious Diseases, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania, ⁵Department of Pneumology, Elias Emergency University Hospital, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania, ⁶Department of Rheumatology, Center of Experimental Rheumatology, University Hospital Zurich, Zurich, Switzerland, ⁷Carol Davila University of Medicine and Pharmacy, Internal Medicine and Rheumatology Department, Cantacuzino Clinical Hospital, Bucharest, Romania, ⁸Internal Medicine and Rheumatology Dept., Cantacuzino Clinical Hospital, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Epidemiology and Public Health Poster II: Rheumatic Diseases Other than Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Tuberculosis (TB) is a major concern in patients receiving TNF inhibitors (TNFi).

Objectives: To assess the incidence of active TB and the efficacy of TB prevention measures in a large, single-center cohort of patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS) receiving TNFi.

Methods:
Data of all patients in whom treatment with TNFi was initiated in our rheumatology clinic from January 1st 2002 until December 31st 2015 have been retrospectively analysed. The cohort was divided into 2 groups per the mandatory latent TB infection (LTBI) screening method at baseline: tuberculin skin test (group TST), and QuantiFERON®-TB Gold test (group QFT). The incidence of active TB was analysed for each group and compared to TB incidence data in general population.

Results:
653 patients were included (344 RA, 52 PsA, 257 AS); 324 patients belonged to the TST and 329 to the QFT group. The number of active TB cases/ time of exposure to TNFi (person-years, PY) was 17/2002.6 and 7/1041.2 respectively, accounting for an incidence of 848.9 and 672.3 cases per 105 PY, about 8 times higher (8.3 and 8.8 for TST, respectively QFT group) than the average TB during the period of exposure to TNFi. LTBI reactivations per total TB cases were only
4/17 and 2/7, respectively, too few to identify statistically significant differences between the 2 LTBI screening protocols. Only 10 patients had pulmonary TB, whereas the rest were disseminated TB (8 cases), TB pleurisy and/or pericarditis (4 cases), one mediastinal lymph node TB and one isolated hepatic TB. Using Pearson chi-square test, we found no significant differences between LTBI group and active TB (Table 1).

**Conclusion:**

In our cohort, new infection TB exceeds reactivation TB, suggesting the necessity of periodical LTBI re-screening.

**Table 1. LTBI screening results and TB occurrence in the 653 TNFi-treated patients.** (Pearson $\chi^2$ test)

<table>
<thead>
<tr>
<th></th>
<th>TST</th>
<th>QFT</th>
<th>All</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=324)</td>
<td>(n=329)</td>
<td>(n=653)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>immuno-</td>
<td>52 (16.0%)</td>
<td>63 (19.1%)</td>
<td>115 (17.6%)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>diagnostic test at baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active TB</td>
<td>17 (5.2%)</td>
<td>7 (2.1%)</td>
<td>24 (3.7%)</td>
<td>0.185*</td>
</tr>
<tr>
<td>Reactivation TB</td>
<td>4 (1.2%)</td>
<td>2 (0.6%)</td>
<td>6 (0.9%)</td>
<td>**</td>
</tr>
<tr>
<td>New infection TB</td>
<td>13 (4.0%)</td>
<td>5 (1.5%)</td>
<td>18 (2.8%)</td>
<td>0.052*</td>
</tr>
<tr>
<td>Total TB incidence</td>
<td>848.9</td>
<td>672.3</td>
<td>788.5</td>
<td>-</td>
</tr>
</tbody>
</table>

(per $10^5$ PY)

|                |           |           |           |         |
| Maximal period of TNFi exposure in group | 2002-2016 | 2011-2016 | 2002-2016 | -       |
| Mean TB incidence in Romania in the respective time period (per $10^5$ PY) | 102.3     | 76.7      | 102.3     | -       |
| TB incidence patients/general population | 8.3       | 8.8       | 7.7       | 0.88†   |

*Pearson $\chi^2$ test comparing TST and QFT. **Reactivation TB cases were too few to perform statistical testing †Pearson $\chi^2$ test comparing total TB incidence in the TST and QFT groups to the average TB incidence in our region in the respective period of exposure.

**Disclosure:** A. M. Gheorghiu, None; A. Garaiman, None; A. Radu, None; A. Soare, None; V. Arama, None; D. Bumbacea, None; R. Dobrota, None; R. Oneata, None; S. Pintilie, None; M. Milicescu, None; I. Ancuta, None; A. Martin, None; M. Sasu, None; C. Ciofu, None; L. Macovei, None; V. Stoica, None; M. Bojinca, None; C. Mihai, None.


**Abstract Number:** 998
Mental Health in Patients with Axial Spondyloarthritis: Increasing Our Understanding of the Disease. Results from the Spanish Atlas

Marco Garrido-Cumbera1, Victoria Navarro-Compán2, David Galvez-Ruiz1, Carlos Jesus Delgado Dominguez1, Pilar Font-Ugalde3, Olta Brace1, Pedro Zarco4, Jorge Chacon-Garcia1 and Pedro Plazuelo-Ramos5, 1Universidad de Sevilla, Seville, Spain, 2Rheumatology, Hospital Universitario La Paz, Madrid, Spain, 3Rheumatology service, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain, 4H Fundación Alcorcón, Alcorcón, Spain, 5CEADE, Madrid, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Epidemiology and Public Health Poster II: Rheumatic Diseases Other than Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: This study’s aim was to assess the association between sociodemographic characteristics, disease progression, and mental health comorbidity with risk of mental disorders (RMD).

Methods: In 2016 a sample of 680 axSpA patients was interviewed as part of the Spanish Atlas. To quantify the RMD, Goldberg’s General Health Questionnaire (GHQ-12) scale was employed. Possible RMD predictors analysed were: sociodemographic characteristics (age, gender, being part of a couple, patient association membership, job status); disease characteristics (BASDAI, spinal stiffness ranging from 0-3, functional limitation in 18 daily activities ranging from 0-3); and mental health comorbidities (depression and anxiety). All clinical variables showed a Cronbach’s alpha coefficient guaranteeing the reliability of the scales used. First, a descriptive analysis was employed to describe the sample and study variables. Second, we performed univariate correlation and homogeneity analyses between each predictor (independent variable) and RMD (GHQ-12). Third, selection of variables that showed statistical significance in the univariate analyses in order to conduct a multiple hierarchical and stepwise regression analysis.

Results: All variables except educational level and thoracic stiffness showed significant univarient correlation with RMD. BASDAI, functional limitation and age showed higher coefficient (R = 0.543, R = 0.378, R = -0.174, respectively). Multiple Hierarchical regression analysis showed as sociodemographic variables explained in great detail the RMD (R² = 83.2%). By contrast, having established sociodemographic as a control variable, the inclusion of depression and anxiety to the model increase the R² value to just 0.6% (p = 0.001), while the inclusion of variables related to the disease characteristics add 5.5% (p = 0.000) to the GHQ-12 punctuation variability. The only variables presenting a significant coefficient different from 0 were BASDAI (0.52, p = 0.000) and functional limitation (0.14, p = 0.004). This suggests that once the sociodemographic and mental comorbidity variables are established, a change to BASDAI levels or functional limitation impacts the GHQ-12 score. In the stepwise regression analysis, four variables (BASDAI, functional limitation, association membership, cervical stiffness) showed a significant relation to GHQ-12 and explained the majority of RMD variability. BASDAI displayed the highest explanatory degree (R² = 0.875).

Table 1. Sample characteristics (n = 474, unless other specified).
Variables | Values (means ± SD or percentage)
---|---
Age, mean ± SD | 45.43 ± 10.78
Sex, No. of men | 233 (49.16%)
Having a couple, No. of participants (N=444) | 386 (86.94%)
Education level, No. of university studies | 185 (39.30%)
Job status, No. of unemployed | 68 (14.35%)
Association Membership | 227 (47.89%)
BASDAI, mean ± SD (N=442) | 5.49 ± 2.17
Cervical stiffness, No. (N=447) | 201 (44.97%)
Thoracic stiffness No. (N=435) | 186 (42.76%)
Lumbar stiffness No. (N=458) | 288 (62.88%)
Functional Limitation, mean ± SD (N=473) | 27.54 ± 12.78
Depression, No. (%) (N=474) | 99 (20.89)
Anxiety, No. (%) (N=474) | 134 (28.27)
GHQ-12, mean ± SD | 18.30 ± 8.01

**Conclusion:** Patients at certain sociodemographic levels are more prone to present a higher BASDAI. Taking these conditions for granted, the degree of disease progression measured by BASDAI is a good indicator of RMD. Therefore, in those with higher disease activity, psychiatric evaluation and intervention should be considered within the medical treatment.

**Disclosure:** M. Garrido-Cumbrera, None; V. Navarro-Compán, None; D. Galvez-Ruiz, None; C. J. Delgado Dominguez, None; P. Font-Ugalde, None; O. Brace, None; P. Zarco, None; J. Chacon-Garcia, None; P. Plazuelo-Ramos, None.


**Abstract Number:** 999

**Association between Smoking with Spinal Level of Stiffness and Functional Limitation in Patients with Axial Spondyloarthritis: Results from the Spanish Atlas**

Marco Garrido-Cumbrera¹, Victoria Navarro-Compán², Jorge Chacon-Garcia¹, Jordi Gratacosas-Masmitja³, David Galvez-Ruiz¹, Eduardo Collantes Estevez⁴, Pedro Zarco⁵ and Olta Brace⁶, ¹Universidad de Sevilla, Seville, Spain, ²Rheumatology, Hospital Universitario La Paz, Madrid, Spain, ³Rheumatology, Hospital Parc Taulí, Sabadell - Barcelona, Spain, ⁴Universidad de Cordoba, Cordova, Spain, ⁵H Fundación Alcorcón, Alcorcón, Spain

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017

Session Title: Epidemiology and Public Health Poster II: Rheumatic Diseases Other than Rheumatoid Arthritis

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM

Background/Purpose: Smoking has been associated with greater disease activity and radiographic progression in patients with Axial Spondyloarthritis (ax-SpA). In addition, radiographic damage has been linked to greater functional limitation. However, clarification is still being sought as to whether or not this association exists. To investigate the association between smoking and both the area of spinal stiffness and functional limitation in patients with ax-SpA.
Methods: A sample of 680 patients diagnosed with ax-SpA was interviewed during 2016 as part of the Spanish Atlas, which aims to promote early referral and improve healthcare and the use of effective treatments in patients with ax-SpA. Tobacco consumption was recorded as: Smoker (62.4%), Occasional Smoker (8.9%) and Non-Smoker (28.7%). Spinal stiffness was assessed in the three different vertebral areas: cervical, dorsal and lumbar. To determine the degree of functional limitation we used a composed index which includes the sum of the degree of limitation in the 18 daily activities well established (dressing, grooming, bathing, tying shoelaces, moving around the home, stairs, getting to/out of bed, toilet, shopping, preparing meals, eating, cleaning, walking, using public transportation, going to the doctor, driving, physical exercise, sexual relations) using an ordinal variable (0=none, 1=little, 2=some and 3=moderate). A descriptive analysis was used to compare the level of stiffness (chi-squared test) and the mean degree of limitation (Kruskal-Wallis test) in the different groups of smokers consumptions. Regression analysis was also used to assess the relation between smoking and degree of limitation (0-54).

Results: 53% were females, mean age 46 years and 77.1% were HLA-B27+. The percentage of patients with stiffness in the lumbar region was significantly higher in habitual/occasional smokers than in non-smokers (89.0%, 93.8%, 83.5% respectively; p<0.01) (Table). The mean degree of functional limitation increased with tobacco consumption, although this difference was not statistically significant (47.9 ± 12.1 vs. 45.1 ± 11.5 vs. 44.8 ± 13.7 respectively; p=0.2). However, regression analysis showed a statistically significant correlation between smoking and functional limitation (r=0.096; p=0.02).

Table 1. Relationship between tobacco consumption and spinal stiffness levels in patients with ax-SpA

<table>
<thead>
<tr>
<th></th>
<th>Smoker</th>
<th>Occasional smoker</th>
<th>Non smoker</th>
<th>P</th>
<th>$X^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical stiffness</td>
<td>84.2%</td>
<td>77.1%</td>
<td>73.1%</td>
<td>0.171</td>
<td>9.044</td>
</tr>
<tr>
<td>Thoracic stiffness</td>
<td>76.0%</td>
<td>76.6%</td>
<td>72.4%</td>
<td>0.408</td>
<td>6.141</td>
</tr>
<tr>
<td>Lumbar stiffness</td>
<td>89.0%</td>
<td>93.8%</td>
<td>83.5%</td>
<td>0.002</td>
<td>20.518</td>
</tr>
</tbody>
</table>

Conclusion: Smoking in patients with ax SpA is associated to greater stiffness in the lumbar region, but is not related to stiffness in the cervical or dorsal regions. Additionally, smoking is associated to the degree of functional limitation in these patients.

Disclosure: M. Garrido-Cumbera, None; V. Navarro-Compán, None; J. Chacon-Garcia, None; J. Gratacos-Masmitja, None; D. Galvez-Ruiz, None; E. Collantes Estevez, None; P. Zarco, None; O. Brace, None.


Abstract Number: 1000

Use of Mutual Information Theory in Development and Refinement of a Predictive Model for Early Identification of Ankylosing Spondylitis

Atul A. Deodhar1, Cody Garges2, Oodaye Shukla2, Theresa Arndt2, Tara Grabowsky2 and Yujin Park3, 1Oregon Health & Science University, Portland, OR, 2HVH Precision Analytics, LLC, King of Prussia, PA, 3Novartis Pharmaceuticals Corporation, East Hanover, NJ

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Epidemiology and Public Health Poster II: Rheumatic Diseases Other than Rheumatoid Arthritis
Session Type: ACR Poster Session B
Background/Purpose: Delayed diagnosis and treatment of ankylosing spondylitis (AS) contribute to the economic, physical and psychological burden on patients and their caregivers. The objective of this analysis was to refine a previously developed predictive mathematical model for AS\textsuperscript{1} based on features observed in the medical histories of patients with and without a diagnosis of AS to aid in the earlier identification of AS.

Methods: This retrospective cohort study used administrative claims data from > 182 million patients in the Truven Health MarketScan® Commercial and Medicare Supplemental Databases from January 2006 to September 2015 (Segment 1) and October 2015 to November 2016 (Segment 2). The AS population in Segment 1 included all patients with ≥ 2 diagnoses of AS (ICD-9-CM 720.0) by rheumatologists ≥ 30 days apart who had ≥ 12 months of continuous enrollment prior to first AS diagnosis. Control patients were matched by age, sex, enrollment period and geographic location and were randomly selected from the same database. Mutual information was used to identify features that differentiated AS from the control population; select features were then used as inputs in development of a suite of predictive models using data from Segment 1.\textsuperscript{1} The optimized predictive model was then tested by observing whether patients predicted to have AS in Segment 1 subsequently received an ICD-10-CM AS diagnosis code (M45.x or M08.1) in Segment 2.

Results: In the initial study, 3 iterations of the predictive risk model (Models 1, 2 and 3a/3b) were developed using data from patients with ≥ 1 ICD-9-CM AS diagnosis during Segment 1, with each subsequent model iteration using additional AS-specific queries to reflect a more real-world situation.\textsuperscript{1} A 2-stage model (Models 4 and 5) was built using patients with ≥ 2 ICD-9-CM AS diagnoses during Segment 1 to improve performance. Model 4 identified patients with AS from the general control population in the database (Figure 1A). To further improve precision, Model 5 was built using 50,000 random patients in Segment 1 who scored above a 0.5 in Model 4 (i.e., were more like patients with AS) as a new control population (Figure 1B). Models 4 and 5 were then combined to identify new patients with AS in Segment 2; of the = 20 million patients who tracked across Segment 1 and Segment 2, 742 patients had an ICD-10-CM AS diagnosis in Segment 2 who did not have an ICD-9-CM diagnosis in Segment 1.

Conclusion: Predictive models for AS diagnosis were developed and refined in this US administrative claims database. Work is ongoing to compare the sensitivity and positive predictive value of these predictive models versus more traditional linear regression models, and future research will validate the model in a separate, commercially insured population database.

Reference:

1.) Garges C, et al. Presented at the ISPOR 22nd Annual International Meeting; May 20-24, 2017; Boston, MA; [Poster PRM85].
**Disclosure: A. A. Deodhar**, Eli Lilly, GSK, Janssen, Novartis, Pfizer, Sun Pharma and UCB, 2,AbbVie, Eli Lilly, Janssen, Novartis, Pfizer and UCB, 9; **C. Garges**, HVH Precision Analytics, LLC, 3; **O. Shukla**, HVH Precision Analytics, LLC, 3; **T. Arndt**, HVH Precision Analytics, LLC, 3; **T. Grabowsky**, HVH Precision Analytics, LLC, 3; **Y. Park**, Novartis Pharmaceuticals Corporation, 3.


**Abstract Number:** 1001

**Persistence, Discontinuation, and Switching Patterns Among Ankylosing Spondylitis Patients Newly Initiating Biologic Therapy**

**Theresa Hunter**¹, Krista Schroeder², Sarah Al Sawah² and David Sandoval Calderon², ¹Global Patient Outcomes and Real World Evidence, Eli Lilly and Company, Indianapolis, IN, ²Eli Lilly and Company, Indianapolis, IN

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Epidemiology and Public Health Poster II: Rheumatic Diseases Other than Rheumatoid Arthritis

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The primary goals of treating Ankylosing Spondylitis (AS) patients are to maximize long-term health-related quality of life through control of symptoms and inflammation, prevention of progressive structural damage, and preservation of function. With two classes of biologic disease modifying agent (bDMARD) currently available, providers have more options to offer to their patients, especially after failing a first biologic. The objective of this study was to describe treatment patterns (persistence, discontinuations, and switch to a 2nd or 3rd line biologic) in the 2 years following the initiation of biologic therapy in AS patients.

**Methods:** Adult patients with ≥ 2 AS diagnoses were included in this retrospective analysis of medical and pharmacy claims data from the Truven MarketScan Commercial Claims database. AS patients who newly initiated a biologic agent (etanercept, adalimumab, golimumab, infliximab, or certolizumab pegol) during the period from January 1, 2009, to December 31, 2013 were selected and indexed on their first biologic during the time period. All patients were required to have a 1-year pre-index clean period of all biologic therapy and continuous enrollment (medical and prescription) 1-year pre-index and 2-years post-index. Patients were excluded if they had ≥2 diagnostic codes for any of the following conditions: Rheumatoid Arthritis, Juvenile Idiopathic Arthritis, Psoriatic Arthritis, Crohn’s Disease, Ulcerative Colitis, Plaque Psoriasis, Hidradenitis Suppurativa, or Uveitis. Demographic, clinical, and treatment patterns were analyzed. Treatment patterns included switching to a new biologic (2 and 3+ lines), discontinuation (≥90-day gap in therapy), or persistence (no gaps in therapy ≥90-days) during the 2-year follow-up period.

**Results:** A total of 1,372 AS patients met the inclusion criteria for this study. The majority of patients (61.7%) were male and the overall mean age of patients was 43.8 years. Adalimumab was the index biologic for 44.1% of patients, followed by etanercept (40.9%), infliximab (10.6%), golimumab (4.3%), and certolizumab pegol (0.1%). During the follow-up period, 33.1% of patients (n=454) were persistent on their index biologic, while 66.9% (n=918) either discontinued their index biologic therapy or switched to a 2nd line biologic. Among the patients who discontinued their first index biologic, 39.1% (n=359) switched to a 2nd line biologic. Of those with a 2nd line biologic, 20.1% (n=72) had 3 or more different biologics prescribed during the follow-up period. From 2009 to 2013, the proportion of new biologic users initiating 2nd line biologic increased over time from 25.2% to 28.8% (average for all four years = 26.2%).

**Conclusion:** This study suggests that approximately two-thirds of AS patients newly initiating on a biologic do not remain on the index therapy 2 years post initiation. More work is needed to understand the reasons for non-persistence and the increasing trend of second line biologic use in this population.

Survival and Years of Potential Life Lost in Connective Tissue Disease and Vasculitis; Data from the Norwegian Connective Tissue Diseases and Vasculitis Registry (NOSVAR)

Torhild Garen¹, Karoline Lerang¹, Anna Maria Hoffmann-Vold², Helena Andersson¹, Øyvind Midtvedt¹, Karin Kilian¹, Ragnar Gunnarsson¹, Birgir Gudbrandsson¹, Gudrun Norby¹, Øyvind Molberg² and Øyvind Palm¹, ¹Department of Rheumatology, Oslo University Hospital, Oslo, Norway, OSLO, Norway, ²Department of Rheumatology, Oslo University Hospital, Oslo, Norway, Oslo, Norway

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Epidemiology and Public Health Poster II: Rheumatic Diseases Other than Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Survival is decreased in patients with connective tissue diseases (CTDs) and vasculitis, however few studies have compared the mortality between the specific diseases prospectively by similar methods for patient’s selection. Here, we aimed to compare survival, standard mortality rates (SMR) and premature mortality between diagnoses of CTDs and vasculitis.

Methods:

All patients included in NOSVAR diagnosed from January 1, 1999 to December 31, 2016, in total 2148 patients were followed up until death or study end. Fifteen controls matched for each individual patient for year of birth, sex and residence area was randomly selected from the Norwegian Central Public Population Register. All controls were alive at time of patients diagnosis. Kaplan-Meier survival probabilities and curves were used to determine survival, and the difference between patients and controls was estimated by the log-rank test (Mantel Cox). In the Standardized mortality ratio (SMR) the number of deaths was divided by number of years of observation for each diagnosis and calculated as the ratio between the observed and expected numbers of death. The years of potential life lost (YPLL) was defined as the years a person would have lived if he or she had not died prematurely (here defined as 60 years of age). The YPLL for each death in patients are summed to represent the total years of potential life lost for all patients in each patient-group. The YPLL (60) rate is found by dividing YPLL by years of observation under the age of 60 in each group.

Results:

During a mean (SD) follow-up time of 9.2 years (4.7), 280/2148 (13%) patients deceased compared to 2885/32186 (9%) of the controls (p<0.001). Patient’s characteristics and demographics are shown in Table 1. Compared to controls, the lowest 5-and 10 years survival was seen in diffuse cutaneous systemic sclerosis (dcSSc) (79 % and 60%), (p<0.001), Antisynthetase syndrome (86% and 73%), (p<0.001), and limited systemic sclerosis, (89% and 75%), (p<0.001) Figure 1). For ANCA vasculitis and controls 5 years survival was 91% vs 95% and 10 years survival was 80 % vs 87%., (p=0.030). Highest SMR was observed for dSSc (5.8) and Antisynthetase syndrome (4.1)(Figure 2) The sum of YPLL60 among patients was 493 years and in matched controls 115 years, indicating a four-fold increase in premature deaths among the patients. The mean YPLL60 was highest in SLE and Takayasu with 19 and 15 years lost, respectively. Both lcSSc and dcSSc had a mean of 7 years lost YPLL60. The ranking of annual rate of YPLL60 for each disease is shown in (Figure 3)

Conclusion:

We show that there is a difference in survival, mortality and YPLL60 among the different CTDs and vasculitis. Methods used supplement each other and highlights the different aspects of outcome among the diagnoses. Systemic sclerosis and Antisynthetase syndrome had the lowest 5 and 10 years survival and the highest rate of premature mortality, but the mean loss of years before 60 years of age were higher in individuals with Takayaus and SLE.

Disclosure: T. Garen, None; K. Lerang, None; A. M. Hoffmann-Vold, None; H. Andersson, None; O. Midtvedt, None; K. Kilian, None; R. Gunnarsson, None; B. Gudbrandsson, None; G. Norby, None; O. Molberg, None; Ø. Palm, None.
Hair Treatments and the Risk of Systemic Lupus Erythematosus: the Michigan Lupus Epidemiology & Surveillance (MILES) Program

Emily C. Somers¹, Christina Mrukowicz², Wendy Marder¹, W. Joseph McCune³, Afton L. Hassett⁴, Suzanna Zick⁵, Siobán Harlow⁶ and Caroline Gordon⁷, ¹Internal Medicine-Rheumatology, University of Michigan, Ann Arbor, MI, ²University of Michigan, Ann Arbor, MI, ³Int Med/Rheum, University of Michigan, Ann Arbor, MI, ⁴Rheumatology, Emory University, Atlanta, GA, ⁵Department of Family Medicine, University of Michigan, Ann Arbor, MI, ⁶Epidemiology Department- School of Public Health, Obstetrics and Gynecology- Medical School, University of Michigan, Ann Arbor, MI, ⁷School of Immunity and Infection, College of Medical and Dental Sciences, University of Birmingham, Birmingham, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: ARHP Epidemiology and Public Health Poster
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Hair dye exposure has been reported as a risk factor for systemic lupus erythematosus (SLE) and connective tissue diseases, though conflicting results exist. We performed a population-based case-control study based on the MILES Program to determine whether hair dyes, rinses and permanents were associated with SLE risk.

Methods:
The MILES Program includes a population-based cohort of SLE cases and controls from southeast Michigan. Detailed data on history of hair treatment exposures prior to SLE diagnosis (i.e., hair dyes, rinses and permanents to curl/straighten hair) were collected, including details regarding frequency, duration, colors used and timing in relation to SLE diagnosis. For controls, we generated a reference date in lieu of a diagnosis date using multiple imputation (SAS PROC MI). Multivariable logistic regression, adjusted for covariates (race, ethnicity, age, county of residence, family income, and history of beauty salon occupation), was used to assess association between hair product use and case/control status.

Results:
In this study population of 654 participants (462 SLE cases, 192 controls), 584 (89.3%) were female, 288 (44%) black, and mean age at baseline visit was 53 years. Primary analyses were restricted to females, due to small numbers in males. In female cases vs controls, hair dye use was reported in 35.1% of cases/38.8% of controls; hair permanents in 55.8%/56.7%; hair rinses in 19.7%/19.6%; and history of beauty salon occupation in 9.1%/6.5%. Odds ratios (95% CIs) adjusted for covariates were: hair dye [0.94 (0.63, 1.40)]; hair rinse [0.91 (0.57, 1.46)]; hair permanent [0.86 (0.57, 1.30)]. Likewise, duration of use, dark color hair dyes, and history of beauty salon occupation were not found to be associated with SLE. Results from analyses stratified by race were similar.

Conclusion:
This population-based case-control study is one of the largest studies to examine the relationship between hair product use and lupus. We found no evidence of an association between any of the treatment types – hair dye, hair rinse, or hair permanents – and risk of lupus.

Disclosure: E. C. Somers, None; C. Mrukowicz, None; W. Marder, None; W. J. McCune, None; A. L. Hassett, None; S. Zick, None; S. Harlow, None; C. Gordon, None.

Arthritis Impact at the State and County Level — United States, 2015
Kamil E. Barbour1, Suson Moss2, Janet Croft2, Jennifer M. Hootman3, Louise Murphy4, Kristina Theis2, Yan Wang2, Hua Lu2, Teresa J. Brady1 and Charles G. Helmick2, 1Arthritis Program, Centers for Disease Control and Prevention, Atlanta, GA, 2Centers for Disease Control and Prevention, Atlanta, GA, 3Centers for Disease Control and Prevention, Kennesaw, GA, 4Division of Population Health, Centers for Disease Control and Prevention, Atlanta, GA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: ARHP Epidemiology and Public Health Poster
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Arthritis, a leading cause of disability, affects 54.4 million US adults. By knowing the state and county level arthritis impact, state-level public health professionals can determine appropriate resource allocation, understand existing disparities, and target dissemination of evidence-based interventions that can reduce arthritis impact.

Methods: To summarize the arthritis burden at the state and county-level, we used data from the 2015 Behavioral Risk Factor Surveillance System, an annual, random-digit–dialed landline and cellphone survey that is representative of the noninstitutionalized adult population aged ≥18 years in the 50 states and territories. Arthritis was defined as a "yes" to "Has a doctor or other health professional ever told you that have some form of arthritis, rheumatoid arthritis, gout, lupus, or fibromyalgia?" For each state, we calculated arthritis prevalence overall and among those with specific comorbidities; among adults with arthritis, we estimated the prevalence of arthritis-attributable activity limitation (AAAL), social participation restriction (SPR), severe joint pain (SJP), physical inactivity (PIA), leisure walking (LW), and arthritis management behaviors; the latter category on management was calculated for the 13 states that collected this information. Age-adjusted (standardized to the projected 2000 U.S. population) percentages were calculated for all prevalence estimates shown below.

Results: For the 50 states and DC in 2015, the median prevalence of arthritis was 23.0% (range: 17.2-33.6%). For arthritis-attributable impact measures among adults with arthritis, median (range) prevalence for AAAL was 49.7% (40.4-59.4%); SPR was 19.7% (12.6-30.4%); and SJP was 29.7% (20.3-46.0%). Median (range) prevalence of arthritis among adults with obesity, heart disease, and diabetes was 30.9% (24.6-41.2%), 44.5% (25.6-72.6%), and 37.3% (27.1-53.7%), respectively. Median (range) prevalence of PIA and LW among adults with arthritis was 35.0% (23.1-47.9%) and 48.0% (38.5-59.5%), respectively. For arthritis management, median (range) prevalence of being told to exercise for their arthritis and lose weight if overweight/obese to manage arthritis symptoms was 58.5% (52.3-61.9%) and 44.5% (35.1-53.2%), respectively; median prevalence of attending a self-management education (SME) course was 14.5% (range=9.1-19.0%). Arthritis prevalence varied considerably by county (range: 13.5%-34.8%).

Conclusion: Arthritis was common -- particularly among those with comorbid conditions -- and varied substantially at both the state and county level. Adults with arthritis have a high prevalence of characteristics that impact quality of life (e.g., AAAL, SPR, and SJP), and a large percentage are PIA and do not participate in LW. Participation in a SME course among adults with arthritis remains low; approximately half of health care providers recommended self-management behaviors. Greater use of evidence-based physical activity and SME interventions could reduce pain and improve function and quality of life for all adults with arthritis including those with comorbidities.

Disclosure: K. E. Barbour, None; S. Moss, None; J. Croft, None; J. M. Hootman, None; L. Murphy, None; K. Theis, None; Y. Wang, None; H. Lu, None; T. J. Brady, None; C. G. Helmick, None.


Abstract Number: 1005

The Prevalence of Patellofemoral Osteoarthritis in China: A Multi-Center Population-Based Cross-Sectional Study

Zhanglai Li1, Qiang Liu1, Changsheng Zhao2, Yuqing Zhang3, Xiaowei Li1 and Jianhao Lin1, 1Arthritis Clinic and Research Center, Peking University People's Hospital,Peking University, Beijing, China, 2Peking University International Hospital, Peking University International Hospital, Beijing, China, 3School Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA

First publication: September 18, 2017
Background/Purpose: To describe the prevalence and risk factors of patellofemoral osteoarthritis (OA) in a Chinese population.

Methods: A multi-center population-based cross-sectional survey was conducted in 2015 in Beijing, Henan and Ningxia, China. 4138 residents aged &ge50 years were recruited using a cluster sampling method. Subjects completed a home interview (including socio-demographic factors, history of knee injury, joint symptoms, job-related physical activity and work history) and had weight-bearing posterior-anterior semi-flexed view of radiographs at tibiofemoral joints and skyline view of radiographs at patellofemoral joints (PF). Height was measured twice for each subject, using a wall-mounted studio meter and weight was assessed using a balance beam scale with a precision to 0.1 kg. BMI was calculated as weight in kilograms divided by height in meters squared. Radiographs were read by two orthopedic surgeons. Each knee was evaluated for the presence of osteophytes (OST), joint space narrowing (JSN) on a 0-3 scale based on OARSI atlas. If two readers disagreed on a patient’s OA status, adjudication session was held with third orthopedic surgeon present. Radiographic OA (ROA) at PF joint was defined if OST score was &ge2 or if JSN score was &ge2 with concurrent grade 1 OST in the PF joint. The kappa for inter-rater reliability was 0.71-0.85 and the intra-rater reliability was 0.85-0.91 prior to adjudication. Knee pain symptoms were asked for each participant using the following questions &Prime Did knee pain occur when going up and down stairs on most days in the past month? &Prime PF symptomatic OA (SxOA) was recorded if both pain and ROA were present at the same knee. We examined the relations of a set of risk factors to the prevalence of PF ROA and SxOA using logistic regression model.

Results: Of 4138 subjects recruited, 533 (12.9%) subjects were excluded from the analysis due to missing knee radiographs. Of the remaining (n=3605) 35.6% (n=1283) were men, mean age was 62.89&plusmn7.58 years, and mean BMI was 25.05&plusmn3.60 kg/m2; 64.4% (n=2322) were women, mean age was 60.86&plusmn7.50 years, and mean BMI was 26.26&plusmn3.81 kg/m2. The prevalence of PF ROA and SxOA was 23.7% and 14.1%, respectively. As shown in Table 1, women, older age, higher BMI, history of knee injury and bicycling &ge2 hours per day lasted less than 30 years were significantly associated with both PF ROA and SxOA. Few years of education was associated with high prevalence of PF ROA, whereas standing &ge2 hours per day lasted less than 30 years was associated with PF SxOA. No statistical significant difference was observed between job-related physical activity and PF ROA/SxOA.

Conclusion: Our study suggests that prevalence of PF ROA and SxOA was high in China. Several potential risk factors for prevalent PF OA were identified and need to be verified in the future prospective cohort studies.

Table 1. Association between risk factor with PF ROA/SxOA
<table>
<thead>
<tr>
<th>Potential risk factors</th>
<th>Level</th>
<th>Radiographic patellofemoral OA</th>
<th>Symptomatic patellofemoral OA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>P-value</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Sex</td>
<td>1.23 (1.01,1.49)</td>
<td><strong>0.034</strong></td>
<td>1.33 (1.06,1.67)</td>
</tr>
<tr>
<td>Education</td>
<td>0.80 (0.66,0.97)</td>
<td><strong>0.026</strong></td>
<td>0.82 (0.65,1.05)</td>
</tr>
<tr>
<td>Age</td>
<td>1.06 (1.04,1.07)</td>
<td>&lt;<strong>0.001</strong></td>
<td>1.06 (1.05,1.08)</td>
</tr>
<tr>
<td>BMI</td>
<td>1.12 (1.10,1.15)</td>
<td>&lt;<strong>0.001</strong></td>
<td>1.12 (1.09,1.15)</td>
</tr>
<tr>
<td>History of knee injury</td>
<td>No</td>
<td>1.38 (1.04, 1.83)</td>
<td><strong>0.026</strong></td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>1.74 (1.28, 2.39)</td>
<td><strong>0.001</strong></td>
</tr>
<tr>
<td>Duration of physical activity at work, year</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Standing &amp;ge2 hours per day</td>
<td>0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>1-29</td>
<td>1.12 (0.87,1.44)</td>
<td>1.33 (1.00,1.77)</td>
</tr>
<tr>
<td></td>
<td>30+</td>
<td>0.86 (0.61,1.21)</td>
<td>0.99 (0.71,1.37)</td>
</tr>
<tr>
<td>Walking &amp;ge2 hours per day</td>
<td>0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>1-29</td>
<td>1.05 (0.81,1.35)</td>
<td>0.94 (0.69,1.29)</td>
</tr>
<tr>
<td></td>
<td>30+</td>
<td>0.91 (0.64,1.30)</td>
<td>0.79 (0.52,1.21)</td>
</tr>
<tr>
<td>Bicycling &amp;ge2 hours per day</td>
<td>0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>1-29</td>
<td>1.33 (1.01,1.74)</td>
<td>1.43 (1.04,1.97)</td>
</tr>
<tr>
<td></td>
<td>30+</td>
<td>1.16 (0.84,1.61)</td>
<td>1.38 (0.71,1.37)</td>
</tr>
<tr>
<td>Bending &amp;ge2 hours per day</td>
<td>0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>1-29</td>
<td>1.06 (0.81,1.40)</td>
<td>1.26 (0.81,1.94)</td>
</tr>
<tr>
<td></td>
<td>30+</td>
<td>1.04 (0.71,1.53)</td>
<td>1.04 (0.71,1.52)</td>
</tr>
<tr>
<td>Squatting &amp;ge30 minutes per day</td>
<td>0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>1-29</td>
<td>1.17 (0.74,1.56)</td>
<td>1.17 (0.87,1.57)</td>
</tr>
<tr>
<td></td>
<td>30+</td>
<td>1.08 (0.40,1.10)</td>
<td>1.28 (0.85,1.94)</td>
</tr>
<tr>
<td>Lifting &amp;ge10kg object per day</td>
<td>0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>1-29</td>
<td>1.20 (0.95,1.53)</td>
<td>1.23 (0.92,1.65)</td>
</tr>
<tr>
<td></td>
<td>30+</td>
<td>1.17 (0.74,1.84)</td>
<td>1.36 (0.82,2.23)</td>
</tr>
<tr>
<td>Climbing &amp;ge2 hours per day</td>
<td>0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>1-29</td>
<td>1.39 (0.75,2.60)</td>
<td>1.21 (0.56,2.58)</td>
</tr>
<tr>
<td></td>
<td>30+</td>
<td>0.83 (0.37,1.86)</td>
<td>1.29 (0.52,3.20)</td>
</tr>
</tbody>
</table>

Disclosure: Z. Li, None; Q. Liu, None; C. Zhao, None; Y. Zhang, None; X. Li, None; J. Lin, None.


Abstract Number: 1006

**Sex Differences in Depressive Symptom Subtypes in Knee Osteoarthritis**

Alan Rathbun1, Megan Schuler2, Elizabeth Stuart3, Michelle Shardell4, Michelle S. Yau5 and Marc Hochberg6, 1Epidemiology and Public Health, University of Maryland School of Medicine, Baltimore, MD, 2Rand Coportation, Boston, MA, 3Mental Health, Biostatistics, and Health Policy and Management, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, 4Translational Gerontology Branch, National Institute on Aging, Baltimore, MD, 5Institute for Aging Research, Hebrew SeniorLife, Harvard Medical School, Boston, MA, 6Department of Medicine, University of Maryland School of Medicine, Baltimore, MD

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017

Session Title: ARHP Epidemiology and Public Health Poster

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM

Background/Purpose: Knee osteoarthritis (OA) is characterized by structural changes in subchondral bone and degradation of articular cartilage, but the pathology does not necessarily lead to pain and functional limitations. Latent and modifiable factors, such as depression, may contribute to or worsen knee OA symptoms. However, depression is clinically heterogeneous and presentation may manifest differently by subtypes and by sex. The objectives were to identify depressive symptom subtypes, examine sex differences across subtypes, and evaluate clinical correlates. Methods: Eligible participants (n=4490) were enrolled in the Osteoarthritis Initiative (OAI) and had or were at risk for symptomatic knee OA. Latent class analysis was applied to symptomology measured by the 20-Item...
Smoking Significantly Reduces Effectiveness and Long-Term Survival of Biologic Treatment in Patients with Rheumatoid Arthritis

Roger Rolon Campuzano1, Andrea Lujan Coronel Ale1, Osvaldo Luis Cerda1, Fernando Dal Pra1, Emilce E Schneeberger1, María de los Angeles Correa2, Marcos Rosemffet1, Emilio Buschiazzo3, Rodrigo Garcia Salinas4, Silvia Papasidero5, Belén Barrios5, Hernán Maldonado Ficco6 and Gustavo Citera7, 1Section of Rheumatology, Instituto de Rehabilitación Psicofísica, Buenos Aires, Argentina, Buenos Aires, Argentina, 2Section Rheumatology, Instituto de Rehabilitación Psicofísica, Buenos Aires, Argentina, Buenos Aires, Argentina, 3Section of Rheumatology, Hospital Señor del Milagro, Salta, Argentina, Salta, Argentina, 4Section of Rheumatology, Hospital Italiano de La Plata, Buenos Aires, Argentina, La Plata, Argentina, 5Section of Rheumatology, Hospital General de Agudos “Dr. E. Tornú”, Buenos Aires, Argentina, Buenos Aires, Argentina, 6section of Rheumatology, Clínica Regional del Sud, Córdoba, Argentina, Córdoba, Argentina, 7Section of Rheumatology, Instituto de Rehabilitación Psicofísica, Buenos Aires, Argentina, Buenos Aires, Argentina

Center for Epidemiological Studies Depression Scale to identify homogenous subtypes with similar patterns of depressive symptoms at study enrollment. Subtype prevalence and item-response probabilities, an indicator of severity within subtype, were estimated separately in men and women. Posterior probability estimates were used to assign each participant to the subgroup for which he or she had the highest probability of membership. Clinical characteristics, including body mass index (BMI), Charlson comorbidity, gait speed, analgesic use, pain severity, and radiographic evidence of knee OA (Kellgren-Lawrence grade ≥ 2), were compared across subtypes by sex. Results: Four depressive symptom subtypes were identified: “No Symptoms,” “Moderate,” “Moderate-Melancholic,” and “Severe.” Item-response probabilities and prevalence estimates significantly differed by sex (P = <0.001). “No Symptoms” was more common in men (79.8%) than women (77.5%) and had low item-response probabilities across all symptoms. “Moderate” was characterized by sadness and anhedonia and occurred more frequently in men (12.2%) than women (11.2%); however, item-response probabilities were higher in women, indicating greater severity. “Moderate-Melancholic” and “Severe” were differentiated from other subtypes by fatigue, loss of appetite, and insomnia and were more common in women (7.0% and 4.2%, respectively) than men (6.4% and 1.7%, respectively); yet, item-response probabilities were higher in men, suggesting greater severity. Comorbidity scores, gait speed, pain scores, and analgesic use were significantly associated with subtype membership among both sexes; radiographic evidence of knee OA was only significant in men, while BMI was only significant in women (Table 1). Conclusion: Study findings indicate the presence of four distinct depressive symptom subtypes that differ in prevalence and clinical presentation by sex among persons who have or are at risk for symptomatic knee OA. Understanding variation in concurrent depressive symptoms among knee OA patients will help inform tailored treatment strategies.

Table 1. Baseline clinical characteristics among men and women enrolled in the Osteoarthritis Initiative by depressive symptom subtype (N=4490).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Men (n=1881)</th>
<th>Women (n=2609)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No Symptoms</td>
<td>Moderate</td>
</tr>
<tr>
<td>(n % or mean sd)</td>
<td>(n=1540)</td>
<td>(n=208)</td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>28.75  4.07</td>
<td>28.93  4.26</td>
</tr>
<tr>
<td>Charlson Comorbidity</td>
<td>0.39  0.89</td>
<td>0.52  1.03</td>
</tr>
<tr>
<td>Gait Speed</td>
<td>1.37  0.20</td>
<td>1.31  0.22</td>
</tr>
<tr>
<td>Analgesic Use</td>
<td>406  26.50</td>
<td>58  27.90</td>
</tr>
<tr>
<td>WOMAC Pain</td>
<td>1.86  2.70</td>
<td>2.62  3.70</td>
</tr>
<tr>
<td>K-L Grade ≥ 2</td>
<td>613  39.80</td>
<td>98  47.10</td>
</tr>
</tbody>
</table>

Table 1. Baseline clinical characteristics among men and women enrolled in the Osteoarthritis Initiative by depressive symptom subtype (N=4490).

<table>
<thead>
<tr>
<th>Variable</th>
<th>No Symptoms</th>
<th>Moderate</th>
<th>Moderate-Melancholic</th>
<th>Severe</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n % or mean sd)</td>
<td>(n=2086)</td>
<td>(n=268)</td>
<td>(n=145)</td>
<td>(n=110)</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>28.14  5.07</td>
<td>29.37  5.63</td>
<td>29.57  6.04</td>
<td>30.39  6.15</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Charlson Comorbidity</td>
<td>0.31  0.68</td>
<td>0.55  1.07</td>
<td>0.60  1.13</td>
<td>0.68  0.94</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gait Speed</td>
<td>1.32  0.21</td>
<td>1.25  0.21</td>
<td>1.21  0.26</td>
<td>1.18  0.22</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Analgesic Use</td>
<td>667  32.00</td>
<td>96.00 36.00</td>
<td>64  44.40</td>
<td>58  52.70</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>WOMAC Pain</td>
<td>2.16  2.99</td>
<td>3.25  3.88</td>
<td>3.87  4.51</td>
<td>4.43  4.63</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>K-L Grade ≥ 2</td>
<td>897  43.00</td>
<td>132  49.30</td>
<td>73  50.30</td>
<td>51  46.40</td>
<td>0.093</td>
</tr>
</tbody>
</table>

BMI, body mass index; K-L, Kellgren-Lawrence; SD, standard deviation; WOMAC, Western Ontario & McMaster Universities Osteoarthritis Index.

Disclosure: A. Rathbun, None; M. Schuler, RAND, 3; E. Stuart, None; M. Shardell, None; M. S. Yau, None; M. Hochberg, None.


Abstract Number: 1007
Background/Purpose: The introduction of biological agents has been an important advance in the treatment of RA. However, they are not exempt from adverse events and their high cost limits access and maintenance of treatment in many circumstances. Our aim was to evaluate the biological treatment patterns in RA patients and their accumulated survival and long-term efficacy using the LUNDEX index.

Methods: Patients ≥ 18 years of age who met ACR/EULAR 2010 criteria for RA and who had started their first biological disease modifying drugs (b-DMARD) between 01/2006 and 12/2017 were included. Socio-demographic variables such as age, sex, employment status, marital status, health coverage, education and number of cohabitants, as well as comorbidities, smoking status (current, past), date of onset of symptoms, disease characteristics and previous DMARDs treatment were recorded. Disease activity and functional capacity were assessed before and after biologic treatment using CDAI and HAQ, respectively. Cumulative drug survival was assessed by Kaplan Meier curves and comparisons using log Rank. LUNDEX was calculated as the product of efficacy (CDAI remission or low disease activity) and percentage of patients who continued to receive biological treatment at different cut-off times.

Results: 347 patients were included, 89.6% were female, median age was 57.80 years (IQR 48-65), 96.5% had positive rheumatoid factor and 60.8% had positive anti-CCP. 70.6% of patients had health insurance, 79.8% were smokers and 47% of them had comorbidities. The first bDMARD was etanercept in 46.8%, adalimumab (ADA) 28.9, certolizumab 7.2%, abatacept 6.4%, golimumab 4.3, tocilizumab 2.6%, rituximab 2.3% and infliximab 1.4%. Only 5.6% of patients received mono-therapy, 53.9% of patients discontinued treatment with bDMARD, and the causes of discontinuation were: lack of provision (33.5%), inefficacy (33%), adverse events (20.3%). Out of the available data the most frequent adverse event was infection. The median survival of the first biological was 31 months (95%CI: 21.8-40.1), without differences between different drugs. CDAI significantly improved over time. Lundex was 45.5% at 6 months and 41.1% at one year. CDAI at 6 months was significantly lower in non smokers vs smokers (11.37±9.6 vs 17.71±14, p=0.03). In Cox regression analysis, smoking status (HR 1.8, 95%CI:1.2-2.8) and younger age (HR: 0.98, 95%CI: 0.96-0.99) were independently associated with lower bDMARD survival rates.

Conclusion: Socioeconomic factors impact on biological survival in our region. Smoking significantly reduces the effectiveness of biological treatment, as well as it reduces drug survival.
mtDNA Cybrids from OA Patients Are Less Efficient Using Glycolysis and Are More Susceptible to Apoptosis Under Stress Conditions

Mercedes Fernandez Moreno1,2, Tamara Hermida-Gómez3, Andrea Dalamao-Fernandez4, M. Eugenia Vazquez Mosquera4, Estefanía Cortés-Pereira1, Morena Scotece4, Sara Relaño-Fernandez5, Ignacio Rego-Pérez1 and Francisco J Blanco6, 1Servicio de Reumatología. Area Genomica. Instituto de Investigación Biomédica de A Coruña (INIBIC). Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidad da Coruña (UDC), A Coruña, Spain, 2CIBER-BBN, Madrid, Spain, 3Rheumatology, INIBIC. Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidad da Coruña (UDC), A CORUÑA, Spain, 4Plataforma de Genómica. Instituto de Investigación Biomédica de A Coruña (INIBIC). Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidad da Coruña (UDC), A Coruña, Spain, 5Servicio de Reumatología. Instituto de Investigación Biomédica de A Coruña (INIBIC). Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidad da Coruña (UDC), A Coruña, Spain, 6Servicio de Reumatología. Instituto de Investigación Biomédica de A Coruña (INIBIC). Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidad da Coruña (UDC). As Xubias, 15006. A Coruña. España, A Coruña, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Genetics, Genomics and Proteomics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Previous studies have showed that chondrocytes from OA patients had mitochondrial alteration in comparison with healthy. However the role of mitochondria in the biological dysfunction of chondrocytes is not totally know. Cybrids are optimal cellular models to study mitochondrial biology and function implications in the cellular behavior, since they carry different mitochondrial variants with the same nuclear background, excluding the variations because of nuclear genome. Purpose: To test the real role of mitochondrial function in OA pathogenesis using mtDNA cybrids.

Methods: mtDNA Cybrids were developed using the cell line 143B.TK- Rho-0 as the nuclear donor, and platelets from patients without and with knee osteoarthritis respectively as mitochondrial donors (N vs OA). The stress response was evaluated analyzed O2− production; percentage of cell survival in presence of H2O2 and the level of apoptotic cells were studied using flow cytometry. The OXPHOS function and glycolytic activity was evaluated by SeaHorse XFp. The metabolic status was evaluated by glucose consumption and lactic acid production.

Results: Cybrids carrying the platelets from OA patients showed significant higher levels O2− than N (36.61% vs 17.79%). Percentage of not viable cell in presence of H2O2 was higher in OA than in N cybrids (40.1 % vs 27.15 %). The percentage of cell in inducing apoptosis condition was higher in OA than in N cybrids (15.68% vs 6.41%). OA cybrids had lower basal respiration (92.07 and 155.5), and maximal respiratory capacity (114.7 and 160.6) than N. The analysis of ATP production was lower in OA than in N cybrids (66.69 vs 101.5). The % spare respiratory capacity for the N was significantly lower than in OA cybrids (107 vs 124.7). Cybrids carrying the mtDNA from OA patients showed higher glucose consumption than N cybrids (43.77 mg/ml vs 31.91 mg/ml) however in the lactic acid production did not exit differences. The glycolytic showed that OA cybrids had lower glycolysis (71.05 vs 85.43) but higher glycolytic reserve than N cybrids (56.60 vs 39.73).

Conclusion: These results showed that the mitochondria obtained from healthy and OA donors had a different behaviour and offer a real rationale for why mitochondria alterations play an important role in OA pathogenesis.

Disclosure: Mercedes Fernandez Moreno, None; Tamara Hermida-Gómez, None; A. Dalamao-Fernandez, None; M. Eugenia Vazquez Mosquera, None; Estefanía Cortés-Pereira, None; Morena Scotece, None; Sara Relaño-Fernandez, None; Ignacio Rego-Pérez, None; Francisco J Blanco, Pfizer Inc, S.
Abstract Number: 1009

Novel Non-Coding RNAs Associated with Rheumatoid Arthritis in Asians By Gene-Based Testing

Aleksander Lenert1 and David W. Fardo2, 1Internal Medicine, Div. of Rheumatology, University of Kentucky, Lexington, KY, 2Biostatistics, College of Public Health, University of Kentucky, Lexington, KY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Genetics, Genomics and Proteomics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Rheumatoid arthritis (RA) is a complex genetics disease driven by multiple genetic contributors as evidenced by association with over 100 risk SNPs by GWAS. However, the majority of risk SNPs are not causal and explain only a small proportion of heritability in RA. Novel approaches for the analysis and interpretation of large-scale genomics data are needed to detect the missing heritability of and gain further insight into RA. Additionally, risk gene and SNP associations differ in European and Asian RA populations (1). Regulatory genetic elements, such as non-coding micro RNAs (miRNA), are thought to play an important role in RA and have been identified by gene-based testing in Europeans with RA (2). Our aim was to identify non-coding genetic elements in Asians with RA with gene-based association testing.

Methods:
Our dataset consisted of 4,873 RA cases and 17,642 controls from GWAS meta-analysis in Asians (1). All RA cases fulfilled the 1987 ACR criteria or were diagnosed by a rheumatologist. We used the Knowledge-based mining system for Genome-wide Genetic studies (KGG v.4) for gene-based association testing using extended Simes procedure (GATES) with SNPs outside the extended MHC [Chr. 6, 25.7-33.3 Mb] (3). Genes were defined as ± 5kb. Genomic control was calculated by median of Chi-square statistic. We accounted for linkage disequilibrium (LD) between SNPs with 1000 Genomes Phase 1 for Asians. Benjamini & Hochberg false discovery rate (FDR) was used to correct for multiple testing. UCSC Genome Browser was used for visualization of findings.

Results:
Our genome analysis build used 6,581,301 million SNPs and a total of 25,550 genes (including 5189 non-coding RNAs); 51.66% of SNPs were located inside genes. A total of 108 genes were found to be significant by GATES (FDR <0.05). Amongst the top genes by GATES, we identified several non-coding RNAs associated with RA in Asians. The significant long non-coding RNAs were TNFRSF14-AS1 (Chr.1 at RA risk locus TNFRSF14-MMEL1), LINC01843 (Chr. 5 near JADE2), LINC00336 (Chr.6 near GGNBP1-BAK1) and LINC001016 (Chr.6 near MLN). The significant miRNAs were MIR3934 (Chr.6 near UQCC2-ITPR3), MIR7159 (Chr. 6 near MLN), MIR4647 (Chr.6 at RA risk locus NFKBIE), MIR3939 (Chr.6 at RA risk locus CCR6), MIR4658 (Chr.7 near C7orf43) and MIR4308 (Chr. 14 near GCH1). There was no overlap of these non-coding RNAs identified in Asians with RA compared with RA in Europeans.

Conclusion:
Through large-scale gene-based association testing, we identified novel non-coding RNA associations specific for RA in Asians. These novel regulatory genetic elements, in addition to established RA risk loci, may improve our understanding of the complex genetics of RA. Non-coding RNAs could also play a role as potential biomarkers and novel drug targets in RA.

References:
Identification of Circulating Biomarkers of Disease Activity and Organ Involvement in ANCA-Associated Vasculitis By Targeted Proteomics

Jun Ishizaki1, Ayako Takemori2, Koichiro Suemori1, Takuya Matsumoto1, Yoko Akita1, Masaki Yasukawa1, Nobuaki Takemori2 and Hitoshi Hasegawa1, 1Department of Hematology, Clinical Immunology and Infectious Diseases, Ehime University Graduate School of Medicine, Ehime, Japan, 2Division of Proteomics Research, Proteo-Science Center, Ehime University, Ehime, Japan
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Genetics, Genomics and Proteomics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Targeted proteomics, which involves quantitative analysis of targeted proteins using selected reaction monitoring (SRM) mass spectrometry, has emerged as a new methodology for discovery of clinical biomarkers. The aim of this study was to identify circulating biomarkers for prediction of disease activity and organ involvement in antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) by using targeted serum proteomics.

Methods: We selected the targeted candidates by an experiment-based approach in which we conducted MS-based serum proteomic profiling of AAV patients before and after treatment. We further selected 87 endothelium-related proteins, which were expected to be present in blood, based on information from publicly available databases. A large-scale SRM assay targeting 135 biomarker candidates was established using a triple quadrupole mass spectrometer coupled with nano-flow liquid chromatography. Target proteins in serum samples from patients in the active and remission (6 months after treatment) stages were quantified using the established assays. Identified marker candidates were further validated by ELISA using serum samples (n=169) collected in a large-cohort Japanese study (RemIT-JAV-RPGN study).

Results: The following proteins were identified as biomarkers for discriminating patients with highly active AAV from those in remission or healthy controls: tenasin C (TNC), C-reactive protein (CRP), tissue inhibitor of metalloproteinase 1 (TIMP1), leucine-rich alpha-2-glycoprotein 1, S100A8/A9, CD93, matrix metalloproteinase 9, and transketolase (TKT). Of these, TIMP1 was the best-performing marker of disease activity, allowing distinction between non-remission (mildly active AAV) and remission. The serum levels of TKT and CD93 were higher in patients with renal involvement than in those without, and predicted renal outcome. The serum level of TNC was elevated significantly in patients with lung infiltration. AAV severity was associated with markers reflecting organ involvement (TKT, CD93 and TNC) rather than inflammation.

Conclusion: We have identified promising biomarkers of disease activity and severity and organ involvement in AAV with targeted proteomics approach using serum samples collected in a large-cohort Japanese study. Especially, our analysis demonstrated the effectiveness of TIMP1 as a marker of AAV activity. In addition, we identified TKT and CD93 as novel markers for evaluation of renal involvement and renal outcome in AAV.

Disclosure: J. Ishizaki, None; A. Takemori, None; K. Suemori, None; T. Matsumoto, None; Y. Akita, None; M. Yasukawa, None; N. Takemori, None; H. Hasegawa, None.


Abstract Number: 1011
Mitochondrial Haplogroups-Mediated Methylation Regulates Apoptosis in Osteoarthritis Cartilage

Ignacio Rego-Pérez1, Estefanía Cortés-Pereira1, Juan Fernández-Tajes Sr.2, Mercedes Fernandez Moreno1, María Eugenia Vazquez Mosquera1, Sara Relaño-Fernandez3, Natividad Oreiro4, Carlos Fernandez-Lopez1 and Francisco J Blanco1, 1Servicio de Reumatología. Area Genómica. Instituto de Investigación Biomédica de A Coruña (INIBIC). Complejo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidade da Coruña (UDC), A Coruña, Spain, 2The Wellcome Trust Center for Human Genetics. McCarthy’s Group. University of Oxford, Oxford, United Kingdom, 3Plataforma de Genómica. Instituto de Investigación Biomédica de A Coruña (INIBIC). Complejo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidade da Coruña (UDC), A Coruña, Spain, 41) Servicio de Reumatología. Instituto de Investigación Biomédica de A Coruña (INIBIC). Complejo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidade da Coruña (UDC). As Xubias, 15006. A Coruña, España, A Coruña, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Genetics, Genomics and Proteomics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Recent studies revealed that haplogroup J associates with a decreased rate of incident knee Osteoarthritis. Among the functional characteristics of this haplogroup, lower rates of apoptosis stand out. In this study we aimed to evaluate if this process is epigenetically regulated.

Methods:
DNA methylation profiling from a previous study performed in knee articular cartilage was obtained from Gene Expression Omnibus database (accession GSE-43191). In that study, cartilage DNA was isolated from 13 samples carrying the haplogroup J and 20 samples carrying the haplogroup H. The differential methylome between J and H haplogroups was obtained using Lumi and Methylumi packages (R bioconductor).

A subsequent validation by RNA-seq was performed in 7 haplogroup J cartilage samples and 9 haplogroup H cartilage samples. Differential expression data between haplogroups were analyzed using Kallisto package (R bioconductor). Gene ontology analyses from methylation and expression approaches were performed using DAVID (https://david.ncifcrf.gov/).

Results:
Gene ontology analysis of the 538 differentially methylated regions between haplogroups J and H revealed that genes involved in the negative regulation of apoptosis (p=0,021) and catalytic activity (p=0,036) were hypomethylated in haplogroup J cartilages. On the contrary, haplogroup H cartilages showed a enrichment of hypomethylated genes involved in the positive regulation of apoptosis (p=0,008); an enrichment of hypomethylated genes involved in the negative regulation of the metabolic processes of nitrogen compounds (p=0,03) and macromolecules (p=0,026) was detected in haplogroup H cartilages.

Subsequent validation by RNA-seq revealed 416 differentially expressed genes between haplogroups H and J, considering an adjusted p-value≤0,005 as well as a logFc≥±4 (Figure 1). Of these genes, 362 were up-regulated in haplogroup J cartilages and 54 up-regulated in haplogroup H. Among the most differentially altered biological processes, an enrichment of over-expressed genes involved in the positive regulation of apoptosis (p=0,047) and cellular adhesion (p=0,0018) was detected in haplogroup H cartilages. On the contrary, an enrichment of up-regulated genes involved in lipid synthesis (p=0,044), Calcium homeostasis (p=0,047), cell signaling (p=0,00031) and immune system development (p=0,0092) was detected in haplogroup J cartilages.

Conclusion:
Mitochondrial haplogroups J and H induce specific methylation and expression profiles in cartilage samples that lead to an epigenetic regulation of apoptosis, being more repressed in cartilages with J haplogroup and more active in cartilages with H haplogroup.
Analysis of microRNAs in Familial Mediterranean Fever

Gil Amarilyo, Nir Pillar, Ilan Ben-Zvi, Daphna Weissglas-Volkov, Jonatan Zalcman, Liora Harel and Noam Shomron

Schneider Children's Medical Center of Israel, Sackler School of Medicine, Tel Aviv University, Petach Tikva, Israel, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel, Chaim Sheba Medical Center, Tel Hashomer, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel, Schneider Children's Medical Center of Israel, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Genetics, Genomics and Proteomics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Familial Mediterranean Fever (FMF) is thought to be inherited as an autosomal recessive trait. However, there are frequent deviations from this model. The aim of this study was to explore epigenetic modifications in patients with FMF.

Methods: Ten patients diagnosed with FMF according to the Tel-Hashomer criteria were recruited from the rheumatology outpatient clinic of Sheba Medical Center, Tel Hashomer, Israel. All patients were homozygous for the M694V mutation, the most common mutation in FMF, and all had the most severe phenotype of the disease. All were in the quiescent phase at the time of the study. Total RNA was drawn from peripheral blood and profiled for microRNA expression using NanoString nCounter technology. Findings were compared to 10 healthy age- and sex-matched control subjects. Statistical analyses were conducted using R software, version 3.2.
preprocessing and normalization followed by differential expression analysis were performed using the R package DESeq2 (25516281) and in house scripts. A priori $P$ values were adjusted for false discovery rate (FDR).

**Results:** Of the 798 mature human miRNAs probed, 103 exhibited reasonable expression levels in these cells. Seven were found to be significantly deregulated in the patients with FMF: three were significantly downregulated compared to control samples (miR-107, let−7d−5p, and miR-148b-3p), and four were significantly upregulated (miR-144-3p, miR-21−5p, miR−4454 and miR-451a), all with an adjusted $P$ value of $<0.01$ (Figure 1).

To ensure that the observed changes were true biological effects and not technical artifacts, we performed Taqman quantitative real time polymerase chain reaction (qRT-PCR) analysis of two of the differentially expressed miRNAs between the patients and controls. Each miRNA was quantified in each sample, and its expression level was normalized to the reference RNA, U6-snRNA. In both groups, the direction of effect and the miRNA expression patterns in the NanoString analysis were consistent with the Taqman measurements ($R^2=0.93$)

**Conclusion:** We identified significant epigenetic changes in patients with clinically quiescent FMF. Further research is warranted in order to elucidate critical FMF manifestation such as susceptibility to early disease, disease severity, risk of the development of amyloidosis, and resistance to colchicine. All these factors might be ultimately explained, at least in part, by epigenetic modifications.

---

**Figure 1**

---

**Disclosure:** G. Amarilyo, None; N. Pillar, None; I. Ben-Zvi, None; D. Weissglas-Volkov, None; J. Zalcman, None; L. Harel, None; A. Livneh, None; N. Shomron, None.


**Abstract Number:** 1013

**HLA-Class II Associations with ANCA-Associated Vasculitis in the Japanese Population: Different Features from European Populations**

Aya Kawasaki$^1$, Fumio Hirano$^2$, Ken-ei Sada$^3$, Shigeto Kobayashi$^4$, Hidehiro Yamada$^5$, Hiroshi Furukawa$^1$, Kenji Nagasaka$^6$, Takahiko Sugihara$^7$, Kunihiro Yamagata$^8$, Takayuki Sumida$^9$, Shigeto Tohma$^{10}$, Shoichi Ozaki$^5$, Seiichi Matsuo$^{11}$, Hiroshi Hashimoto$^{12}$, Hirofumi Makino$^{13}$, Yoshihiro Arimura$^{14}$, Masayoshi Harigai$^{15}$ and Naoyuki Tsuchiya$^1$. $^1$Molecular and Genetic Epidemiology Laboratory, University of Tsukuba, Faculty of Medicine, Tsukuba, Japan, $^2$Departments of Rheumatology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan, $^3$Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical
Background/Purpose: HLA-class II region harbors the strongest genetic factors for ANCA-associated vasculitis (AAV), and differences in the genetic background of HLA-class II may partly explain the epidemiologic differences in AAV between European and Asian populations. HLA-DPB1*04:01, highly prevalent in the European populations, is associated with granulomatosis with polyangiitis (GPA)/PR3-AAV prevalent in the European populations, whereas DRB1*09:01, almost exclusively distributed in Asian populations, is associated with microscopic polyangiitis (MPA)/MPO-AAV, which account for the majority of AAV in Japan. Of interest, although DRB1*09:01 is very rare in the European populations, genome-wide association study (GWAS) detected significant association of a single nucleotide polymorphism (SNP) rs5000634 between DQB1 and DQA2 loci with MPA/MPO-AAV. Whether this association is independent from HLA alleles has not been reported. Another unique feature in Japanese AAV is that only half of the patients with GPA are positive for PR3-ANCA, and the other half are positive for MPO-ANCA. This provides a valuable opportunity to distinguish whether the genetic factors are associated with clinical classification of GPA or ANCA specificity. In the present study, we addressed these two issues in Japanese patients with AAV.

Methods: HLA-DRB1 and DPB1 were genotyped using high-resolution allele typing, and rs5000634 using TaqMan SNP assay. Association was tested in 467 Japanese AAV patients (clinical classification: MPA [285], GPA [92], eosinophilic GPA [56], unclassifiable [34], ANCA specificity: MPO-AAV [376], PR3-AAV [62]) and 596 healthy controls. Among GPA, 36 were single positive for PR3-ANCA (PR3-GPA) and 35 were single positive for MPO-ANCA. The association of DRB1 alleles remained significant after conditioned on rs5000634. When the associations of DRB1 and DPB1 were examined in MPO-GPA and PR3-GPA (Table 2), DPB1*04:01 was associated with PR3-GPA, but slightly decreased in MPO-GPA. In contrast, association of DRB1*08:02 was observed in MPO-GPA, but not in PR3-GPA.

Results: As shown in Table 1, rs5000634A was slightly decreased in MPO-AAV and MPA. However, when conditioned on DRB1*09:01 or DRB1*13:02, the association was no longer significant, while the association of DRB1 alleles remained significant after conditioned on rs5000634. When the associations of DRB1 and DPB1 were examined in MPO-GPA and PR3-GPA (Table 2), DPB1*04:01 was associated with PR3-GPA, but slightly decreased in MPO-GPA. In contrast, association of DRB1*08:02 was observed in MPO-GPA, but not in PR3-GPA.

Conclusion: In Japanese AAV, the genetic contribution of HLA-DQ region GWAS SNP was the secondary one caused by linkage disequilibrium with HLA-DRB1 alleles. Striking differences in HLA-DRB1 and DPB1 associations were observed between MPO-GPA and PR3-GPA, suggesting that HLA may be more strongly associated with ANCA specificity than with clinical classification of GPA.
Table 1. The association of European GWAS SNP rs5000634 with MPA/MPO-AAV was secondary to DRB1 association in the Japanese population.

<table>
<thead>
<tr>
<th></th>
<th>unconditioned</th>
<th>Conditioned on DRB1*09:01</th>
<th>Conditioned on DRB1*13:02</th>
<th>Conditioned on rs5000634</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P</td>
<td>OR (95%CI)</td>
<td>P</td>
<td>OR (95%CI)</td>
</tr>
<tr>
<td>MPO-AAV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DRB1*09:01</td>
<td>1.6E-04</td>
<td>1.58 (1.25-2.00)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>DRB1*13:02</td>
<td>7.0E-05</td>
<td>0.43 (0.28-0.65)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>rs5000634</td>
<td>0.044</td>
<td>0.82 (0.68-1.00)</td>
<td>0.64</td>
<td>0.95 (0.77-1.17)</td>
</tr>
<tr>
<td>MPA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DRB1*09:01</td>
<td>6.4E-04</td>
<td>1.56 (1.21-2.02)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>DRB1*13:02</td>
<td>1.1E-03</td>
<td>0.47 (0.30-0.74)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>rs5000634</td>
<td>0.074</td>
<td>0.83 (0.68-1.02)</td>
<td>0.67</td>
<td>0.95 (0.76-1.19)</td>
</tr>
</tbody>
</table>

Conditional logistic regression analysis was performed under the additive model. OR: odds ratio, CI: confidence interval.

Table 2. Differential association of DRB1*08:02, DRB1*13:02 and DPB1*04:01 with PR3-ANCA single positive GPA and MPO-ANCA single positive GPA.

<table>
<thead>
<tr>
<th></th>
<th>PR3-GPA</th>
<th>MPO-GPA</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AF (%)</td>
<td>P</td>
<td>OR(95%CI)</td>
</tr>
<tr>
<td>DRB1*08:02</td>
<td>1.4</td>
<td>0.72</td>
<td>0.49 (0.07-3.67)</td>
</tr>
<tr>
<td>DRB1*13:02</td>
<td>8.3</td>
<td>1.0</td>
<td>0.93 (0.39-2.20)</td>
</tr>
<tr>
<td>DPB1*04:01</td>
<td>13.9</td>
<td>0.025</td>
<td>2.39 (1.18-4.85)</td>
</tr>
</tbody>
</table>

AF: allele frequency, PR3-GPA: PR3-ANCA positive, MPO-ANCA negative GPA, MPO-GPA: MPO-ANCA positive, PR3-ANCA negative GPA, OR: odds ratio, CI: confidence interval. P values were calculated by Fishers exact test.

Disclosure: A. Kawasaki, None; F. Hirano, Chugai Pharmaceutical Co., Ltd.; Ono Pharmaceuticals; Mitsubishi Tanabe Pharma Co.; UCB Japan; CSL Behring; Towa Pharmaceutical Co., Ltd.; Abbvie Japan Co., Ltd.; Japan Blood Products Organization; Ayumi
The Rheumatic Disease Data Refinery: A Case Study in Integrative Genomics Reveals Complex IFN Signatures in Therapeutic Studies in SLE

Jaclyn N Taroni and Casey S. Greene, Systems Pharmacology and Translational Therapeutics, University of Pennsylvania, Philadelphia, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Genetics, Genomics and Proteomics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Over the past 15 years, more than 10,000 whole tissue biopsies from patients with rheumatic diseases have been deposited into publicly available gene expression databases. Often rheumatic diseases are studied in isolation, but these data can be harnessed to characterize the full catalog of shared molecular patterns perturbed in these disease states. We present plans for a rheumatic disease transcriptomic compendium (Fig 1) and demonstrate feasibility through a case study in SLE whole blood gene expression data.

Methods: We curated experiments from studies of rheumatic diseases from ArrayExpress. For our SLE whole blood case study, we selected 8 experiments from multiple platforms, including data from 2 clinical trials examining the effects of treatments modulating IFN (Lauwerys, et al. Arthritis Rheumatol. 2013; Welcher, et al. Arthritis Rheumatol. 2015.). Cross-platform normalization using quantile normalization was performed. Interferon module gene sets from Chiche, et al. Arthritis Rheumatol. 2014. and unsupervised machine learning algorithms were used to examine the change in IFN signatures during treatment and the overall data structure during the integration process. This is, to our knowledge, the first application of the Chiche, et al. whole blood modular framework to these trials.

Results: We demonstrate that it is possible to integrate SLE whole blood data from multiple platforms and studies and retain underlying biology. We find that expression of Type I IFN module genes are altered following the treatment with the therapeutic vaccine IFN-alpha-kinoid in patients with high baseline Type I signatures, consistent with the therapeutics mechanism of action and the original study (Fig 2). We also find that only putative Type II modules are altered during blockade of IFN-gamma.

Conclusion: We have established the feasibility of a rheumatic disease gene expression compendium that is an order of magnitude larger than any single publicly available experiment. Our results further support the utility of data-driven cross-disease modules and suggest that unsupervised approaches can yield insight into complex molecular patterns altered in rheumatic diseases (Fig 1).
1. Curate over 100 individual experiments sampling multiple tissues and rheumatic diseases

2. Integrate over 10,000 individual samples into a unified rheumatic disease compendium

3. Perform unsupervised machine learning with denoising autoencoders to obtain comprehensive map of perturbed molecular patterns

Fig 1. Overview of the Rheumatic Disease Data Refinery.

Fig 2. Summarized expression values (change from baseline) of IFN modules during treatment with IFN-kinoid (data from Lauwerys, et al. Arthritis Rheumatol. 2013.). Patients were stratified into the following groups: placebo, those with a low Type I (M1.2) signature at base (IFN-negative), and those with a high M1.2 signature at baseline.

Disclosure: J. N. Taroni, None; C. S. Greene, None.


Abstract Number: 1015
Key Genes and Pathways between Rheumatoid Arthritis and Osteoarthritis By Integrative Genome-Wide Gene Expression Profiling Analysis

Rongqiang Zhang¹,², Aimin Yang³, Xiaomei Ren², Jie Zhang³, Xiaoli Yang⁴, Qiling Liu², Na Sun², Puwei Yuan⁵ and Yongmin Xiong⁴,¹School of Public Health, Xi'an Jiaotong University Health Science Center, Key Laboratory of Trace Elements and Endemic Diseases of the National Health and Family Planning Commission, Xi'an 710061, China, Xi'an, China, ²Shaanxi University of Chinese Medicine, Xianyang 712046, China, Xianyang, China, ³School of Public Health, Brown University, Providence, RI 02906, US, Providence, RI, ⁴School of Public Health, Xi'an Jiaotong University Health Science Center, Key Laboratory of Trace Elements and Endemic Diseases of the National Health and Family Planning Commission, Xi'an 710061, China, Xian, China, ⁵Shaanxi University of Chinese Medicine, Xianyang 712046, China, XianYang, China

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Genetics, Genomics and Proteomics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Rheumatoid arthritis (RA) and Osteoarthritis (OA) are two most common types of joint diseases with lots of similar symptoms, and their pathological mechanisms remain largely unknown. Although some key genes and diagnostic markers have been identified by microarray, these biomarkers still cannot reveal the complicated pathogenesis of RA and OA entirely. We conducted a novel integrative analysis of identification the key biomarkers of synovial tissue from RA and OA patients to better understand their difference.

Methods: After screening NCBI GEO database, 3 new expression profiling datasets (GSE 55235, GSE 55584, GSE 55457) met the eligibility criteria (from synovial tissue of RA and OA patients diagnosed according to American Rheumatism Association 1987 revised criteria, detected by the same platform, and sample size >15). A global normalization was performed to minimize the data inconsistency and heterogeneity. Differentially expressed genes (DEGs, p<0.05, FDR<0.05, Fold Change>2) between RA and OA from the 3 datasets were explored by R v3.4.0 software. Gene Ontology and KEGG pathway analysis of the DEGs were conducted by Cytoscape 3.4.0. Protein-protein interaction (PPI) network of the DEGs was obtained from STRING database v9.05.

Results: 375, 242 and 264 DEGs from GSE 55235, GSE 55584 and GSE 55457 datasets were obtained, respectively. Among them, 81 DEGs presented identical expression trends in the 3 datasets, including 50 up-regulated genes (IGHG1, GUSBP11, STAT1, et al) and 31 down-regulated genes (SCRG1, MAB21L2, GHR, et al). The DEGs mainly involved in negative regulation of I-kappa B kinase/NF-kappa B signaling, cellular response to vitamin D pathway, et al(Fig. 1). STAT1 and GHR were the cores of PPI networks of 50 up-regulated proteins and 31 down-regulated proteins, respectively (Fig. 2).

Conclusion: Several apoptosis and vitamin D related pathways were more closely related to RA than OA, which suggested that antioxidative stress therapy and vitamin D might be more effective for RA. STAT1 and GHR (both relate to bone metabolism) are the key genes presenting statistical significant difference between RA and OA. This study provides novel insights into the molecular mechanisms underlying RA and OA, thereby aiding the diagnosis and treatment of the diseases. Well-designed, well-controlled and dependent experiments are needed in future to validate the findings of the present study.

Fig. 1. Networks of key pathways related to RA
Fig. 2. PPI networks of up-regulated (A) and down-regulated DEGs (B)

Disclosure: R. Zhang, None; A. Yang, None; X. Ren, None; J. Zhang, None; X. Yang, None; Q. Liu, None; N. Sun, None; P. Yuan, None; Y. Xiong, None.


Abstract Number: 1016

The Genetic Biomarkers to Predicting Response of TNF Inhibitors Treatment in Rheumatoid Arthritis

So-Young Bang, Youngho Park, Kwangwoo Kim, Young Bin Joo, Soo-Kyung Cho, Chan-Bum Choi, Yoon-Kyoun Sung, Tae-Hwan Kim, Jae-Bum Jun, Hye-Soon Lee and Sang-Cheol Bae, Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), Department of Biology, Kyung Hee University, Seoul, Korea, Republic of (South), Internal Medicine, Department of Rheumatology, St. Vincent's Hospital, The Catholic University of Korea, Suwon, Gyeonggido, Korea, Republic of (South), Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), Hanyang University Guri Hospital, Gyeonggi-do, Korea, Republic of (South), Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Genetics, Genomics and Proteomics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Although pharmacogenetic studies of TNF inhibitors (TNFi) response presented the estimates of high heritability, only few loci with suggestive weak association as biomarkers for TNFi response have been identified. We aimed to identify optimal phenotype for drug response using heritability estimates (h²) and new predictive biomarkers of response to TNFi using genome-wide association studies (GWAS) in the Korean population.

Methods: Disease Activity Scores based on 28 joint counts (DAS28) and Clinical Disease Activity Index (CDAI) were assessed at baseline, and after 6 months in 370 Korean RA patients who started TNFi due to moderate or high disease activity from Hanyang university hospital. Genotypes were generated on the Illumina HumanOmni2.5Exome array (2.5 million variants). Quality control (QC) procedures were applied using the PLINK 1.9 and R 3.2.2 software. We estimated heritability by a linear mixed effect modeling approach (GCTA) for TNFi response using changes (Δ) in DAS28 and CDAI. To identify clinical and genetic variables that influence response to TNFi, a multivariate generalized linear model (GLM) analysis was performed. We also conducted a gene-based analysis [optimal sequence kernel association test (SKAT-O)] of rare variants.
Results: We identified that clinical factors seem to influence the therapeutic good response of TNFi including male, high disease activity score at baseline, BMI. The heritability estimates were found for ΔDAS28 h²=0.44, ΔCDAI h²=0.62, Δprovider global assessment of disease activity (PrGA) h²=0.66, Δswollen joint count (SJC) h²=0.66, Δtender joint count (TJC) h²=0.59, Δpatient global assessment of disease activity (PtGA) h²=0.58, and ΔESR h²=0.49. We identified two novel significant functional SNPs [rs117811759 (UTR3 of SAP18), rs17279819 (exon of SKA3)] associated with response to TNFi, surpassing genome-wide significant threshold (P < 5.0×10−8). Using a gene-based approach, we also identified two genes (SAP18 and SKA3) with significant burden signals after correction for multiple comparisons.

Conclusion: The optimal phenotype based on heritability suggests the use of changes in clinical disease activity index (CDAI) including provider global assessment than DAS28 in pharmacogenetic study. Our study suggests that SAP18 and SKA3 associated with response to TNFi therapy may serve as the useful genetic biomarker in RA patients of Koreans.

Disclosure: S. Y. Bang, None; Y. Park, None; K. Kim, None; Y. B. Joo, None; S. K. Cho, None; C. B. Choi, None; Y. K. Sung, None; T. H. Kim, None; J. B. Jun, None; D. H. Yoo, Celltrion Inc., 5; H. S. Lee, None; S. C. Bae, None.


Abstract Number: 1017

Investigation of Differential Methylation As a Potential Biomarker of Methotrexate Response in Patients with Rheumatoid Arthritis

Nisha Nair1, Darren Plant2,3, Suzanne M Verstappen1, John D Isaacs4, Ann W. Morgan5, Kimme L. Hyrich6, Anne Barton7 and Anthony G. Wilson8, 1Arthritis Research UK Centre of Genetics and Genomics and Centre of Epidemiology, Manchester, United Kingdom, 2Arthritis Research UK Centre for Genetics and Genomics, The University of Manchester, Manchester, United Kingdom, 3NIHR Manchester Musculoskeletal BRU, Central Manchester Foundation Trust and University of Manchester, Manchester Academic Health Science Centre, Manchester, United Kingdom, 4Institute of Cellular Medicine, Newcastle University, Newcastle-upon-Tyne, United Kingdom, 5NIHR-Leeds Musculoskeletal Biomedical Research Unit, Leeds, United Kingdom, 6National Institute of Health Research Manchester Musculoskeletal Biomedical Research Centre, Central Manchester NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, United Kingdom, 7Arthritis Research UK, Centre for Genetics and Genomics, Centre for Musculoskeletal Research, Manchester Academic Health Sciences Centre, The University of Manchester, Manchester, United Kingdom, 8UCD School of Medicine and Medical Science, Conway Institute, University College Dublin, Dublin, Ireland

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Genetics, Genomics and Proteomics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Methotrexate (MTX) is the first-line disease modifying anti-rheumatic drug for the treatment of rheumatoid arthritis (RA). However, many patients do not respond adequately or experience adverse effects, therefore identifying blood-based biomarkers that predict treatment response is a clinical priority. DNA methylation is an epigenetic marker that modifies, but does not alter, DNA sequence, and it is thought that MTX may act, at least in part, by inhibiting intracellular methyl donor status leading to DNA hypomethylation. We aimed to identify differential DNA methylation signatures in whole blood, which may be predictive of response to MTX in patients with RA.

Methods: DNA methylation was measured using the HumanMethylation450 BeadChip in DNA samples from individuals recruited to the Rheumatoid Arthritis Medication Study (RAMS), a one year observational study in the UK including patients with RA starting MTX for the first time. In RAMS, demographic and clinical data are collected prior MTX start (baseline) and at 6 months after commencing MTX. DNA was extracted from whole blood samples collected baseline and at 4 weeks from patients who, at 6 months, had a EULAR good response (n=36) or EULAR poor response (n=36) to MTX (test cohort). Differentially methylated positions (DMPs) between the baseline and 4 weeks, and between good and poor response were identified using linear regression, adjusting for gender, age, cell composition, baseline disease activity score (DAS28), and smoking status. Analyses also compared methylation with changes in DAS28 and the individual DAS28 components over 6 months. DMPs that showed significant differences in the test cohort
were selected for replication by pyrosequencing in an independent group of 100 patients with both baseline and 4 week samples (replication cohort).

**Results:** In the test cohort, differential methylation at 2 CpG sites in samples taken at 4 weeks was associated with response status determined at 6 months (p-value <10^-5). Three additional DMPs were associated with change in tender joint count, whilst three other DMPs were associated with change in swollen joint count, and a further four DMPs associated with change in C-reactive protein. One of the 4 DMPs associated with change in CRP, cg04334751, showed a trend to association in the independent replication cohort (Spearmans Rho p-value =0.058). This CpG site is located close to microRNA, mir182.

**Conclusion:** These preliminary results suggest DNA methylation may provide a biomarker of MTX response but requires additional replication in other cohorts and testing in a prospective study of patients starting MTX for the first time.

**Disclosure:** N. Nair, None; D. Plant, None; S. M. Verstappen, None; J. D. Isaacs, None; A. W. Morgan, None; K. L. Hyrich, None; A. Barton, None; A. G. Wilson, None.


**Abstract Number: 1018**

**Comprehensive Identification of Differentially Methylated Regions Associated with Systemic Sclerosis in Dermal Fibroblasts from African-American Patients**

Paula S. Ramos1,2, Willian da Silveira3, E. Starr Hazard3, Ilia Atanelishvili4, Robert C. Wilson5, Jim C. Oates1, Galina S. Bogatkevich4 and Gary Hardiman1,2,3, 1Department of Medicine, Medical University of South Carolina, Charleston, SC, 2Department of Public Health Sciences, Medical University of South Carolina, Charleston, SC, 3Center for Genomic Medicine, Medical University of South Carolina, Charleston, SC, 4Division of Rheumatology and Immunology, Department of Medicine, Medical University of South Carolina, Charleston, SC, 5Department of Pathology and Laboratory Medicine, Medical University of South Carolina, Charleston, SC

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Genetics, Genomics and Proteomics Poster II  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The etiology and reasons underlying the ethnic disparities in systemic sclerosis (SSc) remain unknown. African-Americans are disproportionately affected by SSc, yet dramatically underrepresented in research. The role of DNA methylation in disease risk remains unclear. This analysis was conducted to comprehensive identify differentially methylated loci associated with SSc in AA.

**Methods:** Genomic DNA was isolated from cultured dermal fibroblasts isolated from 15 AA SSc cases and 15 AA controls. All patients met the 2013 ACR/EULAR classification criteria for SSc, most (93%) presenting with diffuse cutaneous SSc. DNA methylation patterns were profiled through reduced representation bisulfite sequencing (RRBS). Alignment and methylation calling were performed using Bismarck v0.16.3 and the GRCh37/hg19 reference genome. Data was filtered, normalized, and analyzed with RnBeads v1.6.1. Differential methylation analysis was conducted on CpG, promoter, gene and system level.

**Results:** We generated DNA methylation data for over 5 million CpGs in each sample with at least 40x coverage in promoter and CpG islands. Using the Combined Score approach implemented in RnBeads, a total of 97 CpG islands, 197 genes and 112 promoters showed significant differential enrichment in methylation levels between cases and controls. The top differentially methylated loci include, among others, the promoter of SERPINA1 (a protease inhibitor of elastase, plasmin, thrombin and trypsin) and SERPINA3, SERPINA4, SERPINA5, SERPINA11 and SERPINA13P. The SERPIN superfamily is characterized by its function as chaperone proteins and its roles in inflammation and immune function. Enrichment analysis revealed that both hypo- and hypermethylated genes and their promoter regions were enriched for differentiation and immune-related gene ontology terms (hypomethylated regions: IL2-mediated signaling pathway, P=5E-3; and mesenchymal cell differentiation, P=3E-4; hypermethylated regions: type I IFN signaling pathway, P=8E-4; and positive regulation of cell differentiation, P=1E-3).

**Conclusion:** We observed dramatic DNA methylation differences between cases and controls. Interestingly, most of the dysregulated genes can be placed in immune pathways, supporting the role of immune dysregulation in triggering the fibrosis characteristic of SSc.
These add to previous reports of mostly European-Americans that report an enrichment of extracellular matrix-receptor interaction and focal adhesion genes. These data support a role for DNA methylation differences in mediating susceptibility to SSc in AA, and a potentially stronger immune-driven etiology in AA.

Disclosure: P. S. Ramos, None; W. da Silveira, None; E. S. Hazard, None; I. Atanelishvili, None; R. C. Wilson, None; J. C. Oates, None; G. S. Bogatkevich, NIH/NIAMS P60 AR062755, 2, Scleroderma Foundation, 2; G. Hardiman, None.

Abstract Number: 1019

Molecular Profiling of RA Patients Suggests a Differential Involvement of Adaptive and Innate Cell Populations in Response to Anti-TNF Treatment

Victor Farutin1, Thomas Prod'homme1, Kevin McConnell1, Nathaniel Washburn1, Patrick Halvey1, Jamey Guess1, Nur Sibel Gunay1, Jan Hillson2, Carol J. Etzel3, Katherine C. Saunders3, Dimitrios A. Pappas3,4, Anthony Manning1, Leona Ling1 and Ishan Capila1,
1Research, Momenta Pharmaceuticals, Inc., Cambridge, MA, 2Clinical Research, Momenta Pharmaceuticals, Inc., Cambridge, MA, 3Corrona, LLC, Southborough, MA, 4Columbia University, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Genetics, Genomics and Proteomics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Despite the success of anti-TNF therapies in RA, ~ 30 % of patients are non-responders. Several studies have focused on understanding the biology underlying non-response in these patients, and this remains an area of active investigation. We conducted a comprehensive molecular profiling of biologic naïve RA patients being treated with anti-TNF therapy in combination with MTX, prior to initiating (baseline) and following 3 months of treatment. The aim of the study was to understand the molecular mechanisms (other than drug neutralization), that affect clinical response to anti-TNF and to identify potential predictive markers that could allow us to differentiate responders and non-responders at baseline.

Methods:

Two independent cohorts of 52 and 41 RA patients were selected from the Corrona CERTAIN registry. Clinical response at three months was defined according to EULAR criteria. Patients were included in each cohort only if a minimum level of anti-TNF was detected in the 3 month plasma sample to assure drug exposure.

Whole-blood RNA (PAXgene) and plasma samples from baseline and after 3 months of treatment were profiled using a broad array of technologies including RNAseq (Illumina HiSeq2500), shotgun and targeted proteomics, and glycan / glycopeptide analysis. A cell-specific transcriptional data analysis methodology was developed and applied to results of RNAseq analysis to enable characterization of the most common immune cell sub-populations.

Results:

Results from each cohort show a strong treatment-related molecular signature between 3 months and baseline, and also a high level of correlation (p=0.7; permutation p<10^-5), between cohorts. Interestingly, no significant difference could be established between responders and non-responders in terms of treatment signature. Cell-specific transcriptional profiling analysis indicated a decrease in neutrophil markers at 3 months (permutation p<0.01), which is concordant with observed changes in neutrophil counts. Shotgun proteomics in plasma showed a significant reduction of acute phase proteins, including CRP. Results at baseline, comparing responders to non-responders, demonstrated a lower concordance across the two cohorts, however, cell-specific analysis indicated increased representation of innate cell type signatures in responders and, conversely, increased expression of adaptive cell type signatures in non-responders. These results were not only conserved between the two cohorts, but were also observed when this analysis was applied to other independent publicly available RA datasets assessing response to anti-TNF treatment.
Conclusion:
Results from this comprehensive molecular profiling study identified that differences in innate / adaptive immune cell signatures at baseline may be a major contributor to response to anti-TNF treatment within the first 3 months of therapy. These observations were supported by analysis of independent, publicly available RA datasets, and could potentially lead to an approach to patient selection, resulting in improved treatment outcomes.

Disclosure: V. Farutin, Momenta Pharmaceuticals, Inc, 1,Momenta Pharmaceuticals, Inc, 3; T. Prod'homme, Momenta Pharmaceuticals, Inc, 1,Momenta Pharmaceuticals, Inc, 3; K. McConnell, Momenta Pharmaceuticals, Inc., 1,Momenta Pharmaceuticals, Inc, 3; N. Washburn, Momenta Pharmaceuticals, Inc., 1,Momenta Pharmaceuticals, Inc, 3; P. Halvey, Momenta Pharmaceuticals, Inc, 1,Momenta Pharmaceuticals, Inc, 3; J. Guess, Momenta Pharmaceuticals, Inc, 1,Momenta Pharmaceuticals, Inc, 3; N. S. Gunay, Momenta Pharmaceuticals, Inc., 1,Momenta Pharmaceuticals, Inc., 3; J. Hillson, Momenta Pharmaceuticals, Inc, 1,Momenta Pharmaceuticals, Inc, 5,Chemocentryx, 1,Chemocentryx, 3; C. J. Etzel, Corrona, LLC, 3,Merck Human Health, 9; K. C. Saunders, Corrona, LLC, 3; D. A. Pappas, Corrona, LLC, 3,Abbvie, 5,Abbvie, 2,Novartis Pharmaceutical Corporation, 9,Corrona, LLC., 1; A. Manning, Momenta Pharmaceuticals, Inc, 1,Momenta Pharmaceuticals, Inc, 3; L. Ling, Momenta Pharmaceuticals, Inc, 1,Momenta Pharmaceuticals, Inc, 3; I. Capila, Momenta Pharmaceuticals Inc, 3,Momenta Pharmaceuticals Inc, 1.

Abstract Number: 1020

The Inflammatory and Proliferative Synovial Lesion in Post-Infectious Lyme Arthritis Results from Impaired Wound Healing

Robert Lochhead1,2, David Ordonez-Del Valle1,2, Klemen Strle2,3, Sheila Arvika1,2, John Aversa4 and Allen Steere1,2, 1Center for Immunology and Inflammatory Diseases, Massachusetts General Hospital, BOSTON, MA, 2Department of Medicine, Harvard Medical School, BOSTON, MA, 3Department of Immunology and Inflammatory Diseases, Massachusetts General Hospital, BOSTON, MA, 4School of Medicine, Yale University, New Haven, CT
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Genetics, Genomics and Proteomics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Lyme arthritis (LA) is initially triggered by Borrelia burgdorferi infection, but in some patients, the synovitis persists despite 2-3 months of antibiotic therapy and spirochetal killing, called post-infectious LA. As in rheumatoid arthritis (RA), post-infectious LA is characterized by autoimmune inflammation and synovial hyperplasia. Our recent microRNA analysis revealed that antibacterial responses characterized the infectious phase of LA, and impaired wound healing may contribute to inflammatory and proliferative synovitis following resolution of infection. In mice, impaired wound repair and elevated interferon (IFN) responses during B. burgdorferi infection are associated with severe murine LA, but the role of impaired wound healing has not been explored in post-infectious LA or RA.

Methods: High-throughput RNA sequencing was performed using synovial tissue from patients with post-infectious LA (n=14), RA (n=5), and osteoarthritis (OA, n=5), and analyzed using in-house and online bioinformatics tools. Cells expressing IFNγ were identified by intracellular cytokine staining and flow cytometry of cells collected from fresh synovial tissue and synovial fluid. Immunofluorescent (IF) microscopy was used to identify IFNγ-responsive cells from patient synovial biopsies.

Results: 1001 genes were differentially expressed (DE) in post-infectious LA synovial tissue compared with OA tissue, of which 517 (43%) were interferon-regulated genes. In addition, 85/190 (45%) of genes in the response to wounding gene ontology (GO) set were DE in post-infectious LA patients compared with OA patients. Of these, ~1/3 were involved in coagulation, cell proliferation/differentiation, and extracellular matrix (ECM) formation, and were down-regulated in post-infectious LA, but less consistently in RA, compared with OA; whereas ~2/3 were involved in immune activation, IFN responses, and ECM degradation, and were up-regulated in both post-infectious LA and RA, compared with OA. Cytotoxic CD8+ T cells were a major source IFNγ in post-infectious LA and RA synovial tissue, and fibroblasts within foci of active synovitis expressed high levels of IFNγ-inducible HLA-DR molecules.
Conclusion: These data show that impaired wound healing is a previously unrecognized component of the inflammatory-proliferative synovial pathology of post-infectious LA and RA. We propose that dysregulated wound healing in inflamed tissue may potentiate break in immune tolerance during the early stages of autoimmune development. Thus, post-infectious LA provides a natural human model of infection-induced autoimmunity, in which impaired wound healing leads to autoimmune synovial pathology of the chronic inflammatory arthritides, including RA.

Disclosure: R. Lochhead, None; D. Ordonez-Del Valle, None; K. Strle, None; S. Arvikar, None; J. Aversa, None; A. Steere, None.


Abstract Number: 1021

GWAS of Gout in Patients with Hyperuricemia Identified Many Possible New Candidate Risk Alleles

Jing Cui¹, Zhi Zhang¹, Elizabeth Karlson² and Daniel H. Solomon², ¹Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, ²Brigham and Women's Hospital and Harvard Medical School, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Genetics, Genomics and Proteomics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Virtually all gout patients have high levels of uric acid in the blood (hyperuricemia, HU), but approximately 80% of patients with HU will never develop gout. There are a numbers of GWAS that identified risk alleles for hyperuricemia and/or gout using general population as comparison. This study examines genes that might influence the risk of gout among subjects with HU.

Methods: Subjects with HU (uric acid ≥6.5 mg/dl from lab data) and available GWAS data were requested from Partners HealthCare Biobank, a collaborative database that contains linked electronic medical records (EMR), survey data and genomic data for 15,000+ subjects. Gout was defined using a validated EMR algorithm with positive predict value of 0.95. Samples were genotyped from three Illumina MEGA chips. We performed standard quality control (QC) procedures for each file, merged them into one analysis dataset, and applied standard QC again. We restricted our genome-wide association study (GWAS) analysis to the Caucasian population. Principal component analysis (PCA) was performed. Among subjects with HU, association between SNPs and gout was tested using logistic regression assuming a genetic additive model. The first 10 PCAs were utilized as covariates to control for any potential population stratification. We also looked at potential gout and HU SNPs with genome-wide significance among European ancestry from the GWAS Catalog (https://www.ebi.ac.uk/gwas/).

Results: 3146 self-reported Caucasian subjects with HU were identified from the Biobank, with 467 (14.8%) were identified as having gout. The gout group was slightly older (mean ±SD, 72±11 vs 66±14, p<0.0001), more likely to be male (79% vs 56%, p<0.0001) compared to non-gout HU group. 793,514 SNPs passed QC and were utilized in the GWAS. The most significant SNP was rs1481012 in ABCG2 gene with p value of 1.8 x 10^-6, which is a known risk factor for gout. We identified 14 SNPs at p~10^-6 (see Table); 12 were new SNPs and 2 had been previously identified as gout/HU risk SNPs from the GWAS catalog. 53 SNPs were identified at p~10^-5; only 1 is a previously identified gout/HU risk SNP. 623 SNPs were identified at p~10^-4, with only 1 as a known gout/HU SNP.

Conclusion: We carried out a GWAS of gout in patients with HU, and found that some of the risk alleles for gout in the general population are also associated with gout in a population with HU. But, we found many possible new SNPs and some previously identified SNPS were null in the HU population. The null findings may be because of limited power, confounding, or true non associations.

Table  Top 20 SNPs associated with gout compared to hyperuricemia
<table>
<thead>
<tr>
<th>SNP</th>
<th>Chr</th>
<th>BP</th>
<th>Allele</th>
<th>Gene</th>
<th>OR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs1481012</td>
<td>4</td>
<td>89039082</td>
<td>G</td>
<td>ABCG2</td>
<td>0.61</td>
<td>1.8E-06</td>
</tr>
<tr>
<td>kgp2887248</td>
<td>4</td>
<td>89052323</td>
<td>T</td>
<td>ABCG2</td>
<td>0.61</td>
<td>1.8E-06</td>
</tr>
<tr>
<td>rs4148155</td>
<td>4</td>
<td>89054667</td>
<td>G</td>
<td>ABCG2</td>
<td>0.61</td>
<td>1.8E-06</td>
</tr>
</tbody>
</table>

**Known gout/HU risk SNPs from previous GWAS with genome-wide significance**

<table>
<thead>
<tr>
<th>SNP</th>
<th>Chr</th>
<th>BP</th>
<th>Allele</th>
<th>Gene</th>
<th>OR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs7020787</td>
<td>9</td>
<td>12340300</td>
<td>C</td>
<td>-</td>
<td>1.42</td>
<td>1.9E-06</td>
</tr>
<tr>
<td>rs7323513</td>
<td>21</td>
<td>23989516</td>
<td>T</td>
<td>-</td>
<td>0.60</td>
<td>2.9E-06</td>
</tr>
<tr>
<td>rs2367897</td>
<td>12</td>
<td>72492104</td>
<td>G</td>
<td>TRHDE</td>
<td>0.67</td>
<td>2.9E-06</td>
</tr>
<tr>
<td>rs1928873</td>
<td>9</td>
<td>12350656</td>
<td>C</td>
<td>-</td>
<td>0.72</td>
<td>4.4E-06</td>
</tr>
<tr>
<td>rs4760822</td>
<td>12</td>
<td>72479611</td>
<td>T</td>
<td>TRHDE</td>
<td>0.67</td>
<td>5.5E-06</td>
</tr>
<tr>
<td>JHU_2.206047717</td>
<td>2</td>
<td>206047718</td>
<td>A</td>
<td>PARD3B</td>
<td>0.20</td>
<td>1.9E-06</td>
</tr>
<tr>
<td>rs7040701</td>
<td>9</td>
<td>12318093</td>
<td>C</td>
<td>-</td>
<td>1.38</td>
<td>8.0E-06</td>
</tr>
<tr>
<td>rs143936778</td>
<td>5</td>
<td>85185350</td>
<td>A</td>
<td>-</td>
<td>0.41</td>
<td>8.3E-06</td>
</tr>
<tr>
<td>rs113845454</td>
<td>10</td>
<td>53981733</td>
<td>G</td>
<td>PRKG1</td>
<td>0.37</td>
<td>8.3E-06</td>
</tr>
<tr>
<td>JHU_12.72507970</td>
<td>12</td>
<td>72507971</td>
<td>T</td>
<td>TPH2</td>
<td>0.68</td>
<td>1.0E-05</td>
</tr>
<tr>
<td>rs7721690</td>
<td>5</td>
<td>85185350</td>
<td>A</td>
<td>-</td>
<td>1.68</td>
<td>1.1E-05</td>
</tr>
<tr>
<td>rs59996437</td>
<td>3</td>
<td>30845824</td>
<td>T</td>
<td>GADL1</td>
<td>0.20</td>
<td>1.2E-05</td>
</tr>
<tr>
<td>JHU_10.102775026</td>
<td>10</td>
<td>102775027</td>
<td>G</td>
<td>PDZD7</td>
<td>0.65</td>
<td>1.2E-05</td>
</tr>
<tr>
<td>rs10756369</td>
<td>9</td>
<td>12401666</td>
<td>A</td>
<td>-</td>
<td>0.73</td>
<td>1.5E-05</td>
</tr>
<tr>
<td>rs7223247</td>
<td>17</td>
<td>72027224</td>
<td>T</td>
<td>-</td>
<td>0.52</td>
<td>6.2E-06</td>
</tr>
<tr>
<td>rs7040701</td>
<td>9</td>
<td>12318093</td>
<td>C</td>
<td>-</td>
<td>1.38</td>
<td>8.0E-06</td>
</tr>
<tr>
<td>rs143936778</td>
<td>5</td>
<td>85185350</td>
<td>A</td>
<td>-</td>
<td>0.41</td>
<td>8.3E-06</td>
</tr>
<tr>
<td>rs113845454</td>
<td>10</td>
<td>53981733</td>
<td>G</td>
<td>PRKG1</td>
<td>0.37</td>
<td>8.3E-06</td>
</tr>
</tbody>
</table>

**Not found in previous GWAS (new SNPs identified)**

<table>
<thead>
<tr>
<th>SNP</th>
<th>Chr</th>
<th>BP</th>
<th>Allele</th>
<th>Gene</th>
<th>OR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>JHU_9.12340636</td>
<td>9</td>
<td>12340636</td>
<td>T</td>
<td>-</td>
<td>0.60</td>
<td>2.9E-06</td>
</tr>
<tr>
<td>rs7020787</td>
<td>9</td>
<td>12340300</td>
<td>C</td>
<td>-</td>
<td>1.42</td>
<td>1.9E-06</td>
</tr>
<tr>
<td>rs1928873</td>
<td>9</td>
<td>12350656</td>
<td>C</td>
<td>-</td>
<td>0.72</td>
<td>4.4E-06</td>
</tr>
<tr>
<td>rs4760822</td>
<td>12</td>
<td>72479611</td>
<td>T</td>
<td>TRHDE</td>
<td>0.67</td>
<td>5.5E-06</td>
</tr>
</tbody>
</table>

**Disclosure:** J. Cui, None; Z. Zhang, None; E. Karlson, None; D. H. Solomon, None.


**Abstract Number:** 1022

**A Personalized Medicine Approach to Improve the Prediction of Azathioprine-Induced Pancreatic Injury: Preliminary Results**

Tyler Reese¹, Savannah Hurt², Rany Octaria², Alyson Dickson², Prathima Anandi², Vivian Kawai², Kelly Birdwell², Adriana Hung², C. Michael Stein³, QiPing Feng² and Cecilia P. Chung³, ¹Department of Medicine, Vanderbilt University Medical Center, Nashville, TN, ²Vanderbilt University Medical Center, Nashville, TN, ³Medicine, Vanderbilt University Medical Center, Nashville, TN

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Genetics, Genomics and Proteomics Poster II

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Azathioprine (AZA) is used to treat rheumatic diseases and to prevent transplant rejection. There is marked variability in toxicity to azathioprine; one such toxicity is thiopurine-induced acute pancreatitis (TIAP). The cause of TIAP is not known, but a HLA-DRB1*07:01-HLA-DQA1*02:01 haplotype was recently identified as a risk factor, suggesting that pancreatic injury may be immunologically mediated and modified by genetic factors. We aimed to build a cohort of patients who had pancreatic injury while taking AZA to perform pharmacogenetic studies. Here we present preliminary data.

**Methods:** We used the Vanderbilt University Medical Center BioVU resource that contains de-identified medical records linked to a biobank containing DNA samples from 225,000 patients. A validated bioinformatic algorithm was used to assemble a cohort of European American patients taking AZA. Those AZA users with amylase or lipase values that exceeded twice the upper limit of normal or with ICD-9/ICD-10 codes for acute pancreatitis were identified. Each record was reviewed to confirm AZA use at the time and to further classify patients into three not mutually exclusive categories: pancreatic injury (enzyme abnormalities alone), acute pancreatitis
(defined by American College of Gastroenterology Guidelines), or TIAP (Figure 1). The remaining patients served as controls. Age, sex, race, and BMI were compared between groups. All available genotypes from Infinium MEGA<sup>EX</sup>, a platform for genome wide analysis (GWA), were retrieved. After standard quality control measures with removal of variants with minor allele frequency <0.01, we performed an exploratory GWA with 849,934 variants adjusted for age and sex.

**Results:** We identified 3,212 AZA users. Evidence of pancreatic injury based on enzyme abnormalities occurred in 109 patients, of whom 22 and 7 met criteria for pancreatitis and TIAP, respectively. The remaining 3,103 were controls (Figure 1). Patients with pancreatic injury were more likely to be male (p=0.002). MEGA<sup>EX</sup> genotypes were available in 34 cases and 449 controls. Although the results did not reach GWAS statistical significance, variants in two SNPs, rs4859716 (p=3.01x10<sup>-6</sup>) and rs4843192 (p=7.13x10<sup>-6</sup>), differed in patients with pancreatic injury.

**Conclusion:** These preliminary findings suggest that AZA users with pancreatic injury are more likely to be male and that variants in rs4859716 or rs4843192 may be associated with pancreatic injury. The rs4859716 variant is an intergenic variant near the SHROOM3 gene, necessary for epithelial morphogenesis of the gut, and rs4843192 is an intergenic variant near the FOXL1 gene, a tumor suppressor gene whose activity predicts tumor aggressiveness in pancreatic cancer. Further investigation is warranted into clinical and genetic determinants of pancreatic toxicity with azathioprine.

**Disclosure:** T. Reese, None; S. Hurt, None; R. Octaria, None; A. Dickson, None; P. Anandi, None; V. Kawai, None; K. Birdwell, None; A. Hung, None; C. M. Stein, None; Q. Feng, None; C. P. Chung, NIH/NIAMS and Rheumatology Research Foundation, 2.


Abstract Number: 1023
The Autoimmune Discovery Ichip Distinguishes Healthy Individuals (HC) from Those with SLE, Rheumatoid Arthritis (RA), Scleroderma (SSc), Sjogren’s Syndrome (SS), and the Anti-Phospholipid Syndrome (APS)

Chaim Putterman1, Armando Gabrielli2, Alexandra Balbir-Gurman3, Pennina Safer4, Keren Jakobi-Brook4, Rachel Sorek4, Ilana Gluzman4, Steve Wallace5 and Irun R. Cohen4,6, 1Division of Rheumatology, Albert Einstein College of Medicine, Bronx, NY, USA, Bronx, NY, 2Istituto di Clinica Medica dell’Università di Ancona, Ancona, Italy, Ancona, Italy, 3Rheumatology Unit, Rambam Health Care Campus, Rappaport Faculty of Medicine, Technion, Haifa, Israel, Haifa, Israel, 4ImmunArray Ltd., Rehovot, Israel, Rehovot, Israel, 5ImmunArray Inc., VA, USA, Richmond, VA, 6Weizmann Institute of Science, Rehovot, Israel, Rehovot, Israel

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Genetics, Genomics and Proteomics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Current serological tests are not sufficiently accurate in differentiating between HC and those with autoimmune rheumatic diseases. We developed the iCHIP antigen microarray to provide extensive autoantibody profiling in human serum. We previously described the SLE-Key Rule-Out test, which distinguishes SLE patients from HC with 94% sensitivity, 75% specificity, and a negative predictive value (NPV) of 93%1,2,3. Here, we report the use of the autoimmune discovery iCHIP to distinguish between HC and subjects with SLE, RA, SSc, SS, and the APS.

Methods:
We examined IgM and IgG autoantibodies binding to 519 antigens (1038 features) in the sera of HC subjects (N=136), and in patients with SLE (N=30), RA (N=30), SSc (N=40), SS (N=20), and APS (N=16). FDR-adjusted p-values were calculated for each univariate test. Three independent multivariate classification methods were applied: Support Vector Machine (SVM), Quadratic Discriminant Analysis (QDA) and Naive Bayesian classifier (NB). Classifier training and testing were performed based on 10-fold cross validation on all samples, and the performance of each classifier was determined.

Results:
Univariate analysis revealed multiple statistically significant separating reactivities. We found that IgG autoantibody reactivity to the connective tissue antigen receptor leukocyte-associated immunoglobulin-like receptor 1 (LAIR-1) differentiated HC subjects with all of the 5 diseases with a p value of 2.8E-63. Other highly significant autoantigen reactivities included connective tissue proteins such as collagen III (p = 6.5E-26 (IgM)) and collagen II (p = 5E-22 (IgG)). Figure 1 shows anti-LAIR-1 data comparing HC subjects to each of the 5 diseases; each of the three classification methods differentiated between HC and subjects with autoimmune diseases. The typical mean classifier performance was 93% sensitivity, 96% specificity, and 95% accuracy. Interestingly, LAIR-1 appears to function as a “checkpoint” down-regulator of immune reactivity4; thus, it is possible that anti-LAIR-1 represent a target for therapeutic discovery and also may be pathogenic, and predispose to a variety of autoimmune conditions.

Conclusion:
Autoantibody specificities detected by the autoimmune discovery iCHIP successfully distinguished between HC individuals and individuals with several autoimmune rheumatic diseases, including SLE, RA, SSc, SS, and APS. These preliminary results are based on relatively small numbers of serum samples, but are very promising and warrant additional validation in larger cohorts of autoimmune and HC subjects.


Acknowledgements: Authors wish to acknowledge Cohen-Gindi O, Lerner M, Tarnapolski O, Blumenstein Y, Javaherian A, Pitts J, Barton M and Wong E
High-Throughput Proteomic Profiling Identifies Dysregulated Proteins in Neonatal-Onset Multisystem Inflammatory Disease (NOMID) That Respond to IL-1-blocking Treatment

Megha Garg¹,², Brian Sellers³, Adriana Almeida de Jesus⁴, Angélique Biancotto⁵, Foo Cheung⁶ and Raphaela Goldbach-Mansky⁴, ¹National Institutes of Arthritis, Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, ²Translational Autoinflammatory Disease Studies, NIH/NIAID, Bethesda, MD, ³Center for Human Immunology, Autoimmunity and Inflammation, NIH/NHLBI, Bethesda, MD, ⁴Translational Autoinflammatory Disease Studies (TADS), Laboratory of Clinical Investigation and Microbiology (LCIM), NIAID/NIH, Bethesda, MD, ⁵Center for Human Immunology, Autoimmunity and Inflammation (CHI), NHLBI, NIH, Bethesda, MD, ⁶Center for Human Immunology Autoimmunity and Inflammation (CHI), NHLBI, NIH, Bethesda, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Genetics, Genomics and Proteomics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Neonatal-onset multisystem inflammatory disease (NOMID) is an IL-1 mediated autoinflammatory disease caused by a gain-of-function mutations in NLRP3 that results in constitutive activation of IL-1b and specific organ/tissue inflammation and damage. To date no reliable serum biomarkers that identify IL-1 mediated systemic inflammation or inflammatory organ damage particularly CNS inflammation exist. We explore high-throughput proteomic profiling to screen for potential biomarkers.

Methods: Serum samples were obtained from healthy age-matched children (HC), n=8 and 12 NOMID patients(pts.) before and after a median of 42 months (range 3-96mo) after starting IL-1 blocking treatment with anakinra. All patients were in inflammatory remission at the time of blood draw. Using an aptamer-based proteomic assay (SOMAscan) we screened 1129 proteins. To identify biomarkers of exaggerated systemic and tissue specific IL-1-mediated inflammation, we selected proteins that significantly changed with anakinra treatment many were significantly increased or decreased in untreated NOMID vs HC. Mann-Whitney U test and Wilcoxon rank-sum analyses with FDR correction were used for statistical comparison. We determined RNA transcription levels (RNAsseq) of the protein targets in whole blood. RPKMs< 1 characterized low expression in blood cells and suggested that the protein origin might be from non-hematopoietic cells. We also determined protein function.
**Results:** In the SOMAscan Assay we identified 70 proteins that changed in the serum of NOMID pts. before and after treatment (n=12; q<0.05). Of these 15 (21%) were also significantly increased or decreased compared to controls at baseline. Protein levels of 30 proteins decreased and protein levels of 40 increased with treatment. Of these, 63% and 82% respectively had low or no gene expression in whole blood. Protein targets of the IL-1 pathway (IL-1β, soluble IL-1RI, IL-1 RAcP) significantly decreased. Of markers that decreased were those indicating systemic inflammation including complements (i.e CRP, SAA1, C3, C9, CFI) and markers that have been associated with tissue damage including CNS manifestations (CFI TNFSD11A) and hypercoagulabilty (F9) as well as vascular endothelial markers associated with atherosclerosis (PLAUR, CST3). Of the markers that increase, most are associated with growth and tissue regeneration (including growth hormone receptor: GHR, IGFBP3 and -5, NOTCH3, TGFβ), p<0.05 for all.

**Conclusion:** Protein changes with anakinra treatment reveal markers of IL-1 pathway that are not reliably detectable in ELISA assays and transcription assays. These markers need to be validated in other presumed IL-1 mediated diseases. Furthermore, markers of tissue inflammation particulary of CNS inflammation need to be validated in treatment studies to determine their utility in assessing appropriate treatment with IL-1 blocking therapies.

**Disclosure:** M. Garg, None; B. Sellers, SomaLogic, 1; A. Almeida de Jesus, None; A. Biancotto, None; F. Cheung, None; R. Goldbach-Mansky, None.


**Abstract Number:** 1025

**Submetabolome Profiling with Differential Chemical Isotope Labeling Liquid Chromatography Mass Spectrometry and a Universal Metabolome Standard Reveals a Metabolite Profile with 99% Accuracy for Rheumatoid Arthritis**

**Walter P. Maksymowych**, 1, Derrick Blackmore2, Roman Eisner3, Liang Li4 and Zaeem Siddiqi2, 1Department of Medicine, University of Alberta, Edmonton, AB, Canada, 2Medicine, University of Alberta, Edmonton, AB, Canada, 3City of Edmonton, Edmonton, AB, Canada, 4Chemistry, University of Alberta, Edmonton, AB, Canada

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Genetics, Genomics and Proteomics Poster II  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Early diagnosis of rheumatoid arthritis (RA) is hampered by suboptimal accuracy of currently available serological biomarkers. Recent advancements in metabolomic profiling include dansylation liquid chromatography mass spectrometry (LC-MS), resulting in 1000-fold increase in detection sensitivity of amine/phenol-containing metabolites, and universal metabolome-standard (UMS) methodology in conjunction with differential chemical isotope labeling (CIL LC−MS), to provide long-term analytical reproducibility and facilitate metabolome comparisons among different data sets. CIL LC-MS uses different labeling reagents to target chemical group-based submetabolomes to provide in-depth metabolomic analysis. We aimed to identify a metabolite signature with high accuracy for RA.

**Methods:** 12C-dansylation and acid labeling of individual serological samples and 13C-dansylation and acid labeling of pooled samples from 47 age/gender matched healthy control subjects, 52 age/gender matched RA patients, and 46 patients with seropositive myasthenia gravis was undertaken. A total of 7,458 amine/phenol and 9954 organic acid metabolites were combined into a single data set for analysis. Metabolite concentrations were natural-log transformed. Model accuracy estimation was performed using 5-fold cross-validation, and metabolites were selected using within-fold feature selection. Metabolites were ranked using Spearman correlation coefficient, and the top n were selected, with a varying n. Training of the predictive model was done using a linear Support Vector Machine (SVM). After cross-validation, the final model formula was calculated on the entire data set using the same methodology as was evaluated using cross-validation. Cross-validation accuracy was further analyzed using randomly selected metabolites. Data processing and analysis was performed entirely in R (version 3.2.3). SVM was trained using the e1071 package (version 1.6-7) and cross-validation was done using the caret package (version 6.0-64).

**Results:** A total of 5711 metabolites were identified in all samples with orthogonal partial least squares discriminant analysis showing a clear separation of the 3 groups (R2=0.98, Q2=0.80). 34 serum metabolites were identified as potential RA biomarkers with correlation
coefficients ≥0.80. Cross-validation accuracy of top-ranked metabolites, according to Spearman’s correlation, and using a varying number of metabolites shows that 99.1% accuracy for RA versus controls is achieved using only 4 metabolites.

**Conclusion:** CIL LC-MS metabonomic profiling and UMS methodology reveals that serum metabolomes of RA patients differ considerably from healthy and autoimmune disease.

![Graph showing cross-validation accuracy using varying number of metabolites. 99.1% accuracy is achieved using 4 metabolites.](image)

---

**Disclosure:** W. P. Maksymowych, None; D. Blackmore, None; R. Eisner, None; L. Li, None; Z. Siddiqi, None.


**Abstract Number:** 1026

**Gene Expression Analysis Reveals Common Pathways of Tissue Pathogenesis in Lupus Organ Involvement**

**Amrie Grammer**¹, Sarah Heuer¹, Robert Robl¹, Adam Labonte¹, Prathyusha Bachali¹, Sushma Madamanchi¹ and Peter E. Lipsky²,

¹AMPEL BioSolutions and RILITE Research Institute, Charlottesville, VA,
²AMPEL BioSolutions, LLC, Charlottesville, VA

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Monday, November 6, 2017
**Session Title:** Genetics, Genomics and Proteomics Poster II
**Session Type:** ACR Poster Session B
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**
Lupus is a prototypic autoimmune disease characterized by B cell hyperactivity, autoantibody formation and resultant tissue damage. The mechanisms underlying tissue pathology in lupus are not completely understood. Analysis of gene expression in various tissues has been employed in an attempt to develop a better understanding of disease pathogenesis and tissue injury. The current experiments were undertaken to develop a more comprehensive understanding of molecular pathways involved in lupus organ pathogenesis by assessing gene expression profiles so that novel treatment candidates targeting commonly dysregulated cellular functions could be identified.

**Methods:**
Publicly available gene expression profiles were identified in GEO from lupus affected skin, synovium, and kidney. The raw data were downloaded, normalized, curated and assessed for differentially expressed (DE) genes. Correlation with clinical or histologic features was carried out by Weighted Gene Correlation Network Analysis (WGCNA) and variation in pathway activity was determined in individual samples and groups of samples by Gene Set Variation Analysis (GSVA).

**Results:**
More than 300 gene expression profiles from lupus patients and controls were analyzed to determine DE genes (8279 discoid lupus skin, 5465 synovium, 6381 kidney glomerulus WHO class 3/4, 5587 kidney tubulointerstitum WHO class 3/4). Notably, 45% of lupus tissue DE genes were detected in more than one tissue and 439 were differentially expressed in all tissues. Curated STRING-based protein-protein interaction analysis carried out using MCODE in Cytoscape of these 439 DE genes identified a number of gene clusters that
were functionally characterized by both Biologically Informed Gene Cluster Analysis (BIG-C) and IPA. BIG-C identified 13 pathways that were abnormally expressed in all lupus tissues, whereas IPA identified 65 dysregulated pathways shared among these tissues. Using the 45 BIG-C functional categories, GSVA separated lupus tissues from control tissues, identified commonly dysregulated functional pathways, documented individual tissue variation and also largely identified the same functional pathways that emerged from pathway construction generated from DE genes. WGCA identified a number of gene modules that correlated with clinical of histologic features. These modules contained nearly 85% of the DE genes. A number of approaches were employed to connect the dysregulated lupus organ pathways to potential drug candidates, including cross referencing to the Library of Integrated Network Based Cellular Signatures (LINCS). More than 75 potential drug candidates were identified.

Conclusion:

These results indicate that common cellular and molecular pathways can be identified in all of the affected lupus tissues, implying that related processes might be involved in the pathology of multiple organs in this autoimmune disease. Connectivity between lupus organ gene expression abnormalities and candidate drug induced changes in gene expression identified a number of potential novel treatments that could target the commonly dysregulated molecular pathways underlying lupus organ pathology.

Disclosure: A. Grammer, None; S. Heuer, None; R. Robl, None; A. Labonte, None; P. Bachali, None; S. Madamanchi, None; P. E. Lipsky, None.


Abstract Number: 1027

**Quantification of Leukocytes’ Secretome to Guide Diagnosis and Treatment Options in Patients with Suspected Chronic Auto-Inflammatory Syndromes**

Philippe A. Tessier¹, Marie-Pier Longchamps¹, Nathalie Amiable¹, Nathalie Pagé¹, Laetitia Michou², Louis Bessette², Paul R. Fortin¹, Alexandra Albert², Anne-Laure Chetaille² and Martin Pelletier¹, ¹Infectious Diseases and Immunity Research Division, CHU de Québec-Université Laval Research Center, Québec, QC, Canada, ²Division of Rheumatology, Department of Medicine, CHU de Québec-Université Laval, Québec, QC, Canada

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Genetics, Genomics and Proteomics Poster II

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Auto-inflammatory syndromes are inherited conditions characterized by recurrent inflammation (fever, abdominal pain, dermatitis, arthritis). Diagnosis and treatments are challenging as detection rate of mutations in patients with high suspicions for auto-inflammatory syndromes is low, symptoms are reminiscent of other autoimmune diseases, especially Systemic Autoimmune Rheumatic Diseases (SARD), and the cytokines abnormally secreted are unknown. As a consequence, patients can be misdiagnosed, leading to inappropriate treatment, severe complications and substantial socio-economic costs. We hypothesized that the secretion of cytokines by peripheral blood mononuclear cells (PBMC) is an indicator of the disease and could guide the treatment to the most suitable anti-cytokine.

**Methods:** Plasma and peripheral blood mononuclear cells (PBMCs) were obtained from healthy controls, suspected auto-inflammatory patients, and rheumatoid arthritis and systemic lupus erythematosus patients from the CHU de Québec SARD Biobank Repository Database (SBRD). PBMC were stimulated with inflammatory and immune stimuli, and cytokines in the supernatant were analyzed by multiplex assays.

**Results:** The cytokines found in the plasma were similar between healthy donors, SARD patients and suspected auto-inflammatory patients. In contrast, PBMC had a distinct profile of cytokine secretion. Stimulation of PBMCs with IL-15 or anti-Ig (Figure 1) led to differential secretion of members of IL-1 cytokine family, IL-12 and IFNγ in autoimmune, but not auto-inflammatory patients. In
contrast, stimulation with inflammasome activators or pro-inflammatory cytokines led to selective secretion of IL-1α, IL-1β, IL-1RA, IL-18 (Figure 2), IFNγ or IL-12 in suspected auto-inflammatory patients, but not in autoimmune patients.

**Conclusion:** This study demonstrates that analysis of leukocytes’ secretome is reliably more sensitive than serum to reveal cytokine signatures and to predict treatment options in patients with suspected chronic auto-inflammatory syndromes.

**Acknowledgement:** This work was partly funded by the Fondation du Grand défi Pierre Lavoie. We thank Pfizer, Amgen, BMS, Abbvie, Roche, Sanofi-Genzyme and Merck & Co. for their unrestricted financial support of the SBRD.

**Figure 1:** Stimulation of PBMCs with anti-immunoglobulins to activate B cells reveals different cytokine signatures between autoimmune and auto-inflammatory patients

**Figure 2:** Stimulation of PBMCs with inflammasome activators or pro-inflammatory cytokines uncovers abnormal over-secretion of the IL-1 cytokine family member IL-18 by auto-inflammatory patients

**Disclosure:** P. A. Tessier, None; M. P. Longchamps, None; N. Amiable, None; N. Pagé, None; L. Michou, None; L. Bessette, Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Lilly, Novartis, Sanofi, 8, Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Lilly, Novartis, Sanofi, 5, Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Lilly, Novartis, Sanofi, 2; P. R. Fortin, None; A. Albert, None; A. L. Chetaille, None; M. Pelletier, None.

Abstract Number: 1028

**Association of a Non-Synonymous, Loss-of-Function, Variant in NOD2 with Reduced Tissue Damage in ACPA +Ve RA**

Ricardo Segurado¹, Denis Shields¹, Rachel Knevel², Annette H.M. van der Helm-van Mil³, Tom W.J. Huizinga⁴ and Anthony G. Wilson⁵.

¹University College Dublin, Dublin, Ireland, ²Medical and Population Genetics Program, Broad Institute of MIT and Harvard, Cambridge, MA, ³Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, ⁴Department of Rheumatology, LUMC, Leiden, Netherlands, Leiden, Netherlands, ⁵UCD School of Medicine and Medical Science, Conway Institute, University College Dublin, Dublin, Ireland

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017
Session Title: Genetics, Genomics and Proteomics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

**Background/Purpose:**

The functional capacity of individuals with rheumatoid arthritis (RA) is related to the severity of damage to bone and cartilage within joints. This is a highly variable trait that is known to have a significant genetic component. A loss-of-function non-synonymous variant (rs2066844, Arg702Trp) in nucleotide-binding oligomerization domain containing 2 (NOD2) gene, results in lower activation of NF-kB-mediated inflammation and tissue damage in RA. Our hypothesis was that the 702Trp variant is, as a result of reduced inflammatory load, be associated with lower radiological damage in RA.

**Methods:**

The initial study was performed in the British Genetics of RA (GORA) cross-sectional population (N=914), radiological damage was assessed by the Modified Larsen Score (MLS). Genotyping was performed using either the Illumina HumanCoreExome array (N=568) or the Illumina HumanCNV370 Quad v3 array (N=346). Genotypes for rs2066844 were imputed for individuals typed on latter platform using IMPUTE v2. Replication was performed in the Leiden EAC (N=597), with damage assessed at baseline and yearly thereafter using the Sharp-van der Heijde score (SHS) and samples were genotyped on the Illumina iScan platform (Immunochip). RF and ACPA status was available for both populations. Analyses were conducted in R v3.4.0 and SPSS v20. For the combined meta-analysis, we used the most recent measurement on each patient in a zero-inflated negative binomial model adjusted for sex and age at assessment, followed by a fixed-effects meta-analysis of the two summary statistics.

**Results:**

In the discovery GORA population the minor rs2066844 (702Trp) frequency was 5%, similar to the 1000 genomes European frequency (5.1%), genotypes fitted Hardy-Weinberg equilibrium. The minor allele carriage was associated with lower MLS: incidence ratio risk 0.75 (95% CI: 0.60-0.93), p=0.009. The association was only significant in RF+ (p=0.008) or ACPA+ (p=0.013) subgroups. The proportion of variance explained by rs2066844 was 0.007. In the replication Leiden cohort we observed a similar lower yearly progression of SHS score for each minor allele, by 0.95 SHS (95% CI: 0.92-0.99, p=0.006) in all patient and in ACPA positive patients (0.92, 95% CI: 0.87-0.97, p=0.004). Meta-analysis of the two cohorts revealed a significant pooled effect with an IRR of 0.76 (95% CI: 0.64-0.91 , p=0.003).

**Conclusion:** These data reveal a protective effect of rs2066844 minor allele with severity of sero-positive RA that is likely a consequence of the lower inflammatory activity associated with this genotype. Although the overall influence on the variance of tissue damage is modest, in combination with established prognostic biomarkers, it may contribute to the development of prognostic algorithm for RA.

**Disclosure:** R. Segurado, None; D. Shields, None; R. Knevel, None; A. H. M. van der Helm-van Mil, None; T. W. J. Huizinga, None; A. G. Wilson, None.


Abstract Number: 1029
What to Measure after Arthroplasty? Confirmation of a Core Domain Set

Anh Hoang1, Susan M. Goodman2, Mark P. Figgie3, Mathias Bostrom4, Douglas Padgett4, Lisa A. Mandl5,6,7, Peter Sculco8, Alexander McLawhorn9 and Jasvinder A. Singh10, 1Rheumatology, Hospital for Special Surgery, New York, NY, 2Medicine, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, 3Orthopaedic Surgery, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, 4Orthopaedic Surgery, Hospital for Special Surgery, New York, NY, 5Department of Medicine, Hospital for Special Surgery, New York, NY, 6Rheumatology, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, 7Department of Rheumatology, Hospital for Special Surgery, New York, NY, 8Orthopaedic Surgery, Hospital for Special Surgery, New York, NY, 9Hospital for Special Surgery, New York, NY, 10Rheumatology, University of Alabama at Birmingham, Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Health Services Research Poster II: Osteoarthritis and Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The Outcomes Measures in Rheumatology Trials (OMERACT) TJR Working Group has proposed six core domains that would constitute a standardized measurement set that can be used as a tool to compare outcomes among TJR clinical trials. The specific aim was to query two different groups of stakeholders, patients and surgeons, to establish a consensus regarding the domains.

Methods: We e-mailed a survey to 3810 hip/knee TJR patients and 49 hip/knee arthroplasty surgeons at a high-volume orthopedic center of excellence to rate the importance of the six core domains and two additional domains for consideration. Ratings were on a 1 to 9 scale: 1-3 indicating limited or no importance for patients, 4-6 being important, but not critical, and 7-9 being critical. Scores were summarized with median [interquartile range]. Comparisons between the sexes, age groups (< 55 years vs. ≥ 55 years), and participant types (surgeons vs. patients) were made using the Wilcoxon rank-sum test.

Results: 1295 patients (34%) and 21 (43%) surgeons completed the questionnaire. Patient non-responders were similar in age (≥ 55 years, 86%) and gender (57.5% female) to responders. All core domains were confirmed as “critical” by both patients and surgeons. This consensus rating persisted even when compared between the sexes as well as the age groups. The only exception was cost, while “critical” overall, when compared to patients and females respectively, which both surgeons and males scored cost as only “important”, not “critical”. Cost was also rated differently between those < 55 years vs. participants ≥ 55 years: 6 [5, 8] vs. 7 [5, 8], p=0.015.

Conclusion: Our study confirmed that both orthopedic surgeons and TJR patients agree that the OMERACT TJR core domains were critical for patients. These results support a broad endorsement and encourage the identification of candidate outcome instruments to further develop a TJR standardized measurement set.

<table>
<thead>
<tr>
<th>Table 1. Demographic Characteristics (n=1316)</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>743 (56.5%)</td>
</tr>
<tr>
<td>Age Groups</td>
<td></td>
</tr>
<tr>
<td>&lt; 55 years</td>
<td>157 (12%)</td>
</tr>
<tr>
<td>≥ 55 years</td>
<td>1159 (88%)</td>
</tr>
<tr>
<td>Participant Type</td>
<td></td>
</tr>
<tr>
<td>Hip/Knee TJR Patient</td>
<td>1295 (98.5%)</td>
</tr>
<tr>
<td>Orthopedic Surgeon</td>
<td>21 (1.5%)</td>
</tr>
<tr>
<td>Arthritis Conditions (TJR Patients only)</td>
<td></td>
</tr>
<tr>
<td>Osteoarthritis only</td>
<td>1071 (82.7%)</td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
<td>34 (2.6%)</td>
</tr>
<tr>
<td>Another type of arthritis</td>
<td>44 (3.4%)</td>
</tr>
<tr>
<td>Joints aches and pains</td>
<td>66 (5.1%)</td>
</tr>
<tr>
<td>No arthritis or joint aches or pains</td>
<td>80 (6.2%)</td>
</tr>
<tr>
<td>Core Domains</td>
<td>Overall (N=1316)</td>
</tr>
<tr>
<td>--------------------------------------</td>
<td>------------------</td>
</tr>
<tr>
<td>Joint Pain</td>
<td>9 [8, 9]</td>
</tr>
<tr>
<td>Function or functional ability</td>
<td>9 [8, 9]</td>
</tr>
<tr>
<td>Patient Satisfaction</td>
<td>9 [8, 9]</td>
</tr>
<tr>
<td>Revision surgery</td>
<td>8 [5, 9]</td>
</tr>
<tr>
<td>Adverse events</td>
<td>8 [7, 9]</td>
</tr>
<tr>
<td>Death</td>
<td>9 [6, 9]</td>
</tr>
<tr>
<td><strong>Additional Domains for Consideration</strong></td>
<td></td>
</tr>
<tr>
<td>Cost</td>
<td>7 [5, 8]</td>
</tr>
<tr>
<td>Patient participation in work and social activities</td>
<td>8 [6, 9]</td>
</tr>
</tbody>
</table>

Table 3. Ratings of Domains for TJR Clinical Trials Between Males & Females

<table>
<thead>
<tr>
<th>Core Domains</th>
<th>Overall (N=1316)</th>
<th>Female (n=743)</th>
<th>Male (n=573)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joint Pain</td>
<td>9 [8, 9]</td>
<td>9 [8, 9]</td>
<td>8 [7, 9]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Function or functional ability</td>
<td>9 [8, 9]</td>
<td>9 [8, 9]</td>
<td>8 [8, 9]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Patient Satisfaction</td>
<td>9 [8, 9]</td>
<td>9 [8, 9]</td>
<td>8 [8, 9]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Revision surgery</td>
<td>8 [5, 9]</td>
<td>8 [5, 9]</td>
<td>7 [5, 9]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Adverse events</td>
<td>8 [7, 9]</td>
<td>9 [7, 9]</td>
<td>8 [6, 9]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Additional Domains for Consideration</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost</td>
<td>7 [5, 8]</td>
<td>7 [5, 9]</td>
<td>6 [5, 8]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Patient participation in work and social activities</td>
<td>8 [6, 9]</td>
<td>8 [7, 9]</td>
<td>7 [6, 8]</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Disclosure: A. Hoang, None; S. M. Goodman, None; M. P. Figgie, Lima, 7,Mekanika, 1; M. Bostrom, None; D. Padgett, Pixar Bio, 1,DOI Global, 5,Hip Society, American Joint Registry, 9; L. A. Mandi, Boehringer Ingelheim, 2,American College of Physicians, 3,Up To Date, 7; P. Sculco, None; A. McLawhorn, None; J. A. Singh, Takeda and Savient, 2,Savient, Takeda, Regeneron, Merz, Iroko, Bioiberica, Crealta/ Horizon and Allergan pharmaceuticals, WebMD, UBM LLC and the American College of Rheumatology., 5,JAS serves as the principal investigator for an investigator-initiated study funded by Horizon pharmaceuticals through a grant to DINORA, Inc., a 501 (c)(3) entity., 9,JAS is a member of the executive of OMERACT, an organization that develops outcome measures in rheumatology and receives arms-length funding from 36 companies., 9,JAS is the editor and the Director of the UAB Cochrane Musculoskeletal Group Satellite Center on Network Meta-analysis., 9,Jas is a member of the American College of Rheumatology's (ACR) Annual Meeting Planning Committee (AMPC); Chair of the ACR Meet-the-Professor, Workshop and Study Group Subcommittee., 9,a member of the Veterans Affairs Rheumatology Field Advisory Committee, 9.


Abstract Number: 1030

**Healthcare Service Utilization and Costs of Certolizumab Pegol Versus Infliximab Treatment in Patients with Rheumatoid Arthritis**

Joseph Tkacz\(^1\), Edward Lee\(^2\), Robert Low\(^2\), Jeffrey Stark\(^2\), Mohamed Yassine\(^2\) and Brenna Brady\(^1\), \(^1\)Health Analytics LLC, Columbia, MD, \(^2\)UCB Pharma, Smyrna, GA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017

Session Title: Health Services Research Poster II: Osteoarthritis and Rheumatoid Arthritis

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM
Background/Purpose: Prior retrospective claims analyses examining rheumatoid arthritis (RA) treatment costs have shown infliximab (IFX) to be costlier than certolizumab pegol (CZP) across all sites of care (physician office, home, outpatient [OP]), primarily due to lower CZP drug costs. The present study assessed one-year (yr) healthcare resource utilization (HRU) and costs incurred by RA patients (pts) treated with CZP vs IFX.

Methods: Medical and pharmacy claims data (2008–2015) were derived from the Truven MarketScan® database of insured pts matching the inclusion criteria: RA diagnosis, treatment initiation (index date) with CZP or IFX (July/1/2008–December/31/2014), continuous eligibility ±12 months around index date, and age ≥18 yrs. Mean, unadjusted one-yr visits (OP, inpatient [IP], emergency room [ER], and physician office) and costs (pharmacy, medical, and total healthcare) were calculated and compared between groups via Mann-Whitney U tests. These were also assessed using multivariate (MV) regression models and adjusted for treatment (CZP/IFX), prior biologic use (yes/no), gender, age, baseline health, and baseline HRU and costs.

Results: 1,398 RA pts were treated with CZP and 3,592 with IFX. CZP pts were more likely to have prior biologic use than IFX pts (74.0% vs 40.8%, p<0.001; Table 1). In the unadjusted analyses, CZP pts demonstrated increased pharmacy usage (68.7 vs 56.1 fills per pt per yr, p<0.001), but reduced physician office visits (19.8 vs 21.9, p<0.001) and OP hospital-based services (4.4 vs 4.9, p=0.221) compared to IFX pts, resulting in greater overall pharmacy costs but lower medical expenditure than IFX patients (p values <0.001; Figure 1A). In adjusted analyses, MV models controlling for patient and treatment characteristics revealed that prior biologic use was associated with more office visits (p<0.001), OP visits (p<0.001), ER utilization (p<0.001), and elevated total medical costs (p<0.001). Despite the CZP cohort having more biologic-experienced pts, CZP treatment was associated with fewer physician office (p<0.001; Table 2) and OP (p<0.001; Table 2) services compared to IFX pts, but a greater pharmacy spend (p<0.001; Figure 1B). However, CZP treatment was associated with reduced total healthcare costs (p<0.001), with IFX pts incurring over $4,000 per pt per yr more than CZP pts ($46,908 vs $42,867, p<0.001; Figure 1B).

Conclusion: Despite the CZP-treated RA population having a higher rate of prior biologic use, which has been correlated with more severe disease, annual total healthcare costs were higher for IFX-treated RA pts. MV models controlling for demographics and baseline HRU revealed that treatment with CZP was associated with a $4,000 saving per pt per yr compared to treatment with IFX.

References:


Table 1: Baseline patient characteristics

<table>
<thead>
<tr>
<th>Characteristic [a]</th>
<th>CZP</th>
<th>IFX</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>10.5</td>
<td>9.7</td>
<td>0.396</td>
</tr>
<tr>
<td>Pre-period Charlson Comorbidity Index</td>
<td>0.53</td>
<td>0.66</td>
<td>0.290</td>
</tr>
<tr>
<td>Post-period Charlson Comorbidity Index</td>
<td>0.56</td>
<td>0.63</td>
<td>0.110</td>
</tr>
<tr>
<td>Prior biologic use, n (%)</td>
<td>1,034 (74.0)</td>
<td>1,466 (40.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gender, female, n (%)</td>
<td>1,134 (61.1)</td>
<td>2,025 (76.7)</td>
<td>0.050</td>
</tr>
</tbody>
</table>

Note: Significance levels are highlighted in bold (p<0.05). Pre-period: prior to initiating CZP or IFX. Post-period: after initiating CZP or IFX. [a] Mean (SD) unless stated otherwise. PPO = Preferred Provider Organization; PPO: Preferred Provider Organization; SD: standard deviation.

Figure 1: One-year total pharmacy, medical, and healthcare costs per patient

A. Total population (unadjusted)

B. Adjusted population [a]

Table 2: Mean healthcare resource utilization per patient per year from multivariate models

<table>
<thead>
<tr>
<th>Measure, mean (SE)</th>
<th>CZP</th>
<th>IFX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Office Visits</td>
<td>19.1 (0.12)</td>
<td>20.4 (0.09)</td>
</tr>
<tr>
<td>Outpatient Hospital Visits</td>
<td>5.7 (0.05)</td>
<td>4.3 (0.04)</td>
</tr>
<tr>
<td>ER Visits</td>
<td>0.3 (0.01)</td>
<td>0.3 (0.01)</td>
</tr>
<tr>
<td>IP Admissions</td>
<td>0.2 (0.02)</td>
<td>0.2 (0.02)</td>
</tr>
<tr>
<td>Prescription Fills</td>
<td>67.2 (0.83)</td>
<td>49.2 (0.68)</td>
</tr>
</tbody>
</table>

Variables in bold indicate a statistically significant difference between CZP and IFX groups. Poisson loglinear models were fitted for physician office and ER visits. Logistic regression was used for IP and ER utilization (yes/no). Total prescription fills were estimated using gamma models with a log link. SE: standard error.

Disclosure: J. Tkacz, Health Analytics LLC, 3; E. Lee, UCB Pharma, 3; R. Low, UCB Pharma, 3; J. Stark, UCB Pharma, 3; M. Yassine, UCB Pharma, 3; B. Brady, Health Analytics LLC, 3.


Abstract Number: 1031

Developing a Multi-Phase Claims-Based Algorithm to Facilitate the Study of Drug Exposure during Pregnancy

S Phillips1, KE Johnson1, SW Shen2, KJ Woodcroft3, SA Oliveria4 and TA Simon5, 1QuintilesIMS, Seattle, WA, 2Bristol-Myers Squibb, Hopewell, NJ, 3Henry Ford Health System, Detroit, MI, 4QuintilesIMS, New York, NY, 5Bristol-Myers Squibb, Princeton, NJ

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017

Session Title: Health Services Research Poster II: Osteoarthritis and Rheumatoid Arthritis

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM

Background/Purpose: The use of antirheumatic medications during pregnancy may lead to birth defects or other complications. Safety studies are critical, with registries being common but often yielding a small number of cases after years of follow-up. Medical administrative claims data can be used to study large numbers of women and infants more quickly and efficiently, if these claims data
Methods: A multi-phase algorithm is being developed in a phased manner among women aged ≥15 and ≤50 years with ≥1 International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) end of pregnancy code. Women were enrolled and had prescription coverage 340 days prior to the end of pregnancy in the Henry Ford Health System between 1/1/2013 and 9/30/2015. In all phases, algorithms will be developed, applied to claims data and compared to electronic medical records for validation. Positive predictive value (PPV), sensitivity and 95% CI will be calculated. The best performing algorithm developed in each phase will be used to move to the next phase.

Results: A total of 698 women met inclusion criteria. Three algorithms were developed and tested for phase 1. Algorithm 1 (≥1 definitive ICD-9-CM end of pregnancy code) performed best (Table 1). Two algorithms for phase 2 were developed and tested. Algorithm 2 (adjusted delivery date based on selected procedure codes and assigned 245 days to preterm, 273 days to term, and 294 days to post-term) performed best for preterm and term births (Table 2).

Conclusion: End of pregnancy outcomes can be identified in claims data with high PPV and sensitivity. Gestational age can be estimated with reasonable PPV and sensitivity for preterm and term live births. Further analyses are underway for phases 3 and 4.

Table 1. Phase 1: End of Pregnancy Algorithm Summary and Performance Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>PPV (%)</th>
<th>95% CI</th>
<th>Sensitivity (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>94.21</td>
<td>92.18-95.85</td>
<td>96.91</td>
<td>97.76-99.57</td>
</tr>
<tr>
<td>Live birth</td>
<td>95.49</td>
<td>97.04-99.39</td>
<td>97.36</td>
<td>95.04-99.56</td>
</tr>
<tr>
<td>Non-live birth</td>
<td>76.92</td>
<td>71.04-84.49</td>
<td>99.12</td>
<td>99.24-99.86</td>
</tr>
<tr>
<td>Algorithm 2</td>
<td>90.56</td>
<td>88.08-92.71</td>
<td>95.75</td>
<td>95.02-96.01</td>
</tr>
<tr>
<td>Live birth</td>
<td>91.75</td>
<td>89.05-93.88</td>
<td>98.22</td>
<td>98.88-99.15</td>
</tr>
<tr>
<td>Non-live birth</td>
<td>71.06</td>
<td>63.72-79.41</td>
<td>85.22</td>
<td>77.38-91.15</td>
</tr>
<tr>
<td>Algorithm 3</td>
<td>72.70</td>
<td>63.93-82.54</td>
<td>41.32</td>
<td>32.44-50.63</td>
</tr>
</tbody>
</table>

*Live birth and non-live birth data are not necessarily mutually exclusive, as in the case where there is a multiple birth and there is at least one live birth and at least one non-live birth.


Table 2. Phase 2: Estimated Gestational Age Assignment Algorithm Summary and Performance Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>PPV (%)</th>
<th>95% CI</th>
<th>Sensitivity (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm</td>
<td>93.5</td>
<td>78.6-99.2</td>
<td>67.4</td>
<td>51.5-82.9</td>
</tr>
<tr>
<td>Term</td>
<td>94.2</td>
<td>81.5-90.4</td>
<td>80.8</td>
<td>78.4-84.4</td>
</tr>
<tr>
<td>Postterm</td>
<td>40.5</td>
<td>31.6-49.2</td>
<td>89.5</td>
<td>76.2-95.0</td>
</tr>
<tr>
<td>Algorithm 2</td>
<td>93.9</td>
<td>79.2-95.2</td>
<td>65.2</td>
<td>52.4-81.4</td>
</tr>
<tr>
<td>Preterm</td>
<td>94.2</td>
<td>91.2-96.6</td>
<td>80.6</td>
<td>76.4-84.4</td>
</tr>
<tr>
<td>Term</td>
<td>40.7</td>
<td>31.6-49.2</td>
<td>89.5</td>
<td>76.5-95.0</td>
</tr>
</tbody>
</table>

ICD-9-CM=International Classification of Diseases, Ninth Revision, Clinical Modification; PPV=positive predictive value

Disclosure: S. Phillips, Bristol-Myers Squibb, 2, QuintilesIMS, 3; K. Johnson, None; S. Shen, Bristol-Myers Squibb, 3, Bristol-Myers Squibb, 1; K. Woodcroft, None; S. Oliveria, QuintilesIMS, 3; T. Simon, Bristol-Myers Squibb, 3, Bristol-Myers Squibb, 1, 9.

Trends in Hospitalizations Following Heart Failure Diagnosis in Rheumatoid Arthritis

Elena Myasoedova¹, Eric L. Matteson², Sara J. Achenbach³, John M. Davis III⁴, Soko Setoguchi⁵, Sherine E. Gabriel⁶ and Cynthia S. Crowson⁷, ¹Rheumatology, Mayo Clinic, Rochester, MN, ²Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, MN, ³Mayo Clinic, Rochester, MN, ⁴Division of Rheumatology, Mayo Clinic, Rochester, MN, ⁵Rutgers School of Public Health, New Brunswick, NJ, ⁶Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, ⁷Health Sciences Research, Mayo Clinic College of Medicine and Science, Rochester, MN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Health Services Research Poster II: Osteoarthritis and Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The rising prevalence of heart failure (HF) in the general population and associated increased hospitalization costs is a major public health problem. There is a 2-fold increased risk of HF in rheumatoid arthritis (RA) compared to the general population. Little is known about hospitalization rates in patients with RA and HF. We aimed to compare the frequency of and trends in hospitalizations following HF diagnosis in patients with and without RA during 1987-2015.

Methods: The study included a retrospectively identified population-based cohort of patients with incident HF and prior RA (age≥18 years, 1987 ACR criteria) and a comparison cohort of incident HF patients without RA matched 3:1 on age, sex, and year of HF diagnosis. Hospitalizations at the time of HF diagnosis were excluded from analyses. All subjects were followed until death, migration, or 1/1/2015. Person-years methods and rate ratios (RR) from Poisson regression models were used to compare hospitalization rates between the groups. Generalized linear models were used to analyze the length of stay (LOS).

Results: The study included 212 patients with RA (mean age at HF diagnosis 78.3 years; 68% female) and 636 non-RA patients (mean age at HF diagnosis 78.6 years; 68% female). The hospitalization rate following HF diagnosis was higher in RA vs non-RA patients (RR 1.16; 95%CI 1.08-1.25). This difference may be decreasing after 2010 (Figure). The magnitude of the increase was similar in both sexes and across all ages. In patients with available echocardiography, HF with preserved ejection fraction (HFpEF) was not different in RA (57%) vs non-RA (51%; p=0.3). Patients with RA and HF with reduced ejection fraction (HFrEF; RR 1.65; 95%CI 1.29-2.09) but not those with HFpEF (RR 0.80; 95%CI 0.63-1.01) had significantly more hospitalizations than non-RA patients. Following HF diagnosis, RA patients were more likely to be hospitalized for non-cardiovascular causes (RR 1.26; 95%CI 1.14-1.39), but not for HF (RR 0.96; 95%CI 0.76-1.21) or other cardiovascular causes (RR 0.99; 95%CI 0.81-1.20) compared to the non-RA patients. There was no overall difference in hospital LOS in RA vs non-RA patients after HF diagnosis (mean of 5.6 vs 5.3 days, respectively, p=0.31). LOS was higher in earlier years in RA than non-RA and declined faster in RA than non-RA over time, with similar LOS in both groups in recent years (interaction p=0.019). Readmission rates within 30 days of prior discharge were similar in RA and non-RA (p=0.14).

Conclusion: Hospitalization rate following HF diagnosis was 16% higher in RA than in non-RA patients regardless of sex and age. This increased hospitalization risk was mostly among patients with RA who had HFrEF rather than HFpEF, and was predominantly due to non-cardiovascular causes. Increased complexity of management of patients with comorbid RA may play a role in more frequent hospitalizations in the RA cohort.
Burden of Illness in Patients with RA and Anti-Cyclic Citrullinated Peptide Positivity

ML Paudel1, JP Swindle1, J McPheeters1, R Szymialis2 and K Price2, 1Optum, Inc., Eden Prairie, MN, 2Bristol-Myers Squibb, Princeton, NJ
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Health Services Research Poster II: Osteoarthritis and Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: RA is often treated with a biologic DMARD (bDMARD), such as abatacept (ABA) or a TNF inhibitor (TNFi). Real-world data on how economic outcomes vary by bDMARD therapy in patients (pts) with seropositivity to anti-cyclic citrullinated peptide (anti-CCP) are sparse. The objective of this study was to compare healthcare resource utilization (HCRU) and costs among pts with RA and anti-CCP positivity who initiated a new bDMARD therapy. Methods: A retrospective study was conducted using claims data from a large US health plan, linked with laboratory results. Pts were aged ≥18 years with ≥1 diagnosis code for RA (ICD-9-CM 714.x) and ≥1 claim for ABA (identified first) or a TNFi (adalimumab, certolizumab pegol, etanercept, golimumab or infliximab) during Jan 1, 2007–Jul 31, 2015. Cohort assignment was based on index therapy (ABA or first observed TNFi). Pts were required to have ≥18 months of continuous health plan enrollment (≥6 months pre-index [pre-initiation], 12 months post-index [post-initiation]), no pre-index claims for index therapy and anti-CCP positivity (≥20 IU/mL). Per-pt-per-month HCRU and costs (total and RA-related) were calculated separately for the pre- and post-index periods. Independent sample t-tests were used to examine differences by cohort.

Results: Analyses included 203 ABA users and 1066 TNFi users (etanercept=487, adalimumab=331, infliximab=144, certolizumab=60, golimumab=44) with anti-CCP positivity (median age 55 & 52 years, female 88 & 75%, Medicare Advantage 17 & 15%; mean Charlson Comorbidity Index score 1.6 & 1.4, pre-index bDMARD use 48 & <1%). Compared with TNFi users, ABA users experienced greater mean ambulatory visits in pre-index (2.6 vs 2.0, p<0.01) and post-index periods (2.6 vs 1.7, p<0.01). No statistically significant differences (p<0.05) in mean emergency room visits or inpatient days for the pre- or post-index periods were observed between cohorts. Compared with TNFi users, ABA users experienced higher mean costs in pre-index ($2543 vs $932, p<0.01) and post-index periods ($3632 vs $2957, p<0.01). Analyses of RA-related costs and utilization were similar, with the exception that a statistically significant difference was not observed in post-index RA-related costs between ABA and TNFi users ($2660 vs $2306, p=0.06).

Conclusion: Among pts with RA and anti-CCP positivity, unadjusted differences in pre-index ambulatory care and healthcare costs were observed between abatacept and TNFi users, which carried over to post-index cost and HCRU comparisons. These differences appeared to be driven, in part, by greater ambulatory care among abatacept users. Further research is needed to understand additional factors driving pre-index costs among pts initiating bDMARDs to treat RA, to inform multivariable adjusted analyses and ensure comparability of cohorts, as abatacept is likely to be their second line of therapy due to formulary availability.
Table 1. Per-Patient-Per-Month Costs and Healthcare Resource Utilization by Biologic DMARD Group

<table>
<thead>
<tr>
<th>Healthcare costs, USD, mean (SD)</th>
<th>6 months pre-index</th>
<th>12 months post-index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total healthcare costs</td>
<td>2543 (3283) 932 (1668)*</td>
<td>3632 (3480) 2957 (2457)*</td>
</tr>
<tr>
<td>RA-related healthcare costs</td>
<td>1379 (1660) 310 (1168)*</td>
<td>2660 (2567) 2306 (1785)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Healthcare resource utilization, mean (SD)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total ambulatory visits</td>
<td>2.62 (1.86) 1.96 (1.42)*</td>
<td>2.56 (1.73) 1.68 (1.35)*</td>
</tr>
<tr>
<td>Total ER visits</td>
<td>0.11 (0.29) 0.07 (0.28)</td>
<td>0.10 (0.29) 0.06 (0.19)</td>
</tr>
<tr>
<td>Total inpatient days</td>
<td>0.12 (0.72) 0.06 (0.67)</td>
<td>0.12 (0.58) 0.09 (0.47)</td>
</tr>
<tr>
<td>RA-related ambulatory visits</td>
<td>1.02 (0.75) 0.74 (0.48)*</td>
<td>1.15 (0.66) 0.61 (0.46)*</td>
</tr>
<tr>
<td>RA-related ER visits</td>
<td>0.03 (0.09) 0.01 (0.07)</td>
<td>0.02 (0.04) 0.01 (0.06)</td>
</tr>
<tr>
<td>RA-related inpatient days</td>
<td>0.10 (0.69) 0.05 (0.66)</td>
<td>0.11 (0.54) 0.08 (0.43)</td>
</tr>
</tbody>
</table>

Costs and healthcare resource utilization were reported as per-patient-per-month
*p<0.05; statistically significant differences were computed between abatacept and TNFi groups
ER=emergency room; TNFi=TNF inhibitor; USD=United States dollars, adjusted to 2016 dollars

Disclosure: M. Paudel, None; J. Swindle, None; J. McPheeters, None; R. Szymialis, Bristol-Myers Squibb, 1, Bristol-Myers Squibb, 3; K. Price, Bristol-Myers Squibb, 1, Bristol-Myers Squibb, 3.


Abstract Number: 1034

**Presence of Anti-Cyclic Citrullinated Peptide Antibodies Is Associated with Better Treatment Response to Abatacept but Not to TNF Inhibitors in Patients with RA: A Meta-Analysis**

E Alemao¹, R Postema², Y Elbez³, C Mamane⁴ and Axel Finckh⁵, ¹Bristol-Myers Squibb, Princeton, NJ, ²Bristol-Myers Squibb, Uxbridge, United Kingdom, ³Excelya, Boulogne-Billancourt, France, ⁴Mapi, London, United Kingdom, ⁵University Hospital of Geneva, Geneva, Switzerland

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017

Session Title: Health Services Research Poster II: Osteoarthritis and Rheumatoid Arthritis

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM

Background/Purpose: The association between anti-citrullinated protein antibody (ACPA) status and erosions, as well as response to TNF inhibitor (TNFi) treatment, has been explored.¹,² Results based on a large US RA registry study have suggested that anti-cyclic citrullinated peptide (anti-CPP; a surrogate for ACPA) positivity predicts better clinical responses to abatacept, but not to TNFi.³ The objective of this study was to investigate whether ACPA status is associated with clinical responses to abatacept or to TNFi in RA, in the published literature. Methods: A systematic literature review (SLR) was performed to identify published studies and conference abstracts estimating biologic DMARD response according to ACPA status. The SLR was supplemented by additional studies that were identified through expert input. Mantel–Haenszel meta-analysis methods were used to pool risk ratios (RRs) based on ACPA status. In the base-case, response to therapy was assessed using the EULAR response as the primary outcome, while a scenario analysis assessed response by combining various definitions including ACR20 and EULAR for abatacept, and ACR20, DAS28 and EULAR for TNFi therapy. Results: Nineteen studies were included in the meta-analysis: 4 for abatacept, 14 for TNFi and 1 for both treatments. The base-case analysis included 4 of the abatacept and 6 of the TNFi studies and showed a statistically significant positive association between
ACPA positivity and EULAR response for patients treated with abatacept (RR 1.13 [95% CI 1.00, 1.26]; Figure 1), while ACPA positivity was associated with lower EULAR responses to TNFi therapy (RR 0.92 [95% CI 0.86, 0.98]; Figure 2). For the scenario analyses, in which all definitions of response were pooled, the results were consistent with base-case for abatacept (RR 1.18 [95% CI 1.30, 1.35]), while for TNFi therapy, no significant difference by ACPA status was observed (RR 0.97 [95% CI 0.86, 1.10]).

**Conclusion:** This meta-analysis confirms that ACPA-positive RA patients are more likely to achieve response to abatacept treatment compared to ACPA-negative patients. Additionally, the analysis demonstrates that there is no association between ACPA status and response to TNFi therapy, consistent with the findings of previously published studies.1,3


**Risk of Hospitalization Among RA Patients with Multiple Autoimmune Co-Morbidities Differs By DMARD Treatment**

E Alemao, Z Guo and L Burns, Bristol-Myers Squibb, Princeton, NJ

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Health Services Research Poster II: Osteoarthritis and Rheumatoid Arthritis

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM
Background/Purpose: Patients (pts) with autoimmune (AI) disorders are at higher risk of developing another AI disorder; co-occurrence of some AI conditions is reported more frequently than others in RA pts. The objective was to evaluate 6- and 12-month (mo) hospitalization rates in RA pts with multiple AI co-morbidities, treated with abatacept, biologic (b) or conventional (c) DMARDs.

Methods: Administrative claims data from Optum Clinformatics Data Mart (database A) and QuintilesIMS™ PharMetrics Plus (database B) from 2006 to 2015 were used. Inclusion was based on the presence of 2 diagnosis codes for RA plus 1 DMARD prescription, age ≥18 yrs, ≥1 of the 5 most prevalent AI conditions: ankylosing spondylitis (AS), Crohn’s disease, lupus, psoriasis or ulcerative colitis at or before index, ≥3 mo baseline (pre-index date) and 3 mo of follow-up (post-index date). Mutually exclusive treatment groups were classified based on the index prescription using hierarchy of abatacept, other bDMARD and cDMARD. Also, an RA group without record of DMARD (NoDMARD) was identified. Date of first DMARD was index date (for NoDMARD, index date was first diagnosis date). Primary outcome was 6- and 12-mo hospitalizations. Treatment groups were compared using descriptive statistics (Wilcoxon rank-sum test for continuous variables or Pearson’s chi-square test for categorical variables) and using multivariate Cox regression analyses for hospitalization risk. Covariates included in the multivariate analysis were age, sex, region, past hospitalization, physician office visits during past 3 mo, an indicator variable for 714.0x, medication use (steroids, NSAIDs, salicylates, antidyslipidemics), the 5 AI and 18 co-morbidity conditions. Results: A total of 18,964 and 47,105 RA pts with multiple AI co-morbidities from databases A and B, respectively, were included. The mean (SD) age of study population was 55.4 (15.1) yrs in database A and 50.0 (13.0) in database B. Respectively, 4.4%, 20.7%, 41.6% and 33.3% were prescribed abatacept, bDMARD, cDMARD and NoDMARD in database A, and 3.7%, 25.9%, 40.5% and 29.8% in database B. The most common AI co-morbidities in databases A vs B were AS (29 vs 27%), lupus (32 vs 32%) and psoriasis (32 vs 34%). Abatacept-treated pts had higher past hospitalization rates vs bDMARD and cDMARD groups. 6- and 12-mo pooled adjusted hazard ratios for hospitalization were higher for bDMARDs (and cDMARDs) vs abatacept (Table). Results were consistent in both databases.

Conclusion: Among RA pts with multiple AI co-morbidities, adjusted risk of hospitalization in both bDMARD- and cDMARD-treated pts was significantly higher compared with abatacept-treated pts. Though the NoDMARD group had an even higher risk of hospitalization, this should be interpreted with caution as it comprises a heterogeneous pt population

Table. HRs for Hospitalization in RA Patients With Multiple Autoimmune Co-morbidities by DMARDs

<table>
<thead>
<tr>
<th>DMARD</th>
<th>HR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-month hospitalization</td>
<td></td>
<td></td>
</tr>
<tr>
<td>bDMARD (vs abatacept)</td>
<td>1.18 (1.04, 1.33)</td>
<td>0.014</td>
</tr>
<tr>
<td>cDMARD (vs abatacept)</td>
<td>1.27 (1.12, 1.44)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NoDMARD (vs abatacept)</td>
<td>1.92 (1.69, 2.19)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>12-month hospitalization</td>
<td></td>
<td></td>
</tr>
<tr>
<td>bDMARD (vs abatacept)</td>
<td>1.16 (1.05, 1.28)</td>
<td>0.005</td>
</tr>
<tr>
<td>cDMARD (vs abatacept)</td>
<td>1.19 (1.08, 1.32)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NoDMARD (vs abatacept)</td>
<td>1.60 (1.45, 1.76)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

bDMARD=biologic DMARD, cDMARD=conventional DMARD, HR=hazard rate.

Disclosures: E. Alemao, Bristol-Myers Squibb, 1, Bristol-Myers Squibb, 3; Z. Guo, Bristol-Myers Squibb, 3; L. Burns, Bristol-Myers Squibb, 1, Bristol-Myers Squibb, 3.

Abstract Number: 1036

Blood Glucose Changes Surrounding Initiation of Tumor-Necrosis Factor Inhibitors and Conventional Disease-Modifying Anti-Rheumatic Drugs in Veterans with Rheumatoid Arthritis

Patrick R. Wood⁠¹, Evan Manning², Joshua Baker³, Grant Cannon⁴, Lisa Davis⁵, Bryant R. England⁶, Ted R. Mikuls⁷ and Liron Caplan⁸, ¹Rheumatology, University of Colorado School of Medicine, Aurora, CO, ²University of Colorado School of Medicine, Aurora, CO, ³Rheumatology, University of Pennsylvania, Philadelphia, PA, ⁴Salt Lake City VA Medical Center and University of Utah, Salt Lake City, UT, ⁵Div of Rheumatology, Denver Health, Denver, CO, ⁶Division of Rheumatology & Immunology, Department of Internal Medicine, Nebraska-Western IA VA Health Care System & University of Nebraska Medical Center, Omaha, NE, ⁷Internal Medicine, Division of Rheumatology, University of Nebraska Medical Center, Omaha, NE, ⁸Division of Rheumatology, University of Colorado School of Medicine, Aurora, CO

First publication: September 18, 2017

Background/Purpose: There is evidence linking activation of the innate immune system and insulin resistance. Perturbations in glucose homeostasis upon initiation of tumor-necrosis factor inhibitors (TNFis) and conventional DMARDs have been described in small studies, perhaps due to suppression of inflammation. To evaluate this association, we measured glucose before and after initiation of TNFis and DMARDs in a large registry of patients with rheumatoid arthritis (RA).

Methods: Patients enrolled in the Veterans Affairs RA (VARA) registry were retrospectively examined. Subjects were selected who, during study follow-up, initiated treatment with TNFis, prednisone, or DMARDs, and for whom proximate random blood glucose (RBG) or hemoglobin A1C (A1C) values were available. Proximate values were the closest RBG within 2 weeks prior to, and 6 months following, medication initiation. A1C values were the closest A1C within 2 months prior to, and 12 months following, medication initiation. Measurements were compared before and after medication initiations using paired t-tests and multivariate regression, adjusting for demographics and comorbid conditions.

Results: 2111 patients contributed at least one proximate measurement surrounding initiation of any agent. Significant decreases in RBG were associated with 653 hydroxychloroquine-initiation events (-3.68mg/dL, p = 0.04), and increases were noted in RBG surrounding 665 prednisone-initiation events (+5.85mg/dL, p < 0.01). A significant decrease in A1C was noted surrounding 49 sulfasalazine-initiation events (-0.70%, p < 0.01). Multivariate regression analyses suggest sulfasalazine and hydroxychloroquine use as predictors of lower post-medication-initiation blood glucose values; congestive heart failure was also a predictor for higher RBG values after all medication-initiation events. We found no association of TNFi initiation with changes in glucose.

Conclusion: This study quantifies hyperglycemic effects of prednisone initiation. We also observed hypoglycemic effects of sulfasalazine and hydroxychloroquine initiation. TNFi initiation was not observed to impact measured blood glucose. Further large-scale and prospective investigation of DMARD and TNFi blood glucose effects in other populations is warranted.

<table>
<thead>
<tr>
<th>Medication</th>
<th>N</th>
<th>Difference (mg/dL or % glycosylation)</th>
<th>Confidence Interval</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etanercept</td>
<td>311</td>
<td>-0.06</td>
<td>-4.91</td>
<td>4.79</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>302</td>
<td>1.03</td>
<td>-3.41</td>
<td>5.46</td>
</tr>
<tr>
<td>Certolizumab</td>
<td>5</td>
<td>-5.20</td>
<td>-26.60</td>
<td>16.19</td>
</tr>
<tr>
<td>Golimumab</td>
<td>13</td>
<td>-17.61</td>
<td>-37.54</td>
<td>2.31</td>
</tr>
<tr>
<td>Infliximab</td>
<td>147</td>
<td>-1.90</td>
<td>-9.45</td>
<td>5.65</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>831</td>
<td>2.08</td>
<td>-7.48</td>
<td>4.90</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>290</td>
<td>-0.48</td>
<td>-6.84</td>
<td>5.88</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>653</td>
<td>-3.68</td>
<td>-7.15</td>
<td>0.20</td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>335</td>
<td>-0.38</td>
<td>-4.92</td>
<td>4.17</td>
</tr>
<tr>
<td>Prednisone</td>
<td>665</td>
<td>5.85</td>
<td>2.20</td>
<td>9.51</td>
</tr>
</tbody>
</table>

Hemoglobin A1C

<table>
<thead>
<tr>
<th>Medication</th>
<th>N</th>
<th>Difference (mg/dL or % glycosylation)</th>
<th>Confidence Interval</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etanercept</td>
<td>35</td>
<td>-0.17</td>
<td>-0.50</td>
<td>0.17</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>43</td>
<td>0.04</td>
<td>-0.34</td>
<td>0.42</td>
</tr>
<tr>
<td>Certolizumab</td>
<td>1</td>
<td>0.20</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Golimumab</td>
<td>4</td>
<td>-0.65</td>
<td>-3.47</td>
<td>2.17</td>
</tr>
<tr>
<td>Infliximab</td>
<td>20</td>
<td>-0.36</td>
<td>-0.95</td>
<td>0.23</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>107</td>
<td>-0.11</td>
<td>-0.35</td>
<td>0.14</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>51</td>
<td>-0.02</td>
<td>-0.40</td>
<td>0.35</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>98</td>
<td>-0.15</td>
<td>-0.40</td>
<td>0.11</td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>49</td>
<td>-0.70</td>
<td>-1.08</td>
<td>0.31</td>
</tr>
<tr>
<td>Prednisone</td>
<td>68</td>
<td>-0.01</td>
<td>-0.25</td>
<td>0.24</td>
</tr>
<tr>
<td>Predictor variable</td>
<td>Coefficient</td>
<td>Confidence Interval</td>
<td>p value</td>
<td></td>
</tr>
<tr>
<td>-----------------------------------------</td>
<td>-------------</td>
<td>---------------------</td>
<td>---------</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>1.75</td>
<td>-3.80 to 7.30</td>
<td>0.54</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.00</td>
<td>-0.16 to 0.15</td>
<td>0.98</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.02</td>
<td>-3.33 to 3.36</td>
<td>0.99</td>
<td></td>
</tr>
<tr>
<td>Malignancy</td>
<td>0.54</td>
<td>-3.31 to 4.39</td>
<td>0.78</td>
<td></td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td>-1.48</td>
<td>-6.54 to 3.58</td>
<td>0.57</td>
<td></td>
</tr>
<tr>
<td><strong>Congestive Heart Failure</strong></td>
<td><strong>4.69</strong></td>
<td><strong>0.45 to 8.92</strong></td>
<td><strong>0.03</strong></td>
<td></td>
</tr>
<tr>
<td>Chronic Lung Disease</td>
<td>-0.95</td>
<td>-4.16 to 2.27</td>
<td>0.56</td>
<td></td>
</tr>
<tr>
<td>Chronic Kidney Disease</td>
<td>-5.57</td>
<td>-12.67 to 1.52</td>
<td>0.12</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>-0.81</td>
<td>-4.50 to 2.88</td>
<td>0.67</td>
<td></td>
</tr>
</tbody>
</table>

*Medication (comparator is methotrexate)*

<table>
<thead>
<tr>
<th>Medication</th>
<th>Coefficient</th>
<th>Confidence Interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adalimumab</td>
<td>-0.87</td>
<td>-6.83 to 5.09</td>
<td>0.78</td>
</tr>
<tr>
<td>Golimumab</td>
<td>-19.88</td>
<td>-44.57 to 4.82</td>
<td>0.12</td>
</tr>
<tr>
<td>Certolizumab</td>
<td>-7.02</td>
<td>-46.55 to 32.51</td>
<td>0.73</td>
</tr>
<tr>
<td>Infliximab</td>
<td>-3.85</td>
<td>-11.76 to 4.06</td>
<td>0.34</td>
</tr>
<tr>
<td>Etanercept</td>
<td>-2.07</td>
<td>-7.97 to 3.84</td>
<td>0.49</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>-2.66</td>
<td>-8.68 to 3.36</td>
<td>0.39</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>-5.78</td>
<td>-10.38 to -1.17</td>
<td>0.01</td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>-2.56</td>
<td>-8.26 to 3.15</td>
<td>0.38</td>
</tr>
<tr>
<td>Prednisone</td>
<td>3.76</td>
<td>-0.82 to 8.34</td>
<td>0.11</td>
</tr>
</tbody>
</table>

*Medication Class (comparator is conventional DMARDs)*

<table>
<thead>
<tr>
<th>Class</th>
<th>Coefficient</th>
<th>Confidence Interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNFi</td>
<td>0.30</td>
<td>-3.47 to 4.07</td>
<td>0.88</td>
</tr>
<tr>
<td><strong>Glucocorticoid</strong></td>
<td><strong>6.32</strong></td>
<td><strong>2.40 to 10.24</strong></td>
<td><strong>&lt;0.01</strong></td>
</tr>
</tbody>
</table>
Disclosure: P. R. Wood, None; E. Manning, None; J. Baker, None; G. Cannon, Amgen, 2; L. Davis, None; B. R. England, None; T. R. Mikuls, BMS, 2, Ironwood Pharm, 2; Pfizer Inc, 5, NIH, VA, 2; L. Caplan, None.


Abstract Number: 1037

**Biosimilar Knowledge Among US Rheumatologists – a Survey**

Allan Gibofsky\(^1,2\) and Sam Badawi\(^3\), \(^1\)Medicine and Public Health, Hospital for Special Surgery, New York, NY, \(^2\)Rheumatology, Weill Cornell Medicine, and Hospital for Special Surgery, New York, NY, \(^3\)Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT

First publication: September 18, 2017

**SESSION INFORMATION**
Session Date: Monday, November 6, 2017
Session Title: Health Services Research Poster II: Osteoarthritis and Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

**Background/Purpose:**

<table>
<thead>
<tr>
<th>Predictor variable</th>
<th>Coefficient</th>
<th>Confidence Interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>-0.12</td>
<td>-0.60, 0.36</td>
<td>0.63</td>
</tr>
<tr>
<td>Age</td>
<td>0.00</td>
<td>-0.01, 0.02</td>
<td>0.71</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.10</td>
<td>-0.20, 0.40</td>
<td>0.50</td>
</tr>
<tr>
<td>Malignancy</td>
<td>-0.20</td>
<td>-0.50, 0.09</td>
<td>0.17</td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td>0.07</td>
<td>-0.30, 0.43</td>
<td>0.72</td>
</tr>
<tr>
<td>Congestive Heart Failure</td>
<td>-0.07</td>
<td>-0.37, 0.22</td>
<td>0.62</td>
</tr>
<tr>
<td>Chronic Lung Disease</td>
<td>0.14</td>
<td>-0.11, 0.38</td>
<td>0.27</td>
</tr>
<tr>
<td>Chronic Kidney Disease</td>
<td>-0.35</td>
<td>-0.78, 0.07</td>
<td>0.11</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.01</td>
<td>-0.35, 0.38</td>
<td>0.95</td>
</tr>
</tbody>
</table>

Medication (comparator is methotrexate)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Coefficient</th>
<th>Confidence Interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adalimumab</td>
<td>0.17</td>
<td>-0.28, 0.62</td>
<td>0.46</td>
</tr>
<tr>
<td>Golimumab</td>
<td>-0.56</td>
<td>-1.81, 0.70</td>
<td>0.39</td>
</tr>
<tr>
<td>Certolizumab</td>
<td>0.41</td>
<td>-2.06, 2.87</td>
<td>0.75</td>
</tr>
<tr>
<td>Infliximab</td>
<td>-0.30</td>
<td>-0.90, 0.30</td>
<td>0.32</td>
</tr>
<tr>
<td>Etanercept</td>
<td>-0.08</td>
<td>-0.56, 0.40</td>
<td>0.75</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>0.05</td>
<td>-0.37, 0.47</td>
<td>0.81</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>-0.01</td>
<td>-0.36, 0.33</td>
<td>0.94</td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>-0.58</td>
<td>-1.00, -0.16</td>
<td>0.01</td>
</tr>
<tr>
<td>Prednisone</td>
<td>0.11</td>
<td>-0.26, 0.49</td>
<td>0.55</td>
</tr>
</tbody>
</table>

Medication Class (comparator is conventional DMARDs)

<table>
<thead>
<tr>
<th>Medication Class</th>
<th>Coefficient</th>
<th>Confidence Interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNFi</td>
<td>0.06</td>
<td>-0.23, 0.35</td>
<td>0.68</td>
</tr>
<tr>
<td>Glucocorticoid</td>
<td>0.20</td>
<td>-0.13, 0.53</td>
<td>0.23</td>
</tr>
</tbody>
</table>
Four biosimilar tumor necrosis factor α (TNFα) inhibitors have been approved by the FDA in the United States as of April 2017. This survey was developed to evaluate US rheumatologists’ familiarity with biosimilars, the concept of biosimilarity, and the approval process for biosimilars in the treatment of immune-mediated chronic diseases.

Methods:

A 20-question survey was administered by WebMD between December 9 and 14, 2016. Physicians (n=958) who were medscape.com members were invited to participate in an online survey via email. Most survey items used a 5-point Likert scale. Results were summarized descriptively.

Results:

Overall, 131 physicians responded, a response rate of 13.67%. Data were collected from 102 participants who were self-identified rheumatologists, practicing in the US for ≥1 year. All but 1 respondent had prescribed a TNFα monoclonal antibody (mAB) for the treatment of an autoimmune disease. When asked to choose the status of biosimilar development (as of December 2016), the majority (84%) of respondents were aware that an infliximab biosimilar was approved in the US, but only 47% and 34% were aware of the recent approvals of the adalimumab and etanercept biosimilars, respectively. Most physicians were extremely (38%) or moderately (36%) familiar with the FDA’s definition of a biosimilar. Most respondents (71%) were aware that an approved biosimilar was not automatically deemed interchangeable by the FDA. When asked to rate their expectations of biosimilar products, 74% indicated that an interchangeable designation was very or moderately important. Regarding other characteristics of the biosimilar compared with the originator, the majority indicated that effectiveness (96%), safety (96%), and durability of response (95%) were very or moderately important. Regarding treatment initiation, 66% of physicians were extremely likely or likely to initiate biosimilar treatment for a biologic treatment-naïve patient with RA if the approval included efficacy and safety studies in the same indication, whereas 5% and 29% were extremely likely or likely, respectively, to initiate biosimilar treatment for a biologic treatment-naïve patient with a different rheumatologic condition than the one on which the approval was based. Approximately 60% of survey respondents were unlikely to switch therapy from an originator to its biosimilar TNFα mAB in patients who were doing well, regardless of whether the patient had the same or a different rheumatologic indication than the one on which the biosimilar approval was based. Also, 21% of respondents were extremely likely or likely to switch to a biosimilar if the patient was failing on the originator.

Conclusion:

This survey supports a need to further educate US rheumatologists about biosimilars, extrapolation, and interchangeability. Knowledge gaps include a lack of understanding of biosimilarity based on switching, and the availability of currently approved biosimilars.

Disclosure: A. Gibofsky, Pfizer Inc, 1,AbbVie, 1,Amgen, 1,Bristol-Myers Squibb, 1,Johnson & Johnson, 1,Regeneron, 1,AbbVie, 5,AbbVie, 8,Pfizer Inc, 5,Pfizer Inc, 8,Celgene, 8,Novartis Pharmaceutical Corporation, 8,Takeda, 5,Horizon, 5,Relburn, 5,Samumed, 5; S. Badawi, Boehringer Ingelheim, 3.

Impact of Patient Support Program Utilization on Patient Activation Measure Scores Among Patients with Rheumatoid Arthritis

Filip van Den Bosch¹,², Siegfried Wassenberg³, Andrew Östör⁴, Chen Wang⁵, Vishvas Garg⁵ and Jasmina Kalabic⁶, ¹Ghent University Hospital, Ghent, Belgium, ²Rheumatology, Ghent University Hospital, Gent, Belgium, ³Rheumazentrum Ratingen, Ratingen, Germany, ⁴Addenbrooke's Hospital, Cambridge, United Kingdom, ⁵AbbVie Inc., North Chicago, IL, ⁶AbbVie Deutschland GmbH & Co. KG, Ludwigshafen, Germany

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Health Services Research Poster II: Osteoarthritis and Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM
Background/Purpose: AbbVie’s Patient (pt) Support Program (PSP) is offered to pts who are prescribed adalimumab (ADA) for their Rheumatoid arthritis (RA). The purpose of this analysis was to assess the association of Patient Activation Measure (PAM)-13 scores with PSP utilization among pts with moderate to severe RA initiating ADA who had option to enroll in the PSP.

Methods: PASSION (NCT01383421) was a 78-week post-marketing observational study of pts with RA receiving ADA in routine clinical care. Pts from the EU, Israel, Mexico, Puerto Rico, and Australia with an insufficient response to ≥1 disease-modifying antirheumatic drug (DMARD) newly initiating ADA (1 prior biologic DMARD was allowed) were enrolled. Pts were offered a panel of “Core elements” (starter pack, call center/hotline, nursing services, educational material, and injection guide; offered in all participating countries) and “Other elements” (e.g, refill reminders, email communications, newsletters, support groups, home medication delivery, and financial assistance; vary by country) of PSP. Pts were divided in 2 groups based on their participation in the PSP: ever (PSP users) vs never (PSP non-users). The PAM-13 scores were collected at baseline (BL) and at week 78. PAM-13 scores evaluate knowledge, skills, and confidence essential to a pt managing his/her own health. PAM-13 scores were classified a priori into 4 levels (higher level = greater pt involvement in disease management). Multivariate inferential analysis was used to examine the associations between PSP utilization (yes/no) and PAM-13 scores after adjusting for the following BL characteristics: age, gender, race, RA disease duration, prior use of biologic DMARD, BL Health Assessment Questionnaire Disease Index (HAQ-DI), and BL PAM-13 score. The response variable of the model was PAM-13 scores change from BL.

Results: PSP users had significantly larger increase in the PAM-13 scores (2.33, 95% CI 0.05 – 4.61, P=0.045) compared to the BL than the PSP non-users after adjusting for relevant BL characteristics (Figure 1A). Percentage of pts that demonstrated improvement in PAM-13 levels were significantly higher among PSP users vs PSP non-users at week 78 compared to BL (35.7% vs 28.1%, P=0.01) (Figure 1B). Additionally, lower PAM-13 and HAQ-DI BL scores were statistically significantly associated with increases in the PAM-13 scores at week 78 compared to BL.

Conclusion: Among pts with moderate to severe RA that initiated ADA treatment, PSP users reported significantly larger improvement from BL to week 78 in PAM-13 scores compared to the PSP non-users. Greater increase in PAM-13 scores among PSP users (vs. non-users) from baseline to week-78 indicate towards their increased ability in managing their health, gaining confidence and knowledge about their health, and taking action to maintain and improve their health.
Influences for Therapeutic Changes in Rheumatoid Arthritis Patients from the Veterans Affairs Rheumatology Arthritis Registry Who Have Moderate to High Disease Activity

Brian Sauer¹, Jacob R. Stever¹, Chia-Chen Teng, MS¹, Neil Accortt², David Collier² and Grant Cannon¹, ¹Salt Lake City VA Medical Center and University of Utah, Salt Lake City, UT, ²Amgen Inc., Thousand Oaks, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Health Services Research Poster II: Osteoarthritis and Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Current guidelines encourage the measurement of rheumatoid arthritis (RA) disease activity to achieve a low disease state (treat-to-target). Many RA patients with documented moderate to high disease activity, however, remain on their current regimen. This study used clinical and administrative data of US Veterans, identified as having moderate/high disease activity (DAS28≥3.2), to identify patient and treatment characteristics associated with a major change in therapy.

Methods: Patients in the Veterans Affairs (VA) RA registry were included if they had: 1) moderate/high disease activity on the index date, 2) 18-months of VA activity prior to the index and 3) two or more prior DAS28 measures during the preceding 18-months (≥ three months apart). Patients were defined as having a major change in therapy if any of the following occurred within 7 days prior to 30 days after the index date: 1) initiation or escalation of DMARDs, 2) initiation or increase dose of prednisone and/or 3) ≥ 2 joint injections. Disease stability was determined during the observation period prior to the index date using an area under the curve calculation and compared to the index DAS28. Patients were categorized as improving (index DAS28 was ≥ 0.6 points lower), worsening (≥ 0.6 higher) or stable. Poisson multivariable regression was used to explore how demographic, clinical and treatment patterns influenced the initial finding that stability of disease activity was a strong predictor of a major treatment change.

Results: Of the 941 patients who met enrollment criteria only 41% had a major therapeutic change. Major therapeutic changes occurred in 50%, 37% and 30% with worsening, stable and improved DAS28, respectively. In multivariable models, patient demographics and individual components of the DAS28 score were not independently associated with a major therapeutic change. In the full model, the current DAS28, and oral steroids and non-biologic DMARDs in the past year increased the likelihood of a major change. Non-biologic DMARDs in the past 90-days decreased the likelihood of a major change. Table 1 displays the RR with “stable DAS28” as the comparison group after adjustment for demographic, demographic + DAS28 and clinical components and the full model, which added indicators of medication use, surgery, radiographs and comorbidity scores.

Conclusion: More than half the patients did not experience a major change in therapy despite moderate/high disease activity even among those patients with worsening disease. In crude analysis, the likelihood that RA patients with moderate/high RA disease received a change in therapy was highly associated with worsening disease activity, but this effect was diminished when accounting for current DAS28, indicators of non-biologic DMARDs and steroid use in the previous year. The decision to modify therapy is complex and we are conducting chart-review to better understand why providers are not modifying therapy.
Table 1. Effect of stability of disease activity on major therapeutic change after adjustment for patient, clinical and treatment variables

<table>
<thead>
<tr>
<th>Comparators</th>
<th>Crude Model</th>
<th>Demographic Adjusted</th>
<th>Demographic + DAS and components</th>
<th>Full Model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR</td>
<td>LCI</td>
<td>UCI</td>
<td>RR</td>
</tr>
<tr>
<td>Worse vs stable DAS28</td>
<td>1.36</td>
<td>1.07</td>
<td>1.73</td>
<td>1.31</td>
</tr>
<tr>
<td>Improved vs stable DAS28</td>
<td>0.79</td>
<td>0.55</td>
<td>1.14</td>
<td>0.81</td>
</tr>
<tr>
<td>Index DAS28*</td>
<td></td>
<td></td>
<td></td>
<td>1.42</td>
</tr>
<tr>
<td>Oral Steroids</td>
<td></td>
<td></td>
<td></td>
<td>1.42</td>
</tr>
<tr>
<td>Non-Biologic DMARD year</td>
<td></td>
<td></td>
<td></td>
<td>1.69</td>
</tr>
<tr>
<td>Non-Biologic DMARD Rd</td>
<td></td>
<td></td>
<td></td>
<td>0.67</td>
</tr>
</tbody>
</table>

*Variables with significant association from the full model are presented. RR = Risk Ratio, LCI = Lower bound of 95% confidence interval (CI), UCI = Upper bound of the 95% CI

Disclosure: B. Sauer, Amgen, 2; J. R. Stever, None; C. C. Teng, MS, Amgen, 2; N. Accortt, Amgen, 1,Amgen, 3; D. Collier, Amgen, 1,Amgen, 3; G. Cannon, Amgen, 2.


Abstract Number: 1040

**Perceptions of US Community Rheumatologists on Biosimilars**

Janna Radtchenko, Yolaine Smith, Jonathan Kish and Bruce Feinberg, Specialty Solutions, Cardinal Health, Dallas, TX

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017

Session Title: Health Services Research Poster II: Osteoarthritis and Rheumatoid Arthritis

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM

**Background/Purpose:** Biosimilars contain a highly similar version of the active substance of an already approved biologic or “reference product.” Regulatory agencies mandate that safety, efficacy, dosing, route of administration, and immunogenicity are established. The FDA allows extrapolation of safety and efficacy data from one biosimilar indication to another significantly lowering drug development cost. Biosimilars are thereby expected to have a lower price point than their reference product and result in reduced healthcare spending, but that will largely depend on how providers perceive and prescribe them. As of May 2017, four biosimilars have been FDA approved for rheumatologic conditions. We have evaluated the perceptions of U.S. community rheumatologists to identify areas of opportunity to support biosimilar adoption

**Methods:** Using audience response technology, we surveyed 24 community rheumatologists and 20 rheumatology practice managers (PMs) during a live meeting in April 2017. Participating physicians and PMs represented various practice sizes and geographic locations throughout the U.S.

**Results:** Regarding the legal and regulatory aspect of biosimilars and their reference biologics: only 51% of the respondents understood the concept of interchangeability between biosimilars and reference biologic; 76% were unaware of compatibility requirements for reference biologics following a manufacturing change; while only 40% believed biosimilars match the safety and efficacy of their reference biologics. When asked if they or their practice would prescribe a biosimilar approved for anti-rheumatic treatment: 20% would not prescribe at all, only 23% would switch a patient from the reference biologic, and 57% responded that they would prescribe it to patients initiating biologic therapy. The responses to the query, “Which issues are most concerning?” in descending order are: Regulations related to substitutions, understanding when to prescribe a biosimilar versus a reference biologic, and coordinating with pharmacists on substitutions. Information about safety and efficacy, guidelines on when to prescribe a reference biologic versus a biosimilar, and reimbursement information were named as tools for achieving a greater understanding of biosimilars.

**Conclusion:** Significant barriers to biosimilar adoption for rheumatologic conditions exist due to physicians’ perceptions. Education around biosimilar efficacy, safety, appropriate use, and reimbursement may improve perceptions and facilitate usage.

Disclosure: J. Radtchenko, None; Y. Smith, None; J. Kish, None; B. Feinberg, None.
Abstract Number: 1041

Real-World Utilization of Biosimilars for Management of Rheumatoid Arthritis (RA) in the US

Janna Radtchenko, Yolaine Smith, Jonathan Kish and Bruce Feinberg, Specialty Solutions, Cardinal Health, Dallas, TX

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Health Services Research Poster II: Osteoarthritis and Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: A biosimilar product is a biological product highly similar to another FDA-approved biological product, reference product, and has no clinically meaningful differences in safety and effectiveness from the reference product. While four biosimilars have been approved by the FDA in rheumatology in 2016-2017, only one biosimilar infliximab-dyyb (IFX-b) has launched. We have evaluated early uptake of IFX-b in RA following its approval in April 2016 and launch in November 2016.

Methods: Symphony Health longitudinal prescription and medical claims data was used to evaluate the uptake of IFX-b relative to its reference product infliximab (IFX) from biosimilar approval through Q1 2017. The database contains claims records for 279 million unique patients representing an estimated 63% of specialty prescriptions, 58% of medical claims, and 25% of hospital claims in the US. Duration of therapy was defined as days from biologic initiation to the last administration. Time to treatment discontinuation (TTD) was defined as months from biologic initiation to switch or last administration + 90 days if no other biologic was administered. Duration of therapy was described with a Kaplan-Meier curves. Patient characteristics were evaluated using frequencies for categorical and mean and standard deviation (SD) for continuous variables.

Results: Of the 78,481 patients who initiated a biologic/biosimilar therapy for RA since IFX-b approval, 90 (0.1%) were treated with IFX-b and 5,178 (6.6%) were treated with IFX. The first patient started IFX-b in May 2016 and 78 IFX-b patients (86.7%) started in Q1 2017. Of the patients treated with IFX-b, 66 (73.3%) were female, 58 (64.4%) were 65 or older, 1 patient was commercially insured, the rest were with unknown insurance status, 31 (34.4%) were previously treated with IFX, 56 (62.2%) received IFX-b as their first biologic. Mean (SD) age for IFX-b patients was 65.9 (12.4) compared to 55.0 (16.7) for infliximab patients (p<0.0001). Mean (SD) number of prior biologics was 0.5 (0.8) for IFX-b and 0.5 (0.9) for IFX patients. Median (mean) duration was 1.0 (4.5) days for IFX-b and 60.0 (101.2) for IFX (Log Rank P<0.001) due to late IFX-b adoption.

Conclusion: Adoption of IFX-b in the US so far has been low and has not yet significantly impacted the reference biologic. The majority of IFX-b patients received it as first biologic, however a third of them switched from IFX. Duration of therapy on IFX-b is relatively short due to delayed launch. Future monitoring of IFX-b uptake is warranted especially as other approved biosimilars prepare for launch.

Disclosure: J. Radtchenko, None; Y. Smith, None; J. Kish, None; B. Feinberg, None.

Remote Management of Osteoporosis Screening and Treatment in US Veterans Using a Bone Health Team: A Cost-Effectiveness Analysis

Karla L. Miller1, Jordan King2, Phillip Lawrence3, Richard Nelson4, Joanne Lafluer5, Grant Cannon6 and Scott Nelson7, 1Internal Medicine, Veterans Affairs Salt Lake City Health Care System and University of Utah School of Medicine, Salt Lake City, UT, 2Clinical Pharmacy Specialist, Research, Kaiser Permanente Colorado, Aurora, CO, 3Salt Lake City VA Medical Center and Roseman University of Health Sciences, Salt Lake City, UT, 4Epidemiology, Veterans Affairs Salt Lake City Health Care System and University of Utah
Remote Management of Osteoporosis Screening and Treatment in US Veterans using a Bone Health Team: A Cost-effectiveness Analysis

**Background/Purpose:** To evaluate the cost effectiveness of a bone health team (BHT) as a primary prevention service to screen, monitor, and treat Veterans at risk for fragility fractures compared to current clinical practice from the Veteran’s Administration (VA) perspective over a life-time.

**Methods:** We conducted this analysis by adapting a previously validated Markov microsimulation model of osteoporosis incidence and outcomes in the VA. The model was used to estimate fracture events, quality-adjusted life years (QALYs), and direct healthcare costs of using a BHT vs current clinical practice. Model inputs were derived from national sources, published literature, and program estimates from the BHT. Uncertainty in model parameters was assessed by conducting one-way and probabilistic sensitivity analyses.

**Results:** In the base-case, the BHT was associated with a substantially higher proportion of patients with underlying osteoporosis or osteopenia diagnosed and treated with bisphosphonates (osteoporosis: 38.0% vs 6.9%, osteopenia: 25.5% vs 0.2%). This resulted in the BHT strategy being associated with a modestly lower fracture rate than current clinical practice. In probabilistic sensitivity analysis, the BHT was the dominant option; however, in all analyses, no meaningful differences were observed in life-time estimated costs, unadjusted survival, and QALYs between the prevention strategies.

**Conclusion:** A BHT appears to be a potentially cost-effective method for screening and treating US Veterans for osteoporosis compared to no intervention. Quality improvement programs addressing primary prevention of osteoporotic fractures provide a feasible, team-based, approach to this important problem, while unburdening the increasingly limited time and availability of primary care providers.

**Disclosure:** K. L. Miller, None; J. King, None; P. Lawrence, None; R. Nelson, None; J. Lafleur, None; G. Cannon, Amgen, 2; S. Nelson, None.
Abstract Number: 1043

Comparison of the Costs for Hyaluronic Acid and Total Knee Arthroplasty in the Treatment of OA for the Blue Cross/Blue Shield Patient Population

Kevin Ong1, Faizan Niazi2, Edmund Lau3, Peter Shaw2 and Steven Kurtz1, 1Exponent, Inc., Philadelphia, PA, 2Ferring Pharmaceuticals, Inc., Parsippany, NJ, 3Exponent, Inc., Menlo Park, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Health Services Research Poster II: Osteoarthritis and Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Previous HA studies have focused on the Medicare population, but less is known of the treatment patterns and cost of HA relative to knee arthroplasty (KA) and other therapies for younger privately insured patients. We evaluated the overall cost of treating knee OA in a large group of Blue Cross/Blue Shield (BCBS) patients, including those from KA and non-arthroplasty therapies, such as HA, corticosteroid injections, and physical therapy. We hypothesized that non-arthroplasty interventions would account for the majority of knee OA costs in the younger patient population.

Methods: Knee OA-related claims were identified from Blue Health Intelligence claims data (2011-2015). The dataset contains claims for 140+ million unique BCBS members nationwide in the U.S. Cumulative costs (adjusted to November 2016$) were evaluated from a payor perspective and grouped into various categories, such as physical therapy, corticosteroid injections, HA, and KA.

Results: The overall cost of treating knee OA for 1,567,024 knee OA patients over the five-year period was $5.7B (average $3,600/patient). HA accounted for $196.9M (3.5%) of the overall cost, based on 216,523 HA patients (13.8% of knee OA cohort). KA accounted for $3.6B (63.5%) of the overall cost, while office visits, arthroscopy, anesthesia for knee surgery, arthrocentesis, knee imaging, and physical therapy accounted for $229.3M (4.0%), $141.8M (2.5%), $140.8M (2.5%), $124.6M (2.2%), $115.0M (2.0%), and $51.9M (0.91%), respectively. 16.5% of the HA patients subsequently underwent knee arthroplasty during the study period, but HA contributed to 2.8% of their overall knee OA treatment costs compared to KA, which contributed 82.9%. For those who received KA, the median costs for the HA cohort were lower at 1 and 2 years compared to the no-HA cohort, but similar at 3 years and marginally higher at 4 years (Table 1). If the 180,862 HA patients who avoided KA during the study period had, instead, undergone arthroplasty, the cost of KA would be estimated to total $4.8B. Instead, there was a cost savings of $4.3B (90.1%) by utilizing non-arthroplasty therapies.

Conclusion: Non-arthroplasty therapies accounted for about a third of the costs (36.5%) in treating knee OA in our cohort of younger patients. Interventions that were not recommended or determined to have inconclusive evidence by AAOS accounted for 3.5% (HA), 0.12% (corticosteroid), and 0.54% (knee brace) of the overall costs. Although questions have been raised about the effectiveness of HA, the majority of HA patients avoided knee arthroplasty during the study period; they saved an estimated 90.1% by utilizing non-arthroplasty therapies. With the wide spectrum of therapies to treat knee OA, efforts to identify the most appropriate candidates for arthroplasty and non-arthroplasty therapies, such as HA or other non-HA therapies, can help reduce costs to the healthcare system.


Table 1. Knee OA-related costs (median) stratified by HA and knee arthroplasty groups.

<table>
<thead>
<tr>
<th></th>
<th>No HA (Without arthroplasty)</th>
<th>No HA (With arthroplasty)</th>
<th>HA (Without arthroplasty)</th>
<th>HA (With arthroplasty)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=1,247,689</td>
<td>n=162,812</td>
<td>n=180,862</td>
<td>n=35,661</td>
</tr>
<tr>
<td>1 year</td>
<td>$173</td>
<td>$14,832</td>
<td>$1,197</td>
<td>$2,429</td>
</tr>
<tr>
<td>2 year</td>
<td>$198</td>
<td>$24,521</td>
<td>$1,693</td>
<td>$20,588</td>
</tr>
<tr>
<td>3 year</td>
<td>$223</td>
<td>$27,014</td>
<td>$1,939</td>
<td>$27,945</td>
</tr>
<tr>
<td>4 year</td>
<td>$260</td>
<td>$28,066</td>
<td>$2,364</td>
<td>$29,793</td>
</tr>
</tbody>
</table>
Abstract Number: 1044

Medical Care Costs Associated with Rheumatoid Arthritis in the US: A Meta-Analysis

Andrew Hresko¹, Tzu-Chieh Lin² and Daniel H. Solomon³, ¹Tufts Medical School, Boston, MA, ²Health Outcomes, Amgen, Thousand Oaks, CA, ³Brigham and Women's Hospital and Harvard Medical School, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Health Services Research Poster II: Osteoarthritis and Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a morbid, mortal, and costly condition without a cure. Treatments for RA have expanded over the last two decades with the introduction of biologic disease modifying anti-rheumatic drugs (bDMARDs). Biologic DMARDs offer alternatives for patients unresponsive to traditional synthetic DMARDs, but carry an increased financial burden. Detailed understanding of the cost of care for RA patients since the advent of bDMARDs is of importance to policy makers, administrators, and physicians, as the high cost of RA treatments impacts the use of limited medical resources.

Methods: We conducted a systematic literature review and meta-analysis to assess direct annual medical cost for RA patients in the US receiving any treatment regimen for RA since the marketing of the first bDMARD in 1999. Studies were identified through a search of Medline using MeSH search terms related to cost of care and RA. Data were extracted independently by two reviewers (AH and DHS). Total direct medical costs as well as RA-specific costs were calculated using random effects meta-analysis. A subgroup analysis addressed costs for RA patients using bDMARDs.

Results: We found 541 potentially relevant studies and 11 papers met the selection criteria for meta-analysis. Total direct annual medical costs were estimated at $12,509 (95% CI $7,451-21,001) for all RA patients using any treatment regimen (see Figure 1) and $36,053 (95% CI $32,138-40,445) for bDMARD users (see Figure 2). RA-specific annual costs were $3,723 (95% CI $2,408-5,762) for all RA patients using any treatment regimen, representing 30% of total costs for all care. RA-specific annual costs were $20,262 (95% CI $17,480-23,487) for bDMARD users, representing 56% of total costs for all care.

Conclusion: The total and disease-specific direct annual medical cost of patients with RA is substantial. Among bDMARD users, cost of RA care is over half of all direct medical costs. These findings indicate that the burden of RA patients on the US health care system may become outsized compared to the disease’s relatively small prevalence as more patients use bDMARDs in the future. While patients that use bDMARDs have increased annual cost over typical RA patients, the increment is below the total cost of bDMARDs themselves. This discrepancy suggests that either the use of bDMARDs is associated with lower total non-drug direct medical costs or that there are crucial underlying demographic differences between bDMARD and traditional DMARD users.

Figure 1: Total Cost of Care, All Patients

<table>
<thead>
<tr>
<th>Study</th>
<th>Cost ($)</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Michaud</td>
<td></td>
<td>12.45</td>
</tr>
<tr>
<td>Kawaiho</td>
<td></td>
<td>1.87</td>
</tr>
<tr>
<td>Birnbaum</td>
<td></td>
<td>12.3</td>
</tr>
<tr>
<td>Harald (2000)</td>
<td></td>
<td>12.1</td>
</tr>
<tr>
<td>Harald (2002)</td>
<td></td>
<td>12.23</td>
</tr>
<tr>
<td>Harald (2006)</td>
<td></td>
<td>12.29</td>
</tr>
<tr>
<td>Johnson (Lumi)</td>
<td></td>
<td>12.36</td>
</tr>
<tr>
<td>Johnson (Rest)</td>
<td></td>
<td>12.26</td>
</tr>
<tr>
<td>Pooled $12,509 ($7,451-$21,001)</td>
<td></td>
<td>100</td>
</tr>
</tbody>
</table>
The Potential Value of a Shared Decision-Making Intervention for Choices Regarding Triple Therapy in Rheumatoid Arthritis

Nick Bansback1, Tima Mohammadi2, Aslam Anis3, James R. O'Dell4 and Glen Hazelwood5, 1School of Population and Public Health, University of British Columbia, Vancouver, BC, Canada, 2Centre for Health Evaluation and Outcome Sciences, Vancouver, BC, Canada, 3University of British Columbia, School of Population and Public Health, Vancouver, BC, Canada, 4Department of Internal Medicine, University of Nebraska Medical Center, Omaha, NE, 5Division of Rheumatology, University of Calgary, Calgary, AB, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Health Services Research Poster II: Osteoarthritis and Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Previous studies have shown that using Triple Therapy (a combination of 3 generic drugs) prior to a biologic, is the most cost-effective strategy for patients with rheumatoid arthritis. While studies also find that many patients would prefer to trial Triple Therapy prior to a biologic, fewer than 5% of patients do so in the US. We determined the potential value of an intervention that promotes informed shared decision-making between patients and clinicians around triple therapy use after failure of methotrexate.

Methods: We developed an economic model that compared a strategy where patient preferences for triple therapy use were integrated into treatment decisions, versus usual care. A previous study suggests that 59% of patients would choose triple therapy first if provided the comparative evidence of benefits, potential adverse events and dosing schedule. We assumed a cost of $50 for a shared decision making intervention such as a patient decision aid. Patient’s trialling triple therapy first were assumed to switch to a sequence of biologics upon withdrawal. We extrapolated the influence of the initial treatment decision on subsequent disease progression, resource use such as hospitalizations, quality of life, mortality and Quality Adjusted Life Years (QALYs). Various sensitivity analyses were performed. A scenario that incorporated the value patients assign to the process of shared decision-making was also considered.

Results: Incorporating patient preferences into the decision was estimated to reduce average costs for a patient by $40,000 over a lifetime through delaying the introduction of biologic therapy. Even under the most pessimistic assumptions regarding the potential for earlier biologic use delaying joint erosions, only 0.08 QALYs (28 days of full health) over a lifetime were estimated to be lost. The consequent incremental cost-effectiveness ratio for usual care vs the patient preference strategy is over $500,000/QALY. Sensitivity analysis supported this finding. Incorporating the process of shared decision-making offsets the negative QALYs, implying the patient preference strategy saves costs and increases QALYs.
Conclusion: This study demonstrates that systematically giving patients with rheumatoid arthritis who fail methotrexate an informed choice between triple therapy and a biologic as the initial treatment is cost-saving and can even provide more 'benefits' to the patient. This strategy allows patients who prefer biologic therapy to choose it, but saves costs by delaying the biologic initiation in patients who choose triple therapy first. The results suggest that strategies used elsewhere for increasing shared decision-making such as building infrastructure for implementing patients decision aids, or introducing fee codes for shared decision-making, could be cost-effective and should be explored to promote value based prescribing in rheumatology.

Disclosure: N. Bansback, None; T. Mohammadi, None; A. Anis, None; J. R. O'Dell, Medac, 5, Coherus, 5; G. Hazlewood, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-potential-value-of-a-shared-decision-making-intervention-for-choices-regarding-triple-therapy-in-rheumatoid-arthritis

Abstract Number: 1046

Biological and Targeted Synthetic Dmards’ Prior Authorization Time Is Significantly Reduced with Pharmacy Presence in the Rheumatology Clinic

Wendy Ramey1, Kristine M. Lohr2, Matt Zeltner1, Haley Herrell Postonl1, Andrew Johannemann1, Arie D. Schadler1 and Aleksander Lenert3, 1University of Kentucky, Lexington, KY, 2Rheumatology, University of Kentucky, Lexington, KY, 3Internal Medicine, Div. of Rheumatology, University of Kentucky, Lexington, KY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Health Services Research Poster II: Osteoarthritis and Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Treatment with biological DMARDs (bDMARD) and targeted synthetic DMARDs (tsDMARD) has led to improved outcomes for chronic rheumatic diseases. Current treat-to-target (T2T) strategy relies on quick escalation in therapy to achieve disease control. A delay in escalation of therapy may impact clinical outcomes adversely. Insurance prior authorization, required for specialty DMARD approval, represents a significant bottleneck to care. Clinical pharmacists embedded in a collaborative clinical team could optimize rheumatologic care by shortening time to specialty medication authorization. Our aim was to assess the impact of pharmacy support on specialty DMARD approval in an academic rheumatology clinic.

Methods: We performed a retrospective review of patient records followed in the Rheumatology Clinics at the University of Kentucky who were prescribed specialty medications for RA, PsA and AS. All patients were diagnosed by clinical rheumatologists and met ACR, CASPAR or ASAS criteria respectively. We included 8 bDMARDs and 2 tsDMARDs currently prescribed. We collected data during two 6 month periods from prescriptions written pre-pharmacy (1/2014-6/2014) and post-pharmacy establishment (1/2016-6/2016). We excluded the transition to pharmacist period of 7/2014-12/2015. Our primary outcome was the time to authorization defined as time (in days) between rheumatologist's prescribing and pharmacist's completion of authorization for a given specialty DMARD. We compared the mean time to authorization pre- and post-pharmacist establishment in the rheumatology clinic. Statistical analysis was performed with IBM SPSS Statistics 23; continuous variables were analyzed utilizing an independent samples t-test and categorical variables with Pearson's chi-square test.

Results: We screened 423 specialty prescriptions; 112 were eligible for study inclusion. Thirty-one specialty prescriptions from 28 patients were completed pre-pharmacist (Group 1) and 81 specialty prescriptions from 71 patients were completed post-pharmacist (Group 2) (Table 1). There were no significant differences between the groups in baseline characteristics that were tested including age, gender, diagnosis, and type of insurance. The majority of patients were women with RA; most patients had commercial insurance or Medicaid. The mean time to authorization was significantly shorter post-pharmacist compared to pre-pharmacist routine care (6.43±15.48 vs. 52.03±58.64 days, p=0.002).

Conclusion: In a large tertiary academic rheumatology practice, the mean time to authorization of specialty DMARDs was significantly reduced to <7 days with establishment of a clinical pharmacist in a collaborative clinical team, facilitating implementation of T2T strategy.
**Disclosure:** W. Ramey, None; K. M. Lohr, None; M. Zeltner, None; H. Herrell Postonl, None; A. Johannemann, None; A. D. Schadler, None; A. Lenert, None.


**Abstract Number:** 1047

**Cost-Effectiveness of Drug-Level Guided Adalimumab Dosing**

**Zara Izadi**1, Gabriela Schmajuk2, Milena Gianfrancesco3, Laura Trupin4, Kashif Jafri5, Jinoos Yazdany4 and Dhruv Kazi6,  
1Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, CA,  
2San Francisco VA Medical Center,  
University of California San Francisco, San Francisco, CA,  
3Medicine/Rheumatology, University of California, San Francisco, San Francisco, CA,  
4Medicine/Rheumatology, University of California San Francisco, San Francisco, CA,  
5University of California, San Francisco, San Francisco, CA,  
6Department of Medicine, University of California, San Francisco, Zuckerberg San Francisco General Hospital, San Francisco, CA

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Monday, November 6, 2017

---

**Table 1. Baseline Characteristics and Comparison of Time to Authorization of DMARDs**

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (Pre) (N = 32)</th>
<th>Group 2 (Post) (N = 81)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age – year*</td>
<td></td>
<td></td>
<td>0.330</td>
</tr>
<tr>
<td>Mean</td>
<td>47.07±15.68</td>
<td>49.93±12.20</td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>48 (35-56)</td>
<td>51 (42-58)</td>
<td></td>
</tr>
<tr>
<td>Sex – no. (%)*</td>
<td></td>
<td></td>
<td>0.089</td>
</tr>
<tr>
<td>Male</td>
<td>4 (14.3)</td>
<td>22 (27.1)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>24 (75.7)</td>
<td>49 (62.0)</td>
<td></td>
</tr>
<tr>
<td>Diagnosis – no. (%)*</td>
<td></td>
<td></td>
<td>0.859</td>
</tr>
<tr>
<td>RA</td>
<td>22 (71.9)</td>
<td>51 (62.7)</td>
<td></td>
</tr>
<tr>
<td>PsA</td>
<td>5 (17.9)</td>
<td>16 (20.0)</td>
<td></td>
</tr>
<tr>
<td>AS</td>
<td>1 (3.6)</td>
<td>3 (4.2)</td>
<td></td>
</tr>
<tr>
<td>Insurance Type – no. (%)*</td>
<td></td>
<td></td>
<td>0.771</td>
</tr>
<tr>
<td>Commercial</td>
<td>13 (43.3)</td>
<td>27 (33.3)</td>
<td></td>
</tr>
<tr>
<td>Medicaid</td>
<td>12 (40.0)</td>
<td>35 (43.2)</td>
<td></td>
</tr>
<tr>
<td>Medicare</td>
<td>5 (16.7)</td>
<td>13 (16.9)</td>
<td></td>
</tr>
<tr>
<td>Time to Authorization – days</td>
<td></td>
<td></td>
<td>0.0002</td>
</tr>
<tr>
<td>Mean</td>
<td>52.03±25.64</td>
<td>64.3±15.48</td>
<td></td>
</tr>
</tbody>
</table>

* N = represents number of specialty DMARD approvals in each group respectively. *Based on 28 patients in Group 1 and 71 patients in Group 2. Plus-minus (±) values represent standard deviation of the mean. AS = ankylosing spondylitis; PsA = psoriatic arthritis; RA = rheumatoid arthritis; IQR = interquartile range.
Background/Purpose: Adalimumab (ADA) induces and maintains clinical remission in patients with rheumatoid arthritis (RA) and Crohn’s disease (CD) but is an expensive drug. Drug-level and antidrug antibody testing has the potential to facilitate personalization of dosing, particularly the use of less frequent dosing of ADA (de-escalation). The cost-effectiveness of drug-level guided dose de-escalation of therapy is unknown.

Methods: We evaluated the effectiveness (in quality adjusted life years [QALYs]) and cost-effectiveness of a drug-level guided dose-reduction strategy for ADA compared with standard dosing in patients with CD who are in clinical remission, from a health system perspective using a 4-year horizon. We chose CD rather than RA because drug-level guided dose de-escalation studies have not been conducted in RA. We developed a discrete-time Markov simulation model for the analysis, using inputs from published randomized controlled trials and observational studies. The intervention studied was reduction in frequency of ADA dosing from 40mg every other week (EOW) to 40mg every three weeks (ETW) among patients with sustained clinical remission and therapeutic ADA trough levels. Patients who lost clinical remission would undergo drug-level testing. A switch to an alternate biologic was indicated with positive antidrug antibodies or drug resistance (adequate levels despite active symptoms); otherwise the dose was re-escalated back to 40mg EOW. Standard dosing (control arm) involved continuation of 40mg EOW dosing and switch to an alternate biologic on loss of clinical remission.

Results: Among patients with CD in remission on standard dose ADA, reductions in dose yielded similar QALYs but lower costs compared with continuing standard dosing strategy. The difference between the standard and dose-reduction strategies ranged from 0.00 to 0.06 QALYs across the range of probabilities tested (with standard strategy being marginally more effective), but the intervention resulted in cost-savings in every circumstance. In sensitivity analyses, the dose-reduction strategy was the dominant option (less costly and more effective) when ≥87% of patients who were controlled on standard dosing continued to be in remission under the dose-reduction strategy. The findings were most sensitive to the probability of formation of antidrug antibodies after dose reduction and the cost of ADA.

Conclusion: Based on lower costs and similar overall efficacy, dose reduction may be a cost-saving alternative among patients with CD who are in sustained remission with therapeutic ADA levels. These findings suggest that further research to explore drug-level guided tapering in RA may also be warranted. Given the small difference we observed in incremental effectiveness, our proposed strategy may prove to be dominating if future studies also demonstrate that reduced dosing improves the safety of ADA.

<table>
<thead>
<tr>
<th>Table 1: Cost effectiveness rankings by study horizon</th>
</tr>
</thead>
<tbody>
<tr>
<td>Horizon</td>
</tr>
<tr>
<td>---------</td>
</tr>
<tr>
<td>4 years</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>3 years</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>2 years</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>1 year</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

ICER: Incremental cost-effectiveness ratio. Costs are in USD. Difference in incremental effectiveness between the two arms was reduced to 0.00 using a study horizon of 1 year. Cumulative probability of clinical remission at 4 years was 67% in the dose reduction arm versus 74% in standard dosing arm (p=0.2759).

Disclosure: Z. Izadi, None; G. Schmajuk, None; M. Gianfrancesco, None; L. Trupin, None; K. Jafri, None; J. Yazdany, None; D. Kazi, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/cost-effectiveness-of-drug-level-guided-adalimumab-dosing

Abstract Number: 1048

Efficacy of Educating Visiting Pharmacists Regarding Drug Administration for Patients with Rheumatoid Arthritis Who Poorly Adhere to Treatment Regimens

Masatoshi Hayashi, Hiroyuki Matsubara, Kei Funamura, Masataka Maeda and Toshihisa Kanamono, Rheumatology, Nagano Red Cross Hospital, Nagano, Japan, Orthopaedics, Hekinan municipal hospital, Hekinann, Japan

First publication: September 18, 2017

SESSION INFORMATION
Background/Purpose: Patients with rheumatoid arthritis (RA) need to take lifelong oral or injectable medication to alleviate their symptoms and prevent disease progression. However, some patients may not adhere or poorly adhere to treatment and have poor understanding of biological agents. Poor or no adherence may be attributed to the following factors: complex regimen for medications, such as methotrexate (MTX), difficulty in self-administration of injectables due to hand deformities, and forgetfulness due to dementia. This study aimed at determining the effect of educating visiting pharmacists regarding administration of oral medication and injectables for patients with RA who poorly adhere to treatment regimens.

Methods: A prospective analysis was performed by enrolling 21 patients with RA who were treated with different types of medication, including self-injectable biological agents. Two cases were excluded because one had been added on subcutaneous tocilizumab and the other on MTX with increased dosage. The remaining 19 cases did not have any change in their treatment, including dosage or intervals between drug administration, just before and after the pharmacist visit. Baseline characteristics, such as age, Steinblocker Stage and Class, disease duration, use of biological agents, use of MTX and its dosage, use of prednisolone (PSL) and its dosage, presence of dementia, and living or not living alone, were assessed. DAS28-ESR, SDAI and CDAI as markers of RA disease activity were evaluated just before and after the pharmacist visit.

Results: Mean ± SD were as follows: age (years), 74.4 ± 6.1; Stage I, 1; II, 4; III, 6; IV, 8; Class 1, 0; 2, 7; 3, 8; 4, 4; disease duration (months), 144.2 ± 114.5; use of biological agents; 36.8%; use of MTX and its dosage (mg/week), 84.2% and 6.6 ± 2.7; use of PSL and its dosage (mg/day), 47.4% and 4.4 ± 1.2; presence of dementia, 10.5%; living alone, 42.1%. The mean values of DAS28-ESR, SDAI, and CDAI just before and after the pharmacist visit showed improvements; they were 3.56 ± 1.46 and 3.12 ± 1.16 (p = 0.084), 7.99 ± 6.88 and 4.39 ± 3.47 (p = 0.0176), and 6.85 ± 5.74 and 3.90 ± 3.18 (p = 0.0148), respectively. All patients reported satisfaction with the overall effectiveness of the care.

Conclusion: Adherence to treatment in patients with RA may decline with increasing age. For such patients, education regarding oral and injectable medication may be useful in controlling RA activity and avoiding any adverse effects due to consumption of wrong medication. This finding is important for better and safer management of patients with RA in the ageing communities in Japan and other developed countries.

Disclosure: M. Hayashi, None; H. Matsubara, None; K. Funamura, None; M. Maeda, None; T. Kanamono, None.

Heart Rate Variability Testing with Autonomic Nervous System Optimization: Could It Change the Course of Spending for Rheumatoid Arthritis Patients in the U.S.? an Exploratory Minimal Model Analysis

Marita Zimmermann1, Elisabeth Vodicka2, Andrew J Holman3,4,5 and Louis P Garrison2, 1Constants in Global Health, University of Washington, Seattle, WA, 2Consultants in Global Health, University of Washington, Seattle, WA, 3Rheumatology, Pacific Rheumatology Associates Inc PS, Seattle, WA, 4Inmedix, Normandy Park, WA, 5Pacific Rheumatology Research, Seattle, WA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Health Services Research Poster II: Osteoarthritis and Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Autonomic nervous system (ANS) testing with heart rate variability (HRV) has been shown to predict 52-week anti-TNF therapeutic outcomes in rheumatoid arthritis (RA). HRV testing could be combined with the three currently available putative ANS biologic
pathways (vagal nerve stimulation, obstructive sleep apnea, and restless leg [RLS] medications) to improve treatment response for RA patients. We explored the potential costs and health outcomes of introducing HRV testing into RA treatment, both without vs. with ANS optimization.

Methods:

A decision tree exploratory economic model compared HRV testing to standard care in moderate-to-severe biologic-eligible patients over a 10-year time horizon. Patients were stratified by HRV test scores into “low probability of response” and “moderate to high probability of response” (parasympathetic HRV<= vs. >0.12) with positive predictive value (PPV)=33% and negative predictive value (NPV)=100%. We then explored adding ANS optimization (RLS method) based on HRV score, with patients stratified into parasympathetic <= vs. >0.19, PPV=0.63, NPV=0.88. Finally we explored a hypothetical scenario expanding the eligible population to all RA patients using hypothetically analogous ANS-prediction and ANS-enhancement of non-biologic treatment (no study yet done) over a range of potential PPV values (10-25%). We also evaluated model outcomes when biologic utilization was assumed to increase from current 26% of eligible patients to 35-55%. Costs and quality-adjusted life-years (QALYs) per patient and for the US population were estimated. Cost-effectiveness was defined as an incremental cost-effectiveness ratio (ICER) below $150,000/QALY.

Results:

HRV testing in biologic-eligible patients decreased non-effective biologic use, reducing US costs by $9.8B over 10 years with QALYs unchanged. When combined with ANS optimization in biologic-eligible patients, HRV testing could increase costs by $1.5 billion over 10 years and save 102,000 QALYs (ICER $14,000/QALY). Our hypothetical analysis estimated that, among all RA patients, HRV testing with ANS optimization could save $15-20 billion and 780,000 QALYs over 10 years, depending on PPV of the HRV test. In this scenario, if biologic use increased from current uptake, costs could increase from $13 to 98 billion, ICER maintained <$150,000/QALY.
### HRV testing vs. no testing (10 year total)

<table>
<thead>
<tr>
<th>Standard of Care</th>
<th>Incremental Change with HRV Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total costs</td>
<td>$57.33 bil vs. $-9.30 bil</td>
</tr>
<tr>
<td>Biologics</td>
<td>$36.07 bil vs. $-9.84 bil</td>
</tr>
<tr>
<td>QALYs</td>
<td>2,228,036 vs. 0</td>
</tr>
<tr>
<td>ICER</td>
<td>-- vs. --</td>
</tr>
</tbody>
</table>

### HRV testing + ANS optimization vs. no testing or optimization, biologic eligible patients (10 year total)

<table>
<thead>
<tr>
<th>Standard of Care</th>
<th>Incremental Change with HRV Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total costs</td>
<td>$57.33 bil vs. $1.45 bil</td>
</tr>
<tr>
<td>Biologics</td>
<td>$36.07 bil vs. $0.03 bil</td>
</tr>
<tr>
<td>QALYs</td>
<td>2,228,036 vs. 101,765</td>
</tr>
<tr>
<td>ICER</td>
<td>-- $14,244/QALY vs. --</td>
</tr>
</tbody>
</table>

### HRV testing + ANS optimization vs. no testing or optimization, all patients (10 year total), hypothetical analysis

<table>
<thead>
<tr>
<th>Standard of Care</th>
<th>Incremental Change with HRV Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total costs</td>
<td>$207.38 bil vs. $-15.36 bil</td>
</tr>
<tr>
<td>PPV 10%</td>
<td>$122.27 bil vs. $-23.08 bil</td>
</tr>
<tr>
<td>QALYs</td>
<td>9,348,102 vs. 780,335</td>
</tr>
<tr>
<td>ICER</td>
<td>-- $23,049/QALY vs. --</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Standard of Care</th>
<th>Incremental Change with HRV Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total costs</td>
<td>$207.38 bil vs. $19.66 bil</td>
</tr>
<tr>
<td>PPV 25%</td>
<td>$122.27 bil vs. $4.66 bil</td>
</tr>
<tr>
<td>QALYs</td>
<td>9,348,102 vs. 946,503</td>
</tr>
<tr>
<td>ICER</td>
<td>-- $13,100/QALY vs. --</td>
</tr>
</tbody>
</table>

### Conclusion:

The potential US health economic impact of introducing HRV testing and ANS optimization into RA treatment appears substantial and is possibly cost-effective. Additional rigorous studies are warranted in larger patient samples, particularly investigation into non-biologic therapeutic applications.


**Disclosure:** M. Zimmermann, None; E. Vodicka, None; A. J. Holman, Inmedix, 4; L. P. Garrison, None.
Prevalence and Predictors of Knee Replacement Overuse and Underuse in the US

Hassan Ghomrawi\(^1\), Alvin Mushlin\(^2\), Raymond Kang\(^3\), Samprit Banerjee\(^2\), Jasvinder A. Singh\(^4\), Leena Sharma\(^5\), Tuhina Neogi\(^6\), Michael C. Nevitt\(^7\) and Daniel Riddle\(^8\), \(^1\)Surgery and Pediatrics/Center for Healthcare Studies, Feinberg School of Medicine of Northwestern University, Chicago, IL, \(^2\)Healthcare Policy and Research, Weill Cornell Medical College, New York, NY, \(^3\)Center for Healthcare Studies, Feinberg School of Medicine of Northwestern University, Chicago, IL, \(^4\)Rheumatology, University of Alabama at Birmingham, Birmingham, AL, \(^5\)Division of Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL, \(^6\)Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA, \(^7\)Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, CA, \(^8\)Virginia Commonwealth University, Richmond, VA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Health Services Research Poster II: Osteoarthritis and Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The elective nature of knee replacement (KR) creates difficult decisions and the potential for both overuse and underuse. We examined the temporal relationship between needing a KR and actually undergoing one to determine the rates and investigate predictors of overuse and underuse.

Methods: We pooled longitudinal data from the Osteoarthritis Initiative (OAI) and the Multicenter Osteoarthritis (MOST) Study to estimate KR overuse and underuse. These cohorts closely followed 8,002 participants with or at risk of knee OA over multiple years and collected demographic, patient-reported, radiographic, and clinical exam information. To determine need for KR, we longitudinally applied the modified and validated Escobar KR appropriateness criteria (AC) to classify participants as either appropriate or inappropriate for KR (Table 1). Examining the temporal relationship between appropriateness status and KR utilization, we classified participants into: 1) appropriate and had KR (appropriate use), 2) appropriate but did not have KR (potential underuse), and 3) inappropriate but had KR (potential overuse). We used multinomial logistic regression to estimate the association between overuse and underuse and age, sex, race, educational status, obesity categories, CESD depression score>16, SF-12 PCS, Charlson comorbidity score, and living alone. We repeated our analyses by dividing potential underusers into those with and without extreme pain (an indicator of necessity and a likely substantial benefit from KR).

Table 1: Elements of the modified Escobar appropriateness criteria for KR*

Abstract Number: 1050
### Table: 

<table>
<thead>
<tr>
<th>Factor</th>
<th>Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1-&lt;55 years</td>
</tr>
<tr>
<td></td>
<td>2-55-65 years</td>
</tr>
<tr>
<td></td>
<td>3-&gt;65 years</td>
</tr>
<tr>
<td>Knee Stability</td>
<td>1-Preserved mobility and stable joint (&lt;5 degrees flexion contracture and normal or minor medial or lateral gapping in the 20 degrees flexed knee)</td>
</tr>
<tr>
<td></td>
<td>2-Limited mobility and/or unstable joint (&gt;=5 degrees flexion contracture and/or moderate or severe medial or lateral gapping in the 20 degrees flexed knee)</td>
</tr>
<tr>
<td>Compartments involved</td>
<td>1-Uni-compartmental</td>
</tr>
<tr>
<td></td>
<td>2-Bi/ tri-compartmental</td>
</tr>
<tr>
<td>Radiographic findings</td>
<td>1-Slight (KL grade &lt;=3)</td>
</tr>
<tr>
<td></td>
<td>2-Moderate or severe (KL grade = 4)</td>
</tr>
<tr>
<td>Symptomatology</td>
<td>1-Slight (mild overall functional loss and function-related pain [e.g. up to half of WOMAC pain and physical scale items scored from 0 to 11])</td>
</tr>
<tr>
<td></td>
<td>2-Moderate (moderate overall functional loss and function-related pain [e.g. up to half of WOMAC pain and physical scale items scored from 12 to 22])</td>
</tr>
<tr>
<td></td>
<td>3-Intense (intense overall functional loss and function-related pain [e.g. up to half of WOMAC pain and physical scale items scored from 23 to 33]) or</td>
</tr>
<tr>
<td></td>
<td>4-Severe (severe overall functional loss and function-related pain [e.g. up to half of WOMAC pain and physical scale items scored from &gt;=34])</td>
</tr>
</tbody>
</table>

*16 combination of factors, depending on levels involved, determined whether person was appropriate or inappropriate for surgery. Example: for a 54-year-old patient with KL=4 and moderate symptoms TKR is inappropriate; however, if the symptoms are intense or severe TKR becomes appropriate.

### Results:

3,449 of 8,002 participants fell into one of the 3 groups, with 843 (24.4%) classified as appropriate users, 2256 (65.4%) as potential underusers, and 350 (10.1%) as potential overusers. Of potential underusers, 988 (43.8%) were deemed likely to receive substantial benefit. Compared to appropriate use, the odds of underuse were greater in blacks (OR=2.9, 95% CI [2.3, 3.8]). The odds of overuse increased with postgraduate degree, higher SF-12 PCS score, living alone, and decreased with being overweight or obese, having depressive symptoms, and having comorbidities. Distinguishing necessary from not necessary but appropriate in the underuser group increased racial disparities in KR underuse (blacks OR=4.9, 95% CI[3.8, 6.5]), without significantly affecting findings related to the other predictors.

### Conclusion:

We found a substantial proportion of patients either overuse or underuse KR. For the underusers, almost 50% would likely receive substantial benefit if they underwent KR and of these, African Americans are at greatest risk for underuse. Overuse appears to be less of a issue but still occurs approximately 10% of the time. Future work needs to focus on ways of reducing rates of overuse and underuse of KR given the substantial costs and consequences of the procedure.

### Disclosure:

H. Ghomrawi, NIH, QNRF, 2,Haman Medical Corporation, NIH, 5; A. Mushlin, None; R. Kang, None; S. Banerjee, None; J. A. Singh, Takeda and Savient, 2,Savient, Takeda, Regeneron, Merz, Iroko, Bioiberica, Crealta/Horizon and Allergan
Telemicine for Rheumatoid Arthritis in the Alaska Native Population

Elizabeth Ferucci1, Tammy Choromanski1, Gretchen Day2 and Sarah Freeman3, 1Division of Community Health Services, Alaska Native Tribal Health Consortium, Anchorage, AK, 2Clinical and Research Services, Alaska Native Tribal Health Consortium, Anchorage, AK, 3Alaska Native Tribal Health Consortium, Anchorage, AK

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Health Services Research Poster II: Osteoarthritis and Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Access to a rheumatologist and frequent monitoring of disease activity in rheumatoid arthritis (RA) are associated with higher quality of care and improved outcomes. With the current rheumatology workforce shortage in the US and concentration of rheumatologists in urban areas, there is a need for strategies addressing barriers to access. Telemedicine video consultation has been implemented within the Alaska Tribal Health System specialty clinics, including rheumatology. The purpose of this study is to evaluate the impact of telemedicine follow-up for RA on disease activity, quality of care, and access to care and to investigate patient perceptions of telemedicine. This analysis describes the baseline characteristics and perceptions of enrolled study participants.

Methods: Study participants with a diagnosis of RA were recruited when seeing a rheumatologist, either in-person or by telemedicine. At the study visit, participants completed the RAPID3 and a telemedicine survey and agreed to medical record review for demographics, disease characteristics, and measures of quality and access to care. Participants also agreed to telephone contact at 6 and 12 months for follow-up surveys and RAPID3. For data analysis, participants are categorized as being in the telemedicine group if they have had at least one telemedicine visit with a rheumatologist and in the in-person group otherwise.

Results: To date, 65 participants have enrolled in the study (25 telemedicine and 40 in-person). Age, sex, disease duration, and baseline RAPID3 score were similar across groups. The telemedicine group had a higher mean number of rheumatologist visits in the past year (3.3 vs. 2.3, p=0.002). Both groups expressed a preference of seeing a specialist in-person rather than by video and the opinion that it is important for the specialist to physically examine them. However, those seen by telemedicine were more likely to consider telemedicine an acceptable way to receive health services (p=0.008) and to have favorable opinions about other aspects of telemedicine, including respect for culture (p=0.002), patient involvement in decision-making (p<0.001), ability to talk easily and openly to provider (p<0.001), and trusting the equipment to work (p=0.04). Finally, those seen by telemedicine were more likely to consider the care given in video visits to be as good as in-person visits (p<0.001).

Conclusion:
Telemedicine can improve access to care in patients with RA. Although patients in both groups expressed a preference for in-person visits, those seen by telemedicine were more likely to have favorable opinions of it. Whether telemedicine can improve quality of care and disease activity is not yet known.

Disclosure: E. Ferucci, None; T. Choromanski, None; G. Day, None; S. Freeman, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/telemedicine-for-rheumatoid-arthritis-in-the-alaska-native-population
Abstract Number: 1052

Systematic Review of Modelling Approaches and Quality for the Cost Effectiveness of sequential Targeted Therapy in Patients with Rheumatoid Arthritis That Show an Inadequate Response to at Least One Tumor Necrosis Factor Alpha Inhibitor

Aliza Matusevich1, Maria Suarez-Almazor1, Scott B. Cantor2 and Maria A. Lopez-Olivo1, 1Section of Rheumatology and Clinical Immunology, Department of General Internal Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA, Houston, TX, 2Department of Health Services Research, Division of Cancer Prevention and Population Sciences, The University of Texas MD Anderson Cancer Center, Houston, TX, USA, Houston, TX

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Health Services Research Poster II: Osteoarthritis and Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Results from cost-effectiveness analysis (CEAs) comparing treatment options for patients with rheumatoid arthritis (RA) who have an inadequate response to an initial tumor necrosis factor inhibitor (TNFi) have been inconclusive. Our objective was to systematically review the modelling approaches and quality of economic evaluations comparing the cost-effectiveness, cost-utility, or cost-minimization of subsequent TNFi (cycling) versus a therapy with a different mode of action (swapping) in order to understand their discrepant results.

Methods: We searched seven electronic databases until 2016, sources of gray literature and the references of relevant publications. Two independent reviewers screened retrieved citations, including studies published in English-language and economic evaluations comparing second line biological treatments in RA patients. We excluded reviews, conference abstracts and poster presentations. Data extraction was done by one reviewer and crosschecked by another. Reporting quality was evaluated based on the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement. Reported incremental cost-effectiveness ratios (ICERs) were synthetized and adjusted to 2016 US dollars according to rules specified by the Panel on Cost-Effectiveness in Health and Medicine.

Results: Of 4,563 citations, ten economic evaluations comprising 21 comparisons and representing six European countries, Canada and the United States were included. Most studies (8 of 10) were funded by the pharmaceutical industry. There were two discrete event simulations, three microsimulations, two Markov cohort models, two decision trees and one single study-based evaluation. The most common time horizons were lifetime (6/10) and one year (2/10). Seven studies were from a payer perspective. The cohorts were predominantly female (78%), on average aged 53.4 years, disease duration of 10.2 years and baseline health assessment questionnaire (HAQ) of 2.3. Adherence to reporting standards was good with seven studies scoring ≥26 out of 36. The most common failing point was justification of modelling choices. One study did not report any sensitivity analysis, but most performed probabilistic as well as one-way sensitivity analysis. Common influential parameters include rituximab dosing schedule as well as assumptions regarding HAQ progression and conversion to utilities. In the cost-utility analyses, the median ICER was US$25,617 for the swapping strategy, rituximab dominated in half of the comparisons. Of the CEA comparisons, tofacitinib dominated adalimumab while the ICER for abatacept versus infliximab was $20,803 and $27,976 per case of low disease activity and remission respectively. The single cost-minimization study found in favor of rituximab.

Conclusion: Despite disparate modelling approaches it appears that swapping to a targeted agents with an alternative mechanism of action is cost-effective at the $50,000/QALY threshold as ICER’s ranged between $9,323 to 41,467/QALY, dominating in 8 of 20 comparisons.

Disclosure: A. Matusevich, None; M. Suarez-Almazor, Pfizer Inc, 5; S. B. Cantor, None; M. A. Lopez-Olivo, Rheumatology Research Foundation, 2.


Abstract Number: 1053
Impact of Step Therapy Protocols on North Carolina Rheumatologists’ Job Satisfaction and the Quality of Care Received By Their Patients with Rheumatoid Arthritis

Victoria Hamby1, Amanda Nelson2, Antonia Bennett1, Leigh F. Callahan3 and Stacie Dusetzina4, 1Gillings School of Global Public Health, Department of Health Policy and Management, University of North Carolina at Chapel Hill, Chapel Hill, NC, 2Division of Rheumatology, Allergy, and Immunology and Thurston Arthritis Research Center, University of North Carolina at Chapel Hill, Chapel Hill, NC, 3Thurston Arthritis Research Center, University of North Carolina at Chapel Hill, Chapel Hill, NC, 4Eshelman School of Pharmacy and Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Health Services Research Poster II: Osteoarthritis and Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Early diagnosis and treatment of rheumatoid arthritis (RA) is crucial in minimizing disease damage. Step-therapy, a form of prior authorization used by payers to manage costs, determines which medications will be covered and thus affordable. Expansion of the Institute for Healthcare Improvements Triple Aim initiative to the Quadruple Aim initiative added the aim to promote workplace happiness for providers. We examined provider beliefs regarding the role of step-therapy in managing health care costs, quality of care delivered, and on clinical autonomy and job satisfaction in North Carolina. We also evaluated provider awareness and agreement with proposed state policies aimed at streamlining step-therapy exceptions processes.

Methods: In this cross-sectional survey study, a web-based questionnaire was emailed on March 7 and March 16, 2017 to all members of the North Carolina Rheumatology Association. We summarized the data through frequency counts to determine knowledge, beliefs and perception of step-therapy, and chi-square tests were used to compare respondent knowledge of state legislation, NC HB 1048, to their beliefs about autonomy and job satisfaction.

Results: The survey was sent to 118 providers, and the final analysis included 38 completed surveys (effective response rate of 32.2%). Respondents were more likely to be male (58%), report 20+ years in practice (53%), work in a private practice (87%), and see patients with Medicare (34%) or private insurance (38%). Providers disagreed that step-therapy reduced costs for society overall (52%) or patients (57%). Instead, 82% agreed that step-therapy reduced costs for insurance companies. With respect to quality, 92% of providers believed step-therapy negatively impacted the quality of care provided to patients (50% somewhat reduced quality, 42% greatly reduced quality) and 82% of providers agreed that step-therapy delayed beginning proper treatment (50% agree, 31% strongly agree). Nearly 90% of providers reported step-therapy negatively affects their autonomy and 87% reported step-therapy negatively impacting their job satisfaction. When considering the burden of step-therapy on providers, 79% of providers reported step-therapy as being common when prescribing for RA. Most respondents (76%) were directly involved in processing step-therapy paperwork. In addition, half of respondents reported spending >60 minutes on step-therapy paperwork in an average clinic day. Despite the burden of step-therapy, only 47% of providers were aware of proposed NC state legislation to reduce the burden of step-therapy. Notably nearly all surveyed providers agreed with the exceptions proposed within the state legislation.

Conclusion: Providers view step-therapy as a burden without justifiable results for cost and quality. This unjustified burden coupled with provider agreement with state proposed legislation suggests that providers should engage with policy makers to support legislative action on this topic. Additionally, provider groups such as the ACR should create advocacy groups to increase awareness of state and federal legislation.

Disclosure: V. Hamby, None; A. Nelson, QuantiaMD, 9,NIAMS-NIH, 2,RRF, 2; A. Bennett, None; L. F. Callahan, None; S. Dusetzina, None.


Abstract Number: 1054

Healthcare Utilization Profiles in Rheumatoid Arthritis – a Cluster Analysis
Nina Mars1,2, Anne M Kerola2,3, Markku J Kauppi4,5, Matti Pirinen1, Outi Elonheimo6 and Tuulikki Sokka-Isler7, 1Institute for Molecular Medicine Finland (FIMM), University of Helsinki, Helsinki, Finland, 2University of Helsinki, Helsinki, Finland, 3Department of Internal Medicine, Päijät-Häme Central Hospital, Lahti, Finland, 4School of Medicine, University of Tampere, Tampere, Finland, 5Department of Rheumatology, Päijät-Häme Central Hospital, Lahti, Finland, 6FCG Finnish Consulting Group Ltd., Helsinki, Finland, 7Rheumatology, Jyväskylä Central Hospital, Jyväskylä, Finland

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Health Services Research Poster II: Osteoarthritis and Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Utilization patterns in rheumatoid arthritis (RA) are complex. For targeted interventions, patients with special healthcare needs should be recognized. Our aim was to explore healthcare utilization profiles in RA by cluster analysis.

Methods: The RA patients attending Jyväskylä Central Hospital rheumatology unit, Finland, are as of 2007 enrolled prospectively in a structured digital database, from which we identified patients with rheumatology clinic visits in 2012-2014. We combined this clinical data with well-recorded administrative data on fiscal year 2014 on all public healthcare visits, both in primary and specialty care. For each patient, we considered the median of time dependent clinical variables. Clustering variables were disease activity score (DAS28-3), health assessment questionnaire index (HAQ index, 0-3), pain on visual analogue scale (VAS, 0-100) and total annual health services related direct costs (€), excluding out of pocket medication costs. The number of clusters was set based on dendrogram examination. We applied hierarchical clustering with Ward's minimum variance method with Euclidean distance.

Results: Of 844 patients with RA, complete-case analysis (n = 827) derived four clusters. Descriptive statistics are in Table 1 and distributions for DAS28-3 and HAQ index are in Figure 1. Cluster 1 was the largest cluster constituting relatively young patients with low costs, low disease activity, and minimal disability. Cluster 2 was characterized by high pain levels and disability, despite fairly low average DAS28-3. Compared with cluster 2, patients in cluster 3 had high average disease activity and rheumatic disease-related costs, and biologics were more frequently used. Still, they presented with less pain and disability compared with cluster 2. Cluster 4 was small, heterogeneous and characterized by exceptionally high average costs. These patients had costly and severe comorbidities in addition to RA.

Conclusion: Over half of patients had low costs and favorable outcome measures, whereas a fifth was characterized by high disease activity and active treatment of RA, yielding higher costs. Pain and disability did not necessarily relate to high rheumatic disease-related costs. In all clusters, over half of costs were attributable to comorbidities.

Table 1. Descriptive statistics.

<table>
<thead>
<tr>
<th>Cluster</th>
<th>n</th>
<th>Age (mean ± SD)</th>
<th>Disease duration (median)</th>
<th>Pain (mean ± SD)</th>
<th>RF+ (%)</th>
<th>Ever biologics (%)</th>
<th>Number of comorbidities</th>
<th>Mean total costs/patient (€)</th>
<th>Mean rheumatic disease costs/patient (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>467</td>
<td>58.2 ± 16.5</td>
<td>11.8 ± 16.3</td>
<td>12.2 ± 18.3</td>
<td>65</td>
<td>23.3</td>
<td>2.1 ± 2.13</td>
<td>2367</td>
<td>(48.5)</td>
</tr>
<tr>
<td>2</td>
<td>147</td>
<td>65.3 ± 71.1</td>
<td>13.9 ± 16.0</td>
<td>12.6 ± 18.3</td>
<td>71</td>
<td>24.5</td>
<td>2.3 ± 2.83</td>
<td>3785</td>
<td>(44.8)</td>
</tr>
<tr>
<td>3</td>
<td>180</td>
<td>63.3 ± 18.6</td>
<td>16.0 ± 37.2</td>
<td>12.5 ± 15.8</td>
<td>77</td>
<td>43.3</td>
<td>2.8 ± 2.55</td>
<td>6772</td>
<td>(48.5)</td>
</tr>
<tr>
<td>4</td>
<td>33</td>
<td>71.1 ± 47.0</td>
<td>12.9 ± 47.0</td>
<td>12.9 ± 20.9</td>
<td>90</td>
<td>45.5</td>
<td>3.5 ± 5.57</td>
<td>36206</td>
<td>(13.0)</td>
</tr>
</tbody>
</table>

*Of recorded healthcare contacts
A Combination of Self-Reported Symptoms and ACPA Testing Can Identify Individuals with Previously Undiagnosed Inflammatory Arthritis in a Health-Fair Setting

Elizabeth A. Bemis¹, Nicholas Ellinwood², Kaylynn Aiona³, Christopher C. Striebich⁴ and Kevin D. Deane⁵, ¹Epidemiology, Colorado School of Public Health, Aurora, CO, ²Pharmacology and Toxicology Graduate Group, University of California Davis, Davis, CA, ³Denver Health and Hospitals and Colorado School of Public Health, Denver, CO, ⁴Division of Rheumatology, University of Colorado School of Medicine, Aurora, CO, ⁵Division of Rheumatology, University of Colorado School of Medicine, Aurora, CO

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Health Services Research Poster II: Osteoarthritis and Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Early identification and treatment of inflammatory arthritis (IA) and in particular rheumatoid arthritis (RA) can lead to improved outcomes. However, there are often delays in diagnosis. We hypothesized that evaluation of individuals in a health-fair setting could identify those with previously undiagnosed IA/RA. In addition, because performing physical examinations is difficult to perform on a large scale, we sought to evaluate the diagnostic characteristics of self-reported symptoms and antibody testing to identify IA.
Methods:

Subjects who self-reported no prior diagnosis of RA were evaluated from 2012 to 2015 at a Colorado based health-fair. Each subject reported presence/absence and location of joint symptoms in the wrists and hands on a cartoon picture of these joints. All subjects additionally underwent ACPA testing (CCP3, Inova) and a joint examination of the wrists and hands (excluding DIPs) by a rheumatologist who recorded presence/absence of IA. The diagnostic accuracy of symptoms and ACPA as single variables or an overall score were evaluated using regression techniques.

Results:

1703 subjects were evaluated, and 98 (5.8%) were found to have IA (Table 1). Of single joint areas, self-reported symptoms of joint pain, stiffness or swelling in the MCPs had the strongest association with the presence of IA on examination (OR 4.8). CCP3(+) was also significantly associated with IA (OR 3.1) but was present in only 8% of all subjects with IA, and 45 subjects were CCP3(+) without hand/wrist IA. In multivariate analyses, four variables including symptoms in wrists, MCPs, PIPs, and CCP3(+) were significantly associated with IA. When these 4 variables were evaluated as counts, the highest positive predictive value (PPV) for IA was 22% (³3 items present), and the highest negative PV was ~98% (0 items present) (Table 2).

Conclusion:

Health-fair evaluations can be used to identify individuals with IA, some of whom likely have RA due to CCP3(+), and others with potentially other forms of IA. A scoring system using a combination of self-reported joint symptoms and CCP3 testing can be used to identify those with IA in the hands, with varying predictive values depending on the score used. Further evaluations including determining what specific forms of arthritis are identified and cost-effectiveness need to be performed, but overall these findings support a health-fair based approach using questionnaires and ACPA testing as a way to improve identification of IA. Additionally, N=46 CCP3(+) subjects did not have IA, indicating this method could be used to identify individuals at future risk for RA.

<table>
<thead>
<tr>
<th>Table 1. Univariate analyses of differences in demographics, CCP positivity and joint symptoms between subjects with/without IA</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>N</td>
</tr>
<tr>
<td>Mean Age at Visit (Years)</td>
</tr>
<tr>
<td>Percent Female</td>
</tr>
<tr>
<td>N, (%) CCP+</td>
</tr>
<tr>
<td>Self-Reported symptoms of pain, stiffness or swelling on the day of the health-fair evaluation</td>
</tr>
<tr>
<td>Wrist</td>
</tr>
<tr>
<td>MCP</td>
</tr>
<tr>
<td>PIP</td>
</tr>
</tbody>
</table>
Table 2. Counts of symptoms in wrists, MCPs, PIPs, and CCP3 positivity and diagnostic accuracy for inflammatory arthritis

<table>
<thead>
<tr>
<th>Number of Items Positive (joint symptoms in wrists, MCPs, PIPs and positive for CCP3 each get 1 point)</th>
<th>Sensitivity</th>
<th>Positive Predictive Value (PPV)</th>
<th>Specificity</th>
<th>Negative Predictive Value (NPV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 or more*</td>
<td>80.61</td>
<td>11.84</td>
<td>63.36</td>
<td>98.17*</td>
</tr>
<tr>
<td>2 or more</td>
<td>42.86</td>
<td>16.03</td>
<td>86.29</td>
<td>96.11</td>
</tr>
<tr>
<td>3 or more</td>
<td>11.22</td>
<td>22.45</td>
<td>97.63</td>
<td>94.74</td>
</tr>
<tr>
<td>All 4 items</td>
<td>2.04</td>
<td>94.36</td>
<td>100.00</td>
<td>100.00</td>
</tr>
</tbody>
</table>

*Of note, the 1036 subjects who reported no symptoms in their wrists, MCPs and PIPs or had CCP3 positivity, 19 were found to have IA on examination.

Disclosure: E. A. Bemis, None; N. Ellinwood, None; K. Aiona, None; C. C. Striebich, None; K. D. Deane, Inova Diagnostics, Inc., 5.


Abstract Number: 1056

Evolution of Health Care Consumption in the Knee and Hip Osteoarthritis Long Term Assessment Cohort, a French Population Based Cohort of Symptomatic Knee and/or Hip OA Patients

Anne-Christine Rat1,2,3, Jean-Hugues Salmon4, Willy Ngueyon Sime5, Maud Wieczorek6, Alain Saraux7, Claudine Gard8, Francis Guillemin9 and Bruno Fautrel10, 1Inserm, CIC-1433 Epidémiologie Clinique, Vandoeuvre-lès-Nancy, France, 2Rheumatology Department, CHRU Nancy, Vandoeuvre-lès-Nancy, France, 3Université de Lorraine, EA4360, APEMAC, Nancy, France, 4Rheumatology, Rheumatology Department CHU Teaching Hospital Reims, Reims, France, 5CIC 1433 Epidémiologie clinique, Inserm, Nancy, France, 6Université de Lorraine EA 4360 APEMAC, Nancy, France, 7Rheumatology Department, Rheumatology Department, CHU de la Cavale Blanche, Brest, France, Brest Cedex, France, 8Pitié Salpêtrière hospital, Paris, France, 9CHRU Nancy, Clinical Epidemiology and Evaluation, Université de Lorraine, Paris Descartes University, APEMAC, EA 4360, Nancy, France, 10UPMC University Paris 06, Pitié-Salpêtrière Hospital, Paris, France

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Health Services Research Poster II: Osteoarthritis and Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

- **Background/Purpose:** in hip and knee OA, one of the leading causes of global disability, recent population-based data of health care practices and utilization are scarce. Describing trajectories of patients’ patterns of care and their predictive factors is important to adapt health care practices and guide interventions to optimize patients’ use of health care services. The aim of the study was to describe health care utilization trajectories and associated factors of a representative sample of patients with knee or hip symptomatic OA.

- **Methods:** the KHOALA cohort is a French population-based multicenter cohort of 878 patients with symptomatic knee and/or hip OA, aged between 40 and 75 years old recruited between 2007 and 2009. Patients are followed annually by self-report questionnaires. Analyses used the data from the 5 first years of the follow up. We used Latent Class Growth Analyses (LCGA) to define homogeneous trajectories.
subgroups of trajectories based on the individual health care consumptions over time, and logistic regressions to explain the differences between the identified trajectories with baseline characteristics.

**Results:** Among the 878 patients, 609 (69%) were women, 222 (25%) have hip OA, 607 (69%) knee OA and 49 (6%) both hip and knee OA. Groll comorbidity index (0-18) was 3.1 (1.6). The most optimal and clinically relevant models retrieved by LCGA were two group models for consultations with the different health care professionals (primary care physician (PCP), rheumatologist, orthopedic surgeon, physiotherapist), hospitalizations, use of assisting devices and acid hyaluronic (AH) injections, and 3 group models for corticoids injections and use of complementary and alternative medicine (CAM). In multivariate analyses, increasing age was independently associated with the trajectory of high number of consultations with PCP and rheumatologist, and with a high use of corticoids injections or complementary medicine. Impaired mental health was associated with the groups of frequent consultations with PCP, rheumatologists and physiotherapists and with corticoid injections. Pain was only associated with increasing number of orthopedic surgeons consultations and high use of assisting devices. Impaired function abilities were only associated with frequent hospitalizations. Comorbidities are associated with PCP consultations and hospitalizations (frequent use).

**Conclusion:** In multivariate analyses, mental health impairment is the only symptom associated with trajectories of frequent use of medical care while pain is only associated with orthopedic surgeon consultations.

**Disclosure:** A. C. Rat, None; J. H. Salmon, None; W. Ngueyon Sime, None; M. Wieczorek, None; A. Saraux, None; C. Gard, None; F. Guillemin, None; B. Fautrel, AbbVie, Biogen, BMS, Celgene, Hospira, Janssen, Eli Lilly and Company, Novartis, Pfizer, Roche, SOBI Pharma, UCB, 5.


**Abstract Number:** 1057

**Budgetary Impact Analysis of Real-World Dosing Patterns in Matched Cohorts of Rheumatoid Arthritis Patients Treated with Infliximab or Golimumab Intravenous Anti-TNF Medications**

Lorie A. Ellis1, Elisabetta Malangone-Monaco2, Helen Varker2, Diana Stetsovsky3, Maureen Kubacki4, Raphael J. DeHoratius5 and Shelly Kafka4, 1Janssen HECOR Immunology, Horsham, PA, 2Truven Health Analytics, Bethesda, MD, 3Truven Health Analytics, Philadelphia, PA, 4Janssen Scientific Affairs, LLC, Horsham, PA, 5Janssen Scientific Affairs, LLC/Sidney Kimmel School of Medicine, Thomas Jefferson University, Horsham/Philadelphia, PA

**First publication:** September 18, 2017

**SESSION INFORMATION**
Session Date: Monday, November 6, 2017
Session Title: Health Services Research Poster II: Osteoarthritis and Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM
Background/Purpose: Infliximab (IFX) is more frequently selected than golimumab for intravenous use (GLM-IV) in patients with Rheumatoid Arthritis (RA) but differences in dosing and administration recommendations for these products may have budgetary consequences. This study aimed to determine the budgetary impact of IFX and GLM-IV based upon real-world treatment patterns and commercial reimbursement in a matched sample of RA patients.

Methods: Truven Commercial Claims and Encounters and Medicare Supplemental data were used to evaluate maintenance infusion interval, frequency of first or subsequent hour billing code and cost of infusions for adult RA patients starting a new episode of IFX (J1745) or GLM-IV (J1604). Adult patients with ≥12 months continuous enrollment before and after the 1st IFX or GLM-IV claim (index) between 1/1/2014 and 3/31/2016 and no evidence of index medication use 12 months before index were studied. IFX and GLM-IV patients were matched 1:1 on index medication treatment duration, gender, payer type, prior-biologic use and post-index methotrexate (MTX). The payer paid drug plus administration cost was used applied to population treatment patterns. Descriptive statistics summarized key variables (mean, SD, median, n, %). Chi-squared tests determined differences between categorical variables and t-test was used for continuous variables.

Results: A total of 1,094 matched patients were identified (n=547 GLM-IV; n=547 IFX). In both groups, median age was 56 years; 82% were female and 38% had no prior biologic use. Mean (SD) follow-up was 609 (161) days (d) for GLM-IV and 613 (163) days for IFX. Mean (SD) duration of GLM-IV use was 396 (240) d and 397 (239) d for IFX. A total of 3,961 GLM-IV infusions and 4,716 IFX infusions were administered. The proportion of maintenance infusions given every 8 wk was 80% for GLM-IV vs 39% for IFX; 6% of GLM-IV vs 53% of IFX infusions occurred more frequently than every 8 wk (P<0.0001). Mean drug plus administration cost per infusion was $5,846.10 (GLM-IV) and $5,443.66(IFX). Mean GLM-IV administration cost was $224.26 with <1% of infusions having a second hour billing code vs IFX with mean administration cost of $360.36 and 96% of IFX infusions requiring a second hour billing code (P<0.0001). Based upon the average maintenance infusion interval, GLM-IV patients cost approximately $10,507 less than IFX patients in the first year and approximately $6,774 less than IFX patients in subsequent years.

Conclusion: From the commercial health plan perspective, annual GLM-IV drug plus administration cost was less than IFX in RA patients due to differences in real-world dosing and administration. These findings have important implications for population health decision makers.

Disclosure: L. A. Ellis, Janssen, 3,Johnson & Johnson, LLC, 1; E. Malangone-Monaco, Janssen Scientific Affairs, LLC, 5; H. Varker, Janssen Scientific Affairs, LLC, 5; D. Stetsovsky, Janssen Scientific Affairs, LLC, 5; M. Kubacki, Janssen Scientific Affairs, LLC, 3; R. J. DeHoratius, Johnson & Johnson, 3; S. Kafka, Janssen Pharmaceuticals, 3,Johnson & Johnson, 1.


Abstract Number: 1058

Variation in DMARD Therapy Following Methotrexate Failure for Newly-Identified Rheumatoid Arthritis in a National Veterans Health Administration Cohort

John McDougall Jr.1,2, Cynthia Brandt3,4, Melissa Skanderson3, Joseph Goulet3 and Liana Fraenkel5, 1National Clinician Scholars Program, Yale School of Medicine, New Haven, CT, 2Dep't of Rheumatology, Yale School of Medicine, New Haven, CT, 3Veterans Affairs Connecticut Healthcare System, West Haven, CT, 4Emergency Medicine, Yale School of Medicine, New Haven, CT, 5Rheumatology, Rheumatology, Yale University School of Medicine, New Haven, CT, New Haven, CT
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Health Services Research Poster II: Osteoarthritis and Rheumatoid Arthritis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Absent contraindications to conventional DMARD (cDMARD) use, the Veterans Administration (VA) requires a 3-month trial of 2 cDMARDs prior to the use of biologic DMARD (bDMARD), for active rheumatoid arthritis (RA). In this national VA study, we used a time-to-event analysis in cases of newly-identified RA to examine variation between VA Integrated Service Network (VISN) areas in prescriptions following MTX monotherapy.
Methods:

A previously validated, 3-part definition was used to identify patients with RA within the VA Musculoskeletal Disorder (MSD) cohort (N > 5 million, Jan 1, 2000-Dec 31, 2013). The date of the first VA DMARD prescription was used to define both RA diagnosis and RA cohort entry. To limit our analysis to newly-identified RA, we included patients with >1 year in the MSD cohort prior to RA diagnosis. To make our RA cohort as uniform as possible, we included only patients who first received a >90-day period of VA-prescribed MTX monotherapy. Kaplan Meier survival analysis and bivariate logistic regression were used to assess patient demographic and clinical data. After adjusting for significant predictor variables, we used a multivariate logistic regression to examine initial, non-MTX DMARD prescription by VISN.

Results:

A total of 4,823 patients (91% male, median age 64yrs, median observation time 3.91 yrs) met our inclusion criteria. All 21 VISN areas were represented (mean number of RA patients per VISN = 230 pts; range 88-488). Overall, 1,911 patients (40%) were prescribed only MTX monotherapy while observed in the RA cohort. Of the remaining patients who did receive a non-MTX DMARD, 748 (15%) went on to receive a bDMARD, whereas 2,164 (45%) received a cDMARD, as their initial, non-MTX DMARD prescription. The median interval between the first MTX prescription and initial, all non-MTX DMARD prescription was 1.13 years (IQR 0.56-2.25); a Kaplan Meier survival analysis did not show a significant difference between bDMARD and cDMARD interval prescription times (Kaplan Meier log rank p=0.94). Examining regional variation, 8 VISN areas were at statistically higher odds of receiving an initial bDMARD prescription, when compared to the VISN with lowest percentage bDMARD prescriptions (OR range 1.0-3.29, reference cDMARD prescription in VISN 23, see Figure 1).

Conclusion:

Following MTX monotherapy for newly-identified RA, we found a 3-fold variation by VISN in the prescription of biologic versus conventional DMARDs (see Figure 1; base 1.0 [VISN 23] in blue, highest 3.29 [VISN 22] in red). Further work is needed to assess the causes of these differences.

Disclosure: J. McDougall Jr., None; C. Brandt, None; M. Skanderson, None; J. Goulet, None; L. Fraenkel, None.

Abstract Number: 1059

Cost-Effectiveness of Tai Chi Versus Physical Therapy for Knee Osteoarthritis

John B. Wong1, Mei Chung2, Lori Lyn Price3 and Chenchen Wang4,5, 1Tufts Medical Center, Boston, MA, 2Department of Public Health and Community Medicine, Tufts University School of Medicine, Boston, MA, 3Biostatistics Research Center, Institute for Clinical Research and Health Policy Studies, Tufts Medical Center, Boston, MA, 4Rheumatology, Center of Integrative Medicine and Division of Rheumatology, Tufts Medical Center, Boston, MA, 5Division of Rheumatology, Tufts Medical Center, Boston, MA

First publication: September 18, 2017
Background/Purpose: A single-blind randomized comparative effectiveness trial showed that Tai Chi yielded beneficial effects similar to those of a standard course of physical therapy in the treatment of knee osteoarthritis, so we aimed to examine the cost-effectiveness of Tai Chi vs. physical therapy for knee osteoarthritis.

Methods: Using standard microeconomic methods, we developed a simulation model to estimate healthcare resource utilization (hospitalizations, inpatient, outpatient, testing, medications and nutraceutical use) and cumulative effectiveness outcomes (WOMAC pain, WOMAC function, Global Visual Analog Scale and SF36 pain component score) over 12 weeks, 24 weeks, and a year. Based on available data, we fit longitudinal models for each patient. To account for uncertainty in the results and estimates, we performed Monte Carlo simulations incorporating the uncertainty surrounding all estimates. We estimated physical therapy costs at $100 per session for 6 weeks twice a week and group Tai Chi classes at $25 per session at twice a week for 12 weeks and accounted for the adherence observed in the study.

Results: In the 1000 simulations for 12, 24 and 52 weeks, Tai Chi was always less expensive than Physical Therapy, with mean (SD) savings of $289 (47) at 12 weeks, $648 (60) at 24 weeks and $1668 (112) after 52 weeks. The analysis was most sensitive to the cost of PT or Tai Chi. At $25 per session for PT, PT was cost-saving at 12 and 24 weeks but Tai Chi was cost saving at 52 weeks. At $60 per session for Tai Chi, Physical Therapy was cost-saving at 12 weeks, but Tai Chi became cost-effective at 24 and 52 weeks.

In terms of effectiveness for 100 patients with knee OA, Tai Chi improved WOMAC pain (0-500) by 50,925 points over 12 weeks, 220,159 points over 24 weeks and 368,642 points over 52 weeks. Similarly, Tai Chi improved WOMAC function (0-1700) by 93,339 points over 12 weeks, 279,460 points over 24 weeks and 439,979 points over 52 weeks. Lastly, Tai Chi improved SF36 Physical Component Score (0-100) by 13,589 over 12 weeks, 44,197 over 24 weeks and 84,294 over 52 weeks.

Conclusion: Our analysis suggests that Tai Chi is cost-saving relative to physical therapy because it on average both reduces costs and improves outcomes. The results are relatively robust (consistent) when varying the cost of physical therapy and Tai Chi until extreme values were considered. The results suggest that reimbursement for Tai Chi as a treatment for knee osteoarthritis should be considered by health payers.

Disclosure: J. B. Wong, None; M. Chung, None; L. L. Price, None; C. Wang, None.
**Background/Purpose:** Interferon regulatory factor 5 (IRF5) is a key mediator of pathogen-induced immune responses that acts downstream of Toll-like receptors (TLRs), NOD-like receptors (NLRs) and RIG-I-like receptors (RLRs). IRF5 polymorphisms leading to its elevated expression and activation have been detected in patients with autoimmune diseases; yet, the contribution of IRF5 to disease onset and/or severity remains to be fully elucidated. IRF5 typically remains inactive in the cytoplasm of a cell but upon stimulation by external signals, IRF5 undergoes post-translational modification(s), homo-dimerization, and nuclear translocation, where the dimeric protein induces transcription of antiviral and pro-inflammatory genes. Here, we report the evaluation of novel cell-penetrating peptides (CPPs) designed to disrupt IRF5 dimerization which is considered critical for nuclear translocation and function in immune cells.

**Methods:** We designed CPPs targeting IRF5 Helix 2 or Helix 5 regions based on a modelled structure of the IRF5 dimer. CPPs binding to the IRF5 monomer were measured in a time-resolved fluorescence resonance energy transfer (TR-FRET) assay. Potencies of IRF5-CPPs were assessed in an IRF5 dimerization assay using recombinant biotin- and his-tagged IRF5 (222-467, S430D). Cell penetration was first tested in Hela cells with FITC-conjugated CPPs followed by confocal microscopy. The effects of IRF5-CPPs on nuclear localization and phosphorylation of IRF5 in CD14$^+$ monocytes, CD123$^+$BDCA2$^+$ plasmacytoid dendritic cells (pDC) and CD19$^+$ B cells were analyzed on an ImageStream Mark II cytometer following stimulation of peripheral blood mononuclear cells (PBMCs) with CpGA, R848 or SLE serum. Levels of inflammatory cytokines (IL-6, TNFα), IgG and IFNα in PBMCs were measured by AlphaLISA.

**Results:** Biochemical and imaging analyzes showed that IRF5-CPPs are cell permeable, non-cytotoxic at concentrations <50 µM, and directly bind to IRF5 ($K_D = 0.5-0.93 \mu M$). FRET assays revealed that IRF5-CPPs disrupt IRF5 homo-dimerization (IC$_{50}$ = 8.5-10.9 µM). Stimulation of PBMCs with TLR ligands revealed that IRF5-CPPs blocked pro-inflammatory cytokine production (IL-12, TNFα, and IL-6), IgG production in B cells, and IFNα production in pDCs. Inhibition of cytokine and IgG production from primary immune cells correlated with a significant, concentration-dependent reduction in the nuclear localization of phosphorylated IRF5. Similar findings were made in PBMCs derived from patients with systemic lupus erythematosus (SLE) or lupus nephritis (LN).

**Conclusion:** Rational design of novel cell-penetrating peptide inhibitors that target IRF5 dimerization not only provides new tools for the functional interrogation of IRF5 in healthy and disease-relevant cells, but also facilitates the development of new therapeutics to treat inflammatory and autoimmune disorders such as SLE.

**Disclosure:** J. Banga, None; D. Srinivasan, Anthera Pharmaceuticals Inc., LQT Therapeutics, 1,Anthera Pharmaceuticals Inc., 3,LQT Therapeutics, 5,Hoffmann-La Roche Inc., 9; C. C. Sun, EMD Serono Research and Development Institute, Inc., 3; F. Milletti, Roche Pharmaceuticals, 1,Roche Pharmaceuticals, 3; K. S. Huang, None; S. Hamilton, None; A. F. Hoffman, None; Y. G. Qin, None; S. Panicker, None; G. Lu, None; D. Li, None; H. Qian, None; D. R. Bolin, None; L. Liang, None; C. Wartchow, None; N. Fotouhi, None; J. A. DeMartino, EMD Serono, Merck and Co., 1,EMD Serono, 3; S. L. Tan, None; G. Chen, EMD Serono, 1,EMR Serono, 3; B. J. Barnes, None.


**Abstract Number:** 1061

**Cardiac Endothelial Cell Transcriptome Analyses Support a Pathological Role of Metabolic and Inflammasome Genes in Anti-SSA/Ro-Associated Congenital Heart Block**

Sara Rasmussen$^1$, Robert M. Clancy$^2$ and Jill P. Buyon$^2$, $^1$Department of Medicine, Division of Rheumatology, NYU School of Medicine, New York, NY, $^2$NYU School of Medicine, New York, NY

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Innate Immunity and Rheumatic Disease Poster II

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The role of Type I IFN in anti-SSA/Ro-associated Congenital Heart Block (CHB) may include an adverse consequence to the cardiac vasculature. One scenario consistent with injury is that the phenotype of cardiac endothelial cells contributes to Caspase-1/Interleukin-1 converting enzyme (inflammasome) to account for chronic levels of inflammatory cytokines and oxidative stress. This study sought to
test the hypothesis that anti-SSA/Ro-mediated injury to the vasculature occurs via a Type 1 IFN-enriched environment, which acts on the endothelial cells to upregulate the inflammasome along with metabolical changes contributing to damage by decreasing oxygen to the tissue.

**Methods:**

Two sources of endothelial cells were studied. In an in vitro approach, cultured HUVECs were evaluated in the presence and absence of supernatants generated from macrophages treated with ssRNA (hY3) since previous studies have identified macrophages as a potential source of IFN in CHB. Both transcriptomic analyses and cellular metabolism as reflected in the extracellular acidification rate (ECAR) and mitochondrial oxygen consumption (OCR) were analyzed using the Seahorse platform. A second in vivo approach used freshly obtained endothelial cells (DAPI negative cells isolated by flow using antibodies to CD31) from a 19 week fetus dying with CHB and an otherwise healthy 22 week heart.

**Results:**

For the in vitro experiments, IFIT1 (IFN response gene) was significantly increased by 163-fold in HUVECs incubated with hY3 macrophage supernatants compared to HUVECs treated with macrophage supernatants alone (p=0.023, qPCR). The inflammasome components NLRP3 and CASP1 were also significantly increased by 2.8 fold and 2.1 fold in HUVECs treated with hY3 macrophage supernatants vs macrophage supernatants alone (p=0.025, p=0.05, respectively). Reflecting oxidant stress, significant increases in ECAR were observed in the HUVECs treated with hY3 macrophage supernatants compared to macrophage supernatants alone (15±4 mpH/min vs 5±3 mpH/min, p=0.05, N = 3). For bioenergetic health index (BHI), a composite of spare capacity, coupling efficiency, Proton leak and non mitochondrial respiration, there was a trend to be lower EC + hY3 macrophage supernatants vs EC + macrophage supernatants (2.0 vs 3.3, p=0.2, respectively).

Transcriptomes of the two hearts for each isolated endothelial cell fraction were compared. Based on DAVID annotation, data were organized into clusters of closely related genes. The top GO category was the type I IFN signaling pathway with 5 IFN inducible genes in the top 10. Regarding targeted genes with greater than two-fold upregulation (CHB vs control), there were genes within the inflammasome pathway, including IFN inducible NLRC5, which serves to interact with NLRP3, along with well characterized multiprotein oligomer of the inflammasome such as NLRP3, IRF7, IRF9 & CASP1. Inflammasome precursors including IL18, IL1B, & IL1A were also upregulated.

**Conclusion:**

Anti-SSA/Ro-induced cardiac injury may include a previously unappreciated effect on the vasculature mediated by IFN. This vascular effect is reflected in the upregulation of metabolic and inflammasome genes.

**Disclosure:** S. Rasmussen, None; R. M. Clancy, None; J. P. Buyon, None.


**Abstract Number:** 1062

### Ptpn22 Regulates Synovial Slam Family Receptor Expression during Toll-like Receptor-Driven Suppression of Inflammatory Arthritis

**David Ewart**¹, Juan Abrahante Llorèns² and Erik J. Peterson³, ¹Rheumatology, University of Minnesota, Minneapolis, MN, ²Informatics Institute (UMII), University of Minnesota, Minneapolis, MN, ³Center for Immunology/Department of Medicine, University of Minnesota, Minneapolis, MN

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** In innate Immunity and Rheumatic Disease Poster II

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**
Genetic factors contribute strongly to Rheumatoid arthritis (RA) risk. Protein tyrosine phosphatase non-receptor 22 [PTPN22] encodes the hematopoietic-specific Lymphoid Phosphatase [“Lyp”]. A PTPN22 coding variant “LypW” is the most potent non-HLA genetic risk factor for RA. TLR agonists potently suppress inflammatory arthritis in murine models of RA. Our previous work revealed that Lyp promotes induction of type 1 interferon [IFN1] and IFN1-dependent genes during TLR3 agonist treatment of serum transfer arthritis (STA). RA-associated variant LypW shows loss of function behavior in arthritis suppression. The molecular and cellular mechanism(s) by which Lyp promotes IFN1-dependent inflammatory arthritis amelioration are not known. The goal of this study was to analyze the PTPN22-dependent transcriptome within arthritic synovium of animals receiving TLR agonist treatment.

Methods:
Wild-type (WT) or Lyp-deficient (Lyp-/-) mice (n = 6 per genotype) were injected with K/BxN serum on days 0 and 2. On days 4 and 6, half of the mice were given 150 μg poly I:C [pIC], a TLR 3 agonist and arthritis-suppressing agent, by intraperitoneal injection. 12 hours after the second dose of pIC, mice were sacrificed. Total RNA was extracted from ankle synovial aspirates. RNA-Seq mapping, gene quantification and differential expression were done in Bowtie2, Feature Counts and edgeR.

Results:
15 genes were differentially-regulated by pIC in Lyp-/- arthritic synovium. Among the genes with known immune-modulating function, Signaling lymphocytic activation molecular family member 7 [Slamf7] and family member 4 [Slamf4] had the highest fold-change differences between genotypes. pIC treatment robustly upregulated expression of Slamf7 in synovium from arthritic WT mice, but upregulation was markedly attenuated in Lyp-/- animals (figure 1). In contrast, Slamf4 transcripts were reduced after pIC treatment in both genotypes; Slamf4 suppression was greater in Lyp-/- mice. Because SLAM family members are important for innate immunoregulation, we examined TLR-signaled SLAM expression within candidate SLAM-expressing innate immune cells. Preliminary results from studies of TLR3 or TLR4-treated bone marrow-derived macrophages or dendritic cells, or of splenic macrophages after in vivo pIC exposure revealed minimal upregulation of Slamf7, regardless of Lyp genotype. NK cells from pIC-treated animals showed upregulation of surface Slamf7, and suppression of Slamf4, but not in a Lyp-dependent manner.

Conclusion:
TLR agonist treatment induced modulation of SLAMf4 and 7 and is differentially regulated by Lyp during serum transfer arthritis. Preliminary studies do not support the hypothesis that Lyp modulates TLR-stimulated SLAM family receptor expression in key inflammation-regulating innate immune cell types, including dendritic cells, macrophages, or NK cells.

Disclosure: D. Ewart, None; J. Abrahante Lloréns, None; E. J. Peterson, None.


Abstract Number: 1063

Activation of Toll-like Receptor 2 in Human Synovium Explants Increase Tissue Turnover and Secretion of Interleukin-6
Background/Purpose:
The innate immune system is important for initiation and development of OA. Increased degradation of the cartilage release fragments into the synovial fluid, which can then bind to innate immune receptors in the synovium. The aim of this study was to investigate the effect of Toll like receptor 2 (TLR2) activation by synthetic agonists and a synthetic aggrecan 32 amino acid fragment (32-mer) on the tissue turnover and IL-6 secretion, in a human synovial membrane explant model.

Methods:
Human synovial membrane biopsies retrieved from OA patients undergoing total knee replacement were lysed and the presence of TLR2 were investigated by western blotting. Human synovial membrane explants (SME) were prepared from the synovial biopsies: Excess fat was removed and the biopsies were cut into explants of 30±5 mg. The SMEs were cultured for 14 days without treatment (WO), OSM [10ng/mL] + TNFα [20ng/mL] (positive control), Pam2CSK4 in three doses (100 ng/mL, 10 ng/mL, or 1 ng/mL), or Pam3CSK4 in three doses (300 ng/mL, 30 ng/mL, or 3 ng/mL). Furthermore, stimulation with a synthetic aggrecan 32-mer (100000 ng/ml, 10000 ng/ml, 1000 ng/ml, 100 ng/ml and 10 ng/ml, respectively) was evaluated. Release of the neo-epitope biomarkers acMMP3 and C3M were measured by ELISA and secretion of IL-6 was evaluated by western blotting at day 5 and 10 in the conditioned media.

Results:
Western blotting confirmed the presence of TLR2 in untreated OA synovial biopsies (Fig. 1a). Activation of the SMEs were assessed by acMMP3, C3M, and IL-6 release. OSM+TNFα significantly increased the release of IL-6 secretion, acMMP3 (P<0.05), and C3M (P<0.01) (Fig. 1). The TLR2 agonists, Pam2CSK4 and Pam3CSK3, significantly increased the release of acMMP3 at day 10 compared to WO (PAM2CSK4: 100 ng/mL P<0.001, 10 ng/mL P=0.016, Pam3CSK4: 30 ng/mL P=0.001) (Fig. 1c). The overall C3M release was significantly increased by Pam2CSK compared to WO (100 ng/mL P=0.007 and 10 ng/mL: P=0.008) (Fig. 1d). Pam3CSK tended to increase the overall C3M and significantly increased C3M release at day 10 compared to WO (100 ng/mL: P=0.035, 10 ng/mL: P=0.008). The western blotting confirmed increased secretion of IL-6 from SMEs stimulated with Pam2CSK4 (Fig. 1b) and Pam3CSK4 compared to WO. Synthetic aggrecan 32-mer did not show any significant increase of C3M release from the synovium.

Conclusion:
TLR2 is expressed in synovium of OA patients and their activation by synthetic ligands resulted in increased tissue turnover confirmed by release of activated MMP3, acMMP3, and MMP-mediated degradation of type III collagen, C3M. Additionally, activation of TLR2 lead to an increased secretion of the pro-inflammatory cytokine IL-6. A synthetic peptide of the potential biological ligand of TLR2, the aggrecan 32-mer failed to generate a significant C3M response compared to WO. We hypothesize that it may be different with the glycosylated native aggrecan 32-mer.
Characterization of Human Tolerogenic Dendritic Cells Generated with Protein Kinase C Inhibitor and Induction from Patients with Autoimmune Diseases

Hitoshi Hasegawa¹, Takuya Matsumoto¹, Endy Adnan², Jun Ishizaki¹, Koichiro Suemori¹ and Masaki Yasukawa¹, ¹Department of Hematology, Clinical Immunology and Infectious Diseases, Ehime University Graduate School of Medicine, Ehime, Japan, ²Hematology, Clinical Immunology and Infectious Diseases, Ehime University Graduate School of Medicine, Ehime, Japan

First publication: September 18, 2017

SEsson Information
Session Date: Monday, November 6, 2017
Session Title: Innate Immunity and Rheumatic Disease Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Tolerogenic dendritic cells (tDCs) are a promising therapeutic tool for specific induction of immunological tolerance. Human tDCs can be generated ex vivo using various compounds. However, the compound(s) most suitable for clinical application remain undefined. For clinical application of tDCs, three functional characteristics are required: 1) CCR7-dependent migration toward secondary lymphoid organs; 2) efficient induction of functional regulatory T cells; and 3) stability upon exposure to proinflammatory stimuli. We found that DCs (PKCl-tDCs) treated with protein kinase C inhibitor (PKCl) had potent tolerogenic properties. Since aberrant activation of T cells, especially CD4⁺ T cells, plays an important role in the initiation and/or perpetuation of rheumatoid arthritis (RA) and primary Sjögren’s syndrome (pSS), both diseases may be suitable for tolerance-inducing therapy. In this study, we described the characterization of PKCl-tDCs and examined whether PKCl-tDCs could be generated from patients with RA or pSS.
Methods:

1) Generation of human tDCs: Immature DCs (iDCs) were generated from the monocytes by culturing them in X-VIVO medium with GM-CSF and IL-4 for 5 days. To induce mature DCs (mDCs), iDCs were incubated with a maturation cocktail for a further 48 h. Compound-treated tDCs were generated by culturing iDCs with a maturation cocktail in the presence of each compound for 48 h. 2) Other methods: In vitro T cell proliferation assay; cytokine production; phagocytic ability; induction of regulatory T cells; in vitro T regulatory activity; stability of DCs under proinflammatory stimuli; and chemotaxis assay.

Results:

PKCI-tDCs had a semi-mature phenotype, showing high production of IL-10, and efficiently induced IL-10-producing T cells and functional Foxp3^+ regulatory T cells, thus eliciting a strong immunosuppressive function. They also showed CCR7 expression and sufficient capacity for migration toward CCR7 ligands. In addition, PKCI-tDCs were highly stable when exposed to inflammatory stimuli. PKCI inhibited NF-κB activation of both the canonical and non-canonical pathways of DC maturation, thus suppressing the expression of costimulatory molecules and IL-12 production. High production of IL-10 in PKCI-tDCs was due to not only an increase of intracellular cAMP, but also a synergistic effect of increased cAMP and NF-κB inhibition. PKCI-treated DCs from the patients with RA or pSS had similar phenotypes and suppressive properties to those from healthy donors.

Conclusion:

PKCI-tDCs may be useful for tolerance-inducing therapy, since they satisfy the required functional characteristics for clinical-grade tDCs. In addition, PKCI-tDCs were generated from patients with RA or pSS not only before but also after treatment with agents such as methotrexate and prednisolone.

Disclosure: H. Hasegawa, None; T. Matsumoto, None; E. Adnan, None; J. Ishizaki, None; K. Suemori, None; M. Yasukawa, None.


Abstract Number: 1065

Mucosal-Associated Invariant T Cell Deficiency in Systemic Lupus Erythematosus Is Related to an Intrinsic Defect in the Ca2+/Calcineurin/NFAT1 Signaling Pathway

Yong-Wook Park^1, Young-Nan Cho^2, Hye-Mi Jin^1, Tae-Jong Kim^3 and Seung-Jung Kee^4, ^1Rheumatology, Chonnam National University Medical School and Hospital, Gwangju, Korea, Republic of (South), ^2Rheumatology, Chonnam National University Hospital and Medical School, Gwangju, MN, Korea, Republic of (South), ^3Chonnam Nat’l University Medical School&Hospital, Chonnam, Korea, Republic of (South), ^4Laboratory Medicine, Chonnam National University Medical School and Hospital, Gwangju, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Innate Immunity and Rheumatic Disease Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Mucosal-associated invariant T (MAIT) cells contribute to protection against certain microorganism infections and play an important role in mucosal immunity. However, the role of MAIT cells remains enigmatic in autoimmune diseases. Here, we examined the level and function of MAIT cells in patients with rheumatic diseases.

Methods: Patients with systemic lupus erythematosus (SLE; n = 54), rheumatoid arthritis (RA; n = 66), Behçet’s disease (n = 9), ankylosing spondylitis (n = 21), and healthy controls (n = 136) were enrolled in the study. MAIT cell, cytokine and programmed death-1 (PD-1) levels were measured by flow cytometry.

Results: Circulating MAIT cell levels were significantly reduced in systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) patients. In particular, this MAIT cell deficiency was more prominent in CD8^+ and double-negative T cell subsets, and significantly correlated with disease activity, such as SLE disease activity index (SLEDAI) and 28-joint disease activity score (DAS28). Interestingly, MAIT cell frequency was significantly correlated with natural killer T (NKT) cell frequency in SLE patients. IFN-gamma in MAIT
In SLE patients, MAIT cells were poorly activated by alphagalactosylceramide-stimulated NKT cells, thereby showing the dysfunction between MAIT cells and NKT cells. Notably, an elevated expression of PD-1 in MAIT cells and NKT cells was associated with SLE. In RA patients, MAIT cell levels were significantly higher in synovial fluid than in peripheral blood.

**Conclusion:** Our study primarily demonstrates that MAIT cells are numerically and functionally deficient in SLE. In addition, we report a novel finding that this MAIT cell deficiency is associated with NKT cell deficiency and elevated PD-1 expression. These abnormalities possibly contribute to dysregulated mucosal immunity in SLE.

**Disclosure:** Y. W. Park, None; Y. N. Cho, None; H. M. Jin, None; T. J. Kim, None; S. J. Kee, None.

**Abstract Number:** 1066

**Invention and Phenotypic Evaluation of Human IgG4-Knock-in Mice**

Yoshie Gon, Hajime Yoshifuji, Koji Kitagori, Toshiki Nakajima, Kosaku Murakami, Ran Nakashima, Koichiro Ohmura and Tsuneyo Mimori, Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University, Kyoto, Japan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Innate Immunity and Rheumatic Disease Poster II  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** IgG4-related disease (IgG4-RD) is a disorder characterized by elevated serum IgG4 concentration and infiltration of IgG4-positive plasma cells into affected organs, however, the role of IgG4 in the pathophysiology of IgG4-RD is not sufficiently elucidated. Although animal models are required, mice only have IgG1, 2 and 3 subclasses but no IgG4. Therefore, we invented human IgG4 (hIgG4)-knock-in (KI) mice and evaluated their phenotypes.

**Methods:** The hIgG4 gene is inserted in the cite of mouse IgG1 (mIgG1) gene, which is promoted by Th2 cells associated with the pathophysiology of IgG4-RD. In order to preserve the rearrangement system of VDJ region of IgH gene, constant region of hIgG4 gene was only transfected into ES cells of C57BL/6 mice by gene targeting method. 1) We quantitated levels of mRNA extracted from spleens of homozygous (Homo) and heterozygous (Hetero) IgG4-KI mice, respectively. 2) Serum IgG4 levels in Homo, Hetero and wild-type (WT) mice were quantitated by ELISA and turbidimetric immunoassay (TIA) used in daily clinics. 3) To enhance the production of IgG4, we established MRL-lpr/IgG4-KI mice and analyzed them by ELISA and flow cytometry (FCM).

**Results:** 1) Expression of hIgG4 mRNA, mIgG1 mRNA and hIgG4+mIgG1 mRNA were detected in the spleen of Homo, WT and Hetero mice, respectively. 2) hIgG4, mIgG1 and hIgG4+mIgG1 proteins were detected in sera of Homo, WT and Hetero mice, respectively (Fig. 1). Serum hIgG4 level in Homo mice was 7.0 mg/dL by TIA (Table 1). 3) Serum hIgG4 level in MRL-lpr/IgG4-KI Homo mice was increased to 289 mg/dL. We detected the spleen cells that express IgG4 on surface by FCM.

**Conclusion:** The transfected IgG4 gene seemed to work physiologically, as we confirmed secretory IgG4 in blood and membranous IgG4 on spleen cells in the mice. Serum IgG4 level was high in MRL-lpr/IgG4-KI mice. Their histopathology is to be examined.

**Table 1. Serum hIgG4 titer by TIA**

<table>
<thead>
<tr>
<th></th>
<th>B6/WT</th>
<th>B6/IgG4-KI Homo</th>
<th>MRL-lpr</th>
<th>MRL-lpr/IgG4-KI</th>
</tr>
</thead>
<tbody>
<tr>
<td>hIgG4 (mg/dL)</td>
<td>Not detected</td>
<td>7.0</td>
<td>Not detected</td>
<td>289</td>
</tr>
</tbody>
</table>
Clinical Significance of Anti-Dense Fine Speckled 70 and Dense Fine Speckled Pattern in Diagnosis of Systemic Autoimmune Rheumatic Disease

You La Jeon1, Ji Yun Ryu1, Jiyoung Baek1, Woo-In Lee2, Myeong Hee Kim1 and So Young Kang1, 1Department of Laboratory Medicine, School of Medicine, Kyung Hee University and Kyung Hee University Hospital at Gangdong, Seoul, Korea, Republic of (South), 2School of Medicine, Kyung Hee University and Kyung Hee University Hospital at Gangdong, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Innate Immunity and Rheumatic Disease Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The dense fine speckled (DFS) pattern in IIF-ANA on HEp-2 cell is perhaps the most frequently observed pattern in most clinical laboratories. The DFS70 or lens epithelium-derived growth factor p75 (LEDGFp75) is the known corresponding antigen to the DFS pattern. Identification of this antibody can be an evidence to exclude the presence of systemic autoimmune rheumatic diseases (SARD), however this correlation requires more definite clinical correlation. The aim of our study is to confirm the presence of anti-DFS70 in specimens showing DFS pattern by western blot (WB) and enzyme immunoassay (EIA). Also the association between the anti-DFS70 and SARD or certain clinical conditions is discussed.

Methods: A total of 227 serum specimens showing DFS (n=180, only DFS (158) and DFS+other (22)) and homogeneous (H) (n=47, only H (33) and H+other (14)) patterns in IIF-ANA screening test were included. All specimens were tested twice by IIF-ANA and the results interpreted by two separate expert specialists of Laboratory Medicine. The cases with discrepant results between the two interpreters were excluded. The results of first and second test results of IIF-ANA were compared. In-house WB was performed using deriving cell lysate from cultured HeLa cells. Detection of anti-DFS70 IgG was done using a commercial EIA kit. The clinical information regarding disease status or the presence of SARD of subjects was obtained from retrospective review of individual medical records.

Results: Forty four cases (19.4%) showed discrepant reading in their repeated IIF-ANA test results. The majority of those results included the following: 19 cases (DFS pattern in first test result then interpreted as another in second test result, especially 14 cases as H pattern), 9 cases (from DFS pattern to negative), and 13 cases (changed with only combined pattern). There were also 17 other cases in which the results were complex and indeterminable. Among 155 cases with DFS pattern in the second test results of IIF-ANA, 134 cases (86.5%) were positive by WB and 114 cases (73.5%) positive by EIA. WB had covered all cases in which this autoantibody was detected. The number of cases detected of anti-DFS70 are divided into three groups which are as follows; 114 (73.5%) in WB+/EIA+, 114 (73.5%) in WB+/EIA+, 114 (73.5%) in WB+/EIA+.
20 in WB+/EIA-, and 21 in WB-/EIA-. There was no case which showed only EIA positivity. More than half of the patients from each group were referred to the department of dermatology, where many were given their diagnoses of androgenic alopecia. SARD patients with DFS pattern were 1 (SLE) in WB+/EIA+, 3 (1 SSc, 2 RA) in WB+/EIA-, and 1 (RA) in WB-/EIA-.

**Conclusion:** The prevalence of SARD (2.2%) was very low in this study of randomly selected 180 DFS and 47 H pattern cases. This result suggests the utility of anti-DFS70 to exclude SARD when detected. DFS pattern can also provide a clue to exclude SARD based on the results that anti-DFS70 was detected in 86.5% of cases with DFS pattern given that IIF-ANA tests were conducted twice and interpreted carefully by two separate specialists. However presence of a confusing pattern or the absence of monospecific anti-DFS70, additional tests are necessary to rule out the diagnosis of SARD.

**Disclosure:** Y. L. Jeon, None; J. Y. Ryu, None; J. Baek, None; W. I. Lee, None; M. H. Kim, None; S. Y. Kang, None.


**Abstract Number:** 1068

**Impact of TNF Antagonist Treatment on the Gut Microbiome In Vivo**

**Odile Gabay**¹, Jonathan Vicenty², Grant Wunderlin³, Linda Tiffany², Wells Wu⁴, Vahan Simonyan⁵ and Kathleen A Clouse⁶, ¹Office of Biotechnology Products /Center for Drug Evaluation and Research DBRRI, U.S. Food and Drug Administration, Silver Spring, MD, ²Office of Biotechnology Products, Center for Drug Evaluation and Research, DBRRI, U.S. Food and Drug Administration, Silver Spring, MD, ³Center for Drug Evaluation and Research CDER DBRRI, U.S. Food and Drug Administration, Silver Spring, MD, ⁴Center for Biologic Evaluation and Research OMPT, U.S. Food and Drug Administration, Silver Spring, MD, ⁵Center for Biologic Evaluation and Research, U.S. Food and Drug Administration, Silver Spring, MD, ⁶Office of Biotechnology Products /Center for Drug Evaluation and Research, DBRRI, U.S. Food and Drug Administration, Silver Spring, MD

**First publication:** September 18, 2017

**SESSON INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Innate Immunity and Rheumatic Disease Poster II  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Auto-immune diseases are in constant progression in the US. Biologic therapeutics have been used successfully to treat these diseases, but have presented some unique regulatory challenges. Although they can be very efficacious, the response to these therapeutics can initially be quite variable among patients and patients who are initially responsive can develop resistance to them over time. We propose that the gut microbiome could play a role in the initial variability and impact the response to treatments.

**Methods:** Germ Free (GF) mice colonies have been successfully developed in a sterile environment in the CBER/CDER Animal Facility. We used these GF mice to test human monoclonal antibodies and fusion proteins, following a treatment regimen consistent with patient regimens, to evaluate the role of the microbiome when GF mice are compared to conventional mice controls treated in parallel. Our pilot study is analyzed from two different approaches: assessment of taxonomy changes and an immunologic variation in the mouse gut.

**Results:** Our results show a break in the symbiosis of the commensal bacteria communities after TNF antagonist treatment. These mice present a shift in the ratio Firmicutes/Bacteroidetes with a statistically significant increase in this latter family over uncultured bacteria. Differences are reported between males and females and between young (3 month-old) and old (9 month-old) mice. When the mucosal immune system is explored, comparing conventional and GF mice, it appears that the Innate Lymphoid Cells (ILCs) colonizing the lamina propria of the gut have two very different profiles and therefore, are likely to respond differently to cross-talk with commensal bacteria in the gut. A preliminary mechanistic link to the plasticity between ILC1 and LC3 is suggested in older mice.

**Conclusion:** Our results show that the Microbiota indeed plays a regulating role in TNF antagonist treatment, involving a dysbiosis and a regulation through ILCs. This observational study should be followed by *in vivo* functionality studies.

**Disclosure:** O. Gabay, None; J. Vicenty, None; G. Wunderlin, None; L. Tiffany, None; W. Wu, None; V. Simonyan, None; K. A. Clouse, None.
Abstract Number: 1069

Significantly Elevated Serum Protein-Adduction with 4-Hydroxy-2-Nonenal but Not Malondialdehyde in Sjogren’s Syndrome

Biji T Kurien1,2,3, Sona Nuguri4, Bre’ana Byrd5, Joey Maher6, Rohit Thomas4, Huyen Tran7 and R. Hal Scofield8, 1Arthritis and Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, 2U.S. Department of Veterans Affairs Medical Center, Oklahoma City, OK, 3College of Medicine, University of Oklahoma Health Sciences Center, Oklahoma City, OK, 4Oklahoma School of Science and Mathematics, Oklahoma City, OK, 5University of Central Oklahoma, Edmond, OK, 6University of Oklahoma, Norman, OK, 7University of Oklahoma Health Sciences Center, Edmond, OK, 8Arthritis & Clinical Immunology Program, Oklahoma Medical Research Foundation; Department of Medicine, University of Oklahoma Health Sciences Center; US Department of Veterans Affairs Medical Center, Oklahoma City, OK

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Innate Immunity and Rheumatic Disease Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Sjögren’s syndrome (SS) is a chronic inflammatory, autoimmune disorder characterized by diminished lacrimal and salivary gland secretion resulting in keratoconjunctivitis sicca and xerostomia. Autoantibodies, directed against 60 kD Ro protein is found in up to 90% of patients with SS. Free radical mediated oxidative damage has not been well characterized previously in SS. Therefore, we studied oxidative damage (conjugate diene formation) and modification of serum proteins by the lipid peroxidation by-product 4-hydroxy-2-nonenal (HNE) or malondialdehyde (MDA) in SS and age-and sex matched controls.

Methods:

Sixty nine primary SS subjects, 25 age and sex matched subjects that do not meet criteria (incomplete SS), and 18 normal controls were studied. We studied indices of oxidative damage, namely conjugate diene formation, and HNE or MDA-protein adducts in the sera of SS, incomplete SS and normal controls. Sera from SS subjects or normal controls were coated on ELISA plates as antigen. HNE or MDA adducts in serum proteins was determined with rabbit anti-HNE or anti-MDA antibodies purchased commercially. Sera from SS or normal controls were electrophoresed, transferred to nitrocellulose by electroblotting and subjected to immunoblotting with rabbit anti-HNE antibody. For determination of conjugate diene, 25 µl of SS or incomplete SS sera were extracted with chloroform:methanol (2:1) and the samples were centrifuged. Two ml of the clear supernatant was evaporated to dryness at 45°C and reconstituted in one ml methanol. The spectra ranging from 200 to 360 nm was read using a spectrophotometer.

Results:

We found significantly increased oxidative damage in the sera of primary SS subjects compared to normal controls by ELISA and immunoblotting. Serum proteins from SS subjects were found to contain HNE adducts. There was significantly more HNE-modified proteins in SS sera (n=10) compared to controls (n=10; age and sex matched) by ELISA (0.074 ± 0.017 versus 0.046 ± 0.007; p=0.00015; average OD±SD). However, there was no significant difference in MDA-modified proteins between SS and controls by ELISA. When SS sera (n=34) were analyzed by immunoblotting, we found HNE adducts in several serum proteins, and significantly in a 18 kD protein. Control sera did not show significant HNE-modification (n=8). Our preliminary results for conjugate diene formation show that there is no significant difference between conjugate diene levels in the Sjogrens’s syndrome patients (n=25) and incomplete SS subjects (n=25). We are pursuing HNE-modification in the sera of incomplete SS subjects and also identifying the protein bands in SS subjects with HNE adducts by matrix assisted time of flight mass spectrometry.

Conclusion:

Significantly elevated HNE- but not MDA-protein adducts occur in the sera of SS subjects compared to normal controls, showing that oxidative damage occurs in SS.
Phenotypic Characterization of Peripheral Basophil Perturbations in the Antiphospholipid Syndrome

Benjamin Chaigne1, Veronique Le Guern2, Tali-Anne Szwebel1, Romain Paule2, Claire Le Jeunne3, Nathalie Costedoat-Chalumeau4 and Luc Mouton5, 1Service de Médecine Interne, Centre de Référence Maladies Systémiques Autoimmunes Rares d’Ile de France, hôpital Cochin, D.H.U Authors, Assistance Publique-Hôpitaux de Paris, Paris, France; 2Department of Internal Medicine, Department of Internal Medicine, Cochin University Hospital, Paris, France; 3Service de Médecine Interne, Hôpital Cochin, Centre de référence national pour les maladies systémiques autoimmunes rares d’Ile de France, D.H.U Authors, Assistance Publique-Hôpitaux de Paris (AP-HP), Paris, France; 4Service de médecine interne Pôle médecine, Hôpital Cochin, Centre de référence maladies auto-immunes et systémiques rares de l’Ile de France, Paris, France; 5Service de Médecine Interne, Hôpital Cochin, Centre de référence national pour les maladies systémiques autoimmunes rares d’Ile de France, D.H.U Authors, Assistance Publique-Hôpitaux de Paris (AP-HP), Paris, France; Université Paris Descartes Sorbonne Paris, Paris, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Innate Immunity and Rheumatic Disease Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
The antiphospholipid syndrome (APS) is an autoimmune condition characterized by thrombosis, pregnancy complications and the presence of antiphospholipid antibodies. Basophils, which have long been associated with allergy and parasitic infections, are known to be activated and able to enhance the production of autoantibodies in autoimmune diseases, particularly in systemic lupus erythematosus (SLE). Herein we investigated the role of basophils in APS.

Methods:
Peripheral basophils of patients with primary APS, SLE-associated APS (SLE-APS), and healthy controls (HC) were analyzed using flow cytometry.

Results: Forty-three consecutive patients with APS, including 10 patients with SLE-APS, and 20 HC were recruited. None of the patients was treated with corticosteroids or immunosuppressants. Thirty-five (81.4%) patients had lupus anticoagulant, 33 (76.7%) had anti-cardiolipin antibodies, and 24 (55.8%) had anti-ß2 glycoprotein I. Twenty (46.5%) patients had obstetric APS, 20 (46.5%) patients experienced arterial thrombosis and 19 (44.2%) patients experienced venous thrombosis. Six patients (14%) had a catastrophic APS (CAPS). Basophil activation markers revealed a decreased proportion of CD193+ basophils in patients with APS vs HC (63.0% [27.3 – 85.0] vs 90.4% [74.1 – 97.1]; p < 0.05) and an increased mean fluorescence intensity (MFI) of CD69 within basophils in patients with APS vs HC (839 [436 – 1434] vs 318 [103 – 755]; p < 0.05). Basophils functional markers revealed a decreased proportion of CD62L+ basophils in APS vs HC (99.0% [95.6 – 100] vs 100% [99.6 – 100]; p < 0.05), and an increased proportion of HLA-DR+ basophils in APS vs HC (32.3% [16.8 – 77.2] vs 10.0% [3.4 – 21.7]; p < 0.05). There was no difference between patients with APS and patients with SLE-APS, or patients with CAPS. When compared to patients without obstetric APS, patients with obstetric APS (46.5%) had a decreased proportion of CD196+ basophils (25.5% [11.3 – 32.5] vs 31.9% [25.8 – 66.3]; p < 0.05), an increased proportion of CD63+basophils (34.8% [0.25 – 53.3] vs 7.4% [0 – 37.9]; p < 0.05), and an increased proportion of HLA-DR+ basophils (49.0% [23.4 – 79.6] vs 20.8% [8.7 – 70.8]; p < 0.05). Lastly, the proportion of CD154+ basophils was higher in patients who experienced miscarriages than those who did not (47.6% [38.2 – 56.1] vs 19.7%[5.1 - 35.8]; p < 0.01) and MFI of basophil CD62L was higher in patients who experienced fetal death in utero than those who did not (11823 [9862 – 15546] vs 7978 [4628 - 10160]; p < 0.05).

Conclusion:
Main phenotypic characteristics of basophils in APS are an increased expression of CD69 marker, a decreased expression of CD193 marker, and an increased expression of HLA-DR marker suggesting a role for basophils. Patients with obstetric APS differed from other APS patients by a skewed distribution of CD196+, CD63+ and HLA-DR+ basophils.

Disclosure: B. Chaigne, None; V. Le Guern, None; T. A. Szwebel, None; R. Paule, None; C. Le Jeunne, None; N. Costedoat-Chalumeau, None; L. Mouthon, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/phenotypic-characterization-of-peripheral-basophil-perturbations-in-the-antiphospholipid-syndrome

Abstract Number: 1071

Increased Susceptibility of SLE-Prone Mice to Pulmonary Haemophilus Influenzae Infection Was Attributed to Dysfunctions of Innate Immune Responses

Wenchao Li and Lingyun Sun, Department of Rheumatology and Immunology, The Affiliated Drum Tower Hospital of Nanjing University Medical School, Nanjing, China

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Innate Immunity and Rheumatic Disease Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Aside from the disease itself, infections represent the major cause of morbidity and mortality in systemic lupus erythematosus (SLE) patients. Although the daily usage of immunosuppressive drugs is considered to be responsible for the increased rates of infection, inherent defects in immune system should not be overlooked.

Methods: To better understand the proclivity of SLE patients to suffer infections, we infected lupus-prone mice B6/lpr with 1X10^8 CFU of Haemophilus influenzae (Hi) intranasally and monitored bacterial clearance, body weight change and lung pathology after infection. Apoptosis of lung cells was analyzed by TUNEL assay. Immune cells recruited by infection were determined by flow cytometry. Cytokines in the bronchoalveolar lavage fluid (BALF) were measured by ELISA.

Results: Although both wild-type (WT) and B6/lpr mice survived after pulmonary Hi infection, a delay of bacterial clearance and inflammatory resolution was observed in B6/lpr mice(Fig1A-C). Besides, tissue damage was more severe in B6/lpr mice, as more apoptotic cells appeared in the lung on D2 after infection (Fig1D). When looked at the cytokine production, we found that cells from lupus-prone lungs produced much more proinflammatory cytokines IL-6, IL-17 and chemokines MCP-1 and KC. However, TNF-α is comparable between the two groups (Fig2). NK, γδ T and CD4 T cells are very important in control of bacterial infection. Here, we showed that compared with WT controls, in response to infection fewer NK cells were detected in B6/lpr lungs. The numbers of γδ T and CD4 T cells in the lung were not different, but their ability to secrete IFN-γ was significant lower in B6/lpr mice(Fig3).

Conclusion: The increased susceptibility of SLE-prone mice to pulmonary Haemophilus influenzae infection may due to the elevated inflammatory responses and the deficiency of immune cells.
Figure 1.

(A) BALF and Lung CFU (cfu/ml) comparison between B6 and B6/lpr.

(B) Graph showing % of original weight over days post infection for B6 and B6/lpr.

(C) Histological images of B6 and B6/lpr at days 0, 2, and 8.

(D) TUNEL, nuclear, and merge images for B6 and B6/lpr with statistical significance indicated.

Figure 2.

Bar graphs showing MCP-1, KC, TNF-α, IL-6, and IL-17 levels in B6 and B6/lpr with statistical significance indicated.
Disclosure: W. Li, None; L. Sun, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/increased-susceptibility-of-sle-prone-mice-to-pulmonary-haemophilus-influenzae-infection-was-attributed-to-dysfunctions-of-innate-immune-responses](http://acrabstracts.org/abstract/increased-susceptibility-of-sle-prone-mice-to-pulmonary-haemophilus-influenzae-infection-was-attributed-to-dysfunctions-of-innate-immune-responses)

Abstract Number: 1072

**Mutated Peptidylarginine Deiminase from Porphyromonas Gingivalis Is a Target in Rheumatoid Arthritis and Citrullinates Major RA-Autoantigens**

Madeleine Jenning1, Bianka Marklein1, Jimmy Ytterberg2, Gerd R. Burmester1 and Karl Skriner1, 1Department of Rheumatology and Clinical Immunology, Charité - University Medicine Berlin, Free University and Humboldt University Berlin, Berlin, Germany, 2Dept. of Medicine, Rheumatology Unit, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden

**First publication:** September 18, 2017
Background/Purpose: Previous reports showed that peptidylarginine deiminase (PPAD) form *Porphyromonas gingivalis* (*P.g.*) is not able to citrullinate proteins internally. Mutated PPAD (mPPAD) from *P.g.* involved in periodontal disease (PD) cloned out of *P.g.* strain was characterized and analyzed for its reactivity in sera from patients with systemic autoimmune diseases.

Methods: We cloned an enzymatically active recombinant mPPAD from *P.g.* Mutations and citrullination sites were analyzed by DNA sequencing and protein mass spectrometry (MS). Autocitrullination activity, its enzymatic-activity and human autoantigen protein citrullination was investigated by 2D-Elektrophoresis, MS, immunoblot analysis and ELISA. Furthermore we tested anti-mPPAD/cit-mPPAD with human sera (*n*=123) from early rheumatoid arthritis (RA) before and after onset of RA (*n*=30), established RA (*n*=32), systemic lupus erythematosus (*n*=15), osteoarthritis (*n*=16) and healthy blood donors (*n*=30) in ELISA assays. In RA mouse model collagen antibody-induced arthritis (CAIA), mPPAD-containing vesicles from *P.g.* were injected by intraperitoneal injection (IP).

Results: Recombinant mPPAD lacks 43 amino acids at the N-terminus and exhibits so far two new amino acid mutations (aminoacid position 73 (F>L) and 447 (E>V). We were able to demonstrate, mPPAD is enzymatically active over a huge pH-range (3-10) and autocitrullinates at amino acid position 63 the arginine to citrulline. Moreover mPPAD citrullinates major autoantigens in RA (Fibrinogen, Vimentin and hnRNP-A2/B1) which are detectable by RA patient sera and specific anti-citrulline monoclonal antibodies. MPPAD citrullinates HeLa-protein extracts and these specific citrullinated proteins are recognized by RA patient sera. Anti-citrullinated mPPAD antibodies were detected in 41% (*n*=32) of patients with RA but not in SLE (*n*=15), OA (*n*=16) and control sera (*n*=16). In an RA follow-up study (*n*=30), we detected nearly similar antibody-sensitivities for citrullinated mPPAD before and after onset of RA (13/20%). Only a minority (7%) of RA patients show higher mPPAD antibody levels after RA diagnosis. In the CAIA RA mouse model mPPAD containing *P.g.* vesicles when injected IP showed a TLR2-dependent protective anti-inflammatory effect like *P.g.* LPS and Lipomannan.

Conclusion: *P.g.* infection and RA disease diagnosis occurs at different time points and *P.g.* infection induces a TLR2-dependent protective anti-inflammatory effect. We show the first time that mPPAD can citrullinate major human autoantigens internally and their immunologically and diagnostic relevance in RA.

Disclosure: M. Jenning, None; B. Marklein, None; J. Ytterberg, None; G. R. Burmester, None; K. Skriner, None.

**Background/Purpose:** Primary Sjögren’s syndrome (pSS) is a complex heterogeneous systemic autoimmune disease. Biomarkers for patient stratification are scarce. Several single nucleotide polymorphisms within type I interferon (IFN) signaling pathways are associated with pSS. To define novel biomarkers for pSS patient stratification, we analyzed the temporal profile of MAPK/ERK and JAK/STAT signaling networks in PBMCs upon stimulation with IFNα by flow cytometry.

**Methods:** PBMCs from pSS patients and healthy matched donors were stimulated for 15, 30, 60, 120, 180, and 240 min with IFNα at 100 ng / ml. Nine different phospho epitopes were measured, STAT4(pY693), ERK1/2(pT202/pY204), NF-κB p65(pS529), STAT1(pS727), STAT1(pY701), p38 MAPK(pT180/pY182), STAT3(pS727), STAT3(pY705) and STAT5(pY694). Cell surface markers were CD3, CD20 and CD56.

**Results:** Cells from pSS patients display significant differences in basal and IFNα induced phosphorylation levels of numerous signaling proteins compared to cells from healthy donors. PCA using IFNα induced phosphorylation levels after 15 minutes showed clustering of pSS patients and pSS patient subgroups. PCA visualization showed a positive shift for pSS samples away from healthy donor samples with positive movement influenced by changes in phosphorylation of STAT1 Y701 in T, NK and B cells in PC1, and PC2 positive movement influenced by STAT1 Y701 in NK and B cells, and negative movement by STAT3 S727 in T cells. Medicated and SSA- patients grouped closer to healthy donors than non-medicated or SSA+ patients.

**Conclusion:** pSS patients show increased responses to IFNα through STAT1. Increased responses to IFNα may in part drive an up-regulation of interferon induced genes.

**Disclosure:** R. Davies, None; D. Hammenfors, None; B. Bergum, None; P. Vogelsang, None; S. Gavasso, None; J. G. Brun, None; R. Jonsson, None; S. Appel, None.


Abstract Number: 1074

**High Cholesterol Levels By ApoE Defenciency Reduce Bone Destruction in Murine Antigen-Induced Arthritis Via Inhibition of Osteoclastogenesis**

**Giuliana Ascone**¹, Irene Di Ceglie¹, Arjen B. Blom¹, Birgitte Walgreen², Annet W. Sloetjes¹, Peter M. van der Kraan¹, Ernst Lindhout³, Mike Martens³ and Peter L. van Lent¹, ²Experimental Rheumatology, Radboud university medical center, Nijmegen, Netherlands, ³Future Diagnostics Solutions (FDs), Wijchen, Netherlands, ⁴Experimental Rheumatology (272), Radboud university medical center, Nijmegen, Netherlands

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Innate Immunity and Rheumatic Disease Poster II

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by immune complex- deposition in the synovium, leading to increased bone destruction. In RA, joint destruction has been associated with high cholesterol levels, largely transported in low density lipoprotein (LDL) particles and enhanced LDL oxidation (oxLDL). Apolipoprotein E (Apo E) is an important regulator of LDL transportation and its absence strongly elevates LDL levels in the serum, which may lead to increased oxLDL levels during inflammation. In this study, we investigated the effects of high LDL levels on bone destruction during antigen-induced arthritis (AIA), which is largely immune complex driven and how increased LDL/oxLDL levels affect osteoclastogenesis.

**Methods:** AIA was induced by injection of methylated BSA (mBSA) into the right knee joint of Apo E⁺⁻ and wild type (WT) control mice previously immunized with mBSA and complete Freund’s adjuvant (CFA). WT and ApoE⁺⁻ Hoxb8 myeloid precursor cells were differentiated into osteoclasts using 20 ng/mL RANKL and 30 ng/mL M-CSF, then stimulated for 24h with 10 µg/mL LDL/oxLDL. Oil Red O staining was performed to assess lipid uptake by osteoclasts. mRNA levels of NFATc1, DC-STAMP, TRAP, CTR and Cat K were measured by qPCR, whereas TRAP activity in culture supernatants was detected using a spectrophotometric assay. Bone erosion was quantified by histological analysis using an arbitrary scale from 0 to 3 and TRAP⁺ cells were determined using immunohistochemistry.
**Results:** Apo E−/− mice showed significantly higher LDL serum levels than WT controls. Histology showed that at day 21 after AIA induction, bone destruction was significantly decreased in the Apo E−/− mice, as indicated by the reduction of erosion pits (25% reduction from 1.5±0.2 to 1.1±0.1). In line with that, ApoE−/− mice showed a lower number of osteoclasts within the knee joints (36% lower from 20±4 osteoclasts/section in WT mice to 12±5 in ApoE−/− mice), as determined by image analysis of TRAP staining. To study the role of ApoE and high LDL levels on osteoclastogenesis in more detail, we differentiated WT and ApoE−/− myeloid precursor cells (Hoxb8) into osteoclasts and found similar mRNA levels of osteoclast markers. Whereas the number of osteoclasts was comparable between WT and ApoE−/− osteoclasts, we observed significantly decreased mRNA expression of TRAP (2.6 fold decrease) in ApoE−/− cells as compared to WT cells. In line with this, TRAP activity was reduced by 49%, suggesting a decreased osteoclast activity in ApoE−/− cells. Stimulation of osteoclasts by oxLDL strongly impaired cell fusion keeping them in a mononuclear state. mRNA levels of DC-STAMP were significantly down-regulated in both WT and ApoE−/− osteoclasts (1.4 and 2.3 fold decrease, respectively) as well as TRAP activity (49% and 58% reduction in WT and ApoE−/− osteoclasts, respectively), indicating a major role of oxLDL in the inhibition of osteoclastogenesis.

**Conclusion:** High LDL/oxLDL levels by apoE deficiency affect bone destruction by reducing the number of osteoclasts within the synovium during AIA probably by interfering osteoclastogenesis.

**Disclosure:** G. Ascone, None; I. Di Ceglie, None; A. B. Blom, None; B. Walgreen, None; A. W. Sloetjes, None; P. M. van der Kraan, None; E. Lindhout, None; M. Martens, None; P. L. van Lent, None.


**Abstract Number:** 1075

**Higher Frequencies of Lymphocytes Expressing the Natural Killer Group 2D Receptor and Cytotoxic Potential of NK Cells in Patients with Behcet Disease**

**Martin Bonacini**¹, Stefania Croci¹, Alessandra Soriano²,³, Eleonora Calò¹, Alessandro Zerbini¹, Luca Cimino⁴, Francesco Muratore²,⁵, Luigi Fontana⁶, Maria Parmeggiani¹ and Carlo Salvarami²,⁵, ¹Unit of Clinical Immunology, Allergy and Advanced Biotechnologies, Arcispedale Santa Maria Nuova-IRCCS, Reggio Emilia, Italy, Reggio Emilia, Italy, ²Unit of Rheumatology, Arcispedale Santa Maria Nuova-IRCCS, Reggio Emilia, Italy, Reggio Emilia, Italy, ³Campus Bio-Medico, University of Rome, Italy, Roma, Italy, ⁴Unit of Ocular Immunology, Arcispedale Santa Maria Nuova-IRCCS, Reggio Emilia, Italy, Reggio Emilia, Italy, ⁵University of Modena and Reggio Emilia, Italy, Modena, Italy, ⁶Unit of Ophthalmology, Arcispedale Santa Maria Nuova-IRCCS, Reggio Emilia, Italy, Reggio Emilia, Italy

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Innate Immunity and Rheumatic Disease Poster II

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Behçet disease (BD) is a rare, systemic, inflammatory disorder with multiorgan damage and various clinical manifestations such as oral ulcers, genital ulcers and uveitis. Pathogenesis is still unknown but it is considered a MHC-I-opathy. Despite HLA-B51 and some gene polymorphisms have been associated with BD², the diagnosis is based on clinical parameters and currently laboratory tests are only of a little help in the diagnosis of BD. The aims of this study were: 1) to increase the knowledge about BD pathogenesis; 2) to identify laboratory tests which can support BD diagnosis.

**Methods:** Peripheral blood mononuclear cells (PBMCs) were collected from 40 BD patients (according to 1990 ISGB criteria) and 15 healthy subjects, aged and sex matched, used as controls. The frequency of Natural Killer (NK), Natural Killer T cells (NKT) and T cells expressing the Natural Killer Group 2D activating receptor (NKG2D) was assessed by flow cytometry using anti-CD56, anti-CD3 and anti-NKG2D antibodies. NK, NKT and T cells were defined as CD56⁺CD3neg, CD56⁺CD3⁺ and CD56negCD3⁺ cells respectively. Cytotoxic potential of NK cells was evaluated by flow cytometry as the percentage of cells expressing on their surface the degranulation marker CD107a, after incubation with K562 cells, optimal target for NK cell activation³. Statistical analyses were performed by Mann-Whitney and Spearman test. P-values less than 0.05 were considered statistically significant.
Results: A significant increase in the percentages of NKG2D⁺ lymphocytes in the NK, NKT and T lymphocyte gates was detected in BD patients respect to healthy subjects (P < 0.01). ROC curve analysis showed that the evaluation of NKG2D⁺ NKT cell percentage better allowed to discriminate between BD patients and healthy subjects (AUC = 0.7385; P = 0.0071). In particular, a frequency higher than 75% could identify BD patients with a 93.3% specificity and 38.5% sensitivity. After incubation of PBMCs with K562 cells, a significant higher frequency of NK cells expressing CD107a was detected in BD patients respect to healthy subjects (13.4% versus 9.5%, P = 0.0124). In BD patients we also observed a correlation between frequencies of NK cells positive for NKG2D and CD107a (r = 0.3573; P = 0.0255). Instead the median percentages of NKT and T cells expressing CD107a was low: 0.88% and 0.51% and similar between groups.

Conclusion: We found that expression of NKG2D by NK, NKT and T lymphocytes might be involved in the pathogenesis of BD in a subset of patients. BD patients were also characterized by a higher cytotoxic potential of NK cells than healthy subjects. We can speculate that NK and NKT cells of BD patients are more prone to respond to stress signals when exposed on target cells leading to cyclic auto-inflammation. Monitoring both the frequencies of NKT cells positive for NKG2D and of NK cells positive for CD107a after activation with K562 cells could help to identify BD patients.

References:

Disclosure: M. Bonacini, None; S. Croci, None; A. Soriano, None; E. Calò, None; A. Zerbinì, None; L. Cimino, None; F. Muratore, None; L. Fontana, None; M. Parmeggiani, None; C. Salvarani, None.


Abstract Number: 1076

TGF-β1 Induces AXL in Murine and Human Synovium and Protects Ankle Joints, but Not Knee Joints, during Murine Inflammatory Arthritis

Claire E.J. Waterborg, Mathijs G.A. Broeren, Esmeralda N. Blaney Davidson, Marije I. Koenders, Peter L. van Lent, Peter M. van der Kraan and Fons A.J. van de Loo, Experimental Rheumatology, Radboud university medical center, Nijmegen, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Innate Immunity and Rheumatic Disease Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Rheumatoid arthritis (RA) manifests in a symmetrical fashion in anatomically distinct synovial joints. The innate immune system, which plays a crucial role in the pathogenesis of RA, is regulated by anti-inflammatory feedback mechanisms such as the tyrosine kinase receptor family TYRO3, AXL and MER. Of importance, AXL is mainly expressed on sentinel cells. We investigated the synovial expression of AXL and its putative anti-inflammatory role in a macrophage-dependent model of arthritis.

Methods: Tissue sections of ankle and knee joints of naïve mice were studied for protein expression of AXL. KRN serum transfer arthritis was induced in Axl⁻/⁻ and wild-type (WT) mice. Ankle and knee joints were assessed macroscopically and histologically. Naïve WT mice were injected intra-articularly in the knee joint with adenoviruses overexpressing active TGF-β1 or Luciferase. Protein expression of AXL on tissue sections and/or gene expression in synovial biopsies from naïve, arthritic and adenovirus-treated ankle and/or knee joints was examined. Human RA synovium was examined for gene expression. Human monocyte-derived macrophages were treated with recombinant TGF-β1.

Results: When examining naïve murine joints, synovial cells of the ankle joints were AXL positive, but knee joints of the same mice were not, indicating a profound difference between these two weight-bearing joints. To examine whether AXL played a protective role during arthritis, we induced arthritis in Axl⁻/⁻ and WT mice. The ankle joints of Axl⁻/⁻ mice showed an increased macroscopic disease...
score during arthritis development (p<0.001 at day 7). In agreement with this, histology of ankle joints showed significantly increased arthritis pathology in Axl−/− mice. No effect of Axl gene deletion was observed on gonarthritis pathology and the synovial expression of inflammatory genes. To unravel the cause for the noteworthy difference in AXL expression between knee and ankle, we investigated the role of TGF-β, a factor known to induce AXL. As hypothesized, Tgfβ1 expression was significantly higher in synovium of ankle compared to synovium of knee joints in naïve mice (p<0.01), which correlated with Axl expression (Pearson r=0.8860, p=0.0012). In addition, adenoviral overexpression of TGFβ1 induced AXL expression in synovium of knee joints (p<0.05), a tissue devoid of AXL during homeostasis. The TGF-β1-induced AXL expression appeared to be conserved in humans. We observed a correlation between TGFβ1 and AXL expression in human RA synovium (Pearson r=0.7233, p=0.0035) and TGF-β1 stimulation enhanced the expression of AXL in human macrophages (p<0.01).

Conclusion: Our study shows remarkable differences in synovial AXL expression between ankle and knee joints and this is in accordance with the observation that AXL dampens arthritis in ankle but not in knee joints. We provide evidence that these local differences in AXL are due to TGF-β1. It is tempting to speculate that the differences in AXL expression and its innate immune protective effector role could explain the lower arthritis incidence in ankle joints compared to other weight-baring joints in humans (reviewed in DiStefano and Pinney. Semin Arthro. 2010).

Disclosure: C. E. J. Waterborg, None; M. G. A. Broeren, None; E. N. Blaney Davidson, None; M. I. Koenders, None; P. L. van Lent, None; P. M. van der Kraan, Contract research UCB, 2; F. A. J. van de Loo, None.


Abstract Number: 1077

The Lectin Pathway of the Complement System Is Activated in Patients with Systemic Lupus Erythematosus

Anne Troldborg1,2, Steffen Thiel3, Marten Trendelenburg4, Justa Friebus-Kardash5, Josephine Nehring5, Rudi Steffensen6, Søren Werner Karlakov Hansen7, Magdalena Janina Laska1, Bent Deleuran8, Jens Christian Jensenius1, Anne Voss9 and Kristian Stengaard-Pedersen10, 1Biomedicine, Aarhus University, Aarhus, Denmark, 2clinical medicine, Aarhus University, Aarhus, Denmark, 3Institute of Biomedicine, Aarhus University, Aarhus, DK, Aarhus, Denmark, 4Department of Biomedicine, Division of Internal Medicine, Basel, Switzerland, 5University Hospital Basel, Division of Internal Medicine, Basel, Switzerland, 6Department of Clinical Immunology, Aalborg University Hospital, Aalborg, Denmark, 7Department of Cancer and Inflammation Research, University of Souther Denmark, Odense, Denmark, 8Department of Biomedicine, Aarhus University, Aarhus, Denmark, 9Rheumatology, Odense University Hospital, Odense, Denmark, 10Department of Clinical Medicine, Aarhus University Hospital, Aarhus, Denmark

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Innate Immunity and Rheumatic Disease Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

The pathogenesis of Systemic Lupus Erythematosus (SLE) involves complement activation. It is well established that activation of complement through the classical pathway (CP) and deficiencies of this pathway are associated with SLE. Our knowledge about the Lectin Pathway (LP) of complement activation in relation to SLE is very limited. Since the LP is also activated through pattern recognition of, i.e., intracellular components and apoptotic cells, we hypothesize that this pathway is also activated in SLE and could have similar implications as the CP in the development of SLE.

Methods:

We examined the 11 known LP proteins in a large well-defined SLE cohort of 372 SLE patients and 170 controls. We estimated LP protein concentrations using in house developed time resolved immuno-fluorometric assays (TRIFMA). We assessed if changes in concentrations were associated with complement activation and disease activity based on C3 measurements. To follow the protein concentrations over time in relation to disease activity, a cohort of 52 SLE patients followed for five years with repeated blood samples were additionally included.
Results:

Concentrations of the LP proteins were altered in a specific pattern in this cross sectional SLE cohort compared with the controls. The differences in LP proteins observed between patients and controls were associated with complement activation and disease activity based on C3 measurements and SLEDAI. M-ficolin, CL-L1, CL-K1, MASP-3 and MAp19 showed a significant negative correlation with disease activity. When followed over time the concentrations of several LP proteins correlated with SLEDAI and particularly the serine protease, MASP-2, increased with SLE disease activity.

Conclusion:

In this large SLE cohort, specific changes in LP proteins were associated with complement activation and disease activity, indicating that the LP is activated in patients with SLE. These novel findings substantiate the involvement of the LP of complement activation in the complex pathogenesis of SLE.

Disclosure: A. Troldborg, None; S. Thiel, None; M. Trendelenburg, None; J. Friebus-Kardash, None; J. Nehring, None; R. Steffensen, None; S. W. Karlskov Hansen, None; M. J. Laska, None; B. Deleuran, Otezla, 2; J. C. Jørgensen, None; A. Voss, None; K. Stengaard-Pedersen, None.

Abstract Number: 1078

Initial Combination Therapy Versus Step-up Therapy Is More Effective and Less Costly As a Treat to Target Strategy for RA: A Markov Model Based upon the Dutch Rheumatoid Arthritis Monitoring Registry Cohorts

Celine J. van de Laar1, Laura M.M. Steunebrink2, Martijn A.H. Oude Voshaar3 and Harald E. Vonkeman4, 1Transparency in Healthcare B.V., Hengelo, Netherlands, 2Medisch Spectrum Twente - Arthritis Center Twente, Enschede, Netherlands, 3University of Twente, Department of Psychology, Health and Technology, Enschede, Netherlands, 4koningsplein, Medisch Spectrum Twente - Arthritis Center Twente, Enschede, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Adjusting medication of patients with rheumatoid arthritis (RA) until predefined disease activity targets are met, i.e. Treat to Target (T2T), is the currently recommended treatment approach. However, not much is known about long-term cost-effectiveness of different T2T strategies.

We model the 5-years costs and effects of a step-up approach (MTX mono -> MTX + csDMARD combination -> Adalimumab -> second anti-TNF-α) and an initial combination therapy approach (MTX + csDMARD + prednisone if needed -> MTX + csDMARD high dose -> anti-TNF-α’s) from the healthcare and societal perspectives, by adapting a previously validated Markov model.

Methods:

We constructed a Markov model in which 3-monthly transitions between DAS28-defined health states of remission (≤2.6), low (2.6<DAS28≤3.2), moderate (3.2<DAS28≤5.1), and high disease activity (DAS28>5.1) were simulated. Hypothetical patients proceeded to subsequent treatments in case of non-remission at each (3-month) cycle start. In case of remission for two consecutive cycles medication was tapered, until medication-free remission was achieved. Transition probabilities for individual treatment steps were estimated using data of Dutch Rheumatology Monitoring registry Remission Induction Cohort I (step-up) and II (initial combination). Expected costs, utility, and the ICER after 5 years were compared between the two strategies. To account for parameter uncertainty, probabilistic sensitivity analysis was employed through Beta, Normal, and Dirichlet distributions. All utilities, costs, and transition probabilities were replaced by fitted distributions.
Results:

Over a 5-year timespan, initial combination therapy was less costly and more effective than step-up therapy. Initial combination therapy accrued €16226.3 and 3.552 QALY vs €20183.3 and 3.517 QALYs for step-up therapy. This resulted in a negative ICER, indicating that initial combination therapy was both less costly and more effective in terms of utility gained. This can be explained by higher (±5%) remission percentages in initial combination strategy at all time points. More patients in remission means less healthcare and productivity loss costs and more accumulated utility. Additionally, higher remission percentages caused less bDMARD use in the initial combination strategy, again lowering overall costs.

Conclusion:

Initial combination therapy was found to be favourable over step-up therapy in the treatment of Rheumatoid Arthritis, when considering cost-effectiveness. Initial combination therapy resulted in more utility at a lower cost over 5 years.

Figure 1: Cost-effectiveness plane comparing initial combination and step-up therapy


Disclosure: C. J. van de Laar, None; L. M. M. Steunebrink, None; M. A. H. Oude Voshaar, None; H. E. Vonkeman, None.


Abstract Number: 1079

Treat to Target Adherence Measurement Tool Performance in Rheumatoid Arthritis

Rodrigo Garcia Salinas1, Sebastian Magri2 and Facundo Salvatori3, 1Section of Rheumatology, Hospital Italiano de La Plata, Buenos Aires, Argentina, La Plata, Argentina, 2Section of Rheumatology, Hospital Italiano de La Plata, La Plata, Argentina, 3Rheumatology, Hospital Italiano de La Plata, La Plata, Argentina

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM
Background/Purpose: The purpose of the T2T approach in RA is to achieve remission or LDA according to results from objective activity measurements. This strategy has proven clinical benefits, however objective adherence T2T measurement tools are lacked in daily practice. Objectives: To evaluate the setting, usage of a T2T adherence measure: T2T70 and T2T100, and its association with sustained low disease activity (LDAS) as a measure of outcome.

Methods: Prospective study, consecutive patients with RA diagnosis (ACR / EULAR 2010) and follow-up between 1 and 24 months were included. Data from electronic medical record (EHR) were collected. Demographic variables, characteristics of the disease and treatment were recorded. The following T2T characteristics were defined and collected from each patient: number of visits, visits where treatment was adjusted, CDAI measurements, use of ultrasound to measure disease activity and achievement of LDA. Sustained LDA (LDAS) was defined when the patient had 2 or more records of that consecutive state of activity. Measures of adherence to T2T were defined as follows: T2T-70, when therapeutic decisions were accompanied by the measurement of activity by 70% and the interval between visits did not exceed 6 months; And T2T-100, when 100% of the decisions were accompanied with the activity measurement and the interval between each visit did not exceed 6 months. Statistical analysis: a descriptive analysis of the variables was performed and Chi2 test (categorical) and Student or MannWhitney test (continuous) were applied. For multivariate logistic regression analysis we considered as dependent variable LDAs.

Results: 96 patients were included, with a mean follow-up of 15 months (DS 7.8), equivalent to 120.6 patients / year. Eighty percent of the patients were women, mean age 53.7 years (SD 13), disease duration 36 months (RIC, 12-52), 64% had early diagnosis, 85% and 75% positive For FR and ACPA, respectively. According to T2T characteristics, 526 visits were recorded, 270 were treatment adjustment and 208 (78%) of them were performed according to the CDAI value. The frequency of LDAS was 20% (IC95: 12-30). The frequency of T2T-70 compliance was 62.5% (IC95: 52-72) and T2T-100 was 42% (IC95: 32-52). Compliance with T2T-70 and T2T-100 presented a statistically significant association to the achievement of LDAS in the uni and multivariate analysis (p: 0.000). Compliance with T2T-70 and T2T-100 was associated with a shorter time course of disease; And T2T-70 also showed association with early diagnosis.

Conclusion: T2T-70 and T2T-100 adherence were 62% and 42%, respectively, patients who met these criteria reached more LDAS. The early diagnosis and shorter time to disease evolution at baseline were variables that were associated with more compliance of these tools.

Disclosure: R. Garcia Salinas, None; S. Magri, None; F. Salvatori, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/treat-to-target-adherence-measurement-tool-performance-in-rheumatoid-arthritis

Abstract Number: 1080

Electronic Patient Reported Outcomes Increase Pediatric Rheumatology Clinic Operations Efficiency While Increasing Patient and Caregiver Satisfaction

Y. Ingrid Goh1, Talia Goldberg2, Nicholas Lao3 and Brian M. Feldman4, 1Child Health Evalutative Sciences, The Hospital for Sick Children, Toronto, ON, Canada, 2University of Toronto, Toronto, ON, Canada, 3University of Western Ontario, London, ON, Canada, 4Rheumatology, The Hospital for Sick Children, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Electronic Patient Reported Outcomes Increase Pediatric Rheumatology Clinic Operations Efficiency While Increasing Patient and Caregiver Satisfaction

Background/Purpose: Patient reported outcomes (PROs) are powerful tools that facilitate communication between patients and their healthcare team. In paper format, PROs may be incomplete, misplaced and incorrectly scored. Electronic version (e-form) of PROs may reduce the occurrence of these issues. As more healthcare institutions move toward electronic medical systems, it is important to assess its impact on healthcare. Not only is the system impact important, it is imperative to assess patients’ and caregivers’ perspective on these changes. The objectives of this study were to a) determine whether the e-form could improve efficiency; b) assess user satisfaction with the e-form; and c) identify additional improvements to the e-form.
**Methods:** An e-form of the Childhood Health Assessment Questionnaire (CHAQ) and the Quality of My Life (QoML) questionnaire was created in REDCap. Patients/caregivers attending the rheumatology clinic at The Hospital for Sick Children were asked to participate in this quality improvement study by completing both paper and e-form of the PROs (the order of which was determined by a table of random numbers). They were then asked to complete a satisfaction survey which asked them about their experience and for suggestions on how to improve the e-form. Changes in efficiency were compared by noting the time differences between both forms as well as calculating the annual differences in cost. Prior to comparing the times, 2.5 minutes were added to the paper form times to account for scoring and data entry times. Survey results were analysed using descriptive statistics and thematic identification.

**Results:** 197/209 participants completed both forms. The median times to complete the paper forms were longer than completing the e-forms (Table 1). This was more significant when paper forms were completed prior to e-forms.

The Division’s costs for photocopying paper forms amounts to ~ $1000/year, whereas the REDCap database cost ~$300 to build and does not require any additional maintenance funding. Therefore, an e-form results in significant cost savings.

191/209 participants completed the satisfaction survey. 64% (122/191) respondents indicated that they preferred the e-form over the paper form.

Suggestions for improvements included improving the sliding scale mechanism and increasing the text size.

**Conclusion:** Implementation of an e-form resulted in greater efficiency—it was faster and saved money. Patients also liked it better. The e-form should be modified to reflect participants’ suggestions and these modifications should be subsequently assessed.

**Table 1. Time to complete paper vs. electronic form**

<table>
<thead>
<tr>
<th></th>
<th>Randomized to Paper then Electronic Form</th>
<th>Randomized to Electronic then Paper Form</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>New Patient</td>
<td>Follow-Up Patient</td>
</tr>
<tr>
<td>N</td>
<td>17</td>
<td>86</td>
</tr>
<tr>
<td>Median time to complete paper form (mm:ss)</td>
<td>6:17</td>
<td>3:45</td>
</tr>
<tr>
<td>Median total time for paper form completion, scoring and data entry (mm:ss)</td>
<td>8:47</td>
<td>6:15</td>
</tr>
<tr>
<td>Median time to complete electronic form (mm:ss)</td>
<td>3:50</td>
<td>4:10</td>
</tr>
<tr>
<td>P</td>
<td>0.0005</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

**Disclosure:** Y. I. Goh, None; T. Goldberg, None; N. Lao, None; B. M. Feldman, None.

**Abstract Number:** 1081

**Improving Patient-Reported Outcomes Collection and Documentation for Patients with Rheumatoid Arthritis at Multilingual, Safety Net Hospital Rheumatology Clinic**

**Todd Liou**¹, Omotoke Odimayomi¹, Laura Trupin², Jinoos Yazdany² and Mary Margaretten³, ¹University of California San Francisco, San Francisco, CA, ²Medicine/Rheumatology, University of California San Francisco, San Francisco, CA, ³Medicine, University of California San Francisco, San Francisco, CA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Measures and Measurement of Healthcare Quality Poster I

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The Patient-Reported Outcomes Measurement Information System (PROMIS) Physical Function-10a (PF10a) survey is a reliable and valid measure of function in patients with rheumatoid arthritis (RA). National quality measures recommend that
patient-reported outcomes such as PROMIS PF10a be collected regularly in routine care. However, safety net health systems may face barriers in implementing PRO collection, including patients with low health literacy and limited English-language proficiency. Our objective was to increase collection and documentation of the PROMIS PF10a from 0% to 50% for all adult RA patient visits in our diverse, safety net clinic during a 9 month period.

**Methods:** We used the Institute for Healthcare Improvement’s Model for Improvement and Plan-Do-Study-Act (PDSA) methodology over 4 cycles. In cycle 1, PF10a surveys were administered to English-speaking patients, after vitals were taken. Staff offered to read the survey to all patients, an approach commonly used to ensure patients with low health literacy feel comfortable participating. Cycle 2 separated the process of collecting PROMIS PF10a scores into two steps: (1) administering the survey throughout clinic workflow rather than only after vitals were taken and (2) uploading the score into the electronic health record (EHR), which were delegated to a high school research volunteer and medical assistants. Cycle 3 created a folder for the volunteer and medical student team to communicate and track weekly progress. In the final PDSA cycle, the forms were administered to Spanish-speaking patients by language concordant staff.

**Results:** Our rheumatology clinic has approximately 96 RA encounters per month and 70% of the patient population speaks languages other than English (the majority speaking Cantonese or Spanish). The quality improvement project began in the fall of 2016 and PROMIS PF10a score collection percentage was 12.5% after the first PDSA cycle. During the second cycle, the proportion of visits with a completed PROMIS PF10a rose to 22.2%. After the 4th PDSA cycle, there was a sustained improvement over 6 months, with 35.5% of RA patient visits having the PROMIS PF10a collected and recorded in the EHR (Figure).

**Conclusion:** Using an interprofessional team approach and the Model for Improvement, we significantly improved collection and documentation of the PROMIS PF10a measure in a multilingual safety net rheumatology clinic. Although we fell short of our goal of 50% of our RA patient visits, we were able to record the PROMIS PF10a measure for 48.6% of the 212 individual patients seen throughout the course of our project. Efforts are ongoing to expand collection to further engage our clinic staff and volunteers to create a sustainable PRO collection workflow.

![Figure](PROMIS Run Chart (Nov 2016 - Mar 2017). 1-4 correspond to PDSA cycles. A is when research intern was absent due to a 3-week vacation.)

**Disclosure:** T. Liou, None; O. Odimayomi, None; L. Trupin, None; J. Yazdany, None; M. Margaretten, None.

**Abstract Number:** 1082

**Responsiveness and Minimally Clinically Important Differences of Promis Measures in Rheumatoid Arthritis**

Susan J. Bartlett¹, Michelle Jones² and Clifton O. Bingham III³, ¹Department of Medicine, Division of ClinEpi, Rheumatology, Respirology, McGill University, Montreal, QC, Canada, ²Johns Hopkins University School of Medicine, Baltimore, MD, ³Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017
Responsiveness and Minimally Clinically Important Differences of PROMIS Measures in Rheumatoid Arthritis

Background/Purpose: The ability to detect meaningful change in clinical status (responsiveness) is an important aspect of validity. Minimally clinically important difference (MCID) is a patient-centered construct reflecting the smallest difference of value to patients. PROMIS is a generic family of measures developed for use across chronic diseases. We examined the responsiveness and estimated MCIDs of selected PROMIS measures reflecting domains that people with RA have identified.

Methods: Data are from the first two visits of an observational trial in Baltimore, MD. Patients completed PROMIS Physical Function (PF), Pain Interference (PI), Participation Ability (PA), and Fatigue computer adapted tests and other patient-reported outcomes (PROs) using a tablet. At the second visit, patients also completed a 5-point item assessing change in RA status from the previous visit (much worse to much better) and the self-reported health rating. Descriptive statistics were calculated, and ANOVA was used to identify significant differences in scores on 9 PROMIS measures.

Results: The 196 RA patients who completed outcomes at clinical visits approximately 4 months apart were mostly female (81%), white (82%) with a mean age of 55 (13). All met ACR 1987 or 2010 criteria for RA. One-third reported the same health status at both visits (68 [35%]); 13% were a little better; a similar number were much better; 27% were a little worse, and 7% were much worse. Correlations between PROMIS and other measures assessing similar domains ranged from 0.32 to 0.83. Among patients reporting being “much worse”, PROMIS scores worsened from 1.0 to 8.1 points (mean CDAI change 9.2)(Table). Among patients feeling much better, PROMIS scores improved from 1.6 to 6.9 points (mean CDAI change -6.6). Change in PROMIS scores were largest in relation to changing disease activity for symptoms highly relevant to RA (e.g., PI, fatigue, PF); notably patients with worsening in RA did not report higher anxiety or depression scores.

Conclusion: These initial data suggest PROMIS measures are responsive to clinical changes in RA status and contribute to the growing literature supporting the use of PROMIS measures to assess physical, social, emotional and health in people with RA.

Disclosure: S. J. Bartlett, None; M. Jones, None; C. O. Bingham III, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/responsiveness-and-minimally-clinically-important-differences-of-promis-measures-in-rheumatoid-arthritis

Abstract Number: 1083

Rheumatoid Arthritis Patients Achieved Better Quality of Life Than Systemic Lupus Erythematosus Patients at Sustained Remission: The Impact of Disease Diagnosis on Health-Related Quality of Life Outcomes

Virginia Pascual-Ramos1, Irazú Contreras-Yáñez2, Katya Valencia-Quíñones3 and Juanita Romero-Diaz4, 1Department of Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, 2Inmunología y Reumatología, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, 3Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, 4Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico city, Mexico
Background/Purpose: Patients with Systemic Lupus Erythematosus (SLE) and Rheumatoid Arthritis (RA) had profound negative effects on their health-related quality of life (HRQoL) that can be assessed using the 36 item Medical Outcome Study Short-Form survey (SF-36). Remission might have a different impact on patient’s HRQoL depending on the specific disease diagnosis.

In 2004 and 1999, respectively, recent-onset rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) cohorts were initiated; the 36 item Medical Outcome Study Short-Form survey (SF-36) was incorporated to routine assessments from 2005 onwards in the SLE cohort and the SF-36v2 beginning from enrollment in the RA cohort. Objectives of the study were to compare the SF-36v2 scores between patients from both cohorts who achieved sustained remission (SR) and to define the role of disease diagnosis as associated to SF-36v2 normative data.

Methods: SLE and RA were diagnosed based on corresponding ACR classification criteria. Routine assessments were performed every 2-6 months and included at least the SLE disease activity index 2000 update (SLEDAI-2K) for SLE patients, and the Disease Activity Score (28 joints) (DAS28) for RA patients.

SR was considered when RA and SLE patients achieved at least 12 months of continuous follow-up with either SLEDAI-2K=0 or DAS28 ≤2.4, respectively. Up to December 2015, data from 172 RA patients and 211 SLE patients respectively, were reviewed.

SF-36v2 scores were available for the totality of SR assessments. The SF-36v2 licensee performed the re-scoring of the SF-36 that was used in the SLE cohort. In all the cases, Spanish (for México) versions were used and scoring was adjusted by gender and age. Logistic regression models were used to investigate factors associated with normative SF-36v2. Written informed consent was obtained from all patients.

Results: A higher proportion of RA patients achieved SR: 106 (58%) RA patients vs. 75 (30.6%) SLE patients, p≤0.001. SR was achieved earlier in patients from the former group: (mean±SD) follow-up was 30.8±23.9 months vs. 59.4±37.5 months in SLE patients, p≤0.001. The length of time in SR and the number of patients who had a disease flare were similar in both cohorts.

At baseline, RA patients scored significantly lower all the domains of the SF-36v2 and both the mental and physical summary measures, than SLE patients. At SR, RA patients scored better than SLE patients in 6 out of 8 domains of the SF-36v2 and the physical health component summary (Figure).

Age (β: 1.06, 95% CI: 1.02-1.1, p=0.03) and SLE diagnosis (β: 9.64, 95% CI: 3.61-25.75, p≤0.001) were predictors of not achieving normative physical component summary measure.

Conclusion: Patient’s perspective of (absence of) disease activity represents an important aspect of the assessment of rheumatic diseases. RA patients in SR achieved better quality of life than SLE patients.

Figure.
Emdhaq: (electronic multidimensional health assessment questionnaire) to Record and Document eRAPID3 (electronic routine assessment of patient index data3) and eFAST3 (electronic fibromyalgia assessment screening tool3) in Routine Rheumatology Care

Theodore Pincus1, Jacquelin R. Chua2, Shakeel M. Jamal2, Nathaniel Cook3, Niels Steen Krogh4, Anne-Marie Malfait1 and Joel A. Block2, 1Rheumatology, Rush University Medical Center, Chicago, IL, 2Division of Rheumatology, Rush University Medical Center, Chicago, IL, 3Infectious Disease, Rush University Medical Center, Chicago, IL, 4ZiteLab ApS, Copenhagen, Denmark

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: RAPID3 (routine assessment of patient index data) on a multi-dimensional health assessment questionnaire (MDHAQ) distinguishes active from control treatments in RA clinical trials as effectively as disease activity score 28 (DAS28) or clinical disease activity index (CDAI), and is informative to monitor patients with osteoarthritis, spondyloarthropathies, vasculitis, gout, etc. (1). Therefore, many versions of an electronic RAPID3 (eRAPID3) have been developed, although generally mutually incompatible, mimicking electronic medical records (EMRs), and not easily merged into an EMR or into multicenter databases to study patient outcomes (2). More recently, another index of MDHAQ scores, FAST3 (fibromyalgia assessment screening tool3), has been described, which agrees >80% with ACR fibromyalgia (FM) criteria to identify FM (3). Here, we assess eFAST3 and eRAPID3 on an eMDHAQ to recognize possible secondary FM in patients with osteoarthritis (OA) or rheumatoid arthritis (RA).

Methods: A patient- and doctor-friendly eMDHAQ meets HIPAA, privacy and security requirements, and is designed to interface with any EMR, using FHIR (Fast Healthcare Interoperability Resources) for integration and interoperability, although requiring collaboration with the EMR vendor, and to be merged easily into common collaborative research databases. eRAPID3 on an eMDHAQ is a 0-30 sum of a 0-10 physical function (FN) scale and two 0-10 visual analog scales (VAS) for pain (PN) and global assessment (PATGL). eFAST3 on eMDHAQ is a 0-3 scale; 1 point is assigned if PN ≥6/10, RADAI painful joint count ≥16/48, and MDHAQ symptom checklist ≥16/60; FAST3≥2 is clue to FM (3). eRAPID3 and eFAST3 were compared in 89 osteoarthritis (OA) vs 91 rheumatoid arthritis (RA) patients, using STATA to compute means and cross-tabulations.

Results: Mean eRAPID3 scores were 14.9 in OA vs 11.1 in RA patients. eRAPID3 was >12 (high severity) in 59 OA (66%) and 39 RA (43%) patients. eFAST3 ≥2, suggesting secondary FM, was seen in 21 of the 59 OA patients (24% of all OA patients) and 17 of the 39 RA patients (19% of all RA patients) with RAPID3>12 (Table). No patient with RAPID3 <12 had eFAST3 ≥2, suggesting a good screen for the absence of FM. Most patients with RAPID3>12 also had FAST3 <2 (Table), suggesting limited specificity of RAPID3 for FM.

Number of patients with OA or RA according to eRAPID3 vs eFAST3 on eMDHAQ.

(%) are of all OA or RA patients
### Table 1

<table>
<thead>
<tr>
<th>OA n=89</th>
<th>RAPID3 Remission=0-3</th>
<th>RAPID3 Low severity=3.1-6</th>
<th>RAPID3 Moderate severity=6.1-12</th>
<th>RAPID3 High severity&gt;12</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAST3=0</td>
<td>2 (2%)</td>
<td>6 (7%)</td>
<td>14 (16%)</td>
<td>8 (9%)</td>
<td>30 (34%)</td>
</tr>
<tr>
<td>FAST3=1</td>
<td>0</td>
<td>0</td>
<td>8 (9%)</td>
<td>30 (34%)</td>
<td>38 (43%)</td>
</tr>
<tr>
<td>FAST3=2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>13 (15%)</td>
<td>13 (5%)</td>
</tr>
<tr>
<td>FAST3=3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>8 (9%)</td>
<td>8 (9%)</td>
</tr>
<tr>
<td>Total</td>
<td>2 (2%)</td>
<td>6 (7%)</td>
<td>22 (25%)</td>
<td>59 (66%)</td>
<td>89</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>RA n= 91</th>
<th>Remission</th>
<th>Low severity</th>
<th>Moderate severity</th>
<th>High severity</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAST3=0</td>
<td>15 (16%)</td>
<td>20 (22%)</td>
<td>11 (12%)</td>
<td>2 (2%)</td>
<td>48 (53%)</td>
</tr>
<tr>
<td>FAST3=1</td>
<td>0</td>
<td>0</td>
<td>6 (7%)</td>
<td>20 (22%)</td>
<td>26 (29%)</td>
</tr>
<tr>
<td>FAST3=2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>10 (11%)</td>
<td>10 (11%)</td>
</tr>
<tr>
<td>FAST3=3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>7 (8%)</td>
<td>7 (8%)</td>
</tr>
<tr>
<td>Total</td>
<td>15 (16%)</td>
<td>20 (22%)</td>
<td>17 (19%)</td>
<td>39 (43%)</td>
<td>91</td>
</tr>
</tbody>
</table>

**Conclusion:** An eMDHAQ offers reports of eRAPID3 and eFAST3 for improved clinical decisions, doctor-patient communication, and documentation. Further development of the eMDHAQ, eRAPID3, and eFAST3, and interface to the EMR, are needed for optimal value. Rheumatologists and organizations are encouraged to implement an electronic MDHAQ, rather than simply an electronic RAPID3.

**References:**

**Disclosure:** T. Pincus, Theodore Pincus, 7; J. R. Chua, None; S. M. Jamal, None; N. Cook, None; N. S. Krogh, None; A. M. Malfait, Galapagos, Regeneron, Ferring, 5; J. A. Block, None.

**Abstract Number:** 1085

**Application of Lupus Nephritis Quality Measures to Understand Gaps in Care for SLE**

Lisa Gaynon¹, Maria Dall'Era², Patricia P. Katz², Lindsey A. Criswell², Cristina Lanata², Laura Trupin³, Charles G. Helmick⁴ and Jinoos Yazdany³, ¹Internal Medicine, California Pacific Medical Center, San Francisco, CA, ²Medicine/Rheumatology, University of California, San Francisco, San Francisco, CA, ³Medicine/Rheumatology, University of California San Francisco, San Francisco, CA, ⁴Centers for Disease Control and Prevention, Atlanta, GA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Measures and Measurement of Healthcare Quality Poster I

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** In 2012, the ACR released guidelines for monitoring and treatment of lupus nephritis (LN), but studies have yet to evaluate adherence to these recommendations. Using measures from the SLE Quality Indicators Project (Yazdany, et al., 2009) and
new measures derived from ACR guidelines, we evaluated quality of care for LN among patients enrolled in the California Lupus Epidemiology Study (CLUES), a multi-ethnic, population-based cohort study.

**Methods:** We reviewed charts of CLUES patients to evaluate performance on quality measures (N=116 of 281 enrolled in the study to date). Patients were followed either in tertiary academic centers or by community rheumatologists in the study catchment area. Seven quality measures were assessed. For those without LN, we evaluated whether recommended screening processes were completed in the year preceding study enrollment (2014-2016) (urinalysis, urine protein: creatinine ratio and serum creatinine checked every 6 months; C3/C4 and anti-dsDNA levels every 6 months; and blood pressure checked every 3 months). For those with prevalent LN, we looked to see if patients had a renal biopsy at the time of diagnosis, received an immunosuppressant within 30 days of LN diagnosis, and were started on an ACEi/ARB and anti-malarial therapy within 1 year. "Pass rates" (% eligible patients receiving recommended care) for these measures were analyzed for the entire group and compared for tertiary vs community treatment settings using chi-squared tests.

**Results:** Among the 116 patients, 55 had a diagnosis of LN. 75 were followed in tertiary care settings and 41 by community rheumatologists. For patients with no history of LN, 40% had recommended screening of urine and renal function every 6 months, and 45% had screening for immunological activity every 6 months (Table). Adherence to blood pressure checks every 3 months was better (74%). For patients with LN, most patients (87%) had renal biopsies for diagnostic confirmation and 82% were started on an immunosuppressant within 1 month of diagnosis. 80% were placed on an anti-malarial and 68% on a renal protective antihypertensive (ACEi or ARB) within 1 year of diagnosis. We found no differences between community and tertiary care settings in measures assessing the diagnosis and treatment of LN. However, performance on measures examining screening of urine, renal function, immunological activity, and BP for patients with no history of LN was lower among community rheumatologists (see Table).

**Conclusion:** We found relatively high performance on quality measures regarding LN diagnosis and treatment, with no differences between community and tertiary care settings. For patients with no history of LN, we found that screening for renal disease was performed less in community settings. Next steps include reviewing additional records from CLUES and validating our chart review procedures across health care settings.

| Table 1: Quality Measure Pass Rates for the Screening and Treatment of Lupus Nephritis |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
|                                 | With No History of LN (n=61)    |                                 | With LN (n=55)                  |                                 |                                 |                                 |
|                                 | Q1: UA, Urine Protein:Creatinine ratio, Serum Creatinine q6m | Q2: C3/C4, anti-dsDNA q6m | Q3: Blood pressure check q3m | Q4: Renal biopsy done | Q5: Immunosuppression within 1m | Q6: Anti-malarial within 1y | Q7: ACEi/ARB within 1y |
| Academic Clinic (n=36)          | 66.7%                          | 55.6%                          | 86.1%                          | 89.7%                          | 80.0%                          | 84.8%                          | 70.3%                          |
| Community Clinic (n=25)         | 0.0%                           | 29.2%                          | 56.0%                          | 77.8%                          | 85.7%                          | 66.7%                          | 55.6%                          |
| *P*-value                       | <0.01                          | <0.05                          | <0.01                          | 0.357                          | 0.641                          | 0.177                          | 0.398                          |
| Total                           | 40.0%                          | 45.0%                          | 73.8%                          | 86.8%                          | 81.6%                          | 80.0%                          | 67.4%                          |

**Disclosure:** L. Gaynon, None; M. Dall’Era, None; P. P. Katz, Bristol-Myers Squibb, 2; L. A. Criswell, None; C. Lanata, None; L. Trupin, None; C. G. Helmick, None; J. Yazdany, None.
Screening and Intervention of Depression in Rheumatoid Arthritis and Systemic Lupus Erythematosus

Rui Zhang1, Priya Prakash2, Amy Wasserman3, Kirk Sperber4 and Julia Ash5, 1Medicine -Rheumatology, New York Medical College / Westchester Medical Center, Valhalla, NY, 2Rheumatology, NYMC /WMC, Valhalla, NY, 3Medicine - Rheumatology, New York Medical College / Westchester Medical Center, Valhalla, NY, 4New York Medical College / Westchester Medical Center, Valhalla, NY, 5Medicine -Rheumatology, New York Medical College / Westchester Medical Center, Valhalla, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Depression is common and associated with worse outcomes among patients with RA and SLE. Our study assessed depression using Patient Help Questionnaire (PHQ-9) and its correlation with disease activity. We also examined the outcome of intervention on depression score.

Methods: This is a single center cross-sectional study of mainly uninsured patients with RA and SLE in Rheumatology clinic. PHQ-9 scores were collected at each clinic visit. Physicians assessed corresponding disease activity using Clinical Disease Activity Index (CDAI) or SLEDAI. Patients with at least moderate depression (PHQ-9 ≥10) were offered depression intervention, counseling or medications. PHQ-9 was re-administered after intervention.

Results: 45 RA patients with a mean age of 50 years (±12) and 16 SLE patients with a mean age of 42 years (±11) were screened. In RA group 82% were females with average disease duration of 7 (±6) years. In SLE group 94% were females with average disease duration of 8 (±7) years. Depression was diagnosed in 51% of RA patients: 29% mild, 13% moderate and 9% moderately severe (Table 1). Severity of depression positively correlated with disease activity in RA patients (Figure 1, Pearson R=0.636, p <0.001). In contrast, depression was diagnosed in 25% of SLE patients: 12.5% mild and 12.5% moderate and did not correlate with disease activity (Pearson R=0.209). RA patients with moderate/high CDAI had significantly higher PHQ-9 than those with low CDAI (7.7 vs 1.5, p<0.001; 9.6 vs 1.5 p<0.001, t-test). Of 12 patients who met criteria for depression intervention (Table 2), 33% were treated, 33% are pending treatment and 33% declined. With intervention, 2 patients had improved PHQ-9 scores, 1 patient's score worsened confounded by cancer surgery, and 1 patient had no change in score.

Conclusion: Our study shows higher prevalence of depression in RA (51%) and SLE (25%) than in general population (7-12%). Correlation between disease activity and depression score is only found in RA. Depression intervention resulted in PHQ-9 improvement in some patients, supporting the benefit of depression screening and treatment in rheumatology practice.

Figure 1: Correlation between severity of depression and disease activity score in RA

<table>
<thead>
<tr>
<th>Disease Activity</th>
<th>Severity of Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA (CDAI)</td>
<td>Minimal</td>
</tr>
<tr>
<td>Remission (&lt;2.8)</td>
<td>0%</td>
</tr>
<tr>
<td>Low (2.9-10.0)</td>
<td>48.0%</td>
</tr>
<tr>
<td>Moderate (10.1-22.0)</td>
<td>12.5%</td>
</tr>
<tr>
<td>High (22.1-76.0)</td>
<td>7.3%</td>
</tr>
<tr>
<td>SLE (SLEDAI)</td>
<td>Minimal</td>
</tr>
<tr>
<td>Remission (&lt;3)</td>
<td>76.9%</td>
</tr>
<tr>
<td>Mild/Moderate Flare (3-12)</td>
<td>66.7%</td>
</tr>
</tbody>
</table>

Table 1: Prevalence of depression and disease activity in RA and SLE

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Depression Initial Screen (PHQ-9)</th>
<th>Depression Intervention</th>
<th>Post-Intervention (PHQ-9)</th>
<th>Comorbid</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA_01</td>
<td>Moderate (11)</td>
<td>None</td>
<td>Improved (6)</td>
<td>None</td>
</tr>
<tr>
<td>RA_02</td>
<td>Moderate (13)</td>
<td>Yes/ Antidepressant</td>
<td>Withdrawn (16)</td>
<td>Breast cancer</td>
</tr>
<tr>
<td>RA_03</td>
<td>Moderate (10)</td>
<td>Yes/ Counseling</td>
<td>Improved (6)</td>
<td>Hepatitis (under treatment)</td>
</tr>
<tr>
<td>RA_04</td>
<td>Mild/Severe (15)</td>
<td>None</td>
<td>Improved (6)</td>
<td>None</td>
</tr>
<tr>
<td>RA_05</td>
<td>Mild/Severe (19)</td>
<td>None</td>
<td>Pending</td>
<td>None</td>
</tr>
<tr>
<td>RA_06</td>
<td>Moderate (12)</td>
<td>Pending</td>
<td>Pending</td>
<td>DMII, CKD</td>
</tr>
<tr>
<td>RA_07</td>
<td>Mild/Severe (19)</td>
<td>Yes/ Antidepressant</td>
<td>Unchanged (19)</td>
<td>Depression</td>
</tr>
<tr>
<td>RA_08</td>
<td>Moderate (12)</td>
<td>Yes/ Antidepressant</td>
<td>Improved (8)</td>
<td>DMII</td>
</tr>
<tr>
<td>RA_09</td>
<td>Mild/Severe (16)</td>
<td>Pending</td>
<td>Pending</td>
<td>None</td>
</tr>
<tr>
<td>RA_10</td>
<td>Moderate (11)</td>
<td>Pending</td>
<td>Pending</td>
<td>DMII</td>
</tr>
<tr>
<td>SLE_01</td>
<td>Moderate (10)</td>
<td>None</td>
<td>Improved (2)</td>
<td>Thyroid cancer (treated)</td>
</tr>
<tr>
<td>SLE_02</td>
<td>Moderate (10)</td>
<td>Pending</td>
<td>Pending</td>
<td>None</td>
</tr>
</tbody>
</table>

Table 2: Depression intervention outcome in RA and SLE

Disclosure: R. Zhang, None; P. Prakash, None; A. Wasserman, None; K. Sperber, None; J. Ash, None.


Abstract Number: 1087

Rheumatology Clinic Smoking Cessation Protocol Markedly Increases Quit Line Referrals

Christie M. Bartels1, Edmond Ramly2, Daniel Panyard3, Diane Lauver4, Heather Johnson5, Zhanhai Li6, Emmanuel Sampene7, Megan Piper8 and Patrick McBride5, 1Rheumatology/Medicine, University of Wisconsin - Madison, Madison, WI, 2Industrial and Systems Engineering, University of Wisconsin College of Engineering, Madison, WI, 3Population Health, University of Wisconsin School of Medicine and Public Health, Madison, WI, 4University of Wisconsin-Madison School of Nursing, Madison, WI, 5Cardiology/Medicine, University of Wisconsin School of Medicine and Public Health, Madison, WI, 6Biostatistics and Medical
SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Smoking predicts higher incidence, greater severity, and reduced treatment responses in rheumatoid arthritis, lupus, and spondyloarthritis. However, cessation advice and quit line referral occur in just 10% and 0.6% of rheumatology visits, respectively. Primary care staff protocols improve guideline-based care, and electronic referrals increase use of free, state tobacco quit lines by 13-fold. We sought to examine a similar staff protocol in rheumatology using electronic health record (EHR) tools to connect eligible patients to a free, state quit line.

Methods: We conducted a pre- post-analysis of EHR data (2012-16) including our 6-month Quit Connect project. During implementation, cessation experts and project staff provided an hour of Quit Connect protocol training to nurses and medical assistants at three rheumatology clinics. The protocol included EHR prompts to assess smoking status, 30-day readiness to quit or cut back, and willingness to try a quit line. EHR data measured process steps. Referral to the quit line (vs. our published baseline) was the primary outcome. The quit line reported patient outcomes. The IRB exempted this as standard of care with permission to publish.

Logistic regression models examined process measures and referrals pre- and post-protocol. Multivariable process models included age, sex, race, body mass index (BMI), socioeconomic status (SES; defined as ever receiving Medicaid), and comorbidity (Johns Hopkins Adjusted Clinical Groups (ACG) score).

Results: For 54,090 rheumatology visits, 4,601 (9%) reported current smoking. 4,078 pre-protocol visits with patients who smoke (2012-15) were compared to 523 visits after protocol implementation (2016). Documenting smoking status remained high (96 v. 97%). 30-day readiness to quit assessment rose from 3% to 80% post-protocol (Table 1, OR 120, 91-159). Among those asked, 29% reported being ready to quit. Of those ready, 76% had a referral to the state tobacco quit line compared to our pre- rate of 0.6% (OR 26, 6-106). When offered, 71% accepted referrals (54% of ready to quit; 13% of smokers).

Patients with higher comorbidity were less often ready to quit (ACG OR 0.6, 0.4-0.9 unadj.); older patients accepted fewer referrals (OR 0.8, 0.7-0.97 unadj. per 10 yrs.). Adjusted models did not change results.

Among 66 referred patients, 11 (17%) accepted counselling, nicotine replacement, and set a quit date, and 5 more reported a quit in process. Overall, 24% of referred patients set a quit date or reported a quit attempt.

Conclusion: Our Quit Connect protocol for rheumatology staff increased quit line referrals over 20-fold. When asked, a third of patients were ready to quit and half agreed to referral. Given the importance of cessation to reduce immune and cardiopulmonary disease, future rheumatology studies should investigate cessation protocols to leverage quit lines, which are free in all states.

Table 1. Tobacco cessation care pre- and post-protocol implementation

<table>
<thead>
<tr>
<th></th>
<th>Pre n=4,078</th>
<th>Post n=523</th>
<th>Unadj. OR, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ready to quit asked</td>
<td>135 (3%)</td>
<td>421 (80%)</td>
<td>120, 91-159</td>
</tr>
<tr>
<td>Patient ready to quit/cut back</td>
<td>59 (44%)</td>
<td>122 (29%)</td>
<td></td>
</tr>
<tr>
<td>Quit line referral offered</td>
<td>[0.6% historic]</td>
<td>93 (36%)</td>
<td>26, 6-106</td>
</tr>
<tr>
<td>Quit line referral accepted</td>
<td>NA</td>
<td>66 (71%)</td>
<td></td>
</tr>
</tbody>
</table>

Disclosure: C. M. Bartels, Pfizer Inc, 2; E. Ramly, None; D. Panyard, None; D. Lauver, None; H. Johnson, None; Z. Li, None; E. Sampene, None; M. Piper, None; P. McBride, None.

Abstract Number: 1088

Staff Protocol in Rheumatology Clinics Reduces Population-Level Rate of High Blood Pressure
The Centers for Disease Control and Prevention director has said “nothing will save more lives” than protocols to control blood pressure (BP). BP is relevant in rheumatology clinics because it is causally linked to cardiovascular disease. Hypertension control is also one of ten RA quality measures endorsed by ACR and Medicare for 2017 quality payment reporting. Yet, minimal evidence exists on how to improve BP control in busy rheumatology clinics. We previously implemented a staff protocol that doubled timely follow-up after high BPs in rheumatology clinics, and now aimed to examine its impact on population BP control.

Methods: We assessed population trends in the rate of monthly high BPs (% of all visits) before and after the implementation of a staff BP Connect Health protocol in three rheumatology clinics (10/2012-10/2014 vs. 11/2014-12/2016). During implementation, clinical educators trained nurses and medical assistants in an hour-long session on BP in rheumatic diseases, proper BP measurement, and the BP Connect Health protocol steps. Protocols included EHR prompts to re-measure high BPs, and if confirmed high, offer timely primary care follow-up. Follow-up orders automatically routed to scheduling staff for patients with in-network primary care, and printed on after visit materials for all patients. EHR data reported the monthly percentage of adult rheumatology clinic visits with an initial BP >140/90 mmHg.

We performed time series regression with Newey-West standard errors to examine changes in rates of high BPs in the 24 months before and after protocol implementation.

Results: A total of 28,109 pre-protocol rheumatology clinic visits were compared to 28,285 visits after protocol implementation. Monthly rates of high BP, when averaged over the periods before and after implementation, fell from 17% pre- to 8% post-protocol. Time series analysis demonstrated a significant reduction after protocol implementation and continued improvement over time (Figure 1. p<0.003 & p<0.03). Strengths included 2-year protocol feasibility; limitations include our single center pre-post design.

Conclusion: After implementing the rheumatology staff protocol, we observed a 9% reduction in mean rates of high BP across rheumatology clinic populations. Early improvements likely reflected staff BP training, while later improvements may reflect improved follow-up, adherence, and management of BP. Future multi-site studies will test the BP Connect Health protocol in other rheumatology and specialty populations at risk for cardiovascular disease.
Large Variations in Tuberculosis Testing for New Biologic Users with Rheumatoid Arthritis Among Providers in the RISE Registry

Gabriela Schmajuk1, Michael Evans2, Julia Kay3 and Jinoos Yazdany4, 1San Francisco VA Medical Center, University of California San Francisco, San Francisco, CA, 2University of California San Francisco, San Francisco, CA, 3Medicine/Rheumatology, University of California - San Francisco, San Francisco, CA, 4Medicine/Rheumatology, University of California San Francisco, San Francisco, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Tuberculosis (TB) testing prior to biologic DMARD use helps prevent potentially fatal, medication-related adverse events and is a National Quality Forum-endorsed quality measure. We used data from a national registry to describe practice variations on this measure among US rheumatologists.

Methods: The ACR’s RISE is a national registry that passively collects electronic health record (EHR) data on all patients seen by participating practices. As of December 2016, RISE was connected to 632 providers representing an estimated 20% of the US clinical rheumatology workforce. We calculated the proportion patients ≥ 18 with rheumatoid arthritis who were newly prescribed a biologic DMARD or tofacitinib during 2016 and who had TB testing in the 12 months preceding the biologic prescription, by practice and geographic region. We examined associated EHR data for the type of TB test performed (PPD or quantiferon-based assays). Consistent with other national performance analyses, providers with fewer than 30 qualifying patients in the denominator were excluded. Proportions were compared using chi-square tests.

Results: We analyzed data from 18,079 patients across 533 providers and 95 practices. 77% of patients were female, 20% were non-white, and mean age was 58 (SD 13.5). Overall, patient-level performance on the measure was 56%, with a range of 0 to 96% across practices (Figure), and significant variation across regions (Table; p<0.0001). Among the patients in the numerator with a TB test found in the EHR data (N=7828), 93% received a Quantiferon test while 7% had a PPD.

Conclusion: We found large variations in TB testing prior to new biologic DMARD starts across RISE practices. Given that quantiferon-based assays represented the majority of TB screening tests identified, we suspect that PPD testing remains undercaptured in the EHR. As value-based incentive programs become more widespread, accurate capture of performance on patient safety measures will be increasingly important and may require practices to standardize documentation of important safety processes such as TB testing.

Disclaimer: The data presented here was supported by the ACR’s RISE Registry. However, the views expressed represent those of the authors and do not necessarily represent the views of the ACR.
Table. Proportion of RA patients who received T8 test prior to a new biologic prescription, by region.

<table>
<thead>
<tr>
<th>Geographic Region (included U.S. States)</th>
<th>N patients</th>
<th>Mean (%)</th>
<th>95% CI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>New England (CT, ME, MA, NH, RI, VT)</td>
<td>613</td>
<td>83.7</td>
<td>80.7, 86.7</td>
</tr>
<tr>
<td>Mid Atlantic (DE, NJ, NY, PA)</td>
<td>1138</td>
<td>57.1</td>
<td>54.2, 60.1</td>
</tr>
<tr>
<td>East North Central (IL, IN, MI, OH, WI)</td>
<td>1900</td>
<td>64.8</td>
<td>62.6, 67.0</td>
</tr>
<tr>
<td>West North Central (IA, KS, MN, MO, NE, ND, SD)</td>
<td>2980</td>
<td>30.7</td>
<td>29.0, 32.4</td>
</tr>
<tr>
<td>South Atlantic (FL, GA, MD, NC, SC, VA, DC, WV)</td>
<td>5341</td>
<td>61.0</td>
<td>59.6, 62.3</td>
</tr>
<tr>
<td>East South Central (AL, KY, MS, TN)</td>
<td>2926</td>
<td>47.6</td>
<td>45.7, 49.4</td>
</tr>
<tr>
<td>West South Central (AR, LA, OK, TX)</td>
<td>1733</td>
<td>70.2</td>
<td>68.0, 72.3</td>
</tr>
<tr>
<td>Mountain (AZ, CO, ID, MT, NV, NM, UT, WY)</td>
<td>600</td>
<td>71.3</td>
<td>67.6, 75.0</td>
</tr>
<tr>
<td>Pacific (AK, CA, HI, OR, WA)</td>
<td>848</td>
<td>62.4</td>
<td>59.1, 65.7</td>
</tr>
</tbody>
</table>

Disclosure: G. Schmajuk, None; M. Evans, None; J. Kay, None; J. Yazdany, None.


Abstract Number: 1090

A Multidisciplinary Performance Improvement Approach to Achieving Goal Serum Uric Acid Levels in Patients with Gout

Luke Monteagudo¹, Jefferson Roberts², Donna Kido³, Collette Chin³ and Susan Fujii³, ¹Internal Medicine, Tripler Army Medical Center, Honolulu, HI, ²Rheumatology, Tripler Army Medical Center, Honolulu, HI, ³Pharmacy, Tripler Army Medical Center, Honolulu, HI

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: In patients with gout, hyperuricemia leads to inflammation induced by mono-sodium urate crystal deposition. This causes irreversible physical and radiographically evident destruction of the affected joint. Current guidelines recommend a serum uric acid (sUA) level < 6 mg/dL, while data has shown that sUA of < 5 mg/dL has benefit. The aim of this performance improvement project was to assess how to better achieve these goals. We hypothesized that through a multidisciplinary approach, we could more effectively achieve sUA goal levels.

Methods: We enrolled patients with a new or chronic diagnosis of gout. We excluded pregnant women and those under the age of 18. Baseline sUA levels were obtained on all patients. If elevated and not already on urate lowering therapy, patients were started on 100mg Allopurinol daily and 0.6mg Colchicine twice daily. A clinical pharmacist followed our algorithm for a step wise increase in therapy intensity every two weeks, with a corresponding sUA level.

Results: A total of 40 patients participated. The average starting uric acid level of the experimental group was 8.06 mg/dL. After 12 months, 48% (n=19) of patients reached a level below 6 mg/dL. After an average of 18.5 months of enrollment, 33% of patients (n=13) reached a serum uric acid level below 5 mg/dL and 53% (n=21) reached a serum uric acid level below 6 mg/dL.

Conclusion: The aim of our approach to gout treatment is to decrease sUA, gout attacks, and ultimately joint damage. We were able to show that a multidisciplinary approach could improve sUA level compared with primary physicians alone. This effect is due to clinical pharmacists’ ability to perform more frequent sUA evaluations and medication changes for patients. Future work will evaluate secondary end points, like the number of acute care visits and gout attacks during the study period. The summation of this data supports the multidisciplinary approach to the treatment of gout.

Disclosure: L. Monteagudo, None; J. Roberts, None; D. Kido, None; C. Chin, None; S. Fujii, None.
The Utility of Electronic Consultation in the Management of Gout at the Veterans Affairs Medical Center

Juliana Chang1, Michelle DiFiore1 and Maida Wong2,3, 1Internal Medicine, University of California, Irvine, School of Medicine, Orange, CA, 2Rheumatology, University of California, Irvine, School of Medicine, Orange, CA, 3Rheumatology, Tibor Rubin VA Medical Center in Long Beach, Long Beach, CA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Gout is the most common inflammatory arthritis in adults worldwide. It can be managed by primary care physicians (PCPs), but complex cases often require rheumatology input. However, the average wait time for a first rheumatology clinic visit varies from 38 days to 47 weeks. By utilizing electronic consultation (e-consult) which allows two-way communications between referring and rheumatology physicians (pre-consult exchange), rheumatologists can decide whether patients can be managed by addressing the clinical questions electronically, or a face-to-face patient evaluation is necessary. We analyzed the effectiveness of gout management via e-consult compared to PCP and face-to-face rheumatology visits at the VA Medical Center in Long Beach.

Methods: A retrospective study of 133 VA gout patients from 2013 to 2014 was constructed and grouped by their management under rheumatology e-consults (n = 33), rheumatology clinic visits (n = 52), or PCP visits (n = 37). Electronic medical records were reviewed for a 24-month period from their initial gout flare or e-consult date. The effectiveness in management was measured by the change in frequency of gout flares and related emergency department (ED) visits, renal function and serum uric acid levels (sUA).

Results: Of the 48 gout e-consults, 33 cases were resolved electronically, and 15 were converted to rheumatology clinic visits. The wait time for recommendations from e-consult was 3.7 days. Face-to-face clinic visit took 20.3 days after pre-consult exchange (vs 71.3 days for direct clinic consult). Compared to PCP managed patients, both e-consult and rheumatology clinic patients have more gout attacks and related ED visits at baseline (p =0.08). They have fewer attacks in the first 12 months of management, with decreased sUA and improved renal function (p =0.06), (p =0.1), and are more likely to be treated with allopurinol, colchicine, febuxostat and corticosteroids than with NSAIDs alone (p <0.05). E-consult management was comparable but second to rheumatology clinic visits (p not significant), but beyond 12 months, disease activity was stable and similar in all groups.

Conclusion: More effective gout management can be achieved by referring patients with uncontrolled disease to direct rheumatology visits or e-consults in the first 12 months. Patients can be transitioned to PCP management after 12 months if disease is stable. Overall, e-consult serves as a reasonable alternative in managing gout. Clinical questions can be addressed electronically resulting in a shorter wait time and more efficient referrals to the rheumatology clinic.

Disclosure: J. Chang, None; M. DiFiore, None; M. Wong, None.
Background/Purpose: A large proportion of patients with rheumatologic diseases are now being treated with biologic therapies. Estimates of the use of biologics in patients with rheumatoid arthritis (RA), for example, now range from 30-40%. While biologics improve disease outcomes, they also increase the risk of infections, autoimmunity, and possibly malignancy. Screening for these conditions, as well as completion of routine vaccinations, has shown to decrease complication rates. Despite these benefits, compliance with current guideline recommendations tends to be low in practice. Development of The Ottawa Biologic Safety & Screening Tool (OBSST) is a quality initiative at The Ottawa Hospital with the objective to increase compliance with guideline recommendations and ultimately improve patient safety. The Ottawa Hospital is an academic teaching hospital in Ontario, Canada with 1,122 beds, facilitating 1.155 million ambulatory care visits each year. Our rheumatology clinic serves more than 880 patients using biologic therapies.

Methods: A chart review of randomly selected patients (n=50) who started a biologic treatment at our centre from 2011 to 2013 revealed baseline rates of compliance with guidelines. American College of Rheumatology and Canadian Rheumatology Association Guidelines for treatment of rheumatoid arthritis were used to determine screening goals (Singh et al, 2012; Bombardier et al, 2011-2012). The OBSST was then developed using a Nominal Group Technique, and implemented by a multidisciplinary team. OBSST is a checklist reviewing 1) patient characteristics which may preclude the use of certain biologics, 2) recommended laboratory and imaging screening, and 3) vaccination counselling. After one year of OBSST use, a chart review of randomly selected patients (n=50) initiating biologic therapy from October 2015 to September 2016 was completed. Descriptive statistics are reported for pre- and post-implementation rates.

Results: Following implementation of the OBSST, rates of documented Hepatitis B serology increased significantly from 50% to 94% (25/50 to 47/50 patients, P<0.0001). Hepatitis C serology documentation showed similar rates of improvement, from 46% to 98% (23/50 to 49/50 patients, P<0.0001). Prior to the implementation of OBSST, the rate of documented vaccination counselling was low; 6% of patients (3/50) had documented counselling regarding influenza, herpes zoster, and pneumococcal vaccines. With the OBSST, vaccination counselling increased to 98% (49/50, P<0.0001) for influenza, 96% (48/50, P=0.0003) for herpes zoster, and 94% (47/50, P<0.0001) for pneumococcal vaccines. Screening rates for tuberculosis with a TB skin test and chest X-ray were relatively high at baseline. Rates increased with OBSST but not reach statistical significance.

Conclusion: The Ottawa Biologics Safety & Screening Tool, administered by a multidisciplinary team, led to significantly increased rates of recommended screening and vaccine counselling of patients starting biologic therapies. Use of a standardized tool, combined with a team approach, may be beneficial in aligning institutional practices with current guideline recommendations when initiating biologics.

Disclosure: C. Dobrowolski, None; I. Midzic, None; D. Boone, Novartis Pharmaceutical Corporation, 5; A. McCarthy, None; D. Smith, None; J. Thomson, None; S. Izzi, None; S. Humphrey-Murto, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-ottawa-biologics-safety-and-screening-tool

Abstract Number: 1093

Effectiveness of the Outreach Model for Rheumatology Specialty Clinics to On-Reserve First Nations in Canada: System-Level and Individual Measures of Performance and Outcomes

Sujay Nagaraj¹, Claire Barber², Margaret Kargard³, Tyler White³ and Cheryl Barnabe⁴, ¹McCaig Institute for Bone and Joint Health, University of Calgary, Calgary, AB, Canada, ²Medicine, University of Calgary, Calgary, AB, Canada, ³Siksika Health Services, Siksika, AB, Canada, ⁴Department of Community Health Sciences, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada

First publication: September 18, 2017

SESSION INFORMATION
Background/Purpose: Inflammatory arthritis (IA) disproportionately affects Canada’s First Nations population. A Model of Care (MoC) consisting of rheumatology specialty services embedded in the primary care context on-reserve was instituted to reduce barriers to care and improve treatment outcomes. This study assessed the system-level performance of the MoC as well as its effectiveness on disease activity measures and patient-reported outcomes over 7 years (2011 - 2017) at one centre.

Methods: Patients with incident and prevalent IA were enrolled in a longitudinal cohort. Clinical characteristics, disease activity measures, and treatment recommendations were systematically recorded over follow-up. System-level performance was evaluated according to established measures including: wait times for new referral, proportion of patients seen in yearly follow-up, proportion of patients prescribed DMARD treatment, and time to DMARD initiation. Treatment escalation (new DMARD or biologic prescribed) was characterized in relation to disease activity state at each visit. Mixed-model regression was performed to determine rates of change for disease activity measures over time, with adjustment for baseline demographics and disease activity measures.

Results: 59 participants (78% female, mean age 47 (SD 13)) with IA (n=39 RA, n=7 PsA, n=7 SLE and related CTD, n=3 JIA, n=1 SpA, n=2 crystal arthritis; 29 with incident and 30 with prevalent disease, mean 16 (SD 13) years duration) were followed for a mean of 29 (SD 23) months with a mean of 6 (SD 5) visits per participant.

At the system-level, the 50th and 90th percentile wait times were 69 and 695 days, respectively. Only 33% of patients were seen in the benchmark waiting time of 4 weeks but 83% of patients were followed up in each measurement year. Nearly all (96%) of patients received a DMARD in each measurement year and 90% were prescribed a DMARD within 2 weeks of diagnosis.

At the baseline visit, 70% of participants were in DAS28 moderate or high disease activity. Treatment was escalated at 60% of visits where the individual was in moderate or high disease activity. Swollen and tender joint counts significantly improved during follow-up (SJC28 adjusted slope -0.16, 95%CI -0.27 to -0.05, p=0.004; TJC28 adjusted slope -0.16, 95%CI -0.32 to -0.0057, p=0.04.). Pain (adjusted slope -0.014, 95%CI -0.70 to -0.04, p=0.62), MD Global (adjusted slope -0.028, 95%CI -0.095 to 0.040, p=0.42), HAQ (adjusted slope 0.0028, 95%CI -0.0088 to 0.014, p=0.64), and DAS28 (adjusted slope -0.038, 95% CI -0.078 to 0.0016, p=0.060) did not significantly improve over time. Patient global continued to increase over time (adjusted slope 0.081, 95%CI 0.025 to 0.137, p=0.005). No significant differences were found in a sensitivity analysis comparing outcomes for incident and prevalent patients.

Conclusion: Evaluation of the MoC highlighted areas for further improvement. The program met several system-level performance measure targets however patients still experience long wait times. Despite improvement in swollen and tender joint counts, disease activity measures and patient-reported outcomes did not significantly improve during follow-up. This suggests that there are still gaps in meeting relevant outcomes.

Disclosure: S. Nagaraj, None; C. Barber, None; M. Kargard, None; T. White, None; C. Barnabe, None.


Abstract Number: 1094

A Model for Improved Management of Fragility Fractures: Navigating the Fracture Liaison Service

Marcy B. Bolster1, Smriti Cevallos2, Lisa Beyer2, Henry M. Kronenberg2 and Ben Leder2, 1Massachusetts General Hospital, Boston, MA, 2Endocrine, Massachusetts General Hospital, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM
**Background/Purpose:** Fragility fractures are associated with significant morbidity, mortality and healthcare costs, yet most fracture patients are neither evaluated nor treated for their underlying osteoporosis (OP). A Fracture Liaison Service (FLS) can improve OP treatment in patients with fragility fractures, including hip fractures. Our model uses a physician assistant Navigator to coordinate interdisciplinary care and provide a seamless transition between inpatient surgical care and outpatient OP management. The Navigator enhances patient education, facilitates communication amongst all providers, performs diagnostic evaluation as warranted, and initiates OP treatment.

**Methods:** A patient-centered care algorithm (Figure 1) begins in the Emergency Department (ED), continues for inpatient hospital care with Geriatric, FLS and Orthopaedic co-management, and the FLS Navigator then transitions care to the outpatient setting (orthopaedic clinic). Communication between the FLS Navigator and patient's PCP occurs at each step.

**Results:** A comparison of outcomes (Table 1) is made from 1/1/2013-12/31/2013 (Group 1, pre-MGH FLS) to 2/1/2016-1/31/2017 (Group 2, year 1 of MGH FLS). There were 314 hip fragility fractures in Group 1 (66% female, 83% age ≥ 65 years), and 259 fragility fractures in Group 2 (71% female, 91% age ≥ 65 years).

Of 314 Group 1 inpatients treated for a hip fragility fracture, 127 (40%) had a PCP in our health care system. Treatment was prescribed for 7 of 127 (5.5%) patients within 6 months of hip fracture and 11/314 (3.5%) were seen by an OP specialist within 1 year of fracture.

Of 259 Group 2 inpatients, 102 (39%) were seen as an outpatient by the FLS Navigator in the orthopaedic clinic or by a specialist in OP clinic. Of Group 2 patients, 68 (26%) declined a follow up appointment with the FLS Navigator and 32 (12%) did not keep the FLS outpatient appointment. Preliminary data reveal that 62 of 259 (24%) Group 2 patients were receiving OP therapy 6 months post-hospitalization, a greater than 4-fold increase compared to Group 1 (additional data not available for many Group 2 patients due to insufficient time since fracture).

**Conclusion:** The MGH FLS utilizes an innovative model to improve health outcomes, including morbidity, mortality and reduced healthcare costs, in a high risk population. Future goals include increasing the FLS scope to ensure all patients admitted with all fragility fractures are evaluated, improving 6-month treatment rates to >80%, expanding the FLS to fracture patients not requiring inpatient care, and using telemedicine to develop networks with regional hospitals.

---

**Figure 1: Fracture Liaison Service Algorithm**

[Diagram of the FLS algorithm with steps including:]
- Patient to ED* with any fragility fracture
- Admitted for inpatient care
- Orthopaedic and Geriatric co-management
- Establishes partnership & initiates evaluation & management
- Schedules additional follow-up with orthopaedic specialist OR transitioning care back to PCP
- 6 weeks post-hospital orthopaedic follow-up appointment and same-day FLS** Navigator visit
- Orthopaedic follow-up appointment 2 weeks post-hospital
- Scheduling between FLS Navigator and patient

* Emergency Department
** Fracture Liaison Service
Abstract Number: 1095

**Increasing Lipid Panel Monitoring in a Rheumatology Clinic**

Anju Mohan\(^1\) and Beth Scholz\(^2\), \(^1\)Internal Medicine-Rheumatology, University of Texas Health Science Center at Houston, Houston, TX, \(^2\)Internal Medicine - Rheumatology, University of Texas Health Science Center at Houston, Houston, TX

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017

Session Title: Measures and Measurement of Healthcare Quality Poster I

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM

**Background/Purpose:**

Patients with autoimmune conditions are at increased risk for cardiovascular disease (CVD) compared to the general population. It is not routine practice at UT Rheumatology to manage lipids. Since rheumatologists often play the role of PCP for patients with autoimmune diseases, they are at a unique position to modulate the CVD risk. Our aim was to increase the percentage of patients with an annual lipid panel checked to 50% and to prescribe statin therapy for LDL more than or equal to 190 or if the 10-year risk for atherosclerotic cardiovascular disease (ASCVD) is more than or equal to 7.5%.

**Methods:**

Patients over 18 years of age with RA, SLE, Psoriatic arthritis, Polymyositis and Dermatomyositis were included in this study. This quality improvement project was undertaken by a single attending provider at a single clinic location. The baseline data from chart
review was collected from July 2016 to August 2016. The post-intervention data was collected in 3 phases between December 2016 and May 2017. For the first phase of intervention a reminder card with a flowchart was attached to the work stations, and ASCVD risk calculator was downloaded to the provider’s cell phone. For appropriate patients, lipid profiles were ordered and ASCVD risk calculated. If indicated, atorvastatin was prescribed. During the second intervention phase, in addition to the above the provider reviewed the daily schedule and printed appropriate lab orders for each patient the day prior to the visit.

Results:

During baseline period, lipid profiles were ordered on 20% of appropriate patients (5/30) with 13% (4/30) on statins. After the first intervention, lipids were checked in 33% (12/36) with 13.8% (5/36) on statins. During the second intervention phase, lipids were checked in 77% (10/13) with 23% (3/13) on statins. During maintenance (about 3 months later), lipids were ordered on 81% (13/16) with 25% (4/16) placed on statins. It was also noted that 5 of the 65 patients in the intervention phases declined having lipid panel measured.

Conclusion:

The initial intervention did not result in significant improvement. For the second intervention, pre-clinic reviews with labs checks were performed, which increased success. Next steps will involve spread to other rheumatology providers in the clinic and interventions to increase appropriate prescribing of statins based on lipid panel results.

Disclosure: A. Mohan, None; B. Scholz, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/increasing-lipid-panel-monitoring-in-a-rheumatology-clinic

Abstract Number: 1096

Clinical Significance of RNP Antibodies in Diagnosis of Systemic Autoimmune Rheumatic Disease When Detected By Multiplex Immunoassay

Heather Bukiri\textsuperscript{1}, Amish Dave\textsuperscript{2}, Erin Bauer\textsuperscript{2}, Vivian Stone\textsuperscript{2}, Chris Chong\textsuperscript{3} and Punam Verma\textsuperscript{4}, \textsuperscript{1}Graduate Medical Education, Virginia Mason Medical Center, Seattle, WA, \textsuperscript{2}Rheumatology, Virginia Mason Medical Center, Seattle, WA, \textsuperscript{3}Virginia Mason Medical Center, Seattle, WA, \textsuperscript{4}Microbiology/Immunology General Lab, Virginia Mason Medical Center, Seattle, WA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster I
Background/Purpose: A large multicenter healthcare system recently adopted multiplex immunoassay as an initial screen for antinuclear antibody (ANA) with confirmatory reflex testing by immunofluorescence antibody assay (IFA). When both are positive, a 3-tiered cascade reporting algorithm is activated (Figure 1A). This ANA testing method led to an increase in rheumatology referrals for RNP antibody (ab) positivity in patients lacking clinical features of systemic autoimmune rheumatic diseases (SARD). We conducted a multiphase quality improvement project to determine the clinical significance of RNP ab positivity.

Methods: A retrospective review of all ANA tests completed at our institution was conducted from July to September 2016. Specimens positive in the multiplex assay were further reviewed for both RNP ab and ANA by IFA positivity. A titer of ≥ 1:160 was considered positive. Positive RNP ab results (> 1 antibody index (AI)) were characterized as either low (1-3 AI) or high (>3 AI). Two independent physicians conducted chart review on all RNP results to determine if diagnosis of SARD was made. Methods are summarized in Figure 2.

Results: Of 1058 ANA multiplex performed, 183 were positive (17.3%) and 60 were positive for RNP ab. Of the 60 RNP ab positive samples, 28 had negative ANA IFA testing (47%). One-hundred and twenty-three ANAs were positive both multiplex and IFA (11.6%), 32 of which were also RNP ab positive (26.2%). Fifteen out of 32 were positive to only RNP ab, and negative to abs to all other extractable nuclear antigens (ENAs). Thirteen of those 15 patients (87%) had no evidence of SARD. PPV for SARD among RNP ab positive patients, sorted by AI is summarized by Table 1.

Conclusion: Within our testing, an isolated positive RNP ab has a poor PPV for SARD and likely represents type I error. When RNP ab is positive with ≥ 1 additional ab to ENA, there is a higher probability for SARD. The highest probability for SARD exists when RNP ab is >3 AI with ≥ 1 additional ab to ENA. Healthcare systems should consider a modified algorithm for reporting RNP positivity as either low (1-3 AI) or high (>3) to help clarify the clinical significance of RNP ab positivity with multiplex testing (Figure 1B).

![Figure 1: Prior and current algorithms for reporting results of positive ANA testing](image-url)
Table One: Incidence of Systemic Autoimmune Rheumatic Disease\textsuperscript{\textcircled{5}} Between Isolated RNP Ab and Non-Isolated RNP Ab at Varying Titers

<table>
<thead>
<tr>
<th></th>
<th>True Positive</th>
<th>False Positive</th>
<th>Total</th>
<th>Positive Predictive Value for SARD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isolated RNP Ab (&gt;1) AI</td>
<td>2</td>
<td>15</td>
<td>17</td>
<td>11.7%</td>
</tr>
<tr>
<td>Isolated RNP Ab 1-3 AI</td>
<td>1</td>
<td>7</td>
<td>8</td>
<td>12.5%</td>
</tr>
<tr>
<td>Isolated RNP Ab (\geq3) AI</td>
<td>1</td>
<td>6</td>
<td>7</td>
<td>14%</td>
</tr>
<tr>
<td>RNP Ab 1-3 AI with Ab positivity to additional ENA</td>
<td>3</td>
<td>6</td>
<td>9</td>
<td>42.9%</td>
</tr>
<tr>
<td>RNP Ab &gt;3 AI with Ab positivity to additional ENA</td>
<td>9</td>
<td>1</td>
<td>10</td>
<td>90%</td>
</tr>
</tbody>
</table>

\(\text{A board certified rheumatologist made the diagnosis of systemic autoimmune rheumatic disease, which includes systemic lupus erythematosus, Sjogren’s syndrome, systemic sclerosis, polymyositis, dermatomyositis, and rheumatoid arthritis.}\)

Disclosure: H. Bukiri, None; A. Dave, None; E. Bauer, None; V. Stone, None; C. Chong, None; P. Verma, None.


Abstract Number: 1097
Investigating Opportunities for Cost Conscious Care: A Review of Physician Practice in Ordering Anti-Nuclear Antibody Testing at an Academic Community Hospital

Hrudya Abraham, Jorge Espinal and Sindhu Joseph, Internal Medicine, MacNeal Hospital, Berwyn, IL
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
More than 94,000 ANA tests are performed each year resulting in an estimated cost of 2.24 million dollars annually. The American College of Rheumatology Choosing Wisely Campaign emphasizes the appropriate use of autoantibody testing focusing on high value and cost conscious care. Besides rheumatologic diseases, positive ANA results can be seen in several non-rheumatic pathologies and in normal healthy individuals. Improper use of immunologic testing can result in misdiagnosis, patient concerns, inappropriate therapy and wasted health care resources. We sought to review physician practicing habits of utilizing the ANA screen prior to ordering ANA panel, unless otherwise warranted in specific clinical settings.

Methods:
We conducted a retrospective chart review of patients aged 18 years or older admitted to our teaching hospital from Jan 1st, 2012 to December 31st, 2014 who had an ANA screen and/or an ANA panel ordered. Fifty percent of these charts were selected using a random number generator and a total of 625 charts were reviewed. Data was collected on the ANA test that was ordered, date of the test performed, result of the tests, history of prior SLE, history of other autoimmune diseases, and prior positive ANA testing.

Results:
Of the 625 patient charts that were reviewed, five patients (0.8%) had a preexisting diagnosis of SLE and 20 patients (3.2%) had previously been diagnosed with non-SLE autoimmune disorders. 208 (33%) patients had an ANA screen ordered, and 417 (67%) had only an ANA panel. Of those patients who had an ANA screen ordered (208), 73% appropriately had the ANA screen ordered first, and 27% had an ANA screen ordered at the same time or after the ANA panel. In those patients who had an ANA screen ordered, 91% of those screens were negative and 9% were positive. Interestingly, in those patients where only an ANA panel was ordered without any prior ANA screening, only 0.05% (2/417) was actually positive.

Conclusion:
Sixty six percent (417) of patients had an ANA panel ordered without an ANA screen, of which 99.5% were negative, leading to an estimated excess cost of 342,254 dollars over 3 years in this test alone. Our Electronic Medical Recording system has different ANA testing options which currently includes the option to only order an ANA panel without the ANA screen. An expanded ANA panel without specific clinical suspicion may result in falsely positive results leading to unnecessary workup. Our next step in implementing change is to remove the option of ‘ANA panel only’ in our Electronic Medical Recording system, and to replace it with ‘ANA screen with reflex to ANA pattern, titer and panel’ to avoid unnecessary testing.

Disclosure: H. Abraham, None; J. Espinal, None; S. Joseph, None.


Abstract Number: 1098

Glucose-6-Phosphate Dehydrogenase Testing in a US Veterans Healthcare System: Are We Ordering Unnecessary Tests?

Glucose-6-Phosphate Dehydrogenase Testing in a US Veterans Healthcare System: Are We Ordering Unnecessary Tests?

Tracy Driver1, Kevin Hsu2, Meika A. Fang3 and Ari Weinreb3, 1Medicine, Rheumatology, David Geffen School of Medicine at UCLA, Los Angeles, CA, 2Cedars-Sinai Medical Center, Los Angeles, CA, 3VA Greater Los Angeles Healthcare System, Los Angeles,
Glucose-6-phosphate dehydrogenase (G6PD) deficiency is an X-linked genetic defect that causes a non-immune hemolytic anemia affecting more than 400 million people worldwide. When initiating medications with oxidant potential such as sulfasalazine (SSZ), patients are frequently tested for G6PD deficiency. The objectives of this study include determining the prevalence of G6PD deficiency among those tested and characterizing G6PD test ordering patterns.

Methods:
Retrospective chart review was performed using the electronic medical record at the VA Greater Los Angeles Healthcare System. The database was searched for all patients who had a G6PD test ordered between 2009-2014. Data collected included demographics, reasons G6PD testing was done, number of patients who underwent repeat testing, and the specialty of the provider who ordered the test. Prevalence of G6PD deficiency was determined. Descriptive analysis of categorical variables was done with the Chi-Square test. The odds ratio (OR) with 95% confidence interval (CI) was used to evaluate the association between ethnicity and G6PD deficiency.

Results:
G6PD levels were measured in 737 patients. The study population included 661 males (89.7%) and 76 females (10.3%) with a mean age of 56.6 (± SD 14.9). There were 60 (8.1%) patients with G6PD deficiency. The percentage of patients with G6PD deficiency by gender and within each self-reported race/ethnicity was as follows: 8.4% (N=56) males, 5.3% (N=4) females, 18.2% (N=2) American Indian, 17.9% (N=47) African American, 7.7% (N=2) Asian, 2.5% (N=7) Caucasian, 1.1% (N=1) Hispanic, and 100% (N=1) Brazilian. Observed differences in G6PD deficiency prevalence were statistically significant based on gender and self-reported race/ethnicity (p<0.001 for both). Odds ratios were calculated to evaluate the association between race/ethnicity and G6PD deficiency: African American (OR 7.77, [95% CI 4.12-14.66]), American Indian (OR 2.56, [95% CI 0.54-12.12]), Asian (OR 0.94, [95% CI 0.22-4.07]), Caucasian (OR 0.20, [95% CI 0.02-0.82]). Repeated testing was carried out in 105 (14.2%) patients. Reasons for G6PD testing included initiation of SSZ for inflammatory arthritis (52.3%), dapsone for PCP prophylaxis (14.2%), and anemia workup (11.1%). Rheumatology ordered the majority of repeat tests (60.7%) for the following reasons: SSZ (65), hydroxychloroquine initiation (1), anemia workup (4), and dapsone initiation (4).

Conclusion:
G6PD deficiency occurred in 8% of our study population, mainly in African Americans, American Indians, and Asians. Rheumatologists ordered most of the tests measuring G6PD levels primarily before considering SSZ therapy and were more likely to order duplicate tests when compared to other specialists. Unnecessary repeat testing is an issue that could be reduced with pop-up computer reminder. This study supports G6PD deficiency testing for high risk populations, including African Americans, American Indians, and Asians, but routine screening of all rheumatology patients for G6PD deficiency when considering SSZ therapy may not be needed.

Disclosure: T. Driver, None; K. Hsu, None; M. A. Fang, None; A. Weinreb, None.
Background/Purpose: The widespread usage of biologic disease modifying anti-rheumatic drugs (bDMARDs) in rheumatology has increased the risk of hepatitis B virus (HBV) re-activation. The prevalence of chronic HBV infection was estimated at 3.0% and 3.5%, respectively in two large, cross-sectional studies in rheumatoid arthritis and spondyloarthropathies internationally. HBV reactivation (HBVr) after using immunosuppressive medicines has been observed in 6.8% of fulminant hepatitis cases in Japan. We aimed to quantify the knowledge gap in the practice of rheumatologists with regards to management of HBVr in rheumatologic patients using a Canada-wide survey.

Methods: In order to assess the discrepancy in practice with regards to dealing with HBV infection in patients started on biologic and non-biologic DMARDs, we conducted a short pilot survey of 15 rheumatologists and 2 rheumatology fellows at an inter-city rheumatology rounds aimed at assessing any knowledge gap. Subsequently, an expert panel of five hepatologists, two infectious disease specialists and four rheumatologists helped generate a final questionnaire. The final survey included questions regarding chronic hepatitis B monitoring and anti-viral prophylaxis with either biologic or non-biologic DMARDs or corticosteroids. A Canada-wide survey was sent to the Canadian Rheumatology Association (CRA) members. The results were compared to the American Gastroenterology Association (AGA) guidelines.

Results: There were 17 respondents to the pilot survey. Of 7 questions in the pilot survey, there were 47% of questions that were either answered incorrectly or marked “I don’t know”. The final survey was sent to 521 members of CRA. The response rate was 27.25% for a total of 142 responses. Interestingly, 8.8% of the responders thought not to send their HBsAg positive patients to a gastroenterologist, although anti-viral prophylaxis would be indicated and hepatology monitoring. There were 58% of the respondents who would order unnecessary test like anti-HBs for monitoring a patient who is HBsAg positive and is on immunosuppressive medication. Another 43% answered incorrectly to start anti-viral prophylaxis for patients who are HBsAg positive and are on DMARDs.

Conclusion: The results of our survey highlight the knowledge gap in monitoring and treating chronic hepatitis B in rheumatology patients. All patients with hepatitis B surface antigen positivity on immunosuppression including prednisone should be referred to gastroenterologist. Similarly, patients on high risk medicines with hepatitis B core antibody positivity despite hepatitis surface antibody status should be monitored and started early on anti-viral prophylaxis.

Disclosure: Y. Daghistani, None; F. To, None; P. Doyle, None; H. H. Ko, None; M. Krajden, None; J. Kur, None; A. Ramji, None; K. Shojania, None; E. Tam, None; J. Wade, None; E. Yoshida, None; G. Reid, None; S. Erb, None; M. Carruthers, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/hepatitis-b-reactivation-in-rheumatologic-patients

Abstract Number: 1100

Communication between Inpatient and Outpatient Specialty Clinicians: Developing a Better Understanding of Patients with Rheumatoid Arthritis Who Are Admitted to the Hospital

Abraham Tacang¹, Christina Downey², Alfred Denio¹, Eric Newman³ and Lisa L. Schroeder⁴, ¹Rheumatology, Geisinger Medical Center, Danville, PA, ²Geisinger Medical Center, Danville, PA, ³Department of Rheumatology, Geisinger Medical Center, Danville, PA, ⁴Rheumatology, Geisinger Health System, Danville, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster I
Session Type: ACR Poster Session B
Effective communication is essential in caring for medically complex patients with rheumatoid arthritis (RA). Communication between clinicians becomes even more crucial when a patient gets admitted to the hospital. Our study aims to investigate how often communication gaps occur at our institution, focusing primarily on RA patients, and subsequent consequences.

Methods:
This is a retrospective cohort study of RA patients admitted to our institution from July 1, 2015 to June 30, 2016. All patients were seen by a rheumatologist at least twice within a 14-month period prior to the admission date. Data gathered include: admission type based on principal diagnosis (infection, cardiac, surgical, other), baseline glucocorticoid and immunosuppressive therapy, rheumatology service notification of a patient’s current or upcoming admission and communication mode (inpatient consult, clinic visit, telephone encounter, discharge instructions or summary), flare up and/or glucocorticoid dose increase up to 3 months after discharge, appropriate preoperative C-spine xray, appropriate medication continuation or discontinuation, and appropriate re-initiation of discontinued medications.

Results:
Two hundred twenty-nine admissions were included. Rheumatology was notified 57.6% of the time across all admission types. Medications (immunosuppressive and/or glucocorticoid) were appropriately held 36.4% of the time. Medications were rightfully continued for 73% of our patient cohort. Nineteen percent of our patients developed a flare within 3 months after discharge. Only 11% of our patients admitted for surgery had a preoperative C-spine xray. Among our surgical patients, 4 developed non-life-threatening infection and 1 patient had wound healing issues within 3 months after surgery.

Conclusion:
Our retrospective study highlights both gaps in communication between rheumatology and admitting services, and in the care of RA patients admitted to the hospital. To our knowledge, this is the first study to investigate these gaps, and subsequent consequences, among RA patients followed in a large integrated healthcare system. One potential intervention to address the problem in communication is integrating an automated notification system within our electronic record to inform rheumatology clinicians when one of our RA patients is scheduled for an elective surgery, or gets admitted to the hospital. To bridge gaps in patient care, we are exploring ways to increase our rates of appropriate preoperative C-spine xrays, as well as appropriate medication continuation or discontinuation among our RA patients. This will be done through collaboration with our surgeons to establish a standardized evidence-based approach to the perioperative management of patients with RA.

Table 1. Summary data of hospital admissions, Rheumatology notification, and patient outcomes

Table 1. Summary data of hospital admissions, Rheumatology notification, and patient outcomes

Disclosure: A. Tacang, None; C. Downey, None; A. Denio, None; E. Newman, None; L. L. Schroeder, None.


Abstract Number: 1101
Document Patient Status and Support Clinical Decisions: Analysis of Inter-Rater Reliability

Shakeel M. Jamal1, Theodore Pincus2, Isabel Castrejón2, Jacquelin R. Chua1, Aman Kugasia1, Juan Schmukler1, Stacy Weinberg1 and Joel A. Block3, 1Division of Rheumatology, Rush University Medical Center, Chicago, IL, 2Rheumatology, Rush University Medical Center, Chicago, IL, 3Rush University Medical Center, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: A physician global estimate of patient status (DOCGL) on a 0-10 visual analog scale (VAS) is as effective as any rheumatoid arthritis (RA) Core Data Set measure to quantify inflammatory activity in patients selected for clinical trials1. However, in routine care, DOCGL may be affected by joint damage and/or distress (e.g., fibromyalgia, depression, etc.), in addition to inflammation. Different physicians may consider these findings variably in formulating DOCGL. One approach to document the contribution of inflammation, damage, and distress to DOCGL is for the physician to complete 3 additional 0-10 VAS. We analyze inter-rater reliability between two rheumatologists for DOCGL and 3 VAS subscales for inflammation, damage, and distress.

TABLE: Mean and SD for the four physician estimates according to the rheumatologist (rheum) and the fellow, intraclass correlations and levels of concordance and discordance for each estimate. *p<0.003

<table>
<thead>
<tr>
<th>VAS (0-10)</th>
<th>Rheum Mean (SD)</th>
<th>Fellow Mean (SD)</th>
<th>Mean Difference</th>
<th>Intraclass Correlation (95% Confidence Interval)</th>
<th>Rheumatologist (Rheum) and Fellows concordance and discordance by 2/10 units, number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall DOCGL</td>
<td>3.8 (1.9)</td>
<td>3.8 (2.2)</td>
<td>0.01</td>
<td>0.63 (0.46, 0.75)</td>
<td>Rheum&gt; Fellow: 22 (22%)</td>
</tr>
<tr>
<td>DOCINF</td>
<td>1.8 (1.5)</td>
<td>1.5 (1.6)</td>
<td>0.25</td>
<td>0.74 (0.62, 0.82)</td>
<td>Rheum&gt; Fellow: 7 (7%)</td>
</tr>
<tr>
<td>DOCDAM</td>
<td>2.7 (2.2)</td>
<td>2.7 (2.2)</td>
<td>-0.04</td>
<td>0.80 (0.70, 0.86)</td>
<td>Rheum&gt; Fellow: 20 (19%)</td>
</tr>
<tr>
<td>DOCSTR</td>
<td>3.2 (3.0)</td>
<td>2.2 (2.4)*</td>
<td>1.02</td>
<td>0.69 (0.55, 0.79)</td>
<td>Rheum&gt; Fellow: 11 (10%)</td>
</tr>
</tbody>
</table>

Methods: At one academic site, 4 VAS for overall DOCGL, and levels of inflammation [or reversible findings] (DOCINF), organ damage [or irreversible findings] (DOCDAM), and distress [or symptoms not explained by inflammation or damage such as fibromyalgia, depression] (DOCSTR), are scored in patients with all rheumatic diagnoses in routine care. At a weekly fellows’ clinic, the four 0-10 VAS estimates scores were recorded independently by a senior rheumatologist and a rheumatology fellow at the same visit. The estimates of the 2 observers for each subscale were analyzed for mean levels, differences, intraclass correlation coefficients (ICCs), and possible discordance - defined as a difference of 2 units/10 between the 2 observers.

Results: Estimates of 2 rheumatologists were analyzed in 107 patients with different rheumatic diseases. Mean differences ranged from 0.01 for DOCGL to 1.02 for DOCSTR, significant only for DOCSTR (Table). The ICC ranged from 0.63 (DOCDAM) to 0.80 (DOCDAM), a range higher than for joint counts2. Concordance of estimates (within 2/10 units) ranged from 63% (DOCSTR) to 85% (DOCINF).

Conclusion: Good agreement between two observers with different levels of clinical experience was seen for 4 physician 0-10 VAS estimates for overall global assessment, inflammation, damage, and distress. These data extend evidence for the value of physician VAS, as DOCGL distinguishes active from control treatments in rheumatoid arthritis (RA) clinical trials more efficiently than joint counts or laboratory tests1. Mean scores for damage and distress were higher than for inflammation, indicating the possible value for doctors, patients, and payers of quantitating damage, in addition to inflammation, to document patient status and support clinical decisions in routine care.


Disclosure: S. M. Jamal, None; T. Pincus, Theodore Pincus, 7; I. Castrejón, None; J. R. Chua, None; A. Kugasia, None; J. Schmukler, None; S. Weinberg, None; J. A. Block, None.
Abstract Number: 1102


Marc W. Nolan1,2, Morgan M. Brown3 and Elie Gertner1,2, 1Section of Rheumatology, Regions Hospital, St. Paul, MN, 2Division of Rheumatology, University of Minnesota Medical School, Minneapolis, MN, 3HealthPartners Institute, St. Paul, MN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
The ACR in 2013 and the Canadian Rheumatology Association (CRA) in 2015 published their respective Choosing Wisely recommendations to promote evidence-based care and reduce medical services that may have questionable value. HLA-B27 testing was #7 in ACR’s and #2 in CRA's Choosing Wisely list of recommendations. HLA-B27 testing is not to be ordered unless features suggestive of a SpA are present. We sought to assess adherence to CRA’s Choosing Wisely recommendations (presence of 2 or more features or 1 feature with radiographic sacroiliitis) by primary care physicians (PCP) ordering HLA-B27 within a large integrated healthcare system and to identify additional areas for quality improvement.

Methods:
Retrospective analysis of all patients who had HLA-B27 testing at Regions Hospital/Health Partners, a large academic vertically and horizontally integrated healthcare system, from 1/1/2014 - 7/1/2015. Chart review identified features of SpA (defined as inflammatory back pain > 3 months with onset < 45 years old, peripheral synovitis, enthesitis, dactylitis, psoriasis, or uveitis) at the time of HLA-B27 testing. We assessed if any imaging (Xray, CT, or MRI) identifying sacroiliitis +/- 6 months from HLA-B27 order was present, the presence of inflammatory markers (ESR or CRP) +/- 1 month from the HLA-B27 order, and if an eventual diagnosis of SpA was made. Data were analyzed to generate descriptive information regarding frequency, demographics, as well as a cost analysis.

Results:
During the 18 months, a total of 627 tests were ordered; 336 by Rheumatologists, 68 by Ophthalmology, and 223 by PCPs. Age ranged from 1 to 92 years. We focused on PCP ordered HLA-B27 testing habits. Applying Choosing Wisely recommendations, only 31 of 223 tests (13.9%) were ordered correctly; 20 (9%) had two or more features, and 11 (4.9%) had one feature with a positive imaging result. Even if ONE feature alone was allowed to be an indication for testing (as opposed to the CRA recommended TWO), only 38.1% of tests were ordered correctly. In comparison, 80% of tests ordered by rheumatologists had one feature and 35% had at least two. The average cost of HLA-B27 test within our payer system is $70-100. Thus, a cost savings of $15,000-20,000 would have occurred if ordered correctly. This does not include secondary costs of referrals to specialists for positive results.

Conclusion:
Improperly ordered HLA-B27 tests occurred nearly 86% of the time from PCPs within our large integrated healthcare system resulting in a cost of $15,000-20,000. EMR educational implementation plans have been shown to be effective for quality improvement. We are planning on utilizing EMR ordering alerts to aid HLA-B27 ordering that is more consistent with Choosing Wisely recommendations which promote evidence-based care.

Table 1. Demographics and features in HLA-B27 testing between 1/2014 and 7/2015 in a large integrated healthcare system.
<table>
<thead>
<tr>
<th></th>
<th>N (%)</th>
<th>N (%)</th>
<th>N (% of total)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>17 (54.84%)</td>
<td>104 (54.17%)</td>
<td>121 (54.26%)</td>
</tr>
<tr>
<td>Female</td>
<td>14 (45.16%)</td>
<td>88 (45.83%)</td>
<td>102 (45.74%)</td>
</tr>
<tr>
<td>&lt;= 17 years old</td>
<td>0 (0.00%)</td>
<td>26 (13.54%)</td>
<td>26 (11.66%)</td>
</tr>
<tr>
<td>&gt;= 18 years old</td>
<td>31 (100.00%)</td>
<td>166 (86.46%)</td>
<td>197 (88.34%)</td>
</tr>
<tr>
<td>&lt;= 45 years old</td>
<td>22 (70.97%)</td>
<td>106 (55.21%)</td>
<td>128 (57.40%)</td>
</tr>
<tr>
<td>&gt;45 years old</td>
<td>9 (29.03%)</td>
<td>86 (44.79%)</td>
<td>95 (42.60%)</td>
</tr>
<tr>
<td>Inflammatory Back Pain</td>
<td>20 (64.52%)</td>
<td>28 (14.58%)</td>
<td>48 (21.52%)</td>
</tr>
<tr>
<td>Peripheral Synovitis</td>
<td>13 (41.94%)</td>
<td>7 (3.65%)</td>
<td>20 (8.97%)</td>
</tr>
<tr>
<td>Enthesitis</td>
<td>1 (3.23%)</td>
<td>3 (1.56%)</td>
<td>4 (1.79%)</td>
</tr>
<tr>
<td>Dactylitis</td>
<td>5 (16.13%)</td>
<td>0 (0.00%)</td>
<td>5 (2.24%)</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>11 (35.48%)</td>
<td>9 (4.69%)</td>
<td>20 (8.97%)</td>
</tr>
<tr>
<td>Uveitis</td>
<td>3 (9.68%)</td>
<td>7 (3.65%)</td>
<td>10 (4.48%)</td>
</tr>
</tbody>
</table>

Disclosure: M. W. Nolan, None; M. M. Brown, None; E. Gertner, None.


Abstract Number: 1103

Towards Recommendations on Functional Assessment Status Measures for Rheumatoid Arthritis: Preliminary Results from a Systematic Review

Claire Barber¹, JoAnn Zell², Jinoos Yazdany³, Aileen Davis⁴, Linda S. Ehrlich-Jones⁵, Carter Thorne⁶, Donna Everix⁷, Laura Cappelli⁸ and Kaleb Michaud⁹, ¹Medicine, University of Calgary, Calgary, AB, Canada, ²National Jewish Medical Center, Denver, CO, ³Medicine/Rheumatology, University of California San Francisco, San Francisco, CA, ⁴Health Care and Outcomes Rsrch, Toronto Western Research Institute, University Health Network, Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, ON, Canada, ⁵Rehabilitation Institute Chicago, Chicago, IL, ⁶Southlake Regional Health Centre, Newmarket, Newmarket, ON, Canada, ⁷OnMyCare Home Health, Fremont, CA, ⁸Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, ⁹Rheumatology & Immunology, University of Nebraska Medical Center and National Data Bank for Rheumatic Diseases, Omaha, NE

First publication: September 18, 2017
Background/Purpose: Functional status assessment measures (FSAMs) are important outcomes in rheumatology and used to monitor response to treatment and aid in prediction of rheumatic disease outcomes. We conducted a systematic review of FSAMs used in the evaluation of patients with rheumatoid arthritis (RA). In this first phase of the study, we report on the identification and characteristics of the FSAMs. The ultimate objective is to develop American College of Rheumatology (ACR) recommendations for the use of FSAMs in clinical practice and quality measurement.

Methods: A search strategy was developed in consultation with a medical librarian and based on a published strategy for finding studies that evaluate the measurement properties of clinical instruments from the COnsensus-based Standards for the selection of health Measurement Instruments (COSMIN) group. This strategy involves the use of MeSH terms/keywords in three themes: #1 construct search (functional status), #2 population search (rheumatoid arthritis), #3 instrument search (including terms for instruments of interest).

MEDLINE, EMBASE, Cochrane Library and CINHAL were searched from inception until March 16th 2017. Two reviewers independently considered papers for inclusion with disagreements resolved by consensus. FSAMs were included if the primary objective of the study was to develop, validate or establish the psychometric properties of a patient-reported FSAMs. Performance-based measures (e.g., grip strength, walk tests) and FSAMs addressing function of a single body part/region were excluded. Health related quality of life or health status measures that only in part addressed function were also excluded as they captured different constructs.

Results: 11,835 unique citations were found and 649 were selected for full-text review. Twenty-three FSAMs met inclusion criteria including 7 published variations of the Health Assessment Questionnaire (HAQ). Eleven measures were developed in the USA (48%), while the remainder were developed in Europe or with international participation. All of the FSAMs were questionnaires varying in length from 2 to 47 items with the exception of a single visual analogue scale. Eight (35%) FSAMs included questions about the use of assistive devices and one FSAM was specific to valued life activities. Range of scores was also often based on the original HAQ range of 0-3 (52% of measures). Where reported, time to administer scores was universally <10 minutes. Preliminary results indicate that the Patient-Reported Outcomes Measurement Information System (PROMIS) physical function questionnaires were highly robust and were correlated with the HAQ but had fewer ceiling effects, were sensitive to change and had high convergent validity.

Conclusion: There are 23 FSAMs for RA in the published literature of varying complexity. Further evaluation of the FSAMs along the 9 domains of COSMIN rating (internal consistency, reliability, measurement error, hypothesis testing, responsiveness and validity (content, structural, criterion and cross-cultural) is presently ongoing and will help determine final ACR recommendations for FSAM use in clinical practice.

Disclosure: C. Barber, None; J. Zell, None; J. Yazdany, None; A. Davis, Osteoarthritis & Cartilage, 6,OARSI, 6,Ontari Trillium Foundation, 2,The Arthritis Society, 2,Bone and Joint Canada, 6; L. S. Ehrlich-Jones, Eation Vance, 1,Abbott Labs, 1,CMS, 2,NIH-NIAms, 2,Craig H. Neilsen Foundation, 2,NIDILRR, 2,Rehabilitation Institute of Chicago, 3,Rush University Medical Center, 3,University of Illinois at Chicago, 3,Northernwestern University, 3; C. Thorne, AbbVie, Amgen, Celgene, Lilly, Novartis, Pfizer, Sanofi, and UCB, 2,Medexus/Medac, 8,AbbVie, Amgen, Celgene, Centocor, Genzyme, Hospira, Janssen, Lilly, Medexus/Medac, Merck, Novartis, Pfizer, Sanofi, and UCB, 5; D. Everix, None; L. Cappelli, Bristol-Myers Squibb, 2; K. Michaud, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/towards-recommendations-on-functional-assessment-status-measures-for-rheumatoid-arthritis-preliminary-results-from-a-systematic-review

A Genome-Wide Association Study of Gout in People of European Ancestry

Tony R. Merriman1, Murray Cadzow1, Marilyn E. Merriman1, Amanda Phipps-Green1, Ruth Topless1, Abhishek Abhishek2, Mariano Andrés3, Linda A. Bradbury4, Russell Buchanan5, Katie Cremin6, Erika De Guzman6, Janak de Zoya7, Michael Doherty8, Catherine Hill9, Tom W.J. Huizinga10, Tim Jansen11, M. Janssen12, Leo A.B. Joosten13, Fina Kurreeman14, Susan Lester15, Frederic Liote16, Donia Macartney-Coxson17, Hirotaka Matsuo18, Geraldine M. McCarthy19, Sally McCormick20, Rinki Murphy21, Karel Pavelka22, Fernando Perez-Ruiz23, Juan Puig24, Timothy RDJ Radstake25, Philip Riches26, Maureen Rischmueller27, Edward Roddy28, Malcolm Smith29, Eli A. Stahl30, Blanka Stiburkova31, Richard Stubbs32, Anne-Kathrin Tausche33, Rosa Torres34, Rob Walker1, Ken Yamamoto35, Matthew A. Brown6, Hyon K. Choi36, Nicola Dalbeth21, Jeffrey N. Miner37, Alexander So38, Lisa K. Stamp39 and Tanya Major40, 1University of Otago, Dunedin, New Zealand, 2Devision of Rheumatology, University of Nottingham, NG5 1PB, England
A genome-wide association study of gout in people of European ancestry

Background/Purpose: Genome wide association studies (GWAS) have provided considerable insight into the molecular control of urate levels. However, less is known about the progression from asymptomatic hyperuricemia to gout. Our aim was to conduct a GWAS for gout in people of European ancestry using the largest number of cases of gout to date.

Methods: This GWAS (7,431 cases and 105,631 controls) was comprised of three data sets: a mixed New Zealand (NZ), Eurogout, and Ardea Biosciences group (3,961 cases; 1,547 controls; genotyped using the Illumina CoreExome v24 array, 547,644 markers), a composite set from the Health Professionals Follow-Up (HPFS) and Nurses’ Health Studies (NHS) (1,038 cases; 1,095 controls; genotyped using the Illumina OmniExpress v12 array, 730,525 markers), and UK Biobank (2,432 cases; 102,989 controls; genotyped using an Affymetrix Axiom array, 820,967 markers). The UK Biobank genotypes were imputed to ~73.3M SNPs. Neither the NZ/Eurogout/Ardea nor NHS/HPFS genotype sets were imputed. Markers found within all three data sets (234,062) were identified and associated with gout (adjusted for sex and age), within each data set separately, using PLINK v1.9. An inverse-variance weighted meta-analysis of the results was then performed using the meta v4.4 package within R v3.2.3. The overall genome inflation factor was 0.90.

Results: There were nine loci with experiment-wide significance (0.05/234,062; $P < 2 \times 10^{-7}$) for association with gout: ABCG2 (OR=1.77), SLC2A9 (OR=1.69), GCKR (OR=1.24), MLXIPL (OR=1.18), SLC17A1-A4 (OR=1.22), SLC16A9 (OR=1.18), SLC22A12 (OR=1.16), PDZK1 (OR=1.16), TRIM46 (OR=1.15). All nine of these loci have been previously associated with serum urate levels in genome-wide studies with the urate-increasing alleles also associated with increased risk of gout in this study.

Conclusion: Our data emphasize the central importance of genetic involvement in serum urate levels, compared to the genetic involvement in MSU crystal formation, or the innate immune response, in determining gout.
Allopurinol Dose Escalation to Achieve Serum Urate below 6mg/Dl: An Open Label Extension Study

Lisa K. Stamp\textsuperscript{1}, Peter T. Chapman\textsuperscript{2}, Murray Barclay\textsuperscript{3}, Anne Horne\textsuperscript{4}, Christopher Frampton\textsuperscript{1}, Paul Tan\textsuperscript{5}, Jill Drake\textsuperscript{6} and Nicola Dalbeth\textsuperscript{5}, \textsuperscript{1}University of Otago, Christchurch, New Zealand, \textsuperscript{2}Christchurch Hospital, Christchurch, New Zealand, \textsuperscript{3}Medicine, University of Otago, Christchurch, New Zealand, \textsuperscript{4}Department of Medicine, University of Auckland, Auckland, New Zealand, \textsuperscript{5}University of Auckland, Auckland, New Zealand, \textsuperscript{6}Rheumatology, Immunology and Allergy, Christchurch Hospital, Christchurch, New Zealand

\textbf{First publication:} September 18, 2017

\textbf{Background/Purpose:} Allopurinol at higher than CrCL based doses remains controversial due to concerns over increased risk of adverse events (AE). A recent 12month randomized controlled trial (RCT) reported that allopurinol above CrCL-based doses is effective and well tolerated. Here, we report the results of the 12month open label extension phase of this RCT. The aims were to determine the long-term safety and efficacy of allopurinol dose escalation to achieve target serum urate (SU) in people with gout.

\textbf{Methods:} People who completed the first 12months of a randomized, controlled, parallel-group, comparative clinical trial continued into a 12month open label extension study (from Month 12 to 24). Participants randomised to the control group who continued their usual dose of allopurinol for the first 12months began allopurinol dose escalation at month 12 if SU was ≥6mg/dl (control (C)/dose escalation (DE)). Those in the DE arm for the first 12months who had achieved target SU maintained the dose of allopurinol, while those with SU≥6mg/dl continued dose escalation (DE/DE). Allopurinol was increased monthly until SU was <6mg/dl. The primary endpoints were reduction in SU and AEs at month 24. Secondary endpoints included the proportion of individuals with gout flares.

\textbf{Results:} Of the 183 participants who entered the study, 143 (78.1%) completed the month 12 visit and 137 (74.9%) completed month 24. The mean (SE) change in SU from month 12 to month 24 was -1.1 (0.2) mg/dl in the C/DE group and 0.1 (0.2) mg/dl in the DE/DE group (p<0.001) with a mean difference of 1.3mg/dl (95\%CI 0.8-1.7), p<0.001). In the C/DE group mean (SE) SU was 7.13 (0.16) mg/dl at baseline and 5.7 (0.2) mg/dl at final visit, and 7.18 (0.2) mg/dl and 5.4 (0.1) mg/dl in the DE/DE group (Fig). SU was <6mg/dl...
at final visit in 69.1% of the C/DE group and 79.7% in the DE/DE group (p=0.16); odds ratio (OR) 1.8 (95%CI 0.8-3.8). There was a significant reduction in the percentage of individuals having a gout flare in the month prior to month 12 and month 24 in both groups (p<0.001), but no difference between randomised groups (p=0.29). There were similar numbers of AEs and serious AEs between groups. Mild elevations of AST, ALT and ALP were noted while some higher grade abnormalities in GGT were observed.

**Conclusion:** The majority of people with gout can achieve and maintain target SU with dose escalation of allopurinol above CrCL-based doses. Higher doses of allopurinol are well tolerated.

**Disclosure:** L. K. Stamp, Amgen, 8; P. T. Chapman, None; M. Barclay, None; A. Horne, None; C. Frampton, None; P. Tan, None; J. Drake, None; N. Dalbeth, Takeda, AstraZeneca, Abbvie, 9.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/allopurinol-dose-escalation-to-achieve-serum-urate-below-6mgdl-an-open-label-extension-study](http://acrabstracts.org/abstract/allopurinol-dose-escalation-to-achieve-serum-urate-below-6mgdl-an-open-label-extension-study)

**Abstract Number:** 1106

**Association between ABCG2 rs2231142 and Poor Response to Allopurinol: Replication and Meta-Analysis**

Mary Wallace¹, Rebecca Roberts², Payal Nanavati³, Jeffrey N Miner³, Nicola Dalbeth⁴, Ruth Topless⁵, Tony R. Merriman⁶ and Lisa K. Stamp⁷. ¹Surgical Sciences, University of Otago, Dunedin, New Zealand, ²University of Otago, Dunedin, New Zealand, ³Ardea Biosciences, San Diego, CA, ⁴University of Auckland, Auckland, New Zealand, ⁵Department of Biochemistry, University of Otago, Dunedin, New Zealand, ⁶Biochemistry Dept, PO Box 56, University of Otago, Dunedin, New Zealand, ⁷University of Otago, Christchurch, New Zealand

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Monday, November 6, 2017
Background/Purpose: Allopurinol is the most widely used urate-lowering drug. However, some patients treated with allopurinol do not achieve serum urate (SU) treatment target of <6mg/dl, despite daily doses >300mg. ABCG2 rs2231142 has been reported to be associated with poor response to allopurinol, while there are conflicting data on the association between ABCG2 rs10011796 and allopurinol response. The aim of this study was to replicate the association of ABCG2 rs2231142 and rs10011796 with allopurinol response and perform a meta-analysis.

Methods: Participants in the Long-term Allopurinol Safety Study Evaluating Outcomes in Gout Patients (LASSO) with available allopurinol dose, plasma allopurinol, oxypurinol, serum urate and genotyping data from a single visit were studied (n=395). In patients with evidence of adherence to allopurinol therapy (oxypurinol >20μmol/l), good response was defined as serum urate (SU) <6mg/dl on allopurinol ≤300mg/d and poor response as SU≥6mg/dl despite allopurinol >300mg/d. Association of rs2231142 and rs10011796 with poor response was tested in logistic regression models that included age, sex, body mass index (BMI), ethnicity and estimated glomerular filtration rate (eGFR).

Results: 24.3% (96/395) of the LASSO cohort and 13.5% (40/296) of the NZ cohort either did not fit the pre-defined response criteria and/or had plasma oxypurinol suggestive of non-adherence (<20μmol/l) and were therefore excluded. 46.5% (139/299) of patients in the LASSO cohort and 50.8% (130/256) of patients in the NZ cohort were defined as poor responders. There was evidence for association of rs2231142 with allopurinol response (OR=2.35 \text{A allele}, P=7.3x10^{-4}) but not for rs10011796 (OR=1.21 \text{G allele}, P=0.33) in the LASSO cohort using a fully adjusted logistic regression model. Meta-analysis with the Genetics of Gout in Aotearoa study participants provided strong and consistent evidence of an association for rs2231142 with allopurinol response (OR=2.43, P=6.2x10^{-7}), but not for rs10011796 (OR=1.06, P=0.69) (Figure).

Conclusion: This study replicates the association of ABCG2 rs2231142 with poor response to allopurinol. Testing ABCG2 rs2231142 may assist in prediction of SU response in people treated with allopurinol.

Disclosure: M. Wallace, None; R. Roberts, None; P. Nanavati, Ardea Biosciences, 3; J. N. Miner, Ardea Biosciences, 3; N. Dalbeth, Takeda, AstraZeneca, Abbvie, 9; R. Topless, None; T. R. Merriman, Ardea Biosciences, 2; L. K. Stamp, Ardea Biosciences, 2.


Abstract Number: 1107

An Illness By Any Other Name: The Effect of Changing the Disease Label of Gout on the Perceptions of the Illness and Its Management

Keith Petrie\textsuperscript{1}, Kate MacKrill\textsuperscript{1}, Christina Derksen\textsuperscript{2} and Nicola Dalbeth\textsuperscript{1}, \textsuperscript{1}University of Auckland, Auckland, New Zealand, \textsuperscript{2}University of Marburg, Marburg, Germany

First publication: September 18, 2017
Background/Purpose: Gout is a chronic disease caused by deposition of monosodium urate crystals. Although diet is a risk factor, many other factors also contribute to development of gout, including age, male sex, kidney disease and genetic variants. Historical and contemporary narratives frequently depict gout as an acute condition caused by dietary overindulgence. These perceptions of illness may have a negative impact on healthcare-seeking and management strategies. The aim of this study was to examine the effect of changing the disease label of gout on the perceptions of the illness and its management.

Methods: Supermarket shopper participants were recruited into this study (n=189). Participants were advised that the aim of the study was to examine the perceptions of different types of arthritis. Participants were randomised to read an identical description of an illness labelled as either gout or urate crystal arthritis (UCA), and complete a questionnaire examining their perception of the illness, likely causal factors, and the usefulness of various management strategies. The label urate crystal arthritis was selected to represent the core pathophysiological elements of disease, including urate as the causative biochemical substrate, crystal deposition, and joint inflammation. Differences between the two illness labels were tested using independent sample t-tests.

Results: The gout-labelled illness was attributed more to patient behaviour (p = 0.030) through poor diet (p = 0.013) and overconsumption of alcohol (p = 0.039), while the UCA-labelled illness was attributed more to aging (p = 0.006). There were no differences in beliefs about other causal factors. The gout-labelled illness was viewed as under more personal control (p = 0.001) and as more socially embarrassing (p < 0.001), whereas the UCA-labelled illness was viewed as having a more chronic timeline (p = 0.044) and as a more serious condition (p = 0.037). Changing to a healthier diet was perceived as more helpful for the gout-labelled illness (p = 0.014). In contrast, taking long-term medications for the condition was viewed as more helpful for the UCA-labelled illness (p = 0.041). There was no significant difference between the illness labels in perceptions that reducing stress, adopting regular exercise, losing weight or using alternative medicine would be helpful for managing the illness (p for all >0.08).

Conclusion: The negative cultural stereotypes surrounding the disease label gout may be a barrier to effective treatment. Changing the name of the illness from gout to a pathophysiological illness label such urate crystal arthritis may have a positive benefits for patient understanding of the condition and the adoption of effective management strategies.

Disclosure: K. Petrie, None; K. MacKrill, None; C. Derksen, None; N. Dalbeth, Takeda, AstraZeneca, Abbvie, 9.

Effect of Body Mass Index on Serum Urate and Renal Uric Acid Handling Responses to an Oral Inosine Load

Nicola Dalbeth1, Jordyn de Kwant1, Gregory Gamble2, Amanda Phipps-Green3, Anne Horne2, Lisa K. Stamp4 and Tony R. Merriman5, 1University of Auckland, Auckland, New Zealand, 2Department of Medicine, University of Auckland, Auckland, New Zealand, 3University of Otago, Dunedin, New Zealand, 4University of Otago, Christchurch, New Zealand, 5Biochemistry Dept, PO Box 56, University of Otago, Dunedin, New Zealand

First publication: September 18, 2017
Background/Purpose: Increased body mass index (BMI) is an important risk factor for hyperuricemia and gout. It is unknown whether overweight and obesity influence serum urate primarily through increased urate production or reduced renal clearance of uric acid. Inosine is a purine nucleoside that functions as an intermediate in the purine salvage and degradation pathways. Oral administration of inosine allows analysis of the effects of a standardized purine load on both serum urate concentrations and renal uric acid handling. The aim of this study was to determine the influence of body mass index on the response to an inosine load.

Methods: Following an overnight fast, 100 healthy participants, recruited by public advertising, attended a study visit. Exclusion criteria included chronic kidney disease stage 3 or worse, gout, diabetes mellitus and diuretic use. Blood and urine samples were obtained for urate and creatinine, prior to and then 15, 30, 60, 120, and 180 minutes after a single oral 1.5g dose of inosine. Clinical features including age, sex, ethnicity and BMI were recorded. Data were analysed according to increased BMI (25kg/m^2 or more) and low/normal BMI (less than 25kg/m^2). The primary endpoint was change in serum urate and secondary endpoint was change in fractional excretion of uric acid (FEUA). Data were analysed using a mixed models approach to repeated measures.

Results: In the entire study population, oral intake of inosine led to large increases in serum urate (mean increase 1.6mg/dL) and FEUA (mean increase 3.7%) over the 180 minute study period (P<0.0001 for both). Although participants in the increased BMI group (n=52) had higher serum urate concentrations at baseline (age, sex, ethnicity-adjusted P=0.002), this group had a smaller increase in serum urate following the inosine load (age, sex, ethnicity-adjusted ANCOVA P=0.0035, Figure 1A). The two BMI groups had a similar FEUA at baseline (age, sex, ethnicity-adjusted P=0.98), but those in the increased BMI group had a smaller increase in FEUA following the inosine load (age, sex, ethnicity-adjusted ANCOVA P=0.0003, Figure 1B).

Conclusion: People with increased BMI do not have an exaggerated hyperuricemic response to a standardized purine load. However, those with increased BMI do have reduced renal excretion of uric acid following inosine loading. These data demonstrate impaired renal clearance of uric acid following dietary purine intake in those with overweight and obesity.

![Figure 1. A Change in serum urate, and B. Change in FEUA following an oral inosine load in different BMI groups. Data are presented as unadjusted mean (95% CI). Age, sex and ethnicity-adjusted ANCOVA P values are shown.](image-url)

Disclosure: N. Dalbeth, Takeda, AstraZeneca, Abbvie, 9; J. de Kwant, None; G. Gamble, None; A. Phipps-Green, None; A. Horne, None; L. K. Stamp, Amgen, 8; T. R. Merriman, Ardea Biosciences, 2.


Abstract Number: 1109

Sex Differences in Gout Patients: Epidemiology, Flares and Hospitalization Data in a Population Based Cohort

Mohanad Elfishawi1,2,3, Clement J. Michel Jr.4, Cynthia S. Crowson5, Eric L. Matteson6 and Tim Bongartz7, 1Rheumatology, Mayo Clinic, Rochester, MN, 2Rheumatology, Kasr Alainy Hospital, Cairo University, Cairo, Egypt, 3Internal Medicine, Icahn School of Medicine at Mount Sinai, Queens Hospital Center, New York, NY, 4Division of Rheumatology, Mayo Clinic, Rochester, MN, 5Health Sciences Research, Mayo Clinic College of Medicine and Science, Rochester, MN, 6Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, MN, 7Emergency Medicine, Vanderbilt University, Nashville, TN

First publication: September 18, 2017
While gout is the most common form of inflammatory arthritis, there are relatively few studies on the influence of sex with regard to disease presentation and comorbidities as well as flare and hospitalization rates among patients with gouty arthritis. Possible determinants of these outcomes in patients with gouty arthritis based upon sex were evaluated using a population-based cohort.

Methods:

The individual medical records of all patients with a potential diagnosis of gout in a geographically defined area were retrospectively reviewed using a resource insuring complete capture. All individuals with a possible diagnosis of incident gout in 2009-2010 were identified. Incident cases had to fulfill at least 1 of 3 criteria: the 1977 American College of Rheumatology proposed criteria for gout, the Rome or New York criteria. All identified cases were followed up through their records for 5 years after incident gout attack, death or migration, whichever came first. Clinical characteristics were compared using chi-square and rank sum tests. Person-year methods were used to estimate and compare flare and hospitalization rates over time.

Results:

A total of 271 patients (196 males; 72%) with incident gout in 2009-2010 were identified. Females had significantly higher mean (SD) age at diagnosis 66.3 (15.7) years compared to males 57.6 (16.9) years (p<0.001). Although the mean (SD) body mass index (BMI) for females 32.1 (8.9) did not differ from males 32.0 (5.8) (p=0.48), more females were morbidly obese (BMI ≥40 kg/m²) than males (25% vs 8%; p<0.001). Podagra was less common in females than males (51% vs 62%), but this did not reach statistical significance (p=0.10). Females had significantly more chronic kidney disease stage 3/4 (36% vs 20%; p=0.006) while hypertension, diabetes and heart disease were non-significantly increased in females compared to males.

During a median of 4.7 years of follow up, 127 males and 31 females experienced at least one gout flare with no significant difference in the number of involved joints. Males reported a total of 323 flares with a rate of 3.97 person-years (py), higher than the 74 flares experienced by females with a rate of 2.28 per 10 py (rate ratio: 1.73; 95% confidence interval [CI]: 1.36-2.25). This difference persisted after adjustment for multiple flares per person (hazard ratio: 1.51; 95% CI: 1.14-2.00).

In the follow up period, 69 male patients and 41 female patients were hospitalized. Males were hospitalized 169 times for a rate of 2.08 per 10 py which is less than the reported 137 hospitalizations for females with a rate of 4.22 per 10 py (rate ratio: 0.49; 95% CI: 0.39-0.62). However, this difference was no longer significant after accounting for the older age of the females.

Conclusion:

Female patients with gout are older at incidence than males and tend to have more associated common co-morbidities, particularly chronic kidney disease. Podagra is less common in females than males. Female patients tend to have fewer flares as compared to males. Adjusted for age, there was no difference in hospitalization rates between males and females.

Disclosure: M. Elfishawi, None; C. J. Michet Jr., None; C. S. Crowson, None; E. L. Matteson, None; T. Bongartz, None.
SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Metabolic and Crystal Arthropathies Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: To investigate the clinical features and risk of gout recurrence in patients with normouricemia during an acute attack

Methods:
This study was conducted in patients diagnosed with acute gout attack by the presence of urate crystals. Clinical features of normouricemic and hyperuricemic patients were compared. Multivariate analysis was performed to determine whether normouricemic patients during an acute attack were less likely to have a recurrent gout attack.

Results: Among a total of 221 gout patients, 88 (39.8%) had normouricemia during an acute attack. Postsurgical gout (22.7% vs 6.0%, P < 0.001), hemodialysis initiation (9.1% vs 2.3%, P = 0.029) and inflammatory activity were higher in normouricemic patients than in hyperuricemic patients. The frequency of renal insufficiency was lower in normouricemic patients (25.0% vs 53.4%, P < 0.001). However, the recurrence rate of gout attack was not different between the two groups during the follow-up period (24.7% vs 33.0%, P = 0.220). In multivariate analysis, female sex, history of urinary stone, presence of tophi, and use of thiazide were associated with risk of recurrent gout attack, but not with serum urate status during an acute attack (HR 1.075, 95% CI 0.972-1.190, P = 0.159).

Conclusion: Normouricemia during an acute gout attack was more frequently observed in postsurgical episodes, hemodialysis initiation and patients with preserved renal function. The recurrent attack was not associated with serum urate levels during an acute gout attack. Thus, careful follow-up should be considered in gout patients regardless of serum urate levels during an acute attack.

Disclosure: J. S. Lee, None; S. Hong, None; O. C. Kwon, None; B. Ghang, None; W. J. Seo, None; D. H. Lim, None; Y. G. Kim, None; C. K. Lee, None; B. Yoo, None.


Abstract Number: 1111

Protective Effect of Allopurinol Use on Kidney Function Among Patients with Gout and Chronic Kidney Disease

Ana Beatriz Vargas-Santos1, Christine Peloquin2, Yuqing Zhang3,4 and Tuhina Neogi4, 1Internal Medicine - Rheumatology, State University of Rio de Janeiro, Rio de Janeiro, Brazil, 2Clinical Epidemiology Unit, Boston University School of Medicine, Boston, MA, 3School Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, 4Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Metabolic and Crystal Arthropathies Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: There is increasing evidence that allopurinol may be protective of kidney function among hyperuricemic subjects, though clinicians are often cautious about using allopurinol in renal insufficiency. Further, studies have been conflicting and few have involved patients with gout. We sought to evaluate the relation of allopurinol to kidney function among gout patients with chronic kidney disease (CKD) stage 3-4 at the start of therapy.
Methods: We conducted a time-stratified propensity score (PS)-matched cohort study in The Health Improvement Network (THIN), a general practitioner electronic medical records database representative of the UK general population. Our study sample included subjects 18-89 years-old with gout and CKD 3 or 4 who had not previously been on urate-lowering therapy. We used PS matching to minimize the effects of confounding by indication. Specifically, we identified new users of allopurinol among this cohort, and matched them 1:1 with an unexposed subject based on the PS using greedy matching within 1-year cohort accrual blocks. We computed the PS using logistic regression, with incident allopurinol use as the dependent variable and potential confounders that reflect indication for allopurinol use and/or risk of CKD (table) as the independent variables. Subjects were followed from the index date (date of 1st allopurinol prescription for the exposed, and randomly assigned date for the unexposed within the 1-year accrual block) until the last glomerular filtration rate (GFR) assessment within 1 year after the index date (before dialysis, kidney transplant, or death if they occurred), or end of study. We analyzed the relation of incident allopurinol use to the changes in GFR using linear regression adjusted for the potential confounders included in the PS model.

Results: Of those with a diagnosis of gout and CKD 3-4, we PS-matched 9,830 allopurinol initiators to 9,830 non-users, among whom 41% and 42% were female. Other covariates were also well-balanced, with mean age of 74 years, mean BMI of 30 kg/m² and 9% of CKD4 subjects in both groups. Time to post-baseline GFR, and dialysis/transplant were similar in both groups. The mean GFR prior to study entry was 46.8 mL/min among allopurinol initiators and 49.8 mL/min among non-users, while the last GFR within one year was 47.8 and 50.0 mL/min, respectively. Allopurinol initiators had an adjusted mean increase in GFR that was 0.8 mL/min (95% CI 0.6-1.1) greater than that of the non-users (Table).

Conclusion: In this community-based cohort, allopurinol use appeared to confer a renoprotective effect among those with pre-existing CKD 3-4 and gout, suggesting that allopurinol does not contribute to worsening renal function among gout patients with renal insufficiency. Physicians should seek other contributors to renal function decline in patients on allopurinol with concomitant gout and CKD if renal function deteriorates.

Disclosure: A. B. Vargas-Santos, None; C. Peloquin, None; Y. Zhang, None; T. Neogi, None.

Efficacy of High Dose Versus Moderate Dose Prednisone in the Treatment of Acute Gout

Rochella A. Ostrowski¹, Elizabeth Araujo², Richard Hariman³ and Elaine Adams⁴, ¹Division of Rheumatology, Loyola University Medical Center, Maywood, IL, ²Rheumatology and Immunology, Department of Internal Medicine 3, Universitätsklinikum Erlangen, Erlangen, Germany, Erlangen, Germany, ³Rheumatology, Medical College of Wisconsin, Milwaukee, WI, ⁴Rheumatology, Edward Hines Jr Hospital, Veterans Administration, Hines, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Metabolic and Crystal Arthropathies Poster I  
Session Type: ACR Poster Session B  
Session Time: 9:00AM-11:00AM

Background/Purpose:
Despite the use of corticosteroids in acute gout, there exist wide variations in treatment doses and duration. No studies have evaluated the ideal dose of steroids for gout flares. However, occurrences of treatment failure and side effects from treatment warrant an evaluation for the lowest effective dosing. The goal of this double blinded prospective pilot study is to compare efficacies of a moderate dose and high dose prednisone course in treating acute gout.

Methods:
Male subjects age 18 years and older at Edward Hines Jr Hospital VA with acute gout were included. Patients with heart failure exacerbation, uncontrolled diabetes mellitus, infection, pseudogout, or chronic prednisone use were excluded. Subjects were randomized to a high or moderate dose of prednisone (high: 60mg on day 1, decreased by 10mg each day for a 6 day course; moderate: 30mg on day 1, decreased by 5mg each day for 6 days).

The primary endpoint was improvement in pain at 48 hours based on a 200mm visual analog scale. Secondary endpoints included the proportion of patients with resolution of synovitis by Day 7; absence of recurrent flares at 28 days; the proportion of patients who returned to baseline pain by day 7; and the number of days to return to baseline pain levels.

An intention-to-treat approach was used for analysis. Student t-test was used to compare mean values and Fishers exact test was used to compare proportions (STATA 11.1).

Results:
139 patients were screened, and 33 patients were enrolled between September 2007 and December 2014. All patients enrolled were male, with a mean age of 62.2 (± 11.8) and 63.4 (± 15.8) years in the moderate and high dose groups respectively. Results are summarized in Table 1. The mean percent improvement in pain severity at 48 hours was higher in the high dose group (51.9 vs 43.7%), though it did not achieve statistical significance. Of 26 patients examined at day 7, a higher proportion of patients in the moderate dose group experienced resolution of synovitis, though this finding did not reach statistical significance (0.75 in moderate group vs 0.36 in high group).

The proportion of patients back at baseline pain on day 7 was significantly higher in the moderate dose group (0.73 vs 0.26, p=0.013). The time to return to baseline pain levels was also shorter in the moderate dose group but did not achieve statistical significance.

<table>
<thead>
<tr>
<th>Response to Steroid Treatment</th>
<th>Moderate Dose</th>
<th>High Dose</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Percent improvement in pain severity at 48 hours (95% CI)</td>
<td>43.7 (28.7, 58.6)</td>
<td>35.9 (22.5, 71.8)</td>
<td>0.4073</td>
</tr>
<tr>
<td>n=16</td>
<td>n=16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of patients with resolution of synovitis at day 7 (95% CI)</td>
<td>0.75 (0.48, 1.62)</td>
<td>0.38 (0.08, 0.68)</td>
<td>0.002</td>
</tr>
<tr>
<td>n=12</td>
<td>n=14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of patients without recurrence of flares between days 7 and 28 (95% CI)</td>
<td>0.75 (0.52, 0.98)</td>
<td>0.73 (0.49, 0.97)</td>
<td>0.618</td>
</tr>
<tr>
<td>n=16</td>
<td>n=35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of patients who achieved baseline status based on pain scale (95% CI)</td>
<td>0.73 (0.49, 0.98)</td>
<td>0.26 (0.02, 0.51)</td>
<td>0.013</td>
</tr>
<tr>
<td>n=15</td>
<td>n=15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean days to return to baseline status based on pain scale (95% CI)</td>
<td>5.41 (4.23, 6.59)</td>
<td>6.2 (4.46, 7.46)</td>
<td>0.888</td>
</tr>
<tr>
<td>n=17</td>
<td>n=15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of patients who resumed functional status of affected joint at 48 hours (95% CI)</td>
<td>0.88 (0.72, 1.00)</td>
<td>0.87 (0.68, 1.00)</td>
<td>0.659</td>
</tr>
<tr>
<td>n=17</td>
<td>n=15</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusion:
In this randomized double blinded pilot study, there were no significant differences between the response of acute gout to high dose versus moderate dose prednisone at 48 hours and exam findings on day 7. Furthermore, the proportion of patients who returned to baseline pain levels was lower in the high dose group, contrary to what investigators hypothesized would occur. Despite size limitations of this pilot study, our findings warrant larger trials to establish a standardized, evidence based practice for appropriate dosing of steroids in acute gout.

Disclosure: R. A. Ostrowski, None; E. Araujo, None; R. Hariman, None; E. Adams, None.
Risk of Cardiovascular Events in Older Patients with Gout Initiating Probenecid Versus Allopurinol: A Population-Based Cohort Study

Seoyoung C. Kim1, Tuhina Neogi2, Eun Ha Kang3, Jun Liu4, Rishi J. Desai5, MaryAnn Zhang6 and Daniel H. Solomon7,
1Rheumatology, Immunology and Allergy; Pharmacoepidemiology and Pharmacoeconomics, Brigham and Women's Hospital, Boston, MA,
2Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA,
3Division of Rheumatology, Department of Internal Medicine, Division of Rheumatology, Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, Korea, Republic of (South),
4Division of Pharmacoepidemiology and Pharmacoeconomics, Brigham and Women's Hospital, Boston, MA,
5Division of Pharmacoepidemiology and Pharmacoeconomics, Brigham and Women's Hospital, Boston, MA,
6Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA,
7Brigham and Women's Hospital and Harvard Medical School, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Metabolic and Crystal Arthropathies Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Gout is associated with an increased risk of cardiovascular (CV) disease including myocardial infarction (MI), stroke and heart failure (HF). Although both probenecid and allopurinol have been available for treatment of gout for many decades, no studies have directly compared CV safety of these drugs. Both drugs lower uric acid through different mechanisms and have other pharmacologic effects possibly tied to CV disease.

Methods: To determine comparative CV safety of probenecid versus allopurinol, we conducted a cohort study of gout patients enrolled in Medicare (2008-2013). Gout patients aged ≥65 years who initiated probenecid or allopurinol were identified with having continuous enrollment in Parts A/B/D for ≥1 year free of a given drug prior to the 1st dispensing date (i.e., index date). Patients with ESRD, dialysis or renal transplant were excluded. The primary outcome was a composite CV endpoint of MI or stroke using a validated claims-based algorithm (PPV>94%). Secondary outcomes included MI, stroke, coronary revascularization, and HF. Follow-up time started from the day after the index date to the earliest CV endpoint, drug discontinuation, nursing home admission, death, or end of study period. To control for ≥50 potential confounders at baseline, probenecid initiators were matched to allopurinol initiators on a propensity score (PS) with a ratio of 1:3. Incidence rates (IR) and hazard ratios (HR) were estimated in the PS-matched cohort. We also conducted subgroup analyses among patients with no known CV disease or chronic kidney disease (CKD) at baseline.

Results: We included a total of 9,722 probenecid initiators PS-matched on 29,166 allopurinol initiators with mean (± SD) age of 76 (± 7) years and 54% were men. All the baseline covariates were well-balanced between the two PS-matched groups. During the 365-day baseline period prior to the index date, 28% had evidence of CVD, 27% HF, 45% diabetes, and 28% CKD. 71% had any use of colchicine, 48% opioids, and 35% oral steroids at baseline. The IR of MI or stroke per 100 person-years was 2.29 in probenecid and 2.82 in allopurinol initiators with HR of 0.78 (95%CI 0.67-0.90). In the secondary analyses, probenecid was associated with a decreased risk of MI, stroke and HF exacerbation versus allopurinol (see Table). Subgroup analyses in probenecid initiators vs. allopurinol showed consistent results with HR of 0.82 (95%CI 0.67-0.99) for the composite CV endpoint of MI or stroke among those without baseline CV disease and HR of 0.84 (95%CI 0.70-1.01) in those without baseline CKD.

Conclusion: In this large cohort study of 38,888 elderly gout patients enrolled in Medicare, use of probenecid appears to be associated with a modestly decreased risk of CV events including MI, stroke and HF exacerbation compared to allopurinol. Previous research has found direct positive CV effects of probenecid, suggesting that it should be investigated as a potential CV treatment.
Table. Risk of cardiovascular events in probenecid initiators versus allopurinol: 1:3 fixed ratio PS-matched

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Probenecid (n=9,772)</th>
<th>Allopurinol (N=29,166)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Event (n)</td>
<td>Person-years</td>
</tr>
<tr>
<td>MI or stroke</td>
<td>203</td>
<td>8,611</td>
</tr>
<tr>
<td>MI</td>
<td>121</td>
<td>8,670</td>
</tr>
<tr>
<td>Stroke</td>
<td>83</td>
<td>8,695</td>
</tr>
<tr>
<td>Coronary revascularization</td>
<td>213</td>
<td>8,550</td>
</tr>
<tr>
<td>New onset HF a</td>
<td>289</td>
<td>6,665</td>
</tr>
<tr>
<td>HF exacerbation b</td>
<td>590</td>
<td>1,600</td>
</tr>
</tbody>
</table>

* IR is per 100 person-years among the subgroup of patients with no baseline history of HF

a among the subgroup of patients with baseline history of HF, only counting the 1st exacerbation after the index date

Disclosure: S. C. Kim, None; T. Neogi, None; E. H. Kang, None; J. Liu, None; R. J. Desai, None; M. Zhang, None; D. H. Solomon, Amgen, 2.


Abstract Number: 1114

Effects of Diacerein Controlled Release Tablets in Serum Uric Acid Reduction in Treating Subjects with Gout

Ying-Chou Chen Sr.1, Shih-Chueh Chen2, Chung-Tei Chou3, Carl Brown4, Jing-Yi Lee4, Wei-Shu Lu5 and Chang Youh Tsai6,

1Division of Rheumatology, Allergy and Immunology, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung County, Taiwan, 2Department of Endocrinology, Cheng Ching General Hospital, Taichung, Taiwan, 3Division of Allergy-Immunology-Rheumatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, 4Medical Research, TWi Biotechnology, Inc., Taipei, Taiwan, 5TWi Biotechnology, Inc., Taipei, Taiwan, 6Division of Allergy-Immunology-Rheumatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan

First publication: September 18, 2017

SESSION INFORMATION
Background/Purpose: The goal of gout treatment is to reduce serum uric acid (sUA) concentrations below the urate solubility limit. Diacerein is known as an oral IL-1β modulator and also discovered to possess uric acid-lowering effects by inhibiting urate transporter 1 (URAT1). This study was a randomized, placebo-controlled multicenter, 16-week Phase 2 study designed to test the urate-lowering effects, safety and tolerability of diacerein controlled release tablets (CR), which is designed for bioavailability and pharmacokinetic improvement, and adverse effect alleviation as compared with the currently available immediate-release oral formulation.

Methods: The study comprised 4 periods of 4 weeks each: blinded study medication only, combination with febuxostat 40 mg once daily (QD), study medication plus febuxostat with titration to 80 mg febuxostat QD for those not achieving sUA <6 mg/dL, and finally febuxostat alone. A total of 127 subjects with hyperuricemia and gouty arthritis were randomized to diacerein 100 mg or placebo twice daily (BID). Subjects were Asian, primarily male, mean age 47 years, mean duration of gout 8.7 years, and mean sUA 9.0 mg/dL at baseline.

Results: The study was powered to show a difference in proportion of subjects achieving target sUA <6 mg/dL at Week 8 with significance assessed at a 1-sided p-value <0.05. Significantly more diacerein than placebo subjects (64% vs 55%) achieved the endpoint (p = 0.0337). Also, more diacerein subjects achieved sUA <5 mg/dL at Week 8 (39% vs 27%; p=0.0140). The overall flare rate was not different between groups. There were no serious adverse events in either group; 6% of diacerein subjects withdrew due to an adverse event. The most common adverse events with diacerein were diarrhea (27%) and soft stools (13%).

Conclusion: This study showed that treatment with diacerein 100 mg BID increased the odds of achieving the clinical sUA target of <6.0 mg/dL at Week 8, after 4 weeks of treatment with diacerein alone and 4 weeks of diacerein in combination with 40 mg febuxostat QD. Treatment with diacerein was shown to be safe and well tolerated with no new safety trends noted in this study. In combination with a low-dose xanthine oxidase inhibitor, diacerein could be a potential formulation to increase the percentage of gout patients who reach the sUA target without increasing flare rates.

<table>
<thead>
<tr>
<th>Table 1. Demographic and Baseline Characteristics</th>
<th>Diacerein 100 mg BID (N = 67)</th>
<th>Placebo BID (N = 60)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years) – Mean (SD)</strong></td>
<td>47.2 (11.7)</td>
<td>47.5 (13.1)</td>
</tr>
<tr>
<td><strong>Gender – n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>62 (92.5)</td>
<td>59 (98.3)</td>
</tr>
<tr>
<td>Female</td>
<td>5 (7.5)</td>
<td>1 (1.7)</td>
</tr>
<tr>
<td><strong>Race – n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>67 (100)</td>
<td>60 (100)</td>
</tr>
<tr>
<td>sUA (mg/dL) at baseline – Mean (SD)</td>
<td>9.1 (1.7)</td>
<td>8.9 (1.5)</td>
</tr>
<tr>
<td><strong>Weight (kg) – Mean (SD)</strong></td>
<td>76.6 (12.9)</td>
<td>78.1 (15.0)</td>
</tr>
<tr>
<td><strong>Gout duration (yr) – Mean (SD)</strong></td>
<td>9.0 (7.8)</td>
<td>8.3 (8.4)</td>
</tr>
<tr>
<td><strong>Flares in prior year – Mean (SD)</strong></td>
<td>3.0 (3.8)</td>
<td>2.2 (2.4)</td>
</tr>
<tr>
<td><strong>Subjects w/ tophus – n (%)</strong></td>
<td>6 (9.0)</td>
<td>4 (6.7)</td>
</tr>
<tr>
<td><strong>Metabolic disease history – n (%)</strong></td>
<td>41 (61.2)</td>
<td>35 (58.3)</td>
</tr>
</tbody>
</table>

SD = standard deviation.
Table 2. Proportion of Subjects Achieving sUA <6.0 and <5.0 mg/dL at Week 8

<table>
<thead>
<tr>
<th></th>
<th>Diacerein 100 mg BID (N = 67) n/N (%)</th>
<th>Placebo BID (N = 60) n/N (%)</th>
<th>p-value 1-sided</th>
</tr>
</thead>
<tbody>
<tr>
<td>sUA &lt;6.0</td>
<td>43 / 67 (64.2%)</td>
<td>33 / 60 (55.0%)</td>
<td>0.0337</td>
</tr>
<tr>
<td>Odds Ratio (95% CI)</td>
<td>2.1069 (0.9508, 4.6687)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>sUA &lt;5.0</td>
<td>26 / 67 (38.8%)</td>
<td>16 / 60 (26.7%)</td>
<td>0.0139</td>
</tr>
<tr>
<td>Odds Ratio (95% CI)</td>
<td>2.5352 (1.0955, 5.8667)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CI = confidence interval.

Disclosure: Y. C. Chen Sr., None; S. C. Chen, None; C. T. Chou, None; C. Brown, TWi Biotechnology Inc., 3; J. Y. Lee, TWi Biotechnology Inc., 3; W. S. Lu, TWi Biotechnology Inc., 3; C. Y. Tsai, None.


Abstract Number: 1115

Long-Term Adherence to Urate-Lowering Therapy in Gout: Do Not Blame on the Patients

Fernando Perez-Ruiz1 and Sandra Chinchilla2, 1Rheumatology Division, Hospital Universitario Cruces, Baracaldo, Spain, 2BioCruces Health Research Institute, Barakaldo, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Metabolic and Crystal Arthropathies Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: adherence to urate-lowering treatment (ULT) in patients with gout is reported to be lower than 50% in the first year and below 20% at 2-year, and worse than in other chronic conditions such as hypertension, diabetes, or hyperlipidemia. This was to evaluate adherence to ULT both overall and during follow-up, to compare it to the adherence to medications for associated comorbidities, and to explore potential causes for non-adherence to ULT.

Methods: transversal study of a nested cohort of patients in a gout-office hospital setting who were scheduled for a follow-up visit during 6 months in 2016. General data of patients, along with variables related to gout and to comorbid conditions are systematically retrieved at first visit; prescribed ULT, doses, adherence, and serum urate levels were obtained during the follow-up visits. Adherence was retrieved as medication possession rate (MPR) according to pharmacy offices from government electronic databases (including >98% of the general population). Also, MPRs of drugs prescribed for hypertension, diabetes (only oral), and hyperlipidemia were obtained; if more than one drug prescribed for any of the previous, the best adherence per comorbidity treatment was entered. Good adherence was considered as MPR>80 per cent of that prescribed, target serum urate (sUA) as <0.36 mmol/L.

Patients are educated at first visit and encouraged to be adherent from baseline through to follow-up visits.

Results: adherence data were available from de 209 patients who were scheduled for a follow-up visit during the observation period; 14 (6.7%) patients did not attend the visit. This sample was formed by 90% male, only 55% had received ULT previous to first visit, median age was 65 years at follow-up visit, 47% and 44% showed poliarticular and tophaceous disease at baseline, respectively. MPR overall showed a median of 89% (IQR 79-94, N= 209) for ULT (72% showed MPR>80), and 89% (IQR 81-94, N=119), 88% (IQR 79-94, N= 65), and 82% (IQR 77-93, N= 28) for hypertension, hyperlipidemia, and diabetes respectively (p<0.05 only for diabetes).

Adherence was lower for patients who did not attend the scheduled visit (median MPR 58% vs. 86%, MPR > 80, 21% vs. 75%, p<0.01). Adherence was lower during the first year (80%, N=67) compared to 2-3 year period (86%, N=67) or 4 or over (89%, N=75). MPR>80 were 57%, 76% y 81% for the same periods of follow-up, respectively. Good adherence was associated to a rate of target serum urate of 90%, compared to 72% for patients showing MPR<80.
Male gender and un-attendance to scheduled visit were statistically associated to MPR<80 in multivariate analysis; rate of achieving MPR80 was numerically higher with increasing age and overall comorbidity.

**Conclusion:** adherence to ULT measured as MPRs in a cohort of educated patients is good, sustained during follow-up, and similarly good to that for comorbid conditions (hypertension, hyperlipidemia, and diabetes); therefore, we cannot blame poor adherence on the patients any more. Avoiding absenteeism could be an opportunity for further improvement.

**Disclosure:** F. Perez-Ruiz, Asociacion de reumatologos de Cruces, 2,Grünenthal, 5,Grünenthal, 8, Menarini, 5, Menarini, 8; S. Chinchilla, None.


**Abstract Number:** 1116

**Management of Acute Gout in Hospitalized Patients and Risk Factors for Xanthine Oxidase Inhibitor (XOI) Discontinuation or Dose Reduction**

**Dawen Zhang**, Kichul Ko, Michael A. Becker and Reem Jan, Medicine, Rheumatology, University of Chicago, Chicago, IL, Medicine, University of Chicago, Chicago, IL

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Metabolic and Crystal Arthropathies Poster I  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Patients with gout frequently have multiple serious co-morbidities, take concomitant medications, and have complex clinical profiles, making treatment of acute flares in hospital settings difficult. We evaluated the current management of inpatient acute gout in an academic tertiary-care hospital.

**Methods:** Retrospective data review of acute gout flares occurring during hospitalization at the University of Chicago Medical Center in the period 01/01/2013 to 10/01/2015 was undertaken. To be included, a rheumatology consulting service had to have confirmed acute gout (ICD-9 code 274.xx) as a primary or secondary diagnosis. We reviewed demographics, comorbidities, gout flare characteristics, serum uric acid and creatinine levels, and treatment of gout flare. Multivariate logistic regression was performed to determine factors associated with discontinuation or dose reduction of baseline XOI therapy.

**Results:** 112 patients were included in the study. Mean patient age was 63.8 ± 13.7 (SD) years, and 75% were male. Baseline characteristics included a prior history of gout (70%), chronic kidney disease (58%), heart failure (47%), and diabetes mellitus (37%). Active infection (34%) and acute kidney injury (43%) were common preceding the acute gout attack. Mean serum urate levels during flares were 8.2 ± 2.7 (SD) mg/dL, but 29% of values were ≤ 6.0 mg/dL. Treatments for acute attacks included non-steroidal anti-inflammatory drugs (2%), colchicine (18%), intra-articular steroids (49%), and systemic steroids (64%). 79% of systemic steroid administration were administered to patients at high risk for steroid-induced complications, including heart failure, diabetes, active infection, or immediate post-operative status. In patients on baseline XOIs prior to admission, discontinuation or dose reduction occurred in 33% (18/54) of cases. Multivariate logistic regression analysis, when adjusted for age and sex, revealed discontinuation or dose reduction of baseline XOI therapy was more likely in patients with acute kidney injury (OR: 8.34, 95% CI [2.04, 43.22]), but less likely when acute gout was the primary reason for hospitalization (OR: 0.086, 95% CI [0.0038, 0.70]). 23% of patients with a prior history of gout were not on urate lowering therapy despite meeting ARA criteria for acute gout.

**Conclusion:** Acute gout treatment in hospitalized patients is complicated by a high prevalence of comorbidities, multiple concomitant medications, and acute organ dysfunction. Systemic steroids are ordered frequently for hospitalized patients with acute gout that are at risk for steroid-induced complications. Discontinuation or dosage reduction of XOIs during hospitalization commonly occurs during acute kidney injury, but the evidence basis for this remains to be established.

**Disclosure:** D. Zhang, None; K. Ko, None; M. A. Becker, Takeda Pharmaceuticals, 2, Horizon, 2, Ardea Biosciences/AstraZeneca and Ironwood, 2, Takeda Pharmaceuticals, 5, Horizon, 5, Ardea Biosciences/AstraZeneca and Ironwood, 5, CymaBay Therapeutics, 5; R. Jan, None.
the Absolute Risk of Clinically Diagnosed Gout By Serum Uric Acid Levels – Results from 30 Years Follow-up of the Malmö Preventive Project Cohort in Southern Sweden

Meliha C. Kapetanovic, Peter M Nilsson, Carl Turesson, Martin Englund, Nicola Dalbeth, Lieke E.J.M. Scheepers and Lennart TH Jacobsson

1Lund University, Skane University Hospital, Department of Rheumatology, Lund, Sweden, Lund, Sweden, 2Department of Clinical Sciences, Lund University, Skåne University Hospital Malmö, Sweden., Lund, Sweden, 3Department of Rheumatology, Skåne University Hospital, Malmö, Sweden, 4Clinical Sciences Lund, Orthopedics, Clinical Epidemiology Unit, Lund University, Lund, Sweden, 5University of Auckland, Auckland, New Zealand, 6Department of Rheumatology and Inflammation Research, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Metabolic and Crystal Arthropathies Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Hyperuricemia i.e. increased s-uric acid levels (s-UA), is established risk factor for clinical gout. Studies regarding the absolute and relative effect on population level have suggested a dose-dependent increase in risk of developing gout with increasing serum urate level (1). We aimed to explore the long-term risk of developing gout among asymptomatic adults with different levels of baseline hyperuricemia who participated in Malmö Preventive Project (MPP).

Methods: MPP is a screening program for cardiovascular risk factors, alcohol abuse and breast cancer in Malmö, Sweden. Overall, 33,346 individuals (67% male, mean age 45.7 years at inclusion, mean follow up 28.2 years) participated. The study population was screened between 1974 and 1992. A baseline health screening included: questionnaire with 260 questions (socioeconomic factors, alcohol consumption, smoking, physical activity, dietary habits, history of gout and other co-morbidities); physical examination (length, weight, blood pressure), and laboratory tests (s-UA, fasting glucose, s-creatinine). Endpoint was defined as date of first gout diagnosis, death, moving from area or December 31st 2014.

In order to identify all gout diagnoses (using ICD-codes) given at visits to physicians within primary care, specialized in-patient and out-patient specialized care, MPP cohort was linked to regional health care register and to national patient register, respectively. Baseline s-UA levels were stratified into 4 categories: normal levels (≤ 360 µmol /L; 361-405 (levels under tissue solubility of UA); 406-500 and >500. The absolute risks for gout by these s-UA strata are presented and Cox regression models are used to determine the relative risks; unadjusted and age-adjusted.

Results: Overall, 1279 individuals (3.8%), 1018 men (4.5%) and 261 women (2.4%) of these middle-aged subjects developed gout during the follow up. Of those with s-UA 406-500 and >500 µmol/L corresponding absolute risks were 14% and 21.7% (men) and 15.6% and 52.9 (women). Compared to subjects with low s-UA levels, subject with different levels of hyperuricemia had an increase HR for being diagnosed with gout, with HRs varying in men between 3 -15 and in women between 6 -106 (Table).

Conclusion: The risk for developing gout over 30 years in middle-aged subjects was 3.8% but varied considerably with baseline s-UA levels. Compared to normal S-UA levels, having s-UA>500 µmol/L was associated with 15- and 100-fold increased risk of gout in men and women, respectively. These results indicate the risk for developing gout in hyperuricemic subjects may be higher than previously reported.


Table. Risk of developing clinically gout over 30 years in man and women by different levels of baseline s-UA
<table>
<thead>
<tr>
<th>S-UA at baseline (µmol/L)</th>
<th>Absolute risk (%)</th>
<th>HR unadjusted (95%CI)</th>
<th>HR age adjusted (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men ≤360</td>
<td>2.7%</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>361-405</td>
<td>7.0%</td>
<td>2.8 (2.4-3.3)</td>
<td>2.8 (2.4-3.3)</td>
</tr>
<tr>
<td>406-500</td>
<td>14.0%</td>
<td>6.5 (5.6-7.6)</td>
<td>6.5 (5.6-7.6)</td>
</tr>
<tr>
<td>≥501</td>
<td>21.7%</td>
<td>15.3 (11.4-20.6)</td>
<td>15.0 (11.2-20.2)</td>
</tr>
<tr>
<td>Women ≤360</td>
<td>8.3%</td>
<td>6.1 (4.1-9.2)</td>
<td>5.1 (3.4-7.6)</td>
</tr>
<tr>
<td>361-405</td>
<td>15.6%</td>
<td>12.9 (8.4-19.9)</td>
<td>10.9 (7.0-16.8)</td>
</tr>
<tr>
<td>501</td>
<td>52.9%</td>
<td>106.1 (54.1-208.2)</td>
<td>84.7 (43.2-166.4)</td>
</tr>
</tbody>
</table>

Disclosure: M. C. Kapetanovic, None; P. M. Nilsson, None; C. Turesson, None; M. Englund, None; N. Dalbeth, Abbott Laboratories, 8; L. E. J. M. Scheepers, None; L. T. Jacobsson, Abbvie, Cellegem, MSD, Novartis and UCB, 5.


Abstract Number: 1118

Diabetes and Gout: Real-World Evidence Evaluating Patient Characteristics, Treatment Patterns, and Health Care Utilization

Douglas C.A. Taylor¹, An-Chen Fu¹ and Robert Morlock², ¹Ironwood Pharmaceuticals, Inc., Cambridge, MA, ²YourCareChoice, Ann Arbor, MI

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Metabolic and Crystal Arthropathies Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Gout and type 2 diabetes mellitus (T2DM) are common in the United States (US), but little is known about potential associations of T2DM and hyperuricemia/gout with clinical outcomes. This study examined variations in gout severity, management, and health care utilization among gout patients with and without T2DM.

Methods: Data were assessed from a survey of US physicians and patient chart audits. Participating physicians managed the care of ≥50 patients with gout annually; chart audits were of their last 5 consecutive adult patients with confirmed gout. Gout severity was measured by physician global assessment, flares, organ/joint damage, and tophi. Treatment characteristics, presence of clinician-confirmed T2DM, and sociodemographics were identified. Descriptive and multivariate (stepwise logistic regression) statistics analyzed the differences among gout patients with and without clinician-confirmed comorbid T2DM, and assessed urate-lowering therapy (ULT) use and gout control.

Results: Overall, 1159 charts of patients with gout were abstracted (246 with T2DM, 913 without T2DM; 80.50% male; 71.18% Caucasian); for patients with gout aged ≥61, a significantly higher proportion had T2DM than did not have T2DM (68.71% vs 31.29%, P<0.01). Patients with gout and T2DM had longer mean duration of gout (63 vs 41 months), were more likely to have tophi (37% vs 20%), joint damage (24% vs 13%), and clinician-rated severe gout (27% vs 13%) than those without T2DM (all P<0.01). Patients with gout and T2DM were also more likely to receive ULT (86% vs 71%; P<0.01), and among those receiving ULT, T2DM patients treated with allopurinol received a similar mean daily dose (321 mg vs 298 mg; P=0.17). Gout patients with T2DM were more likely to have additional comorbidities (cardiovascular disease, kidney disease, COPD, depression, diabetes, hyperlipidemia, hypertension, obesity, prostate problems [men]) and have chronic pain than those without T2DM (all P<0.05). Gout patients with T2DM reported more office visits (4.1 vs 3.5), were more likely to have an emergency department visit (17% vs 9%), and were more likely to be hospitalized (5% vs
2%) (all \( P<0.01 \)). In both groups, ULT use was associated with better gout control, but the specific factors predictive of ULT use and disease control varied between those with and without T2DM.

**Conclusion:** Gout patients with T2DM were more likely to have a greater impact on health system spending, with additional comorbidities and more severe gout than those without T2DM. These data suggest that patients with gout and T2DM constitute a less healthy group in need of careful monitoring and more aggressive gout management.

**Disclosure:** D. C. A. Taylor, Ironwood Pharmaceuticals, 1, Ironwood Pharmaceuticals, 3; A. C. Fu, Ironwood Pharmaceuticals, 1, Ironwood Pharmaceuticals, 3; R. Morlock, Ironwood Pharmaceuticals, 5.


**Abstract Number:** 1119

**Uncontrolled Gout Patients with Higher Heart Failure Hospitalization Rates in US**

Robert Morlock\(^1\), Pierre Chevalier\(^2\), An-Chen Fu\(^3\) and Douglas C.A. Taylor\(^3\), \(^1\)YourCareChoice, Ann Arbor, MI, \(^2\)IMS Health, Zaventem, Belgium, \(^3\)Ironwood Pharmaceuticals, Inc., Cambridge, MA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Metabolic and Crystal Arthropathies Poster I

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Gout is the most common form of inflammatory arthritis and is caused by elevated serum uric acid (sUA). Elevated sUA is associated with worsened outcomes in patients with heart failure, however, little is known about the association between gout and acute heart failure (AHF). The objective of this study was to assess the impact of gout control on the rate of hospitalization for AHF in a prevalent gout population.

**Methods:** A retrospective analysis using the IMS Pharmetrics Plus database from 01/01/2009 to 12/31/2011. Patients were required to have evidence of “prevalent established gout” (ie, treated with urate-lowering therapy [ULT] or eligible for ULT based on American College of Rheumatology [ACR] guidelines) between 01/01/2009 and 12/31/2009, be aged \( \geq 18 \) years on index date (01/01/2010), and have \( \geq 1 \) sUA measurement reported during the year of evaluation of gout control status. Follow-up extended from 01/01/2010 to 12/31/2011. AHF rate was calculated as percentage of eligible patients having \( \geq 1 \) AHF-related hospitalization over the course of calendar year 2011. In a given calendar year, patients were considered to have controlled gout if they had no elevated sUA (\( \geq 6 \) mg/dL), no diagnosis of tophus, and no flare documented, while uncontrolled gout was defined as \( \geq 1 \) elevated sUA or \( \geq 1 \) tophus diagnosis. The odds ratio (OR) of AHF was modeled using multivariable logistic regression adjusting for gout control status (in previous or current year), gender, age, and Charlson Comorbidity index as covariates.

**Results:** A total of 2,556 eligible gout patients with available sUA data in 2011 were identified in the US of which 67% had uncontrolled gout status (\( n=1,720 \)). The unadjusted AHF hospitalization rates were 1.51% (95% confidence interval [CI]: 0.93%-2.09%) in patients with uncontrolled gout in 2011 and 0.72% (95% CI: 0.14%-1.29%) in patients with controlled gout. After adjusting for the covariates, AHF rate was significantly higher in patients whose gout was uncontrolled during the same year (adjusted OR: 2.66 [\( P=0.037 \)]). Among the patients with available sUA data in 2010 (\( n=2,200 \)), there was a trend indicating that patients with uncontrolled gout in 2010 were at higher risk of AHF hospitalization in 2011 (adjusted OR: 2.54 [\( P=0.059 \)]).

**Conclusion:** This study suggests that patients with uncontrolled gout have a higher risk of being hospitalized for AHF. Further studies would be required to validate this finding on larger samples with availability of sUA data.

**Disclosure:** R. Morlock, Ironwood Pharmaceuticals, 5; P. Chevalier, IMSHealth, 3; A. C. Fu, Ironwood Pharmaceuticals, 1, Ironwood Pharmaceuticals, 3; D. C. A. Taylor, Ironwood Pharmaceuticals, 1, Ironwood Pharmaceuticals, 3.

Less Than Half of Patients Treated with High-Dose Allopurinol Reach Serum Uric Acid Target

Robert Morlock¹, Douglas C.A. Taylor² and Scott Baumgartner³, ¹YourCareChoice, Ann Arbor, MI, ²Ironwood Pharmaceuticals, Inc., Cambridge, MA, ³drB Consulting, Spokane, WA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Metabolic and Crystal Arthropathies Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Although allopurinol is FDA approved for up to 800 mg per day and EMEA authorized for up to 900 mg per day, most patients receive 300 mg per day or less. The objective of this study was to describe physician, patient, and treatment characteristics in gout patients treated with allopurinol and to assess the proportion of patients reaching serum uric acid (sUA) target by allopurinol dose.

Methods: Patient data from a quantitative survey of physicians were utilized and results confirmed through chart review. Initial and current dose of allopurinol, presence of co-morbid conditions, sUA lab results, physician specialty, and patient characteristics were assessed. Data on number of patients achieving target sUA ≤6mg/dL were also collected. Descriptive characteristics are presented as proportions or means and standard deviations (SD). Multivariate and descriptive statistics are used to describe patients with sUA ≤6 mg/dL.

Results: 251 rheumatologists and 250 primary care physicians were interviewed. Of 2505 patients with gout, 1437 (57%) were treated with allopurinol. Use of high-dose allopurinol significantly differed by country with less than 6.5% of patients in France, Germany, and Spain given >300 mg, whereas 10.2%, 19.5%, and 33.6% of patients in Italy, the US, and the UK, respectively, received a daily dose >300 mg (p<0.01). Over 12 months the percentage of patients achieving sUA ≤6.0 mg/dL differed across the 6 countries. Overall, across all countries, only 43.8% and 44.7% of patients achieved sUA <6.0 mg/dL with 301-599 mg and ≥600 mg of allopurinol daily, respectively. A multivariable-adjusted model found patients with tophi (OR 3.42; p<0.01), co-existing alcoholism (OR 1.73; p<0.05), chronic obstructive pulmonary disease (OR 2.02; p<0.05), smoking cessation treatment (3.49; p<0.05), and from the UK (OR 3.98; p<0.01) were more likely to be using >600 mg of allopurinol. Regardless of allopurinol dose, the co-variates UK vs. other countries (OR 3.51; p<0.01), time on therapy >24 months (OR 1.39; p<0.01), and chart-documented co-existing hypertension (OR 1.36; p<0.05) were predictive of achieving sUA <6 mg/dL, whereas physician sub-specialty [general practitioners vs. rheumatologists (OR 0.56; p<0.01)], having tophi (OR 0.72; p<0.05), and chart-documented co-existing alcoholism (OR 0.67; p<0.05), hyperlipidemia (OR 0.74; p<0.05), and kidney stones (OR 0.49; p<0.05) were found to be associated with not achieving sUA <6 mg/dL. After adjusting for confounding factors, over a 12-month period, there was no difference in achieving sUA <6 mg/dL for those treated with high- vs. low-dose allopurinol.

Conclusion: Allopurinol is approved for up to 800 mg in the US and 900 mg in the EU but the majority of patients are treated with ≤300 mg per day. Less than 50% of patients achieve sUA <6 mg/dL at any dose of allopurinol, and those on a higher dose of allopurinol are not more likely to reach this target. These data suggest a need for consideration of new treatment options on top of allopurinol for uncontrolled gout patients.


Allopurinol Treatment for Gout: How Long to Reach Serum Urate Goal?

Jean J. Lim¹,², An-Chen Fu², Jami Giordano², David S. Reasner² and Douglas C.A. Taylor², ¹Tufts University School of Medicine, Boston, MA, ²Ironwood Pharmaceuticals, Inc., Cambridge, MA

Abstract Number: 1121

Allopurinol Treatment for Gout: How Long to Reach Serum Urate Goal?

Jean J. Lim¹,², An-Chen Fu², Jami Giordano², David S. Reasner² and Douglas C.A. Taylor², ¹Tufts University School of Medicine, Boston, MA, ²Ironwood Pharmaceuticals, Inc., Cambridge, MA
Background/Purpose: Urate-lowering therapy (ULT) is essential in chronic gout management. For decades, allopurinol has remained the most frequently prescribed ULT. Reaching a goal of serum urate (sUA) level of <6.0 mg/dL has been suggested by gout management guidelines. However, limited studies have reported time duration needed to reach the sUA goal among allopurinol users. The aim of this study was to estimate time for allopurinol-treated gout patients to reach sUA goal.

Methods: This retrospective study used the Truven Health MarketScan® Database (Commercial). Study cohort included patients with a gout diagnosis during the study period (2010-2015), ≥1 allopurinol prescription fill during 2011-2015 (intake period, the earliest allopurinol date as index date), ≥90 days of allopurinol continuous therapy, ≥2 sUA results (the first sUA test was within 90 days before and 30 days after the index date; the second sUA test was after first sUA test and index date), aged ≥18 years on index date. Prevalent allopurinol users (allopurinol prescription fill during 1 year prior to index date) were excluded. Time duration to sUA goal was estimated from index date until reaching sUA goal of <6.0 mg/dL. Patients not reaching sUA goal were followed until end of therapy, health plan disenrollment, or end of 2015, whichever came first (censor date). Patient characteristics included age, gender, provider specialty, and initial dosage (ID) at the index date (used in subgroup analysis). Survival analyses of Kaplan-Meier estimators and unadjusted Cox proportional hazards regression model were conducted.

Results: There were 1404 patients included in the study cohort (Table 1) with a median time of 8 months to sUA goal (Figure 1). Stratifying by ID, the proportions of patients reaching sUA goal in 1 and 2 years were 36% and 49% with ID <300 mg versus 65% and 77% for patients with ID ≥300 mg (Figure 2).

Conclusion: Patients with gout who do not reach goal within 1 year using allopurinol, regardless of initial dosage, are unlikely to reach goal in the next year and therefore may benefit from additional treatment.
Figure 1. Time-to-event analysis estimating time to achieve sUA goal among gout patients taking allopurinol.

Figure 2. Time-to-event analysis of dosage subgroups estimating time to achieve sUA goal by initial allopurinol dosage (mg/day).

Disclosure: J. J. Lim, Ironwood Pharmaceuticals, Inc., 3; A. C. Fu, Ironwood Pharmaceuticals, 1, Ironwood Pharmaceuticals, 3; J. Giordano, Ironwood Pharmaceuticals, 3; D. S. Reasner, Ironwood Pharmaceuticals, 3; D. C. A. Taylor, Ironwood Pharmaceuticals, 1, Ironwood Pharmaceuticals, 3.

Jean J. Lim1,2, An-Chen Fu2, David S. Reasner2 and Douglas C.A. Taylor2, 1Tufts University School of Medicine, Boston, MA, 2Ironwood Pharmaceuticals, Inc., Cambridge, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Metabolic and Crystal Arthropathies Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Gout is the most common form of inflammatory arthritis, mainly caused by elevated serum uric acid (sUA) levels. The American College of Rheumatology guidelines recommend lowering sUA levels to <6 mg/dL for all patients with gout. Studies reported that elevated sUA levels are also associated with chronic kidney disease (CKD). It is suggested that urate-lowering therapy, predominantly xanthine oxidase inhibitors (XOIs), can potentially slow progression of renal disease. This study aims to estimate the prevalence of CKD among US adult patients with gout, both controlled (sUA <6 mg/dL) and uncontrolled (sUA ≥6 mg/dL), stratified by XOI treatment status.

Methods: The National Health and Nutrition Examination Survey (NHANES) is a large, cross-sectional study conducted by the National Center for Health Statistics using a multistage, complex sampling design. This study utilized NHANES (2007–2012) by combining interviews, physical examinations, and laboratory data. Participants aged ≥20 years with valid gout status, gender, race/ethnicity, and sUA/serum creatinine were included in the study sample. Participants were assumed to have gout if they had ever been told by a doctor or other health professional that they had gout. CKD stages were defined using both estimated glomerular filtration rate (estimated by the Chronic Kidney Disease Epidemiology Collaboration equation) and albumin-creatinine ratio. CKD stages were grouped into “normal to Stage 2 CKD,” “Stage 3a CKD,” and “Stage 3b-5 CKD”. Descriptive analyses were performed accounting for the survey’s complex sampling design to estimate the US population from the study sample.

Results: Out of 15,868 participants in NHANES 2007–2012 (representing 206 M US non-institutionalized population, aged 20 years or older), 715 participants had been told by a doctor that they had gout. These participants represented an estimated total of 7.7 M with gout (US prevalence of 3.7%). Among the gout population, 5.7 M (74%) had kidney function of normal to Stage 2 CKD, 1.1 M (15%) had Stage 3a CKD, and 0.8 M (11%) had Stage 3b-5 CKD. Of the gout population, 22% with normal to Stage 2 CKD, 42% with Stage 3a CKD, and 44% with Stage 3b-5 CKD were currently taking an XOI, most of whom were taking allopurinol. The majority of gout patients were uncontrolled regardless of CKD stage (63% of those with normal to Stage 2 CKD, 62% of those with Stage 3a CKD, and 72% of those with Stage 3b-5 CKD). Among those taking an XOI, 34% were uncontrolled and had normal to Stage 3a CKD (Figure 1).

Conclusion: The majority of non-institutionalized US adults who self-report that they have been diagnosed with gout have uncontrolled gout regardless of CKD stage. Even among those patients with gout who are taking an XOI, 34% are uncontrolled and have normal to Stage 3a CKD, and therefore, may benefit from alternative treatment options indicated for their CKD stage.
Random Urinary Uric Acid/Creatinine Ratio Is Useful in the Estimation of 24-Hour Urine Uric Acid Excretion in Patients with Gout

Sang Tae Choi¹, Seong-Jin Moon² and Eun-Jin Kang³, ¹Internal Medicine, Chung-Ang University College of Medicine, Seoul, Korea, Republic of (South), ²Internal Medicine, Catholic Kwandong University College of Medicine, Incheon, Korea, Republic of (South), ³Internal Medicine, Busan Medical Center, Busan, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Metabolic and Crystal Arthropathies Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Gout is a chronic inflammatory disease resulted from hyperuricemia. The measurement of 24-hour urinary uric acid excretion is frequently used to evaluate disease status and select drugs that lower uric acid level. However, 24-hour urine collection is cumbersome and inconvenient, and sometimes unreliable because of incomplete sampling. Approximately 1 g of creatinine is excreted into the urine on a daily basis, and the ratio of random urine protein to creatinine is known to be closely related to the amount of 24-hour urine protein excretion. Therefore, in this study, we assessed the utility of the random urinary uric acid/creatinine (UA/Cr) ratio in the estimation of 24-hour urine uric acid excretion in patients with gout.

Methods: Eighty-seven patients with gout without any use of uric acid lowering agents were enrolled in this study. The mean age was 49.8 ± 16.8 years old and the male patient was 89.6% (78/87). For the evaluation of uric acid excretion and renal function, patients were collected 24-hour urine. Random urine uric acid and creatinine specimens were gained on the same day of 24-hour urine collection. Chronic kidney disease was defined as a creatinine clearance (CCr) level of less than 60 ml/min/1.73m² measured in 24-hour urine collection sample. Excretion of more than 650 mg of uric acid in the 24-hour urine sample was defined as uric acid over-excretion.

Results: Mean serum uric acid level was 7.77 ± 1.92 mg/dl, and the mean 24-hour uric acid excretion and mean CCr value were 669.6 ± 237.9 mg and 109.6 ± 39.0 ml/min/1.73m², respectively. Random urinary UA/Cr ratio showed good correlation with the 24-hour urine uric acid excretion in the absolute and log-transformed value (γ = 0.413, p < 0.001; γ = 0.585, p < 0.001, respectively). Correlation...
between these two variables was also found in the patients with chronic kidney disease ($\gamma = 0.789, p = 0.011$). In the linear regression analysis, absolute 24-hour urine uric acid excretion was estimated to be $402 \times \text{random urinary UA/Cr ratio} + 218.73$ ($p < 0.001$). The best cut-off value for the random urinary UA/Cr ratio to distinguish between uric acid over-excretion and normal uric acid excretion was 0.533, and its sensitivity and specificity were 35.6% and 97.6%, respectively (AUC = 0.686; 95% CI, 0.576 - 0.796, $p = 0.003$).

**Conclusion:** There was a good correlation between the random urinary UA/Cr ratio and 24-hour urine uric acid excretions. The random urinary UA/Cr ratio would be a useful predictor of 24-hour urine uric acid excretion in patients with gout.

**Disclosure:** S. T. Choi, None; S. J. Moon, None; E. J. Kang, None.


**Abstract Number: 1124**

**Marked Variability of Circulating Urate Concentrations in Banked Samples Based on Sample Type and Assay**

**Evan M. Ryan**$^1$, Michael J. Duryee$^2$, Susan K. Dover$^3$, Elizabeth Schoenecker$^3$, Risa Urbauer$^3$, Flordeliza Faulkner$^3$, Nicole Norotsky$^3$, Harlan Sayles$^1$, Brian W Coburn$^4$, Samuel Pirruccello$^1$, Geoffrey M. Thiele$^1$ and Ted R. Mikuls$^5$, 1University of Nebraska Medical Center, Omaha, NE, 2Internal Medicine Division of Rheumatology, University of Nebraska Medical Center, Omaha, NE, 3U.S. Department of Veterans Affairs, Omaha, NE, 4Division of Rheumatology, University of Nebraska Medical Center, Omaha, NE, 5Internal Medicine, Division of Rheumatology, University of Nebraska Medical Center, Omaha, NE

**First publication:** September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017  
Session Title: Metabolic and Crystal Arthropathies Poster I  
Session Type: ACR Poster Session B  
Session Time: 9:00AM-11:00AM

**Background/Purpose:** Circulating urate is an important biomarker, not only in the detection and management of gout, but also in assessing the risk of related comorbidity. The impact of biobanking processes and assay type on uric acid (UA) measurement has been the subject of limited study but is important given the role of biorepositories in biomarker assessments. Thus, we analyzed banked samples of citrated $p$UA ($p$UA) and serum UA ($s$UA) using two separate assays and compared results to heparinized plasma UA ($p$UA) as part of routine care and abstracted from electronic health data.

**Methods:** Two clinical laboratories, one based at an academic medical center (Lab A) and the other at a VA affiliate (Lab B), measured $p$UA and $s$UA using banked samples from 30 rheumatic disease patients. Samples were collected using acid citrate dextrose ACD (plasma) and SST tubes (serum) between 2003 and 2017 and were stored at -70 °C until analysis. Lab A used the Beckman Coulter AU 5800 analyzer while Lab B used the VITROS URIC Slide method for UA measurement. UA measures were compared to lifetime average $p$UA concentrations measured as part of routine care and abstracted from electronic health data from 15 of the 30 patients.

**Results:** There was no association of $p$UA or $s$UA with year of sample collection. In contrast, mean ($\pm$SD) $s$UA was higher than $p$UA at Lab A (5.9 ± 1.7 mg/dl vs. 3.5 ± 1.5, $p$$<$$0.01$) and Lab B (6.0 ± 1.7 vs. 3.7 ± 1.9, $p$$<$$0.01$). Serum UA values from Lab A and Lab B were highly correlated ($r=0.98, p<0.01$) with less than 5% variability overall. In contrast, $p$UA values from the same samples differed on average by nearly 39% between Lab A and Lab B. Percent differences and correlations for the 4 measures are shown by lab and sample type (Table). Lifetime average $p$UA concentrations measured as part of routine care were similar to $s$UA values obtained from both labs using banked samples, but were on average 50 to 80% higher than $p$UA levels measured on banked samples (Table).

**Conclusion:** We observed a nearly 2-fold difference in UA values measured from banked serum compared to banked citrated plasma. Moreover, $p$UA values showed greater variability when measured in different laboratories with different assays, variability that did not appear to be related to the time elapsed from sample procurement. Compared to $p$UA values, $s$UA measures were much more strongly associated with $p$UA values measured in ‘real-time’ as part of routine care. Although additional study will be needed to understand the mechanisms driving these observations, these results suggest that UA measurement of banked citrated plasma leads to marked assay variability in addition to falsely low concentrations.
## UA Percent Difference and Correlation

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Mean Percent Difference</th>
<th>Correlation coefficient (r)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lab A CpUA vs. Lab A sUA</td>
<td>81.2%</td>
<td>0.83</td>
</tr>
<tr>
<td>Lab B CpUA vs. Lab B sUA</td>
<td>105.9%</td>
<td>0.63</td>
</tr>
<tr>
<td>Lab A sUA vs. Lab B sUA</td>
<td>4.9%</td>
<td>0.98</td>
</tr>
<tr>
<td>Lab B sUA vs. Lab A CpUA</td>
<td>38.5%</td>
<td>0.73</td>
</tr>
</tbody>
</table>

### Ratio of Lifetime Avg. \( \text{HpUA} \) Abstracted from Medical Record and \( sUA / CpUA \) Measured in Lab A and Lab B

<table>
<thead>
<tr>
<th>Lifetime Avg. ( \text{HpUA} / \text{Lab A sUA} )</th>
<th>Mean (SD)</th>
<th>Median (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.92 (0.34)</td>
<td>0.92 (0.39, 1.71)</td>
</tr>
<tr>
<td>Lifetime Avg. ( \text{HpUA} / \text{Lab B sUA} )</td>
<td>0.91 (0.27)</td>
<td>0.96 (0.39, 1.36)</td>
</tr>
<tr>
<td>Lifetime Avg. ( \text{HpUA} / \text{Lab A CpUA} )</td>
<td>1.53 (0.55)</td>
<td>1.54 (0.67, 2.50)</td>
</tr>
<tr>
<td>Lifetime Avg. ( \text{HpUA} / \text{Lab B CpUA} )</td>
<td>1.80 (1.04)</td>
<td>1.57 (0.43, 3.90)</td>
</tr>
</tbody>
</table>

Disclosure: E. M. Ryan, None; M. J. Duryee, None; S. K. Dover, None; E. Schoenecker, None; R. Urbauer, None; F. Faulkner, None; N. Norotsky, None; H. Sayles, None; B. W. Coburn, None; S. Pirruccello, None; G. M. Thiele, None; T. R. Mikuls, BMS, 2,Ironwood Pharm, 2,Pfizer Inc, 5,NIH, VA, 2.


Abstract Number: 1125

**Factors Associated with Acute Gouty Arthritis in Patients Hospitalized with Acute Coronary Syndromes and Congestive Heart Failure**

**Gabriela Montes-Rivera**\(^1\), Carla F Gamarra-Hilburn\(^2\), Lorena González-Sepúlveda\(^3\) and Luis M. Vilá\(^4\), \(^1\)Division of Rheumatology, University of Puerto Rico Medical Sciences Campus, San Juan, PR, \(^2\)Department of Medicine, Division of Rheumatology, University of Puerto Rico Medical Sciences Campus, San Juan, PR, \(^3\)Puerto Rico Clinical and Translational Research Consortium, University of Puerto Rico Medical Sciences Campus, San Juan, Puerto Rico, \(^4\)Department of Medicine, Division of Rheumatology, University of Puerto Rico Medical Sciences Campus, San Juan, Puerto Rico

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Metabolic and Crystal Arthropathies Poster I

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Hyperuricemia and untreated gout appears to be independent prognostic markers for poor all-cause and coronary heart disease mortality in patients with recent acute myocardial infarction. Moreover, gout attacks among patients with acute myocardial infarction are linked with short-term and long-term adverse non-fatal cardiac events. Similarly, serum uric acid levels correlate with morbidity and mortality of patients with congestive heart failure. However, the factors associated with gouty arthritis in patients presenting with acute cardiovascular events are not well known. Thus, we sought to study the demographic and clinical factors in patients with acute coronary syndromes and congestive heart failure who developed acute gout during hospitalization.
Methods: In-patient rheumatology consults of patients admitted to a cardiovascular hospital with either acute coronary syndromes (angina pectoris or myocardial infarction) or congestive heart failure between January 2006 and May 2015 were evaluated. Data on demographic parameters, type of medical insurance, primary diagnosis on admission, comorbidities, and pharmacologic treatment were compared between patients who developed acute gouty arthritis during hospitalization versus those who did not, using Chi-square test, Fisher’s Exact test and Student’s T test, as appropriate. Shapiro-Wilk test was used to assess normal distribution.

Results: A total of 189 patients admitted with acute cardiac events were consulted to the rheumatology service. Of those patients, 83 (43.9%) had acute gouty arthritis during the hospitalization. The mean (SD) age was similar between patients with and without acute gout [57.4 (15.0) vs. 58.7 (15.3) years, p=0.561]. Most patients with acute gout were men (92.8% vs. 33.0%, p < 0.001). Patients with acute gout were more likely to have chronic kidney disease (30.1% vs. 11.3%, p=0.001) and less likely to have systemic lupus erythematosus (0.0% vs. 14.2%, p < 0.001), rheumatoid arthritis (0.0% vs 13.2%, p < 0.001), hypothyroidism (4.8% vs. 15.1%, p=0.023), and exposure to antiplatelet therapy (8.4% vs. 27.4%, p=0.001) than those without acute gout. As expected, patients with acute gout had a previous history of gout (53.0% vs. 27.4%, p < 0.001) and were more commonly taking allopurinol (15.7% vs. 3.8%, p=0.005) and colchicine (19.3% vs. 1.9%, p < 0.001) at the moment of admission than those who did not present acute gout. However, of those with previous history of gout, only 30% were taking allopurinol at the moment of admission. No statistical differences (p > 0.05) were found for type of health insurance, arterial hypertension, diabetes mellitus, dyslipidemia, and exposure to diuretics and angiotensin receptor blockers.

Conclusion: Male gender, chronic kidney disease, and previous history of gout were associated with acute gout attack in this group of patients admitted with acute coronary syndromes and congestive heart failure. The awareness of these factors may help to recognize and manage patients promptly and prevent further complications in this population.

Disclosure: G. Montes-Rivera, None; C. F. Gamarra-Hilburn, None; L. González-Sepúlveda, None; L. M. Vilá, None.

Abstract Number: 1126

High Osteoprotegerin:RANKL Ratios in Synovial Fluid Correlate with the Presence of Calcium Pyrophosphate Crystals

Ian Chang1, Daisy Obiora2, Ann Rosenthal3 and Charlene J. Williams4, 1Medicine/Rheumatology, Medical College of Wisconsin, Milwaukee, WI, 2Urology, Cooper Hospital, Camden, NJ, 3Division of Rheumatology, Medical College of Wisconsin, Milwaukee, WI, 4Department of Biomedical Sciences, Cooper Medical School of Rowan University, Camden, NJ
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Metabolic and Crystal Arthropathies Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Calcium pyrophosphate deposition disease (CPDD) is a common cause of both acute and chronic arthritis in the elderly. It is estimated that twenty percent of patients with knee osteoarthritis (OA) have undiagnosed CPDD based on analysis of synovial fluid performed at the time of joint replacement. Calcium pyrophosphate (CPP) crystals can be difficult to identify in synovial fluid, and no biomarkers for CPPD currently exist.

Familial forms of CPDD have been recognized since the original descriptions of this disease. Associated mutations have been identified at one of two loci. One locus (CCAL2) is comprised of mutations in the ANKH protein, which is an ATP/Pi transporter. The second locus (CCAL2) codes for osteoprotegerin (OPG), a decoy receptor for the RANKL/RANK pathway. Little is known about ANKH and OPG levels in synovial fluids of patients with sporadic CPDD and whether these factors might be biomarkers for CPDD. We set out to measure ANKH, OPG and RANKL levels in synovial fluids from patients with chronic knee effusions with and without CPP crystals.

Methods:
Knee synovial fluids were obtained for diagnostic or therapeutic purposes at an academic rheumatology practice from patients with OA or chronic CPDD. No patients had clinical signs or symptoms of active inflammatory arthritis at the time of joint aspiration. De-identified synovial fluids were used with permission from the local IRB. All fluids were examined for crystals using compensated polarized light microscopy by an expert observer (AKR). Cell counts were not performed. Any fluids containing monosodium urate crystals were discarded. Fluids were aliquoted and stored at -20° C. Levels of OPG, ANKH, and RANKL were measured by ELISA and compared in groups with and without CPP crystals by a Mann Whitney test.

Results:

Thirteen synovial fluid samples were analyzed. Seven samples contained CPP crystals and 6 samples did not contain CPP crystals. Levels of ANK, OPG, and RANKL were measurable in all fluids (Table 1). CPDD fluids had statistically higher mean levels of OPG (p <0.026) and similar levels of RANKL compared to OA fluids. Mean ANKH levels were also higher in fluids with CPP crystals compared to OA fluids but this did not reach statistical significance due to the large variability of values. Mean OPG:RANKL ratios were 84.2 in CPDD fluids and 5.0 in OA fluids.

Table 1.

<table>
<thead>
<tr>
<th></th>
<th>OPG (ng/ug protein)</th>
<th>ANKH (ng/ug protein)</th>
<th>sRANKL (pg/ug protein)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OA</td>
<td>2.6 ± 2.5</td>
<td>8.2 ± 9.4</td>
<td>0.52 ± 0.32</td>
</tr>
<tr>
<td>CPDD</td>
<td>42.1 ± 26.1</td>
<td>64.3 ± 87.4</td>
<td>0.50 ± 0.34</td>
</tr>
</tbody>
</table>

Conclusion:

Synovial fluids from patients with OA or CPDD contain easily measurable quantities of ANKH, OPG, and RANKL. In this small pilot study of well-characterized fluids from patients with and without CPDD, we noted a very high ratio of OPG:RANKL in patients with CPDD. These findings provide additional support for the importance of OPG in CPDD pathogenesis. If validated in a larger study, the OPG:RANKL ratio may be a useful biomarker for CPDD.

Disclosure: I. Chang, None; D. Obiora, None; A. Rosenthal, None; C. J. Williams, None.


Abstract Number: 1127

Replication of Genetic Association of Peroxisome Proliferator-Activated Receptor Gamma-1B with Gout in a New Zealand Polynesian Sample Set

Amara Shaukat1, Tim Jansen2, M. Janssen3, Leo .A.B. Joosten4, Timothy Radstake5, Philip Riches6, Anne-Kathrin Tausche7, Jennie Harre Hindmarsh8, Nicola Dalbeth9, Lisa K. Stamp10 and Tony R. Merriman11,
1Univ Otago, Dunedin, New Zealand, 2VieCuri Medical Center, Venlo, Netherlands, 3Rheumatology Dept, Rijnstate Hospital, Arnhem, Netherlands, 4Internal Medicine, Radboud University Medical Center, Nijmegen, Netherlands, 5Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands, 6University of Edinburgh, Edinburgh, United Kingdom, 7Medizinische Klinik und Poliklinik III, Universitätsklinikum Carl Gustav Carus an der Technischen Universität Dresden, Dresden, Germany, 8Ngati Porou Hauora Charitable Trust, Te Puia Springs, New Zealand, 9University of Auckland, Auckland, New Zealand, 10University of Otago, Christchurch, New Zealand, 11Biochemistry Dept, PO Box 56, University of Otago, Dunedin, New Zealand

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Metabolic and Crystal Arthropathies Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Gout results from formation of monosodium urate (MSU) crystals in the presence of hyperuricemia. Genome wide association studies have provided significant insights into hyperuricemia, however, the genetic basis of the progression from hyperuricemia to gout is still unclear. Previously, Chang et al (Rheumatology 2016;56:457-466) reported an association of the
peroxisome proliferator-activated receptor gamma coactivator 1B (PPARGC1B) missense variant rs45520937 A-allele with gout risk in a Taiwan Han Chinese population (OR= 1.96, P= 4.0 × 10^{−10}) [1]. PPARGC1B is a regulator of NOD-like receptor family pyrin domain containing 3 inflammasome (NLRP3)-activated inflammation. Our aim was to replicate the rs45520937 association in New Zealand (NZ) Polynesian (Māori and Pacific) and European ancestral groups to investigate the association of PPARGC1B variant with gout.

**Methods:** A total of 2645 clinically-ascertained gout cases based on American Rheumatism Association 1977 criteria and 2125 controls were utilized from the NZ population. There were 1143 Māori and Pacific (Polynesian) people with gout and 1241 without gout. The European data set was comprised of people with gout from Germany, The Netherlands and Scotland (n=571), and New Zealand (n=931) and 884 people without gout. Taqman® genotyping of PPARGC1B rs45520937 was undertaken, followed by multivariate-adjusted association analysis in R 3.2.2 version with gout as the outcome.

**Results:** The A-allele was at a lower prevalence in European controls compared to Polynesian controls (0.055 vs 0.418). The A-allele of rs45520937 was associated with increased risk of gout in the Polynesian sample set (OR= 1.17 [1.02-1.35], P=0.02) but not in the European sample set (OR=0.96 [0.73-1.27], P=0.81).

**Conclusion:** We replicated the association between the PPARGC1B risk A-allele of rs45520937 and gout in the NZ Polynesian group. However this association was not evident in the European group suggesting that this population-specific effect is restricted to the Asia-Pacific region. PPARGC1B is one of several inducible nodes, including PPARγ and AMPK-activated protein kinase, in the complex regulatory network for damping NLRP3 inflammasome activation and the inflammatory arthritis phenotype in gout.

**Disclosure:** A. Shaukat, None; T. Jansen, None; M. Janssen, None; L. A. B. Joosten, None; T. Radstake, None; P. Riches, None; A. K. Tausche, None; J. Harre Hindmarsh, None; N. Dalbeth, Takeda, AstraZeneca, Abbvie, 9; L. K. Stamp, Amgen, 8; T. R. Merriman, Ardea Biosciences, 2.


---

### Effect of Urate-Lowering Treatment on the Risk of Urolithiasis in People with Gout

**Wen-Ching Lan**, Kuang-Hui Yu, Shue-Fen Luo, Chang-Fu Kuo and Tien-Ming Chan, Division of Rheumatology, Allergy and Immunology, Chang Gung Memorial Hospital, Taoyuan, Taiwan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Metabolic and Crystal Arthropathies Poster I  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Appropriate dose of urate-lowering therapy (ULT) is needed for gout patients to dissolve existing urate crystals to prevent acute gout attacks and reduce the risk of urate nephropathy and urolithiasis. This study aimed to investigate the associations between ULT use in different doses and the risk of urolithiasis in incident gout patients.

**Methods:**

We conducted a nested case-control study in a cohort of incident gout using the UK-based Clinical Practice Research Data-link (CPRD). Overall, 63,095 people with incident gout 1990–2010 were identified. Among them incidence cases of urolithiasis were identified and they were 1:4 age-, sex- and diagnosis year-matched to patients without urolithiasis Conditional logistic regression was used to estimate the association between cumulative defined daily dose (cDDD) and risk of urolithiasis.

**Results:**

We identified 700 gout patients with incident urolithiasis occurring after the initial diagnosis of gout aged 20-89 matched to 2,800 controls with incident gout but no urolithiasis. After adjusting for body mass index, smoking, alcohol consumption, pertinent drugs and comorbidities, the odds ratio (OR) of urolithiasis associated with use of ULT among gout patients were 1.41 (95% confidence interval
Conclusion:
Short-term and low dose ULT use was associated with an increased risk for urolithiasis while adequate ULT dose results in a neutral effect on urolithiasis risk.

Disclosure: W. C. Lan, None; K. H. Yu, None; S. F. Luo, None; C. F. Kuo, None; T. M. Chan, None.


Abstract Number: 1129

Impact of Diuretics on Urate Lowering Therapy in Patients with Gout: Analysis of an Inception Cohort

Laura Ranieri¹, Carolina Contero², Pedro Zapater³,⁴ and Mariano Andrés¹,⁵, ¹Sección de Reumatología, HOSPITAL GENERAL UNIVERSITARIO DE ALICANTE, Alicante, Spain, ²Departamento de Medicina Clínica, UNIVERSIDAD MIGUEL HERNÁNDEZ, Alicante, Spain, ³Sección de Farmacología Clínica, HOSPITAL GENERAL UNIVERSITARIO DE ALICANTE, Alicante, Spain, ⁴Departamento de Farmacología, Pediatría y Química Orgánica, UNIVERSIDAD MIGUEL HERNÁNDEZ, Alicante, Spain, ⁵Departamento de Medicina Clínica, Universidad Miguel Hernández, Alicante, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Metabolic and Crystal Arthropathies Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Diuretics have been associated with impaired response to allopurinol and refractoriness in gout, but whether this stills after new urate-lowering treatments (ULT) and treat-to-target strategies is unknown. The aim of this study was to assess the impact of the diuretic therapy on the response to ULT in patients with gout.

Methods: Retrospective analysis of an inception cohort of patients with crystal-proven gout (Jan2014-Nov2016). Patients were classified according to the type of ULT received and whether they were on diuretics (loop and/or thiazide) at baseline. The last visit of follow-up was registered. The primary outcome variables were a) reduction of serum uric acid (SUA) levels from baseline; b) achievement of different SUA targets (6, 5, and 4mg/dL); and c) maximum dose of ULT employed. Clinical, laboratory and ULT-related variables were also registered. A comparative analysis was performed according to the use of diuretics, using Student’s t and chi-2 tests, stratified by the type of ULT prescribed. Also, to properly determine the influence of diuretics on gout management (maximum dose of ULT used), a multiple linear regression model was built.

Results: The inception cohort included 225 patients with an average age of 65 years (SD 14.1), 86.2% of them men, with a median duration of gout at inclusion of 4 years (p25-75 1-10) and tophi in 21.3%. Follow-up data was available from 209 patients (92.9%), with a median 9 months of follow-up (4-14). A total of 98 patients (43.6%) were on diuretics, mainly for hypertension (64.7%), heart failure (9.4%), and renal failure (5.9%). These patients were older (p<0.001), had higher rates of females (p<0.001), hypertension (p<0.001), diabetes (p=0.001), and cardiovascular disease (p<0.001), and showed higher SUA (p=0.003) and lower glomerular filtration rate (p<0.001), compared to those not on diuretics. ULT used was allopurinol in 172 patients (82.6%) and febuxostat in 34 (16.5%) – benzbromarone was excluded due to minimal use (two cases). The table shows the outcome comparison according to diuretic treatment, stratified by type of ULT. Except for a lower achievement of SUA<5 in the allopurinol subgroup, no significant differences were found in SUA reduction and targets. Contrary to febuxostat, a trend to lower maximum dose of allopurinol in those on diuretics was noted, also in the bivariate analysis (β=-37.9, p=0.053, R²=0.022); however, this association was lost after multivariate adjustment for baseline characteristics (β=-18.1, p=0.499).

Conclusion: Despite its common use, diuretics currently show no significant impact on the achievement of treatment outcomes in patients with gout.
<table>
<thead>
<tr>
<th>Outcome variable</th>
<th>Diuretic therapy</th>
<th></th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Allopurinol (N=158)</td>
<td></td>
<td>N=92</td>
<td>N=66 (41.8%)</td>
</tr>
<tr>
<td>SUA reduction (mg/dL), mean (SD)</td>
<td></td>
<td>3.1 (1.9)</td>
<td>3.2 (2.0)</td>
</tr>
<tr>
<td>SUA&lt;6 (%)</td>
<td></td>
<td>80.6</td>
<td>74.2</td>
</tr>
<tr>
<td>SUA&lt;5 (%)</td>
<td></td>
<td>60.2</td>
<td>43.9</td>
</tr>
<tr>
<td>SUA&lt;4 (%)</td>
<td></td>
<td>28.0</td>
<td>21.2</td>
</tr>
<tr>
<td>Maximum dose (mg/day), mean (SD)</td>
<td></td>
<td>316.5 (126.9)</td>
<td>278.6 (121.8)</td>
</tr>
<tr>
<td>Febuxostat (N=33)</td>
<td></td>
<td>N=14</td>
<td>N=19 (57.6%)</td>
</tr>
<tr>
<td>SUA reduction (mg/dL), mean (SD)</td>
<td></td>
<td>3.7 (3.4)</td>
<td>5.6 (3.1)</td>
</tr>
<tr>
<td>SUA&lt;6 (%)</td>
<td></td>
<td>70.0</td>
<td>82.4</td>
</tr>
<tr>
<td>SUA&lt;5 (%)</td>
<td></td>
<td>70.0</td>
<td>76.5</td>
</tr>
<tr>
<td>SUA&lt;4 (%)</td>
<td></td>
<td>60.0</td>
<td>58.8</td>
</tr>
<tr>
<td>Maximum dose (mg/day), mean (SD)</td>
<td></td>
<td>80.0 (16.3)</td>
<td>80.0 (25.3)</td>
</tr>
</tbody>
</table>

Disclosure: L. Ranieri, None; C. Contero, None; P. Zapater, None; M. Andrés, Grunenthal, 5.


Abstract Number: 1130

**Can Alcohol Intake in Moderation Lower the Risk of Myocardial Infarction and Mortality Even Among Gout Patients?**

Sarah Keller¹, Sharan K. Rai², Na Lu¹, April Jorge³, Yuqing Zhang⁴ and Hyon K. Choi², ¹Rheumatology, Allergy and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, ²Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, ³Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, ⁴Department of Rheumatology, Allergy and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017

Session Title: Metabolic and Crystal Arthropathies Poster I

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM

**Background/Purpose:** Alcohol is a well-established risk factor for gout. However, more than 60 prospective studies have also shown that moderate alcohol intake is associated with a 25-40% reduced risk of coronary heart disease (CHD) and death. The American Heart Association (AHA) suggests that “If you drink alcohol, do so in moderation.” As gout is associated with an increased risk of CHD and premature mortality, the potential benefit of moderate alcohol use may also apply to gout patients. To address this question, we examined the relationship between alcohol intake, the risk of acute myocardial infarction (AMI) and all-cause mortality among gout patients in a general population context.

**Methods:** We conducted a cohort study using data from an EMR representative of the UK general population. The study population included individuals aged ≥20 years who had a diagnosis of gout between 1995 and 2015. The exposure of interest was the first alcohol intake measured after gout diagnosis. Study endpoints were incident cases of AMI and all-cause mortality. We estimated sex-specific hazard ratios (HR) according to alcohol intake category (i.e., 0, 1-9 [light drinking], 10-24 [moderate drinking], 25-42, and > 42 UK
alcohol units/week (1 unit = 8 mg). In the multivariable-adjusted regression model, we adjusted for age, smoking status, body mass index, duration of gout, presence of tophi, comorbidities, and medication use, including anti-gout medications. We performed a cubic-spline model analysis to depict the dose-response relationship between alcohol intake and all-cause mortality in a continuous manner.

Results: Among 55,584 gout patients (78% male, mean age of 63 years), 1,332 developed AMI and 8,362 died. The mean follow-up time was 5.6 years. As shown in the Figure, there is an apparent U-shaped relationship between alcohol intake after gout onset and the risk of AMI and all-cause mortality. Men who drank a moderate amount of alcohol had a lower risk of AMI and mortality. The multivariable HRs for developing AMI in men with gout were 1.0, 0.76 (95% CI, 0.63-0.93), 0.68 (0.55-0.83), 0.69 (0.53-0.89), and 0.71 (0.52-0.95) for each increasing alcohol intake category. The corresponding HRs for mortality were 1.0, 0.77 (95% CI 0.71-0.82), 0.74 (0.66-0.82), and 0.89 (0.78-1.01). While alcohol use and sample sizes were smaller among women, a similar U-shaped relationship was present. Women who drank > 42 UK units/week had the highest risk of mortality (HR 1.68 95% CI, 1.09-2.61).

Conclusion: This general population-based study indicates that moderate alcohol consumption is associated with a lower risk of AMI and all-cause mortality among gout patients, similar to general population studies. This finding suggest that the AHA recommendation regarding moderate alcohol use may apply to gout patients (for their cardiac health and improved survival) provided that their gout is well-controlled.

Disclosure: S. Keller, None; S. K. Rai, None; N. Lu, None; A. Jorge, None; Y. Zhang, None; H. K. Choi, Selecta, Horizon, 5,AstraZeneca, 2.


Abstract Number: 1131

The Dietary Approaches to Stop Hypertension (DASH) and Mediterranean Diets and Risk of Gout in Women: 28-Year Follow-up of a Prospective Cohort

Sarah Keller1, Sharan K. Rai2, Leo Lu3, Yuqing Zhang4 and Hyon K. Choi2, 1Rheumatology, Allergy and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, 2Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, 3Allergy, Immunology, and Rheumatology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, 4Department of Rheumatology, Allergy and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Metabolic and Crystal Arthropathies Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM
**Background/Purpose:** There is increasing recognition of a gout epidemic, exacerbated by an unhealthy diet and a sedentary lifestyle. Indeed, our recent study among men confirmed that the Western dietary pattern was associated with an increased risk of gout (Rai et al. BMJ 2017). In contrast, the Dietary Approaches to Stop Hypertension (DASH) diet was associated with a lower risk of gout (Rai et al. BMJ 2017). The extrapolation of these findings to women should be done with caution given the substantial difference in uric acid metabolism, gout incidence, and role of estrogen on serum uric acid levels. We aimed to examine the DASH, Mediterranean, and Western diets in relation to gout risk among women.

**Methods:** We evaluated the risk of incident gout in ~70,000 woman who reported a physician diagnosis of gout from 1984-2012. Using dietary intake information obtained from validated Food Frequency Questionnaires, we used a previously derived DASH diet score, emphasizing fruits, vegetables, nuts and legumes, whole grains, low-fat dairy foods, and reduced intake of saturated and total fat and sugar-sweetened beverages (SSBs). We also used a previously derived Mediterranean diet score, based on high intake of monounsaturated fat, plant proteins, whole grains, and fish, moderate intake of alcohol, and low consumption of red meat, refined grains, and sweets. Finally, we used a previously derived Western diet score, characterized by higher intakes of red and processed meats, SSBs, desserts, French fries, and refined grains. We assigned a diet score for each participant and prospectively examined the association between the diets and incident gout risk, adjusting for age, menopausal status, total energy intake, body mass index, diuretic use, hormone therapy use, hypertension, and alcohol and coffee intakes.

**Results:** During 28 years of follow-up, we documented 3,076 cases of incident gout. The DASH diet score was associated with a lower risk for gout (relative risk [RR] for extreme quintiles, 0.68 [CI, 0.60 to 0.76]; P<0.001 for trend). Similarly, the Mediterranean dietary pattern score was associated with a modestly lower risk for gout (RR for extreme quintiles, 0.86 [CI, 0.77 to 0.96]; P=0.05 for trend). In contrast, the Western diet score was associated with an increased risk for gout (RR, 1.56 [CI, 1.37 to 1.79]; P<0.001).

**Conclusion:** The DASH and Mediterranean diets are associated with a lower risk of incident gout in women, although the DASH diet shows an even greater protective benefit; conversely, the Western dietary pattern is associated with an increased risk of gout. These findings confirm the associations observed in the recent study among men and provide the first such prospective evidence among women. The DASH diet appears to offer an attractive dietary approach for gout, as it also reduces blood pressure among patients with hypertension, present in 81% of female gout patients (Zhu et al. Am J Med 2012).
<table>
<thead>
<tr>
<th>Model</th>
<th>Quintile 1</th>
<th>Quintile 2</th>
<th>Quintile 3</th>
<th>Quintile 4</th>
<th>Quintile 5</th>
<th>P for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dash Diet</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of incident gout cases</td>
<td>680</td>
<td>700</td>
<td>751</td>
<td>393</td>
<td>552</td>
<td></td>
</tr>
<tr>
<td>Person-years of follow-up</td>
<td>385859</td>
<td>400700</td>
<td>464194</td>
<td>275779</td>
<td>450160</td>
<td></td>
</tr>
<tr>
<td>Incidence rate (1/1000PYs)</td>
<td>1.76</td>
<td>1.74</td>
<td>1.62</td>
<td>1.43</td>
<td>1.23</td>
<td></td>
</tr>
<tr>
<td>Age-adjusted RR</td>
<td>1.00</td>
<td>0.91</td>
<td>0.81</td>
<td>0.70</td>
<td>0.59</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Age, BMI, alcohol, and calorie-adjusted RR</td>
<td>1.00</td>
<td>0.92</td>
<td>0.85</td>
<td>0.77</td>
<td>0.70</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Multivariable-adjusted</td>
<td>1.00</td>
<td>0.90</td>
<td>0.83</td>
<td>0.74</td>
<td>0.68</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td><strong>Mediterranean diet</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of incident gout cases</td>
<td>745</td>
<td>562</td>
<td>602</td>
<td>496</td>
<td>671</td>
<td></td>
</tr>
<tr>
<td>Person-years of follow-up</td>
<td>419458</td>
<td>340765</td>
<td>369724</td>
<td>342807</td>
<td>503958</td>
<td></td>
</tr>
<tr>
<td>Incidence rate (1/1000PYs)</td>
<td>1.78</td>
<td>1.65</td>
<td>1.63</td>
<td>1.45</td>
<td>1.33</td>
<td></td>
</tr>
<tr>
<td>Age-adjusted RR</td>
<td>1.00</td>
<td>0.95</td>
<td>0.95</td>
<td>0.84</td>
<td>0.75</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Age, BMI, alcohol, and calorie-adjusted RR</td>
<td>1.00</td>
<td>0.99</td>
<td>1.02</td>
<td>0.93</td>
<td>0.89</td>
<td>0.0338</td>
</tr>
<tr>
<td>Multivariable-adjusted</td>
<td>1.00</td>
<td>0.99</td>
<td>1.00</td>
<td>0.91</td>
<td>0.86</td>
<td>0.0048</td>
</tr>
<tr>
<td><strong>Western Diet</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of incident gout cases</td>
<td>485</td>
<td>591</td>
<td>605</td>
<td>620</td>
<td>775</td>
<td></td>
</tr>
<tr>
<td>Person-years of follow-up</td>
<td>408777</td>
<td>397780</td>
<td>390313</td>
<td>388145</td>
<td>391677</td>
<td></td>
</tr>
<tr>
<td>Incidence rate (1/1000PYs)</td>
<td>1.19</td>
<td>1.49</td>
<td>1.55</td>
<td>1.60</td>
<td>2.0</td>
<td></td>
</tr>
<tr>
<td>Age-adjusted RR</td>
<td>1.00</td>
<td>1.17</td>
<td>1.17</td>
<td>1.20</td>
<td>1.53</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Age, BMI, alcohol, and calorie-adjusted RR</td>
<td>1.00</td>
<td>1.13</td>
<td>1.14</td>
<td>1.19</td>
<td>1.52</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Multivariable-adjusted</td>
<td>1.00</td>
<td>1.15</td>
<td>1.16</td>
<td>1.21</td>
<td>1.56</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

Disclosure: S. Keller, None; S. K. Rai, None; L. Lu, None; Y. Zhang, None; H. K. Choi, Selecta, Horizon, 5, AstraZeneca, 2.


Abstract Number: 1132

**Compensated Polarized Microscopy for Crystal Identification Shows High Reliability Among Multiple Observers**

José Antonio Bernal¹, Mariano Andrés²,³, Salvador López-Salguero⁴, Vega Jovani⁵, Paloma Vela³,⁶ and Eliseo Pascual⁷,
¹Reumatología, Hospital Universitario del Vinalopó, Elche, Spain, ²Reumatología, Hospital General Universitario Alicante, Alicante,
SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Metabolic and Crystal Arthropathies Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
The gold standard for crystal-related arthritis diagnosis remains synovial fluid analysis by a microscope fitted with compensated polarized filters as it has been shown an immediate, valid, easy to learn, and reliable procedure (for the last, only in two studies not designed for this purpose). The objective was to analyze the agreement between multiple observers in crystal identification using a compensated polarized optic microscope. Finding good reliability results between multiple observers would reinforce the value of the technique.

Methods:
Cross-sectional, observational study performed at a single center with consecutive synovial fluid sampling. Samples were immediately analyzed when possible or kept refrigerated at 4ºC. Five different observers analyzed samples under a compensated polarized optical microscope to detect and identify crystals, independently and blinded to clinical data. All observations were performed at 400x fields. It was recorded the presence and type of crystal (No crystals; monosodium urate -MSU-; and calcium pyrophosphate dihydrate -CPPD-). Inter-rater agreement by Cohen’s kappa (k) statistic was measure. Also, sub-analyses were performed on a) time of sample visualization (£24 hours or >24 hours of sampling) and b) expertise in crystal identification (£10 years or > 10 years).

Results:
Synovial fluid samples were obtained mostly from knees (67.3%), ankles (13.2%) and wrist (6.8%) of patients seen at rheumatology clinic or during admissions. Main rheumatic diseases were gout (33.8%), rheumatoid arthritis (18.4%), CPPD related arthritis (15%) and arthritis under study (8.3%). A total of 31 samples were analyzed by all five observers (155 observations). Overall k was 0.76 (CI95% 0.63-0.89) thus indicating good agreement. Agreement for detection was k 0.75 (CI95% 0.61-0.90) and k for MSU was 0.91 (CI95% 0.76-1.05) while for CPPD was 0.66 (CI95% 0.47-0.84). Regarding secondary endpoints, no differences were noted neither between observations made before or after 24 hours (p 0.68 for k comparison), nor in expertise in crystal analysis (p 0.63 for k comparison).

Conclusion:
Even requiring agreement among multiple observers, compensated polarized microscopy remains consistent in the detection and identification of crystals in synovial fluid, confirming its high utility in clinical practice.

Disclosure: J. A. Bernal, None; M. Andrés, None; S. López-Salguero, None; V. Jovani, None; P. Vela, None; E. Pascual, AstraZeneca, 5,Grunenthal, 5.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/compensated-polarized-microscopy-for-crystal-identification-shows-high-reliability-among-multiple-observers

Abstract Number: 1133

Are We Ready? Changes in the Profile of Gout Patients over the Last 25 Years

Sandra Chinchilla1,2, Irati Urionagüena2,3 and Fernando Perez-Ruiz1,2,3, 1University of the Basque Country (UPV/EHU), Bilbao, Spain, 2BioCruces Health Research Institute, Barakaldo, Spain, 3Rheumatology Division, Hospital Universitario Cruces, Barakaldo, Spain
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Background/Purpose: Gout is a rising cause of hospital admissions and emergency consults. It has even replaced rheumatoid arthritis as the principal rheumatological condition causing hospitalizations. Some questions arise in this setting: What are the characteristics of our patients? How have they changed over the past years? Our objective is to analyze possible changes in the clinical profile of gout patients during a period of 25 years.

Methods: Data was collected from a prospective cohort of gout patients, from a crystal arthritis clinic in a tertiary hospital (reference population: half a million inhabitants). The period, between 1992 and 2016 (n = 1137) was reviewed, with division into five quinquennia (Q). All patients fulfilled ACR/EULAR 2015 gout classification criteria. When entering the cohort, epidemiologic, clinic, laboratory and imaging data are systematically collected. Variables susceptible to change in time were considered: age, gender, gout clinical data, previous admissions due to gout and comorbidities. Complex patients were defined as those who presented at the first visit with polyarticular disease and/or tophi plus chronic kidney disease and/or cardiovascular disease. Quantitative variables were analyzed with ANOVA and Bonferroni correction; qualitative variables with chi-square test. Inclusion of patients to the cohort was approved by the hospital ethics committee. Data from extreme quinquennia are reported (1stQ: 1992-1996 / 5thQ 2011-2016 or 2ndQ: 1997-2001 / 4th: 2006-2010). All results are statistically significant unless stated otherwise.

Results: Differences were observed regarding age at first visit (1stQ: 54.1 ± 10.9 / 5thQ: 64.6 ± 13.8 years) and gender (1stQ: 2.6% / 5thQ: 12.2% of women, respectively).

Initial comorbidities: See graph 1.

Initial clinical characteristics: See graph 2

The overall prevalence of complex patients was of 67.1%, with increasing incidence through time (1stQ: 53.9% / 5thQ: 77.1%). Globally, less than half of these patients (39.7%) had received urate lowering treatment prior to their first visit.

Conclusion: The profile of gout patients has notably changed in the past 25 years: we have elder, more complex patients, with higher rates of hospital admissions, with severe forms of disease and important comorbidities. Nevertheless, most of these complex patients have not been appropriately started on urate lowering therapy. When considering these results, we believe that a substantial proportion of gout patients will require specialized attention in the coming years.

Graph 1: Initial Comorbidities (%)

Initial comorbidities are shown over time, with categories including cardiovascular disease, renal disease, hypertension, and hyperlipidemia.
A Case Series of Gout and Downs Syndrome – a New Paradigm for Detecting Disease Associations Using Big Data

Ann Igoe1,2,3, Bryan A Roller4,5, Abbinaya Elangovan5,6, Kristin L Kaelber4,6 and David Kaelber4,5,6,7, 1Internal Medicine & Pediatrics, Metrohealth Medical Center, Cleveland, OH, 2Rheumatology, Metrohealth Medical Center, Cleveland, OH, 3Metrohealth Medical Center, Metrohealth Medical Center, Cleveland, OH, 4School of Medicine, Case Western Reserve, Cleveland, OH, 5Center for Clinical Informatics Research and Education, Metrohealth Medical Center, Cleveland, OH, 6Dept of Internal Medicine & Pediatrics, Metrohealth Medical Center, Cleveland, OH, 7Departments of Information Services, Metrohealth Medical Center, Cleveland, OH
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Metabolic and Crystal Arthropathies Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Down syndrome (Trisomy 21) is known to have higher prevalence of certain conditions including cardiac defects, hypothyroidism, hearing defects and early Alzheimer’s disease, but no studies have looked at the association between Downs syndrome and gout.

Objective: The aim of this study is to estimate the prevalence of gout among Down syndrome patients compared to non-down syndrome patients.

Methods: We reviewed electronic health record (EHR) data over 14 years (1999-2013) from 25,840,730 patients using a third-party cloud-based platform (Explorys, Cleveland OH). 994,793 patients from our institution (The MetroHealth System) were analyzed. International Classification of Disease – 9 (ICD-9) diagnoses codes were used to define Downs syndrome and gout. Prevalence data was

Disclosure: S. Chinchilla, Beqa BBK-BioCruces post MIR curso 2016-2017, 2; I. Urionagüena, None; F. Perez-Ruiz, Asociacion de reumatologos de Cruces, 2, Grünenthal, 5, Grünenthal, 8, Menarini, 5, Menarini, 8.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/are-we-ready-changes-in-the-profile-of-gout-patients-over-the-last-25-years

Abstract Number: 1134
compiled among patient diagnoses of Downs syndrome only, gout only, both Downs Syndrome and gout, and neither Downs Syndrome or gout. The odds ratio of a gout diagnosis in a Downs Syndrome patient relative to a non-Downs syndrome patient was calculated

**Results:** Among the almost 26 million patient cohort, the odds ratio of a gout diagnosis in a patient with Downs syndrome diagnosis compared to a patient without Downs syndrome diagnosis was 3.66 [95% CI 3.32-4.03] and within the MetroHealth system subset, the odds ratio was 4.26 [2.81-6.46].

**Conclusion:** In the setting of a Downs syndrome patient presenting with articular pain, gout should be higher on the differential diagnoses than in non-Downs syndrome patients. This study also illustrates the potential of aggregated EHR data from tens of millions of patients to create a new paradigm for case series and disease association identification.

**Table 1:** Metrohealth patients with both DS and gout.

<table>
<thead>
<tr>
<th>Case Series #</th>
<th>Sex</th>
<th>Race/Ethnicity</th>
<th>BMI (Kg/m²)</th>
<th>Age @ 1st Gout Diagnosis</th>
<th>Encounters w/ Gout ICD-9</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>♂</td>
<td>Caucasian</td>
<td>35.5</td>
<td>32</td>
<td>46</td>
</tr>
<tr>
<td>2</td>
<td>♂</td>
<td>Caucasian</td>
<td>24.6</td>
<td>40</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>♂</td>
<td></td>
<td>32.3</td>
<td>61</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>♂</td>
<td>Caucasian</td>
<td>20.1</td>
<td>30</td>
<td>17</td>
</tr>
<tr>
<td>5</td>
<td>♂</td>
<td></td>
<td>21.1</td>
<td>27</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>♂</td>
<td></td>
<td></td>
<td>46</td>
<td>4</td>
</tr>
<tr>
<td>7</td>
<td>♂</td>
<td></td>
<td>32.3</td>
<td>38</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>♂</td>
<td>African American</td>
<td>44.9</td>
<td>38</td>
<td>12</td>
</tr>
<tr>
<td>9</td>
<td>♂</td>
<td>Caucasian</td>
<td>36.2</td>
<td>31</td>
<td>5</td>
</tr>
<tr>
<td>10</td>
<td>♂</td>
<td>African American</td>
<td>45.8</td>
<td>32</td>
<td>55</td>
</tr>
<tr>
<td>11</td>
<td>♂</td>
<td></td>
<td>23.0</td>
<td>31</td>
<td>4</td>
</tr>
<tr>
<td>12</td>
<td>♂</td>
<td></td>
<td></td>
<td>43</td>
<td>1</td>
</tr>
<tr>
<td>13</td>
<td>♂</td>
<td>Caucasian</td>
<td>28.8</td>
<td>41</td>
<td>1</td>
</tr>
<tr>
<td>14</td>
<td>♂</td>
<td></td>
<td>32.3</td>
<td>52</td>
<td>2</td>
</tr>
<tr>
<td>15</td>
<td>♂</td>
<td>Caucasian</td>
<td>22.2</td>
<td>33</td>
<td>1</td>
</tr>
<tr>
<td>16</td>
<td>♀</td>
<td></td>
<td>87</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>17</td>
<td>♂</td>
<td></td>
<td></td>
<td>57</td>
<td>1</td>
</tr>
<tr>
<td>18</td>
<td>♀</td>
<td>Caucasian</td>
<td>38.5</td>
<td>41</td>
<td>2</td>
</tr>
<tr>
<td>19</td>
<td>♀</td>
<td></td>
<td></td>
<td>53</td>
<td>1</td>
</tr>
<tr>
<td>20</td>
<td>♀</td>
<td>Caucasian</td>
<td>27.2</td>
<td>75</td>
<td>10</td>
</tr>
<tr>
<td>21</td>
<td>♂</td>
<td>African American</td>
<td>23.4</td>
<td>43</td>
<td>8</td>
</tr>
<tr>
<td>22</td>
<td>♂</td>
<td></td>
<td>30.1</td>
<td>59</td>
<td>1</td>
</tr>
<tr>
<td>23</td>
<td>♀</td>
<td>African American</td>
<td>37.9</td>
<td>52</td>
<td>8</td>
</tr>
</tbody>
</table>

*a* Demographic and BMI

**Table 2:** Odds of simultaneous DS and gout stratified
<table>
<thead>
<tr>
<th>Attribute</th>
<th>Stratum</th>
<th>Cohorts(^c) (N)</th>
<th>All Cohorts</th>
<th>DS and Both Populations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Both</td>
<td>DS Gout Neither</td>
<td>OR(^a) (CI(^d))</td>
<td>OR(^b) (CI(^d))</td>
</tr>
<tr>
<td>Sex</td>
<td>Female</td>
<td>80 4,890 81,890 13,405,820</td>
<td>2.68 (2.15-3.44)</td>
<td>1 (Ref.)</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>340 5,200 191,310 11,353,200</td>
<td>3.88 (3.48-4.33)</td>
<td>4.00 (3.12-5.11)</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td>Caucasian</td>
<td>260 5,720 159,500 11,435,820</td>
<td>3.26 (2.88-3.69)</td>
<td>1 (Ref.)</td>
</tr>
<tr>
<td></td>
<td>African American</td>
<td>50 1,090 45,100 2,347,990</td>
<td>2.39 (1.80-3.17)</td>
<td>1.01 (0.74-1.38)</td>
</tr>
<tr>
<td></td>
<td>Asian</td>
<td>0 200 10520 542130</td>
<td>n/a (n/a)</td>
<td>n/a (n/a)</td>
</tr>
<tr>
<td></td>
<td>Hispanic</td>
<td>0 300 1820 430390</td>
<td>n/a (n/a)</td>
<td>n/a (n/a)</td>
</tr>
<tr>
<td></td>
<td>Other/Unknown</td>
<td>30 1430 26830 317750</td>
<td>2.48 (1.73-3.57)</td>
<td>0.46 (0.31-0.68)</td>
</tr>
<tr>
<td>BMI</td>
<td>Normal</td>
<td>80 2,220 47,310 3,162,740</td>
<td>2.41 (1.93-3.01)</td>
<td>1 (Ref.)</td>
</tr>
<tr>
<td></td>
<td>Overweight [25-30 Kg/m(^2)]</td>
<td>110 1,830 90,570 3,024,850</td>
<td>2.01 (1.66-2.43)</td>
<td>1.67 (1.24-2.24)</td>
</tr>
<tr>
<td></td>
<td>Obesity Class I [30-35 Kg/m(^2)]</td>
<td>120 1,380 79,290 1,861,410</td>
<td>2.04 (1.69-2.46)</td>
<td>2.41 (1.80-3.23)</td>
</tr>
<tr>
<td></td>
<td>Obesity Class II [35-40 Kg/m(^2)]</td>
<td>90 830 46,920 900,010</td>
<td>2.08 (1.67-2.59)</td>
<td>3.01 (2.20-4.11)</td>
</tr>
<tr>
<td></td>
<td>Obesity Class III [&gt; 40 Kg/m(^2)]</td>
<td>70 580 27,960 514,970</td>
<td>2.22 (1.73-2.85)</td>
<td>3.35 (2.40-4.68)</td>
</tr>
<tr>
<td>Age</td>
<td>&lt; 25</td>
<td>0 4920 500 5259510</td>
<td>n/a (n/a)</td>
<td>n/a (n/a)</td>
</tr>
<tr>
<td></td>
<td>25-29</td>
<td>20 650 1,140 1,516,400</td>
<td>40.93 (26.13-64.11)</td>
<td>1 (Ref.)</td>
</tr>
<tr>
<td></td>
<td>30-34</td>
<td>30 550 2,780 1,594,390</td>
<td>31.28 (21.62-45.26)</td>
<td>1.77 (1.00-3.16)</td>
</tr>
<tr>
<td></td>
<td>35-39</td>
<td>40 520 5,080 1,486,980</td>
<td>22.52 (16.30-31.09)</td>
<td>2.50 (1.44-4.33)</td>
</tr>
<tr>
<td></td>
<td>40-44</td>
<td>40 600 8,800 1,527,330</td>
<td>11.57 (8.40-15.95)</td>
<td>2.17 (1.25-3.75)</td>
</tr>
<tr>
<td></td>
<td>45-49</td>
<td>80 670 12,530 1,571,560</td>
<td>14.98 (11.87-18.90)</td>
<td>3.88 (2.34-6.41)</td>
</tr>
<tr>
<td></td>
<td>50-54</td>
<td>80 800 18,010 1,745,050</td>
<td>9.69 (7.70-12.20)</td>
<td>3.25 (1.97-5.36)</td>
</tr>
<tr>
<td></td>
<td>55-59</td>
<td>60 680 24,000 1,760,990</td>
<td>6.47 (4.97-8.43)</td>
<td>2.87 (1.71-4.81)</td>
</tr>
<tr>
<td></td>
<td>60-64</td>
<td>40 430 28,780 1,633,450</td>
<td>5.28 (3.82-7.30)</td>
<td>3.02 (1.74-5.24)</td>
</tr>
<tr>
<td></td>
<td>65-69</td>
<td>20 170 33,110 1,494,440</td>
<td>5.31 (3.34-8.44)</td>
<td>3.82 (2.01-7.27)</td>
</tr>
<tr>
<td></td>
<td>&gt;70</td>
<td>0 110 137920 5101390</td>
<td>n/a (n/a)</td>
<td>n/a (n/a)</td>
</tr>
</tbody>
</table>
Odds of a DS patient having a gout diagnose relative to a non-DS patient within a particular stratum.

Odds of a DS patient having a gout diagnoses relative to the reference stratum.

Cohorts do not total all 25,840,730 patients because attribute specific data is available for approximately 96% of patients.

All CI intervals are 95%.

Refer

Disclosure: A. Igoe, None; B. A. Roller, None; A. Elangovan, None; K. L. Kaelber, None; D. Kaelber, None.


Abstract Number: 1135

the Incidence of Knee Chondrocalcinosis and Its Risk Factors in Community-Based Cohort

Jae-Bum Jun1, Nam H. Cho2, Yoonah Song3, Seunghun Lee4 and Yoon-Kyoung Sung1, 1Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), 2Department of Preventive Medicine, Ajou University School of Medicine, Suwon, Korea, Republic of (South), 3Department of Radiology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), 4Department of Radiology, Hanyang University Hospital, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Metabolic and Crystal Arthropathies Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Chondrocalcinosis (CC) results from deposition of calcium pyrophosphate dihydrate (CPPD) in articular cartilage. It is a relatively common radiographic finding of the joints, especially the knee. This study investigated the incidence of knee CC and sought to identify the risk factors for the development of knee CC in the general population.

Methods: We used a prospective, ongoing cohort, composed of 5,018 people, which was established in 2001 to investigate the epidemiologic characteristics of major chronic diseases in Korea. The incidence of knee CC was assessed per 1,000 person-years, and the risk factors were explored by Cox proportional hazard regression analyses.

Results: A total of 4,319 patients who did not have knee CC at enrollment, year 2001-2002, were evaluated with a mean follow-up duration of 8.4 years (SD, 4.2 years). The crude incidence of knee CC was 3.19 per 1,000 person-years (women, 3.55; men, 2.70), and the whole cumulative incidence of knee CC was 2.7%. Older age (≥ 55 years) and higher HbA1C were associated with increased risk of knee CC.

Conclusion: This is the first study to report the incidence of knee CC in the general population. Older age and high HbA1C were independent risk factors for development of knee CC.
Urate-Lowering Treatment and Risk of Total Joint Replacement in Patients with Incident Gout: A Population-Based Cohort and Nested Case-Control Study

Jung-Sheng Chen, Chang-Fu Kuo, Ping-Han Tsai, Shue-Fen Luo and Kuang-Hui Yu, Division of Rheumatology, Allergy and Immunology, Chang Gung Memorial Hospital, Taoyuan, Taiwan

First publication: September 18, 2017

SESSON INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Metabolic and Crystal Arthropathies Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
This cohort study aimed to investigate the risk of total joint (hip/knee) replacement (TJR, THR and TKR) among patients with incident gout at initial diagnosis and subsequent periods. Furthermore, we estimate the exposure dose of urate-lowering treatment (ULT) on the TJR risk by using a nested case-control study.

Methods:
An incident gout cohort during 1995 to 2009 was retrieved from the UK Clinical Practice Research Datalink (CPRD) and were age-, sex and general practice-matched in a 1:4 ratio to controls. Multivariate odds ratios (ORs) for TJR at diagnosis and hazard ratios (HRs) for TJR after diagnosis were estimated adjusting for age, gender, Charlson comorbidity index, BMI level, smoking status, alcohol consumption and comorbidities. Adjusted ORs derived from conditional logistic regression were used to estimate the association between cumulative defined daily dose (cDDD) of urate-lowering treatment and TJR using a nested case-control design.

Results:
There were 40,160 incident gout patients diagnosed during study period and matched to 160,640 controls. Gout was associated with adjusted ORs (95% CIs) of 1.34 (1.15–1.57) for THR and 1.24 (1.02–1.51) for TKR at diagnosis. The incidence of both were higher in gout patients compared with their corresponding controls (3.72 vs 2.47 cases/1000 person-years for THR and 3.57 vs 2.31 cases/1000 person-years for TKR). Multivariate HRs (95% CIs) were 1.22 (1.10–1.35) for THR, 1.09 (0.99–1.21) for TKR and 1.14 (1.06–1.23) for...
TJR. Using a nested case-control study with gout cohort, ORs (95% CI) for TJR was 1.00 (0.83–1.20) for 1–180 cDDD of ULT, 1.03 (0.80–1.33) for 180–364 cDDD and 1.09 (0.94–1.27) for >365 cDDD compared with non-ULT user.

Conclusion:

Gout was associated with a higher risk of TJR at diagnosis and the risk continue to rise afterwards. TJR risk was not modified by ULT use after gout diagnosis.

Disclosure: J. S. Chen, None; C. F. Kuo, None; P. H. Tsai, None; S. F. Luo, None; K. H. Yu, None.


Abstract Number: 1137

Urate Lowering to ACR-Recommended Targets Allows Significant Improvement of Severe Gout: A Monocentric Prospective Trial in Vietnam, Using a Systematic Treatment Protocol

Thomas Bardin1,2,3, Quang Nguyen Dinh1, Khoi Tran Minh1, Nghia Le Hieu1, Minh Do Duc4, Pascal Richette5,6 and Matthieu Resche-Rigon3,7, 1French-Vietnamese Gout Research Center, Ho Chi Minh City, Viet Nam, 2Rheumatology, Hôpital Lariboisière, Paris, France, 3Université Paris Diderot, Paris, France, 4Molecular Biology, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City, Viet Nam, 5Rhumatologie, Hôpital Lariboisière, Paris, France, 6Rheumatology Department, Université Paris Diderot, Paris, France, 7Biostatistics, Hôpital Saint-Louis, Paris, France

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Metabolic and Crystal Arthropathies Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Gout is frequent and severe in Vietnam, where urate-lowering drugs (ULD) are seldom used and many patients are treated only with traditional herbal medicine. We looked at the effect of a Treat to Target strategy (T2T) using allopurinol on severe Vietnamese gout.

Methods: One hundred Vietnamese, ULD- free, crystal-proven gout patients (99 men, 1 woman) with a GFR > 60 ml/min, were prospectively followed during an aimed period of 12 months (M) after allopurinol (ALLO) initiation. The median age of patients was 47 years (y), median disease duration 10 y, median BMI 25 kg/m², 91 patients had multiple palpable tophi, 32 had hypertension, 7 type 2 diabetes, 31 dyslipidemia, 47 coronary heart disease, 16 were on long term steroid. Treatment protocol included full patient information, titration of ALLO up to reaching a predefined SUA target (6 mg/dL in 5 patients and 5 mg/dL in 95), flare prophylaxis by colchicine (0.5 to 1mg/d) during the first months, and traditional herbal medicine. At each visit, gout flares from the last visit were counted using a daily diary, palpable tophus size was assessed using a Vernier caliper, SUA was measured. Ultrasound (US) scan was performed at inclusion and every 3 M and allowed search for double contour (DC) sign at the knees and first MTP joints -which were found in all patients at baseline and classified into 4 classes (thick, medium, thin and none)- and measurement of a hand or foot index tophus. Quality of life (gout impact scale (GIS) and function were recorded at inclusion and after 12 M. The effect of SUA lowering was explored by comparing inclusion and 12-M data, in patients who reached their SUA target and those who did not, using standard statistics.

Results:

Eighty four and 68 patients were seen at M6 and M12, respectively. Reasons for loss of follow-up were major improvement (12), alcoholism (2), long distance from the center (8), inter-current disease or personal problem (9), and intolerance to ALLO (4). The mean maximal dose of ALLO was 520 (+165) mg/d and was reached after a median of 2 (+1.3) M. SUA target was obtained in 89 patients. Mean flare rate per M significantly declined from 2.5 on M1 (n=98) to 1.1 at M6 (n=84) (p<0.001), and 0.15 at M12 (n=68) (p<0.001), at a time when all patients were free of prophylactic colchicine, NSAIDs or steroid but remained under herbal treatment, with no significant influence of SUA. GIS significantly similarly strongly improved in all dimensions (p<0.02) except for fear of side effects.
and did not significantly correlate with SUA target. Function significantly (p<0.004) improved, and even more in patients at target (p<0.001). Tophi (p<0.001 for both caliper and US measurements) and DC sign (p<0.03 for all locations) significantly decreased between inclusion and M12 and both decreases correlated with achievement of SUA target (p=0.004 for tophi, and <0.03 for DC disappearance).

Conclusion: The T2T strategy strikingly improved patients. Tophi and DCs decreased, and function improved in correlation with achievement of SUA target. Flare rate dramatically decreased and GIS strongly improved but these changes did not correlate with SUA, suggesting a lack of statistical power or an anti-inflammatory effect of high dose ALLO and/ or herbal medicine.

Disclosure: T. Bardin, None; Q. Nguyen Dinh, None; K. Tran Minh, None; N. Le Hieu, None; M. Do Duc, None; P. Richette, None; M. Resche-Rigon, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/urate-lowering-to-acr-recommended-targets-allows-significant-improvement-of-severe-gout-a-monocentric-prospective-trial-in-vietnam-using-a-systematic-treatment-protocol

Abstract Number: 1138

Investigation on Allele Frequency of Rs3117583 and Rs9263726 in Patients with Hyperuricemia or Gout

Xiaomin Li1, Qiujing Wei2, Naomi Schlesinger3 and Jieruo Gu2, 1Rheumatology, Third affiliated hospital of Sun Yat-sen University, Guangzhou, China, 2Rheumatology, Third affiliated hospital of Sun Yat-sen Universtiy, Guangzhou, China, 3Medicine, Rutgers-Robert Wood Johnson Medical School, New Brunswick, NJ

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Metabolic and Crystal Arthropathies Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Allopurinol, effectively regulates and controls serum uric acid levels but may cause allopurinol-induced life-threatening severe cutaneous adverse reaction (SCAR). Previous studies reported that single nucleotide polymorphisms (SNP) rs3117583 and rs9263726, as well as HLA-B*5801, were genetic markers for allopurinol-induced SCAR. This study aims to investigate the allele frequency of rs3117583 and rs9263726 in patients with hyperuricemia and/or gout, and the possible effect on predicting allopurinol-induced SCAR.

Methods: We enrolled 100 patients with hyperuricemia and/or gout, diagnosed by clinicians at our University in Southern China. Genomic DNA was extracted and the alleles were tested by liquid chip using a Luminex 200 analyzer. Allele frequencies and allele carrying rates were calculated. We investigated the relationship between rs3117583, rs9263726 and HLA-B*5801. We used Plink software to explore the linkage disequilibrium analysis of rs3117583 and rs9263726.

Results: Observed genotype frequencies for rs3117583 (AG&GG) were 22%, while the risk allele G frequency was 11.5%. Similarly, rs9263726(AA&AG) exhibited the same genotype frequencies as rs3117583, and the risk allele frequency was 11.5%. HLA-B*5801 was observed in 19% of patients. Patients who carried the HLA-B*5801 allele, tended to carry the risk allele of rs3117583(G), with an odds ratio (OR) of 25.55 (95%CI:7.28-89.64, p<0.01), and rs9263726, with an OR of 468.00 (95%CI:45.97-4764.48). Rs3117583 showed a weak linkage disequilibrium with rs9263726 (D'=0.58, r²=0.34).

Conclusion: The technology of liquid chip can allow rapid and reliable detection of HLA-B*5801 and SNPs to identify individuals at risk of allopurinol-induced SCAR. Our study suggests that, since there is no strong linkage disequilibrium between rs3117583 and rs9263726, prospective screening combining these two SNPs and HLA-B*5801 genotyping can improve the predictive value of prescreening for allopurinol-induced SCARs in Southern Chinese patients.

Table 1 genotype of rs3117583, rs9263726 and HLA-B*5801 in patients with hyperuricemia and/or gout

<table>
<thead>
<tr>
<th></th>
<th>Rs3117583</th>
<th>Rs9263726</th>
</tr>
</thead>
<tbody>
<tr>
<td>HLA-B*5801 (+)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AA</td>
<td>5</td>
<td>18</td>
</tr>
<tr>
<td>AG</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>GG</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>15</td>
<td>19</td>
</tr>
<tr>
<td>HLA-B*5801(-)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AA</td>
<td>73</td>
<td>1</td>
</tr>
<tr>
<td>AG</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>GG</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>81</td>
<td>4</td>
</tr>
</tbody>
</table>

Table 1 genotype of rs3117583, rs9263726 and HLA-B*5801 in patients with hyperuricemia and/or gout

<table>
<thead>
<tr>
<th></th>
<th>Rs3117583</th>
<th>Rs9263726</th>
</tr>
</thead>
<tbody>
<tr>
<td>HLA-B*5801 (+)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AA</td>
<td>5</td>
<td>18</td>
</tr>
<tr>
<td>AG</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>GG</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>15</td>
<td>19</td>
</tr>
<tr>
<td>HLA-B*5801(-)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AA</td>
<td>73</td>
<td>1</td>
</tr>
<tr>
<td>AG</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>GG</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>81</td>
<td>4</td>
</tr>
</tbody>
</table>
The linkage disequilibrium analysis between rs3117583(A>G) and rs9263726(G>A). A: parameter $D_i$ of linkage disequilibrium analysis; B: parameter $r^2$ of linkage disequilibrium analysis.

Disclosure: X. Li, None; Q. Wei, None; N. Schlesinger, AstraZeneca, 2,AstraZeneca, 2,AstraZeneca, Horizon, Pfizer, BMS, Celgene, 5,AstraZeneca, Horizon, Pfizer, BMS, Celgene, 5; J. Gu, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/investigation-on-allele-frequency-of-rs3117583-and-rs9263726-in-patients-with-hyperuricemia-or-gout

Abstract Number: 1139

Management of Gout – a Survey for Healthcare Providers in South Australia

Nieves Leonardo1 and Julian McNeil2, 1Rheumatology, The Queen Elizabeth Hospital, Woodville South, Australia, 2Rheumatology, Northern Adelaide Local Health Network, Modbury, Australia

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Metabolic and Crystal Arthropathies Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Gout is a treatable arthritis and while the rate of gout in Australia has been steadily rising, drugs used to treat acute gouty arthritis have a variety of toxicities. A South Australian coroner’s case in 2014 drew attention to the fact that there are differences in approach to the treatment of gout that medical professional should be aware off.

We conducted a survey to help understand how South Australian healthcare providers manage Gout.

1. To identify which treatment approaches are favoured for management of acute gouty arthritis
2. To determine whether there are misconceptions in the management of gout according to current recommendations.
3. Whether healthcare providers are familiar with the “treat to target” approach when it comes to management of chronic hyperuricemia.

Methods:
An anonymous voluntary survey was conducted from 1st of May till the 31st of July 2015. The targeted population consisted of general practitioners working in the South Australian Health Care System. A random sample size of 326 was determined with 95% confidence level and confidence interval of 5. The population total was based on 2012 figures of practicing general practitioners which is 2138.
The questionnaire was based on published guidelines for management of gout:

1) Acute symptomatic management: (NSAIDs, colchicine, and prednisolone)
2) Knowledge regarding use of urate lowering therapy
3) Familiarity with different published treatment recommendations.

Ethics and site-specific approval was obtained before the start of the survey.

Results:
A total of 146 responses (response rate 48.6%) were received from general practitioners from both rural and metropolitan areas. At least half of whom see more than one patient with gout per week.

Most responders (63%) managed acute gouty arthritis with non-steroidal anti-inflammatory drugs while 24% uses Colchicine. For those who used colchicine, greater than 50% used a greater than 1.5mg per 24-hour dosing, 2.2% prescribed colchicine 500mcg 2-3 hourly until the patient has diarrhea.

Although, 66% commenced allopurinol and up titrate it, only 17% increased the dose more than 300 mg per day if serum urate remains elevated.

Out of the 146 responders only 27 knew of febuxostat as an alternative therapy for allopurinol, while 83% of responders were not aware of the “Treat to Target” approach.

Conclusion:
Gout is primarily managed by GPs in Australia. In recent years there has been a paradigm shift in terms of management. In published guidelines for acute attack of gouty arthritis the recommended options have been oral NSAIDs, systemic corticosteroid or colchicine. However, there remains to be ambiguity in the published dosing guidelines of colchicine.

Our study is the first to examine gout knowledge, belief and treatment approaches in the South Australian Health care system. Despite the recent coroner’s report and updates in the management of gout there continues to be a gap in our responder’s approach to its management.

We identified that suboptimal management of gout is due to poor dosage adjustment of urate lowering therapy to aim for the target urate level and lack of education with alternative to allopurinol as a urate lowering therapy.

Disclosure: N. Leonardo, None; J. McNeil, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/management-of-gout-a-survey-for-healthcare-providers-in-south-australia

Abstract Number: 1140

Gout Characteristics and Its Association with the Presence of Cardiovascular Disease: A Case-Control Study

Mariano Andrés1,2, Salvador López-Salgueiro1, Francisca Sivera3, Loreto Carmona4, Paloma Vela1,2 and Eliseo Pascual1,5, 1Sección de Reumatología, Hospital General Universitario de Alicante, Alicante, Spain, 2Departamento de Medicina Clínica, Universidad Miguel Hernández, Alicante, Spain, 3Sección de Reumatología, Hospital General Universitario de Elda., Elda, Spain, 4Instituto de Salud Musculosquelética (InMusc), Madrid, Spain, 5Emeritus Professor, Universidad Miguel Hernández, Elche, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Metabolic and Crystal Arthropathies Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM
Background/Purpose: Gout is an independent risk factor for any type of cardiovascular disease (CVD). The exact mechanism behind remains to be elucidated, but persistent crystal-related inflammation is presumed as a key factor. The aim of this study was to assess whether gout characteristics that may indicate a more severe disease and higher inflammatory load are associated with the presence of CVD.

Methods: Case-control study, performed at baseline of an inception cohort including consecutive crystal-proven gout patients seen at a rheumatology unit. Gout features (time since first attack, number of attacks, number of joints ever affected, pattern of presentation, tophi) were registered after interview and physical exam. Presence and duration of CVD (which included coronary heart disease, heart failure, stroke or peripheral artery disease) was registered after interview and records review. Those patients who have suffered from CVD prior to the onset of gout were excluded. Other cardiovascular risk factors, as well as clinical and laboratory variables, were also registered. Odds ratios with 95% confidence intervals (95%CI) for each gout feature were calculated between patients with and without CVD, using a multiple logistic regression model to adjust for confounders.

Results: The inception cohort includes 308 patients; 54 were excluded for this study because gout onset occurred after CVD, so finally 254 cases were analyzed. Mean age was 61.4 years (SD 13.9), being 225 (88.6%) men. Regarding gout, median duration was 5 years (IQR 1-12), median number of reported attacks was 5 (IQR 2-14) that had involved a median of 3 joints (IQR 2-5); presenting attack was monoarticular in 77.4% cases, oligoarticular in 16.7%, and polyarticular in 6%, and 58 patients (22.8%) showed tophi at enrolment. A total of 32 patients (12.6%) had suffered from CVD at enrolment. Table shows the results of logistic regression analysis: time since first attack and polyarticular presentation of gout both significantly associated with the presence of CVD, while other variables showed no association. After multivariate analysis, time since first attack persisted associated with CVD, while polyarticular involvement showed a trend towards significance.

Conclusion: Time since first attack and likely a polyarticular presentation, two variables that may estimate crystal and inflammatory load in gout patients, are independently associated with the presence of CVD, adding evidence to the role of persistent inflammation on its development.

<table>
<thead>
<tr>
<th>Association between gout features and cardiovascular disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple regression</td>
</tr>
<tr>
<td>Multiple regression</td>
</tr>
<tr>
<td>OR (95%CI)</td>
</tr>
<tr>
<td>Time since first attack</td>
</tr>
<tr>
<td>Number of attacks suffered</td>
</tr>
<tr>
<td>Number of ever involved joints</td>
</tr>
<tr>
<td>Joint pattern at presentation</td>
</tr>
<tr>
<td>i. Monoarticular</td>
</tr>
<tr>
<td>ii. Oligoarticular</td>
</tr>
<tr>
<td>iii. Polyarticular</td>
</tr>
<tr>
<td>Tophi</td>
</tr>
</tbody>
</table>

*aOR: adjusted OR for age, gender, hypertension, diabetes, dyslipidemia, smoking background, obesity, and renal failure.

Disclosure: M. Andrés, Grunenthal, 5; S. López-Salguero, None; F. Sivera, AstraZeneca, 5; L. Carmona, None; P. Vela, None; E. Pascual, AstraZeneca, 5, Grunenthal, 5.


Abstract Number: 1141

Initial Results of a Clinical Study to Determine Whether a Tolerizing Regimen of Pegloticase Can Increase the Frequency of Subjects Having Sustained Lowering of Serum Urate
Kenneth Saag1, Mitchell Feinman2, Alan J. Kivitz3, Herbert S. B. Baraf4, Roy Fleischmann5, Arthur Kavanaugh6 and Peter E. Lipsky7,

1Department of Medicine, University of Alabama at Birmingham, Birmingham, AL, 2ACME Research, LLC, Orangeburg, SC, 3Department of Rheumatology, Altoona Center for Clinical Research, Duncansville, PA, 4Center for Rheumatology and Bone Research, Wheaton, MD, 5Southwestern Medical Center at Dallas, University of Texas, Dallas, TX, 6Medicine, University of California, San Diego, La Jolla, CA, 7AMPEL BioSolutions, LLC, Charlottesville, VA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Metabolic and Crystal Arthropathies Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Pegloticase is a pegylated recombinant mammalian uricase approved for treatment of persons with chronic gout refractory to standard urate lowering therapy1. Despite initial reduction of serum urate (sUA) to near 0 mg/dL, patients may lose the urate lowering effect of pegloticase owing to the development of anti-drug antibodies (ADA)2, and as a result, only 42% of treated subjects had sustained urate lowering in the registration trials1. In the absence of stopping rules, infusion reactions (IRs) occurred in 26% of patients in the biweekly dosing regimen compared to 5% of placebo-treated patients. Gout flares occurred in 74% of pegloticase treated subjects in the first 3 months of treatment compared with 51% receiving placebo. Examination of pegloticase pharmacokinetics (PK)2 indicated that the biweekly regimen may not maintain high levels of drug during the first month of therapy, possibly contributing to the immunogenicity of pegloticase. PK modelling suggested that an additional dose of 8 mg of pegloticase 1 week after the initial dose and 1 week before the subsequent dose might be sufficient to maintain high serum pegloticase levels and contribute to the development of high zone tolerance with decreased ADA. The TRIPLE (Tolerization Reduces Intolerance to Pegloticase and Prolongs the Urate Lowering Effect, NCT02598596) was designed to address this question.

Methods: is a multi-center open label trial enrolling subjects with chronic gout whose sUA was not maintained at 6mg/dL or below. Background urate lowering therapy was discontinued and subjects were treated with 3 weekly doses of 8mg pegloticase followed by biweekly administration of 8 mg of pegloticase for a total of 10 doses over 17 weeks. SUA was measured immediately before each dose. After the first administration, dosing was only permitted if the sUA was 6 mg/dL or less. Standard infusion prophylaxis and gout flare prophylaxis was required. The primary outcome was the maintenance of sUA at 6 mg/dL or less throughout the treatment period.

Results: 47 subjects have been enrolled with a mean age of 62.0 +/-15.4 years, and BMI of 30.0 +/-4.5. Subjects have received a total of 282 infusions to date. There has been a total of 2 IRs, both in the same subject (2.1% of subjects with IRs, 0.7% of infusions with IRs). None of these IRs met criteria of anaphylaxis and were thought to be mild/moderate. There have been 5 serious adverse events in 3 subjects, 4 of which were felt to be unrelated to pegloticase and 1 of which was a gout flare. A total of 24 subjects (51.1%) experienced gout flares with each experiencing a mean of 2.2 flares. A total of 5 (10.6%) discontinued treatment before completion of the study. Of the 36 subjects who have completed the treatment regimen, 19 (52.8%) were persistent responders.

Conclusion: The tolerization regimen of pegloticase treatment appears to improve outcomes and is well tolerated. Few IRs were noted as administration of pegloticase was avoided in those with a sUA > 6mg/dL. The tolerization regimen may also be associated with a somewhat higher frequency of subjects achieving a persistent urate lowering effect.

2. Lipsky, PE et al Arth Res Ther 2014, 16:R60

Disclosure: K. Saag, Horizon, Takeda, SOBI, Ironwood, 2,Horizon, Takeda, SOBI, Ironwood, 5; M. Feinman, Horizon Pharma, 8; A. J. Kivitz, Amgen, Abbvie, Celgene, Genentech, Janssen, Merck, Novartis, Pfizer, UCB, Genzyme, Sanofi, Regeneron, Vertex, Horizon, 5; H. S. B. Baraf, Takeda, Horizon, 2,Takeda, Horizon, Ironwood, 5,Horizon Pharma, 8; R. Fleischmann, None; A. Kavanaugh, None; P. E. Lipsky, Horizon Pharma, 5,Horizon Pharma, 2.


Abstract Number: 1142

A Case Control Study of Anakinra Use for Acute Gout in a VA Patient Cohort Reveals Association with East Asian Descent, High Urate Burden, and Increased Co-Morbidities and All-Cause Mortality
Effectiveness of the IL-1 receptor antagonist anakinra, in resolving flares of acute gout, has been reported in several case series. Here, studying a VA gout cohort with a plurality of minorities, we analyzed patient characteristics in those who needed anakinra prescription to control acute gout flares. In doing so we tested the hypothesis that anakinra was prescribed for gout patients who were sicker (more comorbidities and ultimate mortality), and with higher urate burden (uncontrolled hyperuricemia, palpable tophi). We also analyzed ethnic/racial factors, since in East Asians the ABCG2 variant Q141K is very common (with an allele frequency up to 0.5) in gout. An emerging line of investigation links inflammation with the ABCG2 Q141K variant, and is associated with hyperuricemia and subsequent early onset tophaceous gout. ABCG2 Q141K inhibits autophagy and may increase systemic inflammation.

Methods:
More than 6000 patients fulfilling 2015 ACR/EULAR criteria for gout were seen at the VA between 01/2003 and 01/2015, with more than 1300 of these evaluated at least once for management by Rheumatology. During this time period, 14 patients (100% male) received anakinra at varying times, for a total of 55 courses. Demographics of the gout cohort were 52% White, 12% Black, 34% East Asian (including ~25% Pacific Islanders), and 2% other. In retrospective case-control analyses, for each patient, 4 age and gender matched controls were chosen. Each patient’s first visit with the Rheumatology department was analyzed for factors predictive of the patient eventually requiring anakinra for gout. Demographics, urate burden, baseline co-morbidities, and all-cause mortality were analyzed for anakinra use.

Results:
Patients who were prescribed or not prescribed anakinra had no significant difference in mean number of comorbidities, (mean of 3.9 in anakinra, 3.1 in controls), p = 0.08, CI -0.11 to 1.65. Patients receiving anakinra were more likely to have very poorly controlled hyperuricemia and a high body urate burden at baseline (anakinra group 10/14 with tophi vs. controls 17/56 with tophi, p = 0.018; anakinra group had mean serum urate of 10.2 mg/dL vs. 7.6 mg/dL in controls, p = 0.0002). The anakinra treated group had higher all-cause mortality (7/14 in anakinra group, 9/56 in controls p = 0.012) as well as greater predominance of East Asian patients (8/14 in anakinra group vs. 16/56 in control group, p = 0.049). In contrast, the distribution of Black patients was not statistically significant between groups (p = 0.18)

Conclusion:
Anakinra use for acute gout was associated with patient characteristics including East Asian descent, uncontrolled hyperuricemia and a high body urate burden (reflected by palpable tophi), and significant increases in both the number of co-morbidities and all-cause mortality. The results suggest not only that in gout, patients who are sicker and have less poorly controlled serum urate, more frequently require anakinra to help control acute gout flares. Moreover, the possibility that East Asian patients have a genetic predisposition for more refractory inflammation in gout merits further investigation.
Background/Purpose: The poor adherence to urate lowering therapy is due to a lack of appropriate information. This study performed to analyze the effect of education for patients with gout.

Methods: Patients were enrolled by categorizing in two groups, education and non-education. Face-to-face education was conducted by the specialist nurse, and an information leaflet about lifestyle advice and urate lowering therapy was also given to all participants. Non-education group also received an education on their second visit (after two or three month from first visit). The patient satisfaction were assessed using the visual analogue scale (0 to 100 mm) and patients' satisfaction questionnaire. Questionnaire regarding patient's knowledge about gout. Also, we analyzed the serum uric acid level and drug compliance.

Results: A total of 100 patients were randomized to education or non-education group. patients' satisfaction in visual analogue scale was significantly higher in education group (education group: 87.5±24.5 mm, vs. non-education group: 75.4±20.3 mm, \( P=0.008 \)). Also, patients' satisfaction questionnaire was significantly higher in education group (education group: 4.02±0.4, vs. non-education group: 3.71±0.39, \( P<0.001 \)). The level of knowledge about gout was higher in education group (education group: 7.38±2.0, vs. non-education group: 6.08±2.42, \( P=0.004 \)). The serum uric acid level on second visit (after two or three month from first visit) is decreased in education group (baseline: 5.73±1.72 mg/dL, vs. second visit: 5.09±1.62 mg/dL, \( P=0.032 \)). Besides, drug compliance on second visit is improved in education group without statistical significance (baseline: 88.76±18.47 %, vs. second visit: 92.91±11.56 %, \( P>0.05 \)).

Conclusion: Nurse-delivered face-to-face education including the nature of gout and its treatment options is improved the patients' satisfaction and their treatment adherence.

Disclosure: I. S. Yoo, None; C. K. Park, None; J. Kim, None; S. J. Yoo, None; S. C. Shim, Celltrion Inc., 5; S. W. Kang, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-patient-education-for-gout-patients-ameliorate-the-patients-satisfaction-and-serum-uric-acid-level

Abstract Number: 1144

Initiating Colchicine and Urate-Lowering Therapy Reduces Baseline Inflammation, and Improves Vascular Endothelial but Not Smooth Muscle Function in Gout Subjects: Resistance to Endothelial Improvement Among Patients with Cardiovascular Comorbidities

Talia Igel1,2, Aaron Garza Romero2, Virginia Pike3, Yu Guo4, Stuart Katz5, Binita Shah5, Irina Dekiarev2, Svetlana Krasnokutsky Samuels2 and Michael Pillinger2, 1Medicine, Monash University School of Medicine, Melbourne, Australia, 2Medicine/Rheumatology, New York University School of Medicine, New York, NY, 3Medicine/Rheumatology, New York University School of Medicine, Division of Rheumatology, New York, NY, 4Population Health/Statistics, New York University School of Medicine, New York, NY, 5Medicine/Cardiology, New York University School of Medicine, New York, NY

First publication: September 18, 2017
Background/Purpose: We have previously reported that patients with gout have impaired vascular endothelial and smooth muscle responsiveness, but whether initiating appropriate gout therapy ameliorates these impairments, or improves baseline inflammatory status, has not been determined.

Methods: We performed an observational pilot study to assess whether initiating gout therapy improves vascular function as well as markers of inflammation. Subjects meeting ACR classification and treatment criteria for gout, but not actively receiving gout medications, were enrolled. Baseline demographics were obtained. Subjects were given colchicine daily for 6 weeks, followed by addition of urate-lowering therapy (ULT; allopurinol or febuxostat at the discretion of the treating physician) and titration to a target serum urate (sUA) of <6.0 mg/dL, or <5.0 mg/dL for subjects with tophi. hsCRP was measured pre and post the colchicine-only period, and 4 weeks after achieving target sUA. Endothelial responsiveness was assessed using ultrasound as brachial artery dilation in response to application/release of a blood pressure cuff (flow-mediated dilation, FMD). Vascular smooth muscle function was assessed as brachial artery dilation in response to sublingual nitroglycerine (nitrate-mediated dilation, NMD).

Results: 34 male subjects were enrolled, and 28 completed all study phases. Mean age was 57.9 years, and mean BMI 30.3. Co-morbidities included hypertension (HTN, 71%); hyperlipidemia (HL, 50%); coronary artery disease (CAD, 21%); chronic kidney disease (14.7%) and diabetes (6%). 26% were current smokers. Mean baseline sUA was 9.1 mg/dL, and declined after ULT (p baseline vs post-ULT, <0.001) (Table). Baseline hsCRP was elevated, and FMD and NMD reduced, vs healthy controls. We observed a pattern of improvement in hsCRP and FMD after colchicine treatment, and further improvement after ULT initiation (mostly allopurinol), but no NMD improvement. Whereas subjects without comorbidities (HTN, HL, CAD and/or BMI>30) experienced improvements in both hsCRP and FMD, subjects with individual or multiple CV co-morbidities experienced improvement in hsCRP but not FMD. In contrast, smokers experienced improvement in both inflammatory and endothelial parameters in response to treatment.

Conclusion: Initiating colchicine prophylaxis and ULT in gout patients reduces systemic inflammation. Improvement in endothelial function is also observed, but patients with established CV comorbidities may be resistant to endothelial improvement. These data suggest that proper gout treatment may have direct benefit in reducing CV risk. Whether longer term treatment could have additional impact, particularly on patients with established CV comorbidities, remains to be determined.

Table. Responses to colchicine, and to colchicine plus ULT, in gout patients without HTN, HL, CAD or BMI > 30

<table>
<thead>
<tr>
<th></th>
<th>Pre-treatment</th>
<th>On colchicine</th>
<th>On colchicine + ULT</th>
</tr>
</thead>
<tbody>
<tr>
<td>sUA (mg/dL)</td>
<td>9.4</td>
<td>9.4</td>
<td>5.2</td>
</tr>
<tr>
<td>hsCRP (mg/L)</td>
<td>4.2</td>
<td>3.8</td>
<td>2.0</td>
</tr>
<tr>
<td>FMD (endothelial response)</td>
<td>0.6</td>
<td>1.6</td>
<td>3.39</td>
</tr>
<tr>
<td>NMD (smooth muscle response)</td>
<td>22.2</td>
<td>24.2</td>
<td>21.5</td>
</tr>
</tbody>
</table>

Disclosure: T. Igel, None; A. Garza Romero, None; V. Pike, None; Y. Guo, None; S. Katz, None; B. Shah, None; I. Dektiarev, None; S. Krasnokutsky Samuels, Crealta/Horizon, Ironwood, 5; M. Pillinger, AstraZeneca, Crealta/Horizon, Ironwood, Sobi, 5.

Effectiveness of a Multidisciplinary Gout Clinic on Timely Achievement of Serum Uric Acid Goals
SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: ARHP Metabolic and Crystal Arthropathies Poster
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
The concept of a multidisciplinary gout clinic is relatively new in Singapore. Changi General Hospital launched such a clinic in 2014 to provide treat-to-target management of gout in a shared care model of rheumatologists and pharmacists. This study aims to demonstrate the effectiveness of a multidisciplinary gout clinic on the optimization of urate lowering agents to achieve target serum uric acid (sUA) levels.

Methods:
We reviewed case notes and medication records of gout outpatients who were started on either Allopurinol or Febuxostat in the 24 months prior to (pre-group) and 33 months following (post-group) the launch of the multidisciplinary gout clinic. Patients with stage 5 chronic kidney disease or end-stage kidney disease as well as those who defaulted their appointments were excluded.

The primary efficacy end-point was mean time taken to attain goal sUA in patients who achieved target sUA between both pre- and post- groups. Secondary outcomes include percentage of patients who experienced a gout flare at one year of drug initiation, the mean dose of urate lowering therapy required to achieve target sUA levels, the proportion of patients that achieved target sUA of 360µmol/L or less at one year of drug initiation and mean reduction in sUA.

Results:
In 98 eligible subjects enrolled in our study, 50 patients were managed only by the rheumatologist (pre-group) and 48 patients were seen by both the rheumatologist and pharmacist (post-group). Among patients who have achieved target sUA level, the mean time taken to attain target sUA was shorter in the post-group as compared to the pre-group (147 days vs. 314 days, p<0.001). The percentage of patients who experienced a gout flare at one year of drug initiation is lower in those who achieved target sUA levels as compared to those who did not achieve target sUA levels (29.5% vs. 78.4%, p<0.001). The mean (standard deviation) daily allopurinol and febuxostat dose to achieve target sUA levels were 276mg (138mg) and 76mg (37mg) respectively. A higher proportion of patients achieved sUA of 360µmol/L or less at one year of drug initiation in the post-group as compared to pre-group (70.8% vs. 22.0%, p<0.001). The mean change in sUA among pre-group and post group were 113.02 µmol/L vs. 169.27 µmol/L, p=0.049, respectively.

Conclusion:
Our results demonstrate that the implementation of a multidisciplinary gout clinic provides a more timely achievement of target sUA level and the attainment of goal sUA is associated with reduced incidence of gout flares. This suggests that a structured multidisciplinary approach is effective in providing better disease management in gout patients.

Disclosure: K. M. Cheong, None; A. Vasudevan, None; M. Sriranganathan, None; E. Lee, None; S. Yeow, None; P. Ramskay, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/effectiveness-of-a-multidisciplinary-gout-clinic-on-timely-achievement-of-serum-uric-acid-goals

Abstract Number: 1146

Associations between Gout and Cancer in an Nhanes Cohort

Patricia Kachur¹, Venkatesh Gondhi², Yinjin Wert³ and Pramil Cheriyath², ¹Internal Medicine, Ocala Regional Medical Center, Ocala, FL, ²Ocala Regional Medical Center, Ocala, FL, ³Pinnacle Health System, Harrisburg, PA
First publication: September 18, 2017
**Background/Purpose:**

Gout is the most common inflammatory disease in the United States (US), affecting more than 4% of the population. Although uric acid (UA) can function as an antioxidant at low levels, high levels have been postulated to play an important role in the pathogenesis of cancer. Recent evidence has demonstrated that hyperuricemia is associated with excess cancer risk, cancer recurrence, and mortality. However, this may be confounded by common comorbidities such as alcoholism and obesity that likewise increase risk for malignancy. The National Health and Nutrition Examination Survey (NHANES) provides a good basis to study these associations in the general US population.

**Methods:**

11,262 individual from the general population between 2011-2014 were surveyed through the NHANES project using a combination of questionnaires, physical examinations and laboratory studies. Of all subjects, 403 had a diagnosis of gout and 825 had a diagnosis of cancer. Statistical modeling of disease associations were adjusted for age, gender, college education, and the presence of rheumatoid arthritis, smoking status, alcohol use, and BMI. All analyzes were performed using SAS software version 9.4 (Cary, North Carolina).

**Results:**

There was a significantly higher proportion of cancer diagnoses in gout patients (21% vs 7%; p< 0.001). Adjusted multivariate analysis showed that those with gout were 50% more likely to have a diagnosis of malignancy (Odds ratio [OR] = 1.54; 95%CI, 1.16-2.04, p=0.003). Interestingly, patients with rheumatoid arthritis also had a direct association with a diagnosis of cancer (OR 1.6, 95% CI 1.22-2.00, p=0.001), and this was independent of the association with gout. The most common cancer was prostate cancer (25%), followed by breast, cervix, and colon.

**Conclusion:**

Our study shows evidence of an independent association between gout and malignancy. Prostate cancer was the most common type of cancer in this group. The association between gout and cancer warrants further investigation, as confirming these findings have the potential to modify screening practices in those with gout.

| Table 1: Multiple logistic regression model - Demographics and risk factors associated with cancer |
|-----------------|-----------------|-----------------|-----------------|
| Predictors      | Odds Ratio      | 95% CI          | P-Value         |
| Age (18 - 79)   | 1.073           | 1.06 - 1.07     | <.0001          |
| Gender - female | 1.263           | 1.08 - 1.47     | 0.0025          |
| Race - black    | 0.657           | 0.54 - 0.79     | <.0001          |
| Had a college degree | 1.769       | 1.51 - 2.06   | <.0001          |
| Current smoker  | 1.401           | 1.15 - 1.70     | 0.0007          |
| Overweight (BMI>=25) | 0.982       | 0.83 - 1.15     | 0.8275          |
| Rheumatoid arthritis | 1.605      | 1.21 - 2.11     | 0.0008          |
| Gout            | 1.542           | 1.16 - 2.04     | 0.0028          |
| Alcohol use     | 0.936           | 0.77 - 1.12     | 0.4863          |

**Disclosure:** P. Kachur, None; V. Gondhi, None; Y. Wert, None; P. Cheriyath, None.


Abstract Number: 1147
Macrophage Activation Syndrome or Acquired Hemophagocytic Lymphohistiocytosis in Adults: Demographics, Clinical Characteristics, and Survivorship in an American Academic Medical Center

Seema Malkana¹ and Irene Tan², ¹Internal Medicine, Temple University Hospital, Philadelphia, PA, ²Section of Rheumatology, Temple University Lewis Katz School of Medicine, Philadelphia, PA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Macrophage Activation Syndrome, also known as acquired Hemophagocytic Lymphohistiocytosis in adults, is an immune-mediated systemic inflammatory state. It is associated with multisystem organ failure and high mortality. Diagnostic criteria are extrapolated from children with primary Hemophagocytic Lymphohistiocytosis as there is a paucity of literature on adults. Additionally, most recent evidence is reported from non-U.S. populations. These gaps in the literature may contribute to under-recognition and under-diagnosis of adults in the U.S. Study objectives were to characterize the demographic, clinical, and biopsy features of adult Macrophage Activation Syndrome or acquired Hemophagocytic Lymphohistiocytosis at a single American academic medical center; along with treatments, outcomes, and possible predictive factors in the outcomes.

Methods: The study center’s Electronic Health Record was queried for adult patients in the inpatient or outpatient setting between 1/1/2010-8/30/2015 with ICD-9 codes for hyperferritinemia, adult-onset Still’s disease, Macrophage Activation Syndrome, Hemophagocytic Lymphohistiocytosis, or combinations of these. This produced 42 patients. A chart review was performed to confirm diagnosis and patients with only hyperferritinemia or adult-onset Still’s disease were excluded. Patients without primary data or reliable report thereof for the first presentation of the disease were also excluded. A detailed chart review followed.

Results: Thirteen patients met criteria during the study period. As compared to the global literature, the majority of patients with Macrophage Activation Syndrome or acquired Hemophagocytic Lymphohistiocytosis were male at our center and more often autoimmune-triggered as opposed to viral infection-associated. Ten patients (77%) had biopsy findings or elevated biomarkers for Macrophage Activation Syndrome or acquired Hemophagocytic Lymphohistiocytosis, though soluble IL-2 receptor and CD25 were more commonly positive than bone marrow aspirate. Although cardiopulmonary compromise requiring ICU-level care was common, normal renal function was often maintained. Combination immunosuppressive therapy with anakinra was the most common treatment. Importantly, ten of the eleven patients (91%) whose index encounter was at the medical center survived to discharge.

Conclusion: This study reviewed data for adult patients from an American population that is under-represented in the literature. Patient demographics and key clinical features differ from globally observed trends. This may reflect characteristics innate to the study center or the limitations of using EHR-captured data retrospectively. Molecular and biochemical markers can provide a diagnosis when pathognomonic hemophagocytes are not seen in the bone marrow or lymph organs. Combination immunosuppressive therapy remains important but survivorship is difficult to predict without standardization of treatment regimens.

Disclosure: S. Malkana, None; I. Tan, None.


Abstract Number: 1148

Arthritis after Cancer Immunotherapy: Symptom Duration and Treatment Response

Melanie H. Smith¹ and Anne R. Bass²,³, ¹Medicine, New York Presbyterian Hospital (Cornell), New York, NY, ²Rheumatology, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, ³Rheumatology, Hospital for Special Surgery Weill Cornell Medical College, New York, NY
First publication: September 18, 2017
Background/Purpose: Checkpoint inhibitor immunotherapy has fundamentally changed the treatment for an actively expanding list of cancers, however its use is associated with immune related adverse events (irAEs). Rheumatologic manifestations of irAEs remain incompletely characterized and poorly understood. A recently published case series suggested that immunotherapy-induced arthritis is an aggressive process requiring high dose corticosteroids.

Methods: This was a retrospective chart review of all patients with musculoskeletal irAEs first seen by one of the authors prior to October 2016. All patients had been treated for a malignancy with immune checkpoint inhibitors targeting PD-1 (nivolumab, pembrolizumab), PD-L1 (durvalumab) and/or CTLA-4 (ipilimumab, tremelimumab) at Memorial Sloan Kettering Cancer Center between 2013 and 2016.

Results: We identified 10 patients with a mean (± standard deviation) age 63.2 (± 9.7) years (Table 1). Seven patients were treated with a combination of checkpoint inhibitors and three with nivolumab monotherapy. Four patients developed inflammatory polyarthritis, four oligoarthritis and two tenosynovitis. Six were ANA positive and two had anti-CCP antibodies. Mean time from the first dose of immunotherapy until joint involvement was 6.3 (± 4.3) months (Table 2). Of the two patients with the shortest interval between immunotherapy and the onset of arthritis, one had had mild polymyalgia rheumatic (PMR)-like symptoms prior to the initiation of immunotherapy, and the other had a sister with rheumatoid arthritis (RA). All 10 patients were treated with systemic corticosteroids, and eight required 20 mg or less per day of prednisone. Five patients received steroid-sparing agents. The mean time until resolution of joint symptoms after the last dose of immunotherapy was 15.2 (± 4.1) months.

Conclusion: Patients experiencing musculoskeletal irAEs can have a wide variety of manifestations ranging from oligoarthritis and tenosynovitis, to PMR, to a polyarthritis consistent with RA. The onset of arthritis appears to be relatively late compared to other irAEs. Musculoskeletal symptoms can last more than a year after the last dose of immunotherapy, however they can generally be managed with low doses of corticosteroids.

Table 1. Patient Demographics and Arthritis Manifestations

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Malignancy</th>
<th>CELA or PD-L1</th>
<th>Target IT</th>
<th>Poly</th>
<th>Oligo</th>
<th>Teno</th>
<th>Joints</th>
<th>Comments</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>57</td>
<td>M</td>
<td>Melanoma</td>
<td>X</td>
<td>nivolumab</td>
<td>X</td>
<td></td>
<td></td>
<td>knees</td>
<td>ANA+</td>
<td>hypothyroid</td>
</tr>
<tr>
<td>2</td>
<td>74</td>
<td>F</td>
<td>Melanoma</td>
<td>anti-PD-1</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td>wrists</td>
<td>ANA+</td>
<td>neurology</td>
</tr>
<tr>
<td>3</td>
<td>67</td>
<td>M</td>
<td>Melanoma</td>
<td>X</td>
<td>nivolumab</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td>RA, Sjogren's</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>56</td>
<td>F</td>
<td>Melanoma</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td>knees</td>
<td>ANA+</td>
<td>hepatitis, GFRS</td>
</tr>
<tr>
<td>5</td>
<td>63</td>
<td>F</td>
<td>Anal</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td>PMR, ANA+, CCP+</td>
<td>hypothyroid</td>
</tr>
<tr>
<td>6</td>
<td>47</td>
<td>F</td>
<td>Cervical</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td>knees</td>
<td>ANA+</td>
<td>GFRS, hypothyroid, hypothyroid</td>
</tr>
<tr>
<td>7</td>
<td>68</td>
<td>F</td>
<td>Melanoma</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td>RA, ANA+</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>60</td>
<td>M</td>
<td>NSGC</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td>RA, ANA+</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>81</td>
<td>M</td>
<td>Merkel</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td>RA, CCP+</td>
<td>polymyalgia, arthritis</td>
</tr>
<tr>
<td>10</td>
<td>59</td>
<td>M</td>
<td>Melanoma</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td>knee</td>
<td>SIgG 2</td>
<td>hepatitis, polymyalgia, arthritis</td>
</tr>
</tbody>
</table>

IT = immunotherapy; poly = polyarthritis; oligo = oligoarthritis; teno = tenosynovitis; other = other immune-related adverse events; ANA+ = low titer ANA, PMR = polymyalgia rheumatic, RA = rheumatoid arthritis
### Background/Purpose
Relapsing polychondritis (RP) is a rare systemic inflammatory disorder and might often be refractory. Therefore, the discovery of more convenient imaging modality than contrast-CT, MRI and FDG-PET/CT would be required on diagnosis and treatment. The objective is to assess the clinical implications of ultrasonography (US) in monitoring disease activity and diagnosis of RP.

### Methods
Firstly, auricular chondritis of patients with RP (n=5) were assessed by US before and after treatments. Second, the relationship between US findings and other serum inflammatory markers were evaluated. Moreover, the comparisons of US findings between the auricle of patients with RP (n=5), repeated trauma (n=5) which is similar to auricle of RP, and healthy subjects (n=5) were also assessed.

<table>
<thead>
<tr>
<th>Case</th>
<th>Prednisone</th>
<th>Other</th>
<th>Months to onset</th>
<th>Months to resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10 mg daily</td>
<td>Hydroxychloroquine</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>2</td>
<td>5 mg daily</td>
<td></td>
<td>4</td>
<td>14</td>
</tr>
<tr>
<td>3</td>
<td>20 mg daily</td>
<td>Infliximab</td>
<td>7</td>
<td>NA</td>
</tr>
<tr>
<td>4</td>
<td>10 mg bid</td>
<td>Celecoxib</td>
<td>4</td>
<td>NA</td>
</tr>
<tr>
<td>5</td>
<td>15 mg daily</td>
<td></td>
<td>1</td>
<td>NA</td>
</tr>
<tr>
<td>6</td>
<td>30 mg daily</td>
<td></td>
<td>14</td>
<td>NA</td>
</tr>
<tr>
<td>7</td>
<td>20 mg daily</td>
<td></td>
<td>9</td>
<td>20</td>
</tr>
<tr>
<td>8</td>
<td>10 mg daily</td>
<td>Hydroxychloroquine, Sulfasalazine</td>
<td>1</td>
<td>Ongoing (6 months)</td>
</tr>
<tr>
<td>9</td>
<td>20 mg daily</td>
<td>Methotrexate</td>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td>10</td>
<td>50 mg daily</td>
<td>Metyrapone</td>
<td>8</td>
<td>19</td>
</tr>
</tbody>
</table>

*Time from first dose of immunotherapy until onset of musculoskeletal symptoms
**Time from discontinuation of immunotherapy to resolution of symptoms off steroids
NA = patient still on immunotherapy at last visit
IA = intraarticular steroid injection

---

**Disclosure:** M. H. Smith, None; A. R. Bass, Pfizer, 9, Abbot, 9.


---

**Abstract Number:** 1149

**Clinical Implications of Ultrasonography (US) in Monitoring Disease Activity of Relapsing Polychondritis (RP) and Comparative Investigation By US between Auricle of RP, Repeated Trauma and Healthy Subject**

Eri Amano¹, Yoshinori Taniguchi², Satoshi Inotani¹, Hirofumi Nishikawa¹, Tatsuki Matsumoto³, Shuichi Nakayama⁴ and Yoshio Terada², ¹Endocrinology, Metabolism, Nephrology and Rheumatology, Kochi Medical School, Nankoku, Japan, ²Endocrinology, Metabolism, Nephrology and Rheumatology, Kochi University, Kochi, Japan, ³Endocrinology, Metabolism, Nephrology and Rheumatology, Kochi University, Nankoku, Japan, ⁴Kochi Medical School, Nankoku, Japan, ⁵Kochi University, Nankoku, Japan

**First publication:** September 18, 2017
**Results:** US of the auricular chondritis before treatment showed low-echoic swollen auricular cartilage with increased power Doppler signals (PDS) in all cases. US findings corresponded to biopsy findings. After treatment with prednisolone (PSL) combined with methotrexate, the swollen ear completely resolved in all cases. Then, US findings also showed dramatic reductions in swollen cartilage with the decrease in PDS. When serum inflammatory markers completely improved, but US finding remained, 1 of 5 cases showed flare due to PSL tapering. On the other hands, US imaging could differentiate between inflammation, vascular lesions, and tumors in the ear pinna. RP could be differentiated from the damage of repeated trauma (i.e. rugby) with producing subperichondrial serous effusion.

**Conclusion:** US imaging of the external ear and auricular cartilage in RP possibly facilitates evaluation of auricular lesions and monitoring of disease activity, especially when we consider the treatment response and the timing of drug tapering.

**Disclosure:** E. Amano, None; Y. Taniguchi, None; S. Inotani, None; H. Nishikawa, None; T. Matsumoto, None; S. Nakayama, None; Y. Terada, None.


**Abstract Number:** 1150

**Ocular Involvement Is Exclusive with Genital Ulcer and Skin Lesion in the Early Phase of Behçet’s Disease: Nationwide Japanese Registration.**

Nobuyuki Horita¹, Akiko Suwa², Mitsuhiro Takeno³, Takehito Ishido², Yohei Kirino⁴ and Nobuhisa Mizuki⁵, ¹National Human Genome Research Institute, National Institutes of Health, Bethesda, MD, ²Department of Ophthalmology and Visual Science, Yokohama City University Graduate School of Medicine, Yokohama, Japan, ³Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan, ⁴Department of Stem Cell and Immune Regulation, Yokohama City University Graduate School of Medicine, Yokohama, Japan, ⁵Yokohama City University, Yokohama, Japan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017
**Session Title:** Miscellaneous Rheumatic and Inflammatory Diseases Poster I
**Session Type:** ACR Poster Session B
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Behçet's disease (BD) is a chronic inflammatory syndrome with features of multi-organ involvement and presents with mucocutaneous and ocular symptoms. We have previously found that eye involvement was significantly associated with neurologic lesions, while the coexistence with intestinal involvement was uncommon. Moreover, a couple of studies have revealed some phenotypical clustering among the patients with BD. This study aimed to identify the high-risk patients for ocular involvement.

**Methods:** The Japanese Ministry of Health, Labour and Welfare provided the dataset of ongoing nationwide BD registration project. We analyzed newly registered patients who fulfilled the International Study Group (ISG) criteria. To have an overview on the associations between manifestations, we made Yule's Q matrix. After this screening process, we estimated how each risk factor associated with ocular lesions using odds ratio (OR). We also conducted a logistic regression analysis, wherein the ocular lesion was a dependent variable.

**Results:** Among 2399 eligible BD patients, 941 (39%) were men and 1458 (61%) were women with a median age of 37 years (interquartile range (IQR) 29-44 years) (Abstract Table 1). The median duration between onset and registration was 0 year (IQR 0-3). Genital ulceration and skin lesions had Yule's Q values of -0.82 and -0.75, respectively. These values indicated that the absence of genital ulceration and skin lesions were risk factor of ocular involvement. Among 1915 patients with genital ulceration, 383 (20%) had ocular lesions, while among 484 patients without genital ulceration, 348 (72%) had ocular lesions (Abstract Table 2). This yielded an OR of 0.10 (95% CI 0.08-0.12, P<0.001). Among 2308 patients with skin lesions, 664 (29%) had ocular lesions, while among 91 patients without skin ulceration, 67 (74%) had ocular lesions, yielding an OR of 0.15 (95% CI 0.09-0.23, P<0.001). Subgroup analyses constantly replicated these results (Abstract Table 2). The logistic regression analysis identified skin lesion (OR 0.08, 95% CI 0.05-0.13, P<0.001) and genital ulceration (OR 0.08, 95% CI 0.06-0.10, P<0.001) as protective factors or ocular lesions (Abstract Table 3).

**Conclusion:** The absence of genital ulceration and skin lesions were risk factor of ocular involvement of BD.
<table>
<thead>
<tr>
<th></th>
<th>All analyzable cases</th>
<th>International Study Group criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>3213</td>
<td>2399</td>
</tr>
<tr>
<td>Age year, median</td>
<td>38 (IQR 30-49)</td>
<td>37 (IQR 29-47)</td>
</tr>
<tr>
<td>Men</td>
<td>1382 (43%)</td>
<td>941 (39%)</td>
</tr>
<tr>
<td>Women</td>
<td>1831 (57%)</td>
<td>1458 (61%)</td>
</tr>
<tr>
<td>Oral ulceration</td>
<td>3044 (95%)</td>
<td>2399 (100%)</td>
</tr>
<tr>
<td>Onset registration duration</td>
<td>1 (IQR 0-3)</td>
<td>0 (IQR 0-3)</td>
</tr>
<tr>
<td>0 year</td>
<td>1593 (50%)</td>
<td>1222 (51%)</td>
</tr>
<tr>
<td>1-9 years</td>
<td>1237 (39%)</td>
<td>893 (37%)</td>
</tr>
<tr>
<td>10- years</td>
<td>383 (12%)</td>
<td>284 (12%)</td>
</tr>
<tr>
<td>Skin lesion</td>
<td>2673 (83%)</td>
<td>2308 (96%)</td>
</tr>
<tr>
<td>Ocular lesion</td>
<td>891 (28%)</td>
<td>731 (31%)</td>
</tr>
<tr>
<td>Genital ulceration</td>
<td>2101 (65%)</td>
<td>1915 (80%)</td>
</tr>
<tr>
<td>Positive pathergy test</td>
<td>1016 (32%)</td>
<td>975 (41%)</td>
</tr>
<tr>
<td>Arthritis</td>
<td>1620 (50%)</td>
<td>1290 (54%)</td>
</tr>
<tr>
<td>Epididymitis (male only)</td>
<td>126/1382 (9%)</td>
<td>94/941 (10%)</td>
</tr>
<tr>
<td>Gastrointestinal symptom</td>
<td>998 (31%)</td>
<td>633 (26%)</td>
</tr>
<tr>
<td>Vascular lesion</td>
<td>368 (12%)</td>
<td>255 (11%)</td>
</tr>
<tr>
<td>Neurological manifestation</td>
<td>692 (22%)</td>
<td>493 (21%)</td>
</tr>
<tr>
<td>Iris/cyclitis</td>
<td>637 (20%)</td>
<td>523 (22%)</td>
</tr>
<tr>
<td>Retino-uveitis</td>
<td>596 (19%)</td>
<td>480 (20%)</td>
</tr>
<tr>
<td>Patient background</td>
<td>Ocular lesion</td>
<td>Genital ulcer</td>
</tr>
<tr>
<td>--------------------</td>
<td>--------------</td>
<td>---------------</td>
</tr>
<tr>
<td></td>
<td>(+)</td>
<td>(-)</td>
</tr>
<tr>
<td>All cases (N = 2399) Ocular lesion (+)</td>
<td>383</td>
<td>1532</td>
</tr>
<tr>
<td></td>
<td>Ocular lesion (-)</td>
<td>348</td>
</tr>
<tr>
<td>Male (N = 941) Ocular lesion (+)</td>
<td>169</td>
<td>469</td>
</tr>
<tr>
<td></td>
<td>Ocular lesion (-)</td>
<td>229</td>
</tr>
<tr>
<td>Female (N = 1459) Ocular lesion (+)</td>
<td>214</td>
<td>1063</td>
</tr>
<tr>
<td></td>
<td>Ocular lesion (-)</td>
<td>119</td>
</tr>
<tr>
<td>Age &lt; median, -36 years (N = 1145) Ocular lesion (+)</td>
<td>163</td>
<td>776</td>
</tr>
<tr>
<td></td>
<td>Ocular lesion (-)</td>
<td>144</td>
</tr>
<tr>
<td>Age &gt; median, 37- years (N = 1254) Ocular lesion (+)</td>
<td>220</td>
<td>756</td>
</tr>
<tr>
<td></td>
<td>Ocular lesion (-)</td>
<td>204</td>
</tr>
<tr>
<td>Onset-, 0 y (N = 1222) Ocular lesion (+)</td>
<td>170</td>
<td>818</td>
</tr>
<tr>
<td></td>
<td>Ocular lesion (-)</td>
<td>159</td>
</tr>
<tr>
<td>Onset-, 1-9 years (N = 893) Ocular lesion (+)</td>
<td>126</td>
<td>566</td>
</tr>
<tr>
<td></td>
<td>Ocular lesion (-)</td>
<td>157</td>
</tr>
<tr>
<td>Onset-, 10-years (N = 284) Ocular lesion (+)</td>
<td>87</td>
<td>148</td>
</tr>
<tr>
<td></td>
<td>Ocular lesion (-)</td>
<td>32</td>
</tr>
<tr>
<td>All cases (N = 2399) Iridocyclitis (+)</td>
<td>262</td>
<td>1653</td>
</tr>
<tr>
<td></td>
<td>Iridocyclitis (-)</td>
<td>261</td>
</tr>
<tr>
<td>All cases (N = 2399) Retino- uveitis (+)</td>
<td>239</td>
<td>1676</td>
</tr>
<tr>
<td></td>
<td>Retino- uveitis (-)</td>
<td>241</td>
</tr>
<tr>
<td></td>
<td>OR (95%CI)</td>
<td>P</td>
</tr>
<tr>
<td>--------------------------</td>
<td>--------------</td>
<td>-------</td>
</tr>
<tr>
<td>N = 2399</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (10 years)</td>
<td>1.12 (1.04-1.21)</td>
<td>0.004</td>
</tr>
<tr>
<td>Female</td>
<td>0.55 (0.44-0.68)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Skin lesion</td>
<td>0.08 (0.05-0.13)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Genital ulceration</td>
<td>0.08 (0.06-0.10)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Positive pathergy test</td>
<td>0.51 (0.40-0.64)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Arthritis</td>
<td>0.91 (0.74-1.13)</td>
<td>0.397</td>
</tr>
<tr>
<td>Gastrointestinal symptom</td>
<td>0.50 (0.39-0.65)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Vascular lesion</td>
<td>0.98 (0.70-1.37)</td>
<td>0.898</td>
</tr>
<tr>
<td>Neurological manifestation</td>
<td>1.12 (0.86-1.45)</td>
<td>0.394</td>
</tr>
</tbody>
</table>

Disclosure: N. Horita, None; A. Suwa, None; M. Takeno, None; T. Ishido, None; Y. Kirino, None; N. Mizuki, None.


Abstract Number: 1151

Clinical Manifestations of Behçet’s Disease Depending on Sex and Age: Nationwide Japanese Registration

Takehito Ishido, Nobuyuki Horita, Mitsuhiro Takeno, Mizuho Ishido, Yohei Kirino and Nobuhisa Mizuki, 1Department of Ophthalmology and Visual Science, Yokohama City University Graduate School of Medicine, Yokohama, Japan, 2National Human Genome Research Institute, National Institutes of Health, Bethesda, MD, 3Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan, 4Department of Stem Cell and Immune Regulation, Yokohama City University Graduate School of Medicine, Yokohama, Japan, 5Yokohama City University, Yokohama, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Behçet’s disease (BD) has a broad spectrum of clinical phenotypes. Sex differences in BD presentation has been one of the major topics of BD epidemiology. The prevalence of BD was found not to be very different between men and women, whereas that of each symptom showed a clear difference between the sexes. However, it is important to consider age factor in discussing sex differences, because the differences are mainly caused by sex hormone environments in the reproductive age besides sex chromosome gene products. In principle, genetic factors contribute to disease phenotype more prominently in young aged onset patients than elderly ones in any diseases. On contrary, elderly individuals are more exposed environmental factors and the effects are accumulated. Unfortunately, age differences in BD was reported in few studies with smaller numbers of cases.

Methods: The database of newly registered BD was obtained from the Japanese Ministry of Health, Labour and Welfare. Patients who met International Criteria for Behçet's Disease (ICBD) were selected and analyzed. Prevalence of manifestations was compared after stratifying by sex alone, age alone, and simultaneous sex plus age.

Results: Among 6627 ICBD cases, 2651 (40.0%) were men and 3976 (60.0%) were women with a median age of 39 years (IQR 31-50 years) (Abstract Table 1). Ocular lesion was more common in male (odds ratio (male: female) 2.64 (95%CI: 2.35-2.95, P < 0.001) and genital ulceration was more common in female (odds ratio 0.29, 95%CI 0.25-0.32, P < 0.001). Ocular lesion (P < 0.001), arthritis (P < 0.001), and vascular lesions (P < 0.001) were more frequently observed in elderly-registered patients. Contrarily, genital ulceration (P < 0.001), epididymitis of males (P = 0.023), and oral ulceration (P = 0.003) were more common in younger patients. Simultaneous assessment of sex and age revealed that male predominance of ocular involvement was found in the young adult generation, but not in patients over 70 year of age (Abstract Figure 1). A female predominance of genital ulcer was prominently observed in patients 20-59 year of age; however, the sex difference was not found in patients over 60 years of age. Sensitivity analysis using International Study Group criteria replicated the results.
Conclusion: We showed that clinical phenotype in early phase of BD was different depending on onset age and sex.

Abstract Table 1. Demographic and clinical profiles.

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>Intl Criteria for Behçet's Disease</th>
<th>Comparison between sexes</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>7950</td>
<td>6627</td>
<td>M 2651, F 3976</td>
</tr>
<tr>
<td>Age (year) Median</td>
<td>40 (IQR:31-52)</td>
<td>39 (IQR 31-50)</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Sex (Male)</td>
<td>3379/7950 (42.5%)</td>
<td>2651/6627 (40.0%)</td>
<td>Not available</td>
</tr>
<tr>
<td>Oral ulceration</td>
<td>7250/7738 (93.7%)</td>
<td>6500/6589 (98.6%)</td>
<td>OR 0.49 (0.32-0.75), P = 0.001</td>
</tr>
<tr>
<td>Skin</td>
<td>6289/7707 (81.6%)</td>
<td>5674/6530 (86.9%)</td>
<td>OR 0.82 (0.71-0.94), P = 0.006</td>
</tr>
<tr>
<td>Ocular</td>
<td>2801/7518 (37.3%)</td>
<td>2617/6390 (41.0%)</td>
<td>OR 2.58 (2.33-2.86), P &lt; 0.001</td>
</tr>
<tr>
<td>Genital ulceration</td>
<td>4752/7532 (63.1%)</td>
<td>4716/6422 (73.4%)</td>
<td>OR 0.29 (0.25-0.32), P &lt; 0.001</td>
</tr>
<tr>
<td>Positive pathergy test</td>
<td>1568/4772 (32.9%)</td>
<td>1540/4181 (36.8%)</td>
<td>OR 1.20 (1.05-1.36), P = 0.006</td>
</tr>
<tr>
<td>Arthritis</td>
<td>3717/7445 (49.9%)</td>
<td>3294/6301 (52.3%)</td>
<td>OR 0.67 (0.61-0.74), P &lt; 0.001</td>
</tr>
<tr>
<td>Epididymitis in male</td>
<td>289/3032 (9.5%)</td>
<td>247/2397 (10.3%)</td>
<td>Not available</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>2368/7495 (31.6%)</td>
<td>1785/6342 (28.1%)</td>
<td>OR 0.91 (0.81-1.02), P = 0.090</td>
</tr>
<tr>
<td>Vascular</td>
<td>746/6543 (11.4%)</td>
<td>683/5516 (12.4%)</td>
<td>OR 1.55 (1.32-1.82), P &lt; 0.001</td>
</tr>
<tr>
<td>Neurological</td>
<td>1688/7509 (22.5%)</td>
<td>1543/6363 (24.2%)</td>
<td>OR 0.91 (0.81-1.02), P = 0.100</td>
</tr>
<tr>
<td>HLA-B51 positive</td>
<td>1609/3579 (45.0%)</td>
<td>1356/3044 (44.5%)</td>
<td>OR 1.32 (1.14-1.52), P &lt; 0.001</td>
</tr>
</tbody>
</table>

Abstract Figure 1. Subgrouping by sex and age of patients who satisfied International Criteria for Behçet's Disease criteria.

Disclosure: T. Ishido, None; N. Horita, None; M. Takeno, None; M. Ishido, None; Y. Kirino, None; N. Mizuki, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/clinical-manifestations-of-behcets-disease-depending-on-sex-and-age-nationwide-japanese-registration

Abstract Number: 1152
Interleukin-37 As an Independent Disease Activity Marker of Adult-Onset Still’s Disease

Seoung Wan Nam1, SuMan Kang2, Hyoungyoung Kim3, Ga-Young Ahn4, Min Jung Kim3 and Dae-Hyun Yoo1, 1Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), 2Division of Rheumatology, Department of Internal Medicine, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), 3Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), 4Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Diagnosis and accurate measurement of disease activity in adult-onset Still’s disease (AOSD) are still challenging due to its heterogeneous clinical manifestations and the lack of serological markers. A few serological markers, such as ferritin, C-reactive protein (CRP), interleukin (IL)-18 have been suggested but their clinical role is limited. IL-37 is a novel anti-inflammatory cytokine belonging to IL-1 cytokine family. However, there has been no study on the role of IL-37 in AOSD patients.

Objectives: We aimed to investigate the role of IL-37 as a disease activity marker of patients with AOSD.

Methods: A total of 51 patients meeting the Yamaguchi criteria were recruited at a single university hospital. Patients’ clinical data and additional laboratory study including serum IL-18 and IL-37 were acquired both at the definite disease flare status (defined as modified Pouchot score 4 or more) and at the definite disease remission status (with modified Pouchot score 2 or less without significant clinical symptoms for more than a month). AOSD disease activity markers were compared between flare and remission status by Wilcoxon signed rank test and their correlation were evaluated by Spearman’s correlation test.

Results: The mean age of study population was 48.8 ± 2.0. The mean interval between flare and remission was 7.2 ± 0.6 months. There were significantly higher levels of modified Pouchot score, serum ferritin, CRP, IL-18 and IL-37 level in flare status compared to remission (p<0.01) supporting their roles as disease activity markers. IL-37 level positively correlated with other AOSD disease activity markers including modified Pouchot score, CRP, and ferritin at flare status. The sensitivity and specificity of IL-37 for the disease flare status were 80% and 82%, respectively, at a cut-off value of 82.1 pg/mL. The AUC for IL-37 was 0.85 (95% confidence interval of 0.78-0.93). IL-18 level showed highest correlation with ferritin level at flare status (Spearman’s Rho = 0.632, p<0.01). In contrast, IL-37 level had highest correlation with CRP level at flare status (Spearman’s Rho = 0.574, p<0.01). And, there was no significant correlation between IL-18 and IL-37 levels (p=0.13). These differences in the presentation of interactive relationship between cytokines and other disease activity markers suggest the different role of IL-37 from that of IL-18 in activated AOSD status.

Conclusion: IL-37 can be used as an efficient disease activity marker in AOSD patients. And, it has a distinctive role as disease activity marker and inflammatory modulator in AOSD patients.

Table 1. Comparison of AOSD disease activity marker levels between flare and remission status (n=31)

<table>
<thead>
<tr>
<th></th>
<th>Flare</th>
<th>Remission</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modified Pouchot Score</td>
<td>6.0 (4.0, 7.0)</td>
<td>0 (0, 0)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Ferritin</td>
<td>3425.0 (338.4, 9733.0)</td>
<td>60.8 (39.3, 108.1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>CRP</td>
<td>7.6 (3.2, 12.7)</td>
<td>0.4 (0.35, 0.4)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>IL-18</td>
<td>91552.2 (49784.2, 141944.5)</td>
<td>1316.9 (637.2, 6069.9)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>IL-37</td>
<td>231.6 (86.5, 740.1)</td>
<td>28.2 (7.5, 62.6)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Data shown are median [interquartile range]. CRP, C-reactive protein; IL, interleukin.
Rheumatic Manifestations of Whim Syndrome

Ananta Subedi¹, Shubhasree Banerjee¹, Blas Betancourt¹, James D. Katz¹, Peter C. Grayson¹, Elena Cho², Daniel Velez², Philip M. Murphy² and David H. McDermott², ¹National Institute of Arthritis, Musculoskeletal and Skin Disease (NIAMS), Bethesda, MD, ²National Institute of Allergy and Infectious Diseases (NIAID), Bethesda, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: WHIMS (Warts, Hypogammaglobulinemia, Infections, and Myelokathexis Syndrome) is a rare autosomal dominant primary immunodeficiency due to gain of function mutations of the CXC chemokine receptor 4 (CXCR4). CXCR4 signaling is crucial in hematopoietic stem cell homeostasis, and plays an important role in innate and adaptive immune responses. The disease often manifests with recurrent bacterial infections and Human Papilloma Virus (HPV)-induced warts of the hand, feet and genitals. The focus of our study is to characterize the rheumatological manifestations in WHIMS patients.

Methods: Nine patients out of 36 diagnosed with WHIM syndrome enrolled in a treatment protocol were assessed. These 9 patients were identified owing to rheumatological complaints. Demographics, clinical presentation, laboratory data and imaging studies were tabulated to look for common characteristics and patterns of presentation.

Results: The majority of our cohort had onset of rheumatological complaints as children or young adults. Six out of nine were female. The spectrum of initial complaints ranged from arthralgia to overt arthritis. The pattern of joint involvement included asymmetric or symmetric oligo- or polyarthritis involving small and large joints. Three patient exhibited symptoms after a known trigger. In one case, an Oligoarticular small and large joint arthritis postdated a positive urethral chlamydia PCR. Three patients had presentation satisfying a retrospective diagnosis of juvenile idiopathic arthritis. Only one patient had septic arthritis. Another had idiopathic avascular necrosis of the hip in the childhood. We observed that four patients had worsening of joint symptoms temporally related to the treatment of the primary disease. Two patients had tenosynovitis involving the fingers leading to deformity. Auto-antibodies were negative in all eight patients and none were HLA B27 positive. Arthrocentesis data was available in two patients and revealed inflammatory synovial fluid. One of the patients underwent synovial biopsy demonstrating chronic synovitis with T and B lymphocytes. Overall, the response to NSAIDs was variable. Sulfasalazine was used in two of the five patients for purposes of steroid sparing with partial benefit.
Conclusion: Rheumatological manifestations have not previously been reported as a major component of the clinical manifestation of WHIM syndrome. We present the first detailed cataloguing of such manifestations in a cohort of WHIM patients. Our finding of a high prevalence of joint findings warrants further study. The etiology of arthritis in WHIM syndrome is unknown but could relate to impaired clearance of infectious organisms associated with arthritis or alternatively, an increased risk for autoimmune disease. The rheumatological management of these patients is challenging due to the underlying immunodeficiency.

Disclosure: A. Subedi, None; S. Banerjee, None; B. Betancourt, None; J. D. Katz, None; P. C. Grayson, None; E. Cho, None; D. Velez, None; P. M. Murphy, None; D. H. McDermott, None.

Abstract Number: 1154

Use of Including Serum Ferritin and Heme Oxygenase 1 in the Yamaguchi’s Classification for Adult-Onset Still’s Disease: A Multicenter Retrospective Study

Yohei Kirino1, Yasushi Kawaguchi2, Yoshifumi Tada3, Hiroshi Tsukamoto4, Toshiyuki Ota5, Masahiro Iwamoto6, Hiroki Takahashi7, Kohei Nagasawa8, Syuji Takei9, Takahiko Horiuchi10, Hisae Ichida2, Seiji Minota11, Atsuhiisa Ueda1, Akihide Ohta12 and Yoshiaki Ishigatubo13

1Department of Stem Cell and Immune Regulation, Yokohama City University Graduate School of Medicine, Yokohama, Japan, 2Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan, 3Department of Internal Medicine, Division of Rheumatology, Saga University, Saga, Japan, 4Department of medicine and biosystemic science, Kyushu University Hospital, Fukuoka, Japan, 5Department of Rheumatology, Iizuka Hospital, Iizuka, Japan, 6Department of Rheumatology and Clinical Immunology, Jichi Medical University, Shimotsuke, Japan, 7Department of Gastroenterology, Rheumatology and Clinical Immunology, Sapporo Medical School School of Medicine, Sapporo, Japan, 8Rheumatic Disease Center, Sawara Hospital, Sawara, Japan, 9Pediatrics of Developmental Medicine, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima, Japan, 10Department of Internal Medicine, Kyushu University Beppu Hospital, Beppu, Japan, 11Department of Internal Medicine, Division of Rheumatology/Clinical Immunology, Jichi Medical University, Shimotsuke, Japan, 12Saga University School of Medicine, Saga, Japan, 13Yokohama City University, Yokohama, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Yamaguchi’s criteria for classification of adult-onset Still’s disease (AOSD) has been widely applied in clinic despite it was established decades ago. However, hyperferritinemia, which is a hallmark of AOSD, is not included in the criteria. Moreover, the criteria requires differential diagnosis of malignancy, infection, etc., which has been challenging. Heme oxygenase (HO)-1 is a stress-inducible heme degrading enzyme highly expressed in monocyte/macrophage, serum levels of which has been reported as a promising biomarker for AOSD. We here report data on the use of serum ferritin and HO-1 levels in an attempt to improve the classification of AOSD.

Methods: Under the Hypercytokinemia Study Group collaboration, we collected sera from a total of 145 AOSD cases. Three independent experts judged whether the patient is definite AOSD depending on clinical information. These “definite AOSD” patients were further divided into active, remission, and relapse groups, based on their clinical status. Other rheumatic diseases such as ANCA-associated vasculitis, and culture-positive sepsis were included as disease controls. Serum ferritin and HO-1 levels were measured in all of the collected samples by means of ELISA. An association among clinical symptoms, serum ferritin, and HO-1 was explored. Multivariate regression analysis was performed to identify the independent variables associated with definite AOSD diagnosis.

Results: Serum ferritin and HO-1 levels were significantly higher in active and relapsed AOSD cases compared to disease controls, and were reduced by the treatment. Although significant correlation between serum ferritin and HO-1 levels were observed, discrepancy was found in some cases such as patients with iron-deficient anemia (Figure). ROC analysis identified optimal levels of serum ferritin (> 833 ng/ml; sensitivity 77.5%, specificity 81.1%), and HO-1 (>96.4 ng/ml; sensitivity 92.5%, specificity 81.1%) that differentiate AOSD from disease controls. Multivariate analysis identified typical skin rash, lymphadenopathy/splenomegary, seronegative, high HO-1 as independent variables associated with AOSD diagnosis.
**Conclusion:** We confirmed that serum ferritin and HO-1 serve as biomarkers for AOSD. Including biomarkers in the Yamaguchi's criteria may reduce heterogeneity of the included patients, although further validation is necessary.

**Figure:** Comparison of serum ferritin and serum HO-1 in AOSD and disease-controls.

Horizontal and vertical dots indicate cut-off values determined from ROC analysis.

**Disclosure:** Y. Kirino, None; Y. Kawaguchi, None; Y. Tada, None; H. Tsukamoto, None; T. Ota, None; M. Iwamoto, None; H. Takahashi, None; K. Nagasawa, None; S. Takei, Chugai, Eisai, Takeda, Bristol-Myers Squibb, 2, Chugai, Mitsubishi-Tanabe, Pfizer, Ayumi, 8; T. Horiuchi, None; H. Ichida, None; S. Minota, None; A. Ueda, None; A. Ohta, None; Y. Ishigatsubo, None.

**Abstract Number:** 1155

**Impact of Adalimumab on Immunosuppressant Use in Patients with Active and Inactive Non-Infectious Intermediate, Posterior, or Pan-Uveitis in the Ongoing Open Label Study: Visual-III**

Sergio Schwartzman, Alfredo Adan, Hiroshi Goto, Koju Kamoi, Martina Kron, Alexandra P. Song, Kevin Douglas, Sophia Pathai and C. Stephen Foster, 

1 Hospital for Special Surgery, New York, NY, 2 Department of Rheumatology, VU University Medical Center, Amsterdam, Netherlands, 3 Hospital Clinic. Barcelona. Spain, Barcelona, Spain, 4 Tokyo Medical University, Tokyo, Japan, 5 Tokyo Medical and Dental University, Tokyo, Japan, 6 AbbVie Deutschland GmbH & Co. KG, Ludwigshafen, Germany, 7 AbbVie Inc., North Chicago, IL, 8 AbbVie Ltd, Maidenhead, United Kingdom, 9 Massachusetts Eye Research and Surgery foundation and Harvard Medical School, Boston, MA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Miscellaneous Rheumatic and Inflammatory Diseases Poster I

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The morbidity associated with the use of immunosuppressants is well described in patients (pts) with autoimmune ophthalmic disease and presents a challenge to treating physicians. The purpose of this analysis was to determine the impact of adalimumab (ADA) on immunomodular (IMM) use in pts with active and inactive non-infectious uveitis in the ongoing open label study: VISUAL-III.

**Methods:** Adults who met treatment failure criteria in VISUAL-I/VISUAL-II studies (defined as pts with active uveitis) or who successfully completed the parent studies without treatment failure (defined as pts with inactive uveitis) were eligible to enroll in VISUAL-III and received ADA 40-mg every other week for the study duration. Corticosteroids (CS) and/or IMM therapy were permitted as needed. For this analysis, proportion of pts on IMM and percent change in systemic IMM dose were analyzed in pts using medications for immunosuppression. Interim follow-up data from VISUAL-III baseline (week 0) through week-78 are described. In
addition, proportion of pts who achieved a ≥50% reduction in immunosuppression load (CS + IMM) relative to week 8 (for active uveitis) and relative to week 0 (for inactive uveitis) is reported. Data are presented as-observed. Adverse events are reported from first ADA dose up to the data cut-off date of 31-October-2016.

**Results:** Of 424 pts enrolled, 371 (active uveitis; n=242 and inactive uveitis; n=129) were included in the intent-to-treat analysis. Of these 371 pts, 117 (32%) (active uveitis; n=65 (56%) and inactive uveitis; n=52 (44%)) were using IMM at VISUAL-III entry. By week 78, the number of pts using IMM decreased (active uveitis, n=36 and inactive uveitis, n=32). The systemic IMM dose was substantially reduced by week 78 compared to baseline in pts with active and inactive uveitis. In pts with active uveitis using CS + IMM, 47% (52/110) achieved a ≥50% reduction in immunosuppression load relative to week 8, while in pts with inactive uveitis 13% (5/39) achieved a ≥50% reduction in immunosuppression load relative to week 0 (Figure A-B). Adverse Event rates were consistent with previous VISUAL trials.

**Conclusion:** Long-term treatment with ADA suggests decreased IMM dependence along with substantial reduction in IMM dose in pts with active and inactive uveitis.

**References:**

**Disclosure:** S. Schwartzman, Abbvie, Antares, Genentech, Janssen, Lilly, Novartis, Pfizer, Regeneron, Sanofi, and UCB, 5, Abbvie, Janssen, Genentech, Pfizer, UCB, Crescendo, and Novartis, 8; I. Van der Horst-Bruinsma, Abbvie, MSD, UCB, 5, Pfizer, MSD and Abbvie, 2; A. Adan, AbbVie, Santen and Allergan, 9; H. Goto, AbbVie Inc, 9; K. Kamoi, None; M. Kron, AbbVie Inc, 1, AbbVie Inc, 3; A. P. Song, AbbVie Inc, 1, AbbVie Inc, 3; K. Douglas, AbbVie Inc, 1, AbbVie Inc, 3; S. Pathai, AbbVie Inc, 1, AbbVie Ltd, 3; C. S. Foster, Aldeyra (Lexington, MA, USA), Bausch & Lomb Surgical, EyeGate, Novartis, pSivida, and Xoma, 5, Alcon and Allergan, 8, Alcon, Aldeyra, Bausch & Lomb, Clearside Biomedical, Dompe, Icon, Novartis, Santen, Xoma, Aciont and pSivida, 2.

**Abstract Number:** 1156

**Rheumatic Immune Related Adverse Events from Checkpoint Inhibitor Therapy for Cancer: Long-Term Follow up Data**

Cassandra Calabrese1, Elizabeth Kirchner1, Apostolos Kontzias1, Laura Wood2, Brian Rini2, Vamsidhar Velcheti2 and Leonard H. Calabrese1, 1Rheumatic & Immunologic Disease, Cleveland Clinic Foundation, Cleveland, OH, 2Hematology and Oncology, Cleveland Clinic Foundation, Cleveland, OH

**First publication:** September 18, 2017
IgG4-Related Disease

Hypocomplementemia Is Closely Related to IgG Subclasses Other Than IgG4 in IgG4-Related Disease

Ichiro Mizushima1, Kazunori Yamada2, Motohisa Yamamoto3, Takak Maeki4, Shoko Matsui5, Satoshi Hara6, Hiroki Takahashi7, Hideki Nomura8, Shigeyuki Kawa9 and Mitsuhiro Kawano6, 1Kanazawa University Hospital, Kanazawa, Japan, 2Department of Advanced Research in Community Medicine, Kanazawa University Graduate School of Medical Sciences, Kanazawa, Japan, 3First Department of Internal Medicine, Sapporo Medical University School of Medicine, Sapporo, Japan, 4Department of Internal Medicine, Nagaoka Red Cross Hospital, Nagaoka, Japan, 5Health Administration Center, University of Toyama, Toyama, Japan, 6Division of Rheumatology, Kanazawa University Hospital, Kanazawa, Japan, 7Department of Gastroenterology, Rheumatology and Clinical Immunology, Sapporo Medical University School of Medicine, Sapporo, Japan, 8Department of General Medicine, Kanazawa University Hospital, Kanazawa, Japan, 9Center for Health, Safety and Environmental Management, Shinshu University, Matsumoto, Japan

First publication: September 18, 2017
Hypocomplementemia frequently occurs in IgG4-related disease (IgG4-RD), especially IgG4-related kidney disease (IgG4-RKD). This study aimed to investigate the clinical features of IgG4-RD patients (pts) with hypocomplementemia using a large-scale cohort of 328 IgG4-RD pts, in order to clarify the clinical significance and mechanisms of hypocomplementemia.

Methods: We retrospectively evaluated the clinical features at diagnosis of 328 pts diagnosed with IgG4-RD according to the comprehensive diagnostic criteria or each organ-specific diagnostic criteria; the features we evaluated included age; sex; serum IgG4, IgE, CH50, C3, C4, and CRP levels; gaps between serum IgG and IgG4 levels (IgG-IgG4 levels); the serum IgG4/IgG ratio; and the affected organs. These data were longitudinally analyzed over the clinical course for patients whose data were available. Hypocomplementemia was defined as a decrease below the normal range for the serum CH50, C3, or C4 level. We applied multivariate logistic regression analysis to the variables with \( P < 0.05 \) in univariate analysis to search for factors related to hypocomplementemia in the group of all pts, pts with IgG4-RKD, and pts without IgG4-RKD.

Results: The pts comprised 201 men and 127 women (average age 63.9 years). At diagnosis, the average serum IgG4 level was 750 mg/dL (range: 18 to 3,510). Hypocomplementemia was observed in 138 pts (42.1%). The salivary glands were involved in 241 pts, lacrimal glands in 188, pancreas in 85, retroperitoneum/arteries in 82, kidneys in 80, and lungs in 76. Compared with pts without hypocomplementemia, pts with it had significantly higher age (65.0 vs. 63.0 years, \( P = 0.044 \)), serum IgG4 (947 vs. 608 mg/dL, \( P = 0.001 \)) and IgG-IgG4 levels (1,976 vs. 1,428 mg/dL, \( P < 0.001 \)), IgG4/IgG ratio (31.0% vs. 27.2%, \( P = 0.028 \)), and number of involved organs (3.5 vs. 3.0 organs, \( P = 0.007 \)). They also had a higher incidence of renal (34.8% vs. 16.8%, \( P < 0.001 \)), pancreatic (34.1% vs. 20.0%, \( P = 0.005 \)), and lung (29.7% vs 18.4%, \( P = 0.024 \)) involvement. Multivariate logistic regression analysis for all pts indicated that the elevation of IgG-IgG4 levels [per 100 mg/dL, odds ratio (OR) 1.102, 95% confidence interval (CI) 1.036-1.173, \( P = 0.002 \)] and the presence of pancreatic lesions (OR 1.909, 95% CI 1.063-3.428, \( P = 0.031 \)) were independent factors related to hypocomplementemia. Of note, the same analysis in pts with IgG4-RKD showed that only the elevation of IgG-IgG4 levels (per 100 mg/dL, OR 1.227, 95% CI 1.094-1.375, \( P = 0.001 \)) was an independent factor, whereas the presence of pancreatic lesions (OR 1.963, 95% CI 1.048-3.676, \( P = 0.035 \)), but not the elevation of IgG-IgG4 levels (OR 1.046, 95% CI 0.984-1.111, \( P = 0.153 \)), was an independent factor in pts without IgG4-RKD. In IgG4-RKD, both pts with and without hypocomplementemia showed serum IgG4 re-elevation upon relapse of renal lesions. Notably, the pts with hypocomplementemia showed exacerbation of hypocomplementemia and re-elevation of IgG-IgG4 levels, while the pts without it did not.

Conclusion: The present study shows that hypocomplementemia is related to the elevation of IgG subclasses other than IgG4 in IgG4-RD, especially IgG4-RKD.
Background/Purpose: Uveitis are inflammatory processes of the vascular layer of the eye, the uvea, which is divided into iris (anterior uvea), ciliary body (intermediate) and choroid (posterior uvea). Many of these uveitis will have severe repercussions on the visual function and quality of life of the patients. We propose a clinical trial that allows us to evaluate the presence of differences in disease control (frequency and severity of relapses, and need for addition of another drug over time of the study) between biological therapy with adalimumab (ADA) and conventional disease-modifying antirheumatic drugs.

Methods: Prospective interventional study at 2 years of follow-up, type III clinical trial, with a sequential randomization of treatments. A sample size of 92 outpatients from a multidisciplinary autoimmune unit with one rheumatologist and one ophthalmologist, were assigned to ADA, methotrexate (MTX) or cyclosporine (CyA). Inclusion criteria for study selection were: non infectious uveitis, recurrent uveitis (≥ 3 relapses) and 1 episode of previous uveitis with severity criteria. Indicators of inflammation were: decreased visual acuity, tyndall effect, flare, par planitis and cells in vitreous. Severity indicators were: onset of synechiae, band-keratophaty, cataract, cystic macular edema, retinitis, choroiditis and vasculitis. Clinical response was defined as the improvement of one inflammation indicator without worsening of the rest, from 6 months to the end of study. The patients were assessed at 0, 2, 6, 12, 18 and 24 months.

Results: A total of 92 patients were reviewed, 57.6% males. The mean age at initiation of the study was 40.9 ± 14.9 years. The most frequent diagnosis was idiopathic uveitis (66.3%), uveitis associated with autoimmune disease (22.8%) (ankylosing spondylitis 5, psoriatic arthritis 4, juvenile idiopathic arthritis 3, inflammatory bowel disease 3) and primary uveitis due to juvenile idiopathic arthritis "like" (7.6%). Granulomatous uveitis were 68 (73.9%) vs non-granulomatous 24 (26.1%).

Data analyzed showed the 3 drugs groups achieved clinical response maintained in 100% of the cases. Outcome measures to evaluate effectiveness as number of recurrence of uveitis showed significant differences ($x^2_{kruskall-wallis} = 7.146; p=0.028$), with more patients without relapse in ADA group. There was not significative difference in severity uveitis relapse ($x^2_{k-w} = 1.408; p=0.495$) (table 1) or addition of another drug (21 patients, $x^2_{K-W}=0.651; p =0,722$).

Conclusion: In our study we show such as ADA, MTX and CyA therapy are effective in non-infectious uveitis control in the disease inflammation, severity relapse and need for another drug, without statistical difference between groups. A total of 52 patients had at least one relapse over time the study, with better result in ADA group. This fact is very important due to the relation between number of relapse and the structural damage in uveitis.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>UVEITIS RELAPSE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Severity relapse</td>
</tr>
<tr>
<td>ADA</td>
<td>7 (13,4)</td>
</tr>
<tr>
<td>CyA</td>
<td>10 (19,2)</td>
</tr>
<tr>
<td>MTX</td>
<td>16 (30,7)</td>
</tr>
<tr>
<td></td>
<td>33 (63,4)</td>
</tr>
</tbody>
</table>

Disclosure: E. Rubio Romero, None; R. Aguilar Galán, None; R. Menor Almagro, None; A. Muñoz, None; J. Povedano, None.


Abstract Number: 1159

National Recommendations on the Use of Immunomodulatory Drugs in Patients with NON-Infectious NON-Malignant Anterior Uveitis

Gerard Espinosa1, Santiago Muñoz2, Jose M Ruiz de Morales3, Jose M Herreras4 and Miguel Cordero-Coma5, 1Autoimmune Diseases Department. Hospital Clinic de Barcelona, Barcelona, Spain, 2Rheumatology, Hospital Infanta Sofia, Madrid, Spain, 3Complejo Asistencial Universitario de León, León, Spain, 4Ophthalmology, Hospital Universitario, IOBA, Valladolid, Spain, 5Ophthalmology, Hospital de León, Spain, León, Spain

First publication: September 18, 2017

SESSION INFORMATION
Background/Purpose: Anterior uveitis (AU) is the most common pattern of uveitis, that might lead to important ocular complications including blindness. Immunomodulatory drugs have been used in order to prevent recurrences of uveitis. Nevertheless, it is not clear which drug could be preferred in each patient. The aim of the project was to generate recommendations on the use of immunomodulators in adult patients with non-infectious, non-neoplastic anterior uveitis (AU) based on best evidence and experience.

Methods: Delphi methodology was followed. A multidisciplinary panel of 5 experts (2 ophtalmologists, one immunologist, one rheumatologist, one internist) was established, who, in the first nominal group meeting, defined the scope, users, and chapters of the document. A systematic literature review was performed to assess the efficacy and safety of immunomodulators in patients with non-infectious, non-neoplastic AU. All of the exposed above was discussed in a second nominal group meeting and 33 recommendations were generated. Recommendations agreement grade was tested also in 25 additional experts. Recommendations were voted from 1 (total disagreement) to 10 (total agreement). We defined agreement if at least 70% voted ≥7. The level of evidence and grade or recommendation was assessed using the Oxford Centre for Evidence-based Medicine Levels of Evidence.

Results: The 33 recommendations were accepted. They include specific recommendations on patients with non-infectious, non-neoplastic UA, as well as different treatment lines. Methotrexate (MTX) or Sulfasalazine were recommended as a first line drugs in refractory cases to topical treatments in patients with AU and spondyloarthritis, inflammatory bowel disease, psoriasis, idiopathic HLA-B27 positive or negative AU. Etanercept was recommended for patients with TRAPS syndrome, and for those with other autoinflammatory syndromes canakinumab or anakinra. In case of bilateral sarcoidosis, relapsing polychondritis or TINU syndrome, MTX was recommended along with systemic steroids. For patients with a flare of AU and Behçet disease, systemic steroids along with azathioprine or a calcineurin inhibitor were recommended. The indication of an immunomodulatory drug in patients with multiple sclerosis was considered to be decided with a neurologist. For patients refractory to all exposed above and or intolerant, depending on AU type, a change to another classical immunomodulatory drug or to an anti-TNF was recommended (adalimumab, infliximab, certolizumab or ). Except for patients with TINU, etanercept was not recommended because current evidence does not support the use of it to prevent AU flares.

Conclusion: In patients with non-infectious, non-neoplastic AU, these recommendations on the use of immunomodulators might be a guide in order to help in the treatment decision making, due to the lack of robust evidence or other globally accepted algorithms.

Disclosure: G. Espinosa, None; S. Muñoz, None; J. M. Ruiz de Morales, None; J. M. Herreras, None; M. Cordero-Coma, None.

Increased Incidence of Upper and Lower Gastrointestinal Events in Patients with Sarcoidosis: A Population-Based Cohort Study

Patompong Ungprasert1, Cynthia S. Crowson2 and Eric L. Matteson3, 1Rheumatology, Mayo Clinic, Rochester, MN, 2Health Sciences Research, Mayo Clinic College of Medicine and Science, Rochester, MN, 3Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, MN

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Increased Incidence of Upper and Lower Gastrointestinal Events in Patients with Sarcoidosis: A Population-Based Cohort Study

Background/Purpose: An increased incidence of gastrointestinal (GI) events has been observed in patients with autoimmune diseases such as rheumatoid arthritis. However, there is little information about GI complications among patients with sarcoidosis.
Methods: 345 patients (50% female; 90% Caucasian, 5% African-American; mean age 45.6 years) with incident sarcoidosis in 1976-2013 in a geographically well-defined population were identified based on comprehensive individual medical record review. Inclusion to this cohort required physician diagnosis supported by histopathology, compatible clinical presentation, and exclusion of other causes of granulomatous inflammation. A total of 345 sex and age-matched comparators (50% female; 95% Caucasian, 1% African-American; mean age 45.4 years) were also identified from the same underlying population. Medical records of both cases and comparators were individually reviewed for upper and lower GI events. Upper GI events included ulcer, hemorrhage, perforation, obstruction, esophagitis and esophageal varices. Lower GI events included ulcer, hemorrhage, perforation, obstruction, colitis and inflammatory bowel disease. The cumulative incidence of all and individual GI events adjusted for the competing risk of death was estimated. Cox proportional hazards models with adjustment for age, sex, and calendar year were used to compare the rate of development of GI events, individually and in combination, between cases and comparators.

Results: A total of 101 patients with sarcoidosis and 63 comparators developed GI events after index date during a median follow-up of 13.6 years among patients with sarcoidosis and 15.9 years among comparators. After adjusting for age, sex and calendar year, the risk of GI events after index date was significantly higher among patients with sarcoidosis with adjusted hazard ratio (HR) of 1.90 (95% confidence interval (CI), 1.38 – 2.61). The risk was increased for both upper GI events (HR 1.90; 95% CI, 1.27 – 2.83) and lower GI events (HR 1.97; 95% CI, 1.27 – 3.05). Analysis by individual GI event revealed a significantly increased risk of upper GI hemorrhage, upper GI ulcer and diverticulitis as shown in table 1.

Conclusion: This first ever population-based evaluation of GI events in sarcoidosis revealed that patients with this disease have a significantly increased risk of events affecting the upper and lower GI tracts.

Table 1: Hazard ratio of GI events after index date, comparing patients with sarcoidosis with subjects without sarcoidosis

<table>
<thead>
<tr>
<th>Subtype of GI event</th>
<th>HR (95% CI) for all events after index date, adjusting for age, sex and calendar year</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Upper GI events</strong></td>
<td></td>
</tr>
<tr>
<td>Ulcer</td>
<td>2.56 (1.27 – 5.17)</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>2.36 (1.24 – 4.47)</td>
</tr>
<tr>
<td>Perforation</td>
<td>Not available</td>
</tr>
<tr>
<td>Obstruction</td>
<td>1.20 (0.43 – 3.32)</td>
</tr>
<tr>
<td>Esophagitis</td>
<td>1.58 (0.87 – 2.88)</td>
</tr>
<tr>
<td>Esophageal varices</td>
<td>6.51 (0.78 – 54.16)</td>
</tr>
<tr>
<td>Any upper GI events</td>
<td>1.90 (1.27 – 2.83)</td>
</tr>
<tr>
<td><strong>Lower GI events</strong></td>
<td></td>
</tr>
<tr>
<td>Ulcer</td>
<td>3.51 (0.73 – 16.92)</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>1.32 (0.62 – 2.82)</td>
</tr>
<tr>
<td>Perforation</td>
<td>Not available</td>
</tr>
<tr>
<td>Obstruction</td>
<td>Not available</td>
</tr>
<tr>
<td>Diverticulitis</td>
<td>2.29 (1.03 – 5.10)</td>
</tr>
<tr>
<td>Ischemic colitis</td>
<td>2.38 (0.61 – 9.26)</td>
</tr>
<tr>
<td>Infectious colitis</td>
<td>1.99 (0.79 – 5.00)</td>
</tr>
<tr>
<td>Drug-induced colitis</td>
<td>Not available</td>
</tr>
<tr>
<td>Other colitis</td>
<td>Not available</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>1.87 (0.95 – 3.70)</td>
</tr>
<tr>
<td>Any lower GI events</td>
<td>1.97 (1.27 – 3.05)</td>
</tr>
</tbody>
</table>

Disclosure: P. Ungprasert, None; C. S. Crowson, None; E. L. Matteson, None.

**Clinical Characteristics of Ocular Sarcoidosis: A Population Based Study 1976-2013**

Patompong Ungprasert¹, Andrea Tooley², Cynthia S. Crowson³, Eric L. Matteson⁴ and Wendy M. Smith⁵, ¹Rheumatology, Mayo Clinic, Rochester, MN, ²Ophthalmology, Mayo Clinic, Rochester, MN, ³Health Sciences Research, Mayo Clinic College of Medicine and Science, Rochester, MN, ⁴Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, MN, ⁵Department of Ophthalmology, Mayo Clinic, Rochester, MN

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Monday, November 6, 2017
**Session Title:** Miscellaneous Rheumatic and Inflammatory Diseases Poster I
**Session Type:** ACR Poster Session B
**Session Time:** 9:00AM-11:00AM

**Clinical Characteristics of Ocular Sarcoidosis: A Population Based Study 1976-2013**

**Background/Purpose:** To characterize the epidemiology and clinical characteristics of ocular involvement in patients with systemic sarcoidosis.

**Methods:** An inception cohort of patients with systemic sarcoidosis in 1976-2013 in a geographically well-defined population was identified based on comprehensive individual medical record review. Inclusion required physician diagnosis of sarcoidosis supported by histopathology of non-necrotizing granulomata, characteristic radiologic features of intrathoracic sarcoidosis and exclusion of other granulomatous diseases. Medical records of those patients were then reviewed for ocular involvement.

**Results:** A total of 345 incident cases of systemic sarcoidosis were identified. Ocular involvement occurred in 23 patients (mean age 51.8 years, 65% female and 78% Caucasian). The most common ocular disease was uveitis (61%) followed by conjunctival nodule (17%). Other types of ocular involvement that were observed in this cohort included episcleritis, anterior scleritis, conjunctivitis, lacrimal gland involvement, eyelid lesion, dry eye disease and optic neuritis. ACE level was elevated in 83% of patients (10 out of 12 tested patients) while hypercalcemia was found in 46% of patients (6 out of 13 tested patients) in whom these tests were obtained. All patients had intrathoracic involvement of sarcoidosis (hilar adenopathy and/or interstitial infiltration).

Among 14 cases with uveitis, 86% were female; 86% were Caucasian, 7% were African-American and 7% were Native-American. Mean age at diagnosis of uveitis was 56.5 years. Anterior uveitis was the most common type of uveitis (71%) followed by intermediate uveitis (21%), posterior uveitis (7%) and panuveitis (7%). Uveitis was the initial presentation prior to the diagnosis of systemic sarcoidosis in 8 (57%) of 14 uveitis cases. Visual acuity (VA) of patients with uveitis was generally good at diagnosis with the majority of eyes having VA of 20/20 to 20/25 in each eye. Visual outcome was also good; only 2 of 24 affected eyes with adequate follow-up lost more than or equal to 3 lines of VA (define as losing more than or equal to 0.3 logMAR) during follow-up due to uveitis, and only 1 eye had VA worse than 20/200 at last visit.

The majority of patients with sarcoid uveitis in this cohort were treated with topical glucocorticoids for the eyes (78%) and/or oral glucocorticoids (64%). Disease modifying anti-rheumatic agents (DMARDs) and biologic agents were infrequently required (only 1 case with methotrexate and 1 case with hydroxychloroquine).

**Conclusion:** Ocular involvement occurred in 7% of sarcoidosis patients in this first ever population-based study of ocular sarcoidosis. Uveitis was the most common type of ocular disease. Visual outcome was generally good.

**Disclosure:** P. Ungprasert, None; A. Tooley, None; C. S. Crowson, None; E. L. Matteson, None; W. M. Smith, None.

[View Abstract and Citation Information Online](http://acrabstracts.org/abstract/clinical-characteristics-of-ocular-sarcoidosis-a-population-based-study-1976-2013)
Langerhans cell histiocytosis (LCH) is a rare condition, and mostly affects children. Bone is the most commonly involved organ, with bone lesions in 50% of patients. In a recent work, Aricò et al. described that the probability of survival in children suffering from a multisystemic LCH with risk organ involvement was reduced if patients did not have any bony lesion. There is no such study in adult patients in order to know the bone impact on the prognosis.

Methods:
A retrospective monocentric study was performed using data from the patients hospitalized for a LCH at Centre Hospitalier Régional Universitaire de Lille, a university hospital between 2001 and 2015. All patients with LCH and at the age of 18 years or older were included. Patients were excluded if they did not receive any osteoarticular imaging (radiography, bone scan, PET, MRI).

Results:
Our study initially included 70 patients had LCH. After screening 54 patients met the inclusion criteria: 31 had bone localization (BLG) and 23 none (NBLG). The two groups showed differences. The lesion leading to the diagnosis was mostly osteoarticular (18 patients) in BLG and pulmonary (18 patients) in NBLG. The BLG presented more multisystemic form than the NBLG (20 vs 2, p<0.0001). Treatment was required for 14 patients in BLG and for 2 in NBLG. In BLG, 8 patients were treated medically, mostly by corticosteroid therapy and chemotherapy (7), one patient underwent radiotherapy. 6 patients were treated by surgery. In NBLG, 2 patients were treated by corticosteroid therapy. There was no surgery in NBLG (table 1). 3 patients died in BLG, 2 directly related to LCH and one from postoperative infectious complications. One patient died in NBLG from haematological pathology (chronic myelomonocytic leukaemia). The time between diagnosis and death was one, six and 22 months in BLG, 36 months in NBLG. 7 patients presented relapses in BLG. 5 had been treated by medical treatment, one surgically and one had no previous treatment. The time of relapse was six, 8, 12, 14, 16, 52 and 72 months. 4 presented new bone lesions, 1 pulmonary lesions, 1 dermatological lesions and 1 neurologic lesion (table 1). There was no relapse in NBLG. Unfortunately, there was a lack of statistical power to conclude about the bone impact on the prognosis.

Both groups were equivalent for comorbidities (p=0.206 for cancer and p=0.756 for cardiovascular disease), number of smokers and age at diagnosis (36.8+/- 3.0 years vs 36.7+/- 3.0 years, p=0.96 and 25 vs 22, p=0.063, respectively in the bone location group (BLG) and the no bone location group (NBLG).

Conclusion:
Patients with bone location and those with no bone location are two different phenotypes of adult LCH. Patients with bone location are more prone to have a multisystemic relapsing disease. A multicentric study with a larger number patients is needed to bring more robust data to answer about bone impact on the prognosis of adult LCH.

Disclosure: J. G. Letarouilly, None; N. Segaud, None; B. Wallaert, None; P. Y. Hatron, None; R. M. FLIPO, None.
Agent, Rph-104, in Healthy Subjects

Ahmet Gul1, Sibel Ulker2, Recep Selim Turk2, Ugur Onsel Turk2, Cemil Gurgun2, Yan Lavrovsky3, Mikhail Samsonov4, Sebnem Ozen5 and Serdar Altinel6, 1Department of Internal Medicine, Division of Rheumatology, Istanbul University, Istanbul Faculty of Medicine, Istanbul, Turkey, 2Ege University Drug Development and Pharmacokinetics Research and Application Centre (ARGEFAR), Izmir, Turkey, 3R-Pharm Overseas, Inc., San Diego, CA, 4Medical Department, R-Pharm JSC, Moscow, Russian Federation, 5Clinical Trial Department, TRPHARM İlac A.S., Istanbul, Turkey, 6Clinical Trial Department, TRPHARM İlac A.S., Istanbul, Turkey

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Interleukin-1 (IL-1) is highly active pro-inflammatory cytokine, which is responsible for clinical and laboratory findings in hereditary and acquired auto-inflammatory disorders. Blocking IL-1 activity in these conditions results in a rapid and sustained reduction in inflammatory activity and disease severity. RPH-104, a novel heterodimeric fusion protein containing IL-1R1 and IL-1RAcP linked to immunoglobulin heavy chains, highly selectively binds IL-1β, but can also bind IL-1α and IL-1Ra with lower affinity. In this First-in-Human study, we aimed to evaluate safety as well as pharmacokinetic (PK) and pharmacodynamic (PD) parameters of RPH-104.

Methods: A total of 35 healthy volunteers (HV) were enrolled in this randomized, double-blind, placebo-controlled, single-dose study. Five different dosages (4 mg, 20 mg, 40 mg, 80 mg and 160 mg) were tested in cohorts consisted of 7 HV in each. Each HV was hospitalized for 72 hours and followed up to 60 days after subcutaneous (SC) injection of RPH-104. Evaluation of safety data after each subgroup was performed by the Independent Data Monitoring Committee; and the next subgroup could be dosed when the previous dose results did not reveal any risk safety concern.

Results: Totally 35 HV were dosed, 5 HV were administered RPH104 and 2 HV were administered placebo (saline) in each cohort; All 35 HV were included in the safety analysis but 33 HV were included in PK analysis (2 drop outs). Totally 70 adverse events (AE) were reported, none of them were serious. None of the AE was related to the study drug nor leaded to subject withdrawal. All AE were of mild intensity. RPH-104 was safe and well tolerated in terms of AE and other clinical and laboratory parameters at all dose levels. PK parameters of RPH-104 are summarized at Table 1 and Figure 1. Mean terminal elimination half-life ($t_{1/2}$) was similar in all cohorts. Initial results suggest linear PK for RPH-104 at all dose levels. PD analysis are ongoing. However, according to the PD analysis of the first 2 cohorts, administration of RPH-104 resulted in a decrease in Serum Amyloid A levels starting from the first hour post-dose in 20 mg cohort, and they remained suppressed throughout the study which may suggest the first biologic activity of RPH-104. Conclusion: RPH-104 was administered first time in humans, and it was considered safe and well tolerated following single dose SC administration at different dose levels. A linear PK was observed.
Disclosure: A. Gul, None; S. Ulker, None; R. S. Senturk, None; U. Onsel Turk, None; C. Gurgun, None, 5; Y. Lavrovsky, None, 3; M. Samsonov, None, 3; S. Ozen, None, 3; S. Altinel, None, 3.


Abstract Number: 1164

Spectrum of Skin Eruption and Histological Findings in Adult-Onset Still’s Disease and Significance of Atypical Persistent Skin Eruptions
Elina Zuelgaray¹, Maxime Battistella², Camille Sallé de Chou¹, Patrice Cacoub³, François Chasset⁴, Christopher Rein⁵, Nathan Peiffer-Smadja³, Fanny Domont³, Marie Chapalain⁶, Claude Bachmeyer⁴, Laurence Fardet⁶, Bruno Fautrel⁷, Martine Bagot¹ and Jean-David Bouaziz¹,

¹Dermatology Department, Saint-Louis Hospital, Paris, France, ²Pathology Department, Saint-Louis Hospital, Paris, France, ³Department of Internal Medicine and Clinical Immunology, Groupe Hospitalier Pitié-Salpêtrière, Paris, France, ⁴Dermatology Department, Tenon Hospital, Paris, France, ⁵Department of Internal Medicine and Clinical Immunology, Groupe Hospitalier Pitié-Salpêtrière, Paris, France, ⁶Dermatology Department, Mondor Hospital, Paris, France, ⁷UPMC University Paris 06, Pitié-Salpêtrière Hospital, Paris, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Adult-onset Still disease (AOSD) is a rare systemic inflammatory disorder characterized by spiking fevers, polyarthritis and an evanescent salmon-pink maculopapular eruption. Several cases of atypical persistent skin eruption (APSE) have been reported in AOSD to date. APSE could be associated with AOSD poor prognosis and resistance to treatment. We report the second largest series of AOSD with accurate clinical and histological data.

Methods:
A multicenter retrospective study was conducted (6 french centers) including all patients with a diagnosis of AOSD (Yamaguchi and/or Fautrel criteria) with skin involvement and a skin biopsy between 2005 and 2017. Clinical, biological and histological data, delay of diagnosis and treatments used were recorded. A review of all APSE cases described in the literature was also performed.

Results:
Thirty-six patients were included (median age: 46 years-old, female: 69%). Nineteen (53%) presented an APSE (Figure 1). Extracutaneous attempts included: arthralgia/arthritis (94%), lymphadenopathy (36%), hepato/splenomegaly (25%), pericarditis/pleurisy (11%). The following factors seemed to be increased in patients with APSE (n=19) in comparison with patients without APSE (n=17): time to diagnosis (p=0.1), arthritis (p=0.09), liver dysfunction (p=0.08), ferritin level higher than 1,500 ng/mL (p=0.018), number of line of treatments to achieve complete remission (p=0.08). Reactive hemophagocytic syndrome and associated malignancy were similar in both groups. Ninety-four cases of APSE in AOSD were previously reported, characterized by urticarial lesions (with a linear configuration in some cases), pigmented papules or plaques, lichenoid lesions or dermatomyositis-like lesions. Histology of APSE compared with evanescent salmon-pink maculopapular skin eruption displayed increased dermal inflammatory infiltrate and neutrophils, and increased epidermal alterations (dyskeratosis/necrotic keratinocytes, spongiosis).

Conclusion:
Cutaneous clinical and histological spectrum in AOSD is large and should not delay the diagnosis. These results have to be confirmed by large prospective cohorts.

Figure 1: A 58-year-old woman presenting a pruritic APSE (erythematous and pigmented papules and plaques of the cheeks and the leg) (A,B). Skin biopsy of the leg lesion revealed a moderate perivascular and interstitial dermal infiltrate composed of lymphocytes and neutrophils, a dermal oedema and vascular walls infiltrate (C)
Clinical Characteristics of Patients with Late-Onset Familial Mediterranean Fever in Japan

Dai Kishida¹, Masahide Yazaki¹, Akinori Nakamura¹, Ayako Tsuchiya-Suzuki¹, Yasuhiro Shimojima² and Yoshiki Sekijima¹, ¹Department of Medicine (Neurology and Rheumatology), Shinshu University School of Medicine, Matsumoto, Japan, ²Department of Medicine (Neurology and Rheumatology), Shinshu University School of Medicine, Matsumoto, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Familial Mediterranean fever (FMF) is an auto-inflammatory disease characterized by recurrent episodes of fever and polyserositis. Most patients have their first febrile attack before the age of 20. Elderly onset (after 40 years) is very rare, but we do encounter these patients sometimes. Therefore, the aim of this study was to evaluate the demographic, clinical, and genetic characteristics of late-onset FMF patients in the Japanese population.

Methods: We analyzed clinical features and mutations in the MEFV gene of 384 patients, who were referred to our laboratory (Department of Medicine [Neurology and Rheumatology], Shinshu University School of Medicine) between September 2003 and September 2016. All patients were clinically diagnosed with FMF by the Tel-Hashomer criteria. Patients were divided into three groups based on the age of disease onset; group I: 19 years and younger (early-onset group), group II: 20–39 years, group III: 40 years and older (late-onset group). Mutation analysis of the MEFV gene was performed by direct sequencing of the product of polymerase chain reaction amplification for hotspot regions (exons 1, 2, 3, 5, and 10). Differences between categorical variables were analyzed using chi-square test with Bonferroni correction. Continuous variables were evaluated with Kruskal-Wallis test and multiple comparison.

Results: The study enrolled 63 patients (16.4%) who experienced their first FMF attack when older than 40 years. In this patient group, high fever (90.5%) was the most common clinical finding. In contrast, the percentage of patients with peritonitis (66.2% in group I, 66.8% in group II, 34.9% in group III) and pleuritis (47.0% in group I, 36.5% in group II, 27.0% in group III) was significantly lower in late-onset patients compared with early-onset patients. In the late-onset group, the frequency of patients having a mutation in the MEFV gene (57.1%) and a mutation in exon 10 (12.7%), which induces a severe clinical FMF phenotype, was significantly lower than in early-onset patients. The response to colchicine therapy was good (88.6%) and similar in all groups. Family history of FMF was less frequent in the late-onset group.

Conclusion: In Japan, there are a number of FMF patients with late-onset. Our observation indicates that they have a milder form of the disease with less frequent peritonitis and pleuritis and a good response to colchicine treatment. However, careful differential diagnosis
may be needed because they have a lower prevalence of the MEFV gene mutation, especially in exon 10.

Table 1: Comparison of patients between the three groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Group I (n = 153)</th>
<th>Group II (n = 176)</th>
<th>Group III (n = 82)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic features</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at onset (mean)</td>
<td>31 (20-65)</td>
<td>31 (20-55)</td>
<td>31 (20-60)</td>
<td>0.05</td>
</tr>
<tr>
<td>Age at diagnosis (mean)</td>
<td>34 (20-70)</td>
<td>35 (20-70)</td>
<td>35 (20-70)</td>
<td>0.96</td>
</tr>
<tr>
<td>Median birth year (mean)</td>
<td>1960 (1900-1990)</td>
<td>1960 (1900-1990)</td>
<td>1960 (1900-1990)</td>
<td>0.05</td>
</tr>
<tr>
<td>Male/Female</td>
<td>22/78</td>
<td>30/76</td>
<td>21/61</td>
<td>0.92</td>
</tr>
</tbody>
</table>

Clinical symptoms

| Frequency (mean) (per year) | 17 (4.8) | 15 (1.5) | 15 (2.5) | 0.54 |
| Fever (°C) | 13 (95%) | 10 (95%) | 8 (70%) | 0.71 |
| Laboratory | 100 (64.2%) | 110 (60.9%) | 22 (13.6%) | 0.02 |
| Presence | 70 (47.9%) | 82 (51.9%) | 17 (21.3%) | 0.03 |
| Arthritis | 68 (42.7%) | 80 (51.7%) | 29 (35.8%) | 0.23 |

Eculizumab

| Administration of eculizumab | 80 (79%) | 75 (77%) | 80 (98%) | 0.06 |
| Overall response to eculizumab | 80 (79%) | 75 (77%) | 80 (98%) | 0.025 |
| Complete response to eculizumab | 80 (79%) | 75 (77%) | 80 (98%) | 0.025 |

Outcome

| Curing rate of treatment | 100% | 100% | 100% | 1.01 |
| Curing rate for 12 months | 50 (43.5%) | 50 (43.5%) | 10 (12.5%) | 0.01 |
| Probability of cure at 12 months | 40 (30.5%) | 40 (29.5%) | 8 (12.5%) | 0.025 |

*,, ** and *** denote significant differences between Groups I vs II, Groups I vs III, and Groups II vs III, respectively (after Bonferroni correction).

Disclosure: D. Kishida, None; M. Yazaki, None; A. Nakamura, None; A. Tsuchiya-Suzuki, None; Y. Shimojima, None; Y. Sekijima, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/clinical-characteristics-of-patients-with-late-onset-familial-mediterranean-fever-in-japan

Abstract Number: 1166

Systemic Degos Disease: Long Term Survival on Combined Therapy with Eculizumab and Treprostinil

Lee S. Shapiro1,2, Jessica Farrell1,2,3, Roberta Lukasiewicz1,2, Peter A. Merkel4, Douglas Rosing5, Manfred Boehm6, Axia Toledo-Garcia1, Maria Karas7, Maria DeSancho8, Harry McCoy9, Michael Marmulstein10, and Scott Beegle11, 1The Center for Rheumatology, Albany, NY, 2Steffens Scleroderma Center, Albany, NY, 3Pharmacy Practice, Albany College of Pharmacy & Health Sciences, Albany, NY, 4Division of Rheumatology, University of Pennsylvania, Philadelphia, MN, 5Cardiovascular Pulmonary Branch, National Heart, Lung, and Blood Institute (NHLBI), NIH, Bethesda, MD, 6Center for Molecular Medicine, NHLBI/ NIH, Bethesda, MD, 7Division of Cardiology/Department of Medicine, Weill Cornell Medical College, New York, NY, 8Weill Cornell Medical Center, New York, NY, 9Blue Ridge Cancer Care, Blacksburg, VA, 10Albany Associates in Cardiology, Albany, NY, 11Division of Pulmonary and Critical Care Medicine, Albany Medical College, Albany, NY

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Degos disease (Malignant Atrophic Papulosis) is a thrombotic microvasculopathy of complement activation, endothelial cell injury and progressive microvascular obliteration. Lesions are marked by vascular C5b-9 deposition and a type 1 interferon rich microenvironment. Systemic disease historically results in death within 2-3 years, most commonly from gastrointestinal perforations and the resulting sepsis or stroke. There have been no effective treatment options. Experience with this combination therapy for systemic Degos disease has resulted in prolonged survival for our patients with improved quality of life.

Methods:

We performed a retrospective analysis of the clinical outcomes of 4 patients with Degos disease treated with treprostinil and eculizumab.
Patients 1 and 2 were critically ill in late 2009 with gastrointestinal complications of systemic Degos disease. Patient 1, a 51 year old man was started on eculizumab in October 2009. Patient 2, a 25 year old man was started on eculizumab in December 2009. Both patients experienced immediate, dramatic response. Because of disease progression despite ongoing therapy with eculizumab, Patient 2 began therapy with treprostinil in December 2010 and Patient 1 in March 2014. Despite lasting disease damage, both Patient 1 and 2 have regained good quality of life, are in stable health and are working full time.

Patient 3, is a 45 year old woman with cutaneous Degos lesions who developed sudden monocular vision loss and severe eye pain requiring enucleation. Pathologic findings of microvascular changes were consistent with systemic Degos disease. Exploratory laparoscopy in October 2012 revealed innumerable Degos lesions. Based on the experience of the first 2 patients, and difficulty obtaining eculizumab, patient 3 began treatment with treprostinil. Due to inadequate disease control, eculizumab was added. Other than loss of vision in the affected eye, patient remains stable on dual therapy, working full time.

Patient 4 is a 56 year old woman who was seen with a 4 year history of biopsy confirmed cutaneous Degos disease and persistent and 1 year of intermittent episodes of intensifying abdominal pain, pericarditis and peripheral neuropathy suggestive of systemic progression. Laparoscopy detected intestinal and hepatic lesions consistent with Degos disease. Eculizumab was initiated in October 2015 and treprostinil in May 2016. Since patient 4 began this treatment regimen her abdominal pain has resolved. Her condition has been quiet and stable without major disease complication in two years of treatment. Her quality of life is good and she is working full time.

Conclusion:
Systemic Degos disease is extremely rare and our cohort is small (n=4), but these cases provide promising results in terms of patient survival and quality of life. Among our 4 patients, two are approaching the 8-year survival mark. Therapy with eculizumab and treprostinil may be an effective treatment for systemic Degos disease, especially if initiated prior to catastrophic sequelae. Heightened awareness, early assessment for systemic involvement, rapid initiation of treatment and vigilant follow-up have been associated with prolonged survival.

Disclosure: L. S. Shapiro, None; J. Farrell, None; R. Lukasiewicz, None; P. A. Merkel, Actelion, Alexion, Boston Pharm., Bristol-Myers Squibb, ChemoCentryx, Genzyme/Sanofi, GlaxoSmithKline, Genentech/Roche, InflaRx, PrincipioBio, Proteon, Seattle Genetics, 5, Actelion, Bristol-Myers Squibb, CaridianBCT, Celgene, ChemoCentryx, Genentech/Roche, GlaxoSmithKline, Kypha, MedImmune/AstraZeneca, 2, American College of Rheumatology European League Against Rheumatism National Institutes of Health: NHLBI, NIAMS, NIAID, NCATS, ORDR-US Food and Drug Administration The Patient-Centered Outcomes Research Institute The Vasculitis Foundation, 2; D. Rosing, None; M. Boehm, None; A. Toledo-Garcia, None; M. Karas, None; M. DeSancho, None; H. McCoy, None; M. Marmulstein, None; S. Beegle, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/systemic-degos-disease-long-term-survival-on-combined-therapy-with-eculizumab-and-treprostinil

Abstract Number: 1167

Phenotypical Features of Patients with Rheumatologic Manifestations of Common Variable Immunodeficiency

MARIA GUTIERREZ, Kathleen E. Sullivan, Ramsay Fuleihan and Clifton O. Bingham III, Pediatrics, Johns Hopkins University, BALTIMORE, MD, Pediatrics, University of Pennsylvania, Philadelphia, PA, Pediatrics, Ann & Robert H. Lurie Children's Hospital, Chicago, IL, Rheumatology, Johns Hopkins University, Baltimore, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Patients with common variable immunodeficiency (CVID) have a higher incidence of rheumatologic disorders. To delineate this clinical association, we investigated the phenotypical features of patients with CVID affected by these conditions.
Methods:
We conducted a retrospective analysis of 870 pediatric and adult patients with CVID included in the United States Immunodeficiency Network (USIDNET) registry. Outcomes included clinical characteristics (age, gender, ethnicity, rheumatologic diagnosis, comorbidities) and basic immunophenotype (immunoglobulin levels, T- and B- cell counts) in patients with rheumatologic disorders compared with those with non-inflammatory CVID. Demographic and clinical data were compared using chi-square, Fisher’s exact or Wilcoxon-Mann-Whitney tests. For immunological variables, Generalized Estimating Equations (GEE) regression models were built to evaluate the relationship between IgA, IgM, CD19+ B-cell counts and CD4/CD8 ratios and CVID-associated rheumatologic disorders.

Results:
Physician-reported rheumatic diseases were present in 5.9% of patients with CVID (n=51) included in the registry. Although CVID affects both sexes equally, there were more females (3.3:1 female to male ratio) in the rheumatic disease group (p<0.05). Specific disorders included: inflammatory arthritis (n=18), Sjogren’s syndrome (n=11), SLE (n=8), Raynaud’s syndrome (n=8), medium and small vessel vasculitis (n=8), MCTD (n=3), other (n=5). There were no significant differences in the frequency of other CVID complications such as bronchiectasis between the two groups (p>0.05). Additionally, no significant differences in immunoglobulin levels (IgA and IgM), CD19+ B-cells counts or CD4/CD8 ratio were detected.

Conclusion:
These results highlight the coexistence of primary antibody disorders and systemic autoimmune diseases. Importantly, hypergammaglobulinemic, autoantibody-associated disorders such as Sjogren’s syndrome and SLE were among the most common, demonstrating that they can occur even in the setting of a primary antibody deficiency. Basic immunophenotypical parameters demonstrated no significant differences, although characteristics such as specific T- and B-cell subpopulations were not evaluated. Finally, the female predominance in the rheumatic disease group, brings into question whether sex-related factors may play a role in the development of certain CVID manifestations. This study has several limitations, namely the retrospective nature of the analysis, variable amounts of missing data and lack of confirmation of rheumatic diagnosis using current classification data. Nonetheless, these findings should raise awareness for primary antibody immunodeficiencies among patients with rheumatic disorders. Delineating the link between systemic autoimmunity and humoral immunodeficiencies can also provide novel insights into the immune abnormalities underlying these related conditions.

Disclosure: M. GUTIERREZ, None; K. E. Sullivan, None; R. Fuleihan, None; C. O. Bingham III, BMS, 2,BMS, 5.

Abstract Number: 1168

Eosinophilic Fasciitis: Baseline Retrospective Evaluation of Clinical Characteristics and Prognosis in a Cohort of 83 Patients

Robert L. Mango1, Kubra Bugdaycil2, Cynthia S. Crowson3, Margot S. Peters4, Lisa A. Drage5, Julia S. Lehman4 and Vaidehi Chowdhary6, 1Internal Medicine, Division of Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, MN, MN, 2Department of Internal Medicine, Division of Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, MN, MN, 3Health Sciences Research, Mayo Clinic College of Medicine and Science, Rochester, MN, 4Pathology and Dermatology, Mayo Clinic College of Medicine and Science, Rochester, MN, MN, 5Dermatology, Mayo Clinic College of Medicine and Science, Rochester, MN, MN, 6Internal Medicine, Division of Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, MN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Eosinophilic fasciitis (EF) is a rare disease and there have been few published series that include clinical, pathological and serological data. These studies have provided disparate information on clinical course, with high rates of complete resolution and recurrence reported. Furthermore, no clear direction has emerged on the prognostic significance of features initially reported to be characteristic for EF.
Methods: We conducted a retrospective review of all EF patients evaluated at our institution from 1/1/1997 to 12/30/2016. Clinical records were reviewed to confirm the diagnosis of EF. Baseline demographic data, clinical, laboratory features at time of diagnosis and information on clinical course were collected. Kaplan-Meier methods were used to determine response and recurrence rates over time.

Results: We identified 83 patients with eosinophilic fasciitis seen within the study period. The median age of diagnosis was 53 years and the female to male ratio was 1:1. Majority of patients (90%) were diagnosed with combination of clinical features and biopsy, 6 (7%) were diagnosed based on clinical presentation alone, and 2 were diagnosed by clinical and imaging (MRI) features. Mean time to diagnosis from symptom onset was 7.9 months (range 1 – 45). Twenty-one patients (25%) reported exercise as a possible trigger. Groove sign was noted in only 24 (29%). Active inflammatory arthritis was noted in 9 patients at the time of initial EF evaluation, and only one of these had a known diagnosis of rheumatoid arthritis. Muscle weakness was described in 8 (10%), and EMG was interpreted as indicative of inflammatory myopathy in 6/17 (35%). The median absolute eosinophil count was 0.4-x10^9/ml and peripheral eosinophilia was noted in 37/74 patients (50%). Elevated erythrocyte sedimentation rate was seen in 16/70 (23%) and elevated CRP in 33/56 (59%). CK was elevated in 2/40 (5%), but aldolase was elevated in 9/33 (27%). High titer (≥1:320 or ≥ 3 units by ELISA) positive ANA was seen in 5/66 (8%). The median follow up was 2.3 years (range 0.2 – 18.5) among 46 patients with at least one follow up visit. Of those, 35 were initially seen within 1 year of diagnosis, and were included in prognosis analysis. By 3 years, 57% (95% confidence interval [CI] 32 -73%) had achieved a complete response with resolution of skin thickening. The rate of recurrence was 47% (95% CI 20 - 65%) at 3 years.

Conclusion: In a cohort of patients with EF defined by clinical diagnosis, rates of classic features in addition to, complete response and recurrence rates, are similar to those in previously published reports. To our knowledge, this is the largest retrospective cohort study of patients with EF.

Disclosure: None;
K. Bugdayli, None;
C. S. Crowson, None;
M. S. Peters, None;
L. A. Drage, None;
J. S. Lehman, None;
V. Chowdhary, None.


Abstract Number: 1169

**Rapid Improvement with Tocilizumab in Refractory and Severe Uveitic Cystoid Macular Edema**

Nuria Vegas-Revenga^1^, Vanesa Calvo-Rio^1^, Natalia Palmou-Fontana^1^, Marina Mesquida^2^, Alfredo Adan^2^, M. Victoria Hernández^2^, Emma Beltrán^3^, Elia Valls Pascual^4^, David Díaz-Valle^5^, Gisela Díaz-Cordovés^6^, María Luisa Hernández- Grafella^7^, Lucia Martínez-Costa^7^, Inmaculada Calvo^8^, Antonio Atanes^9^, Luis Francisco Linares^10^, Consuelo Mosdeo^11^, Elena Aurrecochea^12^, Miguel Cordero-Coma^13^, Rosalia Demetrio-Pablo^1^, Carlos Fernández-Diaz^14^, Lucia C. Domínguez-Casas^14^, José Luis Martín-Varillas^14^, Belén Atienza-Mateo^14^, Jose L. Hernández^15^, Miguel Angel González-Gay^14^ and Ricardo Blanco^14^, 1Hospital Universitari Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, 2Internal Medicine, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, 3Rheumatology, Hospital del Mar. Barcelona. Spain, Barcelona, Spain, 4Rheumatology, Hospital Universitario de Valencia. Spain, Valencia, Spain, 5Hospital Clinico San Carlos. Madrid. Spain, Madrid, Spain, 6Rheumatology, Hospital Regional Universitario de Málaga. Spain, Málaga, Spain, 7Ophthalmology, Hospital Universitario Doctor Peset. Valencia. Spain, Valencia, Spain, 8Hospital Universitario i Politecnico La Fe. Valencia. Spain, Valencia, Spain, 9Rheumatology, Complejo Hospitalario Universitario A Coruña (CHUAC). Spain, A Coruna, Spain, 10Rheumatology, Hospital Virgen de la Arrixaca. Murcia. Spain, Murcia, Spain, 11Hospital Universitari Vall d'Hebron. Barcelona. Spain, Barcenola, Spain, 12Rheumatology, Hospital de Sierrallana. Torrelavega. Spain, Torrelavega, Spain, 13Ophthalmology, Hospital de León. Spain, León, Spain, 14Rheumatology, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, 15Internal Medicine, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
In uveitis, remission-inducing therapy with even more vigor than does rheumatology is mandatory. Since the eye is so much less forgiving of chronic inflammation than is the joint, with profound life-altering consequences. Cystoid macular edema (CME) is the leading cause of blindness in uveitis.

Our aim was to evaluate the rapid efficacy of Tocilizumab (TCZ) in refractory CME.

**Methods:** Multicentre study of 25 patients with CME due to non-infectious uveitis who had inadequate response or intolerance to traditional treatment with corticosteroids and at least one conventional immunosuppressive drug including in most cases biological therapy (n=22). CME was defined by (OCT >300 μm).

The outcome variables were the degree of inflammation of the anterior chamber and vitreous, visual acuity, macular thickness. The results are expressed as mean ±SD for normally distributed variables, or as median [interquartile range] when are not. Comparison of continuous variables was performed using the Wilcoxon test.

**Results:** 25 patients (17 women/8 men), mean age, 33.6±18.9 years were studied. The associated diseases were: juvenile idiopathic arthritis (9), Behçet's disease (7), Birdshot retinochoroidopathy (4), idiopathic (4), sarcoidosis (1). The ocular pattern was: panuveitis (9), anterior uveitis (7), posterior uveitis (5) and intermediate uveitis (4). Most patients had bilateral involvement (24). Prior to biological therapies patients received: intraocular corticosteroids (22), iv. methylprednisolone (7), methotrexate (MTX) (19), cyclosporine A (CSA) (17), mycophenolate (4), azathioprine (2), leflunomide (2), cyclophosphamide (1), sulfasalazine (1), acetazolamide (1) and thalidomide (1). The biological used before the administration of TCZ were infliximab (8), adalimumab (19), etanercept (2), golimumab (2), rituximab (2), abatacept (3), anakinra (1) and daclizumab (1).

TCZ administration schedule was 8 mg/kg/4 weeks iv. (n=23), every 2 weeks (n=1) and subcutaneously 162 mg/2 week (n=1). TCZ was used in monotherapy (13) or combined with conventional immunosuppressive (12). Most of intraocular inflammation parameters showed a rapid improvement after TCZ onset (**TABLE**), with corticosteroid-sparing effect (15.9±13.6 to 8.5±5.17 mg; p=0.001). Remission was achieved in 8 patients and improvement in 17. After a month, no minor side effects were observed, so no patient had to stop treatment. No side effects were observed.

**Conclusion:** TCZ seems a rapid effective treatment in refractory uveitic CME.

**TABLE**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>1st week</th>
<th>2nd week</th>
<th>1st month</th>
</tr>
</thead>
<tbody>
<tr>
<td>OCT (microns)</td>
<td>415.7±177.15</td>
<td>413.3±162.9*</td>
<td>388.06±158.1*</td>
<td>330.8±104.2*</td>
</tr>
<tr>
<td>mean ± SD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visual acuity</td>
<td>0.39±0.31</td>
<td>0.4±0.31</td>
<td>0.45±0.3*</td>
<td>0.51±0.3*</td>
</tr>
<tr>
<td>mean ± SD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior chamber</td>
<td>1 [0-1]*</td>
<td>0.5 [0-1]*</td>
<td>0 [0-1]*</td>
<td>0 [0-0]*</td>
</tr>
<tr>
<td>cells [median (IQR)]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitritis [median</td>
<td>1 [0-2]</td>
<td>1 [0-1.5]</td>
<td>0 [0-1]*</td>
<td>0 [0-0.5]*</td>
</tr>
<tr>
<td>(IQR)]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*p <0.05 compared with basal data

**Disclosure:** N. Vegas-Revena, None; V. Calvo-Río, None; N. Palmou-Fontana, None; M. Mesquida, None; A. Adan, AbbVie, Santen and Allergan, 9; M. V. Hernández, None; E. Beltrán, None; E. Valls Pascual, None; D. Diaz-Valle, None; G. Díaz-Cordovés, None; M. L. Hernández-Grafella, None; L. Martínez-Costa, None; I. Calvo, None; A. Atanes, None; L. F. Linares, None; C. Modesto, None; E. Aurrecoechea, None; M. Cordero-Coma, None; R. Demetrio-Pablo, None; C. Fernández-Díaz, None; L. C. Dominguez-Casas, None; J. L. Martín-Varillas, None; B. Atienza-Mateo, None; J. L. Hernández, None; M. A. González-Gay, None; R. Blanco, None.


Abstract Number: 1170
High Output Flow Cytometry Array Classifies Subjects with Uveitis Due to Behcet’s Disease and Sarcoidosis

Johannes Nowatzky1, Ezra Resnick2, Julia Manasson3, Cristy Stagnar1 and Olivier Manches4, 1Department of Medicine, Division of Rheumatology, NYU School of Medicine, New York, NY, 2Google Inc., New York, NY, 3Department of Medicine, Division of Rheumatology, New York University School of Medicine, New York, NY, 4EFS Rhône-Alpes-Auvergne "Immunobiology and Immunotherapy in Chronic Diseases", INSERM - French National Institute of Health and Medical Research, Grenoble, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The information content of multi-parametric flow cytometry-based immune-phenotyping experiments is routinely underexploited given the paucity of adequate tools and strategies for large-scale unbiased data analysis.

Methods: We developed and applied a data analysis approach taking into account all mathematically possible combinations of markers in a given flow cytometry panel. We analyzed mined (dx.doi.org/10.5061/dryad.v6st3) flow cytometry data generated from peripheral blood samples of healthy humans and subjects with a uniform ocular patho-phenotype (pan-uveitis) caused by 2 different autoimmune diseases: Behcet's disease and sarcoidosis. Flow data were gated in bivariate plots. We employed combinatorial mathematics to generate a matrix quantifying the representation of all possible cell populations using given sets of markers within the respective starting populations and coded the algorithm in Java. Computed metadata were tested against primary data sets of manually gated cell populations with known markers and immunological properties. External variables defined by biological characteristics of the subjects, i.e., ‘healthy vs diseased’ and ‘Behcet’s uveitis vs Sarcoid uveitis’ were used as independent measures of truth for sample classification.

Results: Our method increased the retrievable information content from each panel exponentially in relation to the number of markers used instead of linearly as in conventional approaches. Computed cell populations matched those in primary data sets. The method enabled clustering of healthy vs diseased subjects using only 4 common markers (CD3, C8, CD197, and CD45), and of sarcoid vs Behcet’s uveitis subjects with minimal error.

Conclusion: Our approach demonstrates that multi-dimensional analysis of flow cytometry data allows meaningful screening of biologically relevant markers enabling classification and characterization of states of health and autoimmune disease. The approach is unbiased and has the potential to facilitate the discovery of cell populations with relevance as potential biomarkers or biological research targets.

Disclosure: J. Nowatzky, None; E. Resnick, None; J. Manasson, None; C. Stagnar, None; O. Manches, None.

Abstract Number: 1171

Mycophenolate Mofetil May Improve Interstitial Pneumonia with Autoimmune Features

Sara S. McCoy1, Zubin Mukadam2, Keith C. Meyer3, Emmanuel Sampene4, Jeffrey P. Kanne5, Christopher A. Meyer5, Maria D. Martin5, Scott W. Aesif6, Laurie Rice7 and Christie M. Bartels8, 1Department of Medicine, Rheumatology Division, University of Wisconsin School of Medicine and Public Health, Madison, WI, 2PULMONARY & CRITICAL CARE, University of Wisconsin School of Medicine and Public Health, Madison, WI, 3PULMONARY & CRITICAL CARE, University of Wisconsin School of Medicine and Public Health, Madison, WI, 4Biostatistics, University of Wisconsin School of Medicine and Public Health, Madison, WI, 5Radiology, University of Wisconsin School of Medicine and Public Health, Madison, WI, 6Department of Pathology and Laboratory Medicine, University of Wisconsin School of Medicine and Public Health, Madison, WI, 7Critical Care Medicine, SSM Health Dean Medical Group, madison, WI, 8Rheumatology/Medicine, University of Wisconsin - Madison, Madison, WI

First publication: September 18, 2017
Background/Purpose: To assess the efficacy of mycophenolate mofetil (MMF) in treatment of adult patients with interstitial pneumonia with autoimmune features (IPAF).

Methods: A retrospective medical record review was performed using electronic health record searches for interstitial lung diseases and either autoimmune diseases or positive ANA in the years 2000-2013 at an academic center. Records were then manually reviewed to include all adult subjects who met European Respiratory Society/American Thoracic Society classification criteria for IPAF and to exclude those with other specific connective tissue diseases. Sociodemographic, clinical, and pulmonary function data were manually abstracted for patients with and without MMF treatment and followed longitudinally from the date of IPAF diagnosis. In this analysis, we examined diffusing capacity for carbon monoxide (DLCO) and forced vital capacity (FVC) recorded over 4 years (24 months before or after MMF initiation) to compare rates of change between treated and untreated and within treated patients.

Results: We identified 52 subjects who met criteria for IPAF, 63% female, ranging from age 31 to 83 years. Of the 52 subjects with IPAF, 28 were treated with MMF and 24 were not treated with MMF. Median time to MMF initiation among those treated was 22 months. Within the MMF group, 11 and 14 subjects had DLCO and FVC measurements, respectively, before and after MMF initiation. Median time to MMF start among those who were treated was 22 months. The average decline in FVC% and DLCO% between the MMF treated and untreated groups was not significantly different (FVC% change p=0.08; DLCO% change p=0.17); however, there was a trend to more rapid decline of both FVC% and DLCO% in the MMF-treated group.

Among subjects treated with MMF, the rate of decline of DLCO (mL/min/mmHg) significantly improved after therapy with MMF (Figure 1, p=0.007). There was not a significant difference in rate of change of FVC (L) before and after MMF treatment (p=0.07) although many stabilized (Figure 2).

Conclusion: MMF therapy stabilized the decline of DLCO and was associated with a trend toward stabilization of FVC in treated IPAF patients. These findings suggest that MMF may slow the progression of PFT changes in IPAF. Further studies are needed to confirm these findings.
Disclosure: S. S. McCoy, None; Z. Mukadam, None; K. C. Meyer, None; E. Sampene, None; J. P. Kanne, None; C. A. Meyer, None; M. D. Martin, None; S. W. Aesif, None; L. Rice, None; C. M. Bartels, Pfizer Inc, 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/mycophenolate-mofetil-may-improve-interstitial-pneumonia-with-autoimmune-features

Abstract Number: 1172

Utility of Interstitial Pneumonia with Autoimmune Features (IPAF) Proposed Criteria in the Classification of Patients with CTD-Associated Interstitial Lung Disease in a Single Centre

Fredeswinda I. Romero-Bueno1, Ana Sofia Pozo2, Maria Jesus Rodriguez-Nieto3, Maria Jose Martinez-Becerra4, Gabriel Herrero-Beaumont5 and Olga Sanchez-Pernaute1, 1Section for Autoimmune Diseases, Rheumatology, Jiménez Díaz Foundation University Hospital, Madrid, Spain, 2Faculty of Medicine, Autonoma University of Madrid, Madrid, Spain, 3Pulmonary Medicine, Jiménez Díaz Foundation University Hospital, Madrid, Spain, 4Immunology, Jiménez Díaz Foundation University Hospital, Madrid, Spain, 5Bone and Joint Research Unit, IIS-Fundacion Jimenez Diaz UAM, Madrid, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The term interstitial pneumonia with autoimmune features (IPAF) has recently been proposed to identify those patients with ILD and clinical and/or serological autoimmune manifestations who do not meet diagnostic criteria for a specific CTD (UCTD-ILD). Our aim was to re-classify our patients with ILD and features of CTD according to the 2015 European Respiratory Society/American Thoracic Society research statement proposed criteria for IPAF and examine their applicability in clinical practice. We also evaluate other clinical tools which might improve their specificity.

Methods: Retrospective review of medical records of 100 patients with ILD attending the multidisciplinary Pulmonary and Rheumatology clinic at our centre between 2011 and 2016. Fulfilment of the proposed IPAF criteria was assessed in all patients who did not meet current criteria for a definite CTD. Additional autoimmune/inflammatory data not included in the IPAF domains, as well as nailfold capillaroscopy findings (available in 47 patients), were also recorded. Analysis was carried out with non-parametric tests and significance laid at 95%.

Results: We identified 62 CTD-ILD, 26 IPAF and 12 non-IPAF patients, with 71% women. Therefore, 68% (26/38) of patients previously regarded as UCTD-ILD were captured by the IPAF criteria. Age at onset was higher in patients from the non-IPAF group (p<0.01). Definite or possible Usual Interstitial Pneumonia (UIP) and Non-Specific Interstitial Pneumonia (NSIP) were found in 41% and 40% of patients, respectively. A non-UIP morphologic pattern predominated in CTD-ILD patients (58%), while NSIP was more frequent than UIP in IPAF (46% versus 27%) and UIP predominated in non-IPAF (67%). Pulmonary hypertension and vasculopathy were associated to UIP (p<0.05). Coexistent hypersensitive pneumonitis was marginally more frequent in IPAF and non-IPAF than in CTD-ILD. There was a 72% of ANA+ and 37% RF+ patients with no differences among groups. In contrast, ACPA and dsDNA were found in 0 but only in 1 non-IPAF case. Interestingly, two patients with antisynthetase antibodies fulfilled both the preliminary criteria for antisynthetase syndrome and for IPAF. As regards items included in the IPAF clinical domain, RP was present in 27% (6/22) of IPAF patients and only in 1 non-IPAF case. No differences were found for arthritis or RP between IPAF and non-IPAF. Capillaroscopy changes were found in 67% (8/12) and 50% (6/12) of non-IPAF and IPAF patients, respectively. Haemolytic anemia, high CRP and LDH, hyperferritinemia and hypertriglyceridemia were associated to a fatal outcome (p<0.05), with no differences between groups.

Conclusion: We found few phenotype differences between patients re-classified as IPAF and those with non-IPAF according to the new criteria. This indicates that the proposed IPAF criteria might not be able to capture all patients with inflammatory and/or isolated features of CTD. In addition, only some of the proposed items for IPAF were prevalent in patients with UCTD-ILD, being the presence of RP a dominant one. The use of capillaroscopy could therefore help characterize a set of patients with UCTD-ILD. Prospective and larger cohorts are needed to confirm these findings.

Disclosure: F. I. Romero-Bueno, None; A. S. Pozo, None; M. J. Rodriguez-Nieto, None; M. J. Martinez-Becerra, None; G. Herrero-Beaumont, None; O. Sanchez-Pernaute, None.
Rheumatic Immune Related Adverse Events Due to Programmed Cell Death Protein 1 (PD-1) Inhibition for Cancer: Comprehensive Analysis of a Whole Cancer Cohort

**Authors:**
- David Liew\(^{1,2,3}\)
- Jessica Leung\(^1\)
- Bonnia Liu\(^1\)
- Jonathan Cebon\(^{3,4}\)
- Albert Frauman\(^{2,3}\)
- Russell Buchanan\(^1\)

**Institutions:**
- \(^1\)Department of Rheumatology, Austin Health, Melbourne, Australia
- \(^2\)Department of Clinical Pharmacology and Therapeutics, Austin Health, Melbourne, Australia
- \(^3\)Department of Medicine, University of Melbourne, Melbourne, Australia
- \(^4\)Olivia Newton-John Cancer Wellness & Research Centre, Melbourne, Australia

**First Publication:** September 18, 2017

**Session Information:**
- **Session Date:** Monday, November 6, 2017
- **Session Title:** Miscellaneous Rheumatic and Inflammatory Diseases Poster I
- **Session Type:** ACR Poster Session B
- **Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Immune checkpoint therapy with programmed cell death protein 1 (PD-1) inhibitors has led to significant survival benefits in the treatment of multiple cancers. This strategy interrupts inhibitory signals within the immune system, but this may additionally cause immune-related adverse events (irAEs) that resemble a spectrum of well-recognised autoimmune conditions. Detailed study of these may also further the understanding of the development of spontaneous autoimmune disease. At present, characterisation of rheumatic irAEs is limited as reports from clinical trials have inadequate detail for this purpose and the current literature largely consists of case series. Few reports describe in detail all rheumatic irAEs in a whole cohort of patients receiving PD-1 inhibitors, which would enable determination of frequency and context to this emerging entity. To the best of our knowledge, we describe the largest such series to date.

**Methods:** A retrospective chart review was performed on all patients dispensed nivolumab or pembrolizumab in 2016 at our center. Patients diagnosed with a non-cutaneous irAE were identified as were patients with undiagnosed symptoms possibly consistent with a rheumatic irAE. Information recorded included details regarding the malignancy and its therapy, the nature of the irAE and its treatment and outcomes.

**Results:** Of the 149 patients, 54 (36.2%) had at least one non-cutaneous irAE. Thyroid irAEs were the most common, occurring in 22 patients (14.8%) followed by rheumatic irAEs, which were diagnosed in 18 patients (12.1%). Of these, 11 were de novo diagnoses and 7 were exacerbations of existing autoimmune disease. A further 4 had symptoms possibly consistent with a rheumatic irAE but without a diagnosis from the treating physician. Inflammatory arthritis was the most common rheumatic irAE, with a diagnosis in 15 patients. The median time to developing a rheumatic irAE was 5 months (range 1-28). Rheumatic irAEs were more common in patients with an oncological response to therapy (RR 10.0, p<0.01) and receiving combination therapy with ipilimumab (RR 3.5, p = 0.016). Most patients were treated with corticosteroids and only 4 patients required introduction of DMARDs. Confirmation by a rheumatologist only occurred in 10 patients but supportive findings on imaging were available in 13 patients, including 8 patients not reviewed by a rheumatologist.

**Conclusion:** Rheumatic irAEs are a relatively common consequence of PD-1 inhibitor therapy, and frequently require the use of corticosteroids. They would benefit from systematic investigation to explore, amongst other characteristics, the apparent association with oncological response to therapy. Our findings also suggest that many rheumatic irAEs are not routinely referred to rheumatological services. While imaging may be able to assist with retrospective identification, if insights are to be made regarding the pathogenesis of the spontaneous diseases from irAEs, consistent rheumatological assessment will be required. A reliance on conventional mechanisms may be insufficient for this purpose and electronic biosurveillance may be necessary.

**Disclosure:** D. Liew, None; J. Leung, None; B. Liu, None; J. Cebon, None; A. Frauman, None; R. Buchanan, None.
Which Definition Should be Used to Determine Colchicine Resistance in Patients with Familial Mediterranean Fever?

Abdulsamet Erden¹, Ezgi Deniz Batu², Alper Sari³, Hafize Emine Sonmez⁴, Berkan Armagan³, Selcan Demir⁴, Esra Furat⁵, Yelda Bilginer⁶, Sule Apras Bilgen¹, Omer Karadag¹, Umut Kalyoncu¹, Sedat Kiraz¹, İhsan Erteli¹, Seza Ozen⁷ and Ali Akdogan³,

¹Department of Internal Medicine, Division of Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Turkey, ²Department of Pediatrics, Division of Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Turkey, ³Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Turkey, ⁴Department of Pediatrics, Division of Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Turkey, ⁵Department of Internal Medicine, Hacettepe University Faculty of Medicine, Ankara, Turkey, ⁶Department of Pediatrics, Division of Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Turkey, ⁷Department of Pediatrics, Division of Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Turkey

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Colchicine is the main therapy for familial Mediterranean fever (FMF); however, around 5-10% of FMF patients are colchicine-resistant. Currently there is no standard and validated definition for colchicine resistance. We aimed to compare the existing definitions for colchicine resistance in both adult and pediatric FMF patients to find out the best definition to determine the colchicine-resistant patients.

Methods: 385 FMF patients were evaluated and patients receiving anti-interleukin-1 (IL-1) treatment were included. Nine different definitions (found out after PubMed search for colchicine resistance in FMF) (Table 1) were applied to all patients. Results were re-analyzed after excluding the patients with no clinical attacks but had persistently high acute phase reactants (APRs) and/or amyloidosis.

Results: Among 385 FMF patients 60 (40 (66.7%) adults, 20 (33.3%) children) were colchicine-resistant. The highest percentage of FMF patients fulfilled the definition 5 (93.3%), while definition 9 had the poorest performance (28%) (Table 2). Significantly higher percentage of adult patients were meeting definitions 4 and 6 than pediatric patients (87.5% vs 50%, p=0.002; 75% vs 40%, p=0.008; respectively) (Table 2). After excluding patients without clinical attacks, the highest percentage of patients fulfilled definition 2 (94.4%). We combined the attack frequency definition (> 1 typical episode per 3 months) of definition 2 and presence of amyloidosis/APR definition (increase in at least two out of three acute phase reactants (C-Reactive Protein, Erythrocyte sedimentation rate, and serum amyloid A) of definition 5 to create a new definition. The new criteria set were met by 59 (98.3%) colchicine-resistant FMF patients.

Conclusion: Definition of colchicine resistance is still controversial. Definitions of colchicine-resistant patients with both clinical and laboratory criteria were met by a higher percentage of patients than without laboratory criteria. However, the proper definitions for the attack-free period and persistence of APRs are still lacking.

Table 1. The definitions for colchicine resistance in familial Mediterranean fever (FMF) in the literature
<table>
<thead>
<tr>
<th>Definition</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Despite taking 2 mg/day of colchicine, at least 1 episode per month</td>
</tr>
<tr>
<td>2</td>
<td>Despite taking 2 mg/day colchicine, more than 1 typical episode per 3 months</td>
</tr>
<tr>
<td>3</td>
<td>Despite receiving 2 mg/day colchicine, 3 or more attacks have been reported in the last 6 months</td>
</tr>
<tr>
<td>4</td>
<td>Despite the fact that adequate doses of colchicine are taken in children and increased doses of 2 mg/day in adults, at least one episode per month during the following 3 months and increased ESR or increased CRP or increased SAA</td>
</tr>
<tr>
<td></td>
<td>Presence of amyloidosis</td>
</tr>
<tr>
<td></td>
<td>Protracted febrile myalgia that needs steroid treatment</td>
</tr>
<tr>
<td></td>
<td>Presence of persistent arthritis</td>
</tr>
<tr>
<td>5</td>
<td>More than 3 episodes in 4-6 months, or more than 6 typical episodes per year, despite adequate doses of colchicine</td>
</tr>
<tr>
<td></td>
<td>An increase in at least two out of three acute phase reactants (CRP, ESR, and SAA) between attacks</td>
</tr>
<tr>
<td>6</td>
<td>1 or more episodes per month despite the use of colchicine at the maximum dose of at least 6 months</td>
</tr>
<tr>
<td></td>
<td>Presence of amyloidosis</td>
</tr>
<tr>
<td>7</td>
<td>At least 1 episode per month despite taking 2 mg/day colchicine</td>
</tr>
<tr>
<td></td>
<td>Persistently elevated AFR</td>
</tr>
<tr>
<td></td>
<td>Organ involvement (especially renal)</td>
</tr>
<tr>
<td></td>
<td>Losing job or not continuing to school</td>
</tr>
<tr>
<td>8</td>
<td>Despite taking 2 mg/day of colchicine (or the maximum dose that can be tolerated), at least 1 episode per month</td>
</tr>
<tr>
<td></td>
<td>Symptoms continue despite 2 mg/day colchicine intake (or maximum tolerable dose)</td>
</tr>
<tr>
<td></td>
<td>SAA, ESR and CRP elevation 1.5 times higher than the normal limit between attacks</td>
</tr>
<tr>
<td>9</td>
<td>Despite 2 mg of colchicine, at least 2 episodes per month and elevation of CRP and/or SAA between attacks</td>
</tr>
</tbody>
</table>

AFR, acute phase reactants; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; FMF, familial Mediterranean fever; SAA, serum amyloid A

Table 2. Number of familial Mediterranean fever (FMF) patients defined as colchicine resistant according to different definitions
### Definitions

<table>
<thead>
<tr>
<th>Definitions</th>
<th>All patients (n=60)</th>
<th>Adult patients (n=40)</th>
<th>Pediatric patients (n=20)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definition 1, n (%)</td>
<td>29 (48.3)</td>
<td>21 (52.5)</td>
<td>8 (40)</td>
<td>0.36</td>
</tr>
<tr>
<td>Definition 2, n (%)</td>
<td>51 (85)</td>
<td>33 (82.5)</td>
<td>18 (90)</td>
<td>0.44</td>
</tr>
<tr>
<td>Definition 3, n (%)</td>
<td>50 (83.3)</td>
<td>32 (80)</td>
<td>18 (90)</td>
<td>0.32</td>
</tr>
<tr>
<td>Definition 4, n (%)</td>
<td>45 (75)</td>
<td>35 (87.5)</td>
<td>10 (50)</td>
<td>0.002</td>
</tr>
<tr>
<td>Definition 5, n (%)</td>
<td>56 (93.3)</td>
<td>36 (90)</td>
<td>20 (100)</td>
<td>0.29</td>
</tr>
<tr>
<td>Definition 6, n (%)</td>
<td>38 (63.6)</td>
<td>30 (75)</td>
<td>8 (40)</td>
<td>0.008</td>
</tr>
<tr>
<td>Definition 7, n (%)</td>
<td>52 (86.7)</td>
<td>37 (92.5)</td>
<td>15 (75)</td>
<td>0.10</td>
</tr>
<tr>
<td>Definition 8, n (%)</td>
<td>54 (90)</td>
<td>34 (85)</td>
<td>20 (100)</td>
<td>0.06</td>
</tr>
<tr>
<td>Definition 9, n (%)</td>
<td>16 (28.3)</td>
<td>14 (35)</td>
<td>2 (10)</td>
<td>0.06</td>
</tr>
</tbody>
</table>

**Disclosure:** A. Erden, None; E. D. Batu, None; A. Sari, None; H. E. Sonmez, None; B. Armagan, None; S. Demir, None; E. Firat, None; Y. Bilginer, None; S. Apras Bilgen, None; O. Karadag, None; U. Kalyoncu, None; S. Kiraz, None; I. Ertenli, None; S. Ozen, Novartis, R-Pharm, Roche, 5; A. Akdogan, None.


**Abstract Number: 1175**

### Rituximab for Idiopathic and IgG4-Related Retroperitoneal Fibrosis

**Rituximab for Idiopathic and IgG4-Related Retroperitoneal Fibrosis**

**Rachel Wallwork**¹, Zachary S. Wallace², Cory A. Perugino³, Amita Sharma⁴ and John H. Stone⁵. ¹Department of Medicine, Massachusetts General Hospital, Boston, MA, ²Division of Rheumatology, Allergy and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, ³Ragon Institute of MGH, MIT and Harvard, Cambridge, MA, ⁴Department of Radiology, Massachusetts General Hospital, Boston, MA, ⁵Massachusetts General Hospital Rheumatology Unit, Harvard Medical School, Boston, MA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Miscellaneous Rheumatic and Inflammatory Diseases Poster I

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Rituximab for Idiopathic and IgG4-Related Retroperitoneal Fibrosis**

**Background/Purpose:** Untreated retroperitoneal fibrosis (RPF) can lead to chronic back and flank pain and/or renal failure. The mainstay of treatment for non-malignant (IgG4-related disease [RD] or idiopathic) RPF is glucocorticoid (GC) therapy which often has insufficient efficacy or is complicated by toxicity. We performed a retrospective review of patients with RPF treated with rituximab (RTX).

**Methods:** We reviewed the database of the Massachusetts General Hospital’s Center for IgG4-RD and identified all patients with RPF treated with RTX who had follow-up (2010-2016). RPF was diagnosed by CT or MRI following commonly accepted radiographic criteria (Lancet 2011;378:338). Demographics, date of diagnosis, symptoms, co-morbidities, laboratory values, use of stents or percutaneous nephrostomy (PCN) tubes, biopsy results, and symptomatic response to treatment were collected from the database. A
board-certified radiologist (AS) reviewed baseline and follow-up imaging. Response to treatment was defined as symptom improvement and/or radiographic improvement defined as reduction in lesion size in at least two radiographic planes (Lancet 2011;378:338).

**Results:** Twenty-six RPF patients received RTX (Table 1). The median age was 55 years (IQR 43, 58) and a majority was male (85%) and former or current smokers (85%). Pathology was available in 20 (77%) patients. In 17/20 (85%) patients, diagnostic features of IgG4-RD were present; in the remaining 3/20 (15%), malignancy and infection were ruled out. Of the six patients not biopsied, 2 (33%) met clinical diagnostic criteria for IgG4-RD and four had typical radiographic idiopathic RPF with no clinical suspicion of infection or malignancy. Ten of 26 (39%) patients had previously failed GC therapy. RTX was used as monotherapy in 20 (77%) patients and in combination with GC in 6 patients (23%); ten (39%) patients required ureteral stents or PCN tubes. Of the 21 patients with baseline symptoms (e.g., pain), all (100%) had improvement. Twenty-two (88%) of the 25 patients with follow-up imaging had radiographic improvement; in the remaining 3 patients, the RPF remained stable. Of the 10 patients with a stent or PCN, 4 (40%) had it successfully removed. Four of the six patients whose stents or PCN were not removed had disease duration for greater than 1 year prior to RTX.

**Conclusion:** In this retrospective study of patients with idiopathic or IgG4-related RPF, peripheral B cell depletion with RTX was highly effective, used as monotherapy in the majority of patients. A striking proportion (85%) of patients were current or former smokers. Future research could explore whether patients with disease for greater than 1 year prior to RTX respond less well.

**Table 1: Baseline Demographics and Features with Treatment Response**

<table>
<thead>
<tr>
<th>Sample Size</th>
<th>26</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at Diagnosis (Median, IQR)</td>
<td>55 (43, 58)</td>
</tr>
<tr>
<td>Male (%)</td>
<td>22 (85%)</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>19 (73%)</td>
</tr>
<tr>
<td>Smoking History</td>
<td>22 (85%)</td>
</tr>
<tr>
<td>Former</td>
<td>16 (62%)</td>
</tr>
<tr>
<td>Current</td>
<td>6 (23%)</td>
</tr>
<tr>
<td>Serum IgG4 Concentration Elevated</td>
<td>11 (42%)</td>
</tr>
<tr>
<td>Other Organ Involvement</td>
<td>6 (23%)</td>
</tr>
</tbody>
</table>

**Diagnostics**

| Typical Radiographic Appearance | 26 (100%) |
| RPF Biopsied | 20 (77%) |
| Diagnostic of IgG4-RD | 17 (65%) |
| Suggestive of IgG4-RD, ruled out malignancy/infection | 3 (12%) |
| Met Clinical Criteria for IgG4-RD (of those not biopsied) | 2 (8%) |

**Presentation**

| Pain (back or flank) | 19 (73%) |
| Renal Failure | 16 (62%) |

**Treatment Approach**

| Prior Treatment with Steroids | 10 (39%) |
| Rituximab with Steroids | 6 (23%) |
| Rituximab Only | 20 (76%) |
| Ureteral Stents or Percutaneous Nephrostomy (PCN) Tube | 10 (39%) |

**Treatment Response**

| Symptomatic Response (N=26) | 21 (100%)* |
| Radiographic Response ** (N=25) | 22 (88%)† |
| Stable (if no reduction in size, N=3) | 3 (100%) |
| Stent or PCN Removed (N=10) | 4 (40%) †† |

* of those with baseline symptoms; ** Response defined as improvement in size in at least 2 planes (e.g., anterior-posterior, cranio-caudal); † of 25 patients with f/u radiology; †† of 10 patients with stents or PCN.

Disclosure: R. Wallwork, None; Z. S. Wallace, None; C. A. Perugino, None; A. Sharma, None; J. H. Stone, Xencor, 2.
Abstract Number: 1176

A Randomized, Open-Label, Dose-Ranging Study of Oral Delayed Release Prednisone in Patients with Untreated Polymyalgia Rheumatica

Jasvinder A. Singh¹ and Lee S. Simon², ¹Medicine, University of Alabama at Birmingham, Alabama, AL, ²SDG LLC Consulting, West Newton, MA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Polymyalgia rheumatica (PMR) is a common condition of unknown etiology with a lifetime risk of 2.43% in women and 1.66% in men.¹ PMR is characterized by pain and stiffness in the neck, shoulders and/or pelvic girdle, and is more severe in the morning with a duration >1 hour in most patients. It is generally agreed that the absence of a prompt response to a moderate glucocorticoid (GC) dose (15 mg prednisone daily) indicates a diagnosis other than PMR.² This higher dose of a GC is associated with more adverse drug effects than lower doses.³ Blood concentrations of interleukin (IL) -6 increase during the night and peak in the early morning hours in parallel with PMR patients’ pain and stiffness.⁴ A timed (delayed) release prednisone preparation (DR GC) was developed to target treatment to the nighttime increase in IL-6.⁵ It has been shown that this formulation provides better control of rheumatoid arthritis symptoms than the same dose of conventional immediate release prednisone (IR GC) taken in the morning and possibly permit a lower initial dose.⁶

Methods: In this preliminary 4-week, randomized, controlled, open-label two period trial, conducted in collaboration with OMERACT, patients with PMR responsive to GC received one of 3 nighttime doses of DR GC (4 mg, 7 mg or 10 mg) for 2 weeks followed by treatment with 15 mg IR GC in the morning for 2 weeks. The primary outcome was the change from baseline in the severity of morning stiffness (measured on a 10-point visual analog scale [VAS]) with DR GC vs that with IR GC with each patient as their own control. Pain was also evaluated using a 10-point VAS.

Results:
A total of 8 patients were enrolled (n=3 for 4 mg DR GC, 1 for 7 mg DR GC, 4 for 10 mg DR GC) and all completed the trial. The mean baseline value for morning stiffness was 5.2, and changes from baseline with 4, 7 and 10 mg DR GC were -4.5, -1.0, and -3.1, respectively. Those for 15 mg IR GC in the patients who received 4, 7, or 10 mg DR GC during the first treatment period were -4.2, -2.5, and -3.9. The mean baseline pain score was 5.2 and the reductions from baseline with 4, 7, and 10 mg DR GC were -4.4, -0.8, and -2.7, respectively. Those for 15 mg IR GC in the patients who received 4, 7, or 10 mg DR GC during the first treatment period were -4.3, -2.0, and -3.6. Two patients treated with 10 mg DR GC experienced mild adverse events (1 mild skin tear and 1 decrease in vitamin D). No adverse events were reported during treatment with 15 mg IR GC.

Conclusion: Results of this small-scale study indicated that a low-dose DR GC has effects on PMR-associated pain and stiffness similar to those of 15 mg IR GC. The efficacy of low-dose DR GC may improve the long-term safety of PMR treatment. These data warrant consideration for initiation of a larger study evaluating the efficacy and safety of DR GC in this patient population.


Disclosure: J. A. Singh, Takeda, Savient, 2,Takeda, American College of Rheumatology, Savient, Regeneron, Merz, Iroko, Bioiberica, Crealta, Horizon, Allergan, WebMD, UBM LLC, 5; L. S. Simon, Horizon Pharma, 1,Horizon Pharma, Roche, 5.
Airway Findings in Patients with Relapsing Polychondritis

Marcela A. Ferrada1, James D. Katz2, Keith A. Sikora3, Allen Clint4, Jeff Kim4, Wendy Goodspeed4, Robert Colbert5, Marcus Chen6, Arlene Sirajuddin4 and Peter C. Grayson2, 1NIAMS, National Institutes of Health, Bethesda, MD, 2National Institute of Arthritis, Musculoskeletal and Skin Disease (NIAMS), Bethesda, MD, 3Pediatric Translational Research Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, 4National Institutes of Health, Bethesda, MD, 5NIAMS/NIH, Bethesda, MD, 6NHLBI, National Institutes of Health, Bethesda, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Relapsing polychondritis (RP) is a rare multiorgan disease. Involvement of the upper and lower airways is associated with significant morbidity and mortality. Isolated airway involvement can be seen in patients with RP. The objective of this study is to determine the prevalence of airway inflammation and damage in patients with RP who endorse clinical symptoms suggestive of airway disease.

Methods:
Patients described in this cohort were selected from a prospective natural history protocol. All patients met McAdams or Damiani’s diagnosis criteria for relapsing polychondritis. Patients were selected if they reported voice changes, choking sensation, shortness of breath or cough. All patients underwent laryngoscopy and dynamic 4D cine computed tomography (CT) scanning of the trachea and central airway obtained during forced exhalation.

Results:
A total of 31 patients have been evaluated in our prospective cohort, 4 adult patients were excluded because of a different CT scan technique was used. 12 patients were younger than 18 years old and one patient did not meet criteria for RP diagnosis. The 14 remaining patients were included in this report. Patient demographic information includes: average age 46.7 years (SD 7.5), 93% female, 86% white. All the patients reported voice changes, dry cough and shortness of breath, and all but one patient reported choking sensation. On laryngoscopy, 86% of the patients had arytenoid swelling (Image 1), 50% of the patients had nasal ulcers, one patient had septal perforation, and no patient had a saddle nose deformity. On dynamic 4D cine CT scans of the airways, 36% of the patients had tracheomalacia, 14% had tracheal calcifications, 14% of the patients had tracheal wall thickening, 14% had bronchomalacia, 21% had bronchial wall thickening, none of the patients had bronchial calcifications, 21% had alveolar opacities and 28 % had air trapping. The percentage of tracheal collapse (Image 2) ranged from 40-87%.

Conclusion:
Airway symptoms such as voice changes, cough, choking sensation and shortness of breath in patients with relapsing polychondritis should be further investigated with laryngoscopy and dynamic 4D cine CT imaging of the airways to assess for airway inflammation and damage. Arytenoid swelling is a common finding in RP and may be indicative of active disease.
Disclosure: M. A. Ferrada, None; J. D. Katz, None; K. A. Sikora, None; A. Clint, None; J. Kim, None; W. Goodspeed, None; R. Colbert, None; M. Chen, None; A. Sirajuddin, None; P. C. Grayson, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/airway-findings-in-patients-with-relapsing-polychondritis

Abstract Number: 1178

Sympathetic Joint Effusion in an Urban Hospital

Jessica L. Barlow¹ and Irene J. Tan²,³ ¹Internal Medicine, Temple University Hospital, Philadelphia, PA, ²Temple University Hospital, Philadelphia, PA, ³Section of Rheumatology, Temple University Lewis Katz School of Medicine, Philadelphia, PA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Sympathetic joint effusion (SJE) or sympathetic synovial effusion (SSE) is a rheumatologic entity that has not been well defined in the medical literature. It is a non-inflammatory synovial fluid collection that is associated with infection or inflammation of an adjacent anatomic structure. The epidemiology and clinical characteristics of SJE/SSE are largely unknown. This knowledge gap has led to a lack of recognition and misdiagnosis by clinicians. Our study aimed to determine incidence, demographic information, and describe the clinical characteristics and potential triggering conditions for this presumptive reactive phenomenon.

Methods:
We conducted a study of patients >18 years of age hospitalized at Temple University Hospital (TUH) between January 31, 2010 and December 10, 2016 who underwent diagnostic arthrocentesis for painful effusions. Individuals with synovial fluid white blood cell count (WBC) in the normal range of 200 WBC/mm3 or less were included. Patients with non-inflammatory range synovial fluid of 200-2,000 WBC/mm3 were excluded to limit confounders. Demographic and clinical data of 72 patients were included for detailed analysis.
Results:

SJE/SSE was seen in 80/882 hospitalized patients (incidence of 9%). Seventy-two patients fulfilled inclusion criteria for detailed chart review. Demographic information revealed: male 46/72 (64%), female 26/72 (36%), African-American 38/72 (53%), Caucasian 16/72 (22%), Hispanic 10/72 (14%), undefined and other 8/72 (11%). Onset was typically acute, with 45/72 (63%) of patients developing symptoms within six days of arthrocentesis. All patients (100%) with SJE/SSE presented with painful effusion, and a minority had physical findings of warmth 23/72 (32%) or erythema 12/72 (17%). Interestingly, nearly a third of patients 21/72 (29%) were misdiagnosed with crystal or septic arthritis based solely on clinical exam, and empiric treatment was often administered prior to arthrocentesis. The most commonly affected joint was the knee 61/72 (85%), followed by the elbow 5/72 (7%), shoulder 3/72 (4%) and hip 3/72 (4%). Identifiable pathology in the affected limb was found in 29/72 (40%) of patients. Infection was the most common etiology, found in 17/29 (59%) of patients, and included cellulitis, abscess, osteomyelitis, septic bursitis, myositis, and necrotizing fasciitis. The majority of cases of SJE/SSE 23/29 (79%) were associated with concomitant infection, DVT or intramuscular hematoma in the affected limb which required specific therapeutic interventions.

Conclusion:

Sympathetic joint effusion or sympathetic synovial effusion (SJE/SSE) is relatively common in hospitalized patients. SJE/SSE may be a sentinel sign for a more serious disorder affecting the same limb. Clinicians should maintain a heightened index of suspicion for SJE/SSE. A search for underlying infection, venous thrombosis, and intramuscular hematoma in the affected limb is warranted when encountering acute painful joint effusion with normal range synovial fluid WBC count.

Disclosure: J. L. Barlow, None; I. J. Tan, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/sympathetic-joint-effusion-in-an-urban-hospital

Abstract Number: 1179

A Multi-Organ Inflammatory Condition with Features of Idiopathic Multicentric Castleman’s Disease and IgG4-Related Disease: An Unrecognized Mimicker of IgG4-RD

Zachary S. Wallace¹, Yasuharu Sato², Kazuichi Okazaki³, Judith Ferry⁴, Hisanori Umehara⁵, Aliyah Sohani⁶, Mitsuhiro Kawano⁷, Nancy Harris⁶, Yoshiya Tanaka⁸, Cory A. Perugino⁹, Satoshi Kubo¹⁰, James Stone⁴, Robert Colvin⁴, Tsutomu Chiba¹¹, John H. Stone¹² and Yoh Zen¹³, ¹Division of Rheumatology, Allergy and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, ²Department of Pathology, Okayama University Graduate School of Medicine, Okayama, Japan, ³Department of Gastroenterology and Hepatology, Kansai Medical University, Osaka, Japan, ⁴Department of Pathology, Massachusetts General Hospital, Boston, MA, ⁵Kyoto University, Kyoto, Japan, ⁶Massachusetts General Hospital, Boston, MA, ⁷Division of Rheumatology, Kanazawa University Hospital, Kanazawa, Japan, ⁸The First Department of Internal Medicine, University of Occupational and Environmental Health, Fukuoka, Japan, ⁹Ragon Institute of MGH, MIT and Harvard, Cambridge, MA, ¹⁰The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, ¹¹Department of Gastroenterology and Hepatology, Kyoto University, Kyoto, MA, ¹²Massachusetts General Hospital Rheumatology Unit, Harvard Medical School, Boston, MA, ¹³Department of Diagnostic Pathology, Kobe University Graduate School of Medicine, Kobe, Japan

First publication: September 18, 2017
Methods: American and Japanese clinicians and pathologists exchanged pathology slides of 60 cases (30 cases from the US, 30 from Japan) accompanied by clinical vignettes. Japanese investigators submitted 15 cases in which they suspected a diagnosis of iMCD and 15 cases they felt were typical IgG4-RD. Cases considered iMCD had at least focal extranodal manifestations. US investigators submitted 12 cases considered to represent IgG4-RD with an elevated CRP and 18 IgG4-RD cases with normal CRP. All investigators were blinded to CRP and IL-6 concentrations as well as treatment responses. The US investigators were blinded to the designated diagnoses of the Japanese cases. The diagnosis of iMCD was evaluated based on expert pathology opinion as well as recently published diagnostic criteria (Fajgenbaum, Blood 2017).

Results: Of the 15 suspected iMCD cases from Japan, 14 had mixed nodal and extranodal manifestations and 1 had pure extranodal abnormalities. All but one had elevated serum IgG4 concentrations. Twelve (80%) had extensive extranodal polyclonal plasma cell infiltrates with increased IgG4-positive plasma cells affecting the kidneys, lungs, and skin that were similar to the lymph node appearance. Nine (60%) fulfilled iMCD diagnostic criteria. When reviewed by expert American pathologists, however, the histopathology of all suspected iMCD cases were considered to be a nonspecific, reactive process characterized by a nonspecific plasmacytic infiltrate without regressed follicles. No association was observed between CRP elevations in the US IgG4-RD cases and whether or not the Japanese investigators considered the case to be IgG4-RD (P=0.5). None of the US IgG4-RD cases were considered iMCD by the Japanese investigators.

Conclusion: A condition characterized by multifocal LAD with polyclonal IgG4+ plasma cell infiltrates, extranodal lesions of similar histologic appearance, and elevated inflammatory markers mimics IgG4-RD and iMCD but is often not clearly classifiable as either condition even with iMCD diagnostic criteria. Although these and similar cases are commonly reported as iMCD, future studies using alternative but common nosology are critical to better characterize them. Furthermore, the diagnosis of IgG4-RD was agreed on regardless of the CRP concentration, suggesting that CRP can be elevated in otherwise typical IgG4-RD and that CRP is not a useful measure to distinguish iMCD and IgG4-RD.

Disclosure: Z. S. Wallace, None; Y. Sato, None; K. Okazaki, None; J. Ferry, None; H. Umehara, None; A. Sohani, None; M. Kawano, None; N. Harris, None; Y. Tanaka, None; C. A. Perugino, None; S. Kubo, Bristol-Myers Squibb, 8; Pfizer Inc, 8; Takeda Pharmaceutical Company Ltd, 8; J. Stone, None; R. Colvin, None; T. Chiba, None; J. H. Stone, Xencor, 2; Y. Zen, None.

Abstract Number: 1180

Multicenter Study on the Rate of Renal Function Deterioration in IgG4-Related Tubulointerstitial Nephritis

Mitsuhiro Kawano1, Ichiro Mizushima2, Takahiro Matsunaga1, Kazunori Yamada3, Satoshi Hara1, Hiroshi Fujii4, Takako Saeki4, Yoshinori Taniguchi5 and Hitoshi Nakashima6, 1Division of Rheumatology, Kanazawa University Hospital, Kanazawa, Japan, 2Kanazawa University Hospital, Kanazawa, Japan, 3Department of Advanced Research in Community Medicine, Kanazawa University Graduate School of Medical Sciences, Kanazawa, Japan, 4Department of Internal Medicine, Nagaoka Red Cross Hospital, Nagaoka, Japan, 5Department of Endocrinology, Metabolism, Nephrology and Rheumatology, Kochi Medical School, Kochi, Japan, 6Div of Nephrol & Rheumatol, Dept of Int Med, Faculty of Medicine, Fukuoka University, Fukuoka, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Only a few reports have focused on the rate of renal function deterioration in IgG4-related tubulointerstitial nephritis (IgG4-TIN). Some cases show acute or progressive chronic renal failure, and others progression of renal failure slowly over one year or more. This study aimed to investigate the rate of renal function deterioration in patients with biopsy proven IgG4-TIN, leading to clarification of the divergence of the deterioration rate of renal function, identifying the factors affecting the deterioration rate, and confirming the influence of the deterioration rate on the final renal function of each case.

Methods: We extracted 18 patients with IgG4-TIN between July 2006 and March 2017 in four hospitals. Based on the rate of renal function deterioration using estimated glomerular filtration rate (eGFR) before starting corticosteroid therapy, we divided them into a rapidly deteriorating group (deterioration rate more than or equal to 4 ml/min/1.73m²/month) (n=8) and a slowly deteriorating group
(deterioration rate less than 4 ml/min/1.73m$^2$/month) (n=10), and retrospectively analyzed various clinical features (age, sex, serum IgG levels, serum IgG4 levels, serum IgE levels, serum complement levels, serum eGFR levels at start of corticosteroid and the last visit, initial dose of prednisolone, multiple organ lesions) during the clinical course in the two groups.

**Results:** The mean age of the 18 patients was 69 years (range: 43 to 81 years). 89% of the patients were male. The average number of affected organs was 4 (range: 1 to 9). All patients had elevated serum IgG4 levels, and average was 977 mg/dL (range: 207 to 2800). In all patients, the diagnosis of IgG4-TIN was made by histopathological confirmation of the kidney biopsy specimen with immunostaining. The mean kidney function decline rate per month before starting corticosteroid therapy was 4.4 ml/min/1.73m$^2$/month. In seven cases, the deterioration rate of kidney function was less than 2 ml/min/1.73m$^2$/month, while 10 cases had a rapid deterioration rate more than 4 ml/min/1.73m$^2$/month. Corticosteroid was effective in all cases, and average recovery of eGFR after corticosteroid therapy was 17.4 ml/min/1.73m$^2$ (range: -0.4 to 46.5). In group A (a slowly deteriorating group), the recovery of eGFR was less than that in group B (a rapidly deteriorating group) (6.4 ml/min/1.73m$^2$ vs. 26.3 ml/min/1.73m$^2$, $P < 0.05$). Hypocomplementemia was more frequent in patients in group A than those in group B ($P < 0.05$). No differences were noted regarding gender, age, eGFR before starting corticosteroid therapy, eGFR at the last visit, the number of affected organs, eosinophil count, serum IgG levels, IgG4, or IgE between the groups.

**Conclusion:** Regarding the deterioration rate of renal function before corticosteroid therapy in patients with IgG4-TIN, there are two groups, i.e. a rapidly deteriorating group and slowly deteriorating group. Hypocomplementemia is associated with the rapid deterioration of renal function, and a slowly deteriorating group shows lower recovery of renal function after the corticosteroid therapy.

**Disclosure:** M. Kawano, None; I. Mizushima, None; T. Matsunaga, None; K. Yamada, None; S. Hara, None; H. Fujii, None; T. Saeki, None; Y. Taniguchi, None; H. Nakashima, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/multicenter-study-on-the-rate-of-renal-function-deterioration-in-igg4-related-tubulointerstitial-nephritis

---

**Serum KL-6 Level Reflects Severity of Interstitial Lung Disease Associated with Connective Tissue Disease**

**Jeong Seok Lee**, Eun Young Lee, Jin Kyun Park, Eun Bong Lee, and Yeong Wook Song, 1Division of Rheumatology, Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea, Republic of (South), 2Division of Rheumatology, Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea, Republic of (South), 3Department of Molecular Medicine and Biopharmaceutical Sciences, Graduate School of Convergence Science and Technology, and College of Medicine, Seoul National University, Seoul, Korea, Republic of (South), 4Department of Molecular medicine and biopharmaceutical science, Seoul National University, Seoul, Korea, Republic of (South)

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Miscellaneous Rheumatic and Inflammatory Diseases Poster I  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Measuring severity of interstitial lung disease (ILD) usually depends on the extent or pattern of imaging findings on computed tomography (CT) and the parameters of pulmonary function test. Krebs von den Lungen 6 (KL-6) is a sialylated glycoprotein mainly expressed on the surface membrane of type II pneumocytes and bronchiolar epithelial cells (1). Serum level of KL-6 had been reported to be associated with presence or outcome of ILD associated with connective tissue diseases (CTD-ILD) (2-4). We aimed to evaluate KL-6 as a potential biomarker reflecting severity of CTD-ILD.

**Methods:** Study population was a retrospective cohort of 464 Korean patients with rheumatoid arthritis (RA), systemic sclerosis (SSc), inflammatory myositis (IM), Sjögren’s syndrome (SS), and systemic lupus erythematosus (SLE) who had concurrent ILD or not. Serum concentration of KL-6 (U/mL) was measured by Nanopia KL-6 assay (SEKISUI MEDICAL, Tokyo), using latex enhanced immunoturbidimetric assay method. Temporally nearest CT and PFT results were collected within 2 years from each serum sampling. Semi-quantitative grade of ILD extent (grade 1: 0-25%, grade 2: 26-50%, grade 3: 51-75%, grade 4: 76-100%) was evaluated by CT scan. Student t-test and Pearson’s coefficient (PC) were applied to evaluate the correlation of KL-6 level and severity of ILD.
Results: The patients with CTD-ILD (n=162) had elevated serum level of KL-6 compared to CTD without ILD (n=302) (mean±SEM, 737.9±57.5 vs 238.2±10.1U/mL, p<0.001) (Fig 1). In subgroup analysis, RA (544.6±100.3 vs 241.7±19.6, p<0.001), SSc (766.4±103.7 vs 224.0±26.3, p=0.002), IM (808.1±99.8 vs 291.4±33.1, p<0.001), and SS or SLE (914.1±227.1 vs 215.0±10.25, p<0.001) also had significant difference according to the presence of ILD. Semi-quantitative grade of ILD in CT scan was significantly proportional to KL-6 level except for grade 1 and 2 (Fig 2). Percent diffusion capacity for carbon monoxide (DLCO%) and forced vital capacity (FVC%) had negative correlation with KL-6 level (PC=-0.587, p<0.001; PC=-0.399, p<0.001, respectively).

Conclusion: Serum levels of KL-6 were increased in CTD-ILD and had good correlation with CT grade, FVC, and DLCO. Higher serum level of KL-6 may reflect severity of CTD-ILD.

Figure 1. Comparison of serum levels of KL-6 in different types of connective tissue disease with or without ILD.

Figure 2. Association of serum level of KL-6 with semi-quantitative grade of chest CT.

Disclosure: J. S. Lee, None; E. Y. Lee, None; J. K. Park, None; E. B. Lee, Green Cross Corp, 2, Pfizer Inc, 5; Y. W. Song, CKD Research Institute, 2.
Petra Budde, Jennifer Marte, Hans-Dieter Zucht, Saurabh Bhandari, Manuel Tuschen, Peter Schulz-Knappe, James Gulley, Christopher Heery, Ravi Madan and Jeffrey Schlom, Protagen AG, Dortmund, Germany, National Cancer Institute, National Institutes of Health, Bethesda, MD, Bavarian Nordic, Inc., Morrisville, NC

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Autoantibodies (AAB) targeting self-antigens can be found in two clinically and immunologically opposing diseases, autoimmune diseases and cancer. While in autoimmune diseases, the immune system is hyperactivated against self-antigens, many tumors suppress the anti-tumor immune response. The therapeutic cancer vaccines PSA-Tricom (Prostvac) is designed to generate an antigen-specific tumor response in metastatic castration-resistant prostate cancer (mCRPC), which is in phase 3 testing. To further augment the immune response, combination therapies of Prostvac with ipilimumab are currently tested in clinical studies. Ipilimumab is an antibody that blocks the immune checkpoint molecule cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4). However, treatment with ipilimumab is associated with immune-related adverse events (irAEs) (1). Since there are no biomarkers for predicting irAEs, we investigated AAB profiles as biomarkers associated with irAE in mCRPC patients treated with prostvac and ipilumumab combination therapy.

Methods: Serum samples from 24 mCRPC patients treated with prostvac and ipiliumab therapy were tested for the presence of serum autoantibodies against 842 preselected antigens. Candidate antigens comprise immune-related and cancer signaling pathway proteins, autoimmune disease antigens, and tumor-associated antigens (TAA). Samples were collected prior to treatment (T0 samples), at 3 and 6 month. IrAEs included rash, elevated aminotransferases, neutropenia, diarrhea, colitis and endocrine irAEs. Overall survival was also captured and correlated with AABs. Autoantibody levels were measured by Luminex FlexMap3D bead based multiplex protein arrays (2) and data were analyzed by significance analysis of microarrays (SAM), Partial least squares regression (PLS) and Pearson’s correlation.

Results: In total, 87 AABs were found that were significantly different in patients with irAEs and those without irAEs (SAM |d|>2.5; Pearson’s correlation |3|>0.35). PLS analysis revealed that AABs associated with irAEs were also associated with overall survival. Gene ontology analysis of pathways, molecular function and cellular localization revealed that AABs predicting irAEs target cancer, cell cycle, cell adhesion and apoptotic pathways. We also found elevated levels of AABs in patients who do not experience irAEs. Interestingly, these 40 AABs target proteins that are involved in inflammatory, adaptive and cellular immune response pathways or are autoimmune disease antigens.

Conclusion: AABs that target antigens involved in cancer signaling pathways are associated with irAEs following prostvac plus checkpoint inhibitor combination therapy. In contrast, AABs targeting immune response pathways were found in patients who do not develop irAEs and may counteract the action of inflammatory molecules. Similarly, anti-cytokine AABs have been found in autoimmune diseases, were they appear to counteract the pathological effects of cytokines (3). Further studies in larger sample sets are needed to confirm these findings.


Disclosure: P. Budde, ProtagenAG, 3; J. Marte, None;

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/autoantibody-profiling-in-prostvac-and-ipilimumab-combination-therapy
Bone Sarcoidosis: A Multicenter Study

Camille Glanowski1, Raphaele Mestiri2, Lisa Bialé3, Thierry Carmoi4, Gaëlle Leroux5, David Saadoun6, Catherine Chapelon-Abric7 and Patrice Cacoub8, 1Internal Medicine, Hôpital d'instruction des armées de Bégin, Bégin, France, 2Hôpital d'instruction des armées du Val-de-Grâce, Paris, France, 3Hôpital d'instruction des armées de Bégin, Bégin, France, 4Service de Médecine Interne, Hôpital d'instruction des armées du Val-de-Grâce, Paris, France, 5Internal Medicine, Pitié-Salpêtrière University Hospital, Paris, France, 6Sorbonne Universités, UPMC Univ Paris 06, UMR 7211, and Inflammation-Immunopathology-Biotherapy Department (DHU i2B), F-75005, Paris, France; INSERM, UMR_S 959, F-75013, Paris, France; CNRS, FRE3632, F-75005, Paris, France; AP-HP, Groupe Hospitalier, Paris, France, 7AP-HP, Groupe Hospitalier Pitié-Salpêtrière, Department of Internal Medicine and Clinical Immunology, F-75013, Paris, France, Paris, France, 8Department of Internal Medicine and Clinical Immunology, Groupe Hospitalier Pitié-Salpêtrière, Paris, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Studies on bone involvement of sarcoidosis (BS) are scarce. To analyze in depth main features, treatments and follow up of patients presenting a BS.

Methods: Among 926 patients with a proved sarcoidosis from four tertiary hospitals in Paris (France) seen between 2000 and 2015, all cases of BS were retrospectively analyzed for demography, clinical features, biological tests and imaging results. Inclusion criteria were a) a bone biopsy with epithelioid granuloma and no casein necrosis, or b) radiological evidence of BS, after exclusion of other diagnoses.

Results: 27 out 926 (2.9%) sarcoidosis patients fullfilled inclusion criteria for BS. Most patients were caucasian (56%), M/F sex ratio 1.5, 30% were active smokers, mean age at sarcoidosis diagnosis was 39±12 yrs and at BS diagnosis 43±11 yrs. Extra-osseous involvement of sarcoidosis was found in lymph nodes (93%), lungs (78%), skin (52%), CNS (33%), ENT (33%), and heart (19%). BS was symptomatic in 15/26 (56%) patients i.e. bone pain (15/15), local inflammation (5/15), bone deformation (3/15), arthritis (4/15), and myalgia (5/15). BS was never the revealing symptom of sarcoidosis. BS was more frequently symptomatic when it was a Perthes-Jüngling osteitis and an appendicular skeleton involvement.

On imaging exams, BS lesions were found at the spine skeleton alone (14/27, 52%), appendicular skeleton alone (10/27, 37%) or both (3/27, 11%). BS lesions had an aspect of pseudo-metastasis (59%), micro-cysts (Perthes-Jungling, 37%) or Paget disease (4%). Bone lesion was unique in 22% and 26% of patients had more than 10 lesions. When a bone biopsy was done it always confirmed the diagnosis (n=9) ; in all other cases extra-osseous biopsies confirmed the diagnosis of sarcoidosis.

Nine patients received a treatment for BS, i.e. prednisone (n=8, 0.25-1 mg/kg/day), hydroxychloroquine (n=8), and methotrexate (n=5). Response to treatment was complete (n=3), partial (n=4) or nul (n=2). Of note, 21 out of 27 patients received an immunosuppressant for a severe form of systemic sarcoidosis (n=11) or for pain (3/15), local inflammation (5/15), bone deformation (3/15), arthritis (4/15), and myalgia (5/15). BS was never the revealing symptom of sarcoidosis. BS was more frequently symptomatic when it was a Perthes-Jüngling osteitis and an appendicular skeleton involvement.

On imaging exams, BS lesions were found at the spine skeleton alone (14/27, 52%), appendicular skeleton alone (10/27, 37%) or both (3/27, 11%). BS lesions had an aspect of pseudo-metastasis (59%), micro-cysts (Perthes-Jungling, 37%) or Paget disease (4%). Bone lesion was unique in 22% and 26% of patients had more than 10 lesions. When a bone biopsy was done it always confirmed the diagnosis (n=9) ; in all other cases extra-osseous biopsies confirmed the diagnosis of sarcoidosis.

Conclusion: Bone involvement remains a rare manifestation of sarcoidosis. It was symptomatic in 56% of patients, mainly when Perthes-Jüngling osteitis and appendicular skeleton involvement were present. Extra-osseous involvement of sarcoidosis were always present at the time of BS diagnosis. Treatment remains difficult with frequent relapses.

Disclosure: C. Glanowski, None; R. Mestiri, None; L. Bialé, None; T. Carmoi, None; G. Leroux, None; D. Saadoun, None; C. Chapelon-Abric, None; P. Cacoub, None.
Response to Methotrexate and Glucocorticoid Injection in New Onset Arthritis after Checkpoint Inhibitor Therapy

Lisa Christ¹, Jan Leipe¹, Ilana Goldscheider², Markus Heppt², Carola Berking², Frank Berger³, Claudia Dechant¹, Alla Skapenko¹ and Hendrik Schulze-Koops¹, ¹Division of Rheumatology and Clinical Immunology, Department of Internal Medicine IV, University of Munich, Munich, Germany, ²Department of Dermatology and Allergology, University of Munich, Munich, Germany, ³Department of Radiology, University of Munich, Munich, Germany

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The recent introduction of biologic agents targeting immunologic checkpoints (immunologic checkpoint inhibitors, ICI) established immunotherapy as a highly effective cancer therapy. ICI that trigger an anti-tumor response by activation of T cells, may also cause immune-related adverse events (irAEs). Characterization of rheumatic adverse events such as arthritis and data on treatment of irAEs are scarce. The aim of this study is to characterize patients with new-onset arthritis under ICI therapy and to assess the efficacy and safety of treatment that aimed to balance anti-tumor and anti-inflammatory therapy.

Methods: In this prospective observational study, patients with melanoma or NSCLC receiving ICI therapy who experienced arthralgias were evaluated for the presence of musculoskeletal inflammation. Data on demographics, ICI regime, time of onset and response to therapy of musculoskeletal irAEs, imaging, joint count, CRP/ESR, and immune serology were collected. Further, clinical response to antiinflammatory therapies including NSAR, glucocorticoids (GC) and methotrexate was assessed before and after an antiinflammatory treatment with VAS GH by patients and two expert rheumatologists aware of all clinical data but blinded for treatment, patient identity and study purpose.

Results: Of 10 patients with arthralgias after initiation of ICI therapy, arthritis was demonstrated in 9 patients: 4 monoarthritis, 3 oligoarthritis (SpA pattern), 2 polyarthritis (RA pattern). PMR-like disease with typical ultrasound findings was evident in 1 case and in 3 cases concurrent with arthritis. Upon first visit in our clinic, CRP levels were elevated in 7 of the patients (5.5 to 107 mg/l) while immune serology was positive only in two patients.

The mean baseline VAS GH patient was 7.4 ± 0.9 and was significantly reduced after a median of 24 weeks of antiinflammatory treatment to 2.0 ± 1.3. Initially, all patients were treated with NSAID and/or systemic GC. Six patients received intraarticular GC. Five patients flared on GC treatment upon tapering and were given methotrexate. Remission was achieved in all and prednisolone could be tapered.

Patients were followed for a median of 272 days, and no safety signal with regard to tumor reappearance was detected.

Retrospective analysis of cancer staging imaging studies revealed good sensitivity for PET-CT in the detection of synovitis, as opposed to contrast-enhanced CT.

Interestingly, in one patient low RF and ACPA titers had been detected when she presented with arthralgias without synovitis five years prior. This patient developed highly active RA one day after the first infusion of nivolumab.

Conclusion: Inflammatory manifestations were associated with high disease burden and not self-limiting. In monarthritides, GC joint injection resulted in long-term remission. In oligo- and polyartarthritides flares were frequent after tapering and, thus, potential side-effects including attenuation of the antitumor efficacy of ICI are a concern. This is the first report on the efficacy and safety of methotrexate as a GC-sparing agent in ICI-induced arthritis.
Acupotomy Therapy for Joint Pain Relief of Knee Osteoarthritis—Systematic Review and Meta-Analysis

Jia Li1, Puwei Yuan2, Rongqiang Zhang1, Bin Chen3, Bo Dong1, Wulin Kang1, Xiaoliang Zhang3, Stephanie Hyon4, Raveendhara R. Bannuru5, William F. Harvey4 and Chenchen Wang4,1 Shaanxi University of Chinese Medicine, Xianyang, China, 2Traditional Chinese Medicine College, Shaanxi University of Chinese Medicine, Xianyang, China, 3Integrative TCM and Western Medicine College, Shaanxi University of Chinese Medicine, Xianyang, China, 4Rheumatology, Center of Integrative Medicine and Division of Rheumatology, Tufts Medical Center, Boston, MA, 5Center of Integrative Medicine and Division of Rheumatology, Tufts Medical Center, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Osteoarthritis—Clinical Aspects Poster I: Clinical Trials and Interventions
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Knee osteoarthritis (KOA) is a major public health problem and a leading cause of long-term pain and disability. Few effective medical treatments for the disease currently exist. Acupotomy has been used as a new type of minimally-invasive surgical treatment for KOA pain. It combines techniques from acupuncture and micro-surgery that separates subcutaneous adhesions and muscle knots, resulting in immediate pain relief. A comprehensive literature review is an important step in understanding its benefits and for guiding treatment for KOA pain. We conducted a systematic review and meta-analysis to evaluate the efficacy of acupotomy for joint pain associated with KOA.

Methods: We performed a search on Cochrane Library, PubMed, EMBASE, 3 universal Chinese databases (CNKI, Wan Fang and VIP), and reference lists of published articles through June 2017. We include randomized controlled trials using acupotomy therapy for KOA patients who met the ACR diagnostic criteria. The effect of acupotomy on joint pain relief was measured with WOMAC pain subscale, VAS and other pain scores. Study quality was evaluated with Jadad criteria. The differences between treatment groups were reported as mean change (P-value).

Results: After screening 721 abstracts, 16 studies met eligibility criteria and were conducted between 2007 and 2015. A total of 1,416 KOA patients (65.2% female, mean age = 59 years, mean symptom duration = 87 months) were included. Table 1 summarizes the trials evaluating the effect of acupotomy therapy on joint pain relief. The typical treatment was once a week, for 1-5 weeks until pain relief. Additional massage therapy after acupotomy was included in four studies. Nine studies used acupuncture (1 traditional acupuncture and 9 electroacupuncture) as controls and others used therapeutic massage, oral nonsteroidal anti-inflammatory analgesics, or intra-articular hyaluronate injection. The overall quality of trials was modest (mean Jadad score=3). Almost all studies reported an effect of acupotomy on joint pain compared to a variety of controls. Figure 1 shows a meta-analysis comparing effects of acupotomy therapy with acupuncture controls on pain relief. A meta-analysis comparing acupotomy with other controls is not reported due to variation in outcomes assessed. Adverse events were not reported.

Conclusion: Acupotomy treatment may improve joint pain associated with KOA. Further rigorously designed and well-controlled RCTs with long-term follow-up are warranted.

Table 1. Sixteen RCTs of Acupotomy Therapy on Knee Osteoarthritis
<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>N</th>
<th>(Age)</th>
<th>Acupotomy therapy</th>
<th>Controls</th>
<th>Duration (weeks)</th>
<th>Pain Mean Difference(^{c}) (P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zeng</td>
<td>2007</td>
<td>24</td>
<td>(63y)</td>
<td>Release soft tissue adhesion (once/wk; 1-3 times until pain relieves)</td>
<td>Acupuncture therapy (30 min, 3 times/1 wk, 3 wks)</td>
<td>3</td>
<td>VAS(^{d}) score: *2.05 (P&lt;0.05)</td>
</tr>
<tr>
<td>Peng</td>
<td>2008</td>
<td>32</td>
<td>(60y)</td>
<td>Release soft tissue adhesion (once/wk; 1-3 times until pain relieves)</td>
<td>Acupuncture therapy (30 min, 3 times/1 wk, 3 wks)</td>
<td>3</td>
<td>VAS score: *0.43 (P&lt;0.05)</td>
</tr>
<tr>
<td>Guo</td>
<td>2009</td>
<td>60</td>
<td>(ND)</td>
<td>Release soft tissue adhesion (once/wk; 1-3 times until pain relieves)</td>
<td>Acupuncture therapy (30 min, 3 times/1 wk, 3 wks)</td>
<td>3</td>
<td>VAS score: *0.97 (P&lt;0.05)</td>
</tr>
<tr>
<td>Zeng</td>
<td>2009</td>
<td>46</td>
<td>(ND)</td>
<td>Release soft tissue adhesion (once/wk; 1-3 times until pain relieves)</td>
<td>Acupuncture therapy (30 min, 3 times/1 wk, 3 wks)</td>
<td>3</td>
<td>VAS score: *1.68 (P&lt;0.01)</td>
</tr>
<tr>
<td>Guo</td>
<td>2010</td>
<td>180</td>
<td>(60y)</td>
<td>Release soft tissue adhesion (once/wk; 1-3 times until pain relieves)</td>
<td>Acupuncture therapy (30 min, 3 times/1 wk, 3 wks)</td>
<td>3</td>
<td>VAS score: *0.3 (P&gt;0.05)</td>
</tr>
<tr>
<td>Li</td>
<td>2011</td>
<td>76</td>
<td>(53y)</td>
<td>1. Release soft tissue adhesion (once/wk, 3 times)</td>
<td>Acupuncture therapy (30 min, 5 times/1 wk, 3 wks)</td>
<td>3</td>
<td>Pain score by HSS(^{f}): *0.9 (P&lt;0.05)</td>
</tr>
<tr>
<td>Zhang</td>
<td>2011</td>
<td>58</td>
<td>(53y)</td>
<td>Release soft tissue adhesion (once/wk; 1-3 times until pain relieves)</td>
<td>Acupuncture therapy (30 min, 3 times/1 wk, 3 wks)</td>
<td>3</td>
<td>Pain score(^{g}) by JOA: *10.89 (P&lt;0.05)</td>
</tr>
<tr>
<td>Guo</td>
<td>2012</td>
<td>180</td>
<td>(60y)</td>
<td>Release tissue under points of pain (once/wk, 3 times)</td>
<td>Acupuncture therapy (30 min, 3 times/1 wk, 3 wks)</td>
<td>3</td>
<td>Pain score of JOA: Walking: ^4.02 (P&lt;0.01)</td>
</tr>
</tbody>
</table>

\(^{a}\) N represents the number of patients. 
\(^{b}\) Age range is provided. 
\(^{c}\) P-values for pain mean difference. 
\(^{d}\) VAS: Visual Analog Scale. 
\(^{e}\) JOA: Japanese Orthopaedic Association. 
\(^{f}\) HSS: Harris Hip Score. 
\(^{g}\) JOA: Japanese Orthopaedic Association.
<table>
<thead>
<tr>
<th>Authors</th>
<th>Age (yrs)</th>
<th>Treatment Details</th>
<th>Outcome Measures</th>
<th>P-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xiong 2014</td>
<td>80 (62y)</td>
<td>Release tissue under points of pain (once/wk, 4times)</td>
<td>Acupuncture therapy (once/day, 6 days)</td>
<td>VAS score: *0.23 (P&lt;0.05)</td>
</tr>
<tr>
<td>Wang 2009</td>
<td>60 (49y)</td>
<td>Release soft tissue adhesion (once/wk; 1-3 times until pain relieves)</td>
<td>Sodium hyaluronate injection (1-2 ml/1 wk, 5wks)</td>
<td>Pain score of WOMAC: *3.23 (P&lt;0.05)</td>
</tr>
<tr>
<td>Zhu 2011</td>
<td>80 (62y)</td>
<td>1. Release soft tissue adhesion by the method named ¡±5 fingers¡± (once/6 days, 3times) 2. Massage therapy to improve joint movement (after acupotomy)</td>
<td>Sodium hyaluronate injection (1-2 ml/6 days, 3wks)</td>
<td>Pain score by HSS: ^3.38 (P&lt;0.05)</td>
</tr>
<tr>
<td>Zheng 2015</td>
<td>80 (61y)</td>
<td>Release tissue under points of pain (once/wk, 5times)</td>
<td>Sodium hyaluronate injection (1-2 ml/1 wk, 5 wks)</td>
<td>VAS score: *0.77 (P&lt;0.05)</td>
</tr>
<tr>
<td>Zhou 2015</td>
<td>100 (58y)</td>
<td>Release tissue under points of pain (once/wk, 5times)</td>
<td>Sodium hyaluronate injection (1-2 ml/1 wk, 5 wks)</td>
<td>VAS score: ^0.1 (P&gt;0.05) Follow-up after a half year of treatment: *3.03 (P&lt;0.05)</td>
</tr>
<tr>
<td>Ding 2014</td>
<td>200 (58y)</td>
<td>1. Release soft tissue adhesion (once/wk, 4times) 2. Massage therapy to improve joint movement (after acupotomy)</td>
<td>Diclofenac sodium (75 mg/d, 2wks, oral pill)</td>
<td>VAS score: *0.13 (P&gt;0.05) Follow-up after a half year of treatment: *2.63 (P&lt;0.05)</td>
</tr>
<tr>
<td>Yao 2010</td>
<td>100 (61y)</td>
<td>1. Release tissue under points of pain (once/wk, 3times); 2. Massage therapy to improve joint movement (after acupotomy)</td>
<td>Diclofenac sodium (25 mg/time, 3times/d, 15 days, oral pill)</td>
<td>Pain score by JOA Walking: ^4.98 (P&lt;0.05) Stair activity: ^4.82 (P&lt;0.01)</td>
</tr>
<tr>
<td>Huang 2007</td>
<td>60 (65y)</td>
<td>Release soft tissue adhesion (once/wk; 1-4 times until pain relieves)</td>
<td>Therapeutic Massage (5 times/wk, 4wks)</td>
<td>Pain score of KSS: ^11.58 (P&lt;0.05)</td>
</tr>
</tbody>
</table>

\[ a \] N= number of patients included; \[ b \] Mean age reported in years; \[ c \] Mean difference was calculated between group comparisons; \[ d \] VAS: Visual Analogue Scale (range 0-10, lower score = better outcome); \[ e \] JOA: Japanese Orthopedic Association (walking subscale range 0-30, higher score = better outcome; stair activity subscale range 0-25, higher score = better outcome); \[ f \] HSS: Hospital for Special Surgery Score (range 0-30, higher score = better outcome); \[ g \] Score = sum of walking pain score and stair activity pain score; \[ h \] WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index (range 0-50, lower score = better outcome); \[ i \] KSS: Knee Society Score (range 0-50, higher score = better outcome); * indicate decrease; ^ indicate increase.
A Simple, Self-Assembled Hydrogel Depot for Localized Treatment of Post-Traumatic Osteoarthritis

Jing Yan, Nitin Joshi, Xueyin He, Sachin Bhaigandani, Kai Slaughter, Nicholas Sherman, Joerg Ermann and Jeffrey Karp

1Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA, 2Brigham and Women's Hospital, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster I: Clinical Trials and Interventions
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Joint injuries, including sports- or combat-related ligamentous tears and fractures, can lead to post-traumatic osteoarthritis (PTOA), a chronic condition that causes pain, disability and limited quality of life. Current treatment options only provide symptomatic relief without modifying the progressive course of the disease, and are plagued by dose- or duration-limiting toxicity. Pharmacologic inhibition of catabolic factors, including cartilage degrading enzymes, pro-inflammatory cytokines and catabolic cell signaling pathways appears to reduce progressive joint damage in preclinical and clinical studies. However, the clinical translation of such disease modifying osteoarthritis drugs (DMOADs) has been hampered by short half-lives following intra-articular administration. Although platforms have been developed for local delivery of therapeutics, most suffer from major drawbacks, including a lack of control points to tune release kinetics and complex design that limits scalability and adaptability to a wide range of DMOADs. A localized drug delivery depot that provides long-term release of DMOADs in response to OA associated local factors like matrix metalloproteinase-2 (MMP-2) would represent an attractive paradigm shift in OA therapy.

Methods: We designed a self-assembled hydrogel depot using small molecules that are Generally Recognized As Safe (GRAS) by the FDA without chemical modifications, and evaluated the hydrogel’s ability to encapsulate an MMP-13 inhibitor (Sigma-Aldrich) and a Cathepsin-K inhibitor (TOCRIS Bioscience). Release studies were performed in vitro to explore the responsiveness of the system to...
MMP-2 and synovial fluid (SF) collected from healthy and arthritic human joints. Hydrogels were evaluated \textit{in vitro} for biocompatibility using chondrocytes and synoviocytes. Therapeutic efficacy of Cathepsin-K inhibitor loaded gels was determined \textit{in vivo} using the medial meniscal tear model of PTOA in Lewis rats.

**Results:** Hydrogels encapsulated both MMP-13 and cathepsin-K inhibitors with high loading efficiencies and showed excellent hydrolytic stability in PBS and synovial fluid from healthy human joints, with cumulative drug release <30% over a 30-day period. The encapsulated DMOADs were released from the hydrogel in response to MMP-2 and synovial fluid collected from arthritic human joints. The release of DMOADs was directly proportional to the dose of enzyme or amount of arthritic synovial fluid added. Drug-loaded gels showed biocompatibility with both chondrocytes and synoviocytes, suggesting their safety for intra-articular administration. In the medial meniscal tear model of PTOA, intra-articular treatment with Cathepsin-K inhibitor-loaded hydrogels resulted in a significant reduction in cartilage damage compared to controls (rats injected with blank hydrogel).

**Conclusion:** Our results suggest that self-assembled hydrogels are a promising strategy for efficient, localized delivery of DMOADs and can offer improved therapeutic benefit in the treatment of PTOA.

**Disclosure:** J. Yan, None; N. Joshi, None; X. He, None; S. Bhagchandani, None; K. Slaughter, None; N. Sherman, None; J. Ermann, Novartis Pharmaceutical Corporation, 5, UCB, 5, Takeda, 5, SPARTAN/GRAPPA, 9; J. Karp, Alivio Therapeutics, 1.


**Abstract Number: 1187**

**Chondroitin Sulfate/Glucosamine Hydrochloride Induce a Reduction in Adrenergic Serum Markers in Osteoarthritis Patients Similar to That Produced By Celecoxib**

**Marta Herrero**\(^1\), Pedro Zapater\(^2,3\), Helena Martinez\(^1\), Rubén Francés\(^3,4\), Josep Vergés\(^5\) and Jose F Horga\(^2\), \(^1\)Clinical R&D Area, Bioiberica, SAU, Barcelona, Spain, \(^2\)Pharmacology Department, Miguel Hernández University, Alicante, Spain, \(^3\)CIBERehd. Carlos III Institute, Madrid, Spain, \(^4\)Medicine Department, Miguel Hernández University, Alicantes, Spain, \(^5\)Osteoarthritis Foundation International, Barcelona, Spain

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Monday, November 6, 2017
**Session Title:** Osteoarthritis – Clinical Aspects Poster I: Clinical Trials and Interventions
**Session Type:** ACR Poster Session B
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Inflammation in osteoarthritis (OA) has been characterized by infiltration of immune cells and secretion of cytokines into synovial tissues. Noradrenaline levels, sympathetic nerve fiber distribution and β2-AR expression in the bone of rats have been associated with subchondral bone loss and increased osteoclast activity. All these data suggest the participation of the adrenergic and immune systems in the development and evolution of OA. However, the relationship among the systemic adrenergic and immune systems activation with OA progression and treatment response is less well known.

**Methods:** Serum samples from patients participants in a 6-month controlled, double blind and randomized clinical trial comparing the efficacy of pharmaceutical grade Chondroitin sulfate/Glucosamine hydrochloride (CS/GH) and Celecoxib (CE) were analyzed to determine cytokines (IL-2, IL-4, IL-6, IL-10, IL-8, IL-1beta using BD™ Cytometric Bead Array (CBA) immunoassay), catecholamines (noradrenaline, adrenaline and dopamine using ELISA LDN®) and the presence of endotoxin or lipopolysaccharide (LPS; LAL test Lonza®).

**Results:** Samples from 100 knee OA patients (age: 62±8 yr.; BMI: 31±6 kg/m\(^2\); 86 females; VAS: 73±15; WOMAC: 369±43) treated with CS/GH (50) or CE (50) were analyzed. There were no baseline differences between treatment groups. After 6 months of treatment, both groups of patients showed a similar reduction in VAS and WOMAC score (Table 1). Serum IL-2, IL-4, IL-6, IL-8, IL-1beta using BD™ Cytometric Bead Array (CBA) immunoassay, catecholamines (noradrenaline, adrenaline and dopamine using ELISA LDN®) and the presence of endotoxin or lipopolysaccharide (LPS; LAL test Lonza®).

**Results:** Samples from 100 knee OA patients (age: 62±8 yr.; BMI: 31±6 kg/m\(^2\); 86 females; VAS: 73±15; WOMAC: 369±43) treated with CS/GH (50) or CE (50) were analyzed. There were no baseline differences between treatment groups. After 6 months of treatment, both groups of patients showed a similar reduction in VAS and WOMAC score (Table 1). Serum IL-2, IL-4, IL-6, IL-8, IL-10 and dopamine levels did not change significantly over treatment. Adrenaline levels were significantly reduced by both treatments. Moreover, serum noradrenaline was reduced only in the group treated with CS/GH although the difference was not significant because of the great data variability. LPS levels were doubled in both treatment groups but attained values remained very low and were accompanied by a small and non-significant increase in IL-1 beta (p=0.07). These effects were similar in patients who attained a clinically meaningful VAS score decrease compared with those who didn't.
Conclusion: Six month treatment with CS/GH reduces significantly and in a similar fashion to NSAID CE the pain intensity and systemic adrenergic activation in patients with OA. Reduction in adrenergic activation was independent of pain response. Further studies are needed to ascertain the relationship between systemic adrenergic changes and subchondral bone loss and osteoclast activity.

Table 1.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th></th>
<th>6-month</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CS/GH</td>
<td>CE</td>
<td>CS/GH</td>
<td>CE</td>
</tr>
<tr>
<td>Adrenaline (pg/mL)</td>
<td>96 (82-119)</td>
<td>98 (76-114)</td>
<td>78 (61-96)*</td>
<td>80 (62-98)*</td>
</tr>
<tr>
<td>Noradrenaline (pg/mL)</td>
<td>1561 (1003-1916)</td>
<td>1540 (952-2643)</td>
<td>1344 (859-1856)</td>
<td>1558 (942-2212)</td>
</tr>
<tr>
<td>LPS (EU/mL)</td>
<td>0.9 (0.5-1.2)</td>
<td>0.7 (0.6-1.3)</td>
<td>1.2 (0.7-2.8)*</td>
<td>1.4 (0.6-2.1)*</td>
</tr>
<tr>
<td>IL-1beta</td>
<td>12.1 (10.2-15.2)</td>
<td>12.5 (10.7-15.4)</td>
<td>15.2 (13.3-15.9)</td>
<td>14.6 (12.5-15.5)</td>
</tr>
<tr>
<td>VAS (0-100) score</td>
<td>75 (66-87)</td>
<td>77 (70-82)</td>
<td>34 (24-50)*</td>
<td>39 (11-60)*</td>
</tr>
<tr>
<td>WOMAC score</td>
<td>371 (342-395)</td>
<td>356 (322-394)</td>
<td>153 (87-220)*</td>
<td>168 (89-284)*</td>
</tr>
</tbody>
</table>

* p < 0.05 vs baseline values (Mann-Whitney-Wilcoxon Test)

Disclosure: M. Herrero, Bioiberica, SA, 3; P. Zapater, Bioiberica SAU, 2; H. Martinez, Bioiberica, SA, 3; R. Francés, None; J. Vergés, None; J. F. Horga, None.


Abstract Number: 1188

Initial Estimates of Efficacy of Intra-Articular 2.5% Polyacrylamide Hydrogel for the Treatment of Knee Osteoarthritis: An Observational Proof-of-Concept Study

Marius Henriksen1,2, Anders Overgaard1 and Henning Bliddal3, The Parker Institute, Copenhagen University Hospital Bispebjerg and Frederiksberg, Copenhagen, Denmark, 2Department of physical therapy, Copenhagen University Hospital Bispebjerg and Frederiksberg, Copenhagen, Denmark, 3The Parker Institute, Department of Rheumatology, Copenhagen University Hospital, Bispebjerg and Frederiksberg, Copenhagen, Denmark

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster I: Clinical Trials and Interventions
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
There is a draught of available effective treatments of knee osteoarthritis (OA) and tests of new therapies are needed. Polyacrylamide hydrogel (PAAG) is a non-toxic, non-degradable synthetic product, used for years in the augmentation of soft tissues. Animal studies have shown that intra-articular (IA) PAAG significantly alleviates lameness and joint effusion over 2 years among horses with OA. Thus, IA injection of PAAG may be a promising treatment for knee OA in humans, albeit with a need for scientific evaluation of efficacy and safety. The present study has been conducted to establish an initial estimate of effectiveness of IA injection of PAAG for the symptomatic treatment of knee OA.
Methods:

Patients with OA of the knee were invited into a prospective open-label cohort study. The patients received IA injection of 3 ml of PAAG (a proprietary 2.5% cross-linked PAAG manufactured by Contura International A/S) twice within 1 month. The WOMAC questionnaire was used to estimate efficacy, and was collected at baseline and after 4, 7 and 13 months. Efficacy was mainly estimated as a change from baseline for the WOMAC pain subscale after 4 months (Normalised to 0-100 points; 100 worst). WOMAC stiffness and WOMAC physical function were measured as secondary estimates of efficacy. The efficacy variables were analyzed using a mixed-effect model repeated measure approach without imputation of missing data. Sensitivity analyses were done using baseline observation carried forward imputation.

Results:

118 patients (62 females) received IA PAAG. Of these there were WOMAC data available from 81 after 4 months, 66 after 7 months, and 47 after 13 months. At baseline the mean WOMAC pain score was 43.7 (SD17.5). There were statistically significant reductions in WOMAC pain after 4 months (mean change -13.3 points [95% CI: -17.3 to -9.3]; P<.0001), which exceeds established minimal clinically important improvements margins of 9 points. Similar results were found in WOMAC stiffness and physical function (figure 1). The improvement was sustained throughout the observation period. In the sensitivity analyses the estimates were generally lower caused by the non-responder imputation approach (table 1).

Conclusion:

These results suggest beneficial effects of IA injection of a 2.5% PAAG on knee OA symptoms, even in the long term (1 year). This is promising but efficacy needs to be confirmed in a randomized study with adequate measures taken to reduce risk of bias.

Figure 1. Changes from baseline in WOMAC. No imputation of missing data.

Table 1. Sensitivity analyses of changes from baseline in WOMAC. Missing data imputed using BOCF technique.

<table>
<thead>
<tr>
<th>Change from baseline in</th>
<th>4 month (n=118)</th>
<th>7 month (n=118)</th>
<th>13 month (n=118)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WOMAC pain</td>
<td>Mean (95% CI)</td>
<td>P</td>
<td>Mean (95% CI)</td>
</tr>
<tr>
<td>-9.5 (-12.1 to -6.9)</td>
<td>&lt;.0001</td>
<td>-7.6 (-10.2 to -5)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>WOMAC stiffness</td>
<td>-6.6 (-9.7 to -3.5)</td>
<td>&lt;.0001</td>
<td>-6.4 (-9.6 to -3.3)</td>
</tr>
<tr>
<td>WOMAC function</td>
<td>-6.6 (-8.5 to -4.6)</td>
<td>&lt;.0001</td>
<td>-4.5 (-6.4 to -2.5)</td>
</tr>
</tbody>
</table>

Disclosure: M. Henriksen, None; A. Overgaard, None; H. Bliddal, AbbVie Inc., Roche, Pfizer, Lilly, 5.


Abstract Number: 1189

Favorable Human Safety, Pharmacokinetics and Pharmacodynamics of the Adams-5 Inhibitor GLPG1972, a Potential New Treatment in Osteoarthritis
Ellen van der Aar1, Sonia Dupont2, Liesbeth Fagard1, Marina De Smet1, David Amantini2, Staffan Larsson3, André Struglics3, L. Stefan Lohmander4, Frédéric Vanhoutte1 and Julie Desrivot2, 1Galapagos NV, Mechelen, Belgium, 2Galapagos SASU, Romainville, France, 3Clinical Sciences, Lund University, Lund, Sweden, 4Orthopaedics, Clinical Sciences Lund, Lund University, Lund, Sweden

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster I: Clinical Trials and Interventions
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Increased aggrecanase activity is a well-known trigger factor for osteoarthritis (OA), initiating loss of cartilage aggrecan that precedes more severe cartilage degradation. A disintegrin and metalloproteinase with thrombospondin motifs-5 (ADAMTS-5) is a key aggrecanase in humans and is a relevant target for the development of disease-modifying OA drugs (DMOADs). GLPG1972 is a potent small molecule inhibitor of ADAMTS-5 displaying high selectivity versus a number of other zinc metalloproteases. The anti-catabolic activity of GLPG1972 was shown in murine and human cartilage explants, and its DMOAD activity was demonstrated in the destabilization of the medial meniscus (DMM) mouse model.
In the current study, the safety, tolerability, pharmacokinetics and pharmacodynamics of GLPG1972 in healthy male subjects were evaluated.

Methods:
GLPG1972 was administered as single oral doses (60 mg up to 2100 mg) or multiple doses (300 mg/day to 1050 mg/day for 14 days) formulated as a solution. Ascending single doses were evaluated in an alternating fashion between two panels of 8 male healthy subjects and multiple doses were evaluated sequentially in 3 groups of 8 male healthy subjects. In both parts, 6 subjects received GLPG1972 and 2 placebo. Plasma and urine were collected at several time points and intervals for the quantification of GLPG1972 by LC-MS/MS. Pharmacodynamics was assessed by measurement of the aggrecan ARGS neoepitope levels in plasma by an enzyme-linked immunosorbent assay.

Results:
Administration of single (up to 2100 mg) and multiple (up to 1050 mg q.d.) ascending oral doses of GLPG1972 in healthy subjects was well tolerated, with no clinically relevant effects on ECGs, vital signs or laboratory parameters.

GLPG1972 given as a single oral dose in fasted state was rapidly absorbed with a median $t_{\text{max}}$ range of 1 to 4 h and eliminated with a terminal half-life of approximately 10 h. The rate of absorption decreased with higher doses, whereas the plasma exposure in terms of AUC increased dose-proportionally. After once-daily dosing for 14 days in fed state, GLPG1972 plasma exposure (both $C_{\text{max}}$ and AUC) increased dose-proportionally over the entire dose range. Pharmacokinetic steady state was reached after 2 dosing days, with minimal accumulation. The excretion of unchanged GLPG1972 in urine over a 24 h period was low (<11% of the administered dose).

The aggrecan ARGS neoepitope levels decreased progressively over time during treatment with GLPG1972 but not with placebo. The extent of the pharmacodynamic effect was similar for the 3 tested doses. The maximal reduction in plasma concentrations of aggrecan ARGS neoepitope was about 60% at day 14 versus baseline. No plateau had been attained on day 14, suggesting that it may take longer to obtain the maximum effect.

Conclusion:
GLPG1972 was shown to be safe and well-tolerated in healthy male subjects with a suitable pharmacokinetic profile and a marked decrease of the aggrecan ARGS neoepitope biomarker, indicating target engagement. These data and the preclinical data package confirm the potential of GLPG1972 to be a potential DMOAD treatment. GLPG1972 will be progressed to a Phase 2 study in osteoarthritis.

Disclosure: E. van der Aar, Galapagos, 3,Galapagos, 1; S. Dupont, Galapagos SASU, 3; L. Fagard, Galapagos, 3; M. De Smet, Galapagos, 5; D. Amantini, Galapagos, 3,Galapagos, 1; S. Larsson, None; A. Struglics, None; L. S. Lohmander, Galapagos, GSK, Johnson and Johnson, 5; F. Vanhoutte, Galapagos, 1; J. Desrivot, Galapagos, 3.

**Orosomucoid 2 Serves As Predictor of Therapeutic Response in Osteoarthritis Patients Treated with Chondroitin Sulfate/Glucosamine Hydrochloride**

Valentina Calamia¹, M Camacho¹, Ignacio Rego-Pérez¹, L González¹, P Fernández-Puente¹, F Picchi¹, Marta Herrero², Helena Martínez², C Ruiz-Romero¹ and Francisco J Blanco³,⁴, ¹Instituto de Investigación Biomédica de A Coruña (INIBIC), A Coruña, Spain, ²Clinical R&D Area, Bioiberica, SAU, Barcelona, Spain, ³RIER-RED de Inflamación y Enfermedades Reumáticas, INIBIC-CHUAC, A Coruña, Spain, A Coruña, Spain, ⁴Rheumatology Division, ProteoRed/ISCIII, Proteomics Group, INIBIC-Hospital Universitario A Coruña, A Coruña, Spain

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Osteoarthritis – Clinical Aspects Poster I: Clinical Trials and Interventions

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

Orosomucoid 2 Serves as Predictor of Therapeutic Response in Osteoarthritis Patients Treated with Chondroitin Sulfate/Glucosamine Hydrochloride


**Background/Purpose:**

The present study explored potential protein biomarkers useful to predict the therapeutic response of osteoarthritis (OA) patients treated with pharmaceutical grade Chondroitin sulfate plus glucosamine hydrochloride (CS+GH) or the COX-2 selective nonsteroidal anti-inflammatory drug Celecoxib, in order to optimize therapeutic outcomes in OA.

**Methods:**

A shotgun proteomic analysis was performed on sera from 80 patients enrolled in the Multicentre Osteoarthritis interVEntion trial with Syzadao (MOVES), employing the iTRAQ labelling technique (Sciex) followed by LC-MALDI-MS/MS analysis. One of the altered proteins was selected to be validated using commercially available ELISA Kit (Uscn Life Science) in the whole MOVES cohort at baseline. Logistic regression models adjusting for the confounder variables of gender, age, BMI, KL grade, VAS score and WOMAC score at baseline, as well as receiver-operating-characteristics (ROC) curves, were used to analyze the accuracy of the measured protein as predictive biomarker for OA treatment.

**Results:**

We employed a quantitative proteomic approach to identify differentially expressed proteins between OA responders and non-responders before starting the pharmacological treatment (Chondroitin sulfate/glucosamine hydrochloride or Celecoxib). Serum levels of orosomucoid 2 (ORM2) were measured by ELISA assays in 451 OA patients (n=229 for CS+GH group and n=222 for Celecoxib group). As shown in figure 1A, baseline ORM2 levels were significantly higher in patients who obtained unfavorable outcome (reduction in WOMAC score <20%) after 6 month of treatment with CS+GH (252,2 vs 195,4 ug/mL; n=51 vs 178; p=0,003), while no statistically significant differences were found in the Celecoxib group (data not shown). Both WOMAC and VAS scores at baseline significantly influence patients response regardless of treatment (p=0,001 and p=0,001 respectively). Notably, if we include baseline ORM2 as covariate, we found a specific interaction between response to CS+GH and baseline ORM2 levels (p=0,012) thus increasing the predictive power of our study (Figure 1B).

**Conclusion:**

Our results show that ORM2 levels significantly correlate with patients response to pharmaceutical grade Chondroitin Sulfate/Glucosamine Hydrochloride suggesting the possibility of its use in predictive assays in order to optimize therapeutic outcomes in OA.
Efficacy and Safety of Cntx-4975 in Subjects with Moderate to Severe Osteoarthritis Knee Pain: 24-Week, Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Study

Randall Stevens1, Dena Petersen2, John Ervin3, Jennifer Nezzer4, Yeni Nieves4, James Campbell1, Kimberly Guedes1, Robin Burges1 and Peter Hanson1, 1Centrexion Therapeutics, Boston, MA, 2Noble Clinical Research, Tucson, AZ, 3Center for Pharmaceutical Research, Kansas City, MO, 4Premier Research, Durham, NC

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster I: Clinical Trials and Interventions
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: CNTX-4975, a highly purified, synthetic trans-capsaicin, targets transient receptor potential vanilloid 1, producing analgesia via reversible desensitization of end terminals of primary afferent pain fibers within the joint. This phase 2 dose-ranging study evaluated CNTX-4975 in subjects with osteoarthritis (OA) knee pain.

Methods: Subjects aged 45–80 years with chronic knee OA and stable moderate to severe knee pain who failed previous oral/intra-articular (IA) analgesics were randomized 2:1:2 to a single IA injection of placebo, CNTX-4975 0.5 mg, or CNTX-4975 1.0 mg. Randomization was stratified by Kellgren-Lawrence (K-L) grade (2–3 vs 4) and body mass index (<30 vs ≥30 kg/m²). The primary efficacy endpoint was area under the curve (AUC) for change from baseline in daily Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) A1 score (pain with walking) through week 12 (analysis of covariance). Additional efficacy endpoints included mean change from baseline in weekly WOMAC A1 score, WOMAC B stiffness subscale, and WOMAC C physical function subscale through week 24 (mixed model for repeated measures). Symptomatic improvements were assessed with modified Outcome Measures in Rheumatology Clinical Trials–Osteoarthritis Research Society International (OMERACT-OARSI) criteria (Table 1). Statistical tests were 2-sided (alpha, 0.10). Safety assessments included treatment-emergent adverse events (TEAEs).

Results: Efficacy was evaluated in 172 subjects (placebo, n=69; CNTX-4975 0.5 mg, n=33; CNTX-4975 1.0 mg, n=70), most with K-L grade 2–3 (placebo, n=62; CNTX-4975 0.5 mg, n=30; CNTX-4975 1.0 mg, n=65). Mean baseline WOMAC A1 pain score was 7.3 (Numeric Pain Rating Scale, 0–10). WOMAC A1 scores (AUC analysis) were significantly improved vs placebo at week 12 with CNTX-4975 0.5 mg (least squares mean difference [LSMD]: −0.8; P=0.07) and 1.0 mg (LSMD: −1.6; P<0.0001) and at week 24 with CNTX-4975 1.0 mg (LSMD: −1.4; P=0.0002). Additional efficacy analyses are reported in Table 2. At week 12, more subjects treated with CNTX-4975 0.5 mg and 1.0 mg met modified criteria for OMERACT-OARSI response (76% [P=0.11] and 86% [P=0.0005], respectively) vs placebo (59%). The incidence of TEAEs was 30% for placebo or CNTX-4975 1.0 mg and 47% for CNTX-4975 0.5 mg at week 24. Most TEAEs were considered unrelated to study treatment. Arthralgia was the most common TEAE with placebo and CNTX-4975 1.0 mg.

Disclosure: V. Calamia, None; M. Camacho, None; I. Rego-Pérez, None; L. González, None; P. Fernández-Puente, None; F. Picchi, None; M. Herrero, Bioiberica, SA, 3; H. Martinez, Bioiberica, SA, 3; C. Ruiz-Romero, None; F. J. Blanco, None.
Conclusion: A single IA injection of CNTX-4975 1.0 mg improved pain with walking, knee stiffness, and physical function and was well tolerated in subjects with moderate to severe OA knee pain.

<table>
<thead>
<tr>
<th>Table 1. Modified OMERACT-OARSI Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Responders</strong></td>
</tr>
<tr>
<td>• ≥50% improvement and 2-point improvement from baseline to the specified week in WOMAC A1 or WOMAC C average score</td>
</tr>
<tr>
<td>• Met ≥2 of the following 3 criteria</td>
</tr>
<tr>
<td>• ≥20% improvement and 1-point improvement in pain</td>
</tr>
<tr>
<td>• ≥20% improvement and 1-point improvement in function</td>
</tr>
<tr>
<td>• Patient Global Impression of Change rated as minimally, much, or very much improved</td>
</tr>
</tbody>
</table>

OMERACT-OARSI: Outcome Measures in Rheumatology Clinical Trials—Osteoarthritis Research Society International; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.

Table 2. Mean Changes from Baseline in Weekly Average Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) A1, WOMAC B, and WOMAC C at Week 12 and Week 24

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>CNTX-4975 0.5 mg (n=33)</th>
<th>CNTX-4975 1.0 mg (n=70)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Week 12</td>
<td>Week 24</td>
</tr>
<tr>
<td>WOMAC A1*</td>
<td>n=30</td>
<td>n=65</td>
</tr>
<tr>
<td>K-L grade 2–3</td>
<td>–0.74</td>
<td>–1.7</td>
</tr>
<tr>
<td>90% CI</td>
<td>(–1.5, 0.01)</td>
<td>(–2.3, –1.1)</td>
</tr>
<tr>
<td>P value</td>
<td>0.11</td>
<td>0.001</td>
</tr>
<tr>
<td>K-L grade 4*</td>
<td>n=3</td>
<td>n=5</td>
</tr>
<tr>
<td>LSMD vs placebo</td>
<td>0.68</td>
<td>3.4</td>
</tr>
<tr>
<td>90% CI</td>
<td>(–2.6, 3.9)</td>
<td>(–6.5, –0.30)</td>
</tr>
<tr>
<td>P value</td>
<td>0.75</td>
<td>0.07</td>
</tr>
<tr>
<td>WOMAC A1*</td>
<td>n=40</td>
<td>n=65</td>
</tr>
<tr>
<td>LSMD vs placebo</td>
<td>–0.99</td>
<td>–1.5</td>
</tr>
<tr>
<td>90% CI</td>
<td>(–1.7, –0.03)</td>
<td>(–2.2, –0.84)</td>
</tr>
<tr>
<td>P value</td>
<td>0.09</td>
<td>0.003</td>
</tr>
<tr>
<td>WOMAC B*</td>
<td>n=40</td>
<td>n=65</td>
</tr>
<tr>
<td>LSMD vs placebo</td>
<td>–0.84</td>
<td>–2.5</td>
</tr>
<tr>
<td>90% CI</td>
<td>(–2.4, 0.75)</td>
<td>(–3.6, –1.2)</td>
</tr>
<tr>
<td>P value</td>
<td>0.36</td>
<td>0.0013</td>
</tr>
<tr>
<td>WOMAC C*</td>
<td>n=40</td>
<td>n=65</td>
</tr>
<tr>
<td>LSMD vs placebo</td>
<td>–5.0</td>
<td>–18.3</td>
</tr>
<tr>
<td>90% CI</td>
<td>(–17.9, 7.9)</td>
<td>(–18.3, 3.8)</td>
</tr>
<tr>
<td>P value</td>
<td>0.62</td>
<td>0.004</td>
</tr>
</tbody>
</table>

AUC: area under the curve; K-L, Kellgren-Lawrence; LSMD, last square mean difference; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Disclosure: R. Stevens, Centrexion Therapeutics, 3; D. Petersen, None; J. Ervin, None; J. Nezzer, None; Y. Nieves, None; J. Campbell, Centrexion Therapeutics, 3; K. Guedes, Centrexion Therapeutics, 3; R. Burges, Centrexion Therapeutics, 3; P. Hanson, Centrexion Therapeutics, 3.


Abstract Number: 1192

Patient Characteristics That Predict the Effect of Laparoscopic Adjustable Gastric Band Weight Loss Surgery on Knee Osteoarthritis Pain

Shannon Chen1, Fernando Bomfim2, Heekoung Youn3, Christine Ren-Fielding4 and Jonathan Samuels5, 1Medicine, NYU Langone Medical Center, New York, NY, 2NYU Langone Medical Center, New York, NY, 3Surgery, NYU Langone Medical Center, New York,
Background/Purpose: Obesity is a modifiable risk factor for knee osteoarthritis (OA), yet diet and exercise often fail to achieve sustained weight loss or knee improvement. Recent studies suggest that bariatric weight loss surgery has a significant impact on both obesity and knee pain in this population. We aimed to quantify knee pain improvement in obese patients opting for the laparoscopic adjustable gastric band (LAGB), and further support its use in refractory knee OA.

Methods: We identified bariatric surgery patients from the New York University Langone Weight Management Program Research Registry (2002-2015) who were ≥18 years old at the time of surgery, reported knee pain pre-operatively, and had no previous history of rheumatoid arthritis, psoriatic arthritis, or lupus. Participants rated their knee pain on a scale from 0 (best) to 10 (worst) at three time points: (1) before bariatric surgery, (2) one year after surgery, and (3) at the time of survey administration. They reported any family history of OA, knee injury or surgery before onset of knee pain, and presence of OA in other joints. We obtained patient height and weight from their charts at the first two time points, and used self-reported weight for the third time point. ANOVA was used to analyze the relationship between change in knee pain rating and various perioperative and postoperative patient characteristics, including baseline age and body mass index (BMI).

Results: Of the 617 bariatric patients eligible for the study, 120 LAGB patients were included. By one year post-LAGB, the BMI decreased by a mean of 11.2 kg/m², and knee pain decreased from 6.88 to 3.34. We found a significant difference in knee pain improvement by age group at one year post-LAGB (p=0.009). Those who had a knee injury prior to onset of knee pain showed less improvement at one year post-LAGB than did those who were injury-free (p=0.04), though a history of knee surgery was not similarly significant. Patients with OA in other joints had less improvement by a margin of 2.75 vs 4.22 (p=0.001). There was no significant relationship between baseline BMI and knee pain improvement at one year post-LAGB, but the subgroup with the highest BMI improvement had the most knee improvement (p=0.043). Though knee pain improvement trended with decreased BMI at one year post-LAGB, the difference between BMI groups was no longer significant at the time of survey administration (mean 9.14 years, median 10 years).

Conclusion: LAGB weight loss surgery results in a significant reduction of knee OA pain, especially in younger patients and those without prior knee injury or other involved joints. This further supports LAGB as a viable treatment option in the algorithm for refractory knee OA pain in obese patients, irrespective of a patient’s degree of obesity.

Table 1. Various perioperative and postoperative factors affecting knee OA pain rating improvement in a cohort of 120 laparoscopic gastric banding patients (2002-2015)
<table>
<thead>
<tr>
<th>Covariate</th>
<th>Mean Knee Pain Improvement ±SD (1 year post-surgery)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at time of surgery (yrs)</td>
<td></td>
<td>0.009</td>
</tr>
<tr>
<td>≤40 (n=22)</td>
<td>4.41 ±2.44</td>
<td></td>
</tr>
<tr>
<td>41-50 (n=35)</td>
<td>4.11 ±2.44</td>
<td></td>
</tr>
<tr>
<td>51-60 (n=44)</td>
<td>3.25 ±2.56</td>
<td></td>
</tr>
<tr>
<td>&gt;60 (n=19)</td>
<td>2.11 ±1.89</td>
<td></td>
</tr>
<tr>
<td>BMI at time of surgery (kg/m²)</td>
<td></td>
<td>0.653</td>
</tr>
<tr>
<td>≤40 (n=23)</td>
<td>3.09 ±2.56</td>
<td></td>
</tr>
<tr>
<td>40-&lt;45 (n=40)</td>
<td>3.90 ±3.13</td>
<td></td>
</tr>
<tr>
<td>45-&lt;50 (n=25)</td>
<td>3.44 ±1.76</td>
<td></td>
</tr>
<tr>
<td>≥50 (n=32)</td>
<td>3.47 ±2.08</td>
<td></td>
</tr>
<tr>
<td>Knee injury before surgery</td>
<td></td>
<td>0.044</td>
</tr>
<tr>
<td>No (n=81)</td>
<td>3.85 ±2.53</td>
<td></td>
</tr>
<tr>
<td>Yes (n=39)</td>
<td>2.87 ±2.34</td>
<td></td>
</tr>
<tr>
<td>Knee surgery before surgery</td>
<td></td>
<td>0.132</td>
</tr>
<tr>
<td>No (n=97)</td>
<td>3.70 ±2.51</td>
<td></td>
</tr>
<tr>
<td>Yes (n=23)</td>
<td>2.83 ±2.37</td>
<td></td>
</tr>
<tr>
<td>Family history of OA</td>
<td></td>
<td>0.749</td>
</tr>
<tr>
<td>No (n=57)</td>
<td>3.46 ±2.64</td>
<td></td>
</tr>
<tr>
<td>Yes (n=63)</td>
<td>3.60 ±2.39</td>
<td></td>
</tr>
<tr>
<td>OA at other anatomic sites</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>No (n=64)</td>
<td>4.22 ±2.47</td>
<td></td>
</tr>
<tr>
<td>Yes (n=56)</td>
<td>2.75 ±2.32</td>
<td></td>
</tr>
<tr>
<td>Change in BMI at 1yr post-surgery (kg/m²)</td>
<td></td>
<td>0.043</td>
</tr>
<tr>
<td>&lt;8 (n=27)</td>
<td>2.59 ±2.12</td>
<td></td>
</tr>
<tr>
<td>8-13 (n=62)</td>
<td>3.60 ±2.43</td>
<td></td>
</tr>
<tr>
<td>&gt;13 (n=31)</td>
<td>4.23 ±2.77</td>
<td></td>
</tr>
</tbody>
</table>

Disclosure: S. Chen, None; F. Bomfim, None; H. Youn, None; C. Ren-Fielding, Apollo, Inc, 2; J. Samuels, None.


Abstract Number: 1193

**A Randomized, Placebo-Controlled, Double-Blind, Phase II Clinical Trial of the First-in-Class Imidazoline-2 Receptor Ligand CR4056 in Pain from Knee Osteoarthritis and Disease Phenotypes**

Lucio C. Rovati¹, Nadia Brambilla¹, Tomasz Blicharski², Nicholas J Probert³, Cristina Vitalini¹, Giampaolo Giacovelli¹, Federica Girolami¹ and Massimo D’Amato¹, ¹Clinical Research Department, Rottapharm Biotech, Monza, Italy, ²Lubelskie Centrum Diagnostyczne, Świdnik, Poland, ³MAC Clinical Research, Manchester, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster I: Clinical Trials and Interventions
**Background/Purpose:** CR4056 is a novel imidazoline-2 receptor (I$_2$R) ligand endowed with potent analgesic activities in several and diverse animal models of nociceptive and neuropathic pain, by innovative modulation of the monoaminergic descending inhibitory pathway (Li JX, Pharmacol Ther 2017). The present proof-of-concept study was undertaken to investigate the efficacy and safety of CR4056 in patients with knee osteoarthritis (OA) pain.

**Methods:** This was a multicenter, prospective, randomized, placebo-controlled, double-blind, parallel group design trial (EudraCT n. 2015-001136-37). Patients with knee OA (ACR clinical and radiological criteria, Kellgren & Lawrence grade 2/3) and moderate to severe pain (score ≥50 on the 0-100 normalized WOMAC pain subscale) were randomized in a 2:1 ratio to a pharmacologically effective dose of oral CR4056 (100 mg b.i.d. in women and 200 mg b.i.d. in men, to assure similar exposure due to slight gender differences in pharmacokinetics) or matching placebo for 14 days. Intention-to-treat (ITT: Worst-Case approach for non-completers) changes in WOMAC pain (primary endpoint) were analysed by the Wilcoxon test in the overall study population and in different OA phenotypes, including patients with a neuropathic pain component (as per the painDETECT questionnaire), or obesity (BMI≥27.5 kg/m$^2$, i.e. the WHO threshold for pre-obesity).

**Results:** A total of 213 patients were blindly randomized at 20 sites in Poland and UK: 92 women to CR4056 100 mg b.i.d., 52 men to 200 mg b.i.d. and 69 overall to placebo, with median (range) WOMAC pain baseline scores of 61 (50;90), 58 (50;90) and 58 (50;84), respectively, that were similar across groups and OA phenotypes. Three patients withdrew with CR4056 100 mg b.i.d., 5 with 200 mg b.i.d. and 6 with placebo. There were no serious adverse events and treatments were equally well tolerated. CR4056 decreased WOMAC pain vs. placebo after only 14 days and with a similar pattern in the overall population and the selected OA phenotypes. While only 21/213 (9.9%) patients had a neuropathic pain component, 73.2% (156 out of 213) had BMI≥27.5 (mean 33.4). In these patients, CR4056 significantly decreased WOMAC pain (Figure) in a clinically relevant fashion: pooled CR4056 ITT median (range) change was -14 (-80;22) vs. 0 (-56;8) with placebo (P=0.011; n=105 and 51, respectively). Secondary pain and function outcomes followed a pattern consistent with the primary endpoint.

**Conclusion:** CR4056 is the first I$_2$R ligand to show analgesic activity in humans. The compound was safe and effective in reducing knee OA pain in this very short phase II trial, especially in overweight and obese patients. This observation prompts longer-term trials and the exploration of possible links between the I$_2$ pathway and the overweight or metabolic OA phenotype altered pain perception. Conversely, a neuropathic pain component had low prevalence in unselected knee OA patients in this study.

**Disclosure:** L. C. Rovati, Rottapharm Biotech, 3; N. Brambilla, Rottapharm Biotech, 3; T. Blicharski, Rottapharm Biotech, 5; N. J. Probert, Rottapharm Biotech, 5; C. Vitalini, Rottapharm Biotech, 3; G. Giacovelli, Rottapharm Biotech, 3; F. Girolami, Rottapharm Biotech, 3; M. D’Amato, Rottapharm Biotech, 3.
Are Bisphosphonates Efficacious in Knee Osteoarthritis? A Meta-Analysis of Randomized Controlled Trials

Mikala C. Osani, Elizaveta Vaysbrot, Raveendhara R. Bannuru, Mia-Cara Musetti and Timothy E. McAlindon, 1 Division of Rheumatology, Tufts Medical Center, Boston, MA, 2 Center of Integrative Medicine and Division of Rheumatology, Tufts Medical Center, Boston, MA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster I: Clinical Trials and Interventions
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
One of the key aspects of osteoarthritis (OA) pathogenesis is subchondral bone remodeling. Bisphosphonates have been touted as disease-modifying agents for OA due to their ability to limit excessive bone remodeling and block osteoclast-mediated pain pathways. Prior meta-analyses on the topic suggested efficacy of bisphosphonates in OA but had major methodological flaws in data extraction and analyses, resulting in misleading conclusions. The latest review combined observational studies with randomized controlled trials (RCTs) in the same analysis, blended various OA sites, and mixed active with placebo comparators; this produced high heterogeneity (I² up to 99%). We aimed to elucidate the true effects of bisphosphonates using rigorously implemented meta-analysis of RCTs. We chose to isolate our analysis to knee OA patients, because this population is more homogenous and has been widely studied.

Methods:
We searched Medline, EMBASE, Google Scholar, Web of Science, and Cochrane Database from inception until April 2017 and hand-searched reference lists. We included only RCTs in knee OA patients that compared any bisphosphonates vs. placebo and reported validated pain and function scales, radiographic progression, and adverse events outcomes. Studies using active comparators or concomitant medications besides NSAIDs and acetaminophen were excluded. We calculated standardized mean differences to account for variation in outcome scales. Random effects meta-analyses were performed.

Results:
We included seven RCTs (3,013 patients, 69% female) (Table 1). Most patients (N=2,767) received oral risedronate, and a majority were taking concomitant NSAIDs. No pain or function outcomes, regardless of dose, route, time point or measuring instrument, revealed statistically significant results (Table 2). Similarly, we found no statistically significant effect on radiographic progression. One small RCT in patients with bone marrow lesions (BML) suggested a reduction in BML size at 6 months. Bisphosphonates displayed good tolerability, with no statistically significant differences in adverse event outcomes vs. placebo.

Conclusion:
Contrary to prior reviews, our analysis showed that bisphosphonates neither provide symptomatic relief nor defer radiographic progression in knee OA. However, these agents may still be beneficial in certain subsets of patients who display high rates of subchondral bone turnover. Future studies should be directed at defining such OA subsets and investigating the effects of bisphosphonates in those patients.
Table 1: Characteristics of included studies

<table>
<thead>
<tr>
<th>Author, year, Study name</th>
<th>No. of patients</th>
<th>Age mean (range)</th>
<th>% females</th>
<th>Intervention vs. comparator</th>
<th>NSAID use, %</th>
<th>Study duration</th>
<th>Overall risk of bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Speciner, 2015, BRISK study</td>
<td>214</td>
<td>63.3 (20-78)</td>
<td>42%</td>
<td>Rosuvastatin 5 vs or 15 mg/day vs. placebo</td>
<td>0%</td>
<td>12 months</td>
<td>Unclear</td>
</tr>
<tr>
<td>Bergman, 2009, KOST trial: efficacy data, N:1, N: 2</td>
<td>1,251</td>
<td>63.8 (19-88)</td>
<td>25%</td>
<td>Rosuvastatin 5 vs or 15 mg/day vs. placebo</td>
<td>0%</td>
<td>24 months</td>
<td>Unclear</td>
</tr>
<tr>
<td>Bergman, 2009, KOST trial: efficacy data, N: 3, N: 4</td>
<td>1,292</td>
<td>63.5 (25-88)</td>
<td>25%</td>
<td>Rosuvastatin 5 vs or 15 mg/day vs. placebo</td>
<td>0%</td>
<td>24 months</td>
<td>Unclear</td>
</tr>
<tr>
<td>Araki, 2014, KOST trial: safety data</td>
<td>2,483</td>
<td>62.1 (20-89)</td>
<td>25%</td>
<td>Rosuvastatin 5 vs or 15 mg/day vs. placebo</td>
<td>0%</td>
<td>24 months</td>
<td>Unclear</td>
</tr>
<tr>
<td>Jukar, 2010</td>
<td>39</td>
<td>47.6 (20-76)</td>
<td>50%</td>
<td>Rosuvastatin 10 mg/week vs. placebo</td>
<td>0%</td>
<td>6 months</td>
<td>High</td>
</tr>
<tr>
<td>Issi, 2012</td>
<td>59</td>
<td>62.4 (19-89)</td>
<td>50%</td>
<td>Rosuvastatin 10 mg/week vs. placebo</td>
<td>0%</td>
<td>12 months</td>
<td>Low</td>
</tr>
<tr>
<td>Rossen, 2015</td>
<td>83</td>
<td>68.4 (19-83)</td>
<td>48%</td>
<td>Rosuvastatin 10 mg/week vs. placebo</td>
<td>0%</td>
<td>4 months</td>
<td>Low</td>
</tr>
<tr>
<td>Veronesi, 2015</td>
<td>88</td>
<td>69.5 (20-87)</td>
<td>48%</td>
<td>Rosuvastatin 10 mg/week vs. placebo</td>
<td>0%</td>
<td>2 months</td>
<td>Low</td>
</tr>
</tbody>
</table>

Table 2: Bisphosphonates vs. Placebo in Knee OA

<table>
<thead>
<tr>
<th>Outcome</th>
<th>N of RCTs</th>
<th>N of patients</th>
<th>Effect estimate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain (last week)</td>
<td>2</td>
<td>8,952</td>
<td>SMD: -0.16 (0.34, 0.02)</td>
</tr>
<tr>
<td>Pain (within 6 months)</td>
<td>2</td>
<td>8,952</td>
<td>SMD: -0.50 (0.18, 0.96)</td>
</tr>
<tr>
<td>Pain (at 12 months)</td>
<td>1</td>
<td>8,952</td>
<td>SMD: -0.40 (0.04, 0.78)</td>
</tr>
<tr>
<td>Pain (at 24 months)</td>
<td>2</td>
<td>8,952</td>
<td>SMD: -0.54 (0.10, 0.98)</td>
</tr>
<tr>
<td>Felson’s questionnaire</td>
<td>2</td>
<td>8,952</td>
<td>SMD: -0.41 (0.10, 0.81)</td>
</tr>
<tr>
<td>All-cause Adverse Events</td>
<td>3</td>
<td>4,292</td>
<td>RR: 1.03 (95% CI: 0.88, 1.21)</td>
</tr>
<tr>
<td>Serious Adverse Events</td>
<td>3</td>
<td>4,292</td>
<td>RR: 1.63 (95% CI: 0.88, 3.00)</td>
</tr>
<tr>
<td>Withdrawals during treatment</td>
<td>8</td>
<td>3,132</td>
<td>RR: 1.08 (95% CI: 0.68, 1.72)</td>
</tr>
<tr>
<td>Withdrawals due to adverse events</td>
<td>3</td>
<td>3,468</td>
<td>RR: 1.07 (95% CI: 0.63, 1.81)</td>
</tr>
</tbody>
</table>

Disclosure: M. C. Osani, None; E. Vaysbrot, None; R. R. Bannuru, None; M. C. Musetti, None; T. E. McAlindon, None.

Abstract Number: 1195

Efficacy and Safety of Subcutaneous Tanezumab in Patients with Knee or Hip Osteoarthritis (NCT01089725)

Charles A. Birbará1, Eugene J. Dabiezies2, Aimee M. Burr3, Robert J. Fountaine4, Michael D. Smith3, Mark T. Brown3, Christine R. West3, Rosalinda H. Arends3 and Kenneth M. Verburg3, 1University of Massachusetts Medical School, Worcester, MA, 2Pensacola Research Consultants, Pensacola, FL, 3Pfizer, Inc., Groton, CT, 4Pfizer, Inc., Groton, CT

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster I: Clinical Trials and Interventions
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Tanezumab (TNZ) is a monoclonal antibody that inhibits nerve growth factor and reduces hip or knee osteoarthritis (OA) pain. A placebo-controlled phase 3 study (NCT01089725), evaluated efficacy of subcutaneous (SC) TNZ (2.5, 5, and 10 mg) and compared therapeutic equivalence of TNZ 10 mg SC to TNZ 10 mg intravenous (IV) every 8 weeks in the treatment of
symptomatic OA. Co-primary endpoints were Western Ontario and McMaster Universities (WOMAC) OA Pain and Physical Function Indices and Patient's Global Assessment of OA (PGAOA) at Week 8.

**Methods:** Patients (N=379) with knee or hip OA were randomized and treated with placebo (n=72), TNZ 2.5 mg SC (n=74), 5 mg SC (n=63), 10 mg SC (n=86) or 10 mg IV (n=84) every 8 weeks. Efficacy analyses included change from baseline in WOMAC Pain and Physical Function subscales, PGAOA, and percentage of patients with ≥30%, ≥50%, ≥70%, and ≥90% improvement in WOMAC Pain. Safety assessments included adverse event (AE) reporting, physical and neurological examinations, and laboratory tests.

**Results:** The study discontinued prematurely due to a FDA partial clinical hold on TNZ non-cancer pain studies; thus no statistical testing was conducted. Since <10% of patients received a second dose at Week 8, efficacy results are described for change from baseline to Week 8 only. Mean (standard error [SE]) change from baseline to Week 8 in WOMAC Pain in TNZ groups ranged from −3.59 (0.26) to −3.89 (0.32); versus −2.74 (0.25) with placebo. Percentage of patients with ≥30%, ≥50%, ≥70%, and ≥90% reductions in WOMAC Pain score at Week 8 was greater in all TNZ groups versus placebo (Figure). Mean (SE) change from baseline to Week 8 in WOMAC Physical Function ranged from −3.13 (0.25) to −3.51 (0.28) with TNZ and −2.26 (0.24) with placebo. For PGAO, mean (SE) change from baseline to Week 8 was −0.90 (0.11) to −1.08 (0.12) with TNZ and −0.78 (0.10) with placebo. Inspection of the efficacy-time curves indicated that onset and duration of analgesia with all SC doses were similar to the 10-mg IV dose over the 8-week dosing interval. Overall incidence of all-causality AEs was highest with TNZ 10-mg IV (52.4%) and placebo (51.4%). No AEs of osteonecrosis were reported by investigators. Two placebo-treated patients and 3 TNZ 2.5-mg SC patients underwent total joint replacements. AEs in ≥5% of patients in any treatment group included arthralgia, paresthesia, hypoaesthesia, worsening OA, headache, and joint swelling; paresthesia and hypoaesthesia occurred only in patients receiving TNZ. Injection site reactions were reported by 4.7%, 3.6%, 2.8%, 2.7% and 0% of those treated with TNZ 10 mg SC, TNZ 10 mg IV, placebo, TNZ 2.5 mg SC and TNZ 5 mg SC, respectively and the majority were mild (none were severe).

**Conclusion:** SC TNZ provided improvements in Pain, Physical Function, and PGAOA at all doses. Efficacy and safety of SC TNZ were generally similar to IV in patients with OA pain.

![Figure: Reduction in WOMAC Pain Subscale for Week 8 (ITT, LOCF)](image)

**Disclosure:** C. A. Birbara, Forest Laboratories Inc, 8,GlaxoSmithKline, 8,Roche Pharmaceuticals, 8; E. J. Dabezies, None; A. M. Burr, Pfizer Inc, 1,Pfizer Inc, 3; R. J. Fountaine, Pfizer Inc, 3; M. D. Smith, Pfizer Inc, 1; M. T. Brown, Pfizer Inc, 1,Pfizer Inc, 3; C. R. West, Pfizer Inc, 1,Pfizer Inc, 3; R. H. Arends, Pfizer Inc, 1,Pfizer Inc, 3; K. M. Verburg, Pfizer Inc, 1,Pfizer Inc, 3.


**Abstract Number:** 1196

**Safety and Efficacy of ABT-981, an Anti–Interleukin-1α/β Dual Variable Domain (DVD) Immunoglobulin, in Subjects with Knee Osteoarthritis: Results from the Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Phase 2 Trial**
Roy Fleischmann1, Henning Bliddal2, Francisco J Blanco3, Thomas J. Schnitzer4, Charles Peterfy5, Su Chen6, Li Wang6, Philip G. Conaghan7, Francis Berenbaum8, Jean-Pierre Pelletier9, Johanne Martel-Pelletier9, Ole Vaeterlein10, Wei Liu6, Gwen Levy6, Lanju Zhang6, Jeroen K. Medema6 and Marc C. Levesque6,
1University of Texas Southwestern Medical Center at Dallas, Metroplex Clinical Research Center, Dallas, TX, 2Parker Institute, Bispebjerg-Frederiksberg Hospital, University of Copenhagen, Copenhagen, Denmark, 3INIBIC-Instituto de Investigaciones Biomédicas de A Coruña-Complexo Hospitalario Universitario de A Coruña, A Coruña, Spain, 4Northwestern Medicine, Feinberg School of Medicine, Chicago, IL, 5Spire Sciences, Inc., Boca Raton, FL, 6AbbVie Inc., North Chicago, IL, 7Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom, 8University Pierre & Marie Curie and Inserm, DHU i2B, APHP, Hospital Saint-Antoine, Paris, France, 9Centre Hospitalier de l'Université de Montréal, Montréal, QC, Canada, 10Bioclinica, Hamburg, Germany

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster I: Clinical Trials and Interventions
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Animal studies suggested that inhibiting IL-1α/β with ABT-981 may reduce pain and slow structural progression in OA. This study (NCT02087904; ILLUSTRATE-K) assessed the safety and efficacy of ABT-981 in subjects with knee OA.

Methods: Subjects (N=350; 347 analyzed) with Kellgren-Lawrence (KL) grade 2–3 knee OA, synovitis on MRI or US, and visual analog scale knee pain score 4–8 (range, 0–10) were randomized to placebo (PBO) or ABT-981 25, 100, or 200 mg subcutaneously (sc) every 2 wk (E2W) for 50 wk. The primary endpoints were change from baseline (BL) in WOMAC pain at wk 16 and change from BL in MRI synovitis at wk 26. Other endpoints included WOMAC function and OMERACT/OARSI response (wk 16, 26, and 52) MRI cartilage volume (wk 26 and 52), and x-ray joint space narrowing (JSN) (wk 52). Continuous efficacy assessments used ANCOVA (main factors: treatment, age group, KL grade; covariates: BL values).

Results: BL demographics and disease characteristics were balanced (KL grade 3, 36.0%–38.8%; mean WOMAC pain (scale 0–50), 26.2–28.4). The primary endpoint of WOMAC pain at wk 16 improved significantly, compared with PBO, with ABT-981 100 mg (P=0.050; Figure 1), but not 25 mg (P=0.834) or 200 mg (P=0.415). WOMAC pain reduction in all ABT-981 groups was sustained from wk 16 to 52, but differences between ABT-981 and PBO for WOMAC pain and other key signs and symptoms were not significant (Table 1). Synovitis-related imaging, cartilage volume endpoints, and JSN were similar between ABT-981 and PBO groups at wk 26 and 52. ABT-981 was well tolerated; serious adverse events (SAEs), treatment-related SAEs, and infections and serious infections were similar with ABT-981 vs PBO (Table 2). Injection site reactions, grade 2/3 neutropenia, and discontinuations due to neutropenia were more frequent with ABT-981 vs PBO. ABT-981 exposures reached steady state after wk 6 and were stable through wk 52. Pharmacodynamic responses (neutrophil and high-sensitivity CRP levels) plateaued at the 100 mg dose and data were similar at 200 mg. The low immunogenicity to ABT-981 did not meaningfully affect outcomes.

Conclusion: ABT-981 was generally well tolerated and met the primary endpoint of reduction in WOMAC pain at wk 16 compared with placebo at a dose of 100 mg, but not at 25 mg or 200 mg; cartilage thickness, synovitis, and other structural endpoints were similar between ABT-981 and PBO.
Table 1. Changes From Baseline in Efficacy Endpoints

<table>
<thead>
<tr>
<th>Signs and Symptoms Endpoints (LOCF data)</th>
<th>Week 16</th>
<th>Week 52</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WOMAC pain (0–10)</strong></td>
<td>PBO (n=85)</td>
<td>25 (n=88)</td>
</tr>
<tr>
<td>p-value vs PBO</td>
<td>-8.9</td>
<td>-9.2</td>
</tr>
<tr>
<td><strong>WOMAC function (0–170)</strong></td>
<td>PBO (n=85)</td>
<td>0.834</td>
</tr>
<tr>
<td>p-value vs PBO</td>
<td>-28.7</td>
<td>-29.8</td>
</tr>
<tr>
<td><strong>OMERACT/OARSI response, %</strong></td>
<td>PBO (n=85)</td>
<td>60.0</td>
</tr>
<tr>
<td>p-value vs PBO</td>
<td>0.311</td>
<td>0.080</td>
</tr>
</tbody>
</table>

Structural Endpoints (observed data)

<table>
<thead>
<tr>
<th>Endpoints</th>
<th>PBO</th>
<th>25</th>
<th>100</th>
<th>200</th>
<th>PBO</th>
<th>25</th>
<th>100</th>
<th>200</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WORMS synovitis/effusion volume</strong></td>
<td>0.07</td>
<td>-0.01</td>
<td>-0.08</td>
<td>-0.07</td>
<td>-0.05</td>
<td>-0.05</td>
<td>-0.06</td>
<td>-0.01</td>
</tr>
<tr>
<td>n</td>
<td>70</td>
<td>76</td>
<td>70</td>
<td>75</td>
<td>59</td>
<td>66</td>
<td>62</td>
<td>66</td>
</tr>
<tr>
<td>p-value vs PBO</td>
<td>0.384</td>
<td>0.095</td>
<td>0.106</td>
<td>0.967</td>
<td>0.923</td>
<td>0.692</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Effusion volume, mL</td>
<td>0.03</td>
<td>0.26</td>
<td>-1.04</td>
<td>-1.49</td>
<td>-1.90</td>
<td>1.17</td>
<td>-0.67</td>
<td>-1.83</td>
</tr>
<tr>
<td>n</td>
<td>60</td>
<td>69</td>
<td>67</td>
<td>68</td>
<td>53</td>
<td>60</td>
<td>60</td>
<td>58</td>
</tr>
<tr>
<td>p-value vs PBO</td>
<td>0.807</td>
<td>0.542</td>
<td>0.385</td>
<td>0.154</td>
<td>0.569</td>
<td>0.977</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Synovial membrane thickness, mm</td>
<td>-0.05</td>
<td>0.01</td>
<td>-0.08</td>
<td>-0.01</td>
<td>-0.07</td>
<td>-0.04</td>
<td>-0.05</td>
<td>-0.02</td>
</tr>
<tr>
<td>n</td>
<td>59</td>
<td>65</td>
<td>59</td>
<td>63</td>
<td>50</td>
<td>59</td>
<td>55</td>
<td>53</td>
</tr>
<tr>
<td>p-value vs PBO</td>
<td>0.145</td>
<td>0.520</td>
<td>0.159</td>
<td>0.474</td>
<td>0.637</td>
<td>0.221</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cartilage volume, mm²</td>
<td>n</td>
<td>28</td>
<td>65</td>
<td>53</td>
<td>66</td>
<td>49</td>
<td>57</td>
<td>50</td>
</tr>
<tr>
<td>Total</td>
<td>-326.9</td>
<td>-255.5</td>
<td>-322.4</td>
<td>-351.0</td>
<td>-598.7</td>
<td>-554.3</td>
<td>-583.1</td>
<td></td>
</tr>
<tr>
<td>p-value vs PBO</td>
<td>0.992</td>
<td>0.948</td>
<td>0.523</td>
<td>0.554</td>
<td>0.970</td>
<td>0.713</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medial</td>
<td>-166.9</td>
<td>-139.5</td>
<td>-163.1</td>
<td>-153.7</td>
<td>-286.8</td>
<td>-317.3</td>
<td>-266.7</td>
<td>-310.9</td>
</tr>
<tr>
<td>p-value vs PBO</td>
<td>0.804</td>
<td>0.904</td>
<td>0.655</td>
<td>0.503</td>
<td>0.670</td>
<td>0.399</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lateral</td>
<td>-159.6</td>
<td>-166.3</td>
<td>-158.0</td>
<td>-204.1</td>
<td>-270.7</td>
<td>-280.9</td>
<td>-287.9</td>
<td>-271.1</td>
</tr>
<tr>
<td>p-value vs PBO</td>
<td>0.860</td>
<td>0.969</td>
<td>0.539</td>
<td>0.820</td>
<td>0.719</td>
<td>0.992</td>
<td></td>
<td></td>
</tr>
<tr>
<td>JSN, mm</td>
<td>n</td>
<td>58</td>
<td>70</td>
<td>64</td>
<td>68</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medial</td>
<td>-0.09</td>
<td>-0.10</td>
<td>-0.11</td>
<td>-0.16</td>
<td>0.14</td>
<td>-0.07</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>JSN, mm</td>
<td>n</td>
<td>58</td>
<td>70</td>
<td>64</td>
<td>68</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p-value vs PBO</td>
<td>0.017*</td>
<td>0.148</td>
<td>0.415</td>
<td>0.065*</td>
<td>0.118</td>
<td>0.065</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data are least squares means unless otherwise noted.

LOCF, last observation carried forward; PBO, placebo; sc, subcutaneous.
*P<0.05 vs PBO. Continuous variables compared with analysis of covariance (ANCOVA) with treatment, age, and KL grade as main factors and baseline as covariate. Categorical variables compared with Cochran-Mantel-Haenszel test with age group and KL grade as stratification factors.

Figure 1. Changes From Baseline Over Time in WOMAC Pain Score (LOCF)

Primary Endpoint

25 mg vs PBO, P=0.834
100 mg vs PBO, P=0.050
200 mg vs PBO, P=0.415

Least-Squares Mean Change From Baseline in WOMAC Pain Score

Week

*P<0.05 from ANCOVA with treatment, age, and KL grade as main factors and baseline as covariate.
Exploring Determinants Predicting Response to Intra-Articular Hyaluronic Acid Treatment in Symptomatic Knee Osteoarthritis

Jean-Pierre Pelletier1, Jean-Pierre Raynauld1, François Abram2, Marc Dorais3, Philippe Delorme4 and Johanne Martel-Pelletier1, 2
1Osteoarthritis Research Unit, University of Montreal Hospital Research Centre (CRCHUM), Montreal, QC, Canada, 2Medical Imaging Research & Development, ArthroLab Inc., Montreal, QC, Canada, 3StatSciences Inc., Notre-Dame-de-l’Île-Perrot, QC, Canada, 4ArthroLab Inc., Montreal, QC, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster I: Clinical Trials and Interventions
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: A major challenge regarding intraarticular hyaluronic acid (IAHA) treatment in knee osteoarthritis (OA) is identifying patients who will benefit most. This study aimed to identify determinants associated with response level to IAHA treatment for symptomatic knee OA.

Methods: Data were from the Osteoarthritis Initiative (OAI) database. Subjects were selected based on the following question: “During the past 6 months, have you had an injection of HA in one or both knees for treatment of arthritis?” Included were subjects with radiographic OA who received a single treatment in one or both knees, and with data on demographics and WOMAC scores at visits before (T0) and after (T1; within 6 months) treatment. Data from the WOMAC pain scores were analyzed for demographic, clinical, and imaging (X-ray; Kellgren-Lawrence [KL] and joint space width [JSW], and MRI; cartilage volume [CV], bone marrow lesions [BML], and synovial fluid effusion size) at T0 and change (T1-T0) over time. Subjects with WOMAC >0 at T0 were included and subdivided based on WOMAC pain score tertile (first=lower pain). Analyses were also done on “responders” (improvement in pain score ≥20%) and “non-responders” (unchanged or worsening of pain score).

Results: Participants (n=310) received a total of 404 treatments (one/knee). WOMAC pain scores at T0 showed in the first and second vs. the third tertile, lower WOMAC score, BMI and KL grade, and greater JSW (p≤0.010), and in the first vs. the third tertile, significantly greater CV and effusion size (p≤0.033). Participants with decrease in pain score ≥20% were greater in the third tertile (p=0.001). Other WOMAC scores (function, stiffness, total) yielded similar results. These indicate a more severe disease in the third tertile. Analyses on participants in the third tertile, pain score ≥28 (greatest probability of improvement in pain with IAHA treatment), showed that responders vs. non-responders were usually younger (p=0.014), with greater medial compartment CV (p=0.046) and a trend
toward lower BML score and greater JSW. In this group, differences between responders and non-responders in all WOMAC score changes were significant (p<0.001). The majority of responders had a reduction in WOMAC scores (except stiffness) of about 40%, while non-responders showed worsening of symptoms. The use of concomitant arthritis medication was similar in both groups.

**Conclusion: This study has successfully allowed the identification of new reliable predictive factors that can identify patients who could best benefit from IAHA treatment. Patients with moderate to severe symptoms, younger, and with greater medial compartment CV are the most likely to respond to treatment with the greatest level of improvement. These predictive factors can potentially be implemented in daily clinical practice and will be a useful guide for physicians.**

**Disclosure:** J. P. Pelletier, Sanofi Canada, 5; J. P. Raynauld, Sanofi Canada, 5; F. Abram, ArthroLab, 3; M. Dorais, ArthroLab, 5; P. Delorme, ArthroLab Inc., 3; J. Martel-Pelletier, Sanofi Canada, 5.


**Abstract Number:** 1198

**Intra-Articular Hyaluronic Acid Delay to Total Knee Arthroplasty By Number of Injection Courses Received: Analysis of an Administrative Database**

Andrew Concoff1, Faizan Niazi2, Peter Shaw2 and Jeffrey Rosen3, 1Rheumatology, St. Jude Medical Center, Fullerton, CA, 2Ferring Pharmaceuticals Inc., Parsippany, NJ, 3Department of Orthopaedics & Rehabilitation, New York Presbyterian Queens; Department of Clinical Orthopaedic Surgery, Weill Medical College of Cornell University, New York, NY

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Monday, November 6, 2017
**Session Title:** Osteoarthritis – Clinical Aspects Poster I: Clinical Trials and Interventions
**Session Type:** ACR Poster Session B
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Total knee arthroplasty (TKA) is the standard surgical treatment for patients with osteoarthritis (OA) that no longer experience symptom relief from conservative or pharmacologic treatments. Intra-articular hyaluronic acid (IA-HA) is a common treatment option for mild to moderate knee OA that provides relief for patients who do not respond to conservative treatment and are not ready for TKA. The primary objective of this study is to determine if there is a correlation between receiving IA-HA injections and a delay to TKA in patients with knee OA compared to patients not receiving IA-HA, and if more courses of IA-HA injections relates to a longer delay to TKA.

**Methods:** This was a retrospective analysis of the Blue Cross/ Blue Shield (BCBS) claims database from October 1st, 2010 through September 30th, 2015. The primary outcome was time to TKA, which was defined as the time from treatment to the time TKA. Kaplan-Meier survival analysis was conducted to determine the TKA-free survival of patients who received IA-HA injections stratified by the number of injection courses received versus those who did not receive any IA-HA injections. A Cox proportional hazards regression analysis was also conducted to compare hazards ratios between the non IA-HA treated group and the IA-HA injection subgroups.

**Results:** A total of 744,734 patients were included in the analysis. Of these, 181,631 received at least one IA-HA injection, while 563,103 did not receive an IA-HA injection. A delay to TKA compared to the non IA-HA treated group was generally observed within the first year after IA-HA treatment for patients treated with 1 injection course, while patients treated with multiple courses demonstrated an incremental increase in delay to TKA with more injections (Figure 1). The model demonstrated a gradual decrease in hazard ratio (HR) with each subsequent course of IA-HA injection in comparison to the no IA-HA injection group, suggesting that the risk of TKA is reduced with subsequent IA-HA courses. The hazard ratio for a single course of injections was 0.85 (95% CI 0.84 - 0.86). The HR for TKA was smallest in the 5 or more injection courses group (HR 0.27, 95% CI 0.25 to 0.28).

**Conclusion:** These results demonstrate that within a large cohort of knee OA patients, individuals who received multiple courses of HA injections had a progressively greater delay to TKA compared to patients who did not receive HA treatment. The results demonstrated that with a greater number of injection courses received over time, there may be a relationship to a longer delay in TKA. Based on these results, multiple, repeat courses of IA-HA injection may be beneficial in substantially delaying TKA in knee OA patients.

**Figure 1: Survival Analysis**
Costs Associated with Osteoarthritis Care Using Intra-Articular Hyaluronic Acid: Analysis of an Administrative Database

Andrew Concoff¹, Faizan Niazi², Peter Shaw² and Jeffrey Rosen³, ¹Rheumatology, St. Jude Medical Center, Fullerton, CA, ²Ferring Pharmaceuticals Inc., Parsippany, NJ, ³Department of Orthopaedics & Rehabilitation, New York Presbyterian Queens; Department of Clinical Orthopaedic Surgery, Weill Medical College of Cornell University, New York, NY, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster I: Clinical Trials and Interventions
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Many treatment options are available for the management of knee osteoarthritis (OA). The need for non-operative management is motivated by the large costs associated with the total knee arthroplasty (TKA) procedure. Intra-articular hyaluronic acid (IA-HA) is a non-operative treatment for knee OA that provides significant pain relief for patients with mild to moderate knee OA. The purpose of this study is to assess the annual insurance claim costs of patients who have undergone IA-HA treatment for knee OA versus those who did not, to determine if IA-HA ultimately results in a lower total annual cost of healthcare for knee OA patients.

Methods: This was a retrospective analysis of the Blue Cross/ Blue Shield (BCBS) claims database from October 1st, 2010 through September 30th, 2015. The primary outcome was the median annual OA related cost of healthcare for patients who received IA-HA vs those who did not for treatment of their knee OA. Additionally, annual costs for patients who have progressed to TKA will be compared between people who have received IA-HA and those who did not receive IA-HA prior to their TKA. Annual cost data specific to professional and facility claims between the two groups are also summarized. Due to the large sample size, comparisons between
healthcare costs were conducted using Mann-Whitney U test. The large sample size has eliminated the need to report p-values, as interpretability is minimal.

**Results:** A total of 744,734 patients were included in the analysis. Of these, 181,631 received IA-HA injections, while 563,103 did not receive an IA-HA injection. In all patients who received TKA, annual costs separated by professional and facility claims are included within Table 1. The analysis demonstrated that the annualized median healthcare costs of patients treated with IA-HA who progressed to TKA was $871.31 (IQR $3.82), while the annualized median healthcare costs of patients who did not receive IA-HA was $2697.28 (IQR $8.25). In all patients, the annualized costs over the course of the study timeframe was $22.20 (IQR $0- $71.52) for patients who received HA, and $21.12 (IQR $0 - $225.88) for patients who did not receive HA.

**Conclusion:** This database analysis concludes that from the initiation of treatment for knee OA until TKA, patients who receive IA-HA have a lower annual median healthcare cost than knee OA patients who do not receive IA-HA. In particular, for individuals who eventually progressed to TKA, receiving IA-HA prior to their TKA resulted in significantly lower annual healthcare costs than those who did not receive IA-HA as a treatment.

Table 1: Total Annual Costs for Included TKA Patients

<table>
<thead>
<tr>
<th></th>
<th>IA-HA Group</th>
<th>Non IA-HA Group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Annual Professional Costs (Median, IQR)</strong></td>
<td>$15.03 (2.64)</td>
<td>$32.14 (6.30)</td>
</tr>
<tr>
<td><strong>Annual Facility Costs (Median, IQR)</strong></td>
<td>$862.64 (3.82)</td>
<td>$2724.39 (8.17)</td>
</tr>
</tbody>
</table>


Abstract Number: 1200

**Updating the Knee Osteoarthritis Intra-Articular Corticosteroid Meta-Analysis with Two Large Trials of Extended-Release Triamcinolone Acetonide (FX006) Versus Placebo**

Philip G. Conaghan¹, Francis Berenbaum², Virginia B. Kraus³, James Johnson⁴ and Scott Kelley⁵, ¹Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom, ²Pierre & Marie Curie University, Saint-Antoine Hospital, Paris, France, ³Duke Molecular Physiology Institute, Duke University School of Medicine, Durham, NC, ⁴Summit Analytical, Denver, CO, ⁵Flexion Therapeutics, Inc., Burlington, MA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Osteoarthritis – Clinical Aspects Poster I: Clinical Trials and Interventions

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** A recent meta-analysis concluded that intra-articular corticosteroids (IACS) for knee osteoarthritis (OA) may be associated with moderate improvement in pain compared with control treatment.¹² Notably, evidence quality was graded “low” due in part to inclusion of many small trials and trial heterogeneity.¹² Only 3 trials were moderate to large in size (≥50 patients/arm), with a variety of control treatments and pain endpoints. Across those 3 trials, at 1–2 weeks, 4–6 weeks, and 3 months post-treatment, standardized mean difference (SMD) corresponded to numbers needed to treat (NNT) of 8, 15, and infinity (indicating that the benefit of treatment cannot be determined; Figure).² FX006 is an extended-release formulation of triamcinolone acetonide for IA injection. We updated the meta-analysis by including data from two large, randomized, placebo-controlled trials of FX006 in patients with knee OA and heuristically compared the analysis of FX006 to the moderate to large trials to help assess the clinical relevance of FX006.
Methods: In studies FX006-2014-006 (NCT02116972) and FX006-2014-008 (NCT02357459), knee OA patients (Kellgren-Lawrence Grade 2 or 3; Average Daily Pain (ADP)-intensity ≥5) received a single IA injection of FX006 40 mg (N=104 and N=161, respectively) or saline-placebo (N=104 and N=163, respectively). ADP was collected for 24 weeks post-injection. SMD (95% CI) was computed for ADP-intensity at 2 weeks, 6 weeks, and 3 months post-treatment using least-squares mean (LSM) difference for FX006 from saline-placebo derived from each trial. Weighted-average SMD (95% CI) for FX006 and corresponding NNT for FX006 vs saline-placebo were determined and compared to NNTs reported for IACS.1,2

Results: FX006 yielded a weighted average SMD (95% CI) of −0.51 (−0.72, −0.31), −0.56 (−0.74, −0.36), and −0.34 (−0.52, −0.14) at 2 weeks, 6 weeks, and 3 months post-treatment, respectively, corresponding to a NNT (95% CI) of 4 (1 to 7), 4 (1 to 6), and 10 (7 to 13) at the corresponding time points (Figure). The magnitude of the FX006 effect is favorable compared with that determined for IACS, with a lower NNT (pooled estimate): 4 vs 8 (1–2 weeks), 4 vs 15 (4–6 weeks), and 10 vs infinity (3 months).

Conclusion: The two large FX006 studies in the expanded analysis demonstrated effective analgesia through 3 months with reduced NNT compared with traditional IACS. Limitations of the heuristic comparison include small sample sizes, trial heterogeneity, non-placebo controls, and other factors among the comparator trials.


Figure. Knee pain in osteoarthritis: meta-analysis of total experimental trials with NNT estimates and comparison to moderate to large trials (at least 50 subjects per arm) of IACS.
Reducing Heterogeneity in OA Clinical Trials: Data from a Phase 2 Study of SM04690, a Novel, Intra-Articular, Wnt Pathway Inhibitor in Knee Osteoarthritis

Philip G. Conaghan1, Anita DiFrancesco2, Christopher J. Swearingen2, Sarah Kennedy2, Ismail Simsek2, Jeymi Tambiah2 and Yusuf Yazici2, 1Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom, 2Samumed, LLC, San Diego, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster I: Clinical Trials and Interventions
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Kellgren-Lawrence [KL] radiographic grading is used to classify knee osteoarthritis (OA), but may not accurately reflect disease progression. Classifying subjects by baseline medial joint space width (mJSW) may be a more specific measure. This hypothesis was assessed in a post-hoc analysis of data from a phase 2, multicenter, 52-week, randomized controlled trial of SM04690, a small molecule Wnt pathway inhibitor in development as a potential disease modifying drug in knee OA.

Methods: In the trial, subjects with KL grade 2-3 knee OA were randomized to a single, 2 mL, intra-articular injection of 0.03 mg, 0.07 mg, 0.23 mg SM04690 or placebo (PBO) into their target (most painful) knee at Day 0. WOMAC Pain and Function were assessed at 0, 4, 13, 26, 39 and 52 weeks, with fixed location radiographic assessment of mJSW at Weeks 0, 26 and 52. Exploratory analysis of clinical outcomes in the intention to treat (ITT) population was conducted by analysis of covariance adjusted for baseline mJSW with multiple imputation. This post-hoc analysis examined a group with baseline mJSW of 2-4 mm in comparison to the full ITT population.

Results: 455 subjects (mean age 60.3 [±8.7] years, BMI 29.9 [±4.6] kg/m², 268 [58.9%] female, 293 [64.4%] KL Grade 3) were enrolled. Contralateral knee KL grade was equal or worse than target knee in 91% of ITT population. 258 subjects had baseline mJSWs of 2-4 mm. At week 52, in the placebo group, imputed mean mJSW change from baseline was -0.14 [SE 0.06] mm. In the ITT population, compared to placebo, imputed mean mJSW changes from baseline were positive for 0.03 mg and 0.07 mg SM04690 doses (Table, figure). In the post-hoc analysis of the smaller 2-4mm mJSW subgroup, heterogeneity was similar to ITT for all doses compared to PBO and for the 0.03 mg and 0.07 mg changes beyond measurement error (>0.13 mm)1 were observed. In addition, improvement in WOMAC Function compared to placebo was seen in the 0.07 mg SM04690 group at Week 52 within the mJSW subgroup (change compared to placebo -13.6, 95% CI (-25.5, -1.7), P=0.025).

Conclusion: Stricter inclusion criteria for mJSW provided a less heterogenous baseline group, reducing sample size by 42% without increasing standard error. When applied to this dataset, meaningful radiographic changes were demonstrated with 0.03 mg and 0.07 mg SM04690 groups compared to placebo. Future trials of structure modification in knee OA should consider specific mJSW inclusion criteria.

1Dupuis et al. OAC 2003
Disclosure: P. G. Conaghan, AbbVie, BMS, Eli Lilly, Novartis, Pfizer, Roche, 5, AbbVie, BMS, Eli Lilly, Novartis, Pfizer, Roche, 8; A. DiFrancesco, Samumed, LLC, 3, Samumed, LLC, 1; C. J. Swearingen, Samumed, LLC, 3, Samumed, LLC, 1; S. Kennedy, Samumed, LLC, 3, Samumed, LLC, 1; I. Simsek, Samumed, LLC, 3, Samumed, LLC, 1; J. Tambiah, Samumed, LLC, 3, Samumed, LLC, 1; Y. Yazici, Samumed, LLC, 3, Samumed, LLC, 1.


Abstract Number: 1202

**A Phase 2A, Placebo-Controlled, Randomized Study of ABT-981, an Anti-Interleukin-1Alpha and -1Beta Dual Variable Domain Immunoglobulin, to Treat Erosive Hand Osteoarthritis**

Margreet Kloppenburg¹, Charles Peterfy², Ida K. Haugen³, Féline Kroon⁴, Su Chen⁵, Li Wang⁵, Wei Liu⁵, Gwen Levy⁵, Roy Fleischmann⁵, Francis Berenbaum⁷, Désirée van der Heijde⁴, Jeroen K. Medema⁵ and Marc C. Levesque⁵, ¹Rheumatology, Leiden University Medical Center, Leiden, Netherlands, ²Spire Sciences, Inc., Boca Raton, FL, ³Diakonhjemmet Hospital, Oslo, Norway, ⁴Leiden University Medical Center, Leiden, Netherlands, ⁴Spire Sciences, Inc., Boca Raton, FL, ⁵Diakonhjemmet Hospital, Oslo, Norway, ⁶University of Texas Southwestern Medical Center at Dallas, Metroplex Clinical Research Center, Dallas, TX, ⁷University Pierre & Marie Curie and Inserm, DHU i2B, APHP, Hospital Saint-Antoine, Paris, France

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Osteoarthritis – Clinical Aspects Poster I: Clinical Trials and Interventions
Background/Purpose: No approved OA therapies reduce pain and slow joint damage. Mouse data suggested that inhibiting IL-1α and -1β with ABT-981 would reduce pain and slow structural progression in EHOA. This study tested the efficacy and safety of ABT-981 in EHOA.

Methods: Subjects with HOA per ACR criteria, ≥3 inflamed IP joints (tender, swollen, or both), hand pain ≥6 (scale 0–10), and ≥1 erosive IP joint on X-ray (Verbruggen-Veys) were randomized to placebo (PBO) or ABT-981 200 mg SC every 2 wk for 26 wk. The primary outcome was AUSCAN hand pain at 16 wk. Subjects had radiographs of both hands and MRI of the index hand at baseline and 26 wk. Both radiographs (Verbruggen-Veys, GUSS™, OARSI, Kellgren-Lawrence [KL]) and MRIs (HOAMRIS) were read by 2 independent central readers. A modified intent-to-treat population (ie, randomized and treated) was analyzed. Continuous efficacy endpoints were assessed using ANCOVA models with treatment and country as main factors and baseline measurements as covariates with LOCF imputation for the primary endpoint.

Results: Of 131 treated subjects (85% women; mean age 66 y), 61/67 randomized to PBO and 49/64 to ABT-981 completed the study; subject characteristics were well matched. AUSCAN pain was not significantly different vs PBO at wk 16 (P=.39; Table 1, Figure). X-ray data and other endpoints also were not statistically different vs PBO (Table 1). ABT-981 significantly decreased hsCRP, neutrophils, IL-1α, and IL-1β. Immunogenicity had no impact on ABT-981 pharmacokinetics. Besides injection site reactions and neutropenia, ABT-981 was well tolerated and safety was similar vs PBO, with no serious infections (Table 2).

Conclusion: Despite adequate pharmacodynamics results, targeting IL-1 may be ineffective in EHOA, as ABT-981 did not improve outcomes.

Table 1

<table>
<thead>
<tr>
<th>1º Endpoint</th>
<th>PBO Baseline, Mean±SD</th>
<th>ABT-981 Baseline, Mean±SD</th>
<th>LS Mean Change±SE at Wk 16</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUSCAN pain (0–50)</td>
<td>39±7</td>
<td>38±6</td>
<td>−10.7±2.4</td>
<td>−9.2±2.3</td>
</tr>
<tr>
<td>2º Endpoints</td>
<td>PBO Baseline, Mean±SD</td>
<td>ABT-981 Baseline, Mean±SD</td>
<td>LS Mean Change±SE at Wk 26</td>
<td></td>
</tr>
<tr>
<td>AUSCAN function (0–90)</td>
<td>69±15</td>
<td>71±13</td>
<td>−14.3±4.2</td>
<td>−16.4±4.0</td>
</tr>
<tr>
<td>Tender joints (0–30)</td>
<td>12±6</td>
<td>12±7</td>
<td>−4.7±1.2</td>
<td>−5.8±1.2</td>
</tr>
<tr>
<td>Swollen joints (0–30)</td>
<td>6±6</td>
<td>6±5</td>
<td>−1.8±0.8</td>
<td>−2.2±0.9</td>
</tr>
<tr>
<td>X-ray erosive joints (0–16)</td>
<td>2±2*</td>
<td>3±2*</td>
<td>0.26±0.08†</td>
<td>0.18±0.08†</td>
</tr>
<tr>
<td>KL score (0–80)</td>
<td>41±13</td>
<td>46±13</td>
<td>0.13±0.19</td>
<td>0.10±0.19</td>
</tr>
<tr>
<td>OARSI JSN (0–58)</td>
<td>28±10</td>
<td>32±9</td>
<td>0.14±0.19</td>
<td>0.03±0.19</td>
</tr>
<tr>
<td>OARSI osteophytes (0–58)</td>
<td>23±11</td>
<td>26±10</td>
<td>0.25±0.15</td>
<td>0.14±0.16</td>
</tr>
<tr>
<td>HOAMRIS synovitis (sum score; 0–52.5)</td>
<td>11±4</td>
<td>10±4</td>
<td>0.92±0.48</td>
<td>0.85±0.51</td>
</tr>
<tr>
<td>HOAMRIS erosive damage (sum score; 0–105)</td>
<td>18±9</td>
<td>17±10</td>
<td>0.26±0.64</td>
<td>0.10±0.67</td>
</tr>
<tr>
<td>HOAMRIS BML (sum score, 0–105)</td>
<td>7±5</td>
<td>5±4</td>
<td>0.11±0.64</td>
<td>0.44±0.66</td>
</tr>
</tbody>
</table>

*Verbruggen-Veys, erosive phase (E) + erosive with remodeling (E/R) or †new E or E/R or R.
Table 2

<table>
<thead>
<tr>
<th></th>
<th>PBO (n=67)</th>
<th>ABT-981 (n=64)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE/serious AE, %</td>
<td>88/3</td>
<td>91/3</td>
</tr>
<tr>
<td>Death, %</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Infection/serious infection, %</td>
<td>51/0</td>
<td>41/0</td>
</tr>
<tr>
<td>Injection site reaction, %</td>
<td>16</td>
<td>36</td>
</tr>
<tr>
<td>Neutropenia by NCI CTCAE grade, n</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G2 (1000 to &lt;1500/mm$^3$)</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>G3 (500 to &lt;1000/mm$^3$)</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>G4 (&lt;500/mm$^3$)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Disclosure: M. Kloppenburg, Pfizer, 2, AbbVie, GlaxoSmithKline, Merck, Levicept, 5; C. Peterfy, Spire Sciences, Inc, 1, Spire Sciences, Inc, 3, Amgen, 8; I. K. Haugen, Abbvie, 5; F. Kroon, None; S. Chen, Abbvie, 1, Abbvie, 3; L. Wang, AbbVie Inc., 1, AbbVie Inc., 3; W. Liu, AbbVie Inc., 3, AbbVie Inc., 1; G. Levy, AbbVie Inc., 1, AbbVie Inc., 3; R. Fleischmann, AbbVie Inc., 2, AbbVie Inc., 5; F. Berenbaum, AbbVie, Pfizer, Regeneron, 5; D. van der Heijde, AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, UCB, 5, Director of Imaging Rheumatology bv., 3; J. K. Medema, AbbVie Inc., 1, AbbVie Inc., 3; M. C. Levesque, AbbVie Inc., 1, AbbVie Inc., 3.


Abstract Number: 1203

Differences in Serum Protein Biomarkers between Combined Glucosamine and Chondroitin Versus Celecoxib Treatment in a Randomized, Double-Blind Trial in Osteoarthritis Patients

Sandi L Navarro¹, Marta Herrero², Helena Martinez², Jon Ladd¹, Yuzheng Zhang¹, Edward Lo¹, David Shelley¹, Timothy W Randolph¹, Yvonne Schwarz¹, Johanna W Lampe¹ and Paul D Lampe¹, ¹Public Health Sciences, Fred Hutchinson Cancer Research Center, Seattle, WA, ²Clinical R&D Area, Bioiberica, SAU, Barcelona, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster I: Clinical Trials and Interventions
Session Type: ACR Poster Session B
Background/Purpose: Non-steroidal anti-inflammatory drugs, e.g., celecoxib, are commonly used for inflammatory conditions, including osteoarthritis (OA), but are associated with adverse effects. Combined glucosamine hydrochloride plus chondroitin sulfate (GH+CS) is commonly used for joint pain and has no known adverse side effects. Evidence from in vitro, animal and human studies suggests that GH and CS have anti-inflammatory activity, among other mechanisms of action.

Methods: In this study, we evaluated a panel of 20 serum proteins involved in inflammation and other metabolic signaling pathways after treatment with pharmaceutical grade 1500 mg GH + 1200 mg CS daily (n=96) versus 200 mg celecoxib once a day (n=93) in a 6-month randomized, parallel, double-blind trial of knee OA patients. All patients had Kellgren and Lawrence grades 2-3 knee OA and moderate-to-severe pain as defined by Western Ontario and McMaster osteoarthritis index (WOMAC) score ≥ 301; on a 0-500 scale. We used linear mixed models adjusted for age, sex, body mass index, baseline serum protein values, and rescue medicine use to assess the intervention effects of each treatment arm separately and between treatments. Benjamini-Hochberg FDR (q<0.05) was used to control for multiple testing.

Results: When evaluating treatments separately, all serum proteins except WNT16 were lower after treatment with GH+CS, while about half of the proteins increased after celecoxib. IL-6 was statistically significantly reduced (by 9%, P=0.001) after GH+CS, and satisfied the FDR threshold of q<0.05. There were statistically significant increases for CCL20, CSF3, and WNT16 after celecoxib (by 7%, 9% and 9%, respectively, P<0.05), but these proteins were no longer statistically significant after controlling for multiple testing. There were no statistically significant differences in any proteins when comparing serum protein concentrations at end of treatment between GH+CS and celecoxib.

Conclusion: The results of this study demonstrate that GH+CS reduces IL-6, an inflammatory cytokine, but is otherwise comparable to celecoxib with regard to effects on other protein biomarkers.

Trial registration number: NCT01425853.

Table 1. Protein biomarker effect sizes after 6 month treatment with combined glucosamine and chondroitin (GH+CS) and celecoxib

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>GH+CS (n=96)</th>
<th>Celecoxib (n=93)</th>
<th>GH+CS versus Celecoxib (n=189)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Effect size</td>
<td>Effect size</td>
<td>Effect size</td>
</tr>
<tr>
<td></td>
<td>(unadjusted)</td>
<td>(adjusted)</td>
<td>(unadjusted)</td>
</tr>
<tr>
<td>C1orf38</td>
<td>-0.08</td>
<td>-0.03</td>
<td>0.55</td>
</tr>
<tr>
<td></td>
<td>0.55</td>
<td>-0.02</td>
<td>0.83</td>
</tr>
<tr>
<td>CCL20</td>
<td>-0.04</td>
<td>-0.02</td>
<td>0.63</td>
</tr>
<tr>
<td></td>
<td>-0.02</td>
<td>0.63</td>
<td>0.07</td>
</tr>
<tr>
<td>CEACAM1</td>
<td>-0.11</td>
<td>-0.03</td>
<td>0.56</td>
</tr>
<tr>
<td></td>
<td>0.56</td>
<td>-0.03</td>
<td>0.73</td>
</tr>
<tr>
<td>CRP</td>
<td>-0.12</td>
<td>-0.04</td>
<td>0.34</td>
</tr>
<tr>
<td></td>
<td>-0.04</td>
<td>0.34</td>
<td>0.74</td>
</tr>
<tr>
<td>CSF3</td>
<td>-0.15</td>
<td>-0.06</td>
<td>0.16</td>
</tr>
<tr>
<td></td>
<td>-0.06</td>
<td>0.16</td>
<td>0.09</td>
</tr>
<tr>
<td>CXCL12</td>
<td>0.06</td>
<td>0.01</td>
<td>0.59</td>
</tr>
<tr>
<td></td>
<td>0.01</td>
<td>0.59</td>
<td>0.44</td>
</tr>
<tr>
<td>HBEGF</td>
<td>-0.15</td>
<td>-0.08</td>
<td>0.24</td>
</tr>
<tr>
<td></td>
<td>-0.08</td>
<td>0.24</td>
<td>0.71</td>
</tr>
<tr>
<td>IL13</td>
<td>-0.04</td>
<td>-0.01</td>
<td>0.85</td>
</tr>
<tr>
<td></td>
<td>-0.01</td>
<td>0.85</td>
<td>0.86</td>
</tr>
<tr>
<td>IL6</td>
<td>-0.24</td>
<td>-0.09</td>
<td>0.01*</td>
</tr>
<tr>
<td></td>
<td>-0.09</td>
<td>0.01*</td>
<td>0.64</td>
</tr>
<tr>
<td>CCSP-1</td>
<td>-0.04</td>
<td>-0.02</td>
<td>0.70</td>
</tr>
<tr>
<td></td>
<td>-0.02</td>
<td>0.70</td>
<td>0.65</td>
</tr>
<tr>
<td>ITGA5</td>
<td>-0.05</td>
<td>-0.01</td>
<td>0.80</td>
</tr>
<tr>
<td></td>
<td>-0.01</td>
<td>0.80</td>
<td>0.70</td>
</tr>
<tr>
<td>MARVELD2</td>
<td>-0.08</td>
<td>-0.02</td>
<td>0.49</td>
</tr>
<tr>
<td></td>
<td>-0.02</td>
<td>0.49</td>
<td>0.76</td>
</tr>
<tr>
<td>MUC3B3</td>
<td>-0.19</td>
<td>-0.08</td>
<td>0.07</td>
</tr>
<tr>
<td></td>
<td>-0.08</td>
<td>0.07</td>
<td>0.99</td>
</tr>
<tr>
<td>NCKIPSD</td>
<td>-0.16</td>
<td>-0.03</td>
<td>0.38</td>
</tr>
<tr>
<td></td>
<td>-0.03</td>
<td>0.38</td>
<td>0.85</td>
</tr>
<tr>
<td>NPR3</td>
<td>-0.12</td>
<td>-0.05</td>
<td>0.22</td>
</tr>
<tr>
<td></td>
<td>-0.05</td>
<td>0.22</td>
<td>0.85</td>
</tr>
<tr>
<td>SFRS12</td>
<td>-0.13</td>
<td>-0.08</td>
<td>0.20</td>
</tr>
<tr>
<td></td>
<td>-0.08</td>
<td>0.20</td>
<td>0.17</td>
</tr>
<tr>
<td>SPP1/Osteopontin</td>
<td>-0.10</td>
<td>-0.04</td>
<td>0.31</td>
</tr>
<tr>
<td></td>
<td>-0.04</td>
<td>0.31</td>
<td>0.77</td>
</tr>
<tr>
<td>THBS4</td>
<td>-0.10</td>
<td>-0.06</td>
<td>0.33</td>
</tr>
<tr>
<td></td>
<td>-0.06</td>
<td>0.33</td>
<td>0.95</td>
</tr>
<tr>
<td>TNFRSF17</td>
<td>-0.16</td>
<td>-0.07</td>
<td>0.09</td>
</tr>
<tr>
<td></td>
<td>-0.07</td>
<td>0.09</td>
<td>0.72</td>
</tr>
<tr>
<td>TSG101</td>
<td>0.14</td>
<td>0.05</td>
<td>0.31</td>
</tr>
<tr>
<td></td>
<td>0.05</td>
<td>0.31</td>
<td>0.10</td>
</tr>
</tbody>
</table>

Values represent effect sizes in biomarker values pre-to-post intervention from: 1 paired t-tests (unadjusted models with the exception of hybridization and plate day); 2 linear mixed regression models adjusted for sex, age, BMI, baseline biomarker values, use of rescue medication, and hybridization and plate day.

3Values represent differences between GH+CS to celecoxib.
This biomarker failed to hybridize for a large proportion of samples and was excluded from analysis.

*Significant with Benjamini-Hochberg FDR $q<0.05$

Disclosure: S. L. Navarro, Bioiberica, SA, 9; M. Herrero, Bioiberica, SA, 3; H. Martinez, Bioiberica, SA, 3; J. Ladd, None; Y. Zhang, None; E. Lo, None; D. Shelley, None; T. W. Randolph, None; Y. Schwarz, None; J. W. Lampe, None; P. D. Lampe, None.


Abstract Number: 1204

**Radiographic Outcomes Were Associated with Pain and Function Responses: Post-Hoc Analysis of Results from a Phase 2 Study of a Small Molecule Wnt Pathway Inhibitor, SM04690, for Knee Osteoarthritis Treatment**

Yusuf Yazici¹, Timothy E. McAlindon², Allan Gibofsky³, Nancy E. Lane⁴, Nebojsa Skrepnik⁵, Eddie Armas⁶, Christopher J. Swearingen¹, Anita DiFrancesco¹, Jeymi Tambiah¹ and Marc Hochberg⁷, ¹Samumed, LLC, San Diego, CA, ²Division of Rheumatology, Tufts Medical Center, Boston, MA, ³Rheumatology, Weill Cornell Medicine, and Hospital for Special Surgery, New York, NY, ⁴Center for Musculoskeletal Health, University of California, Davis School of Medicine, Sacramento, CA, ⁵Tuscon Orthopedics Institute, Tuscon, AZ, ⁶Well Pharma Medical Research, Miami, FL, ⁷Head, Division of Rheumatology & Clinical Immunology; Vice Chair, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster I: Clinical Trials and Interventions
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

**Background/Purpose:** Knee osteoarthritis (OA) is characterized by pain, disability and joint deformity due to articular cartilage degradation and bone remodeling. Wnt signaling is involved in these processes. SM04690, a potential disease modifying knee OA drug (DMOAD) is a small molecule, intra-articular Wnt pathway inhibitor. A phase 2, multicenter, 52-week, single-dose, randomized, placebo-controlled (PBO) trial was conducted, and a post-hoc analysis evaluated associations of radiographic changes with changes in pain and function.

**Methods:** Subjects were randomized to receive a 2 mL injection of 0.03 mg, 0.07 mg, 0.23 mg SM04690 or PBO in target (most painful) knees at Week 0. Western Ontario and McMaster Universities Arthritis Index (WOMAC) Pain [0-50] and Function [0-170] were assessed at Weeks 0, 4, 13, 26, 39 and 52 and target knee radiographs taken at Weeks 0, 26 and 52. Joint space narrowing was assessed by analysis of covariance adjusted for baseline medial joint space width (mJSW) with multiple imputation. A unilateral symptomatic knee subgroup was pre-specified and investigator defined by patient history and examination. Logistic regression analysis estimated associations between mJSW changes and pain and function changes for subjects who achieved combined WOMAC Pain and Function improvement of >50% and >20 [scaled to 100] points.

**Results:** 455 subjects were enrolled (mean age 60.3 ±8.7 years, BMI 29.9 ±4.6 kg/m², 268 [58.9%] female, 293 [64.4%] Kellgren-Lawrence (KL) Grade 3, 164 [36.0%] unilateral symptomatic knee OA). Contralateral knee KL grade was equal / worse in 91% of intention to treat (ITT) population. Subjects who achieved a combined WOMAC Pain and Function improvement as defined above were: a) in ITT: 46 (48%) in 0.03 mg, 58 (55%) in 0.07 mg, 48 (53%) in 0.23 mg and 52 (55%) in PBO; and b) in unilateral symptomatic: 20 (56%) in 0.03 mg, 20 (63%) in 0.07 mg, 23 (64%) in 0.23 mg and 15 (47%) in PBO.

At Week 52, in ITT, PBO mean mJSW change was -0.14 [SE 0.06] mm. Mean mJSW changes in dose groups were 0.10 [SE 0.09] mm (0.03 mg), 0.06 [SE 0.09] mm (0.07 mg), and -0.02 [SE 0.09] mm (0.23 mg). In the unilateral symptomatic group, PBO mJSW change was -0.26 [SE 0.11] mm. Mean mJSW changes in dose groups were 0.24 [SE 0.16] mm (0.03 mg), 0.39 [SE 0.17] mm (0.07 mg, p=0.02), and -0.04 [SE 0.16] mm (0.23 mg) (Figure 1). Logistic regression for ITT showed area under the curve (AUC) > 0.7 was not achieved by any SM04690 dose. In the unilateral symptomatic group, 0.07 mg AUC = 0.78, indicating baseline-adjusted increase in mJSW was concordant with improvement in pain and function (Figure 2).
Conclusion: Radiographic outcomes from this study demonstrated treatment with SM04690 potentially maintained or increased mJSW compared to PBO. In unilateral symptomatic knee OA 0.07 mg subjects, changes in mJSW were predictive of WOMAC pain and function improvement. These data support potential of SM04690 as a DMOAD for treatment of knee OA.

Disclosure: Y. Yazici, Samumed, LLC, 3,Samumed, LLC, 1; T. E. McAlindon, None; A. Gibofsky, Pfizer Inc, 1,AbbVie, 1,Amgen, 1,Bristol-Myers Squibb, 1,Johnson & Johnson, 1,Regeneron, 1,AbbVie, 5,AbbVie, 8,Pfizer Inc, 5,Pfizer Inc, 8,Celgene, 8,Novartis Pharmaceutical Corporation, 8,Takeda, 5,Horizon, 5,Relburn, 5,Samumed, 5; N. E. Lane, LLP2A-Ale, 4; N. Skrepnik, Orthofix, 5,Regeneron, 5,Sanofi-Aventis Pharmaceutical, 5; E. Armas, Samumed, LLC, 2; C. J. Swearingen, Samumed, LLC, 3,Samumed, LLC, 1; A. DiFrancesco, Samumed, LLC, 3,Samumed, LLC, 1; J. Tambiah, Samumed, LLC, 3,Samumed, LLC, 1; M. Hochberg, Bioiberica SA, 5,Bristol Myers Squibb, 5,EMD Serono, 5,Galapagos, 5,IBSA SA, 5,Novartis Pharma AG, 5,Pfizer Inc, 5,Plexxikon, 5,Samumed LLC, 5,Theralogix LLC, 5,TissueGene, 5,NIH, 2,Theralogix LLC, 1.

Abstract Number: 1205

Effectiveness of Low-Dose Radiation Therapy on Symptoms in Knee Osteoarthritis: First Results of a Triple Blinded, Randomized Controlled Trial

E.A.M. Mahler1, M.J.M Minten1, M.M. Leseman-Hoogenboom2, P.M.P. Poortmans2, S.S. Boks3, J.W.J. Bijlsma4, F.H.J. van den Hoogen1,5, A.A. Den Broeder1,5 and C.H.M. van den Ende1,5, 1Rheumatology, Sint Maartenskliniek, Nijmegen, Netherlands, 2Radiation Therapy, Radboud university medical centre, Nijmegen, Netherlands, 3Radiology, Sint Maartenskliniek, Nijmegen,
Background/Purpose: Previous research in animal osteoarthritis (OA) has shown that low-dose radiation therapy (LD-RT) exerts anti-inflammatory effects, but a systematic review concluded that the evidence for its effectiveness in clinical practice is insufficient. Therefore, we wanted primarily to evaluate the effectiveness of LD-RT on symptoms in knee OA patients. In addition, the effects of LD-RT on inflammatory aspects were examined.

Methods: Knee OA patients, aged ≥ 50 years, fulfilling clinical ACR criteria, with a pain score ≥ 5 on a numeric rating scale (0-10), not responding to analgesics and exercise therapy, were included in this triple blinded, sham controlled, randomized clinical trial (RCT). The local Medical Research Ethics Committee approved the study design (study number 2014-275). Patients were randomly allocated 1:1 to the experimental (6x 1Gy LD-RT in two weeks) or sham (6x 0 Gy in two weeks) intervention. The primary outcome was the proportion of responders according to the OMERACT-OARSI responder criteria, 3 months post-intervention. Secondary outcomes were changes in inflammatory aspects assessed by both ultrasound (mean synovial effusion and synovial thickness measured at suprapatellar and both medial and lateral parapatellar recesses) and serum inflammatory markers (erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)). Chi squared tests or t-tests were used to compare differences in proportions and differences in changes to continuous variables, respectively.

Results: Preliminary results enclose the evaluation of 53 patients out of 55 participating patients; 51% was female, mean age 65 years (SD 9) and median body mass index 27 (IQR 24-31) kg/m². A total of 21 out of 53 patients (39.6%) met the OMERACT-OARSI responder criteria at 3 months post-intervention; of whom 10/25 (40%) were assigned to the intervention group and 11/28 (39%) to the sham group. A greater increase in mean synovial thickness in the intervention group than in the sham group was observed (difference intervention minus sham group: 0.07 mm, 95% CI -0.00-0.14). No differences between the two groups in any of the other secondary measures were observed.

Conclusion: Our preliminary results suggest that LD-RT is not effective in reducing symptoms in knee OA patients and has no impact on inflammatory aspects on the short-term. We therefore suggest not using LD-RT for symptom relief in knee OA.

Dutch Trial Register: NTR4574

Trial register number Central Committee on Research Involving Human Subjects (CCMO): NL48752.091.14
<table>
<thead>
<tr>
<th>Table 1 Baseline characteristics of 53 knee OA patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intervention group</strong> (n=25)</td>
</tr>
<tr>
<td><strong>Sociodemographic characteristics</strong></td>
</tr>
<tr>
<td>Age, years</td>
</tr>
<tr>
<td>Women, n (%)</td>
</tr>
<tr>
<td>Body mass index, kg/m², median (IQR)</td>
</tr>
<tr>
<td>Duration of symptoms ≤ 5 years</td>
</tr>
<tr>
<td>NRS pain (0-10)</td>
</tr>
<tr>
<td>Kellgren and Lawrence ≥ 1, n (%)</td>
</tr>
<tr>
<td><strong>Clinical parameters included in the primary outcome</strong></td>
</tr>
<tr>
<td>WOMAC pain (0-100)</td>
</tr>
<tr>
<td>WOMAC function (0-100)</td>
</tr>
<tr>
<td>NRS PGA (0-10)</td>
</tr>
<tr>
<td><strong>Inflammatory parameters included in the secondary outcomes</strong></td>
</tr>
<tr>
<td>Synovial thickness (mm)</td>
</tr>
<tr>
<td>Synovial effusion (mm)</td>
</tr>
<tr>
<td>ESR (mm/h), above upper limit, n (%)</td>
</tr>
<tr>
<td>CRP (mg/l), above upper limit, n (%)</td>
</tr>
</tbody>
</table>

Values are mean (SD) unless stated otherwise; IQR: interquartile range; NRS: numeric rating scale; PGA: patient global assessment; WOMAC pain, function and stiffness, Western Ontario and McMaster University Osteoarthritis Index scale; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein. Higher scores indicate more NRS pain, worse PGA, better scores for WOMAC pain and function.  
* : p < 0.02

<table>
<thead>
<tr>
<th>Table 2 Outcomes: changes (SD) per group and differences (95% CI) between groups between baseline and 3 months post-intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change (SD) in intervention group</td>
</tr>
<tr>
<td><strong>Clinical parameters included in the primary outcome</strong></td>
</tr>
<tr>
<td>WOMAC pain (range 0-100)</td>
</tr>
<tr>
<td>WOMAC function (range 0-100)</td>
</tr>
<tr>
<td>PGA (range 0-10)</td>
</tr>
<tr>
<td><strong>Inflammatory parameters included in the secondary outcomes</strong></td>
</tr>
<tr>
<td>Synovial thickness (mm)</td>
</tr>
<tr>
<td>Synovial effusion (mm)</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
</tr>
<tr>
<td>CRP (mg/l)</td>
</tr>
</tbody>
</table>

ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein. Positive changes indicate less pain, better function, worse PGA, increase in synovial thickness, effusion, ESR, CRP. Positive differences indicate less pain, better function, worse PGA, increase in synovial thickness, effusion, ESR, CRP of intervention group compared to sham group.  
* : p < 0.05

Disclosure: E. A. M. Mahler, None; M. J. M. Minten, None; M. M. Leseman-Hoogenboom, None; P. M. P. Poortmans, None; S. S. Boks, None; J. W. J. Bijlsma, None; F. H. J. van den Hoogen, None; A. A. Den Broeder, None; C. H. M. van den Ende, None.

Chondroitin Sulfate Reduces Pain and Improves Function in Knee Osteoarthritis Significantly Better Than Placebo, Independently of the Definition of Responders

J-Y Reginster, Bone Cartilage Unit, University of Liege, Liege, Belgium
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster I: Clinical Trials and Interventions
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: In addition to the assessment of the two co-primary endpoints – pain and function – regulatory agencies recommend the use of responder rates in percentages as complementary endpoints in order to demonstrate the robustness of the results and their clinical relevance at the level of the individual. Several clinically meaningful responder definitions were in fact proposed by the OMERACT initiative and the OARSI.

Methods: The proportion of responders was calculated among the subjects participating in the CONCEPT study, a double-blind, double-dummy Phase III clinical trial in which they received pharmaceutical grade Chondroitin Sulfate (CS) (800 mg/day, during 6 months) or placebo (PL). The following responder definitions were used: pain reduction of 30% vs baseline (moderate pain relief), pain reduction of 40% vs baseline (moderate-to-substantial pain relief), pain reduction of 50% vs baseline (substantial pain relief). Corresponding responder rates were calculated for the decrease in Lequesne index (LI). Moreover, the rates according to the OMERACT-OARSI responder criteria (scenario F) were calculated.

Results: 404 of the 604 patients recruited in 5 European countries for the CONCEPT study, suffering from knee osteoarthritis (OA) corresponding to the ACR criteria and belonging to the intention to treat population of the study, were included in the analyses. Of these, 199 were treated with CS and 205 with PL. The remaining 200 patients in the control group with active treatment (celecoxib 200 mg/day) were not considered. The responder rates for pain reduction were consistently higher for the CS group than for the PL group. They were 69% and 61% in the CS and the PL group, respectively, for a pain reduction of 30% vs baseline (p=0.098 between groups, chi-square test), 64% and 52% for a pain reduction of 40% vs baseline (p=0.014), and 58% and 40% for a pain reduction of 50% vs baseline (p<0.001). Comparable results were found for the LI. According to the OMERACT-OARSI criteria (scenario F), 66% and 55% of the patients in the CS and the PL group, respectively, were found to be responders after the 6-months of treatment (p=0.021 between groups, chi-square test).

Conclusion: Higher percentages of patients with knee osteoarthritis treated continuously for 6 months with 800 mg/day of pharmaceutical grade Chondroitin Sulfate achieved pre-defined levels of pain relief and/or functional improvement as compared to those receiving placebo. The differences in responder rates were both, statistically significant and clinically relevant.

Disclosure: J. Y. Reginster, IBSA, 2;


Clinical Relevance of Structural Measures in Knee Osteoarthritis: Baseline Values and Change from Baseline Discriminate Patients Subsequently Receiving Knee Replacement

C. Kent Kwoh¹, Hans Guehring², Michael J Hannon³ and Aida Aydemir⁴, ¹University of Arizona Arthritis Center, Tuscan, AZ, ²Merck KGaA, Darmstadt, Germany, ³Medicine, University of Pittsburgh, Pittsburgh, PA, ⁴EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA
First publication: September 18, 2017

SESSION INFORMATION
Background/Purpose: Structural measures of knee OA (KOA) progression include assessment of radiographic joint space width (JSW) and quantitative MRI (qMRI) measurement of cartilage thickness, both of which are endpoints in clinical trials of Disease-modifying Osteoarthritis Drugs (DMOADs). Objectives were 1) to determine if baseline value and 2 year change of medial JSW, and medial and total femorotibial compartment cartilage thickness (MFTC, FTC), are discriminative of the risk of knee replacement (KR); and 2) to evaluate whether these associations differ by sex or Kellgren-Lawrence grade (KLG).

Methods: Osteoarthritis Initiative (OAI) knees were selected based on eligibility criteria typical of a DMOAD trials for KOA: KLG of 2 or 3; medial minimum JSW (minJSW) ≥ 2.5 mm; knee pain at worst in the past 30 days from 4 to 9 on a 10-point scale, or 0 to 3 if pain medication was taken for joint pain; and availability of structural measures over two years. T-tests were used to look for differences in these measures by KR. Area under the receiver operating characteristic curve (AUC) was estimated for each measure using baseline and 2-year change values, in all patients as well as in male/female and in KLG=2/KLG=3 subgroups, to assess the ability of these measures to discriminate knees that went to future KR.

Results: The sample included 627 participants, of which 107 underwent KR, with a median of 6.7 years of follow-up. The 2-year reductions from baseline in all imaging measures were significantly greater in participants who later underwent KR compared with those who did not [Table 1]. Among all participants, the ability of JSW and cartilage thickness to discriminate knees that had future KR was modest (max AUC=0.62); the best discrimination using baseline or 2 year change values was achieved with FTC. Among subgroups, AUCs for 2 year change tended to be numerically higher for males and KLG=2, and pronounced more for fJSW and FTC [Table 2].

Conclusion: 2-year changes in all image measures were important in discriminating knees that will undergo KR. Sex and KLG should be considered as factors in discrimination ability.

<table>
<thead>
<tr>
<th>Imaging Measure</th>
<th>Mean (standard deviation)</th>
<th>Mean Difference (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HS=Yes</td>
<td>HS=No</td>
</tr>
<tr>
<td></td>
<td>N=107</td>
<td>N=520</td>
</tr>
<tr>
<td>Medial JSW [mm]</td>
<td>Baseline</td>
<td>4.39 (1.44)</td>
</tr>
<tr>
<td></td>
<td>2 year Change</td>
<td>-0.03 (0.94)</td>
</tr>
<tr>
<td>FTC [mm]</td>
<td>Baseline</td>
<td>5.25 (1.43)</td>
</tr>
<tr>
<td></td>
<td>2 year Change</td>
<td>-0.09 (0.69)</td>
</tr>
<tr>
<td>MFTC [mm]</td>
<td>Baseline</td>
<td>1.77 (0.32)</td>
</tr>
<tr>
<td></td>
<td>2 year Change</td>
<td>-0.05 (0.15)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Imaging Measure</th>
<th>Mean (standard deviation)</th>
<th>Mean Difference (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All</td>
<td>KLG=2</td>
</tr>
<tr>
<td></td>
<td>N=627</td>
<td>N=107</td>
</tr>
<tr>
<td>Medial JSW [mm]</td>
<td>Baseline</td>
<td>0.50 (0.43, 0.55)</td>
</tr>
<tr>
<td></td>
<td>2 year Change</td>
<td>0.07 (0.50, 0.64)*</td>
</tr>
<tr>
<td>FTC [mm]</td>
<td>Baseline</td>
<td>0.52 (0.46, 0.59)</td>
</tr>
<tr>
<td></td>
<td>2 year Change</td>
<td>0.01 (0.55, 0.60)</td>
</tr>
<tr>
<td>MFTC [mm]</td>
<td>Baseline</td>
<td>0.62 (0.46, 0.59)</td>
</tr>
<tr>
<td></td>
<td>2 year Change</td>
<td>0.00 (0.53, 0.66)</td>
</tr>
<tr>
<td>FTC [mm]</td>
<td>Baseline</td>
<td>0.62 (0.51, 0.66)</td>
</tr>
<tr>
<td></td>
<td>2 year Change</td>
<td>0.01 (0.55, 0.60)</td>
</tr>
</tbody>
</table>

AUC, area under the receiver operating characteristic curve; FTC, total femorotibial compartment cartilage thickness; JSW, joint space width; KLG, Kellgren-Lawrence grade; KR, knee replacement; MFTC, medial femorotibial compartment cartilage thickness.

*p-value<0.05 (Chi-Square test for AUC).
Abstract Number: 1208

Levels of Serum Biomarkers from a Two-Year Multicentre Trial Are Associated with Treatment Response on Knee Osteoarthritis Cartilage Loss As Assessed By MRI: An Exploratory Study

Johanne Martel-Pelletier1, Jean-Pierre Raynauld1, François Mineau1, François Abram2, Patrice Paiement3, Philippe Delorme3 and Jean-Pierre Pelletier1, 1Osteoarthritis Research Unit, University of Montreal Hospital Research Centre (CRCHUM), Montreal, QC, Canada, 2Medical Imaging Research & Development, ArthroLab Inc., Montreal, QC, Canada, 3ArthroLab Inc., Montreal, QC, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster I: Clinical Trials and Interventions
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: There is an obvious need to identify biomarkers that could predict patient response to an osteoarthritis (OA) treatment. This post hoc study explored in a 2-year randomized controlled trial in knee OA patients, the likelihood of some serum biomarkers to be associated with a better response to chondroitin sulfate at reducing cartilage volume loss.

Methods: Eight biomarkers were studied: hyaluronic acid (HA), C reactive protein (CRP), adipin, leptin, N-terminal propeptide of collagen IIα (PIIANP), C-terminal crosslinked telopeptide of type I collagen (CTX-1), matrix metalloproteinase-1 (MMP-1), and MMP-3. Patients were treated with chondroitin sulfate (1200 mg/day; n=57) or celecoxib (200 mg/day; n=62). Serum biomarkers were measured at baseline. The cartilage volume at baseline and its loss at 2 years was assessed by quantitative magnetic resonance imaging (MRI). Statistical analysis included ANCOVA.

Results: As data from the original MOSAIC trial showed no differences in the lateral compartment between the two treatment groups in cartilage volume and loss in any comparison, only the medial compartment and its subregions were studied. Stratification according to the median biomarker levels was used to discriminate treatment effect. In patients with levels of biomarkers of inflammation (HA, leptin and adipin) lower than the median, those treated with chondroitin sulfate demonstrated less cartilage volume loss in the medial compartment, condyle and plateau (p≤0.047). In contrast, chondroitin sulfate treated patients with higher levels of MMP-1 and MMP-3, biomarkers of cartilage catabolism, had less cartilage volume loss in the medial compartment, condyle and plateau (p≤0.050). Patients with higher levels of PIIANP and CTX-1, biomarkers related to collagen anabolism and bone catabolism, respectively, had reduced cartilage volume loss in the medial condyle (p≤0.026) in the chondroitin sulfate group.

Conclusion: This study provides important and novel information about the association of some serum biomarker levels with cartilage degradation, which could help to identify patients who are most likely to be responsive to a treatment. Moreover, data are suggestive of a potentially greater response to chondroitin sulfate treatment on cartilage volume loss in knee OA patients with low level of inflammation and/or greater level of cartilage catabolism.

Disclosure: J. Martel-Pelletier, Bioiberica, 5,ArthroLab, 9; J. P. Raynauld, ArthoLab, 5; F. Mineau, None; F. Abram, ArthroLab, 3; P. Paiement, ArthroLab, 3; P. Delorme, ArthroLab Inc., 3; J. P. Pelletier, Bioiberica, 5,ArthroLab, 9.


Abstract Number: 1209
Phospholipase A2 Group 5 Is a Potential Therapeutic Target for Osteoarthritis Treatment

Ming Liu¹, Andrew Furey², Weidong Zhang³, Sergei Likhodi², Edward Randell², Proton Rahman⁴ and Guangju Zhai², ¹Discipline of Genetics, Faculty of Medicine, Memorial University of Newfoundland, St. John's, NF, Canada, ²Memorial University of Newfoundland, St. John's, NF, Canada, ³Jilin University, Changchun, China, ⁴Rheumatology, St Claires Mercy Hospital, St Johns, NF, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster I: Clinical Trials and Interventions
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: We recently discovered that lysophosphatidylcholines (lysoPCs) to phosphatidylcholines (PCs) ratio was associated with knee osteoarthritis (OA), suggesting that the conversion of PCs to lysoPCs catalyzed by phospholipases A2 (PLA2) was over activated. The aim of the study was to examine the gene expression levels of multiple PLA2 enzymes in human cartilage and identify the specific one that is important in OA.

Methods: Human cartilage samples were collected from patients undergoing total hip/knee joint replacement surgery due to primary OA or hip fractures as controls. RNA was extracted from the cartilage tissues. mRNA levels of three PLA2 enzymes, namely PLA2IIa, IVa, and V, and three cytokines, namely IL-6, IL-1β, and TNF-α were measured by real-time quantitative PCR (qPCR). Expression levels in each sample were calculated as fold changes in relation to the calibrator using Livak method.

Results: A total of 33 OA cases (24 hip OA and 9 knee OA) and 21 healthy controls were included. We found that PLA2V expression level was substantially increased by 445% in OA-affected cartilage compared to OA-free cartilage (p=0.003), but not PLA2IIa and PLA2IVa (p>0.05). Similarly, the expression level of TNF-α was significantly increased by 193% in OA-affected cartilage compared to the OA-free cartilage (p=0.007), but not IL-6 and IL-1β. Further, the expression level of PLA2V was highly correlated with TNF-α expression with a correlation coefficient of 0.71 (p<0.0001).

Conclusion: Our data indicated that inflammatory process was involved in OA and resulted in substantial over expression of PLA2V and excessive conversion of PCs to lysoPCs, suggesting PLA2V could be a novel therapeutic target for OA.

Disclosure: M. Liu, None; A. Furey, None; W. Zhang, None; S. Likhodi, None; E. Randell, None; P. Rahman, Janssen Pharmaceutica Product, L.P., 8,Amgen, AbbVie, BMS, Celgene, Pfizer, Janssen, Wyeth, EliLiyi, Novartis, 8,Amgen, AbbVie, BMS, Celgene, Pfizer, Janssen, Wyeth, EliLiyi, Novartis, 5; G. Zhai, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/phospholipase-a2-group-5-is-a-potential-therapeutic-target-for-osteoarthritis-treatment

Abstract Number: 1210

Non-Responders to Total Joint Replacement Therapy in Osteoarthritis Patients and Novel Metabolic Markers

Guangju Zhai¹, Ming Liu², Quan Li¹, Andrew Furey¹, Weidong Zhang³, Sergei Likhodi¹, Edward Randell¹ and Proton Rahman⁴, ¹Memorial University of Newfoundland, St. John's, NF, Canada, ²Discipline of Genetics, Faculty of Medicine, Memorial University of Newfoundland, St. John's, NF, Canada, ³Jilin University, Changchun, China, ⁴Rheumatology, St Claires Mercy Hospital, St Johns, NF, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster I: Clinical Trials and Interventions
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM
**Background/Purpose:** Osteoarthritis (OA) is the most common form of arthritis, and is the major source of joint pain and disability. The aim of the study was to estimate the percentage of non-responders to total joint replacement therapy (TJR) in OA (hip and knee) patients and identify factors and biomarkers that associated with it.

**Methods:** TJR patients due to OA were recruited at the surgery and followed up for 4 years on average. The WOMAC pain and function subscales at pre- and post-surgery were used to assess the improvement of joint pain and function. Based on the minimal clinically important difference (MCID), participants were classified as non-responders if the change score of less than 7 points (of 20 points total) for WOMAC pain subscale from pre-surgery to post-surgery. For physical function, participants were non-responders if the change score was less than 22 points (of a total of 68) from pre-surgery to post-surgery. Metabolic profiling (186 targeted metabolites) was performed on plasma samples collected at baseline. Demographic and medical information was collected systematically using standardized questionnaires.

**Results:** A total of 242 TJR patients were included, 20% were hip replacements and 80% were knee replacements. 42% of them were males and 58% were females. Mean age was 65.6 ±7.4 years old. 16.5% of the study participants were classified as non-responders to TJR, as they failed to reach MCID for pain. A similar percentage for non-responders was noted for physical function. There was no difference between knee and hip replacements. About 63% of the non-responders as defined by pain score were also non-responders in physical function. No association was noted between the non-responders in pain and physical function and clinical epidemiological factors including age, sex, BMI, and comorbidities (cardiovascular disease, metabolic related disease, and cancers). However, four amino acids – histidine, sarcosine, phenylalaine, and serine levels were significantly associated with non-responders in physical function (all adjusted p values (FDR)<0.05). Phenylalanine level was also associated with non-responders in pain although the significance didn’t pass the multiple testing adjustments by FDR (unadjusted p=0.02).

**Conclusion:** Our data indicated that over 16% of OA patients did not reach MCID from TJR in either pain or physical function and non-responders to TJR were associated with higher levels of several amino acids. While further confirmation is needed, our findings have great potential in the clinical decision-making process when contemplating TJR for knee or hip OA.

**Disclosure:** G. Zhai, None; M. Liu, None; Q. Li, None; A. Furey, None; W. Zhang, None; S. Likhodi, None; E. Randell, None; P. Rahman, Janssen Pharmaceutical Product, L.P., 8,Amgen, AbbVie, BMS, Celgene, Pfizer, Janssen, Wyeth, EliLily, Novartis, 8,Amgen, AbbVie, BMS, Celgene, Pfizer, Janssen, Wyeth, EliLily, Novartis, 5.

**Biomarkers Predictive of Pain Improvement in Knee Osteoarthritis Subjects Treated with the Anti-IL-1α/β Dual Variable Domain Immunoglobulin ABT-981**

Sheng Feng1, Su Chen1, Li Wang1, Charles Peterfy2, Virginia B. Kraus3, Rajesh Kamath1, Lanju Zhang1, Yanping Luo1, Lu Cui1, Jeroen K. Medema1 and Marc C. Levesque1, 1AbbVie Inc., North Chicago, IL, 2Spire Sciences, Inc., Boca Raton, FL, 3Duke University School of Medicine, Durham, NC

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Osteoarthritis – Clinical Aspects Poster I: Clinical Trials and Interventions

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Development of disease-modifying drugs for OA has been challenging, partly due to lack of predictive biomarkers. Our primary objective was to identify baseline (BL) biomarkers predicting greater treatment effects on WOMAC pain among knee OA subjects in the ABT-981 ILLUSTRATE-K trial (NCT02087904).

**Methods:** Subjects (N=347) with Kellgren-Lawrence (KL) grade 2–3 knee OA, synovitis on MRI or ultrasound, and knee pain score 4–8 (range, 0–10) were randomized to placebo (PBO) or ABT-981 25, 100, or 200 mg subcutaneously every 2 wk for 50 wk. The primary endpoints were change from BL (CFB) in WOMAC pain at wk 16 and CFB in MRI synovitis at wk 26. Demographics, patient-reported outcomes (WOMAC, ICOAP, global assessment [PGA]), x-ray joint space width, and Whole Organ MRI Score (WORMS) were determined at BL. The Patient Rule Induction Method, Sequential Batting, and the Adaptive Index Model were used to identify BL predictive biomarkers and OA subsets with greater ABT-981 treatment effects. Continuous efficacy endpoints were assessed using
ANCOVA with treatment, age group, and KL grade as main factors and BL measurements as covariates with LOCF imputation for WOMAC pain.

**Results:** WORMS Global Total Osteophyte Score (GTOS), which semi-quantitatively summates osteophyte severity from 14 regions of the knee, identified a subset of subjects with a greater ABT-981 treatment effect vs PBO; the optimal GTOS cutoff for discriminating treatment effects was 14 (Figure 1). Among subjects with a GTOS ≥14, the PBO WOMAC pain response was markedly reduced and only marginally improved for ABT-981. At wk 16, among subjects with GTOS ≥14, the standardized mean difference (95% CI) of WOMAC pain for the ABT-981 100-mg dose group vs PBO was −0.62 (−0.16 to −1.09) vs −0.30 (0 to −0.61) for all subjects. Compared with the total study population, the 41% of subjects with GTOS ≥14 not only had a greater ABT-981 treatment effect vs PBO on WOMAC pain, but also other measures of OA symptoms (Table 1). BL systemic markers of synovitis (serum C1M and C3M) and potential markers of macrophage activation by IL-1 (serum alkaline phosphatase) were positively associated with greater ABT-981 treatment effects vs PBO but to a lesser extent than GTOS. Other data supported the robustness of the GTOS predictive marker (Table 2).

**Conclusion:** The GTOS biomarker predicted improvement of knee OA pain and other symptoms with ABT-981 treatment. We hypothesize that subjects with more severe osteophytes may have had more inflammation-dependent pain that was less responsive to PBO, suggesting that IL-1 inhibitors should be studied further as a treatment for knee OA symptoms in this subset of patients.

**Disclosure:** S. Feng, AbbVie Inc., 1, AbbVie Inc., 3; S. Chen, AbbVie Inc., 1, AbbVie Inc., 3; L. Wang, AbbVie Inc., 1, AbbVie Inc., 3; C. Peterfy, Spire Sciences, Inc. (which provides imaging services for clinical trials to multiple pharmaceutical companies), 3, Spire Sciences, Inc. (which provides imaging services for clinical trials to multiple pharmaceutical companies), 1; V. B. Kraus, AbbVie Inc., 5; R. Kamath, AbbVie Inc., 1, AbbVie Inc., 3; L. Zhang, AbbVie Inc., 1, AbbVie Inc., 3; Y. Luo, AbbVie Inc., 1, AbbVie Inc., 3; L. Cui, AbbVie Inc., 1, AbbVie Inc., 3; J. K. Medema, AbbVie Inc., 1, AbbVie Inc., 3; M. C. Levesque, AbbVie Inc., 1, AbbVie Inc., 3.
Relation of Incident Bisphosphonate Use to Bone Marrow Lesion Volume in Knee Osteoarthritis

Tuhina Neogi1, Jeffrey Duryea2, Na Lu1, Jingbo Niu1 and Yuqing Zhang1, 1Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA, 2Radiology, Brigham & Women's Hospital/ Harvard Medical School, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster I: Clinical Trials and Interventions
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Bone marrow lesions (BMLs) are important contributors to pain and progression of knee OA. There has been recent interest in bisphosphonates as a potential disease modifier through amelioration of BMLs; however, there is theoretical concern that long-term suppression of bone turnover may be detrimental to healing of BMLs. One randomized controlled trial demonstrated beneficial effects of intravenous zoledronic acid on BML volume at 6 months, though this effect was no longer statistically significant at 12 months. We sought to determine the effect of commonly prescribed oral bisphosphonates on BML volume over 12 months.

Methods: We identified women in the Osteoarthritis Initiative who newly initiated an oral bisphosphonate (alendronate or risedronate) and who had a MRI at the visit at which they reported initiating a bisphosphonate as well as the following clinic visit (i.e., 12 months later) after initiation. We excluded women who reported use of other bone-active agents, such as PTH, calcitonin, or raloxifene. We propensity-score matched (see Table for covariates) bisphosphonate initiators to women who did not initiate bisphosphonate use with greedy matching, and used multiple imputation to address missing covariate data. BML volume was assessed using the sagittal turbo spin echo fat-suppressed intermediate-weighted MR images (slice thickness 3mm). A validated semi-automated process was used to segment the subchondral OA-related BMLs in the distal femur and proximal tibia to determine the total volume of BMLs based upon the number of voxels (0.382 mm$^3$) within the outlined region of interest (intra- and inter-reader reliability: 0.96, 0.97, respectively). We evaluated the mean change in BML volume over 12 months among the bisphosphonate initiators compared with the non-initiators using multiple linear regression, as well as by proportion with changes in BMLs over 12 months.

Results: We identified 145 bisphosphonate initiators, who were well-matched to their comparators (mean age 65, mean BMI 26.2). A similar proportion of bisphosphonate initiators and non-initiators had BMLs at their index visit (51% vs. 47%, p=0.3). The proportion of subjects with decrease, increased, or unchanged BML volumes over time were similar in both groups, though there was a trend towards decreased BMLs in the bisphosphonate initiators (Table). However, mean change in total BML volume for the whole sample, regardless of presence of baseline BMLs, was not significantly different between the two groups (difference in mean change in total BML volume: 98.8mm$^3$, 95% CI -156.6 to +354.2, p=0.4).

Conclusion: In this ‘real-world’ setting of women starting bisphosphonates, we found no clear evidence of benefit or harm of oral bisphosphonate use over a 12-month period on BML volume. Longer term follow-up is likely necessary to better appreciate the effects of bisphosphonates on BMLs in knee OA.

| Table: Relation of incident bisphosphonate use to BML volume change over 12 months |
|---------------------------------|---------------------------------|----------------|
|                                 | Bisphosphonate Initiator (N=145) | Bisphosphonate non-initiator (N=145) | P-value |
| BML volume:                     |                                 |                               |         |
| Decreased                       | 28%                             | 22%                           | p=0.07  |
| Unchanged                       | 32%                             | 36%                           |         |
| Increased                       | 30%                             | 32%                           |         |

Propensity score was adjusted for baseline values of: age, race, BMI, minimum adult weight, marital status, education, income, employment, health insurance, blood pressure, SF-12, activity limitation, comorbidity score, renal disease, WOMAC function, knee pain, gait speed, physical activity, worst IL grade, inflammatory arthritis, prednisone use, total dietary intake, dietary calcium intake, calcium supplement use, vitamin D prescription or supplements, estrogen use, fractures, falls, ovariectomy/hysterectomy, smoker, alcohol use.
Prediction Model for the Two-Year Risk of Fracture Among Older US Women

Annette Adams, Akhila Balasubramanian, Hui Zhou, Robert Platt, Deborah Wenkert, Steven Jacobsen and Eric Johnson,


First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Current algorithms for identifying patients at high risk of fracture focus on long-term risk. We developed simple 10- and 3-predictor models and points-based risk scores to enable pragmatic identification of patients at near-term (12-24 months) risk of fracture. Physicians and patients could benefit from such models to ensure timely care.

Methods: This retrospective cohort study included women ≥50 years who had dual-energy x-ray absorptiometry (DXA) bone mineral density (BMD) data and were members of an integrated healthcare delivery system in the United States. Clinic location determined inclusion in the development vs. validation cohort. Using randomly selected outpatient visits (2008-2012) as index dates, we followed women up to 2 years for the occurrence of “any fracture” – closed fracture other than skull/face/fingers/toes. We adapted our previously validated 10- and 3-predictor models to predict 2-year fracture risks among the subgroup of women with recent BMD T-scores, using Cox regression. We used predictor coefficients from these models to develop risk score points.

Results: 68,589 women in the development cohort (mean±sd age 67.0±9.6 years, 1,816 fractures) and 58,812 women in the validation cohort (age 67.2±9.8 years, 1,440 fractures) had an overall 2-year fracture rate of 2.6% and 2.4%, respectively. We developed a 10-predictor model for “any fracture,” which included age, race/ethnicity, body mass index (BMI), BMD T-score, fracture in the prior year, fall risk, tobacco use, and use of antidepressant, narcotic, and glucocorticoid medications. This model discriminated risk effectively in both the development cohort (c-statistic = 0.75) and the external validation cohort (c-statistic = 0.76). Our reduced, 3-predictor model included age, recent fracture, and BMD T-score, and explained 88.4% of the variation in the 10-variable model. Discrimination was 0.72 in the development and 0.73 in the external validation cohorts. Calibration plots revealed excellent agreement between observed and predicted risks. A 2-year predicted risk ≥10% in the 3-predictor model accounted for 4% of patients and 20% of fractures in the total study population (Table 1). We also developed a points-based risk score for easy implementation of the model to identify patients at high near-term fracture risk (Table 2).

Conclusion: Our data suggest that models using as few as 3 variables can perform well in estimating near-term fracture risk. Our simple models can aid in identification of patients in greatest need of impactful interventions to quickly lower fracture risk.
Table 1. Agreement between observed (Kaplan-Meier) and predicted two-year fracture risks in external validation cohort, with the range of risk score points for the three-predictor model of all fractures.

<table>
<thead>
<tr>
<th>Predicted risk</th>
<th>Number of Patients</th>
<th>Number of any fracture (crude risk, %)</th>
<th>KM observed risk (%)</th>
<th>Mean ± SD predicted risk (%)</th>
<th>Median predicted risk (%) (q1-q3)</th>
<th>Range of risk score points</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 to 1.49%</td>
<td>12,830</td>
<td>86 (0.67)</td>
<td>0.66</td>
<td>0.9 ± 0.3</td>
<td>0.8 (0.7-1.2)</td>
<td>0 to 44</td>
</tr>
<tr>
<td>1.50 to 4.99%</td>
<td>37,280</td>
<td>716 (1.92)</td>
<td>1.79</td>
<td>2.4 ± 0.9</td>
<td>2.3 (1.6-2.9)</td>
<td>47 to 91</td>
</tr>
<tr>
<td>5.00 to 9.99%</td>
<td>6,403</td>
<td>359 (5.61)</td>
<td>5.51</td>
<td>6.8 ± 1.4</td>
<td>6.5 (5.8-7.8)</td>
<td>92 to 120</td>
</tr>
<tr>
<td>10.00 to 14.99%</td>
<td>1,480</td>
<td>151 (10.20)</td>
<td>10.27</td>
<td>11.9 ± 1.4</td>
<td>11.6 (10.6-12.9)</td>
<td>121 to 137</td>
</tr>
<tr>
<td>≥15.00%</td>
<td>819</td>
<td>128 (15.63)</td>
<td>17.12</td>
<td>22.3 ± 7.919.5</td>
<td>21.8 (16.7-25.0)</td>
<td>≥138</td>
</tr>
</tbody>
</table>

Table 2. Contribution of individual predictors to points-based risk score from the three-predictor model

<table>
<thead>
<tr>
<th>Age</th>
<th>Points</th>
<th>BMD T-score</th>
<th>Points</th>
<th>History of fracture</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 to 54</td>
<td>0</td>
<td>&gt;= -1.0</td>
<td>0</td>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>55 to 59</td>
<td>12</td>
<td>-2.5 to &lt; -1.0</td>
<td>29</td>
<td>Yes</td>
<td>40</td>
</tr>
<tr>
<td>60 to 64</td>
<td>19</td>
<td>-3.5 to &lt; -2.5</td>
<td>45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>65 to 69</td>
<td>15</td>
<td>-4.5 to &lt; -3.5</td>
<td>60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>70 to 74</td>
<td>25</td>
<td>&lt; -4.5</td>
<td>71</td>
<td></td>
<td></td>
</tr>
<tr>
<td>75 to 79</td>
<td>42</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>80 to 84</td>
<td>55</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Disclosure: A. Adams, Amgen Inc, 2,Merck Pharmaceuticals, 2,Otsuka, 2; A. Balasubramanian, Amgen, 3,Amgen, 1; H. Zhou, None; R. Platt, Pfizer Inc, 5,Eli Lilly and Company, 5,Amgen, 5,Searchlight Pharma, 5; D. Wenkert, Amgen, 1,Amgen, 5,Alexion Pharmaceuticals, Inc., 5,Amgen, 3; S. Jacobsen, None; E. Johnson, Amgen, 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/prediction-model-for-the-two-year-risk-of-fracture-among-older-us-women

Abstract Number: 1214

Fracture Incidence and Characteristics in Young Adults Age 18 to 49 Years: A Population-Based Study

Joshua N. Farr¹, L. Joseph Melton III¹, Sara J. Achenbach¹, Elizabeth J. Atkinson¹, Sundeep Khosla¹ and Shreyasee Amin², ¹Mayo Clinic, Rochester, MN, ²Rheumatology, Mayo Clinic, Rochester, MN

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: While fractures in both the elderly and pediatric populations have been extensively investigated, comparatively little attention has been given to the age-group in between. Thus, we determined incidence rates for all fractures in young adult residents from a defined geographic population (age range, 18 to 49 years), in 2009-11, and compared the distribution of fracture sites and causes in this young adult cohort with those age ≥50 years old from the same population.
Methods: Using a unique medical records linkage system that allows access to all (inpatient and outpatient) community medical records for the population under study, we identified all fractures that occurred among young adult residents during the 3-year period. All medical records were reviewed by trained nurse abstractors to validate all fractures identified and to determine their antecedent cause (pathological process [e.g., metastatic malignancy], severe trauma [e.g., motor vehicle accidents, falls from greater than standing height] and those due to no more than moderate trauma [by convention, equivalent to a fall from standing height or less]). Comparable results that we previously reported in residents age ≥50 years old (JBMR 2014) were used for comparisons.

Results: During 2009-2011, 2,482 residents age 18-49 years experienced one or more fractures. There were 1,730 fractures among 1,447 men compared to 1,164 among 1,035 women, and the age-adjusted incidence of all fractures was 66% greater among the men (1,882 [95% CI, 1,793-1,971] vs. 1,135 [95% CI, 1,069-1,201] per 100,000 person-years; p<0.001). Of all fractures, 80% resulted from severe trauma compared to 33% in residents age ≥50 years who sustained a fracture in 2009-11. Younger residents (ages 18-49 years) had a greater proportion of fractures than older residents (age ≥50 years) of the hands and feet (40% vs. 18%) with relatively few fractures observed at traditional osteoporotic fracture sites (wrist, shoulder, spine or hip) (14% vs. 43%). Vertebral fractures were still more likely to be due to moderate trauma than at other sites in younger residents, especially in women (57% vs. 32% in men, 26% vs. 72% in women, for severe vs. moderate trauma vertebral fractures, respectively).

Conclusion: In conclusion, whereas elderly populations often fracture from no more than moderate trauma, young adults, and more commonly men, suffer fractures primarily at non-osteoporotic sites due to more significant trauma. The main exception is vertebral fractures in young women, which are still more likely to be secondary to moderate trauma.

Disclosure: J. N. Farr, None; L. J. Melton III, None; S. J. Achenbach, None; E. J. Atkinson, None; S. Khosla, None; S. Amin, None.

Abstract Number: 1215

Chest Radiography As a Screening Tool to Detect Fragile Spine Fractures

Yasuhiro Suyama1, Mitsumasa Kishimoto2, Taiki Nozaki3, Tetsuhiko Okabe4 and Masato Okada2, 1Rheumatology, JR Tokyo General Hospital, Tokyo, Japan, 2Immuno-Rheumatology Center, St. Luke's International Hospital, Tokyo, Japan, 3Radiology, St. Luke’s International Hospital, Tokyo, Japan, 4Radiology, Yokohama City University, Yokohama, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Osteoporosis screening is essential in the management of rheumatoid arthritis, and evaluation of fragile spine fractures is one of the recommended examinations. Digital chest radiography is widely available, and the spine can be evaluated by focusing on its lateral view. Therefore, we assessed the usefulness of lateral-view chest radiography in the screening of fragile spine fractures.

Methods: We retrospectively evaluated patients who newly met the 2010 American College of Rheumatology/European League Against Rheumatism rheumatoid arthritis criteria and underwent osteoporosis screening, including chest radiography, spine radiography, FRAX, and dual-energy X-ray absorptiometry within a 1-month interval, from April 2016 to March 2017. The incidental identification of vertebral fracture was evaluated using a semiquantitative approach by two board-certified musculoskeletal radiologist. Radiography was used as the gold standard by both readers to detect vertebral fractures in the thoracic and lumbar spines. We calculated the sensitivity and specificity of chest radiography and compared these with those of the gold standard performed by each radiologist. In addition, kappa statistics between the radiologists were calculated reproducitively.

Results: We identified 35 eligible patients (Table 1). Both readers agreed that at least one moderate or severe thoracic fracture was present in 6 patients (17.1%) on spine radiography. The kappa statistics between the radiologists who detected fragile spine fractures using lateral-view chest radiography was 0.982 (95% confidence interval: 0.685–1.000). For thoracic vertebral fractures, the sensitivity and specificity of lateral-view chest radiography in detecting fractures were respectively 100% and 97.1% for radiologist 1 and 100% and 97% for radiologist 2. For lumbar vertebral fractures, the sensitivity and specificity were both 100% for radiologists 1 and 2.
Conclusion: Chest radiography is useful for the screening of fragile spine fractures.

Disclosure: Y. Suyama, None; M. Kishimoto, None; T. Nozaki, None; T. Okabe, None; M. Okada, AbbVie Japan, Ayumi Pharmaceutical, Eli Lilly and Company, Mitsubishi Tanabe Pharma, and Ono Pharmaceutical, 2,AbbVie Japan, Ayumi Pharmaceutical, Eli Lilly and Company, Mitsubishi Tanabe Pharma, and Ono Pharmaceutical, 5,AbbVie Japan, Ayumi Pharmaceutical, Eli Lilly and Company, Mitsubishi Tanabe Pharma, and Ono Pharmaceutical, 9.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/chest-radiography-as-a-screening-tool-to-detect-fragile-spine-fractures

Abstract Number: 1216

Odontoid Fractures in the Elderly: An Unknown Osteoporotic Fracture?

Veronique Breuil1, Lauren Natella2, Nicolas Bronsard3, Jeremy Allia2, Laurent Hekayem4, Liana Euler Ziegler5 and Fernand De Peretti6, 1Rheumatology department, Nice, France, 2Rheumatology, CHU Nice, nice, France, 3Orthopedic, CHU Nice, Nice, France, 4Emergency, CHU Nice, Nice, France, 5151 rte de St Antoine de Gines, CHU de Nice -Université Nice Sophia Antipolis, Nice, France, 6orthopedic, CHU Nice, Nice, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Current WHO definition of osteoporosis excludes cervical fractures. However, in atraumatic odontoid fractures, mainly reported by orthopedic surgeons, bone status has not been described yet [1].

To investigate bone status in elderly patients sustaining a low energy odontoid fracture.

Methods:
We conducted a prospective study from January 2016 to January 2017 in patients > 65 years old, hospitalized in Nice University hospital for low energy odontoid fracture. An evaluation of bone status was proposed within 3 months after fracture event. Evaluation included demographic data, clinical risk factors of osteoporosis, bone mineral density (BMD) at spine and hip and vertebral fracture assessment (VFA) by dual X-ray absorptiometry and serum analysis to detect secondary osteoporosis.
Results:

38 patients were hospitalized for odontoid fracture: 8 patients < 65 years always after a major trauma (mean age 37.1 ±14.5 y) and 30 patients ≥ 65 years including 3 after a high energy impact. 27 odontoid fractures followed a low energy impact: 18 women and 9 men, mean age 83.8 y. (±10.7). 8 patients died before bone status assessment (5 men and 3 women), 6 died during hospitalization with a mean delay of 3.5 days (±1.87) and 2 after discharge (1 month and 5 month). 3 patients refused bone status evaluation, 5 were lost to follow-up and 1 is awaiting evaluation. Finally 10 patients had bone status evaluation, all were ≥ 65 y. None had parental history of hip fracture, 1 received aromatase inhibitors for breast cancer and 2 had a history of steroid therapy (> 3 months). 3 patients had previously received hormone replacement therapy, 1 received bisphosphonate for 5 years and 4 had calcium + vitamin D supplements. Lumbar spine mean T-score was -1.45 (±1.08), femoral neck: -2.37 (± .040) and total hip: -1.99 (±0.6). VFA analysis revealed 4 unknown vertebral fractures. The table summarizes population bone status: 8 patients out of 10 fulfilled diagnostic criteria of osteoporosis, including 6 with previous fractures. 2 patients with T-score > -1.DS didn’t have hip BMD assessment because of bilateral hip replacement but had previous major osteoporotic fractures. No secondary osteoporosis was detected. Serum vitamin D concentration was < 30 ng/ml in 5 patients, including 2 with concentration < 10 ng/ml.

<table>
<thead>
<tr>
<th>Lowest T-score</th>
<th>No fracture (n)</th>
<th>Previous minor osteoporotic fracture (n)</th>
<th>Previous major osteoporotic fracture (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-score &gt; -1 DS</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(1 patient: 2 femoral neck fracture,</td>
<td>(1 patient: pelvic and humeral</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>fractures,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Both patients had vertebral</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>fracture on VFA)</td>
</tr>
<tr>
<td>-1 DS &gt; T-score ≥ -2.5</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(1 wrist)</td>
<td>(1 patient: humeral and vertebral</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>fracture on VFA,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1 patient: 5 ribs fractures)</td>
</tr>
<tr>
<td>T-score &lt; -2.5</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(2 wrist fractures)</td>
<td>(vertebral fracture on VFA)</td>
</tr>
</tbody>
</table>

Conclusion:

Our study reveals that odontoid fractures mainly occur in elderly osteoporotic patients after a low energy impact. Although WHO osteoporosis definition excludes cervical fractures, odontoid fracture may be considered as an osteoporotic fracture. Further studies are required to confirm these results.


Disclosure: V. Breuil, None; L. Natella, None; N. Bronsard, None; J. Allia, None; L. Hekayem, None; L. Euler Ziegler, None; F. De Peretti, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/odontoid-fractures-in-the-elderly-an-unknown-osteoporotic-fracture

Abstract Number: 1217

Evaluation of Post Fracture Management in Males at a Veterans Affairs Health System

Nicola Berman1, David Smith2, Virginia Pike3, Craig Tenner4, Michael Pillinger1 and Stephen Honig1, 1Rheumatology, New York University School of Medicine, Division of Rheumatology, New York, NY, 2School of Medicine, New York University School of Medicine, New York, NY, 3Medicine/Rheumatology, New York University School of Medicine, Division of Rheumatology, New York, NY, 4New York University School of Medicine, Internal Medicine, New York, NY

First publication: September 18, 2017
Session Date: Monday, November 6, 2017
Session Title: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

The worldwide incidence of hip fractures in men is rising, and by 2050 is projected to increase by 310%. Increased hip fracture rates may be due to the number of undiagnosed, and therefore untreated, cases of osteoporosis. Established coordinated models for fracture care aim to improve treatment of osteoporosis following fragility fractures, and their implementation has been associated with reduction of subsequent fractures. However, these models vary and have not been uniformly adopted as a standard of care. The aim of this study was to assess osteoporosis management patterns in males with fragility fractures, using a VA system to identify an appropriate population of males at risk for osteoporosis and fractures.

Methods:

We performed a retrospective chart review using the VA Computerized Patient Record System. All patients who underwent bone densitometry (DEXA) between 2011 and 2016, and therefore presumed to be at potentially high risk for osteoporosis and fractures, were identified. Subjects were then stratified into two subgroups: those who had DEXA scans ordered in response to a fragility fracture (subgroup 1), and those who suffered a fragility fracture following their first DEXA (subgroup 2). To identify the impact of treatment on subsequent fractures, post-fracture management was evaluated in both groups. We assessed whether patients were treated following their fracture, whether they sustained a recurrent fracture, and what percentage of treated patients sustained subsequent fractures compared to the percentage of untreated patients who sustained subsequent fractures. Data was collected by three investigators, following a validated algorithm.

Results:

From among 45,000 patients with active records in the study time period, 1848 patients had undergone DEXA. Manual review of records for these 1848 patients identified 485 who had experienced a fragility fracture, including 170 of the 485 patients (9%) who had DEXA scans ordered in response to a fracture (subgroup 1). Overall, 68 (40%) of subgroup 1 patients subsequently suffered a recurrent fracture. 51 (30%) patients in subgroup 1 were treated for osteoporosis following their fracture; of these, 11 (23%) suffered a recurrent fracture, compared with 54 of 119 untreated patients (46%). Further, we evaluated post-fracture care in 315 patients who suffered a fragility fracture after a DEXA was obtained (subgroup 2). 22 of these patients (7%) were on treatment at the time of their initial fracture. Overall, 78 of 315 patients (25%) suffered a second, recurrent fracture. 198 (63%) were initiated on treatment following their first fracture. Among those receiving treatment, 26 of 198 (13%) suffered a recurrent fracture, compared with 28 of the 117 (24%) who did not receive treatment.

Conclusion:

Our data confirms the ability of treatment to reduce the risk of primary and secondary osteoporotic fractures in men, but underline that the number of male patients actually treated in response to DEXA and fracture is well below that mandated by available guidelines. Physicians should be educated on appropriate management of osteoporosis following fractures and an established model of care following fragility fractures may be helpful in this setting.

Disclosure: N. Berman, None; D. Smith, None; V. Pike, None; C. Tenner, None; M. Pillinger, None; S. Honig, None.

Caffeine Consumption and Risk of Osteoporosis: A Cross Sectional Study of 3, 210 Patients from the National Health and Nutrition Examination Survey

Nicola Berman1, Teresa Attina2, Bruce Cronstein1, Stephen Honig1 and Michael Pillinger1, 1Rheumatology, New York University School of Medicine, Division of Rheumatology, New York, NY, 2Pediatrics, New York University School of Medicine, New York, NY
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Adenosine regulates bone metabolism. In vitro studies suggest that direct stimulation of the adenosine A2A receptor increases osteoblasts and diminishes osteoclasts, and thus inhibition of these receptors might promote osteoporosis. Caffeine is a regular part of many adult diets and acts in part by engaging adenosine receptors. However, the impact of caffeine consumption on bone metabolism remains incompletely elucidated. Previous population based studies have demonstrated that caffeine may be associated an increased risk of osteoporotic fractures in post-menopausal females. The National Health and Nutrition Examination Survey (NHANES) is an ongoing CDC assessment of the health and nutritional status of adults and children in the United States, with a particular emphasis on diet. In this study, we leveraged NHANES to assess whether caffeine intake is a risk factor for osteoporosis and resultant fractures.

**Methods:**

We utilized NHANES for the 2013-14 cycle, which included a total of 10,175 subjects. All subjects underwent a 24-hour dietary recall interview to estimate intake of a specified panel of nutrients, caffeine included. Bone mineral density (BMD) was evaluated using Dual Energy X-ray Absorptiometry (DEXA) at the hip and spine. Subjects also answered surveys addressing history of prior fractures and risk factors for osteoporosis. Variables considered for analysis were downloaded from NHANES. Statistical analysis was conducted using STATA 14.2. We examined a subpopulation of patients over the age of 40 (N=3,210) and a further subset of Caucasian females over 50 (N=682). Sampling weights were accounted for unequal probabilities of selection. Univariate and multivariate analysis with logistic regression was used for data analyses. In the multivariate analysis, adjustments were made for age, body mass index, physical activity, prior corticosteroid use, smoking and alcohol.

**Results:**

Baseline characteristics were similar in the two subpopulations. In the subpopulation of men and women over 40, caffeine intake was found to be associated with vertebral spine fractures in the univariate analysis (p=0.01) and decrease in femoral neck BMD (p=<0.001) and spine fractures (p=<0.001) in the multivariate analysis. In the subpopulation of Caucasian women over 50, there was no significant associations from the univariate analysis, however caffeine intake was associated with both hip fractures (p=0.01) and decreased femoral neck BMD (p=0.05) on the multivariate analysis. Of note, in the subpopulation of Caucasian men over 50, there was no significant association between caffeine intake and decreased BMD or fractures.

**Conclusion:**

In women over 50, caffeine intake is associated with a small but significant decrease in bone mineral density at the femoral neck and increased risk of hip fractures. Further, in a cohort of men and women over 40, we observed a significant association of caffeine intake with increased vertebral spine fractures and decreased femoral neck BMD.

**Disclosure:** N. Berman, None; T. Attina, None; B. Cronstein, NIH grant, 2,Arthritis foundation grant, 2,AstraZeneca, 2,Celgene, 2,Eli Lilly & Co., 5,AstraZeneca, 5,Canfite Biopharma, 1; S. Honig, None; M. Pillinger, None.


**Abstract Number:** 1219

**Associations between Muscle Mass and Function with Bone Microarchitecture and Bone Strength in Postmenopausal Women**

Daniel Lobo1, Jackeline C Alvarenga1, Diogo S Domiciano2, Fabiana Benatti1, Bruno Gualano1 and Rosa M R Pereira2,

1Rheumatology Division, Faculdade de Medicina da Universidade de Sao Paulo, Sao Paulo, Brazil, 2Rheumatology Division, Hospital das Clínicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, Brazil

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017
**Session Title:** Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster II
**Session Type:** ACR Poster Session B
Background/Purpose: Most studies on sarcopenia and osteoporosis involve elderly populations. However, because postmenopausal hypoestrogenism is able to negatively modulate bone and muscle mass, it is important to understand the interplay between muscle and bone in early menopause. In addition, there is a paucity of studies investigating the potential influence of muscle mass and function upon bone quality (microarchitecture and strength), which could provide a more comprehensive view of fracture risk in this population. Therefore, the aim of this study was to assess the potential correlations between muscle parameters (mass, strength and function), and bone microarchitecture and strength using high-resolution peripheral computed tomography (HR-pQCT) in postmenopausal women.

Methods: A total of 248 healthy menopausal women (aged 58.0 ± 6.0 years) were evaluated by clinical questionnaire, laboratory and body composition (DXA, Hologic, QDR-4500). Bone quality (density, microarchitecture, strength and cortical porosity) was analyzed by high resolution peripheral computed tomography (distal radius and tibia, XtremeCT, Scanco Medical, Brüttisellen, Switzerland). Functional mobility and muscle performance were measured by handgrip strength (JAMAR model dynamometer), Timed-Stand and Timed Up & Go tests. Balance was assessed by the Berg Balance Scale. The correlation between bone parameters (HR-pQCT) and muscle performance was analyzed by the Spearman test ($p < 0.05$).

Results: At the radius, there were positive correlations between handgrip strength and trabecular bone HR-pQCT parameters (trabecular volumetric bone mineral density [Tb.vBMD]: $r = 0.17$, $p = 0.03$), trabecular thickness [Tb.Th]: $r = 0.16$, $p = 0.04$) and trabecular separation [Tb.Sp]: $r = -0.15$, $p = 0.02$), as well as between muscle strength and bone strength (Stiffness - S: $r = 0.36$, $p < 0.001$). At the tibia, the left leg muscle mass was positively correlated with number of trabeculae (Tb.N) ($r = 0.16$, $p <0.001$), cortical thickness (Ct.Th) ($r = 0.21$, $p = 0.01$) and bone strength (S) ($r = 0.37$, $p <0.001$). There were no significant correlations between HR-pQCT parameters and lower limb functional tests, except between the balance and tibial Tb.vBMD ($r = 0.13$, $p = 0.04$). There was a negative correlation between total body fat and muscle function (timed-stand test: $r = -0.21$, $p <0.001$, balance: $r = -0.21$, $p <0.001$).

Conclusion: In postmenopausal women, muscle strength seems to play a more important role in the upper limb bone (radius) parameters, whereas muscle mass seems to exert a higher influence on the lower limb bone (tibia). These findings suggest a difference on relationship between muscle and bone according to distinct body segments. In addition, the negative correlation between body fat and balance/muscle function indicate that increased body fat mass might confer increased risk of falls in this population. Longitudinal studies are needed to test these assumptions.

Disclosure: D. Lobo, None; J. C. Alvarenga, None; D. S. Domiciano, None; F. Benatti, None; B. Gualano, None; R. M. R. Pereira, None.


Abstract Number: 1220

Effect of Anti-Diabetic Medications on Fracture Risk in Type II Diabetes Mellitus

Youmna Lahoud1, Christine Peloquin1, Yuqing Zhang2 and Devyani Misra3, 1Boston University School of Medicine, Boston, MA, 2School Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, 3Medicine, Section of, Boston University School of Medicine, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Risk of osteoporotic fracture in type II Diabetes Mellitus is conflicting and possibly related to the anti-diabetic medication used. There is evidence to suggest protective effect of some medications (e.g. metformin and sulfonylureas) while others have been associated with increased risk for fractures (e.g. thiazolidinedione and DPP4-inhibitors). Thus, we examined the association of oral anti-diabetic medications with hip fractures risk in community-dwelling older adults with type 2 Diabetes Mellitus.

Methods: We conducted a nested case-control study in men and women ≥ 40 years old with incident (new-onset) type II Diabetes Mellitus, from The Health Improvement Network (THIN), an electronic medical records database from the United Kingdom. For each incident (new-onset) hip fracture case, we selected up to 4 controls matched by age and sex. We categorized the anti-diabetic medications into the following categories: 1) Current use (last prescription within 1 year) of Metformin alone; 2) Current use of...
Sulfonylureas alone; 3) Current use of Thiazolidinediones or DPP4 inhibitors alone; 4) Current use of combinations or others; 5) Current use of any drug with recent switch in category; 6) Remote use of any medications (last prescription >1 year ago) as the reference category. In a multivariable conditional logistic model, we adjusted for alcoholism/heavy drinking, BMI, fall/high risk of falls, smoking and medications (ace inhibitors, anti-osteoporosis medications, anti-seizure drugs, beta-blockers, diuretics, estrogen, glucocorticoids).

**Results:** Among 2673 subjects (mean age 72y; 70% women; 447 incident hip fracture cases and 2226 controls), the hip fractures cases had lower BMI and were more likely to have alcoholism and falls. As shown in Table, compared to remote use of any oral anti-diabetic medications, the odds for hip fracture was reduced by 36% with current metformin use (OR 0.64, 95% CI 0.49-0.84), no different with current use of sulfonylureas (OR 1.02, 95%CI 0.76-1.38) and slightly increased, although not statistically significant, with current Thiazolidinedione or DPP-4 inhibitors (OR 1.29, 95%CI 0.69-2.43) use.

**Conclusion:** We found protective effect of metformin use, no effect of sulfonylureas and possibly adverse effect of Thiazolidinedione and DPP-4 inhibitors on hip fracture risk in this large cohort of older diabetic patients. Clinicians caring for older diabetic patients need to consider fracture risk while selecting anti-diabetic medications.

### Table: Association of Anti-diabetic Medications with Odds of Hip Fracture

<table>
<thead>
<tr>
<th>Oral anti-diabetic medications use</th>
<th>Hip Fracture Cases</th>
<th>Controls</th>
<th>Crude OR</th>
<th>Adjusted OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current Metformin</td>
<td>449</td>
<td>2246</td>
<td>0.57 (0.45, 0.74)</td>
<td>0.65 (0.50, 0.84)</td>
</tr>
<tr>
<td>Current Sulfonylureas</td>
<td>209</td>
<td>602</td>
<td>1.05 (0.79, 1.39)</td>
<td>1.05 (0.78, 1.40)</td>
</tr>
<tr>
<td>Current Thiazolidinedione or DPP-4 inhibitors</td>
<td>16</td>
<td>47</td>
<td>0.99 (0.54, 1.82)</td>
<td>1.24 (0.66, 2.31)</td>
</tr>
<tr>
<td>Current Mixed Use</td>
<td>12</td>
<td>34</td>
<td>1.01 (0.50, 2.03)</td>
<td>1.17 (0.57, 2.37)</td>
</tr>
<tr>
<td>Remote use of any drug (Ref)</td>
<td>99</td>
<td>287</td>
<td>1.0</td>
<td>1.0</td>
</tr>
</tbody>
</table>

**Disclosure:** Y. Lahoud, None; C. Peloquin, None; Y. Zhang, None; D. Misra, None.


Abstract Number: 1221

**Differences in BONE Metabolism between Intermittent and Continuous Treatment with LHRH Agonists in Prostate Cancer Patients**

Karla Arevalo Ruales¹, Jose Ivorra Cortes¹, Cesar David Vera Donoso², Elena Grau Garcia¹, Cristina Alcañiz Escandell¹, Ines Canovas Olmos¹, Inmaculada Chalmeta Verdejo¹, Carlos Feced Olmos¹, Jorge Juan Frago Gil¹, Roxana Gonzalez Mazarío¹, Luis Gonzalez Puig¹, Eztizen Labrador Sanchez¹, Isabel Martinez Cordellat¹, Carmen Najera Herranz¹, Rosa Negueroles Albuixech¹, Jose Eloy Oller Rodriguez¹, Francisco Miguel Ortiz-Sanjuan¹, Elvira Vicens Bernabeu¹, David Hervás Marín³, Marta De la Rubia Navarro¹ and Jose Andres Roman Ivorra¹, ¹Rheumatology Department. Hospital Universitario y Politecnico La Fe, Valencia, Spain, ²Urology Department. Hospital Universitario y Politecnico La Fe, Valencia, Spain, ³Biostatistics Unit. IIS La Fe, Valencia, Spain

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster II

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM
Background/Purpose:
Prostate cancer is the most common male malignancy. It is hormone dependent and androgenic inhibition with LHRH agonists is one of the mainstays of treatment. There are different treatment scheme’s options; continuous or intermittent in order to decrease secondary effects. As for bone effects, LHRH agonists therapy increase bone resorption, reduce bone mineral density (BMD), which leads to an increase in the risk of fracture. The influence of the different treatment schemes in bone metabolism has not been studied enough. The aim of this study is to evaluate the LHRH agonist treatment schemes effect in bone metabolism in prostate cancer patients and to evaluate whether antiresorptive treatment decreases the risk of osteoporosis according to different scheme of LHR agonists.

Methods:
We recruited patients from the Prostate Cancer Protocol of Osteoporotic Risk Assessment. Patients were evaluated in a first visit (month 0) and at 6, 12, 18 and 24 months. We collected the following data: markers of bone turnover (serum BCTX and P1NP), BMD of the lumbar spine, femoral neck, and total hip, LHRH agonists treatment scheme, PSA and testosterone levels, and antiresorptive treatment. Biostatistical analysis with R (3.3.2.) was performed.

Results:
We selected 45 prostate cancer patients without bone metastasis with a minimum follow up of 12 months, 36 of them completed 24 months follow up. The mean age at prostate cancer diagnosis was 68.33 (9.02) years, with a mean Gleason score of 7 (1). 15 patients had intermittent LHRH agonists treatment scheme and 30 had continuous treatment scheme. 17 patients initiated antiresorptive treatment (mostly denosumab), 7 of them under intermittent LHRH agonist therapy. At baseline evaluation 16.7% of patients had osteoporosis and the 45.2% had osteopenia. 43.2% of patients had vitamin D values under 20ng/ml and 31.1% showed increased PTH values. Vitamin D and PTH levels were normalized, with supplementation, during the follow-up. Statistical analysis using a multivariable linear mixed model show that antiresorptive treatment had significant influence in femoral neck and total hip BMD (P<0.001 and P<0.001 respectively). Beta-CTX levels are related to the total hip BMD value (P=0.019) in patients with no antiresorptive treatment. Furthermore, in patients receiving intermittent LHRH agonist scheme and without antiresorptive treatment there was an increase total hip and femoral neck BMD values, in comparison to patients receiving continuous LHRH agonist treatment without antiresorptive treatment who had a decrease of total hip and femoral neck BMD values (coef= 0.89; 95% CI 0.09-1.75 and coef= -0.28; 95% CI -0.99-0.46). No fractures have been detected during the follow up period.

Conclusion:
In our patients cohort we detected a high prevalence of vitamin D deficiency. In patients without antiresorptive treatment, evolution of BMD values correlated to betaCTX levels during the follow-up. Moreover, patients without antiresorptive treatment under intermittent treatment with LHRH agonist display positive effects in total hip BMD values compared to patients receiving continuous LHRH regimen.

Disclosure: K. Arevalo Ruales, None; J. Ivorra Cortes, None; C. D. Vera Donoso, None; E. Grau Garcia, None; C. Alcañiz Escandell, None; I. Canovas Olmos, None; I. Chalmeta Verdejo, None; I. Feded Olmos, None; J. J. Fragio Gil, None; R. Gonzalez Mazario, None; L. Gonzalez Puig, None; E. Labrador Sanchez, None; I. Martinez Cordellat, None; C. Najera Herranz, None; R. Negueroles Albuech, None; J. E. Oller Rodriguez, None; F. M. Ortiz-Sanjuán, None; E. Vicens Bernabeu, None; D. Hervás Marin, None; M. De la Rubia Navarro, None; J. A. Roman Ivorra, None.

Impact of Bariatric Surgery on Bone Mineral Density : Observational Study of 110 Patients Followed up in a Specialised Centre for the Treatment of Obesity in France

Marion Geoffroy1, Isabelle Lambrecht1, Jan Chrusciel2, Isabelle Gaubil-Kaladjian3, Ana Diaz-Cives4, Jean Paul Eschard1 and Jean-Hugues Salmon1, 1Service de Rhumatologie, CHU Reims, Hôpital Maison Blanche, Reims, France, 2Service de Recherche Clinique, CHU Reims, Hôpital Robert Debré, Reims, France, 3Service de Recherche Clinique, CHU Reims, Hôpital Robert Debré, Reims, France, 4Service d’Endocrinologie et nutrition, CHU Reims, Hôpital Robert Debré, Reims, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Background/Purpose: Bariatric surgery is used to treat severe obesity. We aimed to investigate the incidence of significant bone mineral density (BMD) loss at 6 and 12 months after bariatric surgery.

Methods: Observational study performed in a specialised centre for the treatment of obesity in a University Hospital in France. Surface BMD was measured by dual x-ray absorptiometry (DEXA). A reduction of >0.03 g/cm² was considered as significant.

Results: A total of 110 patients were included. A significant reduction in BMD was observed in 63.4% of patients at 6 months, and in 73.9% at 12 months after surgery. No case of osteoporosis was observed. There were 4 cases of osteopenia and one fracture post-surgery. BMD loss was related by univariate analysis to the reduction in Body Mass Index (BMI) (p<0.01), weight loss (p<0.01), fat mass (p<0.01) and lean mass (p<0.01). Multivariate analysis found a significant association between the reduction in BMD and the percent excess weight loss (odds ratio 1.11, 95% confidence interval (1.05-1.18), p<0.001).

Conclusion: There is a significant reduction in BMD at 6 months after surgery in over 60% of patients undergoing bariatric surgery. BMD loss is persistent over time, and predominantly situated at the femoral level, and strongly associated with weight loss. Systematic vitamin and calcium supplementation, as well as follow-up by DEXA scan seems appropriate, with systematic DEXA scan pre- and post-surgery, and annually thereafter until weight has stabilized.

Disclosure: M. Geoffroy, None; I. Lambrecht, None; J. Chrusciel, None; I. Gaubil-Kaladjian, None; A. Diaz-Cives, None; J. P. Eschard, None; J. H. Salmon, None.


Abstract Number: 1223

Inflammatory Bowel Diseases and the Risks of Fracture and Low Mineral Density: Review of the Literature and Meta-Analysis of Observational Cohorts

Paulina Szafors¹, Thomas Barnetche², Cédric Lukas³, Jacques Morel⁴, Cécile Gaujoux-Viala⁵, Bernard Combe⁷ and Hélène Che⁸, ¹Department of Rheumatology, Lapeyronie Hospital and University of Montpellier, Montpellier, France, ²Rheumatology Department, Pellegrin University Hospital, BORDEAUX, France, ³Rheumatology, CHU Lapeyronie and EA2415, Montpellier University, University of Montpellier, France, ⁴Rheumatology, CHU Lapeyronie and Montpellier University, Montpellier, France, ⁵Rheumatology, Nîmes University Hospital and EA2415 Montpellier University, Nîmes, France, ⁶EA 2415, Montpellier University, Nîmes, France, ⁷Department of rheumatology, Lapeyronie Hospital and Montpellier University, Montpellier, France, ⁸Rheumatology, University and Hospital Lapeyronie, University of Montpellier, France
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Inflammatory bowel diseases (IBD), such as Crohn disease (CD) and ulcerative colitis (UC), are associated with a decreased bone mineral density caused by chronic inflammation and corticosteroid use. However, the increase of fracture risk is unknown and data are contradictory across studies.

The aim of our study was to assess the risks of fracture and presence of low bone mineral density (BMD) in patients with IBD compared to the general population.

Methods: A systematic search of literature up to 1st February 2017 was conducted using databases including: MEDLINE (via PUBMED), EMBASE, the Cochrane library and abstracts from the ACR, ASBMR and EULAR congresses 2014-2016. Prospective and retrospective cohort studies were included if they reported the incidence of fractures and/or the measure of BMD by dual energy X-ray absorptiometry (DXA) (expressed in g/cm²) in IBD patients in comparison with healthy controls. Data was extracted by two
independent investigators. Meta-analysis was performed to assess odds-ratios (OR) for each outcome using the inverse variance approach to estimate pooled OR with their 95% confidence interval. Heterogeneity was assessed according to Cochran Q-test and $I^2$ values. Calculations were made with the Cochrane RevMan 5.3 software. P-values less than 0.05 were considered significant.

**Results**: The literature search identified 1165 articles and no congress abstract; a manual search did not retrieve any additional article. Finally, 25 studies met the inclusion criteria. Nine of them reported 2065 fracture events among 42,615 IBD patients and 4825 fracture events among 203,240 healthy controls. Global risk of fracture was increased in IBD patients compared with controls with a pooled OR of 1.50 (95% CI 1.10-2.05; p<0.001, $I^2$=86%). Fracture risk was not significantly increased for any other site (arm, hip, wrist). The analysis of 17 studies concerning BMD showed a significant decrease of BMD and Z-score at three sites. At femoral neck, mean difference (MD) of BMD was -0.05 (95% CI -0.08 to -0.02; p=0.001, $I^2$=60%) and MD of Z-score -0.48 (95% CI -0.64 to -0.33; p<0.0001, $I^2$=0%). These values were respectively -0.08 (95% CI -0.11 to -0.05, p<0.00001, $I^2$=46%) and -0.10 (95% CI -1.52 to -0.50; p=0.07, $I^2$=69%) at total femur, and -0.06 (95% CI -0.10 to -0.03, p=0.0003, $I^2$=87%) and -0.51 (95% CI -0.68 to -0.34; p<0.0001, $I^2$=54%) at lumbar spine.

**Conclusion**: IBD patients have an increased risk of fractures, especially in the spine, and a decrease of BMD at all sites, suggesting the need for regular follow-up and preventing measures.

**Disclosure**: P. Szafors, None; T. Barnetche, None; C. Lukas, None; J. Morel, None; C. Gaujoux-Viala, None; B. Combe, None; H. Che, None.

**Abstract Number**: 1224

**BONE Metabolism in LIVER Transplant Patients Two-Year Study. Influence of Medical Intervention PRIOR to Surgery and Antiresorptive Treatment**

Eztizen Labrador Sanchez1, Elena Grau Garcia1, Karla Arevalo Ruales1, Jorge Juan Frago Gil1, Roxana Gonzalez Mazarion1, Cristina Alcañiz Escandell1, Ines Canovas Olmos1, Inmaculada Chalmeta Verdejo1, Carlos Feced Olimos1, Luis Gonzalez Puig1, Jose Ivolra Cortes1, Isabel Martinez Cordellat1, Carmen Najera Herranz1, Rosa Negueroles Albuixech1, Jose Eloy Oller Rodriguez1, Francisco Miguel Ortiz-Sanjúan1, Elvira Vicens Bernabe1, Victoria Forges Ferrer2, David Hervás Marín2, Marta De la Rubia Navarro1, Angel Moya Herranz2 and Jose Andres Roman Ivorra1

1Rheumatology Department. Hospital Universitario y Politecnico La Fe, Valencia, Spain, 2Biostatistics Unit. IIS La Fe, Valencia, Spain, 3Hepatology Department. Hospital Universitario y politecnico La Fe, Valencia, Spain

**First publication**: September 18, 2017

**SESSION INFORMATION**

**Session Date**: Monday, November 6, 2017

**Session Title**: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster II

**Session Type**: ACR Poster Session B

**Session Time**: 9:00AM-11:00AM
Background/Purpose:

Osteoporosis is a frequent complication in patients with chronic liver diseases, mainly in advanced stages or with evidence of cholestasis. During the first few months after liver transplant (LT) it seems that there is an accelerated bone mass loss and greater fracture risk. The aim of the present study is to evaluate the antiresorptive treatment effect in bone metabolism in patients undergoing LT and to evaluate whether medical intervention prior to LT decreases the risk of osteoporosis.

Methods: We recruited patients from the LT Protocol of Osteoporotic Risk Assessment. The patients were evaluated 3-6 months before surgery, shortly after transplant (month 0) and 6-12-18-24 months after surgery. Data of bone metabolism biomarkers, densitometric values and antiresorptive treatment was collected. Biostatistical analysis with R (3.3.2.) was performed.

Results: We selected 163 LT patients of which 86 completed 24 months follow-up. From the total cohort, 77.8% were men and the mean age at transplantation 54.53 ±9.4 years old. 92.6% of patients were supplemented with vitamin D after surgery and 19.6% initiated antiresorptive treatment. We observed that 25-OHVitamin D, PTH, beta-CTX and P1NP levels were corrected through the follow-up .T-score during the first year of follow-up decreased slightly and at 24 months the tendency was towards increase. This pattern was stronger in lumbar spine (t-score -1.48±1.34 after surgery and -1.28±1.06 at 24 months). Statistical analysis showed that antiresorptive treatment significantly influence lumbar and hip densitometric values (P<0.001 and P<0.001 respectively) as well as P1NP levels (P=0.003 and P=0.012 respectively). Moreover, obesity (P=0.0004), as well as beta-CTX (P=0.029) and 25-OHVitamin D (P=0.024) standardization improved hip densitometric values. Finally, LT patients evaluated before surgery showed better lumbar densitometric values than those evaluated after the transplant (P=0.007).

Conclusion: We observed 25-OHVitamin D levels and bone metabolism biomarkers correction during the first two years after LT. Medical intervention prior to LT as well as antiresorptive treatment seem to play a decisive role in bone mineral density improvement.

Disclosure: E. Labrador Sanchez, None; E. Grau Garcia, None; K. Arevalo Ruales, None; J. J. Fragio Gil, None; R. Gonzalez Mazarro, None; C. Alcañiz Escandell, None; I. Canovas Olmos, None; I. Chalmeta Verdejo, None; C. Feced Olmos, None; L. Gonzalez Puig, None; J. Ivorra Cortes, None; I. Martinez Cordellat, None; C. Najera Herranz, None; R. Negueroles Albuixech, None; J. E. Oller Rodriguez, None; F. M. Ortiz-Sanjuán, None; E. Vicens Bernabeu, None; V. Fornes Ferrer, None; D. Hervás Marin, None; M. De la Rubia Navarro, None; A. Moya Herreia, None; J. A. Roman Ivorra, None.


Abstract Number: 1225

BONE Mineral Density and Vertebral Fractures in Gaucher Disease Patients Treated with Imiglucerase

Maria Silvia Larroude1, Gabriel Aguilar1, Ignacio Rossi1, Lucas Ricardo Brun2 and Guillermo Drelichman3, 1Centro de Diagnostico Rossi, Buenos Aires, Argentina, 2School of Medicine. Rosario National University, Bone Biology Laboratory, Rosario, Argentina, 3Hospital Ricardo Gutierrez, Buenos Aires, Argentina

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Osteopenia and osteoporosis (OP) have been described in patients with Gaucher disease (GD) but there are very few reports about bone mass in GD patients treated with imiglucerase. The aim of this study was to evaluate bone mineral density (BMD) and vertebral fractures (VF) in EG patients treated with imiglucerase.

Methods: We conducted a prospective, observational and descriptive study in 218 GD patients receiving enzyme replacement therapy (imiglucerase, mean dose of 54±15 U/kg [range: 11-120]) with a follow-up of 3 years. BMD was evaluated by DXA (Lunar Prodigy) to measure lumbar spine, total hip or femoral neck and total body according to age. The diagnosis of OP was performed according to WHO and ISCD criteria. The diagnosis of VF was performed with lumbar and dorsal spine by lateral Rx and by whole-body magnetic resonance. Data are expressed as mean±SD and differences were considered significant if p<0.05.
**Results:** 126 women (57.8%) and 92 men (42.2%) were included, mean age 27.9±15.9 years (98% had splenomegaly, 49.2% hepatomegaly and 7.9% were splenectomized). The age at diagnosis was 153±154 months (range 4-702) and the mean age of initiation of treatment was 215±173 months (range 7-835). BMD was normal in 78.2%, 5.2% showed osteopenia/low bone mass (LBM) and 16.6% osteoporosis (OP). During 1 year follow-up (n=97), 10.3% were found with OP and 8.3% with LMB; at the second year (n=89) we found 6.7% OP and 7.9% LMB; while in the third year (n=53) only 3.8% showed OP and 5.6% LBM. This indicates a lower percentage of patients with OP during follow-up (chi², p=0.0216). In the lumbar spine, a significant increase in BMD was found throughout the follow-up (percentage change: 1st year +2.48, 2nd year +4.00%, and 3rd year +6.95%). There was no significant difference in total hip or femoral neck and whole-body BMD. We excluded 25.14% of hip BMD due to the presence of avascular bone necrosis. The increase in BMD was found in <19 years old patients and in premenopausal women. 10 VF were found in females and 13 in males; 31.58% were located in low dorsal vertebrae, 21.05% lumbar, 15.79% dorsolumbar low and 31.58% high dorsal vertebrae without posterior wall compromise. High dorsal VF could only be detected by total body magnetic resonance. 45% of the fractures involved a single vertebra, 55% more than one. According to Genant classification, 13% were grade I and 87% grade II and III.

**Conclusion:** treatment with imiglucerase maintains and increases lumbar spine BMD in GD patients. VF findings in GD patients did not compromise the posterior wall and the whole-body magnetic resonance was useful for detecting high dorsal VF.

**Disclosure:** M. S. Larroude, None; G. Aguilar, None; I. Rossi, None; L. R. Brun, None; G. Drelichman, None.


**Abstract Number: 1226**

**Association of Dorsal Flat Vertebra/Platyspondylia As a Form of Vertebral Dysplasia within Type II Collage Disorders**

Pilar Ahijado-Guzman¹, Raul Veiga², Miguel Cantalejo¹, Justo Ruiz³ and Antonio Zapatero³, ¹Rheumatology Unit. Fuenlabrada’s Hospital, Madrid, Madrid, Spain, ²Rheumatology Unit. Fuenlabrada’s Hospital, Madrid, Fuenlabrada, Spain, ³Department of Internal Medicine. Fuenlabrada’s Hospital, Madrid, Madrid, Spain

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster II

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Defects in the type II collagen gene are described. These predispose humans to various phenotypic combinations in families with skeletal dysplasia, and/or disease by causing deposits of microcrystals and/or early osteoarthritis and/or synovial osteochondromatosis. Flat vertebra is defined as the vertebrae with flattening of the vertebral body, also with irregular surface or with nodules of Schmorl (flat vertebra), in isolation or two a maximum of two vertebral bodies, to distinguish it from Scheuermann's disease.

The purpose of this is to demonstrate the possibility of "dorsal flat vertebra" in relation to pathologies associated with type II collagen disorders.

**Methods:** Patients attending physician since 1994, in whom Type II collagen disease or vertebral dysplasia was suspected, were selected for the study. Their medical history was taken. Also available radiographs, including dorsal lateral spine x-rays, were assessed for a flat vertebra, by triple-observer (two rheumatologists and one radiologist), according to the defined criteria. In all selected patients, a DEXA osteoporosis screening was performed, being both densitometric osteoporosis and chest trauma exclusion criteria.

**Results:** The 84 patients assessed included 43 women and 41 men, with a mean age of 47.1 years, mean weight of 84.6kg in men and 74.4kg in women, and mean height 168.8cm in men and 159cm in women.

From a radiological and clinical point of view it was obtained:

Atypical arthrosis: 64.3%

Synovial osteochondromatosis: 15.5%
Chondrocalcinosis: 7.1%
Lower Dorsal kyphotic apex: 38.1%,
Calcifying enthesopathies: 4.8%,
Exostoses: 4.8%,
Other calcifications: 20.2%,
Scoliosis: 33.3%,
Family history of flat vertebrae: 3.6%,
Dysplastic Peripheral traits: 27.4%,
Personal history of microcrystalline arthritis: 4.8%.

None developed T score suggesting osteoporosis by DEXA.

Conclusion:
The association of dorsal flat vertebra (according to the defined criteria) is seen as a form of vertebral dysplasia within type II collagen disorders.

All patients or their parents were born in small towns, leading to suspicion in endogamy.

Disclosure: P. Ahijado-Guzman, None; R. Veiga, None; M. Cantalejo, None; J. Ruiz, None; A. Zapatero, None.


Abstract Number: 1227

Osteoporosis and Breast Cancer: Can FRAX-Based Risk Factors Accurately Predict Further Fractures at This Setting?

Salvador López-Salguero¹, Laura Ranieri², Juan Carlos Ordoñez³, Mariano Andrés⁴,⁵, Jose Ponce⁶ and Isabel Ibero², ¹Sección de Reumatología, Hospital General Universitario de Alicante, Alicante, Spain, ²Reumatología, Dpt. Rheumatology, Hospital General Universitario Alicante, Alicante, Spain, ³RHEUMATOLOGY, Dpt. Rheumatology, Hospital General Universitario Alicante, Alicante, Spain, ⁴Dpt. Rheumatology, Hospital General Universitario Alicante, Alicante, Spain, ⁵Universidad Miguel Hernández, Elche, Spain, ⁶Oncología, Dpt. Oncology, Hospital General Universitario Alicante, Alicante, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Women with breast cancer (BC) are at risk for the development of bone loss and osteoporosis (OP) mainly due to adjuvant therapies, as aromatase inhibitors (AI). Thus, it would be of special interest in this group of patientes, to know at baseline which factors can predispose to develop fragility fractures (FF) during follow-up, in order to optimize vigilance and treatment.

The purpose of this study is to analyze which risk factors at baseline that can predict the appearance of a new FF in women with BC and OP.

Methods:
Retrospective analysis of consecutive female patients with recent breast cancer (BC) and low bone mineral density (BMD) referred to the osteoporosis outpatient clinic for assessment, as agreed with oncologists. For the purpose of this analysis, only patients with follow-up data (at least six months after baseline visit) were selected. FRAX tool-derived risk factors (age, BMI, DEXA, previous fracture, parent fractured hip, smoking, alcohol, glucocorticoids, rheumatoid arthritis, secondary OP) were taken as explicative variables. Student’s t and chi-2 tests were used to perform comparisons based on the appearance of new FF in the study period.

Results:

Results: A total number of 156 female patients have been assessed up to January 2017. Of the 107 patients in follow-up (68.5%; median time in follow-up 2.1 years p25-75 1.2-3.2). Median age was 62.07 years old (SD±10,35), being 89% of them postmenopausal. 73 (68.2%) were on AI therapy (10 anastrozole, 59 letrozole and 4 exemestane). At baseline, 29 patients (27.1%) showed a FF (15 vertebral; 10 non vertebral; 2 hip; 2 multiple fracture). Antiosteoporotic treatment was recommended in 95 patients (88.7%). During follow-up, 13 FF were seen (12.1%; CI95% 6-19); being 8 of them vertebral, 4 not vertebral, and one multiple fracture; no new hip FF was seen.

After comparison of the different risk factors according to the development of a new FF, no significant association was found (see table).

<table>
<thead>
<tr>
<th></th>
<th>New fragility fracture</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NO (n= 94)</td>
</tr>
<tr>
<td>Age (years old), mean ±SD</td>
<td>62.0 ±10.7</td>
</tr>
<tr>
<td>BMI (kg/m2), mean ±SD</td>
<td>26.5 ±7.1</td>
</tr>
<tr>
<td>Follow-up duration (months) median ±SD</td>
<td>28.6 ±19,4</td>
</tr>
<tr>
<td>DEXA at lumbar spine (T-score) median ±SD</td>
<td>-2.7 ±0,8</td>
</tr>
<tr>
<td>GFR (ml/min) mean ±SD</td>
<td>91.7 ±16.0</td>
</tr>
<tr>
<td>Menopause (%)</td>
<td>93.4</td>
</tr>
<tr>
<td>Previous fracture (%)</td>
<td>27.1</td>
</tr>
<tr>
<td>Parent fractured hip (%)</td>
<td>11.0</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>10.0</td>
</tr>
<tr>
<td>Glucocorticoids (%)</td>
<td>9.9</td>
</tr>
<tr>
<td>Rheumatoid arthritis (%)</td>
<td>3.2</td>
</tr>
<tr>
<td>Aromatase inhibitor (%)</td>
<td>70.9</td>
</tr>
<tr>
<td>Antiosteoporotic treatment (%)</td>
<td>88.4</td>
</tr>
</tbody>
</table>

Conclusion:

In this study no relationship between FRAX-based risk factors and the development of new FF in women with OP and BC was found. As new FF occurred in 12% of cases, it highlights the need for special attention to this singular, secondary form of OP.

Disclosure: S. López-Salguero, None; L. Ranieri, None; J. C. Ordoñez, None; M. Andrés, None; J. Ponce, None; I. Ibero, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/osteoporosis-and-breast-cancer-can-frax-based-risk-factors-accurately-predict-further-fractures-at-this-setting

Abstract Number: 1228

Postmenopausal Breast Cancer Patients on Aromatase Inhibitor Therapy and Their Increased Risk of Fragility Fracture

Anna Lafian1, Julia Suh2 and Karina Torralba3, 1Internal Medicine, Arrowhead Regional Medical Center, Colton, CA, 2Internal Medicine, Loma Linda University, Loma Linda, CA, 3Internal Medicine/Rheumatology, Loma Linda University, Loma Linda, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Background/Purpose: Postmenopausal women with breast cancer have higher osteoporosis risk due to declining estrogen levels and use of aromatase inhibitors (AIs). The American Society of Clinical Oncology (ASCO) update on bone health management in breast cancer elaborated on measures medical oncologists can undertake. Factors conferring high fracture risk are age ≥65, women aged 60-64 with family history of fracture, weight <70kg, prior fragility fracture, postmenopausal state on AIs, and chemotherapy (CT)-induced menopause. Recommendations include annual DXA, calcium and vitamin D for high risk patients, bisphosphonates for patients with T score ≤-2.5. Malignancies such as breast cancer are co-morbidities that rheumatic disease patients are at risk for. The purpose of this IRB-approved Loma Linda University study was to evaluate adherence of oncologists to ASCO guidelines, and to determine fracture rates in our cohort of breast cancer patients on AIs. This is a pilot study examining the practice of one of our breast cancer specialists.

Methods: Oncology clinic data from January-December 2016 was extracted using ICD10 codes related to breast cancer, osteoporosis, osteopenia, which identified 208 encounters. ICD10 code related to use of aromatase inhibitors was applied, resulting in a unique subset of 32 patients. Chart review collected patient demographics (age, sex), presence of metastases, estrogen receptor positivity (ER+), AI used, T-score (by DXA), frequency DXA ordered, anatomic fracture location, re-fracture events, bisphosphonate use, calcium/vitamin D use, current alcohol and tobacco, and thyroid disease.

Results: All 32 patients were ER+, postmenopausal females, with one having CT-induced menopause. Mean age was 70.2. Mean BMI was 26.5. 5 (16%) had thyroid disease. Twelve (39%) reported alcohol use; 1 (3%) was a smoker. Twelve (38%) of patients were on Anastrozole, 3 (9.4%) on Exemestane and 17 (53%) on Letrozole. Based on T-scores, 9 (28%) were osteopenic and 22 (69%) were osteoporotic. Twenty-nine (90%) patients were on appropriate doses of calcium/vitamin D. DXA was obtained annually in 15 (47%) patients. Of those with osteoporosis based on T-score, 17 (77%) were on a bisphosphonate, while 4 (18%) were on denosumab; 1 refused treatment. Overall, 9 fractures occurred; of these, 3 were re-fracture events. Mean age at time of first fracture was 69.3, while mean age at re-fracture was 76.3. Four (44%) occurred in the spine, with 1 due to metastases. Other sites of fracture were: hip (1), hand (1), rib (1), humerus (2). Re-fractures in the spine (2) and hand (1). Six fractures occurred while on bisphosphonates: alendronate (1), risedronate (3), ibandronate (2).

Conclusion: There was great adherence to ASCO bone health guidelines for breast cancer patients on AIs. It would be of interest if the same level of adherence applies to the entire oncology team. We also raise questions about the applicability of fracture risk calculators for this population. Postmenopausal breast cancer patients on AIs may need closer bone health monitoring given their high risk of fracture. Bone health issues related to malignancy should be of concern to all rheumatologists.

Disclosure: A. Lafian, None; J. Suh, None; K. Torralba, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/postmenopausal-breast-cancer-patients-on-aromatase-inhibitor-therapy-and-their-increased-risk-of-fragility-fracture

Abstract Number: 1229

Factors Affecting FRAX Score Calculation & Treatment in Practice

Avneet Vig1, Beverly Johnson2, Tony Francis3 and Barbara Mendez-Agrusa4, 1Montefiore Medical Center, Bronx, NY, 2Jacobi Medical Center, Albert Einstein College of Medicine, Bronx, NY, 3Radiology, Albert Einstein College of Medicine, Bronx, NY, 4Medicine, Department of Rheumatology, Albert Einstein College of Medicine, Bronx, NY
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Osteoporosis-related fractures causes increased disability and morbidity and mortality. The FRAX algorithm quantifies the 10 year probability of a hip or major osteoporotic fracture. This study was initiated after observation of significant discrepancies between FRAX scores generated by the facility machine and those calculated using the online FRAX tool. We aimed to review a series of bone density scans to determine the reason for the discrepancy. Our hypothesis was that providers may not be using the correct measure to calculate the FRAX score.
Methods: This was a retrospective quality improvement study. 700 of 1200 DEXAs from 2013 to 2015 were randomly selected, 168 met the inclusion criteria of osteopenia. Data to calculate the score was obtained from the patient chart. The correct way to calculate the FRAX is to use the femoral neck bone mineral density (BMD) and to select the DEXA machine used. Selecting the femoral neck t-score gives the wrong DEXA result because the normative t-score values used by Hologic differ from the FRAX. Selecting BMD without specifying the machine does not give an accurate score as it defaults to no bone mineral density result. Three separate FRAX scores were calculated: (1) FRAX by femoral neck T-score (T score FRAX), (2) FRAX by femoral neck BMD (No BMD FRAX), and (3) FRAX by BMD with Hologic machine selected (BMD FRAX). The latter score was the gold standard. It was determined whether the patient was ultimately appropriately treated by chart review.

Results: Patients were primarily female (94%), age ranged from 40-89 years old, and race was primarily Hispanic (54.7%) and black (31%). There was a difference when comparing BMD FRAX with the machine generated FRAX (p<.05), and between the BMD FRAX with T-Score BMD (p=0.001). However, these differences were not clinically significant. There were clinically and statistically significant differences when comparing treatment of BMD FRAX with no BMD FRAX (P < .001), all of whom would be over treated if using the latter. Four patients (2.4%) were over treated by FRAX guidelines, however, justification was given for each case. Four patients (2.4%) were undertreated. In 3 of these patients, no FRAX score was mentioned in patient notes and in 1 patient FRAX score was interpreted incorrectly.

Conclusion: Not selecting DEXA machine type can lead to significant overtreatment of patients. Many patients were undertreated due to lack of understanding of FRAX score by clinicians. Further education of clinicians regarding FRAX score use is needed. Modification of the FRAX score calculation may be required to ensure patients are not being over or under treated.

Disclosure: A. Vig, None; B. Johnson, Johnson and Johnson, 1,TREG, 5; T. Francis, None; B. Mendez-Agrusa, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/factors-affecting-frax-score-calculation-treatment-in-practice

Abstract Number: 1230

Comparative Study of Frax® Score in Ecuadorian Population

Genesis Maldonado¹, Carlos Paredes¹, Roberto Guerrero¹, Maricarmen Mieles¹, Maria Jose Intriago¹, O Messina² and Carlos Rios³,
¹Universidad Espíritu Santo, Guayaquil, Ecuador, ²Hospital Argerich, Buenos Aires, Argentina, ³Centro de Reumatología y Rehabilitación CERER, Guayaquil, Ecuador

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Osteoporosis is a systemic skeletal disease characterized by a decrease in bone mineral density with alterations in bone microarchitecture and an increased risk of fracture. The World Health Organization asserts that it is a major public health problem and increases morbidity and mortality in elderly patients. The FRAX® score is a tool that estimates the risk of fracture at 10 years. It was adapted to the Ecuadorian population in 2009. The purpose of this study was to identify the risk of fracture of the Ecuadorian population using the FRAX® Ecuador calculator and compare the results with FRAX® Colombia, Brazil and the United States (Hispanics).

Methods: A retrospective study that included the Ecuadorian population between 40-90 years old, who underwent bone densitometry between 2013-2015, and whose risk of fracture was assessed with FRAX® Ecuador, Colombia, Brazil and the United States (Hispanics). The DXA values considered were: Osteopenia: T Score -1.0 -2.5 and Osteoporosis: T Score ≥2.5.

Results: We analyzed 1154 patients with a mean age of 61.39 [SD 11.07] (26-97). The predominant gender was female with 88.6% (1022) versus 11.4% (132) male. The mean age of menopause was 45.81 [SD 5.5]. The diagnoses according to bone densitometry were: 18.8% (217) normal, 32.3% (373) osteopenia and 48.9% (564) osteoporosis. The risk of major osteoporotic fracture of the population using FRAX® Ecuador was 1.5% (0.3-27%) and hip 0.5% (0-22%). For FRAX Colombia: 3.0% (0.2-40%) for major osteoporotic fracture and 0.8% (0-34%) for hip fracture. For FRAX Brazil: 4.2% (1.2-56) was obtained for major osteoporotic fracture and 1.3% (0-49%) for a hip. Finally, FRAX® USA (Hispanic) had a risk of 5.1% (0.7-59%) for major osteoporotic fracture and 1.2% (0-50%) for hip fracture.
Conclusion: The risk of fracture for the Ecuadorian population according to the FRAX® Ecuador calculator was 1.5% for major osteoporotic fracture and 0.5% for hip fracture. Surprisingly, this population presents a low risk of fracture using the calculator of this country, in comparison to the scores obtained using the FRAX® of Colombia, Brazil and the United States (Hispanic). This may indicate that the risk of fracture may be underestimated with FRAX® Ecuador, although more specific studies are needed.

Disclosure: G. Maldonado, None; C. Paredes, None; R. Guerrero, None; M. Mieles, None; M. J. Intriglio, None; O. Messina, None; C. Rios, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/comparative-study-of-frax-score-in-ecuadorian-population

Abstract Number: 1231

Scope and Consistency of Adherence Related Outcomes in Randomized Controlled Trials of Interventions for Improving Medication Adherence

Ayano Kelly1,2,3,4, Daniel Sumpton3,5,6, Clare O'Sullivan2, Alexa Meara7, Robby Nieuwlaat8, Peter Tugwell9,10,11, Lyn March12,13,14, Allison Tong3,6, Karine Toupin-April15, Francois Nantel16, B.J.F. Van den Bemt (PharmD, PhD)17,18, Mary De Vera19, Vicki Evans20, Willemina Campbell21, Peter Wong22, Rebecca Davey23, Dorcas Beaton24,25,26, Maria Suarez-Almazor27,28,29,30, Geraldine Hassett31,32, Helen I. Keen33,34,35, Therese Dawson36, Luke Crimston-Smith37 and Kathleen Tymms38, 1Rheumatology, Canberra Rheumatology, Canberra, Australia, 2Rheumatology, The Canberra Hospital, Canberra, Australia, 3Centre for Kidney Research, The Children's Hospital at Westmead, Sydney, Australia, 4School of Medicine, Australian National University, Canberra, Australia, 5Department of Rheumatology, Concord Hospital, Sydney, Australia, 6Sydney School of Public Health, University of Sydney, Sydney, Australia, 7Internal Medicine/Rheumatology, The Ohio State University Wexner Medical Center, Columbus, OH, 8Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, ON, Canada, 9Center For Global Health, Institute of Population Health, Ottawa, ON, Canada, 10Institute of Population Health, Center For Global Health, University of Ottawa, Ottawa General Hospital, Ottawa, ON, Canada, 11Center For Global Health, Institute of Population Hlth, Ottawa, ON, Canada, 12Department of Rheumatology, Northern Clinical School, Institute of Bone and Joint Research, Kolling Institute, University of Sydney & Department of Rheumatology, Royal North Shore Hospital, St Leonards, Sydney, Australia, 13Rheumatology, Institute of Bone and Joint Research, Kolling Institute, University of Sydney, Sydney, Australia, 14Rheumatology, University of Sydney, Institute of Bone and Joint Research, Royal North Shore Hospital, St Leonards NSW, Australia, 15Children’s Hospital of Eastern Ontario Research Institute, Ottawa, ON, Canada, 16Medical Affairs, Janssen Inc., Toronto, ON, Canada, 17Pharmacy, Sint Maartenskliniek and Raboudumc, Nijmegen, Netherlands, 18Pharmacy, Sint Maartenskliniek, Nijmegen, Netherlands, 19Pharmaceutical Sciences, The University of British Columbia, Vancouver, BC, Canada, 20Clear Vision Consulting, Canberra, Australia, 21Rheumatology, Toronto Western Hospital, Toronto, ON, Canada, 22Mid-North Coast Arthritis Clinic and University of New South Wales Rural Clinical School, Coffis Harbour, Australia, 23Arthritis ACT, Canberra, Australia, 24Research, Mobility Program Clinical Research Unit, Li Ka Shing Knowledge Institute, St. Michaels Hospital, Toronto, ON, Canada, 25Scientist, Institute for Work & Health, Toronto, ON, Canada, 26Mobility Program Clinical Research Unit, St Michael's Hospital, Toronto, ON, Canada, 27GIM, AT & EC, UT MD Anderson Cancer Center, Houston, TX, 28Section of Rheumatology and Clinical Immunology, Department of General Internal Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA, Houston, TX, 29Section of Rheumatology and Clinical Immunology, Department of General Internal Medicine., The University of Texas MD Anderson Cancer Center, Houston, TX, 30The University of Texas MD Anderson Cancer Center, Houston, TX, 31Rheumatology, Liverpool Hospital, Sydney, Australia, 32Ingham Institute, Sydney, Australia, 33Rheumatology, Royal Perth Hospital, Perth, Australia, 34Leeds, Leeds, United Kingdom, 35School of Medicine and Pharmacology, University of Western Australia, Perth, Australia, 36Rheumatology, Lord Street Specialist Centre, Port Macquarie, Australia, 37Australian National University, Canberra, Australia, 38ANU, Canberra, Australia

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017

Session Title: Patient Outcomes, Preferences, and Attitudes Poster II

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM
**Background/Purpose:** Poor medication adherence attenuates optimal clinical benefits and reduces the overall effectiveness of health systems. A large number of interventions targeting medication adherence have been evaluated in randomized controlled trials (RCTs). However, there is no consensus on which adherence related outcomes should be used in these RCTs. We sought to assess the scope and consistency of adherence related outcome domains and measures in RCTs of medication adherence interventions.

**Methods:** Four reviewers independently extracted the adherence outcome domains and measures from RCTs included in the 2014 Cochrane review of interventions for enhancing medication adherence. Adherence as an outcome domain was classified into phases (using the ABC taxonomy these were divided into initiation, implementation, persistence or phase unclear). The time points, metric and method of aggregation of each outcome measure were also extracted. Contextual factors (any factor that may affect adherence but not measuring adherence itself) were also extracted.

**Results:** From 70 trials, the four adherence outcome domains (initiation, implementation, persistence and phase unclear) were measured using 68 different adherence measures, with a mean of 2 adherence measures per trial (range 1-5). For adherence outcome domains, implementation adherence was reported most frequently (61 trials [87%]), followed by persistence adherence (7 trials [10%]) and initiation adherence (2 trials [3%]). The phase of adherence being measured was unclear in 15 trials [21%]. There were 37 different contextual factors. The six most common contextual factors reported were disease knowledge (7 trials [10%]), medication knowledge (5 trials [7%]), lifestyle adherence (5 trials [7%]), medication satisfaction (4 trials [6%]), clinical care satisfaction (4 trials [6%]), and self efficacy (4 trials [6%]).

**Conclusion:** Implementation adherence is the primary type of adherence outcome domain reported. Adherence measures in RCTs are heterogeneous with a lack of uniformity. Many other factors that may be relevant to adherence are being reported in RCTs however their importance needs further evaluation. Additional work to ensure consistent reporting of robust outcome domains and measures that are relevant to all stakeholders, particularly patients, will improve the value of clinical trials in supporting evidence-based decision-making regarding medication adherence.

**Disclosure:** A. Kelly, None; D. Sumpton, None; C. O'Sullivan, None; A. Meara, None; R. Nieuwlaat, None; P. Tugwell, None; L. March, None; A. Tong, None; K. Toupin-April, None; F. Nantel, Janssen Inc., 3; B. J. F. Van den Bernt (PharmD, PhD), Pfizer Inc, 8; Abbie, 8; Sandoz, 8; UCB, 8; M. De Vera, None; V. Evans, None; W. Campbell, None; P. Wong, Novartis Pharmaceutical Corporation, 5; Roche Pharmaceuticals, 5; Abbott Immunology Pharmaceuticals, 5; R. Davey, None; D. Beaton, None; M. Suarez-Almazor, Rheumatology Research Foundation, 2; G. Hassett, None; H. I. Keen, None; T. Dawson, None; L. Crimston-Smith, None; K. Tymms, None.


Abstract Number: 1232

**The Perceived Impact of Recent-Onset Psoriatic Arthritis Is Different between Genders: A Spanish Multicenter Experience**

Rubén Queiro⁴, Ana Laiz², Carlos Alberto Montilla-Morales³, Eva Galindez-Agirrekoia⁴, Juan J. Bethencourt⁶ and Daniel Seoane⁶, ¹Rheumatology Department. Hospital Universitario Central de Asturias, Oviedo, Spain, ²Rheumatology, HU. Santa Creu i San Pau, Barcelona, Spain, ³Hospital Clínico Universitario de Salamanca, Salamanca, Spain, ⁴Rheumatology Division, Hospital Universitario de Basurto, Bilbao, Spain, ⁵Rheumatology, HU. Canarias, Sta. Cruz de Tenerife, Spain, ⁶Research Unit, Spanish Foundation of Rheumatology, Madrid, Spain

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Patient Outcomes, Preferences, and Attitudes Poster II  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Some studies point to a differential clinical expression between men and women with PsA, but the information on gender differences is very scarce in the earliest stages of the disease. We aimed to describe the baseline characteristics and impact of disease among men and women included in the REAPSER (Recent-Onset PsA Registry of the Spanish Society of Rheumatology) cohort.
Methods:

REAPSER is an observational, multicenter study, with consecutive recruitment, that included adults of both sexes aged 18 yr or older that met CASPAR criteria for PsA, and had duration of less than two years since the appearance of symptoms attributed to PsA (recent-onset PsA). Annual follow-up visits will be carried out for 5 years. Measurements include socio-demographic data, employment status and impact of the disease, family history of PsA and other inflammatory diseases, comorbidities, lifestyle, use of health services, clinical status at disease presentation, anthropometric data, clinical evaluation of PsA manifestations, radiographic progression, analytical determinations, and treatment of the disease. The study has been approved by the ethical committees of the participating centers.

We have analyzed these aspects among men and women, with special emphasis on the perceived impact of the disease between both sexes. Descriptive statistic included central measures with dispersion values. Qualitative variables were compared by Chi-square and Fisher’s exact test. The normal quantitative variables were compared by a Student’s T test and the non-normal quantitative ones by non-parametric tests.

Results:
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>50.2 (13.8)</td>
<td>49.6 (14.1)</td>
<td>NS</td>
</tr>
<tr>
<td>University studies</td>
<td>18.3%</td>
<td>16.2%</td>
<td>NS</td>
</tr>
<tr>
<td>Active worker</td>
<td>65%</td>
<td>49.3%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI</td>
<td>27.3 (4.8)</td>
<td>28.5 (6)</td>
<td>NS</td>
</tr>
<tr>
<td>Waist-hip index</td>
<td>0.94 (0.1)</td>
<td>0.87 (0.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Smoker</td>
<td>29.6%</td>
<td>32.4%</td>
<td>NS</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>45.1%</td>
<td>16.2%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Psoriasis family history</td>
<td>40.1%</td>
<td>45.6%</td>
<td>NS</td>
</tr>
<tr>
<td>PsA family history</td>
<td>8.5%</td>
<td>10.3%</td>
<td>NS</td>
</tr>
<tr>
<td>Charlson’s CI (&gt; 3)</td>
<td>18.3%</td>
<td>17.6%</td>
<td>NS</td>
</tr>
<tr>
<td>Depression</td>
<td>81%</td>
<td>61.8%</td>
<td>0.003</td>
</tr>
<tr>
<td>Common Psoriasis</td>
<td>2.1%</td>
<td>11.8%</td>
<td>0.006</td>
</tr>
<tr>
<td>Pustular Psoriasis</td>
<td>8.5%</td>
<td>19.1%</td>
<td>0.027</td>
</tr>
<tr>
<td>No psoriasis</td>
<td>59%</td>
<td>49%</td>
<td>NS</td>
</tr>
<tr>
<td>Onicopathy</td>
<td>1.5 (0.6-4.4)</td>
<td>1.2 (0.6-3)</td>
<td>NS</td>
</tr>
<tr>
<td>PASI</td>
<td>80.3%</td>
<td>83.8%</td>
<td>NS</td>
</tr>
<tr>
<td>Peripheral pattern</td>
<td>7%</td>
<td>1.5%</td>
<td>NS</td>
</tr>
<tr>
<td>Axial pattern</td>
<td>12.7%</td>
<td>14.7%</td>
<td>NS</td>
</tr>
<tr>
<td>Mixed Pattern</td>
<td>4 (2-7.2)</td>
<td>4 (2-8)</td>
<td>NS</td>
</tr>
<tr>
<td>TJC68</td>
<td>2 (1-4)</td>
<td>2 (0-5)</td>
<td>NS</td>
</tr>
<tr>
<td>SJC66</td>
<td>4.1 (2.2-6)</td>
<td>4.8 (2.4-7.3)</td>
<td>0.008</td>
</tr>
<tr>
<td>BASDAI (0-10)</td>
<td>1.8 (0.4-4.5)</td>
<td>2.9 (1.4-4.7)</td>
<td>0.065</td>
</tr>
<tr>
<td>BASFI (0-10)</td>
<td>31.4%</td>
<td>47.1%</td>
<td>0.028</td>
</tr>
<tr>
<td>Dactylitis</td>
<td>12 (5-20)</td>
<td>21 (10-29.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CI: comorbidity index. PASI: Psoriasis Area and Severity Index. Data are expressed in percentages, mean with SD (Standard Deviation), median and IQR (Interquartile Range).

**PROs**

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
<th>p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain VAS</td>
<td>4 (2-7)</td>
<td>6 (4-7)</td>
<td>0.025</td>
</tr>
<tr>
<td>Pat. global disease activity</td>
<td>5 (3-7)</td>
<td>6 (3-8)</td>
<td>0.042</td>
</tr>
<tr>
<td>PsAID</td>
<td>3.1 (1.5-6.1)</td>
<td>4.2 (2.3-6)</td>
<td>0.063</td>
</tr>
<tr>
<td>HAQ</td>
<td>0.4 (0-1)</td>
<td>0.8 (0.4-1)</td>
<td>0.010</td>
</tr>
</tbody>
</table>

Conclusion:

Female scored higher in several PROs compared to male. Thus the perception of having a severe disease is higher in female. This information could be of help for improving medical care for women with PsA.

Disclosure: R. Queiro, None; A. Laiz, None; C. A. Montilla-Morales, None; E. Galindez-Agirregoikoa, None; J. J. Bethencourt, None; D. Seoane, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-perceived-impact-of-recent-onset-psoriatic-arthritis-is-different-between-genders-a-spanish-multicenter-experience

Abstract Number: 1233

Establishing and Maintaining a Volunteer Charity Rheumatology Clinic: One Clinic’s Experience

Narender Annapureddy1, Michelle J. Ormseth2, Julie Barnes3 and James Gore4, 1Rheumatology and Immunology, Vanderbilt University Medical Center, Nashville, TN, 2Rheumatology, Vanderbilt Medical Center, Nashville, TN, 3Vanderbilt University Medical Center, Nashville, TN, 4Vanderbilt Rheumatology Cool Springs, Franklin, TN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Establishing and Maintaining a Volunteer Charity Rheumatology Clinic: One Clinic’s Experience

Background/Purpose: In 2015, about 16% of adults under age 65 in Tennessee were uninsured. While there are options available for patients to receive primary care (health departments and faith-based benevolent clinics), there were limited options for rheumatology care, creating serious health risks for these patients. We set out to establish volunteer charity clinic to provide consultation and management for adult rheumatology patients who are uninsured.

Methods: The St. Sampson medical clinic was established as a 501c3 nonprofit organization, operating one Saturday per month since 2012. It’s yearly budget of $15,000, mostly for malpractice coverage, and clinic space was donated by the Lupus Foundation of America Mid-South Chapter, Tennessee Rheumatology Society, and Holy Trinity Greek Orthodox Church. The clinic has three Vanderbilt providers, two rheumatologists and a nurse practitioner, and other volunteers for intake. It uses an encrypted, password-protected electronic medical record designed for the clinic and HIPPA-compliant efax to communicate with referring providers. Clinic flow is shown in figure 1.

Results: As of May 2017, we have provided 1538 visits to 560 patients from 33 counties in Tennessee, Kentucky and Mississippi. The majority of diseases treated include rheumatoid arthritis/ other inflammatory arthritis (46%), lupus/ other connective tissue diseases (15%), fibromyalgia syndrome (11%), and psoriatic arthritis (7%). We have secured over $500,000 in free medications, largely for biologic agents through patient assistance programs. We estimate we have donated $186,703 in professional fees (consultations: $94,080; return visits: $92,623) to our patients.

Conclusion: We have been able to establish and maintain a successful volunteer charity rheumatology clinic with limited resources which has provided much needed care for rheumatology patients. Rheumatology is unique as a specialty as clinical history and physical examination play a majority role in diagnosis which was an important factor in being able to establish and sustain a volunteer charity clinic.
How Machine Learning Statistics Can Change the Game of Data Analysis in Rheumatology: The Example a Study with 170 Patients with Rheumatoid Arthritis (ra) or Axial Spondyloarthritis (axspa)

Frédéric Guyard\textsuperscript{1}, Laure Gossec\textsuperscript{2}, Didier Leroy\textsuperscript{3}, Thomas Lafargue\textsuperscript{1}, Michel Seiler\textsuperscript{3}, Charlotte Jacquemin\textsuperscript{4}, Anna Molto\textsuperscript{5}, Jeremie Sellam\textsuperscript{6}, Violine Foltz\textsuperscript{4}, Frédérique Gandjbakhch\textsuperscript{3}, Christophe Hudry\textsuperscript{7}, Stéphane Mitrovic\textsuperscript{4}, Bruno Fautrel\textsuperscript{4} and Hervé Servy\textsuperscript{8}, \textsuperscript{1}IMT, Orange, Nice, France, \textsuperscript{2}UPMC, University Paris 06, Pitié-Salpêtrière Hospital, Paris, France, \textsuperscript{3}Healthcare, Orange, Paris, France, \textsuperscript{4}UPMC University Paris 06, Pitié-Salpêtrière Hospital, Paris, France, \textsuperscript{5}Hôpital Cochin, Department of Rheumatology, Paris Descartes University, Paris, France, \textsuperscript{6}Rheumatology, Saint-Antoine Hospital, Paris, France, \textsuperscript{7}AP-HP Hôpital Cochin, Paris, France, \textsuperscript{8}e-health services, Sanoia, Gemenos, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: A link between flares and physical activity would confirm the objective consequences of flares. In the ActConnect study of patients with RA or axSpA, the initial analyses made with traditional statistical tools on aggregated data found a low magnitude link between flares and physical activity\textsuperscript{(1)}. The objective of this reanalysis was to determine if applying Machine Learning technics (i.e., Big Data statistics) to this dataset, could lead to more accurate results about flares prediction.

Methods: In the ActConnect study, physical activity (steps) were collected through an activity tracker at the minute level, during 3 months for 170 patients, leading to 27 million information points that have been aggregated at the level of 24 hours \textsuperscript{(1)}. Patients also reported weekly their perceived flares. In this reanalysis, multi-class Bayesian classifications were performed to find a link between physical activity and flares / no flares states, using a Machine Learning software belonging to Orange \textsuperscript{(2)}. A normalization was performed to calibrate for each patient their pattern associated with no flares. As the data are sampled by minutes, models were designed using several aggregation intervals (24h, 12h, 4h, 1h) then trained randomly on 70% of data for each interval and tested on the remaining 30%. To evaluate the stability of the models, the complete analysis was done 10 times for each interval of aggregation. The performance of the models was evaluated using patient-reported flares (assessed weekly) as gold standard. Sensitivity, specificity and kappa were assessed.
Results: The modeling performance increased as the aggregation interval decreased. The best performance was evidenced for 1-hour interval (table 1). The increase in the agreement between the true classes and the predicted classes was also reflected in the substantial increase of the Kappa coefficient when the size of the aggregation intervals decreased (for 24 hours, kappa=0.51 [95% confidence interval 0.47, 0.56]; for 1 hour: kappa=0.90 [0.87, 0.92]).

Conclusion: Connected devices bring huge data-flows that cannot be handled with traditional statistical tools without data aggregation. Machine Learning techniques, which can compute raw datasets with minimal aggregation, bring more accurate predictions. These may contribute to a more precise quantification of existing links or to the identification of new links in rheumatological datasets.


2- Khiops software for data mining, PredicSis: [https://khiops.predicsis.com](https://khiops.predicsis.com)

<table>
<thead>
<tr>
<th>Aggregation</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>24h</td>
<td>0.80</td>
<td>0.86</td>
<td>0.48</td>
<td>0.96</td>
</tr>
<tr>
<td>12h</td>
<td>0.83</td>
<td>0.89</td>
<td>0.61</td>
<td>0.96</td>
</tr>
<tr>
<td>4h</td>
<td>0.87</td>
<td>0.95</td>
<td>0.85</td>
<td>0.96</td>
</tr>
<tr>
<td>1h</td>
<td>0.89</td>
<td>0.99</td>
<td>0.96</td>
<td>0.97</td>
</tr>
</tbody>
</table>

Table 1: Performance indicators for various intervals of aggregation of physical activity to detect patient-reported flares

Disclosure: F. Guyard, Orange, 3; L. Gossec, None; D. Leroy, Orange, 3; T. Lafargue, Orange, 3; M. Seiler, Orange, 3; C. Jacquemin, None; A. Molto, None; J. Sellam, None; V. Foltz, None; F. Gandjbakhch, None; C. Hudry, None; S. Mitrovic, None; B. Fautrel, AbbVie, Biogen, BMS, Celgene, Hospira, Janssen, Eli Lilly and Company, Novartis, Pfizer, Roche, SOBI Pharma, UCB, 5; H. Servy, None.


Abstract Number: 1235

**Perceived Stress and Fatigue in Systemic Lupus Erythematosus**

**Patricia P. Katz**, 1, Desiree R Azizoddin, 2 and Meenakshi Jolly, 3, 1 Medicine/Rheumatology, University of California, San Francisco, San Francisco, CA, 2 Department of Medicine and Behavioral Sciences, Rush University, Chicago, IL, 3 Rheumatology, Rush University Medical Center, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017

Session Title: Patient Outcomes, Preferences, and Attitudes Poster II

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM

Background/Purpose: Fatigue is a common and often severe symptom among individuals with systemic lupus erythematosus (SLE). Yet, there is an incomplete understanding of the causes of fatigue. We examined perceived stress and depressive symptoms as potential predictors of fatigue in a large cohort of individuals with SLE.

Methods: Data from two years of the Lupus Outcomes Study (n = 650), obtained through annual structured telephone interviews, were used. All participants had physician-confirmed SLE. Fatigue was measured with the SF-36 Vitality scale (reversed); scores ranged from 0 – 100, with higher scores indicating greater fatigue. The following additional measures were also administered: 4-item Cohen Perceived Stress scale (PS), Centers for Epidemiological Studies Depression scale (CESD); Systemic Lupus Activity Questionnaire (SLAQ, self-reported disease activity), and Brief Index of Lupus Damage (BILD; self-reported lupus damage). Cross-sectional
multivariate linear regression analyses examined the association of CESD and PS on fatigue. Longitudinal analyses were then conducted to identify predictors of increases in fatigue. Three longitudinal regression models were constructed. The first examined the association of CESD at time 1 (T1) with fatigue at time 2 (T2), controlling for T1 fatigue, age, sex, disease duration, SLAQ, BILD, comorbid conditions, self-report of fibromyalgia, obesity, and pain (SF-36 Pain subscale). The second model then added PS at T1, and the third added decrease in PS from T1 to T2.

**Results:** Sample characteristics are shown in Table 1. In cross-sectional analyses, both CESD and PS were significantly associated with fatigue (Table 2). In longitudinal analyses, T1 CESD was a significant independent predictor of T2 fatigue (Table 2, Model 1). When T1 PS was added (Model 2), PS was a significant predictor of T2 fatigue but CESD was no longer significant. The further addition of T1-T2 decrease in PS increased the predictive power of the model (Model 3), and decline in PS was associated with a significant decrease in fatigue.

**Conclusion:** Both depressive symptoms and perceived stress were associated with concurrent fatigue. While depressive symptoms initially predicted subsequent increases fatigue, the effects were mediated by perceived stress. Furthermore, a decrease in perceived stress was associated with a decrease in fatigue. These results suggest that perceived stress plays an important role in SLE fatigue and may be an important focus of interventions to reduce fatigue.

<table>
<thead>
<tr>
<th>Table 1. Characteristics of sample, n = 650</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>T1 SLE activity (0 – 10)</td>
</tr>
<tr>
<td>T1 BILD (0 – 12)</td>
</tr>
<tr>
<td>T1 Pain (0 – 100)*</td>
</tr>
<tr>
<td>T1 CES-D score</td>
</tr>
<tr>
<td>T1 Fatigue (0 – 100)</td>
</tr>
<tr>
<td>T1 Perceived stress score (0 – 16)</td>
</tr>
<tr>
<td>T1-T2 decline in stress (≥ 2 points)</td>
</tr>
</tbody>
</table>

* Lower scores reflect higher pain

<table>
<thead>
<tr>
<th>Table 2. Multivariate analysis results</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cross-sectional analysis</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>CESD</td>
</tr>
<tr>
<td>Perceived stress</td>
</tr>
<tr>
<td>T1-T2 decrease in perceived stress</td>
</tr>
<tr>
<td>Model R²</td>
</tr>
</tbody>
</table>

• Tabled values are beta (p-value) from multivariate linear regression analysis
• Cross-sectional analyses controlled for T1 age, sex, disease duration, self-reported disease activity and damage, pain, comorbid conditions, self-report of fibromyalgia, and obesity.
• Longitudinal analyses controlled for the above plus T1 fatigue.
The Influence of Testimonials on Patient Decision-Making

Changchuan Jiang¹, Ellen Peters² and Liana Fraenkel³, ¹Yale University, New Haven, CT, ²Decision Research, Eugene, OR, ³Rheumatology, Rheumatology, Yale University School of Medicine, New Haven, CT

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Testimonials have been shown to have a strong influence on patient decision-making. Patients are increasingly accessing the Internet as a source of medical information. In this study, we sought to examine whether the presence and order of patients’ testimonials influenced participant’s willingness to take a medication, subjective knowledge, and risk perceptions.

Methods: We administered a survey to senior Mechanical workers (≥ 50 years old; not on medication for osteoporosis or osteopenia) to examine the influence of online medication reviews on participants’ stated willingness to take an osteoporosis medication. We first described osteoporosis and its complications and subsequently asked participants to imagine themselves as a patient with this disease in a clinical encounter during which a physician recommended treatment. Participants’ received information describing outcomes using one of three randomly distributed versions: Icon arrays, icon arrays followed by narrative reviews, or narrative reviews followed by icon arrays. Numeracy was measured using the Rasch-based Numeracy Scale. Participant’s willingness to take a medication, subjective knowledge, perceived benefit, riskiness, and worry related to the medication were measured on 10-point scales before and after reading the description of the medication presented in one of the three versions. We examined whether the presence and order of online testimonials influenced participant’s willingness to take the described medication using a linear regression including age, sex, race, education, previous history of osteoporosis/fracture. Numeracy as a main effect and effect modifier were also included in the model. Similar models were used to examine the influence of online testimonials on participant’s subjective knowledge, perceived benefit, riskiness, and worry.

Results: 499 valid responses were included in the analyses. The mean (SD) age was 59 (7), and the majority were female (61%), white (74%) and college graduate (56%). We found no significant differences in participant’s willingness (p=0.21), subjective knowledge (p=0.43), perceived benefit (p=0.12), riskiness (p=0.51), and worry (p=0.06) across the three groups. Participants with higher numeracy were significantly more willing take the medication (p=0.04). Race was associated with riskiness and worry, with minority subjects having significantly higher scores on both scales. In contrast, participants with personal history of osteoporosis/low bone density were more likely to perceive greater benefit of the medication (p=0.04).

Conclusion: In this study, we found no main effect of the presence or order of online testimonials on participants’ decision-making. Interestingly, willingness and perceptions related to risks and benefits were each associated with different personal characteristics.

Disclosure: C. Jiang, None; E. Peters, None; L. Fraenkel, None.

Group Strength Training in Rheumatology Patients: Results of an Exercise Survey
Primary care (PC) patients have shown significant interest in a community-based group strength training (GST) program, especially among those in poor health\(^1\). Exercise is known to reduce inflammation, improve symptoms such as fatigue and poor mental health, and has proven benefits in rheumatoid arthritis (RA), osteoarthritis (OA) and fibromyalgia (FMS). Group exercise program design improves adherence in PC patients but it is unknown the effect on exercise adherence in rheumatology patients. In this study, we examined the interest of rheumatology patients and the effect of comorbidities in pursuing an organized GST program. We hypothesized that rheumatology patients would be as interested in a GST program compared to a previous study of PC patients.

**Methods:**

We conducted a cross-sectional survey of rheumatology patients from a rheumatology practice in central Pennsylvania in February and April 2017. This survey\(^1\), modified for rheumatology patients, assessed self-reported interest of patients in GST programs in addition to demographics, comorbidities, and quality of life measures. Logistic regression was used to quantify interest in a GST. PC data from the study by Sciamanna et al were used for comparative analysis for the primary outcome, interest in a GST program.

**Results:**

A total of 397 of 656 patients returned surveys with a response rate of 61.6%. Patients had a mean age of 52, 80% were female, with RA (39.0%), FMS (21.4%), and OA (19.7%) as the most common rheumatology diagnoses. 50.1% of rheumatology patients were interested in a GST program and there was no difference of interest compared to the PC patients\((X^2=2.04, p=0.15)\). Perceived health was worse in rheumatology patients (45.1%) compared to PC patients (18.8%). However, there was no difference in interest in a GST for rheumatology patients with poor health compared to patients with good health (OR=0.9, p=0.8, Table 1). Female rheumatology patients were more interested in GST than male patients (OR=3.7, p=0.001). Patients with a BMI of 25-30 (OR=2.2, p=0.04) or >30 (OR=1.7, p=0.12) were also more interested compared to those with a normal BMI. There was no difference in interest in GST regardless of rheumatology disease or measured comorbidities.

**Conclusion:**

Over 50% of rheumatology patients were interested in a GST exercise program design. While rheumatology patients have worse perceived health than published PC health perceptions, interest in GST remained the same. Our data suggests that rheumatologists can recommend GST for their patients regardless of disease, medical comorbidities, perceived mental or physical health or education level. Future studies should examine if a GST program design improves exercise adherence in rheumatology patients.

**Reference:**

<table>
<thead>
<tr>
<th>Item</th>
<th>Odds Ratio</th>
<th>Confidence Interval</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age Group</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-44 [reference]</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>45-54 0.57</td>
<td>(0.27, 1.23)</td>
<td>0.15</td>
<td></td>
</tr>
<tr>
<td>55-64 1.16</td>
<td>(0.53, 2.54)</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>≥65 0.8</td>
<td>(0.33, 1.91)</td>
<td>0.61</td>
<td></td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male [reference]</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Female 3.67</td>
<td>(1.76, 7.63)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td><strong>Smoking Status</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-smoker [reference]</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Smoker 0.54</td>
<td>(0.26, 1.12)</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td>1.2</td>
<td>(0.62, 2.32)</td>
<td>0.6</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td>1.63</td>
<td>(0.63, 4.22)</td>
<td>0.31</td>
</tr>
<tr>
<td><strong>High Cholesterol</strong></td>
<td>1.11</td>
<td>(0.58, 2.16)</td>
<td>0.75</td>
</tr>
<tr>
<td><strong>Coronary Artery Disease</strong></td>
<td>0.9</td>
<td>(0.27, 2.97)</td>
<td>0.87</td>
</tr>
<tr>
<td><strong>BMI Group</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 25.0 [reference]</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>25.0-30.0 2.18</td>
<td>(1.05, 4.52)</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>&gt; 30 1.72</td>
<td>(0.87, 3.41)</td>
<td>0.12</td>
<td></td>
</tr>
<tr>
<td><strong>Days of Aerobic Activity/Week</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 [reference]</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>1-3 0.83</td>
<td>(0.44, 1.56)</td>
<td>0.56</td>
<td></td>
</tr>
<tr>
<td>4-7 1.63</td>
<td>(0.74, 3.58)</td>
<td>0.23</td>
<td></td>
</tr>
<tr>
<td><strong>Days of Strength Training/Week</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 [reference]</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>1-3 1.57</td>
<td>(0.83, 2.97)</td>
<td>0.17</td>
<td></td>
</tr>
<tr>
<td>4-7 0.3</td>
<td>(0.12, 0.76)</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td><strong>Self-Reported Health</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excellent, Very Good, or Good [reference]</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Fair or Poor 0.92</td>
<td>(0.48, 1.76)</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td><strong>Days of Poor Physical Health/Month</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 [reference]</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>1-9 1.84</td>
<td>(0.74, 4.56)</td>
<td>0.19</td>
<td></td>
</tr>
<tr>
<td>≥ 10 2.16</td>
<td>(0.87, 5.37)</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td><strong>Days of Poor Mental</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### The Development of the Lupus Foundation of America—Rapid Evaluation of Activity in Lupus (LFA-REAL™) Patient-Reported Outcome (PRO) to Evaluate Lupus Disease Activity

**Anca Askanase**¹, Samantha Nguyen², Miya Okado², Nancy Leidy³ and Joan T. Merrill⁴, ¹Rheumatology, Columbia University Medical Center, New York, NY, ²Rheumatology, Columbia University College of Physicians & Surgeons, New York, NY, ³Evidera, Bethesda, MD, ⁴Oklahoma Medical Research Foundation, Oklahoma City, OK

**First publication:** September 18, 2017

#### SESSION INFORMATION

**Session Date:** Monday, November 6, 2017  
**Session Title:** Patient Outcomes, Preferences, and Attitudes Poster II  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The LFA REAL™ is designed as two complimentary disease activity measures in order to integrate clinician and patient input. The current report updates progress of the LFA REAL™ patient-reported outcome (PRO).  

**Methods:** The PRO was developed in accordance with FDA guidance. After preliminary concept identification work, a qualitative study was performed with 25 adult participants with SLE, including 10 who participated in concept elicitation (Phase 1) and 15 for cognitive debriefing interviews (Phase 2). A semi-structured guide was employed by trained interviewers. Qualitative data were analyzed using ATLAS.ti software v7.5. A coding dictionary was developed based on the interview guide and concepts of interest. At the completion of the interviews, participants completed the draft PRO and measures to characterize the sample (SF-36, socio-demographic, clinical data questionnaires).

**Results:** Mean age of participants was 45.6 [22-69], 88% were female and all had SLE diagnosis confirmed by their rheumatologists. The mean SF-36 physical component score (PCS) for the sample was 29.8 (±9.1), and mental component scores MCS was 46.4 (±11.6). Phase 1 elicited symptom saturation (detailed in Table 1) and mapping of the draft PRO while Phase 2 debriefed instructions, items, response options for content clarity, comprehensiveness and content validity of the draft PRO. With a recall period of 4 weeks, the PRO asks patients to evaluate their overall progress and severity of symptoms associated with current lupus activity along a series of visual analogue scales. Instructions are brief and guide the patient to active as opposed to longstanding symptoms that are more likely due to damage. The PRO allows for global, organ-based or symptom specific disease assessments from the patient’s perspective.

**Conclusion:** Results of this qualitative study address the content validity of the LFA-REAL PRO. As expected, fatigue or tiredness was spontaneously reported by 90% of patients. 100% of patients spontaneously brought up arthritis, which may be more important to this group than previously estimated and substantiates the approach to break down arthritis into joint pain, stiffness and swelling in this PRO. Shortness of breath and fever was also more common than expected. Quantitative validation of the PRO will be performed to characterize the psychometric properties of the PRO against other PROs used in lupus trials. After validation, the LFA-REAL system is
intended for clinical practice and clinical trial use.

**Disclosure:** A. Askanase, None; S. Nguyen, None; M. Okado, None; N. Leidy, Evidera PPD, 3; J. T. Merrill, None.


**Abstract Number:** 1239

**Web Based Educational Intervention to Improve Cardiovascular Disease Knowledge Among RA Patients**

Meenakshi Jolly¹, Aman Kugasia², Carlos Cordova³, Josheen Fair³, Eleftheria Steinig⁴, Rasa Kazkaukaite⁵, Lisa Walt⁶, Mondira Sengupta⁷ and Joel A. Block², ¹Rush, Chicago, IL, ²Division of Rheumatology, Rush University Medical Center, Chicago, IL, ³Rheumatology, Rush University Medical Center, Chicago, IL, ⁴Northwestern University, Chicago, IL, ⁵Rush University, Chicago, IL, ⁶American Hospital Association, Chicago, IL, ⁷John H Stroger Hospital of Cook County, Chicago, IL

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Patient Outcomes, Preferences, and Attitudes Poster II  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The major cause of mortality in patients with Rheumatoid Arthritis (RA) is cardiovascular disease (CVD). However traditionally, very few RA patients receive screening and treatment for modifiable CVD risk factors; rates as low as 27-45%. The primary objective was to (a) evaluate baseline cardiovascular risk awareness (CVRA) in patients with RA and to (b) compare CVRA among RA patients before, and immediately after, a web-based educational intervention (EI).
Methods: Consecutive patients at two academic centers with a diagnosis of RA of at least 3 months’ duration were enrolled. Patients completed questionnaires on demographics, RA and CVRA. CVRA was measured using the Heart Disease Knowledge Questionnaire (HDKQ; 30 items), and the Heart Disease Fact Questionnaire-RA (HDFQ-RA; 13 items); and were administered at baseline and immediately after EI. The EI consisted of a 28-minute educational video developed specifically to address CVRA in the context of RA. Experts in CVD prevention, educational intervention and RA were involved in developing the EI. The video also included RA patient testimonials to normalize health behavior change and provide motivation. This short video focused primarily on CVD issues pertinent to RA patients. These included exercise in the context of RA, the control of RA, and medications. The EI and the questionnaires were pilot tested on set of RA patients. General linear model analyses for repeated measures were used to compare within person changes in CVRA. Effect size (ES) were calculated for observed improvements in CVRA.

Results: 86 RA patients participated. The average age was 55.2±14.3 years (mean ± SD); 90% were women. Self-reported CVD risks were: post-menopause (69%), smoking (20%), hypertension (41%), diabetes mellitus (DM; 28%), sedentary lifestyle (61%), poorly controlled RA (47%) and current steroid use (35%). Ninety-five percent were taking medications for RA; most commonly methotrexate (61%) and biologics (68%). Less than half of the participants correctly answered 8/30 HDKQ and 2/13 HDFA-RA listed in Table 1. Average total scores for correct responses for HDKQ and HDFA-RA at baseline were 63% and 78%; which improved to 67% (p=0.02, ES 0.25) and 89% (p <0.001, ES=0.71) respectively after EI. Improvements in CVRA after EI on specific questions of HDKQ and KDFA-RA are shown in Table 1. The largest improvements were noted for RA specific CVRA items.

Conclusion: General understanding of CVRA is poor among RA patients, specifically RA-specific CVD risks. However, a simple and short educational intervention resulted in large improvement in CVRA, specific to their RA. This EI may serve as a cost effective intervention that could potentially increase screening for CVD risks and behavior changes in RA. Further studies are ongoing to evaluate if the knowledge gains are retained over time and if they result in changes in health behaviors.

Disclosure: M. Jolly, Pfizer Inc, 2,LupusPRO, 7; A. Kugas, None; C. Cordova, None; J. Fair, None; E. Steinig, None; R. Kazkaia, None; L. Walt, None; M. Sengupta, None; J. A. Block, None.

Abstract Number: 1240

Active Disease Is Associated with Dependency in Inflammatory Arthritis

Havva Ozturk Durmaz1, Alper Sari2, Berkan Armagan2, Abdulsamet Erden3, Levent Kilic2, Omer Karadağ4, Sedat Kiraz2, Sule Apras Bilgen3 and Umut Kalyoncu3, 1Physical Medicine and Rehabilitation, Ahi Evran University Faculty of Medicine, Kirsehir, Turkey, 2Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Turkey, 3Department of Internal Medicine, Division of Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Turkey, 4Vasculitis and Lupus Clinic, Addenbrooke’s Hospital, University of Cambridge, Cambridge, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM
**Background/Purpose:** The independency is one of the major concerns according to patients' perspective. For instance, independency is top ranking problem in psoriatic arthritis patients and it take part in PsA core set domain (1). The objectives of this study were to assess level of independency and its correlation with disease activity.

**Methods:** Patients with inflammatory arthritis were consecutively recruited. Age, sex, disease duration, education level, DMARD usage were recorded. Independence was assessed with visual activity scale (VAS)-independence (0-100 mm) according to patients' perspective. VAS - independence more than 40/100 mm were defined as "dependent patient". All patients were assessed with patient global assessment (PGA), physician global assessment (PhGA), pain VAS, fatigue VAS, swollen (66 joints), and tender joint counts (68 joints). Other measures were BASDAI, BASFI, ASDAS-CRP, DAS-28, SDAI, CDAI, and HAQ. Correlation of outcome measures with independence-VAS were calculated.

**Results:** Total 194 (66% female) patients (88 RA, 87 AS, 19 PsA) were enrolled to study. Mean age was 47.1±12 years-old and mean disease duration was 9.5 (7.8) years. 83 (42.8%) patients had less or equal than 5 years educational level and 104 (53.6%) patients had regular occupations. 88 (45.4%) patients were used biological DMARD. Independence-VAS score was zero in 141 (72.6%) patients and 28 patients (14.4%) had more or equal than 40 mm independence VAS score. Female patients were more frequently dependent than male patients (19.5% vs 4.5%, p=0.005). There was no difference at age, disease duration, incoming, occupation, disease type, biological DMARD usage according to dependence status. Dependent patients had worst disease activity and functional status (Table 1). Correlation of independence-VAS with other outcome measures were followed; HAQ (r=0.70), BASFI (r=0.64), BASDAI (r=0.58), PhGA (r=0.57), pain-VAS (0.57), PGA (r=0.52), CDAI (r=0.51), ASDAS-CRP (r=0.51), SDAI (r=0.48), fatigue-VAS (r=0.46),DAS-28 (r=0.42), TJC-68 joints (r=0.39), SJC-66 joints (r=0.27).

**Conclusion:** Being independenct is a major goal according to patients' perspective. Independency is closely related with functional disability and disease activity. However, when assessed with VAS score, a floor effect can be seen. For inflammatory arthritis patients, we need a well-defined instruments for the assessment of independence.

**Reference:**

**Table 1: Independence level and disease activity scores**

<table>
<thead>
<tr>
<th></th>
<th>Independence VAS ≥40 mm n=28</th>
<th>Independence VAS &lt; 40 mm n=166</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>PhGA</td>
<td>63 (21)</td>
<td>28 (20)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PGA</td>
<td>69 (25)</td>
<td>34 (23)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pain-VAS</td>
<td>73 (29)</td>
<td>31 (26)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fatigue-VAS</td>
<td>73 (25)</td>
<td>39 (26)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DAS-28</td>
<td>3.8 (1.1)</td>
<td>2.9 (1.3)</td>
<td>0.004</td>
</tr>
<tr>
<td>SDAI</td>
<td>19.1 (10.1)</td>
<td>10.9 (8.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>CDAI</td>
<td>17.4 (9.6)</td>
<td>9.3 (8.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BASDAI</td>
<td>6.4 (2.1)</td>
<td>2.5 (2.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BASFI</td>
<td>5.5 (2.7)</td>
<td>1.6 (1.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ASDAS</td>
<td>3.61 (0.88)</td>
<td>2.08 (1.10)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>1.0 (0.5)</td>
<td>0.33 (0.37)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>


**Disclosure:** H. Ozturk Durmaz, None; A. Sari, None; B. Armagan, None; A. Erden, None; L. Kilic, None; O. Karadag, None; S. Kiraz, None; S. Apras Bilgen, None; U. Kalyoncu, None.


**Abstract Number:** 1241
Understanding Differences in Patient Definitions of RA Flares Using Omeract Core Domains

Gabriela L. Maica1, Michelle Frits2, Christine Iannaccone3, Taysir G. Mahmoud4, Clifton O. Bingham III5, Vivian P. Bykerk6, Michael Weinblatt7 and Nancy A. Shadick8, 1Department of Rheumatology, Allergy, and Immunology, Brigham and Women's Hospital, Boston, MA, 2Brigham and Women's Hospital, Boston, MA, 3Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA, 4Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 5Rheumatology, Johns Hopkins University, Baltimore, MD, 62-005, Mt Sinai Hospital, Toronto, ON, Canada, 7Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 8Rheumatology Immunology & Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Flare is an important, distinct feature of RA, often rendering patients immobile and contributing to a poor quality of life. Recently, there has been consensus on the domains that constitute a flare (OMERACT Flare Core Domains); however, variations in patients’ definition of a flare continue to be observed. This study seeks to evaluate how demographic and clinical characteristics contribute to these differences.

Methods: Subjects enrolled in a prospective RA registry completed a qualitative flare survey which included the open ended question “What does a flare mean to you?” Responses were categorized into the OMERACT Core Domains (pain, function, swollen/tender joints, fatigue, stiffness, patient global, participation) and research domains (emotional distress, sleep disturbance). DAS28-CRP3 was collected at the same visit. Univariate analyses evaluated demographics such as age, gender and clinical characteristics, including a disease state variable that combined the DAS and flare status (yes/no in the past 6 months) into 4 groups (low DAS/no flare, low DAS/flare, moderate-high DAS/no flare, and moderate-high DAS/flare). Logistic regression analyses were used to model each of the above domains as the outcome with age, gender, and disease state as covariates.

Results: Among the 503 subjects, 84% were female, mean age (SD) was 61 years (13), and mean disease duration was 18 years (11.7). The mean DAS score was 2.3 (0.93). 55% reported at least 1 flare in the past 6 months. Of the 8 OMERACT Core Domains, this cohort reported on average 2.5 (1.3) domains when asked to define a flare. Pain (80%), physical function (44%), and painful joints (36%) were the most commonly recorded. 5 domains showed an association between flare definition and patient characteristics in individual logistic regression models (Table). When looking at DAS alone, we found no variations in patient reported domains to be statistically significant. Additional OR comparisons of DAS/flare status (moderate-high DAS/flare vs. moderate-high DAS/no flare) suggested high DAS influences a patient’s definition to include participation regardless of flare status.

Conclusion: Patients reported at least one of 8 OMERACT Core domains when defining a flare, however, these domains vary by patients’ demographic and clinical states. Furthermore, when a patient’s current disease activity and experience of recent flare are evaluated together, differences in patients’ descriptions of a flare are observed. Patients are more attuned to a flare as pain and fatigue when flaring in a low disease state. Considering a flare as a decrease in participation is influenced more by being in moderate-high disease activity. Variations in patients’ flare definitions can lend insight into how physicians approach patients and potentially shed light on the reasoning behind discordance between patient-clinician flare definitions.
<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>OMERACT Flare Domains</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
<th>Model 4</th>
<th>Model 5</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pain</td>
<td>1.0 (0.99, 1.03)</td>
<td>0.99 (0.98, 1.01)</td>
<td>0.99 (0.97, 1.01)</td>
<td>0.96 (0.93, 0.99)</td>
<td>0.95 (0.92, 0.98)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female (n=388)</td>
<td></td>
<td>1.1 (0.58, 2.09)</td>
<td>4.97 (1.75, 14.1)</td>
<td>1.3 (0.53, 3.29)</td>
<td>2.4 (0.31, 18.8)</td>
<td>0.35 (0.12, 0.98)</td>
</tr>
<tr>
<td>Low DAS28-CRP3/Flare*</td>
<td></td>
<td>2.2 (1.29, 3.76)</td>
<td>1.9 (1.15, 3.22)</td>
<td>1.8 (0.93, 3.67)</td>
<td>1.4 (0.45, 4.31)</td>
<td>0.47 (0.17, 1.29)</td>
</tr>
<tr>
<td>Moderate- High DAS28-CRP3/No Flare* (n=198)</td>
<td></td>
<td>0.46 (0.18, 1.22)</td>
<td>0.61 (0.13, 2.81)</td>
<td><strong>4.4 (1.37, 13.9)</strong></td>
<td>1.998 (0.22, 18.4)</td>
<td>2.2 (0.43, 10.96)</td>
</tr>
<tr>
<td>Moderate- High DAS28-CRP3/Flare* (n=54)</td>
<td></td>
<td>1.5 (0.69, 3.22)</td>
<td>1.9 (0.95, 3.97)</td>
<td>2.0 (0.79, 5.15)</td>
<td>2.5 (0.65, 9.99)</td>
<td>0.34 (0.04, 2.77)</td>
</tr>
</tbody>
</table>

*Compared to reference group Low DAS28-CRP3/No Flare (n= 186)
Methods: Surveys were both mailed and administered in clinic to adult patients with pSLE seen in an adult SLE clinic. Demographics including sex, race, age, employment (full time, part time, not working) marital status (single, married, partnered, divorced) and education level (< high school, high school, college degree, graduate degree) were collected. Patients reported preparedness for transition as: completely prepared, mostly prepared, neutral, mostly unprepared or completely unprepared. The modified Medical Outcomes Study Social Support Survey (mMOS SS, range 8-40 points, higher scores indicate more support) and the Brief Illness Perception Questionnaire (IPQ, range 0-80 points, higher scores indicate increased perceptions of illness) were completed. We calculated Spearman rank correlations between variables and self-reported transition preparedness. Discrimination was assessed with the receiver-operating characteristic (area under the curve, AUC). Two multivariable logistic regression models, each including race, marital and employment status, educational level, and mMOS SS in one model and IPQ in the other, were analyzed to identify factors associated with transition preparedness.

Results: Of 258 surveys distributed, 30 patients (12%) responded. Average age was 28 ± 5 years, (range 21-38), 27 (90%) were female. The cohort was 60% (n=18) white, 10% (n=3) black, 10% (n=3) Hispanic and 17% (n=5) Asian. Twenty subjects (67%) were single, 67% were employed full time and 67% had a college degree. Fourteen subjects (47%) reported feeling completely or mostly prepared, 9 (30%) were neutral and 6 (20%) felt mostly or completely unprepared for transition. Higher social support per the mMOS SS was positively correlated with preparedness (Spearman rho = 0.42, p=0.02). Prepared subjects (n=14) vs. unprepared subjects (n=6) had significantly higher mMOS SS scores (35 ±6 vs. 28±7, p=0.02); AUC =0.83. In a multivariable model, high mMOS SS scores were predictive of preparedness (p=0.03). In contrast, high IPQ were negatively correlated with preparedness (Spearman rho = -0.48, p<0.01). Mean IPQ scores were significantly lower in prepared vs. unprepared patients (32±13 vs. 47±12, p=0.02); AUC=0.76. Lower IPQ scores were predictive of preparedness in the multivariable model (p=0.02).

Conclusion: In an adult group of pSLE patients, self-reported lack of preparedness for transition was strongly associated with low social support and increased cognitive and emotional representations of illness. The transition from pediatric to adult care for SLE may be improved by implementing appropriate support systems.

Disclosure: M. B. Son, None; D. Zurakowski, None; D. J. Kreps, None; S. Case, None; K. H. Costenbader, None.

Abstract Number: 1243

Clarifying Patient-Determined Barriers in Living with Systemic Lupus Erythematosus Treatment: A Qualitative Ethnographic Approach

Jerik Leung1, Deepali Sen2 and Alfred Kim3, 1Internal Medicine/Rheumatology, Washington University School of Medicine, Saint Louis, MO, 2Division of Rheumatology, Washington University School of Medicine, St. Louis, MO, 3IM/Rheumatology, Washington University School of Medicine, St. Louis, MO
SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The patient-specific experience of living with SLE is underreported. While there are data addressing factors influencing the quality of life of patients with SLE, these studies primarily derive from the perspective of the health care provider, not the patient. Changing to the patient perspective will likely improve our understanding of living with SLE, including reasons for medical noncompliance and socioeconomic differences in disease severity. Using an approach drawing from the sociological tool of ethnography, we performed extensive field observations and semi-structured interviews with a cohort (n=9) from the Lupus Clinic at Washington University School of Medicine to understand the patient perspective during the diagnosis of SLE and subsequent care.

Methods: Consented adult patients with SLE were recruited for this study during their scheduled clinic visits. We used a conventional ethnographic methodology to view the SLE experience from the patient perspective. Through long-form, semi-structured interviews (60-70 minutes) and field observations of interviewees, interviewees were encouraged to openly express their experience with SLE. 15 interviews across 9 individuals (6 individuals were interviewed twice) were performed. Interviews took place in a variety of locations including subject’s homes, cafes, public libraries, and clinic office rooms. We determined a core list of questions for each round of interviews. The initial round was based from a review of existing literature on barriers in SLE care and the authors’ clinical experience with perceived unmet needs among individuals with SLE. The second round centered on core themes which emerged from the first round of interview data and were often specific to the interviewee. Audio of interview data was recorded, transcribed, and analyzed using thematic analysis in NVivo 11.0 software.

Results: The dominant theme among patients with SLE is the deterioration of their social structure due to ambiguity and invisibility. Ambiguity derived from the protean nature of SLE disease activity, which disallowed individuals from complying with societal expectations of punctuality and reliability. Additionally, the common debilitating symptoms of SLE (e.g. chronic pain, fatigue, poor sleep quality) are largely invisible to others. Interviewees often attributed this invisibility to creating mistrust among non-SLE individuals in their social networks.

Conclusion: Ambiguity and invisibility contribute to poor quality of life in patients with SLE, with a particular negative effect on the patients’ social networks. These data have the potential to alter how providers administer SLE care. For example, loss of social structure may lead to depression and anxiety, promoting a negative view of having SLE, and driving medication and office visit noncompliance, both of which are major barriers to appropriate SLE care. Awareness of the social implications of having SLE—which are largely underaddressed by clinicians—unlock a potential to vastly improve outcomes by rethinking the doctor-patient interaction and services the health care field offer for these patients.

Disclosure: J. Leung, None; D. Sen, None; A. Kim, Kypha, Inc., 2,Exagen Diagnostics, 5,NIH/NIAMS, 2,Department of Defense, 2,Rheumatology Research Foundation, 2,Doris Duke Foundation, 2,Midwest Strategic Pharma-Academic Research Consortium, 2.


Abstract Number: 1244

Are Chinese-American Rheumatology Patients Who Use Traditional Chinese Medicine Less Adherent to Prescribed Western Medications?

Kai Sun1, Jackie Szymonifka2, Henghe Tian3, Ya Ju Chang4, Jennifer Leng5 and Lisa A. Mandl6, 1Hospital for Special Surgery/Weill Cornell medicine, New York, NY, 2Rheumatology, Hospital for Special Surgery, New York, NY, 3Internal Medicine, New York University School of Medicine, New York, NY, 4Mount Sinai Beth Israel, New York, NY, 5Immigrant Health and Cancer Disparities laboratory, Memorial Sloan Kettering Cancer Center, New York, NY, 6Rheumatology, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY

First publication: September 18, 2017
Background/Purpose: High adherence is crucial for the management of rheumatic diseases. Nonadherence is more common among immigrants and minorities and may contribute to known outcome disparities. Chinese-American patients commonly use Traditional Chinese Medicine (TCM) and have worse outcomes in lupus and rheumatoid arthritis. Adherence among Chinese-American rheumatology patients has not been previously studied, and whether TCM use affects adherence to prescribed rheumatic disease medications is unknown.

Methods: Subjects were recruited from two rheumatology clinics that serve a predominantly Chinese-American immigrant population. Inclusion criteria were Chinese ethnicity, Mandarin or English fluency, and actively followed and prescribed ≥1 non-pro re nata (PRN), non-intravenous medication for a systemic rheumatic disease by rheumatologist. TCM use, adherence, Patient-Reported Outcomes Measurement Information System (PROMIS) domains, and other variables were assessed using validated instruments available in English and Chinese. Adherence was classified as high or medium/low based on the 8-item Morisky Medication Adherence Scale. Medication complexity was assessed using the Medication Regimen Complexity Index; higher score indicates more complexity. Chart review was performed to gather additional clinical data. Parametric and nonparametric statistics were performed as appropriate. Multivariable logistic regression using step-wise selection was used to assess factors independently associated with high adherence.

Results: 230 enrolled, median age 55 years (range 20-97), 65% female, 71% ≤ high school education, 70% Medicaid, and 22% reported English fluency. 50% reported TCM use in the past year, most frequently tuina massage (47%), acupuncture (45%), and herbs (37%). The three most common diagnoses were RA (41%), SLE (17%), and spondyloarthritis (15%), with median time since diagnosis of 4.1 years (range 0.2-52). High adherence to western medicine was found in 28.3%, while 37.4% and 34.4% had medium and low adherence. Both herb and non-herb TCM users had better rates of high adherence to western medicine compared to TCM nonusers (33% and 39% vs. 20% respectively, p=0.02). In multivariable analysis, high adherence was independently associated with TCM use (Odds Ratio [OR] 3.2, 95% confidence interval [CI] 1.6-6.7, p=0.002), older age (OR 1.1, 95% CI 1.03-1.1, p<0.001), unemployment (OR 4.1, 95% CI 1.5-11, p=0.005), married/living with partner (OR 2.3, 95% CI 1.2-5.9, p=0.02), more complex rheumatologic medication regimen (OR 1.1, 95% CI 1.02-1.2, p=0.02), and lower levels of anxiety (OR 0.9, 95% CI 1.02-1.1, p=0.001).

Conclusion: Among poorly integrated, low education, and low socioeconomic status Chinese-American rheumatology patients, high adherence rate was poor. TCM use was statistically significantly associated with high adherence to western medication. TCM use does not appear to represent an alternate but rather complementary approach to disease management. Future studies should evaluate whether TCM use is associated with disease activity and outcomes over time.

Disclosure: K. Sun, None; J. Szymonifka, None; H. Tian, None; Y. J. Chang, None; J. Leng, None; L. A. Mandl, Boehringer Ingelheim, 2,American College of Physicians, 3,Up To Date, 7.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/are-chinese-american-rheumatology-patients-who-use-traditional-chinese-medicine-less-adherent-to-prescribed-western-medications

Abstract Number: 1245

Transition in Work Status and Quality of Life in People with Inflammatory Arthritis

Wiebke Bartels1, Eric C. Sayre2, Pam Rogers3 and Diane Lacaille4, 1Science, University of British Columbia, Vancouver, BC, Canada, 2Arthritis Research Canada, Richmond, BC, Canada, 3Rheumatology, Arthritis Research Canada, Richmond, BC, Canada, 4University of British Columbia, Arthritis Research Canada, Richmond, BC, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: People with inflammatory arthritis (IA) frequently have to stop working due to their arthritis. It is assumed that economic and psychosocial consequences of premature work cessation lead to reduced well-being. Yet, patients who were struggling at
work could experience an improvement in quality of life. Our objective was to evaluate the association between transition in work status and changes in quality of life (QoL) in patients with inflammatory arthritis (IA).

**Methods:** We conducted a prospective study using data from the RCT of an employment intervention, the Making it Work program, aimed at helping people with IA stay employed. Participants were recruited from rheumatologist practices, consumer organization (Arthritis Consumer Experts), and advertisements. Eligibility criteria included: IA diagnosis, employed, age 19-59, and concerns about arthritis affecting ability to work. Surveys were administered online at baseline and every 6 mos for up to 3.5 years. Working status was defined as “Currently working” vs. “currently not working” if not working for any reason (incl. sick leave). Working status over two consecutive surveys was categorized as: 1) Remaining working; 2) Stopping work; 3) Remaining not working; or 4) Returning to work. QoL was measured using EQ5D-Index (0-1) and EQ5D-VAS (0-100). Linear GEE models were used to predict changes in EQ5D-Index and EQ5D-VAS scores between 2 consecutive surveys, acc. to work transitions, after controlling for potential confounders.

**Results:** The sample includes all RCT subjects with at least two consecutive surveys by 12/2016 (N= 367 people; 948 pairs of surveys; 77% females, mean age: 46yrs, 54% with RA, AS: 20%; PsA: 14%; SLE: 12%). Amongst people working at the first survey, stopping work (vs. remaining at work) was associated with worsening in QoL (EQ-index and EQ-VAS). Amongst those not working at the first survey, returning to work (vs. remaining off work) was associated with improvement in QoL (EQ-Index; not signif. for EQ-VAS) (Table 1). We observed little to no change in QoL when people remained in the same work status (data not shown).

**Conclusion:** Our results suggest that remaining employed or returning to work is beneficial for QoL in workers with IA. This provides useful information to guide people with arthritis in their decisions about continuing, stopping, or returning to work; and provides evidence in support of initiatives aimed at helping individuals with IA remain employed.

**Disclosure:** W. Bartels, None; E. C. Sayre, None; P. Rogers, None; D. Lacaille, None.


**Abstract Number:** 1246

**Patient Preferences Associated with the Use of Treatments for Psoriatic Arthritis: Results of a Conjoint Analysis**
Yihua Xu1, Lavanya Sudharshan1, Ming-Ann Hsu2, Andrew Koenig3, Joseph C Cappelleri4, Wen Liu5, Tim Smith6 and Margaret Pasquale1,
1Comprehensive Health Insights Inc., Louisville, KY, 2Pfizer Inc, Groton, CT, 3Pfizer Inc, Collegeville, PA, 4Statistics, Pfizer Inc, New London, CT, 5Humana Inc., Louisville, KY, 6Pfizer Inc, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: As Psoriatic Arthritis (PsA) treatment choices continue to expand, it is important to consider patient preferences for treatment modalities for PsA. Involving patients in treatment decisions can influence adherence and outcomes of therapy, which has a large impact on treatment outcomes.

Methods: A choice-based conjoint survey was mailed to 2,800 randomly selected patients enrolled in Humana Inc. Medicare and commercial plans (1,400 patients each). Patients were 18-80 years old and had been diagnosed with PsA (≥2 claims with a diagnosis code ICD-9-CM: 696.0 /ICD-10 CM: L40.5) between 1/1/2012 and 9/30/2016. Attributes for comparison included route of administration, frequency of administration, ability to reduce daily joint pain and swelling, likelihood of serious infections, improvement in the ability to perform daily tasks and activities, achieving clear or almost clear skin, and cost. Part-worth utilities (preference scores) and attribute importance scores (AIS) were estimated separately for patients enrolled in Medicare and commercial plans, using hierarchical Bayesian models after adjustment for demographic and clinical characteristics (age, sex, region, years since first PsA diagnosis, Deyo-Charlson comorbidity score, disease severity, and prior injectable/infusion experience). Mean AIS scores were used to rank order patient preferences for the attributes.

Results: A total of 468 patients (258 Medicare and 210 commercial; response rate of 16.7%) returned the survey (mean age ± standard deviation Medicare: 66.7 ± 7.6 years/Commercial: 51.4 ± 10.7 years; proportion female Medicare: 58.1%/Commercial: 56.2%). The top three attributes of importance for patients enrolled in Medicare plans were (in order) route of administration, cost, and then improvement in the ability to perform daily tasks and activities. The top three attributes of importance for patients enrolled in commercial plans were (in order) cost, route of administration, followed by frequency of administration (Figure 1). For both health plans, oral formulation was preferred relative to self-injection and intravenous routes of administration, and lower cost was preferred. For the commercial plans, less frequency of administration was preferred; for Medicare plans, more improvement in ability to perform daily tasks and activities was preferred.

Conclusion: Route of administration and cost are among the most important and common considerations for patients diagnosed with PsA and surveyed in this study. Gaining a better understanding of the attributes considered important to patients may help inform payer policies and prescriber selections regarding therapy that may lead to higher patient satisfaction, improved medication adherence, and ultimately treatment outcomes.

Figure 1.

Data are represented as mean, standard deviation.

For each plan, the sum of the average importance scores across attributes equaled 100.
Coexisting Fibromyalgia in Patients with Rheumatoid Arthritis Worsens Scores for Pain, Physical Function and Depression

Dylan Ruebeck1, Judith Baumhauer2 and Allen P. Anandarajah3, 1Internal Medicine, University of Rochester Medical Center, Rochester, NY, 2Orthopedics, University of Rochester Medical Center, Rochester, NY, 3Dept of Rheumatology, Univ of Rochester Medical Ctr, Rochester, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Quality of life (QOL) measures as assessed by Patient Reported Outcome Measurement Information System (PROMIS) can contribute essential information about the status of or a change in the physical, emotional, and social health outcomes of people living with chronic diseases compared with the general population. Rheumatoid arthritis (RA) is a chronic inflammatory disease that is associated with pain and progressive joint damage resulting in decreased function and changes in mood. The reliability of PROMIS in assessment of RA has been validated. Fibromyalgia (FMS) is a condition characterized by diffuse chronic pain associated with tenderness of joints and muscles along with fatigue, sleep disturbances and often poor mental health. FMS affects 10-20% of patients with RA and thus can negatively affect the pain and depression assessments. The impact of FMS on the quality of life measures as assessed by PROMIS in RA patients is not known.

Purpose: Compare pain, physical function and depression scores as assessed by PROMIS in patients with RA and FMS and assess the effect of coexisting fibromyalgia on these scores in RA patients.

Methods: This is a single center retrospective assessment of prospectively collected PROMIS data in all RA and FMS patients between January 2016 and April 2017 at an academic center RA clinic. The PROMIS t-scores are obtained as standard of care in all patients seen at the rheumatology clinic. ICD-10 diagnosis codes were used to identify patients with RA (M06.9 to M08.00) and FMS (M79.7). The t-scores for pain interference, physical function and depression during their rheumatology visits were retrieved and a mean calculated when more than one score was available. Age, gender, disease duration and medications were also recorded. The mean PROMIS scores were compared between patients with RA, FMS and FMS coexisting with RA.

Results: A total of 392 patients were identified with RA, FMS and coexisting FMS and RA but only 230 patients had complete PROMIS scores: 169 RA, 28 FMS and 33 with both. Mean age was similar between RA and FMS with RA groups, 56.7 (+/- 14.9) and 55.0 (+/- 9.3), respectively. The FMS cohort was slightly younger at 52.3 (+/- 10.7). A larger proportion of females were in the FMS (27/28; 96.4%) and FMS and RA group (31/33; 93.9%) compared with the RA patients (126 /169; 74.6%). The scores for pain (63.7 +/- 5.9) and depression (54.8 +/- 9.6) were significantly (p < 0.05) higher in patients with FMS coexisting with RA patients compared with RA only, (55.0 +/- 8.3) and (46.7 +/- 6.7), respectively. Additionally, the scores for physical function were significantly (p < 0.05) lower among RA and FMS compared to RA only, (37.5 +/- 5.4) and (44.6 +/- 8.9), respectively. Interestingly, FMS patients had scores for pain (64.6 +/- 5.9), physical function (37.4 +/- 6.5) and depression (54.3 +/- 8.6) that were similar to patients with FMS and RA.

Conclusion: These results show that patients with RA have a worse quality of life as assessed by PROMIS than the average US population (t-score =50) but coexistence of FMS in patients with RA negatively impacts PROMIS t-scores for pain, depression and physical function even further. This suggests that treatment aimed at FMS is needed to improve the QOL in these patients.

Disclosure: D. Ruebeck, None; J. Baumhauer, None; A. P. Anandarajah, None.
Evaluation of Validated Patient Reported Outcome Measures to Assess Sensitivity to Change in Patients with Systemic Sclerosis and Gastroesophageal Reflux Disease — a Scleroderma Clinical Trials Consortium Collaborative Project

Zsuzsanna McMahan1, Tracy M. Frech2, David Lim3, Veronica J. Berrocal4, Cosimo Bruni5, Marco Matucci-Cerinic6, Vanessa Smith7, Karin Melsons8, Susanna Proudman9, Jinyu Zhang10, Fabian A Mendoza11, Melanie Woods3 and Dinesh Khanna3,

1Department of Internal Medicine, Johns Hopkins University, Baltimore, MD, 2Division of Rheumatology, University of Utah, Salt Lake City, UT, 3University of Michigan, Ann Arbor, MI, 4Div of Rheumatology, University of Michigan, Ann Arbor, MI, 5Department of Experimental and Clinical Medicine, Division of Rheumatology, University of Florence, Firenze, Italy, 6Dept of Medicine/Div of Rheum, University of Florence, Firenze, Italy, 7Faculty of Internal Medicine, Ghent University, Ghent, Belgium, 8Ghent University, Gent, Belgium, 9Discipline of Medicine, University of Adelaide, Adelaide, Australia, 10Thomas Jefferson University, Philadelphia, PA, 11Jefferson Institute of Molecular Medicine and Scleroderma Center, Rheumatology Division, Department of Medicine, Thomas Jefferson University, Philadelphia, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The UCLA SCTC GIT 2.0 and NIH PROMIS GI Symptoms Scales are validated in scleroderma to assess patient-reported gastrointestinal (GI) involvement. We sought to determine whether longitudinally administered reflux-specific domains of the UCLA GIT 2.0 and PROMIS are effective in capturing change in GI symptoms following therapeutic intervention in an international cohort of scleroderma patients with gastroesophageal reflux disease (GERD).

Methods: Six scleroderma centers participated in this longitudinal observational cohort study. Patients with active GERD, defined as symptoms for at least 3 of the last 7 days, were recruited during routine clinical visits. Patient-reported outcomes (PROs) were captured at baseline and again at 4 weeks follow-up. Effect size and standardized response mean (SRM) were calculated to assess the sensitivity to change and a range of 0.20-0.49 was interpreted as small magnitude, 0.50-0.79 as moderate magnitude, and >=0.80 as large magnitude.

Results: 115 subjects with systemic sclerosis and active GERD were recruited. The average age was 53.7 ± 13.3 years, with a mean disease duration of 12.7 years. Patients were more likely to be female (81%), and there was a similar distribution of patients with diffuse and limited cutaneous disease (43% vs. 48%, respectively). Mean body mass index was 25.9 ± 6.2. The mean UCLA GIT 2.0 Reflux score was 0.98 ± 0.63 (N=112) and mean PROMIS score was 53.5 ± 8.1 (0.3 SD above the US population; N=64). The UCLA GIT 2.0 and PROMIS had a significant correlation coefficient at baseline (-0.60, p=0.000000219). In patients where both the UCLA GIT 2.0 and PROMIS were available (N=57), the changes were associated with a small effect size and SRM during 4-week follow-up (Table 1). For subjects who reported improvement, the effect size and SRM were moderate (-0.62 and -0.54) for UCLA GIT 2.0, and large (-1.03 and -1.02) for NIH PROMIS.

<table>
<thead>
<tr>
<th>Table 1. Effect size and standardized response means across patient groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient-Reported Outcome Scales</td>
</tr>
<tr>
<td>Effect size</td>
</tr>
<tr>
<td>UCLA SCTC GIT 2.0</td>
</tr>
<tr>
<td>NIH PROMIS</td>
</tr>
</tbody>
</table>

Conclusion: In this unique large international cohort, both the UCLA GIT 2.0 and PROMIS are sensitive to change. UCLA GIT 2.0 and PROMIS have a large correlation for the assessment of GERD in systemic sclerosis. Although the change was of small magnitude, statistical correlation was demonstrated.
What Factors Predict Good Patient Experiences of Switching from Reference Etanercept (EnbrelTM) to an Etanercept Biosimilar (BenepaliTM) in a South West London General Hospital?

Laura Attipoe, Samir Patel, Robin Birt, Jennifer Crooks and Antigoni Grigoriou, Rheumatology, Kingston Hospital, Kingston, London, England, Kingston, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

The introduction of biological (BG) drugs in the last 20 years has revolutionised the treatment of patients with inflammatory arthritis (IA). The development of cheaper biosimilar (BS) drugs, analogous to existing licensed BG therapies, has significant cost benefits for the treatment of IA.

In 2016, our Hospital's Rheumatology Department switched all patients on reference etanercept (E) to an etanercept biosimilar (B). Patients were informed of their switch during a routine clinic appointment or by letter/phone.

In non privatised health settings it is inevitable that hospitals will continue switching patients from BG to their BS counterparts once efficacy, safety and licensing rights have been established. Little is known about how best to switch patients. We devised a questionnaire to investigate our patient’s experiences of switching and gain feedback on factors that could be improved.

Methods:

In May 2017, 355 anonymised questionnaires were sent to our patients with IA who had switched from E to B. We received 107 responses. Questions were semi-structured using Likert scales and focused on diagnosis, treatment history, how patients were informed of their switch and any effects they had from the switch itself.

Results:

Rheumatoid arthritis represented 68% of patients, Psoriatic Arthritis 16% and Ankylosing Spondylitis 11%. 64% were female, 36% male. 20% were 18-49 years and 80% were ≥ 50 years. 29% of patients had a disease duration of 1-10 years and 71% > 10 years. 44% were on monotherapy and 39% combined with Methotrexate.

65% of patients were informed of the switch by their rheumatology doctor, the remainder informed by their nurse/delivery company. 90% of patients were informed face to face in clinic with the remainder informed by phone/letter. 6% of patients were not given any information about B, the rest were given verbal or written information. 45% of patients found their switching experience excellent or very good, 44% was satisfactory. However 9% found their experience poor or very poor. From those patients 32% expressed that their experiences would have improved if they were given the option of switching and 21% if they were given more information about B. 39% experienced side effects (SE) whilst switching.

Factors significantly involved in patients’ having a poor experience of switching were longer disease duration (p 0.042), not feeling sufficiently supported (p 0.000000079) and experiencing SE after switching (p 0.0018). There were no significant differences when looking at age, gender, the type of clinician informing the patient of the switch, whether patients were informed in person or by phone/letter or the type of information patients were given about the switch (verbal or written).
Conclusion:
Switching onto BS is a phenomenon that is likely to continue with a need to improve patients’ experience of switching. Longer disease duration, less support from clinicians and SE from switching contribute to poor experiences. Reducing SE in patients who have switched is fundamental, including those occurring via the nocebo effect. Adequate information given in advance, having opportunities to ask questions and having a point of contact after switching are factors that patients express as important.

Disclosure: L. Attipoe, None; S. Patel, None; R. Birt, None; J. Crooks, None; A. Grigoriou, None.

Abstract Number: 1250

Outcomes in Real-World Patients with Early Aggressive Rheumatoid Arthritis

Keith Knapp1,2, Eric Mueller1,2 and Gary Craig1,2, 1Arthritis Northwest PLLC., Spokane, WA, 2Discus Analytics LLC., Spokane, WA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The window of opportunity to address early rheumatoid arthritis (RA) in patients (pts) is well documented. However early aggressive (agr) RA needs further study to identify optimal treatment patterns. This study compares outcomes of early agr RA to early non-agr patients on their first DMARD.

Methods: Pts>18 years and clinically diagnosed with RA in the JointMan database between 1 Jan 2009 and 31 Mar 2017 were included. Test pts had erosions on imaging and were positive for either anti-cyclic citrullinated peptide (ACPA) or rheumatoid factor (RF) within 6 months of their diagnosis. Controls had non-agr early RA with no erosions on imaging and were RF- and ACPA-.

Outcomes using composite disease activity metrics (DAM - DAS28, DAS28-CRP, SDAI, CDAI, and Rapid3) and 8 clinical metrics (tender & swollen joint counts, patient global, pain, physician global physician disease, ESR, and CRP) were tracked at baseline (first DMARD initiation), 6, 12, and 18 months follow up. Index date was the date of the first DMARD. Baseline was defined as the encounter immediately prior to the index date, but no greater than 12 months. Percentage change in each metric from baseline was calculated and differences between test and control (normally distributed) were compared with Welch’s T-Test (significance level of 0.05).

Results: 618 patients were included in the analysis, 177 (28.6%) were test. Compared to controls, test pts were older (60 vs 53 years), but less likely female (71.8 vs 77.8%). There was significant difference between test and controls at baseline for ESR, CRP and all DAMs (p=0.034, 0.013, and <0.022 respectively) except Rapid3. The percentage change was significant between cohorts at 18 months for all DAMs (p=0.0001); DAS28-CRP had the greatest difference in percentage change (test -36.14 vs -28.94%), while the average swollen joint count was significantly different at all time points.

Conclusion: Early agr RA is distinct both at baseline and in its progression to that of non-agr RA. Close clinical monitoring may be necessary to ensure agr pts respond to therapy.
Disease Activity Metric | Baseline | 6 Months | 12 Months | 18 Months
---|---|---|---|---
DAS28-CRP | 0.002 | 0.027 | 0.525 | 0.0001
DAS28 | 0.002 | 0.168 | 0.415 | 0.0001
CDAI | 0.022 | 0.066 | 0.979 | 0.0001
SDAI | 0.003 | 0.224 | 0.902 | 0.0001
Rapid3 | 0.774 | 0.734 | 0.551 | 0.0001
Tender Joint Count | 0.280 | 0.639 | 0.552 | 0.0001
Swollen Joint Count | 0.000 | 0.009 | 0.029 | 0.0001
Patient Global | 0.963 | 0.823 | 0.602 | 0.0001
MD Global | 0.152 | 0.710 | 0.675 | 0.0001
MD Disease | 0.129 | 0.724 | 0.832 | 0.0001
Patient Pain | 0.524 | 0.707 | 0.490 | 0.0001
ESR | 0.034 | 0.226 | 0.248 | 0.0001
CRP | 0.013 | 0.222 | 0.039 | 0.0001

The p-values from Welch's T-Test comparing early aggressive vs early non-aggressive RA.

Disclosure: K. Knapp, Discus Analytics, 1; E. Mueller, Discus Analytics, 4, Genentech and Biogen IDEC Inc., 8; G. Craig, Discus Analytics, 4, Arthritis Northwest, 4, Bristol-Myers Squibb, 5, Bristol-Myers Squibb, 8, UCB, 8, Celgene, 8, Genentech and Biogen IDEC Inc., 8, Abbvie, 8, Premera Blue Cross, 9.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/outcomes-in-real-world-patients-with-early-aggressive-rheumatoid-arthritis

Abstract Number: 1251

**Chinese Patient Reported Index with Rheumatoid Arthritis (CPRI-RA): Reliability, Validity and Agreement with DAS28 and HAQ**

Man Han1, Xun Gong1, Xiao-po Tang1, Hong-xiao Liu2, Jian Liu3, Xin-chang Wang4, Jun-li Zhang5, Shi Chen6, Qing-chun Huang7, Yong-fei Fang8, Qing-jun Wu9, Dong-yi He10, Zhen-bin Li11, Yue Wang12, Hong Jiang13, Ming-li Gao14, Wei Liu15, Ying Liu16, Zhengxi Li17, Zhong-wen Zhao18, Cheng-wu Wang19, Wei-chao Liu20, Hai-dong Wang21, Yu-qian Lou22, Qing-liang Meng23, Chong-jie Ruan24, Yan-ming Xie25 and Quan Jiang26, 1Rheumatology, Guang’anmen Hospital, China Academy of Chinese Medical Sciences, Beijing, China, 2Department of Rheumatology, Guang’anmen Hospital, China Academy of Chinese Medical Sciences, Beijing, China, 3The First Affiliated Hospital of Anhui University of Traditional Chinese Medicine, Hefei, China, 4Rheumatology, The Second Affiliated Hospital of Zhejiang University of Traditional Chinese Medicine, Hangzhou, China, 5Rheumatology, The Fifth Hospital of Xi’an City, Xi’an, China, 6Rheumatology, Peking University People’s Hospital, Beijing, China, 7Rheumatology, Guangzhou Provincial Hospital of Traditional Chinese Medicine, Guangzhou, China, 8Rheumatology, Southwest Hospital, Third Military Medical University, Chongqing, China, 9Rheumatology, Peking Union Medical College Hospital, Beijing, China, 10Institute of Arthritis Research, Shanghai Academy of Chinese Medical Sciences, Guanghua Integrative Medicine Hospital, Shanghai, China, 11Rheumatology, Bethune international peace hospital, Shi jiazhuang, China, 12Jiangsu Provincial Hospital of Traditional Chinese Medicine, Nanjing, China,
Background/Purpose: The use of patient reported outcomes (PROs) has become increasingly popular in the chronic disease management, disease monitoring and the assessment of drug efficacy. However, very few studies on rheumatoid arthritis (RA) have come down to PROS in China. We initiated CPRI-RA based on Chinese RA population, which include not only arthritis symptoms, physical function but also fatigue, appetite, emotional wellness and self-efficacy. We aimed to measure the reliability and the validity of CPRI-RA and evaluate the correlation and agreement with DAS28 and HAQ.

Methods: Nationwide multicenter cross-sectional and longitudinal studies were designed to recruit RA patients who fulfilled 1987 ACR classification criteria. Demographics, clinical and laboratory data were collected and CPRI-RA, DAS-28 and HAQ were recorded. Intensive treated patients with moderately to severely active RA were followed up regularly for 12-week and 24-week periods to track the changes of CPRI-RA, DAS-28 and HAQ scores. The reliability was measured using the Cronbach α coefficient and the validity was analyzed by the construct validity using factor analysis method. Agreement between CPRI-RA and DAS28 was analyzed by the weighted kappa value. The correlation between CPRI-RA and DAS28, HAQ was analyzed by Pearson correlations. The linear mixed-effects model was adopted to analyze the dynamic correlation and consistency between the indices.

Results: A total of 1868 RA patients (83.08% women, mean±SD age 54.79±12.62 years, disease duration 6.18±7.68 years, DAS28 5.56±1.36) from 19 provinces and 23 hospitals completed the cross-sectional survey and 186 active RA patients(85.48% women, mean±SD age 48.18±10.61 years, disease duration 1.77±1.52 years, DAS28 5.71±1.06) participated in the longitudinal study. The overall Cronbach α value was 0.756 and the Guttman split-half coefficient was 0.733, indicating CPRI-RA had good internal consistency and stability. Three factors extracted by factor analysis (cumulative 53.199%) reflected the physical status, social and psychological properties of RA patients, which provided evidence for good construct validity. HAQ versus CPRI-RA scores were significantly correlated (r=0.581, P<0.0001), and DAS28 versus CPRI-RA scores were significantly correlated at higher levels (r=0.640, P<0.0001). The weighted kappa value was 0.4215 (P <0.0001) for DAS28 versus CPRI-RA, indicating fair agreement of the indices. Dynamically, HAQ versus CPRI-RA scores and DAS28 versus CPRI-RA scores were both significantly correlated (r=0.4464, r=0.4622, P<0.0001). The dynamic trends of the three indices were highly consistent.

Conclusion: CPRI-RA, a reliable, feasible and valid PRO scale, can provide similar quantitative information to DAS28 and HAQ. The results support the incorporating of CPRI-RA into the routine assessment and dynamic monitoring of RA.
**Abstract Number: 1252**

**Real-World Oral Methotrexate Adherence Measured Electronically in Patients with Established Rheumatoid Arthritis**

Kaleb Michaud\(^1,2\), Rebecca Schumacher\(^2\), Bernard Vrijens\(^3\), Eric Tousset\(^3\), Gorana Dasic\(^4\), Connie Chen\(^4\), Ekta Agarwal\(^4\) and Maria Suarez-Almazor\(^5\), \(^1\)University of Nebraska Medical Center, Omaha, NE, \(^2\)National Data Bank for Rheumatic Diseases, Wichita, KS, \(^3\)WestRock Healthcare, Visé, Belgium, \(^4\)Pfizer Inc, New York, NY, \(^5\)Section of Rheumatology and Clinical Immunology, Department of General Internal Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA, Houston, TX

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Patient Outcomes, Preferences, and Attitudes Poster II  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** While weekly methotrexate (MTX) remains the gold standard treatment for patients with RA, studies suggest that MTX adherence may be sub-optimal and could be associated with side effects, poor outcomes, and unnecessary switching to other DMARDs. We set out to assess MTX adherence in patients with RA using electronic medication monitoring in a real-world non-clinical setting.

**Methods:** Patients were participants in the National Data Bank for Rheumatic Diseases (NDB) longitudinal survey-based study that reported oral MTX initiation independent of other treatments within a year of September 2016. Study patients used a Medication Event Monitoring System (MEMS®) to accurately record when they accessed their MTX pills and completed the Beliefs about Medications Questionnaire (BMQ). The BMQ assesses "General" beliefs about medications and also those taken for a "Specific" condition (RA). While validated in several chronic disease, the BMQ has never been studied in RA. After 24 weeks the MEMS data were retrieved and baseline patient characteristics were summarized by categorical adherence level.

**Results:** Of the 119 eligible patients invited, 62 enrolled and 32 had completed the study by May 2017. Mean (SD) MTX experience at the first time of MEMS use was 7.4 (5.0) months. Nine (28%) patients had perfect adherence, 7 (22%) had 1 interrupted week, 8 (25%) had ≥2 interrupted weeks, and 8 (25%) had major adherence deviations, including treatment discontinuation. On average, 80% of dosing intervals were between 6 and 8 days and MTX dose was taken in 77% of the monitored weeks. The table compares baseline characteristics between adherence categories. There was a significant difference in Non-Hispanic Caucasian and BMQ-General-Overuse response between patients with ≤1 interrupted weeks and ≥2 (94 vs. 63%, p=0.03 and 11.1 vs. 9.4, p=0.02, respectively). There were also clinically significant differences in functional assessment (HAQ-II 0.7 vs. 1.2) and fatigue (VAS 2.9 vs. 4.9).

**Conclusion:** This study demonstrated the feasibility of using remote electronic medication monitoring in a participatory US RA population; yet, even with such participation biases, half had important adherence interruptions with MTX. Patients with beliefs that medicines are overused by doctors were most likely to be adherent while Non-Caucasian race and worse function and fatigue were less likely. Next steps include a larger and longer follow-up and investigating early intervention to improve MTX adherence.


Table. Baseline characteristics of RA patients by 24-week MTX adherence (≤1 vs ≥2 interrupted weeks)
<table>
<thead>
<tr>
<th></th>
<th>All (SD)</th>
<th>Adherent (SD)</th>
<th>Non-Adherent (SD)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>32</td>
<td>9+7=16</td>
<td>8+8=16</td>
<td></td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>60 (11)</td>
<td>60 (12)</td>
<td>60 (12)</td>
<td>0.89</td>
</tr>
<tr>
<td>Male (%)</td>
<td>7</td>
<td>13</td>
<td>0</td>
<td>0.17</td>
</tr>
<tr>
<td>Non-Hispanic Caucasian (%)</td>
<td>77</td>
<td>94</td>
<td>63</td>
<td>0.03</td>
</tr>
<tr>
<td>Education (yrs)</td>
<td>14.8 (2.1)</td>
<td>14.8 (2.0)</td>
<td>14.8 (2.2)</td>
<td>0.75</td>
</tr>
<tr>
<td>Disease duration (yrs)</td>
<td>16 (13)</td>
<td>18 (13)</td>
<td>14 (13)</td>
<td>0.37</td>
</tr>
<tr>
<td>Comorbidity Index (0-9)</td>
<td>1.6 (1.8)</td>
<td>1.2 (2.1)</td>
<td>2.0 (1.4)</td>
<td>0.21</td>
</tr>
<tr>
<td>HAQ-II (0-3)</td>
<td>0.95 (0.76)</td>
<td>0.70 (0.74)</td>
<td>1.20 (0.70)</td>
<td>0.06</td>
</tr>
<tr>
<td>Pain VAS (0-10)</td>
<td>3.3 (2.5)</td>
<td>3.3 (2.6)</td>
<td>3.4 (2.4)</td>
<td>0.89</td>
</tr>
<tr>
<td>Global severity VAS (0-10)</td>
<td>3.7 (2.6)</td>
<td>3.5 (2.9)</td>
<td>3.9 (2.4)</td>
<td>0.64</td>
</tr>
<tr>
<td>Fatigue VAS (0-10)</td>
<td>3.9 (3.1)</td>
<td>2.9 (2.9)</td>
<td>4.9 (2.9)</td>
<td>0.06</td>
</tr>
<tr>
<td>MTX use (months)</td>
<td>7.4 (5.0)</td>
<td>8.0 (5.8)</td>
<td>7.1 (4.2)</td>
<td>0.61</td>
</tr>
<tr>
<td>BMQ-General-Overuse (4-20)</td>
<td>10.6 (3.0)</td>
<td>11.8 (3.4)</td>
<td>9.4 (2.1)</td>
<td>0.02</td>
</tr>
<tr>
<td>BMQ-General-Harm (4-20)</td>
<td>8.0 (2.9)</td>
<td>8.8 (3.4)</td>
<td>7.3 (2.0)</td>
<td>0.13</td>
</tr>
<tr>
<td>BMQ-Specific-Necessity (5-25)</td>
<td>20.4 (4.1)</td>
<td>19.4 (4.7)</td>
<td>21.4 (3.4)</td>
<td>0.19</td>
</tr>
<tr>
<td>BMQ-Specific-Concerns (5-25)</td>
<td>17.3 (4.5)</td>
<td>16.9 (4.5)</td>
<td>17.7 (4.6)</td>
<td>0.62</td>
</tr>
</tbody>
</table>

Disclosure: K. Michaud, None; R. Schumacher, None; B. Vrijens, None; E. Tousset, None; G. Dasic, None; C. Chen, Pfizer, Inc, 1,Pfizer, Inc, 3; E. Agarwal, Pfizer Inc, 1,Pfizer Inc, 3; M. Suarez-Almazor, Bristol-Myers Squibb, 5,Pfizer Inc, 5.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/real-world-oral-methotrexate-adherence-measured-electronically-in-patients-with-established-rheumatoid-arthritis

Abstract Number: 1253

**Patient Reported Outcomes Explain the Lack of Agreement between Physician and Patient Perceived Remission in Early Rheumatoid Arthritis**

Samina A. Turk1,2, Linda A. Rasch3, Willem F. Lems4,5, Lilian van Tuyl3, Dirkjan van Schaardenburg4,6 and Marieke M. Ter Wee5,7, 1Rheumatology, Amsterdam Rheumatology and Immunology Center | Reade, Amsterdam, Netherlands, 2Rheumatology, Amsterdam Rheumatology and Immunology Center | Academic Medical Center, Amsterdam, Netherlands, 3Amsterdam Rheumatology and Immunology Center | VU University, Amsterdam, Netherlands, 4Amsterdam Rheumatology and Immunology Center | Reade, Amsterdam, Netherlands, 5Rheumatology, Amsterdam Rheumatology and Immunology Center | VU University, Amsterdam, Netherlands, 6Amsterdam Rheumatology and Immunology Center | Academic Medical Center, Amsterdam, Netherlands, 7Epidemiology and Biostatistics, VU University, Amsterdam, Netherlands

First publication: September 18, 2017
Background/Purpose:

Rheumatoid arthritis (RA) patients increasingly reach a state of absence of disease activity, or remission. However, the proportion of patients classified as in remission varies substantially between definitions and are often determined by disease activity score (DAS) of the joints. But, the importance of patients’ perspective is increasingly recognized, which often result in discordance between patients and physician assessment.

Objectives:

First, agreement between patient-perceived, physician-perceived remission and clinical response and remission definitions was determined in early RA patients. Second, the differences in clinical and patient-reported outcomes, in patients in physician-perceived remission, between patients in and not in self-perceived remission were assessed.

Methods:

In early RA patients receiving COBRA-light treatment, DAS44, ACR/EULAR Boolean-based remission, EULAR good and ACR70 response were determined after 12 weeks. Agreement percentages and kappa values between patient-perceived, physician-perceived remission and clinical response and remission definitions were calculated. In patients in physician-perceived remission, improvement in clinical and patient-reported outcomes (RAID) were compared between patients in and not in self-perceived remission.

Results:

Eighty-four consecutive patients were included (mean age 50 years, 67% female). Agreement between the assessed outcome measures differed enormously. The agreement between physician-perceived and patient-perceived remission was 64% (kappa 0.25, p<0.01). Physician-perceived remission (cut-off VAS ≤20 mm) had the best agreement with EULAR good response (86%, kappa 0.58, p<0.01). Agreement between patient-perceived remission was 69% for EULAR good and ACR70 response (kappa 0.36, p<0.01; kappa 0.40, p<0.01, respectively). Patients not in self-perceived remission improved less on components of the RAID, especially on pain, sleep and emotional well-being.

Conclusion:

One-third of the early RA patients disagreed with the physician on being in remission. Those patients had less improvement on components of the RAID, especially on pain, sleep and emotional well-being. Together with the variability in clinical response and remission definitions, these results highlight the need to increase patient involvement in their own health care decisions.

Table. Agreement between different definitions of response and remission.
Physician-Physician- Patient-remission remission remission perceived perceived perceived (≤10 mm) (≤20 mm) remission remission remission

Physician-perceived remission (≤10 mm) 86% 67% 74% 79% 60% 57%
P=0.000  K=0.650  K=0.318  K=0.439  K=0.484  K=0.281  K=0.248

Physician-perceived remission (≤20 mm) x 64% 64% 86% 45% 48%
P=0.000  K=0.254  K=0.454  K=0.576  K=0.117  K=0.175

Patient-perceived remission 67% 64% 46% 69% 69% 67%
P=0.003  K=0.318  K=0.254  K=0.516  K=0.356  K=0.398  K=0.354

DAS44 remission 74% 64% 46% x 83% 64% 67%
P=0.000  K=0.439  K=0.454  K=0.516  K=0.516  K=0.622  K=0.343  K=0.392

EULAR good response 79% 86% 69% 83% x 52% 50%
P=0.000  K=0.484  K=0.576  K=0.356  K=0.622  K=0.220  K=0.199

ACR70 response 60% 45% 69% 64% 52% x 74%
P=0.000  K=0.281  K=0.117  K=0.398  K=0.343  K=0.220  K=0.359

Boolean remission 57% 48% 67% 67% 50% 74% x
P=0.001  K=0.248  K=0.175  K=0.354  K=0.392  K=0.199  K=0.359
P=0.002  K=0.005  P=0.000  P=0.000  P=0.002  P=0.001

Numbers are presented as level of agreement (%), kappa value (K) and p-value (P).

Figure.
Abstract Number: 1254

Eliciting the Research Priorities of Parents and Children with Juvenile Myositis

Colleen K. Correll1, Mitali Dave2, Anne Paul3, Vincent Del Gaizo4 and Esi Morgan5, 1Pediatrics, University of Minnesota, Minneapolis, MN, 2Cure JM Foundation, Encintas, CA, 3Anderson Center for Health Systems Excellence, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 4Parent Partner, Whitehouse Station, NJ, 5Cincinnati Children's Hospital, Cincinnati, OH

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The Patient-Centered Outcomes Research Institute (PCORI) aims to improve the quality and relevance of research by conducting research that is of highest priority to patients and to engage patients at all phases of research. As a project of the PCORI-supported Patient Powered Research Network, PARTNERS (Patients, Advocates and Rheumatology Teams Network for Research and Service), we surveyed parents of children with juvenile myositis (JM) to identify what research questions are most important to them.

Methods: This research prioritization exercise was conducted through web-based surveys, a focus group, and a Delphi process. In November, 2016 a survey link, comprised of 3 open-ended questions to assess what concerns patients/families found most important, was emailed to members of the Cure JM Foundation listserv and posted on Cure JM social media sites. Parents, patients ≥13 years old and family/friends were included. Common themes on research areas of interest were identified from the survey and further characterized through a focus group consisting of parents of children with JM at the annual Cure JM conference in February, 2017. A final survey was created based upon these themes and emailed to the Cure JM listserv and posted to its social media sites in April, 2017. Survey respondents were asked to rank the themes most important to them. Responses were weighted and the 6 most important themes were identified.

Results: There were 138 respondents to the initial survey (77% parents, 11% patients, 12% family/friends). Response rate could not be calculated because the number of potential respondents from social media sites is unknown. From this survey, 23 concerns were identified. The 3 most common concerns were long-term effects of medications, long-term effects of juvenile myositis, and triggers for disease flare. The 23 concerns were further characterized into 20 research priorities during a 9-member focus group. The final ranking survey asked respondents to rank the 7 most important priorities from the 20 themes. There were 365 survey respondents (75% parents, 15% patients, 10% family/friends). The following were ranked in order as the most important research priorities: a cure, new treatments with less side effects, triggers for disease flare, treatment side effects (such as steroids), standards to measure disease activity/remission, genetic/environmental causes of the disease. These research priorities were formally presented at the Global Conference on Myositis and the Childhood Arthritis and Rheumatology Research Alliance annual meetings to help frame the juvenile myositis research agenda.

Conclusion: Patient centered research prioritization is increasingly recognized as a valuable tool in conducting high-quality research, yet there is a lack of publication describing patient/family preferences, especially in pediatrics. Here, we demonstrate a successful program from which we assessed patient/family research priorities in order to inform a joint research agenda process for the juvenile myositis research community.
Abstract Number: 1255

Using PROs to Guide Patient-Centered Conversations and Care in Inflammatory Arthritis: The Clinician Perspective

Susan J. Bartlett1, Katherine Clegg Smith2, Elaine de Leon2, Michelle Jones3, Anna Kristina Gutierrez4, Allie Butanis5 and Clifton O. Bingham III6. 1Department of Medicine, Division of ClinEpi, Rheumatology, Respiriology, McGill University, Montreal, QC, Canada, 2Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, 3Johns Hopkins University School of Medicine, Baltimore, MD, 4Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, 5Rheumatology, Johns Hopkins School of Medicine, Baltimore, MD, 6Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Although patient-reported outcomes (PROs) are routinely collected for research and quality purposes, they have not been routinely incorporated into the routine care of patients. Clinicians are best able to provide chronic disease care that is patient-centered when they have a better understanding of their patients’ lived experiences. We hypothesized that having PRO results describing the range of symptoms and impacts of living with RA during clinic visits would provide insight into patient priorities, values, and preferences and facilitate SDM around treatment choices. Evidence for the impact of PROs on patient management from the clinician’s perspective are presented.

Methods: Participants with RA in an observational study at an academic arthritis center completed PROMIS fatigue, pain, physical function, sleep, and participation on a tablet in the waiting room. Reports of results in numerical and graphical formats were available during the visit for review. Semi-structured interviews were used to query the experiences of rheumatologists and rheumatology fellows on the impact of PROs on RA patient management.

Results: Data are from interviews with 4 rheumatologists and 6 fellow trainees. Among rheumatologists, access to real-time PROMIS results that could be addressed during the visit was highly valued. All stated that completing questionnaires helped patient feel “heard” and discussing results made it clear that patients’ experiences mattered. Several said reports prompted them to ask about symptoms they may have overlooked. There was concern that some symptoms (depression, anxiety) may have little to do with RA; identifying these without a clear pathway to resources was potentially problematic. All noted that how they used results differed depending on the needs of specific patients and the nature of the visit. While rheumatologists felt able to control the time spent discussing results, fellows expressed less certainty about their ability to control conversations, the value of additional PROs for RA care, or its impact on decision-making. Fellows also reported greater discomfort discussing results if they had not yet built a rapport with patients.

Conclusion: Expanded real-time assessments of RA symptom and impacts on day-to-day life as part of routine care appears to offer important new information to make RA care more patient-centered by informing discussions and facilitating shared decision-making around treatment. For trainees, the value of additional symptom information was balanced by concerns about greater time challenges, ways to integrate results into discussions and care plans, and availability of resources to address new problems that were identified. Results highlight opportunities to enhance broader communication skills training around potentially sensitive topics and quality of life in rheumatology training programs.

Funding PCORI IP2-PI0000737 and SC14-1402-10818.

Disclosure: S. J. Bartlett, None; K. Clegg Smith, None; E. de Leon, None; M. Jones, None; A. K. Gutierrez, None; A. Butanis, None; C. O. Bingham III, None.


Abstract Number: 1256
Uptake of Influenza and Pneumococcal Vaccination in Inflammatory Arthritis

Kieran Murray1 and Douglas J. Veale2, 1Rheumatology, Rheumatology Specialist Registrar, Dublin 4, Ireland, 2Rheumatology, St. Vincent's University Hospital, Dublin 4, Ireland

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Inflammatory arthritides such as RA and PsA increase infection risk. The Centre for Disease Control and Prevention (CDC) recommends vaccination against i. influenza for all adults annually and ii. pneumococcus for all ‘at-risk’ adults (> 65 years, specific conditions or those taking certain immunosuppressants). The aim of this study was to examine patients’ knowledge, uptake and attitudes to influenza and pneumococcal vaccination, and to assess opportunities to increase vaccination rates in our inflammatory arthritis clinic.

Methods:
Patients attending the inflammatory arthritis clinic in St Vincent’s University Hospital, Dublin completed an anonymous 23 question worksheet while awaiting their physician. Demographic details, medical history, medications, knowledge about vaccinations, vaccination status, reasons for lack of vaccination and attitudes regarding willingness to use a smart phone for healthcare record were recorded.

Results:
125 patients responded, 79% were female and 71% were over 50 years of age. 83% had completed high school. Half of the patients had RA. 23% of patients were using methotrexate, 17% oral steroids and 34% an injectable biologic.

Awareness that rheumatological conditions increase risk of infection was reported by 51%, while 54% were aware that their medications can increase the infection risk. 67% were aware influenza vaccination was recommended, most commonly via their primary care physician (PCP) at 42%. 10% learnt of the need for vaccination through television or radio.

55% were up to date with their ‘flu’ vaccination, mainly (68%) via their PCP. 4% of patients received their last vaccine in hospital. Stated reasons for not being adequately vaccinated included lack of awareness (23%) and fear of side effects (15%).

66% were aware pneumococcal vaccination might be indicated, 42% were informed by their PCP. None were informed by television or radio. 47% of respondents were up to date with their pneumococcal vaccination, mainly (82%) via their PCP. 2% had been vaccinated in the hospital. 59% of those not adequately vaccinated cited lack of awareness as the reason.

75% of patients had access to a smart phone. 76% were willing to use their smart phone for their healthcare record and reminder re vaccinations.

Conclusion:
Patient awareness of the risk of infection associated with disease and treatment was low. Although over two thirds were aware of influenza and pneumococcal vaccination recommendations, significantly fewer patients were up-to-date with their vaccinations. The majority of vaccinations took place in the community. The use of mass media and mobile technology may be an effective means of increasing vaccination uptake.

Disclosure: K. Murray, None; D. J. Veale, None.


Abstract Number: 1257
A Scoping Review of Contextual Factors of Patient Decision Aids in Osteoarthritis

Alexa Meara¹, Karine Toupin-April², Bev Shea³, Liana Fraenkel⁴, Jennifer Barton⁵, Peter Brooks⁶, Maarten de Wit⁷ and Peter Tugwell⁸
1Internal Medicine/Rheumatology, The Ohio State University Wexner Medical Center, Columbus, OH, 2Children’s Hospital of Eastern Ontario Research Institute, Ottawa, ON, Canada, 3University of Ottawa, Ottawa, ON, Canada, 4Yale University, New Haven, CT, 5Oregon Health and Science University, Portland, OR, 6The University of Queensland, Sidney, Australia, 7EULAR standing committee of PARE, Zurich, Switzerland, 8Center For Global Health, Institute of Population Hlth, Ottawa, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Patient decision aids (PDAs) have been developed to help patients make informed health care decisions that are consistent with their values and preferences. Patients diagnosed with osteoarthritis (OA) can choose from a wide array of treatments, such as physical therapy, exercise, medication, joint injections, and surgery (when indicated). OMERACT Filter 2.0 highlights the importance of measuring relevant contextual factors (i.e., any factors that indirectly influence the process or outcomes of interventions) in clinical studies evaluating PDAs. However, very few studies have assessed these factors. A Cochrane Systemic Review published in 2017 performed an in-depth review of benefits of PDAs and performed subgroup analyses based on the timing of the use of PDAs (i.e., before or during a consultation) but did not find any impact. The current study sought to systematically search the literature in order to appraise and summarize contextual factors that were assessed in randomized controlled trials (RCTs) of PDAs in OA.

Methods: We conducted a scoping literature review using Medline, Embase, AMED, PsycInfo and Cochrane Central from inception of the databases to June 14 2017. The search strategy was based on the Cochrane systematic review of PDAs and MeSh terms related to OA. Citations were included if they reported on RCTs evaluating PDAs compared to any control group in patients with OA.

Results: 235 citations were identified after removal of duplicates and six RCTs of PDA in OA were included. Of the six included trials, four were about the effectiveness of PDAs for knee arthroplasty and two others were for overall management of OA. Three RCTs measured PDA format as the main predictor of decision making outcomes (i.e., internet vs. DVD PDAs, and paper-based educational booklet vs. video-booklet PDA). One of these RCTs also examined the impact of patient testimonials. A fourth trial measured the setting in which the PDA was used (i.e., community or academic hospital setting) and another trial conducted subgroup analyses for patients’ characteristics. Format and content of the PDA and patients’ younger age (i.e., 50-55 years old), sex (female) and willingness to undergo surgery at baseline were linked to better decision-making outcomes.

Conclusion:
Contextual factors assessed in RCTS of PDAs in OA include format, content and setting of the PDA and patients’ characteristics. There is a need for more research to assess contextual factors in PDA RCTs in rheumatology to fulfill the OMERACT filter 2.0. Potential contextual factors to consider include the timing in which PDAs are used and the interface between the PDA and patients (e.g., tailoring to patients’ health literacy, understanding, etc). Future work will be also be needed to assess contextual factors of PDAs in other prevalent rheumatic conditions.

Disclosure: A. Meara, None; K. Toupin-April, None; B. Shea, None; L. Fraenkel, None; J. Barton, None; P. Brooks, None; M. de Wit, None; P. Tugwell, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/a-scoping-review-of-contextual-factors-of-patient-decision-aids-in-osteoarthritis

Abstract Number: 1258

Divided By a Common Language: Challenges in Physician-Patient Communication Limit Patient Understanding and Support in Systemic Sclerosis with Interstitial Lung Disease (SSc-ILD)
Background/Purpose:
Systemic sclerosis is a potentially life-threatening, clinically diverse, and rare condition. The prognosis and course of disease is difficult to predict and treatment is complex. This can be challenging to understand or explain, posing challenges for effective physician-patient communication. Our study explored communication between physicians and patients with SSc-ILD to assess communication and understanding and identify information gaps and needs.

Methods:
23 20-minute consultations between physicians (rheumatologists, pulmonologists) and patients (19 real, 4 actors) with diagnosed SSc-ILD across 5 countries were directly observed and video/audio recorded. SSc-ILD (limited/diffuse) of all severities, with a range of other organ involvement, was represented. None of the discussants were known to one another. Consultations were analysed using linguistic techniques based on interactional sociolinguistic discourse analysis to understand the pattern and meaning of communication, whether the needs of both participants were met, and the level of understanding between participants.

Results:
The following issues inhibited effective communication between patients and physicians:

1. 1. Consultation pattern: In most consultations, patients were given little opportunity to explain their concerns or ask questions. Physicians solicited the patient’s story but quickly diverted it to extract clinical information. During effective consultations, patients were invited to tell their story, guided by physicians, who also gathered clinical information. Physicians used techniques to check and demonstrate understanding, express empathy and build rapport.

1. 2. Use and meaning of language: Physicians used plain language in their explanations but often reverted to medical terminology when the issue became complex. Patients often used medical terminology with limited understanding of the terms. Hence, some physicians mistakenly believed patients had a better understanding than they actually had.

1. 3. Cognitive models: Physicians and patients had different ways of understanding SSc-ILD based on their knowledge, experiences, expectations and beliefs. This determined what information patients shared and how they interpreted information from physicians. Differences in cognitive models between patients and physicians were responsible for misunderstandings.

Conclusion:
Communication challenges between patients and physicians limit joint understanding of SSc-ILD and may result in both parties missing important information and patients being less aware of self-help management approaches. Strategies should be developed with physicians to facilitate effective communication and increase patient understanding and support.

Disclosure: C. Denton, None; B. Laird, None; L. Moros, None; J. L. Luna Flores, None.

Abstract Number: 1259
a Transition Toolkit

Nadia Luca1, Evelyn Rozenblyum2, April Elliott3, Lynn R. Spiegel4, Nicole Johnson5, Sara Aholu6, Yvonne Brandelli3, Carolyn Johns7, Stephanie Luca8, Dianne P. Mosher9, Gordon Soon10, Karine Toupin-April11, Gabriela Uifalusi3 and Jennifer N. Stinson12, 1Pediatric Rheumatology, University of Calgary, Alberta Children's Hospital, Calgary, AB, Canada, 2Royal University Hospital, Saskatoon, SK, Canada, 3Alberta Children's Hospital, Calgary, AB, Canada, 4Rheumatology/Pediatrics, The Hospital for Sick Children, Toronto, ON, Canada, 5Alberta Children's Hospital, University of Calgary, Calgary, AB, Canada, 6Hospital for Sick Children, Toronto, ON, Canada, 7Alberta Health Services, Calgary, AB, Canada, 8The Hospital for Sick Children, Toronto, ON, Canada, 9Med, University of Calgary, Calgary, AB, Canada, 10Pediatric Rheumatology, Hospital for Sick Children, Toronto, ON, Canada, 11Children's Hospital of Eastern Ontario Research Institute, Ottawa, ON, Canada, 12Anesthesia and Pain Medicine, The Hospital for Sick Children, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Transition from pediatric to adult care is an important process for adolescents and young adults with Juvenile Idiopathic Arthritis (JIA). A seamless transition is critical for optimal health outcomes; however, young people are faced with obstacles at the patient, caregiver, and health care system levels. A “transition tool-kit” provides a standardized approach to the transition process and has the potential to overcome some of the existing barriers. A needs assessment was conducted to determine the most important features and tools that Canadian users would value in a transition tool-kit.

Methods:
Participants were recruited from four Canadian rheumatology centres. In total, 22 individual interviews and 12 semi-structured focus groups (with approximately 4-7 participants in each) were conducted, including all user types (adolescents, young adults, caregivers, and pediatric and adult health care providers [HCPs]). Discussion focused on preparations, concerns and wishes regarding the transition process, and how these issues could be addressed using a transition tool-kit. The qualitative data were transcribed and analyzed by two coders using simple descriptive content analysis (NVivo 10). Demographic and disease-related data were analyzed using descriptive statistics.

Results:
In total, 20 adolescents (60% female; mean age = 15.9±1.3 years), 12 young adults (58.3% female; mean age = 20.3±1.8 years), 26 caregivers (88.5% female), 20 pediatric HCP (90% female; mean number of years practicing = 14.3±7.6), and 8 adult HCP (87.5% female; mean number of years practicing = 12.0±13.8) participated.

The main themes from the qualitative analysis include:

(1) Preparation for transition: most participants expressed concerns about transition and felt that patients were not properly prepared; however, a small number of adolescent participants expressed no concerns.

(2) Treatment decision making: most participants agreed that patients should be the ultimate decision makers following discussion with their caregivers and HCPs. Patients and caregivers identified the importance of access to accurate and comprehensive disease- and medication-related information from HCPs and online resources prior to making a treatment decision.

(3) Transition tools: participants felt that a tool-kit would streamline the transition process and provided suggestions for potential components, such as a calendar feature to remind patients of appointments and to take medication, an online self-guided JIA resource website, a smartphone app for tracking and managing symptoms, and a resource to help manage JIA in college or university. Most participants thought that the tool-kit would be best suited as a website or mobile application.

Conclusion:
Overall, participants felt that adolescents are not adequately prepared for transition, and had a positive response to the concept of a transition tool-kit. Key components of this tool-kit were identified by users, with a priority on resources for self-management and
shared decision-making. Next steps include the development of a standardized transition tool-kit, which will incorporate existing tools and development of new tools as necessary.

Disclosure: N. Luca, None; E. Rozenblyum, None; A. Elliott, None; L. R. Spiegel, None; N. Johnson, None; S. Ahola Kohut, None; Y. Brandelli, None; C. Johns, None; S. Luca, None; D. P. Mosher, None; G. Soon, None; K. Toupin-April, None; G. Uifalusi, None; J. N. Stinson, None.

Abstract Number: 1260

Lupus Diagnosis: Process and Patient Experience

Rossi Daly, Roushanac Partovi and Patricia Davidson, Lupus Foundation of America, Washington, DC

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Delays in lupus diagnosis and misdiagnosis are sources of concern, as uncontrolled disease activity and early damage can increase mortality risk. The purpose of this study is to analyze the diagnostic process through the patient perspective and provide insight into unmet needs in lupus diagnosis.

Methods:
This cross-sectional study draws from a one-time online national survey conducted between December 2015 and January 2016 among 3,022 adults who self-reported a lupus diagnosis. To assess patient perspective on the diagnosis process, participants answered questions regarding symptoms pre-diagnosis, the provider(s) they discussed symptoms with, and the time frame to diagnosis. Descriptive statistics were conducted on demographic information and all diagnosis process measures.

Results:
Respondent characteristics are described in Table 1.

This analysis provides a detailed look at the diagnostic process from the patient perspective. Beginning with the symptoms prompting a first visit, musculoskeletal symptoms and fatigue illustrate the non-specificity experienced by nearly half of the respondents (Table 2). Of importance, a majority of respondents (73.2%) specifically made an appointment to discuss these symptoms, 72% discussing them with a primary care provider. Of those who discussed symptoms with other types of providers, over 75% also discussed the symptoms with a rheumatologist. Leading up to respondents’ diagnosis, more than half reported being told there was nothing wrong with them or that their symptoms were psychological (54.1%). Furthermore, 41% of respondents reported being told they had something other than lupus, and concurrently, nearly 40% of individuals waited more than one year from the onset of symptoms to receive an accurate diagnosis. At the time of diagnosis, over one third of respondents (34.5%) reported having severe symptoms.

Conclusion:
The findings of this study suggest the need to provide ongoing education to both primary care and specialty providers in diagnosing lupus. Qualitative responses in this study, not reported here, also suggest that poor provider-patient communications may contribute to the delay in diagnosis. Lastly, describing the providers and care settings typically involved in diagnosis can be useful for creating a framework to identify future areas of intervention and/or research.
Table 1. Background characteristics of respondents (n = 3,022)*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>2823 (91.5)</td>
</tr>
<tr>
<td>Male</td>
<td>196 (6.5)</td>
</tr>
<tr>
<td>Geographic location</td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>560 (18.6)</td>
</tr>
<tr>
<td>(Sub)urban</td>
<td>2446 (81.4)</td>
</tr>
<tr>
<td>Insurance</td>
<td></td>
</tr>
<tr>
<td>Private</td>
<td>1833 (65.7)</td>
</tr>
<tr>
<td>Medicaid/Medicare</td>
<td>851 (34.3)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>Young adults (18-24)</td>
<td>81 (2.7)</td>
</tr>
<tr>
<td>Adults (25-54)</td>
<td>2604 (85.2)</td>
</tr>
<tr>
<td>Older adults (65-79)</td>
<td>337 (11.2)</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>1749 (57.9)</td>
</tr>
<tr>
<td>African American</td>
<td>544 (18)</td>
</tr>
<tr>
<td>Asian</td>
<td>90 (3)</td>
</tr>
<tr>
<td>Latino</td>
<td>399 (13.2)</td>
</tr>
<tr>
<td>Other races</td>
<td>240 (7.9)</td>
</tr>
</tbody>
</table>

* Individual items may not add to total due to missing data.

Table 2. Characteristics of patient experience in diagnosis process (n = 3,022)*

<table>
<thead>
<tr>
<th>Top symptoms prompting visit</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Musculoskeletal</td>
<td>1365 (32.2)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>1295 (44.6)</td>
</tr>
<tr>
<td>Skin rash</td>
<td>986 (26.2)</td>
</tr>
<tr>
<td>詈 of test visit</td>
<td></td>
</tr>
<tr>
<td>Annual appointment</td>
<td>420 (14.9)</td>
</tr>
<tr>
<td>Appointment made for symptoms</td>
<td>2044 (75.7)</td>
</tr>
<tr>
<td>Emergency room</td>
<td>360 (9.9)</td>
</tr>
</tbody>
</table>

First provider discussed symptoms with

<table>
<thead>
<tr>
<th>Provider</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCP</td>
<td>2046 (72.3)</td>
</tr>
<tr>
<td>Pediatric</td>
<td>41 (2.8)</td>
</tr>
<tr>
<td>Ortho-ED</td>
<td>92 (3.1)</td>
</tr>
<tr>
<td>Rheumatologist</td>
<td>201 (6.7)</td>
</tr>
<tr>
<td>Dermatologist</td>
<td>198 (6.9)</td>
</tr>
<tr>
<td>ER Physician</td>
<td>146 (4.8)</td>
</tr>
<tr>
<td>Other</td>
<td>97 (3.2)</td>
</tr>
</tbody>
</table>

Lupus mentioned in their visit

<table>
<thead>
<tr>
<th>Response</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>2093 (70.3)</td>
</tr>
<tr>
<td>Yes</td>
<td>784 (26.7)</td>
</tr>
</tbody>
</table>

Provider response pre-diagnosis

<table>
<thead>
<tr>
<th>Response</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unknown what is wrong</td>
<td>1317 (46.6)</td>
</tr>
<tr>
<td>More something other than lupus</td>
<td>1235 (44.7)</td>
</tr>
<tr>
<td>Nothing is wrong</td>
<td>93 (3.1)</td>
</tr>
</tbody>
</table>

Is it psychological

<table>
<thead>
<tr>
<th>Response</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>763 (25.9)</td>
</tr>
</tbody>
</table>

Time to diagnosis

<table>
<thead>
<tr>
<th>Duration</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 1 month</td>
<td>1815 (60.2)</td>
</tr>
<tr>
<td>1-3 months</td>
<td>579 (19.3)</td>
</tr>
<tr>
<td>4-6 months</td>
<td>330 (11.2)</td>
</tr>
<tr>
<td>7-11 months</td>
<td>289 (9.5)</td>
</tr>
<tr>
<td>1-2 years</td>
<td>414 (14.4)</td>
</tr>
<tr>
<td>3+ years</td>
<td>75 (2.5)</td>
</tr>
</tbody>
</table>

Severity at ED

<table>
<thead>
<tr>
<th>Severity</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>496 (33.2)</td>
</tr>
<tr>
<td>Moderate</td>
<td>1114 (77.0)</td>
</tr>
<tr>
<td>Severe</td>
<td>326 (34.3)</td>
</tr>
<tr>
<td>Life-threatening</td>
<td>40 (1.3)</td>
</tr>
</tbody>
</table>

* Individual items may not add to total due to missing data and multiply coded responses.

1 Rahman P, Gladman D, Urowitz M, Hallett D. Early damage as measured by the SLICC/ACR damage index is a predictor or mortality in systemic lupus erythematosus. Lupus 2001; 10: 93-96.

Disclosure: R. Daly, None; R. Partovi, None; P. Davidson, None.


Abstract Number: 1261

The Effects of Disease Burden, Helplessness, and Pain on Depressive Symptoms in Rheumatoid Arthritis and Systemic Lupus Erythematosus

Sera Ramadan1, Perry M. Nicassio2, George Karpouzas3 and Sarah Ormseth4, 1Internal Medicine, Dignity Health St. Mary Medical Center, Long Beach, CA, 2Cousins Center for PNI, UCLA, LA, CA, 3Division of Rheumatology, Harbor-UCLA Medical Center, Torrance, CA, 4Rheumatology, Harbor-UCLA Medical Center, Torrance, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster II
Session Type: ACR Poster Session B
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** This research tested an integrated framework examining patient global assessment of disease activity (PtGA), maladaptive illness beliefs and pain as determinants of mood disturbance in rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) patients.

**Methods:** The data of 232 patients (RA = 110, SLE = 122) were used to evaluate the hypothesized model in which PtGA (rated on a 10-cm visual analogue scale) directly and indirectly predicted mood disturbance (Center for Epidemiologic Studies Depression Scale and SF-36 Mental Health) through maladaptive illness beliefs (Arthritis Helplessness Index) and pain (SF-36 Pain and pain visual analog scale). Using EQS 6.1, multigroup structural equation modeling (SEM) was employed to test the model as well as the potential moderating role of diagnosis (RA compared to SLE).

**Results:** The model fit the data well for both patient groups [for RA: CFI = 1.00, $\chi^2(6) = 1.93$, $p = .926$, RMSEA < .001; for SLE: CFI = 1.00, $\chi^2(6) = 2.04$, $p = .916$, RMSEA < .001]. However, there were some differences in the significance and magnitude of paths between model variables, which were further assessed in multigroup analyses. As hypothesized, in both patient groups PtGA had direct positive effects on maladaptive illness beliefs and pain, and pain predicted greater mood disturbance. Moreover, illness beliefs were associated with mood disturbance for RA patients and SLE patients, though the nature of that relation was different for the two groups. Among RA patients, maladaptive illness beliefs directly predicted mood disturbance ($\beta = .42, p < .001$) whereas for SLE patients, the effect of illness beliefs on mood was indirect (mediated by pain; $\beta_{\text{indirect}} = .39, p < .001$). Multigroup SEM results further indicated that while illness beliefs predicted higher levels of pain in both patient groups, the effect of was significantly stronger for lupus patients (RA: $\beta = .23, p = .006$; SLE: $\beta = .44, p < .001$).

**Conclusion:** These findings suggest that maladaptive illness beliefs and pain may serve as mechanisms through which PtGA influences mood disturbance in both RA and SLE. Multigroup structural equation modeling elucidated differences between groups in the mediating pathways connecting PtGA to mood disturbance and have important implications for the development of targeted interventions to enhance mood regulation in RA and SLE patients.

![Figure 1. Structural model with standardized path coefficients for Rheumatoid Arthritis (Lupus) subgroups.](image)

*Note: pathway set to 1.0. Dashed line indicate significant between-group differences in the magnitude of the structural path: Pt = Patient; SF-36 = Short Form-36; VAS = visual analogue scale; CES-D = Center for Epidemiologic Studies Depression scale.*

**Disclosure:** S. Ramadan, None; P. M. Nicassio, None; G. Karpouzas, None; S. Ormseth, None.


**Abstract Number:** 1262

**Stability of Two Short Medication Adherence Questionnaires over Time for Follow-up in Patients with Rheumatoid Arthritis**

Raquel Sweezie¹, Charles H. Goldsmith², Imy Chiu³, Anna Gutlin³, Sharron Sandhu⁴ and Mary J. Bell⁵, ¹Division of Rheumatology, Sunnybrook Health Sciences Centre, Toronto, ON, Canada, ²Simon Fraser University, Vancouver, BC, Canada, ³Rheumatology, Sunnybrook Health Sciences Centre, Toronto, ON, Canada, ⁴Medicine, University of Toronto, Toronto, ON, Canada, ⁵University of Toronto, Toronto, ON, Canada

**First publication:** September 18, 2017

**SESSION INFORMATION**
Background/Purpose: Adherence to disease modifying anti-rheumatic drug (DMARD) therapy is suboptimal in patients with rheumatoid arthritis (RA). Efficient, low-cost measures are required for better monitoring of medication adherence in the rheumatology clinic. Self-report tools are the most efficient and cost-effective measures available. A 5-item version of the Compliance Questionnaire Rheumatology (CQR5) was developed from the original 19-item version to reduce patient burden. Long-term reliability (stability) of this questionnaire has not yet been evaluated over a period equivalent to RA patient follow-up (3 to 6 months). Therefore, we looked at stability of the CQR5 and the 9-item Medication Adherence Report Scale (MARS9), another short medication adherence tool that has been shown to be valid in a sample of RA patients.

Methods: RA patients (disease duration ≥ 1 year) taking at least one DMARD prescription were randomly selected from a rheumatology outpatient clinic database. Patients were assessed at baseline and three months. Demographic data were collected at baseline. At each visit, medication adherence was assessed with the CQR5 and MARS9. Each item on the CQR5 was scored on a four point Likert scale (1 = strongly disagree, 4 = strongly agree). Scores for each item were then summed into a total score which varied between 0 and 20. For the MARS9, each item was scored on a five point Likert scale (1 = always, 5 = never) and item scores were summed into a total score varying from 9 to 45. On both questionnaires, higher scores indicated greater adherence. Stability analysis was performed with the intraclass correlation coefficient (ICC) and the mean difference between measurements obtained at baseline and three months.

Results: 100 RA patients, ages [mean(SD)] 60.75(12.67) years, were recruited. 4 patients dropped out, therefore 96 were included in the analysis. In this sample, the CQR5 and MARS9 demonstrated good and fair stability, respectively [ICC_CQR5 = 0.73(CI 95% = 0.61 to 0.81); ICC_MARS9 = 0.43(CI 95% = 0.24 to 0.58)]. One-sample t-tests showed that the differences in measurement from baseline to three months were not significantly different from zero (p > 0.05) for both the CQR5 [mean(SD) = -0.22 (1.57)] and MARS9 [mean(SD) = -0.15 (4.18)]. The CQR5 and MARS9 had similar mean differences but variability for the MARS9 was larger than for the CQR5, indicating greater consistency across measurements for the CQR5.

Conclusion: We demonstrated stability of a short, rheumatology-specific adherence questionnaire in a time frame similar to RA patient follow-up. Our results also suggest that the CQR5 may be a more stable measure of medication adherence than the MARS9 when it is used in a rheumatology clinic setting.

Disclosure: R. Sweezie, None; C. H. Goldsmith, None; I. Chiu, None; A. Gutlin, None; S. Sandhu, None; M. J. Bell, None.


Abstract Number: 1263

Relevance and Utility of Patient Reported Outcomes Measurement Information System (PROMIS®) Instruments in SLE: A Qualitative Study

Shanthini Kasturi1, Madeline Epsten2, Adena Batterman3, Roberta Horton3, Juliette Kleinman3, Jillian Rose3, Jackie Szymonifka2, Laura Robbins4 and Lisa A. Mandl1, 1Rheumatology, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, 2Rheumatology, Hospital for Special Surgery, New York, NY, 3Social Work Programs, Hospital for Special Surgery, New York, NY, 4Education & Academic Affairs, Hospital for Special Surgery, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM
Background/Purpose: The measurement of patient reported outcomes is a priority for patient-centered high value care. This is particularly true in chronic systemic diseases such as SLE, which can have a significant ongoing impact on quality of life. PROMIS instruments are precise, reliable, and valid measures of physical, mental, and social health, but their relevance and potential value in the clinical care of SLE patients has not been explored. The aims of this study were to evaluate SLE patient perspectives on the relevance and potential utility of PROMIS computerized adaptive tests (CATs) and PROMIS10.

Methods: Adult outpatients meeting 1997 ACR SLE classification criteria were recruited from an SLE Center of Excellence. Subjects completed 12 PROMIS CATs, the PROMIS10, and participated in focus groups (women) or structured interviews (men). Focus groups and interviews explored the relevance of PROMIS domains, the potential value of PROMIS instruments in routine medical care, and identified missing domains. Transcripts were analyzed for recurring themes and concepts using grounded theory.

Results: Twenty eight women and 4 men with SLE participated in 4 focus groups and structured interviews (table 1). Participants reported that PROMIS instruments, especially CATs, reflected their experience with lupus, with women prioritizing domains of fatigue, pain interference, physical function, sleep disturbance, and cognitive abilities as most relevant, and men selecting fatigue, sleep disturbance, anxiety, pain interference, and pain behavior. Subjects identified body image, intimate relationships, pregnancy, and relationships with providers as important areas not addressed by PROMIS. Participants were enthusiastic about using PROMIS in their medical care, citing utility in validating their experience, tracking symptoms and disease progression, facilitating communication with providers, and guiding treatment plans. A recurring theme in the focus groups and interviews was the importance of doctors reviewing the survey results.

Conclusion: SLE patients endorse PROMIS instruments as relevant, valuable, and potentially useful in improving clinical care. These data identify domains of importance to SLE patients, including men’s greater emphasis on mental health, and areas where there is a need to develop PROMIS instruments. Further longitudinal studies are essential to explore how to most effectively integrate PROMIS measures in routine clinical care.

Table 1. Socio-Demographic Characteristics of Participants (n=32)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (IQR) years</td>
<td>39 (33, 53.5)</td>
</tr>
<tr>
<td>Disease duration, median (IQR) years</td>
<td>11.6 (6.4, 24.2)</td>
</tr>
<tr>
<td>Female</td>
<td>28 (87.5%)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>6 (21.4%)</td>
</tr>
<tr>
<td>Black or African American</td>
<td>14 (50.0%)</td>
</tr>
<tr>
<td>Asian</td>
<td>3 (10.7%)</td>
</tr>
<tr>
<td>Other</td>
<td>5 (17.9%)</td>
</tr>
<tr>
<td>Ethnicity, Hispanic</td>
<td>9 (28.1%)</td>
</tr>
<tr>
<td>Insurance Type</td>
<td></td>
</tr>
<tr>
<td>Medicaid</td>
<td>18 (56.3%)</td>
</tr>
<tr>
<td>Medicare</td>
<td>5 (15.6%)</td>
</tr>
<tr>
<td>Third party/private</td>
<td>9 (28.1%)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
</tr>
<tr>
<td>Some high school or less</td>
<td>1 (3.1%)</td>
</tr>
<tr>
<td>High school graduate</td>
<td>2 (6.3%)</td>
</tr>
<tr>
<td>Some college</td>
<td>12 (37.5%)</td>
</tr>
<tr>
<td>College graduate</td>
<td>10 (31.3%)</td>
</tr>
<tr>
<td>Advanced degree</td>
<td>7 (21.9%)</td>
</tr>
<tr>
<td>Employment (Full or Part Time)</td>
<td>10 (31.3%)</td>
</tr>
<tr>
<td>On Disability</td>
<td>18 (58.1%)</td>
</tr>
</tbody>
</table>

Disclosure: S. Kasturi, None; M. Epsten, None; A. Batterman, None; R. Horton, None; J. Kleinman, None; J. Rose, None; J. Szymonifka, None; L. Robbins, None; L. A. Mandl, Boehringer Ingelheim, 2, American College of Physicians, 3, Up To Date, 7.

Abstract Number: 1264
Responsiveness of Patient Reported Outcomes Measurement Information System (PROMIS®) Computerized Adaptive Tests (CATs) in Systemic Lupus Erythematosus (SLE)

Shanthini Kasturi¹, Jackie Szymonifka², Jessica R. Berman³, Kyriakos A. Kirou¹, Alana B. Levine¹, Lisa R. Sammaritano¹ and Lisa A. Mandl¹, ¹Rheumatology, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, ²Rheumatology, Hospital for Special Surgery, New York, NY, ³Rheumatology, Hospital for Special Surgery Weill Cornell Medical College, New York, NY

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: PROMIS CATs are precise measures of quality of life with construct validity in SLE. The longitudinal responsiveness (sensitivity to change) of PROMIS CATs in SLE patients is unknown. We aimed to evaluate the responsiveness of PROMIS CATs in SLE outpatients using patient and physician-derived anchors.

Methods: Adult SLE patients were recruited from an SLE Center of Excellence. Subjects completed 14 selected PROMIS CATs at two visits a minimum of one month apart. SLE disease activity was measured with a patient global assessment of change, a physician global assessment and the physician-derived SELENA-SLEDAI. Responsiveness of PROMIS scores was evaluated using known-groups validity. Changes in PROMIS scores from baseline to follow up were compared across groups of patients who differed in their patient global assessment of change, physician global assessment, and SELENA-SLEDAI using Wilcoxon rank-sum tests.

Results: A diverse cohort of 228 SLE patients completed baseline surveys (table 1), with 190 (83%) completing a follow up survey. Using the patient-based anchor, there was a trend towards responsiveness across 11 PROMIS CATs (table 2), with statistically significant changes in T-scores with improvement and worsening of health status in Physical Function (effect size 0.15, 0.01, and -0.14 \( p < 0.02 \) with “better”, “same”, and “worse” health status respectively), Pain Interference (0.0, 0.0, 0.25 \( p < 0.02 \)), and Anger (-0.37, -0.08, 0.0 \( p < 0.03 \)) CATs. Using the physician global assessment and SELENA-SLEDAI as anchors, there was no notable trend or statistically significant change in scores across groups, with the exception of the Applied Cognition-Abilities CAT (0.34, -0.01, 0.0 \( p < 0.01 \)) when the SELENA-SLEDAI was used as an anchor.

Conclusion: PROMIS CATs showed modest responsiveness to patient-reported, but generally not physician-derived changes in lupus health status. These data suggest that certain PROMIS CATs are precise and sensitive tools which may be used to measure and monitor important aspects of the patient experience of lupus not captured by physician-derived metrics. Further studies are needed to evaluate the role of PROMIS in optimizing longitudinal disease management in SLE.

Table 1. Baseline Characteristics of Participants (n = 228)
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median [IQR] years</td>
<td>37 [29, 49]</td>
</tr>
<tr>
<td>Disease duration, median [IQR] years</td>
<td>10.6 [5.7, 16.4]</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>20 (8.8%)</td>
</tr>
<tr>
<td>Female</td>
<td>208 (91.2%)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>87 (38.2%)</td>
</tr>
<tr>
<td>Black or African-American</td>
<td>64 (28.1%)</td>
</tr>
<tr>
<td>Asian</td>
<td>26 (11.4%)</td>
</tr>
<tr>
<td>Other</td>
<td>38 (16.7%)</td>
</tr>
<tr>
<td>Not Reported</td>
<td>13 (5.7%)</td>
</tr>
<tr>
<td>Ethnicity, n (%)</td>
<td></td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>65 (28.5%)</td>
</tr>
<tr>
<td>Not Hispanic or Latino</td>
<td>155 (68.0%)</td>
</tr>
<tr>
<td>Not Reported</td>
<td>8 (3.5%)</td>
</tr>
<tr>
<td>Insurance, n (%)</td>
<td></td>
</tr>
<tr>
<td>Medicaid</td>
<td>82 (36.0%)</td>
</tr>
<tr>
<td>Medicare</td>
<td>22 (9.7%)</td>
</tr>
<tr>
<td>Third party/private</td>
<td>124 (54.4%)</td>
</tr>
</tbody>
</table>

Table 2. Responsiveness of PROMIS CATs: Changes in PROMIS T-Score (median [IQR]) by Anchor Type
<table>
<thead>
<tr>
<th>Patient Global Rating of Change</th>
<th>Better (n=77)</th>
<th>Same (n=79)</th>
<th>Worse (n=34)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ability to Participate in Social Roles</td>
<td>1.3 [-3.3, 5.4]</td>
<td>0.0 [-3.5, 2.0]</td>
<td>0.0 [-4.6, 1.9]</td>
<td>0.19</td>
</tr>
<tr>
<td>Anger</td>
<td>-4.1 [-9.1, 0.0]</td>
<td>-0.9 [-6.1, 5.6]</td>
<td>0.0 [-7.1, 8.4]</td>
<td>0.03</td>
</tr>
<tr>
<td>Anxiety</td>
<td>-3.5 [-7.7, 1.4]</td>
<td>-0.4 [-4.3, 3.4]</td>
<td>-0.2 [-6.1, 6.7]</td>
<td>0.13</td>
</tr>
<tr>
<td>Applied Cognition-Abilities</td>
<td>1.4 [-2.8, 4.4]</td>
<td>0.0 [-4.4, 3.5]</td>
<td>0.3 [-5.3, 3.6]</td>
<td>0.30</td>
</tr>
<tr>
<td>Applied Cognition-General Concerns</td>
<td>-0.9 [-6.2, 2.3]</td>
<td>0.0 [-3.8, 4.1]</td>
<td>-0.8 [-6.9, 7.1]</td>
<td>0.47</td>
</tr>
<tr>
<td>Depression</td>
<td>-1.5 [-7.2, 2.8]</td>
<td>0.0 [-4.7, 5.5]</td>
<td>3.7 [-7.0, 10.2]</td>
<td>0.15</td>
</tr>
<tr>
<td>Fatigue</td>
<td>-1.6 [-6.6, 3.5]</td>
<td>0.0 [-5.2, 4.3]</td>
<td>-1.5 [-3.9, 5.5]</td>
<td>0.51</td>
</tr>
<tr>
<td>Mobility</td>
<td>1.2 [-1.8, 3.4]</td>
<td>0.0 [-3.9, 2.3]</td>
<td>0.0 [-2.7, 2.6]</td>
<td>0.26</td>
</tr>
<tr>
<td>Pain Behavior</td>
<td>-1.3 [-4.3, 1.7]</td>
<td>0.0 [-3.7, 2.6]</td>
<td>1.0 [-2.8, 4.8]</td>
<td>0.07</td>
</tr>
<tr>
<td>Pain Interference</td>
<td>0.0 [-6.7, 0.4]</td>
<td>0.0 [-2.5, 4.1]</td>
<td>2.5 [-2.7, 5.4]</td>
<td>0.02</td>
</tr>
<tr>
<td>Physical Function</td>
<td>1.3 [-1.2, 4.7]</td>
<td>0.1 [-2.3, 2.4]</td>
<td>-1.2 [-4.2, 1.9]</td>
<td>0.02</td>
</tr>
<tr>
<td>Satisfaction with Social Roles &amp; Activities</td>
<td>1.8 [-2.4, 5.0]</td>
<td>0.0 [-4.6, 4.8]</td>
<td>0.0 [-5.8, 3.4]</td>
<td>0.21</td>
</tr>
<tr>
<td>Sleep Disturbance</td>
<td>0.0 [-5.9, 2.5]</td>
<td>-1.5 [-5.7, 1.8]</td>
<td>-0.4 [-4.3, 5.1]</td>
<td>0.50</td>
</tr>
<tr>
<td>Sleep-Related Impairment</td>
<td>-0.8 [-7.6, 5.4]</td>
<td>0.0 [-6.7, 4.4]</td>
<td>-0.2 [-3.7, 5.2]</td>
<td>0.95</td>
</tr>
<tr>
<td>SELENA-SLEDAI (Possible score range from 0 to 46)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥ 3 point decrease (n=37)</td>
<td>&lt; 3 point change (n=128)</td>
<td>≥ 3 point increase (n=31)</td>
<td>p-value</td>
</tr>
<tr>
<td>Ability to Participate in Social Roles</td>
<td>0.0 [-3.0, 1.9]</td>
<td>0.0 [-3.6, 4.8]</td>
<td>-0.1 [-4.0, 2.3]</td>
<td>0.66</td>
</tr>
<tr>
<td>Anger</td>
<td>-4.1 [-9.8, 2.8]</td>
<td>-1.9 [-6.5, 3.5]</td>
<td>-0.9 [-6.1, 7.7]</td>
<td>0.38</td>
</tr>
<tr>
<td>Anxiety</td>
<td>-2.5 [-9.2, 1.9]</td>
<td>-0.5 [-5.8, 3.4]</td>
<td>-1.8 [-5.7, 0.0]</td>
<td>0.40</td>
</tr>
<tr>
<td>Applied Cognition-Abilities</td>
<td>3.0 [0.0, 8.4]</td>
<td>-0.1 [-4.4, 3.3]</td>
<td>0.0 [-1.8, 3.9]</td>
<td>0.01</td>
</tr>
<tr>
<td>Applied Cognition-General Concerns</td>
<td>0.0 [-2.1, 3.2]</td>
<td>0.0 [-5.2, 2.8]</td>
<td>0.0 [-8.5, 7.7]</td>
<td>0.62</td>
</tr>
<tr>
<td>Depression</td>
<td>0.0 [-7.2, 7.3]</td>
<td>0.0 [-6.0, 4.4]</td>
<td>0.0 [-5.3, 4.0]</td>
<td>0.81</td>
</tr>
<tr>
<td>Fatigue</td>
<td>-1.5 [-4.7, 2.9]</td>
<td>-0.1 [-5.5, 4.6]</td>
<td>-2.2 [-3.9, 7.0]</td>
<td>0.93</td>
</tr>
<tr>
<td>Mobility</td>
<td>0.6 [-1.2, 2.6]</td>
<td>0.0 [-2.6, 1.4]</td>
<td>1.4 [-5.8, 0.8]</td>
<td>0.84</td>
</tr>
<tr>
<td>Response</td>
<td>Score 0</td>
<td>Score 2.8</td>
<td>Score 4.2</td>
<td>p-value</td>
</tr>
<tr>
<td>----------</td>
<td>----------</td>
<td>-----------</td>
<td>-----------</td>
<td>---------</td>
</tr>
<tr>
<td>Pain Behavior</td>
<td>0.0 [-5.4, 1.7]</td>
<td>-0.1 [-3.5, 2.6]</td>
<td>-0.5 [-2.7, 4.3]</td>
<td>0.59</td>
</tr>
<tr>
<td>Pain Interference</td>
<td>-1.3 [-6.5, 1.0]</td>
<td>0.0 [-2.6, 4.1]</td>
<td>0.0 [-5.4, 6.6]</td>
<td>0.07</td>
</tr>
<tr>
<td>Physical Function</td>
<td>0.1 [-1.6, 3.4]</td>
<td>0.5 [-2.2, 3.4]</td>
<td>0.2 [-3.8, 4.5]</td>
<td>0.89</td>
</tr>
<tr>
<td>Satisfaction with Social Roles &amp; Activities</td>
<td>1.6 [-2.5, 4.2]</td>
<td>0.0 [-4.0, 5.1]</td>
<td>-1.5 [-8.1, 4.9]</td>
<td>0.48</td>
</tr>
<tr>
<td>Sleep Disturbance</td>
<td>-1.5 [-7.0, 1.1]</td>
<td>0.0 [-5.0, 2.8]</td>
<td>-2.3 [-5.1, 1.6]</td>
<td>0.60</td>
</tr>
<tr>
<td>Sleep-Related Impairment</td>
<td>-0.6 [-3.1, 5.8]</td>
<td>0.0 [-7.4, 4.4]</td>
<td>0.0 [-6.6, 5.9]</td>
<td>0.54</td>
</tr>
<tr>
<td>Physician Global Assessment (Possible score range from 0 to 3)</td>
<td>≥ 1 point decrease (n=22)</td>
<td>&lt; 1 point change (n=151)</td>
<td>≥ 1 point increase (n=13)</td>
<td>p-value</td>
</tr>
<tr>
<td>Ability to Participate in Social Roles</td>
<td>0.1 [-3.0, 3.2]</td>
<td>0.0 [-3.6, 4.6]</td>
<td>-1.6 [-5.0, 0.0]</td>
<td>0.25</td>
</tr>
<tr>
<td>Anger</td>
<td>0.4 [-6.1, 7.7]</td>
<td>-2.8 [-7.8, 3.5]</td>
<td>0.2 [-3.3, 7.7]</td>
<td>0.10</td>
</tr>
<tr>
<td>Anxiety</td>
<td>0.4 [-4.5, 6.1]</td>
<td>-1.6 [-6.9, 2.1]</td>
<td>-0.2 [-3.6, 8.0]</td>
<td>0.17</td>
</tr>
<tr>
<td>Applied Cognition-Abilities</td>
<td>0.0 [-3.4, 3.5]</td>
<td>0.0 [-3.7, 3.9]</td>
<td>1.9 [-1.8, 6.7]</td>
<td>0.72</td>
</tr>
<tr>
<td>Applied Cognition-General Concerns</td>
<td>1.4 [-1.3, 4.9]</td>
<td>0.0 [-5.3, 2.8]</td>
<td>1.5 [-8.0, 5.1]</td>
<td>0.18</td>
</tr>
<tr>
<td>Depression</td>
<td>2.1 [-4.5, 6.3]</td>
<td>0.0 [-6.8, 4.3]</td>
<td>3.4 [-2.4, 8.7]</td>
<td>0.26</td>
</tr>
<tr>
<td>Fatigue</td>
<td>-0.7 [-6.4, 3.3]</td>
<td>-0.8 [-5.3, 3.7]</td>
<td>-1.6 [-3.4, 7.0]</td>
<td>0.83</td>
</tr>
<tr>
<td>Mobility</td>
<td>0.1 [-2.5, 1.8]</td>
<td>0.0 [-2.5, 2.9]</td>
<td>-0.8 [-6.2, 3.6]</td>
<td>0.52</td>
</tr>
<tr>
<td>Pain Behavior</td>
<td>0.0 [-2.8, 3.1]</td>
<td>-0.5 [-4.2, 2.2]</td>
<td>-0.9 [-2.7, 4.3]</td>
<td>0.60</td>
</tr>
<tr>
<td>Pain Interference</td>
<td>0.0 [-4.5, 4.0]</td>
<td>0.0 [-4.6, 3.2]</td>
<td>0.8 [-2.7, 6.1]</td>
<td>0.50</td>
</tr>
<tr>
<td>Physical Function</td>
<td>0.1 [-4.2, 4.2]</td>
<td>0.7 [-2.1, 3.5]</td>
<td>-1.2 [-3.0, 0.7]</td>
<td>0.48</td>
</tr>
<tr>
<td>Satisfaction with Social Roles &amp; Activities</td>
<td>-1.9 [-6.3, 4.2]</td>
<td>0.0 [-3.2, 5.0]</td>
<td>0.0 [-6.2, 5.8]</td>
<td>0.39</td>
</tr>
<tr>
<td>Sleep Disturbance</td>
<td>0.3 [-4.7, 5.2]</td>
<td>-1.1 [-5.6, 1.7]</td>
<td>0.6 [-5.1, 5.1]</td>
<td>0.25</td>
</tr>
<tr>
<td>Sleep-Related Impairment</td>
<td>0.7 [-1.6, 5.8]</td>
<td>-0.6 [-7.7, 4.6]</td>
<td>0.1 [-2.1, 5.9]</td>
<td>0.15</td>
</tr>
</tbody>
</table>

Disclosure: S. Kasturi, None; J. Szymonifka, None; J. R. Berman, None; K. A. Kirou, None; A. B. Levine, None; L. R. Sammaritano, None; L. A. Mandl, Boehringer Ingelheim, 2, American College of Physicians, 3, Up To Date, 7.
Impaired Cardiac Function in Juvenile Mixed Connective Tissue Disease Compared with Controls

Birgit Nomeland Witzczak¹, Siri Opsahl Hetlevik², Zoltan Barth¹,³, Thomas Schwartz⁴,⁵, Berit Flato²,⁶, Vibke Lilleby²,⁶ and Ivar Sjaastad¹,⁶,⁷

¹Institute for Experimental Medical Research, Oslo University Hospital, Oslo, Norway, Oslo, Norway, ²Department of Rheumatology, Oslo University Hospital, Rikshospitalet, Oslo, Norway, Oslo, Norway, ³Department of Pathophysiology and Gerontology, Medical School, University of Pécs, Pécs, Hungary, Pécs, Hungary, ⁴Oslo University Hospital and University of Oslo, Institute for Experimental Medical Research, Oslo, Norway, ⁵Department of Infectious Diseases, Oslo University Hospital, Oslo, Norway, Oslo, Norway, ⁶Institute for Clinical Medicine, University of Oslo, Oslo, Norway, Oslo, Norway, ⁷Department of Cardiology, Oslo University Hospital, Oslo, Norway, Oslo, Norway

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster II: Lupus and Related Disorders, Myositis, Scleroderma and Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Juvenile MCTD (JMCTD) is a heterogenic autoimmune disease, with SLE-, SSc- and PM/DM and RA like manifestations. Cardiac involvement is known in juvenile SLE, SSc, JDM and JIA, but data is limited in JMCTD. Adult MCTD is more benign than other CTDs, and cardiac involvement is mainly subclinical. Mortality, however, is mostly related to cardiac causes. Aim of study was to compare cardiac function in JMCTD patients with controls, and explore associations between cardiac function and disease characteristics.

Methods: 50 patients and 50 matched controls were examined median 14.9 years after disease onset. Cardiac function was assessed by echocardiography; LV systolic function was assessed by biplane ejection fraction (EF) and normalized mitral annulus displacement (long axis strain (LAS)); LV diastolic function was assessed by early diastolic tissue velocity (E’), early diastolic transmitral flow (MV E), and early/late diastolic transmitral flow ratio (MV E/A ratio). LV dysfunction was defined as EF≤61.6%, LAS≤15.3%, or E’≤9.3m/s, all defined by mean values -2 standard deviations in controls. Disease activity was assessed by SLEDAI, Juvenile Arthritis Disease Activity Score (JADAS), anti-RNP-levels and positive rheumatoid factor (RF). Patients were classified with SLE-like, SSc-like or PM-like findings.

Results: Table 1 shows characteristics and cardiovascular parameters in patients and controls. 86% were female; Mean age in patients was 27.4 years. EF and LAS were lower in patients than controls (P≤0.001 and P=0.045), but within normal range. MV E and MV E/A ratio were also impaired in patients (P ≤0.029). LV dysfunction was present in 16% patients versus 4% controls (P=0.046).

At follow-up, JADA was associated with lower EF (rsp= -0.283, p=0.049); Positive RF and higher SLEDAI at follow-up were associated with higher LAS (rsp= 0.318, P=0.026 and rsp= 0.281, P=0.048). Long duration of prednisolone treatment was associated with EF≤61.6% (rsp=0.340, P=0.016).

In final multivariable regression models (table 2), PM-like findings at diagnosis was an independent predictor of impaired EF (P=0.001), male sex was independent predictor of impaired LAS (P=0.002), and long disease duration was independent predictor of impaired E’ (P≤0.001).

Conclusion: LV cardiac function was impaired in JMCTD patients compared with controls. Subclinical LV dysfunction was present in 16% of the patients. PM-like manifestation at diagnosis, male sex and long disease duration predicted impaired cardiac function. Our results suggest that cardiac involvement in JMCTD varies among the different clinical phenotypes.
Table 1. Characteristics and cardiovascular parameters in JMCTD patients and controls

<table>
<thead>
<tr>
<th></th>
<th>JMCTD Patients n=50</th>
<th>Controls n=50</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Female sex</strong></td>
<td>43 (86%)</td>
<td>43 (86%)</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Variables assessed at diagnosis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLE-like findings (n=49)</td>
<td>46 (94%)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>SSc-like findings (n=49)</td>
<td>12 (25%)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>PM-like findings (n=49)</td>
<td>15 (31%)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Anti-RNP, U/L (n=48)</td>
<td>240 (240-999)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Positive RF (n=42)</td>
<td>26 (62%)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Variables assessed at follow-up</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease duration, years</td>
<td>14.9 (6.6-23.0)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Age, years</td>
<td>27.4 (9.9)</td>
<td>28.5 (9.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Height, cm (n=49 pairs)</td>
<td>166.0 (7.5)</td>
<td>169.6 (8.6)</td>
<td>0.022</td>
</tr>
<tr>
<td>BMI, kg/m² (n=49 pairs)</td>
<td>22.8 (3.5)</td>
<td>23.5 (3.0)</td>
<td>0.279</td>
</tr>
<tr>
<td>SBP, mmHg (n=47 pairs)</td>
<td>111.9 (14.5)</td>
<td>114.8 (11.9)</td>
<td>0.233</td>
</tr>
<tr>
<td>DBP, mmHg (n=47 pairs)</td>
<td>64.8 (15.0)</td>
<td>67.9 (8.6)</td>
<td>0.177</td>
</tr>
<tr>
<td>Total duration of prednisolone (months)</td>
<td>12 (2-40)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>SLE-like findings</td>
<td>27 (54%)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>SSc-like findings</td>
<td>34 (68%)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>PM-like findings</td>
<td>2 (4%)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Disease activity measures at follow-up</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRP, mg/L (n=41 pairs)</td>
<td>0.70 (0.50-1.90)</td>
<td>0.60 (0.50-0.90)</td>
<td>0.108</td>
</tr>
<tr>
<td>ESR, mm (n=47 pairs)</td>
<td>8.5 (5.0-16.0)</td>
<td>4.0 (2.0-7.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anti-RNP, U/L (n=49)</td>
<td>199 (38-240)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Positive RF (n=49)</td>
<td>17 (35%)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>SLEDAI</td>
<td>0 (0-0)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>JADA (n=49)</td>
<td>0 (0-0)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Echocardiography data at follow-up</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV ejection fraction, EF, %</td>
<td>65.8 (4.5)</td>
<td>69.6 (4.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV length, mm</td>
<td>77.4 (7.2)</td>
<td>79.6 (6.3)</td>
<td>0.109</td>
</tr>
<tr>
<td>MA displacement, mm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MV medial, mm</td>
<td>13.7 (1.9)</td>
<td>14.3 (1.5)</td>
<td>0.094</td>
</tr>
<tr>
<td>MV lateral, mm</td>
<td>15.1 (1.7)</td>
<td>16.5 (2.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>Long Axis Strain% (LAS%)</td>
<td>18.68 (1.94)</td>
<td>19.40 (2.07)</td>
<td>0.044</td>
</tr>
<tr>
<td>MV E velocity, m/s</td>
<td>0.82 (0.12)</td>
<td>0.90 (0.16)</td>
<td>0.015</td>
</tr>
<tr>
<td>MV E/A ratio</td>
<td>1.95 (0.46)</td>
<td>2.16 (0.56)</td>
<td>0.029</td>
</tr>
<tr>
<td>E’ (cm/s)</td>
<td>12.38 (1.63)</td>
<td>12.86 (1.79)</td>
<td>0.129</td>
</tr>
</tbody>
</table>

Values are mean (SD) or median (IQR) or number (%). Anti-RNP, anti-ribonuceloprotein antibodies; BMI, body mass index; CRP, c-reactive protein; DBP, diastolic blood pressure; E’, early diastolic tissue velocity; ESR, erythrocyte sedimentation rate; JADA, Juvenile Arthritis Disease Activity Score; LA, left atrium; LAS, long axis strain; LV, left ventricular; MA, mitral annulus; MV A, late diastolic transmitral flow; MV E, early diastolic transmitral flow; NA, not applicable; RF, rheumatoid factor; SBP, systolic blood pressure; SLEDAI, systemic lupus erythematosus disease activity index, SLICC, Systemic Lupus International Collaborating Clinics/ACR Damage Index; n=50 pairs or 50 patients or 50 controls unless otherwise stated.
Table 2. Uni-and multivariable linear regression for predictors of cardiac left ventricular function in JMCTD at follow up.

<table>
<thead>
<tr>
<th>Predictor at diagnosis</th>
<th>Univariable Linear Regression</th>
<th>Multivariable Linear Regression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$R^2$</td>
<td>Unstandardized</td>
</tr>
<tr>
<td>EF biplane, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(LV systolic function)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male sex</td>
<td>0.026</td>
<td>-2.0 (-5.7, 1.6)</td>
</tr>
<tr>
<td>Disease duration, years at FU</td>
<td>0.001</td>
<td>0.02 (-0.12, 0.15)</td>
</tr>
<tr>
<td>RNP, g/l</td>
<td>0.002</td>
<td>0.0 (-0.004, 0.003)</td>
</tr>
<tr>
<td>RF positive</td>
<td>0.015</td>
<td>1.1 (-1.8, 4.1)</td>
</tr>
<tr>
<td>SLE-like findings</td>
<td>0.021</td>
<td>-2.7 (-8.1, 2.7)</td>
</tr>
<tr>
<td>SSc-like findings</td>
<td>0.015</td>
<td>-1.3 (-4.3, 1.7)</td>
</tr>
<tr>
<td>PM/DM-like findings</td>
<td>0.120</td>
<td>-3.4 (-6.0, -0.7)</td>
</tr>
<tr>
<td>LAS, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(LV systolic function)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male sex</td>
<td>0.206</td>
<td>-2.5 (-3.9, -1.19)</td>
</tr>
<tr>
<td>Disease duration, years at FU</td>
<td>0.010</td>
<td>0.02 (-0.04, 0.08)</td>
</tr>
<tr>
<td>RNP, g/l</td>
<td>0.000</td>
<td>0.0 (-0.002, 0.001)</td>
</tr>
<tr>
<td>RF positive</td>
<td>0.068</td>
<td>1.1 (-0.2, 2.3)</td>
</tr>
<tr>
<td>SLE-like findings</td>
<td>0.092</td>
<td>-2.4 (-4.7, -0.2)</td>
</tr>
<tr>
<td>SSc-like findings</td>
<td>0.018</td>
<td>-0.6 (-1.9, 0.7)</td>
</tr>
<tr>
<td>PM/DM-like findings</td>
<td>0.018</td>
<td>-0.6 (-1.8, 0.6)</td>
</tr>
<tr>
<td>E’ m/s</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(LV diastolic Function)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male sex</td>
<td>0.009</td>
<td>-0.4 (-1.8, 0.9)</td>
</tr>
<tr>
<td>Disease duration, years at FU</td>
<td>0.174</td>
<td>-0.07 (-0.11, -0.03)</td>
</tr>
<tr>
<td>RNP, g/l</td>
<td>0.091</td>
<td>-0.001 (-0.002, 0.000)</td>
</tr>
<tr>
<td>RF positive</td>
<td>0.001</td>
<td>0.1 (-1.0, 1.1)</td>
</tr>
</tbody>
</table>
Covariates chosen for multivariable linear regression were variables with \( P \leq 0.20 \) in univariable regression and without multicollinearity in the multivariate models. Backward regression based on all potential predictors was performed as sensitivity analysis. \( P \)-value for inclusion was 0.05. Variables were removed by backward regression (\( P=0.10 \)).

Disclosure: B. N. Witczak, None; S. O. Hetlevik, None; Z. Barth, None; T. Schwartz, None; B. Flato, None; V. Lilleby, None; I. Sjaastad, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/impaired-cardiac-function-in-juvenile-mixed-connective-tissue-disease-compared-with-controls](http://acrabstracts.org/abstract/impaired-cardiac-function-in-juvenile-mixed-connective-tissue-disease-compared-with-controls)

Abstract Number: 1266

**Geographic Variation in Use of Echocardiography at Diagnosis and Detection of Acute Cardiac Disease in Youth with Systemic Lupus Erythematosus**

Joyce C. Chang\(^1\), Andrea M. Knight\(^2\), Laura M. Mercer-Ross\(^3\), Rui Xiao\(^4\) and Pamela F. Weiss\(^5\), \(^1\)Center for Clinical Epidemiology and Biostatistics, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, \(^2\)Division of Rheumatology, Center for Pediatric Clinical Effectiveness & PolicyLab, Children's Hospital of Philadelphia, Philadelphia, PA, \(^3\)Division of Cardiology, Children's Hospital of Philadelphia, Philadelphia, PA, \(^4\)Department of Biostatistics and Epidemiology, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, \(^5\)Division of Rheumatology, Center for Pediatric Clinical Effectiveness, Children's Hospital of Philadelphia, Philadelphia, PA

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017

Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster II: Lupus and Related Disorders, Myositis, Scleroderma and Vasculitis

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM

Background/Purpose: Child-onset systemic lupus erythematosus (SLE) is a chronic autoimmune condition with a high risk of organ damage. There are no guidelines on the use of echocardiography to detect cardiac manifestations. We aim to describe utilization of echocardiograms in youth with SLE, assess regional variation, and compare baseline echocardiogram use with subsequent rates of new cardiac diagnoses.

Methods: Using the Clininformatics™ DataMart (OptumInsight, Eden Prairie, MN) de-identified US administrative claims data from 2000-2013, we identified youth ages 10-24 years with an incident diagnosis of SLE (\( \geq 3 \) ICD-9 SLE codes 710.0, \( >30 \) days apart). Multivariable logistic regression with forward selection was used to identify factors associated with echocardiogram use during the baseline period from 1 year preceding to 6 months after SLE diagnosis. Linear regression was used to evaluate the association between echocardiogram use by census division and the proportion of imaged youth subsequently diagnosed with their first acute cardiac manifestation (pericarditis, myocarditis, endocarditis), at or after the baseline echocardiogram.

Results: Among 699 youth with new-onset SLE, 26% underwent echocardiogram at baseline. Youth hospitalized at diagnosis had the highest odds of baseline echocardiogram (OR 6.1, 95%CI 3.8-9.8), while youth with psychiatric diagnoses had lower odds (OR 0.5, 95%CI 0.3-0.7) (Table). There was significant geographic variability in echocardiogram use by census division after adjustment for other subject characteristics. The prevalence of acute cardiac manifestations at any time in the total cohort was 10%, ranging from 0-19% by division. There was a positive linear association between the proportion of youth in each division undergoing echocardiography and the proportion of those imaged who were subsequently diagnosed with new acute cardiac manifestations (Figure).
Conclusion: There is significant geographic variability in the use of peri-diagnostic echocardiograms in youth with SLE. Divisions with more widespread use of baseline echocardiograms diagnosed greater proportions of imaged youth with new acute cardiac manifestations following echocardiography. The results suggest the low frequency of cardiac diagnoses in divisions using few echocardiograms may partially reflect under detection. This underscores the need to obtain echocardiograms in large numbers of unselected youth with SLE to determine whether routine echocardiography is warranted to identify cardiac disease that would otherwise be missed or manifest in an acute clinical setting.

Disclosure: J. C. Chang, None; A. M. Knight, None; L. M. Mercer-Rosa, None; R. Xiao, None; P. F. Weiss, None.

Blood Pressure Control over Time in Childhood-Onset Systemic Lupus Erythematos

Pinar Ozge Avar Aydin¹, Jian Shan², Hermine I. Brunner¹ and Mark Mitsnefes³, ¹Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, ²Peking Union Medical College Hospital, Peking, China, Peking, China, ³Cincinnati Children’s Hospital Medical Center, Cincinnati, OH

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster II: Lupus and Related Disorders, Myositis, Scleroderma and Vasculitis

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM

Background/Purpose: Cardiovascular disease (CVD) is the leading cause of increased long-term morbidity and mortality in systemic lupus erythematosus (SLE). As an important modifiable risk factor for CVD, hypertension (HTN) is prevalent in patients with SLE and causes early cardiovascular aging and progression of the renal and cardiac disease. The aims of this longitudinal retrospective study were to determine the prevalence of HTN, evaluate longitudinal trend in blood pressure control, and assess risk factors for HTN in childhood-onset SLE (cSLE).

Methods: Between January 2012 and December 2016, demographic and clinical data of consecutive visits including sitting blood pressure, disease activity as measured by the SLE disease activity index (SLEDAI), presence of lupus nephritis, medication use, and results of the standard laboratory testing from cSLE diagnosis to the last visit were extracted from medical records of patients with cSLE admitted to the rheumatology clinic.

Results: 110 patients with cSLE were recruited: 79% female; 35% blacks; mean age at the baseline visit 13.3 ± 3.0 years; median follow-up duration 29.5 months; 19% had lupus nephritis. Twenty-nine percent of patients had HTN and 23% had pre-hypertension at the baseline visit. Patients with HTN had higher disease activity, more frequent renal involvement, lower eGFR, and were more obese than patients without HTN. In the multivariate analysis, the presence of nephritis, obesity, and high extra-renal disease activity (SLEDAI score ≥ 10) were independent predictors of HTN at the baseline. No significant changes in blood pressure control were observed in patients without nephritis. Patients with nephritis had less stage 1 and 2 HTN, and more prehypertension at the last follow-up compared to the baseline.

Conclusion: While hypertension is known feature of lupus nephritis, our results indicate that hypertension is common and persistent in cSLE without kidney disease with about one third of patients having uncontrolled elevated BP almost 3 years after onset of lupus. In addition to renal disease, obesity and high overall disease activity were identified as independent predictors of HTN in these patients.

Disclosure: P. O. Avar Aydin, None; J. Shan, None; H. I. Brunner, None; M. Mitsnefes, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/blood-pressure-control-over-time-in-childhood-onset-systemic-lupus-erythematous

Abstract Number: 1268

Risk Factors for Bone Loss in Juvenile-Onset Systemic Lupus Erythematosus: A Prospective Study

Luiz A Sousa1, Juliane Paupitz1, Nadia E Aikawa2, Liliam Takayama1, Valéria F. Caparbo1 and Rosa M R Pereira3, 1Rheumatology Division, Faculdade de Medicina da Universidade de Sao Paulo, Sao Paulo, Brazil, 2Rheumatology Division, Faculdade de Medicina da Universidade de Sao Paulo, Sao Paulo, Brazil, 3Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, Brazil

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster II: Lupus and Related Disorders, Myositis, Scleroderma and Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Juvenile-onset systemic lupus erythematosus (JoSLE) is associated with low bone mass for age and fractures, nevertheless risk factors and predictors of bone involvement are poorly understood in this condition. The aim of this study was to evaluate the risk factors for bone mass loss in patients with JoSLE analyzing clinical and laboratory data and bone microarchitecture parameters.
Methods: This study enrolled a sample of 49 female JoSLE patients, all of them with diagnosis, according to ACR classification criteria (2012 SLICC). All these patients were evaluated at baseline and after 3.5 years of follow-up in relation to: clinical data associated with the disease, lifestyle habits, treatment, laboratory tests including bone turnover markers (N-terminal propeptide of type 1 collagen - P1NP; C-terminal telopeptide of type 1 collagen - CTX), areal bone mineral density (aBMD) by dual X-ray absorptiometry (DXA) at lumbar spine and hip and parameters of bone microarchitecture by high-resolution peripheral quantitative computed tomography (HR-pQCT) at distal tibia and radius. Vertebral fractures were analyzed using DXA (VFA, Genant’s method). aBMD changes above the least significant change were considered significant. Based on the difference between final and baseline aBMD value, the patients were divided into 3 groups: aBMD gain (BG), aBMD loss (BL) and aBMD no change (NC).

Results: The mean age of patients was 18.7 ± 3.3 years and the mean disease duration was 6.0 ± 3.9 years. Sixty-one percent of patients presented aBMD gain, 18.4% aBMD loss and 22.4% remained stable over this period of follow-up. Comparing the BL group with the BG group, there was a higher frequency of alcohol consumption (33.3 vs. 0%, p = 0.009), a higher frequency of inadequate calcium intake (66.7 vs. 26.7%, p = 0.047) and lower serum levels of baseline P1NP (52.42 ± 33.56 vs. 119.72 ± 85.78 ng/mL, p = 0.036) in the former group. Moreover, a worse evolution of HR-pQCT bone parameters: trabecular volumetric density at tibia (-16.36 ± 15.71 vs. -1.55 ± 10.83 mg/cm³, p = 0.003) and cortical thickness at tibia (-0.025 ± 0.09 vs. 0.054 ± 0.07 mm, p = 0.009) was observed in the BL group. In addition, a higher frequency of renal activity was observed when the BL and NC groups were associated and compared to the BG group (52.6 vs. 23.3%, p = 0.036). No significant differences were observed regarding other clinical, laboratory and microarchitecture bone parameters and treatment.

Conclusion: This is the first longitudinal study in the literature that analyzed the risk factors of bone mass loss in JoSLE patients. The authors emphasize the importance of evaluating not only renal disease activity, but also lifestyle habits, mainly alcoholism and calcium intake in these young women. Furthermore, this study suggests that trabecular and cortical bone compartments were deteriorated in this disease and that low serum levels of P1NP may be a predictor of bone involvement in JoSLE.

Disclosure: L. A. Sousa, None; J. Paupitz, None; N. E. Aikawa, None; L. Takayama, None; V. F. Caparbo, None; R. M. R. Pereira, None.

View Abstract and Citation Information Online: http://acrabstracts.org/abstract/risk-factors-for-bone-loss-in-juvenile-onset-systemic-lupus-erythematosus-a-prospective-study

Abstract Number: 1269

Investigating Time Trends in Incident Pediatric Lupus across Ethnic Groups in Toronto, Canada—a Large, Multiethnic Metropolitan Area

Laura Y Feldman1, Patrick Brown2, Linda T Hiraki1,3 and Earl Silverman3, 1Child Health Evaluative Sciences, The Hospital for Sick Children, Toronto, ON, Canada, 2Department of Statistical Sciences, University of Toronto, Toronto, ON, Canada, 3Division of Rheumatology, The Hospital for Sick Children, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster II: Lupus and Related Disorders, Myositis, Scleroderma and Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Lupus incidence rates are known to differ by ethnicity among children and adults, with African ancestry as a risk factor for incident lupus, compared to those of European ancestry. Changes in a city’s ethnic demographic over time make it challenging to determine if changes in lupus incidence rates over time reflect population ethnic groups changes. We aimed to investigate whether lupus incidence rates have increased over time and whether trends over time differed by ethnic groups in Toronto, Canada—a large, multiethnic metropolitan area served by a tertiary care, pediatric lupus clinic.

Methods: Demographic information, including sex, self-identified ethnicity, age at diagnosis and region of residence, were prospectively collected on all children aged <18 years who were diagnosed with lupus between 1994 and 2015 in the pediatric lupus clinic at the Hospital for Sick Children (SickKids), Toronto. Only children living in Toronto were included in this analysis; those travelling to SickKids from outside of Toronto were excluded. Overall lupus incidence rates and 95% confidence intervals (95%CI) were calculated using population denominators for Toronto that were obtained from the Census of Canada, which is conducted every
Results: From 1994 to 2015, 503 children living in Toronto were diagnosed with lupus at SickKids, corresponding to an overall lupus incidence rate of 1.92 per 100,000 person-years (95%CI 1.75–2.09). Overall lupus incidence rates were highest among Chinese (3.77, 95%CI 2.96–4.58) and Black (3.62, 95%CI 2.88–4.35) children and lowest among White children (0.74, 95%CI 0.59–0.88). After adjusting for sex and age at diagnosis, the lupus incidence rate was found to increase by 5% each year from 1994 to 2015 (IRR 1.05, 95%CI 1.03–1.06). Interaction terms between the year and ethnicity were not statistically significant.

Conclusion: Pediatric lupus incidence increased over time in Toronto. While lupus incidence rates were substantially higher among Black and Chinese children, compared to White children, trends in the increase of lupus incidence did not differ over time between ethnic groups, but may reflect the changing ethnic population in Toronto.

Disclosure: L. Y. Feldman, None; P. Brown, None; L. T. Hiraki, None; E. Silverman, None.

Comparison of Clinical and Serological Features of Juvenile and Adult-Onset Neuropsychiatric Lupus in Spanish Patients

Sandra Garrote-Corr1, Alina Boteanu2, Walter A. Sifuentes-Giraldo1, Antia Garcia-Fernández1, Maria Luz Gámir-Gámir1 and Antonio Zea Mendoza1, 1Rheumatology, Hospital Universitario Ramón y Cajal, Madrid, Spain, 2Rheumatology, Hospital Universitario Ramon y Cajal, Madrid, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster II: Lupus and Related Disorders, Myositis, Scleroderma and Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Neuropsychiatric (NP) manifestations are a main cause of morbidity and mortality in juvenile-onset systemic lupus erythematosus (jSLE). Some studies suggest that they are more frequent and severe in jSLE than in adult-onset SLE (aSLE). We performed a study to compare the clinical and serological profile of pediatric and adult patients with neuropsychiatric lupus (NPSLE) treated in a Spanish tertiary center.

Methods: A retrospective study of patients with jSLE (age of onset: 0-18y) and aSLE (age of onset: >18y) seen in our center during the period 1988-2016 was performed. Case definitions of the American College of Rheumatology were used to identify NPSLE manifestations. Demographics, clinical and serological data were obtained through a review of their medical records.

Results: A total of 69 patients with NPSLE were included, aSLE 41 (59%) and jSLE 28 (41%), the comparison of groups is presented in the table. Most of them were Caucasian (92%), mean age at diagnosis in adults was 36.4 years (range: 19-68) and 13.9 years (range: 8-18) in children. The proportion of males was higher in the latter group. The mean duration of the disease was significantly greater in adults, as well as the time from SLE diagnosis to NP manifestation onset, although without significant difference. Central NP manifestations were the most frequent in both groups (aSLE 93%, jSLE 96%) regarding to the peripheral manifestations (aSLE 12%, jSLE 11%). The most frequent manifestations in aSLE were headache (29%), cerebrovascular disease (27%), seizures (17%) and myelopathy (15%), whereas in jSLE were seizures (46%), headache (29%), mood disorder/depression (25%), psychosis (18%) and autonomic disorders (18%). A significant group of patients presented ≥ 2 central manifestation during their evolution (aSLE 32%, jSLE 41%), with the mean number of manifestations in adults being 1.36 (range: 1-3) and in children 1.44 Range: 1-4 ). Patients with jSLE developed lupus nephritis (LN) with a significantly higher frequency, as well as higher titres of anti-DNA antibodies, erythrocyte sedimentation rate (ESR) and hypocomplementemia. During the study period there was mortality in 2 cases of aSLE and 2 jSLE (5% and 7%, respectively).
Juvenile NPSLE & Adult NPSLE & p-value  

| & Nº of patients & 28 (41%) & 41 (59%) & - |
| & Women:men & 20:8 & 39:2 & 0.0060* |
| & Time of disease (months) & 19.8 & 232.5 & 0.0001* |
| & NPSLE at onset & 7 (25%) & 11 (27%) & 0.8651 |
| & Time from diagnosis to NP manifestation (months) & 42.4 & 87.1 & 0.1268 |
| & Lupus nephritis & 16 (57%) & 9 (22%) & 0.0028* |
| & Antiphospholipid syndrome & 5 (18%) & 10 (24%) & 0.5182 |
| & ANA ≥ 1/1280 & 8 (29%) & 11 (27%) & 0.8736 |
| & Anti-DNA ab (IU/ml) & 178.9 & 39.4 & 0.0005* |
| & Anti-Ro/SSA ab & 10 (36%) & 17 (41%) & 0.6308 |
| & Anticardiolipin ab & 4 (14%) & 10 (24%) & 0.3054 |
| & Anti-ß2 glycoprotein I ab & 5 (18%) & 7 (17%) & 0.9328 |
| & Lupus anticoagulant & 8 (29%) & 10 (24%) & 0.6977 |
| & Cryoglobulins & 6 (21%) & 3 (7%) & 0.0874 |
| & ESR (mm/h) & 53.8 & 35.7 & 0.0199* |
| & CRP mg/l & 4.6 & 4.7 & 0.9687 |
| & C3 low (< 80 mg/dl) & 22 (79%) & 16 (39%) & 0.0012* |
| & C4 low (< 16 mg/dl) & 22 (79%) & 13 (32%) & 0.0001* |

Conclusion: Our results corroborate that juvenile patients with NPSLE present higher disease activity compared to adults. There was no significant difference in the time from SLE diagnosis to NP manifestation onset, but tended to be shorter in JSLE. The spectrum of NPSLE was varied both groups and an important proportion developed ≥ 2 manifestation. Mortality continues to be important in NPSLE in both age groups.

Disclosure: S. Garrote-Corral, None; A. Boteanu, None; W. A. Sifuentes-Giraldo, None; A. García-Fernández, None; M. L. Gámir-Gámir, None; A. Zea Mendoza, None.


Abstract Number: 1271

**Associations between Systemic Lupus Susceptibility (SLE) Loci and Anti-Phospholipid Antibody (aPL) Positivity in Childhood-Onset SLE (cSLE)**

Linda T Hiraki1,2, France Gagnon3, Earl Silverman2, Deborah M. Levy2, Sima Abu Alsaoud4 and Karl Everett1,3, 1Child Health Evaluative Sciences, The Hospital for Sick Children, Toronto, ON, Canada, 2Division of Rheumatology, The Hospital for Sick Children, Toronto, ON, Canada, 3Epidemiology, Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada, 4Rheumatology, The Hospital for Sick Children, Toronto, ON, Canada

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017  
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster II: Lupus and Related Disorders, Myositis, Scleroderma and Vasculitis  
Session Type: ACR Poster Session B  
Session Time: 9:00AM-11:00AM

Background/Purpose: Genome-wide association studies have identified nearly 60 susceptibility loci for systemic lupus erythematosus (SLE). However, few studies have investigated their influence on specific disease manifestations. Antiphospholipid
antibodies (aPL) are present in 30-40% of those with SLE and are major risk factors for thrombosis in childhood-onset SLE (cSLE). We hypothesized that SLE susceptibility loci are also associated with antiphospholipid antibody-positivity in cSLE.

**Methods:** We tested 41 SLE-related single nucleotide polymorphisms (SNPs) for association with lupus anticoagulant (LA) positivity and the presence of anti-cardiolipin (aCL) antibodies among cSLE patients diagnosed and followed at the Hospital for Sick Children, Toronto. Participants were genotyped on the Illumina Immunochip. Untyped SNPs were imputed from a 1000 genomes reference panel. Associations between SNPs and antibody status (positive/negative) were tested individually under the additive model and in a weighted genetic risk score.

**Results:** Among our sample of 348 cSLE patients, 56 were positive for LA and 144 were aCL-positive. The median age of SLE diagnosis was 13 (interquartile range: 11 – 15) and 19% were male. Of the 41 SNPs tested, 38 were genotyped or imputed with high quality. A one unit increase in SLE genetic risk score was associated with a 20% increase in odds of LA positivity (odds ratio (OR) 1.20; 95% CI: 0.88, 1.64) and a 13% increased odds of aCL (OR 1.13, 95% CI: 0.90 – 1.44) after adjustment for sex, age of SLE onset and ancestry. Though few were statistically significant, suggestive associations with antibody status were also seen for several of the individual SNPs included in the genetic risk score.

**Conclusion:** Our findings suggest that specific genetic variants related to SLE onset may underlie the development of aPL in cSLE patients.

**Disclosure:** L. T. Hiraki, None; F. Gagnon, None; E. Silverman, None; D. M. Levy, None; S. Abu Alsaoud, None; K. Everett, None.


**Abstract Number:** 1272

**Cluster Analysis of Autoantibodies and Their Relationship with Demographic and Clinical Features in Pediatric Systemic Lupus Erythematosus in the Childhood Arthritis and Rheumatology Research Alliance Legacy Registry**

**Ginger Janow**¹, Uptej Khalsa² and Tracy Andrews³, ¹Pediatric Rheumatology, Joseph M Sanzari Children’s Hospital, Hackensack Meridian Health Network, Hackensack, NJ, ²Pediatrics, Newark Beth Israel Medical Center, Children's Hospital of New Jersey, Newark, NJ, ³Research, Hackensack University Medical Center, Hackensack Meridian Health, Hackensack, NJ

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster II: Lupus and Related Disorders, Myositis, Scleroderma and Vasculitis

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Systemic Lupus Erythematosus (SLE) is a chronic, heterogeneous, multisystem autoimmune disease characterized, in part, by the presence of autoantibodies. The spectrum of disease presents a challenge when discussing disease course, outcomes and treatment. While autoantibody clusters have been described in adult lupus, there is little data examining relationships among specific autoantibody clusters and disease manifestations in pediatric SLE (pSLE) patients. The objective of this study is to identify distinct autoantibody clusters and their role in the development of unique disease profiles within an exclusively pSLE cohort.

**Methods:** We conducted a cross-sectional analysis of pSLE patients in the CARRA legacy database (of N=989), ages 1-19 years. Patients without a complete autoantibody profile (including anti-dsDNA, anti-Sm, anti-RNP, anti-Ro, and anti-La antibodies) were excluded. A cohort of 198 patients were analyzed. Two-step cluster analysis was performed to identify subsets of patients with similar autoantibody patterns. Additional frequency analysis and logistic regression were completed to assess for cluster/disease manifestation associations.

**Results:** Demographic variables were similar between the entire pSLE cohort and the subset of 198 patients included in our analysis. Anti-dsDNA was the most prevalent autoantibody (66.2%), followed by anti-Smith (50%), Anti-RNP (47%), anti-RO (45%), and
anti-LA (23.2%). The most prevalent manifestations were immunologic disorder (86.9%), hematological disorder (65.7%), arthritis (64.1%), renal disorder (54%), and malar rash (45.5%). Four distinct antibody clusters were identified: Cluster 1 (all 5 antibodies present, n=53), Cluster 2 (anti-RNP, anti-Smith, anti-dsDNA, n=50), Cluster 3 (anti-dsDNA only, n=51), and Cluster 4 (anti-Ro, anti-La, anti-RNP and anti-dsDNA, n=44). The distribution of African American patients was statistically different across clusters, with the lowest percentage in cluster 3 (p=0.0067). There were roughly twice as many white patients in cluster three as in the other three clusters with a p-value approaching significance (p=0.0634). Patients in Cluster 1 were on average younger than patients in Cluster 2 at age of onset and at first visit to a rheumatologist. Clusters 2 and 3 had the highest frequency of neuropsychiatric manifestations (40% and 50%, respectively). The remaining clinical manifestations were equally distributed among clusters. For individual antibodies, patients with an anti-La antibody were 61% less likely to develop arthritis and 79% less likely to develop serositis. Patients were three times more likely to have hematological manifestations when anti-RNP antibodies were present, and 73% less likely if anti-Smith antibodies were present.

**Conclusion:** Our data suggests that autoantibodies in pSLE do tend to cluster, which could potentially represent subsets of disease. However, in our sample, there was not a robust correlation amongst clinical manifestations and clusters. Future research is needed to better define these clusters in larger populations.

**Disclosure:** G. Janow, None; U. Khalsa, None; T. Andrews, None.


**Abstract Number:** 1273

**Patient Health Questionnaire-9 Utilization for the Detection of Depression in Adolescents and Young Adults with Lupus Nephritis**

Peter Yorgin¹, Eleanor Lazarow² and Robert Sheets³, ¹Pediatrics, Rady Children's Hospital/University of California San Diego, San Diego, CA, ²Social Work, Rady Children's Hospital, San Diego, CA, ³Pediatrics, Rady Children's Hospital/UCSD, San Diego, CA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster II: Lupus and Related Disorders, Myositis, Scleroderma and Vasculitis  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The PHQ-9 is a self-administered depression screening questionnaire. Patients with a PHQ-9 score of 0-4 have no depression, 5-9, mild; 10-14, moderate; 15-19, moderately severe; and 20-27, severe. A score ≥10 has a sensitivity of 88% and a specificity of 88% for major depression. Hypothesis: The PHQ-9 is a useful screening tool to identify depression in pediatric LN patients.

**Methods:** A retrospective study cohort was identified using Slicer Dicer, an electronic medical record tool. Between 11/30/14 and 5/30/16, out of 1,602,679 in the database, there were 94 patients with LN. 60 subjects remained after exclusion criteria were applied. Data from a hospital survey of all Nephrology and Rheumatology patients, after introduction of the PHQ-2 score (5/1/16 to 1/31/17), was analyzed.

**Results:** 50 subjects were female, 10 were male, with a mean age of 17.4 ± 3.4 yrs. 39 subjects (65%) were Hispanic. 29 subjects (48% of all subjects) had a diagnosis of depression discoverable in EMR notes but only 14 subjects (23%) had a diagnosis of depression in their problem list. Only 2 of the 10 males had a diagnosis of depression.

Of the 45 of the 60 patients (75%) seen in the lupus multidisciplinary clinic, 27 of the 45 (60%) subjects had ≥1 PHQ-9 result. The 27 subjects (48%) who had discoverable PHQ-9 results, were not more likely to have a diagnosis of depression that those subjects who did not have PHQ-9 screening testing (p = 0.11). Only 2 of 15 (13%) subjects not followed in lupus clinic had ≥1 PHQ-9 value (p=0.0024). 2 the 7 subjects had PHQ-9 values recorded after referral to the Lupus Transition Clinic.
18 PHQ-9 values were ≥10 (14 moderate depression, 4 moderately severe depression, mean PHQ-9: 5.1 ± 5.1). 8 patients were not previously known to be depressed and 2 patients were suicidal. There was dramatic PHQ-9 score variability over time.

The PHQ-9 was made available to other sub-specialty groups once the study was presented to the hospital EMR group. Patient demand quickly outstripped the supply of psychiatric resources. The PHQ-9 was removed and PHQ-2 was substituted (Table 1) while a behavioral referral pathway was created.

Study patients using the PHQ-9 were more likely to report depression than general Rheumatology (p <0.01) or Nephrology (p <0.01) patients using the PHQ-2.

**Conclusion:** Slicer Dicer is a quick and effective means to identify study populations of interest in EPIC.

30% of subjects had PHQ-9 scores ≥10 and cases of new depression were detected. Thus, the PHQ-9 was a useful tool to identify LN patients with depression.

The use of the PHQ-9 questionnaire was used more often in a multidisciplinary LN setting with social workers and a physician “champion” for PHQ-9 use.

Hospitals utilizing the PHQ-9 need to be ready with increased psychological services for the newly identified patients who are depressed.

It is unclear if the PHQ-2 is equally useful in identifying depressed LN patients.

Key study limitations include: the failure to utilize the PHQ-9 for all LN patients and visits, some PHQ-9 were completed by nurses or social workers acting as a scribe for the patient, there was no evaluation of relationship between PHQ-9 values and SLEDAI-2K values and corticosteroid doses.

**Disclosure:** P. Yorgin, None; E. Lazarow, None; R. Sheets, None.

**Abstract Number:** 1274

**Anti-MDA5 Autoantibodies Associated with Juvenile Dermatomyositis Constitute a Distinct Phenotype in North America**

**Gulnara Mamyrova**1, Takayuki Kishi2, Ira N Targoff3, Rodolfo V Curiel4, Frederick W Miller2 and Lisa G Rider2, 1Rheumatology, George Washington University School of Medicine and Health Sciences, Washington, DC, 2Environmental Autoimmunity Group, National Institute of Environmental Health Sciences, National Institutes of Health, Bethesda, MD, 3VA Medical Center, University of Oklahoma Health Sciences Center, and Oklahoma Medical Research Foundation, Oklahoma City, OK, 4George Washington University School of Medicine and Health Sciences, Washington, DC

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Title:** Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster II: Lupus and Related Disorders, Myositis, Scleroderma and Vasculitis

**Session Type:** ACR Poster Session B

**Session Date:** Monday, November 6, 2017

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Anti-MDA5 autoantibodies (Abs) have been associated with clinically amyopathic and classic dermatomyositis (DM), with rapidly progressive interstitial lung disease (ILD) and poor prognosis in Japanese patients (pts). The aim of this study was to examine the frequency and characteristics of anti-MDA5 Abs associated with juvenile DM (JDM) in North America.

**Methods:** Demographic, clinical, laboratory and outcome features of 34 pts with anti-MDA5 Abs were compared to those of 60 Ab (MSA/MAA) negative, 164 anti-p155/140 Ab+ and 116 MJ Ab+ JDM and JCTM/DM pts meeting probable or definite Bohan and
Results: Anti-MDA5 Abs were identified in 34 (7.5%) pts from a cohort of 453 JDM and JCTM/DM pts. Characteristics of MDA5 Ab+ compared to MSA/MAA-, anti-p155/140 Ab+ and anti-MJ Ab+ pts are shown in the Table. MDA5+ were older at diagnosis and had a slower disease onset compared to p155/140 + and MJ Ab+. Anti-MDA5 Ab+ had lower serum CK levels and more frequent fever, weight loss, adenopathy, arthralgia, arthritis, abnormal PFTs, dyspnea, ILD compared to MSA/MAA-, p155/140+ and MJ Ab+. The median skeletal, pulmonary, constitutional and overall total clinical system scores at diagnosis were higher in MDA5 Ab+ (p<0.0001). There were no differences in gender distribution, delay to diagnosis, and onset severity among the four groups. Total number of medications received was fewer (4.0 [IQR 3-6] vs. 5.0 [IQR 4-8], p=0.04), treatment duration was shorter (23.2 mths [IQR 13-54] vs. 38.2 [IQR 22-66], p=0.04) in MDA5 Ab+ vs. p155/140 Ab+. MDA5 Ab+ had fewer flares (48% vs. 71%, p=0.035) and shorter time to discontinue steroid therapy (24.7 mths [IRQ 16-37] vs. 33.0 [IRQ 18-61], p=0.046) vs. p155/140 Ab+. Multivariable analysis revealed weight loss, arthritis and lower serum CK level as significantly associated with anti-MDA5 Ab+ vs Ab-, whereas weight loss, arthritis, arthralgia, ILD were significantly associated with anti-MDA5 Ab+ vs. p155/140 Ab+, and weight loss, arthritis, ILD, lower serum aldolase level, older age at diagnosis were significantly associated with anti-MDA5 Ab+ vs. MJ Ab+. There were no differences in disease course, status at most recent evaluation, and mortality of MDA5 Ab+ vs. other Ab groups.

Conclusion: Anti-MDA5 Abs are seen in a distinct subset of JDM with frequent arthritis, arthralgia, weight loss, adenopathy, and ILD, but lower serum CK and aldolase. MDA5+ have comparable outcomes, but with the ability to discontinue steroids more rapidly and less frequent flares compared to p155/140 Ab+ pts.
<table>
<thead>
<tr>
<th></th>
<th>Anti-MDA5 Ab+ Median [IQ range] or %</th>
<th>MSA/MAA-* Median [IQ range] or %</th>
<th>Anti-p155/140 Ab+ Median [IQ range] or %</th>
<th>Anti-MJ Ab+* Median [IQ range] or %</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=34</td>
<td></td>
<td>N=60</td>
<td>N=164</td>
<td>N=116</td>
</tr>
<tr>
<td>Age at diagnosis (yr)</td>
<td>9.4 [6.6-13.4]</td>
<td>7.6 [5.3-11.4]</td>
<td>7.2 [4.7-11.0]</td>
<td>6.3 [4.5-9.9]</td>
</tr>
<tr>
<td>Slow onset speed (3-6 mo)</td>
<td>50.0</td>
<td>36.2</td>
<td>23.9 [3]</td>
<td>23.5 [3]</td>
</tr>
<tr>
<td>ANA titer</td>
<td>40 [0-320]</td>
<td>40 [0-320]</td>
<td>480 [80-1280]</td>
<td>80 [0-320]</td>
</tr>
<tr>
<td>Fever</td>
<td>58.8</td>
<td>43.3</td>
<td>31.1 [3]</td>
<td>40.5 [1]</td>
</tr>
<tr>
<td>Constitutional System Score</td>
<td>0.5 [0.5-0.75]</td>
<td>0.25 [0.25-0.5] [4]</td>
<td>0.25 [0.25-0.5]</td>
<td>0.25 [0.25-0.5]</td>
</tr>
<tr>
<td>Highest CK (nrl ≤ 252U/L)</td>
<td>211.0 [85.5-276.5]</td>
<td>745.5 [293.0-3029.0] [4]</td>
<td>476.0 [226.5-2153.0] [4]</td>
<td>1669.0 [438.0-5280.0] [4]</td>
</tr>
<tr>
<td>Muscle System Score</td>
<td>0.29 [0.16-0.43]</td>
<td>0.29 [0.15-0.48]</td>
<td>0.29 [0.17-0.43]</td>
<td>0.43 [0.29-0.57]</td>
</tr>
<tr>
<td>Arthritis</td>
<td>85.3</td>
<td>41.7 [4]</td>
<td>42.1 [4]</td>
<td>47.0 [4]</td>
</tr>
<tr>
<td>Contractures</td>
<td>47.1</td>
<td>48.3</td>
<td>59.1 [4]</td>
<td>63.5 [4]</td>
</tr>
<tr>
<td>Skeletal System Score</td>
<td>0.5 [0.5-1.0]</td>
<td>0.0 [0.0-0.5] [4]</td>
<td>0.0 [0.0-0.5]</td>
<td>0.5 [0.0-1.0]</td>
</tr>
<tr>
<td>Raynaud’s phenomenon</td>
<td>17.6</td>
<td>10.0</td>
<td>9.8 [2]</td>
<td>3.5 [2]</td>
</tr>
<tr>
<td>Shawl sign</td>
<td>20.6</td>
<td>15.3</td>
<td>30.2 [1]</td>
<td>7.8 [1]</td>
</tr>
<tr>
<td>Photosensitivity</td>
<td>48.5</td>
<td>47.5</td>
<td>63.1 [4]</td>
<td>35.7 [4]</td>
</tr>
<tr>
<td>Calcinosis</td>
<td>32.4</td>
<td>48.3</td>
<td>31.7 [4]</td>
<td>35.3 [4]</td>
</tr>
<tr>
<td>“Mechanic” hands</td>
<td>14.7</td>
<td>5.1</td>
<td>4.3 [1]</td>
<td>1.8 [1]</td>
</tr>
<tr>
<td>Cutaneous System Score</td>
<td>0.31 [0.22-0.42]</td>
<td>0.24 [0.14-0.33] [2]</td>
<td>0.30 [0.22-0.39]</td>
<td>0.22 [0.14-0.31] [4]</td>
</tr>
<tr>
<td>Abnormal PFT</td>
<td>28.6</td>
<td>10.9</td>
<td>23.9 [3]</td>
<td>23.3 [3]</td>
</tr>
<tr>
<td>Dyspnea on exertion</td>
<td>44.1</td>
<td>15.0 [3]</td>
<td>18.5 [3]</td>
<td>25.0 [1]</td>
</tr>
<tr>
<td>Pulmonary System Score</td>
<td>0.0 [0.0-0.2]</td>
<td>0.0 [0.0-0.0] [1]</td>
<td>0.0 [0.0-0.13]</td>
<td>0.0 [0.0-0.17]</td>
</tr>
<tr>
<td>Overall/Total System Score</td>
<td>0.28 [0.24-0.35]</td>
<td>0.17 [0.12-0.26] [4]</td>
<td>0.20 [0.13-0.28]</td>
<td>0.22 [0.16-0.32] [3]</td>
</tr>
<tr>
<td>Chronic Disease Course</td>
<td>45.5</td>
<td>37.3</td>
<td>65.6 [4]</td>
<td>45.9 [4]</td>
</tr>
<tr>
<td>Mortality</td>
<td>2.9</td>
<td>3.3</td>
<td>1.2 [4]</td>
<td>1.7 [4]</td>
</tr>
</tbody>
</table>

*Significant differences from anti-MDA5+: 1p <0.05; 2p <0.01; 3p <0.005; 4p < 0.001

Note that percentages may not reflect the number divided by the total number of subjects, if data missing

**Disclosure:** G. Mamyrova, Cure JM, 2; T. Kishi, The Myositis Association, 2; I. N. Targoff, Consultant to the Oklahoma Medical Research Foundation Clinical Immunology Laboratory for myositis testing, 5; R. V. Curiel, Cure JM, BMS, 2; F. W. Miller, None; L. G. Rider, None.


Abstract Number: 1275
101 Juvenile Myositis Patients Characterized By Myositis Specific Antibodies: Disease Activity and Damage over 60 Months

Lauren M. Pachman1,2, Megan L. Curran3, Gabrielle A. Morgan4, IRA Targoff5, Hua Huang6, Dong Xu7 and Chiang-Ching Huang8

1Cure JM Program of Excellence in Juvenile Myositis Research, Stanley Manne Children’s Research Institute, affiliated with Ann & Robert H. Lurie Children’s Hospital of Chicago, Chicago, IL, 2Pediatric Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL, 3Pediatric Immunology/Rheum, UCSF, San Francisco, CA, 4Cure JM Program of Excellence in Myositis Research, Chicago, IL, 5internal Medicine, The University of Oklahoma, Norman, OK, 6Joseph J. Zilber School of Public Health, Milwaukee, WI, 7Pediatric Rheumatology, Stanley Manne Research Center, Chicago, IL, 8Biostatistics, Joseph J. Zilber School of Public Health, Milwaukee, WI

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster II: Lupus and Related Disorders, Myositis, Scleroderma and Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The impetus for this investigation was the specific questions from parents of JM patients pertaining to the physician’s expectations about their child’s disease course. The data in this study provides a window with which to study the anatomy of the first five years of response to current therapies available for JM children, classified by Myositis Specific Antibody (MSA).

Methods: Two groups: inception patients since diagnosis (n=36); referral patients (n=65) were assessed at diagnosis/referral and at 6, 12, 24, 36, 60 months. MSA was determined by immunoprecipitation and immunoblot (Oklahoma Research Lab). Nailfold capillary end row loops (ERL) were assayed using a Nikon Coolpix P6000 camera attached to a Dermlite II ProHR (18x). TNF-α-308 (A/G) polymorphisms in the promotor region were determined as previously reported. Calcifications: Physician inspection identified the calcific deposits, or when clinically appropriate, they were located by radiographic study, and designated as mild, moderate or severe. Lunar Prodigy measured bone mineral density. Data Collection and Analysis: Study data was prospectively obtained and stored in a MEDLOG database. Statistical analysis was performed using R version 3.3.1(www.r-project.org). For each clinical variable, a two sample t-test or the Wilcoxon Rank Sum test was performed as appropriate for the comparison between two defined patient groups. To test for the equality of more than two means, Tukey’s HSD test in conjunction with ANOVA was performed for all pairwise comparisons among means

Results: The 2 groups were similar: myositis onset age, race, gender, duration of untreated disease, abnormal MRI and initial Disease Activity Scores (DAS). The inception group had higher values for SGOT (p=0.008), CPK (p=0.014), LDH (p=0.0014), aldolase (p=0.0076) and neopterin (p=0.0033) than the referred. By 60 months, the referral DAS total score > inception (p=0.05). Myositis specific antibody (MSA) frequencies for the 93 juvenile dermatomyositis (JDM): negative (33.3%); combination of anti p155/140 and ant-Mi-2 (positive or indeterminate) (6.5%); p155/140+ (40.9%), Mi-2 (6.5%); MJ (11.8%), MDA5 (1.1%). The eight U1RNP overlap myositis patients had a higher DAS muscle score at 60 months than MSA negative (p=0.008), and anti p155/140 (p=0.002). Disease/treatment related damage: cataracts (35%), lipodystrophy (30%), fractures (28%), abnormal pulmonary function (2/19 tested; 10.3%), and calcification (17%). At 60 months, chronic calcifications (n=7) were associated with decreased mean nailfold capillary end-row loop (ERL) count (p=0.002) and lipodystrophy (p=0.027).

Conclusion:

Conclusion: 1) At 60 months, referral JDM and overlap patients each had a higher DAS, but all patients improved; 2) 21.7% had > 1 MSA; 3) cataracts and lipodystrophy were each present in 30% patients; 4) ERL count ≤5 was associated with calcinosis; 5) lipodystrophy was associated with calcinosis, but not ERL count.

Disclosure: L. M. Pachman, None; M. L. Curran, None; G. A. Morgan, None; I. Targoff, None; H. Huang, None; D. Xu, None; C. C. Huang, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/101-juvenile-myositis-patients-characterized-by-myositis-specific-antibodies-disease-activity-and-damage-over-60-months

Abstract Number: 1276
Nail Fold Capillary Changes Are Associated with Pulmonary, but Not with Cardiac Involvement in Juvenile Dermatomyositis

Zoltán Barth¹,²,³, Thomas Schwartz²,⁴, Berit Flato⁵,⁶, Akos Koller⁷,⁸, May Brit Samersaw-Lund⁹, Ivar Sjaastad¹⁰,¹¹ and Helga Sanner⁶, ¹Bjørknes College, Oslo, Norway, ²Oslo University Hospital and University of Oslo, Institute for Experimental Medical Research, Oslo, Norway, ³Medical School, University of Pecs, Institute for Translational Medicine, Pecs, Hungary, ⁴Institute for Experimental Medical Research, Institute for Clinical Medicine, University of Oslo, Oslo, Norway, ⁵Institute for Clinical Medicine, University of Oslo, Oslo, Norway, Oslo, Norway, ⁶Department of Rheumatology, Oslo University Hospital, Rikshospitalet, Oslo, Norway, Oslo, Norway, ⁷University of Physical Education, Institute of Natural Sciences, Budapest, Hungary, ⁸Medical School, University of Pecs, Department of Neurosurgery, Pecs, Hungary, ⁹Oslo University Hospital, Rikshospitalet, Department of Respiratory Medicine, Oslo, Norway, ¹⁰Department of Cardiology, Oslo University Hospital, Oslo, Norway, Oslo, Norway, ¹¹Institute for Experimental Medical Research, Oslo University Hospital and University of Oslo, Oslo, Norway, Oslo, Norway

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster II: Lupus and Related Disorders, Myositis, Scleroderma and Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Juvenile dermatomyositis (JDM) is a rare autoimmune disease of unknown origin, characterised primarily by cutaneous rashes and symmetrical weakness of the proximal skeletal muscles. Other organs can also be affected with characteristic changes in the involved tissues, in which local inflammation and impaired microcirculation probably have pathogenic role. Microvascular abnormalities are easily assessable in the nail folds by capillaroscopic examination (Nail Fold Capillaroscopy, NFC), and might mirror microvascular involvement in other organs. We aimed to examine the association between alterations in nailfold capillary network and pulmonary and cardiac involvement in JDM patients with medium- to long-term disease duration.

Methods: Fifty-nine JDM patients were examined after disease onset median 16.8 (2-38) years. Nailfold capillary density (NCD) was assessed by NFC and patients were divided into ‘Low NCD’ (<6.0 cap/mm) and ‘Normal NCD’ (≥6.0 cap/mm) groups. Pulmonary involvement was assessed by pulmonary function test (PFT; forced vital capacity, FVC; total lung capacity, TLC; diffusing capacity for carbon monoxide, DLCO) and high resolution CT imaging (interstitial lung disease, ILD; airway disease). PFT parameters are presented as predictive values. Additionally, the patients were also grouped by PFT values: a ‘low’ value was defined as less than the 5th percentile of the predicted value. Cardiac measures included echocardiography and conventional, as well as Holter ECG measures. Systolic cardiac function was assessed by long axis strain (LAS), diastolic function was measured by early diastolic tissue velocity (e’). Arrhythmias and heart rate variability were assessed by ECG.

Results: The low NCD group presented lower FVC and TLC without difference in FVC/DLCO ratio. Moreover, patients with low NCD presented more frequently low DLCO and abnormalities in PFT/HRCT than those patients with normal NCD. There were no significant association between NCD and cardiac measures.

Conclusion: Nail fold capillary alterations in JDM patients after median 16.8 years disease duration was associated with pulmonary involvement, and might be a useful tool to detect patients at risk for pulmonary complications. Further studies are needed to confirm the applicability of NCD as a biomarker for lung involvement in JDM after medium to long term disease duration.

Disclosure: Z. Barth, None; T. Schwartz, None; B. Flato, None; A. Koller, None; M. B. Samersaw-Lund, None; I. Sjaastad, None; H. Sanner, None.


Abstract Number: 1277

Longitudinal Predictors of Physical Function in Juvenile Myositis
Juvenile myositis (JM) is marked by skin rashes, proximal muscle weakness, and deconditioning causing potentially severe disability. Studies examining long-term physical function in JM remain scant. This study aims to define longitudinal predictors of physical function in JM.

Methods:

JM patient data collected prospectively at routine clinic visits from January 2000 to June 2014 at Ann & Robert H. Lurie Children’s Hospital of Chicago was used in this study. Only patient visits with documented Childhood Health Assessment Questionnaire (CHAQ) summary scores were included for analysis. Demographic/clinical variables were extracted, including: gender, race, duration of untreated disease, Disease Activity Score (DAS) - muscle/skin domains, Childhood Myositis Assessment Scale (CMAS), muscle enzymes (i.e. CPK, AST, LDH, aldolase), nailfold capillary end row loops (NFC-ERL), von Willebrand factor antigen (vWFα), calcinosis, lipodystrophy, possible markers of disease severity (i.e. NK cell absolute counts, TNFα-308A allele), and treatments. Descriptive statistics were calculated. CHAQ was dichotomized (0 vs. >0) as most scores equaled zero. Generalized estimating equations for binary data specifying logit link function were used to evaluate effects for each covariate with a main effect for time. Covariates were univariably analyzed at \( p < 0.10 \), with all univariably significant covariates entered into a multivariable model for CHAQ > 0 using a manual backward selection method.

Results:

Table 1 describes the study sample (i.e. \( n = 187 \) patients with 2293 study visits and median follow-up 3.58 years). The following univariably significant covariates (at \( p < 0.10 \)) were included in the multivariable model: time (years from visit 0) \( (p < 0.0001) \), black race \( (p = 0.035) \), DAS-skin \( (p = 0.006) \), DAS-muscle \( (p < 0.0001) \), CMAS \( (p < 0.0001) \), LDH \( (p = 0.005) \), aldolase \( (p = 0.013) \), NFC-ERL \( (p = 0.002) \), abnormal vWFα \( (p = 0.0001) \), lipodystrophy \( (p < 0.0001) \), cyclosporine \( (p = 0.0725) \), and IV solumedrol \( (p = 0.0002) \). Complete data for the multivariable model was available for 892 study visits from all 187 unique patients. Significant adjusted associations persisted in the multivariable model for CMAS \( (OR: 0.91, p < 0.0001) \), aldolase \( (OR: 1.1, p = 0.0024) \), and lipodystrophy \( (OR: 2.2, p = 0.0126) \), with a trend towards significance for NFC-ERL \( (OR: 0.84, p = 0.0502) \).

Conclusion:

To our knowledge, this is the largest longitudinal study of prospectively collected physical function data yet reported in JM. Measures of muscle weakness/inflammation (i.e. CMAS, aldolase) predict long-term physical function. The relationships between lipodystrophy, vasculopathy (i.e. NFC-ERL), and physical function warrant closer attention and replication.
Disclosure: K. Ardalan, None; H. L. Palac, Abbvie, Inc, 3; J. Lee, None; M. Wolfe, None; G. A. Morgan, None; L. M. Pachman, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/longitudinal-predictors-of-physical-function-in-juvenile-myositis](http://acrabstracts.org/abstract/longitudinal-predictors-of-physical-function-in-juvenile-myositis)

Abstract Number: 1278

**Growth and Puberty in Juvenile Dermatomyositis a Longitudinal Multinational Cohort Study**

Ellen Nordal1,2, Angela Pistorio3, Marite Rygg3, Gabriella Giancane4, Michäel Hofer3, Jose Antonio Melo-Gomes4, Blanca Bica4, Ximean Norambuena1, Valda Stanevicha3, Rebecca ten Cate5, Olga Vougiouka4, Jurgen Brunner4, Guenther Dannecker4, Polyxeni Pratsidou-Gertsi4, Gabriele Simonini4, Helen Venning4, Serena Pastore4, Angelo Ravelli6, Alberto Martini7 and Nicolino Ruperto7, 1Department of Pediatrics, University Hospital of Northern Norway, Tromsø, Norway, 2Department of Clinical medicine, UIT, the Arctic University of Norway, Tromsø, Norway, 3Istituto Giannina Gaslini - Pediatrica II, Reumatologia - PRINTO, Genoa, Italy, 4Istituto Giannina Gaslini - Pediatrica II, Reumatologia - PRINTO, Genova, Italy, 5Pediatric Rheumatology, Leiden University Medical Center, Leiden, Netherlands, 6University of Genova, IRCCS Istituto Giannina Gaslini, Genova, Italy, 7Istituto Giannina Gaslini, Genoa, Italy

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster II: Lupus and Related Disorders, Myositis, Scleroderma and Vasculitis

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM
Background/Purpose: Children with juvenile dermatomyositis (JDM) are at risk of growth failure and delayed puberty because of inflammatory disease activity and side effects of corticosteroid treatment. Knowledge on growth and pubertal development in JDM is very limited. Our aim was to study growth and puberty in a multicenter longitudinal prospective cohort of juvenile dermatomyositis (JDM).

Methods: Anthropometric and pubertal data in children ²18 years with recent onset or flare of JDM from 31 countries were studied. Growth failure was defined as parent-adjusted z-score < -1.5, and height deflection z-score < -0.25/year.

Results: Height and weight from four follow-up visits during two years in 196/275 (71.3 %) of the children included in the original JDM study were analyzed. There was a significant reduction in parent-adjusted height z score over time in females (p<0.0001) and males (p=0.001) with significant gender difference (p<0.05), but also catch-up growth at the final study visit were seen. Median BMI z score peaked at 6 months (p<0.0001) and was still significantly above baseline at the final study visit at a median of 26 months (p=0.007) with no gender difference. Females with a disease duration ³12 months after onset had significantly lower parent-adjusted height z score (p=0.002) with no catch-up growth. Delayed pubertal onset, pubertal duration and delayed menarche was found in a substantial number of the participants as shown in the table. Growth failure at base line was the main determinant of growth failure at the final study visit (OR: 53.4).

Conclusion: Children with JDM of long duration are at high risk of having a lower than expected height and a delayed pubertal development.

TABLE Growth and pubertal characteristics at the final study visit of 196 participants in a longitudinal JDM cohort

<table>
<thead>
<tr>
<th></th>
<th>Girls (N=116)</th>
<th>Boys (N=80)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Growth failure</td>
<td>20/97 (20.6%)</td>
<td>11/73 (15.1%)</td>
</tr>
<tr>
<td>Height deflection</td>
<td>29/116 (25.0%)</td>
<td>25/80 (31.3%)</td>
</tr>
<tr>
<td>Age at B2 females(n=37)/T2 males (n=23), mean (SD)</td>
<td>11.1 (1.9)</td>
<td>12.8 (1.6)</td>
</tr>
<tr>
<td>Menarche registered</td>
<td>31/55 (56.4%)</td>
<td>n.a.</td>
</tr>
<tr>
<td>Delayed menarche</td>
<td>7/31 (22.6%)</td>
<td>n.a.</td>
</tr>
<tr>
<td>Late pubertal onset</td>
<td>23/37 (62.2%)</td>
<td>15/23 (65.2%)</td>
</tr>
<tr>
<td>Delayed puberty</td>
<td>20/55 (36.4%)</td>
<td>11/27 (40.7%)</td>
</tr>
</tbody>
</table>
Numbers are frequencies (%) unless otherwise specified. Delayed menarche was defined as age of menarche >14 years, delayed pubertal onset was defined as age at Tanner B2 >12 years or age at Tanner T2 >13 years, delayed puberty was defined as a delay in pubertal onset, pubertal tempo or menarche.

Disclosure: E. Nordal, None; A. Pistorio, None; M. Rygg, None; G. Giancane, None; M. Hofer, Novartis and AbbVie, 5; J. A. Melo-Gomes, None; B. Bica, None; X. Norambuena, None; V. Stanevicha, None; R. ten Cate, None; O. Vougiouka, None; J. Brunner, None; G. Dannecker, None; P. Pratsidou-Gertsì, None; G. Simonini, None; H. Venning, None; S. Pastore, None; A. Ravelli, None; A. Martini, GASLINI Hospital, 3,Astellas, AstraZeneca, Bristol-Myers Squibb, Italfarmaco, and MedImmune, 8,AbbVie Inc., AstraZeneca, Bristol-Myers Squibb, Janssen Biologies B.V., Eli Lilly and Co., “Francesco Angelini”, GlaxoSmithKline, Italfarmaco, Novartis, Pfizer, Roche, Sanofi Aventis, Schwarz Biosciences GmbH, Xoma, and Wyeth Pharmaceuticals, 2; N. Ruperto, BMS, Hoffman-La Roche, Janssen, Novartis, Pfizer and Sobi, 2,Abbvie, Ablynx, AstraZeneca, Baxalta Biosimilars, Biogen Idec, Boehringer, Bristol Myers Squibb, Eli-Lilly, EMD Serono, Gilead Sciences, Janssen, Medimmune, Novartis, Pfizer, Rpharm, Roche, Sanofi., 5,Abbvie, Ablynx, AstraZeneca, Baxalta Biosimilars, Biogen Idec, Boehringer, Bristol Myers Squibb, Eli-Lilly, EMD Serono, Gilead Sciences, Janssen, Medimmune, Novartis, Pfizer, Rpharm, Roche, Sanofi., 8.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/growth-and-puberty-in-juvenile-dermatomyositis-a-longitudinal-multinatinal-cohort-study

Abstract Number: 1279

Risk Factors for Achieving a Drug-Free Remission in Patients with Juvenile Dermatomyositis

Tomokazu Nagakura1, Takuma Ito2, Masateru Kusuda2, Tuyoshi Yamatou2, Tomohiro Kubota2, Yuuichi Yamasaki2, Yukiko Nonaka2, Tomoko Takezaki2, Harumi Akaike3, Yasuhiro Imanaka2 and Syuji Takei4, 1Pediatrics, The Holy Mother of Grace Hospital Home for Children and Persons with Severe Motor and Intellectual Disabilities, Usuki, Japan, Usuki, Japan, 2Department of Pediatrics, Kagoshima University Graduate School of Medical and Dental Sciences, Kagoshima, Japan, Kagoshima, Japan, 3Department of Pediatrics, Department of Pediatrics, Kagoshima University Graduate School of Medical and Dental Sciences, Kagoshima, Japan, Kagoshima, Japan, 4Department of Pediatrics, Kagoshima University Graduate School of Medical and Dental Sciences, Kagoshima, Japan, Kagoshima, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster II: Lupus and Related Disorders, Myositis, Scleroderma and Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Juvenile dermatomyositis (JDM) is the most common idiopathic inflammatory myopathy in children. Approximately one-third of JDM patients attain drug-free remission (DFR) without relapse; however, there exist patients who are refractory to glucocorticoid therapy with or without immunomodulating agents. The purpose of this study was to examine the risk factors for achieving DFR in patients with JDM.

Patients and Methods: JDM patients referred to the Kagoshima University Hospital between 1994 and 2015 were enrolled. Demographic, clinical and laboratory data were retrospectively collected from medical records. DFR was defined as a condition that patients maintained symptom-free status with normal laboratory test for at least 1 year after withdrawal of all medications. The following parameters were evaluated as the related factors for achieving DFR in JDM patients: sex, age at onset, disease duration and clinical manifestations at starting therapy, laboratory data such as creatine kinase (CK) and aldolase (ALD), and initial treatment (intravenous methylprednisolone pulse therapy and/or methotrexate). Episodes of disease relapse and development of subcutaneous calcinosis during the disease course was also analyzed. Mann-Whitney U test and Chi-square test were used for comparison of
continuous and categorical variables, respectively. Cumulative DFR rates were analyzed by Kaplan-Meier methods with log-rank test.

**Results:** A total of 40 JDM patients (18 male and 22 female patients) were involved. The mean age at onset was 6.2 ± 4.1 years, and the mean disease duration at starting the therapy was 0.6 ± 0.8 years. During the entire observation period, 22 patients had achieved sustained DFR (DFR group) while 18 patients were still on medication at the final visit (no-DFR group). Cumulative DFR rates of all patients were 21.6%, 35.6% and 58.6% at 3, 5 and 7 years after initiation of drug therapy, respectively. There were no significant differences between DFR group and no-DFR group with regard to sex, age at onset, disease duration by starting initial therapy, the presence or absence of skin ulcer and interstitial pneumonia. As to laboratory tests, the maximum serum levels of ALD (ALDmax) were significantly higher in no-DFR group than that in DFR group (p=0.0202), though the serum CKmax showed no difference between the two groups. In addition, Kaplan-Meyer analysis revealed that the cumulative DFR rates were significantly lower in patients with ALDmax ≥20 IU/L (p=0.0079, Figure 1) and patients with relapse (p<0.0001) or subcutaneous calcinosis (p=0.0035) during the disease course.

**Conclusion:** ALDmax ≥20IU/L at starting therapy, and presence of episodes of relapse or subcutaneous calcinosis during the disease course may be predictors for a refractory disease course in JDM. Therefore, more prolonged and/or more aggressive therapies are needed to attain DFR in these patients.

**Disclosure:** T. Nagakura, None; T. Ito, None; M. Kusuda, None; T. Yamatou, None; T. Kubota, None; Y. Yamasaki, None; Y. Nonaka, None; T. Takezaki, None; H. Akaike, None; Y. Nerome, None; H. Imanaka, None; S. Takei, Chugai, Eisai, Takeda, Bristol-Myers Squibb, 2,Chugai, Mitsubishi-Tanabe, Pfizer, Ayumi, 8.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/risk-factors-for-achieving-a-drug-free-remission-in-patients-with-juvenile-dermatomyositis

**Abstract Number: 1280**

**Clinical Outcomes of Juvenile Dermatomyositis Patients Treated with TNF-Inhibitors: A Retrospective Chart Review**

Katelyn Banschbach1, Ellen Go1 and Stacey Tarvin2, Indiana University School of Medicine, 2riley Hospital for Children, Indiana University

**Katelyn Banschbach¹, Ellen Go² and Stacey Tarvin³, ¹Indiana University School of Medicine, Indianapolis, IN, ²Pediatrics, Indiana University School of Medicine, Indianapolis, IN, ³Riley Hospital for Children, Indiana University, Indianapolis, IN

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017
**Background/Purpose:** To analyze the clinical outcomes of TNF-inhibitors as a steroid-sparing agent in the treatment of juvenile dermatomyositis (JDM).

**Methods:** We performed a retrospective chart review on a total of 15 patients from 1997 to 2011 who were diagnosed with probable or definite JDM based on the Bohan and Peter criteria (1975). All patients were between the ages of 3-16 years at diagnosis and had exposure to TNF-inhibitor therapy. Patient demographic information, clinical history, medication history including dose, time between diagnosis and TNF-inhibitor use, and significant adverse events were reviewed. Outcome was defined based on medication changes, clinical history, and presence of adverse events.

**Results:** Infliximab was the most frequently administered TNF-inhibitor. Ten patients were treated with infliximab, four with etanercept, and one with adalimumab. Infliximab dose ranged from 3 to 15mg/kg/dose every 4 weeks. Twelve of 15 patients had at least a 50% reduction in oral steroid dose after TNF therapy and 20% of all patients were able to stop all medications. In the infliximab cohort, 60% were able to discontinue steroids and 30% were able to reduce the steroid dose by half. Among patients that improved, average time from diagnosis to initiation of TNF therapy was 12 (±11.6) months. All patients received methotrexate and oral steroids prior to initiation of an anti-TNF agent. In addition, 10 patients were previously treated with IV methylprednisolone (IVMP), 10 with IV immunoglobulin, and 5 with hydroxychloroquine. Three patients were on IVMP at the start of TNF therapy and two discontinued the IVMP infusions while taking biologics. Three patients had infections that resulted in discontinuation of anti-TNF medications. Two patients, both taking infliximab, required hospitalization. There were no reported deaths or incidence of malignancy. In all patients, TNF therapy was held for infection and was not restarted due to baseline stability of disease.

**Conclusion:** JDM is the most common inflammatory myopathy in children. It is a multisystem disorder associated with significant morbidity and risk of long-term disability if untreated. In this cohort, TNF-inhibitors were typically used as a 3rd or 4th line therapy. The majority of infliximab-treated patients had a substantial decrease in overall steroid exposure and a significant percentage were able to stop steroids. Infection was the most common adverse event reported but this did not lead to any life-threatening morbidity and reversed after discontinuing the biologic. The use of TNF-inhibitors in JDM patients is still controversial. However, this data supports further investigation into the use of TNF-inhibitors, particularly infliximab, as a therapeutic option in children with refractory JDM.

**Disclosure:** K. Banschbach, None; E. Go, None; S. Tarvin, None.

**Plasma CXCL4 As a Biomarker in Juvenile Systemic Sclerosis**

**Katharine Moore**1,2, Marvin J. Fritzler3, Marisa S. Klein-Gitelman4, Ann M Reed5, Tzielan Lee6 and Anne Stevens7,8, 1Pediatrics, University of Colorado, Aurora, CO, 2Pediatric Rheumatology, Children's Hospital Colorado, Aurora, CO, 3Medicine, University of Calgary, Calgary, AB, Canada, 4Division of Pediatric Rheumatology/PDD PTD, Lurie Children's Hospital of Chicago/Northwestern University, Chicago, IL, 5Rheumatology, Duke University, Durham, NC, 6Pediatric Rheumatology, Stanford University, Palo Alto, CA, 7University of Washington, Department of Pediatrics, Seattle, WA, 8Center for Immunity and Immunotherapies, Seattle Children's Research Institute, Seattle, WA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster II: Lupus and Related Disorders, Myositis, Scleroderma and Vasculitis

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM
Background/Purpose: Juvenile systemic sclerosis (jSSc) is a severe and heterogeneous autoimmune vasculopathy. Pulmonary fibrosis is the highest independent predictor of mortality, yet currently there are no known biomarkers associated with organ involvement, response to therapy, or prognosis in jSSc. CXCL4 is a chemoattractant for neutrophils and fibroblasts. Elevated peripheral levels of CXCL4 have been associated with pulmonary fibrosis, pulmonary hypertension, and overall disease progression in adult SSc. The purpose of this study was to evaluate whether CXCL4 levels are elevated in jSSc patients as compared to healthy pediatric controls and patients with other rheumatologic illnesses, and to determine whether there is an association with jSSc disease manifestations.

Methods: In this multi-center case-control study, plasma samples from 28 patients with jSSc, 26 with localized scleroderma (jLS), 36 with juvenile systemic lupus erythematosus (jSLE), and 35 age-matched healthy controls were tested for CXCL4. Testing was done on a Luminex 200 luminometer (Eve Technologies, Calgary, AB). CXCL4 plasma concentration was compared between diseases and controls. The CXCL4 level was then correlated with specific disease manifestations, including the presence of pulmonary hypertension and pulmonary fibrosis on HRCT.

Results: The mean (± 95% CI) level of CXCL4 in jSSc patients was 24,358 ± 6047 ng per milliliter, which was significantly higher than in controls (12,455 ± 5032 ng/mL; p=.001). Mean CXCL4 in both jLS patients (20,692 ± 4513 ng/mL) and in jSLE (18,165 ± 4360 ng/mL) were also significantly higher than in controls, but to lesser extent (p=.01 and p=.04, respectively). When the Bonferroni correction was applied, only the jSSc cohort was significantly different from controls. There was no significant difference in CXCL4 level between the sub-classifications of jSSc (diffuse versus limited cutaneous SSc). Within the jSSc cohort, there were three patients with PH and a mean CXCL4 level of 41,768 ng/mL (range 3,472 - 79,585), compared to 24,565±19,731 ng/mL for 17 patients with pulmonary fibrosis, and 24,600±8,927 ng/mL for patients without cardiopulmonary involvement.

Conclusion: Levels of plasma CXCL4 were elevated in patients with jSSc and, in a small number of patients, were higher with the presence of pulmonary hypertension. Levels did not correlate with HRCT-confirmed pulmonary fibrosis in this cohort. These findings suggest that CXCL4 may have value as a biomarker in jSSc, but further prospective studies of an inception cohort are needed.

Disclosure: K. Moore, None; M. J. Fritzler, Inova Diagnostics, Inc., 5,Werfen International, 5,Eurimmun GmbH, 5,Alexion Pharmaceuticals, Inc., 5; M. S. Klein-Gitelman, Janssen Pharmaceutica Product, L.P., 2,Pfizer Inc, 2,UCB biosciences, 2,Abbvie, 2,Lupus Foundation of America, 2,NIH/LFA/Cure JM/Arthritis Foundation, 2,Up to Date, 7; A. M. Reed, None; T. Lee, None; A. Stevens, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/plasma-cxcl4-as-a-biomarker-in-juvenile-systemic-sclerosis

Abstract Number: 1282

Assessing the Prevalence of Juvenile Systemic Sclerosis in Childhood Using Administrative Claims Data from the United States

Ivan Foeldvari1, Timothy Beukelman2 and Fenglong Xie3, 1Hamburg Center for Pediatric and Adolescent Rheumatology, Hamburg, Germany, 2Pediatric Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 3Division of Clinical Immunology & Rheumatology, University of Alabama at Birmingham, Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster II: Lupus and Related Disorders, Myositis, Scleroderma and Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Juvenile systemic Sclerosis (jSSc) is an orphan disease. There are some data regarding the incidence, but nearly no data exist regarding the prevalence of jSSc. To plan prospective trials, it is very important to gain data regarding the prevalence of jSSc.

Methods:
We used Truven MarketScan® commercial insurance claims data from the United States for the years 2010 through 2014, inclusive. In each individual calendar year, we identified all persons in the claims data who were less than 16 years old. Among these persons, we identified all persons with at least 1 physician diagnosis code for systemic sclerosis (ICD-9 710.1) and then removed any person with a diagnosis code for localized scleroderma (ICD-9 701.0). From this remaining group of patients, we identified patients with at least one filled prescription or infusion claim for immunosuppressant medications often used to treat systemic sclerosis, namely methotrexate, mycophenolate mofetil, or cyclophosphamide. We assumed these children had jSSc and calculated the estimated prevalence and 95% confidence interval using a Poisson distribution.

Results:

The results for each calendar year are shown in the Table. Very few children received diagnosis codes for systemic sclerosis. Approximately 70% of these patients did not have concurrent diagnoses of localized scleroderma, but only approximately 14% of those had treatment with immunosuppressant medications often used to treat systemic sclerosis. The prevalence estimates were approximately 3 per 1 million children and were relatively stable from year to year.

<table>
<thead>
<tr>
<th>Year</th>
<th>N of Total Children</th>
<th>Diagnosis Code for Systemic Sclerosis</th>
<th>No Diagnosis Code for Localized Scleroderma</th>
<th>Use of Methotrexate, Mycophenolate Mofetil, or Cyclophosphamide</th>
<th>Estimated Prevalence per 1,000,000 Children [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>5,888,868</td>
<td>254</td>
<td>186</td>
<td>23</td>
<td>3.9 [2.5-5.9]</td>
</tr>
<tr>
<td>2011</td>
<td>6,231,475</td>
<td>249</td>
<td>185</td>
<td>22</td>
<td>3.5 [2.2-5.3]</td>
</tr>
<tr>
<td>2012</td>
<td>6,278,116</td>
<td>217</td>
<td>170</td>
<td>26</td>
<td>4.1 [2.7-6.1]</td>
</tr>
<tr>
<td>2013</td>
<td>4,950,018</td>
<td>175</td>
<td>120</td>
<td>17</td>
<td>3.4 [2.0-5.5]</td>
</tr>
<tr>
<td>2014</td>
<td>4,933,522</td>
<td>138</td>
<td>91</td>
<td>14</td>
<td>2.8 [1.6-4.8]</td>
</tr>
</tbody>
</table>

Conclusion:

Using diagnosis codes and medication usage from administrative claims, we estimated the prevalence of jSSc to be approximately 3 per 1 million children.

Disclosure: I. Foeldvari, None; T. Beukelman, None; F. Xie, None.


Abstract Number: 1283

**Male Patients Have a More Severe Course As Female Patients with Diffuse Juvenile Systemic Scleroderma? Results from the Juvenile Scleroderma Inception Cohort**

**Ivan Foeldvari**1, Jens Klotsche2, Ozgur Kasapcopur3, Amra Adrovic4, Valda Stanevich5, Maria Teresa Terreri6, Ekaterina Alexeeva7, Maria M. Katsicas8, Vanessa Smith9, Rolando Cimaz10, Mikhail Kostik11, Thomas J. A. Lehman12, Jordi Anton13, Walter A. Sifuentes-Giraldo14, Flavio Sztajnbok15, Tadey Avcin16, Mahesh Janarthanan17, Maria José Santos18, Dana Nemkova19, Cristina Battagliotti20, Despina Eleftheriou21, Liora Harel22, Tilmann Kallinich23, K Minden24, Susan Mary Nielsen25, Kathryn S. Torok26, Yosef Uziel27, Anne Stevens28, Clarissa Pilkington29 and Nicola Helmus1, 1Hamburg Center for Pediatric and Adolescent Rheumatology, Hamburg, Germany, 2Epidemiology unit, German Rheumatism Research Center, Berlin, Germany, 3Pediatric Rheumatology, Istanbul University, Cerrahpasa Medical School, Department of Pediatric Rheumatology, Istanbul, Turkey, 4Department of Pediatric Rheumatology, Istanbul University, Cerrahpasa Medical School, Istanbul, Turkey, 5Pediatric cathedra, Riga Stradiņš University, Riga, Latvia, 6Pediatric Rheumatology Unit, Federal University of Sao Paulo (UNIFESP - Universidade Federal de Sao Paulo), Sao Paulo, Brazil, 7Children's Health of RAMS and IM Sechenov First Moscow State Medical University, Moscow, Russian Federation, 8Service of Immunology & Rheumatology., Hospital de Pediatría Prof Dr JP Garrahan, Buenos Aires, Argentina, 9Faculty of Internal Medicine, Ghent University, Ghent, Belgium, 10Pediatrics, Ospedale Pediatrico Anna Meyer, Florence, Italy, 11Hospital Pediatrics, State Pediatric Medical University, Saint-Petersburg, Russia, 12Pediatric Rheumatology, Hospital for Special Surgery Weill Cornell Medical College, New York, NY, 13pediatric Rheumatology, University Childrens Hospital, Barcelona, Spain, 14Rheumatology, Hospital Universitario Ramón y Cajal, Madrid, Spain, 15Universidade Federal do Rio de Janeiro, Rio de Janeiro,
In adult systemic scleroderma patients male have a more severe course. This issue was never evaluated in a larger juvenile scleroderma cohort.

Methods:

Patients with jSSc were included worldwide to the jSScI cohort. We compared the demographics and clinical characteristics of male and female dcjSSc patients at the time of the enrollment into the jSScI.

Results:

Sixty-two dcjSSc patients were enrolled until April 2016. 11/62 (18%) of the patients were male (M) and 51/62 female (F) (82%). The mean age of the onset of Raynaud symptoms was 8.0 in M and 9.4 years in the F patients and the non-Raynaud symptoms was 8.2 in M and 10.0 in F patients. At the time of the enrollment the mean MRSS was 24.3 in M and 17.3 in F patients. Anti-Scl 70 positivity was found in 4/11 (36.4%) in M and 14/49 (28.6%) in F patients. Anticientromere positivity occurred in 2/11 (18.2%) in M and 0/23 (0%) in F patients (p=0.035). Capillary changes were present in 8/11(73%) of the M and 30/51 (59%) of F patients, but 36% of M and F had already history of ulcerations. 7/11 (64%) of the M and 21/51 (41%) of the F patients had cardiopulmonary involvement. Pulmonary hypertension occurred in F patients (n=6). 7/11 (64%) of M and 11/51 (22%) of F patients had signs of interstitial lung disease (p=0.005). No renal crisis was observed till enrollment. 37% in both sexes had gastrointestinal involvement. Patient global disease damage was on a VAS (0-100) 56.9 in M and in 38.4 in F (p=0.014) and patient global disease activity was 58.8 in M and 41.9 in M (p=0.024). Physician global of disease activity on a VAS was 58.9 in M and 36.9 in F (p=0.004) and physician global disease damage was 60.2 in M and 31.2 in F (p=0.001).

Conclusion:

Male patients had a significantly more severe disease course at time point of enrollment. This finding overlaps to the observation in adult cohorts.

Disclosure: I. Foeldvari, None; J. Klotsche, None; O. Kasapcopur, None; A. Adrovic, None; V. Stanevicha, None; M. T. Terreri, None; E. Alexeeva, None; M. M. Katsicas, None; V. Smith, None; R. Cimaz, None; M. Kostik, None; T. J. A. Lehman, None; J. Anton, None; W. A. Sifuentes-Giraldo, None; F. Sztajnbok, None; T. Avcin, None; M. Janarthanan, None; M. J. Santos, None; D. Nemkova, None; C. Battagliotti, None; D. Eleftheriou, None; L. Harel, None; T. Kallinich, None; K. Minden, None; S. M. Nielsen, None; K. S. Torok, None; Y. Uziel, None; A. Stevens, None; C. Pilkington, None; N. Helmus, None.


Abstract Number: 1284
The Localized Scleroderma Quality of Life Instrument (LoSQI): Initial Validation in Pediatric Localized Scleroderma

Christina K. Zigler¹, Kaveh Ardalan², Kaila Schollaert-Fitch³, Heidi Jacobe⁴ and Kathryn S. Torok³, ¹Physical Medicine & Rehabilitation, University of Pittsburgh, Pittsburgh, PA, ²Division of Rheumatology, Ann & Robert H. Lurie Children’s Hospital of Chicago, Chicago, IL, ³Pediatric Rheumatology, University of Pittsburgh Med Ctr, Pittsburgh, PA, ⁴Department of Dermatology, University of Texas Southwestern Medical Center, Dallas, TX

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster II: Lupus and Related Disorders, Myositis, Scleroderma and Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
There is a current need to integrate health related quality of life (HRQoL) into outcomes for clinical trials (Chang & Reeve, 2005). For pediatric localized scleroderma (LS), large gaps continue to exist in regards to the impact of LS on QoL, and clinical trials have been limited by the lack of valid patient-reported outcomes (PROs). Our group developed the pediatric LS Quality of Life Instrument (LoSQI) to meet this need. The LoSQI includes 3 domains (skin sensations, physical functioning, body image and social support) and an optional subscale (systemic medication side effects). The goal of this project was to provide validity evidence for the LoSQI scores in children with LS.

Methods:
The study had two phases (1) a pilot study and (2) a field test. The main purpose of the pilot study was to obtain input from pediatric LS patients regarding the under- and over- representation of the included content domains, understandability and readability of the survey items, and appropriateness of the recall period. Semi-structured interviews were used. The main goal of the field test was to provide quantitative validity evidence from multiple sources including patterns of missing or skipped items, reliability coefficients, and convergent and divergent validity. Patients were recruited from specialized scleroderma clinics at two sites: the Children’s Hospital of Pittsburgh and the UT Southwestern Medical Center.

Results:
Seventeen patients (ages 8-17) were enrolled into the pilot study and 74 patients aged 11-20 years were enrolled for the field test. Only 4% of the sample (3/74) had missing or skipped items. Internal consistency was excellent (all coefficients >0.8; Table 1) and test re-test reliability was >0.7 for the total score. The LoSQI had moderate to strong relationships with other PROs, but limited correlations with physician reported measures of disease activity and damage (Table 2).

Conclusion:
Initial evidence supports the reliability and validity of the LoSQI to measures HRQoL in pediatric patients. Limited correlations to physician reported outcomes suggest that the LoSQI measures unique information and should be an additional outcome measured in future clinical trials. Additional examination into the responsiveness of the scale to change is needed.

Table 1. Reliability coefficients for LoSQI.

<table>
<thead>
<tr>
<th>Scores</th>
<th>Number of items</th>
<th>Cronbach’s alpha (n = 74)</th>
<th>Test re-test reliability (n= 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Domain 1: Skin sensations</td>
<td>4</td>
<td>0.88</td>
<td>0.60</td>
</tr>
<tr>
<td>Domain 2: Physical functioning</td>
<td>8</td>
<td>0.90</td>
<td>0.70</td>
</tr>
<tr>
<td>Domain 3: Body image and social support</td>
<td>7</td>
<td>0.93</td>
<td>0.66</td>
</tr>
<tr>
<td>LoSQI Total Score</td>
<td>21</td>
<td>0.94</td>
<td>0.72</td>
</tr>
<tr>
<td>Domain 4: Medication side effects (n = 41, 17)</td>
<td>11</td>
<td>0.82</td>
<td>0.77</td>
</tr>
</tbody>
</table>
Table 2. Relationships of the LoSQI total score to patient, parent, and physician reported outcomes.

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>n</th>
<th>Pearson’s r</th>
<th>Spearman’s rho</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient Reported Outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDLQI/DLQI</td>
<td>61</td>
<td>0.82</td>
<td>0.78</td>
</tr>
<tr>
<td>VAS-patient</td>
<td>47</td>
<td>0.56</td>
<td>0.54</td>
</tr>
<tr>
<td><strong>Physician Reported Outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mLoSSI (activity)</td>
<td>56</td>
<td>-0.06</td>
<td>0.05</td>
</tr>
<tr>
<td>LoSDI (damage)</td>
<td>56</td>
<td>0.30</td>
<td>0.27</td>
</tr>
<tr>
<td>PGA-activity</td>
<td>34</td>
<td>-0.07</td>
<td>0.09</td>
</tr>
<tr>
<td>PGA-damage</td>
<td>34</td>
<td>0.34</td>
<td>0.48</td>
</tr>
<tr>
<td>PGA-severity</td>
<td>34</td>
<td>0.41</td>
<td>0.48</td>
</tr>
<tr>
<td><strong>Parent Reported Outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VAS-parent</td>
<td>34</td>
<td>0.71</td>
<td>0.54</td>
</tr>
<tr>
<td>Peds QL Family Impact</td>
<td>45</td>
<td>-0.75</td>
<td>-0.59</td>
</tr>
</tbody>
</table>

CDLQI/DLQI = Children’s Dermatology Life Quality Index; VAS = Visual Analogue scale; mLoSSI = Localized Scleroderma Skin Severity Index; LoSDI = Localized Scleroderma Damage Index; PGA = Physician Global Assessment.

Disclosure: C. K. Zigler, None; K. Ardalān, None; K. Schollaert-Fitch, None; H. Jacobe, None; K. S. Torok, None.


**Abstract Number:** 1285

**Extracutaneous Involvement Is Common in Juvenile Localized Scleroderma and Associated with a Higher Level of Perceived Disease Impact**

Suzanne C. Li1, Tracy Andrews2, Mallory Chen3, Kathryn S. Torok4, Elena Pope5, Katie G. Stewart6, Gloria C. Higgins7, C. Egla Rabinovich8, Ronald M. Laxer9, Kathleen Haines10, Marilyn Punaro11, Heidi Jacobe12 and Kathleen O’Neil13, 1Pediatrics, Joseph M Sanzari Children’s Hospital, Hackensack Meridian Health, Hackensack, NJ, 2Research, Hackensack University Medical Center, Hackensack Meridian Health, Hackensack, NJ, 3Williams College, williamstown, MA, 4Pediatric Rheumatology, University of Pittsburgh Med Ctr, Pittsburgh, PA, 5Section of Dermatology, The Hospital for Sick Children, Hospital for Sick Children, Toronto, ON, Canada, 6Pediatric Rheumatology, Texas Scottish Rite Hospital, Dallas, TX, 7Pediatric Rheumatology Ohio State University, Nationwide Childrens Hospital, Columbus, OH, 8Pediatric Rheumatology, Duke University Medical Center, Durham, NC, 9Div of Rheumatology, The Hospital for Sick Children, Toronto, ON, Canada, 10Joseph M Sanzari Children’s Hospital, Hackensack Meridian Health, Hackensack, NJ, 11Texas Scottish Rite Hospital for Children, Dallas, TX, 12Department of Dermatology, University of Texas Southwestern Medical Center, Dallas, TX, 13Pediatric Rheumatology, Riley Hospital for Children, Indianapolis, IN

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster II: Lupus and Related Disorders, Myositis, Scleroderma and Vasculitis

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Juvenile localized scleroderma (jLS) is often associated with deep tissue and extracutaneous involvement (ECI), putting children at risk for severe morbidity such as hemiatrophy, arthritis, and seizures. Few studies have prospectively evaluated occurrence of ECI or its impact on jLS health related quality of life (HRQoL). Our multicenter, multidisciplinary group (LOCUS, Localized scleroderma Clinical and Ultrasound Study) conducted a study to identify factors associated with ECI in jLS.

**Methods:**
We conducted a prospective observational cohort study of active and inactive jLS patients. Inclusion criteria included diagnosis of jLS by a pediatric rheumatologist or dermatologist, onset < 16 years, and willingness to complete questionnaires. Ethical board approval was obtained at each site.

At each of the 3 study visits, physicians scored clinical disease features and Physician Global Assessments of activity and damage. Parents scored two global assessments (100 mm visual analog scales): 1) Impact of disease on their child’s life at time of visit (Impact VAS, anchors No Impact, Very Large Impact), and 2) Disease activity (Activity VAS, anchors Not Active, Very Active). Parents also noted if specific symptoms or problems had occurred since the prior visit or in past 2 months. Physicians completed LS treatment and ECI forms. The ECI form was a checklist of specific problems for 8 organ systems, with option to list additional items.

Descriptive statistics, Spearman correlations, and least squares means were performed. Models were built by choosing variables that had a significant correlation with Impact VAS scores, followed by elimination of variables based on log-likelihood scores.

**Results:** Of the 90 subjects, 55.6% had ECI - mostly musculoskeletal including joint contracture (27), bone size difference (23), and myalgia (12). Factors associated with ECI included higher PGA-Damage and Impact VAS scores, mixed morphea subtype, limb involvement, RF positivity, and systemic treatment (Table). No association was found with gender, age of onset, disease duration, or ANA positivity. High impact VAS was associated with altered sensation at skin lesion site, joint problems, difficulty playing, and missing school (r= 0.209-0.322). Modeling to identify variables associated with higher Impact VAS scores identified female sex (OR 10.7, 95% CI 3.9 to 29.5, p <0.001), active disease (OR 2.9, 95% CI 1.2 to 6.8, p = 0.014), and ECI (OR 2.8, 95% CI 1.3 to 5.9, p = 0.008).

**Conclusion:** Most jLS subjects had ECI, which occurred within a few years of disease onset. Several associated factors were identified, and subjects with ECI were found to have higher physician rated damage and parent rated impact scores. The odds of higher impact scores were strongly associated with female sex. There is a need for more study to better evaluate variables associated with development of ECI and its impact on HRQoL.

Characteristics of Subjects with and without ECI
<table>
<thead>
<tr>
<th></th>
<th>All (90)</th>
<th>+ ECI (50)</th>
<th>No ECI (40)</th>
<th>P value (+ vs No ECI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender: Female: Male</td>
<td>70 : 20</td>
<td>39 : 11</td>
<td>31 : 9</td>
<td>NS</td>
</tr>
<tr>
<td>Age at Disease Onset, median years, (IQR)</td>
<td>7.9 (5.0, 10.0)</td>
<td>7.7 (4.8, 9.8)</td>
<td>8 (5.3, 10)</td>
<td>NS</td>
</tr>
<tr>
<td>Disease Duration at Study Entry, median years (IQR)</td>
<td>2.75 (1.4, 5.0)</td>
<td>3 (1.6, 5.3)</td>
<td>2.2 (1.1, 5)</td>
<td>NS</td>
</tr>
<tr>
<td>Race: Caucasian</td>
<td>70</td>
<td>37</td>
<td>33</td>
<td>NS</td>
</tr>
<tr>
<td>African American</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>7</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Mixed</td>
<td>10</td>
<td>8</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Ethnicity: Hispanic</td>
<td>13</td>
<td>7</td>
<td>6</td>
<td>NS</td>
</tr>
<tr>
<td>Active Disease Status</td>
<td>66</td>
<td>37</td>
<td>29</td>
<td>NS</td>
</tr>
<tr>
<td>LS Subtype: Circ superficial</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>0.005</td>
</tr>
<tr>
<td>Circumscibed deep</td>
<td>12</td>
<td>5</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Linear trunk or limb</td>
<td>31</td>
<td>18</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Linear head</td>
<td>10</td>
<td>3</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Generalized morphea</td>
<td>7</td>
<td>4</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Mixed morphea</td>
<td>26</td>
<td>20</td>
<td>6</td>
<td>0.007</td>
</tr>
<tr>
<td>Mixed Morphea Subtype</td>
<td>26</td>
<td>20</td>
<td>6</td>
<td>0.007</td>
</tr>
<tr>
<td>Anatomic site: Head</td>
<td>15</td>
<td>6</td>
<td>9</td>
<td>0.046</td>
</tr>
<tr>
<td>Neck or Trunk</td>
<td>28</td>
<td>14</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Limb</td>
<td>48</td>
<td>32</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Family History of Autoimmune disease</td>
<td>53</td>
<td>35</td>
<td>18</td>
<td>0.021</td>
</tr>
<tr>
<td>RF positivity (denominator = number of subjects who were tested)</td>
<td>6/33</td>
<td>6/14</td>
<td>0/19</td>
<td>0.011</td>
</tr>
<tr>
<td>Elevated IgG or IgE level</td>
<td>9/38</td>
<td>9/22</td>
<td>0/16</td>
<td>0.003</td>
</tr>
</tbody>
</table>
Performance of Juvenile Scleroderma Classification Criteria for Juvenile Systemic Sclerosis. Results from the Jssc Inception Cohort

Jens Klotsche, Ivan Foeldvari, Ozgur Kasapcopur, Vanessa Smith, Flavio Sztajnbok, Maria M. Katsicas, Rolando Cimaz, Mahesh Janarthanan, Jordi Anton, Mikhail Kostik, Dana Nemkova, Walter A. Sifuentes-Giraldo, Valda Stanivitch, Kathryn S. Torok, Simone Appenzeller, Tadey Avcein, Lillemor Berntson, Liora Harel, Tilmann Kallinich, Maria José Santos, Maria Teresa Terreri, Yosef Uziel, and Nicola Helmus.

Disclosure: S. C. Li, None; T. Andrews, None; M. Chen, None; K. S. Torok, None; E. Pope, None; K. G. Stewart, None; G. C. Higgins, None; C. E. Rabinovich, None; R. M. Laxer, None; K. Haines, None; M. Punaro, None; H. Jacobe, None; K. O'Neil, None.


Abstract Number: 1286
Juvenile systemic sclerosis (jSSc) is a rare disease during childhood. Classification criteria for jSSc were published in 2007. They include a major criterion that is required and 20 minor criteria from which at least two are required for classification. The objective of this study was to investigate the distribution of the single minor classification criteria in patients with jSSc in relation to sex and the age at disease onset in a prospective cohort study.

Methods:

Data from the prospective international inception cohort for jSSc was used to investigate the proportion of jSSc patients fulfilling the 20 minor criteria. 48 patients with a jSSc disease duration of less than 2.5 years were included in the analyses. Age at disease onset (AO) was categorized into two groups (<12 (AO G1) /≥ 12 (AO G2) years). Latent class analysis (LCA) was used to identify distinct groups of patients which share a similar pattern of minor criteria for jSSc.

Results:

The mean physician global on a visual analogue scale was 46 (sd=26) at enrolment, 37 (77.1%) were female, and 31 (64.6%) patients had diffuse subtype. Raynaud’s phenomenon (90%), ANA positivity (87%), and nailfold capillary abnormalities (77%) were the most present minor criteria. Patients in group AO G1 met more often only 2 or 3 minor criteria (23% versus 11%), whereas almost 40% in AO G2 (versus 23% in AO G1) met more than 5 criteria. Patients in AO G2 had more often sclerodactyly (83%/47%), decreased DLCO (62%/38%) and were more often ANA positive (100%/72%) than in AO G1. LCA in patients of AO G2 resulted in two groups. In the first group, the leading minor criteria were sclerodactyly, Raynaud’s phenomenon, nailfold capillary abnormalities and SCL-70 positivity. The second group was characterized by patients with nailfold capillary abnormalities, Raynaud’s phenomenon, decreased DLCO, reflux and arthritis. Female patients fulfilled in mean significantly more minor criteria than boys (4.3 versus 5.1). Differences were highest in nailfold capillary abnormalities (84%/55%), gastro-esophageal reflux (30%/0%), and arthritis (35%/9%). No case with dysphagia, renal crisis, atrial hypertension, neuropathy and carpal tunnel syndrome was documented at enrolment.

Conclusion:

Patients with a jSSc disease onset before the age of 12 and males met significantly less minor criteria than patients with a later onset and females. We could recognize 2 patterns of presentation of jSSc over the age at onset of 12, which was not described before. We have to observe in the long term follow up, how fare to be part of a cluster present a prognostic factor for morbidity and mortality.

Disclosure: J. Klotsche, None; I. Foeldvari, None; O. Kasapcopur, None; V. Smith, None; F. Sztajnbok, None; M. M. Katsicas, None; R. Cimaz, None; M. Janarthanan, None; J. Anton, None; M. Kostik, None; D. Nemkova, None; W. A. Sifuentes-Giraldo, None; V. Stanevicha, None; K. S. Torok, None; S. Appenzeller, None; T. Avcin, None; L. Berntson, None; L. Harel, None; T. Kallinich, None; M. J. Santos, None; M. T. Terreri, None; Y. Uziel, None; N. Helmus, None.


Abstract Number: 1287

Cone Beam Computed Tomography for the Assessment of Linear Scleroderma of the Face
Linear scleroderma of the face (LSF) is a very disabling condition and, to date, standardized and validated methods for assessing and monitoring the disease progression are lacking. The Cone Beam Computed Tomography (CBCT) is an imaging technique with good sensitivity for both soft and bony tissues, fast to be performed with no need for patient sedation. Of interest, the radiation exposure is 50 times lower than a traditional CT scan, being the ideal technique for a repeated use. We investigated whether CBCT may represent a reliable tool for assessing patients with LSF and monitoring their course over time.

Methods: Ten consecutive patients with LSF, aged 3-21 years, and 5 age-matched healthy controls underwent CBCT assessment. The transverse sections of CBCT scan, in digital format, were analyzed according with three arbitrarily selected anatomic levels: mandibular condyle (MC), floor of the maxillary sinus (MS) and mandibular foramen (MF). Measurements of both affected and unaffected side of the face were made by a standardized methodology. From the intersection axes, an origin point was generated and from this one, 30° and 60° lines, crossing bony and soft structures, were drawn. For each given degree, the soft tissue thickness and the total thickness (bony and soft tissues) of the right and left side were calculated by using the software Onis 2.4 free edition. Twenty-four measures for each subject (two for each side, right and left, of the three transverse sections) were therefore evaluated. Five raters, all physicians, after a two-hour training session, evaluated LSF patients’ and controls’ CBCTs twice and blindly one from the other. The intra-rater reliability was assessed by the repeatability coefficient and the inter-rater reliability by the Intraclass Correlation Coefficient (ICC) and interpreted as follows: ICC values range 0.75-1 excellent reliability, 0.4-0.74 good reliability, <0.4 poor reliability.

Results: CBCT was fast and well tolerated by the patients even the youngest. The intra-rater concordance resulted optimal as the repeatability coefficient ranged between 0.77 and 0.99. The inter-rater concordance for the total thickness, among the assessors, was also excellent with mean ICC value of 0.75 (SD 0.16) for patients and 0.89 (SD 0.09) for controls. The mean ICC for the soft tissue thickness was 0.49 (SD 0.24) for patients and 0.66 (SD 0.28) for controls, respectively. 58.3% of the measurements for patients and 91.2% of those for controls showed excellent ICC results (> 0.75). The best performances were obtained at the level of the MF and MC sections.

Conclusion: CBCT is a reliable method to assess and monitor skin and bone changes in patients with LSF. It is a fast, reproducible and reasonably safe technique. A prospective validation to confirm its relevance in evaluating the disease progression is ongoing.

Disclosure: F. Zulian, None; C. Di Giovanni, None; S. Puggina, None; A. Meneghel, None; S. Trainito, None; G. Martini, None.
Renal disease is the most common manifestation of pediatric anti-neutrophil cycloplasmic antibody (ANCA) associated vasculitis (AAV). Renal disease course and early trajectories have not been well studied. The aim of this project was to describe renal disease at time of diagnosis (TOD) and follow glomerular filtration rate (GFR) trajectories over 12-months.

Methods:

PedVas is a multi-center international study that is currently collecting clinical and biological data from children with chronic vasculitis. The clinical data is stored in ARChiVe (A Registry for Childhood Vasculitis). Patients entered into ARChiVE with granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA) and renal disease were included. Renal disease was defined as biopsy confirmed pauci-immune glomerulonephritis OR dialysis dependence at TOD. Patients had to be less than 18 years of age at TOD. GFR was estimated using the bedside Schwartz formula. GFR based outcomes were reported as proportion of children with normal GFR (>90 ml/min/1.73m²), mildly reduced (MildR) (60-89 ml/min/1.73m²), moderately reduced (ModR) (30-59 ml/min/1.73m²), severely reduced (SR) (15-29 ml/min/1.73m²), and renal failure (RF) (<15 ml/min/1.73m², or requirement of dialysis).

Results:

109 patients met inclusion criteria. 64% were female. 81% had GPA and 19% had MPA. No patients with EGPA had renal disease. Median age at diagnosis was 13.8 years (range 3.9 to 17.8 yrs). Ethnicity data was available for 83% of patients. Of those, 61% were Caucasian, 13% East Indian/South Asian, 9% Hispanic, and 17% other (Asian, Black, Aboriginal, Mixed, or Other). Renal manifestations at TOD included: hematuria (92%), proteinuria (84%), hypertension (29%), oliguria (20%), and nephrotic syndrome (14%). 29 patients (27%) required dialysis at TOD. Cyclophosphamide (CYC) and/or rituximab (RTX) were used as primary induction treatments in 93% of patients. 10% of patients received both CYC and RTX. 30% of patients also received plasmapheresis. All patients received corticosteroids.

At TOD, 36% of patients had a normal GFR. The remaining patients had reduced GFRs as follows: 6% MildR, 16% ModR, 12% SR, and 30% RF. By post-induction (4-6 months following diagnosis), 28% of patients had a normal GFR, 32% MildR, 17% ModR, 4% SR, and 19% RF. 71 patients had complete 12-month visit data. 21 patients (30%) had normal GFR, 34% MildR, 17% ModR, 3% SR, 14% RF, and 2 patients had been transplanted. Of the 21 patients with normal GFR, 17 (81%) had achieved a normal GFR by post-induction. Of patients requiring dialysis at TOD, 85% had ModR GFR or worse at 12-months, 50% remained on dialysis or were transplanted.

Conclusion:

More than half of children with AAV associated renal disease have moderately reduced renal function or worse at diagnosis. In this cohort, only modest improvements in GFR were seen by post-induction, and minimal improvements were seen beyond that despite aggressive treatment. At 12-months, only 30% of children had normal GFRs. The majority of patients who required dialysis at TOD continued to have significantly reduced renal function at 12-months.

Disclosure: K. Morishita, None; A. Chen, None; C. Mammen, None; A. Rivera, None; D. Cabral, None.
Medium Vessel Chronic Vasculitis – a Pediatric Vasculitis Initiative (PedVas) Study

Angelyne Rivera¹, Kimberly Morishita², David Cabral² and Raashid Luqmani³, ¹Pediatrics, BC Children's Hospital and University of British Columbia, Vancouver, BC, Canada, ²BC Children's Hospital and University of British Columbia, Vancouver, BC, Canada, ³Nuffield Department of Orthopaedics Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster II: Lupus and Related Disorders, Myositis, Scleroderma and Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Classification of chronic vasculitis to clinically or etiologically meaningful groups has been challenging. In 2008, the 1990 ACR classification criteria for GPA was adapted for children as the 2008 EULAR/PRINTO/PRES criteria. In 2017, ACR/EULAR proposed new criteria for classifying GPA using new knowledge, and based on data from 1500 adult patients in the Diagnosis and Classification Criteria in Vasculitis (DCVAS) initiative. We aimed to evaluate the 2017 criteria for GPA in a cohort of children and compare the 2008 criteria.

Methods: Time of diagnosis data was retrieved from the international Registry of Childhood Vasculitis (ARChiVe) in PedVAS. The 2017 Classification criteria and scoring system are shown in Table 1 with adaptations of criteria to align with the available ARChiVe dataset. All patients except Takayasu (TAK) were included. Classification of GPA versus not GPA patients by both the 2017 and 2008 criteria was computed from data, and sensitivity / specificity measured against Expert classification. Expert Opinion was determined as follows: If physician submitted diagnosis matched both 1990 and 2008 criteria for GPA, or not GPA, the diagnosis was considered as verified; an expert (KM or DC) evaluated clinical vignettes of remaining patients and verified the diagnosis if it matched submitted diagnosis. Both experts evaluated remaining patients and when consensus could not be reached patients were considered unclassifiable.

Results: After applying the 1990 and 2008 criteria for GPA in all 376 included patients (Table 2), those fulfilling both criteria matched submitted diagnosis of GPA in 163; and for those not fulfilling either criteria there was a matched submitted diagnosis that was not-GPA in 89. Clinical vignettes of the remaining 124 patients underwent expert review for classification. Ultimately 245 patients had GPA and 131 did not. The 2017 criteria for GPA and the 2008 criteria were each applied to all patients and sensitivity specificity respectively measured against Expert classification: 2017 criteria 93% and 72%, and 2009 criteria 95% and 70%. The 2017 criteria classified 6 additional patients.

Conclusion: Performance of the 2017 and 2008 classification criteria was similar but applicability of the 2017 criteria across the ages is valuable; low specificity may reflect relatively low non GPA numbers and exclusion of TAK. The value of criteria in both adults and children will be best assessed if classification to GPA is seen to be mutually exclusive of classification to other closely related diseases, when these criteria also become available from DCVAS.
Disclosure: A. Rivera, None; K. Morishita, None; D. Cabral, None; R. Luqmani, None.

Preterm Birth Phenotypes in Women with Autoimmune Diseases

Kathleen D. Kolstad, Jonathan A. Mayo, Lorinda Chung, Yashaar Chaichian, Victoria M. Kelly, Maurice Druzin, David K. Stevenson, Gary M. Shaw and Julia F Simard
1 Rheumatology, Stanford University Medical Center, Stanford, CA, 2 Stanford University Medical Center, Stanford, CA, 3 Rheumatology, Stanford University Medical Center, Palo Alto, CA, 4 Medicine, Immunology & Rheumatology Division, Stanford School of Medicine, Stanford, CA, 5 Palo Alto Medical Foundation, Palo Alto, CA, 6 Obstetrics & Gynecology, Stanford School of Medicine, Stanford, CA, 7 Pediatrics - Neonatology, Stanford University, Stanford, CA, 8 Pediatrics, Division of Neonatology and Developmental Medicine, Stanford School of Medicine, Stanford, CA, 9 Division of Epidemiology, Health Research and Policy Department, Stanford School of Medicine, Stanford, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Reproductive Issues in Rheumatic Disorders Poster
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Systemic autoimmune diseases expose patients to chronic inflammation, immune dysregulation, and vascular abnormalities; complications that can impact obstetric outcomes. The goal of this study was to investigate preterm birth (PTB) phenotypes in women with a variety of autoimmune diseases in large population-based data.

Methods:
Maternally linked hospital and birth certificate records for all live singleton births in California between 2007 and 2011 were analyzed (n=2,481,516) using data provided by the California Office of Statewide Health Planning and Development (OSHPD). Prevalent autoimmune disease at delivery was identified by ICD-9 codes for Systemic Lupus Erythematosus (SLE), Discoid Lupus Erythematosus (DLE), Systemic Sclerosis (SSc), Rheumatoid Arthritis (RA), Polymyositis/Dermatomyositis (DM/PM), and Juvenile Idiopathic Arthritis (JIA). Patients with more than one of these diagnoses were classified as “overlap”. PTB was assessed overall (20-36 weeks) and partitioned into phenotypes including pre-term premature rupture of membranes (PPROM), spontaneous, and medically induced PTB. Adjusted multivariable Poisson regression models estimated risk ratios (RR) and corresponding 95% confidence intervals for the above PTB outcomes (relative to term deliveries) for each autoimmune disease compared to the general obstetric population adjusting for maternal age, race/ethnicity, body mass index, smoking, education, payer, parity, and prenatal care.

Results:
There were 4,458 births to 4,156 distinct mothers with autoimmune diseases (SLE n=2,419, RA n=1,649, SSc n=106, DLE n=114, JIA n=198, DM/PM n=43, Overlap n=164). Greater than 90% of women in all groups initiated prenatal care in the first five months of pregnancy and were nonsmokers. Compared to the general population, patients with systemic autoimmune diseases were more likely to deliver prematurely (Table). This increased risk persisted for all disease groups for spontaneous PTB and the majority of disease groups for both PPROM and medically indicated PTB at 32-36 weeks of gestation, with the exception of DLE.

Conclusion:
These results indicate that women with systemic autoimmune diseases have an elevated risk of preterm delivery, both spontaneous and medically indicated. Therefore, preconception counseling and close monitoring during pregnancy is important. Despite the differences in these autoimmune conditions, the risks were consistently elevated for PTB outcomes, which may provide insight into the underlying mechanism of these obstetric complications.
<table>
<thead>
<tr>
<th>Autoimmune Disease</th>
<th>Overall PTB</th>
<th>PPROM</th>
<th>Spontaneous PTB</th>
<th>Medically Indicated PTB</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>RR (95% CI)</td>
<td>N</td>
<td>RR (95% CI)</td>
</tr>
<tr>
<td>SLE</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>176984</td>
<td>1.0 (ref)</td>
<td>36986</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>Yes</td>
<td>578</td>
<td>3.22 (2.97,3.49)</td>
<td>99</td>
<td>2.95 (2.42,3.59)</td>
</tr>
<tr>
<td>DLE</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>177541</td>
<td>1.0 (ref)</td>
<td>37082</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>Yes</td>
<td>21</td>
<td>2.33 (1.52,3.58)</td>
<td>3</td>
<td>1.64 (0.53,5.09)</td>
</tr>
<tr>
<td>SSC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>177533</td>
<td>1.0 (ref)</td>
<td>37074</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>Yes</td>
<td>29</td>
<td>3.73 (2.60,5.37)</td>
<td>11</td>
<td>7.08 (3.92,12.8)</td>
</tr>
<tr>
<td>RA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>177316</td>
<td>1.0 (ref)</td>
<td>37020</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>Yes</td>
<td>246</td>
<td>2.06 (1.82,3.32)</td>
<td>65</td>
<td>2.57 (2.01,3.28)</td>
</tr>
<tr>
<td>JIA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>177530</td>
<td>1.0 (ref)</td>
<td>37075</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>Yes</td>
<td>32</td>
<td>2.40 (1.70,3.39)</td>
<td>10</td>
<td>3.50 (1.88,6.51)</td>
</tr>
<tr>
<td>DM/PM</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>177546</td>
<td>1.0 (ref)</td>
<td>37083</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>Yes</td>
<td>16</td>
<td>5.32 (3.26,6.88)</td>
<td>2</td>
<td>4.01 (1.00,16.1)</td>
</tr>
<tr>
<td>Overlap</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>177531</td>
<td>1.0 (ref)</td>
<td>37082</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>Yes</td>
<td>31</td>
<td>2.54 (1.78,3.61)</td>
<td>3</td>
<td>1.25 (0.40,3.86)</td>
</tr>
</tbody>
</table>

Table 1. Preterm Birth (PTB) at 20-36 weeks of gestation in women with the autoimmune diseases compared to the general obstetric population. Systemic Lupus Erythematosus =SLE, Discoid Lupus Erythematosus=DLE, Systemic Sclerosis=SSc, Rheumatoid Arthritis=RA, Polymyositis/Dermatomyositis=DM/PM, and Juvenile Idiopathic Arthritis =JIA, Preterm Premature Rupture of Membranes=PPROM.

Disclosure: K. D. Kolstad, None; J. A. Mayo, March of Dimes, 2; L. Chung, None; Y. Chaichian, Novartis Research Foundation, 5, John & Marcia Goldman Foundation, 3, V. M. Kelly, None; M. Druzin, March of Dimes, 2; D. K. Stevenson, March of Dimes, 2; G. M. Shaw, March of Dimes, 2; J. F. Simard, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/preterm-birth-phenotypes-in-women-with-autoimmune-diseases

Abstract Number: 1291

Preterm Delivery Phenotypes in SLE Pregnancies

Julia F Simard, Marios Rossides, Anna-Karin Wikstrom, Gary M. Shaw, and Maurice Druzin. 1Medicine, Division of Immunology & Rheumatology, Stanford School of Medicine, Stanford, CA, 2Medicine, Immunology & Rheumatology Division, Stanford School of Medicine, Stanford, CA, 3Medicine Solna, Clinical Epidemiology Unit, Karolinska Institutet, Stockholm, Sweden, 4Department of Women’s and Children’s Health, Uppsala University, Uppsala, Sweden, 5Pediatrics, Division of Neonatology and Developmental Medicine, Stanford School of Medicine, Stanford, CA, 6Obstetrics & Gynecology, Stanford School of Medicine, Stanford, CA.

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017

Session Title: Reproductive Issues in Rheumatic Disorders Poster

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM

Background/Purpose: Women with systemic lupus erythematosus (SLE) are at greater risk of preterm delivery compared to women without lupus. A significant proportion of SLE pregnancies are complicated by maternal factors and delivery is medically indicated (iatrogenic). For example, preeclampsia risk is increased in SLE pregnancies. We investigated the types of preterm deliveries in SLE (iatrogenic vs spontaneous), and estimated the proportion mediated by preeclampsia.

Methods: Women with and without SLE with singleton pregnancies were identified from SLINK, a Swedish register-based cohort, 2001-2013. Maternal SLE was defined as ≥2 SLE-coded discharge diagnoses from the National Patient Register and ≥1 SLE code from an appropriate specialist. Preterm delivery was defined as ≤37 weeks gestation, extremely and very preterm as <32 weeks. Spontaneous preterm birth was defined as due to preterm contractions or premature rupture of the membranes (PPROM). Iatrogenic was defined as planned C-section or induced labor. Maternal/fetal complications were stratified by maternal SLE, parity, and...
Long-Term Follow-up of 320 Children Born to Mothers with Systemic Autoimmune Diseases: A Multicentre Survey from 24 Rheumatology Centers in Italy

Maria Grazia Lazzaroni, Cecilia Nalli, Laura Andreoli, Chiara Carini, Marilia Rodrigues, Francesca Dall’Ara, Elena Bartolon-Bocci, Roberto Gerli, Maria Gerosa, Cecilia B. Chighizola, Pier Luigi Meroni, Luigi Sinigaglia, Paola Coniglio, Roberto Perricone, Ada Corrado, Francesco Paolo Cantatore, Salvatore D’Angelo, Ignazio Olivieri, Maria Favaro, Maddalena Larosa, Andrea Doria, Amelia Ruffatti, Elena Generali, Carlo Selmi, Marianna Meroni, Maurizio Cutolo, Melissa Padovan, Marcello Govoni, Giulia Pazzola, Carlo Salvarani, Susanna Peccatori, Giuseppe Paolazzi, Imma Prevete, Giovanni Minisola, Gian Domenico Sebastiani, Antonio Brucato, Véronique Ramoni, Roberto Caporalí, Carlo Maurizio Montecucco, Viola Signorini, Chiara Tani, Marisa Mocci, Marica Trevisani, Nazzarena Malavolta, Marta Vadacca, Antonella Aflerta, Ester Vivaldelli, Armin Maier, Elisa Visalli, Rosario Foti, Carolina Benigno, Lucia Zuliani, Armando Gabrielli, Corrado Campochiaro, Elena Baldissera, Maria Grazia Sabbadini, Nicoletta Romeo and Angela Tincani, University and Spedali Civili of Brescia, Brescia, Italy, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal, University and Azienda Ospedaliera di Perugia, Perugia, Italy, Istituto Ortopedico Gaetano Pini, University of Milan, Milan, Italy, University and Policlinico San Matteo of Pavia, Pavia, Italy, Policlinico Tor Vergata of Rome, Rome, Italy, Ospedali Riuniti of Foggia, Foggia, Italy, San Carlo Hospital of Potenza, Potenza, Italy, University and Azienda Ospedaliera di Padova, Padova, Italy, Unità di Reumatologia, Dipartimento di Medicina-DIMED, University di Padova., Padova, Italy, Rheumatology and Clinical Immunology, Humanitas Research Hospital, Rozzano (MI), Italy, Humanitas Research Hospital of Milan, Rozzano, Italy, Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, IRCCS A.O.U. San Martino-IST, University of Genova, Genoa, Italy, Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, IRCCS San Martino, Genoa, Italy, OUC of Rheumatology, University Hospital S. Anna, Cona Ferrara, Italy, Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy, Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy, Struttura Complessa Medicina Interna, ASST Papa Giovanni XXIII, Bergamo, Italy, Ospedale Papa Giovanni XXIII of Bergamo, Policlinico San Matteo of Pavia, Bergamo, Pavia, Italy, University and Policlinico San Matteo di Pavia, Pavia, Italy, University of Pisa, Pisa, Italy, Rheumatology Unit, University of Pisa, Pisa, Italy, Policlinico S.Orsola-Malpighi, Azienda Ospedaliero-Universitaria of Bologna, Bologna, Italy, University of Milan, Italy, Milan, Italy, Tincani Armando Gabrielli, Montecucco Giovanni Minisola Padovan 9 University of Pisa, Pisa, Italy, Pavia, Italy, Rome, Roma, Italy, Emilia, Reggio-Emilia, Italy, Hospital S. Anna, Cona Ferrara, Italy, and Academic Division of Clinical Rheumatology, Department of Internal Medicine, IRCCS A.O.U. San Martino-IST, University of Humanitas Research Hospital, Istituto Auxologico Italiano, University of Milan, Milan, Italy, Policlinico S.Orsola-Malpighi, Azienda Ospedaliero-Universitaria of Bologna, Bologna, Italy, University of Pisa, Pisa, Italy, and Azienda Ospedaliera San Camillo of Rome, Roma, Italy, Rheumatology, San Camillo Forlanini Hospital, Roma, Italy, Struttura Complessa Medicina Interna, ASST Papa Giovanni XXIII, Bergamo, Italy, Ospedale Papa Giovanni XXIII of Bergamo, Policlinico San Matteo of Pavia, Bergamo, Pavia, Italy, University and Policlinico San Matteo di Pavia, Pavia, Italy, University of Pisa, Pisa, Italy, Rheumatology Unit, University of Pisa, Pisa, Italy, Policlinico S.Orsola-Malpighi, Azienda Ospedaliero-Universitaria of Bologna, Bologna, Italy, University of Pisa, Pisa, Italy, Tincani Armando Gabrielli, Montecucco Giovanni Minisola Padovan 9 University of Pisa, Pisa, Italy, Pavia, Italy, Rome, Roma, Italy, Emilia, Reggio-Emilia, Italy, Hospital S. Anna, Cona Ferrara, Italy, and Academic Division of Clinical Rheumatology, Department of Internal Medicine, IRCCS A.O.U. San Martino-IST, University of Humanitas Research Hospital, Istituto Auxologico Italiano, University of Milan, Milan, Italy, Policlinico S.Orsola-Malpighi, Azienda Ospedaliero-Universitaria of Bologna, Bologna, Italy, University of Pisa, Pisa, Italy.
SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Reproductive Issues in Rheumatic Disorders Poster
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Rheumatic Diseases (RD) frequently affect women during reproductive age, therefore counseling on family planning is crucial for their quality of life. Children's outcome is a major topic, but no large studies are available. This study aimed at assessing the long-term health conditions of children born to women with RD.

Methods: 24 Italian Rheumatology Centers distributed the questionnaire (65 multiple-choice and 12 open-answer questions) to consecutive patients (aged 18-55) during September 2015. Data were analyzed subdividing children upon maternal diagnosis: Chronic Arthritides (CA) and Connective Tissue Diseases (CTD).

Results: Data were collected for 320 children (166 males, 52%) born to 184 mothers (63 CA and 121 CTD). At the time of interview, children had a mean age of 17.1±9.6 years. Pre-term delivery (<37 w) was observed in 72 cases (22.5%), including 13 (4%) cases born <34 w. The occurrence of an autoimmune/inflammatory disease (AIID) and/or neurodevelopmental disorders (ND)/learning disabilities (LD) is reported in Table 1. Twelve children (3.7%) were diagnosed with an AIID, mostly coeliac disease (8/12, 67%). Eleven children (3.4%) were diagnosed as having a ND and/or LD by a Pediatric Neuropsychiatrist. To rule out the possible effects of in utero exposure to maternal autoantibodies and/or anti-rheumatic drugs in the pathogenesis of ND, data on such exposures were retrieved for 280 children (87.5%) and a comparison was performed between affected (n=11) and not-affected children (n=258) as reported in Table 2.

Conclusion: The long-term follow-up of children born to mothers with RD in this large, multicenter study of randomly interviewed women did not raise particular concerns in terms of relevant health problems. In particular, each AIID did not display a significantly increased frequency as compared to the literature (e.g. 2.5% coeliac disease as compared to 1-2% in the general pediatric population, GPP). Children with ND/LD had a tendency to cluster in the group of mothers with CTD, especially after maternal diagnosis, with a higher frequency as compared to GPP (7.9% vs 3%). No particular association with the in utero exposure to either autoantibodies or drugs was found. Therefore, our data suggest that the development of ND/LD in children of patients with RD cannot be linked exclusively to maternal disease. The results of this study can be reassuring for patients with RD about problems in the offspring possibly related to their disease.

Acknowledgements: Statistical analysis supported by an unrestricted grant by UCB Pharma. The authors wish to thank Patients Associations and Participants to the survey.
Disclosure: M. G. Lazzaroni, None; C. Nalli, None; L. Andreoli, None; C. Carini, None; M. Rodrigues, None; F. Dall’Ara, None; E. Bartoloni-Bocci, None; R. Gerli, None; M. Gerosa, None; C. B. Chighizola, None; P. L. Meroni, None; R. Perricone, None; A. Corrado, None; F. P. Cantatore, None; S. D’Angelo, None; I. Olivieri, None; M. Favaro, None; M. Larosa, None; A. Doria, GSK, Pfizer, 8,Italian Association of Lupus Patients, 2,GSK, Pfizer, AstraZeneca, Celgene, Eli Lilly, Baxalta, 5; A. Ruffatti, None; E. Generali, None; C. Selmi, None; M. Meroni, None; M. Cutolo, None; M. Padovan, None; M. Govoni, None; G. Pazzola, None; C. Salvareni, None; S. Peccatori, None; G. Paolazzi, None; I. Prevete, None; G. Minisola, None; G. D. Sebastiani, None; A. Brucato, None; V. Ramoni, None; R. Caporali, None; C. Montecucco, None; V. Signorini, None; C. Tani, None; M. Mosca, None; M. Trevisani, None; N. Malavolta, None; M. Vadacca, None; A. Afeltra, None; E. Vivaldelli, None; A. Maier, None; E. Visalli, None; R. Foti, None; C. Benigno, None; L. Zuliani, None; A. Gabrielli, None; C. Campochiaro, None; E. Baldissera, None; M. G. Sabbadini, None; N. Romeo, None; A. Tincani, None.

Table 1. Autoimmune/inflammatory diseases and neuropsychiatric disorders in 320 children, distributed according to maternal diagnosis and timing of pregnancy; CA, chronic arthritis; CTDs, connective tissue diseases; SGA, Small for Gestational Age; LD, learning disabilities (LD).

Table 2. Exposure to maternal autoantibodies and anti-rheumatic drugs in children affected by neuropsychiatric disorders.


Abstract Number: 1293
Indications for Cesarean Delivery in Systemic Lupus Erythematosus Pregnancies

Evelyne Vinet1, Paul R. Fortin2, Stéphanie Roberge3, Emmanuel Bujold4 and Nils Chaillet5, 1Divisions of Rheumatology and Clinical Epidemiology, McGill University Health Centre, Montreal, QC, Canada, 2Infectious Diseases and Immunity Research Division, CHU de Québec-Université Laval Research Center, Québec, QC, Canada, 3Centre de recherche du CHU de Québec-Université Laval, Québec, QC, Canada, 4Reproduction, mother and youth health, Centre Hospitalier de l'Université Laval (CHUL), Québec, QC, Canada. 5Département d’obstétrique et gynécologie et département de Médecine de famille et médecine d’urgence, Université de Sherbrooke, Sherbrooke, QC, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Reproductive Issues in Rheumatic Disorders Poster
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Pregnant SLE women are at increased risk of cesarean delivery compared to pregnant women from the general population. Yet, to date, no one has evaluated the indications for cesarean delivery in SLE pregnancies. Using the large population-based “QUAlity of care, obstetrics RISK MAnagement, and mode of delivery (QUARISMA)” cohort, we assessed indications for cesarean delivery in SLE pregnancies versus unaffected pregnancies.

Methods: The QUARISMA cohort includes 184,952 pregnancies and was established as part of a cluster-randomized, controlled trial, which aimed to evaluate the effect of a 1.5-year intervention, involving audits of indications for cesarean delivery and feedback to healthcare professionals, at 32 hospitals in Quebec (2008-2011). The intervention had a small effect on the rate of cesarean delivery (Chaillet, NEJM, 2015). As part of the trial, in-hospital data, including maternal SLE status and information on indications for cesarean delivery, were abstracted by trained professionals from the medical records.

For the present study, we individually matched 4:1 SLE pregnancies to unexposed pregnancies on maternal age, parity, body mass index (BMI), hospital of delivery, QUARISMA intervention group, and intervention period. We identified cesarean deliveries in SLE and unexposed pregnancies, and ascertained their indications. We performed multivariate analyses to estimate the risk of cesarean delivery for any indications, as well as the risk of cesarean delivery for fetal distress (e.g. cardiac distress, prematurity, intra-uterine growth restriction, stillbirth), maternal disease, and/or preeclampsia in SLE pregnancies versus controls, adjusting for BMI and multiple births.

Results: We identified 122 SLE pregnancies and 488 unexposed pregnancies. Cesarean deliveries occurred in 35/122 (29%) of SLE pregnancies versus 132/488 (27%) of unexposed pregnancies. Among the 35 SLE cesarean deliveries, indications included (but were not limited to) cardiac distress in 34%, prematurity in 29%, maternal disease in 20%, and preeclampsia in 11%. Among the 132 unexposed cesarean deliveries, 28% were due to cardiac distress, 10% to prematurity, 4% to maternal disease, and 6% to preeclampsia. In multivariate analyses, there was a trend for an increased risk of cesarean delivery for any indications in SLE versus unexposed pregnancies (OR 1.6; 95% CI 0.9,2.9). Moreover, SLE pregnancies had a substantially increased risk of cesarean delivery for fetal distress, preeclampsia, and/or maternal disease versus unexposed pregnancies (OR 2.6; 95% CI 1.2,5.3).

Conclusion: Cesarean deliveries in SLE pregnancies are more often due to fetal distress, preeclampsia, and/or maternal disease than cesarean deliveries in pregnancies from the general population.

Disclosure: E. Vinet, None; P. R. Fortin, None; S. Roberge, None; E. Bujold, None; N. Chaillet, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/indications-for-cesarean-delivery-in-systemic-lupus-erythematosus-pregnancies

Abstract Number: 1294

Time to Pregnancy in Women with Systemic Lupus Erythematosus

Meriem El bakali1, Sasha Bernatsky2, Christian A. Pineau3 and Evelyne Vinet4, 1Division of Rheumatology, McGill University Health Centre, Montreal, QC, Canada, 2Divisions of Rheumatology and Clinical Epidemiology, Research Institute of the McGill University Health Centre, Montreal, QC, Canada.
Background/Purpose: Women diagnosed with systemic lupus erythematosus (SLE) during the reproductive period have fewer children than unaffected women. Multiple disease-related factors might influence family size in SLE women, including impaired fertility. However, until now, no one has assessed if women with SLE have a prolonged time to pregnancy (TTP). Therefore, we aimed to measure TTP in women with SLE of reproductive age and compare the occurrence of delayed TTP (i.e. ≥12 months) to general population figures.

Methods: Female subjects with SLE from the Montreal General Hospital Lupus Clinic, aged 18-45 years, were enrolled between 2012 and 2017. SLE diagnosis was defined in accordance with the American College of Rheumatology classification criteria for SLE. At baseline and annual follow-up visits, the investigators administered a detailed reproductive questionnaire, wherein the TTP was measured. The TTP was assessed retrospectively for all pregnancies occurring prior to the baseline visit and prospectively for all pregnancies occurring over the follow-up period. Disease damage index [i.e. SLICC damage index (SDI) score] and the mean disease activity (i.e. SLEDAI score) over a maximum of 5 years were recorded, as well as previous cyclophosphamide (i.e. ever/never) and other relevant drug exposures. Descriptive statistics were calculated.

Results: A total of 333 women with SLE completed the questionnaire. Among these women, 135 never had a pregnancy and 198 conceived at least once. In women having ≥1 pregnancies, we identified 400 pregnancies for which the TTP was assessed. The TTP was measured retrospectively in 347 pregnancies, of which 226 and 121 respectively occurred prior and after SLE diagnosis. We observed a TTP ≥12 months in 4.9% (95% CI 2.6, 8.8) of pregnancies occurring prior to diagnosis and in 9.1% (95% CI 4.9, 16.0) of pregnancies after diagnosis.

43 pregnancies occurred over the study period and 11.6% (95% CI 4.4, 25.9) had a TTP ≥12 months. None of the women with prolonged TTP had prior cyclophosphamide exposure nor were exposed to steroids while attempting to conceive. However, they tended to be slightly older (median 33 vs 31 years) and more likely to have a SDI ≥1 [60% (95% CI 17, 92) vs 28% (95% CI 14, 47)] compared to women with TTP < 12 months.

Conclusion: Our findings suggest that the occurrence of delayed TTP after SLE diagnosis is similar to that of the general population, which has been consistently reported at approximately 10%. However, larger observational studies, including notably an unexposed group of women without SLE, are needed to confirm our results.

Disclosure: M. El bakali, None; S. Bernatsky, None; C. A. Pineau, None; E. Vinet, None.
Background/Purpose: SLE pregnancies are complicated due to risk for maternal disease exacerbation and potential for fetal and neonatal complications. With careful pre-pregnancy counseling and monitoring during pregnancy, most women with SLE can anticipate a successful pregnancy. Less is known about pregnancy courses in women with other connective tissue diseases (oCTD). Our purpose was to compare pregnancy outcomes in women with SLE with outcomes in women with oCTD and with other inflammatory rheumatic diseases.

Methods: The German pregnancy register Rhekiss is designed as nationwide, web-based longitudinal observational cohort study. Pregnant patients with confirmed diagnosis of inflammatory rheumatic disease are eligible to be enrolled until the 20th week of pregnancy. At baseline, sociodemographic parameters, disease severity, obstetric history, comorbidities and antibody status are reported. During each trimester, disease activity, flares, drug treatment and adverse pregnancy outcomes are documented. After birth, the outcome and child development during the first two years of life are collected.

Results: Until April 2017, data from 455 patients were available (SLE [n=104]; other connective tissue diseases [oCTD, including UCTD, MCTD and Sjögren’s Syndrome, n=77] and patients with other inflammatory rheumatic diseases [oIRD, including rheumatoid arthritis [RA], juvenile RA, psoriatic arthritis, and spondyloarthritis, n=271]). 192 women had already completed their pregnancy. Approximately 80% of all pregnancies were planned. At enrollment, disease activity (physicians’ global assessment, 0-10) was 1.6±1.5 [SLE] vs. 1.7±1.5 [oCTD] and 2.5±2.1 [oIRD]. HCQ was used in 63% [SLE] vs. 50% (oCTD) and 5% [oIRD]. Antiphospholipid-Syndrome was present in 14.2% [SLE] vs. 2.6% [oCTD] and 0.7% [oIRD]. The overall live birth rate was 93.7% [88.9% [SLE] vs 94.7% [oCTD] vs 95.4% [oIRD]]. Mean birth weight in singletons born at term was 3117 g [SLE] vs. 3131 g [oCTD] and 3477 g [oIRD]. Severe adverse pregnancy outcome included preterm birth [25% [SLE] vs 16.7% [oCTD] vs 16.3% [oIRD]]. Serious infections were documented in six preterm born newborns (all mothers had SLE or oCTD). Two neonatal deaths occurred (one in a baby born to a mother with SLE and APS who developed severe HELPP syndrome in her 23rd week of pregnancy after inadvertent stopping of anticoagulation, the other death occurred in a preterm twin delivered in the 25th week of pregnancy by a mother with oCTD and triple aPl positivity.

Conclusion: Our real world data show that although most patients with SLE or oCTD have a successful outcome of pregnancy, compared to patients with oIRD, substantial more adverse pregnancy outcomes occurred in these women despite of a high rate of planned pregnancies. Prematurity is the main cause for serious complications.

Disclosures: Rhekiss is a collaborative project of the Rheumazentrum Rhein-Ruhr e.V. Düsseldorf and the DRFZ Berlin, jointly funded by both institutions.

Disclosure: R. Fischer-Betz, None; C. Bungartz, None; M. Schneider, Protagen AG, 5; J. Richter, UCB Pharma GmbH, 9; A. Weiss, None; A. Zink, AbbVie, BMS, MSD, Pfizer, Roche, UCB, 8; A. Strangfeld, BMS, MSD, Pfizer, Roche, Sanofi-Aventis, 8.


Abstract Number: 1296

Hydroxychloroquine Level Decreases throughout Pregnancy: Implications for Maternal and Neonatal Outcomes

Stephen Balevic1, Michael Cohen-Wolkowiez2, Amanda M. Eudy3, Laura E. Schanberg4 and Megan E. B. Clowse5, 1Rheumatology, Adult and Pediatric, Duke University Medical Center, Durham, NC, 2Pharmacometrics Center, Duke Clinical Research Institute, Durham, NC, 3Duke University Medical Center, Chapel Hill, NC, 4Pediatrics, Duke University Medical Center, Durham, NC, 5Duke University Medical Center, Durham, NC

First publication: September 18, 2017
Session Title: Reproductive Issues in Rheumatic Disorders Poster
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Pregnancy in women with active rheumatic disease often result in poor neonatal outcomes. Prior data suggests that hydroxychloroquine (HCQ) can reduce disease activity and flares in pregnant women with systemic lupus. Due to significant increases in the volume of distribution and renal clearance, we hypothesize that HCQ levels decrease during pregnancy, thereby increasing the risk for worsened maternal disease activity and thus poor neonatal outcomes. We tested the relationship between HCQ levels and maternal/neonatal outcomes in a prospective pregnancy cohort.

Methods: We enrolled pregnant patients with rheumatic disease from a single center on a stable HCQ dose between 2013-2016 into an observational study. Frozen serum samples were sent to NMS laboratories and analyzed using high performance liquid chromatography/tandem mass spectrometry. HCQ levels were defined as non-therapeutic (<100 ng/mL) or therapeutic (≥100 ng/mL). Categorical outcomes were analyzed using Fisher’s Exact Test and continuous outcomes were analyzed using linear regression models.

Results: 50 patients were enrolled in the study; 28 (56%) had systemic lupus, 7 (14%) had rheumatoid arthritis, and the remainder had undifferentiated connective tissue disease or other rheumatic diseases. Concomitant medications included corticosteroids in 14 (28%) and azathioprine in 9 (18%). Median HCQ levels for all patients at the most common dose (400 ng) trended down throughout pregnancy and returned near baseline post-partum (p=0.08) (Figure 1, excluding levels <100 ng/mL). Of all patients, 24% had at least one visit with HCQ levels < 100 ng/mL (29% SLE and 18% non-SLE). Excluding one outlier, mean physician global assessment (PGA) scores in lupus patients decreased by 0.07 per 100 ng/mL increase in HCQ level (p=0.04). There was no relationship between HCQ levels and C3, C4, or double-stranded DNA antibody in lupus patients. When analyzed by HCQ level closest to delivery, 100% of lupus patients with HCQ levels <100 ng/mL delivered prematurely (n=4), whereas only 24% of individuals with levels ≥100 ng/mL delivered prematurely (n=21), (p=0.01). In non-lupus patients, there was no difference in prematurity by HCQ level category.

Conclusion: In this small cohort of patients, HCQ levels declined as pregnancy progressed, suggesting a physiologic effect of pregnancy on drug levels and the potential need to optimize dosing. Lupus PGA scores improved with increasing HCQ levels. All lupus patients with HCQ levels <100 ng/mL delivered prematurely, suggesting a role for therapeutic drug monitoring.

Acknowledgements: This work was supported by funding from the Derfner Foundation.

Disclosure: S. Balevic, None; M. Cohen-Wolkowiez, Cempra Pharmaceuticals, Jacobus Pharmaceuticals, Commense, Dyax, 9; A. M. Eudy, None; L. E. Schanberg, Sanofi, Swedish Orphan Biovitrum, 9; M. E. B. Clowse, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/hydroxychloroquine-level-decreases-throughout-pregnancy-implications-for-maternal-and-neonatal-outcomes

Abstract Number: 1297

Hydroxychloroquine in Lupus Pregnancy: A Meta-Analysis of Individual Participant Data
Amanda M. Eudy1, Michelle Petri2, Rebecca Fischer-Betz3, Abeer Mokbel4, Cecilia Nalli5, Laura Andreoli5, Angela Tincani6, Yair Molad7, Stephen Balevic8 and Megan E. B. Clowse1,

1Rheumatology, Duke University Medical Center, Durham, NC, 2Medicine (Rheumatology), Johns Hopkins University School of Medicine, Baltimore, MD, 3Department of Rheumatology and Hiller Research Unit, University Hospital Duesseldorf, Duesseldorf, Germany, 4Department of Rheumatology and Rehabilitation, Cairo University Hospital, Cairo, Egypt, 5Rheumatology and Clinical Immunology, Spedali Civili and University of Brescia, Brescia, Italy, 6Spedali Civili and University of Brescia, Brescia, Italy, 7Rheumatology Unit, Rabin Medical Center, Beilinson Hospital, Petach Tikva, and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel, 8Rheumatology, Adult and Pediatric, Duke University Medical Center, Durham, NC

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Reproductive Issues in Rheumatic Disorders Poster
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Our current knowledge about how to treat lupus in pregnancy derives from small prospective or retrospective cohorts, and how best to manage lupus nephritis remains unknown. The goal of this individual participant meta-analysis was to pool data from multiple prospective cohorts to answer the clinical question of whether hydroxychloroquine (HCQ) treatment is beneficial from the decision point of the first trimester.

Methods: PubMed, Embase, and the Cochrane Database of Systematic Reviews were searched for prospective cohorts of pregnancies among women with lupus. Data from each cohort were collected and analyzed individually. HCQ use was defined as use any time during pregnancy. Outcomes of interest included fetal loss, preterm birth (<37 weeks gestation), and high disease activity (PGA ever >1, SLEDAI ever >4, or a report of a flare, depending on available data). Logistic regression models estimated log odds ratios (OR) and standard errors individually in all cohorts. Pooled ORs were calculated by random-effect models using the generic inverse variance method in Review Manager. Primary analysis included only women with first trimester visits (5 cohorts). Sensitivity analyses included all women (6 cohorts), and subgroup analyses included patients with a history of nephritis.

Results: 46 potential cohorts were identified from 2811 manuscripts. Seven cohorts met inclusion criteria and agreed to participate. The current analysis included 811 pregnancies from six cohorts, of which 70% were exposed to HCQ during pregnancy.

Fetal Loss: When limited to only patients with a 1st trimester visit, a 52% decrease in fetal loss was observed (OR: 0.48; 95% CI: 0.24, 0.94; Table 1). Among all patients there was a modest decrease in fetal loss among HCQ users, but the association was stronger among women with a history of nephritis (Figure 1).

Preterm Birth: No association with HCQ use during pregnancy and preterm birth was observed among women with a 1st trimester visit (OR: 0.78; 95% CI: 0.47, 1.30), among all women, and among women with nephritis.

Disease Activity: Among patients with a 1st trimester visit, there was a decrease in high disease activity among HCQ users (OR: 0.62; 95% CI: 0.37, 1.05), particularly among women with a history of nephritis. Among all patients, there was no association of HCQ use and high disease activity during pregnancy.

Conclusion: Our results suggest that HCQ may decrease the risk of fetal loss, and the benefits are seen most among women with nephritis. The heterogeneity of data collection suggests a unified approach to identify larger cohorts of lupus pregnancies is needed.
Tough Choices: Understanding the Medication Decision-Making Process for Women with Inflammatory Arthritis during Pregnancy and Lactation

Tayseer Haroun1, Amanda M. Eudy2,3,4,5, Malithi Jayasundara2, W. Benjamin Nowell6,7, Jeffrey R. Curtis8, Charlotte Whitney White9, Rachelle Crow-Hercher9, Seth D. Ginsberg10 and Megan E. B. Clowse4,11, 1Department of Medicine/Division of Rheumatology, Duke University Medical Center, Durham, NC, 2Rheumatology, Duke University Medical Center, Durham, NC, 3Duke University, Durham, NC, 4Division of Rheumatology, Department of Medicine, Duke University Medical Center, Durham, NC, 5Duke University Medical Center, Chapel Hill, NC, 6CreakyJoints/Global Health Living Foundation, Upper Nyack, NY, 7Global Healthy Living Foundation, Upper Nyack, NY, 8Division of Clinical Immunology and Rheumatology, University of Alabama at...
SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Reproductive Issues in Rheumatic Disorders Poster
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
With new data demonstrating medication compatibility in pregnancy and lactation, it is important to understand how this information can best reach patients. We sought to identify the decision-making process and gaps in knowledge for women of childbearing age regarding their use of rheumatic medication.

Methods:
A cross-sectional study conducted in collaboration with an online arthritis community from March to June 2017. After an e-mail invitation members provided consent by clicking their unique link to the online survey. Participants were women aged 18-50 years with inflammatory arthritis.

Results:
The majority of 250 women who took the survey were white (83%), not Hispanic (82%), college graduates (69%) and had rheumatoid arthritis (80%); average current age was 39.5yrs and age at diagnosis was 26yrs. Sixty eight (27%) women had pregnancies following their arthritis diagnosis and each reported about her most recent pregnancy. Of these, 31% stopped methotrexate (MTX) and 22% stopped TNF-inhibitor (TNFi) prior to pregnancy; 53% took prednisone, DMARDs or biologics during pregnancy. Fifteen percent had inadvertent MTX exposure during their most recent pregnancy. Prednisone was the most common medication in pregnancy and lactation, followed by NSAIDs and TNFi. Most women reported taking medications by physician instruction, but a minority stopped despite physician reassurances.

Of the 37 women who breastfed their last infant (76% of live born infants), 20 (54%) reported taking at least one anti-rheumatic medication (prednisone, DMARD, or biologic) beyond NSAIDs. Prednisone was by far the most common medication used in lactation (17) with only 5 women using a TNFi. Many avoided arthritis medications while breastfeeding: 86% reported either stopping breastfeeding to take medications or avoiding medications to breastfeed. This caused significant distress for some women: “...I decided it would be better for my baby to be able to hold her, than to be breastfed” and “For the first 6 months I flared while breast feeding and... I would have my spouse hold the baby up to my breasts (to) breast feed. I was in bed for 6 months.”

Most women (69%) were very worried about the impact of their medications on a pregnancy. A majority of women talked to their doctor, most commonly a rheumatologist (89%) or obstetrician (OB) (78%), about the risks of medications on pregnancy, with fewer talking to a high-risk OB (39%). Women had the highest level of confidence in the high-risk OB (76% very confident) followed by their rheumatologist (58%) and OB (38%). Among women consulting more than one provider, most (75%) reported receiving a consistent message from their clinicians about medications in pregnancy and lactation. Many women (61%) also searched online for more information.

Conclusion:
As many as half of women reported discontinuing arthritis medications during pregnancy and/or lactation, sometimes suffering with arthritis activity to avoid any perceived risk to the fetus or newborn. Clinical data suggests that many rheumatic medications may be compatible with pregnancy and lactation, but more education is necessary to support women’s decision making about arthritis treatment.

Disclosure: T. Haroun, None; A. M. Eudy, None; M. Jayasundara, None; W. B. Nowell, Global Healthy Living Foundation, 3; J. R. Curtis, Crescendo Biosciences, 2,Crescendo Biosciences, 5; C. Whitney White, None; R. Crow-Hercher, None; S. D. Ginsberg, None; M. E. B. Clowse, Pfizer, Janssen, 5,UCB Pharma, 5.

Patient-Reported Disease Activity and Adverse Pregnancy Outcomes in Systemic Lupus Erythematosus and Rheumatoid Arthritis

Nathaniel Harris¹, Amanda M. Eudy² and Megan E. B. Clowse², ¹Duke University School of Medicine, Durham, NC, ²Division of Rheumatology, Department of Medicine, Duke University Medical Center, Durham, NC
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Reproductive Issues in Rheumatic Disorders Poster
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Patient-reported measures of disease activity may provide useful adjuncts to physician-reported measures in identifying pregnancies at greater risk for adverse pregnancy outcomes. Little is known about the utility of these measures in SLE patients, and most analyses in patients with RA use only a single measure of disease activity or disability.

Methods: Data on pregnancy outcomes were collected on 225 patients with SLE or RA enrolled in a prospective registry at a single academic center from 2008-2016. Disease activity was measured by physician global assessment (PGA) in SLE and RA, as well as joint counts in RA. The primary patient-reported measure used was the Health Assessment Questionnaire (HAQ); we also tested the utility of pain and general health visual-analog scales. Univariate and multivariable regression models adjusted for race, education, living status, and BMI were used to assess the relationship between patient and physician-reported measures of disease activity and adverse pregnancy outcomes.

Results: Among 145 women with SLE, the mean age was 30 and 50% were African American. Among the 80 women with RA, mean age was 33; nearly 80% were white. Women with RA were more likely to be living with a spouse or partner (85% vs 68%) and were more likely to have completed at least 4 years of college (75% vs 52%). Nearly 50% of women with lupus were Ro+, and 17% percent had a history of lupus nephritis.

In women with RA, patient-reported disease activity was associated with preterm birth (OR 5.9 (95% CI: 1.5-23.9)), and gestational age (beta -1.5 weeks (-2.6, -0.4)). In addition, physician assessment of disease activity predicted preterm (OR 2.1 (1.2-3.5)) and small for gestational age births (OR 1.8 (1.03-3.1), and gestational age in weeks (beta -0.6 weeks (-0.9, -0.02)). On the other hand, for women with SLE, patient-reported measures, including HAQ, pain and general health, were not associated with adverse pregnancy outcomes. However, physician’s global assessment was associated with preterm birth (OR 2.9 (1.6-3.3)), C-section delivery (OR 2.3 (1.0-5.3)), and preeclampsia (OR 2.8 (1.3-6.3)) in SLE patients. The results do not appear to be driven by nephritis or aPL syndrome.

Conclusion: Patient-reported measures of disease activity in RA patients may provide useful adjuncts for physicians to identify pregnancies at higher risk for adverse events. This suggests that increased activity on a patient-reported measure should prompt action during an RA pregnancy. In contrast, in SLE, while the physician-reported measures correlated with pregnancy outcome, the patient-reported measures did not. Our findings provide additional support for the use of patient-reported measures among women with inflammatory arthritis in pregnancy and impetus for the development of patient-reported measures that more accurately reflect lupus disease activity.

Disclosure: N. Harris, None; A. M. Eudy, None; M. E. B. Clowse, Pfizer, Janssen, 5,UCB Pharma, 5.


The Italian Registry of Autoimmune Congenital Heart Block (Lu.Ne Registry): Report of the First Year of Activity

Micaela Fredi¹, Laura Andreoli², Tiziana Bertero³, Alesandra Bortoluzzi⁴, Silvia Breda⁵, Veronica Cappa⁶, Fulvia Ceccarelli⁷, Rolando Cimaz⁸, Salvatore De Vita⁹, Emma Di Poi¹⁰, Franco Franceschini¹¹, Maria Gerosa¹², Marcello Govoni⁴, Ariela Hoxha¹³,
Andrea Lojacono14, Luca Marozio15, Alessandro Mathieu16, Antonina Minniti17, Marina Muscarà18, Melissa Padovan4, Matteo Piga16, Roberta Priori7, Véronique Ramoni19, Amelia Ruffatti13, Marta Tonello13, Sonia Zatti20, Stefano Calza6, Antonio Brucato5 and Angela Tincani2, 1Department of Rheumatology and Clinical Immunology, Rheumatology and Clinical Immunology, Spedali Civili of Brescia, Brescia, Italy, 2Rheumatology and Clinical Immunology, Spedali Civili and University of Brescia, Brescia, Italy, 3Ospedale Mauriziano, Torino, Italy, 4UOC of Rheumatology, University Hospital S. Anna, Cona Ferrara, Italy, 5Struttura Complessa Medicina Interna, ASST Papa Giovanni XXIII, Bergamo, Italy, 6Unit of Biostatistics and Biomathematics & Unit of Bioinformatics, Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy, 7UO Complessa Reumatologia, Policlinico Umberto I Università Sapienza di Roma, Rome, Italy, 8Pediatric Rheumatology, Anna Meyer Children's Hospital-University of Firenze, Florence, Italy, 9Rheumatology Clinic, Academic Hospital S. M. della Misericordia, Medical Area Department, University of Udine, Italy, Udine, Italy, 10Clinica di Reumatologia, Azienda Sanitaria Universitaria Integrata di Udine, Udine, Italy, 11Rheumatology and Clinical Immunology, Spedali Civili of Brescia, Brescia, Italy, 12Istituto Ortopedico Gaetano Pini, University of Milan, Milan, Italy, 13Unità di Reumatologia, Dipartimento di Medicina-DIMED, Università di Padova., Padova, Italy, 14Obstetrics and Gynecology, Spedali Civili and University of Brescia, Brescia, Italy, 15Ginecologia e Ostetricia 1, Dipartimento di Scienze Chirurgiche, Università di Torino, Torino, Italy, 16Unit and Chair of Rheumatology, University Hospital of Cagliari, Cagliari, Italy, 17UO Complessa Reumatologia, Policlinico Umberto I Università Sapienza di Roma, Roma, Italy, 18Reumatologia ASST Ospedale Niguarda, Milano, Italy, 19Rheumatology, Rheumatology, IRCCS Policlinico San Matteo Foundation and University of Pavia, Pavia, Italy, 20U.O. Ginecologia e Ostetricia ASST Spedali Civili, Brescia, Italy

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Reproductive Issues in Rheumatic Disorders Poster  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Neonatal Lupus (NL) is a rare syndrome caused by placental transfer of maternal anti-Ro/SSA and anti-La/SSB autoantibodies to the fetus. Cardiac manifestations may comprise autoimmune congenital heart block (CHB) and dilated cardiomyopathy (DCM). The prevalence of CHB has been estimated as 1-2% in anti-Ro/SSA-positive women while the recurrence rate is 16-19%. The rarity of these conditions requires the establishment of collaborative registries in order to improve our knowledge on the management of CHB. Here we report the preliminary data of the Italian Registry of the autoimmune congenital heart block, which was created in the frame of the Italian Society for Rheumatology in 2016.

**Methods:**

The aim was to collect retrospective and prospective pregnancies complicated with CHB in patients with anti-Ro/SSA and/or anti-La/SSB antibodies. The study was approved by the Ethic Committee of the Promoting Centre in July 2016 and it has been approved by other eight Italian Institutions. Data regarding demography, maternal treatment before and after CHB detection, neonatal outcome, maternal and neonatal follow-up were collected through an online electronic datasheet prepared in a Research Electronic Data Capture (REDCap) platform. Two-tailed Student’s t-test for continuous variables, Fisher’s exact test or Yates’s Chi squared test for categorical variables were applied. The statistical software Stata/SE14.2 was used.

**Results:**

Seventy-five pregnancies complicated with the detection of CHB were collected in 73 women. CHB was detected in utero in 68 cases (90.6%), 5(6.7%) neonatal cases, 2(2.7%) unknown. Demographic description of the cohort, degree of CHB and treatment are reported in the table. The death of the child was observed in 17 (23.2%) cases: 7 fetal-deaths, 5 termination of pregnancy and 5 postnatal death. Maternal and fetal risk factors for fetal mortality were analyzed for possible associations. At univariate analysis, factors associated with death were hydrops (p=0.065) and pericardial effusion (p=0.025).

**Conclusion:**

The Lu.Ne registry is an ongoing project aiming at collecting all cases of CHB referred to Italian Rheumatology Centres. Our preliminary data confirmed that hydrops and pericardial effusion are risk factors for fetal death. Conversely, we found that the majority of the mothers (58%) whose pregnancy was affected by CHB had a formal diagnosis of systemic autoimmune disease. This is in contrast with other registries showing that usually CHB was incidentally detected in healthy women. Probably such discrepancy
is related to the recruiting Centres all belonging to Rheumatology Society. The collection of CHB cases from Gynecological and Pediatric Cardiology Centres, planned in the next months, will complete our analysis

Disclosure: M. Fredi, None; L. Andreoli, None; T. Bertero, None; A. Bortoluzzi, None; S. Breda, None; V. Cappa, None; F. Ceccarelli, None; R. Cimaz, None; S. De Vita, None; E. Di Poi, None; F. Franceschini, None; M. Gerosa, None; M. Govoni, None; A. Hoxha, None; A. Lojacono, None; L. Marozio, None; A. Mathieu, None; A. Minniti, None; M. Muscarà, None; M. Padovan, None; M. Piga, None; R. Priori, None; V. Ramoni, None; A. Ruffatti, None; M. Tonello, None; S. Zatti, None; S. Calza, None; A. Brucato, None; A. Tincani, None.


Abstract Number: 1301

**Congenital Heart Defects in Children Born to Mothers with Rheumatic Disease and Anti-Ro and/or Anti-La Antibodies**

**Julie Couture**¹, Linda T Hiraki², Franklin Silverio¹, Deepika Sharma¹ and Earl Silverman³, ¹Pediatrics, The Hospital for Sick Children, Toronto, ON, Canada, ²Child Health Evaluative Sciences, The Hospital for Sick Children, Toronto, ON, Canada, ³Division of Rheumatology, The Hospital for Sick Children, Toronto, ON, Canada

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017  
Session Title: Reproductive Issues in Rheumatic Disorders Poster  
Session Type: ACR Poster Session B  
Session Time: 9:00AM-11:00AM

**Background/Purpose:** Transplacental passage of maternal anti-Ro IgG is thought to be critical in initiating inflammation leading to congenital heart block in neonatal lupus erythematosus (NLE). Congenital heart block is the most frequent manifestation of cardiac NLE. To date, the majority of studies have focused on babies born to mothers with systemic lupus erythematosus (SLE) or congenital heart block babies born to anti-Ro and/or anti-La mothers. In this large cohort study, we aimed to determine the proportion of babies born to anti-Ro and/or anti-La positive mothers with SLE, Sjögren syndrome or rheumatoid arthritis (RA), with congenital heart defects (CHD).
Methods: The Hospital for Sick Children offers serial fetal echocardiography for women with anti-Ro and/or anti-La antibodies. Babies born to anti-Ro and/or anti-La mothers are referred to the NLE clinic for follow-up. We performed an observational study of our large, single-centre NLE clinic cohort, on whom prospective data has been collected since 1984. We included all infants, seen in our clinic, born to mothers positive for anti-Ro and/or anti-La antibodies, with SLE, Sjögren syndrome or RA. Among them we identified infants with cardiac NLE disease diagnosed either prenatally or postnatally. We identified those babies with CHD, including septal defects, patent ductus arteriosus, and other rare structural heart defects. We compared the proportion of babies with CHD, with and without NLE congenital heart block using Fisher’s exact test.

Results: A total of 451 children were included. Seven (1.6%) children had CHD. The most frequently observed CHD were ventricular septal defects and patent ductus arteriosus. Among cases with congenital heart block (N=28), the frequency of CHD was further increased, with 3 (10.7%) children diagnosed with at least one CHD. This was significantly higher when compared to the rate of CHD among babies without congenital heart block (0.9%, p < 0.006).

Conclusion: In our NLE clinic cohort of children born to mothers with anti-Ro and/or anti-La antibodies and SLE, Sjögren syndrome or RA, we observed higher rates of CHD among those with congenital heart block when compared to our NLE clinic babies without congenital heart block. This suggests a common pathway in the development of congenital heart block and CHD. The precise role of maternal antibodies in the development of CHD requires further investigation and replication.

Disclosure: J. Couture, None; L. T. Hiraki, None; F. Silverio, None; D. Sharma, None; E. Silverman, None.


Abstract Number: 1302

Luteinized Unruptured Follicle Syndrome in Young Female with Juvenile Idiopathic Arthritis

Renato B. B. Tomioka1, Gabriela R.V. Ferreira2, Nadia E Aikawa3, Gustavo A.R. Maciel1, Paulo C. Serafini1, Edmund Baracat1, Lucia M A Campos4, Cláudia Goldenstein-Schainberg3, Rosa M R Pereira3, Eloisa Bonfa5 and Clovis A Silva2, 1Discipline of Gynecology, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, 2Pediatric Rheumatology Unit, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, 3Rheumatology Division, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, 4Pediatric Rheumatology Unit, Instituto da Criança, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo, São Paulo, Brazil, 5Rheumatology Divison, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Reproductive Issues in Rheumatic Disorders Poster
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Juvenile idiopathic arthritis (JIA) may be active during reproductive age, therefore ovarian function and future fertility are relevant issues for its female population. Nonsteroidal antiinflammatory drugs (NSAIDs) may impair fertility inducing luteinized unruptured follicle syndrome (LUF) in adults rheumatoid arthritis patients however there is no study evaluating this condition in female adolescent and young adults with JIA. Thus, our objective was to assess LUF in three groups: JIA patients with NSAIDs vs. JIA without NSAIDs vs. healthy controls.

Methods: Twenty-three adolescent and young adult female JIA patients (ILAR criteria) and 11 healthy females were studied by pelvic ultrasound repeated 2 to 3 times monitoring for follicular development and ovulation in one menstrual cycle. Exclusion criteria included: presence of current gestation or lactation; hypothalamic-pituitary-ovarian axis dysfunction; end-stage renal disease; contraindication or refusal to suspend the use of hormonal contraceptives for at least 6 months; thyroid diseases; history of surgery or pelvic irradiation or neoplasia; use of gonadotrophin releasing hormone analogs; obesity in virgin patients due to the difficulty of performing the abdominal ultrasonography; polycystic ovarian syndrome; amenorrhea; and presence of another systemic autoimmune disease. JIA patients and healthy controls were systematically assessed for menstrual flow duration and cycle length. LUF syndrome
was defined by pelvic ultrasound with a dominant ovarian follicle without signs of follicular rupture, with elevation of progesterone in blood sample in the luteal phase of the menstrual cycle and LH detected in the urine.

**Results:** Comparison between JIA patients with (n=8) vs. JIA without NSAIDs (n=15) and healthy controls (n=11) revealed that the frequency of LUF syndrome was significantly higher in the former group [2(25%) vs. 0% vs. 0%, p=0.049]). Of note, the two patients with LUF syndrome had normal menstrual cycles and used naproxen 500 mg bid. Further comparison between JIA patients with and without NSAIDs, and healthy controls showed similar mean in three groups regarding levels of Anti-Müllerian hormone (AMH) [3.4 (0.47-5.0) vs. 3.4 (0.6-13.9) vs. 3.3 (0.49-10.6) ng/mL, p=0.909], estradiol [43 (32.7-160) vs. 47 (25.8-119) vs. 41.5 (18.9-61) pg/mL, p=0.436], FSH [6.3 (5-10) vs. 6.4 (5-12) vs. 6.8 (4-10), p=0.662], LH [8 (6.3-9.6) vs. 7.7 (4.1-28.7) vs. 7.6 (4.4-14.4) IU/L, p=0.686], antral follicle count [15.5 (8-19) vs. 19 (6-40) vs. 22 (7-33), p=0.240] and ovarian volume mL [6.1 (3.2-7.8) vs. 4.5 (2-15.8) vs. 4.6 (2.8-7.4), p=0.363]. No differences were evidenced in three groups regarding white race, body mass index, duration and length of menstrual cycles (p>0.05). The frequencies of prednisone, methotrexate and biological agents were similar in two JIA groups (p>0.05).

**Conclusion:** The present study identified an increased incidence of LUF syndrome in JIA patients using NSAIDs. We further demonstrated that reduced ovarian reserve does not seem to contribute to this condition.

**Disclosure:** R. B. B. Tomioka, None; G. R. V. Ferreira, None; N. E. Aikawa, Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP #2015/03756-4 to NEA), 2; G. A. R. Maciel, None; P. C. Serafini, None; E. Baracat, None; L. M. A. Campos, None; C. Goldenstein-Schainberg, None; R. M. R. Pereira, None; E. Bonfa, None, 2; C. A. Silva, Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP #2014/14806-0 and 2015/03756-4 to CAS), Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq 303422/2015-7 - 1A to CAS), 2.


**Abstract Number:** 1303

**Polycystic Ovarian Syndrome in Rheumatic Disease**

Cuoghi Edens¹ and Maria Antonelli², ¹Division of Pediatric Infectious Diseases and Rheumatology and Division of Rheumatology, Rainbow Babies and Children's Hospital and University Hospitals Cleveland Medical Center, Cleveland, OH, ²Department of Medicine/Division of Rheumatology, Case Western Reserve University School of Medicine, MetroHealth Medical Center, Cleveland, OH

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Reproductive Issues in Rheumatic Disorders Poster

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Polycystic ovarian syndrome (PCOS) is a common entity in the general population associated with polycystic ovaries, oligomenorrhea, difficulty conceiving, hormone abnormalities, metabolic comorbidities, and hirsutism. Prevalence ranges from 3-10%. Fertility issues, menstrual cycle irregularities, and metabolic conditions are common in those with rheumatic disease as well. The prevalence of PCOS in those with rheumatic disease is unknown.

**Methods:** Utilizing a secure cloud-based platform, Explorys, we conducted a retrospective cross-sectional study of females 10-50 years of age. The diagnosis of PCOS was determined if the subject had polycystic ovaries and 1/10 known findings associated with PCOS (Table 1). Our inclusion criteria was limited by the existence of Systematized Nomenclature for Medicine-Clinical Term (SNOMED-CT), as the Explorys database is ontology based. A SNOMED-CT does not exist for PCOS. Diseases of interest included: systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), dermatomyositis (DM), psoriasis (PsO), ankylosing spondylitis (AS), psoriatic arthritis (PsA), and juvenile idiopathic arthritis (JIA). Disease-specific searches excluded all other rheumatic diseases of interest in this study and endocrinopathies. Table 2 summarizes the findings of each patient population. Chi-squared testing was performed to compare prevalence of PCOS between rheumatic diseases.
Results: In our analysis, there was significant prevalence of PCOS between SLE and RA, PsO, PsA, and AS as well as RA and PsO and PsA with p-values <0.01. There was also significance between JIA and PsA, PsO, and AS. In our Explorys population, PCOS prevalence was found to be low, however recognized underreporting of PCOS and known lack of medical care for this diagnosis may account for this. In our data set, our disease specific prevalence was similar to reported values, validating our cohort.

Conclusion: PCOS prevalence in rheumatic diseases nears that of the general population. There is a significantly increased prevalence in those with PsA, PsO, and AS. It should be considered as a diagnosis in those who have oligomenorrhea, infertility, or signs of hyperandrogenization.

<table>
<thead>
<tr>
<th></th>
<th>Explorys</th>
<th>SLE</th>
<th>RA</th>
<th>DM</th>
<th>PsO</th>
<th>PsA</th>
<th>AS</th>
<th>JIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCOS</td>
<td>126330</td>
<td>1120</td>
<td>1540</td>
<td>50</td>
<td>1340</td>
<td>290</td>
<td>150</td>
<td>160</td>
</tr>
<tr>
<td>Total</td>
<td>14209420</td>
<td>34300</td>
<td>39480</td>
<td>1290</td>
<td>30740</td>
<td>6020</td>
<td>3150</td>
<td>4570</td>
</tr>
<tr>
<td>Prevalence</td>
<td>0.009</td>
<td>0.033</td>
<td>0.039</td>
<td>0.039</td>
<td>0.044</td>
<td>0.048</td>
<td>0.048</td>
<td>0.035</td>
</tr>
</tbody>
</table>

Disclosure: C. Edens, None; M. Antonelli, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/polycystic-ovarian-syndrome-in-rheumatic-disease

Abstract Number: 1304

Lack of Uptake of Prophylactic Human Papilloma Virus (HPV) Vaccination Among Women with SLE in Saginaw Valley, a High Risk Population

J. Patricia Dhar1,2, Lynnette Essenmacher3, Renee Dhar4, Neli Ragina5 and Robert Sokol6, 1Internal Medicine, Wayne State University School of Medicine, Detroit, MI, 2Internal Medicine, Central Michigan University College of Medicine, Saginaw, MI, 3Wayne State University School of Medicine, Detroit, MI, 4CMED medical student, Central Michigan University College of Medicine, Mt. Pleasant, MI, 5Foundational Sciences, Central Michigan University College of Medicine, Mount Pleasant, MI, 6Department of Obstetrics & Gynecology, Wayne State University School of Medicine, Detroit, MI

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Reproductive Issues in Rheumatic Disorders Poster
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Women with SLE are at increased risk for cervical neoplasia likely due to infection with high risk (HR) HPV and thus should be considered for HPV vaccination. We previously showed qHPV vaccine to be safe and immunogenic in women
with SLE. We sought to determine frequency of HRHPV infection and uptake of HPV vaccination in our regional female lupus population. The qHPV vaccine was approved for use in 2006 for women ages 9-26 years.

**Methods:** Data were analyzed from our electronic health records (EPIC) for women with ICD 10 or ICD 9 billing codes for SLE seen June 6, 2007 - May 1, 2017 at our regional medical center which services a large urban, suburban & rural population. This study was approved by the Central Michigan University/Covenant Medical Center institutional review board. Statistical analyses consisted of student’s t-test, chi square, and Z test for proportions using SPSS v. 24 software.

**Results:** 1349 women with SLE were seen at our regional medical center, mean age=53 yrs., of which 70.8%=Caucasian, 20.8%=African American, and the rest other race/ethnicity, with 49% having exposure to cigarette smoke. HRHPV testing was performed in only 195 of these women (14.5%, mean age=50 years), of which 33 (16.9%) were positive. Those testing positive for HRHPV were slightly younger (P<0.05) than those testing negative, with no statistical difference in smoking or race between the 2 groups (Table 1).

<table>
<thead>
<tr>
<th></th>
<th>HPV + (n=33)</th>
<th>HPV – (n=162)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean, SD)</td>
<td>45.8 (11.2) y</td>
<td>50.9 (12.8) y</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Race (n, %)</td>
<td></td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>White</td>
<td>22 (66.7%)</td>
<td>117 (72.2%)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>8 (24.2%)</td>
<td>34 (21.0%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>3 (9.1%)</td>
<td>11 (6.8%)</td>
<td></td>
</tr>
<tr>
<td>Smoke Exposure (n, %)</td>
<td></td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Yes</td>
<td>17 (51.5%)</td>
<td>71 (43.8%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>16 (48.5%)</td>
<td>91 (56.2%)</td>
<td></td>
</tr>
</tbody>
</table>

Comparing our proportion testing positive for high risk HPV (0.169) vs. NHANES* (0.088), we calculated a z=3.99 (p<0.001) indicating HPV infection is significantly higher (2X) in our regional female SLE population. Of the 238 women who were eligible to receive an HPV vaccine, only 16.0% (38/238) were tested for HRHPV with 9 being positive, and only 4.6% (11/238) were vaccinated. Of the 11 that were vaccinated, only one woman had testing for HRHPV and this female was positive for HR HPV.

**Conclusion:** HPV infection is 2 fold increased in our regional female lupus population compared to population controls. Despite the fact that HPV related cervical disease and neoplasia are increased in women with SLE, the frequency of testing for HRHPV testing is low (14.5%) and vaccination rate even lower (4.6%) in our region. This highlights the importance of the need for monitoring for HRHPV and including HPV vaccination as part of general health care in this vulnerable population. Promoting awareness of this problem with primary care doctors and the lupus community would improve uptake of prophylactic HPV vaccination and be beneficial to gynecologic health in women with SLE.


**Disclosure:** J. P. Dhar, Merck, Inc., 2; L. Essenmacher, None; R. Dhar, None; N. Ragina, None; R. Sokol, None.


**Abstract Number:** 1305

**Use of Estrogen-Containing Contraceptives Among SLE Women with and without Contraindications to Estrogen**

Arielle Mendel1, Sasha Bernatsky2, Yvan St.Pierre3, Christian Pineau4 and Evelyne Vinet5, 1Rheumatology, McGill University, Montreal, QC, Canada, 2Divisions of Rheumatology and Clinical Epidemiology, Research Institute of the McGill University Health Centre, Montreal, QC, Canada, 3McGill University Health Centre, Montreal, QC, Canada, 4Rheumatology, McGill University Health Center, Montreal, QC, Canada, 5Divisions of Rheumatology and Clinical Epidemiology, McGill University Health Centre, Montreal, QC, Canada

**First publication:** September 18, 2017
Background/Purpose: Estrogen-containing contraceptives may be contraindicated in specific medical conditions due to an increased risk of cardiovascular and thromboembolic events. Women with SLE are at increased risk of having medical contraindications to estrogen use. We assessed the prevalence of estrogen-containing contraceptives in reproductive-aged SLE women with and without possible contraindications.

Methods: Premenopausal women aged 18-45 enrolled in the Systemic Lupus International Collaborating Clinics (SLICC) Registry (2000-2017) were enrolled within 15 months of SLE onset and evaluated yearly to update drug use, including estrogen-containing contraceptives. We assessed the presence of World Health Organization (WHO) category 3 (theoretical or proven risks usually outweighing advantages of use) or category 4 (unacceptable health risk if used) contraindications to estrogen-containing contraceptives. Examples included smoking and age ≥35, hypertension, migraine with aura, positive antiphospholipid antibodies (aPL), and stroke. High disease activity defined as a SLEDAI score >12 or use of >0.5 mg/kg/d of prednisone were also evaluated as relative contraindications since safety of estrogen in this population has not been established.

Results: We identified 1224 SLE women of reproductive age, who contributed 7756 visits. We observed ≥1 possible contraindications to estrogen in 648 (53%) subjects at enrolment and at 4376 (56%) visits over the study period. At baseline, 124 (10%) women were using estrogen-containing contraceptives and among these, 33 (27%) had ≥1 possible contraindication. Across all study visits, estrogen-containing contraceptives were used by 6% (95% CI 5-7) of women with ≥1 possible contraindication vs 12% (95% CI 11-13) of women without any contraindication. Among women using estrogen-containing contraceptives, the most frequently observed WHO category-3 or -4 contraindications were hypertension (44%), positive aPL (32%), and migraine with aura (27%).

Conclusion: In a large international prospective SLE cohort, more than half of SLE women of reproductive age had ≥1 possible contraindication to estrogen-containing contraceptives. Overall use of estrogen-containing contraceptives was low in SLE women (10%) compared to women of reproductive age in the general population (usually above 35%). Estrogen-containing contraceptives were used in 6% of women with possible contraindications. Further work is needed to explore prescribers’ characteristics and prescription patterns over time, and to determine long-term outcomes associated with this exposure.
Table 1. Baseline characteristics of reproductive-aged SLE women, overall and among those using estrogen-containing contraceptives with and without 1 or more possible contraindications to estrogen

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total population (n=1224)</th>
<th>Estrogen-containing contraceptive users (n=124)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Without contraindication (n=91)</td>
</tr>
<tr>
<td><strong>Age, mean (SD)</strong></td>
<td>29.8 (7.6)</td>
<td>26.6 (5.9)</td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Years of education prior to college or university, mean (SD)</td>
<td>11.7 (1.8)</td>
<td>11.9 (1.8)</td>
</tr>
<tr>
<td></td>
<td>3.6 (2.0)</td>
<td>4.0 (2.5)</td>
</tr>
<tr>
<td></td>
<td>760 (62)</td>
<td>65 (71)</td>
</tr>
<tr>
<td>Any post-secondary education, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ethnicity, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>209 (17)</td>
<td>8 (8)</td>
</tr>
<tr>
<td>Native North American</td>
<td>5 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Black</td>
<td>22 (18)</td>
<td>14 (11)</td>
</tr>
<tr>
<td>Caucasian</td>
<td>486 (40)</td>
<td>84 (68)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>212 (17)</td>
<td>8 (7)</td>
</tr>
<tr>
<td>Indian subcontinent</td>
<td>39 (3)</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Other</td>
<td>48 (4)</td>
<td>5 (4)</td>
</tr>
<tr>
<td><strong>Country of origin, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canada</td>
<td>265 (22)</td>
<td>24 (26)</td>
</tr>
<tr>
<td>United States</td>
<td>349 (29)</td>
<td>35 (39)</td>
</tr>
<tr>
<td>Mexico</td>
<td>170 (14)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>241 (20)</td>
<td>22 (24)</td>
</tr>
<tr>
<td>Iceland</td>
<td>13 (1)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Spain</td>
<td>19 (2)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Sweden</td>
<td>24 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Switzerland</td>
<td>2 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td></td>
<td>Denmark</td>
<td>Turkey</td>
</tr>
<tr>
<td>---------------</td>
<td>---------</td>
<td>--------</td>
</tr>
<tr>
<td>Disease duration, years, mean (SD)</td>
<td>0.46 (0.4)</td>
<td>0.41 (0.3)</td>
</tr>
<tr>
<td>BMI, kg/m², mean (SD)</td>
<td>24.6 (5.7)</td>
<td>24.5 (4.2)</td>
</tr>
</tbody>
</table>
Table 2. Frequency of contraindications to estrogen use across all study visits among SLE women using estrogen-containing contraceptives with 1 or more possible contraindications

<table>
<thead>
<tr>
<th>Contraindications to estrogen-containing contraceptives</th>
<th>SLE women using estrogen-containing contraceptives with 1 or more contraindication (n= 255 visits)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension, n (%)*/**</td>
<td>114 (45)</td>
</tr>
<tr>
<td>Antiphospholipid antibodies, n (%)**</td>
<td>82 (32)</td>
</tr>
<tr>
<td>Migraine with aura, n (%)**</td>
<td>69 (27)</td>
</tr>
<tr>
<td>History of venous thromboembolism, n (%)*/**</td>
<td>24 (9)</td>
</tr>
<tr>
<td>SLEDAI score &gt;12, n (%)‡</td>
<td>21 (8)</td>
</tr>
<tr>
<td>Prednisone use ≥0.5 mg/kg/d, n (%)‡</td>
<td>19 (7)</td>
</tr>
<tr>
<td>Ischemic stroke, n (%)**</td>
<td>14 (6)</td>
</tr>
<tr>
<td>Smoker aged ≥35, n (%)*/**</td>
<td>10 (4)</td>
</tr>
<tr>
<td>Valvular heart disease with pulmonary hypertension, n (%)**</td>
<td>9 (4)</td>
</tr>
<tr>
<td>Ischemic heart disease, n (%)**</td>
<td>4 (2)</td>
</tr>
<tr>
<td>Diabetes ≥ 20 years, n (%)*/**</td>
<td>3 (1)</td>
</tr>
<tr>
<td>History of breast cancer, n (%)**</td>
<td>1 (0)</td>
</tr>
<tr>
<td>Peripheral vascular disease, n (%)**</td>
<td>1 (0)</td>
</tr>
</tbody>
</table>

*World Health Organization (WHO) Grade 3: theoretical or proven risks usually outweigh the advantages [1]

** WHO Grade 4: unacceptable health risk, method not to be used [1]

‡ Safety in this population has not been established


Disclosure: A. Mendel, None; S. Bernatsky, None; Y. St.Pierre, None; C. Pineau, None; E. Vinet, None.


Abstract Number: 1306
Predictors of Contraceptive Use Among Reproductive-Age Women with Rheumatic Diseases

Mehret Birru Talabi¹ and Sonya Borrero², ¹Rheumatology and Clinical Immunology, University of Pittsburgh School of Medicine, Pittsburgh, PA, ²Internal Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Reproductive Issues in Rheumatic Disorders Poster
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Contraception helps reproductive-age women with rheumatic diseases to avoid or plan pregnancies so that disease quiescence on safe medications may first be achieved. However, little is known about contraceptive usage among these women. This study examines the prevalence and predictors of prescription contraception among women receiving rheumatologic care from a large, multi-site health care system in Pittsburgh, Pennsylvania.

Methods: We examined administrative data for women aged 18-50 years with ≥ 1 of 18 rheumatic diagnoses based on ICD-9 codes, and ≥ 2 visits to a rheumatology outpatient clinic between years 2013 and 2014. Prescription contraceptive methods were identified and categorized by highest level of efficacy. Highly-effective contraceptive methods included female sterilization, intrauterine devices, and subdermal implants; records of these procedures were abstracted from years 2003-2014. Moderately-effective methods included pills, rings, patches, and injections. Patients’ medications were categorized by FDA pregnancy risk classes (Class A/B/C medications: lower fetal risk, Class D/X medications: higher fetal risk). Logistic regression was used to evaluate associations of 1) any prescription contraception or 2) use of highest efficacy contraception, adjusting for frequency of visits to health care providers, medications by FDA pregnancy risk class, and demographic variables (age, race, marital status). Women with prior record of hysterectomies (n=97) were excluded from analyses.

Results: In our sample of 2631 women, most were married (52.6%) and White (82.2%), with mean age of 39.6 (S.D. 7.7). Antiphospholipid antibody syndrome (35.5%), rheumatoid arthritis (23.3%), systemic lupus erythematosus (19.4%), and Sjogren’s Syndrome (18.8%) were the most common diagnoses. Women had a median of 3 rheumatology visits, but most had no documented visits with primary care providers (PCP) (59.8%) or gynecologists (68.3%) over the 2-year study timeframe. Contraception was prescribed to 32.6% of women, and 8.8% used highly-effective methods. Class D or X medications were prescribed to 71.2% of women. Younger age (aOR:0.9; 95%CI:0.92-0.96), ≥1 visits with a PCP (aOR:1.8; 95%CI:1.6-2.2) or gynecologist (aOR:3.6; 95%CI:3.0-4.3), or ≥ 2 rheumatology visits (aOR:1.2; 95%CI:1.0-1.4), were associated with prescription contraception. Fetotoxic versus safer medication prescription was not associated with overall prescription contraception, but was associated with prescription of highly-effective contraception (aOR:2.1; 95%CI:1.4-3.0), as was younger age (aOR:0.97; 95%CI:0.95-0.99), and at least 1 visit with a PCP (aOR:1.6; 95%CI:1.2-2.1) or gynecologist (aOR:3.6; 95%CI:2.7-4.8).

Conclusion: Overall prescription contraceptive prevalence was low in this sample. Care from PCPs or gynecologists enhanced the prescription of contraception-- particularly with highly-effective methods. Increasing referrals to these women’s health providers is one approach to improving contraceptive care for reproductive-age women with rheumatic diseases.

Disclosure: M. Birru Talabi, None; S. Borrero, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/predictors-of-contraceptive-use-among-reproductive-age-women-with-rheumatic-diseases

Abstract Number: 1307

Contraceptive Use in Patients with Rheumatologic Disease on Teratogenic Medications: Rate of Use and Related Factors

Shanley O'Brien¹ and Megan Krause², ¹Department of Internal Medicine, Division of Allergy, Clinical Immunology, & Rheumatology, Kansas University Medical Center, Kansas City, KS, ²Division of Allergy, Clinical Immunology, and Rheumatology, Kansas University Medical Center, Kansas City, KS

Disclosures: This abstract contains no conflict of interest
Background/Purpose: Rheumatologic diseases can affect females of reproductive age. Medications utilized for treatment of these diseases can be associated with harmful consequences in pregnancy. Unfortunately, not all women receive contraception despite this risk.

Methods: A retrospective chart review conducted at a single tertiary care center identified the most recent 500 women between ages 18-50 seen in outpatient rheumatology clinic with ICD codes for rheumatoid arthritis, systemic lupus erythematosus, vasculitis, and systemic sclerosis who had been prescribed methotrexate, leflunomide, mycophenolate mofetil, or cyclophosphamide between 06/01/2008-06/01/2016. Individuals were allowed to be included in multiple categories if they had received multiple diagnoses and different immunosuppressants over the time of follow-up. Additional data collected included: age at office visit, self-reported race, primary language, marital status, and type of contraception. Contraception was identified by searching medication lists, past medical/surgical history, and procedure codes. Fisher’s exact test and chi-square were utilized.

Results: Of the 500 women, 62 (12%) were between ages 18-29, 127 (25%) were 30-39, and 311 (62%) were 40-50. Almost half were married (243, 49%). The vast majority were English speaking (478, 96%). Individuals who self reported as white represented 301 (60%), black 127 (25%), other 46 (9%), Asian 15 (3%), Native American 5 (1%), two races 4 (1%), Pacific Islander 1 (0.2%), and unknown 1 (0.2%). Rheumatoid arthritis was the most common diagnosis (338, 68%), followed by systemic lupus erythematosus (188, 38%), systemic sclerosis (69, 14%), and vasculitis (33, 7%). Methotrexate was the most common medication (342, 68%), followed by mycophenolate mofetil (191, 38%), leflunomide (76, 15%), and cyclophosphamide (25,5%).

In total, 290 women (58%) received some form of contraception. The most common forms of contraception were hysterectomy (104, 21%) and combination hormone therapy (oral contraceptives and vaginal ring) (95, 19%). The following forms of contraception were also used with rates as follows: tubal ligation in 56 (11%), intrauterine devices in 34 (7%), medroxyprogesterone injections in 21 (4%), progesterone implant in 8 (2%), and progesterone only pill in 1 patient (0.2%).

Women who self-reported as white race were more likely to utilize contraception (63%) than non-white patients (50%) (p=0.003). There was no statistically significant difference in the rates of contraception based on age, marital status, disease, or immunosuppressant utilized.

Conclusion: This study identifies that contraception is not being utilized in all patients when it would be recommended. Self-reported race/ethnicity was one factor associated with different rates of contraception. Understanding the magnitude of patients not receiving contraception and factors associated with this will better inform strategies to help improve rates of contraception in those exposed to teratogens.

Disclosure: S. O'Brien, None; M. Krause, None.


Abstract Number: 1308

Answering Reproductive Health Questions That Your Patients Want to Know: Impediments to Family Building and Risks of Contraception

Malithi Jayasundara1, Amanda M. Eudy2, Tayseer Haroun3, W. Benjamin Nowell4, Jeffrey R. Curtis5, Rachelle Crow-Hercher6, Charlotte Whitney White6, Seth D. Ginsberg7 and Megan E. B. Clowse8.1Rheumatology, Duke University, Durham, NC, 2Duke University, Durham, NC, 3Department of Medicine/Division of Rheumatology, Duke University Medical Center, Durham, NC, 4Global Healthy Living Foundation, Upper Nyack, NY, 5University of Alabama at Birmingham, Birmingham, AL, 6Arthritis Power, Upper Nyack, NY, 7Global Healthy Living Foundation, CreakyJoints, Upper Nyack, NY, 8Duke University Medical Center, Durham, NC

First publication: September 18, 2017
Background/Purpose:

Women with arthritis wonder whether they will be able to have the children they desire. They also worry that oral contraceptives may worsen their arthritis. Working with the Patient Governors of an inflammatory arthritis network, we developed a reproductive survey to answer these questions.

Methods:

The survey was developed in a collaboration between the research and patient teams. The survey was distributed via email to the network’s participant list and consent was implied the women clicked on the link to join the anonymous survey. This study is limited by selection and recall bias.

Results:

From March to June 2017 14,711 invitations were sent with 250 female responses. Self-reported diagnoses of RA (80%) and SpA (24%) were hampered by many women reporting multiple diagnoses. The majority of respondents were white (83%), non-Hispanic (82%), with a college degree (69%).

Of all women, 59% had fewer children than they desired due to arthritis and 36% had the full number they wanted. Women who had fewer children had an earlier age of diagnosis compared to those did not (24.5yrs vs 31.6yrs, p<0.0001). The most common fears limiting family size were 1.) being unable to care for a child (85%), 2.) arthritis medications would harm child (61%), and 3.) the child would get arthritis (52%).

Of the women who tried to conceive after their arthritis diagnosis, 44% reported infertility (23% with physician-diagnosed infertility and 42% taking >1yr to conceive). Unexplained infertility (39%) was the most common cause, followed by ovulation dysfunction (37%), endometriosis (26%), and uterine/tubal issues (26%). Women with physician-diagnosed infertility were younger at arthritis diagnosis than fertile women (24.6yrs vs 31.4yrs, p=0.007). Half of the women with infertility used multiple forms of assisted reproductive technology, including oral (27) and injectable (16) medications and IVF (7).

Of the women not pregnant, trying to become pregnant, or in a same-sex relationship, 35% reported currently using highly effective, 32% effective, and 33% ineffective contraception; 28% of women taking methotrexate were using ineffective contraception.

Of the 135 of women who report ever using OCP, 70% report no impact of the pills on their arthritis; 9% had improved arthritis and 10% had worsened arthritis. At the time of the survey, 20% of women were currently taking OCPs: more prior OCP users noted worsening of arthritis with the drugs than current OCP users (16% prior vs 2% current users, p=0.02)

Half of women noticed an effect of their menstrual cycle on their arthritis disease activity with the vast majority reporting worsening just prior to (60%) or during menstruation (36%). Multiple women reported that taking OCPs continuously, and thus avoiding their monthly menses, seemed to decrease their pre-menstrual flares.

Conclusion:

More than half of the women report having fewer children than they had ideally wanted, largely due to infertility and concerns about their medications and difficulty mothering. The frequency of ineffective contraceptive use among women on methotrexate remains unacceptably high. Fear of OCPs appears to be unfounded and continuous OCP use may provide relief for women with menses-related arthritis flares.

Disclosure: M. Jayasundara, None; A. M. Eudy, None; T. Haroun, None; W. B. Nowell, Pfizer, BMS, Lilly, Merck, JandJ, GSK, Mallincrodt, 1; J. R. Curtis, Amgen, Pfizer, Crescendo Bio, Corrona, 2,AbbVie, Roche/Genentech, BMS, UCB, Myriad, Amgen, Janssen, Pfizer, Corrona, 5; R. Crow-Hercher, None; C. Whitney White, None; S. D. Ginsberg, None; M. E. B. Clowse, Pfizer, Janssen, 5,UCB Pharma, 5.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/answering-reproductive-health-questions-that-your-patients-want-to-know-impediments-to-family-building-and-risks-of-contraception
Characteristics and Outcomes of Prospectively Reported Pregnancies Exposed to Certolizumab Pegol from a Safety Database

Megan E. B. Clowse1, Angela E. Scheuerle2, Christina D Chambers3, Anita Afzali4, Alexa Kimball5, John J. Cush6, Maureen Cooney7, Laura Shaughnessy7, Mark Vanderkelen8 and Frauke Förger9, 1Division of Rheumatology, Department of Medicine, Duke University Medical Center, Durham, NC, 2UT Southwestern Medical Center, Dallas, TX, 3UC San Diego School of Medicine, San Diego, CA, 4University of Washington Harborview Medical Center, Seattle, WA, 5Beth Israel Deaconess Medical Center, Boston, MA, 6Baylor Scott & White Research Institute, Dallas, TX, 7UCB Pharma, Raleigh, NC, 8UCB Pharma, Braine-l’Alleud, Belgium, 9Inselspital, University of Bern, Bern, Switzerland

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Reproductive Issues in Rheumatic Disorders Poster
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Anti-tumor necrosis factor medications (anti-TNFs) are effective in controlling chronic inflammatory diseases, but information about their use and safety in pregnancy is limited. Consequently, anti-TNFs are often discontinued early in gestation. Certolizumab pegol (CZP), a PEGylated, Fc-free anti-TNF approved for treatment of rheumatic diseases and/or Crohn’s disease, has no active placental transfer. This project provides information on pregnancy outcomes in women receiving CZP, especially those with early pregnancy exposure.

Methods: Prospective and retrospective data on maternal CZP exposure, including timing and duration, outcomes, comorbidities, and major malformations were extracted from the UCB Pharma safety database through March 6, 2017. This analysis was limited to prospective reports to avoid bias associated with retrospective submissions. Numbers of live births, miscarriages, elective abortions, stillbirths, and major congenital malformations were ascertained.

Results: From a total of 1541 maternal CZP-exposed pregnancies, 1137 were reported prospectively, of which 528 pregnancies (including 10 twins) had 538 known outcomes: 459 live births (85%), 47 miscarriages (9%), 27 elective abortions (5%), and 5 stillbirths (1%) (Figure). Of the 459 live births, 8 (1.7%) cases of major congenital malformations were reported (vesicoureteral reflux, club foot, congenital heart disease, cerebral ventricle dilatation, polydactyly, anal fistula, accessory auricle, and hydronephrosis). Of the 528 prospective pregnancies with known outcomes, 436 (83%) were exposed during the 1st trimester, when most organogenesis occurs; 202 out of the 436 were exposed during the entire pregnancy.

Conclusion: This analysis represents the largest cohort of pregnant women exposed to an anti-TNF for management of chronic inflammatory diseases. Although these data should be interpreted with caution, there is no observed increased risk of major malformations or other adverse pregnancy outcomes with CZP use compared to baseline, as reported for the US general population by the Centers for Disease Control and Prevention (3%). The data are reassuring for women of childbearing age considering treatment with CZP.
Maternal and Fetal Outcomes in a Cohort of Patients Exposed to Tumor Necrosis Factor Inhibitors throughout Pregnancy

Geneviève Genest¹, Karen Spitzer² and Carl Laskin³, ¹Allergy-Immunology, McGill University and McGill University Health Center, Montreal, QC, Canada, ²Trio Fertility, Toronto, ON, Canada, ³Medicine, Rheumatology and Obstetrics and Gynecology, University of Toronto and LifeQuest Centre for Reproductive Medicine, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Reproductive Issues in Rheumatic Disorders Poster
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Tumor Necrosis Factor inhibitors (TNFi) are increasingly used during pregnancy but are frequently withheld in the second or third trimester to minimize transplacental transfer to the fetus. It is our practice to recommend uninterrupted TNFi treatment throughout pregnancy to avoid the risk of peri- or postpartum disease flare. We evaluated the maternal and fetal outcomes of women who continued their TNFi treatment throughout pregnancy compared to women who interrupted TNFi during pregnancy.

Methods:

Women seen in our clinic from 11/2010-6/2017 with RA, PsA, JIA or AS having been exposed to TNFi during pregnancy were prospectively followed throughout pregnancy and during the postpartum period. Maternal age, medical comorbidities and medication was recorded at the initial visit and disease activity was assessed throughout the follow up period. Adverse pregnancy outcomes were...
recorded as were the following fetal outcomes: birthweight, neonatal hospitalization and congenital anomalies. Pregnancies were divided into 2 groups: Group 1 included patients who stopped their TNFi at any time during pregnancy and Group 2 included patients who continued their TNFi throughout pregnancy.

Results:

There were 36 women with 42 pregnancies in this cohort. Mean maternal age was 31.9 in Group 1 and 33.9 in Group 2. In Group 1, 11 women had 13 pregnancies and 11 live births. There were 2 first trimester losses (2/13, 15%) one in the setting of active RA. Four pregnancies (4/13, 30.7%) were complicated by a disease flare; one patient with RA miscarried; two patients, one with RA and the other with PsA resumed TNFi therapy. Another patient with AS and IBD failed to achieve disease control after resuming her TNFi and required switching to another TNFi peripartum. Six other patients (6/13, 46%) flared postpartum (4 patients with RA, 1 AS, 1 JIA). In total, 10/13 (77%) flared during or after pregnancy.

In Group 2, 25 women had 29 pregnancies and 31 live births. Three (3/28, 10.7%) adverse pregnancy outcomes were reported in 2 patients. One patient had a twin pregnancy and delivered at 33 weeks after developing PPROM at 32 weeks in the setting of a JIA flare. Her second pregnancy was complicated by active JIA before and throughout gestation and HELLP syndrome necessitating a C-section at 39 weeks. Another patient with comorbid APS underwent a C-section at 36 weeks for suspicion of HELLP syndrome. Three (3/29, 10.3%) postpartum flares occurred: one patient with IBD and AS developed anti-infliximab antibodies and responded to another TNFi; one patient with RA required treatment with a different class of biologics; and another was treated with a corticosteroid injection and hydroxychloroquine. There were no other adverse pregnancy outcomes. All offspring were born healthy, with no congenital abnormalities, and all were appropriate size for gestational age. No neonatal infections were reported. Therefore, a total of 4/29 (13.7%) pregnancies were associated with a flare during or after pregnancy.

Conclusion:

Women who discontinued their TNFi during pregnancy, had a higher risk of peri- or post-partum flare compared to those that continued their TNFi throughout pregnancy. TNFi were not felt to be responsible for gestational complications in group 2.

Disclosure: G. Genest, None; K. Spitzer, None; C. Laskin, Abbott Laboratories, 5.


Abstract Number: 1311

Pregnancy Outcome in Chinese Women with Rheumatic Disease Treated By Leflunomide (LEF)

Yan Zhao1, lingxun shen2, zongwen shuai3, Hengli Zhao4, Weinan Lai5, Xiaoling Lai6, Shaoying Zhang7, Xuequn Wang8, Shaoxian Hu9, Wenli Chen10, Wei Ji11, Hua Wei12, Qi Zhang13, Lixia Pang14, huaxiang Liu15, Qiang Shu15, Jun-li Zhang16, Yating Zhou17, Qiong Jiang18, Huaxiang Wu19, Jing Xue19, Ganping Bai20, Li Zhang20 and Fei Xiao21. 1Rheumatology, Peking Union Medical College Hospital, Beijing, China, 2Wuhan Union Hospital, wuhan, China, 3The First Affiliated Hospital of Anhui University, Hefei, China, 4Yantai Hospital of Traditional medicine University, Yantai, China, 5Nanfang Hospital, Guangzhou, China, 6Guangxi Hospital of Traditional Chinese Medicine, Nanning, China, 7Yiling Hospital, Yiling, China, 8The First Affiliated Hospital of Xinyang, Xinyang, China, 9Tongji hospital, wuhan, China, 10Wuhan Central Hospital, wuhan, China, 11Jiangsu Province Hospital of TCM, Nanjing, China, 12Subei People's Hospital, Yangzhou, China, 13Dongying central hospital, Dongying, China, 14Dongying Hospital, Dongying, China, 15Qiu hospital of Shandong University, Jinan, China, 16Rheumatology, The Fifth Hospital of Xi'an City, Xi’an, China, 17Xian No5 Hospital, Shandong, China, 18Taizhou Hospital, Taizhou, China, 19The Second Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou, China, 20Chongqing Southwest Hospital, Chongqing, China, 21Gothic Internet Technology Corporation, Shanghai, China

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Reproductive Issues in Rheumatic Disorders Poster
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM
**Background/Purpose:**

LEF is a first line DMARD. Due to the teratogenic effects in offspring of rats in preclinical study, the patients who plan to get pregnant are advised to withdraw the drug before pregnancy and take cholestyramine (CHL) simultaneously.

To evaluate the outcome of pregnancy of Chinese women with rheumatic disease treated by LEF in real world practice.

**Methods:** The patients with rheumatic disease treated by LEF who planned to get pregnant in the near future were included. The patients withdrew the LEF and were prescribed with CHL for drug clearance, 8 g, tid, for 11 days. The patients were followed up regularly. The medication and pregnancy outcome were recorded. The informed consent was obtained for all patients included.

**Results:**

66 patients cared by 43 doctors from 34 hospitals across China were enrolled. The mean age of patients were 31.54±4.63 (23-46) years old, including 39 (59.09%) patients with RA, 21 (31.82%) patients with SLE, 3 (4.55%) patients with ctd, 1 (1.52%) patient with IgAN, 1 (1.52%) patient with takayasu arteritis, and 1 (1.52%) patient with Sjogren syndrome. The mean disease course was 6.72±2.87 (2-19) years. The mean medication time with Lef was 34.20±23.86 (2-94) months. The mean dose was 16.15±4.90 (10-20) mg. The drug combination during peripregnancy included glucocorticoid, CsA, HCQ, FK506.

There were 36 patients who had live birth: 33 patients with singleton and 3 with twins; 31 patients used CHL and 5 did not; 33 planned to get pregnant (using CHL after withdrawal of LEF) and 3 had accidental pregnancy. The mean interval between withdrawal of LEF and being pregnant was 10.40±6.16 (-3-25) months; the mean interval between administration of CHL and being pregnant was 7.20±6.21 (-4-21) months. The children were healthy: mean age of 27.50±36.46 (1-228) months; 31 children of full-term birth, 5 of premature delivery, mean gestational age of 38.17±2.56 (28-40) weeks, 18% being low birth weight, mean birthweight of 2951.57±694.02 (1100-4200) g; Apgar score of 9.87±0.50 (8-10). The physical, mental and intellectual developments of offsprings are normal.

There were 9 (13.64%) patients who had abnormal pregnancy: 8 patients used CHL and 1 did not; all planned to get pregnant. The mean interval between withdrawal of LEF and being pregnant was 11.92±4.61 (6-18) months; the mean interval between administration of CHL and being pregnant was 8.86±5.69 (3-18) months. Among them, 5 had embryo (56%) development ceasing, 2 (22%) had spontaneous abortion, 1 (11%) had Down's syndrome, and 1 (11%) had labor induction due to relapse.

Due to the relapse of rheumatic disease, 12 (18.18%) patients resumed using immunosuppressive drugs including MTX and LEF, resulting in terminating the preparation of pregnancy. 9 (13.64%) patients are successfully got pregnant and ongoing with good conditions so far.

**Conclusion:**

To our knowledge, this is the largest study about pregnancy outcomes with the treatment of lef. The teratogenic effects was not found, however, the spontaneous abortion and embryo development ceasing are worthy of attention. For the sake of safety, the patients who plan to get pregnant are encouraged to use CHL for drug clearance.

**Disclosure:** Y. Zhao, None; L. Shen, None; Z. Shuai, None; H. Zhao, None; W. Lai, None; X. Lai, None; S. Zhang, None; X. Wang, None; S. Hu, None; W. Chen, None; W. Ji, None; H. Wei, None; Q. Zhang, None; L. Pang, None; H. Liu, None; Q. Shu, None; J. L. Zhang, None; Y. Zhou, None; Q. Jiang, None; H. Wu, None; J. Xue, None; G. Bai, None; L. Zhang, None; F. Xiao, None.


**Abstract Number:** 1312

**Pregnancy Outcomes in Male Patients Using Anti-Tumor Necrosis Factor Alpha Patients with Inflammatory Arthritis; Hur-BIO Real Life Experiences**

Oguz Abdullah Uyaroglu1, Emrah Seyhoglu1, Abdulsamet Erden2, Levent Kilic2, Berkan Armagan2, Alper Sari2, Omer Karadag3, Ali Akdogan2, Sule Apras Bilgen3, Sedat Kiraz2, Ihsan Erentli3 and Umut Kalyoncu2, 1Internal Medicine, Hacettepe University Faculty of Medicine, Ankara, Turkey; 2Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Turkey; 3Department of Internal Medicine, Divison of Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Turkey

**First publication:** September 18, 2017
Background/Purpose:

A significant part of patients with inflammatory arthritis are at their reproductive ages. Anti-tumor necrosis factor-alpha (Anti-TNF) agents are one of the relevant treatment options for inflammatory arthritis which may cause fetal morbidity and mortality. Anti-TNF studies for pregnancy outcomes are mostly related with maternal exposure. In male patients, there are limited studies related to the fetal risks associated with the use of anti-TNF alfa agents before preconception period.

The objective of this study was to assess fetal loss, who used to anti-TNF agents during preconception period in male patients with inflammatory arthritis.

Methods:

A questionnaire was performed to 160 male patients admitted to our outpatient clinic between July 2015 and July 2016 who use anti-TNF alfa agents. Patients were asked whether their wife’s had got pregnant after the start of anti-TNF agents. If their wife’s had got pregnant we asked about pregnancy outcomes.

Results:

Totally, 42 (39 AS, 2 RA, 1 PsA) male patients’ wife had pregnancy during patients continue to anti-TNF agents. General characteristics of the patients whose wife had got pregnant was shown in the table. The mean age of patients was 36.4 ± 5.2 years. Median disease duration was 10 (IQR=11) years. Thirty-eight (90.5%) patients had live births and all newborns were healthy. The median gestation week was 39 (IQR = 3) weeks. Four (10.5%) births were preterm (ended in <37 gestation week). Mean birth weight of newborns was 3229 gram (gr) (SD = 582). Thirty-one (81.6%) newborn had normal (2500-4000 gr) birth weights. Four had low and 3 had high birth weights.

One pregnancy of a RA patient using etanercept and methotrexate was terminated due to oligohydramnios at 37th gestation week. The birth weight was 2850 gr and newborn was healthy.

One pregnancy of 35-years-old male AS patient using Adalimumab was ended in live birth in normal gestational week and normal birth weight but newborn diagnosed as Angelman Syndrome in the following.

Three (7.9%) out of 38 live births hospitalized in intensive care unit after delivery. The indications of ICU admission were unknown.

On the other hand, 3 (7.1%) pregnancies were ended in spontaneous abortions and 1 (2.4%) pregnancy were terminated with curettage. No congenital malformations were found in connection to paternal exposure.

Conclusion:

Our study is one of the most extensive studies which provides the male number of patients and the pregnancy outcomes related to men in the literature. Study results suggest that anti-TNF drugs could be safe following paternal exposure.

Table. General characteristics of the patients participating in the study
<table>
<thead>
<tr>
<th>Patients whose wife had got pregnant</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)= 45 (27.6)</td>
</tr>
</tbody>
</table>

<p>| Age, mean (SD) | 36.4 (5.2) |</p>
<table>
<thead>
<tr>
<th>Disease, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AS</td>
</tr>
<tr>
<td>RA</td>
</tr>
<tr>
<td>PsA</td>
</tr>
<tr>
<td>Duration of disease, year, median (IQR)</td>
</tr>
<tr>
<td>Biologic Agents, n (%)</td>
</tr>
<tr>
<td>----------------------</td>
</tr>
<tr>
<td>Adalimumab</td>
</tr>
<tr>
<td>Etanercept</td>
</tr>
<tr>
<td>Infliximab</td>
</tr>
<tr>
<td>Golimumab</td>
</tr>
<tr>
<td>Duration of biological agent use, month, mean (SD)</td>
</tr>
</tbody>
</table>

Disclosure: O. A. Uyaroglu, None; E. Seyhoğlu, None; A. Erden, None; L. Kilic, None; B. Armagan, None; A. Sari, None; O. Karadag, None; A. Akdogan, None; S. Apras Bilgen, None; S. Kiraz, None; I. Ertenli, None; U. Kalyoncu, None.


Abstract Number: 1313

**Oral Corticosteroid Use during Pregnancy and Risk of Preterm Birth in Women with Rheumatoid Arthritis**

Kristin Palmsten¹, Gretchen Bandoli², Diana L Johnson¹, Ronghui Xu³,⁴ and Christina D Chambers¹, ¹Department of Pediatrics, University of California, San Diego, La Jolla, CA, ²Pediatrics, University of California, San Diego, La Jolla, CA, ³Department of
Background/Purpose:
There are limited data regarding gestational timing of oral corticosteroid (OCS) use during pregnancy and risk of preterm birth. The objective was to compare preterm birth risk in pregnant women with rheumatoid arthritis according to timing of OCS and disease modifying antirheumatic drug (DMARD) use.

Methods:
This study included pregnant women (n=537) with rheumatoid arthritis who enrolled in the MothertoBaby Autoimmune Diseases in Pregnancy Study (2003-2014) before 20 weeks’ gestation. Information on medication use and pregnancy characteristics was collected by telephone interview at up to 3 time points during pregnancy and once after delivery, plus by medical record review. Exposures were classified into mutually exclusive groups: neither OCS nor DMARD (reference) OCS only, DMARD only, and both OCS and DMARD according to any use during the 1st trimester, 2nd trimester, and 90 days prior to gestational week 37 or delivery date, whichever occurred first. Modified Poisson regression was used to estimate relative risks (RR) and 95% confidence intervals (CI) between exposure and preterm birth, with separate models for each exposure window. Models were adjusted for year, maternal age, race/ethnicity, socio-economic status, overweight, autoimmune comorbidities, multiple gestation, nonsteroidal anti-inflammatory drug use, Health Assessment Questionnaire (HAQ) score at enrollment, and gestational age at enrollment.

Results:
During pregnancy, 55% of women used OCS (of which 98% used prednisone), 68% used biologics, and 31% used non-biologic DMARDs. Median HAQ score at enrollment was 0.25 for neither OCS nor DMARD, 0.38 for OCS only, 0.25 for DMARD only, and 0.5 for OCS and DMARD use in the 1st trimester. Preterm birth risk was 6% in women who did not use OCS or DMARD during the 1st trimester, and the adjusted RR was 3.3 (CI: 1.1-9.5) for 1st trimester OCS, 1.7 (CI: 0.6-4.7) for DMARD, and 3.1 (CI: 1.2-8.0) for DMARD and OCS. Preterm birth risk was 13% in women who did not use OCS or DMARD during the 2nd trimester, and the adjusted RR was 1.5 (CI: 0.9-2.5) for 2nd trimester OCS, 0.6 (CI: 0.3-1.2) for DMARD, and 1.5 (CI: 0.9-2.6) for DMARD and OCS. Preterm birth risk was 11% in women who did not use OCS or DMARD in the 90 days before delivery or gestational week 37, and the adjusted RR was 1.8 (CI: 1.1-3.1) for OCS, 0.8 (CI: 0.4-1.7) for DMARD, and 1.9 (CI: 1.1-3.4) for DMARD and OCS.

Conclusion:
Early and late pregnancy OCS use with or without DMARD use was associated with an increased risk of preterm birth compared with women who did not use OCS or DMARD. DMARD use alone was not associated with an increased risk of preterm birth. The OCS and preterm birth association was strongest for 1st trimester use partly due to low preterm birth risk in the 1st trimester reference group. Results may reflect residual confounding by RA severity.

Disclosure: K. Palmsten, None; G. Bandoli, None; D. L. Johnson, None; R. Xu, None; C. D. Chambers, AbbVie, 2,Amgen, 2,Bristol Myers Squibb, 2,Celgene, 2,Janssen Pharmaceuticals Product, L.P., 2,Pfizer Inc, 2,Roche Pharmaceuticals, 2,Seqirus, 2,GSK, 2,UCB, 2,Sanofi-Aventis Pharmaceutical, 2.


Abstract Number: 1314

Pregnancy Outcomes in Patients with Psoriasis: A Nationwide Population-Based Study
Meng-Jiun Chiou1, Yu-Hui Huang2, Chang-Fu Kuo1, Kuang-Hui Yu1, Shue-Fen Luo1 and Yao-Fan Fang1, 1Division of Rheumatology, Allergy and Immunology, Chang Gung Memorial Hospital, Taoyuan, Taiwan, 2Department of Dermatology, Chang Gung Memorial Hospital, Taoyuan, Taiwan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Reproductive Issues in Rheumatic Disorders Poster
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
The pregnancy outcomes in women with psoriasis have rarely been investigated. This nationwide population study aimed to estimate the risks of adverse maternal and neonatal outcomes in women with psoriasis compared with the general population.

Methods:
Among 2,350,339 singleton pregnancies identified using the Taiwan National Health Insurance and national birth registry between 2001 and 2012, 3,669 pregnancies were delivered by psoriasis patients. Odds ratios (ORs) and 95% confidence intervals (CIs) for maternal and Neonatal outcomes were estimated adjusted for age, sex, Charlson comorbidity score, birth year, maternal nationality and socioeconomic status using an adjusted generalized estimating equation model.

Results:
Pregnancies with psoriasis were associated with an adjusted OR (95% CIs) of 1.06 (1.01-1.12) for Cesarean delivery, 1.40 (1.09-1.81) for gestational hypertension, 1.53 (1.25-1.86) for preeclampsia, 1.47 (1.04-2.08) for antepartum hemorrhage, 1.59 (1.36-1.86) for severe postpartum hemorrhage, 1.13 (1.00-1.28) for gestational diabetes. Neonatal outcomes were also poorer, with an OR (95% CIs) of 1.51 (1.12-2.03) for stillbirth, 1.30 (1.16-1.45) for low birth weight, 1.11 (1.00-1.24) for prematurity, 1.12 (1.02-1.24) for small for gestational age, 1.49 (1.01-2.19) for an Apgar score <7 at 5 minutes.

Conclusion:
Both maternal and neonatal outcomes are worse in women with psoriasis than in the general population.

Disclosure: M. J. Chiou, None; Y. H. Huang, None; C. F. Kuo, None; K. H. Yu, None; S. F. Luo, None; Y. F. Fang, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/pregnancy-outcomes-in-patients-with-psoriasis-a-nationwide-population-based-study

Abstract Number: 1315

Influence of Rheumatoid Arthritis and Axial Spondyloarthritis on Pregnancy Complications, Pregnancy Outcome and Delivery Mode

Frauke Förger1, Stephanie van den Brandt2, Astrid Zbinden3, Monika Ostensen3 and Peter M. Villiger3, 1Inselspital, University of Bern, Bern, Switzerland, 2Clinical Immunology and Rheumatology, University of Amsterdam, Amsterdam, Netherlands, 3Rheumatology, Immunology and Allergology, Inselspital, University of Bern, Bern, Switzerland

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Reproductive Issues in Rheumatic Disorders Poster
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM
Background/Purpose: To analyze pregnancy complications, pregnancy outcome and delivery mode in patients with rheumatoid arthritis (RA) and axial spondyloarthritis (axSpA).

Methods: Patients with RA and axSpA were compared with those of matched healthy controls (HC) with respect to pregnancy complications, pregnancy outcome and delivery mode. Patients and controls were prospectively followed at the University of Bern once at each trimester and two months postpartum. To identify risk factors for adverse pregnancy outcomes and delivery modes, multivariable logistic regression analyses were performed. Differences in birth weight of neonates in patients and references were examined in multivariable linear regression analyses.

Results: We analyzed 244 pregnancies, of which 96 pregnancies occurred in 86 RA patients, 78 in 70 axSpA patients and 70 in 70 healthy women. Compared with healthy pregnant controls, pregnant women with RA and axSpA showed a higher risk for pregnancy complications (gestational diabetes, preeclampsia, infection, preterm premature rupture of membranes) as well as for small for gestational age infants and for preterm deliveries. Active disease in both RA and axSpA was a risk factor for preterm delivery. Compared to neonates born to healthy mothers, those born to women with RA showed a mean reduction in birth weight of 414.4 gm and those born to women with axSpA had a mean reduction in birth weight of 254.4 gm. Regarding delivery mode, most women had vaginal deliveries (RA: 51.0%, axSpA: 57.7%, HC: 72.9%). We found an increased risk of caesarean section (C section) in women with RA compared with healthy controls which was not seen in axSpA patients. The risk of elective C section and emergency C section was not increased in RA and axSpA patients compared to the healthy control group.

Conclusion: Autoimmune inflammatory diseases such as RA and axSpA are risk factors for adverse pregnancy outcome. Since maternal disease activity is a risk factor for preterm delivery, disease activity should be sufficiently controlled during pregnancy.

Disclosure: F. Förger, UCB Pharma, 2,Mepha, Roche, UCB Pharma, 8; S. van den Brandt, None; A. Zbinden, None; M. Ostensen, None; P. M. Villiger, None.

Abstract Number: 1316

Risk of Preterm Delivery Associated with Perinatal Exposure to Dmards in Women with Inflammatory Arthritis: A Population-Based Cohort Study

Nicole W. Tsao1,2, Eric C. Sayre2, Mohsen Sadatsafavi1, J. Antonio Avina-Zubieta2,3, Stephanie Ensworth4 and Mary A. De Vera1,2, 1Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada, 2Arthritis Research Canada, Richmond, BC, Canada, 3Division of Rheumatology, Department of Medicine, University of British Columbia, Vancouver, BC, Canada, 4University of British Columbia, Vancouver, BC, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Reproductive Issues in Rheumatic Disorders Poster
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Given the limited data on impacts of perinatal medication use, our objective was to investigate the association between conventional synthetic DMARD (csDMARD) use preconception and during pregnancy and risk of preterm deliveries.

Methods: We linked population-based health data in British Columbia, Canada from 2002 to 2012 on all physician visits, hospital admissions, and dispensed medications with a perinatal registry. Essential data from this registry included date of conception according to ultrasound-confirmed gestational age or last menstrual period. We created a pregnancy cohort of women with inflammatory arthritis using a case definition of 2 outpatient physician ICD9 codes for RA, ankylosing spondylitis, JIA, PsA, or connective tissue diseases and adult systemic vasculitides, ≥ 2 months and ≥ 2 years apart. We grouped csDMARDs according to accepted safety profiles - antimalarials, gold, CSA, and SSZ (Group 1); and MTX, LEF, AZA, CYC, chlorambucil, penicillamine, MMF, and minocycline (Group 2) – and determined perinatal exposure over two periods: as binary use (yes/no) during the 90 days preconception and as time-dependent use during pregnancy from date of conception until delivery. We used Cox proportional hazards models to evaluate the association between csDMARDs exposure preconception and/or during pregnancy and risk of preterm
delivery, defined as live births with gestational age (GA) < 37 weeks, while adjusting for baseline and time-dependent covariates. Subgroup analyses were conducted according to csDMARD groups.

**Results:** There were 610 pregnancies in 512 women and 5639 pregnancies in 4078 women with and without csDMARDs exposure, respectively (Table 1). There were 562 (10%) and 138 (23%) preterm deliveries in unexposed and exposed pregnancies, respectively, with mean GA at delivery at 38.5 weeks (SD 2.06) in unexposed pregnancies, 38.3 (2.46) in Group 1, and 37.1 (2.96) in Group 2. The adjusted hazard ratio (HR) for exposure to csDMARDs preconception and during pregnancy and risk of preterm delivery was 2.12 (95% CI 1.63-2.76) (Table 2). In subgroup analyses, the risk of preterm delivery was highest in those exposed to Group 2 csDMARDs during pregnancy (HR 3.92, 95% CI 1.45-10.62).

**Conclusion:** Our findings suggest a risk of preterm delivery associated with exposure to csDMARDs preconception and during pregnancy. This may have been impacted by disease activity and differences in inflammatory arthritis types between exposure groups. Nonetheless, with mean GA of neonates approximating term delivery, it is important to consider the risks and benefits of medication use during pregnancy.

| Table 1. Characteristics of pregnant women with inflammatory arthritis exposed and unexposed to csDMARDs preconception and during pregnancy |
|---|---|---|
| Characteristics | Exposed to csDMARDs | Unexposed to csDMARDs |
| | N (%) | | N (%) |
| | 512 women, 610 pregnancies | 4078 women, 5369 pregnancies |
| **Current pregnancy** | | |
| Age at delivery (mean (SD)) | 32 (5) | 31 (5) |
| Multiparous | 335 (55) | 3356 (60) |
| **Obstetrical history** | | |
| Prior preterm delivery | 50 (8) | 308 (5) |
| Prior spontaneous abortion | 161 (27) | 1424 (25) |
| Prior neonatal death | <5 | 34 (0.6) |
| Prior stillbirth | 17 (3) | 62 (1) |
| Prior low birth weight | 26 (4) | 162 (3) |
| Prior congenital anomaly | 6 (1) | 50 (1) |
| **Inflammatory arthritis type** | | |
| Rheumatoid arthritis | 387 (63) | 1402 (25) |
| Psoriasis/psoriatic arthritis | 77 (13) | 3366 (60) |
| Juvenile idiopathic arthritis | 28 (5) | 73 (1) |
| Connective tissue diseases and adult systemic vasculitides | 280 (46) | 786 (14) |
| Ankylosing spondylitis | 38 (6) | 378 (7) |
| **csDMARD use** | | |
| Group 1 | 499 (82) | - |
| Group 2 | 189 (31) | - |
| **Other medication use** | | |
| Biologics | 26 (4) | 44 (0.8) |
| Glucocorticoids | 211 (35) | 211 (4) |
| Traditional NSAIDs | 158 (26) | 525 (9) |
| COX2 NSAIDs | 45 (7) | 62 (1) |
| Antidepressants | 100 (17) | 598 (11) |
| Anxiolytics | 49 (8) | 295 (5) |
| **Comorbidities** | | |
| Mood disorders | 32 (5) | 250 (4) |
| Anxiety | 63 (10) | 548 (10) |
| Asthma | 3 (0.5) | 30 (0.5) |

*percentages do not add to 100 as each pregnancy can be exposed to more than one category of csDMARDs

#other medication use during 90 days preconception and/or during pregnancy
<table>
<thead>
<tr>
<th>Models*</th>
<th>Exposure groups</th>
<th>Hazard ratio</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1</td>
<td>All csDMARDs</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Preconception only vs. unexposed</td>
<td>1.37</td>
<td>1.03-1.82</td>
</tr>
<tr>
<td></td>
<td>During pregnancy only vs. unexposed</td>
<td>1.93</td>
<td>0.80-4.65</td>
</tr>
<tr>
<td></td>
<td>Preconception AND during pregnancy vs. unexposed</td>
<td>2.12</td>
<td>1.63-2.76</td>
</tr>
<tr>
<td>Model 2</td>
<td>Group 1 csDMARDs</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Preconception only vs. unexposed</td>
<td>1.40</td>
<td>1.02-1.90</td>
</tr>
<tr>
<td></td>
<td>During pregnancy only vs. unexposed</td>
<td>1.86</td>
<td>0.77-4.48</td>
</tr>
<tr>
<td></td>
<td>Preconception AND during pregnancy vs. unexposed</td>
<td>1.87</td>
<td>1.40-2.49</td>
</tr>
<tr>
<td>Model 3</td>
<td>Group 2 csDMARDs</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Preconception only vs. unexposed</td>
<td>1.58</td>
<td>1.02-2.44</td>
</tr>
<tr>
<td></td>
<td>During pregnancy only vs. unexposed</td>
<td>3.92</td>
<td>1.45-10.62</td>
</tr>
<tr>
<td></td>
<td>Preconception AND during pregnancy vs. unexposed</td>
<td>2.64</td>
<td>1.75-3.98</td>
</tr>
</tbody>
</table>

*All models were adjusted for baseline covariates including maternal characteristics (maternal age, neighborhood income quintile, parity, number of visits to rheumatologist, hospitalizations, and maternal body mass index); obstetrical history (prior premature births, spontaneous abortions, low birth weight births, congenital anomalies, neonatal deaths, stillbirths, total prior hospital admissions, number of antenatal visits); use of medications (glucocorticoids, traditional NSAIDs, COX2 NSAIDs, biologic DMARDs, anxiolytics, antidepressants); and comorbidities (asthma, depression, anxiety). All models were also adjusted for time-dependent covariates during pregnancy, namely use of medications (traditional NSAIDs, COX2 NSAIDs, biologic DMARDs, anxiolytics, antidepressants).

**Disclosure:** N. W. Tsao, None; E. C. Sayre, None; M. Sadatsafavi, None; J. A. Avina-Zubieta, None; S. Ensworth, None; M. A. De Vera, None.


**Abstract Number:** 1317

**Obstetric Outcomes in Women with Rheumatoid Arthritis: Results from Nationwide Inpatient Sample Database 2003-2011**

Shweta Kishore¹, Varun Mittal², Venkataraman Palabindala³, Shradha Ahuja³ and Vikas Majithia¹,⁴, ¹Division of Rheumatology, University of Mississippi, Jackson, MS, ²Division of Hematology and Oncology, Albert Einstein Healthcare Network, Philadelphia, PA, ³Division of Hospital Medicine, University of Mississippi, Jackson, MS, ⁴Jackson VA Medical Center and University of Mississippi, Jackson, MS

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Reproductive Issues in Rheumatic Disorders Poster

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Fertility is reduced in patients with Rheumatoid Arthritis (RA) due to unknown cause. Few studies mostly involving single center cohorts have addressed pregnancy outcomes in RA. This study was undertaken to determine the frequency of complications occurring during pregnancy for women with RA and to compare these outcomes with the general obstetric population by using the largest inpatient care database.

**Methods:** By using the 2003-2011 Nationwide Inpatient Sample of Healthcare Cost and Utilization Project, we estimated the number of obstetric hospitalization, deliveries and caesarean deliveries in women between the age group 18-50 years. Patients hospitalized with RA as one of the top three diagnoses were identified. Demographic characteristics and in-hospital outcomes were recorded for both RA and control group. Then we compared maternal and pregnancy complications for all pregnancy-related admissions for women with and without RA. Multivariate logistic regression analysis was used to obtain adjusted odds ratio (OR).

**Results:** The total number of obstetric hospitalization was 42.32 million of which 31439 were women with diagnosis of RA. The maternal age of RA population was higher (30.5 years) than that in the control group (27 years) (p < 0.001). After adjusting for potential confounders, maternal RA population had a significantly higher prevalence of hypertensive diseases, premature rupture of
membranes, antepartum hemorrhage, preterm delivery, intrauterine growth retardation and cesarean delivery. However, the prevalence of postpartum hemorrhage and the risk of inpatient mortality were not different between two groups. The frequencies of the above outcomes along with Odds Ratio are provided in Table 1.

**Conclusion:** Based on our study of national cohort, we conclude that women with RA have a higher risk of adverse outcomes of pregnancy than do pregnant women without RA and thus close antenatal and post delivery monitoring need to be performed in order to reduce complications. The mean maternal age of RA population is higher likely secondary to infertility. Further studies are needed to examine these findings in relation to severity of disease, medications used and the presence of other comorbidities.

**References:**


**Disclosure:** S. Kishore, None; V. Mittal, None; V. Palabindala, None; S. Ahuja, None; V. Majithia, None.


**Abstract Number: 1318**

**Abnormal Cerviovaginal Cytology in Adolescents with Systemic Lupus Erythematosus: A Retrospective Case Series**

Jennifer Kurkowski¹, Martha Curry², Marietta deGuzman³, Jane Geyer⁴ and Oluyemisi Adeyemi-Fowode⁵, ¹Department of Obstetrics and Gynecology, Baylor College of Medicine, Texas Childrens Hospital, Houston, TX, ²Pediatric rheumatology, Baylor College of Medicine and Texas Childrens Hospital, Houston, TX, ³Baylor College of Medicine, Division of Pediatric Rheumatology, Houston, TX, ⁴Baylor College of Medicine, Division of Pediatric and Adolescent Gynecology, Houston, TX, ⁵Department of Obstetrics and Gynecology, Baylor College of Medicine and Texas Childrens Hospital, Houston, TX

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** ARHP Reproductive Issues in Rheumatic Disorders Poster

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Guidelines recommend screening for cervical cancer in women starting at age 21 but according to the American Congress of Obstetricians and Gynecologists, exceptions should be made for those with HIV and those with weakened immune systems. It is recommended that sexually active adolescents with weakened immune systems should be screened six months apart in the first year after they begin having sex and then continue with annual pap tests. Though studies are limited, it appears that the prevalence of an
abnormal Papanicolaou (Pap) smear is significantly increased in patients with SLE. The purpose of this study was to examine pap smear results among SLE adolescent patients at our institution.

**Methods:**

An IRB approved retrospective chart review was performed on SLE female patients < 21 years. Patients were identified using ICD-9 codes between the years 2000-2016. Sexually active patients with a history of a pap smear were included in the study. Data reviewed included demographics, menarchal status, age of coitarche, contraceptive use, human papillomavirusvirus vaccine (HPV) status, use of immunosuppressive medication and pathology reports. Fisher exact test was used to determine statistical significance.

**Results:**

18 patients met inclusion criteria. Mean age of SLE diagnosis was 13.6 ± 3.4 years while the average age of menarche was 12.6 ± 1.4 years. All patients were sexually active and the mean age of onset of sexual activity of 16.2 ± 1.8 years, mean age of initial pap smear was 18.4 ± 1.7 years with 44% having a pap smear within the first year of coitarche. Majority were on immunosuppressive medication (94.4%) and 88.9% were on teratogenic medication. Although all utilized progestin-only contraception, only 39% used Long Acting Reversible Contraception and only 39% reported consistent condom use. 83.3% reported ever receiving HPV vaccine. 9/18 (50%) had abnormal pap smears, 4 were atypical squamous cells of undetermined significance (ASCUS) and 5 were Low-grade squamous intraepithelial lesion (LSIL). Plan of care was for repeat pap smear in 1 year in all but one patient with ASCUS pap who underwent a colposcopy with biopsy result of mild chronic endocervicitis and squamous metaplasia. Average age of coitarche was 16 years in both groups. Mean time frame between coitarche to the initial pap smear was 1.66 years and 2.77 years, HPV vaccination rate was 77.8% and 88.8% for those with normal and abnormal pap results respectively. Only 22.2% reported consistent condom use in the abnormal pap smear group compared to 55.6% in the normal pap smear group. Fisher exact test revealed no statistically significant difference (P value 0.1534).

**Conclusion:**

No high-grade dysplasia on pap smear was noted in this small retrospective study of sexually active adolescent SLE patient. 50% of our sample size had an abnormal pap smear. Despite its limitations and small sample size, this study provides further evidence that women with SLE are at increased risk of developing cervical changes. Larger studies with inclusion of a control group are needed to conclude pap-testing recommendations in the adolescent SLE population.

**Disclosure:** J. Kurkowski, None; M. Curry, None; M. deGuzman, None; J. Geyer, None; O. Adeyemi-Fowode, None.


**Abstract Number:** 1319

**TAS05567 Is a Novel Potent and Selective Spleen Tyrosine Kinase Inhibitor That Attenuates Disease Severity in Animal Models of Autoimmune Diseases**

Hiroaki Hayashi, Ryusuke Kaneko, Manabu Tayama, Shunsuke Demizu, Daichi Akasaka, Hiroki Irie, Aki Kawagishi, Yoshio Ogino, Teruhiro Utsugi, Eiji Sasaki and Yoshikazu Iwasawa, TAIHO PHARMACEUTICAL CO., LTD., Tsukuba, Japan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Rheumatoid Arthritis – Animal Models Poster II

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Spleen tyrosine kinase (Syk) is a non-receptor cytoplasmic tyrosine kinase. B-cell receptor (BCR) and Fc receptor-mediated syk signaling pathways lead to activation of several immune cells, including B-cells, macrophages and osteoclast. In these cells, Syk plays an essential role in diverse cellular responses, such as production of inflammatory mediators and differentiation. These roles of Syk in immunologic processes make it an attractive target for the development of therapeutic drugs against autoimmune diseases. We
identified TAS05567 as a highly selective syk inhibitor and assessed its therapeutic potential in rheumatoid arthritis (RA) as well as in immune thrombocytopenic purpura (ITP).

Methods:

In vitro biochemical assay was performed with available kinase assay panels. Anti-IgM-induced phosphorylation of BLNK and PLCγ2 was detected by flow cytometry in B cells. TNF-α production from monocytes induced by IgG was measured by ELISA. Effect of TAS05667 on the intracellular calcium level of basophilic cells was evaluated with FLIPR Calcium assay. Mature osteoclasts were detected with TRAP staining.

Rat CIA model: Lewis rats were immunized with a bovine type II collagen emulsion on day -14 and -7. To evaluate the therapeutic efficacy of TAS05567 in a rat collagen-induced arthritis (CIA) model, TAS05567 was started to administer for 14 consecutive days when the overt clinical signs of disease were observed. Swelling in hind paws were measured by a plethysmometer. At the end of the treatment period, the hind paws were removed to analyze histopathological changes.

Mouse ITP model: C57BL/6 mice were injected with anti-CD41 antibody and bled the following day to measure platelets count by a hematology analyzer. IVIg used as a positive control was intravenously administered once and TAS05567 was orally administered for 2 days.

Results:

TAS05567 showed high potency against enzymatic activity of Syk (IC_{50} = 0.37 nM) and only inhibited 4 kinases with inhibitory activity of 191 off-target kinases tested (>70% within 135-fold of Syk IC_{50}). TAS05567 also inhibited BCR-dependent phosphorylation of BLNK and PLCγ2 in B cells with IC_{50} of 1.8 nM and 23 nM, respectively. TAS05567 effectively inhibited FcγR-mediated TNF-α production in monocytes (IC_{50} = 27 nM) and FcεR-mediated calcium flux in basophilic cells (IC_{50} = 52 nM). Furthermore, TAS05567 suppressed mature osteoclast differentiation from precursor cells in a dose-dependent manner.

In the established rat CIA model, TAS05567 dose-dependently suppressed paw swelling compared with vehicle. In the histological analysis, TAS05667-treated mice had a marked reduction in the severity of inflammation, pannus, cartilage destruction and bone destruction.

In the mouse ITP model, thrombocytopenia was induced by intravenous injection of anti-CD41 antibody. TAS05567 significantly protected symptoms of thrombocytopenia and exhibited more potent efficacy than IVIg in this model.

Conclusion:

Our study demonstrates a novel Syk inhibitor, TAS05567, showed potent efficacy in both RA and ITP models. These data suggest that TAS05567 would be an attractive therapeutic agent for autoimmune diseases including RA and ITP.

Disclosure: H. Hayashi, None; R. Kaneko, None; M. Tayama, None; S. Demizu, None; D. Akasaka, None; H. Irie, None; A. Kawagishi, None; Y. Ogino, None; T. Utsugi, None; E. Sasaki, None; Y. Iwasawa, None.


Abstract Number: 1320

TAS5315, a Novel Bruton’s Tyrosine Kinase Inhibitor, Ameliorates Inflammation and Bone Erosion in Murine Model for Rheumatoid Arthritis

Yohei Yoshiga¹, Fumihiro Hosoi¹, Satoru Iguchi¹, Ryuusuke Kaneko², Yoshinori Nakachi¹, Daichi Akasaka², Kenji Tanakà², Kazuhiko Yonekura², Teruhiro Utsugi², Eiji Sasaki² and Yoshikazu Iwasawa², ¹TAIHO PHARMACEUTICAL CO., LTD., TSUKUBA, Japan, ²TAIHO PHARMACEUTICAL CO., LTD., Tsukuba, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Animal Models Poster II
Background/Purpose:

The erosions of bone and cartilage are a cardinal feature of rheumatoid arthritis (RA) and associated with disease severity and poor functional outcome. Although several anti-inflammatory drugs improve symptoms of articular inflammation, they are less effective against bone erosion. The bone erosions in RA are associated with aberrant activations of osteoclasts induced by pro-inflammatory cytokines and receptor activator of nuclear factor κB ligand (RANKL). Bruton’s tyrosine kinase (BTK), which is expressed in immune cells and mature osteoclast, is reported to be a key molecule in inflammatory response and bone resorption. Thus, targeting BTK may be efficacious against not only inflammation but also bone erosion through direct regulation of activation of effector cells such as B cells, macrophages and osteoclasts in RA.

In this study, we evaluated the effect of TAS5315, a novel BTK inhibitor, on the expression of inflammatory factors from macrophages and osteoclasts activation compared with BTK inhibitor CC-292, and bone erosion by time-dependent micro-CT analysis in mouse collagen-induced arthritis (CIA).

Methods:

Kinase selectivity of TAS5315 was assessed by available kinase assay panels. The effects of TAS5315 on macrophages and osteoclasts were assessed by examining phosphorylation of BTK, expression of inflammatory factors, osteoclast differentiation and bone resorptions compared with that of BTK inhibitor CC-292. TAS5315 were orally administrated once a day for 21 consecutive days in an established mouse CIA model. Disease severity was evaluated by clinical score of paw swelling. Changes in bone mineral density (BMD) and bone erosion by TAS5315 were assessed using time-dependent micro-CT analysis.

Results:

TAS5315 selectively inhibited the enzyme activity of BTK and had less off target inhibition against other kinases. TAS5315 dose-dependently suppressed the expression of inflammatory factors (TNFα and IL-8) in macrophages. TAS5315 showed more potent efficacy against phosphorylation of BTK, osteoclastogenesis and bone resorbing activity in osteoclasts compared with CC-292. In established mouse CIA model, TAS5315 significantly ameliorated paw swelling in a dose-dependent manner and showed the anti-inflammatory effects in pathological analysis at a dose of 0.1 mg/kg. Most importantly, TAS5315 also showed repair of bone erosion and improvements of BMD from joint destruction in the initial treatment by micro-CT analysis.

These data suggests that TAS5315 indicated more potent efficacy on joint damage as well as inflammation, and also improved bone erosion in murine model for RA through direct inhibitory effects against osteoclasts function.

Conclusion:

Our study demonstrates that TAS5315 could be a promising RA therapeutic agent by improving bone erosion as well as inflammation.

Disclosure: Y. Yoshiga, None; F. Hosoi, None; S. Iguchi, None; R. Kaneko, None; Y. Nakachi, None; D. Akasaka, None; K. Tanaka, None; K. Yonekura, None; T. Utsugi, None; E. Sasaki, None; Y. Iwasawa, None.


Abstract Number: 1321

Inhibition of the Mechanistic Target of Rapamycin Pathway and Glutaminolysis Facilitates the Expansion of Myeloid-Derived Suppressor Cells and Synergistically Ameliorates Arthritis in SKG Mice

Yo Ueda¹, Takaichi Okano¹, Hirotaka Yamada¹, Yoshihide Ichise¹, Ikuko Naka², Soshi Takahashi³, Sho Sendo⁴, Kengo Akashi², Akira Onishi⁵, Jun Saegusa⁴ and Akio Morinobu³, ¹Department of Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, Kobe, Japan, ²Kobe University Graduate School of Medicine, Kobe, Japan, ³Department of Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, Kobe, Japan, ⁴Rheumatology and Clinical
Background/Purpose: Myeloid-derived suppressor cells (MDSCs) are a heterogeneous population of immature cells that increase in the pathological state such as tumor or inflammation and have the immunosuppressive ability. MDSCs have been reported to ameliorate arthritis in several mice models. The mechanistic target of rapamycin (mTOR) pathway and glutaminolysis are known to be activated in the differentiation from myeloid progenitors to mature myeloid cells such as dendritic cells, macrophages, or osteoclasts. The aim of this study is to evaluate the facilitative effects of the inhibition of mTOR pathway and glutaminolysis on MDSCs in a mouse model of rheumatoid arthritis.

Methods: Bone marrow (BM) cells from untreated Balb/c mice were cultured for 5 days under granulocyte–macrophage colony-stimulating factor (GM-CSF) stimulation with four patterns of drugs; 1) DMSO (control), 2) rapamycin, 3) 6-Diazo-5-oxo-L-norleucine (DON; a glutamine analogue), or 4) the combination of rapamycin and DON. Cultured BM cells were analyzed by flow cytometry. Cultured MDSCs were isolated by manual MACS and analyzed their immunosuppressive characters by co-culture with CFSE-dyed CD4+ T cells. The four patterns of drugs described above were administered intraperitoneally to arthritic SKG mice induced by Zymosan A injection.

Results: We found that DON administration (separately or in combination) significantly suppressed the differentiation from BM cells to dendritic cells in vitro. Most DON-treated BM cells showed the phenotype of MDSCs, large part of which were Ly6G+ cells (the phenotype of polymorphonuclear MDSCs; PMN-MDSCs). On the other hand, rapamycin administration (separately or in combination) significantly increased the TGF-b expression and the inhibitory capacity of Ly6G+ PMN-MDSCs. The combination of rapamycin and DON was the most effective to suppress arthritis in SKG mice among these four treatment patterns (see Fig 1).

Conclusion: The combination of rapamycin and DON facilitates the expansion of PMN-MDSCs in vitro and synergistically ameliorates arthritis in SKG mice in vivo.

Disclosure: Y. Ueda, None; T. Okano, None; H. Yamada, None; Y. Ichise, None; I. Naka, None; S. Takahashi, None; S. Sendo, None; K. Akashi, None; A. Onishi, None; J. Saegusa, None; A. Morinobu, None.
Tissue Folate Dysregulation Is Associated with Disease Activity and Methotrexate Response in Collagen-Induced Arthritis

Leon van Haandel¹, Rakesh Singh², Paul Kiptoo³, Teruna Siahaan³, Mara L Becker⁴ and Ryan Funk⁵, ¹2401 Gillham Road, Children's Mercy, Kansas City, MO, ²Department of Pharmacy Practice, University of Kansas Medical Center, Kansas City, KS, ³Department of Pharmaceutical Chemistry, University of Kansas, Lawrence, KS, ⁴Rheumatology, Children's Mercy Kansas City, Kansas City, MO, ⁵University of Kansas Medical Center, Kansas City, KS

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Animal Models Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Methotrexate (MTX) is an anti-metabolite inhibitor of folate-dependent biochemical pathways and is effective in reducing disease activity in autoimmune arthritis. This work seeks to investigate the relationship between dysregulation of folates and response to MTX in the collagen-induced arthritis (CIA) mouse model, with respect to biomarker identification and drug development.

Methods: Arthritis was induced in male DBA/1 mice at 7-9 weeks of age by intradermal injection of chicken-collagen in complete Freund’s adjuvant (Day 0) with a booster injection at Day 19 (n=25) and compared to healthy controls (n=5). Subcutaneous MTX injections of 0, 2, 10, 20, and 50 mg/kg were given weekly beginning at Day 14 for a total of 6 weeks. Arthritis disease activity was assessed by paw volume measurement and a 16-point clinical disease score. Mice were sacrificed at Day 54 and tissue samples were collected. Erythrocyte and liver tissue samples were evaluated for folate content by ultra-performance liquid chromatography tandem mass spectrometry. Liver tissue samples were analyzed for folic acid (FA), tetrahydrofolate (THF), 5-methyl-THF (5mTHF) and formyl-THF (fTHF), and RBCs were analyzed for 5mTHF content.

Results: Induction of arthritis in mice had no significant effect on RBC 5mTHF levels, but caused a marked dysregulation of liver folate. Compared to healthy controls, untreated disease mice were found to have a 37% reduction in liver 5mTHF (8.89±1.84 vs 5.58±1.10 pmol/mg, p=0.01) and a 57% increase in liver fTHF (3.54±0.63 vs 5.57±0.68 pmol/mg, p=0.003), with no significant impact on liver THF or FA content. Treatment with MTX resulted in a dose-dependent reduction in RBC 5mTHF, with a 32% reduction in the 50 mg/mL treatment group (p<0.05) that is similar to those observed in patients treated with low-dose MTX. Interestingly, MTX at 50 mg/mL also caused a 42% increase in liver 5mTHF (p=0.03) and a 47% reduction in liver fTHF (p=0.003), resulting in levels similar to those seen in the healthy control mice. Decreased paw volumes across the animals studied were associated with reduced RBC 5mTHF (r=0.63, p=0.004) and reduced liver THF (r=0.62, p=0.002), and reduced liver fTHF (r=0.48, p=0.03). Similarly, reduced disease activity scores were associated with reduced RBC 5mTHF (r=0.59, p=0.008) and increased liver 5mTHF (r=0.67, p=0.0006).

Conclusion: Together, this data suggests that induction of autoimmune arthritis is associated with the dysregulation of tissue folates in the CIA mouse model, and is at least partially reversed by treatment with MTX. The increased ratio of fTHF to 5mTHF is hypothesized to reflect increased oxidation of folates under pro-inflammatory conditions. The finding that measurements of disease activity are associated with the effect of MTX on folates supports the role of folates as a therapeutic target and biomarker of drug response in autoimmune arthritis.
Crucial Roles for Toll-like Receptor 9 in the Pathogenesis of Erosive Autoimmune Arthritis and during Osteoclastogenesis

Anita Fischer¹, Brigitte Meyer¹, Birgit Niederreiter², Erik Lönnblom³, Rikard Holmdahl⁴ and Günter Steiner², ¹Internal Medicine III, Division of Rheumatology, Medical University Vienna, Vienna, Austria, ²Rheumatology, Medical University of Vienna, Vienna, Austria, ³Department of Medical Biochemistry & Biophysics, Karolinska Institute, Stockholm, Sweden, ⁴Department of Medical Biochemistry and Biophysics, Karolinska Institute, Stockholm, Sweden

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Animal Models Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Release and insufficient removal of endogenous nucleic acids may be involved in triggering harmful autoimmune reactions important in the initiation of systemic autoimmune diseases including rheumatoid arthritis (RA). Nucleic acid sensing molecules, such as the endosomal Toll-like receptors (TLRs) 3, 7 and 9, have been linked to pathogenic autoimmune processes, particularly in systemic lupus erythematosus, but their role in RA is less obvious. Data previously obtained in rats with pristane-induced arthritis (PIA) suggested involvement of TLR9 in the pathogenesis of this arthritis model (Hoffmann MH et al. J Autoimmun. 2011; 36:288). Interestingly, rats with PIA develop autoantibodies associated with RA including rheumatoid factor, anti-RA33 and antibodies to carbamylated proteins (Stoop JN et al. Ann Rheum Dis 2015; 74:949). It was therefore the aim of this study to gain more insight into the role of TLR9 in the pathogenesis of autoimmune arthritis by investigating the effects of TLR9 inhibition in rats with PIA.

Methods: Arthritis was induced in DA rats with the mineral oil pristane. Rats were treated with a TLR9 antagonist or a control oligonucleotide every other day, starting one before disease induction. Arthritis was scored using established scoring systems, inflammation and bone erosion were quantified by histological analysis. Expression of TLR9 and other nucleic acid sensing TLRs was quantified by RT-PCR and Western blotting; activation (phosphorylation) of various signal transduction molecules was determined by Western blotting. Furthermore, the role of TLR9 in osteoclast differentiation and activation was investigated in vitro using an established murine bone marrow culture system.

Results: Clinical signs of arthritis were significantly (p<0.05) reduced by 30-50% in animals treated with the TLR9 antagonist. Histological analyses revealed significantly (p<0.05) diminished inflammation, cartilage degradation, bone erosion and reduced numbers of osteoclasts in joints of animals treated with the TLR9 antagonist. Furthermore, serum levels of IL-6, AGP and RF were significantly decreased and expression and activation of NF-kB in lymph nodes appeared to be reduced. However, when treatment was started after onset of arthritis TLR9 inhibition had no effect on arthritis development and severity. Remarkably, mRNA levels of TLR7 and TLR9 strongly differed in the course of in vitro osteoclastogenesis. Whereas TLR7 expression did not change throughout osteoclastogenesis, expression of TLR9 was higher in precursor cells than in mature osteoclasts and partial inhibition of osteoclastogenesis was seen when cultures were exposed to the TLR9 antagonist, whereas a TLR7 antagonist was ineffective.

Conclusion: These results suggest a crucial role for TLR9 in the T cell-dependent initiation phase of PIA and thus important involvement of endogenous DNA presumably released during apoptosis and/or necrosis (induced by pristane in lymphoid organs) in the initiation of autoimmune arthritis and during osteoclastogenesis. The relevance of these findings for human RA needs to be further elucidated in future experiments.

Disclosure: A. Fischer, None; B. Meyer, None; B. Niederreiter, None; E. Lönnblom, None; R. Holmdahl, None; G. Steiner, None.
Angiotensin II Type I Receptor Deficiency Exacerbates Erosive Bone Destruction of hTNF-Transgenic Arthritis Mice

Takafumi Mito1, Tomoyuki Mukai1, Shunichi Fujita1, Shoko Kodama1, Akiko Nagasu1, Teruki Sone2 and Yoshitaka Morita1,
1Department of Rheumatology, Kawasaki Medical School, Kurashiki, Okayama, Japan, 2Department of Nuclear Medicine, Kawasaki Medical School, Kurashiki, Okayama, Japan

Methods: To investigate the effect of exogenous Ang II, Ang II (1 μg/kg/min) was infused by osmotic pumps from 12 to 16 weeks of age in wild-type and human TNF-transgenic (hTNF-tg) mice. As controls, H2O was infused by osmotic pumps in each genotype. The swelling of the paws was graded as arthritis score once per week until 16 weeks of age. The bone property of the talus of the hind paws was analyzed by micro-computed tomography (CT) to assess the extent of bone erosion. Inflammation, bone erosion, and osteoclast formation were evaluated by histological analysis. To examine the role of endogenous AT1R on the erosive bone destruction, AT1R deficient (AT1R-KO) mice were crossed with hTNF-tg. Inflammation and bone erosion were evaluated as described above.

Results: Micro-CT and histological analyses revealed that systemic administration of Ang II significantly augmented bone erosion on hind paws in hTNF-tg mice. Ang II increased the number of osteoclasts around the talus. The severity of clinical arthritis and the histological degree of inflammatory cell infiltration were not affected by Ang II infusion. Interestingly, genetic deletion of AT1R also resulted in more severe bone destruction in hTNF-tg mice without affecting the clinical severity of arthritis.

Conclusion: Both systemic administration of Ang II and genetic deletion of AT1R exacerbated bone destruction in hTNF-tg mice. These results suggest that Ang II is likely to be involved in the TNF-induced bone destruction, and the binding of Ang II to the receptors other than AT1R may be important in the process. Our findings have important implication for the present clinical use of AT1R blockers in patients with rheumatoid arthritis.
Immune Responses to Peptides Containing Homocitrulline or Citrulline in the DR4-Transgenic Mouse Model of Rheumatoid Arthritis

Patrick Lac¹, Sheri Saunders¹, Elena Tutunea-Fatan¹, Lillian Barra², David Bell³ and Ewa Cairns², ¹Microbiology and Immunology, The University of Western Ontario, London, ON, Canada, ²Medicine, Microbiology and Immunology, The University of Western Ontario, London, ON, Canada, ³Medicine, The University of Western Ontario, London, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Animal Models Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Antibodies to proteins/peptides containing citrulline (commonly measured using cyclic citrullinated peptide, CCP2) are hallmarks of Rheumatoid Arthritis (RA). These antibodies are strongly associated with the expression of the Shared Epitope (SE), a major risk factor for RA. RA patients also generate antibodies to homocitrulline-containing proteins/peptides. The latter antibodies are often referred to as anti-carbamylated protein antibodies (Anti-CarP). Citrulline and homocitrulline are structurally similar. There is evidence supporting an important role for immune responses to citrulline in the pathogenesis of RA. We hypothesize that immune responses to homocitrulline are related to citrulline (cross-reactive) and are also arthritogenic. We aimed to study: (1) the relationship between homocitrulline and citrulline immune responses using an established mouse model of RA: DR4-transgenic (DR4tg) mice that express human SE, (2) whether homocitrulline immune responses are dependent on the SE and (3) induce arthritis in this animal model.

Methods:
We used DR4tg mice on a C57BL/6 (B6) background; these mice express the human SE, lack endogenous murine MHC class II and are known to develop immune responses to citrulline and arthritis when immunized with citrullinated fibrinogen. DR4tg and B6 mice were immunized subcutaneously with a homocitrullinated peptide (HomoCitJED). We examined immune responses to HomoCitJED and CitJED, which have an identical number of modified amino acids on the same peptide backbone. Splenic T cell proliferation was evaluated by ³H-thymidine incorporation assay. IgG anti-HomoCitJED, anti-CitJED, and anti-CCP2 antibodies were screened by enzyme-linked immunosorbent assay (ELISA). Antibody cross-reactivity was examined by inhibition with CitJED and HomoCitJED. Some HomoCitJED immunized mice also received intra-articular injection (IA) of HomoCitJED and joint swelling was measured using calipers.

Results:
HomoCitJED immunized DR4tg mice developed early T and B cell responses to HomoCitJED and late responses to CitJED. These mice also developed anti-CCP2 antibodies. In some mice, antibodies to HomoCitJED were also reactive to CitJED. B6 mice immunized with HomoCitJED developed late T and B cell responses to HomoCitJED, but did not generate responses to CitJED or anti-CCP2 antibodies. Unlike DR4tg mice, anti-HomoCitJED antibodies from B6 mice did not react to CitJED. DR4tg mice immunized with HomoCitJED developed knee swelling following IA injections of HomoCitJED.

Conclusion: DR4tg mice immunized with HomoCitJED developed immune responses to CitJED, indicating cross-reactivity. CitJED immune responses were dependent on the SE. HomoCitJED responses occurred in the absence of the SE (B6 mice); however, they developed earlier in DR4tg SE-expressing mice. HomoCitJED is immunogenic and its intra-articular presence is required for knee swelling in DR4tg mice.

Disclosure: P. Lac, None; S. Saunders, None; E. Tutunea-Fatan, None; L. Barra, None; D. Bell, None; E. Cairns, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/immune-responses-to-peptides-containing-homocitrulline-or-citrulline-in-the-dr4-transgenic-mouse-model-of-rheumatoid-arthritis

Abstract Number: 1326
Alpha-Glucosidase Inhibitors Alter Gut Microbiota and Ameliorate Collagen-Induced Arthritis

Lingshu Zhang1,2, Pingfang Song2, Xiaowei Zhang2, Christina Metea2, Matthew Schleisman2, Lisa Karstens2, Eric Leung2, Jun Zhang3, Qiang Xu2,4, Yi Liu2, Mark Asquith5 and Cong-Qiu Chu6,7, 1Department of Rheumatology, West China Hospital, Sichuan University, Chengdu, China, 2Oregon Health & Science University, Portland, OR, 3MD Anderson Cancer Center, Houston, TX, 4Guangzhou University of Chinese Medicine, Guangzhou, China, 5Department of Rheumatology and Immunology, West China Hospital of Sichuan University, Chengdu, China, 6Rheumatology, Oregon Health & Science University, Portland, OR, 7Rheumatology, VA Portland Health Care System, Portland, OR

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Animal Models Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Acarbose, an alpha-glucosidase inhibitor anti-diabetic drug exhibited anti-arthritic effects. The mechanism that acarbose exerts its anti-arthritic effects is not fully understood. Since > 90% of acarbose is not absorbed, we hypothesized that acarbose influences the gut microbiota that affects the course of arthritis. We tested this hypothesis in a collagen-induced arthritis (CIA) model.

Methods: CIA was induced by intradermal injection of chicken collagen type II (CII) emulsified in complete Freund’s adjuvant in male DBA/1 mice. Acarbose, miglitol (a control drug) in drinking water were administered daily at 500 mg/kg via oral gavage. In the prophylactic regimen, mice were treated 7 days prior to the induction of CIA, and in the therapeutic regimen, mice were treated on the day of immunization. All mice were euthanized on day 55 after immunization. Fecal pellets were collected before immunization, during onset of arthritis and after treatment for identification of bacteria using 16S rDNA sequencing. Intestines and spleen were harvested for isolation of lymphocytes and analysis for changes of Th17 and Treg cells. Serum was obtained for analysis of cytokines and autoantibodies to CII.

Results: Administration before induction of CIA, acarbose significantly reduced the incidence of arthritis and attenuated clinical severity of arthritis. This was accompanied by a significant reduction of levels of anti-CII antibodies compared to those of drinking water treated or miglitol treated groups of mice (P < 0.05). The frequency of Th17 cells was significantly decreased in the intestinal lamina propria in both acarbose and miglitol prophylactic treatment (P < 0.001). Prophylactically treated mice with acarbose showed significantly increased CD4+CD25+Foxp3+ Treg cells (P < 0.01) with elevation of Helios+ (P < 0.01) and CCR6+ (P < 0.05). Mice prophylactically treated with miglitol also showed an increase of CD4+CD25+Foxp3+ Treg cells (P < 0.01) with increased CCR6+ (P < 0.05) in the mucosal sites. Furthermore, a remarkable alteration in microbial community was observed in both acarbose and miglitol treated mice. Bacterial diversity and richness in mice with arthritis were significantly lower than those in acarbose treated groups (P < 0.05). The frequency of Firmicutes was significantly reduced after arthritis onset but was restored after treatment with acarbose. The frequency of Lactobacillus, Anaeroplasma, Adlercreutzia, RF39 and Corynebacterium was significantly higher in control groups than in acarbose or mitiligol treated, while Oscillospira, Desulfovibrio and Ruminococcus enriched in acarbose or mitiligol treated groups.

Conclusion: These data demonstrated that alpha-glucosidase inhibitors, in particular acarbose alleviated CIA. The therapeutic effect was through regulation of Th17/Treg cells in the intestinal mucosal immunity which might be resulted from impact of these drugs on gut microbial community. These inexpensive antidiabetic drugs with an excellent safety profile are potentially useful for management of rheumatoid arthritis.

Disclosure: L. Zhang, None; P. Song, None; X. Zhang, None; C. Metea, None; M. Schleisman, None; L. Karstens, None; E. Leung, None; J. Zhang, None; Q. Xu, None; Y. Liu, None; M. Asquith, None; C. Q. Chu, None.


Abstract Number: 1327
Decreased Inflammatory Arthritis in Human Serum Paraoxonase 1 Transgenic Mice

Christina Charles-Schoeman\textsuperscript{1}, Ani Shahbazian\textsuperscript{2}, Jennifer Wang\textsuperscript{3}, Victor Grijalva\textsuperscript{4} and Srinivasa T. Reddy\textsuperscript{4}, \textsuperscript{1}University of California, Los Angeles, Los Angeles, CA, \textsuperscript{2}Medicine-Rheumatology, University of California, Los Angeles, Los Angeles, CA, \textsuperscript{3}UCLA, Los Angeles, CA, \textsuperscript{4}Medicine-Cardiology, University of California, Los Angeles, Los Angeles, CA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Animal Models Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Paraoxonase 1 (PON1) is an HDL-associated protein, which hydrolyzes biologically active oxidized phospholipids and prevents oxidation of lipids in LDL and HDL. Increased lipid peroxidation and oxidized LDL have been implicated in the pathogenesis of rheumatoid arthritis (RA), and we previously reported low PON1 activity in active RA patients. The current work evaluated the effects of PON1 gene overexpression in the collagen antibody induced arthritis (CAIA) and the K/BxN serum transfer induced arthritis (STIA) models of RA.

Methods:

Mice homozygous for the PON1 human transgene [PON1Tg] and wild type littermate control mice [WT] were injected intraperitoneally (n = 10 per group) with either 5mg of collagen antibody cocktail (Chondrex) on day 0, and 50ug of LPS on day 3 (CAIA), or 200ul of pooled K/BxN serum on days 0 and 2 (STIA). Arthritis activity was assessed using caliper measurements of hind limbs and clinical scores 3 times weekly until sacrifice at 2 weeks. PON1 activity was assessed using paraoxon (paraoxonase), dihydrocumarin (lactonase), and phenylacetate (arylesterase) as substrates (\textit{A&R} 2013; 65: 2765). Lipids were assessed by standard assays, and a luminex cytokine/chemokine panel analysis was performed for STIA group of mice.

Results:

PON1Tg mice had significantly lower arthritis activity compared to WT mice in both CAIA and STIA models (Table). Arthritis activity was more severe in STIA. PON1 activity was strongly correlated with arthritis activity using all 3 assays of PON1 function ($r$ values= -0.5 to -0.7; all $p$ values<0.05); higher PON1 activity was associated with lower arthritis activity by joint scores. WT mice had significant increases in triglycerides (TG) and significant decreases in both total cholesterol (TC) and unesterified cholesterol (UC) post arthritis induction. In contrast, PON1Tg mice had no significant changes in TG, TC, or UC, but had significant increases in HDL cholesterol post arthritis induction in STIA. A trend was noted for lower serum IL-6 concentrations post arthritis in the PON1Tg mice (11±6 pg/ml) compared to WT mice (15±7 pg/ml), however no significant correlations of serum cytokine/chemokine levels with arthritis activity were noted.

Conclusion:

Overexpression of the human PON1 transgene in two mouse models of RA was associated with reduction of inflammatory arthritis activity, which correlated strongly with serum PON1 activity. Further investigation of mechanisms behind these findings is warranted to evaluate potentially novel lipid pathways for treatment of RA.
<table>
<thead>
<tr>
<th></th>
<th>PONTg</th>
<th>WT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CAIA Model</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PON1 activity [Pre]</td>
<td>268 ± 66*</td>
<td>121 ± 38</td>
</tr>
<tr>
<td>(nmoles/minute/ml)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (months)</td>
<td>8.6 ± 0.6</td>
<td>8.7 ± 0.6</td>
</tr>
<tr>
<td>Sex (% female)</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Final total joint score</td>
<td>3.7 ± 1.8*</td>
<td>5.8 ± 1.2</td>
</tr>
<tr>
<td>Final hind limb caliper assessment (average both limbs-mm)</td>
<td>319 ± 27</td>
<td>341 ± 23</td>
</tr>
<tr>
<td>PON1 activity [Post]</td>
<td>164 ± 45*</td>
<td>109 ± 28</td>
</tr>
<tr>
<td>(nmoles/minute/ml)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDL Cholesterol (mg/dL) [Pre]</td>
<td>86 ± 18</td>
<td>84 ± 22</td>
</tr>
<tr>
<td>HDL Cholesterol (mg/dL) [Post]</td>
<td>91 ± 21</td>
<td>91 ± 19</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL) [Pre]</td>
<td>133 ± 29</td>
<td>124 ± 24</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL) [Post]</td>
<td>116 ± 28</td>
<td>119 ± 22</td>
</tr>
<tr>
<td>Lactonase Activity [Pre]</td>
<td>24 ± 2*</td>
<td>14 ± 4</td>
</tr>
<tr>
<td>Lactonase Activity [Post]</td>
<td>23 ± 2*</td>
<td>14 ± 3</td>
</tr>
<tr>
<td>Arylesterase Activity [Pre]</td>
<td>134 ± 9*</td>
<td>91 ± 26</td>
</tr>
<tr>
<td>Arylesterase Activity [Post]</td>
<td>145 ± 12*</td>
<td>82 ± 12</td>
</tr>
<tr>
<td><strong>STIA Model</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PON1 activity [Pre]</td>
<td>241 ± 42*</td>
<td>64 ± 18</td>
</tr>
<tr>
<td>(nmoles/minute/ml)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (months)</td>
<td>3.6 ± 0.5</td>
<td>3.9 ± 0.9</td>
</tr>
<tr>
<td>Sex (% female)</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Final total joint score</td>
<td>7.4 ± 2.0*</td>
<td>9.9 ± 1.9</td>
</tr>
<tr>
<td>Final hind limb caliper assessment (average both limbs-mm)</td>
<td>375 ± 34</td>
<td>398 ± 19</td>
</tr>
<tr>
<td>PON1 activity [Post]</td>
<td>186 ± 46*</td>
<td>58 ± 17</td>
</tr>
<tr>
<td>(nmoles/minute/ml)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lactonase Activity [Pre]</td>
<td>18 ± 2*</td>
<td>9 ± 2</td>
</tr>
<tr>
<td>Lactonase Activity [Post]</td>
<td>23 ± 3*</td>
<td>13 ± 2</td>
</tr>
<tr>
<td>Arylesterase Activity [Pre]</td>
<td>142 ± 14*</td>
<td>71 ± 10</td>
</tr>
<tr>
<td>Arylesterase Activity [Post]</td>
<td>144 ± 13*</td>
<td>74 ± 12</td>
</tr>
<tr>
<td>HDL Cholesterol (mg/dL) [Pre]</td>
<td>48 ± 11</td>
<td>62 ± 25</td>
</tr>
<tr>
<td>HDL Cholesterol (mg/dL) [Post]</td>
<td>68 ± 19#</td>
<td>57 ± 19</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL) [Pre]</td>
<td>91 ± 19</td>
<td>101 ± 22</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL) [Post]</td>
<td>111 ± 27</td>
<td>88 ± 18#</td>
</tr>
<tr>
<td>Unesterified Cholesterol (mg/dL) [Pre]</td>
<td>8 ± 2</td>
<td>10 ± 3</td>
</tr>
<tr>
<td>Unesterified Cholesterol (mg/dL) [Post]</td>
<td>8 ± 2</td>
<td>6 ± 2#</td>
</tr>
<tr>
<td>Triglycerides (mg/dL) [Pre]</td>
<td>25 ± 7</td>
<td>12 ± 1</td>
</tr>
<tr>
<td>Triglycerides (mg/dL) [Post]</td>
<td>19 ± 5</td>
<td>23 ± 9#</td>
</tr>
<tr>
<td>Free Fatty Acids (mg/dL) [Pre]</td>
<td>51 ± 7</td>
<td>71 ± 33</td>
</tr>
<tr>
<td>Free Fatty Acids (mg/dL) [Post]</td>
<td>59 ± 12</td>
<td>58 ± 12</td>
</tr>
</tbody>
</table>

PONTg= mice homozygous for the PON1 human transgene. WT= wild type littermate control mice. CAIA = collagen antibody induced arthritis. STIA = serum transfer induced arthritis. Pre=prior to arthritis induction. Post= after arthritis induction.

*p<0.05 compared to WT. # p<0.05 compared to “Pre” value of same group and test.
A Dual ICOS/CD28 Antagonist ICOSL Variant Ig Domain (vIgDTM) Potently Suppresses Mouse Collagen-Induced Arthritis and Human Xenograft Graft Vs. Host Disease (GvHD)

Stacey Dillon¹, Katherine Lewis¹, Ryan Swanson², Lawrence Evans², Michael Kornacker³, Steve Levin², Martin Wolfson⁴, Erika Rickel², Susan Bort², Sherri Mudri¹, Aaron Moss¹, Michelle Seaberg¹, Janhavi Bhandari⁴, Sean MacNeil⁴, Joe Hoover⁴, Mark Rixon⁴ and Stanford Peng⁵, ¹Translational Sciences, Alpine Immune Sciences, Seattle, WA, ²Immunology, Alpine Immune Sciences, Seattle, WA, ³Protein Engineering, Alpine Immune Sciences, Seattle, WA, ⁴Protein Therapeutics, Alpine Immune Sciences, Seattle, WA, ⁵Clinical, R&D, Alpine Immune Sciences, Seattle, WA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Animal Models Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Our proprietary variant Ig domain (vIgD) platform creates novel, therapeutically-applicable protein domains with tailored specificity and affinity. These vIgDs are created through directed evolution of immunoglobulin superfamily (IgSF) proteins, which are key components of the immune system that include well-known family members such as PD-1, PD-L1, and CTLA-4. CD28 and Inducible T-cell Costimulator (ICOS) are two related costimulatory molecules within the IgSF which are expressed on T cells and interact with CD80/CD86 and ICOS ligand (ICOSL), respectively. Both play critical roles in T cell activation and adaptive immunity. We have used our vIgD platform to generate human ICOSL-Fc vIgDs capable of binding both ICOS and CD28, blocking the interaction of these costimulatory molecules with their respective receptors.

Methods: ICOSL-Fc molecules were evaluated in vitro in mixed lymphocyte reactions (MLR) generated using negatively-selected human pan T cells mixed with activated human monocyte-derived dendritic cells, and in vivo in standard mouse models of delayed type hypersensitivity (DTH), collagen-induced arthritis (CIA), and human-mouse xenograft PBMC-NSG™ graft versus host disease (GvHD).

Results: ICOSL-Fc fusion proteins containing variant ICOSL domains significantly attenuate T cell activation in vitro as assessed by suppressed proliferation and cytokine production in MLR. They also reduce mouse DTH reactions in vivo. ICOSL-Fc molecules mediate significant disease reduction, matching or exceeding CTLA-4-Ig comparators targeting only the CD28 pathway in mouse CIA, and in the human PBMC-NSG™ GvHD model. ICOSL-Fc suppresses the production of anti-collagen antibodies in CIA, likely reflecting the key roles CD28 and ICOS play in follicular helper T cell differentiation and T-dependent antibody responses.

Conclusion: Efficacy in vitro and in vivo of ICOSL-Fc is superior to wild-type ICOSL domains due to the induced alterations in affinity for cognate ligand (ICOS) and through specifically directed changes in ICOSL-Fc’s ability to bind additional counter-structures (i.e. CD28). Thus, vIgDs like these ICOSL variants can be developed to acquire unique biochemical properties that can potentially significantly enhance their therapeutic utility as immunomodulatory agents. This vIgD therapeutic platform has broad potential to enhance the activity of biologics in treatment of autoimmune and other disorders driven or subject to modulation by IgSF proteins, such as cancer and infectious diseases. Preclinical development of ICOSL-Fc has been initiated to support clinical studies.
A Quantitative Framework for Evaluating Drug Combination Treatment in Rat Collagen-Induced-Arthritis Model

Amy Meng², Julie Di Paolo², Shringi Sharma³ and Anita Mathias³, ¹Clinical Pharmacology, Gilead Sciences, Foster City, CA, ²Immunology and Inflammation Biology, Gilead Sciences, Foster City, CA, ³Gilead Sciences, Foster City, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Animal Models Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Filgotinib (FIL), a JAK1 inhibitor, and GS-9876, a SYK inhibitor, are currently being evaluated as once-daily monotherapy in subjects with rheumatoid arthritis (RA). A preclinical study was conducted to compare the efficacy of FIL + GS-9876 in combination versus monotherapy of each agent in a rat collagen-induced arthritis (CIA) model. A semi-mechanistic pharmacokinetic/pharmacodynamic (PK/PD) model was developed to 1) characterize the exposure (plasma concentration)-response...
(ankle diameter) relationship following mono- and combination therapy, and 2) provide a quantitative assessment of PD interaction between the two drugs.

**Methods:** Monotherapy (FIL at 3 doses 1, 3, or 5 mg/kg, QD or GS-9876 5 mg/kg BID) and the combination (FIL 1, 3 mg/kg QD and GS-9876 5 mg/kg, BID) treatments were administered to CIA rats. FIL was co-administered with the active metabolite to reflect the PK profile in humans. Dexamethasone at 0.075 mg/kg QD was the positive control. Dosing was initiated at the peak of inflammation (day 17-20) and continued through the chronic disease phase until day 34. Population PK models were developed to characterize FIL and GS-9876 concentration versus time profiles. Disease progression, assessed as the change in ankle diameter over time, was described by equation 1 (indirect response model), and drug effect (monotherapy and combination) by equations 2 and 3 (Figure 1; Ref: Minto et al., 2000). The analysis was conducted using a nonlinear mixed-effects modeling approach (NONMEM 7.3) and R v3.3.2 was used for processing/visualizing data.

**Results:** The model adequately described the PK of FIL/GS-9876 and the exposure-response relationship, following monotherapy and combination therapy. The results indicated a dose/exposure dependent reduction in ankle paw diameter following FIL monotherapy. Furthermore, a synergistic effect on efficacy was observed (based on an estimated β value >1) following treatment with the combination compared with either agent alone. Simulations (of various dose levels) indicated an exposure dependent increase in efficacy following combination treatment, with a plateau at doses ≥ FIL 3 mg/kg QD + GS-9876 5 mg/kg BID.

**Conclusion:** The PK/PD model demonstrated a synergistic interaction between FIL and GS-9876, thereby suggesting the utility of simultaneously targeting the JAK and SYK receptor pathways for RA. Furthermore, the model provides a quantitative framework for screening various drug combinations (of two or more drugs) in CIA rats and may help in selecting efficacious combinations for clinical assessment.


**Disclosure:** A. Meng, Gilead Sciences, 3; Gilead Sciences, 1; J. Di Paolo, Gilead Sciences, 3; Gilead Sciences, 1; S. Sharma, Gilead Sciences, 3; Gilead Sciences, 1; A. Mathias, Gilead Sciences, 3; Gilead Sciences, 1.

**Abstract Number:** 1330

**Rhesus Theta Defensin 1 (RTD-1) Suppresses Disease-Associated Genes and Induces Anti-Inflammatory Expression Signature in Synovial Tissues of Rat Model of Rheumatoid Arthritis**
Background/Purpose: Theta (θ) defensins are the only known macrocyclic peptides found in the Animal kingdom and are exclusively expressed in Old World monkeys. θ-defensins were discovered as antimicrobial effector molecules in rhesus macaque neutrophils, but later found to possess immune regulatory activity. Rhesus macaque theta defensin-1 (RTD-1), the prototype θ-defensin, down-regulates expression of pro-inflammatory cytokines by macrophages stimulated with TLR agonists, reduces lethality in bacteremic and severely septic mice and also dose-dependently inhibits MAP kinase and NF-κB pathways in LPS-stimulated monocytes and macrophages. We recently showed that systemic administration of RTD-1 to rats with established pristane-induced arthritis (PIA), a model of rheumatoid arthritis (RA) rapidly arrests and induces resolution of arthritis. Pathogenesis of RA involves inflammation of the synovium, joint erosion and the dysregulation of immune signaling and cytokine gene expression pathways. We hypothesized that RTD-1 regulates the gene expression and signaling pathways in inflamed synovial tissues.

Methods: PIA was induced in DA rats and RNA-seq analysis was performed on synovial tissue RNA harvested from naïve and diseased rats, and from rats with PIA that were treated with vehicle or RTD-1. Bioinformatics analysis was used to investigate changes in gene expression in treated and untreated animals. These changes in gene expression were validated by quantitative real time PCR. Ingenuity Pathway Analysis (IPA) was used to identify signaling pathway targets of RTD-1.

Results: RNA-seq analysis revealed differential expression of 258 and 107 synovial tissue genes by 3 days and 5 days of RTD-1 treatment respectively (False Discovery Rate p < 0.05; fold change > ±1.5-fold). qPCR analysis of 12 genes confirmed the RTD-1 regulation detected with RNA-seq. Bioinformatics analyses revealed that RTD-1 treatment modulates genes involved in leukocyte migration, extracellular matrix, rheumatoid arthritis, regulation of cytokine activity and in additional immune response pathways. Analysis of gene expression data by IPA identified, among others, inhibition of pathways stimulated by proinflammatory cytokines such as TNFα, IL-1β, IL-6 and activation of anti-inflammatory nuclear receptor pathways after 5 days of RTD-1 treatment, consistent with resolution of disease.

Conclusion: RTD-1 regulates genes and signaling pathways that are operative in RA and experimental arthritis and induces an anti-inflammatory gene signature in treated PIA rats. RTD-1 regulated genes and pathways include targets for FDA-approved treatments for RA underscoring the potential for RTD-1 as a future new treatment for RA.

Disclosure: P. Tongaonkar, None; V. Punj, None; A. Subramanian, None; D. Tran, Oryn Therapeutics, 3; K. Trinh, None; J. Schaal, None; P. S. Gulko, Oryn Therapeutics, 9; A. Oullette, Oryn Therapeutics, 4; M. Selsted, Oryn Therapeutics, 4.


Abstract Number: 1331

A Pathogenic Role of Porphyomonas Gingivalis Fimbriae (FimA) in Periodontitis-Associated Rheumatoid Arthritis

Ji-Won Kim¹, Jennifer Lee², Yeon-Sik Hong³, Sung-Hwan Park² and Ji Hyeon Ju², ¹Medicine, Division of Rheumatology, Department of Internal Medicine, Seoul St. Mary’s Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea, Republic of (South), ²Division of Rheumatology, Department of Internal Medicine, Seoul St. Mary’s Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea, Republic of (South), ³Division of Rheumatology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea, Republic of (South)

First publication: September 18, 2017
Background/Purpose: Periodontitis induced by oral pathogen *Porphyromonas gingivalis* (Pg) has been suggested to be associated with rheumatoid arthritis (RA). Pg peptidyl arginine deiminase-mediated citrullination and induction of anti-citrullinated protein antibodies seems to contribute to the development of RA, however, the exact mechanism remains unknown. We hypothesized that the fimbriae -flexible appendages on the bacterial cell surface- of Pg (FimA) play an important role in the link between Pg infection and RA development by serving as attachment pili and helping invasion into host cells of RA patients.

Methods: Collagen induced arthritis (CIA) induced mice were periodontally infected with Pg or Pg pre-incubated with anti FimA antibody (Ab). The number of oral anaerobic bacteria, and the degree of alveolar bone loss was determined to examine the severity of periodontitis. Joint inflammation and destruction was investigated by histological analysis and micro CT. Bacterial invasion into human gingival fibroblast (HGF) cell line or RA synovial fibroblast (RASF) was measured by electron microscopy and immunohistochemical analysis.

Results: Oral inoculation of Pg in CIA mice increased the number of total oral anaerobic bacteria, aggravated alveolar bone loss, and exacerbated synovitis and joint bone destruction. However, pre-incubation of Pg with anti-FimA Ab led to a significant reduction in the severity of both oral disease and arthritis. Moreover, FimA Ab pretreatment attenuated Pg attachment and aggregation on HGF and RASF. Pg was found in the joints of CIA mice, which suggests that orally inoculated Pg migrated to inflamed joints carried within the dendritic cells, macrophages, and neutrophils recruited to arthritic joints. However, FimA Ab treated-Pg was not found in the joints of CIA mice.

Conclusion: These results suggest that Pg fimbriae play a pathogenic role in Pg infection associated RA development. Disrupting Pg fimbriae suppresses the periodontitis and bacterial migration to the arthritic joints and thus, ameliorates joint inflammation in RA.

Disclosure: J. W. Kim, None; J. Lee, None; Y. S. Hong, None; S. H. Park, None; J. H. Ju, None.


Abstract Number: 1332

Periostin Deficiency Exacerbates Joint Inflammation and Bone Destruction in Mouse Models of Rheumatoid Arthritis

Yun-Hong Cheon, Division of Rheumatology, Department of Internal Medicine, Gyeongsang National University School of Medicine, Jinju, Korea, Republic of (South)  
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017  
Session Title: Rheumatoid Arthritis – Animal Models Poster II  
Session Type: ACR Poster Session B  
Session Time: 9:00AM-11:00AM

Background/Purpose:

Periostin (POSTN), a matricellular protein, is involved in many fundamental biological processes such as bone metabolism, cell proliferation, cell invasion, and angiogenesis. Also, POSTN has been shown to be involved in many aspects of inflammation, wound fibrosis and recruitment several immune cells. Although POSTN expression has been reported to promote migration and invasion of fibroblast-like synoviocyte (FLS) in vitro, there is no study to investigate the role of POSTN in mouse models of rheumatoid arthritis (RA). This study was performed to assess the function of POSTN in 3 mouse models of arthritis, K/BxN serum transfer arthritis (STA), collagen-induced arthritis (CIA) and collagen-antibody induced arthritis (CAIA).

Methods:
Periostin level in synovial fluid from RA and osteoarthritis (OA) patients were measured by ELISA. The expression of periostin FLS was stained by immunohistochemistry. STA, CIA and CAIA was induced in POSTN⁻/⁻ and POSTN⁺/+ mice. Arthritis was monitored in 3 mouse models of arthritis using defined criteria (clinical and histologic). Osteoclastogenesis was assessed using bone marrow monocytes (BMM) cultures from POSTN⁻/⁻ and POSTN⁺/+ mice.

Results:

POSTN level in synoviocyte tissue were increased in patient with RA compare to OA patient. In STA studies, the clinical score and hind paw thickness were significantly increased in POSTN⁻/⁻ mice compared with POSTN⁺/+ mice. Mean histologic severity scores including synovial inflammation, bone erosion and cartilage damage were increased in diseased joints from POSTN⁻/⁻ mice compared with those from POSTN⁺/+ mice. The IL-1β was increased in the serum, and TNF-α, IL-1β, and MMPs were increased in the ankle of POSTN⁻/⁻ mice than wild type control. BMMs from POSTN⁻/⁻ mice showed increased osteoclast formation compared with BMMs from POSTN⁺/+ mice. Similarly, in CAIA and CIA model, both mean clinical severity scores and ankle joint swelling were significantly increased in POSTN⁻/⁻ mice compared with POSTN⁺/+ mice.

Conclusion:

This study suggests that POSTN contributes to pathogenesis of RA and might have a potential protective role in RA.

Disclosure: Y. H. Cheon, None;


Abstract Number: 1333

Mortality of Tumor Necrosis Factor Transgenic Arthritic Mice with Interstitial Lung Disease Occurs with Pulmonary Arteriole Thickening and Right Ventricular Hypertrophy but Is Not Associated with Inducible Nitric Oxide Synthase Dependent Inflammatory Cell Infiltration

Richard Bell¹, Emily Wu¹,², Homaira Rahimi³ and Edward Schwarz¹,⁴,⁵, ¹Center for Musculoskeletal Research, University of Rochester, Rochester, NY, ²Department of Immunology, Microbiology, and Virology, University of Rochester, Rochester, NY, ³Rheumatology, University of Rochester/Golisano Children's Hosp, Rochester, NY, ⁴University of Rochester, Rochester, NY, ⁵Univ of Rochester Med Ctr, University of Rochester School of Medicine and Dentistry, Rochester, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Animal Models Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Rheumatoid arthritis associated interstitial lung disease (RA-ILD) occurs in up to 15% of RA patients, whose median survival expectancy after diagnosis is only 2.6 years. The tumor necrosis factor-transgenic (TNF-Tg) mouse model of RA develops cellular ILD with increased mortality, which is presumed to be from lung and cardiac failure secondary to ILD. In the context of arthritis, inducible nitric oxide synthase (iNOS) is detrimental to clearance of immune cells from the joint, and selective iNOS inhibitors restore lymphatic flow. Thus, we hypothesize that ILD pathology is decreased in iNOS⁻/⁻ x TNF-Tg mice.

Methods: To test this, female TNF- Tg, iNOS⁻/⁻, iNOS⁻/⁻ x TNF-Tg and WT littermates were weighed and scanned with μCT to investigate differences in ILD at 2, 3 and 4 months (Mixed Model with Tukey’s Post-Hoc, ***p<0.001). The mice were euthanized at 4 months to perform histology on the hearts and lungs for histomorphometry (ANOVA, **p<0.01). In a separate cohort, iNOS⁻/⁻ x TNF-Tg, TNF-Tg and WT littermate were aged to investigate lifespan differences.
Results: There were no differences in weight or lifespan between the iNOS<sup>−/−</sup> x TNF-Tg and TNF-Tg, both failing to gain weight from 2mo and dying at 5mo. However, μCT 3D reconstructions of 4 months old WT (A), iNOS<sup>−/−</sup> (B), TNF-Tg (C) and iNOS x TNF-Tg (D) show preservation of air space and decrease in tissue volume in the iNOS<sup>−/−</sup> x TNF-Tg (Fig 1, Air = Green, Tissue = Orange). Quantification reveals a significant increase in air volume at 3 and 4 months in iNOS<sup>−/−</sup> x TNF-Tg compared to TNF-Tg (E, 3mo: 229±26μm<sup>3</sup> vs 116±32μm<sup>3</sup>, p<0.001; 4mo: 225±48μm<sup>3</sup> vs 133±42μm<sup>3</sup>, p<0.001), similar to WT and iNOS<sup>−/−</sup> (4mo: 219±51μm<sup>3</sup> and 227±28μm<sup>3</sup>). Furthermore, tissue volume was significantly decreased at 4mo in iNOS<sup>−/−</sup> x TNF-Tg compared to TNF-Tg (F, 438±55μm<sup>3</sup> vs 606±51μm<sup>3</sup>, p<0.001). Lung histomorphometry confirmed these μCT results finding more white area and less total cells in iNOS<sup>−/−</sup> x TNF-Tg compared to TNF-Tg. Interestingly, iNOS<sup>−/−</sup> x TNF-Tg and TNF-Tg had severe arteriole thickening (Green Arrows in Fig 2, B and C) in the lung (Fig 2 D, 0.01±0.01mm<sup>2</sup> and 0.007±0.005mm<sup>2</sup>) compared to WT (0.002±0.001mm<sup>2</sup>, p<0.001). The right ventricle was also thicker in iNOS<sup>−/−</sup> x TNF-Tg and TNF-Tg than WT (Fig 2 H, 726±108μm<sup>2</sup>, 664±35μm<sup>2</sup> vs 359±85μm<sup>2</sup>, p<0.01).

Conclusion: This study demonstrates for the first time that the cellularity of ILD in this model of RA is iNOS dependent, and is not associated with decreased lifespan. Moreover, lung arteriole thickening and right ventricular hypertrophy are consistent with pulmonary hypertension, likely causing cardiac failure and increased mortality in TNF-Tg mice.

Disclosure: R. Bell, None; E. Wu, None; H. Rahimi, None; E. Schwarz, Janssen Pharmaceutica Product, L.P., 9,Lilly Inc., 9.


Abstract Number: 1334
Identification of Key Regulators for Resolution of Chronic Inflammatory Arthritis through a Systems Approach

Jin-Sun Kong Sr. 1, Ji-Hwan park 2, Seung-Ah Yoo Sr. 1, Jung Hee Koh 3, Daeehee Hwang 4 and Wan-Uk Kim Sr. 5, 1 The Catholic University of Korea, Center for Integrative Rheumatoid Transcriptomics and Dynamics, seoul, Korea, Republic of (South), 2 Center for Plant Aging Research, DGIST, Daegu 42988, South Korea, Daegu, Korea, Republic of (South), 3 Division of Rheumatology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea, Republic of (South), 4 Center for Plant Aging Research, DGIST, Daegu 42988, South Korea, Department of New Biology, DGIST, Daegu 42988, South Korea, Daegu, Korea, Republic of (South), 5 The Catholic University of Korea, Department of Internal Medicine, seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Animal Models Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Collagen-induced arthritis (CIA), a representative animal model of chronic inflammatory arthritis, follows phases of induction, peak of inflammation and resolution. This study aims to identify the key regulator genes that change with time course in animal models of rheumatoid arthritis through dynamics analysis.

Methods: We first investigated gene expression profiles in the synovial tissues of mice with CIA at early, peak, resolution phase of arthritis using microarray analysis and identified differentially expressed genes (DEGs) associated with arthritis resolution. We built a resolution-associated network model describing interactions among these DEGs and then selected three hub-like genes from the network model, which can significantly contribute to regulating function of the resolution-associated network. We examined the level of gene expression in the synovial tissues and the function of selected genes in resolution of CIA.

Results: From time-course gene expression profiles of CIA synovial tissues, we identified 2237 resolution-related genes, and found that these genes were significantly associated with Toll-like receptor and T and B cell receptor signaling pathways. Network analysis of these resolution-related genes further selected three hub genes, Itgb1, RPS3 and YwhaZ, that can be predominantly responsible for arthritis resolution. These genes were highly expressed in independent synovial tissues at resolution phase. Particularly, the expression of Itgb1, RPS3 and YwhaZ was elevated in regulatory T cells and alternatively-activated macrophages (M2) that are involved in restoration of chronic inflammation. Moreover, recombinant Itgb1, RPS3, and YwhaZ dose-dependently reduced pro-inflammatory cytokine expression in peritoneal macrophages and splenocytes. To test a potential application of proteins from selected genes for detecting the arthritis resolution, the levels of proteins from the selected genes also were analyzed in mice serum and urine of patients with rheumatoid arthritis (RA). As a result, serum YwhaZ concentration was higher at resolution phase than at peak phase among the three proteins from selected genes. Additionally, YwhaZ concentrations in the urine of patients with rheumatoid arthritis were associated with the degree of treatment response; YwhaZ levels increased significantly after treatment in good response group (n=23) while the protein level before and after treatment were not different in moderate (n=12) or none (n=25) response group.

Conclusion: Our comprehensive analysis of gene profile contributing to arthritis resolution reveals novel anti-arthritic genes, Itgb1, RPS3, and YwhaZ. We anticipate that Itgb1, RPS3 and YwhaZ will be novel targets for predict the arthritis resolution and could be therapeutic targets for chronic inflammatory arthritis.

Disclosure: J. S. Kong Sr., None; J. H. park, None; S. A. Yoo Sr., None; J. H. Koh, None; D. Hwang, None; W. U. Kim Sr., the National Research Foundation of Korea, 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/identification-of-key-regulators-for-resolution-of-chronic-inflammatory-arthritis-through-a-systems-approach

Abstract Number: 1335

p62/SQSTM1 Modulates Bone Erosions in a Murine Model of Rheumatoid Arthritis
Rheumatoid arthritis (RA) is characterised by massive bone erosions leading to irreversible joint destructions. In this context, the multi-adapter protein p62/SQSTM1 is of interest because apart from its involvement in autophagy, p62/SQSTM1 also interacts with TNFalpha signalling pathways and has the ability to bind directly to TRAF6 resulting in the stimulation of osteoclastogenesis. Here, we sought to investigate, whether based on these signalling characteristics, p62/SQSTM1 is functionally involved in human RA and in animal models of the disease.

Methods:

Tissue samples of RA (n=30) and OA (n=9) patients were analysed to identify correlations between p62 expression and RA diagnosis, disease duration and medication. Furthermore, mice were generated that carry a shortened, but functional mutant of p62 with defective signal transduction domains (p62aaD69-251) for interbreeding studies with arthritic hTNFtg mice. The resulting genotypes (wt, hTNFtg, p62aaD69-251 and hTNFtg/ p62aaD69-251/wt) were scored for clinical parameters (paw swelling, grip strength, weight) for 14 weeks. To quantify the extent of inflammation, cartilage degradation and number of osteoclasts, joints of 14 wks old mice were embedded into paraffin and stained with toluidine blue and TRAP. In addition, bone marrow derived monocytes (BMDMs) were isolated from all genotypes and osteoclastogenesis was studied using an established osteoclast formation assay. To investigate the underlying signalling pathways, cells were treated with TNFalpha at different time points, and MAPK activation was studied by Western blot analyses.

Results:

A significant correlation of p62 expression with RA and prolonged disease duration and specific treatment was found (p<0.05). In our animal studies, histology revealed only minor changes in the number and size of osteoclasts between p62aaD69-251 and wt animals suggesting that under physiological conditions, regulatory mechanisms compensate for the lack of the signal transduction domains of p62. Compared to wt cells, however, BMDMs of p62aaD69-251 mice showed a significantly increased osteoclastogenic potential (+28.9% vs hTNFtg BMDMs), in particular when stimulated with TNFalpha in vitro (+30.6% vs hTNFtg BMDMs). Crossing of p62aaD69-251 mice with hTNFtg animals resulted in a dramatic increase in the severity of joint damage in the hTNFtg/p62aaD69-251/wt mice as determined clinically and by histomorphometry, showing a significant increase of inflammation area (+113.9% vs hTNFtg) and the number and size of osteoclasts in vivo (+278.5% vs hTNFtg). Interestingly, MAPK activation studies only showed minor differences between wt and p62aaD69-251 BMDMs.

Conclusion:

In summary, our human expression data as well as the functional mouse data suggest that p62 is an important regulator of TNFalpha mediated joint damage. They indicate that the loss of the TRAF6 and aPKCs binding domains of p62 has important consequences for osteoclastogenesis under inflammatory conditions.

Disclosure: A. Korb-Pap, None; A. Römer-Hillmann, None; M. Heitzmann, None; M. Kato, None; K. Klein, None; C. Ospelt, None; S. Gay, None; S. Buergis, None; T. Pap, Orthogen, 5; T. Weide, None; A. Gessner, None; H. Pavenstädt, None.
Unique Role for miR429 in RA and Acute Model of Arthritis

Jonatan Hervoso¹, W. Alexander Stinson¹, Yuxuan Du², Sarah Arwani¹, Ellen Cealey¹, David A. Fox¹ and M. Asif Amin¹, ¹Division of Rheumatology and Clinical Autoimmune Center of Excellence, University of Michigan, Ann Arbor, MI, Ann Arbor, MI, ²Division of Rheumatology and Clinical Autoimmune Center of Excellence, University of Michigan, Ann Arbor, MI, Ann Arbor, MI, MI

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Animal Models Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is characterized by inflammation and subsequent infiltration of peripheral blood monocytes (MNs) into the synovial tissue (ST). Micro (mi)RNAs are non-coding RNAs which regulate many physiological and pathological functions at the posttranscriptional level. We performed miRNA PCR array and found a panel of miRNAs, including miR429, were highly expressed in response to TNF-α in MNs. Hence we examined the contribution miR429 and one of its target genes, PAK2, in MN chemotaxis and acute inflammatory arthritis.

Methods: The expression of miR429 in RA and NL MNs was assessed via quantitative (q)PCR. RA MNs and RA fibroblast-like synoviocytes (FLS) were transfected with inhibitors and mimics of miR429 for 24 hours. Then these cells were stimulated with TNF-α for 25 minutes to determine phosphorylation of signaling molecules by Western blotting. We transfected U937 cells, a human leukemic MN lymphoma cell line, and NL MNs with miR429 mimics and inhibitors and performed chemotaxis. To investigate the role of miR429 in acute inflammation, miR429 shRNA or control shRNA were packaged into lentivirus and injected into mouse knees 30 minutes prior to administration of TNF-α or Zymosan. Mouse knee circumference was measured before injections and again 24 hours later. Following euthanasia, knees were harvested for immunofluorescence staining or homogenized for analysis of inflammatory cytokines.

Results: Non-stimulated RA MNs had a 2.6 fold increase in miR429 expression compared to non-stimulated Normal (NL) MNs by qPCR. We also found that miR429 is inducible, TNF-α induced significantly higher miR429 expression in NL MNs compared to non-stimulated MNs. With regards to MN migration, inhibition of miR429 decreased migration of U937 cells and MNs in response to MCP1/CCL2, suggesting a role for miR429 in MN migration. TNF-α upregulation of phospho-Erk, -JNK and -NFkB was decreased when RA MNs were transfected with miR429 inhibitor. Similarly, a decrease of TNF-α induced phospho-Erk, -JNK and -NFkB was observed in RA FLS. Furthermore we also determined that a miR429 target gene, PAK2, was downregulated when miR429 was inhibited in RA MNs and RA FLS. Additionally, TNF-α and Zymosan treated mouse knee swelling was significantly reduced in mice injected with miR429 inhibitor compared to control, indicating that miR429 is critical to arthritis development in vivo. We also found decreased ingress of leukocytes into mouse knee cryosections treated with miR429 inhibitor.

Conclusion: miR429 expression is increased with TNF-α stimulation and has higher levels in RA compared to NL MNs. miR429 plays an essential role in the migration of MNs and also regulates phosphorylation of signaling molecules and PAK2 transcription factor. Additionally mice treated with miR429 inhibitor showed decreased inflammation indicating the importance of miR429 in acute inflammation and MN recruitment. This data suggests that miR429 may be a therapeutic target in MN dependent diseases.

Disclosure: J. Hervoso, None; W. A. Stinson, None; Y. Du, None; S. Arwani, None; E. Cealey, None; D. A. Fox, None; M. A. Amin, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/unique-role-for-mir429-in-ra-and-acute-model-of-arthritis

Abstract Number: 1337

ASN002, a Novel Dual SYK/JAK Inhibitor, Demonstrates Strong Efficacy in a Rat Model of Collagen-Induced Arthritis
SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Animal Models Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Spleen tyrosine kinase (SYK) and Janus kinase (JAK) mediate signaling in immune cells and hematopoietic cells important for the initiation and progression of rheumatoid arthritis (RA). JAK inhibitors have demonstrated clinical efficacy in RA and exert their biological activity principally by blockade of proinflammatory cytokine signaling. ASN002 is a novel potent dual inhibitor of SYK and JAK kinases, currently in clinical development for auto-immune (atopic dermatitis) and oncology indications. To date, more than 70 patients and subjects have received single or multiple oral, daily doses of ASN002. Here we demonstrate that ASN002 inhibits both SYK and JAK signaling pathways and cellular functions in both immune cells and osteoclasts; and is efficacious in both early and late stage rat models of collagen induced arthritis (CIA).

Methods: Cell lines, osteoclast progenitors, fresh human peripheral blood mononuclear cells (PBMCs) or isolated immune cells were cultured with various stimulating agents and inhibition of JAK or SYK mediated cell signaling or functions were measured by flow cytometry, proliferation assays or cytokine production. Osteoclast differentiation and bone resorption were assessed using the tartrate resistant acid phosphatase (TRAP) activity assay and collagen type 1c telopeptide (CTx) release by ELISA. ASN002, was tested for in vivo efficacy in an early and late stage rat CIA model. Dosing was initiated at either Day 14 (early model) or Day 18 (late model). Efficacy measures were arthritic scores, edema, and histopathology and radiographic assessments of the ankles.

Results: ASN002 is a potent inhibitor of SYK, JAK1, JAK2, JAK3 and TYK2 kinases with IC50 values of 5, 46, 4, 11, and 8 nM in biochemical assays respectively. In mechanistic cell-based studies, ASN002 strongly suppressed the SYK and JAK family kinase signaling pathways as measured by phosphorylation of LAT (a SYK substrate), and phosphorylation of signal transducers and activators of transcription (STAT). Cytokine induced phosphorylation of STAT in fresh human PBMCs was also suppressed. Human T and B cell proliferation and other cellular functions such as cytokine release were inhibited by AN002 at nM levels. ASN002 also demonstrated nM level inhibition of osteoclast progenitor differentiation and bone resorption by osteoclasts. In the rat CIA model, ASN002 showed dose-dependent efficacy (3-30 mg/kg/day) and significantly reduced arthritic scores and paw edema in both early and late stage models. ASN002 showed a greater decrease in histopathology scores (82%) at 10 mg/kg, than either Tofacitinib (39%) or Fostamatinib (37%) alone.

Conclusion: ASN002 is an orally bioavailable, potent dual inhibitor of SYK and JAK kinases. It effectively inhibits SYK and JAK mediated cell signaling and functions. ASN002 significantly improved all efficacy measures in the rat CIA model, at lower exposures than those achieved in human studies to date. These data support the development of ASN002 for the treatment of autoimmune and inflammatory diseases, including rheumatoid arthritis and psoriatic arthritis. A Phase Ib study in patients with atopic dermatitis is in progress.


Abstract Number: 1338

Important Role of CD11c+ Dendritic Cells in Inflammatory Arthritis

Antonia Puchner¹, Victoria Saferding¹, Michael Bonelli², Harald Leiss³, Gerhard Krönke⁴, René Pfeifle⁵, Josef S. Smolen⁶, Kurt Redlich⁷ and Stephan Blüml⁶, ¹Medical University of Vienna, Austria, Vienna, Austria, ²Rheumatology, Medical University of Vienna, Vienna, Austria, ³Rheumatology, Medical University Vienna, Vienna, Austria, ⁴Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, Erlangen, Germany., Erlangen, Austria, ⁵Department of Internal Medicine 3 and Institute for Clinical Immunology, University of Erlangen-
Dendritic cells (DCs) are important antigen presenting cells (APCs) and therefore they play an important role in bridging the innate and the adaptive immune response. DCs can be divided in different subsets with specific functions. As powerful APCs, DCs are thought to play an important role in the induction of autoimmune diseases such as rheumatoid arthritis. However, the active role of DCs in joint inflammation is not known yet.

Methods:
We analyzed histological sections of K/BxN serum transfer arthritis as well as hTNFtg arthritis for the presence of CD11c+ cells by immunohistochemistry. We also performed synovial biopsies and analyzed the cellular composition of the inflammatory infiltrate with respect to DCs. We used CD11c-diptheria toxin receptor (DTR) transgenic mice, which express the human diphtheria-toxin receptor under the CD11c promoter, allowing for specific depletion of CD11c+ cells by administration of diphtheria toxin (DT). K/BxN serum transfer arthritis was induced, and mice were given either DT or PBS or in wt and BARF3 deficient mice. In addition CD11c DTR mice were crossed into hTNFtg animals and also received either DT or PBS. The severity of arthritis was determined clinically and histologically.

Results:
We show that Cd11c+ cells are present in significant numbers in the synovia of K/BxN and TNF driven arthritis. Both CD8+ CD11c+ and CD11b+CD11c+, can be found in synovial tissue. Upon depletion of CD11c+ cells clinical signs of K/BxN serum transfer arthritis were significantly reduced. Histological analysis found reduced synovial inflammation after the depletion of CD11c+ cells in K/BxN arthritis. In addition, local bone destruction and the number of osteoclasts was also significantly reduced. Analysis of K/BxN arthritis in wt mice and BATF3-/- mice, which lack a subset of DCs, namely CD8+CD11+ DCs, revealed no difference in arthritis severity between the two groups. In addition to K/BxN arthritis, we found that also in TNF-driven arthritis depletion of CD11c+ cells led to a striking reduction of synovial inflammation and a complete depletion of osteoclasts.

Conclusion: These data show that in addition to initiating an adaptive immune response, CD11c+ dendritic cells, are also involved in innate effector mechanisms of inflammatory arthritis. Especially CD11b+CD11c+ and monocyte derived inflammatory seem to play a role in inflammatory arthritis, suggesting that they could be an important therapeutic target for patients suffering from inflammatory arthritis.

Disclosure: A. Puchner, None; V. Saferding, None; M. Bonelli, None; H. Leiss, None; G. Krönke, None; R. Pfeifle, None; J. S. Smolen, AbbVie, Eli Lilly, Janssen, MSD, Pfizer Inc, Roche, 2,AbbVie, Amgen, AstraZeneca, Astro, Celgene, Celtrion, Eli Lilly, GSK, ILTOO, Janssen, MedImmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, UCB, 5,AbbVie, Amgen, AstraZeneca, Astro, Celgene, Celtrion, Eli Lilly, GSK, ILTOO, Janssen, MedImmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, UCB, 8; K. Redlich, None; S. Blüml, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/important-role-of-cd11c-dendritic-cells-in-inflammatory-arthritis

Abstract Number: 1339

Role of Hexokinase-2 in Synovial Lining Hypertrophy in Murine Arthritis

Marta Fernandez Bustmanate, Jeffrey Smith, Adam Paul Croft, Gary S. Firestein, Chris Buckley, Shigeaki Miyamoto and Monica Guma, Medicine, UCSD, San Diego, CA, Pharmacology, UCSD, La Jolla, CA, Institute of Inflammation and Ageing,
SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Animal Models Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Recent studies indicate that fibroblast-like synoviocyte (FLS) glucose metabolism is altered in rheumatoid arthritis (RA). Hexokinases (HKs) catalyze the first step in glucose metabolism. HK2, which constitutes the principal HK inducible isoform, is mostly expressed in the lining of RA synovial tissue but not in OA tissue. Fibroblast-like synoviocytes (FLS) are a key component of RA hypertrophic and invasive synovium, and display unique aggressive features, including increased migration and invasion. We hypothesize that HK2 expression in FLS contributes to the synovial lining hypertrophy and plays a critical role in the arthritic joint bone and cartilage damage.

Methods: HK2 expression was determined in joints from wild-type (WT) and arthritic mice by immunohistochemistry (IHC). HK2 expression by qPCR in CD45negPDPNpos subpopulation obtained after collagenase digestion and magnetic beads isolation was also performed. To study the effect of HK2 overexpression, we injected 1010 particles of adenovirus (ad) carrying HK2 (ad-HK2) or GFP (ad-GFP) into the right or left knee respectively in WT mice. After 14 days, we collected the knees and H&E and safranin O staining was performed. Double color IHC was performed to confirm HK2 overexpression in FLS and to determine FLS activation with alpha-smooth muscle active (a-sma) staining. We also used HK2F/F mice, harboring Col1a1-Cre, in order to delete HK2 in non-hematopoietic cells including FLS. Serum transfer K/BxN arthritis was induced injecting intraperitoneally 150ml of serum. Clinical scores were assessed daily and histopathological studies were performed on joints harvested on day 12.

Results: HK2 was highly expressed by IHC in the synovial lining of arthritic joints from mice after serum transfer K/BxN arthritis. After CD45neg enrichment, PDPNpos cells had higher expression of HK2 in the arthritic joint (1.04 ± 0.4 in normal joints vs 1.8 ± 0.3 in arthritic joints; p=0.03). Over-expression of HK2 after intra-articular injection of ad-HK2 in normal knees dramatically increased synovial lining thickness (p=0.03). Double color IHC confirmed HK2 expression in FLS after ad-HK2 injection and showed elevated a-sma expression in the hypertrophic lining. Safranin O staining revealed a higher proteoglycan loss in the cartilage from ad-HK2 injected knees compared with control knees. Finally, deletion of HK2 in Col1a1 expressing cells significantly decreased arthritis severity (clinical score at day 12 was 9 ± 2.5 in WT mice vs. 6.1 ± 3.2 in HK2F/FCol1a1-Cre; p=0.02). Histopathological studies at day 12 showed significantly less synovial hypertrophy (p=0.04), infiltration (p=0.05); bone erosion (p=0.05) and cartilage damage (p=0.03).

Conclusion: HK2 expression is elevated in the synovial intimal lining of arthritic mice. Over-expression of HK2 in the synovial lining promotes hypertrophy of healthy synovium as well as FLS activation and cartilage damage. HK2 deletion in FLS ameliorates disease severity of arthritis. Taken together, the data suggest that HK2 is involved in FLS activation and synovial hypertrophy and could play a role in RA. HK2 inhibitors could serve as a new therapeutic option for the treatment of RA.

Disclosure: M. Fernandez Bustmanate, None; J. Smith, None; A. P. Croft, None; G. S. Firestein, None; C. Buckley, None; S. Miyamoto, None; M. Guma, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/role-of-hexokinase-2-in-synovial-lining-hypertrophy-in-murine-arthritis

Abstract Number: 1340

Is Depression in Patients with Rheumatoid Arthritis Associated with Disease Activity? Comparative Study between Germany and Brazil

Harriet Morf1, Olga Seifert2, Geraldo Castelar-Pinheiro3, Ana Beatriz Vargas-Santos4 and C Baerwald5, 1Department of Internal Medicine, University Hospital, Erlangen, Germany, 2University of Leipzig, Leipzig, Germany, 3Universidade do Estado do Rio de Janeiro - UERJ, Rio de Janeiro, Brazil, 4Internal Medicine - Rheumatology, State University of Rio de Janeiro, Rio de Janeiro, Brazil, 5Department of Rheumatology, University of Leipzig, Germany, Leipzig, Germany
Rheumatoid Arthritis (RA) can be associated with psychologic disorders and especially depression. About 13–20% of patients have clinical significant depression (Matcham F et al, 2013). Systemic inflammation could lead not only to inflammation in affected organs, but also mediates behavior abnormalities including depression symptoms.

**Purpose:** To characterise the inflammatory marker level and diseases activity in RA patients with depression.

**Methods:**

176 german RA outpatients: age 62.4 ± 12.3 years, mean duration of disease 14.3 ± 10.4 years, DAS28 3.3 ± 1.3, HAQ 1.0 ± 0.75; as well 91 brazilian RA outpatients: age 56.3 ± 12.6 years, mean duration of disease 15.9 ± 8.5 years, DAS28 3.4 ± 1.51, HAQ 1.89 ± 0.85 could be included in this study. RA was diagnosed according to the ACR/EULAR Criteria 2010 and the following questionnaires were utilised: Beck depression inventory (BDI) (Beck et al., 1988), painDETECT (Freyhagen et al., 2006), visual analogue scale for pain (VAS), Short Form Health Survey (SF – 36) and Health Assessment Questionnaire (HAQ-DI). The participants were classified in 2 groups according to BDI I-II (BDI ≤ 13 – no signs of depression; BDI > 13 signs of depression) (Beck et al, 1996). The cut-off of C-reactive protein (CrP) was 5mg/l.

**Results:**

About 22.9 % of german RA patients were diagnosed with associated depression. It was divided into mild (64.1 %), moderate (28.2 %) and severe depression (7.7 %). Depressive patients had a higher level of CrP compare to patients without signs of depression (7.18 ± 3.39 vs 5.25 ± 1.41, p = 0.001). There was an association between CrP and clinical symptoms of depression (BDI: r = 0.226, p = 0.003), as well as pain (VAS: r = 0.184, p = 0.017), HAQ (r = 0.291, p = 0.002) and physical quality of life (r = -0.337, p < 0.0001). In depressive patients we found higher disease activity (DAS 28) (p<0.001). Depressive patients showed 25.8% with high disease activity and 45.2% with moderate disease activity. Only 12.9% were in remission and 16.1 % in low disease activity. In patients without depressive symptoms were 43.6% in remission and 17.8% showed low disease activity. Only 5% had a high disease activity and 33.7% with moderate disease activity. Concerning to brazilien population of RA patients it was found that 44 % of patients were diagnosed with associated depression. It was divided into mild (53.7 %), moderate (29.3 %) and severe depression (17.1 %). Brazilien RA patients with mild depression showed a higher CrP-level compare to patients with moderate depression (p < 0.05). Depressive patients had higher levels of disease activity (p= 0.004). 8.3% in remission and 75% in moderate disease activity. Only 16.7% had high disease activity. In patients without depression we found 16.7% in remission and 25.0% showed low disease activity. 41.7% had moderate disease activity and 16.7% with high disease activity.

**Conclusion:**

The study indicates that RA-related depression could be associated with inflammatory markers and diseases activity. In RA-population with higher prevalence of depression we could find higher CRP- levels than in population with lower prevalence. It suggests the need for management strategies that specifically target depression as part of an overall RA- management program.

**Disclosure:** H. Morf, None; O. Seifert, None; G. Castelar-Pinho, None; A. B. Vargas-Santos, None; C. Baerwald, None.


**Abstract Number:** 1341

The Impact of Anti-Cyclic Citrullinated Peptide Seropositivity on Erosion Prevalence Among Patients with RA of Varying Disease Duration
Background/Purpose: Little is known regarding the prevalence of erosive disease in a contemporary cohort of patients with RA and whether erosive disease prevalence differs by disease duration and seropositivity to anti-citrullinated protein antibodies (ACPA). The aim of this study was to characterize the proportion of patients with RA with erosive disease by disease duration category and stratified by positive and negative serological status (anti-cyclic citrullinated peptide [anti-CCP], a surrogate for ACPA).

Methods: We identified patients with RA aged ≥18 years who were enrolled in the Corrona registry (October 2001–June 2016), with available disease duration, radiographic/MRI/ultrasound studies and serological status based on anti-CCP. Patients were grouped based on RA disease duration (0–2, 3–5, 6–10 and >10 years from diagnosis). Unadjusted prevalence erosion rates were calculated based on the proportion of patients with reports of erosions present on joint radiographs/MRIs/ultrasounds. Seropositivity was based on laboratory results (anti-CCP ≥20 U/mL) at enrollment in the Corrona registry. Chi-squared tests were used to assess differences in prevalence rates.

Results: There were 9759 patients who met inclusion criteria. Most were women (76%), middle-aged (mean [SD] 57 years [14]), with moderate disease activity (mean [SD] CDAI 14.7 [13.4]). Prior use of at least one biologic or targeted synthetic DMARD had occurred in 41% of patients. Overall, the prevalence of erosive disease was 28.6%, with higher prevalence among anti-CCP+ (35.4%) vs anti-CCP− (20.1%) patients (p<0.001, chi-squared test). The prevalence of erosions increased with increasing disease duration (p<0.001; Table). For each disease duration group, the prevalence of erosions was higher in patients who were anti-CCP+ compared with those who were anti-CCP−.

Conclusion: Erosions were common in this cohort of patients, and prevalence of erosions increased with longer disease duration. Patients who were anti-CCP+ had higher rates of prevalent erosions than those who were anti-CCP− with similar disease duration.

Table. Prevalence of Erosions According to Disease Duration and Serological Status

<table>
<thead>
<tr>
<th>Disease duration (years)</th>
<th>Overall</th>
<th>0–2</th>
<th>3–5</th>
<th>6–10</th>
<th>&gt;10</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>(905/4699)</td>
<td>(475/1678)</td>
<td>(469/1404)</td>
<td>(946/1978)</td>
</tr>
<tr>
<td>Serological status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-CCP+</td>
<td>22.1</td>
<td>(546/2473)</td>
<td>(306/934)</td>
<td>(341/816)</td>
<td>(740/1245)</td>
</tr>
</tbody>
</table>

Data are % (n/N) CCP=cyclic citrullinated peptide

Disclosure: L. R. Harrold, Corrona, 1,Pfizer Inc, 2,Roche Pharmaceuticals, 5,Corrona, 3; K. Price, Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1; H. J. Litman, Corrona, 3; S. Connolly, Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1; E. Alemao, Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1; S. Rebello, Corrona, 3; W. Hua, Corrona, 3; J. Kremer, Corrona, 1,AbbVie, BMS, Genentech, Lilly, Novartis, Pfizer, 2,Corrona, 3,Genentech and Biogen IDEC Inc., 8.
Comprehensive Provider Judgment Outweighs Disease Activity Measures in the Decision to Not Escalate Therapy in Patients with Moderate to Severe Rheumatoid Arthritis

Jacob R. Stever1, Brian Sauer2, Chia-Chen Teng, MS1, Neil Accortt3, David Collier4 and Grant Cannon1, 1Salt Lake City VA Medical Center and University of Utah, Salt Lake City, UT, 2IDEAS Center and Division of Epidemiology, HSR&D SLC VA Medical Center and University of Utah, Salt Lake City, UT, 3Center for Observational Research, Amgen, Inc., Thousand Oaks, CA, 4Amgen, Inc., Thousand Oaks, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Title:
Comprehensive provider judgment outweighs disease activity measures in the decision to not escalate therapy in patients with moderate to severe rheumatoid arthritis.

Authors:
Stever, Sauer, Teng, Accortt, Collier, Cannon.

Background/Purpose:
We evaluated US Veterans with RA in the Veterans Affairs Rheumatoid Arthritis (VARA) registry with moderate/severe disease activity (DAS28>3.2) and noted that of 941 patients with DAS>3.2, 559 (59%) did not have a change in RA therapy. We reviewed medical chart notes to determine provider reasoning for not modifying therapy despite documented moderate/severe RA disease activity.

Methods:
US Veterans included in VARA had 1) moderate/severe disease activity (DAS28³3.2) on the index date, 2) 18 months of VA data prior to the index date and 3) no major change to their medical therapy within 7 days before to 90 days after the index date. A major change was 1) initiation or escalation of DMARDs and/or prednisone and/or 2) 2 joint injections. There were 220 patients from 9 VARA registry sites randomly selected for chart review and the reasons documented in the patient record for continuing on therapy were recorded. In all patients, a Comprehensive provider judgment (CPJ) was made by the chart reviewer (JS) for each patient and categorized as mild or moderate/severe disease on the basis of text notes by the provider using these terms or similar comments on disease state. The CPJ was based on text notes and not physician global assessment by visual analog scale (VAS).

Results:
The reasons for continuing current therapy despite DAS28>3.2 are listed in Table 1. A CPJ reported as mild was the predominant reason for no major change in therapy in 149 (68%) patients. CPJ mild patients had lower tender joint counts, swollen joint count, and physician global assessment. This CPJ of mild disease activity was not associated with other parameters evaluated including patient global assessment, ESR, CRP, and Heath Assessment Questionnaire (HAQ) (Table 2).

Conclusion:
The most common reason that RA patients remain on current therapy despite a documented DAS28>3.2 is a comprehensive provider judgment of acceptable disease activity. Many cases involved patients with a low numbers of tender and swollen joints. This observation suggests that a value of DAS28>3.2 may frequently occur in patients that most providers do not accept as having
moderate/severe disease with sufficient confidence to direct therapy. These data emphasize the need for a better understanding of factors in addition to disease activity measures directing therapy in clinical practice.

Table 2. Comparison of patients with mild disease activity by Comprehensive Provider Judgment (CPJ) to patients with moderate disease activity by CPJ. Mean (95% Confidence interval)

<table>
<thead>
<tr>
<th>Baseline Demographic and Clinical Data</th>
<th>Patients with No Change in Therapy at Index Date</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All (N=220)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>66.6 (65.3-67.9)</td>
</tr>
<tr>
<td>Methyl Cellosolve N (h) (ESR)</td>
<td>194 (84.2%) (183.9-205.5)</td>
</tr>
<tr>
<td>Disease Duration (years)</td>
<td>14.9 (12.2-16.6)</td>
</tr>
<tr>
<td>Tender Joint Count (0-28)</td>
<td>4.0 (3.2-4.7)</td>
</tr>
<tr>
<td>Swollen Joint Count (0-28)</td>
<td>2.5 (2.2-3.1)</td>
</tr>
<tr>
<td>Patient Global Assessment (0-100)</td>
<td>46.6 (43.9-49.8)</td>
</tr>
<tr>
<td>Physician Global Assessment (0-100)</td>
<td>28.4 (25.0-31.3)</td>
</tr>
<tr>
<td>Visual Analog Pain Score (0-100)</td>
<td>5.0 (4.6-5.5)</td>
</tr>
<tr>
<td>HAQ (0-3.0)</td>
<td>1.0 (1.0-1.1)</td>
</tr>
<tr>
<td>ESR (mm/hr)</td>
<td>31.0 (26.2-35.7)</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>1.1 (0.9-1.4)</td>
</tr>
<tr>
<td>DAS28 at index date</td>
<td>4.2 (4.1-4.3)</td>
</tr>
<tr>
<td>Average DAS28 before index date*</td>
<td>3.9 (3.6-4.0)</td>
</tr>
</tbody>
</table>

* Average DAS28 scores during 18 month observation period before index date as area under the curve calculation.

Table 1. Reason for continuing RA therapy without change despite moderate/severe disease activity (DAS28 >3.2) (n=220)

<table>
<thead>
<tr>
<th>Reason for continuing RA therapy without change</th>
<th>DAS28 &gt;3.2 (n=220)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comprehensive Provider Judgment (CPJ) of RA as mild/controlled</td>
<td>149 (68%)</td>
</tr>
<tr>
<td>Provider recommended continuing current therapy with anticipating improvement</td>
<td>13 (5.9%)</td>
</tr>
<tr>
<td>Patient with low adherence to prescribed therapy</td>
<td>13 (5.9%)</td>
</tr>
<tr>
<td>Patients disagreed with provider recommendation for major change</td>
<td>7 (3.1%)</td>
</tr>
<tr>
<td>Non-RA musculoskeletal disease activity explained symptoms</td>
<td>6 (3.0%)</td>
</tr>
<tr>
<td>No increase in therapy recommended because of pending procedure</td>
<td>2 (0.9%)</td>
</tr>
<tr>
<td>Patient requested additional time to consider therapy change before accepting change</td>
<td>2 (0.9%)</td>
</tr>
<tr>
<td>Provider waiting for imaging or laboratory results to decide on therapy changes</td>
<td>2 (0.9%)</td>
</tr>
<tr>
<td>Active Hepatitis C</td>
<td>3 (1.4%)</td>
</tr>
<tr>
<td>Change of Medication by non-RA provider</td>
<td>3 (1.4%)</td>
</tr>
<tr>
<td>Reason for persistence on therapy could not determine by chart review</td>
<td>24 (10.5%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>220 (100%)</td>
</tr>
</tbody>
</table>

Disclosure: J. R. Stever, None; B. Sauer, Amgen, 2; C. C. Teng, MS, Amgen, 2; N. Accortt, Amgen, 1, Amgen, 3; D. Collier, Amgen, 1, Amgen, 3; G. Cannon, Amgen, 2.


Abstract Number: 1343

Gingival Bleeding and Periodontitis in Japanese Patients with Rheumatoid Arthritis: Results from the IORRA Cohort Study

Takefumi Furuya1, Eisuke Inoue2, Shigeru Maeda3, Eichi Tanaka1, Katsunori Ikari1, Ayako Nakajima1, Atsuo Taniguchi1 and Hisashi Yamanaka1, 1Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan, 2Division of Medical Informatics, St. Marianna University School of Medicine, Kawasaki, Japan, 3Department of Dental Anesthesiology, Okayama University Hospital, Okayama, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017

Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM
Background/Purpose: Oral health is an important issue for patients with rheumatoid arthritis (RA) because periodontitis is a potential risk factor for RA and RA patients have been reported to have a significantly increased incidence of periodontitis compared to healthy individuals. We previously reported that 40% of Japanese RA patients disclosed receiving dental treatment in the previous 6 months (J Bone Miner Metab, 2017; 35: 344-350). Limited data exist in the literature concerning periodontitis in Japanese RA patients. This study aimed to evaluate periodontitis in our Institute of Rheumatology Rheumatoid Arthritis (IORRA) cohort.

Methods: The IORRA cohort was established in 2000 as a single institute-based large cohort of Japanese RA patients. More than 122 publications have described various characteristics of Japanese RA patients using this cohort. Patients with RA enrolled in the IORRA cohort completed self-administered questionnaires as part of the 2016 October/November IORRA surveys, which included gingival bleeding during tooth brushing and periodontitis diagnosed by dentists in the previous 6 months (April to September 2016). Logistic regression analyses were used to evaluate associations between gingival bleeding during tooth brushing, periodontitis, and clinical variables.

Results: Among 5,660 Japanese patients with RA who participated in the cohort (median age, 62 years old; females, 86%), 31% and 18% reported having gingival bleeding during tooth brushing and periodontitis diagnosed by a dentist, respectively, in the previous 6 months. Among 1,211 patients with RA treated with anti-resorptive drugs (bisphosphonates and denosumab) (median age, 69 years old; females, 95%), 26% and 19% reported having gingival bleeding during tooth brushing and periodontitis diagnosed, respectively, in the previous 6 months. Among Japanese patients with RA, younger age, ever-smoker status, disease activity score (DAS) 28, and Japanese health assessment questionnaire disability index (JHAQ-DI) were significantly associated with gingival bleeding during tooth brushing, and older age, female sex, ever-smoker status, DAS28, and JHAQ-DI were significantly correlated with periodontitis (Table). Among Japanese RA patients treated with anti-resorptive drugs, younger age and patient general visual analogue scale (VAS) were significantly associated with gingival bleeding during tooth brushing, and older age was associated with periodontitis diagnosis in the previous 6 months.

Conclusion: In Japanese patients with RA, many patients experienced gingival bleeding during tooth brushing and were diagnosed with periodontitis by dentists. Age, female sex, ever-smoker status, general health status, disease activity, and disability may be associated with periodontitis in Japanese patients with RA.

Table. Factors associated with gingival bleeding during tooth brushing and periodontitis

<table>
<thead>
<tr>
<th>Variables</th>
<th>Gingival bleeding during tooth brushing</th>
<th>Periodontitis diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients receiving anti-resorptive drugs</td>
<td>All patients receiving anti-resorptive drugs</td>
</tr>
<tr>
<td>Age, per 10 years</td>
<td>0.70 (0.66-0.74)</td>
<td>0.66 (0.57-0.76)</td>
</tr>
<tr>
<td>Female sex</td>
<td>1.07 (0.87-1.33)</td>
<td>—</td>
</tr>
<tr>
<td>Ever smokers</td>
<td>1.17 (1.01-1.36)</td>
<td>—</td>
</tr>
<tr>
<td>General VAS, 10 cm</td>
<td>—</td>
<td>1.07 (1.01-1.14)</td>
</tr>
<tr>
<td>DAS28</td>
<td>1.15 (1.04-1.27)</td>
<td>—</td>
</tr>
<tr>
<td>JHAQ-DI</td>
<td>1.34 (1.20-1.49)</td>
<td>—</td>
</tr>
</tbody>
</table>

Odds ratios (95% confidence intervals)

Disclosure: T. Furuya, UCB, 8,Bristol-Myers Squibb, 8,Takeda, 8,Eisai, 8,Chugai, 8,Pfizer Inc, 8,Ono, 8,Asahi Kasei, 8; E. Inoue, None; S. Maeda, None; E. Tanaka, Abbvie, 8,Abumi, 8,Bristol-Myers Squibb, 8,Chugai, 8,Eisai, 8,Nippon Kayaku, 8,Pfizer Inc, 8,Takeda, 8,UCB, 8; K. Ikari, Bristol-Myers Squibb, 8,Abbbie, 8,Eisai, 8,Asahi Kasei, 8,Asastelas, 8,Chugai, 8,Hisamitsu, 8,Janssen Pharmaceutica Product, L.P., 8,Taisho Toyama, 8,Takeda, 8,Santen, 8,Tanabe-Mitsubishi, 8,Kaken, 8; A. Nakajima, Nippon-Kayaku, 5,Bristol-Myers Squibb, 8,Chugai, 8,Novartis Pharmaceutical Corporation, 8,Pfizer Inc, 8,Senim, 8,Tanabe-Mitsubishi, 8; A. Taniguchi, Pfizer Inc, 8; H. Yamanaka, MSD, 2,Asstelales, 2,AbbVie, 2,MS, 2,Kaken, 2,UCB, 2,Ono, 2,Ayumi, 2,Eisai, 2,Daichi-Sankyo, 2,Takeda, 2,Tanabe-Mitsubishi, 2,Chugai, 2,Nipponshinaku, 2,Pfizer Inc, 2,Pfizer Inc, 8,YL biologics, 8,Takeda, 8,Nipponkonayaku, 8,Chugai, 8,Tanabe-Mitsubishi, 8,Daiichi-Sankyo, 8,Asstelas, 8.
Impact of Fibromyalgic RA on Composite Scores; Results from a Longitudinal Study of RA Patients Initiating BDMARD Therapy

Hilde B Hammer1, Sella A. Provan2, Brigitte Michelsen3, Till Uhlig4, Jon Lampa5 and Tore K Kvien6, 1Rheumatology, Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, 2Department of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, 3Rheumatology, Hospital of Southern Norway trust, Kristiansand, Norway, 4Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, 5Karolinska Institute, Department of Medicine, Rheumatology Unit, Stockholm, Sweden, Stockholm, Sweden, 6On behalf of the NOR-DMARD registry, Oslo, Norway

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
The composite scores DAS28, CDAI and SDAI all include number of tender and swollen joints (of 28). Rheumatoid arthritis (RA) patients with tender to swollen joint count difference (TSJD) >0 had reduced composite score remission and TSJD of ≥7 was shown to have ≥ 80% sensitivity and specificity to have “fibromyalgic RA” (FM-RA) (Pollard et al. Rheumatology 2010). Ultrasonography (US) is a sensitive imaging technique to detect synovitis including grey scale synovitis (GS) and power Doppler (PD) activity. The present purpose was to explore the impact of FM-RA on the composite scores in comparison to other clinical assessments including US in a longitudinal study of established RA patients initiating bDMARD therapy.

Methods:
A total of 209 patients with RA (mean (SD) age 53 (13) years, disease duration 10 (9) years, 81% women, 79% anti-CCP positive) were included when initiating bDMARDs and assessed at baseline and after 1, 2, 3, 6 and 12 months with joint pain VAS, patient’s global VAS, RAID score, MHAQ, clinical examinations (performed by a study nurse; assessor’s disease activity VAS, tender and swollen joint counts (of 28) and laboratory variables (ESR and CRP). All US examinations (semi-quantitative scoring (0-3)) of GS and PD (PIP 2-3, MCP 1-5, wrist (radiocarpal, intercarpal, radioulnar), elbow, knee, tibiotalar, MTP 1-5 and ext.carpi ulnaris/tib.post.tendons bilaterally) were performed by one rheumatologist (HBH) (Siemens Acuson Antares, excellence version, 5-13 MHz probe). To explore the impact of tender minus swollen joint count, patients were divided into three groups depending on TSJD at baseline; Gr.1=≤0 (n=125), Gr.2=1-6 (n=62), Gr.3=≥7 (n=22, FM-RA). Statistical calculations included frequency of DAS28(ESR), CDAI, SDAI and ACR/EULAR (Boolean) remission, one-way ANOVA and cross-tabs.

Results:
There were significantly higher DAS28(ESR), CDAI, SDAI, joint pain VAS, patient’s global VAS, RAID score and M-HAQ in the FM-RA group at all time points (p≤0.003), while there were no differences between the groups regarding assessor’s global VAS or ESR/CRP. On the other hand, sum scores GS and PD were higher in Gr.1 and 2 (figure 1). The table illustrates that the FM-RA group has a very low percentage of composite score remission both at 6 and 12 months follow-up.

Conclusion:
In spite of having the lowest degree of US pathology, the 10.5% FM-RA patients had significantly higher levels of all the commonly used composite scores at all time points and they seldom reached remission. Thus, the small RA-FM group should be identified and other than composite scores should be used for assessing their disease activity.
### Table: Percentages of patients in composite score remission

<table>
<thead>
<tr>
<th></th>
<th>6 months</th>
<th></th>
<th>12 months</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group 1; TSJD≤0</td>
<td>Group 2; TSJD=1-6</td>
<td>Group 3; TSJD=7, FM-RA</td>
<td>Group 1; TSJD≤0</td>
</tr>
<tr>
<td>DAS28</td>
<td>27.2</td>
<td>11.4</td>
<td>2.3</td>
<td>26.3</td>
</tr>
<tr>
<td>SDAI</td>
<td>15.2</td>
<td>7.1</td>
<td>1.1</td>
<td>17.8</td>
</tr>
<tr>
<td>CDAI</td>
<td>12.5</td>
<td>6.5</td>
<td>1.6</td>
<td>16.4</td>
</tr>
<tr>
<td>Boolean</td>
<td>13.0</td>
<td>7.1</td>
<td>1.1</td>
<td>14.5</td>
</tr>
</tbody>
</table>

### Disclosure:

H. B. Hammer, AbbVie Norway, 2, Abbvie, 8, Novartis Pharmaceutical Corporation, 5, Pfizer Inc, 8, Roche Pharmaceuticals, 8; S. A. Provan, None; B. Michelsen, None; T. Uhlig, None; J. Lampa, None; T. K. Kvien, AbbVie, 2, Pfizer Inc, 2, Roche Pharmaceuticals, 2, UCB, 2, BMS, 2, MSD, 2, AbbVie, 5, Pfizer Inc, 5, BMS, 8, MSD, 8, Roche Pharmaceuticals, 8, UCB, 8, AbbVie, 8.


**Abstract Number: 1345**

**Tender Joints Have Low Associations with Patient’s Evaluation of Joint Pain and Ultrasound Findings Explored at Joint Level in Patients with Rheumatoid Arthritis**

Hilde B Hammer¹, Joseph Sexton¹, Sella A. Provan², Brigitte Michelsen³,⁴ and Tore Kvien⁵, ¹Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, ²Department of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, ³Rheumatology, Hospital of Southern Norway trust, Kristiansand, Norway, ⁴Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, ⁵Diakonhjemmet Hospital, Oslo, Norway

**First publication:** September 18, 2017

### SESSION INFORMATION

**Session Date:** Monday, November 6, 2017

**Session Title:** Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM
Background/Purpose:

In patients with rheumatoid arthritis (RA) the pain experience in joints with different degrees of joint inflammation is highly individual and dependent upon the pain threshold. The composite scores all include tender joints as an approximation of disease activity. Ultrasonography (US) is sensitive for assessment of joint inflammation (synovitis (grey scale, GS) and vascularization (power Doppler, PD)). The present objective was to cross-sectionally explore the associations at joint level between joint pain experienced by the patient, presence of pain by external pressure (tender joint), presence of joint swelling and the degree of US pathology.

Methods:

174 patients with established RA (mean (SD) age 52 (13) years, disease duration 10 (8) years, 82% women, 79% anti-CCP positive, 80% on DMARDs (MTX in 74%) and 55.2% on prednisolone (mean (SD) dosage of 4.5 (5.8) mg) were assessed before initiating bDMARD treatment. The presence of patient reported joint pain (PRJP) was assessed at joint level by use of a manikin including 32 joints (bilateral wrist, MCP1-5, PIP2-3, elbow, knee, ankle, MTP1-5). Each joint was scored 0-3 reflecting the level of spontaneous joint pain the last day. The same 32 joints were scored 0-3 for US pathology (GS and PD). An experienced study nurse assessed the presence of tenderness and swelling (MTP1-5 scored as one joint). Correlations of sum scores (PRJP, GS, PD and tender/swollen joints) were assessed by use of Spearman. Associations at joint level was explored using Cohens kappa, with transforming semi-quantitative scores to categorical (PRJP: 0=0, 1-3=1; US GS 0-1=0 (as score 1 may also be seen in healthy joints), 2-3=1; US PD 0=0, 1-3=1).

Results:

Correlations between sum scores showed moderate to high correlations between PRJP and tender joints as well as between swollen joints and US GS/PD (table1, *p<0.05, **p<0.001). At joint level, the associations between PRJP, tender and swollen joints were low, while US (GS/PD) had strong associations with swollen joints (table 2).

Conclusion:

Sum scores of tender joints and PRJP were correlated, but they had low or none associations with sum scores of swollen joints and GS/PD. On the other hand, there were high correlations between sum scores of swollen joints and US. At joint level, there were surprisingly low association between tender joints and PRJP. In addition, tender joints had low associations with swollen joints and GS/PD US findings. However, also at joint level, swollen joints and US findings were associated. The present findings raise questions regarding the prominent role of tender joints in composite disease activity measures for RA.

<table>
<thead>
<tr>
<th>Spearman correlations for sum scores</th>
<th>Sum score PRJP</th>
<th>Sum tender joints</th>
<th>Sum swollen joints</th>
<th>Sum US GS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sum tender joints</td>
<td>0.54**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sum swollen joints</td>
<td>0.32**</td>
<td>0.21*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sum US GS</td>
<td>0.26**</td>
<td>0.03</td>
<td>0.69**</td>
<td></td>
</tr>
<tr>
<td>Sum US PD</td>
<td>0.26**</td>
<td>-0.1</td>
<td>0.64**</td>
<td>0.88**</td>
</tr>
</tbody>
</table>

| Cohens kappa values on joint level (Standard error) (all joints, n=5568) |
|-----------------------------|----------------|-----------------|-------------------|-----------|
|                             | Swollen | Tender | PRJP | US GS |
| Tender                      | 0.32 (0.02) |      |     |       |
| PRJP                        | 0.25 (0.02) | 0.34 (0.02) |     |       |
| US GS                       | 0.57 (0.02) | 0.21 (0.02) | 0.23 (0.02) |       |
| US PD                       | 0.56 (0.01) | 0.20 (0.02) | 0.25 (0.02) | 0.74 (0.01) |

Disclosure: H. B. Hammer, AbbVie Norway, 2, Abbvie, 8, Novartis Pharmaceutical Corporation, 5, Pfizer Inc, 8, Roche Pharmaceuticals, 8; J. Sexton, None; S. A. Provan, None; B. Michelsen, None; T. Kvien, AbbVie, Biogen, BMS, Celltrion, Eli Lilly and Company, Janssen, Merck-Serono, MSD, NOvartis, Oktal, Orion Pharma, Hospira/Pfizer, Riche, Samsung, Sandoz, UCB, 5.

Abstract Number: 1346
Selective Effect of Rituximab on IgG4 Anti-CCP Autoantibodies in Rheumatoid Arthritis Patients

Mercedes Rincon1,2, Sarah Kelso3, Janice Bunn4 and Sheldon Cooper5, 1Department of Medicine/Rheumatology, University of Vermont, Burlington VT, VT, 2Department of Medicine/Immunobiology, University of Vermont, Burlington, VT, 3Department of Medicine/Rheumatology, University of Vermont, Burlington, VT, 4Mathematics and Statistics, University of Vermont, Burlington, VT, 5Department of Medicine/Rheumatology, University of Vermont, Burlington, VT

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Autoantibodies have long been recognized to be present in patients with RA, but it is more recent that autoantibodies against citrullinated proteins (anti-CCP) are emerging as contributors to Rheumatoid Arthritis (RA) pathogenesis. While depletion of CD20 B cells by rituximab clearly has a major beneficial effect in RA, it remains unclear whether this effect is associated with decreased autoantibody production. We recently reported that tocilizumab, a monoclonal antibody to the IL-6 receptor (IL-6R), specifically reduces the levels of IgG4 anti-CCP antibodies (Abs), but not IgG1 anti-CCP Abs, and that IL-6 promotes isotype switching to IgG4. No previous studies have examined whether rituximab treatment has an isotype-specific effect on autoantibody production. The objective of this study was to determine if rituximab has a specific effect on IgG4 versus IgG1 anti-CCP Abs in RA

Methods: RA patients who were starting a new biologic treatment or switching to a new biologic were consented to enter an accompanying laboratory study. Blood specimens were obtained prior to the first treatment (time 0), and 6-9 months later. Serum samples and peripheral blood mononuclear cells were collected. Levels of total anti-CCP antibodies (Abs), IgG1-anti-CCP and IgG4-anti-CCP Abs in serum were determined. Total levels of IgG1 and IgG4 in serum were also determined

Results: While some RA patients have no detectable IgG4 anti-CCP Abs, there is a fraction of RA patients with higher levels of IgG4 anti-CCP Abs than IgG1 anti-CCP Abs (about 40%). Rituximab treatment had no significant effect on IgG1 anti-CCP Abs levels, but it caused a marked reduction in the levels of IgG4 anti-CCP Abs. The total anti-CCP Abs levels were significantly reduced with rituximab, but the reduction was less pronounced due to the minimal effect on the IgG1 subclass antibodies. The reduction in IgG4 anti-CCP Ab levels by rituximab was not caused by a reduction in the total IgG4 serum immunoglobulin levels, as determined by spearman correlation

Conclusion: Rituximab specifically reduces the levels of IgG4 anti-CCP antibodies but has minimal effect on IgG1 levels and IgG1 anti-CCP antibodies. This effect on IgG4 could be masked if total Ig anti-CCP antibody levels are tested. The results from these studies reveal a novel effect of rituximab on autoantibody levels that has been questioned. Considering the emerging relevance of anti-CCP antibodies in the pathogenesis of RA, the specific effect of rituximab on IgG4 autoantibodies could be a novel mechanism for this biologic.

Disclosure: M. Rincon, None; S. Kelso, None; J. Bunn, None; S. Cooper, None.

Abstract Number: 1347

Ultrasonography and Synovial Histology in the RA Patients in Remission

Asami Abe1, Hajime Ishikawa2 and Kunihiko Wakaki3, 1Rheumatology, Niigata Rheumatic Center, Shibata, Japan, 2Department of Rheumatology, Niigata Rheumatic Center, Shibata, Japan, 3Pathology, Niigata Prefectural Shibata Hospital, Shibata, Japan

First publication: September 18, 2017

SESSION INFORMATION
Background/Purpose: In the treatment of rheumatoid arthritis (RA), the early diagnosis and early medical treatment via tight control have become increasingly important with the advent of biological therapy. Ultrasonography (US) for the affected joints enables the evaluation of synovial hypertrophy, effusion and bone erosion in real time. US is a reliable method that can detect more erosive sites than radiography. US is now utilized widely and is a reliable tool among rheumatologists for diagnosing RA and evaluating the disease activity. However, many patients have swollen, deformed and painful joints due to overuse and advancing bone destruction. This study was conducted to clarify the relationship between the systemic disease activity, local disease activity using US and a synovial histopathological evaluation in RA patients in remission (Disease Activity Score [DAS] 28-ESR[4]<2.6).

Methods: Between March 2011 and April 2017, 176 joints were surgically treated among all RA patients in remission, and synovial biopsies were performed at the time of surgery. Among them, a total of 52 fingers, 32 wrists, 57 ankles, 12 elbows, 3 shoulders and 17 knees were investigated. Just before surgery, the US probe was placed on the joints to evaluate the activity of local synovitis. The maximum grade of power Doppler (PD) signal was determined, ranging from 0 to 3. The serum C reactive protein (CRP), matrix metalloproteinase-3 (MMP-3) and DAS28 values were also examined just before surgery. A histopathological examination of the gathered synovium at the surgical site was performed using the Rooney score (RS). Biological disease-modifying antirheumatic drugs (BIO) were used in 73 cases, namely infliximab in 8 cases, etanercept in 10, adalimumab in 10, tocilizumab in 28, abatacept in 5, certolizumab pegol in 2 and golimumab in 10.

Results: The PD score was grade 0 in 76 cases, 1 in 61 cases, 2 in 30 cases and 3 in 9 cases. The average CRP was 0.17 mg/dL, and MMP-3 was 94.6 ng/mL, both low values. The three items of lymphocytes in the RS score showed low values, while synoviocyte hyperplasia and fibrosis showed high values due to a secondary reaction after inflammation at the joints. Group L consisted of 76 joints of grade 0, Group H included 61 joints of grade 1, 30 joints of grade 2 and 9 joints of grade 3. The values of MMP-3, synovium hyperplasia, lymphocyte infiltration and blood vessel hyperplasia were markedly low in Group L. Small Joints (SJ) consisted of 144 joints with fingers, wrists, feet and ankles. Large Joints (LJ) consisted of 32 joints with elbows, shoulders and knees. The values of MMP-3, synovium hyperplasia and high value were markedly low in SJ cases with blood vessel hyperplasia. Patients using BIO showed low values for CRP, synovium hyperplasia and lymphocyte infiltration.

Conclusion: The systemic disease activities, as indicated by DAS28, CRP and MMP-3, of RA patients in remission were low. However, synovitis was clearly present based on ultrasonography and histological findings of the surgical joints of PD-positive RA patients in remission.

Disclosure: A. Abe, None; H. Ishikawa, None; K. Wakaki, None.

Abstract Number: 1348

Swollen Joint Count, but Not Inflammatory Cytokines, Differs By Frequency of Fish Consumption in a Cross-Sectional Rheumatoid Arthritis Cohort

Sara K. Tedeschi1, Joan Bathon2, Jon T. Giles3, Tzu-Chieh Lin4, Kazuki Yoshida5 and Daniel Solomon1, 1Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA, 2Division of Rheumatology, Columbia University, College of Physicians & Surgeons, New York, NY, 3Division of Rheumatology, Columbia University College of Physicians & Surgeons, New York, NY, 4Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 5Brigham and Women's Hospital, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM
**Background/Purpose:** Omega-3 fatty acids downregulate pro-inflammatory cytokines, thus have been of interest as adjunctive rheumatoid arthritis (RA) therapy for decades. We previously reported an inverse association between disease activity measured by DAS28-CRP and frequency of fish consumption in an RA cohort. The present study tested whether individual components of DAS28-CRP or other inflammatory cytokines were related to frequency of fish intake.

**Methods:** We conducted a cross-sectional analysis using baseline data from participants in a prospective cohort study of cardiovascular disease in RA. Frequency of fish consumption was assessed by a baseline food frequency questionnaire assessing usual diet in the past year. DAS28-CRP was calculated using tender joint count (TJC), swollen joint count (SJC), and C-reactive protein (CRP) measured at baseline. Multivariable, total energy-adjusted linear regression models provided effect estimates and 95% confidence intervals (CI) for frequency of non-fried fish consumption (never to <1/month, 1/month to <1/week, 1/week, and ≥2/week) on baseline TJC, SJC, and natural log (ln)-transformed cytokine levels. We also estimated the difference in each outcome associated with increasing fish consumption by one serving per week. A sensitivity analysis additionally adjusted for pack-years.

**Results:** Among 176 participants, 60% were female and median age was 59 years (interquartile range [IQR] 53-65). Seventy-nine percent were seropositive (RF or anti-CCP), median disease duration was 9 years (IQR 5-17), and median DAS28-CRP was 3.5 (IQR 2.9-4.3). Current medications taken as mono- or combination therapy included non-biologic disease modifying anti-rheumatic drugs (DMARDs) in 87%, biologic DMARDs in 46%, glucocorticoids in 39%, and fish oil supplements in 9%. Twenty percent ate fish never to <1/month and 18% ate fish ≥2 times/week. In adjusted linear regression models, subjects consuming fish ≥2 times/week had a significantly lower SJC compared with subjects who ate fish never to <1/month (difference -3.51 [95% CI -5.87, -1.16]) (Table). For each additional serving of fish per week, SJC was significantly reduced by 1.18 (95% CI -2.03, -0.33). We did not observe differences in TJC or ln-transformed cytokine levels based on frequency of fish consumption. Further adjustment for smoking produced similar results.

**Conclusion:** Differences in SJC according to frequency of fish consumption may explain our previous observation that higher intake of fish was associated with lower disease activity as measured by DAS28-CRP in RA patients.

<table>
<thead>
<tr>
<th>Frequency of fish consumption</th>
<th>Difference in outcome per 1 additional serving of fish/week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome</td>
<td>Adjusted $\beta$-coefficient* (95% CI)</td>
</tr>
<tr>
<td></td>
<td>Adjusted $\beta$-coefficient*+ (95% CI)</td>
</tr>
<tr>
<td>SJC</td>
<td></td>
</tr>
<tr>
<td>0 (ref)</td>
<td>-1.99 (-3.91, -0.06)</td>
</tr>
<tr>
<td></td>
<td>-2.80 (-5.02, -0.57)</td>
</tr>
<tr>
<td></td>
<td>-3.51 (-5.87, -1.16)</td>
</tr>
<tr>
<td>TJC</td>
<td></td>
</tr>
<tr>
<td>0 (ref)</td>
<td>-0.22 (-3.83, 3.39)</td>
</tr>
<tr>
<td></td>
<td>-0.81 (-4.99, 3.36)</td>
</tr>
<tr>
<td></td>
<td>-2.09 (-6.51, 2.32)</td>
</tr>
<tr>
<td>CRP#</td>
<td></td>
</tr>
<tr>
<td>0 (ref)</td>
<td>-0.40 (-0.95, 0.14)</td>
</tr>
<tr>
<td></td>
<td>-0.45 (-1.09, 0.18)</td>
</tr>
<tr>
<td></td>
<td>-0.55 (-1.22, 0.11)</td>
</tr>
<tr>
<td>IL-6#</td>
<td></td>
</tr>
<tr>
<td>0 (ref)</td>
<td>-0.29 (-0.67, 0.09)</td>
</tr>
<tr>
<td></td>
<td>-0.09 (-0.53, 0.35)</td>
</tr>
<tr>
<td></td>
<td>-0.38 (-0.84, 0.09)</td>
</tr>
<tr>
<td>ICAM#</td>
<td></td>
</tr>
<tr>
<td>0 (ref)</td>
<td>-0.13 (-0.29, 0.02)</td>
</tr>
<tr>
<td></td>
<td>-0.04 (-0.22, 0.14)</td>
</tr>
<tr>
<td></td>
<td>-0.09 (-0.28, 0.10)</td>
</tr>
<tr>
<td>fibrinogen#</td>
<td></td>
</tr>
<tr>
<td>0 (ref)</td>
<td>-0.07 (-0.19, 0.05)</td>
</tr>
<tr>
<td></td>
<td>-0.003 (-0.14, 0.13)</td>
</tr>
<tr>
<td></td>
<td>-0.10 (-0.24, 0.04)</td>
</tr>
<tr>
<td>e-selectin#</td>
<td></td>
</tr>
<tr>
<td>0 (ref)</td>
<td>-0.29 (-0.57, -0.01)</td>
</tr>
<tr>
<td></td>
<td>-0.35 (-0.68, -0.04)</td>
</tr>
<tr>
<td></td>
<td>-0.26 (-0.59, 0.08)</td>
</tr>
</tbody>
</table>

Abbreviations: CI: confidence interval  SJC: swollen joint count  TJC: tender joint count  CRP: C-reactive protein  IL-6: interleukin 6  ICAM: intercellular adhesion molecule

* $\beta$-coefficient (95% CI) from linear regression models adjusted for total energy intake, age in decades, sex, body mass index in kg/m$^2$ (<25, 25 to <30, $\geq$30), CES-Depression score (continuous), married (yes/no), biologic DMARD use (yes/no), fish oil supplement use (yes/no)

+ $\beta$-coefficient (95% CI) from a term representing the median frequency of fish consumption per week in each exposure group, which represents the difference in outcome per 1 additional serving of fish/week

#All cytokines are natural log-transformed

Disclosure: S. K. Tedeschi, None; J. Bathon, None; J. T. Giles, None; T. C. Lin, None; K. Yoshida, None; D. Solomon, None.


Abstract Number: 1349

**Treat to Target: What’s the Target?**

Philip Dunn$^1$, Jonida Cote$^1$, Eric Newman$^2$ and Lester Kirchner$^1$, $^1$Geisinger Medical Center, Danville, PA, $^2$Department of Rheumatology, Geisinger Medical Center, Danville, PA

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017

Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM

Background/Purpose:
The 2015 ACR RA treatment guidelines focus on measuring disease activity and provide a guideline driven treat to target strategy. We hope to understand patients’ personal choices of disease measures and treatment targets and how it compares to their physicians.

Methods:
This is a cross sectional study of the first 120 RA patients defined by the 1987 or 2010 ACR criteria seen in our clinic from 1/16/17 to 3/13/17.

Before the routine care visit, each patient was given a questionnaire of traditional and personalized RA measures and asked which they prefer using to determine their treat to target goal. The patient was asked to rank each traditional (disease activity, functional status, patient global, physician global, joint pain/swelling) and personalized (ADLs, exercise, work, leisure, sleep) measure 1 to 5 (1 - most important and 5 - least important). Physicians completed the survey for each respective patient. Comparisons were made on both traditional and personalized physician and patients’ ranking responses.

Percent agreement, Wilcoxon signed rank test and weighted kappa coefficients were used to understand the change in agreement between physicians and patients.

Results:
Most patients (70%) and physicians (64%) believe a combination of traditional and personalized measures should be used to determine their RA treatment goal (Table 1).

<table>
<thead>
<tr>
<th>Traditional vs. Personalized Measures</th>
<th>Physicians</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Traditional</td>
<td>3 (27.3%)</td>
<td>17 (14.2%)</td>
</tr>
<tr>
<td>Personalized</td>
<td>1 (9.1%)</td>
<td>9 (7.5%)</td>
</tr>
<tr>
<td>Combination</td>
<td>7 (63.6%)</td>
<td>84 (70.0%)</td>
</tr>
<tr>
<td>Neither</td>
<td>0 (0%)</td>
<td>10 (8.3%)</td>
</tr>
</tbody>
</table>

As an overall group, both patients and physicians believe that functional status and disease activity are the most important traditional measures based on average ranking. Also, there is agreement in joint pain/swelling (p=0.36). Being able to complete ADLs is the most important personalized measure based on average ranking (Table 2).

<table>
<thead>
<tr>
<th>Traditional Measures</th>
<th>Physician</th>
<th>Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Functional Status</td>
<td>1.8</td>
<td>2.2</td>
</tr>
<tr>
<td>Disease Activity</td>
<td>2.1</td>
<td>2.9</td>
</tr>
<tr>
<td>Tender/Swollen Count</td>
<td>2.5</td>
<td>2.7</td>
</tr>
<tr>
<td>Patient Global</td>
<td>4.0</td>
<td>3.2</td>
</tr>
<tr>
<td>Physician Global</td>
<td>4.6</td>
<td>4.1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Personalized Measures</th>
<th>Physician</th>
<th>Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADLs</td>
<td>1.2</td>
<td>1.5</td>
</tr>
<tr>
<td>Work</td>
<td>3.2</td>
<td>3.5</td>
</tr>
<tr>
<td>Travel/Leisure</td>
<td>3.3</td>
<td>3.8</td>
</tr>
<tr>
<td>Sleep</td>
<td>3.4</td>
<td>2.8</td>
</tr>
<tr>
<td>Exercise</td>
<td>3.9</td>
<td>3.4</td>
</tr>
</tbody>
</table>

On an individual level, patient and physician level of agreement measured by weighted kappa coefficient is random (-0.024 to 0.283) and percent agreement showed a low of 20% (95% CI: 12.8%, 27.2%) for disease activity and high of 62% (95% CI: 53.0%, 70.4%) for ADLs.
Conclusion:

To our knowledge, this is the first study to analyze patient preference in addition to a treat to target management of RA.

Using disease activity as a measure for a treat to target approach has improved RA patient care. However, this study shows that on an individual patient level, even physicians who know their patients well cannot predict what measure(s) are most important to them as an individual.

To provide population care that is patient-centered, we recommend setting a patient specific measure/goal (traditional or non-traditional) based on personal importance in addition to following guideline driven care (i.e. disease activity measure).

Disclosure: P. Dunn, None; J. Cote, None; E. Newman, None; L. Kirchner, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/treat-to-target-whats-the-target

Abstract Number: 1350

Ultrasound Detected Tenosynovitis in Rheumatoid Arthritis Patients in Clinical Remission

Florencia Beatriz Mollerach, Josefina Marin, Johana Zacaria, Marina Scolnik, Javier Rosa, Santiago Ruta and Enrique R. Soriano, 1 Rheumatology Unit, Internal Medicine Service, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina, 2 Rheumatology Unit, Internal Medicine Service, Hospital Italiano de Buenos Aires, Instituto Universitario Hospital Italiano de Buenos Aires, and Fundacion PM Catoggio, Buenos Aires, Argentina, 3 Rheumatology Unit, Internal Medicine Service, Hospital Italiano de Buenos Aires, CABA, Argentina, 4 Rheumatology Unit, Internal Medicine Service, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: ultrasound (US) has demonstrated subclinical synovitis in rheumatoid arthritis (RA) patients in clinical remission, but there is less information regarding US tenosynovitis. The aims of the present study were to evaluate prevalence of US detected tenosynovitis in RA patients in clinical remission, its association with other features of the disease and to assess whether US detected tenosynovitis could add to US synovitis in order to define US remission in these patients.

Methods: consecutive RA patients (2010 ACR/EULAR criteria) in clinical remission according to DAS28<2.6 were included. All patients underwent US examination by the same rheumatologist using a MyLab 70 machine (Esaote) provided with a linear probe (6-18 MHz). Synovitis and tenosynovitis were defined according to OMERACT preliminary definitions. Grayscale (GS) and Power Doppler US (PDUS) were graded for both tenosynovitis and synovitis from 0 to 3. The following tendons were bilaterally assessed: 1st to 6th extensor tendon compartments at wrist level, 2nd to 5th finger flexor tendons and posterior tibial and peroneal tendons. Joints assessed bilaterally were: wrist, 1st to 5th MCP and 2nd to 5th proximal IP. US remission was defined as the absence of both GSUS grade ≥ 2 and any PDUS signal at both joint and tendon level.

Results: 60 RA patients were included (table). GSUS tenosynovitis grade ≥ 2 and PDUS tenosynovitis were found in 14 (23%, CI95%;12-34) and in 13 (21.7%, CI95%;10-32) RA patients in clinical remission, respectively. The most frequent involved tendons were:6th extensor wrist compartment, 3rd finger flexor and posterior tibial.

Mean erythrosedimentation rate (ESR) and DAS28 values were higher in patients with US detected tenosynovitis than those without US tenosynovitis (19 vs 12.3, p=0.016 and 2.2 vs 1.9, p=0.025, respectively). In multivariate analysis, the only feature associated with the presence of US tenosynovitis was ESR (OR:1.11, 95%CI: 1.02-1.22). ESR showed an area under the ROC curve for the detection of US tenosynovitis of 0.71.
Twenty-nine (48.3%, CI95%: 35-60) patients had US detected synovitis and were not classified as in US remission. Adding data of US detected tenosynovitis, 6 more patients would have been classified as not in US remission, giving a total of 35 (58.3%; CI95%: 45-70) (p=0.272).

**Conclusion:** about a quarter of RA patients in clinical remission had US detected tenosynovitis. The only feature associated with this US finding was the presence of higher levels of ESR. If US tenosynovitis is considered alongside with synovitis in the definition of US remission, a small number of patients would be added.

<table>
<thead>
<tr>
<th>Features</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean (SD)</td>
<td>59.6 (13.2)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>51 (85)</td>
</tr>
<tr>
<td>Disease duration (months), median (IQR)</td>
<td>55.5 (26.5-102)</td>
</tr>
<tr>
<td>Positive RF, n (%)</td>
<td>37 (61.6)</td>
</tr>
<tr>
<td>Positive antiCCP, n (%)</td>
<td>46 (76.6)</td>
</tr>
<tr>
<td>ESR, mean (SD)</td>
<td>13.9 (7.8)</td>
</tr>
<tr>
<td>DAS28, mean (SD)</td>
<td>1.9 (0.4)</td>
</tr>
<tr>
<td>DMARDs, n (%)</td>
<td>53 (88.3)</td>
</tr>
<tr>
<td>Biologic therapy with TNFi, n (%)</td>
<td>12 (20)</td>
</tr>
<tr>
<td>Tofacitinib, n (%)</td>
<td>2 (3.3)</td>
</tr>
<tr>
<td>US remission, n (%; CI95%)</td>
<td>25 (41.6; 28-54)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No US remission</th>
<th>US detected only synovitis, n (%; CI95%)</th>
<th>21 (35; 22-47)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>US detected only tenosynovitis, n (%; CI95%)</td>
<td>6 (10; 2-17)</td>
</tr>
<tr>
<td></td>
<td>US detected both synovitis and tenosynovitis, n (%; CI95%)</td>
<td>8 (13.3; 4-22)</td>
</tr>
<tr>
<td>Total, n (%; CI95%)</td>
<td></td>
<td>35 (58.3; 45-70)</td>
</tr>
</tbody>
</table>

**Disclosure:** F. B. Mollerach, None; J. Marin, None; J. Zacariaz, None; M. Scolnik, None; J. Rosa, None; S. Ruta, None; E. R. Soriano, Abbvie, BMS, Novartis, Janssen, Pfizer, Roche, UCB, 2, Abbvie, BMS, Novartis, Janssen, Pfizer, Roche, UCB, 5, Abbvie, BMS, Novartis, Janssen, Pfizer, Roche, UCB, 8.

**Minimal Clinically Important Improvement (MCII) of RAPID3 (ROUTINE ASSESSMENT OF PATIENT INDEX DATA 3), an INDEX of ONLY Patient Self-Report Scores in Rheumatoid Arthritis (RA): Similar Performance to DAS28 and CDAI**

**Michael Ward**¹, Isabel Castrejón², Martin J. Bergman³, Lori C. Guthrie⁴, Maria I. Alba⁴ and Theodore Pincus², ¹NIH/NIAMS, Bethesda, MD, ²Rheumatology, Rush University Medical Center, Chicago, IL, ³Drexel University College of Medicine, Philadelphia, PA, ⁴NIAMS/NIH, Bethesda, MD

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Monday, November 6, 2017
**Session Title:** Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
**Session Type:** ACR Poster Session B
**Session Time:** 9:00AM-11:00AM
Background/Purpose: No single “gold standard” measure is available to assess patients with rheumatoid arthritis (RA) in clinical trials and routine care, as in hypertension, diabetes, and other diseases. Therefore, an index of several measures, such as a DAS28 (Disease Activity Score-28) and CDAI (Clinical Disease Activity Index), based on 7 RA core data set measures, is needed. However, the only quantitative data collected in many (most) patients at routine rheumatology care visits are laboratory tests. RAPID3 (routine assessment of patient index data), which includes only patient self-report scores, is considerably more feasible than DAS28 or CDAI for routine care, distinguishes active from control treatments in RA clinical trials similarly and is correlated significantly with these indices. A minimal clinically important improvement (MCII) to aid in planning and interpretation of changes in disease activity/severity in clinical trials as well as in routine care has not been established for RAPID3, and is presented here.

Methods: Post hoc analyses were performed of a longitudinal study of 250 patients with active RA, in whom results of treatment escalation were assessed quantitatively, as described previously (1). All 7 RA core data set measures were collected at baseline and after treatment escalation. RAPID3 is the sum of 3 0-10 measures for a 0-10 (converted from 0-3) physical function scale and 0-10 visual analog scales (VAS) for pain and patient global assessment, total=0-30. DAS28-ESR and CDAI were computed as described in the literature. Patient judgment of improvement was recorded independently as “improved”, “the same” or “worsened”, and dichotomized as improved vs same/worsened to generate receiver operating characteristic (ROC) curves, to determine MCII as changes that had a specificity of 0.80 for improvement. Sensitivity to change was assessed as standardized response means (SRM).

Results: Among 250 patients, 167 (66.8%) reported improvement. Each composite index was sensitive to change, with SRMs ranging from -0.79 to -0.98 (Table). The mean ROC curve area ranged from 0.77 for DAS28-ESR to 0.80 for RAPID3 (Table). With a criterion of a specificity of 0.80, the MCII were -3.5 for RAPID3, -1.17 for DAS28-ESR, and −12.5 for CDAI. MCII were in a similar range of 11.6% to 16.8% of maximum score (Table).

Table. Changes in rheumatoid arthritis activity measures during the study.

<table>
<thead>
<tr>
<th>Measure (range)</th>
<th>Baseline (%)</th>
<th>Follow-up (%)</th>
<th>Mean change (95% CI)</th>
<th>SRM (95% CI)</th>
<th>ROC Curve Area (95% CI)</th>
<th>MCII (95% CI)</th>
<th>% of Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAPID3 (0–30)</td>
<td>16.3 ± 6.3</td>
<td>11.1 ± 6.7</td>
<td>-5.2 ± 6.5</td>
<td>-0.79</td>
<td>0.80</td>
<td>-3.5</td>
<td>11.6%</td>
</tr>
<tr>
<td>DAS28-ESR (0–9.4)</td>
<td>6.16 ± 1.2</td>
<td>4.8 ± 1.38</td>
<td>-1.31 ± 1.34</td>
<td>-0.98</td>
<td>0.77</td>
<td>-1.17</td>
<td>12.4%</td>
</tr>
<tr>
<td>CDAI (0–76)</td>
<td>36.8 ± 13.5</td>
<td>23.0 ± 13.6</td>
<td>-13.7 ± 14.1</td>
<td>-0.98</td>
<td>0.78</td>
<td>-12.5</td>
<td>16.4%</td>
</tr>
</tbody>
</table>

* SRM = standardized response mean; CI = confidence interval

Conclusion: MCII for RAPID3 were similar in ROC curve areas and SRM to DAS28 and CDAI. Knowledge concerning MCII thresholds can improve planning and interpretation of data from clinical trials and routine clinical care.


Disclosure: M. Ward, None; I. Castrejón, None; M. J. Bergman, None; L. C. Guthrie, None; M. I. Alba, None; T. Pincus, Theodore Pincus, 7.


Abstract Number: 1352

The Relevance of Elevated CRP As an Inclusion Criterion in Clinical Trials in Patients with Rheumatoid Arthritis

Craig Scoville1, Jessica L. Suboticki2, Sheng Zhong3 and Edward C. Keystone4, 1Idaho Falls Arthritis Clinic, Idaho Falls, ID, 2AbbVie Inc., Mettawa, IL, 3AbbVie Inc., North Chicago, IL, 4Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada
SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Elevated C-reactive protein (CRP) is often used as an entry criterion in clinical trials (CT) with rheumatoid arthritis (RA) patients (pts), resulting in the potential exclusion of pts with active disease and high screen failure rates. This analysis assessed the relevance of requiring an elevated CRP (≥1 mg/dL) as an inclusion criterion for clinical, functional, and radiographic outcomes.

Methods:
This post hoc analysis used data from 2 randomized CTs in RA pts with an inadequate response to methotrexate (MTX). In DE019, pts on background MTX received adalimumab (ADA) or placebo (PBO)2; in MUSICA, pts received either 7.5 or 20 mg MTX, along with ADA3. MUSICA data were used to confirm observations from DE019. Pts were subgrouped by CRP level at entry (CRP <1 mg/dL, ≥1 mg/dL). Baseline (BL) demographics and disease characteristics were summarized for each group. Clinical efficacy was assessed through swollen/tender joint count (S/TJC) at 66/68 joints, pain, patient global assessment (PtGA), physician global assessment (PhGA), CRP, clinical disease activity index (CDAI), 28-joint disease activity score based on CRP (DAS28-CRP), and proportions of pts achieving ACR20/50/70. Functional outcomes were assessed by the disability index of the health assessment questionnaire (HAQ-DI), and radiographic outcomes by the modified total Sharp score (mTSS). Outcomes were assessed in pts with CRP <0.8 mg/dL in DE019, which included pts with CRP levels as low as 0.75 mg/dL. Observed data are reported at week 24.

Results:
In DE019, 183 pts (89 and 94 in the ADA and PBO arms, respectively) had CRP <1 mg/dL and 224 pts (118 and 106, respectively) had CRP ≥1 mg/dL. Pts with elevated CRP had higher BL disease activity compared with those with CRP <1 mg/dL at entry (not shown). After 24 wks of treatment with ADA, pts in both CRP subgroups experienced significant improvements in most clinical and functional outcomes vs PBO (Table). In pts with CRP <0.8 mg/dL, the ACR20 response rate difference (30.4, p<.001) and the difference in ΔmTSS (-1.3, p<.05) for ADA vs PBO treatment were still significant. Compared to pts with CRP <1 mg/dL, pts with elevated CRP experienced greater clinical and functional improvements. However, within the ADA subgroups, pts with elevated CRP had smaller differences vs PBO in mTSS, perhaps reflecting higher joint damage at BL. In general, similar trends were observed in MUSICA (not shown).

Conclusion: While pts with elevated CRP at entry experienced larger improvements from BL in clinical and functional outcomes upon treatment, significant improvements in most outcomes were also observed in those without elevated CRP at entry (as low as 0.75 mg/dL), suggesting that an elevated CRP may not be required to see differences between active and inactive treatment.

References:
1. Von Vollenhoven et al. 2015, Arthritis Rheumatol 67: 2855-2860
### Disease characteristics at Week 24 in patients with CRP <1 or ≥1 mg/dL at entry in DE019

<table>
<thead>
<tr>
<th></th>
<th>CRP &lt;1</th>
<th>Difference</th>
<th>CRP ≥1</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PBO n=79</td>
<td>ADA n=74</td>
<td>PBO n=75</td>
<td>ADA n=101</td>
</tr>
<tr>
<td>TJC68</td>
<td>-13.2</td>
<td>-17.2</td>
<td>-3.2</td>
<td>-11.7</td>
</tr>
<tr>
<td>SJC66</td>
<td>-7.1</td>
<td>-11.1</td>
<td>-4.3**</td>
<td>-6.7</td>
</tr>
<tr>
<td>Pain</td>
<td>-13.0</td>
<td>-24.5</td>
<td>-11.7***</td>
<td>-20.3e</td>
</tr>
<tr>
<td>PtGA</td>
<td>-11.0</td>
<td>-24.2</td>
<td>-13.2***</td>
<td>-20.7c</td>
</tr>
<tr>
<td>PhGA</td>
<td>-24.4</td>
<td>-35.0</td>
<td>-10.2**</td>
<td>-28.0e</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>-0.26f</td>
<td>-0.49</td>
<td>-0.24**</td>
<td>-0.38</td>
</tr>
<tr>
<td>CRP</td>
<td>0.1</td>
<td>0.02</td>
<td>-0.08*</td>
<td>-0.54</td>
</tr>
<tr>
<td>DAS28-CRP</td>
<td>-1.19</td>
<td>-1.92</td>
<td>-0.75***</td>
<td>-1.26c</td>
</tr>
<tr>
<td>CDAI</td>
<td>-15.9</td>
<td>-22.7</td>
<td>-7.6***</td>
<td>-15.7c</td>
</tr>
<tr>
<td>ACR20, n/N (%)</td>
<td>32/79(41)</td>
<td>50/74(68)</td>
<td>27***</td>
<td>30/72(42)</td>
</tr>
<tr>
<td>ACR50, n/N (%)</td>
<td>9/79(11)</td>
<td>34/74(46)</td>
<td>35***</td>
<td>11/72(15)</td>
</tr>
<tr>
<td>ACR70, n/N (%)</td>
<td>6/79(8)</td>
<td>19/74(26)</td>
<td>18**</td>
<td>0/72(0)</td>
</tr>
<tr>
<td>mTSS</td>
<td>0.93a</td>
<td>-0.32b</td>
<td>-1.30**</td>
<td>1.63g</td>
</tr>
</tbody>
</table>

Change from baseline values and least square mean differences (using ANCOVA) are reported for continuous endpoints. p-values for binary endpoints are calculated based on chi-square test or Fisher’s exact test. ****, ***, *: p <.001, .01 and .05, respectively for differences between treatment groups for change from BL. Missing values are not imputed.

a\n\n\nb\n\n\nc\n\n\nd\n\n\ne\n\n\nf\n\n\ng\n\n\nh\n\n\ni\n\n\nj

TJC68, tender joint count at 68 joints; SJC66, swollen joint count at 66 joints; PtGA, patients global assessment of disease activity; PhGA, physician’s global assessment of disease activity; HAQ-DI, disability index of health assessment questionnaire; CRP, C-reactive protein; DAS28-CRP, 28-joint disease activity score based on CRP; CDAI, clinical disease activity index; mTSS, modified total Sharp score; ACR20/50/70, 20, 50 and 70% improvement in the American College of Rheumatology criteria


**Abstract Number:** 1353

**Is Joint Damage Due to Secondary Osteoarthritis (OA) Clinically As Important As Inflammation in Contemporary Management of Rheumatoid Arthritis (RA)?**
Background/Purpose: Measures to assess patients with rheumatoid arthritis (RA) reflect primarily inflammatory activity in patients who meet inclusion criteria for selection into clinical trials. However, many patients seen in routine care (and some in clinical trials) have structural joint damage and/or patient distress in addition to inflammatory activity, which may affect RA indices. Thus, a patient with 0 swollen joints, an erythrocyte sedimentation rate of 15, 14 tender joints and patient global assessment of 80/100 (or 8/10) would have a DAS28 of 5.1 and CDAI of at least 22 (even if physician global assessment is 0), suggesting high disease activity, although the high score results from damage and/or distress. We have added to a physician global assessment (DOCGL) 0-10 visual analog scale (VAS) 3 three 0-10 VAS for inflammation, damage, and distress, as well as estimates of the proportion of clinical management decisions attributed to each (%inflammation+ %damage+ %distress, total=100%). We hypothesized that a greater proportion of clinical decisions in RA may be attributed to structural damage than to inflammation as a result of modern therapeutics, by comparing scores in routine care patients.

Methods: At one academic center, all patients complete an MDHAQ/RAPID3 prior to seeing the rheumatologist. Physicians complete 4 0-10 VAS for DOCGL, inflammation (i.e., reversible disease) (DOCINF), damage (i.e., structural irreversible disease) (DOCDAM), and distress (i.e., fibromyalgia, depression, etc.) (DOCSTR). The rheumatologist also records estimates of the proportion of clinical management decisions attributed to %inflammation, %damage, and % distress, total=100%. Patients were classified in 5 groups for DOCINF and DOCDAM VAS as 0-2, 2.1-4, 4.1-6, 6.1-8, and 8.1-10, and for % of clinical decisions as 0-20%, 21-40%, 41-60%, 61-80%, and 81-100%, and compared using t tests and analysis of variance (ANOVA).

Results: In a cross-sectional analysis of a single random visit of 98 RA patients, mean physician DOCINF 0-10 VAS was 2.8, lower than 3.8 for DOCDAM (Table). The mean proportion of management decisions attributed to inflammation was 39%, lower than 52% for damage (Table) (9% for distress- data not shown). Minimal 0-2.0 VAS scores for DOCINF were seen in 48 patients vs 30 for DOCDAM, while 4.1-10 VAS were estimated in 20 patients for DOCINF (8+2+10) vs 29 for DOCDAM (12+15+2). More than 40% of management decisions was attributed to damage in 59 patients (24+20+15) (vs 22 for 0-20%), vs to inflammation in 42 patients (18+15+9) (same as 0-20%) (Table).

<table>
<thead>
<tr>
<th>Measure</th>
<th>Inflammation</th>
<th>Damage</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>2.8 (2.4)</td>
<td>3.8 (2.3)</td>
</tr>
<tr>
<td>0-2.0</td>
<td>48 (49%)</td>
<td>30 (31%)</td>
</tr>
<tr>
<td>2.1-4.0</td>
<td>30 (31%)</td>
<td>39 (41%)</td>
</tr>
<tr>
<td>4.1-6.0</td>
<td>8 (8%)</td>
<td>12 (12%)</td>
</tr>
<tr>
<td>6.1-8.0</td>
<td>10 (10%)</td>
<td>15 (15%)</td>
</tr>
<tr>
<td>8.1-10.0</td>
<td>2 (2%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>% Decision</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean % of 100%</td>
<td>39% (29)</td>
<td>52% (30)</td>
</tr>
<tr>
<td>0-20%</td>
<td>42 (43%)</td>
<td>22 (22%)</td>
</tr>
<tr>
<td>21-40%</td>
<td>14 (14%)</td>
<td>17 (17%)</td>
</tr>
<tr>
<td>41-60%</td>
<td>18 (18%)</td>
<td>24 (24%)</td>
</tr>
<tr>
<td>61-80%</td>
<td>15 (15%)</td>
<td>20 (20%)</td>
</tr>
<tr>
<td>81-100%</td>
<td>9 (9%)</td>
<td>15 (15%)</td>
</tr>
<tr>
<td>Total</td>
<td>98</td>
<td>98</td>
</tr>
</tbody>
</table>

Conclusion: Structural joint damage appears more prominent than inflammatory activity in physician clinical management decisions in a cross-section of RA patients at this time. Quantitative physician estimates of damage as well as inflammation may clarify management decisions in patients with RA, as damage remains a significant challenge in routine clinical care.
Fatigue, Poor Health and Mood Disturbance Persist in Rheumatoid Arthritis and Psoriatic Arthritis Patients Despite Disease Remission: The OPAL Deeper Study

Paul Bird¹, Hedley Griffiths², Geoff Littlejohn³, Peter Youssef⁴, Fred Joshua⁵, Peter Nash⁶, Julien De Jager⁷, Tegan Smith⁸, Janet Sanburg⁹ and Kathleen Tymms¹⁰, ¹University of New South Wales, Sydney, Australia, ²Barwon Rheumatology Service, Geelong, Australia, ³Medicine, Monash, Melbourne, Australia, ⁴Royal Prince Alfred Hospital, Camperdown, Sydney, Australia, ⁵Combined Rheumatology Practice, Sydney, NSW, Australia, ⁶University of Queensland, Brisbane, Australia, ⁷University Of Queensland, Southport, Australia, ⁸OPAL, Sydney, Australia, ⁹OPAL, Melbourne, Australia, ¹⁰ANU, Canberra, Australia

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Patient reported outcomes are recognized as increasingly important in defining the full burden of disease experienced by patients with rheumatic disease. Traditional measures of remission (DAS28, CDAI, SDAI, Rapid 3) are important in the treat-to-target paradigm as measures of response to treatment, but it is increasingly recognized that these measures cannot capture the full yoke that subjects with rheumatic disease endure. Furthermore, as modern rheumatology advances, it is increasingly difficult to capture the complete spectrum of the patient response to therapies using traditional measures. This primary objective of this study was to examine the relationship between DAS28CRP and fatigue, health, and mood using a novel electronic PRO delivery system.

Methods:

We utilized the Optimising Patient Outcome in Australian rheumatoLogy (OPAL) database employing a unique electronic questionnaire delivery system to obtain PRO information from rheumatology patients on a quarterly basis and/or prior to patient-physician consultation. The software enables an email to be delivered to the patient automatically, and the patient is invited to complete a validated PRO questionnaire by smartphone, tablet or desktop. Completed questionnaires are securely fed back into the patient’s electronic health record (EHR) for discussion at the next consultation. PRO’s collected included fatigue (FACIT-F), mood (PHQ-2), overall health (SF-1) and RAPID3 components. PROs were correlated with DAS28CRP using Pearson product-moment correlation coefficient.

Results:

12,575 PROs have been returned from 1625 unique patients with a completion rate of approximately 70%. There was a weak correlation between fatigue and DAS28CRP (R²=-0.40); CDAI (R² =-0.41) HAQ-DI (-0.60). However, a significant proportion of patients in low disease activity (LDA) and remission reported ongoing fatigue. Patient perception of their overall health was similar with 22% of patients in remission and 33% of patients in LDA reporting fair or poor health. Furthermore, 41% of patients in LDA and 31% of patients in remission reported feeling down in the previous 2 weeks.

Conclusion:

Fatigue, mood disturbance, and poor health are reported by a considerable proportion of subjects in DAS28CRP LDA and remission. These results underline the importance of PROs in documenting the full impact of rheumatic disease and the patient response to therapy.
Disclosure: P. Bird, Celgene Corporation, 2,Abbott Laboratories, 2,Pfizer Inc, 5,Bristol-Myers Squibb, 5,Janssen Pharmaceutical Product, L.P., 5,Novartis Pharmaceutical Corporation, 5; H. Griffiths, None; G. Littlejohn, None; P. Youssef, None; F. Joshua, None; P. Nash, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Hospira, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, 5,AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Hospira, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, 8,AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Hospira, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB, 2; J. De Jager, None; T. Smith, None; J. Sanburg, None; K. Tymms, None.


Abstract Number: 1355

14-3-3η: Useful for More Than the Diagnosis of Rheumatoid Arthritis?

Lisa Zickuhr1, Maryam Pourpaki2, Martha M. Brooks3 and Amy Joseph4, 1Rheumatology, Cleveland Clinic Foundation, Cleveland, OH, 2Rheumatology, Advocate Christ Medical Center at Chicago, Oak Lawn, IL, 3Rheumatology, St. Louis VA Medical Center, St. Louis, MO, 4Rheumatology, Veterans Administration Central Office, St. Louis, MO

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Chronic hepatitis C virus (HCV) infection can masquerade as rheumatoid arthritis (RA). Distinguishing between the two is important because treatments differ. 14-3-3η has been explored in RA. When combined with traditional antibodies, high titers of 14-3-3η improve the accuracy of RA diagnosis. The utility of measuring 14-3-3η is not well understood in viral infections, such as HCV. We measure the incidence of 14-3-3η in patients with chronic HCV infection with long-standing arthralgias and compare it to the incidence in patients with long-standing RA to assess its utility in differentiating the two.

Methods: We recruited patients at the VA St. Louis Health Care System in St. Louis, MO, with an established diagnosis of either RA per 2010 ACR/EULAR Classification Criteria for RA or chronic HCV infection (defined as a detectable HCV viral load) with arthralgias of at least three joints. We obtained clinical information from chart review and physical exam at time of enrollment. We measured serum 14-3-3η titers with a quantitative sandwich ELISA (Quest Diagnostics Nichols Institute, San Juan Capistrano, CA), defining presence of 14-3-3η as a serum titer >0.19ng/mL. Chi-squared analysis compared the incidence of 14-3-3η in the two groups (α = 0.05).

Results:
### RA (N = 14) HCV (N=21)

<table>
<thead>
<tr>
<th></th>
<th>RA (N=14)</th>
<th>HCV (N=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>N (%)</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>2 (14.3%)</td>
<td>1 (4.8%)</td>
</tr>
<tr>
<td>Male</td>
<td>12 (85.7%)</td>
<td>20 (95.2%)</td>
</tr>
<tr>
<td>Age ± STD (years)</td>
<td>65.1 ± 8.8</td>
<td>63.7 ± 3.5</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>12 (85.7%)</td>
<td>7 (33.3%)</td>
</tr>
<tr>
<td>African American</td>
<td>--</td>
<td>1 (4.8%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>--</td>
<td>1 (4.8%)</td>
</tr>
<tr>
<td>Other (Asian, Native American)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Duration of Joint Disease ± STD (years)</td>
<td>11.9 ± 12.2</td>
<td>18.7 ± 11.1</td>
</tr>
<tr>
<td>Number of Joints Involved ± STD</td>
<td>14 ± 5</td>
<td>3.5 ± 0.5</td>
</tr>
<tr>
<td>Active Disease, Synovitis at Time of Enrollment</td>
<td>2 (14.3%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>12 (85.7%)</td>
<td>1 (4.8%)</td>
</tr>
<tr>
<td>DMARDs</td>
<td>2 (14.3%)</td>
<td>--</td>
</tr>
<tr>
<td>Biologics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serologies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rheumatoid Factor (RF)</td>
<td>11 (78.6%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Anti-Citrullinated Peptide (CCP)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence of 14-3-3 η</td>
<td>2 (14.3%)</td>
<td>1 (4.8%)</td>
</tr>
<tr>
<td>Erosions on X-ray</td>
<td>3 (21.4%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

Both groups had long-standing joint disease of more than ten years. All RA patients met 2010 ACR/EULAR Classification Criteria for RA, and all HCV patients had detectable viral loads. Only two (14.3%) RA patients and 1 (4.8%) HCV patient had elevated 14-3-3η. Chi-square showed no significant association between 14-3-3η positivity and diagnosis of either RA or HCV ($X^2 = 0.73$, $p=0.39$). Of the two RA patients with elevated 14-3-3η, both (100%) had RF and anti-CCP antibodies, and one (50%) had active disease, with synovitis at time of enrollment and radiographic erosions. The HCV patient with elevated 14-3-3η was RF positive.

**Conclusion:** We show a low incidence of 14-3-3η in a cohort of patients with long-standing RA or chronic HCV with arthralgias, lower than what was reported previously. In our cohort, 14-3-3η did not distinguish between joint pain from RA or chronic HCV infection. This suggests it is not useful in patients with long symptom duration. Most of our RA cohort’s disease was controlled on therapy. Therefore, detection of 14-3-3η may be most useful early in the disease course and may be a good biomarker of disease activity. Additional studies correlating 14-3-3η positivity with disease activity and duration are warranted.

**Disclosure:** L. Zickuhr, None; M. Pourpaki, None; M. M. Brooks, None; A. Joseph, None.

**View Abstract and Citation Information Online** - [http://acrabstracts.org/abstract/14-3-3%ce%b7-useful-for-more-than-the-diagnosis-of-rheumatoid-arthritis](http://acrabstracts.org/abstract/14-3-3%ce%b7-useful-for-more-than-the-diagnosis-of-rheumatoid-arthritis)

**Abstract Number:** 1356

**Is ACPA-Positive RA Still a More Severe Disease Than ACPA-Negative RA? a Longitudinal Cohort Study in RA-Patients Treated from 2000 Onwards**

Aleid C. Boer¹, Annelies Boonen² and Annette H.M. van der Helm-van Mil³

¹Rheumatology, Leiden University Medical Center, Leiden, Netherlands
²Department of Internal Medicine, Division of Rheumatology, Maastricht University Medical Centre+, Maastricht, The Netherlands
³Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Background/Purpose:**

Anti-citrullinated-protein antibodies (ACPA)-positive rheumatoid arthritis (RA) is considered as more severe than ACPA-negative RA, because of its association with joint destruction. Clinically relevant joint destruction is now infrequent, thanks to adequate disease suppression. According to patients, important outcomes are pain, fatigue and independence. We evaluated if ACPA-positive RA-patients diagnosed ≥2000 have more severe self-reported limitations and impairments including restrictions at work than ACPA-negative RA-patients.

**Methods:**

492 ACPA-positive, 450 ACPA-negative 2010-criteria-positive RA-patients included in the Leiden Early Arthritis Clinic cohort ≥2000 were compared for self-reported pain, fatigue, disease activity, general wellbeing (measured by numerical rating scales) and physical function (measured by the health assessment questionnaire, HAQ) and also work restrictions including absenteeism at baseline and during 4-year follow-up. Linear mixed models were used.

**Results:**

At disease presentation, ACPA-negative patients had more severe pain, fatigue, self-reported disease activity-scores and functional disability (p<0.05), although absolute differences were small. During follow-up ACPA-negative patients remained somewhat more fatigued (p=0.002), whereas other patient-reported impairments and limitations were similar. 38% ACPA-negative and 48% ACPA-positive patients reported absenteeism (p=0.30), with median 4 days missed in both groups in the last 3 months. Also restrictions at work among employed patients and restrictions with household work were not statistically different at baseline and during follow-up.

**Conclusion:**

In current rheumatology practice, ACPA-positive RA is not more severe than ACPA-negative RA in terms of for patients relevant outcomes including physical functioning and restrictions at work. This implies that effort to further improve the disease course should not restrict to ACPA-positive patients.

**Disclosure:** A. C. Boer, None; A. Boonen, None; A. H. M. van der Helm-Van Mil, None.

**Abstract Number:** 1357

**Anti-Cyclic Citrullinated Peptide Antibody Positive Rheumatoid Arthritis Patients with Comorbid Post-Traumatic Stress Disorder Have Higher Serum Cytokine Expression**

Bryant R. England¹, Harlan Sayles², Geoffrey M. Thiele², Kaleb Michaud², Jeremy Sokolove³, Grant Cannon⁴, Andreas Reimold⁵, Gail S. Kerr⁶, Liron Caplan⁷, Joshua Baker⁸ and Ted R. Mikuls⁹, ¹Division of Rheumatology & Immunology, Department of Internal Medicine, Nebraska-Western IA VA Health Care System & University of Nebraska Medical Center, Omaha, NE, ²University of Nebraska Medical Center, Omaha, NE, ³Division of Immunology and Rheumatology, Stanford University Medical Center, Mountain View, CA, ⁴Salt Lake City VA Medical Center and University of Utah, Salt Lake City, UT, ⁵Hospital of Southern Norway, Kristiansand, Norway, ⁶VAMC, Georgetown University, Washington, DC, ⁷Division of Rheumatology, University of Colorado School of Medicine, Aurora, CO, ⁸Rheumatology, University of Pennsylvania, Philadelphia, PA, ⁹Internal Medicine, Division of Rheumatology, University of Nebraska Medical Center, Omaha, NE

**First publication:** September 18, 2017
Background/Purpose: We have previously shown that rheumatoid arthritis (RA) patients with Post-Traumatic Stress Disorder (PTSD) have higher disease activity measures, due primarily to patient reported measures including higher tender joint counts, pain, and worse patient global scores. However, a recent systematic review and meta-analysis reported increased serum expression of IL-1, IL-6, and IFN-γ in PTSD patients (Passos IC et. al., Lancet Psychiatry, 2015). The purpose of this study was to compare serum cytokine/chemokine expression in RA patients with and without PTSD.

Methods: Participants were enrollees in a multicenter, longitudinal observational cohort of US Veterans with RA categorized as having PTSD, other anxiety or depression, or neither based on administrative codes. Serum cytokines/chemokines were measured from banked serum at enrollment using a multiplex bead-based assay. Cytokines (CKs) were modeled using an overall cytokine (CK) score (log-transformed), the number of elevated cytokines (>2 SD above mean), and by individual CKs (log-transformed). CK score and number of elevated CKs were compared between groups using ANOVA and \( \chi^2 \). The association of PTSD with CK parameters was assessed using multivariable least squares and negative binomial regression adjusted for age, sex, race, and smoking status. Analyses were additionally stratified by anti-CCP status.

Results: Of 1,460 RA subjects with mean (SD) age of 64 (11) years, RA duration 11 (11) years, were 91% male, 76% anti-CCP positive, and 80% current or former smokers, 9% had PTSD, 24% had other depression/anxiety, and 67% had neither psychiatric condition. In unadjusted comparisons, those with PTSD had higher CK scores (P=0.02) and a greater number of elevated CKs (P=0.02, Figure 1). In multivariable least squares and negative binomial regression models, CK score and number of positive CKs were associated with PTSD, though this was limited to those who were anti-CCP positive (Table 1). Anxiety/depression subjects without PTSD had similar CK scores and number of elevated CKs as controls. PTSD was associated with heightened expression of several individual CKs (IL-1, IL-2, IL-6, IL-10, GM-CSF, IFN-γ, MCP-1).

Conclusion: Anti-CCP positive RA patients with PTSD have a higher serum cytokine expression in comparison to those without PTSD. These findings support an objective measure of increased inflammation in RA patients with comorbid PTSD. Exploration of a potential mechanistic inflammatory link between RA and PTSD and contributions of specific cytokines will require future study.
Table 1. Associations of Serum Cytokines with PTSD in Rheumatoid Arthritis

<table>
<thead>
<tr>
<th></th>
<th>No Depression, Anxiety or PTSD</th>
<th>Depression or Anxiety</th>
<th>PTSD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Values, mean (SD)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cytokine score</td>
<td>2.33 (0.89)</td>
<td>2.39 (0.91)</td>
<td>2.56 (0.93)</td>
</tr>
<tr>
<td>Cytokine number positive</td>
<td>1.08 (2.23)</td>
<td>1.23 (2.42)</td>
<td>1.64 (2.75)</td>
</tr>
<tr>
<td><strong>All subjects</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cytokine score</td>
<td>Reference</td>
<td>0.055 (-0.055, 0.165)</td>
<td><strong>0.193 (0.026, 0.361)</strong></td>
</tr>
<tr>
<td>Cytokine number positive</td>
<td>Reference</td>
<td>0.145 (-0.051, 0.341)</td>
<td><strong>0.355 (0.197, 0.513)</strong></td>
</tr>
<tr>
<td><strong>Anti-CCP positive</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cytokine score</td>
<td>Reference</td>
<td>-0.027 (-0.170, 0.117)</td>
<td>0.193 (-0.018, 0.405)</td>
</tr>
<tr>
<td>Cytokine number positive</td>
<td>Reference</td>
<td>-0.036 (-0.272, 0.201)</td>
<td><strong>0.339 (0.162, 0.517)</strong></td>
</tr>
<tr>
<td><strong>Anti-CCP negative</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cytokine score</td>
<td>Reference</td>
<td>-0.048 (-0.266, 0.171)</td>
<td>-0.074 (-0.410, 0.261)</td>
</tr>
<tr>
<td>Cytokine number positive</td>
<td>Reference</td>
<td>0.184 (-0.403, 0.771)</td>
<td>-0.233 (-0.588, 0.092)</td>
</tr>
</tbody>
</table>

*Values represent b coefficients (95% confidence interval)

*P < 0.05; ** P < 0.01

Models adjusted for age, sex, race, and smoking status.

**Disclosure:** B. R. England, None; H. Sayles, None; G. M. Thiele, None; K. Michaud, None; J. Sokolove, None; G. Cannon, Amgen, 2; A. Reimold, Bristol-Myers Squibb, 2,Janssen Pharmaceutica Product, L.P., 2,Pfizer, 2,Human Genome Sciences, 2,Novartis, 2; G. S. Kerr, Janssen, BMS, Genetech, Pfizer, 2; L. Caplan, None; J. Baker, None; T. R. Mikuls, BMS, 2,Ironwood Pharm, 2,Pfizer Inc, 5,NIH, VA, 2.


**Abstract Number:** 1358

**Relationship between Serum Protein Pattern and High Disease Activity in Patients with Rheumatoid Arthritis**

**Pavel Horak**¹, Anna Petráčková², Martina Skácelová³, Eva Kriegová⁴, Petra Schneiderová⁵ and František Mrázek⁵, ¹III. Department of internal medicine, III. Department of Internal Medicine, Faculty of Medicine and Dentistry, Palacký University of Olomouc, Olomouc, Czech Republic, ²Department of Immunology, Department of Immunology, Faculty of Medicine and Dentistry, Palacky University of Olomouc, Olomouc, Czech Republic, ³III. Department of Internal Medicine, Faculty of Medicine and Dentistry, Palacký University of Olomouc, Olomouc, Czech Republic, ⁴Department of Immunology, Faculty of Medicine and Dentistry, Palacky University of Olomouc, Olomouc, Czech Republic, ⁵Department of Immunology, Faculty of Medicine and Dentistry, Palacky University of Olomouc, Olomouc, Czech Republic

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures  
Session Type: ACR Poster Session B  
Session Time: 9:00AM-11:00AM  

**Background/Purpose:** Rheumatoid arthritis (RA) is a chronic autoimmune disease that primarily affects joints. There is still limited information of serum biomarkers suitable for effective monitoring of disease activity. To assess RA-associated serum protein signature using highly sensitive multiplex Proximity Extension ImmunoAssay (PEA) and its relationship with disease activity evaluated by activity score (DAS28).

**Methods:** We investigated the serum levels of 92 inflammation-related proteins in 78 Czech patients with RA and 38 age-matched healthy control (C) subjects using a highly sensitive innovative multiplex PEA (Proseek Multiplex, Olink Bioscience, Sweden). Statistical tests (Mann-Whitney U test, Benjamini-Hochberg correction, Spearman correlation) were performed using GenEx (Sweden), $P$-value ≤ 0.05 was considered as significant.

**Results:**
Top-ranked proteins distinguishing RA and C ($P_{corr}<0.0001$) were sTNFSF14, sulfotransferase 1A1, IL-6, axin 1, CCL7, caspase 8, oncostatin M, sirtuin 2, sTGFα, CCL3, sHGF, sCD40, STAMBP, FGF23, CXCL10, and sSLAMF1. Of them, upregulation of sulfotransferase 1A1, axin 1, and GDNF was not reported in RA yet. Disease activity positively correlated with CCL20 ($r=0.495$, $P=0.000004$), CCL7 ($r=0.442$, $P=0.00005$), CXCL1, CXCL9, IL-6, sCDCP1, GDNF, CXCL10 ($r>0.30$, $P<0.006$), and negatively correlated with IL-12B and sCD244 ($r<-0.304$, $P<0.007$). Subanalysis of protein pattern in patient phenotypes is ongoing.

**Conclusion:** Among the entire panel, the chemokines CCL20, CCL7, CXCL1, CXCL9, CXCL10 and GDNF appeared to be the most useful serum markers for evaluation of the disease activity of patients with RA. Further multivariate analysis is needed to identify pattern associated with high disease activity.

Acknowledgement: Grant support: MZ CR VES15-28659A, IGA_LF_2017_009

Disclosure: P. Horak, None; A. Petráčková, None; M. Skácelová, None; E. Kriegová, None; P. Schneiderová, None; F. Mrázek, None.


Abstract Number: 1359

**M-DAS28, M-SDAI and M-CDAI Performance in a Cohort of RA Patients with and without Concomitant Fibromyalgia**

Julia Sosa1, Silvana Karina Pérez1, Maria Julia Santa Cruz1, Maria Alejandra Medina1, Silvia Beatriz Papasidero1, Diana Klajn2, Jose Angel Caracciolo1, Maria de los Angeles Correa3, Roger Rolón4, Gustavo Citera4, Maria Constanza Bertolaccini5, LL Gonzalez6, L Vargas7 and Oscar Rillo7, 1Rheumatology Department, Hospital General de Agudos Dr. Enrique Tornú, Buenos Aires, Argentina, 2Research Committee, Hospital General de Agudos Dr. Enrique Tornú, Buenos Aires, Argentina, 3Section Rheumatology, Instituto de Rehabilitación Psicofísica, Buenos Aires, Buenos Aires, Argentina, 4Rheumatology Department, Instituto de Rehabilitación Psicofísica, Buenos Aires, Argentina, 5Rheumatology, Hospital Angel Cruz Padilla, Tucumán, Argentina, 6Hospital Angel Cruz Padilla, Tucumán, Argentina, 7Rheumatology Department, Hospital General de Agudos Dr. Ignacio Pirovano, Buenos Aires, Argentina

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures  
Session Type: ACR Poster Session B  
Session Time: 9:00AM-11:00AM
Background/Purpose: Fibromyalgia has been reported in approximately 20% of Rheumatoid Arthritis (RA) patients. Several studies have shown that the presence of Fibromyalgia (FM) is associated with a significant increase in patient-reported outcomes (PROs). Therefore, traditional composite measures usually employed for the assessment of disease activity in RA, would not be able to discriminate between RA activity and FM symptoms. Baker et al. developed modified disease activity scores based on DAS28, SDAI and CDAI (M-DAS28, M-SDAI, M-CDAI). Interestingly, these scores of which all self-reported measures were excluded, showed a better correlation with synovitis detected on magnetic resonance imaging (MRI). By excluding the tender joint count and the patient’s global assessment of disease activity, these new activity scores would represent a useful tool to better determine RA activity in patients with concomitant FM. The aim of this study was to evaluate the M-DAS28, M-SDAI and M-CDAI performance in a cohort of RA patients with and without concomitant FM. Methods: Cross-sectional observational study that included consecutive patients with diagnosis of RA (ACR/EULAR 2010 criteria) with and without concomitant FM (ACR 1990 and/or ACR 2010 criteria). Other connective tissue disorders (except secondary Sjögren’s Syndrome) were excluded. Demographic and RA characteristics, and disease activity measures were collected. Patients were divided into 2 groups: RA and RA+FM. Statistical analysis: Mean differences between traditional and modified scores in RA patients with and without FM were analyzed. A linear regression model evaluating the effect of FM presence on score difference was performed, adjusting by covariates that proved significant on bivariate analysis. Results: A total of 130 patients were included, 90% women, mean age was 53 years (SD 12.3). Thirty-five patients had RA+FM (27%). Mean duration of RA was 66 months (IQR 23-120). The only difference between the groups with and without FM was the presence of nodular disease (11.4% vs 32.6%, p=0.01). The difference between traditional and modified scores was higher and statistically significant in the RA+FM group (Table 1). This difference remained after adjusting for sex, age and nodular disease (Table 2). Conclusion: RA activity assessed by these new modified disease activity scores in patients with RA and concomitant FM was lower than that measured by traditional ones. Therefore, these new modified scores could avoid a disease activity overestimation in RA patients with FM, resulting in a better tool to achieve the “Treat to Target” premises.

<table>
<thead>
<tr>
<th>Score difference</th>
<th>Mean increment</th>
<th>CI 95%</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAS28ESR-MDAS28ESR (N=128)</td>
<td>1.68 (0.17)</td>
<td>3.00 (0.57)</td>
<td>0.0023</td>
</tr>
<tr>
<td>DAS28CRP-MDAS28CRP (N=119)</td>
<td>1.24 (0.16)</td>
<td>2.70 (0.61)</td>
<td>0.0015</td>
</tr>
<tr>
<td>SDAI – MSDAI (N=119)</td>
<td>10.06 (1.56)</td>
<td>19.80 (4.56)</td>
<td>0.0193</td>
</tr>
<tr>
<td>CDAI - MCDAI (N=130)</td>
<td>7.35 (1.46)</td>
<td>15.74 (4.06)</td>
<td>0.0158</td>
</tr>
</tbody>
</table>

SE= Standard error

<table>
<thead>
<tr>
<th>Score difference</th>
<th>Mean increment</th>
<th>CI 95%</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAS28ESR-MDAS28ESR</td>
<td>1.50 (0.60-2.40)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>DAS28CRP-MDAS28CRP</td>
<td>1.55 (0.63-2.48)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>SDAI – MSDAI</td>
<td>10.78 (3.23-18.34)</td>
<td>0.005</td>
<td></td>
</tr>
<tr>
<td>CDAI - MCDAI</td>
<td>11.34 (3.80-18.89)</td>
<td>0.0258</td>
<td></td>
</tr>
</tbody>
</table>

Disclosure: J. Sosa, None; S. K. Pérez, None; M. J. Santa Cruz, None; M. A. Medina, None; S. B. Papasidero, None; D. Klajn, None; J. A. Caracciolo, None; M. D. L. A. Correa, None; R. Rolón, None; G. Citera, Novartis, Pfizer Inc, 2,AbbVie, Bristol-Myers Squibb, Janssen, Novartis, Pfizer Inc, 5; M. C. Bertolaccini, None; L. Gonzalez, None; L. Vargas, None; O. Rillo, None.


Abstract Number: 1360
Validation of the Health Assessment Questionnaire-Upper Extremity (HAQUP) in Patients with Rheumatoid Arthritis

Juan Manuel Bande¹, José Ángel Caracciolo¹, Silvia Beatriz Papasidero¹, María Julia Santa Cruz², María Alejandra Medina¹, Diana Klajn³, María Gabriela Battaglia⁴, Julieta Giantinoto⁴ and Florencia Pelagagge⁴, ¹Rheumatology Department, Hospital General de Agudos Dr. Enrique Tornú, Buenos Aires, Argentina, ²Section of Rheumatology, Hospital General de Agudos Dr. Enrique Tornú, Buenos Aires, Argentina, ³Research Committee, Hospital General de Agudos Dr. Enrique Tornú, Buenos Aires, Argentina, ⁴Occupational Therapy Department, Hospital General de Agudos Dr. Enrique Tornú, Buenos Aires, Argentina

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: HAQ is considered the gold standard for the evaluation of functional capacity in patients with RA, even though it doesn’t focus in any particular anatomical region. With the objective of assessing functional incapacity of the hand in elderly patients with osteoarthritis, Baron et al. (1987) used a modified version of the HAQ which was calculated as the mean value for those categories involving mostly upper extremities and named it ‘HAQUP’. This instrument has not been validated in patients with RA. Given the high prevalence of upper limb involvement in this disease and the lack of useful tools in daily clinical practice targeting the functional capacity of this anatomical sector, the aim of this study was to validate HAQUP in patients with RA.

Methods: Analytical, observational, prospective cross-sectional study. We included consecutive patients ≥ 18 years with diagnosis of RA (ACR/EULAR 2010). Socio-demographic data, characteristics of the disease, disease activity parameters and treatment were recorded. Patients completed the following self-administered questionnaires: HAQ-A (Argentine Spanish Version), HAQUP, Functional Index for Hand OsteoArthritis (FIHOA) and Quick Disabilities of the Arm, Shoulder and Hand (Quick DASH). In a subgroup of patients, an occupational therapist made an objective evaluation of the functional capacity of upper limbs using the Sequential Occupational Dexterity Assessment (SODA). The reproducibility of the questionnaire was assessed in 30 patients who completed HAQUP in a second visit, 10 to 15 days. Statistical analysis: Population characteristics were described. Reliability was assessed using the Cronbach test. Construct validity was analyzed through the correlation with other functional capacity questionnaires and disease activity parameters using the Spearman coefficient. Reproducibility was estimated using test-retest reliability. A linear regression model was constructed with HAQUP as the outcome variable and those variables that were statistically significant in bivariate analysis.

Results: We included 100 patients, 83% women, mean age 57.9 years (SD 11.6). The median HAQ-A was 0.88 (IQR 0.25-1.50). Cronbach's alpha test was 0.94. The intra-item correlation did not show redundant questions. HAQUP showed excellent correlation with HAQ-A (r = 0.93); FIHOA (r = 0.89); Quick DASH (r = 0.91) and SODA (r = -0.84). It also showed good correlation with DAS28 (r = 0.68) and other composite disease activity indices as well as with other parameters of the disease [visual analog scale (VAS) for pain, patient and physician global, 28 tender joint count (TJC), 68 TJC, 28 swollen joint count (SJC) and 66 SJC]. There was no correlation between HAQUP and age or disease duration. The reproducibility of the questionnaire was 0.82. Multiple linear regression adjusted for age and sex showed patient global VAS as the main determinant of HAQUP, followed by the presence of morning stiffness and 66 SJC.

Conclusion: HAQUP was found to be reliable, valid and reproducible in patients with RA, representing a useful tool for the evaluation of the functional capacity of the upper limbs in these patients.

Disclosure: J. M. Bande, None; J. Á. Caracciolo, None; S. B. Papasidero, None; M. J. Santa Cruz, None; M. A. Medina, None; D. Klajn, None; M. G. Battaglia, None; J. Giantinoto, None; F. Pelagagge, None.


Abstract Number: 1361
How Often Do Rheumatologists Use Valid Prognostic Factors of Rheumatoid Arthritis? the ProgresAR Project

Teresa Oton-Sanchez¹, Loreto Carmona², Sara Luján³, Ana Royo³, Jose Luis Baquero⁴ and Santiago Muñoz-Fernandez⁵, ¹InMusc. Instituto de Salud Músculo-Esquelética, Madrid, Spain, ²Instituto de Salud Musculoesquelética (InMusc), Madrid, Spain, ³Medical Department Bristol-Myers Squibb, Madrid, Spain, ⁴Scientific Department Scientia Salus, Madrid, Spain, ⁵Rheumatology, Hospital Universitario Infanta Sofia. Universidad Europea, Madrid, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Prognostic factors facilitate decisions on treatment and follow-up of patients with rheumatoid arthritis (RA). Rheumatologists might use factors with poor link to evidence in clinical practice. The ProgresAR project aims to 1) benchmark the use of the most commonly known prognostic factors in RA in daily clinical practice, and 2) to contrast their use with the strength of association of these factors with poor outcome.

Methods: We performed an overview of systematic reviews of factors associated with disability, mortality, remission, and radiological progression in RA. Then, a panel of rheumatologists, removed and added factors to the selection. Following, a review in matrix was carried out for each factor and outcome. In parallel, a group of 42 rheumatologists randomly selected was surveyed. The use of each factor was recorded on a Likert scale from 1 (none) to 9 (always) generating 3 categories: 1-3 under use; 4-6 intermediate and 7-9 high use.
### Prognostic factors

<table>
<thead>
<tr>
<th>Sociodemographic data</th>
<th>Use M (IQR)</th>
<th>Radiological progression</th>
<th>Disability</th>
<th>Mortality</th>
<th>Remission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advanced age</td>
<td>5 (4)</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female gender</td>
<td>6 (4)</td>
<td>C NN</td>
<td>C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low educational level</td>
<td>5 (3)</td>
<td>N</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low sociocultural level</td>
<td>6 (4)</td>
<td>N N</td>
<td>N</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medical history and clinical presentation</th>
<th>Use M (IQR)</th>
<th>Radiological progression</th>
<th>Disability</th>
<th>Mortality</th>
<th>Remission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interstitial lung disease</td>
<td>8 (1)</td>
<td>N</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very young onset</td>
<td>7 (3)</td>
<td>N N</td>
<td>C</td>
<td>NN</td>
<td></td>
</tr>
<tr>
<td>Disease duration</td>
<td>8 (3)</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Comorbidity and toxic habits</th>
<th>Use M (IQR)</th>
<th>Radiological progression</th>
<th>Disability</th>
<th>Mortality</th>
<th>Remission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobacco use</td>
<td>8 (2)</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td>6 (2)</td>
<td>C P</td>
<td>P</td>
<td>N</td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>6 (3)</td>
<td>N</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline low bone mineral density</td>
<td>6 (2)</td>
<td>NN</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular disease or risk factors</td>
<td>8 (1)</td>
<td>N N</td>
<td>N</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other comorbidities (infections, liver disease, chronic kidney disease …)</td>
<td>8 (2)</td>
<td>N N</td>
<td>N</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Questionnaires or indices</th>
<th>Use M (IQR)</th>
<th>Radiological progression</th>
<th>Disability</th>
<th>Mortality</th>
<th>Remission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activity (DAS28 score, SDAI…)</td>
<td>9 (1)</td>
<td>N</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Function (HAQ)</td>
<td>7 (2)</td>
<td>C NN</td>
<td>NN</td>
<td>N</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Biomarkers</th>
<th>Use M (IQR)</th>
<th>Radiological progression</th>
<th>Disability</th>
<th>Mortality</th>
<th>Remission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid factor</td>
<td>9 (2)</td>
<td>NNN</td>
<td>N</td>
<td>N</td>
<td></td>
</tr>
<tr>
<td>Anti-citrullinated peptide antibodies (ACPA)</td>
<td>9 (1)</td>
<td>NNNN</td>
<td>N</td>
<td>NN</td>
<td>NN</td>
</tr>
<tr>
<td>Acute phase reactants</td>
<td>9 (1)</td>
<td>N</td>
<td></td>
<td>N</td>
<td></td>
</tr>
<tr>
<td>Calprotectin</td>
<td>2 (2)</td>
<td>N</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interleukin-2</td>
<td>1 (1)</td>
<td>NN</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Receptor Activator for Nuclear Factor K B Ligand</td>
<td>1 (2)</td>
<td>N</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin D deficit</td>
<td>6 (4)</td>
<td>NN</td>
<td></td>
<td>NN</td>
<td>NN</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genetic markers</th>
<th>Use M (IQR)</th>
<th>Radiological progression</th>
<th>Disability</th>
<th>Mortality</th>
<th>Remission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shared epitope</td>
<td>2 (4)</td>
<td>NNN</td>
<td>N</td>
<td>NN</td>
<td>NN</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Image data</th>
<th>Use M (IQR)</th>
<th>Radiological progression</th>
<th>Disability</th>
<th>Mortality</th>
<th>Remission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasound synovitis with Doppler signal</td>
<td>7 (2)</td>
<td>NN</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osteitis by magnetic resonance</td>
<td>4 (4)</td>
<td>NN</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erosions by magnetic resonance</td>
<td>4 (4)</td>
<td>NNN</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erosions by radiography</td>
<td>9 (1)</td>
<td>NNN</td>
<td>N</td>
<td>N</td>
<td></td>
</tr>
<tr>
<td>Erosions by ultrasound</td>
<td>7 (3)</td>
<td>N</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

M: median; IQR: interquartile range; C: controversial; N/n: negative effect; P: positive effect. The number of letters indicates the strength of the association, from weak (N) to strong (NNNN). Lowercase (n) indicates an intermediate assessment.

**Results:** The reviews identified 36 prognostic factors that were further reduced to 28. The survey was completed by 42 rheumatologists. Table 1 shows, for each factor, the reported frequency of use and the strength of association with the various outcomes.

**Conclusion:** Rheumatoid factor, ACPA, and erosions by radiography are well recognized and strong predictors that are used frequently. Osteitis and erosions by magnetic resonance and shared epitope have good evidence but minor use. Disease duration and smoking are frequently used as prognostic factors despite weak association with outcome, similarly to activity and acute phase reactants at baseline. Subsequently, we will test whether displaying the evidence makes rheumatologists change opinions.
Assessing the Quality, Reliability and Readability of Online Health Information Regarding Rheumatoid Arthritis

Mathew Reynolds¹, David Ta¹ and Russell Buchanan², ¹Department of Rheumatology, Austin Health, Heidelberg, Australia, ²Department of Rheumatology, Austin Health, Melbourne, Australia

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Rheumatoid arthritis is a common autoimmune disease with complex pathophysiology and varied treatment options, which accounts for many visits to health care professionals. With increasing use of the internet, we assessed the quality, reliability and readability of online information relating to rheumatoid arthritis.

Methods:

The search phrase ‘rheumatoid arthritis’ was used with the three most commonly accessed internet search engines (Google, Bing and Yahoo) to identify websites. The first 25 ‘hits’ (excluding duplicates and excluded websites) for each search were assessed for quality using the DISCERN instrument (score 16-80 points), reliability using the four JAMA benchmarks (assessing authorship, attribution of references, currency (date of posted content) and disclosure of conflict of interest) and readability using the Gunning Fog Index (ideal score 7-8).

Results:

There was significant concordance between the hits returned from each search engine with a total of 27 unique websites identified. The average DISCERN score was 44.9 (SD 10.7), and ranged from 29-62.

Websites that appeared earlier in searches did not have higher DISCERN scores (Pearson correlation -0.09).

The Top 5 websites by DISCERN score are seen in Table 1.

The mean number of JAMA benchmarks was 1.5 (SD 1.05), with currency present in 21/27 (77.8%), appropriate authorship in 8/27 (29.6%), attribution of references in 11/27 (40.7%) and disclosure of interest in only 1/27 (3.7%) of websites.

The average readability of the websites was 13.3 (SD 4.0) using the Gunning Fog Index.

Conclusion:

The overall quality of online health information relating to rheumatoid arthritis, as assessed by the DISCERN instrument, is only fair. Reliability, as measured by the JAMA benchmarks was of variable quality. Whilst the majority of websites provided dates of posted and updated content, references were available for less than half. The remaining benchmarks were poorly represented.

The readability of websites is higher than recommended for near-universal understanding, requiring an average of year 12 equivalent or higher education for understanding.
This assessment highlights the need for clinicians to provide patients with quality written information regarding rheumatoid arthritis or be able to direct them to websites with high quality information.

<table>
<thead>
<tr>
<th>Name</th>
<th>Address</th>
<th>DISCERN score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
<td><a href="https://patient.info/health/rheumatoid-arthritis-leaflet">https://patient.info/health/rheumatoid-arthritis-leaflet</a></td>
<td>61</td>
</tr>
<tr>
<td>Mayo Clinic</td>
<td><a href="http://www.mayoclinic.org/diseases-conditions/rheumatoid-arthritis/home/ovc-20197388">http://www.mayoclinic.org/diseases-conditions/rheumatoid-arthritis/home/ovc-20197388</a></td>
<td>60</td>
</tr>
</tbody>
</table>

Disclosure: M. Reynolds, None; D. Ta, None; R. Buchanan, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/assessing-the-quality-reliability-and-readability-of-online-health-information-regarding-rheumatoid-arthritis

Abstract Number: 1363

Disease Duration and Shared Epitope, but Not Smoking History, Are Associated with Peptidylarginine Deiminase 4-Antibody Development in Rheumatoid Arthritis

Laura Cappelli¹, Maximilian Konig¹, Pooja Naik², Arvin Saleh³, Allan C. Gelber³, Clifton O. Bingham III⁴ and Erika Darrah⁵,
¹Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, ²Department of Medicine, Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, ³Johns Hopkins University School of Medicine, Baltimore, MD, ⁴Rheumatology, Johns Hopkins University, Baltimore, MD, ⁵Department of Medicine/Division of Rheumatology, The Johns Hopkins University School of Medicine, Baltimore, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Clinical characteristics and biomarkers help clinicians predict disease features in rheumatoid arthritis (RA). Both peptidylarginine deiminase 4 (PAD4) antibodies and smoking have been associated with common clinical characteristics in RA, namely erosive disease, anti-CCP positivity, and interstitial lung disease. Whether smoking is etiologically linked to developing PAD4 antibodies, however, is unknown. We evaluated whether smoking history was associated with PAD4 antibody development in RA.

Methods: Adults with physician-diagnosed RA were drawn from a longitudinal cohort followed at the Johns Hopkins Arthritis Center. PAD4 and PAD3/4 cross-reactive antibodies were measured by immunoprecipitation; anti-CCP levels were measured by ELISA. Genotyping for shared epitope (SE) alleles was performed. Clinical data were drawn from patient/physician reported and historical sources.

Results: Among the 274 patients with RA, demographics did not significantly differ in those with PAD4, PAD3/4 and without PAD4 antibodies (table 1). Disease duration was longer in PAD4 and PAD3/4 antibody positive groups compared with the PAD4 negative group, whereas presence of SE was higher in the PAD4 antibody group. Both PAD4 and PAD3/4 positive groups were more likely to be anti-CCP positive. There was no significant difference in smoking history between groups, but there was a trend toward lower frequency of current smokers among those with PAD4 antibodies. In subsequent analyses, all those with PAD4 antibodies were grouped (PAD4 only and PAD3/4). In stratified analyses (table 2), smoking history remained unassociated with PAD4 antibody status, and was inversely associated with having PAD4 antibodies in those with SE, although not statistically significant. In multivariable models adjusting for disease duration, SE, race and sex, smoking remained unassociated with PAD4 antibody presence, while longer disease duration and having SE were positively associated with PAD4 antibodies (table 3).

Conclusion: Smoking history was not associated with the development of PAD4 or PAD3/4 cross-reactive antibodies in this cohort with RA. The lack of association persisted in multivariable analyses accounting for potentially confounding features. Having shared epitope and longer disease duration, however, were associated with developing PAD4 antibodies.
<table>
<thead>
<tr>
<th>Variable</th>
<th>PAD negative (P0) (n=206)</th>
<th>PAD 4 Ab only (P4) (N= 34)</th>
<th>PAD 3/4 Ab (XR) (N= 34)</th>
<th>p-value XR vs P0</th>
<th>p-value P4 vs P0</th>
<th>p-value XR vs P4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex- N (%)</td>
<td>163 (79%)</td>
<td>27 (79%)</td>
<td>28 (82%)</td>
<td>0.66</td>
<td>0.99</td>
<td>0.76</td>
</tr>
<tr>
<td>Race- N (%)</td>
<td>White 165 (80%)</td>
<td>White 28 (82.4%)</td>
<td>White 27 (79%)</td>
<td>0.91</td>
<td>0.99</td>
<td>0.95</td>
</tr>
<tr>
<td></td>
<td>Black 27 (13%)</td>
<td>Black 4 (11.8%)</td>
<td>Black 4 (12%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Asian/Other 14 (7%)</td>
<td>Asian/Other 2 (6%)</td>
<td>Asian/Other 3 (9%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age- median (IQR)</td>
<td>57 (49-66)</td>
<td>55 (47-68)</td>
<td>51.5 (46-64)</td>
<td>0.14</td>
<td>0.70</td>
<td>0.33</td>
</tr>
<tr>
<td>Disease duration (yrs)- median (IQR)</td>
<td>6 (2-12)</td>
<td>15.5 (8-27)</td>
<td>15.5 (7-26)</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>0.77</td>
</tr>
<tr>
<td>Smoking status- N (%)</td>
<td>Never 110 (54%)</td>
<td>Never 18 (53%)</td>
<td>Never 22 (65%)</td>
<td>0.10</td>
<td>0.87</td>
<td>0.18</td>
</tr>
<tr>
<td></td>
<td>Former 71 (35%)</td>
<td>Former 13 (38.2%)</td>
<td>Former 12 (35%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Current 24 (12%)</td>
<td>Current 3 (8.8%)</td>
<td>Current 0 (0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CCP positive- N (%)</td>
<td>116 (57%)</td>
<td>30 (88.2%)</td>
<td>30 (88.2%)</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>1.0</td>
</tr>
<tr>
<td>Shared Epitope- N (%)</td>
<td>112 (54%)</td>
<td>28 (82.4%)</td>
<td>22 (64.7%)</td>
<td>0.26</td>
<td>&lt;0.01</td>
<td>0.10</td>
</tr>
<tr>
<td>Erosions- N (%)</td>
<td>88 (43%)</td>
<td>17 (54.8%)</td>
<td>22 (65%)</td>
<td>0.07</td>
<td>0.46</td>
<td>0.42</td>
</tr>
<tr>
<td>CDAI- median (IQR)</td>
<td>7.9 (3-16)</td>
<td>7 (2.8-11.5)</td>
<td>3.7 (1.5-9.5)</td>
<td>0.04</td>
<td>0.37</td>
<td>0.21</td>
</tr>
<tr>
<td>On a csDMARD-N (%)</td>
<td>184 (90%)</td>
<td>28 (82%)</td>
<td>28 (82%)</td>
<td>0.20</td>
<td>0.21</td>
<td>1.0</td>
</tr>
<tr>
<td>On methotrexate-N (%)</td>
<td>127 (63%)</td>
<td>20 (59%)</td>
<td>24 (71%)</td>
<td>0.33</td>
<td>0.73</td>
<td>0.31</td>
</tr>
<tr>
<td>On a biologic- N (%)</td>
<td>89 (44%)</td>
<td>17 (50%)</td>
<td>16 (47%)</td>
<td>0.71</td>
<td>0.49</td>
<td>0.81</td>
</tr>
</tbody>
</table>

P0= PAD4 antibody negative; XR= PAD3/4 cross-reactive antibody; P4= PAD4 antibody only
Table 2: Stratified analyses of the association between smoking history and PAD4 antibody status

<table>
<thead>
<tr>
<th>Smoking History</th>
<th>Odds ratio</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>With Shared Epitope</td>
<td>0.67</td>
<td>0.25</td>
</tr>
<tr>
<td>Without Shared Epitope</td>
<td>0.94</td>
<td>0.90</td>
</tr>
<tr>
<td>Females</td>
<td>0.86</td>
<td>0.65</td>
</tr>
<tr>
<td>Males</td>
<td>0.63</td>
<td>0.46</td>
</tr>
<tr>
<td>Disease duration &gt; 10 years</td>
<td>0.88</td>
<td>0.75</td>
</tr>
<tr>
<td>Disease duration &lt; 10 years</td>
<td>0.82</td>
<td>0.66</td>
</tr>
</tbody>
</table>

Table 3: Unadjusted and adjusted associations between clinical variables and presence of PAD4 antibodies

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio (unadjusted)</th>
<th>p-value</th>
<th>Odds Ratio (adjusted)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>1.12</td>
<td>0.74</td>
<td>0.88</td>
<td>0.74</td>
</tr>
<tr>
<td>Non-white Race</td>
<td>0.95</td>
<td>0.87</td>
<td>1.45</td>
<td>0.34</td>
</tr>
<tr>
<td>Ever Smoker</td>
<td>0.81</td>
<td>0.46</td>
<td>0.78</td>
<td>0.41</td>
</tr>
<tr>
<td>Disease duration &gt; 10 years</td>
<td>3.64</td>
<td>&lt; 0.01</td>
<td>3.46</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Presence of Shared epitope</td>
<td>2.35</td>
<td>&lt; 0.01</td>
<td>2.29</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Disclosure: L. Cappelli, Bristol-Myers Squibb, 2; M. Konig, None; P. Naik, None; A. Saleh, None; A. C. Gelber, None; C. O. Bingham III, None; E. Darrah, patent, 9.


Abstract Number: 1364

Incidence of Rheumatoid Arthritis in a Cohort of First Degree Relatives from the Studies of the Etiology of Rheumatoid Arthritis

Diraj R. Karnani¹, Lindsy J. Forbess², Michael Weisman³, Kevin D. Deane⁴, V. Michael Holers⁵ and Jill M. Norris⁶, ¹Department of Rheumatology, Cedars Sinai Medical Center, Los Angeles, CA, ²Medicine, Division of Rheumatology, Cedars-Sinai Medical Center, Los Angeles, CA, ³Cedars-Sinai Medical Center Division of Rheumatology, Los Angeles, CA, ⁴Division of Rheumatology, University of Colorado School of Medicine, Aurora, CO, ⁵Rheumatology Division, University of Colorado School of Medicine, Aurora, CO, ⁶Department of Epidemiology, Colorado School of Public Health, Aurora, CO

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
**Background/Purpose:** First-degree relatives (FDRs) of patients with rheumatoid arthritis (RA) are at increased risk for developing RA compared to the general population. The purpose of the study reported herein was to evaluate the incidence rate of RA from a local cohort of FDRs that was initiated in 2004.

**Methods:** FDRs of patients with RA from Cedars-Sinai Medical Center (CSMC) enrolled in the Studies of the Etiology of RA (SERA, a multicenter prospective cohort of FDRs of probands with RA) were studied (Kolfenbach 2009). Participants were enrolled between 2004 and 2011, providing an average of 9.5 years of follow-up. FDRs who live in Southern California within approximately 150 miles of CSMC were contacted by phone and asked if they were given a diagnosis of RA by a rheumatologist or if they reported pain in one or more joints, and/or swelling or morning stiffness. If they had symptoms, but were not yet diagnosed with RA, they were evaluated in clinic by a rheumatologist and underwent testing for CCP antibodies (CCP 3.1).

**Results:** 250 FDRs enrolled in SERA between 2004 and 2011 and seen at CSMC who live in Southern California were contacted by telephone. 73 out of 250 subjects (29.2%) were reached to date. 2/73 FDRs (3%) reported a diagnosis of RA by a rheumatologist. Both FDRs diagnosed with RA were seronegative at the time of enrollment in the SERA cohort. One who was initially seronegative in 2007 seroconverted in 2011, with CCP2 and RF IgG positivity – she was diagnosed with RA in 2014. The second FDR diagnosed with RA remained seronegative for the duration of follow-up, even post-diagnosis. 9 of 73 FDRs (12.3%) had arthralgias defined as pain in one or more joints. Of these, 4 of the 9 have been evaluated to date by a rheumatologist in clinic without evidence of RA; none were CCP positive.

**Conclusion:** Our local cohort follow-up suggests that FDRs of patients with RA develop RA at a higher rate than the general population with an incidence rate of 3% in FDRs versus 0.4% in the general population over 10 years\(^1\). This is an ongoing effort to prospectively evaluate the risk of development of RA from a subgroup of FDRs established in the United States (SERA).

**References:**


**Disclosure:** D. R. Karnani, None; L. J. Forsbess, None; M. Weisman, None; K. D. Deane, Inova Diagnostics, Inc., 5; V. M. Holers, None; J. M. Norris, None.

**Abstract Number: 1365**

**Correlation of the Multi-Biomarker Disease Activity Score with Composite Rheumatoid Arthritis Disease Activity Measures: A Systematic Review and Meta-Analysis**

Tate Johnson\(^1\), Kyle A. Register\(^2\), Cynthia Schmidt\(^3\), James R. O'Dell\(^4\), Ted R. Mikuls\(^5\), Kaleb Michaud\(^1\) and Bryant R. England\(^6\), 
\(^1\)University of Nebraska Medical Center, Omaha, NE, \(^2\)Division of Rheumatology and Immunology, University of Nebraska Medical Center, Omaha, NE, \(^3\)McGoogan Library of Medicine, University of Nebraska Medical Center, Omaha, NE, \(^4\)Department of Internal Medicine, University of Nebraska Medical Center, Omaha, NE, \(^5\)Internal Medicine, Division of Rheumatology, University of Nebraska Medical Center, Omaha, NE, \(^6\)Division of Rheumatology & Immunology, Department of Internal Medicine, Nebraska-Western IA VA Health Care System & University of Nebraska Medical Center, Omaha, NE

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM
Background/Purpose: The regular assessment of disease activity is necessary to implement a treat-to-target management approach in RA. The Multi-Biomarker Disease Activity (MBDA) Score is a novel tool developed to facilitate RA disease activity assessment, but there have been conflicting reports on the ability of the MBDA score to assess RA disease activity. Therefore, we performed a systemic review of MBDA in RA and meta-analysis of the correlation between the MBDA and composite RA disease activity measures.

Methods: We conducted a systematic review and meta-analysis of published manuscripts on the MBDA in RA (registered with PROSPERO) by searching MEDLINE, EMBASE, Scopus, Google Scholar, and the Cochrane Library from their inception to March 7, 2017, adhering to the PRISMA guidelines. We included studies reporting correlations of MBDA with composite RA disease activity measures and completed a meta-analysis to calculate a pooled estimate. Studies only assessing MBDA performance in separate cohorts or time points were modeled as separate studies. We performed a random-effects meta-analysis of correlation coefficients using the DerSimonian-Laird model for measures assessed in ≥3 cohorts. In sensitivity analyses, we allowed each study to only contribute one cohort and transformed correlation coefficients to Fisher’s Z scores prior to meta-analysis. Heterogeneity was assessed using the Cochran Q test.

Results: The systematic review identified 18 reports examining the MBDA in RA, with 6 of these (n=9 cohorts) reporting correlations with composite RA disease activity measures. Results from meta-analysis demonstrated a moderate to strong correlation of the MBDA with DAS28-CRP \( (r=0.53, 95\% \text{ CI } 0.40-0.67, \text{ Figure 1}) \). Heterogeneity was marginally significant by Cochrane Q \( (p = 0.07) \). Results were similar following conversion of correlation coefficients to Fisher’s Z scores \( (r=0.54, 95\% \text{ CI } 0.40-0.66) \) and using only one cohort (baseline) per study \( (r=0.61, 95\% \text{ CI } 0.52-0.70) \). The MBDA demonstrated similar correlations with the Simple Disease Activity Index (SDAI) and a slightly less robust correlation with the Clinical Disease Activity Index (CDAI) with significant heterogeneity across relevant studies (Table 1). There was a moderate to strong correlation between Δ-MBDA with Δ-DAS28-CRP (Table 1).

Conclusion: The MBDA demonstrates moderate to strong correlations with DAS28-CRP and SDAI, but less robust correlations with CDAI. Since CRP is a common component of MBDA, DAS28-CRP, and SDAI, additional study is needed to assess whether MBDA correlates with RA disease activity measures lacking CRP.

Table 1. Random-effects meta-analysis of the correlation of MBDA with composite RA disease activity measures

<table>
<thead>
<tr>
<th></th>
<th>N cohorts</th>
<th>Pooled r</th>
<th>95% CI</th>
<th>Cochrane Q</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MBDA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDAI</td>
<td>4</td>
<td>0.38</td>
<td>0.19-0.56</td>
<td>12.36</td>
<td>0.006</td>
</tr>
<tr>
<td>SDAI</td>
<td>3</td>
<td>0.51</td>
<td>0.29-0.73</td>
<td>11.34</td>
<td>0.003</td>
</tr>
<tr>
<td><strong>ΔMBDA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ΔDAS28-CRP</td>
<td>3</td>
<td>0.51</td>
<td>0.38-0.64</td>
<td>1.67</td>
<td>0.44</td>
</tr>
</tbody>
</table>

*Significance of Cochrane Q test for heterogeneity

Disclosure: T. Johnson, None; K. A. Register, None; C. Schmidt, None; J. R. O'Dell, Medac, 5,Coherus, 5; T. R. Mikuls, BMS, 2,Ironwood Pharm, 2,Pfizer Inc, 5,NIH, VA, 2; K. Michaud, None; B. R. England, None.
Evaluation of Synovial Fluid 14-3-3η Protein As a Marker of Joint Damage in Rheumatoid Arthritis Patients

Nevin Hammam\textsuperscript{1,2}, Shaimaa Salah\textsuperscript{3}, Anthony Marotta\textsuperscript{4} and Emad F. Kholef\textsuperscript{5}, \textsuperscript{1}Rheumatology and Rehabilitation Department, University of Assiut, Assiut, Egypt, \textsuperscript{2}University of Alberta, Edmonton, AB, Canada, \textsuperscript{3}Rheumatology, Rehabilitation and Physical Medicine department, Faculty of Medicine, Assiut, Assiut, Egypt, \textsuperscript{4}Augurex Life Sciences Corp., Vancouver, BC, Canada, \textsuperscript{5}Clinical Pathology Department, Aswan University Hospital, Aswan, Egypt

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Rheumatoid arthritis (RA) is a chronic inflammatory disease that results in severe joint damage and physical disability, therefore, the discovery of new marker(s) for joint destruction is needed. Serum 14-3-3η protein is a novel diagnostic marker for RA, and also involved in joint damage (1, 2). 14-3-3η protein has been reported to be expressed at significantly higher levels in synovial fluid (SF) of RA patients when compared with matched serum by immunoblot analysis (1). Correlation of serum 14-3-3η protein with clinical variables, autoantibodies, inflammatory markers, and radiologic damage has been examined in RA (2). These associations have never been examined for RA synovial fluid (SF) 14-3-3η protein. In this study, we quantified SF 14-3-3η by ELISA and determined the association of serum and SF 14-3-3η protein with clinical, laboratory and radiographic damage in RA.

Methods:
RA patients diagnosed according to 2010 ACR criteria were included. Serum and SF samples were obtained from all patients at the same day and 14-3-3η protein levels were measured using the quantitative 14-3-3η ELISA kit (Augurex Life Sciences Corp). A 14-3-3η cut-off of $\geq 0.19$ ng/ml, the diagnostic cut-off was employed. Radiological damage was evaluated using Sharp/van der Heijde score (SHS). Spearman or Pearson correlations to compare relationships and Mann-Whitney U test for groups difference were used for statistical analysis.
Results:
A total of 39 RA patients, mean age of 38 years, with 87.2% being female were included. Their mean disease duration was 9.3 years, and 48.7% of patients had moderate DAS28. Mean SF14-3-3η protein levels were 2 fold higher than mean serum protein levels (3.7 vs 1.7 ng/ ml). The prevalence of 14-3-3η protein positivity was higher in SF compared with serum from RA patients; 82.1% versus 69.2%, respectively. Although there was significant correlation between SF 14-3-3η protein levels and ESR (p=0.036), no significant association was found between serum or SF 14-3-3η protein levels with DAS28 or autoantibodies in RA. There was significant correlation between serum and SF 14-3-3η protein levels (p<0.05) in RA patients. Serum and SF 14-3-3η protein levels were positively correlated with SHS (p<0.001). RA patients who were serum or SF 14-3-3η protein positive showed significant difference in SHS but not in clinical and laboratory features when compared with 14-3-3η negative patients.

Conclusion:
14-3-3η levels are significantly higher in SF than in matched serum. Serum and SF14-3-3η protein levels correlate with radiographic damage. This study further substantiates 14-3-3η as a mechanistic joint damage marker for RA.

References:

Circulating Microbial Small RNAs Are Altered in Patients with Rheumatoid Arthritis

Michelle J. Ormseth1, Shilin Zhao2, Ryan Allen2, Joseph F. Solus2, Quanhu Sheng2, Yan Guo2, Fei Ye2, Marisol Ramirez2, Kasey Vickers2 and C Michael Stein2, 1Medicine, Vanderbilt University Medical Center, Nashville, TN, 2Vanderbilt University Medical Center, Nashville, TN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM
**Background/Purpose:** Small RNAs (sRNAs), such as microRNAs, are important regulators of biological processes and serve as important biomarkers of disease. We found that approximately half of sRNAs in human plasma fail to map to the human genome, but many map to microbial genomes. sRNAs, human and non-human alike, may alter cellular function. Thus, non-human plasma sRNAs may serve as an effector compartment of the human microbiome, an area of great interest in rheumatoid arthritis (RA). Our objective was to determine if sRNAs of microbial origin are altered in RA plasma.

**Methods:** RNA was extracted from plasma from 165 patients with RA and 91 controls frequency-matched for age, race and sex. Purified plasma RNA was used to prepare sRNA cDNA libraries. Sequencing was performed using Illumina NextSeq500. Using TIGER, an in-house sRNA-seq analysis pipeline, high quality reads were first aligned to the human genome allowing for 1 mismatch. Remaining reads were aligned to 57 genomes of bacteria previously found to be altered in RA. Separately, remaining reads were aligned to representative genomes of 207 human microbiome bacteria, 8 fungi, and 167 environmental bacteria. Differential expression analysis of sRNA and microbial genome counts were performed using DESeq2, adjusting for age, race, sex and batch, with 5% false discovery rate. Benjamini and Hochberg method was used for multiple test correction.

**Results:** Three microbial sRNAs, of variable length of the same sRNA were increased approximately 2-fold in the plasma of RA patients compared to control subjects (P=0.001 to P=0.02). These sRNAs mapped to multiple bacterial genomes of the human microbiome and environment. The three microbial sRNAs have an identical seed region, which in the case of miRNAs, is the region that binds with complementarity to target mRNAs to alter translation. This microbial sRNA seed region is predicted to target several human genes which are altered in RA including CARD8, IL17RA, and TRAF1. Comparing genome counts of RA-specific bacteria, *Lactobacillus salivarius* was significantly decreased in RA vs control (P=0.03). Comparing genome counts of representative genomes of human microbiome, fungi and environmental bacteria, *Anaerobaculum hydrogeniformans* (P=0.01), *Staphylococcus epidermidis* (P=0.04), *Sphingobacterium spiritivorum* (P=0.04), and *Staphylococcus aureus* (P=0.04) were significantly decreased in RA compared to control subjects.

**Conclusion:** Microbial plasma small RNAs are altered in patients with RA. Three microbial plasma sRNAs were increased significantly in RA and are predicted to target genes associated with RA. Further studies will determine the role of these microbial sRNAs in RA.

**Disclosure:** M. J. Ormseth, None; S. Zhao, None; R. Allen, None; J. F. Solus, None; Q. Sheng, None; Y. Guo, None; F. Ye, None; M. Ramirez, None; K. Vickers, None; C. M. Stein, None.

**View Abstract and Citation Information Online** - http://acrabstracts.org/abstract/circulating-microbial-small-rnas-are-altered-in-patients-with-rheumatoid-arthritis

**Abstract Number:** 1368

**Small RNA Sequencing Identifies Plasma microRNA Panel for Rheumatoid Arthritis Diagnosis**

Michelle J. Ormseth¹, Joseph F. Solus², Quanhu Sheng², Yan Guo², Fei Ye², Ryan Allen², Kasey Vickers² and C Michael Stein², ¹Medicine, Vanderbilt University Medical Center, Nashville, TN, ²Vanderbilt University Medical Center, Nashville, TN

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Small noncoding RNAs (sRNAs), such as microRNAs (miRNAs), are regulators of biological processes and serve as important biomarkers of disease. Most previous plasma sRNA studies in inflammatory autoimmune diseases have relied on PCR or microarrays to quantify candidate miRNAs based on limited information about their function; however, unbiased sRNA sequencing could reveal new miRNA markers of disease. We hypothesized that plasma miRNAs are altered in patients with rheumatoid arthritis (RA) compared to control subjects and some may serve as markers of RA diagnosis.
**Methods:** This cross-sectional study included patients with 167 patients with RA, and 91 age, race and sex matched control subjects. Sequencing was done by Illumina NextSeq500. High quality reads were mapped to the human genome using Bowtie1. MiRBase21.0 was used to quantify miRNAs. miRNA reads were compared between RA and control subjects by DESeq2 with adjustment for age, race sex, and batch with 5% false discovery rate and multiple test correction by Benjamini and Hochberg method, and separately by random forest analysis. The top 12 differentially expressed miRNAs were validated by qPCR. A miRNA qPCR panel for RA diagnosis was developed using logistic regression, whose discrimination capacity was assessed by area under the receiver operative characteristic curve (AUC).

**Results:** Of 262 reliably mapped microRNAs, 107 were significantly altered >1.5-fold in patients with RA. Among the top 12 differentially expressed miRNAs identified by both DESeq2 and random forest analysis, miR-22-3p, miR-22-5p, miR-24-3p, miR-29c-3p, miR-30e-5p, miR-130a-3p, miR-140-3p, miR-221-3p, and miR-345-5p remained significantly altered and reliably detectable when validated by qPCR (Table). A panel including miR-22-3p, miR-24-3p, and miR-140-3p had AUC=0.81 for distinguishing between RA and control subjects. This panel remained robust distinguishing between control subjects and both seronegative RA (AUC=0.85) and seropositive RA (AUC=0.79).

**Conclusion:** Several plasma miRNAs identified by sRNA sequencing are altered in patients with RA compared to control subjects and may serve as novel diagnostic markers of RA. Further validation is necessary to confirm these findings.

<table>
<thead>
<tr>
<th></th>
<th>RA (fM)</th>
<th>Control (fM)</th>
<th>Fold difference</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>miR-22-3p</td>
<td>58.10 [45.30, 74.50]</td>
<td>15.10 [10.80, 21.00]</td>
<td>3.85</td>
<td>8.45E-12</td>
</tr>
<tr>
<td>miR-22-5p</td>
<td>1.18 [0.89, 1.56]</td>
<td>0.39 [0.25, 0.61]</td>
<td>2.99</td>
<td>1.25E-07</td>
</tr>
<tr>
<td>miR-24-3p</td>
<td>3.98 [2.95, 5.37]</td>
<td>1.32 [0.85, 2.06]</td>
<td>3.01</td>
<td>1.19E-06</td>
</tr>
<tr>
<td>miR-29c-3p</td>
<td>1.46 [1.18, 1.80]</td>
<td>0.56 [0.41, 0.77]</td>
<td>2.59</td>
<td>5.32E-09</td>
</tr>
<tr>
<td>miR-130a-3p</td>
<td>5.00 [3.51, 7.12]</td>
<td>1.27 [0.81, 1.97]</td>
<td>3.94</td>
<td>8.56E-08</td>
</tr>
<tr>
<td>miR-140-3p</td>
<td>1.22 [1.00, 1.49]</td>
<td>0.25 [0.17, 0.37]</td>
<td>4.93</td>
<td>2.12E-13</td>
</tr>
<tr>
<td>miR-221-3p</td>
<td>9.96 [7.48, 13.20]</td>
<td>3.04 [2.15, 4.31]</td>
<td>3.27</td>
<td>6.78E-09</td>
</tr>
<tr>
<td>miR-345-5p</td>
<td>0.06 [0.04, 0.09]</td>
<td>0.02 [0.01, 0.03]</td>
<td>3.62</td>
<td>1.72E-04</td>
</tr>
</tbody>
</table>

The geometric mean [interquartile range] is presented based on qPCR adjusted for triple spike-in control.

**Disclosure:** M. J. Ormseth, None; J. F. Solus, None; Q. Sheng, None; Y. Guo, None; F. Ye, None; R. Allen, None; K. Vickers, None; C. M. Stein, None.

**View Abstract and Citation Information Online** - [http://acrabstracts.org/abstract/small-rna-sequencing-identifies-plasma-microrna-panel-for-rheumatoid-arthritis-diagnosis](http://acrabstracts.org/abstract/small-rna-sequencing-identifies-plasma-microrna-panel-for-rheumatoid-arthritis-diagnosis)

**Abstract Number:** 1369
Interferon Gamma Signature Genes and CXCL10 As New Biomarkers in Early Stage of Rheumatoid Arthritis

Kijun Lee¹, Jennifer Lee², Hong-Ki Min³, Sang-Heon Lee⁴, Sung-Hwan Park⁵, Ji Hyeon Ju⁶ and Hoyoun Kim¹,
¹The Catholic University of Korea, Seoul, Korea, Republic of (South), ²Division of Rheumatology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea, Republic of (South), ³Konkuk University Medical Center, Seoul, Korea, Republic of (South), ⁴Konkuk University School of Medicine, Seoul, Korea, Republic of (South), ⁵Division of Rheumatology, Department of Internal Medicine, Seoul St. Mary’s Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea, Republic of (South), ⁶Division of Rheumatology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The purpose of this study is to explore new biomarkers for early diagnosis of rheumatoid arthritis (RA). For better discrimination power, we especially investigated the samples of early RA (eRA) patients with the onset of RA less than 2 year.

Methods: Gene expression profiles of peripheral mononuclear cells (PBMC) and CD4⁺ T cells obtained patients with eRA, advanced RA (aRA, disease duration more than 2 year) and osteoarthritis (OA) were investigated using microarray. PBMC from 11 patients with eRA and CD4⁺ T cells from 10 patients with eRA were analyzed compared to patients from aRA and OA. Quantitative real-time PCR (qRT-PCR) was performed to verify the results of microarray. The concentrations of representative cytokines were measured with enzyme-linked immunosorbent assay (ELISA) kits.

Results: We identified 52 differentially expressed genes (DEGs) with more than 1.5-fold higher expression values and 27 DEGs with lower expression on microarray of PBMC of eRA patients compared to OA (p < 0.05). 29 genes were highly upregulated in CD4⁺ T cells of patients with eRA compared to aRA and OA (3-fold, p < 0.05). The top 10 genes were mainly interferon signature genes and related chemokine including CXCL10 (chemokine C-X-C motif ligand 10; 225-fold, p = 0.004), IFIT3 (interferon-induced protein with tetratricopeptide repeats 3; 85-fold, p = 0.0002), IFIT1 (interferon-induced protein with tetratricopeptide repeats 1; 33-fold, p = 0.002), RSAD2 (radical S-adenosyl methionine domain containing 2; 23-fold, p = 0.001), TNFAIP6 (tumor necrosis factor, alpha-induced protein 6; 15-fold, p = 0.005), SLAMF7 (SLAM family member 7; 14-fold, p = 0.008), IFI44 (interferon-induced protein 44; 14-fold, p = 0.0003), IFIH1 (interferon induced with helicase C domain 1; 13-fold, p = 0.0002), OASL (2-5-oligoadenylate synthetase-like; 11-fold, p = 0.0002), HERC5 (HECT and RLD domain containing E3 ubiquitin protein ligase 5; 11-fold, p = 0.0003). The differentially expressed genes were verified using qRT-PCR. Elevated levels of IFN-¥ and CXCL10 were demonstrated in patients with eRA. The concentrations of representative cytokines were measured with enzyme-linked immunosorbent assay (ELISA) kits.

Conclusion: Our study defined that IFN-¥ signature genes in CD4⁺ T cells and level of IFN-¥ in serum were highly presented in the early stages of rheumatoid arthritis. In addition, we found CXCL10, which supposed to be stimulated by IFN-¥, was significantly increased not only in the gene level but also in the protein level of peripheral blood from eRA. IFN-¥ signature as well as CXCL10 could be useful as biomarkers in patients with the early stage of rheumatoid arthritis.

Table 1. The concentration of IFN-¥ and CXCL10 in eRA compared to aRA.

<table>
<thead>
<tr>
<th>Protein Level</th>
<th>eRA (µg/mL)</th>
<th>aRA (µg/mL)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFN-¥</td>
<td>34</td>
<td>21</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Mean ± SEM</td>
<td>39.1 ± 4.9</td>
<td>24.2 ± 6.7</td>
<td></td>
</tr>
<tr>
<td>Median (ng/mL)</td>
<td>38.9 (10.2-72.5)</td>
<td>12.3 (5.5-141.5)</td>
<td></td>
</tr>
<tr>
<td>CXCL10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SEM</td>
<td>190.8 ± 104.8</td>
<td>67.9 ± 33.2</td>
<td>0.017</td>
</tr>
<tr>
<td>Median (ng/mL)</td>
<td>179.5 (63.7-102.5)</td>
<td>57.3 (44.4-132.5)</td>
<td></td>
</tr>
</tbody>
</table>

Table 1 notes: SEM: the standard error of the mean

Disclosure: K. Lee, None; J. Lee, None; H. K. Min, None; H. R. Kim, None; S. H. Lee, None; S. H. Park, None; J. H. Ju, None; H. Kim, None.
Higher Disease Activity in Current Smokers with Established RA: Is It Disease, Damage or Disability?

Emily Keeler¹, Danielle Feger², Nancy J. Olsen¹ and Rayford R. June³, ¹Medicine/Rheumatology, Penn State Hershey Medical Center, Hershey, PA, ²Medicine/Rheumatology, Penn State College of Medicine, Hershey, PA, ³Rheumatology, Penn State Hershey Medical Center, Hershey, PA

First publication: September 18, 2017

Abstract Number: 1370

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Smoking is an important environmental risk factor for development of rheumatoid arthritis (RA). Smoking has been linked to lower rates of disease remission, incomplete response to DMARD therapy, and elevated serum levels of pro-inflammatory cytokines. Former smokers respond equally well to DMARD treatment as never smokers. In established RA patients, it is unknown if smoking cessation improves RA-associated outcomes. We aimed to investigate the association of tobacco use and disease activity in established RA patients. We hypothesized that current tobacco use in established RA is associated with increased DAS28-CRP and is affected by RA-associated comorbidities.

Methods: We performed a case control study on 95 patients with RA. Patients were consented and enrolled in the Penn State Investigation of Remission in Rheumatoid Arthritis cohort. Disease activity was measured by DAS28-CRP. Smoking was categorized as current, former or never status. Chi-square (X²) or Fisher’s exact test were used to test for differences between categorical variables, and ANOVA or Kruskal-Wallis test were used for continuous variables. The primary outcome was the association of smoking status with DAS28-CRP. Multivariable linear regression was performed with covariates including age, education, pack years, disability as measured by the modified health assessment questionnaire (MHAQ), nodules, hypertension, periodontitis, and disease duration.

Results: RA subjects had an average age of 55.5 years, 74% were female and > 90% were Caucasian. Subjects had established RA with a mean disease duration of 10.9 years, 87% were seropositive, and mean DAS28-CRP was 3.36. 89.3% of patients met the 2010 ACR/EULAR classification criteria for RA. 19% percent were current smokers and 36% were former smokers, who were 10 years older than current smokers (p<0.05). Mean DAS28-CRP was significantly higher (p=0.003) in current smokers (4.40) compared to former (3.26) and never (2.95) smokers. Current smokers had a lower odds of being in remission than never smokers (OR=0.14, p=0.02). Rheumatoid nodules were more prevalent in current smokers (p=0.06). Level of education was inversely associated with DAS28-CRP (p<0.0001). Median MHAQ scores were significantly higher in current smokers (0.75) than former smokers (0; p=0.02). MHAQ scores were strongly associated with DAS28-CRP (p<0.0001). There was no difference in DAS28-CRP scores between smoking groups when controlled for MHAQ score, education, and periodontitis.

Conclusion: Current smokers with established RA have higher disease activity and are significantly less likely to be in remission. Smoking status and RA disease activity are strongly associated with disability, education level, and periodontal scores, implying both a socioeconomic and pathophysiologic basis for this association. Effects of smoking cessation on RA outcomes would be of interest.
Table 1: Patient demographics, disease characteristics, and comorbidities.

<table>
<thead>
<tr>
<th></th>
<th>Overall (95)</th>
<th>Current Smoker (18)</th>
<th>Former Smoker (34)</th>
<th>Never Smoker (43)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Mean (SD)</td>
<td>55.5 (13.54)</td>
<td>52.2 (12.91)</td>
<td>62.0 (11.70)</td>
<td>51.9 (13.53)</td>
<td>0.002</td>
</tr>
<tr>
<td>Female (%)</td>
<td>70 (73.7%)</td>
<td>12 (66.7%)</td>
<td>26 (76.5%)</td>
<td>32 (74.4%)</td>
<td>0.74</td>
</tr>
<tr>
<td>BMI, Mean (SD)</td>
<td>29.7 (7.15)</td>
<td>29.0 (5.31)</td>
<td>30.7 (7.10)</td>
<td>29.2 (7.89)</td>
<td>0.6</td>
</tr>
<tr>
<td>Pack years, Mean (SD)</td>
<td>9.2 (14.1)</td>
<td>18.6 (13.7)</td>
<td>17.4 (16.4)</td>
<td>0 (0.59)</td>
<td></td>
</tr>
<tr>
<td>Disease Duration, Mean (SD)</td>
<td>10.9 (10.0)</td>
<td>12.7 (12.0)</td>
<td>11.6 (10.5)</td>
<td>9.6 (8.8)</td>
<td>0.53</td>
</tr>
<tr>
<td>Seropositive for RF or CCP (%)</td>
<td>76 (87.4%)</td>
<td>15 (83.3%)</td>
<td>27 (87.1%)</td>
<td>34 (89.5%)</td>
<td>0.78</td>
</tr>
<tr>
<td>MHAQ, Median (IQR)</td>
<td>0.125 (0.625)</td>
<td>0.75 (0.75)</td>
<td>0 (0.38)</td>
<td>0.13 (0.38)</td>
<td>0.002</td>
</tr>
<tr>
<td>DAS28-CRP</td>
<td>3.36 (1.38)</td>
<td>4.40 (1.20)</td>
<td>3.26 (1.33)</td>
<td>2.95 (1.28)</td>
<td>0.003</td>
</tr>
<tr>
<td>Remission (DAS28-CRP&lt;2.6) (%)</td>
<td>28 (37.8%)</td>
<td>2 (13.3%)</td>
<td>10 (35.7%)</td>
<td>16 (51.6%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Rheumatoid Nodules</td>
<td>28 (30.1%)</td>
<td>9 (50.0%)</td>
<td>11 (32.4%)</td>
<td>8 (19.5%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>31 (32.6%)</td>
<td>4 (22.2%)</td>
<td>16 (47.1%)</td>
<td>11 (25.6%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Peripontitis (%)</td>
<td>28 (29.5%)</td>
<td>7 (38.9%)</td>
<td>10 (29.4%)</td>
<td>11 (25.6%)</td>
<td>0.58</td>
</tr>
</tbody>
</table>

Disclosure: E. Keeler, None; D. Feger, None; N. J. Olsen, None; R. R. June, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/higher-disease-activity-in-current-smokers-with-established-ra-is-it-disease-damage-or-disability](http://acrabstracts.org/abstract/higher-disease-activity-in-current-smokers-with-established-ra-is-it-disease-damage-or-disability)

Abstract Number: 1371

**Development of an Adjusted Multi-Biomarker Disease Activity (MBDA) Score for Rheumatoid Arthritis (RA) That Accounts for Age, Sex and Adiposity, with Subsequent Evaluation of Ability to Predict Risk for Radiographic Damage**

Jeffrey R. Curtis¹, Darl D. Flake II², Michael Weinblatt³, Nancy A. Shadick⁴, Mikkel Østergaard⁵, Merete Lund Hetland⁶, Cecilie Heegaard Brahe⁶, Yong Gil Hwang⁷, Daniel E. Furst⁸, Vibeke Strand⁹, Carol J. Etzel⁰, Dimitrios A. Pappas¹¹, Xingbin Wang¹², Ching Chang Hwang¹³, Carol J. Etzel⁰, Alexander Gutin², Elena Hitraya¹² and Jerry S. Lanchbury², ¹Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL, ²Myriad Genetics Inc., Salt Lake City, UT, ³Brigham and Women’s Hospital, Boston, MA, ⁴Rheumatology Immunology & Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ⁵Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Rigshospitalet, Denmark, Copenhagen, Denmark, ⁶Copenhagen Center for Arthritis Research, Copenhagen, Denmark, ⁷Rheumatology & Clinical Immunology, University of Pittsburgh, Pittsburgh, PA, ⁸David Geffen School of Medicine at UCLA, Los
SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The MBDA score, based on 12 serum proteins, is a validated tool for assessing disease activity in RA patients. MBDA biomarkers may be influenced by age, sex and adiposity. The objective of this study was to develop and validate an adjusted MBDA score that accounted for these three factors, using BMI or serum leptin as proxies for adiposity.

Methods: The MBDA score as a continuous variable was adjusted to account for age, sex and a proxy for adiposity (serum leptin) using data from 325,781 RA patients for whom MBDA tests had been ordered as part of routine care. Leptin values came from the MBDA test. As an alternative to using leptin to adjust for adiposity, a cohort of 1411 patients from 5 studies/registries (BRASS, CERTAIN, InFoRM, OPERA, RACER) was used to adjust for BMI, which was not available in the larger cohort, adding this BMI adjustment to that for age/sex from the larger cohort. Both types of adjusted MBDA score use the low, moderate, and high disease activity cutpoints of the original MBDA score. The two types of adjusted MBDA score and other variables were then evaluated for the prediction of radiographic progression (RP) in the 2 cohorts with available radiographic data (OPERA and BRASS) using univariate and multivariate linear regression analyses. Rate of RP was assessed as the change in modified total Sharp score ($D_mTSS$) per year after MBDA testing. Prediction of RP was evaluated using the original and adjusted MBDA scores and compared with conventional measures, as well as DAS28 without CRP or ESR (DAS28*).

Results: The MBDA score increased with age, BMI and leptin concentration. In univariate analysis of the combined OPERA and BRASS cohorts (n = 555), the significant variables predicting $D_mTSS$ were leptin-adjusted MBDA score, seropositivity for RF or anti-CCP, BMI-adjusted MBDA score, MBDA score, BMI, CRP, baseline $mTSS$, disease duration, DAS28-CRP, SDAl, CDAI and DAS28* (Table 1). The leptin-adjusted and BMI-adjusted MBDA scores were the first and third most significant univariate predictors of $D_mTSS$. To compare them directly, DAS28-CRP, MBDA score, BMI-adjusted MBDA score and leptin-adjusted MBDA score were combined in pairs in regression analyses of $D_mTSS$; the BMI-adjusted (p = 0.0027) and leptin-adjusted MBDA score were significant (p = 0.00063) after adjusting for DAS28-CRP (p = 0.87 and 0.74, respectively) and the leptin-adjusted MBDA score was significant (p = 0.024 and 0.020, respectively) after adjusting for either the MBDA (p = 0.32) or BMI-adjusted MBDA scores (p = 0.094).

Conclusion: We developed two adjusted MBDA scores that combine molecular and biometric variables to account for age, sex, and adiposity. One of them, the leptin-adjusted MBDA score, significantly outperformed DAS28-CRP and the original MBDA score in predicting radiographic progression in RA patients. These results suggest that the leptin-adjusted MBDA score may offer improved clinical utility for the personalized management of patients with RA.

Table 1. Univariate Linear Regression Analysis of the Association of Clinical and Laboratory Variables with $D_mTSS$ in the OPERA and BRASS Combined Cohort

<table>
<thead>
<tr>
<th>Variable</th>
<th>n</th>
<th>F-statistic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leptin-adjusted MBDA Score</td>
<td>555</td>
<td>17.1</td>
<td>0.000040</td>
</tr>
<tr>
<td>RF or Anti-CCP Status</td>
<td>555</td>
<td>14.8</td>
<td>0.00013</td>
</tr>
<tr>
<td>BMI-adjusted MBDA Score</td>
<td>555</td>
<td>14.4</td>
<td>0.00016</td>
</tr>
<tr>
<td>MBDA Score</td>
<td>555</td>
<td>12.9</td>
<td>0.000956</td>
</tr>
<tr>
<td>BMI</td>
<td>555</td>
<td>10.9</td>
<td>0.001</td>
</tr>
<tr>
<td>log(CRP)</td>
<td>555</td>
<td>6.8</td>
<td>0.0093</td>
</tr>
<tr>
<td>Baseline $mTSS$</td>
<td>555</td>
<td>5.3</td>
<td>0.022</td>
</tr>
<tr>
<td>log(Disease duration + 1)</td>
<td>401</td>
<td>4.8</td>
<td>0.030</td>
</tr>
<tr>
<td>DAS28-CRP</td>
<td>536</td>
<td>4.6</td>
<td>0.032</td>
</tr>
<tr>
<td>SDAl</td>
<td>533</td>
<td>4.3</td>
<td>0.040</td>
</tr>
<tr>
<td>CDAI</td>
<td>533</td>
<td>3.9</td>
<td>0.049</td>
</tr>
<tr>
<td>DAS28*</td>
<td>536</td>
<td>3.1</td>
<td>0.079</td>
</tr>
<tr>
<td>Gender</td>
<td>555</td>
<td>1.5</td>
<td>0.23</td>
</tr>
<tr>
<td>Smoking Status</td>
<td>478</td>
<td>0.8 (2 df)</td>
<td>0.46</td>
</tr>
<tr>
<td>Age</td>
<td>555</td>
<td>0.1</td>
<td>0.76</td>
</tr>
</tbody>
</table>

DAS28* = DAS28 with no CRP or ESR component, i.e., $0.56(TJC28)^{0.5} + 0.28(SJC28)^{0.5} + 0.014(GH)$. 

First publication: September 18, 2017
A Single Immunosignature Test Accurately Discriminates RA from Related Autoimmune and Inflammatory Disorders

*Theodore M. Tarasow*, 1 Robert Gerwien, 1 Jonathan Melnick, 1 Scott A. Melville and Chaim Putterman, 1 HealthTell, Inc., San Ramon, CA, 2 Division of Rheumatology, Albert Einstein College of Medicine, Bronx, NY, USA, Bronx, NY

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Rheumatoid Arthritis (RA) is a chronic inflammatory autoimmune disease primarily targeting the synovium. RA is B-cell driven, and is associated with autoantibody production. The clinical heterogeneity in RA and overlapping symptoms with other diseases can pose diagnostic challenges, especially in early disease. An accurate diagnostic tool or a means to further stratify patients could have a significant impact on patient care.

Immunosignature (IS) technology permits differential diagnosis of related autoimmune diseases based on distinct serum autoantibody profiles, as determined by binding to a microarray containing 126K distinct peptides with an average length of 9 amino acids. Our unique approach to peptide microarray fabrication, combining photolithography with optimized peptide chemistry and MALDI-based quality control, enables low-cost, rapid, and reproducible testing.

Here, the IS technology was applied to the serological differentiation of RA from other rheumatic diseases (inflammatory and non-inflammatory) and healthy controls.

**Methods:**

379 serum samples were prospectively collected, including RA (n=95), systemic lupus erythematosus (SLE) (n=75), Sjögren’s syndrome (SS) (n=20), osteoarthritis (OA) (n=24), fibromyalgia (n=22), other disease (OD) (n=76) and healthy controls (HC) (n=59). Subjects with rheumatological diseases were diagnosed based on ACR criteria. There were no significant differences in gender, race, or ethnicity across all groups. Antibody(IgG)-peptide binding was quantified and peptides with significant intensity differences between contrasting groups were identified by Bonferroni adjusted t-test. Support vector machine classifiers were trained using the most distinguishing peptides between contrasts. Classifier performance was evaluated by a cross-validation routine that included feature selection, model training, and model testing.
Results:

The number of significant peptides that discriminate RA from other groups and classification cross-validated area under the curve (cvAUC) values are summarized in the table below.

<table>
<thead>
<tr>
<th>Contrast</th>
<th>Samples</th>
<th>Significant Peptides</th>
<th>cvAUC (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA vs. HC</td>
<td>154</td>
<td>3,062</td>
<td>0.80 (0.78-0.83)</td>
</tr>
<tr>
<td>RA vs. other rheumatic diseases*</td>
<td>239</td>
<td>328</td>
<td>0.70 (0.66-0.74)</td>
</tr>
<tr>
<td>RA vs. SLE</td>
<td>170</td>
<td>201</td>
<td>0.80 (0.76-0.85)</td>
</tr>
<tr>
<td>RA vs. OA</td>
<td>119</td>
<td>130</td>
<td>0.73 (0.67-0.78)</td>
</tr>
<tr>
<td>RA vs. Fibromyalgia</td>
<td>117</td>
<td>753</td>
<td>0.78 (0.73-0.83)</td>
</tr>
<tr>
<td>RA vs. SS</td>
<td>115</td>
<td>20</td>
<td>0.66 (0.60-0.73)</td>
</tr>
</tbody>
</table>

*Other rheumatic diseases = SLE, SS, OA, psoriatic arthritis (11), gout (9), seronegative spondyloarthropathy (2), pseudogout (1)

Conclusion:

Using IS technology, RA is best discriminated from patients with SLE and HC. Nevertheless, RA can also be differentiated from closely-related conditions such as SS with modest cvAUCs. The results presented represent a step toward creating a single test using a small serum sample capable of multi-classification across a range of symptomatically related diseases and in patients with conditions referred to rheumatologic evaluation. Whether diagnostic accuracy would be improved by combining results from standard serological tests is being studied. Verification in cohorts from other sites and validation in blinded studies would allow for further model refinement to create a robust diagnostic assay.

Disclosure: T. M. Tarasow, HealthTell, 3,HealthTell, 1; R. Gerwien, HealthTell, 3,HealthTell, 1; J. Melnick, HealthTell, 3,HealthTell, 1; S. A. Melville, HealthTell, 3,HealthTell, 1; C. Putterman, HealthTell, 2,HealthTell, 5.

Abstract Number: 1373

Ultrasound of Subtalar Joint Synovitis in Patients with Rheumatoid Arthritis: Results of an Omeract Reliability Exercise Using Consensual Definitions

George A. W. Bruyn¹, Heidi Siddle², Petra Hanova³, Felicie Costantino⁴, Annamaria Iagnocco⁵, Andrea Delle Sedie⁶, Marwin Gutierrez⁷, Hilde B. Hammer⁸, Elizabeth Jernberg⁹, Damien Loeuille¹⁰, Carlos Pineda¹¹, Mihaela Cosmina Micu¹², Ingrid Moller¹³, Bethan Richards¹⁴, Maria S. Stoenoiu¹⁵, Takeshi Suzuki¹⁶, Lene Terslev¹⁷, Violeta Vlad¹⁸, Robert Wonink¹⁹, MA D'Agostino²⁰ and Richard J. Wakefield²¹, ¹Dept of Rheumatology, MC Groep hospitals, Lelystad, Netherlands, ²University of Leeds, Leeds, United Kingdom, ³Institute of Rheumatology and Department of Rheumatology, 1st Faculty of Medicine, Charles University in Prague, Prague, Czech Republic, ⁴Hôpital Universitaire Ambroise Pare, Paris, France, ⁵Academic Rheumatology Unit, Università degli Studi di Torino, Torino, Italy, ⁶Department Rheumatology, University of Pisa, Pisa, Italy, ⁷Rheumatology, Instituto Nacional de Rehabilitación, Mexico City, Mexico, ⁸Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, ⁹University of Washington, Seattle, WA, ¹⁰Rheumatology, CHRU Vandoeuvre les Nancy, Nancy, France, ¹¹Instituto Nacional de Rehabilitacion, Mexico, Mexico, ¹²Division of Rheumatology, Department of Rehabilitation II, Clinical Rehabilitation Hospital, Cluj Napoca, Romania, ¹³Instituto de Poal, Barcelona, Spain, ¹⁴University of New South Wales, Sydney, Australia, ¹⁵Service de Rhumatologie, Cliniques Universitaires Saint-Luc, Institut de Recherche Expérimentale et Clinique (IREC), Université catholique de Louvain,, Brussels, Belgium, ¹⁶Division of Allergy and Rheumatology, Japanese Red Cross Medical Center, Tokyo, Japan, ¹⁷Copenhagen Center for
SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: To evaluate the intra- and interobserver reliability of the ultrasonographic (US) assessment of subtalar joint (STJ) synovitis in patients with rheumatoid arthritis (RA).

Methods: Following a 2-round Delphi consensus process on US-defined STJ synovitis in patients with RA, twelve sonographers conducted an US reliability exercise on 10 RA patients with ankle/rearfoot pain using a 16-8 MHz linear probe. The anteromedial, postero medial, and posterolateral STJ was assessed ultrasonographically using B-mode and power Doppler (PD) techniques according to an agreed US protocol and using a 4-grade semiquantitative grading score for synovitis (synovial hypertrophy (SH) and power Doppler (PD) signal) and a dichotomous score for the presence of joint effusion (JE). Intraobserver reliability was calculated by Cohen’s kappa. Interobserver reliability was computed by Light’s kappa. Weighted k coefficients with absolute weighting were computed for B-mode and PD signal.

Results: Overall intra- and interobserver agreement for the STJ was 83% and 69%; overall intra- and interobserver agreement for SH, PD signal and JE, was 81(51-100)% , 88 (67-100) %, and 80 (72-88)% , respectively, and 69 (60-74)% , 76 (66-83)% , and 60 (54-65)% respectively. Mean weighted Cohen’s kappa for SH, PD, and JE, was 0.80 (0.62-0.98) , 0.61 (0.48-0.73) , and 0.52 (0.36-0.67) , respectively. Weighted Cohen’s kappa for SH, PD, and JE in the anteromedial, postero medial and posterolateral STJ was -0.04-0.79, 0.42-0.95, and 0.28-0.77; 0.31-1, -0.65-0.65, and -0.2-0.69; 0.66-1, 0.52-1, and 0.42-0.88, respectively. Weighted Light kappa for SH was 0.67 (95%CI 0.58-0.74), 0.46 (0.35-0.59) for PD, and 0.16 (0.08-0.27) for JE. Weighted Light kappa for SH, PD, and JE was 0.63 (0.45-0.82),0.33 (0.19-0.42) and 0.09 (-0.01-0.19), for the anteromedial STJ; 0.49 (0.27-0.64), 0.35 (0.27-0.4), and 0.04 (-0.06-0.1) for posteromedial STJ, and 0.82 (0.75-0.89), 0.66 (0.56-0.8), and 0.18 (0.04-0.34) for posterolateral STJ, respectively.

Conclusion: Ultrasound is a reliable imaging technique for assessing synovitis of the STJ in patients with RA. The most reliable site to assess STJ synovitis in patients with RA is the posterolateral probe position.

Disclosure: G. A. W. Bruyn, None; H. Siddle, None; P. Hanova, None; F. Costantino, None; A. Iagnocco, None; A. Delle Sedie, None; M. Gutierrez, None; H. B. Hammer, None; E. Jernberg, None; D. Loueille, None; C. Pineda, None; M. C. Micu, None; I. Moller, None; B. Richards, None; M. S. Stoenoiu, None; T. Suzuki, None; L. Terslev, None; V. Vlad, None; R. Wonink, None; M. D'Agostino, BMS, AbbVie, Novartis, 8; R. J. Wakefield, None.


Abstract Number: 1374

Flares in Patients with Rheumatoid Arthritis Are Strongly Associated with Worse Clinical Outcomes but Are Difficult to Predict

Katie Bechman1, L. Tweehuysen2, James Galloway3, Andrew P. Cope4 and Margaret Ma1, 1Academic Rheumatology Department, Kings College London, London, United Kingdom, 2Rheumatology, Sint Maartenskliniek, Nijmegen, Netherlands, 3King's College Hospital, Department of Rheumatology, London, London, United Kingdom, 4Academic Department of Rheumatology in the Division of Immunology, Infection and Inflammatory Diseases (DIIID), King's College London, London, Great Britain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Background/Purpose: Disease flares in RA are associated with radiographic progression\(^1\) and functional deterioration\(^2\). Predicting flare is of direct relevance to clinical practice, particularly in patients with low disease activity (LDA) in whom treatment tapering may be considered. The aim of this study was to investigate various biomarkers as predictors of flare in patients with LDA and to evaluate the impact of flare on 12-months clinical outcomes.

Methods: The REMIRA study was a prospective cohort study in which adult RA patients on stable DMARD treatment with a DAS28 < 3.2 for > 1 month were included.\(^3\) At baseline and during every 3 months for 1 year, clinical (DAS28), functional (HAQ-DI, EQ-5D, SF36), serum (MBDA, calprotectin, CXCL10) and imaging (ultrasound) data were collected. Flare was defined as an increase in DAS28 >1.2 or >0.6 if concurrent DAS28 ≥3.2 compared to baseline. Univariate Cox regression analyses were used to identify baseline predictors of flare. Subsequently, multivariate analyses were used to calculate HR for flare, adjusted for age, gender, DAS28, CRP, ESR, ultrasound and MBDA score. Linear regression analyses were performed to compare 12-months clinical outcomes between patients with and without a flare.

Results: In total 152 patients were included of whom 46 (30%) patients experienced a flare. Several baseline characteristics were associated with flare in univariate analyses (DAS28, ESR, CRP, PGA, HAQ-DI and EQ-5D) (Figure 1). The strongest magnitude of association was seen with HAQ-DI and EQ-5D. Baseline MBDA score, calprotectin, CXCL10 and ultrasound were not predictive of flare. A sensitivity analysis limited to flares with a rise in MBDA score to >44 (high disease activity) did show a relationship between baseline MBDA value and flare risk (1.07, 95% CI 1.02 to 1.11; \(p=0.005\)). In the multivariate analysis only HAQ-DI remained a significant independent predictor of flare (adjusted HR 1.76, 95% CI 1.05-2.93). Adjusting for baseline values, patients who flared had significantly worse clinical outcomes at month 12 (Table 1).

Conclusion: Flares occur frequently in RA patients with LDA and are associated with worse clinical outcomes after 1 year. However we found no strong predictors of flare, which may highlight a challenge in attempting to reduce flare rates or in considering patients for treatment tapering.

Table 1: Outcomes in flare versus no flare group

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Unadjusted</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAS</td>
<td>0.50</td>
<td>0.37 to 0.63</td>
<td>0.00</td>
</tr>
<tr>
<td>Higher score at worse</td>
<td>0.19</td>
<td>0.04 to 0.33</td>
<td>0.01</td>
</tr>
<tr>
<td>SD-BMI</td>
<td>0.1</td>
<td>0.01 to 0.26</td>
<td>0.00</td>
</tr>
<tr>
<td>Lower score at worse</td>
<td>-0.11</td>
<td>-0.18 to -0.05</td>
<td>0.00</td>
</tr>
<tr>
<td>SVI-ESR</td>
<td>0.21</td>
<td>0.14 to 0.28</td>
<td>0.00</td>
</tr>
<tr>
<td>Lower score at worse</td>
<td>-0.42</td>
<td>-0.52 to -0.32</td>
<td>0.00</td>
</tr>
<tr>
<td>SVI-MCS</td>
<td>0.1</td>
<td>0.00 to 0.24</td>
<td>0.05</td>
</tr>
<tr>
<td>Lower score at worse</td>
<td>-0.11</td>
<td>-0.23 to 0.00</td>
<td>0.16</td>
</tr>
<tr>
<td>NALC</td>
<td>0.84</td>
<td>0.75 to 0.93</td>
<td>0.00</td>
</tr>
<tr>
<td>Lower score at worse</td>
<td>-0.72</td>
<td>-0.83 to -0.62</td>
<td>0.00</td>
</tr>
<tr>
<td>USA</td>
<td>0.01</td>
<td>0.00 to 0.02</td>
<td>0.05</td>
</tr>
<tr>
<td>Higher score at worse</td>
<td>0.00</td>
<td>0.00 to 0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Old age</td>
<td>0.00</td>
<td>0.00 to 0.00</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Disclosure: K. Bechman, None; L. Tweehuysen, None; J. Galloway, MSD, 5, UCB, 5, Bristol Myers Squibb, 5, Pfizer Inc, 5, Celgene, 5; A. P. Cope, None; M. Ma, None.


Abstract Number: 1375

Foot Arthritis: Poor Prognosis Factor in RA

Sung-Hae Chang1, Sung Won Lee2, Mi-II Kang3 and Seong Yong Kim4. 1Soonchunhyang University Cheonan Hospital, Cheonan, Korea, Republic of (South), 2Division of Rheumatology, Department of Internal Medicine, Department of Rheumatology, Soonchunhyang University Cheonan Hospital, Cheonan, Korea, Republic of (South), 3Dankuk University Hospital, Cheonan, Korea, Republic of (South), 4Application Statistics, Hoseo University, Cheonan, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The objective of the current study is to evaluate the clinical importance of foot and ankle joint arthritis.

Methods: Data from Korean Biologic Registry (KoBio) data were analyzed. Foot and/or ankle arthritis defined as one or more swollen and/or tender joint among 1st-5th metatarsal or ankle joints. A chi-square analysis was employed to calculate the relative risk (RR) of remission for patients with foot and/or ankle arthritis among. Marginal model was applied to assess prognostic effect of foot and/or ankle arthritis adjusting positive rheumatoid factor, anti-CCP antibody and radiographic abnormalities.
Results: A total of 2026 patients (biologic disease modifying anti-rheumatic drugs, R, n=1400 non-biologic DAMRDs treatment group, C, n=626) at baseline, 1554 patients (R, n=1046, C, n=508) at 1 year follow-up, 1068 patients (R, n=712, C, n=356) at 2 year follow-up, and 472 patients (R, n=327, C, n=145) were enrolled. At baseline evaluation, prevalence of foot synovitis was 29.4% of total patients (595 of 2026). Patients with foot or ankle arthritis (Group 1) were less likely to achieve clinical remission (using Disease Activity Score 28 ESR, DAS-28 ESR) compared to patients without foot and ankle arthritis (Group 2); remission rate of Group 1 vs Group 2 was 11.7% vs 39.7% (p<0.001) at 1 year, 18.1% vs 40.1% (p<0.001) at 2 year, and 23.1% vs 44.5% (p<0.001) at 3 year follow-up. They were also tend to have functional impairment (using Routine Assessment of Patients Index Data, RAPID3); remission rate of Group 1 vs Group 2 was 5.0% vs 20.4% (p<0.001) at 1 year, 9.0% vs 18.5% (p<0.001) at 2 year, and 3.1% vs 20.3% (p<0.05) at 3 year follow-up. Even among patients without radiographic abnormalities (joint space narrowing or erosion) in baseline foot x-ray, Group 1 patients showed significantly low clinical remission rate; remission rate of Group 1 vs Group 2 was 12.9% vs 40.7% (p<0.001) at 1 year, 15.3% vs 41.3% (p<0.001) at 2 year, and 26.2% vs 47.7% (p<0.001) at 3 year follow-up. Presence of foot and/or ankle arthritis at baseline or at any time point of observation period was associated with poor prognosis (Table 1, 2).

Conclusion: Foot and/or ankle arthritis is associated with less achievement of clinical remission.

Table 1. Impact of foot or ankle arthritis at baseline assessment for remission

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Relative Risk</th>
<th>Estimate</th>
<th>Standard Error</th>
<th>95% Confidence Limits</th>
<th>Z</th>
<th>Pr &gt;</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-0.1604</td>
<td>0.2089</td>
<td>-0.2270</td>
<td>-0.5429</td>
<td>-2.4</td>
<td>0.0161</td>
<td></td>
</tr>
<tr>
<td>1 y follow-up</td>
<td>4.9420</td>
<td>1.6018</td>
<td>0.1225</td>
<td>1.5167</td>
<td>15.03</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>2 y follow-up</td>
<td>5.9429</td>
<td>1.7145</td>
<td>0.1426</td>
<td>1.6046</td>
<td>19.94</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>3 y follow-up</td>
<td>7.1614</td>
<td>1.9627</td>
<td>0.1713</td>
<td>1.8090</td>
<td>23.75</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Foot or ankle arthritis at baseline</td>
<td>-0.7662</td>
<td>0.2116</td>
<td>-0.3536</td>
<td>-0.1619</td>
<td>-4.71</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Functional impairment</td>
<td>-0.6995</td>
<td>0.2213</td>
<td>-0.1505</td>
<td>-0.1001</td>
<td>-8.17</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Anti-CCP positivity</td>
<td>-0.6470</td>
<td>0.1933</td>
<td>-0.3830</td>
<td>-0.1036</td>
<td>-4.79</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>0.7417</td>
<td>0.0464</td>
<td>0.0293</td>
<td>-0.2906</td>
<td>-1.87</td>
<td>0.0607</td>
<td></td>
</tr>
<tr>
<td>Disease duration</td>
<td>0.9391</td>
<td>0.0122</td>
<td>0.0042</td>
<td>-0.0203</td>
<td>-2.85</td>
<td>0.0040</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Impact of foot or ankle arthritis with normal foot x-ray at baseline evaluation for remission

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Relative Risk</th>
<th>Estimate</th>
<th>Standard Error</th>
<th>95% Confidence Limits</th>
<th>Z</th>
<th>Pr &gt;</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-0.8454</td>
<td>0.2089</td>
<td>-0.1818</td>
<td>-0.5518</td>
<td>-3.91</td>
<td>0.0001</td>
<td></td>
</tr>
<tr>
<td>1 y follow-up</td>
<td>4.9420</td>
<td>1.6018</td>
<td>0.1225</td>
<td>1.5167</td>
<td>15.03</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>2 y follow-up</td>
<td>5.9429</td>
<td>1.7145</td>
<td>0.1426</td>
<td>1.6046</td>
<td>19.94</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>3 y follow-up</td>
<td>7.1614</td>
<td>1.9627</td>
<td>0.1713</td>
<td>1.8090</td>
<td>23.75</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Foot or ankle arthritis at baseline</td>
<td>-0.7662</td>
<td>0.2116</td>
<td>-0.3536</td>
<td>-0.1619</td>
<td>-4.71</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Anti-CCP positivity</td>
<td>-0.6470</td>
<td>0.1933</td>
<td>-0.3830</td>
<td>-0.1036</td>
<td>-4.79</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>0.7417</td>
<td>0.0464</td>
<td>0.0293</td>
<td>-0.2906</td>
<td>-1.87</td>
<td>0.0607</td>
<td></td>
</tr>
</tbody>
</table>

Disclosure: S. H. Chang, None; S. W. Lee, None; M. I. Kang, None; S. Y. Kim, None.
Abstract Number: 1376

Diagnostic Performance of 7 Different Anti-Cyclic Citrullinated Peptide Antibody and 6 Rheumatoid Factor Assays in a Primary Diagnostic, Consecutive Rheumatological Population in a Secondary Care Hospital

Lieve Van Hoovels¹, Julie Jacobs¹, Bert Vander Cruyssen², Stefanie Van den Breeml¹, Patrick Verschueren³ and Xavier Bossuyt⁴,
¹Laboratory medicine, OLV Hospital, Aalst, Belgium, ²Rheumatology, OLV hospital, Aalst, Belgium, ³Division of Rheumatology, University Hospital Leuven, Leuven, Belgium, ⁴Laboratory medicine, University Hospital Leuven, Leuven, Belgium

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

The clinical diagnosis of rheumatoid arthritis (RA) remains a challenge, making serological markers most interesting. The 2010 ACR/EULAR classification criteria for RA take into account two serological markers: anti-cyclic citrullinated peptide (ACPA) and rheumatoid factor (RF).

The objective of this study is to evaluate the diagnostic performance of 6 RF and 7 ACPA assays in a secondary care hospital

Methods:

From January 2014 to June 2015, all unique patients who for the first time underwent laboratory testing for a rheumatologic disease at the OLV hospital Aalst were included. Review of the medical records was done and the diagnosis was registered and reviewed by the consulting rheumatologist. Patients were categorized into three groups: RA, rheumatologic disease control group (RDCG) and disease control group (DCG). For all RA patients the fulfillment of the ACR classification criteria (1987 and 2010) was checked. Six commercial RF assays (Zenit, Phadia, Inova, Roche, Abbott, Euroimmun (EI)) and 7 commercial ACPA assays (Zenit, Phadia, BIOFlash Inova (BF), Roche, Abbott, EuroDignostica (ED), EI) were tested and diagnostic performance (sensitivity, specificity, receiver operating characteristics (ROC) curve analysis, likelihood ratio (LR)) evaluated.

Results:

We included 594 patients: 44 (7.4%) RA, 247 (41.6%) RDGC and 225 (37.9%) DCG. For 78 (13.1%) the diagnosis remained undifferentiated. Most of the included RA patients fulfilled the ACR classification criteria (94.3% 1987; 78.56% 2010).

Sensitivities for RF range from 35.7-44.3% and for ACPA from 35.7-41.4% (Table 1), lower than normally described. Demographic patient features, like older patients, could be partly responsible for this low RF/ACPA positivity. The low false positive reactivities in the control patient cohorts are also quite remarkable for RF, as RF is historically known as a more aspecific serological RA marker. Since the control group consists of a primary diagnostic, consecutive rheumatological population, they represent the real life setting in this secondary care hospital, reflecting the true diagnostic usefulness of the RF/ACPA analyses. A negative serological test result will not exclude RA. For RF the importance of a weak positive result (1-3 times cut-off value) depends on the assay used. For ACPA a weak positive result is of diagnostic importance. Strong positive RF or ACPA results can aid in the diagnosis of RA as they have a high LR for RA (>10 for all assays), except for two RF assays (from Inova and Euroimmun).

Conclusion:

The aid of the serological reactivities in the diagnosis of RA is dependent on the choice of the RF (especially) or ACPA assay used due to the lack of harmonization. Demographic features of the patient population and the possible low serological positive RA pretest probability will also influence the usefulness of these serological tests.
Disclosure: L. Van Hoovels, None; J. Jacobs, None; B. Vander Cruyssen, None; S. Van den Bremt, None; P. Verschueren, AbbVie, Bristol-Myers Squibb, Eli Lilly & Doehme, Pfizer, Roche, Sanofi, and UCB, 5, Pfizer chair for early RA management at KU Leuven, 6; X. Bossuyt, None.


Abstract Number: 1377

The Serum Levels of Semaphorin 4D Are Associated with Disease Activity As Well As Radiographic Progression in Patients with Rheumatoid Arthritis

The Serum Levels of Semaphorin 4D Are Associated with Disease Activity As Well As Radiographic Progression in Patients with Rheumatoid Arthritis

Ji Hyoun Kim1, You-Jung Ha2, Sang Wan Chung3, Eun Ha Kang2, Yeong Wook Song4,5 and Yun Jong Lee6, 1Division of Rheumatology, Department of Internal Medicine, Seoul National University Bundang Hospital, Division of Rheumatology, Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam-si, Korea, Republic of (South), 2Division of Rheumatology, Department of Internal Medicine, Division of Rheumatology, Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam-si, Korea, Republic of (South), 3Department of Internal Medicine, Department of Internal Medicine, Sarang Hospital, Incheon, Korea, Republic of (South), 4Department of Molecular Medicine and Biopharmaceutical Sciences, Graduate School of Convergence Science and Technology, and College of Medicine, Seoul National University, Seoul, Korea, Republic of (South), 5WCU Department of Molecular Medicine and Biopharmaceutical Sciences, Medical Research Institute, Seoul National University College of Medicine, Seoul, Korea, Republic of (South), 6Division of Rheumatology, Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM
**Background/Purpose:** Progranulin (PGRN) and semaphorins (sema) are known to be involved in immune responses as well as bone remodeling process. The aim of this study was to investigate the clinical significance of serum levels of PGRN, sema3A, and sema4D in patients with RA.

**Methods:** Blood samples were collected from 85 RA patients who satisfied 2010 ACR/EULAR classification criteria for RA and 43 age- and gender-matched healthy controls. The serum levels of PGRN and sema3A/4D were determined using ELISA. Additionally, TNF-\(\alpha\), IL-6, IL-23, RANK ligand, osteoprotegerin, and osteopontin were measured using magnetic bead-based multiplex assays. RA disease activity was assessed by DAS28 and structural joint damage was assessed by plain radiographs using the modified Sharp/van der Heijde score (SHS) at baseline and after an average 2-year follow-up period. \(\Delta\) SHS \(\geq\) 1 unit/year was defined as having radiographic progression.

**Results:** Serum levels of PRGN were significantly increased in patients with RA, compared with healthy controls (31.0 [24.5-39.1] vs 25.9 [21.1-31.0] ng/mL, \(p=0.001\)), while those of sema4D did not differ between two groups. Although the serum levels of sema3A were below the detection range in most samples, the serum sema3A level in RA patients was significantly elevated in comparison with the level in the controls (0.44 [0-1.90] vs 0 [0-0.19] ng/mL, \(p<0.001\)). In RA patients, serum concentrations of sema4D were found to be correlated with those of IL-6 (\(\bar{y}=0.514\), \(p<0.001\)) and IL-23 (\(\bar{y}=0.234\), \(p=0.031\)) and PGRN was negatively correlated with osteopontin. Serum sema4D levels showed positive correlations with ESR (\(\bar{y}=0.336\), \(p=0.002\)), CRP (\(\bar{y}=0.337\), \(p=0.002\)), DAS28 (\(\bar{y}=0.240\), \(p=0.029\)) and \(\Delta\) SHS/year (\(\bar{y}=0.244\), \(p=0.025\)). However, the levels of PGRN and sema3A were not associated with disease activity or joint damage. RA patients with radiographic progression had significantly higher serum sema4D levels than those without progression (127.5 [66.4-230.2] vs 81.9 [52.1-106.9] ng/mL, \(p=0.018\)).

**Conclusion:** Serum sema4D levels were associated with disease activity as well as radiographic progression in RA patients, although its levels were comparable between RA patients and controls. These findings suggest that sema4D might play a role in RA-related joint damage and is a possible biomarker reflecting inflammatory burden and radiographic progression in patients with RA.

**Disclosure:** J. H. Kim, None; Y. J. Ha, None; S. W. Chung, None; E. H. Kang, None; Y. W. Song, None; Y. J. Lee, None.


**Abstract Number:** 1378

**Low HDL Level As a Clinical Marker of Disease Activity in Rheumatoid Arthritis Patients**

**Rocio Gamboa-Cárdenas**\(^1\), Manuel Ugarte-Gil\(^2\), Francisco Zevallos\(^1\), Mariela Medina\(^1\), Zoila Rodriguez-Bellido\(^1\), Claudia Erler-Fitzcarrald\(^1\), Omar Sarmiento-Velasquez\(^1\), Cristina Reategui-Sokolova\(^1\), Victor Pimentel-Quiroz\(^1\), José Alfaro\(^1\), Mariano Cucho-Venegas\(^1\), Risto Perich-Campos\(^3\) and Cesar A. Pastor-Asurza\(^1\), \(^1\)Rheumatology, Hospital Guillermo Almenara Irigoyen. EsSalud, Lima, Peru, \(^2\)Peru, GLADEL, Lima, Peru, \(^3\)Rheumatology, Hospital Guillermo Almenara Irigoyen, Lima, Peru

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Monday, November 6, 2017
**Session Title:** Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
**Session Type:** ACR Poster Session B
**Session Time:** 9:00AM-11:00AM
Background/Purpose: In contrast to high evidence of HDL inflammatory function in cardiovascular risk in rheumatoid arthritis (RA) patients, there is scarce data about the total HDL levels as a marker of RA disease activity.

Methods: A cross-sectional study in Rheumatology department of Hospital Almenara EsSalud. Lima Perú. Subjects were recruited consecutively from our RA cohort. RA was defined with ACR 87/ACR EULAR 2010 RA criteria, without overlap syndromes except Sjögren, current infections or pregnancy. For these analyses hospitalized patients, with recent medical/surgical procedures or severe anemia (less than 7 g/dL) were excluded. Clinical interview, chart review, physical examination (included 28 joint count), health questionnaires, Visual analogue scales and laboratory sampling including a complete lipid profile were performed in the same day. A univariable and multivariable linear regression models were performed in order to determine if HDL levels were associated with disease activity (DAS 28 or CDAI) independently of disease duration, gender, age at diagnosis, socioeconomic status, use of conventional DMARDs, biologics, current corticosteroid dose, CRP, anti CCP, RF, and metabolic syndrome.

Results: Two hundred and seventy-eight patients were included, all Mestizos, 92.8% were female, disease duration was 15.16 (11.92) and age at diagnosis 44.08 (13.92) years. The most frequent socioeconomic statuses were low: 30.9%, middle 33.1% and high 33.8%. Current prednisone dose was 4.50 mg/d (3.30). Patients with current convectional DMARD use were 97.1 % and 6.1 % with biologic agent; RF level was 290.39 (474, 17) UI/ml and anti CCP 544, 98 (132.37) U/ml. Level of HDL was 56.98 (1326, 37) mg/dL and LDL 120.76 (33.00) mg/L. One hundred and three patients (37.1 %) had metabolic syndrome. DAS 28 media score was 4.69 (1.22) and CRP level 11.76 (21.41) mg/dL. In the multivariate analysis HDL cholesterol level was associated with DAS 28 score (B= -0.016: CI: -0.26 - -0.01; p=0.04) independently of other variables. HDL cholesterol level was also independently associated with CDAI score (B = 0.14 CI -0.24 - -0.04 p= 0.009)

Conclusion: Low HDL cholesterol level was associated with higher disease activity in RA patients, independently of other known classical factors. A more careful evaluation of active disease could be performed in patients with this potential marker, in clinical practice.

Disclosure: R. Gamboa-Cárdenas, None; M. Ugarte-Gil, None; F. Zevallos, None; M. Medina, None; Z. Rodriguez-Bellido, None; C. Elera-Fitzcarrald, None; O. Sarmiento-Velasquez, None; C. Reategui-Sokolova, None; V. Pimentel-Quiroz, None; J. Alfaro, None; M. Cucho-Venegas, None; R. Perich-Campos, None; C. A. Pastor-Asurza, None.


Abstract Number: 1379

Epithelial Neutrophil-Activating Peptide 78/C-X-C Motif Chemokine 5 in the Insulin Resistance of Patients with Rheumatoid Arthritis

Hiurma Sanchez-Perez1, Beatriz-Segura Tejera2, De Vera-González AM3, Alejandra González Delgado4, Jose M Olmos5, José Luis Hernandez6, Begoña Ubilla7, Raquel Lopez-Mejias8, Miguel Angel González-Gay9 and Ivan Ferraz-Amaro10, 1Rheumatology, Rheumatology Division, Hospital Universitario de Canarias, La Laguna. Tenerife, Spain, 2Rheumatology section, Hospital Germans Trias i Pujol, Badalona, Spain, 3Central Laboratory Division, University Hospital of Canary Islands, Tenerife, Spain, 4Central Laboratory Division. Hospital Universitario de Canarias, Tenerife, Spain, Tenerife, Spain, 5Division of Internal Medicine. Hospital Universitario Marqués de Valdecilla, IDIVAL.Universidad de Cantabria. RETICEF, Santander, Spain, 6Internal Medicine, Hospital Universitario Marqués de Valdecilla. IDIVAL, Santander, Spain, 7Epidemiology, Genetics and Atherosclerosis Research Group on Systemic Inflammatory Diseases, IDIVAL, Santander, Spain, 8Epidemiology, Genetics and Atherosclerosis Research Group on Systemic Inflammatory Diseases, Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain, 9Rheumatology, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Johannesburg, South Africa, 10Rheumatology, Hospital Universitario de Canarias, La Laguna, Tenerife, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM
Background/Purpose: It is known that the chemokine molecule CXCL5 (C-X-C motif chemokine 5 or epithelial neutrophil activating peptide 78 -ENA78-) is a link between obesity, inflammation, and insulin resistance (IR) in general population. Similarly, chronic inflammation has been found to deteriorate IR and impair pancreatic beta cell function in rheumatoid arthritis (RA) patients. The aim of this study was to explore the role of CXCL5 in the IR of RA patients.

Methods: Cross-sectional study that encompassed 141 non-diabetic patients with RA. IR by homeostatic model assessment (HOMA2), insulin and C-peptide serum levels and lipid profile, and CXCL5 serum levels were assessed in patients. A multivariable regression analysis, adjusted for IR related factors, was performed to evaluate how CXCL5 is related to IR, disease activity and disease characteristics in RA patients.

Results: Insulin and C peptide serum levels did strongly correlated between them (r²=0.913, p<0.001) but not with CXCL5 (insulin r²=-0.034, p=0.69; C peptide r²=-0.050, p=0.56). Interestingly, while glucocorticoids were related with insulin (beta coef. 2.56 [95%CI 0.31-5.42], p=0.080), C-peptide serum levels (beta coef. 1.69 [95%CI 1.09-2.28], p=0.000), and HOMA2-IR (beta coef. 0.34 [95%CI -0.02-0.70], p=0.06) and HOMA2-%B-C peptide (beta coef. 51 [95%CI 31-70], p=0.000), the use of prednisone was not associated with CXCL5 serum levels (beta coef. -6 [95%CI -74-63], p=0.87). C reactive protein (beta coef. 0.2 [95%CI -1.4-1.9], p=0.80) and disease activity through DAS28 (beta coef. 13 [95%CI -14-41], p=0.34) also disclosed no relation with CXCL5. Other disease characteristics like disease duration, presence of rheumatoid factor or anti-citrullinated protein antibodies, or use of methotrexate or anti-TNF alpha therapies were not related with CXCL5 serum levels. Additionally, CXCL5 did neither explained HOMA2-IR (beta coef. -0.00 [95%CI -0.00-0.00], p=0.21) nor beta cell production, using HOMA2-%B-C peptide (beta coef. -0.05 [95%CI -0.12-0.02], p=0.17), through multivariable regression analysis.

Conclusion: CXCL5 is not related to RA disease characteristics or IR in RA patients. This could imply that the mechanisms that lead to IR of RA patients are different from those from general population.

Disclosure: H. Sanchez-Perez, None; B. S. Tejera, None; D. V. G. AM, None; A. González Delgado, None; J. M. Olmos, None; J. L. Hernandez, None; B. Ubilla, None; R. Lopez-Mejías, None; M. A. González-Gay, None; I. Ferraz-Amaro, None.


Abstract Number: 1380

Serum Galectin-3 in Rheumatoid Arthritis Compared with Healthy Controls and Subjects with Prediabetes before and after High-Intensity Interval Training

Brian J. Andonian1, David Bartlett2, Virginia B. Kraus3, Janet Huebner2, William E. Kraus4 and Kim M. Huffman5, 
1Rheumatology, Duke University Medical Center, Durham, NC, 2Duke University, Durham, NC, 3Duke Molecular Physiology Institute, Duke University School of Medicine, Durham, NC, 4Duke University School of Medicine, Durham, NC, 5School of Medicine, Division of Rheumatology, Immunology and Molecular Physiology and Durham VA Medical Center, Duke University, Durham, NC

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Rheumatoid arthritis (RA) is associated with significant cardiovascular disease (CVD), sarcopenic obesity, and mortality. Galectin-3 is a biomarker associated with inflammation, fibrosis, and increased risk of CVD and all-cause mortality. We aimed to: 1) explore clinical relationships between RA and galectin-3; and 2) investigate changes in galectin-3 in patients with RA and prediabetes mellitus (PD) before and after a novel high-intensity interval training (HIIT) program.

Methods:
All RA patients in this study satisfied 1987 ACR criteria. Serum galectin-3 was measured in 47 persons with RA; concentrations were compared among older RA (age>55yrs; n=24), younger RA (<55 y, n=23), and older, age, sex and BMI-matched healthy controls (>55 y, n=12). In a second study, we compared galectin-3 in older RA (age<50; n=12) to older PD (age<50; n=9), before and after 10 weeks of HIIT. Student's t-tests and Wilcoxon signed rank tests were used to compare outcome variables. Correlations were compared using Spearman’s rho.

**Results:**

As compared to both the younger RA group (7.85±4.0(SD) ng/mL, p=0.390) and older healthy controls (6.89±1.9, p=0.042), the older RA group had higher concentrations of galectin-3 plasma concentrations (8.80±3.5). In the total RA group (n=47), galectin-3 was significantly and positively correlated with age (r=0.39), BMI (r=0.32), prednisone use (r=0.42), plasma IL-6 (r=0.29), and thigh cross-sectional area (r=0.46); it was negatively correlated with thigh muscle density (r=-0.44; p<0.05 for all). In the HIIT study, as compared to the PD group, the RA group was younger (63.9±7.2 vs 71.4±4.9, p=0.05) and thinner (27.4±9.3 vs 29.4±3.0, p<0.05). After HIIT, galectin-3 did not change in either group, but both baseline and post-HIIT galectin-3 were greater in the RA group compared to the PD group (pre: 12.21±6.7 vs 8.73±2.3, p=0.118; post: 11.99±4.2 vs 8.71±2.3, p=0.056). A decrease in galectin-3 was also correlated with an increase in absolute peak VO\textsubscript{2} in the total group (r=-0.47, p=0.03) and in RA (r=-0.57, p=0.05).

**Conclusion:**

In RA, greater galectin-3 plasma concentrations associate with traditional cardiovascular risk factors including age and adiposity, as well as with RA-specific risk factors, including prednisone use and IL-6. The importance of RA-specific risks is emphasized by greater galectin-3 in RA even when comparing to an older, heavier, prediabetic cohort. While HIIT did not change mean galectin-3 concentrations, reductions in galectin-3 were associated with cardiorespiratory fitness improvements in RA. These findings suggest that galectin-3 may represent a novel risk factor for CVD in RA, and that CVD risk in RA may be modulated by exercise training.

**Disclosure:** B. J. Andonian, None; D. Bartlett, None; V. B. Kraus, None; J. Huebner, None; W. E. Kraus, None; K. M. Huffman, None.

**Abstract Number:** 1381

**Skeletal Muscle Cytokine and Myostatin Responses to High-Intensity Interval Training in Rheumatoid Arthritis Contrasted with Prediabetes Mellitus**

Brian J. Andonian\textsuperscript{1}, David Bartlett\textsuperscript{2}, Virginia B. Kraus\textsuperscript{3}, Janet Huebner\textsuperscript{2}, William E. Kraus\textsuperscript{4} and Kim M. Huffman\textsuperscript{5},

\textsuperscript{1}Rheumatology, Duke University Medical Center, Durham, NC, \textsuperscript{2}Duke University, Durham, NC, \textsuperscript{3}Duke Molecular Physiology Institute, Duke University School of Medicine, Durham, NC, \textsuperscript{4}Duke University School of Medicine, Durham, NC, \textsuperscript{5}School of Medicine, Division of Rheumatology, Immunology and Molecular Physiology and Durham VA Medical Center, Duke University, Durham, NC

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Sarcopenic obesity and the associated risk of cardiovascular disease (CVD) and mortality in rheumatoid arthritis (RA) may be related to dysregulated skeletal muscle remodeling (Huffman et al. Arthritis Research & Therapy (2017); 19:12). Skeletal muscle remodeling relies on coordinated signaling through cytokines and myokines. We hypothesized that exercise training-induced alterations in muscle cytokines and myokines would reprogram muscle remodeling differently in (RA) versus those with prediabetes (PD). In this study, we investigated relationships between skeletal muscle cytokines and myostatin in patients with RA and PD before and after a high-intensity interval-based training (HIIT) program.
Methods:

All RA patients in this study satisfied 1987 ACR criteria. Body composition was assessed with Bod Pod. Using vastus lateralis biopsies, muscle (m) cytokines, mIL-1β, mIL-6, mIL-8, mTNF-α, mIL-10, and myostatin were quantified in RA (n=12) and pre-DM (n=9) before and after a 10-week supervised HIIT program. Continuous variables were compared using Students t-tests and Wilcoxon signed rank tests, dependent on normality. Correlations between muscle cytokines and clinical variables were compared using Spearman's rho.

Results:

The RA group was younger (age 63.9 vs 71.4 y; p<0.05) and thinner (BMI 27.4 vs 29.4 kg/m²; p<0.05) with similar cytokine yet lower muscle myostatin concentrations (Table 1). For both groups after HIIT training, there were no significant responses in cytokines or myostatin concentrations. While overall body composition changes were small in RA, an increase in lean mass correlated with decreases in mIL-6, mIL-1 β, and mTNF-α. A decrease in body fat percentage was correlated with a decrease in mTNF-α.

Conclusion:

While muscle cytokines in RA were comparable to an older, heavier, prediabetic group, RA myostatin was lower. As a potent negative regulator of skeletal muscle growth and hypertrophy, lower muscle myostatin suggests that in RA, sarcopenic obesity may be related to impaired myostatin signaling. Although 10 weeks of HIIT did not significantly alter mean group cytokine or myostatin concentrations, reductions in RA muscle cytokines were associated with improved body composition (greater lean mass and less body fat percentage). Thus, HIIT may improve coordination of cytokines and myokines critical for skeletal muscle remodeling.

Table 1

<table>
<thead>
<tr>
<th>Skeletal Muscle Concentrations (pg/mL/µg)</th>
<th>All participants (n=21)</th>
<th>Rheumatoid arthritis (n=12)</th>
<th>Pre-diabetes mellitus (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-HIIT</td>
<td>Post-HIIT</td>
<td>Pre-HIIT</td>
</tr>
<tr>
<td>IL-1β</td>
<td>0.023(0.075)</td>
<td>0.008(0.006)</td>
<td>0.007(0.005)</td>
</tr>
<tr>
<td>IL-6</td>
<td>0.022(0.053)</td>
<td>0.015(0.008)</td>
<td>0.010(0.006)</td>
</tr>
<tr>
<td>IL-8</td>
<td>0.123(0.234)</td>
<td>0.117(0.132)</td>
<td>0.112(0.212)</td>
</tr>
<tr>
<td>TNF-α</td>
<td>0.013(0.026)</td>
<td>0.010(0.006)</td>
<td>0.008(0.007)</td>
</tr>
<tr>
<td>IL-10</td>
<td>0.012(0.023)</td>
<td>0.006(0.004)</td>
<td>0.009(0.012)</td>
</tr>
<tr>
<td>Myostatin</td>
<td>41.201(87.883)</td>
<td>26.764(16.079)</td>
<td>16.621(7.463)</td>
</tr>
</tbody>
</table>

Continuous variable data are presented as means (SD). IL interleukin, TNF tumor necrosis factor, HIIT high intensity interval training

*p < 0.05 for comparisons between RA and pre-diabetes mellitus groups

Disclosure: B. J. Andonian, None; D. Bartlett, None; V. B. Kraus, None; J. Huebner, None; W. E. Kraus, None; K. M. Huffman, None.


Abstract Number: 1382

Characteristics of Patients with Rheumatoid Arthritis and Atlanto-Axial Pannus
Formation of pannus, an inflammatory tissue mass, in the atlanto-axial joint of the cervical spine is an important sequela of rheumatoid arthritis (RA). Atlanto-axial pannus may result in spinal cord injury if not recognized in a timely manner. The purpose of this study was to further characterize patients with RA and atlanto-axial pannus in order to more accurately identify these patients in clinical practice.

Methods:

Subjects were identified by free text searching the Partners HealthCare Research Patient Data Registry for the terms ‘atlanto-axial’ and ‘pannus’ in cervical spine magnetic resonance imaging (MRI) reports between January 1, 2001 and December 31, 2015. RA diagnoses were verified by chart review conducted by 2 reviewers. Data were extracted regarding demographics, prior cervical spine surgery, years since RA diagnosis, clinical presentation, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels, presence of rheumatoid factor or anti-cyclic citrullinated peptide (CCP) antibody, and surgery or medication change after MRI demonstrating pannus.

Results:

Seventy-four patients were identified with pannus in the atlanto-axial joint, and 27 of these patients had a confirmed diagnosis of RA, including 5 with juvenile rheumatoid arthritis (JRA). At the time of MRI, the mean age of patients with pannus and RA was 58 years. The median number of years since RA diagnosis was 21 years (range 5-69 years). Most patients were female (85%) and white (78%). Fifteen percent of patients had undergone cervical spine surgery prior to the identification of atlanto-axial pannus. The most common specialty to provide referral for cervical spine MRI was rheumatology (59%). The vast majority of patients reported neck pain (85%), and only 11% reported associated traumatic injury. Only 41% had an abnormal neurologic exam, most commonly an abnormal sensory exam (15%). Eighty-one percent of patients had ESR or CRP checked within 3 months of MRI (mean ESR 39 ± 33 millimeters per hour, median CRP 6.4 milligrams per liter (interquartile range 13.0)). Sixty-seven percent of patients were seropositive, and 67% had been treated with biologic therapy prior to MRI. Only 15% of patients underwent cervical spine surgery after MRI, but all of these patients reported improvement in their symptoms post-operatively. The majority of patients had no change in their RA medications after MRI demonstrating pannus (81%).

Conclusion:

The majority of patients with atlanto-axial pannus had long-standing RA, but pannus was also reported as soon as 5 years after RA diagnosis. Atraumatic neck pain in a patient with RA should prompt consideration of atlanto-axial pannus, and clinicians should not be dissuaded by a normal neurologic exam. Interestingly, the proportion of patients with seronegative RA and pannus formation in our study was similar to the frequency of seronegative disease in the general RA population. Most of the patients in our study were diagnosed in the pre-biologics era. It needs to be shown whether treatment of RA with biologics will result in a lower incidence of atlanto-axial pannus in the future.

Disclosure: J. Williams, None; A. Joyce, None; G. Gaviola, None; Z. Isaac, None; J. Ermann, Novartis Pharmaceutical Corporation, 5,UCB, 5,Takeda, 5,SPARTAN/GRAPPA, 9.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/characteristics-of-patients-with-rheumatoid-arthritis-and-atlanto-axial-pannus

Abstract Number: 1383
IMPACT of Smoking in the Expression of Periodontitis and Anticitrullinated Protein Antibodies in Rheumatoid Arthritis

Jerián González Febles1, Jorge Luis Garnier Rodríguez2, Fernando Sánchez-Alonso3, Sagrario Bustabad4, Federico Díaz-González5, Mariano Sanz Alonso1 and Beatriz Rodriguez Lozano6, 1Periodontology, Universidad Complutense de Madrid, Madrid, Spain, 2Odontology, Dental Clinic Garnier, S/C Tenerife, Spain, 3Unidad de Investigación, Spanish Society of Rheumatology, Madrid, Spain, 4Rheumatology, Servicio de Reumatología. Hospital Universitario de Canarias, La Laguna, Tenerife, Spain, 5Servicio de Reumatología. Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain, 6Rheumatology, Hospital de Canarias, S/C Tenerife, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Environmental, genetic and epigenetic factors can induce citrullination of structural peptides by the enzyme PAD, which induce anti-citrullinated protein antibodies (ACPA) preceding RA. Among the environmental factors are cigarette smoke, infections, such as P. gingivalis and A. actinomycetemcomitans in periodontitis (PD) and Prevotella copri of intestinal microflora, and silica dust. Given the implication of these two exogenous factors, tobacco and PD in citrullination, and tobacco enhancer factor in PD, we studied: 1. The risk of smoking for developing advanced PD in patients with RA. 2. Possible influence of smoking on the expression of severe PD and ACPA in RA patients.

Methods: Observational, cross-sectional study in RA patients older than 18yo (ACR/EULAR 2010), with ≥4 teeth, without tooth cleaning nor antibiotic intake 6 months previously. Socio-demographic and anthropometric variables included smoking status, social indicators such as Graffar scale, stress level, and co-morbidities such as diabetes mellitus, dyslipidemia, ischemic cardiovascular disease. Serum ACPA detection: semiquantification Ab IgG against citrullinated peptides (ELISA) with Immunoscan CCPlus® test kit. Euro Diagnostica: positive >25 U/mL; ACPA title stratification: Low (25–75), moderate (76–300) and high (>300). Periodontal parameters: plaque index (PI), Bleeding on probing (Bop), probing pocket depth, recession, clinical attachment level (CAL). CAL loss was categorized according to European Workshop 2005 (Tonetti)1: T level 0 (absence), TL1 (mild), TL2 (severe). Statistical analysis: t-student, Kruskal Wallis, Chi-cuadrado by Stata program 13.1.

Results: We studied 187 patients, F/M 78.6%/21.4%, mean age 54.4 yo Follow-up time 8.8 yo Rheumatoid Factor positive 74.2%, ACPA positive in 114/168 patients (67.86%). Smoking habit: Current smoker (19.25%), former smoker (24.6%); low socioeconomical status (36.4%) / relative poverty (33.7%).PD was observed in 97.3%; TL1 52.4%, TL2 44.9%. A “risk gradient” was observed for PD related to smoking habit: former smoker OR 1.62 (95% CI 0.81–3.27),p=0.174; smokers, OR 2.27 (95% CI 1.05–4.91), p=0.037. When analyzing the influence of smoking on PD development according to ACPA profile, a gradient effect of developing severe PD was observed from former smokers OR 2.37 (IC95% 0.52–7.64) to current smokers OR 6.99 (IC95% 1.53–32.07) (p=0.029) in ACPA(-) patients. This relationship was not observed in ACPA (+) patients (p=0.383).

Conclusion: 1. There is a “risk gradient” to develop PD in RA in relation to past or current exposure to tobacco, so that, although not significant, former smokers are at greater risk than non-smokers, and current smokers have a significant risk 2.3 times higher. 2. This risk gradient is shown in ACPA (-) patients, but not in ACPA (+) patients, which suggests an independent relationship between PD and ACPA (+) RA.

Disclosure: J. González Febles, None; J. L. Garnier Rodriguez, None; F. Sánchez-Alonso, None; S. Bustabad, Gebro, 2; F. Díaz-González, None; M. Sanz Alonso, None; B. Rodriguez Lozano, None.


Abstract Number: 1384

Physician Global Assessments for Disease Activity in Rheumatoid Arthritis Are All over the Map!
Background/Purpose: Assessments of disease activity in rheumatoid arthritis (RA) determine the course of treatment. Physician global assessments of disease activity (MD globals) are important outcomes in trials as they are part of the CDAI (Clinical Disease Activity Index) and SDAI (Simple Disease Activity Index) composite scores. MD globals may vary between physicians based on their age, sex, practice setting, experience (number of patients seen per year), and years in practice. Our research goal was to determine which factors contribute to the variability of MD globals. We expected assessments to be lower as physician experience increased (i.e. once you have been in practice a long time, you have seen the worst, so this would reset the global assessments for less active patients to a lower value relative to less experienced rheumatologists).

Methods: After obtaining ethics approval, we surveyed rheumatologists who were members of the Canadian Rheumatology Association with RA patient scenarios where each was rated as a MD global for disease activity from 0 – 10. The cases covered a range of disease activity; to determine extreme cases and cases in between. There were some scenarios where a change in status was given (i.e. a rating with one disease state and then the patient returned and another rating was given by each participant when the patient was obviously better or worse). Means, t tests, and correlations were used to analyze the responses.

Results: We received 145 responses from eligible physicians spanning the above categories (approximately 40% response rate). Contrary to our original hypothesis, MD global assessments were not significantly different between physicians in any category (number of RA patients seen per year, years of experience, age, sex, type of practice [community vs. university], and self-reported expertise in RA). Moreover, the range of answers for the same scenario was as high as 7.6 out of a possible 10, indicating vast discrepancies between physicians. We checked to ensure the questions were not answered backwards by individuals using the scenarios where a patient changed disease activity over time. The agreement was highest in the extreme scenarios (very low and very high disease activity, but in the spectrum in between agreement was extremely poor). Some scenarios outlined changes in individual patients, however physicians surveyed were often in disagreement as to how well the patient recovered or worsened. The change in MD globals between one time and the next in the cases had better agreement than the actual scores (i.e. most agreed that a patient had worsened or improved).

Conclusion: This research emphasizes the need to establish stringent evaluation criteria of disease activity as rated by the physician in RA; particularly if remission and low disease activity is used clinically by CDAI or SDAI. Perhaps a catalogue examples of patient scenarios of MD globals that range from 0 to 10 should be developed, standardized and agreed upon; to decrease the wide variability of ranking by rheumatologists.

Disclosure: M. Turk, None; J. E. Pope, AbbVie, Amgen, Bayer, BMS, Celtrion, Eli Lilly and Company, Merck, Novartis, Pfizer, Roche, UCB, 5,Amgen, Bayer, BMS, GSK, Merck, Novartis, Pfizer, Roche, UCB, 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/physician-global-assessments-for-disease-activity-in-rheumatoid-arthritis-are-all-over-the-map

Abstract Number: 1385

Decisional Conflict in Doctor – Patient Discussions about Disease Modifying Anti-Rheumatic Drugs

Rohit Nallani1 and Richard W Martin2, 1Michigan State University, College of Human Medicine, Grand Rapids, MI, 2Medicine, Rheumatology, Michigan State University, College of Human Medicine, Grand Rapids, MI

First publication: September 18, 2017

SESSION INFORMATION
Background/Purpose: There are few published studies describing patient-physician discussions about initiating new rheumatoid arthritis (RA) medications in real world settings. The purpose of this study is to describe the incidence of these discussions, levels of decisional conflict and its correlation with primary adherence.

Methods: We conducted a prospective observational study of consecutive RA patients attending a routine rheumatology clinic visits. Immediately after the visit, we identified all patients whom had a discussion about starting a new medication. We conducted immediate written and 30-day post-visit telephone surveys. This assessed patient preference, actions and decisional conflict about starting the proposed medication.

Results: Of 580 RA patients seen during the observation period, 104 (17.9%) patients confirmed discussing a new medication. 91 (87.5%) completed the follow up survey. Demographics: mean age = 55.4 years, 79.8% female, 7.7% minority, 3.8% with inadequate health literacy RA duration 7.5 years, and mean CDAI 20 (range 0-50). 65.4% of discussions involved adding or changing disease modifying drug therapy (DMARD). Mean post-visit Decisional Conflict Scale score (DCS) was 18.3 (SD: 18.8), with 11.8% demonstrating high DCS. Mean 30 day DCS was 16.1 (SD: 18.4). There was no difference between immediate post-visit and 30 day DCS (p=.47). While 97.1% of patients intended to start the discussed medication, primary adherence was 68.3% at 30 days. Most patients identified “Too Risky” as the reason for primary non-adherence. There was no significance difference in decisional conflict between patients considering DMARD vs. non-DMARD therapy.

Conclusion: Discussions to start or change medications occurred daily in community rheumatology practice. Despite short times of deliberation after visits, patients reported high levels of feeling informed about benefits and harms and had relatively low levels of decisional conflict. This raises questions about the depth and quality of patient deliberation following physician - patient discussions about initiating new DMARD therapy.

References:

Disclosure: R. Nallani, None; R. W. Martin, None.


Abstract Number: 1386

Tenosynovitis in the Forefoot at Disease Presentation Is Specific for RA: Results from a Cross-Sectional MRI Study in Early Arthritis

Yousra J. Dakkak1, Debbie M. Boeters2, Annette H.M. van der Helm-van Mil2 and M. Reijnierse3, 1Rheumatology, Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, 2Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, 3Department of Radiology, Leiden University Medical Center, Leiden, Netherlands

First publication: September 18, 2017
The foot is a preferential location for rheumatoid arthritis (RA)-manifestation, but physical examination of the metatarsophalangeal (MTP) joints is difficult. Magnetic Resonance Imaging (MRI) is sensitive in depicting inflammation at an early stage; it detects synovitis, bone marrow edema (BME) and tenosynovitis. MRI detected inflammation in the MTP joints has not been studied thoroughly in an early arthritis setting, but may increase our understanding of forefoot inflammation. This cross-sectional MRI study thoroughly examined the forefoot to identify inflammatory findings that are specific for RA compared to other arthritides.

**Methods:**

218 patients presenting with early arthritis (93 RA, 125 other arthritides) underwent contrast-enhanced 1.5T MRI of unilateral MTP 1-5-joints. BME, synovitis and tenosynovitis were scored by two readers according to OMERACT rheumatoid arthritis MRI scoring system (RAMRIS), and Haavardsholm et al. Comparisons between RA and other arthritides were made at joint level.

**Results:**

1090 MTP-joints were studied. RA-patients more often had MRI-detected inflammation in any of the MTP-joints than other arthritides (74 vs 61%, p=0.038). Tenosynovitis was associated with RA; the association was strongest for MTP 5 (OR 12.8, 95% CI 2.9-57.1), followed by MTP 1 (OR 3.1, 95% CI 1.3-7.3). Inflammation in RA was present at both the flexor and extensor tendons. The specificity of tenosynovitis was high, ranging between 89-98% at the different MTPs. The sensitivity for RA ranged 16-19%.

In addition, BME in MTP 3-5 was associated with RA, as well as synovitis in MTP 3-5. Of these joints, MTP 5 showed the strongest associations (BME: OR 5.2, 95% CI 2.1-12.9, synovitis: OR 6.0, 95% CI 2.8-13.1).

**Conclusion:**

MRI detected inflammation including BME, synovitis and tenosynovitis was increased at the level of MTP 5 joints of RA patients, this is in line with MTP 5 being a preferential location for erosion development. Previous studies have shown that tenosynovitis in wrist and MCP joints is associated with RA; the present study is the first demonstrating in an early arthritis setting that tenosynovitis in MTP joints is also specific for RA.

**Disclosure:** Y. J. Dakkak, None; D. M. Boeters, None; A. H. M. van der Helm-van Mil, None; M. Reijnierse, None.

**In-Depth Temperature of Small and Large Joints Assessed By Microwave Radiometry As an Additional Biomarker in Rheumatoid Arthritis**

**Katerina Laskari**¹, George Pentazos¹, George Konstantonis¹, Ioannis Raftakis², Elias Siros³ and Petros P Sfikakis¹,

¹Rheumatology Unit, 1st Dept. of Propaedeutic Internal Medicine, Joined Academic Rheumatology Program, Athens University Medical School, Athens, Greece, ²Rheumatology Department, Asklepion General Hospital, Athens, Greece, ³Institute of Materials Research and Innovation, University of Bolton, Bolton, United Kingdom

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Microwave Radiometry (MR) is an easy-to-perform, rapid, non-invasive, objective method, able to measure in-depth tissue temperature. In a proof-of-concept study using joint ultrasound as reference method, we showed that an increased in-depth knee joint temperature detected by MR in the absence of relevant clinical signs reflects the presence of subclinical synovial inflammation in rheumatoid arthritis (RA) (1).
We aimed to test the hypothesis that a ‘thermo-score’ constructed as the sum of MR-derived temperatures of small and large joints reflects global disease activity levels in RA.

Methods:
Consecutive RA patients (N=61) underwent clinical, laboratory and MR (RTM 01 RES microwave computer based system, Bolton, UK) assessments, as well as joint ultrasound. Unselected patients with active disease (N=19) were re-examined 2 months after treatment initiation. Age- and sex-matched healthy individuals (N=23) and patients with osteoarthritis (N=23) served as controls. We created a ‘thermo-score’ by summing the relative temperatures (Dt) of 7 small joints (wrist, 2nd-3rd metacarpophalangeal, 2nd-3rd proximal interphalangeal, 2nd and 5th metatarsophalangeal) of the clinically dominant hand and foot, based on the German US7 ultrasound score (2), as well as of 3 large joints (elbow, knee, lower leg) of the clinically dominant arm and leg. The relative temperature (Dt) was calculated as the difference between the reference and a control point for each joint, thus, resulting in lower Dt values in inflamed versus healthy joints. Among healthy individuals examined 2 months apart ‘thermo-score’ values were repeatable (ICC=0.714).

Results:
The baseline ‘thermo-score’ could discriminate RA patients in high [mean (SD)=7.36 (1.68)], moderate [mean (SD)=9.71 (1.70)], low disease activity [mean (SD)=10.74 (1.37)] and remission [mean (SD)=11.63 (1.71)] (p<0.001 by Kruskal-Wallis test). Healthy subjects [mean (SD)=11.84 (2.42)] and patients with osteoarthritis [mean (SD)=10.99 (3.05)] had comparable values with RA patients in remission and low activity, respectively. Among RA patients, the ‘thermo-score’ correlated inversely to the DAS28 disease activity score (p<0.001), tender joint count (p<0.001), swollen joint count (p=0.028), patient’s visual analogue scale (p<0.001), CRP (p=0.014), ESR (p=0.013), as well as the standard Ultrasound Scores of 7 joints (2) (all p<0.05). Notably, individual ‘thermo-score’ changes from baseline to follow-up mirrored the corresponding DAS28 changes in 15/19 patients.

Conclusion:
In-depth temperatures of small and large joints detected by MR allow the construction of a ‘thermo-score’ that reflects the global disease activity levels in RA and may serve as an additional biomarker. Optimization of MR equipment and technique may result in an objective measurement of RA disease activity in clinical practice.

References

Disclosure: K. Laskari, None; G. Pentazos, None; G. Konstantonis, None; I. Raftakis, None; E. Sioreis, None; P. P. Sfikakis, None.


Abstract Number: 1388

Fatigue Is Strongly Associated with the Patient Global Assessment and May Affect Disease Severity and Clinical Remission in Patients with Rheumatoid Arthritis: A Cross-Sectional Study from IORRA, a Large Observational Cohort of Japanese Rheumatoid Arthritis Patients

Naoki Sugimoto1, Eiichi Tanaka1, Eisuke Inoue1,2, Kumiko Saka1, Eri Sugano1, Naohiro Sugitani1, Moeko Ochiai1, Yoko Shimizu1, Rei Yamaguchi1, Katsunori Ikari1, Ayako Nakajima1, Atsuo Taniguchi1 and Hisashi Yamanaka1, 1Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan, 2Division of Medical Informatics, St. Marianna University School of Medicine, Kawasaki, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
**Background/Purpose**: Fatigue is a common complaint in patients with rheumatoid arthritis (RA)\(^1\). However, its impact on disease activity and clinical remission in patients with RA has not been explored thoroughly in daily clinical practice\(^2\). The aim of this study was to investigate how fatigue is related to disease activity and clinical remission in patients with RA.

**Methods**: Among Japanese patients with RA in the Institute of Rheumatology, Rheumatoid Arthritis (IORRA) cohort study in April 2015, fatigue was measured based on the checklist of individual strength (CIS) 8R (normal, CIS 8R≤26; heightened fatigue, 27≤CIS 8R≤34; severe fatigue, CIS 8R≥35). We performed a cross-sectional investigation of the association between fatigue severity and the 28-joint disease activity score (DAS28) and its components (swollen joint counts, tender joint counts, erythrocyte sedimentation rate and patient global assessment [PtGA]) with an ordered logistic regression analysis. We also analyzed the contribution of patient demographic and clinical factors to fatigue severity among the variables with significance in an ordered logistic regression analysis by analysis of variance (ANOVA).

**Results**: Among 5,679 RA patients (mean age, 61.4 years; female, 85.8%; mean DAS28 score, 2.62; mean CIS 8R, 28.3), fatigue severity was normal in 2,152 patients (37.9%, [mean age, 61.0 years; female, 82.0%]), heightened in 1,489 patients (26.2%, [mean age, 61.0 years; female, 86.7%]) and severe in 1,383 patients (24.4%, [mean age, 57.5 years; female, 90.4%]). The proportion of corticosteroid use (normal fatigue, 22.0%; heightened fatigue, 30.3%; and severe fatigue, 40.3%) and non-steroidal anti-inflammatory drug [NSAID] use (normal fatigue, 38.8%; heightened fatigue, 52.0%; and severe fatigue, 62.7%) was significantly higher with fatigue severity (\(P = 0.0010\) and 0.0327, respectively). The DAS28 score was significantly associated with fatigue severity (mean DAS28 score: normal fatigue, 2.30; heightened fatigue, 2.63; and severe fatigue, 2.98; \(P = 0.0443\)). The DAS28 remission rate significantly decreased with fatigue severity (normal, 65.5%; heightened, 51.5%; and severe, 40.0%; \(P < 0.0001\)). Of the four components of the DAS28 score, only PtGA had a significant association with fatigue severity (mean PtGA [mm]: normal fatigue, 11.7; heightened fatigue, 24.7; and severe fatigue, 40.2; \(P < 0.0001\)). Among the six variables with significance in an ordered logistic regression analysis (gender, PtGA, pain, the Japanese version of the Health Assessment Questionnaire [J-HAQ] score, corticosteroid use and NSAID use), PtGA had the strongest contribution to fatigue severity (81.0%), followed by the J-HAQ score (9.4%), gender (3.2%) and NSAID use (3.1%).

**Conclusion**: Fatigue was strongly associated with PtGA and affected the evaluation of disease activity and clinical remission in patients with RA, suggesting that evaluating fatigue may be important for controlling disease activity in patients with RA in daily practice.


**Disclosure**: N. Sugimoto, Takeda Pharmaceutical and Bristol Myers Squibb, 8; E. Tanaka, Abbvie, Eisai Pharmaceutical, Chugai Pharmaceutical, Bristol Myers Squibb, Astellas Pharmaceutical, Pfizer, Takeda Pharmaceutical, and Ayumi Pharmaceutical, 8; E. Inoue, None; K. Saka, None; E. Sugano, None; N. Sugitani, None; M. Ochiai, None; Y. Shimizu, None; R. Yamaguchi, None; K. Ikari, Astellas, UCB, Bristol-Meyers, Pfizer, Eisai, Tanabe-Mitsubishi, Chugai, AbbVie, Janssen Pharmaceutical, Otsuka, Kaken, Asahi-Kasei, Hisamitsu and Takeda, 8; A. Nakajima, Bristol-Meyers, Mitsubishi Tanabe Pharma, Nippon Kayaku Co. Ltd., Novartis Pharma, Pfizer, Siemens Healthcare Diagnostics K.K. and Takeda Pharmaceutical Company, 8; A. Taniguchi, AbbVie, Eisai, Takeda, Tanabe-Mitsubishi, Teijin Pharma, Pfizer, 8; H. Yamanaka, MSD, Astellas, AbbVie, BMS, Kaken, UCB, Ono, Ayumi, Eisai, Daiichi-Sankyo, Takeda, Tanabe-Mitsubishi, Chugai, Nipponshinyaku and Pfizer Inc 2,Pfizer Inc, YL biologics, Takeda, Nipponkayaku, Chugai, Tanabe-Mitsubishi, Daiichi-Sankyo and Astellas, 8.


**Abstract Number**: 1389

**Serum Progranulin Antibodies (PGRN-abs) in Rheumatoid Arthritis Patients Being Negative for RF-IgM and ACCP-IgG**

**Gunter Assmann**\(^1\), Silke Zinke\(^2\), Moritz Gerling\(^3\), Natalie Fadle\(^3\), Klaus Dieter Preuss\(^3\), Michael Pfreundschuh\(^3\) and Lorenz Thurner\(^3\), \(^1\)Medicine I, University Medical School of Saarland, 66424, Germany, \(^2\)Rheumapraxis, Rheumatology Center Berlin - Lichtenberg, Berlin, Germany, \(^3\)Medicine I, Jose Carreras Center, University of Saarland, Homburg, Germany
Background/Purpose: Until recently, most research on progranulin (PGRN) had been focused on its role in neurogenerative diseases as frontotemporal dementia. After the detection of elevated PGRN serum levels in patients with autoimmune arthritis we discovered antibodies against PGRN in a protein array-based screening of serum from various different rheumatic diseases. Furthermore, serum PGRN antibodies (PGRN-abs) have been proved to have neutralizing effect on PGRN serum levels; in addition, serum PGRN presented preferentially in a phosphorylated stage in PGRN-abs positive patients. Here we conducted the study to evaluate the prevalence of PGRN-abs in sera of rheumatoid arthritis patients being seronegative according to RF and ACCP.

Methods: PGRN-abs were determined in sera of 257 RA patients with positivity for RF-IgM and/or ACCP-IgG and in sera of 224 seronegative RA patients, which were prospectively included in the study from 2013-2015. Healthy serum donors n=97 served as control cohort. All RA patients have fulfilled the revised ACR/EULAR classification criteria for RA from 2011. The ELISA detecting PGRN-abs as well as the phosphorylated stage of PGRN were applied as previously described. Subgroup analyses has stratified the RA cohort into diseases duration (less or more than 2 years) as well as gender, age of diagnoses, erosive course of diseases and the occurrence of tumor necrosis factor inhibitor failure (TNFi-failure). The statistics were performed with Mann-Whitney-U test evaluating the differences between seronegative, seropositive RA, and healthy controls; using the chi2 test differences between different RA subgroups were investigated. p-value of < 0.05 were considered significant.

Results: PGRN-abs were detected in 24.5% of seropositive RA and in 22.3% of RF/ACCP negative RA (OR 1.43, CI 0.93-2.21, p=0.106), Figure 1. In healthy controls (n=97) one serum was positive for PRGN-abs. Phosphorylated stage of PGRN were tested positive in sera of 33 of 36 PGRN-abs positive RA patients and negative in all 158 RA without PGRN-abs. Patients (n=107 out of 481) could be retrospectively stratified into early RA defined by diseases duration less than 2 years; early RA patients showed in 18.7% PGRN-abs compared to not-early RA patients (n=201; data missing) with 22.7% (OR 0.82; CI 0.52-1.30, p=0.397). Erosive disease as well as TNFi failure patients were significantly more frequently PGRN-abs positive (28.4%, 29.9%, respectively).

Conclusion: Here we present the first study evaluating the PGRN-abs in sera of patients with seropositive and seronegative RA. Testing PGRN-abs in sera of RA patients seems to reduce the fraction of seronegative status in RA patients by more than 20%. In what way PGRN-abs can be used as diagnostic biomarker has to be further demonstrated in larger cohort of RA patients.
Agreement between the DAS28-ESR and the DAS28-CRP and Factors Related to the Discrepancies between Disease Activity Levels According to These 2 Scores in Patients with Early Rheumatoid Arthritis

Cécile Gaujoux-Viala, Mohamed Belkacemi, Alain Cantagrel, Bruno Fautrel and Bernard Combe, 1 Rheumatology, Nîmes University Hospital and EA2415 Montpellier University, Nîmes, France, 2EA2415 Montpellier University, Montpellier, France, 3Rheumatology, Toulouse University Hospital and Toulouse University, Toulouse, France, 4UPMC University Paris 06, Pitié-Salpêtrière Hospital, Paris, France, 5Rheumatology, CHU Lapeyronie and Montpellier University, Montpellier, France

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: DAS28 is often used as a treatment decision tool in patients with rheumatoid arthritis (RA) in the daily clinic. Although different versions of DAS28 have previously been validated, and although disease activity thresholds are the same, it is not clear whether DAS28-ESR and DAS28-CRP can be used interchangeably in individual patients.

Objectives: The aims of our study were to examine the agreement between these two DAS28 versions in individual early RA patients in the daily clinic and to identify factors related to the discrepancies between disease activity levels according to these 2 scores.

Methods: Baseline and 6 months data from 677 patients with early RA (ACR EULAR 2010) were extracted from the French cohort of early arthritis ESPOIR (at least 2 swollen joints for less than 6 months, DMARD naïve) and were used to calculate DAS28-ESR and DAS28-CRP. Disease activity levels according to the DAS thresholds and EULAR responses were assessed.

Intraclass correlation coefficient [ICC] and weighted kappa (k) were calculated. The Bland-Altman method was used to examine the bias between the DAS scores and the 95% limits of agreement (LoA).

Multivariate logistic regression was used to determine the patient and RA features independently associated with discrepancies between disease activity levels according to DAS28-ESR and DAS28-CRP.

Results: The mean value of DAS28-CRP (5.04±1.16 at M0 and 3.38±1.33 at M6) was smaller than that of mean DAS28-ESR (5.33±1.24 at M0 and 3.51±1.42 at M6).

Agreement between the scores was excellent: ICC=0.93 at M0 and M6. Agreement between disease activity levels according to the 2 scores was good: k=0.70 at M0 and 0.75 at M6. Agreement between EULAR responses at M6 according to the 2 scores was good: k=0.78. At M0, the bias of DAS28-CRP was -0.28 (LoA -1.16, 0.59) and -0.14 (LoA -1.17,0.89) at M6.

There were discrepancies between disease activity levels according to the 2 scores in 122 (18.6%) patients at M0 with clear difference in moderate (88 patients for DAS28-CRP vs 29 for DAS28-ESR) and high disease activity (18 patients for DAS28-CRP vs 80 for DAS28-ESR), and in 171 (28.1%) patients at M6 with clear difference in remission (42 patients for DAS28-CRP vs 29 for DAS28-ESR) and high disease activity (9 patients for DAS28-CRP vs 32 for DAS28-ESR).

At M0, presence of erosion (OR 95%CI=1.76 [1.07-2.90]), better mental component of the SF36 (OR 95%CI=2.14 [1.38-3.31]), fewer tender joint counts (TJC) and better physical component of the SF36 (PCS) (with significant interaction between TJC and PCS) were associated with discrepancies between disease activity levels according to the 2 scores. At M6, only being male (OR 95%CI=1.62 [1.09-2.41]) was associated with discrepancies.

Conclusion: DAS28-CRP significantly underestimated disease activity compared to DAS28-ESR. Agreement was high between the 2 scores, good for disease activity levels and EULAR responses. In the individual patient, however, the two scores may differ considerably. The scores should not be used interchangeably in the daily clinic without caution.

Disclosure: C. Gaujoux-Viala, None; M. Belkacemi, None; A. Cantagrel, None; B. Fautrel, None; B. Combe, None.
Ultrasound Response to Tocilizumab in Surgically Replaced Joints and Surgically Operated Joint Areas of Rheumatoid Arthritis Patients

Evan Choate¹, Gurjit S. Kaeley², Jenny Brook³, John Fitzgerald⁴, David Elashoff⁵ and Veena K. Ranganath⁶
¹David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA, ²Rheumatology, University of Florida College of Medicine, Jacksonville, Jacksonville, FL, ³Medicine, David Geffen School of Medicine, UCLA, Los Angeles, CA, ⁴David Geffen School of Medicine, Division of Rheumatology, Department of Internal Medicine, University of California, Los Angeles, Los Angeles, CA, ⁵David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA, ⁶Medicine/Rheumatology, University of California, Los Angeles, Los Angeles, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Rheumatoid Arthritis (RA) disease activity outcomes are used for treatment decisions (ie. DAS28-ESR). Surgically operated joints (SOJ) are assumed not to respond to therapy and are often not included in standard trials. This analysis examines whether a therapeutic benefit is conferred to SOJ over six months, as measured by grey-scale synovial hypertrophy (GSUS) and power Doppler (PDUS) synovitis scores.

Methods: 20 RA patients with SOJ enrolled in an open-label 24-week tocilizumab study. Participants’ joints were identified as SOJ (replaced, fusion, arthroscopy, tendon) or as a non-operated joint (NOJ). Joint assessments occurred at baseline, 1-mos, 3-mos, and 6-mos for: tender joint (0/1), swollen joint (0/1), GSUS (0-3), and PDUS (0-3). GSUS and PDUS images were captured for 32 joints including bilateral MCPs, PIPs, wrist, medial/lateral parapatellar knee recesses, and MTP 2-5. Maximum GSUS and PDUS scores across the views for each joint were calculated. Mean GSUS and PDUS scores from SOJ were compared to NOJ over time by mixed effects linear models analysis. GSUS and PDUS compared baseline to 6months using mixed effects models, while TJ and SJ used McNemar test.

Results: A significant difference between NOJ and SOJ over 6mos was seen for GSUS and PDUS (both p<0.0001) (Figure 1). There was a significant improvement in TJ for NOJ (p=0.02), however no difference seen in SOJ for SJ or TJ (Table 1). Of 37 SOJ joints assessed by ultrasound, 78% of joints had PDUS>1 and 86% of joints had GSUS>1 at baseline, while NOJ had 43% and 64% respectively. There was a significant GSUS response seen for the overall set of SOJ from baseline to 6-months (p=0.03), and a trend for PDUS (p=0.07).

Conclusion: RA activity measures such as DAS28-ESR require strict parameters to provide patient prognosis and treatment efficacy. Traditional trials exclude operated joints from measurement and analysis. This study suggests that SOJ joints exhibit significant synovitis. Response to tocilizumab over six months, by GSUS. Further research is needed to validate these findings, and this study suggests that ultrasound RA clinical studies should assess response in both SOJ and NOJ.
Table 1: Therapeutic response over six months in NOJ and SOJ

<table>
<thead>
<tr>
<th></th>
<th>Non-Operated Joints (NOJ)</th>
<th>Surgically Operated Joints (SOJ)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Month 6</td>
</tr>
<tr>
<td>Tender Joint (Y)</td>
<td>564 (31.8%)</td>
<td>799 (33.5%)</td>
</tr>
<tr>
<td>Swellen joint (Y)</td>
<td>32.6%</td>
<td>17.1%</td>
</tr>
<tr>
<td>FUSIS (0-3)</td>
<td>413 (1.10)</td>
<td>357 (0.98)</td>
</tr>
<tr>
<td>GSUS (0-3)</td>
<td>1.25 (1.11)</td>
<td>1.06 (1.63)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tender Joint (Y)</td>
<td>55 (20.3%)</td>
<td>53 (18.9%)</td>
</tr>
<tr>
<td>Swellen joint (Y)</td>
<td>27.1%</td>
<td>11.3%</td>
</tr>
<tr>
<td>FUSIS (0-3)</td>
<td>37 (2.12)</td>
<td>33 (1.46)</td>
</tr>
<tr>
<td>GSUS (0-3)</td>
<td>2.24 (1.82)</td>
<td>1.70 (1.66)</td>
</tr>
</tbody>
</table>

Disclosure: E. Choate, None; G. S. Kaeley, None; J. Brook, None; J. Fitzgerald, None; D. Elashoff, None; V. K. Ranganath, Genentech and Biogen IDEC Inc., 2, Pfizer Inc, 2, Bristol-Myers Squibb, 2, Bristol-Myers Squibb, 5.


Abstract Number: 1392

Effect Size Comparison of Ultrasound Measures in Rheumatoid Arthritis

Veena K. Ranganath¹, David Elashoff², Jenny Brook³, Ami Ben-Artzi⁴, Geraldine Navarro⁵, Lynnette Avedikian-Tatosyan⁶, George Karpouzas⁷, William Martin⁸, Tanaz A. Kermani⁹, Soo Choi¹⁰ and Gurjit S. Kaeley¹¹, ¹Medicine/Rheumatology, University of California, Los Angeles, Los Angeles, CA, ²David Geffen School of Medicine., University of California, Los Angeles, Los Angeles, CA, ³Medicine, David Geffen School of Medicine, UCLA, Los Angeles, CA, ⁴Medicine, Cedars, Beverly Hills, CA, ⁵Medicine, Division of Rheumatology, David Geffen School of Medicine, UCLA, Los Angeles, CA, ⁶Healthcare Partners, Los Angeles, CA, ⁷Division of Rheumatology, Harbor-UCLA Medical Center, Torrance, CA, ⁸Rheumatology, University of Florida College of Medicine, Jacksonville, Jacksonville, FL

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Currently there are several outcome metrics used for the assessment and quantification of musculoskeletal (MSK) ultrasound inflammatory burden in rheumatoid arthritis (RA). This study compares the effect sizes of MSK ultrasound metrics in RA. Effect size is an important factor that judges the robustness of response in a standardized fashion and impacts power and sample size calculations in clinical trials.
Methods:

This study was an open-label 24 week trial of 54 RA patients starting tocilizumab IV recruited from two rheumatology clinic sites. Inclusion criteria required DAS28-ESR>4.4 and power Doppler (PDUS) >10. At baseline patients started 4mg/kg dosing and were dose escalated to 8mg/kg at 12 weeks if the DAS28-ESR>3.2. Joints examined by ultrasound included bilateral MCPs, PIPs, wrist midline/radioulnar, medial/lateral parapatellar knee recesses, and MTP 2-5. Joint images of PDUS and grey-scale synovial hypertrophy (GSUS) were assessed based on a semiquantitative scale (0-3). Ultrasound measure means were calculated: maximum PDUS by joint, PDUS by view, German US7 PDUS (wrist, MCP/PIP 2/3, MTP2/5), modified Global OMERACT-EULAR Synovitis Score (GLOESS) 22 (all except shoulder, elbow, ankle, hindfoot), modified GLOESS 9 (excludes elbow, shoulder), GLOESS 4 (MCP2-5), PDUS dichotomous (0 vs 1,2,3), PDUS dichotomous (0,1 vs 2,3), GSUS US7, GSUS max joint, and GSUS by view. Cohen’s d effect sizes were computed as the mean change in the measure from baseline to 4, 12, and 24 weeks of the study divided by the standard deviation of the changes.

Results: 54 RA patients enrolled in the trial and 44 patients completed the study. Of all the MSK ultrasound measures calculated, the PDUS dichotomous 0 vs 1,2,3 had the largest effect size of 0.92 at 24 weeks and the GLOESS 4 demonstrated the smallest effect size at 0.55 (Figure 1). The US7 PDUS measure also performed well with the second best effect size of 0.85 at 24 weeks.

Conclusion: Effect sizes are important in clinical trials to judge if the response was robust and meaningful. It has important implications for calculating the power and sample size in randomized clinical trials. For MSK ultrasound outcome measures, the PDUS dichotomous measure of 0 vs 1,2,3 had a large effect size and GLOESS measures had moderate effects sizes. Based on this study, a simple PDUS dichotomous measure of 34 joints will decrease the sample size by approximately 60% compared to utilizing the GLOESS 4.

Disclosure: V. K. Ranganath, Genentech and Biogen IDEC Inc., Pfizer Inc, 2,Bristol-Myers Squibb, 2,Bristol-Myers Squibb, 5; D. Elashoff, None; J. Brook, None; A. Ben-Artzi, None; G. Navarro, None; L. Avedikian-Tatosyan, None; G. Karpouzas, None; W. Martin, None; T. A. Kermani, None; S. Choi, None; G. S. Kaeley, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/effect-size-comparison-of-ultrasound-measures-in-rheumatoid-arthritis

Abstract Number: 1393

Patient Characteristics, Treatment Strategy or Investigator Effect: An Analysis of Factors Driving Variation in Outcomes in Early Rheumatoid Arthritis

Cheryl Barnabe1, Orit Schieir2, Glen Hazlewood1, Susan J. Bartlett3, Carol A Hitchon4, Janet E. Pope5, Gilles Boire6, Edward C. Keystone7, Diane Tin8, B Harauvi9, Vivian P. Bykerk10 and Carter Thorne11, 1Division of Rheumatology, University of Calgary, Calgary, AB, Canada, 2Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada, 3Department of Medicine, Division of ClinEpi, Rheumatology, Respiriology, McGill University, Montreal, QC, Canada, 4University of Manitoba, Winnipeg, MB, Canada, 5Department of Medicine, Division of Rheumatology, University of Western Ontario, St Joseph's Health Care, London, ON, Canada, 6Rheumatology Division, Centre Hospitalier Universitaire de Sherbrooke and Universite de Sherbrooke, Sherbrooke, QC, Canada, 7University of Toronto, Toronto, ON, Canada, 8The Arthritis Program, Southlake Regional Health Centre, Newmarket, ON, Canada, 9Institut de Recherche en Rhumatologie de Montréal (IRRMM), Montreal, QC, Canada, 102-005, Mt Sinai Hospital, Toronto, ON, Canada, 11University of Toronto, Newmarket, ON, Canada

First publication: September 18, 2017
Outcomes in ERA are largely thought to reflect individual prognostic factors and treatment strategy employed. We hypothesize that an additional factor may be the provider, who could influence outcomes through their educational and practice experience, approach to patient interactions, and practice resources. We have undertaken an analysis of remission outcomes across 11 ERA clinics, demonstrating significant variation in rates of remission. In this analysis, we incorporate patient characteristics, treatment strategy and investigator effect in understanding this variation.

Methods: Data were analyzed for ERA patients with >1 year of follow-up, enrolled at sites with >40 patients at baseline and >30 patients with 2 years of follow-up data. Multiple linear regression was applied to predict DAS28 remission at 12 months, with all continuous variables centered at the mean prior to entry in the models. Covariates in the model were patient characteristics (age, sex, symptom duration at initiation of treatment, education, comorbidities, smoking status, seropositive status and baseline DAS28 and HAQ scores); treatment strategy (oral methotrexate monotherapy, subcutaneous methotrexate monotherapy, methotrexate-based combinations, triple therapy, biologic therapy and steroid); and investigative site characteristics (volume of recruitment; academic or community practice; solo vs group; allied health resources available; teaching site; and the proportion of investigators at that site by sex, age cohort, location of training, training years and practice type (rheumatology alone or also providing internal medicine services).

Results:
1,633 participants with mean age 54 years, 73% female, and mean DAS28 4.9 (SD 1.4) were included. At 12 months, 49% of patients across all sites had achieved DAS28 remission (site range 22%-80%) and the frequency of sustained DAS28 remission over all follow-ups was 52% (site range 29-71%). There were significant differences between centers in the means of patient characteristics and frequency of use of treatment strategies (oral methotrexate monotherapy 8%, subcutaneous methotrexate monotherapy 6%, methotrexate-based combination therapy 36%, triple therapy 11%, and biologics 14%). 27% of sites were community-based practices, 45% systematically incorporated allied health professionals in the care plan, 82% were a teaching site, 64% were group recruitment sites with a mean of 5 investigators per site, and 62% of the investigators were female. In the model, investigator age, location of training, training year and practice type were excluded due to collinearity with the other characteristics. Patient characteristics of age, sex, comorbidities, smoking status, seropositive status, baseline DAS28 scores were significant factors in remission (all p<0.04). The specific treatment strategy had no significant effect, except for use of oral steroids. The presence of learners had a negative impact on remission (coefficient -0.50, 95%CI -0.76 to -0.24).

Conclusion: Patient prognostic factors contribute greatly to the variation in remission outcomes, with treatment strategy and investigator/investigative site factors having lesser contributory roles.

Disclosure: C. Barnabe, None; O. Schieir, None; G. Hazlewood, None; S. J. Bartlett, PROMIS, 6,Pfizer Inc, UCB, Lilly, 5; C. A. Hitchon, None; J. E. Pope, Abbvie, Amgen, Bayer, BMS, Celtrion, Eli Lilly and Company, Merck, Novartis, Pfizer, Roche, UCB, 5,Amgen, Bayer, BMS, GSK, Merck, Novartis, Pfizer, Roche, UCB, 2; G. Boire, None; E. C. Keystone, Pfizer Inc, 2,Pfizer Inc, 5,Pfizer Inc, 8; D. Tin, None; B. Harraoui, BMS, Janssen, Roche Speakers bureau: Pfizer, UCB, 2,AbbVie, Amgen, BMS, Celgene, Janssen, Merck, Pfizer, Roche, Sandoz, UCB, 5; V. P. Bykerk, None; C. Thorne, AbbVie, Amgen, Celgene, Lilly, Novartis, Pfizer, Sanofi, and UCB; has served as a consultant for AbbVie, Amgen, Celgene, Centocor, Genzyme, Hospira, Janssen, Lilly, Medexus/Medac, Merck, Novartis, Pfizer, Sanofi, and UCB, 2,Medexus/Medac, 8.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/patient-characteristics-treatment-strategy-or-investigator-effect-an-analysis-of-factors-driving-variation-in-outcomes-in-early-rheumatoid-arthritis

Abstract Number: 1394

Comparison of Improvements in Disease Activity between Classes of Biologic Disease Modifying Anti-Rheumatic Drugs in Routine Clinical Practice: Findings from a Large Contemporaneous Real World Cohort
Background/Purpose: RA is estimated to affect approximately 1.3 million adults in the US and accounts for a significant proportion of US health care spend with direct medical costs of over $70 billion a year. The primary driver of cost in RA are the specialty drug classes. Given the cost differential between available RA treatments, it is critical to ensure that patients are receiving optimal therapy at the optimal time. We compared improvements in disease activity between biologic DMARD classes, in a large cohort of patients with RA, under conditions of routine clinical practice.

Methods: The OM1 platform collects, links, and leverages, structured and unstructured data from electronic medical records (EMR) and other sources in an ongoing and continuously updating manner. The OM1 RA Cohort includes data on >75,000 patients treated by rheumatologists. Disease activity measures (measured and identified using advanced natural language processing) were available in 59,326 patients and established American College of Rheumatology cutpoints were used to define disease severity. There were an average of 9.1 (imputed + observed) disease activity measures per patient. The analysis included patients who were treated with the same biologic disease modifying anti-rheumatic drug (bDMARD) for a 6-month period and had disease activity measures at baseline and at 6 months.

Results: The mean±SD age was 60±14 years, 76% of the cohort was female, and 71% Caucasian.

At baseline, 23% of patients were in remission, and 36%, 24% and 17% had low, moderate and high disease activity, respectively. Total and swollen joint counts were available in ~40% of the cohort and erythrocyte sedimentation rate was available in 70%. During the study period, 44% of the cohort received nonbiologic DMARD and 45% bDMARD; tumor necrosis factor inhibitor (TNF-inhibitor) accounted for 77% of bDMARD. The figure presents proportion of patients treated with bDMARD (categorized as TNF-inhibitor, n=9,574, 18% [95% CI: 17%-18%], and other bDMARD, n=5,877, 14% [13%-15%] for naive and non-naive patients combined), with moderate to severe disease at baseline, who achieved low or remission status within the subsequent 6 months. Analysis was stratified by whether they had documented prior treatment with biologics.

Conclusion:

Using a data driven platform that enables large scale assessment (patient characteristics, treatment patterns, clinical outcomes) of patients, we found that naive patients treated with TNF-inhibitors showed the most improvement in disease activity overall. Among non-naive patients the TNF-inhibitor group had the highest proportion of patients achieving remission or low disease activity over a 6-month treatment period.
Abstract Number: 1395

Patient Reported Outcomes in Rheumatoid Arthritis: Best Domain, Best Interface

Iris Navarro-Millán1, Anna Cornelius-Schecter1, Aprajita Jagpal2, Bernadette Johnson3, Liana Fraenkel4, Monika M. Safford1 and Jeffrey R. Curtis2, 1Weill Cornell Medical College, New York, NY, 2Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 3Clinical Immunology & Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 4Rheumatology, Rheumatology, Yale University School of Medicine, New Haven, CT, New Haven, CT

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Quantifiable measures of patients’ symptoms such as patient reported outcomes (PROs) provides the physician with quantifiable information of subjective symptoms experienced by patients with rheumatoid arthritis (RA). Electronic tools that include instruments that physicians value to inform their treatment recommendations are limited since collection of this type of data can be time consuming and requires personnel to administer them. To determine which PRO domain, are most commonly used by rheumatologists when treating RA patients and best ways to administered them at the point of care.

Methods: We developed a survey following qualitative data of 4 nominal groups and 25 rheumatologists. Items were aggregated into topic groups and categorized by themes. We used the items/responses generated in the nominal groups to develop the questions and responses of the survey. The survey included multiple choice questions and others included a scale where participants graded specific items into: 1) very important; 2) Important; 3) Somewhat important; 4) Not important; 5) do not assess. Rheumatologists who are a part of the American College of Rheumatology membership were invited to participate. The survey was deployed via Qualtrics. We used proportions to describe the results of this survey.

Results: We invited 600 rheumatologists and 56 responded to the survey (ongoing survey). The majority of the respondents were between 35 and 54 years of age; 64% male. The aspects that physicians graded as very important are shown in figure 1. The majority of them valued medication compliance, aspects related to physical function, and quality of life were. While the Patient-Reported Outcomes Measurement Information System (PROMIS) was known by 16 respondents, only 1 rheumatologist was using it regularly in practice. There were 16 and 25 respondents who collect MDHAQ and RAPID3 on most of all office visits, respectively. The majority of the respondents were interested in having PRO data collected electronically and synchronized with the electronic health record (64%).

Conclusion: Electronic collection of PROs that incorporates medication compliance, patient function and that it has an interface with the electronic health record will make the collection of PROs more feasible for physicians. While PROMIS instruments was known by a small number of respondents only 1 was using it. Educating physicians about these questionnaires can increase its use in clinical
Can 3 0-10 Physician Visual Analog Scales (VAS) to Assess Levels of Inflammation, Damage and Distress Offer Comprehensive Quantitative Data That May be As Informative As Detailed, Formal Swollen and Tender Joint Counts?

MJ Bergman¹ and Theodore Pincus², ¹Drexel University College of Medicine, Philadelphia, PA, ²Rheumatology, Rush University Medical Center, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Management of patients with rheumatoid arthritis (RA) remains primarily according to a patient history and physical examination, unlike in many other chronic diseases, in which a “gold standard” biomarker, such as a laboratory test provides the primary basis for clinical management. A need for quantitative measures has led to a count of tender and swollen joints. A formal joint count is standard in clinical trials and clinical research, but not at most patient visits. Perhaps this phenomenon suggests that a joint examination without a formal quantitative joint count may be adequate, e.g., it matters considerably whether a patient has, say, 2 vs 12 swollen joints, but not necessarily whether the patient has 1 vs 2 or 11 vs 12 swollen joints. Furthermore, joint counts have relatively poor test-retest reliability, and can be affected by phenomena other than inflammatory activity, such as joint damage and/or distress. An alternative approach to quantify a clinical encounter involves 3 physician visual analog scales (VAS) for inflammation, damage and distress to supplement a physician global assessment, as analyzed here.

Methods: At one private practice rheumatology site, all patients complete a patient self-report MDHAQ/RAPID3 at each visit. The rheumatologist performs a formal 28-joint count of tender (TJC) and swollen (SJC) joints, and then completes four 0-10 VAS, for overall global assessment, inflammation, damage, and distress. A random visit of 259 RA patients was studied for mean values, and correlations of the 4 physician VASs with SJC and TJC. Because correlations may be artefactually elevated if many patients have a value for a zero for the two variables compared, correlations also were calculated of patients whose SJC was >1.

Results: Mean values for the 0-10 VASs were 2.09 for physician global assessment, 2.50 for inflammation, 1.47 for damage and 0.74 for distress, as well as 4.17 for patient global assessment (Table). Mean SJC 28 was 5.15, and TJC 28 2.54. SJC was correlated at significantly higher levels with the inflammation VAS, r=0.766 than the damage VAS, r=0.235, or distress VAS, r=0.030. In patients only with SJC >1, the correlation of SJC with the inflammation VAS was somewhat lower, r=0.688, but remained significantly higher
than other correlations with physician VAS. The correlation of TJC was similar for overall global, inflammation and distress. The 4 VAS required about 15 seconds to complete vs about 90 seconds for a 28 joint count.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Mean value±SD</th>
<th>Correlation with SJC</th>
<th>Correlation with TJC</th>
<th>Correlation with SJC&gt;1</th>
<th>Correlation with TJC&gt;1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician global assessment VAS</td>
<td>2.09±2.18</td>
<td>0.415</td>
<td>0.372</td>
<td>0.333</td>
<td>0.338</td>
</tr>
<tr>
<td>Inflammation VAS</td>
<td>2.50±2.04</td>
<td>0.766</td>
<td>0.389</td>
<td>0.688</td>
<td>0.344</td>
</tr>
<tr>
<td>Damage VAS</td>
<td>1.47±1.81</td>
<td>0.235</td>
<td>0.062</td>
<td>0.174</td>
<td>0.016</td>
</tr>
<tr>
<td>Distress VAS</td>
<td>0.74±1.55</td>
<td>0.030</td>
<td>0.345</td>
<td>0.017</td>
<td>0.272</td>
</tr>
<tr>
<td>SJC28</td>
<td>5.15±5.32</td>
<td>-----</td>
<td>0.386</td>
<td>-----</td>
<td>0.411</td>
</tr>
<tr>
<td>TJC28</td>
<td>2.54±4.95</td>
<td>0.368</td>
<td>-----</td>
<td>0.411</td>
<td>-----</td>
</tr>
<tr>
<td>Patient global assessment VAS</td>
<td>4.17±2.83</td>
<td>0.312</td>
<td>0.369</td>
<td>0.241</td>
<td>0.350</td>
</tr>
</tbody>
</table>

VAS=visual analog scale, SJC= swollen joint count, TJC= tender joint count

**Conclusion:** 3 physician VAS for inflammation, damage and distress may provide a useful tool to document a physician assessment of patient status and the rationale for clinical decisions, e.g., not escalating anti-inflammatory therapy in a patient with high RA index score who does not have high scores for inflammation but rather high scores for damage and/or distress.

**Disclosure:** M. Bergman, None; T. Pincus, Theodore Pincus, 7.


**American College of Rheumatology Response Rates Determined Using 28 Versus 68/66 Joint Count in Patients with Rheumatoid Arthritis Receiving Tofacitinib in Phase 3 Studies**

**Josef S. Smolen**¹, William Shergy², Grace C. Wright³, Ryan DeMasi⁴, Kenneth Kwok⁵, Christopher F Mojcik⁵, Noriko Ikuni⁵, Svitlana Tatulych⁶ and Gustavo Citera⁷, ¹Medical University of Vienna and Hietzing Hospital, Vienna, Austria, ²Rheumatology Associates of North Alabama, Huntsville, AL, ³NYU Langone Medical Center, New York, NY, ⁴Pfizer Inc, Collegeville, PA, ⁵Pfizer Inc, New York, NY, ⁶Pfizer Inc, Groton, CT, ⁷Instituto de Rehabilitación Psicofísica, Buenos Aires, Argentina

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Rheumatoid Arthritis – Clinical Aspects Poster II: Pathophysiology, Autoantibodies, and Disease Activity Measures

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM
**Background/Purpose:** Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). In a clinical trial setting, standard criteria for measuring the effectiveness of treatments in patients with RA include American College of Rheumatology (ACR) response rates (defined as the proportion of patients with an improvement of 20/50/70%, respectively, in tender and swollen joint counts and 20/50/70% improvement in 3 of the 5 core components [patient and physician global assessments, pain, disability, and an acute phase reactant] between time points). Tender and swollen joint counts are typically assessed by counting 68 and 66 joints, respectively. However, the use of a 28 joint count is considered a valid and reliable way to determine ACR response rates, and a 28 joint count has been used to determine ACR response rates in the recently completed ORAL Strategy (NCT02187055) Phase 3b/4 study of tofacitinib. The current post-hoc analysis was conducted to determine whether ACR response rates in six Phase 3 studies of tofacitinib varied when a 28 joint count vs a 68/66 joint count was used.

**Methods:** Data from patients with active RA who received tofacitinib 5 or 10 mg twice daily (BID) in six randomized, double-blind Phase 3 studies (ORAL Step [NCT00960440], ORAL Solo [NCT00814307]; ORAL Scan [NCT00847613], ORAL Sync [NCT00856544], ORAL Standard [NCT00853385], and ORAL Start [NCT01039688]) were included in this analysis. ACR20/50/70 response rates were determined using 28 joint counts and compared with ACR20/50/70 response rates obtained in the respective study using the full joint count (68/66 joints). ACR response rates were assessed at the time of the primary endpoints of the studies (Month 3 in ORAL Step and ORAL Solo; Month 6 in all other studies). All analyses were based on the full analysis set; missing data were imputed using non-responder imputation.

**Results:** Overall, the ACR20/50/70 response rates of 3141 tofacitinib-treated patients were determined; 1558 (49.6%) and 1583 (50.4%) patients were randomized to receive tofacitinib 5 and 10 mg BID, respectively. At the primary endpoint, ACR20/50/70 response rates measured using the 28 joint count were generally similar to those determined using the full joint count within each study (Table). ACR20/50/70 response rates of placebo-treated patients were also generally similar when measured using the 28 and 68/66 joint counts (data not shown).

**Conclusion:** The results of this post-hoc analysis suggest that the use of a 28 joint count in tofacitinib-treated patients with RA provides similar ACR response rates as the use of a full joint count (68/66 joint count).

**References:**

Table. ACR20/50/70 response rates from six Phase 3 studies determined using 28 and 68/66 joint counts (FAS, NRI)

<table>
<thead>
<tr>
<th>Joint count</th>
<th>ACR20</th>
<th>ACR50</th>
<th>ACR70</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ORAL Step (Month 3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>28 JC, %</td>
<td>40.9</td>
<td>46.6</td>
<td>11.4</td>
</tr>
<tr>
<td>n/N</td>
<td>54/132</td>
<td>62/133</td>
<td>15/132</td>
</tr>
<tr>
<td>95% CI</td>
<td>35.7-46.1</td>
<td>40.8-52.4</td>
<td>11.0-15.4</td>
</tr>
<tr>
<td>68/66 JC, %</td>
<td>41.7</td>
<td>48.1</td>
<td>13.6</td>
</tr>
<tr>
<td>n/N</td>
<td>55/132</td>
<td>64/132</td>
<td>18/132</td>
</tr>
<tr>
<td>95% CI</td>
<td>36.5-46.9</td>
<td>42.8-53.2</td>
<td>13.1-15.1</td>
</tr>
<tr>
<td>ORAL Solo (Month 3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>28 JC, %</td>
<td>68.2</td>
<td>62.8</td>
<td>13.7</td>
</tr>
<tr>
<td>n/N</td>
<td>145/241</td>
<td>152/242</td>
<td>33/241</td>
</tr>
<tr>
<td>95% CI</td>
<td>63.4-73.0</td>
<td>57.9-67.3</td>
<td>9.4-18.0</td>
</tr>
<tr>
<td>68/66 JC, %</td>
<td>59.8</td>
<td>65.7</td>
<td>15.4</td>
</tr>
<tr>
<td>n/N</td>
<td>144/241</td>
<td>159/242</td>
<td>37/241</td>
</tr>
<tr>
<td>95% CI</td>
<td>54.0-65.6</td>
<td>60.1-71.3</td>
<td>10.8-20.3</td>
</tr>
<tr>
<td>ORAL Scan (Month 6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>28 JC, %</td>
<td>51.1</td>
<td>60.5</td>
<td>13.6</td>
</tr>
<tr>
<td>n/N</td>
<td>158/309</td>
<td>187/309</td>
<td>42/309</td>
</tr>
<tr>
<td>95% CI</td>
<td>45.6-56.7</td>
<td>55.1-66.0</td>
<td>9.8-17.4</td>
</tr>
<tr>
<td>68/66 JC, %</td>
<td>51.5</td>
<td>61.8</td>
<td>14.6</td>
</tr>
<tr>
<td>n/N</td>
<td>159/309</td>
<td>191/309</td>
<td>45/309</td>
</tr>
<tr>
<td>95% CI</td>
<td>45.9-57.0</td>
<td>56.4-67.2</td>
<td>10.6-18.5</td>
</tr>
<tr>
<td>ORAL Sync (Month 6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>28 JC, %</td>
<td>49.8</td>
<td>55.3</td>
<td>12.2</td>
</tr>
<tr>
<td>n/N</td>
<td>155/311</td>
<td>171/309</td>
<td>38/311</td>
</tr>
<tr>
<td>95% CI</td>
<td>44.3-55.4</td>
<td>49.8-60.9</td>
<td>8.6-15.9</td>
</tr>
<tr>
<td>68/66 JC, %</td>
<td>52.7</td>
<td>58.3</td>
<td>13.2</td>
</tr>
<tr>
<td>n/N</td>
<td>164/311</td>
<td>180/309</td>
<td>41/311</td>
</tr>
<tr>
<td>95% CI</td>
<td>47.2-58.3</td>
<td>52.8-63.8</td>
<td>9.4-16.9</td>
</tr>
<tr>
<td>ORAL Standard (Month 6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>28 JC, %</td>
<td>59.0</td>
<td>51.5</td>
<td>18.9</td>
</tr>
<tr>
<td>n/N</td>
<td>98/196</td>
<td>101/196</td>
<td>37/196</td>
</tr>
<tr>
<td>95% CI</td>
<td>43.0-57.0</td>
<td>44.5-58.5</td>
<td>13.4-24.4</td>
</tr>
<tr>
<td>68/66 JC, %</td>
<td>51.5</td>
<td>52.6</td>
<td>19.9</td>
</tr>
<tr>
<td>n/N</td>
<td>101/196</td>
<td>103/196</td>
<td>39/196</td>
</tr>
<tr>
<td>95% CI</td>
<td>44.5-58.5</td>
<td>45.6-59.5</td>
<td>14.3-25.5</td>
</tr>
<tr>
<td>ORAL Start (Month 6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>28 JC, %</td>
<td>69.1</td>
<td>76.9</td>
<td>25.5</td>
</tr>
<tr>
<td>n/N</td>
<td>255/369</td>
<td>303/394</td>
<td>94/369</td>
</tr>
<tr>
<td>95% CI</td>
<td>64.4-73.8</td>
<td>72.7-81.1</td>
<td>54.0-57.8</td>
</tr>
<tr>
<td>68/66 JC, %</td>
<td>71.3</td>
<td>76.1</td>
<td>31.0</td>
</tr>
<tr>
<td>n/N</td>
<td>263/369</td>
<td>300/394</td>
<td>121/394</td>
</tr>
<tr>
<td>95% CI</td>
<td>66.6-75.9</td>
<td>71.9-80.4</td>
<td>21.0-29.9</td>
</tr>
</tbody>
</table>

ACR, American College of Rheumatology; BID, twice daily; CI, confidence interval; FAS, full analysis set; JC, joint count; NRI, non-responder imputation

Disclosure: J. S. Smolen, Abbvie, Eli Lilly, Janssen, MSD, Pfizer Inc, Roche, 2,Abbvie, Amgen, AstraZeneca, Astro, Celgene, Celtrion, Eli Lilly, GSK, ILTOO, Janssen, MedImmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, UCB, 5,AbbVie, Amgen, AstraZeneca, Astro, Celgene, Celtrion, Eli Lilly, GSK, ILTOO, Janssen, MedImmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, UCB, 8; W. Shergy, None; G. C. Wright, AbbVie, Amgen, BMS, Eli Lilly, Janssen, MEDAC, Pfizer Inc, Regeneron, UCB, 5,AbbVie, Amgen, Bristol-Myers Squibb, Eli Lilly, Genentech, UCB, 8; R. DeMasi, Pfizer Inc, 1, Pfizer Inc, 3; K. Kwok, Pfizer Inc, 1, Pfizer Inc, 3; C. F. Mojicik, Pfizer Inc, 1, Pfizer Inc, 3; N. Iikuni, Pfizer Inc, 1, Pfizer Inc, 3; S. Tatulych, Pfizer Inc, 1, Pfizer Inc, 3; G. Citera, Novartis, Pfizer Inc, 2, AbbVie, Bristol-Myers Squibb, Janssen, Novartis, Pfizer Inc, 5.


Abstract Number: 1398

**Sleep and Physical Activity: An Objective Profile of People with Rheumatoid Arthritis**

Sean McKenna\(^1\), Marie Tierney\(^2\), Sandy Fraser\(^3\), Aoife O'Neill\(^4\) and Norelee Kennedy\(^1\), \(^1\)Department of Clinical Therapies, University of Limerick, Ireland, Limerick, Ireland, \(^2\)Discipline of General Practice, National University of Galway, Ireland, Galway,
SESSION INFORMATION

**Session Date:** Monday, November 6, 2017
**Session Title:** ARHP Rheumatoid Arthritis – Clinical Aspects Poster
**Session Type:** ACR Poster Session B
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Regular physical activity is important for people with rheumatoid arthritis (RA). Sleep requirements for adults should be on a ‘sleep needs spectrum’ of between 7 to 9 hours per day. Poor sleep is a common complaint among people with RA, which may have an effect on their activity levels and well-being. There is evidence that physical activity and exercise can impact sleep quality and disturbances in other chronic disease populations therefore, examining how they could affect sleep in people with RA is important. There is a lack of objective information regarding total sleep time (TST) and its relationship with physical activity and disease related variables in people with RA.

**Methods:** Aim of the study was to objectively measure sleep and energy expenditure in people with RA and to determine if relationships exist between sleep, physical activity and related disease variables among people with RA. A cross-sectional study design was used to recruit people with RA attending rheumatology outpatient clinics. Participants had to have a confirmed diagnosis of RA according to the American College of Rheumatology (ACR) classification criteria to be included in the study. A SenseWear™armband was applied to the right upper arm and participants were encouraged to wear same for 24 hours a day for 8 days. Subjects were contacted 3 times during the week to remind them to continue to wear the monitor. Four valid days with 95% wear time was determined as the measurement criteria.

**Results:** Seventy five (75) participants completed period of monitoring, with 32 subjects having the required wear time. The mean TST was 5.7 (SD 1.11) hours per night, with a median 1.25 (IQR 1.88) hours of daily physical activity. Sleep time had a positive significant relationship with physical activity (p=0.018); physical activity also demonstrated a negative significant relationship with functional limitation (p=0.009); physical activity energy expenditure further demonstrated a significant negative correlation with disease activity (p=0.011) and low disease activity was strongly correlated with improved global health (p<0.001). Therefore, those who were more active had the longest TST, with reduced functional limitations. Those who expended more energy had lower disease activity with improved global health. Physical activity correlated with lower CRP levels and CRP levels had in turn a significant relationship to global health (p=0.034).

**Conclusion:** This study has demonstrated that people with RA who are more physically active have longer TST. Disease related factors and function variables also correlate with sleep, with lower CRP, lower DAS, lower HAQ and increased global health in those with higher physical activity levels and longer TST. These findings are significant given recent information that sleep is commonly reduced in people with RA and that people with RA have lower physical activity profiles.

People with RA have varied sleep patterns and fall below the required ‘sleep needs spectrum’. Future research should specifically investigate the effect of physical activity and exercise on sleep and from this, the most effective exercise prescription, the ideal approach to exercise delivery and how compliance can be promoted.

**Disclosure:** S. McKenna, None; M. Tierney, None; S. Fraser, None; A. O’Neill, None; N. Kennedy, None.


**Abstract Number:** 1399

**Tissues Are Differently Modulated By Tocilizumab and Methotrexate; Assessment of Connective Tissue Metabolites in the Ambition Study**

Anne C. Bay-Jensen¹, Anne Sofie Siebuhr¹, Christian S. Thudium² and Morten Asser Karsdal¹, ¹Rheumatology, Nordic Bioscience, Herlev, Denmark, ²Biomarkers and Research, Nordic Bioscience, Herlev, Denmark

**First publication:** September 18, 2017
Background/Purpose: The response to any treatment in rheumatoid arthritis (RA) is assessed by symptomatic changes, such as swollen joint count and DAS28. However, such assessments do not provide information regarding the effect of the treatment at the tissue level. Chronic inflammation has a detrimental effect resulting in elevated levels of tissue remodeling and the release of extracellular matrix (ECM) metabolites into the circulation. The tissues consist mainly of interstitial matrix, basement membrane and cells, which are all affected by auto-immune disorders. Tissue metabolites can be measured in serum as biomarkers of tissue remodeling and may give insight to effect at the tissue level of different interventions. The purpose was to investigate if tissue remodeling is differently modulated by tocilizumab (TCZ) and methotrexate (MTX). This was conducted by measurement of tissue metabolites in serum of the RA patients participating in the phase III clinical trial.

Methods: The AMBITION study, a phase III RCT with tocilizumab vs. Methotrexate in which TCZ monotherapy (8 mg/kg every 4 weeks) was compared to methotrexate monotherapy over 24 weeks in patients with moderate-severe RA (AMBITION, NCT00109408). TCZ is a compound that inhibits the IL-6 receptor. Tissue metabolites were measured in baseline and 8-weeks sera (n=319) by ECM specific ELISAs: Connective tissue remodeling was measured by C3M (type III collagen degradation), basement membrane remodeling by C4M (type IV collagen), inflammation by C-reactive protein (CRP) and its metabolite CRPM. Comparison between groups were done by ANCOVA adjusting for age, gender, BMI and disease duration.

Results: Tissue remodeling was increased by 10% in the placebo group. The connective tissue remodeling was significantly (p<0.001) inhibited by both MTX and TCZ compared to placebo. The inhibition with TCZ was 14% greater than that of MTX (P=0.0005). Basement membrane remodeling was likewise inhibited by both MTX and TCZ; the effect of TZC was 20% greater than MTX (p<0.0001). In contrast, MTX had no or limited effect on CRP and its metabolite CRPM compared to placebo or baseline. TCZ reduced the level to 27% and 73% of baseline, respectively. Although the effect of TCZ was much greater when assessing CRP, this was the least significant response marker, due to the huge placebo modulation, as well as the general high variation in response. Only changes in CRP was correlated to 8-week changes in DAS (rho=0.27, p=0.001) in the TCZ group. In the MTX group all changes in markers were correlated to change in DAS (rho=0.28 to 0.41, p<0.001). In contrast, only changes in C4M and CRP were significantly correlated with DAS changes (rho=0.31, p<0.05).

Conclusion: Chronic inflammation results in an increased amount of tissue remodeling. There was a significant difference in the magnitude of effect MTX and TCZ on tissue remodeling. In addition there was a disconnect between tissue remodeling and change in disease activity, which was treatment dependent.

Disclosure: A. C. Bay-Jensen, Nordic Bioscience Diagnostic, 3; A. S. Siebuhr, Nordic Bioscience Diagnostic, 3; C. S. Thudium, Nordic Bioscience Diagnostic, 3; M. A. Karsdal, Nordic Bioscience Diagnostic, 3.

Abstract Number: 1400

Beneficial Effect of Anti-IL-6 Blockade on Insulin Resistance and Insulin Sensitivity in Patients with Rheumatoid Arthritis

Raquel López-Mejías¹, Fernanda Genre¹, Sara Remuzgo-Martínez¹, Begoña Ubiña¹, Veronica Mijares¹, Jaime Calvo-Alen², Javier Llorca³, Santos Castañeda⁴ and Miguel Angel González-Gay⁵. ¹Epidemiology, Genetics and Atherosclerosis Research Group on Systemic Inflammatory Diseases, Rheumatology Division, IDIVAL, Santander, Spain, ²Rheumatology Department, Hospital Universitario Araba, Vitoria-Gasteiz, Spain, ³Department of Epidemiology and Computational Biology, School of Medicine, University of Cantabria, and CIBER Epidemiología y Salud Pública (CIBERESP), IDIVAL, Santander, Spain, ⁴Hospital Universitario La Princesa. IIS-IP. Madrid. Spain, Madrid, Spain, ⁵Epidemiology, Genetics and Atherosclerosis Research Group on Systemic Inflammatory Diseases, Rheumatology Division, IDIVAL. School of Medicine, University of Cantabria., Santander, Spain

First publication: September 18, 2017
Background/Purpose: Systemic inflammation, insulin resistance, and endothelial dysfunction were implicated in the development of cardiovascular disease in rheumatoid arthritis (RA) [1-3]. Since insulin resistance can promote endothelial dysfunction and IL-6 blockade yields a rapid improvement of endothelial function [4], we aimed to assess whether IL-6 blockade may also result in a reduction of insulin serum levels and improvement of insulin resistance in patients with RA.

Methods: 50 Spanish patients on treatment with anti-IL-6 monoclonal antibody-Tocilizumab who fulfilled the 2010 classification criteria for RA [5] were recruited. Patients with diabetes mellitus or plasma glucose > 110 mg/dl were excluded. Fasting blood samples were taken for determination of plasma glucose and serum insulin levels immediately prior to (time 0) and after (time 60 minutes) Tocilizumab infusion. Insulin resistance was assessed by the homeostasis model assessment for insulin resistance (HOMA) and insulin sensitivity was evaluated by the quantitative insulin sensitivity check index (QUICKI).

Results: A marked reduction in the serum insulin levels was observed following Tocilizumab infusion (mean ± standard deviation (SD): 10.60 ± 5.80 µU/ml versus 7.61 ± 5.08 µU/ml, p<0.0001). In addition, a decrease in the insulin/glucose index was observed in patients with RA after Tocilizumab dose (mean ± SD: 0.12 ± 0.06 versus 0.08 ± 0.05, p<0.0001). Furthermore, a significant improvement of insulin resistance (HOMA: mean ± SD: 2.61 ± 2.05 versus 1.65 ± 1.14, p=0.0003) and insulin sensitivity (QUICKI: mean ± SD: 0.34 ± 0.003 versus 0.37 ± 0.04, p<0.0001) was found following Tocilizumab infusion.

Conclusion: Our study confirms a rapid beneficial effect of Tocilizumab on insulin resistance and insulin sensitivity in RA patients treated with this drug. It may support the long-term use of drugs that act blocking IL-6 function to reduce the mechanisms implicated in the development of atherosclerosis in patients with RA.


RL-M is supported by the Miguel Servet I programme of the Spanish Ministry of Economy and Competitiveness through the grant CP16/00033. FG is recipient of a Sara Borrell postdoctoral fellowship from the “Instituto Carlos III de Salud” at the Spanish Ministry of Health (Spain) (CD15/00095). SR-M is supported by funds from the RETICS Program (RIER) (RD16/0012/0009).

Disclosure: R. López-Mejías, None; F. Genre, None; S. Remuzgo-Martínez, None; B. Ubilla, None; V. Mijares, None; J. Calvo-Alen, None; J. Llorca, None; S. Castañeda, None; M. A. González-Gay, None.

Abstract Number: 1401

Persistence of Mast Cell-Rich Synovitis Is Associated with Lack of Response to Synthetic Disease Modifying Anti-Rheumatic Drugs in Patients with Early Rheumatoid Arthritis

Felice Rivellese, Frances Humby, Sara Pagani, Alessandra Nerviani and Costantino Pitzalis, Centre for Experimental Medicine and Rheumatology, William Harvey Research Institute, Barts and The London, School of Medicine and Dentistry, Queen Mary University of London, London, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Mast cells (MCs) are immune cells infiltrating the synovial membrane and implicated in the pathogenesis of Rheumatoid Arthritis, but their strict contribution to disease development and progression is still unclear. We have previously shown an association between synovial MCs and disease severity in early RA patients. Aim of this study was to analyse the presence of MCs in the synovia of RA patients at baseline and 6 months after treatment with synthetic DMARDs in relationship with disease parameters and response to treatment.

Methods: DMARD-naïve patients with early (<12 months) RA (n=20) fulfilling the 2010 ACR/EULAR criteria were recruited as part of the Pathobiology of Early Arthritis Cohort at Barts Health NHS Trust. Synovial tissue was obtained by ultrasound-guided synovial biopsy at baseline and 6 months after treatment with synthetic DMARDs. Sequentially cut sections were stained by IHC for CD117+ MCs and immune cells (CD20+ B cells, CD3+ T cells, CD68+ macrophages and CD138+ plasma cells). Patients were classified according to the presence or absence of MCs, and MC density (n/mm²) was calculated by automated cell counting (cellSens, Olympus). Upon SQ scoring (0-4), sections were stratified into synovial pathotypes according to the degree of immune cell infiltration: (i) Lymphoid- grade 2/3 B cell aggregates, CD20≥ 2 and/or CD138>2 ii) Myeloid- CD68 SL≥ 2, CD20≤1 and/or CD3≥1, CD138≤2 and iii) Fibroid- CD68 SL<2 and CD3, CD20, CD138<1.

Results: At baseline, the presence of synovial MCs was significantly associated with synovial inflammation (high synovitis score 60.7% in MC+ vs 16% in MC-, p<0.05) and lymphoid aggregates (lymphoid pathotype 64.4% in MC+ Vs 16.1% in MC-). Additionally, MCs were associated with systemic inflammation and disease activity (e.g. DAS-28 5.96 in MC+ vs 5.18 in MC-, p<0.05). Treatment with synthetic DMARDs induced a partial reduction in MC numbers (mean MC at baseline 14.2/mm² at 6; at 6 months 8.2/mm², p=0.094). Accordingly, synovial MCs were still present at 6 months in 45% of patients (9/20), in association with synovitis and lymphoid aggregates (high synovitis score and lymphoid pathotype 44.4% in MC+ vs 0% in MC-, p<0.05). Additionally, the presence of MCs at 6 months was associated with a higher DAS28 (4.08 in MC+ vs 2.41 in MC-, p<0.05) and a lower rate of remission (DAS28<2.6 22.2% in MC+ vs 72.7% in MC-, p<0.05).

Conclusion: Here we show that treatment with synthetic DMARDs in early RA patients partially reduces the number of synovial mast cells and their persistence (MC-rich synovitis) is associated with lack of response to DMARDs. This exploratory study confirms the relevance of MCs as part of the inflammatory infiltrate in the synovia of RA patients, warranting further investigations to clarify their role in disease progression and response to treatment.

Disclosure: F. Rivellese, None; F. Humby, None; S. Pagani, None; A. Nerviani, None; C. Pitzalis, None.

In RA, Becoming Seronegative over the 1st Year of DMARD Treatment Does Not Improve Chances of Drug-Free Remission in the Long-Term

Emma de Moel¹, Veerle Derksen¹, LA Trouw¹, Holger Bang², Yvonne P. Goekoop-Ruiterman³, GM Steup-Beekman¹⁴, Tom W.J. Huizinga⁵, Cornelia F Allaart⁵, Rene E.M. Toes¹ and Diane van der Woude⁶, ¹Rheumatology, Leiden University Medical Center, Leiden, Netherlands, ²Orgentec Diagnostika GmbH, Mainz, Germany, ³Rheumatology, HAGA hospital, The Hague, Netherlands, ⁴Rheumatology, Haaglanden Medical Center, The Hague, Netherlands, ⁵Department of Rheumatology, LUMC, Leiden, Netherlands, ⁶Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Patients with RA harbor autoantibodies of various isotypes and directed against several post-translational modifications. Baseline seropositivity is a poor prognostic factor for sustained drug-free remission (SDFR). However, autoantibody levels may change and patients may become seronegative under treatment. It is unknown how often this happens, and whether decreasing levels or becoming seronegative early in disease, indicating disappearance of serological autoimmunity, improves chances
of SDFR. To investigate this, we measured a large variety of autoantibodies, including isotypes, in RA patients over time and investigated whether changes in their levels and/or presence associated with SDFR.

Methods: In sera of 381 seropositive RA patients in the IMPROVED study\(^1\), we measured, at 4 month intervals over the first year of treatment: IgG, IgM, and IgA isotypes for anti-cyclic citrullinated peptide-2, rheumatoid factor, anti-carbamylated protein antibodies, and autoantibodies against 4 citrullinated and 2 acetylated peptides. We investigated whether changes in antibody levels and seroconversion from positive to negative for each individual antibody was favorable for SDFR (drug-free DAS44<1.6 lasting ≥1 year until last follow-up).

Results: For all 14 antibodies, median levels decreased significantly between baseline and 4 months and then stabilized. The prevalence of seroconversion from positive to negative between 0-12 months varied substantially depending on the autoantibody and occurred in 3% (anti-CCP2 IgG) to 66% (anti-CarP IgA) of patients positive at baseline. We hypothesized that greater level decreases and seroconversion, reflecting disappearance of the underlying immunopathology, might be favorable for the long-term outcome SDFR, an outcome approximating disease curation. Surprisingly, greater median decreases in levels were not associated with higher chance of SDFR. Furthermore, we found no evidence that rates of SDFR were higher in patients who seroconverted compared those who stayed seropositive, for all antibodies analyzed (see Figure).

Conclusion: Autoantibody levels decrease and seroconversion from positive to negative occurs under treatment, but these changes do not seem to translate to apparent clinical long-term benefits with regard to SDFR. This suggests that in these patients, despite the disappearance of measurable serological autoimmunity, other immunopathological processes sustain the disease.

References:

\(^{1}\)Heimans, AR&T 2016, 18:23.

![Figure](http://acrabstracts.org/abstract/in-ra-becoming-seronegative-over-the-1st-year-of-dmard-treatment-does-not-improve-chances-of-drug-free-remission-in-the-long-term)
SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The Mediterranean Diet has been associated with lower mortality and risk of cardiovascular diseases and cancer. Although its components have been analyzed in several studies, only two studies have investigated the association between Mediterranean diet and risk of rheumatoid arthritis (RA) and reported no association.

Methods: Data on 1726 incident cases and 3683 controls, matched on age, gender and residential area, from the Epidemiological Investigation of RA (EIRA), a population-based case-control study, was used to estimate the association between the Mediterranean dietary score and the risk of RA. The score, ranging from 0 to 9, was calculated using a 124-item food frequency questionnaire. Odds ratios (ORs) and their 95% confidence intervals (CIs) were calculated using conditional logistic regressions, and multivariable models were adjusted for body mass index, educational level, physical activity, use of dietary supplements, energy intake, and smoking.

Results: In the EIRA study (median age 53), 23.5% of the cases and 27.9% of the controls had a high adherence to the Mediterranean diet (a score between 6 and 9). An high adherence reduced the odds of developing RA by 23% (OR 0.76; 95% CI, 0.62-0.92) as compared to low adherence (a score between 0 and 2). The odds ratio was even lower among men (OR 0.49; 95% CI, 0.33-0.72), but no association was found among women (OR 0.89; 95% CI, 0.71-1.11). The inverse association was observed for rheumatoid factor (RF) positive (OR 0.66; 95% CI, 0.52-0.84), but not negative RA (OR 0.93; 95% CI, 0.66-1.30), and for antibodies to citrullinated peptides (ACPA) positive, but not ACPA-negative RA (Table 1).

Conclusion: In this large population-based case-control study, the Mediterranean diet score was inversely associated with risk of RA. The association was stronger among men than among women and no significant association was observed for seronegative RA.

Acknowledgments: This study was supported by grant from Forte (grant registration number 2015–00689).

Conflict of interest: The authors declare that they have not conflict of interest.

Table 1. Odds ratios of RA, overall and stratified by gender and ACPA, according to categories of the Mediterranean diet score

<table>
<thead>
<tr>
<th>Mediterranean Diet Score</th>
<th>0-2</th>
<th>3</th>
<th>4-5</th>
<th>6-9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>376/604</td>
<td>299/649</td>
<td>646/1403</td>
<td>405/1027</td>
</tr>
<tr>
<td>OR crude</td>
<td>0.76 (0.59-0.95)</td>
<td>0.76 (0.65-0.90)</td>
<td>0.64 (0.54-0.76)</td>
<td></td>
</tr>
<tr>
<td>OR adjusted</td>
<td>0.80 (0.63-1.03)</td>
<td>0.85 (0.72-1.01)</td>
<td>0.76 (0.62-0.92)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>251/438</td>
<td>218/450</td>
<td>473/1007</td>
<td>313/762</td>
</tr>
<tr>
<td>OR crude</td>
<td>0.85 (0.68-1.07)</td>
<td>0.83 (0.69-1.01)</td>
<td>0.73 (0.59-0.90)</td>
<td></td>
</tr>
<tr>
<td>OR adjusted</td>
<td>0.91 (0.71-1.16)</td>
<td>0.95 (0.77-1.16)</td>
<td>0.89 (0.71-1.11)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>125/166</td>
<td>81/199</td>
<td>173/396</td>
<td>92/265</td>
</tr>
<tr>
<td>OR crude</td>
<td>0.58 (0.41-0.83)</td>
<td>0.63 (0.47-0.85)</td>
<td>0.46 (0.33-0.65)</td>
<td></td>
</tr>
<tr>
<td>OR adjusted</td>
<td>0.60 (0.41-0.88)</td>
<td>0.65 (0.47-0.91)</td>
<td>0.49 (0.33-0.72)</td>
<td></td>
</tr>
<tr>
<td>ACPA positive</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>271/371</td>
<td>210/392</td>
<td>437/840</td>
<td>261/652</td>
</tr>
<tr>
<td>OR crude</td>
<td>0.74 (0.59-0.93)</td>
<td>0.72 (0.59-0.87)</td>
<td>0.56 (0.45-0.69)</td>
<td></td>
</tr>
<tr>
<td>OR adjusted</td>
<td>0.80 (0.63-1.02)</td>
<td>0.82 (0.67-1.01)</td>
<td>0.69 (0.55-0.88)</td>
<td></td>
</tr>
<tr>
<td>ACPA negative</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>103/173</td>
<td>88/188</td>
<td>205/400</td>
<td>144/273</td>
</tr>
<tr>
<td>OR crude</td>
<td>0.82 (0.58-1.18)</td>
<td>0.91 (0.67-1.23)</td>
<td>0.91 (0.66-1.26)</td>
<td></td>
</tr>
<tr>
<td>OR adjusted</td>
<td>0.82 (0.56-1.20)</td>
<td>0.93 (0.67-1.29)</td>
<td>0.97 (0.68-1.29)</td>
<td></td>
</tr>
</tbody>
</table>
Figure 1. Continuous association (with 95% confidence interval) of the Mediterranean diet score with RA, modeled using restricted cubic splines.

Disclosure: D. Di Giuseppe, None; K. Johansson, None; J. Askling, None; L. Alfredsson, None.


Abstract Number: 1404

Hydrogen Sulfide Metabolism and Rheumatoid Arthritis

Alexis Guice¹, Richa Dhawan², Sibile Pardue³ and Christopher Kevil⁴, ¹INTERNAL MEDICINE, LSU UNIVERSITY HEALTH, SHREVEPORT, LA, ²INTERNAL MEDICINE, SECTION OF RHEUMATOLOGY, LSU UNIVERSITY HEALTH, SHREVEPORT, LA, ³LSU UNIVERSITY HEALTH, SHREVEPORT, LA, ⁴PATHOLOGY,MOLECULAR CELLULAR PHYSIOLOGY AND CELL BIOLOGY AND ANATOMY, LSU UNIVERSITY HEALTH, SHREVEPORT, LA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Hydrogen sulfide (H2S) is an endogenous gasotransmitter known to play a role in inflammation. While levels of hydrogen sulfide have been studied in patient populations with cardiovascular disease, there has been little research of H2S levels in plasma of subjects with autoimmune diseases such as rheumatoid arthritis (RA). H2S bioavailability is regulated through its conversion into different biochemical forms. Past H2S studies concerning rheumatoid arthritis have not employed analytical biochemistry to measure biochemical forms of H2S, specifically the free H2S, acid-labile sulfide, and bound sulfane sulfur. Thus, the aim of this study was to measure these metabolites of H2S in rheumatoid arthritis subjects and compare them to non-RA individuals over time.

Methods:

Thirty control non-RA and thirty RA subjects were selected based on specific criteria and consented in the University Health Rheumatology Clinic. Subjects with diabetes were excluded from the study. Following consent, 10 ml of venous blood was collected into a BD microtainer plasma separator tube with heparin. Samples were prepared for detecting H2S pools. Hydrogen sulfide can be
released from acid-labile sulfide form in 100 mM phosphate buffer (pH 2.6) with or without the reductant TCEP. Sulfide levels were measured by derivatization of hydrogen sulfide with excess monobromobimane (MBB) in 50 mM Tris-HCl buffer. The fluorescent product sulfide-dibimane was then measured by RP-HPLC with a fluorescence detector. An F test was performed on the data to check for a significant difference in variances. Because the variances differed significantly with some populations, the Mann-Whitney test was performed.

Results:

Subjects with RA had significantly higher levels of acid labile sulfur (p=0.009) and total sulfide (p=0.04) at the one month blood draw. Additionally, acid labile sulfide levels (p=0.04) and total sulfide levels (p=0.01) were greater in control males as compared to females at the 6-month blood draw. White male control’s H2S levels were found to have an upward trend over the 6 months.

Conclusion:

This research serves as a pilot study comparing the different biochemical forms of H2S (free, acid-labile, and bound) in the plasma of RA subjects versus control subjects. The method used in this study is unique, validated and quantitative because, unlike any prior studies on H2S, the MBB method analytically measures different forms of H2S in the plasma. Our findings show that acid labile and total H2S levels are higher in RA subjects than controls at the one month visit. Further studies are needed to determine the relationship of medications, disease activity, and diet during various time points of disease progression.
of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 2Division of Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 3Divisions of Genetics and Rheumatology, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 4Department of Surgery, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 5Arthritis and Tissue Degeneration Program and the David Z. Rosensweig Genomics Research Center, Hospital for Special Surgery, New York, NY, 6Institute of Inflammation and Ageing, University of Birmingham, Birmingham, United Kingdom, 7Medicine, University of Pittsburgh, Pittsburgh, PA, 8Medicine-Allergy, Immunology and Rheumatology, University of Rochester Medical Center, Rochester, NY, 9Broad Institute, Cambridge, MA, 10Centre for Experimental Medicine and Rheumatology, William Harvey Research Institute, Barts and The London, School of Medicine and Dentistry, Queen Mary University of London, London, United Kingdom, 11Medicine, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, 12University of California San Diego, La Jolla, CA, 13Stanford University School of Medicine, Stanford, CA, 14Medicine, Stanford University School of Medicine, Stanford, CA, 15Medicine, University of California San Diego, La Jolla, CA, 16Department of Medicine, Division of Rheumatology, Northwestern University Feinberg School of Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, 17Laboratory Medicine, Hospital for Special Surgery, New York, NY, 18Institute of Inflammation and Ageing (IIA), University of Birmingham, Birmingham, United Kingdom, 19University of Rochester Medical Center, Rochester, NY, 20Lazare Research Bldg, University of Massachusetts Medical School, Worcester, MA, 21The Broad Institute and Harvard, Cambridge, MA, 22Harvard Medical School, Boston, MA, 23Massachusetts General Hospital, Charlestown, MA, 24Broad Institute of MIT and Harvard, Cambridge, MA, 25The Feinstein Institute for Medical Research, Northwell Health, Manhasset, NY, 26Rheumatology & Clinical Immunology, University of Pittsburgh, Pittsburgh, PA, 27Medicine, Division of Rheumatology, University of Colorado Denver, Aurora, CO, 28Division of Rheumatology, Hospital for Special Surgery, New York, NY, 29Brigham and Women's Hospital and Harvard Medical School, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Discovery and application of new therapies for rheumatoid arthritis (RA) has been hampered by multiple factors, including disease heterogeneity and the lack of well established approaches to analyze the synovial target tissue. The goal of the Accelerating Medicines Partnership (AMP) program is to deconstruct RA through cellular and molecular profiling of synovial tissue and matched peripheral blood from individuals with RA. During phase 1 of the AMP – RA program, we tested the feasibility of applying cytometric and transcriptomic analyses to synovial tissues from RA patients recruited from clinical sites across the network.

Methods:

Patient Enrollment. A multicenter cross-sectional study of individuals undergoing elective surgical procedures and a prospective observational study of synovial biopsy from RA ≥ age 18 with at least one inflamed joint were recruited from 10 contributing sites in the network.

Tissue Processing. Synovial tissues were cryopreserved on site then shipped to a central processing site for tissue disaggregation, cell sorting, mass cytometry and RNA-seq. Synovial tissue quality and grading of synovitis were evaluated via histologic analysis (H and E staining).

Analytic Pipelines. Cellular composition of RA and osteoarthritic (OA) synovial tissue was determined by flow cytometry and mass cytometry. RNA-seq was performed in parallel.

Results:

58 synovial tissues acquired from 22 synovial biopsies and 36 elective surgical procedures (20 RA and 16 OA) were analyzed by combination of flow cytometry, mass cytometry, and RNA-seq. Synovial cellular composition determined by flow cytometry and mass cytometry were highly consistent in T cells (r=0.98), B cells (r=0.96), myeloid cells (r=0.64), endothelial cells (r=0.81) and synovial fibroblasts (r=0.93), validating synovial analysis by mass cytometry of synovial tissue. Whereas RA synovial tissue obtained from elective surgical procedures exhibited varied degrees of inflammation with mean Krenn inflammation score (0-3) of 0.94 (S.D.=0.51), synovial tissues obtained from biopsies revealed significantly higher Krenn inflammation score than OA (1.68 vs 0.73; p=0.02) and higher abundance of lymphocytes by flow cytometry (67% vs 8%; p<0.001). Lymphocytic infiltration assessed by
cytometry was significantly correlated with histologic inflammation score \( (p<0.001, r=0.58) \), further supporting the fidelity of flow cytometric assessment of cryopreserved synovial tissue. Principle component analysis of synovial cell flow cytometry data identified 3 RA arthroplasty samples with inflammatory features resembling that seen in RA biopsies. Consistent with this analysis, these arthroplasty samples also showed higher inflammation score of inflammation by histology \( (2.0 \text{ vs } 0.77, p<0.001) \). Ongoing transcriptomic profiling of sorted synovial cells demonstrate molecular heterogeneity in RA synovium.

**Conclusion:**

In Phase 1 of the AMP-RA program, robust cell yield from synovial tissue enables mass and flow cytometric data. These results lay the ground work for the larger phase 2 of the Accelerating Medicines Partnership (AMP) – RA network, which will utilize >100 independent samples.

**Disclosure:** K. Wei, Roche Pharmaceuticals, 2; D. Rao, None; F. Zhang, None; C. Fonseka, None; K. Slowikowski, None; J. Keegan, None; L. T. Donlin, None; J. Turner, None; M. J. McGechy, None; N. Meednu, None; D. Lieb, None; S. Kelly, None; S. M. Goodman, None; D. L. Boyle, None; W. H. Robinson, None; P. J. Utz, None; G. S. Firestein, None; H. Perlman, None; E. F. DiCarlo, None; C. Pitzalis, None; A. Filer, None; B. Boyce, None; E. M. Gravallese, Abbott Immunology Pharmaceuticals, 2,Lilly, Inc, 2,New England Journal of Medicine, 3,Up to Date, 7,Lilly Inc., 5,Sanofi/Genzyme, 5; C. Nusbaum, None; J. Lederer, None; N. Hacohen, None; P. Gregersen, None; L. W. Moreland, None; M. Holers, None; V. P. Bykerk, None; S. Raychaudhuri, Pfizer Inc, 2, Roche Pharmaceuticals, 2; M. Brenner, None; J. H. Anolik, None.


**Abstract Number:** 1406

**Methods for Generating Multiple High-Dimensional Analyses of Cryopreserved Synovial Tissue Developed By the Accelerating Medicines Partnership RA/SLE Network**

Deepak Rao1, Laura T. Donlin2, Kevin Wei3, Nida Meednu4, Jason Turner5, Mandy J. McGechy6, Fumitaka Mizoguchi7, Joshua Keegan8, James Lederer9, Maria Gutierrez-Arcelus10, Kamil Slowikowski11, Kaylin Muskat12, Joshua Hillman12, Cristina Rozo13, Edd Ricker14, Thomas Eisenhaure15, David Lieh15, Shuqiang Li15, Edward Browne15, Chad Nusbaum15, William H. Robinson16, Stephen Kelly17, Alessandra B. Pernis18, Lionel Ivashkiv19, Susan M. Goodman20, Ellen M. Gravallese21, Michael Holers22, Nir Hacohen23, Costantino Pitizalis17, Peter Gregersen24, Vivian P. Bykerk25, Larry W. Moreland26, Gary Firestein27, Soumya Raychaudhuri28, Andrew Filer29, David L. Boyle30, Michael Brenner10 and Jennifer H. Anolik4, 1Division of Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 2Arthritis and Tissue Degeneration Program and the David Z. Rosensweig Genomics Research Center, Hospital for Special Surgery, New York, NY, 3Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 4Medicine- Allergy, Immunology and Rheumatology, University of Rochester Medical Center, Rochester, NY, 5Institute of Inflammation and Ageing, University of Birmingham, Birmingham, United Kingdom, 6Medicine, University of Pittsburgh, Pittsburgh, PA, 7Department of Rheumatology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University (TMDU), Tokyo, Japan, 8Brigham and Women's Hospital, Boston, MA, 9Department of Surgery, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 10Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 11Division of Medicine and Rheumatology, Brigham and Women's Hospital, Harvard Medical Schoo, Boston, MA, 12University of California, San Diego, San Diego, CA, 13Hospital for Special Surgery, New York, NY, 14Weill Cornell Graduate School of Medical Sciences, New York, NY, 15Broad Institute, Cambridge, MA, 16Stanford University School of Medicine, Stanford, CA, 17Centre for Experimental Medicine and Rheumatology, William Harvey Research Institute, Barts and The London, School of Medicine and Dentistry, Queen Mary University of London, London, United Kingdom, 18David Z. Rosensweig Genomics Research Center, Hospital for Special Surgery, New York, NY, 19Medicine, Hospital for Special Surgery, New York, NY, 20Medicine, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, 21Lazare Research Bldg, University of Massachusetts Medical School, Worcester, MA, 22Medicine, Division of Rheumatology, University of Colorado Denver, Aurora, CO, 23Harvard Medical School, Boston, MA, 24The Feinstein Institute for Medical Research, Northwell Health, Manhasset, NY, 252-005, Mt Sinai Hospital, Toronto, ON, Canada, 26Rheumatology & Clinical Immunology, University of Pittsburgh, Pittsburgh, PA, 27EGG, St Cloud, France, 28Division of Medicine and Rheumatology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, 29Institute of
Inflammation and Ageing (IIA), University of Birmingham, Birmingham, United Kingdom, University of California San Diego, La Jolla, CA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Detailed analyses of cells from rheumatoid arthritis (RA) synovium may identify cell phenotypes and functions that drive tissue pathology and joint damage. The AMP RA/SLE network aims to deconstruct RA pathology using multiple high-dimensional analyses of cells obtained from rheumatoid synovium. These studies hold the potential to identify novel therapeutic strategies to counteract pathologic inflammatory responses in RA.

Methods: We developed a method to cryopreserve intact synovial tissue for downstream analyses of viable cells. Synovial tissue fragments were cryopreserved in a 10% DMSO-containing solution, then thawed and disaggregated. Synovial cells were analyzed using a 35-marker mass cytometry panel. In parallel, synovial cell populations, including fibroblasts, T cells, B cells, and macrophages, were flow-cytometrically sorted for low-input and plate-based single cell RNAseq transcriptomics.

Results: Intact cryopreserved synovial tissue yielded high numbers of viable cells after a thawing protocol followed by tissue dissociation. Cells isolated from cryopreserved tissue demonstrated intact expression of lineage markers by flow cytometry, comparable to freshly processed tissues. Optimization of synovial tissue dissociation performed across 6 sites, utilizing >30 arthroplasty and >20 synovial biopsy samples, yielded a consensus dissociation protocol of tissue digestion with 100ug/mL of liberase TL enzyme, which provided high cell yields, preserved surface markers, and minimized variability in RNAseq transcriptomes across replicates.

Arthroplasty samples were mechanically dissociated after enzymatic digestion by gentleMACS. To reduce cell losses when using smaller synovial biopsies, biopsy samples were mechanically dissociated by rapid, continuous magnetic stirring during enzymatic digestion and passage through an 18-gauge syringe. Cryopreserved tissue dissociated by these methods could be analyzed by multiple high-dimensional analyses. Mass cytometry revealed 1) diverse fibroblast phenotypes, 2) clear separation of memory B cells from antibody-secreting cells, and 3) multiple phenotypes of activated CD4+ and CD8+ T cells. To complement mass cytometry analysis, a flow cytometric sorting strategy was developed to collect fibroblasts, macrophages, T cells, B cells for bulk and single cell RNAseq transcriptomics. RNAseq of total synovial cells revealed a transcriptomic effect of tissue dissociation, compared to intact synovial tissue. Nonetheless, RNAseq of sorted cell populations demonstrated robust separation of synovial lymphocytes, fibroblasts, and macrophages. Single cell RNAseq by CelSeq2 yielded transcriptomes of over 1000 genes/cell and demonstrated characteristic lineage markers in the expected cell populations.

Conclusion: We propose that this method of acquisition of viable cells from cryopreserved tissue can serve as a model for centralized generation of multiple, robust high-dimensional analyses of synovial samples acquired in multi-site studies. Integrated analysis of these datasets in a large patient cohort may help define the molecular heterogeneity of RA pathology and identify new therapeutic targets and biomarkers.

Disclosure: D. Rao, None; L. T. Donlin, None; K. Wei, None; N. Meednu, None; J. Turner, None; M. J. McGeechay, None; F. Mizoguchi, None; J. Keegan, None; J. Lederer, None; M. Gutierrez-Arcelus, None; K. Slowikowski, None; K. Muskat, None; J. Hillman, None; C. Rozo, None; E. Ricker, None; T. Eisenhaure, None; D. Lieb, None; S. Li, None; E. Browne, None; C. Nusbaum, None; W. H. Robinson, None; S. Kelly, None; A. B. Pernis, Kadmon corporation, 2; L. Ivashkiv, None; S. M. Goodman, None; E. M. Gravallese, Abbott Immunology Pharmaceuticals, 2,Lilly, Inc, 2,New England Journal of Medicine, 3,Up to Date, 7,Lilly Inc., 5,Sanofi/Genzyme, 5; M. Holers, None; N. Hacohen, None; C. Fitzalis, None; P. Gregersen, None; V. P. Bykerk, None; L. W. Moreland, None; G. Firestein, None; S. Raychaudhuri, Pfizer Inc, 2,Roche Pharmaceuticals, 2; A. Filer, None; D. L. Boyle, None; M. Brenner, None; J. H. Anolik, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/methods-for-generating-multiple-high-dimensional-analyses-of-cryopreserved-synovial-tissue-developed-by-the-accelerating-medicines-partnership-rasle-network

Abstract Number: 1407
Huntingtin Interactin Protein 1 (HIP1) Regulates Invasiveness, Actin Filament and Lamellipodia Formation in Rheumatoid Arthritis Fibroblast-like Synoviocytes (FLS)

Teresina Laragione, Carolyn Harris, Erjing Gao and Percio S. Gulko, Medicine/Rheumatology, Icahn School of Medicine at Mount Sinai, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Huntingtin-interacting protein 1 (Hip1) is an arthritis severity and joint damage gene recently discovered in rodent models of arthritis. Hip1 regulates fibroblast-like synoviocytes (FLS) invasiveness, and FLS invasiveness strongly correlates with joint damage. Previous studies suggested that Hip1 regulates PDGFR signaling in rodent cells. In the present study we aimed at determining whether Hip1 mediates PDGFβ and EGF-induced invasion in RA-derived FLS.

Methods: FLS cell lines from RA patients were transfected with siRNA targeting Hip1 or controls. Knock-down was confirmed with qPCR and western blot. Invasion was studied in a well-established two-chamber assay through Matrigel, where lower chamber contained either PDGFβ (50ng/ml), EGF (1ug/ml) in SFM. Cell were also treated with PDGFβ for 5, 15 and 30 minutes and analyzed by immunofluorescence for pFAK localization and actin cytoskeleton. Total cell lysates from RA FLS stimulated with PDGF were used to quantify matrix metalloproteases (MMP1-3, 8-10, 12, 13), as well as total and phospho-FAK.

Results: siRNA Hip1 knock down in RA FLS (n=6) significantly reduced invasiveness induced by PDGFβ (40% reduction; p=0.03) and EGF (50%; p=0.005) compared with siRNA control cells. Hip1 knock-down cells had fewer thick actin filaments and developed an unusual star-like morphology unable to take the polarized shape typically required for movement and invasion, with impaired formation of lamellipodia. Total levels of phospho-FAK did not differ between Hip1 knock-down and control FLS. However, in Hip1 knock-down FLS phospho-FAK distribution was significantly different from controls and distant from the cell periphery. Levels of MMPs were not affected by siRNA Hip1.

Conclusion: We describe a new role for Hip1 in the regulation of EGF and PDGF-induced invasiveness of RA FLS, and show that in the absence of Hip1 the cells takes an unusual and non-invading morphology without lamellipodia. These new findings provide new understanding of events regulating FLS behavior in RA and have the potential to generate a new prognostic biomarkers and a new intra-cellular target for therapies aimed at reducing joint damage.

Disclosure: T. Laragione, None; C. Harris, None; E. Gao, None; P. S. Gulko, none, 9.


Abstract Number: 1408

The Cation Channel TRPV2 Decreases Rheumatoid Arthritis Fibroblast-like Synoviocyte Invasiveness By Inhibiting RhoA Activation, Cell Adhesion and Actin Cytoskeleton Changes

Teresina Laragione, Carolyn Harris, Erjing Gao and Percio S. Gulko, Medicine/Rheumatology, Icahn School of Medicine at Mount Sinai, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster II
Background/Purpose: We have recently identified the non-selective cation channel TRPV2 (transient receptor potential vanilloid subfamily, type 2 channel) as a new central mediator of arthritis and fibroblast-like synoviocyte (FLS) invasiveness. TRPV2 activation by the synthetic agonists O1821 and LER13 suppressed invasiveness of FLS from DA rats, B6 mice and RA FLS and reduced disease severity and joint damage in collagen induced arthritis (CIA) and KRN serum-induced arthritis. However, the mechanism of action of TRPV2 agonists was incompletely understood. In this study we characterized the cell signaling events and mechanisms mediating the TRPV2 suppressive activity in FLS.

Methods: FLS cell lines developed from RA patients were pre-treated with O1821 (or vehicle) for 30 minutes, followed by either a) adhesion to multiple substrates (collagen I/II/IV, fibronectin, laminin, tenascin, vitronectin or BSA), b) cell lysis for Milliplex MAPK pathway analyses or RhoA/Rac1/Cdc42 activation assay, or c) for quantification of total matrix metalloproteases (MMPs). The active form of MMP2 was quantified on a Zymogram using supernatants from FLS cultured on Matrigel. Actin filaments and pFAK localization on FLS were analyzed by immunofluorescence.

Results: O1821 significantly reduced FLS adhesion to laminin, tenascin, vitronectin, and type IV collagen suggesting an inhibitory effect on different integrins. O1821 decreased pFAK (tyr397) levels and prevented pFAK co-localization with lamellipodia. Additionally, O1821 reduced actin filament thickness inducing a disorganized filament distribution and keeping the cells in a round and non-polarized shape. O1821 prevented the formation of lamellipodia and reduced levels of activated RhoA, while the activator CN03 bypassed that effect. We detected no significant effect of O1821 on MMPs, Cdc42, Rac1, MAPK pathway phosphorylated members p38, Jnk, Erk, CREB, Akt, Stat3, Stat5, p70S6K or NFkB.

Conclusion: We describe new cellular and signaling processes regulated by TRPV2 suggesting that it suppresses RhoA activation to prevent actin filament changes required for cell mobility and invasion, including adhesion, polarization of cell morphology and the formation of lamellipodia. These observations provide new understanding into the mechanism of action of arthritis and invasion suppressive TRPV2 agonists that are being developed toward therapeutic use.

Disclosure: T. Laragione, None; C. Harris, None; E. Gao, None; P. S. Gulko, none, 9.


Abstract Number: 1409

Ursolic Acid Promotes Apoptosis of Rheumatoid Arthritis Synovial Fibroblasts By Upregulating Noxa Expression and Recruiting E3 Ligase Mule to Degrade Mcl-1

Eugene Kim1, Solomon Agere1, Sadik Khuderr and Salahuddin Ahmed1, 1Department of Pharmaceutical Sciences, Washington State University, College of Pharmacy, Spokane, WA, 2Department of Medicine, University of Toledo, Toledo, OH

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: In our previous study, we discovered that ursolic acid (UA), a pentacyclic triterpenoid with anti-inflammatory properties, induces apoptosis in synovial fibroblasts from rheumatoid arthritis patients (RASFs) by upregulating Noxa and downregulating Mcl-1. To examine the molecular mechanism of UA-mediated apoptosis, we tested early signaling pathways that may activate Noxa expression as well as potential mechanisms of Noxa-mediated proteasomal degradation of Mcl-1 in human RASFs.

Methods: Human RASFs were treated with UA (5-10 μM) to determine the activated signaling pathways by Western blotting and qRT-PCR methods. The spatial association of Noxa with Mcl-1 and other E3 ligases was studied using immunoprecipitation (IP), immunofluorescence (IF), and proximal ligation assay (PLA) methods. The ubiquitination of Mcl-1 was studied using denatured IP.
**Results:** Treatment of RASFs with UA (5-10 μM) resulted in a time- and dose-dependent increase in Noxa, but decrease in Mcl-1 expression. Addition of proteasome inhibitor (MG132) showed no further increase in Noxa expression, suggesting transcriptional activation as a potential mechanism behind UA-induced Noxa expression. Evaluation of the signaling pathways showed that UA induced temporal expression of hypoxia-inducible factor-1 α (HIF-1α) in RASFs. Furthermore, our results showed that UA utilizes Akt, p38-MAPK, and JNK/SAPK signaling pathways to activate Noxa expression in RASFs. Utilizing inhibitors of JNK/SAPK (SP600125), p38-MAPK (SB203580), Akt (LY294002), and HIF-1α (HIF-1α inhibitor) pathways, we showed that inhibition of JNK/SAPK pathway significantly reduced UA-mediated upregulation of Noxa. In addition, the results from PLA and IF studies in UA-treated RASFs showed that Noxa co-localizes with Mcl-1 predominantly in the non-nuclear compartment of the cell, suggesting its association with Mcl-1 in ‘priming’ Mcl-1 for proteosomal degradation. Interestingly, the IP of Mcl-1 under denatured condition after UA treatment and subsequent Western blot analysis showed an increase in K48-linked, but not K63-linked, ubiquitin chains tagged to Mcl-1. This K48 polyubiquitylation of Mcl-1 appears to be mediated by Mule, a HECT domain containing E3 ubiquitin-protein ligase, since UA treatment of RASFs preferentially induced the recruitment of Mule rather than SCFβ-TrCP to Noxa/Mcl-1 complex to facilitate Mcl-1 degradation.

**Conclusion:** Taken together, these results suggest that UA induces Noxa expression via JNK pathway and facilitates Mcl-1 association with E3 ubiquitin ligase Mule to activate Mcl-1 degradation that sensitizes RASFs to apoptosis. These findings not only unveil a novel mechanism of UA in inducing apoptosis of RASFs, but also a potential new approach to treat RA.

**Disclosure:** E. Kim, None; S. Agere, None; S. Khuder, None; S. Ahmed, None.


**Abstract Number: 1410**

**Tyrosine Kinase Receptor Axl Is Down Regulated in Highly Inflamed Rheumatoid Synovium and Negatively Correlates with Markers of Disease Activity**

**Alessandra Nerviani**, Sara Pagani, Daniele Mauro, Frances Humby, Stephen Kelly, Felice Rivellesi, Gloria Lliso Ribera, Myles J. Lewis, Michele Bombardieri and Costantino Pitzalis, 1Centre for Experimental Medicine and Rheumatology, William Harvey Research Institute, Barts and The London, School of Medicine and Dentistry, Queen Mary University of London, London, United Kingdom, 2Rheumatology, Centre for Experimental Medicine and Rheumatology, William Harvey Research Institute, Barts and The London, School of Medicine and Dentistry, Queen Mary University of London, London, United Kingdom, 3William Harvey Research Institute, Centre for Experimental Medicine and Rheumatology, William Harvey Research Institute, Barts and The London, School of Medicine and Dentistry, Queen Mary University of London, London, United Kingdom

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster II  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Emerging evidence highlighted the role of Tyro3, Axl and Mer Tyrosine Kinase receptors (TAMs) and their ligands Gas6 and ProteinS in the pathogenesis of autoimmunity; however, little is known about their expression and function in Rheumatoid Arthritis (RA). Axl is able to inhibit the pro-inflammatory cascade in Antigen-Presenting-Cells. Its soluble form (sAxl) behaves as a potent decoy receptor for the ligand Gas6, thus playing an essential role in regulating TAMs functions. Given the crucial role of Axl receptor and its ligand Gas6 in controlling inflammation, we aimed to characterise their expression and function in RA.

**Methods:**

Biologic samples were collected from patients with early inflammatory arthritis (disease duration <12 months) DMARDs and steroids-naïve; all patients underwent an US-guided synovial biopsy of the most inflamed accessible joint before starting treatment. Only patients diagnosed with RA according to ACR/EULAR 2010 criteria were included in this study. Axl/Gas6 expression was evaluated: i) in synovial tissue at gene expression level by next generation sequencing (81 patients); ii) in synovial tissue at protein
Results:

Axl mRNA levels, but not GAS6, were significantly down regulated in highly inflamed synovial tissues containing B/T cells ectopic structures compared to non-lymphoid synovitis (p<0.001) and negatively correlated with the synovitis score (r -0.48). Axl gene expression showed a significant strong negative correlation with indexes of disease activity, including ESR, CRP, swollen joint count and DAS28. At protein level, Axl was predominantly detected in cells forming the lining layer or in close association with blood vessels, independently of the synovial pathotype. In RA synovial fluids, sAxl was significantly more abundant in patients characterised by high-inflamed lymphoid synovitis compared to non-lymphoid (28.55 ± 12.99 ng/ml versus 4.86 ± 2.18 ng/ml, p<0.05); moreover, synovial fluid levels of sAxl positively correlated with the synovitis score (r 0.55) and with systemic inflammation (sAxl/ESR r 0.56). In an in vitro system of cultured RA FLS, sAxl shedding and release in the supernatant was significantly increased upon treatment with TNFα in comparison with untreated synovial fibroblasts.

Conclusion:

Axl is down regulated in highly inflamed RA synovial tissues and negatively correlates with multiple markers of disease activity. It can be shed and released into the synovial fluid and its levels are higher in presence of high-inflamed synovitis and positively correlate with systemic inflammation. TNFα is able to enhance Axl proteolytic cleavage from RA synovial fibroblasts. In conclusion, the dysregulation of the TAM system could provide a novel mechanistic explanation of the persistent inflammation characterizing the RA joints but could also be potentially exploited for therapeutic strategies in order to regain tissue homeostasis.

Disclosure: A. Nerviani, None; S. Pagani, None; D. Mauro, None; F. Humby, None; S. Kelly, None; F. Rivellese, None; G. Lliso Ribera, None; M. J. Lewis, None; M. Bombardieri, None; C. Pitzalis, None.


Abstract Number: 1411

Protein Tyrosine Phosphatase Non-Receptor 22 / C-Src Tyrosine Kinase Complex Down-Regulated in Patients with Rheumatoid Arthritis

Sara Remuzgo-Martínez1, Fernanda Genre1, Raquel López-Mejías1, Santos Castañeda2, Alfonso Corrales1, Pablo Moreno Fresneda2–3, Begoña Ubilla1, Verónica Mijares1, Virginia Portilla1, Jesús González-Vela1, Trinitario Pina1, J. Gonzalo Ocejo-Vinyals4, Juan Irure-Ventura4, Ricardo Blanco1, Javier Martín5, Javier Llorca6 and Miguel Angel González-Gay7, 1Epidemiology, Genetics and Atherosclerosis Research Group on Systemic Inflammatory Diseases, IDIVAL, Santander, Spain; 2Rheumatology Division, Hospital Universitario La Princesa, IIS-IP, Madrid, Spain; 3Rheumatology, Rheumatology Division, Hospital Universitario La Princesa, IIS-IP, Madrid, Spain; 4Immunology Division, Hospital Universitario Marqués de Valdecilla, Santander, Spain; 5Instituto de Parasitología y Biomedicina ‘López-Neyra’, CSIC, PTS Granada, Granada, Spain; 6Department of Epidemiology and Computational Biology, School of Medicine, University of Cantabria, and CIBER Epidemiología y Salud Pública (CIBERESP), IDIVAL, Santander, Spain; 7Epidemiology, Genetics and Atherosclerosis Research Group on Systemic Inflammatory Diseases, IDIVAL and School of Medicine, University of Cantabria, Santander, Spain

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Protein tyrosine phosphatase non-receptor 22 (PTPN22) binds to C-Src tyrosine kinase (CSK) forming a key regulator complex in autoimmunity1. In this regard, PTPN22 is the main non-HLA genetic risk factor involved in rheumatoid arthritis (RA) susceptibility2 and several PTPN22 single-nucleotide polymorphisms (SNPs) have been significantly related with RA3. Moreover, PTPN22 expression profiles have been proposed as biomarkers of RA4. Nevertheless, the potential influence of PTPN22 SNPs on PTPN22 expression in RA has not been elucidated and there is no information of the role of CSK in RA. Accordingly, we
determined if the most relevant PTPN22 (rs2488457, rs2476601 and rs33996649) and CSK (rs34933034 and rs1378942) polymorphisms may influence on PTPN22 and CSK expression in peripheral blood of RA patients when compared to healthy controls.

Methods:

PTPN22 and CSK mRNA expression was assessed by quantitative real-time PCR in peripheral blood samples from 89 patients with RA, who met the 1987 ACR and the 2010 ACR/European League Against Rheumatism criteria for RA\(^5\-\,6\), and 43 healthy controls recruited from Hospital Universitario Marqués de Valdecilla (Santander, Spain) and Hospital Universitario La Princesa (Madrid, Spain). PTPN22 (rs2488457, rs2476601 and rs33996649) and CSK (rs34933034 and rs1378942) were genotyped by TaqMan SNP genotyping assays. Differences in PTPN22 and CSK expression between patients and controls stratified according to their genotype for each SNP were analyzed by Student’s t test. All the results were adjusted by sex, age at time of study and cardiovascular risk factors.

Results: A significant down-regulation of PTPN22 expression in patients with RA carrying PTPN22 rs2488457 and rs2476601 mutant alleles compared to controls was observed (p=0.009 and p=0.008, respectively). Furthermore, patients with RA carrying CSK rs1378942 mutant allele showed a significantly lower CSK expression than healthy individuals (p<0.0001).

Conclusion: Our study shows for the first time that the mutant allele of PTPN22 rs2488457, PTPN22 rs2476601 and CSK rs1378942 influences on the down-regulation of PTPN22 and CSK, respectively, in RA. The transcriptional suppression of this PTPN22/CSK complex, may have a noteworthy clinical relevance in patients with RA, playing an important role in disease diagnosis and progression.


Fundings: This study was supported by European Union FEDER funds and “Fondo de Investigación Sanitaria” (grant PI12/00060 and PI15/00525) from the Instituto de Salud Carlos III (ISCIII, Health Ministry, Spain). This work was also partially supported by RETICS Programs RD12/0009 (RIER) from ISCIII, and in part by grants from the European IMI BTCure Programme. SR-M is supported by funds from the RETICS Program (RIER) from the ISCIII (RD16/0012/0009). FG is a recipient of a Sara Borrell postdoctoral fellowship from the ISCIII (CD15/00095). RL-M is supported by funds of the Miguel Servet type I programme from the ISCIII (CP16/00033).

Disclosure: S. Remuzgo-Martínez, None; F. Genre, None; R. López-Mejías, None; S. Castañeda, None; A. Corrales, None; P. Moreno Fresneda, None; B. Ubilla, None; V. Mijares, None; V. Portilla, None; J. González-Vela, None; T. Pina, None; J. G. Ocejo-Vinyals, None; J. Irure-Ventura, None; R. Blanco, None; J. Martín, None; J. Llorca, None; M. A. González-Gay, None.


Abstract Number: 1412

**Yra-1909 suppresses Production of Pro-Inflammatory Mediators and MMPs through Downregulating Akt, p38, JNK and NF-κb Activation in Rheumatoid Arthritis Fibroblast-like Synoviocytes**

Hyun Jung Yoo\(^1,\)\(^2\), Jeong Yeon Kim\(^1\), Shin Eui Kang\(^1\), Ji Seok Yoo\(^3\), Yong Nam Lee\(^3\), Dong Goo Lee\(^3\), Ji Soo Park\(^1\), Eun Bong Lee\(^4\), Eun Young Lee\(^4\) and Yeong Wook Song\(^2,\)\(^5\), \(^1\)Department of Molecular Medicine and Biopharmaceutical Sciences, Graduate School of Convergence Science and Technology, Seoul National University, Seoul, Korea, Seoul, Korea, Republic of (South), \(^2\)Division of Rheumatology, Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea, Seoul, Korea, Republic of (South), \(^3\)Central R&D Institute, Yungjin Pharm Co., Ltd., Suwon, Korea, Suwon, Korea, Republic of (South), \(^4\)Division of Rheumatology, Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea, Republic of (South), \(^5\)Department of Molecular Medicine and Biopharmaceutical Sciences, Graduate School of Convergence Science and Technology, and College of Medicine, Seoul National University, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Background/Purpose: Rheumatoid arthritis (RA) is characterized by hyperplastic synovial pannus tissue, which mediates destruction of cartilage and bone. Fibroblast-like synoviocyte (FLS) are a key component of the invasive pannus and have a major role in the initiation and perpetuation of destructive joint inflammation. *Stauntonia hexalphylla* (Lardizabalaceae) is widely distributed in Korea, Japan and China, and is a popular herbal supplement in Korean and Chinese folk medicine owing to its analgesic, sedative, and diuretic properties. However, the exact pharmacological effects of *S. hexalphylla* extract, particularly its effect on inflammation, are not known. We investigated the suppressive effects of *S. hexalphylla* extract, YRA-1909 on the aggressiveness of lipopolysaccharide (LPS) - induced RA-FLS.

Methods: RA-FLS were cultured from synovial specimens obtained from RA patients undergoing joint replacement therapy. Inflammatory cytokines/chemokines level was measured by multiplex cytokine ELISA. Matrix metalloproteinase-2 (MMP-2) activity was measured using gelatin zymography. The expression of p-ERK1/2, p-p38, p-JNK and p-Akt was detected by Western blot analysis. The location of NF-κB p65 and expression of pro-inflammatory mediators in RA-FLS was detected by immunofluorescence microscope.

Results: YRA-1909 inhibited the production of pro-inflammatory cytokines, chemokines and matrix metalloproteinases (MMPs) including tumor necrosis factor-α, interleukin-6 (IL-6), IL-17A, CXCL8, CXCL10, MMP-1, 2, 3, 9 and 13 in RA-FLSs. Moreover, YRA-1909 suppressed LPS-induced MMP-2 enzyme activity and expression of MMP-2 and MMP-9 in RA-FLSs. YRA-1909 inhibited LPS-induced nuclear factor kappa B (NF-κB) activation by reducing the phosphorylation of p65 at Ser468 and Ser536. YRA-1909 also suppressed nucleus translocation of p65. Furthermore, YRA-1909 suppressed LPS-induced phosphorylation Akt and mitogen-activated protein kinases (MAPKs), including JNK1/2, and p38 signaling.

Conclusion: YRA-1909 reduces production of inflammatory cytokines/chemokines via inhibition of MMP-2 activity and MAPKs-NF-κB signaling pathway in activated RA-FLS. These observations suggest that YRA-1909 might be useful for the development of new anti-inflammatory agents.

Disclosure: H. J. Yoo, None; J. Y. Kim, None; S. E. Kang, None; J. S. Yoo, None; Y. N. Lee, None; D. G. Lee, None; J. S. Park, None; E. B. Lee, None; E. Y. Lee, None; Y. W. Song, None.

role in antigen presentation. Our aim was to investigate if AIRE is expressed and can regulate gene transcription in primary RA-FLS and if AIRE is present in synovial tissue in RA.

Methods:

Primary FLS were stimulated by proinflammatory cytokines for 12-24 hours before qPCR, confocal microscopy and ImageStreamX flow cytometry for AIRE expression. Stimulated or unstimulated control or AIRE-silenced RA-FLS samples were subjected to RNA seq. Differential gene expression and pathway analyses were performed. Synovial tissues from RA and control osteoarthritis (OA) patients were subjected to confocal microscopy.

Results: No AIRE expression was detected in unstimulated FLS. However, AIRE mRNA expression was induced up to 222±102 fold by IL-1β in RA-FLS compared with unstimulated (p=0.009, n=3). In OA-FLS AIRE was induced 39±9 fold (p<0.0001, n=6) by IL-1β and 10±5 fold (p=0.011) by TNF compared with unstimulated. A synergistic effect was seen using IL-1β + TNF (66±33 fold, p=0.009). The AIRE induction was significantly higher in RA than OA-FLS (p=0.009). AIRE protein expression was detected in stimulated RA-FLS. RNAseq analysis identified 55 (adjP-value<0.05) genes regulated by AIRE in RA-FLS of which 33 are annotated as interferon-γ response genes. The top-ranked network by pathway analysis was "Dermatological diseases and conditions, organismal injury and abnormalities, connective tissue disorders" with a score of 38. AIRE expressing cells were present in lining and sublining in RA but not in OA synovium.

Conclusion:

AIRE is induced by TNF and IL-1β in primary RA-FLS and regulates the expression of interferon-γ response genes suggesting an immune-modulatory role in these cells. AIRE is expressed in the RA synovium supporting a role of AIRE in arthritis.

Disclosure: B. Bergström, None; C. Lundqvist, None; H. Carlsten, None; O. Ekwall, None; A. K. Hultgård Ekwall, None.


Abstract Number: 1414

Stimulation with Resistin Upregulates Chemokine Production By Fibroblast-like Synoviocytes from Patients with Rheumtoid Arthritis

Hiroshi Sato1, Sei Muraoka1, Natsumi Kurunoki1, Shotaro Masuoka1, Soichi Yamada1, Toshio Imai2, Shinichi Kawai3 and Toshihiro Nanki1, 1Division of Rheumatology, Department of Internal Medicine, Toho University School of Medicine, Tokyo, Japan, 2KAN Research Institute, Inc., Kobe, Japan, 3Department of Inflammation and Pain Control Research, Toho University School of Medicine, Tokyo, Japan
First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Adipose tissue synthesizes and releases physiologically active molecules that are known as adipokines. Resistin, an adipokine, has been widely studied the regulation of glucose homeostasis and insulin sensitivity. Moreover, resistin also plays an important role of inflammation. We previously reported that serum level of resistin correlated with the disease activity of rheumatoid arthritis (RA). However, the pathogenic role of resistin has not been elucidated. In this study, we examined the stimulatory effect of resistin on fibroblast-like synoviocytes (FLSs) form RA patients.

Methods: Expression of resistin and the receptor, adenylyl cyclase-associated protein 1 (CAP1), in the synovial tissue from RA and osteoarthritis (OA) was examined by immunohistochemistry. FLSs were incubated with resistin for 18 hours. Then, total RNA was extracted, and the gene expression profile was analyzed by RNA sequencing. Concentration of chemokines in the culture supernatant was determined by enzyme-linked immunosorbent assay (ELISA). Expression of CAP1 was examined by RT-PCR and Western blotting. To verify signaling of resistin, we pretreated FLSs with a PKA inhibitor, KT5720, or transfected siRNA for CAP1 before stimulation with resistin.
**Results:** Resistin and CAP1 was abundantly expressed in the RA synovial tissue. Resistin expression was minimal in the OA synovium. Double immunofluorescence staining revealed that CD68-positive macrophages expressed resistin in RA synovium. CAP1 was expressed by cadherin-11-positive FLSs in RA. RT-PCR and Western blotting showed that *in vitro* cultured FLSs also expressed CAP1. RNA sequencing revealed that expressions of 18 genes, including 7 chemokines (CXCL1, CXCL2, CXCL3, CXCL5, CXCL6, CXCL8 and CCL2), from RA FLSs were increased more than 2 folds by stimulation with resistin. Production of CXCL8 and CCL2 in the culture supernatant of FLSs was increased by resistin. Pretreatment with KT5720 or transfection with CAP1 siRNA suppressed resistin-induced CXCL8 production by FLSs.

**Conclusion:** Resistin might play an important role in the pathogenesis of RA via upregulation of chemokine production in the synovial tissue.

**Disclosure:** H. Sato, None; S. Muraoka, None; N. Kusunoki, None; S. Masuoka, None; S. Yamada, None; T. Imai, None; S. Kawai, None; T. Nanki, None.


Abstract Number: 1415

**TNF-Induced IRF1 Is Critical for the Inflammatory Gene Expression in Fibroblast-like Synoviocytes**

**Michael Bonelli**¹, Karolina von Dalwigk², Birgit Niederreiter¹, Thomas Pap³, Josef S. Smolen⁴, Hans Peter Kiener¹ and Thomas Karonitsch¹, ¹Rheumatology, Medical University of Vienna, Vienna, Austria, ²Department of Rheumatology, Medical University of Vienna, Vienna, Austria, ³Institute of Musculoskeletal Medicine, University Hospital Muenster, Muenster, Germany, ⁴Medical University Vienna, Division of Rheumatology, Department of Internal Medicine III, Vienna, Austria

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster II

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Fibroblast-like synoviocytes (FLS) are increasingly recognised as major pathogenic cells in synovial inflammation of patients with Rheumatoid Arthritis (RA). In response to pro-inflammatory stimuli, such as TNF, FLS produce vast amounts of cytokines and chemokines that help to recruit and activate immune cells and drive the local inflammatory process. The pathways and transcription factors that determine the inflammatory response in FLS are, however, largely unexplored. Here, we investigated the potential contribution of the transcription-factor IRF1 to the inflammatory gene expression in FLS.

**Methods:** Expression of IRF1 in synovial tissue samples (12 RA and 8 osteoarthritis (OA) patients) was assessed by immunohistochemistry (IHC). Moreover, FLS were isolated according to established protocols and cultured using 2-D or 3-D culture techniques. IRF1 expression in response to TNF was determined by western blots, qPCR, immunofluorescence microscopy or IHC. FLS were also stimulated with TNF in the presence or absence of IRF1 siRNA pools. Expression of pro-inflammatory cytokines and chemokines was measured by qPCR.

**Results:** IRF1 expression was significantly increased in rheumatoid synovial tissues as compared to patients with OA on protein level. RA-FLS stimulation with TNF *ex vivo* caused rapid upregulation of IRF1 and proved the involvement of TNF in the regulation of IRF1. Immunofluorescence analysis further revealed that IRF1 was mainly localized in the nucleus of TNF-stimulated FLS. Moreover, also chronic TNF exposure of FLS grown in a 3-D synovial tissue culture system promoted the expression of IRF1. SiRNA-mediated knockdown of IRF1 in FLS significantly reduced the TNF-induced expression of pro-inflammatory cytokines and chemokines, such as IL6, CCL7, CXCL11 and TNFSF13B, which confirmed the role of IRF1 as a critical regulator of proinflammatory genes in RA FLS.

**Conclusion:** Our data reveal that IRF1 is crucial for the inflammatory response of FLS and support the idea that IRF1 might be an exciting therapeutic target in patients with RA.
Higher Expression of Type 1 Interferon in Synovitis of Patient with Undifferentiated Arthritis before They Met Rheumatoid Arthritis Criteria Compared to Established Rheumatoid Arthritis. a Retrospective Study with 14 Years of Follow-up

Andrea Cuervo1, Raquel Celis2, Julio Ramírez3, Alicia Usategui4, Regina Faré5, M. Victoria Hernández6, Virginia Ruiz-Esquide3, Jose Inciarte-Mundo7, Raimon Sanmartí8, Jose L. Pablos9 and Juan D. Cañete7, 1Arthritis Unit. Rheumatology Dpt, Arthritis Unit, Rheumatology Dpt, Hospital Clinic of Barcelona and IDIBAPS, Barcelona, Spain, 2Arthritis Unit, Rheumatology Department, Arthritis Unit, Rheumatology Dpt, Hospital Clinic of Barcelona and IDIBAPS, Barcelona, Spain, 3Rheumatology Service, Hospital Clínica de Barcelona, Barcelona, Spain, 4Grupo de Enfermedades Inflamatorias y Autoinmunes, Instituto de Investigación Hospital 12 de Octubre (i+12), Madrid, Spain, 5Instituto de Investigación Hospital 12 de Octubre (i+12), Madrid, Spain, 6Hospital Clinic. Barcelona. Spain, Barcelona, Spain, 7Rheumatology Department, Arthritis Unit, Rheumatology Dpt, Hospital Clinic of Barcelona, Barcelona, Spain, 8Arthritis Unit, Rheumatology Dpt, Hospital Clinic of Barcelona, Barcelona, Spain, 9Servicio de Reumatologia, Hospital 12 de Octubre, Madrid, Spain

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Undifferentiated Arthritis (UA) is defined as an inflammatory oligo/poly arthritis that does not fulfil criteria for a definitive diagnosis. Delay in diagnosis and treatment leads to poor prognosis. The aim is to identify synovial biomarkers that may be useful to diagnose patients with early UA.

Methods: Retrospective longitudinal study. Patients with UA followed in our Arthritis Unit, who underwent arthroscopy between 2000 and 2014. Synovial biopsy were stained by immunohistochemistry (IHQ) with the following antibodies: antiCD3 (T cells), antiCD20 (B cells), antiCD79 (preplasma cells), antiCD138 (plasma cells), antiCD31(vessels), antiCD68 (macrophages), antiCD15 (neutrophils), antiCD117 (mast cells), antihsp47 (fibroblasts), and quantified by Digital Image Analysis (Olympus). The same antibodies were evaluated in RA and PsA control groups. A transcriptomic analysis was performed to study different pathways of inflammation; only the Type 1 Interferon pathway shown differences between RA and PsA, IHQ with MxA (one of the gene of Type 1 IFN signature) was performed.

Results: 54 UA and 78 controls were included. Table 1 shows the clinical, serological and demographic characteristics at time of synovial biopsy. Among patients with UA, 24 (44%) patients met criteria for RA and 30 (56%) for PsA during follow-up. Synovitis of patients with UA had higher macrophage(CD68+) density in total tissue(p=0.008) and sublining(SL)(p=0.012) than the control group. The UA that evolved to RA had a higher density of CD3 T lymphocytes than the control RA group(p=0.014). No differences were observed in cells of adaptive immunity(CD20 B lymphocytes, CD138 plasma cells), innate immunity(CD117 mast cells, CD15 neutrophils), vessels(CD31) between the 4 groups. The area(%) stained by anti-hsp47 (synovial fibroblasts) in SL was higher in the RA control group than in the PsA(p=0.003). The expression of MxA was increased in pre-RA Group compare to RA control (p=0.036) especially in patients with synovial lymphoidneogenesis.

Conclusion: This is the first immunohistological study of synovitis in a significant group of patients with UA who developed AR or PsA during follow-up. Although there are some differences between the UA and control groups in the density of CD68+
macrophages and lymphocytes T CD3+, these do not appear to be useful for an early diagnosis of UA. On the other hand, unlike the results of some previous studies, we not found differences between the cellular infiltrate (adaptive immunity, innate immunity or vessels) in patients with RA and PsA. The Type 1 Interferon pathway could be a biomarker in patients with UA who develop RA, but a prospective study would be necessary to validate this results. The fact that some patients with UA were undergoing treatment prior to synovial biopsy and its retrospective character limit the results of this study.


Disclosure: A. Cuervo, None; R. Celis, None; J. Ramírez, Gebro, 2; A. Usategui, None; R. Faré, None; M. V. Hernández, None; V. Ruiz-Esquide, None; J. Inciarte-Mundo, None; R. Sanmarti, None; J. L. Pablos, None; J. D. Cañete, None.


Abstract Number: 1417

Mitophagy Defect in Fibroblast-like Synoviocytes of Rheumatoid Arthritis Is Improved By Pyruvate Treatment

Jeong Yeon Kim¹,², ShinEui Kang³,⁴, Hyun Jung Yoo¹,⁵, Ji Soo Park¹,², Sehui Shon¹,², Eun Young Lee², Eun Bong Lee⁵ and Yeong Wook Song¹,⁶, ¹Department of Molecular Medicine and Biopharmaceutical Sciences, Graduate School of Convergence Science and Technology, Seoul National University, Seoul, Korea., Seoul, Korea, Republic of (South), ²Division of Rheumatology, Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea., Seoul, Korea, Republic of (South), ³Department of Molecular Medicine and Biopharmaceutical Sciences, Graduate School of Convergence Science and Technology, Seoul National University, Seoul, Korea., Seoul, Korea, Republic of (South), ⁴Division of Rheumatology, Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea., Seoul, Korea, Republic of (South), ⁵Division of Rheumatology, Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea, Republic of (South), ⁶Department of Molecular Medicine and Biopharmaceutical Sciences, Graduate School of Convergence Science and Technology, and College of Medicine, Seoul National University, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017

Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster II

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM

Background/Purpose:

Fibroblast-like synoviocytes (FLS) in the synovial intimal lining produce pro-inflammatory cytokines resulting in increase of joint inflammation. Recent studies about the cellular metabolism in FLS offered novel approaches to understand the inflammation in rheumatoid arthritis (RA). However, it has been unknown about mitochondrial dysfunction and metabolic change in RA. Mitochondria are very dynamic organelle and dysfunctional mitochondria are removed by mitophagy for cellular homeostasis. In addition, it was reported that mitochondrial dysfunction may be induced by mitophagy defect and that treatment with pyruvate protects fibroblast senescence induced by mitochondrial dysfunction. In this study, we show that RA FLS has mitophagy defect which was improved by treatment with pyruvate.

Methods:

To analyze mitochondrial function in RA FLS, we determined mitochondria membrane potential by TMRM staining and FACS analysis. Mitochondrial respiration and glycolysis were measured using a Seahorse Bioscience Extracellular Flux Analyzer (XF24). Defective mitochondria are degraded by autophagy. We analyzed LC3b and p62 protein levels by Western-blotting. Cells were transfected with GFP-tagged LC3 expression vector. Mitochondria were stained by MitoTracker Deep Red and analyzed by confocal microscopy. Mitophagy was evaluated by transmission electron microscopy (TEM). The pyruvate effect on mitophagy process was
analyzed by the change of fluorescence of mitochondria-targeted mKeima (mt-mKeima) using confocal microscopy. Pro-inflammatory cytokines were measured by qRT–PCR and ELISA.

**Results:**

Mitochondrial membrane potential (MMP), oxygen consumption rate (OCR) and the extracellular acidification rate (ECAR) were significantly increased in RA FLS compared with OA FLS. We also found that the abundance of LC3-b protein and p62 protein in RA FLS and the increase of colocalization of GFP-LC3 puncta with mitochondria in RA FLS. In addition, TEM and mt-mKeima confocal analysis revealed the accumulation of abnormal mitochondria and the dysregulation of mitophagy in RA FLS compared with OA FLS. Interestingly, these mitophagy defect and metabolic change such as increase of OCR, ECAR and MMP in RA FLS recovered by treatment with pyruvate. In addition, pyruvate decreased IL-6 and IL-8 production in RA-FLS.

**Conclusion:**

Pyruvate improved mitophagy defect and suppressed proinflammatory cytokine production in RA FLS.

**Disclosure:** J. Y. Kim, None; S. Kang, None; H. J. Yoo, None; J. S. Park, None; S. Shon, None; E. Y. Lee, None; E. B. Lee, None; Y. W. Song, None.


**Abstract Number: 1418**

**The Value of Adalimumab Trough Levels and Clinical Assessments in Predicting Clinical Response in Patients with Established Rheumatoid Arthritis and an Inadequate Response to Methotrexate**

Josef S. Smolen, Nael Mostafa, Xin Huang, Peter Noertersheuser, Ben Klünder, Kun Chen, Jasmina Kalabic, Iain Sainsbury, Ruud Oerlemans, Stefan Florentinus and Gerd R. Burmester, 1Medical University Vienna, Division of Rheumatology, Department of Internal Medicine III, Vienna, Austria, 2AbbVie Inc., North Chicago, IL, 3AbbVie Deutschland GmbH & Co. KG, Ludwigshafen, Germany, 4AbbVie, Nederland, Hoofddorp, Netherlands, 5Rheumatology and Clinical Immunology, Charité - University Medicine Berlin, Free University and Humboldt University Berlin, Berlin, Germany

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Low trough levels of the tumor necrosis factor inhibitor, adalimumab (ADL), and anti-ADL antibodies (AAA) were reported to be correlated with lack of response at later time points in patients (pts) with rheumatoid arthritis (RA). 1

**Objective:** To assess the ability of ADL trough levels and clinical assessments at Week 12 to predict clinical remission (REM) after 24 weeks (wks) of treatment with ADL +/- methotrexate (MTX) in established RA pts.

**Methods:** Data from MTX inadequate responders (MTX-IR) pts with established RA with available measurement of ADL trough levels and clinical assessments at Wks 12 and 24 from several clinical trials were pooled: for pts who received ADL+MTX combination therapy from DE009, DE019, M10-261 and M13-390; for pts who received ADL monotherapy from DE011, M10-261 and M13-390. Efficacy endpoints at Wk 24 were DAS28-CRP <2.6 and DAS28-CRP low disease activity (LDA, <3.2), remission (REM) and LDA by simplified disease activity index (SDAI, ≤3.3 and ≤11 respectively); REM and LDA by clinical disease activity index (CDAI, ≤2.8 and ≤10 respectively). Each of the pooled datasets was randomly and equally split into training and testing sets. Predictive modeling was performed on the training set, and the best-performing model was selected and validated in the testing set. The performance of the final model was reported based on the testing set.
Results: Based on the cutoffs selected by the predictive model, ADL concentrations at Wk 12 were only slightly predictive for Wk 24 clinical assessment in the ADL monotherapy group, but not in the ADL+MTX group (Table 1). However, based on achievement of the specified CDAI, SDAI or DAS28-CRP score at Wk 12 (selected by the model), pts were correctly predicted to reach Wk 24 REM or LDA with an accuracy of 80-90% and area under the receiver operating characteristic curve (AUC) of 75-90% (Table 2). As an example, pts on ADL monotherapy with DAS28 < 3.3 at Wk 12 had 60% and 70% chance of reaching Wk 24 DAS28-CRP<2.6 and LDA respectively, whereas pts with DAS28 ≥ 3.3 had 0% and 7% chance of achieving Wk 24 DAS28-CRP<2.6 and LDA, respectively (Table 2). Pts on ADL+MTX with Wk 12 SDAI<12.5 had a 25% and 77% chance of achieving SDAI REM and LDA at Wk 24, respectively.

Conclusion: The ADL concentrations at Week 12 selected by the prediction model were weak predictors of disease control at 6 months, especially for pts on ADL+MTX combination therapy. However, using the model-selected cutoffs of composite clinical endpoints at Wk 12, disease control after 6 months of ADL +/- MTX treatment could be correctly predicted in 70-80% of pts.

Table 1. Ability of Week 12 Drug Concentration to Predict Disease Control at Week 24 in Patients Treated with ADL +/- MTX

<table>
<thead>
<tr>
<th>Week 24 Endpoints</th>
<th>Week 12 Cutoff</th>
<th>High conc (µg/ml)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADL Monotherapy</td>
<td>DAS28 &lt; 2.6</td>
<td>&gt;7.62</td>
<td>0.36 (11)</td>
<td>0.05 (42)</td>
<td>0.67</td>
<td>0.85</td>
<td>0.95</td>
</tr>
<tr>
<td></td>
<td>CDAI REM</td>
<td>&gt;7.62</td>
<td>0.27 (11)</td>
<td>0.05 (42)</td>
<td>0.60</td>
<td>0.83</td>
<td>0.95</td>
</tr>
<tr>
<td></td>
<td>SDAI REM</td>
<td>&gt;7.62</td>
<td>0.27 (11)</td>
<td>0.05 (42)</td>
<td>0.60</td>
<td>0.83</td>
<td>0.95</td>
</tr>
<tr>
<td></td>
<td>DAS28 LDA</td>
<td>&gt;6.53</td>
<td>0.42 (12)</td>
<td>0.12 (41)</td>
<td>0.50</td>
<td>0.84</td>
<td>0.88</td>
</tr>
<tr>
<td></td>
<td>CDAI LDA</td>
<td>&gt;6.47 (11)</td>
<td>0.34 (43)</td>
<td>0.46</td>
<td>0.90</td>
<td>0.46</td>
<td>0.90</td>
</tr>
<tr>
<td></td>
<td>SDAI LDA</td>
<td>&gt;6.06 (12)</td>
<td>0.42 (12)</td>
<td>0.17 (41)</td>
<td>0.42</td>
<td>0.83</td>
<td>0.83</td>
</tr>
<tr>
<td>ADL + MTX Combination Therapy</td>
<td>DAS28 &lt; 3.6</td>
<td>&gt;9.03</td>
<td>0.34 (46)</td>
<td>0.34 (46)</td>
<td>0.54</td>
<td>0.85</td>
<td>0.77</td>
</tr>
<tr>
<td></td>
<td>CDAI REM</td>
<td>&gt;7.63</td>
<td>0.12 (8)</td>
<td>0.12 (8)</td>
<td>0.95</td>
<td>0.48</td>
<td>0.10</td>
</tr>
<tr>
<td></td>
<td>SDAI REM</td>
<td>&gt;7.03</td>
<td>0.11 (79)</td>
<td>0.16 (62)</td>
<td>0.57</td>
<td>0.48</td>
<td>0.11</td>
</tr>
<tr>
<td></td>
<td>DAS28 LDA</td>
<td>&gt;8.87</td>
<td>0.41 (49)</td>
<td>0.42 (83)</td>
<td>0.35</td>
<td>0.62</td>
<td>0.41</td>
</tr>
<tr>
<td></td>
<td>CDAI LDA</td>
<td>&gt;4.50</td>
<td>0.42 (106)</td>
<td>0.44 (32)</td>
<td>0.75</td>
<td>0.24</td>
<td>0.42</td>
</tr>
<tr>
<td></td>
<td>SDAI LDA</td>
<td>&gt;3.09</td>
<td>0.45 (85)</td>
<td>0.47 (85)</td>
<td>0.45</td>
<td>0.45</td>
<td>0.54</td>
</tr>
</tbody>
</table>

Table 2. Ability of Selected Week 12 Clinical Scores to Predict Disease Control at Week 24 in Patients Treated with ADL +/- MTX

<table>
<thead>
<tr>
<th>Week 24 Endpoints</th>
<th>Week 12 Cutoff</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADL Monotherapy</td>
<td>DAS28 &lt; 2.6</td>
<td>0.90</td>
<td>0.60</td>
<td>1.00</td>
<td>0.93</td>
<td>0.96</td>
</tr>
<tr>
<td></td>
<td>CDAI REM</td>
<td>0.94</td>
<td>0.63</td>
<td>1.00</td>
<td>0.94</td>
<td>0.97</td>
</tr>
<tr>
<td></td>
<td>SDAI REM</td>
<td>0.90</td>
<td>0.60</td>
<td>1.00</td>
<td>0.91</td>
<td>0.95</td>
</tr>
<tr>
<td></td>
<td>DAS28 LDA</td>
<td>0.70</td>
<td>0.67</td>
<td>0.98</td>
<td>0.70</td>
<td>0.88</td>
</tr>
<tr>
<td></td>
<td>CDAI LDA</td>
<td>0.93</td>
<td>0.70</td>
<td>0.91</td>
<td>0.87</td>
<td>0.78</td>
</tr>
<tr>
<td></td>
<td>SDAI LDA</td>
<td>0.90</td>
<td>0.80</td>
<td>0.91</td>
<td>0.89</td>
<td>0.81</td>
</tr>
<tr>
<td>ADL + MTX Combination Therapy</td>
<td>DAS28 &lt; 3.3</td>
<td>0.90</td>
<td>0.60</td>
<td>1.00</td>
<td>0.93</td>
<td>0.96</td>
</tr>
<tr>
<td></td>
<td>CDAI REM</td>
<td>0.94</td>
<td>0.63</td>
<td>1.00</td>
<td>0.94</td>
<td>0.97</td>
</tr>
<tr>
<td></td>
<td>SDAI REM</td>
<td>0.90</td>
<td>0.60</td>
<td>1.00</td>
<td>0.91</td>
<td>0.95</td>
</tr>
<tr>
<td></td>
<td>DAS28 LDA</td>
<td>0.70</td>
<td>0.67</td>
<td>0.98</td>
<td>0.70</td>
<td>0.88</td>
</tr>
<tr>
<td></td>
<td>CDAI LDA</td>
<td>0.93</td>
<td>0.70</td>
<td>0.91</td>
<td>0.87</td>
<td>0.78</td>
</tr>
<tr>
<td></td>
<td>SDAI LDA</td>
<td>0.90</td>
<td>0.80</td>
<td>0.91</td>
<td>0.89</td>
<td>0.81</td>
</tr>
</tbody>
</table>

Disclosure: J. S. Smolen, AbbVie Inc, 2,AbbVie Inc, 5; N. Mostafa, AbbVie Inc, 1,AbbVie Inc, 3; X. Huang, AbbVie Inc, 1,AbbVie Inc, 3; P. Noertersheuser, AbbVie Inc, 1,AbbVie Inc, 3; B. Klünder, AbbVie Inc, 1,AbbVie Inc, 3; K. Chen, AbbVie Inc, 1,AbbVie Inc, 3; J. Kalabic, AbbVie Inc, 1,AbbVie Inc, 3; I. Sainsbury, AbbVie Inc, 1,AbbVie Inc, 3; R. Oerlemans, AbbVie Inc, 1,AbbVie Inc, 3; S. Florentinus, AbbVie Inc, 1,AbbVie Inc, 3; G. R. Burmester, AbbVie Inc, Bristol-Myers Squibb, Merck, Roche, Pfizer, and UCB, 2,AbbVie Inc, Bristol-Myers Squibb, Merck, Roche, Pfizer, and UCB, 5,AbbVie Inc, Bristol-Myers Squibb, Merck, Roche, Pfizer, and UCB, 8.


Abstract Number: 1419
Characteristics of Patients with Early Rheumatoid Arthritis Who Have a Delayed Response to Treatment with Methotrexate in Monotherapy or in Combination with Adalimumab

Josef S. Smolen\textsuperscript{1}, Xianwei Bu\textsuperscript{2}, Xin Wang\textsuperscript{2}, Jessica L. Suboticki\textsuperscript{3} and Arthur Kavanaugh\textsuperscript{4}, \textsuperscript{1}Medical University Vienna, Division of Rheumatology, Department of Internal Medicine III, Vienna, Austria, \textsuperscript{2}AbbVie Inc., North Chicago, IL, \textsuperscript{3}AbbVie Inc., Mettawa, IL, \textsuperscript{4}Medicine, University of California, San Diego, La Jolla, CA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: In patients (pts) with rheumatoid arthritis (RA), treat-to-target recommendations call for adjustment of treatment if a target is not met within 3-6 months (mths) of initiation. While some pts continue therapy beyond 3-6 mths despite not achieving the target, it’s unclear if they still can achieve the target, and how the timing of target attainment impacts long-term outcomes.

Objective: To evaluate clinical, functional, and radiographic outcomes based on initial time to low disease activity (LDA) attainment among early RA pts who are naïve to MTX, or are MTX-insufficient responders (MTX-IR).

Methods: This post hoc analysis included pts receiving MTX in monotherapy or in combination with adalimumab (ADA) in 2 randomized, controlled trials (RCTs) of MTX-naïve pts with early RA: PREMIER included a 104-week (wk) RCT\textsuperscript{1}; OPTIMA included a 26 wk RCT followed by treatment adjustments based on a target of LDA at wks 22 and 26\textsuperscript{2}. Pts not achieving stable LDA received open-label (OL) ADA+MTX for an additional 52 wks (MTX-IR). Pts were subgrouped by treatment and time to first LDA event [SDAI ≤11: 0-<3 mths, 3-≤6 mths, >6-≤12 mths]. The following were summarized for each subgroup: mean values and change from baseline (Δ) in SDAI, HAQ-DI and modified total Sharp score (mTSS). The proportions of pts achieving SDAI remission (REM) at 1 year (yr) were assessed.

Results: Roughly equal proportions of pts on MTX alone experienced their first LDA response between 0-<3 mths (21%), 3-≤6 mths (21%), and >6-≤12 mths (17%). More pts on ADA+MTX experienced LDA within 3 mths (0-<3: 45% and 56% for MTX-naïve and MTX-IR backgrounds, respectively), with smaller proportions in the 3-≤6 mths (19% for both MTX-naïve and –IR backgrounds), and >6-≤12 mths groups (14% and 4% for MTX-naïve and MTX-IR backgrounds). Approximately 50% of the 0-<3 mth group across treatments achieved SDAI REM at 1 yr. Interestingly, 10%, 14%, and 8% of the MTX, ADA+MTX (MTX-naïve), and ADA+MTX (MTX-IR) pts who first experienced LDA after 6 mths were in SDAI REM at 1 yr.

Among MTX-naïve pts, pts on ADA+MTX had greater ΔHAQ and smaller ΔmTSS than pts on MTX alone at Wks 26 and 52 (Table 1). Regardless of their time to first SDAI LDA response, pts on MTX monotherapy or ADA+MTX experienced comparable improvements in SDAI, HAQ-DI and comparable ΔmTSS at Wks 26 and 52.

Conclusion: Pts on ADA+MTX achieved a first SDAI LDA response earlier than pts on MTX monotherapy, regardless of whether they were MTX-naïve or MTX-IR. More pts with a very early response went on to achieve SDAI REM at 1 yr. However, pts with a longer time (>6 mths) to their first SDAI LDA response had comparable clinical, functional and radiographic outcomes compared to pts who responded earlier (within 3 or 6 mths). Therefore, achieving a clinical response in the direction of the treatment target, even if not yet achieving it, may be sufficient to continue therapy in appropriate pts.
The Ability of Patients with Early Rheumatoid Arthritis to Taper Low-Dose Glucocorticoids on Methotrexate Monotherapy and in Combination with Adalimumab

Josef S. Smolen1, Prashanth Sunkureddi2, Jaclyn K. Anderson3, Jenny Griffith3, Dingfeng Jiang3, Kun Chen3, Jessica L. Suboticki4 and Arthur Kavanaugh5, 1Division of Rheumatology, Medical University of Vienna and Hietzing Hospital, Vienna, Austria, 2Clear Lake Rheumatology, Nassau Bay, TX, 3AbbVie Inc., North Chicago, IL, 4AbbVie Inc., Mettawa, IL, 5Medicine, University of California, San Diego, La Jolla, CA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017

Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM
Background/Purpose: Low dose glucocorticoids (GCs) are recommended in combination with ≥1 synthetic DMARDs as part of the initial treatment strategy in rheumatoid arthritis (RA), with taper recommended as quickly as is clinically feasible. The purpose of this analysis was to evaluate the ability of patients (pts) with early RA receiving MTX monotherapy or adalimumab (ADA)+MTX to taper and discontinue low-dose GCs and associated impact on outcomes.

Methods: This post hoc analysis included MTX naïve pts receiving PBO+MTX or ADA+MTX in the double-period OPTIMA trial. Pts achieving stable low disease activity (sLDA; DAS28 <3.2 at wks 22 and 26) during the first 26 wks (P1) continued blinded therapy (MTX, ADA continuation) for an additional 52 wks (P2). PBO+MTX pts not achieving sLDA were offered open-label (OL) ADA+MTX in P2 (OL ADA rescue). Pts receiving GCs (≤10 mg/d) at baseline (BL) continued a stable dose through P1; tapering ≤1mg/EOW was permitted in P2. Pts were categorized by GC use in each treatment group. The proportions of pts discontinuing GC were summarized. Outcomes were assessed as change from wk 26 to wk 78. Adverse events (AEs) were summarized.

Results: Of the 926 pts who entered P2 (RA disease duration ~4 months), 207/460 (45%) and 188/466 (40%) in the initial PBO+MTX and ADA+MTX groups, respectively, had GC treatment at BL. BL characteristics appeared similar between pts receiving and not receiving GCs. In P1, the proportions of pts achieving sLDA between those receiving and not receiving GCs in the PBO+MTX group were similar (51% without and 49% with GCs), while in the ADA+MTX group a higher proportion of pts achieved sLDA without GCs (58% without vs 42% with GCs). At the beginning of P2, 54/112 (48%) and 45/105 (43%) pts in the MTX and ADA continuation groups, respectively, were on GCs; 145/348 (42%) pts in the OL ADA rescue group received GCs. Of these pts, equal proportions [57% (n=31), 56% (n=25), and 57% (n=83) from the MTX continuation, ADA continuation, and OL ADA rescue groups, respectively] discontinued GCs during P2. Although slight increases in disease activity were observed, GC discontinuation across the different groups did not result in clinically meaningful changes through wk 78 (Table). Within the 3 P2 treatment groups, the AE profile appeared similar between those receiving and not receiving GCs.

Conclusion: Approximately 60% of early RA pts receiving PBO+MTX or ADA+MTX along with GCs whose treatment was modified based on attainment of sLDA were able to discontinue their GC use without clinically meaningful worsening in disease activity, structural damage or decreases in function. As the current analysis is limited by its retrospective, uncontrolled nature, further studies are needed to prospectively evaluate the ability of pts with early RA to taper or discontinue GCs.

Reference:
Kensuke Kume1, Kanzo Amano2, Susumu Yamada1, Toshikatsu Kanazawa3 and Kazuhiko Hatta4, 1Rheumatology, Hiroshima Clinic, Hiroshima, Japan, 2rheumatology, hiroshima clinic, Hiroshima, Japan, 3rheumatology, hiroshima clinic, hiroshima, Japan, 4Rheumatology, Hatta Clinic, Kure, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Patients with rheumatoid arthritis (RA) have an increased cardiovascular (CV) risk. We should have strategies for primary cardiovascular prevention in RA. We reported Tofacitinib(Tofa) plus methotrexate improve arterial stiffness in RA. How about Tofa monotherapy. To examine the effect of Tofa monotherapy on arterial stiffness with CV disease in conventional DMARDs resistant RA patients in a cohort study design.

Methods: 16 RA patients with moderate to severe active disease despite conventional DMARDs treatment (disease activity score: DAS28>3.2) were received Tofa monotherapy. Arterial stiffness was assessed with cardio-ankle vascular index (CAVI) and augmentation index corrected for a heart rate of 75 beats per minute (AIx@75) at baseline and 24 weeks follow-up. Clinical data were collected at regular visits. CAVI is very similar to pulse wave velocity (PWV), and CAVI measures arterial wall stiffness independent of blood pressure and it is superior to brachial ankle PWV as an index of arterial stiffness.No new all treatments(statin, low lipids drug, and etc.) were allowed.

Results: Treatment with Tofa monotherapy attenuated the CAVI significantly from baseline to 24 weeks follow up(13.62 ± 1.96 and 11.44± 1.65%; p = 0.021). Treatment with Tofa monotherapy attenuated the Aix@75 significantly from baseline to 24 weeks follow up(38.7 ± 11.6, 35.2 ± 8.6 %; p = 0.024). DAS 28-ESR score improved significantly from baseline to 24 weeks(5.56±1.29, 2.61±1.45: p = 0.01). On the other hand, fasting serum total cholesterol TC was significantly increased from baseline to follow-up at 24 weeks (187±28.2mg/dL, 209±19.8mg/dL, p = 0.021). No patients suffered from new CV disease.

Conclusion: These findings suggest that Tofa monotherapy not only reduced RA disease activity but also limited vascular damage despite up-regulating cholesterol in patients conventional DMARDs resistant active RA, as well as Tofa plus methotrexate.

Takaki A et al. Cardio-ankle vascular index is superior to brachial ankle pulse wave velocity as an index of arterial stiffness. Hypertens Res.2008 Jul; 31(7):1347-55

Disclosure: K. Kume, None; K. Amano, None; S. Yamada, None; T. Kanazawa, None; K. Hatta, None.
Background/Purpose: Steroids are used to reduce inflammation and pain among rheumatoid arthritis (RA) patients, but they can cause harmful side effects, and in some patients, difficulty to discontinue/taper the dose. Adalimumab (ADA) has been shown to be effective in treating RA patients with a well-established safety profile. The objective of this study was to determine if patients on ADA treatment were able to discontinue or lower the dose of steroids post-ADA initiation.

Methods: Biologic naïve RA patients who initiated ADA after 2008, and with at least 6 months of continuous therapy were included in the study. The difference in mean steroid dose from ADA initiation (baseline) to 6 months was evaluated for all ADA initiators and by type of therapy (monotherapy/combination therapy with methotrexate). Paired t-tests were used to compare changes. The distribution of steroid dose categories (0 mg, >0 to 5 mg, >5 to 10 mg, >10 to 15 mg and >15 mg) at baseline and 6 months was also described and stratified by ADA monotherapy and combination therapy. Descriptive characteristics at baseline were examined; appropriate tests of comparisons (1-way ANOVA/chi-square/Kruskal-Wallis) were used to compare across type of therapy.

Results: Among 713 biologic naïve ADA initiators who were eligible to participate in the study, 239 (34%) used steroids during the 6 month follow up period: 109 at initiation only, 94 at initiation and follow-up, and 38 at follow-up only. The mean (SD) age of the study population was 55.4 (12.3) years, 73% were female, and the mean (SD) disease duration was 5.1 (7.4) years. Mean (SD) clinical disease activity index at baseline was 20.1 (14.9), with ~70% in moderate/severe disease activity (CDAI>10) and a mean (SD) functional disability index score of 0.5 (0.5) as measured by the modified health assessment questionnaire. Mean steroid dose at baseline was 6.1 mg (6.1) and over the 6 months of therapy, the steroid dose reduced to a mean (SD) dose of 3.6 mg (5.0), with a mean (SD) change of 2.5 mg (8.0) (p<0.0001). Similar dose reductions were seen in ADA monotherapy and combination therapy groups (data not shown). As seen in the table below, approximately 53% of the 201 patients who were on steroids at ADA initiation were able to discontinue the steroid by 6 months.

Conclusion: In this real world study of ADA initiators, approximately half of the patients who received concomitant steroids at initiation were able to discontinue the steroid by 6 months. For those who continued steroids at 6 months, patients were on average able to significantly reduce their dose.

Figure. Distribution of steroid dose at ADA initiation vs steroid dose at the 6-month follow-up visit for all initiators (N=239)
Abstract Number: 1423

Patterns of Prednisone Use in US Patients with Rheumatoid Arthritis Initiating Treatment with Tocilizumab in Routine Clinical Practice

Dimitrios A. Pappas¹, Carol J. Etzel², Jennie Best³, Steve Zlotnick², Taylor Blachley², Gioia Persuitte² and Joel Kremer⁴,
¹Columbia University, New York, NY, ²Corrona, LLC, Southborough, MA, ³Genentech, Inc., South San Francisco, CA, ⁴Albany Medical College and The Center for Rheumatology, Albany, NY
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: There are limited data regarding the impact of tocilizumab (TCZ) treatment on prednisone use in patients with rheumatoid arthritis (RA). The objective of this study was to examine prednisone use among US patients with RA who initiated TCZ in routine clinical practice, overall and stratified by initiation of TCZ as monotherapy (TCZ mono) or in combination with a conventional synthetic DMARD (csDMARD; TCZ combo).

Methods: TCZ-naïve patients enrolled in the Corrona RA registry (NCT01402661) who initiated TCZ on or after January 1, 2010; had a 12-month follow-up visit without discontinuation of TCZ and had prednisone dose information available at the time of TCZ initiation (baseline) and follow-up were included. Outcomes included the proportion of patients with changes in prednisone use (initiation, discontinuation, dose escalation or reduction ≥ 5 mg) and change in Clinical Disease Activity Index (CDAI) score at 12 months. Outcomes were assessed in the overall population and stratified by initiation of TCZ mono or TCZ combo. Baseline patient characteristics were compared between the TCZ mono and TCZ combo groups using 2-sample $t$ tests or Wilcoxon rank-sum tests for continuous variables and chi-square or Fisher exact tests for categorical variables.

Results: Of the 648 eligible patients, 29% initiated TCZ mono and 71% initiated TCZ combo. Patients who initiated TCZ mono were older (mean age, 60.5 vs 57.9 years; $P = 0.01$), weighed less (mean weight, 174.0 vs 184.4 pounds; $P = 0.01$), were less likely to have private insurance (71.8% vs 79.3%; $P = 0.04$) and had used fewer csDMARDs ($P < 0.001$) and tumor necrosis factor inhibitors ($P = 0.03$) compared with TCZ combo. At baseline, 222 patients (34.3%) were receiving prednisone and 426 (65.7%) were not. Changes in prednisone use, including discontinuation and dose reduction ≥ 5 mg, were observed within 6 months after TCZ initiation. Of the patients on prednisone at baseline, 30.6% had discontinued prednisone and 13.1% had decreased the dose after 12 months of TCZ therapy (Table 1). Of those not on prednisone at baseline, only 8.5% initiated prednisone over 12 months of TCZ therapy (Table 1). Changes in prednisone use were not different between TCZ mono and TCZ combo, and there were no differences in CDAI improvement between patients using prednisone vs not using prednisone at baseline, overall or stratified by TCZ mono vs TCZ combo (Table 1).

Conclusion: A considerable proportion of patients initiating TCZ were able to discontinue or lower the dose of prednisone over 12 months. Changes in prednisone use were observed within 6 months after TCZ initiation, were similar regardless of whether TCZ was administered as monotherapy or in combination with csDMARDs and did not result in differences in the observed decrease in disease activity.
**Table 1. Distribution of Prednisone Use and Change in CDAI Score at 12 Months in Patients With RA Who Initiated TcZ as Monotherapy or With a csDMARD**

<table>
<thead>
<tr>
<th>Prednisone Use</th>
<th>Disease Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No Change, n (%)</td>
</tr>
<tr>
<td>All TcZ initiators (N = 648)</td>
<td></td>
</tr>
<tr>
<td>Not on prednisone (n = 426; 66.8%)</td>
<td>390 (91.5)</td>
</tr>
<tr>
<td>On prednisone (n = 222; 34.2%)</td>
<td>115 (51.8)</td>
</tr>
<tr>
<td>TcZ monotherapy initiators (n = 188; 29.0%)</td>
<td></td>
</tr>
<tr>
<td>Not on prednisone (n = 124; 66.0%)</td>
<td>105 (84.7)</td>
</tr>
<tr>
<td>On prednisone (n = 64; 34.0%)</td>
<td>30 (46.9)</td>
</tr>
<tr>
<td>TcZ + csDMARD initiators (n = 468; 71.0%)</td>
<td></td>
</tr>
<tr>
<td>Not on prednisone (n = 302; 65.7%)</td>
<td>285 (94.4)</td>
</tr>
<tr>
<td>On prednisone (n = 158; 34.3%)</td>
<td>85 (53.8)</td>
</tr>
</tbody>
</table>

CDAI, Clinical Disease Activity Index; csDMARD, conventional synthetic disease-modifying antirheumatic drug; N/A, not applicable; RA, rheumatoid arthritis; TcZ, tocilizumab.

* Includes patients with changes in dose of < 5 mg.

Disclosure: D. A. Pappas, Corrona, LLC, 3,AbbVie, 2,AbbVie, 5; C. J. Etzel, Corrona, LLC, 3,Merck Human Health, 9; J. Best, Genentech, Inc., 3,Genentech, Inc., 1; S. Zlotnick, Genentech, Inc., 3,Genentech, Inc., 1; T. Blachley, Corrona, LLC, 3; G. Pursiute, Corrona, LLC, 3; J. Kremer, Corrona, LLC, 3,Corrona, LLC, 1,AbbVie, Amgen, Bristol-Myers Squibb, Genentech, GlaxoSmithKline, Lilly, Pfizer, Regeneron, Sanofi, 5.


**Abstract Number: 1424**

**Impact of Glucocorticoid Therapy on the Efficacy of SC Abatacept or Adalimumab in RA Patients with Inadequate Response to MTX: A Post Hoc Analysis of Data from a Head-to-Head Trial**

Yannick Degboé1,2, Michael Schiff3, Michael Weinblatt4, Roy Fleischmann5, HA Ahmad6 and Arnaud Constantin2,7, 1Toulouse University Hospital, Toulouse, France, 2Université Paul Sabatier, Toulouse, France, 3University of Colorado, Denver, CO, 4Brigham and Women’s Hospital, Boston, MA, 5University of Texas Southwestern Medical Center, Dallas, TX, 6Bristol-Myers Squibb, Princeton, NJ, 7Purpan University Hospital, Toulouse, France

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** In patients with RA, low-dose glucocorticoids (GCs) have been shown to increase clinical, functional, and radiographic efficacy when combined with conventional synthetic DMARDs;1 however, evidence for potentiation of bDMARD efficacy is lacking. The objective was to assess the impact of low-dose GCs on the efficacy of SC abatacept or adalimumab in biologic-naïve patients with active RA and inadequate response to MTX enrolled in the AMPLE trial (NCT00929864).2,3

**Methods:** In this post hoc analysis, efficacy outcomes were compared based on GC therapy at baseline (≤10 mg/day vs no GC) in patients receiving abatacept or adalimumab. Outcomes assessed were: mean change from baseline in DAS28 (CRP), HAQ-DI and modified total Sharp score (mTSS) over time; CDAI and SDAI remission rates, proportion of patients with DAS28 (CRP) < 2.6 and with improvement in HAQ-DI score ≥ 0.3, and radiographic non-progression rates (TSS ≤ SDC [2.2 points]) at Years 1 and 2. 

**Results:** The analysis included 317/318 patients treated with abatacept + MTX (161 GC, 156 no GC) and 326/328 treated with adalimumab +
MTX (162 GC, 164 no GC). Baseline demographics and adverse events during follow-up were similar across groups. At baseline, patients treated with GC had more severe radiographic disease (mean [SD] TSS: abatacept/GC 23.9 [37.9] vs abatacept/no GC 15.8 [26.9], adalimumab/GC 22.8 [32.6] vs adalimumab/no GC 15.6 [23.7]). Baseline disease activity (mean [SD] DAS28 [CRP]) was similar across groups: abatacept/GC 5.7 (1.1) vs abatacept/no GC 5.3 (1.2), adalimumab/GC 5.6 (1.1) vs adalimumab/no-GC 5.5 (1.1). Mean change (95% CI) from baseline in DAS28 (CRP) was significantly greater in the abatacept/GC than in the abatacept/no-GC subgroup at Month 6 (-2.24 [-2.45, -2.04] vs -1.94 [-2.14, 1.74]; p=0.0293), but not at Year 1 or 2, and did not differ significantly by GC treatment in adalimumab-treated patients. The proportions of patients in CDAI or SDAI remission or with DAS28 (CRP) <2.6 were similar in GC and no GC subgroups for both treatments (Figure). Radiographic progression rates at Years 1 and 2 and mean change from baseline in mTSS over 2 years were the same regardless of GC use. The proportion of patients with improvement in HAQ-DI score ≥0.3 was higher in the abatacept/GC subgroup than the abatacept/no GC subgroup at 6 months (70.47 vs 57.64%; p=0.0289) but not at later time points and was not seen in adalimumab-treated patients.

Conclusion: The use of low-dose GC with abatacept or adalimumab in RA patients with inadequate response to MTX has no impact on short-term and medium-term outcomes. This finding could be because patients who entered this trial had active disease despite background GC use and they responded to the addition of an active medication.


---

Disclosures: Y. Degboé None; M. Schiff, AbbVie, BMS, Eli Lilly, JNJ, UCB, 5,AbbVie, BMS, 8; M. Weinblatt, Amgen, BMS, Crescendo Bioscience, UCB, DxtTerity, Sanofi, 2,Amgen, BMS, Crescendo Bioscience, UCB, AbbVie, Lilly, Pfizer, Roche, 5; R. Fleischmann, AbbVie, Amgen, Astellas, AstraZeneca, BMS, Celgene,EMD-Serono, Janssen, Eli Lilly, Merck, Novartis, Pfizer, Roche, Sanofi-Genzyme, UCB, 2,AbbVie, Amgen, BMS, Celgene, GSK, Janssen, Eli Lilly, Novartis, Pfizer, Roche, Sanofi-Genzyme, UCB, 5; H. Ahmad, Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1, 9; A. Constantin, AbbVie, BMS, Lilly, Pfizer, Procter and Gamble, Sanofi, UCB, 5.


Abstract Number: 1425

**Treatment Patterns in Patients with Rheumatoid Arthritis Newly Initiated on Biologic and Non-Biologic Therapy Enrolled in a North American Clinical Registry**
Background/Purpose: Many treatment options are currently available to patients with rheumatoid arthritis (RA), including tumor necrosis factor inhibitors (TNFi’s). While combination therapy of TNFi’s or other biologics with a conventional synthetic disease-modifying antirheumatic drug (csDMARD; commonly methotrexate, leflunomide, sulfasalazine, or hydroxychloroquine) is thought to be the most effective treatment option, few studies have examined changes in treatment initiation over time. This study describes RA treatment patterns among patients newly initiated on biologic and non-biologic therapy over time.

Methods: This retrospective, cohort study included adult patients with RA enrolled in the Corrona RA registry who initiated monotherapy with a biologic or csDMARD or combination therapy between January 1, 2004, and December 31, 2015. Patients were required to have ≥ 6 months of follow-up time after initiation of therapy, with at least one follow-up visit. Patients could belong to one of five cohorts: TNFi monotherapy, other biologic monotherapy, csDMARD monotherapy, combination therapy with TNFi + csDMARD, or combination therapy with other biologic + csDMARD. Cohorts were defined by the first treatment initiation after enrollment into Corrona and were mutually exclusive. The primary outcome of interest was time on therapy. Time periods of interest were 2004-2007, 2008-2011, and 2012-2015; these were based on the year of enrollment into Corrona. Data were analyzed descriptively by cohort.

Results: There were 8,027 patients in this analysis. Overall, the majority of patients were female (77%), white (82%), and biologic-naïve (60%), with mean (SD) duration of RA 7.9 (9.2) years. 9.6%, 4.6%, 37.2%, 37.6%, and 11.0% of patients initiated TNFi monotherapy, other biologic monotherapy, csDMARD monotherapy, combination therapy with TNFi + csDMARD, and combination therapy with other biologic + csDMARD, respectively. Over time, treatment initiation between monotherapy and combination therapy has not changed: about half of patients initiated monotherapy and half combination therapy, mostly TNFi + csDMARD (Table). Mean CDAI at treatment initiation has remained similar within the TNFi monotherapy cohort over the three time periods. Patients who initiated csDMARD monotherapy had the lowest CDAI at treatment initiation, while TNFi and other biologic monotherapy and both combination therapy cohorts had comparable CDAI. Time on drug has remained stable for TNFi monotherapy and decreased for all other cohorts; in the most recent time period, time on drug was similar among all cohorts.

Conclusion: In the Corrona registry, over time, treatment initiation between monotherapy and combination therapy has changed little. Mean time on drug has decreased over time, likely due to the availability of more treatment options and/or the emphasis on achievement of treat-to-target goals.

Table. Disease Activity, RA Duration, and Persistence Among Different Therapy Cohorts Over Time

<table>
<thead>
<tr>
<th>Time period</th>
<th>TNFi</th>
<th>Other biologic</th>
<th>csDMARD</th>
<th>TNFi + csDMARD</th>
<th>Other biologic + csDMARD</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004-2007</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>98</td>
<td>121</td>
<td>29.4</td>
<td>21.2</td>
<td>19.5</td>
<td>1044</td>
</tr>
<tr>
<td>CDAI</td>
<td>18.1</td>
<td>12.9</td>
<td>39.8</td>
<td>19.5</td>
<td>14.5</td>
<td>19.3</td>
</tr>
<tr>
<td>RA duration</td>
<td>10.0</td>
<td>8.8</td>
<td>6.7</td>
<td>7.1</td>
<td>8.1</td>
<td>11.8</td>
</tr>
<tr>
<td>Persistence*</td>
<td>23.3</td>
<td>21.6</td>
<td>29.4</td>
<td>26.7</td>
<td>19.1</td>
<td>20.8</td>
</tr>
<tr>
<td>2008-2011</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>312</td>
<td>112</td>
<td>11.2</td>
<td>5.5</td>
<td>1225</td>
<td>3174</td>
</tr>
<tr>
<td>CDAI</td>
<td>21.1</td>
<td>14.8</td>
<td>38.6</td>
<td>16.7</td>
<td>13.1</td>
<td>24.5</td>
</tr>
<tr>
<td>RA duration</td>
<td>8.6</td>
<td>9.4</td>
<td>8.9</td>
<td>9.2</td>
<td>8.8</td>
<td>9.9</td>
</tr>
<tr>
<td>Persistence*</td>
<td>28.5</td>
<td>27.7</td>
<td>26.7</td>
<td>26.3</td>
<td>24.4</td>
<td>26.7</td>
</tr>
<tr>
<td>2012-2015</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>360</td>
<td>95.5</td>
<td>21.3</td>
<td>6.4</td>
<td>1340</td>
<td>3309</td>
</tr>
<tr>
<td>CDAI</td>
<td>22.5</td>
<td>14.8</td>
<td>13.9</td>
<td>16.4</td>
<td>12.4</td>
<td>23.5</td>
</tr>
<tr>
<td>RA duration</td>
<td>8.8</td>
<td>9.5</td>
<td>12.3</td>
<td>10.7</td>
<td>8.1</td>
<td>10.4</td>
</tr>
<tr>
<td>Persistence*</td>
<td>23.0</td>
<td>14.7</td>
<td>16.9</td>
<td>22.9</td>
<td>23.5</td>
<td>18.7</td>
</tr>
</tbody>
</table>

* Mean time on drug

Disclosure: P. J. Mease, AbbVie, Amgen, Bristol Myers Squibb, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB Pharma, 2,AbbVie, Amgen, Bristol Myers Squibb, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB Pharma, 5,Abbvie, Amgen, Bristol Myers Squibb, Celgene, Genentech, Janssen, Novartis, Pfizer, UCB Pharma, 8; N. Accortt, Amgen, 1,Amgen, 3; M. Liu, Corrona, 3; S. Rebello, Corrona, LLC, 3; M. Gharaibeh, Amgen, 1,Amgen, 3; D. Collier, Amgen, 1,Amgen, 3.

Higher Levels of Interleukin-6 As Well As Soluble Interleukin-6 Receptor Leads to Worse Clinical and Radiographic Prognosis in Rheumatoid Arthritis Patients Treated with Tocilizumab

Naoshi Nishina, Yuko Kaneko, Keiko Yoshimoto and Tsutomu Takeuchi, Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** We have already reported that baseline levels of soluble interleukin-6 receptor (sIL-6R), target of tocilizumab, predicted response to tocilizumab treatment in rheumatoid arthritis (RA) patients. However, there is a report that interleukin (IL)-6 is also one of predictors. The aim of this study is to investigate the association of baseline levels of both IL-6 and sIL-6R with clinical and radiographic response to tocilizumab in patients with RA.

**Methods:** Consecutive RA patients at our institution who received tocilizumab as the first biologic agent from April 2010 to April 2013 were included. Serum levels of sIL-6R and IL-6 were measured by electrochemiluminescence assay at week 0, 4, 24, and 52. According to baseline levels of sIL-6R and IL-6, patients were divided into 3 groups using K-means clustering. Clinical response and radiographic progression were compared among the 3 groups. Differences among 3 groups were analyzed by analysis of variance (ANOVA)

**Results:** Fifty six patients were enrolled. Distribution of sIL-6R and IL-6 at week 0 is shown in Figure 1 and the clusters were named as Group 1, 2 and 3. Mean levels of sIL-6R and IL-6 of Group 1 (n=29) were 46.2 ng/mL and 3.9 pg/mL; Group 2 (n=7), 65.4 ng/mL and 32.8 pg/mL; and Group 3 (n=20), 100.4 ng/ml and 5.6 pg/mL, respectively. Baseline characteristics were comparable among the groups except for RA activity. Mean disease activity score (DAS28-ESR) was higher in Group 2 compared to Group 1 and 3 (4.9 vs 6.2 vs 5.0 for Group 1, 2, and 3, respectively; p=0.02 by ANOVA). Time course of mean DAS28-ESR is shown in Figure 2. Although significant difference was observed only at week 24, mean DAS28-ESR of Group 2 tended to be higher than those of Group 1 and Group 3 (p=0.21, 0.02, and 0.08, respectively at week 4, 24, and 52). Mean yearly progression of van der Heijde modified total Sharp score was worse in Group 2 but without statistical significance (0.2 vs 2.1 vs 0.2, for Group 1, 2, and 3, respectively; p=0.07) as shown in Figure 3.

**Conclusion:** Despite lower levels of sIL-6R, patients with very high levels of IL-6 showed worse clinical and radiographic response to tocilizumab in RA. IL-6 as well as sIL-6R could be strong indicators for the effectiveness of tocilizumab.

![Figure 1. IL-6/sIL-6R at baseline](image-url)


Abstract Number: 1427
Monitoring of Absolute Lymphocyte Count in Patients with Rheumatoid Arthritis Treated with Tofacitinib

Gerd R. Burmester¹, Zoltan Szekanecz², Pinaki Biswas³, Sriram Krishnaswami⁴, Christopher F Mojcik³, Hernan Valdez³, Jamie Geier³ and Sander Strengholt⁵, ¹Rheumatology and Clinical Immunology, Charité - University Medicine Berlin, Free University and Humboldt University Berlin, Berlin, Germany, ²University of Debrecen Faculty of Medicine, Debrecen, Hungary, ³Pfizer Inc, New York, NY, ⁴Pfizer Inc, Groton, CT, ⁵Pfizer Inc, Capelle aan den IJssel, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor for the treatment of RA. Lymphopenia is a frequent feature of RA,¹ and RA medications may also affect absolute lymphocyte count (ALC). Previous analyses showed an increased rate of serious infection (SI) in tofacitinib-treated patients (pts) whose ALCs were <500 cells/mm³, which was the basis for the recommendation to adopt the ALC <500 cells/mm³ threshold for treatment discontinuation. Here we describe the association between ALC and infection events in the tofacitinib RA clinical development program.

Methods: Data were pooled from pts in 19 RA studies (2 Phase [P] 1; 9 P2; 6 P3; 2 long-term extension [LTE] studies [1 LTE ongoing at time of analysis; database not locked at March 2015 cut-off]) across all tofacitinib doses (1, 3, 5, 10, 15, 30 mg twice daily and 20 mg once daily). Exposure-adjusted incidence rates (IRs; pts with event/100 pt-years) and 95% confidence intervals (CIs) for SIs, opportunistic infections (OIs), and herpes zoster (HZ; all reported cases, both serious and non-serious) were calculated for ALC categories: ≥2000, ≥1500–<2000 (normal reference range), ≥1000–<1500, ≥750–<1000, ≥500–<750, and <500 cells/mm³. Numbers needed to harm (NNH) were calculated as reciprocals of the differences in IRs relative to the ALC ≥1500–<2000 category.

Results: Of the 6194 pts (tofacitinib exposure: 19,229 pt-years) in this analysis, 527 (8.5%) reported SIs (IR 2.74 [95% CI: 2.51, 2.98]). The IR for SI in pts with normal ALC (≥1500–<2000 cells/mm³) was 2.49 (2.06, 2.98). IRs were similar in pts with ALC ≥750–<1500 cells/mm³, but increased by 75% to 4.36 (3.10, 5.96) and by 234% to 8.31 (3.05, 18.10) for ALCs ≥500–<750 and <500 cells/mm³, respectively, relative to pts with normal ALC (Figure); however, CIs were wider in the ≥500–<750 and <500 cells/mm³ ALC categories due to smaller pt numbers. For all ALC categories except <500 cells/mm³, IRs for SI with tofacitinib were within the range of published rates for biologic DMARDs (3.04–5.45).² For NNH, 179 and 53 more pts in the ≥750–<1500 and ≥500–<750 cells/mm³ categories, respectively, would need to be treated to experience 1 additional SI event compared with pts with normal ALC ≥1500 cells/mm³. A similar pattern was observed with IRs for OI (0.21 [0.10, 0.38] for normal ALC vs 0.89 [0.38, 1.76] and 1.39 [0.04, 7.75] for ALCs ≥500–<750 and <500 cells/mm³, respectively). There was a trend for increased HZ risk with decreased ALC; IR differences between ALC categories were <2-fold with overlapping CIs and did not inform the selection of an appropriate ALC threshold.

Conclusion: These findings support the recommendation to discontinue tofacitinib in pts with ALC <500 cells/mm³ to decrease the risk of SI. Discontinuation at higher thresholds results in further decreases in SI incidence but also excludes a larger number of pts who will not develop a SI.

References:
Disclosure: G. R. Burmester, Pfizer Inc, 2, Pfizer Inc, Eli Lilly, 5; Z. Szekanecz, None; P. Biswas, Pfizer Inc, 1, Pfizer Inc, 3; S. Krishnaswami, Pfizer Inc, 1, Pfizer Inc, 3; C. F. Mojcik, Pfizer Inc, 1, Pfizer Inc, 3; H. Valdez, Pfizer Inc, 1, Pfizer Inc, 3; J. Geier, Pfizer Inc, 1, Pfizer Inc, 3; S. Streng Holt, Pfizer Inc, 1, Pfizer Inc, 3.


Abstract Number: 1428

Discovery and Characterization of JNJ-61178104, a Bispecific Antibody Against Human Tumor Necrosis Factor (TNF) Alpha and Interleukin (IL)-17A

Fang Shen1, Jennifer F. Nemeth2, Brian Jones1, Ann Cai1, Shannon Hitchcock3, Thai Dinh2, Ravi Malaviya1 and Tatiana Ort1, 1Immunology, Janssen R&D, Spring House, PA, 2Janssen Biotech, Janssen R&D, Spring House, PA, 3Immunology, Janssen R&D, Springhouse, PA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Tumor necrosis factor alpha (TNFa) and interleukin (IL)-17A are pleiotropic cytokines implicated in the pathogenesis of several autoimmune diseases including Rheumatoid Arthritis (RA) and Psoriatic Arthritis (PsA). It has been suggested that TNFa and IL-17A drive independent actions on cellular inflammatory responses resulting in significantly increased proinflammatory mediator...
Targeting both TNFa and IL-17A has been proposed to have potential to achieve better and long lasting efficacy with a favorable safety profile in RA and PsA.

Methods:

JNJ-61178104 is a novel human anti-TNF-a and anti-IL‑17A bispecific antibody. The affinities of JNJ-61178104 binding to TNFa and IL-17A were assessed by surface plasmon resonance. The functional activity of JNJ 61178104 was evaluated in several preclinical cell based assays to characterize neutralization in the conditions where only one or both cytokines were present. Given the bispecific nature of JNJ-61178104, the ability to neutralize both TNFa and IL-17A simultaneously was assessed in a co-culture model. To evaluate pharmacodynamics (PD) activity of JNJ-61178104 in vivo, Balb/c mice were treated with intranasal instillation of TNFa and IL-17A to induced acute lung inflammation. Proinflammatory cytokine production was assessed by ELISA and cellular influx was enumerated in lung lavage.

Results:

JNJ-61178104 binds to both TNFa (KD= 1.88~2.11 x 10⁻¹¹ M) and IL-17A (KD= 2.20~4.53 x 10⁻¹¹ M) with high affinity and inhibits binding of human TNFa to its receptors (IC₅₀ = 0.92~1.96 nM) or human IL-17A to IL-17RA receptor (IC₅₀ = 1.18 nM). JNJ-61178104 also potently neutralizes soluble TNFa (IC₅₀ = 0.22~1.33 nM), transmembrane TNFa (IC₅₀ = 0.74 nM), IL-17A- and IL 17A/F heterodimer (IC₅₀ = 0.32~3.06 nM) -mediated responses in multiple cell based assays.

In a co-culture system consisting of human synovial-like-fibroblast cells isolated from an RA donor and activated human Th1/Th17 cells, either parental anti-TNFa antibody or parental anti-IL-17A antibody only partially inhibit cytokines production, while JNJ-61178104 inhibited IL-6 and GROa production in a dose dependent manner similarly to the combination of parental antibodies.

In the acute pharmacodynamics model, while the parental anti-TNFa antibody or parental anti-IL-17A antibody dosed at 10 mg/kg partially attenuated cell accumulation in the lung, treatment with the JNJ 61178104 at 1 mg/kg, 3 mg/kg, and 10 mg/kg resulted in a significant, dose dependent inhibition of cell influx, with a near complete ablation of total cells/neutrophils in the lung with the highest dose of 10 mg/kg.

Conclusion:

Overall, JNJ-61178104 demonstrated potent functional neutralization of both TNFa and IL-17A driven inflammatory responses in vitro and in vivo preclinical models. Favorable pharmacological profile of JNJ-61178104, i.e., along with significant clinical experience with both TNFα and IL-17A pathways in RA and PsA subjects support the clinical investigation of JNJ-61178104 in autoimmune and inflammatory disease.

Disclosure: F. Shen, Johnson & Johnson, 3,Johnson & Johnson, 1; J. F. Nemeth, Johnson & Johnson, 3,Johnson & Johnson, 1; B. Jones, Johnson & Johnson, 3; A. Cai, Johnson & Johnson, 3; S. Hitchcock, Johnson & Johnson, 3; T. Dinh, Johnson & Johnson, 3; R. Malaviya, Johnson & Johnson, 3,Johnson & Johnson, 1; T. Ort, Johnson & Johnson, 3,Johnson & Johnson, 1.

Incidence Rates of Adverse Events with Death As an Outcome during Abatacept Treatment in RA: Results from an Integrated Data Analysis from 16 Clinical Trials

D Fleming1, TA Simon1, A Torbeyns2, U Meier-Kriesche1 and A Johnsen1, 1Bristol-Myers Squibb, Princeton, NJ, 2Bristol-Myers Squibb, Braine l’Alleud, Belgium

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM
**Background/Purpose:** Patients with RA have a 1.5–2-fold increased risk of mortality compared with the general population. The association between mortality rates and different RA treatments has been investigated: increased (glucocorticoids), decreased (MTX), and no impact of treatment on mortality (TNF inhibitors) have been reported. To date, the impact of treatment with the selective T-cell co-stimulation modulator abatacept on mortality across clinical trials have not been comprehensively reported.

**Methods:** The risk of mortality in adult patients with RA treated with abatacept was investigated using an integrated safety database, which included 16 short- and long-term clinical trials of both SC and IV abatacept (N=7044). Of the 16 trials in this analysis, 9 were double-blind (DB), placebo-controlled studies (n=4138; non-biologic DMARD was a background therapy for all patients). Incidence rates (IRs) (95% CI) per 100 person-years (p-y) of deaths were calculated as the number of patients experiencing an event with death as the outcome divided by the total number of p-y of exposure. The p-y of exposure was censored at the time of onset of the first event with an outcome of death, discontinuation, or end of study. **Results:** Most patients were women; mean duration of RA was 8 years and <10% had a history of a prior biologic therapy (Table 1). During the DB, controlled period, IRs for overall deaths were 0.5 and 1.0 in the abatacept and placebo groups, respectively, with overlapping 95% CIs (Table 2). The most frequent causes of death were in the cardiovascular and infection System Organ Classes. In the cumulative population on abatacept, the most frequent causes of death were pneumonia (IR [95% CI]: 0.09 [0.05, 0.14]) and cardiac arrest (0.05 [0.03, 0.09]). IRs were similar with overlapping 95% CIs within each age group, with the highest IR in patients aged >65 years (1.73 [1.3, 2.3]), as expected. These rates are within the ranges reported in the literature.

**Conclusion:** The data from this ongoing assessment of abatacept safety are consistent with the current known benefit–risk profile of abatacept. In the DB phases, the overall IRs of death (95% CI) were 0.5 (0.3, 0.9) on abatacept and 1.0 (0.5, 1.6) on placebo. In the cumulative abatacept population, IR was 0.7 (0.5, 0.8), similar to both the DB population and published literature.


<table>
<thead>
<tr>
<th>Table 1. Demographics and Disease Characteristics of Patients Treated in the Abatacept RA Clinical Trial Program</th>
</tr>
</thead>
<tbody>
<tr>
<td>Double-blind period</td>
</tr>
<tr>
<td>Abatacept (n=2863)</td>
</tr>
<tr>
<td>Mean (SD) age, years</td>
</tr>
<tr>
<td>Female, %</td>
</tr>
<tr>
<td>White, %</td>
</tr>
<tr>
<td>Mean (SD) disease duration, years*</td>
</tr>
<tr>
<td>Mean (SD) HAQ-DI score</td>
</tr>
<tr>
<td>Corticosteroid use, %</td>
</tr>
<tr>
<td>MTX use, %</td>
</tr>
<tr>
<td>Prior biologic, %</td>
</tr>
</tbody>
</table>

*Discharge duration at baseline was defined as per protocol for each study

<table>
<thead>
<tr>
<th>Table 2. Events With Death as an Outcome During the Double-Blind, Placebo-Controlled and Cumulative Periods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Double-blind period</td>
</tr>
<tr>
<td>Abatacept (n=2863)</td>
</tr>
<tr>
<td><strong>Overall deaths</strong></td>
</tr>
<tr>
<td><strong>Causes by System Organ Class</strong></td>
</tr>
<tr>
<td>Cardiovascular</td>
</tr>
<tr>
<td>Infections and infestations</td>
</tr>
<tr>
<td>Infections (HIV, mycobacterium and unspecified)</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
</tr>
<tr>
<td>Gastrointestinal</td>
</tr>
<tr>
<td>Injury, poisoning and procedural complications</td>
</tr>
<tr>
<td>Nervous system</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal</td>
</tr>
<tr>
<td><strong>Investigations</strong></td>
</tr>
<tr>
<td>Vasovagal</td>
</tr>
<tr>
<td><strong>Infections</strong></td>
</tr>
<tr>
<td>Hiv/AIDS</td>
</tr>
<tr>
<td><strong>Hematologic and lymphatic system</strong></td>
</tr>
<tr>
<td><strong>Infections</strong></td>
</tr>
<tr>
<td><strong>Lymphoma and leukaemia</strong></td>
</tr>
<tr>
<td><strong>Malignant neoplasms</strong></td>
</tr>
</tbody>
</table>

*Includes data up to 56 (Phase III) or 152 (Phase II) days post last ED visit. Events with missing Exclusion Term or Inclusion Term may have had events in different SOCs that lead to death. ROC (system Organ Class).

**Disclosure:** D. Fleming, Bristol-Myers Squibb, 3; T. Simon, Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1, 9; A. Torbeyns, Bristol-Myers Squibb, 3; U. Meier-Kriesche, Bristol-Myers Squibb, 3; A. Johnsen, Bristol-Myers Squibb, 1,Bristol-Myers Squibb,
Switching from Synthetic to Biologic Dmards – Is There an Insufficient Use of Methotrexate?

Lisa Baganz\textsuperscript{1}, Adrian Richter\textsuperscript{1}, Yvette Meißner\textsuperscript{2}, Matthias Schneider\textsuperscript{3}, Anke Liebhaber\textsuperscript{4}, Ilka Schwarze\textsuperscript{5}, Anja Strangfeld\textsuperscript{6} and Angela Zink\textsuperscript{7}, \textsuperscript{1}German Rheumatism Research Center, Berlin, Germany, \textsuperscript{2}Programme Area Epidemiology, German Rheumatism Research Center, Berlin, Germany, \textsuperscript{3}Department of Rheumatology, Univ. Duesseldorf, Duesseldorf, Germany, \textsuperscript{4}Rheumatologist, Halle, Germany, Halle, Germany, \textsuperscript{5}Rheumatologist, Leipzig, Germany, Leipzig, Germany, \textsuperscript{6}Epidemiology, German Rheumatism Research Center, Berlin, Germany, \textsuperscript{7}German Rheumatism Research Centre and Charité University Medicine, Berlin, Germany

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: A recent US-study suggests considerable underuse of MTX and too early switches to biologic (b)DMARDs before using a high MTX dose or changing the route of administration. We investigated doses of MTX, route of administration and time to treatment escalation with bDMARDs in Germany.

Methods: The biologics register RABBIT (Rheumatoid Arthritis: Observation of biologic therapy) comprises a control group of patients who were enrolled when starting csDMARDs after failure of at least one csDMARD therapy (mostly MTX monotherapy). We selected \(n=1,608\) patients starting either with MTX monotherapy, MTX + another csDMARD or triple therapy (MTX plus hydroxychloroquine and sulfasalazin). In a sub-cohort of patients recruited between 2009 and 2013 \((n=1,151)\) information about the route of administration was available.

Results: \(1,210\) patients (75.2\%) were enrolled at start of MTX plus another csDMARD, \(356\) patients (22.1\%) starting MTX monotherapy and \(42\) patients (2.6\%) with triple therapy. The proportions of male and seropositive patients were higher in MTX combination and triple therapy \((p<0.05)\). Disease severity (DAS28) at baseline and physical function were not significantly different. Larger differences were found in the sub-cohort: patients treated with subcutaneous (sc) MTX were significantly younger, had a higher DAS28, higher doses of glucocorticoids (GC) and less physical function at baseline \((p<0.01)\).

Overall, \(266\) (16.5\%) patients were escalated to a bDMARD within the 1\textsuperscript{st} year of observation. Only 53 patients (3.3\%) switched to a bDMARD within 3 months after enrollment; without an impact of calendar time \((p=0.23)\). In recent years, escalation to bDMARD therapy occurred earlier (Fig. 1). The median time to a bDMARD was highest \((p<0.01)\) in MTX monotherapy (366d) compared to MTX combination (266d) and triple therapy (150d).

In year one, the average doses of MTX did not vary between the treatment regimens: MTX mono (15.2mg), combination (15.6mg), triple (15.0mg). In patients who switched to a bDMARD, 28.2\% 95\%CI [23.0; 34.1] had prior high doses (>20 mg) of MTX and 54.1\% [47.9; 60.2] had GC doses ≥5 mg/d which was significantly higher than in patients who maintained csDMARD therapy (MTX >20mg; 17.7\% [15.7;19.9], GC ≥5mg: 32.3\% [29.8; 34.9]). Stratified by route of administration, doses were significantly higher with sc MTX (16.8mg [16.4; 17.1]) vs. oral (14.8mg [14.5; 15.1]) but more patients \((p<0.01)\) with sc MTX (21.6\%) were switched to a bDMARD compared to oral MTX (10.9\%).

Conclusion: Our data suggest that German rheumatologists use different strategies after insufficient response to MTX before switching to a bDMARD: MTX dose increase, change to sc MTX, combination with other csDMARDs or increase in GC dose. The results of the US-study\textsuperscript{1} could not be confirmed.
Serum Trough Levels of Adalimumab Inversely Correlate with Disease Activity in Patients with Inflammatory Arthritis

Daman Langguth¹, Peter Wong², Alison Bowling³, Hanish Bagga⁴, Di Freeman⁴ and Emma Ford⁵, ¹Immunology, Sullivan Nicolaides Pathology, Brisbane, Australia, ²Mid-North Coast Arthritis Clinic and University of New South Wales Rural Clinical School, Coffs Harbour, Australia, ³School of health and human sciences, Southern Cross University, Coffs Harbour, Australia, ⁴Mid-North Coast Arthritis Clinic, Coffs Harbour, Australia, ⁵Mid North Coast Arthritis Clinic, Coffs Harboyr, Australia

First publication: September 18, 2017

BACKGROUND/PURPOSE:
Targeted blockade of TNF has been a major advance in the treatment of rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS). However, many patients lose response to a TNF inhibitor. One possible mechanism for this is development of anti-drug antibodies (ADAb).

However, there is no standardised assay for detection of ADAb. It can be difficult to determine if ADAb have in vivo neutralising ability. Serum trough drug levels may be a more robust biomarker. We sought to determine if serum trough levels of adalimumab (ADL) correlated with disease activity in patients with RA, PsA and AS.

METHODS:
Methods:

This was a prospective observational cohort study in bDMARD-naïve patients aged 18-80 yo with RA, PsA and AS commencing ADL. Serum samples were collected 24 hours before a dose of ADL at baseline and months 4, 10 and 16. GRIFOLS Proteomika – Promonitor™ ELISA assays were used to determine serum trough drug levels. These were correlated with the following measures: DAS28, SDAI, RAPID3, CRP, ESR for RA and PsA; and BASDAI, ASDAS, CRP, ESR for AS. Samples with a serum trough ADL level <0.01 μg /ml were assayed for ADAb.

Spearman correlation coefficients (rho values) and multiple regression analysis were used to assess relationship between variables. The significance threshold was set at p<0.05 (2-tailed).

Results:

There was a negative correlation between serum trough ADL levels and DAS28 (r= -0.73, p=0.001) and SDAI (r= -0.50, p=0.05) in RA patients (n=7). Disease remission (DAS28<2.6) was associated with a serum trough ADL > 5 μg/ml. A negative correlation was found between serum trough ADL levels and BASDAI (r= -0.52, p <0.001), ASDAS-ESR (r= -0.47, p <0.001) and ASDAS-CRP (r= -0.48, p <0.001) in patients with AS (n=22). A serum trough ADL level of 5-8 μg/ml was associated with lower ASDAS-ESR and ASDAS-CRP scores. Of the 32 blinded samples with a serum trough ADL <0.01 μg/ml, 26 were found to be baseline samples (ie, prior to ADL exposure). Of the remaining (non-baseline) samples, 5 had ADAb (mean±sem: 386± 158IU/ml) while 1 had no detectable ADAb (<10 IU/ml).

Conclusion:

There was a moderately strong negative correlation between serum trough ADL levels and markers of disease activity in RA (DAS28, SDAI) and AS (ASDAS-ESR, ASDAS-CRP, BASDAI). A serum trough ADL level of > 5 mcg/ml was associated with DAS28 remission in RA. A serum trough ADL level of 5-8 mcg/ml was associated with lower ASDAS-ESR and ASDAS-CRP scores. ADAb were present in almost all samples with undetectable serum trough ADL levels. Serum trough drug levels may be useful in dose titration of, or choice of bDMARD.

Disclosure: D. Langguth, Sullivan Nicolaides Pathology, 3,Roche Pharmaceuticals, 5,Novartis Pharmaceutical Corporation, 5; P. Wong, Novartis Pharmaceutical Corporation, 5,Roche Pharmaceuticals, 5,Abbott Immunology Pharmaceuticals, 5; A. Bowling, None; H. Bagga, Abbott Immunology Pharmaceuticals, 5; D. Freeman, None; E. ford, None.


Abstract Number: 1432

The Prognostic Value of IgA Subtypes of Rheumatoid Factor and Anti-Citrullinated Protein Antibodies (ACPA) for Prediction of Therapeutic Responses to TNF Inhibitory Therapy in Patients with Rheumatoid Arthritis

Daniela Sieghart1, Farideh Alasti2, Paul Studenic1 and Günter Steiner2, 1Medical University Vienna, Division of Rheumatology, Department of Internal Medicine III, Vienna, Austria, 2Rheumatology, Medical University of Vienna, Vienna, Austria

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Rheumatoid factor (RF) and Anti-Citrullinated Protein antibodies (ACPA) are the most specific diagnostic markers of rheumatoid arthritis (RA). These antibodies are predominantly of the IgM (RF) or IgG (ACPA) isotype. The presence of IgA subtypes was reported but their added diagnostic and prognostic value has still not been fully elucidated. It was therefore the
Objective of this study was to (i) determine the prevalence of IgA-RF and IgA-ACPA in patients with RA and (ii) to investigate their potential predictive value regarding response to treatment with methotrexate (MTX) and TNF inhibitors.

Methods:
To determine the diagnostic sensitivity and specificity sera from 255 RA patients, 258 disease controls and 100 healthy subjects were tested for the presence of IgA-RF and IgA-ACPA by EliA (Thermo Fisher Scientific). IgM-RF and IgG-ACPA were routinely measured by nephelometry and the anti-CCP EliA, respectively. Therapeutic responses to MTX and TNF inhibitors (TNFi) were analyzed in an inception cohort (n=104) who had started their DMARD therapy at our clinic. To define therapeutic responses simplified disease activity score (SDAI) and American College of Rheumatology (ACR) responses were calculated.

Results:
Diagnostic specificity was 95% for IgA-RF and 98% for IgA-ACPA, respectively. Among the 255 RA patients, 49% had at least one type of IgA antibody: 45% were IgA-RF positive (as compared to 61% IgM-RF positivity) and 31% were IgA-ACPA positive (56% IgG-ACPA positivity). Importantly, 10.5% of IgA-RF positive patients (i.e. 5% of the total cohort) were negative for IgM-RF (and half of also them for IgG-ACPA) while - apart from two exceptions- all IgA-ACPA positive patients had also IgG-ACPA. Thus, the added diagnostic value of IgA-RF was approximately 5% whereas IgA-ACPA only marginally increased the sensitivity of ACPA testing. Remarkably, the percentage of patients showing a SDAI50 response to TNFi was significantly lower in patients positive for IgA-RF and/or IgA-ACPA (p<0.0001) compared to IgA negative patients: while 58% of IgA negative (but IgM-RF and/or IgG-ACPA positive) patients showed a SDAI50 response only 25% of the IgA positive ones were responders. Interestingly, IgA-ACPA positive/IgA-RF negative patients were the poorest responders with only one out of nine patients showing a SDAI50 response whereas 4/13 IgA-RF positive/IgA-ACPA negative patients were responders. Seronegative patients also showed a significantly decreased SDAI50 response (p<0.001) to TNFi compared to IgM-RF/IgG-ACPA positive patients without IgA antibodies. Similar results were obtained when ACR20 was used as primary response criteria. Interestingly, no difference between the various groups was seen with respect to treatment with MTX.

Conclusion: Apart from a moderate added diagnostic value of IgA-RF, IgA subtypes and particularly IgA-ACPA appear to be strongly associated with a diminished therapeutic response to TNF blocking biological drugs, irrespectively of IgM-RF and IgG-ACPA. Therefore their determination may help in further stratification of RA patients and therapeutic decision making.

Disclosure: D. Sieghart, None; F. Alasti, None; P. Studenic, None; G. Steiner, Thermo Fisher Scientific adia GmbH, 2.


Abstract Number: 1433

Tailoring Second-Line Biologic Therapy in Rheumatoid Arthritis: New Findings on the Usefulness of Antibody Status to Optimise Drug Selection

Muhammad Shipa1, Maria Di Cicco2, Emese Balogh2, Aneela Mian3, Dev Mukerjee4 and Euthalia Roussou2, 1Rheumatology and General internal Medicine, North Middlesex University Hospital NHS trust, London, United Kingdom, 2Barking Havering and Redbridge University hospitals NHS Trust, London, United Kingdom, 3Rheumatology, King's College London, London, United Kingdom, 4Rheumatology, North Middlesex University Trust, London, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Treatment of rheumatoid arthritis (RA) has been revolutionized by the introduction of Tumour Necrosis Factor alpha inhibitors (TNFi). However a significant proportion of patients fails to respond (primary failure) or may lose the initial response over time (secondary failure). Whether a second TNFi or Biologics with Different Mode of Action [ BDMA; Rituximab (RTX), Abatacept (ABT), Tocilizumab (TCZ)] should be used, who had secondary failure still needs to be defined. The aim was to retrospectively compare the efficacy of second TNFi versus BDMA after secondary failure and to investigate whether there was an association between response and antibody status [Rheumatoid Factor (RF) and Anti CCP].

**Methods:**

This was a retrospective observational real life data analysis from two hospitals of North-East London serving diverse ethnic population. The list of the RA patients (defined by 2010 ACR/EULAR criteria), who had secondary failure to first line TNFi from 2010 to 2016, was obtained. The study population were randomly selected using ‘RESEARCH RAMDOMIZER’ software. Response to treatment was defined as the achievement of at least moderate response at six months according to EULAR response criteria.

**Results:**

A total of 422 patients were included in the analysis: 211 in each group (TNFi and BDMA). Male/female ratio was 1:3 and the mean age was of 61.4 years (SD ± 12.1). Baseline DAS28 (SD) scores were higher in BDMA group than in the TNFi group: [5.90(0.6) vs 5.20(0.8); p<0.01].

Table 1 describes response rates according to biologic subcategories and autoantibody status. This reflects 74 patients responded to second TNFi (35%) compared to 148 patients who responded in the BDMA group (70%) (p<0.01); Number need to treat (NNT) was 2.9. The response rates were better in seropositive if receiving RTX (85%) or TCZ (68%), while poorer on ABT (46%), p<0.01. In contrast, for seronegative patients RTX response was poor (35%), but markedly better response observed on ABT or TCZ (83% and 74% respectively).

Table 1: Comparison between TNFi and different BDMA according antibody status [Rheumatoid Factor (RF) and Anti CCP]

<table>
<thead>
<tr>
<th></th>
<th>Total (N=422)</th>
<th>TNFi (N=211)</th>
<th>BDMA (N=211)</th>
<th>p Value</th>
<th>RTX (N=99)</th>
<th>ABT (N=55)</th>
<th>TCZ (N=57)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responders (%)</td>
<td>74 (35%)</td>
<td>148 (70%)</td>
<td>130 (62%)</td>
<td>&lt;0.01</td>
<td>74 (75%)</td>
<td>36 (65%)</td>
<td>40 (70%)</td>
<td>0.90</td>
</tr>
<tr>
<td>Sero (+) (%) : Sero (-) (%)</td>
<td>134 (63%) : 77 (37%)</td>
<td>130 (62%) : 81 (38%)</td>
<td>0.80</td>
<td>73 (74%) : 26 (26%)</td>
<td>26 (47%) : 29 (53%)</td>
<td>31 (54%) : 26 (46%)</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Sero (+) Responders (%)</td>
<td>48 (36%)</td>
<td>98 (75%)</td>
<td>&lt;0.01</td>
<td>62 (85%)</td>
<td>12 (46%)</td>
<td>21 (68%)</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>Sero (-) Responders (%)</td>
<td>26 (34%)</td>
<td>50 (61%)</td>
<td>0.01</td>
<td>9 (35%)</td>
<td>24 (83%)</td>
<td>17 (74%)</td>
<td>&lt;0.01</td>
<td></td>
</tr>
</tbody>
</table>

*Footnote: Sero (+) = seropositive, Sero (-) = seronegative, N= number.*

**Conclusion:**

RA patients who had secondary failure to the initial TNFi, had greater response rate (nearly 3:1), if treated with a BDMA instead of another TNFi. Our findings suggest that seropositive patients may be benefitted from switching to RTX or TCZ, meanwhile seronegative patients may do better with ABT or TCZ.

**Disclosure:** M. Shipa, None; M. Di Cicco, None; E. Balogh, None; A. Mian, None; D. Mukerjee, None; E. Roussou, None.


**Abstract Number:** 1434
COX-2 Inhibitor Contributes Cell Death in Rheumatoid Arthritis Fibroblast-like Synoviocytes Via PI3K/AKT/mTOR Signaling Pathway Triggered By Autophagy

Sang-Hyon Kim¹, Jihye Bang², Ji-Min Kim¹, Chang-Nam Son¹, Jin-Nyeong Chae¹ and Hye-Jin Jeong³, ¹Division of Rheumatology, Department of Internal Medicine, Keimyung University Dongsan Medical Center, Keimyung University School of Medicine, Daegu, Republic of Korea, Daegu, Korea, Republic of (South), ²Division of Rheumatology, Department of Internal Medicine, Dongsan Medical Center, Keimyung University School of Medicine, Daegu, Korea, Republic of (South), ³Department of Rheumatology, Keimyung University Dongsan Medical Center, Daegu, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Recently, the possibilities that autophagy regulates apoptosis resistance and hyperplasia of fibroblast-like synoviocytes (FLS) were also presented. The aim of this study is to investigate the influence of COX-2 inhibitor on viability of rheumatoid arthritis (RA) FLS and to reveal how COX-2 inhibitor affects the viability of RAFLS.

Methods: RA synovial tissue was obtained from patients during total knee replacement surgery or arthroscopy. FLS was cultured with COX-2 inhibitor, caspase inhibitor (z-VAD-fmk), autophagy inhibitor (3-methyladenine; 3-MA), knockdown of si-autophagy protein 5 (Atg5) or si-Beclin1. Cell viability was measured by MTS assay and by cell count using trypan blue staining. The expression of autophagy flux was analyzed by western blot and apoptosis activation was measured caspase3/7 activity assay.

Results: Synoviocyte from RA patients showed that COX-2 inhibitor attenuated cell proliferation and promoted apoptosis. A kind of COX-2 inhibitor dose-dependently decreased cell viability (IC50 of 120 μM) of RAFLS. COX-2 inhibitor also increased the expression of conversion of LC3-I to LC3-II, Atg5, Beclin1, p62 and decreased expression of lysosomal associated membrane protein 1 (LAMP1) in RAFLS. Combination of autophagy by 3-MA, si-Atg5 or si-Beclin1 restored viability of RAFLS by COX-2 inhibitor. COX-2 inhibitor decreased expression of phosphorylation-AKT signaling pathway. And, COX-2 inhibitor-induced autophagic cell death via ROS-dependent effect in RAFLS.

Conclusion: Taken together, this study indicated that COX-2 inhibitor induced apoptosis, inhibiting RA-FLS proliferation while promoting autophagic cell death by the PI3K/AKT/mTOR signaling pathway. Then, autophagy regulation may be an effective therapeutic strategy in inflammatory autoimmune disease such as RA.

Disclosure: S. H. Kim, None; J. Bang, None; J. M. Kim, None; C. N. Son, None; J. N. Chae, None; H. J. Jeong, None.


Abstract Number: 1435

Consistent Inhibition of Joint Destruction By Denosumab in Important Subgroups of Japanese Patients with Rheumatoid Arthritis: Pooled Analysis of Phase 2 and 3 Studies

Yoshiya Tanaka¹, Tsutomu Takeuchi², Satoshi Soen³, Naoki Ishiguro⁴, Hisashi Yamanaka⁵, Toshiyuki Yoneda⁶, Sakae Tanaka⁷, Takaya Nitta⁸, Naoki Okubo⁹, Harry K. Genant¹⁰ and Désirée van der Heijde¹¹, ¹University of Occupational and Environmental Health, Kitakyushu, Japan, ²Keio University School of Medicine, Tokyo, Japan, ³Kindai University Nara Hospital, Ikoma, Japan, ⁴Orthopaedic Surgery, Nagoya University Graduate School of Medicine, Nagoya, Japan, ⁵Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan, ⁶Indiana University School of Medicine, Indianapolis, IN, ⁷Department of Orthopaedic Surgery, Faculty of Medicine, The University of Tokyo, Bunkyo-ku, Japan, ⁸Daiichi Sankyo Co., Ltd., Tokyo, Japan, ⁹DaiichiSankyo CO., LTD., Tokyo, Japan, ¹⁰University of California, San Francisco, CA, ¹¹Leiden University Medical Center, Leiden, Netherlands

Abstract Number: 1435
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Denosumab is a fully human monoclonal antibody (IgG2 subclass) that inhibits bone resorption by blocking RANKL. Phase 2 (DRIVE) and phase 3 (DESIRABLE) studies demonstrated that denosumab inhibited progression of joint destruction in Japanese patients with rheumatoid arthritis (RA). The results of subgroup analyses of DRIVE study have already been reported in ACR 2014. The subgroup analyses of DRIVE and DESIRABLE studies were undertaken to understand whether denosumab was broadly effective upon progression of the joint destruction in RA patients.

Methods:
These analyses used pooled data from two randomized, multicenter, double-blind placebo control trials in RA patients treated with denosumab [60 mg every 6 months (Q6M) or 60 mg every 3 months (Q3M)] or placebo. All patients continued conventional synthetic DMARDs (including MTX) and a supplement of calcium and vitamin D throughout the study. The modified total Sharp score (mTSS), the bone erosion score (ES) and the joint space narrowing score (JSN) were assessed by the modified Sharp van der Heijde method. Subgroup analyses were conducted according to risk factors for radiographic damage.

Results:
A total of 909 patients were included (306 in placebo, 302 in Q6M and 301 in Q3M). Denosumab significantly inhibited the progression of mTSS and ES from baseline to 12 months compared to placebo, whereas denosumab didn’t have an effect on JSN. The incidence of adverse events (AEs), serious AEs and AEs leading to discontinuation of study drug were similar among treatment groups. Each subgroup with a specific risk factor for radiographic damage showed consistent results for the mTSS in total group.

<table>
<thead>
<tr>
<th>Subgroup Description</th>
<th>Placebo N = 306</th>
<th>Placeso N = 302</th>
<th>Denosumab 60 mg N = 301</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td></td>
<td>P-Value</td>
<td>P-Value</td>
<td>P-Value</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.50 (3.73)</td>
<td>0.68 (3.30)</td>
<td>0.002</td>
</tr>
<tr>
<td>RA disease duration (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 3</td>
<td>1.32 (3.43)</td>
<td>0.91 (3.46)</td>
<td>0.024</td>
</tr>
<tr>
<td>≥ 3</td>
<td>1.95 (4.39)</td>
<td>0.81 (2.86)</td>
<td>0.034</td>
</tr>
<tr>
<td>CRP (mg/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 1.0</td>
<td>1.19 (2.95)</td>
<td>0.51 (2.30)</td>
<td>0.0007</td>
</tr>
<tr>
<td>≥ 1.0</td>
<td>3.34 (6.47)</td>
<td>2.49 (5.72)</td>
<td>0.0033</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 28</td>
<td>1.05 (2.77)</td>
<td>0.41 (2.00)</td>
<td>0.0018</td>
</tr>
<tr>
<td>≥ 28</td>
<td>2.77 (5.44)</td>
<td>1.89 (4.93)</td>
<td>0.1760</td>
</tr>
<tr>
<td>RF status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>0.70 (1.99)</td>
<td>0.50 (2.14)</td>
<td>0.0722</td>
</tr>
<tr>
<td>Positive</td>
<td>1.94 (4.35)</td>
<td>1.08 (3.75)</td>
<td>0.0072</td>
</tr>
<tr>
<td>Anti-CCP antibody</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>0.16 (0.82)</td>
<td>0.03 (1.26)</td>
<td>0.1193</td>
</tr>
<tr>
<td>Positive</td>
<td>2.10 (4.33)</td>
<td>1.15 (3.69)</td>
<td>0.0008</td>
</tr>
<tr>
<td>TJC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 2</td>
<td>1.04 (2.82)</td>
<td>0.43 (2.12)</td>
<td>0.0798</td>
</tr>
<tr>
<td>3 to 5</td>
<td>1.56 (3.46)</td>
<td>1.03 (3.40)</td>
<td>0.6393</td>
</tr>
<tr>
<td>≥ 6</td>
<td>1.77 (4.26)</td>
<td>1.09 (3.37)</td>
<td>0.0083</td>
</tr>
<tr>
<td>SJC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 10</td>
<td>1.55 (3.93)</td>
<td>0.74 (3.39)</td>
<td>0.0006</td>
</tr>
<tr>
<td>≥ 10</td>
<td>1.43 (3.44)</td>
<td>1.10 (3.14)</td>
<td>0.7198</td>
</tr>
<tr>
<td>Glucocorticoid use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absence</td>
<td>1.25 (3.01)</td>
<td>0.91 (3.34)</td>
<td>0.0445</td>
</tr>
<tr>
<td>Presence</td>
<td>1.97 (4.78)</td>
<td>0.82 (3.25)</td>
<td>0.0169</td>
</tr>
</tbody>
</table>

N = Number of patients who received ≥ 1 dose of investigational product and had a baseline and at least 1 post-baseline measurement of the radiograph score. RA=rheumatoid arthritis, CRP=C-reactive protein, ESR=erythrocyte sedimentation rate, RF=rheumatoid factor, Anti-CCP=anti-cyclic citrullinated peptide, TJC=tender joint count, SJC=swollen joint count

The same tendency was observed in ES.
Conclusion:

Denosumab inhibited the progression of the joint destruction at 12 months in Japanese patients with RA in subgroup analyses based on pooled data of DRIVE and DESIRABLE studies. These results indicate that denosumab broadly inhibits the progression of joint destruction in RA patients with risk factors for radiographic damage.

Disclosure: Y. Tanaka, Mitsubishi Tanabe Pharma, Takeda Pharmaceutical, Bristol-Myers, Chugai Pharmaceutical, Astellas Pharma, AbbVie, MSD, DaiichiSankyo, Pfizer, Kyowa-Kirin, Eisai, Ono Pharmaceutical, 2, DaiichiSankyo, Astellas Pharma, Pfizer, Mitsubishi Tanabe Pharma, Bristol-Myers, Chugai Pharmaceutical, YL Biologies, Eli Lilly, Sanofi, Janssen, UCB, 8; T. Takeuchi, Astellas Pharma, Bristol–Myers, Chugai Pharmaceutical, DaiichiSankyo, Takeda Pharmaceutical, Teijin Pharma, AbbVie, Asahikasei Pharma, Mitsubishi Tanabe Pharma, Pfizer Japan, Taiho Toyama Pharma, Eisai, AYUMI Pharmaceutical, 2, Astra Zeneca, Eli Lilly Japan, Novartis Pharma, Mitsubishi Tanabe Pharma, AbbVie, Nipponkayaku, Janssen Pharmaceutical, Astellas Pharma, Taiho Pharmaceutical, 5, AbbVie, Bristol–Myers, Chugai Pharmaceutical, Mitsubishi Tanabe Pharma, Pfizer Japan, and Astellas Pharma, DaiichiSankyo, 8; S. Soen, Eisai, DaiichiSankyo, Takeda Pharmaceutical, 2, Asahikasei Pharma, Astellas Pharma, Eisai, MSD, Ono Pharmaceutical, DaiichiSankyo, Takeda Pharmaceutical, Chugai Pharmaceutical, Teijin Pharma, Pfizer Japan, 8; N. Ishiguro, Abbott, Astellas Pharma, Bristol-Myers, Chugai Pharmaceutical, DaiichiSankyo, Eisai, Hisamitsu, Janssen Pharmaceutical, Kaken Pharmaceutical, Mitsubishi Tanabe Pharma, Otsuka Pharmaceutical, Pfizer, Takeda Pharmaceutical, Taisho Toyama Pharmaceutical, UCB, 2, AbbVie, Astellas Pharma, Bristol-Myers, Chugai Pharmaceutical, DaiichiSankyo, Eisai, Hisamitsu, Janssen Pharmaceutical, Mitsubishi Tanabe Pharma, Otsuka Pharmaceutical, Pfizer, Takeda Pharmaceutical, Taisho Toyama Pharmaceutical, UCB, 8; H. Yamanaka, MSD, Astellas Pharma, AbbVie, BMS, Kaken Pharmaceutical, UCB, Ono, Ayumi Pharmaceutical, Eisai, DaiichiSankyo, Takeda Pharmaceutical, Mitsubishi Tanabe Pharma, Chugai Pharmaceutical, Teijin Pharma, Torii, Nipponshinyaku, Pfizer, 2, Pfizer, YL biologies, Takeda Pharmaceutical, Teijin, BMS, Nipponkayaku, Chugai Pharmaceutical, Mitsubishi Tanabe Pharma, DaiichiSankyo, Astellas Pharma, 5; T. Yoneda, Indiana University, 3, DaiichiSankyo, 5; S. Tanaka, Amgen, Astellas Pharma, BioPharma, DaiichiSankyo, Teijin Pharma, Asahi Kasei Pharma, Ono Pharmaceutical, Eli Lilly, Pfizer, MSD, Astellas Pharma, AbbVie, Eisai, Kaken Pharmaceutical, Johnson & Johnson, Taisho Toyama Pharmaceutical, Mitsubishi Tanabe Pharm, 5, The Japanese Orthopaedic Association Corporation, Director, the Japanese Society for Bone and Mineral Research, Chief Director, Japan College of Rheumatology, Director, 6; T. Nitta, DaiichiSanyo, 3; N. Okubo, DaiichiSanyo, 3; H. K. Genant, DaiichiSanyo, Pfizer, Amgen, Bioclinica, Eli-Lilly, Janssen, Servier, Novartis Pharmaceutical, Takeda Pharmaceutical, Merck, Biomarin, Clemencia, Agnovos, Regeneron, 5; D. van der Heijde, Imaging Rheumatology bv., 3, AbbVie, Amgen, Astellas Pharma, AstraZeneca, BMS, Boeringer Ingelheim, Celgene, DaiichiSankyo, Eli-Lilly, Galapagos, Gilead, Janssen, Merck, Novartis Pharmaceuticals, Pfizer, Regeneron, Roche Pharmaceutical, Sanofi, UCB, 5.


Abstract Number: 1436

Therapeutic Drug Monitoring on Rheumatoid Arthritis Patients with Reduced Doses of Intravenous Tocilizumab

Virginia Ruiz-Esquide1, Carla Bastida2, Mariona Pascal3, Jordi Yagüe3, Dolors Soy2 and Raimon Sanmartí1, 1Rheumatology Service, Hospital Clinic de Barcelona, Barcelona, Spain, 2Pharmacy Service, Hospital Clinic de Barcelona, Barcelona, Spain, 3Immunology Service, Hospital Clinic de Barcelona, b, Spain

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Tocilizumab (TCZ) is an effective treatment for rheumatoid arthritis (RA). There is great variability in intravenous (iv) TCZ serum concentrations among individuals. Moreover, initial drug dosage approver by Regulatory Agencies (FDA and EMA) differs. Empirical dose de-escalation strategies are being fostered in patients with disease remission.
The purpose of the study was to examine TCZ serum concentrations at the different prescribed doses in RA. Secondary objectives were to evaluate the relationship between drug serum concentrations and laboratory parameters of disease activity.

**Methods:**

Prospective, observational, single-center study conducted in a university tertiary hospital. Enrolled RA patients received iv TCZ at a dose range from 4 to 8 mg/kg every 28 days. Demographic characteristics and clinical laboratory data were obtained at study entry. Blood samples for drug concentration testing were collected from the third TCZ dose onwards, just before TZC infusion and, when possible, once a week until the next drug administration.

**Results:**

A total of 35 patients (88.6% women, 80% Caucasian) were included. Mean age ± SD was 54.1 ± 12.3 and the median [range] of disease duration was 11.1 [2.9-48.5]. Median [range] treatment duration with iv TCZ was 36.5 [3-68] months. 54% of patients received the standard dose of 8 mg/kg whereas the rest received reduced doses (23% were on 6 mg/kg and 23% on 4 mg/kg) due to persistent remission/low disease activity. 20 patients (57.1%) were being treated with low steroid dose and 24 (68.6%) were on concomitant DMARD, mainly methotrexate.

Regarding drug concentration testing, a total of 109 samples were obtained. Nineteen patients participated to multiple drug sampling between two drug administrations and in the 17 remaining patients, a pre-dose sample was drawn. Mean TCZ concentrations are displayed in table 1. No significant differences were observed in median pre-dose TCZ concentration values (54 samples) between patients on 8 and 6 mg/kg whereas significant lower drug levels were observed in those taking 4 mg/kg.

According to inflammatory parameters, mean C-reactive protein (CRP) concentration was significantly lower in those patients with trough TCZ concentrations >1 µg/mL compared to those <1 µg/mL (0.066 mg/dL vs 0.689 mg/dL, respectively; p<0.001). This difference was not observed with calprotectin serum concentrations (2.260 µg/mL vs 2.143 µg/mL).

**Conclusion:**

Trough TCZ serum concentrations do not differ between patients on an 8 and 6 mg/kg regimen. Therefore, according to the pharmacokinetics observed in our study, a maintenance dose of iv TCZ 6 mg/kg would be appropriate for most RA patients. Although CRP levels are significantly higher in patients with trough iv TCZ concentrations <1 µg/mL, serum calprotectin did not show the same tendency.

Table 1. Mean (± standard deviation) intravenous tocilizumab serum concentrations at different prescribed doses within time.

<table>
<thead>
<tr>
<th>Time (days)</th>
<th>TCZ 8 mg/kg</th>
<th>TCZ 6 mg/kg</th>
<th>TCZ 4 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-infusion (C_{trough})</td>
<td>8.91 ± 6.0</td>
<td>5.68 ± 9.1</td>
<td>0.79 ± 1.2</td>
</tr>
<tr>
<td>T7</td>
<td>84.82 ± 33.9</td>
<td>48.88 ± 18.6</td>
<td>26.06 ± 6.4</td>
</tr>
<tr>
<td>T14</td>
<td>46.40 ± 19.8</td>
<td>30.98 ± 11.5</td>
<td>15.16 ± 5.3</td>
</tr>
<tr>
<td>T21</td>
<td>21.63 ± 9.5</td>
<td>19.65 ± 10.5</td>
<td>7.11 ± 4.4</td>
</tr>
<tr>
<td>T28 (C_{trough})</td>
<td>10.63 ± 7.3</td>
<td>10.29 ± 10.8</td>
<td>1.32 ± 2.3</td>
</tr>
</tbody>
</table>

**Disclosure:** V. Ruiz-Esquide, None; C. Bastida, None; M. Pascal, None; J. Yagüe, None; D. Soy, None; R. Sanmartí, None.


**Abstract Number: 1437**

**C-Reactive Protein Levels in Patients with or without Structural Progression: A Post-Hoc Analysis from a Phase 3 Tofacitinib Trial**

**Roy Fleischmann**1, Carol A Connell2, Haiyun Fan3 and Sander Strengholt4, 1Metroplex Clinical Research Center and University of Texas Southwestern Medical Center, Dallas, TX, 2Pfizer Inc, Groton, CT, 3Pfizer Inc, Collegeville, PA, 4Pfizer Inc, Capelle aan den IJssel, Netherlands

**First publication:** September 18, 2017

**SESSION INFORMATION**
Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). We examined high sensitivity C-reactive protein (hsCRP) levels in relation to structural progression in patients with RA receiving tofacitinib or methotrexate (MTX).

Methods: This was a post-hoc analysis of data from a Phase 3, randomized, double-blind controlled trial of tofacitinib monotherapy vs MTX (ORAL Start [NCT01039688]) in patients with early RA who were naïve to therapeutic doses of MTX. Patients were randomized to tofacitinib 5 mg twice daily (BID), tofacitinib 10 mg BID, or MTX titrated up to 20 mg/week. hsCRP levels through Month (M) 24 were analyzed descriptively for patients with structural progression at M12 (change from baseline in modified Total Sharp Score [mTSS] >0.5; mTSS progressors) and those without structural progression at M12 (mTSS non-progressors). The proportions of patients who were mTSS non-progressors at M6, M12, and M24 were summarized for patients with baseline hsCRP level ≤7 mg/L and >7 mg/L.

Results: A total of 885 patients who had mTSS assessments at M12 were included in this analysis, of whom 345 received tofacitinib 5 mg BID, 371 received tofacitinib 10 mg BID and 169 received MTX. Mean baseline hsCRP levels were similar across treatment groups, but M12 mTSS progressors appeared to have a higher mean baseline hsCRP vs non-progressors in all treatment groups (Figure). On a group level, patients who were mTSS progressors at M12 generally had numerically higher mean hsCRP levels vs mTSS non-progressors over 24 months (Figure); effect was generally greater with MTX vs tofacitinib groups. At M24, mean changes from baseline in hsCRP appeared higher for M12 progressors (-21.5 to -27.8 mg/L across groups) vs non-progressors (-12.6 to -16.7 mg/L across groups). Rates of mTSS non-progression appeared to be numerically higher at M6, M12, and M24 in patients with baseline hsCRP ≤7 mg/L vs those with baseline hsCRP >7 mg/L (Table). At M24, among patients with baseline hsCRP >7 mg/L, 59.5% of patients treated with MTX and 77.0% and 79.6% treated with tofacitinib 5 mg and 10 mg BID, respectively, were mTSS non-progressors, compared with 77.1%, 85.6% and 90.8%, respectively, among patients with baseline CRP ≤7 mg/L (Table).

Conclusion: Patients with RA receiving tofacitinib 5 mg or 10 mg BID or MTX who showed structural progression at M12 generally had numerically higher mean hsCRP levels through M24. Numerically higher rates of non-progression were observed over time in patients with baseline hsCRP ≤7 mg/L vs >7 mg/L. At M24, structural progression was lower with tofacitinib vs MTX, regardless of baseline hsCRP level.
Figures. Mean hsCRP levels over 24 months according to mTSS progression at M12 in patients receiving A) tofacitinib 5 mg BID, B) tofacitinib 10 mg BID, or C) MTX.

A) Tofacitinib 5 mg BID

- Progressors, N = 61
- Non-progressors, N = 294

B) Tofacitinib 10 mg BID

- Progressors, N = 51
- Non-progressors, N = 325

C) MTX

- Progressors, N = 53
- Non-progressors, N = 116

Progressors were defined as those patients with change from baseline in mTSS score ≥ 3 at M12.
BID: twice daily; CI: confidence interval; hsCRP: high sensitivity C-reactive protein; M: month; mTSS: modified Total Sharp Score; MTX: methotrexate.
Is It Necessary to Weight By Weight the Dosage of MTX in RA Patients? Results from Observational Analysis of Baseline Data of a Phase III Trial

Alain Saraux¹, Christophe Hudry², Elena Zinovieva³ and Hélène Herman-Demars³, ¹Rheumatology Department, Rheumatology Department, CHU de la Cavale Blanche, Brest, France, Brest Cedex, France, ²AP-HP Hôpital Cochin, Paris, France, ³Medical Department Nordic Pharma, Paris, France

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: In inflammatory rheumatic diseases, pharmacokinetics of MTX may be modified by patients’ weight [1]. The rheumatologists are though reluctant to prescribe a high dosage to patients with a low weight. On the other hand, international guidelines (ACR and EULAR [2, 3]) do not recommend any weight adaptation concerning MTX dose. Following which, rheumatologists generally do not increase MTX dosage above 25 mg/wk for patients with high weight. Our goal was to evaluate the MTX dosage used in routine practice to treat RA as compared the patients’ weight.
Methods: We used the baseline data of SELFi study. This phase III trial included patients treated by MTX (≥ 3 months, oral or SC) randomized in two arms: MTX in prefilled syringes or MTX autoinjector. The primary objective of the study was to compare the arms in terms of HAQ and treatment adhesion at 6 months. In this preliminary post-hoc analysis, we evaluated in four groups <50kg, 50-74.9 kg, 75-99.9 kg, and >100 kg the mean dosage of MTX in mg/kg, the proportion of patient receiving <10, 10 to 14.9, 15 to 19.9, ≥ 20 mg/wk, and the proportion of patients receiving < or ≥ 0.3 mg/kg/wk. We also evaluated the factors associated to the use of ≥ 0.3 mg/kg/wk using univariate or multivariate analyses.

Results: Between Sept 2015 and Sept 2016 SELFi study recruited 264 patients (192 women and 72 men); mean age: 58.4±13.2 years. Mean weight of women/men was 67.3±13.5 kg and 81.5±13.7 kg respectively (p<0.0001). The difference of BMI between men and women was statistically significant: 25.8±5.3 for women and 26.9±3.9 for men (p=0.014). Absolute value of MTX dosage was the same for both genders: 15.4 mg/wk in women vs 15.9 in men (p=0.36). Although, the proportion of women and men receiving ≥ 15mg/wk dosage is not statistically different (75.5% vs 84.7%, p=0.11), 17.7% of women vs only 2.9% of men received ≥0.3 mg/kg/wk (p=0.002). While the patients <50kg receive 0.29 mg/kg/wk for the other groups this parameter is decreased to 0.24, 0.19 et 0.16 mg/kg/wk for the tree other groups. Results of the univariate analysis show that the prescription of MTX ≥ 0.3 mg/kg/wk is associated with the female gender (p<0.002), the height (p<0.001) and the weight (p<0.0001). In multivariate analysis, only the weight remains associated (p<0.0001). However, the MTX dosage <0.3 mg/kg/wk was not associated with higher disease activity, but the study was designed to consider patients with low disease activity.

Conclusion: Weight does not seem to influence the MTX dosage in RA patients. Although the dosage of MTX in mg/wk seems slightly higher in men vs women, it is significantly lower in mg/kg/wk. These results raise the question of the utilization of mg/kg/wk MTX dosage rather than the absolute value in mg/wk. On this basis, it would be interesting to design a randomized controlled trial to further explore these findings.


Disclosure: A. Saraux, Nordic Pharma, 5; C. Hudry, Nordic Pharma, 5; E. Zinovieva, Nordic Pharma, 3; H. Herman-Demars, Nordic Pharma, 3.

Factors Influencing the Prescription of Tocilizumab Alone or in Combination with Dmards in Rheumatoid Arthritis Patients in a Real Life Setting. Pooled Analysis of 2 Observational Studies

Alain Saraux1, René-Marc Flipo2, Bernard Combe3, Jacques Tebib4, Christelle Baffie5, Isabelle Idier6 and Alain Cantagrel7,

1Rheumatology Department, Rheumatology Department, CHU de la Cavale Blanche, Brest, France, Brest Cedex, France,
2Rheumatology, Department of Rheumatology, CHU Teaching Hospital Lille, France., Lille, France,
3Rheumatology, Lapeyronie Hospital, Montpellier I university, Montpellier, France,
4Rheumatology, University Hospital, Hospices civils de Lyon, Lyon, France,
5Statistics, Altizem on behalf of Roche, Boulogne Billancourt, France,
6Medical department, Chugai Pharma France, Paris La Defense, France,
7Department of Rheumatology, Purpan Hospital, Toulouse III University, Toulouse, France, Toulouse, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Tocilizumab (TCZ) as monotherapy (Mono) is nowadays a standard treatment in rheumatoid arthritis (RA) for patients in whom methotrexate (MTX) gives an inadequate response1.
The objective was to describe factors influencing the use of TCZ in Mono or in combination with DMARDs (Combo) in real-life practice in RA patients (pts).

Methods:

Analysis: pooled data of 2 prospective, multicentre, observational studies (Spare-1 n=307, Act-solo n=577). Patients: RA pts requiring TCZ treatment according to their physician. Treatment: TCZ as prescribed in real life. Endpoint: Evaluation of factors influencing the use of TCZ in Mono or in Combo. Data collected: demographic characteristics, past medical history, RA characteristics and history including previous RA treatments, TCZ treatment strategy (in Mono or Combo). Statistical analysis: Pts fulfilling inclusion and non-inclusion criteria and with ≥1 TCZ infusion were analyzed. 1- descriptive analysis 2- Univariate and multivariate analysis to determine factors influencing the use of TCZ in Mono. 3.-A propensity score was built to balance baseline characteristics.

Results:

884 pts were analysed at inclusion. Pts’ characteristics: 57% of the pts were >55 years old, 78.4% female, mean RA duration 10.7±9.1 years, 84.3% positive for RF and/or ACPA, 77.5 % with erosive disease, CRP 19.4±26.2 mg/l, mean DAS28-ESR 5.14±1.27. Comorbidities were: diabetes 8%, high blood pressure (HBP) 28%, dyslipidemia 20%, osteoporosis 21%, others 56%. Past RA treatment included csDMARDs in 98.2% and biologics in 73.8% (median=2 [1-6]). TCZ was initiated as Mono in 39% of pts and in Combo in 61%, with MTX in 78.5% of Combo pts (mean dose 16.1±4.5mg). Steroids were used in 78.5% of pts (mean dose 11±6.8mg). In the multivariate analysis variables associated with a TCZ prescription in Mono were: number of previous bDMARD (1 bDMARD, OR=1.30 [0.88-1.93], 2 bDMARD OR=2.32 [1.55-3.45], ≥ 3 bDMARD, OR=1.21 [0.78-1.90] p<.001), HBP OR=1.45 [1.05-2.00], p=0.025, osteoporosis OR=1.63 [1.14-2.33], p=0.007, CRP ≥10mg/l OR=1.61 [1.21-2.15], p=0.001. At 12 months, mean DAS28-ESR was 2.41±1.28 and 2.29±1.23 with 74.7% and 77% of pts in DAS28 LDA in Mono and Combo respectively. No differences were observed between Mono and Combo groups on other efficacy data. This remains true when weighting by the propensity score.

Conclusion:

This pooled analysis suggests that TCZ in monotherapy is used more often in previously heavily treated, with higher inflammatory markers and with comorbidities such as HBP or osteoporosis.


Disclosure: A. Saraux, None; R. M. Flipo, Chugai Pharma France, 5,Roche SAS, 5; B. Combe, Chugai Pharma France, 5,Roche SAS, 5; J. Tebib, None; C. Baffie, Roche SAS, 3; I. Idier, Chugai Pharma France, 3; A. Cantagrel, None.

The Effectiveness of Zoster Vaccine in RA Patients Subsequently Treated with Tofacitinib

Kevin Winthrop1, Ann Wouters2, Ernest Choy3, Chudy Nduaka4, Pinaki Biswas2, Lisy Wang5, Jennifer Hodge2, Irina Lazariciu6, Koshika Soma5, Christopher F Mojcik2, Elie Needle7 and William F C Rigby8, 1Oregon Health & Science University, Portland, OR, 2Pfizer Inc, New York, NY, 3CREATE Center, Division of Infection and Immunity, Cardiff University School of Medicine, Cardiff, United Kingdom, 4Pfizer Inc, Collegeville, PA, 5Pfizer Inc, Groton, CT, 6QuintilesIMS, Saint-Laurent, QC, Canada, 7Pfizer Inc, Pearl River, NY, 8Geisel School of Medicine at Dartmouth, Lebanon, NH

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: RA patients (pts) are at increased risk of herpes zoster (HZ), and ACR guidelines recommend vaccination in pts aged ≥50 years prior to starting biologic DMARDs or tofacitinib. Tofacitinib is an oral Janus kinase inhibitor for the treatment of RA. Live zoster vaccine (LZV) has shown 70% efficacy in immunocompetent adults aged 50–59 years, and 51% efficacy in those aged ≥60 years. We previously reported that RA pts on background methotrexate who started 3 months of treatment with tofacitinib after LZV had similar varicella zoster virus (VZV)-specific immunity to placebo (PBO) pts, and that their VZV immunity at Week (Wk) 6 post-vaccination was comparable with healthy individuals aged ≥50 years. The objective of this study was to evaluate the long-term effectiveness of LZV in pts with RA, via the incidence of HZ after treatment with tofacitinib for up to 27 months.

Methods: The initial study involved 112 RA pts given LZV and randomized 2–3 wks later to tofacitinib 5 mg twice daily (BID) or PBO for 12 wks (A3921237 [NCT02147587]). At 14 wks post-vaccination, pts joining the long-term extension ORAL Sequel study (NCT00413699) initiated open-label treatment with tofacitinib 5 or 10 mg BID. The incidence of post-vaccination HZ after tofacitinib exposure up to 27 months (based on an extended follow-up beyond the January 2016 data snapshot) was evaluated. Among HZ cases, we analyzed measures of VZV-specific immunity with average immunity after LZV.

Results: 112 pts were randomized to PBO (n=57) or tofacitinib 5 mg BID (n=55). 100 pts continued to receive tofacitinib in ORAL Sequel. Five cases (not adjudicated) of HZ occurred, with an incidence rate (pts with events per 100 pt-years) of 3.60 (95% confidence interval 1.17, 8.39) (#1: 202 days [219 days post-LZV], #2: 267 days [281], #3: 702 days [748], #4: 699 days [741], #5: 446 days [544] after initiation of tofacitinib). Cases #1–#4 were monodermatomal; case #5 involved 5 dermatomes. All cases resolved with treatment. Cases #1, #4, and #5 had undetectable ELISPOT measures at baseline and at Wk 6 post-vaccination, indicating a lack of VZV-specific immunity. Cases #2 and #3 responded adequately to vaccination by both immunoglobulin G (IgG) and ELISPOT measures, but had lower-than-average VZV IgG levels, both at baseline and at Wk 6 (Table).

Conclusion: LZV prior to treatment with tofacitinib is effective at boosting IgG levels and cell-mediated immunity towards VZV. Of the 5 pts who developed HZ, 3 did not have any measurable cell-mediated response, and 2 had a low humoral response.

3. Winthrop K et al. Arthritis Rheumatol 2015;67:Abstract 12L.

Acknowledgment: The authors would like to acknowledge Lisa McNeil.

Table. VZV ELISPOT and IgG Levels

<table>
<thead>
<tr>
<th>Case 1 (HZE 210 days after zoster vaccine)</th>
<th>Case 2 (HZE 281 days after zoster vaccine)</th>
<th>Case 3 (HZE 748 days after zoster vaccine)</th>
<th>Case 4 (HZE 741 days after zoster vaccine)</th>
<th>Case 5 (HZE 544 days after zoster vaccine)</th>
<th>Study A3921237 Tofacitinib 5 mg BID 20-24</th>
</tr>
</thead>
<tbody>
<tr>
<td>VZV (IgG) ELISPOT at baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(SPC 12/16 PMBC)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25 (LOD)</td>
<td>1</td>
<td>25 (LOD)</td>
<td>25 (LOD)</td>
<td>25 (LOD)</td>
<td>48</td>
</tr>
<tr>
<td>VZV (IgG) ELISPOT at Wk 6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(SPC 12/16 PMBC)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25 (LOD)</td>
<td>7</td>
<td>5</td>
<td>25 (LOD)</td>
<td>25 (LOD)</td>
<td>70</td>
</tr>
<tr>
<td>Change from baseline in VZE ELISPOT at Wk 6 (SPC fold; SPC 12/16 PMBC)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.00</td>
<td>1.85</td>
<td>2.04</td>
<td>1.00</td>
<td>1.00</td>
<td>1.50</td>
</tr>
<tr>
<td>VZV (gG) IgG at baseline (gG/ELISA units/ml)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>304</td>
<td>37</td>
<td>37</td>
<td>332</td>
<td>332</td>
<td>301</td>
</tr>
<tr>
<td>VZV (gG) IgG at Wk 6 (gG/ELISA units/ml)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>464</td>
<td>71</td>
<td>187</td>
<td>332</td>
<td>332</td>
<td>403</td>
</tr>
<tr>
<td>Change from baseline in VZE IgG at Wk 6 (gG/ELISA units/ml)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.98</td>
<td>1.92</td>
<td>1.91</td>
<td>0.88</td>
<td>1.97</td>
<td>2.31</td>
</tr>
</tbody>
</table>

Disclosure: K. Winthrop, Bristol-Myers Squibb, 2,AbbVie, Bristol-Myers Squibb, Eli Lilly, Galapagos, Pfizer Inc, UCB, 5; A. Wouters, Pfizer Inc, 1,Pfizer Inc, 3; E. Choy, BioCancer, Pfizer Inc, Roche, UCB, 2,Amgen, Biogen, Chugai Pharma, Eli Lilly, Janssen, Novartis, Pfizer Inc, Regeneron, Roche, R-Pharm, Sanofi, 5,Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Chugai Pharma, Eli Lilly, Hospira, MSD, Novartis, Pfizer Inc, Regeneron, Roche, Sanofi-Aventis, UCB, 8; C. Nduaka, Pfizer Inc, 1,Pfizer Inc, 3; P. Biswas, Pfizer Inc, 1,Pfizer Inc, 3; L. Wang, Pfizer Inc, 1,Pfizer Inc, 3; J. Hodge, Pfizer Inc, 1,Pfizer Inc, 3; I. Lazariciu, QuintilesIMS, 3,Pfizer Inc, 5; K. Soma, Pfizer Inc, 1,Pfizer Inc, 3; C. F. Mojcik, Pfizer Inc, 1,Pfizer Inc, 3; E. Needle, Pfizer Inc, 1,Pfizer Inc, 3; W. F. C. Rigby, Roche, 5.
Evaluation of Ultrasound-Detecting Efficacy of Abatacept By Profiling Multiple Serum Cytokines, Chemokines and Bone-Related Biomarkers in Rheumatoid Arthritis Patients: Kyushu Multicenter Rheumatoid Arthritis Ultrasound Prospective Observational Cohort Study

Shinya Kawashiri1,2,3, Ayako Nishino3,4, Nobutaka Eiraku3, Tamami Yoshitama3, Naoki Matsuoka3, Toshiyuki Aramaki3, Yukitaka Ueki3, Akitomo Okada3, Hiroaki Hamada3, Shuji Nagano3, Keita Fujikawa3 and Atsushi Kawakami1,3, 1Department of Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, 2Departments of Community Medicine, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, 3Kyushu multicenter rheumatoid arthritis ultrasound prospective observational cohort study group, Nagasaki, Japan, 4Center for Comprehensive Community Care Education, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: We have been prospectively investigating therapeutic efficacy of biologic or targeted synthetic DMARDs in patients with rheumatoid arthritis (RA) by ultrasound (US) in Kyushu region, Japan from June 2013. In this study, we have investigated efficacy of abatacept (ABT) by US indices and tried to find the correlations of those with serum cytokines, chemokines and bone-related biomarkers.

Methods: Forty-seven RA patients, registered and completed ABT therapy for 6 months, were enrolled from the Kyushu multicenter RA US prospective observational cohort study. They gave their informed consent to be subjected to the protocol that was approved by the Institutional Review Board of each center. We evaluated clinical disease activity, US synovitis score [22 joints including bilateral 1st-5th metacarpophalangeal (MCP) joints, proximal interphalangeal (PIP) joints and wrist joints semi-quantitatively examined by grey-scale (GS) and power Doppler (PD) from 0 to 3] and serum levels of 38 kinds of cytokine and chemokine biomarkers (multi-suspension array), bone-related biomarkers[TRACP-5b (EIA), sRANKL (ELISA), multi-suspension array; DKK-1, osteocalcin (OC), osteoprotegerin (OPG), osteopontin (OPN) and sclerostin (SOST)], rheumatoid factor (RF), anti-cyclic citrullinated peptide antibodies (ACPA), matrix metalloproteinase-3 (MMP-3) at baseline, 3 and 6 months. Variables predicting PD non-responder defined that sum of PD score from 22 joints did not improve at 6 months were assessed.

Results: The median of disease duration was 82 months and that of DAS28-CRP was 4.49 at baseline. Clinical disease activity, US synovitis score, RF titer and MMP-3 significantly improved at 3 and 6 months from baseline (p<0.001). In addition, most of cytokines, chemokines and bone-related biomarkers were down- or up-regulated by ABT therapy. A multivariate logistic regression analysis revealed that longer disease duration (OR 1.01, 95%CI 1.01-1.03, p=0.0003), low PDUS synovitis score (OR 0.75, 95%CI 0.54-0.92, p=0.0010) and high DKK-1 (OR 1.11, 95%CI 1.01-1.25, p=0.027) at baseline was predictive of PD non-responder (Table 1).

Conclusion: Cytokines, chemokines and bone-related biomarker differently changed after introduction of ABT therapy. Therapeutic response of ABT evaluated by US indices may be predicted by baseline bone-related biomarkers such as DKK-1.

Table 1. Multivariate regression analysis to predict power Doppler non-responder at 6 months
<table>
<thead>
<tr>
<th>Comparison</th>
<th>OR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease duration</td>
<td>1.01</td>
<td>1.01</td>
<td>1.03</td>
</tr>
<tr>
<td>PDUS synovitis score</td>
<td>0.75</td>
<td>0.54</td>
<td>0.92</td>
</tr>
<tr>
<td>DKK-1 100 increase</td>
<td>1.11</td>
<td>1.01</td>
<td>1.25</td>
</tr>
</tbody>
</table>

Variables with a p value less than 0.02 in univariate analysis were used in multivariate models.

CI, confidence interval; OR, odds ratio

Disclosure: S. Kawashiri, None; A. Nishino, None; N. Eiraku, None; T. Yoshitama, None; N. Matsuoka, None; T. Aramaki, None; Y. Ueki, None; A. Okada, None; H. Hamada, None; S. Nagano, None; K. Fujikawa, None; A. Kawakami, None.


Abstract Number: 1442

**Corticosteroid Sparing Effect of Non-TNF Targeted Biologics, Rituximab, Abatacept and Tocilizumab in Common Practice: Data from 3183 Patients Enrolled in the French Society of Rheumatology Registries**

Jacques-Eric Gottenberg¹, Jacques Morel², Arnaud Constantin³, Thomas Bardin⁴, Alain Cantagrel⁵, Bernard Combe², Maxime Dougdos⁶, René-Marc Flipo⁷, Alain Saraux⁸, Thierry Schaeverbeke⁹, Jean Sibilia¹⁰, Martin Soubrier¹¹, Olivier Vittecoq¹²,¹³, Gabriel Baron¹⁴, Elodie Perrodeau¹⁵, Philippe Ravault¹⁴ and Xavier Mariette¹⁶, ¹CNRS, Immunopathologie et Chimie Thérapeutique/Laboratory of Excellence Medalis, Institut de Biologie Moléculaire et Cellulaire, Strasbourg, France, ²Rheumatology, CHU Lapeyronie and Montpellier University, Montpellier, France, ³Rheumatology, CHU Purpan - Hopital Pierre-Paul Riquet, Toulouse, France, ⁴Clinique de Rhumatologie, Hospital Lariboisiere, Paris Cedex 10, France, ⁵Department of Rheumatology, Purpan Hospital, Toulouse III University, Toulouse, France, ⁶Rheumatology, Paris Descartes University, Paris, France, ⁷Rheumatology, Department of Rheumatology, CHU Teaching Hospital Lille, France, Lille, France, ⁸Rheumatology, Brest University Hospital, Brest, France, ⁹Department of Rheumatology, Bordeaux University Hospital, BORDEAUX, France, ¹⁰Department of Rheumatology, Strasbourg University Hospital, Strasbourg, France, ¹¹Rheumatology, Department of Rheumatology, CHU Gabriel Montpied, Clermont-Ferrand, France, ¹²INSERM U905 & Normandy University, Institute for Research and Innovation in Biomedicine, Rouen, France, ¹³Rheumatology Department and INSERM U 905, CHU Rouen, Rouen, France, ¹⁴Hôpital Hôtel Dieu, Paris, France, ¹⁵Epidemiology, Hopital Hotel Dieu, Paris Descartes University, Paris, France, ¹⁶Université Paris-Sud, AP-HP, Hôpitaux Universitaires Paris-Sud, Paris, France

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017

Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM

Background/Purpose:

Little is known regarding the corticosteroid sparing effect of non-TNF biologics in rheumatoid arthritis (RA).

Objectives: To compare the corticosteroid sparing effect of non-TNF biologics in daily practice in RA.
Methods:
Autoimmunity and Rituximab (AIR), Orencia and Rheumatoid arthritis (ORA) and REGistry–RoAcTEmra (REGATE) are three prospective registries promoted by the French Society of Rheumatology for patients who initiate rituximab (RTX), abatacept (ABA), or tocilizumab (TCZ), as intravenous drugs.

The observational data were used to emulate a target trial with 3 groups: patients receiving rituximab, abatacept and tocilizumab. A propensity-score approach was used to adjust for differences in observed factors that might affect both treatment assignment and outcome and to emulate randomization.

Change in oral corticosteroid dosage was analyzed by 3 different approaches regardless of drug discontinuation: delta decrease ≥ 5 mg/d compared to baseline dose, final daily dose ≤ 5 mg/d, and total discontinuation of corticosteroids in patients receiving the drug at baseline. To compare these outcomes, we used logistic regression with weighted GEEs, with drug as the only covariate.

Results:
At enrollment, 77.7, 74.4 and 66.5% of patients treated with RTX (n= 1619), ABA (n= 623) and TCZ (n= 941) had daily oral corticosteroid (mean (SD dose): 11.8 (8.8), 11.2 (8.3), 10.3 (7.2) mg/ day, respectively).

- Delta decrease ≥ 5 mg of the daily dose compared to enrollment
At 6 months, such a decrease was observed in 31.6, 41.6 and 48.4% of RTX, ABA and TCZ-treated patients respectively (p=0.003 for the comparison between TCZ and RTX, no significant difference between ABA and TCZ). At 12 months, such a decrease was observed in 43.1, 51.9 and 62.2% of RTX, ABA and TCZ-treated patients respectively (p< 0.001 between TCZ and RTX). At 24 months, it was observed in 58.3, 62 and 71% of patients, respectively.

- Daily dose ≤ 5 mg/d
At 6 months, a daily dose ≤ 5 mg/d was observed in 26.4, 37.8 and 52.9% of patients, treated with RTX, ABA and TCZ respectively (p< 0.001 between TCZ and RTX). At 12 months, it was observed in 44.7, 53.5 and 72.2% of patients, respectively (p< 0.001 between TCZ and RTX). At 24 months, a daily dose ≤ 5 mg/d was observed in 66.1, 67.1% and 75.8% of patients, respectively (p=0.001 between TCZ and RTX).

- Discontinuation of oral corticosteroids
At 6 months, in patients initially treated with steroids, oral corticosteroids were discontinued in 9.7, 13.7 and 15.6% of patients respectively treated with RTX, ABA and TCZ. At 12 months, they were discontinued in 11.5, 23.4 and 24.9% of patients, respectively (p= 0.003 between ABA and RTX, p< 0.001 between TCZ and RTX). At 24 months, steroids were discontinued in 20.5, 31.5 and 38% of patients, respectively.

Conclusion:
These results demonstrate a corticosteroid-sparing effect for all 3 of the non-TNF targeted biologics in around half of the patients at 12 months. However, only 21% to 38% of patients with baseline oral corticosteroids use could discontinue corticosteroids at 24 months, which emphasizes the need to continue to enlarge the armamentarium of new biologic and targeted DMARDs in RA.

Disclosure: J. E. Gottenberg, BMS, Gilead, Medimune,Pfizer SanofiAventis, Roche, Ucb, 2; J. Morel, None; A. Constantin, None; T. Bardin, None; A. Cantagrel, None; B. Combe, None; M. Dougdos, AbbVie, Lilly, Merck, Novartis, Pfizer, Sanofi, and UCB., 2,Abbvie, Lilly, Merck, Novartis, Pfizer, Sanofi, and UCB., 5; R. M. Flipo, Chugai Pharma France, 5,Roche SAS, 5; A. Saraux, None; T. Schaeverbeke, None; J. Sibilia, None; M. Soubrier, None; O. Vittecoq, None; G. Baron, None; E. Perrodeau, None; P. Ravaud, None; X. Mariette, None.


Abstract Number: 1443

Adverse Drug Reactions Due to Disease Modifying Drugs in a Cohort of Patients with Incident Rheumatoid Arthritis
Background/Purpose: There is a well-known risk of developing adverse drug reactions (ADR) in rheumatology due, mainly, to the Disease Modifying Drugs (DMARD) used. After more than twenty years using DMARD, there is no doubt about their efficacy in rheumatoid arthritis (RA), but it is necessary to increase our knowledge of their ADR, especially those that lead to discontinuation in real life. Purpose: to describe the incidence and characteristics of ADR to DMARD in patients with incident RA as well as the factors related to their development.

Methods: An observational longitudinal study was conducted. Patients: all recent onset RA patients diagnosed between April 15th 2007 and 31st June 2011 followed in outpatient clinic at Hospital Clinico San Carlos until December 31st 2016, which used any DMARD (synthetic and biologic). Primary outcome: development of an ADR that required discontinuation of the DMARD (moderate: discontinuation; severe: discontinuation and hospitalization or death as a result of the ADR). Incidence rates of discontinuation (IR) per 100 patient-years were estimated using survival techniques with their respective 95% confidence interval [CI]. Comparisons between associated factors were run by Cox bivariate and multivariate regression models. Results were expressed by hazard ratio (HR) and [CI].

Results: We included 1054 courses of DMARD treatment in 405 patients (2277.9 patient-years). 78.3% were women with a mean age at diagnosis of 57±15 years. Median time to the first DMARD was 0.3 ±0.6 days. 16.3% of patients were taking biological DMARD, 73.3% were using monotherapy and 89% were taking corticoids. There were 369 ADR in 212 patients, 88.9% of them moderate. Gastrointestinal was the most frequent cause of ADR (26.3%), followed by infections (12.2%). Incidence rates are shown in table 1. In the multivariate analysis (table 2) after adjusting by age and sex, number of concomitant DMARD was directly related to more risk. Regarding type of DMARD, Abatacept had the highest risk of ADR development (HR: 4.9[2.1-11.2]) compared to the other drugs followed by Gold (HR: 1.6[1-2.6]) and Leflunomide (HR: 1.4[1.1-1.9]). Methotrexate was the safest drug compared with the others (0.6[0.5-0.8]).

Conclusion: The IR of ADR estimated was 16.2%, being gastrointestinal the main cause followed by infections. We have found differences in discontinuation rates among DMARD due to ADR, being Abatacept, Gold and Leflunomide the drugs with the highest risk. Methotrexate is a protective factor for the development of ADR. Caution should be taken in patients receiving combined therapy and with certain comorbidities.
<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>patient-years</th>
<th>n</th>
<th>IR</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Global</strong></td>
<td>2277.9</td>
<td>369</td>
<td>16.2</td>
<td>14.6-17.9</td>
</tr>
<tr>
<td>Women</td>
<td>1835.4</td>
<td>296</td>
<td>16.1</td>
<td>14.4-18.1</td>
</tr>
<tr>
<td>Men</td>
<td>442.5</td>
<td>73</td>
<td>16.5</td>
<td>13.1-20.7</td>
</tr>
<tr>
<td><strong>By therapy regimen</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monotherapy</td>
<td>1609.5</td>
<td>200</td>
<td>12.4</td>
<td>10.8-14.3</td>
</tr>
<tr>
<td>Double therapy</td>
<td>568.9</td>
<td>132</td>
<td>23.2</td>
<td>19.6-27.5</td>
</tr>
<tr>
<td>Triple therapy</td>
<td>99.4</td>
<td>37</td>
<td>37.2</td>
<td>26.9-51.4</td>
</tr>
<tr>
<td><strong>By type of DMARD</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Synthetic</td>
<td>2048.3</td>
<td>326</td>
<td>15.9</td>
<td>14.3-17.7</td>
</tr>
<tr>
<td>Biological</td>
<td>229.5</td>
<td>43</td>
<td>18.7</td>
<td>13.9-25.3</td>
</tr>
<tr>
<td><strong>By drug</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abatacept</td>
<td>8.3</td>
<td>5</td>
<td>60.6</td>
<td>25.2-145.5</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>81.5</td>
<td>10</td>
<td>12.3</td>
<td>6.6-22.8</td>
</tr>
<tr>
<td>Antimalarials</td>
<td>749.7</td>
<td>157</td>
<td>20.9</td>
<td>17.9-24.5</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>19</td>
<td>3</td>
<td>15.7</td>
<td>5.1-48.8</td>
</tr>
<tr>
<td>Certolizumab</td>
<td>16</td>
<td>4</td>
<td>24.8</td>
<td>9.3-66.2</td>
</tr>
<tr>
<td>Etanercept</td>
<td>65.2</td>
<td>12</td>
<td>18.4</td>
<td>10.5-32.4</td>
</tr>
<tr>
<td>Golimumab</td>
<td>9.1</td>
<td>5</td>
<td>54.9</td>
<td>22.9-131.9</td>
</tr>
<tr>
<td>Infliximab</td>
<td>18.4</td>
<td>6</td>
<td>32.7</td>
<td>14.7-72.7</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>340.4</td>
<td>85</td>
<td>25</td>
<td>20.2-30.9</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>1463.5</td>
<td>206</td>
<td>14.1</td>
<td>12.3-16.1</td>
</tr>
<tr>
<td>Gold</td>
<td>83.6</td>
<td>33</td>
<td>39.5</td>
<td>28-55.5</td>
</tr>
<tr>
<td>Rituximab</td>
<td>26.3</td>
<td>1</td>
<td>3.8</td>
<td>0.5-27</td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>154</td>
<td>45</td>
<td>29.2</td>
<td>21.8-39.1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>Hazard ratio CI 95% p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monotherapy</td>
<td>1 - -</td>
</tr>
<tr>
<td>Double therapy</td>
<td>2</td>
</tr>
<tr>
<td>Triple therapy</td>
<td>4.2</td>
</tr>
<tr>
<td>Biologics vs Synthetic DMARD</td>
<td>0.8</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>1.8</td>
</tr>
<tr>
<td>Liver disease</td>
<td>2</td>
</tr>
<tr>
<td>Cancer</td>
<td>1.3</td>
</tr>
</tbody>
</table>

Disclosure: Z. Rosales Rosado, None; D. Freites Núñez, None; C. Lajas Petisco, None; E. Pato Cour, None; L. Leon, None; J. Font Urgelles, None; J. A. Jover Jover, None; L. A. Alcazar, None.

Abstract Number: 1444

Targeted Therapeutic Delivery to Cartilage with Knottin Proteins

Emily Girard, Michelle Cook Sangar, Gene Hopping, Fiona Pakiam and James Olson, Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Arthritic diseases affect more than 50 million Americans and, although there are many etiologies, the common manifestation of the disease is pain and limited mobility (1). Delivery of therapeutics to alleviate symptoms and perturb disease progression is limited by the risk of systemic toxicity (2). Intra-articular therapeutic administration is limited to accessible joints and cannot address disseminated disease (3). We have identified a panel of cysteine-knot peptides that target to cartilage in rodents following systemic administration. This work characterizes the in vivo pharmacokinetics of cartilage-targeting knottins and assesses the potential for translation to arthritis therapeutics in the clinic.

Methods: Whole body autoradiography (WBA) was used to evaluate biodistribution of knottin peptides in rodents. Radioactive signal of 14C-KNT-17R (100 nmol, IV) was quantified in the knee and intervertebral disc (IVD) between 5 min and 96hr. Delivery of a cargo was assessed after KNT-17R conjugation to the fluorophore Cy5.5 (10nmol IV, 3hr) or Dexamethasone (100nmol IV, 3 and 24hr). Accumulation in knee and IVD were assessed by fluorescent microscopy and WBA. Binding to human cartilage explants was assessed by microscopy or liquid scintillation counting after overnight incubation with 10mM 14C or Cy5.5 labeled peptide.

Results: Two independent time course experiments show that peptide KNT-17R distributes rapidly and persists in all types of cartilage in the mouse. The peak signal intensity of 60+/−14 % injected dose/g (knee) and 34+/− 8 % injected dose/g (IVD) was observed 30 min after administration. Peak signal did not significantly decline until after 3 hours (knee) or 8 hours (IVD). Fluorescent microscopy further demonstrated that Cy5.5-KNT-17R accumulated in cartilage of the knee and IVD. Dexamethasone-KNT-17R accumulated in the knee at 41+/−14 % injected dose/g and in the IVD at 20+/−3 % injected dose/g after 3 hours. Signal intensity in cartilage was too low to measure in mice treated with 14C-Dexamethasone. KNT-17R was found to bind to human cartilage with significantly greater intensity than negative control peptide KNT-15R by fluorescence microscopy and liquid scintillation counting.

Conclusion: This work demonstrates cartilage accumulation by a systemically administered knottin peptide. The peptide is able to deliver a steroid payload to cartilage in multiple clinically relevant joints. Binding to human cartilage explants establishes evidence that a knottin peptide may have promise in the treatment of arthritis in humans.

1. Hootman, Arthritis Rheumatol 2016. 68, 1582-1587
2. Evans, Nat Rev Rheumatol 2014 10, 11-22
3. Larsen, J Pharm Sci 2008 97, 4622-4654

Disclosure: E. Girard, None; M. Cook Sangar, None; G. Hopping, None; F. Pakiam, None; J. Olson, Blaze Bioscience, 4.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/targeted-therapeutic-delivery-to-cartilage-with-knottin-proteins

Abstract Number: 1445

Effect of Methotrexate (MTX), and MTX Plus Colchicine (CCH) on the Expression and Activity of NLRP3 Inflammasome in Patients with Early Rheumatoid Arthritis (RA)
Background/Purpose: NLRP3 inflammasome is an intracellular protein complex involved in the production of pro-inflammatory cytokines as IL-1β and IL-18, which has been reported to have a role in the pathogenesis of RA. Since CCH is a potent inhibitor of NLRP3, we hypothesized that it may significantly modify the expression and function of this molecular complex, reducing the inflammatory phenomenon in RA. Accordingly, the aim of this study was to evaluate the possible effect of CCH administration on the expression and activity of NLRP3 in patients with early RA.

Methods: We selected consecutive patients with RA according to the ACR/EULAR 2010 criteria with ≤12 months of evolution and were randomly assigned to 2 groups: MTX (15 mg/week); or MTX (15 mg/week) plus CCH (1.5 mg/day). Inflammasome expression by monocytes was assessed by two-color flow cytometry (CD14+NLRP3+ cells), and its function was estimated through the analysis of Caspase-1 activity (colorimetric assay). Clinical activity was assessed by HAQ-DI, CDAI, SDAI and DAS28-ESR at 0, 1 and 3 months.

Results: Twenty DMARD naive patients have been recruited, their main characteristics are shown in table 1. In a preliminary analysis of 7 patients in the MTX group and 6 patients in the MTX+CCH group after 1 month of treatment, and 3 patients in the MTX group and 4 patients in the MTX+CCH group after 3 months of treatment, all patients had increased levels of caspase-1 activity and NLRP3; patients in the MTX group had a significant change in its expression at 1 month (Table 2), however that difference was not subsequently detected at month 3. In contrast, patients in the MTX+CCH group showed a significant decrease in the expression and activity of NLRP3 at 1 and 3 months (p<0.05). Moreover, a significant improvement in clinical parameters was observed in both at months 1 and 3. We will present follow-up all patients.

Conclusion: Our preliminary data suggest that CCH administration is associated with sustained decrease in the expression and activity of the NLRP3 inflammasome. This phenomenon might contribute to decrease inflammation and may help to achieve low disease activity.
Clinical Significance of Serum Levels of ROM (reactive oxygen metabolities) at 12 Weeks during Treatment with Biologic Agents As a Predictor for the 52-Week Remission

Arata Nakajima1, Masato Sonobe1, Shinji Taniguchi1 and Koichi Nakagawa2, 1Orthopaedics, Toho University Sakura Medical Center, Sakura-city, Chiba, Japan, 2Toho University Sakura Medical Center, Sakura-city, Chiba, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Oxidative stress induced by reactive oxygen species is thought to be an important mechanism that underlies joint destruction and synovial proliferation. We have shown that serum levels of reactive oxygen metabolities (ROM) at 12 weeks during treatment with biologic agents (BAs) are predictive for the DAS28-remission at 52 weeks. However, it has not been elucidated whether ROM is also a predictor for the CDAI-, SDAI- or Boolean-remission at 52 weeks.

Methods: Fifty-four BA-naïve RA patients (mean age: 59.8±13.6 y, disease duration: 7.26±10.8 y) were included in this study. Association between ROM, CRP, MMP-3, DAS28, CDAI, SDAI, and HAQ at 12 weeks and the CDAI-, SDAI-, and Boolean-remission at 52 weeks was investigated. To measure ROM, the d-ROM test was performed using the FRAS4 analyzer (Wismarl, Italy). In order to identify predictor(s) for the 52-week remission, a multivariate logistic regression analysis was performed and an ROC analysis was also performed to determine their cut-off values.

Results: CDAI and SDAI at baseline was 17.8±11.6 and 20.4±13.0, respectively but decreased to 5.54±11.6 and 6.21±13.1 at 52 weeks and the remission rate for CDAI, SDAI and Boolean was 54, 57 and 56%, respectively. Significant factors at 12 weeks between the remission and non-remission group at 52 weeks were (1) ROM, DAS28, CDAI, and HAQ for the CDAI-remission, (2) ROM, DAS28, CDAI, and HAQ for the SDAI-remission, (3) ROM, DAS28, and HAQ for the Boolean-remission (Table 1). A multivariate logistic regression analysis revealed that ROM at 12 weeks was associated with the CDAI-remission (p=0.032, OR: 0.991, 95%CI: 0.983-0.999), SDAI- and Boolean-remission (p=0.006, OR: 0.988, 95%CI: 0.980-0.997) at 52 weeks. ROC analyses demonstrated that AUC for the CDAI-remission was 0.702 and the cut-off value was 389.5 U.Carr (sensitivity: 52.4%, specificity: 91.7%). AUC for the SDAI- and Boolean-remission was 0.746 and the cut-off value was 389.5 U.Carr (sensitivity: 55.0%, specificity: 92.3%, Figure 1).

Conclusion: These results suggest that neither CRP nor MMP-3 can be a predictor for the remission during early stage of treatment with BAs. Instead, ROM at 12 weeks was a predictor for the CDAI-, SDAI-, and Boolean-remission at 52 weeks. Serum levels of
ROM will be a useful biomarker in the current treatment strategy aiming at the early remission of RA.

Table 1. Comparison of the factors at 12 weeks between the remission and non-remission groups at 52 weeks

<table>
<thead>
<tr>
<th></th>
<th>ROM (U/l)</th>
<th>CRP (mg/dL)</th>
<th>MDA (nmol/l)</th>
<th>DDA28</th>
<th>CDAI</th>
<th>SDM</th>
<th>HbA1c</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remission</td>
<td>312±56.7</td>
<td>0.08±2.02</td>
<td>1.88±1.12</td>
<td>4.36±5.38</td>
<td>4.19±5.09</td>
<td>4.19±5.09</td>
<td>0.20±0.32</td>
</tr>
<tr>
<td>Non-reminssion</td>
<td>395±136</td>
<td>0.67±2.55</td>
<td>1.38±1.24</td>
<td>3.32±1.84</td>
<td>11.1±15.5</td>
<td>10.7±15.3</td>
<td>0.67±0.65</td>
</tr>
<tr>
<td>p</td>
<td>0.015*</td>
<td>0.019*</td>
<td>0.017*</td>
<td>0.045*</td>
<td>0.049*</td>
<td>0.049*</td>
<td>0.016*</td>
</tr>
</tbody>
</table>

A cut-off value corresponds to 395.5 U/l (indicated as an asterisk). ROM, reactive oxygen metabolites.

Figure 1. The ROC curve for ROM at 12 weeks to predict the 52-week remission.

Disclosure: A. Nakajima, None; M. Sonobe, None; S. Taniguchi, None; K. Nakagawa, None.


Abstract Number: 1447

Smoking Reduces Efficacy of Biologics Differently By Target Cytokines in Rheumatoid Arthritis

Kentaro Kuzuya1, Yukihiro Saeki2, Jun Hashimoto3, Shirou Oshima4, Masato Matsushita5, Souichirou Tuji4, Yoshinori Harada6, Maiko Yoshimura6, Satoru Teshigawara6 and Hidetoshi Matsuoka1, 1Rheumatology and Allegology, Osaka-Minami Medical Ctr, Kawachinagano, Japan, 2Dept of Clinical research, Osaka-Minami Medical Ctr, Osaka, Japan, 3Rheumatology/Orthopaedics, Osaka-Minami Medical Ctr, Kawachinagano, Japan, 4Division of Rheumatology, Osaka-Minami Medical Ctr, Osaka, Japan, 5Rheumatology, Osaka-Minami Medical Ctr, Osaka, Japan, 6Osaka-Minami Medical Ctr, Kawachinagano, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Biologiccs (Bio) have shown outstanding efficacy and became one of the most effective drugs in the treatment of RA. However, several issues remain, including adverse effect (AE), therapeutic failure (Failure), and expensiveness. On the other hand, cumulative evidence has suggested that some genetic and environmental factors affects responsiveness of anti-rheumatic drugs including Bio. Smoking is thought to be one of crucial environmental factors. The purpose of this study is to investigate the influence of smoking on Bio treatment in RA.

**Methods:** The association between smoking habit and discontinuation of Bio treatment was analyzed on Japanese RA patient cohort (11940 patients). Smoking habit was assessed by questionnaire and the patients were divided into three groups as current smoker, never smoker, ever smoker. The total percentages of discontinuation were analyzed according to four categories: Failure, adverse effect (AE), Remission, and others. The association between the causes of discontinuation of Bio and smoking habit was analyzed statistically.

**Results:** 3,187 (26.7%) of the total registered patients were treated with one or more Bio during 6 years. Among them, 584, 1,321, 397, 223, and 73 patients were treated with IFX, ETN, ADA, TCZ, ABT and GLM respectively. Failure in the current smoker group was significantly more frequent than never smoker and ever smoker groups (OR=0.678, 95%CI:0.482~0.967, OR=0.577, 95%CI:0.357~0.869, respectively). Among therapeutic targets, patients treated with TNF inhibitors (IFX, ETN, ADA, GLM) showed more significant association between smoking habit and Failure than those treated with either IL-6 inhibitor (TCZ) or T cell inhibitor (ABT).

**Conclusion:** Smoking reduced responsiveness of treatment by Bio in RA, especially when treated with TNF inhibitors. Smoking cessation may reduce failure of treatment by Bio in RA.

**Disclosure:** K. Kuzuya, None; Y. Saeki, None; J. Hashimoto, None; S. Oshima, None; M. Matsushita, None; S. Tuji, None; Y. Harada, None; M. Yoshimura, None; S. Teshigawara, None; H. Matsuoka, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/smoking-reduces-efficacy-of-biologics-differently-by-target-cytokines-in-rheumatoid-arthritis

**Abstract Number:** 1448

**Prospective, Intervention, Multicenter, Non-Inferiority Study of Utility of Therapeutic Drug Monitoring with Respect to the Efficacy and Cost of Adalimumab Tapering in Patients with Rheumatic Diseases**

Catalina Gómez Arango1, Maria Luz Garcia Vivar2, Eduardo Úcar Angulo1, Iñigo Gorostiza3, Clara Eugenia Perez2, Juan Ramon De Dios4, Belen Alvarez5, Ana Ruibal Escriberno6, Claudia Stoye5, Margarida Vasques5, Joaquin Belzunegui Otano7, Antonio Escobar3, Ziortza Trancho8, Ainhoa Ruiz del Agua9, Lorena Del Rio9, Cristina Jorquera10, Antonio Martinez9 and Daniel Nagore9,

1Rheumatology Department; Basurto University Hospital, Bilbao, Spain, 2RHEUMATOLOGY, Rheumatology Department; Basurto University Hospital, Bilbao, Spain, 3Research Unit, Basurto Univeristy Hospital, Bilbao, Spain, 4Rheumatology Department. Hospital Universitario de Araba, Vitoria, Spain, 5Rheumatology, Hospital Universitario de Araba, Vitoria, Spain, 6Rheumatology, Hospital Universitario de Araba, Vitoria, Spain, 7Donostia University Hospital, San Sebastian, Spain, 8Unidad de Investigación, Hospital Universitario de Basurto, Bilbao, Spain, 9R&D, Progenika-Grifols, Derio, Spain, 10Hospital Universitario de Basurto, Bilbao, Spain

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Adalimumab (ADL) tapering based on clinical assessment is an usual practice, especially in patients in remission. The objective of INGEBIO was to analyze how personalized management guided by Therapeutic Drug Monitoring (TDM) in rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS) patients impacts the annual direct costs to the
Health System and the quality-adjusted life year (QALY) gained with respect to conventional practice in Spain. Second, to evaluate the effectiveness of TDM in the reduction of the number of days with high disease activity compared with conventional practice.

**Methods:** In a pragmatic, non-randomized, non-inferiority trial, adult patients treated with ADL (40 mg sc) who remained clinically stable for at least 6 months were recruited in 3 sites. Patients were grouped in Control (CG) and Intervention groups (IG) according to the site. ADL frequency was adjusted based on physician criteria. Patients are assessed at 8 visits for up to 18 months. Trough ADL and anti-ADL antibodies levels are measured with Promonitor-ADL and Promonitor-ANTI-ADL (Progenika). TDM data were released only to the IG, and blinded to the CG. Physicians in the IG were not obliged to follow any therapeutic algorithm based on TDM results but could use tests to alter doses based on their clinical judgement. Endpoints include DAS28, BASDAI, BASFI and HAQ-DI scores at every time point. Cost-effectiveness is evaluated according to associated costs and QALY.

**Results:** A total of 169 patients were recruited, but 19 were lost to follow-up (disease, N IG, N CG, %) (RA, 25, 29, 36.0%; PsA, 30, 18, 32.0%; and AS, 43, 5, 32.0%). Median disease duration was 124.0, 105.5 and 129.0 months for RA, PsA and AS, respectively. At baseline, 9 (17.3%) and 28 (28.6%) patients had low disease activity, 43 (82.7%) and 70 (71.4%) patients were in remission, and median trough ADL levels were 5.76 and 5.04 mg/L in the CG and IG, respectively. Patients were in remission/low activity an average of 475.2 vs 460.2 days in the CG and IG, respectively. The number of flares in the CG and IG was 47 and 66, respectively. The rate of flares per patient-year of FU was 0.639 vs 0.463 in the CG and IG, respectively (a difference of -0.176; CI95%: -0.379 to 0.0289). The risk of flare is 27.5% lower in the IG (IRR= 0.7252; CI95%: 0.4997 to 1.0578). Median time to first flare was 136,5 and 145 days in the CG and IG, respectively. Quality of life (EQ-5D-5L) was significantly better in the IG at visits 2 (p=0.001) and 3 (p=0.035); EQ-5D-5L was higher (although not statistically significant) in the IG in the remaining visits. Mean QALY were 1.145 and 1.076 during FU per intervention and control patient, respectively (gain of 0.069). Average cost of Humira per patient-year was 10,664.54€ vs 9,856.45€ (-808.08€, 8% savings) in the CG and IG, respectively.

**Conclusion:** BDM-guided management is not inferior to clinically based management for maintaining remission after 18 months and is associated with fewer flares, better quality of life and lower treatment costs during the course of treatment.

**Disclosure:** C. Gómez Arango, None; M. L. García Vivar, None; E. Úcar Angulo, None; I. Gorostiza, None; C. E. Perez, None; J. R. De Dios, None; B. Alvarez, None; A. Ruibal Escribano, None; C. Stoye, None; M. Vasques, None; J. Belzunegui Otano, None; A. Escobar, None; Z. Tranch, None; A. Ruiz del Agua, Progenika, 3; L. Del Rio, Progenika, 3; C. Jorquera, None; A. Martínez, Progenika, 3; D. Nagore, Progenica, 3.

**Abstract Number:** 1449

**Development of a Predictive Score of Successful TNF Inhibitor Tapering in Patients with Rheumatoid Arthritis Remission**

Clothilde Barral1, David Hajage2, Bruno Fautrel3, Pierre Lafforgue1, Florence Tubach2 and Thao Pham1, 1Rheumatology, APHM, Aix Marseille Univ, Marseille, France, 2APHP, Pitié Salpêtrière Hospital, Département Biostatistics and Public health, Pharmacoepidémiology center (Cephepi), 75018 75013, Paris, France, Paris, France, 3Rheumatology, AP-HP Pitié-Salpêtrière Hospital / Pierre and Marie Curie University Paris 6 GRC-08 (EEMOIS), Paris, France

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Tapering trials confirmed the feasibility of TNF inhibitors (TNFi) tapering for a relevant proportion of patients in remission and/or low disease activity. However, there are no consensual predictors of a good response to therapeutic spacing among patients with
rheumatoid arthritis (RA) in remission. We aimed to develop a predictive score of successful TNFi tapering.

Methods:

Post-hoc analysis of a controlled trial of a tapering strategy in RA patients, fulfilling ACR 1987 criteria, treated with subcutaneous TNFi with sustained remission, randomized to either spacing or maintaining TNFi. We used the data of the Spacing arm.

Performances of several variables (DAS28, SDAI, CDAI, CRP, ACPA status, HAQ, patient/physician global assessment, and boolean remission criteria) were assessed for the prediction of successful TNFi tapering, defined as reaching at least 25% tapering of the full regimen during at least 6 months, using sensitivity (Se) and specificity (Spe) for dichotomous variables, or the area under the ROC curve (AUC) and its 95% confidence interval for continuous variables.

A predictive score of successful tapering was constructed using LASSO regression modeling to avoid overfitting (R software version 3.2.1).

Results:

The main characteristic of the 64 patients of the Spacing arm were the following (mean ± SD): age 54.3 ± 10.7 years, disease duration 8.3 ± 5.4 years, and DAS 28 1.9 ± 0.6.

The baseline variables were similar between patients who failed or succeeded at TNFi spacing, except for the HAQ score (0.30 in the group success and 0.89 in the failure group, p = 0.01) and the CRP (2.35 mg/l versus 3.48 mg/l, respectively, p=0.02).

Baseline variable performance in predicting successful TNFi spacing: None of the tested variables was able to predict successful TNFi spacing, except the HAQ score and the CRP. A HAQ threshold ≥ 1.125 had a Spe of 93% and an AUC: 0.713 (CI95%: 0.540-0.886). A CRP threshold ≥ 6.8 mg/l had a Spe of 0.97 and an AUC: 0.689 (CI95%: 0.547-0.831).

Predicting score: A composite score able to predict successful TNFi spacing has been elaborated, including ACPA status, Boolean criteria, SDAI, CRP and HAQ. A 0.5 threshold predicted successful TNFi spacing with Spe = 100% and Se = 54% (AUC: 0.829; CI95%: 0.671 - 0.986).

Conclusion:

The remission maintenance in rheumatoid arthritis after TNFi spacing is possible. Our results showed that in a population of RA patients in remission with TNFi, baseline HAQ and CRP are independent predictor factors of successful tapering. We have developed a composite index able to predict successful TNFi spacing, with an AUC of 0.829 and a 100% Spe. A validation study will be needed to confirm its ability to select patients for treatment decrease.

Disclosure: C. Barral, None; D. Hajage, None; B. Fautrel, None; P. Lafforgue, None; F. Tubach, None; T. Pham, None.

Influence of Immunogenicity to the First Anti-TNF Therapy on Response to the Second Biologic Agent in RA Patients

Patricia Bogas¹, Chamaïda Plasencia-Rodriguez¹, Alejandro Balsa¹, Dora Pascual-Salcedo², Gema Bonilla¹, Enrique Moral Coro¹, Carolina Tornero¹, Laura Nuño¹, Diana Peiteado³, Ana Martínez⁴ and Borja Hernández¹, ¹Hospital Universitario La Paz, Madrid, Spain, ²Immuno-Rheumatology Research group, La Paz University Hospital, Madrid, Spain, ³Rheumatology, La Paz University Hospital, Madrid, Spain, ⁴Immuno-Rheumatology research group, La Paz University Hospital, MADRID, Spain

First publication: September 18, 2017

Abstract Number: 1450

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Background/Purpose: There is currently no consensus on selecting a therapeutic target in patients (pts) non-responsive to their first TNF inhibitors (TNFi). The development of anti-drug antibodies (ADA) is a frequent cause of secondary inefficacy in our pts with TNFi and there is evidence that those who develop ADA at their 1st TNFi achieve a higher degree of response to the second one, compared to ADA- pts. Thus ADA measurement can help in choosing a therapeutic target in pts who failed to respond to their 1st TNFi. The objective of this study was to assess if development of ADA to the 1st TNFi determines better response when switching to a 2nd TNFi versus a nonTNFi. As secondary objective, it was analyzed whether the presence or absence of ADA to a 1st TNFi influences the efficacy of a 2nd TNFi

Methods: Of a total of 110 pts that switched from infliximab or Adalimumab to a 2nd biologic agent (Etanercept, Rituximab, Tocilizumab, Adalimumab, Abatacept, Certolizumab and Infliximab), only 60, who had measured drug levels (DL)/ADA at discontinuation of the 1st TNFi, were included. Clinical response was evaluated with DAS28, Delta-DAS28 (ΔDAS28) and EULAR response (E-resp) at 6 (v-6) and 12 (v-12) months after initiating 2nd biologic agent and at the last visit prior to drug discontinuation or ending of the study for those who did not interrupt the biological therapy (v-end). DL/ADA levels were measured by ELISA. T tests and Fisher’s exact test were used to test statistical differences. Analysis was performed using SPSS version 20.0

Results: Within the 60 pts who had measured DL/ADA at suspension of the 1st TNFi, 26 (43%) were ADA-. In this ADA- subpopulation, 50% changed to a 2nd TNFi; at v-6 there were no differences between switchers to a 2nd TNFi and switchers to a nonTNFi in DAS28 (3.7±2.1 TNFi vs 4.2±1.1 nonTNFi, p=0.286), ΔDAS28 (1.4±2 TNFi, 1±1.2 nonTNFi, p=0.374) and resp-E (75% good/moderate resp in TNFi, 40% in nonTNFi, p=0.064). At v-12, switchers to a 2nd TNFi showed a lower DAS28 (2.5±0.6 TNF-i, 3.9±0.9 nonTNFi, p=0.009) and a higher good E-resp rate with a marginally significant difference (80% in TNFi, 22% in nonTNFi, p=0.071). However, at v-end, pts with a 2nd nonTNFi had better response (DAS28 > 5.1 in 50% of TNFi pts, 0% of nonTNFi, p=0.044). Likewise ΔDAS28 at v-end was higher in the nonTNFi group (0.7±1.7 TNFi, 1.7±0.8 nonTNFi, p=0.06). Along these lines, the good/moderate E-resp rate was higher in switchers to a nonTNFi (30% in TNFi, 92% in nonTNFi, p=0.006). In ADA+ subpopulation (n=34), no differences were found at v-end, pts with a 2nd nonTNFi had better response (DAS28 > 5.1 in 50% of TNFi pts, 0% of nonTNFi, p=0.044). Likewise ΔDAS28 at v-end was higher in the nonTNFi group (0.7±1.7 TNFi, 1.7±0.8 nonTNFi, p=0.06). Among these, the good/moderate E-resp rate was higher in switchers to a nonTNFi (30% in TNFi, 92% in nonTNFi, p=0.006). In ADA+ subpopulation (n=34), no differences were found at v-end, pts with a 2nd nonTNFi had better response (DAS28 > 5.1 in 50% of TNFi pts, 0% of nonTNFi, p=0.044). Likewise ΔDAS28 at v-end was higher in the nonTNFi group (0.7±1.7 TNFi, 1.7±0.8 nonTNFi, p=0.06). Among these, the good/moderate E-resp rate was higher in switchers to a nonTNFi (30% in TNFi, 92% in nonTNFi, p=0.006). In pts who changed to a 2nd TNFi, those with ADA to 1st TNFi had a higher good response rate than ADA- pts (65% in ADA +, 30% in ADA-, p=0.07).

Conclusion: The development of ADA to the first TNFi entails a better response when switching to a 2nd TNFi, with a similar efficacy to the pts who switched to a nonTNFi. In those pts who did not develop immunogenicity to the 1st TNFi, there is a better response when changing therapeutic target. The ADA measurement can help to select the pts who can benefit from a 2nd TNFi.

Disclosure: P. Bogas, None; C. Plasencia-Rodriguez, None; A. Balsa, None; D. Pascual-Salcedo, None; G. Bonilla, None; E. Moral Coro, None; C. Tornero, None; L. Nuño, None; D. Peiteado, None; A. Martínez, None; B. Hernández, None.
Background/Purpose:

RA is a burdensome for most of the patients, comorbidities usually provide additional disadvantages the course of RA. The possible effects of comorbidities on selection of biological DMARDs in RA patients were not frequently assessed.

Objectives: The objective of this study was to assess effects of comorbidities and multimorbidities on biological DMARDs choose, timing of biological DMARDs and response of biological DMARDs.

Methods:

Hacettepe University Biologic Registry (HUR-BIO) is single center biological DMARD registry. After 2012, all known comorbidities reported by patients were evaluated by a standard questionnaire. HUR-BIO included 1235 patients with RA and 998 patients were assessed for comorbidities. Assessed comorbidities were obesity, diabetes, hypertension, hyperlipidemia, osteoporosis, coronary heart disease, cerebrovascular event, chronic kidney disease, hepatitis B, tuberculosis, amyloidosis, and cancer.

Multimorbidity defined as more than 1 comorbidity. Disease duration, initial date of biological DMARDs, initial and overall biological DMARD choose were recorded. DAS-28 responses were compared to comorbidity presence and multimorbidity.

Results:

Totally, 998 RA patients were enrolled. The mean age was 53.1 (12.5) and mean disease duration (SD) was 11.7 (7.5) years. At least one comorbidity was detected in 689 (69.1%) patients, 375 (37.9%) patients had multimorbidity. Patients had mean 1.36 ± 1.32 comorbidity. Patients with comorbidity were older (56.2 ± 11.3 vs 46.1 ± 12.4, p<0.001), more frequently female (83% vs 74%, p=0.01), worst functional disability (HAQ score 1.0 (0-2.9), vs 0.77 (0-2.5), p<0.001) and highest baseline patient global assessment score (70 (0-100) vs 60 (10-100), p=0.004). The median duration of first biological DMARDs prescription were 60 (3-552) months after RA diagnosis. For multimorbidity patients, the median first biological prescription duration were longer than patients without multimorbidity patients (72 (3-552) vs 60 (3-396) months, p<0.001). The physicians prescribe anti-TNF biological drugs less frequently than other biologic DMARDs in patients with at least one comorbidity (66.2% vs 74.5%, p=0.007) or multimorbidity (34.6% vs. 43.5%, p=0.006). Patients with comorbidities and multimorbidity achieved to DAS-28 remission less frequently than patients without comorbidity (31.6% vs 42.6%, p=0.012 and 27.2% vs 39.7%, p=0.001, respectively).

Conclusion:

Physicians were postpone to prescribe biological DMARDs in patients with multimorbidity. Furthermore, comorbidity may have a negative effect on the treatment response. This situation may rise from both late start of the efficient treatment and additional burden effect of the comorbidities on the course of RA disease.

Disclosure: B. Armagan, None; A. Sari, None; A. Erden, None; L. Kilic, None; E. C. Erdat, None; O. Karadag, None; A. Akdogan, None; S. Apras Bilgen, None; I. Ertenli, None; S. Kiraz, None; U. Kalyoncu, None.

Handling of Missing Data, Protocol Violation and Performance of Intention-to-Treat Analysis in the Randomized Controlled Trials of Drug Therapy of Rheumatoid Arthritis

Fawad Aslam1, Karina Torralba2 and Nasim A. Khan3, 1Rheumatology, Mayo Clinic, Scottsdale, AZ, 2Division of Rheumatology, Department of Internal Medicine, Loma Linda University, Loma Linda, CA, 3Rheumatology, University of Arkansas for Medical Sciences and Central Arkansas Veterans Healthcare System, Little Rock, AR

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017

Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports

Session Type: ACR Poster Session B
**Background/Purpose:** Intention-to-treat (ITT) method is recommended to analyze Randomized Controlled Trials (RCTs). It requires analyzing all participants per the assigned intervention group at randomization to prevent treatment effect estimation bias. In practice, RCTs have subjects with protocol deviations and/or missing outcomes. Incorrect analysis of these subjects may give biased results\(^1,2\). Single imputation methods like “last observation carried forward (LOCF)” are discouraged as they may bring bias, and don’t adjust for the uncertainty of imputation\(^3\). We studied the ITT principle application, protocol deviations and missing outcome data handling in RCTs of rheumatoid arthritis (RA) drug therapy.

**Methods:** MEDLINE and Cochrane Central Register of Controlled Trials database were searched to identify parallel-design, English language, original RCT reports of drug therapy for RA with clinical primary and efficacy outcome(s) published in 2002-3, 2006-7 and 2010-11. Two reviewers assessed each RCT for the primary outcome(s) analysis and handling of missing data.

**Results:** 134 RCTs were eligible and enrolled a median (interquartile range, IQR) of 160 (59-381) patients. A median (IQR) of 83 (70-90) % remained enrolled until trial completion. 92 (67%) RCTs lost >10% to follow-up for the primary outcome. 84 (62.7%) reported using ITT analysis, 10 (7.5%) reported modified ITT analysis, and 40 (29.9%) mentioned no such term. 63 (47%) RCTs actually performed true ITT analysis (analyzed all patients as randomized, although 7 RCTs had missing data with undefined approach to imputation). 32 (23.9%) performed a modified ITT analysis [percent analyzed: 97 (95-99)] with exclusion of following categories: those without post-baseline assessment (17); no intervention received (12), and non-eligibility (1). 20 RCTs analyzed only those completing the trial per the study protocol [percent analyzed: 89 (86-97)], while for 19 RCTs patients exclusion reason was unclear [percent analyzed: 91 (69-93)]. Only 5 RCTs had all subjects complete the trials. Only 92 of the 129 (71%) RCTs with a missing final outcome described missing primary outcome handling which included: LOCF (51), non-responder assignment to those with missing data (29), calculation by interpolation (5). Only 2 RCTs did sensitivity analyses with different missing data assumptions. Experimental intervention efficacy could be assessed for 124 RCTs. The percentage of positive RCTs (statistical significance favoring experiment intervention) according to analytic method were: ITT (66%), modified ITT (87%), per-protocol (67%) and unclear (50%) [\(p = 0.056\), Likelihood Ratio test].

**Conclusion:** A considerable variation in reporting and application of ITT principle in the RCTs exists. In about 30% RCTs, per-protocol or unclear analytic methods were used. Similar number of RCTs with missing data did not address handling of such data. Vast majority of RCTs used the non-recommended single imputation methods for missing data. A better description of subjects selected for final statistical analysis and approaches to deal with missing outcomes are needed.

References:

2. Sedgwick P. BMJ 2015;350:h681

Disclosure: F. Aslam, None; K. Torralba, None; N. A. Khan, None.
**Session Date:** Monday, November 6, 2017  
**Session Title:** Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM  

**Background/Purpose:** The addition of biological (b) and new targeted synthetic (ts) DMARDs agents in chronic inflammatory arthritides (CIAs) therapeutic strategies has improved the possibility of controlling disease activity and slowing the progression of joint damage. However their impact on work participation is unclear.

Objective: to assess the effect of biological and tsDMARDs versus conventional treatments in patients with CIAs on work outcomes: employment, presenteeism and absenteeism.

**Methods:** A systematic review of the literature using Pubmed-Medline and the Cochrane library was performed until January 2017. All randomized controlled trials (RCT) and controlled cohorts (CC) comparing work outcomes in patients with rheumatic diseases such as rheumatic arthritis (RA), ankylosing spondylarthritis (AS) and psoriatic arthritis (PsA) treated with biological or tsDMARDs versus conventional therapies were selected. Statistical analysis determined in each study effect size (ES) or odds-ratios (OR) as appropriate to assess the magnitude of treatment effect. Pooled ES and OR were computed by meta-analysis. A random effect model was used in case of heterogeneity.

**Results:**

Thirty three RCTs and 8 CCs were analyzed ie 12306 patients with conventional treatment and 21328 patients with bDMARD or tsDMARD (6610 Infliximab, 5613 Etanercept, 3820 Adalimumab, 672 Golimumab, 2935 Certolizumab, 691 Abatacept, 444 Sirukumab, 351 Baricitinib); 26 studies included 29592 patients with RA, 10 studies included 2226 patients with AS and 5 studies included 1816 patients with PsA.

This meta-analysis showed in patients treated by bDMARD vs conventional treatment:

- a significant decrease of accumulated missed workdays at week 24: ES -0.34 IC95%[-0.6; -0.08] and at week 52: ES -0.04 IC95% [-0.29; 0.2],
- a significant decrease of patients loosing hours due to CIAs: RR 0.63 IC95%[0.48; 0.83],
- a significant improvement in VAS productivity: ES -1.81 IC95%[-2.61; -1.01] and in activity impairment (WPAI): ES -10,57 IC95% [-13,99; -7.14].
- For the employment loss, the positive effect of bDMARDs was nearly significant: OR 0.60 IC95% [0.33; 1.09].

**Conclusion:** Despite the heterogeneity of the data, this meta-analysis showed the beneficial effect of bDMARDs on both absenteeism and presenteeism in CIAs. Thus the high cost of biologic agents could be partly balanced with savings in indirect costs.

**Disclosure:** C. Traverson, None; A. Tubery, None; C. Hua, Abbvie,BMS, Pfizer, 5; F. Barchechath-Flaisler, Roche Pharmaceuticals, 5; C. Lukas, Abbvie, BMS, Celgene, Janssen, MSD, Novartis, Pfizer, Sanofi, Schering, Roche- Chugai, UCB, 5; B. Combe, Pfizer, UCB, 2, BMS, Janssen, Lilly, MSD,Pfizer, Roche-Chugai, UCB, 8, Abbvie, BMS, Janssen, Lilly, MSD, Novartis, Pfizer, Roche-Chugai, UCB, 5; J. Morel, Abbvie, BMS, Celgene, Janssen, Medac, MSD, Novartis, Pfizer, Sanofi, Schering, Roche-Chugai, UCB, 5; C. Gaujoux-Viala, Pfizer Inc, 2, Abbvie, BMS, Celgene, Janssen, Medac, MSD, Nordic Pharma, Novartis, Pfizer, Sanofi, Roche-Chugai, UCB, 5.


**Abstract Number:** 1454

**Association of Poor Prognostic Factors with Medication Persistence Among Adult RA Patients within a Community of Rheumatology Clinics**

Damemarie Paul¹, Laura McDonald², Aarti Rao³, Ruthwik Anupindi⁴ and Keith Knapp⁵,⁶, ¹HEOR, Bristol Myers Squibb, Lawrence Township, NJ, ²CORDS, Bristol Myers Squibb, Uxbridge, United Kingdom, ³Analytics, Mu-Sigma, Bengaluru, India,
Background/Purpose: A fixed treatment paradigm often exists for Rheumatoid Arthritis (RA) patient (pts)\(^1\). However, RA is a heterogeneous disease and differences in pts’ serostatus affect disease progression. For pts receiving targeted disease modifying antirheumatic drug (tDMARD) (biologics and JAK inhibitors), this study compares the differences in treatment factors such as persistence, adherence and medication effectiveness for pts with versus those without poor prognostics factors (PPF).

Methods: Pts ≥18 years and satisfying either ACR 1987 or 2010 criteria in the JointMan database between 1 Jan 2009 and 31 Mar 2017 were included. Pts were required to have at least one record for either anti-citrullinated protein antibodies (ACPA) or rheumatoid factor (RF) at baseline (study period start date to index treatment initiation + 30 days). Pts who were ACPA positive (+) only, RF+ only or dual+ were considered PPF positive (PPF+) and pts who were both ACPA and RF negative (-) were controls (PPF-). First tDMARD prescription date was considered as the index date.

Persistence, measured as number of days from index date to first switch from, or discontinuation of the index tDMARD or end of study period, whichever came first, was reported for the two cohorts. Persistence was stratified by cohort and PPF+ subgroups. Kruskal-Wallis test compared median persistence with a significance level of 0.05. Comparisons for all treatment factors will be conducted in the same way.

Results: 797(71%) out of the 1,122 pts included in the analysis were PPF+. Compared to controls, PPF+ pts were older (59 vs 56 yrs) and less likely to be females (73 vs 81%). Overall, median persistence was greater for the PPF+ cohort (420 vs 379 days) but not significant. Comparison of the PPF+ subgroups to controls showed significant differences in persistence between ACPA+ and dual+ pts versus controls. Intragroup comparison of PPF+ subgroups also showed that dual+ pts had substantially lower persistence compared to ACPA+ and RF+ subgroups. ACPA+ pts remained on tDMARD therapy the longest. (ACPA+: 577, RF+: 484, dual+: 344 days)

Table1: Persistence (days) by subgroups of PPF

<table>
<thead>
<tr>
<th>Descriptive Statistics</th>
<th>Cohort Subgroups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PPF+</td>
</tr>
<tr>
<td></td>
<td>ACPA+ (N=163)</td>
</tr>
<tr>
<td></td>
<td>ACPA+ and RF+ (N=265)</td>
</tr>
<tr>
<td>Median(IQR)</td>
<td>577(217-1533)</td>
</tr>
<tr>
<td></td>
<td>344(152-640)</td>
</tr>
<tr>
<td>p-value</td>
<td>0.0016</td>
</tr>
<tr>
<td></td>
<td>0.0434</td>
</tr>
<tr>
<td>&lt;.0001</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td></td>
<td>N/A</td>
</tr>
</tbody>
</table>

Conclusion:

In this study, tDMARD persistence varied based on PPF status. Scientific evidence also demonstrates a correlation between serostatus and RA disease progression. PPF status may need to be considered in tDMARD assignment decisions. Further analysis to evaluate the effect of PPF status on other treatment factors is needed.

Disclosure: \textbf{D. Paul}, Bristol-Myers Squibb, 3; \textbf{L. McDonald}, BMS, 3; \textbf{A. Rao}, None; \textbf{R. Anupindi}, None; \textbf{K. Knapp}, Discus Analytics, 1.

View Abstract and Citation Information Online - \url{http://acrabstracts.org/abstract/association-of-poor-prognostic-factors-with-medication-persistence-among-adult-ra-patients-within-a-community-of-rheumatology-clinics}

Abstract Number: 1455
Investigation of Poor Prognostic Factors Among Rheumatoid Arthritis Patients in Turkbio Registry

Nevsun Inanc1, Zeynep Erturk1, Gulsen Ozen1, Ediz Dalkilic2, Suleyman Serdar Koca3, Gerçek Can4, Ahmet Karatas5, Yavuz Pehlivan6, Ayten Yazici7, Ayse Cefle7, Servet Akar8, Soner Senel9, Burak Oz9, Nurullah Akkoe10, Haner Direskeneli1 and Fatos Onen11, 1Rheumatology, Marmara University, School of Medicine, Rheumatology, Istanbul, Turkey, 2Department of Internal Medicine, Division of Rheumatology, Uludag University, School of Medicine, Rheumatology, Bursa, Turkey, 3Rheumatology, Firat University, School of Medicine, Rheumatology, Elazig, Turkey, 4Rheumatology, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey, 5Department of Rheumatology, Firat University, School of Medicine, Rheumatology, Elazig, Turkey, 6Rheumatology, Uludag University, School of Medicine, Rheumatology, Bursa, Turkey, 7Rheumatology, Kocaeli University, School of Medicine, Rheumatology, Kocaeli, Turkey, 8Rheumatology, Izmir Katip Celebi University, School of Medicine, Rheumatology, Izmir, Turkey, 9Rheumatology, Kayseri Erciyes University, School of Medicine, Rheumatology, Kayseri, Turkey, 10Rheumatology, Private Practice, Rheumatology, Izmir, Turkey, 11Rheumatology, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: TURKBIO is the Turkish version of Danish DANBIO rheumatologic database which has been established in 2011. In 2016, the EULAR RA management guideline recommended assessment of certain prognostic factors while deciding the treatment strategy after the first csDMARD failure. However, it is unknown how frequent these factors are in bDMARD and tsDMARD initiators and how they affect the treatment response in RA patients. We examined the frequency and influence of these poor prognostic factors on treatment response in bDMARD and tsDMARD initiating RA patients enrolled in TURKBIO.

Methods: Seven poor prognostic factors were investigated in 898 RA patients started bDMARD and tsDMARD in TURKBIO: (1) Moderate to high disease activity (2) Elevated acute phase reactants (3) High swollen joint counts (≥ 4) (4) High RF/ACPA titers (5) Combinations of the above (6) Erosions (7) Failure of ≥ 2 csDMARDs. The frequencies of these factors at treatment initiation and influence of these on achievement of DAS28-CRP remission/remission+low disease activity (LDA) at the 6th month of treatment were evaluated in overall any bDMARD and tsDMARD-receiving RA patients and in subgroups of individual drugs including TNF inhibitors (TNFi), abatacept (ABA), rituximab (RTX), tocilizumab (TCZ) and tofacitinib (TOFA). The presence of these factors in patients who stayed on or were withdrawn from the bDMARDS and tsDMARD were also determined.

Results: Among the seven prognostic factors; factors 1, 2, 4, 6, and 7 were found in over 60% of patients while factors 3 and 5 were present in about 30% of the patients. Factors 1 and 3 were more frequent in patients who were in moderate/high disease activity compared to those in remission + low disease activity at the 6th month of treatment (Table). Similarly, factors 1 and 3 were determined at higher percentage in non-remission than remission group (Factor 1: 93.4% vs. 82.2%, p<0.001; factor 3: 43% vs. 30.7%, p=0.002). These two factors were also significantly more frequent in patients withdrawn from the treatment than in patients who stayed on treatment (Factor 1: 93% vs. 85%, p<0.001; factor 3: 41% vs. 34%, p=0.038). In TNFi group besides factors 1 and 3, factors 5 and 7 were also significantly more frequent in non-remission group than in remission group whereas, in the RTX group, only factor 1 was significantly more frequent in remission group compared to non-remission group. For the other bDMARDS and tsDMARD we did not find any difference in poor prognostic factors among patients who did achieve remission and did not.

Conclusion: Five of the seven poor prognostic factors were detected more than half of the RA patients at bDMARD and tsDMARD initiation in TURKBIO. Patients with poor prognostic factors especially factors 1 and 3 achieved remission less frequently. Additionally, there was a relationship between bDMARDS and tsDMARD withdrawal and factors 1 and 3. The influence of these factors was mainly observed in TNFi receiving group.
Table. Frequencies of poor prognostic factors in RA patients initiating bDMARDs and tsDMARD.

<table>
<thead>
<tr>
<th>Factors</th>
<th>Remission+low disease activity, %</th>
<th>Moderate+high disease activity, %</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Factor 1:</strong> Moderate to high disease activity</td>
<td>95.9</td>
<td>83.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Factor 2:</strong> Elevated acute phase reactants</td>
<td>100</td>
<td>99.5</td>
<td></td>
</tr>
<tr>
<td><strong>Factor 3:</strong> High swollen joint counts (≥4)</td>
<td>47.1</td>
<td>31.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Factor 4:</strong> High RF/ACPAters</td>
<td>68.3</td>
<td>71.9</td>
<td>0.465</td>
</tr>
<tr>
<td><strong>Factor 5:</strong> Combinations of the factors 1, 2, 3, 4</td>
<td>31.3</td>
<td>25.9</td>
<td>0.284</td>
</tr>
<tr>
<td><strong>Factor 6:</strong> Erosions</td>
<td>56.5</td>
<td>65.6</td>
<td>0.332</td>
</tr>
<tr>
<td><strong>Factor 7:</strong> Failure of ≥2 csDMARDs</td>
<td>69.4</td>
<td>69.0</td>
<td>0.918</td>
</tr>
</tbody>
</table>

* Disease activity was assessed by using DAS28-CRP at the 6th month of treatment

Disclosure: N. Inanc, None; Z. Erturk, None; G. Ozen, None; E. Dalkilic, AbbVie, 2,AbbVie, MSD, Roche, UCB and Pfizer, 9; S. S. Koca, None; G. Can, None; A. Karatas, None; Y. Pehlivan, None; A. Yazıcı, None; A. Cefle, None; S. Akar, None; S. Senel, None; B. Oz, None; N. Akkoc, None; H. Direskeneli, None; F. Onen, None.


Abstract Number: 1456

**Synergistic Reversal of Arthritis By Synoviocyte-Targeted Therapy and TNF Immunomodulation**

Christian Secchi1,2,3, Karen M. Doody2, Mattias N. D. Svensson2,4, Frances Humby5, Rebecca Hands5, Eugenio Santelli1,2, Cristiano Sacchetti2,6, Kuninobu Wakabayashi7, Dennis J. Wu8, Ardira Aliko9, Piotr Mydel9,10, Tsuyoshi Kasama7, David L. Boyle11, Francesco Galimi12, Michel L. Tremlay13, Gary S. Firestein6, Costantino Pitzalis5, Stephanie Standford8,14 and Nunzio Bottini2,4: 1Medicine, University of California San Diego, San Diego, CA, 2Cellular Biology, La Jolla Institute for Allergy and Immunology, La Jolla, CA, 3Medicine, National Institute of Biostructures and Biosystems, University of Sassari Medical School, Sassari, Italy, 4Department of Medicine, University of California San Diego, La Jolla, CA, 5Centre for Experimental Medicine and Rheumatology, William Harvey Research Institute, Barts and The London, School of Medicine and Dentistry, Queen Mary University of London, London, United Kingdom, 6Medicine, University of California San Diego, La Jolla, CA, 7Div of Rheumatology, Showa University School of Med, Shinagawa-ku Tokyo, Japan, 8University of California San Diego, San Diego, CA, 9University of Bergen, Bergen, Norway, 10Clinical Science, Broegelmann Research Laboratory, Bergen, Norway, 11University of California San Diego, La Jolla, CA, 12National Institute of Biostructures and Biosystems, University of Sassari Medical School, Sassari, Italy, 13Goodman Cancer Centre, McGill University, Montréal, QC, Canada, 14La Jolla Institute for Allergy and Immunology, La Jolla, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Background/Purpose:
Despite the availability of immunosuppressive disease-modifying anti-rheumatic agents (DMARDs), many rheumatoid arthritis (RA) patients still fail to achieve remission. Fibroblast-like synoviocytes (FLS) are non-immunological joint-lining cells that become invasive during RA. Non-immunosuppressive agents targeting FLS in combination with DMARDs have the potential to improve control of RA without enhancing the risk of infections. We recently reported that disrupting the interaction between the receptor protein tyrosine phosphatase sigma (RPTPσ) and the proteoglycan syndecan-4 using an RPTPσ decoy biologic (RPTPσ-Ig1&2) reduces FLS cartilage invasion. Here we examined the therapeutic potential of RPTPσ-Ig1&2 in combination with tumor necrosis factor-a (TNF) inhibition.

Methods:
The relationship between RPTPσ and TNF was evaluated in RA FLS, murine FLS and collagen-induced arthritis (CIA) mice by qPCR. The anti-rheumatic effect of RPTPσ-Ig1&2 was assessed in spontaneous KBxN (sKBxN) and collagen antibody induced arthritis (CAIA). Also, RPTPσ-Ig1&2 was administered to CIA mice either alone or in combination with a mouse anti-TNF receptor agent.

Results:
TNF was found to negatively regulate the expression of RPTPσ in RA FLS (P<0.0001). Anti-TNF treatment of CIA mice increased the joint expression of RPTPσ (P=0.031). RPTPσ-Ig1&2 administration attenuated arthritis in multiple mouse models (sKBxN P<0.001; CAIA P<0.001, CIA P=0.0079). Combining RPTPσ-Ig1&2 with anti-TNF receptor treatment enhanced the reversal of CIA (P<0.0001).

Conclusion:
Our study provides the first evidence that an FLS-targeting therapy is efficacious in multiple mouse models of RA and enhances TNF blockade in experimental arthritis.

Disclosure: C. Secchi, None; K. M. Doody, None; M. N. D. Svensson, None; F. Humby, None; R. Hands, None; E. Santelli, None; C. Sacchetti, None; K. Wakabayashi, None; D. J. Wu, None; A. Aliko, None; P. Mydel, None; T. Kasama, None; D. L. Boyle, None; F. Galimi, None; M. L. Tremblay, None; G. S. Firestein, None; C. Pitzalis, None; S. Standford, None; N. Bottini, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/synergistic-reversal-of-arthritis-by-synoviocyte-targeted-therapy-and-tnf-immunomodulation

Abstract Number: 1457

Perioperative Management of Methotrexate and Tumor Necrosis Factor Inhibitor Combination Therapy in Rheumatoid Arthritis Patients

Hsin-Hsuan Juo1,2 and Bernard Ng1,3, 1rheumatology, University of Washington, seattle, WA, 2rheumatology, VA Puget Sound Health Care System, seattle, WA, 3Rheumatology, VA Puget Sound Health Care System, seattle, WA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM
Background/Purpose:

Rheumatoid arthritis (RA) patients have a higher frequency of requiring surgical procedures and worse surgical outcome. However, literature regarding post-surgical infectious outcome associated with combination of modifying anti-rheumatic drugs (DMARDs) and biologics is scare. The aim of the study is to assess whether the risk of post-operative infectious complications among RA patients is affected by discontinued methotrexate (MTX) and Tumor Necrosis Factor Inhibitor (TNFi) prior to surgery during perioperative period.

Methods:

Using the United States Veterans Affairs (VA) databases, we identified surgical procedures in a 18-year cohort of RA patients, who were on at least 1 DMARDs or 1 biologic agent in the perioperative period. Surgeries were divided into the following groups: patients treated with methotrexate (MTX) and etanercept (ETA) combination therapy, and those treated MTX and adalimumab (ADA) combination therapy. MTX is continued throughout the surgery. The risk of infection is compared among groups that continue vs discontinue within 90 days, 60 days and 30 days of the surgery. Infection includes pneumonia, urinary tract infection and wound infection. Primary endpoints are total infectious complication. Unconditional multilevel mixed effect logistic regression model was used for analysis. Covariates include chronic steroid use status and modified Charlson score. Statistical significance is defined as p<0.05.

Results:

Table 1. Post-operative infection with MTX continued and TNFi discontinued within 90 days

<table>
<thead>
<tr>
<th>Continue methotrexate</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>P value</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continue (reference) vs discontinue</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discontinue &gt;90 days</td>
<td>0.64</td>
<td>0.28–1.47</td>
<td>0.29</td>
<td>811</td>
</tr>
<tr>
<td>etanercept</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discontinue &lt;90 days</td>
<td>1.04</td>
<td>0.26–4.17</td>
<td>0.96</td>
<td>811</td>
</tr>
<tr>
<td>etanercept</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>etanercept</td>
<td>1.74</td>
<td>0.51–5.98</td>
<td>0.38</td>
<td>685</td>
</tr>
<tr>
<td>etanercept</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Post-operative infection with MTX continued and TNFi discontinued within 60 days

<table>
<thead>
<tr>
<th>Continue methotrexate</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>P value</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continue (reference) vs discontinue</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discontinue &gt;60 days</td>
<td>0.68</td>
<td>0.30–1.51</td>
<td>0.34</td>
<td>820</td>
</tr>
<tr>
<td>etanercept</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discontinue &lt;60 days</td>
<td>0.76</td>
<td>0.15–3.77</td>
<td>0.73</td>
<td>820</td>
</tr>
<tr>
<td>etanercept</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>etanercept</td>
<td>2.64</td>
<td>0.75–9.27</td>
<td>0.13</td>
<td>691</td>
</tr>
<tr>
<td>etanercept</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Post-operative infection with MTX continued and TNFi discontinued within 30 days

<table>
<thead>
<tr>
<th>Continue methotrexate</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>P value</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continue (reference) vs discontinue</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discontinue &gt;30 days</td>
<td>0.65</td>
<td>0.29–1.45</td>
<td>0.29</td>
<td>830</td>
</tr>
<tr>
<td>etanercept</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discontinue &lt;30 days</td>
<td>1.11</td>
<td>0.21–5.82</td>
<td>0.90</td>
<td>830</td>
</tr>
<tr>
<td>etanercept</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>etanercept</td>
<td>2.09</td>
<td>0.41–10.53</td>
<td>0.37</td>
<td>702</td>
</tr>
<tr>
<td>etanercept</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusion:

When MTX is continued through surgery for patients with RA, there is a trend towards lower risk of post-operative infection when TNFi was discontinued before surgery. Sensitivity analyses of TNFi discontinuation at 30-60-90 days before surgery yielded similar results. However, the reduced infection risks did not reach statistical significance. This could be because of the heterogeneity of surgeries in our study. Further analyses looking at specific types of surgeries may help to ascertain this.

Disclosure: H. H. Juo, None; B. Ng, None.

Correlation of Multi-Biomarker Disease Activity Score with Clinical Disease Activity Measures for the JAK1-Selective Inhibitor Filgotinib As Monotherapy and in Combination with Methotrexate in Rheumatoid Arthritis Patients

Mark C. Genovese¹, René Galien², Yang Pan³, Annegret Van der Aa⁴, Corinne Jamoul⁴, Pille Harrison⁴, Chantal Tasset⁴, Lovely Goyal³, Wanying Li³ and Jacqueline Tarrant³, ¹Stanford University Medical Center, Palo Alto, CA, ²Galapagos SASU, Romainville, France, ³Gilead Sciences, Foster City, CA, ⁴Galapagos NV, Mechelen, Belgium

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The JAK1 selective inhibitor filgotinib (GLPG0634, GS-6034) was efficacious as both add-on to methotrexate (MTX) and monotherapy in two 24-week phase 2B studies in active rheumatoid arthritis (RA) patients with inadequate response to MTX (DARWIN 1 and 2)¹. We evaluated the utility of a Multi Biomarker Disease Activity (MBDA) score in relation to clinical disease activity assessments in patients treated with filgotinib.

Methods: Serum samples from RA patients receiving either a stable dose of MTX and PBO, filgotinib 100mg or 200mg QD (DARWIN 1), or placebo (PBO) or filgotinib monotherapy at 100mg or 200mg once daily (QD, DARWIN 2), were collected and analyzed at baseline and week 12 with the MBDA test (Crescendo Biosciences, CA, US). Spearman’s rank correlations between MBDA score and clinical measures (e.g. DAS28-CRP, SJC28, TJC28) were estimated at baseline and week 12 and for their changes from baseline to week 12.

Results: At baseline, median MBDA scores were the same for both DARWIN 1 and 2 studies (58) with statistically significant correlation observed between MBDA score and DAS28-CRP (r=0.43, r=0.48, respectively, both p<0.001). There was weak correlation of MBDA score with SJC28 and TJC28 for DARWIN 1 (r=0.2, 0.11; p=0.01, ns) and DARWIN 2 (r=0.19, 0.17; both p<0.05). At week 12, statistically significant correlations were observed in 200mg filgotinib monotherapy cohort between MBDA score and DAS28, SJC28, and TJC28 (r=0.6, 0.36, 0.46; p<0.001, <0.01, <0.001) that were less so in 100mg (r=0.33, 0.16, 0.15; p<0.05, ns, ns) and PBO (r=0.49, 0.40, 0.22; p<0.001, <0.01, ns) treatment groups. When comparing change from baseline at week 12, the MBDA only correlated to DAS28-CRP for 200mg filgotinib monotherapy and PBO groups (r=0.36, 0.39; p<0.01). There was no statistically significant correlation between MBDA and clinical measures (or between their changes from baseline) for filgotinib on a background of MTX at week 12.

Conclusion: The MBDA score significantly correlated with disease activity measures in subjects treated with filgotinib as monotherapy for 12 weeks. Despite similar baseline associations and treatment efficacy no correlation was observed between MBDA score and DAS28-CRP for filgotinib with MTX add-on.


Figure: Scatter plot of MBDA score vs. DAS28-CRP at week 12 for DARWIN 1 and DARWIN 2
Lack of Drug-Drug Interaction between Filgotinib, a JAK-1 Selective Inhibitor, and a Representative Hormonal Contraceptive Medication, Levonorgestrel/Ethinyl Estradiol

Rebecca Begley¹, Kacey Anderson², Timothy R. Watkins¹, Jing Shen¹, Hao Zheng¹, Eugene Vass¹, Ann Qin², Brian P. Kearney² and Yan Xin², ¹Gilead Sciences, Inc., Foster City, CA, ²Clinical Pharmacology, Gilead Sciences, Inc., Foster City, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Filgotinib is a potent and selective JAK1 inhibitor in clinical development for treatment of inflammatory diseases, including rheumatoid arthritis and inflammatory bowel diseases. Filgotinib does not inhibit or induce CYP or UGT metabolic enzymes in vitro, and did not alter the pharmacokinetics (PK) of midazolam, a sensitive CYP3A substrate, in healthy subjects. In order to support the use of filgotinib in fertile women, this Phase I study was conducted to rule out unanticipated interactions of filgotinib on the PK of a representative oral contraceptive (OC), levonorgestrel (LEVO)/ethinyl estradiol (EE).

Methods:
This was an open-label, randomized, two-way crossover study in healthy female subjects. Subjects received a single dose of LEVO (150 ug)/EE (30 ug) alone (Treatment A; reference), or in combination with multiple-dose filgotinib (200 mg once daily; 15 days; Treatment B; test). PK sampling was performed for 120 hours following administration of the OC, and safety was assessed throughout the study. An analysis of variance using a mixed-effects model was applied to the natural logarithmic transformation of PK parameters (AUC and C_{max}) for EE and LEVO. Geometric-least squares means (GLSM) ratios and 90% confidence intervals (90%CI) of PK parameters were estimated for the test vs reference treatments, and were compared against pre-specified lack of PK alteration boundaries of 70 to 143%. The PK of filgotinib was evaluated as well, and compared against historical values.

Results:

The study enrolled 24 subjects. All subjects completed study treatments; 1 subject discontinued after the last PK draw, due to withdrawal of consent. The mean (range) age of subjects was 37 (21-45) years, 21 (87.5%) were white, and 24 (100%) were of Hispanic or Latino ethnicity.

Coadministration of OC with filgotinib resulted in comparable exposures of LEVO and EE. The GLSM ratios (90%CI) for AUC_{inf}, AUC_{last} and C_{max} of LEVO were 94.9 (90.2, 99.8), 94.2 (89.1, 99.6) and 105 (94.8, 117), respectively; corresponding values for EE were 114 (109, 118), 113 (109, 117) and 114 (106, 122). The GLSM ratios (90%CI) were contained within the pre-specified lack of interaction bounds (70 ‑ 143%), indicating a lack of interaction of filgotinib on OC. Exposures of filgotinib were consistent with historical data.

Study treatments were generally well tolerated; 3 (12.5%) and 6 (25.0%) of subjects experienced an adverse event (AE) during Treatments A and B, respectively. No serious or severe AEs occurred; all AEs reported were Grade 1 (mild). Of the AEs reported only one (headache) was recorded as related to study drug (during Treatment B), and it was not distinctly attributed to LEVO/EE versus filgotinib. All laboratory abnormalities were Grade 1, and there were no clinically significant trends in laboratory abnormalities, vital sign measurements, or ECG recordings.

Conclusion:

Co-administration with filgotinib did not alter the PK of levonorgestrel/ethinyl estradiol. Hormonal contraceptives can be allowed as an effective contraception method for subjects on filgotinib treatment.


**Abstract Number:** 1460

**Predictive Factors Associated with Successful Down-Titration of Biologics for Rheumatoid Arthritis Patients in Clinical Practice**

Takaaki Komiya1, Kaoru Minegishi-Takase2, Natsuki Sakurai1, Yuichiro Sato1, Hideto Nagai3, Naoki Hamada3, Yumiko Sugiyama3, Naomi Tsuchida1, Yutaro Soejima3, Yosuke Kunishita3, Hiroto Nakano3, Daiga Kishimoto3, Koji Kobayashi2, Reikou Kamiyama3, Ryusuke Yoshimi3, Yukiko Asami2, Yohei Kirino3, Shigeru Ohno4 and Hideaki Nakajima3, 1Stem Cell and Immune Regulation, Yokohama City University Graduate School of Medicine, Yokohama, Japan, 2Center for Rheumatic Diseases, Yokohama City University Medical Center, Yokohama, Japan, 3Department of Stem Cell and Immune Regulation, Yokohama City University Graduate School of Medicine, Yokohama, Japan, 4Center for Rheumatic Disease, Yokohama City University Medical Center, Yokohama, Japan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Background/Purpose: Randomized clinical trials have shown that if a patient is in sustained remission, biological disease-modifying anti rheumatic drugs (bDMARDs) therapy can be tapered in rheumatoid arthritis (RA). However, little is known about down-titration of bDMARDs in the real world. We retrospectively analyzed our cohort to determine the frequency and predictive factors associated with the successful down-titration of bDMARD in RA patients in our two university hospitals.

Methods: This study included consecutive RA patients who fulfilled 1987 ACR and/or 2010 ACR/EULAR classification criteria and treated with bDMARD (infliximab, adalimumab, etanercept, golimumab, certolizumab-pegol, tocilizumab, and abatacept) for longer than 6 months. The patients receiving stable and standard dose treatment were defined as SD group, while the patients receiving down-titration were defined as DT group. We retrospectively reviewed clinical charts and compared the route of administration, concomitant medication use, laboratory data, X-ray findings and patient characteristics at the beginning of bDMARD between SD group and DT group. Statistical analyses were performed using univariate and multivariate analysis.

Results: A total of 347 patients (age 62.5±13.8 years old, female 83.6%, disease duration 12.3±8.5 years) were included in this analysis, 255 (73.5%) and 92 (26.5%) patients belonged to SD and DT groups, respectively. Five (1.4%) patients experienced disease flare after down-titration of bDMARD after 8.4±5.7 months. There was no significant difference between SD group and DT group in disease duration, route of administration, prevalence of the anti-citrullinated protein antibody and the rheumatoid factor, TJC, SJC, PGA, DAS28-ESR, and X-ray at baseline. In the univariate analyses of baseline data, there were statistically significant differences in the rates of bDMARD naïve patients, age at onset, age at the beginning of bDMARD, concomitant oral corticosteroid use, and CRP levels between SD group and DT group (57.1% vs 76.4%, \( p = 0.001 \), 51.0 ± 14.6 vs 47.1 ± 14.9, \( p = 0.03 \), 59.6 ± 13.7 vs 55.5 ± 14.6, \( p = 0.02 \), 43.1% vs 34.8%, \( p = 0.04 \), and 1.9 ± 2.5 vs 1.1 ± 1.3, \( p = 0.03 \), respectively). Multivariate statistical analysis revealed the low level of serum CRP at baseline were associated with successful down-titration (\( p = 0.03 \), odds ratio = 0.81, 95% CI: 0.663-0.990).

Conclusion: Down-titration of biologics might be achieved in RA patients who have the following factors at the beginning of bDMARD: bDMARD naïve, younger age, no concomitant use of corticosteroid, and low level of serum CRP.
Disclosure: T. Komiya, None; K. Minegishi-Takase, None; N. Sakurai, None; Y. Sato, None; H. Nagai, None; N. Hamada, None; Y. Sugiyama, None; N. Tsuchida, None; Y. Soejima, None; Y. Kunishita, None; H. Nakano, None; D. Kishimoto, None; K. Kobayashi, None; R. Kamiyama, None; R. Yoshimi, None; Y. Asami, None; Y. Kirino, None; S. Ohno, None; H. Nakajima, None.


Abstract Number: 1461

The Relationship between Serum IL-37 and Disease Activity in Patients with Rheumatoid Arthritis: Post-Hoc Analysis of Planetra Study

Seoung Wan Nam¹, Hyuk Hee Kwon², Ga-Young Ahn³, Min Jung Kim² and Dae-Hyun Yoo¹, ¹Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), ²Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), ³Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

Background/Purpose:
Rheumatoid Arthritis (RA) is a chronic inflammatory disorder affecting synovial joints. Multiple pro- and anti-inflammatory cytokine are thought to play a major role in the development of the disease. IL-37 is an anti-inflammatory cytokine which belongs to IL-1 family superfamily and regulates inflammation. We investigated the association of IL-37 with disease activity in RA patients, who were treated with infliximab for 30 weeks.

Methods:
Patients were recruited from the PLANETRA study (NCT01217086). Patients with active RA were treated with CT-P13 or infliximab originator (INX). We measured the serum levels of IL-37 at week 0 (baseline) and at 30 weeks after treatment. Other demographic, laboratory and clinical variables were evaluated simultaneously. Mann-Whitney or Wilcoxon signed rank test was performed to determine the difference between two groups and Spearman’s correlation coefficient was used to test for correlations between to variables. The values described are the median values.

Results:
66 patients with active RA (53 females and 13 males, 54 White and 12 Asians) were analyzed and median age of patients was 50 years. Compared to baseline, all measured clinical and laboratory parameters and serum IL-37(from 46.1 to 25.2 pg/ml, p=0.011) were significantly reduced. There was a correlation between IL-37 and CRP at the time of screening, and IL37 correlated with ESR, CRP, DAS28-ESR, DAS28-CRP and PGAD at week 30. IL-37 levels at 30 weeks after treatment, were lower in patients with DAS28<3.2 than in patients with DAS28>3.2 (DAS28-ESR; 0.0 in DAS28<3.2, 30.6 in DAS28>3.2, p=0.002, DAS28-CRP; 0.0 in DAS28<3.2, 34.3 in DAS28>3.2, p=0.010). IL-37 levels decreased significantly in the EULAR good & moderate response group (DAS28-ESR; 42.2 at week 0, 0.0 at week 30, p=0.006, DAS28-CRP; 44.8 at week0, 18.5 at week 30, p=0.001), but not in non-responder group. According to the median level of IL-37, CRP was higher in the high group (n=29) at screening, and CRP, ESR DAS28-ESR, DAS28-CRP, HAQ and PAP were higher in high group at week 30.

Conclusion:
Serum levels of IL-37 is elevated in active RA patients and is associated with disease activity measures of RA.

Table1. Laboratory and clinical parameters at baseline and 30 weeks after treatment

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline (median)</th>
<th>week 30 (median)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-CCP Ab-positive, no(%)</td>
<td>55 (83.3)</td>
<td>52 (78.8)</td>
<td>0.261</td>
</tr>
<tr>
<td>Joint count</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TJC (28 joints)</td>
<td>14.5 (3-28)</td>
<td>2.5 (0-24)</td>
<td>0.000</td>
</tr>
<tr>
<td>SJC (28 joints)</td>
<td>10.0 (3-25)</td>
<td>1.5 (0-12)</td>
<td>0.000</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>0.85 (0.04-9.25)</td>
<td>0.31 (0.02-8.90)</td>
<td>0.011</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>38.0 (24-138)</td>
<td>20.5 (2-86)</td>
<td>0.000</td>
</tr>
<tr>
<td>DAS28-ESR</td>
<td>6.54 (4.50-8.42)</td>
<td>3.90 (1.35-6.82)</td>
<td>0.000</td>
</tr>
<tr>
<td>DAS28-CRP</td>
<td>5.70 (3.44-7.57)</td>
<td>3.25 (1.15-6.44)</td>
<td>0.000</td>
</tr>
<tr>
<td>HAQ</td>
<td>1.6 (0-2.4)</td>
<td>1.0 (0-2.1)</td>
<td>0.000</td>
</tr>
<tr>
<td>IL-37</td>
<td>46.1 (0-552.2)</td>
<td>25.2 (0-630.5)</td>
<td>0.011</td>
</tr>
</tbody>
</table>
Induction of Immune Tolerance through an Epitope-Specific Vaccine Induces Clinical Amelioration in Patients with Rheumatoid Arthritis

Jin Hui Sherlynn Chan, Theodorus van den Broek, Jing Yao Leong, Maura Rossetti, Roberto Spreafico and Salvatore Albani

SingHealth Translational Immunology and Inflammation Centre (STIIC), Duke-NUS Medical School, Singapore, Singapore, University Medical Center of Utrecht, Utrecht, Netherlands, University of California, Los Angeles, Los Angeles, CA, Synthetic Genomics, La Jolla, CA, KK Women's and Children's Hospital, Singapore, Singapore

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

The manipulation of immune tolerance using immune checkpoints such as PD-1 is gaining progressive attraction in diseases such cancer where such manipulation would be clinically relevant. In our previous studies, we have identified an antigenic epitope which contributes to autoimmune inflammation in rheumatoid arthritis. Using dnaJP1, a peptide derived from the pro-inflammatory dnaJ proteins, we have concluded Phase I and II clinical trials in which clinical amelioration was associated with the induction of immune tolerance to dnaJP1. Here, we hypothesize that clinical amelioration relies on immunomodulatory mechanisms of immune tolerance involving the reactivation of immune checkpoints.

Methods:

PBMCs obtained at the end of the Phase II trial (Day168), from clinical responders treated with dnaJP1 (n=6) and clinical non-responders treated with placebo (n=10) were studied for gene expression by quantitative PCR and multi-coloured flow cytometry with antibody panels designed to investigate the T cell immunomes. Flow cytometry results were analysed by clustering with Multi-Dimensional Automated Reduction and Visualization (MARVis), an in-house customised machine learning software.

Results:

Analysis of PBMCs with the MARVis software employed in this study allowed for the identification of immune subsets and the dissection of complex interactions between immune cell populations at a level which was unachievable before. Examination of the T cell immunomes of dnaJP1 responders and placebo non-responders revealed that clinical amelioration is an outcome of an active process of tolerization. More specifically, the induction of immune tolerance appears to depend on the generation of a population of CD4+ FoxP3+ regulatory T (Treg) cells in which PD-1 plays an active role in enhancing the production of anti-inflammatory cytokines such as TGFβ. This vital observation is complemented by the reshaping of the effector T (Teff) cell compartment which is accompanied by a significant decline in the expression of pro-inflammatory cytokines such as IL-17A and IFNγ between the start and
the end of epitope-specific immunotherapy. In parallel, epitope-specific immunotherapy also elicited a subset of antigen-experienced memory T cells (CD4+CD45RO+CD69+TGFβ+) which are reliant on tolerogenic pathways.

Conclusion:

We have taken a holistic approach in identifying the mechanisms dictating the induction of immune tolerance. Our data paves the way for a vaccine-like approach for epitope-specific immunotherapy in rheumatoid arthritis. This novel approach relies on the restoration of the balance amongst various immune checkpoints and will contribute significantly to the development of clinically effective therapies in RA.

References

1 Prakken et al., 2004, PNAS
2 Koffeman et al., 2009, Arthritis & Rheumatism

Additional Disclosure: S. Albani is the inventor of patents owned by Singhealth & UCSD

Disclosure: J. H. S. Chan, None; T. van den Brock, None; J. Y. Leong, None; M. Rossetti, None; R. Spreafico, None; S. Albani, None.


Abstract Number: 1463

Interaction between Methotrexate and BAFF for Preventing Immunization Against TNF-α Inhibitors By Increasing Adenosine and Regulatory B-Cell Subsets

Samuel Bitoun1, Gaetane Nocturne2, Bineta Ly3, Juliette Pascaud4, Alain Pruvo5 and X Mariette6, 1INSERM U1184, IMVA, Paris Sud University, LabEx LERMIT, Le Kremlin Bicêtre, France, 2INSERM U1184, IMVA, Paris Sud University, LabEx LERMIT, Le Kremlin Bicêtre, France, 3INSERM U1184, Paris Sud University, Kremlin Bicêtre, France, 4U1184 IMVA, Università Paris Sud, Le Kremlin-Bicêtre Cedex, France, 5CEA - DRF/iBiTec-S - LabEx LERMIT - MetaboHUB-Paris, Gif sur Yvette, France, 6INSERM U1184, Université Paris-Sud, Hôpitaux Universitaires Paris-Sud, Le Kremlin-Bicêtre, France

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

TNFα inhibitors (TNFi) can be immunogenic in patients with autoimmune diseases. B-cell activating factor transgenic mice (BAFFtg) are a model of autoimmune disease since they present with lupus and Sjögren-like manifestations. Prolonged treatment with TNFi in this model leads to anti-drug antibodies (ADA). In humans, low dose Methotrexate (MTX) diminishes immunization against TNFi. MTX favors the release of adenosine monophosphate (AMP), which, via the CD73 ectoenzyme will be transformed in adenosine, a powerful immune-regulatory mediator. We thus sought to investigate the role of MTX in BAFFtg mice to identify the mechanism of action involved in this tolerance.

Methods:

BAFFtg mice treated with adalimumab or etanercept for 52 weeks with or without MTX for 3 consecutive days starting the day of TNFi, were studied. Drug concentration and ADA were monitored with Theradiag® assays. WT and BAFFtg mice splenocytes and B1 peritoneal cells were compared for surface markers either involved in MTX-related purinergic metabolism (CD73 CD39) or B-
cell regulatory function (IL-10 or Breg precursors: CD21hi CD24hi CD23+ cells). Detection of adenosine on sorted B-cells was performed using mass spectrometry-coupled with HPLC.

**Results:**

In BAFFtg mice, a short course of MTX treatment starting the day of the TNFi administration prevented immunization against TNFi and maintained drug concentration over 52 weeks (Fig A). The same experiments made in WT mice led to controversial results. BAFFtg mice splenic B-cells expressed more CD73 (median: 21.7% vs 10.9% for WT) (Fig B) leading to more adenosine production (Fig B) when exposed to AMP known to be released by cells upon MTX exposure. BAFFtg splenocytes also expressed more IL-10 (B10 cells) and B1 peritoneal cells express more CD73. Tolerization with MTX further increased B10 and Breg precursors (Fig C).

**Conclusion:**

In BAFFtg mice, immunization against TNFi can be prevented for a year by a single course of MTX if administered concomitantly with the first TNFi injection. This supports an interaction between MTX and BAFF to prevent ADA formation. The mechanism of this specific tolerance could involve interaction between extracellular release of AMP induced by MTX and increase of CD73 in BAFFtg mice, which in turn may increase adenosine and IL-10 regulatory B cells.

**Disclosure:** S. Bitoun, None; G. Nocturne, None; B. Ly, None; J. Pascaud, None; A. Pruvost, None; X. Mariette, Bristol-Myers Squibb, LFB, Pfizer, GSK, UCB, 9, Biogen, Pfizer, UCB, 2.


Abstract Number: 1464
Relation of HLA-DRB1 Genotype to the Efficacies of Abatacept and Tocilizumab in Patients with Rheumatoid Arthritis

Kensuke Oryoji, The Center for Rheumatology, Matsuyama Red Cross Hospital, Ehime, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: To investigate whether clinical efficacy of abatacept (ABT) and tocilizumab (TCZ) differs depending on whether or not HLA-DRB1 Shared Epitope (SE) is present in patients with rheumatoid arthritis.

Methods: HLA-DRB1 genotype of patients treated with ABT (n=78) and TCZ (n=78) was identified. HLA-DRB1 0101,0102,0401,0404,0405,0408,1001 was defined as SE. Retention rate and clinical efficacy were assessed by Cox proportional hazard model and multiple regression analysis.

Results: The patients with SE positive were 51 in ABT (65%) and 53 in TCZ (68%). The retention rate of ABT was significantly higher in SE positive patients than in SE negatives. (p <0.0001, log rank), and the retention rate of TCZ was not significantly different in both group.

Average CDAI at 24 week was 3.5/10.7 in SE positive/negative group with ABT (p<0.0001, ANOVA), and 6.3/5.8 with TCZ (p = 0.87). Multivariable Cox hazard regression model, in which age, sex, disease duration, ACPA titer, RF titer, MHAQ, prior use of biological agents, MTX dose, oral steroid dose, and SDAI and CRP at baseline were adjusted, revealed that, compared with SE-positive, SE-negative had a higher abatacept discontinuation due to lack of efficacy (adjusted HR=9.2, 95% CI: 2.8-30.4), but was not significant in TCZ (p = 0.41). In addition, the predictor of CDAI at 24 week by multiple regression analysis was SE (p<0.0001) in ABT but SE was not predictive in TCZ.

Conclusion: ABT is effective in SE positive group, but TCZ is not relevant for SE.

Disclosure: K. Oryoji, Abbvie, Chugai, Tanabe-Mitsubishi, Astellas, Eisai, Janssen, Pfizer, UCB, Ono., 8;


Abstract Number: 1465

Cost per Response for Abatacept Versus Adalimumab in Patients with Seropositive, Erosive, Early Rheumatoid Arthritis in the US, Germany, Spain and Canada

J Foo1, JM Rodriguez Heredia2, C Polanco Sánchez3, M Mtiabaa4, KH Herrmann5, E Alemao6, R Postema7 and C Baerwald8, 1Mapi Group, Houten, Netherlands, 2Hospital Universitario de Getafe, Madrid, Spain, 3Bristol-Myers Squibb, Madrid, Spain, 4Bristol-Myers Squibb, Montréal, QC, Canada, 5Bristol-Myers Squibb, Munich, Germany, 6Bristol-Myers Squibb, Princeton, NJ, 7Bristol-Myers Squibb, Uxbridge, United Kingdom, 8University Hospital, Department of Internal Medicine, Rheumatology Unit, Leipzig, Germany

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Background/Purpose: RA is a chronic, inflammatory disorder leading to disability and reduced quality of life. Effective treatment with biologic DMARDs poses a significant economic burden. The Abatacept versus adalimumab comparison in bioLogic-naïve RA subjects with background methotrexate (AMPLE) trial was a head-to-head, randomized study comparing SC abatacept with SC adalimumab. A recent post hoc analysis showed improved efficacy for abatacept in patients with seropositive, erosive early RA (defined as: disease duration ≤6 months, RF or anti-citrullinated protein antibody seropositivity and ≥1 radiographic erosion) compared with adalimumab. Methods: A previously published decision tree was used to compare the cost per response of abatacept and adalimumab in a cohort of 1000 patients over a 2-year time horizon. Clinical inputs were based on a post hoc analysis of the AMPLE trial in patients with or without seropositive, erosive early RA. Response was based on ACR20/50/70/90 and HAQ-DI. Unit costs for direct medical costs of AEs were based on local tariffs for disease-related groups and the ex-manufacturer price, including mandatory reductions, pay-back and transparent discounts for drugs. Results: The cost per response in patients with seropositive, erosive early RA favored SC abatacept compared with SC adalimumab for ACR20, ACR50, ACR70, ACR90 and HAQ-DI across all countries (Table). Cost per ACR90 and HAQ-DI response consistently favored SC abatacept in patients with or without seropositive, erosive early RA in all countries. The cost per CDAI and SDAI remission also favored SC abatacept in patients with seropositive, erosive early RA in all countries; however, the cost per DAS28 remission favored SC adalimumab in the US and Canada. Results in patients without seropositive, erosive early RA were less consistent for SC abatacept, except in Germany and Spain where the cost of abatacept is lower than the cost of adalimumab.


Disclosure: J. Foo, Bristol-Myers Squibb, 5; J. Rodriguez Heredia, None; C. Polanco Sánchez, Bristol-Myers Squibb, 3; M. Mtibaa, Bristol-Myers Squibb, 9; Bristol-Myers Squibb, 3; K. Herrmann, Bristol-Myers Squibb, 1; Bristol-Myers Squibb, 3; E. Alemao, Bristol-Myers Squibb, 3; Bristol-Myers Squibb, 1; R. Postema, Bristol-Myers Squibb, 1; Bristol-Myers Squibb, 3; C. Baerwald, AbbVie, BMS, Chugai, MSD, Pfizer, Roche, UCB, 5, AbbVie, BMS, Chugai, MSD, Pfizer, Roche, UCB, 8.


Abstract Number: 1466

The Effects of Rituximab and B-Cells Depletion on the Inflammatory and Pro-Thrombotic Profile of Leucocytes of Rheumatoid Arthritis Patients and on the Vascular Endothelium

Irene Cecchi¹, Carlos Perez-Sanchez², Patricia Ruiz-Limon³, Ivan Arias de la Rosa³, Maria Carmen Abalos-Aguilera³, Yolanda Jiménez-Gómez², Rafaela Ortega-Castro², Eduardo Collantes-Estévez², Alejandro Escudero-Contreras³, Massimo Radin⁴, Nuria Barbarroja², Dario Roccatello⁵, Savino Sciascia⁶ and Chary Lopez-Pedrera⁷, ¹Center of Research of Immunopathology and Rare Diseases- Coordinating Center of Piemonte and Valle d’Aosta Network for Rare Diseases, Department of Clinical and Biological Sciences, University of Turin, Italy, Turin, Italy, ²Rheumatology service, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain, ³Rheumatology Service, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain, ⁴Department of Clinical and Biological Sciences, Center of Research of Immunopathology and Rare Diseases- Coordinating Center of Piemonte and
SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Cardiovascular disease (CVD) constitutes a relevant cause of morbidity and mortality in Rheumatoid Arthritis (RA) patients. Rituximab (RTX) has been proved to be effective in the treatment of RA, indicating that B-cells play a crucial role in the pathogenesis of the disease, not only through the production of autoantibodies. Moreover, B-cells seem to be important in the development of CVD. However, the effect of RTX in the context of CVD in RA patients has not been fully elucidated yet. Therefore, the aims of this study were to evaluate the mechanism of action of RTX on immune and endothelial cells and to investigate the effect of B-cells depletion in the context of CVD in RA patients.

Methods: The analysis includes 10 RA patients with moderate-high disease activity based on Disease Activity Score using 28 joints. To evaluate the influence of B-cells depletion on the inflammatory profile of T-cells, purified lymphocytes from 6 RA patients were treated with RTX (1µg/ml) for 24 hours. B-cells depletion was assessed by flow cytometry and the changes in the inflammatory profile were analyzed by RT-PCR. Following, to identify changes in the activity of crucial mediators in the production of pro-inflammatory cytokines, a western blot was performed on extracted proteins from purified lymphocytes of the 6 RA patients treated with RTX. In a second set of experiments, supernatant from cultured lymphocytes of 6 RA patients, in the presence or in the absence of RTX, was added to cultured endothelial cells (HUVECs) and monocytes isolated from Healthy Donors (HDs) and the response was analyzed by RT-PCR. Finally, serum from 4 RA patients at baseline and after 3 months of therapy with RTX, was added to HUVECs and monocytes isolated from HDs and the response was analyzed by RT-PCR.

Results: In parallel to a significant depletion of B-cells, we observed a downregulation of the pro-inflammatory profile of T-lymphocytes, as shown by a significant drop of IL1, IL6, IL17, IFNγ, and TNFα genes expression levels. We also found a decrease in the phosphorylation and protein expression of STAT-3 and p38 in lymphocytes treated with RTX, compared to non-treated T-cells. HUVECs and monocytes cultured with supernatant of RA-lymphocytes treated with RTX, showed a decrease in the expression levels of various pro-thrombotic factors (i.e. TF, IL8, and VEGF) as well as cell-adhesion molecules (i.e. V-CAM, I-CAM and e-Selectin). Both HUVECs and monocytes, treated with serum of RA patients after 3 months of therapy with RTX, showed a reduced expression of genes related to their pro-thrombotic and pro-inflammatory profile.

Conclusion: Overall, RTX showed a beneficial effect in the context of CVD in RA patients, through the modulation of the inflammatory and pro-thrombotic profile of distinct leukocytes subtypes and vascular endothelial cells. Supported by CTS-794, ISCIII (PI15/01333; RIER RD16/0012/0015)

Disclosure: I. Cecchi, None; C. Perez-Sanchez, None; P. Ruiz-Limon, None; I. Arias de la Rosa, None; M. C. Abalos-Aguilera, None; Y. Jiménez-Gómez, None; R. Ortega-Castro, None; E. Collantes-Estévez, None; A. Escudero-Contreras, None; M. Radin, None; N. Barbarroja, None; D. Roccatello, None; S. Sciascia, None; C. Lopez-Pedrera, EFPIA, 2.


Abstract Number: 1467

Changes in the Immune Response of RA Patients Induced By 1 Year of Tocilizumab
**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Tocilizumab, a humanized anti-human IL-6 receptor antibody that blocks the signaling of IL-6/IL-6R complex, is an effective treatment in chronic inflammatory rheumatoid arthritis (RA). Although IL-6 contributes significantly to RA pathology, it is unknown how tocilizumab regulates the immune response of these patients.

**Methods:** Heparinized blood and clinical data from 47 RA patients were collected before treatment (t0) and after 12 months (t12m). Plasmatic cytokines were measured by ELISAs and phenotyping of circulating T CD4+ lymphocytes (memory, naïve, Tregs and Th subsets) was analyzed by flow cytometry.

**Results:**

Clinical and disease characteristics of the patients are shown in table 1. At t0 and at t12m, the concentrations of IL-6 and IL-10 and the concentrations of IL-17, VEGF and IL-22 correlated. After 12m with tocilizumab, the concentrations of sIL-6R and IL-10 significantly increased. Despite the decrease of CD4+ T lymphocytes, the percentages of Tregs and the Treg subset CD45RA+ significantly increased. No differences were observed in the percentages of Th1, Th2 and Th17 between t0 and t12m. However, the percentages of Th9 and Th9 CD45RO+ significantly decreased (Table 2). When patients were segregated according to EULAR response to tocilizumab (NR= no responders, R= responders), sIL6R (at t12m, NR=652±83 vs. R=1731±160 ng/ml, p=0.02) and monocytes/ul (at t12m, NR=840±40 vs. R=610±30, p=0.02) decreased and the ratio t12m/t0 of TregCD45RO+ increased (NR=0.49±0.15 vs. R=0.91±0.005, p=0.01) only in those patients with good or moderate response.

**Conclusion:** Despite the blocking of IL-6/IL-6R in all RA patients, changes in soluble mediators and T cell subsets were different between EULAR responders and non-responders to tocilizumab. Further information would be necessary to understand the immunological mechanisms operating in the different groups of patients.

**Table 1. Baseline demographic and disease characteristics of the RA patients**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age; years (mean±SD)</td>
<td>53.8±11.1</td>
</tr>
<tr>
<td>Women; n (%)</td>
<td>40 (85.1)</td>
</tr>
<tr>
<td>Years of disease (mean±SD)</td>
<td>12.7±8.4</td>
</tr>
<tr>
<td>Positive Rheumatoid Factor; n (%)</td>
<td>31 (66%)</td>
</tr>
<tr>
<td>Positive ACPAs; n (%)</td>
<td>35 (74.5%)</td>
</tr>
<tr>
<td>Tocilizumab on monotherapy</td>
<td>17 (36.2%)</td>
</tr>
<tr>
<td>Used as first line biologic therapy; n (%)</td>
<td>14 (29.8%)</td>
</tr>
<tr>
<td>DAS28 (mean±SD)</td>
<td>5.65±1.15</td>
</tr>
<tr>
<td>CDAI (mean±SD)</td>
<td>28.2±13.3</td>
</tr>
<tr>
<td>ESR; mm/h (mean±SD)</td>
<td>46.5±30.8</td>
</tr>
<tr>
<td>CRP; mg/l (mean±SD)</td>
<td>24.9±30.8</td>
</tr>
</tbody>
</table>
Table 2. Immunological parameters at baseline and after 1 year of treatment

<table>
<thead>
<tr>
<th></th>
<th>t0</th>
<th>t12m</th>
<th>(paired t-test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG</td>
<td>1193.55 ± 66.83</td>
<td>915.52 ± 65.94</td>
<td>0.001</td>
</tr>
<tr>
<td>IgA</td>
<td>309.03 ± 21.60</td>
<td>232.14 ± 18.39</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IgM</td>
<td>156.09 ± 14.00</td>
<td>128.30 ± 15.86</td>
<td>0.195</td>
</tr>
<tr>
<td>Monocytes</td>
<td>0.67 ± 0.07</td>
<td>0.66 ± 0.08</td>
<td>0.445</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>4.82 ± 0.33</td>
<td>3.93 ± 0.33</td>
<td>0.017</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>2.22 ± 0.16</td>
<td>2.11 ± 0.15</td>
<td>0.287</td>
</tr>
<tr>
<td>IL6 pg/ml</td>
<td>670.52 ± 129.89</td>
<td>849.74 ± 183.31</td>
<td>0.066</td>
</tr>
<tr>
<td>sIL6R ng/ml</td>
<td>332.59 ± 45.10</td>
<td>1592.92 ± 158.32</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IL17 pg/ml</td>
<td>2044.40 ± 945.86</td>
<td>1481.00 ± 638.81</td>
<td>0.187</td>
</tr>
<tr>
<td>IL22 pg/ml</td>
<td>4960.60 ± 1261.10</td>
<td>5461.28 ± 1288.02</td>
<td>0.414</td>
</tr>
<tr>
<td>VEGF pg/ml</td>
<td>590.07 ± 227.16</td>
<td>566.15 ± 246.19</td>
<td>0.261</td>
</tr>
<tr>
<td>IL10 pg/ml</td>
<td>100.00 ± 39.00</td>
<td>119.00 ± 18.00</td>
<td>0.035</td>
</tr>
<tr>
<td>CD4 (% lymphocytes)</td>
<td>46.99 ± 1.58</td>
<td>44.92 ± 1.22</td>
<td>0.041</td>
</tr>
<tr>
<td>Treg (% CD4+ T cells)</td>
<td>6.66 ± 0.28</td>
<td>7.38 ± 0.27</td>
<td>0.026</td>
</tr>
<tr>
<td>Th1 (% CD4+ T cells)</td>
<td>7.79 ± 1.05</td>
<td>6.72 ± 0.51</td>
<td>0.420</td>
</tr>
<tr>
<td>Th17 (% CD4+ T cells)</td>
<td>10.78 ± 1.85</td>
<td>6.81 ± 0.48</td>
<td>0.130</td>
</tr>
<tr>
<td>Th2 (% CD4+ T cells)</td>
<td>8.53 ± 1.35</td>
<td>6.41 ± 0.32</td>
<td>0.220</td>
</tr>
<tr>
<td>Th9 (% CD4+ T cells)</td>
<td>13.75 ± 1.85</td>
<td>6.78 ± 0.64</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Disclosure: C. Diaz-Torné, None; P. Estrada, None; P. Moya, None; M. A. Ortiz, None; D. de la Fuente, None; M. Moreno, None; N. Busquets, None; J. Ramírez, Gebro, 2; C. Moragues, None; S. Ros, None; E. Casado Burgos, None; V. Torrente, None; E. Garcia, None; M. Pujol, None; A. Ponce, None; S. Vidal, None; J. J. de Agustín, None.


Abstract Number: 1468

Abatacept Retention Rates, Overall and By Participating Country, and Prognostic Factors of Retention in Patients with RA: 2-Year Results from a Real-World Observational Study

Rieke Alten1, HM Lorenz2, X Mariette3, HG Nüßlein4, M Galeazzi5, F Navarro6, M Chartier7, Y Elbez8, C Rauch9 and M Le Bars7, 1Schlosspark-Klinik University Medicine, Berlin, Germany, 2University Hospital, Heidelberg, Germany, 3Université Paris-Sud, Paris, France, 4University of Erlangen, Nürnberg, Germany, 5University of Siena, Siena, Italy, 6Hospital Universitario Virgen Macarena, Seville, Spain, 7Bristol-Myers Squibb, Rueil-Malmaison, France, 8Excelya, Boulogne-Billancourt, France, 9Bristol-Myers Squibb, Munich, Germany

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: ACTION (NCT02109666) was the first prospective international non-interventional study designed to provide long-term real-world data on abatacept retention in patients (pts) with RA. The 1-y interim analyses of ACTION were reported previously.1
Methods: ACTION is a 2-y observational study of pts with moderate-to-severe RA who initiated IV abatacept as first- or second/further-line biologic therapy in routine clinical practice in Europe and Canada (May 2008–Dec 2013). Here we report the primary outcome of the study, ie 2-y crude abatacept retention rate with 95% CI (overall and by treatment line), estimated by Kaplan–Meier analysis. Additional study outcomes were crude retention rates by participating country, prognostic factors of retention, identified by backward selection method in multivariate models, and EULAR response by treatment line and RF/anti-citrullinated protein antibody (ACPA) seropositivity, compared by Fisher’s exact test.

Results: In total, 2350/2364 enrolled pts were evaluable for analysis: 673 (28.6%) biologic naïve and 1677 (71.4%) biologic failures. Some expected differences in baseline characteristics were seen between groups and were reported previously. The 2-y retention rate was 47.9% (95% CI 45.7, 50.0) in the overall population, and was higher in biologic-naïve (54.5% [50.4, 58.3]) vs -failure pts (45.2% [42.7, 47.7]; p<0.001); main reasons for abatacept discontinuation were lack of efficacy (61.4 vs 67.7%) and safety (21.3 vs 21.2%). By country, overall retention rates were 37.5–66.7%; rates were highest in Belgium (66.7%) and Austria (60.5%). Retention rates were higher in biologic-naïve vs -failure pts (Figure). Predictors of higher abatacept retention included: RF/ACPA seropositivity (p=0.030 biologic naïve; p=0.028 biologic failure); diabetes (p=0.044 biologic naïve); geographic location, Canada, Spain and Italy vs Germany (p<0.001 biologic naïve); and abatacept combination therapy (p<0.001 biologic failure). Only high Patient Global Assessment, ie ≥70, (p=0.009 biologic failure) predicted lower retention. At 2 y, a greater proportion of biologic-naïve vs -failure pts had good/moderate EULAR response (p=0.005); RF and/or ACPA seropositivity was associated with a significantly better response (p=0.007).


Disclosure: R. Alten, Bristol-Myers Squibb, 2; H. Lorenz, AbbVie, Bristol-Myers Squibb, Roche-Chugai, UCB, MSD, GSK, SOBI, Medac, Novartis, Janssen-Cilag, AstraZeneca, Pfizer, Actelion, 5; X. Mariette, Bristol-Myers Squibb, LFB, Pfizer, GSK, UCB, 9,Biogen, Pfizer, UCB, 2; H. Nüßlein, None; M. Galeazzi, None; F. Navarro, Pfizer, MSD, AbbVie, Bristol-Myers Squibb, Roche, 2,Pfizer, MSD, Roche, UCB, AbbVie, Bristol-Myers Squibb, 8,Pfizer, MSD, Roche, UCB, AbbVie, Bristol-Myers Squibb, Janssen, Lilly, 5; M. Chartier, Bristol-Myers Squibb, 3; Y. Elbez, None; C. Rauch, Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1, 9; M. Le Bars, Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1, 9.
Treatment Paradigms in Real-World Practice: Biologic Agent Use Prior to and after Discontinuation of Abatacept

Rieke Alten1, H-M Lorenz2, X Mariette3, H Nüßlein4, M Galeazzi5, F Navarro6, M Chartier7, Y Elbez8, C Rauch9 and M Le Bars7,
1Schloßpark-Klinik University Medicine, Berlin, Germany, 2University Hospital, Heidelberg, Germany, 3Université Paris-Sud, Paris, France, 4University of Erlangen-Nuremberg, Nuremberg, Germany, 5University of Siena, Siena, Italy, 6Hospital Universitario Virgen Macarena, Seville, Spain, 7Bristol-Myers Squibb, Rueil-Malmaison, France, 8Excelya, Boulogne-Billancourt, France, 9Bristol-Myers Squibb, Munich, Germany

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: ACTION is a 2-year, observational study of patients (pts) with moderate-to-severe RA who initiated IV abatacept in Canada and Europe (NCT02109666). The objective was to determine pt biologic (b)DMARD use prior to initiation and after discontinuation of abatacept overall and by treatment line in ACTION. Methods: Pts with RA initiated IV abatacept as first- or second-/further-line therapy. Biologic-naïve and biologic-failure pts were enrolled during three periods between May 2008 and December 2013. Pts could switch administration routes (IV to SC) during treatment. Crude retention rates (Kaplan–Meier) were compared by log-rank test.

Results: Of the 2364 pts enrolled, 2350 were evaluable for analysis: 673 (28.6%) were biologic naïve and 1677 (71.4%) biologic failures. Baseline characteristics differed: biologic-failure pts had longer RA duration, higher CRP levels and prevalence of radiographic erosions, and lower rates of chronic obstructive pulmonary disease and neoplasms vs biologic-naïve pts. Most biologic-failure pts (96.7%) had previously received ≥1 TNF inhibitor (TNFi): 48.7% had received 1 and 48.0% ≥2 TNFi; 56.6% had received ≥2 bDMARDs. The overall 2-year retention rate was 47.9% and was higher for biologic-naïve vs biologic-failure pts (54.5 vs 45.2%; p<0.001); the most common reasons for abatacept discontinuation were inefficacy (61.4 vs 67.7%) and safety (21.3 vs 21.2%). In pts who discontinued abatacept, 83.0% started a bDMARD ≤6 months after discontinuation (Table), most commonly abatacept IV. Mean (SD) days from stopping abatacept to starting a bDMARD was similar for biologic-naïve (93.4 [51.3]) and biologic-failure pts (93.6 [48.0]). Among pts who restarted abatacept, 62 (80.5%) biologic-naïve and 158 (85.0%) biologic-failure pts were considered to have discontinued as the time from last dose was >84 (IV) or >28 (SC) days, and thus were no longer temporary discontinuations, as predefined in the protocol. Three pts discontinued for bad compliance, 3 for lack of efficacy, 3 for remission/major improvement, 12 for safety and 15 for surgery. A good/moderate EULAR response was achieved by 76.7% of pts at the last follow-up before abatacept discontinuation and 58.3% at abatacept restart; mean (SD) DAS28 (CRP) was 3.2 (1.1) and 3.8 (1.4), respectively.

Conclusion: Prior to abatacept treatment, over half of biologic-failure pts had received ≥2 bDMARDs and most had received a TNFi. After initial discontinuation (protocol defined), over one-third of pts restarted abatacept.

Original abstract © EULAR/BMJ. First presented at EULAR 2017 and published in Ann Rheum Dis 2017;76 (Suppl 2):AB0267. Any reprints, promotional options, education material etc have to be done through the original source (ARD/BMJ).
Table

<table>
<thead>
<tr>
<th>Biologic naïve</th>
<th>Biologic failure</th>
<th>Biologic failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=186</td>
<td>n=526</td>
<td>n=186</td>
</tr>
<tr>
<td>None</td>
<td>35 (18.8)</td>
<td>86 (16.3)</td>
</tr>
<tr>
<td>Abatacept</td>
<td>77 (41.4)</td>
<td>186 (35.4)</td>
</tr>
<tr>
<td>IV</td>
<td>71 (38.2)</td>
<td>170 (32.3)</td>
</tr>
<tr>
<td>SC</td>
<td>6 (3.2)</td>
<td>16 (3.0)</td>
</tr>
<tr>
<td>TNFi</td>
<td>41 (22.0)</td>
<td>74 (14.1)</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>10 (5.4)</td>
<td>12 (2.3)</td>
</tr>
<tr>
<td>Etanercept</td>
<td>13 (7.0)</td>
<td>21 (4.0)</td>
</tr>
<tr>
<td>Infliximab</td>
<td>7 (3.8)</td>
<td>13 (2.5)</td>
</tr>
<tr>
<td>Certolizumab</td>
<td>7 (3.8)</td>
<td>17 (3.2)</td>
</tr>
<tr>
<td>Golimumab</td>
<td>4 (2.2)</td>
<td>11 (2.1)</td>
</tr>
<tr>
<td>Other bDMARD</td>
<td>33 (17.7)</td>
<td>180 (34.2)</td>
</tr>
<tr>
<td>Anakinra</td>
<td>1 (0.5)</td>
<td>4 (0.8)</td>
</tr>
<tr>
<td>Rituximab</td>
<td>6 (3.2)</td>
<td>58 (11.0)</td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>26 (14.0)</td>
<td>118 (22.4)</td>
</tr>
</tbody>
</table>

Data are n (%)
bDMARD=biologic DMARD; TNFi=TNF inhibitor

Disclosure: R. Alten, Bristol-Myers Squibb, 2; H. M. Lorenz, AbbVie, Bristol-Myers Squibb, Roche-Chugai, UCB, MSD, GSK, SOBI, Medac, Novartis, Janssen-Cilag, AstraZeneca, Pfizer, Actelion, 5, AbbVie, Bristol-Myers Squibb, Roche-Chugai, UCB, MSD, GSK, SOBI, Medac, Novartis, Janssen-Cilag, AstraZeneca, Pfizer, Actelion, 9; X. Mariette, Bristol-Myers Squibb, LFB, Pfizer, GSK, UCB, 9, Biogen, Pfizer, UCB, 2; H. Nüßelein, AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, UCB, 5, AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, UCB, 8; M. Galeazzi, None; F. Navarro, Pfizer, MSD, AbbVie, Bristol-Myers Squibb, Roche, 2, Pfizer, MSD, Roche, UCB, AbbVie, Bristol-Myers Squibb, 8, Pfizer, MSD, Roche, UCB, AbbVie, Bristol-Myers Squibb, Janssen, Lilly, 5; M. Chartier, Bristol-Myers Squibb, 3; Y. Elbez, None; C. Rauch, Bristol-Myers Squibb, 3, Bristol-Myers Squibb, 1, 9; M. Le Bars, Bristol-Myers Squibb, 3, Bristol-Myers Squibb, 1.


Abstract Number: 1470

Impact of Anti-Drug Antibody and Injection Site Reaction on Efficacy: 24-Week Results from a Phase III Study Comparing SB4 (etanercept biosimilar) with Reference Etanercept in Patients with Rheumatoid Arthritis

Jiri Vencovsky1, Paul Emery2, Edward C. Keystone3, Jeehoon Ghil4, Soo Yeon Cheong4 and Evelyn Hong4, 1Institute of Rheumatology, Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, 2NIHR-Leeds Musculoskeletal Biomedical Research Unit and Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom, 3University of Toronto, Toronto, ON, Canada, 4Samsung Bioepis Co., Ltd., Incheon, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Background/Purpose: SB4 is approved by the European Commission as a biosimilar of the reference etanercept (ETN). The phase III clinical study results have been reported previously.\(^1\,^2\) Data to date shows no correlation between the development of anti-drug antibody (ADA) and clinical response or adverse events with etanercept treatment. The objective of this study was to investigate the impact of the presence of ADA or injection site reaction (ISR) on efficacy in patients with rheumatoid arthritis (RA) treated with SB4 or ETN up to week 24.

Methods: In this phase III randomized, double blind study, patients with moderate to severe RA received 50 mg/week of either SB4 or ETN with background methotrexate (MTX) for 52 weeks. Efficacy, safety and immunogenicity were assessed.

Results: Up to week 24, the incidence of ADA (2 patients [0.4%] in SB4 vs 39 patients [13.1%] in ETN, \(p<0.001\)) and the incidence of ISR (9 patients [3.0%] in SB4 vs 48 patients [16.2%] in ETN, \(p<0.001\)) were significantly lower in SB4 compared to ETN. Due to the low incidence of ADA in the SB4 treatment group, the impact of ADA on efficacy could not be evaluated. Within the ETN treatment group at week 24, there was a trend towards increased efficacy (ACR20, ACR-N, change in DAS28, remission and low disease activity based on DAS28, SDAI, or CDAI) in patients without detectable ADA compared to patients with ADA (Table). In regards to ISR, efficacy tended to be higher in patients who did not experience ISR compared to those who did within each treatment group.

There was no correlation between the presence of ADA and incidence of ISR. In patients without detectable ADA and patients with ADA, respectively, 3.0% (9/297) vs. 0.0% (0/2) of patients from SB4 group and 16.3% (42/248) vs. 15.4% (6/39) of patients from the ETN group experienced ISR.

Conclusion: Significantly fewer patients from SB4 developed ADA or experienced ISR compared to ETN, however the efficacy was still comparable between SB4 and ETN in patients without detectable ADA and in patients who did not experience ISR. Within the ETN group, there was a trend towards increased efficacy in patients without detectable ADA compared to patients with ADA. In both SB4 and ETN group, patients without ISR tended to have higher efficacy than patients with ISR. There was no correlation between the presence of ADA and ISR.

References

<table>
<thead>
<tr>
<th>Table. Efficacy at week 24 by presence of ADA and ISR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>ACR20</td>
</tr>
<tr>
<td>ACR50</td>
</tr>
<tr>
<td>ACR70</td>
</tr>
<tr>
<td>ACR-N</td>
</tr>
<tr>
<td>Change in DAS28</td>
</tr>
<tr>
<td>Change in CDAI</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>ACR20</td>
</tr>
<tr>
<td>ACR50</td>
</tr>
<tr>
<td>ACR70</td>
</tr>
<tr>
<td>ACR-N</td>
</tr>
<tr>
<td>Change in DAS28</td>
</tr>
</tbody>
</table>

Data are presented as either n(%) or mean ± standard deviation. ACR20: 50% of American College of Rheumatology 20% improvement in 20 weeks; ACR-N: numeric index of the ACR response; ADA: anti-drug antibody; CDAI: clinical disease activity index; DAS28: disease activity index measured by 28 joints; ISR: injection site reactions; LDA: low disease activity; SDAI: simplified disease activity index.
Flare Incidence and Predictive Factors in a Population of Patients with Rheumatoid Arthritis Under Optimised Treatment with Adalimumab and Infliximab

Amara Pieren¹, Dora Pascual-Salcedo², Pilar Aguado³, Gema Bonilla⁴, Eugenio De Miguel⁵, Irene Monjo⁶, Laura Nuño³, Diana Peiteado³, Alejandro Villalba³, Enrique Moral Coro⁴, C. Tornero⁷, Patricia Bogas⁴, Alejandro Balsa³ and Chamaida Plascencia-Rodriguez⁴¹, ¹Rheumatology, Hospital La Paz, Madrid, Spain, ²Immuno-Rheumatology Research group, La Paz University Hospital, Madrid, Spain, ³Rheumatology, La Paz University Hospital, Madrid, Spain, ⁴Hospital Universitario La Paz, Madrid, Spain, ⁵Rheumatology, University Hospital La Paz, IdiPaz, Madrid, Spain, ⁶Internal Medicine, Hospital Universitario La Paz, MADRID, Spain, ⁷Rheumatology, Rheumatology. La Paz University Hospital, Spain., Madrid, Spain

First publication: September 18, 2017
Conclusion: We noted a high proportion of flares in our cohort of optimised patients. However, flares were controlled with dosage readjustment without needing a change of the treatment. Independently correlated predictive factors for flares were a higher disease activity measured by DAS and not being in therapeutic range in the pre-optimisation visit.

Disclosure: A. Pieren, None; D. Pascual-Salcedo, None; P. Aguado, None; G. Bonilla, None; E. De Miguel, None; I. Monjo, None; L. Nuño, None; D. Peiteado, None; A. Villalba, None; E. Moral Coro, None; C. Tornero, Alexion Pharmaceuticals, Inc., 9; P. Bogas, None; A. Balsa, None; C. Plasencia-Rodriguez, None.


Abstract Number: 1472

Body Mass Index Does Not Affect Response to Rituximab in Patients with Rheumatoid Arthritis: Results from Turkbio Registry

Suleyman Serdar Koca1, Ahmet Karatas2, Burak Oz3, Ediz Dalkilic4, Gerçek Can5, Yavuz Pehlivan6, Ayten Yazici7, Nevsun Inanc8, Ayse Cefe9, Zeyen Erturk10, Servet Akar11, Soner Senel12, Merih Birlik13, Nurullah Akkoc14 and Fatos Onen15, 1Department of Rheumatology, Firat University School of Medicine, Elazig, Turkey, 2Department of Rheumatology, Firat University, School of Medicine, Rheumatology, Elazig, Turkey, 3Rheumatology, Firat University, School of Medicine, Rheumatology, Elazig, Turkey, 4Department of Internal Medicine, Division of Rheumatology, Uludag University, School of Medicine, Rheumatology, Bursa, Turkey, 5Rheumatology, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey, 6Department of Rheumatology, Uludag University, Bursa, Turkey, 7Rheumatology, Kocaeli University, Kocaeli, Turkey, 8Department of Internal Medicine, Division of Rheumatology, Marmara University, Istanbul, Turkey, 9Rheumatology, Kocaeli University, School of Medicine, Rheumatology, Kocaeli, Turkey, 10Department of Rheumatology, Marmara Univeristy School of Medicine, Istanbul, Turkey, 11Rheumatology, Izmir Katip Celebi University, School of Medicine, Rheumatology, Izmir, Turkey, 12Rheumatology, Kayseri Erciyes University, School of Medicine, Rheumatology, Kayseri, Turkey, 13Department of Rheumatology, Dokuz Eylul University School of Medicine, Izmir, Turkey, 14Rheumatology, Private Practice, Rheumatology, Izmir, Turkey, 15Rheumatology, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Adipose tissue produces several inflammatory mediators. Thus, obesity affects the disease course and the responses to the anti-rheumatic agents in inflammatory diseases. Several previous reports have documented that obesity decrease the response rate to anti-TNF-α agents in rheumatoid arthritis (RA). The aim of the study was to determine whether body mass index (BMI) is involved in the response to rituximab in RA.

Methods: Data on patient characteristics, diagnosis, previous treatment and outcomes have been collected since 2011 in Turkish Biologic (TURKBIO) Registry. By the end of May 2017, 206 RA patients, received rituximab from the TURKBIO registry, were included in the analysis. Demographic and clinical data including age, sex, disease type, disease duration, and previous or current treatment with DMARDs and biological drug durations are stored in the database. Kaplan-Meier survival analysis was performed to estimate the drug survival. Subgroups were compared by log-rank.

Results: 32.5% patients were normal/underweight, 67.5% were overweight and 28.6% were obese. Mean age, female percentage, DAS28-CRP and VAS were higher in obese patients than non-obese ones (Table 1). Rituximab treatment was ongoing 71.2% in obese and 63.3% in non-obese patients (p=0.279). Median drug survival duration was 77 months in obese patients and 62 months in non-obese ones (p=0.053). Estimated drug survival rates for rituximab were not statistically significantly different in the obese and non-obese patients (Fig. 1).

Conclusion: We noted a high proportion of flares in our cohort of optimised patients. However, flares were controlled with dosage readjustment without needing a change of the treatment. Independently correlated predictive factors for flares were a higher disease activity measured by DAS and not being in therapeutic range in the pre-optimisation visit.

Disclosure: A. Pieren, None; D. Pascual-Salcedo, None; P. Aguado, None; G. Bonilla, None; E. De Miguel, None; I. Monjo, None; L. Nuño, None; D. Peiteado, None; A. Villalba, None; E. Moral Coro, None; C. Tornero, Alexion Pharmaceuticals, Inc., 9; P. Bogas, None; A. Balsa, None; C. Plasencia-Rodriguez, None.

Abstract Number: 1472

Body Mass Index Does Not Affect Response to Rituximab in Patients with Rheumatoid Arthritis: Results from Turkbio Registry

Suleyman Serdar Koca1, Ahmet Karatas2, Burak Oz3, Ediz Dalkilic4, Gerçek Can5, Yavuz Pehlivan6, Ayten Yazici7, Nevsun Inanc8, Ayse Cefe9, Zeyen Erturk10, Servet Akar11, Soner Senel12, Merih Birlik13, Nurullah Akkoc14 and Fatos Onen15, 1Department of Rheumatology, Firat University School of Medicine, Elazig, Turkey, 2Department of Rheumatology, Firat University, School of Medicine, Rheumatology, Elazig, Turkey, 3Rheumatology, Firat University, School of Medicine, Rheumatology, Elazig, Turkey, 4Department of Internal Medicine, Division of Rheumatology, Uludag University, School of Medicine, Rheumatology, Bursa, Turkey, 5Rheumatology, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey, 6Department of Rheumatology, Uludag University, Bursa, Turkey, 7Rheumatology, Kocaeli University, Kocaeli, Turkey, 8Department of Internal Medicine, Division of Rheumatology, Marmara University, Istanbul, Turkey, 9Rheumatology, Kocaeli University, School of Medicine, Rheumatology, Kocaeli, Turkey, 10Department of Rheumatology, Marmara University School of Medicine, Istanbul, Turkey, 11Rheumatology, Izmir Katip Celebi University, School of Medicine, Rheumatology, Izmir, Turkey, 12Rheumatology, Kayseri Erciyes University, School of Medicine, Rheumatology, Kayseri, Turkey, 13Department of Rheumatology, Dokuz Eylul University School of Medicine, Izmir, Turkey, 14Rheumatology, Private Practice, Rheumatology, Izmir, Turkey, 15Rheumatology, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Adipose tissue produces several inflammatory mediators. Thus, obesity affects the disease course and the responses to the anti-rheumatic agents in inflammatory diseases. Several previous reports have documented that obesity decrease the response rate to anti-TNF-α agents in rheumatoid arthritis (RA). The aim of the study was to determine whether body mass index (BMI) is involved in the response to rituximab in RA.

Methods: Data on patient characteristics, diagnosis, previous treatment and outcomes have been collected since 2011 in Turkish Biologic (TURKBIO) Registry. By the end of May 2017, 206 RA patients, received rituximab from the TURKBIO registry, were included in the analysis. Demographic and clinical data including age, sex, disease type, disease duration, and previous or current treatment with DMARDs and biological drug durations are stored in the database. Kaplan-Meier survival analysis was performed to estimate the drug survival. Subgroups were compared by log-rank.

Results: 32.5% patients were normal/underweight, 67.5% were overweight and 28.6% were obese. Mean age, female percentage, DAS28-CRP and VAS were higher in obese patients than non-obese ones (Table 1). Rituximab treatment was ongoing 71.2% in obese and 63.3% in non-obese patients (p=0.279). Median drug survival duration was 77 months in obese patients and 62 months in non-obese ones (p=0.053). Estimated drug survival rates for rituximab were not statistically significantly different in the obese and non-obese patients (Fig. 1).
**Table 1.** Clinical and laboratory data in obese an non-obese patients

<table>
<thead>
<tr>
<th></th>
<th>Obese patients</th>
<th>Non-obese patients</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>60 (34-80)</td>
<td>56 (21-85)</td>
<td>0.013</td>
</tr>
<tr>
<td>Disease duration, years</td>
<td>10.5 (2-36)</td>
<td>12 (2-36)</td>
<td>0.713</td>
</tr>
<tr>
<td>Females, %</td>
<td>89.8</td>
<td>70.7</td>
<td>0.004</td>
</tr>
<tr>
<td>RF positivity, %</td>
<td>87.2</td>
<td>78.9</td>
<td>0.220</td>
</tr>
<tr>
<td>Anti-CCP positivity, %</td>
<td>73.9</td>
<td>75.7</td>
<td>0.814</td>
</tr>
<tr>
<td>Basal ESR, mm/h</td>
<td>34 (13-84)</td>
<td>32 (1-100)</td>
<td>0.199</td>
</tr>
<tr>
<td>Basal CRP, mg/dl</td>
<td>10.5 (2-75)</td>
<td>8.5 (0-87)</td>
<td>0.383</td>
</tr>
<tr>
<td>Basal DAS28</td>
<td>4.8 (2-7.1)</td>
<td>4.3 (1.7-6.6)</td>
<td>0.020</td>
</tr>
<tr>
<td>Basal HAQ</td>
<td>1.15 (0.25-2.88)</td>
<td>1.25 (0-2.88)</td>
<td>0.869</td>
</tr>
<tr>
<td>Basal VAS - Patient Pain</td>
<td>75 (40-100)</td>
<td>52 (0-100)</td>
<td>0.003</td>
</tr>
<tr>
<td>Basal VAS - Physician</td>
<td>61.5 (6-90)</td>
<td>50 (0-90)</td>
<td>0.121</td>
</tr>
<tr>
<td>AESR, mm/h</td>
<td>-17.5 (-43-11)</td>
<td>-4 (-45-29)</td>
<td>0.114</td>
</tr>
<tr>
<td>ΔCRP, mg/dl</td>
<td>-10 (-67-4)</td>
<td>0 (-69-67)</td>
<td>0.031</td>
</tr>
<tr>
<td>ADAS28</td>
<td>-1.6 (-4.4-0.4)</td>
<td>-0.9 (-4-0)</td>
<td>0.785</td>
</tr>
<tr>
<td>ΔHAQ</td>
<td>-0.25 (-1.87-0.98)</td>
<td>-0.38 (-2.75-1.5)</td>
<td>0.674</td>
</tr>
<tr>
<td>AVAS - Patient Pain</td>
<td>-30 (-59-2)</td>
<td>-30 (-85-11)</td>
<td>0.431</td>
</tr>
<tr>
<td>AVAS - Physician</td>
<td>-43 (-63-4)</td>
<td>-32.5 (-80-20)</td>
<td>0.625</td>
</tr>
<tr>
<td>Rituximab ongoing, %</td>
<td>71.2</td>
<td>63.3</td>
<td>0.279</td>
</tr>
</tbody>
</table>

Data are expressed as median (min-max). Δ reflects the changes between basal and 6th month.

*RF*: rheumatoid factor; *CCP*: cyclic citrullinated peptide; *ESR*: erythrocyte sedimentation rate; *CRP*: C-reactive protein; *DAS*: disease activity score; *HAQ*: Health Assessment Questionnaire; *VAS*: visual analog scale.

**Conclusion:** It is known that adipose tissue increases TNF-α level and enhances cellular immunity. Since its act on humoral immunity may be limited, obesity does not affect the response to rituximab.

Golimumab Improves Work Productivity and Activity Impairment in Patients with Rheumatoid Arthritis (RA), Ankylosing Spondylitis (AS) and Psoriatic Arthritis (PsA): Interim Results from a Non-Interventional Trial in Germany

Klaus Krüger1, Sven Remstedt2, Astrid Thiele3 and Ines Klaudius4, 1Praxiszentrum St. Bonifatius München, München, Germany, 2Rheuma Praxis Berlin, Berlin, Germany, 3Krankenhaus St. Josef Wuppertal, Wuppertal, Germany, 4MSD Sharp & Dohme GmbH, Haar, Germany
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
In Germany no prospective data are available for Golimumab (GLM) in patients with RA, AS and PsA regarding outcomes evaluating work productivity and activity in daily life. It is the aim of this study to show the benefit of GLM in work productivity and activity for RA, AS and PsA pts in Germany. The analysis was performed by the validated WPAI (Work Productivity Activity Impairment) as primary endpoint. WPAI is rated to be the most psychometrically validated and frequently used instrument for measuring of health-related work-productivity.

Methods:
As primary endpoint the change of work productivity impairment and ability for daily activities in month 3 (V1) versus baseline visit (V0) was evaluated. All 4 subscores of the WPAI were analyzed: disease related absence from work (absenteeism), working while sick (presenteeism), total work productivity impairment (TWPI) and activity impairment with TWPI as primary score. In addition an evaluation of the activity impairment in the mITT population (modified-Intention-To-Treat) was performed.

Results:
749 pts were included in the study (all patients who started with GLM); thereof 664 pts formed the mITT population (at least V0 and V1 documented). 469 (RA=150, AS=168, PsA=151) of 664 pts were included in the analysis of the primary efficacy endpoint, as they were employed at V0.
Figure 1: Overview of WPAI scores including relevant standard deviations of RA pts; for all p<0.05 (mean difference of TWPI is based on 76 / 150 pts, due to the fact that for 74 pts entries for the WPAI questionnaire were missing).

Figure 2: Overview of WPAI scores including relevant standard deviations of AS pts; for all p<0.05 (mean difference of TWPI is based on 104 / 168 pts, due to the fact that for 64 pts entries for the WPAI questionnaire were missing).

Figure 3: Overview of WPAI scores including relevant standard deviations of PsA pts; for all p<0.05 (mean difference of TWPI is based on 80 / 151 pts, due to the fact that for 71 pts entries for the WPAI questionnaire were missing).

Conclusion:
GLM s.c. 1 x monthly is an effective treatment in pts. with RA, AS and PsA. All scores of the WPAI showed a significant (p< 0.05) reduction in mean score values in each indication. GLM leads to an improvement of work productivity and daily activities in all pts. already within the first 3 months of treatment.


A Higher DAS28P, the Subjective Proportion of the DAS28, Predicts a Favorable Response to Abatacept in Rheumatoid Arthritis

***Jeong Seok Lee1, HA Ahmad2, Seung-Cheol Shim3, Sang-Cheol Bae4, Yeong Wook Song5 and Eun Young Lee6, 1Division of Rheumatology, Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea, Republic of (South), 2Bristol-Myers Squibb, Princeton, NJ, 3Division of Rheumatology, Department of Internal Medicine, Daejeon Rheumatoid & Degenerative Arthritis Center, Chungnam National University Hospital, Daejeon, Korea, Republic of (South), 4Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), 5WCU Department of Molecular Medicine and Biopharmaceutical Sciences, Medical Research Institute, Seoul National University College of Medicine, Seoul, Korea, Republic of (South), 6Seoul National University College of Medicine, Seoul, Korea, Republic of (South)***

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Time:** 9:00AM-11:00AM

**Session Title:** Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports

**Session Type:** ACR Poster Session B

**Background/Purpose:** Response prediction of certain biologic agents for the treatment of rheumatoid arthritis (RA) is still an unmet need in real-world clinical practice. To reduce trial and error, discovering easily-accessible predictive markers for treatment response would be beneficial both for patients and healthcare systems. The patient-reported components tender joint count (TJC) and visual analogue score (VAS-GH) of the 28-joint disease activity score (DAS28) has been termed DAS28P and investigated as a predictor to the response to biologic agents, mostly TNF inhibitors (1, 2). We aimed to evaluate DAS28P as a predictor of EULAR response to abatacept in patients with RA.

**Methods:** The study population was a prospective cohort of Korean patients with RA who were followed up for a nationwide post-marketing survey of abatacept. By applying 6 month last observation carried forward method, 341 patients were involved in the analysis stratified upon the EULAR response criteria (3). Univariate analysis including chi-square test or Kruskal Wallis test were conducted for demographic factors, medical history, and clinical indices. Correlation of DAS28P with DAS28-ESR, change of DAS28-ESR, and EULAR response group were evaluated by Pearson’s coefficient (PC) or Student t-test. Logistic regression analysis was used to predict good to moderate EULAR response to abatacept in the study population.

**Results:** Presence of comorbidities, previous exposure to biologic agents, baseline DAS28-ESR, three of its components (tender joint counts, VAS global health, and ESR) and baseline DAS28P were significantly associated with EULAR response of abatacept at 6 months. Baseline DAS28P had positive correlation with baseline DAS28-ESR (PC=0.529, p<0.001) (Fig 1A) and negative correlation with interval change of DAS28-ESR (PC=-0.275, p<0.001) (Fig 1B). Stratified upon EULAR response, a group with good or moderate response had higher baseline DAS28P and lower interval change (Fig 1C, 1D). ROC curve of DAS28P and EULAR response revealed significant association (AUC=0.590, p=0.014). Logistic regression analysis showed that a DAS28P cutoff of >0.44 had the strongest association (OR=4.84, p=0.001) with good to moderate EULAR response (Table 1).

**Conclusion:** The subjective proportion of baseline DAS28, the DAS28P, is predictive of response to abatacept with a higher baseline DAS28P associated with a favorable therapeutic response of abatacept at 6 months after treatment initiation.
Table 1. Logistic regression analysis to find predictive factors for good to moderate EULAR response.

<table>
<thead>
<tr>
<th>Variables</th>
<th>β</th>
<th>S.E</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-3.426</td>
<td>1.351</td>
<td>1.81 (1.07-3.04)</td>
<td>0.011</td>
</tr>
<tr>
<td>Biologics (naive vs experienced)</td>
<td>0.795</td>
<td>0.133</td>
<td>0.51 (0.32-0.82)</td>
<td>0.005</td>
</tr>
<tr>
<td>DAS28-P</td>
<td>-4.072</td>
<td>2.799</td>
<td>0.26 (0.13-0.51)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TJC</td>
<td>-0.231</td>
<td>0.056</td>
<td>0.79 (0.71-0.88)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VAS/GFH</td>
<td>-0.006</td>
<td>0.012</td>
<td>0.99 (0.95-1.00)</td>
<td>0.024</td>
</tr>
<tr>
<td>ESR</td>
<td>-0.016</td>
<td>0.007</td>
<td>0.99 (0.98-1.01)</td>
<td>0.598</td>
</tr>
<tr>
<td>DAS28-ESR</td>
<td>1.277</td>
<td>0.373</td>
<td>3.58 (1.73-7.44)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Comorbidity (no vs yes)</td>
<td>-0.237</td>
<td>0.157</td>
<td>1.90 (0.87-3.97)</td>
<td>0.032</td>
</tr>
<tr>
<td>DAS28-P cut-off (&gt;=0.44 vs &lt;0.44)</td>
<td>-0.789</td>
<td>0.244</td>
<td>4.26 (1.86-12.62)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Disclosure: J. S. Lee, None; H. Ahmad, Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1, 9; S. C. Shim, Celltrion Inc., 5; S. C. Bae, None; Y. W. Song, None; E. Y. Lee, None.


Abstract Number: 1475

Collection of Anti-Rheumatic Medication Data from Both Patients and Rheumatologists Shows Strong Agreement in a Real World Clinical Cohort

Mohammad Movahedi, Angela Cesta, Xiuying Li and Claire Bombardier, Toronto General Hospital Research Institute, University Health Network, Toronto, ON, Canada
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Collection of Anti-Rheumatic Medication (ARM) information from both patients and rheumatologists is considered a strength for Rheumatoid Arthritis (RA) registries and cohorts. However, it is important to assess the agreement between these two data sources. We aimed to examine the agreement between patient and rheumatologist reported ARM use, their administration routes, and start and stop dates in the Ontario Best Practices Research Initiative (OBRI).

Methods:

Adult Patients enrolled in the OBRI who consented to both patient interviews and rheumatologist evaluations were included. Patients in the OBRI are interviewed every six months, while rheumatologist assessments are conducted as per routine care. For this analysis, we included patients who enrolled in OBRI on or after Sep 1st 2010 and compared ARM use reports where rheumatologist visits and interviews occurred within 60 days of each other. ARM included conventional synthetic Disease-Modifying Antirheumatic Drugs (csDMARDs) and biologic DMARDs (bDMARDs). Cohens’ Kappa statistics of agreement between the two data sources were calculated for ARM use and administration route. Kappa values 0.61-0.80 were considered to represent good and 0.81-1.00 as very good agreement. To examine factors associated with agreement, a multivariate backward stepwise logistic regression was used to model the odds of agreement for ARM use. The absolute time gap (days) for starts and stops dates between patient reports and rheumatologist reports were also assessed and presented by median and interquartile range (IQR) in a subset analysis.

Results:

2,154 patients (78.7% female) were included with a mean (SD) age at OBRI enrolment of 57.8 (12.6) year. Mean (SD) disease parameters were: disease duration: 8.4 years (9.9); DAS28: 4.2 (1.6); physician global: 4.0 (2.5); and health assessment questionnaire (HAQ) disability Index: 1.1 (0.8). For csDMARDs use, the prevalence was 74.2% based on patient reports and 76.6% based on rheumatologist reports. The prevalence of bDMARDs use was approximately 20.0% based on both reports.

Overall agreement for ARM use between patient and rheumatologist reports was good. In the regression model, increased HAQ-pain index (OR: 0.66; 95% CI: 0.60-0.73) and physician global (OR: 0.95; 95% CI: 0.92-0.98) were significantly associated with lower agreement. By contrast, post-secondary education (OR: 1.20; 95% CI: 1.02-1.40), and seeing an academic rheumatologist (OR: 1.47; 95% CI: 1.25-1.73) were significantly associated with higher agreement between the two data sources.

There was good and very good agreement for reported administration route of bDMARDs and csDMARDs, respectively. The median absolute time gap (IQR) of start dates and stop dates for ARM use reported by the two data sources was 7 days (1-27) and 19 days (5-48), respectively.

Conclusion:

The results of this analysis suggest that ARM reports from the two data sources have strong agreement in the OBRI. This agreement is even better for patients who have post-secondary education and are being treated by an academic rheumatologist.

Disclosure: M. Movahedi, None; A. Cesta, None; X. Li, None; C. Bombardier, Canada Research Chair in Knowledge Transfer for Musculoskeletal Care and a Pfizer Research Chair in Rheumatology, 6.


Abstract Number: 1476

Effect of Treat-to-Target Tocilizumab- and Methotrexate-Based Strategies on Health-Related Quality of Life in Newly Diagnosed Rheumatoid Arthritis Patients: Results of the U-Act-Early Trial

Xavier M Teitsma¹, Johannes WG Jacobs¹, Paco MJ Welsing², Attila Pethö-Schramm³, Michelle EA Borm⁴, Jacob M. van Laar⁵, Floris PJ Lafeber⁵ and Johannes W.J. Bijlsma². ¹Department of Rheumatology & Clinical Immunology, University Medical Center Utrecht, Utrecht, Netherlands, ²Rheumatology and Clinical Immunology, University Medical Center Utrecht, Utrecht, Netherlands,
**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Patient-reported outcomes are, in addition to other efficacy and safety related outcomes, important reflections of effectiveness and adverse effects of a therapy. The Outcomes Measures in Rheumatology Clinical Trials (OMERACT) initiative therefore strongly endorses to monitor also health-related quality of life (HRQoL) in rheumatoid arthritis (RA) studies. In the U-Act-Early strategy trial, initiation of tocilizumab (TCZ) has been proven more efficacious for reducing disease activity when compared to a step-up methotrexate strategy in disease modifying anti-rheumatic drugs (DMARD)-naïve patients with early RA. Here we report the effect of the strategies in this treat-to-target trial on HRQoL, as measured by the five dimensional EuroQol (EQ-5D) questionnaire.

**Methods:** In U-Act-Early, 317 early RA patients were randomized (1:1:1) to initiate methotrexate (MTX), TCZ or TCZ+MTX therapy and were treated to target until sustained remission (disease activity score assessing 28 joints (DAS28) <2.6 with ≤4 swollen joints for ≥24 weeks) was achieved. Hydroxychloroquine, as part of the initial treatment regimen, was added if remission was not achieved. If after 12 additional weeks the target still was not reached, patients switched to a subsequent treatment regimen: those in the TCZ arm or in the MTX arm switched to TCZ+MTX therapy; patients who started with TCZ+MTX switched to standard of care. We used a linear mixed model to analyze the differences between groups in change from baseline over time in EQ-5D utility scores (anchored at “0” (dead) and “1” (perfect health)) and the corresponding visual analogue scale (EQ-VAS, range 0-100). ANCOVA was used for between-group comparisons of scores at week 12, 24, 52 and 104.

**Results:** Significant greater improvements over time were found in EQ-5D scores in patients in the TCZ+MTX arm, compared to the MTX arm (p=0.02), but not compared to the TCZ arm (p=0.09, Fig. 1). No significant differences were found over time between the strategies in EQ-VAS scores (p≥0.14). When evaluating between-group differences at specific time-points, improvements were significantly greater at week 12 in both TCZ strategies in EQ-5D (TCZ+MTX vs MTX, p=0.04; TCZ vs MTX, p=0.01) and EQ-VAS scores (TCZ+MTX vs MTX, p<0.01; TCZ vs MTX, p=0.04), when compared to the MTX strategy. After 24 weeks, significance only remained in the EQ-5D score in favor of the TCZ+MTX strategy (TCZ+MTX vs MTX, p<0.01).

**Conclusion:** Initiating a treat-to-target TCZ-based strategy in DMARD-naïve patients with early RA resulted in significant improvements in HRQoL when compared to initiation of step-up MTX therapy, in line with current standards.

**Disclosure:** X. M. Teitsma, None; J. W. Jacobs, None; P. M. Welsing, None; A. Pethö-Schramm, F Hoffmann-La Roche, 3; M. E. Borm, Roche Nederland BV, 3; J. M. van Laar, MSD, Pfizer, Eli Lilly, and BMS, 5; F. P. Lafeber, Roche Nederland BV, 2; J. W. J. Bijlsma, Roche, AbbVie, Bristol-Myers Squibb, Merck Sharp & Dohme, Pfizer, and UCB, 2.

Patient-Reported Outcomes As Independent Measures of Treatment Success with Sirukumab, an Anti-IL6 Cytokine Monoclonal Antibody, in Patients with Active Rheumatoid Arthritis: Post-Hoc Analysis of 2 Placebo-Controlled Phase 3 Trials

Vibeke Strand¹, Rita Ganguly², Nan Li², Prasheen Agarwal³, Shihong Sheng³, Kaiyin Fei³, Kelly McQuarrie³ and Sharon Popik³,
¹Division of Immunology/Rheumatology, Stanford University, Stanford, CA, ²GlaxoSmithKline, Collegeville, PA, ³Janssen Research & Development, LLC, Spring House, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Sirukumab, a selective, high-affinity, human anti–IL-6 monoclonal antibody, is in development for rheumatoid arthritis (RA) and other diseases. Effects of sirukumab on RA symptoms and disease activity and health-related physical and emotional well-being were evaluated in 2 phase 3 randomized controlled trials (RCTs) in RA pts with inadequate responses to conventional DMARDs (SIRROUND-D) or TNF inhibitors (TNFi; SIRROUND-T). Across both RCTs, significant improvements were observed in all 8 SF-36 domains with both evaluated sirukumab doses (50 mg q4w and 100 mg q2w) versus placebo (PBO; P<0.001).

Methods: In both RCTs, eligible pts were randomized (1:1:1) to treatment with SC sirukumab 50 mg q4w, sirukumab 100 mg q2w, or PBO. Durations of PBO treatment were 52 and 24 wks, respectively, in SIRROUND-D and SIRROUND-T. Efficacy of sirukumab was evaluated using traditional RA endpoints. This analysis included SDAI and CDAI scores and the following patient-reported outcomes (PROs): pt global assessment of disease activity, pain (0-10 VAS), HAQ-DI, FACIT-Fatigue, and SF-36 health survey. In this post-hoc analysis, correlations between changes from baseline (BL; at Wks 16 [primary endpoint] or 24) in disease activity, symptoms, and SF-36 domain scores were evaluated. Last observation carried forward was used for imputing missing data.

Results: For changes from BL to Wk 16 in SIRROUND-T, correlation coefficients (r) were low to moderate between all 8 SF-36 domains and SDAI (r ranging from −0.535 to −0.208) and CDAI (−0.526 to −0.209; Table). Low to moderate correlations were also observed between changes from BL to Wk 16 in 7 of 8 SF-36 domains and pt global assessment scores (r ranging from −0.461 to −0.267) in SIRROUND-T, and a high correlation was observed for the remaining domain, bodily pain (−0.665 to −0.619). Moderate correlations were observed between changes from BL to Wk 16 in the SF-36 bodily pain, physical function, social function, and role-physical domains and changes in HAQ-DI (r ranging from −0.560 to −0.310). Moderate to high correlations were observed for changes from BL to Wk 16 in 7 of 8 SF-36 domains and FACIT-Fatigue scores (r ranging from 0.392 to 0.627; Table). As anticipated, changes from BL to Wk 16 in VAS pain and SF-36 bodily pain domain were highly correlated (r ranging from −0.672 to −0.661; Table). Correlations were generally higher with sirukumab than placebo. Similar correlations were observed in changes from BL to Wk 16 in SIRROUND-D. These correlations were maintained at Week 24 in both RCTs.

Conclusion: Results of these analyses highlight the importance of PROs, including SF-36 and FACIT-Fatigue, as independent measures of treatment success. Although some SF-36 domains are moderately correlated with clinical responses, these findings indicate that SF-36 captures aspects of patient well-being not covered by standard measures of RA symptoms and disease activity.
Abstract Number: 1478

Inadequate Clinical Response to Sirukumab, an Anti-IL-6 Monoclonal Antibody, Can be Predicted after a Single Dose of Treatment in Patients with Rheumatoid Arthritis

Shruti Daga1, Daniel Aletaha2, Benjamin Hsu3, Jennifer Gilbride4, Jacquie Christie5, Matthew Loza5, Bidisha Dasgupta5, Kim Campbell1, Kurt Brown6, Ravi Rao5 and Paul P. Tak5, 1GlaxoSmithKline, Uxbridge, United Kingdom, 2Department of Medicine III, Division of Rheumatology, Medical University of Vienna, Vienna, Austria, 3Janssen Research & Development, LLC, Spring House, PA, 4Sum of Squares Ltd, Hertfordshire, United Kingdom, 5GlaxoSmithKline, Stevenage, Hertfordshire, United Kingdom, 6GlaxoSmithKline, Collegeville, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster II: Prognostic Factors, Imaging and Miscellaneous Reports
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Response to therapy in rheumatoid arthritis (RA) is heterogeneous. Early identification of patients (pts) who are unlikely to achieve a meaningful clinical response may inform decisions to stop treatment in individual pts (Wijbrandts and Tak;
Mayo Clin Proc; in press). This would improve benefit:risk ratio in pts who continue treatment, and allows earlier cycling to alternate treatments for those who do not respond. Sirukumab (SIR) is a human monoclonal antibody that selectively binds to the cytokine IL-6 with high affinity, and has demonstrated efficacy in Phase 3 RA studies. This post hoc analysis explored whether lack of change in Clinical Disease Activity Index (CDAI) after a single dose of SIR could be used to identify pts with a low likelihood of clinical response after continued treatment.

**Methods:** We evaluated clinical response to SIR in two Phase 3 clinical trials in anti-TNF inadequate responders (IRs; SIRROUND-T; Aletaha D, et al. Lancet. 2017;389(10075):1206-1217) and DMARD IRs (SIRROUND-D) using CDAI - a simple composite measure of disease activity which does not include measurement of inflammatory markers. In both studies pts were randomized 1:1:1 to placebo, SIR 50 mg every 4 weeks (q4w), or SIR 100 mg every 2 weeks (q2w). We evaluated whether a change from baseline in CDAI >0 (representing worsening) at Week 4 could predict clinical outcomes including ACR20 (primary endpoint) and DAS28 (CRP)≤3.2 at Week 16 in pts receiving SIR 50mg q4w in SIRROUND-T. Analyses were repeated for Week 24 outcomes, SIR 100 mg q2w and in SIRROUND-D.

**Results:** A significantly greater proportion of pts achieved the primary endpoint of Week 16 ACR20 response on both doses of SIR compared to placebo in SIRROUND-T and -D (p<0·001). Worsening in CDAI at Week 4 after a single dose of SIR 50mg q4w was predictive of non-response at Week 16 in SIRROUND-T: 22% (65/291) of pts had CDAI worsening at Week 4; of these pts more than 85% did not achieve ACR20 or DAS28 (CRP)≤3.2 at Week 16 (NPV in Table 1). The 22% of pts with CDAI worsening at Week 4 could consider stopping SIR at Week 4 based on predicted non-response. In the remaining subgroup of pts, there was an approximate 20% relative increase in ACR response rates compared to the overall population rates. Results were comparable for the SIR 100 mg q2w dose, Week 24 outcomes, and for both doses in SIRROUND-D (Table 1).

**Conclusion:** SIR has demonstrated robust efficacy in RA. Lack of clinical efficacy at 16 weeks can be predicted using worsening from baseline in CDAI after a single dose of SIR 50mg. This approach can be further refined using different cut-offs and methods of prediction. It can also be extended to determine probabilities of achieving other outcomes, e.g. remission, which may be specific to the individual pt. These results have the potential to enable early treatment discontinuation decisions for individuals who are unlikely to respond to continued therapy.
Table 1. Predictive values of ACR20 and DAS28 (CRP) ≤3.2 after 16 and 24 weeks of treatment with sirukumab 50mg q4w and 100 mg q2w based on change from baseline to Week 4 in CDAI.

<table>
<thead>
<tr>
<th></th>
<th>ACR20</th>
<th>DAS28 (CRP) ≤3.2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Week 16</td>
<td>Week 24</td>
</tr>
<tr>
<td>Week 4 CDAI change from baseline</td>
<td>SIRROUND-T (anti-TNF inadequate responders)</td>
<td></td>
</tr>
<tr>
<td>Sirukumab 50 mg q4w N=292 CDAI change &gt; 0 (NPV) ≤ 0 (PPV)</td>
<td>56/65 (86.2%) 118/226 (47.8%)</td>
<td>54/65 (83.1%) 114/226 (50.4%)</td>
</tr>
<tr>
<td>Sirukumab 100 mg q2w N=292 CDAI change &gt; 0 (NPV) ≤ 0 (PPV)</td>
<td>43/50 (86.0%) 125/242 (51.7%)</td>
<td>39/50 (78.0%) 114/242 (47.1%)</td>
</tr>
<tr>
<td>Sirukumab 50 mg q4w N=556 CDAI change &gt; 0 (NPV) ≤ 0 (PPV)</td>
<td>64/80 (80.0%) 288/476 (60.5%)</td>
<td>61/80 (76.3%) 279/476 (58.6%)</td>
</tr>
<tr>
<td>Sirukumab 100 mg q2w N=558 CDAI change &gt; 0 (NPV) ≤ 0 (PPV)</td>
<td>67/88 (76.1%) 278/470 (59.1%)</td>
<td>61/88 (69.3%) 286/470 (60.9%)</td>
</tr>
</tbody>
</table>

Data presented are n/N (%) of patients not achieving (NPV) or achieving (PPV) clinical outcomes of interest.

CDAI – Clinical Disease Activity Index, ACR20 – American College of Rheumatology response 20%, DAS28 (CRP) – Disease Activity Score, analyzed using C-reactive protein, TNF – Tumor Necrosis Factor, DINAID – Disease Modifying Anti-Rheumatic Drug, NPV – Negative Predictive Value, PPV – Positive Predictive Value.

CDAI change from baseline > 0 is considered worsening; CDAI change from baseline ≤ 0 is considered maintenance or improvement of response.

Disclosure: S. Daga, GlaxoSmithKline, 3,GlaxoSmithKline, 1; D. Aletaha, AbbVie, Pfizer, Grünenthal, Merck Medac, UCB, Mitsubishi/Tanabe, Janssen, and Roche, 2,AbbVie, Pfizer, Grünenthal, Merck Medac, UCB, Mitsubishi/Tanabe, Janssen, and Roche, 5; B. Hsu, Johnson & Johnson, 1,Johnson & Johnson, 3; J. Gilbride, Sum of Squares Ltd, 3,GSK, 9; J. Christie, GlaxoSmithKline, 3,GlaxoSmithKline, 1; M. Loza, Johnson & Johnson, 1,Johnson & Johnson, 3; B. Dasgupta, Johnson & Johnson, 3; K. Campbell, Johnson & Johnson, 3,Johnson & Johnson, 1; K. Brown, GlaxoSmithKline, 3,GlaxoSmithKline, 1; R. Rao, GlaxoSmithKline, 3,GlaxoSmithKline, 1; P. P. Tak, GlaxoSmithKline, 3,GlaxoSmithKline, 1.


Abstract Number: 1479

**Difference in Clinical Presentation between Female and Male Patients with Primary Sjogren’s Syndrome at Diagnosis and in Long-Term Follow-up**

**Jorge Ramírez**¹, Marika Kvarnstrom², Susanna Brauner³, Chiara Baldini⁴, Per Eriksson⁵, Thomas Mandl⁶, Katrine Brække Norheim⁷, Svein Joar Johnsen⁸, Daniel S. Hammenfors⁹,¹⁰, Malin V. Jonsson¹¹, Kathrine Skarstein¹²,¹³, Johan G. Brun⁹,¹⁰, Lars Rönnblom¹⁴, Helena Forsblad D’Elia¹⁵, Sara Magnusson Bucher¹⁶, Elke Theander¹⁷, Roald Omdal⁸, Roland Jonsson⁹,¹⁰, Gunnel Nordmark¹⁸, and Marie Wahren-Herlenius¹⁹, ¹Unit of Experimental Rheumatology, Department of Medicine, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, Solna, Sweden, ²Unit of Rheumatology, Department of Medicine, Karolinska
Institutet, Karolinska University Hospital, Stockholm, Sweden, Stockholm, Sweden, 3Department of Clinical Neuroscience, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, Stockholm, Sweden, 4Internal Medicine, Rheumatology Unit, University of Pisa, Pisa, Italy, 5Division of Rheumatology, Department of Clinical Experimental Medicine, Linköping University, Linköping, Sweden, Linköping, Sweden, 6Department of Rheumatology, Skåne University Hospital, Malmö, Sweden, Lund, Sweden, 7Department of Internal Medicine, Clinical Immunology Unit, Department of Internal Medicine, Stavanger University Hospital, Stavanger, Norway, Stavanger, Norway, 8Clinical Immunology Unit, Department of Internal Medicine, Stavanger University Hospital, Stavanger, Norway, Stavanger, Norway, 9Broegelmann Research Laboratory, Department of Clinical Science, University of Bergen, Bergen, Norway, Bergen, Norway, 10Department of Rheumatology, Haukeland University Hospital, Bergen, Norway, Bergen, Norway, 11Section for Oral and Maxillofacial Radiology, Department of Clinical Dentistry, University of Bergen, Bergen, Norway, Bergen, Norway, 12Gade Laboratory for Pathology, Department of Clinical Medicine, University of Bergen, Bergen, Norway, 13Department of Pathology, Haukeland University Hospital, Bergen, Bergen, Norway, 14Rheumatology and Science for Life Laboratory, Department of Medical Sciences, Uppsala University, Uppsala, Sweden, Uppsala, Sweden, 15Department of Public Health and Clinical Medicine, Rheumatology, Umeå University, Umeå, Sweden., 16Department of Rheumatology, Faculty of Medicine and Health, Örebro University, Örebro, Sweden, Örebro, Sweden, 17Department of Rheumatology, Skåne University Hospital, Malmö, Sweden, Malmö, Sweden, 18Department of Medical Sciences, Section of Rheumatology, Uppsala University, Uppsala, Sweden, Uppsala, Sweden, 19Unit of Experimental Rheumatology, Department of Medicine, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, Stockholm, Sweden

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Sjögren's Syndrome Poster II: Clinical Research
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Despite men being less prone to develop autoimmune diseases, male sex has been associated with a more severe disease course in several systemic autoimmune diseases. In the present study, we aimed to identify differences in clinical presentation between the sexes at the time of diagnosis and during long-term follow-up of primary Sjögren’s syndrome (pSS), and to establish whether male sex is associated with a more severe form of pSS.

Methods:

Incident, treatment naïve patients (n=199, 186 females and 13 males) from Stockholm, Sweden were prospectively included during a 5-year period and examined for items of classification criteria for pSS as well as extraglandular manifestations (EGM). Serum was sampled at the time of diagnosis and anti-Ro52/SSA levels measured by ELISA. Replication of significant findings was confirmed in an independent cohort of incident pSS patients from Pisa, Italy (n=377, 368 females and 9 males), and meta-analysis performed.

We further studied a cohort of 967 patients with prevalent pSS (899 females and 68 males) from Scandinavian clinical centers. The mean follow-up time (years) was 8.8 ± 7.6 for women and 8.5 ± 6.2 for men (ns). Clinical data including serological and hematological parameters, glandular, EGM and comorbidities were compared between men and women.

Results:

An increased frequency of EGM in men at diagnosis was observed and replicated (p=0.05, p=0.0003, and p_{meta}=0.002, respectively). This related to pulmonary involvement, vasculitis and lymphadenopathy being more common in men, for whom a lower age at diagnosis was observed in the exploratory cohort. Additionally, SSA positive male patients had significantly higher levels of anti-Ro52 levels than their female counterparts (p=0.02).

After long-term follow-up, male patient serology was characterized by more frequent positivity for anti-SSA and anti-SSB (p=0.02), and ANA (p=0.02). Also, men with pSS were more frequently diagnosed with interstitial lung disease (p=0.008), lymphadenopathy (p=0.04) and lymphoma (p=0.007). Conversely, concomitant hypothyroidism was more common among female patients (p=0.009).

Conclusion:

Our analysis of two independent cohorts of incident pSS and a large cohort of prevalent pSS demonstrates significant differences between women and men with pSS. Notably, men present with more EGM, enhanced serological profile and a higher frequency of lymphoma development.
Risk of Ischemic Stroke in Sjögren’s Syndrome Patients: A Systematic Review and Meta-Analysis

Jirapat Teerakanok¹, Daniel Cordoba², Sakolwan Suchartlikitwong³ and Kenneth Nugent⁴, ¹Internal medicine, Texas Tech University health and sciences center, Lubbock, TX, ²Internal Medicine, Texas Tech University Health and Sciences Center, Lubbock, TX, ³Internal medicine, Texas Tech University Health Sciences Center, Lubbock, TX, ⁴Internal Medicine, Texas Tech University Health Sciences Center, Lubbock, TX
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Sjögren’s Syndrome Poster II: Clinical Research
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Primary Sjögren’s syndrome (SS) is an autoimmune disease of the exocrine glands with lymphocytic infiltration into lacrimal and salivary glands. Autoimmune diseases increase cardiovascular risk by premature vascular damage. There were observational studies on the risk of ischemic stroke in primary SS patients, but results have been inconclusive. We conducted a meta-analysis to compare incidence of ischemic stroke in SS and normal populations.

Methods: Two investigators searched published articles in EMBASE and PubMed database from 1980 to the end of February 2017 using the terms “Sjögren’s syndrome”, “ischemic stroke”, “stroke”, “cerebrovascular accident”, “cerebrovascular disease”, “cerebrovascular disorder”, “cerebral infarction”, “cerebral ischemia”, “brain infarction” and “brain ischemia”. Manual searching in the conferences abstract database from 2002-2016 was performed. Inclusion criteria were 1) observational studies (cohort, case control, cross sectional studies), 2) studies comparing incidence of ischemic stroke in SS and normal population, 3) studies providing relative risk (RR), odds ratio (OR), or standardized incidence ratio (SIR) with 95% confidence interval (CI). Quality assessment of studies was performed using Newcastle-Ottawa quality assessment scale. Review Manager 5.3 software was used to perform data analysis. Studies were combined by the generic inverse variance method described by Dersimonian and Laird. We used a random-effect model because of the variance in the studies. Cochran’s Q test was used to calculate $I^2$ to measure heterogeneity across studies. A funnel plot was used to assess for publication bias.

Results: Five studies (3 cohort studies, 1 case control study, and 1 cross sectional study) were met our criteria with 9,514 patients with primary SS. The pooled risk ratio for ischemic stroke in primary SS patients compared to control populations was 1.21 (95% CI 0.97-1.50), heterogeneity was moderate with $I^2$ of 60%, there was no evidence of publication bias from funnel plot.

Conclusion: We found no statistically significant increased risk for ischemic stroke in primary SS patients compared to the normal population, but more studies are needed to clarify the association between these two conditions.

Disclosure: J. Teerakanok, None; D. Cordoba, None; S. Suchartlikitwong, None; K. Nugent, None.
Risk of Ischemic Heart Disease in Sjögren’s Syndrome Patients: A Systematic Review and Meta-Analysis of Observational Studies

Jirapat Teerakanok1, Sakolwan Suchartkitwong2, Thammasak Mingbunjerdsuk3, Praveen Ratanasrimetha3, Yuttiwat Vorakunthada3 and John S. Pixley3, 1Internal medicine, Texas Tech University health and sciences center, Lubbock, TX, 2Internal medicine, Texas Tech University Health Sciences Center, Lubbock, TX, 3Internal Medicine, Texas Tech University Health Sciences Center, Lubbock, TX

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Sjögren's Syndrome Poster II: Clinical Research
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) are associated with an increased risk of ischemic heart disease (IHD). The risk of IHD in patients with Sjögren’s syndrome (SS) from previous observational studies has been inconclusive. Therefore, we conducted a meta-analysis to compare incidence of IHD in SS patients to normal populations.

Methods: Two investigators (J.T. and S.S.) searched published articles in EMBASE and PubMed database from 1980 to the end of May 2017 using the terms “Sjögren’s syndrome” and terms of ischemic heart disease. The diagnosis of Sjögren’s syndrome was made by physicians (primary care, rheumatologist) or retrieved from medical records using ICD-9-CM code 710.2. A manual search in the conferences abstract database from 2002-2017 was performed. Inclusion criteria were 1) observational studies (cohort, case control, cross sectional studies), 2) studies comparing incidence of IHD in SS and normal populations. Exclusion criteria were pediatric patients and non English-language articles. Quality assessment of studies was performed using Newcastle-Ottawa quality assessment scale. Review Manager 5.3 software was used to perform data analysis. We used a random-effect model because of the variance in the studies. Cochran’s Q test was used to calculate I² to measure heterogeneity across studies. A funnel plot was used to assess for publication bias.

Results: We identified 243 studies from the search. Five studies met our criteria (3 cohort studies, one case-controlled study and one cross-sectional study) with total 21,261 SJS patients. The pooled risk ratio for IHD in SJS patients compared to control populations was 1.27 (95% CI 0.91-1.79).

Conclusion: This meta-analysis did not find statistically significant increased risk of IHD in SJS patients compared to the general population.

Disclosure: J. Teerakanok, None; S. Suchartkitwong, None; T. Mingbunjerdsuk, None; P. Ratanasrimetha, None; Y. Vorakunthada, None; J. S. Pixley, None.
Preliminary Population-Based Incidence and Prevalence Estimates of Primary Sjogren’s Syndrome from the Manhattan Lupus Surveillance Program

Peter M. Izmirly1, Isabella Wan2, Sara Sahl3, Jill P. Buyon4, H. Michael Belmont5, Jane E. Salmon6, Anca Askanase7, Joan Baton8, Laura Geraldino-Pardilla7, Yousaf Ali9, Ellen M. Ginzler10, Chaim Putterman11, Caroline Gordon12, Charles G. Helmick13 and Hilary Parton14, 1Medicine, Division of Rheumatology, New York University School of Medicine, New York, NY, 2Medicine/Rheumatology, New York University School of Medicine, New York, NY, 3Pediatrics, Harbor-University of California at Los Angeles Medical Center, Torrance, CA, 4Department of Medicine, Division of Rheumatology, New York University School of Medicine, New York, NY, 5Medicine, New York University School of Medicine, New York, NY, 6Division of Rheumatology, Hospital for Special Surgery, Weill Cornell Medicine, New York, NY, 7Rheumatology, Columbia University College of Physicians & Surgeons, New York, NY, 8Division of Rheumatology, Columbia University, College of Physicians & Surgeons, New York, NY, 9Medicine/Rheumatology, Icahn School of Medicine at Mount Sinai, New York, NY, 10Rheumatology, Division of Rheumatology, Department of Medicine, SUNY Downstate Medical Center, Brooklyn, NY, 11Division of Rheumatology, Albert Einstein College of Medicine, Bronx, NY, USA, Bronx, NY, 12Rheumatology Research Group, Institute of Inflammation and Ageing, College of Medical and Dental Sciences, University of Birmingham, Birmingham, United Kingdom, 13Centers for Disease Control and Prevention, Atlanta, GA, 14Bureau of Epidemiology Services, New York City Department of Health and Mental Hygiene, Long Island City, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Sjögren's Syndrome Poster II: Clinical Research
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The extant epidemiologic data of Primary Sjögren’s Syndrome (pSS) remains limited with few published estimates for the general population and little data regarding racial/ethnic populations in the U.S. The Manhattan Lupus Surveillance Program (MLSP) is a population-based registry comprised of patients with Systemic Lupus Erythematosus (SLE) and related diseases including pSS treated in New York County (Manhattan) that was developed to determine the incidence and prevalence of SLE among Manhattan residents. Leveraging MLSP data we provide estimates of the prevalence and incidence of pSS during 2007 and 2007-09, respectively, in Manhattan across the major racial/ethnic populations (black, Hispanic, Asian, white).

Methods: MLSP cases were identified from hospitals, rheumatologists, and state population databases. Case screening was performed using ICD-9 codes, including 710.2 for SS. Charts were abstracted and final diagnosis was coded for Manhattan residents with one of the screening ICD-9 codes. pSS was defined using three case definitions: 1) a physician (regardless of specialty for cases hospitalized and not seen by a Rheumatologist) stating the diagnosis of pSS; 2) a rheumatologist’s diagnosis of pSS 3) a diagnosis of pSS with documentation of patient complaints of dry eyes and/or dry mouth and autoantibodies defined as a positive anti-SSA and/or anti-SSB antibody or a positive rheumatoid factor and antinuclear antibody titer >1:320.

Results: Based on the diagnosis of pSS found in the medical chart, the preliminary age-adjusted overall prevalence and incidence rates of pSS in Manhattan were 9.8 and 2.6 per 100,000, respectively, Table 1. The overall prevalence and incidence rates were 6 times higher among women than men, and rates among women were also higher within racial/ethnic groups. The prevalence of pSS was 17.4 among Asian women, 17.2 among white women 10.2 among Hispanic women, and 8.5 among black women, though confidence intervals overlapped, Table 1. The incidence of pSS was 7.1 among Asian women, 4.2 among white women, 2.2 among black women, and 2.0 among Hispanic women. Restricting the case definition to a rheumatologist diagnosis or to cases with symptoms and autoantibodies reduced both the prevalence and incidence of pSS, though there were similar trends in gender and racial/ethnic differences, Table 1. The average age ±SD at diagnosis among incident cases was 52.4 ±18.4 years among women and 58.1 ±17.3 years among men. The average age ±SD at diagnosis among incident cases was 48.6 ±18.2 years among Asians, 55.0 ±19.2 years among whites, 48.0 ±12.5 years among blacks, and 57.3 ±19.7 years among Hispanics.

Conclusion: Using data from a large population-based registry revealed substantial gender disparities in pSS among Manhattan residents. These data also provided epidemiologic estimates for the major racial/ethnic populations in the U.S.
<table>
<thead>
<tr>
<th>Table 1: Age-adjusted rates of Sjogren's Syndrome among Manhattan residents, overall and by sex and race/ethnicity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prevalent Cases, 2007</strong></td>
</tr>
<tr>
<td>Total</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td><strong>Incident cases, 2007-2009</strong></td>
</tr>
<tr>
<td>Total</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td><strong>Race/ethnicity</strong></td>
</tr>
<tr>
<td><strong>Primary Sjogren's</strong></td>
</tr>
<tr>
<td>Non-Hispanic White</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Non-Hispanic Black</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Hispanic</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Non-Hispanic Asian</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td><strong>Primary Sjogren's with Rheumatologist Diagnosis</strong></td>
</tr>
<tr>
<td>Non-Hispanic White</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Non-Hispanic Black</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Hispanic</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Non-Hispanic Asian</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td><strong>Primary Sjogren's modified definition</strong></td>
</tr>
<tr>
<td>Non-Hispanic White</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
</tr>
<tr>
<td>----------------------</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Non-Hispanic Black</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Hispanic</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Non-Hispanic Asian</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
</tbody>
</table>

Rates are per 100,000 Manhattan residents. Denominator data is based on 2007 intercensal population estimates from the NYC DOHMH Bureau of Epi Services (2000-2014 files).

Data are age adjusted to the US 2000 Standard Population.

Cases were assigned to one of five mutually exclusive race/ethnicity categories: non-Hispanic white, non-Hispanic black, non-Hispanic Asian, Hispanic, and non-Hispanic other. Non-Hispanic cases identified with more than one race were categorized as non-Hispanic other.

Incidence of Cancer in a Cohort of Patients with Primary Sjögren Syndrome

**Martin Brom**¹, Sebastian Moyano¹, Marina Scolnik² and Enrique R. Soriano³, ¹Rheumatology Unit, Internal Medicine Service, Hospital Italiano de Buenos Aires, Instituto Universitario Hospital Italiano de Buenos Aires, and Fundacion PM Catoggio, Buenos Aires, Argentina, ²Rheumatology Unit, Internal Medicine Service, Hospital Italiano de Buenos Aires, CABA, Argentina, ³Rheumatology Unit, Internal Medicine Service, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina

**First publication:** September 18, 2017

**Session Information**

**Session Date:** Monday, November 6, 2017

**Session Title:** Sjögren's Syndrome Poster II: Clinical Research

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Several neoplasia have been associated with Sjögren Syndrome (SS), being non-Hodgkin lymphoma the most frequent one. Our objective was to evaluate the incidence of all type of cancer in a cohort of patients with primary SS.

**Methods:** A retrospective descriptive study was performed in a university hospital with its own health insurance and captive population. Electronic medical records of SS patients were reviewed between 01/01/2000 and 12/31/2015. We included patients fulfilling ACR 2012 or American-European Consensus Group (AECG) 2002 SS criteria, or patients diagnosed as Primary SS by the treating rheumatologist. We registered and analyzed demographic, clinical and histopathologic information available on their medical records.
Incidence rate of cancer with their 95% CI was calculated. Patients were followed up until the end of study, death, loss of follow up, or when a diagnosis of cancer was performed. Incidence was compared with statistics on general population from United Kingdom (UK) as there is no full data available in the country where the study was performed.

**Results:** One hundred fifty-seven patients with Primary SS were included, and followed for 1158 patient/years. Table 1 shows patients’ characteristics. 15 patients developed a neoplasia during follow up: 3 lymphomas (two MALT lymphomas of the parotid and one disseminated non-Hodgkin lymphoma), 1 Multiple Myeloma, 4 Skin (non – melanoma) neoplasia and 7 solid organ cancer (4 Breast, 1 Lung, 1 Uterus, 1 Tongue). Table 2 shows the cohort cancer incidence rates and comparison with statistics from general population. Non- Hodgkin Lymphomas showed an increased incidence in SS patients. All 3 patients with lymphoma were females, with anemia, leukopenia, thrombocytopenia and high erythrocyte sedimentation rate. In multivariate logistic regression analysis only thrombocytopenia was associated with an increased risk of cancer in general (OR 7, CI 95% 1.9-25.7).

**Conclusion:** We only found an increased rate of non- Hodgkin lymphomas in this cohort of SS patients. Other types of cancer incidence rates were in ranges expected for general population.

Table 1. SS patients’ characteristics

<table>
<thead>
<tr>
<th>SS patients (n=157)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Females, n (%)</td>
<td>150 (95.5)</td>
</tr>
<tr>
<td>Mean age at diagnosis, years (SD)</td>
<td>49.4 (19)</td>
</tr>
<tr>
<td>Dry eyes, n (%)</td>
<td>152 (96.8)</td>
</tr>
<tr>
<td>Dry mouth, n (%)</td>
<td>139 (89.1)</td>
</tr>
<tr>
<td>Salivary gland enlargement, n (%)</td>
<td>26 (16.6)</td>
</tr>
<tr>
<td>Arthralgia, n (%)</td>
<td>106 (67.5)</td>
</tr>
<tr>
<td>Arthritis, n (%)</td>
<td>14 (9)</td>
</tr>
<tr>
<td>ANA +, n (%)</td>
<td>153 (96.8)</td>
</tr>
<tr>
<td>Anti Ro +, n (%)</td>
<td>149 (94.9)</td>
</tr>
<tr>
<td>Anti La +, n (%)</td>
<td>94 (60.3)</td>
</tr>
<tr>
<td>Rheumatoid Factor +, n (%)</td>
<td>66 (44.9)</td>
</tr>
<tr>
<td>Anti CCP +, n/n performed (%)</td>
<td>3/45 (6.7)</td>
</tr>
<tr>
<td>Low C3/C4, n/n performed (%)</td>
<td>30/111 (27)</td>
</tr>
<tr>
<td>Elevated erythrocyte sedimentation rate, n (%)</td>
<td>130 (83.3)</td>
</tr>
<tr>
<td>Hypergammaglobulinemia, n (%)</td>
<td>95 (63)</td>
</tr>
<tr>
<td>Cryoglobulinemia +, n/n performed (%)</td>
<td>5/50 (10)</td>
</tr>
<tr>
<td>Anemia, n (%)</td>
<td>47 (30.1)</td>
</tr>
<tr>
<td>Leukopenia, n (%)</td>
<td>51 (32.7)</td>
</tr>
<tr>
<td>Thrombocytopenia, n (%)</td>
<td>23 (14.7)</td>
</tr>
<tr>
<td>Compatible Salivary Glands biopsy, n/n performed (%)</td>
<td>24/32 (75)</td>
</tr>
<tr>
<td>Confirmatory dry eye test, n/n performed (%)</td>
<td>49/68 (72)</td>
</tr>
<tr>
<td>Follow up in years, median (IQR)</td>
<td>7.7 (8)</td>
</tr>
<tr>
<td>Deaths during follow up, n (%)</td>
<td>2 (1.2)</td>
</tr>
</tbody>
</table>

Table 2. Neoplasia incidence rate in this SS cohort compared to general statistics

<table>
<thead>
<tr>
<th>Neoplasia</th>
<th>Incidence rate in this SS cohort per 100,000 person/years (95% CI)</th>
<th>Incidence in general Population per 100,000 person/years (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non Hodgkin Lymphomas</td>
<td>260 (50 – 750)</td>
<td>22.9 (22.5-23.3)*</td>
</tr>
<tr>
<td>Multiple Myeloma</td>
<td>86 (2- 480)</td>
<td>9.3 (9.1-9.6) *</td>
</tr>
<tr>
<td>Skin (non – melanoma)</td>
<td>340 (94- 880)</td>
<td>223.6 (222.4-224.8) *</td>
</tr>
<tr>
<td>Breast</td>
<td>340 (94- 880)</td>
<td>172 (170-173)**</td>
</tr>
<tr>
<td>Lung</td>
<td>86 (2- 480)</td>
<td>79.3 (78.6-80)*</td>
</tr>
<tr>
<td>Uterus</td>
<td>86 (2- 480)</td>
<td>29.8 (29.2-30.4)*</td>
</tr>
<tr>
<td>Tongue</td>
<td>86 (2- 480)</td>
<td>19.2 (18.8-19.5)***</td>
</tr>
</tbody>
</table>

* UK incidence data

**UK incidence in women

*** UK Head and neck cancer incidence rate
**Association between Primary Sjogren’s Syndrome, Arterial Stiffness and Subclinical Atherosclerosis: A Systematic Review and Meta-Analysis**

**Wai Chung Yong, Anawin Sanguankeo and Sikarin Upala, Bassett Medical Center, Cooperstown, NY**

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Sjögren's Syndrome Poster II: Clinical Research  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Abstract**

**Background/Purpose:** In rheumatoid arthritis and systemic lupus erythematosus, cardiovascular disease is frequently a major cause of mortality or morbidity. Studies have shown that acute systemic inflammation and chronic systemic vasculitis are associated with endothelial dysfunction and atherosclerotic plaque formation, subsequently leading to cardiovascular disease. The studies of atherosclerosis in primary Sjogren syndrome (PSS) are still inconclusive to date. This meta-analysis aimed to explore the association of subclinical atherosclerosis and arterial stiffness in PSS.

**Methods:** A comprehensive search of the CENTRAL, MEDLINE and Embase databases was performed from 2000 through January 2017. The inclusion criterion was observational studies evaluating the association between primary Sjogren syndrome, subclinical atherosclerosis and arterial stiffness by measuring pulse wave velocity (PWV) and intima media thickness (IMT). Definitions of PSS and methods to assess PWV and IMT were recorded for each study. Different locations of IMT were assessed including common carotid, internal carotid, and femoral arteries. Pooled mean difference (MD) of PWV and IMT and 95% confidence interval (CI) were calculated using a random-effect meta-analysis. The between-study heterogeneity of effect size was quantified using the $Q$ statistic and $I^2$.

**Results:** Data were extracted from 10 observational studies involving 789 subjects. Pooled result demonstrated a significant increase in PWV in patients who have PSS compared with controls (MD=1.30 m/s; 95% CI: 0.45 – 2.15, p-value=0.003, $I^2 = 82\%$). Patients with PSS also have higher IMT (MD=0.10 mm; 95% CI: 0.07-0.14, p-value<0.01, $I^2 = 49\%$).

**Conclusion:** Our study suggests that PSS is associated with arterial stiffness and subclinical atherosclerosis. Further studies need to be conducted in order to find the correlation of subclinical atherosclerosis in PSS with cardiovascular event, the pathophysiologic changes of arterial stiffness in PSS, and the benefit of statins, because controlling cardiovascular risk factors or disease activity could potentially help avoid progression of atherosclerosis to an overt cardiovascular disease.
Abstract Number: 1485

Association between Primary Sjogren’s Syndrome, Cardiovascular and Cerebrovascular Events: A Systematic Review and Meta-Analysis

Wai Chung Yong, Anawin Sanguankeo and Sikarin Upala, Bassett Medical Center, Cooperstown, NY
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Sjögren's Syndrome Poster II: Clinical Research
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Abstract

Background/Purpose: Studies have demonstrated that acute systemic inflammation and chronic systemic vasculitis are associated with endothelial dysfunction and atherosclerotic plaque formation, subsequently leading to cardiovascular or cerebrovascular disease. In rheumatoid arthritis and systemic lupus erythematosus, the tendency of atherosclerosis is a major cause of mortality. Patients with primary Sjogren syndrome (PSS) may have a higher frequency of subclinical atherosclerosis, but studies on cardiovascular or cerebrovascular events in this population are limited with conflicting results. This meta-analysis aimed to explore the risk of cardiovascular and cerebrovascular event in PSS.

Methods: A comprehensive search in the CENTRAL, MEDLINE and Embase databases was performed from 1990 through January 2017. The inclusion criterion was observational studies evaluating the association between PSS and cardiovascular disease or cerebrovascular event. PSS is defined using American College of Rheumatology or American European Consensus criteria. Outcomes are diagnosis of ischemic heart disease, myocardial infarction, ischemic stroke or hemorrhagic stroke. Pooled odds ratio (OR) of cerebrovascular event or cardiovascular event and their 95% confidence interval (CI) were calculated using a random-effect meta-analysis to compare risk between those who have PSS and controls. The between-study heterogeneity of effect-size was quantified using the $Q$ statistic and $I^2$.

Results: Data were extracted from five observational studies involving 94,426 subjects. Pooled result demonstrated no significant difference in risk of having cardiovascular disease or cerebrovascular event in patients who have PSS compared with controls (OR=1.24; 95% CI: 0.96-1.61, p-value=0.10, $I^2$ = 67%). Subgroup analyses showed no difference in risk for cerebrovascular event...
(OR=1.26; 95% CI: 0.93-1.69, p-value=0.13, $I^2 =$ 72%), and cardiovascular disease (OR=1.30; 95% CI: 0.67-2.53, p-value=0.43, $I^2 =$ 72%).

**Conclusion:** Our study has not shown an increased risk of cardiovascular or cerebrovascular event in patient with PSS. Further studies need to be conducted in order to find the correlation of subclinical atherosclerosis in PSS with cardiovascular or cerebrovascular event.

Disclosure: W. C. Yong, None; A. Sanguankeo, None; S. Upala, None.
Interstitial Lung Disease in Primary Sjögren’s Syndrome: Clinical Presentation, Serological Biomarkers and Long Term Outcome

Chiara Baldini1, Ilaria Puxeddu2, Martina Orlandi3, Francesco Ferro4, Elena Elefante4, Nicoletta Luciano4, Marco Matucci-Cerinic3, Paola Migliorini2 and Marta Mosca4, 1Internal Medicine, Rheumatology Unit, University of Pisa, Pisa, Italy, 2Allergology and Clinical Immunology Unit, University of Pisa, Pisa, Italy, 3Rheumatology Unit, University of Florence, Florence, Italy, 4Rheumatology Unit, University of Pisa, Pisa, Italy

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Sjögren’s Syndrome Poster II: Clinical Research
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Interstitial lung disease (ILD) is a rare but potentially severe manifestation of primary Sjögren’s syndrome (pSS). The aims of this study were to: 1) analyze clinical presentation, characteristics and outcome of ILD in pSS; 2) evaluate predictive factors associated with ILD onset and evolution; 3) explore whether the inflammatory chemokines RANTES, IL-8 and MCP-1 may be associated to pSS-related ILD.

Methods: Patients with a diagnosis of pSS (AECG 2002) were included in this single center study. Demographic, clinical and radiological data were collected retrospectively. Serum levels of RANTES, MCP-I and IL-8 were measured by commercial ELISA kits in a subgroup of pSS patients with and without ILD.

Results: We included in this study 285 (12 M:273 F) patients with pSS. Eighteen out of 285 (6.3%) presented ILD: 12/18 NSIP and 6/18 UIP pattern. Patients with ILD were more frequently males (4/18 (22%) vs 8/267 (3%), p=0.004) and older at the diagnosis with respect to non-ILD pSS patients (62±13 vs 50±13 yrs, p=0.000). The clinical presentation of ILD was acute-subacute in 8 cases, slow progressive in 3 and subclinical in 7 patients. ILD diagnosis preceded pSS diagnosis in 8/18 cases. These patients presented more often a UIP pattern (5/8 vs 1/10, p=0.04). Patients were treated with steroids in monotherapy (7/18) or in association with immunosuppressive drugs (11/18) including cyclophosphamide (n=4), azathioprine (n=5), mycophenolate mofetil (n=1) and rituximab (n=1). During the disease course 5 patients improved, 11 were stabilized and 2 worsened. Patients that at the end of the follow-up presented a DLCO <60%, were more frequently positive for anti-Ro/SSA antibodies (p=0.04) and all presented a UIP pattern (p=0.000). Finally, circulating levels of RANTES, but not of IL-8 and MCP-1 were significantly able to discriminate pSS-ILD from non-ILD pSS patients (620.4±318.4 vs 280.2±180.9, p=0.02).

Conclusion: This study showed that, despite rare, ILD can be a presenting feature of pSS especially in males and older patients. The inflammatory chemokine RANTES, promoting lymphocyte infiltration, may play a role in the pathophysiology of pSS-related ILD and may have a role as diagnostic biomarker for ILD especially in less symptomatic pSS patients.

Disclosure: C. Baldini, None; I. Puxeddu, None; M. Orlandi, None; F. Ferro, None; E. Elefante, None; N. Luciano, None; M. Matucci-Cerinic, None; P. Migliorini, None; M. Mosca, None.

Salivary Gland Ultrasonography (SGUS) and Subclinical Parotid Involvement: Usefulness of SGUS in the Identification of a Subset of Patients with Sjögren’s Syndrome at Higher Risk for Extraglandular Disease Manifestations

Abstract Number: 1487
SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Sjögren's Syndrome Poster II: Clinical Research
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Salivary gland ultrasonography (SGUS) has recently appeared as a promising tool for the diagnosis and the early stratification of patients affected by primary Sjögren’s syndrome (pSS). In particular, the SGUS score has been reported as correlated with the ESSDAI score, suggesting that patients with more prominent pathological findings at the SGUS may have a higher disease activity. In this study, we aimed at correlating the SGUS score with the single domains of the ESSDAI and of the ClinESSDAI in order to better investigate any eventual association and correlation between SGUS abnormalities and pSS clinical and biological features.

Methods: Patients with pSS (AECG 2002) were prospectively enrolled in this study. All subjects had a standardized evaluation which included laboratory testing and a complete rheumatologic evaluation. SGUS was carried out by the same radiologist blinded to the diagnosis and the following US parameters were recorded: size, parenchymal echogenicity and inhomogeneity in the parotid and submandibular glands on both sides. A modified version of the De Vita score was used to grade the echostructure alterations of the salivary glands.

Results: One hundred and forty consecutive pSS patients (137 F: 3 M, age = 56.7±13 yrs) were enrolled in this study. Out of them 59/140 patients showed no pathological findings at the SGUS examination and 81/140 presented at least some mild alterations. The mean SGUS score was 1.97± 2.20 (range 0-8). The mean ESSDAI was 3.10±4.33 (range 0-33). The total SGUS score significantly correlated with both the ESSDAI (r=0.340, p=0.000) and the ClinESSDAI (r=0.263, p=0.002). In particular the biological domain of the ESSDAI were significantly correlated to both partial parotid scores (r=0.379, p=0.000) and submandibular scores (r=0.200, p=0.02). By contrast, only partial parotid scores (but not the partial submandibular scores) significantly correlated with the ClinESSDAI (r=0.253, p=0.03) and, particularly with glandular (r=0.279, p=0.001), ematological (r=0.185, p=0.03) and skin domains (r=0.188, p=0.03). Total and partial parotid SGUS scores inversely correlated with the age of the patients at pSS diagnosis (r=-0.168, p=0.04 and r=-0.208, p=0.01).

Conclusion: This study demonstrated that patients with US pathological findings in their parotid glands, also in the absence of evident glandular swelling, presented a more aggressive disease phenotype. SGUS may therefore be useful in clinical practice to identify patients with subclinical parotid involvement who may deserve a closer monitoring and a more aggressive treatment.

Disclosure: C. Baldini, None; N. Luciano, None; F. Ferro, None; E. Elefante, None; R. Talarico, None; C. Tani, None; M. Mosca, None.


Abstract Number: 1488

Correlation between Lung Ultrasound, HRCT Findings and Pulmonary Function Tests in Primary Sjögren’s Syndrome (pSS)-Associated Interstitial Lung Disease

Francesco Ferro1, Alessandra Bulleri2, Andrea Delle Sedie1, Simone Barsotti1, Nicoletta Luciano1, Elisa Cioffi3, Elena Elefante1, Gianfranco Puppo4, Marta Mosca1 and Chiara Baldini5, 1Rheumatology Unit, University of Pisa, Pisa, Italy, 2Radiology Unit, University of Pisa, Pisa, Italy, 3Rheumatology Unit, Rheumatology Unit, University of Pisa, Pisa, Italy, 4Pneumology Unit, University of Pisa, Pisa, Italy, 5Internal Medicine, Rheumatology Unit, University of Pisa, Pisa, Italy
First publication: September 18, 2017
Background/Purpose: Recently, pleural irregularity (PI), a new lung ultrasound (US) sign, has been proposed as an emerging tool for the diagnosis of interstitial lung disease (ILD) in connective tissue diseases. However, few data are available regarding its role in the evaluation of ILD associated to primary Sjögren’s syndrome (pSS). Aim of this study was to assess the accuracy of PI-US in detecting pSS-associated ILD by correlating PI-US findings with chest high-resolution computed tomography (HRCT) and pulmonary function tests.

Methods: Eighteen patients with pSS-associated ILD were included in the study. HRCT and tests of pulmonary function were performed in each patient. PI-US was performed by a single operator using a MyLab-25 (Esaote), 10 MHz, 5 cm linear probe. PI was defined as the loss of the normal hyperechoic linear pleural contour (score 0-2: normal, minimal and major changes at each intercostal space). PI US total score represented the sum of partial scores assigned to 6 lung fields (2 for the anterior, 2 for postero-superior and 2 for postero-inferior chest surface). Abnormal findings at HRCT were quantified by an expert radiologist according to the Warrick score.

Results: We included in this study 18 patients with pSS-related associated ILD (14 F:4 M, mean age =68.8 ±9.9 yrs). The median PI-US score was 45 (range 25.5-73.5). Both PI-US total score and partial postero-inferior PI-US score strongly correlated with the Warrick HRCT score (r= 0.813, p=0.000 and r= 0.914, p=0.000). Regarding pulmonary function tests, the Warrick HRCT score correlated with FVC (r=-0.753, p=0.001), TLC (r=-0.853, p=0.000), and DLCO (r=-0.834, p=0.000). Similarly, PI-US total score and partial PI-US postero-inferior score correlated inversely with FVC (r=-0.849, p=0.000 and r=-0.836, p=0.000), TLC (r=-0.895, p=0.000 and r=-0.829, p=0.000), and DLCO (r=-0.953, p=0.000 and r=-0.883, p=0.001). Finally, both PI-US score and PI-US of the infero-posterior field (but not Warrick HRCT score) directly correlated with FEV1/SVC (r=0.701, p=0.004 and r=0.619, p=0.01) and with FEV1/FVC (r=0.600, p=0.02 and r=0.501, p=0.05).

Conclusion: This study demonstrated a high correlation between PI-US, HRCT findings and pulmonary function tests, supporting the use of lung ultrasonography in clinical practice for the assessment of pSS-associated ILD. The exclusive correlation between PI-US scores and both FEV1/SVC and FEV1/FVC seemed to indicate a higher sensitivity of PI-US with respect to HRCT in ILD assessment. Further studies are warranted to clarify the role of PI-US for the early diagnosis of ILD.

Disclosure: F. Ferro, None; A. Bulleri, None; A. Delle Sedie, None; S. Barsotti, None; N. Luciano, None; E. Cioffi, None; E. Elefante, None; G. Puppo, None; M. Mosca, None; C. Baldini, None.

Development and Validation of a Questionnaire to Assess Healthcare Utilization and Access in Cohorts of Patients with Primary Sjögren’s Syndrome

Chiara Seghier1, Chiara Baldini2, Luca Quartuccio3, Francesco Ferro4, Saviana Gandolfo5, Salvatore De Vita6 and Stefano Bombardieri4, 1Istituto di Management Scuola Superiore Sant'Anna, Pisa, Italy, 2Internal Medicine, Rheumatology Unit, University of Pisa, Pisa, Italy, 3Rheumatology Clinic, DSMB, University of Udine, Udine, Italy, Udine, Italy, 4Rheumatology Unit, University of Pisa, Pisa, Italy, 5Rheumatology Clinic, Medical Area Department, University of Udine, Udine, Italy, 6Rheumatology Clinic, Academic Hospital S. M. della Misericordia, Medical Area Department, University of Udine, Italy, Udine, Italy

First publication: September 18, 2017
Background/Purpose: The geographic variation in healthcare service utilization and quality across and within countries is well documented. Part of this geographic variation is linked to differences in population health and needs. However, some of the variation may be unwarranted and driven by factors other than health needs, such as provider discretion, the availability and distribution of resources, financing and reimbursement models (Wennberg 2011). In this study, we identified the need for instruments to collect comparable data in Europe to establish practice profiles in the treatment and management of patients with Primary Sjögren’s Syndrome (pSS).

Methods: We describe the development and preliminary validation of a questionnaire to pSS to collect information on access to and intensity of treatments and services (e.g. diagnostic testing, hospitalizations, specialist visits), patients’ satisfaction with the care received and socio-demographic data (e.g. age, sex, education level). A short questionnaire is also administered to specialists treating the selected pSS to collect data on the organization of the clinical centers and involvement and relations with other healthcare professionals besides clinical information of the selected patients.

Results: The pilot version of the questionnaire was administered to 50 pSS in the clinical centre of Pisa (Italy) and counted 22 closed-ended questions. Three questionnaires out of 50 were returned incomplete. Mean (SD) age was 60 (12.2) years and 96% of the sample was female. The majority of the respondents had a primary or secondary school (59%). Construct validity was supported by the questionnaire's ability to discriminate between groups with different levels of activity of the disease and socio-demographic characteristics. Disease activity was significantly associated with frequency of rheumatologic visits and diagnostic tests (p<0.001). The total number of specialists involved in the care other than the rheumatologist varies significantly among patients. As expected, the most frequently involved were the ophthalmologist (90%) and the dentist (58%). Additionally, patients with lower education have attended on average less specialists than those with a high school or university degree (p<0.001).

Conclusion: Preliminary results confirm that the questionnaire is a valid instrument to assess patterns of care for pSS in terms of access and utilization and in relation to clinical and socio-demographic characteristics of patients. Further analysis will be conducted in other clinical centers within the European Horizon 2020 project “HarmonicSS” to verify the generalizability and additional psychometric properties of the instrument.

Disclosure: C. Seghieri, None; C. Baldini, None; L. Quartuccio, None; F. Ferro, None; S. Gandolfo, None; S. De Vita, None; S. Bombardieri, None.

Abstract Number: 1490

Cardiovascular Morbidity and Mortality in Primary Sjögren Syndrome: A Systematic Review and Meta-Analysis

Aurélie Beltai1, Cédric Lukas2, Cécile Gaujoux-Viala3, Bernard Combe4, Jacques Morel4 and Thomas Barnetche5, 1Department of rheumatology, Teaching hospital Lapeyronie and University of Montpellier, Montpellier, France, 2Rheumatology, CHU Lapeyronie and EA2415, Montpellier University, University of Montpellier, France, 3Rheumatology, Nîmes University Hospital and EA2415 Montpellier University, Nîmes, France, 4Rheumatology, CHU Lapeyronie and Montpellier University, Montpellier, France, 5Rheumatology, CHU Pellegrin, Bordeaux, France, Bordeaux, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Sjögren's Syndrome Poster II: Clinical Research
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: It is well documented that patients with immune-mediated inflammatory diseases (IMID) like rheumatoid arthritis are exposed at an increased risk of cardiovascular disease. Primary Sjögren syndrome (PJS) is a progressive autoimmune disease characterized by a chronic inflammation of exocrine glands and a functional deficit of the salivary and lachrymal glands, biological inflammation being infrequent. The purpose of this article was to investigate the association between PJS and an increase of the cardiovascular morbidity and mortality.
Methods: We performed a systematic review of available articles on the databases of MEDLINE and the COCHRANE library from their dates of inception to January 2017 and recent abstracts from ACR and EULAR meetings, searching for studies reporting observed cardiovascular morbidity and cardiovascular mortality in PJS and having a comparison group. The relative risks of cardiovascular morbidity and mortality associated with PJS were collected and pooled in meta-analysis using Review Manager Software (Cochrane collaboration). Random effects meta-analyses were conducted, and forest plots were constructed to summarize the risk ratio estimates and their 95% confidence intervals. The heterogeneity between studies was assessed using the Cochran’s Q-test and the I2 value.

Results: 457 studies were retrieved, among which 26 involving 61254 PJS patients met the inclusion criteria and were analyzed after the selection procedure was applied. Ten studies involving 32 907 PJS patients were included in the meta-analysis. The studies showed that patients with PJS had a significantly increased prevalence of coronary morbidity (relative risk (RR) = 1.75, 95%CI : 1.36-2.25; p<0.0001), cerebrovascular morbidity (RR= 1.46, 95%CI : 1.43-1.49, p<0.00001), heart failure rate (odd ratio (OR)=2.54, 95%CI: 1.30 – 4.97, p=0.007), thromboembolic morbidity ( RR= 1.78, 95% confidence interval (CI) :1.41- 2.25, p<0.00001), and a trend to increased cardiovascular mortality ((RR)= 1.48, 95%CI : 0.77-2.85, p=0.24) compared to the control population without IMID.

Conclusion: This meta-analysis demonstrates that PJS is associated with an increased cardiovascular morbidity suggesting that these patients should also been proposed for a screening of cardiovascular comorbidities and specific preventive interventions.

Disclosure: A. Beltai, None; C. Lukas, None; C. Gaujoux-Viala, None; B. Combe, None; J. Morel, None; T. Barnetche, None.

Abstract Number: 1491

Is There a Seasonal Effect on Fatigue, Pain, and Dryness in Primary Sjögren’s Syndrome? Data from the Prospective Assess Cohort and from 3 Randomized Controlled Trials

Pierre-Marie DURET1, Nicolas MEYER2, Alain Saraux3, Valérie Devauchelle-Pensec4, Jean Sibilia5, Raphaele Seror6, Véronique Le-Guern7, Claire Larroche8, Aleth Perdriger9, Xavier Mariette10 and Jacques-Eric Gottenberg11, 1Rhumatology, Hautepierre Hospital, STRASBOURG, France, 2clinical research, Hautepierre Hospital, STRASBOURG, France, 3Rheumatology, Brest University Hospital, Brest, France, 4Department of Rheumatology, Brest University Hospital, Brest, France, 5Department of Rheumatology, Strasbourg University Hospital, Strasbourg, France, 6Center for Immunology of Viral Infections and Autoimmune Diseases, Assistance Publique – Hôpitaux de Paris, Hôpitaux Universitaires Paris-Sud, Le Kremlin-Bicêtre, Université Paris Sud, INSERM, Paris, France, Paris, France, 7service de médecine interne, Department of Internal Medicine, Referral Center for Rare Autoimmune and Systemic Diseases, Hôpital Cochin, AP–HP, Université Paris Descartes, Paris, France, 8Internal Medicine, Paris, France, 9Service de Rhumatologie, CHRU de Rennes, Rennes, France, 10Université Paris-Sud, AP-HP, Hôpitaux Universitaires Paris-Sud, Paris, France, 11CNRS, Immunopathologie et Chimie Thérapeutique/Laboratory of Excellence Medalis, Institut de Biologie Moléculaire et Cellulaire, Strasbourg, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Sjögren's Syndrome Poster II: Clinical Research
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

A seasonal effect was reported on fatigue and pain in rheumatoid arthritis. We speculated that fall and winter could be associated with increased fatigue and pain and that spring and summer could be associated with increased dryness. If a seasonal effect plays a role on patients’s symptoms, it has to be taken into account in clinical trials and also in daily practice.

Our objective was to assess a seasonal effect on fatigue, pain and dryness.
Methods:
The data (date, VAS pain, fatigue, dryness) were extracted from three negative placebo-controlled randomized controlled trials (infliximab (n= 103 patients), hydroxychloroquine (JOQUER, n= 120 patients) and rituximab (TEARS n=120)) and from the ASSESS prospective cohort (n= 395 patients). VAS pain, fatigue and dryness were analyzed at each visit for each patient, according to the day of the year, the month of the year, and the season. Linear mixed models were fitted with a fixed time effect (month, with or without cosinus transformation, or season effect, in distinct models) with a random subject effect used to take into account the repeated structure of the data and analyze a potential cyclic effect. Statistical analyses were performed using R3.3.1 with the LME4 and HGLM libraries.

Results:
744, 584, 848 and 682 pain, fatigue and dryness VAS were collected on 632 subjects in spring, summer, fall and winter, respectively. Mean (SD) pain VAS was 52.2 (27.9), 55.1 (28.1), 51.0 (28.7) and 51.7 (28.4) in spring, summer, fall and winter, respectively. Mean (SD) fatigue was 61.9 (23.2), 62.2 (25.2), 60.0 (25.5), 61.9 (24.2), respectively. Mean (SD) dryness was 58.9 (21.8), 61.2 (22.9), 56.9 (22.8), and 57.9 (23.8), respectively (Figure 1). No significant difference was observed in pain, fatigue and dryness, according to the day of the year, the month or the season (all p-values >0.05). Variations from month to month or season to season of mean pain, fatigue and dryness were mild (maximum between-months variation for pain was 7.22 on a 100-unit scale). All observed fluctuations were well lower than MCIIs for fatigue, dryness and pain (20, 10 and 10 point on a 100-point scale, respectively, ref 1).

Conclusion:
Intensity of perceived dryness, pain and fatigue do not seem to have meaningful fluctuations according to seasons or months. Therefore, the impact on the main symptoms of the disease in randomized trial is not biased by a seasonal effect.

Ref 1 : Gottenberg JE, et al. JAMA 2014

Disclosure: P. M. DURET, None; N. MEYER, None; A. SARAUX, None; V. DEVAUCHELLE-PENSEC, Roche-Chugai provided me tocilizumab for the SEMAPHORER study, 2; J. SIBILIA, None; R. SEROR, None; V. LE-GUERN, None; C. LARROCHE, None; A. PERDRIGER, None; X. MARIETTE, None; J. E. GOTTENBERG, BMS, Gilead, Medimune,Pfzer SanofiAventis, Roche, Ucb, 2.

Total Body Water Correlates with Ocular Sicca Symptoms in Primary SjöGren’s Syndrome

Gabriela Hernandez-Molina1, Paloma Almeda-Valdés2, Guadalupe López-Carrasco2, Miguel Astudillo-Angel1, Victor Zamora-Legoff3, Carlos Aguilar-Salinas4 and Ivette Cruz-Bautista5, 1Immunology and Rheumatology, Instituto Nacional de Ciencias Medicas y Nutricion SZ, Mexico City, Mexico, 2Endocrinology, Instituto Nacional de Ciencias Medicas y Nutricion SZ, Mexico City, Mexico, 3Rheumatology and Immunology, Instituto Nacional de Ciencias Medicas y Nutricion SZ, Mexico D.F., Mexico, 4Endocrinology, Instituto Nacional de Ciencias Medicas y Nutricion SZ, Mexico D.F., Mexico, 5Instituto Nacional de Ciencias Medicas y Nutricion SZ, Mexico City, Mexico

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Sjögren's Syndrome Poster II: Clinical Research
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Patients with primary Sjögrens’ syndrome (PSS) suffer from severe alterations in both the quality and quantity of saliva and tears. Body water represents around 50-55% of the body weight. Tears contain 98% of water and saliva 99.5%. We evaluated the percentage of total body water (TBW) among patients with PSS assessed its correlation with the severity of sicca symptoms.

Methods: We included 85 patients with PSS and 85 non-diabetic controls matched by gender, age (±3 years) and body mass index (±1kg/m²) (BMI). We assessed the Schirmer-I test, non-stimulated whole salivary flow (NSWSF) and ocular staining. We evaluated ocular as well as oral symptoms during the past 15 days, using for each symptom, a VAS scale (0-10, a higher score implies worst symptoms). We obtained the TBW percentage with a bioelectric impedance analysis (BIA-SECA-514, Hamburgo).

Results: 80% were women, mean age 54.8±13.7 years and mean disease duration 11.5±7.52 years. The percentage of TBW was similar among patients and controls (PSS 46.85±4.6 vs. 46.9±4.5, p=0.88). However among the patients, the TBW negatively correlated with age (ρ=-0.25, p=0.02), disease duration (ρ=-0.30, p=0.005), BMI (ρ=-0.78, p<0.001) and the ocular VAS scale (ρ=-0.28, p=0.01), but not with the NSWSF or the oral VAS scale. When we compared the patients in the 25% percentile (group with the lowest % of water) vs. the remaining patients, the former group was older (56.6±8.1 vs. 54±14.2, p=0.02), with longer disease duration (12.4±5.9 vs. 10.8±7.12, p=0.03), lower scores at the Schirmer test (1 (range 0-8) vs. 2 (range 0-9), p=0.01), higher BMI (31.1±5.1 vs. 23.7±2.9, p=0.001) as well as with higher ocular VAS scores (8.3±1.4 vs. 6.7±2.5, p=0.007). At the linear regression analysis, the variables that remained associated with the TBW were disease duration (b -0.22, p=0.001), BMI (b -0.76, p<0.001) and the ocular VAS scale (b-0.15, p<0.001).

Conclusion: Patients with PSS had similar TBW percentages than controls. However among PSS patients, the TBW had a negative correlation with the intensity of ocular symptoms independently of disease duration, age and BMI.

Disclosure: G. Hernandez-Molina, None; P. Almeda-Valdés, None; G. López-Carrasco, None; M. Astudillo-Angel, None; V. Zamora-Legoff, None; C. Aguilar-Salinas, None; I. Cruz-Bautista, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/total-body-water-correlates-with-ocular-sicca-symptoms-in-primary-sjogrens-syndrome

Abstract Number: 1493

Characteristics of Korean Primary Sjogren’s Syndrome and Comparison of 3 Different Classification Criteria for Primary Sjogren’s Syndrome: Data from Korean Kiss Cohort

Ji-Won Kim1, Jennifer Lee2, Yeon-Sik Hong3, Sung-Hwan Park2 and Ji Hyeon Ju2, 1Medicine, Division of Rheumatology, Department of Internal Medicine, Seoul St. Mary’s Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea,
SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Sjögren's Syndrome Poster II: Clinical Research
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The objective of this study is to introduce the clinical and laboratory characteristics of Korean primary Sjogren’s syndrome (pSS) patients enrolled in Korean Initiative of Sjogren’s Syndrome (KISS). We also sought to compare the performance of newly proposed 2016 American College of Rheumatology (ACR)/European League-Against Rheumatism (EULAR) criteria to 2002 American-European Consensus Group (AECG) and 2012 ACR classification criteria for primary pSS in a well characterized registry.

Methods: Patients with pSS from 12 university affiliated hospitals in Korea were enrolled from Oct 2013 to JAN 2017. The patients were diagnosed with pSS by either fulfilling 2002 AECG or 2012 ACR classification criteria. Data of clinical manifestations and various laboratory findings were obtained.

Results: Data at inclusion were available in 458 patients. The mean age was 51.9 ± 11.8 years. Four hundred fifty patients (98.3%) were female. Mean disease duration was 33.9 ± 46.7 months. Most common extraglandular manifestation was arthralgia (47.8%) followed by Raynaud’s phenomenon (15.7%) and lymphadenopathy (13.5%). Median [interquartile range] ESSDAI and ESSPRI was 2 [0-5], 5 [4-6.7], respectively. Among 458 patients, 328 patients had sufficient data to determine the fulfillment of each criteria. All three criteria were met by 307 patients. Among 3 patients by whom 2016 ACR/EULAR criteria were not met, one 2002 AECG+ 2012 ACR+ had negative anti Ro or La while positive antinuclear antibody and rheumatoid factor with more than 3 ocular staining score. Two 2002 AECG+ 2012 ACR- showed no ocular sign and negative anti Ro or La while had positive focus score. Ninety-six patients had results of all items in 2016 criteria, 95 met the criteria.

Conclusion: We successfully established a nationwide pSS registry in Korea, which represents the characteristics of Korean pSS patients. The newly proposed 2016 ACR/EULAR criteria were met by most of the patients diagnosed with pSS according to previous criteria.

Disclosure: J. W. Kim, None; J. Lee, None; Y. S. Hong, None; S. H. Park, None; J. H. Ju, None.

Abstract Number: 1494

Validation of New Criteria in “The Guidance for Diagnosis of Sjögren’s Syndrome in Pediatric Patients”

Minako Tomiita1, Ichiro Kobayashi2, Yuzaburo Inoue3, Nami Okamoto4, Naomi Iwata5, Yukiko Nonaka6, Ryoki Hara7, Hiroaki Umebayashi8, Yasuhiro Itoh9 and Masaaki Mori10, 1Department of Allergy and Rheumatology, Chiba Children's Hospital, Chiba, Japan, 2Department of Allergy and Rheumatology, Chiba Children’s Hospital, Sapporo, Japan, 3Department of Pediatrics, Chiba University Graduate School of Medicine, Chiba, Japan, 4Pediatrics, Graduate School of Medicine, Osaka Medical College, Takatsuki, Japan, 5Department of Immunology and Infectious Diseases, Aichi Children's Health and Medical Center, Obu, Japan, 6Department of Pediatrics, Kagoshima University Graduate School of Medical and Dental Sciences, Kagoshima, Japan, Kagoshima, Japan, 7Department of Pediatrics, Yokohama City University, Graduate School of Medicine, Yokohama, Japan, 8Department of Rheumatics, Miyagi Children’s Hospital, Sendai, Japan, 9Department of Pediatrics, Nippon Medical School, Tokyo, Japan, 10Department of Lifetime Clinical Immunology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan

First publication: September 18, 2017
Background/Purpose: Sjögren’s syndrome (SS) has been thought rare during pediatric age. Because patients in this age group lack sicca symptoms, the diagnosis of SS is often difficult by currently available diagnostic or classification criteria, and accordingly needs new criteria. Japanese Pediatric Sjögren’s syndrome Study Group has developed new criteria for diagnosis of SS in pediatric patients (Table 1,2). This criteria has been approved by both the board of the Pediatric Rheumatology Association of Japan and the board of the Japanese Society for Sjögren’s syndrome. In this criteria, patients are classified into 5 groups: definite, probable, possible, need follow-up or non-SS. In the present study, we compared the sensitivity of our criteria with 4 major criteria, and evaluated which criteria is most suitable for identifying SS patients in the early stage.

Methods: We enrolled 41 pediatric patients who were diagnosed as having SS with unanimity by 10 pediatric rheumatologists. They were categorized into primary SS (pSS), secondary SS (sSS) and primary to secondary SS (psSS), which was diagnosed as primary SS at diagnosis but developed other collagen diseases during follow-up. We classified those patients into 5 groups according to our criteria, and examined whether each patient fulfilled the major criteria: revised American-European Consensus Group classification criteria (AECG), the revised Japanese diagnostic criteria (JPN), ACR classification criteria (ACR), American College of Rheumatology/European League Against Rheumatism Classification Criteria for primary Sjögren’s syndrome (A/E).

Results: The numbers of patients were as follows: pSS 25, sSS 11 and psSS 5. According to our criteria, patients were classified into definite 33, probable 2 or possible 6 at the first visit, and 38, 3 or 0 at the last visit. No patient was diagnosed as non-SS. In the other 4 criteria, the most sensitive was JPN, followed by A/E and ACR among all patients group (Table 3). However, even by using JPN criteria, there was 12% of pSS patients diagnosed as non-SS at the last visit.

Conclusion: Our new criteria is useful for diagnosis of pediatric SS, and make it possible to recognize SS-associated complications at an early stage.

Table 1: Scoring
<table>
<thead>
<tr>
<th>Glandular score</th>
<th>Salivary gland</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labial salivary gland biopsy</td>
<td>1 (&lt;1 focus / 4mm²), 2 (≥1 focus / 4mm²)</td>
<td></td>
</tr>
<tr>
<td>Sialography (conventional or MRI)</td>
<td>2 (Rubin-Holt stage ≥1)</td>
<td></td>
</tr>
<tr>
<td>Salivary scintigraphy</td>
<td>1 (Deceased in uptake or secretion)</td>
<td></td>
</tr>
<tr>
<td>Decreased salivary flow (counted if at least one other test is positive)</td>
<td>1 (Saxon test ≤ 2.0g / 2min, or Salivary flow rate ≤ 1.5ml / 15min, or Gum test ≤ 10ml / 10min)</td>
<td></td>
</tr>
<tr>
<td>Lacrimal gland</td>
<td>2 (Schirmer test &lt; 5mm/5min and Rose-Bengal test van Bijsterveld score ≥3, or Schirmer test &lt; 5mm/5min and fluorescein test (+), or ACR score ≥3)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Classification

<table>
<thead>
<tr>
<th>Serological score</th>
<th>Glandular score</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥6</td>
<td>≥2</td>
</tr>
<tr>
<td>5</td>
<td>Probable</td>
</tr>
<tr>
<td>4</td>
<td>Probable</td>
</tr>
<tr>
<td>3</td>
<td>Probable</td>
</tr>
<tr>
<td>2</td>
<td>Probable</td>
</tr>
<tr>
<td>1</td>
<td>Possible</td>
</tr>
<tr>
<td>0</td>
<td>Need follow-up</td>
</tr>
</tbody>
</table>

Table 3: Sensitivity of each criteria
<table>
<thead>
<tr>
<th></th>
<th>1st visit</th>
<th></th>
<th></th>
<th>Last visit</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>pSS</td>
<td>sSS</td>
<td>psSS</td>
<td>pSS</td>
<td>sSS</td>
<td>psSS</td>
</tr>
<tr>
<td>AECG fulfilled</td>
<td>20 (%)</td>
<td>18.2</td>
<td>20</td>
<td>36</td>
<td>36.4</td>
<td>20</td>
</tr>
<tr>
<td>AECG (objective items) fulfilled</td>
<td>28</td>
<td>-</td>
<td>40</td>
<td>40</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>JPN fulfilled</td>
<td>72</td>
<td>90.9</td>
<td>100</td>
<td>88</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>ACR fulfilled</td>
<td>52</td>
<td>72.7</td>
<td>100</td>
<td>72</td>
<td>72.7</td>
<td>100</td>
</tr>
<tr>
<td>A/E fulfilled</td>
<td>60</td>
<td>-</td>
<td>100</td>
<td>76</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Our criteria</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Definite</td>
<td>72</td>
<td>90.9</td>
<td>100</td>
<td>88</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Probable</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>12</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Possible</td>
<td>20</td>
<td>9.1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Disclosure: M. Tomiita, None; I. Kobayashi, None; Y. Inoue, None; N. Okamoto, None; N. Iwata, None; Y. Nonaka, None; R. Hara, None; H. Umebayashi, None; Y. Itoh, None; M. Mori, None.


Abstract Number: 1495

Longitudinal Changes in EULAR Sjögren’s Syndrome Patient Reported Index in Routine Clinical Practice

Ji Hyoun Kim¹, You-Jung Ha², Eun Ha Kang², Yeong Wook Song³,¹ and Yun Jong Lee⁵, ¹Division of Rheumatology, Department of Internal Medicine, Seoul National University Bundang Hospital, Division of Rheumatology, Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam-si, Korea, Republic of (South), ²Division of Rheumatology, Department of Internal Medicine, Division of Rheumatology, Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, Korea, Republic of (South), ³WCU Department of Molecular Medicine and Biopharmaceutical Sciences, Medical Research Institute, Seoul National University College of Medicine, Seoul, Korea, Republic of (South), ⁴Department of Molecular Medicine and Biopharmaceutical Sciences, Graduate School of Convergence Science and Technology, and College of Medicine, Seoul National University, Seoul, Korea, Republic of (South), ⁵Department of Internal Medicine, Division of Rheumatology, Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam-si, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Sjögren’s Syndrome Poster II: Clinical Research
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: This study aimed to investigate the longitudinal changes in EULAR Sjögren’s Syndrome Patient Reported Index (ESSPRI) and to study clinical features associated with favorable ESSPRI changes in Korean patients with primary Sjögren’s syndrome (pSS).

Methods:

At baseline and after a median 6.6 [interquartile range, 4.9–8.4] years, 41 pSS patients were evaluated through ESSPRI, EULAR Sjögren's syndrome disease activity index (ESSDAI), EULAR Sicca Score (ESS), health-related quality of life (HRQOL) questionnaires (SF-36), Xerostomia Inventory (XI), and visual analog scale (VAS) for exocrine and extra-exocrine symptoms. Also, we collected data for used medications and laboratory results. Favorable outcome (F) group was defined as patients who had improved ESSPRI (from baseline ESSPRI ≥5 to follow-up ESSPRI <5) or the maintenance of satisfactory symptom state (ESSPRI <5) and unfavorable (UF) group was those with worsening of ESSPRI (from baseline ESSPRI <5 to follow-up ESSPRI ≥5) or the maintenance of unsatisfactory symptom state (ESSPRI ≥5).

Results: During the follow-up period, ESSPRI was significantly increased from 4.11 [3.22–5.56] to 5.33 [3.50–6.67] (p < 0.05) and SF-36 scores were not changed in pSS patients even though XI scores (p=0.01) and oral dryness (p<0.05) were significantly
decreased in the total enrolled patients. Hyper-gamma-globulinemia (p<0.001) and anemia (p<0.05) were improved but ESSDAI was not changed. When compared between F (n=17) and UF (n=24) group, F group exhibited significantly lower VAS levels of oral or eye dryness (both p<0.05), XI scores (p<0.05), and ESS scores (p<0.00) than UF group at baseline. Also, F group had more patients with Raynaud's phenomenon (19.5% versus 9.8%, p<0.05). In spite that baseline physical component summary (PCS) scores were comparable and F group was less likely to take cholinergic (12.2% versus 46.3%, p=0.001) or immuno-modulatory (7.3% versus 31.7%, p<0.05) drugs, F group showed significantly better PCS scores at final follow-up than UF group (p < 0.001).

Conclusion:

In routine clinical practice, most values for subjective or objective assessments including ESSPRI and HRQOL were not significantly improved during the follow up periods in pSS patients. pSS patients with less severe sicca symptom are more likely to have a favorable course, based on ESSPRI status.

Disclosure: J. H. Kim, None; Y. J. Ha, None; E. H. Kang, None; Y. W. Song, None; Y. J. Lee, None.

Abstract Number: 1496

The Performance of Different Classification Criteria in Patients with Primary Sjögren’s Syndrome and Analysis of Their Contribution for Definitive Diagnosis, When Either Criteria Used Alone or in Combination

Zehra Kosuva Ozturk, Gokce Kenar, Handan Yarkan, Berrin Zengin, Гercek Can, Fatos Onen and Merih Birlik

1internal medicine, dokuz eyulu university, izmir, Turkey, 2Rheumatology, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey, 3Rheumatology, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey, 4Rheumatology, Dokuz Eylul University Faculty of Medicine, izmir, Turkey

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Sjögren's Syndrome Poster II: Clinical Research
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Many classification criteria sets have for primary Sjögren's Syndrome (pSS). We aimed to compare the performance of 3 classification criteria sets for pSS, to determine the agreement between each other and expert opinion and to investigate diagnostic contribution with any combined use of these criteria. For those assessments, American-European Consensus Criteria (AECG), American Collage of Rheumatology (ACR) / Sjögren International Clinical Alliance (SICCA) criteria and L.S. Martin et.al. criteria named Mathematical model (M.model) had chosen.

Methods: 86 patients(F:96%,mean age:51.7±11.8) with the diagnosis of pSS were enrolled to the study. Expert opinion had been taken as gold standard for pSS diagnosis. Patients were questioned for eye/mouth dryness. Antinuclear antibody, complement, anti-Ro-La, serum protein electrophoresis, rheumatoid factor, break-up time (BUT) and Schirmer, minor salivary gland biopsy results were analysed cautiously. The aforementioned criteria sets, were implemented to assess the classification. The percentage of exact agreement and Kappa test was calculated.

Results: Number of patients classified as pSS according to ACR/SICCA, AECG and M.model criteria were 75 (87%), 63 (73%) and 58(67%) respectively. 9 patients (10%) did not fulfill any of these 3 criteria but they were diagnosed as pSS according to expert opinion (Figure). The Kappa test was moderate between the ACR/SICCA and AECG criteria and slightly low between the M.model with the AECG and ACR/SICCA criteria (Table 1). According to our proposed combination model, number of patients classified as pSS, either AECG or M.model was 74; either AECG or ACR/SICCA model was 76; either ACR/SICCA or M.model was 77 (Table 2). In the triple combination of our model, if all 3 criteria used concomitantly, only 46 of patients fulfill the criteria simultaneously; however if any of 3 criteria sets used 77 patients fulfill as pSS.

Conclusion: In this study, ACR/SICCA classification criteria for pSS was found the most compatible criteria set with expert opinion.
Table 1. The agreement between three pSS classification criteria sets (%, Kappa test)

<table>
<thead>
<tr>
<th></th>
<th>AECG</th>
<th>ACR/SICCA</th>
<th>M.MODEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>AECG</td>
<td>%83 K:0.50</td>
<td>%68 K:0.25</td>
<td></td>
</tr>
<tr>
<td>ACR/SICCA</td>
<td>%83 K:0.50</td>
<td>%75 K:0.34</td>
<td></td>
</tr>
<tr>
<td>M.MODEL</td>
<td>%68 K:0.25</td>
<td>%75 K:0.34</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Number of patients fulfilling classification criteria

<table>
<thead>
<tr>
<th>Classification criteria (n) (%)</th>
<th>According to 1 criteria</th>
<th>According to either of 2 criteria</th>
<th>According to either of 3 criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ACR/SICCA</td>
<td>AECG or ACR/SICCA</td>
<td>AECG or ACR/SICCA or M.model</td>
</tr>
<tr>
<td></td>
<td>75 87.2</td>
<td>77 89.5</td>
<td>77 89.5</td>
</tr>
<tr>
<td></td>
<td>63 73.2</td>
<td>76 88.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>58 67.4</td>
<td>74 86</td>
<td></td>
</tr>
</tbody>
</table>

Disclosure: Z. Kosuva Ozturk, None; G. Kenar, None; H. Yarkan, None; B. Zengin, None; G. Can, None; F. Onen, None; M. Birlik, None.


Abstract Number: 1497

Clinical and Laboratory Features of Patients with Focal Lymphocytic Sialadenitis on Minor Salivary Gland Biopsy for Sicca Symptoms: A 16 Year Experience

Bibi Ayesha1, Ruth Fernandez-Ruiz2, Devin Shrock3, Rebecca Tuetken4, Scott Lieberman5, Elizabeth Field6 and Namrata Singh7,  
1Internal Medicine and Division of Rheumatology, MD, BRONX, NY; 2Internal Medicine, University of Iowa Hospitals and Clinics, Iowa City, IA; 3Pathology, MD, Iowa, IA, 4MD, PhD, Iowa, IA; 5Division of Rheumatology, Stead Family Department of Pediatrics, Carver College of Medicine, University of Iowa, Iowa City, IA; 6Iowa City VA, Iowa City, IA; 7VA Nebraska-Western Iowa Health Care System and University of Iowa, Omaha, IA

First publication: September 18, 2017

SESSION INFORMATION
Background/Purpose: Focal lymphocytic sialadenitis (FLS) on minor salivary gland biopsy (MSGB) is one of the classification criteria for Sjögren’s syndrome (SS). As no diagnostic criteria exist, there is a need for timely diagnosis of seronegative patients (SSA and SSB antibody negative), to allow earlier intervention and prevent end-organ damage. There are only a few studies on how seronegative patients with FLS on MSGB differ clinically from seropositive patients (SSA and/or SSB antibody positive). Therefore, the objective of our study was to compare the clinical and laboratory features of patients with and without autoantibodies (anti-SSA and/or anti-SSB) among those with FLS on MSGB. As a secondary objective, we compared the clinical and laboratory features of those with and without FLS on MSGB among the seronegative patients only.

Methods: Cases > 18 years old with a MSGB performed at the University of Iowa Hospital and Clinics between 1/1/2000-12/31/2016 were identified, excluded patients with incomplete clinical and laboratory data. Then data was extracted by retrospective chart review. Fisher’s exact test or chi-square test was used to compare categorical variables between the groups; student’s t-test was used for comparison of continuous variables.

Results: During the study period 230 patients had MSGB done for sicca symptoms, 51 patients were excluded due to incomplete clinical data. FLS on MSGB was found in 133 patients, 27% (37/133) were seropositive and 72% (96/133) were seronegative. Dry eyes, dry mouth, fibromyalgia and depression, predominated as statistically significant clinical features in the seronegative group compared to the seropositive group (Table1 – Among all MSGB positive patients, comparison of the clinical and laboratory features of those with and without SSA antibody and/or SSB antibody). Symptomatic seronegative patients who underwent MSGB were 137, and no FLS on MSGB was found in 41 patients. Smoking predominated as a statistically significant variable (p=0.0003) in the seronegative patients with no FLS on biopsy, whereas seronegative patients with a positive biopsy tended to be older and have more sicca symptoms.

Conclusion: Identifying the subset of symptomatic SS patients, who are seronegative is challenging. When patients have sicca symptoms, associated with other clinical features like fatigue, inflammatory arthritis, peripheral nervous system clinical symptoms; with no serological markers, these patients should be considered for a further evaluation by MSGB. Smoking can also cause sicca symptoms with no FLS on MSGB, this should be considered while evaluating the patients with sicca symptoms.

Disclosure: B. Ayesha, None; R. Fernandez-Ruiz, None; D. Shrock, None; R. Tuetken, None; S. Lieberman, None; E. Field, None; N. Singh, None.


Abstract Number: 1498
Long-Term Cohort of Patients with a Clinical Diagnosis of Sjogren’s Syndrome: Activity Index and Patient Reported Outcome Performance

Anna Viola Taulaigo¹, Maria Francisca Moraes-Fontes¹, Melissa Fernandes², Vera Bernardino² and Tiago Ramires³, ¹Unidade de Doenças Auto-imunes, Hospital Curry Cabral, Centro Hospitalar de Lisboa Central, Lisboa, Portugal, ²Unidade de Doenças Auto-imunes, Hospital Curry Cabral, Centro Hospitalar de Lisboa Central, Lisboa, Portugal, ³Unidade de Doenças Auto-imunes, Hospital Curry Cabral, Centro Hospitalar de Lisboa Central, Lisboa, Portugal; Serviço de Medicina Interna, Hospital Espírito Santo, Évora, Portugal, Lisbon, Portugal

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Sjögren’s Syndrome Poster II: Clinical Research
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: There have been three classification proposals for Sjögren’s Syndrome (SS) over the past 15 years (1-3). The 2016 criteria require a diagnostic work-up which includes at least evaluation of focus score (FS) in minor salivary gland (MSG) biopsy, anti-SSA antibodies, Schirmer’s test, unstimulated whole salivary flow (UWS), and ocular staining score (OSS), the last two tests being unavailable at our centre. Patients have to score ≥4 points to fulfill the ACR-EULAR criteria for SS (3 points for FS≥1 and antiSSA positivity, 1 point for UWS ≤0.1 ml/min, Schirmer ≤5 mm/5min and OSS ≥59). In some of our longstanding patients, MSG biopsies performed at disease onset scored negative and have not been repeated, either because they are judged to be unnecessary by the attending physician or due to patient refusal. While ESSDAI reflects SS biological activity, ESSPRI is claimed to be disease-specific for SS (4) and both scores have been validated (5). The aim of this study was to investigate EULAR Sjögren Syndrome Disease Activity Index (ESSDAI) and EULAR Sjögren Syndrome Patient Reported Outcome (ESSPRI) in a monocentric sicca syndrome cohort, all of whom have a working clinical diagnosis of SS.

Methods: Cross sectional study carried out at our AID Unit from January to December 2016. Inclusion criteria: 1) sicca syndrome symptoms as main complaint and clinical diagnosis of SS; 2) absence of any other known autoimmune disease (AID) at inclusion time; 3) follow up in AID Unit of at least 1 year. Demographic and clinical features, previous diagnostic investigation, ongoing therapeutics and fulfillment of sequential classification criteria were recorded. ESSDAI activity (Low <5, moderate 5 – 13, high ≥14) and ESSPRI-Patient acceptable symptom state (PASS < 5 points) (5) were performed once in each patient. Parameters were analyzed according to disease duration. Univariate statistical analysis was performed using the Wilcoxon Mann-Whitney test for non-parametric distributed data.

Results: Overall, between January and May 2017, 45 consecutive patients were included, of which 18 (40%) met 2002; 7 (16%) 2012; and 15 (33%) the 2016 SS classification criteria. Median age was 63 years (y), IQR 57-72, range 29-83; 100% female; median disease duration was 12 y, IQR 8-19; range 2-36; median ESSDAI and ESSPRI were, respectively 0, IQR 0-2; range 0-17 and 5, IQR 3,7-7, range 0 – 10. Two patients were diagnosed with lymphoma, one prior to enrolling time. Disease duration was greater than 10 y in 29 (64%) and smaller or equal to 10 y in 16 (35%) patients. Approximately half of the patients in each group were on hydroxychloroquine (200 mg/day) and ≤5 mg/day of prednisolone. Both groups presented low biological activity (only 2 patients had a score above 14, one due to renal and another due to lung involvement). There were no statistically significant demographic or clinical differences according to disease duration.

Conclusion: Regardless of disease duration, patients presented low biological activity but remained symptomatic with a PASS ≥ 5. ESSDAI and ESSPRI provide important information and therapeutic stratification, particularly as regards the need for new therapies that provide symptomatic relief.

Disclosure: A. V. Taulaigo, None; M. F. Moraes-Fontes, None; M. Fernandes, None; V. Bernardino, None; T. Ramires, None.


Abstract Number: 1499

Major Salivary Gland Ultrasonography Bed-Side and Still Image Scoring – a Pilot Comparison in Juvenile Sjögren’s Syndrome

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Sjögren's Syndrome Poster II: Clinical Research
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Adding major salivary gland ultrasonography (SGUS) improves the diagnostics of primary Sjögren’s syndrome (pSS). Juvenile Sjögren’s syndrome (jSS) is a rare, poorly defined disease. With regard to the late onset of sicca-symptoms and current lack of diagnostic criteria, a non-invasive diagnostic method is warranted for jSS. The aim of this study was to evaluate SGUS bed-side scoring (realtime) and still/2D-image scoring, and to investigate whether imaging findings differ in the parotid and the submandibular glands.

Methods:
Patients were recruited from Brazil (n=40), Norway (n=11), and Spain (n=5) in the period 2016-2017. SGUS of the parotid and submandibular glands had been performed bed-side in all patients, using linear high-frequency transducers (6-15 MHz), and glands characterized as normal or SS-like. Still/2D-images from 26 patients were available for re-evaluation by the same experts (DSH and MVJ).

Results:
Mean age at diagnosis was 12.1 years (range 4-17), with first symptoms at 10.1 years (range 3-17). Time from onset of symptoms until diagnosis was 1.8 years (range -2-8). Oral and ocular symptoms were reported by 16/26 and 18/26 patients, respectively. Reduced tear-production was detected in 9/25 patients, and hyposalivation in 11/26 patients. Focus score was available in 19/20 cases. Anti-Ro/SSA-titer was elevated in 23/26, and anti-La/SSB in 12/26. AECG and ACR/EULAR diagnostic criteria was fulfilled by 21/26 patients. The female:male ratio was 23:3.

When comparing the total SGUS score, pathological changes were noted in 18/26 patients using realtime images, as compared to 24/26 using still/2D-images (p=0.027, κ=0.316).

In the realtime images SGUS pathological changes were detected in 16/26 parotid glands (15/16 in both right and left gland, p<0.001, κ=0.920), and 15/26 submandibular glands (14/15 in both right and left gland, p<0.001, κ=0.842). In four cases, pathological changes were detected only in the parotid glands (n=2) or only in the submandibular glands (n=2).

In the still/2D-images pathological changes were detected in 19/26 parotid glands (17/19 in both right and left gland, p<0.001, κ=0.821), and 21/26 submandibular glands (18/21 in both right and left gland, p=0.029, κ=0.425).

When comparing the glands separately, pathological changes were reported in 2D/still images of glands that had been diagnosed as normal using realtime images; 3/10 cases in the right parotid (p=0.001, κ=0.742), 2/11 cases in the left parotid (p=0.001, κ=0.839), 6/11 cases in the right submandibular (p=0.004, κ=0.490) and 5/11 cases in the left submandibular (p=0.001, κ=0.581).

Conclusion:
Although containing a limited number of patients, our study highlights important challenges in the clinical applications of SGUS. Notable differences were observed when comparing still/2D-images to realtime evaluation, especially in cases with normal-appearing
Longitudinal Analysis of Different Therapeutic Strategies in Patients with Primary Sjögren’s Syndrome

Kristen Davies¹, Kamran Mirza¹, Jessica Tam², Marian Regan³, Saravanan Vadivelu⁴, Gavin Clunie⁵, Jacqueline Andrews⁶, Elizabeth Price⁷, Steve Young-Min⁸, Ian Giles⁹, Bhaskar Dasgupta¹⁰, Cathy Lawson¹¹, Nagui Gendi¹², Neil J. McHugh¹³, Michele Bombardieri¹⁴, Costantino Pitzalis¹⁴, Nurhan Sutcliffe¹⁴, Simon Bowman¹⁵, Dennis Lendrem¹⁶,¹⁷ and Wan-Fai Ng²,¹⁸ ¹Institute of Cellular Medicine, Musculoskeletal Research Group, Institute of Cellular Medicine, Newcastle University, Newcastle-Upon-Tyne, UK, Newcastle-Upon-Tyne, United Kingdom, ²Musculoskeletal Research Group, Institute of Cellular Medicine, Newcastle University, Newcastle-Upon-Tyne, UK, Newcastle-Upon-Tyne, United Kingdom, ³Royal Derby Hospital, Derby, UK, Derby, United Kingdom, ⁴Queen Elizabeth Hospital, Gateshead, UK, Gateshead, United Kingdom, ⁵Ipswich Hospital NHS Trust, Ipswich, UK, Ipswich, United Kingdom, ⁶Leeds Teaching Hospitals NHS Trust, Leeds, UK, Leeds, United Kingdom, ⁷Great Western Hospital, Swindon, UK, Swindon, United Kingdom, ⁸Queen Alexander Hospital, Portsmouth, UK, Portsmouth, United Kingdom, ⁹Centre for Rheumatology, University College London, Centre for Rheumatology, University College London, UK, London, United Kingdom, ¹⁰Rheumatology, Southend University Hospital NHS Foundation Trust, Southend, UK, Westcliff-on-Sea, United Kingdom, ¹¹Harrogate District Hospital, Harrogate, UK, Harrogate, United Kingdom, ¹²Basildon and Thurrock University Hospital, Basildon, UK, Basildon, United Kingdom, ¹³Royal National Hospital for Rheumatic Diseases, Bath, UK, Bath, United Kingdom, ¹⁴Barts Health NHS Trust & Barts and the London School of Medicine & Dentistry, London, UK, London, United Kingdom, ¹⁵Department of Rheumatology, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK, Birmingham, United Kingdom, ¹⁶Musculoskeletal Research Group, Institute of Cellular Medicine, Newcastle University, Newcastle-Upon-Tyne, UK, Newcastle-Upon-Tyne, United Kingdom, ¹⁷Newcastle-Upon-Tyne Hospitals NHS Foundation Trust, Newcastle-Upon-Tyne, UK, Newcastle, United Kingdom, ¹⁸Newcastle-Upon-Tyne Hospitals NHS Foundation Trust, Newcastle-Upon-Tyne, UK, Newcastle-Upon-Tyne, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Sjögren's Syndrome Poster II: Clinical Research
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Primary Sjögren’s syndrome (pSS) is a systemic autoimmune rheumatic disease characterised by sicca features and systemic manifestations such as pain and fatigue. The classic therapeutic approach for pSS is based upon symptomatic treatment of sicca manifestations with immunosuppression for more severe disease. To date, there has been no longitudinal analysis of medication use for patients with pSS.

Methods: We used data from the United Kingdom Primary Sjögren’s Syndrome Registry to identify patients with sufficient follow-up data including their current medications. Patients who were not on medication at visit 1 but who were on medication at visit 2 were included. Those patients who were not on medication at visit 1 or visit 2 were included for comparison. The medication regimes were group into four categories: Hydroxychloroquine (HCQ), Immunosuppression, NSAIDs and Analgesics. The differences in characteristics and patient-reported scores between each group were evaluated by analysis of variance. Paired data between the two visits was evaluated by a paired t-test.

Results: 98 patients had sufficient data to be included. The median time between visits was 4 years and was not different between groups (p=0.48). Patient-reported scores at visit 1 revealed significant differences in physical fatigue (p=0.017) and pain (p=0.049)
between the groups. Patients treated with HCQ, Immunosuppression, NSAIDs or Analgesia (N=87) showed a worsening of physical and mental fatigue, pain and dryness whereas the inverse was true for those patients not treated (N=11). In particular, patients who were started on analgesics reported higher physical fatigue (p=0.03), mental fatigue (p=0.005) and pain (p=0.16) at visit 2. Haematological analysis reveal that patients treated with HCQ had a lower ESR (p=0.045), IgG (p=0.0044) and IgM (p=0.0031) whereas those treated with other immunosuppressives only had a lower IgM (p=0.0035).

**Conclusion:** Whilst HCQ appears to reduce the clinical parameters associated with active disease in patients with pSS, it was not accompanied by improvement in patient-reported symptoms at visit 2. Symptomatic treatments in the form of NSAIDs or analgesics appear to be associated with worsening patient-reported scores whereas those not treated with any medication seem to improve at visit 2. Despite the limitations with this analysis our data suggest that HCQ, immunosuppressive therapies and symptomatic medications are ineffective in improving patients’ symptoms.

<table>
<thead>
<tr>
<th>Regime</th>
<th>Visit 1 (Mean)</th>
<th>Visit 2 (Mean)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HCQ (N=20)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical Fatigue</td>
<td>3.40</td>
<td>3.65</td>
<td>0.41</td>
</tr>
<tr>
<td>Mental Fatigue</td>
<td>2.83</td>
<td>2.98</td>
<td>0.69</td>
</tr>
<tr>
<td>Pain</td>
<td>3.5</td>
<td>4.05</td>
<td>0.13</td>
</tr>
<tr>
<td>Dryness</td>
<td>3.70</td>
<td>3.85</td>
<td>0.74</td>
</tr>
<tr>
<td><strong>Immunosuppression (N=19)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical Fatigue</td>
<td>4.07</td>
<td>4.58</td>
<td>0.15</td>
</tr>
<tr>
<td>Mental Fatigue</td>
<td>2.84</td>
<td>2.97</td>
<td>0.74</td>
</tr>
<tr>
<td>Pain</td>
<td>4.21</td>
<td>4.68</td>
<td>0.24</td>
</tr>
<tr>
<td>Dryness</td>
<td>4.32</td>
<td>5.00</td>
<td>0.097</td>
</tr>
<tr>
<td><strong>NSAIDs (N=15)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical Fatigue</td>
<td>4.21</td>
<td>4.46</td>
<td>0.33</td>
</tr>
<tr>
<td>Mental Fatigue</td>
<td>3.70</td>
<td>4.13</td>
<td>0.22</td>
</tr>
<tr>
<td>Pain</td>
<td>4.40</td>
<td>4.70</td>
<td>0.43</td>
</tr>
<tr>
<td>Dryness</td>
<td>4.20</td>
<td>4.67</td>
<td>0.15</td>
</tr>
<tr>
<td><strong>Analgesics (N=33)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical Fatigue</td>
<td>3.60</td>
<td>4.20</td>
<td>0.03</td>
</tr>
<tr>
<td>Mental Fatigue</td>
<td>2.91</td>
<td>3.66</td>
<td>0.0051</td>
</tr>
<tr>
<td>Pain</td>
<td>3.94</td>
<td>4.40</td>
<td>0.16</td>
</tr>
<tr>
<td>Dryness</td>
<td>4.09</td>
<td>4.48</td>
<td>0.17</td>
</tr>
<tr>
<td><strong>No medications (N=11)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical Fatigue</td>
<td>2.18</td>
<td>1.78</td>
<td>0.26</td>
</tr>
<tr>
<td>Mental Fatigue</td>
<td>1.81</td>
<td>1.77</td>
<td>0.91</td>
</tr>
<tr>
<td>Pain</td>
<td>2.36</td>
<td>2.09</td>
<td>0.59</td>
</tr>
<tr>
<td>Dryness</td>
<td>2.64</td>
<td>2.18</td>
<td>0.41</td>
</tr>
</tbody>
</table>

Figure 1: Patient Reported Scores at Visit 1 and Visit 2 with p-values determined using the paired t-test.

**Disclosure:** K. Davies, None; K. Mirza, None; J. Tarn, None; M. Regan, None; S. Vadivelu, None; G. Clunie, None; J. Andrews, None; E. Price, None; S. Young-Min, None; I. Giles, None; B. Dasgupta, None; C. Lawson, None; N. Gendi, None; N. J. McHugh, None; M. Bombardieri, GSK, Amgen/MedImmune and UCB, 5; C. Pitzalis, None; N. Sutcliffe, None; S. Bowman, I have consulted in the field of Sjogren's for: AstraZeneca/MedImmune, BMS, Celgene, Eli Lilly, Glenmark, GSK, MTPharma, Novartis, Ono, Takeda, UCB, xtlbio). Roche provided Rituximab for the TRACTISS Study, 5; D. Lendrem, None; W. F. Ng, None.


**Abstract Number:** 1501
Sexual Dysfunction and Vaginal Dryness Are Common in Female Patients with Early, Active Primary Sjögren’s Syndrome

Jolien F. van Nimwegen, Greetje S. van Zuiden, Frans G.M. Kroese, Suzanne Arends and Hendrika Bootsma, Rheumatology and Clinical Immunology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Sjögren's Syndrome Poster II: Clinical Research
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The objective of this study was to evaluate the prevalence of sexual dysfunction and vaginal dryness in female patients with early, active primary Sjögren’s syndrome (pSS), and to explore the association with patient characteristics, symptoms, disease activity, and exocrine gland function.

Methods: Between September 2015 and May 2017, 52 female pSS patients were included in an RCT studying the efficacy and safety of abatacept (NCT02067910). Inclusion criteria were fulfilment of the AECG criteria, EULAR Sjögren Syndrome Disease Activity Index (ESSDAI) ≥5, disease duration ≤7 years and positive salivary gland biopsy. The present analysis concerns data from the baseline visit. ESSDAI, unstimulated whole salivary flow (UWS), stimulated whole salivary flow (SWS), Schirmer’s test, ocular staining score (OSS), immunoglobulin G, and rheumatoid factor were determined. Patients completed a questionnaire including the Female Sexual Function Index (FSFI), EULAR Sjögren Syndrome Patient Reported Index (ESSPRI), numeric rating scale (NRS, range 0-10) for vaginal, ocular and oral dryness, and EuroQol five dimensions questionnaire (EQ-5D). Patients who did not have intercourse due to lack of a sexual partner were excluded from analyses involving the FSFI, as this may cause low FSFI scores while no sexual dysfunctioning is present. Sexual dysfunction was defined as FSFI<26.55\(^1\). Associations between FSFI, vaginal dryness and other clinical parameters were explored using Spearman’s correlation coefficient.

Results: Of the 52 included patients, 26 (50%) were premenopausal. Median vaginal dryness score was 6.0. 32 patients (62%) did not have intercourse in the past four weeks. Reasons for not having intercourse were low sexual desire (n=10), dyspareunia (n=7), lack of a sexual partner (n=7), vaginal dryness (n=4) and other (n=4). Median FSFI score was 14.4. Sexual dysfunction was present in 40 patients (89%). Sexual dysfunction was associated with age, vaginal dryness, and ESSPRI total and pain subdomain (table 1). Vaginal dryness was associated with age, ESSPRI total and dryness subdomain scores, and with ocular and oral dryness. In premenopausal patients, sexual dysfunction was associated with ESSPRI fatigue subdomain (ρ=-0.450, p=0.036) and MFI reduced activity (ρ -0.520, p=0.013). In postmenopausal patients, sexual dysfunction was associated with ESSPRI total (ρ=-0.426, p=0.043) and pain subdomain scores (ρ=-0.459, p=0.027), EQ-5D score (ρ=-0.500, p=0.015), and MFI reduced motivation (ρ=-0.611, p=0.002).

Conclusion: Sexual dysfunction and vaginal dryness are highly prevalent in female patients with early, active pSS, and should be included in the outcome measures of clinical trials. Sexual dysfunction and vaginal dryness are associated with symptoms of pSS in pre- and postmenopausal women, but not with systemic disease activity or salivary and tear gland function.

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Spearman correlation coefficients</th>
<th>FSFI*</th>
<th>NRS vaginal dryness</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median (IQR) or Mean ± SD</td>
<td>ρ</td>
<td>p-value</td>
</tr>
<tr>
<td>Age</td>
<td>48.4 ± 14.3</td>
<td>-0.399</td>
<td>0.007</td>
</tr>
<tr>
<td>Disease duration</td>
<td>2.0 (0.0-4.0)</td>
<td>0.102</td>
<td>NS</td>
</tr>
<tr>
<td>FSFI*</td>
<td>14.4 (5.3-23.2)</td>
<td>-</td>
<td>-0.463</td>
</tr>
<tr>
<td>NRS vaginal dryness</td>
<td>6.0 (4.3-8.0)</td>
<td>-0.463</td>
<td>0.001</td>
</tr>
<tr>
<td>ESSPPI</td>
<td>7.0 (5.4-7.7)</td>
<td>-0.418</td>
<td>0.004</td>
</tr>
<tr>
<td>Dryness</td>
<td>7.0 (6.0-8.0)</td>
<td>-0.161</td>
<td>NS</td>
</tr>
<tr>
<td>Fatigue</td>
<td>7.0 (6.3-8.0)</td>
<td>-0.273</td>
<td>NS</td>
</tr>
<tr>
<td>Pain</td>
<td>7.0 (4.3-8.0)</td>
<td>-0.446</td>
<td>0.001</td>
</tr>
<tr>
<td>NRS ocular dryness</td>
<td>7.0 (5.0-8.0)</td>
<td>-0.140</td>
<td>NS</td>
</tr>
<tr>
<td>NRS oral dryness</td>
<td>7.5 (6.0-8.0)</td>
<td>-0.166</td>
<td>NS</td>
</tr>
<tr>
<td>EQ-5D</td>
<td>0.70 ± 0.15</td>
<td>0.108</td>
<td>NS</td>
</tr>
<tr>
<td>ESSDAI</td>
<td>14.0 (10.0-18.8)</td>
<td>0.158</td>
<td>NS</td>
</tr>
<tr>
<td>Immunoglobulin G</td>
<td>18.5 (13.5-24.6)</td>
<td>0.067</td>
<td>NS</td>
</tr>
<tr>
<td>Rheumatoid factor</td>
<td>24.0 (6.2-67.8)</td>
<td>-0.026</td>
<td>NS</td>
</tr>
<tr>
<td>UWS</td>
<td>0.05 (0.01-0.15)</td>
<td>-0.090</td>
<td>NS</td>
</tr>
<tr>
<td>SWS</td>
<td>0.20 (0.06-0.42)</td>
<td>-0.156</td>
<td>NS</td>
</tr>
<tr>
<td>Schirmer**</td>
<td>1.8 (0.0-11.8)</td>
<td>-0.282</td>
<td>NS</td>
</tr>
<tr>
<td>Ocular staining score**</td>
<td>5.8 (3.6-8.9)</td>
<td>0.259</td>
<td>NS</td>
</tr>
</tbody>
</table>

Higher FSFI scores indicate better sexual function. P values are given for significant correlation coefficients (p≤0.05). *N=45 (excluding 7 patients who did not have sexual intercourse due to lack of a sexual partner). **Mean of right and left eye.

Disclosure: J. F. van Nimwegen, None; G. S. van Zuiden, None; F. G. M. Kroese, None; S. Arends, None; H. Bootsma, None.

Comparison of Classification Criteria for Sjögren’s Syndrome from 2002 and 2016 in an Incident Cohort Diagnosed 2007 to 2011 from Stockholm County Sweden

Mariika Kvarnstrom and Marie Wahren-Herlenius, Unit of Rheumatology, Department of Medicine, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, and Unit of Experimental Rheumatology, Department of Medicine, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Sjögren's Syndrome Poster II: Clinical Research
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Comparison of classification criteria for Sjögren's syndrome from 2002 and 2016 in a 5 year cohort of incident patients diagnosed 2007 to 2011 from Karolinska University Hospital, Stockholm County, Sweden.

The current American-European Consensus Criteria (AECC) from 2002 has been the most widely used and applied all over the world. New classification criteria for Sjögren's Syndrome was published in 2016, designed in collaboration between ACR and EULAR. They are made up of a scoring system in which 4 points are required for classification. The weight/score is as follows:

- Labial salivary gland biopsy (?) with focal lymphocytic sialadenitis and focus score of ≥1 foci/4 mm2 – 3
- Anti-SSA/Ro positive – 3
- Ocular Staining Score ≥5 (or van Bijsterveld score ≥4) in at least 1 eye – 1
- Schirmer’s test ≤5 mm/5 minutes in at least 1 eye – .1
- Unstimulated whole saliva flow rate ≤0.1 ml/minute – 1

We wanted to examine the consistency between the different classification criteria.

Methods:

We compared a cohort of all diagnosed patients with primary Sjögren's syndrome between the years 2007 to 2011 at the Dep. of Rheumatology at Karolinska University Hospital in Stockholm Sweden. Data on the item Ocular Staining Score ≥5 was not available since it is not included in AECC. The cohort consisted of 199 patients all fulfilling the 2002 AECC. Another eight patients did not fulfill the criteria but were regarded as possible Sjögren syndrome under development by the rheumatologist investigating them.

Results:

196 of the 199 pSS patients also fulfilled the new criteria from 2016. The three patients who did not, only had SSB autoantibodies and no positive biopsy. Of eight patients with suspicion of Sjögren under development, three fulfilled
the new criteria.

**Conclusion:**

The classification criteria for Sjögren’s syndrome from 2002 and 2016 are consistent. This study indicates a possibility that the new criteria may be more sensitive early in the disease development, as long as the classification is not based on autoantibody positivity against SSB.

**Disclosure:** M. Kvarnstrom, None; M. Wahren-Herlenius, None.


Abstract Number: 1503

**The Prevalence of Axial Spondyloarthritis in Israel**

Sara Borok Lev-Ran¹, Hagit Sarvagyl-Maman², Victoria Furer³, Sara Pel⁴, Iddo Drukman⁵, Gideon Flusser⁶ and Ori Elhayam⁶, ¹Tel Aviv Sourasky Medical Center and the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel, ²Tel Aviv Sourasky Medical Center and the Sackler Faculty of Medicine, Tel Aviv University, Tel-aviv, Israel, ³Rheumatology, Tel-Aviv Sourasky Medical Center and the Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel, ⁴Rheumatology, Tel-Aviv Sourasky Medical Center and the Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel, ⁵Radiology, Tel Aviv Medical Center, Tel Aviv, Israel, ⁶Rheumatology, Tel Aviv Sourasky Medical Center and the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The concept of axial Spondyloarthritis (SpA) as defined by the ASAS criteria is relatively new. While the prevalence of Ankylosing spondylitis is around 0.5%, the exact prevalence of axial SpA in the general population is unknown. To evaluate the prevalence of axial SpA according to the ASAS classification criteria among the Israeli population of Jewish origin.

**Methods:** The study composed of 3 steps: 1) preliminary screening of the general population based on an internet screening survey of 4000 Israelis of Jewish origin, aged 18-45, which form a representative sample of the general population. Those answering positively to the question of suffering from lower back pain (LBP) for more than 3 months continued to the second step questionnaire. 2) step 2 comprised of 11 questions pertaining to inflammatory back pain (IBP) and other SpA features such as arthritis, enthesitis, uveitis, dactylitis, psoriasis, Crohn's disease or colitis, and family history of SpA. Those who answered positively to at least one of the questions were invited to undergo further evaluation by a rheumatologist. Those who agreed moved to the 3rd step and were invited to the department of rheumatology. 3) the evaluation included a clinical form comprising the SpA features as specified in the ASAS criteria, imaging (X-RAY and MRI of the sacroiliac joints) and laboratory evaluation (CRP and HLA-B27).
**Results:** A total of 4012 people were screened via the internet survey. Of these, 1440 (36%) suffered from LBP for more than 3 months. 467 fulfilled the ASAS criteria for inflammatory back pain (32%) while 30-60% described at least one characteristic of inflammatory back pain, 11% arthralgia/arthritis, 12% dactylitis and 13% enthesitis. Four percent reported uveitis, 3.5% on psoriasis and 2% on Crohn's disease or colitis. 1389 (35%) of them continued to step 2 and 981 (70%) answered positively to at least one of the SpA feature questions and were invited to be examined by a rheumatologist. 417 agreed and 60 kept their appointment. 3 patients were further excluded based on the exclusion criteria. HLA-B27 returned negative in all but one patient. The MRI showed findings compatible with sacroiliitis in 20 patients (active and/or chronic). Fifteen patients complied with the ASAS classification criteria for axial SpA resulting in an estimated prevalence of at least 0.4%.

**Conclusion:** The estimated prevalence of axial SpA is at least 0.4%. Taking into consideration the proportion of patients with IBP (6%), the prevalence is probably much higher and is between 0.4 and at least 1%. Internet screening for IBP may be a useful tool for detection of axial SpA.

**Disclosure:** S. Borok Lev-Ran, None; H. Sarvagyl-Maman, None; V. Furer, None; S. Pel, None; I. Drukman, None; G. Flusser, None; O. Elkayam, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/the-prevalence-of-axial-spondyloarthritis-in-israel](http://acrabstracts.org/abstract/the-prevalence-of-axial-spondyloarthritis-in-israel)

**More Than 10 Percent Patients with Recent Onset Chronic Mechanical Back Pain Fulfill the Modified NY Criteria for Sacroiliitis**

**Anna Molto**¹, Laure Gossec², Violaine Foltz², Romain Beaufort³, Jean Denis Laredo⁴, Pascal Richette⁵, Philippe Dieude⁶, Philippe Goupille⁷, Antoine Feydy⁸ and Maxime Dougados⁹, ¹Hôpital Cochin, Department of Rheumatology, Paris Descartes University, Paris, France, ²UPMC University Paris 06, Pitié-Salpérière Hospital, Paris, France, ³Private Practice., Paris, France, ⁴Radiology Department, Lariboisière Hospital, Paris, France, ⁵Rheumatology Department, Université Paris Diderot, Paris, France, ⁶Université Paris-Diderot, Paris, France, ⁷Department of Rheumatology, CHRU de Tours; and Université François-Rabelais de Tours, Tours, France, ⁸Univ. Paris Descartes, PRES Sorbonne Paris Cité, Service de radiologie B, Hôpital Cochin, Assistance Publique - Hôpitaux de Paris, Paris, France, ⁹Department of Rheumatology, Paris Descartes University, Hôpital Cochin, Paris, France

First publication: September 18, 2017

**SESSION INFORMATION**
**Session Date:** Monday, November 6, 2017
**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
**Session Type:** ACR Poster Session B
**Session Time: 9:00AM-11:00AM**

**Background/Purpose:** only scarce data are available regarding the diagnostic value of pelvic Xrays abnormalities suggestive of axial spondyloarthritis (axSpA) in patients with recent onset back pain to distinguish mechanical chronic back pain (CBP) and axSpA.

**Objective:** To evaluate the prevalence of sacroiliac abnormalities suggestive of axSpA in a non-axSpA CBP population and to compare its prevalence to an recent onset axSpA cohort.
Methods:

Study design: Observational cross-sectional national multicentre study. Patients: a) Recent onset axSpA patients: first, a sample of 100 patients representative in terms of imaging abnormalities of the global DESIR (1) axSpA cohort (> 3 months but <3 years), based on the results of the previously published central reading of baseline films of DESIR(2) were selected (e.g. 21% of patients fulfilling the modified NY criteria (mNY)). b) CBP patients: consecutive in- and outpatients consulting for recent (>3months but <5years) mechanical CBP, initiating before the age of 45y and with a maximum age of 50y, in four tertiary care Hospitals were included in the study. Imaging: Pelvic Xrays were performed in both groups with an identical protocol. Central reading: an experienced reader (AM) centrally read X-ray films, blinded for clinical diagnosis.

Statistical analysis: prevalence of lesions suggestive of axSpA and the fulfilment of the mNY criteria for radiographic sacroiliitis were compared in both groups. Sensitivity, specificity and positive likelihood ratio of each lesion for the diagnosis of axSpA were calculated.

Results:

A total of 98 patients with CBP were included, and compared to 100 axSpA patients. Age and gender were comparable (mean (SD) 36.2 (9.9) vs. 32.2 (8.7)y, and 41.8% and 45% males, in the CBP vs. axSpA groups, respectively).

Patients with axSpA had consistently more lesions suggestive of axSpA than CBP patients (Table), and presence of erosions showed the best positive likelihood ratio. The fulfilment of mNY criteria presented also a high positive likelihood ratio (LR+).

<table>
<thead>
<tr>
<th>LESIONS</th>
<th>CBP n=98</th>
<th>axSpA n=100</th>
<th>p</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR+</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Erosion</td>
<td>9/97 (9.3%)</td>
<td>35 (35.0%)</td>
<td>&lt;0.001</td>
<td>0.4 (0.3, 0.5)</td>
<td>0.9 (0.8, 0.9)</td>
<td>3.8 (1.9, 7.4)</td>
</tr>
<tr>
<td>• Sclerosis</td>
<td>21/97 (21.6%)</td>
<td>50 (50.0%)</td>
<td>&lt;0.001</td>
<td>0.5 (0.4, 0.6)</td>
<td>0.8 (0.7, 0.9)</td>
<td>2.3 (1.5, 3.5)</td>
</tr>
<tr>
<td>• Joint widening</td>
<td>13/97 (13.4%)</td>
<td>25 (25.0%)</td>
<td>0.06</td>
<td>0.3 (0.2, 0.4)</td>
<td>0.9 (0.8, 0.9)</td>
<td>1.9 (1.0, 3.4)</td>
</tr>
<tr>
<td>• Joint narrowing</td>
<td>11/97 (11.3%)</td>
<td>21 (21.0%)</td>
<td>NS</td>
<td>0.2 (0.1, 0.3)</td>
<td>0.9 (0.8, 0.9)</td>
<td>1.9 (0.9, 3.6)</td>
</tr>
<tr>
<td>• Partial ankylosis</td>
<td>7/97 (7.2%)</td>
<td>11 (11.0%)</td>
<td>NS</td>
<td>0.1 (0.1, 0.2)</td>
<td>0.9 (0.9, 0.9)</td>
<td>1.5 (0.6, 3.8)</td>
</tr>
<tr>
<td>• Total ankylosis</td>
<td>0</td>
<td>3 (3.0%)</td>
<td>NS</td>
<td>0.0 (0.0, 0.1)</td>
<td>1.0 (0.9, 1.0)</td>
<td>NA*</td>
</tr>
<tr>
<td>Modified NY criteria (Y/N)</td>
<td>11/95 (11.6%)</td>
<td>35 (35.0%)</td>
<td>&lt;0.001</td>
<td>0.4 (0.3,0.5)</td>
<td>0.9 (0.8,0.9)</td>
<td>3.0 (1.6, 5.6)</td>
</tr>
</tbody>
</table>

* NA = not applicable, since one of the categories is 0, Specificity can not be calculated.

Conclusion:

Prevalence of sacroiliac lesions suggestive of axSpA in pelvic Xrays of patients with recent onset CBP is high, but significantly lower when compared to recent onset axSpA. Presence of erosions and fulfilment of mNY criteria were the best performing features for axSpA recognition even in an early disease stage.
Gender Bias in the Inheritance of Ankylosing Spondylitis

Karim Doughem¹, Michael Weisman², Lianne S. Gensler³, Mohammad H. Rahbar⁴, MinJae Lee⁴, Laura A. Diekman⁵, Matt Brown⁶, Michael Ward⁷ and John D. Reveille⁵, ¹Rheumatology, The University of Texas-McGovern Medical School, Houston, TX, ²Cedars-Sinai Medical Center Division of Rheumatology, Los Angeles, CA, ³Medicine/Rheumatology, UCSF, San Francisco, CA, ⁴Biostatistics/Epidemiology/Research Design (BERD) Core | Center for Clinical and Translational Sciences, University of Texas-McGovern Medical School, Houston, TX, ⁵Rheumatology, University of Texas-McGovern Medical School, Houston, TX, ⁶Translational Genomics Group, Institute of Health and Biomedical Innovation, Queensland University of Technology, Translational Research Institute, Brisbane, Australia, Brisbane, Australia, ⁷NIH/NIAMS, Bethesda, MD

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Spondyloarthopathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

There are few studies of the heritability of ankylosing spondylitis (AS) in families, a disease where hereditary factors play a dominant role in disease pathogenesis. One study (Calin et al, Lancet 1999; 354: 1687-90) showed that in families with affected parent: offspring pairs, the mother was more likely to be affected compared to the father. This study aims to better understand the pattern of inheritance of this disease in familial AS and to determine whether exists gender bias in disease inheritance in parent: offspring pairs in familial AS.

Methods:

Two cohorts were examined comprising 105 affected parent:offspring pairs, including one taken from 865 AS patients meeting modified New York Criteria enrolled in a longitudinal study of outcome who were administered a questionnaire querying spondyloarthritits symptoms in their first degree relatives (the proband recall cohort) and a second from 210 AS probands enrolled in a study of familial AS genetics, where the diagnoses were confirmed by either review of pelvic radiographs of affected family members or by radiographic reports thereof (the radiographic cohort). We tested whether the proportion of affected fathers was same as that of affected mothers and also evaluated the gender association between affected parents and offspring by conducting a test of one sample proportion and Chi-square test, respectively, at a 5% level of significance. All parent:offspring pairs were HLA-B27 positive.
Results: Overall, in 105 parent:offspring pairs, the father was the more likely affected parent after combining the parent: offspring pairs from the proband recall and the radiographic cohorts (p = 0.003). In the proband recall cohort there were 54 parent:offspring pairs and the father was more likely to be the affected parent compared to the mother (p = 0.007). In the radiographic cohort there were 51 affected parent: offspring pairs. Here a trend was also seen for greater paternal involvement, although the results were not statistically significant (p = 0.12).

Next it was tested whether affected parents are more likely to transmit the disease to their same or opposite gender offspring. In the radiographic cohort, the father and son were affected in 26 of 55 (47%) of father:offspring pairs whereas there in an affected mother:son pair in 12 of 24 (50%) of mother:offspring pairs (p = 0.40). Similar results were seen in the proband recall cohort-28/36 (77%) father:son versus 12/17 (71%) affected mother:son pairs, or in the combined cohorts (p = 0.07). Overall, sons were more likely to be affected than daughters (p = 0.0003) in the proband recall and combined cohorts.

Conclusion: In affected parent:offspring pairs with AS, the father is more likely to be affected than the mother, and there is greater likelihood for transmission to male versus female offspring, perhaps reflecting the male gender bias known to exist in this disease. There were no significant differences in parental transmission AS to same gender versus opposite gender offspring.

Disclosure: K. Doughem, None; M. Weisman, None; L. S. Gensler, Janssen Pharmaceutica Product, L.P., 5,Novartis Pharmaceutical Corporation, 5,Amgen, 2,UCB, 2,AbbVie, 2; M. H. Rahbar, None; M. Lee, None; L. A. Diekman, None; M. Brown, None; M. Ward, None; J. D. Reveille, Janssen, Novartis, 5,UCB, Eli Lilly, 2.


Abstract Number: 1506

Similarities and Differences between Patients Fulfilling Non-Radiographic Axial Spondyloarthritis and Undifferentiated Spondyloarthritis Criteria: Results from the Esperanza Cohort

Antonio Juan¹, Xavier Juanola², Eugenio De Miguel³, Eduardo Collantes-Estevez⁴, Juan Carlos Quevedo⁵, Elena Alonso⁶ and Victoria Navarro-Compán⁷, ¹Hospital Universitario Son Llàtzer. Rheumatology, Palma de Mallorca, Spain, ²Rheumatology, Hospital Universitario de Bellvitge, Barcelona, Spain, ³Rheumatology, University Hospital La Paz, IdiPaz, Madrid, Spain, ⁴Rheumatology, IMIBIC-Hospital Universitario Reina Sofia, Cordoba, Spain, ⁵H. Universitario de Gran Canaria Dr. Negrín., Las Palmas., Spain, ⁶Hospital Universitario Virgen del Rocio, A Curuña, Spain, ⁷Rheumatology, Hospital Universitario La Paz, Madrid, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Traditionally, patients with spondyloarthritis (SpA) were classified in five subgroups: ankylosing spondylitis (AS), psoriatic arthritis, arthritis associated with inflammatory bowel disease, reactive arthritis and undifferentiated SpA (uSpA). Nowadays, the ASAS criteria classify patients in peripheral SpA and axial SpA (axSpA), being the latest classified in two groups: classical AS and non-radiographic axSpA (nr-axSpA). Whether or not patients with nr-axSpA represent the same group of patients that used to be classified as uSpA remains unclear. The purpose is to evaluate the similarities and differences between patients with predominant axial disease classified currently as nr-axSpA versus those traditionally classified as uSpA.

Methods:
Baseline data from the ESPeranza program (a multicenter national initiative to early diagnose SpA between 2008 and 2011) was used. Inclusion criteria for this program were: age <45 years, symptoms duration 3-24 months and with inflammatory back pain -IBP- or asymmetrical arthritis or spinal/joint pain plus ≥1 SpA features). For this study, only patients with predominant axial manifestation were selected. Demographic, clinic, laboratory and image results were compared between two groups: i) 182 patients with nr-axSpA according to ASAS criteria, and ii) 166 patients classified as uSpA defined as fulfilling ESSG/Amor criteria in absence of sacroiliitis (mNY), psoriasis, inflammatory bowel disease and reactive arthritis. In order to get a deeper knowledge of the differences between nr-axSpA and uSpA, we also compared: i) 88 patients only classified as nr-axSpA, ii) 72 patients only classified as uSpA; iii) 94 patients fulfilling both criteria.

Results:
Results are shown in table 1 and table 2. Compared to patients classified as uSpA patients with nr-axSpA were younger, had HLA-B27 positive more frequently and higher values of CRP. On the other hand, they had history of SpA less frequently and lower values for BASDAI, BASFI and ASQoL.

Table 1: Results are presented in mean ± standard deviation for continuous variables and n (%) for categorical variables.

<table>
<thead>
<tr>
<th>nr-axSpA</th>
<th>Undifferentiated SpA</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)= 182</td>
<td>N (%) = 166</td>
</tr>
<tr>
<td>Age (years)</td>
<td>31.5 ± 7.1</td>
</tr>
<tr>
<td>Male</td>
<td>108 (61)</td>
</tr>
<tr>
<td>HLA-B27</td>
<td>142 (80.2)</td>
</tr>
<tr>
<td>Dactylitis</td>
<td>11 (6.2)</td>
</tr>
<tr>
<td>Enthesitis</td>
<td>46 (26.0)</td>
</tr>
<tr>
<td>BASDAI</td>
<td>3.7 ± 2.2</td>
</tr>
<tr>
<td>BASFI</td>
<td>2.1 ± 2.2</td>
</tr>
<tr>
<td>BASMI</td>
<td>1.2 ± 1.1</td>
</tr>
<tr>
<td>ASQoL</td>
<td>5.6 ± 4.6</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>10.3 ± 15.4</td>
</tr>
</tbody>
</table>

Table 2
Both, nr-axSpA & undifferentiated SpA N (%) = 94

Only nr-axSpA N (%) = 88

Only undifferentiated SpA N (%) = 72

<table>
<thead>
<tr>
<th></th>
<th>Both, nr-axSpA &amp; undifferentiated SpA</th>
<th>Only nr-axSpA</th>
<th>Only undifferentiated SpA</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>30.9 ± 7.3</td>
<td>32.2 ± 6.9</td>
<td>35.2 ± 6.9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Male</td>
<td>61 (64.9)</td>
<td>50 (56.8)</td>
<td>34 (47.2)</td>
<td>0.2</td>
</tr>
<tr>
<td>Family history</td>
<td>48 (51.1)</td>
<td>21 (23.9)</td>
<td>30 (41.7)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>HLA-B27</td>
<td>81 (86.2)</td>
<td>65 (73.9)</td>
<td>6 (8.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BASDAI</td>
<td>3.7 ± 2.3</td>
<td>3.8 ± 2.1</td>
<td>4.7 ± 2.3</td>
<td>0.01</td>
</tr>
<tr>
<td>BASFI</td>
<td>2.2 ± 2.2</td>
<td>2.1 ± 2.1</td>
<td>2.9 ± 2.5</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>BASMI</td>
<td>1.0 ± 1.2</td>
<td>1.4 ± 0.9</td>
<td>1.6 ± 1.1</td>
<td>0.2</td>
</tr>
<tr>
<td>ASQoL</td>
<td>5.9 ± 4.7</td>
<td>5.2 ± 4.5</td>
<td>7.4 ± 5.2</td>
<td>0.01</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>10.7 ± 14.3</td>
<td>9.8 ± 16.5</td>
<td>5.1 ± 9.1</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

*p value for differences between nr-axSpA and undifferentiated SpA (Student-t test for continuous variables and Pearson Chi-square test for categorical variables)

Conclusion:

Compared with patients traditionally classified as uSpA, patients who are currently classified as nr-axSpA are diagnosed earlier, are more frequently HLA-B27 carriers and have higher disease activity according to objective parameters. On the other hand, they report lower values for patient reported outcomes.

Disclosure: A. Juan, None; X. Juanola, None; E. De Miguel, None; E. Collantes-Estevez, None; J. C. Quevedo, None; E. Alonso, None; V. Navarro-Compán, None.


Abstract Number: 1507

Comparison of the Clinical and Imaging Arms of the Assessment of Spondyloarthritis International Society Classification Criteria and Parameters of Objective Inflammation in Patients with Non-Radiographic Axial Spondyloarthritis

Robert B.M. Landewé¹, Joachim Sieper², Atul A. Deodhar³, Helena Marzo-Ortega⁴, Robert G. Lambert⁵, Mei Li⁶, Xin Wang⁶ and Jaclyn K. Anderson⁶, ¹University of Amsterdam, Amsterdam, Netherlands, ²Charité Universitätsmedizin Berlin, Berlin, Germany, ³Oregon Health & Science University, Portland, OR, ⁴NIHR LBRC, Leeds Teaching Hospitals Trust and LIRMM, University of Leeds, Leeds, United Kingdom, ⁵University of Alberta, Edmonton, AB, Canada, ⁶AbbVie Inc., North Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Background/Purpose: Assessment of SpondyloArthritis international Society (ASAS) recommendations for use of TNF inhibitors (TNFi) in axial SpA include active disease and a positive expert opinion, which includes consideration of serum acute phase reactant and/or imaging results that indicate active inflammation and/or risk of radiographic progression. Little is known about the characteristics of patients (pts) with non-radiographic axial SpA (nr-axSpA) who fulfill criteria for TNFi use. Here we characterize the clinical phenotype of nr-axSpA pts enrolled in the ABILITY-3 adalimumab study in terms of ASAS classification criteria and parameters of objective inflammation at baseline.

Methods: ABILITY-3 enrolled adult pts with nr-axSpA defined as fulfilling ASAS classification criteria but not modified New York radiologic criteria for ankylosing spondylitis (AS). Pts were required to have a minimum baseline disease activity (defined as Ankylosing Spondylitis Disease Activity Score ≥2.1, BASDAI ≥4, and total back pain score ≥4), objective evidence of inflammation (in ≥1 of the following: MRI of the SI joints, MRI of spine, and/or elevated high-sensitivity CRP [each centrally evaluated]), and an inadequate response to ≥2 NSAIDs. Pts received open-label adalimumab 40 mg every other wk for 28 wks during period 1. Pts achieving sustained remission (wks 16–28) were randomized into the double-blind period 2. Here, we analyzed whether enrolled patients fulfilled the imaging arm of the ASAS classification criteria (sacroiliitis on imaging plus ≥1 SpA feature), the clinical arm (presence of HLA-B27 plus ≥2 SpA features), or both arms, and which objective parameters of inflammation were present.

Results: 673 of 1506 screened pts were enrolled; screen failures were commonly due to pelvic x-ray consistent with AS (24.7%), not fulfilling ASAS classification criteria (29.3%), or lack of objective evidence of inflammation (22.1%). Overall, 664 pts (98.7%) fulfilled the ASAS criteria, of which 447 (67.6%) fulfilled the imaging arm, 513 (77.4%) the clinical arm, and 296 (44.0%) both arms. At baseline, 662 (98.4%) pts had objective evidence of active inflammation. Most pts (74.0%) had evidence of MRI inflammation, 31.4% had MRI inflammation only, 42.6% were MRI positive and had elevated hsCRP, and 24.1% had elevated hsCRP only (Table).
### Table. Baseline Characteristics and Parameters of Objective Evidence of Inflammation

<table>
<thead>
<tr>
<th>Characteristic, n (% of total population)</th>
<th>Total Population (n=673)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD, y</td>
<td>37.3±11.1</td>
</tr>
<tr>
<td>Male</td>
<td>330 (49.0)</td>
</tr>
<tr>
<td>White</td>
<td>651 (96.7)</td>
</tr>
<tr>
<td>Symptom duration, mean ± SD, y</td>
<td>7.7±7.7</td>
</tr>
<tr>
<td>Positive HLA-B27 status(^a)</td>
<td>515 (76.6)</td>
</tr>
<tr>
<td>Elevated hsCRP</td>
<td>451 (67.0)</td>
</tr>
<tr>
<td>MRI evidence of inflammation(^b)</td>
<td></td>
</tr>
<tr>
<td>SI joint and/or spine</td>
<td>498 (74.0)</td>
</tr>
<tr>
<td>+ Elevated hsCRP</td>
<td>287 (42.6); 57.6% of MRI+</td>
</tr>
<tr>
<td>+ Normal hsCRP</td>
<td>211 (31.4); 42.4% of MRI+</td>
</tr>
<tr>
<td>SI joint only</td>
<td>316 (47.0)</td>
</tr>
<tr>
<td>Spine only</td>
<td>50 (7.4)</td>
</tr>
<tr>
<td>SI joint AND spine</td>
<td>130 (19.3)</td>
</tr>
<tr>
<td>Elevated hsCRP only (MRI normal)(^c)</td>
<td>162 (24.1)</td>
</tr>
<tr>
<td>Positive MRI for SI joint AND spine AND elevated hsCRP</td>
<td>90 (13.4)</td>
</tr>
<tr>
<td>Negative MRI for SI joint AND spine AND normal hsCRP</td>
<td>11 (1.6)</td>
</tr>
</tbody>
</table>

HLA-B27, human leukocyte antigen-B27; hsCRP, high-sensitivity C-reactive protein; MRI, magnetic resonance imaging; SI, sacroiliac.

\(^a\) 1 pt had missing HLA-B27 data from the central laboratory.

\(^b\) 4 pts had missing MRI imaging (spine only, n=1; SI joint only, n=2; SI joint and spine, n=1).

\(^c\) Elevated hsCRP = greater than the upper limit of normal for the lab.

**Conclusion:** An important proportion of screened nr-axSpA pts with clinically active disease did not present with objective measures of inflammation, and would not be candidates for biologics per ASAS recommendation. Many pts fulfilled both imaging and clinical arms of the ASAS criteria with more fulfilling the clinical vs imaging arm. Nearly 60% of pts who presented with MRI inflammation also had elevated hsCRP, suggesting hsCRP assessment as the first step in evaluating pts for objective inflammation due to low cost and ease of obtainment, unless MRI is required for diagnosis.

**Disclosure:** R. B. M. Landewé, Abbott/AbbVie, Ablynx, Amgen, Astra-Zeneca, Bristol Myers Squibb, Celgene, Janssen (formerly Centocor), Galapagos, GlaxoSmithKline, Novartis, Novo-Nordisk, Merck, Pfizer, Roche, Schering-Plough, TiGenix, UCB, and Wyeth, 5,Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, and Wyeth, 2,Abbott/AbbVie, Amgen, Bristol Myers Squibb, Janssen (formerly Centocor), Merck, Pfizer, Roche, Schering-Plough, UCB, and Wyeth, 8; J. Sieper, AbbVie, Janssen, Lilly, Merck, Novartis, Pfizer, Sun Pharma and UCB, 5,AbbVie, Janssen, Lilly, Merck, Novartis, and Pfizer, 8; A. A. Deodhar, Amgen, Abbvie, Eli Lilly, GlaxoSmithKline, Janssen, Novartis, Pfizer, and UCB, 2,Eli Lilly, Janssen, Janssen, Novartis, Pfizer, and UCB, 9; H. Marzo-Ortega, Janssen and Pfizer, 2,AbbVie, Celgene, Janssen, Novartis and UCB, 5,AbbVie, Celgene, Janssen and UCB, 8; R. G. Lambert, Abbott/AbbVie, BioClinica, Janssen, and Parexel, 5; M. Li, AbbVie, 3,Abbvie, 1; X. Wang, Abbvie, 3,AbbVie, 1; J. K. Anderson, Abbvie, 3,Abbvie, 1.
Validation of Self-Reported Inflammatory Back Pain Score Compared to Rheumatology Consultation in University Students

Nelly Ziade¹, Fouad Fayad¹ and Lea el-Khoury², ¹Rheumatology, Hotel Dieu de France Hospital and Saint Joseph University, Beirut, Lebanon, ²Saint-Joseph University, Beirut, Lebanon

Abstract Number: 1508

Validation of self-reported inflammatory back pain score compared to rheumatology consultation in university students

Background/Purpose: Low Back Pain (LBP) is a major public health problem affecting all ages, mostly young adults. University students may be vulnerable due to sedentary lifestyle and high stress levels. LBP is usually self-limited but a small proportion may have inflammatory back pain (IBP), a cornerstone symptom of axial spondyloarthritis, often overlooked. The objective of the study is to test an auto-questionnaire for IBP screening in educated young individuals, compared with the rheumatologist consultation as gold standard.

Methods: University students of three faculties (Medicine, Engineering and Sciences at Saint-Joseph University) were invited to respond to an auto-questionnaire about the presence and characteristics of LBP. Items related to IBP from the ASAS, Calin and Berlin criteria were collected. The students were then invited to a rheumatology consultation. Correlations between IBP score according to ASAS, Calin and Berlin criteria were studied between the auto-questionnaire and the rheumatology consultation.

Results: 611 students completed the auto-questionnaire (66.5%). 154 (25.2%) gave their consent to be contacted, 85 (55.2%) could be reached for consultation at the time of this report. Responders differed from non-responders by LBP (presence), age (older), BMI (higher), year of study (higher), habits such as smoking, alcohol consumption, caffeine consumption and sports activities (higher). 44% of students reported having at least one LBP episode during the past year (59.5% in medicine vs 25.5% in others, p<0.001). LBP correlated with specialty, caffeine consumption, sleep hours, walking when studying and anxiety in multivariate analysis. 8.6% of LBP were chronic, 84.8% were recurrent (>2/year) and 31.6% were highly recurrent (>4/year). IBP was found in 17.5% (ASAS), 12.3% (Calin) and 8.8% (Berlin) of interviewed LBP. The correlation with the medical interview was acceptable, with agreement ranging from 73.68 to 85.96%.

Conclusion: LBP is more frequent in medical university students compared to others. The correlation between the auto-questionnaire and the rheumatology consultation was acceptable, which makes the auto-questionnaire a suitable screening tool in educated individuals.

Table 1. Participants characteristics and habits, per specialty.
Table 2. Low Back Pain scores, compared between self-declaration and rheumatology consultation (in 57 interviewed LBP)

<table>
<thead>
<tr>
<th></th>
<th>Medicine</th>
<th>Engineering and Science</th>
<th>Total</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (%)</td>
<td>333 (54.5%)</td>
<td>278 (45.5%)</td>
<td>611</td>
<td></td>
</tr>
<tr>
<td>Male Gender N (%)</td>
<td>152 (45.6%)</td>
<td>170 (61.2%)</td>
<td>322 (52.7%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean Age (SD)</td>
<td>20.73 (2.04)</td>
<td>18.54 (0.88)</td>
<td>19.73 (1.95)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (SD)</td>
<td>22.53 (3.21)</td>
<td>22.25 (3.29)</td>
<td>22.40 (3.23)</td>
<td>0.294</td>
</tr>
<tr>
<td>Smoking N (%)</td>
<td>30 (9.0%)</td>
<td>22 (7.9%)</td>
<td>52 (8.5%)</td>
<td>0.629</td>
</tr>
<tr>
<td>Alcohol consumption N (%)</td>
<td>136 (40.8%)</td>
<td>104 (37.4%)</td>
<td>240 (39.4%)</td>
<td>0.387</td>
</tr>
<tr>
<td>Caffeine consumption N (%)</td>
<td>255 (76.6%)</td>
<td>166 (55.7%)</td>
<td>421 (68.9%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Regular Sports N (%)</td>
<td>221 (66.4%)</td>
<td>206 (74.1%)</td>
<td>427 (69.9%)</td>
<td>0.038</td>
</tr>
<tr>
<td>PHQ4-a (Anxiety %)</td>
<td>20.7</td>
<td>25.8</td>
<td>23.0</td>
<td>0.137</td>
</tr>
<tr>
<td>PHQ4-b (Depression %)</td>
<td>12.9</td>
<td>25.2</td>
<td>18.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Laptop hours/day</td>
<td>2.56</td>
<td>2.44</td>
<td>2.56</td>
<td>0.042</td>
</tr>
<tr>
<td>Television hours/day</td>
<td>1.48</td>
<td>1.65</td>
<td>1.55</td>
<td>0.012</td>
</tr>
<tr>
<td>Study Satisfaction %</td>
<td>83.4</td>
<td>80.4</td>
<td>82.0</td>
<td>0.199</td>
</tr>
<tr>
<td>Sleep satisfaction %</td>
<td>47.3</td>
<td>41.0</td>
<td>44.0</td>
<td>0.292</td>
</tr>
</tbody>
</table>

Disclosure: N. Ziade, None; F. Fayad, None; L. el-Khoury, None.


Abstract Number: 1509

**Similarities and Differences between Non-Radiographic and Radiographic Axial Spondyloarthritis**

Denis Poddubnyy1, Robert D Inman2, Joachim Sieper1, Servet Akar3, Santiago Muñoz-Fernández4 and Maja Hojnik5, 1Charité Universitätsmedizin Berlin, Berlin, Germany, 2Toronto Western Hospital, Toronto, ON, Canada, 3Rheumatology, Izmir Katip Celebi University, School of Medicine, Rheumatology, Izmir, Turkey, 4Hospital Universitario Infanta Sofia, Universidad Europea, Mardid, Spain, 5AbbVie, Ljubljana, Slovenia

First publication: September 18, 2017
Background/Purpose: Differences between non-radiographic and radiographic axial spondyloarthritis (axSpA) – such as a higher prevalence of females and lower level of acute phase reactants in non-radiographic axSpA (nr-axSpA) – have been reported in national observational studies, mostly from Europe. This analysis compared demographic and clinical characteristics of patients (pts) with nr-axSpA and radiographic axSpA (ankylosing spondylitis, AS) in a large multinational cohort of pts with recently diagnosed axSpA.

Methods: PROOF is a prospective observational study evaluating clinical and radiographic outcomes in axSpA pts in rheumatology clinical practice in 29 countries. Pts with axSpA fulfilling ASAS classification criteria were eligible if diagnosed ≤1 year prior to study enrolment. Investigator’s confidence with the axSpA diagnosis was ascertained on a numeric rating scale (NRS 0-10) at enrolment and end of follow-up. At baseline, demographic and clinical data related to the diagnosis, disease activity, quality of life and work productivity, as well as conventional radiographs of the sacroiliac joints were collected. Classification as nr-axSpA or AS was based on results of the assessment of sacroiliac radiographs. Available radiographs were assessed by a local reader and then by a central reader according to grading system of modified New York criteria. In the case of a disagreement in classification (nr-axSpA or AS), the radiograph was evaluated by the 2nd central reader, who was blinded to previous assessments and final classification was made based on the decision of 2 out of 3 readers.

Results: Of the 2126 pts enrolled in PROOF, 1281 (60.3%) pts were classified as AS and 845 (39.7%) as nr-axSpA according to investigators. Confidence with the axSpA diagnosis was 8.7±1.8. Final classification according to central assessment of sacroiliac radiographs was confirmed in 1583 pts included in this analysis. A total of 987 pts (62.3%) were classified as AS and 596 (37.7%) as nr-axSpA. AS pts expectedly had longer symptom duration, more frequently had elevated and higher CRP and were more often male and treated with TNF inhibitors (Table). In addition, HLA-B27 positivity was more frequent among AS pts, while pts with nr-axSpA had a significantly higher prevalence of enthesitis, psoriasis, and inflammatory bowel disease (IBD). Prevalence of other SpA features was comparable between the two subgroups of axSpA. Mostly, pt-reported outcomes reflecting burden of disease were comparable between the two subgroups, but BASDAI was significantly higher in the nr-axSpA subgroup (Table).

Conclusion: There were a few differences between nr-axSpA and AS pts in the PROOF cohort. Clinical constellation of female sex, low CRP, enthesitis, psoriasis, and IBD in nr-axSpA pts appears to reflect a phenotype less prone to structural damage in the sacroiliac joints. However, clinical burden of disease was comparable between the two subgroups of axSpA.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>nr-axSpA (N = 544)</th>
<th>AS (N = 1039)</th>
<th>P-value(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean ± SD</td>
<td>35.5 ± 9.8</td>
<td>34.5 ± 11.1</td>
<td>.070</td>
</tr>
<tr>
<td>Duration since back pain onset, months, mean ± SD</td>
<td>48.7 ± 69.2</td>
<td>62.4 ± 90.9</td>
<td>.001</td>
</tr>
<tr>
<td>Duration since diagnosis, months, mean ± SD</td>
<td>2.8 ± 5.6</td>
<td>4.0 ± 20.2</td>
<td>.119</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>264 (48.5)</td>
<td>737 (71.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>SpA parameters</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HLA-B27 (+), n (%)</td>
<td>254 (55.3)(^b)</td>
<td>591 (69.0)(^c)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Inflammatory back pain, n (%)</td>
<td>512 (94.1)</td>
<td>991 (95.4)</td>
<td>.279</td>
</tr>
<tr>
<td>Peripheral arthritis, n (%)</td>
<td>171 (31.4)</td>
<td>343 (33.0)</td>
<td>.535</td>
</tr>
<tr>
<td>Enthesitis (heel), n (%)</td>
<td>214 (39.3)</td>
<td>348 (33.5)</td>
<td>.023</td>
</tr>
<tr>
<td>Dactylitis, n (%)</td>
<td>32 (5.9)</td>
<td>57 (5.5)</td>
<td>.732</td>
</tr>
<tr>
<td>Uveitis, n (%)</td>
<td>49 (9.0)</td>
<td>106 (10.2)</td>
<td>.477</td>
</tr>
<tr>
<td>Psoriasis, n (%)</td>
<td>54 (9.9)</td>
<td>59 (5.7)</td>
<td>.003</td>
</tr>
<tr>
<td>IBD, n (%)</td>
<td>23 (4.2)</td>
<td>18 (1.7)</td>
<td>.004</td>
</tr>
<tr>
<td>Good response to NSAIDs, n (%)</td>
<td>324 (59.6)</td>
<td>636 (61.2)</td>
<td>.551</td>
</tr>
<tr>
<td>Family history of SpA, n (%)</td>
<td>101 (18.6)</td>
<td>196 (18.9)</td>
<td>.946</td>
</tr>
<tr>
<td>Elevated CRP, n (%)</td>
<td>178 (32.7)</td>
<td>555 (53.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Number of positive SpA parameters, mean ± SD</td>
<td>3.5 ± 1.4</td>
<td>3.8 ± 1.4</td>
<td>.001</td>
</tr>
<tr>
<td>CRP, mg/l, mean ± SD</td>
<td>11.5 ± 19.5</td>
<td>17.6 ± 24.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>ASDAS-CRP, mean ± SD</td>
<td>2.8 ± 1.1</td>
<td>3.0 ± 1.1</td>
<td>.004</td>
</tr>
<tr>
<td>BASDAI, points NRS (0-10), mean ± SD</td>
<td>4.8 ± 2.4</td>
<td>4.3 ± 2.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Patient global, points NRS (0-10), mean ± SD</td>
<td>5.0 ± 4.8</td>
<td>4.8 ± 4.6</td>
<td>.183</td>
</tr>
<tr>
<td>BASFI, points NRS (0-10), mean ± SD</td>
<td>3.4 ± 2.5</td>
<td>3.3 ± 2.5</td>
<td>.815</td>
</tr>
<tr>
<td>SF-12v2, physical component score, mean ± SD</td>
<td>40.9 ± 8.9</td>
<td>41.0 ± 8.8</td>
<td>.698</td>
</tr>
<tr>
<td>SF-12v2, mental component score, mean ± SD</td>
<td>42.9 ± 10.9</td>
<td>43.7 ± 10.4</td>
<td>.166</td>
</tr>
<tr>
<td>WPAI-SHP – total activity impairment, mean ± SD</td>
<td>44.9 ± 28.1</td>
<td>43.1 ± 27.4</td>
<td>.208</td>
</tr>
<tr>
<td>Current Treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSAIDs, n (%)</td>
<td>428 (78.7)</td>
<td>800 (77.0)</td>
<td>.485</td>
</tr>
<tr>
<td>Methotrexate, n (%)</td>
<td>40 (7.4)</td>
<td>63 (6.1)</td>
<td>.335</td>
</tr>
<tr>
<td>Sulfasalazine, n, (%)</td>
<td>117 (21.5)</td>
<td>253 (24.4)</td>
<td>.212</td>
</tr>
<tr>
<td>Steroids, n (%)</td>
<td>40 (7.4)</td>
<td>85 (8.2)</td>
<td>.624</td>
</tr>
<tr>
<td>Analgesics, n (%)</td>
<td>98 (18.0)</td>
<td>144 (13.9)</td>
<td>.033</td>
</tr>
<tr>
<td>TNF α inhibitors, n (%)</td>
<td>48 (8.8)</td>
<td>165 (15.9)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

\(^a\)P-values from two-sided t-test for scale variables and Fisher’s exact test for categorical variables.

\(^b\)N = 459; \(^c\)N = 856.

nr-axSpA = non-radiographic axial spondyloarthritis; AS = Ankylosing spondylitis; SD= standard deviation; SpA = spondyloarthritis; HLA-B27 = human leukocyte antigen B27; IBD = inflammatory bowel disease; NSAIDs = non-steroidal anti-inflammatory drugs; CRP=C-reactive protein; ASDAS-CRP = Ankylosing Spondylitis Disease Activity Score containing CRP; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; NRS = numeric rating scale; BASFI = Bath Ankylosing Spondylitis Functional Index; SF-12v2=Short form 12-item health survey; WPAI-SHP = Work productivity impairment Questionnaire–specific health problem; TNF = tumor necrosis factor.
Similarities and Differences between Osteitis Condensans Ilii and Axial Spondyloarthritis Patients Presenting with Chronic Back Pain in a Rheumatology Setting

Henning Weineck¹, Joachim Listing², Torsten Diekhoff¹, Kay-Geert Hermann¹, Joachim Sieper¹ and Denis Poddubnyy¹,² ¹Charité Universitätsmedizin Berlin, Berlin, Germany, ²German Rheumatism Research Centre, Berlin, Germany
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Osteitis condensans ilii (OCI) is regarded as a non-inflammatory disorder, which is considered to be induced by mechanical stress (e.g., by pregnancy and delivery). An extended sclerosis of the sacroiliac joints without erosions or ankyloses is the most characteristic imaging feature. More recently, paraarticular bone marrow edema has been described on magnetic resonance imaging, which can occur early but also intermittently later in the course of the disease. The clinical characteristics of OCI patients have not been well described. To date, there are no published systematic data on the characteristics of OCI as compared to axial spondyloarthritis (axSpA).

The objective of this matched case-control study was to investigate demographic, clinical, and lab characteristics of OCI as compared to axSpA.

Methods:
Using medical database search we have identified n=103 patients aged ≥18 years who were diagnosed with OCI upon presentation with chronic back pain in the Early Spondyloarthritis Clinic of the rheumatology department in the Charité University Hospital between January 2010 and May 2015. These patients were contacted in order to obtain an informed consent and to complete a survey on the disease-related history. N=60 OCI patients who
provided an informed consent and completed the survey were included in the final analysis. These patients were matched with a 1:2 ratio according to the back pain duration to patients with definite axSpA diagnosed in the same setting in order to compare demographic, clinical and lab characteristics.

**Results:**

The main characteristics of the two groups are presented in the table. Most importantly, all but 2 patients with OCI were females and had a significantly lower prevalence of inflammatory back pain, lower level of CRP stressing a rather non-inflammatory nature of this condition. All patients were referred because of possible axSpA, therefore SpA features, although being lower than in axSpA patients (table), were higher than can generally be expected in chronic back pain patients. This is probably the reason why a statistical significance in comparison to axSpA was observed for uveitis only. There was no difference in age of back pain onset. Signs of sacroiliitis at physical examination were only slightly more frequent in axSpA; there were no differences in spinal mobility. The level of symptoms (BASDAI) and the perceived level of functional disability (BASFI) were comparable between groups. 83% of female patients with OCI reported a history of at least one pregnancy with a mean number of pregnancies of 3 (median=3, range 1-8).

**Conclusion:**

OCI manifesting with chronic back pain starting before 45 years of age represents an important differential diagnosis for axSpA. A constellation of a female sex (with a history of pregnancies), negative HLA-B27 and negative CRP seems to be of differential diagnostic value as compared to axSpA.
Table. Demographic, clinical and lab characteristics of OCI as compared to axSpA in the rheumatology setting.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>OCI N=60</th>
<th>axSpA N=120</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>40.3±10.0</td>
<td>39.4±11.3</td>
<td>0.56</td>
</tr>
<tr>
<td>Female sex, %</td>
<td>96.7%</td>
<td>41.7%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age at back pain onset, years</td>
<td>29.7±9.0</td>
<td>30.5±9.0</td>
<td>0.55</td>
</tr>
<tr>
<td>Back pain duration, years</td>
<td>9.1±7.9</td>
<td>8.9±8.0</td>
<td>n.a.***</td>
</tr>
<tr>
<td>HLA-B27 positive, %</td>
<td>35.2%</td>
<td>84.2%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CRP, mg/l</td>
<td>2.1±2.1</td>
<td>11.3±27.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Elevated CRP (&gt;5mg/l), %</td>
<td>7.1%</td>
<td>41.3%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Inflammatory back pain, %</td>
<td>39.5%</td>
<td>80.7%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Good response to NSAIDs, %</td>
<td>70.5%</td>
<td>69.7%</td>
<td>0.85</td>
</tr>
<tr>
<td>Peripheral arthritis, %</td>
<td>4.5%</td>
<td>12.5%</td>
<td>0.13</td>
</tr>
<tr>
<td>Enthesitis of the heel, %</td>
<td>4.8%</td>
<td>15.8%</td>
<td>0.09</td>
</tr>
<tr>
<td>Dactylitis, %</td>
<td>0%</td>
<td>5.0%</td>
<td>0.48</td>
</tr>
<tr>
<td>Uveitis, %</td>
<td>0%</td>
<td>11.7%</td>
<td>0.02</td>
</tr>
<tr>
<td>Psoriasis, %</td>
<td>5.6%</td>
<td>3.3%</td>
<td>0.69</td>
</tr>
<tr>
<td>Inflammatory bowel disease, %</td>
<td>1.8%</td>
<td>2.5%</td>
<td>1.00</td>
</tr>
<tr>
<td>Family history of SpA, %</td>
<td>32.7%</td>
<td>20.8%</td>
<td>0.19</td>
</tr>
<tr>
<td>BASDAI, NRS points (0-10)</td>
<td>4.6±2.0</td>
<td>4.0±2.0</td>
<td>0.15</td>
</tr>
<tr>
<td>BASFI, NRS points (0-10)</td>
<td>3.4±2.2</td>
<td>3.1±2.3</td>
<td>0.54</td>
</tr>
<tr>
<td>Meinei's test positive, %</td>
<td>37.5%</td>
<td>62.5%</td>
<td>0.27</td>
</tr>
<tr>
<td>Patrick's test positive, %</td>
<td>45.8%</td>
<td>69.6%</td>
<td>0.52</td>
</tr>
<tr>
<td>Tenderness in the SI area, %</td>
<td>75.6%</td>
<td>66.7%</td>
<td>1.00</td>
</tr>
<tr>
<td>Schober's test, cm</td>
<td>4.2±0.9</td>
<td>4.6±2.1</td>
<td>0.33</td>
</tr>
<tr>
<td>Lateral spinal flexion, cm</td>
<td>15.6±15.0</td>
<td>15.3±4.5</td>
<td>0.89</td>
</tr>
</tbody>
</table>

*p-values of conditional logistic regression, mixed linear models, where appropriate
**Matching variable

Disclosure: H. Weineck, None; J. Listing, None; T. Diekhoff, None; K. G. Hermann, None; J. Sieper, None; D. Poddubnyy, None.


Abstract Number: 1511

Real-Life Performance of the ASAS Health Index in Routine Care of Patients with Spondyloarthritis

Uta Kiltz, Thomas Wiatr, Xenofon Baraliakos, Kirill Fedorov and Jürgen Braun, Rheumazentrum Ruhrgebiet, Herne, Germany
First publication: September 18, 2017
Background/Purpose: The ASAS Health Index (ASAS HI) have been developed to measure health and impairment in functioning in patients with spondyloarthritis (SpA). Its measurement properties have already been evaluated in a cohort study. So far, its association with structural damage has not been examined. The purpose is to investigate the relationship between clinical data, function and health as assessed by the ASAS HI and to investigate the influence of structural spinal damage in patients with axial SpA (axSpA) on the ASAS HI.

Methods: Patients fulfilling ASAS classification criteria for axial SpA (axSpA) were recruited prospectively. Information was collected on clinical assessments (ASAS HI, NRS pain, BASDAI, ASDAS, BASFI, BASMI), laboratory parameters and spinal x-rays. Imaging were scored using mSASSS by two independent readers. The relationship between ASAS HI and other health outcomes was evaluated by Spearman correlation.

Results: A total of 150 patients (57 nr-axSpA and 93 AS patients) were included: 68.7% male, mean (SD) age 46.4 (14.1), symptom duration 18.7 (13.5) and diagnosis since 11.4 (11.8) years, and HLA-B27 positive in 82.0%. Values of clinical assessments were ASAS HI 7.4 (4.1), BASDAI 4.7 (2.3), ASDAS 2.7 (1.1), BASMI 3.3 (1.8), pain 5.7 (2.7), and BASFI 4.7 (2.6). An elevated CRP level was found in 34.8% of the patients. Radiographs of the sacroiliac (SI) joint and the spine were available in 138 patients, 38.0% of which had syndesmophytes and 7.5% a bamboo spine. The median (IQR) mSASSS value was 4.3 (IQR 1.0-22.1) in AS und 0.2 (IQR 0.0-1.4) in nr-axSpA patients. Patients received a treatment with NSAIDs (62.7%), DMARDs (20.9%) and/or biologics (49.4%). Significant correlation of ASAS HI was noted for BASMI (0.5), BASDAI (0.7), ASDAS (0.5) and BASFI (0.8). No correlations were found for ASAS HI and any of the results for radiographic damage (mSASSS 0.2, syndesmophytes 0.01, bamboo spine 0.2) and CRP level (0.07). Startifying patient population by symptom duration (cut-off 3 years) does not change the results.

Conclusion: Measures of function and spinal mobility correlate well with the ASAS HI in patients with SpA. Probably due to relatively low mSASSS scores at baseline, the influence of structural changes as measured by mSASSS on the ASAS HI was rather limited in this study. Further study in more severely affected patients is needed to study the association of physical activity, spinal mobility, function and radiographic damage.

Disclosure: U. Kiltz, None; T. Wiatr, None; X. Baraliakos, None; K. Fedorov, None; J. Braun, None.


Abstract Number: 1512

Is Sacroiliac Imaging the All-Decisive Factor in the Diagnosis of Early Axial Spondyloarthritis? Data from the Spondyloarthritis Caught Early (SPACE) Cohort

Zineb Ez-Zaitouni1, Robert B.M. Landewé2, Miranda van Lunteren1, Pauline Bakker1, Karen M Fagerli3, Roberta Ramonda4, Lennart TH Jacobsson5, Désirée van der Heijde6 and Floris van Gaalen7, 1Rheumatology, Leiden University Medical Center, Leiden, Netherlands, 2Amsterdam Rheumatology & Immunology Center, Amsterdam, Netherlands, 3Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, 4Rheumatology Unit, University of Padova, Padova, Italy, 5Department of Rheumatology and Inflammation Research, Sahlgrenska Academy, University of
Background/Purpose:
Imaging of the sacroiliac joints plays a pivotal role in the recognition of axSpA. However, interpretation of imaging is challenging and has led to concerns of overreliance on imaging possibly leading to incorrect diagnoses of axSpA. Given these controversies, surprisingly little is known about how rheumatologists actually integrate sacroiliac imaging results in the diagnostic work-up of patients suspected of axSpA. Therefore, we evaluated the influence of sacroiliac imaging on diagnosis and rheumatologists’ confidence in diagnosis of patients with chronic back pain (CBP) suspected of early axSpA.

Methods:
Baseline data from 513 patients from the SPACE cohort which includes patients with CBP (≥3 months, ≤2 years, onset <45 years) were analysed. All patients underwent a full work-up including MRI and radiography of the sacroiliac joints. Rheumatologists were asked to provide a diagnosis before and after taking imaging into account. Also, a level of confidence (LoC) regarding the diagnosis on an 11-point numerical scale (0: not confident at all to 10: very confident) was documented.

Results:
Before imaging, 317/513 (62%) CBP patients were diagnosed with axSpA. Of these patients, 178/317 (56%) did not have sacroiliitis on MRI or radiography, and after imaging rheumatologists changed diagnosis to ‘no axSpA’ in 81/178 (46%) patients. Of the patients without axSpA before imaging, 35/196 (18%) had sacroiliitis on imaging. After imaging, 28/35 (80%) patients were diagnosed with axSpA and in 7/35 (20%) patients the diagnosis remained ‘no axSpA’. In general, diagnostic confidence increased significantly following imaging (all patients’ average LoC 6.2 to 7.4, p<0.001). Overall, imaging results not in line with the diagnosis (n=213) before imaging led to a change in diagnosis in 109 (51%) patients.

Conclusion:
In CBP patients suspected of axSpA sacroiliac imaging increases diagnostic confidence. However, the number of changes in diagnosis suggests that imaging is an important but not the all-decisive factor in axSpA diagnosis.
Abstract Number: 1513

**Clinical Characteristics and Peripheral Joint Involvement at the Time of Diagnosis of Non-Radiographic Axial Spondyloarthritis Patients in the United States and Europe**

Atul A. Deodhar¹, Theresa Hunter², David Sandoval Calderon³, Steve Lobosco⁴, Rachel Moon⁴ and Gary Milligan⁵, ¹Oregon Health & Science University, Portland, OR, ²Global Patient Outcomes and Real World Evidence, Eli Lilly and Company, Indianapolis, IN, ³Eli Lilly and Company, Indianapolis, IN, ⁴Adelphi Real World, Macclesfield, United Kingdom, ⁵Adelphi Real World, Macclesfield,, United Kingdom

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Timely identification of nr-axSpA may lead to earlier intervention to reduce symptoms, improve function, and reduce disease burden. The purpose of this study was to compare the clinical characteristics that are present at the time of diagnosis of nr-axSpA patients in the US and EU.
Methods: Nr-axSpA patients from the 2015 SpA Disease Specific Programme, a cross-sectional, multi-national survey of patients and rheumatologists conducted in France, Germany, Italy, Spain, United Kingdom, and the United States were analyzed. Rheumatologists completed patient record forms containing patient demographics, clinical measurements and symptomology at diagnosis.

Results: Data from 391 rheumatologists (299 EU/92 US) and 1,995 patients with nr-axSpA (1513 EU/482 US) were included in this analysis. In the US and EU, at the time of diagnosis patients had similar rates of IBP, back pain for more than 3 months, and a family history of SpA (Table 1). Patients in the US were significantly more likely to have peripheral joint involvement at diagnosis than patients in the EU. In the US, patients that had peripheral joint involvement at diagnosis were significantly more likely to have had IBP that was previously diagnosed as mechanical back pain (p=0.002) and have back pain for greater than 3 months (p=0.035) at diagnosis when compared to patients that did not have peripheral joint involvement at diagnosis. In the EU, patients that had peripheral joint involvement at diagnosis were significantly more likely to have elevated ESR (p<0.001) and alternating buttock pain (p=0.002) when compared to patients that did not have peripheral joint involvement at diagnosis. In the US and EU, patients that had peripheral joint involvement at diagnosis were significantly more likely to have elevated CRP, morning stiffness for more than 30 minutes, dactylitis, enthesitis, tendonitis, synovitis, and arthritis at diagnosis when compared patients that did not have peripheral joint involvement at diagnosis (Table 2).

Conclusion: Nr-axSpA patients in the US and EU share a range of clinical features at diagnosis. However, patients in the US were more likely to have peripheral joint involvement at diagnosis than patients in the EU. Furthermore, nr-axSpA patients in the US and EU with peripheral joint involvement at diagnosis were associated with a worse symptom profile versus patients without peripheral joint involvement.

Table 1. Comparison of symptoms of nr-axSpA patients at diagnosis in the US vs. EU

<table>
<thead>
<tr>
<th>Symptoms at Diagnosis</th>
<th>USA</th>
<th>EU</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral joint involvement</td>
<td>50.8</td>
<td>23.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>IBP or spinal pain</td>
<td>69.3</td>
<td>67.6</td>
<td>0.5016</td>
</tr>
<tr>
<td>Age of onset of IBP less than 45 years</td>
<td>48.5</td>
<td>48.2</td>
<td>0.9167</td>
</tr>
<tr>
<td>Back pain for more than 3 months</td>
<td>56.0</td>
<td>54.9</td>
<td>0.7128</td>
</tr>
<tr>
<td>IBP that was previously diagnosed as mechanical back pain</td>
<td>27.4</td>
<td>27.3</td>
<td>1.0000</td>
</tr>
<tr>
<td>Family history of spondyloarthritis</td>
<td>20.7</td>
<td>20.9</td>
<td>1.0000</td>
</tr>
<tr>
<td>Morning stiffness for more than 30 minutes</td>
<td>57.9</td>
<td>51.8</td>
<td>0.0210</td>
</tr>
<tr>
<td>Elevated CRP</td>
<td>37.1</td>
<td>37.1</td>
<td>1.0000</td>
</tr>
<tr>
<td>Elevated ESR</td>
<td>37.3</td>
<td>25.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HLA-B27 positive</td>
<td>46.5</td>
<td>49.5</td>
<td>0.2293</td>
</tr>
</tbody>
</table>

Table 2. Comparison of symptoms of nr-axSpA patients with peripheral joint involvement at diagnosis vs. nr-axSpA patients without peripheral joint involvement at diagnosis
### Symptoms at Diagnosis

<table>
<thead>
<tr>
<th>Symptoms at Diagnosis</th>
<th>USA</th>
<th></th>
<th>EU</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>% With Symptoms</td>
<td>p-value</td>
<td>% With symptoms</td>
<td>p-value</td>
<td></td>
</tr>
<tr>
<td>Back pain for &lt; 3 months</td>
<td>60.8</td>
<td>0.0348</td>
<td>59.1</td>
<td>0.0764</td>
</tr>
<tr>
<td>IBP previously diagnosed as mechanical back pain</td>
<td>33.9</td>
<td>0.0015</td>
<td>30.1</td>
<td>0.1943</td>
</tr>
<tr>
<td>Morning stiffness for more than 30 minutes</td>
<td>63.3</td>
<td>0.0165</td>
<td>61.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Alternating buttock pain</td>
<td>15.9</td>
<td>1.0000</td>
<td>40.3</td>
<td>0.0020</td>
</tr>
<tr>
<td>Elevated ESR</td>
<td>40.8</td>
<td>0.1108</td>
<td>42.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Elevated CRP</td>
<td>45.3</td>
<td>0.0002</td>
<td>48.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Dactylitis</td>
<td>10.6</td>
<td>0.0451</td>
<td>12.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Enthesitis</td>
<td>26.1</td>
<td>0.0004</td>
<td>28.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Tendonitis</td>
<td>22.0</td>
<td>&lt;0.0001</td>
<td>14.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Active Synovitis</td>
<td>23.3</td>
<td>&lt;0.0001</td>
<td>21.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Arthritis</td>
<td>42.4</td>
<td>&lt;0.0001</td>
<td>27.8</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

**Disclosure:** A. A. Deodhar, AbbVie, Amgen, Eli Lilly, GlaxoSmithKline, Janssen, Novartis, Pfizer, UCB Pharma, 2; Eli Lilly, Janssen, Novartis, Pfizer, UCB Pharma, 2; T. Hunter, Eli Lilly and Company, 3; D. S. Calderon, Eli Lilly and Company, 1; Eli Lilly and Company, 3; S. Lobosco, Adelphi Real World, 3; R. Moon, Adelphi Real World, 3; G. Milligan, Adelphi Real World, 3.


**Abstract Number:** 1514

**Phenotype Differences in HLA-B27 Positive Versus Negative Patients with Ankylosing Spondylitis in a Population That Show Relatively Weaker Association with HLA-B27**

**Handan Yarkan**¹, Zhixiu Li², Gokce Kenar³, Sedat Capar⁴, Fernur Çapa⁵, Rudi Steffensen⁶, Servet Akar⁷, Dilek Solnaz⁸, Pinar Cetin⁹, Berrin Zengin³, Erika de Guzman¹⁰, Katie Cremin²,Gerçek Can¹¹, Zeynep Yüce⁵, Ismail Sari¹², Fatos Onen¹³, Matt Brown² and Nurullah Akkcö¹⁴, ¹Rheumatology, Dokuz Eylül University Faculty of Medicine, İzmir, Turkey, ²Translational Genomics Group, Institute of Health and Biomedical Innovation, Queensland University of Technology, Translational Research Institute, Brisbane, Australia, Brisbane, Australia, ³Rheumatology, Dokuz Eylül University Faculty of Medicine, Izmir, Turkey, ⁴Statistics, Dokuz Eylül University School of Medicine, Izmir, Turkey, ⁵Department of Molecular Medicine, Dokuz Eylül University Health Sciences Institute, IZMIR, Turkey, ⁶Department of Clinical Immunology, Aalborg University Hospital, Aalborg, Denmark, ⁷Rheumatology, İzmir Katip Celebi University, School of Medicine, Rheumatology, İzmir, Turkey, ⁸Rheumatology, İzmir Katip Celebi University, School of Medicine, Rheumatology, Izmir, Turkey, ⁹Rheumatology, Dokuz Eylül University Faculty of Medicine, izmir, Turkey, ¹⁰Translational Genomics Group, Institute of Health and Biomedical Innovation, Queensland University of Technology, Translational Research Institute, Brisbane, Australia, Brisbane, Austria, ¹¹TURKBIO, İzmir, Turkey, ¹²Rheumatology, Toronto Western Hospital, University of
The association of HLA-B*27 and ankylosing spondylitis (AS) is relatively weak in some populations. The aim of this study is to compare the clinical manifestations between HLA-B*27+ and HLA-B*27− patients in a Turkish AS population, which has been reported to have a low HLA-B*27 prevalence.

Methods:

A total of 881 AS patients and 900 healthy controls were included in the analysis. All patients fulfilled the modified New York criteria for AS. Clinical and demographic parameters were compared between the HLA-B*27+ and HLA-B*27− patients. Group comparisons were performed using t-tests for continuous measures that were normally distributed and x2 tests were used for categorical measures.

Results:

HLA-B*27 was positive in 64% of patients (n=561) and 6.3% of controls (n=57). All results are summarized in Table 1. Seventy-four percent of the HLA-B*27+ patients and 60% of HLA-B*27− patients were male (<0.001). HLA-B*27+ patients had a younger age at symptom onset, as well as a shorter delay in diagnosis. Moreover, uveitis and a family history for AS were significantly more frequent among HLA-B*27+ AS patients, whereas co-existent psoriasis and inflammatory bowel disease (IBD) were more frequent among HLA-B*27− patients. Further, HLA-B27+ patients had a 22% higher CRP (P<0.05) and 13% higher ESR (P=0.06) than HLA-B*27− patients. Prevalence of peripheral arthritis, dactylitis, biologic use, hip replacement surgery, family history for psoriasis or IBD or uveitis were not different between the two groups. Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI) and Bath Ankylosing Spondylitis Metrology Index (BASMI) were also similar in both groups.

Conclusion:

The results of this study conducted in an AS population with a relatively low prevalence of HLA-B*27 are in line with those of other studies performed in other populations. HLA-B*27+ AS patients are more likely to be males and have an earlier age of symptom onset, and a shorter delay in diagnosis as compared to AS patients lacking HLA-B*27. Moreover, HLA-B*27+ AS patients show a greater risk for occurrence of acute anterior uveitis, a greater familial occurrence, and an elevated CRP/ESR, the latter suggesting that HLA-B*27 carriage influences degree of inflammation in AS.
<table>
<thead>
<tr>
<th></th>
<th>$HLA$-$B^*$27$^+$</th>
<th>$HLA$-$B^*$27$^-$</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>415 (%74)</td>
<td>154 (%59.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age, Mean ± SD (year)</td>
<td>43.8 ± 12.2</td>
<td>45.5 ± 12.4</td>
<td>0.07</td>
</tr>
<tr>
<td>Age at diagnosis, Mean ± SD (year)</td>
<td>34.1 ± 11.9</td>
<td>38.1 ± 12.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age of symptom onset, Mean ± SD (year)</td>
<td>27.4 ± 10.1</td>
<td>30.2 ± 11.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of axial symptoms Mean ± SD(year)</td>
<td>16.5 ± 11.1</td>
<td>15.3 ± 11.1</td>
<td>0.18</td>
</tr>
<tr>
<td>Delay in diagnosis, Mean ± SD (year)</td>
<td>6.9 ± 8</td>
<td>8.6 ± 9.2</td>
<td>0.009</td>
</tr>
<tr>
<td>Family history</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family history of AS, n (%)</td>
<td>207 (36.9%)</td>
<td>50 (19.5%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Family history of psoriasis, n (%)</td>
<td>15 (2.7%)</td>
<td>9 (3.5%)</td>
<td>0.5</td>
</tr>
<tr>
<td>Family history of uveitis, n (%)</td>
<td>12 (3.7%)</td>
<td>2 (1.3%)</td>
<td>0.13</td>
</tr>
<tr>
<td>Family history of IBD, n (%)</td>
<td>8 (2.5%)</td>
<td>4 (2.5%)</td>
<td>0.99</td>
</tr>
<tr>
<td>Peripheral arthritis, n (%)</td>
<td>249 (44.4%)</td>
<td>112 (43.6%)</td>
<td>0.83</td>
</tr>
<tr>
<td>Enthesitis, n (%)</td>
<td>222 (39.6%)</td>
<td>110 (42.8%)</td>
<td>0.4</td>
</tr>
<tr>
<td>Psoriasis, n (%)</td>
<td>14 (2.5%)</td>
<td>14 (5.4%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Uveitis, n (%)</td>
<td>135 (24.1%)</td>
<td>27 (10.5%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IBD, n (%)</td>
<td>14 (2.5%)</td>
<td>24 (9.3%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dactylitis, n (%)</td>
<td>39 (7%)</td>
<td>27 (10.5%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Current biologic use, n (%)</td>
<td>168 (29.9%)</td>
<td>73 (28.4%)</td>
<td>0.6</td>
</tr>
<tr>
<td>Ever biologic use, n (%)</td>
<td>183 (32.6%)</td>
<td>79 (30.7%)</td>
<td>0.6</td>
</tr>
<tr>
<td>Hip prothesis, n (%)</td>
<td>25 (4.5%)</td>
<td>9 (3.5%)</td>
<td>0.52</td>
</tr>
<tr>
<td>Elevated CRP, n (%)</td>
<td>353 (62.9%)</td>
<td>135 (52.5%)</td>
<td>0.005</td>
</tr>
<tr>
<td>CRP Mean ± SD (mg/l)</td>
<td>21.9 ± 26.2</td>
<td>18 ± 25.6</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>ESR, Mean ± SD (mm/h)</td>
<td>BASDAI, Mean ± SD</td>
<td>BASFI, Mean ± SD</td>
</tr>
<tr>
<td>--------------------------</td>
<td>-----------------------</td>
<td>-------------------</td>
<td>-----------------</td>
</tr>
<tr>
<td></td>
<td>33 ± 25.6</td>
<td>3.7 ± 2.4</td>
<td>2.9 ± 2.7</td>
</tr>
<tr>
<td></td>
<td>29.3 ±23.9</td>
<td>3.9 ± 2.3</td>
<td>3 ± 2.6</td>
</tr>
<tr>
<td></td>
<td>0.06</td>
<td>0.22</td>
<td>0.57</td>
</tr>
</tbody>
</table>

**Disclosure:** H. Yarkan, None; Z. Li, None; G. Kenar, None; S. Capar, None; F. Çapa, None; R. Steffensen, None; S. Akar, None; D. Solmaz, None; P. Cetin, None; B. Zengin, None; E. D. Guzman, None; K. Cremin, None; G. Can, None; Z. Yüce, None; I. Sari, None; F. Onen, None; M. Brown, None; N. Akkoc, None.


Abstract Number: 1515

**Improvements in Enthesitis Scores with Certolizumab Pegol Treatment in Males and Females with Active Axial Spondyloarthritis Are Maintained to Week 204**

Maxime Dougados¹, Philip J Mease², Joachim Sieper³, Peter C. Taylor⁴, Natasha de Peyrecave⁵, Tommi Nurminen⁶ and Jürgen Braun⁷, ¹Rheumatology Department, Paris-Descartes University and Cochin Hospital, Paris, France, ²Swedish Medical Center and University of Washington, Seattle, WA, ³Charité University Hospital, Berlin, Germany, ⁴Nuffield Dept. of Orthopaedics, Rheumatology and Musculoskeletal, Sciences, Kennedy Institute of Rheumatology, University of Oxford, Oxford, United Kingdom, ⁵UCB Pharma, Slough, United Kingdom, ⁶UCB Pharma, Monheim, Germany, ⁷Rheumazentrum Ruhrgebiet, Herne, Germany

**First publication:** September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017

Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM

**Background/Purpose:** Axial spondyloarthritis (axSpA), characterized by spinal inflammation, is also associated with extra-spinal manifestations including inflammation of the entheses (enthesitis). Enthesitis is equally prevalent throughout the axSpA disease spectrum and can severely reduce patients’ (pts) quality of life. RAPID-axSpA (NCT01087762) was a long-term, phase 3 study in axSpA pts with/without radiographic sacroiliitis treated with certolizumab pegol (CZP). Here we report improvements in tenderness at enthesal sites in males and females with axSpA treated with CZP for <4 years.

**Methods:** RAPID-axSpA was double-blind and placebo (PBO)-controlled to Wk24, dose-blind to Wk48 and open-label to Wk204. Pts fulfilled ASAS axSpA classification criteria with/without radiographic sacroiliitis (AS/nr-
axSpA) and had active disease. Enthesitis was assessed by the Maastricht Ankylosing Spondylitis Enthesitis Score (MASES; count of 0–13 tender sites)\(^1\) at baseline (BL) and through to study completion/early withdrawal. Data are shown for all pts randomized to CZP (200 mg Q2W/400 mg Q4W) at BL, or where noted, for those reporting tenderness at BL. Observed case (OC) data are reported, with last observation carried forward (LOCF) imputation used where noted. Model-based analyses were run to evaluate effects independently associated with MASES outcomes (data not shown).

**Results:** Of 218 pts (83 female, 135 male) randomized to CZP at Wk0, 148 (67.9%) exhibited ≥1 tender site (MASES ≥1) at BL (AS: 78/121 [64.5%]; nr-axSpA: 70/97 [72.2%]). AxSpA females had mean (SD) MASES of 4.8 (4.0) at BL, with 84.3% reporting ≥1 tender site, compared to 57.8% for axSpA males whose mean (SD) was 2.7 (3.3). BL data were similar for AS and nr-axSpA females: 28/33 (84.8%) AS pts and 42/50 (84.0%) nr-axSpA pts reported ≥1 tender site and mean MASES = 4.6 and 4.9, respectively. At Wk204, mean MASES (OC/LOCF) was reduced to 1.0/1.1 (AS) and 2.0/2.5 (nr-axSpA). In males, mean MASES at BL = 2.4 (AS), 3.1 (nr-axSpA); Wk204 = 0.7/0.8 (AS), 0.6/0.7 (nr-axSpA). No notable differences were observed between enthesal sites in the resolution of tenderness at Wks24 and 204, with resolution in 70.5–83.6% sites affected at BL by Wk204 (Table). New onset of tenderness was rare: 1/107 pts (0.9%) without Achilles tenderness at BL reported tenderness at Wk204 (observed data).

**Conclusion:** In CZP-treated males and females across the broad axSpA spectrum with enthesal tenderness, improvements were maintained in all MASES sites. Females reported higher BL MASES than males. Improvements in MASES at Wk204 were greater for AS females than AS males, and were similar in both genders for nr-axSpA pts. A high percentage of pts with positive BL MASES at a particular site achieved total resolution in the affected area by Wk24, which was maintained to Wk204.

**References:**


**Table:** Resolution of tenderness in enthesal sites at Weeks 24 and 204, in patients randomized to CZP at baseline in the RAPID-axSpA trial

<table>
<thead>
<tr>
<th>AxSpA (n=218)</th>
<th>AS (n=121)</th>
<th>nr-axSpA (n=97)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Enthesal site</strong></td>
<td><strong>Absence of enthesitis at BL</strong></td>
<td><strong>Absence of enthesitis at BL</strong></td>
</tr>
<tr>
<td></td>
<td><strong>n (%)</strong></td>
<td><strong>n (%)</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Wk 24</strong></td>
<td><strong>Wk 204</strong></td>
</tr>
<tr>
<td><strong>MASES ≥1 at baseline (any site)</strong></td>
<td>148</td>
<td>75 (50.7)</td>
</tr>
<tr>
<td><strong>Achilles tendon</strong></td>
<td>52</td>
<td>32 (61.5)</td>
</tr>
<tr>
<td><strong>Anterior superior iliac spine</strong></td>
<td>61</td>
<td>40 (65.6)</td>
</tr>
<tr>
<td><strong>Costochondral 1</strong></td>
<td>61</td>
<td>36 (59.0)</td>
</tr>
<tr>
<td><strong>Costochondral 7</strong></td>
<td>61</td>
<td>38 (62.3)</td>
</tr>
<tr>
<td><strong>Iliac crest</strong></td>
<td>61</td>
<td>56 (69.1)</td>
</tr>
<tr>
<td><strong>L5 spinous process</strong></td>
<td>77</td>
<td>49 (63.6)</td>
</tr>
<tr>
<td><strong>Posterior iliac spine</strong></td>
<td>91</td>
<td>63 (69.2)</td>
</tr>
</tbody>
</table>

Week 24 and 204 data use LOCF imputation. Combined Wk0 CZP 200 mg Q2W+400 mg Q4W data for patients with baseline enthesitis. Presence of enthesitis defined as tenderness at either contralateral site. Absence of enthesitis defined as MASES = 0, or as the absence of tenderness at the affected site where individual sites are reported. BL: Baseline; L5: Fifth lumbar vertebral body.
Disclosure: M. Dougados, Abbvie, Pfizer, Eli Lilly, Merck, Novartis, 5, Abbvie, Pfizer, Eli Lilly, Merck, Novartis, 2; P. J. Mease, AbbVie, Amgen, BMS, Celgene, Janssen, Eli Lilly, Merck, Novartis, Pfizer, Sun, UCB Pharma, Zynerba, 5, AbbVie, Amgen, BMS, Celgene, Janssen, Eli Lilly, Novartis, Pfizer, Sun, UCB Pharma, 2, AbbVie, Amgen, BMS, Celgene, Genentech, Janssen, Novartis, Pfizer, UCB Pharma, 8; J. Sieper, Abbott, Merck, Pfizer, UCB Pharma, Novartis, Eli Lilly, Janssen, 5, AbbVie, Merck, Pfizer, UCB Pharma, Novartis, Eli Lilly, Janssen, 8; P. C. Taylor, AbbVie, Biogen, GSK, Janssen, Eli Lilly, Novartis, Pfizer, Sanofi, UCB Pharma, 5, Abide Therapeutics, Galapagos, Janssen, Eli Lilly, UCB Pharma, 2; N. de Peyrecave, UCB Pharma, 3; T. Nurminen, UCB Pharma, 3; J. Braun, Abbott, BMS, Celgene, Celltrion, Chugai, Johnson & Johnson, MSD, Novartis, Pfizer, Roche, UCB Pharma, 5, Abbott, BMS, Celgene, Celltrion, Chugai, Johnson & Johnson, MSD, Novartis, Pfizer, Roche, UCB Pharma, 2.


Abstract Number: 1516

Effectiveness of Certolizumab Pegol in Patients with Uveitis Associated to Spondyloarthritis Refractory to Other Tumour Necrosis Factor Inhibitors

M. Victoria Hernández1, Marina Mesquida1, Victor Llorens2, Maite Sainz de la Maza2, Ricardo Blanco3, Vanesa Calvo4, Olga Maiz5, Ana Blanco6, Ana Urruticoechea-Arana7, Juan Ramon De Dios8, Pilar Ahijado-Guzman9, Enrique Judez10, Patricia Tejón11, M Soledad Peña12, Francisca Sivera13, Alfredo Adan1 and Raimon Sanmarti14, 1Hospital Clinic. Barcelona. Spain, Barcelona, Spain, 2Ophthalmology Department. Hospital Clínic of Barcelona, Barcelona, Spain, 3Rheumatology, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, 4Rheumatology Department. Hospital Universitario Marqués de Valdecilla., Santander, Spain, 5Hospital Donostia. Spain, San Sebastian, Spain, 6Ophthalmology Department. Hospital Donostia, San Sebastian, Spain, 7Rheumatology Department. Hospital Can Misses, IBIZA, Spain, 8Rheumatology Department. Hospital Universitario de Araba, Vitoria, Spain, 9Rheumatology Unit. Fuenlabrada’s Hospital, Madrid, Madrid, Spain, 10Rheumatology Department. Hospital de Albacete, Albacete, Spain, 11Rheumatology Department. Hospital Universitario General de Castellón, Castellon, Spain, 12Ophthalmology Department. Hospital Universitario General de Castellón, Castellon, Spain, 13Sección de Reumatología, Hospital General Universitario de Elda., Elda, Spain, 14Arthritis Unit, Rheumatology Dpt, Hospital Clinic of Barcelona, Barcelona, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthopathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Uveitis is a common extra-articular manifestation in patients with spondyloarthritis (SpA) requiring, in most severe cases, the use of biological therapy, especially tumour necrosis factors inhibitors (TNFi). Currently, the most frequently TNFi used are infliximab and adalimumab. However, in cases of failure or adverse events related to these drugs, other TNFi (with indication for SpA patients) such as certolizumab pegol (CZP) could be an effective option
for both uveitis and SpA control, as we have previously reported (1). Our purpose is to analyze the effectiveness and
safety profile of CZP in patients with SpA-associated- uveitis refractory to previous immunosuppressive or
biological therapy.

Methods:
Observational, multicentric, retrospective study. Inclusion criteria were: patients with SpA and with a diagnosis of
uveitis (confirmed by an Ophtalmologist) as main extra-articular SpA manifestation, refractory to previous
immunosuppressive or biological agents and who received CZP for at least 6 months. Variables analyzed: age, sex,
diagnosis, type of uveitis, duration since the first uveitis episode and number of eyes affected; previous treatment
(NSAID, disease-modifying anti-rheumatic drugs (DMARDs), immunosuppressive, biological therapy); outcome
and time to follow-up.

Results:
Twenty-two eyes of 13 patients (10 men); age 50.4 ± 11.7 (range 29-71 years) were included in the study. Diagnosis
were: ankylosing spondylitis (n=7), psoriatic arthritis (n=4), non-radiographic axial SpA (n=1) and SpA associated
to inflammatory bowel disease (n=1). Type of uveitis: 14 anterior (63.6%), 6 panuveitis (27.2%), and 2 intermediate
uveitis (9.1%). Mean disease duration was 161.7 ± 138.5 months (range 5-420). 84.6% patients had previously
received biological therapy (53.8% > 2 biological agents). 69.2% received CZP in monotherapy and 5 patients
received concomitant treatment: 4 methotrexate and 1 azathioprine. In all cases CZP was started due to inefficacy to
previous treatment except for 2 cases whose primary reason was the concurrence of adverse events or intolerance.
After a follow-up of 17.8 ± 9.9 months (range 6-39), 8 patients are still on CZP treatment. Thirteen eyes showed
improvement of visual acuity (59.1%), 7 remained stable and 2 worsened. During the follow-up no serious adverse
events were reported. Five cases withdrew CZP treatment: 2 due to worsening of articular symptoms but with no
uveitis activity; 1 due to persistence of macular edema and 2 due to uveitis activity. Two patients switched to
infliximab, one to golimumab, one to adalimumab and one required switch to tocilizumab due to persistence of
macular edema. In all 13 patients except 2, CZP achieved a good control of SpA activity.

Conclusion:
CZP demonstrates moderate effectiveness in patients with SpA-associated-uveitis refractory to previous TNFi
treatment, with a good safety profile.


Disclosure: M. V. Hernández, None; M. Mesquida, None; V. Llorens, None; M. Sainz de la Maza, None; R.
Blanco, None; V. Calvo, None; O. Maíz, None; A. Blanco, None; A. Urruticoechea-Arana, None; J. R. De Dios,
None; P. Ahijado-Guzman, None; E. Judez, None; P. Tejón, None; M. S. Peña, None; F. Sivera, None; A. Adan,
AbbVie, Santen and Allergan, 9; R. Sanmarti, None.

Effectiveness and Retention Rate of Certolizumab Pegol in Spondyloarthritis. Real Life Data

Rosa Expósito1, Carlos M Gonzalez2, Rosa García-Portales3, Ana Urruticoechea-Arana4, Jose Ramon Lamua5,
Maria del Pilar Navarro6, José Santos Rey Rey7 and Manuel Fernández8, 1Rheumatology, Hospital Comarcal de
Laredo. Spain, Laredo, Spain, 2Rheumatology, Hospital general Universitario Gregorio Marañón, Madrid, Spain,
SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Spondyloarthopathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Certolizumab pegol (CZP) is available for patients with spondyloarthritis (SpA), including ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axialSpA). CZP has a different molecular structure, the only Fc free PEGylated antiTNF and monovalent. Thus, CZP represents an alternative for solution NSAIDs refractory patients suffering with SpA.

Objective: To evaluate the effectiveness and safety of CZP in a real word setting in SpA patients.

Methods: Multicentric cohort of SpA patients treated with CZP according to routine clinical practice. The study was approved by the local Ethics Committee. Maximum follow-up was 12 months. Clinical response was evaluated through BASDAI, ASDAS,BASFI and MASES scores. Safety variables: discontinuation rate.

Results: 336 patients with axSpA were included: 56.5% male, mean age 45.8 (±12.1) years, median disease time 4.3 (range 0, 49.5) years, 68.5% HLAB27 positive, never smokers 64.7%. Prior bDMARD exposure: (27.2% none; 37.9% 1, 35% ≥2). At baseline, 36.8% had concomitant csDMARDs. Mean duration on treatment with CZP was 10.3 months. 31.8% of patients had peripheral arthritis and 42.7% enthesitis at baseline.

Statistically significant differences in BASDAI, BASFI, ASDAS and MASES were observed at the last visit comparing with baseline (Table 1). In the last observation, 41.0% of the patients achieved BASDAI50, 34% were in ASDAS remission (ASDAS<1.3) and 49% presented a minimal clinical response (ΔASDAS≥ 1.1). Percentage of patients with enthesitis at baseline (42.9%) was reduced to 16.8% at the end of the observation. Finally, 46.3% had resolution of the enthesitis (MASES=0)

Table 1. Evolution of the disease activity variables.

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Last visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>BASDAI evolution</td>
<td>6,2±1.6</td>
<td>3,9±2.2 *</td>
</tr>
<tr>
<td>BASFI evolution</td>
<td>5,6±2.1</td>
<td>3,7 ±2.3 *</td>
</tr>
<tr>
<td>ASDAS evolution</td>
<td>3.7±2.7</td>
<td>2,4 ±2.2 *</td>
</tr>
<tr>
<td>MASES score</td>
<td>3,9 ±2.7</td>
<td>1,2 ±1.8 *</td>
</tr>
</tbody>
</table>

*p<0,001, Wilcoxon’s test

According to Kaplan-Meier analysis, the drug survival of CZP is 83.3% (Figure1), and similar retention rates were observed independently if CZP were used as monotherapy (82.9%) or in combination with csDMARDs (82.6%).

Figure 1.
56/336 (16.7%) withdrawn CZP treatment: 34/336 (10.1%) due to lack of efficacy, 16/336 (4.8%) due to adverse event and 6/336 (1.8%) for other reason. Serious adverse event was found in 23/336 (6.8%) patients.

**Conclusion:** Real life experience from this nationwide rheumatology study, demonstrated the effectiveness and safety of CZP in patients with SpA, with a significant reduction of BASDAI, BASFI, ASDAS and MASES scores.

*This publication has been possible thanks to a grant of UCB Pharma to the technical companies which have been managing the data collection and the statistical analyses. The results are independent of UCB Pharma.*

**Disclosure:** R. Expósito, None; C. M. Gonzalez, MSD, Celgene, Novartis, Abbvie, Janssen, 5,MS, Celgene, Novartis, UCB, Janssen, 8; R. García-Portales, UCB Pfizer, Roche, 8,Celgene, 5; A. Urruticoechea-Arana, None; J. R. Lamua, None; M. D. P. Navarro, None; J. S. Rey Rey, UCB, Abbvie, Pfizer BMS, Roche, Celgene, 8; M. Fernández, None.

**Abstract Number:** 1518

**Certolizumab Pegol Effectiveness and Retention Rate in Psoriatic Arthritis. Real Life Data**

Arantxa Conesa¹, Manuel Fernández², Rosa Expósito³, Jose Campos⁴, Jose Ramon Lamua⁵, Maria del Pilar Navarro⁶, Paula Rubio-Muñoz⁷, Pilar Ahijado-Guzman⁸ and **Carlos M Gonzalez**⁹, ¹Hospital Clínico Universitario de Valencia, Valencia, Spain, ²Hospital Universitario de Guadalajara, Guadalajara, Spain, ³Rheumatology, Hospital Comarcal de Laredo. Spain, Laredo, Spain, ⁴Rheumatology, Hospital Universitario Puerta de Hierro Majadahonda, Madrid, Spain, ⁵Hospital del Henaes, Madrid, Spain, ⁶Hospital de Fuenlabrada, Fuenlabrada, Spain, ⁷Rheumatology, Hospital Universitari Germans Trias i Pujol, Badalona, Spain, ⁸Rheumatology Unit. Fuenlabrada’s Hospital, Madrid, Madrid, Spain, ⁹Rheumatology, Hospital General Universitario Gregorio Marañón, Madrid, Spain

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B  
Session Time: 9:00AM-11:00AM

Background/Purpose: To evaluate the effectiveness and safety of Certolizumab Pegol (CZP) in a real world setting in Psoriatic Arthritis (PsA) patients.

Methods: Multicentric cohort of PsA patients treated with CZP according to routine clinical practice. Study approved by local Ethics Committee. Maximum time of observation is 12 months. Effectiveness variables: SJC, TJC, PtGA, PhGA and DAS28-CRP. Safety variables: discontinuation rate.

Results: 262 patients with PsA were included: 43.5% male, mean (SD) age 49.9 (±11.9) years, median disease duration 5.0 (0, 40.2) years, 14.9% of patients were HLAB27 positive, BMI (kg/m²) 26.9 (±4.7) and never smokers 70.3%. Regarding extra-articular manifestations ever: Psoriasis (90%; PASI≥10 4.9%), enthesitis (44.4%), dactylitis (41.9%), nail disease (32%), inflammatory bowel diseases (4.9%). 37.3% of the PsA patients had erosions and a 3% arthritis mutilans (N=8). 48.9% patients received 1 prior csDMARDs and 52.1% at least 2 csDMARDs. Prior bDMARD received (28.4% none; 38.1% 1, 33.5% ≥2). 29.6% of PsA patients received CZP in monotherapy. Mean duration on treatment with CZP 10 m (78.2%).

Statistically significant differences in SJC, TJC and DAS28[CRP] were observed at the last visit comparing with baseline (Table 1). In the last observation, 47.1% of the patients had a DAS28 response (reduction of ≥1.2 from baseline). The percentage of patients with enthesitis at baseline (25.4%) was reduced to 9.5% at the end of the observation; 73.2% of the patients had a total resolution of the enthesitis (MASES=0). The percentage of patients with dactylitis at baseline (29.1%) decreased to 8.6% in the last observation; 82.5% of these patients had a total resolution of the dactylitis.

Table 1. Evolution of clinical variables of activity

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Last observation</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAS28-crp; mean±SD</td>
<td>4.6±0.9 (N=210)</td>
<td>3.8±1.0 (N=132)*</td>
</tr>
<tr>
<td>TJC evolution; mean±SD</td>
<td>7.2±5.1 (N=228)</td>
<td>4.0±4.0 (N=188)*</td>
</tr>
<tr>
<td>SJC evolution; mean±SD</td>
<td>5.0±3.7 (N=212)</td>
<td>2.8±2.8 (N=137)*</td>
</tr>
</tbody>
</table>

*p<0.001, Wilcoxon’s test

The drug survival of CZP is 78.2% (Figure1), and similar retention rates were observed independently if CZP were used as monotherapy (79.2%) or in combination with DMARDs (78.9%).

Figure 1.
262 patients were included in the safety analysis, 21.8% withdrawn treatment: 12.6% due to lack of efficacy, 5.3% due to intolerance and 3.8% other reasons.

**Conclusion:** Real life experience from this nationwide study, demonstrated the effectiveness and safety of CZP in PsA patients (bionaive only: 28.4%), with a significant reduction of DAS28, enthesitis and dactilytis. CZP survival seems to be similar regardless of csDMARDs concomitant use.

This publication has been possible thanks to a grant of UCB Pharma to the technical companies which have been managing the data collection and the statistical analyses. The results are independent of UCB Pharma.

**Disclosure:** A. Conesa, None; M. Fernández, None; R. Expósito, None; J. Campos, None; J. R. Lamua, None; M. D. P. Navarro, None; P. Rubio-Muñoz, None; P. Ahijado-Guzman, None; C. M. Gonzalez, MSD, Celgene, Novartis, Abbvie, Janssen, 5, MSD, Celgene, Novartis, Janssen, UCB Pharma, 8.


**Abstract Number:** 1519

**Certolizumab Pegol Effectiveness in Radiographic and Non-Radiographic Axial Spondyloarthritis. a Nationwide Study**

**Carlos M Gonzalez**1, Rosa Expósito2, Rosa García-Portales3, Ana Urruticoechea-Arana4, Jose Ramon Lamua5, María del Pilar Navarro6, José Santos Rey Rey7, Manuel Fernández8 and Mercedes Morcillo9, 1Rheumatology, Hospital general Universitario Gregorio Marañón, Madrid, Spain, 2Rheumatology, Hospital Comarcal de Laredo. Spain, Laredo, Spain, 3Rheumatology, Hospital Virgen de la Victoria, Málaga, Spain, 4Rheumatology Department. Hospital Can Misses, IBIZA, Spain, 5Hospital del Henares, Madrid, Spain, 6Hospital de Fuenlabrada, Fuenlabrada, Spain, 7Hospital Virgen de la Salud, Toledo, Spain, 8Guadalajara, Guadalajara, Spain, 9Rheumatology, Hospital El Escorial, San Lorenzo de el Escorial, Spain

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017
**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
**Session Type:** ACR Poster Session B
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Certolizumab pegol (CZP) is a PEGylated Fab’ fragment of a humanized anti-TNF antibody with high affinity to TNF. RAPID-axSpA trial investigated the efficacy and safety of CZP in patients with axSpA, including ankylosing spondylitis (AS) and non-radiographic (nr)-axSpA, and has shown CZP to improve the signs and symptoms of axSpA over 4 years.

Objective: To investigate the effectiveness of CZP in a real word setting in axSpA patients including AS and nr-axSpA.

**Methods:** Multicentric cohort of axial spondyloarthritis patients treated with CZP according with the clinical practice. Study was approved by local Ethics Committee. Maximum time of observation is 12 months. Clinical response was assessed by BASDAI and ASDAS.

**Results:**
336 patients with axSpA were included and 333 were classified: 228 (68.5%) patients with AS, 95 (28.5%) patients with nr-axSpA and 10 (3%) patients with peripheral SpA. The baseline characteristics of the patients are shown in Table 1.

Table 1. Baseline demographic and clinical characteristics of the patients with ankylosing spondyloarthritis and patients with non-radiographic axial SpA.

<table>
<thead>
<tr>
<th></th>
<th>AS</th>
<th>nr-axSpA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean, yr)</td>
<td>46.4±11.9 (N=207)</td>
<td>43.8±12.1 (N=77)</td>
</tr>
<tr>
<td>Male sex</td>
<td>63.2% (N=228)</td>
<td>45.3% (N=95)</td>
</tr>
<tr>
<td>Evolution of the disease (median, yr)</td>
<td>5.6 (N=207)</td>
<td>2.2 (N=77)</td>
</tr>
<tr>
<td>Never smokers</td>
<td>75.1% (N=201)</td>
<td>80.2% (N=86)</td>
</tr>
<tr>
<td>HLA-B27 positive</td>
<td>73.7% (N=190)</td>
<td>59.7% (N=72)</td>
</tr>
<tr>
<td>Uveitis ever</td>
<td>30.2% (N=159)</td>
<td>11.7% (N=60)</td>
</tr>
<tr>
<td>Peripheral arthritis</td>
<td>25% (N=228)</td>
<td>37.9% (N=95)</td>
</tr>
<tr>
<td>Enthesitis</td>
<td>43.6% (N=133)</td>
<td>45.9% (N=74)</td>
</tr>
<tr>
<td>Biologics treatment previous</td>
<td>(N=165)</td>
<td>(N=65)</td>
</tr>
<tr>
<td>0</td>
<td>23.0%</td>
<td>32.3%</td>
</tr>
<tr>
<td>1</td>
<td>40.0%</td>
<td>35.4%</td>
</tr>
<tr>
<td>&gt;1</td>
<td>36.9%</td>
<td>32.3%</td>
</tr>
<tr>
<td>BASDAI mean±SD 0-10 NRS</td>
<td>6.3±1.6 (N=190)</td>
<td>5.9±1.4 (N=73)</td>
</tr>
<tr>
<td>BASFI mean±SD</td>
<td>5.9±2.0 (N=164)</td>
<td>4.9±2.0 (N=61)</td>
</tr>
<tr>
<td>ASDAS mean</td>
<td>3.9±2.6 (N=227)</td>
<td>3.1±2.6 (N=95)</td>
</tr>
<tr>
<td>CRP mean (mg/L)</td>
<td>12.1 (N=227)</td>
<td>9.0 (N=95)</td>
</tr>
<tr>
<td>Treatment with NSAIDs</td>
<td>83.0% (N=206)</td>
<td>84.4% (N=77)</td>
</tr>
<tr>
<td>Treatment with DMARDs</td>
<td>35.9% (N=206)</td>
<td>35.0% (N=77)</td>
</tr>
</tbody>
</table>

No statistically significant differences were observed in BASDAI and ASDAS between both subpopulation (AS and nr-axSpA) (Table 2). In the last visit of the patients, BASDAI50 was observed in 39.7% of AS patients and 44.6% of nr-axSpA. 29.1% and 45.7% of the patients presented ASDAS remission within the AS and nr-axSpA population, respectively.

Table 2. Evolution of clinical variables of activity

<table>
<thead>
<tr>
<th></th>
<th>AS</th>
<th>nr-axSpA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Last visit</td>
</tr>
<tr>
<td>BASDAI evolution</td>
<td>6.3±1.6 (N=190)</td>
<td>3.9±2.2 (N=190)</td>
</tr>
<tr>
<td>ASDAS evolution</td>
<td>3.9±2.6 (N=227)</td>
<td>2.6±2.4 (N=227)</td>
</tr>
<tr>
<td>CRP mean</td>
<td>12.1 (N=227)</td>
<td>6.8 (N=334)</td>
</tr>
</tbody>
</table>

Conclusion:
In this nationwide real-life study, effectiveness of CZP was demonstrated in both Radiographic and Non-Radiographic Axial Spondyloarthritis.

This publication has been possible thanks to a grant of UCB Pharma to the technical companies which have been managing the data collection and the statistical analyses. The results are independent of UCB Pharma.

Disclosure: C. M. Gonzalez, MSD, Celgene, Novartis, Abbvie, Janssen, 5, MSD, Celgene, Novartis, UCB, Janssen, 8; R. Expósito, None; R. García-Portales, UCB, Pfizer, Roche, 8, Celgene, 5; A. Urruticoechea-Arana, None; J. R. Lamua, None; M. D. P. Navarro, None; J. S. Rey Rey, UCB, Abbvie, Pfizer, BMS, Roche, Celgene, 8; M. Fernández, None; M. Morcillo, Pfizer Inc, UCB, Janssen, 8.

Abstract Number: 1520

**Golimumab Retention Rate in Patients with Spondyloarthritis. Differences between Ankylosing Spondylitis and Non-Radiographic Axial Spondyloarthritis**

Belen Serrano¹, Carlos M Gonzalez², Roberto González³, Julia Martínez-Barrio⁴, Juan Gabriel Ovalles-Bonilla⁵, Juan Carlos Nieto⁵, Iustina Janta², Larissa Valor³, Francisco Javier López Longo⁶ and Indalecio Monteagudo², ¹Rheumatology, Hospital General Universitario Gregorio Marañón, Genoa, Italy, ²Rheumatology, Hospital General Universitario Gregorio Marañón, Madrid, Spain, ³Rheumatology, Hospital general Universitario Gregorio Marañón, Madrid, Spain, ⁴Servicio de Reumatología, Hospital General Universitario Gregorio Marañón, Madrid, Spain, ⁵Instituto de Investigación Sanitaria Gregorio Marañón, Madrid, Spain, ⁶Facultad de Medicina, Universidad Complutense de Madrid, Madrid, Spain

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The efficacy of Golimumab (GLM) treatment in spondyloarthritis (SpA) has been widely documented. The aim of this study was to analyze the long-term retention of GLM and to identify independent predictors of retention in patients with SpA.

Methods: Prospective monocentric cohort of SpA patients treated with GLM according with clinical practice. Study was approved by local Ethics Committee. Demographic and clinical variables were analyzed with Cox proportional hazard regression model.

Results: 105 patients were included, 49 (46.7%) Ankylosing Spondylitis (AS), 40 (38.1%) non-radiographic axial SpA (nr-AxSpA) and 16 (15.2%) peripheral SpA. The baseline characteristics of the patients are shown in Table 1. Mean follow-up time 23.8 months (SD 20.9). Mean survival time was 47.2 months (95% CI: 39.4-54.9). Age, gender, HLA-B27, radiographic or nr-AxSpA and previous biological use were significant in the univariate analysis. Concomitant DMARD had no influence on GLM retention rate (HR: 1.2; 95% CI: 0.6-2.4; p: 0.6).
Table 1. Baseline demographic and clinical characteristics of the patients.

<table>
<thead>
<tr>
<th></th>
<th>All (axial and peripheral SpA)</th>
<th>AS</th>
<th>nr-AxSpA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age -mean (SD)-years</td>
<td>45.1 (13.2)</td>
<td>51.1 (10.8)</td>
<td>39.8%</td>
</tr>
<tr>
<td>Male gender %</td>
<td>49.5%</td>
<td>61.2%</td>
<td>47.5%</td>
</tr>
<tr>
<td>Mean evolution time (SD) years</td>
<td>11.8 (12.3)</td>
<td>18.8 (10.1)</td>
<td>7.3 (10.3)</td>
</tr>
<tr>
<td>HLA-B27</td>
<td>69.6%</td>
<td>90.7%</td>
<td>52.6%</td>
</tr>
<tr>
<td>Uveitis</td>
<td>16.2%</td>
<td>24.5%</td>
<td>10.0%</td>
</tr>
<tr>
<td>Back pain -mean (SD)</td>
<td>7.5 (7.0)</td>
<td>6.5 (2.4)</td>
<td>9.1 (10.7)</td>
</tr>
<tr>
<td>BASDAI -mean (SD)</td>
<td>6.2 (1.6)</td>
<td>6.3 (2.1)</td>
<td>6.2 (1.2)</td>
</tr>
<tr>
<td>BASFI -mean (SD)</td>
<td>5.8 (2.3)</td>
<td>6.0 (2.4)</td>
<td>5.4 (2.1)</td>
</tr>
<tr>
<td>CRP mg/dl Mean (SD)</td>
<td>1.1 (1.7)</td>
<td>1.5 (2.1)</td>
<td>0.65 (1.4)</td>
</tr>
<tr>
<td>Concomitant DMARD %</td>
<td>29.8%</td>
<td>31.3%</td>
<td>7.5%</td>
</tr>
<tr>
<td>Biological Therapy naïve %</td>
<td>45.7%</td>
<td>30.6%</td>
<td>60%</td>
</tr>
</tbody>
</table>

Upon Cox regression analysis, patients with AS had significant better retention rate compared to nr-AxSpA (HR: 2.1; 95% CI: 1.1-4.2; p<0.035). There was a numerically better GLM retention rate in patients treated previously with less number of biologicals, but did not reach statistical significance. 39/105 (37%) withdraw GLM treatment. 26/39 (66,7%) due to lack of efficacy, 6/39 (15,4%) due to adverse events and 7/39 (17,5%) due to other reasons.

Conclusion: Real-world Golimumab retention rate in patients with Spondyloarthritis was good and did not depend on concomitant treatment with DMARD. Patients with Ankylosing Spondylitis had a better Golimumab retention rate than patients with non-radiological Axial Spondyloarthritis. A better retention rate was expected in patients who had previously used less biological, but was not found due probably to the low effectiveness of Golimumab in patients with non-radiological Axial Spondyloarthritis.

Disclosure: B. Serrano, None; C. M. Gonzalez, MSD, Celgene, Novartis, Abbvie, Janssen, 5, MSD, Celgene, Novartis, Janssen, UCB Pharma, 8; R. González, None; J. Martínez-Barrio, None; J. G. Ovalles-Bonilla, Pfizer,
Impact of Time Since Diagnosis, Age, and Number of Prior Non-Steroidal Anti-Inflammatory Drugs on 52-Week Clinical Response to Adalimumab in Patients with Ankylosing Spondylitis

Joachim Sieper\textsuperscript{1}, Atul A. Deodhar\textsuperscript{2}, Maja Hojnik\textsuperscript{3}, Ying Zhang\textsuperscript{4} and Maxime Dougados\textsuperscript{5}, \textsuperscript{1}Charité Universitätsmedizin Berlin, Berlin, Germany, \textsuperscript{2}Oregon Health & Science University, Portland, OR, \textsuperscript{3}AbbVie, Ljubljana, Slovenia, \textsuperscript{4}AbbVie Inc., North Chicago, IL, \textsuperscript{5}René Descartes University and Hôpital Cochin, Paris, France

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Spondyloarthopathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Ankylosing spondylitis (AS) patients (pts) were found to respond better to TNF inhibitors (TNFi) if treated early in the disease course.\textsuperscript{1} The actual disease onset and hence disease duration is not always known. Previously, younger age was found to have the largest positive impact on clinical outcomes following 12 weeks (wks) of adalimumab (ADA) treatment.\textsuperscript{2} The objective of this analysis was to examine the impact of time since diagnosis, age, and number of prior NSAIDs as surrogates for disease duration on clinical outcomes in AS pts from ATLAS trial treated with ADA for 52 wks.

**Methods:** ATLAS\textsuperscript{3,4} was a phase 3 randomized double-blind placebo(PBO)-controlled trial evaluating the safety and efficacy of originator ADA in pts with active AS who failed NSAID therapy. In this post hoc analysis, pts who received at least one dose of ADA during the PBO-controlled period or open label extension and received prior NSAID(s) at baseline (BL) were categorized by BL: (1) time since diagnosis (<2 vs ≥2; <5 vs ≥5; <10 vs ≥10 years [y]), (2) age (<35, 35–45, and >45 y), and (3) number of prior NSAIDs (≤ 2 vs >2). The effect of time since diagnosis, age, and number of prior NSAIDs on AS outcome measures following 52 wks of ADA treatment was examined.

**Results:** At wk 52, 274 pts had received at least one dose of ADA and had at least one prior NSAID at BL. A majority of pts were ≥5 y since AS diagnosis (188 [68.6%]), ≤45 y of age (163 [59.5%]), HLA-B27+ (213 [77.7%]), and had ≤2 prior NSAIDs (158 [57.7%]). Pts with shorter time since diagnosis were generally younger (late thirties). Across all subcategories, >70% of pts were male. The BL disease activity measures were numerically similar across
most categories. Following 52 wks of ADA treatment, the proportions of pts achieving ASAS20 and ASAS40 responses were numerically higher and mean decreases in BASDAI and BASFI scores from BL larger in subcategories with shorter time since diagnosis, younger age, and fewer prior NSAIDs (Table). There were significant differences in ASAS40, BASDAI, and BASFI scores between time since diagnosis (<2 vs ≥2 and <5 vs ≥5 y) and age (<35 vs >45 y) subcategories.

Conclusions: Following 52 wks of ADA treatment, shorter time since diagnosis and younger age were associated with greater clinical responses and improvements in disease activity and functionality. Although younger age (<35 vs >45 y) had significant positive impact on the clinical outcomes similar to wk 12 results, shorter time since diagnosis (<2 vs ≥2 and <5 vs ≥5 y) was also associated with better 52-wk clinical outcomes. These results suggest that early effective treatment intervention may improve long-term clinical outcomes in AS pts.

References:


Table. Clinical Responses Following 52 Weeks of ADA Treatment in Patients Categorized by Time Since Diagnosis, Age, and Prior NSAID(s).

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>&lt;2 (n=53)</th>
<th>≥2 (n=217)</th>
<th>&lt;5 (n=186)</th>
<th>≥5 (n=188)</th>
<th>&lt;10 (n=126)</th>
<th>≥10 (n=128)</th>
<th>&lt;35 (n=76)</th>
<th>≥35 (n=87)</th>
<th>&lt;45 (n=111)</th>
<th>≥45 (n=118)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASAS20, n (%)</td>
<td>39 (73%)</td>
<td>103 (96%)</td>
<td>126 (61%)</td>
<td>133 (71%)</td>
<td>107 (82%)</td>
<td>82 (66%)</td>
<td>68 (83%)</td>
<td>61 (76%)</td>
<td>67 (70%)</td>
<td>71 (64%)</td>
</tr>
<tr>
<td>ASAS40, n (%)</td>
<td>25 (48%)</td>
<td>109 (41%)</td>
<td>104 (44%)</td>
<td>111 (60%)</td>
<td>96 (76%)</td>
<td>70 (59%)</td>
<td>65 (86%)</td>
<td>56 (66%)</td>
<td>61 (55%)</td>
<td>61 (53%)</td>
</tr>
<tr>
<td>ΔBASDAI, mean (SD)</td>
<td>-4.1 (2.8)</td>
<td>-3.9 (2.6)</td>
<td>-3.9 (2.5)</td>
<td>-3.9 (2.4)</td>
<td>-3.6 (2.7)</td>
<td>-2.9 (2.6)</td>
<td>-2.9 (2.4)</td>
<td>-3.7 (2.7)</td>
<td>-3.2 (2.0)</td>
<td>-3.2 (2.0)</td>
</tr>
<tr>
<td>ΔBASFI, mean (SD)</td>
<td>-2.6 (2.4)</td>
<td>-2.7 (2.2)</td>
<td>-2.7 (2.2)</td>
<td>-2.1 (2.0)</td>
<td>-2.4 (2.3)</td>
<td>-2.1 (2.0)</td>
<td>-2.7 (2.4)</td>
<td>-2.3 (1.9)</td>
<td>-2.0 (2.9)</td>
<td>-2.5 (2.1)</td>
</tr>
</tbody>
</table>

#values are based on Pearson’s Chi-square test for comparison. *P < 0.01; **P < 0.05; #P < 0.05.

Disclosure: J. Sieper, AbbVie, Lilly, Janssen, Merck, Novartis, Pfizer, Roche, Sun Pharma, and UCB, 2,AbbVie, Lilly, Janssen, Merck, Novartis, Pfizer, Roche, Sun Pharma, and UCB, 5,AbbVie, Lilly, Janssen, Merck, Novartis, Pfizer, Roche, Sun Pharma, and UCB, 9; A. A. Deodhar, AbbVie, Amgen, Eli Lilly, Glaxo-Smith-Kline, Merck-Sharp-Dohme, Novartis, Pfizer, Sun Pharma, and UCB, 2,AbbVie, Amgen, Eli Lilly, Glaxo-Smith-Kline, Merck-Sharp-Dohme, Novartis, Pfizer, Sun Pharma, and UCB, 5; M. Hojnik, Abbvie, 1,abbvie, 3; Y. Zhang, AbbVie, 3,AbbVie; 1; M. Dougados, AbbVie, Lilly, Merck, Novartis, Pfizer, Sanofi, and UCB, 2,AbbVie, Lilly, Merck, Novartis, Pfizer, Sanofi, and UCB, 5.


Abstract Number: 1522
Patients with Ankylosing Spondylitis Had Better Adalimumab Survival Than Patients with Non-Radiographic Axial Spondyloarthritis

Alper Sari¹, Berkan Armagan¹, Abdulsumet Erden², Levent Kilic¹², Omer Karadag²³, Ali Akdoğan¹, Umut Kalyoncu² and İhsan Ertenli¹, ¹Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Turkey, ²Department of Internal Medicine, Division of Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Turkey, ³Vasculitis and Lupus Clinic, Addenbrooke’s Hospital, University of Cambridge, Cambridge, United Kingdom
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Patients with ankylosing spondylitis had better adalimumab survival than patients with non-radiographic axial spondyloarthritis

Background/Purpose: Drug survival rate is generally accepted as a reliable indicator of both efficacy and safety profile of a biological DMARD. We aimed to evaluate survival rates of adalimumab (ADA) in ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nrAxSpA) patients registered in HUR-BIO (Hacettepe University Rheumatology Biologic Registry) and potential predictors of drug continuation.

Methods: HUR-BIO is a monocentric database of biologics including 1938 SpA patients by January 2017. All AS and nrAxSpA patients in HUR-BIO prescribed ADA at least once were enrolled in the study. Patients who were prescribed ADA within 6 months period before analysis defined as drug continuing. Reasons for ADA discontinuation were categorized as adverse events (AEs), inefficacy (primary and secondary) and others. Kaplan-Meier analysis was used to estimate ADA survival rates. Potential predictors of ADA continuation were evaluated using Cox proportional regression model in only AS patients due to small number of patients in nrAxSpA group.

Results: In total, 421 AS and 103 nrAxSpA patients were analyzed. Median duration of ADA usage was 14.5 (0-139.2) months in AS and 8.7 (0-84.2) months in nrAxSpA group. Baseline characteristics of patients were shown in Table 1. Among AS patients, ADA was discontinued due to inefficacy in 70 (30.4%) and adverse events in 39 (17.0%). The reason for ADA discontinuation was inefficacy in 28 (48.3%) and adverse events in 5 (8.6%) nrAxSpA patients. Figure 1 represents the Kaplan-Meier plots of ADA survival. Log-rank between AS and nrAxSpA patients was found as p=0.044. Cox proportional regression model failed to demonstrate any predictor of ADA discontinuation in AS patients.

Conclusion: In this single center biological SpA cohort, ADA had better drug survival in AS patients compared with nrAxSpA consistent with literature¹. Although certain factors such as uveitis, baseline increased acute phase reactants, and being biological naïve were associated with better ADA survival in univariate analysis, we could not demonstrate any predictors in Cox regression analysis.

References
<table>
<thead>
<tr>
<th></th>
<th>AS Continue (n=191)</th>
<th>AS Discontinue (n=230)</th>
<th>P</th>
<th>nrAxSpA Continue (n=44)</th>
<th>nrAxSpA Discontinue (n=59)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (min-max)</td>
<td>38.4 (18.0-65.9)</td>
<td>38.0 (12.0-65.9)</td>
<td>0.27</td>
<td>34.1 (17.1-63.4)</td>
<td>34.5 (17.0-51.3)</td>
<td>0.79</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>118 (61.8)</td>
<td>121 (52.6)</td>
<td>0.06</td>
<td>22 (50.0)</td>
<td>18 (30.5)</td>
<td>0.04</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>73 (38.2)</td>
<td>109 (47.4)</td>
<td></td>
<td>22 (50.0)</td>
<td>41 (69.5)</td>
<td></td>
</tr>
<tr>
<td>Disease duration, months</td>
<td>55.4 (1.2-475.6)</td>
<td>56.8 (1.5-431.8)</td>
<td>0.55</td>
<td>18.2 (1.6-104.8)</td>
<td>24.0 (1.3-182.9)</td>
<td>0.27</td>
</tr>
<tr>
<td>Disease duration ≥5 years, n</td>
<td>68 (35.6)</td>
<td>61 (26.5)</td>
<td>0.13</td>
<td>10 (22.7)</td>
<td>8 (13.5)</td>
<td>0.15</td>
</tr>
<tr>
<td>History of smoking, n (%)</td>
<td>115 (60.2)</td>
<td>113 (49.1)</td>
<td>0.13</td>
<td>22 (50.0)</td>
<td>31 (52.5)</td>
<td>0.79</td>
</tr>
<tr>
<td>History of uveitis, n (%)</td>
<td>34 (17.8)</td>
<td>22 (9.6)</td>
<td>0.03</td>
<td>4 (9.0)</td>
<td>7 (11.9)</td>
<td>0.65</td>
</tr>
<tr>
<td>Previous biologic use, n (%)</td>
<td>35 (18.3)</td>
<td>75 (76.1)</td>
<td>0.001</td>
<td>10 (22.7)</td>
<td>12 (20.3)</td>
<td>0.77</td>
</tr>
<tr>
<td>Baseline BASDAI</td>
<td>53 (0-94)</td>
<td>53 (0-94)</td>
<td>0.21</td>
<td>55 (8-91)</td>
<td>55 (9-92)</td>
<td>0.92</td>
</tr>
<tr>
<td>Baseline BASFI</td>
<td>38 (0-98)</td>
<td>46 (0-99)</td>
<td>0.09</td>
<td>45 (2-85)</td>
<td>45 (1-96)</td>
<td>0.87</td>
</tr>
<tr>
<td>Baseline back pain VAS</td>
<td>60 (0-100)</td>
<td>60 (5-100)</td>
<td>0.29</td>
<td>70 (0-90)</td>
<td>70 (1-90)</td>
<td>0.35</td>
</tr>
<tr>
<td>ESR, mm/h (min-max)</td>
<td>23 (2-120)</td>
<td>18 (0-120)</td>
<td>0.002</td>
<td>10 (2-69)</td>
<td>10 (2-97)</td>
<td>0.64</td>
</tr>
<tr>
<td>CRP, mg/dL (min-max)</td>
<td>1.37 (0.1-26.7)</td>
<td>1.20 (0.1-28.0)</td>
<td>0.013</td>
<td>0.52 (0.1-6.4)</td>
<td>0.60 (0.1-10.6)</td>
<td>0.95</td>
</tr>
<tr>
<td>ESR &gt; UL, n (%)</td>
<td>98 (51.3)</td>
<td>93 (40.4)</td>
<td>0.04</td>
<td>13 (29.5)</td>
<td>16 (27.1)</td>
<td>0.85</td>
</tr>
<tr>
<td>CRP &gt; UL, n (%)</td>
<td>118 (61.8)</td>
<td>134 (58.3)</td>
<td>0.58</td>
<td>14 (31.8)</td>
<td>23 (39.0)</td>
<td>0.44</td>
</tr>
<tr>
<td>Syndesmophits on X-ray, n (%)</td>
<td>56 (46.3)</td>
<td>65 (53.7)</td>
<td>0.06</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 1. ADA survival rates in AS and nrAxSpA patients

Disclosure: A. Sari, None; B. Armagan, None; A. Erden, None; L. Kilic, None; O. Karadag, None; A. Akdogan, None; U. Kalyoncu, None; I. Ertenli, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/patients-with-ankylosing-spondylitis-had-better-adalimumab-survival-than-patients-with-non-radiographic-axial-spondyloarthritis](http://acrabstracts.org/abstract/patients-with-ankylosing-spondylitis-had-better-adalimumab-survival-than-patients-with-non-radiographic-axial-spondyloarthritis)
Secukinumab Demonstrates Rapid and Sustained Efficacy in Ankylosing Spondylitis Patients with Normal or Elevated Baseline CRP Levels: Pooled Analysis of Two Phase 3 Studies

Jürgen Braun1, Joachim Sieper2, Robert B.M. Landewé3, Xenofon Baraliakos1, Corinne Miceli-Richard4, Ruvie Martin5, Brian Porter5, Kunal Gandhi5 and Désirée van der Heijde6, 1Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany, 2Charité University Medicine Berlin, Berlin, Germany, 3University of Amsterdam and Atrium Medical Center, Amsterdam, Netherlands, 4Department of Rheumatology, Hôpital Bicêtre, Paris, France, 5Novartis Pharmaceuticals Corporation, East Hanover, NJ, 6Leiden University Medical Center, Leiden, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Inhibition of IL-17A with secukinumab is an approved therapy for patients (pts) with AS.1 It has been previously reported that response rates with TNFα inhibitors (TNFi) are higher in AS pts with elevated baseline (BL) CRP levels;2-4 however, this relationship is unclear for IL–17A-inhibition. This post-hoc analysis assessed the response to secukinumab treatment in AS pts with normal or elevated BL CRP from the phase 3 MEASURE 1 and MEASURE 2 studies over 3 years.

Methods: The study designs of MEASURE 1 and 2 have been reported elsewhere.1 This analysis pooled data from all pts with available BL CRP levels in the 2 studies who received subcutaneous (s.c.) secukinumab 150 mg (approved dose; N = 197) or placebo (PBO; N = 195). Efficacy endpoints included ASAS20/40, BASDAI, BASDAI50, AS disease activity score (ASDAS) inactive disease, and ASAS partial remission (ASAS PR) in pts stratified by BL CRP as defined by the central lab: normal (<5 mg/L) or elevated (≥5 mg/L). Data are presented using non-responder imputation through Week (Wk) 16 and multiple imputation from Wk 20–156 for binary variables, and mixed-effect model repeated measure for all time points through Wk 156 for continuous variables.

Results: Overall, 36.5% (143/392) of pts with normal CRP and 63.5% (249/392) of pts with elevated CRP at BL were included in this pooled analysis. The proportion (36% and 64%) of pts with normal and elevated BL CRP was similar in the secukinumab 150 mg and PBO groups. BL demographic/clinical characteristics were balanced across the normal and elevated BL CRP groups (mean age ± SD: 43.8 ± 12.0 and 41.0 ± 12.5 years, mean time since diagnosis ± SD: 7.0 ± 8.7 and 7.2 ± 7.9 years, mean BASDAI ± SD: 6.7 ± 1.5 and 6.4 ± 1.5, respectively). At Wk 16, the ASAS20 and ASAS40 response rates were improved with secukinumab 150 mg vs PBO in pts with normal or elevated BL CRP (Figure and Table). The treatment effect of secukinumab 150 mg vs PBO at Wk 16 was significant in pts with a normal or elevated BL CRP for all other outcomes, except for ASAS PR in the normal BL CRP group (P = 0.07; Table). Results were sustained or further improved through 156 wks of secukinumab treatment in both groups.

Conclusion: Secukinumab 150 mg demonstrated efficacy in AS pts with either normal or elevated BL CRP, with greater magnitude of response in pts with elevated BL CRP.
### Table. Summary of Clinical Efficacy

<table>
<thead>
<tr>
<th>Clinical outcomes</th>
<th>Normal Baseline CRP (&lt;5 mg/L)</th>
<th>Elevated Baseline CRP (≥5 mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pooled secukinumab 150 mg s.c. (N = 72)</td>
<td>Pooled PBO (N = 71)</td>
</tr>
<tr>
<td><strong>ASAS20, %</strong></td>
<td>16</td>
<td>56.9§</td>
</tr>
<tr>
<td></td>
<td>156</td>
<td>61.3</td>
</tr>
<tr>
<td><strong>ASAS40, %</strong></td>
<td>16</td>
<td>34.7†</td>
</tr>
<tr>
<td></td>
<td>156</td>
<td>42.4</td>
</tr>
<tr>
<td><strong>BASDAI, mean change from baseline</strong></td>
<td>16</td>
<td>-2.2†</td>
</tr>
<tr>
<td></td>
<td>156</td>
<td>-2.7</td>
</tr>
<tr>
<td><strong>BASDAI50, %</strong></td>
<td>16</td>
<td>27.8§</td>
</tr>
<tr>
<td></td>
<td>156</td>
<td>40.4</td>
</tr>
<tr>
<td><strong>ASDAS inactive disease, %</strong></td>
<td>16</td>
<td>19.4‡</td>
</tr>
<tr>
<td></td>
<td>156</td>
<td>28.9</td>
</tr>
<tr>
<td><strong>ASAS PR, %</strong></td>
<td>16</td>
<td>12.5</td>
</tr>
<tr>
<td></td>
<td>156</td>
<td>14.4</td>
</tr>
</tbody>
</table>

*P < 0.0001; †P < 0.001; §P < 0.01; ‡P < 0.05 versus placebo; missing values were imputed as non-response at Week 16. Multiple imputation and MMRM presented at Week 156 included n = 56 and 103 in the normal baseline CRP and elevated baseline CRP groups, respectively. Multiple imputation and MMRM data included patients (87/125) who continued in the extension trial for MEASURE 1 and all patients for MEASURE 2 at Week 156. For BASDAI, LS mean change from baseline was presented using MMRM at Weeks 16 and 156. ASAS, Assessment of SpondyloArthritis international Society criteria; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; LS, least squares; MMRM, mixed-effect model repeated measures; N, number of patients with available baseline CRP (normal or elevated) included in this pooled analysis at Week 16; n, number of patients in this pooled analysis at Week 156; PBO, placebo; PR, partial remission.

**Disclosure:** J. Braun, AbbVie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wylem), Roche, Sanofi-Aventis, UCB, 2, AbbVie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wylem), Roche, Sanofi-Aventis, UCB, 5, AbbVie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wylem), Roche, Sanofi-Aventis, UCB, 8; J. Sieper, AbbVie Inc., Pfizer Inc., and Merck, 2, AbbVie Inc., Pfizer Inc., Merck, UCB, and Novartis, 5, AbbVie Inc., Pfizer Inc., Merck, and UCB, 8; R. B. M. Landewé, Abbott/AbbVie, Ablynx, Amgen, Astra-Zeneca, Bristol-Myers Squibb, Centocor,
Real-World Use of Secukinumab Among Biologic-Naïve and Biologic-Experienced Patients with Ankylosing Spondylitis in the United States

Kurt R. Oelke1, Rahul Garg2, Yunfeng Li3, Xing Liu4, Huanxue Zhou4 and Yujin Park3, 1Rheumatic Disease Center, Glendale, WI, 2PRO Unlimited, Inc, East Hanover, NJ, 3Novartis Pharmaceuticals Corporation, East Hanover, NJ, 4KMK Consulting, Inc, Morristown, NJ

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Secukinumab is a fully human anti–interleukin-17A monoclonal antibody approved for the treatment of patients with moderate to severe ankylosing spondylitis (AS). A limited number of studies have evaluated the use of secukinumab in a real-world setting since its approval in the United States on January 15, 2016. The objective of this analysis was to describe the demographic and clinical characteristics of patients with AS who were treated with secukinumab in routine clinical practice, stratified by previous biologic experience.

Methods: Retrospective data from the Symphony Health Solutions Lx commercial claims database were used to identify patients with AS who had ≥ 1 secukinumab treatment between January 15, 2016 and December 31, 2016. Patients eligible for inclusion were ≥ 18 years of age who had the diagnosis of AS (ICD-10-CM Code M45 or M08.1; ICD-9-CM Code 720.0) and ≥ 1 pharmacy or medical claim in the 12 months prior to their first secukinumab treatment (index date), and any pharmacy or medical claim > 30 days after the index date. Patient demographics and secukinumab dosage were examined at the index date. Clinical characteristics, comorbidities and treatment history in the 12 months prior to the index date were identified and presented for biologic-naïve and biologic-experienced patients with AS.
Results: A total of 543 patients who initiated secukinumab were included in this study; the mean (SD) age of included patients was 46.4 (12.3) years and 51.6% were female. Of the 543 patients, 358 patients (65.9%) had received another biologic in the previous 12 months, and 185 patients (34.1%) were biologic naïve. Patient demographics, clinical characteristics and treatment history were mostly similar between the two cohorts (Table 1). Most patients (59.1%) initiated secukinumab with the 150-mg dose (biologic experienced, 62.3%; biologic naïve, 53.0%); nearly two-thirds of all patients (64.5%) received a full loading regimen. A higher proportion of biologic-naïve patients had prior tsDMARD use compared with biologic-experienced patients (9.2% vs 2.8%); however, both cohorts were similar in prior NSAID, oral corticosteroid and csDMARD use. Among biologic-experienced patients, the most common biologics previously used were adalimumab (41.3%) and etanercept (31.3%). Overall, the most prevalent comorbidities were hypertension (25.4%), cancer (20.4%), rheumatoid arthritis (19.7%) and hyperlipidemia (19.5).

Conclusion: In this retrospective, administrative claims-based study, approximately two-thirds of patients with AS who initiated secukinumab used biologics in the previous 12-month period. While most patients initiated secukinumab at the approved dose of 150 mg, nearly 40% of patients initiated secukinumab at a dose of 300 mg. These results provide early insights into real-world use of secukinumab among biologic-naïve and biologic-experienced patients with AS in the United States.

Table 1. Demographics, clinical characteristics and treatment history of patients with AS treated with secukinumab stratified by previous biologic experience

<table>
<thead>
<tr>
<th></th>
<th>Overall (N = 543)</th>
<th>Biologic Experienced (n = 358)</th>
<th>Biologic Naïve (n = 185)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), years</td>
<td>46.4 (12.3)</td>
<td>45.7 (12.0)</td>
<td>47.8 (13.0)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>280 (51.6)</td>
<td>182 (50.8)</td>
<td>98 (53.0)</td>
</tr>
<tr>
<td>Region, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>South</td>
<td>165 (30.4)</td>
<td>114 (31.8)</td>
<td>51 (27.6)</td>
</tr>
<tr>
<td>Northeast</td>
<td>135 (24.9)</td>
<td>85 (23.7)</td>
<td>50 (27.0)</td>
</tr>
<tr>
<td>West</td>
<td>123 (22.7)</td>
<td>77 (21.5)</td>
<td>46 (24.9)</td>
</tr>
<tr>
<td>Midwest</td>
<td>119 (21.9)</td>
<td>81 (22.6)</td>
<td>38 (20.5)</td>
</tr>
<tr>
<td>Index dose, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>150 mg</td>
<td>321 (59.1)</td>
<td>223 (62.3)</td>
<td>98 (53.0)</td>
</tr>
<tr>
<td>300 mg</td>
<td>222 (40.9)</td>
<td>135 (37.7)</td>
<td>87 (47.0)</td>
</tr>
<tr>
<td>Received full loading regimen, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>350 (64.5)</td>
<td>237 (66.2)</td>
<td>113 (61.1)</td>
</tr>
<tr>
<td>No</td>
<td>193 (35.5)</td>
<td>121 (33.8)</td>
<td>72 (38.9)</td>
</tr>
<tr>
<td>Physician specialty, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rheumatology</td>
<td>436 (80.3)</td>
<td>295 (82.4)</td>
<td>141 (76.2)</td>
</tr>
<tr>
<td>Internal medicine</td>
<td>30 (5.5)</td>
<td>16 (4.5)</td>
<td>14 (7.6)</td>
</tr>
<tr>
<td>Other specialties</td>
<td>21 (3.9)</td>
<td>11 (3.1)</td>
<td>10 (5.4)</td>
</tr>
<tr>
<td>Unknown/missing</td>
<td>56 (10.3)</td>
<td>36 (10.1)</td>
<td>20 (10.6)</td>
</tr>
<tr>
<td>Treatment history, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSAID</td>
<td>144 (26.5)</td>
<td>100 (27.9)</td>
<td>44 (23.8)</td>
</tr>
<tr>
<td>Oral corticosteroid</td>
<td>167 (30.8)</td>
<td>116 (32.4)</td>
<td>51 (27.6)</td>
</tr>
<tr>
<td>csDMARD</td>
<td>155 (28.5)</td>
<td>109 (30.4)</td>
<td>46 (24.9)</td>
</tr>
<tr>
<td>tsDMARD</td>
<td>27 (5.0)</td>
<td>19 (2.6)</td>
<td>8 (4.3)</td>
</tr>
<tr>
<td>Biologic&lt;sup&gt;1&lt;/sup&gt;</td>
<td>358 (65.9)</td>
<td>358 (100.0)</td>
<td>—</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>148 (27.3)</td>
<td>148 (41.3)</td>
<td>—</td>
</tr>
<tr>
<td>Etanercept</td>
<td>112 (20.6)</td>
<td>112 (31.3)</td>
<td>—</td>
</tr>
<tr>
<td>Certolizumab</td>
<td>66 (12.2)</td>
<td>66 (18.4)</td>
<td>—</td>
</tr>
<tr>
<td>Golimumab</td>
<td>62 (11.4)</td>
<td>62 (17.3)</td>
<td>—</td>
</tr>
<tr>
<td>Infliximab</td>
<td>61 (11.2)</td>
<td>61 (17.0)</td>
<td>—</td>
</tr>
<tr>
<td>Comorbidities, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>138 (25.4)</td>
<td>79 (22.1)</td>
<td>59 (31.9)</td>
</tr>
<tr>
<td>Cancer</td>
<td>111 (20.4)</td>
<td>67 (18.7)</td>
<td>44 (23.8)</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>107 (19.7)</td>
<td>68 (19.0)</td>
<td>39 (21.1)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>106 (19.5)</td>
<td>72 (20.1)</td>
<td>34 (18.4)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>87 (16.0)</td>
<td>58 (16.2)</td>
<td>29 (15.7)</td>
</tr>
<tr>
<td>Depression</td>
<td>83 (15.3)</td>
<td>53 (14.8)</td>
<td>30 (16.2)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>68 (12.5)</td>
<td>54 (15.1)</td>
<td>14 (7.6)</td>
</tr>
<tr>
<td>Obesity</td>
<td>62 (11.4)</td>
<td>41 (11.5)</td>
<td>21 (11.4)</td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
<td>61 (11.2)</td>
<td>39 (10.9)</td>
<td>22 (11.9)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>58 (10.7)</td>
<td>44 (12.3)</td>
<td>14 (7.6)</td>
</tr>
<tr>
<td>Other skin diseases</td>
<td>48 (8.8)</td>
<td>30 (8.4)</td>
<td>18 (9.7)</td>
</tr>
</tbody>
</table>

AS, ankylosing spondylitis; csDMARD, conventional synthetic disease-modifying antirheumatic drug; NSAID, nonsteroidal anti-inflammatory drug; tsDMARD, targeted synthetic disease-modifying antirheumatic drug.

* Loading regimen consists of secukinumab doses at weeks 0, 1, 2, 3 and 4 followed by maintenance dosing every 4 weeks thereafter.

1 Does not include ustekinumab, since it is not currently approved for the treatment of AS.

Disclosure: K. R. Oelke, Novartis Pharmaceuticals Corporation, 5; AbbVie, Amgen, Bristol-Meyers Squibb, Pfizer, 8; R. Garg, PRO Unlimited, Inc, 3; Y. Li, Novartis Pharmaceutical Corporation, 3; X. Liu, KMK Consulting, Inc, 3; H. Zhou, KMK Consulting, Inc, 3; Y. Park, Novartis Pharmaceuticals Corporation, 3.
Characteristics and Treatment Patterns Among Patients with Psoriatic Arthritis Initiating Subcutaneously Administered Biologics: Descriptive Analyses from a US Claims Database

Kurt R. Oelke1, Rahul Garg2, Peter Hur3, Olivier Chambenoit3, Amar Q. Majjhoo4, Stephani Gray5, Kate Higgins5 and Jacqueline B. Palmer3, 1Rheumatic Disease Center, Glendale, WI, 2PRO Unlimited, Inc, East Hanover, NJ, 3Novartis Pharmaceuticals Corporation, East Hanover, NJ, 4Shores Rheumatology, St. Clair Shores, MI, 5Truven Health Analytics, Cambridge, MA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: To better understand the real-world efficacy of biologics for the treatment of psoriatic arthritis (PsA), there is a need to evaluate the persistence and adherence with biologics among patients with PsA seen in routine clinical practice. This study described the patient demographics, disease characteristics and treatment patterns of patients with PsA who initiated a subcutaneously administered (SC) biologic in a US claims database.

Methods: Patients with ≥ 1 pharmacy claim for an FDA-approved SC biologic between 01/15/2016 and 01/31/2017 were identified from the Truven Health Analytics MarketScan Commercial and Medicare Supplemental Databases. Eligible patients were aged ≥ 18 years at the time of biologic initiation (index date) and were continuously enrolled with medical and pharmacy claims ≥ 12 months prior to (baseline period) and ≥ 6 months after the index date. Patients had ≥ 1 PsA diagnosis (ICD-9-CM 696.0 or ICD-10-CM L40.5x) and no pharmacy claims for the index biologic during the baseline period. Patient demographics were assessed at the index date; clinical characteristics and treatment history were examined during the baseline period. Biologic discontinuation, number of days persistent and adherence (proportion of days covered) with the index biologic were evaluated over the 6-month follow-up period.

Results: A total of 2208 eligible SC biologic initiations were identified in patients with PsA, including adalimumab (n = 946), certolizumab pegol (n = 171), etanercept (n = 589), golimumab (n = 94) and secukinumab (n = 408), with mean follow-up of 253 to 275 days. Demographics and clinical characteristics were similar across biologic groups (Table 1). A lower proportion of patients initiating adalimumab or etanercept had prior biologic use (28% and 37%, respectively) compared with certolizumab pegol (72%), golimumab (68%) and secukinumab (76%). The 6-month discontinuation rate was lowest with secukinumab (12%), followed by adalimumab (16%), golimumab (18%), certolizumab pegol (20%) and etanercept (22%). Mean days persistent on the index biologic ranged from 153 days (etanercept) to 164 days (secukinumab). The mean proportion of days covered was similar among secukinumab, adalimumab, etanercept and golimumab (0.73-0.76) and lowest for certolizumab pegol (0.63) (Table 2).

Conclusion: Patients who initiated secukinumab had the lowest discontinuation rate and highest number of days persistent over 6 months compared with the other SC biologics assessed.
Table 1. Baseline Demographics, Clinical Characteristics and Treatment History in Patients With PsA Who Initiated a Biologic (N = 2208 Initiations)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adalimumab n = 946</th>
<th>Certolizumab Pegol n = 171</th>
<th>Etanercept n = 589</th>
<th>Golimumab n = 94</th>
<th>Secukinumab n = 408</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>48.6 (11.8)</td>
<td>51.7 (11.7)</td>
<td>49.5 (11.5)</td>
<td>49.4 (9.1)</td>
<td>50.0 (10.8)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>529 (55.9)</td>
<td>119 (69.0)</td>
<td>341 (57.9)</td>
<td>64 (68.1)</td>
<td>232 (50.9)</td>
</tr>
<tr>
<td>Geographic region, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Northeast</td>
<td>167 (17.7)</td>
<td>22 (12.9)</td>
<td>96 (16.8)</td>
<td>24 (25.5)</td>
<td>97 (23.8)</td>
</tr>
<tr>
<td>North Central</td>
<td>158 (20.9)</td>
<td>21 (12.3)</td>
<td>114 (19.4)</td>
<td>32 (32.8)</td>
<td>66 (16.2)</td>
</tr>
<tr>
<td>South</td>
<td>450 (47.6)</td>
<td>104 (60.8)</td>
<td>285 (48.4)</td>
<td>47 (50.0)</td>
<td>199 (49.6)</td>
</tr>
<tr>
<td>West</td>
<td>133 (14.1)</td>
<td>23 (13.5)</td>
<td>90 (15.3)</td>
<td>11 (11.7)</td>
<td>55 (13.5)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (0.1)</td>
<td>1 (0.6)</td>
<td>1 (2.2)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Length of follow-up, mean (SD)</td>
<td>274.6 (66.0)</td>
<td>270.5 (62.7)</td>
<td>272.4 (66.6)</td>
<td>273.1 (53.7)</td>
<td>253.1 (48.4)</td>
</tr>
<tr>
<td>Deyo-Charlson Comorbidity Index, mean (SD)</td>
<td>0.6 (1.2)</td>
<td>1.0 (1.4)</td>
<td>0.8 (1.3)</td>
<td>0.9 (1.2)</td>
<td>0.8 (1.4)</td>
</tr>
<tr>
<td>Baseline comorbidities, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psoriasis</td>
<td>649 (69.6)</td>
<td>98 (57.3)</td>
<td>359 (61.6)</td>
<td>48 (51.1)</td>
<td>304 (74.6)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>148 (15.6)</td>
<td>35 (20.5)</td>
<td>54 (16.0)</td>
<td>15 (16.0)</td>
<td>74 (18.1)</td>
</tr>
<tr>
<td>Depression</td>
<td>137 (14.5)</td>
<td>27 (15.5)</td>
<td>106 (18.0)</td>
<td>19 (20.2)</td>
<td>64 (15.7)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>137 (14.5)</td>
<td>30 (17.5)</td>
<td>96 (16.3)</td>
<td>14 (14.8)</td>
<td>68 (16.7)</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>241 (25.5)</td>
<td>58 (33.9)</td>
<td>145 (24.6)</td>
<td>36 (38.3)</td>
<td>113 (27.7)</td>
</tr>
<tr>
<td>Prior biologic use, n (%)</td>
<td>261 (27.6)</td>
<td>123 (71.9)</td>
<td>218 (37.6)</td>
<td>64 (68.1)</td>
<td>311 (72.6)</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>0</td>
<td>87 (50.2)</td>
<td>172 (29.2)</td>
<td>23 (24.5)</td>
<td>113 (27.7)</td>
</tr>
<tr>
<td>Certolizumab pegol</td>
<td>14 (1.5)</td>
<td>0</td>
<td>17 (2.9)</td>
<td>12 (12.8)</td>
<td>42 (10.3)</td>
</tr>
<tr>
<td>Etanercept</td>
<td>192 (20.3)</td>
<td>48 (28.1)</td>
<td>0</td>
<td>25 (26.5)</td>
<td>72 (17.6)</td>
</tr>
<tr>
<td>Golimumab</td>
<td>3 (0.3)</td>
<td>8 (4.7)</td>
<td>9 (1.5)</td>
<td>0</td>
<td>35 (8.6)</td>
</tr>
<tr>
<td>Infliximab</td>
<td>23 (2.4)</td>
<td>16 (9.4)</td>
<td>18 (3.1)</td>
<td>10 (10.6)</td>
<td>35 (8.6)</td>
</tr>
<tr>
<td>Secukinumab</td>
<td>13 (1.4)</td>
<td>3 (1.8)</td>
<td>9 (1.5)</td>
<td>3 (3.2)</td>
<td>0</td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>35 (3.7)</td>
<td>12 (7.0)</td>
<td>20 (3.4)</td>
<td>9 (9.6)</td>
<td>100 (24.5)</td>
</tr>
<tr>
<td>Number of unique biologic treatments, mean (SD)</td>
<td>0.3 (0.5)</td>
<td>0.9 (0.7)</td>
<td>0.4 (0.6)</td>
<td>0.9 (0.7)</td>
<td>1.0 (0.7)</td>
</tr>
</tbody>
</table>

PsA, psoriatic arthritis.

Table 2. Persistence and Adherence With Index Biologic Therapies Over 6 Months of Follow-Up in Patients With PsA (N = 2208 Initiations)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adalimumab n = 946</th>
<th>Certolizumab Pegol n = 171</th>
<th>Etanercept n = 589</th>
<th>Golimumab n = 94</th>
<th>Secukinumab n = 408</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistence</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discontinuation of index biologic, n (%)</td>
<td>154 (16.3)</td>
<td>34 (19.9)</td>
<td>131 (22.2)</td>
<td>17 (18.1)</td>
<td>50 (12.3)</td>
</tr>
<tr>
<td>Days persistent on index biologic, mean (SD)</td>
<td>159.7 (47.1)</td>
<td>155.0 (51.6)</td>
<td>153.0 (51.6)</td>
<td>157.0 (50.3)</td>
<td>164.3 (43.0)</td>
</tr>
<tr>
<td>Switched biologic after discontinuation, n (%)</td>
<td>30 (19.5)</td>
<td>7 (20.6)</td>
<td>24 (18.3)</td>
<td>6 (35.3)</td>
<td>11 (22.0)</td>
</tr>
<tr>
<td>Days to switch, mean (SD)</td>
<td>108.9 (15.2)</td>
<td>103.9 (17.3)</td>
<td>106.8 (12.4)</td>
<td>105.5 (15.5)</td>
<td>106.8 (11.6)</td>
</tr>
<tr>
<td>Adherence</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of days covered, mean (SD)</td>
<td>0.76 (0.25)</td>
<td>0.63 (0.25)</td>
<td>0.73 (0.27)</td>
<td>0.73 (0.26)</td>
<td>0.74 (0.24)</td>
</tr>
</tbody>
</table>

PsA, psoriatic arthritis.

* Patients with a gap of ≥ 90 days were considered to have discontinued.

† Days persistent (i.e., time to discontinuation) was defined as the time from index prescription fill to the last day on drug or hand prior to a gap of ≥ 90 days without the index drug, or the end of follow-up if no gap was observed.

‡ Proportion of days covered was defined as the sum of the number of days with the drug on hand divided by the number of days of follow-up.

Disclosure: K. R. Oelke, Novartis Pharmaceuticals Corporation, 5,AbbVie, Amgen, Bristol-Meyers Squibb, Pfizer, 8; R. Garg, Novartis Pharmaceuticals Corporation, 9,PRO Unlimited, Inc, 3; P. Hur, Novartis Pharmaceuticals Corporation, 3; O. Chambenoit, Novartis Pharmaceuticals Corporation, 3; A. Q. Majjhoo, Novartis Pharmaceuticals Corporation, 5,Novartis Pharmaceuticals Corporation, 8,Novartis Pharmaceuticals Corporation, 9; S. Gray, Truven Health Analytics, 3; K. Higgins, Truven Health Analytics, 3; J. B. Palmer, Novartis Pharmaceuticals Corporation, 3.


Abstract Number: 1526

Shift Analysis of Spinal Radiographic Progression after 2 Years of Secukinumab in Ankylosing Spondylitis – Detailed Results from a Phase 3 Trial
Background/Purpose: An overall low rate of spinal radiographic progression with the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) was reported with secukinumab (SEC), a fully human interleukin 17A (IL-17A) inhibitor in the 2-year (2y) uncontrolled ankylosing spondylitis (AS) MEASURE 1 study (1). The objective of this analysis was to investigate those patients whose mSASSS either increased or decreased at 2 yr (Wk 104) in more detail.

Methods: In the MEASURE 1 trial patients received subcutaneous SEC 75mg or 150mg or placebo (PBO) every 4 weeks up to 2 years. Analysis of radiographic progression of the cervical and lumbar spine was performed in X-ray completers using mean mSASSS of two experienced readers blinded to time sequence of the images. To supplement the established published analysis we now performed an analysis using only vertebral edges (VE) scores where both readers were in agreement, and the scores of the initial PBO group were merged and included in the analysis. Progression in mSASSS at 2y vs. baseline (BL) was defined by a change of >1.838 (smallest detectable change, SDC), while ‘improvement’ was defined by < -1.838 and no change by ‑1.838 to 1.838. Furthermore, a shift analysis was performed to explore the course of radiographic progression based on the occurrence of syndesmophytes, evaluating an increase of an mSASSS of 0 or 1 to 2 or 3 vs. a decrease in mSASSS from 2 or 3 to 1 or 0 on single VE from BL to 2y.

Results: A total of 257 patients were X-ray completers at Wk104. Overall, 13.2% patients showed an increase and 6.2% patients showed a decrease of mSASSS as defined. BL demographics and clinical characteristics of patients with mSASSS progression, ‘improvement’ and stable scores were similar.

A total of 4947 VE could be analyzed. No mSASSS change to Wk104 was seen in 4891/4947 (98.9%) VEs, mSASSS increase in 46/4947 (0.9%) VEs and mSASSS decreased in 10/4947 (0.2%) VEs. Of interest, in 9 out of 10 VEs with an mSASSS decrease at Wk104, a change of -2 or -3 was recorded.

Overall, 4291 VEs had no syndesmophytes (86.7%) and 656 VEs (13.3%) had syndesmophytes at BL. Development of a new syndesmophyte was seen in 32/4291 (0.7%) VEs whereas 9/656 VEs syndesmophytes at BL (1.4%) were no longer detected at Wk104. An increase of mSASSS to 2 or 3 was found in 13 out of 173 VEs (0.08%) with an mSASSS score 1 or 2 at BL.

Conclusion: This detailed exploratory analysis at the vertebral unit level complements the previous analysis (1) based on adjudicated scores from blinded readers. This analysis shows that the radiographic status remained stable in almost 99% of VEs in secukinumab-treated patients. The previously reported proportion of patients showing a decrease in mSASSS change is confirmed by the scores at the VE level. Since this is most probably due to background noise it requires further investigation which may include a reevaluation of images. Only the mSASSS at BL was predictive of radiographic progression. These findings may influence future radiographic studies and analyses.

Disclosure: X. Baraliakos, None; J. Braun, Abbott, BMS, Celgene, Celltrion, Chugai, Johnson & Johnson, MSD, Novartis, Pfizer, Roche, UCB Pharma, 5,Abbott, BMS, Celgene, Celltrion, Chugai, Johnson & Johnson, MSD, Novartis, Pfizer, Roche, UCB Pharma, 2; A. Widmer, Novartis AG, 3; A. Das Gupta, Novartis Pharmaceutical Corporation, 3; A. Readie, Novartis Pharmaceutical Corporation, 3; B. Porter, Novartis Pharmaceutical Corporation, 1,Novartis Pharmaceutical Corporation, 3; C. Gaillez, Novartis Pharma AG, BMS, 1,Novartis Pharma AG, 3.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/shift-analysis-of-spinal-radiographie-progression-after-2-years-of-secukinumab-in-ankylosing-spondylitis-detailed-results-from-a-phase-3-trial

Abstract Number: 1527

Do TNF Inhibitors Alter the Natural History of Ankylosing Spondylitis By Impacting the Incidence and Prevalence of Comorbidities and Extra-Articular Manifestations?

Atul A. Deodhar¹, Kevin Winthrop², Benjamin Chan², Sarah A. R. Siegel², Lisa Pisenti³, Jeffrey Stark³, Robert Y. Suruki⁴, Rhonda L. Bohn⁴, Huifeng Yun⁵, Lang Chen⁵ and Jeffrey R. Curtis⁵, ¹Division of Arthritis & Rheumatic Diseases OP09, Oregon Health & Science University, Portland, OR, ²Oregon Health & Science University, Portland, OR, ³UCB Pharma, Smyrna, GA, ⁴UCB Pharma, Raleigh, NC, ⁵University of Alabama at Birmingham, Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Treatment with TNF inhibitors (TNFi) has led to a reduction in signs and symptoms, and improvement in physical function and quality of life in patients with ankylosing spondylitis (AS). Whether TNFi impact the incidence of AS-related comorbidities and extra-articular manifestations (EAMs) is not known.

Methods: We conducted a retrospective cohort study using three commercial insurance claims databases (Multi-Payer Claims Database [MPCD; 2007–2010], Truven MarketScan® [2010–2014], and the US Medicare Fee-for-Service Claims data [2006–2014]) to evaluate EAMs (uveitis, psoriasis, inflammatory bowel disease) and comorbidities (cardiac, renal, pulmonary, neurologic) in AS patients diagnosed by a rheumatologist (index date), having 6 months baseline data prior to index date, and drug-specific exposures after AS diagnosis. Three mutually-exclusive hierarchical exposure groups were examined: (1) no therapy or prescription of non-steroidal anti-inflammatory drugs (NSAIDs), (2) conventional disease-modifying antirheumatic drugs (DMARDs), and (3) TNFi. Prevalence of comorbidities were ascertained in 12-month periods (6 months pre- and post-index date). Incidence of comorbidities and EAMs were ascertained during the period following treatment initiation and the earliest of death, loss of medical coverage, end of study, first outcome occurrence, treatment discontinuation, or initiation of therapy at a higher level in exposure hierarchy. Comparisons were made using the mid-p exact test (α=0.05).

Results: Out of nearly 40 million beneficiaries, 63,052 patients were included. Table 1 shows the prevalence of comorbidities and EAMs of AS by treatment exposures, stratified by data source. Comorbidities were more common in Medicare AS patients compared to MPCD or MarketScan®. Table 2 shows the incidence rates of outcomes by
treatment exposures, stratified by data source. Despite the possibility of patients with more severe disease receiving TNFi treatment, their crude incidence of certain cardiac, pulmonary and neurologic comorbidities was lower compared to those treated with NSAIDs or DMARDs alone, although they had higher incidence of some EAMs.

**Conclusion:** This was the largest investigation of the prevalence and incidence of comorbidities and EAMs of AS within the US, and suggests TNFi to be disease-modifying. In the absence of control for confounding, these findings should be considered preliminary.

**Table 1: Prevalence of comorbidities and EAMs during 12 months (per 100 patient-years), stratified by data source**

<table>
<thead>
<tr>
<th>Demographics</th>
<th>MPCD</th>
<th>MarketScan®</th>
<th>Medicare</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>1,102</td>
<td>421</td>
<td>2,286</td>
</tr>
<tr>
<td>Age, mean (years)</td>
<td>41</td>
<td>42</td>
<td>49</td>
</tr>
<tr>
<td>% Female</td>
<td>38.1</td>
<td>44.4</td>
<td>39.9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Specific manifestation</th>
<th>MPCD</th>
<th>MarketScan®</th>
<th>Medicare</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic insufficiency</td>
<td>1.0</td>
<td>1.0</td>
<td>1.9</td>
</tr>
<tr>
<td>Conduction block</td>
<td>0.2</td>
<td>0</td>
<td>1.1</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0.3</td>
<td>0.5</td>
<td>0.2</td>
</tr>
<tr>
<td>Crohn’s disease</td>
<td>5.9</td>
<td>4.0</td>
<td>3.4</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>3.1</td>
<td>2.5</td>
<td>1.9</td>
</tr>
<tr>
<td>Amyloidosis</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>IgA nephropathy</td>
<td>0.3</td>
<td>0.2</td>
<td>0.1</td>
</tr>
<tr>
<td>Nephrotic syndrome</td>
<td>0.2</td>
<td>0.2</td>
<td>0.1</td>
</tr>
<tr>
<td>Acute pulmonary edema</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Interstitial lung disease</td>
<td>0</td>
<td>0</td>
<td>0.1</td>
</tr>
<tr>
<td>Restrictive lung disease</td>
<td>6.7</td>
<td>0.4</td>
<td>1.7</td>
</tr>
<tr>
<td>Celiac disease syndrome</td>
<td>0</td>
<td>0</td>
<td>0.2</td>
</tr>
<tr>
<td>Spinal cord compression</td>
<td>0.2</td>
<td>0</td>
<td>0.3</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>4.3</td>
<td>1.5</td>
<td>1.9</td>
</tr>
<tr>
<td>Peripheral arteries</td>
<td>6.5</td>
<td>5.4</td>
<td>2.4</td>
</tr>
<tr>
<td>Ulcers</td>
<td>6.1</td>
<td>7.3</td>
<td>6.2</td>
</tr>
</tbody>
</table>
Table 2: Crude incidence rates of comorbidities and EAMs per 100 patient-years by treatment exposures: (1) TNFi vs NSAIIds/no treatment, (2) TNFi vs DMARDs, stratified by data source

<table>
<thead>
<tr>
<th></th>
<th>MPCD</th>
<th>MarketScan</th>
<th>Medicare</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TNFi</td>
<td>NSAIIds/no treatment or DMARDs</td>
<td>p value</td>
</tr>
<tr>
<td>Aortic insufficiency</td>
<td>1.3</td>
<td>1.9</td>
<td>NS</td>
</tr>
<tr>
<td>Conduction block</td>
<td>0.3</td>
<td>3.9</td>
<td>0.029</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0.3</td>
<td>2.0</td>
<td>NS</td>
</tr>
<tr>
<td>Restrictive lung disease</td>
<td>4.7</td>
<td>3.0</td>
<td>0.003</td>
</tr>
<tr>
<td>Spinal cord compression</td>
<td>2.5</td>
<td>1.6</td>
<td>0.053</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>0.9</td>
<td>2.0</td>
<td>0.008</td>
</tr>
<tr>
<td>Crohn’s disease</td>
<td>0.1</td>
<td>0.3</td>
<td>NS</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>3.5</td>
<td>1.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Urine</td>
<td>5.0</td>
<td>4.9</td>
<td>NS</td>
</tr>
</tbody>
</table>

|                  | TNFi | NSAIIds/no treatment or DMARDs | p value | TNFi | NSAIIds/no treatment or DMARDs | p value |
|------------------|------|------------|----------|
| Aortic insufficiency | 1.3  | 0.5 | NS | 1.2  | 1.5 | NS | 3.2  | 4.7 | <0.001 |
| Conduction block | 0.3  | 0 | NS | 1.1  | 1.4 | NS | 2.9  | 4.2 | <0.001 |
| Myocardial infarction | 0.3  | 0 | NS | 0.2  | 0.3 | NS | 0.7  | 1.2 | <0.001 |
| Restrictive lung disease | 4.7  | 3.6 | NS | 4.8  | 4.1 | NS | 3.9  | 3.7 | NS |
| Pneumonia | 2.5  | 0.9 | 0.041 | 3.1  | 3.2 | NS | 2.4  | 2.6 | NS |
| Ulcerative colitis | 0.9  | 0.6 | 0.029 | 1.8  | 2.4 | NS | 5.9  | 7.7 | <0.001 |
| Urine | 0.1  | 0 | NS | 0.3  | 0.4 | NS | 0.4  | 0.6 | NS |

*Only significant data are shown. NS: Not significant.*

**Disclosure:** A. A. Deodhar, Amgen, Eli Lilly, GSK, Janssen-Cilag, Novartis, UCB Pharma, 2, Eli Lilly, Janssen-Cilag, Novartis, UCB Pharma, 5; K. Winthrop, BMS, 2, UCB Pharma, Roche, Lilly, Pfizer, GSK, AbbVie, Galapagos, BMS, 5; B. Chan, None; S. A. R. Siegel, None; L. Pisenti, UCB Pharma, 3; J. Stark, UCB Pharma, 3; R. Y. Suruki, UCB Pharma, 3; R. L. Bohn, UCB Pharma, 3, Bohn Epidemiology LLC, 4; H. Yun, BMS, 2; L. Chen, None; J. R. Curtis, UCB Pharma, Janssen-Cilag, Amgen, Roche, Myriad Genetics, Lilly, Novartis, BMS, Pfizer, 2, UCB Pharma, Janssen-Cilag, Amgen, Roche, Myriad Genetics, Lilly, Novartis, BMS, Pfizer, 5.


**Abstract Number:** 1528

Secukinumab Provides Rapid and Sustained Pain Relief in Ankylosing Spondylitis Patients with Normal or Elevated Baseline CRP Levels and Correlated with Improvement in Fatigue

Atul A. Deodhar¹, Philip G. Conaghan², Tore K Kvien³, Vibeke Strand⁴, Lawrence Rasouliyan⁵, Brian Porter⁶, Steffen Jugl⁷ and Kunal Gandhi⁸, ¹Oregon Health & Science University, Portland, OR, ²University of Leeds, Leeds,
Background/Purpose: Secukinumab has demonstrated sustained efficacy in patients (pts) with active AS. We investigated improvement in pain and fatigue scores from baseline (BL) through Week (Wk) 104 in AS pts stratified by BL CRP status and prior use of TNF inhibitor (TNFi) therapy from the MEASURE 2 trial.

Methods: The MEASURE 2 study design has been reported previously. This post-hoc analysis assessed the mean change from BL in total spinal and nocturnal pain scores (by visual analog scale) using mixed-effect model repeated measure analysis through Wk 16 (least squares mean change) and observed data from Wk 20–104 (mean change). The results are reported for the overall population, pts stratified by BL CRP level (normal [<5 mg/L] or elevated [≥5 mg/L]), and by prior use of TNFi (TNFi-naïve vs TNFi-inadequate responder/intolerant [TNFi-IR]) for the approved secukinumab 150 mg subcutaneous dose. The proportion of pts reporting clinically meaningful improvements (≥20% mean change from BL) in spinal pain scores was also assessed. The correlations between pain (spinal or nocturnal) and functional assessment of chronic illness therapy–fatigue (FACIT–Fatigue) score and response (improvement ≥4 points) were also evaluated.

Results: In the overall population (N = 219), secukinumab 150 mg-treated pts (n = 72) reported rapid reductions across pain scores by Wk 1, which were sustained or further improved through Wk 104: mean change (secukinumab vs placebo [PBO]) in spinal pain: Wk 1 (−10.6 vs −3.6, P <0.05), Wk 16 (−29.0 vs −11.4, P <0.0001), and Wk 104 (secukinumab: −36.4); mean change in nocturnal pain: Wk 1 (−12.7 vs −1.7, P <0.001), Wk 16 (−30.3 vs −10.1, P <0.0001), and Wk 104 (secukinumab: −38.6). Furthermore, 63% of pts on secukinumab reported clinically meaningful improvements vs PBO in spinal pain as early as Wk 3 (36%, P <0.01), increasing to 78% at Wk 104. Secukinumab improved pain scores to a similar extent, irrespective of BL CRP status (Table). At Wk 16, moderate correlations were observed between spinal or nocturnal pain and fatigue (FACIT–Fatigue score: −0.49/−0.48 [P <0.05 for both correlations]; FACIT–Fatigue response: −0.48/−0.51 [P <0.05 for both correlations]). Improvements in pain scores and correlations between pain and fatigue showed similar trends among TNFi-naïve and TNFi-IR pts, with a greater magnitude of improvement observed in the TNFi-naïve group (Table).

Conclusion: Secukinumab provides rapid and sustained pain relief through 104 wks of therapy in AS pts with normal or elevated BL CRP levels and in TNFi-naïve and TNFi-IR pts. Pain relief showed a positive correlation with improvement in fatigue.

Table. Summary of Results

By Baseline CRP

<table>
<thead>
<tr>
<th>Pain scores</th>
<th>Normal Baseline CRP (&lt;5 mg/L)</th>
<th>Elevated Baseline CRP (≥5 mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Secukinumab 150 mg (N = 27)</td>
<td>Secukinumab 150 mg (N = 45)</td>
</tr>
<tr>
<td></td>
<td>PBO (N = 26)</td>
<td>PBO (N = 48)</td>
</tr>
<tr>
<td></td>
<td>P-value</td>
<td>P-value</td>
</tr>
<tr>
<td>Spinal Pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>−34.6</td>
<td>−26.7</td>
</tr>
<tr>
<td>104</td>
<td>−31.2</td>
<td>−40.2</td>
</tr>
<tr>
<td>Nocturnal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>−30.2</td>
<td>−31.6</td>
</tr>
<tr>
<td>104</td>
<td>−28.6</td>
<td>−41.1</td>
</tr>
</tbody>
</table>

By TNFi Status

<table>
<thead>
<tr>
<th>Pain scores</th>
<th>TNFi-Naive</th>
<th>TNFi-IR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Secukinumab 150 mg (N = 44)</td>
<td>Secukinumab 150 mg (N = 28)</td>
</tr>
<tr>
<td></td>
<td>PBO (N = 45)</td>
<td>PBO (N = 29)</td>
</tr>
<tr>
<td></td>
<td>P-value</td>
<td>P-value</td>
</tr>
<tr>
<td>Spinal pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>−33.2</td>
<td>−22.5</td>
</tr>
<tr>
<td>104</td>
<td>−37.7</td>
<td>−33.7</td>
</tr>
<tr>
<td>Nocturnal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>−35.4</td>
<td>−22.8</td>
</tr>
<tr>
<td>104</td>
<td>−40.5</td>
<td>−34.8</td>
</tr>
</tbody>
</table>

Correlation coefficient

<table>
<thead>
<tr>
<th>Pain scores</th>
<th>Week</th>
<th>FACIT–Fatigue score</th>
<th>FACIT–Fatigue response</th>
<th>FACIT–Fatigue score</th>
<th>FACIT–Fatigue response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spinal pain</td>
<td>16</td>
<td>−0.51</td>
<td>−0.45</td>
<td>−0.42</td>
<td>−0.49</td>
</tr>
<tr>
<td>104</td>
<td></td>
<td>−0.59</td>
<td>−0.68</td>
<td>−0.55</td>
<td>−0.68</td>
</tr>
<tr>
<td>Nocturnal</td>
<td>16</td>
<td>−0.55</td>
<td>−0.59</td>
<td>−0.31</td>
<td>−0.34</td>
</tr>
<tr>
<td>pain</td>
<td>104</td>
<td>−0.50</td>
<td>−0.56</td>
<td>−0.51</td>
<td>−0.61</td>
</tr>
</tbody>
</table>

$P$-values and LS mean change at Week 16 from MMRM analysis and mean change at Week 104 from observed data; $\dagger n = 39$ (150 mg) for TNFi-naive and $n = 20$ (150 mg) for TNFi-IR; N, number of patients randomized; €Pearson correlation coefficients calculated for FACIT–Fatigue score and polyserial correlation coefficients calculated for FACIT–Fatigue response; £FACIT–Fatigue response dichotomized (using observed data), as 1 if FACIT–Fatigue score improvement ≥4 points, otherwise 0; ‡$P<0.05$ for all values, $P$-value calculated from the Chi-Square likelihood ratio test; FACIT–Fatigue, Functional Assessment of Chronic Illness Therapy–Fatigue; LS, least squares; MMRM, mixed-effect model repeated measure; PBO, placebo.

Disclosure: A. A. Deodhar, AbbVie Inc., Amgen, Eli Lilly, GSK, Janssen, Novartis, Pfizer Inc., UCB, 2,Eli Lilly, Janssen, Novartis, Pfizer, UCB, 5; P. G. Conaghan, AbbVie, BMS, Eli Lilly, Novartis, Pfizer, Roche, 5,AbbVie, BMS, Eli Lilly, Novartis, Pfizer, Roche, 8; T. K. Kvien, AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz, UCB, 5,AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz, UCB, 8; V. Strand, AbbVie, Amgen, BMS, Boehringer Ingelheim, Celgene, Celltrion, CORRONA, EMD Serono, Genentech/Roche, GSK, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sandoz, Sanofi, UCB, 5; L. Rasouliyan, Novartis Pharmaceutical Corporation, 5,RTI Health Solutions, 3; B. Porter, Novartis Pharmaceutical Corporation, 1,Novartis Pharmaceutical Corporation, 3; S. Jugl, Novartis Pharma AG, 1,Novartis Pharma AG, 3; K. Gandhi, Novartis Pharmaceutical Corporation, 1,Novartis Pharmaceutical Corporation, 3.
Secukinumab Demonstrates Consistent Safety over Long-Term Exposure (up to 3 years) in Patients with Active Ankylosing Spondylitis: Pooled Analysis of Three Phase 3 Trials

Atul A. Deodhar1, Xenofon Baraliakos2, Helena Marzo-Ortega3, Joachim Sieper4, Mats Andersson5, Brian Porter6 and Todd Fox5, 1Oregon Health & Science University, Portland, OR, 2Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany, 3NIHR LBRC, LTHT and LIRMM, UoL, Leeds, United Kingdom, 4Charité University Medicine Berlin, Berlin, Germany, 5Novartis Pharma AG, Basel, Switzerland, 6Novartis Pharmaceuticals Corporation, East Hanover, NJ

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Secukinumab has demonstrated a consistent and reliable safety profile in three Phase 3 studies in ankylosing spondylitis (AS): MEASURE 1 (NCT01358175), MEASURE 2 (NCT01649375), and MEASURE 3 (NCT02008916).1–4 Here, we report long-term (up to 3 years) pooled safety and tolerability data for secukinumab from these three studies (data cut-off: June 25, 2016).

Methods: Overall, 371, 219, and 226 patients with active AS were randomized in MEASURE 1, MEASURE 2, and MEASURE 3, respectively. Study design, efficacy, and safety results of these studies have been reported elsewhere.4,5 Secukinumab doses differed in the studies and included intravenous 10 mg/kg or subcutaneous (s.c.; 75–300 mg) multi-dose loading, followed by s.c. maintenance dosing (75, 150, or 300 mg). Data collected up to the last patient performing the Week (Wk) 156 visit in MEASURE 1, the Wk 104 visit in MEASURE 2, and the Wk 52 visit in MEASURE 3 were pooled at the individual patient level. Exposure-adjusted incidence rates were calculated to account for differences in treatment exposure, and safety analyses included all patients who received ≥1 dose of secukinumab.

Results: A total of 794 patients were included in the analysis (representing 1706.3 patient-years of exposure). The exposure-adjusted incidence rates of adverse events (AEs) and serious AEs with secukinumab across the entire safety period were 146.8 and 6.2 per 100 patient-years, respectively. Nasopharyngitis, diarrhea, headache and upper respiratory tract infections were the most frequently reported AEs (Table). The incidences of serious infections, Candida infections, uveitis, and inflammatory bowel disease were low and consistent with previous reports over shorter exposure periods1 (Table). No cases of suicidal ideation or depression were reported.

Conclusion: Secukinumab was well tolerated during long term treatment (representing 1706.3 patient-years of exposure) in patients with AS, with a favorable safety profile consistent with previous reports, with no new safety signals.
## References

## Table: Summary of pooled safety across 3 AS studies (Entire safety period)

<table>
<thead>
<tr>
<th></th>
<th>N=794</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total exposure, patient-years</td>
<td>1706.3</td>
<td></td>
</tr>
<tr>
<td>Minimum–maximum exposure (days)</td>
<td>1–1530</td>
<td></td>
</tr>
<tr>
<td>Death, n (%)</td>
<td>3 (0.4)</td>
<td></td>
</tr>
</tbody>
</table>

**EAIR per 100 Patient-years (95% CI)**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE</td>
<td>146.8 (135.9, 158.4)</td>
</tr>
<tr>
<td>Any SAE</td>
<td>6.2 (5.0, 7.6)</td>
</tr>
</tbody>
</table>

**Frequent AEs**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasopharyngitis</td>
<td>12.3 (10.5, 14.3)</td>
</tr>
<tr>
<td>Headache</td>
<td>6.0 (4.9, 7.4)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>5.7 (4.6, 7.1)</td>
</tr>
<tr>
<td>Upper respiratory tract infections</td>
<td>5.1 (4.1, 6.4)</td>
</tr>
</tbody>
</table>

**AEs of special interest**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious infections and infestations</td>
<td>1.1 (0.7, 1.8)</td>
</tr>
<tr>
<td><em>Candida</em> infections</td>
<td>0.7 (0.4, 1.2)</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>0.7 (0.4, 1.2)</td>
</tr>
<tr>
<td>Crohn’s disease</td>
<td>0.5 (0.2, 0.9)</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>0.2 (0.1, 0.6)</td>
</tr>
<tr>
<td>Uveitis</td>
<td>1.3 (0.8, 2.0)</td>
</tr>
<tr>
<td>MACE</td>
<td>0.7 (0.4, 1.2)</td>
</tr>
</tbody>
</table>

^Adverse events that occurred in Any secukinumab group with an EAIR >5 during the entire safety period.

^Includes 8 cases of Crohn’s disease, of which 5 were de novo and 3 were flares in patients with a history of Crohn’s disease at baseline. 2All cases of uveitis (n=22) were flares in patients with a history of uveitis at baseline.

**AE, adverse event; AS, ankylosing spondylitis; CI, confidence interval; EAIR, exposure adjusted incidence rate per 100 patient-years; MACE, major adverse cardiac events; N, number of patients in the analysis; n, number of patients with event; SAE, serious adverse event**

**Disclosure:** A. A. Deodhar, AbbVie, Amgen, Eli Lilly, GSK, Janssen, Novartis, Pfizer, and UCB, 2,Eli Lilly, Janssen, Novartis, Pfizer, and UCB, 9; X. Baraliakos, AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Werfen, 2,AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Werfen, 5,AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Werfen, 8; H. Marzo-Ortega, Janssen and Pfizer, 2,Abbvie, Celgene, Janssen, Novartis and UCB, 5,Abbvie, Celgene, Janssen and UCB, 8; J. Sieper, AbbVie, Boehringer Ingelheim, Janssen, Novartis, Merck, Lilly, Pfizer, and UCB, 2,AbbVie, Boehringer Ingelheim, Janssen, Novartis, Merck, Lilly, Pfizer, and UCB, 5; M. Andersson, Novartis Pharma AG, 3; B. Porter, Novartis Pharmaceutical Corporation, 1,Novartis Pharmaceutical Corporation, 3; T. Fox, Novartis Pharma AG, 1,Novartis Pharma AG, 3.


**Abstract Number:** 1530
Improvements in Sleep Problems and Pain in Patients with Active Ankylosing Spondylitis Treated with Intravenous Golimumab: 28-Week Results of the Phase III Trial

Atul A. Deodhar1, John D. Reveille2, Eric K. H. Chan3, Steven Peterson4, Nan Li4, Elizabeth C. Hsia5, Lilianne Kim4, Kim Hung Lo4, Diane D. Harrison4 and Chenglong Han6, 1Division of Arthritis & Rheumatic Diseases OP09, Oregon Health & Science University, Portland, OR, 2University of Texas McGovern Medical School, Houston, TX, 3Janssen Global Services, LLC, Raritan, NJ, 4Janssen Research & Development, LLC, Spring House, PA, 5Janssen Research & Development, LLC/University of Pennsylvania, Spring House/Philadelphia, PA, 6Janssen Global Services, LLC, Malvern, PA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: To investigate the effect of intravenously administered (IV) golimumab (GLM, 2 mg/kg), an anti-TNFα monoclonal antibody, on sleep problems, total back pain (TBP), and night back pain (NBP) in adult patients with active AS.

Methods: GO-ALIVE is a Phase 3, multicenter, randomized, double-blind, placebo (PBO)-controlled trial. Patients (≥18 years) had a diagnosis of definite AS (modified New York criteria) and BASDAI ≥4, TBP visual analog scale (VAS) ≥4, and CRP ≥0.3mg/dL. At baseline, 208 patients were randomized to IV GLM 2mg/kg (N=105) at Wk0, 4, and every 8 weeks or placebo (N=103) at Wk0, 4, and 12, with crossover to IV GLM at Wk16 and through Wk52. Sleep problems were assessed using the Medical Outcomes Study Sleep Scale (MOS-SS, range 0-100), a generic instrument designed to assess six dimensions of sleep: Sleep disturbance, Somnolence, Sleep adequacy, Snoring, Awaken short of breath or headache, and Quantity of sleep/optimal sleep during the past 4 weeks. The six dimensions are also used to generate the composite Sleep Problems Index (SPI). An increase in score from baseline represents improvement. TBP and NBP over the past week were assessed using VAS (0-10 cm; 0=no pain, 10=most severe pain). Wk28 results are presented here. Unadjusted p-values of least square mean differences between treatment groups were based on analysis of covariance controlling for prior anti-TNF therapy.

Results:
Mean changes in MOS-SS Sleep Index and 6 subscales are presented in Table 1. Greater mean improvement (p<0.05) in the MOS-SS sleep index and 4 subscales at Wk8 was observed in GLM compared to PBO, and in the sleep index and 4 subscales at Week 16. Mean improvements from baseline to Week 16 in patient’s assessment of TBP (cm) were greater (p<0.001) in GLM than PBO (-2.70 vs -0.86 and -3.15 vs -1.15, respectively), and after PBO crossed over to GLM, the differences diminished at Wk28 (-3.14 vs -3.34, respectively). Mean improvements at Wk8 and 16 from baseline in patient’s assessment of NBP (cm) were also greater (p<0.001) in GLM than PBO (-3.03 vs -0.87 and -3.44 vs -0.85, respectively), and differences diminished at Wk28 (-3.47 vs -3.39, respectively). Changes from baseline in all subscales of MOS-SS were correlated (Spearman correlations ranging between -0.10 and -0.45) with TBP and NBP at Wk8, 16, and 28 (p values <0.05), with the exception of Snoring and both TBP and NBP at Wk16. Change in NBP was associated with change in Sleep Problem Index at all 3 time points (p=0.002, p=0.001, and p=0.031, respectively). In the general linear model, most of the association between change in TBP and change in Sleep Problem Index was explained by the association between change in NBP and change in Sleep Problem Index.

Conclusion:
Adult patients with active AS treated with IV GLM showed improvements in sleep problems, TBP, and NBP. NBP
improvement was associated with improvement in sleep problems.

Table 1. Summary of mean (standard deviation) changes in MOS-SS and its subscales.

<table>
<thead>
<tr>
<th></th>
<th>GLM N=104</th>
<th>PBO N=102</th>
<th>GLM N=104</th>
<th>PBO N=102</th>
<th>GLM N=104</th>
<th>PBO* N=102</th>
</tr>
</thead>
<tbody>
<tr>
<td>MOS-SS</td>
<td>Week 8</td>
<td>Week 16</td>
<td>Week 28</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD) change from baseline in:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep problems index:</td>
<td>5.10 (7.86)</td>
<td>1.72 (7.36)</td>
<td>6.63 (7.18)</td>
<td>2.49 (8.16)</td>
<td>6.58 (8.05)</td>
<td>5.88 (8.29)</td>
</tr>
</tbody>
</table>
p<0.001 | p<0.001 |
| Sleep disturbance: | 4.44 (8.81) | 1.32 (7.09) | 6.08 (7.76) | 2.37 (7.88) | 6.32 (8.42) | 5.07 (8.17) |
p=0.001 | p<0.001 |
| Somnolence: | 3.37 (7.34) | 1.21 (8.58) | 5.27 (7.05) | 1.47 (8.18) | 4.82 (7.87) | 4.54 (7.81) |
p=0.016 | p<0.001 |
| Sleep adequacy: | 3.12 (8.24) | 1.80 (8.59) | 4.14 (8.36) | 2.09 (8.93) | 3.73 (7.88) | 5.75 (10.15) |
p=0.037 | p=0.001 |
| Snoring: | 1.97 (7.71) | 0.82 (6.58) | 1.24 (7.72) | 1.04 (6.24) | 1.90 (7.39) | 0.89 (7.28) |
p=0.30 | p=0.012 |
| Awaken short of breath or headache: | 4.64 (12.44) | 1.15 (10.02) | 4.08 (12.26) | 1.50 (11.20) | 4.19 (12.50) | 3.00 (11.21) |
p=0.043 | p=0.98 |
| Quantity of sleep/optimal sleep: | 0.13 (0.57) | 0.10 (0.52) | 0.13 (0.59) | 0.01 (0.57) | 0.16 (0.56) | 0.19 (0.56) |
p=0.43 | p=0.019 |

*At Wk28, PBO has crossed over to GLM

Disclosure: A. A. Deodhar, Amgen, Abbvie, GSK, Elli Lilly, Janssen, Novartis, Pfizer, UCB, 2,Elli Lilly, Janssen, Novartis, Pfizer, UCB, 6; J. D. Reveille, Janssen, 5; E. K. H. Chan, Janssen Global Services, LLC, 3,Johnson & Johnson, 1; S. Peterson, Janssen Research & Development, LLC, 3,Johnson & Johnson, 1; N. Li, Janssen Research & Development, LLC, 3,Johnson & Johnson, LLC, 1; E. C. Hsia, Janssen Research & Development, LLC, 3,Johnson & Johnson, LLC, 1; K. H. Lo, Janssen Research & Development, LLC, 3,Johnson & Johnson, LLC, 1; L. Kim, Janssen Research & Development, LLC, 3,Johnson & Johnson, LLC, 1; D. D. Harrison, Janssen Research & Development, LLC, 3,Johnson & Johnson, LLC, 1; C. Han, Janssen Global Services, LLC, 3,Johnson & Johnson, LLC, 1.

Effects of Intravenous Golimumab on Patient-Reported Outcomes in Active Ankylosing Spondylitis: 28-Week Results of the Phase 3 Trial

John D. Reveille¹, Atul A. Deodhar², Eric K.H. Chan³, Steven Peterson⁴, Nan Li⁴, Elizabeth C. Hsia⁵, Lilianne Kim⁴, Kim Hung Lo⁴, Diane D. Harrison⁴ and Chenglong Han⁶, ¹University of Texas McGovern Medical School, Houston, TX, ²Division of Arthritis & Rheumatic Diseases OP09, Oregon Health & Science University, Portland, OR, ³Janssen Global Services, LLC, Raritan, NJ, ⁴Janssen Research & Development, LLC, Spring House, PA, ⁵Janssen Research & Development, LLC/University of Pennsylvania, Spring House/Philadelphia, PA, ⁶Janssen Global Services, LLC, Malvern, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: To evaluate patient-reported outcomes (PRO) of physical functioning, mental health functioning, health state, and health-related quality of life (HRQoL) in patients (pts) with active AS treated with intravenous (IV) golimumab (GLM), an anti-TNFα monoclonal antibody.

Methods: GO-ALIVE is a Phase 3, multicenter, randomized, double-blind, placebo(PBO)-controlled trial. Pts (≥18 years) had a diagnosis of definite AS (modified New York criteria) and BASDAI ≥4, total back pain visual analog scale (VAS) ≥4, and CRP ≥0.3mg/dL. At baseline, 208 pts were randomized to IV GLM 2mg/kg (N=105) at Wks0, 4, and every 8 wks or PBO (N=103) at Wks0, 4, and 12, with crossover to IV GLM at Wk16. PRO instruments included: SF-36, a generic instrument designed to measure physical & mental health functioning; EQ-5D VAS, a generic measure of current health state; and AS Quality of Life (ASQoL), a disease-specific instrument designed to measure impact of AS on HRQoL. SF-36 scores range from 0-100; higher scores indicate better functioning. It has Physical (PCS) and Mental Component Summary (MCS) and 8 subscales (physical functioning, role-physical, body pain, general health, vitality, social functioning, role-emotional, & mental health). EQ-5D has a scale of 0-100 (0=worst health you can imagine; 100=best health you can imagine). ASQoL assesses sleep, mood, motivation, ability to cope, activities of daily living, independence, relationships, & social life in pts with AS; range: 0-18, higher scores indicating worse HRQoL. Unadjusted p-values of least square mean differences between treatment groups were based on analysis of covariance controlling for prior anti-TNF therapy.

Results: Table summarizes mean changes from baseline at Wks8, 16, and 28. Mean improvements in SF-36 PCS/MCS were greater in the IV GLM group than PBO at Wk8 (6.83 vs 2.07, p<0.001; 5.56 vs 1.67, p=0.006, respectively) and maintained through Wk16 (8.52 vs 2.87, p<0.001; 6.47 vs 0.84, p<0.001, respectively). Greater mean improvements in all SF-36 subscales were observed in the IV GLM group at Wks8 & 16 compared to PBO (p<0.01, with the exception of the role-emotional subscale [p=0.058]). Proportion of pts achieving clinically meaningful change (≥5) in SF-36 PCS/MCS was higher in IV GLM than PBO at Wks8 & 16 (PCS: 58.1 vs 27.2, 67.6 vs 35.9, respectively; MCS: 48.6 vs 34.0, 54.3 vs 29.1, respectively; p<0.05 for all). Mean EQ-5D VAS improvements were greater (p<0.001) in IV GLM than PBO at Wks8 & 16 (17.61 vs 6.63, 20.32 vs 4.79, respectively). Greater mean improvements in ASQoL observed in IV GLM compared to PBO at Wks8 & 16 (-4.5 vs -1.5, p<0.001, -5.4 vs -1.8, p<0.001, respectively). By Wk28, after PBO crossover to IV GLM, mean improvement in PCS, MCS, EQ-5D VAS, and ASQoL was similar between the two treatment arms.
**Conclusion:** Adult pts with active AS treated with IV GLM showed marked improvements in physical functioning, mental health functioning, health state, and HRQoL.

| Table Summary of mean (standard deviation) changes in SF-36, EQ-5D, and ASQoL |
|---------------------------------|--------------------|--------------------|
|                                 | IV GOLIMUMAB 2mg/kg | PLACEBO            |
| **Patients**                    | 105                | 103                |
| **Mean (SD) change from baseline in SF-36 PCS:** |                     |                    |
| Week 8                          | 6.83 (6.90)        | 2.07 (5.66)        |
| (p<0.001)                       |                    |                    |
| Week 16                         | 8.52 (7.54)        | 2.87 (6.11)        |
| (p<0.001)                       |                    |                    |
| Week 28                         | 9.08 (8.02)        | 9.29 (7.09)        |
| **Mean (SD) change from baseline in SF-36 MCS:** |                     |                    |
| Week 8                          | 5.56 (9.26)        | 1.67 (8.80)        |
| (p=0.006)                       |                    |                    |
| Week 16                         | 6.47 (9.12)        | 0.84 (9.82)        |
| (p<0.001)                       |                    |                    |
| Week 28                         | 6.16 (10.19)       | 5.60 (9.70)        |
| **Mean (SD) change from baseline in EQ-5D VAS:** |                     |                    |
| Week 8                          | 17.61 (24.02)      | 6.63 (19.88)       |
| (p<0.001)                       |                    |                    |
| Week 16                         | 20.32 (24.59)      | 4.79 (23.47)       |
| (p<0.001)                       |                    |                    |
| Week 28                         | 20.52 (27.86)      | 22.45 (23.08)      |
| **Mean (SD) change from baseline in ASQoL:** |                     |                    |
| Week 8                          | -4.5 (4.71)        | -1.5 (3.90)        |
| (p<0.001)                       |                    |                    |
| Week 16                         | -5.4 (5.01)        | -1.8 (4.50)        |
| (p<0.001)                       |                    |                    |
| Week 28                         | -5.3 (5.24)        | -5.3 (4.84)        |

**Disclosure:** J. D. Reveille, Janssen, 5; A. A. Deodhar, Amgen, Abbvie, GSK, Elli Lilly, Janssen, Novartis, Pfizer, UCB, 2,Elli Lilly, Janssen, Novartis, Pfizer, UCB, 6; E. K. H. Chan, Johnson & Johnson, LLC, 1,Janssen Global Services, LLC, 3; S. Peterson, Janssen Research & Development, LLC, 3,Johnson & Johnson, LLC, 1; N. Li, Janssen Research & Development, LLC, 3,Johnson & Johnson, LLC, 1; E. C. Hsia, Janssen Research &
Development, LLC, 3,Johnson & Johnson, LLC, 1; L. Kim, Janssen Research & Development, LLC, 3,Johnson & Johnson, LLC, 1; K. H. Lo, Janssen Research & Development, LLC, 3,Johnson & Johnson, LLC, 1; D. D. Harrison, Janssen Research & Development, LLC, 3,Johnson & Johnson, LLC, 1; C. Han, Janssen Global Services, LLC, 3,Johnson & Johnson, LLC, 1.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/effects-of-intravenous-golimumab-on-patient-reported-outcomes-in-active-ankylosing-spondylitis-28-week-results-of-the-phase-3-trial

Abstract Number: 1532

Safety and Efficacy of Intravenous Golimumab in Adult Patients with Active Ankylosing Spondylitis: Results through 1 Year

John D. Reveille1, Atul A. Deodhar2, Diane D. Harrison3, Lilianne Kim3, Kim Hung Lo3 and Elizabeth C. Hsia4,
1 University of Texas McGovern Medical School, Houston, TX, 2Division of Arthritis & Rheumatic Diseases OP09, Oregon Health & Science University, Portland, OR, 3 Janssen Research & Development, LLC, Spring House, PA, 4 Janssen Research & Development, LLC/University of Pennsylvania, Spring House/Philadelphia, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Subcutaneous (SC) golimumab (GLM) is currently approved for adult patients (pts) with RA, PsA, and AS. The GO-ALIVE study was designed to evaluate the safety and efficacy of IV GLM in adult pts with active AS.

Methods: GO-ALIVE is a Phase 3, multicenter, randomized, double-blind, placebo (PBO)-controlled trial. Pts (≥18 yrs) had a diagnosis of definite AS (per modified New York criteria) and BASDAI ≥4, total back pain visual analogue scale ≥4, and CRP ≥0.3mg/dL. Pts were randomized (1:1) to IV GLM 2mg/kg at weeks (wks) 0, 4, and every 8 wks or PBO at wks 0, 4, and 12, with crossover to GLM at wk16 through wk52. Up to 20% of pts could have had a prior anti-TNF agent (other than GLM), and up to 10% of pts could have complete ankylosis of the spine. The primary endpoint was ASAS20 at wk16. Other assessments included BASDAI, BASFI, and enthesitis (UCSF index). Missing data were imputed using LOCF. Pts were monitored for adverse events (AEs). Efficacy and safety data through wk52/wk60 are reported here.

Results: 208 pts were randomized and received study agent (PBO: 103; GLM: 105); 5.8% had complete ankylosis of the spine. 17 pts (PBO, n=4; PBO to GLM, n=5; GLM, n=8) discontinued study agent through week 60. At wk 16, greater proportions of pts in the GLM group as compared to PBO had ASAS20 (73% vs 26%), ASAS40 (48% vs 9%), ASAS partial remission (16% vs 4%), and BASDAI50 (41% vs 15%) and GLM pts had greater mean improvements in BASFI (-2.4 vs. -0.5). After crossover to GLM at wk16, clinical efficacy in the PBO group approached that in the endpoint group was ASAS20 at wk16. Other assessments included BASDAI, BASFI, and enthesitis (UCSF index). Missing data were imputed using LOCF. Pts were monitored for adverse events (AEs). Efficacy and safety data through wk52/wk60 are reported here.

Analyses of subset outcome of pts with complete AS were similar to results presented. Treatment groups were comparable at baseline. Adverse events were similar in the 2 groups with the exception of injection site reactions, which were greater in the GLM group (14% vs 1%). No new safety signals were observed.

Conclusion: IV GLM demonstrated clinical efficacy and safety in pts with active AS through 1 year.
of GLM. Of these, 55.4% had ≥1 adverse event (AE), including 3.4% who had a serious AE (SAE). Infections were
the most common type of AE (32.8%). One pt who screened negative for tuberculosis was diagnosed with
pulmonary TB. There were no deaths, malignancies, or opportunistic infections.

**Conclusion:** Response to IV GLM 2mg/kg was maintained through wk52 and comparable between patients who
were randomized to GLM versus those who switched to GLM at wk 16. Through wk60, the safety profile was
consistent with other anti-TNFs, including SC GLM.

<table>
<thead>
<tr>
<th>Table. Efficacy at week 52</th>
<th>Placebo → Golimumab 2 mg/kg</th>
<th>Golimumab 2 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients randomized, n</td>
<td>103</td>
<td>105</td>
</tr>
<tr>
<td><strong>Clinical efficacy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASAS20, n (%)</td>
<td>67 (65.0%)</td>
<td>79 (75.2%)</td>
</tr>
<tr>
<td>ASAS40, n (%)</td>
<td>53 (51.5%)</td>
<td>59 (56.2%)</td>
</tr>
<tr>
<td>BASDAI 50, n (%)</td>
<td>57 (55.3%)</td>
<td>59 (56.2%)</td>
</tr>
<tr>
<td>BASDAI 70, n (%)</td>
<td>36 (35.0%)</td>
<td>35 (33.3%)</td>
</tr>
<tr>
<td>Change from baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>in BASFI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>102</td>
<td>105</td>
</tr>
<tr>
<td>mean (SD)</td>
<td>-2.6 (2.5)</td>
<td>-2.7 (2.5)</td>
</tr>
<tr>
<td>ASAS partial remission, n (%)</td>
<td>25 (24.3%)</td>
<td>26 (24.8%)</td>
</tr>
<tr>
<td>Change from baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>in BASMI (linear)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>101</td>
<td>100</td>
</tr>
<tr>
<td>mean (SD)</td>
<td>-0.4 (0.7)</td>
<td>-0.4 (0.6)</td>
</tr>
<tr>
<td>Change from baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>in enthesitis*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>85</td>
<td>87</td>
</tr>
<tr>
<td>mean (SD)</td>
<td>-3.6 (4.0)</td>
<td>-3.8 (5.0)</td>
</tr>
</tbody>
</table>

* Among pts with enthesitis at baseline (PBO→GLM: n=85; GLM: n=87).

ASAS20/40, ≥20%/40% improvement in ASsessment in Ankylosing Spondylitis (ASAS) International Working
Group criteria; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing
Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; SD, standard deviation.

**Disclosure:** J. D. Reveille, Janssen, 5; A. A. Deodhar, Amgen, Abbvie, GSK, Elli Lily, Janssen, Novartis, Pfizer,
UCB, 2,Eli Lilly, Janssen, Novartis, Pfizer, UCB, 6; D. D. Harrison, Janssen Research & Development, LLC,
3,Johnson & Johnson, LLC, 1; L. Kim, Janssen Research & Development, LLC, 3,Johnson & Johnson, LLC, 1; K.
H. Lo, Janssen Research & Development, LLC, 3,Johnson & Johnson, LLC, 1; E. C. Hsia, Janssen Research &
Development, LLC, 3,Johnson & Johnson, LLC, 1.

**View Abstract and Citation Information Online** - [http://acrabstracts.org/abstract/safety-and-efficacy-of-
Efficacy of Switching Biological Dmards in Patients with Axial Spondyloarthritis: Results from a Systematic Literature Review

Victoria Navarro-Compán1, Chamaida Plasencia-Rodriguez2, Eugenio De Miguel3, Petra Diaz del Campo4, Alejandro Balsa3 and Jordi Gratacos-Masmitja5, 1Rheumatology, Hospital Universitario La Paz, Madrid, Spain, 2University Hospital La Paz, IdiPaz, Madrid, Spain, 3Rheumatology, University Hospital La Paz, IdiPaz, Madrid, Spain, 4Research Unit, Spanish Society of Rheumatology, Madrid, Spain, 5Rheumatology, Parc Tauli Hospital Universitari, Sabadell, Barcelona, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Approximately 30-50% of patients with axial SpA (axSpA) who receive a first bDMARD do not respond well. Current practice in these patients is switching to another bDMARD but the scientific evidence for this attitude is sparse. The aims of this study were: First, to investigate if switching biological DMARDs (bDMARDs) after the failure to prior bDMARD is efficacious in patients with axSpA. Secondly, to evaluate the influence on this efficacy of: i) the reason to discontinue prior TNF inhibitor (TNFi), ii) changing the type of TNFi and iii) changing the target.

Methods: A systematic literature review until January 2017 was performed using Medline, EMBASE and Cochrane databases. The research question was formulated according to the PICOS method: Population (axSpA patients with failure to at least one bDMARD); Intervention (second or consecutive bDMARD); Outcome (clinical response according to ASAS, BASDAI or ASDAS criteria); and Study design (longitudinal studies with at least 50 patients and 12 weeks of follow-up). Data were extracted by two independent reviewers using a specific form. Results are shown as relative frequencies (%).

Results: In total, 9 studies out of 1,862 citations were included. Most of them were observational studies reporting data from national registries and only two used data from clinical trials. In these studies, 1,956 patients (91% AS and 9% nr-axSpA) switched to a second bDMARD (97% TNFi and 3% IL-17i) and 170 to a third bDMARD (all TNFi). The most common reason was inefficacy, followed by intolerance or adverse events related to the administered drug. Baseline characteristics (median -range-) of patients who switched bDMARDs were: age 43 (38-46) years old, 67% (54-80) males, 77% (62-84) HLA-B27+, and BASDAI before switching drugs 6.2 (5.2-7.1). As a control group, data from 4,191 patients after receiving the first bDMARD were analysed.

Time to assess response after switching was 6 (3-12) months. The criteria to define clinical response were heterogeneous. Clinical response (BASDAI50) after a second TNFi was achieved by 25-56% of patients compared to 50-72% after the first TNFi. Also, 47% of patients switching to IL-17i after a TNFi responded (ASAS40) compared to 66% in those who received IL-17i as first line (Figure). The response after switching was not influenced by the reason to discontinue, type of prior TNFi or changing the target.

Conclusion: In patients with axSpA, switching to a second bDMARD (a TNFi or IL-17i) after prior TNFi is efficacious. Nevertheless, the clinical response is lower than the observed in patients naive to bDMARD. So far, the reason to discontinue prior bDMARD or the type of bDMARD have not been identified as predictors of response. Published evidence for switching to a third bDMARD is lacking.
Figure: Efficacy as first, second and third bDMARD in patients with axial spondyloarthritis.

*IL-17i only in MEASURE1&2 study.

Disclosure: V. Navarro-Compán, None; C. Plasencia-Rodriguez, None; E. De Miguel, None; P. Diaz del Campo, None; A. Balsa, None; J. Gratacos-Masmitja, None.


Abstract Number: 1534

Comparison of Long Term Anti-Tnf Survival in Patients with Ankylosing Spondylitis and Non-Radiographic Axial Spondyloarthritis; Data from Turkbio Registry

Gercek Can1, Ediz Dalkılıç2, Yavuz Pehlivanoğlu2, Soner Senel3, Servet Akar4, Dilek Solmaz5, Suleyman Serdar Koca6, Nevşun İnan7, Pamir Atagunduz7, Ayten Yazıcı8, Ayse Cefle8, Berna Goker9, Berrin Zengin1, Sadettin Uslu10, Nurullah Akkoc11 and Fatos Onen1, 1Rheumatology, Dokuz Eylül University Faculty of Medicine, İzmir, Turkey, 2Rheumatology, Uludag University Faculty of Medicine Rheumatology, bursa, Turkey, 3Rheumatology, Erciyes University Faculty of Medicine Rheumatology, kayseri, Turkey, 4Rheumatology, İzmir Katip Celebi University, School of Medicine, Rheumatology, İzmir, Turkey, 5Rheumatology, İzmir Katip Celebi University, School of Medicine, Rheumatology, İzmir, Turkey, 6Rheumatology, Firat University Faculty of Medicine, elazığ, Turkey, 7Rheumatology, Marmara University Faculty of Medicine Rheumatology, istanbul, Turkey, 8Rheumatology, Kocaeli University Faculty of Medicine Rheumatology, kocaeli, Turkey, 9Rheumatology, Gazi University of Faculty of Medicine, ankara, Turkey, 10Rheumatology, Dokuz Eylül University Faculty of Medicine, İzmir, Turkey, 11Rheumatology, Private Practice, Rheumatology, İzmir, Turkey

First publication: September 18, 2017
SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Limited data are available on anti-TNF survival in non-radiographic axial spondyloarthritis (nr-axSpA) patients and their long-term survival in ankylosing spondylitis (AS). The aim of the study was to evaluate long-term survival of the first anti-TNF drug treatment among patients with AS and nr-axSpA enrolled in the TURKBIO database and to compare the discontinuation rates for infliximab (INF), etanercept (ETN), and adalimumab (ADA) in each of the two groups.

Methods: All AS and nr-axSpA patients receiving biological therapies registered in the TURKBIO database between the dates of October 2011 and April 2017 were included in the study. AS diagnosis was made according to modified New York classification criteria and nr-axSpA according to ASAS AxSpA classification criteria. Demographic and clinical data, the date of starting to use biological drug, using frequency and dose of biological drugs, BASFI, BASDAI, BASMI, ASDAS scores, date and reason for discontinuing to use drug were collected. Baseline characteristics and drug survival rates were compared between AS and nr-axSpA patients. Drug survival was calculated by the Kaplan-Meier method and risk for discontinuation among treatment groups compared by Long Rank test.

Results: A total of 924 patients were included in the study (AS, n = 871 and nr-axSpA, n = 53). More than half of the patients with AS were male (60.7% in AS vs 34.0% in nr-axSpA group, p<0.001). AS patients had longer symptom duration (104.90±79.06 vs 75.11±45.29 months, p<0.036) compared to nr-axSpA. Median levels of CRP and ESR were similar for nr-axSpA (CRP: 27.03 ± 34.71, ESR: 30.50 ± 25.77) and AS (CRP: 22.32 ± 29.95, ESR: 35.40 ± 22.91). The scores of BASFI, BASDAI and ASDAS were found to be similar in both groups. Median BASDAI scores at first TNFi initiation were higher in patients with nr-axSpA than in patients with AS (58.65 ± 18.21, 51.06 ± 18.91, p=0.030). Cumulative drug survival rates did not show significant difference among INF (at 59. months:18.5%), ADA (at 71. months: 39.5%) and ETN (at 51. months: 24.2%) in nr-axSpA group (p=0.699) (Figure 1). Similarly, drug survival rates at 78, 77, 78. months for 3 anti-TNF drugs had shown no difference in AS patients (INF (at 78. months: 38.1%), ADA (at 77. months: 52.4%), ETN (at 78. months: 39.0%)) (p=0.151) (Figure 2). Cumulative survival rates in AS patients (at 78. months:42.2%) were found to be significantly higher than that (at 71. months:28.2%) in nr-axSpA patients (p<0.001) (Figure 3).

Conclusion: In contrast to the literature that revealed similar short term survival rates for anti-TNF drugs in patients with AS and nr-axSpA, we found higher survival rates in patients with AS compared to patients with nr-axSpA in this long-term observational study. A limitation of the study may be the low number of nr-axSpA patients using anti-TNF, related to the requirements of social insurance system.

Disclosure: G. Can, None; E. Dalkılıc, None; Y. Pehlivan, None; S. Senel, None; S. Akar, AbbVie, BMS, MSD, Novartis, Pfizer, Roche, and UCB, 2, AbbVie, BMS, MSD, Novartis, Pfizer, Roche, and UCB, 5, AbbVie, BMS,
Abstract Number: 1535

Study of Potential Clinical and Biologic Predictors of Maintaining Good Response at 1 Year Follow-up, in Patients with Ankylosing Spondylitis Under Dose Reduction of TNFi Treatment

Mireia Moreno1, Caridad Pontes2, Ferran Torres3, Agusti Sellas-Fernandez4, Miriam Almirall5, Juan Carlos Torre-Alonso6, Teresa Clavaguera7, Carlos Rodriguez-Lozano8, Luis Francisco Linares9, Ana Urruticoechea-Araná10, Eduardo Collantes-Estevez11, Rosa Morla12, Delia Reina13, Eduardo Cuende14, Pedro Zarco15, Cruz Fernandez-Espartero16, Rosario García-Vicuña17, Jesus Sanz18, Xavier Juanola19, Antoni Vallano20, Francisco J Blanco21, Raimon Sanmartí22, Gonzalo Calvo23, Cristina Avendaño24, Eugenio De Miguel25, Roser Vives26, Raul Veroz Gonzalez27, Carlos Alberto Montilla-Morales28 and Jordi Gratacos-Masmitja29, 1Rheumatology, Parc Tauli Hospital Universitari, Sabadell, Spain, 2Clinic Pharmacology, Parc Tauli Hospital Universitari. I3PT. UAB, Sabadell, Spain, 3Hospital Clinic de Barcelona, Barcelona, Spain, 4Rheumatology, Hospital Universitario Valle Hebron, Barcelona, Spain, 5Rheumatology, Hospital del Mar, Barcelona, Spain, 6H Monte Naranco, Oviedo, Spain, 7Rheumatology. Palamós Hospital, Rheumatologist, Catalonia, Spain, 8Rheumatology, Hospital Universitario Dr. Negrin, Gran Canaria, Spain, 9Rheumatology, Hospital Virgen de la Arrixaca. Murcia. Spain, Murcia, Spain, 10Rheumatology Department. Hospital Can Misses, IBIZA, Spain, 11Rheumatology, IMIBIC-Hospital Universitario Reina Sofia, Cordoba, Spain, 12Rambla Vella, 14, Hospital La Tecla, Tarragona, Spain, 13Rheumatology, Hospital de Sant Joan Despi Moisés Broggi, Barcelona, Spain, 14University Hospital Príncipe de Asturias, Immune System Diseases, Rheumatology department, Alcalá de Henares, Madrid, Spain, 15H Fundación Alcorcón, Alcorcón, Spain, 16Rheumatology, Hospital de Mostoles, Madrid, Spain, 17Rheumatology, Hospital Universitario de La Princesa. IIS La Princesa, Madrid, Spain, 18Rheumatology, Hospital Universitario Puerta de Hierro Majadahonda, Madrid, Spain, 19Rheumatology, Hospital Universitario de Bellvitge, Barcelona, Spain, 20Clinic pharmacology, Hospital Universitari Bellvitge, Barcelona, Spain, 21Servicio de Reumatología. Area Genomica. Instituto de Investigación Biomédica de A Coruña (INIBIC). Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidade da Coruña (UDC), A Coruña, Spain, 22Arthritis Unit, Rheumatology Dpt, Hospital Clinic of Barcelona, Barcelona, Spain, 23Clinic pharmacology, Hospital Clinic Barcelona, Barcelona, Spain, 24Clinic pharmacology, Hospital Puerta de Hierro, Madrid, Spain, 25Medicine, Universidad Autonoma Madrid, MADRID, Spain, 26Clinic pharmacology, Parc Tauli Hospital Universitari. I3PT. UAB, Sabadell, Spain, 27Hospital de Mérida, Mérida, Spain, 28Hospital Clinico Universitario de Salamanca, Salamanca, Spain, 29Rheumatology, Parc Tauli Hospital Universitari, Sabadell, Barcelona, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthopathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Background/Purpose:

Some clinical guidance recommends empirical TNFi dose reductions in AS patients despite lack of robust supportive evidence. Recently, we communicated that a strategy of dose reduction in patients with persistent clinical remission is not inferior to full doses. While it has been suggested that drug level monitoring may guide optimization and prevent overtreatment in rheumatoid arthritis patients on TNFi therapy, there is no conclusive data on biomarkers that may help the monitoring of TNFi treatment in AS. The objective of the present study was to explore potential clinical and biologic predictors of poor clinical response, defined as not meeting low disease activity (LDA) defined as: BASDAI, physician global assessment and patient and nocturnal axial pain, all <4, after 1 year of follow-up.

Methods:

This is a nested study on a prospective multicenter, parallel controlled and randomized open-label clinical trial testing non-inferiority of dose reduction vs maintenance of full doses in patients with remission while treated with any antiTNF drug (REDES-TNF, NCT01604629 / EudraCT 2011-005871-18). The study included and analyzed a total of 113 AS patients (55 full dose arm and 58 reduced dose arm) with persistent clinical remission under TNFi.

Clinical variables analyzed incuded ASDAS-CRP, ASAS response criteria, BASDAI, BASFi and quality of life (ASQoL). Blood samples for measurement of TNFi levels, antibodies anti-drug and inflammatory mediators were collected whenever possible within the 24 hours before TNFi Injection. Plasma levels of TNF alpha, IL-6, esclerostin (SOST) and dickkopf-related protein 1 (DKK-1), high sensitivity CRP (hs-CRP). All TNF inhibitor concentrations were measured by capture ELISA with available commercial kits, and antibodies against drugs were analysed by a homemade two-site (bridging) ELISA.

Results: BASFI, ASQoL and the type of TNFi used were all significantly associated with the probability of LDA after 1 year in univariate models, but only the type of TNFi (Infliximab) and BASFI continued to be significant in multivariate models. Since type of TNFi was not randomized, no conclusions can be derived on whether infliximab is having poor outcomes or used differentially. The treatment effect (dose group assigned) did not show significant heterogeneity according to either BASFI (p=0.5244) nor type of TNFi (p=0.887) suggesting that dose reduction is not predictive of poor outcome. Plasma levels for inflammatory biomarkers and drug levels were available for 55 subjects (29 in full dose group and 26 in experimental group); of all of biomarkers analyzed, only values for hs-CRP were higher in subjects not meetign LDA at 1 year. Univariate methods for clinical and analytical biomarkers showed poor predictive value, with lower bonds of 95% CI for ROC AUC values always below 0.62; multivariate methods were unfeasible since no combination of factors improved the univariate models.

Conclusion: Baseline BASFI and high hs-CRP serum levels have been identified as potential markers of poor prognosis of LDA at 1 year, regardless of dose reduction or not. Further studies may include these markers and explore additional factors in order to build a predictive model for persistent LDA.
Patient Preferences in Medication for Treatment of Spondyloarthritis: A Qualitative Study

Maureen Dubreuil1, Christian Frese2, Shing Law3, Liana Fraenkel4, Elena Losina5 and Tuhina Neogi6, 1Clinical Epidemiology, Boston University School of Medicine, Boston, MA, 2Boston University School of Medicine, Boston, MA, 3Rheumatology, Boston Medical Center, Boston, MA, 4Rheumatology, Rheumatology, Yale University School of Medicine, New Haven, CT, New Haven, CT, 5Orthopaedic and Arthritis Center for Outcomes Research, Department of Orthopedic Surgery, Brigham & Women's Hospital, Boston, MA, 6Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Medications used in the treatment of spondyloarthritis (SpA) include nonsteroidal anti-inflammatory drugs (NSAIDs) and biologics, with each class having distinct characteristics that patients may consider. Qualitative research in rheumatoid arthritis (RA) and psoriasis has shown that patients place highest value on medications that improve pain and function, have low risk of adverse events, and can be administered at home. Little data exist on SpA patient preferences regarding medications characteristics.

Methods: Through a review of records from an urban academic arthritis clinic, adult patients with ankylosing spondylitis or psoriatic arthritis were invited to participate in one of four focus group sessions. Participants were required to have been prescribed either an NSAID or biologic medication within the past year and to speak English fluently. Literature in RA/psoriasis and a SpA expert informed development of a facilitator script with questions to address SpA symptoms, medication efficacy and side effects, cost/availability and other concerns. During each 2-hour session, a trained facilitator guided patients through a semi-structured interview with the following four questions: (1) “What made you decide to start treatment for your arthritis condition?”, (2) “What about your medication made you hesitant to take it?”, (3) “Do you wish you were taking another type of medication for your condition, and if so, why?”, and (4) “Are you glad to be taking your current medication, and if so, why?” Audio recordings were transcribed and coded by two coders using an inductive reasoning approach to identify themes (NVIVO11 software).

Results: Sixteen SpA patients participated in one of the focus group sessions. The median age was 52 (range 23-65), 50% were female, 63% had psoriatic arthritis and 75% used a TNF inhibitor. Themes are detailed in the Table, and included: control of pain and stiffness, durability of medication efficacy, preventing irreversible damage, maintenance of mobility and ability to work or fulfill social roles, avoidance of side effects, avoidance of needles, alternative treatments, and long-term affordability/access.

Conclusion: SpA patient focus groups identified some factors influencing medication preferences that were similar to RA or psoriasis patients. SpA patients expressed concern for a treatment’s ability to maintain or restore one’s occupational or social role, to avoid surgeries and prevent damage, and for long-term affordability/access to medications. This study provides insights into SpA patients’ medication preferences to guide future quantitative analyses and shared decision making in clinical care.
<table>
<thead>
<tr>
<th>Table. Selected themes and quotations from SpA focus groups on medication preferences</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1: Reducing pain/stiffness</strong></td>
</tr>
<tr>
<td>“It hurts so bad, seems like it’s pulling my spine out of my back and I can’t walk when that happens because I be in so much pain in trying to get in bed – it’s horrible.”</td>
</tr>
<tr>
<td><strong>2: Maintaining/restoring independence</strong></td>
</tr>
<tr>
<td>“I gotta live – I gotta move around, I gotta walk, I gotta go to the store, I gotta go to the bathroom, I gotta come back to the hospital… I just gotta. I need the job. I need to be able to get up, to function. It don’t have to be 90%, just let me function 70% of the day. Where I can fix something to eat, can get up and wash, go to the bathroom.”</td>
</tr>
<tr>
<td><strong>3. Preventing disease progression</strong></td>
</tr>
<tr>
<td>“Well for me, I’m thinking about getting worse. You know. Because I thought that these drugs that’s what it’s supposed to do is make it so that it doesn’t get worse. But it is getting worse. I can feel it.”</td>
</tr>
<tr>
<td><strong>4: Medication durability and maintained affordability/access</strong></td>
</tr>
<tr>
<td>“The [medication name], now that I’m taking it, and if it’s taken away from me, the withdrawal. After 90 days and it’s out your system, then what? You get a flare-up. What do you do then? You just run to the emergency room. You get a $500 bill. $300 for the ambulance. To drive the ambulance because you can’t get up, walk. Or take yourself to the hospital…The withdrawal of the medication already being in your system and then it’s out. Then… you go back to that pain like it never left. But it gets worse. It’s worse than it was the day that you picked up that medication.”</td>
</tr>
<tr>
<td><strong>5: Avoiding injections</strong></td>
</tr>
<tr>
<td>When my doctor prescribed [medication name] to me, I’m frightened of needles too, it’s my first time ever shooting myself in a needle, you know? I mean, I did heroin but I never shot up. And to inject myself every Thursday and I have to wait until the last minute and I know I gotta do it before midnight – I’ll go all the way till that last second”</td>
</tr>
<tr>
<td><strong>6. Long term affordability/access</strong></td>
</tr>
<tr>
<td>“It’s something that gave me my life back four months ago- I might not be able to afford it. I get something that helps and I feel it was gonna be taken away from me…I don’t make that much money. I live by myself and I gotta do everything by myself. I don’t get welfare, I don’t get food stamps, get nothing. My job, they – you know, give you health benefits – I can’t get all those benefits! I won’t be able to eat. And before I take my medicine, I gotta eat…I just wish I didn’t have to take it ‘cause I can’t afford it.”</td>
</tr>
<tr>
<td><strong>7. Concern about side effects</strong></td>
</tr>
<tr>
<td>“I had a fear when I first started taking [medication name], of the side effects. My immune system, all of those. I was afraid that I’m going to be the one person that’s going to come down with everything that could possibly go wrong. I was afraid of lymphoma. But I realized my pain and I had to do what I had to do and it all turned out well in the long run but that was my biggest fear, of the side effects”</td>
</tr>
</tbody>
</table>
Determinants of Patient-Reported Improvement after Administration of Biological Treatment in Axial Spondyloarthritis: A Cross-Sectional Study

Julianna Hirsch¹, Michal Nudel², Shira Ginsburg³, Haya Hussein³, Karina Zilber³, Lisa Kaly³, Doron Rimar³, Nina Boulman³, Abid Awisat³, Hily Wollach², Michael Rozenbaum³, Itzhak Rosner³ and Gleb Slobodin³, ¹Ruth and Bruce Rappaport Faculty of Medicine, Technion, Haifa, Haifa, Israel, ²Mifrakim Tz’eirim, Haifa, Israel, ³Bnai-Zion Medical Center, Haifa, Israel

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Efficacy of biological treatment in patients with axial spondyloarthritis (SpA) varies and is dependent on both disease-related and patient-related factors. The goal of this study was to examine variables correlating with patient-reported performance of biologic agents in an Israeli cohort of patients with axial SpA.

Methods: Patients with a clinical diagnosis of axial SpA, either followed in the Rheumatology Unit of Bnai Zion Medical Center (BZMC) or members of the Mifrakim Tz’eirim, the Israeli Association of Young Patients with Rheumatic Diseases (MT), were requested to fill out questionnaires concerning the efficacy of their current treatment, clinical symptoms, dietary habits, mood status, physical activity, working status and basic demographic and disease-related data. Efficacy of treatment was estimated as percentage of global improvement in the disease status. Improvement of 70% or more was considered as clinically significant. Variables of interest were compared between groups of patients, those who achieved or failed to achieve clinically significant improvement. t-test or chi square test were used for group comparisons, as appropriate. Values of p<0.05 were considered significant.

Results: A total of 197 patients with axial SpA filled out the questionnaires by phone or via e-mail. Of 107 patients followed in BZMC, 73 were diagnosed with ankylosing spondylitis and 34 with non-radiographic axial SpA. Details of the diagnosis of axial SpA in the 90 patients enrolled from MT were not available, but these patients did not differ from BZMC patients by reported disease-related features, except from the prevalence of uveitis (15% vs 28%, p=0.02). Ninety-one patients (85%) from the BZMC cohort and 63 patients (70%) from the MT cohort had received biological therapy. Of these, treatment-induced global improvement in the disease status of ≥70% was reported by 100 patients: 64 patients from BZMC and 36 from MT cohorts, respectively (p=0.14). These 100 patients were compared to the second group of 54 patients who failed to achieve 70% improvement. The groups did not differ significantly in age, gender ratio, body mass index, presence of family history of SpA, symptom duration, diagnostic delay, prevalence of peripheral joint involvement, diarrhea, uveitis, psoriasis, self-reported stress or depression, dietary preferences, smoking, insomnia or physical activity (p<0.05 for all comparisons). Patients from the group with limited response to biological therapy were older at the time of diagnosis (37.4±10.6 vs 32.3±10.0 years old,
p=0.004), had lower education level (13.1±3.4 vs 14.9±3.2 years schooling, p=0.001), reported more heel pain (p<0.001), widespread pain (p<0.001), unexplained fatigue (p=0.002), consumed less alcohol (p=0.016) and were less employed during the study period (p=0.009).

**Conclusion:** Improvement after administration of biological treatment in patients with axial SpA correlates with some well-defined disease and patient-related factors. Awareness of these factors may enable refinement of treatment when matched for treatment expectations.

**Disclosure:** J. Hirsch, None; M. Nudel, None; S. Ginsburg, None; H. Hussein, None; K. Zilber, None; L. Kaly, None; D. Rimar, None; N. Boulman, None; A. Awisat, None; H. Wollach, None; M. Rozenbaum, None; I. Rosner, None; G. Slobodin, None.

**Abstract Number:** 1538

**Comparative Effectiveness of Early Versus Delayed Anti-TNF-α Treatment in Axial Spondyloarthritis**

Herman F Mann¹, Jakub Zavada², Šárka Forejtová³, Lenka Szczykova⁴, Zlatuše Křístková⁴ and Karel Pavelka¹, ¹ATTRA, Prague, Czech Republic, Prague, Czech Republic, ²Institute of Rheumatology, Prague, Czech Republic, ³Institute of Rheumatology and Department of Rheumatology, 1st Faculty of Medicine, Charles University, Czech Republic, Prague, Czech Republic, ⁴Institute of Biostatistics and Analyses. Faculty of Medicine, Masaryk University, Brno, Czech Republic

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Anti-TNF-α agents are the mainstay of pharmacotherapy for patients with axial spondyloarthritis (AxSpA) who failed treatment with NSAIDs. A little is known about the influence of early versus delayed treatment initiation on their clinical efficacy.

**Methods:** Baseline demographic data and efficacy parameters of patients starting their first anti-TNF-α treatment ≤ 3 years (EARLY) or > 3 years (DELAYED) after diagnosis of AxSpA from the Czech national registry ATTRA were compared. ATTRA is a centralized prospective computerized registry of patients receiving bDMARD therapy for rheumatic diseases collecting data on efficacy, safety and quality of life of all patients treated in the Czech Republic. Anti-TNF-α therapy was indicated for patients with AxSpA who have failed treatment with NSAIDs with CRP ≥ 1mg/dl and BASDAI score ≥ 4.

**Results:** Data from 1899 axSpA patients were available for analysis. 689 patients started treatment ≤ 3 years and 1210 > 3 years after the diagnosis of AxSpA. There was no difference in gender distribution (72% males) or mean CRP level (2.5 mg/dl) at the time of treatment initiation between EARLY and DELAYED groups. Patients in the EARLY group were significantly younger (mean age 36.4 ± 10.4 vs 42.2 ± 10.9 years; P < 0.001) with shorter symptom duration (8.1 ± 7.4 vs 15.1 ± 9.0 years; P < 0.001). EARLY patients were less likely to be HLA B27
positive (87.9% vs 93.2%; P < 0.001). Disease activity was assessed using BASDAI at months 0, 3, 6, 12, 18 and 24. Activity was higher in the DELAYED group at all timepoints with statistically significant differences at baseline (6.4 ± 1.7 vs 6.2 ± 1.7; P = 0.003), 6 (2.5 ± 1.9 vs 2.3 ± 1.8; P = 0.038), 18 (2.3 ± 1.8 vs 1.9 ± 1.7; P = 0.001) and 24 months (2.3 ± 1.8 vs 2.0 ± 1.8; P = 0.049). There was no difference in survival on therapy between the groups with 85% patients remaining on the initial treatment at 1 year and 77% at 2 years. Radiographic progression was not assessed.

Conclusion: AxSpA patients starting anti-TNF-α therapy later than 3 years after diagnosis had slightly higher activity before and during treatment, however the differences were small and survival on therapy was not different compared to patients with earlier treatment initiation.

Acknowledgement: This study was supported by the project of MHCR for conceptual development of research organization 00023728

Disclosure: H. F. Mann, None; J. Zavada, None; Š. Forejtova, None; L. Szczukova, None; Z. Křístková, None; K. Pavelka, None.


Abstract Number: 1539

High Retention Rate and Sustained Responses with Secukinumab 150mg in Patients with Active Ankylosing Spondylitis: 3-Year Results from a Phase 3 Study

Alan J. Kivitz¹, Helena Marzo-Ortega², Clarence Legerton³, Joachim Sieper⁴, Ricardo Blanco⁵, Martin Cohen⁶, Evie Maria Delicha⁷, Susanne Rohrer⁷ and Hanno Richards⁷, ¹Altoona Center for Clinical Research, Duncansville, PA, ²NIHR LBRC, LTHT and LIRM, UoL, Leeds, United Kingdom, ³Low Country Rheumatology, Articularis Healthcare, Charleston, SC, ⁴University Clinic Benjamin Franklin, Berlin, Germany, ⁵Hospital Universitario Marqués de Valdecilla, Santander, Spain, ⁶McGill University, Montreal, QC, Canada, ⁷Novartis Pharma AG, Basel, Switzerland

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthopathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Secukinumab provided sustained improvement in the signs and symptoms of ankylosing spondylitis (AS) over 2 years in the MEASURE 2 study (NCT01649375).¹,² Here we report the efficacy and safety of secukinumab over 3 years from the study.

Methods: 219 patients (pts) with active AS were randomized to subcutaneous secukinumab 150 mg (72 pts), 75 mg (73 pts) or placebo (PBO, 74 pts) at baseline. At Week (Wk) 16, PBO treated pts were re-randomized 1:1 to secukinumab 150 or 75 mg, irrespective of clinical response. Pts initially randomized to secukinumab and those who
switched from PBO to secukinumab at Wk 16 were included in the analysis (secukinumab 150 mg, N = 106 and secukinumab 75 mg, N = 105). Outcome measures at Wk 156 included ASAS20 and 40, ASDAS-CRP inactive disease, ASAS5/6, BASDAI, SF-36 PCS and ASAS partial remission. Analyses stratified by anti-TNFα status (anti–TNFα-naïve and anti-TNFα inadequate response [IR]) were pre-specified. Data are reported as observed. Safety analyses included all pts who received ≥1 dose of secukinumab.

Results: At Wk 156, the completion rate for secukinumab 150 mg was 81.1% (86/106), compared to 72.4% (76/105) for 75 mg. The higher discontinuation rate for 75 mg was in part due to lack of efficacy or patient/guardian decision. Efficacy observed across endpoints from Wks 52 to 156 is summarized in the Table. Higher responses were observed in the 150 mg group. Improvements in ASAS20 and ASAS40 responses were sustained in anti–TNFα-naïve and anti–TNFα-IR pts (Table). Over the entire study period, the mean exposure [± SD] to secukinumab was 914.3 ± 315.5 days. The safety and tolerability profile of secukinumab was consistent with previous reports; nasopharyngitis, upper respiratory tract infection, diarrhoea and bronchitis were the most frequently reported adverse events (AEs). The exposure-adjusted incidence rates with secukinumab for AEs of interest were serious infections/infestations (1.5), Crohn's disease (0.6), malignant/unspecified tumours (0.6) and major adverse cardiovascular events (0.6) per 100 pt-years.

Conclusion: Secukinumab 150 mg provided sustained response in the signs and symptoms along with physical function through 3 years in pts with AS, with over 80% retention rate. The safety profile remained favourable and was consistent with previous reports.1,2


<table>
<thead>
<tr>
<th>Variable</th>
<th>Secukinumab</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Week 52</td>
<td>Week 156</td>
<td>Week 52</td>
<td>Week 156</td>
</tr>
<tr>
<td>ASAS20, % responders (n/N)</td>
<td>74.2 (69/93)</td>
<td>70.1 (61/87)</td>
<td>57.0 (53/93)</td>
<td>60.9 (53/87)</td>
</tr>
<tr>
<td>ASAS40, % responders (n/N)</td>
<td>52</td>
<td>19.4 (18/93)</td>
<td>24.1 (21/87)</td>
<td>21.9 (21/84)</td>
</tr>
<tr>
<td>ASDAS-CRP inactive disease, % pts (n/N)</td>
<td>52</td>
<td>61.3 (57/93)</td>
<td>56.6 (51/87)</td>
<td>62.5 (55/88)</td>
</tr>
<tr>
<td>ASAS 5/6, % responders (n/N)</td>
<td>52</td>
<td>-3.2 ± 2.3</td>
<td>-3.3 ± 2.5</td>
<td>-2.5 ± 2.2</td>
</tr>
<tr>
<td>BASDAI, mean change±SD (N)</td>
<td>7.6 ± 7.4</td>
<td>8.8 ± 8.8</td>
<td>6.4 ± 7.3</td>
<td></td>
</tr>
<tr>
<td>SF-36 PCS, mean change±SD (N)</td>
<td>52</td>
<td>32.2 (28/87)</td>
<td>31.3 (27/86)</td>
<td>11.1 (9/81)</td>
</tr>
</tbody>
</table>

Analysis by anti-TNFα status

<table>
<thead>
<tr>
<th>Variable, % responders (n/N)</th>
<th>Anti–TNFα-naïve</th>
<th>Anti–TNFα IR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week</td>
<td>Secukinumab 150 mg</td>
<td>Secukinumab 75 mg</td>
</tr>
<tr>
<td>ASAS20</td>
<td>52</td>
<td>80.0 (48/60)</td>
</tr>
<tr>
<td>156</td>
<td>72.9 (43/59)</td>
<td>61.4 (35/57)</td>
</tr>
<tr>
<td>ASAS40</td>
<td>52</td>
<td>62.3 (36/60)</td>
</tr>
<tr>
<td>156</td>
<td>64.4 (38/59)</td>
<td>42.1 (24/57)</td>
</tr>
</tbody>
</table>

ASAS, Assessment of Spondyloarthritis International Society criteria; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score-C reactive protein n, number of responders; N, number of pts in the treatment group with evaluation; SD, standard deviation; SF-36 PCS, Short Form-36 physical component summary.
Comparison of Radiologic Parameters of Ankylosing Spondylitis Treated with Anti-TNF-α Versus Non-Steroidal Anti-Inflammatory Drugs and Sulfasalazine

Seung Min Son, Orthopaedic surgery, Pusan National University Yangsan Hospital, Yangsan, Korea, Republic of (South)
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthopathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
There are many studies about impact of TNF-inhibitors on radiographic progression but little data are available on the relationship between treatment agents and sagittal balance in AS. We focus on radiological aspects related to treatment agents and compare sagittal balance treated with anti-TNF-α to non-steroidal anti-inflammatory drugs and sulfasalazine.

Methods:
One hundred thirty three consecutive AS patients were enrolled prospectively. AS patients were eligible to participate in the trial if they were in medical treatment with same treatment agents at least from 1 year. All patients were treated with NSAIDs and sulfasalazine first. 69 patients were showed excellent outcome of pain control with same agents (Group A). But 64 patients complained of intractable low back pain even though treated with same agents. After at least 3 months, we changed treatment agents for these patients to anti-TNF-α therapy (Group B). Radiographic parameters, that is, sacral slope (SS), pelvic tilt (PT), pelvic incidence (PI), thoracic kyphosis (TK), lumbar lordosis (LL), horizontal distance between C7 plumb line and the posterosuperior corner of the sacrum (C7PL), sacrofemoral distance (SFD), C7PL/SFD ratio (C7/SFD), spinosacral angle (SSA), spinopelvic angle (SPA), C2-C7 lordosis (CL), C2-C7 sagittal vertical axis (C2-C7 SVA) were measured. For the assessment of
Results:

Significantly differences were observed at baseline between two groups. Mean ESR, CRP, and BASDAI were significantly higher in group B. Patients in group B had significantly higher TK compared with group A. In comparison between both groups after treatment, patients in group B had significantly higher lumbar lordosis after treatment. And clinical outcomes including ESR, CRP, BASDAI were significantly lower in group B. At the comparisons between before and after treatment in both groups, there was no significant difference among radiologic parameters in group A. Only BASDAI score had lower after treatment in group A. But in group B, lumbar lordosis and cervical lordosis were significantly increased after treatment. And ESR, CRP, and BASDAI were significantly lower than before treatment. Correlation analysis revealed significant relationships between radiologic parameters and BASDAI. Under multiple regression analysis, lumbar lordosis was the significant predictor for BASDAI.

Conclusion:

This study shows a clear association between treatment agents and radiologic parameters in AS. Furthermore, patients in group B and patients in group A were found to be significantly different in terms of sagittal radiologic parameters like thoracic kyphosis and lumbar lordosis. In addition, correlation analysis revealed significant relationships between radiologic parameters and clinical outcomes. Anti-TNF-α treatment improved lumbar lordosis and made slow thoracic kyphotic progression with improvement of clinical outcomes in AS.

Disclosure: S. M. Son, None;

Background/Purpose:

Large-scale observational cohorts identified in national biological registries may be used to study effectiveness of biological disease modifying drugs (bDMARDs) in ankylosing spondylitis (AS). However, aggregation of data and generalizability of results depends on whether baseline characteristics and disease activity are comparable across countries.

The aims of this interim report, which is part of an ongoing collaborative project between the five Nordic countries, were to explore the following in AS patients who started first line treatment with a bDMARD during 2010-2016 A) baseline characteristics and disease activity per country, B) prescription rate of first line bDMARD per capita per country in 2016.

Methods:

An observational, prospective cohort study conducted in parallel in the 5 Nordic countries. Data regarding the numbers of AS patients (ICD10 code M45) who initiated bDMARD treatment during 2010-2016 were collected from the Nordic rheumatologic biological registries SRQ (Sweden), NOR-DMARD (6 Norwegian treatment centres), DANBIO (Denmark), ROB-FIN (Finland) and ICEBIO (Iceland).

For the calculation of prescription rate, background population numbers (year 2016) were retrieved from each country.

No statistical comparisons were conducted for the current interim analysis.

Results:

In total, 4392 bDMARD treatment initiations were identified in AS patients 2010-2016 (Sweden 1986, Norway 663, Denmark 970, Finland 623, Iceland 150). Demographics and baseline characteristics are presented in Table. The age at start of bDMARD and the proportion of HLA-B27-positivity appeared similar across the countries whereas there seemed to be differences in baseline disease activity, use of conventional synthetic (cs)DMARDS and rate of smoking.

The crude incidence rate of first line bDMARD start in 2016 ranged from 1.3 (Finland) to 10.7 (Iceland), per 100000 capita.

Conclusion:
The biological registries of the Nordic countries can be used to conduct large scale observational studies in AS. However, despite the relatively homogenous populations and health-care systems in the region, variations in the incidence of bDMARD use and in the patient baseline characteristics were observed. National differences in disease classification and in treatment strategies need to be explored further and taken into account when interpreting merged data from several countries.

BG and UL contributed equally to the writing of this abstract.

Acknowledgements: partly funded by a grant from Nordforsk and Foreum

| Table. Baseline characteristics in patients with ankylosing spondylitis starting a first bDMARD 2010-2016 in the five Nordic countries, and incidence rate for start of bDMARD in 2016 |
|-----------------------------------------------|----------------|----------------|----------------|----------------|----------------|
| Number of patients                          | Iceland       | Norway         | Sweden         | Denmark        | Finland        |
| Baseline characteristics                     |                |                |                |                |                |
| Age, years, mean (SD)                        | 41 (13)        | 42 (12)        | 43 (14)        | 42 (13)        | 41 (11)        |
| Females, %                                   | 36             | 41             | 31             | 29             | 39             |
| HLA-B27 positive, %                          | 90             | 90             | NA             | 83             | 89             |
| Current smoking, %                           | 25             | 24             | 17             | 27             | 26             |
| Concomitant csDMARD, %                       | 23             | 11             | 24             | 15             | 72             |
| Swollen joints, %                            | 24             | 18             | 26             | 15             | 23             |
| Prednisolone, %                              | 3              | NA             | 7              | 1              | 17             |
| BASDAI, mean (SD)                            | 6.3 (1.7)      | 4.9 (2.1)      | 5.3 (2.1)      | 5.9 (1.9)      | 3.5 (2.5)      |
| CRP mg/L, median (IQR)                       | 7 (11)         | 5 (9)          | 8 (16)         | 9 (17)         | 8 (16)         |
| ASDAS, mean (SD)                             | 3.8 (0.7)      | 3.0 (0.9)      | 3.2 (1.0)      | 3.6 (1.0)      | 2.7 (1.0)      |
| BASFI, median (IQR)                          | 4.7 (2.2)      | NA             | 3.8 (3.8)      | 5.1 (3.5)      | 2.2 (3.9)      |
| PGA, mm, mean (SD)                           | 73 (16)        | 53 (24)        | 55 (24)        | 69 (22)        | 46 (27)        |
| HAQ, median (IQR)                            | 0.9 (0.8)      | 0.5 (0.5)      | 0.6 (0.8)      | 0.8 (0.5)      | NA             |
| Incidence rate for start of bDMARD $^3$      | 10.7           | 4.2            | 3.2            | 2.8            | 1.3            |

1) ≥1 swollen joint at baseline
2) Patient global assessment
3) Crude incidence rate for first line bDMARD in 2016 per 100'000 capita

Disclosure: B. Glintborg, Abbvie, Biogen, 2; U. Lindström, None; K. Aaltonen, AbbVie, BMS, Janssen, MSD, Pfizer, Roche and UCB, 2; E. K. Kristianslund, None; B. Gudbjornsson, Actavis, Celgene, MSD, Pfizer, 2; K.
Chatzidionysiou, None; J. Askling, AbbVie, Eli Lilly, Janssen, Merck, Pfizer, Roche, UCB, Samsung, 2; D. Nordström, AbbVie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, UCB, 8; M. Lund Hetland, Orion, BMS, AbbVie, Biogen, Pfizer, MSD, 2; D. Di Giuseppe, None; L. Dreyer, MSD, UCB and Janssen Pharmaceutical, 8; T. S. Jørgensen, AbbVie, Roche, Novartis, UCB, and Biogen, 8; L. E. Kristensen, Pfizer, AbbVie, Amgen, UCB, Celgene, BMS, Biogen, Forward Pharma, MSD, Novartis, Eli Lilly, and Janssen pharmaceuticals, 8; K. Eklund, None; G. Grondal, None; S. Ernestam, None; J. Joensuu, Pfizer Inc, 8; T. K. Kvien, AbbVie, 2, Pfizer Inc, 2, Roche Pharmaceuticals, 2, UCB, 8, AbbVie, 5, Pfizer Inc, 5, BMS, 8, MSD, 8, Roche Pharmaceuticals, 8, UCB, 8, AbbVie, 8; E. Lie, AbbVie, Celgene, Hospira and Pfizer, 8; K. M. Fagerli, None; A. J. Geirsson, None; H. Jonsson, None; L. T. Jacobsson, Abbvie, Celegen, MSD, Novartis and UCB, 5.

Inequity in Biologic DMARD Prescription for Spa across the Globe: Results from the Multi-Centre, Cross-Sectional, ASAS Comospa Study

Elena Nikiphorou1, Désirée van der Heijde2, Sam Norton3, Robert B.M. Landewé4, Anna Moltó5, Maxime Dougados6, Filip van Den Bosch7 and Sofia Ramiro8, 1LUMC, Leiden, Netherlands, 2Leiden University Medical Center, Leiden, Netherlands, 3Academic Rheumatology, King’s College London, London, United Kingdom, 4Amsterdam Rheumatology & Immunology Center, Amsterdam, Netherlands, 5Paris Descartes University, Paris, France, 6Paris-Descartes University, Paris, France, 7Rheumatology, Ghent University Hospital, Gent, Belgium, 8Rheumatology, Department of Rheumatology, LUMC, Leiden, Netherlands, Leiden, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The value of biologic DMARDs (bDMARDs) in SpA is well recognized but global access to these treatments can be limited due to high cost and other factors. This study explores variation in the use of bDMARDs in SpA across countries and to what extent socio-economic (SE) factors may explain variation.

Methods: Patients fulfilling the ASAS SpA criteria in the multi-national, cross-sectional ASAS COMOSPA study were studied. Multi-level logistic regression models with random intercept for country were constructed with current use of bDMARDs as the dependent variable. Contribution of socio-economic factors using country health expenditures and gross domestic product (GDP) (all low vs medium/high tertiles) as independent country-level factors, was explored in models adjusted for socio-demographic as well as clinical variables known to determine bDMARD-use in SpA.

Results: In total, 3370 patients from 22 countries were included (mean [SD] age 43 [14] years; 66% male; 88% axial disease). Across countries, 1275 (38%) were bDMARD users. Crude mean bDMARD-use varied between 5% (China) to 74% (Belgium). After adjustment for relevant socio-demographic and clinical variables, important variation in bDMARD-use across countries remained (Figure, p<0.001). Country-level socio-economic factors, specifically higher health expenditures were related to higher bDMARD uptake (Table), though not meeting
statistical significance (OR 1.96; 95% CI 0.94, 4.10). Similar findings were found with country GDP (OR 1.93; 95% CI 0.91, 4.06).

**Conclusion:** There remains important residual variation across countries in bDMARD uptake of patients with SpA followed in specialized SpA centers. This is despite adjustment of well-known factors for bDMARD use such as clinical and country-level socio-economic factors.

**Table.** bDMARD: univariable and multivariable analyses with socio-demographic, clinical and treatment variables as well as indicators of the country socio-economic welfare included.

<table>
<thead>
<tr>
<th>Independent predictors</th>
<th>Univariable analysis bDMARD use OR (95% CI)</th>
<th>Multivariable analysis bDMARD use OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Country health expenditure (high/medium vs low)</td>
<td>1.71 (0.84, 3.50)</td>
<td>1.96 (0.94, 4.10)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>1.01 (1.00, 1.01)</td>
<td>1.00 (0.99, 1.01)</td>
</tr>
<tr>
<td>Male gender (vs females)</td>
<td>1.18 (1.01, 1.39)</td>
<td>1.26 (1.04, 1.53)</td>
</tr>
<tr>
<td>Axial (vs peripheral) disease</td>
<td>1.48 (1.16, 1.89)</td>
<td>1.62 (1.15, 2.28)</td>
</tr>
<tr>
<td>ASDAS (CRP based)</td>
<td>0.82 (0.76, 0.89)</td>
<td>0.80 (0.73, 0.87)</td>
</tr>
<tr>
<td>Sacroiliitis on X-ray</td>
<td>1.75 (1.44, 2.12)</td>
<td>1.41 (1.12, 1.78)</td>
</tr>
<tr>
<td>History of extra-articular manifestations</td>
<td>1.46 (1.25, 1.70)</td>
<td>1.31 (1.08, 1.58)</td>
</tr>
<tr>
<td>Total NSAID score (0-100) in last 3 months</td>
<td>0.99 (0.99, 1.00)</td>
<td>0.99 (0.99, 1.00)</td>
</tr>
<tr>
<td>Past csDMARD use</td>
<td>2.31 (1.96, 2.73)</td>
<td>2.08 (1.72, 2.52)</td>
</tr>
<tr>
<td>Past bDMARD use</td>
<td>2.64 (2.13, 3.28)</td>
<td>2.48 (1.93, 3.19)</td>
</tr>
<tr>
<td>Education (secondary/university vs primary)</td>
<td>0.79 (0.62, 1.00)</td>
<td>0.76 (0.52, 1.13)</td>
</tr>
</tbody>
</table>
Figure. bDMARD uptake (%) by country. Adjusted % use shown with 95% CI based on models with socio-economic, socio-demographic and clinical variables. Crude bDMARD uptake also shown (orange squares). Countries ranked by health expenditure: low (left) to high (right).

Disclosure: E. Nikiphorou, None; D. van der Heijde, None; S. Norton, None; R. B. M. Landewé, None; A. Moltó, None; M. Dougados, Abbvie, Pfizer, Lilly, Merck, Novartis, 5, Abbvie, Pfizer, Lilly, Merck, Novartis, 2; F. van Den Bosch, None; S. Ramiro, None.


Abstract Number: 1543

Real-World Effectiveness of TNF Inhibition in Spondyloarthritis. Data from a Large Nationwide Prospective Cohort – the British Society for Rheumatology Biologics Register for Ankylosing Spondylitis

Gareth T. Jones1, Andrew Keat2, Ejaz Pathan3 and Gary J. Macfarlane4, 1Epidemiology Group, School of Medicine, Medical Sciences and Nutrition, University of Aberdeen, Aberdeen, United Kingdom, 2Rheumatology, Northwick Park Hospital, London, United Kingdom, 3Department of Rheumatology, Aberdeen Royal Infirmary, Aberdeen, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthopathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM
Background/Purpose:

TNF inhibition has revolutionised the treatment of axial spondyloarthritis (AxSpA). Much of what we know about the use of these drugs comes from randomised controlled trials (RCTs). However, RCT populations are highly selected, often from specialist centres, and there are potential threats to external validity – i.e. that the treatment effect in this sub-group of patients is not representative of the wider eligible patient population.

The aim of the current study, using a large, nationally representative patient registry, was to (a) determine the effectiveness of TNF inhibition in a large ‘real-world’ patient population; and (b) examine predictors of treatment failure.

Methods:

The British Society for Rheumatology (BSR) Biologics Register for Ankylosing Spondylitis recruits patients with AxSpA newly starting TNF inhibition. At baseline, clinical and patient-reported data is collected from the medical notes and patient questionnaires. Patients are followed up at 3, 6 and 12 months, and treatment failure was defined as failure to achieve an ASAS20 response by 1yr – a composite outcome comprising patient global assessment, pain, function, and inflammation.

Logistic regression was used to determine the relationship between baseline clinical and patient-reported characteristics and treatment failure.

Results:

Data were available on 354 patients recruited between Apr-2013 and Sep-2016, of whom 127 (36%) had failed to achieve an ASAS20 response by 1yr. There was no difference in age between those who did / did not achieve an ASAS20 response, nor by gender.

Patients with peripheral joint disease were significantly less likely to achieve ASAS20 response than other patients (OR: 1.90; 95%CI: 1.13-3.19). There was some evidence that patients with non-radiographic disease and those who were HLA-B27 negative were less likely to respond than other patients, although this did not reach statistical significance (see Table). Similarly, no clear or significant association was observed with disease activity or function.

Conclusion:

We have shown, in this real-world AxSpA patient population receiving their first TNF inhibitor, around two-thirds achieve satisfactory treatment response within 1yr. This is reassuringly comparable to the proportion of responders in randomised clinical trial populations. There are few strong predictors of treatment response and it may be that some patients have other conditions (e.g. fibromyalgia) that may be less likely to respond to biologic therapy. Early identification of patients who fail to respond within 1yr remains a clinical challenge, emphasising the importance of early monitoring after commencing these therapies.
<table>
<thead>
<tr>
<th>Baseline exposure</th>
<th>OR (95%CI) for failure to achieve ASAS20 response by 1yr</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (quartiles)</strong></td>
<td></td>
</tr>
<tr>
<td>18-34yrs</td>
<td>1.00</td>
</tr>
<tr>
<td>34-44yrs</td>
<td>0.86 (0.43-1.69)</td>
</tr>
<tr>
<td>44-54yrs</td>
<td>1.11 (0.58-2.13)</td>
</tr>
<tr>
<td>54-82yrs</td>
<td>1.27 (0.68-2.36)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.00</td>
</tr>
<tr>
<td>Female</td>
<td>1.19 (0.74-1.90)</td>
</tr>
<tr>
<td><strong>Extra-spinal features (Yes versus No)</strong></td>
<td></td>
</tr>
<tr>
<td>Peripheral joint involvement</td>
<td>1.90 (1.13-3.19)</td>
</tr>
<tr>
<td>Uveitis</td>
<td>0.72 (0.42-1.22)</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>1.11 (0.56-2.20)</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>1.29 (0.69-2.41)</td>
</tr>
<tr>
<td><strong>Modified New York criteria</strong></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>1.00</td>
</tr>
<tr>
<td>Negative</td>
<td>1.22 (0.78-1.91)</td>
</tr>
<tr>
<td><strong>HLA-B27</strong></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>1.00</td>
</tr>
<tr>
<td>Negative</td>
<td>1.67 (0.95-2.94)</td>
</tr>
<tr>
<td><strong>Disease activity (BASDAI)</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;4.0</td>
<td>1.93 (0.81-4.56)</td>
</tr>
<tr>
<td>4.0-4.9</td>
<td>1.00</td>
</tr>
<tr>
<td>5.0-5.9</td>
<td>1.01 (0.44-2.32)</td>
</tr>
<tr>
<td>6.0-6.9</td>
<td>0.66 (0.29-1.52)</td>
</tr>
<tr>
<td>7.0-7.9</td>
<td>0.98 (0.45-2.10)</td>
</tr>
<tr>
<td>8.0-8.9</td>
<td>0.66 (0.28-1.58)</td>
</tr>
<tr>
<td>&gt;=9.0</td>
<td>1.46 (0.52-4.13)</td>
</tr>
<tr>
<td><strong>Function (BASFI)</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;4.0</td>
<td>1.94 (0.79-4.79)</td>
</tr>
<tr>
<td>4.0-4.9</td>
<td>1.00</td>
</tr>
<tr>
<td>5.0-5.9</td>
<td>1.34 (0.50-3.58)</td>
</tr>
<tr>
<td>6.0-6.9</td>
<td>0.66 (0.24-1.85)</td>
</tr>
<tr>
<td>7.0-7.9</td>
<td>1.68 (0.66-4.32)</td>
</tr>
<tr>
<td>8.0-8.9</td>
<td>2.08 (0.82-5.27)</td>
</tr>
<tr>
<td>&gt;=9.0</td>
<td>2.43 (0.93-6.35)</td>
</tr>
</tbody>
</table>

**Disclosure:** G. T. Jones, AbbVie, 2,Pfizer Inc, 2,UCB, 2; A. Keat, None; E. Pathan, None; G. J. Macfarlane, Pfizer, AbbVie and UCB, 2.


**Abstract Number:** 1544

**The Effect of Extraarticular Manifestations on Tumor Necrotic Factor α Inhibitor Drug Survival in Patients with Ankylosing Spondylitis: Nationwide Data from the Korean College of Rheumatology Biologics (KOBIO) Registry**
Yunsuek Kim, Internal medicine, Soonchunhyang university Seoul hospital, Seoul, Korea, Republic of (South)
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The tumor necrosis factor α inhibitor (TNFi) therapy has been shown to be remarkably effective in ankylosing spondylitis (AS). However, almost 30% of AS patients stop TNFi or switch to another TNFi because of inefficacy or adverse effects, annually. The objective of our study was to assess the predictors of TNFi drug survival including extraarticular manifestations, using nationwide registry in Korea.

Methods: Data were obtained from the Korean College of Rheumatology BIOlogics (KOBIO) registry which is multi-center based national wide data from 53 tertiary care hospitals in Korea. Demographics, clinical features, laboratory findings, disease activity indices (BASDAI, ASDAS-ESR, ASDAS-CRP), and extraarticular manifestataions (uveitis, enthesitits, dactylitis, psoriasis, inflammatory bowel disease) were studied in patients with AS during the TNFi therapy. We analyzed the drug survival of 5 TNFi agents (etanercept, infliximab, infliximab biosimilar, adalimumab, and golimumab) and the factors affect drug survival especially in terms of extraarticular manifestations. To verify affecting factors, univariable and multivariable cox regression analysis were performed.

Results: Of 1482 AS patients starting TNFi drugs from Dec 2012 to Jan 2017 were included. In baseline, there was no difference of demographics, disease activity and extraarticular manifestations between continued and discontinued TNFi group except gender distribution, CRP, platelet counts, and HLA-B27 positivity. The effect of extraarticular manifestations including uveitis (unadjusted HR: 0.92, 95% CI 0.57 to 1.48 p value 0.74), enthesitits, dactylitis, psoriasis, and inflammatory bowel disease on TNFi drug survival was not statistically significant. But peripheral arthritis was statistically significantly associated with TNFi drug survival (unadjusted HR: 2.21 95% CI 1.66 to 2.95, adjusted HR 1.38 95% CI 1.01 to 1.88). Of disease activity indices, higher level of ASDAS-ESR showed statistical significance in TNFi drug survival (unadjusted HR: 1.87 95% CI 1.73 to 2.03, adjusted HR: 2.23 95% CI 2.00 to 2.63). Golimumab had higher retention rate to TNFi therapy than etanercept during 3 years of follow-up period (unadjusted HR: 0.46 95% CI 0.31 to 0.68, adjusted HR: 0.65 95% CI 0.43 to 0.99).

Conclusion: In national wide KOBIO registry, extraarticular manifestations including uveitis could not affect TNFi drug survival. But the development of peripheral arthritis during TNFi therapy had higher risk of discontinuance of its treatment in AS patients.

Disclosure: Y. Kim, None;


Abstract Number: 1545

Evaluation of the Adherence to Recommendations for Tnfα Blockers Use and Its Impact over 5 Years of Follow-up in Early Axial Spondyloarthritis. Data from the DESIR Cohort
Background/Purpose: Several recommendations have been published for the use of TNFα blockers (TNFb) in patients with axial Spondyloarthritis (axSpA). However, there is only sparse data on the adherence to these recommendations in daily clinical practice and the long-term impact of adhering to them. In this study, we aimed: a) to describe the adherence to the 2006 and 2016 ASAS/EULAR recommendations for TNFb initiation and continuation; b) to evaluate the impact of the adherence to these recommendations over 5 years of follow-up.

Methods: Data from the early axSpA patients from the DESIR cohort (first 5 years of follow-up) were analysed. We evaluated the adherence to 2006 and 2016 ASAS/EULAR recommendation for: a) TNFb initiation (patients were considered adherent if they initiated a TNFb when they met the conditions to do so according to recommendations or did not initiate a TNFb when conditions were not met) and; b) TNFb continuation (considering only those patients who initiated TNFb). Predictive factors and the impact of the adherence to these recommendations over 5 years were explored by multivariate logistic regression and mixed models with random effects, respectively.

Results: Out of the 708 patients included in the analysis, 440 (62.15%) and 389 (54.94%) were adherent to 2006 and 2016 recommendations for TNFb initiation, respectively. Patients adhering to 2006 recommendations for TNFb initiation were more frequently male [49.5% vs. 40.7%, OR 1.45 (95%CI 1.07-1.98)] and had more frequently a high level of education (university studies) [62.0%, vs. 53.7%, OR 1.43 (95%CI 1.05-1.95)] against patients not adhering. Patients adherent to 2006 and/or 2016 recommendations for TNFb initiation showed significantly lower levels in BASFI, SF-36 (mental and physical components) and in the number of days of sick leave over the 5 years of follow-up [10.7 ± 44.1 vs. 19.4 ± 58.4 days, p<0.001, in adherent vs. non-adherent patients for 2016 recommendations, respectively].

Among the 258 patients who initiated TNFb over follow-up, 232 (93.93%) continued the treatment. Among these, adherence to TNFb continuation recommendations was observed in 47.37% and 49.39% of patients, for 2006 and 2016 recommendations, respectively. Better outcomes over 5 years of follow-up were found in the group of patients adhering to recommendations for TNFb continuation (Table 1).

Conclusion: This study suggests that adherence to recommendations in the initiation and continuation of TNFb leads to better long-term outcomes in terms of quality of life and sick leave.
Table 1. Impact of the adherence to recommendations for TNFβ continuation over 5 years of follow-up.

<table>
<thead>
<tr>
<th></th>
<th>2006 RECOMMENDATIONS FOR TNFβ CONTINUATION</th>
<th>2016 RECOMMENDATIONS FOR TNFβ CONTINUATION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adherence to 2006 rec. for continuation</td>
<td>Adherence to 2016 rec. for continuation</td>
</tr>
<tr>
<td></td>
<td>n = 117</td>
<td>n=122</td>
</tr>
<tr>
<td>BasFI over 5 years</td>
<td>26.3 (22.1)</td>
<td>27.1 (21.9)</td>
</tr>
<tr>
<td>(0-100)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SF-36 mental component</td>
<td>42.0 (11.7)</td>
<td>42.1 (11.6)</td>
</tr>
<tr>
<td>over 5 years (0-100)</td>
<td>0.002</td>
<td>0.010</td>
</tr>
<tr>
<td>SF-36 physical component</td>
<td>41.5 (9.3)</td>
<td>41.1 (9.3)</td>
</tr>
<tr>
<td>over 5 years (0-100)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sick leave over 5</td>
<td>20.9 (57.7)</td>
<td>21.6 (59.7)</td>
</tr>
<tr>
<td>years (days)</td>
<td>0.030</td>
<td>0.042</td>
</tr>
</tbody>
</table>

1Mixed model for adherence vs. no adherence.

All results are presented as mean and Standard Deviation (SD)

Disclosure: C. López-Medina, None; M. Dougados, Abbvie, Pfizer, Eli Lilly and Company, Novartis, UCB, Merck, Roche, BMS UCB, 2, Abbvie, Pfizer, Eli Lilly and Company, Novartis, UCB, Merck, Roche, BMS, UCB, 5; E. Collantes-Estévez, None; A. Molto, None.


Abstract Number: 1546

Comparative Effectiveness of Secukinumab and Golimumab in Ankylosing Spondylitis: Assessed By Matching-Adjusted Indirect Comparison Using Pivotal Phase 3 Clinical Trial Data

Walter P. Maksymowych1, Ernest Choy2, Yusuf Yazici3, Jessica A. Walsh4, Howard Thom5, Chrysostomos Kalyvas6, Todd Fox7, Kunal Gandhi8 and Steffen Jugl7, 1Radiology & Diagnostic Imaging, University of Alberta, Edmonton, AB, Canada, 2Section of Rheumatology, Cardiff University, Cardiff, Great Britain, 3School of Medicine, New York University School of Medicine, New York City, NY, 4Division of Rheumatology, University of Utah, Salt Lake City, UT, 5School of Social and Community Medicine, University of Bristol, Bristol, United Kingdom, 6Real World Strategy and Analytics, MAPI Group, Houten, Netherlands, 7Novartis Pharma AG, Basel, Switzerland, 8Novartis Pharmaceuticals Corporation, East Hanover, NJ

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Background/Purpose:

No data are available from head-to-head randomized controlled trials (RCTs) between secukinumab 150mg (SEC; an anti-IL-17A) and golimumab 50mg (GOL; a TNF inhibitor [TNFi]) in patients with active AS. Matching-Adjusted Indirect Comparison (MAIC) is a method supported and used in decision-making by UK National Institute for Health and Care Excellence (NICE). It ensures comparisons across effectively balanced trial populations. This study assessed the comparative effectiveness of SEC and GOL up to week 24 using MAIC with pooled individual patient data (IPD) from the RCTs MEASURE 1 (M1) and MEASURE 2 (M2) and published aggregate data from GO-RAISE.

Methods:

IPD from the pooled SEC arms of M1 and M2 (n=197) were weighted to match the baseline characteristics of the GOL arm from GO-RAISE (n=138). Pooled data were used to maximize the effective sample size (ESS) for SEC. Placebo arms were also matched; placebo-adjusted comparisons were possible only until week 16 because patients could receive active treatment from this time onwards. Logistic regression determined weights for age, sex, BASFI, disease duration, CRP and previous TNFi therapy. Variables were selected by expert opinion and regression analyses. Recalculated outcomes from M1, M2 (SEC, ESS=102; placebo, ESS=81) were compared with GO-RAISE (GOL, n=138; placebo, n=78). Pairwise comparisons – reported as odds ratios (ORs [95% CIs]) – were performed for Assessment of SpondyloArthritis international Society (ASAS) 20, 40 and partial remission (PR) responses at nearest-equivalent time points across trials: weeks 12 (SEC)/14 (GOL), 14 (GOL)/16 (SEC) and 24 (SEC and GOL). Strict thresholds were avoided when interpreting p values in line with American Statistical Association 2016 guidance.

Results:

There was no evidence of differences in ASAS 20 and 40 responses between SEC and GOL at weeks 12/14 and 14/16 (both placebo-adjusted). At week 24, non-placebo-adjusted ASAS 20 and 40 responses were higher with SEC than GOL (OR [95% CI]: 1.58 [0.93–2.69] p=0.089 and 1.58 [0.94–2.64] p=0.084, respectively). There was no evidence of differences in ASAS PR responses between SEC and GOL at weeks 12/14, 14/16 and 24. A sensitivity analysis that also matched for BASDAI score yielded similar results.

Conclusion:

There was no evidence of differences in ASAS responses between SEC and GOL in placebo-adjusted analyses. In non-placebo-adjusted analyses, SEC showed higher ASAS 20 and 40 responses than GOL at week 24.
Disclosure: W. P. Maksymowych, AbbVie, 2, Pfizer, 2, Sanofi, 2, AbbVie, 5, Amgen, 5, Eli Lilly, 5, Janssen, 5, Merck, 5, Novartis, 5, Pfizer, 5, Sanofi, 5, UCB, 5; E. Choy, Pfizer Inc, 2, Roche Pharmaceuticals, 2, UCB, 2, BioCancer, 2, Amgen, 5, Biogen Idec, 5, Bristol-Myers Squibb, 5, Chugai, 5, Eli Lilly and Company, 5, Janssen Pharmaceutica Product, L.P., 5, Novartis Pharmaceutical Corporation, 5, Pfizer Inc, 5, Regeneron, 5, Roche Pharmaceuticals, 5, R-Pharm, 5, Sanofi-Aventis Pharmaceutical, 5, Bristol-Myers Squibb, 8, Chugai, 8, Hospira, 8, Pfizer Inc, 8, Janssen Pharmaceutica Product, L.P., 8, Regeneron, 8, Eli Lilly and Company, 8, Roche Pharmaceuticals, 8, Sanofi-Aventis Pharmaceutical, 8, UCB, 8; Y. Yazici, Celgene, 2, BMS, 2, Genentech, 2, Celgene, 5, BMS, 5, Novartis, 5; J. A. Walsh, Novartis, 5; H. Thom, Eli Lilly, 5, F Hoffman-La Roche, 5, Novartis Pharma AG, 5, Pfizer, 5; C. Kalyvas, MAPI Group, 3; T. Fox, Novartis Pharma AG, 1, Novartis Pharma AG, 3; K. Gandhi, Novartis Pharmaceuticals Corporation, 1, Novartis Pharmaceuticals Corporation, 3; S. Jugl, Novartis Pharma AG, 1, Novartis Pharma AG, 3.


Abstract Number: 1547

Dose Tapering of TNFi in Patients with Axial Spondyloarthritis: An Observational Cohort Study from Nationwide Korean College of
Rheumatology Biologic Registry (KOBIO)

Jun Won Park¹, Jin Kyun Park¹, Kichul Shin², Yong-Beom Park³, Eun Bong Lee¹, Yeong Wook Song⁴ and Eun Young Lee¹, ¹Division of Rheumatology, Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea, Republic of (South), ²Kyungnam villa #102, Division of Rheumatology, Department of Internal Medicine, SMG-SNU Boramae Medical Center, Seoul, Korea, Republic of (South), ³Yonsei University Severance Hospital, Seoul, Korea, Republic of (South), ⁴Division of Rheumatology, Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: To compare the clinical efficacy of dose-tapering strategy of tumor-necrosis factor inhibitor (TNFi) with that of standard-dose TNFi treatment in patients with spondyloarthritis (SpA)

Methods: This observational cohort study was based on prospectively registered data of nationwide KOBIO registry. A total of 776 SpA patients with available data and more than one year of TNFi adherence were included. Quantification of TNFi dosage were expressed using dose-quotient (DQ), which was calculated as \((\text{actual prescribed dose/standard dose}) \times (\text{standard dosing interval/actual dosing interval})\) annually. We used linear mixed model to estimate the change in disease activity (ASDAS-CRP, BASDAI and BASFI) over 3 years between the two strategies. Classifying as dose-tapering was based on both mean DQ of patients (individual level) and DQs of all 1-year observations from all patients (time level). Incidence of discontinuation of TNFi due to inefficacy and adverse event were also compared.

Results: At the individual level, patients with mean DQ<1.0 (tapering group, n=322) were more likely to have obesity (33.5% vs. 29.4%, p<0.001) and be first TNFi users (82.9% vs. 75.1%, p=0.009) and showed higher CRP level (2.6±3.1 vs. 2.1±2.6 mg/dL, p=0.039) than those with standard-dose TNFi (standard-dose group, n=454). Other baseline clinical factors including age, gender, smoking status, HLA-B27 positivity, and disease activity were comparable. Change in ASDAS-CRP over time in the tapering group was not significantly different from that in the standard-dose group (p value for time*group=0.872). This result was consistent after adjustment for baseline factors (age, obesity, HLS-B27 and definite sacroiliitis) which showed relevant interaction with ASDAS-CRP changes (figure 1). At the time level, 186 (24.0%), 204 (35.6%) and 95 (41.9%) patients received reduced dose of TNFi during 0–1, 1–2 and 2–3-year period, respectively. There was no significant interaction between yearly DQ and relevant ASDAS-CRP change (p value for time*DQ=0.435) (figure 2). In the multivariable model, difference in ASDAS-CRP between the standard-dose TNFi and tapering TNFi over the entire follow-up was 0.10 (95% CI=-0.01 to 0.21). Two treatment strategies showed comparable efficacy regarding BASDAI and BASFI. Incidences of drug discontinuation due to inefficacy and adverse events between the two groups were also comparable (figure 2).

Conclusion: In SpA patients with at least one year of TNFi adherence, dose-tapering of TNFi showed a comparable clinical efficacy to standard-dose TNFi treatment.
Disclosure: J. W. Park, None; J. K. Park, None; K. Shin, None; Y. B. Park, None; E. B. Lee, Green Cross Corp, 2, Pfizer Inc, 5; Y. W. Song, None; E. Y. Lee, None.


Abstract Number: 1548

Opioid Use in Patients with Ankylosing Spondylitis

Victor S. Sloan¹, Anna Sheahan¹, Jeffrey Stark² and Robert Y. Suruki¹, ¹UCB Pharma, Raleigh, NC, ²UCB Pharma, Smyrna, GA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Background/Purpose: The use or misuse of opioids has become a major public health issue in the USA. It is estimated that the economic burden of misuse of prescription opioids is approximately $78 billion/year, and by 2009, opioid deaths outnumbered deaths from motor vehicle accidents. In the 2000s, new standards from The Joint Commission led to increased prescribing of opioids for non-cancer pain.

Ankylosing spondylitis (AS) is a serious, chronic inflammatory condition primarily involving the axial skeleton; progressive spinal pain is a hallmark of the disease. Recent treatment guidelines recommend use of non-steroidal anti-inflammatory drugs (NSAIDs) as initial pharmacotherapy, and TNF inhibitors (TNFi) in patients with insufficient response to NSAIDs; anti-IL17 therapies are not mentioned due to paucity of data and timing, and the use of opioids is not addressed. We performed an initial analysis to attempt to assess the use of opioids in patients with AS.

Methods: Patients aged ≥18 years with AS (ICD9 720.0, ICD10 M45.X) were identified in the Truven MarketScan® database during the period 2011 to 2016. The period following the first AS medical code (i.e. index date) was then examined for claims for opioid medication dispensing. The concomitant use of TNFi and/or NSAIDs during the same follow-up period was also ascertained. Anti-IL17 therapies were not included in this analysis due to insufficient exposure data.

Results: Of the 56,236 patients with AS in the database, 27,347 (48.6%) had ≥1 opioid claim during the follow-up period. Among this subset of opioid-exposed AS patients, 9,808 (35.9%) also had a claim for a TNFi, 17,539 (64.1%) had a claim for an NSAID, and 20,449 (74.8%) received an NSAID and/or a TNFi during the follow-up period. The exposure rates were similar when the analysis was restricted to AS patients with ≥2 opioid claims during the follow-up period.

Conclusion: Opioid use is common among patients with AS. Of the AS patients using opioids in this analysis, approximately one-quarter were using only opioids and no medications recommended in treatment guidelines. In addition to the well-recognized public health and societal issues around opioid treatment, lack of therapies directed at inflammation almost certainly results in suboptimal treatment of this serious inflammatory condition. Further analyses are warranted to better assess the reasons for the lack of appropriate therapies and to understand which practitioners are prescribing the opioids; this methodology is unable to identify alternating use of medication types. Given the high usage of opioids in AS, appropriate circumstances for their use should be defined, and educational efforts should be made to help guide practitioners and patients to more appropriate therapies.

References:


Disclosure: V. S. Sloan, UCB Pharma, 3; A. Sheahan, UCB Pharma, 3; J. Stark, UCB Pharma, 3; R. Y. Suruki, UCB Pharma, 3.

Abstract Number: 1549
A Non-Medical Switch from Originator Infliximab to Biosimilar CT-P13 in 36 Patients with Ankylosing Spondylitis: 6 – Months Clinical Outcomes from the Czech Biologic Registry Attra

Šárka Forejtová1, Jakub Zavada1, Lenka Szczukova2, Katerina Jarosova1, Tom Philipp3 and Karel Pavelka4,
1Institute of Rheumatology and Department of Rheumatology, 1st Faculty of Medicine, Charles University, Czech Republic, Prague, Czech Republic, 2Institute of Biostatistics and Analyses, Faculty of Medicine, Masaryk University, Brno, Brno, Czech Republic, 3Department of Rheumatology and Physiotherapy, Thomayer Hospital, Prague, Praha 4, Czech Republic, 4Institute of Rheumatology, Prague, Czech Republic, Prague, Czech Republic
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: A non-medical switch from originator (INX, Remicade) to biosimilar infliximab (CT-P13, Remsima) was conducted in 36 patients with ankylosing spondylitis (AS) in one clinical center. The aim of the study was to compare measures of disease activity 3 months before and 3 months after the switch, and to monitor effectiveness and safety of treatment within 6 months after the switch.

Methods: Measures of disease activity (BASDAI, CRP) 3 months before and 3 months after switch were compared. Measures of disease activity (BASDAI, ASDAS, CRP, ESR), quality of life (HAQ, RAPID 3, EUROQOL) and patient satisfaction with treatment assessed by Treatment Satisfaction Questionnaire for Medication (TSQM) questionnaire were evaluated in month 0, 3 and 6 after the switch. Mean ±SD and absolute/relative frequencies were used to describe continuous and categorical variables. P-value of Wilcoxon pair test was used when assessing significance of 3 and 6 months change.

Results: 36 patients with AS were switched from Remicade to Remsima. Prior INX treatment duration was 86.2±34.7 months. The baseline characteristics are shown in table 1. Comparison of change in BASDAI and CRP 3 months before and after the switch is shown in table 2. The evolution of disease activity measures and patient reported outcomes (PROMs) and TSQM over 6 months after the switch is shown in table 3. There was no serious adverse event. One patient had a reverse switch to INX because of his request.
### Table 1: Baseline characteristics.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Descriptive statistics</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (women)</td>
<td>N (%)</td>
<td>6 (15.8 %)</td>
</tr>
<tr>
<td>Age at diagnosis (years)</td>
<td>Mean ± SD</td>
<td>27 ± 8</td>
</tr>
<tr>
<td>Disease duration (to treatment with Remsima)</td>
<td>Median (5.; 95. perc.)</td>
<td>27 (12; 39)</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>16 ± 9</td>
<td></td>
</tr>
<tr>
<td>Median (5.; 95. perc.)</td>
<td>15 (5; 40)</td>
<td></td>
</tr>
<tr>
<td>Age at the start of treatment (with Remsima)</td>
<td>Mean ± SD</td>
<td>44 ± 10</td>
</tr>
<tr>
<td>Median (5.; 95. perc.)</td>
<td>42 (28; 68)</td>
<td></td>
</tr>
<tr>
<td>Remicade - line of biologic treatment</td>
<td>N (%)</td>
<td>34 (89.5 %)</td>
</tr>
<tr>
<td>1</td>
<td>N (%)</td>
<td>3 (7.9 %)</td>
</tr>
<tr>
<td>2</td>
<td>N (%)</td>
<td>1 (2.6 %)</td>
</tr>
<tr>
<td>Glucocorticoids - previous therapy</td>
<td>N (%)</td>
<td>3 (7.9 %)</td>
</tr>
<tr>
<td>Number of sDMARD - previous therapy</td>
<td>N (%)</td>
<td>11 (30.6 %)</td>
</tr>
<tr>
<td>0</td>
<td>N (%)</td>
<td>21 (58.3 %)</td>
</tr>
<tr>
<td>1</td>
<td>N (%)</td>
<td>4 (11.1 %)</td>
</tr>
<tr>
<td>Glucocorticoids - concomitant therapy</td>
<td>N (%)</td>
<td>3 (7.9 %)</td>
</tr>
<tr>
<td>sDMARD - concomitant therapy</td>
<td>N (%)</td>
<td>4 (10.5 %)</td>
</tr>
<tr>
<td>HLA-B27 positivity</td>
<td>N (%)</td>
<td>34 (89.5 %)</td>
</tr>
<tr>
<td>Number of swollen joints</td>
<td>Mean ± SD</td>
<td>0 ± 0</td>
</tr>
<tr>
<td>Median (5.; 95. perc.)</td>
<td>0 (0; 0)</td>
<td></td>
</tr>
</tbody>
</table>

### Table 2: Comparison of parameters 3 months before and after switch

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Descriptive statistics</th>
<th>3 months before start of Remsima (M-3)</th>
<th>Start of Remsima (M0)</th>
<th>3 months after start of Remsima (M3)</th>
<th>Change before start of Remsima</th>
<th>Change after start of Remsima</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>BASDAI</td>
<td>Mean ± SD</td>
<td>0.92 ± 1.35</td>
<td>1.71 ± 1.27</td>
<td>1.35 ± 1.32</td>
<td>0.8 ± 1.3</td>
<td>-0.4 ± 0.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Number of patients</td>
<td></td>
<td>38</td>
<td>38</td>
<td>36</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRP</td>
<td>Mean ± SD</td>
<td>2.41 ± 2.46</td>
<td>2.91 ± 2.06</td>
<td>3.89 ± 8.65</td>
<td>0.6 ± 3.4</td>
<td>0.9 ± 8.9</td>
<td>0.162</td>
</tr>
<tr>
<td>Number of patients</td>
<td></td>
<td>38</td>
<td>38</td>
<td>36</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Wilcoxon pair test for difference between changes M-3 → 0M and 0M → M3.
Table 3 Comparison of parameters at the start of treatment and after 3 and 6 months.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Start of treatment with Remsima</th>
<th>3 months</th>
<th>6 months</th>
<th>p-value*</th>
<th>p-value**</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BASDAI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>1.71 ± 1.27</td>
<td>1.35 ± 1.32</td>
<td>1.15 ± 1.19</td>
<td><strong>0.004</strong></td>
<td><strong>0.012</strong></td>
</tr>
<tr>
<td>Number of patients</td>
<td>38</td>
<td>36</td>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ASDAS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>1.34 ± 0.63</td>
<td>1.19 ± 0.70</td>
<td>1.13 ± 0.58</td>
<td><strong>0.028</strong></td>
<td>0.361</td>
</tr>
<tr>
<td>Number of patients</td>
<td>38</td>
<td>36</td>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CRP</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>2.91 ± 2.06</td>
<td>3.89 ± 8.65</td>
<td>3.10 ± 3.93</td>
<td><strong>0.041</strong></td>
<td>0.841</td>
</tr>
<tr>
<td>Number of patients</td>
<td>38</td>
<td>36</td>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Erythrocyte sedimentation rate</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>4.03 ± 2.89</td>
<td>7.25 ± 8.45</td>
<td>6.83 ± 5.88</td>
<td><strong>0.011</strong></td>
<td><strong>0.007</strong></td>
</tr>
<tr>
<td>Number of patients</td>
<td>38</td>
<td>36</td>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Disease activity (VAS)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>2.05 ± 1.49</td>
<td>2.03 ± 1.54</td>
<td>1.63 ± 1.28</td>
<td>0.716</td>
<td>0.135</td>
</tr>
<tr>
<td>Number of patients</td>
<td>38</td>
<td>36</td>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pain (VAS)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>19.08 ± 14.61</td>
<td>15.69 ± 12.88</td>
<td>13.96 ± 11.70</td>
<td>0.195</td>
<td><strong>0.035</strong></td>
</tr>
<tr>
<td>Number of patients</td>
<td>38</td>
<td>36</td>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fatigue (VAS)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>23.68 ± 20.09</td>
<td>22.50 ± 14.12</td>
<td>22.71 ± 19.00</td>
<td>0.609</td>
<td>0.585</td>
</tr>
<tr>
<td>Number of patients</td>
<td>38</td>
<td>36</td>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HAQ</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>0.43 ± 0.44</td>
<td>0.38 ± 0.35</td>
<td>0.31 ± 0.34</td>
<td>0.384</td>
<td>0.360</td>
</tr>
<tr>
<td>Number of patients</td>
<td>38</td>
<td>36</td>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>MDHAQ - RAPID3</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>5.60 ± 3.73</td>
<td>4.48 ± 3.16</td>
<td>4.08 ± 3.23</td>
<td>0.063</td>
<td><strong>0.026</strong></td>
</tr>
<tr>
<td>Number of patients</td>
<td>38</td>
<td>36</td>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>EUROQOL</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>0.751 ± 0.185</td>
<td>0.805 ± 0.122</td>
<td>0.829 ± 0.123</td>
<td>0.021</td>
<td>0.033</td>
</tr>
<tr>
<td>Number of patients</td>
<td>37</td>
<td>36</td>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TSQM questionnaire</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Effectiveness</td>
<td>83.3 ± 18.3</td>
<td>73.3 ± 24.1</td>
<td>64.4 ± 25.2</td>
<td><strong>0.002</strong></td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Number of patients</td>
<td>38</td>
<td>37</td>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Side-effects</td>
<td>75.0 ± 18.2</td>
<td>71.3 ± 25.6</td>
<td>58.3 ± 29.5</td>
<td>0.705</td>
<td>0.593</td>
</tr>
<tr>
<td>Number of patients</td>
<td>5</td>
<td>5</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Convenience</td>
<td>78.8 ± 13.4</td>
<td>79.3 ± 13.8</td>
<td>74.5 ± 13.9</td>
<td>0.736</td>
<td><strong>0.012</strong></td>
</tr>
<tr>
<td>Number of patients</td>
<td>38</td>
<td>37</td>
<td>24</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Global satisfaction *Mean ± SD*  
82.9 ± 13.0  
80.3 ± 17.4  
73.4 ± 22.4  
0.371  
0.095  

*Number of patients*  
38  
37  
24  

*Wilcoxon pair test. difference between values at the start of the treatment and after 3 months.*  

**Wilcoxon pair test. difference between values at the start of the treatment and after 6 months.*

**Conclusion:** We have observed no consistent trend of change in disease activity measures and PROMs that would suggest a decrease in efficacy in the limited time frame of our study. The mild decrease in patients' satisfaction assessed by TSQM that was not correlated with other PROMs may have been caused by a nocebo effect. Our study supports the results of other real life studies indicating no decrease of efficacy after a non-medical switch from originator to biosimilar infliximab.

**Acknowledgements:** Supported by project 00023728 from Ministry of Health in the Czech Republic

**Disclosure:** Š. Forejtová, None; J. Zavada, None; L. Szczukova, None; K. Jarosova, None; T. Philipp, None; K. Pavelka, None.


**Abstract Number:** 1550

**One-Year Clinical Outcomes in 1623 Patients with Inflammatory Arthritis Who Switched from Originator to Biosimilar Etanercept – an Observational Study from the Danish Danbio Registry**

Bente Glintborg¹, Emina Omerovic¹, Kamilla Danebod¹, Dorte Vendelbo Jensen¹, Henrik Nordin¹, Anne Gitte Loft¹, Stavros Chrysidis¹, Johnny Lillegund Raun¹, Oliver Hendricks¹, Hanne Lindegaard¹, Jakob Espesen¹, Susanne Jakobsen¹, Inger Marie J. Hansen¹, Jolanta Grydehøj¹, Emil Dalgaard¹, Dorte Dalsgaard Pedersen¹, Natalia Manilo², Lis Smedegaard Andersen³, Salome Kristensen¹, Asta Linauskas¹, Niels Steen Krogh⁴ and Merete Lund Hetland⁵, ¹The DANBIO registry and the Danish Departments of Rheumatology, Copenhagen, Denmark, ²Center for Rheumatology and Spine Diseases, Copenhagen University Hospital Frederiksberg, Copenhagen, Denmark, ³Department of Rheumatology, The DANBIO registry and the Danish Departments of Rheumatology, Copenhagen, Denmark, ⁴The DANBIO Registry, Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Rigshospitalet, Copenhagen, Denmark, ⁵The DANBIO registry and the Danish Departments of Rheumatology, Glostrup, Denmark

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**
According to Danish national guidelines issued in April 2016, a non-medical switch from originator (ETA, Enbrel) to biosimilar Etanercept (SB4, Benepali) (50 mg s.c.) was conducted for economic reasons in patients with inflammatory rheumatic diseases treated in routine care. Changes in disease activity 3-months pre-switch and 0-3 months after the switch were comparable.\(^1\)

We aimed to investigate the 1-year retention rates and reasons for withdrawal in ETA-treated patients (pts) with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondyloarthritis (SpA) who switched to SB4 ("switchers") and to characterize ETA treated patients, who did not switch to SB4 ("non-switchers").

**Methods:**

Patients were monitored prospectively in the DANBIO registry. Reasons for SB4 withdrawal were categorized as adverse events (AE), lack of effect (LOE) or other. Baseline characteristics associated with SB4 withdrawal were explored by multivariable Cox regression analyses stratified by diagnosis (RA/PsA/SpA) and included gender/age/concomitant methotrexate (MTX)/SB4 dose/patient’s global score (PGS). Comparisons of switchers (at baseline = first SB4 treatment) versus non-switchers (per April 1\(^{st}\) 2016) were by Chi-square/Mann-Whitney.

**Results:**

A total of 2,030 ETA treated patients were identified, of which 1,623 (80%) were switched to SB4.

In switchers, 276 patients (18%) stopped SB4 treatment during follow-up, mainly due to LOE (54%) or AE (28%) (Table). In RA, characteristics associated with withdrawal were no concomitant MTX and higher PGS (all \(p<0.05\)) whereas gender, age and SB4 dose were insignificant. In PsA, associated factors were female gender, higher PGS and lower SB4 doses, whereas no significant factors were found in SpA.

Compared to non-switchers, switchers more frequently had PsA (22%/12%), received co-medication with methotrexate (48%/42%), were men (40%/35%), were rarely treated with 25 mg ETA (1%/43%) doses and had lower PGS (29(13-54)mm /33(14-62)mm) (median(IQR)), (all \(p<0.05\)) whereas age was similar.

**Conclusion:**

Of 2030 ETA treated patients, 80% conducted a nationwide, non-medical switch from originator ETA to biosimilar SB4. 18% of switchers withdrew during 1-year follow-up. Comparison of the withdrawal rate with a historic ETA treated patient cohort is ongoing and will be presented at the ACR. In RA and PsA withdrawal was associated with higher patient’s global scores. Some channeling to non-medical switching was observed, since non-switchers differed in baseline characteristics and often received 25 mg ETA.

**References:**

1) Glintborg et al. 10.1136/annrheumdis-2017-eular

Table. Baseline demographics and 1-year treatment outcomes among ETA switchers
<table>
<thead>
<tr>
<th>Number, n</th>
<th>Rheumatoid arthritis</th>
<th>Psoriatic arthritis</th>
<th>Axial spondyloarthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%)</td>
<td>937</td>
<td>351</td>
<td>335</td>
</tr>
<tr>
<td>692 (74%)</td>
<td>160 (46%)</td>
<td>113 (34%)</td>
<td></td>
</tr>
</tbody>
</table>

**Baseline demographics according to diagnosis***

| Age, years | 60 (48-69) | 52 (43-61) | 48 (39-57) |
| Concomitant MTX | 59% | 48% | 15% |
| In remission** | 65% | 70% | 28% |
| Patient’s global score (VAS), mm | 29 (13-55) | 30 (12-53) | 30 (12-53) |
| HAQ | 0.8 (0.1-1.3) | 0.5 (0.0-1.0) | 0.4 (0.0-0.8) |
| Prior ETA treatment duration, yrs | 6.1 (3.7-8.8) | 4.5 (3.0-7.5) | 4.7 (2.9-6.9) |

**1-year treatment outcomes***

| Withdrawal during follow-up, n (%) | 177 (19%) | 52 (15%) | 47 (14%) |
| Prior ETA treatment duration in withdrawers, yrs | 5.6 (2.8-8.9) | 3.7 (2.7-6.3) | 3.2 (1.5-5.2) |

**Reasons for withdrawal (total n=276):**

Lack of effect 45%, adverse events 28%, other 5%, several reasons 3%, cancer 3%, remission 2%, pregnancy 2%, death 1%, infection 1%, surgery <1%, not stated 10%

Numbers are medians (interquartile ranges) unless otherwise stated.

Abbreviations: VAS: visual analogue scale, ETA: originator Etanercept, SB4: biosimilar etanercept

* Baseline is according to first SB4 dose

** DAS28<2.6, ASDAS<1.3

*** Median follow-up was 316(254-345)days

Disclosure: B. Glintborg, Abbvie, Biogen, 2; E. Omerovic, None; K. Danebod, None; D. V. Jensen, None; H. Nordin, None; A. G. Loft, AbbVie, MSD, Novartis, Pfizer, Roche, UCB, 2; S. Chrysidis, None; J. L. Raun, None; O. Hendricks, Abbvie, Roche, Novartis, 2; H. Lindegaard, None; J. Espesen, None; S. Jakobsen, None; I. M. J. Hansen, Roche Pharmaceuticals, 2; J. Grydehøj, None; E. Dalgaard, None; D. Dalsgaard Pedersen, None; N. Manilo, None; L. Smødeggaard Andersen, None; S. Kristensen, None; A. Linauskas, None; N. S. Krogh, None; M. Lund Hetland, Orion, BMS, AbbVie, Biogen, Pfizer, MSD, 2.


Abstract Number: 1551
Avoidance of Physical Activity Leads to Reduced Inflammatory Enthesitis on Ultrasound

Kim Wervers1, Irene Herrings1, Jolanda J. Luime2, Marlies Moed1, Ilja Tchetverikov3, Andreas H. Gerards4, J.M.W. Hazes5 and Marijn Vis2, 1Erasmus Medical Centre, Rotterdam, Netherlands, 2Rheumatology, Erasmus Medical Centre, Rotterdam, Netherlands, 3Albert Schweitzer Hospital, Dordrecht, Netherlands, 4Sint Franciscus Vlietland Group, Schiedam, Netherlands, 5Department of Rheumatology, Erasmus Medical Centre, Rotterdam, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Enthesitis is one of the manifestations of psoriatic arthritis (PsA), but no clear definition for the diagnosis exists. To further evaluate the added value of sonographic evaluation of entheses in diagnosing enthesitis, more knowledge on factors associated with sonographic enthesitis is needed. We aim to evaluate which clinical characteristics are associated with sonographic enthesitis changes in a cross-sectional PsA population.

Methods: established PsA patients were asked to participate, irrespective of enthesitis complaints. Patients were interviewed on history of musculoskeletal complaints (MSC), more specifically if they had complaints during activities and whether they avoided physical activities (during exercise, work, household tasks, hobbies, chores). Tenderness was determined in the MASEI entheses and those in the Leeds Enthesitis Index (LEI) and Maastricht Ankylosing Spondylitis Enthesitis Score (MASES). Previously we showed that a modified Madrid Sonographic Enthesitis Index (MASEI, i.e. excluding knee enthesis thickness and scoring PD-signal semi-quantitatively) distinguishes entheses of PsA patients from those of healthy volunteers. A sonographist unaware of clinical findings scored the modified MASEI. Multivariable linear regressions of structural (erosions, calcifications, structure) and inflammatory (thickness, bursitis and PD) modified MASEI scores were performed (transformed for a better distribution). Variables included age, gender, PsA duration, medication use (non/nsaids vs. sDMARDs vs. bDMARDs), LEI + MASES and avoidance (no vs. yes).

Results: 84 PsA patients participated (45 males, mean age 55, median disease duration 8 years). Median modified MASEI was 12 (IQR 7.25-17), with a structural component score of 7 (3-10) and inflammatory component score of 6 (3.5-8.5). 8 patients used no medication or NSAIDs only, 36 used sDMARDs and 40 used bDMARDs. 45 patients reported avoiding activities. In a multivariable analysis, inflammatory modified MASEI was negatively associated with avoidance (i.e. fewer inflammatory changes in patients reporting avoidance) and positively associated with age, BMI and use of biologics. Structural MASEI was positively associated with age only.

Conclusion: Avoiding physical activities is associated with fewer inflammatory changes of the entheses. More inflammatory changes are seen in older or overweight patients and patients on biologics, in the latter possibly due to more active disease.
Table 1. Univariable and multivariable linear regression analysis of inflammatory and structural summary scores of MASEI

<table>
<thead>
<tr>
<th></th>
<th>inflammatory modified MASEI</th>
<th>structural modified MASEI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Univariable</td>
<td>Multivariable</td>
</tr>
<tr>
<td>age</td>
<td>0.018</td>
<td>[0.005, 0.031]</td>
</tr>
<tr>
<td>gender (female vs. male)</td>
<td>0.156</td>
<td>0.162</td>
</tr>
<tr>
<td>BMI</td>
<td>0.030</td>
<td>0.031</td>
</tr>
<tr>
<td>medication use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>non/ins/ads vs. sDMARDs</td>
<td>0.365</td>
<td>0.392</td>
</tr>
<tr>
<td>non/ins/ads vs. bDMARDs</td>
<td>0.484</td>
<td>0.588</td>
</tr>
<tr>
<td>yrs/disease duration</td>
<td>0.005</td>
<td>-0.021</td>
</tr>
<tr>
<td>LeL + MASES</td>
<td></td>
<td></td>
</tr>
<tr>
<td>avoidance (no vs. Yes)</td>
<td>-0.415</td>
<td>[-0.739, -0.098]</td>
</tr>
</tbody>
</table>

Data shown as β [95% CI], inflammatory and structural modified MASEI square root+1 transformed. Modified MASEI: MASEI with new PD scoring method: 1: one spot of PD, 1.5: some spots of PD, 2: confluent signal, 3: severe signal) and without knee entheses thickness. Structural components: erosions, calcifications, structure. Inflammatory components: bursitis, thickness and PD signal.

Disclosure: K. Wervers, None; I. Herrings, None; J. J. Luime, None; M. Moed, None; I. Tchetverikov, None; A. H. Gerards, None; J. M. W. Hazes, None; M. Vis, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/avoidance-of-physical-activity-leads-to-reduced-inflammatory-enthesitis-on-ultrasound

Abstract Number: 1552

Persistency of Tumor Necrosis Factor Inhibitor Therapy in US Patients with Ankylosing Spondylitis: Data from the Corrona Psoriatic Arthritis/Spondyloarthritis (PsA/SpA) Registry

Philip J Mease1, Désirée van der Heijde2, Chitra Karki3, Mei Liu3, Yujin Park4 and Jeffrey D. Greenberg5,
1Swedish Medical Center and University of Washington, Seattle, WA, 2Leiden University Medical Center, Leiden, Netherlands, 3Corrona, LLC, Southborough, MA, 4Novartis Pharmaceuticals Corporation, East Hanover, NJ, 5New York University School of Medicine, New York, NY

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017

Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM

Background/Purpose: There are limited data regarding persistency of TNF inhibitor (TNFi) therapies in patients with ankylosing spondylitis (AS) treated in real-world clinical practice. The objective of this analysis was to evaluate time to discontinuation of a TNFi therapy in patients with AS in the US-based Corrona Psoriatic Arthritis/Spondyloarthritis (PsA/SpA) Registry.

Methods: This analysis included all patients with AS aged ≥ 18 years enrolled in the Corrona PsA/SpA registry between April 2013 and January 2015 who were receiving or initiated a TNFi therapy at the time of registry enrollment (index visit) and had ≥ 1 follow-up visit. Patient demographics, clinical characteristics, patient-reported outcomes (PROs) and treatment history at baseline were summarized descriptively. Median (95% CI) time from enrollment to discontinuation of the index TNFi therapy was estimated using Kaplan-Meier analysis.
Results: Of the 179 patients included in the analysis, 30.3% were female, 91.8% were white, mean (SD) age was 47.8 (14.0) years and mean (SD) body mass index was 29.3 (6.9) kg/m\(^2\) (Table 1). The mean (SD) disease duration was 18.3 (12.7) years, and 89.9% of patients had received prior biologic therapy. At baseline, the mean (SD) Bath Ankylosing Spondylitis Disease Activity Index and Bath Ankylosing Spondylitis Functional Index scores were 3.9 (2.5) and 3.2 (2.8), respectively, and patients reported mean (SD) pain and fatigue scores of 38.1 (30.2) and 45.5 (29.4), respectively; additional disease activity measures and PROs are described in Table 1. A total of 57 patients (31.8%) discontinued their index TNFi therapy during follow-up. The median (95% CI) time from enrollment to TNFi discontinuation was 41 (34 to not estimable) months (Figure 1).

Conclusion: Approximately 30% of patients with AS who received a TNFi therapy at time of enrollment in the Corrona PsA/SpA registry and had ≥ 1 follow-up visit discontinued their index TNFi therapy, with a median time to discontinuation of 41 months. These results provide insight into the persistency of TNFi therapy in US patients with AS in a real-world setting.

### Table 1. Patient Demographics, Clinical Characteristics and Treatment History at the Index Visit Among Patients With AS With ≥ 1 Follow-Up Visit in the Corrona PsA/SpA Registry

<table>
<thead>
<tr>
<th>Characteristic*</th>
<th>Patients With AS With ≥ 1 Follow-Up Visit N = 179</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>47.8 (14.0)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>54 (30.3)</td>
</tr>
<tr>
<td>White, n (%)</td>
<td>157 (91.8)</td>
</tr>
<tr>
<td>BMI, kg/m(^2)</td>
<td>29.3 (6.9)</td>
</tr>
<tr>
<td>BMI (in kg/m(^2)) classifications, n (%)</td>
<td></td>
</tr>
<tr>
<td>Normal/underweight (&lt; 25.0)</td>
<td>47 (26.9)</td>
</tr>
<tr>
<td>Overweight (25.0 to &lt; 30.0)</td>
<td>61 (34.9)</td>
</tr>
<tr>
<td>Obese (≥ 30.0)</td>
<td>67 (38.3)</td>
</tr>
<tr>
<td>Disease duration, years</td>
<td>18.3 (12.7)</td>
</tr>
<tr>
<td>History of prior biologic use, n (%)</td>
<td>161 (99.9)</td>
</tr>
<tr>
<td>≥ 2 prior biologics</td>
<td>48 (26.8)</td>
</tr>
<tr>
<td>History of prior csDMARD use, n (%)</td>
<td>66 (39.9)</td>
</tr>
<tr>
<td>History of prior prednisone use, n (%)</td>
<td>18 (10.1)</td>
</tr>
<tr>
<td>Current prednisone use, n (%)</td>
<td>10 (5.6)</td>
</tr>
<tr>
<td>BASDAI (0-10)</td>
<td>3.9 (2.5)</td>
</tr>
<tr>
<td>BASFI (0-10)</td>
<td>3.2 (2.8)</td>
</tr>
<tr>
<td>ASDAS-CRP</td>
<td>1.9 (0.8)</td>
</tr>
<tr>
<td>Patient pain (VAS, 0-100)</td>
<td>38.1 (30.2)</td>
</tr>
<tr>
<td>Patient fatigue (VAS, 0-100)</td>
<td>45.5 (29.4)</td>
</tr>
<tr>
<td>HAQ (0-2)</td>
<td>9.5 (0.6)</td>
</tr>
<tr>
<td>WPFI domains</td>
<td></td>
</tr>
<tr>
<td>Absenteeism (% work time missed)</td>
<td>6.8 (17.8)</td>
</tr>
<tr>
<td>Presenteeism (% impairment while working)</td>
<td>23.0 (23.7)</td>
</tr>
<tr>
<td>Work productivity loss (% overall work impairment)</td>
<td>26.1 (26.0)</td>
</tr>
<tr>
<td>Activity impairment (% activity impairment)</td>
<td>33.2 (30.9)</td>
</tr>
</tbody>
</table>

AS, ankylosing spondylitis; ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score using C-reactive protein; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BMI, body mass index; csDMARD, conventional synthetic disease-modifying antirheumatic drug; HAQ, Health Assessment Questionnaire; VAS, visual analog scale; WPFI, Work Productivity and Activity Impairment Questionnaire.

* All values are presented as mean (SD) unless otherwise stated.
Discontinuation of Tumor Necrosis Factor Inhibitor Therapy in US Patients with Ankylosing Spondylitis: Data from the Corrona Psoriatic Arthritis/Spondyloarthritis (PsA/SpA) Registry

Philip J Mease\textsuperscript{1}, Désirée van der Heijde\textsuperscript{2}, Chitra Karki\textsuperscript{3}, Mei Liu\textsuperscript{3}, Yujin Park\textsuperscript{4} and Jeffrey D. Greenberg\textsuperscript{5},
\textsuperscript{1}Swedish Medical Center and University of Washington, Seattle, WA, \textsuperscript{2}Leiden University Medical Center, Leiden, Netherlands, \textsuperscript{3}Corrona, LLC, Southborough, MA, \textsuperscript{4}Novartis Pharmaceuticals Corporation, East Hanover, NJ, \textsuperscript{5}New York University School of Medicine, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

**Background/Purpose:** There is a need to better characterize patients with ankylosing spondylitis (AS) who discontinue vs continue TNF inhibitor (TNFi) therapies in real-world clinical settings. The objective of this study was to compare patient characteristics and disease outcomes in patients with AS who continued vs discontinued a TNFi therapy by their second follow-up visit in the US-based Corrona Psoriatic Arthritis/Spondyloarthritis (PsA/SpA) Registry.

**Methods:** All patients with AS aged ≥ 18 years enrolled in the Corrona PsA/SpA Registry between April 2013 and January 2015 who were receiving or initiated a TNFi agent at the time of registry enrollment (index visit) and had ≥ 2 follow-up visits were included. Patients were assigned to a cohort based on continued or discontinued use of their TNFi at the second follow-up visit (mean [SD] follow-up, 17.8 [7.1] months). Patient demographics, clinical characteristics, patient-reported outcomes (PROs) and treatment history at baseline were compared between cohorts using t-tests for continuous variables and chi-square or Fisher’s exact tests for categorical variables. Reasons for discontinuation of the index TNFi were summarized descriptively. Mean changes from baseline in clinical disease activity measures and PROs were assessed at second follow-up and compared between cohorts using unadjusted mean differences.

**Results:** Of the 155 included patients, 37 (23.9%) discontinued their index TNFi therapy by the second follow-up visit, including 24 patients who switched to another biologic. Patients who discontinued their index TNFi were significantly older (52.1 vs 46.6 years), more likely to be obese (59.5% vs 34.2%) and had significantly worse mean BASDAI (4.8 vs 3.5) and BASFI (4.2 vs 2.8) scores at the index visit compared with those who continued their TNFi. Of the 37 patients who discontinued their index TNFi, 18 provided reasons for discontinuation; the most common provider-reported reasons for discontinuation were lack of effect (n = 6), side effects (n = 4) and other reasons (n = 5). Patients who discontinued their index TNFi had worse outcomes with respect to disease activity and PROs at the second follow-up visit compared with those who continued their TNFi; however, differences between the groups did not reach statistical significance (Table 1).

**Conclusion:** Patients with AS in the Corrona PsA/SpA Registry who discontinued their index TNFi therapy by the second follow-up visit were older, more likely to be obese and had higher disease activity at baseline compared with patients who continued their TNFi. Differences in clinical disease activity measures and PROs at the second follow-up visit between those who discontinued vs continued their TNFi did not reach statistical significance, possibly due to small sample size. These results provide insight into patient characteristics and disease outcomes in patients with AS who discontinue vs continue TNFi therapy.

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Mean (SD) Change From Baseline</th>
<th>Unadjusted Difference, β (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ASDAS</strong></td>
<td>-0.09 (0.69)</td>
<td>0.36 (0.82)</td>
<td>0.45 (0.03 to 0.92)</td>
</tr>
<tr>
<td><strong>BASDAI (0-10)</strong></td>
<td>-0.15 (1.62)</td>
<td>-0.62 (1.87)</td>
<td>-0.67 (-1.41 to 0.06)</td>
</tr>
<tr>
<td><strong>BASFI (0-10)</strong></td>
<td>-0.10 (1.49)</td>
<td>-0.24 (1.94)</td>
<td>-0.14 (-0.77 to 0.48)</td>
</tr>
<tr>
<td><strong>SPARCC enthesis (0-16)</strong></td>
<td>-0.20 (1.76)</td>
<td>-0.41 (1.24)</td>
<td>-0.20 (-0.82 to 0.41)</td>
</tr>
<tr>
<td><strong>HAQ (0-3)</strong></td>
<td>0.03 (0.31)</td>
<td>0.02 (0.43)</td>
<td>-0.02 (-0.16 to 0.12)</td>
</tr>
<tr>
<td><strong>Patient pain (VAS, 0-100)</strong></td>
<td>-1.81 (23.60)</td>
<td>1.39 (18.84)</td>
<td>3.19 (-5.92 to 12.31)</td>
</tr>
<tr>
<td><strong>Patient fatigue (VAS, 0-100)</strong></td>
<td>-3.78 (21.94)</td>
<td>-3.08 (25.66)</td>
<td>4.36 (-12.92 to 4.32)</td>
</tr>
</tbody>
</table>

**Table 1. Change From Baseline in Clinical and Patient-Reported Outcomes at the Second Follow-Up Visit in Patients With AS Who Continued vs Discontinued a TNFi Therapy.**

AS, ankylosing spondylitis; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; HAQ, Health Assessment Questionnaire; SPARCC, Spondyloarthritis Research Consortium of Canada; TNFi, tumor necrosis factor inhibitor; VAS, visual analog scale; WP A, Work Productivity and Activity impairment questionnaire.
Discontinuation and Switching Patterns By TNFi Line of Therapy in Patients with Psoriatic Arthritis—Results from the Corrona Psoriatic Arthritis/Spondyloarthritis (PsA/SpA) Registry

Philip J Mease, Chitra Karki, Mei Liu, YouFu Li, Peter Hur and Jeffrey D. Greenberg, Swedish Medical Center and University of Washington, Seattle, WA, Corrona, LLC, Southborough, MA, University of Massachusetts Medical School, Worcester, MA, Novartis Pharmaceuticals Corporation, East Hanover, NJ, New York University School of Medicine, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthopathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Few real-world studies have characterized the use of first- vs second-line tumor necrosis factor inhibitors (TNFis) in US patients with psoriatic arthritis (PsA). This study examined disease characteristics and described patterns of TNFi use through the first follow-up visit (≈ 6 months) in patients with PsA who initiated a first- vs second-line TNFi in the US Corrona PsA/SpA Registry.

Methods: This study included adult patients with PsA enrolled in the Corrona PsA/SpA Registry who initiated first- or second-line TNFi therapy between March 2013 and September 2016 with ≥ 1 follow-up visit. Patient demographics, disease characteristics and patient-reported outcomes were assessed at the time of TNFi initiation (baseline) and compared between cohorts using two-sample t-tests for continuous variables and chi-square or Fisher’s exact tests for categorical variables. The proportions of patients who continued their index TNFi, discontinued without switching, or switched to another biologic at the time of the first follow-up visit was examined and compared between cohorts.

Results: Of the 230 patients with PsA who had ≥ 1 follow-up visit (median [IQR] time to first follow-up, 6.8 [6.0, 9.7] months), 139 patients initiated a first-line TNFi and 91 patients initiated a second-line TNFi. At baseline, patients who initiated a second-line TNFi had higher enthesitis and dactylitis counts, were less likely to be in minimal disease activity and had worse pain and fatigue compared with patients who initiated a first-line TNFi; however, these differences were not statistically significant (Table 1). A higher proportion of patients initiating a first-line TNFi continued their TNFi at the first follow-up visit than those initiating a second-line TNFi (76.3% vs 59.3%; P = 0.001). Among first-line initiators, 19.4% and 4.3% discontinued their index TNFi without switching, or
switched to another biologic, respectively, compared with 22.0% and 18.7% of patients initiating a second-line TNFi (Figure 1; both \( P = 0.001 \)). Of the 17 first- and 19 second-line TNFi initiators with provider-reported reasons for discontinuing or switching TNFis, the most common reasons were lack of effect (44.4% and 60.0%, respectively) and adverse effects (27.8% and 10.0%, respectively).

**Conclusion:** Patients with PsA initiating a second-line TNFi were more likely to discontinue or switch therapies compared with patients initiating a first-line TNFi, with the most common reason for discontinuation/switch due to lack of effect. These findings from a US registry suggest potential unmet needs for patients with PsA when using TNFis as a second-line therapy in a real-world setting.

**Table 1. Baseline Demographic, Disease and Patient-Reported Characteristics of Patients With PsA at the Time of Initiation of First- or Second-Line TNFi**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>First-Line TNFi n = 139</th>
<th>Second-Line TNFi n = 91</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>51.8 (13.9)</td>
<td>53.3 (11.8)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>74 (53.6)</td>
<td>56 (62.2)</td>
</tr>
<tr>
<td>White, n (%)</td>
<td>130 (96.3)</td>
<td>80 (93.0)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>31.7 (8.5)</td>
<td>32.0 (6.7)</td>
</tr>
<tr>
<td>Disease duration, years</td>
<td>9.3 (9.3)</td>
<td>12.4 (10.1)</td>
</tr>
<tr>
<td>History of comorbid conditions, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>15 (10.8)</td>
<td>15 (16.5)</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>15 (10.8)</td>
<td>12 (13.2)</td>
</tr>
<tr>
<td>Any cancer</td>
<td>10 (7.2)</td>
<td>7 (7.7)</td>
</tr>
<tr>
<td>Serious infections</td>
<td>3 (2.2)</td>
<td>5 (5.5)</td>
</tr>
<tr>
<td>SPARCC enthesis (0-16)</td>
<td>0.8 (1.9)</td>
<td>1.4 (3.0)</td>
</tr>
<tr>
<td>Dactylitis count (0-20)</td>
<td>0.3 (1.2)</td>
<td>0.5 (1.4)</td>
</tr>
<tr>
<td>BSA, % affected</td>
<td>4.4 (6.5)</td>
<td>4.9 (9.1)</td>
</tr>
<tr>
<td>MDA, n (%)</td>
<td>38 (35.8)</td>
<td>19 (27.5)</td>
</tr>
<tr>
<td>CDAI</td>
<td>14.0 (9.9)</td>
<td>12.9 (6.2)</td>
</tr>
<tr>
<td>Patient global skin assessment (VAS 0-100)</td>
<td>55.5 (27.2)</td>
<td>50.1 (29.5)</td>
</tr>
<tr>
<td>Patient pain (VAS 0-100)</td>
<td>42.5 (29.7)</td>
<td>49.7 (29.1)</td>
</tr>
<tr>
<td>Patient-reported fatigue (VAS 0-100)</td>
<td>44.2 (28.4)</td>
<td>50.2 (29.6)</td>
</tr>
<tr>
<td>HAQ (0-3)</td>
<td>0.8 (0.7)</td>
<td>0.9 (0.7)</td>
</tr>
<tr>
<td>EQ-SD (0-1)</td>
<td>0.7 (0.2)</td>
<td>0.7 (0.2)</td>
</tr>
<tr>
<td>WPAl domains</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Work time missed</td>
<td>1.6 (5.8)</td>
<td>8.6 (21.5)</td>
</tr>
<tr>
<td>% Impairment while working</td>
<td>23.2 (20.8)</td>
<td>28.0 (28.3)</td>
</tr>
<tr>
<td>% Overall work impairment</td>
<td>23.8 (21.2)</td>
<td>29.7 (30.7)</td>
</tr>
<tr>
<td>% Activity Impairment</td>
<td>35.9 (30.7)</td>
<td>36.5 (30.9)</td>
</tr>
</tbody>
</table>

BSA, body surface area; CDAI, Clinical Disease Activity Index; EQ-5D, EQ 5 Dimensions questionnaire; HAQ, Health Assessment Questionnaire; MDA, minimal disease activity; PsA, psoriatic arthritis; SPARCC, Spondyloarthritis Research Consortium of Canada; TNFi, tumor necrosis factor inhibitor; VAS, visual analog scale; WPAl, Work Productivity and Activity Impairment questionnaire.

* All values were calculated based on available data and are presented as “mean (SD)” unless otherwise stated. All variables had < 20% missing data except for MDA (n = 106/99).

1 \( P < 0.05 \)

1 MDA was defined as “Yes” if a patient met ≥ 5 of the 7 following categories (Costes LC, et al. Ann Rheum Dis. 2010;69[1]:48-53): tender joint count ≤ 1, swollen joint count ≤ 1, BSA ≤ 3%, patient pain VAS ≤ 15, patient global activity VAS ≤ 20, HAQ ≤ 0.5, tender enthesal points ≤ 1.
Disclosure: P. J. Mease, Celgene, Novartis, AbbVie, Amgen, BMS, Lilly, Pfizer and UCB, 2, Celgene, Corrona, Novartis, AbbVie, Amgen, BMS, Crescendo, Genentech, Janssen, Lilly, Merck, Pfizer and UCB, 5, AbbVie, Amgen, BMS, Crescendo, Celgene, Genentech, Janssen, Pfizer and UCB, 8; C. Karki, Corrona, LLC, 3; M. Liu, Corrona, LLC, 3; Y. Li, University of Massachusetts Medical School, 3; P. Hur, Novartis Pharmaceuticals Corporation, 3; J. D. Greenberg, Corrona, LLC, 1, Corrona, LLC, 3, Eli Lilly, Genentech, Janssen, Novartis, Pfizer, 5.

Abstract Number: 1555

Treatment Changes By Joint Activity and Skin Severity in Patients with Comorbid Psa and Pso

Philip J Mease1, Carol J. Etzel2, Jeffrey Lisse3, April W Armstrong4, William J Huster3, Sabrina Rebello2, Rhiannon Dodge2, Talia M Muram3, Sarah Al Sawah3, Mwangi J Murage2, Jeffrey D Greenberg2 and William Malatestinic3, 1Swedish Medical Center and University of Washington, Seattle, WA, 2Corrona, LLC, Southborough, MA, 3Eli Lilly and Company, Indianapolis, IN, 4Keck School of Medicine, University of Southern California, Los Angeles, CA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017

Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Treatment of both joint and skin symptoms is important for overall disease management of patients with psoriatic arthritis and comorbid psoriasis\textsuperscript{1,2}. The objective of this study was to characterize treatment changes and the reasons in patients with comorbid PsA and PsO through 12 months of follow-up after enrollment into Corrona registry. Changes in joint/skin severity at the 12 month visit vs at enrollment were also evaluated.

Methods: Enrollment visit data from the Corrona PsA/SpA registry were obtained from 3/21/2013-9/30/2016 on patients with PsA diagnosed by a rheumatologist with a history of PsO. Patients were categorized into the following drug status groups: no change in therapy or change (reduction, addition or switch) in therapy. Reasons for discontinuation were categorized as: efficacy, safety, other, or unreported. Change in joint activity and skin severity from enrollment to 12 month visit were classified by change in category of CDAI, BSA or both. CDAI categories were as Low: ≤10, Moderate: 10<CDAI≤22, and High: >22. BSA was categorized as Low: ≤3%, Moderate: >3 to 10%, and High: >10%.

Results: 647 patients had CDAI, BSA, and known drug status. Majority (n=369, 57%) of patients had no changes in therapy. 278 patients had a change in therapy. Reasons for change were: no reason (70.9%, n=197), efficacy (10.4%; n=29); safety (5.8%; n=16), and other (12.9%; n=36). For patients whose joint or skin severity improved or worsened, the median change in BSA and CDAI scores was ≥ 4. Improvement in either joint or skin severity were seen in 135 (21%) and 138 (21%) patients, respectively. Worsening of either joint or skin severity were seen in 113 (18%) and 52 (8%) patients, respectively. No change in both joint and skin severity was seen in 281 (43%) patients. Patients with improvement in both joint and skin severity saw the greatest median reduction in CDAI and had the second largest median decrease in BSA, while those who worsened in both had the greatest median increase in CDAI and BSA scores (Table 1).

Conclusion: The majority of patients had no change in therapy and no change in either joint or skin severity after 12 months of follow-up. Patients with improvement in both joint and skin severity saw a large median reduction in CDAI and BSA while those who worsened had the greatest median increase in CDAI and BSA. Further study of the real-world impact of therapy changes on subsequent joint activity and skin severity is needed.

Table 1: Changes in Joint Activity and Skin Severity at 12 month FU visit

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>%</th>
<th>Δ in CDAI median (IQR)</th>
<th>Δ in BSA median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improve on both</td>
<td>39</td>
<td>6.0</td>
<td>-9.2 (-18.7, -3.1)</td>
<td>-7.0 (-14.0, -3.0)</td>
</tr>
<tr>
<td>Improve in Skin, no change in Joints</td>
<td>89</td>
<td>13.8</td>
<td>0.0 (2.5, 2.4)</td>
<td>-8.0 (-12.0, -4.0)</td>
</tr>
<tr>
<td>Improve in Joints, no change in Skin</td>
<td>85</td>
<td>13.1</td>
<td>-7.3 (-12.5, -3.5)</td>
<td>0.0 (-1.0, 0.0)</td>
</tr>
<tr>
<td>No Change in both</td>
<td>281</td>
<td>43.4</td>
<td>-0.1 (-2.4, 1.2)</td>
<td>0.0 (-1.0, 0.0)</td>
</tr>
<tr>
<td>Worsen in Skin, Improve in Joints</td>
<td>11</td>
<td>1.7</td>
<td>-5.5 (-8.0, -2.2)</td>
<td>4.0 (2.0, 8.0)</td>
</tr>
<tr>
<td>Worsen in Joints, Improve in Skin</td>
<td>10</td>
<td>1.5</td>
<td>6.6 (4.0, 11.1)</td>
<td>-4.5 (-12.0, -4.0)</td>
</tr>
<tr>
<td>Worsen in Skin, No change in Joints</td>
<td>29</td>
<td>4.5</td>
<td>-0.5 (-0.8, 1.0)</td>
<td>4.0 (3.0, 9.0)</td>
</tr>
<tr>
<td>Worsen in Joints, No change in Skin</td>
<td>91</td>
<td>14.1</td>
<td>6.5 (2.6, 10.5)</td>
<td>0.0 (-1.0, 0.0)</td>
</tr>
<tr>
<td>Worsen in Both</td>
<td>12</td>
<td>1.9</td>
<td>10.0 (6.5, 18.8)</td>
<td>6.0 (3.5, 8.0)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>647</td>
<td>100.0</td>
<td>-0.3 (-4.0, 2.5)</td>
<td>0.0 (-2.0, 0.0)</td>
</tr>
</tbody>
</table>

References:


Efficacy of Biologics and New Anti-Inflammatory Agents Used in the Treatment of Active Psoriatic Arthritis: Systematic Literature Review and Network Meta-Analysis of the Evidence.

Mahdi Gharaibeh1, Yingxin Xu2, Joseph Lee3, Madhura Chitnis2 and David Collier4, 1Amgen Inc., Thousand Oaks, CA, 2Evidera, Bethesda, MD, 3Evidera, Bethesda, MD, 4Amgen, Inc, Terni, Italy
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Psoriatic arthritis (PsA) is an inflammatory arthritis associated with psoriasis. Biologics are usually the first-line FDA-approved disease-modifying anti-rheumatic drug (DMARD) treatment; however, no published network meta-analysis (NMA) has presented efficacy results by prior biologic experience. The aim of this study is to compare the efficacy of treatments in moderate-to-severe PsA in biologic-naïve and biologic-exposed patients (pts).

Methods:
MEDLINE, Embase, Cochrane Central Register of Controlled Trials, and conference databases for the European League Against Rheumatism, American College of Rheumatology (ACR), and British Society for Rheumatology in 2015 and 2016 were searched for randomized controlled trials published from 1/2009 to 4/2017. Treatments included were tumor necrosis factor inhibitors (TNFis; etanercept ETN, adalimumab ADA, infliximab IFX, certolizumab pegol CZP, and golimumab GOL), IL-17 inhibitors (secukinumab SEC, ixekizumab, and brodalumab BRO), phosphodiesterase 4 Inhibitor (apremilast APR) and IL-12/23 blocker (ustekinumab UST). Outcomes of interest were the proportion of pts achieving ≥20% improvement in ACR response criteria (ACR20) and proportion achieving Psoriatic Arthritis Response Criteria (PsARC) at 12 and 24 weeks; these were the most commonly used outcomes in RCTs. A Bayesian NMA estimated the comparative efficacy of these regimens via the best fitting random- or fixed-effects model.

Results:
Among 34 trials identified, 16 PsA trials for biologic-naive therapy were included, of which 5 trials also reported data for biologic-exposed pts. Pts in placebo arms received best standard of care (BSC), including non-steroidal anti-inflammatory drugs with concomitant conventional non-biologic DMARDs; BSC served as the common comparator in the NMA. Full results are shown in Table 1. For ACR20 at 12 weeks in a biologic-naive population, the odds ratio (OR) of response for TNFis vs. BSC ranged from 3.36 for CZP to 19.49 for ETN and from 2.33 for BRO280 to 2.54 for APR in other biologics. At 24 weeks, the OR of response for TNFis vs. BSC ranged from 4.28 for CZP to 11.26 for GOL and from 2.64 for UST45 to 6.77 for SEC150 in other biologics. For ACR20 at 24 weeks in a biologic-exposed population, the OR of response for the TNFi CZP was 12.38 and ranged from 2.97 for SEC150 to 5.65 for SEC300 in other biologics. For PsARC at 12 weeks in a biologic-naive population, the OR of response for TNFis ranged from 4.22 for ADA to 24.75 for ETN while it ranged from 5.02 for IFX to 13.8 for GOL100 at 24 weeks in other biologics.

**Conclusion:**

Response rates vary greatly with DMARD treatment. There was a trend for higher odds of response with TNFis vs. other treatments in biologic-naive PsA pts. There were too few biologic-exposed outcomes to draw any conclusions. The results of this NMA suggest that TNFis show improved response for joint outcomes in PsA pts.

<table>
<thead>
<tr>
<th>Biologics vs. BSC*</th>
<th>Biologic Naïve PsA</th>
<th>Biologic Exposed PsA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ACR 20 @12wks</td>
<td>ACR 20 @24wks</td>
</tr>
<tr>
<td><strong>Adalimumab</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Etanercept</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Golimumab 50mg</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Golimumab 100mg</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Infliximab</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Certolizumab (Pooled)</strong></td>
<td>3.36 [1.3, 5.28]</td>
<td>2.64 [1.36, 5.28]</td>
</tr>
<tr>
<td><strong>Apremilast 30mg</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.54 [1.4, 4.59]</td>
<td>--</td>
</tr>
<tr>
<td><strong>Brodalumab 140mg</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.37 [0.6, 10.61]</td>
<td>--</td>
</tr>
<tr>
<td><strong>Brodalumab 280mg</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.33 [0.54, 10.8]</td>
<td>--</td>
</tr>
<tr>
<td><strong>Ustekinumab 45mg</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.32 [1.68, 6.47]</td>
<td>--</td>
</tr>
<tr>
<td><strong>Ustekinumab 90mg</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.28 [1.78, 10.57]</td>
<td>--</td>
</tr>
<tr>
<td><strong>Secukinumab 150mg</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>6.77 [3.54, 14.28]</td>
<td>--</td>
</tr>
<tr>
<td><strong>Secukinumab 300mg</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>6.27 [2.41, 16.76]</td>
<td>--</td>
</tr>
</tbody>
</table>

*BSC: NSAIDs (51 to 86%), MTX (36 to 71%), other cDMARDs (2 to 7%).
Abstract Number: 1557

Treatment Patterns in Psoriatic Arthritis: Experience from a Real-World Setting

Martin Brom¹, Sebastian Moyano¹, Florencia Beatriz Mollerach², Luciano Fernando Lo Giudice³, Maria Laura Acosta Felquer¹, Marina Scolnik⁴, Santiago Ruta⁴ and Enrique R Soriano⁵, ¹Rheumatology Unit, Internal Medicine Service, Hospital Italiano de Buenos Aires, Instituto Universitario Hospital Italiano de Buenos Aires, and Fundacion PM Catoggio, Buenos Aires, Argentina, ²Rheumatology Unit, Internal Medicine Service, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina, ³Rheumatology section, Internal Medicine Unit, Hospital Italiano de Buenos Aires and Fundacion PM Catoggio, CABA, Argentina, ⁴Rheumatology Unit, Internal Medicine Service, Hospital Italiano de Buenos Aires, CABA, Argentina, ⁵Argentina, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthopathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Both EULAR (European League Against Rheumatism) and GRAPPA (Group for Research and Assessment of Psoriasis and Psoriatic Arthritis) recently published treatment guidelines for Psoriatic Arthritis (PsA). Despite them, it remains unclear how physicians approach the management of PsA since there are few studies in the real world.

The purpose of the study was to describe treatment patterns (treatment discontinuation, switches, and therapy add-ons) for PsA patients in a real-world setting.

Methods:
A Retrospective descriptive study was performed in a university hospital with its own health insurance and captive population. All patients fulfilling Classification Criteria for Psoriatic Arthritis (CASPAR) with at least 3 visits of follow-up were included. Electronic medical records were reviewed between 01/01/2000 and 05/31/2017.

Results:
A total of 275 patients with PsA were included, with a median follow-up of 5.3 years (IQR: 2.1-10.2). Demographical data can be found in Table 1.

First line treatment were NSAIDs in 9.45% of the patients, traditional DMARD (tDMARD) in 88%, being methotrexate the most frequent one (76%), and biologic DMARDs (bDMARD) in 2.18%. None received
combination of tDMARDs. Reasons for switching or discontinuation were: lack of response 41%, adverse events 35%, remission 12% and suspension by the patient 12%.

bDMARD were used in 29.5% of the patients. As monotherapy in 55.4 % of the cases, and combined with methotrexate and leflunomide in 38.5 % and 6% respectively.

Survival rate of DMARDs at the end of follow up was 40% for tDMARD and 72% for bDMARD.

Additional information on both tDMARD and bDMARD can be found in Table 2.

At end of follow up mean DAS28 was 3.1 (SD: 1.4), mean HAQ: 0.42 (SD: 0.6), and 51% of patients fulfilled Minimal Disease Activity (MDA) criteria.

**Conclusion:**

In this real-world data, 40% of the patients continued with the first tDMARD after 5 years of follow up and only one third of patients required bDMARD. Drug survival was very good both for tDMARDs and bDMARDs.

Table 1

<table>
<thead>
<tr>
<th>Total PsA patients</th>
<th>275</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males, n (%)</td>
<td>162 (58.91)</td>
</tr>
<tr>
<td>Axial involvement, n (%)</td>
<td>40 (14.5%)</td>
</tr>
<tr>
<td>Median follow up time, years (IQR)</td>
<td>5.3 (2.1-10.2)</td>
</tr>
<tr>
<td>Mean age at diagnosis of Psoriasis, years (SD)</td>
<td>35.1 (16.9)</td>
</tr>
<tr>
<td>Mean age at diagnosis of PsA, years (SD)</td>
<td>48.3 (15.1)</td>
</tr>
<tr>
<td>Median time between diagnosis of Psoriasis and PsA, years (IQR)</td>
<td>13.1 (5.3-22.9)</td>
</tr>
<tr>
<td>Median time between first musculoskeletal symptom and diagnosis of PsA, years (IQR)</td>
<td>0.6 (0.2-2.1)</td>
</tr>
</tbody>
</table>
Table 2

<table>
<thead>
<tr>
<th>Treatment</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAIDs as first line</td>
<td>26 (9.45)</td>
</tr>
<tr>
<td>tDMARD as first line</td>
<td>243 (88%)</td>
</tr>
<tr>
<td>bDMARD as first line</td>
<td>6 (2.18)</td>
</tr>
<tr>
<td>tDMARD ever</td>
<td>249 (90.54)</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>218 (87.55)</td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>15 (6.02)</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>15 (6.02)</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>1 (0.4)</td>
</tr>
</tbody>
</table>

Median time from diagnosis to start of tDMARD, years (IQR) 0.3 (0.07-3.1)

Survival of first tDMARD at 3rd year, % (CI 95%) 52 (44-59)
Survival of first tDMARD at 5th year, % (CI 95%) 40 (32-48)
Combination of tDMARD ever, n (%) 13 (4.73)

Survival of first bDMARD at 3rd year, % (CI 95%) 81 (66-90)
Survival of first bDMARD at 5th year, % (CI 95%) 72 (54-85)

Disclosure: M. Brom, None; S. Moyano, None; F. B. Mollerach, None; L. F. Lo Giudice, None; M. L. Acosta Felquer, None; M. Scolnik, None; S. Ruta, None; E. R. Soriano, AbbVie, Janssen, Novartis, Pfizer Inc, UCB, 2,AbbVie, Janssen, Novartis, Pfizer Inc, UCB, 5,AbbVie, Janssen, Novartis, Pfizer Inc, UCB, 8.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/treatment-patterns-in-psoriatic-arthritis-experience-from-a-real-world-setting

Abstract Number: 1558

Changes in Blood Pressure with TNF Inhibitors for Psoriatic Arthritis

Birju D. Bhatt, J. Lynn Palmer, Jeffrey R. Curtis, Sathya Velkuru and Joel Kremer, Medicine, div-of Rheumatology, Albany Medical College, Albany, NY, Corrona Research Foundation, Albany, NY, Rheumatology & Immunology, University of Alabama at Birmingham, Birmingham, AL, Medicine, Albany Medical College, Albany, NY, Albany Medical College and the Center for Rheumatology, Albany, NY

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Spondyloarthopathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM
Background/Purpose:

Psoriasis is a complex disorder with cutaneous and rheumatological manifestations affecting 2-3% of the population of the Western world. The prevalence of hypertension (HTN) in patients with psoriasis has been well documented; about 30% of all psoriatic arthritis (PsA) patients have HTN. Treatment of PsA has also been shown to improve certain cardiovascular risks. We hypothesized that blood pressure was related to PsA disease activity. We also evaluated the relationship between PsA and blood pressure as it relates to initiation of TNF inhibitors (TNFi).

Methods:

We utilized the CORRONA database and examined patients with PsA from March 2013 to January 2017. Descriptive statistics were used to summarize patient demographic and clinical data at baseline (first visit in CORRONA database). An analysis of variance was made to determine associations between 3 categories of MD-defined psoriatic body surface area (BSA) and systolic blood pressure (SBP) and diastolic blood pressure (DBP). Spearman correlations were made between continuous values of systolic or diastolic blood pressure and BSA and clinical disease activity index (CDAI) using all visits. We also looked at changes in SBP or DBP between visits correlated with changes in CDAI in those who were initiated on TNFi while they were in the registry. LOESS curves were generated to visualize relationships between variables.

Results:

1481 patients with PsA were identified, who had a total of 6109 registry visits. When body surface area (BSA) of psoriasis was categorized into ² 2%, 3-10% and >10% in analysis of variance, SBP was higher with increased BSA (p=0.0048, F=7.26, r²=0.025). DBP was also higher with an increased BSA (p<0.0001, F=15.28, r²=0.005). SBP was positively correlated with CDAI (p=0.0057, r=0.037), as was DBP (p=0.0012, r=0.044). The association between SBP change and CDAI change in those who were initiated with a TNFi showed an overall decrease in SBP that was not statistically significant (p=0.26, r= -0.041). In addition, DBP change and CDAI change in those who initiated a TNFi also showed a non-statistically significant decrease (p=0.13, r= -0.054).

Conclusion:

In patients with PsA, there was a significant positive relationship between blood pressure and both psoriasis BSA and joint disease activity, measured by CDAI. We also conclude that clinically, the initiation of TNFi did decrease blood pressure, but the decrease was not significant. We believe that this is the first study to look at relationships between the initiation of TNFi treatment and blood pressure in PsA patients.
Residual Disease Activity in Psoriatic Arthritis Triggers Treatment Adjustment in Only a Quarter of Patients in Daily Clinical Practice

Leonieke van Mens¹, Sadaf Atiqi², Inka Fluri², Marleen van de Sande³, Arno van Kuijk⁴ and Dominique Baeten¹,
¹AMC, Amsterdam Immunology and Rheumatology Center, Amsterdam, Netherlands, ²Amsterdam Immunology and Rheumatology Center, Amsterdam, Netherlands, ³Clinical Immunology and Rheumatology, Amsterdam Rheumatology and immunology Center, Academic Medical Center/University of Amsterdam, Amsterdam, Netherlands, ⁴Reade, Amsterdam Immunology and Rheumatology Center, Amsterdam, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthopathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: With expanding therapeutic possibilities for the treatment of psoriatic arthritis (PsA) it will be increasingly important to determine residual disease and define when to adjust treatment. The rationale behind treatment decisions in current daily clinical practice and the relation with residual disease activity has not been investigated.

The aim of this study was to assess the current clinical practice on defining residual disease and the subsequent treatment decisions made in PsA patients.
Methods: This cross sectional study included 142 consecutive PsA patients who visited the outpatient clinic. The treating rheumatologist scored disease activity and her/his opinion on the presence of residual disease and the subsequent treatment decisions made. Patients scored patient disease activity scores.

Results: Two thirds (90/142) of the patients had musculoskeletal residual disease activity, with half of those having even moderate to high disease activity according to CDAI. There were no differences between the groups with or without residual disease activity in gender, disease duration, comorbidity, current treatment duration or number of previously used cDMARDS. Residual disease activity was more frequently reported in patients treated with a cDMARD only or a 2nd TNFi. 74% of the patients with residual disease activity were currently treated with either a cDMARD only or a first TNFi, suggesting that treatment modification could be an option. Of the 90 patients with residual disease, in 21(23%) treatment adjustment was initiated. Treatment changes were considered less frequent in those patients treated with a 2nd TNFi. No differences were seen in disease activity and demographics between those with or without a treatment adjustment. Judgment by the physician and/or patient rather than objective hurdles to treatment intensification (absence of additional treatment options, lack of compliance, intolerance) drove the decision not to modify treatment.

Conclusion: In almost 2/3 of the patients there was a presence of residual disease activity but only resulted in treatment adjustment in only a minority. As the adjustment could not be explained by comorbidities or a lack of treatment options there is clearly a further need for research to understand why disease activity does not lead to treatment adjustment in these cases.

Disclosure: L. van Mens, None; S. Atiqi, None; I. Fluri, None; M. van de Sande, Novartis, Eli Lilly, Boehringer Ingelheim, Abbvie, 5; A. van Kuijk, UCB, Pfizer, MSD, Janssen, 2, Novartis, Celgene, 5; D. Baeten, UCB, 3.
regarding treatment initiation and maintenance. The purpose of this analysis was to determine predictors of long-term mMDA response following adalimumab (ADA) treatment in pSpA pts from the ABILITY-2 study.

Methods: ABILITY-2\textsuperscript{2} was a phase 3 randomized, double-blind trial evaluating the efficacy and safety of 40 mg ADA every other week versus placebo (PBO) over 12 weeks (wks) followed by open-label (OL) ADA for 144 wks in pts with pSpA. This post-hoc analysis included pts who received at least one dose of ADA during the PBO-controlled period or OL extension. The mMDA for pSpA was defined as achieving at least 5 out of the following 6 criteria: 1) TJC78 ≤1; 2) SJC76 ≤1; 3) pt pain visual analog scale (VAS) ≤15 of 100 mm; 4) pt global activity (PtGA) VAS ≤20 of 100 mm; 5) HAQ-DI ≤0.5; and 6) tender enthesal points ≤1 (Leeds Enthesitis Index [LEI] or Spondyloarthritis Research Consortium of Canada [SPARCC] Enthesitis Index). In this post hoc analysis, multiple logistic regression with stepwise variable selection was used to determine predictors of long-term (yrs 1-3) and sustained (defined as mMDA for at least 24 consecutive wks) mMDA responses. Variable selection of baseline (BL) pt demographics and disease characteristics were performed with and without mMDA response at after 12 wks of ADA exposure (mMDA12) as a candidate.

Results: In pSpA pts treated with ADA, mMDA (5/6 LEI or SPARCC) was achieved by almost 41%, 49%, and 50% of pts at yrs 1, 2, and 3, respectively and sustained mMDA response was achieved by 42% of pts. Regardless of mMDA definition, achieving mMDA response after 12 wks of ADA exposure was a robust positive predictor of attaining both long-term mMDA at yrs 1-3 and sustained mMDA (Figure). In the model examining the BL predictors (model without mMDA12), age, BL enthesitis and BL BASDAI scores were most commonly selected as negative predictors for achieving long-term and sustained mMDA. Other selected predictors included BL dactylitis, physician’s global assessment, hsCRP, and male sex; however, these predictors were not consistently selected for all time points or sustained mMDA.

Conclusion: Early mMDA response is a stronger and more consistent predictor of long-term mMDA, whether at 1, 2, or 3 yrs or sustained over time, than BL characteristics. The 5/6 versions of mMDA could be an appropriate treatment target in pSpA pts.

References:


**Figure. Odds Ratio for Predictors of Long-term (years 1-3) and Sustained mMDA responses**

*Only variables selected by stepwise selection model are shown (model selected variables are significant at P<0.05). mMDA= modified minimal disease activity response; LEI = Leeds enthesitis index; SPARCC = Spondyloarthritis Research Consortium of Canada enthesitis index; hsCRP = high sensitivity C-reactive protein; PhGA = physician’s global assessment of disease activity; BASDAI = Bath ankylosing spondylitis disease activity index; SJC76 = swollen joint count (76 joints); CI = confidence interval.*

**Disclosure:** L. C. Coates, AbbVie, Boehringer-Ingelheim, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Sun Pharma, and UCB, 2,AbbVie, Boehringer-Ingelheim, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Sun Pharma, and UCB, 5,AbbVie, Boehringer-Ingelheim, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Sun Pharma, and UCB, 9; S. Abraham, AbbVie, Celgene, Novartis, Pfizer, and UCB, 2,AbbVie, Celgene, Novartis, Pfizer, and UCB, 5,AbbVie, Celgene, Novartis, Pfizer, and UCB, 9; W. Tillett, Sonya Abraham, MRCP, PhD, 2,Sonya Abraham, MRCP, PhD, 5,Sonya Abraham, MRCP, PhD, 9; P. J. Mease, AbbVie, Amgen, Bristol Myers, Celgene, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, Sun Pharma, and UCB, 2,AbbVie, Amgen, Bristol Myers, Celgene, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, Sun Pharma, and UCB, 5,AbbVie, Amgen, Bristol Myers, Celgene, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, Sun Pharma, and UCB, 9; S. Ramiro, None; T. Wu, Abbvie, 1,Abbvie, 3; X. Wang, Abbvie, 3,Abbvie, 1; A. L. Pangan, AbbVie, 1,AbbVie, 3; I. H. Song, AbbVie, 1,Abbvie, 3.

Network Meta-Analysis of Targeted Immunomodulators in the Treatment of Biologic-Naïve Psoriatic Arthritis

Vibeke Strand¹, M. Elaine Husni², Rakesh Singh³, Keith Betts⁴, Yan Song⁵, Jenny Griffith³ and Arijit Ganguli³, ¹Stanford University, Palo Alto, CA, ²Cleveland Clinic, Cleveland, OH, ³AbbVie Inc., North Chicago, IL, ⁴Analysis Group, Inc., Los Angeles, CA, ⁵Analysis Group, Inc., Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is an inflammatory condition characterized by peripheral arthritis and psoriatic skin lesions requiring therapies that control both skin and joint symptoms. In the absence of head-to-head trials, indirect comparison provides informative evidence for decision makers. This study compared the clinical (ACR 20/50/70; PASI 75/90) and cost-effectiveness outcomes of targeted immunomodulators (TIMs) among PsA patients without prior biologic treatment via a network meta-analysis (NMA).

Methods: A systematic literature review was conducted to identify Phase 3 randomized controlled trials (RCTs) for tumor necrosis factor-α inhibitors (TNFi’s: adalimumab [ADA], certolizumab pegol [CZP], etanercept [ETN], golimumab [GOL], and infliximab [INF]), an interleukin-17A inhibitor (secukinumab [SEC]), an interleukin-12/23 inhibitor (ustekinumab [UST]), and a phosphodiesterase-4 inhibitor (apremilast [APR]) in active PsA. Joint (ACR 20/50/70) and skin (PASI 75/90) responses at Week 24 were estimated via Bayesian NMA among biologic-naïve patients. Treatment costs were based on Wholesale Acquisition Cost as of May 8, 2017 and included drug acquisition and administration costs. Incremental costs per responder relative to placebo were calculated as incremental treatment costs during 24 weeks divided by response rate difference vs. placebo.

Results: Eleven RCTs that reported ACR and/or PASI responses at Week 24 among biologic-naïve PsA patients were included. GOL, ADA, and SEC 150 had higher ACR 20 response than other TIMs. In terms of ACR 50, INF, ETN, and ADA had higher efficacy compared with other TIMs (Table 1). With respect to ACR 70 and PASI responses, ADA, INF, and GOL had higher efficacy than other TIMs. In terms of cost-effectiveness, INF ($50,812 for ACR 50/$35,227 for PASI 75), ADA ($78,608/$41,093), and GOL ($80,533/$37,443) were associated with lower incremental costs per additional ACR 50 responder and per additional PASI 75 responder than other TIMs (Figure 1A). A similar ranking of these drugs was observed in ICPR for ACR 70 and PASI 90 (Figure 1B).

Conclusion: At Week 24, INF, GOL, and ADA had the lowest incremental cost per responder for joint and skin outcomes in PsA patients without prior biologic treatments.
Table 1. ACR 20/50/70 and PASI 75/90 response rates at Week 24

<table>
<thead>
<tr>
<th></th>
<th>ACR response rates</th>
<th>PASI response rates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ACR 20</td>
<td>ACR 50</td>
</tr>
<tr>
<td><strong>PBO</strong></td>
<td>17.5% (15.5%, 19.6%)</td>
<td>6.3% (5.0%, 7.8%)</td>
</tr>
<tr>
<td><strong>ADA</strong></td>
<td>62.0% (48.6%, 74.4%)</td>
<td>40.2% (24.7%, 60.2%)</td>
</tr>
<tr>
<td><strong>APR</strong></td>
<td>32.9% (24.4%, 42.8%)</td>
<td>12.7% (6.3%, 25.2%)</td>
</tr>
<tr>
<td><strong>CZP</strong></td>
<td>47.6% (35.2%, 60.8%)</td>
<td>22.2% (13.3%, 35.9%)</td>
</tr>
<tr>
<td><strong>ETN</strong></td>
<td>50.9% (35.8%, 66.5%)</td>
<td>44.0% (24.4%, 69.2%)</td>
</tr>
<tr>
<td><strong>GOL</strong></td>
<td>62.4% (46.6%, 77.0%)</td>
<td>37.3% (20.0%, 62.6%)</td>
</tr>
<tr>
<td><strong>INF</strong></td>
<td>57.1% (40.6%, 72.9%)</td>
<td>54.5% (30.2%, 81.2%)</td>
</tr>
<tr>
<td><strong>SEC 150</strong></td>
<td>58.5% (46.8%, 69.7%)</td>
<td>36.4% (23.8%, 52.5%)</td>
</tr>
<tr>
<td><strong>SEC 300</strong></td>
<td>56.2% (39.1%, 72.3%)</td>
<td>32.8% (17.7%, 53.4%)</td>
</tr>
<tr>
<td><strong>UST 45</strong></td>
<td>35.3% (26.6%, 45.2%)</td>
<td>19.0% (11.3%, 31.0%)</td>
</tr>
<tr>
<td><strong>UST 90</strong></td>
<td>41.1% (31.8%, 51.3%)</td>
<td>21.6% (13.1%, 34.4%)</td>
</tr>
</tbody>
</table>

[1] PASI 75 and PASI 90 responses for APR and CZP were not reported among biologic naïve population.

Figure 1. Incremental cost per responder over 24 weeks (ACR 50 vs. PASI 75 and ACR 70 vs. PASI 90)

[1] ICPR for ACR 50 and ACR 70 in CZP were $173,601 and $201,998. ICPR for ACR 50 and ACR 70 in APR were $250,338 and $4,659,629.
PASI responses were not reported for CZP and APR in the biologic-naïve population.

Disclosure: V. Strand, AbbVie, Alder, Amgen, BMS, Celgene, Genentech, Janssen, Novartis, Pfizer, and UCB, 5,AbbVie, Amgen, BMS, Celgene, Genentech, Janssen, Novartis, Pfizer, and UCB, 9; M. E. Husni, Celgene, AbbVie, Genentech, Bristol-Myers Squibb, Pfizer, Novartis, and Janssen, 9; R. Singh, AbbVie, 3,AbbVie, 1; K. Betts, Analysis Group, which has received consulting fees from AbbVie to partner on this research, 3; Y. Song,
Biological DMARD Efficacy in Psoriatic Arthritis: A Systematic Review and Meta-Analysis on ACR Response Criteria, PASI Response Criteria, HAQ-DI, Enthesitis and Dactylitis Outcomes

**Numa Simons**¹, Yannick Degboé¹, Thomas Barnetche², Alain Cantagrel¹, Adeline Ruysen-Witrand¹ and Arnaud Constantin¹.¹Rheumatology, Purpan Hospital, Toulouse III University, Toulouse, France, ²FHU ACRONIM, Pellegrin Hospital, Bordeaux University, Bordeaux, France

**First publication:** September 18, 2017

**SESSION INFORMATION**
- **Session Date:** Monday, November 6, 2017
- **Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II
- **Session Type:** ACR Poster Session B
- **Session Time:** 9:00AM-11:00AM

**Background/Purpose:**
We are currently witnessing a diversification of the available biotherapies (bDMARDs) for psoriatic arthritis (PsA), with the arrival of new classes of medication. Those treatment options are new, and there is no consensual hierarchy in the use of those medications, and no head-to-head comparative study. The present meta-analysis aims to evaluate the respective efficacy of TNF inhibitors, IL-17 inhibitor (ustekinumab), IL-12/23 inhibitor (secukinumab), and CTLA4-Ig (abatacept), on ACR response criteria, PASI response criteria, HAQ-DI, enthesitis and dactylitis outcomes in PsA.

**Methods:**
Randomised controlled trials assessing TNF inhibitors, ustekinumab, secukinumab or abatacept in psoriatic arthritis were selected through the MedLine database, ACR and EULAR scientific meeting archives. ACR20, ACR50, ACR70, PASI75 and PASI90 response rates and the proportion of patients with residual dactylitis or enthesitis were collected at the time of evaluation of the primary endpoint. The pooled response risk ratios (RRs) and 95% confidence intervals (95%CI) were quantified for the standard dose of anti-TNF (golimumab 50 mg), ustekinumab (45 mg), secukinumab (150 mg) or abatacept (125 mg) in comparison with placebo. A meta-analysis was performed using the inverse variance approach and statistical heterogeneity was assessed with the Cochran Q-test and I² values.

**Results:**
15 RCTs were selected for the meta-analysis. Anti-TNF, secukinumab, ustekinumab and abatacept showed higher ACR20 response rates, with RRs (95%CIs) ranging from 3.51 (2.92, 4.22) to 1.77 (1.31, 2.39), in comparison with placebo. Anti-TNF, secukinumab and ustekinumab showed higher ACR50 (see table) and ACR70 response rates, with RRs (95%CIs) ranging from 6.87 (4.53, 10.43) to 2.89 (1.96, 4.27) and 10.80 (6.25, 18.66) to 4.29 (2.04, 8.99), respectively, in comparison with placebo. Anti-TNF, secukinumab and ustekinumab showed higher PASI75...
response rates, with RRs (95% CIs) ranging from 16.61 (6.38, 43.26) to 5.54 (3.01, 10.21), in comparison with placebo. Anti-TNF, secukinumab and ustekinumab showed a lower proportion of residual enthesitis, with RRs (95% CIs) ranging from 0.65 (0.50, 0.84) to 0.83 (0.71, 0.97), while only anti-TNF and secukinumab showed a lower proportion of residual dactylitis, with RRs (95% CI) ranging from 0.48 (0.31, 0.74) to 0.53 (0.43, 0.65), in comparison with placebo.

Conclusion:

In this meta-analysis, bDMARDs showed higher ACR20/50/70 and PASI75 response rates and a lower proportion of residual enthesitis and dactylitis, in comparison with placebo. However, the respective efficacy of bDMARDs, quantified using ORs or NNTs (data not shown), is variable among the different outcomes measures, in particular for enthesitis and dactylitis. Head-to-head studies are needed to draw definitive conclusions on potential efficacy differences between bDMARDs in PsA patients.

Disclosure: N. Simons, None; Y. Degboé, Pfizer Inc, 2; T. Barnetche, None; A. Cantagrel, None; A. Ruyssen-Witrand, None; A. Constantin, None.

Long-Term Effects of TNF-Alpha Inhibitors on Bone Mineral Density and the Incidence of Vertebral Fractures in Patients with...
Ankylosing Spondylitis

Kim Beek¹, Mignon van der Weijden¹, WF Lems², Christiaan van Denderen³, M. Nurmohamed⁴ and Irene van der Horst - Bruinisma⁵, ¹Rheumatology, Amsterdam Rheumatology immunology Centre/VUmc and Reade, Amsterdam, Netherlands, ²Amsterdam Rheumatology and immunology Center | VU University Medical Center, Amsterdam, Netherlands, Amsterdam, Netherlands, ³Rheumatology, Jan van Breemen Research Institute | Reade, Amsterdam, Netherlands, ⁴Rheumatology, Amsterdam Rheumatology and immunology Center, Reade, Amsterdam, Netherlands, ⁵ARC, Amsterdam, Netherlands, Amsterdam, Netherlands

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: ARHP Spondylarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Ankylosing Spondylitis (AS) is not only characterized by pathological bone formation leading to ankylosis, but also by bone loss which may lead to vertebral fractures (VFx). TNF-alpha inhibitors (TNFi) have proven to be effective in blocking the inflammation process. A few studies also showed an increase of Bone Mineral Density (BMD) in AS patients treated with TNFi but the incidence of VFx after two years of treatment was increased.

Methods:

Consecutive TNFi naive patients diagnosed with AS according to the Modified New York criteria were included. Patients were recruited from the VUmc and the Amsterdam Outpatient clinic Reade and were treated with TNFi for 4 years. BMD at hip and lumbar spine (LS) were measured at baseline, after 2 and 4 years. T-scores were categorized as ‘normal BMD’, ‘osteopenia’ and ‘osteoporosis’, based on the WHO osteoporosis criteria. The incidence of VFx was determined by two observers using the Genant method.

Results:

In total, 70 AS patients with complete datasets (67.1% male) were included. The mean age was 41.6 years and the disease duration (time since diagnosis) was 9.8 years. At baseline 42% of the patients had a decreased BMD of the hip and 34% of the spine, of whom 19 patients (27%) had both a decreased hip BMD as well as a decreased lumbar BMD. The BMD of spine and hip improved after 2 and 4 years of TNFi treatment (Table 1). In 7 patients (10%), 8 VFx were observed both at baseline and after 2 years. After 4 years of TNFi-treatment 11 VFx were observed in 9 patients.

After 4 years, 2 out of 9 patients with >1 VFx had a decreased BMD at hip and lumbar spine whereas the other 7 patients had a normal BMD. The majority of VFx was localized in the mid or lower thoracic spine.

Table 1: BMD measurement in spine and hip of 70 AS patients treated with TNFi.
After 2 years of TNFi

<table>
<thead>
<tr>
<th>Condition</th>
<th>Baseline</th>
<th>After 2 years of TNFi</th>
<th>After 4 years of TNFi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteopenia LS*</td>
<td>23 (32.9)</td>
<td>19 (27.1)</td>
<td>21 (30.0)</td>
</tr>
<tr>
<td>Osteoporosis LS</td>
<td>6 (8.6)</td>
<td>3 (4.3)</td>
<td>2 (2.9)</td>
</tr>
<tr>
<td>Abnormal BMD LS</td>
<td>29 (41.5)</td>
<td>21 (31.4)</td>
<td>23 (32.9)</td>
</tr>
<tr>
<td>Osteopenia total hip</td>
<td>22 (31.4)</td>
<td>19 (27.1)</td>
<td>16 (22.9)</td>
</tr>
<tr>
<td>Osteoporosis total hip</td>
<td>2 (2.9)</td>
<td>2 (2.9)</td>
<td>3 (4.3)</td>
</tr>
<tr>
<td>Abnormal BMD total hip**</td>
<td>24 (34.3)</td>
<td>21 (30.0)</td>
<td>19 (27.2)</td>
</tr>
<tr>
<td>Patients with VFx</td>
<td>7 (10.0)</td>
<td>7 (10.0)</td>
<td>9 (12.9)</td>
</tr>
<tr>
<td>Total number of VFx</td>
<td>8</td>
<td>8</td>
<td>11</td>
</tr>
</tbody>
</table>

*Lumbar Spine

**N=68, because 2 patients had a total hip replacement

Abnormal BMD = osteopenia and/or osteoporosis according to WHO guideline

Vertebral fractures (VFx) are presented in number of patients with a VFx and the actual prevalence of VFx. Outcomes are presented in n (%)

**Conclusion:**

The percentage of relatively young AS patients with a decreased BMD at baseline of the hip and lumbar spine was high (34-41%). After 4 years of TNFi-treatment the BMD of the lumbar spine improved in 8.6% of the patients and of the hip in 7.2% of the patients. At baseline, several vertebral fractures were found and a few additional vertebral fractures were observed after 4 years of treatment.

**Disclosure:** K. Beek, None; M. van der Weijden, None; W. Lems, None; C. van Denderen, None; M. Nurmohamed, None; I. van der Horst - Bruinsma, None.


Abstract Number: 1564

**Treatment Patterns, Survival and Long-Term Effectiveness of Biological Agents in Psoriatic Arthritis Patients**

Marina Natalia Fornaro¹, Fernando Dal Pra², Emilce E Schneeeberger², Osvaldo Luis Cerda², Margarita Landi², María de los Angeles Correa³, Rodrigo Garcia Salinas⁴, Sebastian Magri⁵, Raul Sueldo⁶, María Julia Santa Cruz⁷, Emilio Buschiazzo⁸ and Gustavo Citera⁹, ¹Section of Rheumatology, Instituto de Rehabilitación Psicofísica, Buenos Aires, Argentina, ²Section of Rheumatology, Instituto de Rehabilitación Psicofísica, Buenos Aires, Argentina, ³Section of Rheumatology, Instituto de Rehabilitación Psicofísica, Buenos Aires, Argentina, ⁴Section of Rheumatology, Hospital Italiano de La Plata, Buenos Aires, Argentina, ⁵Section of Rheumatology, Hospital Italiano de La Plata, La Plata, Argentina, ⁶Section of Rheumatology, Hospital Angel Cruz Padilla, Tucumán, Argentina, ⁷Section of Rheumatology, Hospital General de Agudos Dr. Enrique Tornú, Buenos Aires, Argentina, ⁸Section of
Rheumatology, Hospital Señor del Milagro, Salta, Argentina, Salta, Argentina, 9Section of Rheumatology, Instituto de Rehabilitación Psicofísica, Buenos Aires, Argentina, Buenos Aires, Argentina

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: ARHP Spondyarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The incorporation of biological disease modifying drugs (b-
DMARD) has substantially improved the outcome of patients with Psoriatic Arthritis (PsA). Our aim was to evaluate b-DMARD’s patterns, their accumulated survival and long-term efficacy in patients with PsA using the Lund Efficacy Index (LUNDEX).

**Methods:** A retrospective multicentric study was carried out through the collection of medical records data. Patients aged ≥ 18 years with PsA by CASPAR criteria who had started therapy with b-DMARD were included. Socio-demographic and clinical data were collected. We consigned beginning date of b-DMARD, concomitant treatment, suspension or change of b-DMARD, reasons of the suspensions. A therapeutic response was defined according to minimal disease activity (MDA) at 6 and 12 months and then annually since the beginning of biological treatment. Statistical analysis: Student T test and Chi2 test for univariate analysis. Cumulative survival was assessed using Kaplan Meier curves and comparisons using Log Rank. Multivariate Cox regression analysis was performed.

**Results:** Seventy-two patients with PsA were included, 39 (54.2%) were men. The median of age was 54.5 years (IQR 45-61) and median disease duration was 11 years (IQR 6-15). 71.2% (n=42) of patients had comorbidities. Regarding the first biological agent, 45.8% received Adalimumab (ADA), 36.1% Etanercept (ETN), 5.6% Certolizumab, 4.2% Infliximab and Ustekinumab, 1.4% Golimumab. 25.4% (n=15) received them as monotherapy. 79.7% received NSAIDs, 61% Methotrexate, 25.9% Prednisone (≤10 mg/day), 12.1% Leflunomide and 1.7% Sulfasalazine as concomitant treatment. 35.8% (n=19) of patients stopped taking the first biologic. The mean survival of b-DMARD was 82 months (SD±7.4). Causes of suspension were inefficacy (43%), lack of provision (28.6%), side effects (14.3%), and others. The LUNDEX for the first biologic was 24.7% at 6 months and 44.3% at 1 year. The mean survival of ADA was 90 months (SD±10.4) and for ETN 79 months (SD±12). Older patients (>55 years old) and obese patients (BMI ≥30) had less drug survival. In the Cox's regression analysis, after adjusting for different confounders, older age was the main variable associated with less drug survival: HR=1.064 (CI=1.01-1.11) (figure 1). LUNDEX was lower in obese vs non-obese patients, 16% vs 66% at 1 year, 10.5 vs 74.9% at 2 years and 5.9 vs 81.8% at 3 years.

**Conclusion:** The mean survival of the first biologic was 82 months. Older age and obesity were associated with lower survival of biologic therapy.

Figure 1: Drug survival of patients less than 55 years older and older than 55 years old.

**Disclosure:** M. N. Fornaro, None; F. Dal Pra, None; E. E. Schneeberger, None; O. L. Cerda, None; M. Landi, None; M. D. L. A. Correa, None; R. Garcia Salinas, None; S. Magri, None; R. Sueldo, None; M. J. Santa Cruz, None; E. Buschiazzo, None; G. Citera, Novartis, Pfizer Inc, 2,AbbVie, Bristol-Myers Squibb, Janssen, Novartis, Pfizer Inc, 5.


**Abstract Number:** 1565

**Depression and Fatigue in Patients with Ankylosing Spondylitis**

Ji Hui Shin¹, Sun Ju Ahn² and Tae-Hwan Kim³, ¹rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), ²Medical Research Coordinator, Hanyang University Hospital for Rheumatic Disease Research Center, Seoul, Korea, Republic of (South), ³Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South)

**First publication:** September 18, 2017
Background/Purpose: 
Ankylosing spondylitis (AS) is a chronic inflammatory disease that leads to bony ankyloses. The disease occurs in early adulthood, a critical stage in life, causing physical and mental problems. There are many researches on the degrees of ankyloses and activity of the disease, but studies correlating AS with psychological effects—such as depression and fatigue—are rarer. Therefore, we sought to identify depression status in patients with AS and to find correlations among depression, fatigue, and disease activity.

Methods: The subjects of the study were 300 patients with AS, whose data were collected in the hospital from March 2017 to April 2017. All subjects agreed to participate in the research. The data were collected based on the self-reported survey that inquires general features (sex, age, and disease period) and the level of depression measured by CES-D. Based on the CES-D score, the patients were grouped depending on depression level (0-15: normal, 16-21: moderate, 22 : severe). Depression levels were compared to the disease activity measured by BASDAI, BASFI, ESR, CRP and fatigue level, measured by FACIT-F. The collected data were statistically analyzed utilizing SPSS statistics 24.0.

Results: 82.7 % of the patients were male, and average age and disease duration were 37.9 years old and 7.21 years. 21 percent of the patients reported smoking, and 55 % drinking. 3.3 % were diagnosed with depression, with a BASDAI of 3.35 and BASFI of 1.72. ESR and CRP were 19.02 mm/hr and 1.25 mg/dl each. The average of CES-D, or level of depression, was 11.12, which is normal, but 22.1 % of the patients had a moderate depression level. The degree of depression correlated with BASDAI, BASFI, and FACIT-F, but it was unrelated with disease duration. The fatigue level was 15.5, which is normal, and was less than the degree of depression. Fatigue showed a correlation with depression and disease activity. Depression was shown to be correlated with diseases activity (BASDAI, BASFI), but fatigue was not.

Conclusion:
22 % of the patients with AS showed a moderate level of depression, which need intensive treatment. Depression levels correlated with disease activity, but it was unrelated with disease period. It seems that the aftereffects of AS continue after the onset of the disease. This study may contribute to reducing disease activity and improving AS patients’ quality of life by regulating depression and fatigue.

Disclosure: J. H. Shin, None; S. J. Ahn, None; T. H. Kim, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/depression-and-fatigue-in-patients-with-ankylosing-spondylitis

Abstract Number: 1566

Elevated IL-1 Expression Levels in Mesenchymal Stem Cells Derived from Spondyloarthritis Patients Might be Linked to Increased Osteoblast Mineralization

Gerlinde Layh-Schmitt¹, Breanna Nguyen¹, Emily Lazowick¹, Stephen R. Brooks² and Robert Colbert¹, ¹National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD,
Background/Purpose: Axial spondyloarthritis (AxSpA) is an immune–mediated inflammatory disease involving the spine and sacroiliac joint. AxSpA is characterized by vertebral trabecular bone loss and progressive bone formation in the spine. To date, the root cause of osteoproliferation and aberrant bone formation is unknown. Therefore, we evaluated, (i) whether bone progenitor cells (mesenchymal cells (MSCs) and osteoblasts (OBs)) derived from AxSpA patients (P) exhibit differences in their capacity to form mineralizing osteoblasts in comparison to healthy controls (HC), and (ii) whether inflammatory cytokines alter osteoblastogenesis and gene expression patterns in MSCs.

Methods: We used MSCs derived from induced pluripotent stem cells (iPSCs) generated from P and HC skin fibroblasts. MSCs from 3 HC and 5 P were differentiated into mineralizing osteoblasts. The influence of cytokines (combination of IFNγ/TNFα and IL-1β) and the IL-1 receptor antagonist (IL-ra) on MSCs and osteoblastogenesis was examined. The degree of osteoblast calcification was measured by alizarin red stain. Cell numbers were determined by DAPI staining. Whole transcriptome expression profiles were established for MSCs with and without cytokine treatments by using RNA-seq and Nanostring. (3 HC and 4P). Standard approaches and statistical methods were used to analyze the data.

Results: On average, OBs derived from P (n=5) exhibited a 1.4 fold higher mineralization capacity compared to OBs from HC (n=3) (p<0.05; Mann Whitney test). Interestingly, in all tested P IL-1α (n= 4) or IL-1β (n=3) mRNA levels were enriched compared to HC up to 5 fold (p<0.05). Stimulation with IFNγ & TNFα induced IL-1α and IL-1β up to 20-fold and COX2 up to 15-fold. Incubation of P and HC MSC lines with IL-1β for 24h induced IL-1β, IL-1α and COX2 expression 5,10-20, and 3-5 fold (p<0.05), respectively. Treatment of MSCs for 48h with IL-1β before differentiation, led to a 25% increase of OB numbers and the degree of mineralization was up 2.5 fold (p<0.05). This effect was prevented by IL-1ra, which inhibited base line mineralization by 15%.

Conclusion: The results suggest that, under certain conditions, IL-1 can enhance proliferation of bone progenitors and osteoblast mineralization by auto- or paracrine mechanisms. Interestingly, exogenous IL-1β induced IL-1α, IL1β, and COX2 in MSCs correlated with increased proliferation and mineralization of OB. Since COX2 is crucial for the synthesis of prostaglandin E2 (PGE2) which can mediate aberrant ossification through β-catenin stabilization, we will evaluate whether PGE2 and β-catenin are increased in patient cell lines in future studies.

Disclosure: G. Layh-Schmitt, None; B. Nguyen, None; E. Lazowick, None; S. R. Brooks, None; R. Colbert, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/elevated-il-1-expression-levels-in-mesenchymal-stem-cells-derived-from-spondyloarthritis-patients-might-be-linked-to-increased-osteoblast-mineralization

Abstract Number: 1567
A Mitogen-Associated Protein Kinase (MAPK) Associated Kinase 2 Inhibitor Decreases in Vitro Th17 and Monocyte Inflammatory Responses in Spondyloarthritis

Davide Simone, Hui Shi, Nuha Ansar, Alison Davies, Karen Doig and Paul Bowness, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The current biologic treatment for Ankylosing Spondylitis (AS) and Psoriatic Arthritis (PsA) are limited to TNF-α inhibitors (TNFi) and, more recently, IL-17A monoclonal antibodies. These treatments work in a percentage of patients and are not effective against all the disease manifestations. Targeting cellular pathways leading to the production of inflammatory cytokines is a new and appealing therapeutic approach for inflammatory conditions. The inhibition of the mitogen-activated protein kinase (MAPK), attempted in the past in Rheumatoid Arthritis (RA), yielded undesirable effects, including toxicity and tachyphylaxis. We aimed to assess the in vitro efficacy of a small molecule inhibiting the MAPK-associated protein kinase 2 (MK2) in limiting the cytokine response in T-cells (including Th17), and in monocytes derived from patients with inflammatory arthritis.

Methods: CD4+ T cells and monocytes were isolated from peripheral blood mononuclear cells (PBMCs) of AS (n=16), PsA (n=12), RA patients (n=11) and healthy controls (HC, n=7) and stimulated for six days under either neutral (Th0) or Th17-promoting conditions in the presence of MK2 inhibitor (CC0786512, Celgene) or control (DMSO). The level of IL-17A, IFN-γ, GM-CSF, IL-17F in the culture was measured using Cytokine Bead Array (CBA). Cells were also stained for intracellular cytokines and Foxp3 and analysed by flow cytometry. Cytotoxicity and proliferation were also assessed with Annexin V/7-AAD staining and CFSE dilution. Monocytes were stimulated with lipopolysaccharide (LPS) for 18 hours and treated with CC0786512 and the secretion of TNF-a, IL-6, MIP-1α, MCP-1, GM-CSF measured with ELISA or CBA.

Results: CC0786512 effectively inhibited secretion of IL-17A, GM-CSF and IL-17F in CD4+ T cells from AS and PsA (Figure), with negligible effects on viability or cell proliferation. The compound worked on T cells cultured both in neutral (Th0) and in vitro Th17 polarising conditions, with effects in samples derived from TNFi-treated and TNFi-naive patients. The inhibition of MK2 reduced the number of Th17 cells generated under Th17 driving conditions, and in particular of Th17 cells co-expressing IFN-γ. In monocytes, the MK2 inhibition resulted in reduced TNF-a, MIP-1α and MCP-1 secretion.

Conclusion: Our results indicate that the MK2 inhibitor significantly inhibits both Th17 T cell and monocyte immune responses in cells derived from patients with AS and PsA. Our results encourage further investigation and make MK2 a promising novel therapeutic target in the treatment of Spondyloarthritis.
Disclosure: D. Simone, Celgene, 2; H. Shi, Celgene, 2; N. Ansar, None; A. Davies, None; K. Doig, None; P. Bowness, Celgene, 2.


Existence Number: 1568

**Existence of IL-6 and IL-17 Mediated Inflammation Amplifier Loop in Reactive Arthritis**

Ramnath Misra1, Sandeep Kumar2, Rajeev Singh3, Abhisek Singh4, Daisuke Kamimura5, Smriti Chaurasia2, Yasunobu Aria6, Tori Austria7, Ratnadeep Mukherjee8, Balachandran Ravindran9, Vikas Agarwal2 and Masaaki Murakami10, 1Clinical Immunology, Sanjay Gandhi Postgraduate of Medical Sciences, Lucknow, India, 2Clinical Immunology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, 3Biochemistry, King George Medical University, Lucknow, India, 4Division of Molecular Neuroimmunology, Post Doctoral Fellow, Sapporo, Japan, 5Molecular Neuroimmunology, Lecturer, Sapporo 060-0815, Japan, 6Division of Molecular Neuroimmunology, Assistant Professor, Sapporo 060-0815, Japan, 7Division of Molecular Neuroimmunology, Special appointed - Assistant Professor, Sapporo 060-0815, Japan, 8Institute of Life Sciences, Ph D student, Bhubaneswar, India, 9Institute of Life Sciences, Distinguished Scientist, Bhubaneswar, India, 10Institute of Genetic Medicine, Director, Sapporo 060-0815, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Spondyloarthopathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM
**Background/Purpose:** F759 mice with a single amino-acid substitution in signal transducer subunit of IL-6 receptor gp130 (Y759F) develops arthritisspontaneously due to IL-17A and IL-6 mediated synergistic activation of positive-feedback loop of NF-kB signaling (inflammation amplifier). We sought to see whether this mechanism is operational in Reactive arthritis.

**Methods:** Arthritis was induced with oral feeding of *salmonella enterica* followed by ankle microbleeding in the ankle joints of F759 mice. Sera IL-6 along with IL-6 mRNA and STAT3 phosphorylation in synovium were measured. Further, exosomes isolated from sera of salmonella infected and control mice and were injected into the joints of mice, and measured the expression of proinflammatory cytokine, chemokines and growth factor. On the other hand, sera and synovial fluid of patients with ReA multiple cytokines, chemokines and growth factors were also measured. Finally, synovial fibroblasts (FLS) were cultured to purity and stimulated with IL-6, IL-17, IL-6 plus IL-17 and IL-6 were measured to see synergistic activation.

**Results:** IL-6 in sera of arthritic mice were significantly higher (p<0.05) than control mice along with increase STAT3 phosphorylation in the synovium. Though, oral infection itself not sufficient to induce arthritis but if infection is followed by microbleeding then it significantly induces the arthritis in these mice (Fig-1). Further, exosomes from salmonella infected mice induced arthritis in ankle joint and significantly increased IL-6 expression (p<0.05). Similarly, in comparison to IL-6 and IL-17 alone these cytokines synergistically induced more IL-6 production from FLS isolated from ReA patients (Fig-2). Finally, we found that SF concentrations of effectors of inflammation amplifiers like IL-6, CCL-20, PLGF and FGF-basic were significantly higher in patients with ReA/uSpA as compared to osteoarthritis patients. Further, levels of these factors were also high in SF compared to sera in ReA patients.

**Conclusion:** Data of mice and patients support that synovitis in ReA is perpetuated by inflammation amplifier or synergistic induction of IL-6 and IL-17.

**Figure 1:** Oral infection of *Salmonella* followed by microbleeding into the ankle joint induces clinical symptoms of arthritis.

**Figure 2:** Activation of FLS isolated from ReA patients with IL-6 and IL-17 alone and synergistically with both cytokines and measurement of IL-6 level in culture supernatant.
Isotretinoin Induced Seronegative Spondyloarthropathy: Magnetic Resonance Imaging As Diagnostic and Prognostic Biomarker

Basant Elnady1,2, Dalia Desouky3,4, Tohamy Elkhouly5,6, Noha Dawoud7,8 and Hanady Kewan9,10, 1Assistant professor of rheumatology and rehabilitation, department of rheumatology and rehabilitation · faculty of medicine, Benha university, Benha, Egypt, 2Rheumatology consultant ,Rheumatology division ,Al Hada Armed Forcec Hospital, Taif, Saudi Arabia, 3Assistant professor of public health and community medicine,department of public health and community medicine,Faculty of medicine, menoufia University, menoufia, Egypt, 4Assistant professor of public health and community medicine, department of family and community medicine· faculty of medicine, taif university, Taif, Saudi Arabia, 5Assistant professor of radiology, radiology department · faculty of medicine, Benha university, Benha, Egypt, 6Radiology consultant , Department of radiology ,Alhada Armed Forces Hospital, Taif, Saudi Arabia, 7department of dermatology , andrology, and STDs, faculty of medicine, Menoufia university, menoufia, Egypt, 8department of dermatology, Alhada armed forces hospital, Tafi, Ksa, taif, Saudi Arabia, 9Department of radio-diagnosis, Faculty of medicine, Mansoura University., Mansoura, Egypt, 10Radiology consultant ,Department of radiology, Al Hada Armed Forces Hopital, taif, Saudi Arabia

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Recent data has revealed occurrence of musculoskeletal manifestations in particular sacroiliitis and inflammatory back pain (IBP) secondary to isotretinoin therapy for acne vulgaris, accordingly our study conducted to detect the prevalence of isotretinoin triggered rheumatic side-effects, with close clinical and radiological follow up to assess the drug impact on musculoskeletal system.

Methods:
513 acne patients on isotretinoin therapy were enrolled from dermatology out patients’ clinic, screened for musculoskeletal manifestations related features resulting from isotretinoin therapy, all patients were HLA B27 negative. At baseline C-reactive protein (CRP), Magnetic resonance imaging (MRI) sacroiliac joint, onset of IBP and pain score were reported. MRI proven sacroiliitis, has been scored with semi-quantitative score. Clinical and radiological follow up of our patients were done, patients who met ASAS classification criteria for spondyloarthropathy (SpA) were assessed for disease activity by Ankylosing Spondylitis Disease Activity Score (ASDAS) (3). MRI for sacroiliac joints and CRP were repeated three weeks after being symptomless, with isotretinoin discontinuation.
Results:

513 acne patients were enrolled, 123 (23.9%) developed IBP, and 88 (17.1%) developed arthralgia and arthritis. The mean onset of IBP was (2.1±0.85) months, with mean baseline pain score of (4.34±3.09). MRI proven sacroiliitis was found in (0.13%) of total number of acne patients, and (42.27%) of symptomatic patients, baseline CRP was (32.05±17.23 mg/L) and (3.4±2.7 mg/L) after being symptomless. 51.9% of the symptomatic patients had fulfilled the ASAS criteria for axial SpA, 97.6% of patients were treated with NSAID, however 2.4% were treated with anti TNF biologic. all cases normalized within 9 months, the mean time of normalization was (6.27±1.7) months. There was significant positive correlation for MRI scores, with pain, ASAS scores, baseline CRP. Unilateral sacroiliitis patients had significant rapid improvement than bilateral sacroiliitis (P<0.05).

Conclusion: Isotretinoin induced SpA is quite common side effect. Early rheumatologic assessment, and intervention is recommended. MRI is the modality of choice in early detection, and follow up of isotretinoin induced sacroiliitis.

MRI (a) axial T1WI, (b) axial STIR, showing early bilateral acute sacroiliitis evidenced by edema signal (dark signal in T1WI and bright in STIR) of both sacral and iliac sides.
Follow up MRI in (c) coronal and (d) axial STIR images revealed marked resolution of the previously reported bilateral sacroiliitis.
Table 1. Correlation between MRI scores, and different study variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>MRI score</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td></td>
</tr>
<tr>
<td>GAGS score</td>
<td>0.396</td>
<td>0.004</td>
</tr>
<tr>
<td>Pain score</td>
<td>0.465</td>
<td>0.001</td>
</tr>
<tr>
<td>ASAS score</td>
<td>0.416</td>
<td>0.002</td>
</tr>
<tr>
<td>CRP level at diagnosis</td>
<td>0.693</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dose of isotretinoin/kg</td>
<td>0.21</td>
<td>0.135</td>
</tr>
</tbody>
</table>

**GAGS score**: global acne grading system score

Figure (1). Kaplan-Meier survival analysis for normalization of MRI (during 9 months follow up) among acne patients

Disclosure: B. Elnady, None; D. Desouky, None; T. Elkhouly, None; N. Dawoud, None; H. Kewan, None.

Monocytes from Male Patients with Ankylosing Spondylitis Display Decreased Osteoclastogenesis and Decreased RANKL/OPG Ratio

Valéria F. Caparbo¹, Carla G.S. Saad¹, Julio C. B. Moraes², Artur J de Brum-Fernandes³ and Rosa M R Pereira⁴, ¹Rheumatology Division, Faculdade de Medicina da Universidade de Sao Paulo, Sao Paulo, Brazil, ²Rheumatology Division, Faculdade de Medicina da Universidade de Sao Paulo, Sao Paulo, Brazil, ³Rheumatology Division, Université de Sherbrooke, Rheumatology Division, Canada, Sherbrooke, QC, Canada, ⁴Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, Brazil

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Ankylosing Spondylitis (AS) is a chronic inflammatory disease characterized by new bone growth that leads to syndesmophyte formation and subsequent vertebral ankyloses, although AS patients frequently present with low bone mineral density and fractures that can be associated with systemic inflammation and decreased mobility. In fact, acute stages of inflammation in these patients showed mononuclear cell infiltrates, including increased number of osteoclasts (OCs). However, studies that evaluated osteoclastogenesis in AS patients presented different results, and some of them have demonstrated a decrease in osteoclast differentiation in AS patients. There is no data regarding the influence of clinical disease parameters, inflammatory markers and therapy in AS osteoclastogenesis. Thus, the main objective of this study is to determine if the osteoclastogenic capacity of peripheral blood mononuclear cells (PBMCs) is different in male patients with AS compared to healthy controls and to investigate the relationship between osteoclastogenesis and clinical parameters.

Methods: Eight-five male AS patients had mean of age 42.6±9.0yrs and a mean of disease duration 17.4±9.7yrs. PBMCs from AS patients and 59 healthy controls were tested for CD16+ cells and induced to differentiation. After 21 days, the cells were tested to TRAP (tartrate-resistant acid phosphatase) and the apoptosis was detected using TACs TdT blue in situ. Serum levels of nuclear factor-kB ligand (RANKL) and osteoprotegerin (OPG) were evaluated in both groups.

Results: PBMCs from male AS patients had fewer CD16+ cells (25.06±8.59 vs 28.59±10.20, p=0.026) and produced fewer osteoclasts (647.66±669.4 vs 764.43±561.9, p=0.014) compared to controls. Apoptosis occurred less frequently in osteoclasts obtained from AS patients than in osteoclasts from the control group. A lower RANKL/OPG was observed in AS patients compared to controls (0.046±0.035 vs 0.068±0.071, p=0.046). AS patients taking NSAID (non-steroidal anti-inflammatory drugs) presented no difference regarding the number of OCs produced and the percentage of CD16+ cells compared to controls (p>0.05). However, patients taking TNFi inhibitors (TNFi) presented with lower OC numbers than the control group. A generalized linear model with gamma distribution analysis (including disease duration, NSAID and TNFi use) demonstrated that disease duration was negatively associated with osteoclastogenesis: for each year of disease duration, a decrease of 16.6% in the mean osteoclast number was found (p<0.001).

Conclusion: Monocytes from male AS patients display a lower capacity to generate osteoclasts in vitro compared to cells from controls. This difference was not observed in AS patients taking NSAIDS, differently osteoclastogenesis in AS patients using TNFi. Osteoclastogenesis was negatively correlated with disease duration. These finding supports the idea that osteoclasts play a role in the physiopathology of bone disease in AS patients.
Bimekizumab Dual Inhibition of IL-17A and IL-17F Provides Evidence of IL-17F Contribution to Chronic Inflammation in Disease-Relevant Cells

Ash Maroof¹, Remi Okoye¹, Tim Smallie¹, Dominique Baeten²,³, Sophie Archer¹, Catherine Simpson¹, Meryn Griffiths¹ and Stevan Shaw¹, ¹UCB Pharma, Slough, United Kingdom, ²UCB Pharma, Brussels, Belgium, ³University of Amsterdam, Amsterdam, Netherlands
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: IL-17A and IL-17F share structural homology and have similar biologic function.¹ Although the contribution of IL-17A to immune-mediated inflammatory diseases has been widely reported,¹,² the role of IL-17F is less well characterized. Bimekizumab, a humanized monoclonal IgG1 antibody, developed to neutralize both IL-17A and IL-17F potently and selectively, is under clinical development as a treatment for immune-mediated diseases such as PsA and psoriasis. This study aimed to assess the involvement of IL-17F in chronic inflammation in tissue from patients with PsA and disease-relevant cells, and to determine the effect of dual neutralization of IL-17A and IL-17F in suppressing inflammation, compared with blockade of IL-17A alone.

Methods: Synovial and lesional skin tissue from patients with PsA was probed by immunostaining for expression of IL-17F protein. Primary normal human dermal fibroblasts (NHDFs) and synoviocytes from patients with PsA, in the presence of TNF, were stimulated with recombinant IL-17A and IL-17F. Using cytokine-specific blocking antibodies, the individual and combined effects of IL-17A and IL-17F were explored using a complex in vitro model (synoviocytes from patients with PsA and primary NHDFs were treated with proinflammatory mediators from supernatant [SN] of sorted Th17 cells) and transcriptional as well as migratory studies were performed.

Results: IL-17F expression was observed in tissue biopsies from patients with PsA. In primary NHDFs and synoviocytes from patients with PsA, stimulation with recombinant IL-17F promoted production of proinflammatory mediators, such as IL-6 and IL-8, though to a lesser extent than with recombinant IL-17A. Treatment of Th17 SN-stimulated synoviocytes from patients with PsA with bimekizumab led to greater reductions of IL-6 (42% lower, p<0.05) and IL-8 (35% lower, p<0.05) production than IL-17A inhibition. Bimekizumab treatment of Th17 SN-stimulated primary NHDFs also reduced production of IL-6 (35% lower, p<0.0001) and IL-8 (57% lower, p<0.0001) more than IL-17A alone. Combining IL-17A + IL-17F monoclonal antibodies produced similar results to bimekizumab. Levels of expression of 27 inflammation-linked genes, including CXCL1, CXCL2, CXCL3, and IL-15RA, were lower with dual neutralization of IL-17A and IL-17F by bimekizumab versus IL-17A inhibition. Suppression of neutrophil and monocyte (Fig.) migration was substantially greater with bimekizumab than with blockade of IL-17A alone.
Conclusion: Dual neutralization of IL-17A and IL-17F provides evidence for the contribution of IL-17F to inflammation in joints and skin beyond IL-17A alone. Dual inhibition of IL-17A and IL-17F by bimekizumab may provide an effective treatment for immune-mediated inflammatory diseases such as PsA.

References:


Disclosure: A. Maroof, UCB Pharma, 3,UCB Pharma, 9; R. Okoye, UCB Pharma, 3; T. Smallie, UCB Pharma, 3; D. Baeten, UCB Pharma, 3,UCB Pharma, 2,University of Amsterdam, 3; S. Archer, Crescendo Biologics; UCB Pharma, 3; C. Simpson, UCB Pharma, 3; M. Griffiths, UCB Pharma, 3; S. Shaw, UCB Pharma, 3,UCB Pharma, 9.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/bimekizumab-dual-inhibition-of-il-17a-and-il-17f-provides-evidence-of-il-17f-contribution-to-chronic-inflammation-in-disease-relevant-cells

Abstract Number: 1572

MHC Associations of Ankylosing Spondylitis in East Asians Are Driven By HLA-B Amino-Acid Position 97, Confirming Findings in European Descent Subjects

Geng Wang1, Adrian Cortes2, So-Young Bang3, Paul Leo4, Matthew Brown4, Tae-Hwan Kim5 and Huji Xu1,
1Department of Rheumatology and Immunology, Shanghai Changzheng Hospital, Second Military Medical University, Shanghai, China, 2Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, United Kingdom, 3Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea,
SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Whilst HLA-B27 is the MHC allele associated with AS, there is strong evidence indicating that other HLA-B alleles and MHC genes are involved in the disease. Large studies in European case-control cohorts have demonstrated risk associations with HLA-B*40 and multiple other HLA-B, -A and class II alleles, and demonstrated that in that ethnic group the amino-acid sequence at position 97 in HLA-B is the key determinant of HLA associations with AS (Cortes et al, Nat Com, 2015). A recent study in Korean AS cases and controls additionally identified association at HLA-C*15:02 (Kim et al, Arthritis Res Ther, 2015). In the current study, we examined in an expanded East Asian cohort the MHC associations of AS.

Methods: 1637 Chinese, Taiwanese and Korean AS cases meeting the modified New York Criteria for AS, and 1589 ethnically matched controls, were genotyped with the Illumina Immunochip, including a dense coverage of the MHC region. HLA genotypes and amino-acid composition was imputed using the SNP2HLA program using the Korean HLA reference panel (n=413) and association tested using logistic regression using 10 principal components to control for population stratification effects. Only HLA types with imputation information scores >0.8 were considered.

Results: Strong association was seen with HLA-B*27 (odds ratio (OR) 158, P=10-127). Controlling for this association, risk association is seen with HLA-B*40 (OR=8.22, P=7.66x10^-83). Controlling for both HLA-B*27 and –B*40, no other HLA-B associations are seen (P>0.05). At amino-acid level the strongest association seen in uncontrolled analysis was with histidine or tyrosine at position 9 in HLA-B (p=10^-155), but association at P<10^-100 was seen with multiple HLA-B amino acids at P<10^-100 including asparagine (found on HLA-B*27 alleles) at position 97, previously reported to be the main amino-acid determining HLA-B associations with AS. Controlling for HLA-B27 alone, or with –B27 and –B40, the strongest HLA amino-acid association remains with HLA-B position 97 (serine, found on HLA-B*7, *8, *15, *2707, *40, *41, *48; P=10^-115 and 10^-71 respectively)

Conclusion: This study confirms in East Asians that the primary amino-acid driver of HLA associations in AS is amino-acid position 97, which remains associated with AS independently of both HLA-B*27 and –B*40, the two key driver alleles in this ethnicity.

Disclosure: G. Wang, None; A. Cortes, None; S. Y. Bang, None; P. Leo, None; M. Brown, None; T. H. Kim, None; H. Xu, None.


Abstract Number: 1573
**In Vivo Phosphorylation of p38 in Monocytes Is Enhanced in Patients with Axial Spondyloarthritis (axSpA) at the Time of Diagnosis**

Antti Kuuliala, Krista Kuuliala, Riitta Koivuniemi, Mari Hämäläinen, Eeva Moilanen, Hannu Kautiainen, Heikki Repo, Marjatta Leirisalo-Repo, 1 Bacteriology and Immunology, University of Helsinki, Helsinki, Finland, 2 Rheumatology, Helsinki University Hospital, Helsinki, Finland, 3 Helsinki University Hospital, Helsinki, Finland, 4 Rheumatology, University of Helsinki, Helsinki, Finland, 5 The Immunopharmacology Research Group, University of Tampere School of Medicine and Tampere University Hospital, Tampere, Finland, 6 The Immunopharmacology Research Group, Faculty of Medicine and Life Sciences, University of Tampere and Tampere University Hospital, Tampere, Finland, 7 Unit of Primary Health Care, University of Helsinki and Helsinki University Hospital, Helsinki, Finland

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster II  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Host response to microbes is considered to contribute to the pathogenesis to axSpA and other HLA-B27 associated diseases. The p38 MAP kinase pathway plays an important role in the resistance of bacterial replication in HLA-B27 expressing human monocytic U937 cells (Sahlberg AS et al: Arthritis Rheum 2007;56:2652). This prompted us to study the phosphorylation of the MAP kinases p38, extracellular signal-regulated kinase (ERK)1/2 and c-Jun-N-terminal kinase (JNK) in patients with axSpA.

**Methods:** The study comprised 20 patients [10 men, 10 women, mean age 31.1 years (range 22-48), 19/20 patients HLA-B27 positive, time from first period of back pain mean 5.9 years (range 0.3-16), mean BASDAI 4.4 (SD 1.7)] referred to rheumatology unit for diagnostic workup due to back pain. Radiological sacroiliitis was observed in 1/18 patients, and inflammation in sacroiliac joints by MRI was observed in 17/20 patients. The patients were diagnosed to have axSpA fulfilling the Assessment of SpondyloArthritis international Society (ASAS) classification criteria. We included 26 patients [7 men, 19 women, mean age 49 years, range 19-79, mean DAS28 4.0 (SD 1.3)] with early untreated RA fulfilling the 2010 ACR/EULAR classification criteria as a disease control group, and 18 adult volunteers (9 men, 9 women, mean age 39 years, range 25-70) as healthy controls. Whole blood phosphospecific flow cytometry was used to reveal phosphorylation of p38, ERK1/2 and JNK in nonstimulated monocytes, and in monocytes stimulated by E. coli-derived lipopolysaccharides (LPS), whole cells of E. coli or lipoteichoic acid (LTA). Fluorescence histograms for monocyte pERK1/2-PE-CF594, pJNK-AlexaFluor647 and pp38-PE-Cy7 were created and fluorescence intensities were expressed as relative fluorescence units (RFU). Phosphorylation capability of MAP kinases was determined by fold-increase, i.e. the ratio of RFU of the stimulated sample to the nonstimulated one. Significance of difference between axSpA and RA patients and healthy subjects was tested by ANCOVA, adjusted for high sensitivity (hs)CRP levels.

**Results:** Basal phosphorylation level of p38 in axSpA monocytes was significantly higher than that in healthy subjects’ monocytes (P=0.009), while the difference between RA and healthy subjects was not statistically significant. The respective phosphorylation levels of ERK1/2 and JNK did not differ significantly between the 3 subject groups. The fold-increases of p38 phosphorylation in axSpA monocytes upon LPS or E.coli stimulation were significantly lower than those in healthy subjects’ monocytes (P=0.004 and 0.002, respectively), while the respective differences between RA and healthy subjects were not statistically significant. The p38 RFU values of the stimulated monocytes did not differ significantly between the 3 subject groups. The fold-increases of ERK1/2 and JNK phosphorylation did not differ significantly between the 3 subject groups.
Conclusion: Enhanced monocyte baseline phosphorylation of p38 suggests in vivo preactivation of monocytes in patients at the time of diagnosis of axSpA.

Disclosure: A. Kuuliala, None; K. Kuuliala, None; R. Koivuniemi, None; M. Hämäläinen, None; E. Moilanen, None; H. Kautiainen, None; H. Repo, None; M. Leirisalo-Repo, None.

Abstract Number: 1574

Gut Microbiota Perturbations in Reactive Arthritis

Julia Manasson1, Nan Shen2, Helga R. Garcia Ferrer3,4, Carles Ubeda5, Isa Iraheta3,4, Adriana Heguy6, Joan M. Von Feldt7, Luis R. Espinoza8, Abraham Garcia Kutzbach9, Leopoldo N. Segal10, Alexis Ogdie11, Jose C. Clemente2 and Jose U. Scher12, 1Department of Medicine, Division of Rheumatology, New York University School of Medicine, New York, NY, 2Department of Genetics and Genomic Sciences, Icahn Institute for Genomics and Multiscale Biology, Icahn School of Medicine at Mount Sinai, New York, NY, 3Guatemalan Association against Rheumatic Diseases (AGAR), Guatemala City, Guatemala, 4Universidad Francisco Marroquin, Guatemala City, Guatemala, 5Institute for Research in Public Health, Valencia, Spain, 6Department of Pathology, New York University Genome Technology Center, New York University School of Medicine, New York, NY, 7Hospital of the University of Pennsylvania, Philadelphia, PA, 8Internal Medicine, LSU Health Sciences Center, New Orleans, LA, 9Internal Medicine, Rheumatology Unit (AGAR), Francisco Marroquin University, School of Medicine, Guatemala City, Guatemala, 10Department of Medicine, Division of Pulmonary and Critical Care, New York University School of Medicine, New York City, NY, 11Division of Rheumatology, Department of Medicine, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, 12New York University School of Medicine, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Reactive arthritis (ReA) is an inflammatory condition occurring several weeks after gastrointestinal (GI) or genitourinary (GU) infections. HLA-B27 positivity is considered a risk factor, though not necessarily predictive of disease incidence. Among non-genetic factors, the intestinal microbiome may play a role in disease susceptibility. The objective of this study was to characterize the gut microbiota and host gene interactions in ReA.

Methods: Adult ReA (n=32) and control (n=32) subjects with preceding GI and/or GU infections that did not develop arthritis were prospectively recruited in Guatemala, a highly prevalent geographic region for this disease. Clinical variables, HLA status, and fecal samples were collected. Fecal DNA was extracted and high-throughput sequencing of the V4 hypervariable region of bacterial 16S rRNA was performed using the MiSeq Illumina platform (150 bp read length, paired-end protocol) to determine intestinal microbiota composition. Data was analyzed with Quantitative Insights into Microbial Ecology (QIIME), R, Linear discriminant analysis Effect Size (LEfSe), and co-occurrence networks.
**Results:** ReA subjects showed no significant differences from controls in gut bacterial alpha or beta diversity. Furthermore, there were no differences when subjects were grouped by prior exposure to antibiotics or sulfasalazine. However, there was a higher abundance of *Erwinia* and *Pseudomonas*, and increased prevalence of typical enteropathogens associated with ReA. In fact, at least one enteropathogen was present in 71.9% of ReA subjects vs 46.8% of controls (p<0.05). LEfSe analysis showed that subjects with ultrasound evidence of enthesitis were enriched in *Campylobacter*, while subjects with uveitis and radiographic sacroiliitis were respectively enriched in *Erwinia* and *unclassified Ruminococcaceae*, and both enriched in *Dialister* (log LDA >2). Host genetics, particularly HLA-A24, were associated with differences in gut microbiota diversity irrespective of disease status. We determined several co-occurring taxa that were also predictive of HLA-A24 status, including *Ruminococcaceae-Rikenellaceae-Coriobacteriaceae* and *Prevotellaceae-unclassified Sphingobacteriales-Elusimicrobiaceae*.

**Conclusion:** This is the first culture-independent study characterizing the gut microbial community of ReA. Although bacterial factors correlated with disease presence and clinical features of ReA, host genetics also appeared to be a major independent driver of intestinal community composition. Understanding of these gut microbiota-host-genetic relationships may further clarify the pathogenesis of ReA and related spondyloarthropathies.

**Disclosure:** J. Manasson, None; N. Shen, None; H. R. Garcia Ferrer, None; C. Ubeda, None; I. Iraheta, None; A. Heguy, None; J. M. Von Feldt, None; L. R. Espinoza, None; A. Garcia Kutzbach, None; L. N. Segal, None; A. Ogdie, Pfizer, 2,AbbVie, Celgene and Pfizer, 2,Novartis, Takeda and Pfizer, 5; J. C. Clemente, None; J. U. Scher, NIAMS-NIH, 2.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/gut-microbiota-perturbations-in-reactive-arthritis](http://acrabstracts.org/abstract/gut-microbiota-perturbations-in-reactive-arthritis)

**Abstract Number: 1575**

**JMJD3 Epigenetically Regulate Ankylosing Spondylitis Inflammation through Th17 Differentiation**

Hongxiao Liu¹, Ziqi Xu¹, Xinghua Feng¹, Xiaoyan Feng², Heqiu Zhang², Quan Jiang¹, Yanan Zhao³, Yuyang Wang¹ and Zhe Zhao¹, ¹Department of Rheumatology, Guang’anmen Hospital, China Academy of Chinese Medical Sciences, Beijing, China, ²Department of Vaccine Engineering, Beijing Institute of Basic Medical Sciences, Beijing, China, ³Department of Rheumatology, Guang’anmen Hospital, China Academy of Chinese Medical Sciences, BeiJing, China

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster II  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

JMJD3 epigenetically regulate ankylosing spondylitis inflammation through Th17 differentiation

**Background/Purpose:** Inflammation is the initial stage of ankylosing spondylitis (AS), looking for possible inflammatory regulator will have a great significance in AS treatment. Jumonji domain-containing protein D3 (JMJD3) could specifically demethylate the 27th lysine of histones H3(H3K27), which was found in inflammation and many autoimmune diseases. The most important functions of JMJD3 are regulating the differentiation of T cell subsets. JMJD3 specifically de-methylated H3K27 trimethylation in the promoter sequence of the retinoid-acid
receptor-related orphan receptor c (RORc) gene, which is considered to be the beginning of Th17 differentiations. As we know, Th17 has been determined its important role in AS inflammation. So this research aims to explore the epigenetic regulation of JMJD3 in AS inflammation through Th17 differentiations.

**Methods:** A total of 40 AS patients in active stage and 20 healthy controls (25.2±4.1 years) participated in the experiments. All patients were met with the modified New York criteria. 20 of them whose BASDAI¡Ý4 were classified into AS-Active group(25.8±7.1years), others were classified into AS-Stable group(31.2±8.4years). The serum level of IL-17 was detected by ELISA. The proteins were all detected by Western blotting. The mRNA were detected by quantitative PCR.

![Graphs](image)

**Results:** As in Figure1. The serum IL-17 levels were significantly higher in AS-active patients. The level of JMJD3 is significant higher in AS-active. The methylation level of H3K27 was reduced in AS-active than in others. The protein level of RORc is higher in AS-active and AS-stable, but in transcriptional level the AS-active group was higher than other two groups.

In Figure 2. The protein level and phosphorylated level of JAK2 and STAT3 were higher in AS-active. The transcriptional level were higher too.
Conclusion: Our study found that JMJD3 catalyzes the demethylation of H3K27 might be an important epigenetic mechanisms in AS inflammatory. The highly expression of JMJD3 in active AS patients may leading to the higher expression of RORc, and could activation the signal transduction through JAK2/STAT3 pathway, inducing a large number of IL-17 secretions. That could be the beginning of the differentiation and function of Th17, and JMJD3 maybe the core epigenetic regulator in this inflammation process. These exciting findings have broad implications for finding possible biomarkers in the inflammatory of AS, and may give us a new possible point of view from the epigenetic regulation mechanism of Th17 in the inflammation stage of AS.

Disclosure: H. Liu, None; Z. Xu, None; X. Feng, None; X. Feng, None; H. Zhang, None; Q. Jiang, None; Y. Zhao, None; Y. Wang, None; Z. Zhao, None.

Abstract Number: 1576

IL-23 Promotes Fecal Microbiota Dysbiosis Associated with Susceptibility to Spondyloarthritis and Ileitis in ZAP-70 Mutant SKG Mice

Linda Rehaume, Nicholas Matigian, Kate Ormerod, Alicia Kang, Richard Linedale, Olga Zbarskaya, Kristine Kikly, Joshua Daly, Nancy Lachner, Philip Hugenholtz, Mark Morrison, Kim-Anh Lê Cao and Ranjeny Thomas, 1 The University of Queensland Diamantina Institute, Translational Research Institute, Brisbane, Australia, 2 Australian Centre for Ecogenomics, The University of Queensland, Brisbane, Australia, 3 Biotechnology Discovery Research, Eli Lilly and Co, Indianapolis, IN, 4 School of Mathematics and Statistics, Centre for Systems Genomics, The University of Melbourne, Melbourne, Australia

First publication: September 18, 2017

SESSION INFORMATION
Identification of disease-associated or protective bacteria may elucidate new biomarkers or probiotic supplements for people suffering from SpA, or for people at-risk of disease development. The colitogenic *Prevotella copri* was associated with new-onset rheumatoid arthritis, and *Prevotella* spp. were increased in the cecum of HLA-B27 transgenic rats. In ankylosing spondylitis patients, several bacterial families, including *Porphyromonadaceae*, were increased. *Lactobacillus murinus* protects against murine colitis, and ileitis does not occur in germ-free BALB/c ZAP-70W163C-mutant (SKG) mice. Thus, microbes are associated with SpA disease progression and regulation but it is unclear how the microbial community structure differs as a result of genetic susceptibility to SpA, or the impact of additional pro-inflammatory triggers. Since SpA is IL-23- and microbe-dependent in SKG mice, we examined the relationship between IL-23, gut dysbiosis and SpA development in response to microbial β-1,3-glucan (curdlan).

**Methods:**

Altered Schaedler flora (ASF)-colonized SKG and BALB/c mice were treated one day prior to curdlan, and then weekly, with anti-IL-23 p19-specific mAb or isotype control mAb, or with curdlan or vehicle control. SPF-SKG mice were treated weekly with anti-IL-23 or isotype mAb for 3 weeks, then with curdlan or vehicle control. Fecal samples were collected longitudinally and the microbiota community profiles were analyzed by RT-PCR and sequencing of the 16S rRNA gene using Illumina MiSeq technology. Sequence data was analyzed using QIIME and mixOmics platforms. Arthritis, spondylitis and ileitis were assessed histologically.

**Results:**

After colonizing germ-free mice with ASF, 4/8 bacterial strains were detected in ASF-SKG and ASF-BALB/c mice: *Clostridium* sp., *Lactobacillus murinus*, *Mucispirillum schaedleri* and *Parabacteroides* sp. The relative abundance of *L. murinus* increased in mice treated with curdlan and anti-IL-23 mAb compared with curdlan alone or with isotype mAb. Treatment of naïve SPF-SKG mice with anti-IL-23 mAb significantly altered the fecal microbiota composition relative to isotype mAb treatment for prolonged periods. These shifts persisted after washing out anti-IL-23. The microbiota composition of mice treated with isotype mAb and curdlan was distinct to that of mice treated with anti-IL-23 mAb with curdlan or saline, both of which clustered together regardless of curdlan or saline treatment.

**Conclusion:**

Interaction of the microbiota with the immune system of SKG mice alters the composition of both a simplified consortium and an unrestricted bacterial community. Curdlan triggers the decline of a gut-protective *Lactobacillus* species within a simplified consortium. Moreover, IL-23 modifies the host’s support for this gut-protective species. Treatment of SPF-SKG mice with anti-IL-23 mAb not only suppresses SpA development but shifts the fecal microbiota composition and prevents the usual outgrowth of bacteria associated with arthritis and inflammatory bowel disease in response to curdlan. Our results suggest that positive feedback between host IL-23 and dysbiosis predisposes to a host gut environment hostile to gut-protective species and SpA development.

**Disclosure:** L. Rehaume, None; N. Matigian, None; K. Ormerod, None; A. Kang, None; R. Linedale, None; O. Zbarskaya, None; K. Kikly, Eli-Lilly and Company, 3; J. Daly, None; N. Lachner, None; P. Hugenholtz, None; M. Morrison, None; K. A. Lê Cao, None; R. Thomas, None.

Deciphering the Role of the Tissue Microenvironment in Shaping the Immune Landscape in Psoriatic Arthritis

Jin Hui Sherlynn Chan1, Ying Ying Leung2, Warren Fong2, Yi Wei Yeo2, Bhairav Paleja1, Liyun Lai1, Suzan Saidin1, Camillus Chua1, Sharifah Nur Hazirah1, Su Li Poh1, Andrea Hsiu Ling Low2 and Salvatore Albani1,3, 1SingHealth Translational Immunology and Inflammation Centre (STIIC), Duke-NUS Medical School, Singapore, Singapore, 2Singapore General Hospital, Singapore, Singapore, 3KK Women's and Children's Hospital, Singapore, Singapore

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Psoriatic arthritis (PsA) occurs in a third of patients with psoriasis (Ps) and up to 30% of patients with PsA do not have an adequate response to any treatment. The precise pathogenesis of PsA/Ps remains unknown and its understanding is crucial for the development of new therapies. We hypothesize that the microenvironment plays a crucial role in shaping the pathogenic immune response. To address this, we utilize a dual approach to decipher the transcriptome of the skin microenvironment and the immunomes of PsA patients with active disease. This multi-dimensional strategy will enable the distillation of immune cell subsets in the periphery that can potentiate pathogenic responses in the microenvironment.

Methods:
Skin punch biopsies of psoriatic and morphologically normal sites and paired whole blood were obtained from patients (n=3) with active PsA requiring intensification of treatment. Total RNA extracted from the skin punch biopsies and gene expression analysis was performed with Nanostring. Peripheral Blood Mononuclear Cells (PBMCs) from PsA patients (n=3) and sex-matched healthy donors (n=3) were stimulated with PMA-Ionomycin, stained with 37 phenotypic T cells markers and interrogated with the CyTOF platform. Dimensional reduction and unsupervised clustering analyses were performed with Multi-dimensional Automated Reduction and Visualization (MARVis), an in-house customised machine learning software.

Results:
Nanostring results revealed that gene signatures enriched in psoriatic skin (like GZMA, GZMB, ARG1, NOS2) are suggestive of inflammation mediated by subsets of immune cells such as neutrophils, CD8+ T cells and macrophages. Moreover, several immunoattractant chemokines like CCL20, CXCL13 and CXCL2 were expressed at higher levels in psoriatic skin compared to morphologically-normal skin. Given the enrichment of chemokines in the microenvironment, we next examined the immune cell subsets in the peripheral blood which may be responding to these chemical signals. We studied the systemic immune profiles of these patients with CyTOF and noticed significant differences in the immunomes of PsA patients compared to healthy donors. Specifically, in PsA patients, we observed a decline in the Mucosal Associated Invariant T (MAIT) population displaying an immune-modulatory phenotype (TCRvα7.2+CD8+CD161+CCR6+IFNγ+) and an enrichment in activated CD8+ T effector cells (CD8+CCR6+CXCR3+Tbet+GranB+). The expression of CCR6 is indicative of the migratory potential of these pro-inflammatory T cells in response to CCL20 to sites such as the skin and joints.
Conclusion:

Our approach of analysing the psoriatic skin transcriptome and immunome exemplifies the role of microenvironment in shaping the systemic immune response. We observed at the skin level, that the microenvironment secretes a cocktail of chemokines that may serve to shape the composition of the peripheral immunome and affect the relative proportion of cells infiltrating the lesions. These preliminary findings warrant further analysis on a larger PsA patient cohort and will improve the understanding of the pathogenesis of Ps and PsA and facilitate the identification of novel immune therapeutic targets.

Disclosure: J. H. S. Chan, None; Y. Y. Leung, None; W. Fong, None; Y. W. Yeo, None; B. Paleja, None; L. Lai, None; S. Saidin, None; C. Chua, None; S. Nur Hazirah, None; S. L. Poh, None; A. H. L. Low, None; S. Albani, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/deciphering-the-role-of-the-tissue-microenvironment-in-shaping-the-immune-landscape-in-psoriatic-arthritis

Abstract Number: 1578

The Initiation, but Not the Persistence, of Experimental Spondyloarthritis in HLA-B27/Huβ2m Transgenic Rats Is Crucially Dependent on the IL-23 Axis

Melissa van Tok1,2, Songqing Na3, Joel Taurog4, Dominique Baeten2,5 and Leonie van Duivenvoorde1,2,

1Amsterdam Rheumatology and Immunology Center, Academic Medical Center/University of Amsterdam, Amsterdam, Netherlands, 2Clinical Immunology and Rheumatology/Experimental Immunology, Academic Medical Center/University of Amsterdam, Amsterdam, Netherlands, 3Eli Lilly and Company, Indianapolis, IN, 4Dept Int Med-Rheum Dis Div, University of Texas Southwestern Medical Center, Dallas, TX, 5Clinical Immunology and Rheumatology, Amsterdam Rheumatology and Immunology Center, Academic Medical Center/University of Amsterdam, Amsterdam, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: IL-17A is a central driver of spondyloarthritis (SpA) pathology. IL-17A production was originally proposed to be IL-23 dependent. Emerging preclinical and clinical evidence from SpA-related diseases such as Crohn’s disease suggest, however, that IL-17A and IL-23 have a partially overlapping but distinct biology. We aimed to assess to what extend IL-17A is dependent on IL-23 in SpA by selectively targeting the IL-23R in HLA-B27/Huβ2m transgenic rat model of SpA, which we showed previously to be IL-17A-dependent.

Methods: HLA-B27/Huβ2m tg rats were immunized with low dose heat-inactivated M. tuberculosis to induce experimental SpA. Rats were treated with anti-mouse/rat chimeric IL-23R antibody or vehicle in a prophylactic (treatment initiation before onset of symptoms) or therapeutic (treatment initiation after onset of clinical symptoms) experiment. Spondylitis and arthritis were clinically scored, hind limb swelling was measured. Ex vivo cytokine expression was measured in lymph nodes and spleen. Serum samples were analyzed for anti-IL23R exposure.
Results: During prophylactic treatment, 58% and 67% of the rats in the control group developed spondylitis and arthritis, respectively. The average arthritis score at the end of the study was 3.9±1.1 and the average hind paw swelling was 0.35±0.09 cm$^3$. Prophylactic treatment completely protected against the development of spondylitis and arthritis (figure 1). In the therapeutic treatment strategy, however, anti-IL23R treatment failed to reduce incidence or decrease the severity of experimental SpA (figure 1). The differential effect of IL-23R targeting in the initiation phase versus established disease could not be explained by pharmacokinetic differences, serum analyses revealed similar exposure levels. Mechanistically, the expression of downstream effector cytokines such as IL-17A (p<0.05) and IL-22 (p<0.01) was reduced in the popliteal lymph nodes of rats treated prophylactically with anti-IL23R versus controls, with a similar trend in spleen. Accordingly, IL-17A production upon ex vivo re-stimulation was reduced in samples from prophylactically treated rats. In contrast, similar popliteal lymph node expression data in samples from the therapeutic experiment indicate no difference in IL-17A and IL-22 expression in the anti-IL23R treated rats compared to controls.

Conclusion: IL-17A expression and production is dependent on the IL-23 axis in the initiation phase of experimental SpA but not in established disease. Accordingly, targeting of this axis with an anti-IL23R antibody completely prevented the onset of arthritis and spondylitis in HLA-B27/Huβ2m transgenic rats, but failed to reduce axial and peripheral joint inflammation in established disease. The cellular origin of IL-23-independent IL-17A production and the relevance to human SpA remains to be investigated.

Disclosure: M. van Tok, None; S. Na, Eli Lilly and Company, 1,Eli Lilly and Company, 3; J. Taurog, Abbvie; Anges; Inc; Celgene, 5; D. Baeten, UCB, 3; L. van Duivenvoorde, None.

Monocyte-Derived Dendritic Cells (MDDCs) from Spondyloarthritis (SpA) Patients Exhibit a Coordinated Downregulation of the Cholesterol (chol) Biosynthesis Pathway That Relates to Lipid Overload

Maxime Breban¹, Clémence Desjardin², Emmanuel Chaplais³, Alice Talpin³, Felicie Costantino⁴, Christophe Hue⁵, Aude Jobart-Malfait⁵, Benoit Maury⁶, Stanislas Grassin-Delyle³, Nelly Bonilla⁷, Ariane Leboime⁸, Roula Said Nahal⁹, Franck Letourneur⁷, Sébastien Jacques⁷, Anne Boland¹⁰, Jean-François Deleuze¹⁰, Gilles Chiocchia¹¹ and Henri-Jean Garchon³,⁶,¹²

¹Rheumatology, Ambroise Paré Hospital (AP-HP), Versailles Saint Quentin en Yvelines University, INSERM UMR1173, Boulogne-Billancourt, France, ²INSERM UMR1173, Montigny-le-Bretonneux, France, ³Inserm U1173, Montigny-le-Bretonneux, France, ⁴Hôpital Universitaire Ambroise Pare, Paris, France, ⁵INSERM-U1173, University of Versailles Saint-Quentin-en-Yvelines, France, Montigny-le-Bretonneux, France, ⁶University of Versailles Saint-Quentin, Simone Veil school of Health Sciences, Montigny-le-Bretonneux, France, ⁷Institut Cochin, Inserm U1016, Paris, France, ⁸Ambroise Paré Hospital Division of Rheumatology, Assistance Publique des Hopitaux de Paris, Boulogne-Billancourt, France, ⁹Ambroise Paré Hospital, Boulogne-Billancourt, France, ¹⁰Centre National de Recherche en Génomique Humaine, Evry, France, ¹¹Service d'Immunologie, Ambroise Paré Hospital, University of Versailles Saint-Quentin-en-Yvelines, Boulogne, France, Boulogne-Billancourt, France, ¹²Ambroise Paré Hospital Division of Genetics, AP-HP, Boulogne-Billancourt, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthopathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Gene expression studies are useful to investigate the pathogenesis of complex diseases. The critical role of antigen-presenting cells such as dendritic cells (DCs) being suspected in SpA, we wished to study their particular biology, starting from unbiased transcriptomic experiment.

Methods:
MDDCs were obtained from circulating CD14+ monocytes after 7 days of culture with GMCSF + IL-4. Transcriptomes were profiled using Affymetrix microarrays (HuGene 1.0 ST) and further confirmed by RNA-seq (78 million paired-end reads (2x100 nt) per sample). Differentially expressed (DE) genes between SpA (ASAS criteria) and healthy controls (HC) were listed with LIMMA. Functional annotation was performed with DAVID and InnateDB. RT-qPCR was used to test the reproducibility of the signature over time. Intra-cellular lipid droplets (LD) volume and number were quantified by Bodipy® labeling and confocal microscopy. Cellular content of chol pathway metabolites was quantified by mass spectrometry (MS).

Results:
For transcriptomic analysis, we generated 3 lists of DE genes (nominal p < 0.01) comparing (A) HLA-B27+ SpA (n=40) to B27-neg HC (n=30), (B) B27+ HC (n=44) to B27-neg HC and (C) B27+ SpA to B27+ HC. Subtraction A–B and intersection with C yielded a robust list of 68 genes affected by SpA controlling for unrelated HLA-B27 effect. Analysis of functional pathways revealed a significant overrepresentation of genes involved in chol
biosynthesis and its regulation (p < 1x10^{-4}). Five of the 6 genes in this pathway (SQLE, MSMO1, LDLR, INSIG1, SREBF2) were downregulated in SpA. These findings were confirmed by RNA-seq on the same samples and by qPCR on a new series of samples drawn from the same group of individuals (11 SpA vs. 10 HC). Using MS, we evidenced a significant increase of chol and 27-OH-chol content in MDDC from another panel of SpA (n = 14) compared to HC (n = 8) (p < 0.05), suggesting that downregulation of cholesterol synthesis might be secondary to chol overload. Consistently, there was a highly significant increase in the size (p = 5x10^{-4}) and overall volume (p < 2x10^{-4}) of LD in SpA (n=12) compared to HC (n=11) MDDCs (Figure). Importantly, there was no difference of total nor fractionated chol plasma levels between SpA and controls.

**Conclusion:**

Our study identified a downregulation of the chol synthesis pathway in MDDCs from SpA patients that seems to be secondary to lipid overload in those cells. Our findings are consistent with a state of pre-activation of those cells that could lead to a strong inflammatory response to endogenous or environmental stimuli.

**Figure:**

![Mean total LD volume/cell](image)

**Disclosure:** M. Breban, None; C. Desjardin, None; E. Chaplais, None; A. Talpin, None; F. Costantino, None; C. Hue, None; A. Jobart-Malfait, None; B. Maury, None; S. Grassin-Delyle, None; N. Bonilla, None; A. Leboime, None; R. Said Nahal, None; F. Letourneur, None; S. Jacques, None; A. Boland, None; J. F. Deleuze, None; G. Chiocchia, None; H. J. Garchon, None.


Abstract Number: 1580

**HLA-B27/ Human β2-Microglobulin (β2m) Transgenic Drosophila Expresses Specific Cross-Vein Less (CVL) and Small-Eye Phenotypes Resulting from Disruption of the BMP/TGFβ Signaling Pathway**
SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The association between HLA-B27 and spondyloarthritis (SpA) remains unexplained more than 40 years after its discovery. To further explore the pathogenic role of HLA-B27, we produced transgenic Drosophila for several human HLA-B alleles, associated (B*2705, B*2704) or not (B*0702) with SpA, and for the b2m invariant chain partner.

Methods: Transgenes were expressed with different drivers in the wing or eye imaginal discs (i.e. the precursor tissues of the adult fly wing or eye). Their expression was examined by PCR and Western-blot. Cell surface or intra-cellular levels of unfolded (HC10 antibody) and well-folded (ME1 and W6/32 antibodies) HLA-B were examined by FACS and by immunofluorescence (IF). Genetic interactions with candidate genes controlling several signaling pathways were addressed.

Results: IF experiments revealed high levels of well-folded HLA-B27 alleles on the cell surface, but less of the HLA-B*0702. FACS analysis confirmed that HLA-B*2705/b2m and HLA-B*2704/b2m better fold than HLA-B*0702/b2m, in Drosophila. Co-expression of HLA-B27 (B2705 or B2704) alleles and b2m in the wing tissue specifically induced the loss of posterior and anterior cross-veins leading to a CVL phenotype. Furthermore, the eye size was reduced when HLA-B27 alleles (but not HLA-B*0702) were expressed in this tissue with b2m. Genetic interaction tests for candidate signaling pathways involved in the eye and wing development showed a selective decrease of the Bone Morphogenetic Protein (BMP) signaling when HLA-B*2705/b2m was expressed with no evidence for ER stress induction. Those results were confirmed by the decreased phosphorylation of the transcription factor MAD. Altogether, our results allow us to hypothesize that HLA-B*2705 could act downstream of the BMP receptor. Moreover, overexpression of the Drosophila SMAD7 homolog Dad, a negative regulator of the BMP pathway, was observed. Interestingly, transcriptomic study showed that SpA-prone HLA-B27/b2m transgenic rat lines also exhibit a specific increase of SMAD7 in their dendritic cells.

Conclusion: HLA-B27 seems to have a better capacity to fold and reach the cell surface than HLA-B*0702, in the absence of the class-I MHC peptide-loading complex machinery. CVL and small-eye phenotypes resulting from the expression of both SpA-associated HLA-B27 subtypes (i.e. B*2705 and B*2704) but not of HLA-B*0702 was induced by disrupting MAD phosphorylation. Those results highlight the effectors (rSMADs) and inhibitor (SMAD7) of the BMP/TGFb pathway as candidate targets for the pathogenic role of HLA-B27 in SpA.

Disclosure: B. Grandon, None; N. Jah, None; A. Rincheval-Arnold, None; I. Guénal, None; S. Gaumer, None; C. Andre, None; M. Breban, None; G. Chiocchia, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/hla-b27-human-%ce%b22-microglobulin-%ce%b22m-transgenic-drosophila-expresses-specific-cross-vein-less-cvl-and-small-eye-phenotypes-resulting-from-disruption-of-the-bmptgf%ce%b2-signaling-pathway
Differential Involvement of Synovial and Enthesal Inflammation in Mediating Pathological IL23 Axis Signaling in Spondyloarthritis

Ed Purdue¹, Josselyn Galdamez¹, Madeline Epsten², Rima Abhyankar³, Kathleen Hoyt⁴, Michelle Lewis⁴, Devan Dove⁴, Jon Hill⁵, Alexander Klimowicz⁴, Gerald Nabozny⁶, Joseph Wahle⁴ and Lisa A. Mandl⁷, ¹Research, Hospital for Special Surgery, New York, NY, ²Rheumatology, Hospital for Special Surgery, New York, NY, ³Hospital for Special Surgery, New York, NY, ⁴Department of Immunology and respiratory discovery research, Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT, ⁵Department of Discovery research, Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT, ⁶gerald.nabozny@boehringer-ingelheim.com, Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT, ⁷Rheumatology, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Although accumulating evidence continues to point toward a critical role for IL23 signaling in spondyloarthritis (SpA), the cellular and molecular events involved, as well as the respective contributions of enthesial and synovial inflammation, remain incompletely understood. In this study we have combined ex vivo organ culture of enthesial and synovial explants from SpA patients and controls with in-situ hybridization (ISH) and gene expression analysis of synovial tissue to further delineate the molecular and cellular pathogenesis underlying SpA.

Methods: Under an HSS IRB approved protocol, patients undergoing total hip replacement (THR) were recruited into 3 groups: SpA (either psoriatic arthritis or ankylosing spondylitis, meeting ASAS or CASPAR criteria or were being treated with DMARDS/biologics); HO (OA patients a previous contralateral THR who had history of post-THR heterotopic ossification) and OA (OA patients a previous contralateral THR with no history of HO. For Phase 1 of this study (n=15/group), synovial tissue was collected intra-operatively and immediately aliquoted into RNAlater for RNA isolation and subsequent sequencing, or OCT for ISH analysis. For Phase 2 (n=10/group), enthesal tissue (ligamentum teres) and synovial tissue were cultured +/- RORgT inhibitor (2 hours) followed by +/- cytokine stimulation (hTNF/hIL23) for 24 and 48 hours. These cultures were analyzed via MSD for secreted cytokines and via TaqMan RT-PCR.

Results:

RNA sequencing identified the presence of a macrophage signature with elevation of MMPs and MARCO in SpA tissue. Additionally preliminary ISH analysis has shown a potential enrichment of CD163 positive macrophages in areas of synovial inflammation. Expression analysis of ALI cultured explants also identified a remarkable enrichment of MARCO-positive macrophages in synovium (cf enthesis) and, consistent with the RNA sequencing of whole tissue, induction of MMP production in synovium following cytokine stimulation. In contrast enthesal tissue that had a lower MMP and MARCO signature, responded to cytokine stimulation with induction of IL17A/F and IFNg. Importantly, this latter effect was most pronounced in SpA patients and inhibited by an ROR inhibitor.

Conclusion:
Our results suggest that the synovial and entheseal tissues in SpA patients have distinct cellular phenotypes and differential responses to cytokines and involvement of RORγt signaling. In line with previous observations (refs) a prominent macrophage signature is seen in the synovium, and this is associated with elevation of MMP induction in SpA. Whereas entheseal tissue produced IL17 and IFNγ in response to TNF and IL23, consistent with the presence of a resident population of IL23R positive T cells at this site in SpA.

Disclosure: E. Purdue, Boehringer Ingelheim Pharmaceuticals, 2; J. Galdamez, None; M. Epsten, None; R. Abhyankar, None; K. Hoyt, Boehringer Ingelheim Pharmaceuticals Inc, 3; M. Lewis, Boehringer Ingelheim Pharmaceuticals Inc, 3; D. Dove, Boehringer Ingelheim Pharmaceuticals Inc, 3; J. Hill, Boehringer Ingelheim Pharmaceuticals Inc, 3; A. Klimowicz, Boehringer Ingelheim Pharmaceuticals Inc, 3; G. Nabozny, Boehringer Ingelheim, 3; J. Wahle, Boehringer Ingelheim Pharmaceuticals Inc, 3; L. A. Mandl, Boehringer Ingelheim, 2, American College of Physicians, 3, Up To Date, 7.


Abstract Number: 1582

**RORγt Inhibition Selectively Targets Pathogenic Subsets of Human iNKT and γδ-T Cells Enriched in Spondyloarthritis While Preserving Tissue Protective IL-22 Responses**

Koen Venken1,2, Mark Labadia3, Kathleen Hoyt3, Anita Wayne3, Robert Hughes3, Michael Turner3, Dustin Smith4, Christian Harcken4, Tine Decruy5,6, Joseph Wahle7, Chao-Ting Wang3, Peggy Jacques8, Sofie Van Gassen9, Gaëlle Varkas10, Heleen Cypers10, Filip van Den Bosch11, Yvan Saëys9, Gerald Nabozny12 and Dirk Elewaut13,14,

1Department of Rheumatology, Faculty of Medicine and Health Sciences, Laboratory for Molecular Immunology and Inflammation, Ghent, Belgium, 2VIB Inflammation Research Center, Ghent University, Ghent, Belgium, 3Research and Development Boehringer-Ingelheim, Ridgefield, CT, 4Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT, 5Laboratory for Molecular Immunology and Inflammation, Department of Rheumatology, Faculty of Medicine and Health Sciences, Ghent University, De Pintelaan 185, 9000 Ghent, Belgium, Ghent, Belgium, 6VIB Inflammation Research Center, Ghent, Belgium, 7Department of Immunology and respiratory discovery research, Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT, 8Ghent University Hospital, Ghent, Belgium, 9Department of Applied Mathematics, Computer Science and Statistics, Ghent University, Ghent, Belgium, 10Laboratory for Molecular Immunology and Inflammation, Department of Rheumatology, VIB, Ghent University and Ghent University Hospital, Ghent, Belgium, 11Rheumatology, Ghent University Hospital, Gent, Belgium, 12gerald.nabozny@boehringer-ingelheim.com, Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT, 13VIB Inflammation Research Center, University of Ghent, Ghent, Belgium, 14Department of Rheumatology, Laboratory for molecular immunology and inflammation, Ghent, Belgium

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017
Session Title: Spondyloarthopathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Dysregulated IL-23/IL-17 responses have been linked to a myriad of inflammatory diseases including psoriasis, psoriatic arthritis and other forms of spondyloarthritides (SpA). IL-23/IL-17 inflammation is controlled by RORγt, the key Thelper17 (Th17) cell transcriptional regulator. RORγt is also expressed by subsets of innate-like T cells, including invariant natural killer T (iNKT) and γδ-T cells, but how this contributes to inflammatory disorders such as SpA is still unclear.

Methods:

Blood samples were obtained from 27 healthy control subjects and 33 patients with newly diagnosed SpA (following ASAS 2010 criteria). Synovial fluid (SF) was obtained from patients with an active knee synovitis and an indication for aspiration. Patients were treatment naïve or under treatment with a NSAID and/or DMARD (Methotrexate, Sulfasalazin), but naïve for treatment with biologicals at the time of sampling. PBMC and SFMC were isolated from patient samples and were directly analyzed by multi-color flow cytometry for analysis of iNKT cells (CD3+6B11+ TCRVβ11+), γδ-T cells (CD3+TCRγδ+) and CD161+ and CD161- conventional Tconv (T cells excluded from innate-like T cells). Rorc and Il-23r mRNA expression on specific T cell subsets was measured by means of PrimeFlow RNA Assays. Flow cytometric data were analysed by standard gating procedures using FlowJo software and further explored by FlowSOM, a novel method for computational multi-color flow cytometry. Furthermore, sorted γδ-T cells and iNKT cells were cultured in the presence of αGalCer (for iNKT) or aCD3/aCD28Ab (γδ-T cells) with addition of IL-23, IL-1β, TGFB1 and IL-2 (IL-23 cocktail) in the presence or absence of a RORγt inhibitor. Cytokine production of cells was determined by intracellular flow cytometric staining or in supernatants by multiplex protein assays (MSD). In addition, phenotypical analyses were done by qPCR with specific primers for IL-23R, IL-17A and F; IL-22 and RORC.

Results:

Here, we describe a unique population of RORγt+T-betloPLZF- iNKT and TCRγδ-hi T cells (γδ-T cells with a high expression of the γδTCR), present in healthy peripheral blood. iNKT and γδ-hi T cells showed marked IL-23 mediated Th17-like immune responses and are clearly enriched within inflamed joints. Interestingly, in-depth metacenter analyses by FlowSOM iterations showed skewing of novel iNKT cell subsets, already detectable in the blood of SpA patients. RORγt blocked Th17 cell function and inhibited IL-17 production while surprisingly preserved IL-22 production by iNKT and γδ-T cells. Further FlowSOM analyses showed that RORγt inhibition impacts distinctive IL-17+ iNKT cell subsets while preserving IL-22 subsets.

Conclusion:

Overall, these findings highlight a unique diversity of human RORγt+ innate-like T cells and underscore the potential of RORγt antagonism to modulate aberrant Type 17 responses.

Disclosure: K. Venken, None; M. Labadia, Boehringer Ingelheim, 3; K. Hoyt, Boehringer Ingelheim, 3; A. Wayne, Boehringer Ingelheim, 3; R. Hughes, Boehringer Ingelheim, 3; M. Turner, Boehringer Ingelheim, 3; D. Smith, Boehringer Ingelheim, 3; C. Harcken, Boehringer Ingelheim, 3; T. Decruy, None; J. Wahle, None; C. T. Wang, Boehringer Ingelheim, 3; P. Jacques, None; S. Van Gassen, None; G. Varkas, None; H. Cypers, None; F. van Den Bosch, None; Y. Saeyes, None; G. Nabozny, Boehringer Ingelheim, 3; D. Elewaut, Scientific Research Flanders; Research Council Ghent University; Interuniversity Attraction Pole., 2,Boehringer Ingelheim; Pfizer; UCB; Merck; Novartis; Janssen; Abbvie, 5.


Abstract Number: 1583
Increase in Arginase Activity and Related Arginine Metabolites in Patients with Rheumatoid Arthritis (RA) and Psoriatic Arthritis (PsA): Potential Mechanisms for Endothelial Dysfunction

M. Elaine Husni1, Vandana Rai2, Marcia Leon Rabanal3 and Unnikrishnan Chandrasekharan4, 1Cleveland Clinic, Cleveland, OH, 2Cellular and Molecular Medicine, Cleveland Clinic Foundation, Cleveland, OH, 3Rheumatology, Cleveland Clinic Foundation, Cleveland, OH, 4Department of Cellular and Molecular Medicine, Cleveland Clinic, Cleveland, OH

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: A high prevalence of CVD exists among patients with PsA and RA. The cardiovascular morbidity and mortality are hypothesized to be due in part to persistent systemic inflammation. Chronic inflammation promotes endothelial dysfunction with reduced vascular reactivity, leading to CVD. L-arginine metabolism is critical for maintaining normal endothelial homeostasis, and arginases are the central enzymes in the urea cycle that catalyze L-arginine to L-ornithine and urea. L-arginine is also the sole source of nitric oxide (NO), an enhancer of endothelial function as well as modulator of insulin sensitivity, whose production is catalyzed by NO synthases (NOS). Elevated arginase activity diminishes L-arginine bioavailability, thus decreasing NO production, which may lead to CVD by promoting endothelial dysfunction. Furthermore, elevated arginase activity leads to excessive production of ornithine leading to vascular problems. The aim of this study is to identify specific pathways leading to aberrant L-arginine metabolism as a potential cause of the increased CVD risk observed in RA and PsA patients.

Methods: Liquid chromatography-mass spectrometry was used to measure plasma levels of L-arginine and its metabolites [L-ornithine, L-citrulline, asymmetric dimethylarginine (ADMA) and symmetric dimethylarginine (SDMA)]. Global arginine bioavailability ratio (GABR, ratio of L-arginine to L-ornithine + L-citrulline) and arginine methylation index (ArgMI, ADMA + SDMA/MMA) values in RA and PsA were compared to those in control subjects. Plasma arginase activity was measured using Quantichrom Arginase Assay kit, according to the manufacturer’s instructions. Correlations between L-arginine metabolites and cardiovascular risk factors are analyzed using spearman correlation.

Results: There was a 400% and 160% increased level of plasma arginase activity in RA (n=119) and PsA (n=233) subjects, respectively, as compared to controls (n=148). Also, RA patients with existing CVD had higher arginase activity than RA patients without CVD. In addition, we found increased abundance of methylated arginines in RA and PsA. Compared to controls, the RA patients showed significantly lower levels of plasma L-arginine, and GABR and elevated levels of ADMA, SDMA and ArgMI. Arginase activity and L-ornithine were elevated in RA, while the level of L-citrulline was diminished. In comparison to controls, the PsA patients also showed lower levels of plasma L-arginine as well as elevated levels of plasma ADMA and SDMA.
Conclusion: Elevated plasma arginase activity and dimethylarginine in RA and PsA subjects may contribute to impair NO generation, which may lead to accelerated atherosclerosis. Future studies should explore potential therapeutic interventions targeting dysregulation of arginine metabolism.

Disclosure: M. E. Husni, AbbVie, Genentech, Bristol-Myers Squibb, Pfizer, Novartis, and Janssen, 9; V. Rai, None; M. Leon Rabanal, None; U. Chandrasekharan, None.

Chlamydia-Infected Macrophages: “Trojan Horses” for Dissemination of IL-23 and TNF-Mediated Inflammation in SKG Mouse Reactive Arthritis

Athan Baillet, Zaied Ahmed Bhuyan, Claire Douillard, Aurélie Bozon, Charles Armitage, Xavier Romand, Minh Vu Chuong Nguyen, Bertrand Favier, Timothy Wells, Kenneth Beagley and Ranjeny Thomas, 1Université Grenoble-Alpes, GREPI EA7408, Grenoble, France, 2The University of Queensland Diamantina Institute, Translational Research Institute, Brisbane, Australia, 3Institute of Health & Biomedical Innovation, Biomedical Sciences, Faculty of Health, Queensland University of Technology, Brisbane, Australia

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthopathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM
Background/Purpose: The sterile inflammatory arthritis associated with spondylitis, uveitis and rash, known as reactive arthritis, commences a few weeks after certain gastrointestinal or genitourinary infections, including Salmonella and Chlamydia in genetically-susceptible patients. ZAP-70W163C mutant BALB/c mice (known as SKG) develop a syndrome highly similar to human reactive arthritis after vaginal infection with *C. muridarum*. In that model, Chlamydial DNA was found in splenic and lymph node CD11b+ cells distant from the site of infection. We hypothesized that monocytes and macrophages disseminate pro-inflammatory *C. muridarum* pathogen-associated inflammatory molecules (PAMPS) to distant sites in susceptible SKG mice to induce inflammatory cytokine-mediated pathology.

Methods: Female SKG and BALB/c mice were genitally infected with *C. muridarum*. Arthritis was assessed weekly for 12 weeks post-infection. Joint sections were scored after sacrifice and genital tracts were analyzed 1 week post-infection. We compared *Hspa5*, *Tgtp1*, IL-23 expression by RT-qPCR in genital tract from SKG mice before or 1 week after infection. Anti-TNF or isotype were delivered either immediately after infection or after arthritis developed. We engineered *C. muridarum* expressing luciferase and GFP (pGFP-Luc-CM) to monitor in vivo uptake and dissemination. We depleted macrophages from Chlamydia-infected SKG mice with clodronate liposomes.

Results: SKG but not BALB/c mice developed typical histological features of chronic reactive arthritis but remained autoantibody-negative, from 5 weeks after genital infection. When applied at infection, anti-TNF blocked *C. muridarum*-induced reactive arthritis in SKG mice. Seven weeks post-infection, SKG but not BALB/c mice developed inflammatory salpingitis. One week post-infection, we observed *C. muridarum* dissemination in the upper genital tract of SKG but not BALB/c mice. After infection with pGFP-Luc-CM, *C. muridarum* GFP signal was exclusively found in CD11b+Ly6g-Ly6c+F4/80+MHC class II+ macrophages in both strains. Expression of macrophage *Tgtp1* and *IL23a* but not *Hspa5* expression was upregulated one week after *C. muridarum* infection and returned to baseline levels 5 weeks after infection. *Tgtp1* and *IL23a* mRNA expression were highly correlated (Figure) in genital tract one week upon infection. Depletion of macrophages using clodronate liposomes just prior to infection prevented arthritis.

Conclusion: These data indicate that macrophages, IL-23 and TNF are required for the development of Chlamydia-induced reactive arthritis in SKG mice. Macrophages exclusively take up Chlamydia from the site of infection and, in susceptible mice/individuals, upregulate autophagy and IL-23 production and transport persistent bacteria to distant sites such as upper genital tract and joints to trigger TNF-mediated inflammatory pathology.

Disclosure: A. Baillet, None; Z. A. Bhuyan, None; C. Douillard, None; A. Bozon, None; C. Armitage, None; X. Romand, None; M. V. Chuong Nguyen, None; B. Favier, None; T. Wells, None; K. Beagley, None; R. Thomas, None.
Role of Corticosteroids in Subclinical Atherosclerosis in SLE: A Systematic Review and Meta-Analysis

Ehsan Rajabioostami1, Kam Newman2, Sreelakshmi Panginikkod1, Shahrzad Mohammadiankhansari1, Nader Mehri3, Roshanak Habibi4 and Manish Jain5,
1Internal Medicine, Presence Saint Francis Hospital, Evanston, IL, 2Rheumatology, Eisenhower Medical Center, Rancho Mirage, CA, 3Social Gerontology, Miami University, Oxford, OH, 4Presence Saint Francis Hospital, Evanston, IL, 5Rheumatology, Presence Saint Francis Hospital, Evanston, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Atherosclerosis in SLE results from a complex interplay between traditional risk factors, SLE-specific factors, chronic inflammation and multifaceted effects of SLE therapeutics. In particular, corticosteroids may exert a double-edged effect by increasing traditional risk factors on one hand and inhibiting the inflammatory process on the other. In this meta-analysis, we aim to determine the association between corticosteroids and subclinical atherosclerosis in SLE patients and investigate the influence of strength, duration and cumulative dose of steroids.

Methods:
A comprehensive literature search was conducted in Cochrane Library, Scopus, MEDLINE, PubMed and EMBASE for articles published in English from January 1985 through June 2016 in adult age group. Studies were eligible if they presented the dose of steroid administered to the SLE group and used mean CIMT as evaluated by high-resolution ultrasound (surrogate marker of subclinical atherosclerosis). Two independent reviewers performed study selection and data extraction. All articles with multiple publications were considered for data extraction but only one was used for final analysis. The required data to estimate the effect-sizes associated with each study was extracted. Using Hedges’ random-effect model, the estimated effect-sizes were pooled together. Heterogeneity was explored using subgroup analysis and meta-regression technique. Publication bias was tested using funnel plot and Eggers test.

Results:
Out of 254 citations, 24 studies were eligible. Disease characteristics and quality score of the studies are shown in Table 1. The pooled effect size showed statistically significant increase in subclinical atherosclerosis in SLE patients (SMD=0.821, P=0.000; 95% CI, 0.512 to 1.22). In a univariate meta-regression model, corticosteroid consumption significantly increased the risk of subclinical atherosclerosis in SLE patients (B=0.018, P= 0.027; 95% CI, 0.002 to
Result also showed, there was insignificant relationship between the duration as well as cumulative dose and the risk of subclinical atherosclerosis in SLE patient. Subgroup analysis showed that the above association of corticosteroid and subclinical atherosclerosis in SLE patients is not affected by the dose of the steroid.

Conclusion:

Our findings concluded that corticosteroids increase the risk of early atherosclerosis in SLE patients. We also found that subclinical atherosclerosis is not influenced by the strength, duration or cumulative dose of steroids. The biggest challenge to this analysis is the heterogeneity of the studies included. Further research is needed to better understand the adjusted effect of SLE disease activity in the role of steroids in subclinical atherosclerosis.

Table 1.

| Study          | Size | Age (y) | SLE duration | Steroid Average Dose (mg/d) | Steroid Dosage | Steroid Consumption (%) | SLEDA[i] | NOS[ii] |
|----------------|------|---------|--------------|-----------------------------|----------------|-------------------------|----------|
| Abdel-Wahab 2013 | 20   | 25.6    | 5.2          | NA[iii]                     | H[iiv]         | 100                    | 23.6     |
| Ajeganova 2015  | 111  | 48.6    | 9            | 4.3                         | L[v]           | 60.4                   | 2        |
| Cacciapaglia 2009 | 33   | 47      | NA           | L                           | 94             | 14.4                   | 7        |
| Colombo 2009    | 80   | 42.6    | 15           | NA                         | M[vi]          | 100                    | 2.8      |
| Elshishtawy 2012 | 50   | 23.06   | 2.29         | 19.9                       | M              | 100                    | 28.16    |
| Gheita 2012-13  | 92   | 30.18   | 28           | 13.91                      | M              | 91.3                   | 8.585    |
| Gheita 2012     | 45   | 26.13   | 27.37        | 22.33                      | H              | 100                    | 7.31     |
| Ghosh 2009      | 60   | 34      | 5            | 9                          | M              | 86.6                   | 4        |
| Jackson 2006    | 32   | 47.5    | 13           | 3.6                        | L              | 60                     | 1.75     |
| Jung 2014       | 102  | 38.8    | 6.5          | 2.6                        | L              | 73.5                   | 4.4      |
| Leeuw 2007      | 55   | 43      | 12           | 7.5                        | M              | 42                     | 2        |
| Mak 2011        | 55   | 40      | 4.5          | 13.28                      | M              | 87                     | 7        |
| Nowak 2012      | 16   | 44.4    | 6.5          | NA                         | M              | 87.5                   | 10       |
| Ozgen 2011      | 22   | 34      | 4.1          | 7.1                        | L              | 91                     | 8        |
| Ozgen 2011      | 26   | 34      | 3.8          | 8.3                        | M              | 84.6                   | 8.3      |
| Raafat 2014     | 36   | 27.9    | 28.1         | 4.1                        | 24.5           | H                      | 100      |
| Roman 2003      | 197  | 44      | 12.1         | 10                         | M              | 90                     | 4        |
| Sato 2007       | 39   | 5.1     | 19           | 9.4                        | M              | 100                    | 1.85     |
| Shang 2008      | 32   | 46      | 11           | 8.6                        | M              | 93.75 (94)             | 1        |
| Smrzova 2013    | 63   | 38.38   | 31           | 11.91                      | M              | 97                     | 7.22     |
| Somers 2012     | 95   | 37.6    | NA           | 9.2                        | M              | 62.1                   | 4        |
| Valdivielso 2008 | 26  | 34      | 5.11         | L                          | 61             | 5.58                   | 6        |
| Valer 2013      | 100  | 41.54   | 4.25         | 19.47                      | M              | 81                     | 4        |
| Zhang 2009      | 111  | 34.4    | 9.4          | 12.34                      | M              | 100                    | 6        |

[i] SLE Disease Activity Index

[ii] Newcastle–Ottawa Scale
Resistant Hypertension Is Associated with Inflammation, Renal Function, and Increased Mortality in Patients with Systemic Lupus Erythematosus

Jocelyn Gandelman¹, Megan Shuey², April Barnado³, Li Wang⁴, C. Michael Stein³ and Cecilia P. Chung³,
¹Vanderbilt University School of Medicine, Nashville, TN, ²Department of Pharmacology, Vanderbilt University, Nashville, TN, ³Medicine, Vanderbilt University Medical Center, Nashville, TN, ⁴Department of Biostatistics, Vanderbilt University Medical Center, Nashville, TN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Resistant hypertension (RHTN) is defined as blood pressure that remains >140/90 mm Hg despite concurrent use of three different antihypertensive drugs. RHTN has an incidence of 0.7 cases per 100 person-years among patients with hypertension and is associated with a 47% increased risk of cardiovascular events. However, there is no information about RHTN in SLE. Therefore, we estimated the incidence of RHTN in patients with SLE and compared demographic characteristics, immunologic markers, renal function, and mortality in patients who did and did not develop RHTN.

Methods: Patients with SLE were identified from the electronic health records at an academic medical center using a validated algorithm that has a positive predictive value of 94%. The diagnosis of RHTN required the use of 3 antihypertensive drugs concurrently and a mean blood pressure >140/90 mm Hg during the following six months, or the use of > 4 antihypertensive drugs simultaneously. Age, sex, race, immunologic laboratory results, creatinine concentrations at the time of first visit for SLE were compared among patients who developed RHTN and those who did not. Mortality was estimated and compared among patients with and without RHTN during subsequent follow-up.

Results: Of 1,135 patients with SLE identified, 27 were excluded due to pre-existing RHTN present before the first ICD9 code for SLE. Ninety-one patients (8.9%) developed RHTN and 1,017 did not over a follow-up of 7,689 person-years, with an incidence rate of 1.2 cases/100 person-years. Age and sex distribution were similar in patients
who developed RHTN and those who did not (Table 1), but patients with RHTN were more likely to be African American (p<0.001), and had lower C3 (p=0.01), higher CRP (p<0.001), higher erythrocyte sedimentation rate (p<0.001), and higher creatinine (p<0.001) at baseline (Table 1). Twenty one patients with resistant hypertension and 111 patients without resistant hypertension died. A logistic regression model indicated higher mortality associated with RHTN [odds ratio: 2.45, (95% CI 1.45-4.14), p<0.001].

Conclusion: Patients with SLE have an incidence rate of RHTN of 1.2 cases/100 person-years, which is higher than that reported in a population of patients with hypertension. RHTN is more frequent in African-American than Caucasian lupus patients and those with low C3 levels, higher inflammatory markers, and increased creatinine. RHTN is associated with increased mortality in patients with SLE.

Table: Patient Characteristics at the time of first ICD9 Code for SLE

<table>
<thead>
<tr>
<th></th>
<th>RHTN n=91</th>
<th>No RHTN n=1017</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>42 [22-56]</td>
<td>39 [27-51]</td>
<td>0.59</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>82 (90.1%)</td>
<td>914 (89.9%)</td>
<td>0.94</td>
</tr>
<tr>
<td>Caucasian, n (%)</td>
<td>43 (47.3%)</td>
<td>702 (69.0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>African American, n (%)</td>
<td>43 (47.3%)</td>
<td>231 (22.7%)</td>
<td></td>
</tr>
<tr>
<td>Race other or unknown, n (%)</td>
<td>5 (5.5%)</td>
<td>84 (8.3%)</td>
<td></td>
</tr>
<tr>
<td>Immunologic markers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C3, mg/dl**</td>
<td>96 [69-123]</td>
<td>111 [82-132]</td>
<td>0.01</td>
</tr>
<tr>
<td>C4 ,mg/dl**</td>
<td>19 [14-28]</td>
<td>20 [12-28]</td>
<td>0.62</td>
</tr>
<tr>
<td>CRP, mg/L**</td>
<td>10.4 [2.8-41.7]</td>
<td>3.5 [1.0-12.2]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ESR, mm/hr**</td>
<td>40 [18-78]</td>
<td>25 [10-49]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>1.0 [0.8-1.6]</td>
<td>0.8 [0.7-1.0]</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Data were analyzed using chi-squared tests for categorical variables and Wilcoxon’s rank sum test for continuous variables. P<.05 was considered significant.

** The total SLE population was n= 1108, unless otherwise noted for the following variables: C3 (n=1007), C4 (n=914), CRP (n=757), ESR (n=947), Creatinine (n=1090)

Disclosure: J. Gandelman, None; M. Shuey, None; A. Barnado, None; L. Wang, None; C. M. Stein, Lupus Research Alliance, 2; C. P. Chung, NIH/NIAMS and Rheumatology Research Foundation, 2.


Abstract Number: 1587

Mycobacterial Infection in Systemic Lupus Erythematosus: Clinical Significance and Associated Factors. Data from the Registry of Patients
with SLE of the Spanish Society of Rheumatology (RELESSER)

Ana Lois-Iglesias1, Víctor del Campo-Pérez2, Iñigo Rúa-Figueroa3, Coral Mouruño-Rodriguez4, Francisco Javier López Longo5, María Galindo6, Jaime Calvo-Alen7, Jesús Ibañez Ruán8, Alejandro Olivé9, Rafael-Benito Melero González4, Antonio Fernandez-Nebro10, José Antonio Bernal11, Celia Erausquin12, Eva Tomero13, María Loreto Horcada14, Esther Uriarte15, Mercedes Freire16, Carlos Alberto Montilla-Morales17, Ana Sánchez Atrio18, Alina Boteanu19, Elvira Díez Alvarez20, Javier Narváez21, Víctor Martínez Taboada22, Lucía Silva Fernández23, Esther Ruiz Lueca24, Jose Luis Andreu25, José Hernández Beirain26, Marian Gantes27, Blanca Hernández-Cruz28, Jose Javier Perez Venegas29, Ángela Pecondón Español30, Nuria Lozano-Rivas31, Monica Ibanez Barcelo32, Gema Bonilla33, Vicente Torrente34, Ivan Castellvi35, Juan José Alegre36, Mireia Moreno37, José Luis Marenco de la Fuente38, Cesar Magro-Checa39, Tomás Vázquez Rodríguez40, Victor Quevedo41, Patricia Richi42, Maria Teresa Oton Sanchez43 and JM Pego-Reigosa44. 1Rheumatology, University Hospital A Coruña, A Coruña, Spain, 2Preventive Medicine and Epidemiology, EOXI Vigo, Vigo, Spain, 3Rheumatology Division, Hospital Doctor Negrín, Las Palmas GC, Spain, 4Rheumatology, EOXI Vigo, Vigo, Spain, 5Rheumatology, Hospital Gregorio Marañón, Madrid, Spain, 6Servicio de Reumatología, Hospital 12 de Octubre, Madrid, Spain, 7Rheumatology, Txagorritxu Hospital, Araba, Vitoria, Vitoria, Spain, 8POVISA, Rheumatology, Vigo, Spain, 9Rheumatology, Hospital Germans Trias i Pujol, Badalona, Spain, 10Rheumatology, Regional University Hospital of Málaga, Malaga, Spain, 11Reumatología, Hospital Universitario del Vinalopó, Elche, Spain, 12Rheumatology, Hospital de Gran Canaria Dr Negrín, Las Palmas GC, Spain, 13Hospital La Princesa. Madrid., Madrid, Spain, 14Rheumatology, Complejo Hospitalario de Navarra, Pamplona, Spain, 15Reumatología, Hospital de Donosti, Donostia, Spain, 16Servicio de Reumatología. Instituto de Investigación Biomédica de A Coruña (INIBIC). Complexo HospitalarioUniversitario de A Coruña (CHUAC). Sergas. Universidade da Coruña (UDC). A Coruña, Spain, 17Hospital Clínico Universitario de Salamanca, Salamanca, Spain, 18University Hospital Príncipe de Asturias, Immune System Diseases, Rheumatology Department, Alcalá de Henares, Madrid, Spain, 19University Hospital Ramón y Cajal, Madrid, Spain, 20Complejo Asistencial Universitario de León. León. Spain, 21Rheumatology Department, Hospital de Bellvitge. Barcelona. Spain, L’Hospitalet de Llobregat, Spain, 22Rheumatology, Hospital Marqués de Valdecilla, Santander, Spain, 23Arthritis Research UK Centre for Epidemiology, Centre for Musculoskeletal Research, Manchester Academic Health Science Centre, The University of Manchester, Manchester, United Kingdom, 24Hospital de Basurto, Bilbao, Spain, 25Rheumatology, Hospital Universitario Puerto de Hierro Majadahonda, Madrid, Spain, 26Rheumatology, Hospital Insular de Gran Canaria, Las palmas Gran Canarias, Spain, 27Rheumatology, Hospital Universitario de Canarias, La Laguna; Tenerife, Spain, 28Rheumatology, Hospital Universitario Virgen Macarena, Sevilla, Spain, 29Rheumatology, Hospital de Jerez de la Frontera, Jerez de la Frontera, Spain, 30Rheumatology, Hospital Miguel Servet, Zaragoza, Spain, 31Rheumatology, Hospital Virgen de la Arrixaca, murcia, Spain, 32H. Son Llatzer, Palma de Mallorca, Spain, 33Hospital Universitario La Paz, Madrid, Spain, 34Hospital Sant Joan de Déu, Esplugues de Llobregat, Spain, 35Rheumatology, Hospital Universitari de la Santa Creu i Sant Pau, Barcelona, Spain, 36Sección de Reumatología Hospital Universitario Dr Peset Valencia, Valencia, Spain, 37Rheumatology, Hospital Universitari Parc Taulí, Sabadell, Spain, 38Rheumatology, Hospital de Valme, Seville, Spain, 39Department of Rheumatology, Leiden University Medical Center, Leiden, Spain, 40Rheumatology, Hospital Lucus Augusti, Lugo, Spain, 41Rheumatology, Hospital de Monforte, Lugo, Spain, 42Hospital Infanta Sofia, Madrid, Spain, 43Rheumatology Department. Hospital Universitario Puerta de Hierro Majadahonda, Majadahonda, Spain, 44Rheumatology Section, Hospital de Meixoeiro, Pontevedra, Spain, Vigo, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Background/Purpose:

The aim of this work is to study the prevalence of mycobacterial infection (M.I.), the associated factors and their clinical significance in patients included in a large SLE cohort.

Methods:

Retrospective descriptive study of RELESSER patients with a history of M.I. and analysis of the factors associated with the infection of this etiology.

Results:

In RELESSER 3,658 SLE patients were included. 90% are women with a mean age of 32.9 years. 93% are Caucasians. The mean follow-up time (± S.D.) was 120.2 (± 87.6) months. 705 (19.3%) patients had at least a serious infection, 1,227 serious infections occurred. M.I. were diagnosed in 42 patients (1.2% of all RELESSER patients, 3.4% of all serious infections), 85.7% women. The incidence rate of mycobacterial infection was 1 per 1,000 patients/year (95%CI:0.7-1.4).

M.I. presentation was pulmonary in 18 (42.9%) patients and extrapulmonary in 24 (57.1%) patients [joints in 8 (19.0%) patients, soft tissue in 6 (14.3%) and other sites in 10 (23.8%)]. The extrapulmonary form was associated with the use of immunosuppressants: 84.6% of the 13 patients treated with immunosuppressive drugs versus 44.4% of the 27 patients without (p=0.01). We did not observe this association with the use of corticosteroids.

To study the factors associated with mycobacterial infection, we performed a bivariate analysis including the variables associated with severe infection identified in RELESSER (age, sex, ethnicity, use of corticosteroids, immunosuppressants, antimalarials, previous admission by SLE activity, use of rituximab, use of anti-TNF, Katz severity index, SDI damage index, SLEDAI activity index and Charlson comorbidity index). There is a statistically significant association with previous admission by SLE activity (RR:2.9, 95-95%:1.3-6.2, p=0.007), renal impairment (RR:2.0, CI 95%:1.1-3.7, p=0.04), the Katz score (RR:2.1, 95% CI:1.1- 4.0, p=0.04) and the Charlson index (RR: 2.5; 95% CI: 1.3-4.8, p=0.009). The accumulated damage (SDI> 0) was closely associated with significance:RR: 2.0; 95% CI: 1.0-4.0, p=0.07. The use of immunosuppressants was associated with a significant increase in the risk of mycobacterial infection: RR:4.3; 95% CI:2.2-8.3, p=0.31.

Two patients (4.8%) died (1 respiratory and 1 extrapulmonary). The mean survival after diagnosis in these cases was 21 days.

Conclusion:

M.I. in RELESSER affects 1.15% of patients. Its incidence rate is 1 per 1,000 patients/year (95%CI:0.7-1.4). Extrapulmonary localization affects more than half of the patients and is associated with the use of immunosuppressants. Previous admission by SLE activity, renal involvement, severity of SLE, and increased number of associated comorbidities are factors associated with the existence of mycobacterial infection.
“Neoplasia in Patients with Systemic LUPUS Erythematosus in Spain: Relesser Registry DATA”

Ana Urruticoechea-Arana1, Iñigo Rúa-Figueroa2, Maria Auxiliadora Martín3, Fernando Sánchez-Alonso4, Francisco Javier López Longo5, María Galindo6, Alejandro Olivé7, Jaime Calvo-Alen8, Antonio Fernandez-Nebro9 and JM Pego-Reigosa10, 1Rheumatology, Hospital de Can Mises, Ibiza, Spain, 2Rheumatology Division, Hospital Doctor Negrín, Las Palmas GC, Spain, 3Research Unit of Spanish Society of Rheumatology,, Madrid, Spain, 4Unidad de Investigación, Spanish Society of Rheumatology, Madrid, Spain, 5Rheumatology, Hospital Gregorio Marañón, Madrid, Spain, 6Servicio de Reumatología, Hospital 12 de Octubre, Madrid, Spain, 7Rheumatology, Hospital Germans Trias i Pujol, Badalona, Spain, 8Rheumatology, Txagorritxu Hospital, Araba, Vitoria, Vitoria, Spain, 9Rheumatology, Regional University Hospital of Málaga, Málaga, Spain, 10Rheumatology Section, Hospital de Meixoeiro, Pontevedra, Spain, Vigo, Spain

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

There is limited evidence on the risk of neoplasia in autoimmune diseases such as systemic lupus erythematosus. The objective of this study is to analyze the incidence of cancer in the Spanish population with SLE and the factors associated in its development: RelesSER Registry Data.

Methods:

We calculated the incidence density of malignant neoplasms, the standardized incidence ratio and the average time to develop the first neoplasm after diagnosis of SLE in patients of the SLE registry of the Spanish Rheumatology Society (RelesSER) fulfilling ACR97 criteria. We carried out a bivariate analysis of the associated factors to neoplasms and multivariate by logistic regression.

Results:

A total of 3607 patients (90.4% female) were included. We registered 140 neoplasms in women (4.3%) and 14 in men (4%) (p<0.821). Incidence density 7.3 / 1000 patient-years (95%CI:4.85-10.98) (7.39 in patient-years women and 6.93 in men) without significant differences. After stratification by gender and age, cancer appeared in 3.2% of the women aged under 45 versus 3.8% of the men; 4.1% of women aged 45-65 years versus 5.9% of men and a
5.3% of women 65 and older versus 2.5% of men the same age. The standardized incidence ratio (SIR) was 2.16; 1.51 in men and 2.38 in women, highest for women under 65 years old. The SIR for > 65 years was 0.98; 0.59 in men and 1.55 in women.

The average time until de development of the first malignant neoplasm was 10 years (RI:5.75-17.00), being lower in women [9.5(RI:5.00-17.0) years] than in men [ 12.5(8.75-17.5)] and in patients under 45 years versus over 45 years [8.0(RI:5.00-16.00)].

Malignant neoplasms were the cause of death in 10% of the patients (15/154), predominantly hematological and breast cancers, both at 19% followed by lung cancer in 14.3%.

Factors associated to malignant neoplasms in the bivariate analysis are shown in (table 1). No immunosuppressive therapy was associated with the development of neoplasms. In the multivariate model, adjusted for age and time of disease duration, age was the only significant variable (OR:1.030; 95%CI: 1.003-1.059; p=0.029) with a trend for ACE inhibitors use (OR:1.866; 95%CI: 0.808-4.306; p= 0.144), SLEDAI (last visit) (OR :0.904; 95%CI: 0.806-1.015; p= 0.089, SLICC/ACR DI) (without neoplasias) (OR: 1.160; 95%CI: 0.961- 1.401; p= 0.123), and duration of the disease in months (OR: 1.003; 95% CI: 1.000–1.006; p= 0.068).

Conclusion:

The incidence of neoplasia in Spanish women with SLE is higher than expected for age and gender. Malignant neoplasms were the cause of death in 10% of the patients, predominating hematological and breast cancers followed by lung cancer.

Acknowledgements:"The RelesSER registry has been supported by the FIS (ISCIII) - European Regional Development Fund (FEDER), fellowship PI11 / 02857." It has also been partially funded by: GSK, UCB, Roche and Novartis."

Table1- Factors associated to malignant neoplasms in the bivariate analysis

<table>
<thead>
<tr>
<th></th>
<th>Cáncer</th>
<th>Control</th>
<th>Value of p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, men %</td>
<td>4</td>
<td>96</td>
<td>0.821</td>
</tr>
<tr>
<td>Gender, women %</td>
<td>4.3</td>
<td>95.7</td>
<td>0.821</td>
</tr>
<tr>
<td>Age at last evaluation, years, mean (DS)</td>
<td>57.74 (14.38)</td>
<td>46.17 (14.58)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SLICC*, median [p25-p75]</td>
<td>1.00 [0.00-3.00]</td>
<td>0.00 [0.00-1.00]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CHARLSON*, median [p25-p75]</td>
<td>3 [2.00-4.00]</td>
<td>1 [1.00-3.00]</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Disclosure: A. Urruticoechea-Arana, None; I. Rúa-Figueroa, None; M. A. Martín, None; F. Sánchez-Alonso, None; F. J. López Longo, None; M. Galindo, None; A. Olivé, None; J. Calvo-Alen, None; A. Fernandez-Nebro, None; J. Pego-Reigosa, None.


Abstract Number: 1589

A Multicriteria Decision Analysis for the Development of New Systemic Lupus Erythematosus Classification Criteria
SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

EULAR and ACR are supporting multi-phase development of SLE classification criteria based on weighted criteria and a continuous probability scale. Prior steps included criteria generation, criteria reduction through Delphi and Nominal Group Technique exercises, literature review for sensitivity/specificity of candidate criteria, and organization of candidate criteria into seven clinical and three immunologic domains. Our next goals were to refine definitions of candidate criteria, determine relative weights using multicriteria decision analysis (MCDA), and identify a threshold score on a continuous scale for SLE classification.

Methods:

An SLE Expert Panel (9 North American, 8 European) submitted 167 unique cases, with range of SLE probability. Experts scored 20 representative cases using the candidate criteria and rank-ordered them. In a two day meeting, experts reviewed inter-rater reliability of scoring, refined criteria definitions, and participated in a MCDA exercise using 1000Minds™ software. Experts were presented with a series of decisions between two cases, each with different criteria from two domains (e.g. oral ulcers [cutaneous] and acute pericarditis [serositis] vs. alopecia [cutaneous] and pleural effusion [serositis]). Experts anonymously voted for the case more likely to be classified as SLE. Votes were discussed until consensus was reached for each decision. Using the consensus decisions, 1000Minds™ calculated criteria weights, assigned a total score to each of remaining 147 cases and rank-ordered the cases. Experts voted on whether each case should be classified as SLE. The score of the last case for which consensus was achieved was the threshold score. Experts repeated the MCDA for criteria whose calculated weights were inconsistent with expert opinion until group consensus was achieved.
Results:

Inter-rater reliability was good; human data entry error, not following instructions, and differing interpretations of criteria definitions accounted for discrepancies. Arthritis and pericarditis definitions were modified through group discussion. The MCDA involved 74 pairwise decisions. Cranial neuropathy and Class VI lupus nephritis were removed as they added little to SLE classification. MCDA was repeated for the arthritis and cutaneous domains as initial weights did not match expert opinion. Criteria weights and scores were re-calculated. Experts reached consensus for SLE classification for case scores >83.

Conclusion:

Using an iterative process, the expert panel refined and weighted candidate criteria definitions and determined a threshold score of >83 for SLE classification. Validation is the next step.

Disclosure: S. K. Tedeschi, None; S. Johnson, None; D. Boumpas, None; D. I. Daikh, None; B. Diamond, None; T. Doerner, None; S. Jacobsen, None; D. L. Kamen, None; W. J. McCune, None; M. Mosca, None; R. Ramsey-Goldman, None; G. Ruiz-Irastorza, None; M. Schneider, None; J. S. Smolen, None; M. Urowitz, None; D. Wofsy, None; M. Aringer, None; R. P. Naden, None; K. H. Costenbader, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/a-multicriteria-decision-analysis-for-the-development-of-new-systemic-lupus-erythematosus-classification-criteria

Abstract Number: 1590

Prolonged Antimalarial Treatment Increases the Risk for Severe Brady-Arrhythmias in Systemic Lupus Erythematosus

Konstantinos Tselios1, Dafna D Gladman2, Paula Harvey3, Jiandong Su4 and Murray Urowitz5, 1Medicine, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, 2Rheumatology, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, 3Cardiology, Women's College Hospital, University of Toronto, Toronto, ON, Canada, 4University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, 5Centre for Prognosis Studies in the Rheumatic Diseases, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Severe brady-arrhythmias [complete atrioventricular block (cAVB) and sick sinus syndrome (SSS)] have a prevalence of 0.04% and 0.8% in the general population respectively and are sparsely reported in systemic lupus erythematosus (SLE). Immune-mediated damage to the conduction system and atherosclerosis represent the most important risk factors. However, several case reports raised the possibility that antimalarials (AM) may play a role. The aim of the present study is to analyze the characteristics and associated factors of such arrhythmias in a defined lupus cohort.
Methods: The database of a large lupus clinic was searched for patients who received a permanent pacemaker (PPM) from 2000 to December 2016. Demographic, clinical, immunological and therapeutic data along with electrocardiographic (ECG) and echocardiographic (ECHO) variables were analyzed (based on the last available ECG and ECHO, respectively). Patients with a PPM due to brady-arrhythmias (cases) were compared with age-, sex- and disease duration-matched (±5 years) patients without a PPM (controls, 1:2 ratio). Statistical analysis was performed with SAS 9.0; \( p<0.05 \) was considered significant.

Results: Out of 1366 patients, 18 (14 females) received a PPM, 13 with cAVB (prevalence 0.95%) and 5 with SSS (0.37%). Six patients (33.3%) had coronary artery disease (CAD) whereas four (22.2%) had cardiac surgery shortly before PPM implantation. Seven patients (38.9%) did not have any risk factors (coronary angiography at the time of PPM implantation was normal in all of them, no prior structural heart disease). Six of these 7 patients developed ocular toxicity due to chronic AM treatment (all were taking AM for 22.6 years on average) shortly before or after PPM. One patient received a PPM two years after renal transplantation. A comparison between cases and controls for associated factors is shown in Table 1.

<table>
<thead>
<tr>
<th>Variable (at PPM implantation)</th>
<th>Cases (n=18)</th>
<th>Controls (n=34)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>55.14 ± 17.42</td>
<td>58.9 ± 13.06</td>
<td>0.158</td>
</tr>
<tr>
<td>Disease duration (y)</td>
<td>23.1 ± 13.5</td>
<td>21.9 ± 12.3</td>
<td>0.774</td>
</tr>
<tr>
<td>CAD (angina and/or MI and/or PTCA) ever</td>
<td>6 (33.3%)</td>
<td>3 (8.8%)</td>
<td>0.021</td>
</tr>
<tr>
<td>Myocarditis ever</td>
<td>2 (11.1%)</td>
<td>2 (5.9%)</td>
<td>0.414</td>
</tr>
<tr>
<td>Endocarditis ever</td>
<td>4 (22.2%)</td>
<td>4 (11.8%)</td>
<td>0.248</td>
</tr>
<tr>
<td>Valvular surgery ever</td>
<td>2 (11.1%)</td>
<td>0 (0%)</td>
<td>N/A</td>
</tr>
<tr>
<td>Pulmonary arterial hypertension ever</td>
<td>2 (11.1%)</td>
<td>4 (11.8%)</td>
<td>0.414</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>27.35 ± 5.98</td>
<td>25.92 ± 5.47</td>
<td>0.569</td>
</tr>
<tr>
<td>Hypertension ever</td>
<td>16 (88.9%)</td>
<td>22 (64.7%)</td>
<td>0.013</td>
</tr>
<tr>
<td>Hyperlipidemia ever</td>
<td>12 (66.7%)</td>
<td>13 (38.2%)</td>
<td>0.05</td>
</tr>
<tr>
<td>Diabetes ever</td>
<td>4 (22.2%)</td>
<td>3 (8.8%)</td>
<td>0.206</td>
</tr>
<tr>
<td>Smoking ever</td>
<td>8 (44.4%)</td>
<td>13 (38.2%)</td>
<td>0.08</td>
</tr>
<tr>
<td>SLEDAI-2K</td>
<td>2.11 ± 3.38</td>
<td>3.62 ± 4.09</td>
<td>0.136</td>
</tr>
<tr>
<td>AMS up to 2 years before PPM</td>
<td>2.06±3.17</td>
<td>3.11±3.46</td>
<td>0.199</td>
</tr>
<tr>
<td>SLICC/DI</td>
<td>3.83 ± 2.23</td>
<td>2.74 ± 2.88</td>
<td>0.1</td>
</tr>
<tr>
<td>End-stage renal disease</td>
<td>2 (11.1%)</td>
<td>2 (5.9%)</td>
<td>0.317</td>
</tr>
<tr>
<td>eGFR</td>
<td>63.27 ± 23.85</td>
<td>78.24 ± 32.16</td>
<td>0.025</td>
</tr>
<tr>
<td>Cumulative steroid dose</td>
<td>58.17 ± 49.86</td>
<td>42.44 ± 46.23</td>
<td>0.313</td>
</tr>
<tr>
<td>Years on antimalarials</td>
<td>15.44 ± 6.83</td>
<td>11.62 ± 9.95</td>
<td>0.013</td>
</tr>
</tbody>
</table>

CAD: coronary artery disease, MI: myocardial infarction, PTCA: percutaneous transluminal coronary angioplasty, AMS: Adjusted Mean SLEDAI-2K, eGFR: estimated Glomerular Filtration Rate

Table 1. Comparison between patients with severe brady-arrhythmia and controls for demographic variables, prior heart disease, atherosclerotic risk factors and disease-related variables.

Significant differences in ECG variables included 1st degree AVB \([16.7\% \text{ vs. } 0\%, p=0.02]\), right bundle branch block \([55.6\% \text{ vs. } 3.3\%, p<0.001]\) and left anterior fascicular block \([44.4\% \text{ vs. } 0\%, p<0.001]\). ECHO variables revealed a significant difference in the prevalence of septal hypertrophy \([46.7\% \text{ vs. } 25\%, p=0.014]\). Multi-variate analysis revealed that prolonged AM treatment was the only independent factor associated with the development of such arrhythmias \([OR=1.15, 95\% CI=1.01-1.31, p=0.035]\).

Conclusion: The prevalence of cAVB in SLE was approximately 24-fold that of the general population. Prolonged AM treatment increases the risk for severe brady-arrhythmias and may be considered as their cause in the absence of...
other risk factors. Certain ECG characteristics (RBBB, LAFB) may represent indicators of an ongoing damage in the conduction system and should be monitored in such patients.

**Disclosure:** K. Tselios, None; D. D. Gladman, Abbvie, 2,Amgen, 2,Celgene, 2,BMS, 2,Janssen Pharmaceutica Product, L.P., 2,Eli Lilly and Company, 5,Novartis Pharmaceutical Corporation, 2,Pfizer Inc, 2,UCB, 2; P. Harvey, None; J. Su, None; M. Urowitz, None.

**Abstract Number: 1591**

**Monophasic Disease Course Pattern in Systemic Lupus Erythematosus**

Konstantinos Tselios¹, Dafna D Gladman², Zahi Touma³, Jiandong Su⁴, Nicole Anderson² and Murray Urowitz⁵; ¹Medicine, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, ²Rheumatology, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, ³Rheumatology, University of Toronto, Division of Rheumatology, Institute of Health Policy, Management and Evaluation, Toronto, ON, Canada, ⁴University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, ⁵Centre for Prognosis Studies in the Rheumatic Diseases, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Disease course in systemic lupus erythematosus (SLE) is believed to follow three distinct patterns over time, namely relapsing-remitting, persistently active and prolonged quiescent. We recently showed that a small subgroup of patients might follow a course characterized by an initial active clinical presentation, followed by complete clinical remission, occasionally with no medications. The aim of the present study was to assess the prevalence, demographic, clinical and immunological characteristics of such patients.

**Methods:** The inception cohort a large lupus clinic (patients enrolled within 18 months from diagnosis) was investigated. Selected patients had a minimum follow-up of 10 years and no interval greater than 18 months between consecutive visits. Prolonged clinical remission was defined as clinical SLEDAI-2K=0 (serology excluded), achieved within the first five years since diagnosis and maintained for ≥10 years. Descriptive statistics were used.

**Results:** Of 883 inception patients, 382 met inclusion criteria. Twenty-seven (24 females, 21 Caucasians) achieved prolonged clinical remission (prevalence 7.1%) in 1.6 ± 1.3 years (median 1.2) since diagnosis. Mean age at diagnosis was 39±14.1 years. Clinical manifestations at diagnosis included muco Cutaneous involvement in 19 (70.4%), arthritis in 16 (59.3%), serositis in 5 (18.5%), nephritis in 7 (25.9%), central nervous system in 2 (7.4%) and cytopenias in 15 (55.6%). Immunological and therapeutic characteristics are shown in Table 1.
Cumulative glucocorticoid dose over 10 years was 18.1±12.4 grams. Beyond 10 years, 7 patients (25.9%) relapsed at a mean of 15.2±3.8 years since diagnosis (four with musculoskeletal and/or skin involvement). In the remaining three patients (two with nephritis and one with catastrophic antiphospholipid syndrome), the flare occurred during or shortly after pregnancy. Twenty of the 27 patients (5.2% of the entire cohort) sustained remission for the entire length of follow-up (17.8±6.7 years) and thus had pure monophasic disease. Twelve patients (44.4%) were not taking any medications after 10 years. Three patients died (11.1%), one from lung cancer and two from unknown cause.

**Conclusion:** A monophasic disease course was observed in 5.2% of our inception SLE patients, while approximately half of them maintained remission without any medications after 10 years from diagnosis.

**Disclosure:** K. Tselios, None; D. D. Gladman, None; Z. Touma, None; J. Su, None; N. Anderson, None; M. Urowitz, GlaxoSmithKline, 5.


**Abstract Number:** 1592

### Antimalarial-Induced Cardiomyopathy in Systemic Lupus Erythematosus

**Konstantinos Tselios**¹, Mery Deeb², Dafna D Gladman³, Paula Harvey⁴, Shadi Akhtari⁴, Susanna Mak⁵, Jagdish Butany⁶ and Murray Urowitz⁷, ¹Medicine, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, ²Division of Rheumatology, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, ³Rheumatology, Toronto Western Hospital, University of Toronto, Toronto, ON, Canada, ⁴Cardiology, Women's College Hospital, University of Toronto, Toronto, ON, Canada, ⁵Mecklinger Family and Posluns Family Cardiac Catheterization Research Laboratory, University of Toronto, Mount Sinai Hospital, Toronto, ON, Canada, ⁶Department of Pathology and Laboratory Medicine, University Health Network, Toronto, ON, Canada, ⁷Centre for Prognosis Studies in the Rheumatic Diseases, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada
Background/Purpose: Antimalarials (AM) are currently recommended for the management of all patients with systemic lupus erythematosus (SLE) without specific contra-indications. Their main adverse effect is retinal damage, however heart disease has been described in isolated cases. The aim of this study is to describe a series of patients with AM-induced cardiomyopathy (AMIC) in a defined lupus cohort.

Methods: Patients attending the Lupus Clinic and diagnosed with definite [based on endomyocardial biopsy (EMB)] and possible [based on cardiac magnetic resonance (CMR) and other investigations] AMIC were included.

Results: Eight female patients (age 62.5 years, disease duration 35 years, AM use duration 22 years, all medians) were diagnosed with AMIC in the past two years during evaluation for cardiovascular disease. Diagnosis was based on EMB in three, showing extensive vacuolation of the cardiomyocytes and intracytoplasmic myelinoid and curvilinear bodies. CMR was highly suggestive of AMIC in another four patients with features including ventricular hypertrophy and/or atrial enlargement and late gadolinium enhancement in a non-vascular pattern. Another patient was diagnosed based on complete atrioventricular block, left ventricular and septal hypertrophy along with AM-related ocular toxicity. Clinical presentation was that of congestive heart failure in two patients and syncope in one; investigations in the remaining patients were initiated based on abnormal cardiac troponin I (cTnI) and brain natriuretic peptide (BNP). All patients had abnormal cTnI and BNP whereas 7/8 also had chronically elevated creatine phosphokinase (CPK). Right bundle branch block (RBBB) was present in 4 patients, while two of them also had left anterior fascicular block (LAFB). Apart from atrial and/or ventricular hypertrophy, all patients had interventricular septum (IVS) hypertrophy and moderate diastolic dysfunction. During follow-up, one patient died due to refractory heart failure; she was complicated with septic shock during ICU hospitalization. In 5/7 patients, hypertrophy regression and a steady decrease of heart biomarkers was observed. Coronary angiography was performed in 6/8 patients and was normal. Daily hydroxychloroquine dose exceeded 6.5mg/kg in three patients. Details are shown in Table 1.

Conclusion: AMIC is a rare, probably under-recognized, complication of prolonged AM treatment. It usually presents as a hypertrophic, restrictive cardiomyopathy particularly affecting IVS with or without conduction abnormalities. Heart-specific biomarkers and serum CPK may be of value for early diagnosis.
<table>
<thead>
<tr>
<th>No.</th>
<th>Age</th>
<th>SLE/AM duration (y)/AM type</th>
<th>ECG</th>
<th>TTE</th>
<th>CMR</th>
<th>Biomarkers</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>74</td>
<td>44/13/HCQ</td>
<td>RBBB, LAFB</td>
<td>LVH, RVH, LA, RA, IVSH, LGE, low LVEF, DD</td>
<td>LVH, RVH, LA, RA, IVSH</td>
<td>BNP, cTnI, CPK</td>
<td>Regression of hypertrophy, steady decrease of biomarkers over 2 years, conduction abnormalities deteriorated with 1st degree AVB and atrial fibrillation</td>
</tr>
<tr>
<td>2</td>
<td>68</td>
<td>22/22/CQ</td>
<td>RBBB, LAFB</td>
<td>LVH, RVH, LA, RA, IVSH, DD</td>
<td>LVH, RVH, LA, RA, IVSH, LGE</td>
<td>BNP, cTnI, CPK</td>
<td>Regression of hypertrophy, steady decrease of biomarkers over 2 years, conduction abnormalities</td>
</tr>
<tr>
<td>3</td>
<td>65</td>
<td>53/45/HCQ</td>
<td>Normal</td>
<td>LVH, IVSH</td>
<td>LVH, LA, IVSH, LGE</td>
<td>BNP, cTnI, CPK</td>
<td>No significant regression of hypertrophy after 6 months, no decrease of heart biomarkers</td>
</tr>
<tr>
<td>4</td>
<td>59</td>
<td>38/19/HCQ</td>
<td>Normal</td>
<td>LVH, IVSH, LA, RA</td>
<td>LVH, IVSH</td>
<td>BNP, cTnI</td>
<td>Regression of hypertrophy after 6 months, decrease of heart biomarkers</td>
</tr>
<tr>
<td>5</td>
<td>74</td>
<td>27/24/HCQ</td>
<td>1st degree AVB, atrial flutter</td>
<td>LVH, IVSH, LA</td>
<td>LVH, RVH, IVSH, LA, RA</td>
<td>BNP, cTnI, CPK</td>
<td>Patient succumbed due to refractory heart failure, complicated with septic shock</td>
</tr>
<tr>
<td>6</td>
<td>54</td>
<td>38/22/HCQ</td>
<td>Normal</td>
<td>LVH, IVSH</td>
<td>LVH, IVSH, LGE</td>
<td>BNP, cTnI, CPK</td>
<td>No data on follow-up</td>
</tr>
<tr>
<td>7</td>
<td>49</td>
<td>32/23/CQ</td>
<td>RBBB</td>
<td>LVH, RVH, IVSH, LA</td>
<td>LVH, RVH, IVSH, LA</td>
<td>BNP, cTnI, CPK</td>
<td>Regression of hypertrophy, all biomarkers normalized after 18 months</td>
</tr>
<tr>
<td>8</td>
<td>60</td>
<td>9/9/HCQ</td>
<td>RBBB, cAVB</td>
<td>LVH, IVSH</td>
<td>ND</td>
<td>BNP, cTnI, CPK</td>
<td>Biomarkers decreasing after 9 months</td>
</tr>
</tbody>
</table>


Disclosure: K. Tselios, None; M. Deeb, None; D. D. Gladman, None; P. Harvey, None; S. Akhtari, None; S. Mak, None; J. Butany, None; M. Urowitz, None.


Abstract Number: 1593

Development of Quality Indicator Set of Systemic Lupus Erythematosus in Japan
First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: A QI set for systemic lupus erythematosus (SLE) was developed in the United States. However, this does not necessarily conform to the Japanese medical condition. Instead, they could be a burden to the estimators because they need to look up the medical chart records. The aim of this study was to develop a QI set systematically for Japanese SLE patients that we can evaluate easily using electronic health data.

Methods: We used a validated process that combined available scientific evidence and expert consensus to develop a QI set for SLE. First, we performed a literature review to retrieve all clinical practice guidelines (CPGs) and QI development studies that are relevant to SLE by using the Ovid MEDLINE and Elsevier EMBASE databases. The CPGs were defined as follows: ① organizing the panel committee, ② implementation of the literature review, and ③ implementation of the grading quality of evidence and strength of recommendations. Second, we extracted the candidate QI items that can be evaluated by using electronic health data (administrative and laboratory data) from the final selected literature. Third, we used a modification of the RAND/UCLA Appropriateness Method. An interdisciplinary expert panel that comprised seven rheumatologists, one primary care physician, one dermatologist, and one obstetrician convened to discuss the evidence and provide final ratings on the appropriateness. Before the face-to-face meeting, we shared via e-mail the rating sheet and documents that summarized the scientific evidence to panelists and asked them to rate the appropriateness of each QI (the first round of rating). At the face-to-face meeting, each panelist received an anonymous summary of the rankings by the other members of the group. The discussion was aimed at determining whether different ratings resulted from real clinical disagreement. After several
Results: We found 3621 articles through the initial search. After the title and abstract screening, 224 articles were further analyzed. Finally, four literatures on CPGs and 30 studies on QI development were identified. Seventeen potential indicators were extracted as candidate QI items from these literatures. Ten expert panel members evaluated the 17 potential indicators in the first round of rating and face-to-face meeting among the panelists and then excluded three indicators. At the second round of rating, the panelists re-rated the appropriateness of the 14 items and removed two items. Accordingly, we selected the remaining 12 indicators as the final QI set. The median appropriateness of these 12 indicators was at least 7.5, and the percentage of agreement of all the items exceeded 80%. The areas covered included assessment of disease activity, treatment, and drug toxicity monitoring. All the indicators can be measured by using existing electronic health data alone, without medical record review, and all are process indicators.

Conclusion: We identified 12 QIs for assessment of SLE patients based on administrative data. This study may contribute to the spread of QIs in the area of rheumatology in Japan.

Disclosure: N. Yajima, None; K. E. Sada, None; S. Fukuma, None; Y. Tsujimoto, None; S. Shimizu, None; K. Niihata, None; T. Mimori, None; Y. Tanaka, None; T. Takeuchi, None; M. Sugiura, None; H. Kohsaka, None; N. Tamura, None; M. Kuwana, None; H. Kameda, None; A. Yoshiiide, None; T. Azuma, None; T. Matsui, AbbVie GK, Ayumi Pharmaceutical Corporation, Chugai Pharmaceutical Co., Ltd., CSL Behring K.K., Japan Blood Products Organ, 2; K. Suzuki, None; R. Takahashi, None; S. Fukuhara, None; T. Atsumi, None.

Bone Turnover Markers in Adults with Systemic Lupus Erythematosus

Aliese Sarkissian¹, Vidya Sivaraman², Sharon Bout-Tabaku³, Stacy P. Ardoin⁴, Melissa Moore-Clingenpeel⁵, Holly Steigelman⁶, Kelly Morris⁷ and Sasigarn Bowden⁸, ¹Pediatric Rheumatology, Nationwide Children's Hospital and The Ohio State University Medical Center, Columbus, OH, ²Pediatric Rheumatology, Nationwide Children's Hospital, Columbus, OH, ³Rheumatology, Nationwide Children's Hospital, Columbus, OH, ⁴Pediatrics and Rheumatology, Nationwide Children's Hospital and The Ohio State University, Columbus, OH, ⁵Research, Nationwide Children's Hospital, Dublin, OH, ⁶The Ohio State University Wexner Medical Center, Columbus, OH, ⁷Rheumatology and Immunology, The Ohio State University, Columbus, OH, ⁸Pediatric Endocrinology, Nationwide Children's Hospital and The Ohio State University, Columbus, OH

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a systemic inflammatory disease which has an increased risk for comorbid osteoporosis, related to the disease and long term corticosteroid therapy. Bone turnover markers (BTMs) reflect the process of bone formation and resorption; imbalances in this process are associated with
bone loss and osteoporosis. Changes in BTMs have been observed in SLE patients with conflicting results. This study examined the association between BTMs and their relationship to disease activity.

Methods: SLE patients were identified from a university research registry and biorepository of patients with rheumatic disease. Demographics, disease activity, medication use and laboratory data were collected. Serum was assayed for C-terminal telopeptide of type 1 collagen (CTX), a bone resorption marker, and osteocalcin (OC), a bone formation marker. Serum CTX index, expressed as a ratio of measured CTX value to upper limit of normal value for age and gender, was used for analysis. The patients were stratified by SLE disease activity index (SLEDAI): a score of <3 (low disease activity) and ≥3 (higher disease activity). We analyzed correlations between BTMs and variables that have known associations.

Results: Serum levels of BTMs were measured in 42 subjects of which 88% were white females with a median age of 36 years, and 19% had lupus nephritis or chronic kidney disease. Most were on ongoing corticosteroid treatment (68%) and 47% were on vitamin D supplementation. Only 36% had a serum vitamin D level >30 ng/mL and 32% were insufficient (20-30 ng/mL) and 32% were deficient (<20 ng/mL). The median OC value was 13.5 ng/mL (normal 9-42), and the median CTX index was 0.54. Subjects with a higher SLEDAI score had lower median OC level compared to those with low SLEDAI score (median [IQR] of 11 [10, 16] vs. 18 [13, 22], p=0.02). There were no significant differences in CTX between these two groups. There was a positive correlation between the CTX index and OC (r = 0.537, p<0.01).

Conclusion: SLE patients with higher disease activity had lower OC levels than in those with low disease activity, suggesting that inflammation may suppress bone formation. There was no difference in CTX index between patients with higher and low disease activity. Bone formation and resorption markers were positively correlated in our SLE cohort, suggesting a coupled bone turnover state. The next step is to determine if corticosteroid dosage plays a role in the decreased bone formation observed in this cohort.

Disclosure: A. Sarkissian, None; V. Sivaraman, None; S. Bout-Tabaku, None; S. P. Ardoin, None; M. Moore-Clingenpeel, None; H. Steigelman, None; K. Morris, None; S. Bowden, None.

Abstract Number: 1595

Prevalence and Predictors of Depression in Patients with Systemic Lupus Erythematosus: Results from the Korean Lupus Network (KORNET) Registry

Kyung-Eun Lee¹, Ji-Hyoun Kang², Dong-Jin Park² and Shin-Seok Lee², ¹Chonnam National University Medical School and Hospital, Gwangju, Korea, Republic of (South), ²Rheumatology, Chonnam National University Medical School and Hospital, Gwangju, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM
Background/Purpose: Depression is more common in patients with systemic lupus erythematosus (SLE) than in the general population. However, few studies have investigated predictors of depression in SLE patients and those studies have shown inconsistent results. This study evaluated the prevalence of, and risk factors for, depression in ethnically homogeneous Korean SLE patients.

Methods: In this study, 505 consecutive SLE patients were enrolled from KORNET registry. Demographic variables, SLE manifestations, laboratory findings, PGA, SLEDAI-2000, and SLICC damage index were recorded at enrollment. Based on the previous study, SLE Patients were identified as having depressive symptoms using the Beck Depression Inventory (BDI) ≥ 16, and we categorized the SLE patients, according to the BDI total score, into four groups: Group I (BDI 0–9), Group II (BDI 10–15), Group III (BDI 16–23) and Group IV (BDI 24–63). Multivariate logistic regression analyses were performed to identify independent risk factors for depression in SLE patients.

Results: Of the 505 patients, SLE patients were categorized as follows: Group I (n = 320), Group II (n = 88), Group III (n = 65), and Group IV (n = 32). In our cohort, total 97 (19.2%) patients were diagnosed as having depression (Group III and Group IV). The SLE patients with higher BDI score were older, and had higher proportions of current smokers and SLICC score >1, and on the other hands, lower levels of income and education. In the serologic findings, patients with higher BDI score had lower anti-dsDNA positivity and conversely higher aCL positivity. In the multivariate analysis, the following variables were remained as significant predictors of depression in SLE patients: current smokers, lower education and income levels, aCL positivity, and SLICC score >1.

Conclusion: Our results found that depression was prevalent in patients with SLE and multifactorial factors were associated with depression in SLE. Our study helps to guide target programs for those at high risk for depression in SLE.

Disclosure: K. E. Lee, None; J. H. Kang, None; D. J. Park, None; S. S. Lee, None.


Abstract Number: 1596

Effect of the Metabolic Syndrome on Organ Damage, Renal Function and Mortality in Patients with Systemic Lupus Erythematosus: A Longitudinal Analysis

Chi Chiu Mok¹, Sau Mei Tse¹ and Ling Yin Ho², ¹Medicine, Tuen Mun Hospital, Hong Kong, Hong Kong, ²Dept of Medicine, Tuen Mun Hospital, Hong Kong SAR, Hong Kong

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
To study the effect of the metabolic syndrome (MetS) on organ damage, renal function and mortality in patients with SLE.

Methods:

Consecutive patients who fulfilled ≥4 ACR criteria for SLE and were assessed for the presence of MetS between 2010 and 2011 were included. The MetS was defined by the updated joint consensus criteria, using the Asian criteria for central obesity, when ≥3 of the following were present: (1) Increased waist circumference to ≥90cm in men or 80cm in women; (2) Elevated blood pressure to ≥130/85mmHg or requiring drug therapy; (3) Elevated serum triglyceride level to ≥1.7mmol/L; (4) Reduced serum HDL-cholesterol to ≤1.0mmol/L in men and ≤1.3mmol/L in women; and (5) Elevated fasting glucose level to ≥5.6mmol/L. Longitudinal data regarding change in renal function (4-variable eGFR), new organ damage, vascular events and mortality were retrieved from our cohort database. The association of the MetS with new organ damage and mortality was studied by logistic regression.

Results:

577 SLE patients were studied (93% women; age 41.2±13.4 years; SLE duration 9.3±7.2 years). All were ethnic Chinese and the mean follow-up was 66.3±1.8 months. The mean body mass index of the patients was 22.3±3.9kg/m² (11% >27kg/m²). A total of 85 (14.7%) patients qualified the MetS (28% fulfilling waist; 20% fulfilling blood pressure; 25% fulfilling triglyceride; 33% fulfilling HDL and 9.2% fulfilling glucose criteria). New organ damage and vascular (coronary, cerebrovascular and peripheral vascular) events developed in 128 (22%) and 23 (4.0%) patients, respectively. The commonest new arterial events were stroke(50%), acute coronary syndrome(33%) and peripheral vascular disease(17%). Thirty-nine(6.8%) patients died (infection 36%; vascular causes 18%; cancer 15%; lung fibrosis 8%; suicide 3%). Patients with the MetS (N=85), when compared to those without (N=492), had significantly higher SDI accrual at last visits (0.70±1.0 vs 0.26±0.6; p<0.001). Regarding individual systems, the increase in SDI scores in the ocular, renal, cardiovascular, musculoskeletal and endocrine (new diabetes mellitus) systems were significantly higher in the MetS group of patients. Patients with the MetS had a significantly greater decline in eGFR over time (-18.2±27% vs -7.80±19%; p=0.002). New vascular events (11% vs 2.8%; p=0.001), all-cause mortality (14% vs 5.5%; p=0.003), vascular mortality (7.1% vs 0.2%; p<0.001) were significantly more common in patients with MetS. Logistic regression revealed that the MetS was significantly associated with new damage in the ocular (OR 2.77[1.05-7.34]; p=0.04, renal (OR 4.72[1.86-12.0]; p=0.001), cardiovascular (OR 3.66[1.03-12.9]; p=0.04) and endocrine system (OR 41.9[4.93-357]; p=0.001), adjusted for age, sex, SLE duration and the antiphospholipid antibodies. The MetS increased the risk of new vascular events (OR 2.94[1.18-7.31];p=0.02), all-cause mortality (OR 1.60[0.73-3.47];p=0.24) and vascular mortality (OR 30.3[3.42-268];p=0.002) after adjustment for the same covariates.

Conclusion:

In this 5-year longitudinal study, the MetS is significantly associated with new organ damage, more renal function decline, vascular events and mortality in patients with SLE.

Disclosure: C. C. Mok, None; S. M. Tse, None; L. Y. Ho, None.


Abstract Number: 1597

Arthritis and Hydroxychloroquine Are Associated with Decreased Risk of Macrophage Activation Syndrome Among Adults Hospitalized with SLE
Kristin D'Silva1, Ezra Cohen2, David J. Kreps3, Mary Beth Son2 and Karen H. Costenbader3, 1Internal Medicine, Brigham and Women's Hospital, Boston, MA, 2Boston Children's Hospital, Boston, MA, 3Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

**First publication**: September 18, 2017

**SESSION INFORMATION**

**Session Date**: Monday, November 6, 2017

**Session Title**: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities

**Session Type**: ACR Poster Session B

**Session Time**: 9:00AM-11:00AM

**Background/Purpose**: Macrophage activation syndrome (MAS) is an uncommon but potentially fatal complication of SLE. We conducted a case-control study comparing hospitalized adults with SLE with and without MAS to better understand risk factors associated with development of MAS.

**Methods**: Within our large academic hospital lupus registry (n= 2094 SLE patients with ≥ 4 ACR criteria, 1970-2016), we identified patients ≥ age 18 with a hospital admission. We identified SLE patients with MAS among them by screening for a ferritin > 5,000 ng/ml during a hospital admission, excluding patients with end stage renal disease, iron overload and cirrhosis, and confirming MAS diagnosis by medical record review. For each case, we chose 4 hospitalized SLE patients without MAS, matched on dates of SLE diagnosis (± 1 year) and hospital admission (± 1 year). We collected demographic and clinical factors from the medical records. We employed conditional logistic regression models to identify factors associated with MAS.

**Results**: We identified 21 SLE patients hospitalized with MAS and matched them to 84 adults hospitalized with SLE but without MAS. The most common causes of admission among SLE controls were lupus flare (48%; 30% with nephritis) and infection (30%). Cases and controls had similar age at SLE diagnosis (29 vs. 30 years), proportion of females (76 vs. 85%), median area-level income ($52,122 vs. $64,178), racial distribution, and length of time between SLE diagnosis and hospitalization (2,010 vs. 1,849 days) (all p-values >0.05). Among cases, mean SLE Disease Activity Index (SLEDAI) scores at admission (31 vs. 21, p=0.002) and length of stay (17 vs. 3 days, p<0.0001) were higher than among controls. Mortality was 19% among cases and 1% among controls (p=0.01). In multivariable models, the presence of prior arthritis (OR 0.09, 95%CI 0.01-0.62) and hydroxychloroquine use on admission (OR 0.21, 95%CI 0.05-0.94) were associated with decreased MAS risk, while higher SLEDAI scores were associated with increased MAS risk (OR 1.11, 95% CI 1.03-1.19) (Table). There were no differences in other ACR criteria or medication use at time of admission.

**Conclusion**: The finding that hydroxychloroquine was associated with a reduced risk of MAS among hospitalized SLE patients is novel. Hydroxychloroquine is a SLE-stabilizing medication associated with reducing SLE flares and organ complications. In addition, the presence of arthritis may signify a distinct SLE phenotype with a decreased risk of hematologic manifestations, or reflect that patients with arthritis are more likely to receive hydroxychloroquine. Although the comparison group in this study was seriously ill SLE patients admitted to the hospital with mean SLEDAI score of 21, the association of highly elevated SLEDAI on admission with increased MAS risk is important for clinicians, as SLE patients with extremely active disease may be at highest MAS risk.
Table. Conditional Logistic Regression comparing Characteristics in Adult SLE MAS Cases to hospitalized SLE Controls, Odds Ratios and 95% Confidence Intervals

<table>
<thead>
<tr>
<th></th>
<th>Univariable Models OR and 95%CI (N=106)</th>
<th>Multivariable Models OR 95%CI (N=106)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sociodemographic Factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at SLE diagnosis</td>
<td>1.00 (0.96-1.03)</td>
<td>1.00 (0.95-1.04)</td>
</tr>
<tr>
<td>Female</td>
<td>0.60 (0.19-1.88)</td>
<td>0.80 (0.19-3.31)</td>
</tr>
<tr>
<td>Median Household Income**</td>
<td>0.99 (0.99-1.01)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>0.49 (0.17-1.41)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>2.04 (0.76-5.49)</td>
<td></td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>0.63 (0.07-5.89)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>2.11 (0.49-9.00)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>0.67 (0.08-5.54)</td>
<td></td>
</tr>
<tr>
<td><strong>Clinical Manifestations upon Admission</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malar rash</td>
<td>1.18 (0.42-3.28)</td>
<td></td>
</tr>
<tr>
<td>Discoid lesions</td>
<td>1.35 (0.41-4.39)</td>
<td></td>
</tr>
<tr>
<td>Photosensitivity</td>
<td>0.85 (0.30-2.40)</td>
<td></td>
</tr>
<tr>
<td>Oral ulcers</td>
<td>1.66 (0.52-5.29)</td>
<td></td>
</tr>
<tr>
<td>Arthritis</td>
<td><strong>0.23 (0.08-0.72)</strong></td>
<td><strong>0.09 (0.01-0.62)</strong></td>
</tr>
<tr>
<td>Serositis</td>
<td>0.63 (0.23-1.72)</td>
<td></td>
</tr>
<tr>
<td>Renal involvement</td>
<td>2.32 (0.80-6.77)</td>
<td></td>
</tr>
<tr>
<td>Neurologic involvement</td>
<td>1.60 (0.48-5.30)</td>
<td></td>
</tr>
<tr>
<td>Hematologic involvement</td>
<td>4.32 (0.96-19.3)</td>
<td></td>
</tr>
<tr>
<td>Immunologic disorders</td>
<td>1.19 (0.41-3.49)</td>
<td></td>
</tr>
<tr>
<td>Antinuclear antibody</td>
<td>0.63 (0.12-3.22)</td>
<td></td>
</tr>
<tr>
<td>Number of ACR criteria at time of hospitalization</td>
<td>1.06 (0.83-1.35)</td>
<td></td>
</tr>
<tr>
<td>Mean SLEDAI score</td>
<td><strong>1.07 (1.02-1.11)</strong></td>
<td><strong>1.11 (1.03-1.19)</strong></td>
</tr>
<tr>
<td><strong>Medications upon Admission</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td><strong>0.23 (0.07-0.72)</strong></td>
<td><strong>0.21 (0.05-0.94)</strong></td>
</tr>
<tr>
<td>Prednisone</td>
<td>1.48 (0.60-3.70)</td>
<td></td>
</tr>
<tr>
<td>Azathioprine or 6-Mercaptopurine</td>
<td>0.80 (0.09-6.85)</td>
<td></td>
</tr>
<tr>
<td>Mycophenolate mofetil</td>
<td>0.45 (0.05-4.00)</td>
<td></td>
</tr>
</tbody>
</table>
Table:

| Methotrexate | 2.00 (0.18-22.06) |

*Multivariable model included age, sex, race, presence of arthritis, hydroxychloroquine use, SLEDAI score.

** Zip code-level median household income from U.S. Census data

* Which include rituximab, cyclophosphamide, anakinra, cyclosporine, tacrolimus and IVIG not included as too few patients receiving.

Disclosure: K. D'Silva, None; E. Cohen, None; D. J. Kreps, None; M. B. Son, None; K. H. Costenbader, None.


Abstract Number: 1598

Shrinking Lung Syndrome in Systemic Lupus Erythematosus Patients: A Diagnosis We Should Suspect More Often

Didem Saygin\(^1\), Chris Lau\(^2\), Marco Lopez-Velazquez\(^3\) and Kristin B. Highland\(^4\), \(^1\)Internal Medicine, Department of Internal Medicine, Cleveland Clinic, Cleveland, Cleveland, OH, \(^2\)Pulmonary and Critical Care, Cleveland Clinic, Cleveland, OH, \(^3\)Internal Medicine, Cleveland Clinic, Cleveland, OH, \(^4\)Rheumatology.org, Cleveland Clinic, Cleveland, OH

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Shrinking lung syndrome (SLS) is a rare pulmonary manifestation of systemic lupus erythematosus (SLE) characterized by dyspnea, pleuritic chest pain, restriction on pulmonary function test (PFT), and signs of diaphragm dysfunction without evidence of significant pleuroparenchymal disease. We believe that lack of diagnostic criteria leads to misdiagnosis of SLS. Diagnosis of SLS requires careful evaluation of respiratory mechanics which includes spirometry, lung volumes, diffusion capacity, change in FEV1 (forced expiratory volume in one second) from sitting to supine, and consideration for specific diaphragm testing such as Sniff test, ultrasonography or electromyography (EMG). Careful consideration for mimickers of SLS such as obesity, pleural and central nervous system diseases should be considered since each has different management strategies. We report clinical, imaging and PFT characteristics of SLS in order to better understand the physiology seen in SLS and to increase awareness on this unsuspected entity.

Methods: We performed an electronic search of patients seen at the Cleveland Clinic between January 2005 – February 2017 with ICD-10 codes for SLE, restrictive lung disease, diaphragm dysfunction, or pleurisy. Clinical data were retrieved from the electronic medical records.
**Results:** Our search revealed 462 patients with SLE who had PFT results and a diagnostic code for restrictive lung disease, diaphragm dysfunction, or pleurisy. 38 of them were initially suspected to have SLS based on the opinion of their treating physician. Yet, only 27 patients had lung volumes (71%), and 20 had sitting/supine spirometry (53%). 35 had a chest X ray and/or computed tomography (92%). Sniff testing was performed in 7 cases, and showed abnormality in 70% of cases. EMG was done in 11 cases, and showed paresis/paralysis in 50% of cases. None had ultrasound of the diaphragm.

Ultimately, 8 out of 38 patients had a SLS diagnosis (Table). 30 patients had an alternative diagnosis including obesity (n=9), pleurisy (n=7), interstitial lung disease (n=4), severe pleural disease (n=4), asthma (n=2), emphysema (n=1), pneumonia (n=1) and rib fracture (n=1). 18 patients had a BMI >30 (47%), 5 had BMI >40 (13%). When present, lung volumes were useful to differentiate a restrictive pattern between diaphragm dysfunction and obesity related restriction. Diaphragmatic eventration and bibasilar infiltrates were the most common radiographic findings in SLS patients.

**Conclusion:** Our study showed that the majority of patients suspected with SLS had an alternative diagnosis. Almost one third of patients with suspected SLS did not have lung volumes or diaphragmatic function analysis done and almost half of these patients did not have sitting/supine spirometry performed. SLS is a diagnosis of exclusion and a comprehensive evaluation to exclude other reasons for a restrictive ventilatory defect is essential.

<table>
<thead>
<tr>
<th>Patients</th>
<th>FEV1%</th>
<th>FVC%</th>
<th>TLC%</th>
<th>RV%</th>
<th>FRC%</th>
<th>ERV</th>
<th>DLCO%</th>
<th>Sit/Sup reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>43%</td>
<td>39%</td>
<td>72%</td>
<td>109%</td>
<td>86%</td>
<td>0.31</td>
<td></td>
<td>-42%</td>
</tr>
<tr>
<td>2</td>
<td>61%</td>
<td>54%</td>
<td>59%</td>
<td>87%</td>
<td>58%</td>
<td>0.19</td>
<td>50%</td>
<td>-24%</td>
</tr>
<tr>
<td>3</td>
<td>72%</td>
<td>69%</td>
<td>75%</td>
<td>81%</td>
<td>76%</td>
<td>0.73</td>
<td>69%</td>
<td>-10%</td>
</tr>
<tr>
<td>4</td>
<td>37%</td>
<td>36%</td>
<td>55%</td>
<td>73%</td>
<td>47%</td>
<td>0.06</td>
<td>38%</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>26%</td>
<td>23%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>63%</td>
<td>-27%</td>
</tr>
<tr>
<td>6</td>
<td>31%</td>
<td>31%</td>
<td>48%</td>
<td>98%</td>
<td>57%</td>
<td>0.35</td>
<td>43%</td>
<td>-25%</td>
</tr>
<tr>
<td>7</td>
<td>29%</td>
<td>26%</td>
<td>55%</td>
<td>127%</td>
<td>66%</td>
<td>0.17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>48%</td>
<td>51%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>30%</td>
<td>-36%</td>
</tr>
<tr>
<td>Mean (+SD)</td>
<td>43±16%</td>
<td>41±15%</td>
<td>61±10%</td>
<td>96±19%</td>
<td>65±14%</td>
<td>0.31</td>
<td>49±14%</td>
<td>-27±11</td>
</tr>
</tbody>
</table>

**Disclosure:** D. Saygin, None; C. Lau, None; M. Lopez-Velazquez, None; K. B. Highland, None.


**Abstract Number:** 1599
GRADE-Based Recommendations for the Diagnosis and Monitoring of Systemic Lupus Erythematosus in Canada

Stephanie Keeling1, Zainab Alabdurubalnabi2, J. Antonio Avina-Zubieta3, Susan Barr4, Louise Bergeron5, Sasha Bernatsky6, Josiane Bourré-Tessier7, Ann E. Clarke8, Alexandra Baril-Dionne9, Jan Dutz2, Stephanie Ensworth10, Aurore Fifi-Mah11, Paul R. Fortin12, Dafna D Gladman13, Derek Haaland14, John G. Hanly15, Linda T Hiraki16, Sara Hussein9, Kimberly Legault17, Deborah M. Levy16, Lily Lim18, Mark Matsos19, Emily McDonald20, Jorge Medina-Rosas21, Jordi Pardo Pardo22, Christine A. Peschken23, Christian Pineau24, Janet E. Pope25, Tamara Rader26, Jennifer Reynolds2, Earl Silverman16, Manon Suitner9, Konstantinos Tselios27, Murray Urowitz28, Zahi Touma29, Evelyne Vinet30 and Nancy Santesso17,

1Department of Medicine, University of Alberta, Division of Rheumatology, Edmonton, AB, Canada, 2Medicine, University of British Columbia, Vancouver, BC, Canada, 3Division of Rheumatology, Department of Medicine, University of British Columbia, Vancouver, BC, Canada, 4Medicine, University of Calgary, Calgary, AB, Canada, 5Canadian Arthritis Patient Alliance, Toronto, ON, Canada, 6Divisions of Rheumatology and Clinical Epidemiology, Research Institute of the McGill University Health Centre, Montreal, QC, Canada, 7Rheumatology, University of Montreal, Montreal, QC, Canada, 8Division of Rheumatology, University of Calgary, Calgary, AB, Canada, 9Université de Montréal, Montreal, QC, Canada, 10University of British Columbia, Vancouver, BC, Canada, 11University of Calgary, Calgary, AB, Canada, 12Medicine, CHU de Quebec - Universite de Laval, Quebec, QC, Canada, 13Centre for Prognosis Studies in The Rheumatic Diseases, Toronto Western Hospital, Krembil Research Institute, Toronto, ON, Canada, 14Rheumatology, Clinical Immunology & Allergy, McMaster University, Barrie, ON, Canada, 15Division of Rheumatology, Department of Medicine and Department of Pathology, Queen Elizabeth II Health Sciences Centre and Dalhousie University, Halifax, NS, Canada, 16Division of Rheumatology, The Hospital for Sick Children, Toronto, ON, Canada, 17McMaster University, Hamilton, ON, Canada, 18Hospital for Sick Children, Toronto, ON, Canada, 19Medicine, McMaster University, McMaster, ON, Canada, 20Medicine, McGill University, Montreal, QC, Canada, 21Rheumatology, Universidad de la Sabana, Bogota, Colombia, 22Centre for Practice Changing Research, Ottawa Hospital Research Institute, Ottawa, ON, Canada, 23RR 149G, Univ of Manitoba, Winnipeg, MB, Canada, 24Division of Rheumatology, McGill University Health Centre, Montreal, QC, Canada, 25Department of Medicine, Division of Rheumatology, University of Western Ontario, St Joseph's Health Care, London, ON, Canada, 26The Ottawa Hospital - General Campus, Trials Search Coordinator Knowledge Translation Specialist Cochrane Musculoskeletal Group Centre for Practice Changing Research, Ottawa, ON, Canada, 27Medicine, University of Toronto, Toronto, ON, Canada, 28Centre for Prognosis Studies in the Rheumatic Diseases, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, 29Rheumatology, University of Toronto, Division of Rheumatology, Institute of Health Policy, Management and Evaluation, Toronto, ON, Canada, 30Divisions of Rheumatology and Clinical Epidemiology, McGill University Health Centre, Montreal, QC, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: To develop GRADE-based recommendations for the diagnosis and monitoring of systemic lupus erythematosus patients in Canada.
**Methods:** Recommendations were developed using the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach. The Canadian SLE Working Group (panel of Canadian rheumatologists and patient representative from CAPA (Canadian Arthritis Patient Alliance)) was created. Questions for recommendation development were identified based on a survey of SLE practice patterns of Canadian Rheumatology Association members. Systematic literature reviews of randomized controlled trials and observational studies were conducted. Evidence to Recommendation Tables were prepared and presented to the panel at two face-to-face meetings for discussion and voting during and post-meeting online.

**Results:** There are fourteen recommendations for diagnosing and monitoring lupus patients (Table 1). Three recommendations focused on diagnosis, disease activity and damage assessment and suggested a validated disease activity score per visit and annual damage score. One strong recommendation was made for cardiovascular risk assessment and conditional recommendations for osteoporosis (2) and osteonecrosis (1). Three conditional recommendations were made for peripartum assessments, one on cervical cancer screening, and two on hepatitis B and C screening. A strong recommendation was made for annual influenza vaccination.

**Conclusion:** These are the first GRADE-based recommendations for the diagnosis and monitoring of SLE internationally. Evidence is moderate to low quality resulting in more conditional versus strong recommendations. Additional studies and special attention to pediatric lupus populations and patient preferences are needed.

**Table 1. Summary of Recommendations With Strength of Evidence for the Diagnosis and Monitoring of SLE in Canada**
<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Strength of Recommendation</th>
<th>Quality of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. We recommend that all adult and pediatric patients suspected of SLE be referred to a lupus specialist, most often a rheumatologist, to confirm diagnosis and be involved in ongoing care.</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
<tr>
<td>2. For adult and pediatric patients with SLE, we suggest assessing disease activity with a validated instrument of disease activity during baseline and follow up visits.</td>
<td>Conditional</td>
<td>Low</td>
</tr>
<tr>
<td>3. For adult and pediatric patients with SLE, we suggest assessing disease damage annually with a validated measure.</td>
<td>Conditional</td>
<td>Low</td>
</tr>
<tr>
<td>4. For adult lupus patients, we recommend that indicators of obesity, smoking status, diabetes, blood pressure and a basic lipid profile be measured upon diagnosis of SLE and be reassessed periodically according to current recommendations in the general population and be used to inform the cardiovascular risk assessment.</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
<tr>
<td>5. For adult patients with SLE, we suggest assessing the risk of osteoporosis and fractures every 1 to 3 years using a detailed history and focused physical examination, and measuring bone mineral density in patients with other risk factors according to recommendations in the general population.</td>
<td>Conditional</td>
<td>Low</td>
</tr>
<tr>
<td>6. For all adults with SLE, we suggest screening 25-hydroxyvitamin D as part of the assessment for risk of osteoporosis and fractures.</td>
<td>Conditional</td>
<td>Low</td>
</tr>
<tr>
<td>7. For adult patients with SLE who do not have</td>
<td>Conditional</td>
<td>Low</td>
</tr>
</tbody>
</table>
clinical symptoms suggestive of osteonecrosis, we suggest not screening for or performing investigations for osteonecrosis. For patients who have suspected clinical symptoms of osteonecrosis, we suggest radiographs as the initial imaging modality rather than MRI or bone scan with SPECT according to recommendations in the general population.

8. For women with SLE, we suggest that anti-Ro and anti-La antibodies be measured immediately prior to pregnancy or during the first trimester.

| 8. For women with SLE | Conditional | Low |

9. For pregnant women with SLE, we suggest that uterine and umbilical Doppler studies be performed in the second or third trimester, or at the time of a suspected flare.

| 9. For pregnant women with SLE | Conditional | Low |

10. For women with prior or active lupus nephritis who are pregnant, we suggest measuring serum creatinine and urine protein to creatinine ratio every 4-6 weeks, or more frequently if clinically indicated. We suggest blood pressure and urinalysis be measured prior to pregnancy and every 4-6 weeks until 28 weeks, every 1-2 weeks until 36 weeks and then weekly until delivery.

| 10. For women with prior or active lupus nephritis who are pregnant | Conditional | Low |

11. All female adult patients with SLE who are or have been sexually active, regardless of sexual orientation, we suggest annual cervical cancer screening rather than screening every 3 years at least up to the age of 69.

| 11. All female adult patients with SLE who are or have been sexually active | Conditional | Low |

12. We recommend that adults and children with SLE receive an annual

| 12. We recommend that adults and children with SLE receive an annual | Strong | Moderate |
inactivated influenza vaccination in a single dose. 13/14. For adults and pediatric patients with a diagnosis of SLE and high-risk behaviours for HBV and/or HCV acquisition, we recommend screening for Hepatitis B surface antigen and/or Hepatitis C and repeating according to recommendations for the general population. For patients being considered for immunomodulatory therapy, we suggest screening for HBV before starting treatment.

| Disclosure: | S. Keeling, None; Z. Alabdurubalnabi, None; J. A. Avina-Zubieta, None; S. Barr, None; L. Bergeron, None; S. Bernatsky, None; J. Bourré-Tessier, None; A. E. Clarke, UCB, 2; A. Baril-Dionne, None; J. Dutz, None; S. Ensworth, None; A. Fifi-Mah, None; P. R. Fortin, None; D. D. Gladman, Amgen, AbbVie, BMS, Celgene, Eli Lilly, Janssen, Novartis, Pfizer and UCB., 2; D. Haaland, None; J. G. Hanly, None; L. T. Hiraki, None; S. Hussein, None; K. Legault, None; D. M. Levy, None; L. Lim, None; M. Matsos, None; E. McDonald, None; J. Medina-Rosas, None; J. Pardo Pardo, None; C. A. Peschken, None; C. Pineau, None; J. E. Pope, AbbVie, Amgen, Bayer, BMS, Celtrion, Eli Lilly and Company, Merck, Novartis, Pfizer, Roche, UCB, 5.Amgen, Bayer, BMS, GSK, Merck, Novartis, Pfizer, Roche, UCB, 2; T. Rader, None; J. Reynolds, None; E. Silverman, None; M. Suitner, None; K. Tselios, None; M. Urowitz, None; Z. Touma, None; E. Vinet, None; N. Santesso, None.


Abstract Number: 1600

Lupus Nephritis Is Associated with Increased Rates of Hospitalization for Adverse Events on a Glucocorticoid Toxicity Index and in-Hospital Mortality Compared with Non-Renal Lupus and Matched Controls: An Analysis of Insurance Claims Data

Katherine Belendiuk¹, Huong Trinh², Matthew Cascino¹, Leonard Dragone¹, Daniel Keebler¹, Jay Garg¹ and Paul Brunetta¹, ¹Genentech, Inc., South San Francisco, CA, ²Genentech, South San Francisco, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Background/Purpose: Systemic lupus erythematosus (SLE) is heterogeneous in its clinical prognosis and lupus nephritis (LN) is a major cause of morbidity and mortality among children and adults with SLE. LN patients typically receive higher doses of corticosteroids (CS) than do non-renal SLE patients. The excess burden of disease and treatment on hospitalization and in-hospital death associated with SLE and LN remains incompletely understood. This study characterized rates of hospitalizations, CS-related reasons for hospitalization, and in-hospital mortality of SLE and LN pts compared to: 1) each other; 2) matched controls.

Methods: Retrospective cohort study using the Truven Healthcare MarketScan® Commercial Claims and Encounters and Medicare Supplemental and Coordination of Benefits database from 1999 to 2014. LN and SLE cohorts were based on validated algorithms using claims data.\(^1,2\) Controls with claims for non-autoimmune conditions were matched on age and gender at index date. All pts had ≥ 365 days of enrollment ± index date. End of study was the first of end of enrollment or database, or date of death. Potentially CS-related reasons for hospitalization were evaluated on a claims-based modification of adverse events (AEs) on a CS toxicity index.\(^3\)

Results: 54,813 SLE pts w/o renal involvement and 8,839 LN pts were identified. LN adults had the longest hospitalizations (Table 1): Incidence rate ratios (IRRs) confirm statistically significantly higher rates of hospitalization and in-hospital mortality for LN compared to SLE and for both disease groups compared to controls (Figure 1). LN was associated with increased incidence of several potentially CS-related AEs (e.g. diabetes, aseptic necrosis of bone, depression) as the primary reason for hospitalization compared with the non-renal SLE group (Table 2).

Conclusion: The medical need for safe and effective treatments of LN and SLE remains unmet. The retrospective, claims-based results do not permit pt-level assessment of the relative contributions of disease severity, treatment, and other potential confounders of these findings. Ongoing analyses are examining the role of steroid exposure on CS-related hospitalizations.


| Table 1. Incidence Rates for Hospitalizations and In-Hospital Mortality and Length of Hospitalization |
|-----------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Age Group | LN cohort | Non-renal SLE cohort | Non-Al control for LN | Non-Al control for SLE |
|-----------|-----------|-----------------|-----------------|-----------------|-----------------|
| Hospitalization | Adults (N=8466) | Peds (N=373) | Adults (N=53557) | Peds (N=1216) | Adults (N=8466) | Peds (N=373) | Adults (N=53557) | Peds (N=1216) |
| 28.24 (37.25, 19.25) | 55.41 (48.57, 52.45) | 13.47 (13.06, 19.60) | 9.59 (6.99, 10.67) | 5.86 (5.19, 6.62) | 1.52 (0.83, 2.68) | 5.48 (5.00, 5.97) | 1.88 (1.39, 2.42) |
| In-Hospital Mortality | 0.07 (0.00, 0.13) | 0.09 (0.06, 0.12) | 0.08 (0.04, 0.13) | 0.09 (0.06, 0.13) | 0.07 (0.06, 0.09) | 0.13 (0.08, 0.18) |
| Days of Hospitalization | 23 (25, 28) | 19 (23, 28) | 10 (12, 16) | 7 (6, 9) | 5 (4, 6) | 7 (6, 10) |
| Mean (SD) | 23.0 (35.97) | 19.9 (28.20) | 10.1 (19.15) | 11.1 (19.36) | 5.1 (7.54) | 5.2 (7.24) | 5.9 (8.42) | 5.4 (8.42) |

Table values are Incidence Rates Per 100 Person-Years (95% CI)
Figure 1. Incidence Rate Ratios for Adult Hospitalizations and In-Hospital Mortality

Table 2: Incidence Rates and Incidence Rate Ratios of Potentially Glucocorticoid-Related Safety Events as Primary Reason for Hospitalization

<table>
<thead>
<tr>
<th>Event</th>
<th>LN cohort (N=8466)</th>
<th>SLE cohort (N=3597)</th>
<th>IRR (95% CI) LN vs. SLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Pressure</td>
<td>1.131 (1.014, 1.257)</td>
<td>0.131 (0.116, 0.148)</td>
<td>8.6 (7.319, 10.103)</td>
</tr>
<tr>
<td>Endocrine</td>
<td>0.096 (0.003, 0.137)</td>
<td>0.016 (0.011, 0.022)</td>
<td>5.97 (3.028, 9.024)</td>
</tr>
<tr>
<td>Bone Health</td>
<td>1.143 (1.026, 1.27)</td>
<td>0.439 (0.411, 0.47)</td>
<td>2.60 (2.297, 2.947)</td>
</tr>
<tr>
<td>Fracture</td>
<td>0.863 (0.759, 1.003)</td>
<td>0.369 (0.262, 0.416)</td>
<td>2.339 (1.997, 2.633)</td>
</tr>
<tr>
<td>Hip Replacement</td>
<td>0.115 (0.009, 0.12)</td>
<td>0.115 (0.009, 0.120)</td>
<td>NA</td>
</tr>
<tr>
<td>Aseptic Necrosis of Bone</td>
<td>0.252 (0.196, 0.314)</td>
<td>0.054 (0.046, 0.058)</td>
<td>4.664 (3.484, 6.244)</td>
</tr>
<tr>
<td>Cataract</td>
<td>0.035 (0.018, 0.063)</td>
<td>0.040 (0.026, 0.051)</td>
<td>3.5 (1.577, 7.305)</td>
</tr>
<tr>
<td>Muscle and Tendon</td>
<td>0.035 (0.018, 0.063)</td>
<td>0.040 (0.026, 0.051)</td>
<td>3.5 (1.577, 7.305)</td>
</tr>
<tr>
<td>Eye</td>
<td>0.006 (0.003, 0.023)</td>
<td>0.001 (0.001, 0.004)</td>
<td>0.362 (0.289, 1.304)</td>
</tr>
<tr>
<td>Oedema</td>
<td>0.003 (0.001, 0.018)</td>
<td>0.001 (0.001, 0.004)</td>
<td>1.881 (1.288, 2.757)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>0.004 (0.002, 0.016)</td>
<td>0.002 (0.001, 0.005)</td>
<td>1.881 (1.288, 2.757)</td>
</tr>
<tr>
<td>Diabetic Neutropathy</td>
<td>0.015 (0.014, 0.024)</td>
<td>0.009 (0.006, 0.014)</td>
<td>1.94 (1.872, 2.018)</td>
</tr>
<tr>
<td>Diabetic Nephropathy</td>
<td>0.015 (0.014, 0.024)</td>
<td>0.009 (0.006, 0.014)</td>
<td>1.94 (1.872, 2.018)</td>
</tr>
<tr>
<td>Diabetic Retinopathy and Diabetic Retinal</td>
<td>0 (0.006, 0.012)</td>
<td>0 (0.006, 0.012)</td>
<td>NA</td>
</tr>
<tr>
<td>Oedema and Diabetic Eye Disease</td>
<td>0 (0.006, 0.012)</td>
<td>0 (0.006, 0.012)</td>
<td>NA</td>
</tr>
<tr>
<td>Diabetic Nephropathy</td>
<td>0.015 (0.014, 0.024)</td>
<td>0.009 (0.006, 0.014)</td>
<td>1.94 (1.872, 2.018)</td>
</tr>
<tr>
<td>Diabetic Retinopathy and Diabetic Retinal</td>
<td>0 (0.006, 0.012)</td>
<td>0 (0.006, 0.012)</td>
<td>NA</td>
</tr>
<tr>
<td>Oedema and Diabetic Eye Disease</td>
<td>0 (0.006, 0.012)</td>
<td>0 (0.006, 0.012)</td>
<td>NA</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>0.015 (0.014, 0.024)</td>
<td>0.009 (0.006, 0.014)</td>
<td>1.94 (1.872, 2.018)</td>
</tr>
<tr>
<td>Skin</td>
<td>0.015 (0.014, 0.024)</td>
<td>0.009 (0.006, 0.014)</td>
<td>1.94 (1.872, 2.018)</td>
</tr>
<tr>
<td>Neuropsychiatric</td>
<td>0.015 (0.014, 0.024)</td>
<td>0.009 (0.006, 0.014)</td>
<td>1.94 (1.872, 2.018)</td>
</tr>
<tr>
<td>All</td>
<td>0.006 (0.003, 0.023)</td>
<td>0.001 (0.001, 0.004)</td>
<td>0.362 (0.289, 1.304)</td>
</tr>
<tr>
<td>Psychosis</td>
<td>0.003 (0.001, 0.018)</td>
<td>0.001 (0.001, 0.004)</td>
<td>1.881 (1.288, 2.757)</td>
</tr>
<tr>
<td>Hallucination</td>
<td>0 (0.006, 0.012)</td>
<td>0 (0.006, 0.012)</td>
<td>NA</td>
</tr>
<tr>
<td>Delusion</td>
<td>0.003 (0.002, 0.005)</td>
<td>0.001 (0.001, 0.003)</td>
<td>1.881 (1.288, 2.757)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>0 (0.006, 0.012)</td>
<td>0 (0.006, 0.012)</td>
<td>NA</td>
</tr>
<tr>
<td>Mania</td>
<td>0.015 (0.014, 0.024)</td>
<td>0.009 (0.006, 0.014)</td>
<td>1.94 (1.872, 2.018)</td>
</tr>
<tr>
<td>Cognitive Disorder</td>
<td>0 (0.006, 0.012)</td>
<td>0 (0.006, 0.012)</td>
<td>NA</td>
</tr>
<tr>
<td>Depression</td>
<td>0.006 (0.003, 0.023)</td>
<td>0.001 (0.001, 0.004)</td>
<td>1.881 (1.288, 2.757)</td>
</tr>
</tbody>
</table>

Hydroxychloroquine Non-Adherence Is Associated with Higher Sledai Scores in a Predominantly Hispanic Population

Alexandra Perel-Winkler1, Kayla Neville1, James Miceli1, Samantha Nguyen1, Miya Okado1, Laura Geraldino-Pardilla1, Teja Kapoor1, Jon T. Giles2 and Anca Askanase1, 1Rheumatology, Columbia University College of Physicians & Surgeons, New York, NY, 2Division of Rheumatology, Columbia University College of Physicians & Surgeons, New York, NY
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Non-adherence to medication has been shown to impact mortality, morbidity, and health care utilization in SLE and ranges from 40-80% depending on the methods used to assess compliance. Hydroxychloroquine (HCQ) is a key component of SLE therapy. HCQ levels are a sensitive method to assess medication adherence in lupus. Our study assessed the feasibility of HCQ measurement and its impact on SLE activity in a multiethnic, predominantly Hispanic, population.

Methods: SLE patients from the Columbia Lupus Center meeting ACR/SLICC criteria, treated with HCQ for >6 months, reporting adherence to HCQ were included. HCQ testing was done by high performance liquid chromatography on whole blood by the Exagen Laboratory. Non-adherence was defined as a HCQ level of < 500ng/ml. The association between HCQ and disease activity measured by SLEDAI-2K was evaluated in a multivariate model that included all variables showing an association at p<0.2 in univariate analysis (demographics, SLE variables, age, sex, race/ethnicity). Statistical significance was considered p£0.05

Results: 108 patients, average age 38 (range 19-66) and 91% female, 62% Hispanic, and average SLEDAI of 4.3 (range 0-20) were included. 41% of patients had HCQ<500 demonstrating non-adherence; 19% had undetectable levels. Of the patient demographics and SLE characteristics, Hispanic ethnicity, being primarily a Spanish speaker, having higher eGFR, organ involvement and a diagnosis of depression had a trend towards significance in univariate analysis (Table 1). There was a significant association between having had CNS involvement and higher HCQ levels. Higher SLEDAI was significantly associated with lower HCQ levels (Table 2) (p<0.001). After adjusting for age, sex, ethnicity, education, depression, smoking, organ involvement, current steroid use, and immunosuppression, HCQ levels were significantly associated with SLE disease activity measured by SLEDAI (p<0.004). Average adjusted SLEDAI in non-adherent patients was 5.8 (IQR 4.8, 6.8), and 3.3 in adherent patients (IQR 2.5, 4.2).

Conclusion: These data suggest that HCQ levels <500 ng/ml are significantly correlated with higher disease activity scores and explain 32% percent of the SLEDAI variability. Testing for HCQ levels is an easy and reliable way to evaluate medication adherence in SLE. Levels <500ng/ml should be discussed with the patients and the reasons for non-adherence should be further explored. A diagnosis of depression had a strong trend towards associating with non-compliance emphasizing the importance of screening and treating this co-morbidity.
Disclosure: A. Perel-Winkler, None; K. Neville, None; J. Miceli, None; S. Nguyen, None; M. Okado, None; L. Geraldino-Pardilla, None; T. Kapoor, None; J. T. Giles, None; A. Askanase, Exagen, 2.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/hydroxychloroquine-non-adherence-is-associated-with-higher-sle-dai-scores-in-a-predominantly-hispanic-population](http://acrabstracts.org/abstract/hydroxychloroquine-non-adherence-is-associated-with-higher-sle-dai-scores-in-a-predominantly-hispanic-population)

Abstract Number: 1602

Fatigue in Systemic Lupus: The Role of Disease Activity and Its Mediators

Desiree R Azizoddin¹, Meenakshi Jolly², Joel A. Block³ and Perry M. Nicassio⁴, ¹Department of Medicine and Behavioral Sciences, Rush University, Chicago, IL, ²Rush, Chicago, IL, ³Division of Rheumatology, Rush University Medical Center, Chicago, IL, ⁴Cousins Center for PNI, UCLA, LA, CA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017

Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities

Session Type: ACR Poster Session B
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease that leads to a variety of negative health outcomes. Though treatment continues to advance, fatigue remains one of the most salient, unaddressed patient complaints. Understanding the mechanisms of fatigue can help guide the development of interventions to improve health outcomes. The aim was to evaluate the role of six variables (disease activity, insomnia, depression, stress, pain, and physical functioning) towards fatigue in individuals with SLE.

**Methods:** 116 ethnically-diverse, primarily female participants (91%) with SLE, receiving care at university medical centers, completed assessments of disease activity, and quality of life outcomes (FACIT-FT, Insomnia Severity Index, Perceived Stress Scale (PSS-4), Pain Inventory, Depression-PHQ-9, and LupusPRO-physical function). All patients met ACR classification criteria for SLE and did not have concurrent diagnosis of fibromyalgia. Multivariate linear and stepwise regression analyses were conducted with fatigue (FACIT-FT) as the dependent variable and above six variables as independent variables.

**Results:**

Mean(SD) age was 39.80(13.9) years; 50% were African American, 21% Caucasian, 13% Hispanic, 9% Asian, and 8% other. Mean(SD) FACIT-FT was 18.6(11.8). Collectively, these six variables explained 57% variance in fatigue; wherein depression, stress and pain were significant independent predictors of fatigue on the multivariate model, but not disease activity, sleep or physical health. Largest magnitude of effect on fatigue was with stress ($\beta 0.77$, 95% CI0.17, 1.38, $p=0.01$) followed by depression ($\beta 0.66$, 95% CI0.21, 1.10, $p=0.005$). On stepwise regression analysis, stress, depression and pain collectively explained 56% of variance in fatigue in SLE. All three were independent correlates of fatigue, and the largest contribution to fatigue was again from stress ($\beta0.84$, 95% CI 0.27,1.42, $P=0.005$), followed by depression ($\beta0.79$, 95% CI 0.44,1.14, $p=<0.001$).

**Conclusion:**

Stress and depression are the largest and independent contributors to fatigue among patients with SLE without concurrent fibromyalgia. Disease activity, sleep and physical health were not associated with fatigue in patients with SLE without concurrent fibromyalgia. Evaluation of stress and depression needs to be incorporated during assessment of SLE patients, especially in context of fatigue. This stress-depression-fatigue model needs further validation in a longitudinal study.

**Table 1.** Demographics and general characteristics (n=116)
<table>
<thead>
<tr>
<th></th>
<th>M</th>
<th>SD</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td></td>
<td></td>
<td>105</td>
<td>(90.5)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>39.80</td>
<td>(13.87)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td></td>
<td></td>
<td>58</td>
<td>(50.0)</td>
</tr>
<tr>
<td>Caucasian</td>
<td></td>
<td></td>
<td>24</td>
<td>(20.7)</td>
</tr>
<tr>
<td>Hispanic</td>
<td></td>
<td></td>
<td>15</td>
<td>(12.9)</td>
</tr>
<tr>
<td>Asian</td>
<td></td>
<td></td>
<td>10</td>
<td>(8.6)</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td>9</td>
<td>(7.8)</td>
</tr>
<tr>
<td>Marital Status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td></td>
<td></td>
<td>61</td>
<td>(52.6)</td>
</tr>
<tr>
<td>Married/lives with partner</td>
<td></td>
<td></td>
<td>27</td>
<td>(23.3)</td>
</tr>
<tr>
<td>Divorced</td>
<td></td>
<td></td>
<td>7</td>
<td>(6.0)</td>
</tr>
<tr>
<td>Widowed</td>
<td></td>
<td></td>
<td>1</td>
<td>(0.9)</td>
</tr>
<tr>
<td>Not reported</td>
<td></td>
<td></td>
<td>4</td>
<td>(3.4)</td>
</tr>
<tr>
<td>Education level</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than high school</td>
<td></td>
<td></td>
<td>5</td>
<td>(4.3)</td>
</tr>
<tr>
<td>High school</td>
<td></td>
<td></td>
<td>37</td>
<td>(31.9)</td>
</tr>
<tr>
<td>College/University degree</td>
<td></td>
<td></td>
<td>56</td>
<td>(48.6)</td>
</tr>
<tr>
<td>Graduate degree</td>
<td></td>
<td></td>
<td>12</td>
<td>(10.3)</td>
</tr>
<tr>
<td>Employment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unemployed</td>
<td></td>
<td></td>
<td>11</td>
<td>(9.5)</td>
</tr>
<tr>
<td>Work part-time</td>
<td></td>
<td></td>
<td>12</td>
<td>(10.3)</td>
</tr>
<tr>
<td>Work full-time</td>
<td></td>
<td></td>
<td>44</td>
<td>(37.9)</td>
</tr>
<tr>
<td>Homemaker</td>
<td></td>
<td></td>
<td>7</td>
<td>(6.0)</td>
</tr>
<tr>
<td>Student</td>
<td></td>
<td></td>
<td>4</td>
<td>(3.4)</td>
</tr>
<tr>
<td>On disability</td>
<td></td>
<td></td>
<td>27</td>
<td>(23.3)</td>
</tr>
<tr>
<td>Retired</td>
<td></td>
<td></td>
<td>5</td>
<td>(4.3)</td>
</tr>
<tr>
<td>Not available</td>
<td></td>
<td></td>
<td>4</td>
<td>(3.4)</td>
</tr>
<tr>
<td># of ACR Criteria met</td>
<td>5.00</td>
<td>(4.15)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PGA</td>
<td>0.59</td>
<td>(0.51)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SDI</td>
<td>0.64</td>
<td>(1.03)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prednisone</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active use</td>
<td></td>
<td></td>
<td>77</td>
<td>(62.4)</td>
</tr>
<tr>
<td>dose (mg/day)</td>
<td>11.362</td>
<td>(15.17)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>8.69</td>
<td>(7.21)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note. SDI: SLICC/ACR Damage Index. SS: SELENA-SLEDAI. PGA: Physician Global Assessment
Table 2. Regression analyses models for fatigue

<table>
<thead>
<tr>
<th></th>
<th>Multivariate Model</th>
<th>Hierarchical Model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R^2    beta</td>
<td>95% CI</td>
</tr>
<tr>
<td>Disease Activity</td>
<td>-0.03  -0.47,0.41</td>
<td>0.890</td>
</tr>
<tr>
<td>Stress</td>
<td>0.77   0.17,1.38</td>
<td>0.010</td>
</tr>
<tr>
<td>Depression</td>
<td>0.66   0.21,1.10</td>
<td>0.005</td>
</tr>
<tr>
<td>Pain</td>
<td>0.22   0.10,0.43</td>
<td>0.040</td>
</tr>
<tr>
<td>Sleep</td>
<td>0.16   -0.20,0.52</td>
<td>0.390</td>
</tr>
<tr>
<td>Physical Health</td>
<td>-0.03  -0.13,0.07</td>
<td>0.560</td>
</tr>
</tbody>
</table>

Disclosure: D. R. Azizoddin, None; M. Jolly, Pfizer Inc, 2,Medimmune, celpen, boehringer ingelheim, aurinia, 7; J. A. Block, None; P. M. Nicassio, None.


Abstract Number: 1603

**Lupus Low Disease Activity State: Can We Relax the Definition and Still Achieve Low Risk of SLE-Related Damage?**

Michelle Petri¹, Daniel Goldman² and Laurence S Magder³, ¹Medicine (Rheumatology), Division of Rheumatology, Johns Hopkins University School of Medicine, MD, USA, Baltimore, MD, ²Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, ³Epidemiology and Public health, University of Maryland School of Medicine, Baltimore, MD

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017

Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM

**Background/Purpose:** Lupus low disease activity state (LLDAS) is a systemic lupus erythematosus (SLE) outcome measure that combines low disease activity and a 7.5 mg limit on prednisone. We have previously shown that there is a dose-response reduction in SLICC/ACR organ damage by percentage of time spent in LLDAS. We now show which components of LLDAS are most important.

**Methods:** Lupus low disease activity state (LLDAS) was defined by Franklyn et al as a SLEDAI <=4, PGA <=1.0, no major organ activity, and no new activity and prednisone use <= 7.5 mg/d. Using a large clinical cohort, we looked at the risk of organ damage among those who satisfied this definition 75% of the time. Then we looked at the risk of organ damage (by SLICC/ACR Damage Index) among those who satisfied modifications of this definition.
Results: Table 1 shows the risk of damage if LLDAS is present at 75% of previous visits, if some of the requirements for LLDAS are relaxed. If we define LLDAS in the standard way and patients satisfy this definition 75% of the time, damage is experienced in 0.62% of subsequent months. If we use the same definition but allow a prednisone dose of up to 10 mg/day, we still observed a relatively low risk of damage (0.59% per month) among those who achieve that standard 75% of the time.

Table 1: Risk of new damage in a person month in subgroups defined by LLDAS on treatment, after relaxing some of the requirements. The percentages refer to the risk of damage for months that meet the criterion in 75% of preceding follow-up.

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Number of months and instances of damage among those who satisfy the criterion to the left at least 75% of the person-time.</th>
<th>Number of person-months observed</th>
<th>Number of months with an increase in damage</th>
<th>Percentage of months in which damage occurred</th>
</tr>
</thead>
<tbody>
<tr>
<td>LLDAS (original definition)</td>
<td></td>
<td>13,141</td>
<td>82</td>
<td>0.62%</td>
</tr>
<tr>
<td>LLDAS, but allow SLEDAI up to 5</td>
<td></td>
<td>13,198</td>
<td>82</td>
<td>0.62%</td>
</tr>
<tr>
<td>LLDAS, but allow SLEDAI up to 6</td>
<td></td>
<td>13,382</td>
<td>84</td>
<td>0.63%</td>
</tr>
<tr>
<td>LLDAS, but no SLEDAI requirement</td>
<td></td>
<td>13,382</td>
<td>84</td>
<td>0.63%</td>
</tr>
<tr>
<td>LLDAS, but allow Prednisone up to 10 mg/d</td>
<td></td>
<td>14,561</td>
<td>86</td>
<td>0.59%</td>
</tr>
<tr>
<td>LLDAS, but allow Prednisone up to 15 mg/d</td>
<td></td>
<td>15,721</td>
<td>97</td>
<td>0.64%</td>
</tr>
<tr>
<td>LLDAS, but allow Prednisone up to 20 mg/d</td>
<td></td>
<td>15,928</td>
<td>108</td>
<td>0.68%</td>
</tr>
<tr>
<td>LLDAS, but no limit on Prednisone</td>
<td></td>
<td>16,399</td>
<td>111</td>
<td>0.68%</td>
</tr>
<tr>
<td>LLDAS, but allow PGA up to 1.5</td>
<td></td>
<td>14,641</td>
<td>100</td>
<td>0.68%</td>
</tr>
<tr>
<td>LLDAS, but no PGA requirement</td>
<td></td>
<td>15,334</td>
<td>107</td>
<td>0.70%</td>
</tr>
</tbody>
</table>

Table 2 shows the risk of damage if some of the requirements for LLDAS are made more stringent. A more stringent SLEDAI or lower dose of prednisone did not result in a lower damage risk and reduced the number of patients who achieved those stricter goals. The lowest risk was seen if LLDAS was modified to require a PGA of 0 (risk=51%), but this stringent standard was only achieved for a small percentage of the follow-up.

Table 2: Risk of new damage in a person month in subgroups defined by LLDAS on treatment, after making some of the requirements more stringent. The percentages refer to the risk of damage for months that meet the criterion in 75% of preceding follow-up.
<table>
<thead>
<tr>
<th>Criterion</th>
<th>Number of months and instances of damage among those who satisfy the criterion to the left at least 75% of the person-time.</th>
<th>Number of person-months observed</th>
<th>Number of months with an increase in damage</th>
<th>Percentage of months in which damage occurred</th>
</tr>
</thead>
<tbody>
<tr>
<td>LLDAS (original definition)</td>
<td>13,141</td>
<td>82</td>
<td>0.62%</td>
<td></td>
</tr>
<tr>
<td>LLDAS, but require PGA &lt;= 0.5</td>
<td>8,221</td>
<td>46</td>
<td>0.56%</td>
<td></td>
</tr>
<tr>
<td>LLDAS, but require PGA&lt;=0.2</td>
<td>1,922</td>
<td>12</td>
<td>0.62%</td>
<td></td>
</tr>
<tr>
<td>LLDAS, but require PGA=0</td>
<td>1,753</td>
<td>9</td>
<td>0.51%</td>
<td></td>
</tr>
<tr>
<td>LLDAS, but require SLEDAI &lt;=3</td>
<td>12,115</td>
<td>72</td>
<td>0.59%</td>
<td></td>
</tr>
<tr>
<td>LLDAS, but require SLEDAI&lt;=2</td>
<td>11,815</td>
<td>69</td>
<td>0.58%</td>
<td></td>
</tr>
<tr>
<td>LLDAS, but require SLEDAI&lt;=1</td>
<td>7,943</td>
<td>46</td>
<td>0.58%</td>
<td></td>
</tr>
<tr>
<td>LLDAS, but require SLEDAI=0</td>
<td>7,624</td>
<td>45</td>
<td>0.59%</td>
<td></td>
</tr>
<tr>
<td>LLDAS, but require Prednisone&lt;=5</td>
<td>12,482</td>
<td>76</td>
<td>0.61%</td>
<td></td>
</tr>
<tr>
<td>LLDAS, but require Prednisone=0</td>
<td>8,661</td>
<td>55</td>
<td>0.64%</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** Our findings suggest that a relaxed definition of LLDAS (allowing for greater levels of SLEDAI and higher doses of prednisone) might still be a realistic target for clinical care, if the goal is to reduce the risk of later organ damage.

**Disclosure:** M. Petri, Anthera Inc, 5,GlaxoSmithKline, 5,EMD Serono, 5,Eli Lilly and Company, 5,Bristol Meyer Squibb, 5,Amgen, 5,United Rheumatology, 5,Global Academy, 5,Exagen, 2; D. Goldman, None; L. S. Magder, None.


**Abstract Number:** 1604

**Validation of Remission and Lupus Low Disease Activity State As Predictors of Organ Damage in SLE**

Michelle Petri¹, Daniel Goldman² and Laurence S Magder³,⁴ ¹Medicine (Rheumatology), Division of Rheumatology, Johns Hopkins University School of Medicine, MD, USA, Baltimore, MD, ²Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, ³Epidemiology and Public Health, Johns Hopkins University School of Medicine, Baltimore, MD, ⁴Epidemiology and Public health, University of Maryland School of Medicine, Baltimore, MD  
**First publication:** September 18, 2017
Background/Purpose: Outcome measures that combine control of SLE activity and prednisone reduction are clinically relevant. A clinical goal in SLE is to reduce risk of long-term organ damage. We assessed whether two recently proposed disease activity outcomes were predictive of future damage.

Methods: For each month of follow-up in a large SLE cohort, we determined whether the patient was in Clinical Remission (as defined by the DORIS working group) or lupus low disease activity state (LLDAS) (as defined by Franklyn et al). Clinical Remission was defined as a PGA<0.5, clinical SLEDAI=0 and no prednisone or immunosuppressants. Clinical Remission on Treatment allowed for prednisone<=5mg/day and immunosuppressant use. LLDAS was defined as a SLEDAI <=4, PGA <=1.0, no major organ activity, and no new activity. LLDAS on treatment allowed for prednisone use <= 7.5 mg/d and immunosuppressants. Damage was defined using the SLICC/ACR Damage index.

Results: There were 81,118 person-months observed among 2,026 patients (92% female, 53% Caucasian, 39% African-American). Table 1 shows the rates of damage, per person month, in subgroups defined by Remission or LLDAS.

Table 1. Rates of new damage, in subgroups defined by past levels of disease activity
<table>
<thead>
<tr>
<th>Percentage of Prior Months in:</th>
<th>Number of person-months observed</th>
<th>Number of months with an increase in SLICC/ACR Damage Index</th>
<th>Rate of damage per 100 person months</th>
<th>Rate Ratios</th>
<th>P-values</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Remission</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>35,772</td>
<td>406</td>
<td>1.13</td>
<td>1.0 (Ref)</td>
<td></td>
</tr>
<tr>
<td>Not none, but &lt; 25%</td>
<td>14,358</td>
<td>102</td>
<td>0.71</td>
<td>0.60 (0.48,0.75)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>25% to 50%</td>
<td>6573</td>
<td>50</td>
<td>0.76</td>
<td>0.66 (0.46,0.94)</td>
<td>0.023</td>
</tr>
<tr>
<td>50% to 75%</td>
<td>3845</td>
<td>27</td>
<td>0.70</td>
<td>0.63 (0.42,0.97)</td>
<td>0.035</td>
</tr>
<tr>
<td>75%+</td>
<td>1,641</td>
<td>10</td>
<td>0.61</td>
<td>0.58 (0.30,1.15)</td>
<td>0.12</td>
</tr>
<tr>
<td><strong>Clinical Remission on Treatment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not none, but &lt; 25%</td>
<td>16,491</td>
<td>250</td>
<td>1.52</td>
<td>1.0 (Ref)</td>
<td></td>
</tr>
<tr>
<td>25% to 50%</td>
<td>20,169</td>
<td>170</td>
<td>0.84</td>
<td>0.54 (0.44,0.67)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>50% to 75%</td>
<td>14,344</td>
<td>103</td>
<td>0.72</td>
<td>0.46 (0.36,0.60)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>75%+</td>
<td>8,396</td>
<td>54</td>
<td>0.64</td>
<td>0.43 (0.30,0.60)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LLDAS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>30,366</td>
<td>343</td>
<td>1.13</td>
<td>1.0 (Ref)</td>
<td></td>
</tr>
<tr>
<td>Not none, but &lt; 25%</td>
<td>10,880</td>
<td>106</td>
<td>0.97</td>
<td>0.86 (0.69,1.07)</td>
<td>0.18</td>
</tr>
<tr>
<td>25% to 50%</td>
<td>5012</td>
<td>40</td>
<td>0.80</td>
<td>0.70 (0.51,0.98)</td>
<td>0.037</td>
</tr>
<tr>
<td>50% to 75%</td>
<td>8,494</td>
<td>60</td>
<td>0.71</td>
<td>0.63 (0.48,0.83)</td>
<td>0.0010</td>
</tr>
<tr>
<td>75%+</td>
<td>7,527</td>
<td>46</td>
<td>0.61</td>
<td>0.54 (0.40,0.73)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>LLDAS on Treatment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>7,656</td>
<td>117</td>
<td>1.53</td>
<td>1.0 (Ref)</td>
<td></td>
</tr>
<tr>
<td>Not none, but &lt; 25%</td>
<td>10,555</td>
<td>134</td>
<td>1.27</td>
<td>0.83 (0.65,1.06)</td>
<td>0.14</td>
</tr>
<tr>
<td>25% to 50%</td>
<td>12,686</td>
<td>129</td>
<td>1.02</td>
<td>0.66 (0.51,0.85)</td>
<td>0.0013</td>
</tr>
<tr>
<td>50% to 75%</td>
<td>18,151</td>
<td>133</td>
<td>0.73</td>
<td>0.48 (0.37,0.61)</td>
<td>0.0010</td>
</tr>
<tr>
<td>75%+</td>
<td>13,141</td>
<td>82</td>
<td>0.62</td>
<td>0.40 (0.30,0.54)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Damage rates were relatively low when LLDAS was achieved at least 50% of the time. These rates were similar to those experienced by patients who met a more stringent treatment restriction with Remission on Treatment at least
Conclusion: Percent time in LLDAS had a clear dose response for rate ratios of organ damage. The equivalence of LLDAS and DORIS remission on treatment is welcome news, as LLDAS on treatment > 50% of the time is an easier goal to achieve (3 times more person-months observed in our cohort) and more realistic as a clinical trial outcome.

Disclosure: M. Petri, Anthera Inc, 5,GlaxoSmithKline, 5,EMD Serono, 5,Eli Lilly and Company, 5,Bristol Meyer Squibb, 5,Amgen, 5,United Rheumatology, 5,Global Academy, 5,Exagen, 2; D. Goldman, None; L. S. Magder, None.


Abstract Number: 1605

Lupus Low Disease Activity State Protects Against Most Subtypes of Organ Damage in SLE

Michelle Petri1, Daniel Goldman2 and Laurence S Magder3, 1Medicine (Rheumatology), Division of Rheumatology, Johns Hopkins University School of Medicine, MD, USA, Baltimore, MD, 2Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, 3Epidemiology and Public health, University of Maryland School of Medicine, Baltimore, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: In SLE the most common types of organ damage are osteoporotic fractures and cataracts. Other types of organ damage, such as end stage renal disease, are more life-threatening. We asked whether achieving the Lupus Low Disease Activity State (LLDAS) was protective against all – or only some – types of organ damage in SLE.

Methods: LLDAS was defined as by Franklyn et al: SLEDAI <=4, PGA<=1, prednisone <=7.5 mg/day, no major organ involvement (renal, CNS, serositis, vascular, or constitutional), no recent increase in disease activity. Each month of each follow-up was classified based on the proportion of prior months that the patient was in LLDAS. The rate of each damage event (expressed in rate per year) was calculated in each class. P-values were constructed to assess the significance of trends in rates by proportion of months in LLDAS based on a logistic regression model. If a patient had the specific damage prior to cohort entry, then they were not included. The patients were 92% female, 53% Caucasian, 39% African-American.

Results: Table 1 shows the specific type of organ by percent time that LLDAS was achieved, based on a logistic regression model treating percent time in LLDAS as a quantitative predictor.

Table 1: Rates of specific damage per person year and prior LLDAS experience
<table>
<thead>
<tr>
<th>Damage Type</th>
<th>Number of events/Number of person years (Rate per 1000 person years)</th>
<th>P-value for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;25%</td>
<td>25-50%</td>
</tr>
<tr>
<td>Arthritis (deforming or erosive)</td>
<td>15/1358 (11.0)</td>
<td>1/972 (1.0)</td>
</tr>
<tr>
<td>Avascular Necrosis</td>
<td>36/1214 (29.7)</td>
<td>13/867 (15.0)</td>
</tr>
<tr>
<td>Cataract</td>
<td>57/1199 (47.6)</td>
<td>26/838 (31.0)</td>
</tr>
<tr>
<td>Claudication</td>
<td>0/1506 (0.0)</td>
<td>4/1049 (3.8)</td>
</tr>
<tr>
<td>Cognitive Impairment</td>
<td>11/1413 (7.8)</td>
<td>9/955 (9.4)</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>13/1411 (9.2)</td>
<td>6/1004 (6.0)</td>
</tr>
<tr>
<td>Cranial or Peripheral Neuropathy</td>
<td>20/1374 (14.6)</td>
<td>14/935 (15.0)</td>
</tr>
<tr>
<td>CVA</td>
<td>23/1386 (16.6)</td>
<td>13/1004 (12.9)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>19/1387 (13.7)</td>
<td>9/988 (9.1)</td>
</tr>
<tr>
<td>DVT</td>
<td>4/1493 (2.7)</td>
<td>4/1033 (3.9)</td>
</tr>
<tr>
<td>End Stage Renal Disease</td>
<td>26/1463 (17.8)</td>
<td>5/1027 (4.9)</td>
</tr>
<tr>
<td>GFR&lt;50%</td>
<td>11/1397 (7.9)</td>
<td>0/993 (0.0)</td>
</tr>
<tr>
<td>Infarction or resection of bowel below duodenum</td>
<td>25/1295 (19.3)</td>
<td>18/944 (19.1)</td>
</tr>
<tr>
<td>Malignancy</td>
<td>41/1429 (28.7)</td>
<td>22/982 (22.4)</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>21/1493 (14.5)</td>
<td>10/999 (10.0)</td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>5/1506 (3.3)</td>
<td>1/1057 (0.9)</td>
</tr>
<tr>
<td>Osteoporosis with fracture or vertebral collapse</td>
<td>60/1323 (45.5)</td>
<td>33/889 (37.1)</td>
</tr>
<tr>
<td>Pericarditis for 6 months or pericardecotomy</td>
<td>4/1470 (2.7)</td>
<td>2/1049 (1.9)</td>
</tr>
<tr>
<td>Pleural Fibrosis</td>
<td>13/1478 (8.8)</td>
<td>9/1004 (9.0)</td>
</tr>
<tr>
<td>Premature gonadal failure</td>
<td>13/1350 (9.6)</td>
<td>3/986 (3.0)</td>
</tr>
<tr>
<td>Proteinuria 24hr ≥3.5g</td>
<td>5/1314 (3.8)</td>
<td>0/962 (0.0)</td>
</tr>
<tr>
<td>Condition</td>
<td>Count/Total (Percentage)</td>
<td>Count/Total (Percentage)</td>
</tr>
<tr>
<td>------------------------------------------</td>
<td>--------------------------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>Pulmonary Fibrosis</td>
<td>23/1361 (16.9)</td>
<td>12/943 (12.7)</td>
</tr>
<tr>
<td>Pulmonary Hypertension</td>
<td>15/1381 (10.9)</td>
<td>14/960 (14.6)</td>
</tr>
<tr>
<td>Retinal change or optic atrophy</td>
<td>10/1452 (6.9)</td>
<td>7/974 (7.2)</td>
</tr>
<tr>
<td>Ruptured Tendon</td>
<td>16/1484 (10.8)</td>
<td>8/997 (8.0)</td>
</tr>
<tr>
<td>Extensive scarring of panniculum other than scalp and pulp space</td>
<td>6/1420 (4.2)</td>
<td>2/1001 (2.0)</td>
</tr>
<tr>
<td>Seizures requiring therapy for at least 6 months</td>
<td>9/1415 (6.4)</td>
<td>5/995 (5.0)</td>
</tr>
<tr>
<td>Significant Tissue Loss</td>
<td>4/1494 (2.7)</td>
<td>2/1048 (1.9)</td>
</tr>
<tr>
<td>Skin ulceration present for more than 6 months</td>
<td>4/1476 (2.7)</td>
<td>2/1026 (1.9)</td>
</tr>
<tr>
<td>Valvular Disease</td>
<td>10/1444 (6.9)</td>
<td>8/1007 (7.9)</td>
</tr>
</tbody>
</table>

**Conclusion:** Time in LLDAS was protective against most major organ damage, including myocardial infarction, stroke, and end stage renal disease. It was not protective against DVT damage (likely because the initial DVT was due to antiphospholipid antibodies), pulmonary fibrosis, pulmonary hypertension, cognitive impairment, or malignancy. It was not protective against cataract, which is associated with lower doses of prednisone than the 7.5 mg cut-off of the LLDAS.

**Disclosure:** M. Petri, Anthera Inc, 5,GlaxoSmithKline, 5,EMD Serono, 5,Eli Lilly and Company, 5,Bristol Meyer Squibb, 5,Amen, 5,United Rheumatology, 5,Global Academy, 5,Exagen, 2; D. Goldman, None; L. S. Magder, None.


**Abstract Number:** 1606

**Cancer in an SLE Inception Cohort: Smoking May out-Perform Tumor Markers As a Risk Predictor**

Sasha Bernatsky¹, Murray Urowitz², John G Hanly³, Ann E. Clarke⁴, Marvin J. Fritzler⁵, Caroline Gordon⁶, Juanita Romero-Diaz⁷, Graciela S. Alarcón⁸, Sang-Cheol Bae⁹, Michelle Petri¹⁰, Joan T. Merrill¹¹, Daniel J. Wallace¹², Paul R. Fortin¹³, Dafna D Gladman¹⁴, David A. Isenberg¹⁵, Anisur Rahman¹⁶, Susan Manzi¹⁷, Ola Nived¹⁸, Gunnar K. Sturfelt¹⁹, Christine A. Peschken²⁰, Jorge Sanchez-Guerrero²¹, Guillermo Ruiz-Irastorza²², Cynthia Aranow²³, Ronald F van Vollenhoven²⁴, Asad Zoma²⁵, Kristján Steinsson²⁶, Munther A Khamashta²⁷, Ellen M. Ginzler²⁸, Anca Askanase²⁹, Kenneth C. Kalunian³⁰, Mary Anne Dooley³¹, S. Sam Lim³², Diane L. Kamen³³, Søren Jacobsen³⁴, Manuel Ramos-Casals³⁵, Murat Inanc³⁶, Jennifer LF Lee³⁷ and Rosalind Ramsey-Goldman³⁸, ¹Divisions of Rheumatology and Clinical Epidemiology, Research Institute of the McGill University
Health Centre, Montreal, QC, Canada, 2Centre for Prognosis Studies in the Rheumatic Diseases, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, 3Division of Rheumatology, Department of Medicine and Department of Pathology, Queen Elizabeth II Health Sciences Centre and Dalhousie University, Halifax, NS, Canada, 4Division of Rheumatology, University of Calgary, Calgary, AB, Canada, 5Medicine, University of Calgary, Calgary, AB, Canada, 6Rheumatology Research Group, Institute of Inflammation and Ageing., College of Medical and Dental Sciences, University of Birmingham, Birmingham, United Kingdom, 7Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico city, Mexico, 8University of Alabama at Birmingham, Birmingham, AL, 9Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), 10Medicine (Rheumatology), Division of Rheumatology, Johns Hopkins University School of Medicine, MD, USA, Baltimore, MD, 11Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 12Rheumatology, Cedars-Sinai Medical Center, Beverly Hills, CA, 13Université Laval, CHU de Québec, Québeque, QC, Canada, 14Department of Medicine, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, 15Centre for Rheumatology, Division of Medicine, University College London, London, United Kingdom, 16Rayne Institute, Centre for Rheumatology Research, UCL Division of Medicine, London, United Kingdom, 17Medicine, Allegheny Health Network, Pittsburgh, PA, 18Department of Rheumatology, University Hospital, Lund, Sweden, 19Department of Rheumatology, Univ Hospital Lund, Lund, Sweden, 20RR 149G, Univ of Manitoba, Winnipeg, MB, Canada, 21Division of Rheumatology, Toronto Western Hospital, Toronto, AB, Canada, 22Biocruces Health Research Institute, Barakaldo, Spain, 23Autoimmune and Musculoskeletal Disease, The Feinstein Institute for Medical Research, Manhasset, NY, 24AMC, F4-214, Amsterdam Rheumatology and Immunology Center, Amsterdam, Netherlands, 25University of Glasgow, Glasgow, United Kingdom, 26Rheumatology, Univ. Hospital, Reykjavik, Iceland, 27Lupus Research Unit, Lupus Research Unit, The Rayne Institute, King's College London School of Medicine, St Thomas' Hospital, London, United Kingdom, 28Rheumatology, Division of Rheumatology, Department of Medicine, SUNY Downstate Medical Center, Brooklyn, NY, 29Rheumatology, Columbia University, New York, NY, 30Division of Rheumatology, Allergy & Immunology, UCSD School of Medicine Center for Innovative Therapy, La Jolla, CA, 31UNC Kidney Centre, Chapel Hill, NC, 32Division of Rheumatology, Emory University School of Medicine, Atlanta, GA, 33Medicine/Rheumatology & Immunology, Medical University of South Carolina, Charleston, SC, 34Center for Rheumatology and Spine Diseases, Rigshospitalet, Copenhagen, Denmark, 35Hospital Clinic, Barcelona, Spain, 36Department of Internal Medicine, Division of Rheumatology, Istanbul University, Istanbul Faculty of Medicine, Istanbul, Turkey, 37Research Institute of the McGill University Health Centre, Montreal, QC, Canada, 38FSM, Northwestern University, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: We assessed incident cancers in a large inception SLE cohort, and examined demographic and clinical factors, including tumor-related autoantibodies against proliferating cell nuclear antigen (PNCA) and centromere protein B (CENP-B).

Methods: Patients with new-onset SLE were enrolled at 32 centres. Incident cancers were recorded by physicians at annual visits, confirmed by chart review. Of 1,848 patients enrolled from 2000-2011, we studied 1,676 who had at least one follow-up visit. Multivariate survival regression was performed, with baseline demographics (age, sex, race), drugs (corticosteroids, anti-malarial drugs, immunosuppressives), smoking, SLEDAI-2K, and calendar year.
Serology was available in 29 cancer cases and 1114 cancer-free patients. Subjects were followed until death, last visit, or end of the interval for this analysis (August 2015).

**Results:** Of the 1,676 patients evaluated, the majority (88.7%) were female, and 828 (49.4%) were Caucasian. Mean age at SLE diagnosis was 34.6 (standard deviation 13.3) years. At baseline, 1085 (64.7%) patients were never-smokers, with the remainder being current (n=248) or ex-smokers (n=342). Mean follow up was 7 years.

We observed 45 cancers in 45 subjects, occurring at a mean SLE duration of 4.6 (SD 3.1) years. Cancers included breast (9), non-melanoma skin (8), lung (5), prostate (5), head and neck (4), hematologic (3) cervical (3), thyroid (2), melanoma (2) and one each of medulloblastoma, renal carcinoma, carcinoid, thymoma, and dermatofibrosarcoma. Baseline anti-PNCA and anti-CENP-B antibodies were respectively found in 80 (7.2%, 95% CI 5.8, 8.9) and 26 (2.2%, 95% CI 1.6,3.4) of cancer-free patients, and none of the 29 cancer cases where serology was tested (including all 5 lung cancers).

Univariate hazard regression suggested that across all cancers, events were more common in whites and older patients; similar trends were evident in the multivariate analyses, but 95% CIs around the adjusted hazard ratio, HR, estimates were relatively wide.

<table>
<thead>
<tr>
<th>Analyses for all cancers</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at enrolment</td>
<td>1.05 (1.03, 1.07)</td>
<td>1.04 (1.02, 1.07)</td>
</tr>
<tr>
<td>White</td>
<td>2.95 (1.52, 5.72)</td>
<td>2.03 (0.99, 4.14)</td>
</tr>
<tr>
<td>Disease duration</td>
<td>0.91 (0.39, 2.15)</td>
<td>0.83 (0.34, 2.05)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>1.72 (0.85, 3.48)</td>
<td>1.55 (0.75, 3.19)</td>
</tr>
<tr>
<td>Ever used steroids</td>
<td>1.06 (0.51, 2.21)</td>
<td>1.66 (0.75, 3.67)</td>
</tr>
<tr>
<td>Ever used antimalarialins</td>
<td>1.11 (0.59, 2.09)</td>
<td>0.92 (0.48, 1.78)</td>
</tr>
<tr>
<td>Ever immunosuppressives</td>
<td>0.84 (0.46, 1.54)</td>
<td>1.00 (0.51, 1.96)</td>
</tr>
<tr>
<td>SLEDAL 2K</td>
<td>0.94 (0.88, 1.00)</td>
<td>0.96 (0.89, 1.03)</td>
</tr>
<tr>
<td>Calendar year at enrolment</td>
<td>1.05 (0.94, 1.16)</td>
<td>1.05 (0.94, 1.17)</td>
</tr>
</tbody>
</table>

For lung cancer specifically, the adjusted hazard regression showed age and smoking were factors clearly associated with risk (adjusted HR for smoking 31.4, 95% CI 3.0, 327.1).

**Conclusion:** This was a first look at potentially predictive factors, including baseline levels of two tumor-associated antibodies, for cancer risk in a large inception SLE cohort. At a mean follow up time of 7 years, baseline smoking was more helpful in identifying future cancer events (specifically lung cancer), than baseline anti-tumor antibodies. However, additional work will assess a broader range of tumor-associated antibodies and follow-up over a longer period.

**Disclosure:** S. Bernatsky, None; M. Urowitz, None; J. G. Hanly, None; A. E. Clarke, None; M. J. Fritzler, Inova Diagnostics, Inc., 5; C. Gordon, None; J. Romero-Diaz, None; G. S. Alarcón, None; S. C. Bae, None; M. Petri, Anthera Inc, 5,GlaxoSmithKline, 5,EMD Serono, 5,Eli Lilly and Company, 5,Bristol Meyer Squibb, 5,Amgen, 5,United Rheumatology, 5,Global Academy, 5,Exagen, 2; J. T. Merrill, Anthera Pharmaceuticals, Lilly, EMD Serono, GlaxoSmithKline and Biogen., 5; D. J. Wallace, None; P. R. Fortin, None; D. D. Gladman, None; D. A. Isenberg, EMD Serono, Inc, 5; A. Rahman, None; S. Manzi, Exagen, 2,Exagen, 7,Exagen, 5; O. Nived, None; G. K. Sturfelt, None; C. A. Peschken, None; J. Sanchez-Guerrero, None; G. Ruiz-Irastorza, None; C. Aranow, None; R. F. van Vollenhoven, AbbVie, Amgen, Biostech, BMS, Celgene, Crescendo, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, UCB, and Vertex, 2,AbbVie, Amgen, Biostech, BMS, Celgene, Crescendo, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, UCB, and Vertex, 5,AbbVie, Amgen, Biostech, BMS, Celgene, Crescendo, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, UCB, and Vertex, 5,AbbVie, Amgen, Biostech, BMS, Celgene, Crescendo, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, UCB, and Vertex, 5,AbbVie, Amgen, Biostech, BMS, Celgene, Crescendo, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, UCB, and Vertex, 5,AbbVie, Amgen, Biostech, BMS, Celgene, Crescendo, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, UCB, and Vertex, 9; A. Zoma, None; K. Steinsson, None; M. A. Khamashta, None; E. M. Ginzler, None; A. Askane, None;
Tumor-Related Autoantibodies and Cancers in SLE: A Case-Control Study from a Single Centre

Sasha Bernatsky¹, Ann E. Clarke², Joyce Rauch³, Christian Pineau⁴, Evelyne Vinet⁵ and Marvin J. Fritzsche⁶,
¹Divisions of Rheumatology and Clinical Epidemiology, Research Institute of the McGill University Health Centre, Montreal, QC, Canada, ²Division of Rheumatology, University of Calgary, Calgary, AB, Canada, ³Division of Rheumatology, Research Institute of the McGill University Health Centre, Montreal, QC, Canada, ⁴Rheumatology, McGill University Health Center, Montreal, QC, Canada, ⁵Divisions of Rheumatology and Clinical Epidemiology, McGill University Health Centre, Montreal, QC, Canada, ⁶Medicine, University of Calgary, Calgary, AB, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Patients with systemic lupus (SLE) have altered cancer profiles compared to the general population, with a higher risk of some cancers (e.g. lymphoma) and apparently a lower risk of others (e.g. breast). Tumor-associated antibodies to centromere proteins and other antigens have been reported in many types of cancers (including lymphoma and breast) and may serve as diagnostic or prognostic indicators. Our purpose was to compare the prevalence of an array of tumor-associated antibodies in SLE patients with and without cancer.

Methods: We performed a case-control study nested within a large cohort of SLE patients followed at a clinic in Montreal, Canada. These patients have been consecutively enrolled and followed yearly with sera stored at each visit. Cancer events were ascertained by linkage with the Quebec tumor registry. In this analysis, we performed a cross-sectional analysis of antibodies in 23 SLE patients who developed a new cancer after SLE cohort entry, and compared them to 23 SLE cancer-free controls, frequency matched for sex, race/ethnicity and time since cohort entry. We assessed antibodies that in the literature had previously been suggested as associated with cancer in rheumatic disease and/or general populations. These included, but were not limited to, antibodies against anti-centromere protein (CENP), proliferating cell nuclear antigen (PCNA), Scl-70, and RNA polymerase III.

Results: Of the cancers in the 23 SLE patients, 11 were lymphoma, 8 were breast, two were endometrial, and 1 each were colon and kidney. The average age at cancer diagnosis was 52.3 years (standard deviation, SD 13.1) and the median SLE duration at cancer diagnosis was 14 years. The vast majority (91.3%) of the SLE patients with cancer were white and all but two of the SLE cancer cases were women.

For all antibodies examined, there were trends for higher levels in SLE cancer cases as a group, versus cancer-free SLE controls. Certain antibodies were found more often in specific cancer types, such as anti-RNA Pol III antibodies in breast cancer, and anti-CENPF1, anti-CENPF-4, and anti-centromere antibodies in lymphoma.
**TABLE AND FIGURE SHOW MEDIAN LEVELS OF ANTIBODIES IN EACH GROUP**

<table>
<thead>
<tr>
<th></th>
<th>CENPF1 (n=18)</th>
<th>CENPF4 (n=19)</th>
<th>PCNA (n=21)</th>
<th>Scl70 (n=20)</th>
<th>Centromere</th>
<th>Th/To-Rpp38</th>
<th>RNA Pol III</th>
<th>Th/To-Rpp25</th>
<th>PM/Scl D2</th>
</tr>
</thead>
<tbody>
<tr>
<td>breast</td>
<td>56.5</td>
<td>111.5</td>
<td>33.5</td>
<td>87.5</td>
<td>69</td>
<td>41.5</td>
<td>50.25</td>
<td>170.5</td>
<td>25</td>
</tr>
<tr>
<td>lymphoma</td>
<td>63</td>
<td>145</td>
<td>39</td>
<td>46</td>
<td>85</td>
<td>85</td>
<td>59</td>
<td>132.5</td>
<td>21</td>
</tr>
<tr>
<td>all</td>
<td>63</td>
<td>117</td>
<td>39</td>
<td>71</td>
<td>70</td>
<td>45</td>
<td>53.5</td>
<td>138</td>
<td>25</td>
</tr>
<tr>
<td>controls</td>
<td>54</td>
<td>104</td>
<td>28</td>
<td>63</td>
<td>41</td>
<td>29</td>
<td>29</td>
<td>84</td>
<td>20</td>
</tr>
</tbody>
</table>

**Conclusion**: In the SLE patients with cancer, the levels of certain tumor-related antibodies tended to be higher than the levels in SLE patients who were cancer-free. This may suggest potential roles for these as cancer markers, but further research is needed.

**Disclosure**: S. Bernatsky, None; A. E. Clarke, UCB, 2; J. Rauch, None; C. Pineau, None; E. Vinet, None; M. J. Fritzler, Inova Diagnostics, Inc., 5.


**Abstract Number**: 1608

**Entheseseal Involvement in Systemic Lupus Erythematosus: An Ultrasound Study**

**Andrea Di Matteo**¹, Emilio Filippucci², Edoardo Cipolletta², Valentina Lato², Jana Humakova³, Iulia Satulu⁵, Rossella De Angelis² and Walter Grassi², ¹Polytechnic University of Marche, Rheumatology Clinic, Jesi, Italy, ²Polytechnic University of Marche, Rheumatology Clinic, jesi, Italy, ³1st Faculty of Medicine, Institute of Rheumatology and Department of Rheumatology, Prague, Czech Republic, ⁴University Hospital Motol, Department of Pediatric and Adult Rheumatology, Prague, Czech Republic, ⁵Rheumatology Department, Internal Medicine Clinic, Kalmar County Hospital, kalmar, Sweden

**First publication**: September 18, 2017

**SESSION INFORMATION**

**Session Date**: Monday, November 6, 2017

**Session Title**: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities

**Session Type**: ACR Poster Session B
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

A recent study revealed ultrasound (US) findings indicative of enthesal involvement in a small group of patients with systemic lupus erythematosus (SLE), raising the hypothesis that enthesis could be a missing target in the evaluation of musculoskeletal manifestations in SLE. With the present study, we aimed at exploring by US the prevalence and distribution of lower limb enthesal abnormalities in a larger cohort of SLE patients, comparing the US features of SLE-enthesopathy with those of psoriatic arthritis (PSA) patients and of healthy subjects. We also examined the clinical and serologic associations of SLE-enthesopathy.

**Methods:**

We included 165 patients: 65 with SLE, 50 with PSA and 50 healthy subjects. The physical examination and the US evaluation were performed in the same day by independent rheumatologists at the following anatomic sites: the patellar insertion of the quadriceps tendon, the proximal and distal insertions of the patellar tendon, the calcaneal insertion of the Achilles tendon and of the plantar fascia. The US pathological findings, identified according to the definition of the OMERACT US Task Force, were correlated with clinical enthesitis. US enthesitis scores, based on the scoring system proposed by D’Agostino et al., were correlated with disease activity indices, serologic and clinical parameters.

**Results:**

We scanned 1650 entheses: 650 in SLE patients, 500 in PSA patients and in 500 in healthy subjects. The prevalence and distribution of the US abnormalities is reported in Table 1. In the patients with SLE, the US examination revealed one or more US abnormalities in 117 out of 650 entheses (18%) and in at least one enthesis of 44 out of 65 patients (67.7%). There was no statistical difference between SLE patients and healthy subjects about the US finding indicative of enthesal structural damage (enthesophyte, erosion, calcification), whereas US findings of “active” enthesitis (Doppler signal, hypoechogenicity, enthesal thickening) were found significantly higher in SLE patients than in healthy subjects, especially at the patellar and Achilles tendon insertions. There was a weak correlation (k=0.29) between clinical enthesitis and the presence of at least one US enthesal pathological finding, which increased when clinical enthesitis was correlated only with Doppler signal (k=0.38). D’agostino enthesitis scores correlated with age (p=0.005, f²=0.2) and SLEDAI 2-k (p=0.002, f²=0.24) and BILAG-MS (p=0.008, f²=0.17).

**Conclusion:**

This study revealed a considerable burden of enthesal abnormalities in SLE patients, especially at the patellar and Achilles tendon entheses. The US pattern of “active” enthesitis was the most frequently detected. Enthesal involvement in SLE patients correlated with high disease activity (as documented by SLEDAI 2-k) and with more severe musculoskeletal involvement, as evaluated by MS-BILAG.
Abstract Number: 1609

Telomere Length and Coronary Artery Atherosclerosis in Patients with Systemic Lupus Erythematosus

Nathan Stein¹, Joseph F. Solus¹, Annette M. Oeser¹, Paolo Raggi², C Michael Stein¹ and Michelle J. Ormseth³,
¹Vanderbilt University Medical Center, Nashville, TN, ²University of Alberta, Edmonton, AB, Canada, ³Medicine, Vanderbilt University Medical Center, Nashville, TN

First publication: September 18, 2017

SEASON INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Coronary atherosclerosis increases with age but is more prevalent in patients with systemic lupus erythematosus (SLE) independent of chronological age; this increased prevalence has been suggested to reflect accelerated biological aging in SLE. Telomeres protect chromosomal ends from shortening after replication, and telomere length is indicative of biological age. We examined the hypothesis that reduced telomere length, reflecting accelerated biological aging, is associated with inflammation, disease activity and damage, cardiometabolic risk factors, and coronary atherosclerosis in patients with SLE.

Methods: We performed a cross-sectional study in 126 patients with SLE. Telomere length was measured from whole blood DNA using real-time quantitative PCR as telomeric product to a single-copy gene product ratio (T/S ratio). Inflammation was assessed by high sensitivity C-reactive protein (CRP). SLE disease activity and damage were assessed by Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and the Systemic Lupus International Collaborating Clinics Classification Criteria (SLICC), respectively. Homeostatic Model Assessment (HOMA) was used to assess degree of insulin resistance. Framingham Risk Score (FRS) was determined based on the American Heart Association criteria. Coronary artery calcium score was measured by electron beam computed tomography. Spearman correlation and linear or logistic regression models adjusting for age, race, and sex were used to determine the association between telomere length and clinical variables.

Results: Patients with SLE were predominantly female (91%) and Caucasian (65%) with median age 41 years. Telomere length was inversely associated with age ($\rho=-0.43, P<0.001$) and CRP ($\rho=-0.31, P<0.001$, Padj<0.001) but not with SLEDAI or SLICC scores (Table). Higher triglycerides ($\rho=-0.21, P=0.02$ Padj=0.007) and FRS ($\rho=-0.43, P<0.001$, Padj=0.03) were inversely associated with telomere length independent of age, race and sex. Systolic blood pressure and waist-hip ratio were inversely associated with telomere length, but the relationship was attenuated after adjustment. High-density and low density lipoproteins, diastolic blood pressure, HOMA, and coronary artery calcium score were not associated with telomere length (Table).

Conclusion: Telomere length was significantly inversely associated with chronological age in SLE; it was also inversely associated with some cardiometabolic risk factors such as triglycerides, FRS, and CRP independent of age,
race, and sex. However, coronary artery calcium score was not independently associated with telomere length, suggesting that factors other than accelerated biological aging are responsible for increased atherosclerosis in SLE.

<table>
<thead>
<tr>
<th>Table. Relationship between telomere length and disease-related and cardiometabolic risk factors in SLE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rho (ρ)</strong></td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>SLEDAI</td>
</tr>
<tr>
<td>SLICC</td>
</tr>
<tr>
<td>CRP</td>
</tr>
<tr>
<td>Systolic BP</td>
</tr>
<tr>
<td>Diastolic BP</td>
</tr>
<tr>
<td>Waist-hip ratio</td>
</tr>
<tr>
<td>HOMA</td>
</tr>
<tr>
<td>Triglycerides</td>
</tr>
<tr>
<td>HDL</td>
</tr>
<tr>
<td>LDL</td>
</tr>
<tr>
<td>FRS</td>
</tr>
<tr>
<td>Coronary calcium</td>
</tr>
</tbody>
</table>

*Adjusted for age, race and sex. SLEDAI= Systemic Lupus Erythematosus Disease Activity Index, SLICC= Systemic Lupus International Collaborating Clinics Classification Criteria, CRP=high sensitivity C-reactive protein, BP=blood pressure, HOMA= Homeostatic Model Assessment, HDL=high density lipoprotein, LDL= low density lipoprotein, FRS= Framingham risk score.

Disclosure: N. Stein, None; J. F. Solus, None; A. M. Oeser, None; P. Raggi, None; C. M. Stein, None; M. J. Ormseth, None.


Abstract Number: 1610

The Impact of Alcohol Use on Cardiovascular Events and Overall Mortality in Women with Systemic Lupus Erythematosus

April Jorge¹, Leo Lu², Yuqing Zhang³, Sharan K. Rai⁴ and Hyon K. Choi⁴, ¹Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, ²Allergy, Immunology, and Rheumatology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, ³School Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, ⁴Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA

First publication: September 18, 2017
Background/Purpose: Women with SLE have an increased risk of cardiovascular disease (CVD) and premature death. In the general population, moderate alcohol intake is associated with a cardioprotective effect. However, there is no data on the effect of alcohol intake in women with SLE, and it is unclear whether providers should advise SLE patients to avoid drinking. We examined the impact of alcohol consumption on risk of myocardial infarction (MI) and all-cause mortality in women with SLE in a general population setting. As a control lifestyle exposure, we also investigated the impact of current smoking on these endpoints.

Methods: We conducted a population-based cohort study of female patients with SLE using a medical record database representative of the general population of the UK. The exposure of interest was alcohol intake at cohort entry. Outcomes were incident cases of MI and all-cause mortality. We estimated hazard ratios (HR) of each outcome according to alcohol intake categories (i.e., 0, 1-14 [light-moderate drinking], and 15+ [heavy drinking] UK alcohol units/week [1 unit = 8 mg]). Multivariable Cox-proportional hazard models adjusted for age, smoking status, body mass index, duration of SLE, comorbidity index, and medication use.

Results: Among 2625 individuals with SLE (mean age 53.2 years), 1262 were non-drinkers, 1199 were light-moderate drinkers and 164 were heavy drinkers. Of each group by alcohol intake, 20.2%, 26.2% and 46.3% were current smokers, respectively. The mean duration of SLE at cohort entry was 9.3 years for non-drinkers, 8.8 years for light-moderate drinkers, and 8.2 years for heavy drinkers. Over mean follow up of 6.8 years, the overall mortality rates were 23.9, 12.8, and 19.5 deaths/1000 person-years (PY) for the non-drinkers, light-moderate drinkers, and heavy drinkers, respectively. Compared with non-drinkers, the multivariable HR of overall mortality for light-moderate alcohol intake was 0.69 (95% CI, 0.53-0.89). The multivariable HR of incident MI for light-moderate alcohol consumption was 0.53 (95% CI 0.28-1.00) relative to non-drinkers. In contrast, for current smokers, the multivariable HRs were 1.93 (95% CI 1.44-2.58) for mortality and 1.59 (95% CI 0.77-3.29) for incident MI.

Conclusion: These findings provide population-based evidence that women with SLE who consume light-moderate alcohol intake have lower incidence of MI and overall mortality when compared with non-drinkers. This protective effect from light-moderate alcohol use is seen in contrast with an increased risk of mortality associated with smoking, another lifestyle factor that correlates with alcohol intake including in this study population. For their cardioprotection and improved survival, women with SLE with light-moderate alcohol consumption may be advised that they do not need to refrain from alcohol intake, whereas smoking cessation should be strongly implemented.
Disclosure: A. Jorge, None; L. Lu, None; Y. Zhang, None; S. K. Rai, None; H. K. Choi, Selecta, Horizon, 5, AstraZeneca, 2.


Abstract Number: 1611

Increased Body Mass Index May Not be a Risk Factor for the Development of Lupus Nephritis

Yu Pei Chock, Abhijeet Danve, Wei Fu and Michelle Petri, 1Rheumatology, Yale University, New Haven, CT, 2Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, 3Medicine (Rheumatology), Division of Rheumatology, Johns Hopkins University School of Medicine, MD, USA, Baltimore, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Studies have indicated that increased body mass index (BMI) is a risk factor for development of Chronic Kidney Disease (CKD). Obesity is a low grade inflammatory state which leads to CKD by lipotoxicity, increased leptin levels, cytokine mediated glomerular injury and fibrosis. Systemic Lupus Erythematosus (SLE) is associated with...
high leptin levels and dyslipidemia. We studied BMI as a possible predictor for development of lupus nephritis in SLE.

Methods:

We performed a retrospective cross sectional study on a longitudinal lupus cohort. Patients were enrolled from year 1987 to 2015. We compared the demographic information, clinical information, lab results between patients with and without lupus nephritis (Table 1) and between patients with SLE with and without obesity (Table 2). Mean and Inter- quartile ranges were reported for continuous variables, such as age and BMI value. T- test was used to compare patients between the groups. Number and percentages were shown for categorical variables and chi-square test was utilized for comparison.

Results:

Total of 1362 patients with SLE fulfilling revised ACR criteria were included in this analysis; 60.9% were Caucasian and 32.8% African American. 596 had biopsy-proven lupus nephritis however 524 patients were excluded because they had proteinuria before or at cohort entry. Only first available BMI were analyzed: 32.7% were obese (BMI > 30 kg/m2), 27.2% overweight (BMI: 25 -29.9 kg/m2), 37.5% normal (BMI: 18.5 - 24.9 kg/m2) and 2.6% underweight (BMI < 18.5 kg/m2). 39.4% (537) patients were on steroids at first BMI measurement. Results are described in Table 1, 2 and 3.

Conclusion:

Obesity was not associated with the development of lupus nephritis. Obese patients with SLE had lower disease activity as measured by SLEDAI, dsDNA titers and complement levels.

Table 1: SLE patients with vs. without Lupus Nephritis (P < 0.05 in bold)
<table>
<thead>
<tr>
<th></th>
<th>Lupus Nephritis (N = 72)</th>
<th>SLE without Lupus Nephritis (N= 1290)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age when BMI are measured</strong></td>
<td>32.07 (10.85)</td>
<td>42.53 (20.45)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Kidney Biopsy Age</strong></td>
<td>35.14 (12.05)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>20 (27.78%)</td>
<td>811 (62.87%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Asian</td>
<td>5 (6.94%)</td>
<td>36 (2.79%)</td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>42 (58.33%)</td>
<td>404 (31.32%)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>5 (6.94%)</td>
<td>39 (3.02%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>6 (8.33%)</td>
<td>76 (5.89%)</td>
<td>0.4387</td>
</tr>
<tr>
<td><strong>Age when SLE was diagnosed</strong></td>
<td>27.39 (10.87)</td>
<td>35.46 (18.38)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>BMI (continuous)</strong></td>
<td>26.93 (8.1)</td>
<td>28.02 (8.68)</td>
<td>0.1855</td>
</tr>
<tr>
<td><strong>BMI (Categorical)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underweight</td>
<td>32 (44.44%)</td>
<td>475 (36.82%)</td>
<td>0.6242</td>
</tr>
<tr>
<td>Normal Weight</td>
<td>2 (2.78%)</td>
<td>38 (2.95%)</td>
<td></td>
</tr>
<tr>
<td>Overweight</td>
<td>19 (26.39%)</td>
<td>372 (28.84%)</td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td>19 (26.39%)</td>
<td>405 (31.4%)</td>
<td></td>
</tr>
<tr>
<td><strong>SLEDAI (continuous score)</strong></td>
<td>5.04 (4)</td>
<td>2.13 (4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>SLEDAI (&gt;=2 )</strong></td>
<td>65 (90.28%)</td>
<td>690 (53.61%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Urine protein creatinine ratio (&gt; 0.5)</strong></td>
<td>2 (12.5%)</td>
<td>4 (0.67%)</td>
<td>0.0089</td>
</tr>
<tr>
<td><strong>Anti dsDNA (&gt;=10)</strong></td>
<td>40 (59.7%)</td>
<td>252 (20.31%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Low C3 (&lt;79)</strong></td>
<td>37 (53.62%)</td>
<td>178 (14.19%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Low C4 (&lt;12)</strong></td>
<td>27 (39.13%)</td>
<td>146 (11.67%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>ESR (&gt;=20)</strong></td>
<td>47 (70.15%)</td>
<td>576 (47.56%)</td>
<td>0.0004</td>
</tr>
</tbody>
</table>

Table 2: Comparison of disease activity and laboratory data between patients with and without obesity
<table>
<thead>
<tr>
<th></th>
<th>SLE patients with obesity (N=692)</th>
<th>SLE patients without obesity (N=1512)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLEDAI (continuous score)</td>
<td>1.94 (3)</td>
<td>2.45 (4)</td>
<td>0.0019</td>
</tr>
<tr>
<td>SLEDAI (&gt;=2)</td>
<td>210 (49.41%)</td>
<td>547 (58.44%)</td>
<td>0.0022</td>
</tr>
<tr>
<td>Urine protein creatinine ratio (&gt; 0.5)</td>
<td>1 (0.51%)</td>
<td>5 (1.19%)</td>
<td>0.67</td>
</tr>
<tr>
<td>Anti- dsDNA (&gt;= 10)</td>
<td>75 (18.43%)</td>
<td>217 (24.03%)</td>
<td>0.0261</td>
</tr>
<tr>
<td>Low C3 (&lt;79)</td>
<td>20 (4.88%)</td>
<td>195 (21.31%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Low C4 (&lt;12)</td>
<td>23 (5.62%)</td>
<td>150 (16.43%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ESR (&gt;20)</td>
<td>238 (60.41%)</td>
<td>387 (43.68%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Table 3: Association between BMI and Lupus Nephritis

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>P Value</th>
<th>Adjusted OR*</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (continuous)</td>
<td>0.98</td>
<td>0.2153</td>
<td>0.99 (0.95,1.03)</td>
<td>0.5111</td>
</tr>
<tr>
<td>BMI (Categorical)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underweight</td>
<td>0.78</td>
<td>0.7414</td>
<td>0.76 (0.17,3.42)</td>
<td>0.7171</td>
</tr>
<tr>
<td>Normal Weight</td>
<td>Reference</td>
<td>Reference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overweight</td>
<td>0.76</td>
<td>0.3525</td>
<td>0.86 (0.47,1.60)</td>
<td>0.6403</td>
</tr>
<tr>
<td>Obesity</td>
<td>0.70</td>
<td>0.2237</td>
<td>0.87 (0.47,1.64)</td>
<td>0.6735</td>
</tr>
</tbody>
</table>

*Adjusted for age, sex and ethnicity

**Disclosure:** Y. P. Chock, None; A. Danve, Janssen Pharmaceuticals, 6; W. Fu, None; M. Petri, Anthera Inc, 5,GlaxoSmithKline, 5,EMD Serono, 5,Eli Lilly and Company, 5,Bristol Meyer Squibb, 5,Amgen, 5,United Rheumatology, 5,Global Academy, 5,Exagen, 2.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/increased-body-mass-index-may-not-be-a-risk-factor-for-the-development-of-lupus-nephritis](http://acrabstracts.org/abstract/increased-body-mass-index-may-not-be-a-risk-factor-for-the-development-of-lupus-nephritis)

Abstract Number: 1612

**Primary Respiratory Disease in Patients with Systemic Lupus Erythematosus: Data from the Spanish Rheumatology Society**
Lupus Registry (RELESSER) Cohort


1Rheumatology Department, Hospital de Bellvitge, Barcelona, Spain, 2Rheumatology, Hospital Universitario de Bellvitge, Barcelona, Spain, 3Unidad de Investigación, Spanish Society of Rheumatology, Madrid, Spain, 4Rheumatology Division, Hospital Doctor Negrin, Las Palmas GC, Spain, 5Rheumatology, Hospital Gregorio Marañón, Madrid, Spain, 6Servicio de Reumatología, Hospital 12 de Octubre, Madrid, Spain, 7Rheumatology, Hospital de Serrallana. Torrelavega. Cantabria, Spain, Alava, Spain, 8Rheumatology, Hospital Universitario Puerta de Hierro Majadahonda, Madrid, Spain, 9RHEUMATOLOGY, Hospital general universitario de Alicante, Alicante, Spain, 10Sección de Reumatología Hospital Universitario Dr Peset Valencia, Valencia, Spain, 11Rheumatology, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, 12Hospital Universitario Reina Sofia, Universidad Europea de Madrid, Madrid, Spain, 13Hospital Universitario La Paz, Madrid, Spain, 14Rheumatology, Hospital Universitario Ramon y Cajal, Madrid, Spain, 15Complejo Asistencial Universitario de León. León. Spain, León, Spain, 16Rheumatology, Regional University Hospital of Málaga, Malaga, Spain, 17Servicio de Reumatología. Instituto de Investigación Biomédica de A Coruña (INIBIC). Complejo HospitalarioUniversitario de A Coruña (CHUAC), Sargas. Universidade da Coruña (UDC), A Coruña, Spain, 18Rheumatology, Hospital Universitario de Canarias, La Laguna; Tenerife, Spain, 19Rheumatology, Hospital Madrid Norte Sanchinarro, Madrid, Spain, 20Rheumatology, Hospital Universitario de La Princesa. IIS La Princesa, Madrid, Spain, 21Rheumatology, Hospital Insular de Gran Canaria, Las palmas Gran Canarias, Spain, 22Rheumatology, Hospital de Navarra, Pamplona, Spain, 23Rheumatology, Hospital Povisa, Vigo, Spain, 24Rheumatology, Hospital Son LLatzer, Palma de Mallorca, Spain, 25Rheumatology, Hospital Virgen de la Arrixaca, murcia, Spain, 26Rheumatology, Hospital de Valme, Seville, Spain, 27Rheumatology, EOXI Vigo, Vigo, Spain, 28Hospital Clínico Universitario de Salamanca, Salamanca, Spain, 29Rheumatology, Parc Tauli Hospital Universitari, Sabadell, Spain, 30Rheumatology, Hospital Germans Trias i Pujol, Badalona, Spain, 31Rheumatology Department. Hospital Universitario Puerta de Hierro Majadahonda, Majadahonda, Spain, 32Rheumatology, Hospital Miguel Servet, Zaragoza, Spain, 33Rheumatology, Hospital de Basurto, Bilbao, Spain, 34University Hospital Príncipe de Asturias, Immune System Diseases, Rheumatology Department, Alcalá de Henares, Madrid, Spain, 35Rheumatology, Hospital Marína Baixa, Villajoyosa (Alicante), Spain, 36Rheumatology, Hospital Universitario Virgen de la Macarena, Sevilla, Spain, 37Rheumatology, Hospital Universitario de Donosti, San Sebastian, Spain, 38Rheumatology, Hospital Universitario Lucus Augusti, Lugo, Spain, 39Rheumatology Section, Hospital de Meixoeiro, Pontevedra, Spain, Vigo, Spain

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
**Background/Purpose:** To assess the prevalence, risk factors and impact on mortality of primary respiratory disease in a large retrospective cohort.

**Methods:** All adult patients in the Spanish Rheumatology Society Lupus Registry (RELESSER) who meet ≥ 4 ACR-97 SLE criteria were retrospectively investigated for the presence of primary pleuropulmonary manifestations.

**Results:** A total of 3215 patients were included: 91% were female, their mean (SD) age at diagnosis was 37 yrs (13.5), and the median follow-up time was 136 (97.7) months.

At least one pleuropulmonary manifestation was present in 11.3% (365) of the patients (289 (79.2%) patients developed only one manifestation; the rest had two or more). The mean duration of SLE until the appearance of the first respiratory manifestation was 5.8 (SD: 8.3) years.

The most common manifestation was pleurisy, which occurred in 21.1% (680) of the patients, followed by acute lupus pneumonitis (or interstitial alveolitis/pneumonitis according with BILAG 2004 definition) in 3.6% (118); pulmonary thromboembolism (including lung infarction) 2.9% (95); primary pulmonary hypertension 2.4% (79); diffuse interstitial lung disease (or pulmonary fibrosis according with SLICC ACR Damage Index 1996) 2% (65); alveolar hemorrhage (BILAG 2004 definition) 0.8% (28); and shrinking lung syndrome (BILAG 2004 definition) 0.8% (28).

Twenty six patients with acute lupus pneumonitis and six patients with alveolar hemorrhage finally developed interstitial lung disease/pulmonary fibrosis.

In the multivariable analysis, the variables independently associated with the presence of pleuropulmonary manifestation were older age at disease onset (OR 1.03; 95% CI 1.02-1.04), higher SLEDAI scores (OR 1.03; 95% CI 1.00-1.07), the presence of Reynaud’s phenomenon (OR 1.41; 95% CI 1.09-1.84), secondary antiphospholipid syndrome (OR 2.20; 95% CI 1.63-2.96), anti-RNP positivity (OR 1.32; 95% CI 1.00-1.75), and the previous or concomitant presence of severe lupus nephritis (including classes III, IV, V and mixed III/IV + V) (OR 1.48; 95% CI 1.12-1.95), neuropsychiatric manifestations (OR 1.49; 95% CI 1.11-2.02), primary cardiac disease (OR 2.91; 95% CI 1.90-4.15), vasculitis (OR 1.81; 95% CI 1.25-2.62), hematological manifestations (OR 1.31; 95% CI 1.00-1.71) and gastrointestinal manifestations, excluding hepatitis (OR 2.05; 95% CI 1.14-3.66).

Sixty-one (1.89%) patients with pleuropulmonary manifestations died over the follow-up period. Although the mortality rate was low, the development of respiratory disease was associated with lower survival (survival rates 95.6% versus 82.2%; p=0.030). After adjusting for known confounders in the multivariable Cox regression model pleuropulmonary manifestations remained a risk factor for diminished survival (HR: 3.13; 95% CI 1.56–6.28, p=0.001).

**Conclusion:** Primary respiratory disease is not uncommon in patients with SLE and independently contributed to a decreased survival in these patients. This complication occurs mainly in patients with active and severe disease (with previous or concomitant major organ involvement other that lung) and seems to be associated with the positivity of antiphospholipid and anti-Sm antibodies.

**Disclosure:** J. Narváez, None; H. Borrell, None; F. Sánchez-Alonso, None; I. Rúa-Figueroa, None; F. J. López Longo, None; M. Galindo, None; J. Calvo-Alén, None; J. L. Andreu, None; M. Andres, None; J. J. Alegre, None; R. Blanco, None; T. Cobo-Ibáñez, None; G. Bonilla, None; A. Boteanu, None; E. Diez Alvarez, None; A. Fernandez-Nebro, None; M. Freire, None; M. Gantes, None; P. García de la Peña, None; R. García-Vicuña, None; J. Hernández Beirain, None; M. L. Horcada, None; J. Ibañez, None; A. Juan, None; N. Lozano-Rivas, None; J. L. Marenco de la Fuente, None; R. B. Melero González, None; C. A. Montilla-Morales, None; M. Moreno, None; A. Olivé, None; M. T. Oton Sanchez, None; A. Pecondon-Españo1, None; E. Ruiz Lucea, None; A. Sánchez Atrio, None; G. Santos-Soler, None; F. Toyos, None; E. Uriarte Isacelaya, None; T. R. Vazquez Rodriguez, None; J. M. Nolla, None; J. Pego-Reigosa, None.
Natural History of Disease Activity and Damage in Patients with Cutaneous Lupus Erythematosus on Standard of Care Treatments Using Longitudinal Registries from Two Academic Dermatology Centers

Noelle M. Teske¹, Khor Jia Ker²,³, Rui Feng⁴, Benjamin F. Chong¹ and Victoria P Werth⁵, ¹Dermatology, University of Texas Southwestern Medical Center, Dallas, TX, ²Dermatology, National Skin Centre, Singapore, Singapore, ³Dermatology, University of Pennsylvania, Philadelphia, PA, ⁴Department of Biostatistics and Epidemiology at the Hospital of the University of Pennsylvania, Philadelphia, PA, ⁵University of Pennsylvania and the VA Medical Center, Philadelphia, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The natural disease course of patients with cutaneous lupus erythematosus (CLE) on standard-of-care treatments is not fully characterized. We sought to characterize their disease course by obtaining Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) scores in these patients over time. We identified clinical and demographic features associated with different disease activity and damage trends.

Methods: This was a prospective cohort study of patients with CLE who had CLASI scores collected from ≥3 study visits within a 2-year time period. Patients were recruited from outpatient dermatology clinics at University of Texas Southwestern Medical Center and University of Pennsylvania from January 2007 to August 2016. Disease activity and damage trends were evaluated by net area under the curve (AUC) in CLASI scores/time and change in CLASI scores/time (slope). We defined “improving” and “worsening” trends by net AUC/time ≤-4 and ≥4, respectively. If net AUC/time was between -4 and 4, we used the best-fit slope to classify “improving” (m≤-1), “worsening” (m≥1) or “stable” (-1<m<1) trends. These metrics were compared between patient subgroups separated by demographics and clinical characteristics using Mann-Whitney and Kruskal-Wallis tests (continuous variables) and chi-squared tests (categorical variables). Linear regression models were used to compare CLASI score trends between groups.

Results: 83 patients with CLE were included, with mean follow-up time of 3.6 years. 81.8% patients with initial CLASI activity (CLASI-A) scores ≥10 (N=33) had improving disease activity, compared with 16.0% of those with initial CLASI-A ≤9 (N=50). Patients with baseline CLASI-A ≤9 had higher percentages of stable (56.0% vs. 9.1%) and worsening disease activity (28.0% vs. 9.1%) than those with initial CLASI-A ≥10 (p<0.0001). Linear regression analyses showed significant improvement in CLASI-A scores over time in patients with baseline CLASI-A ≥10 (p<0.0001), baseline CLASI damage (CLASI-D) ≥10 (p=0.0001), African Americans (p=0.049), and CLE disease duration ≤1 year (p=0.01). 46.4% patients with baseline CLASI-D ≥10 (N=28) had improving disease damage trends, compared with 5.4% of those with initial CLASI-D ≤9 (N=55), respectively. Patients with baseline CLASI-D ≤9 had higher percentages of stable (67.3% vs. 35.7%) and worsening disease activity (27.3% vs. 17.9%) than those
with initial CLASI-A ≥10 (p=0.0003). Patients with baseline CLASI-A or CLASI-D ≥10 showed negative net AUC/time and slopes (Table).

**Conclusion:** Most patients with high and low baseline CLASI-A and -D showed improving and stable trends, respectively. This natural disease course data may be used as historical controls for future clinical trials.

**Table. Net AUC/time and slope in sub-groups of patients with baseline CLASI scores ≥10 or ≤9**

<table>
<thead>
<tr>
<th></th>
<th>CLASI-A&lt;9 (N=50)</th>
<th>CLASI-A≥10 (N=33)</th>
<th>p-value</th>
<th>CLASI-D&lt;9 (N=55)</th>
<th>CLASI-D≥10 (N=28)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Net AUC/time</td>
<td>0.71 (3.55)</td>
<td>-6.65 (7.57)</td>
<td>&lt;0.0001</td>
<td>1.45 (2.65)</td>
<td>-1.19 (5.16)</td>
<td>0.003</td>
</tr>
<tr>
<td>(mean (SD))</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slope</td>
<td>0.16 (2.00)</td>
<td>-3.39 (5.65)</td>
<td>0.0001</td>
<td>0.74 (2.04)</td>
<td>-0.88 (3.12)</td>
<td>0.02</td>
</tr>
<tr>
<td>(mean (SD))</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Disclosure:** N. M. Teske, None; K. J. Ker, None; R. Feng, None; B. F. Chong, Biogen Idec, 2; V. P. Werth, Biogen Idec, 2.


**Abstract Number:** 1614

“Do You Know What I Mean?” a Tool to Understand What Lupus Patients Comprehend

Alexa Meara¹, Alexa Meara¹, Juliette Yedimenko², Juliette Yedimenko³, Holly Steigelman², Stacy P. Ardoin⁴ and Ellen Peters⁵, ¹Internal Medicine/Rheumatology, The Ohio State University Wexner Medical Center, Columbus, OH, ²The Ohio State University Wexner Medical Center, Columbus, OH, ³The Ohio State University, Columbus, OH, ⁴Pediatric & Adult Rheumatology, The Ohio State University Wexner Medical Center, Columbus, OH, ⁵Decision Research, Eugene, OR

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Long-term SLE treatment is often complex due to changing clinical manifestations, disease fluctuation, and frequent medication changes. Treatment can be daunting especially to the 25-60% of SLE patients who have cognitive and neuropsychiatric deficits. Patients cannot collaborate in making effective and shared and informed choices with physicians without understanding their own baseline health status and treatment options. The
goal of this project was to identify the level of SLE patients’ comprehension of their medication regimens and disease outcomes. To our knowledge, a disease comprehension questionnaire has never been used in SLE patients.

**Methods:** Patients > 18 years were recruited from The Ohio State University Lupus Vasculitis Glomerulonephritis (LVG) clinic. After IRB approval, patient demographics and medical history was collected. A 25 item true/false disease questionnaire (Tables 2) was developed, and a small focus group of SLE patients helped ensure feasibility, understanding and appropriate literacy. The comprehension questionnaire was administered to SLE patients in clinic during routine visits.

**Results:** 32 SLE patients completed the questionnaire. Patient characteristics are summarized in Table 1. Table 2 shows the frequency of incorrect answers. Approximately 33% of the patients did not know that heart disease was associated with SLE. Over 15% of patients did not know that SLE affected bone health and over 25% of the patients did not recognize the side of effects of prednisone. On the other hand, 100% patients recognized SLE disease manifestations and management vary.

**Conclusion:** One-third of SLE patients did not recognize the burden of heart or metabolic bone disease associated with the diagnosis of SLE. In addition, SLE patients did not understand the myriad possible side effects of prednisone, one of the most common drugs prescribed for SLE. Patients appeared to not appreciate the gravity of disease comorbidities and medication side affects, however, they did appreciate the heterogeneity of the disease and its treatment. Similar studies with larger samples are needed to develop educational processes that ensure patient understanding leading to improved shared decision making.

<table>
<thead>
<tr>
<th>Table 1 Patient Demographics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (years)</td>
</tr>
<tr>
<td>Gender % (female)</td>
</tr>
<tr>
<td>Race</td>
</tr>
<tr>
<td>Highest Education Completed</td>
</tr>
<tr>
<td>Annual Household Income, median ($)</td>
</tr>
<tr>
<td>HS (High School)</td>
</tr>
<tr>
<td>Table 2: True/False Comprehension Questions (correct answer indicated immediately after each one)</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>All lupus patients should be on hydroxychloroquine (or similar medication) unless your doctor tells you to stop (True)</td>
</tr>
<tr>
<td>Heart disease is the number one cause of death of lupus patients (True)</td>
</tr>
<tr>
<td>All medications have some side effects (True)</td>
</tr>
<tr>
<td>Lupus does not increase the risk of heart disease (False)</td>
</tr>
<tr>
<td>Active lupus will not affect you or the baby during pregnancy (False)</td>
</tr>
<tr>
<td>Lupus can cause weakening of your bones (True)</td>
</tr>
<tr>
<td>If you have lupus and you smoke, its no worse for you then if you have lupus and you don’t smoke (False)</td>
</tr>
<tr>
<td>Most patients need multiple medications to control their disease (True)</td>
</tr>
<tr>
<td>Controlling your lupus decreases your risk of disability (True)</td>
</tr>
<tr>
<td>Prednisone when stopped abruptly, can cause life threatening consequences (True)</td>
</tr>
<tr>
<td>If you know someone who has lupus, you can expect to have the same things happen to you (False)</td>
</tr>
<tr>
<td>Prednisone is not a steroid (False)</td>
</tr>
<tr>
<td>Exercise can improve your bone and heart health (True)</td>
</tr>
<tr>
<td>All patients with lupus will develop kidney disease (False)</td>
</tr>
<tr>
<td>Most people with lupus, when on the correct medication, can live a life similar to someone who does not have lupus (True)</td>
</tr>
<tr>
<td>Sun exposure does not increase your risk for lupus flares (False)</td>
</tr>
<tr>
<td>It is not important to monitor blood work regularly in patients with lupus to see if their disease is active or not (False)</td>
</tr>
<tr>
<td>If your doctor suggests a medication and the medication does not work for you, then your doctor has failed you (False)</td>
</tr>
<tr>
<td>Lupus can never be cured, but can be managed (True)</td>
</tr>
<tr>
<td>Starting a new medication is a bad idea because you will definitely get the side effects (False)</td>
</tr>
<tr>
<td>Because your doctor prescribed a medication for you, it is guaranteed to work for you (False)</td>
</tr>
<tr>
<td><strong>True/False Questions about the medication: Prednisone</strong></td>
</tr>
<tr>
<td><strong>(correct answer indicated immediately after each one)</strong></td>
</tr>
</tbody>
</table>
Assessment of a Cognitive Impairment Measure in Systemic Lupus Erythematosus

Nicole Davidson¹, Alexa Meara², Holly Steigelman³, Songzhu Zhao⁴, Guy Brock⁵, Wael Jarjour⁶, Brad H. Rovin⁷, Samir parikh⁴, Hareth M. Madhoun⁸, Lee Hebert⁹, Isabelle Ayoub⁴ and Stacy P. Ardoin¹⁰, ¹The Ohio State University, The Ohio State University, Columbus, OH, ²Internal Medicine/Rheumatology, The Ohio State University Wexner Medical Center, Columbus, OH, ³The Ohio State University Wexner Medical Center, Columbus, OH, ⁴The Ohio State University, Columbus, OH, ⁵Department of Biomedical Informatics and Center for Biostatistics, The Ohio State University Wexner Medical Center, Columbus, OH, ⁶Department of Rheumatology/Medicine, Ohio State University, Columbus, OH, ⁷Ohio State University Medical Center, Columbus, OH, ⁸Rheumatology/Immunology, The Ohio State University Wexner Medical Center, Columbus, OH, ⁹Medicine, Ohio State University Medical Center, Columbus, OH, ¹⁰Pediatric & Adult Rheumatology, The Ohio State University Wexner Medical Center, Columbus, OH

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease which can impact the central nervous system in multiple ways, including development of cognitive dysfunction. Cognitive dysfunction is commonly reported in SLE and difficult to detect. Currently used diagnostic methods including neurocognitive testing batteries are time consuming, costly and challenging to implement in clinic. This project used the Self-Administered Gerocognitive Exam (SAGE) screening test for cognitive impairment, a simple patient-completed paper test, validated for dementia, diabetes and other diseases but not SLE.

Methods:

The patient population included 118 patients participating in The Ohio State University Lupus, Vasculitis and Glomerulonephritis Registry. All subjects provided informed consent, completed the SAGE instrument and supplied demographic and medical history information. Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and Systemic Lupus International Collaborative Clinics Damage Index (SLICC-DI) were completed on all subjects. SAGE instruments, scored by a trained individual, were grouped into two categories: normal (SAGE score > 16) and abnormal (SAGE score ≤ 16). Univariate analysis was performed to assess the relationship between normal and abnormal SAGE scores and several clinical variables. Variables with p < 0.15 from the univariate analysis were initially included in multivariable logistic regression modeling. Variables with p>0.05 were subsequently removed sequentially from multivariate model using the backward selection strategy.

Results: Of the 118 subjects in this study, 97 scored in the normal range (>16) and 21 scored in the abnormal range (≤ 16). Race, ethnicity, education level and household income were significantly associated with univariate analysis with normal versus abnormal SAGE scores at the p<0.15 level were initially included in the multivariable model (Table 1). Abnormal SAGE scores were associated with higher overall SLICC DI scores but not with a neuropsychiatric-specific SLICC DI score. In multivariable analysis there was an independent association between abnormal SAGE score and higher SLICC DI score (odds ratio (OR) = 1.44, 95%CI 1.01-1.11, p-value=0.03),
Hispanic ethnicity (OR=43.4, 95%CI 3.1-601, p-value=0.005) and lower household income (OR=11.9 for ≤$15,000 vs >$50,000, 95%CI 2.45-57.8, p-value=0.002).

**Conclusion:**

Study results show a significant independent relationship between neurocognitive impairment as measured by SAGE score and higher lupus related damage as measured by SLICC DI scores. Abnormal SAGE scores were associated with lower household income and Hispanic ethnicity, which may suggest language barriers and a need for a Spanish version of the instrument. Finally, the SAGE was feasible to measure in the clinic setting. Further validation studies in SLE are needed.
<table>
<thead>
<tr>
<th></th>
<th>Normal SAGE score (N=97)</th>
<th>Abnormal SAGE score (N=21)</th>
<th>P-value&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (%)</td>
<td>N (%)</td>
<td></td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>86 (88.66)</td>
<td>20 (95.24)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>11 (11.34)</td>
<td>1 (4.76)</td>
<td>0.6904</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>65 (67.01)</td>
<td>7 (33.33)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>25 (25.77)</td>
<td>12 (57.14)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>7 (7.22)</td>
<td>2 (9.52)</td>
<td><strong>0.0126</strong></td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>2 (2.06)</td>
<td>3 (14.29)</td>
<td></td>
</tr>
<tr>
<td>Not Hispanic or Latino</td>
<td>95 (97.94)</td>
<td>18 (85.71)</td>
<td><strong>0.0388</strong></td>
</tr>
<tr>
<td><strong>Household Income</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>up to $15,000</td>
<td>11 (13.41)</td>
<td>10 (58.82)</td>
<td></td>
</tr>
<tr>
<td>$15,001 - $50,000</td>
<td>35 (42.68)</td>
<td>4 (23.53)</td>
<td></td>
</tr>
<tr>
<td>&gt; $50,000</td>
<td>36 (43.90)</td>
<td>3 (17.65)</td>
<td><strong>0.0002</strong></td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤High school/GED</td>
<td>17 (18.09)</td>
<td>9 (42.86)</td>
<td></td>
</tr>
<tr>
<td>College &lt; four years</td>
<td>22 (23.40)</td>
<td>4 (19.05)</td>
<td></td>
</tr>
<tr>
<td>College ≥4 years</td>
<td>48 (51.06)</td>
<td>7 (33.33)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>7 (7.45)</td>
<td>1 (4.76)</td>
<td><strong>0.1236</strong></td>
</tr>
<tr>
<td><strong>Antidepressant</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>30 (30.93)</td>
<td>6 (28.57)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>67 (69.07)</td>
<td>15 (71.43)</td>
<td>0.8316</td>
</tr>
<tr>
<td><strong>Hydroxychloroquine</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>85 (87.63)</td>
<td>18 (85.71)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>12 (12.37)</td>
<td>3 (14.29)</td>
<td>0.7294</td>
</tr>
<tr>
<td><strong>Immunosuppressant</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>60 (61.86)</td>
<td>15 (71.43)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>37 (38.14)</td>
<td>6 (28.57)</td>
<td>0.4086</td>
</tr>
<tr>
<td><strong>Narcotic</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>28 (28.87)</td>
<td>7 (33.33)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>69 (71.13)</td>
<td>14 (66.67)</td>
<td>0.6845</td>
</tr>
<tr>
<td><strong>Other Neuroactive</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>34 (35.05)</td>
<td>9 (42.86)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>63 (64.95)</td>
<td>12 (57.14)</td>
<td>0.5004</td>
</tr>
<tr>
<td><strong>Prednisone</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>66 (68.04)</td>
<td>15 (71.43)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>----------------</td>
<td>---</td>
<td>---</td>
<td>----------</td>
</tr>
<tr>
<td>Feel Sad/Depressed</td>
<td>31 (31.96)</td>
<td>6 (28.57)</td>
<td>0.7616</td>
</tr>
<tr>
<td>Yes</td>
<td>12 (12.37)</td>
<td>3 (14.29)</td>
<td></td>
</tr>
<tr>
<td>Occasionally</td>
<td>31 (31.96)</td>
<td>6 (28.57)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>54 (55.67)</td>
<td>12 (57.14)</td>
<td>0.9419</td>
</tr>
<tr>
<td>SLICC DI Sore</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>41 (44.09)</td>
<td>5 (23.81)</td>
<td>0.0871</td>
</tr>
<tr>
<td>1 or higher</td>
<td>52 (55.91)</td>
<td>16 (76.19)</td>
<td>0.0871</td>
</tr>
<tr>
<td><strong>Mean (SD)</strong></td>
<td></td>
<td></td>
<td>P-value²</td>
</tr>
<tr>
<td>Age (years)</td>
<td>41.40 (12.82)</td>
<td>43.67 (12.50)</td>
<td>0.4626</td>
</tr>
<tr>
<td>Prednisone Dose (mg)</td>
<td>5 (0, 60)</td>
<td>5 (0, 40)</td>
<td>0.6919</td>
</tr>
<tr>
<td>SLEDAI Score</td>
<td>2 (0, 31)</td>
<td>2 (0, 16)</td>
<td>0.8680</td>
</tr>
<tr>
<td>SLICC DI Score</td>
<td>1 (0, 9)</td>
<td>2 (0, 7)</td>
<td>0.0465</td>
</tr>
</tbody>
</table>


¹ P-value from chi-squared test or Fisher’s exact test
² P-value from t-test
³ P-value from Wilcoxon-Mann-Whitney test

**Disclosure:** N. Davidson, None; A. Meara, None; H. Steigelman, None; S. Zhao, None; G. Brock, None; W. Jarjour, None; B. H. Rovin, None; S. parikh, None; H. M. Madhoun, None; L. Hebert, None; I. Ayoub, None; S. P. Ardoin, not applicable, 9.


**Abstract Number: 1616**

**Early and Late Onset Biopsy Proven Lupus Nephritis without Other Associated Autoimmune Diseases: Severity and Long-Term Outcome**

Michelle Lopes¹, Laryssa Santos², Luciana Seguro³ and Eloisa Bonfa⁴, ¹Rheumatology, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, ²Rheumatology, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, BR, São Paulo, Brazil, ³Rheumatology Division, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, ⁴Rheumatology Division, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil

**First publication:** September 18, 2017
**Background/Purpose:** Lupus nephritis (LN) usually develops within the first years of Systemic Lupus Erythematosus (SLE) onset and rarely after that. There are scarce studies comparing early versus late onset nephritis (before vs. five years of diagnosis). In the only two reports available, the lack of renal biopsy and inclusion of elderly patients in one and the non exclusion of concomitant APS and other associated autoimmune diseases in the other preclude a definitive conclusion about their findings. The aim of this study was to compare the severity and long-term outcome (after 7 years) in these two groups: early and late-onset nephritis.

**Methods:** 77 patients with biopsy-proven LN with more than 7 years of follow-up were included. Patients were divided in two groups: early-onset nephritis (n=62) and late-onset nephritis (n=15). Clinical and laboratorial data were obtained using a standardized electronic chart database protocol carried out at 1-6 months interval and established in 2000. In order to minimize bias, patients >50 years or with concomitant autoimmune diseases were excluded. Variables evaluated at the LN presentation were SLEDAI, creatinine, albumin, anti-DNA positivity and nephritis class. Variables evaluated at the long-term outcome (after 7 years) were SDI, creatinine, dialysis and mortality. T test, Fisher and Mann Whitney were used for comparison.

**Results:** The average time of LN presentation was 0.9±1.4 years for the early-onset group and 10.6±3.6 years for the late-onset group. Of note, both groups had similar nephritis duration (13.5±4.2 vs. 13.1±2.9 years, p=0.69) and comparable mean ages (30.1±10.5 vs. 35.4±10.0 years, p=0.08) allowing a more accurate comparison between groups. Regarding severity, groups were alike at nephritis onset: SLEDAI (8.5 [min-max.: 4-22] vs. 7[min-max.: 6-17] p=0.14), creatinine (1.49 mg/dl±1.21 vs. 1.48±0.99, p=0.95); albumin (2.59 mg/dl±0.84 vs. 2.84±0.65 p=0.23); proteinuria (5.27 ±4.7 vs. 3.95±2.1 mg/dl, p=0.05); proliferative nephritis (53%[n=33] vs. 40%[n=6] p=0.37). There was also no difference in the long-term outcomes between the groups: SDI (1 [min-max.0 – 5] vs. 1 [min-max.:0 – 4], p=0.73); creatinine (1.93mg/dl±2.4 vs. 2.1±2.6, p=0.34); dialysis (16.1% [n=10] vs. 20.0% [n=3], p=0.70); mortality (14.5% [n=9] vs. 0% [n=0], p=0.19).

**Conclusion:** On the present study we demonstrated that late-onset nephritis is comparable to early-onset nephritis concerning clinical, laboratory and histological features at presentation. In addition, we provided novel evidence that long-term outcomes in biopsy proven severe lupus patients without other associated autoimmune diseases are comparable in both groups. These findings suggest that treatment targets and therapeutic interventions should be the same for these patients.

**Disclosure:** M. Lopes, None; L. Santos, None; L. Seguro, None; E. Bonfa, None, 2.
SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Increased rates of co-existing autoimmune diseases in the systemic lupus erythematosus (SLE) population have been reported. Little is known about the prevalence of autoimmune diseases in cutaneous lupus erythematosus (CLE) without SLE (CLE-only) patients. To address this knowledge gap, we sought to assess frequencies of and clinical factors associated with concomitant autoimmune diseases in patients with CLE-only.

Methods: A cross-sectional pilot study was conducted between November 2008 and February 2017 among patients enrolled in the Cutaneous Lupus Registry at University of Texas Southwestern Medical Center. Participants with CLE who met 4 out of 11 American College of Rheumatology (ACR) criteria for SLE were excluded. For each patient, we collected demographic and clinical information including concomitant autoimmune disease diagnoses, which were confirmed by other subspecialty records, and listed by Hayter and Cook. The primary and secondary outcomes was presence of ≥1 autoimmune disease and individual autoimmune diseases, respectively. Univariable (e.g. chi-squared tests) and multivariable analyses (e.g. logistic regression) were used to compare differences in outcomes between CLE-only patients with and without co-existing autoimmune diseases.

Results: Of the 129 patients with CLE-only, 17.8% (23/129) were found to have a co-existing autoimmune disease. Rheumatoid arthritis and Sjogren’s syndrome (3.1% each) were the most frequent autoimmune diseases, followed by Grave’s disease and alopecia areata (2.3% each) (Table). Univariable analyses showed that CLE-only patients who were Caucasian (p=0.03), non-smokers (p=0.008), have subacute cutaneous lupus (p=0.04), or have positive anti-nuclear antibodies (p<0.0001) were more likely to have a concomitant autoimmune disease. Based on our multivariable analyses, CLE-only patients who were Caucasian (Odds ratio (OR):3.07, p=0.03), had non-smoking histories (OR:3.34, p=0.02), and had positive anti-nuclear antibodies (OR:5.03, p=0.002) were highly associated with having autoimmune diseases.

Conclusion: Our cohort of CLE-only patients, particularly those with Caucasian race, non-smoking history, and anti-nuclear antibodies, showed higher prevalence of co-existing autoimmune diseases than what is reported in the general population (4.5%). Patients with CLE-only should be monitored closely for development of concomitant autoimmune conditions.

Table 1: Frequencies of autoimmune diseases in patients with CLE-only
<table>
<thead>
<tr>
<th>Autoimmune disease</th>
<th>CLE-only frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid arthritis</td>
<td>4 (3.1%)</td>
</tr>
<tr>
<td>Sjogren’s syndrome</td>
<td>4 (3.1%)</td>
</tr>
<tr>
<td>Alopecia areata</td>
<td>3 (2.3%)</td>
</tr>
<tr>
<td>Grave’s disease</td>
<td>3 (2.3%)</td>
</tr>
<tr>
<td>Hashimoto’s thyroiditis</td>
<td>2 (1.6%)</td>
</tr>
<tr>
<td>Morphea</td>
<td>2 (1.6%)</td>
</tr>
<tr>
<td>Addison’s disease</td>
<td>1 (0.8%)</td>
</tr>
<tr>
<td>Chronic inflammatory demyelinating polyneuropathy</td>
<td>1 (0.8%)</td>
</tr>
<tr>
<td>Guillain-Barre syndrome</td>
<td>1 (0.8%)</td>
</tr>
<tr>
<td>Idiopathic Immune thrombocytopenic purpura</td>
<td>1 (0.8%)</td>
</tr>
<tr>
<td>Microscopic polyangiitis</td>
<td>1 (0.8%)</td>
</tr>
<tr>
<td>Multiple sclerosis</td>
<td>1 (0.8%)</td>
</tr>
<tr>
<td>Pernicious anemia</td>
<td>1 (0.8%)</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>1 (0.8%)</td>
</tr>
</tbody>
</table>

*One participant had 3 coexisting autoimmune diseases and another participant had 2.


**Disclosure:** E. Kunzler, None; L. S. Hynan, None; B. F. Chong, None.


**Abstract Number:** 1618

**Risk Factors for Development of Early Infectious and Non-Infectious Complications in Systemic Lupus Erythematosus Patients Undergoing Major Surgery**

**Lauro Quintanilla-González**, Gonzalo Torres-Villalobos and Andrea Hinojosa-Azaola, 1Immunology & Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, 2Department of Experimental Surgery, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, 3Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Background/Purpose: Systemic Lupus Erythematosus (SLE) is an autoimmune disease with increased cardiovascular and infectious complications due to subclinical atherosclerosis, disease activity and treatment-related factors. The aim of this study was to identify risk factors for early infectious and non-infectious complications in SLE patients undergoing major surgery.

Methods: Retrospective comparative cohort study including patients with SLE (≥4 ACR criteria) that underwent major non-cardiac surgery between 2010-2015, and non-SLE patients paired 1:1 according to age, gender and type of surgery. Demographics, comorbidities, SLE variables, preoperative laboratory and risk assessment were analyzed. Main outcome was development of infectious, non-infectious complications and mortality 30 days after surgery. Differences between groups were evaluated: Student t-test or Mann-Whitney U test (continuous variables); Chi-square or Fisher’s exact test (categorical variables). Univariate logistic regression and multivariate analyses were done.

Results: 382 patients (191 SLE, 191 non-SLE) were included. Disease duration of SLE patients at surgery was 132 (0-468) months. Table 1 shows characteristics of surgical SLE and non-SLE patients. Variables associated with infectious complications in SLE patients: use of prednisone (OR 1.81, 95%CI 1.13-2.90, p=0.01); anemia (OR 2.43, 95%CI 1.45-4.08, p=0.001); hypoalbuminemia (OR 2.58, 95%CI 1.55-4.30, p<0.001), and lymphopenia (OR 2.43, 95%CI 1.52-3.89, p<0.001). Multivariate analysis retained hypoalbuminemia, anemia and lymphopenia. Variables associated with non-infectious complications: anemia (OR, 1.93, 95%CI 1.03-3.64, p=0.03) and hypoalbuminemia (OR 2.11, 95%CI 1.16-3.86, p=0.01). More patients with SLE died (p=0.02). Table 2 shows characteristics of SLE patients with and without any postoperative complication. Variables associated with any complication: SLEDAI-2K (OR 1.1, 95%CI 1.01-1.20, p=0.02); nephritis (OR 10.08, 95%CI 1.21-83.63, p=0.03); use of aspirin (OR 2.68, 95%CI 1.19-6.02, p=0.01); low C3 (OR 2.00, 95%CI 1.06-3.80, p=0.03); anemia (OR 2.68, 95%CI 1.39-5.18, p=0.003); hypoalbuminemia (OR 3.49, 95%CI 1.83-6.66, p<0.001), and lymphopenia (OR 2.36, 95%CI 1.30-4.26, p=0.004). Only use of aspirin was retained in multivariate analysis. More patients with complications died (p<0.001).

Conclusion: SLE patients present higher frequency of postoperative early complications and mortality compared to non-SLE patients. Hypoalbuminemia, anemia, lymphopenia and use of aspirin are independent risk factors.

Table 1

\[
\begin{array}{|c|c|}
\hline
\text{Variable} & \text{OR} (95\% \text{CI}) \text{ p-value} \\
\hline
\text{Prednisone} & 1.81 (1.13-2.90) \text{ 0.01} \\
\text{Anemia} & 2.43 (1.45-4.08) \text{ 0.001} \\
\text{Hypoalbuminemia} & 2.58 (1.55-4.30) \text{ <0.001} \\
\text{Lymphopenia} & 2.43 (1.52-3.89) \text{ <0.001} \\
\text{SLEDAI-2K} & 1.1 (1.01-1.20) \text{ 0.02} \\
\text{Nephritis} & 10.08 (1.21-83.63) \text{ 0.03} \\
\text{Aspirin} & 2.68 (1.19-6.02) \text{ 0.01} \\
\text{Low C3} & 2.00 (1.06-3.80) \text{ 0.03} \\
\text{Anemia} & 2.68 (1.39-5.18) \text{ 0.003} \\
\text{Hypoalbuminemia} & 3.49 (1.83-6.66) \text{ <0.001} \\
\text{Lymphopenia} & 2.36 (1.30-4.26) \text{ 0.004} \\
\end{array}
\]
<table>
<thead>
<tr>
<th>Variable</th>
<th>SLE (n=191)</th>
<th>Non-SLE (n=191)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female gender</td>
<td>169 (88)</td>
<td>169 (88)</td>
<td>1</td>
</tr>
<tr>
<td>Age at surgery-years</td>
<td>39 (19-76)</td>
<td>39 (18-74)</td>
<td>0.72</td>
</tr>
<tr>
<td><strong>Comorbidities</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td>80 (42)</td>
<td>95 (50)</td>
<td>0.15</td>
</tr>
<tr>
<td>Smoking</td>
<td>60 (31)</td>
<td>57 (30)</td>
<td>0.82</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>15 (8)</td>
<td>25 (13)</td>
<td>0.13</td>
</tr>
<tr>
<td>Hypertension</td>
<td>78 (41)</td>
<td>59 (31)</td>
<td>0.05</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>58 (30)</td>
<td>38 (20)</td>
<td>0.02</td>
</tr>
<tr>
<td>Cardiac failure</td>
<td>10 (5)</td>
<td>4 (2)</td>
<td>0.17</td>
</tr>
<tr>
<td>ESRD</td>
<td>51 (27)</td>
<td>41 (21)</td>
<td>0.28</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>11 (6)</td>
<td>2 (1)</td>
<td>0.02</td>
</tr>
<tr>
<td>Cancer</td>
<td>17 (9)</td>
<td>30 (16)</td>
<td>0.06</td>
</tr>
<tr>
<td><strong>Preoperative risk according to type of surgical procedure</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>0</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Medium</td>
<td>180 (94)</td>
<td>180 (94)</td>
<td>1</td>
</tr>
<tr>
<td>High</td>
<td>11 (6)</td>
<td>11 (6)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Surgery indication</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elective procedure</td>
<td>133 (70)</td>
<td>148 (77)</td>
<td>0.1</td>
</tr>
<tr>
<td>Urgent procedure</td>
<td>45 (24)</td>
<td>35 (18)</td>
<td>0.25</td>
</tr>
<tr>
<td>Emergency procedure</td>
<td>13 (7)</td>
<td>8 (4)</td>
<td>0.37</td>
</tr>
<tr>
<td><strong>Charlson comorbidity index-%</strong></td>
<td>85 (19)</td>
<td>90 (21)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Use of prednisone before surgery</strong></td>
<td>109 (57)</td>
<td>25 (13)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Steroids during surgery</strong></td>
<td>116 (61)</td>
<td>106 (56)</td>
<td>0.3</td>
</tr>
<tr>
<td><strong>Equivalent prednisone dose during surgery-mg</strong></td>
<td>50 (6.25-1250)</td>
<td>50 (12.5-1250)</td>
<td>0.29</td>
</tr>
<tr>
<td><strong>Use of immunosuppressants before surgery</strong></td>
<td>84 (44)</td>
<td>13 (7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Preoperative laboratory characteristics at surgery</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin—g/dl</td>
<td>11.9 (4.9-17.5)</td>
<td>12.7 (5.1-23.1)</td>
<td>0.04</td>
</tr>
<tr>
<td>Leukocytes/mm$^3$</td>
<td>6800 (13.4-29400)</td>
<td>7400 (300-29000)</td>
<td>0.01</td>
</tr>
<tr>
<td>Neutrophils/mm$^3$</td>
<td>4803 (765-27636)</td>
<td>4695 (12.9-22344)</td>
<td>0.73</td>
</tr>
<tr>
<td>Lymphocytes/mm$^3$</td>
<td>961 (82-3496)</td>
<td>1598 (0-4640)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Platelets—K/ul</td>
<td>210 (6-490)</td>
<td>249 (2-585)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum creatinine—mg/dl</td>
<td>0.8 (0.2-21.4)</td>
<td>0.7 (0.1-20.4)</td>
<td>0.92</td>
</tr>
<tr>
<td>Albumin—g/dl</td>
<td>3.9 (0.6-5.2)</td>
<td>4.1 (0.9-5.4)</td>
<td>0.001</td>
</tr>
<tr>
<td>Anemia</td>
<td>129 (68)</td>
<td>105 (55)</td>
<td>0.01</td>
</tr>
<tr>
<td>Hypoalbuminemia</td>
<td>59 (31)</td>
<td>30 (16)</td>
<td>0.001</td>
</tr>
<tr>
<td>Lymphopenia &lt;1000</td>
<td>103 (54)</td>
<td>37 (19)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Surgical time—hours</td>
<td>2.5 (0.7-8.4)</td>
<td>2.3 (0-9)</td>
<td>0.98</td>
</tr>
<tr>
<td>Parameter</td>
<td>Group 1</td>
<td>Group 2</td>
<td>p-value</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>---------------</td>
<td>---------------</td>
<td>---------</td>
</tr>
<tr>
<td>Bleeding—ml</td>
<td>135 (5-7000)</td>
<td>150 (10-5000)</td>
<td>0.84</td>
</tr>
<tr>
<td>Blood transfusion—units</td>
<td>0 (0-9)</td>
<td>0 (0-6)</td>
<td>0.17</td>
</tr>
<tr>
<td>Days of mechanical ventilation</td>
<td>0 (0-24)</td>
<td>0 (0-19)</td>
<td>0.11</td>
</tr>
<tr>
<td>Days of intensive care unit</td>
<td>0 (0-31)</td>
<td>0 (0-31)</td>
<td>0.57</td>
</tr>
<tr>
<td>Total days of hospital stay</td>
<td>7 (0-236)</td>
<td>6 (1-70)</td>
<td>0.13</td>
</tr>
<tr>
<td>Complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any complication</td>
<td>82 (43)</td>
<td>58 (30)</td>
<td>0.01</td>
</tr>
<tr>
<td>Days after surgery</td>
<td>3 (0-30)</td>
<td>3 (1-21)</td>
<td>0.59</td>
</tr>
<tr>
<td>Infectious postoperative complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(any)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septic shock</td>
<td>10 (5)</td>
<td>7 (4)</td>
<td>0.62</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>13 (7)</td>
<td>5 (3)</td>
<td>0.08</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>12 (6)</td>
<td>11 (6)</td>
<td>1</td>
</tr>
<tr>
<td>Surgical wound</td>
<td>5 (3)</td>
<td>2 (1)</td>
<td>0.44</td>
</tr>
<tr>
<td>Bacteremia</td>
<td>3 (2)</td>
<td>5 (3)</td>
<td>0.72</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>6 (3)</td>
<td>2 (1)</td>
<td>0.28</td>
</tr>
<tr>
<td>Abdominal sepsis</td>
<td>16 (8)</td>
<td>15 (8)</td>
<td>1</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2 (1)</td>
<td>0</td>
<td>0.49</td>
</tr>
<tr>
<td>Prosthetic</td>
<td>1 (0.5)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>0</td>
<td>1 (0.5)</td>
<td>1</td>
</tr>
<tr>
<td>Non-infectious postoperative</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>complications (any)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombosis</td>
<td>8 (4)</td>
<td>2 (1)</td>
<td>0.1</td>
</tr>
<tr>
<td>Bleeding</td>
<td>8 (4)</td>
<td>6 (3)</td>
<td>0.78</td>
</tr>
<tr>
<td>Hemorrhagic shock</td>
<td>8 (4)</td>
<td>5 (3)</td>
<td>0.57</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>2 (1)</td>
<td>0</td>
<td>0.49</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>3 (2)</td>
<td>0</td>
<td>0.24</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>10 (5)</td>
<td>8 (4)</td>
<td>0.81</td>
</tr>
<tr>
<td>Hypocalcaemia</td>
<td>0</td>
<td>7 (4)</td>
<td>0.01</td>
</tr>
<tr>
<td>Second intervention</td>
<td>17 (9)</td>
<td>7 (4)</td>
<td>0.05</td>
</tr>
<tr>
<td>Second hospitalization</td>
<td>12 (6)</td>
<td>6 (3)</td>
<td>0.22</td>
</tr>
<tr>
<td>Hospital stay &gt; 31 days</td>
<td>12 (6)</td>
<td>3 (2)</td>
<td>0.03</td>
</tr>
<tr>
<td>Postoperative death</td>
<td>11 (6)</td>
<td>2 (1)</td>
<td>0.02</td>
</tr>
<tr>
<td>Days from surgery to death</td>
<td>4 (1-25)</td>
<td>6 (1-10)</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 2
<table>
<thead>
<tr>
<th>Variable</th>
<th>With complications (n=82)</th>
<th>Without complications (n=109)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>71 (87)</td>
<td>98 (90)</td>
<td>0.5</td>
</tr>
<tr>
<td>Age at SLE diagnosis-years</td>
<td>25 (12-75)</td>
<td>24 (8-63)</td>
<td>0.63</td>
</tr>
<tr>
<td>Age at surgery-years</td>
<td>36 (19-76)</td>
<td>39 (19-72)</td>
<td>0.64</td>
</tr>
<tr>
<td>Disease duration at surgery-months</td>
<td>108 (0-468)</td>
<td>156 (0-456)</td>
<td>0.04</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td>31 (38)</td>
<td>49 (45)</td>
<td>0.37</td>
</tr>
<tr>
<td>Smoking</td>
<td>26 (32)</td>
<td>34 (31)</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>4 (5)</td>
<td>11 (10)</td>
<td>0.27</td>
</tr>
<tr>
<td>Hypertension</td>
<td>38 (46)</td>
<td>40 (37)</td>
<td>0.18</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>24 (29)</td>
<td>34 (31)</td>
<td>0.87</td>
</tr>
<tr>
<td>Cardiac failure</td>
<td>5 (6)</td>
<td>5 (5)</td>
<td>0.74</td>
</tr>
<tr>
<td>ESRD</td>
<td>24 (29)</td>
<td>27 (25)</td>
<td>0.51</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>7 (9)</td>
<td>4 (4)</td>
<td>0.21</td>
</tr>
<tr>
<td>Cancer</td>
<td>8 (10)</td>
<td>9 (8)</td>
<td>0.8</td>
</tr>
<tr>
<td>SLE criteria at diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malar rash</td>
<td>43 (52)</td>
<td>57 (52)</td>
<td>1</td>
</tr>
<tr>
<td>Discoid lupus</td>
<td>3 (4)</td>
<td>9 (8)</td>
<td>0.23</td>
</tr>
<tr>
<td>Photosensitivity</td>
<td>33 (40)</td>
<td>34 (31)</td>
<td>0.22</td>
</tr>
<tr>
<td>Oral ulcers</td>
<td>35 (43)</td>
<td>45 (41)</td>
<td>0.88</td>
</tr>
<tr>
<td>Arthritis</td>
<td>66 (80)</td>
<td>91 (83)</td>
<td>0.7</td>
</tr>
<tr>
<td>Serositis</td>
<td>22 (27)</td>
<td>27 (25)</td>
<td>0.86</td>
</tr>
<tr>
<td>Renal involvement</td>
<td>44 (54)</td>
<td>48 (44)</td>
<td>0.19</td>
</tr>
<tr>
<td>Neurologic involvement</td>
<td>4 (5)</td>
<td>8 (7)</td>
<td>0.56</td>
</tr>
<tr>
<td>Hematologic</td>
<td>47 (57)</td>
<td>62 (57)</td>
<td>1</td>
</tr>
<tr>
<td>Immunologic-n+/n (%)</td>
<td>67/72 (93)</td>
<td>82/96 (85)</td>
<td>0.14</td>
</tr>
<tr>
<td>Positive ANA-n+/n (%)</td>
<td>70/73 (96)</td>
<td>93/103 (90)</td>
<td>0.24</td>
</tr>
<tr>
<td>Positive anti-dsDNA-n+/n (%)</td>
<td>60/67 (90)</td>
<td>77/96 (80)</td>
<td>0.13</td>
</tr>
<tr>
<td>Secondary APS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLEDAI-2K before surgery</td>
<td>4 (0-16)</td>
<td>2 (0-18)</td>
<td><strong>0.04</strong></td>
</tr>
<tr>
<td>SLICC/ACR damage index before surgery</td>
<td>2 (0-8)</td>
<td>1 (0-6)</td>
<td>0.16</td>
</tr>
<tr>
<td>Severe SLE manifestation before surgery</td>
<td>13 (16)</td>
<td>13 (12)</td>
<td>0.52</td>
</tr>
<tr>
<td>Time since last severe SLE manifestation-days</td>
<td>45 (13-90)</td>
<td>43 (15-90)</td>
<td>0.93</td>
</tr>
<tr>
<td>Hemolytic anemia</td>
<td>0</td>
<td>2 (15)</td>
<td>0.48</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>3 (23)</td>
<td>2 (15)</td>
<td>1</td>
</tr>
<tr>
<td>Lupus nephritis</td>
<td>7 (54)</td>
<td>1 (8)</td>
<td><strong>0.03</strong></td>
</tr>
<tr>
<td>Serositis</td>
<td>2 (15)</td>
<td>1 (8)</td>
<td>1</td>
</tr>
<tr>
<td>Constitutional symptoms</td>
<td>0</td>
<td>3 (23)</td>
<td>0.22</td>
</tr>
<tr>
<td>Cutaneous</td>
<td>0</td>
<td>2 (15)</td>
<td>0.48</td>
</tr>
<tr>
<td>Preoperative SLE treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prednisone</td>
<td>51 (62)</td>
<td>58 (53)</td>
<td>0.23</td>
</tr>
<tr>
<td>Prednisone dose-mg</td>
<td>10 (2.5-75)</td>
<td>7.5 (2.5-100)</td>
<td><strong>0.03</strong></td>
</tr>
<tr>
<td>Drug</td>
<td>Value 1 (n)</td>
<td>Value 2 (n)</td>
<td>P-value</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>-------------</td>
<td>-------------</td>
<td>---------</td>
</tr>
<tr>
<td>Prednisone dose ≥10 mg/d</td>
<td>31 (61)</td>
<td>25 (43)</td>
<td>0.08</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>4 (5)</td>
<td>1 (0.9)</td>
<td>0.16</td>
</tr>
<tr>
<td>Cyclophosphamide dose-mg</td>
<td>1000 (500-1200)</td>
<td>1000 (1000)</td>
<td>1</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>23 (28)</td>
<td>35 (32)</td>
<td>0.63</td>
</tr>
<tr>
<td>Azathioprine dose-mg</td>
<td>50 (25-150)</td>
<td>75 (50-200)</td>
<td>0.17</td>
</tr>
<tr>
<td>Mycophenolate mofetil</td>
<td>10 (12)</td>
<td>9 (8)</td>
<td>0.46</td>
</tr>
<tr>
<td>Mycophenolate mofetil dose-mg</td>
<td>1500 (500-3000)</td>
<td>1000 (750-2500)</td>
<td>0.4</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>1 (1)</td>
<td>3 (3)</td>
<td>0.63</td>
</tr>
<tr>
<td>Methotrexate dose-mg</td>
<td>15 (15-15)</td>
<td>10 (7.5-17.5)</td>
<td>0.65</td>
</tr>
<tr>
<td>Antimalarials</td>
<td>32 (39)</td>
<td>34 (31)</td>
<td>0.28</td>
</tr>
<tr>
<td>Aspirin</td>
<td>19 (23)</td>
<td>11 (10)</td>
<td>0.01</td>
</tr>
<tr>
<td>Oral anticoagulants</td>
<td>13 (16)</td>
<td>16 (15)</td>
<td>0.84</td>
</tr>
</tbody>
</table>

Preoperative serologic characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value 1 (n)</th>
<th>Value 2 (n)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive anti-dsDNA-n+/n (%)</td>
<td>50/75 (67)</td>
<td>61/80 (76)</td>
<td>0.21</td>
</tr>
<tr>
<td>Low complement C3-n+/n (%)</td>
<td>47/74 (64)</td>
<td>39/84 (46)</td>
<td>0.03</td>
</tr>
<tr>
<td>Low complement C4-n+/n (%)</td>
<td>39/73 (53)</td>
<td>41/82 (50)</td>
<td>0.74</td>
</tr>
<tr>
<td>Charlson comorbidity index-%</td>
<td>82 (23)</td>
<td>87 (16)</td>
<td>0.39</td>
</tr>
<tr>
<td>Steroids during surgery</td>
<td>45 (56)</td>
<td>70 (64)</td>
<td>0.29</td>
</tr>
<tr>
<td>Equivalent prednisone dose during surgery-mg</td>
<td>50 (12.5-1250)</td>
<td>50 (6.2-1250)</td>
<td>0.99</td>
</tr>
</tbody>
</table>

Preoperative laboratory characteristics at surgery

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value 1 (n)</th>
<th>Value 2 (n)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin—g/dl</td>
<td>10.8 (4.9-16.3)</td>
<td>12.7 (5.2-17.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Leukocytes/mm³</td>
<td>6450 (13.4-29400)</td>
<td>7100 (1800-17200)</td>
<td>0.35</td>
</tr>
<tr>
<td>Neutrophils/mm³</td>
<td>5152 (765-27636)</td>
<td>4547 (972-14635)</td>
<td>0.64</td>
</tr>
<tr>
<td>Lymphocytes/mm³</td>
<td>726 (140-2840)</td>
<td>1074 (82-3496)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Platelets—K/ul</td>
<td>203 (6-418)</td>
<td>217 (32-490)</td>
<td>0.07</td>
</tr>
<tr>
<td>Serum creatinine—mg/dl</td>
<td>1 (0.2-21)</td>
<td>0.7 (0.3-16.7)</td>
<td>0.29</td>
</tr>
<tr>
<td>Albumin—g/dl</td>
<td>3.5 (0.6-5)</td>
<td>4 (1.3-5.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anemia</td>
<td>65 (79)</td>
<td>64 (59)</td>
<td>0.003</td>
</tr>
<tr>
<td>Hypoalbunminemia</td>
<td>38 (46)</td>
<td>21 (20)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lymphopenia &lt;1000</td>
<td>54 (66)</td>
<td>49 (45)</td>
<td>0.005</td>
</tr>
<tr>
<td>Postoperative death</td>
<td>11 (13)</td>
<td>0</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

SLE activity 30 days after surgery

<table>
<thead>
<tr>
<th>Activity</th>
<th>Value 1 (n)</th>
<th>Value 2 (n)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenia</td>
<td>3 (4)</td>
<td>0</td>
<td>0.07</td>
</tr>
<tr>
<td>Nephritis</td>
<td>2 (3)</td>
<td>0</td>
<td>0.18</td>
</tr>
<tr>
<td>Diffuse alveolar hemorrhage</td>
<td>3 (4)</td>
<td>0</td>
<td>0.07</td>
</tr>
<tr>
<td>Myocarditis</td>
<td>1 (1)</td>
<td>0</td>
<td>0.42</td>
</tr>
<tr>
<td>Serositis</td>
<td>1 (1)</td>
<td>0</td>
<td>0.42</td>
</tr>
<tr>
<td>Seizures</td>
<td>1 (1)</td>
<td>0</td>
<td>0.42</td>
</tr>
<tr>
<td>Cutaneous</td>
<td>1 (1)</td>
<td>0</td>
<td>0.42</td>
</tr>
</tbody>
</table>
The Impact of Disease Characteristics on Habitual Physical Activity and Sedentary Behavior Among Patients with Systemic Lupus Erythematosus (SLE)

Alexandra Legge¹, Chris Blanchard¹ and John G. Hanly², ¹Department of Medicine, Queen Elizabeth II Health Sciences Centre and Dalhousie University, Halifax, NS, Canada, ²Division of Rheumatology, Department of Medicine and Department of Pathology, Queen Elizabeth II Health Sciences Centre and Dalhousie University, Halifax, NS, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Patients with systemic lupus erythematosus (SLE) are at increased risk for atherosclerotic cardiovascular disease (ASCVD). As sedentary behavior and lack of physical activity are known ASCVD risk factors, we evaluated habitual physical activity levels among SLE patients using accelerometry. We also investigated the association between SLE disease characteristics and the amount of habitual physical activity and sedentary behavior performed by SLE patients.

Methods: For this cross-sectional study, patients were recruited from an SLE clinic at a single academic medical center. All participants met the ACR classification criteria for SLE. Validated instruments were used to measure disease activity (SLEDAI-2K), organ damage [SLICC/ACR Damage Index (SDI)], and functional status (HAQ). Laboratory data included ESR and serum CRP. Habitual physical activity was measured using triaxial accelerometers worn during waking hours for seven consecutive days. Minutes per day of sedentary time, light activity, and moderate-vigorous physical activity (MVPA) were recorded. SLE disease characteristics associated with time spent performing MVPA and time in sedentary behavior were identified using multivariable linear regression, adjusting for demographic factors including age, sex, race, and education.

Results: There were 109 SLE patients (92% female) with mean (SD) age 52.3 (14.5) years, SLEDAI-2K 2.1 (2.4), and SDI 1.5 (2.1). High levels of sedentary behavior were observed [mean (SD) sedentary time 10.1 (1.2) hours/day], accounting for 78.6% of total accelerometer wear time. Mean (SD) MVPA was low [32.6 (22.5) minutes/day]. Only 13/109 participants (11.9%) met the Canadian Physical Activity Guidelines for MVPA (≥ 150 minutes/week in 10 minute bouts). In univariable linear regression, SLE disease characteristics significantly associated with MVPA performance included the SDI (β = -0.183; p=0.004), SLEDAI-2K (β = -0.133; p=0.004), and ESR (β = -0.208; p=0.004). In multivariable analysis, both the HAQ (β = -0.191;
p=0.002) and SLEDAI-2K (β = -0.175; p=0.005) remained significantly associated with time spent performing MVPA. Specifically, higher HAQ and SLEDAI-2K scores were associated with lower MVPA performance. After adjustment for MVPA performance, none of the SLE disease characteristics we evaluated were significantly associated with time spent in sedentary behavior.

**Conclusion:** SLE patients demonstrate suboptimal levels of habitual MVPA, as well as high sedentary behavior. Our results highlight the potential negative impact of disease activity and functional disability on habitual physical activity in SLE. The findings identify a subgroup of SLE patients at increased risk for physical inactivity and will help inform the design of effective interventions to improve habitual physical activity levels in this population.

**Disclosure:** A. Legge, None; C. Blanchard, None; J. G. Hanly, None.


**Abstract Number:** 1620

**Habitual Physical Activity, Sedentary Behavior and Cardiovascular Disease Risk Burden in Systemic Lupus Erythematosus (SLE)**

Alexandra Legge¹, Chris Blanchard¹ and John G. Hanly², ¹Department of Medicine, Queen Elizabeth II Health Sciences Centre and Dalhousie University, Halifax, NS, Canada, ²Division of Rheumatology, Department of Medicine and Department of Pathology, Queen Elizabeth II Health Sciences Centre and Dalhousie University, Halifax, NS, Canada

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Patients with SLE are at increased risk for atherosclerotic cardiovascular disease (ASCVD). As sedentary behavior and lack of physical activity (PA) have been identified as ASCVD risk factors in the general population, we investigated the relationship between habitual PA levels and estimated 10-year ASCVD risk among patients with SLE. We also evaluated the association between habitual PA levels and individual ASCVD risk factors in SLE.

**Methods:** For this cross-sectional study, patients were recruited from an SLE clinic at a single academic medical center. All participants met the ACR classification criteria for SLE. Patients were excluded if they had a prior history of ASCVD. Habitual PA was measured using triaxial accelerometers worn during waking hours for seven consecutive days. Minutes per day of total sedentary time, prolonged sedentary bouts (≥30 uninterrupted sedentary minutes), light activity, and moderate-vigorous physical activity (MVPA) were recorded. Cardiovascular risk factors included body mass index, blood pressure, fasting glucose and lipid profile. Ten-year ASCVD risk was calculated using the 2013 American College of Cardiology (ACC) / American Heart Association (AHA) risk assessment tool. Associations between time spent in each PA category and calculated 10-year ASCVD risk were assessed using multivariable linear regression models. The relationships between PA at each intensity level and individual cardiovascular risk markers were also evaluated using multivariable linear regression, adjusting for age and gender.
**Results:** There were 100 SLE patients (mean ± SD age 52.4 ± 14.4 years, 92% female). Participants spent a total of 10.0 hours/day being sedentary, 2.2 hours/day engaged in light activity, and 29.8 minutes/day engaged in MVPA. Median (IQR) time spent in prolonged sedentary bouts was 35.4 (36.8) minutes/day, with 21% of participants spending > 1 hour/day in prolonged sedentary behavior. Only 11% of participants met the Canadian Physical Activity Guidelines for MVPA (≥ 150 minutes/week in 10 minute bouts). Regression models demonstrated that time spent in MVPA was inversely associated with calculated 10-year ASCVD risk ($R^2 \Delta = 0.10; p=0.001$). Time spent in prolonged sedentary bouts was positively associated with 10-year risk of ASCVD ($R^2 \Delta = 0.06; p=0.016$), independent of time spent in MVPA ($R^2 \Delta = 0.03; p=0.049$). MVPA performance was also inversely associated with both systolic ($R^2 \Delta = 0.07; p=0.005$) and diastolic blood pressure ($R^2 \Delta = 0.07; p=0.007$), after adjusting for age, gender, and antihypertensive use. Neither total sedentary time nor time spent in light activity were significantly associated with 10-year ASCVD risk, nor were they associated with any of the individual cardiovascular risk markers we evaluated.

**Conclusion:** Among patients with SLE, those at higher risk for ASCVD perform less MVPA. Prolonged sedentary behavior is associated with ASCVD risk in SLE, independent of MVPA performance. Our findings highlight the need for effective PA interventions to increase habitual MVPA levels and reduce prolonged sedentary time in this high-risk population.

**Disclosure:** A. Legge, None; C. Blanchard, None; J. G. Hanly, None.


**Abstract Number:** 1621

**Prevalence of Cognitive Impairment in Systemic Lupus Erythematosus Assessed By the Automated Neuropsychological Assessment Metrics**

Zahi Touma¹, Robin Green², Lesley Ruttan³, Sabrina Lombardi³, Carmela Tartaglia⁴, Nicole Anderson⁵, Jiandong Su⁶, Kenneth Colosimo⁶, Michelle Vitti⁶, Dennisse Bonilla⁶, Joan E. Wither⁵, Marvin J. Fritzler⁷ and Dorcas Beaton⁸

¹Rheumatology, University of Toronto, Division of Rheumatology, Institute of Health Policy, Management and Evaluation, Toronto, ON, Canada, ²Brain and Therapeutics, Toronto Rehabilitation Institute, Toronto, ON, Canada, ³Toronto Rehabilitation Institute, Toronto, ON, Canada, ⁴University of Toronto, Krembil Neurosciences Centre, Toronto, ON, Canada, ⁵Rheumatology, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, ⁶University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, ⁷Medicine, University of Calgary, Calgary, AB, Canada, ⁸Mobility Program Clinical Research Unit, St Michael's Hospital, Toronto, ON, Canada

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The screening and diagnosis of Cognitive Impairment (CI) in Systemic Lupus Erythematosus (SLE) patients is often delayed. CI diagnosed according to the American College of Rheumatology (ACR)-SLE battery is associated with a remarkable administrative and cost burden. The Automated
Neuropsychological Assessment Metrics (ANAM) is a promising computerized battery of tests that is easy to administer. In our recent systematic review, we found a CI prevalence of 34% by ANAM (95% CI: 25-44%) and by the comprehensive batteries 38% (95% CI: 33-43%). We aimed to determine the prevalence of CI based on the ANAM (v4) GNS Battery using different definitions for CI.

Methods: Consecutive SLE patients, aged 18-65 years, who attended the University of Toronto Lupus Clinic between July 2016 and April 2017 and agreeing to participate were included. Patients were administered the ANAM (v4) GNS, which consists of 15 subtests that evaluate key neurocognitive domains (processing speed, attention, memory, visuospatial processing, and executive functioning). ANAM throughput scores were used to provide an estimate of ‘cognitive efficiency’. Patient scores were compared to a normative sample of age and gender-matched healthy controls to obtain z-scores. Cognitive impairment was operationalized on the ANAM as a z-score of $\leq -1.5$ (as compared to controls) on $\geq 2$ subtests, or $\leq -2.0$ on $\geq 1$ subtests. The finger tapping subtest scores for both dominant and non-dominant hands were averaged to calculate a single subtest z-score. The two subtests for simple reaction times were also averaged to calculate a single summary z-score for both tests. Descriptive statistics were used.

Results: Of the 105 patients, 90.6% female, 45.6% were Caucasian, 16.7% Blacks, 5.3% Asians and 32.6% others. The mean age at SLE diagnosis was 28.0 ± 10.0 and lupus duration at enrolment was 16.3 ± 10.0 years.

Thirty-eight (35.5%) patients had CI based on $z \leq -1.5$ on $\geq 2$ subtests and 43 (40.2%) patients based on $z \leq -2.0$ on $\geq 1$ subtests (Table 1). The prevalence of CI in each of the 15 subtests varied from 3.8-26.4% ($z \leq -1.5$) and 0.9-17.0% ($z \leq -2.0$) (Table 2).

Conclusion: A high prevalence of CI, varying between 35.5-40.2% ($z \leq -1.5$ in $\geq 2$ subtests and $z \leq -2.0$ in $\geq 1$ subtests respectively) was identified by the ANAM in this cohort of young SLE patients. The CI prevalence of 35.5-40.2% is similar to the reported prevalence with ANAM and the comprehensive batteries found in SLE literature. Future studies should address the validity of ANAM (v4) GNS Battery against ACR-SLE battery.

<table>
<thead>
<tr>
<th>Number of Subtests</th>
<th>No. (%) of Patients that scored $z \leq -1.5$</th>
<th>No. (%) of Patients that scored $z \leq -2.0$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>47 (43.9%)</td>
<td>64 (59.8%)</td>
</tr>
<tr>
<td>$\geq 1$</td>
<td>60 (56.1%)</td>
<td>43 (40.2%)</td>
</tr>
<tr>
<td>$\geq 2$</td>
<td>38 (35.5%)</td>
<td>20 (18.7%)</td>
</tr>
<tr>
<td>$\geq 3$</td>
<td>28 (26.1%)</td>
<td>12 (11.2%)</td>
</tr>
<tr>
<td>$\geq 4$</td>
<td>23 (21.5%)</td>
<td>8 (7.5%)</td>
</tr>
<tr>
<td>$\geq 5$</td>
<td>17 (15.9%)</td>
<td>8 (7.5%)</td>
</tr>
<tr>
<td>$\geq 6$</td>
<td>12 (11.2%)</td>
<td>8 (7.5%)</td>
</tr>
<tr>
<td>$\geq 7$</td>
<td>7 (6.5%)</td>
<td>2 (1.9%)</td>
</tr>
<tr>
<td>$\geq 8$</td>
<td>6 (5.6%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>$\geq 9$</td>
<td>5 (4.8%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>$\geq 12$</td>
<td>2 (1.9%)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>

Number of patients with $z$-scores $\leq -1.5$ overlap with patients with $z$-scores $\leq -2$
Table 2. Prevalence of patients with throughput z-scores of ≤-1.5 and ≤-2.0 (N=107)

<table>
<thead>
<tr>
<th>Performance Test</th>
<th>No. (%) of Patients that scored z ≤-1.5</th>
<th>No. (%) of Patients that scored z ≤-2.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple Reaction Time</td>
<td>23 (21.5%)</td>
<td>16 (15.0%)</td>
</tr>
<tr>
<td>Code Substitution - Learning</td>
<td>9 (8.4%)</td>
<td>2 (1.9%)</td>
</tr>
<tr>
<td>Procedural Reaction Time</td>
<td>18 (16.8%)</td>
<td>8 (7.5%)</td>
</tr>
<tr>
<td>Mathematical Processing</td>
<td>14 (13.2%)</td>
<td>5 (4.7%)</td>
</tr>
<tr>
<td>Matching to Sample</td>
<td>20 (18.7%)</td>
<td>7 (6.5%)</td>
</tr>
<tr>
<td>Code Substitution - Delayed</td>
<td>20 (18.7%)</td>
<td>4 (3.7%)</td>
</tr>
<tr>
<td>Simple Reaction Time (R)</td>
<td>28 (26.4%)</td>
<td>18 (17.0%)</td>
</tr>
<tr>
<td>Go/No-Go</td>
<td>4 (3.8%)</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>Logical Relations</td>
<td>21 (19.8%)</td>
<td>10 (9.4%)</td>
</tr>
<tr>
<td>Spatial Processing</td>
<td>16 (15.1%)</td>
<td>8 (7.5%)</td>
</tr>
<tr>
<td>Tower Puzzle</td>
<td>7 (6.7%)</td>
<td>3 (2.9%)</td>
</tr>
<tr>
<td>Tapping - Right Hand</td>
<td>8 (7.9%)</td>
<td>5 (5.0%)</td>
</tr>
<tr>
<td>Tapping - Left Hand</td>
<td>8 (8.1%)</td>
<td>3 (3.0%)</td>
</tr>
<tr>
<td>2-Choice Reaction Time</td>
<td>20 (19.0%)</td>
<td>10 (9.5%)</td>
</tr>
<tr>
<td>Running Memory CPT</td>
<td>19 (18.1%)</td>
<td>12 (11.4%)</td>
</tr>
</tbody>
</table>

Number of patients with z-scores ≤-1.5 include patients with z-scores ≤-2

Disclosure: Z. Touma, None; R. Green, None; L. Ruttan, None; S. Lombardi, None; C. Tartaglia, None; N. Anderson, None; J. Su, None; K. Colosimo, None; M. Vitti, None; D. Bonilla, None; J. E. Wither, None; M. J. Fritzler, Inova Diagnostics, Inc., 5; D. Beaton, None.


Abstract Number: 1622

Associations Among Classification Criteria Items within Systemic Lupus Erythematosus

Zahi Touma¹, Ricard Cervera², Ralph Brinks³, Chiara Tani⁴, Bimba F. Hoyer⁵, Karen H. Costenbader⁶, Valentina Lorenzoni⁷, Gian Sebastiani⁸, Sandra V. Navarra⁹, Eloisa Bonfà¹⁰, Rosalind Ramsey-Goldman¹¹, Sara K. Tedeschi¹², Thomas Doerner¹³, Sindhu Johnson¹⁴, Martin Aringer¹⁵ and Marta Mosca¹⁶, ¹Rheumatology, University of Toronto, Division of Rheumatology, Institute of Health Policy, Management and Evaluation, Toronto, ON, Canada, ²Department of Autoimmune Diseases, Hospital Clinic, Barcelona, Spain, ³Hiller Center for Research in Rheumatology, Dusseldorf, Germany, ⁴University of Pisa, Pisa, Italy, ⁵Charité University Medicine, Department of Medicine/Rheumatology and Clinical Immunology and German Rheumatism Research Centre Berlin (DRFZ), ⁶Rheumatology, University of Toronto, Division of Rheumatology, Institute of Health Policy, Management and Evaluation, Toronto, ON, Canada, ⁷Department of Autoimmune Diseases, Hospital Clinic, Barcelona, Spain, ⁸Hiller Center for Research in Rheumatology, Dusseldorf, Germany, ⁹University of Pisa, Pisa, Italy, ¹⁰Charité University Medicine, Department of Medicine/Rheumatology and Clinical Immunology and German Rheumatism Research Centre Berlin (DRFZ), ¹¹Rheumatology, University of Toronto, Division of Rheumatology, Institute of Health Policy, Management and Evaluation, Toronto, ON, Canada, ¹²Department of Autoimmune Diseases, Hospital Clinic, Barcelona, Spain, ¹³Hiller Center for Research in Rheumatology, Dusseldorf, Germany, ¹⁴University of Pisa, Pisa, Italy, ¹⁵Charité University Medicine, Department of Medicine/Rheumatology and Clinical Immunology and German Rheumatism Research Centre Berlin (DRFZ), ¹⁶Rheumatology, University of Toronto, Division of Rheumatology, Institute of Health Policy, Management and Evaluation, Toronto, ON, Canada, ¹⁷Department of Autoimmune Diseases, Hospital Clinic, Barcelona, Spain, ¹⁸Hiller Center for Research in Rheumatology, Dusseldorf, Germany, ¹⁹University of Pisa, Pisa, Italy, ²⁰Charité University Medicine, Department of Medicine/Rheumatology and Clinical Immunology and German Rheumatism Research Centre Berlin (DRFZ), ²¹Rheumatology, University of Toronto, Division of Rheumatology, Institute of Health Policy, Management and Evaluation, Toronto, ON, Canada, ²²Department of Autoimmune Diseases, Hospital Clinic, Barcelona, Spain, ²³Hiller Center for Research in Rheumatology, Dusseldorf, Germany, ²⁴University of Pisa, Pisa, Italy, ²⁵Charité University Medicine, Department of Medicine/Rheumatology and Clinical Immunology and German Rheumatism Research Centre Berlin (DRFZ),
SESSION INFORMATION

Session Date: Monday, November 6, 2017

Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM

Background/Purpose:

An EULAR/ACR –sponsored project is currently developing new weighted SLE classification criteria including laboratory/clinical items. Combinations of symptoms appear commonly in SLE arguing against lupus as one single disease entity. Moreover, if such “clusters (buckets)” exist this would distort the weightings. It is important to ensure the independence of potential criteria items from each other. We evaluated the interrelationship between candidate criteria items in 2 cohorts.

Methods:

International Early SLE Cohort: 389 SLE patients diagnosed within the last 3 years, from 7 academic centers in Asia (Manila), Europe (Berlin, Pisa), North America (Boston, Chicago, Toronto) and South America (São Paulo). Data on all ACR 1997, SLICC 2012 and 30 additional items were collected.

Tetrachoric correlation coefficients (rho) assessed the association between different items of the same domain (rho 0.2-0.3 borderline and rho > 0.3 meaningful correlation). Mucocutaneous, hematologic and neurological items were examined to avoid overrepresentation.

Euro-Lupus Cohort: 1000 SLE patients from 12 universities (7 European countries). The baseline patient data set was used for the analysis. The complete correlation matrix of the Euro-Lupus clinical data was analyzed. The significant associations identified in the international cohort were validated in the Euro-Lupus cohort.

Results:

Mucocutaneous items: Only malar rash resulted in a correlation ≥ 0.2 with photosensitivity, alopecia, and oral ulcers. Neurological items: Only seizure and the non-criteria symptom migraine showed a correlation ≥ 0.2. Serologic items: A high degree of correlation was found for anti-Śm with anti-RNP, and anti-dsDNA, for anti-Ro with anti-La, and between anti-phospholipid antibodies. Other correlations are represented in Table 1.
With the exception of the correlation between malar rash and oral ulcers, all associations between mucocutaneous manifestations were independently confirmed in the Euro-Lupus cohort.

Correlation matrix of the Euro-Lupus cohort: \( \rho \geq 0.2 \) were only found for fever with alopecia and with nephritis, for lymphadenopathy with fever and with hepatitis, and for Libman-Sacks endocarditis with cardiomyopathy (Figure 1).

**Conclusion:** Significant associations were observed among specific clinical and serologic criteria items in the international cohort, and these results were externally validated in the Euro-Lupus cohort. These results will be considered in the ongoing development of new SLE classification criteria.

### Table 1. Correlation with \( \rho \geq 0.2 \) among cutaneous manifestations, neurological and serologic in the international early SLE cohort

<table>
<thead>
<tr>
<th>Manifestations</th>
<th>Items</th>
<th>Tetrachoric rho</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mucocutaneous</strong></td>
<td>Malar rash vs alopecia</td>
<td>0.250</td>
</tr>
<tr>
<td></td>
<td>Malar rash vs photosensitivity</td>
<td>0.299</td>
</tr>
<tr>
<td></td>
<td>Malar rash vs oral ulcer</td>
<td>0.216</td>
</tr>
<tr>
<td><strong>Neuro</strong></td>
<td>Seizure vs Migraine</td>
<td>0.217</td>
</tr>
<tr>
<td><strong>Serologic</strong></td>
<td>Anti-Sm vs Anti-dsDNA</td>
<td>0.334</td>
</tr>
<tr>
<td></td>
<td>Anti-Sm vs anti-Ro</td>
<td>0.240</td>
</tr>
<tr>
<td></td>
<td>Anti-Sm vs anti-RNP</td>
<td>0.606</td>
</tr>
<tr>
<td></td>
<td>Anti-Ro vs anti-La</td>
<td>0.541</td>
</tr>
<tr>
<td></td>
<td>Anti-Cardiolipin IgG vs IgM</td>
<td>0.382</td>
</tr>
<tr>
<td></td>
<td>Anti-Cardiolipin IgG vs LAC</td>
<td>0.286</td>
</tr>
<tr>
<td></td>
<td>Anti-Cardiolipin IgG vs anti-beta2-GPI</td>
<td>0.510</td>
</tr>
<tr>
<td></td>
<td>Anti-Cardiolipin IgM vs anti-beta2-GPI</td>
<td>0.403</td>
</tr>
<tr>
<td></td>
<td>LAC vs anti-beta2-GPI</td>
<td>0.256</td>
</tr>
<tr>
<td></td>
<td>Anti-dsDNA vs anti-cardiolipin IgM</td>
<td>0.219</td>
</tr>
<tr>
<td></td>
<td>Anti-dsDNA vs anti-cardiolipin IgM</td>
<td>0.219</td>
</tr>
</tbody>
</table>

All \( p \) were < 0.001

List of all studied items but not represented in this table: Discoid rash, subacute rash, stroke, transitory attack, cognitive impairment, seizure, psychosis, migraine, and ANA.
Prevalence of Cognitive Impairment in Systemic Lupus Erythematosus Assessed By a Comprehensive Neuropsychological Battery

Zahi Touma¹, Robin Green², Carmela Tartaglia³, Lesley Ruttan⁴, Sabrina Lombardi⁴, Nicole Anderson⁵, Jiandong Su⁶, Kenneth Colosimo⁶, Michelle Vitti⁶, Dennisse Bonilla⁶, Joan E. Wither⁵, Marvin J. Fritzler⁷ and Dorcas Beaton⁸, ¹Rheumatology, University of Toronto, Division of Rheumatology, Institute of Health Policy, Management and Evaluation, Toronto, ON, Canada, ²Brain and Therapeutics, Toronto Rehabilitation Institute, Toronto, ON, Canada, ³University of Toronto, Krembil Neurosciences Centre, Toronto, ON, Canada, ⁴Toronto Rehabilitation Institute, Toronto, ON, Canada, ⁵Rheumatology, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, ⁶University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, ⁷Medicine, University of Calgary, Calgary, AB, Canada, ⁸Mobility Program Clinical Research Unit, St Michael's Hospital, Toronto, ON, Canada

First publication: September 18, 2017
**Background/Purpose:** Cognitive impairment (CI) is a common neurobehavioural manifestation of SLE. In our recent systematic review, the prevalence of CI was 38% (95% CI: 33-43%) with a wide variation (15-79%), which may be due to differences in CI definitions and selection of neuropsychological tests across studies. We aim to report the prevalence of CI in a large cohort using a comprehensive battery (CB) of tests in which we operationalized the classification of CI.

**Methods:** Consecutive consenting SLE patients, aged 18-65 years, who attended a single center (Jul 2016-Apr 2017) were recruited. Patients were administered a CB that evaluates the major cognitive domains: Manual motor speed and dexterity, simple attention and processing speed, visual-spatial construction, verbal fluency, learning and memory (visuospatial and memory), executive functioning (untimed and timed).

Patient scores were compared to a normative sample of age- and gender-matched healthy controls to obtain z-scores. CI was operationalized on the CB as a z-score of ≤-1.5 (as compared to controls) on ≥2 domains, z ≤-2.0 on ≥1 domain or either. Descriptive statistics were used.

**Results:** Of the 105 patients (91% female), the mean age at SLE diagnosis was 28.4 ± 10.2 and disease duration at enrolment was 15.0 ± 10.1 years. The prevalence of CI was 40.0% (z≤-1.5 in ≥2 domains), 44.8% (z≤-2.0 in ≥1 domains) and 55.2% for either.

Prevalence of patients with domain z-scores of ≤-1.5 and ≤-2.0 varied from 7.6-49.5% and 0-24.8% respectively (**Fig 1**). The most affected domain was learning and memory (visuospatial and memory) in 52 (49.5%) patients based on z≤-1.5 on ≥ 2 subtests and 26 (24.8%) patients based on z≤-2.0 in ≥ 1 subtest.

The prevalence of patients with subtest z-scores of ≤-1.5 and ≤-2.0 from 2.3-44.4% and 0.0-32.2% respectively (**Table 1**).

**Conclusion:** Prevalence of CI using our CB ranged between 40.0-44.8 % (z≤-1.5 in ≥2 domains and z≤-2.0 in ≥1 domains respectively) and 55.2% for either, which was higher than the pooled prevalence from previous reports of 38%. These differences in CI prevalence across studies could be attributed to different factors including the heterogeneity in patients’ demographics/comorbidities, sample size, the use of different metrics to determine CI, and the lack of a standardized definition of CI. Further studies are required to identify the best definition for CI and its metrics.
Table 1. Prevalence of patients with subtest z-scores of ≤-1.5 and ≤-2.0 (n=105)
<table>
<thead>
<tr>
<th>Domains</th>
<th>Comprehensive Battery Subtest</th>
<th>No. (%) of Patients that scored z≤-1.5</th>
<th>No. (%) of Patients that scored z≤-2.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manual motor speed and dexterity</td>
<td>Finger Tapping Test</td>
<td>40 (44.4)</td>
<td>29 (32.2)</td>
</tr>
<tr>
<td></td>
<td>Dominant Hand</td>
<td>33 (37.1)</td>
<td>22 (24.7)</td>
</tr>
<tr>
<td></td>
<td>Non-Dominant Hand</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simple attention and processing speed</td>
<td>Trails A</td>
<td>11 (10.7)</td>
<td>2 (1.9)</td>
</tr>
<tr>
<td></td>
<td>Stroop colour naming</td>
<td>7 (6.7)</td>
<td>3 (2.9)</td>
</tr>
<tr>
<td></td>
<td>Stroop word reading</td>
<td>10 (9.5)</td>
<td>3 (2.9)</td>
</tr>
<tr>
<td>Visual-spatial construction</td>
<td>RCFT Copy</td>
<td>30 (29.1)</td>
<td>23 (22.3)</td>
</tr>
<tr>
<td>Verbal fluency</td>
<td>COWAT</td>
<td>12 (11.4)</td>
<td>6 (5.7)</td>
</tr>
<tr>
<td></td>
<td>ANIMALS</td>
<td>7 (7.2)</td>
<td>4 (4.1)</td>
</tr>
<tr>
<td>Learning and memory:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visuospatial</td>
<td>RCFT Delay Recall</td>
<td>29 (28.4)</td>
<td>17 (16.7)</td>
</tr>
<tr>
<td></td>
<td>RCFT Delay Recognition</td>
<td>16 (15.8)</td>
<td>10 (9.9)</td>
</tr>
<tr>
<td>Verbal</td>
<td>HVLT-R Delayed Recall</td>
<td>32 (31.7)</td>
<td>23 (22.8)</td>
</tr>
<tr>
<td></td>
<td>HVLT-R Recognition</td>
<td>34 (33.7)</td>
<td>24 (23.8)</td>
</tr>
<tr>
<td></td>
<td>HVLT-R total recall</td>
<td>41 (40.6)</td>
<td>18 (17.8)</td>
</tr>
<tr>
<td>Executive functioning:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Untimed</td>
<td>Stroop (interference score)</td>
<td>2 (2.3)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td></td>
<td>WAIS Letter-Number</td>
<td>3 (2.9)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td></td>
<td>Consonant Trigrams (used lower value from 18 second or 36 second)</td>
<td>14 (13.3)</td>
<td>9 (8.6)</td>
</tr>
<tr>
<td></td>
<td>WAIS-III Digit Symbol</td>
<td>5 (4.8)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Executive timed</td>
<td>Trails B</td>
<td>20 (19.4)</td>
<td>6 (5.8)</td>
</tr>
</tbody>
</table>

Number of patients with z-scores ≤-1.5 include patients with z-scores ≤-2
Abstract Number: 1624

SLE Disease Activity Index Glucocorticosteroid Index (SLEDAI-2KG) Identifies More Responders Than Sledai-2K

Zahi Touma1, Dafna D Gladman2, Jiandong Su3, Nicole Anderson4 and Murray Urowitz4, 1Rheumatology, University of Toronto, Division of Rheumatology, Institute of Health Policy, Management and Evaluation, Toronto, ON, Canada, 2Rheumatology, Toronto Western Hospital, University of Toronto, Toronto, ON, Canada, 3University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, 4Rheumatology, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Systemic Lupus Erythematosus Disease Activity Index-2000 (SLEDAI-2K) is one of the most commonly used disease activity indices in clinical practice and research but this index doesn't account for severity within each descriptor. Moreover, in clinical trials, the use of standard of care (SoC), which includes glucocorticosteroid (GCS) often confounds trial results.

We developed and validated a novel lupus disease activity index, SLEDAI-2K GCS (SLEDAI-2KG), that describes disease activity while accounting for GCS dose. SLEDAI-2KG has the same descriptors as SLEDAI-2K in addition to a new descriptor “GCS” with different weight scores based on the dose of GCS. Furthermore, SLEDAI-2KG has a low administration burden and a simple scoring system similar to SLEDAI-2K.

We aimed to compare the performance of SLEDAI-2K and SGI in identifying responders in response to SoC.

Methods:
Patients seen between January 2011 and January 2014, at a single lupus centre, with active disease (SLEDAI-2K ≥6) and on prednisone ≥ 10 mg/day, and with follow up visits within 5-24 months were studied. Treatment was determined based on the judgment of the treating rheumatologist.

Response to SoC therapy, at first follow up visit, was assessed by SLEDAI-2K and SLEDAI-2KG. Responders were defined based on the decrease in SLEDAI-2K and SGI score by ≥4. The performance of SLEDAI-2K and SGI was also compared using different cut-off points; 5, 6 and 7. Descriptive analysis was used in the analysis.

Results:

111 patients met the inclusion criteria of the study and were further analyzed. Patients’ characteristics are represented in table 1. The mean age of the patients at baseline visit was 35.75 ± 11.51 years and the SLE duration was 9.02 ± 7.74. The mean follow-up to 1st visit was 7.68 ± 2.95 months. Mean SLEDAI-2K and SLEDAI-2KG at baseline was 12.39 ± 6.03 and 17.08 ± 6.73 respectively. The mean prednisone dose at baseline was 22.94 ± 14.19 mg/day.

SLEDAI-2KG identified more responders at 6 months (92% vs. 84%) and at 12 months (89% vs. 76%) compared to SLEDAI-2K. SLEDAI-2KG also identified more responders with cut off points5, 6 and 7 (Table 2).

Conclusion:

The novel index, SLEDAI-2KG, is superior to SLEDAI-2K in identifying responders at 6 and 12 months accounting for steroid dose and thus adjusting for severity within each descriptor of SLEDAI-2K. SLEDAI-2KG has the ability to enhance analyses in clinical trials to differentiate between responders on minimal and moderate/large doses of GCS.

<table>
<thead>
<tr>
<th>Table 1. Patient characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Variables</strong></td>
</tr>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>Age at baseline</td>
</tr>
<tr>
<td>SLE duration at baseline</td>
</tr>
<tr>
<td>Ethnicity</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Months from baseline to 1st follow up</td>
</tr>
<tr>
<td>SLEDAI-2K at baseline</td>
</tr>
<tr>
<td>Prednisone dose at baseline</td>
</tr>
<tr>
<td>SLEDAI-2KG at baseline</td>
</tr>
<tr>
<td>SLEDAI-2K at 1st follow up</td>
</tr>
<tr>
<td>Prednisone dose at 1st follow up</td>
</tr>
<tr>
<td>SLEDAI-2KG at 1st follow up</td>
</tr>
</tbody>
</table>
### Table 2. Responders by SLEDAI-2K and SLEDAI-2KG in 111 patients

<table>
<thead>
<tr>
<th>Indices</th>
<th>Percentage of responders at 6 months</th>
<th>Percentage of responders at 12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≥3</td>
<td>≥4</td>
</tr>
<tr>
<td>SLEDAI-2K</td>
<td>84%</td>
<td>84%</td>
</tr>
<tr>
<td>SLEDAI-2KG</td>
<td>95%</td>
<td>92%</td>
</tr>
<tr>
<td>Additional</td>
<td>11%</td>
<td>8%</td>
</tr>
</tbody>
</table>

**Disclosure:** Z. Touma, GlaxoSmithKline, 5; D. D. Gladman, Amgen, AbbVie, BMS, Celgene, Eli Lilly, Janssen, Novartis, Pfizer and UCB., 2; J. Su, None; N. Anderson, None; M. Urowitz, GlaxoSmithKline, 5.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/sle-disease-activity-index-glucocorticosteroid-index-sledai-2kg-identifies-more-responders-than-sledai-2k](http://acrabstracts.org/abstract/sle-disease-activity-index-glucocorticosteroid-index-sledai-2kg-identifies-more-responders-than-sledai-2k)

**Abstract Number:** 1625

**Incidence and Outcomes of Venous Thromboembolism in Hospitalized Patients with Systemic Lupus Erythematosus: Results from Nationwide Inpatient Sample Database 2003-2011**

Shweta Kishore¹, Varun Mittal², Shradha Ahuja³ and Vikas Majithia⁴, ¹Division of Rheumatology, University of Mississippi, Jackson, MS, ²Division of Hematology and Oncology, Albert Einstein Healthcare Network, Philadelphia, PA, ³Division of Hospital Medicine, University of Mississippi, Jackson, MS, ⁴Jackson VA Medical Center and University of Mississippi, Jackson, MS

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Venous thromboembolism (VTE) is a major cause of mortality and morbidity in hospitalized patients. Hospitalized patients with autoimmune disorders are particularly at risk of VTE. The National Inpatient Sample database was analyzed to determine trends in rate of hospitalization and mortality from VTE in hospitalized systemic lupus erythematosus (SLE) patients to assess its impact.

**Methods:** 2003-2011 National Inpatient Sample database of Healthcare Cost and Utilization Project was queried to identify all adults (age ³ 18 years) with SLE. SLE patients hospitalized with VTE as one of the top three diagnoses were identified. Demographic characteristics and in-hospital outcomes of this population were compared to SLE patients without a VTE diagnosis. Multivariate logistic regression analysis was used to obtain adjusted odds ratio (OR).
Results: The total number of hospitalized patients with SLE was 299,595 of which 6266 (2.09%) had VTE. Mean age of the study population was 51 years of and 89% were females. Mean age of SLE patients with VTE was lower than those without VTE (49 vs 51 years). Rate of VTE was higher in African Americans as compared to Caucasians or Hispanics (2.5% vs 2.0%) and in males when compared to females (2.9% vs 2.0%).

After adjusting for potential confounders, compared to those without VTE, SLE patients with VTE had significantly higher inpatient mortality (2.6% vs. 2.0%, OR 1.22 (CI 1.12 – 1.33, p = .001), longer length of stay (LOS) (5 vs. 4 days, OR 2.29 (CI 2.23 – 2.35), p < .001) and higher cost of hospitalization ($26000 vs. $20000, OR 1.46 (CI 1.39 – 1.55), p < .001), greater disability at discharge (OR 1.31 (CI 1.27 – 1.35), p < .001) (Table 1).

Conclusion: VTE in hospitalized patients with SLE is associated with significantly higher inpatient mortality, greater disability at discharge, increased length of stay and higher cost of hospitalization. In this database patients with SLE and VTE were younger. Male sex and African-American race may be associated with an increased risk of VTE in patients with SLE. This cross-sectional study would help in the development and implementation of appropriate prophylactic strategies in high risk SLE population. Further studies are needed to understand the effect of autoimmune diseases on VTE risk among hospitalized patients.

References:


Table 1. Outcomes

<table>
<thead>
<tr>
<th>Variable</th>
<th>All Patients</th>
<th>VTE</th>
<th>No VTE</th>
<th>OR</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient Mortality</td>
<td>9132 (2.6%)</td>
<td>164 (2.0%)</td>
<td>5098 (2.0%)</td>
<td>1.22 (CI 1.12 – 1.33)</td>
<td>0.001</td>
</tr>
<tr>
<td>LOS Median (IQR), Days</td>
<td>4 (3-7)</td>
<td>6 (3-8)</td>
<td>4 (3-7)</td>
<td>1.31 (CI 1.27 – 1.55)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total charges ($10,000) Median (IQR)</td>
<td>2.0 (1.1-3.9)</td>
<td>2.6 (1.4-4.9)</td>
<td>2.0 (1.1-3.9)</td>
<td>2.44 (CI 1.35 – 1.55)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Moderate to severe disability at discharge</td>
<td>77904 (25.0%)</td>
<td>1675 (29.3%)</td>
<td>76228 (25.9%)</td>
<td>2.39 (CI 2.03 – 2.80)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data are presented as Numbers of patients (%) or Median (± IQR).

Disclosure: S. Kishore, None; V. Mittal, None; S. Ahuja, None; V. Majithia, None.


Abstract Number: 1626

Childhood-Onset Predicts Increased Steroid-Related Damage Among Adults with Systemic Lupus Erythematosus

Merav Heshin-Bekenstein1, Emily von Scheven2, Aimee O. Hersh3, Laura Trupin4, Edward H. Yelin4 and Erica Lawson1, 1Pediatric Rheumatology, University of California San Francisco, San Francisco, CA, 2Division of Rheumatology, Department of Pediatrics, University of California San Francisco, San Francisco, CA, 3Pediatrics/Rheumatology, University of Utah, Salt Lake City, UT, 4Medicine/Rheumatology, University of California San Francisco, San Francisco, CA

First publication: September 18, 2017
**Session Information**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Childhood-onset SLE (cSLE) often presents with severe disease, managed with high-dose steroids. However, little is known about differences in long-term steroid toxicity between adults with cSLE and adult-onset SLE (aSLE). The goal of this study was to determine whether adults with cSLE are at increased risk for steroid-related and total disease damage as compared to aSLE, and whether they accumulate more disease damage over time.

**Methods:** Data derive from the 2005-2012 cycles of the Lupus Outcomes Study, a cohort of adults with SLE confirmed by chart review using ACR classification criteria, followed by annual telephone surveys. The Brief Index of Lupus Damage (BILD), a validated, patient-reported measure, was used to assess SLE-associated damage. Participants age 18-63 were included in the analysis (N=897). Those diagnosed at age < 18 years were defined as cSLE (N=113). Outcome variables included total BILD scores at baseline and follow-up (mean=6.3±1.7 years between assessments), and presence of steroid-related damage at any point during the study. Steroid-related damage was defined as a self-reported history of cataracts, osteoporosis, avascular necrosis (AVN) or diabetes mellitus (DM). Logistic regression and negative binomial regression were used to compare cSLE and aSLE groups, adjusting for sex, ethnicity, baseline age and baseline disease duration. General health predictors (hypertension, obesity) and medication predictors (steroid use ever) associated with steroid-related damage were included in the steroid damage analysis.

**Results:** Participants with cSLE were younger (mean age 32±10 vs. 47±10; p<0.001), more likely to be male (12% vs 7%; p=0.05) and less likely to be white (41% vs. 57%; p<0.001). Mean age at diagnosis was 14 (±3) for the cSLE vs. 33 (±10) for aSLE group. Median disease duration was 16 years (range 4-50) for participants with cSLE and 12 years (range 0-42) for aSLE. Nearly all participants reported a history of steroid use. There was no difference in unadjusted frequency of steroid-related damage between cSLE and aSLE groups (59% vs. 60%). However, in adjusted analysis, participants with cSLE were twice as likely to report steroid-related damage (72% vs. 58%, p<0.0001, OR 2.0, 95% CI 1.2-3.4). Steroid-related damage also increased significantly with increased disease duration for both groups (Figure 1). Mean damage score at baseline and increase in damage score over 6.3±1.7 year follow up did not differ between groups in unadjusted or adjusted analyses.

**Conclusion:** In this large cohort of adults with SLE, childhood-onset predicted increased risk of steroid-related damage. Participants with cSLE and aSLE continued to accumulate disease-related damage at similar frequencies over time. More aggressive use of steroid-sparing management strategies during childhood may be important to prevent increased risk of steroid-related damage in adulthood.
Changes in Heart Rate Variability Reflect Changes in Clinical Status and Patient Reported Outcomes in Systemic Lupus Erythematosus: A Longitudinal Analysis

Aikaterini Thanou1, Stavros Stavrakis2, Justin Reynolds3, Stan Kamp1, Paul Kamp1, Judith A. James4 and Joan T. Merrill5, 1Arthritis and Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, 2University of Oklahoma Health Sciences Center, Ok, OK, 3University of Oklahoma Health Sciences Center, Oklahoma City, OK, 4Arthritis & Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 5Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation, Oklahoma City, OK

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: We have previously observed associations between systemic lupus erythematosus (SLE) disease activity and heart rate variability (HRV) between 2 time points (1). We aim to prospectively test the hypothesis that HRV reflects longitudinal changes in clinical status and patient reported outcomes.

Methods: HRV was evaluated using a 5 min ECG in SLE patients who completed a minimum of 2 visits in an ongoing clinical trial. HRV parameters were calculated in the time domain (RMSSD and pNN50) and frequency domain [high frequency (HF), low to high frequency (LF/HF) ratio]. A mixed effects linear model with generalized
estimating equations was used to compare changes in HRV between paired visits and to examine linear associations between HRV and clinical scores. All models were adjusted for baseline HRV.

**Results:** Forty nine patients (age 44.9 ± 11.7, 46 female) were followed in 413 paired visits (median time between visits 1 month). BILAG was inversely associated with RMSSD (β=-1.39±0.01; p<0.0001). BILAG, SLEDAI and PGA were directly associated with the LF/HF ratio (β=0.96±0.02; p<0.0001, 0.42±0.10; p<0.0001 and 0.83±0.09; p<0.0001, respectively). Changes in BILAG were inversely associated with changes in RMSSD and pNN50 (β=-7.0±1.9; p=0.003 and -1.6±0.04; p<0.0001, respectively). BILAG changes were also directly associated with changes in the LF/HF ratio (β=0.78±0.05; p<0.0001). Categorical improvement (≥1 letter grade improvement in BILAG and no new BILAG A/B) occurred in 77 (19%) visit pairs (group 1) and no improvement or worsening in 335 (81%) (group 2). RMSSD and HF increased in group 1 vs. group 2 (group difference=-33.3±10.1; p=0.001 and -30.9±4.1; p<0.0001, respectively), and the LF/HF ratio decreased in group 1 vs. group 2 (group difference=3.1±0.8; p=0.002). The average per visit changes in HRV in groups 1 and 2 are listed in Table 1.

Changes in Physical Component Summary (PCS) of SF36v2 were inversely related to changes in SLEDAI and PGA (β=-0.39±0.14; p=0.006 and -0.19±0.02; p<0.0001, respectively). Changes in Mental Component Summary (MCS) were inversely related to changes in BILAG, SLEDAI and PGA (β=-0.23±0.07; p=0.0001, -0.31±0.10; p=0.002 and -0.08±0.03; p=0.008, respectively). PCS was related to HF (β=0.67±0.28, p=0.01) and MCS was inversely related to the LF/HF ratio (β=-0.11±0.03, p=0.0001). Changes in PCS were related to changes in pNN50 (β=0.21±0.05, p<0.0001) and LF/HF (β=0.17±0.06, p=0.003) and changes in MCS were related to changes in HF (β=1.57±0.18; p<0.0001).

**Conclusion:** Changes in HRV reflect changes in clinical status and patient reported outcomes in patients with SLE. These data suggest that HRV may be a simple non-invasive tool used to gauge or predict clinical improvement in SLE. Further studies are warranted.

### Table 1. Average per visit changes in HRV in groups 1 and 2.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1</th>
<th>Group 2</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RMSSD</td>
<td>2.9±1.2</td>
<td>-3.5±1.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HF</td>
<td>6.9±0.4</td>
<td>0.5±0.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PNN50</td>
<td>0.10±0.23</td>
<td>-0.15±0.20</td>
<td>0.81</td>
</tr>
<tr>
<td>LF/HF</td>
<td>-0.83±0.07</td>
<td>0.13±0.07</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>


**Disclosure:** A. Thanou, None; S. Stavrakis, None; J. Reynolds, None; S. Kamp, None; P. Kamp, None; J. A. James, None; J. T. Merrill, Anthera Pharmaceuticals, Lilly, EMD Serono, GlaxoSmithKline and Biogen., 5.


**Abstract Number:** 1628

**Atrial Fibrillation/Flutter Hospitalizations Among Patients with SLE and Diabetes Compared to the General U.S. Medicaid Population**

Sarah Chen¹, Medha Barbhaiya², Michael A. Fischer³, Hongshu Guan⁴, Candace H. Feldman⁵, Brendan M. Everett⁶ and Karen H. Costenbader⁷, ¹Brigham and Women's Hospital, Boston, MA, ²Rheumatology, Immunology
SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: SLE patients have increased cardiovascular disease (CVD) risk, including higher risk of stroke, compared to age- and sex-matched diabetes mellitus (DM) patients. Although DM confers high risk of developing atrial fibrillation/flutter (AF), AF prevalence rates, a contributor to stroke, among SLE patients are unknown. We investigated rates and risks of AF hospitalization among SLE patients compared to age- and sex-matched DM and general Medicaid population.

Methods: We used Medicaid Analytic eXtract (MAX) data, containing all billing claims for Medicaid patients from the 29 most populated US states, 2007-2010. We included patients ages 18-65 in three separate cohorts: prevalent SLE, prevalent DM, and a non-SLE, non-DM general Medicaid cohort. We required >3 ICD-9 codes for SLE or DM, each separated by >30 days. Index date was the date of the 3rd diagnosis code. The general Medicaid cohort was selected by using non-SLE, non-DM ICD-9 codes on the same date as SLE index date. All cohorts required baseline period of 6 months of continuous Medicaid enrollment prior to the index date. Each SLE patient was matched to 2 DM, and 4 non-SLE, non-DM patients by age at index date, and sex. Subjects were followed from index date until death, disenrollment or end of follow-up. We used ICD-9 codes to identify outcomes of AF within primary or secondary hospital discharge diagnoses and calculated rates of first AF hospitalization events per 1,000 person-years. We used Cox regression models to calculate hazard ratios (HR) for first AF hospitalization events. In a secondary analysis, we excluded those with baseline AF.

Results: 40,212 SLE patients were matched to 80,424 DM and 160,848 general Medicaid patients. In all cohorts, 92% were female and mean age was 40.3 (+12.1) years. Mean follow up was 1.8 (+1.1) years for SLE, 1.8 (+1.1) years for DM, and 1.6 (+1.2) years for general Medicaid patients. Baseline CVD was prevalent in 18% SLE, 13% DM and 1% general Medicaid cohorts. Baseline prevalence of AF was 1% in SLE, <1% in DM and <1% in general Medicaid cohorts. Anticoagulant use was present in 7% of SLE vs 2% of DM patients (p<0.001). Beta-blocker use was similar between SLE and DM cohorts (11% in both). AF hospitalization rates per 1,000 person-years were similar in SLE vs DM, and nearly double that in the general Medicaid cohort (Table). The adjusted HR for first AF hospitalization was increased among DM (HR 1.9, 95% CI 1.6-2.3) and SLE (HR 1.4, 95% CI 1.1-1.8) patients compared to the general patients, and remained increased after excluding patients with baseline AF.

Conclusion: First AF hospitalization rate among SLE patients was double that of the general non-SLE, non-DM Medicaid population, and similar to the rate among age- and sex-matched DM patients. Adjusted HRs for first AF hospitalization among SLE patients was as high as in DM patients. As DM is a known AF contributor, the similarly elevated risk among SLE patients warrants further investigation.
Table. Rates and Multivariable Hazard Ratios for Hospitalizations for Atrial Fibrillation/Flutter* among SLE, and age- and sex-matched DM and General (non-SLE, non-DM) Medicaid Population, 2007-2010

<table>
<thead>
<tr>
<th>Cohort†</th>
<th>Events</th>
<th>Person-years</th>
<th>Rate‡ (95% CI)</th>
<th>Including all patients HR§ (95% CI)</th>
<th>Excluding patients with baseline atrial fibrillation/flutter</th>
</tr>
</thead>
<tbody>
<tr>
<td>General Medicaid</td>
<td>207</td>
<td>250,762</td>
<td>0.8 (0.7-1.0)</td>
<td>1.0 (ref)</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>SLE</td>
<td>119</td>
<td>74,151</td>
<td>1.6 (1.3-1.9)</td>
<td>1.4 (1.1-1.8)</td>
<td>1.5 (1.2-1.9)</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>240</td>
<td>147,584</td>
<td>1.6 (1.4-1.9)</td>
<td>1.9 (1.6-2.3)</td>
<td>1.5 (1.2-1.8)</td>
</tr>
</tbody>
</table>

* Atrial fibrillation/flutter: By primary or secondary hospitalization ICD-9 diagnosis codes 427.31, 427.32
† Cohort: SLE cohort defined as >3 SLE ICD-9 codes (710.0), each separated by >30 days; DM cohort defined as >3 ICD-9 codes (249.XX, 250.XX, 357.2, 362.01-362.06, 366.41), 1:2 matched by age, sex to SLE cohort; General Medicaid cohort defined as any non-SLE, non-DM ICD-9 code on same date as SLE index date, 1:4 matched by age, and sex to SLE cohort
‡ Rate: Rate of first atrial fibrillation/flutter hospitalization events per 1000 person-years of follow-up
§ HR: Hazard ratio for first atrial fibrillation/flutter hospitalization event adjusted for: age, sex, race/ethnicity, US region of residence, zip-code level socioeconomic status, Charlson comorbidity index; Two separate Cox proportional hazard models: 1) including all patients, 2) excluding patients who had baseline atrial fibrillation/flutter diagnosis

Disclosure: S. Chen, None; M. Barbhaiya, None; M. A. Fischer, None; H. Guan, None; C. H. Feldman, None; B. M. Everett, None; K. H. Costenbader, None.


Abstract Number: 1629

**Disease Activity Is an Independent Predictor of Leukopenia in a Large International SLE Cohort**

Rangi Kandane-Rathnayake\(^1\), Vera Golder\(^2\), Worawit Louthrenoo\(^3\), Sargunan Sockalingam\(^4\), Aisha Lateef\(^5\), Yuan An\(^6\), Leonid Zamora\(^7\), Yeong-Jian Wu\(^8\), Shue-Fen Luo\(^9\), Madelynn Chan\(^10\), Fiona Goldblatt\(^11\), Chak Sing Lau\(^12\), Zhan-Guo Li\(^13\), Sandra V. Navarra\(^7\), Mandana Nikpour\(^14\), Eric F Morand\(^15\) and **Alberta Y. Hoi**\(^2\), \(^1\)Rheumatology, Monash University, Melbourne, Australia, \(^2\)Centre for Inflammatory Diseases, Monash University, Melbourne, Australia, \(^3\)Division of Rheumatology, Department of Internal Medicine, Chiang Mai University, Chiang Mai, Thailand, \(^4\)University of Malaya, Kuala Lumpur, Malaysia, \(^5\)Medicine, Division of Rheumatology, National University Hospital of Singapore, Singapore, Singapore, \(^6\)Peking University People's Hospital, Beijing, China, \(^7\)Rheumatology, University of Santo Tomas Hospital, Manila, Philippines, \(^8\)Chang Gung University, Taoyuan County, Taiwan, \(^9\)Division of Rheumatology, Allergy and Immunology, Chang Gung Memorial Hospital, Taoyuan, Taiwan, \(^10\)Tan Tock Seng Hospital, Singapore, Singapore, \(^11\)Flinders University, Adelaide, Australia, \(^12\)Univ Dept
Background/Purpose: Leukopenia is commonly seen in SLE, but its predictors are not well understood, as it can be a result of disease activity or bone marrow suppression from immunosuppressive medications.

Methods: Data from 6071 visits in 1352 patients from a multinational lupus cohort were analysed. All patients met either ACR criteria (91%) or SLICC classification criteria (98.5%). Only patients with ≥2 visits were included in the analysis. Leukopenia was defined according to Common Terminology Criteria for Adverse Events (V3), of at least grade 2 (moderate) severity i.e. total white cell count<3 or lymphocyte count<0.8 or neutropenia<1.5. The generalised estimating equation method was used to examine longitudinal associations of leukopenia with factors including demographics (age, gender, ethnicity, SLE family history), serology (low complement/anti-dsDNA positivity), disease characteristics such as SLE Disease Activity Index (SLEDAI-2k) score, flare, physician global assessment (PGA), damage accrual Lupus Low Disease Activity State (LLDAS), and medication use.

Results: Thirty-five percent of patients had at least one episode of leukopenia over 1585 patient-years (24% of all visits). SLEDAI-2k≥6, flare, and PGA>1 were all significantly associated with increased odds of leukopenia (p<0.01). Low complement and high ESR were also significantly associated with leukopenia (p<0.01). In contrast, LLDAS was significantly associated with reduced odds of leukopenia, with an unadjusted odds ratio (OR) = 0.71, 95% CI 0.62-0.81, p<0.01. The only immunosuppressant that was significantly associated with leukopenia was rituximab, OR 2.4, 95% CI 1.17-4.91, p=0.02. Azathioprine and leflunomide use had weak associations with leukopenia but did not reach statistical significance in univariable analysis (p-value 0.09 and 0.08 respectively). Neither methotrexate or mycophenolate use was associated with leukopenia. After adjustment in multivariable analysis models, statistically significant associations with leukopenia remained for SLEDAI≥6 (OR 1.33, 95% CI: 1.09 to 1.62; p <0.01), ESR>25 ( OR ESR>25 = 1.36, 95%CI 1.14-1.61; p<0.01), rituximab (OR 3.11, 95% CI 1.45-6.65; p<0.01) and azathioprine use (OR 1.58, 95% CI 1.24-2.01; p<0.01); the association of LLDAS with reduced odds of leukopenia also remained significant (OR = 0.56, 95% CI: 0.46 to 0.68; p-value<0.01).

Conclusion: SLE disease activity is a significant predictor of leukopenia, and leukopenia is negatively associated with LLDAS. Of the medications commonly used in SLE, rituximab and azathioprine were significantly associated with leukopenia.

Disclosure: R. Kandane-Rathnayake, None; V. Golder, None; W. Louthrenoo, None; S. Sockalingam, None; A. Lateef, None; Y. An, None; L. Zamora, None; Y. J. Wu, None; S. F. Luo, None; M. Chan, None; F. Goldblatt, None; C. S. Lau, None; Z. G. Li, None; S. V. Navarra, None; M. Nikpour, None; E. F. Morand, None; A. Y. Hoi, None.
Achievement of Lupus Low Disease Activity State (LLDAS) in the Early Phase of Systemic Lupus Erythematosus Prevent Damage Accrual

Matteo Piga, Alberto Floris, Giulia Cappellazzo, Alessandro Mathieu and Alberto Cauli, Unit and Chair of Rheumatology, University Hospital of Cagliari, Cagliari, Italy
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The Asia-Pacific Collaboration Group has recently proposed the definition of Lupus Low Disease Activity state (LLDAS). This potential target in SLE treatment has been applied so far in a few longstanding SLE cohorts with not homogeneous disease duration. The present study aims to assess attainability and outcome of the LLDAS in the early stages of systemic lupus erythematosus (SLE) diagnosis and management.

Methods: LLDAS prevalence was evaluated at 6 (T1) and 18 (T2) months after treatment initiation (T0) in a monocentric cohort of 107 (median disease duration 9.7 months) prospectively followed Caucasian SLE patients. Reasons for failure to achieve LLDAS were also investigated. Multivariate models were built, using co-variates with p<0.1 at univariate analysis, to identify factors associated with failure to LLDAS achievement and to investigate the relationship between LLDAS and SLICC/Damage Index (SDI) accrual.

Results: Forty-seven (43.9%) patients were in LLDAS at T1 and 48 (44.9%) at T2. The most frequent unmet LLDAS criteria was the prednisolone dose ≤7.5mg/day (unmet in 83% of no-LLDAS at T1). The disease manifestations with the highest persistence rate during follow-up were: increased anti-dsDNA (persistently present in 85.7% and 67.5% of cases at T1 and T2, respectively), low complement (73.2% and 66.3%) and renal abnormalities (46.4% and 28.6%). Renal involvement at T0 was significantly associated with failure to achieve LLDAS both at T1 (OR: 7.8, 95%CI: 1.41-43.40; p=0.019) and T2 (OR: 3.87, 95%CI 1.41-10.6; p=0.008). In regard of organ damage, 27 SDI-items (9 of them steroid-related) were recorded in 23 (21.5%) patients at T2. Presence of any organ damage (SDI ≥1) at T2 was significantly associated to no-LLDAS at T1 (OR: 5.01, 95%CI 1.51-16.63; p=0.009) and age at diagnosis (OR: 1.05 per year, 95%CI 1.01-1.09; p=0.020).

Conclusion: LLDAS is a promising target in the early stages of SLE management being attainable and negatively associated to damage accrual. However, it seems to poorly fit to patients with renal involvement and a greater consensus should be reached on the definition of significant serological disorders and minimal acceptable prednisolone dose.

Disclosure: M. Piga, None; A. Floris, None; G. Cappellazzo, None; A. Mathieu, None; A. Cauli, None.


Abstract Number: 1631

Hospital Readmissions for SLE in the United States: A National Database Study
Hospital Readmissions For SLE In The United States: A National Database Study

**Background/Purpose:** Systemic lupus erythematosus (SLE) is associated with significant mortality and morbidity, and increased hospital readmissions. Data about readmissions among SLE patients on a national level in the United States is sparse. The aim of this study was to describe unplanned hospital readmission rates among adult SLE patients and assess predictors of readmission.

**Methods:** We analyzed the 2013 National Readmission Database (NRD) to quantify readmission rates among SLE patients. We identified comorbidities and reasons for unplanned 30-day readmissions using administrative codes. We then used survey logistic regression to elucidate predictors for unplanned readmissions using adjusted odds ratios (aOR) and 95% confidence intervals (CI).

**Results:** Among 7926 patients with SLE, 1641 had at least one unplanned 30-days readmissions (20.7%). 39% of readmissions were related to SLE (Figure 1A). Readmitted patients were more likely to be young, have glomerulonephritis (GN), chronic kidney disease (CKD), pericarditis, pleuritis, thrombocytopenia and longer length of hospital stay. Significant predictors of SLE included age 18-25 years, CKD, GN, pericarditis, psychosis, anemia, thrombocytopenia, length of stay > 4 days, patients having Medicare and Medicaid insurance, home health care and against medical advice discharges after adjusting for socio-demographics, comorbidities and hospital characteristic (Figure 1). Cost of hospitalization was $12,522 in patients without readmission compared to $15,716 for index admission in patients with readmission (Figure 2). Cost of readmission was an additional $14,409.

**Conclusion:** In NRD, 20.7% of patients admitted with a primary diagnosis of SLE were readmitted within 30 days. This underscores the importance of close outpatient follow up in the post discharge period especially in high-risk patients with co-morbidities. Readmissions were associated with significant cost.
SLE Characteristics Associated with Modified Framingham Risk Score in Patients without Clinical Cardiovascular Disease

Elizabeth George¹, Thania Perez², Nelson Perez³, Anca Askanase⁴ and Laura Geraldino-Pardilla⁵, ¹Rheumatology, Columbia University College of Physicians and Surgeons, New York, NY, ²Columbia University College of Physicians & Surgeons, New York, NY, ³Hospital Regional Universitario Jose Maria Cabral y Baez, Santiago, Dominican Republic, ⁴Rheumatology, Columbia University College of Physicians & Surgeons, New York, NY, ⁵Columbia University, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Cardiovascular disease (CVD) is a leading cause of mortality in SLE and identifying those at risk remains challenging. While in the general population the Framingham Risk Score (FRS) and high-sensitivity CRP (hsCRP) are good predictors of CVD, in SLE their value remains controversial due to the known underperformance of the FRS and the variability of hsCRP levels. Interestingly high prevalence of nonspecific ST-T segment (NST-T) abnormalities was noted in an SLE inception cohort. While in the general population NST-T abnormalities are associated with increased risk of cardiovascular events, in SLE this association remains
unknown. Therefore, we sought to identify SLE characteristics associated with the modified FRS (mFRS) as a surrogate outcome for CVD, with a particular interest in NST-T and hsCRP.

**Methods:** Adult SLE patients without clinical CVD continuously seen at a University Lupus Center between April 2016 and March 2017, meeting 1997 ACR classification criteria for SLE were studied. Patient characteristics including demographics, SLE-specific features, medication use, traditional CVD risk factors, 12-lead electrocardiogram (EKG), and hsCRP, were ascertained. High-level hsCRP was defined as ≥75th percentile. Univariable and multivariable linear regression models were constructed to test the association of NST-T and high-level hsCRP with the mFRS.

**Results:** One hundred and thirty five SLE patients (baseline characteristics in table 1) were studied. In univariable analyses, presence of NST-T abnormalities (0.389, p=0.025), high-level hsCRP (0.421, p=0.033), and the SLICC/ACR Damage Index (SDI) (0.24, p=0.004) were significantly associated with a higher mFRS. After adjusting for variables associated with NST-T abnormalities, hsCRP, and the SDI, respectively, including total protein, Female sex and use of methotrexate these associations remained statistically significant (NST-T:0.816, p=0.024; hsCRP75:0.527, p=0.017; and SDI:0.193, p=0.016)(Figure 1).

**Conclusion:** EKG nonspecific ST-T abnormalities, high-level hsCRP and the SDI are all independently associated with a higher mFRS in SLE patients without clinical CVD.
Disclosure: E. George, None; T. Perez, None; N. Perez, None; A. Askanase, Exagen, 2; L. Geraldino-Pardilla, None.


Abstract Number: 1633
Use of Emergency Department (ED) and Resulting Hospitalization By Patients with Systemic Lupus Erythematosus (SLE) in a Predominantly Afro-Caribbean Inner-City Cohort

Maushmi Savjani1, Justin Levinson2 and Ellen M. Ginzler3, 1Internal Medicine, Division of Rheumatology, Department of Medicine, SUNY Downstate Medical Center, Brooklyn, NY, 2Medicine, Division of Rheumatology, Department of Medicine, SUNY Downstate Medical Center, Brooklyn, NY, 3Rheumatology, Division of Rheumatology, Department of Medicine, SUNY Downstate Medical Center, Brooklyn, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Given the complexity, chronicity and associated co-morbidities, management of SLE poses a challenge. Despite established care in private and fellow/resident clinics, our patients often go to ED, resulting in inappropriate and costly hospitalizations. Our aim is to reduce ED visits with appropriate outpatient rheumatology care, instate appropriate ED rheumatology consults, and reduce unnecessary hospitalizations.

Methods:
We reviewed SLE patients seen by the Rheumatology Division at least once from 7/2013 to 6/2015, quantifying ED visits and subsequent hospitalization or discharge from 1/2010 to 6/2015. We compared age at SLE diagnosis, SLE duration when first seen by us, and insurance status of “ED users” (at least 1 ED visit) with “ED non-users” (no ED visits). Frequency of ED rheumatology consults among hospitalized vs. discharged patients was noted. After introduction of education tools (Medical ground Rounds presentation of our data and implementation of required rheumatology rotation by our EM-IM residents), we re-assessed the relationship between ED visit frequency and clinic visits in ED user vs. non-users.

Results:
363 SLE patients had 1700 ED visits (range 1-72), leading to 774 hospitalizations over a 5.5-year period. 25 excluded due to lack of data. Among 338 patients, 95 were ED non-users and 243 were ED users, totaling 1608 ED visits with 727 hospitalizations. Among ED users, 61(25%) had no hospitalizations; 34 (14%) were followed privately vs. 201(83%) in clinic. 33(35%) private and 62(65%) clinic patients had no ED visits (Table 1). Only 112 (7%) of ED visits had a rheumatology consult in the ED; 68 (61%) were hospitalized and 44 (39%) were discharged. Pre- and post-educational tools introduction data presented in Table 2.

Conclusion:
Our SLE cohort had frequent ED visits followed by high rate of hospitalization. The difference in mean age at SLE diagnosis, mean SLE duration and insurance status between ED users vs. non-users was small. Only 14% of patients followed privately had any ED visits compared to 83% of clinic patients, yet the % of non-users was higher in clinic patients. Rheumatology consult was requested in only 7%, yet 39% resulted in discharge from the ED, potentially preventing unnecessary hospitalization. Pre- and post-educational tools showed reduction in ED visits and hospitalization among ED users, however, a decrease in clinic visits could be confounded by loss to follow-up. Consistent outpatient care in those not requiring hospitalization and case managers for high-risk patients should reduce inappropriate ED visits and subsequent hospitalizations.
Table 1: Comparisons between ED Users vs Non-users from January 2010 to June 2015

<table>
<thead>
<tr>
<th></th>
<th>ED users (at least 1 visit) n = 243</th>
<th>ED non-users (no ED visits) n = 95</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age at SLE Diagnosis (years)</td>
<td>30.89</td>
<td>32.30</td>
</tr>
<tr>
<td>Mean SLE duration when 1st seen by Rheumatology Division (years)</td>
<td>3.59</td>
<td>4.81</td>
</tr>
<tr>
<td>Without Insurance</td>
<td>6 (2.4%)</td>
<td>5 (5.3%)</td>
</tr>
<tr>
<td>Followed Privately</td>
<td>34 (14%) =&gt; 143 ED visits =&gt; 51 hospitalizations</td>
<td>33 (35%)</td>
</tr>
<tr>
<td>Followed in Fellow/Resident Clinic</td>
<td>201 (83%) =&gt; 1465 ED visits =&gt; 676 hospitalizations</td>
<td>62 (65%)</td>
</tr>
<tr>
<td>Seen only as Inpatient Consultation</td>
<td>8 (3.3%)</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 2: Relationship between ED visit frequency and Clinic visits pre- and post-educational tools introduction (Medical Ground Rounds and Rheumatology Rotation requirement for EM-IM residents). Private patients and those seen only as inpatient consults were excluded.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ED visits</td>
<td>Clinic visits</td>
</tr>
<tr>
<td>ED non-users n = 95</td>
<td>0</td>
<td>348</td>
</tr>
<tr>
<td>ED users n = 234</td>
<td>562 (2.8/pt)</td>
<td>1370 (6.82/pt)</td>
</tr>
</tbody>
</table>

Disclosure: M. Savjani, None; J. Levinson, None; E. M. Ginzler, GlaxoSmith Kline, Aurinia, Genentech, Ablynx, Janssen, 2.

Body Mass Index and Disease Activity in Systemic Lupus Erythematosus- a Paradoxical Relationship?

George Stojan¹, Wei Fu² and Michelle Petri³, ¹Medicine, Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, ²Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, ³Medicine (Rheumatology), Division of Rheumatology, Johns Hopkins University School of Medicine, MD, USA, Baltimore, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Obesity is more common in patients with SLE compared to the general population. The prevalence of obesity among SLE patients is between 28 and 50 percent. Despite the high prevalence of obesity in this population, the effect of obesity on disease activity in SLE has not been studied. We hypothesized that the BMI at cohort entry was predictive of future disease activity and that changes in BMI during cohort follow up were associated with disease activity independent of corticosteroid treatment.

Methods:
2406 patients in a prospective SLE cohort had their weight assessed at each visit. Patients were categorized into five predetermined groups based on weight: low (BMI<20 kg/m²), normal weight (reference, BMI 20-24.9 kg/m²), overweight (25-29.9 kg/m²), obese (BMI 30-34.9 kg/m²), and severely obese (BMI>35 kg/m²). To calculate adjusted mean of SLEDAI over time, we only included patients attending the clinic at 3 month intervals for a minimum of 3 visits. 1896 patients were included in the analysis. 1763 (93.0%) were females. Majority (53.0%) were Caucasians, 39.0% African American. A within-person analysis was then performed to assess whether a person’s disease activity level changed if a person’s BMI changed.

Results:
Adjusted mean of SLEDAI over time did not differ between different BMI groups (table 1). SLEDAI significantly decreased by 0.03 with one unit increase in BMI (table 2). In Table 3, we calculated association between mean centered BMI (BMI – individual average BMI) and mean centered SLEDAI (SLEDAI – individual average SLEDAI) which showed a similar association.

Table 1. Adjusted Mean of SLEDAI Over Time by BMI at Entry Visit
<table>
<thead>
<tr>
<th>BMI</th>
<th>N (%)</th>
<th>SLEDAI Mean (SD)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (Reference)</td>
<td>655(34.5)</td>
<td>2.7(2.4)</td>
<td>REF</td>
</tr>
<tr>
<td>Low</td>
<td>183(9.7)</td>
<td>2.9(2.2)</td>
<td>1</td>
</tr>
<tr>
<td>Overweight</td>
<td>531(28)</td>
<td>2.5(2.1)</td>
<td>1</td>
</tr>
<tr>
<td>Obese</td>
<td>290(15.3)</td>
<td>2.6(2.1)</td>
<td>1</td>
</tr>
<tr>
<td>Severely Obese</td>
<td>237(12.5)</td>
<td>2.5(2.1)</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 2. Association of Disease activity with continuous BMI

<table>
<thead>
<tr>
<th>Mean difference (95% CI)</th>
<th>P value</th>
<th>Adj. Mean difference (95%CI)*</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>-0.03 (-0.04, 0.01)</td>
<td>&lt;0.0001</td>
<td>-0.03(-0.04,-0.02)</td>
</tr>
</tbody>
</table>

* Adjust for age, race and prednisone at visit

Table 3. Association of mean centered SLEDAI with mean centered BMI

<table>
<thead>
<tr>
<th>Mean difference (95% CI)</th>
<th>P value</th>
<th>Adj. Mean difference (95%CI)*</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Centered BMI</td>
<td>-0.06(-0.07,-0.05)</td>
<td>&lt;0.0001</td>
<td>-0.06(-0.07,-0.05)</td>
</tr>
</tbody>
</table>

* Adjust for age, race and prednisone at visit

**Conclusion:**

Body weight at cohort entry was not predictive of future disease activity. There was an inverse correlation between changes in body mass index and disease activity even after adjusting for prednisone use. This is the first evidence to our knowledge of an obesity paradox in systemic lupus.

**Disclosure:** G. Stojan, None; W. Fu, None; M. Petri, Anthera Inc, 5,GlaxoSmithKline, 5,EMD Serono, 5,Eli Lilly and Company, 5,Bristol Meyer Squibb, 5,Amgen, 5,United Rheumatology, 5,Global Academy, 5,Exagen, 2.


**Abstract Number: 1635**

**Cachexia in Systemic Lupus Erythematosus- an Underrecognized Syndrome**

George Stojan1, Laurence S Magder2,3 and Michelle Petri4, 1Medicine, Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, 2Epidemiology and Public Health, Johns Hopkins University
SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Cachexia is a syndrome that may accompany a range of diseases, including cancer, chronic heart failure, chronic obstructive pulmonary disease, and rheumatoid arthritis. It is associated with central and systemic increases of pro-inflammatory factors, and with decreased quality of life, poor responses to pharmacological treatment and shortened survival. Despite an abundance of data from other inflammatory diseases, cachexia in systemic lupus erythematosus remains a largely undescribed syndrome.

Methods:

2406 patients in a prospective SLE cohort had their weight assessed at each visit. Patients were categorized into five predetermined groups based on weight: low (BMI<20 kg/m²), normal weight (reference, BMI 20-24.9 kg/m²), overweight (25-29.9 kg/m²), obese (BMI 30-34.9 kg/m²), and severely obese (BMI>35 kg/m²). Cachexia was defined based on modified Fearon criteria as 5% stable weight loss in 6 months without starvation relative to the average weight in all prior cohort visits AND/OR weight loss >2% without starvation relative to the average weight in all prior cohort visits and a BMI <20. Risk of cachexia within 5 years of cohort entry was based on Kaplan Meier estimates. Differences by patient characteristics were based on log-rank test.

Results:

Table 1: Risk of Cachexia within 5 years of cohort entry
<table>
<thead>
<tr>
<th>Patient Characteristic</th>
<th>Risk of Cachexia within 5 years of cohort entry (95% CI)</th>
<th>P-value for difference by patient characteristic</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (n=2452)</td>
<td>53% (51%, 56%)</td>
<td></td>
</tr>
<tr>
<td>Age Group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30 (n=805)</td>
<td>60% (56%, 64%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>30-44 (n=987)</td>
<td>51% (47%, 55%)</td>
<td></td>
</tr>
<tr>
<td>45-59 (n=528)</td>
<td>46% (41%, 52%)</td>
<td></td>
</tr>
<tr>
<td>60+ (n=132)</td>
<td>57% (46%, 67%)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White (n=1309)</td>
<td>63% (54%, 72%)</td>
<td>0.050</td>
</tr>
<tr>
<td>Black (n=183)</td>
<td>52% (48%, 55%)</td>
<td></td>
</tr>
<tr>
<td>Other (n=960)</td>
<td>53% (50%, 57%)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female (n=2266)</td>
<td>51% (42%, 60%)</td>
<td>0.62</td>
</tr>
<tr>
<td>Male (n=186)</td>
<td>53% (51%, 56%)</td>
<td></td>
</tr>
<tr>
<td>Initial BMI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20 (n=220)</td>
<td>73% (66%, 79%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>20-24.9 (n=782)</td>
<td>59% (55%, 68%)</td>
<td></td>
</tr>
<tr>
<td>25-29.9 (n=632)</td>
<td>64% (59%, 68%)</td>
<td></td>
</tr>
<tr>
<td>30+ (n=635)</td>
<td>37% (33%, 41%)</td>
<td></td>
</tr>
</tbody>
</table>

1Based on Kaplan-Meier estimates

2Based on a log-rank test.

Table 2: Rate ratio comparing those with prior disease manifestation to those without with respect to incidence of cachexia.
Prior Disease Manifestation | Rate Ratio (95% CI) | P-value  
--- | --- | ---  
Malar Rash | 1.1 (0.9, 1.2) | 0.41  
Discoid Rash | 0.8 (0.7, 0.9) | 0.0002  
Photosensitivity | 0.9 (0.8, 1.0) | 0.013  
Oral Ulcers | 1.0 (0.9, 1.1) | 0.82  
Musculoskeletal | 0.8 (0.7, 0.9) | 0.0023  
Serositis | 1.1 (1.0, 1.3) | 0.027  
Neurologic | 1.1 (0.9, 1.4) | 0.22  
Renal | 1.2 (1.1, 1.4) | 0.0004  
Hematologic | 1.0 (0.9, 1.2) | 0.59  
Immunologic | 1.1 (0.9, 1.3) | 0.22  
ANA | 0.9 (0.7, 1.2) | 0.68  

Table 3: Rate ratio comparing those with recent activity to those without with respect to incidence of cachexia

Disease Activity in preceding 3 months as measured by components of SLEDAI | Rate Ratio (95% CI) | P-value  
--- | --- | ---  
Skin activity | 1.1 (0.9, 1.3) | 0.25  
Musculoskeletal activity | 0.9 (0.8, 1.1) | 0.51  
Renal activity | 1.3 (1.1, 1.5) | 0.0048  
Hematologic Activity | 0.9 (0.7, 1.1) | 0.34  
Serositis Activity | 1.2 (0.9, 1.7) | 0.20  
CNS activity | 0.9 (0.6, 1.3) | 0.53  
Vasculitis Activity | 1.2 (0.7, 1.9) | 0.52  
Constitutional Activity | 1.3 (0.6, 2.9) | 0.44  

Conclusion:

Within five years of cohort entry, half of the Hopkins Lupus cohort patients develop cachexia as defined by Fearon criteria; those younger than 30 years of age and those with a BMI below 20 are at highest risk of cachexia.

While patients with discoid rash and musculoskeletal manifestations were less likely to develop cachexia, renal lupus carried the highest cachexia risk.

Cachexia is an underrecognized syndrome in patients with lupus which is predominantly seen in patients with lupus nephritis. Further studies are needed to elucidate the implications of cachexia in the response to treatment, long term outcomes, quality of life, as well as its role as a potential cardiovascular risk factor in SLE.

Disclosure: G. Stojan, None; L. S. Magder, None; M. Petri, Anthera Inc, 5,GlaxoSmithKline, 5,EMD Serono, 5,Eli Lilly and Company, 5,Bristol Meyer Squibb, 5,Amgen, 5,United Rheumatology, 5,Global Academy, 5,Exagen, 2.


Abstract Number: 1636
Body Mass Index at Disease Onset Is Predictive of Future Organ Damage in Systemic Lupus Erythematosus

George Stojan\textsuperscript{1}, Wei Fu\textsuperscript{2} and Michelle Petri\textsuperscript{3}, \textsuperscript{1}Medicine, Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, \textsuperscript{2}Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, \textsuperscript{3}Medicine (Rheumatology), Division of Rheumatology, Johns Hopkins University School of Medicine, MD, USA, Baltimore, MD

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Obesity is more common in patients with SLE compared to the general population. The prevalence of obesity among SLE patients is between 28 and 50 percent. Despite the high prevalence of obesity in this population, the effect of weight on future organ damage in SLE has not been studied. We hypothesized that the body mass index at cohort entry was predictive of future organ damage as measured by the SLICC Damage Index.

Methods:

2406 patients in a prospective SLE cohort had their weight assessed at each visit. Patients were categorized into five predetermined groups based on weight: low (BMI<20 kg/m\textsuperscript{2}), normal weight (reference, BMI 20-24.9 kg/m\textsuperscript{2}), overweight (25-29.9 kg/m\textsuperscript{2}), obese (BMI 30-34.9 kg/m\textsuperscript{2}), and severely obese (BMI>35 kg/m\textsuperscript{2}). A Poisson regression analysis was used to estimate association between damage after cohort entry defined as the SLICC damage index and categorical BMI at cohort entry.

Results:

Table 1. SLICC damage index over time based on BMI at entry into the cohort
<table>
<thead>
<tr>
<th>Damage</th>
<th>Low (OR, 95% CI)</th>
<th>P value</th>
<th>Overweight (OR, 95% CI)</th>
<th>P value</th>
<th>Obesity (OR, 95% CI)</th>
<th>P value</th>
<th>Severely Obesity (OR, 95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Cataract Ever</td>
<td>1.08 (0.68, 1.74)</td>
<td>0.7363</td>
<td>1.31 (0.95, 1.79)</td>
<td>0.0958</td>
<td>1.68 (1.19, 2.36)</td>
<td><strong>0.0031</strong></td>
<td>1.59 (1.1, 2.3)</td>
<td><strong>0.014</strong></td>
</tr>
<tr>
<td>Retinal Change OR optic atrophy</td>
<td>2.86 (1.15, 7.15)</td>
<td><strong>0.0243</strong></td>
<td>1.6 (0.71, 3.63)</td>
<td>0.2569</td>
<td>1.36 (0.53, 3.69)</td>
<td>0.5524</td>
<td>1.93 (0.74, 5.02)</td>
<td>0.1754</td>
</tr>
<tr>
<td>Cognitive impairment OR Major Psychosis</td>
<td>1.53 (0.63, 3.94)</td>
<td>0.3735</td>
<td>1.67 (0.85, 3.31)</td>
<td>0.138</td>
<td>1.61 (0.73, 3.59)</td>
<td>0.2411</td>
<td>0.59 (0.17, 2.04)</td>
<td>0.4069</td>
</tr>
<tr>
<td>Seizures requiring therapy for 6 months</td>
<td>2.39 (0.68, 8.37)</td>
<td>0.1742</td>
<td>1.23 (0.43, 3.8)</td>
<td>0.7148</td>
<td>1.51 (0.43, 5.3)</td>
<td>0.5235</td>
<td>0.46 (0.06, 3.81)</td>
<td>0.4719</td>
</tr>
<tr>
<td>Cerebral Vascular Accident ever or resection not for malignancy</td>
<td>0.25 (0.06, 1.02)</td>
<td>0.0541</td>
<td>1.11 (0.66, 1.85)</td>
<td>0.7026</td>
<td>1.17 (0.64, 2.15)</td>
<td>0.6161</td>
<td>1.05 (0.53, 2.06)</td>
<td>0.8915</td>
</tr>
<tr>
<td>Cranial or peripheral neuropathy</td>
<td>0.96 (0.43, 2.18)</td>
<td>0.9293</td>
<td>1.47 (0.88, 2.45)</td>
<td>0.137</td>
<td>1.13 (0.59, 2.17)</td>
<td>0.7144</td>
<td>1.38 (0.72, 2.64)</td>
<td>0.3287</td>
</tr>
<tr>
<td>Transverse myelitis</td>
<td>3.58 (0.22, 56.95)</td>
<td>0.3664</td>
<td>1.23 (0.08, 19.67)</td>
<td>0.8819</td>
<td>4.52 (0.41, 49.62)</td>
<td>0.2175</td>
<td>2.76 (0.17, 44.01)</td>
<td>0.4716</td>
</tr>
<tr>
<td>Estimated or measured GFR &lt; 50%</td>
<td>1.99 (0.67, 5.86)</td>
<td>0.2126</td>
<td>1.23 (0.49, 3.09)</td>
<td>0.6537</td>
<td>0.75 (0.21, 2.76)</td>
<td>0.6685</td>
<td>1.23 (0.38, 3.95)</td>
<td>0.7301</td>
</tr>
<tr>
<td>Proteinuria 3.5gm/24 hours</td>
<td>1.19 (0.24, 5.86)</td>
<td>0.8279</td>
<td>1.03 (0.32, 3.35)</td>
<td>0.9635</td>
<td>1.51 (0.43, 5.3)</td>
<td>0.5235</td>
<td>1.38 (0.35, 5.48)</td>
<td>0.6455</td>
</tr>
<tr>
<td>End-Stage renal disease</td>
<td>1.11 (0.36, 3.34)</td>
<td>0.8645</td>
<td>1.14 (0.52, 2.47)</td>
<td>0.743</td>
<td>1.56 (0.68, 3.62)</td>
<td>0.2961</td>
<td>0.64 (0.18, 2.22)</td>
<td>0.4795</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>1.02 (0.42, 2.5)</td>
<td>0.9608</td>
<td>0.76 (0.39, 1.51)</td>
<td>0.4384</td>
<td>0.97 (0.45, 2.09)</td>
<td>0.9339</td>
<td>1.97 (1.03, 3.77)</td>
<td><strong>0.039</strong></td>
</tr>
<tr>
<td>Pulmonary fibrosis</td>
<td>1.19 (0.59, 2.39)</td>
<td>0.6194</td>
<td>1.07 (0.64, 1.78)</td>
<td>0.7985</td>
<td>1.36 (0.77, 2.39)</td>
<td>0.2941</td>
<td>1.38 (0.76, 2.52)</td>
<td>0.2921</td>
</tr>
<tr>
<td>Pleural fibrosis</td>
<td>1.28 (0.47, 3.5)</td>
<td>0.633</td>
<td>1.67 (0.85, 3.31)</td>
<td>0.138</td>
<td>0.65 (0.21, 1.94)</td>
<td>0.4362</td>
<td>0.99 (0.36, 2.71)</td>
<td>0.9798</td>
</tr>
<tr>
<td>Pulmonary infarction OR resection not for malignancy</td>
<td>3.58 (0.22, 56.95)</td>
<td>0.3664</td>
<td>1.23 (0.08, 19.67)</td>
<td>0.8819</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td>Angina OR coronary artery bypass</td>
<td>0.55 (0.13, 2.42)</td>
<td>0.4293</td>
<td>1.23 (0.58, 2.64)</td>
<td>0.5884</td>
<td>2.78 (1.35, 5.5)</td>
<td><strong>0.0053</strong></td>
<td>2.34 (1.06, 5.15)</td>
<td><strong>0.0349</strong></td>
</tr>
<tr>
<td>Myocardial infarction ever</td>
<td>1.28 (0.47, 3.5)</td>
<td>0.633</td>
<td>0.97 (0.44, 2.12)</td>
<td>0.9374</td>
<td>1.94 (0.91, 4.13)</td>
<td>0.0878</td>
<td>1.38 (0.56, 3.38)</td>
<td>0.4788</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>0.89 (0.26, 3.14)</td>
<td>0.8621</td>
<td>0.62 (0.23, 1.63)</td>
<td>0.3305</td>
<td>1.13 (0.43, 2.98)</td>
<td>0.8059</td>
<td>2.3 (1.01, 5.26)</td>
<td><strong>0.0477</strong></td>
</tr>
<tr>
<td>Valvular disease</td>
<td>0.67 (0.2, 2.28)</td>
<td>0.5224</td>
<td>0.62 (0.27, 1.43)</td>
<td>0.26</td>
<td>0.28 (0.07, 1.22)</td>
<td>0.0903</td>
<td>1.21 (0.52, 2.9)</td>
<td>0.6708</td>
</tr>
<tr>
<td>Pericarditis OR pericardectomy</td>
<td>3.58 (0.73, 17.58)</td>
<td>0.1164</td>
<td>1.64 (0.37, 7.32)</td>
<td>0.5135</td>
<td>1.51 (0.25, 8.96)</td>
<td>0.6529</td>
<td>0.92 (0.18, 8.1)</td>
<td>0.9432</td>
</tr>
<tr>
<td>Claudication</td>
<td>1.19 (0.24, 5.86)</td>
<td>0.8279</td>
<td>1.64 (0.57, 4.71)</td>
<td>0.3541</td>
<td>1.13 (0.28, 4.48)</td>
<td>0.8628</td>
<td>0.46 (0.06, 3.81)</td>
<td>0.4719</td>
</tr>
<tr>
<td>Condition</td>
<td>Odds Ratio (95% CI)</td>
<td>p-value</td>
<td>Odds Ratio (95% CI)</td>
<td>p-value</td>
<td>Odds Ratio (95% CI)</td>
<td>p-value</td>
<td></td>
<td></td>
</tr>
<tr>
<td>---------------------------------------------------------------------------</td>
<td>---------------------</td>
<td>---------</td>
<td>---------------------</td>
<td>---------</td>
<td>---------------------</td>
<td>---------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Significant tissue loss ever</td>
<td>7.16 (1.32, 38.77)</td>
<td>0.0224</td>
<td>2.88 (0.75, 11.08)</td>
<td>0.1242</td>
<td>2.76 (0.39, 19.51)</td>
<td>0.3084</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Venous thrombosis with swelling, ulceration, OR venous stasis</td>
<td>1.49 (0.73, 3.06)</td>
<td>0.0436</td>
<td>1.70 (1.02, 2.83)</td>
<td>0.1938</td>
<td>1.61 (0.85, 3.06)</td>
<td>0.1449</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infarction or resection of bowel</td>
<td>1.49 (0.73, 3.06)</td>
<td>0.0436</td>
<td>1.70 (1.02, 2.83)</td>
<td>0.1938</td>
<td>1.61 (0.85, 3.06)</td>
<td>0.1449</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stricture OR Upper GI tract surgery ever</td>
<td>1.23 (0.17, 8.73)</td>
<td>0.8335</td>
<td>1.23 (0.17, 8.73)</td>
<td>0.8335</td>
<td>1.38 (0.13, 15.17)</td>
<td>0.7913</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pancreatic insufficiency</td>
<td>1.79 (0.16, 19.63)</td>
<td>0.6339</td>
<td>1.23 (0.17, 8.73)</td>
<td>0.8335</td>
<td>1.38 (0.13, 15.17)</td>
<td>0.7913</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscle atrophy or weakness</td>
<td>2.62 (1.23, 5.62)</td>
<td>0.0129</td>
<td>1.32 (0.66, 2.64)</td>
<td>0.439</td>
<td>1.29 (0.53, 3.12)</td>
<td>0.573</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deforming or erosive arthritis</td>
<td>1.04 (0.52, 2.81)</td>
<td>0.3315</td>
<td>0.81 (0.54, 1.23)</td>
<td>0.3315</td>
<td>0.96 (0.63, 1.46)</td>
<td>0.8419</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osteoporosis w/ fracture or vertebral collapse</td>
<td>1.51 (0.81, 2.79)</td>
<td>0.0321</td>
<td>2.76 (0.56, 13.6)</td>
<td>0.3084</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avascular necrosis</td>
<td>1.15 (0.58, 2.31)</td>
<td>0.7799</td>
<td>0.95 (0.51, 1.78)</td>
<td>0.7799</td>
<td>0.8665 (0.44, 1.79)</td>
<td>0.7468</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>1.99 (0.67, 5.86)</td>
<td>0.2126</td>
<td>1.30 (0.69, 2.46)</td>
<td>0.4409</td>
<td>1.25 (0.42, 3.71)</td>
<td>0.1786</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ruptured Tendon</td>
<td>1.23 (0.17, 8.73)</td>
<td>0.8335</td>
<td>1.23 (0.17, 8.73)</td>
<td>0.8335</td>
<td>1.38 (0.13, 15.17)</td>
<td>0.7913</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extensive scarring of panniculum other than scalp and pulp space</td>
<td>1.23 (0.17, 8.73)</td>
<td>0.8335</td>
<td>1.23 (0.17, 8.73)</td>
<td>0.8335</td>
<td>1.38 (0.13, 15.17)</td>
<td>0.7913</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin ulceration</td>
<td>1.23 (0.17, 8.73)</td>
<td>0.8335</td>
<td>1.23 (0.17, 8.73)</td>
<td>0.8335</td>
<td>1.38 (0.13, 15.17)</td>
<td>0.7913</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Premature Gonadal Failure</td>
<td>1.99 (0.67, 5.86)</td>
<td>0.2126</td>
<td>1.30 (0.69, 2.46)</td>
<td>0.4409</td>
<td>1.25 (0.42, 3.71)</td>
<td>0.1786</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.19 (0.12, 11.4)</td>
<td>0.8782</td>
<td>0.41 (0.04, 3.94)</td>
<td>0.4409</td>
<td>1.51 (0.25, 8.96)</td>
<td>0.6529</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malignancy</td>
<td>1.49 (0.73, 3.06)</td>
<td>0.0436</td>
<td>1.70 (1.02, 2.83)</td>
<td>0.1938</td>
<td>1.61 (0.85, 3.06)</td>
<td>0.1449</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

/ : data is not sufficient for calculating odds ratios

**Conclusion:**

Patients with low BMI at cohort entry are almost three times more likely to have retinal change and two times more likely to develop deforming or erosive arthritis.

Overweight patients at cohort entry are 70% more likely to have Infarction or resection of bowel and 58% more likely to develop cancer.

Obese patients at cohort entry are 68% more likely to develop cataract; almost three times more likely to have angina or coronary artery bypass; almost five times more likely to have venous thrombosis.

Severely obese patients at cohort entry are 59% more likely to develop cataract; almost two times more likely to have pulmonary hypertension; two times more likely to have angina or coronary artery bypass, and two times more...
likely to have cardiomyopathy.

Disclosure: G. Stojan, None; W. Fu, None; M. Petri, Anthera Inc, 5,GlaxoSmithKline, 5,EMD Serono, 5,Eli Lilly and Company, 5,Bristol Meyer Squibb, 5,Amgen, 5,United Rheumatology, 5,Global Academy, 5,Exagen, 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/body-mass-index-at-disease-onset-is-predictive-of-future-organ-damage-in-systemic-lupus-erythematosus

Abstract Number: 1637

Sexual Function in Married Indian Women with Systemic Lupus Erythematosus

Benzeeta Pinto¹, Sandeep Grover², Manish Rathi³ and Aman Sharma⁴, ¹PGIMER, CHANDIGARH, India, ²PGIMER, Chandigarh, India, ³Department of Nephrology,, Postgraduate Institute of Medical Education and Research, Chandigarh, India, ⁴Internal Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh, India

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: This study was carried out to evaluate the impact of disease activity, damage, marital satisfaction, fatigue, psychosocial comorbidity and QoL on sexual function in women with SLE.

Methods: Hundred and twelve premenopausal married women with SLE were included in a one year prospective longitudinal study. Disease activity and damage were assessed using SELENA–SLEDAI and SLICC/ACR damage Index (SDI) respectively. Female sexual function index (FSFI) and Couple Satisfaction Index (CSI) were used to evaluate sexual function and marital satisfaction. QoL was assessed using LupusPRO. Depression, anxiety and Fatigue were assessed using Patient Health Questionnaire 9 (PHQ9), Generalised Anxiety Disorder 7 (GAD7) and Fatigue severity scale (FSS).

Results: The mean age was 34.0±6.8 years. Mean SELENA SLEDAI was 3.67±4.2 and mean SDI was 0.25±0.62. Median steroid dose was 7.5mg of prednisolone. Impaired sexual function was found in 60.7%. More than 90% of the patients reported problems in desire, arousal and lubrication (Table 1). Seventy four percent of the patients had dysfunction in one or more domains. SLEDAI and dose of steroids had a negative correlation with total score of FSFI (Table 2). The mean score of CSI was 130.39±26.17. Eighteen patients (16.1%) had CSI lower than the cut off score (104.5) suggestive of marital distress. There was a significant correlation between FSFI and CSI (r=0.343, p<0.001). There was a correlation between lupus symptoms, cognition, pain vitality, coping, satisfaction with care and total non HRQoL scores of LupusPRO and total score of FSFI (Table 3). On multivariate regression significant
predictors of sexual function were couple satisfaction, corticosteroid dose and SLEDAI (adjusted R square=0.349, p=0.014).

**Conclusion:** Sexual function is impaired in women with SLE. Disease activity and marital satisfaction were the most important factors influencing sexual function.

Table 1: Female sexual function index in 112 patients and comparison with other studies

<table>
<thead>
<tr>
<th>Domain</th>
<th>Cut off scores (Min, Max)</th>
<th>% of Patients with scores &lt; cut off</th>
<th>Our study (n=112)</th>
<th>Morales et al (n=65)</th>
<th>Tseng et al (n=171)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desire</td>
<td>4.28 (1.2,6)</td>
<td>104 (92.9%)</td>
<td>2.97 ± 1.08</td>
<td>3.24 ± 1.49</td>
<td>3.1 ± 0.9</td>
</tr>
<tr>
<td>Arousal</td>
<td>5.08 (0,6)</td>
<td>106 (94.6%)</td>
<td>2.80 ± 1.55</td>
<td>3.92 ± 1.74</td>
<td>4.0 ± 1.0</td>
</tr>
<tr>
<td>Lubrication</td>
<td>5.45 (0,6)</td>
<td>102 (91.1%)</td>
<td>3.6 ± 1.82</td>
<td>3.80 ± 1.93</td>
<td>4.8 ± 0.9</td>
</tr>
<tr>
<td>Orgasm</td>
<td>5.05 (0,6)</td>
<td>76 (67.9%)</td>
<td>3.8 ± 1.98</td>
<td>4.22 ±1.85</td>
<td>4.6 ± 1.0</td>
</tr>
<tr>
<td>Satisfaction</td>
<td>5.04 (0,6)</td>
<td>59 (52.7%)</td>
<td>4.51 ± 1.76</td>
<td>4.67 ± 1.65</td>
<td>4.9 ± 1.1</td>
</tr>
<tr>
<td>Pain</td>
<td>5.51 (0,8,6)</td>
<td>53 (47.3%)</td>
<td>4.42 ± 2.19</td>
<td>4.11 ± 2.03</td>
<td>4.4 ± 1.1</td>
</tr>
<tr>
<td>Total Score</td>
<td>26.55 (2,36)</td>
<td>68 (60.7%)</td>
<td>22.14 ± 9.22</td>
<td>24.45 ± 8.04</td>
<td>25.7 ± 4.7</td>
</tr>
</tbody>
</table>

Table 2: Spearman correlation of various domains of FSFI with demographic and disease characteristics
<table>
<thead>
<tr>
<th></th>
<th>Desire</th>
<th>Arousal</th>
<th>Lubrication</th>
<th>Orgasm</th>
<th>Satisfaction</th>
<th>Pain</th>
<th>Total FSFI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>-0.121</td>
<td>-0.028</td>
<td>-0.061</td>
<td>-0.062</td>
<td>-0.078</td>
<td>0.202(*)</td>
<td>-0.049</td>
</tr>
<tr>
<td></td>
<td>(0.202)</td>
<td>(0.769)</td>
<td>(0.52)</td>
<td>(0.517)</td>
<td>(0.412)</td>
<td>(0.033)</td>
<td>(0.606)</td>
</tr>
<tr>
<td><strong>Duration of marriage</strong></td>
<td>-0.17</td>
<td>-0.125</td>
<td>-0.115</td>
<td>-0.093</td>
<td>-0.124</td>
<td>0.280(**)</td>
<td>-0.091</td>
</tr>
<tr>
<td></td>
<td>(0.073)</td>
<td>(0.188)</td>
<td>(0.225)</td>
<td>(0.328)</td>
<td>(0.194)</td>
<td>(0.003)</td>
<td>(0.341)</td>
</tr>
<tr>
<td><strong>No of living children</strong></td>
<td>-0.108</td>
<td>-0.059</td>
<td>-0.051</td>
<td>0.062</td>
<td>0.004</td>
<td>0.271(**)</td>
<td>0.031</td>
</tr>
<tr>
<td></td>
<td>(0.258)</td>
<td>(0.539)</td>
<td>(0.595)</td>
<td>(0.514)</td>
<td>(0.967)</td>
<td>(0.004)</td>
<td>(0.743)</td>
</tr>
<tr>
<td><strong>Disease duration</strong></td>
<td>0.058</td>
<td>0.077</td>
<td>0.093</td>
<td>0.007</td>
<td>0.049</td>
<td>0.198(*)</td>
<td>0.087</td>
</tr>
<tr>
<td></td>
<td>(0.546)</td>
<td>(0.418)</td>
<td>(0.329)</td>
<td>(0.945)</td>
<td>(0.606)</td>
<td>(0.037)</td>
<td>(0.36)</td>
</tr>
<tr>
<td><strong>SLEDAI</strong></td>
<td>-0.256(**)</td>
<td>-0.227(*)</td>
<td>-0.187(*)</td>
<td>-0.178</td>
<td>-0.15</td>
<td>-0.286(**)</td>
<td>-0.209(*)</td>
</tr>
<tr>
<td></td>
<td>(0.006)</td>
<td>(0.016)</td>
<td>(0.048)</td>
<td>(0.061)</td>
<td>(0.114)</td>
<td>(0.002)</td>
<td>(0.027)</td>
</tr>
<tr>
<td><strong>SDI</strong></td>
<td>-0.023</td>
<td>-0.118</td>
<td>-0.053</td>
<td>-0.086</td>
<td>-0.142</td>
<td>0.008</td>
<td>-0.098</td>
</tr>
<tr>
<td></td>
<td>(0.813)</td>
<td>(0.214)</td>
<td>(0.58)</td>
<td>(0.365)</td>
<td>(0.134)</td>
<td>(0.935)</td>
<td>(0.306)</td>
</tr>
<tr>
<td><strong>Dose of Steroids</strong></td>
<td>-0.172</td>
<td>-0.276(**)</td>
<td>-0.253(**)</td>
<td>-0.221(*)</td>
<td>-0.248(*)</td>
<td>-0.141</td>
<td>-0.258(**)</td>
</tr>
<tr>
<td></td>
<td>(0.082)</td>
<td>(0.004)</td>
<td>(0.01)</td>
<td>(0.024)</td>
<td>(0.011)</td>
<td>(0.152)</td>
<td>(0.008)</td>
</tr>
<tr>
<td><strong>Marital satisfaction (CSI)</strong></td>
<td>0.304(**)</td>
<td>0.208(*)</td>
<td>0.173</td>
<td>0.351(**)</td>
<td>0.353(**)</td>
<td>0.304(**)</td>
<td>0.343(**)</td>
</tr>
<tr>
<td></td>
<td>(0.001)</td>
<td>(0.028)</td>
<td>(0.067)</td>
<td>(&lt;0.001)</td>
<td>(&lt;0.001)</td>
<td>(0.001)</td>
<td>(&lt;0.001)</td>
</tr>
<tr>
<td><strong>Fatigue (FSS)</strong></td>
<td>-0.148</td>
<td>-0.227(*)</td>
<td>-0.111</td>
<td>-0.116</td>
<td>-0.137</td>
<td>-0.347(**)</td>
<td>-0.186(*)</td>
</tr>
<tr>
<td></td>
<td>(0.118)</td>
<td>(0.016)</td>
<td>(0.243)</td>
<td>(0.224)</td>
<td>(0.15)</td>
<td>(&lt;0.001)</td>
<td>(0.05)</td>
</tr>
<tr>
<td><strong>Depression (PHQ9)</strong></td>
<td>-0.205(*)</td>
<td>-0.165</td>
<td>-0.182</td>
<td>-0.182</td>
<td>-0.066</td>
<td>-0.342(**)</td>
<td>-0.195(*)</td>
</tr>
<tr>
<td></td>
<td>(0.03)</td>
<td>(0.082)</td>
<td>(0.055)</td>
<td>(0.055)</td>
<td>(0.487)</td>
<td>(&lt;0.001)</td>
<td>(0.039)</td>
</tr>
<tr>
<td><strong>Anxiety (GAD7)</strong></td>
<td>-0.219(*)</td>
<td>-0.138</td>
<td>-0.104</td>
<td>-0.207(*)</td>
<td>-0.104</td>
<td>-0.238(*)</td>
<td>-0.201(*)</td>
</tr>
<tr>
<td></td>
<td>(0.021)</td>
<td>(0.147)</td>
<td>(0.274)</td>
<td>(0.029)</td>
<td>(0.274)</td>
<td>(0.011)</td>
<td>(0.034)</td>
</tr>
</tbody>
</table>

*p<0.05,** p<0.01 {top line- Spearman Rho ; bottom line - (p value)}

Table 3: Correlation of various domains of Lupus PRO with FSFI domains
<table>
<thead>
<tr>
<th></th>
<th>Desire</th>
<th>Arousal</th>
<th>Lubrication</th>
<th>Orgasm</th>
<th>Satisfaction</th>
<th>Pain</th>
<th>Total FSFI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lupus Symptoms</td>
<td>0.136</td>
<td>0.228(*)</td>
<td>0.153</td>
<td>0.211(*)</td>
<td>0.092</td>
<td>0.419(**)</td>
<td>0.206(*)</td>
</tr>
<tr>
<td></td>
<td>(0.153)</td>
<td>(0.016)</td>
<td>(0.108)</td>
<td>(0.025)</td>
<td>(0.334)</td>
<td>(&lt;0.001)</td>
<td>(0.029)</td>
</tr>
<tr>
<td>Cognition</td>
<td>0.298(**)</td>
<td>0.234(*)</td>
<td>0.093</td>
<td>0.142</td>
<td>0.057</td>
<td>0.291(**)</td>
<td>0.207(*)</td>
</tr>
<tr>
<td></td>
<td>(0.001)</td>
<td>(0.013)</td>
<td>(0.33)</td>
<td>(0.137)</td>
<td>(0.55)</td>
<td>(0.002)</td>
<td>(0.029)</td>
</tr>
<tr>
<td>Lupus Medication</td>
<td>0.159</td>
<td>0.039</td>
<td>-0.057</td>
<td>-0.007</td>
<td>0.018</td>
<td>0.154</td>
<td>0.026</td>
</tr>
<tr>
<td></td>
<td>(0.093)</td>
<td>(0.683)</td>
<td>(0.554)</td>
<td>(0.939)</td>
<td>(0.848)</td>
<td>(0.104)</td>
<td>(0.786)</td>
</tr>
<tr>
<td>Procreation</td>
<td>0.004</td>
<td>-0.06</td>
<td>-0.144</td>
<td>-0.086</td>
<td>-0.008</td>
<td>0.106</td>
<td>-0.058</td>
</tr>
<tr>
<td></td>
<td>(0.963)</td>
<td>(0.53)</td>
<td>(0.131)</td>
<td>(0.366)</td>
<td>(0.931)</td>
<td>(0.266)</td>
<td>(0.545)</td>
</tr>
<tr>
<td>Physical Health</td>
<td>0.139</td>
<td>0.198(*)</td>
<td>0.08</td>
<td>0.056</td>
<td>0.07</td>
<td>0.174</td>
<td>0.116</td>
</tr>
<tr>
<td></td>
<td>(0.143)</td>
<td>(0.036)</td>
<td>(0.4)</td>
<td>(0.558)</td>
<td>(0.461)</td>
<td>(0.067)</td>
<td>(0.221)</td>
</tr>
<tr>
<td>Pain Vitality</td>
<td>0.213(*)</td>
<td>0.293(**)</td>
<td>0.13</td>
<td>0.218(*)</td>
<td>0.134</td>
<td>0.300(**)</td>
<td>0.245(**)</td>
</tr>
<tr>
<td></td>
<td>(0.024)</td>
<td>(0.002)</td>
<td>(0.172)</td>
<td>(0.021)</td>
<td>(0.158)</td>
<td>(0.001)</td>
<td>(0.009)</td>
</tr>
<tr>
<td>Emotional Health</td>
<td>0.227(*)</td>
<td>0.143</td>
<td>-0.024</td>
<td>0.087</td>
<td>0.083</td>
<td>0.193(*)</td>
<td>0.133</td>
</tr>
<tr>
<td></td>
<td>(0.016)</td>
<td>(0.133)</td>
<td>(0.804)</td>
<td>(0.363)</td>
<td>(0.386)</td>
<td>(0.042)</td>
<td>(0.161)</td>
</tr>
<tr>
<td>Body Image</td>
<td>0.176</td>
<td>0.271(**)</td>
<td>0.096</td>
<td>0.144</td>
<td>0.087</td>
<td>0.11</td>
<td>0.172</td>
</tr>
<tr>
<td></td>
<td>(0.063)</td>
<td>(0.004)</td>
<td>(0.316)</td>
<td>(0.13)</td>
<td>(0.361)</td>
<td>(0.247)</td>
<td>(0.07)</td>
</tr>
<tr>
<td>Desires-goals</td>
<td>0.102</td>
<td>0.154</td>
<td>0.107</td>
<td>0.074</td>
<td>0.051</td>
<td>0.145</td>
<td>0.118</td>
</tr>
<tr>
<td></td>
<td>(0.286)</td>
<td>(0.105)</td>
<td>(0.26)</td>
<td>(0.44)</td>
<td>(0.591)</td>
<td>(0.127)</td>
<td>(0.214)</td>
</tr>
<tr>
<td>Social Support</td>
<td>0.058</td>
<td>0.046</td>
<td>-0.083</td>
<td>0.082</td>
<td>0.104</td>
<td>-0.049</td>
<td>0.066</td>
</tr>
<tr>
<td></td>
<td>(0.545)</td>
<td>(0.628)</td>
<td>(0.382)</td>
<td>(0.389)</td>
<td>(0.277)</td>
<td>(0.606)</td>
<td>(0.489)</td>
</tr>
<tr>
<td>Coping</td>
<td>0.151</td>
<td>0.214(*)</td>
<td>0.162</td>
<td>0.295(**)</td>
<td>0.259(**)</td>
<td>0.086</td>
<td>0.257(**)</td>
</tr>
<tr>
<td></td>
<td>(0.112)</td>
<td>(0.023)</td>
<td>(0.087)</td>
<td>(0.002)</td>
<td>(0.006)</td>
<td>(0.368)</td>
<td>(0.006)</td>
</tr>
<tr>
<td>Satisfaction with care</td>
<td>0.092</td>
<td>0.208(*)</td>
<td>0.07</td>
<td>0.342(**)</td>
<td>0.224(*)</td>
<td>0.11</td>
<td>0.239(*)</td>
</tr>
<tr>
<td></td>
<td>(0.333)</td>
<td>(0.027)</td>
<td>(0.46)</td>
<td>(&lt;0.001)</td>
<td>(0.018)</td>
<td>(0.249)</td>
<td>(0.011)</td>
</tr>
<tr>
<td>Total HRQOL</td>
<td>0.234(*)</td>
<td>0.235(*)</td>
<td>0.049</td>
<td>0.133</td>
<td>0.093</td>
<td>0.334(**)</td>
<td>0.179</td>
</tr>
<tr>
<td></td>
<td>(0.013)</td>
<td>(0.013)</td>
<td>(0.607)</td>
<td>(0.162)</td>
<td>(0.331)</td>
<td>(&lt;0.001)</td>
<td>(0.059)</td>
</tr>
<tr>
<td>Total non HRQOL</td>
<td>0.121</td>
<td>0.210(*)</td>
<td>0.066</td>
<td>0.280(**)</td>
<td>0.220(*)</td>
<td>0.102</td>
<td>0.241(*)</td>
</tr>
<tr>
<td></td>
<td>(0.204)</td>
<td>(0.026)</td>
<td>(0.489)</td>
<td>(0.003)</td>
<td>(0.02)</td>
<td>(0.283)</td>
<td>(0.011)</td>
</tr>
</tbody>
</table>

*p<0.05, **p<0.01 {top line- Spearman Rho; bottom line - (p value)}

Disclosure: B. Pinto, None; S. Grover, None; M. Rathi, None; A. Sharma, None.


Abstract Number: 1638

**High Genetic Risk Score Is Associated with Increased Organ Damage in SLE**
Sarah Reid1, Andrei Alexsson1, Martina Frodlund2, Johanna K Sandling1, Elisabet Svennungsson3, Andreas Jönsen4, Christine Bengtsson5, Iva Gunnarsson3, Anders A. Bengtsson4, Solbritt Rantapaa-Dahlqvist5, Maija-Leena Eloranta1, Ann-Christine Syvänen6, Christopher Sjöwall2, Lars Rönnblom1 and Dag Leonard1, 1Rheumatology and Science for Life Laboratory, Department of Medical Sciences, Uppsala University, Sweden, Uppsala, Sweden, 2Department of Clinical and Experimental Medicine, Linköping University, Sweden, Linköping, Sweden, 3Rheumatology Unit, Department of Medicine, Karolinska Institute, Karolinska University Hospital, Stockholm, Sweden, 4Lund University, Department of Clinical Sciences, Rheumatology, Lund, Sweden, 5Dept of Public Health and Clinical Medicine/Rheumatology, Umeå University, Sweden, Umeå, Sweden, 6Uppsala University, Department of Medical Sciences, Molecular Medicine and Science for Life Laboratory, Uppsala, Sweden

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Systemic lupus erythematosus (SLE) is a chronic, autoimmune disease with a complex genetic etiology. Over 80 risk genes for SLE have been identified and some genetic variants have demonstrated association with specific disease manifestations, such as STAT4 and nephritis. The overall effect of a patient's hereditary risk factors on disease severity has so far not been studied. We therefore assessed the relationship between high genetic risk and development of organ damage in SLE.

Methods:
Patients with SLE, who met at least 4 ACR criteria (n = 1012), were genotyped using a 200K Immunochip SNP Array (Illumina). A genetic risk score (GRS) was assigned to each patient based on the single nucleotide polymorphisms (SNPs) which in previous studies have shown association (p<5x10^-8) with SLE according to Morris, et al (Nat Genet, 2016. 48(8): p. 940-6). For 32 loci the SLE GWAS SNP was available on the ImmunoChip. For each SNP, the natural logarithm of the odds ratio (OR) for SLE susceptibility was multiplied by the number of risk alleles in each individual. The sum of all products for each patient was defined as the GRS. Information regarding organ damage according to Systemic Lupus International Collaborating Clinics / American College of Rheumatology Damage Index (SLICC-DI), disease manifestations, antibody profile, medication, current disease activity, age at diagnosis and sex was retrieved from medical records. Statistical analyzes were performed using Statistica 13.2 (Statsoft).

Results:
In an ordinal regression model, with SLICC-DI (0, 1, 2, 3, 4 and >4 points) as outcome and age and GRS as independent variables, an association was found between GRS and SLICC-DI (OR1.16 (1.03-1.31), p=0.015). The relationship was more pronounced for patients under 60 years of age (OR1.30 (1.11-1.52) p=7.1x10^-4). Using a linear regression model, a negative relationship was observed between GRS and age at diagnosis (β = -0.13, p=1.5x10^-5). When analyzing the 11 SLE criteria (ACR-82) using a logistic regression model associations were observed between GRS and nephritis (OR 1.26 (1.09-1.45), p=0.0015), the immunological criteria (OR 1.31 (1.13-1.51), p = 3.2x10^-4) and arthritis (OR 0.84 (0.71-1.00), p=0.044). A high GRS was also associated with presence of anti-dsDNA (OR 1.37 (1.15-1.62), p=9.4x10^-7) and low complement levels (OR 1.32 (1.03-1.68), p=0.044). No
association was observed between GRS and disease activity at the time of follow-up and there was no difference in GRS between men and women with SLE.

**Conclusion:**

In patients with SLE, there is an association between a high genetic risk score and early disease onset. In addition, patients with high genetic risk scores have a higher risk of developing permanent organ damage compared to individuals with fewer risk genes. Our findings indicate that genetic profiling of patients with SLE may provide a tool for predicting severity of the disease.

**Disclosure:**

S. Reid, None; A. Alexsson, None; M. Frodlund, None; J. K. Sandling, None; E. Svenungsson, None; A. Jönsen, None; C. Bengtsson, None; I. Gunnarsson, None; A. A. Bengtsson, None; S. Rantapaa-Dahlqvist, None; M. L. Eloranta, None; A. C. Syvänen, None; C. Sjöwall, None; L. Rönnblom, None; D. Leonard, None.


**Abstract Number: 1639**

**Longitudinal Evolution in a Nationwide Cohort Originally Classified As Mixed Connective Tissue Disease**

Silje Reiseter¹, Ragnar Gunnarsson², Jukka Corander³, Johanna Haydon⁴, May Brit Lund⁵ and Øyvind Molberg¹, ¹Oslo University Hospital, Oslo, Norway, ²Department of Rheumatology, Oslo University Hospital, Oslo, Norway, OSLO, Norway, ³Departement of Biostatistics, University of Oslo, Oslo, Norway, ⁴Rheumatology, Vestre Viken Hospital, Drammen, Norway, ⁵Respiratory Medicine, Oslo University Hospital, Oslo, Norway

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Ever since Mixed Connective Tissue Disease was presented as a distinct entity in 1972, it has been discussed whether MCTD represents an undifferentiated, transient or stable phenotype. Previous studies have been inconclusive regarding frequency of diagnostic converters (i.e. cases evolving from MCTD to another well-defined rheumatic disorder) potentially causing different research cohorts of SLE and SSc. The aims of this study were to evaluate the prevalence of MCTD patients evolving into another well-defined rheumatic disorder, and to assess the disease activity and prevalence of remission in MCTD patients after long term follow-up.

**Methods:** 118 patients were included from the Norwegian MCTD cohort. Patients were defined as having evolved from MCTD if the antibody profile together with the clinical features were compliant with another well-defined rheumatic disorder. Remission was defined by the combined presence of SLEDAI equal zero and EUSTAR less than 2.5. Possible predictors of stable phenotype and remission were assessed by logistic regression.

**Results:** The mean (SD) time between study inclusion and follow-up was 7 (2) years. 9 % of the MCTD patients had evolved into another specific rheumatic disorder (6 SLE, 4 RA, 3 SSc and 1 ASA, Fig. 1). The presence of puffy
hands before or at study inclusion predicted a stable MCTD phenotype at follow-up in univariate regression analysis (OR: 6.5, CI: 1.6 - 27.1, P=0.010). SLEDAI-2K scores were found to decrease over time and over 90% of patients had EUSTAR index activity < 2.5. The prevalence of remission was 28% at inclusion and 46% at follow-up. 30% were in remission during the observational period and at follow-up (extended remission) and 13% of patients were in remission at inclusion, during the observational period and at follow-up (durable remission, Fig. 2). One of the strongest predictors of remission was increasing FVC % pred at inclusion (Table 1).

**Conclusion:** Our results strengthen the view of MCTD as a distinct rheumatic condition as only a small proportion of patients evolved into another well-defined rheumatic disorder. Durable remission in MCTD is infrequent, however the SLEDAI-2K scores and EUSTAR activity index demonstrate that MCTD patients appear to have milder disease activity than SLE and SSc patients.
SLICC Damage Index Is Associated with Tubulointerstitial Nephritis on Lupus Nephritis Biopsies

Cianna Leatherwood, Brigham and Women's Hospital, Boston, MA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

SLICC Damage Index is associated with Tubulointerstitial Nephritis on Lupus Nephritis Biopsies

Kristin D’ Silva, Paul Hoover, Gearoid McMahon, Sushrut Waikar, Helmut Rennke, Karen Kostenbader

Background/Purpose: The presence of tubulointerstitial nephritis (TIN) on lupus nephritis renal biopsy has been associated with a poorer prognosis. Clinical factors associated with this biopsy finding have not been clearly defined. The purpose of this retrospective cohort study was to investigate clinical and laboratory characteristics associated with TIN in patients diagnosed with lupus nephritis. We predicted low C4, elevated 24-hour urinary protein and elevated dsDNA antibodies would be associated with the presence of TIN.
Methods: Biopsy reports of all renal biopsies performed at a single academic medical center between 1996 and 2015 showing Class II-VI lupus nephritis were reviewed. The definition of TIN included interstitial inflammation, tubular atrophy or fibrosis, and was abstracted from the biopsy report. All biopsies were interpreted by senior pathologists. Demographics, clinical variables and labs at the time of biopsy were assessed by chart review. Univariable analyses and then multivariable regression models were used to identify potential factors associated with tubulointerstitial nephritis.

Results: 165 initial lupus nephritis biopsies were identified; 119 had acute (n=5) or chronic interstitial nephritis (n= 97) or both (n=17). The average patient age was 36 years, 85% were female, and dsDNA antibody was positive in 85%. ISSN lupus nephritis biopsy classes overall were 9% II, 25% III, 40% IV and 24% V, and class was not statistically associated with presence of TIN. There were no statistically significant differences between groups in duration of SLE at biopsy, prior medications, age or race (Table). In univariable analyses, presence of TIN was associated with lower hemoglobin [10.5 vs. 11 g/dL, p= 0.02], higher creatinine [1.0 vs. 0.8 mg/dL, p= 0.01], higher 24-hour urinary protein (2.62 vs. 1.4 gm, p= 0.04), and higher SLICC damage index [4 vs. 2, p= 0.0016] compared to no TIN. Elevated SLICC damage index (DI) was associated with the presence of tubulointerstitial nephritis [OR 1.03 (95% CI 1.01, 1.05)] after controlling for age, race, sex, and 24-hour urinary protein.

Conclusion: TIN was a common finding on lupus nephritis biopsy and not associated with ISSN Class. Several laboratory findings related to more severe renal impairment were associated with TIN, but in multivariable models only SLICC-DI remained significantly associated. This suggests that increasing SLE-related systemic damage in lupus nephritis patients is associated with increased risk of TIN. Interestingly, SLE duration was not associated with TIN. Further work is needed to clarify the relationship between overall SLE damage and TIN in order to identify patients at highest risk for this potentially adverse pathology.
Table. Clinical Factors Potentially Associated with Tubulointerstitial Nephritis on Lupus Nephritis Biopsy

<table>
<thead>
<tr>
<th></th>
<th>Tubulointerstitial nephritis (n= 119)</th>
<th>No Tubulointerstitial nephritis (n= 46)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean</td>
<td>36 (±13)</td>
<td>38 (± 12)</td>
<td>0.55</td>
</tr>
<tr>
<td>Duration of SLE at biopsy (years), mean</td>
<td>6 (±8)</td>
<td>7 (±9)</td>
<td>0.58</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>101 (85%)</td>
<td>39 (85%)</td>
<td>0.98</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White, n(%)</td>
<td>39 (35%)</td>
<td>18 (39%)</td>
<td></td>
</tr>
<tr>
<td>Black, n(%)</td>
<td>41 (36%)</td>
<td>13 (28%)</td>
<td>0.55</td>
</tr>
<tr>
<td>Asian, n(%)</td>
<td>13 (12%)</td>
<td>6 (13%)</td>
<td></td>
</tr>
<tr>
<td>Hispanic, n(%)</td>
<td>19 (12%)</td>
<td>7 (15%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1 (1%)</td>
<td>2(4%)</td>
<td></td>
</tr>
<tr>
<td><strong>Laboratory Values</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin (g/dL), mean</td>
<td>10.5 (±2)</td>
<td>11 (±1.3)</td>
<td>0.02</td>
</tr>
<tr>
<td>Anti-dsDNA (IU/mL), median</td>
<td>172 [51, 488]</td>
<td>108 [24, 777]</td>
<td>0.61</td>
</tr>
<tr>
<td>Anti-RNP positive, n(%)</td>
<td>44 (44%)</td>
<td>19 (44%)</td>
<td>0.95</td>
</tr>
<tr>
<td>Antiphospholipid antibodies**</td>
<td>25 (25%)</td>
<td>8 (21%)</td>
<td>0.66</td>
</tr>
<tr>
<td>C4 (mg/dL), median</td>
<td>9 [6.5, 16.5]</td>
<td>9.5 [7, 15]</td>
<td>0.96</td>
</tr>
<tr>
<td>Creatinine (mg/dL), median</td>
<td>1.0 [0.7, 1.7]</td>
<td>0.8 [0.6, 1.0]</td>
<td>0.01</td>
</tr>
<tr>
<td>24-hr urinary protein (g/24 hr), median</td>
<td>2.62 [1.1, 4.5]</td>
<td>1.4 [0.5, 3.2]</td>
<td>0.04</td>
</tr>
<tr>
<td>Serum albumin, mean</td>
<td>3 (±0.7)</td>
<td>3.4 (±0.6)</td>
<td>0.004</td>
</tr>
<tr>
<td><strong>Clinical factors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior high dose glucocorticoid***, n(%)</td>
<td>39 (36%)</td>
<td>12 (30%)</td>
<td>0.49</td>
</tr>
<tr>
<td>Prior immunosuppression****, n(%)</td>
<td>29 (27%)</td>
<td>6 (15%)</td>
<td>0.19</td>
</tr>
<tr>
<td>Prior NSAIDs, n(%)</td>
<td>25 (23%)</td>
<td>11 (28%)</td>
<td>0.58</td>
</tr>
<tr>
<td>SBP ≥140mmHg or DBP≥ 90mmHg, n(%)</td>
<td>28 (25%)</td>
<td>6 (14%)</td>
<td>0.14</td>
</tr>
<tr>
<td>SLICC-DI score******, median</td>
<td>4 [1.6]</td>
<td>2 [1.3]</td>
<td><strong>0.002</strong></td>
</tr>
</tbody>
</table>

*Continuous variables evaluated with t-test or Wilcoxon and binary and categorical variables were assessed using chi-squared tests or Fisher’s exact as appropriate.

** positive vs. negative or not tested

***glucocorticoid ≥ 20 mg/day for past 30 days

**** receiving azathioprine, cyclophosphamide, mycophenolate mofetil, rituximab, cyclosporine or tacrolimus at the time of biopsy

***** Systemic Lupus Erythematosus International Collaborating Clinics damage index
Indications for Initial Renal Biopsy in Systemic Lupus Erythematosus: A Systematic Review of the Literature

Andrew McKinnon¹, Annaliese Tisseverasinghe², Susan Barr³, Paul R. Fortin⁴, John G. Hanly⁵, Stephanie Keeling⁶ and Christine A. Peschken², ¹Internal Medicine, University of Manitoba, Winnipeg, MB, Canada, ²Rheumatology, University of Manitoba, Winnipeg, MB, Canada, ³Medicine, University of Calgary, Calgary, AB, Canada, ⁴Division of Rheumatology, Department of Medicine, CHU de Québec-Université Laval, Québec, QC, Canada, ⁵Division of Rheumatology, Department of Medicine and Department of Pathology, Queen Elizabeth II Health Sciences Centre and Dalhousie University, Halifax, NS, Canada, ⁶Department of Medicine, University of Alberta, Division of Rheumatology, Edmonton, AB, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Lupus nephritis (LN) is an important cause of morbidity and mortality in patients with systemic lupus erythematosus (SLE). An initial renal biopsy (RB) is currently recommended by most experts, but clinical practice varies. With recent changes in treatment paradigms for LN the role of RB in deciding treatment has been questioned. In addition, a recent systematic review found the interpretation of RB findings to be unreliable. Therefore, we systematically reviewed the evidence for an initial biopsy in LN patients.

Methods:
Medline, Embase, Scopus, and Cochrane Library databases were searched using the search terms systemic lupus erythematosus, lupus nephritis and renal biopsy among others. The search was English-language restricted; randomized controlled trials (RCTs), observational, case control, cohort and cross-sectional studies were included. The quality of the studies was assessed using the Newcastle-Ottawa Scale and Quality in Prognostic Studies tool. Two reviewers reviewed citations for inclusion/exclusion at each stage (title, abstract and full text review).

Results:
A total of 776 references were identified after removal of duplicates. No relevant RCTs were found. No studies directly examined the role of RB compared to clinical parameters (CP) in deciding treatment. No studies assessing renal outcome were found that included a comparator arm of patients without RB. Two related studies showed that RB added marginally to short and long-term prediction of renal outcome when added to CP alone; however these were >30 years old and used WHO criteria resulting in high risk of bias. Fifteen studies looked at clinicopathologic correlation of RB findings and CP. Most studies were relatively small, with large variation in populations studied,
CP reported, and outcome measures described; 7 were >25 years old. Results were conflicting. Several studies found that poor CP (acute renal failure, hypertension) showed good correlation with Class IV & V histology on RB, as well as poor renal survival. No clear correlation between degree of proteinuria and LN biopsy class was found. Three studies found that in the setting of low grade proteinuria and normal renal function, many patients had Class III, IV, or V LN on RB; 2 studies did not find a correlation between RB findings and proteinuria. Three studies found higher titres of anti-dsDNA antibodies correlated with proliferative LN, 1 study in Hispanic patients did not. Two studies found low C4 and higher c1q antibodies correlated with proliferative LN on RB. Two studies found that RB findings predicted renal outcome, 2 did not. In 4 studies, RB identified non-LN causes of renal disease; ranging in frequency from 5-9%. Four citations found thrombotic microangiopathy in addition to LN in 30-50% of patients.

**Conclusion:**

The evidence that an initial RB changes management or prognosis in LN is of low quality due to high risk of bias. There is some evidence that RB may serve to identify non-SLE glomerular or other changes that influence management and outcome. As RB remains the clinical standard, is generally required for entry into clinical trials, and is being considered for inclusion in classification criteria, further research into the role, utility and reliability of RB is required.

**Disclosure:** A. McKinnon, None; A. Tisseverasinghe, None; S. Barr, None; P. R. Fortin, None; J. G. Hanly, None; S. Keeling, None; C. A. Peschken, None.


**Abstract Number:** 1642

**Role of Plaque in Predicting Cardiovascular Events in Women with Lupus over a 20 Year Followup**

Erika Joyce¹, Linda Santelices², Jennifer Mall², Kristy Huysman², Amy Xiaoqin Tang³, Michael Anderson², Jennifer Elliott⁴, Amy H. Kao⁵,⁶ and Susan Manzi², ¹Internal Medicine, Allegheny Health Network, Pittsburgh, PA, ²Medicine, Allegheny Health Network, Pittsburgh, PA, ³Lupus Center of Excellence, Allegheny Health Network Research Institute, Pittsburgh, PA, ⁴Allegheny Health Network, Pittsburgh, PA, ⁵EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA, ⁶EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA), Billerica, MA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The increased risk of premature cardiovascular disease (CVD) in systemic lupus erythematosus (SLE) patients has been well reported. Multiple series have demonstrated a higher incidence of accelerated subclinical atherosclerosis, carotid plaque formation, as well as myocardial infarction (M.I.) within these patients. Herein we report the 20-year incidence of cardiovascular events within a large prospectively followed single-institution female SLE patient cohort.
Methods: A single institution group of women previously diagnosed with SLE were prospectively followed. Baseline characteristics, including cardiovascular disease (CVD) risk factors (Framingham score, presence of carotid plaque, and carotid intima-media thickness), SLE specific risk factors (SLE diagnosis duration, Systemic Lupus International Collaborating Clinics (SLICC) damage score), and glucocorticoid use duration were collected. The incidence of CVD events (hard events: myocardial infarction (MI), coronary artery bypass graft (CABG), cerebrovascular accident (CVA), percutaneous transluminal coronary angioplasty (PTCA), fatal cardiac arrest ; soft events: transient ischemic attack (TIA), acute heart failure, angina, pulmonary embolus (PE)) were followed. Events and information were collected by chart review, patient interview, or National Death Index causes of death. A cox regression analysis was performed to identify independent risk factors for cardiovascular events (CVE’s).

Results: A total of 289 SLE women were enrolled, 89 were removed from the analysis either due to previous CV events or being lost to follow-up. After a median follow-up of 18 years the overall incidence CVE’s was 109 (hard: 43, soft: 66). Baseline Framingham Score (p=<0.001), carotid IMT (p=0.013), carotid plaque (p= 0.038), SLE disease duration (p=0.002), and glucocorticoid use duration (p=<0.001) significantly predicted an increased incidence of hard CVE’s. The mean time to any first CVE was 9.5 years in patients with baseline carotid plaque versus 12 years in patients without carotid plaque. The mean time to any hard CVE was 6.9 years in patients with baseline carotid plaque versus 11.7 years in patients without carotid plaque.

Conclusion: To the best of our knowledge this data represents the longest follow up of CVE’s in a large female SLE cohort. This data re-affirms the synergistic effect of SLE, carotid plaque, and traditional CV risk factors towards the development of CVE’s.

Disclosure: E. Joyce, None; L. Santelices, None; J. Mall, None; K. Huysman, None; A. X. Tang, None; M. Anderson, None; J. Elliott, None; A. H. Kao, EMD Serono, Inc, 3; S. Manzi, Exagen, 2,Exagen, 5,Exagen, 7, GSK, 5, UCB, 5, AstraZeneca, 6, Lupus Foundation of America, 9, AstraZeneca, 2, Human Genome Sciences/GSK, 2, Amgen, 2, Bristol-Myers Squibb, 2.


Abstract Number: 1643

15 Year Comparative Analysis of Cardiovascular Events in Female Subjects with Lupus Versus Controls

Erika Joyce1, Kristy Huysman2, Linda Santelices2, Michael Anderson2, Amy H. Kao3, Jennifer Elliott4, Jennifer Mall2, Amy Xiaoqin Tang5 and Susan Manzi2, 1Internal Medicine, Allegheny Health Network, Pittsburgh, PA, 2Medicine, Allegheny Health Network, Pittsburgh, PA, 3EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA, 4Allegheny Health Network, Pittsburgh, PA, 5Lupus Center of Excellence, Allegheny Health Network Research Institute, Pittsburgh, PA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM
Background/Purpose: The multi-organ sequelae of systemic lupus erythematosus (SLE) may include nephritis, alveolar hemorrhage, and cardiovascular disease. Our long term follow up of female SLE subjects has documented the incidence of cardiovascular events, and the predictive nature of carotid ultrasound. To our knowledge, there is a paucity of prospective comparative data of female SLE subjects with age and race adjusted controls. Herein we compare the 15-year incidence of cardiovascular events (CVE’s) within a large prospectively followed single-institution female SLE and control subject cohort.

Methods: A cohort of women diagnosed with SLE, and a race adjusted group of controls were enrolled and prospectively followed for 15 years. Baseline CV risk factors including hypertension, diabetes, lipid panel, and Framingham risk score were assessed. Within the SLE cohort a Systemic Lupus International Collaborating Clinics (SLICC) score was recorded. CVE’s and information were collected by chart review and subject interview.

Results: A total of 267 women without previous CV events (148 with SLE, and 119 controls) were included in the analysis. A total of 52 patients had a CVE, 48 SLE patients versus 4 control patients (p<0.001). The mean time to first CVE was 11.4 yrs in SLE women and 11.7 yrs in control women. SLE diagnosis at baseline was associated with more than 9-fold increased risk for any incident CV event (p = 0.002), after adjusting for traditional Framingham risk score.

Within this SLE cohort, SLICC score was predictive of any CVE (p=0.042).

Conclusion: This comparative analysis demonstrates the increased incidence of CV events within SLE subjects. Further, the impact of SLE is independent of traditional risk factors including the Framingham risk score. This underscores the importance of proactive management of CVE risk in SLE subjects.

Disclosure: E. Joyce, None; K. Huysman, None; L. Santelices, None; M. Anderson, None; A. H. Kao, EMD Serono, Inc, 3; J. Elliott, None; J. Mall, None; A. X. Tang, None; S. Manzi, Exagen, 2,Exagen, 5,Exagen, 7,GSK, 5,UCB, 5,AstraZeneca, 6,Lupus Foundation of America, 9,AstraZeneca, 2,Human Genome Sciences/GSK, 2,Amgen, 2,Bristol-Myers Squibb, 2.


Abstract Number: 1644

Less Than Seven Hours of Sleep per Night Is Associated with Transitioning to Systemic Lupus Erythematosus

Kendra A. Young1, Melissa E. Munroe2, Joel M. Guthridge3, Diane L. Kamen4, Gary S. Gilkeson5, Michael Weisman6, David Karp7, John B. Harley8, Daniel J. Wallace6, Judith A. James9 and Jill M. Norris10,

1Epidemiology, University of Colorado Denver, Aurora, CO, 2Arthritis and Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, 3Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, OKC, OK, 4Medicine/Rheumatology & Immunology, Medical University of South Carolina, Charleston, SC, 5Department of Medicine, Medical University of South Carolina, Charleston, SC, 6Cedars-Sinai Medical Center Division of Rheumatology, Los Angeles, CA, 7Rheumatology, UT Southwestern Med Ctr, Dallas, TX, 8Center for Autoimmune Genomics and Etiology (CAGE), Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 9Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 10Department of Epidemiology, Colorado School of Public Health, Aurora, CO

First publication: September 18, 2017

SESSION INFORMATION
Background/Purpose: Systemic lupus erythematosus (SLE) is a complex autoimmune disease with a relatively unknown etiology. The quality and quantity of sleep has been shown to have significant impacts on health. However, the role of sleep in the etiology of human SLE has not been studied. We examined whether reported sleep duration at baseline was prospectively associated with transitioning to SLE at follow-up in individuals at risk for SLE, independent of early clinical manifestations associated with SLE such as depression, fatigue, anxiety, or medication use.

Methods: 436 individuals who reported having a relative with SLE but who did not have SLE themselves at baseline were evaluated again an average of 6.3 years later. Fifty-six individuals transitioned to SLE by follow-up (>4 cumulative ACR criteria verified by medical record review). Sleep duration, medication use, and clinical manifestations such as depression, fatigue, anxiety, or prednisone use, were assessed by questionnaire; ACR criteria were confirmed by medical record. We dichotomized sleep duration as <7 hours of sleep a night or ≥ 7 hours of sleep a night, based on the Institute of Medicine recommendations. Generalized estimating equations, accounting for correlation within families, were used to assess associations between baseline sleep and the outcome of transitioning to SLE. In addition, to determine if the association between sleep duration and SLE was independent of early SLE symptoms, we additionally adjusted for other sleep associated variables at baseline, including depression, prednisone use, chronic fatigue, anxiety and number of ACR criteria. All multivariable models were adjusted for age, sex, and race.

Results: Sleeping less than the recommended 7 hours of sleep per night was greater in those who transitioned compared to those who did not transition to SLE (61% versus 34%, p=0.0002; OR: 2.8, 95% 1.6-4.9). A higher proportion of those who transitioned reported sleep medication and prednisone use, depression, fatigue, and anxiety at baseline. Those who transitioned to SLE were more likely to sleep less than 7 hours a night at baseline than those who did not transition to SLE adjusting for age, sex and race (OR: 2.9, 95% CI 1.6-5.1) (Model 1 in Table 1). This association remained after adjustment for baseline conditions and early pre-clinical manifestations that could affect sleep, including prednisone use, depression, chronic fatigue, anxiety, and number of ACR criteria.

Conclusion: Lack of sleep may be associated with transitioning to SLE, independent of early clinical manifestations of SLE that may influence sleep duration. Sleep loss may deregulate immune responses, leading to increased inflammatory cytokines and increased white blood cell and natural killer cell counts. Further prospective evaluation of sleeping patterns and biomarkers in at-risk individuals is warranted.

Table 1. Less Than Seven Hours of Sleep a Night is Associated with Transitioning to SLE.
<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
<th>Model 4</th>
<th>Model 5</th>
<th>Model 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep &lt;7 hours</td>
<td>2.9 (1.6-5.1)</td>
<td>2.1 (1.1-4.2)</td>
<td>2.5 (1.4-4.6)</td>
<td>2.1 (1.1-3.9)</td>
<td>2.5 (1.4-4.5)</td>
<td>2.3 (1.2-4.5)</td>
</tr>
<tr>
<td>Prednisone Use</td>
<td>-</td>
<td>15.5 (7.7-31.4)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Self-reported depression</td>
<td>-</td>
<td>-</td>
<td>3.6 (1.9-6.7)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Self-reported chronic fatigue</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>18.3 (7.7-43.1)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Self-reported anxiety</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2.8 (1.6-5.0)</td>
<td>-</td>
</tr>
<tr>
<td>ACR criteria:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>0-1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>13.4 (5.3-34.3)</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>180.8 (27.8-1174.4)</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

All models adjusted for age, sex and race (nonEA).

**Disclosure:** K. A. Young, None; M. E. Munroe, None; J. M. Guthridge, None; D. L. Kamen, None; G. S. Gilkeson, None; M. Weisman, None; D. Karp, None; J. B. Harley, None; D. J. Wallace, None; J. A. James, None; J. M. Norris, None.

**View Abstract and Citation Information Online** - [http://acrabstracts.org/abstract/less-than-seven-hours-of-sleep-per-night-is-associated-with-transitioning-to-systemic-lupus-erythematosus](http://acrabstracts.org/abstract/less-than-seven-hours-of-sleep-per-night-is-associated-with-transitioning-to-systemic-lupus-erythematosus)

**Abstract Number:** 1645

**Tobacco Exposure and Relationship with Severe Damage in Systemic Lupus Erythematosus Patients**

Micaela Ana Cosatti¹, Sebastian Muñoz², Natalia Tamborenea³, Mercedes Argentina Garcia⁴, Ana Curti⁵, Ana Maria Capuccio⁶, Oscar Rillo⁷, Patricia Imamura⁸,⁹,¹⁰, Emilce Schneeberger¹¹, Fernando Dal Pra¹², Marcela Ballent¹³, Mario Luis Cousseau¹⁴, Jorge Velasco Zamora¹⁵, Veronica Saurit¹⁶, Sergio M.A. Toloza¹⁷,¹⁸, Maria Danielsen¹⁹, Veronica Bellomio²⁰, Cesar Graf²¹, Sergio Paia²², Javier Cavallasca²³, Bernado Pons-Estel²⁴, Jose Moreno²⁵, Monica Patricia Diaz²⁶, Paula Alba²⁷, Marcela Verando²⁸, Guillermo Tate²⁹, Eduardo Mysler³⁰, Judith Sarano³¹, Emma Civit³¹, Fabian Risueño³², Pablo Alvarez Sepúlveda³³, Maria Silvia Larroude³⁶, Marcos Mendez³⁴, Andrea Conforti³⁵, Debora Sohn³⁶, Danith Medina Bornachera³⁷, Samanta Malm- Green³⁸, Analia Alvarez³⁹, Claudia Andrea Helling⁴⁰, Susana Roverano⁴¹, Gisela Pendón⁴², M. Mayer⁴³, Josefina Marin⁴⁴, Cecilia Catoggio⁴⁵, Alicia Eimon⁴⁶ and Cecilia N. Pisoni⁴⁷, ¹Section Rheumatology and Immunology, CEMIC, CABA, Argentina, ²Rheumatology Unit, Hospital “Dr. Juan A. Fernández”, CABA, Argentina, ³OMI, Buenos Aires, Argentina, ⁴Rheumatology Unit, HIGA San Martín La Plata, La Plata, Argentina, ⁵rheumatology, Hospital de
SESSION INFORMATION

**Session Date:** Monday, November 6, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** to assess relationship between smoking exposure and organ damage accrual measured by Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index for Systemic Lupus Erythematosus score (SLICC-SDI) in consecutive patients with systemic lupus erythematosus (SLE) from Argentina.

**Methods:** 623 consecutive SLE patients (fulfilling ≥4, 1997 ACR criteria) were included in this cross-sectional study. Sociodemographic and disease related variables including SLICC-SDI score and smoking status were collected.

Patients currently smoking were considered “smokers”, and “non-smokers” those who never smoked and previous smokers.

SLICC-SDI was divided into 2 categories < 3 and ≥ 3 severe damage (this cut off was previously reported in the literature).
Descriptive statistics and frequency distributions were used to describe the population studied. Chi-square was used to test differences between groups for categorical variables. Continuous variables were examined using student’s t-test and Mann-Whitney (Wilcoxon) test for non-normally distributed variables. Univariate analyses and multivariate logistic regression model were calculated.

Results:

623 patients were included in the analysis, 89% women, and median age was 38 (IQR 30-46) years. Eighty-four per cent were non-smokers and 16 % were current smokers. Fifty seven per cent were white, and 43% were non-white (mestizo and Amerindian). Seventy four per cent had >12 years of formal education.

Median disease duration was 9 years (IQR4-13). Median number ACR criteria met were 6 (IQR 5-7), mean SLICC-SDI score was 1.16 (SD 1.75) for non-smokers and 1.43 (SD 1.89) for current smokers (p 0.915).

Table 1 describes ACR criteria in smokers and non-smokers. Discoid lupus was significantly associated with smoking exposure.

<table>
<thead>
<tr>
<th>SLE criteria</th>
<th>All patients n:623</th>
<th>Non-smokers n: 515</th>
<th>Current smokers n: 108</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malar rash, n(%)</td>
<td>445 (71)</td>
<td>372 (71)</td>
<td>73 (75)</td>
<td>0.465</td>
</tr>
<tr>
<td>Discoid lupus, n (%)</td>
<td>67 (11)</td>
<td>51 (10)</td>
<td>16 (16)</td>
<td>0.053</td>
</tr>
<tr>
<td>Photosensitivity, n (%)</td>
<td>432 (69)</td>
<td>366 (70)</td>
<td>66 (67)</td>
<td>0.641</td>
</tr>
<tr>
<td>Arthritis/ arthralgias, n(%)</td>
<td>529 (85)</td>
<td>444 (85)</td>
<td>85 (87)</td>
<td>0.610</td>
</tr>
<tr>
<td>Ulcers, n(%)</td>
<td>268 (43)</td>
<td>220 (42)</td>
<td>48 (49)</td>
<td>0.194</td>
</tr>
<tr>
<td>Neurologic, n(%)</td>
<td>79 (13)</td>
<td>64 (12)</td>
<td>15 (15)</td>
<td>0.395</td>
</tr>
<tr>
<td>Hematologic disorder, n (%)</td>
<td>304 (49)</td>
<td>254 (48)</td>
<td>50 (51)</td>
<td>0.631</td>
</tr>
<tr>
<td>Serositis, n (%)</td>
<td>197 (32)</td>
<td>170 (32)</td>
<td>27 (28)</td>
<td>0.345</td>
</tr>
<tr>
<td>Renal disease, n(%)</td>
<td>279 (45)</td>
<td>240 (46)</td>
<td>39 (40)</td>
<td>0.273</td>
</tr>
<tr>
<td>Immunologic, n(%)</td>
<td>454 (74)</td>
<td>384 (74)</td>
<td>72 (73)</td>
<td>0.90</td>
</tr>
<tr>
<td>Antinuclear antibodies, n (%)</td>
<td>615 (99)</td>
<td>517 (99)</td>
<td>98(99)</td>
<td>0.905</td>
</tr>
</tbody>
</table>

Eighty-three per cent of patients had SLICC-SDI <3 and 17 % had ≥ 3. In patients with SLICC-SDI ≥ 3: 21% were smokersand 15% of patients with <3 SLICC-SDI were current smokers (p 0.081).

Univariate analysis comparing demographical and clinical characteristics of both groups are described in Table 2.
All patients N=623 SLICC<3 N= 515 SLICC≥3 N=108 p
Female, n (%) 556 (89) 461(89) 95 (88) 0.636
White race, n (%) 317 (57) 271 (58) 45 (55) 0.639
Age, years (median IQR) 38 (30-46) 36 (29-45) 43 (33-54) <0.001
SLE ACR criteria (median IQR) 6 (5-7) 6 (5-7) 7 (6-8) <0.001
Disease duration years (median IQR) 7 (4-13) 7 (3-12) 10 (6-16) <0.001
Age at diagnosis, years (median IQR) 28 (21-37.5) 28 (21-36) 30 (21-37.5) 0.05
Education>12 years, n (%) 461 (74) 381 (74) 78 (72) 0.655
Current smokers, n (%) 98 (16) 77 (15) 23 (21) 0.081
Hydroxychloroquine (HCQ) , n (%) 579 (93) 479(93) 100 (93) 0.761
Steroids, n (%) 467 (75) 386 (75) 85 (79) 0.409
Cyclophosphamide (CF), n (%) 149 (24) 103 (20) 46 (43) < 0.01
Azathioprine (AZA), n (%) 181 (29) 134 (26) 49 (45) < 0.01
Micofenolate mofetil, (MMF), n (%) 255 (21) 108 (21) 18 (17) 0.254

In the multiple regression analysis considering SLICC-SDI score ≥3 as dependent variable (adjusting by smoking exposure, age, sex,race, disease duration, > 12 years of education, corticosteroids, CF, AZA and HCQ exposure), we found that smoking (OR 1. 90, CI 95% 1.04- 3.46, p 0.035), age (OR 1.33, CI 95% 1.00-1.75, p 0.044), and CF exposure (OR 2.64, CI 95% 1.41-4.97, p 0.002) were associated to SLICC ≥3.

Conclusion: Tobacco exposure, older age and cyclophosphamide use were associated to SLICC-SDI ≥3.

Disclosure: M. A. Cosatti, None; S. Muñoz, None; N. Tamborenea, None; M. A. García, None; A. Curti, None; A. M. Capuccio, None; O. Rillo, None; P. Imamura, None; E. Schneeberger, None; F. Dal Pra, None; M. Ballent, None; M. L. Coussseau, None; J. Velasco Zamora, None; V. Saurit, None; S. M. A. Toloza, None; M. Danielsen, None; V. Bellomio, None; C. Graf, None; S. Paira, None; J. Cavallasca, None; B. Pons-Estel, None; J. Moreno, None; M. P. Diaz, None; P. Alba, None; M. Verando, None; G. Tate, None; E. Mysler, None; J. Sarano, None; E. Civit, None; F. Risueño, None; P. Alvarez Sepúlveda, None; M. S. Larroude, None; M. Mendez, None; A. Conforti, None; D. Sohn, None; D. Medina Bornachera, None; S. Malm-Green, None; A. Alvarez, None; C. A. Helling, None; S. Roverano, None; G. Pendón, None; M. Mayer, None; J. Marin, None; C. Catoggio, None; A. Eimon, None; C. N. Pisoni, None.


Abstract Number: 1646

Cardiovascular disease in Systemic Lupus Erythematosus. The road to hell is paved with good intentions

Sophie Mavrogeni¹ and Loukia Koutsogeorgopoulou², ¹CMR Department, Onassis Cardiac Surgery Center, Athens, Greece, ²Department of Pathophysiology, Rheumatology Unit, National Kapodistrian University of Athens, Athens, Greece
First publication: September 18, 2017
Background/Purpose: Accurate diagnosis of cardiovascular involvement in systemic lupus erythematosus (SLE) remains challenging, because echocardiography (echo), the cornerstone tool used, has serious limitations. We hypothesized that cardiovascular magnetic resonance (CMR) detects cardiac lesions in SLE patients, missed by echo.

Methods: Between 2005-2015, eighty asymptomatic SLE patients, aged 37±6 yrs, 72F/8M with normal echo, under treatment with antimalarials, have been evaluated using a 1.5 T system. LV-RV ejection fraction, T2 ratio (oedema imaging) and late gadolinium enhancement (LGE) (fibrosis imaging) were assessed. Acute and chronic lesions were characterised as LGE-positive plus T2>2 or T2<2, respectively. According to LGE, lesions were characterized as: a) diffuse subendocardial, b) subepicardial and c) subendocardial /transmural, due to vasculitis, myocarditis and myocardial infarction, respectively.

Results: Abnormal CMR findings were identified in 22/80 (27.5 %) asymptomatic SLE patients with normal echo, including 4/22 with recent onset of silent myocarditis, 9/22 with past myocardial infarction (6 inferior and 3 anterior subendocardial infarction), 5/22 with past myocarditis (subepicardial scar in inferolateral wall) and 4/22 with diffuse subendocardial fibrosis (DSF), due to vasculitis. No correlation between CMR findings and inflammatory indices was identified.

Conclusion: CMR in asymptomatic SLEs with normal echo can assess occult cardiac lesions including vasculitis, myocarditis and myocardial infarction, missed by echo that can influence both rheumatic and cardiac treatment and further risk stratification; therefore, it should be included in the diagnostic algorithm of SLE.

Disclosure: S. Mavrogeni, None; L. Koutsogeorgopoulou, None.


Abstract Number: 1647

A Lupus Low Disease Activity State Is Associated with Reduced Flare, Lower Organ Damage Accrual, and Better Quality of Life in Patients with Systemic Lupus Erythematosus

Ji-Hyoun Kang¹, Kyung-Eun Lee², Dong-Jin Park¹ and Shin-Seok Lee¹, ¹Rheumatology, Chonnam National University Medical School and Hospital, Gwangju, Korea, Republic of (South), ²Chonnam National University Medical School and Hospital, Gwangju, Korea, Republic of (South)

First publication: September 18, 2017
Background/Purpose: To identify the potential predictors of a lupus low disease activity state (LLDAS), and the relationship between LLDAS and disease flare, organ damage, and quality of life in Korean patients with systemic lupus erythematosus (SLE).

Methods: The study followed 181 SLE patients from a single center for three years. LLDAS was defined as follows: (1) SLE Disease Activity Index (SLEDAI)-2K ≤ 4, with no activity in major organ systems; (2) no new lupus disease activity compared with the previous assessment; (3) SLEDAI Physician Global Assessment ≤ 1; (4) a current prednisolone (or equivalent) dose ≤ 7.5 mg daily; and (5) well-tolerated standard maintenance doses of immunosuppressive drugs. We assessed data annually and divided 4 groups according to the number of LLDAS; LLDAS = 0, 1, 2, and 3. Univariate and multivariate analyses were performed to identify predictors of LLDAS.

Results: Of the 181 patients, 16.0% attained LLDAS on three consecutive years. Each group shows as follows; no LLDAS (n=30), LLDAS = 1 (n=60), LLDAS = 2 (n=62), and LLDAS = 3 (n=29). The patients who had higher number of LLDAS had shorter duration of symptoms, lower anti-histone antibody positivity, lower cumulative prescribed dose of prednisolone at baseline, lower mean PGA, lower mean SLEDAI, lower mean Mental Component Summary in SF-36, lower change in SLICC/ACR damage index, and a lower frequency of flare. In the multivariate analysis, LLDAS was significantly associated with lower mean PGA (OR = 0.671, 95% CI: 0.112–0.989, p = 0.019) and a reduced risk of flare after adjusting for confounders (OR = 0.012, 95% CI: 0.001–0.448, p = 0.017).

Conclusion: Attaining LLDAS was associated with an improved outcome, as represented by a decreased rate of disease flare, lower organ damage accrual, and better quality of life in Korean patients with SLE.

Disclosure: J. H. Kang, None; K. E. Lee, None; D. J. Park, None; S. S. Lee, None.


Abstract Number: 1648

Assessment of Outcome in Lupus Nephritis Patients: A Retrospective Analysis of a Single Center Cohort over 20 Years

Lihi Shemesh Eisen1, Talia Weinstein2, Irena Litinsky3, David Levartovsky1, Ilana Kaufman1, Marina Anouk4, Valerie Aloush4, Jonathan Wollman5, Jacob N. Ablin6, Uri Arad1, Mark Berman1, Victoria Furer1, Ari Polachek7, Ofir Elalouf8, Sara Borok Lev-Ran1, Reut Zemach9, Tali Eviatar1, Michael Zisapel1, Hagit Sarvagyl-Maman10, Dan Caspi11, Ori Elkayam4 and Daphna Paran4, 1Rheumatology, Tel-Aviv Sourasky Medical Center and the Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel, 2Nephrology, Tel-Aviv Sourasky Medical Center and the Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel, 3Rheumatology, Tel Aviv Sourasky Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel, 4Rheumatology, Tel Aviv Sourasky Medical Center and the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel, 5Rheumatology, Tel-Aviv Sourasky Medical Center and the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel, 6Internal Medicine H, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, 7Rheumatology, Tel Aviv Sourasky Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel, 8Rheumatology, Toronto Western Hospital, University of Toronto, Toronto, ON, Canada, 9Tel Aviv Sourasky Medical Center and the Sackler Faculty
SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Lupus Nephritis (LN) is a severe SLE manifestation, leading to a six-fold increased risk of death. This study aims to assess the outcome of patients with LN and the effect of change in management guidelines on outcome.

Methods: Retrospective analysis of all SLE patients with LN followed at the Tel Aviv Medical Center over a period of 20 years. Data included: sex, age at SLE diagnosis, age at LN diagnosis, number and timing of LN flares (rise in proteinuria to > 500 mg/d) and remissions (proteinuria < 500 mg/d and normal creatinine or < 10% of normal if baseline abnormal), creatinine, C3, C4 and anti-dsDNA at LN diagnosis, induction and maintenance therapy. Renal biopsy findings were obtained from pathology records. Patients with non-lupus related renal disease were excluded.

Results: LN was diagnosed in 90 patients (28% of the SLE cohort), F-76, M-14. The majority were Caucasian (n=81). Median follow up was 11.5 years, age at SLE diagnosis was 30.3+12 years, mean time to first LN episode was 3.3+5.6 years. LN was present at SLE diagnosis in 47 patients. Mean serum creatinine at diagnosis was >1.1 mg/dl in 35% and > 2mg/dl in 10% of patients. At first episode mean proteinuria was 3230+2402 mg/d, C3 was 67.5+23.6 mg/dl, C4 was 13.1+9 mg/dl. Anti-dsDNA was positive in 80% of patients. Renal biopsies available for review (n=79) demonstrated: class III -19%, class IV - 48.1%, class V - 21.5%, class III+V- 5.1%, class IV+V - 3.8%, isolated antiphospholipid nephropathy- 2.5%. For induction treatment 95% received oral prednisone, 21% received additional IV pulse methylprednisolone, 43% - IV cyclophosphamide (CYC), 42% - mycophenolate mofetil (MMF), 19% - azathioprine, 9% - prednisone alone, 4% - rituximab, 11% - other (tacrolimus, cyclosporine, rituximab+CYC, azathioprine+cyclosporine). The regime of IV CYC (low / high dose) varied mainly depending on year of treatment (before / after 2009). Eighty-five percent received hydroxychloroquine (HCQ). Out of 7 patients who stopped HCQ, 5 had a LN flare. Maintenance therapy included MMF -50%, azathioprine-27%, high dose IV CYC -10%, prednisone alone -9%, other - cyclosporine, tacrolimus -4%. Remission was achieved in 79.9% of the patients. Among patients treated before 2009, 85.9% achieved remission, while in those treated since 2009, when use of MMF was more prevalent, 75% achieved remission. The mean time from LN presentation to remission was 2.7+2.9 years. Among patients who achieved remission, 29.6% experienced a flare after the induction phase: 81% flared once, 19% flared twice. The median time from remission to first flare was 4 years, and from second remission to second flare 3.5 years. Eleven patients (12.2%) developed ESRD, 6 were diagnosed before 2009. Six patients (6.7%) died (ESRD-1; infection-3; severe thrombotic event -1; brain hemorrhage-1), 5 of whom had been diagnosed > 10 years ago, 4 received high dose CYC induction therapy.

Conclusion: In this cohort of LN patients, a high percentage achieved remission (79.9%), however rates of remission and ESRD did not improve when comparing patients treated before or after 2009, suggesting that changes in treatment strategies during this period have not significantly changed the outcome of LN.

Disclosure: L. Shemesh Eisen, None; T. Weinstein, None; I. Litinsky, None; D. Levartovsky, None; I. Kaufman, None; M. Anouk, None; V. Aloush, None; J. Wollman, None; J. N. Ablin, None; U. Arad, None; M. Berman, None; V. Furer, None; A. Polachek, None; O. Elalouf, None; S. Borok Lev-Ran, None; R. Zemach, None; T. Eviatar, None; M. Zisapel, None; H. Sarvagy-Maman, None; D. Caspi, None; O. Elkayam, None; D. Paran, XTL Biopharmaceuticals, 5.
Abstract Number: 1649

Sleep Disturbances in Systemic Lupus Erythematosus (SLE)

Patricia P. Katz¹, Sofia Pedro² and Kaleb Michaud³, ¹Medicine/Rheumatology, University of California, San Francisco, San Francisco, CA, ²National Data Bank for Rheumatic Diseases, Wichita, KS, ³University of Nebraska Medical Center, Omaha, NE

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Sleep disturbances (SD) are reported to be common in SLE, but relatively few studies have addressed the issue. We examined the frequency and severity of self-reported SD among individuals with SLE and identified predictors of SD.

Methods: Data were from the National Data Bank for Rheumatic Diseases (NDB), for which participants complete questionnaires every 6 months. In one questionnaire, items about the presence of physician-diagnosed obstructive sleep apnea (OSA) and restless-leg syndrome (RLS), use of continuous positive air pressure (CPAP) devices, and symptoms of RLS, as well as the Medical Outcomes Study Sleep Scale (MOS-S) were included. The MOS-S yields 5 subscales; results are shown here only for one (Sleep Problems Index I, SPI-I). Frequencies of reports of OSA, RLS, CPAP use, and RLS symptoms were tabulated. Multivariate regression analyses identified independent predictors of OSA and RLS (logistic regression) and SPI-I scores (linear regression). Potential predictors included age, sex, race, education, smoking, Rheumatic Disease Comorbidity Index (RDCI)¹, chronic obstructive pulmonary disease (COPD), asthma, meeting fibromyalgia criteria, obesity (BMI ≥ 30 kg/m²), disease duration, pain, prednisone and other medication use, and disease activity (Systemic Lupus Activity Questionnaire, SLAQ²) and damage (Brief Index of Lupus Damage, BILD³).

Results: Subject characteristics are shown in Table 1 (n = 385). 24% reported physician-diagnosed OSA and 20% RLS, compared to ~2-4% and ~10%, respectively, in the general population. 14% used CPAP, and 33% had RLS symptoms. Mean SPI-I was 36.0 (±34.1), ~0.5 standard deviation higher than a population sample mean. Independent predictors of OSA were greater age, obesity, asthma, RDCI, and disease activity (Table 2). Predictors of RLS were RDCI and disease activity. Worse scores on SPI-I were associated with younger age, non-white race, higher RDCI, and greater pain and disease activity.

Conclusion: Both OSA and RLS were more common in SLE than in the population; SPI-I scores were also worse. Some predictors of SDs were similar to predictors in the population (age, obesity), but disease activity was also associated with SD. Research in SLE has linked SDs to worse outcomes. Previous research in other conditions suggests that SDs might also be a cause of increased disease activity through heightened inflammation. Further research is needed to tease out disease-specific causes and effects of SD in SLE.

¹ England BR. Arthritis Care Res 2015; 6: 865
Table 1. Subject characteristics (n = 385)

<table>
<thead>
<tr>
<th></th>
<th>Mean ± SD or % (n)</th>
<th>Mean ± SD or % (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>60.9 ± 12.4</td>
<td>25.7±12.6</td>
</tr>
<tr>
<td>Female</td>
<td>94.0 (362)</td>
<td>4.0 ± 2.9</td>
</tr>
<tr>
<td>White</td>
<td>84.9 (327)</td>
<td>11.1 ± 7.6</td>
</tr>
<tr>
<td>Current smoker</td>
<td>3.4 (13)</td>
<td>3.7 ± 2.3</td>
</tr>
<tr>
<td>Obese (BMI≥30)</td>
<td>34.6 (133)</td>
<td>26.8 (88)</td>
</tr>
<tr>
<td>Asthma</td>
<td>13.3 (50)</td>
<td>34.5 (146)</td>
</tr>
<tr>
<td>COPD</td>
<td>7.0 (27)</td>
<td>6.8 ± 6.1</td>
</tr>
<tr>
<td>RDCI (0 – 9)</td>
<td>2.7 ± 1.9</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Significant independent predictors of sleep disturbances

<table>
<thead>
<tr>
<th></th>
<th>Obstructive Sleep Apnea (OSA)*</th>
<th>Restless Leg Syndrome (RLS)*</th>
<th>Sleep Problems Index I (SPI-I)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.05 (1.01, 1.09)</td>
<td>(ns)</td>
<td>-0.22 (.01)</td>
</tr>
<tr>
<td>White race</td>
<td>(ns)</td>
<td>(ns)</td>
<td>-6.3 (.02)</td>
</tr>
<tr>
<td>Obesity</td>
<td>5.3 (2.6, 10.8)</td>
<td>(ns)</td>
<td>(ns)</td>
</tr>
<tr>
<td>Asthma</td>
<td>2.7 (1.04, 7.0)</td>
<td>(ns)</td>
<td>(ns)</td>
</tr>
<tr>
<td>RDCI</td>
<td>1.3 (1.1, 1.6)</td>
<td>1.2 (1.05, 1.5)</td>
<td>1.15 (.03)</td>
</tr>
<tr>
<td>Pain rating</td>
<td>(ns)</td>
<td>(ns)</td>
<td>2.0 (&lt;.0001)</td>
</tr>
<tr>
<td>SLAQ</td>
<td>1.07 (1.01, 1.13)</td>
<td>1.1 (1.01, 1.04)</td>
<td>0.7 (.0002)</td>
</tr>
</tbody>
</table>

* Tabled values are odds ratio (95% CI) from multiple logistic regression analyses
† Tabled values are beta (p-value) from multiple linear regression analysis. Higher scores reflect greater sleep problems

Disclosure: P. P. Katz, Bristol-Myers Squibb, 2; S. Pedro, None; K. Michaud, National Data Bank for Rheumatic Diseases, 3.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/sleep-disturbances-in-systemic-lupus-erythematous-sle](http://acrabstracts.org/abstract/sleep-disturbances-in-systemic-lupus-erythematous-sle)
The Montreal Cognitive Assessment Questionnaire (MoCA): A Promising Screening Tool for Cognitive Dysfunction in SLE

Nathalie Chalhoub and Michael Luggen, Division of Immunology, Allergy, and Rheumatology, University of Cincinnati College of Medicine, Cincinnati, OH

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Cognitive dysfunction (CD) is among the most common neuropsychiatric manifestations in SLE. However, the diagnosis is oftentimes delayed and occasionally overlooked because of the lack of a sensitive and practical screening test. Several methods have been used to ascertain CD in patients with SLE, including traditional neuropsychological testing (NPT) and the Automated Neuropsychologic Assessment Metrics (ANAM), a computerized battery of symbol based tests measuring many of the same cognitive domains as NPT. Both are time-consuming, relatively costly, and not readily available. The Montreal Cognitive Assessment Questionnaire (MoCA) is a one-page performance-based screening test that has been validated to identify mild cognitive impairment in the elderly and, in preliminary work done by us, appeared to hold promise in SLE as well. This study aims to further evaluate the MoCA as a screening tool for the diagnosis of CD in SLE.

Methods: Patients with SLE fulfilling the American College of Rheumatology criteria were recruited. All subjects were administered the ANAM test and the MoCA questionnaire. MoCA scores were compared to the total throughput score (TTS) (correct responses/time for the responses), a standard measure of performance of the ANAM. Individual MoCA questions were also compared to TTS to identify the MoCA questions with the strongest correlation with CD. The classification of normal or abnormal by the ANAM was compared to that of the MoCA using various cutoffs. Sensitivity, specificity, likelihood ratios and predictive values were also computed at the various cut-offs for the MoCA.

Results: In total, 74 patients were evaluated. Of these, 15 (20 %) were identified by the ANAM as having cognitive dysfunction in comparison with 33 (44.6 %) by the MoCA using the standard cutoff of 26. The scores were significantly correlated ($r = 0.51$, $p < 0.001$). Six out of the 10 MoCA questions showed significant correlation with the ANAM score with the assessment of visuospatial and executive function being the most highly correlated with CD ($p = 0.000199$). Using the standard cutoff of 26, the sensitivity of the MoCA was 93%, specificity 68%, and negative predictive value 98%. All other cut-offs were inferior.

Conclusion: The MoCA appears to be a promising and practical screening tool for identification of patients with SLE at risk for cognitive dysfunction.

Table 1. MoCA Performance Characteristics

<table>
<thead>
<tr>
<th>Cutoff</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR+</th>
<th>LR-</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>0.6</td>
<td>0.81</td>
<td>3.16</td>
<td>0.49</td>
<td>0.45</td>
<td>0.89</td>
</tr>
<tr>
<td>25</td>
<td>0.73</td>
<td>0.75</td>
<td>2.92</td>
<td>0.36</td>
<td>0.42</td>
<td>0.92</td>
</tr>
<tr>
<td>26</td>
<td>0.93</td>
<td>0.68</td>
<td>2.9</td>
<td>0.10</td>
<td>0.42</td>
<td>0.98</td>
</tr>
<tr>
<td>27</td>
<td>0.93</td>
<td>0.47</td>
<td>1.75</td>
<td>0.15</td>
<td>0.31</td>
<td>0.97</td>
</tr>
<tr>
<td>28</td>
<td>1</td>
<td>0.25</td>
<td>1.33</td>
<td>0</td>
<td>0.25</td>
<td>1</td>
</tr>
</tbody>
</table>
Screening in Patients at High Risk of Hydroxychloroquine Retinal Toxicity

Anna Viola Taulaigo1, Maria Francisca Moraes-Fontes1, Eunice Patarata2, Sara Guerreiro Castro2 and Arnaldo Dias-Santos3, 1Unidade de Doenças Auto-imunes, Hospital Curry Cabral, Centro Hospitalar de Lisboa Central, Lisbon, Portugal, 2Unidade de Doenças Auto-imunes, Hospital Curry Cabral, Centro Hospitalar de Lisboa Central (CHLC), Lisbon, Portugal, Lisbon, Portugal, 3Serviço de Oftalmologia, Hospital de Santo António dos Capuchos, CHLC, Lisbon, Portugal, Lisbon, Portugal

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Despite effectiveness and favourable safety profile, antimalarials have the potential to cause irreversible macular retinopathy and vision loss. Screening methods still vary among clinicians but have evolved over the last decade (1, 2) and the optimal dose of hydroxychloroquine (HCQ) is now set at ≤5 mg/kg real body weight, above which the risk of retinal toxicity increases (3). HCQ in Portugal comes only as a 400 mg pill and in 10 pills per package, both of which, are neither friendly for optimizing safe dosing nor for promoting compliance. Once a patient is in a high risk group, yearly follow-up is recommended. The aim of the study is to test the frequency of retinal hydroxychloroquine toxicity in a single-centre cohort.

Methods:

Cross-sectional study conducted between January 2016 and May 2017, of a convenience sample of chronically compliant patients, characterized according to demographic and clinical phenotype, duration, current and cumulative dose of HCQ. The screening strategy consisted of automated threshold visual fields and objective test: spectral domain-OCT, fundus autofluorescence and multifocal electroretinogram. Toxicity was diagnosed on the basis of...
compatible visual fields defects together with at least one positive objective test, upon confirmation. Univariate statistical analysis was performed using the Wilcoxon Mann-Whitney (WMW) and Chi-Square (CS) tests for non-parametric distributed data.

Results:

Of the 62 patients screened, 32 (51%) had no prior ophthalmological examination. Median age was 46 years (y), IQR 37-60; range 27-83; 59 (95%) were female; the majority, 28 (45%) took HCQ due to SLE, 4 (6%) for Sjögren syndrome, 12 (19%) for UCTD, 11 (18%) for incomplete/cutaneous forms of lupus and 7 (11%) for other CTD. No patient had concomitant renal or liver disease. Median duration and cumulative dose were respectively 8 y (IQR 3 – 12; range 0.4 –31) and 1168 g (IQR 584 – 2044; range 36 -8760). Retinal toxicity was confirmed in 6 SLE- and further diagnosed in 1 non-SLE-patients; in all HCQ was stopped (overall: 2/7 screen naïve; 1/7 on tamoxifen; 1/7 with visual loss). Toxicity was correlated to disease (p=0,003) and HCQ therapy (p=0,002) duration, cumulative HCQ dose (p=0,001) and SLE (p=0,04) – Table I. Dose adjustments to ≤ 5 mg/kg were performed in 13 patients.

Conclusion:

Using a standardised referral protocol for HCQ retinopathy screening led to cessation of therapy due to toxicity (11%) and adjustment of daily dosing (21%). This study serves as a reminder that regular adjustment of dose and retinal toxicity screening is mandatory in patients subjected to prolonged HCQ therapy and reinforces lobbying for more flexible dosages. In addition, HCQ toxicity raises the need for alternative therapies in patients with CTD.

Table I. Univariate analysis comparing patients according to retinal toxicity

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Retinal toxicity (n=7)</th>
<th>No Retinal toxicity (n=55)</th>
<th>P value (*sig)</th>
<th>Statistical test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age y (mean±SD)</td>
<td>50±11</td>
<td>49±16</td>
<td>0,764</td>
<td>WMW</td>
</tr>
<tr>
<td>Non-Caucasian (n, %)</td>
<td>1 (14)</td>
<td>7 (13)</td>
<td>1.000</td>
<td>CS</td>
</tr>
<tr>
<td>Disease duration y (mean±SD)</td>
<td>21±9</td>
<td>10±7</td>
<td>0,003*</td>
<td>WMW</td>
</tr>
<tr>
<td>Duration HCQ therapy y (mean±SD)</td>
<td>17±7</td>
<td>8±6</td>
<td>0,002*</td>
<td>WMW</td>
</tr>
<tr>
<td>Current HCQ &gt; 5 mg/kg (n, %)</td>
<td>6 (86)</td>
<td>38 (69)</td>
<td>0,06</td>
<td>CS</td>
</tr>
<tr>
<td>Cumulative HCQ g (mean±SD) SLE (n, %)</td>
<td>2976±1381</td>
<td>1253±1339</td>
<td>0,001*</td>
<td>WMW</td>
</tr>
</tbody>
</table>

Disclosure: A. V. Taulaigo, None; M. F. Moraes-Fontes, None; E. Patarata, None; S. Guerreiro Castro, None; A. Dias-Santos, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/screening-in-patients-at-high-risk-of-hydroxychloroquine-retinal-toxicity

Abstract Number: 1652

Trajectories of Quality of Life in an Iception Cohort of Lupus Patients and Their Determinants
First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Systemic lupus erythematosus (SLE) is a chronic disease with varying disease activity levels and morbidities over time; this can affect patients’ health related quality of life (QoL). In clinical practice, we observed substantial heterogeneity in how patients’ QoL evolve over time. This study aims to: 1) Determine if there are latent classes of QoL trajectories (T) among SLE patients as measured by the Medical Outcome Survey Short Form 36 (SF-36) and 2) Identify predictors of different latent class membership.

Methods:
This is a single centre retrospective longitudinal inception SLE cohort. Annual SF-36 has been collected prospectively per clinical protocol. Only patients with ≥3 SF-36 questionnaires, and the 1st must be within 2 years of diagnosis were studied. The primary outcomes are the physical component (PCS) and mental component scores (MCS) of the SF36.

Group based trajectory model was performed using Proc Traj (SAS). One model each was fitted for the PCS and MCS. We tested 2 to 6 class solutions. The best model was determined by a combination of clinical plausibility and statistical criteria: number of patients in each group and model fitting statistic Bayesian Information Criterion (BIC). Models with the lowest BIC and groups containing > 5% of the total sample size were selected as the final models. Predictive effects of baseline variables (listed in table 1) on class membership were tested by logistic regressions.

Results:
171 patients with follow up to 10 years were analyzed. Patient characteristics are represented in table 1.

For PCS, 2 classes of T were identified: T1 low PCS with slight improvement over time (54.6%) and T2 persistently very low PCS (45.4%) (Figure 1). For MCS, 3 classes of T were identified: T1 persistently very low MCS (28.4%), T2 low MCS improving over time (32.4%) and T3 average MCS and improving over time (39.2%).

After adjusting for other factors, PCS T2 was significantly associated with older age at SLE diagnosis (OR 0.95 [95% CI 0.92-0.97, p 0.0001]) adjusting baseline disease activity (OR 1.04 [95% CI 0.998-1.09, p 0.06]) and antimalarial treatment (OR 0.36 [95% CI 0.09-1.49, p 0.16]). Regressions did not show significant results for MCS.

Conclusion:
The physical (PCS) and mental health components (MCS) of SF36 follows distinct classes of trajectory in SLE. Some patients have persistently very low PCS and MCS while others show mild improvement from below average to near or above average scores. Younger age at lupus diagnosis was associated with better PCS trajectory (T2).

**Figure 1. SF-36 trajectories over time.** (A) PCS trajectories and (B) MCS trajectories over time.
<table>
<thead>
<tr>
<th>Factors</th>
<th>Value</th>
<th>PCS T1</th>
<th>PCS T2</th>
<th>p</th>
<th>T1</th>
<th>T2</th>
<th>T3</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at SLE diagnosis</td>
<td>SD</td>
<td>14.60</td>
<td>10.07</td>
<td>.01</td>
<td>11.33</td>
<td>14.90</td>
<td>13.59</td>
<td>.66</td>
</tr>
<tr>
<td>Gender</td>
<td>F</td>
<td>80 (86.0%)</td>
<td>71 (91.0%)</td>
<td>.31</td>
<td>45 (91.8%)</td>
<td>47 (87.0%)</td>
<td>59 (86.8%)</td>
<td>.66</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Asian</td>
<td>6 (6.5%)</td>
<td>11 (14.1%)</td>
<td>.31</td>
<td>1 (2.0%)</td>
<td>9 (16.7%)</td>
<td>7 (10.3%)</td>
<td>.01</td>
</tr>
<tr>
<td></td>
<td>Black</td>
<td>17 (18.3%)</td>
<td>10 (12.8%)</td>
<td>.31</td>
<td>11 (22.4%)</td>
<td>3 (5.6%)</td>
<td>13 (19.1%)</td>
<td>.01</td>
</tr>
<tr>
<td></td>
<td>Caucasian</td>
<td>60 (64.5%)</td>
<td>47 (60.3%)</td>
<td>.31</td>
<td>35 (71.4%)</td>
<td>33 (61.1%)</td>
<td>39 (57.4%)</td>
<td>.01</td>
</tr>
<tr>
<td></td>
<td>Others</td>
<td>10 (10.8%)</td>
<td>10 (12.8%)</td>
<td>.31</td>
<td>2 (4.1%)</td>
<td>9 (16.7%)</td>
<td>9 (13.2%)</td>
<td>.01</td>
</tr>
<tr>
<td>Secondary school or higher</td>
<td>Yes</td>
<td>82 (88.2%)</td>
<td>72 (92.3%)</td>
<td>.44</td>
<td>44 (89.8%)</td>
<td>50 (92.6%)</td>
<td>60 (88.2%)</td>
<td>.01</td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td>Yes</td>
<td>7 (7.5%)</td>
<td>5 (6.4%)</td>
<td>.77</td>
<td>6 (12.2%)</td>
<td>3 (5.6%)</td>
<td>3 (4.4%)</td>
<td>.23</td>
</tr>
<tr>
<td>Baseline_SLEDAI-2K</td>
<td>Mean ± SD</td>
<td>9.30 ± 6.54</td>
<td>12.06 ± 9.57</td>
<td>.02</td>
<td>9.43 ± 7.44</td>
<td>10.87 ± 8.60</td>
<td>11.13 ± 8.33</td>
<td>.51</td>
</tr>
<tr>
<td>SDI at year 1</td>
<td>Mean ± SD</td>
<td>0.25 ± 0.76</td>
<td>0.37 ± 0.79</td>
<td>.29</td>
<td>0.35 ± 0.66</td>
<td>0.15 ± 0.41</td>
<td>0.40 ± 1.02</td>
<td>.19</td>
</tr>
<tr>
<td>Prednisone</td>
<td>Yes</td>
<td>81 (87.1%)</td>
<td>65 (83.3%)</td>
<td>.48</td>
<td>40 (81.6%)</td>
<td>45 (83.3%)</td>
<td>61 (89.7%)</td>
<td>.41</td>
</tr>
<tr>
<td>Anti-malarial</td>
<td>Yes</td>
<td>89 (95.7%)</td>
<td>72 (92.3%)</td>
<td>.34</td>
<td>47 (95.9%)</td>
<td>51 (94.4%)</td>
<td>63 (92.6%)</td>
<td>.75</td>
</tr>
<tr>
<td>Immunosuppressants</td>
<td>Yes</td>
<td>22 (23.7%)</td>
<td>21 (26.9%)</td>
<td>.62</td>
<td>10 (20.4%)</td>
<td>14 (25.9%)</td>
<td>19 (27.9%)</td>
<td>.64</td>
</tr>
</tbody>
</table>

All factors are at baseline

**Disclosure:** W. Fung, None; L. Lim, None; J. Su, None; Z. Touma, None.


**Abstract Number:** 1653

**Factors Influencing on Health-Related Quality of Life in Female Systemic Lupus Erythematosus Patients with Fibromyalgia**

**Kyung Min Ko**¹, Jun-Ki Min² and Su-Jin Moon³, ¹Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea, Republic of (South), ²Bucheon St. Mary's Hospital, Division of Rheumatology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Bucheon, Korea, Republic of (South), ³Bucheon St. Mary's Hospital, Division of rheumatology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Bucheon, Korea, Republic of (South)

**First publication:** September 18, 2017
Background/Purpose: Health-related quality of life (HRQoL) among systemic lupus erythematosus (SLE) patients is reduced, and fibromyalgia contribute to the decreased HRQoL. The objective of the present study is to evaluate the contributing factors for reduced HRQoL in female SLE patients regarding the presence of fibromyalgia.

Methods: The HRQoL measurement was made using the SF-36 and Euroqol EQ-5D. Sleep quality, fatigue severity, fibromyalgia severity, and SLE disease associated variables were measured.

Results: The scores of HRQoL, including overall scores as well as the physical component summary (PCS) and mental component summary (MCS), were lower in female SLE patients with fibromyalgia (n = 41), than in those without fibromyalgia (n = 111). SLE patients with fibromyalgia showed higher SLE disease activity, and more severe fatigue score, depressive mood and deteriorated sleep quality, compared with patients without fibromyalgia. In SLE patients with fibromyalgia, education level, severity of SLE organ damage, fatigue severity, sleep quality, depressive mood and fibromyalgia severity were significantly correlated with EQ-5D, whereas age, income, SLE disease activity, steroid dose, and disease duration were not correlated with EQ-5D. On the other hand, education level did not show significant correlation with EQ-5D in SLE patients without fibromyalgia. Multivariate logistic regression analysis revealed that depressive mood and SLE disease activity are independent contributing factors for deteriorated HRQoL in female SLE patients with fibromyalgia. In SLE patients without fibromyalgia, sleep quality in addition to SLE disease activity and depressive mood plays as a independent predictor for poor HRQoL.

Conclusion: The quality of life in SLE patients can be improved by managing depressive mood and improving sleep quality. Physicians may need to pay more attention to sleep both in patients with fibromyalgia and in those without fibromyalgia.

Table 1. Logistic regression analysis to identify the contributing factors of deteriorated HR-QoL (T1 by EQ-5D vs T2 and T3) in female SLE patients with fibromyalgia (n = 41)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate linear regression analysis</th>
<th>Multivariate regression analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Exp(B)</td>
<td>95% CI</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;Junior high school</td>
<td>4.4</td>
<td>0.319-60.6</td>
</tr>
<tr>
<td>Senior high school</td>
<td>12.1</td>
<td>1.31-111.3</td>
</tr>
<tr>
<td>Bachelor</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>SLICC-ACR damage index</td>
<td>1.895</td>
<td>1.002-3.583</td>
</tr>
<tr>
<td>SELENA-SLEDAI score</td>
<td>1.316</td>
<td>1.032-1.676</td>
</tr>
<tr>
<td>FACIT fatigue score (&lt;30)</td>
<td>3.167</td>
<td>0.827-12.12</td>
</tr>
<tr>
<td>PHQ9</td>
<td>1.22</td>
<td>1.068-1.393</td>
</tr>
</tbody>
</table>

Disclosure: K. M. Ko, None; J. K. Min, None; S. J. Moon, None.

Predictive Factors According to Type of Infection in Systemic Lupus Erythematosus Patients: Data from a Multi-Ethnic, Multi-National, Latin-American Cohort


First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster II: Damage and Comorbidities
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: While infections are one of the main causes of mortality in systemic lupus erythematosus (SLE), the type of infections and the factors predisposing to them have not been properly evaluated. The aim of the present study was to identify predictive factors accounting for the different types of infections in SLE patients.

Methods: A multi-ethnic, multi-national cohort from nine countries was utilized for these analyses. The following type of infections were considered: skin, lung, urinary tract, digestive tract and gynecological. Cox regression models were used to evaluate the predictors of new infections (global and per organs involved) using a backward elimination procedure. Potential predictors were demographic factors, clinical manifestations, SLEDAI, SDI and treatment at baseline.
Results: Predictive factors of skin infections were dose of prednisone between 15 and 60mg/d (HR: 1.73; CI: 1.16-2.57) and ≥60mg/d (HR: 1.63; CI: 1.01-1.91), lymphopenia (HR: 1.38; CI: 1.01-1.91), shorter disease duration at baseline (HR: 0.94; CI: 0.91-0.97), and previous infections (HR: 1.77; CI: 1.18-2.65). Predictive factors of lower airway infections were previous infections (HR: 2.39; CI: 1.38-4.13), lung involvement (HR: 2.81; CI: 1.38-5.71), and shorter disease duration at baseline (HR: 0.94; CI: 0.90-0.98). Predictive factors of urinary tract infections were higher damage at baseline (HR: 1.17; CI: 1.02-1.35), older age at diagnosis (HR: 1.02; CI: 1.01-1.03), shorter disease duration at baseline (HR: 0.93; CI: 0.89-0.96), female gender (HR: 3.03; CI: 1.11-8.23), and Mestizo ethnicity (HR: 1.98; CI: 1.29-3.04). Predictive factors of digestive tract infections were higher disease activity at baseline (HR: 0.94; CI: 0.91-0.97), female gender (HR: 3.03; CI: 1.11-8.23), and Mestizo ethnicity (HR: 1.98; CI: 1.29-3.04). Predictive factors of gynecological infections were dose of prednisone between 15 and 60mg/d (HR: 2.05; CI: 1.05-3.99) and higher disease activity at baseline (HR: 1.03; CI: 1.01-1.07).

Conclusion: Female gender, older age at diagnosis, lower socioeconomic status, lower educational level, shorter disease duration, lymphopenia, previous infections, lung involvement, higher damage accrual, higher disease activity, dose of prednisone >15mg/d, and Mestizo ethnicity were predictive of at least one type of infection.

Disclosure: V. R. Pimentel-Quiroz, None; M. Ugarte-Gil, None; G. J. Pons-Estel, None; D. Wojdyla, None; M. Cardiel, None; V. Pascual-Ramos, None; I. García-De La Torre, None; L. Barile, None; M. C. Amigo, None; L. H. Silveira, None; M. J. Sauza del Pozo, None; M. Guibert-Toledano, None; G. A. Reyes, None; A. Iglesias-Gamarra, None; G. Vasquez, None; J. Fernando Molina, None; J. A. Gómez-Puerta, AbbVie,BMS, Pfizer, Roche, 8; L. A. Gonzalez, None; R. Chacón-Díaz, None; M. H. Esteva Spinetti, None; I. Abadi, None; E. M. Acevedo-Vásquez, None; J. Alfaro-Lozano, None; I. Segami, None; L. Massardo, None; O. Neira, None; E. Sato, None; E. Bonfa, None, 2; E. Borba, None; G. S. Alarcón, None; B. Pons-Estel, None.


Abstract Number: 1655

Interferon b Blockade Rescues Human BM-MSC Osteoblastogenesis Defects in Systemic Lupus Erythematosus

Lin Gao1, Jennifer H. Anolik2 and R. John Looney3, 1medicine- allergy, immunology and rheumatology, University of Rochester Medical Center, Rochester, NY, 2Medicine- Allergy, Immunology and Rheumatology, University of Rochester Medical Center, Rochester, NY, 3University of Rochester Medical Center, Rochester, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Bone marrow mesenchymal stromal cells (BM-MSCs) are multipotent stem cells that can differentiate into chondrocytes, osteoblasts and adipocytes. SLE has been implicated as a stem cell disorder with impaired immunomodulatory function of SLE BM-MSCs and improvement of lupus nephritis with healthy MSCs transplantation has been suggested. However, the exact differentiation defects of SLE BM-MSCs have not been addressed, nor are the potential interventions studied. Our previous work indicates upregulation of IFNβ specific genes in human SLE bone marrow derived MSCs compared to normal bone marrow MSC. In addition, our data also
suggest that IFNβ and MAVS (Mitochondrial antiviral-signaling protein) form a positive feedback loop which leads to a senescence-like phenotype in SLE BM-MSCs and impairs MSC immunomodulatory function. Here we set out to investigate the differentiation defects of SLE BM-MSCs and potential intervention approaches.

**Methods:** The SLE patients recruited in this proposal satisfy the ACR classification criteria for SLE. BM-MSCs were isolated with Ficoll centrifugation (1.073 g/ml) and phenotyped using flow cytometry. In vitro studies included real-time PCR, western blotting and osteoblastogenesis analysis.

**Results:** We compared 3 age paired BM aspirates from healthy controls and SLE patients. BM-MSCs from SLE patients and healthy controls were isolated and cultured. The MSC surface markers are positive for CD73, CD90 and CD105, but negative for CD34 and CD45 in both healthy and SLE BM-MSCs after culture. No difference was observed in the surface markers between SLE and healthy BM-MSCs. However, SLE MSCs display significantly reduced osteoblastogenesis markers, such ALP (6 fold, \( p < 0.05 \)), RUNX2 (8 fold, \( p < 0.05 \)), OCN (4 fold, \( p < 0.05 \)) and BSP (4 fold, \( p < 0.05 \)). The osteoblast induction and ALP staining analysis for osteoblastogenesis also suggested a reduced differentiation with the SLE BM-MSCs. In contrast to the downregulation of osteoblast markers, the expression of IFNb is increased 5 fold (\( p < 0.05 \)) in SLE BM-MSCs. When BM-MSCs from healthy controls were treated with IFNb for 6 hours, reduced ALP (12 fold, \( p < 0.05 \)), RUNX2 (11 fold, \( p < 0.05 \)), OCN (8 fold, \( p < 0.05 \)) and BSP (7 fold, \( p < 0.05 \)) were observed, suggesting that IFNb plays an important role in inhibiting SLE BM-MSC differentiation into osteoblasts. Conversely, when IFNb neutralizing antibody was applied to SLE BM-MSCs, the osteoblastogenesis markers were significantly enhanced.

**Conclusion:** IFN-I signature is an important feature of SLE. IFNb has distinct features as compared to IFNα, higher affinity binding to IFN-I receptors, distinct gene transcripts and induction of senescence in non-hematopoietic cells. Our present work suggests that SLE BM-MSCs produce IFNb, mediating a decrease in osteoblastogenesis capacity. Our work sheds lights on the SLE BM pathogenesis. Moreover, the successful rescue of the SLE BM-MSCs osteoblastogenesis defect with an IFNb neutralizing antibody highlights IFNb as a new potential therapeutic target for SLE treatment.

**Disclosure:** L. Gao, None; J. H. Anolik, None; R. J. Looney, AstraZeneca, 5.


**Abstract Number:** 1656

**Type I Interferon Drives the Dysregulation of Plasmacytoid and Myeloid Dendritic Cells in Systemic Lupus Erythematosus and Antiphospholipid Syndrome**

Lucas L. van den Hoogen1, Aridaman Pandit1, Giovanni Palla2, Marzia Rossato3, Ruth D.E. Fritsch-Stork4, Joel A.G. van Roon5 and Timothy R.D.J. Radstake1, 1Rheumatology and Clinical Immunology, Laboratory of Translational Immunology, University Medical Center Utrecht, Utrecht, Netherlands, 2Rheumatology and Clinical Immunology, Laboratory of Translational Medicine, University Medical Center Utrecht, Utrecht, Netherlands, 3Department of Rheumatology & Clinical Immunology, Laboratory of Translational Immunology, University Medical Center Utrecht, Utrecht, Netherlands, 4Department of Rheumatology and Clinical Immunology, University Medical Center Utrecht, Utrecht, Netherlands, 5Department of Rheumatology & Clinical Immunology, University Medical Center Utrecht, Utrecht, Netherlands

**First publication:** September 18, 2017

**SESSION INFORMATION**
Dendritic cells (DC) are the sentinel cells of the immune system that potently activate T-cells, making them important players in the pathophysiology of systemic autoimmune diseases. The most prominent alteration in the immune system of patients with systemic lupus erythematosus (SLE) or antiphospholipid syndrome (APS) is the upregulation of type I interferon (IFN) inducible genes, known as the IFN signature. This signature is related to disease activity and the occurrence of vascular disease and is considered a promising therapeutic target. Plasmacytoid DC (pDC) are held responsible for the increased type I IFN (IFNα) production in SLE and APS, however, little is known on the molecular mechanisms that underlie increased type I IFN production by pDC in SLE and APS. Here we investigated the causes and consequences of increased type I IFN signaling on the dysregulation of both pDC and myeloid DC (mDC) in patients with SLE and APS.

Methods:

pDC and mDC were isolated from peripheral blood of patients with SLE (n=20), SLE+APS (n=10) and primary APS (PAPS, n=10) and healthy controls (n=12). RNA was extracted and used for RNA sequencing (RNAseq) to identify differentially expressed genes in pDC and mDC of SLE, SLE+APS and PAPS patients as compared with HC. Differential gene expression in pDC and mDC was compared between patients with (IFN-high) or without (IFN-low) a type I IFN signature. The effects of IFNα and TLR7 agonists on purified pDC were analyzed by RT-qPCR and flow cytometry. The effect of IFNα on cytokine production and the expression of T-cell stimulating molecules on pDC and mDC was measured by flow cytometry.

Results:

pDC and mDC shared an upregulation of type I IFN inducible genes in SLE, SLE+APS and PAPS as compared with HC. The expression of TLR7 and its downstream intermediates were increased in both pDC and mDC in all three patient groups as compared with HC. In pDC, not mDC, increased expression of TLR7 was confined to IFN-high patients (p<0.001). mDC of IFN-high patients showed an increased expression of genes involved in the activation of B- and T-cells (p<0.001). In vitro, IFNα upregulated TLR7 expression in pDC and augmented TLR7 mediated IFNα production. In contrast to pDC, in mDC IFNα priming enhanced TLR7 mediated TNFα production as well as the expression of T-cell stimulating molecules.

Conclusion:

IFNα has different effects on pDC and mDC. pDC of IFN-high SLE and APS patients are primed for type I IFN production through upregulation of TLR7. This results in a pathogenic loop of IFNα production by pDC, sustaining an increased activation status of both pDC and mDC in SLE and APS. Intervening in this loop potentially attenuates the dysregulation of DC in SLE and APS.

Disclosure: L. L. van den Hoogen, None; A. Pandit, None; G. Palla, None; M. Rossato, None; R. D. E. Fritsch-Stork, None; J. A. G. van Roon, None; T. R. D. J. Radstake, None.


Abstract Number: 1657
SLE Patients with Active Interferon Pathways Showed More Systemic Disease Involvement Than Patients with Inactive Interferon Pathways

Rufei Lu1,2, Joel M. Guthridge3, Cristina Arriens4, Teresa Aberle1, Stan Kamp1, Melissa E. Munroe1, Tim Gross1, Wade DeJager1, Susan Macwana1, Virginia C. Roberts1, Stephen Apel5, Hua Chen1, Hem Gurung1, Eliza Chakravarty4, Katherine Thanou1, Joan T. Merrill6 and Judith A. James7,8, 1Arthritis and Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, 2Medicine and Pathology, University of Oklahoma Health Sciences Center, Oklahoma City, OK, 3Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, OKC, OK, 4Arthritis & Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, 5Oklahoma Medical Research Foundation, Oklahoma City, OK, 6Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 7Arthritis & Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 8Department of Medicine, University of Oklahoma Health Sciences Center, Oklahoma City, OK

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a clinically diverse disease with a complicated pathophysiology highlighted in part by interferon (IFN) pathway dysregulation. Recent studies demonstrated that most pediatric SLE patients exhibit unabated IFN activities measured by microarray transcriptional scores. This study assessed the prevalence of these IFN active modules in adult SLE and determined association of these IFN active modules with lupus clinical features.

Methods: Gene expression profiles and associated IFN activities (IFN) of whole peripheral blood from 176 SLE patients who met ACR disease classification criteria were evaluated using modular transcriptional analysis based on Illumina Beadchip microarray data per (PMC2727981). ACR criteria and sub-criteria, clinical manifestations, comorbidities, and autoantibody positivity history were extracted from medical records by rheumatology trained investigators using a standard protocol. Lupus Severity Index (LSI) was calculated by two methods (Katz: 8330033; Montgomery: PMC4800735). Proportionality, chi-square, and mixed conditional logistic regression tests were used to analyze prevalence differences as well as to detect co-variate effects among different populations.

Results: One hundred patients were found to have active IFN pathways, while 76 patients had inactive IFN pathways by gene expression modules. Gender and ethnicity were not associated with IFN activation status in this adult SLE population. Patients with active IFN (mean: 29, range: 22 Ð 44) had earlier disease onset than patients with inactive IFN (37.5, 28 Ð 44; p<0.05). Patients with inactive IFN were more likely to report myalgias (68.7% vs 42.5%; Odds Ratio, 2.04) and arthralgias (79.1% vs 60%; OR, 3.23) compared to IFN active patients (p<0.05). However, hematologic (72.5% vs 35.8%; OR, 4.76; p<0.001) and renal (37.5% vs 10.4%; OR, 5.00; p<0.001) criteria were more common in IFN active patients. IFN active patients were also more likely to have autoantibody specificities to dsDNA (61.3% vs 28.5%; OR, 2.78; p<0.01), RNP (51.3% vs 14.9%; OR, 5.88; p<0.01), Ro (63.8% vs 14.9%; OR, 3.57; p<0.01), Sm (32.5% vs 10.4%; OR, 4.17; p<0.01), La (33.0% vs 11.9%; OR, 10.00; p<0.01), and Ribosomal P (11.3% vs 0.00%; OR, N/A; p<0.01) compared to IFN inactive patients. Overall, SLE patients with active IFN had higher Montgomery LSI [5.44, (4.65 Ð 5.65) vs 5.07, (4.43 Ð 5.65); p<0.05] and Katz LSI [4, (2.75 Ð 6.00) vs 2, (1.5 Ð 3.5); p<0.001] than IFN inactive patients.

Conclusion: In the current study, 57% of adult SLE patients had active IFN pathways and these patients were more likely to have renal, hematologic, and immunologic involvement compared to IFN inactive patients and scored higher
Interferon Related Soluble Mediator Concentrations Significantly Correlate with Disease Activity in SLE Patients with Active Interferon Pathways

Rufei Lu¹, Cristina Arriens², Teresa Aberle³, Stan Kamp³, Melissa E. Munroe³, Tim Gross¹, Wade DeJager³, Susan Macwana³, Virginia C. Roberts³, Stephen Apel⁴, Hua Chen³, Eliza Chakravarty⁵, Katherine Thanou³, Joan T. Merrill⁶ and Judith A. James⁷, ¹Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, ²Arthritis & Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, ³Arthritis and Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, ⁴Oklahoma Medical Research Foundation, Oklahoma City, OK, ⁵Oklahoma Medical Research Foundation, Oklahoma City, OK, ⁶Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, ⁷Arthritis & Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Interferon (IFN) pathways are dysregulated in a subset of patients with systemic lupus erythematosus (SLE). IFN dysregulation likely contributes to SLE pathogenesis and influences the disease course.
This study examined correlations between IFN transcriptional modular scores, biologically relevant soluble mediators, and SLE disease activity in patients with or without the IFN signature.

**Methods**: Adult SLE patients (n=49) meeting \( \geq 4 \) ACR classification criteria provided longitudinal samples at times of low (SLEDAI<6) and high (SLEDAI\( \geq 6 \)) disease activity. Immune pathway activity was evaluated by modular transcriptional analysis of Illumina Beadchip Microarray gene expression data in 98 patient samples and 20 age, race and gender matched healthy controls. Plasma soluble mediators (n=23) and antinuclear antibodies (n=11) were assessed by multiplex-bead based assays and ELISAs. Non-parametric paired tests were used for intra-individual univariate analyses, conditional logistic regression for multivariate analyses.

**Results**: Within a given individual, IFN signatures remained active and did not change with disease activity. In patients with active IFN signatures (n=29), several soluble mediators were elevated during high compared to low disease activity. These included MIG (median 168 pg/mL vs. 100 pg/mL; \( p<0.01 \)), IFNa (5.82 pg/mL vs. 3.69 pg/mL; \( p<0.01 \)), MCP1 (240 pg/mL vs. 209 pg/mL; \( p<0.01 \)), BLyS (1.88 ng/mL vs. 1.18 ng/mL, \( p<0.01 \)), TNFRI (2.82 ng/mL vs. 1.98 ng/mL, \( p<0.05 \)) and TNFRII (622 pg/mL vs. 552 pg/mL, \( p<0.01 \)). Additionally, patients with active IFN signatures showed higher M4.11 plasma cell module scores and dsDNA concentrations during high vs. low disease activity (\( p<0.05 \)). Periods of high disease activity in patients with active IFN signatures were best distinguished by M4.11 plasma cell module scores, BLyS, MIG and hemoglobin in multivariate logistic modeling (\( p<0.01 \)).

**Conclusion**: Although IFN activity correlates with disease severity in lupus populations, IFN module scores may not correlate significantly with intra-individual changes in disease activity. In contrast, plasma concentrations of IFN- and TNF-related soluble mediators significantly correlated with SLEDAI scores, suggesting that longitudinal monitoring of soluble mediators may be useful in individuals at increased risk of disease flares.

**Disclosure**: R. Lu, None; C. Arriens, Exagen, 2; T. Aberle, None; S. Kamp, None; M. E. Munroe, None; T. Gross, None; W. DeJager, None; S. Macwana, None; V. C. Roberts, None; S. Apel, None; H. Chen, None; E. Chakravarty, None; K. Thanou, None; J. T. Merrill, Anthera Pharmaceuticals, Lilly, EMD Serono, GlaxoSmithKline and Biogen., 5; J. A. James, None.
Identification of Long Noncoding RNA RP11-2B6.2 As a Positive Regulator through Type I Interferon Pathway in Lupus Nephritis

Yuanjia Tang1, Zhuojun Liao1, Zhixin Xue1, Lingling Wu1 and Nan Shen1,2,3,4, 1Shanghai Institute of Rheumatology, Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China, 2Center for Autoimmune Genomics and Etiology, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH, 3Institute of Health Sciences, Shanghai Institutes for Biological Sciences (SIBS), Chinese Academy of Sciences (CAS) & Shanghai Jiao Tong University School of Medicine (SJTUSM), Shanghai, China, 4Shanghai Institute of Rheumatology, Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China, Shanghai, China

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Long noncoding RNAs (lncRNAs) have recently been identified to be tightly linked to diverse human diseases. Systemic lupus erythematosus (SLE) is a common autoimmune disease. Renal involvement is the most frequent and serious complication. Type I interferon (IFN) and a group of inflammatory cytokines induced by type I IFN in human renal mesangial cells (HRMCs) play a vital role in lupus nephritis (LN). In this study we screened and investigated the contribution of the lncRNA RP11-2B6.2 to the pathogenesis of LN involved in the abnormal activation of type I IFN pathway.

Methods:
The high throughput RNA-seq data from kidney biopsies of LN patients and controls was applied to screen for candidate lncRNA and confirm its relationship with clinical data. Rapid amplification of cDNA ends (RACE) was adopted to identify the full length and exact sequences of lncRNA. In situ hybridization was adopted to identify the lncRNA location of cell nucleus and cytoplasm. Quantitative real-time polymerase chain reaction (RT-qPCR) and western blotting was used to detect the RNA and protein expression of lncRNA and individual genes relevant to type I IFN pathway respectively. Dual-luciferase reporter assay was used to detect the promoter transcriptional activity of genes.

Results:
The expression of lncRNA RP11-2B6.2 was significantly increased in the kidney tissues from LN patients compared with those from healthy controls, and positively correlated with the degree of disease activity and renal injury. Additionally, the expression of lncRNA RP11-2B6.2 can be stimulated by type I IFN. Silencing RP11-2B6.2 significantly reduced the expression of a group of interferon-stimulating genes (ISGs) including IFIT1, OAS1, etc., Furthermore, lncRNA RP11-2B6.2 affected the expression of IFN alpha and beta receptor subunit 1 (IFNAR1) and its promoter transcriptional activity, phosphorylation of Jak1 and Stat1, and the luciferase activity induced by interferon stimulated response element (ISRE).

Conclusion:
Long noncoding RNA RP11-2B6.2 is a positive regulator of the type I IFN signaling pathway in LN. LncRNA RP11-2B6.2 may contribute to the pathogenesis of LN and provide a potentially therapeutic target.

Disclosure: Y. Tang, None; Z. Liao, None; Z. Xue, None; L. Wu, None; N. Shen, None.


Abstract Number: 1660

Prolactin Induces an Interferon Signature in Monocytes and Drives IRF1-HAT Interactions

Yiu Tak Leung¹, Lihua Shi², Kelly Maurer², Li Song³ and Kathleen E. Sullivan⁴, ¹Temple University, Philadelphia, PA, ²Immunology ARC 1216, The Children's Hospital of Philadelphia, Philadelphia, PA, ³Allergy Immunology, Children's Hospital of Philadelphia, Philadelphia, PA, ⁴Pediatrics, University of Pennsylvania, Philadelphia, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Epigenetic changes in systemic lupus erythematosus (SLE) offer a potential explanation for the chronicity of disease. We previously found that interferon regulatory factor-1 (IRF1) binding sites were highly enriched in histone H4 acetylation (H4ac) peaks in SLE monocytes. IRF1 directly interacts with histone-modifying enzymes. IRF1 is a downstream immune response mediator that plays an important role in the interferon (IFN) pathway. IRF1 is highly inducible by prolactin (PRL), a hormone implicated in the pathogenesis of SLE. PRL is involved in immune response modulation through the JAK/STAT/IRF1 pathway. Our studies extend this by defining a pivotal role for PRL in induction of histone modifying enzymes that alter the balance of histone acetylation and IRF1 activation and downstream chromatin effects.

Methods: Primary monocytes and THP-1 cells were treated with recombinant human PRL. Flow cytometry for H4ac were run on the Accuri C6 with isotype controls. Real-time quantitative reverse transcription polymerase chain reaction (qRT-PCR) evaluated the effects of PRL stimulation on expression of HATs/HDACs and interferon-response genes. Western blot, immunoprecipitation and ChIP assays defined PRL effects on HAT/HDAC protein expression and interactions with IRF1. IRF1 knockdown experiments were performed using a lentivirus system.

Results:

Flow cytometry found significantly increased total H4ac, H4K5, H4K8, H4K12, and H4K16 acetylation in primary monocytes stimulated by PRL.

qRT-PCR studies of HAT/HDAC expression patterns showed increases in PCAF, CBP, P300, GCN5 and ATF2 expression in THP-1 cells stimulated by prolactin that was time-dependent.

Western blot assays found that nuclear levels of IRF1, PCAF, p300, CBP, ATF2, TIP60, MOF and HBO1 increased with PRL stimulation; HDAC3 decreased with PRL stimulation.
IRF1 co-immunoprecipitation assays found IRF1-binding with PCAF, P300, CBP and ATF2 in both unstimulated and stimulated states. IRF1 interactions with p300, CBP and ATF2 increased at 1-2 hrs of PRL stimulation. ChIP assays revealed increased IRF1 binding to PRL-response genes TGFb and ID1; increased H4ac was seen at the promoter of ID1 with PRL stimulation.

IRF1 knock-down experiments validated that PRL effects on HATs are IRF1-dependent. PRL-induced increases in the gene expression of PCAF, CBP, ATF2 and TIP60 were abrogated in the IRF1 knock-down cells as compared to controls.

PRL effects on the IFN signature genes were defined by qRT-PCR. CXCL10, IFIT1, IFIT3, B2M, OAS1 and CD40 expression levels were significantly increased by 4-hrs of PRL stimulation. Longer exposure to PRL stimulation also found further significant increases in the expression of IFIT1, IFIT3, CXCL10, MX1, B2M, CD40, OAS1, OASL and NOD2 after 2 wks.

**Conclusion:** Prolactin has long been associated with autoimmunity. These studies provide key insights into the mechanisms. These data demonstrate that prolactin stimulation induces IRF1 activation and a pattern of acetylated H4 that corresponds to the changes seen in SLE. We found dominant effects at the level of epigenetics, an area not previously explored with respect to prolactin effects in autoimmunity.

---

**Disclosure:** Y. T. Leung, None; L. Shi, None; K. Maurer, None; L. Song, None; K. E. Sullivan, None.


---

**Abstract Number:** 1661

**STAT4 Regulates Pathogenic IL-21 and IFN-γ in Tfh Cells in Murine and Human Lupus**

Fotios Koumpouras¹, XueMei Dong², Jason Weinstein² and Joseph E. Craft³, ¹Internal Medicine, Rheumatology, Yale University School of Medicine, New Haven, CT, ²Rheumatology, Yale University School of Medicine, New Haven, CT, ³Department of Internal Medicine/Rheumatology, Yale University School of Medicine, New Haven, CT

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster I

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Follicular helper T cells (Tfh) cells regulate the germinal center (GC) response by delivery of contact-dependent interactions and cytokines including IL-4, IFN-γ and IL-21. JAK-STAT signaling plays an important role in regulating these cytokines associated biological responses. Signal Transducer and Activator of Transcription proteins (STATs) are intracellular transcriptional factors that are activated and recruited to the cytokine receptors through phosphorylation by Janus Kinase (JAK).

There are several STATs (STAT1, STAT2, STAT3, STAT4, STAT5 and STAT6) in mammalian cells. STAT4 is the only STAT that demonstrates the genetic association to disease susceptibility in human systemic lupus by a number of Genome-Wide Association Studies. These genetic associations lie in the single-nucleotide polymorphisms (SNPs) among the noncoding regions. STAT4 SNP at rs7574865, which locates intron 3, is associated with increased
sensitivity to IFNa signaling and gene expression, and suggests that these genetic variants may affect disease susceptibility through the gene’s transcription.

Role of STAT4 in disease pathology is still unclear. STAT-4 in human SLE has not been robustly studied.

**Methods:** B6.Sle1.Yaa mice were sacrificed at 2, 4, and 6 months of age flow cytometry plots of Tfh cells or Th1 cells were obtained using FLOW. Flow cytometry plots of intracellular staining for the transcription factors Bcl6 and T-bet in Tfh cells over time were also performed. 40 ml peripheral blood was drawn during the clinical visit. Serum was separated and stored in -80°C. Mononuclear cells from the peripheral blood was isolated using Ficoll-Paque, suspended in serum with 10% DMSO and store in -80 degree for STAT4 assay.

**Results:** In young lupus mice, Tfh cells co-express the Tfh and Th1 cell transcription factors Bcl6 and T-bet, respectively; with a decline of both in Tfh cells as the disease progresses. However, Tfh cells continue to co-produce similar levels of both IL-21 and IFN-γ during the progression of murine lupus. Transcriptional analysis of lupus-Tfh cells at different stages of disease revealed an increased STAT4 gene signature as the disease progresses. Moreover, we observed that lupus-Tfh cells continue to phosphorylate STAT4 (pSTAT4) as the disease worsens, consistent with the prolonged production of pathogenic IL-21 and IFN-γ. In the blood of lupus patients, activated (CD4+CD45RA−) T cells also secrete IL-21 and IFN-γ. STAT4 activity was measured in these cells using FLOW. Unstimulated CD4+CD45RA− T cells from lupus patients had an increase in pSTAT4 compared to that of healthy controls. Furthermore, pSTAT4 was further increased with IFN-a or IL-12 stimulation in the lupus patients compared to controls.

**Conclusion:** In SLE, T-bet and Bcl6 expression decline in Tfh cells, while increased STAT4-guided expression appears to drive pathogenic cytokine production, providing a potential therapeutic target for SLE.

**Disclosure:** F. Koumpouras, None; X. Dong, None; J. Weinstein, None; J. E. Craft, L2 Diagnostics, New Haven, CT, 4, UV Thapeutics, 1.


Abstract Number: 1662

**High Type I Interferon Activity Is Associated with Active Class III/IV Lupus Nephritis in European-American Lupus Patients Independent of dsDNA Antibodies**
Lupus nephritis (LN) is one of the most severe types of organ involvement in systemic lupus erythematosus (SLE), despite the recent advances in immunosuppressive therapies. High type I interferon (IFN) is a heritable risk for SLE, and some previous studies have suggested a link between high IFN and lupus nephritis. However, little is known about the relationships between high levels of IFN and the subtypes of LN, and whether IFN is more associated with anti-dsDNA antibodies or with clinical nephritis.

Methods: We studied 197 EA SLE patients and measured type I IFN in sera by performing WISH IFN bioassay as described previously. Subtypes of LN were confirmed by renal biopsy review. Complements, anti-dsDNA and other auto-antibodies were measured in the clinical laboratory, and standard clinical cut-offs were used to define a positive result. Non-parametric analyses were used to compare IFN data with the antibody data.

Results: IFN level and SLEDAI score was positively correlated (r=0.30, p<0.0001, Spearman) in our cross-sectional evaluation. EA subjects with a high levels of IFN (IFN score ≥2) were more likely to have renal manifestations compared to the subjects with a low levels of IFN(IFN score <2) (p<0.001, OR=3.4, Fisher’s exact test). In addition, the incidence rate of class III/IV LN was significantly higher among patients with a high levels of IFN compared to the patients with low levels of IFN (p=0.0197, OR=5.1, Fisher’s exact test). Notably, IFN level was significantly higher in active class III/IV LN compared to inactive class III/IV LN (p<0.001 Mann-Whitney U) and this was not observed in non-class III/IV LN populations.. Positivity of ds-DNA antibody did not show significant difference between inactive class III/IV LN and active class III/IV LN, and the correlation between SLEDAI and IFN was driven by the dsDNA and complement variables.

Conclusion: Our data support an association between type I IFN and class III/IV nephritis that is independent of overall SLEDAI and anti-dsDNA antibodies, suggesting that IFN is involved in renal pathogenesis. These data also suggest that IFN could predict renal disease activity or the future risk of developing LN, especially class III/IV LN in EA SLE patients.

Disclosure: T. Iwamoto, None; J. M. Dorschner, None; M. A. Jensen, None; D. Vsetecka, None; S. Amin, None; A. Makol, None; F. C. Ernst, None; T. Osborn, None; K. Moder, None; V. Chowdhary, None; T. B. Niewold, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/high-type-i-interferon-activity-is-associated-with-active-class-%e2%85%a2%e2%85%a3-lupus-nephritis-in-european-american-lupus-patients-independent-of-dsdna-antibodies

Abstract Number: 1663
De Novo Mutation in ACACB in Childhood Onset SLE Highlights a Novel Role As Modulator of Nucleic Acid Sensor-Driven Type I Interferon Responses

**Isaac Harley**¹, Hanna Schulz¹, John Cambier², Leah C. Kottyan³, John B. Harley⁴, V. Michael Holers⁵, Hermine I. Brunner⁶, Kristine Kuhn¹, Kevin D. Deane¹ and Kenneth Kaufman⁷, ¹Division of Rheumatology, University of Colorado School of Medicine, Aurora, CO, ²Department of Immunology & Microbiology, University of Colorado School of Medicine, Aurora, CO, ³Center for Autoimmune Genomics and Etiology (CAGE), Division of Allergy and Immunology, Cincinnati Children's Hospital, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, ⁴Center for Autoimmune Genomics and Etiology (CAGE), Cincinnati Children's Hospital Medical Center, Cincinnati, OH, ⁵Medicine, Division of Rheumatology, University of Colorado Denver, Aurora, CO, ⁶Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, ⁷Center for Autoimmune Genomics and Etiology (CAGE), Cincinnati Children's Hospital Medical Center; US Department of Veterans Affairs Medical Center, Cincinnati, OH

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster I  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Rare variants provide important opportunity for mechanistic insight as they carry substantial effect sizes and provide deep insight into disease etiopathogenesis. To date, several pathways have been identified as monogenic causes of SLE or similar syndromes of systemic autoimmunity, particularly with the severe manifestations of childhood onset SLE. In several other disease phenotypes, such as autism spectrum disorders, with severe presentation in childhood, exome-wide sequencing approaches of both unaffected parents and affected children have identified causal de novo mutations and thus identified novel genes that were not amenable to the GWAS approach. With this approach, we identified a novel SLE candidate gene, ACACB, which encodes the acetyl-CoA carboxylase beta subunit (ACC-beta) (see below). This enzyme functions in many tissues as a regulator of fatty acid oxidation and was previously defined as a key modulator of innate immune response through its role supporting the anabolic demands of activated dendritic cells.

**Methods:** In order to define de novo mutations in SLE, we performed an exome-wide sequencing study in a trio consisting of an SLE proband and her parents. Quality control and Mendelian errors were filtered using a validated analysis pipeline (CASSI) as previously described [1]. Functional studies of a gene containing a de novo variant, ACACB, were then performed using 5-(Tetradecyloxy)-2-furoic acid (TOFA), an inhibitor of ACACB. THP1-Blue ISG cells that have stable integration of an interferon regulatory factor (IRF)-inducible secreted alkaline phosphatase reporter construct were treated with TOFA to confirm a role for ACACB in type I interferon response (Invivogen). P-values presented were adjusted for multiple comparisons using the Holm-Sidak method with alpha = 0.05.

**Results:** Inhibition studies with TOFA revealed that type I interferon activity in response to several nucleic acid ligands was impaired in the setting of ACC-beta inhibition as measured by secreted alkaline phosphatase activity. Specifically, in comparison to vehicle treatment, TOFA treated cells demonstrated 10-20% dose-dependent reduction of type I interferon activity in response to the STING ligand cGAMP (P < 0.01), 10-15% dose-dependent reduction of type I interferon activity in response to the transfection of the cytosolic DNA and RNA sensor ligand poly(dA:dT) (P < 0.01) and non-significant trend towards dose-dependent reduction of type I interferon activity in response to the TLR-7/TLR-8 ligand R848 (resiquimod).
**Conclusion:** ACACB is a candidate SLE susceptibility gene for childhood onset SLE. Inhibition of the activity of ACC-beta, its product, modulates type I interferon response to several SLE autoantigen relevant pattern recognition receptor ligands. By defining ACACB as a candidate mutation in SLE, fatty acid beta-oxidation is defined as a potential novel druggable target for SLE therapy. ACC inhibitors in development to treat non-alcoholic steatohepatitis may find utility if repurposed to treat human SLE.


**Disclosure:** I. Harley, None; H. Schulz, None; J. Cambier, None; L. C. Kottyan, None; J. B. Harley, None; V. M. Holers, None; H. I. Brunner, None; K. Kuhn, None; K. D. Deane, Inova Diagnostics, Inc., 5; K. Kaufman, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/de-novo-mutation-in-%ce%b1c%ce%b2-in-childhood-onset-sle-highlights-a-novel-role-as-modulator-of-nucleic-acid-sensor-driven-type-i-interferon-responses](http://acrabstracts.org/abstract/de-novo-mutation-in-%ce%b1c%ce%b2-in-childhood-onset-sle-highlights-a-novel-role-as-modulator-of-nucleic-acid-sensor-driven-type-i-interferon-responses)

Abstract Number: 1664

**Serum FAS, Ferritin, Igfbp2, sTNFR2 As Markers for Tracking Mucocutaneous and Musculoskeletal Flares in SLE Patients**

Kamala Vanarsa¹, Samar Soliman², Aubrey Swilling³, Joan T. Merrill⁴ and Chandra Mohan², ¹Biomedical Engineering, University of Houston, Houston, TX, ²Biomedical Engineering, University of Houston, Houston, TX, ³University of Houston, Houston, TX, ⁴Oklahoma Medical Research Foundation, Oklahoma City, OK

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster I  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Systemic lupus erythematosus (SLE) is a chronic multi-systemic autoimmune disease, with a broad spectrum of clinical manifestations and unpredictable disease course with periods of flares and remission. Over the past few years, several biomarkers have been reported to be elevated in SLE, though the utility of these markers in monitoring disease progression remains unclear. The main objective of the current study is to assess the performance of serum FAS, sTNFRII, Igfbp2 and Ferritin as biomarkers for tracking lupus flares in non-renal SLE patients.

**Methods:**

Serum samples were obtained over 4 consecutive visits (<4 months apart) from 29 SLE patients from Oklahoma Medical Research Foundation (OMRF). All patients met ACR requirements for diagnosis of SLE and none of them had lupus nephritis, though they had mucocutaneous and/or musculoskeletal disease manifestations. Serum FAS, sTNFRII, Igfbp2 and ferritin were assayed in all 29 patients by ELISA and related to SLEDAI and BILAG disease activity indices.

**Results:**
All four tested serum proteins correlated significantly with SLEDAI and BILAG in SLE: FAS ($r= 0.36$, $p < 0.0001$ for SLEDAI & $r= 0.29$, $p= 0.0002$ for BILAG), Ferritin ($r= 0.13$, $p=0.0494$ for SLEDAI & $r= 0.22$, $p= 0.0035$ for BILAG), Igfbp2 ($r= 0.24$, $p= 0.0013$ for SLEDAI & $r= 0.18$, $p= 0.0106$ for BILAG) and sTNFRII ($r= 0.30$, $p <0.0001$ for SLEDAI & $r= 0.19$, $p= 0.0112$ for BILAG). We next examined serial changes in all 4 biomarkers with changes in disease activity. In some patients 2-3 of the tested biomarkers were predictive of changes in disease activity while in others all 4 tested markers emerged as good indicators of disease activity changes. In studying a total of 72 patient follow-up intervals, FAS and Ferritin exhibited the highest concordance with concurrent disease activity (58-62%), followed by Igfbp2 (50%) and sTNFRII (46%), all of which were superior to the performance of complement C3, C4 and anti-DNA. Furthermore, combining FAS to other tested molecules increased its ability to track concordant disease activity changes in SLE (81% for FAS±Ferritin; 76% for FAS±Igfbp2 and FAS±sTNFRII).

**Conclusion:**

Serum FAS and Ferritin emerge as potential serum markers for predicting mucocutaneous and musculoskeletal disease flares in SLE patients.

---

**Disclosure:** K. Vanarsa, None; S. Soliman, None; A. Swilling, None; J. T. Merrill, None; C. Mohan, None.


**Abstract Number:** 1665

**Soluble Programmed Cell Death Protein 1 As a Biomarker for Systemic Lupus Erythematosus**

Shinya Hirahara, Yasuhiro Katsumata, Yasushi Kawaguchi and Hisashi Yamanaka, Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017
**Session Title:** Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster I
**Session Type:** ACR Poster Session B
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Programmed cell death protein 1 (PD-1/CD279) is a cell surface receptor that belongs to the extended CD28/CTLA-4 family and is expressed on T cells and pro-B cells. PD-1 plays an important role in down regulating the immune system by preventing the activation of T-cells. Soluble PD-1 (sPD-1), which is produced by the alternative splicing, can functionally block the regulatory effect of membrane-bound PD-1 on T cell activation. We aimed to retrospectively evaluate the usefulness of serum sPD-1 as a biomarker for systemic lupus erythematosus (SLE).

**Methods:** In the period from 2010 through 2016, serum samples from 74 hospitalized patients due to active SLE were retrieved from the Tokyo Women’s Medical University SLE Biorepository. Serum samples from 20 patients with systemic sclerosis (SSc) were similarly retrieved from the Tokyo Women’s Medical University SSc Biorepository and served as controls. Sera from 21 healthy subjects were also used as controls. These samples had been previously collected and stored for unspecified medical studies under general consents. All of the SLE and SSc patients fulfiled the 1997 revised ACR criteria for SLE and the 2013 ACR/EULAR criteria for SSc, respectively. We measured the levels of sPD-1 by enzyme-linked immunosorbent assay (ELISA) kit in sera of patients with SLE.
and SSc, and healthy controls, and compared them. Clinical and laboratory data including the SLE Disease Activity Index 2000 (SLEDAI-2K) scores were also retrospectively collected from the medical records. Associations between the levels of serum sPD-1 and clinical information were retrospectively and statistically analyzed.

**Results:** In the study population with SLE patients, 69 were female, the median age was 35, the median anti-dsDNA antibodies titer was 9.9, and the median SLEDAI-2K score was 12. The levels of serum sPD-1 in SLE patients with SLEDAI-2K ≥6 were significantly higher than those in SLE patients with SLEDAI-2K <6, patients with SSc, and healthy controls ($p < 0.05$ in all comparisons), whereas there was no significant difference in other comparisons (Figure). Among the SLE patients, the levels of sPD-1 were moderately correlated with the titers of anti-dsDNA antibodies and the SLEDAI-2K scores, and were moderately and inversely correlated with the levels of C3 and C4. The levels of sPD-1 were significantly higher in SLE patients with arthritis, myositis, rash, mucosal ulcers, fever, thrombocytopenia, or leucopenia than those without ($p < 0.05$ in all comparisons). In addition, the levels of sPD-1 were higher in patients positive for anti-dsDNA antibodies than those negative among SLE patients with SLEDAI-2K ≥6 ($p < 0.01$). The sPD-1 levels decreased significantly following treatment among SLE patients ($p < 0.05$).

**Conclusion:** The findings from the present study suggested that serum sPD-1 can serve as a new biomarker reflecting disease activity in patients with SLE.

---


**Abstract Number:** 1666

**Anti-Mitochondrial Autoantibodies in Systemic Lupus Erythematosus and Their Association with Disease Manifestations**

Yann Becker¹, Renee Claude Loignon¹, Genevieve Marcoux¹, Anne-Sophie Julien², Imene Melki¹, Lihi Eder³, Eric Wagner¹, Martin Pelletier¹, Marie-Josee Hebert⁴, Clemence Belleannce¹, Joyce Rauch⁵, Melanie Dieude⁴, Paul R. Fortin⁶ and Eric Boilard¹, ¹CHU de Quebec and Universite Laval, Quebec City, QC, Canada, ²CHU de Quebec - Universite Laval, Quebec City, QC, Canada, ³Women's College Research Institute, Women's College Hospital,
Background/Purpose: Eukaryotic cells contain organelles called mitochondria that govern energy supply and control of cell death. Whereas damaged organs or activated cells can extrude their mitochondria, which is suggested to trigger innate immunity, it is less well known whether extracellular mitochondria are also recognized by the adaptive immune system.

Methods: We improved methodologies for isolation of pure mitochondria from human and mouse cells and tissues, and designed ELISA to measure the presence of antibodies directed against mitochondrial outer membrane and mtDNA in mouse models, and patients with systemic lupus erythematosus (SLE) \( (n=170, \text{Table 1}) \), compared to controls \( (n=44) \) and patients with antiphospholipid syndrome (APS) \( (n=12) \) or primary biliary cirrhosis (PBC) \( (n=12) \). Carotid ultrasounds were available in 113 patients. Spearman’s correlation analysis was used to explore whether antibody levels were associated with the following outcomes: SLEDAI-2K, SDI and carotid ultrasound plaques and intima-media thickness (CIMT) as surrogates for vascular damage.

Results: Antibodies against mitochondrial outer membrane and mtDNA were increased in a mouse model of SLE. In humans, the levels of antibodies recognizing the outer mitochondrial membrane and mtDNA were significantly higher in SLE patients than in controls, APS patients and PBC patients (Table 2). Antibodies against mtDNA were associated with a lower likelihood of previous thrombotic events and higher disease activity measured by SLEDAI-2K, the latter being entirely explained by the high correlation between commercial assays for antibodies to double stranded DNA and our assay for mtDNA antibodies. While antibodies against the mitochondrial outer membrane were not associated with the measured disease characteristics, their presence was not completely explained by the presence of anti-cardiolipin, suggesting that other mitochondrial targets exist. Oxidation of the mitochondrial surface had no impact on autoantibody recognition of mitochondrial antigens.

Conclusion: This study provides useful insights into optimized methodologies for assessing mitochondrial antibodies in mice and humans, providing an appreciation of the anti-mitochondrial antibody repertoire and its role in autoimmunity. These findings further support the concept that extracellular mitochondria provide an important source of circulating autoantigens that may be clinically relevant in SLE.

Table 1: Demographic and clinical variables for SLE patients
<table>
<thead>
<tr>
<th>Demographic variable</th>
<th>SLE patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=170 except if (n-missing)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>20-78</td>
</tr>
<tr>
<td>Range, years</td>
<td>47 ± 15 (49)</td>
</tr>
<tr>
<td>Mean ± S.D (median), years</td>
<td></td>
</tr>
<tr>
<td>Disease duration</td>
<td>0-57</td>
</tr>
<tr>
<td>Range, years</td>
<td>16 ± 17 (19)</td>
</tr>
<tr>
<td>Median ± IQR (mean), years</td>
<td></td>
</tr>
<tr>
<td>Gender, female, n (%)</td>
<td>170 (100)</td>
</tr>
<tr>
<td>Married, n (%)</td>
<td>88 (52)</td>
</tr>
<tr>
<td>Ethnicity, n (%) (n-1)</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>36 (21)</td>
</tr>
<tr>
<td>Asian</td>
<td>30 (18)</td>
</tr>
<tr>
<td>Black</td>
<td>8 (5)</td>
</tr>
<tr>
<td>Others</td>
<td></td>
</tr>
<tr>
<td>Education &gt; Grade 8, n (%)</td>
<td>162 (95)</td>
</tr>
<tr>
<td>Employment, n (%)</td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>38 (22)</td>
</tr>
<tr>
<td>Disabled / Sick-leave</td>
<td>67 (39)</td>
</tr>
<tr>
<td>Pre-menopausal, n (%)</td>
<td>77 (45)</td>
</tr>
<tr>
<td>Smoker[^1], n (%)</td>
<td>15 (9)</td>
</tr>
<tr>
<td>Ex-smoker, n (%)</td>
<td>39 (25)</td>
</tr>
<tr>
<td>Years since quitting, Median ± IQR (mean)</td>
<td>15 ± 18 (15)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>55 (32)</td>
</tr>
<tr>
<td>BP syst, Mean ± S.D (median), mmHg</td>
<td>120 ± 16 (120)</td>
</tr>
<tr>
<td>BP dia, Mean ± S.D (median), mmHg</td>
<td>74 ± 9 (74)</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>10 (6)</td>
</tr>
<tr>
<td>IMC, n (%)</td>
<td></td>
</tr>
<tr>
<td>&lt; 18.5</td>
<td>89 (52)</td>
</tr>
<tr>
<td>18.5 – 24.9</td>
<td>40 (24)</td>
</tr>
<tr>
<td>Range, cm</td>
<td>Mean ± S.D (median), cm</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>25.0 – 29.9</td>
<td>34 (20)</td>
</tr>
<tr>
<td>³ 30.0</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Waist hip ratio (n-1)</th>
<th>0.61-1.12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range</td>
<td>0.83 ± 0.08 (0.83)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medication, n (%)</th>
<th>40 (24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticoagulation or anti-platelet[iii] (n-1)</td>
<td>124 (73)</td>
</tr>
<tr>
<td>Antimalarial</td>
<td>78 (46)</td>
</tr>
<tr>
<td>Prednisone</td>
<td>25 (15)</td>
</tr>
<tr>
<td>Lipid lowering</td>
<td>6 (4)</td>
</tr>
<tr>
<td>Diabetes medication</td>
<td></td>
</tr>
</tbody>
</table>

[i] Current regular smoking, any amount.

[iii] Currently prescribe.

**Table 2: Variables of interest for SLE patients**
<table>
<thead>
<tr>
<th>Variable of interest (n-missing)</th>
<th>Patients (n=170 except when specified)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMtDNA IgG mean</td>
<td>0.00-1.78</td>
</tr>
<tr>
<td>Range</td>
<td>0.31 ± 0.48 (0.46)</td>
</tr>
<tr>
<td>Median ± IQR (mean)</td>
<td></td>
</tr>
<tr>
<td>Anti-mitochondrial outer membrane IgG mean</td>
<td>0.14-3.11</td>
</tr>
<tr>
<td>Range</td>
<td>0.61 ± 0.42 (0.71)</td>
</tr>
<tr>
<td>Median ± IQR (mean)</td>
<td></td>
</tr>
<tr>
<td>Lupus Anticoagulant n (%) (n-7)</td>
<td>18 (11)</td>
</tr>
<tr>
<td>Antiphospholipids antibody present, n (%) (n-6)</td>
<td>22 (13)</td>
</tr>
<tr>
<td>ACA[ii] positive, n (%)</td>
<td>12 (7)</td>
</tr>
<tr>
<td>ACA IgG (ref range 0-13) (n=158, if positive)</td>
<td>3-90</td>
</tr>
<tr>
<td>Range, GPL-U/mL</td>
<td>28 ± 33 (29)</td>
</tr>
<tr>
<td>Median ± IQR (mean), GPL-U/mL</td>
<td></td>
</tr>
<tr>
<td>ACA IgM (ref range 0-4.2) (n=158, if positive)</td>
<td>1-41</td>
</tr>
<tr>
<td>Range, MPL-U/mL</td>
<td>6 ± 7 (8)</td>
</tr>
<tr>
<td>Median ± IQR (mean), MPL-U/mL</td>
<td></td>
</tr>
</tbody>
</table>

Disclosure: Y. Becker, None; R. C. Loignon, None; G. Marcoux, None; A. S. Julien, None; I. Melki, None; L. Eder, None; E. Wagner, None; M. Pelletier, None; M. J. Hebert, None; C. Belleannee, None; J. Rauch, None; M. Dieude, None; P. R. Fortin, None; E. Boilard, None.


Abstract Number: 1667
Increased Levels of BAFF in SLE Patients Correlates with Neutrophil Activation and Autoantibody Production

Andrew Vasconcellos¹, John Marken¹, Ting Wang¹,², Christian Lood³ and Natalia V. Giltiay¹, ¹Division of Rheumatology, Department of Medicine, University of Washington, Seattle, WA, ²Department of Rheumatology, Peking Union Medical College Hospital, Chinese Academy of Medical Science and Peking Union Medical College, Beijing, China, ³Division of Rheumatology, Division of Rheumatology, Department of Medicine, University of Washington, Seattle, WA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Neutrophil (PMN) activation and neutrophil extracellular trap (NET) formation are implicated in the pathogenesis of Systemic Lupus Erythematosus (SLE), particularly in the acceleration of organ and vascular damage. Lupus neutrophils can drive B-cell activation and auto-antibody (Ab) production, at least in part, by production of type-I interferons and B-cell activating factor (BAFF) and, by exposing self-antigens (Ags), such as oxidized mitochondrial DNA and cardiolipin. The presence of anti-cardiolipin Abs in SLE patients has been associated with an increased risk of cardiovascular events due to atherosclerosis. Still, little is known about the potential link between neutrophil abnormalities, B-cell activation, and auto-Ab production. This study was undertaken to test whether PMN activation and NET formation contribute to increased BAFF levels and auto-Ab production in SLE patients.

Methods: BAFF levels were analyzed in serum samples from 60 SLE patients with varying levels of disease activity and 20 healthy controls (HC) by ELISA. Plasma levels of NETs and 8-OHdG were measured by ELISA. Anti-dsDNA titers complement and CRP levels were obtained from clinical records. Autoantibody reactivities were assessed by microarray.

Results: Mean BAFF levels were significantly higher in SLE patients, as compared to HC (2785.25 vs 924.29 pg/mL, p< 0.0001). After defining a cut-off for BAFF levels at 1429.4 pg/mL (mean + 3SD HC), around 60% of SLE patients were identified to have elevated BAFF levels. No associations between BAFF titers and gender, ethnicity, and age at diagnosis were found. Although BAFF levels did not associate significantly with the overall SLEDAI scores, we found a significant correlation between BAFF levels and increased CRP levels, and decreased serum C3 and C4 levels, suggesting an association with ongoing immune complex (IC)-driven disease. Compatible with this hypothesis, levels of ICs, measured by an in vitro assay, correlated with BAFF levels (r=0.38, p=0.02). Asking if BAFF levels correlated with neutrophil activation, we observed that serum-mediated neutrophil activation, as well as the cell-free 8-OHdG DNA, an inflammatory NET-derived component, both correlated with BAFF levels (r=0.34, p<0.05 for both analyses), consistent with PMN activation contributing to elevated BAFF levels in SLE. Microarray data revealed positive correlations between BAFF levels and IgG auto-reactivity against M2-mitochondrial antigen, sphingomyelin, phosphatidylinositol, β2 glycoprotein and cardiolipin.

Conclusion: We found an association between heightened BAFF production and markers of PMN activation and particularly increased levels of inflammatory oxidized DNA, compatible with the release of BAFF during NETosis. Our data support the hypothesis that neutrophils, through IC-mediated activation, release BAFF as well as key auto-Ags such as dsDNA and mitochondrial components, including cardiolipin, which may contribute to the production of pathogenic auto-Abs. These results provide new insights into how neutrophils and BAFF may contribute to the development of cardiovascular disease and help identify new effective therapies for SLE patients.
Disclosure: A. Vasconcellos, None; J. Marken, None; T. Wang, None; C. Lood, None; N. V. Giltiay, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/increased-levels-of-baff-in-sle-patients-correlates-with-neutrophil-activation-and-autoantibody-production

Abstract Number: 1668

Identification of a Serum Measure of Lupus Nephritis Activity That Detects Molecular Pathways and Mechanisms Implicated in Renal Damage

Mikhail Olferiev¹, Dina Greenman², David Fernandez¹, Kerry Merritt¹, Kyriakos A. Kirou¹ and Mary K. Crow³,
¹Hospital for Special Surgery, New York, NY, ²Mary Kirkland Center for Lupus Research, Hospital for Special Surgery, New York, NY, ³Department of Medicine, Hospital for Special Surgery, New York, NY
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Up to 60% of SLE patients develop renal involvement, and renal injury is an important predictor of mortality in patients with SLE. Kidney biopsy is the gold standard for diagnosis of active lupus nephritis (LN), and active LN is associated with proteinuria, active urinary sediment and/or a rise in serum creatinine. Urine protein/creatinine ratio is often used to monitor LN activity over time, and proteinuria is accepted as the most effective predictor of the long-term outcome of LN. However, none of these measures has proved sufficient for identification and analysis of the biologic events that underlie the development of active LN. We analyzed extensive laboratory and clinical data and blood gene expression data in relation to urine protein to identify an informative measure of LN activity over time.

Methods: Forty-seven LN patients were studied. Clinical and laboratory data were collected for an average (range) of 6 (2-12) years. Longitudinal random urine protein/creatinine ratio data were compared to 72 laboratory and clinical parameters in a linear mixed model. Illumina HT-V4 Bead array data (3-13 time points/patient) were obtained from PBMC of 30 LN patients and compared to proteinuria and serum albumin levels.

Results: In a longitudinal analysis of LN patients, serum albumin was the parameter that was most significantly (negatively) correlated with proteinuria (p<0.00001). In addition, serum albumin correlated significantly with serum calcium, sodium, bilirubin, erythrocyte sedimentation rate (ESR), urine red blood cells (URBC) and urine white blood cells (UWBC) (p<0.05) in a multivariate model. In an analysis of longitudinal PBMC gene transcript data, proteinuria did not correlate with any transcript after correction for multiple testing (FDR 0.05). In contrast, serum albumin correlated with 120 transcripts in PBMC from LN patients. Functional analysis of the obtained genes indicates enrichment of transcripts specifically expressed in neutrophils (e.g., DEFA4, MMP8, MMP9, ELANE, ARG1) and genes related to cell-cycle and DNA-damage pathways (p<0.01).

Conclusion: Proteinuria is an indicator of worsening LN. However, its usefulness as a marker is limited by concurrent urinary tract infections, circadian rhythms, oliguria and other factors. Through study of a longitudinal series of LN samples we demonstrate that serum albumin levels negatively correlate with classical measures of renal involvement, including proteinuria, URBC, and UWBC and might herald a renal flare. Moreover, serum albumin levels identified gene transcripts in blood that may reflect significant molecular mechanisms that contribute to LN flare, allowing novel insights into the pathogenesis of LN.
Anti-Mitochondria DNA Antibody As an Improved Biomarker for Systemic Lupus Erythematosus

Yangsheng Yu¹, Kalika Mahato¹, Suyang Xu¹, Jenna Mu¹, Amanda Zhang¹, James R. O'Dell², Lynell W. Klassen², Michelene Hearth-Holmes³ and Kaihong Su¹,

¹Pathology and Microbiology, University of Nebraska Medical Center, Omaha, NE, ²Department of Internal Medicine, University of Nebraska Medical Center, Omaha, NE, ³Internal Medicine/Rheumatology Division, Univ. of Nebraska Medical Center, Omaha, NE

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Anti-dsDNA antibodies are highly specific for systemic lupus erythematosus (SLE) and often associate with lupus nephritis. Extracellular nucleosome DNA released from apoptotic or necrotic cells are thought to be the source of DNA autoantigens in SLE. Recent studies show that mitochondria DNA (mtDNA) may play an important role in driving the production of anti-DNA autoantibodies and type I interferons in SLE. Since mtDNA are rich in unmethylated CpG islands, mtDNA may represent a distinct class of autoantigens in SLE. The purpose of this study was to compare autoantibodies to mtDNA and nucleosome-associated DNA in SLE and their association with lupus nephritis and other disease parameters.

Methods:

144 patients who fulfilled the 1997 American College of Rheumatology criteria for SLE were recruited at the University of Nebraska Medical Center (UNMC). 123 healthy controls (matched with SLE patients in demographics, about 80% female with an average age of 37, about 50% Caucasians, 30% African Americans, and 15% Hispanic) were recruited at the community of UNMC. Blood serum samples were tested for anti-mtDNA antibodies using Enzyme-linked immunosorbent assay (ELISA) with PCR-amplified human mtDNA as the capturing antigen. The anti-dsDNA NcX antibodies were determined using ELISA-based kit from Euroimmun. The data were summarized from three independent experiments.

Results:

The anti-mtDNA antibodies are significantly higher in patients with SLE (n = 144, mean optical density units OD = 0.80; SD = 0.90) than healthy controls (n = 123, mean OD = 0.19; SD = 0.11) with a p value less than 0.0001 (by two-tailed Mann-Whitney test). Using the mean + 2 x SD of healthy controls as the cut off for positivity, 51.4% of
SLE patients are tested positive for anti-mtDNA antibodies while 41% of the same SLE cohort are tested positive for anti-dsDNA-NcX. Anti-mtDNA antibody levels are also more significantly correlated with SLEDAI (Pearson r = 0.53, p = 0.0001), and reversely correlated with C3 and C4 levels (Pearson r = -0.4, p = 0.0001; Pearson r = 0.21 , p = 0.01, respectively) than anti-dsDNA-NcX antibody levels. Furthermore, increased percentage of SLE patients with active lupus nephritis were tested positive for anti-mtDNA (65%) than anti-dsDNA NcX (52%).

**Conclusion:**

We have developed a simple anti-mtDNA ELISA assay that has 10% higher sensitivity for SLE and 13% higher sensitivity for active lupus nephritis, compared to the widely used anti-dsDNA NcX ELISA assay (Euroimmun). The anti-mtDNA antibodies also have better correlations with SLEDAI, C3, and C4 levels. Therefore, anti-mtDNA antibody may serve as an improved biomarker for SLE.

**Disclosure:** Y. Yu, None; K. Mahato, None; S. Xu, None; J. Mu, None; A. Zhang, None; J. R. O'Dell, Medac, 5, Coherus, 5; L. W. Klassen, None; M. Hearth-Holmes, None; K. Su, None.


**Abstract Number: 1670**

**HMGB1-TLR4 Axis in Patients with Neuropsychiatric Systemic Lupus Erythematosus**

**Qin Huang**¹, Chao Yuan², Hao Ren¹ and Min Yang¹, ¹Department of Rheumatology, Nanfang Hospital, Southern Medical University, Guangzhou, China, ²Department of Neurology, Nanfang Hospital, Southern Medical University, Guangzhou, China

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster I

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Neuropsychiatric Systemic Lupus Erythematosus (NPSLE) is a severe complication of SLE, including a variety of neurological and psychiatric features. Previous studies have demonstrated the close relationship between NPSLE and inflammation. High mobility group protein B1 (HMGB1), a highly conserved protein secreted by innate immune cells in response to pathogenic products and released by injured or dying cells, occupies a central role in the pathogenesis of both sterile and infectious inflammation. Recent studies have shown an association between HMGB1 and chronic inflammation and autoimmunity. Toll-like receptor 4 (TLR4) is the primary receptor of endogenous extracellular HMGB1 in mediating macrophage activation, cytokine release, and tissue injury. HMGB1-TLR4 signaling pathway is the up-stream pathway of NF-KB, which could upregulate the expression of various cytokines and other inflammatory mediators. The objective of the study was to explore the potential mechanism of HMGB1-TLR4 axis in NPSLE.

**Methods:** The study population consisted of 107 SLE patients and 43 age- and sex-matched healthy controls. 73 SLE patients had active disease. 36 of these had NPSLE. Clinical and serological parameters were assessed according to routine procedures. HMGB1 and TLR4 levels were measured by ELISA. Statistical analyses were performed by using the chi-square test and the t-test.
Results: Central nervous system (CNS) manifestations accounted for 94% (34/36 patients), while involvement of the peripheral nervous system (PNS) was 6% (2/36 patients). The majority of the manifestations were Seizure disorders (n=17; 47.2%), Headache (n=12; 33.3%), Cognitive dysfunction (n=10; 27.8%), Psychoses (n=8; 22.2%). Within the group of active patients those with NP manifestations had higher HMGB1 levels (0.451 (0.292 to 0.583)) compared to active patients with non-NP manifestations (0.356 (0.098 to 0.436)). In patients with NP (0.429 (0.313 to 0.526)) and non-NP (0.375 (0.196 to 0.478)) manifestations during active periods of the disease, TLR4 levels significant increased in comparison to the controls. TLR4 levels were significantly higher in active patients (0.401 (0.196 to 0.526)) compared to quiescent patients. There was a significant positive correlation between levels of HMGB1 and TLR4 in the total patients group (P<0.0001, r=0.939). We observed a correlation between HMGB1 levels and SLEDAI (P<0.0001, r=0.804). Also, TLR4 levels showed a significant correlation with SLEDAI (P<0.0001, r=0.809). HMGB1 levels correlated with anti-dsDNA levels (P<0.0001, r=0.558). Similarly, TLR4 showed a correlation with anti-dsDNA levels (P<0.0001, r=0.522). We observed a negative correlation in the total SLE group between C3, C4 and HMGB1 levels (P<0.0001, r=-0.545 and P<0.0001, r=-0.270 respectively). Also, TLR4 showed a significant negative correlation with C3 and C4 (P<0.0001, r=-0.559 and P<0.0001, r=-0.285 respectively).

Conclusion: Our data suggest that HMGB1-TLR4 axis plays an important role in the pathogenesis of SLE as well as NPSLE.

Disclosure: Q. Huang, None; C. Yuan, None; H. Ren, None; M. Yang, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/hmgb1-tlr4-axis-in-patients-with-neuropsychiatric-systemic-lupus-erythematosus

Abstract Number: 1671

Complement C4 Gene Copy Number Variations Bestow Large Ranges of Serum C4 Protein Levels in Chinese Patients with Systemic Lupus Erythematosus (SLE) and Contribute to Organ and Cardiovascular Damages over Time

Chi Chiu Mok¹, Emily King², Bi Zhou³, Gakit Yu⁴, Yee Ling Wu⁵ and CHACK-YUNG Yu⁶, ¹Rheumatology, Tuen Mun Hospital, Hong Kong, Hong Kong, ²Pediatrics, Nationwide Children's Hospital, Columbus, OH, ³Center for Molecular and Human Genetics, The Research Institute at Nationwide Children's Hospital and The Ohio State University, Columbus, OH, ⁴Center for Molecular and Human Genetics, Nationwide Children's Hospital, Columbus, OH, ⁵Center for Molecular and Human Genetics, The Research Institute at Nationwide Children's Hospital, Columbus, OH, ⁶Pediatrics, Ohio State Univ, Columbus, OH

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Human SLE is characterized by fluctuating serum levels of complement proteins. There are frequent copy number variations (CNVs) of complement C4A and C4B genes among different individuals. Previously, we demonstrated that C4A deficiency is a strong genetic risk factor for SLE. Our current objectives are
to investigate how CNVs of C4 contribute to the great variability of C4 serum levels and how deficiencies of C4A or C4B modulate the clinical presentations, including organ damage, of SLE.

Methods: Our study population included 499 patients from Hong Kong, who fulfilled ≥4 of the 2013 ACR/SLICC criteria for SLE. Among them 93% were women, the mean age of SLE onset was 32.8±13.0 years, and SLE duration was 14.4±7.6 years. Gene copy numbers (GCNs) of total C4 (C4T), C4A and C4B were determined by real-time PCRs. Serial serum levels over the past 5 years for C4 and C3 of each patient were retrieved through the laboratory data registry system. Serum C4 and C3 levels are shown as mg/100 ml (unit). Clinical manifestations and organ damage of SLE were correlated with CNVs of C4 genes and serum levels. Continuous data between groups were compared by t-tests and categorical data by $\chi^2$ analyses. Logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals for effects of C4 CNVs on cumulative clinical manifestations of SLE and accrued organ damage, adjusted for durations of disease.

Results: Serum levels for C4 varied from 1-84 units (Median: 17) and for C3 from 8-314 units (Median: 86). There was a very strong correlation between C4 and C3 protein levels ($R= 0.70$, $p= 5.3\times 10^{-75}$). The GCN of C4T varied between 2 and 9 with a median of 4 copies (54%), followed by 2 and 3 copies (21%). Each additional gene copy correlated to an increase of 4 and 6 units for the mean and maximum serum C4 levels, respectively. A higher GCN of C4T ($\geq 3$ vs $<3$) was protective against the development of neuropsychiatric disorder over time [OR 0.45 (0.21-0.98), $p=0.04$]. A high GCN of C4L ($\geq 3$ vs $<3$), or the absence of C4S (GCN=0), was negatively associated with the occurrence of thrombocytopenia [OR 0.64 (0.42-0.97), $p=0.04$]. A high GCN of C4B was associated with damage to any organ [OR 1.76 (1.05-2.93), $p=0.03$], but a high GCN of C4A ($\geq 3$ vs $<3$) was associated with cardiovascular damage [OR 2.30 (1.06-5.00), $p=0.04$]. Among the SLE patients studied, 18.3% had persistently low levels of C4 (mean ≤10.0 units). These patients mostly had GCNs of C4T=2 or 3 [OR 4.02 (2.47-6.56), $p= 4.7\times 10^{-8}$], or C4B=0 or 1 [OR 3.06 (1.31-4.84), $p= 0.005$]. Patients with persistently low C4 levels had increased prevalence of mucosal ulceration [OR 2.09 (1.15-3.78), $p=0.02$], lymphopenia [OR 1.76 (1.01-3.05), $p=0.045$] and gastrointestinal disorders [OR 2.52 (1.31-4.84), $p= 0.005$].

Conclusion: CNVs of C4 genes confer great variability of serum C4 levels among SLE patients. While C4A deficiency contributes to genetic predisposition of SLE, persistently low levels of serum C4 among patients were strongly correlated with low GCN of total C4 and C4B deficiency. Elucidating C4-CNVs may have prognostic significance of SLE as high GCNs of C4B and C4A appeared to correlate with organ damage and cardiovascular disease, respectively.

Disclosure: C. C. Mok, None; E. King, None; B. Zhou, None; G. Yu, None; Y. L. Wu, None; C. Y. Yu, None.


Abstract Number: 1672

Cytokines and Autoantibody Cluster-Interaction in Systemic Lupus Erythematosus. a Systems Medicine Approach

Julian Barahona-Correa, Yovana Pacheco, Diana M. Monsalve, Manuel Rojas, Yhojan Rodríguez, Juliana Saavedra, Mónica Rodríguez-Jiménez, Ruben Mantilla, Carolina Ramirez-Santana, Nicolás Molano-González and Juan-Manuel Anaya, Center for Autoimmune Diseases Research (CREA), School of Medicine and Health Sciences, Universidad del Rosario, Bogota, Colombia

First publication: September 18, 2017

SESSION INFORMATION
Background/Purpose:

Evidence supports the existence of different sub-phenotypes and the pivotal role of cytokines and autoantibodies in systemic lupus erythematosus (SLE). Cytokines interact in a highly complex network. Thus, understanding how these complex non-linear processes are connected and observed in real-life settings is a major challenge. Cluster approaches may assist in the identification of these sub-phenotypes, which represent such a phenomenon and may contribute to the development of personalized medicine. Therefore, we analyzed the relationship between autoantibodies and cytokine clusters in SLE.

Methods:

This was an exploratory study in which 70 consecutive women with established SLE (ACR 1997) were assessed. Clinical characteristics, including disease activity (by SLAQ), a 14-autoantibody profile (by IFI and ELISA), and a panel of 15 serum cytokines (by cytometric bead array) were measured simultaneously. Mixed-cluster methodology was used to define autoantibody and cytokine clusters. Bivariate and multivariate analyses, including a heteroscedastic regression model, were done to identify associations between clusters and related variables.

Results:

Three clusters of autoantibodies were defined (Figure 1): neutral, 2) aPL-dominant, and 3) ENA-dominant. Eight cytokines disclosed levels above the threshold (as compared to healthy controls), allowing to find 4 clusters (Figure 2): 1) neutral, 2) chemotactic, 3) IL-6/G-CSF dominant, and 4) IFNα/Pro-inflammatory. Further, the disease activity was associated with cytokine clusters (Figure 3A), which, in turn, were associated with autoantibody clusters (Figure 3B).

Conclusion:

These results support the existence of SLE cytokine-driven sub-phenotypes. They provide insight for a new taxonomy, encourage the practice of personalized medicine, and support proof-of-principle studies.

Figure 1. Autoantibody clusters.
Figure 2. Cytokine clusters.

A. Disease activity by cytokine cluster.

B. Cytokine and autoantibody clusters interaction.
Disclosure: J. Barahona-Correa, None; Y. Pacheco, None; D. M. Monsalve, None; M. Rojas, None; Y. Rodríguez, None; J. Saavedra, None; M. Rodríguez-Jiménez, None; R. Mantilla, None; C. Ramírez-Santana, None; N. Molano-González, None; J. M. Anaya, None.


Abstract Number: 1673

**Human C4 Gene Copy Number Influences Cell-Bound Complement Activation Product (CB-CAP) C4d in Systemic Lupus Erythematosus**

Chau-Ching Liu¹, Joseph Ahearn², Amy Xiaoqin Tang², Yee Ling Wu³, CHACK-YUNG Yu³ and Susan Manzi², ¹Lupus Center of Excellence, Allegheny Health Network Research Institute, Pittsburgh, PA, ²Lupus Center of Excellence, Allegheny Health Network Research Institute, Pittsburgh, PA, ³Center for Molecular and Human Genetics, The Research Institute at Nationwide Children's Hospital, Columbus, OH

First publication: September 18, 2017

SESSION INFORMATION

**Session Date:** Monday, November 6, 2017

**Session Title:** Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster I

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

Background/Purpose: Human complement C4 protein is the product of two isotypic genes C4A and C4B that are located on chromosome 6 in various copy numbers. Recent studies by us and others have demonstrated that cell-bound complement activation product (CB-CAP) C4d is a valuable diagnostic and monitoring biomarker for systemic lupus erythematosus (SLE). The current study was based upon the hypothesis that CB-CAP C4d levels may be influenced not only by SLE disease status but also by C4 gene copy number variation (CNV). Specifically, a low C4 gene copy number may lead to persistently low CB-C4d levels in some SLE patients, thereby reducing the diagnostic sensitivity of CB-C4d as biomarkers in such patients. This study was focused on elucidating the correlation between C4 gene CNV and CB-C4d levels in patients with SLE so as to improve the utility of CB-CAP biomarker assays for lupus diagnosis, monitoring and stratification.
Methods: We conducted a cross-sectional study of 195 SLE patients. Variations in gene copy numbers for total C4, C4A, and C4B genes were determined using various genotyping technologies. CB-C4d levels on peripheral blood cells of respective patients were measured by flow cytometry. Correlations between CB-C4d levels and C4 gene CNV were examined by statistical analysis using Kruskal-Wallis test and post hoc pairwise comparison as well as linear regression analysis (for continuous variables). Categorical variables were analyzed using Fisher’s exact test or chi-square test.

Results: The results demonstrated that higher CB-C4d levels, particularly those of T cell-bound C4d (T-C4d) and B cell-bound C4d (B-C4d), were associated with increasing numbers of C4 genes. Patients with greater than 4 copies of the C4 genes were more likely to be in the highest quartile of T-C4d/B-C4d levels than were patients with fewer copies of the C4 genes. Remarkably, patients with no C4A genes (homozygous C4A deficiency) had normal/low T-C4d/B-C4d. Patients with partial C4 genetic deficiencies were more likely to be missed as false negatives using individual CB-CAPs (e.g. BC4d alone) for the diagnosis of SLE. Not all CB-CAPs were influence equally by C4 CNV.

Conclusion: Together, results of the present study suggest a positive correlation of T-C4d and B-C4d levels with CNV of the C4 gene, particularly the C4A gene, in patients with SLE. These observations support our hypothesis that individual CB-CAP C4d levels such as TC4d and BC4d should be interpreted with simultaneous determination of C4 gene copy numbers as well as other CB-CAPs such as EC4d, PC4d, RC4d, etc. as components of lupus biomarker panels for diagnosis, monitoring and stratification.

Disclosure: C. C. Liu, Exagen Diagnostics, 7; J. Ahearn, Exagen Diagnostics, 7; A. X. Tang, None; Y. L. Wu, None; C. Y. Yu, None; S. Manzi, Exagen Diagnostics, 7.


Abstract Number: 1674

Combining Medications That Lower Systemic Oxidative Stress Is Associated with Less Atherosclerosis in Systemic Lupus Erythematosus

Jim C. Oates, Medical Service, Ralph H. Johnson VA Medical Center, Charleston, SC; Division of Rheumatology & Immunology, Department of Medicine, Medical University of South Carolina, Charleston, SC

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: No single medication has been demonstrated as effective in reducing atherosclerosis or cardiovascular events in systemic lupus erythematosus (SLE), possibly due to the heterogeneity of mechanisms leading to atherosclerosis. However, selecting medications that affect final common pathways to atherosclerosis may be effective. Oxidative stress induces endothelial dysfunction and oxidation of LDL, both of which increase atherosclerotic plaque formation. We hypothesized that medications associated with reduced oxidative stress will also have a reduced association with atherosclerosis and that combining medications will be associated with further reductions in atherosclerosis and oxidative stress.
Methods: SLE patients meeting ACR criteria with inactive disease (SLE Disease Activity Index < 4) were enrolled. Bilateral carotid total atherosclerotic plaque area (TPA) was determined by ultrasound and reported as a percent of the mean (TPA%) for age and sex matched non-SLE controls in a large, high risk hypertension clinic. Serum was digested into amino acids and analyzed for durable oxidative modifications to serum protein tyrosine (ortho-tyrosine + meta-tyrosine (omTyr)) by high performance liquid chromatography and electrochemical detection as a surrogate marker for systemic oxidative stress and reported as (omTyr/Tyr)*100,000. Concurrent medications associated with reduced omTyr were included in the analysis. Patients were categorized by the number of these medications (0-4) they were taking. Groups were compared by Mann-Whiteny U tests, and correlations were performed by Spearman correlation.

Results: Among 50 SLE patients (90% female, 96% African American, median age=44), mycophenolate, (MMF) angiotensin converting enzyme inhibitor (ACE), statin, and hydroxychloroquine (HDQ) use were all associated with a trend to lower TPA% and omTyr (with ACE inhibitors associated with a significantly less TPA%, median(interquartile range) = 0 (0-24) vs. 116 (0-448), p = 0.02). The number of these medications taken together trended to lower omTyr and TPA% (Figure) and correlated negatively with omTyr (r = -0.31, p – 0.04).

Conclusion: In other populations, both ACE and statins are associated with lower cardiovascular events and reduced oxidative stress. MMF reduces expression of inducible nitric oxide synthase, an enzyme source of oxidative stress that is overexpressed in lupus nephritis, while HDQ reduces oxidative stress and improves endothelial function in murine lupus and is associated with lower cardiovascular events in human SLE. This is the first study to our knowledge to evaluate its association with oxidative stress and atherosclerosis in human SLE. This cross sectional study inspires the hypothesis that combining medications chosen by their ability to reduce the sources of systemic oxidant stress may be more effective than any one medication to reduce atherosclerosis in SLE.

Disclosure: J. C. Oates, None;


Abstract Number: 1675

SLE Comprises Four Immune-Phenotypes, Which Differ Regarding HLA-DRB1 and Clinical Associations

Lina Marcela Diaz Gallo1, Emeli Lundström1, Vilija Oke1, Kerstin Elvin2, Yee Ling Wu3, Johanna Gustafsson1, Andreas Jönsen4, Dag Leonard5, Agneta Zickert6, Gunnel Nordmark7, Anders A. Bengtsson4, Johanna K Sandling7, Anders A. Bengtsson4, Johanna K Sandling7, Lars Rönnblom8, Iva Gunnarsson1, CHACK-YUNG Yu9, Leonid Padyukov10 and Elisabet Svenungsson10,
1Department of Medicine, Rheumatology Unit, Department of Medicine Solna, Rheumatology Unit, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, Stockholm, Sweden, 2Dept. of Clinical Immunology
SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: SLE is a remarkably heterogeneous disease including diverging clinical symptoms, autoantibodies and genetic susceptibility. Hitherto unrecognized patterns may define sub-phenotypes with different pathogenesis and specific treatment needs. Based on autoantibody profile we therefore investigated phenotypic clusters and explored cluster associations with clinical manifestations and one of the most important genetic risk factors for SLE, HLA-DRB1 alleles.

Methods: 908 SLE patients (fulfilling 1982 ACR criteria) of European Caucasian origin and 3654 age- gender- and ethnicity-matched healthy controls (HC) were included. We determined the occurrence of 13 autoantibodies: dsDNA, nucleosomes, ribosomal P, RNP68, RNPA, Sm, Sm/RNP, SSA52, SSA60, SSB, aCL-IgG/IgM and ab2GP1. HLA-DRB1 typing was performed by sequence-specific primer polymerase chain reaction assay. Cluster analysis was done using Gower distance matrix, followed by partition around medoids cluster calculation and Silhouette metric for number of clusters validation. Chi-square test, odds ratios (OR), 95% confidence intervals and false discovery rate p value (p) were calculated for the association tests (within brackets).

Results: Four (1-4) clusters were defined based on autoantibody occurrence.

1) 29%, dominated by anti-SSA52/60/SSB positivity is strongly associated with HLA-DRB1*03 when compared to HC (4.1[3.4-4.9] p=6.4E-56) and other clusters (2.9[93.3-3.6] p=1.1E-19). Discoid lesions were more common vs. other clusters (1.8[1.3-2.6] p= 0.02).

2) 29 %, dominated by anti-SmRNP/Sm/DNA/RNPA/RNP68/nucleosome, was specifically associated with HLA-DRB1*15 when compared to HC (1.7[1.6-2.1] p=5.7E-6) and other clusters (1.5[1.1-1.9] p=0.01). Nephritis was common vs. other clusters (1.9[1.4-2.7] p= 2.0E-3)

3) 24 %, dominated by anti-B2GP1/aCL-IgG/IgM, was associated with HLA-DRB1*04 when compared with other clusters (1.8[1.4-2.4] p=2E-4). More thrombotic events vs. other clusters were observed in this group (1.84 [1.3-2.6] p=0.01)

4) 18 % was negative for the 13 tested autoantibodies and was not associated with any specific HLA-DRB1 alleles and it was not associated as risk factor for any of the evaluated clinical manifestations.

Conclusion: We demonstrate that immune-phenotypes/clusters in SLE can fit into a frame of HLA-DRB1 alleles and that the overall association between SLE and HLA-DRB1*03 and HLA-DRB1*15 seems to be driven mainly by clusters 1 and 2, respectively. We also confirm previous observations that autoantibody clusters associate with
clinical symptoms. We believe that these results could be used to redefine SLE, determine predictive biomarkers and inclusion criteria for clinical trials.

Disclosure: L. M. Diaz Gallo, None; E. Lundström, None; V. Oke, None; K. Elvin, None; Y. L. Wu, None; J. Gustafsson, None; A. Jönsen, None; D. Leonard, None; A. Zickert, None; G. Nordmark, None; A. A. Bengtsson, None; J. K. Sandling, None; L. Rönnblom, None; I. Gunnarsson, None; C. Y. Yu, None; L. Padyukov, None; E. Svennungsson, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/sle-comprises-four-immune-phenotypes-which-differ-regarding-hla-drb1-and-clinical-associations

Abstract Number: 1676

Improving Sensitivity to Change of the Modified Rodnan Skin Score over Time

Annel M. Fernandez1, Robert F. Spiera2, Jackie Szymonifka2 and Jessica K. Gordon2, 1Medicine- Rheumatology/Research, Hospital For Special Surgery, New York, NY, 2Rheumatology, Hospital for Special Surgery, New York, NY
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
The Modified Rodnan Skin Score (MRSS) assesses global dermal thickness through the examination of 17 body areas scored by clinical palpation using a 4 point Likert scale (0 = normal skin; 1 = mild thickness; 2 = moderate thickness; 3 = severe thickness). The MRSS, due to its reliability, reproducibility, validity and responsiveness to change, has been used as the primary outcome measure in numerous clinical trials in systemic sclerosis. It has been observed that finger MRSS scores remain relatively static over time in the context of clinical trials. We tested this clinical observation using our MRSS data and further tested the hypothesis that modifying the MRSS to exclude assessment of fingers would improve sensitivity to change of the MRSS.

Methods:
This was a retrospective study using compiled MRSS data from three single institution investigator-initiated clinical trials. Sixty-one patients were followed for a total of 593 visits, with a mean of 9.7 visits per patient (range 2-19), and a median follow-up of 17.7 months (range 0.9 – 54.2 months). We compared the proportion of visits that demonstrates a change from baseline using finger-only MRSS (0-6) and a “fingerless” MRSS (0-45), using Fisher’s exact test. We used linear mixed effects modeling to evaluate whether the MRSS excluding finger scores changed at similar rates to finger-only MRSS scores over time. To assess the correlation between “fingerless” MRSS and “standard” MRSS (0-51), we used Spearman partial correlation.

Results:
Finger-only MRSS were unchanged in 62% (331/532) of follow up visits whereas 45 point MRSS excluding fingers were unchanged in only 14% (72/532) of follow-up visits (p=0.009). The finger-only MRSS scores did not show any significant change over time. However, the “fingerless” MRSS decreased by a mean of 0.24 points per month (p<0.001). Although the 45 point MRSS are slightly lower given that fewer body parts are being assessed, the rate of change over time did not differ significantly from the standard 51 point MRSS with a correlation coefficient of 0.99.

**Conclusion:**

Our study demonstrated skin scores of fingers show lower propensity for change than skin scores of other body areas. The rate of change of the MRSS excluding fingers was not significantly different than the standard MRSS, but may result in a greater percent change. Future studies should consider removing the finger skin score from the MRSS score to improve sensitivity to change over time and assess whether this better reflects changes in patient-level outcomes.

| Mixed Effects Model Comparing 6 point (Finger-Only) versus 45 (Fingerless) MRSS |
|---------------------------------|---------|---------|
| Mixed Effects Modeling Term     | β Coefficient ± Standard Error | p-value |
| Intercept                       | 22.70 ± 0.59                | < 0.001 |
| Group=finger-only score         | -17.47 ± 0.39               | < 0.001 |
| Group="fingerless” score        | reference                   | --      |
| Time                            | -0.24 ± 0.02                | < 0.001 |
| Interaction of time and finger-only score | 0.24 ± 0.02 | < 0.001 |
| Interaction of time and “fingerless” score | reference | --      |

**Disclosure:** A. M. Fernandez, None; R. F. Spiera, Roche-Genetech, 2,GSK, 2,BMS, 2,Celgene, 2,Boehringer Ingelheim, 2,Cytori, 2,Chemocentryx, 2,Corbus Pharmaceuticals, 2,Prism, 2,Roche-Genetech, 5,GSK, 5,Boehringer Ingelheim, 5; J. Szymonifka, None; J. K. Gordon, Corbus Pharmaceuticals, 2,Cumberland Pharmaceuticals, 2,Bayer Pharmaceuticals, 2.

**View Abstract and Citation Information Online** - [http://acrabstracts.org/abstract/improving-sensitivity-to-change-of-the-modified-rodnan-skin-score-over-time](http://acrabstracts.org/abstract/improving-sensitivity-to-change-of-the-modified-rodnan-skin-score-over-time)

**Abstract Number:** 1677

**Low Baseline Impedance in Proximal Esophagus and Decreased Pspw Index May Related with Pathogenesis of Interstitial Lung Disease in Systemic Sclerosis**

Yunseok Kim¹, **Hyun-Sook Kim**², Joon Seong Lee¹ and Jung Ran Choi³, ¹Internal medicine, Soonchunhyang university Seoul hospital, Seoul, Korea, Republic of (South), ²Soonchunhyang university school of medicine, Seoul, Korea, Republic of (South), ³Department of Internal Medicine, Pohang St. Mary Hospital, Pohang, Korea, Republic of (South)

**First publication:** September 18, 2017
SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Interstitial lung disease (ILD) is a common but fatal complication of systemic sclerosis (SSc). Gastroesophageal reflux disease (GERD) may be related to pathogenesis of ILD, but some study failed to show relationship between acidic GER and ILD. Our aims are to find relevant reflux parameters related to ILD in patients with SSc using high-resolution esophageal manometry (HRM) and multichannel intraluminal impedance and pH monitoring (MII-pH).

Methods: Of the consecutive 16 female patients with SSc, 9 patients showed ILD (SSc-ILD, median age 45 years, range 25-55) by HRCT and 7 patients didn’t (SSc-N, age 49.5 y, 31-62). They all received esophageal HRM (Given Imaging, Los Angeles, CA, USA) and MII-pH (Sandhill Scientific, Inc.; Highland Ranch, CO, USA). We compared HRM parameters (Chicago ver 3.0) and MII-pH parameters including baseline impedance (BI) and post-reflux swallow-induced peristaltic wave (PSPW) index between two groups.

Results: SSc-ILD showed significantly low FVC%pred and DLCO% compared with SSc-N (mean ± SD, 72.2±17.1% vs. 101.3±14.2; 56.1±12 vs. 71.9±13.2, respectively, P<0.05) In HRM, absent contractility, ineffective esophageal motility and normal peristalsis were 6, 2, 1 in SSc-ILD and 1, 4, 2 in SSc-N. LES pressure was significantly low in SSc-ILD compared with SSc-N (13.7±6.4 vs. 24.0±11.3 mmHg, p<0.05). IRP, DCI, and UES pressure were not different between two groups. In MII-pH, all reflux % time using pH and impedance according to acidity or position, number of reflux events, and proximal extent were not different between two groups. However, mean bolus clearance time was longer in SSc-ILD than SSc-N [median 14 sec (IQR 13-28) vs. 11 sec (8.5-12.8), p<0.05]. BI except the most distal esophagus were significantly low in SSc-ILD than SSc-N (1099.2±327W vs. 2066.1±754.6W, 1032.9±483.2W vs. 2118.4±742.2W, 1190.7±745.3W vs. 2498.3±528.2W, p<0.005; 1257.8±959.7W vs. 2695.7±841.2W, P<0.01; 1239.9±907.4W vs. 2327.9±542.3W, P<0.05 at 17, 15, 9, 7, and 5 cm above the LES). PSPW index was significantly low in SSc-ILD than SSc-N [median 0 (IQR 0-0.03) vs. 0.16 (0.07-0.45), p<0.05].

Conclusion: Pathogenic mechanisms of ILD in SSc may relate to proximal esophageal reflux (low proximal esophageal BI) and decreased clearance mechanisms due to esophageal involvement of SSc.

Disclosure: Y. Kim, None; H. S. Kim, None; J. S. Lee, None; J. R. Choi, None.


Abstract Number: 1678

Pathogenic Mechanisms of Esophageal Peristaltic Dysfunction By High Resolution Manometry in Patients with Systemic Sclerosis

Hyun-Sook Kim1, Yunseok Kim2, Jung Ran Choi3 and Joon Seong Lee2, 1Soonchunhyang university school of medicine, Seoul, Korea, Republic of (South), 2Internal medicine, Soonchunhyang university Seoul hospital, Seoul, Korea, Republic of (South), 3Department of Internal Medicine, Pohang St. Mary Hospital, Pohang, Korea, Republic of (South)
Background/Purpose: Pathogenic mechanisms of esophageal involvement in systemic sclerosis (SSc) were suggested as neural dysfunction due to impairment of microcirculation to intramural neuron in early stage, followed by atrophy of smooth muscle (SM) portion, and finally extensive fibrosis. According to the esophageal high resolution manometry (HRM) finding, three are three categories in SSc patients; normal peristalsis, ineffective esophageal motility (IEM), and absent contractility (AC). Our hypothesis is IEM of HRM finding in SSc patients may reflect neural dysfunction with/without SM atrophy and AC may reflect severe SM atrophy or extensive fibrosis. Aims of our study are to evaluate the esophageal reserved function of neuronal reflexes and muscle contractility in these three groups of SSc.

Methods: Patients diagnosed with SSc who underwent HRM during recent 3 years were retrospectively included (22 female, ages 25-75). Seventeen patients of them were underwent multichannel intraluminal impedance and pH (Imp-pH) study also. We analyzed LES pressure, HRM metrics according to the Chicago classification version 3, including distal contractile integral (DCI), DCI ratio of single swallow and multiple rapid swallow (MRS) test, and reflux parameters and the post-reflux swallow-induced peristaltic wave (PSPW) index by Imp-pH test. According to the HRM findings, patients were classified as 3 groups (normal HRM, n=5; IEM, n=8, and AC, n=9). We compared SM contractility by DCI, neuronal peristaltic reserve function by MRS test using HRM and the PSPW index using Imp-pH study in normal, IEM, and AC groups. Parameters among 3 groups were analyzed by ANOVA on ranks.

Results: DCI was significantly lower in AC and IEM group than normal group [median 0.00 (IQR 0.00-35.23), 172.80 (77.05-522.35), and 834.30 (789.85-2294.63) mmHg×s×cm respectively, p<0.001]. DCI ratio of MRS/single swallow was lower in AC group than normal group [0.00 (0.00-0.08) vs. 1.00 (0.45-1.19), P=0.030]. Other HRM parameters including LES pressure were not different among three groups. PSPW index was lower in AC group than IEM and normal groups [8.95 (3.20-16.70), and 17.60 (10.0-35.40) % respectively, p=0.023]. PSPW appearance time until 120 seconds were tended to variable in IEM group and AC group than normal group [SD 34.28 (32.29-44.89), 27.60 (16.97-32.03) and 19.60 (17.95-28.02) seconds respectively, p=0.079]. Other reflux parameters were not different among 3 groups.

Conclusion: The AC using HRM may reflect all of SM atrophy, fibrosis and neuronal dysfunction and the IEM using HRM may reflect SM atrophy and mild to moderate neuronal dysfunction in patients with SSc (Figure 1).
Cosimo Bruni¹, Vanessa Maestripieri², Giulia Tesei³, Marco Chiostri⁴, Serena Guiducci³, Silvia Bellando-Randone¹, Maria Boddi⁴ and Marco Matucci-Cerinic³ ¹Department of Experimental and Clinical Medicine, Division of Rheumatology, University of Florence, Firenze, Italy, ²Department of Internal Medicine, Division of Medicine for Care Complexity III, University of Florence, Florence, Italy, ³Department of Experimental and Clinical Medicine, Division of Rheumatology, University of Florence, Florence, Italy, ⁴Department of Heart and Vessels, Division of Cardiology I, University of Florence, Florence, Italy

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Renal Resistive Index (RRI), measured by Doppler ultrasound, reflects changes in both renal vascular and tubular-interstitial compartments and systemic vascular compliance related to age and comorbidities (arterial hypertension, diabetes, hyperuricaemia, etc). As renal injury in younger decades may occur also for RRI <0.70, the use of this cut-off may underestimate. RRI was previously investigated in small SSc samples not considering possible confounding medical conditions. The objectives of the study were: to describe RRI in our SSc population, to test both fixed 0.70 RRI cut-off and SSc-age-adjusted cut-offs in reflecting renal and other organ involvement, to analyse the prognostic value of baseline RRI and RRI Δ change in predicting clinical worsening.

Methods: SSc patients classified through ACR/EULAR 2013 criteria, ≥18 years were enrolled after informed consent. Baseline Data on RRI, laboratory, instrumental and therapeutic features were retrospectively collected. SSc-age-adjusted pathologic cut-offs were created dividing the population in age quartiles and considering RRI values >75th percentile as pathologic (Table 1A). Clinical worsening was defined in case of any event listed in Table 1B. Data were analysed as appropriate with SPSS vers. 20.0.

Results: 250 SSc patients (mean disease duration 7.2±8.3 years) were eligible. RRI showed significant correlations with age (ρ=0.56, p<0.001) and creatinine clearance (ρ=-0.38, p<0.001), as well as significant associations with general population RRI determinants. When considering RRI absolute value and 0.70 cut-off, only comorbidities, renal function, sPAP and E/A, DLCO and late NVC pattern were associated. Conversely, new SSc-age-adjusted RRI cut-offs could not detect early renal damage but were significantly associated with various disease related skin and lung fibrotic manifestations, as well as vasculopathic complications (Table 2A). After a mean follow-up of 3.6±2.6 years, while RRI absolute values and 0.70 RRI cut-off showed no significant value, SSc-age-adjusted RRI cut-offs were significantly predictive for cardiac, lung and renal worsening (Table 2B). On the other hand, RRI Δ changes in 3 years (100 pts) and 5 years (60 pts), were not sensitive or predictive for worsening.

Conclusion: in clinical practice, different age-SSc-adjusted or non-adjusted RRI cut-offs may be used to evaluate renal and extrarenal involvement, resembling DLCO for parenchymal and vascular lung involvement. These RRI cut-offs may be considered as possible predictors of kidney, lung and cardiac worsening in SSc patients.
Higher Baseline Monocyte Count Is Associated with More Extensive Skin Involvement and Higher Mortality in Systemic Sclerosis

Vishnu Mohan¹, Purvesh Khatri², Samuel Theodore¹, Julio Charles¹, Hau Pham¹, Deepthi Nair¹, Madeleine Scott², John D. Reveille¹, Maureen D. Mayes¹ and Shervin Assassi¹, ¹University of Texas McGovern Medical School, Houston, TX, ²Stanford University, Stanford, CA

First publication: September 18, 2017
Background/Purpose:

Macrophages are the primary inflammatory cell type present in the systemic sclerosis (SSc) skin. Circulating monocytes can give rise to profibrotic inflammatory cells such as alternatively activated macrophages in the fibrotic end-organ such as skin and lung. Despite their importance, there are no previous studies examining the clinical correlates of peripheral blood monocyte count in SSc. The primary objective of the present study was to examine the association of monocyte count with clinical variables and survival in the prospective Genetics Versus Environment In Scleroderma Outcome Study (GENISOS) cohort.

Methods:

Monocyte count was prospectively obtained at enrollment in 429 patients. All patients had disease duration less than 5 years (from the first non-Raynaud’s phenomenon symptom) and fulfilled the 2013 ACR/EULAR criteria. Modified Rodnan Skin Score (mRSS) and forced vital capacity % predicted (FVC%) were also obtained prospectively. SSc related autoantibodies were determined in the divisional laboratory using gold standard methods. After mean follow-up of 8.3 years, 129 patients had died.

Results:

The mean disease duration at enrollment was 2.4 years and the majority of patients had diffuse cutaneous involvement (60.4%). Higher monocyte count was associated with diffuse cutaneous disease type (b=59.4, p=0.012). Furthermore, higher monocyte count was significantly associated with higher baseline mRSS (r=0.17, p=0.001) while there was no correlation with baseline FVC%. There was a trend for association of higher monocyte counts with RNA polymerase III positivity (b=55.2, p=0.055) while there was no association with other SSc-related autoantibodies. Higher monocyte count also correlated with lower disease duration at the baseline visit (r=-0.11, p=0.022)

In the multivariable cox regression analysis after adjustment for age at enrollment, monocyte count was associated with higher mortality (p=0.028). Next, patients were classified based on normal vs. high monocyte count as reported by the clinical laboratory. SSc patients with a high monocyte count had higher mortality even after adjustment for age and baseline mRSS (see Table).

Conclusion:

Higher peripheral blood monocyte count was associated with shorter disease duration, more extensive skin disease, and higher mortality. This study provides clinical support for relevance of monocytes and bone marrow derived macrophages in SSc pathogenesis.

<table>
<thead>
<tr>
<th>Clinical Variable</th>
<th>Hazard ratio</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>High monocyte count at enrollment</td>
<td>2.65</td>
<td>1.07 - 6.57</td>
<td>0.035</td>
</tr>
<tr>
<td>Age at enrollment</td>
<td>1.02</td>
<td>1.01 – 1.04</td>
<td>0.003</td>
</tr>
<tr>
<td>mRSS at enrollment</td>
<td>1.01</td>
<td>0.99 – 1.02</td>
<td>0.243</td>
</tr>
</tbody>
</table>

Disclosure: V. Mohan, None; P. Khatri, None; S. Theodore, None; J. Charles, None; H. Pham, None; D. Nair, None; M. Scott, None; J. D. Reveille, None; M. D. Mayes, None; S. Assassi, Bayer Healthcare, 2,Biogen Idec, 2,Reata, 5,Boehringer Ingelheim, 5.
An Evaluation of Two Novel Techniques Utilising a Smartphone Digital Camera in the Assessment of Nailfold Capillaries in Suspected Scleroderma-Spectrum Disorders: A Single-Center Cross-Sectional Study

Matthew Parker, Neil McGill and Michael Oliffe

Rheumatology, Royal Prince Alfred Hospital, Sydney, Australia, University of Sydney, Sydney, Australia

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Nailfold capillaroscopy is a non-invasive, sensitive and specific technique used in the diagnosis of scleroderma-spectrum disorders. Abnormalities predict progression from Raynauds phenomenon to connective tissue disease, sometimes years in advance, as well as serious complications such as pulmonary hypertension. Its inclusion in the most recent diagnostic criteria for systemic sclerosis enable them to perform better to identify patients with early systemic sclerosis in particular, important for prognostication, risk stratification, screening regimen and hopefully, in future, therapeutic intervention.

The current gold standard techniques are nailfold videocapillaroscopy and widefield microscopy. The equipment required for both remains expensive and relatively inaccessible, typically only available in centers with a special interest. Novel approaches utilizing new technologies may help improve accessibility to the wider rheumatology community.

We sought to evaluate the novel combination of a smartphone digital camera with two devices, a commercially produced lens attachment and a dermatoscope, with both techniques offering the possibility of a rapid bedside evaluation at a fraction of the cost of other techniques.

Objectives:
The primary aim was to evaluate the diagnostic performance of digital photographs taken with a smartphone camera using both a lens attachment and, separately, a dermatoscope. The secondary aims were to assess the influence of prior capillaroscopy experience and familiarity with the novel techniques on diagnostic accuracy.

Methods:
This was a single-center cross-sectional study. All patients referred for capillaroscopy between May 2016 and January 2017 were eligible for inclusion. Patients nailfolds were classified by widefield microscopy before proceeding, double-blinded, to have their nailfolds photographed using both novel techniques. Randomized
photographs were assessed after the completion of enrolment by three independent investigators. Sensitivity, specificity, inter- and intra-observer variability were calculated.

**Results:**

65 participants contributed 1040 digital photographs for independent assessment by three investigators. The smartphone-lens technique performed with moderate sensitivity (65%; 58-72) and high specificity (90%; 84-96). The smartphone-dermatoscope technique performed with higher sensitivity (74%; 66-82) and excellent specificity (95%; 88-100) and was used more accurately by a novice. Prior assessor experience with nailfold capillaroscopy in general and prior experience with the novel techniques positively modulated the diagnostic accuracy.

**Conclusion:**

New technologies, in this case utilising a smartphone camera, could help improve accessibility to nailfold capillaroscopy, an important diagnostic tool and putative biomarker in scleroderma-spectrum disorders, whilst retaining accurate results.

<table>
<thead>
<tr>
<th>Capillaroscopy Experience</th>
<th>True Positive (n)</th>
<th>True Negative (n)</th>
<th>False Positive (n)</th>
<th>False Negative (n)</th>
<th>Sensitivity (CI)</th>
<th>Specificity (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Novice</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SMARTPHONE-LENS</td>
<td>12</td>
<td>36</td>
<td>6</td>
<td>11</td>
<td>52% (45-59)</td>
<td>86% (80-92)</td>
</tr>
<tr>
<td>SMARTPHONE-DERMATOSCOPE</td>
<td>16</td>
<td>38</td>
<td>4</td>
<td>7</td>
<td>70% (62-78)</td>
<td>90% (84-96)</td>
</tr>
<tr>
<td><strong>Intermediate</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SMARTPHONE-LENS</td>
<td>15</td>
<td>41</td>
<td>1</td>
<td>8</td>
<td>65% (58-72)</td>
<td>98% (91-100)</td>
</tr>
<tr>
<td>SMARTPHONE-DERMATOSCOPE</td>
<td>17</td>
<td>41</td>
<td>1</td>
<td>6</td>
<td>74% (66-82)</td>
<td>98% (91-100)</td>
</tr>
<tr>
<td><strong>Expert</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SMARTPHONE-LENS</td>
<td>15</td>
<td>38</td>
<td>4</td>
<td>8</td>
<td>65% (58-72)</td>
<td>90% (84-96)</td>
</tr>
<tr>
<td>SMARTPHONE-DERMATOSCOPE</td>
<td>17</td>
<td>40</td>
<td>2</td>
<td>6</td>
<td>74% (66-82)</td>
<td>95% (88-100)</td>
</tr>
</tbody>
</table>

**Disclosure:** M. Parker, None; N. McGill, None; M. Oliffe, None.


**Abstract Number:** 1682

**Significance of Anti-Topoisomerase I Antibodies in Routine Clinical Testing**

Anne E Tebo\(^1\), Robert L. Schmidt\(^2\) and Tracy M. Frech\(^3\), \(^1\)University of Utah, Salt Lake City, UT, \(^2\)Pathology, University of Utah, Salt Lake City, UT, \(^3\)Division of Rheumatology, University of Utah, Salt Lake City, UT

**First publication:** September 18, 2017
Background/Purpose: The 2013 classification criteria for systemic sclerosis (SSc) provide 3 points (towards a 9 point diagnosis) for patients who have an anti-topoisomerase I (anti-Scl-70) antibody. From a clinical practice standpoint, in the absence of other stigmata of SSc, the significance of the presence of an anti-Scl-70 antibody result remains unclear. The purpose of this project was to determine the clinical relevance of anti-Scl-70 antibodies detected by multiplex testing for patients receiving routine clinical evaluation at our institution.

Methods: Results for patients positive for anti-Scl-70 antibodies (cut-off: >41 AU/mL positive) at the University of Utah over a period of 8 years were retrospectively reviewed. All patients with a positive anti-Scl-70 antibody had a manual chart review for other SSc classification criteria information.

Results: There were 3331 unique patient samples evaluated during the investigation period, 51 (1.53%) were positive for anti-Scl-70 antibodies with 5 patients lost to follow-up. Of the available anti-Scl-70 antibody-positive patients (n=46), 17 (37%) met the diagnostic criteria for SSc, 11 (23.9%) were diagnosed with other types of lung disease [sarcoidosis, pulmonary embolism, empyema, and constrictive bronchiolitis], the remaining patients had immune-mediated diseases [n=12] or no reported clinical diagnosis [n=6]. All anti-Scl-70 antibody patients with SSc were also positive for antinuclear antibodies (ANA) compared to those without disease (100% vs. 46.4%, p<0.0001). The median level of anti-Scl-70 antibodies was significantly higher in patients with SSc compared to those without disease [158 AU/mL vs. 60 AU/mL, p<0.0001, Figure 1]. Using logistic regression, an estimated probability of 1 for SSc was attained at anti-Scl-70 antibody level of approximately 200 AU/mL (Figure 2).

Conclusion: In this retrospective study, a positive ANA test and significantly elevated titers (>5x cut-off) of anti-Scl-70 may be predictive of SSc. The role of underlying lung pathology on the pathogenesis of developing a low titer anti-Scl-70 antibody without an ANA may warrant further study.
Smoking Behaviour and the Progression of Organ Manifestations in Systemic Sclerosis: A Longitudinal European Scleroderma Trials and Research Group Study

Veronika K. Jaeger¹, Gabriele Valentini², Eric Hachulla³, Franco Cozzi⁴, Oliver Distler⁵, Paolo Airò⁶, Lazlo Czirjak⁷, Yannick Allanore⁸, Elise Siegert⁹, Edoardo Rosato¹⁰, Marco Matucci-Cerinic¹¹, Lisa Maria Bambara¹², Joerg C. Henes¹³, Patricia Carreira¹⁴, Vanessa Smith¹⁵, Francesco Del Galdo¹⁶, Christopher Denton¹⁷, Susanne Ullman¹⁸, Ellen de Langeh¹⁹, Valeria Riccieri²⁰, Juan José Alegre²¹, Simona Rednic²², Ulf Müller-Ladner²³ and Ulrich A. Walker¹, ¹Department of Rheumatology, University Hospital Basel, Basel, Switzerland, ²Second University of Naples, Naples, Italy, ³Department of Internal Medicine, Université de Lille, Lille, France, ⁴Division of Rheumatology, Rheumatology Unit, Department of Medicine, University of Padova, Padova, Italy, ⁵Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland, ⁶Rheumatology and Clinical Immunology Unit, Spedali Civilini of Brescia, Brescia, Italy, ⁷Department of Rheumatology and Immunology, University of Pécs, Pécs, Hungary, ⁸Department of Rheumatology, University Paris Descartes and Cochin Hospital, Paris, France, ⁹Rheumatology and Clinical Immunology, University Hospital Charité, Berlin, Germany, ¹⁰Sapienza University of Rome, Rome, Italy, ¹¹Dept of Medicine/Div of Rheum, University of Florence, Florence, Italy, ¹²University of Verona, Verona, Italy, ¹³Department of Internal Medicine II, Division of Rheumatology, University Hospital Tuebingen, Tuebingen, Germany, ¹⁴Department of Rheumatology, Hospital Universitario 12 de Octubre, Madrid, Spain, ¹⁵Faculty of Internal Medicine, Ghent University, Ghent, Belgium, ¹⁶Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds and NIHR Leeds Musculoskeletal Biomedical Research Unit, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom, ¹⁷Department of Rheumatology, University College London, Royal Free Hospital, London, United Kingdom, ¹⁸Department of Dermatology, Copenhagen University Hospital, Copenhagen, Denmark, ¹⁹Department of Rheumatology, University Hospitals Leuven, Leuven, Belgium, ²⁰Divisione di Reumatologia, Università di Roma La Sapienza, Roma, Italy, ²¹Sección de Reumatología Hospital Universitario Dr Peset Valencia, Valencia, Spain, ²²Clinica Reumatologie, University of Medicine & Pharmacy,
Background/Purpose:

Systemic sclerosis (SSc) is a rare, multisystem autoimmune disorder. It is characterized by generalized microangiopathy, in the pathogenesis of which hypoxia and oxidative stress have been implicated. Tobacco inhalation increases free radicals and strongly promotes vascular damage. So far, data available with regards to a role of tobacco exposure with SSc severity and progression are scarce.

We aimed to assess the associations of smoking with the speed of worsening of organ manifestations, namely lung involvement (forced vital capacity, FVC; forced expiratory volume, FEV1/FVC ratio; diffusing capacity for carbon monoxide corrected for alveolar volume, DLCO/VA), skin involvement (modified Rodnan skin score; mRSS), and digital ulcers (DU) in the European scleroderma trials and research (EUSTAR) database.

Methods:

Adult SSc patients from the EUSTAR cohort with a follow-up visit 12-24 months after the baseline visit and available data on their smoking habits were included.

The associations of smoking behavior (never smokers vs ex-smokers vs current smokers) with the change in disease manifestations between baseline and follow up were assessed using multivariable linear or logistic regression analyses adjusting for age, sex, autoantibody status, disease duration, SSc subset. Missing data were imputed using multiple imputations.

Results:

Of the 3,319 patients included (mean age 57 years, standard deviation [SD] 14; 85% female; 29% diffuse SSc), 66% of patients stated that they never smoked, 23% were ex-smokers and 11% were current smokers. The average ex-smokers had smoked 18 pack-years (SD 21) during a time of 19 years (SD 12) and quit smoking 15 years (SD 13) ago. The average current smoker smoked 27 pack-years (SD 30) during a time of 30 years (SD 13).

On average, the FEV1/FVC ratio changed from 96.5 (SD 14) at baseline to 96.0 (SD 13) at follow up. In current smokers, the ratio decreased significantly faster during the observation period than in never smokers after adjustment (β=-4%, p<0.001). This was not observed in ex-smokers (p=0.7).

The DLCO/VA decreased on average from 78.4 (SD 17) to 76.8 (SD 17). The decrease of DLCO/VA during the observation period was not associated with smoking behavior.

The mRSS changed between baseline and follow-up from an average of 7.7 (SD 8) to 7.3 (SD 7); the change in mRSS was not strongly and clinically meaningfully associated with smoking behavior.

Smoking behavior was not associated with the presence of DU at baseline. The occurrence of new DU during the observation period in patients without any DU prior to or at baseline was negatively associated with current smoking (OR 0.5, p=0.03) but not with previous smoking (OR 1.1, p=0.7).
Conclusion:

The adverse effect of smoking on bronchial airways that is known in the general population is replicated in the SSc population. The lack of a measurable adverse effect of smoking on the speed of worsening of cutaneous and pulmonary SSc manifestations argues against a major role of tobacco associated free radicals and vasoconstriction in the pathogenesis of SSc vasculopathy and fibrosis. Similarly, our data do not support an adverse effect of smoking on the presence or absence of DU.

Disclosure: V. K. Jaeger, None; G. Valentini, None; E. Hachulla, None; F. Cozzi, None; O. Distler, Actelion, 5,Bayer, 5,Biogen Idec, 5,Boehringer Ingelheim, 5,ChemomAb, 5,espeRare Foundation, 5,Genentech/Roche, 5,GlaxoSmithKline, 5,Inventiva, 5,Lilly, 5,Medac, 5,MedImmune, 5,Mitsubishi Tanabe Pharma, 5,Pharmacyclics, 5,Novartis Pharmaceutical Corporation, 5,Pfizer Inc, 5,Sanoﬁ, 5,SiNoxa, 5,UCB in the area of potential treatments of scleroderma and its complications, 5,Patent mir-29 for the treatment of systemic sclerosis licensed, 5,Actelion, 2,Bayer, 2,Biogen Idec, 2,Boehringer Ingelheim, 2,ChemomAb, 2,espeRare Foundation, 2,Genentech/Roche, 2,GlaxoSmithKline, 2,Inventiva, 2,Lilly, 2,Medac, 2,MedImmune, 2,Mitsubishi Tanabe Pharma, 2,Pharmacyclics, 2,Novartis, 2,Pfizer Inc, 2,Sanoﬁ, 2,SiNoxa, 2,UCB in the area of potential treatments of scleroderma and its complications, 2,Patent mir-29 for the treatment of systemic sclerosis licensed; P. Airò, None; L. Czirjak, None; Y. Allanore, None; E. Siegert, None; E. Rosato, None; M. Matucci-Cerinic, None; L. M. Bambara, None; J. C. Henes, None; P. Carreira, None; V. Smith, None; F. Del Galdo, None; C. Denton, None; S. Ullman, None; E. de Langhe, None; V. Riccieri, None; J. J. Alegre, None; S. Rednic, None; U. Müller-Ladner, None; U. A. Walker, None.


Abstract Number: 1684

Effectiveness and Safety of Tacrolimus Following Intravenous Cyclophosphamide Pulse Therapy As the Treatment of Systemic Sclerosis-Associated Interstitial Lung Disease

Yuki Ichimura, Yasushi Kawaguchi, Kae Takagi, Akiko Tochimoto, Tomoaki Higuchi, Yasuhiro Katsumata and Hisashi Yamanaka, Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic sclerosis (SSc) is the disease characterized by organ fibrosis with unknown etiology, and pulmonary involvement is one of major cause of death. However, the treatment of interstitial lung disease (ILD) in SSc is limited. Although intravenous cyclophosphamide pulse therapy (IVCY) is effective and widely used, the effect of the therapy does not last for a long time. In this reason, IVCY therapy followed by somewhat immunosuppressants may be needed, but it is uncertain which immunosuppressant is better for ILD in SSc. In Japan, tacrolimus, one of calcineurin inhibitors, is frequently used for the treatment of ILD in
polymyositis/dermatomyositis and idiopathic interstitial pneumonia. We examined the effect of sequential IVCY therapy followed by tacrolimus and low-dose corticosteroids in SSc-associated ILD (SSc-ILD).

**Methods:** This retrospective, observational study was performed in a single center in Japan. Twenty consecutive patients with SSc-ILD who received IVCY as first therapy in our hospital from April 2010 to March 2014 were enrolled. The protocol of IVCY is the dose of 400 to 500 mg/body surface area (m$^2$)/4 weeks and performed 3 to 6 times. In this study, we divided them two groups: treated with tacrolimus and low-dose corticosteroids following IVCY (TAC group); only low-dose corticosteroids after IVCY (IVCY group). We assessed the follow-up for 3 years after IVCY therapy in each group. Disease deterioration of ILD was defined as fulfilling more than 2 following criteria: deterioration of symptoms; expanding lung fibrosis in CT scan; DLCO decreasing more than 5% from baseline in lung function test. All data were collected from medical record retrospectively. Data analysis was assessed using JMP Pro 13.

**Results:** Ten patients were in TAC group, and other 10 patients IVCY group. Age (50 ± 14 year-old in TAC group vs. 57 ± 17 year-old in IVCY group; mean ± SD) and Duration of illness (2.6 ± 3.5 years vs. 2.4 ± 1.8 years) were same in each group. No difference was observed in pulmonary function test at baseline in each group (%VC: 79.5 ± 16.1% vs. 87.4 ± 18.8%, %DLCO: 59.5 ± 11.5% vs. 63.7 ± 14.6%). After 3-year follow up, 2 patients revealed disease progression, who were IVCY group. No case in Tac group showed disease progression. In TAC group, a case stopped taking tacrolimus due to adverse event, thrombocytopenia. Any cases in TAC group did not show neither renal crisis nor elevation of creatinine.

**Conclusion:** Tacrolimus following IVCY may be one of therapeutic choice for SSc-ILD, with good tolerance.

**Disclosure:** Y. Ichimura, None; Y. Kawaguchi, None; K. Takagi, None; A. Tochimoto, None; T. Higuchi, None; Y. Katsumata, Chugai Pharmaceutical Co., Ltd., Astellas Pharma Inc., Takeda Pharmaceutical Company Limited., Bayer Yakuhin, Ltd., AYUMI Pharmaceutical Corporation, 5; H. Yamanaka, MSD, 2, Astellas, 2, AbbVie, 2, BMS, 2, Kaken, 2, UCB, 2, Ono, 2, Ayumi, 2, Eisai, 2, Daiichi-Sankyo, 2, Takeda, 2, Tanabe-Mitsubishi, 2, Chugai, 2, Nipponshinyaku, 2, Pfizer Inc, 2, Pfizer Inc, 8, YL biologics, 8, Takeda, 8, Nipponkayaku, 8, Chugai, 8, Tanabe-Mitsubishi, 8, Daiichi-Sankyo, 8, Astellas, 8.


Abstract Number: 1685

**Factors Associated with the 6-Minute Walk Distance in Patients with Systemic Sclerosis**

Sébastien Sanges1, Jonathan Giovannelli2, Vincent Sobanski3, Céline Podevin2, Sandrine Dubois-Morell2, Hélène Maillard4, Marc Lambert4, Nicolas Lamblin5, Pascal De Groot5, Jean-François Bervar6, Pierre-Yves Hatron7, Eric Hachulla8 and David Launay9, 1Université Lille Nord de France, Faculté de Médecine Henri Warembourg, Lille, Lille, France, 2Service de Médecine Interne, Centre National de Référence de la Sclérodermie Systémique, Lille, France, 3Univ. Lille, U995, Lille Inflammation Research International Center (LIRIC), F-59000 Lille, France, 4Department of internal medicine, Hôpital Claude Huriez, CHRU Lille, France, Lille, France, 5Service de Cardiologie, Lille, France, 6Service de Pneumologie, Lille, France, 7Univ Lille, CHU Lille, F-59000 Lille, France, Lille, France, 8CHU Lille, Département de Médecine Interne et Immunologie Clinique, F-59000 Lille, France, Lille, France, 9Service de Médecine Interne, Centre National de Référence des Maladies Systémiques Rares, Hôpital Claude Huriez, CHRU Lille, Lille, France

First publication: September 18, 2017
Background/Purpose:

To assess the associations between the 6-minute walk distance (6MWD) and various disease parameters in patients with systemic sclerosis (SSc).

Methods:

Consecutive patients followed in our SSc National Reference Centre were included in this cross-sectional study if they fulfilled the 2013 ACR/EULAR criteria for SSc. Data were prospectively collected during a comprehensive evaluation that included a 6-minute walk test, clinical assessment, biological results, pulmonary function tests, transthoracic echocardiography, composite scores (EScSG-AI, Medsger, HAQ-DI) and treatments.

Associations of the 6MWD with various disease parameters were assessed by linear regression in univariate analyses, then in several multivariate models.

Results:

The study population comprised 298 patients (females: 81%; mean age: 58.2 ± 13.3 years old; limited cutaneous SSc: 82%; interstitial lung disease (ILD): 42%; pulmonary arterial hypertension (PAH): 6%). The 6MWD was significantly and independently associated with gender, age, initial heart rate, heart rate variation during the test, PAH and CRP levels. Muscle involvement, joint involvement and ILD were not independently associated with the 6MWD.

Conclusion:

During SSc, the 6MWD is independently associated with heart rate variation (possibly implying a role for chronotropic incompetence in exercise intolerance), with PAH but not ILD (suggesting that pulmonary vasculopathy may have a greater impact than parenchymal involvement on functional limitation), and with global markers of disease activity. These results give further insight to clinicians on how to interpret the 6MWD in the context of SSc.

Disclosure: S. Sanges, None; J. Giovannelli, None; V. Sobanski, None; C. Podevin, None; S. Dubois-Morell, None; H. Maillard, None; M. Lambert, None; N. Lamblin, None; P. De Groote, None; J. F. Bervar, None; P. Y. Hatron, None; E. Hachulla, None; D. Launay, None.


Abstract Number: 1686

Topical Nitroglycerine (NTG) Vs Matching Vehicle in Secondary Raynaud Phenomenon (RP) – a Double-Blind Crossover Study of Subjective and Physiologic Responses to Controlled Cold Challenge
Background/Purpose: A topical therapy for either prevention or palliation of attacks would offer unique advantages to selected patients with Raynaud phenomenon (RP). This study used 0.9% nitroglycerine (NTG) in a microemulsion formulation compared to vehicle to investigate clinical and physiologic responses to repetitive controlled cold challenge in individuals with RP secondary to connective tissue disease (CTD).

Methods: 65 subjects with CTD including 32 with systemic sclerosis (SSc), agreed to stop ongoing Rx for RP. Routinized assessments included 30 minutes of acclimatization at 22.2° C +/- 2.2 followed by up to 16 minutes in a cold room maintained at 4.4° C +/- 2.2 and 60 minutes of recovery. Finger temperature was monitored at regular intervals and subjects completed 10 cm VAS scales for numbness, tingling and pain as well as for overall RP attack severity. A Main Raynaud Symptom (MRS; most bothersome symptom of pain, numbness, or tingling) was chosen for each individual based on their highest VAS score during a baseline cold challenge. Active Rx or vehicle as placebo was applied in a blinded randomized sequence 30 minutes prior to each cold challenge with each treatment studied twice. An optional second application during cold exposure was permitted. An enriched subset of subjects responding to NTG but not to placebo was identified from the results of the first paired cold challenges for a subanalysis of responses in the final two cold challenges.

Results:

<table>
<thead>
<tr>
<th></th>
<th>Topical NTG</th>
<th>Vehicle</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Main Raynaud Sx</td>
<td>-20.77 mm</td>
<td>-19.56 mm</td>
<td>0.64</td>
</tr>
<tr>
<td>% Responders*</td>
<td>33/64 51.6%</td>
<td>32/64 50%</td>
<td>0.93</td>
</tr>
<tr>
<td>MRS Enriched**</td>
<td>-18.70 mm</td>
<td>-13.76 mm</td>
<td>0.45</td>
</tr>
<tr>
<td>AUC Skin Temp***</td>
<td>857.5</td>
<td>848.0</td>
<td>NS</td>
</tr>
</tbody>
</table>

* Responders – subjects with > 15 mm improvement in MRS VAS

** Enriched Subset – Vascana response > 10 mm AND vehicle response < 15 mm on VAS during first paired cold challenge VAS
*** Area Under Curve - integral of skin temperature across time during cold exposure (degree-minutes)

**Conclusion:** Topical NTG was not superior to vehicle placebo in reducing symptoms of RP during controlled cold challenge. Although the VAS response in Main Raynaud Symptom was meaningful (-20.77 mm), response to placebo was of similar magnitude. This was also true of analysis of an enriched subset designed to exclude placebo responders. Skin temperature during cold challenge was chosen as an indirect measure of digital perfusion. The lack of difference in physiologic response mirrors the subjective measures. Placebo response remains a critical issue in RP trials. This is in spite of choice of a uniform population, personalization of definitions of response (self-selected MRS), a cold challenge designed to closely match in-life experiences and repetitive testing.

**Disclosure:** D. Khanna, Actelion, Bayer, BoehringerIngelheim, Chemomab, Corbus, Covis, Cytori,Eicos, EMD Serono, Genentech/Roche, Gilead, GSK, Sanofi-Aventis,UCB Pharma, 5,NIH/NIAMS, NIH/NIAID,Bayer, BMS, Genentech/Roche, Pfizer, 2,Eicos, 4; L. Mendez, None; R. Namas, None; M. E. Csuka, None; P. Caldron, None; J. A. Molitor, Shire Human Genetic Therapies Inc., 5; A. J. Kivitz, AbbVie, Pfizer, Genentech, UCB, Sanofi/Regeneron and Celgene, 5,Celgene, Pfizer, Sanofi/Regeneron and Genentech, 8; P. Waller, None; L. Shapiro, None; S. Najam, None; A. Khan, None; V. D. Steen, CSL Behring, 2,cytori, 5,Reata, 5,bayer, 5,bayer, 5; A. Chadha, None; J. R. Seibold, Athersys, BriaCell Therapeutics, Pacific Therapeutics, Cytori, 1,Bayer, Boehringer-Ingelheim, Covis, Cytori, Eiger, Eicos, EMD Serono, Ironwood, OctaPharma, Medac, 5.


**Abstract Number:** 1687

**Efficacy of Rituximab for Connective Tissue Disease-Associated Interstitial Lung Disease: A Single Center Study of 28 Patients**

Sunny Patel¹, Samina Hayat², Gloria Caldito³ and Kristen Erickstad¹, ¹Rheumatology, Louisiana State University Health Sciences Center Shreveport, Shreveport, LA, ²Rheumatology/Internal Medicine, Louisiana State University Health Sciences Center Shreveport, Shreveport, LA, ³Neurology, Louisiana State University Health Sciences Center Shreveport, Shreveport, LA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster II

**Session Time:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Interstitial lung disease (ILD) is a severe pulmonary complication associated with connective tissue diseases (CTDs), resulting in substantial morbidity and mortality. Despite advances in immunosuppressive drugs, there remains limited data on treatment for this challenging clinical entity. This study aims to evaluate the efficacy of rituximab (RTX) in patients with CTD-ILD and determine factors correlated with outcomes at 6 and 12 months post-RTX.

**Methods:**
We analyzed data for 28 patients with CTD-ILD, all of whom met ACR classification criteria for a specific CTD. ILD was confirmed by high-resolution CT chest (HRCT) and pulmonary function tests with forced vital capacity (FVC) and diffusion capacity of lung for carbon monoxide (DLCO). We compared the HRCT chest findings, %FVC and %DLCO at time of diagnosis and at 6 and 12 months post-RTX treatment. We classified the HRCT chest findings at diagnosis into 3 groups, from mild to severe, and used the same semi-quantitative scoring system to evaluate for changes after treatment with RTX. We defined change in %FVC and %DLCO where improvement is an increase in FVC≥10% or DLCO ≥15%, worsening is a decrease in FVC≥10% or DLCO≥15% and stabilization is a change in FVC<10% or DLCO<15%. Multiple patient characteristics (Table 1) were tested for their correlations with each outcome using separate univariate analysis with the chi-square/Fisher test or Wilcoxon rank sum test.

Results:

Majority of the patients were female and African American with median age of 59. The median duration for CTD and ILD was 2 years and 1 year, respectively (Table 1). The proportions of patients whose FVC, DLCO and HRCT Chest status remained stable or improved post-RTX at 6 and 12 months were all significantly higher than 50% (Table 2). Furthermore, the proportions of patients who remained stable or improved were higher at 12 months than at 6 months. The median %change in FVC at 6 months was +3% and at 12 months was +3.5%. The median %change in DLCO at 6 months was +1.5% and at 12 months was +7%. Race, prior immunosuppressive drugs and CTD duration were all significantly associated with the observed outcomes (Table 3).

Conclusion:

Based on this single center retrospective study, RTX appears to be an acceptable and effective therapy for CTD-ILD. RTX may help to fill an unmet therapeutic need for CTD-ILD and larger randomized clinical trials are needed.

Table 1: Summary Statistics on Patient Characteristics and Outcomes (N=28)

<table>
<thead>
<tr>
<th>Characteristic / Outcome</th>
<th>Number (%) or Mean±SD, Median, Range</th>
<th>Number Non-missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>24 (85.7)</td>
<td>22</td>
</tr>
<tr>
<td>Male</td>
<td>4 (14.3)</td>
<td></td>
</tr>
<tr>
<td>Race:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>24 (85.7)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>4 (14.3)</td>
<td></td>
</tr>
<tr>
<td>CTD Type:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RA</td>
<td>14 (50.0)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>14 (50.0)</td>
<td></td>
</tr>
<tr>
<td>Active prednisone use before RTX treatment</td>
<td>14 (50.0)</td>
<td></td>
</tr>
<tr>
<td>HRCT Chest at diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>1 (4.6)</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>18 (64.3)</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>3 (13.0)</td>
<td></td>
</tr>
<tr>
<td>HRCT Chest at 6 months post-RTX</td>
<td>1 (4.6)</td>
<td></td>
</tr>
<tr>
<td>Worsened</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stable</td>
<td>18 (64.3)</td>
<td></td>
</tr>
<tr>
<td>Improved</td>
<td>3 (13.0)</td>
<td></td>
</tr>
<tr>
<td>HRCT Chest at 12 months post-RTX</td>
<td>21 (75.0)</td>
<td></td>
</tr>
<tr>
<td>Stable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improved</td>
<td>2 (8.7)</td>
<td></td>
</tr>
<tr>
<td>FVC/DLCO at 6 months post-RTX</td>
<td>2 (11.1)</td>
<td></td>
</tr>
<tr>
<td>Worsened</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stable</td>
<td>12 (42.9)</td>
<td></td>
</tr>
<tr>
<td>Improved</td>
<td>4 (22.2)</td>
<td></td>
</tr>
<tr>
<td>FVC/DLCO at 12 months post-RTX</td>
<td>1 (7.1)</td>
<td></td>
</tr>
<tr>
<td>Worsened</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stable</td>
<td>10 (35.7)</td>
<td></td>
</tr>
<tr>
<td>Improved</td>
<td>3 (10.7)</td>
<td></td>
</tr>
<tr>
<td>Number of immunosuppressive drugs prior to RTX</td>
<td>1.43±1.03, 1.0, 0 – 4</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>57.7±13.8, 59.0, 26 – 71</td>
<td></td>
</tr>
<tr>
<td>CTD duration (years)</td>
<td>5.0±7.4, 2.0, 1 – 28</td>
<td></td>
</tr>
<tr>
<td>IBD duration (years)</td>
<td>2.9±3.1, 1.0, 0 – 13</td>
<td></td>
</tr>
<tr>
<td>% FVC at diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>64.8±19.7%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% FVC at 6 months</td>
<td>65.8±19.1%, 66%, 31 – 97%</td>
<td>22</td>
</tr>
<tr>
<td>% FVC at 12 months</td>
<td>66.9±37.8%, 66%, 32 – 101%</td>
<td>20</td>
</tr>
<tr>
<td>% DLCO at diagnosis</td>
<td>47.7±13.4%, 43%, 24 – 78%</td>
<td>18</td>
</tr>
<tr>
<td>% DLCO at 6 months</td>
<td>47.9±14.3%, 49%, 22 – 76%</td>
<td>17</td>
</tr>
<tr>
<td>% DLCO at 12 months</td>
<td>60.8±12.9, 53.9%, 24.0 – 66%</td>
<td>14</td>
</tr>
</tbody>
</table>

*Calculated on non-missing values*
Table 2: Proportion of Patients Whose FVC/DLCO Status and HRCT Chest Status
At 6 and 12 Months of RTX Treatment Stabilized or Improved

<table>
<thead>
<tr>
<th>Stable/Improved Outcome</th>
<th>Proportion (P)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC/DLCO Status at 6 months post-Rituximab (N=18)</td>
<td>88.9%</td>
<td>0.001**</td>
</tr>
<tr>
<td>FVC/DLCO Status at 12 months post-Rituximab (N=14)</td>
<td>92.8%</td>
<td>0.001**</td>
</tr>
<tr>
<td>HRCT Finding at 6 months post-Rituximab (N=22)</td>
<td>95.4%</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>HRCT Finding at 12 months post-Rituximab (N=23)</td>
<td>100%</td>
<td>&lt;0.001**</td>
</tr>
</tbody>
</table>

For testing null hypothesis P=0.5 versus our research hypothesis that P≥0.8 (Rituximab is an effective therapy)
**Significant at 1% level of significance (p-value<0.01)

Table 3: Factors Significantly Associated with Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Significant Factor(s)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC/DLCO Status at 6 months post-Rituximab (N=18)</td>
<td># of Prior Immunosuppressive drugs Stable/improved (16); Median=1. Worsened (2); Median=3</td>
<td>0.03*</td>
</tr>
<tr>
<td>FVC/DLCO Status at 12 months post-Rituximab (N=14)</td>
<td>none</td>
<td></td>
</tr>
<tr>
<td>HRCT Chest status at 6 months post-Rituximab (N=22)</td>
<td>none</td>
<td></td>
</tr>
<tr>
<td>HRCT Chest status at 12 months post-Rituximab (N=23)</td>
<td>NA (all 23 stabilized/improved)</td>
<td></td>
</tr>
<tr>
<td>Change in FVC at 6 months post-Rituximab (N=19)</td>
<td>Race White (N=4); Median=6.5% Black (N=15); Median=2.0%</td>
<td>0.03*</td>
</tr>
<tr>
<td>Change in FVC at 12 months post-Rituximab (N=16)</td>
<td>Race White (N=6); Median=5.0% Black (N=10); Median=3.0% RA-CTD use Yes (N=8); Median=3.0% No (N=8); Median=7.5%</td>
<td>0.06*</td>
</tr>
<tr>
<td>Change in DLCO at 6 months post-Rituximab (N=8)</td>
<td>Race White (N=2); Median=20.0% Black (N=6); Median=13.5% CTD duration (years) R22 - 0.8</td>
<td>0.04*</td>
</tr>
<tr>
<td>Change in DLCO at 12 months post-Rituximab (N=9)</td>
<td>Race White (N=3); Median=15.0% Black (N=6); Median=13.5%</td>
<td>0.05*</td>
</tr>
</tbody>
</table>

*Significant at 5% level of significance (p-value<0.05)
**Not significant at 5% level but significant at 10% level (p-value<0.01)

Disclosure: S. Patel, None; S. Hayat, None; G. Caldito, None; K. Erickstad, None.

Abstract Number: 1688

Stem Cell-Enriched Lipotransfer Substantially Improves Measures of Appearance and Function Due to Facial Fibrosis in Systemic Sclerosis

Aurora Almadori1,2, Caroline Ryan2, Michelle Griffin3, Esther Hansen4, Christopher Denton5 and Peter Butler6,7, 1Plastic Surgery, Royal Free NHS Foundation Trust London Hospital, London, United Kingdom, 2Division of Surgery and Interventional Science, UCL, London, United Kingdom, 3Division of Surgery and Interventional Science, UCL, London, United Kingdom, 4Clinical Psychology, Plastic Surgery, Royal Free London NHS Foundation Trust Hospital, London, United Kingdom, 5Department of Rheumatology, University College London, Royal Free Hospital, London, United Kingdom, 6Plastic Surgery, Royal Free London NHS Foundation Trust Hospital, London, United Kingdom, 7Division of Surgery and Interventional Science, UCL, London, United Kingdom
Systemic scleroderma (SSc) is characterised by fibrosis of the skin and underlying connective tissue structures, together with localised loss of subcutaneous fat. Oro-facial fibrosis in systemic sclerosis (SSc) is almost always present in established cases and has major impact on oro-facial function, facial appearance, and quality of life. Based upon theoretical rationale for antifibrotic potential and improvement in connective tissue bulk we have evaluated the benefit of autologous stem cell enriched lipotransfer in a large cohort of SSc patients with a mean follow up period of 12 months after treatment, and objective assessment of clinical benefit including validated outcome tools.

Methods:

62 SSc patients with oro-facial fibrosis were assessed following oro-facial treatment with autologous stem cell enriched lipotransfer. Mean age was 56 (±11.59), 98% were female, 42% were affected by dcSS subset, and mean disease duration was 15.18 years (±8.81). Efficacy was assessed by pre- and post-operative mouth function (Mouth Handicap in Systemic Sclerosis Scale, MHISS), validated psychological measurements (Darriford Appearance Scale, DAS24; Hospital Anxiety and Depression Scale-anxiety, HADS; Brief Fear of Negative Evaluation Scale, BFNE; Visual Analogic Scale for mood, emotion, and distress, VAS), and volumetric assessment (3dMD imaging system).

Results:

We found a significant improvement of mouth function (MHISS) (6.85 ± 5.07) (p<0.0001) and all the psychological measures: DAS 24 (12.1 ± 9.5) (p<0.0001); HADS-anxiety (2.8 ± 3.2) (p<0.0001), HADS-depression (2.0 ± 3.1) (p<0.0001); BFNE (2.9 ± 4.3) (p<0.0001); VAS (3.56 ± 4.1) (p<0.0001). Multiple procedures further improved MHISS (p<0.05), DAS (p<0.0001) and VAS (p=0.01) scores. Disease subset or concomitant immunosuppression did not appear to affect outcome measures. Injected volume was retained variably in all facial areas: cheeks (93.7%), nasolabial folds (81.9%), nose (67.4%), chin (68.2%), upper lips (35.5%) and lower lips (27.3%). Concurrent immunosuppressive treatment with did not appear to influence the safety of efficacy of lipotransfer.

Conclusion:

Autologous stem cell enriched lipotransfer is a feasible treatment that reversed the effects of oro-facial fibrosis in SSc in this open cohort study. It has been shown to be both feasible and beneficial. Our findings warrant further testing in a randomised controlled trial.

Disclosure: A. Almadori, None; C. Ryan, None; M. Griffin, None; E. Hansen, None; C. Denton, None; P. Butler, None.


Abstract Number: 1689
Using Electronic Health Record Algorithms to Accurately Identify Patients with Systemic Sclerosis

Lia Jamian, Leslie Crofford and April Barnado, Medicine, Vanderbilt University Medical Center, Nashville, TN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a rare, chronic, autoimmune disease with high morbidity and mortality. The electronic health record (EHR) represents a powerful tool to study rare disorders such as SSc. Currently, there are no validated algorithms to identify SSc patients in the EHR. We sought to develop algorithms that incorporated not only billing codes but also labs and keywords to identify SSc patients accurately.

Methods: We analyzed data from a de-identified version of Vanderbilt’s EHR called the Synthetic Derivative (SD) that contains over 2.8 million subjects with longitudinal clinical data. Within the SD, we identified 1899 potential SSc patients with at least one count of the SSc ICD-9 (710.1) code. Of these potential subjects, we randomly selected 200 as a training set for chart review to identify true case status. A subject was defined as a case if diagnosed with SSc by a Vanderbilt or external rheumatologist, dermatologist, or pulmonologist. Potential subjects were then classified as either 1) cases, 2) not cases with alternative diagnoses noted, 3) unconfirmed if there was uncertainty in the diagnosis, or 4) missing if clinical documentation was missing. A priori, we selected the following potential algorithm components based on clinical knowledge and available data: SSc ICD-9 code, positive anti-nuclear antibody (ANA) (titer ≥ 1:80), and a keyword of Raynaud’s phenomenon (RP) in the clinic notes. Positive predictive values (PPVs) and sensitivity were calculated for combinations of the above algorithm components.

Results: Of the 200 subjects in the training set, 81 were true cases on chart review, 65 not cases, 17 unconfirmed, and 37 with missing clinical documentation. The PPV for using 1 count of the SSc ICD-9 code was 50%, 68% for ≥ 2 counts, 82% for ≥ 3 counts, and 90% for ≥ 4 counts. PPVs increased when a positive ANA or RP keyword was added to the ICD-9 code. The algorithms with the highest PPVs of 96% were 1) ≥ 4 counts of the SSc ICD-9 code and RP keyword, 2) ≥ 3 counts of the SSc ICD-9 code and ANA positive and RP keyword, and 3) ≥ 4 counts of the SSc ICD-9 code and ANA positive and RP keyword (Table 1). The algorithm with the highest combined PPV of 81% and sensitivity of 95% was ≥ 1 count of the SSc ICD-9 code and RP keyword. Conclusion: We have developed novel algorithms to identify SSc subjects in the EHR using not only billing codes but also labs and keywords with a PPV of 96%. These algorithms will allow researchers to identify and study patients with SSc more efficiently and accurately in the EHR.

Table 1.
<table>
<thead>
<tr>
<th>Algorithm*</th>
<th>Positive Predictive Value</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Counts of the ICD-9 code (710.1)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 1</td>
<td>50%</td>
<td>N/A</td>
</tr>
<tr>
<td>≥ 2</td>
<td>68%</td>
<td>85%</td>
</tr>
<tr>
<td>≥ 3</td>
<td>82%</td>
<td>77%</td>
</tr>
<tr>
<td>≥ 4</td>
<td>90%</td>
<td>67%</td>
</tr>
<tr>
<td><strong>ANA positive(^£) AND ≥ 1 count of 710.1</strong></td>
<td>45%</td>
<td>81%</td>
</tr>
<tr>
<td>ANA positive AND ≥ 2 counts</td>
<td>70%</td>
<td>81%</td>
</tr>
<tr>
<td>ANA positive AND ≥ 3 counts</td>
<td>88%</td>
<td>67%</td>
</tr>
<tr>
<td>ANA positive AND ≥ 4 counts</td>
<td>93%</td>
<td>58%</td>
</tr>
<tr>
<td><strong>Raynaud’s phenomenon (RP) keyword AND ≥ 1 count of 710.1</strong></td>
<td>81%</td>
<td>95%</td>
</tr>
<tr>
<td>RP keyword AND ≥ 2 counts</td>
<td>91%</td>
<td>80%</td>
</tr>
<tr>
<td>RP keyword AND ≥ 3 counts</td>
<td>94%</td>
<td>71%</td>
</tr>
<tr>
<td>RP keyword AND ≥ 4 counts</td>
<td>96%</td>
<td>67%</td>
</tr>
<tr>
<td><strong>ANA positive AND RP keyword AND ≥ 1 count of 710.1</strong></td>
<td>74%</td>
<td>78%</td>
</tr>
<tr>
<td>ANA positive AND RP AND ≥ 2 counts</td>
<td>94%</td>
<td>76%</td>
</tr>
<tr>
<td>ANA positive AND RP AND ≥ 3 counts</td>
<td>96%</td>
<td>64%</td>
</tr>
<tr>
<td>ANA positive AND RP AND ≥ 4 counts</td>
<td>96%</td>
<td>57%</td>
</tr>
<tr>
<td><strong>ANA positive OR RP keyword AND ≥ 1 count of 710.1</strong></td>
<td>49%</td>
<td>98%</td>
</tr>
<tr>
<td>ANA positive OR RP AND ≥ 2 counts</td>
<td>72%</td>
<td>90%</td>
</tr>
<tr>
<td>ANA positive OR RP AND ≥ 3 counts</td>
<td>89%</td>
<td>76%</td>
</tr>
<tr>
<td>ANA positive OR RP AND ≥ 4 counts</td>
<td>93%</td>
<td>67%</td>
</tr>
</tbody>
</table>

*All algorithms included at least one or more counts of the Systemic Sclerosis ICD-9 (710.1). \(^£\)ANA positive defined as titer ≥ 1:80.

Disclosure: L. Jamian, None; L. Crofford, None; A. Barnado, None.
Nailfold Capillary Counts Are Associated with Clinical Manifestations in Connective Tissue Disease Japanese Patients

Atsushi Kondo¹, Tomohiro Kameda¹, Miharu Izumikawa¹, Hiromi Shimada², Shusaku Nakashima¹, Risa Wakiya¹, Mikiya Kato¹, Norimitsu Kadowaki¹ and Hiroaki Dobashi¹, ¹Internal Medicine Division of Hematology, Rheumatology, and Respiratory Medicine, Kagawa University, Kagawa, Japan, ²Department of Internal Medicine, Division of Hematology, Rheumatology and Respiratory Medicine, Faculty of Medicine, Kagawa University, Kagawa, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Connective tissue diseases (CTD) patients have various clinical manifestation including pulmonary hypertension (PH) and digital ulcer (DU). Especially, Raynaud’s phenomenon (RP) is one of the common symptoms. On the other hand, “abnormal nailfold capillaries” are important as the findings that suggest RP associated with CTD. They are included in one of the items of classification criteria for Scleroderma (SSc) in 2013 Classification Criteria for Systemic Sclerosis (ACR/EULAR). Recently, some reports presented the usefulness of nailfold capillaroscopy (NFC) in SSc. NFC findings showed enlarged/giant capillaries, fresh or old haemorrhages, avascular areas, ramified/bushy capillaries. These findings are known as “scleroderma pattern” features. Additionally, there are some reports that nailfold capillary low density in SSc related with merger of DU, PH and interstitial pneumonia (IP).

In this study, we clarify the association between nailfold capillary density and clinical manifestation by analysis of the case in our institution.

Methods:

We enrolled Japanese CTD patients including SSc, Systemic Lupus erythematosus (SLE), Mixed Connective Tissue Disease (MCTD), Sjögren’s syndrome (SS), Dermatomyositis (DM) from May 2016 to May 2017 in our institution.

We measured total nailfold capillary count per 1µm from second to fifth finger by NFC “OptiPiX Capillaroscopy Clinic 1.7.x”. In addition, we investigated relationship with NFC findings and clinical manifestation (or laboratory data) such as current and previous DU, RP, PH and IP.

Results:

We enrolled 107 CTD patients (100 females, 7 males; 42 SSc, 25 SLE, 16 PM/DM, 9 MCTD, 16 SS). Total nailfold capillary counts significantly decreased in all CTD patients with current DU (p= -0.4333, p = 0.0003), previous DU (p= -0.4202, p = 0.0004), RP (p= -0.3350, p = 0.006) and PH (p= -0.3683, p = 0.0023). In addition, Total nailfold capillary counts associated with current DU (p= -0.3855, p = 0.0477) and previous DU (p= -0.4481, p = 0.0191) in
SSc patients and PH (ρ = -0.8281, p = 0.0418) in MCTD patients. There is no significant difference between “scleroderma pattern” features and clinical manifestation.

Conclusion:

Our study revealed that total nailfold capillary counts were associated with clinical manifestation in CTD patients. We suggest that nailfold capillary density may predict clinical manifestation with CTD patients.

Disclosure: A. Kondo, None; T. Kameda, None; M. Izumikawa, None; H. Shimada, None; S. Nakashima, None; R. Wakiya, None; M. Kato, None; N. Kadowaki, None; H. Dobashi, None.

Risk of Development of Definite Disease in Patients with Early Systemic Sclerosis

Cintia Zumstein Camargo, Maria Izabel Arismendi and Cristiane Kayser, Rheumatology Division, Universidade Federal de São Paulo, São Paulo, Brazil

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

The diagnosis of systemic sclerosis (SSc) in the early stages of the disease is frequently a challenge. In 2001, LeRoy and Medsger proposed criteria for the classification of early SSc, defined by the presence of Raynaud’s phenomenon (RP) associated with scleroderma specific antibodies and/or typical scleroderma changes on nailfold capillaroscopy (NFC). After the development of the 2013 ACR/EULAR classification criteria for SSc, which is more sensitive than previous, there are still a group of patients affected by early SSc who do not meet the 2013 ACR/EULAR criteria. Factors associated with disease evolution in these patients are not well recognized. This study aimed to evaluate the disease evolution and to identify predictors of evolution to definite SSc (ACR/EULAR classification criteria for SSc) in patients with early SSc.

Methods:

In this prospective study 46 consecutive patients with early SSc (2001 LeRoy and Medsger criteria), were evaluated at baseline and at 3 years of follow-up. Clinical evaluation and widefield nailfold capillaroscopy using a stereomicroscope (10–40x magnification) were performed in all subjects at baseline and at the end of the study. At the end of follow-up, the fulfillment of the 2013 ACR/EULAR criteria was also assessed in each patient. The following parameters were determined by NFC: number of enlarged and giant capillaries, the number of microhaemorrhages, and the avascular score. The scleroderma pattern was classified as early, active and late.

Results:
After 3 years, 34 patients with early SSc were reevaluated (mean age 53 ± 12.7 years) and 12 patients were lost to follow-up. Eight (23.5%) patients with early SSc developed definite SSc. A higher frequency of puffy fingers at baseline was observed in the group of patients who developed definite SSc compared to those who did not (37.5% vs 0%, respectively; p=0.01). A higher proportion of patients with early SSc who progressed to definite SSc presented a significant increase in the number of giant capillaries (50% vs 7.7%, respectively; p=0.02) and a increase in the avascular score compared with those who remained with a diagnosis of early SSc (50% vs 0%, respectively; p=0.01). A higher frequency of active pattern in NFC at baseline was also observed in patients who progressed to definite SSc compared with those who did not (57.1% vs 6.3%, respectively; p=0.02). By multivariate analysis, increase in the number of giant capillaries (OR=12.0, 95% CI 1.6-88.7, p=0.02), and an active pattern in NFC (OR=30.0, 95% CI 2.1-421.1, p=0.01) were independent risk factors for developing definite SSc in patients with early SSc.

Conclusion:

In this prospective study, patients with early SSc who developed definite disease showed a worsening in capillaroscopic parameters including an increase in the number of giant capillaries and in the avascular score during a follow-up of 3 years. The presence of an active pattern and an increase in the number of giant capillaries in NFC were independent predictive risk factors for developing definite SSc in patients with early SSc.

Disclosure: C. Z. Camargo, None; M. I. Arismendi, None; C. Kayser, None.


Abstract Number: 1692

Decreased Lean Body Mass, Body Fat and Bone Mineral Density in Scleroderma Patients Are Associated with Disease Activity and Physical Activity

Sabina Oreska¹, Maja Spiritovic¹,², Petr Cesak², Michal Cesak², Hana Storkanova¹, Katerina Kubinova¹, Martin Klein¹, Lucia Vernerova¹, Olga Ruzickova¹, Herman F Mann³, Karel Pavelka¹, Ladislav Senolt¹, Jiri Vencovsky¹, Radim Becvar¹ and Michal Tomcik¹, ¹Institute of Rheumatology, Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, Prague, Czech Republic, ²Faculty of Physical Education and Sport, Charles University, Prague, Czech Republic, Prague, Czech Republic, ³Experimental and Clinical Rheumatology, Institute of Rheumatology, Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, Prague, Czech Republic

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic sclerosis (SSc) is characterized by fibrosis of the skin and visceral organs, especially digestive tract, and musculoskeletal involvement, which limit mobility/self-sufficiency of patients, and
can have a negative impact on body composition. The aim of our study was to assess body composition and physical activity of SSc patients and healthy controls (HC).

**Methods:** 59 patients with SSc [50 females, 9 males; mean age 52.1; disease duration 6.7 years; limited cutaneous (lcSSc,36)/diffuse cutaneous (dcSSc,23)] and 36 age-/sex-matched HC (30 females, 6 males, mean age 51.4) without rheumatic/tumor diseases or manifest cardiovascular event were included. SSc patients fulfilled ACR/EULAR 2013 criteria. Anthropometric parameters and body composition were assessed (by densitometry-iDXA Lunar, and by bioelectric impedance-BIA-2000-M), and physical activity was evaluated using Human Activity Profile (HAP) questionnaire. Routine biochemistry analysis was performed after 8 hours of fasting. Disease activity was evaluated by EUSTAR SSc activity score. Data are presented as mean±SD.

**Results:** Compared to HC, patients with SSc had significantly lower body-mass index (BMI: 26.4±3.3 vs. 22.4±4.3 kg/m², p<0.0001) and body fat % assessed by both iDXA (BF%: 37.2±6.6 vs. 32.6±8.2%, p=0.0014) and BIA (BF%: 31.1±6.4 vs. 24.6±7.8%, p<0.0001), and a trend to decreased visceral fat weight (0.9±0.9 vs. 0.5±0.5kg, p=0.0670). Compared to HC, SSc patients demonstrated significantly decreased lean body mass assessed by both iDXA (LBM: 46.6±7.5 vs. 40.9±6.8kg, p=0.0003) and BIA (LBM: 53.2±8.7 vs. 47.7±7.0kg, p=0.0017), and increased extracellular mass/body cell mass (ECM/BCM) ratio (1.03±0.1 vs. 1.29±0.4, p<0.0001), which reflects worse muscle predispositions for physical exercise, aerobic fitness/performance, and usually increases with deteriorating nutritional status. Compared to HC, SSc patients had significantly lower bone mineral density (BMD: 1.16±0.10 vs. 1.05±0.11g/cm², p<0.0001), and were currently able to perform less energetically demanding physical activities according to HAP score (84.7±6.6 vs. 64.1±17.2, p<0.0001). Disease activity negatively correlated with BF% (r=-0.324, p=0.014), and physical activity (HAP) positively correlated with BMD (r=0.276, p=0.034) and negatively with ECM/BCM (r=-0.625, p<0.0001).

**Conclusion:** Compared to healthy age-/sex-matched individuals we found significant negative changes in body composition of our SSc patients, which are associated with their disease activity and physical activity, and could reflect their nutritional status, and gastrointestinal and musculoskeletal involvement.

**Acknowledgement:** Supported by AZV-16-33574A, GAUK-214615.

**Disclosure:** S. Oreska, None; M. Spiritovic, None; P. Cesak, None; M. Cesak, None; H. Storkanova, None; K. Kubinova, None; M. Klein, None; L. Vernerova, None; O. Ruzickova, None; H. F. Mann, None; K. Pavelka, None; L. Senolt, None; J. Vencovsky, Samsung Bioepis Co., Ltd., Biogen, 5; R. Becvar, None; M. Tomcik, None.


**Abstract Number:** 1693

**To What Extend Do Auto-Antibodies Help to Identify High-Risk Patients in Systemic Sclerosis?**

Maaike Boonstra1, Jaap Bakker2, Maarten K. Ninaber3, Nina Ajmone Marsan4, Tom W.J. Huizinga5 and Jeska K. de Vries-Bouwstra6, 1Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, 2Clinical Chemistry and Laboratory Medicine, Leiden University Medical Center, Leiden, Netherlands, 3Pulmonology, Department of Pulmonology, Leiden University Medical Center, Leiden, Netherlands, 4Heart and Lung Center, Leiden University Medical Center, Leiden, Netherlands, 5Rheumatology, Leiden University Medical Center, Leiden, Netherlands, 6Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands

**First publication:** September 18, 2017
Background/Purpose: In Systemic Sclerosis tight monitoring during the first years of disease is required in order to detect organ complications timely. Although a clear pathophysiologic role of disease specific auto-antibodies has never been confirmed, these antibodies are associated with distinct clinical futures, strongly indicating that their prevalence is of relevance. Therefore we aimed to evaluate to what extent disease specific auto-antibodies in Systemic Sclerosis improve clinical subsetting, identifying high-risk disease.

Methods: Clinical clusters of patients were determined, using data from the Combined Care In Systemic Sclerosis cohort, Leiden University Medical Center. Hierarchical clustering based on Ward Method was performed on Principal Component Analysis scores of solely baseline clinical variables. To determine disease-risk, 5-year mortality rates since first non-Raynaud phenomenon were assessed. Prevalence of disease specific auto-antibodies in each cluster was studied. Second, the cluster process was repeated, taking auto-antibodies into account. Clinical and auto-antibody characteristics of obtained clusters were compared to clustering based on clinical variables alone.

Results: Of 407 patients, 91% (n=371) fulfilled ACR/EULAR 2013 criteria. Prevalence of auto-antibodies was: anti-centromere 37%, anti-topoisomerase 24%, anti-RNA polymerase III 5%, anti-fibrillarin 4% and anti-Pm/Scl 5%. Clinical cluster analysis identified 4 different clusters with two clusters showing higher than average mortality (resp. 17% and 7% vs. total group mortality of 4% (n=15)). Adding auto-antibody status to the cluster process resulted in 5 clusters, with an additional cluster 5 with frequent RNA polymerase III (18%, n=14; mortality rate 8%). The total number of patients clustered to a cluster with higher than average mortality-risk increased indicating the need of more intensive screening in a larger group of patients.

Conclusion: Auto-antibodies partially contribute to risk-stratification and clinical subsetting in Systemic Sclerosis. We hypothesize that additional characteristics of auto-antibodies like isotypes might reflect their pathophysiological role, and that the value of autoantibodies as biomarkers for severe disease might increase when adding these characteristics.

Disclosure: M. Boonstra, None; J. Bakker, None; M. K. Ninaber, None; N. Ajmone Marsan, None; T. W. J. Huizinga, None; J. K. de Vries-Bouwstra, None.


Abstract Number: 1694

Efficacy of an Intensive 24-Week Physiotherapy Programme in Scleroderma Patients – Preliminary Data from a Single-Center Controlled Study

Maja Spiritovic¹,², Hana Smucrova¹, Sabina Oreska¹, Hana Storkanova¹, Petr Cesak², Adela Rathouska¹, Olga Ruzickova¹, Herman F Mann¹, Karel Pavelka¹, Ladislav Senolt¹, Jiri Vencovsky¹, Radim Becvar¹ and Michal Tomcik¹

¹Institute of Rheumatology, Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, Prague, Czech Republic, ²Faculty of Physical Education and Sport, Charles University, Prague, Czech Republic, Prague, Czech Republic
**Background/Purpose:** Involvement of skin and musculoskeletal system in systemic sclerosis (SSc) leads to loss of function, disability and reduced quality of life. Data on efficacy of non-pharmacologic care in SSc is very limited due to variety in studied interventions/outcomes. The aim of our study was to address the limitations of existing studies, and evaluate the effect of a controlled, long-term (24-week intervention, 24-week follow-up), intensive (1h physiotherapy + 0.5h occupational therapy twice weekly, and home-exercise for 0.5h 5x weekly), tailored physiotherapy programme on function/impairment of hands/face, and quality of life/disability in cohorts with a substantial number of SSc patients.

**Methods:** All patients fulfilled ACR/EULAR 2013 criteria, had skin involvement of hands/mouth, and were consecutively recruited from 2014 to 2016 at the Institute of Rheumatology in Prague. Both groups received educational materials and instructions for home exercise at baseline, however, only intervention group underwent the intensive physiotherapy programme. At months 0,3,6,12 all patients were assessed by a physician (physical examination, mRSS, EUSTAR SSc activity score, Medsger SSc severity score), and a physiotherapist blinded to intervention [validated measurements (dFTP-delta finger to palm, inter-incisor/inter-lip distance, grip strength using Baseline dynamometer); tests (HAMIS-Hand Mobility In Scleroderma)], patients filled out patient reported outcomes/questionnaires (CHFS-Cochin Hand Function Scale, MHISS-Mouth Handicap In SSc Scale, HAQ, SHAQ, SF-36) and provided blood for routine laboratory analysis and biobanking. Normality of data was tested, inter-group analysis was performed with 2-way ANOVA, and intra-group analysis by Friedman’s test with Dunn’s post hoc test.

**Results:** 25 SSc patients (22 female/3 male, 14 limited cutaneous (lc)SSc/11 diffuse cutaneous (dc)SSc, median of age 54.0 and disease duration 7.0 years, mRSS 12) were recruited into the intervention group (IG) and 29 patients into the control group (CG) (25 female/4 male, 16 lcSSc/13 dcSSc, median of age 49.0 and disease duration 5.0 years, mRSS 11). Compared to observed statistically significant deterioration in CG over the period of m0-m6, we found statistically significant improvement in dFTP, grip strength, HAMIS, inter-incisor and inter-lip distance (Table 1). Only numerical improvement in IG compared to numerical deterioration in CG, which have not reached statistical significance, were observed in patient reported outcomes (CHFS, MHISS, HAQ, SHAQ, SF-36).

**Conclusion:** Our physiotherapy program not only prevented the natural course of progressive deterioration of function of hands/mouth (observed in the control group), but led to a significant improvement in monitored parameters, which was clinically meaningful in a substantial proportion of patients.

**Acknowledgement:** Supported by AZV-16-33574A.
<table>
<thead>
<tr>
<th>Parameter (unit)</th>
<th>Intervention group</th>
<th>Control group</th>
<th>Intra-group analysis (Friedman+Dunn)</th>
<th>Inter-group analysis (2WA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>m0: 5.7 ± 0.5</td>
<td>m0: 6.6 ± 0.5</td>
<td>m0-m3: p&lt;0.001</td>
<td>m0-m3: p&lt;0.01</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>m3: 6.2 ± 0.5</td>
<td>m3: 6.1 ± 0.4</td>
<td>m3-m6: p&lt;0.05</td>
<td>m3-m6: p&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>m6: 6.8 ± 0.6</td>
<td>m6: 5.8 ± 0.4</td>
<td>m0-m6: p&lt;0.001</td>
<td>m0-m6: p&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>m0: 17.2 ± 1.8</td>
<td>m0: 16.6 ± 1.3</td>
<td>m0-m3: p&lt;0.05</td>
<td>m0-m3: p=NS</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>m3: 19.2 ± 1.9</td>
<td>m3: 14.9 ± 1.4</td>
<td>m3-m6: p=NS</td>
<td>m3-m6: p=NS</td>
<td></td>
</tr>
<tr>
<td>m6: 19.7 ± 1.9</td>
<td>m6: 13.9 ± 1.9</td>
<td>m0-m6: p&lt;0.001</td>
<td>m0-m6: p&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>m0: 9.8 ± 1.3</td>
<td>m0: 3.9 ± 1.1</td>
<td>m0-m3: p&lt;0.01</td>
<td>m0-m3: p&lt;0.01</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>m3: 7.1 ± 1.2</td>
<td>m3: 6.4 ± 1.2</td>
<td>m3-m6: p&lt;0.01</td>
<td>m3-m6: p&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>m6: 4.1 ± 0.9</td>
<td>m6: 9.3 ± 1.1</td>
<td>m0-m6: p&lt;0.001</td>
<td>m0-m6: p&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>m0: 30.6 ± 1.6</td>
<td>m0: 32.9 ± 1.3</td>
<td>m0-m3: p&lt;0.01</td>
<td>m0-m3: p&lt;0.001</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>m3: 33.3 ± 1.6</td>
<td>m3: 30.2 ± 1.4</td>
<td>m3-m6: p=NS</td>
<td>m3-m6: p=NS</td>
<td></td>
</tr>
<tr>
<td>m6: 36.2 ± 2.0</td>
<td>m6: 29.8 ± 1.4</td>
<td>m0-m6: p&lt;0.001</td>
<td>m0-m6: p&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>m0: 39.2 ± 1.6</td>
<td>m0: 41.7 ± 1.1</td>
<td>m0-m3: p&lt;0.01</td>
<td>m0-m3: p&lt;0.05</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>m3: 42.4 ± 1.7</td>
<td>m3: 39.9 ± 1.2</td>
<td>m3-m6: p=NS</td>
<td>m3-m6: p=NS</td>
<td></td>
</tr>
<tr>
<td>m6: 44.6 ± 1.8</td>
<td>m6: 40.0 ± 1.3</td>
<td>m0-m6: p&lt;0.001</td>
<td>m0-m6: p=NS</td>
<td></td>
</tr>
</tbody>
</table>

Acronyms: SEM, standard error of the mean; Friedman, Friedman’s test; Dunn, Dunn’s post hoc test; 2WA, two way ANOVA, dFTP, delta finger to palm; HAMIS, Hand Mobility in Scleroderma; m0, month 0 (= at the baseline); m3, month (= in the middle of intervention period); m6, month 6 (= at the end of intervention); p, p-value; NS, not significant.

Disclosure: M. Spiritovic, None; H. Smucrova, None; S. Oreska, None; H. Storkanova, None; P. Cesak, None; A. Rathouska, None; O. Ruzickova, None; H. F. Mann, None; K. Pavelka, None; L. Senolt, None; J. Vencovsky, Samsung Bioepis Co., Ltd., Biogen, 5; R. Becvar, None; M. Tomcik, None.

Abstract Number: 1695

Baseline Characteristics and Outcomes in a Retrospective Cohort of Patients with Systemic Sclerosis Related Interstitial Lung Disease

Robert L. Mango1, Eric L. Matteson2, Cynthia S. Crowson3, Jay H. Ryu4 and Ashima Makol2, 1Internal Medicine, Division of Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, MN, MN, 2Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, MN, 3Health Sciences Research, Mayo Clinic College of Medicine and Science, Rochester, MN, 4Division of Pulmonary and Critical Care Medicine, Mayo Clinic College of Medicine and Science, Rochester, MN
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Interstitial lung disease (ILD) is a major contributor to morbidity and mortality in systemic sclerosis (SSc). We sought to identify the distribution of clinical characteristics, comorbidities, pulmonary disease patterns, and outcomes in a retrospective cohort of SSc-ILD.

Methods: A retrospective review of medical records was conducted to identify patients with SSc seen at a single tertiary referral center in 2000-2013 within 1 year of ILD diagnosis. All patients met the 2013 ACR/EULAR classification criteria for SSc. Patients were included only if at least 1 year of follow up data was available. Baseline demographics, comorbidities and clinical characteristics were collected, in addition to pulmonary function tests, lung imaging, and echocardiogram for 3 years after ILD diagnosis. Cox models were used to examine associations between potential risk factors and progression or mortality.

Results: A total of 126 patients with SSc-ILD were identified (87 [69%] female; mean age: 57.5, range 31-82 years). Based on high resolution chest CT (or biopsy when available), 108 (86%) were characterized as nonspecific interstitial pneumonia (NSIP), 17 (13%) as usual interstitial pneumonia (UIP), 1 as unclassifiable ILD. Pulmonary hypertension (PHTN) was noted in 44 (35%) at baseline, and this did not differ between ILD subtypes. Patients with UIP were more likely than those with NSIP to have chronic obstructive pulmonary disease (COPD) at baseline (24% vs 5%, p = 0.005). 89% had limited cutaneous SSc, 7% had diffuse cutaneous, and 4% SSc sine scleroderma. SSc specific serologies (i.e., SCL-70, centromere, and/or RNA Pol III) were positive in 56 (46%) patients, somewhat more common in NSIP than UIP (49% vs 25%; p=0.07). Baseline initial forced vital capacity (FVC) and diffusion capacity (DLco) were not significantly different between ILD subtypes. Progression to DLco < 40% predicted or too ill to perform DLco was noted in 44 (35%) at baseline, and this did not differ between ILD subtypes. Patients with UIP were more likely than those with NSIP to have chronic obstructive pulmonary disease (COPD) at baseline (24% vs 5%, p = 0.005). 89% had limited cutaneous SSc, 7% had diffuse cutaneous, and 4% SSc sine scleroderma. SSc specific serologies (i.e., SCL-70, centromere, and/or RNA Pol III) were positive in 56 (46%) patients, somewhat more common in NSIP than UIP (49% vs 25%; p=0.07). Baseline initial forced vital capacity (FVC) and diffusion capacity (DLco) were not significantly different between ILD subtypes. Progression to DLco < 40% predicted or too ill to perform DLco was noted in 39% (95% CI 30% – 48%) by 3 years and did not significantly differ between ILD patterns (p=0.64). Risk factors for progression included baseline DLco (p < 0.001), FVC (p = 0.001) and PHTN (p = 0.002). Only 5 patients progressed to FVC < 50% predicted. During a median of 5.0 years of follow-up, five-year survival was 86% (95% CI 80 - 92%), and was only marginally worse in UIP than NSIP (hazard ratio [HR]: 2.0; p=0.057). Risk factors for mortality included comorbid COPD, hypertension and those identified for progression. The presence of inflammatory arthritis at baseline (16 patients, 13%) appeared to be a good prognostic indicator for mortality (HR 0.21, 95% CI 0.05 - 0.89).

Conclusion: Outcomes were overall somewhat better in SSc-ILD compared with those described in idiopathic pulmonary fibrosis, consistent with previous studies of connective tissue disease related ILD. ILD subtype had marginal prognostic significance in this cohort of patients with SSc-ILD. Baseline FVC and DLco, comorbid COPD, hypertension, and pulmonary hypertension at any time were risk factors for a poor prognosis. These findings
highlight the importance of a thorough baseline pulmonary evaluation in predicting outcomes in patients with SSc-ILD.

Disclosure: R. L. Mango, None; E. L. Matteson, None; C. S. Crowson, None; J. H. Ryu, None; A. Makol, None.


Abstract Number: 1696

**Performance of Forced Vital Capacity and Lung Diffusion Cut-Points for Associated Radiographic Interstitial Lung Disease in Systemic Sclerosis**

Kimberly Showalter¹, Aileen Hoffmann², Gerald W. Rouleau³, David Aaby⁴, Julia (Jungwha) Lee⁵, Carrie Richardson⁶, Jane Dematte⁷, Rishi Agrawal⁸, Rowland W. Chang⁹ and Monique Hinchcliff¹⁰, ¹Internal Medicine, McGaw Medical Center of Northwestern University, Chicago, IL, ²Department of Medicine, Division of Rheumatology, Northwestern University Feinberg School of Medicine, Northwestern University, Chicago, IL, ³Northwestern University, Chicago, IL, ⁴Northwestern University Feinberg School of Medicine, Chicago, IL, ⁵Preventive Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, ⁶Department of Rheumatology, Johns Hopkins University, Baltimore, MD, ⁷Pulmonology, Northwestern University Feinberg School of Medicine, Chicago, IL, ⁸Radiology, Northwestern University Feinberg School of Medicine, Chicago, IL, ⁹Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL, ¹⁰Department of Medicine Division of Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Forced vital capacity (FVC) and carbon monoxide diffusion (DLCO) are used to screen for systemic sclerosis associated interstitial lung disease (SSc-ILD). The purpose of this cross-sectional study was to determine the sensitivity, specificity, and negative predictive values (NPV) of FVC and DLCO thresholds for SSc-ILD on chest high-resolution computed tomography (HRCT) scans.

Methods: Patients fulfilled American College of Rheumatology 2013 SSc criteria and had undergone at least one HRCT and pulmonary function test (PFT). An experienced thoracic radiologist quantified ILD on HRCT. Receiver operating characteristic curves were generated to determine optimal % predicted FVC and DLCO cut-points, defined as the greatest combined sensitivity and specificity, for radiographic ILD. Established "normal" PFT thresholds and screening algorithms combining FVC and DLCO were evaluated. Sub-analysis was performed according to anti-topoisomerase I (Scl-70) autoantibody status.

Results: A total of 265 patients fulfilled study criteria (82% women, 49% diffuse cutaneous SSc, 30% +Scl-70), and 188 (71%) had radiographic ILD. Of those with ILD, 59 out of 188 (31%) had "normal" FVC (>80% predicted), and 65 out of 151 (43%) had "normal" DLCO (>60% predicted). There were 31 out of 214 (14%) patients who had
FVC and DLCO both within ŐnormalÓ range. Predicted FVC <=80% (sensitivity 0.69, specificity 0.74), and DLCO <=62% (sensitivity 0.60, specificity 0.70) were the optimal thresholds for ILD (Table 1, Figure 1). All evaluated FVC and DLCO threshold combinations had a NPV <0.70 for radiographic ILD. In patients with positive vs. negative Scl-70, the NPV of % predicted FVC <80 (0.05 vs. 0.57) and DLCO <60 (0.10 vs. 0.48) was lower for radiographic ILD (Table 1).

Conclusion: Radiographic ILD is prevalent in SSc patients despite normal PFTs. No observed % predicted FVC or DLCO threshold combinations yielded a high NPV for SSc-ILD screening. A % predicted FVC >=80 and DLCO >=60 in SSc patients, especially those with positive vs. negative Scl-70 autoantibodies, should not obviate consideration of HRCT for ILD evaluation. However, it remains to be shown if detection of ILD in asymptomatic patients with normal PFTs improves clinical outcomes.

**Figure 1. Receiver Operating Characteristic Curves.** Receiver operating characteristic (ROC) curves for % predicted forced vital capacity (FVC) and diffusing capacity of the lung for carbon monoxide (DLCO) for associated radiographic interstitial lung disease (ILD) in systemic sclerosis.
Table 1. Performance of pulmonary function test thresholds for prevalent radiographic interstitial lung disease on chest high resolution computed tomography images in patients with systemic sclerosis

<table>
<thead>
<tr>
<th>Individual PFT Threshold – Entire cohort</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC % predicted (n=265)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;80 (conventional and optimal)</td>
<td>0.686</td>
<td>0.727</td>
<td>0.860</td>
<td>0.487</td>
</tr>
<tr>
<td>DLCO % predicted (n=214)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;60 (conventional)</td>
<td>0.576</td>
<td>0.698</td>
<td>0.821</td>
<td>0.407</td>
</tr>
<tr>
<td>&lt;62 (optimal)</td>
<td>0.603</td>
<td>0.698</td>
<td>0.827</td>
<td>0.422</td>
</tr>
<tr>
<td>&lt;70 (alternative)</td>
<td>0.801</td>
<td>0.508</td>
<td>0.796</td>
<td>0.516</td>
</tr>
<tr>
<td>&lt;80 (alternative)</td>
<td>0.921</td>
<td>0.317</td>
<td>0.764</td>
<td>0.625</td>
</tr>
<tr>
<td>Combination of PFT Thresholds % predicted</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FVC &lt;80 and DLCO &lt;60</td>
<td>0.457</td>
<td>0.810</td>
<td>0.852</td>
<td>0.383</td>
</tr>
<tr>
<td>FVC &lt;80 or DLCO &lt;60</td>
<td>0.788</td>
<td>0.571</td>
<td>0.815</td>
<td>0.529</td>
</tr>
<tr>
<td>FVC &lt;80 and DLCO &lt;62</td>
<td>0.490</td>
<td>0.810</td>
<td>0.860</td>
<td>0.398</td>
</tr>
<tr>
<td>FVC &lt;80 or DLCO &lt;62</td>
<td>0.795</td>
<td>0.556</td>
<td>0.811</td>
<td>0.530</td>
</tr>
<tr>
<td>FVC &lt;80 and DLCO &lt;70</td>
<td>0.609</td>
<td>0.762</td>
<td>0.860</td>
<td>0.449</td>
</tr>
<tr>
<td>FVC &lt;80 or DLCO &lt;70</td>
<td>0.688</td>
<td>0.429</td>
<td>0.784</td>
<td>0.574</td>
</tr>
<tr>
<td>FVC &lt;80 and DLCO &lt;80</td>
<td>0.656</td>
<td>0.730</td>
<td>0.853</td>
<td>0.469</td>
</tr>
<tr>
<td>FVC &lt;80 or DLCO &lt;80</td>
<td>0.940</td>
<td>0.270</td>
<td>0.755</td>
<td>0.654</td>
</tr>
</tbody>
</table>

Antinuclear Scl-70 Positive Patients

| FVC <80 (n=78)                          | 0.750       | 0.050       | 0.983                     | 0.050                     |
| DLCO <60 (n=62)                         | 0.700       | 1.000       | 1.000                     | 1.000                     |
| FVC <80 or DLCO <60                     | 0.850       | 0.500       | 0.981                     | 0.100                     |

Antinuclear Scl-70 Negative Patients

| FVC <80 (n=183)                         | 0.633       | 0.730       | 0.775                     | 0.574                     |
| DLCO <60 (n=180)                        | 0.500       | 0.683       | 0.703                     | 0.477                     |
| FVC <80 or DLCO <60                     | 0.744       | 0.566       | 0.720                     | 0.596                     |

PFT = pulmonary function test; FVC = forced vital capacity; DLCO = diffusing capacity of the lung for carbon monoxide. FVC >=80% and DLCO >=60% predicted represents traditional cut points based on 95% confidence interval in healthy population.

Disclosure: K. Showalter, None; A. Hoffmann, None; G. W. Rouleau, None; D. Aaby, None; J. Lee, None; C. Richardson, None; J. Dematte, None; R. Agrawal, None; R. W. Chang, None; M. Hinchcliff, None.


Abstract Number: 1697

Unique Characteristics of Scleroderma Among African Americans: A Population Based Study

Sarah M. Compton1, Richard M. Silver2 and Diane L. Kamen3, 1Internal Medicine, Medical University Of South Carolina, Charleston, SC, 2Division of Rheumatology and Immunology, Department of Medicine, Medical University of South Carolina, Charleston, SC, 3Medicine/Rheumatology & Immunology, Medical University of South Carolina, Charleston, SC

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Systemic sclerosis (SSc) is a rare autoimmune disease categorized on the basis of skin involvement as either limited or diffuse cutaneous SSc, the latter of which manifests in more severe skin and internal organ involvement. SSc disproportionately affects women and literature suggests African American (AA) patients experience autoimmune diseases differently than other ethnic/racial groups. We sought to validate these observations utilizing a longitudinal cohort of SSc patients, comparing disease characteristics between AAs and non-AAs.

Methods:
Data were collected as part of an ongoing IRB-approved longitudinal registry of SSc patients, including demographics, clinical disease manifestations and other medical history. Patients were seen over a 12-year period at a single academic center. Retrospective chart review was additionally performed to confirm age of onset, SSc disease type, and selected criteria for SSc to assess severity of disease. PearsonÔs chi-squared and FisherÔs Exact testing were performed for categorical measures. Two-sample t-tests were performed for continuous measures. Significance was set at alpha = 0.05.

Results:
A total of 236 patients with SSc (80.9% female, 35.2% AA) were identified. Demographics and clinical characteristics are shown in Table 1. AA patients developed SSc at a significantly younger age compared to the non-AA patient subset (41.8±13.3 yrs., 48.7±13.2 yrs., respectively, p<0.01). Females developed SSc at a younger age than males (45.1±13.9 yrs., 51.3±11.0 yrs, p<0.01). Diffuse SSc was significantly more common in AA patients (p<0.01). Males overall were more likely to have diffuse SSc than limited SSc (68.3%, p<0.01).

Interstitial lung disease was significantly more common in AA patients (68.5%, p=0.02). The higher prevalence of lung disease among AAs was not attributed to smoking status, as a significantly higher proportion of non-black SSc patients were smokers. Although not statistically significant, AA patients had a higher prevalence of restrictive lung disease based on forced vital capacity percent predicted <70% (46.0% versus 31.9% p=NS). Overall mortality was 7.2% in AA patients compared to 3.9% in non-AA patients with SSc (p=NS).

Conclusion:
In conclusion, we found that AA SSc patients tend to be younger and more often have diffuse cutaneous disease than non-AA SSc patients, consistent with findings among other AA populations. Although not statistically significant, AA patients trended towards a higher prevalence of restrictive lung pattern on pulmonary function testing and a higher mortality rate. These data support the conclusion that AAs have more severe disease with a more unfavorable SSc prognosis. Further investigation into the multifactorial causes for this disparity is needed in order to identify strategies to reduce them.
Quantitative Analyze of Peripheral Vascular Bed in Patients with Systemic Sclerosis By Using Photoacoustic Imaging Technology: A Pilot Study

Yasuyoshi Kusanagi¹, Rika Suzuki¹, Dai Murakoshi², Kazuhiro Hirota², Kaku Irisawa², Takatsugu Wada², Shinpei Okawa³, Miya Ishihara³, Fumihiko Kimura¹ and Kenji Itoh¹, ¹Department of Hematology and Rheumatology, Division of Internal medicine, National Defense Medical College, Saitama, Japan, ²Medical Systems R&D Center, R&D Management Headquarters, Fujifilm Corporation, Kanagawa, Japan, ³Department of Medical Engineering, National Defense Medical College, Saitama, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Objectives: The aim of this study is to evaluate the usefulness of photoacoustic imaging (PAI) for quantitative analysis of the peripheral vascular bed in patients with systemic sclerosis (SSc).
**Background/Purpose:** PAI is a technique that uses the photoacoustic effect of living tissues. Pulsed short-length light waves excite the living tissue to produce strong ultrasonic waves in accordance with the absorbance of substances in the tissue. These ultrasonic waves can be detected with ultrasound probes, and reconstructed as an ultrasound image. Detecting the ultrasonic wave which is produced by 750 nm wavelength pulsed laser-excited hemoglobin enables small blood vessels of low flow velocities to be visualized without using contrast agents. The quantitative evaluation of digital vascular bed volume in patients with SSc may enable us to diagnose SSc earlier, and to determine the progression and severity of the disease.

Patients and **Methods:** Nine patients with SSc, two patients with systemic lupus erythematosus (SLE) complicating Raynaud's phenomenon as disease control (DC), and three healthy adult volunteers as healthy control (HC) were enrolled in the study. The volume of the vascular bed was measured in the proximal and distal sites of fingers 2–5 bilaterally using PAI.

**Results:** The volume of the digital vascular bed in 37 sites of SSc patients, 21 sites of HC, and 14 sites of DC could be obtained. All SSc patients showed a severely decreased digital vascular bed volume in both proximal and distal sites of all measured fingers, and the vascular bed volumes were significantly lower compared with HC. DC showed a tendency of decreased digital vascular bed, but not significantly compared with HC.

**Conclusion:** PAI is a useful device for determining digital vasculopathy by quantitative analysis of vascular bed volume. More data with clinical signs, and comparison with other modalities such as color Doppler sonography, will provide the information to determine the prognosis of peripheral ischemic damage, and the effectiveness of treatments to improve peripheral circulation.

![Image](image.jpg)

**Figure 1.** Three-dimensional projection image of the scanned photoacoustic signal from laser-excited hemoglobin in human finger (A). Enhanced PAI imaging of HC (left) compared with SSc patient (right) (B).
Figure 2. Volume of the digital vascular bed at a site 5 mm proximal from the PIP joint (A), and halfway between the PIP and DIP joints (B). SSc: patients with systemic sclerosis, HC: healthy control, DC: disease control

Disclosure: Y. Kusanagi, None; R. Suzuki, None; D. Murakoshi, None; K. Hirota, None; K. Irisawa, None; T. Wada, None; S. Okawa, None; M. Ishihara, None; F. Kimura, None; K. Itoh, None.


Abstract Number: 1699

A 10-Year National Trend in Acute Coronary Syndrome Among Hospitalized Patients with Systemic Sclerosis

Yiming Luo¹, Jiehui Xu², Yumeng Wen¹, Changchuan Jiang¹, Shuyang Fang¹, Mustafa Kagalwalla¹, Xin Wei¹ and Bing Yue¹, ¹Department of Medicine, Mount Sinai St Luke's and Mount Sinai West Hospitals, Icahn School of Medicine at Mount Sinai, New York, NY, ²Department of Biostatistics, Mailman School of Public Health, Columbia University Medical Center, New York, NY
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Systemic sclerosis (SSc) is a systemic autoimmune disorder characterized by microvascular changes, excessive fibrous tissue deposition and systemic inflammation. Previous studies showed that systemic sclerosis is an
independent risk factor for coronary artery disease and involved not only accelerated epicardial atherosclerosis, but also small vessel disease and vasospasm. The aim of this study is to analyze the temporal trend of acute coronary syndrome (ACS) in hospitalized patients with SSc, mortality and other outcomes from 2005 to 2014. We also compared the in-hospital mortality in ACS hospitalizations in patients with and without SSc.

Methods:

We conducted a retrospective study using data from National Inpatient Sample (NIS) from 2005 to 2014. Diagnoses were identified using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes. Patients with a diagnosis of ACS (ICD 9 code 410 excluding 410.x2 and 411.1) and SSc (ICD 9 code 710.1) were included. Patients younger than 18 years old were excluded. Primary outcome was the temporal trend of the ratio of ACS hospitalizations compared to all-cause hospitalizations from 2005 to 2014. Secondary outcome was the temporal trend of age-adjusted in-hospital mortality, length of stay and total hospital charges over the study period of time. We also compared the age-adjusted in-hospital mortality in ACS hospitalizations in patients with and without SSc. Logistic regression was used for statistical analysis of hospitalization ratio and age-adjusted in-hospital mortality and linear regression was used for length of stay and total hospital charges.

Results:

A total of 66,392 ACS hospitalizations in adult patients with SSc from 2005 to 2014 were identified. Compared with all-cause hospitalizations, the ratio of ACS hospitalizations were stable (3.57% in 2005 and 3.58% in 2014, p = 0.822) among patients with SSc, while the ratio was decreased (3.76% in 2005 and 3.19% in 2014, p < 0.001) among general adult populations. Age-adjusted in-hospital mortality was significantly higher in those with SSc compared to non-SSc (OR 2.25, 95% CI 1.95 - 2.60, p < 0.001) and did not change significantly (16.99% in 2005 and 16.19% in 2014, p = 0.412) from 2005 to 2014. Length of stay decreased significantly (7.42 days in 2005 and 6.13 days in 2014, p = 0.044) and total hospital charges increased significantly (55,280 in 2005 and 76,486 in 2014, p = 0.001) over the 10 year period.

Conclusion:

Our study shows that ACS hospitalizations in SSc patients have more than doubled risk of death compared to those without SSc and both the ratio of ACS hospitalizations and age-adjusted in-hospital mortality failed to decrease over time. Our study highlights that there is a critical gap in preventing and treating ACS in SSc populations.

Disclosure: Y. Luo, None; J. Xu, None; Y. Wen, None; C. Jiang, None; S. Fang, None; M. Kagalwalla, None; X. Wei, None; B. Yue, None.


Abstract Number: 1700

Focusing on Pulmonary Vascular Disease at Early Stage of Systemic Sclerosis: Exercise-Induced Pulmonary Arterial Hypertension and Gene Co-Expression Networks Involved in Its Pathogenesis

Yoshinobu Koyama1, Soichiro Fuке2, Yoshiharu Sato3 and Toshie Higuchi1, 1Center for Autoimmune Diseases, Division of Rheumatology, Japan Red Cross Okayama Hospital, Okayama, Japan, 2Department of Cardiology, Japan Red Cross Okayama Hospital, Okayama, Japan, 3DNA Chip Research Inc, Yokohama, Japan

First publication: September 18, 2017
Background/Purpose: Pulmonary arterial hypertension (PAH) is prominent as a vascular involvement in systemic sclerosis (SSc), which remains a leading cause of death in spite of current best treatments. As the pulmonary vascular disease (PVD) can be well compensated for, more than a half of the pulmonary circulation is impaired before early PAH is detected. Although recent studies focused on molecular basis of the PVD, the underlying mechanisms have not been fully elucidated, especially at early stage of SSc. In this study, we try to detect the subclinical PVD and to detect a gene co-expression network involved in the pathogenesis of exercise-induced PAH at early stage of SSc.

Methods: Total of 93 cases without PAH symptoms (NYHA I) with either Raynaud phenomenon (RP: n=80), skin sclerosis (n=51) or SSc-related autoantibody (anti-RNP: n=15, centromere: n=50, topoisomerase-1: n=3, RNA polymerase III: n=3) were enrolled. To detect the latent PAH, exercise DE with Master’s two-step stress was carried out. Systolic PAP (sPAP) was determined by maximum velocities of tricuspid regurgitation jets, and exercise induced pulmonary hypertension (exPH) group was segregated from normal response group (exN) with using the definition of a sPAP greater than 40 mm Hg during exercise, or a exercise increase in sPAP by greater than 20 mm Hg. Meanwhile, genome-wide gene expression analysis was performed with using whole peripheral blood from some of these patients (n=74). Total RNAs were extracted and multiplex sequencing was done. After quantifying the expressions of transcripts, co-expression modules were identified by weighted gene co-expression network analysis (WGCNA). And then, pathway enrichment analysis (PathVisio) was performed to investigate the module.

Results: In clinical test items, the level of serum BNP was high in exPH group, whereas there were no significant differences between exPH and exN group in the results of total skin score, pulmonary function and thermography after 0°C-stress test. The SSc-related autoantibody positive was a risk factor for exPH (odds ratio=1.62); especially, anti-RNP positive seems to be prominent (odds ratio=2.10). Based on the gene expression analysis, 19 co-expression modules were identified by WGCNA. Pathway enrichment analysis revealed that modules related with the titer of anti-RNP antibody were enriched with genes of type2 interferon signaling pathway.

Conclusion: The paradigm of SSc-PAH management should ideally be aimed at detecting early PVD and starting treatment prior to fulfilling the criteria for PAH. Although it remains a major challenge, individuals who require early therapeutic intervention are possible to be segregated by the follow-up with exercise DE. By this study, the crucial genes involved in the pathogenesis of exercise-induced PAH have not been completely elucidated. However, it is noteworthy that anti-RNP autoantibody, shown as an important risk factor for exercise-induced PAH, seemed to be related with type 2 interferon signaling pathway. It may show a hint for therapeutic intervention at the early stage of the disease to prevent the aggravation of PVD.


Disclosure: Y. Koyama, None; S. Fuke, None; Y. Sato, None; T. Higuchi, None.
Can Durometer Differentiate Limited Versus Diffuse Cutaneous Systemic Sclerosis?

Vivek Nagaraja¹, Amber Young¹, Veronica J. Berrocal² and Dinesh Khanna¹, ¹Department of Medicine, University of Michigan Scleroderma Program, Ann Arbor, MI, ²Department of Biostatistics- School of Public Health, University of Michigan, Ann Arbor, MI

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The durometer is a handheld device that measures the hardness of a surface. It has been used to measure skin hardness in patients with diffuse cutaneous systemic sclerosis (dcSSc), and was found to be feasible, reliable, and responsive to change in a trial and US cohort [1, 2]. The objective of this study is to assess if durometer can differentiate skin hardness in patients with limited cutaneous SSc (lcSSc) vs. dcSSc.

Methods: This is a single center cross-sectional study. Durometer assessment was performed at two areas – forearm and thigh by same observer. At each of these areas, three values were assessed and a median score was reported separately for each area. We assessed the correlation between durometer and mRSS at the forearm and thigh using the Pearson’s correlation coefficient. Paired t-test was used to assess the difference in the mean durometer scores between sub-groups (with p-value less than 0.05).

Results: A total of 45 patients participated in this study – healthy controls (N=21), dcSSc (N=14), and lcSSc (N=10). Majority of patients were females across the groups (dcSSc 64%, lcSSc 80%, HC 76%). The mean (SD) durometer reading of 3 groups were: at the forearm, 19.22 for HC, 24.28 for lcSSc, and 34.53 for dcSSc; at the thigh, 19.39 for HC, 28.68 for lcSSc, and 31.04 for dcSSc. The mean [SD] overall mRSS was 3.89[2.47] in lcSSc and 16.38[7.5] in dcSSc. We found statistically significant correlations in the forearm measurements between median durometer scores and mRSS in dcSSc (0.56, p<0.05), but not in lcSSc (0.36, p=0.34). Durometer was able to differentiate lcSSc from dcSSc (median durometer scores 34.53 units vs. 24.28 units for lcSSc, p=0.006) but not in the thigh (median durometer scores 31.04 units vs. 28.68 units for lcSSc, p=0.53; Table).

Conclusion: Durometer was able to differentiate skin hardness in dcSSC vs lcSSc patients when measured in the forearm.

Table: Mean [SD] durometer scores between the groups

<table>
<thead>
<tr>
<th>Location</th>
<th>Mean Durometer Scores</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HC [SD]</td>
<td>dcSSc [SD]</td>
</tr>
<tr>
<td>Forearm</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>19.22 [2.75]</td>
<td>34.53 [7.88]</td>
</tr>
<tr>
<td></td>
<td>34.53 [7.88]</td>
<td>24.28 [8.19]</td>
</tr>
<tr>
<td>Thigh</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>19.39 [3.64]</td>
<td>31.04 [8.28]</td>
</tr>
</tbody>
</table>
HC – healthy controls; DcSSc – diffuse cutaneous systemic sclerosis; LcSSc – limited cutaneous systemic sclerosis

References:


Disclosure: V. Nagaraja, None; A. Young, None; V. J. Berrocal, None; D. Khanna, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/can-durometer-differentiate-limited-versus-diffuse-cutaneous-systemic-sclerosis

Abstract Number: 1702

Disease Progression in Systemic Sclerosis Patients with Concomitant or Isolated Interstitial Lung Disease and Pulmonary Arterial Hypertension in the Scleroderma Cohort Singapore

Maria Noviani1, Seyed Ehsan Saffari2, Sandra Mei Yu Kua1, Grace Yin Lai Chan3, Gim Gee Teng4, Weng Giap Law5, Amelia Santosa4, Anita Yee Nah Lim4, Swee Cheng Ng1 and Andrea Hsiu Ling Low1,

1Department of Rheumatology and Immunology, Singapore General Hospital, Singapore, Singapore, Singapore, 2Center for Quantitative Medicine, Duke-NUS Medical School, Singapore, Singapore, Singapore, 3Department of Rheumatology, Allergy and Immunology, Tan Tock Seng Hospital, Singapore, Singapore, Singapore, 4Division of Rheumatology, University Medicine Cluster, National University Health System, Singapore, Singapore, Singapore, Singapore, 5Department of Rheumatology, Allergy and Immunology, Tan Tock Seng Hospital, Singapore, Singapore, Singapore, Singapore

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Pulmonary arterial hypertension (PAH) and interstitial lung disease (ILD) are leading causes of mortality in patients with systemic sclerosis (SSc). We aimed to determine factors associated with disease progression in SSc patients with concomitant ILD-PAH, PAH alone or ILD alone in the Scleroderma Cohort Singapore.

Methods:
In this multi-centre study involving 3 tertiary Rheumatology institutions (January 2008 to June 2016), factors associated with progression in full vital capacity (predicted FVC ≥10% decrease from baseline), NT-proBNP (≥4x
baseline) and New York Heart Association (NYHA ≥1 class progression) were identified among SSc patients with ILD-PAH, PAH alone and ILD alone. Stepwise multivariable logistic regression analyses were performed to determine independent factors associated with worse outcomes. Inclusion criteria were fulfillment of the ACR 2013 classification criteria for SSc and significant pulmonary involvement. ILD was based on high resolution computed tomography scan and predicted FVC <70%. Patients with suspected PAH based on echocardiographic systolic pulmonary arterial pressure (PAP) ≥50mmHg, and definite PAH based on right heart catheterization findings of mean PAP ≥25mmHg and pulmonary capillary wedge pressure (PCWP) ≤15 mmHg were included. In patients with PCWP >15mmHg, those with mixed pre- and post-capillary PH based on transpulmonary gradient >12mmHg were also included in the PAH group analyses.

Results:

Among 541 subjects, 88 (16%) had ILD, 49 (9%) PAH and 44 (8%) concomitant ILD-PAH (Table 1). Of 93 patients classified to have PAH or ILD-PAH, 56 (60%) were based on echocardiography and 37 (40%) on right heart catheterization. Patients with ILD-PAH had increased risk of NT-proBNP progression; additionally, telangiectasia and baseline NYHA ≥II increased the risk of NT-proBNP progression. SSc disease duration and malabsorption increased the risk of NYHA progression. Reflux/ dysphagia and malabsorption increased the risk of FVC progression (Table 2).

Conclusion:

SSc patients with concomitant ILD-PAH had worse clinical outcomes based on surrogate biomarker NT-proBNP. We also identified other risk factors associated with increased risk of disease progression in SSc patients with pulmonary involvement.
Table 1. Demographics and Clinical Characteristics

<table>
<thead>
<tr>
<th></th>
<th>ILD (n=88)</th>
<th>PAH (n=49)</th>
<th>ILD-PAH (n=44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%)</td>
<td>(84.1%)</td>
<td>43 (87.8%)</td>
<td>39</td>
</tr>
<tr>
<td>Ethnicity, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chinese</td>
<td>55</td>
<td>36 (73.5%)</td>
<td>29</td>
</tr>
<tr>
<td>Malay</td>
<td>13</td>
<td>8 (16.3%)</td>
<td>9 (20.5%)</td>
</tr>
<tr>
<td>Indian</td>
<td>11</td>
<td>4 (8.2%)</td>
<td>3 (6.8%)</td>
</tr>
<tr>
<td>Others</td>
<td>9</td>
<td>1 (2%)</td>
<td>3 (6.8%)</td>
</tr>
<tr>
<td>Age at cohort entry, years (mean ± SD)</td>
<td>53.4 ± 11.8</td>
<td>57.3 ± 13.5</td>
<td>59.5 ± 12.6</td>
</tr>
<tr>
<td>Follow up duration from entry, years (mean ± SD)</td>
<td>4.6 ± 2.1</td>
<td>4.7 ± 2.1</td>
<td>4.8 ± 2.2</td>
</tr>
<tr>
<td>Age at SSc diagnosis, years (mean ± SD)</td>
<td>46.5 ± 12.1</td>
<td>51.1 ± 16.4</td>
<td>53.6 ± 15.1</td>
</tr>
<tr>
<td>SSc Subtype, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DcSSc</td>
<td>43 (48.9%)</td>
<td>13 (27.1%)</td>
<td>13 (30.2%)</td>
</tr>
<tr>
<td>LcSSc</td>
<td>28 (31.8%)</td>
<td>22 (45.8%)</td>
<td>19</td>
</tr>
<tr>
<td>MCTD</td>
<td>17 (19.3%)</td>
<td>13 (27.1%)</td>
<td>11</td>
</tr>
<tr>
<td>Antibodies, n (%)*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-centromere</td>
<td>3</td>
<td>11 (32.4%)</td>
<td>3 (10.3%)</td>
</tr>
<tr>
<td>Anti-Scl-70</td>
<td>49 (60.5%)</td>
<td>10 (20.4%)</td>
<td>17</td>
</tr>
<tr>
<td>Anti-Ro</td>
<td>21 (31.3%)</td>
<td>15 (34.1%)</td>
<td>9 (23.7%)</td>
</tr>
<tr>
<td>Treatment, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral vasculopathy:</td>
<td>61 (69.3%)</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>CCB, ACE-I, ARB</td>
<td>31 (63.3%)</td>
<td>10 (65.9%)</td>
<td>10</td>
</tr>
<tr>
<td>Peripheral vasculopathy:</td>
<td>10 (11.4%)</td>
<td>9 (18.4%)</td>
<td>2</td>
</tr>
<tr>
<td>PC, PDE5i, ETA</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parenteral nutrition</td>
<td>63 (2.3%)</td>
<td>1 (2.0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Immunosuppression:</td>
<td>25 (2.0%)</td>
<td>23 (2.0%)</td>
<td>22 (2.0%)</td>
</tr>
<tr>
<td>MTX, CYC, MMF</td>
<td>71 (3.6%)</td>
<td>51 (3.6%)</td>
<td>36 (3.6%)</td>
</tr>
<tr>
<td>PAH: PC, PDE5i, ETA</td>
<td>N/A</td>
<td>27 (55.1%)</td>
<td>27 (55.1%)</td>
</tr>
</tbody>
</table>

*The denominator for

NOTE: DcSSc: diffuse cutaneous systemic sclerosis; LcSSc: limited cutaneous systemic sclerosis; MCTD: mixed connective tissue disease; CCB: calcium channel blocker; ACE-I: angiotensin converting enzyme inhibitor; ARB: angiotensin receptor blocker; PC: prostacyclin; PDE-5i: phosphodiesterase type 5 inhibitor; ETA: endothelin receptor antagonist; MTX: methotrexate; CYC: cyclophosphamide; MMF: mycophenolate mofetil; PAH: pulmonary arterial hypertension.
(%) calculation was based on number of subjects tested for the respective antibodies.

**Table 2. Multivariable Logistic Regression**

<table>
<thead>
<tr>
<th></th>
<th>Adjusted Odds Ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NT-proBNP progression</td>
<td>0.916 (0.847, 0.990)</td>
<td>0.0269</td>
</tr>
<tr>
<td>Age at censor date</td>
<td>0.916 (0.847, 0.990)</td>
<td>0.0269</td>
</tr>
<tr>
<td>Cumulative telangiectasia</td>
<td>36.84 (2.933, 462.8)</td>
<td>0.0052</td>
</tr>
<tr>
<td>Baseline NYHA Class</td>
<td>35.98 (1.858, 696.6)</td>
<td>0.0178</td>
</tr>
<tr>
<td>II,III, or IV (vs. I)</td>
<td>35.98 (1.858, 696.6)</td>
<td>0.0178</td>
</tr>
<tr>
<td>ILD-PAH subgroup (vs. PAH only)</td>
<td>8.386 (1.295, 54.3)</td>
<td>0.0256</td>
</tr>
<tr>
<td>NYHA progression</td>
<td>3.332 (1.144, 9.704)</td>
<td>0.0273</td>
</tr>
<tr>
<td>Cumulative malabsorption</td>
<td>1.099 (1.027, 1.177)</td>
<td>0.0064</td>
</tr>
<tr>
<td>SSc duration at cohort entry</td>
<td>1.099 (1.027, 1.177)</td>
<td>0.0064</td>
</tr>
<tr>
<td>SSc subgroup</td>
<td>3.475 (1.124, 10.74)</td>
<td>0.0720</td>
</tr>
<tr>
<td>ILD-PAH subgroup (vs. ILD only)</td>
<td>3.475 (1.124, 10.74)</td>
<td>0.0720</td>
</tr>
<tr>
<td>PAH subgroup (vs. ILD only)</td>
<td>1.876 (0.545, 6.455)</td>
<td>0.9912</td>
</tr>
<tr>
<td>FVC progression</td>
<td>1.876 (0.545, 6.455)</td>
<td>0.9912</td>
</tr>
<tr>
<td>Baseline reflux/dysphagia</td>
<td>3.106 (1.095, 8.811)</td>
<td>0.0331</td>
</tr>
<tr>
<td>Cumulative malabsorption</td>
<td>7.405 (1.767, 31.03)</td>
<td>0.0062</td>
</tr>
<tr>
<td>ILD-PAH subgroup (vs. ILD only)</td>
<td>7.405 (1.767, 31.03)</td>
<td>0.0062</td>
</tr>
</tbody>
</table>

**NOTE:** NYHA: New York Heart Association; FVC: forced vital capacity.

Disclosure: M. Noviani, None; S. E. Saffari, None; S. M. Y. Kua, None; G. Y. L. Chan, None; G. G. Teng, None; W. G. Law, None; A. Santosa, None; A. Y. N. Lim, None; S. C. Ng, None; A. H. L. Low, None.


Abstract Number: 1703

**A Double-Blind, Randomized, Placebo-Controlled, Dose-Escalation, Multi-Center Study of a Single Intravenous Infusion of Allogeneic Mesenchymal Precursor Cells in Patients with Rheumatoid Arthritis and Incomplete Response to at Least One Tnfa Inhibitor**
Allogeneic STRO-3 immunoselected mesenchymal precursor cells (MPCs) derived from bone marrow of healthy donors are a potent, homogeneous cell population which can be activated by pro-inflammatory cytokines to release factors which polarize pro-inflammatory monocytes and T cells to an anti-inflammatory state. This is the first in human trial to assess safety, tolerability and efficacy of MPC therapy in biologic refractory RA, a disease driven by monocyte and T cell activation.

Methods:

Patients must have been positive for rheumatoid factor (RF) and/or anti-cyclic citrullinated peptide (anti-CCP3) antibodies but without extra-articular disease (other than RA nodules) and without severe functional limitation. ACR functional classes I, II and III were acceptable for entry. Safety endpoints were adverse events, vital signs, physical examination, clinical laboratory tests, ECG, and chest x-ray. Efficacy endpoints included ACR 20/50/70, ACR-N, ACR core components, HAQ and DAS28. Patients were randomized to receive one IV infusion of MPC 1 million cells/kg (n=16), 2 million cells/kg (n=16), or placebo (n=16) in 2 sequential dose cohorts. The primary study period was 12 weeks, with complete follow-up through 52 weeks.

Results: Patients in all 3 treatment groups were comparable in mean age (55 y), gender (73% women), duration of RA (13 years), and prior biologic exposure. MPC infusions were well-tolerated with no adverse infusion reactions and few serious adverse events noted during the 52-week study period, with 85% of patents completing all follow-up. HLA Class I sensitization was observed in MPC treatment groups, however without association with increased adverse events overall. We previously reported favorable efficacy results for both MPC groups at 12 weeks for ACR50 and ACR70 rates and ACR core components, with greater efficacy in the 2M/kg group (Durability of treatment effect observed at 12 weeks in the 2M/kg group was assessed by ACR-N and is shown to be significant compared to placebo through 12 and 39 weeks by time-integrated analysis of mean ACR-N area under the curve (AUC)

Conclusion:

A single infusion of MPCs was well-tolerated in RA patients. While the efficacy results are encouraging, further assessment including dose optimization is needed. The current trial is a unique early phase trial whose results show promise and support future development of MPCs for biologic-refractory RA patients, a subset of the RA population with substantial remaining medical need.

Disclosure: S. Kafaja, None; D. Skerrett, mesoblast inc, 3; S. Itescu, mesoblast inc, 3; D. E. Furst, Grant/Research Support: Amgen,BMS Novartis, Pfizer, Roche/Genentech,Corbus. Consultant:AbbVie, Amgen,
Non-Randomized Controlled Trial to Evaluate the Effect of Extracorporeal Shock Wave Therapy on Digital Ulcers in Systemic Sclerosis

Tonomori Ishii1, Yasushi Kawaguchi2, Osamu Ishikawa3, Naruhiko Takasaawa4, Takao Kodera5, Hidekata Yasuoka6, Yuichi Takahashi7, Osamu Takai8, Izaya Nakaya9, Hiroshi Fujii10, Yukiko Kamogawa10, Yuko Shirota10, Tsuyoshi Shirai10, Yoko Fujita11, Shinichiro Saito12, Hiroaki Shimokawa13 and Hideo Harigae10

1Clinical Research, Innovation and Education Center, Tohoku University Hospital, Sendai, Japan, 2Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan, 3Department of Dermatology, Gunma University Graduate School of Medicine, Gunma, Japan, 4Department of Internal Medicine, Tohoku Medical and Pharmaceutical University Wakabayashi Hospital, Sendai, Japan, 5Division of Hematology and Rheumatology, Tohoku Medical and Pharmaceutical University, Sendai, Japan, 6Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, 7Yufamilly Clinic, Sendai, Japan, 8Osaki Citizen Hospital, Sendai, Japan, 9Department of Nephrology and Rheumatology, Iwate Prefectural Central Hospital, Morioka, Japan, 10Department of Hematology and Rheumatology, Tohoku University Graduate School of Medicine, Sendai, Japan, 11Department of Hematology and Rheumatology, Tohoku University Graduate School of Medicine, Sendai, Japan, 12IMS Meirikai Sendai General Hospital, Sendai, Japan, 13Department of Cardiovascular Medicine, Tohoku University Graduate School of Medicine, Sendai, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Patients with systemic sclerosis (SSc) often display Raynaud’s phenomenon, which causes digital skin ulcers. Since these ulcers are not associated with autoimmune factors, conventional immunosuppressive therapies, vasodilators, and anticoagulants are often ineffective. Extracorporeal shock wave therapy (ESWT) at low energy is shown to be effective in stimulating numerous growth factors endogenously, inducing angiogenesis and healing of injuries and wounds. This study evaluated ESWT for treatment of refractory skin ulcers caused by SSc and assessed its efficacy and safety.

Methods: We enrolled 60 patients with SSc and refractory digital ulcers with no response to intravenous prostaglandin E1 therapy at least 4 weeks. Of these, 30 were treated with ESWT and 30 received conventional treatment. Patients in the conventional treatment group were permitted to use any currently available therapies. Patients in the ESWT group continued pre-study treatments.
Results: The mean decrease in the number of ulcers at 8 weeks was 4.47 in the ESWT group and 0.83 in the conventional treatment group and the difference was significant (p<0.0001). The proportion of subjects whose total number of ulcers decreased by 70% or more at 8 weeks was 26.7% in the conventional treatment group and 70.0% in the ESWT group and this was also significant (p<0.0008). The average number of new ulcers in the 8 weeks after the start of treatment was 1.57 in the conventional group and 0.23 in the ESWT group. No serious adverse events associated with ESWT were reported during the study period.

Conclusion: After 8 weeks, ESWT demonstrated clinically meaningful improvement in SSc patients with refractory digital ulcers. This treatment is well-tolerated and minimally invasive, can be repeated without adverse effects, and requires no anesthesia. Overall, the results of our study suggest that ESWT is a novel and efficacious treatment that can be added to pharmacologic therapy.

Disclosure: T. Ishii, Chugai, Ono, Pfizer, Mitsubishi-Tanabe, Astellas, 8; Y. Kawaguchi, None; O. ishikawa, None; N. takasaawa, None; T. kodera, None; H. yasuoka, None; Y. takahashi, None; O. takai, None; I. Nakaya, None; H. Fujii, None; Y. Kamogawa, None; Y. shirotia, None; T. Shirai, None; Y. Fujita, None; S. saito, None; H. Shimokawa, None; H. Harigae, None.


Abstract Number: 1705

Inhibition of EZH2 Stops Fibrosis and Improves Angiogenesis in Scleroderma

Pei-Suen Tsou¹, Phillip L. Campbell², M. Asif Amin³, Patrick Coit¹, David Fox⁴, Dinesh Khanna⁵ and Amr H Sawalha¹, ¹Division of Rheumatology, University of Michigan, Ann Arbor, MI, ²Rheumatology, Division of Rheumatology, University of Michigan Medical Center, Ann Arbor, MI, ³Division of Rheumatology and Clinical Autoimmune Center of Excellence, University of Michigan, Ann Arbor, MI, ⁴Department of Medicine [Division of Rheumatology], University of Michigan Medical System, Ann Arbor, MI, ⁵University of Michigan, Ann Arbor, MI

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Scleroderma (SSc) is a complex disease that involves activation of the immune system, vascular complications, and tissue fibrosis. Although the pathogenesis of this disease is largely unknown, epigenetic dysregulation has been implicated. In this study, we focused on the histone methyltransferase enhancer of zest homolog 2 (EZH2), which is the catalytic component of the polycomb represser complex 2 and mediates trimethylation of lysine 27 of histone 3 (H3K27me3). It has been reported that EZH2 regulates angiogenesis, and it is also involved in fibrosis. We hypothesize that EZH2 contributes to impaired angiogenesis and enhanced fibrosis in SSc, and inhibition of EZH2 improves these key events in SSc.
**Methods:** Dermal endothelial cells (ECs) and fibroblasts were isolated from biopsies from healthy subjects or patients with diffuse cutaneous SSc. EZH2 was overexpressed using an EZH2 vector. Inhibition of EZH2 was achieved by using EZH2 inhibitor DZNep or EZH2 siRNA. Angiogenesis was assessed by an *in vitro* Matrigel tube formation assay. The scratch wound assay was used to evaluate fibroblast migration. The effect of DZNep (50mg/kg/day for 14 days) *in vivo* was assessed in a bleomycin-induced skin fibrosis model. A t-test was used to compare differences between groups, and a p-value of <0.05 was considered significant. Genome-wide DNA methylation was evaluated using the Illumina Infinium Methylation EPIC BeadChip Array.

**Results:** EZH2 and H3K27me3 were significantly elevated in SSc ECs and fibroblasts compared to healthy controls. Overexpression of EZH2 in normal ECs led to significant decrease in tube formation, while decrease in EZH2 in SSc ECs, achieved by siRNA or DZNep treatment, restored normal angiogenesis. In SSc fibroblasts, DZNep treatment dose-dependently reduced EZH2, as well as pro-fibrotic COL1A1, TGFBI, and FRA2. In addition, DZNep significantly reduced pro-angiogenic genes VEGF and FGF2, as well as genes involved in DNA methylation, including DNMT1, DNMT3A, and MECP2. EZH2 inhibition in SSc fibroblasts also led to genome-wide changes in the methylene, and the expression of differentially methylated genes was confirmed by qPCR, including anti-fibrotic IL7 and migration-involved LRRC16A, both hypermethylated and downregulated. In the scratch wound assay, DZNep-treated SSc fibroblasts showed wider wound width at 48 hours post-injury compared to untreated SSc fibroblasts. The gene expression profiles and scratch wound results were further confirmed in EZH2-overexpressing normal fibroblasts, as these cells showed a pro-fibrotic phenotype, mimicking what was seen in SSc fibroblasts. In a bleomycin prevention model, DZNep successfully prevented significant skin fibrosis to occur, assessed by both skin thickness and hydroxyproline analysis.

**Conclusion:** EZH2 is overexpressed in SSc ECs and fibroblasts, and this overexpression is profibrotic and results in impaired angiogenesis in this disease. Inhibition of EZH2 restored normal angiogenesis in SSc ECs, and normalized the pro-fibrotic phenotype in SSc fibroblasts as well as in an animal model. Targeting EZH2 or EZH2-regulated genes may open new therapeutic avenues for patients with SSc.

**Disclosure: P. S. Tsou, None; P. L. Campbell, None; M. A. Amin, None; P. Coit, None; D. Fox, None; D. Khanna, Actelion, Bayer, BoehringerIngelheim, Chemomab, Corbus, Covis, Cytori,Eicos, EMD Serono, Genentech/Roche, Gilead, GSK, Sanofi-Aventis, UCB Pharma, 5,NIH/NIAMS, NIH/NIAID,Bayer, BMS, Genentech/Roche, Pfizer, 2,Eicos, 4; A. H. Sawalha, None.


**Abstract Number:** 1706

**Dipeptidyl-Peptidase-4 (DPP4) Promotes Fibroblast Activation and Is a Potential Molecular Target for Treatment of Fibrosis**

**Alina Soare**¹, Hermina Györfy¹, Alexandru Matei¹, Clara Dees¹, Chih-Wei Chen¹, Andreas Ramming², Georg Schett³ and Jörg Distler¹,

¹Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Erlangen, Germany, ²Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Erlangen, Germany, ³Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, Erlangen, Germany.

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017
**Background/Purpose:**

Dipeptidyl-peptidase-4 (DPP4) has been reported to identify a dermal fibroblast lineage involved in scarring and its inhibition leads to reduced scar formation. Its role in tissue fibrosis, however, is unknown. The aim of the study was to characterize DPP4 positive cells and their mechanism of action and to evaluate the antifibrotic effect of DPP4 inhibition in different preclinical models of systemic sclerosis (SSc).

**Methods:** Expression of DPP4 in human and murine skin was analyzed by immunofluorescence and Western blot. Mouse fibroblasts were isolated and DPP4 positive cells properties were assessed. Two DPP4 inhibitors were tested in two concentrations administered oral in bleomycin-induced skin fibrosis and in sclerodematous chronic graft-versus-host disease (scl-cGvHD) model. Pulmonary and dermal fibrosis was induced by bleomycin in DPP4 knockout (KO) mice and wildtype littermates. The antifibrotic effects were assessed by hydroxyproline assay, quantification of myofibroblasts and analyses of the dermal thickness. Fibrosis of the lungs was additionally evaluated by computer tomography scans (CT). Inflammatory infiltrates were assessed by CD45 staining.

**Results:** DPP4 positive fibroblasts were increased in fibrotic skin of SSc patients and also in murine models of fibrosis. DPP4 expression is induced by TGF-β in an Erk-dependent manner. DPP4-expressing fibroblasts were activated and strongly expressed alpha smooth muscle actin (SMA) and stress fibers after TGF-β stimulation. These cells also released increased amounts of collagen. Furthermore, DPP4-positive fibroblasts showed a higher proliferation rate and an increased migratory capacity. Pharmacological inhibition of DPP4 reduced the release of collagen and the expression of myofibroblast markers. DPP4-KO mice are less sensitive to bleomycin-induced pulmonary fibrosis as shown by milder changes on CT, reduced Ashcroft scores and reduced hydroxyproline content. DPP4-KO mice also show reduced skin fibrosis upon bleomycin challenge. Moreover, treatment with DPP4 inhibitors in pharmacologically relevant and well tolerated doses demonstrated potent antifibrotic effects in bleomycin-induced skin fibrosis and experimental scl-cGvHD mouse model with reduced dermal thickening, decreased collagen deposition and reduced myofibroblast counts. Treatment with DPP4 inhibitors also reduced leukocyte infiltrations into the skin. No anti-fibrotic effects of DPP4 inhibition were observed in DPP4-KO mice, confirming that the antifibrotic effects of DPP4 inhibitors are not mediated by off-target effects. Mechanistically, inhibition of DPP4 selectively interferes with the TGF-β induced activation of ERK signaling, but does not inhibit TGF-β induced SMAD signaling, or other non-canonical TGF-β pathways involving Fra2, c-Jun, p38, Akt or STAT3.

**Conclusion:** DPP4 characterizes an activated subpopulation of fibroblasts in SSc. However, DPP4 does not only serve as an activation marker, but is also functionally required for fibroblast activation and tissue fibrosis. These results may have direct translational implications as DPP4 inhibitors are already in clinical use for diabetes.

**Disclosure:** A. Soare, None; H. Györfy, None; A. Matei, None; C. Dees, None; C. W. Chen, None; A. Ramming, None; G. Schett, None; J. Distler, 4D Science, 1,Anamar Medical, Active Biotech, Array Biopma, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, GSK, Novartis, Sanofi-Aventis, UCB, 2,Actelion Pharmaceuticals US, Active Biotech, Anamar, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi, UCB, 5.

**View Abstract and Citation Information Online** - [http://acrabstracts.org/abstract/dipeptidyl-peptidase-4-dpp4-promotes-fibroblast-activation-and-is-a-potential-molecular-target-for-treatment-of-fibrosis](http://acrabstracts.org/abstract/dipeptidyl-peptidase-4-dpp4-promotes-fibroblast-activation-and-is-a-potential-molecular-target-for-treatment-of-fibrosis)
Effect of Anabasum (JBT-101) on Gene Expression in Skin Biopsies from Subjects with Diffuse Cutaneous Systemic Sclerosis (dcSSc) and the Relationship of Baseline Molecular Subsets to Clinical Benefit in the Phase 2 Trial

Viktor Martyanov1, Yolanda Nesbeth2, Guoshuai Cai1, Tammara A. Wood1, Jake Reder2, Scott Constantine3, Barbara White3, Robert F. Spiera4 and Michael L. Whitfield1, 1Department of Molecular and Systems Biology, Geisel School of Medicine at Dartmouth, Hanover, NH, 2Celdara Medical, LLC, Lebanon, NH, 3Corbus Pharmaceuticals, Inc., Norwood, MA, 4Rheumatology, Hospital for Special Surgery, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Anabasum (JBT-101) is a non-immunosuppressive, synthetic, CB2 agonist that resolves inflammation and fibrosis in animal models of SSc and reduces TGF-β and collagen production by dcSSc fibroblasts. It showed evidence of clinical benefit in dcSSc in the Phase 2 trial JBT101-SSc-001 (NCT02465437). To provide additional data on the impact of anabasum on SSC, gene expression was analyzed in skin biopsies from trial subjects.

Methods:
Gene expression data at baseline and end of treatment (Day 85) were used for differential gene expression, pathway enrichment and intrinsic subset assignment, comparing paired skin biopsies from anabasum-treated (N=23) and placebo-treated (N=13) subjects. Overall response was an ACR Composite Response Index in dcSSc (CRISS) score of ≥ 0.2 and skin response was a decrease in modified Rodnan Skin Score (mRSS) ≥ 5 points.

Results:
1937 genes were differentially expressed in anabasum arm (False Discovery Rate ≤ 5%) from baseline to Day 85. Genes downregulated from baseline at Day 85 were enriched in inflammatory response, extracellular matrix (ECM) organization, collagen metabolism, response to cytokine and angiogenesis (Bonferroni-corrected p ≤ 0.05). Genes upregulated from baseline at Day 85 were involved in lipid metabolism. These changes were not observed in the placebo arm.

Most CRISS (83%) and all mRSS improvers in the placebo arm were assigned to normal-like intrinsic gene expression subset whereas in the anabasum arm most CRISS (75%) and mRSS (79%) improvers were classified as inflammatory or fibroproliferative (Figure 1C and 1D). Scleroderma Disease Severity Score (SDSS), a gene expression-based mRSS surrogate, decreased at Day 85 in anabasum-treated (Figure 1E, p = 0.0029) but not placebo-treated subjects (Figure 1F, p = 0.9576).
Conclusion:

Anabasum induced clinically relevant molecular responses by modulating inflammatory and fibrotic genes and pathways consistent with the resolution of innate immune signaling. Changes in gene expression in the skin of anabasum-treated subjects were accompanied by improvement in CRISS, mRSS and SDSS. Majority of anabasum improvers had increased baseline inflammatory or fibroproliferative gene expression in skin whereas placebo improvers nearly all had increased normal-like gene expression at baseline. This suggests that the normal-like subset identifies subjects that are more likely to improve spontaneously. This report supports further clinical testing of efficacy of anabasum in dcSSc.

Figure 1. Effect of anabasum (JBT-101) on gene expression in dcSSc. Changes in inflammatory response pathway in anabasum (A) and placebo (B) arms. Clinical improvers by treatment arm and intrinsic gene expression subset as defined by mRSS (C) and CRISS (D). Changes in SDSS (quantitative surrogate of mRSS) in anabasum (E) and placebo (F) arm. For panels A/B and E/F, p-values are for paired t-test. For panels C and D, p-values are for Fisher’s exact test.

Disclosure: V. Martyanov, None; Y. Nesbeth, Celdara Medical, LLC, 3; G. Cai, None; T. A. Wood, Celdara Medical, LLC, 5; J. Reder, Celdara Medical, LLC, 1,Celdara Medical, LLC, 3,Celdara Medical, LLC, 4,Celdara Medical, LLC, 6; S. Constantine, Corbus Pharmaceuticals, Inc., 1,Corbus Pharmaceuticals, Inc., 3; B. White, Corbus Pharmaceuticals, 1,Corbus Pharmaceuticals, 3; R. F. Spiera, Roche-Genetech, 2,GSK, 2,BMS, 2,Celgene, 2,Boehringer Ingelheim, 2,Cytori, 2,Chemocentryx, 2,Corbus Pharmaceuticals, 2,Prism, 2,Roche-Genetech, 5,GSK, 5,Boehringer Ingelheim, 5; M. L. Whitfield, Corbus, UCB, glaxosmithkline, 5,Celdara medical llc, 9.

Molecular Imaging Biomarkers for Personalized Medicine Strategies in Systemic Sclerosis-Related Interstitial Lung Disease

Janine Schniering¹, Martina Benesova²,³, Matthias Brunner⁴, Carol A. Feghali-Bostwick⁵, Roger Schibli²,³, Oliver Distler⁶, Cristina Müller²,³ and Britta Maurer⁶, ¹Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, Switzerland, Zurich, Switzerland, ²Department of Chemistry and Applied Biosciences, Department of Chemistry and Applied Biosciences, Swiss Federal Institute of Technology, Zurich, Switzerland, Zurich, Switzerland, ³Center for Radiopharmaceutical Sciences ETH-PSI-USZ, Center for Radiopharmaceutical Sciences ETH-PSI-USZ, Paul Scherrer Institute, Villigen-PSI, Switzerland, Villigen PSI, Switzerland, ⁴Department of Rheumatology, Center of Experimental Rheumatology, University Hospital Zurich, Zurich, Switzerland, Zurich, Switzerland, ⁵Division of Rheumatology and Immunology, Division of Rheumatology and Immunology, Medical University of South Carolina, Charleston, SC, United States, Charleston, SC, ⁶Department of Rheumatology, Center of Experimental Rheumatology, University Hospital Zurich, Zurich, Switzerland

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Interstitial lung disease (ILD) is a life-threatening complication in SSc. In recent years, distinct genomic and molecular subtypes in SSc-ILD were identified and molecular targeted therapies are now within reach. However, personalized medicine approaches are still lacking since clinical tools for individualized patient stratification are not yet available. Here, we aimed to assess nuclear imaging of key molecular markers of inflammation and/or fibrosis as novel biomarkers for the stage-dependent assessment of ILD in the murine model of bleomycin (BLM)-induced lung fibrosis.

Methods:
The expression of folate receptor β (FR-β), integrin αvβ3 and somatostatin receptor 2 (SSTR2) were analyzed in lung biopsies from patients with idiopathic pulmonary fibrosis (IPF), SSc-ILD, and healthy subjects as well as from BLM-treated mice and saline-treated controls using immunohistochemistry and RT-PCR (n=4-11). Single Photon Emission Computed Tomography (SPECT) and Positron Emission Tomography (PET) were performed at days 3, 7, and 14 after BLM instillation using the integrin αvβ3-specific ¹⁷⁷Lu-c(RGDfK)-ligand, the FR-β-specific ¹⁸F-Azafol and the SSTR2-specific ¹⁷⁷Lu-DOTA-NOC. Additionally, ¹⁸F-FDG-PET and pulmonary CT scans were performed. The specific lung uptake of the radiotracers over time was assessed by ex vivo SPECT or PET/CT scans and quantified by biodistribution studies (n=3-9).

Results:
Expression of integrin αvβ3, FR-β and SSTR2 was significantly elevated in lung tissues from patients with SSc-ILD and IPF at the mRNA or protein level (p<0.05). Similarly, FR-β expression increased time-dependently in lungs of BLM-treated mice, but not of controls at the gene and protein level with highest expression at days 3 or 7, the
inflammatory stages of BLM-induced lung fibrosis (p<0.01). In contrast, expression of integrin αvβ3 and SSTR2 was most strongly upregulated at days 7 and 14 at the protein, but not at the mRNA level in BLM-treated mice, and thus in the inflammatory and in the fibrotic stages (p<0.01). 18F-FDG-PET and lung CT scans detected changes of glucose metabolism and ILD morphology in BLM-treated mice. However, compared with these routinely employed, yet unspecific imaging techniques, molecular targeted imaging of integrin αvβ3, FR-β and SSTR2 specifically detected ILD and discriminated lung inflammation and/or fibrosis in correspondence with the changes at the tissue level. The specific lung uptake of 177Lu-c(RGDfK)-ligand, 18F-Azafol, and 177Lu-DOTA-NOC as compared to the unspecific uptake of 18F-FDG in diseased lungs over time was shown by biodistribution studies and ex vivo lung scans.

Conclusion:

Our data suggest that stage-dependent visualization of ILD with radiotracers that target key markers of lung inflammation and/or fibrosis shows promise for clinical application. As opposed to unselective imaging techniques such as 18F-FDG-PET and lung CT scans, the introduction of specific nuclear imaging biomarkers for individualized management of SSc-ILD patients could represent the first step towards precision medicine in SSc-ILD.

Disclosure: J. Schniering, None; M. Benesova, None; M. Brunner, None; C. A. Feghali-Bostwick, None; R. Schibli, Merck & Cie, 2; O. Distler, Actelion, Bayer, BiogenIdec, Boehringer Ingelheim, ChemomAb, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmacycials, Novartis, Pfizer, Sanofi, Sinoa and UCB, 2,Actelion, Bayer, BiogenIdec, Boehringer Ingelheim, ChemomAb, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmacycials, Novartis, Pfizer, Sanofi, Sinoa and UCB, 5,mir-29 for the treatment of systemic sclerosis, 9; C. Müller, Merck & Cie, 2; B. Maurer, AbbVie, Protagen, EMDO, Novartis, German SSce Society, 2,Pfizer, Roche, Actelion, MSD, 9,mir-29 for the treatment of systemic sclerosis, 9.


Abstract Number: 1709

**Classical Monocytes in the Pathogenesis of Early Diffuse Cutaneous Systemic Sclerosis**

**Julia Dunn**¹, Salina Dominguez¹, Philip J. Homan¹, Carla Cuda¹, Dinesh Khanna², Shervin Assassi³, Tracy M. Frech⁴, Harris Perlman⁵, Deborah R. WInter¹ and Monique Hinchcliff⁶, ¹Department of Medicine Division of Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL, ²University of Michigan, Ann Arbor, MI, ³University of Texas McGovern Medical School, Houston, TX, ⁴Division of Rheumatology, University of Utah, Salt Lake City, UT, ⁵Department of Medicine, Division of Rheumatology, Northwestern University Feinberg School of Medicine, Northwestern University Feinberg School of Medicine,, Chicago, IL, ⁶Northwestern University Institute for Public Health and Medicine, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017

Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster II
Background/Purpose: In light of heterogeneous clinical manifestations in systemic sclerosis (SSc), transcriptional analysis of fibrotic tissue and circulating leukocytes may illuminate conserved processes driving inflammation and fibrosis. Prior studies of sorted circulating monocytes and lymphocytes from patients with SSc revealed an interferon gene expression signature. We hypothesized that classical monocytes play an important role in SSc pathogenesis and are responsible for the observed interferon signature in SSc.

Methods: Whole blood was obtained from patients enrolled in the Prospective Registry of Early Systemic Sclerosis (PRESS) study, and from age-, sex-, and race-matched healthy controls. The PRESS cohort includes patients with early (< 2 years’ duration since first non-Raynaud symptom attributed to SSc) diffuse cutaneous SSc (swollen hands or sclerodactyly PLUS ≥1 of the following: anti-topoisomerase I or anti-RNA polymerase III serum autoantibodies; proximal skin involvement; tendon friction rubs) who are recruited at participating US scleroderma centers. RNA was isolated from classical monocytes obtained by fluorescence-activated cell sorting and subjected to RNA-seq using Illumina NextSeq 500.

Results: We identified approximately 6500 genes that were differentially expressed in two or more patients (Z score > 2) compared to healthy controls –this ensured inclusion of genes that are dysregulated only in a subset of the patient population. Hierarchal clustering of patients based on expression of these 6500 genes revealed three prospective disease subtypes, each with a distinct profile of disease-regulated genes. No significant clinical variables were attributable to any subtype, although there is a trend toward increased mRSS in the third subtype (S3). Subtypes one (S1) and two (S2) were both enriched for genes involved in chemotaxis/motility and regulated cell death; however, S1 was also associated with inflammation and cytokine production while S2 linked to TGFβ signaling and extracellular matrix remodeling. Genes upregulated in S3 were involved in myeloid activation. Furthermore, 19 previously reported interferon-related genes were significantly (p<0.05) upregulated in the patient cohort compared to controls. By examining interferon-related gene expression in the three subtypes, we observe subtype-specific upregulation in S1 (e.g. TIMP2), S1 and S2 (TIMP1 and OASL), S2 and S3 (IRF7), or S3 (OAS1).

Conclusion: We observed that transcriptional profiling of classical monocytes reveals patient subtypes with distinct disease-regulated genes. Interferon-related genes, which are upregulated globally in monocytes from SSc patients, are also upregulated in specific disease subtypes. These insights provide us with a framework through which to interrogate the transcriptional profile of sorted macrophages from skin biopsies and other fibrotic tissues, which will ultimately improve our understanding of systemic inflammation and end-organ fibrosis in SSc.

Disclosure: J. Dunn, None; S. Dominguez, None; P. J. Homan, None; C. Cuda, None; D. Khanna, Actelion, Bayer, BoehringerIngelheim, Chemomab, Corbus, Covis, Cytori,Eicos, EMD Serono, Genentech/Roche, Gilead, GSK, Sanofi-Aventis,UCB Pharma, 5,NIH/NIAMS, NIH/NIAID,Bayer, BMS, Genentech/Roche, Pfizer, 2,Eicos, 4; S. Assassi, None; T. M. Frech, None; H. Perlman, None; D. R. Winter, None; M. Hinchcliff, None.
Yongqing Wang1, Shadia Nada2, Nezam Altorok2 and Bashar Kahaleh2, 1University of Toledo, Toledo, OH, 2Medicine/Rheumatology, University of Toledo, Toledo, OH

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

The accumulation of myofibroblasts in fibrotic tissue plays an important role in the pathogenesis of scleroderma (SSc) fibrosis. Recent studies have shown that myofibroblasts can originate from endothelial cells through Endo-MT. TGFβ is involved in the generation of tissue fibrosis through multiple pathways including Endo-MT. MicroRNA-126 (miR-126) is expressed mainly in microvascular endothelial cells (MVECs), and has been shown to inhibit TGFβ induced FoxO3/Smad 4 signaling by direct repression of phosphoinositol-3 kinase regulatory subunit 2 (PIK3R2), a negative regulator of the PIK3/Akt signaling pathway. In this study we investigated the expression levels of miR-126 and TGFβ Endo-MT responses in SSc and control MVECs.

Methods:

MVECs were isolated from involved SSc skin and matched healthy subjects. The expression of miR-126 was detected by qPCR and in situ hybridization followed by quantitative densitometry analysis. Endo-MT was induced by TGFβ1 (10ng/ml) for 48 hours and assessed by expression levels of Mesenchymal Mark genes which include CNN1(Sm-Calp), Collagen type1 (COL1), fibronectin (FN), NOTCH3 and vimentin (VIM) using qPCR. The expression levels of PIK3R2 were examined by qPCR and western analysis. The expression of miR-126 was inhibited in control-MVECs by transfecting cells with hsa-miR-126 inhibitor and enhanced in SSc-MVECs by transfecting cells with hsa-miR-126 Mimic.

Results:

miR-126 expression levels in SSc-MVECs and skin biopsies were significantly down regulated by over 10 fold in SSc-MVECs and 2.32 fold in SSc skin when compared to control. Co-localization of miR-126 and endothelial specific marker CD31 were also observed in skin biopsies. The base line expression of mesenchymal marker genes was similar in SSc and control-MVECs. Addition of TGFβ to control MVECs resulted in increased mRNA expression levels of FN (1.75 folds ± 0.12), COL1 (2.11 folds±0.16), SM-calponin (1.65 folds ±0.10). Whereas an enhanced responses to TGFβ were seen in SSc-MVECs with 3.52 fold ± 0.32 for FN, 4.63 fold ± 0.50 for COL1 and 8.66 fold ± 0.68 for Sm-Calp. Control-MVECs transfected with miR-126 inhibitor repressed miR-126 expression levels by 78% for up to 96 hours as measured by qPCR. This was associated with significant upregulation of miRNA and protein expression levels of PIK3R2 and enhanced TGFβ-induced COL1, FN and Sm-Calp mRNA expression levels. Whereas overexpression of miR-126 by hsa-miR-126 Mimic transfection to SSc-MVECs resulted in upregulation of miR-126 expression levels and reduced expression of PIK3R2, it also resulted in significantly decreased TGFβ1-induced COL1, FN and Sm-Calp mRNA expression.

Conclusion:

The data demonstrate that miR-126 is a crucial regulator of TGFβ- induced Endo-MT. Down-regulation of microRNA-126 in SSc-MVECs enhances Endo-MT induced by TGFβ by directly targeting PIK3R2. Inhibition of miR-126 in control-MVECs resulted in increased Endo-MT responses to TGFβ, whereas forced expression of miR-126 in SSc-MVECs reduced TGFβ-Endo-MT responses. Upregulation of MiR-126 expression may be an effective therapeutic strategy in SSc and other fibrosis diseases in which Endo-MT plays a pathogenetic role.
Disclosure: Y. Wang, None; S. Nada, None; N. Altorok, None; B. Kahaleh, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/down-regulation-of-microrna-126-in-scleroderma-microvascular-endothelial-cells-enhances-the-transition-of-endothelial-to-mesenchymal-cells-endo-mt-induced-by-tgf%ce%b2-through-down-regulating-pi3ak

Abstract Number: 1711

SIRT1 May Protect Against Systemic Sclerosis-Related Pulmonary Fibrosis By Decreasing Pro-Inflammatory and Pro-Fibrotic Processes

Haiyan Chu1, Shuai Jiang2, Qingmei Liu3, Feng Qian4, Xiaodong Zhou5, Maureen D. Mayes6, Li Jin7 and Jiucun Wang8, 1MOE Key Laboratory of Contemporary Anthropology, State Key Laboratory of Genetic Engineering and Ministry of Education Key Laboratory of Contemporary Anthropology, Collaborative Innovation Center for Genetics and Development, School of Life Sciences, Fudan University, Shanghai, China, 2State Key Laboratory of Genetic Engineering and Ministry of Education Key Laboratory of Contemporary Anthropology, Collaborative Innovation Center for Genetics and Development, School of Life Sciences, Fudan University, Shanghai, China, 3State Key Laboratory of Genetic Engineering and Ministry of Education Key Laboratory of Contemporary Anthropology, Collaborative Innovation Center for Genetics and Development, School of Life Sciences, Fudan University, Shanghai, Chile, 4Ministry of Education Key Laboratory of Contemporary Anthropology, School of Life Sciences, Fudan University, Shanghai, China, 5Internal Medicine-Rheumatology, University of Texas McGovern Medical School, Houston, TX, 6University of Texas McGovern Medical School, Houston, TX, 7State Key Laboratory of Genetic Engineering, Collaborative Innovation Center for Genetics and Development, School of Life Sciences, Fudan University, Shanghai, China, 8State Key Laboratory of Genetic Engineering, Collaborative Innovation Center for Genetics and Development, School of Life Sciences, Fudan University, Shanghai, CN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Interstitial lung disease (ILD) is the leading cause of death in systemic sclerosis (SSc). Sirtuin1 (SIRT1) is a deacetylase with known anti-inflammatory and anti-fibrotic activity; the role of SIRT1 in SSc-ILD is unclear.

Methods:
Total RNA was extracted from peripheral blood mononuclear cells (PBMCs) isolated from SSc patients (n=86). In in vivo studies, mice were administered intratracheal bleomycin (BLM) (2.5 U/kg) to induce pulmonary fibrosis. Resveratrol (Res, 25 mg/kg) was fed daily from the third day before BLM instillation for the Prevention Study or 10 days post-BLM for the Treatment Study. Histological analysis was performed to assess lung inflammation/fibrosis. Immunofluorescence staining was used to identify the cell type expressing SIRT1. For in vitro studies, human lung fibroblasts were treated with TNF-aerfa (10 ng/ml)/TGF-beita (10 ng/ml) with or without SIRT1 activator (Res, 50 uM)/plasmid or inhibitor (Nicotinamide, 20 mM) /siRNA. Real-time PCR or Western blotting was used to measure mRNA or protein level (including SIRT1, P65 acetylation, Smad3 and mTOR phosphorylation).
Results:

The expression of SIRT1 in PBMCs of SSc patients with ILD (n=59) was significantly lower than that in SSc patients without ILD (n=27) (0.77±0.04 vs. 1.16±0.13, Fig.1A). Further analysis found the decreased expression of SIRT1 was correlated with dcSSc and the presence of ATA. In the in vivo studies, SIRT1 activation with Res reduced lung inflammation and fibrosis when it was administered either as prevention or as therapy, as evidenced by histological analysis (Fig.1B), decreased inflammatory gene expression and cytokine production as well as collagen production (mRNA level: Col1α1 reduced 72.5%, Col1α2 reduced 76.7% and Col3α1 reduced 72.3%; collagen content reduced 39.8%. Fig.1C-D). SIRT1 was expressed in aera-SMA+ myofibroblasts in mouse lung tissue, indicating an inhibitory effect of SIRT1 on myofibroblasts (Fig.1F). Moreover, SIRT1 activation or overexpression inhibited TNF-aera-induced inflammatory responses in vitro while depletion of SIRT1 in fibroblasts enhanced inflammation; and these effects were related to the decrease or increase in the acetylation of NF-kappaB, respectively (Fig.1G). These results were consistent with data of our in vivo experiments that Res treatment increased SIRT1 expression level and activity and blunted NF-kappaB signaling (Fig.1E). In addition, SIRT1 activation or exogenous overexpression inhibited collagen production in vitro (Fig.1H) via inactivation of TGF-beta/Smad3 and mTOR signaling.

Conclusion:

SIRT1 loss contributed to BLM induced pulmonary fibrosis and may play a role in SSc-ILD, while SIRT1 activation was effective for both the early (inflammatory) and late (fibrotic) stages of BLM induced fibrosis. Thus, SIRT1 could be a promising therapeutic target in the treatment of SSc-ILD.
Disclosure: H. Chu, None; S. Jiang, None; Q. Liu, None; F. Qian, None; X. Zhou, None; M. D. Mayes, None; L. Jin, None; J. Wang, None.


Abstract Number: 1712

Microbial and Metabolic MULTI-Omic Correlations in Systemic Sclerosis Patients

Chiara Bellocci¹, Alvaro Fernández-Ochoa², Gaia Montanelli¹, Barbara Vigone³, Alessandro Santaniello³, Christian Milani⁴, Rosa Quirantes-Piné², Isabel Borras Linares², Marco Ventura⁴, Antonio Segura Carretero², Marta Alarcón-Riquelme⁵,⁶ and Lorenzo Beretta³, ¹Scleroderma Unit, Referral Center for Systemic Autoimmune Diseases, Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico di Milano, Milano, Italy, ²Department of Analytical Chemistry, University of Granada, Granada, Spain, ³Scleroderma Unit, Referral Center for Systemic Autoimmune Diseases, Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico di Milano, Milano, Italy, ⁴Department of Life Sciences, Università degli studi di Parma, Parma, Italy, ⁵Centro de Genómica e Investigación Oncológica (GENYO), Pfizer-Universidad de Granada-Junta de Andalucía, Granada, Spain, ⁶Institute for Environmental Medicine, Karolinska Institutet, Stockholm, Sweden

First publication: September 18, 2017

SESSION INFORMATION
Background/Purpose:

The gastro-intestinal tract (GIT) is frequently involved in Systemic sclerosis (SSc). Perturbation in the gut microbiota may affect the body well-being and function and intestinal disbiosis has been associated with a number of autoimmune diseases, including SSc. To date no attempt has been made to characterize the functional consequences of intestinal disbiosis in SSc and autoimmunity.

Methods:

A total of 59 SSc patients and 28 healthy controls (HCs) were included. Intestinal microbiota was studied via 16s-RNA sequencing on stool samples; in parallel, plasma metabolites were analyzed by high-performance liquid chromatography coupled to electrospray ionisation and quadrupole time-of-flight mass spectrometry (HPLC-MS-ESI-QTOF). Interaction models capable of explaining the disease were built via data mining algorithms with internal validation (20 x 10-fold cross-validation) and feature selection. Microbic and metabolic results were correlated by means of Spearman’s rho and results corrected via 100K-fold permutation testing. The severity of intestinal symptoms was assessed via the UCLA GIT questionnaire.

Results:

random forest model showed that HCs and SSc patients differ at the genus taxonomic rank (AUROC = 0.706 ± 0.023). Model reduction identified 9 genera relevant to the disease status (AUROC = 0.711 ± 0.042). A naïve Bayes algorithm found a unique metabolic pattern associated with SSc (AUROC = 0.707 ± 0.029) with just 17 relevant metabolites after feature selection (AUROC = 0.744 ± 0.029). Cross correlation between the 9 genera and the 17 metabolites (Figure, left panel) found significant interactions between desulfovibrio and alpha-N-Phenylacetyl-L-glutamine (rho = 0.389, p_c = 0.03) and 2,4-dinitrobenzenesulfonic acid (rho = 0.39, p_c = 0.029). Gut microbiota of SSc patients was capable of explaining 12.7 ± 4.1% of the variance of GIT scores. A model of 10 bacteria could jointly discriminate HCs and SSc patients with or without intestinal involvement (weighted AUROC = 0.679 ± 0.021). Among these bacteria, desulfovibrio was significantly associated with the presence of intestinal involvement (figure, right panel).

Conclusion:

SSc patients present unique microbial and metabolic fingertips. SSc-related disbiosis is characterized by an increase in pro-inflammatory microbial groups which compete with commensal bacteria. This microbiomic shift may promote the accumulation of metabolites, including a a sulfonate compound which has direct pro-inflammatory and immuno-modulating properties and that may serve as electron acceptor in anaerobic respiration of desulfovibrio strains. The toxic end-product of desulfovibrio respiratory metabolism (hydrogen sulfide) may contribute to intestinal damage and altered motility.

This work received support from the EU/EFPIA IMI Joint Undertaking PRECISESADS grant n° 115565.

www.precisesads.eu
Defining Genetic Risk for Scleroderma Renal Crisis in RNA-Polymerase III Antibody Positive Patients

Edward Stern¹, Sandra Guerra¹, Harry Chinque¹, David Gonzalez Serna², Markella Ponticos¹, Javier Martin², Maureen D. Mayes³, Shervin Assassi⁴, Carmen Fonseca¹ and Christopher Denton⁵, ¹UCL Centre for Rheumatology and Connective Tissue Diseases, London, United Kingdom, ²Instituto de Parasitología y Biomedicina López-Neyra, Granada, Spain, ³Internal Medicine/Rheumatology, University of Texas Health Science Center at Houston, Houston, TX, ⁴University of Texas McGovern Medical School, Houston, TX, ⁵Department of Rheumatology, University College London, Royal Free Hospital, London, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Scleroderma renal crisis (SRC), characterised by accelerated hypertension and acute kidney injury, is a life-threatening complication of systemic sclerosis (SSc). Most SSc cases have a disease-specific circulating antibody, including the anti Scl-70, anti-centromere and anti RNA polymerase III (ARA) antibodies. Previous studies confirm ARA as a powerful serological predictor of SRC, and cases of SRC more than 5 years after the diagnosis of SSc are rare. We developed an innovative approach to identify genetic susceptibility loci for SRC, comparing ARA positive patients with and without the occurrence of SRC.

Methods:
From a well-characterised SSc cohort (n=415), we selected 100 ARA+ patients with more than 5 years of follow-up data. 50 had a history of SRC and 50 had not developed SRC. All cases were of northern European ancestry. Cases were genotyped using the Illumina Human Omni-express chip. Quality control checks were performed in PLINK (Hardy-Weinberg equilibrium p <0.001; genotyping rate >90%). Based on the results of logistic regression analysis, ten SNPs were put forward for validation in a separate US cohort of 256 ARA+ patients (40 SRC+), using ThermoFisher TaqMan genotyping probes. Immunohistochemistry (IHC) was performed on SRC biopsy samples to identify proteins associated with our genes of interest.

Results:

After quality control checks, 641,489 SNPs were analysed in the first cohort. In logistic regression analysis of our initial cohort, the SNPs within genes and gene regions most strongly associated with SRC were for POU2F1 (p=4.12 x 10^-5), CTNND2 (p=2.92 x 10^-5), HECW2 (p=2.71 x 10^-5), GRIA3 (p=2.16 x 10^-5) and GPATCH2L (p=2.06 x 10^-5). The SNP within the GPATCH2L region was also significantly associated with SRC in our validation cohort (p=0.025). GPATCH2L polymorphisms have been associated with essential hypertension in previous GWAS analysis.

Polymorphisms in the CTNND2 gene have been demonstrated to be associated with pulmonary arterial hypertension, another vascular complication of SSc, in previous studies. We performed IHC for this protein on 8 renal biopsy samples from confirmed cases of SRC and 8 normal human kidney controls (see figure). Tubular epithelial staining was present in cases and controls. Glomerular staining was markedly increased in the SRC cases compared with controls, with 5 cases showing significant staining in this compartment compared with 0 controls (Fisher's Exact p=0.026).

Conclusion:

A novel autoantibody-based extreme phenotype method identifies risk alleles for SRC within a rare disease cohort. Using genetic and histological validation methods we identify CTNND2 and GPATCH2L as candidates for investigation of SRC aetiopathogenesis.

![Image of immunohistochemistry results]

Anti-CTNND2 antibody staining of renal biopsies: A. SRC B. Normal kidney control C. IgG control.

Disclosure: E. Stern, None; S. Guerra, None; H. Chique, None; D. Gonzalez Serna, None; M. Ponticos, None; J. Martin, None; M. D. Mayes, None; S. Assassi, None; C. Fonseca, None; C. Denton, Actelion, Pfizer,
Inhibition of Hedgehog A cyltransferase Alleviates the Profibrotic Effects of Transforming Growth Factor β in Systemic Sclerosis

Ruifang Liang1, Rosebeth Kagwiria2, Clara Dees3, Yun Zhang4, Oliver Distler5, Georg Schett6 and Jörg Distler7,

1 Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, Department of Internal Medicine 3 and Institute for Clinical Immunology, Friedrich-Alexander-University of Erlangen-Nuremberg and University Hospital Erlangen, Erlangen, Germany, 2 Department of Internal Medicine 3 and Institute for Clinical Immunology, Friedrich-Alexander-University of Erlangen-Nuremberg and University Hospital Erlangen, Erlangen, Germany, 3 Department of Internal Medicine 3 and Institute for Clinical Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Erlangen, Germany, 4 Department of Internal Medicine 3 and Institute for Clinical Immunology, Department of Internal Medicine 3 and Institute for Clinical Immunology, Friedrich-Alexander-University of Erlangen-Nuremberg and University Hospital Erlangen, Erlangen, Germany, 5 Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland, 6 Department of Internal Medicine 3 – Rheumatology and Immunology, Department of Internal Medicine 3 and Institute for Clinical Immunology, Friedrich-Alexander-University of Erlangen-Nuremberg and University Hospital Erlangen, Erlangen, Germany, 7 Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Erlangen, Germany

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Hedgehog acyltransferase (Hhat) catalyzes the attachment of the fatty acid palmitate onto Sonic Hedgehog (Shh), a modification essential for Shh signaling activity. Palmitoylation of Shh by Hhat is required for multimerization of Shh proteins to large signaling complexes, which is particularly required for exocrine Shh signaling. Hhat has been identified as a potential target for cancer therapy especially in malignancies characterized by Shh overexpression. Hedgehog signaling activates fibroblasts in vitro and in vivo and plays a prominent role in tissue fibrosis in Systemic sclerosis (SSc). The aim of this study was to evaluate the role of Hhat in the pathogenesis of SSc.

Methods: Expression of Hhat in human and murine skin was analyzed by immunohistochemistry and immunofluorescence. The effects of small interfering RNA (siRNA) induced knockdown of Hhat on TGFβ signaling were analyzed in cultured human fibroblasts in vitro and in the mouse models of bleomycin-induced skin fibrosis and DNA topoisomerase I (topo I) induced fibrosis in vivo. The anti-fibrotic effect on skin was assessed by hydroxyproline assay, alpha smooth muscle cells quantification and measuring the dermal thickness.
**Results:** Increased expression of Hhat was detected by immunohistochemistry in skin biopsies from SSc patients as compared to healthy volunteers, with a particularly strong expression in fibroblasts. The expression of Hhat was induced in fibroblasts *in vitro* and *in vivo* in a TGFβ-dependent manner. Stimulation with TGFβ increased the mRNA and protein levels of Hhat in cultured fibroblasts. Moreover, TGF-β receptor I (TBR)-induced dermal fibrosis upregulated Hhat expression, whereas treatment with a specific inhibitor of TβRI prevented the induction of Hhat in bleomycin-induced skin fibrosis. The TGFβ-induced upregulation of Hhat required Smad3 and knockdown of Smad3 prevented the stimulatory effects of TGFβ on Hhat expression. We also demonstrate that the TGFβ-dependent induction of Hhat is sufficient to promote hedgehog signaling with enhanced activity in reporter assays and increased transcription of hedgehog target genes such as *Ptch-1* and *Ptch-2*. Vice versa, inactivation of Hhat ameliorates the stimulatory effects of TGFβ on fibroblasts. Knockdown of Hhat by siRNA reduced collagen release and myofibroblast differentiation in TGFβ-stimulated fibroblasts. Moreover, inactivation of Hhat also ameliorated experimental dermal fibrosis. Knockdown of Hhat by injection of Hhat siRNA /atelocollagen complexes into the skin effectively ameliorated dermal thickening, reduced myofibroblast counts and decreased collagen content in bleomycin-induced fibrosis. Dermal fibrosis induced by challenge of mice with topoisomerase I was also ameliorated by knockdown of Hhat.

**Conclusion:** We demonstrate that Hhat is regulated in SSc in a TGFβ-dependent manner. Hhat in turn promotes hedgehog signaling, which directly contributes to the stimulatory effects of TGFβ on fibroblasts. Inactivation of Hhat reduces TGFβ-dependent fibroblast activation and ameliorates experimental fibrosis. These data provide first evidence that targeting Hhat may be a novel target for the treatment of fibrosis.

**Disclosure:** R. Liang, None; R. Kagwiria, None; C. Dees, None; Y. Zhang, None; O. Distler, 4 D Science, Actelion, Active Biotec, Bayer, Biogen Idec, Boehringer Ingelheim Pharma, BMS, ChemomAb, EpiPharm, Ergonex, espeRare foundation, GSK, Roche-Genentech, Inventiva, Lilly, medac, MedImmune, Mitsubishi Tanabe, Pharmacyclics, Pfizer, Sanofi, Seroda, 2; G. Schett, None; J. Distler, 4D Science, 1, Anamar Medical, Active Biotech, Array Biopma, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, GSK, Novartis, Sanofi-Aventis, UCB, 2, Actelion Pharmaceuticals US, Active Biotech, Anamar, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi, UCB, 5.


**Abstract Number:** 1715

**Mitochondrial DNA Mutations and Respiratory Chain Dysfunction in Lung Fibrosis of Systemic Sclerosis**

Veronika K. Jaeger¹, Dirk Lebrecht²³, Andrew G. Nicholson⁴⁵, Athol U Wells⁵⁶, Suresh George⁷, Amiq Gazdhar⁸, Michael Tamm⁹, Nils Venhoff², Thomas Geiser⁸ and **Ulrich A. Walker¹, ¹Department of Rheumatology, University Hospital Basel, Basel, Switzerland, ²Department of Rheumatology and Clinical Immunology, Medical Center - University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany, ³Department of Pediatrics and Adolescent Medicine, Division of Pediatric Hematology and Oncology, Medical Center, Faculty of Medicine, University of Freiburg, Freiburg, Germany, ⁴Department of Histopathology, Royal Brompton Hospital, Royal Brompton and Harefield NHS Foundation Trust, London, United Kingdom, ⁵National Heart and Lung Institute, Imperial College, London, United Kingdom, ⁶Interstitial Lung Disease Unit, Royal Brompton Hospital, Royal Brompton and Harefield NHS Foundation Trust, London, United Kingdom, ⁷Royal Brompton and Harefield National Health Service Foundation Trust, London, United Kingdom, ⁸Department of Pulmonary Medicine, University Hospital Bern, Bern, Switzerland, ⁹Department of Pneumology, University Hospital Basel, Basel, Switzerland

**First publication:** September 18, 2017
Background/Purpose:
Recent data have implemented reactive oxygen species (ROS) in the etiology of interstitial lung disease (ILD) in systemic sclerosis. Recent data from bleomycin mice have suggested a role of large-scale somatically acquired mutations in mitochondrial DNA (mtDNA) and consecutive respiratory chain dysfunction as a trigger of ROS formation and lung fibrosis.

Methods:
Lung biopsies from patients with idiopathic interstitial pneumonitis and systemic sclerosis (n=31) were analyzed for mitochondrial functions and compared with biopsies from 13 healthy controls (HC). From 17 patients we had simultaneous biopsies from the upper and lower lung.

Results:
Malondialdehyde as a marker of ROS formation was increased in ILD (p=0.007). The median proportion of mtDNA containing the pathogenic common deletion was 22.5% in ILD patients, compared to 0% in HC. This translated into a 3.8-fold diminishment of mtDNA-encoded cytochrome c-oxidase (COX2), but not nucleus-encoded (COX4) respiratory chain subunits in ILD compared to controls (p<0.0001) and a 33% diminishment of mtDNA-encoded cytochrome c-oxidase activity (p=0.001 vs. controls). In all patients, the more fibrotic lower lungs had significantly more malondialdehyde (p=0.0004), mtDNA deletions (p=0.0006), and cytochrome c-oxidase dysfunction (p=0.0003) than the less-fibrotic upper lung counterparts. Conversely, lower lungs had significantly less (p=0.0003) mtDNA-encoded COX2 subunits in comparison to non-mtDNA-encoded COX4 subunits (Figure). There was no association of any mitochondrial parameter with smoking status or age, and no difference between biopsies from patients with systemic sclerosis and non-specific interstitial pneumonitis.

Conclusion:
Our data support a role of mtDNA-mutations and consecutive respiratory chain dysfunction as a trigger and perpetuator of ROS formation in both, idiopathic interstitial pneumonitis and ILD of patients with systemic sclerosis.
TGFβ-Dependent Upregulation of XIAP Fosters Fibroblast Activation and Tissue Fibrosis By Promoting Canonical Wnt Signaling

Christina Bergmann¹, Ludwig Hallenberger¹, Amelie Brandt¹, Benita Merlevede¹, Clara Dees², Chih-Wei Chen³, Christian Beyer¹, Oliver Distler⁴, Georg Schett⁵ and Jörg Distler⁶, ¹Department of Internal Medicine 3 and Institute for Clinical Immunology, Friedrich-Alexander-University of Erlangen-Nuremberg and University Hospital Erlangen, Erlangen, Germany, ²Department of Internal Medicine 3 and Institute for Clinical Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Erlangen, Germany, ³Department of Internal Medicine 3 – Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Erlangen, Germany, ⁴Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland, ⁵Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, Erlangen, Germany., Erlangen, Germany, ⁶Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Erlangen, Germany

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster II
Background/Purpose:

Aberrant activation of profibrotic pathways is a key feature of systemic sclerosis (SSc). Extensive evidence characterizes TGFβ- and canonical WNT-signaling as key drivers of fibroblast activation. The crosstalk between those pathways, however, remains largely enigmatic. A better understanding of the interplay of different profibrotic pathways may be key to the development of effective targeted therapies.

XIAP (X-linked inhibitor of apoptosis protein) is an ubiquitously expressed member of the IAP protein family with important functions in tissue turnover and cell motility. XIAP was recently described as positive regulator of canonical Wnt signaling in embryogenesis. The aim of this study is to characterize the role of XIAP in fibrotic disease in SSc and to analyze the effects XIAP inhibition in vitro and in vivo.

Methods:

XIAP-expression was analyzed by qPCR, IF and Western blot. XIAP was targeted pharmacologically with Embelin. The activation of the canonical Wnt pathway was assessed by analyses of Wnt target genes and by TOPflash/FOPflash luciferase reporter assay. The interaction of XIAP with TLE3 was analyzed by co-immunoprecipitation. In vivo, XIAP inhibition was analyzed in three different models of fibrosis.

Results:

The expression of XIAP is increased in the skin of SSc patients compared to matched healthy individuals with a particularly prominent staining in fibroblasts. In addition, XIAP-expression is increased in experimental fibrosis models. The induction of XIAP in SSc in experimental fibrosis was mimicked by TGFβ in cultured fibroblasts. Moreover, targeted inhibition of TGFβ signaling prevented the induction of XIAP in experimental fibrosis. The upregulation of XIAP augmented the stimulatory effects of recombinant WNT proteins on fibroblasts. Inhibition of XIAP reduced the Wnt1-induced activation of normal dermal fibroblasts with reduced expression of myofibroblast markers and decreased collagen release. In addition, XIAP inhibition reverted the activated fibroblast phenotype in SSc fibroblasts. Inhibition of XIAP also demonstrated potent antifibrotic effects in experimental fibrosis in bleomycin-induced dermal fibrosis, in Topoisomerase-I-induced (TopoI) dermal and pulmonary fibrosis and in Wnt10b-transgenic mice. The inhibitory effects of Embelin on fibroblast activation were associated with impaired canonical WNT signaling with reduced TCF-dependent transcription in reporter assays and reduced levels of WNT target genes such as Axin2 in cultured fibroblasts and in fibrotic tissues. Mechanistically, we demonstrate that XIAP interacts with the endogenous antagonist TLE3 to regulate canonical WNT signaling.

Conclusion:

XIAP is upregulated in SSc fibroblasts in a TGFβ-dependent manner and promotes fibroblast activation by fostering canonical WNT signaling. XIAP thus serves to integrate TGFβ- and WNT signaling as two core pathways in SSc. XIAP-inhibition demonstrated antifibrotic effects in vitro and in vivo in non-toxic concentrations. Inhibition of XIAP may thus be a novel approach to target aberrant canonical WNT signaling in fibrotic diseases.

Disclosure: C. Bergmann, None; L. Hallenberger, None; A. Brandt, None; B. Merlevede, None; C. Dees, None; C. W. Chen, None; C. Beyer, None; O. Distler, 4 D Science, Actelion, Active Biotec, Bayer, Biogen Idec, Boehringer Ingelheim Pharma, BMS, ChemomAb, EpiPharm, Ergonex, espeRare foundation, GSK, Roche-Genentech, Inventiva, Lilly, medac, MedImmune, Mitsubishi Tanabe, Pharmacies, Pfizer, Sanofi, Seroda, 2; G. Schett, None; J. Distler, 4D Science, 1, Anamar Medical, Active Biotec, Array Biopma, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, GSK, Novartis, Sanofi-Aventis, UCB, 2, Actelion Pharmaceuticals US, Active Biotec, Anamar, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi, UCB, 5.
Skin Commensal Bacteria Might Affect Wound Repair in SSc By Prevenitng Fibroblast Activation and By Provoking Chronic Inflammatory Reaction

Masaya Yokota¹, Janine Schniering¹, Oliver Distler² and Britta Maurer³, ¹Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, Switzerland, Zurich, Switzerland, ²Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland, ³Department of Rheumatology, Center of Experimental Rheumatology, University Hospital Zurich, Zurich, Switzerland

First publication: September 18, 2017

Background/Purpose: Chronic digital ulcers (DU) due to peripheral microangiopathy are a major complication in systemic sclerosis (SSc). Chronic wounds are often enriched in bacteria without overt clinical signs of infection and inflammation. Current treatment comprises vasodilation, local disinfection, mechanical wound cleaning and antibiotics. Data on the role of skin commensal bacteria on wound repair are conflicting with both beneficial and detrimental effects. A recent study provided evidence for previously unknown direct interactions between skin bacteria, dermal cells and extracellular matrix proteins even in normal skin. Therefore, we investigated whether skin commensal bacteria might be involved in wound healing responses in SSc.

Methods: Wound swabs of SSc patients with DU (n=36) were subjected to microbial analysis. The presence of skin commensals in human skin sections processed under sterile conditions was examined by Gram stain and IF. Dermal fibroblasts isolated from healthy controls (HC; n=4) and patients with diffuse cutaneous SSc (dcSSc; n=3) were stimulated with heat-killed S. epidermidis (HKSE) and S. aureus (HKSA). The concentration of IL-6, IL-8 and MCP-1 (monocyte chemoattractant protein-1) in cell culture supernatants was measured by ELISA. Expression of collagen type 1 (COL1A1) and alpha-smooth muscle actin (α-SMA) was evaluated by qPCR, ELISA and Western blotting. Expression of stress fibers and α-SMA was examined by phalloidin staining and IF. Cell proliferation was evaluated with a colorimetric assay. Contractility was analyzed by collagen gel contraction assay.

Results: Superficial and deep wound swabs (n=60) showed that 65% of wounds were primarily colonized with skin commensals including SA and SE. Gram-stain and IF of skin sections of HC and dcSSc (n=3 each) revealed Gram-positive bacteria in the deeper dermis and the epidermis. Upon HKSE/A stimulation, the secretion of IL-6 and IL-8 was increased in both HC and dcSSc fibroblasts, but MCP-1 was increased in dcSSc only. In HKSE/A-stimulated dermal fibroblasts, expression of α-SMA on mRNA and protein level was decreased in both HC (0.53/0.56-fold, p<0.05 each) and dcSSc (0.62/0.60-fold, p=0.06 each) whereas expression of COL1A1 was not changed. Moreover, simultaneous stimulation with HKSE and TGF-β revealed an inhibitory effect of HKSE on TGF-β-induced α-SMA expression on mRNA and protein level in both HC (0.69-fold, p=0.06) and dcSSc (0.49-fold, p=0.06). HKSE-stimulated fibroblasts also showed increased proliferation in dcSSc, but less in HC (1.85-fold vs. 1.27-fold, p=0.20). Accordingly, the expression of stress fibers was more abundant in dcSSc compared to HC. The contractility of
dermal fibroblasts upon HKSE stimulation was decreased in both HC and dcSSc (relative gel area to untreated cells; 116% vs. 114%).

**Conclusion:** Skin commensals inhibit the activation of dermal fibroblasts, but provoke strong inflammatory responses and increase proliferation. Our data indicate that bacterial exposure of dermal fibroblasts might result in chronic activation of innate immune responses with detrimental effects on wound repair.

**Disclosure:** M. Yokota, None; J. Schniering, None; O. Distler, Actelion, Bayer, BiogenIdec, Boehringer Ingelheim, ChemomAb, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Novartis, Pfizer, Sanofi, Sinoxa and UCB, 2,Actelion, Bayer, BiogenIdec, Boehringer Ingelheim, ChemomAb, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Novartis, Pfizer, Sanofi, Sinoxa and UCB, 5,mir-29 for the treatment of systemic sclerosis, 9; B. Maurer, AbbVie, Protagen, EMDO, Novartis, German SSc Society, 2,Pfizer, Roche, Actelion, MSD, 9,mir-29 for the treatment of systemic sclerosis, 9.

Endomyocardial biopsies (n=10 each) from SSc patients and healthy controls were screened by immunohistochemistry. CD14+ monocytes isolated from peripheral blood of SSc patients and healthy donors were differentiated towards a myofibroblast phenotype by stimulation with TGF-β1, IL-4, IL-10 and IL-13 [10ng/ml each]. In addition, CD14+ monocytes were co-cultured in 2D and 3D models with dermal fibroblasts originated from SSc patients or healthy subjects, or with adult healthy cardiac fibroblasts. TGF-β signalling was blocked by SD208 (TGFBR1), A83-01 (SMAD2) and (5Z)-7-Oxozeaenol (TAK1) inhibitors. Gene expression and protein secretion were evaluated by qPCR, Western blot, protein array, immunofluorescence and ELISA.

Results: The myocardium, lungs and skin of SSc patients revealed an extended collagen I deposition and the presence of CD14+ elongated cells in the fibrotic tissue. Stimulated monocytes acquired a myofibroblast-like phenotype with increased expression of collagen I (p<0.0001), fibronectin (p<0.05), and α smooth muscle actin (α-SMA) in comparison to untreated cells. Similarly, CD14+ monocytes exposed to dermal or cardiac fibroblasts acquired spindle shape and expressed higher levels of profibrotic genes. The process of monocyte-to-myofibroblast differentiation employed both canonical and non-canonical TGF-β signalling pathways. Blocking of the TGF-β receptor I and canonical SMAD-dependent pathway resulted in the abrogation of collagen I secretion by monocytes (p=0.002). In contrast, TAK1 inhibitor decreased fibronectin expression, while having no effect on collagen I expression. CD14+ monocytes from SSc patients were characterised by higher secretion of CXCL10 (p<0.001), which was significantly decreased after cytokine stimulation (p<0.001). Additionally, a tendency towards higher secretion of CCL20, CCL22, Leukemia Inhibitory Factor and Neurotrophin-3 was observed for SSc monocytes.

Conclusion: Here we demonstrated the capability of peripheral blood monocytes to differentiate towards the functional myofibroblast phenotype, designating these cells as one of the potential sources of pathological tissue myofibroblasts in SSc. Additionally, these cells sustained pro-fibrotic cytokines secretion, highlighting their important regulatory functions in the fibrogenesis in SSc.

Disclosure: M. Rudnik, None; M. Stellato, None; V. Milleret, None; P. Blysztzuk, None; B. Maurer, AbbVie, Protagen, EMDO, Novartis, German SSc Society; 2.Pfizer, Roche, Actelion, MSD, 9,mir-29 for the treatment of systemic sclerosis, 9; K. Klingel, None; J. C. Henes, None; K. Sotlar, None; M. Ehrbar, None; O. Distler, Actelion, Bayer, BiogenIdec, Boehringer Ingelheim, ChemomAb, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Novartis, Pfizer, Sanofi, Sinoxa and UCB, 2,Actelion, Bayer, BiogenIdec, BoehlerIngelheim, ChemomAb, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Novartis, Pfizer, Sanofi, Sinoxa and UCB, 5,mir-29 for the treatment of systemic sclerosis, 9; G. Kania, Bayer, 2.

Abstract Number: 1719

Accelerated Wound Healing in Megakaryocyte/Platelet-Specific Fli1 Knockout Mice Due to the up-Regulated Expression of Interferon-γ

Megumi Hirabayashi1, Yoshihide Asano2, Takashi Yamashita1, Ryosuke Saigusa1, Shunsuke Miura3, Kouki Nakamura1, Takuya Miyagawa1, Takashi Taniguchi1, Ayumi Yoshizaki1 and Shinichi Sato2, 1Dermatology, University of Tokyo, Graduate School of Medicine, Tokyo, Japan, 2Applied Chemistry, University of Tokyo, Graduate School of Medicine, Tokyo, Japan, 3University of Tokyo, Graduate School of Medicine, Tokyo, Japan, 4Department of Dermatology, Graduate School of Medicine, The University of Tokyo, Bunkyo-ku, Japan

First publication: September 18, 2017

SESSION INFORMATION
**Background/Purpose:** Fli1 deficiency, a potential predisposing factor of systemic sclerosis (SSc), induces SSc-like phenotypes in dermal fibroblasts, endothelial cells, keratinocytes, and macrophages. However, it is still unclear how Fli1 deficiency affects the phenotype of platelets. Hence we aim to investigate the biological effect of Fli1-deficient platelets in vivo by utilizing megakaryocyte/platelet-specific Fli1 (Fli1 MPcKO) knockout mice (Fli1<sup>flox/flox</sup>, Pf4-Cre).

**Methods:** Wound was generated by 8-mm punch device on the back skin of mice. Vascular structure was visualized by FITC-dextran injection. mRNA expression of target genes and collagen contents were assessed by quantitative reverse transcription PCR and hydroxyproline assay, respectively.

**Results:** Since Fli1 MPcKO mice macroscopically appeared normal, wound healing experiments were applied. Wound closure was accelerated in Fli1 MPcKO mice at Day 2 compared with control littermates, although there was no significant difference in the overall duration of wound closure between these two strains. When the expression profile of tissue remodeling-related factors was evaluated, interferon-g expression was significantly decreased in Fli1 MPcKO mice on Day 2. In the epithelized skin, collagen contents and the number of newly formed vasculature were much greater in Fli1 MPcKO mice than in control littermates. In addition, the number of a-smooth muscle actin-positive fusiform cells was increased in Fli1 MPcKO mice. Importantly, a mild skin injury, such as subcutaneous injection of PBS, induced extensive tissue fibrosis in Fli1 MPcKO mice.

**Conclusion:** Megakaryocyte/platelet-specific Fli1 deficiency promotes wound healing through the induction of myofibroblast differentiation and angiogenesis at least partially due to the downregulation of interferon-g. The activation of platelets with altered phenotype may contribute to the development of pathological skin fibrosis, including SSc.

---

**Disclosure:** M. Hirabayashi, None; Y. Asano, None; T. Yamashita, None; R. Saigusa, None; S. Miura, None; K. Nakamura, None; T. Miyagawa, None; T. Taniguchi, None; A. Yoshizaki, None; S. Sato, None.


**Abstract Number: 1720**

**TGF-ß-Induced Tissue Fibrosis in TBRIcaCol1Cre Transgenic Mice Is Abrogated By the Second Generation Tyrosine Kinase Inhibitor SKI-606 (Bosutinib)**

**Peter J. Wermuth** and Sergio A. Jimenez, Jefferson Institute of Molecular Medicine, Division of Connective Tissue Diseases and Scleroderma Center, Thomas Jefferson University, Philadelphia, PA

**First publication:** September 18, 2017

---

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster II
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Bosutinib (SKI-606), a second-generation tyrosine kinase inhibitor that blocks the activity of the BCR-ABL kinase responsible for Philadelphia chromosome positive chronic myeloid leukemias, also inhibits the activity of the Src family of nine non-receptor tyrosine kinases. Activation of Src kinases via phosphorylation of their catalytic regions can be stimulated by PDGF and TGF-β resulting in strong profibrotic cascade signaling. Furthermore, Src kinases are major regulators of the profibrotic activity of focal adhesion kinase (FAK), which promotes the differentiation of quiescent fibroblasts to activated myofibroblasts. Thus, the purpose of this study was to test the antifibrotic activity of Bosutinib *in vivo* on TGF-β induced skin and pulmonary fibrosis employing the well-characterized TBRIcaCol1Cre transgenic mouse model of tissue fibrosis.

**Methods:** TBRIcaCol1Cre transgenic mice with a tamoxifen-inducible constitutively active TGFβ receptor 1 allele in cells expressing Cre recombinase under the control of the Col1a promoter were implanted with subdermal osmotic pumps dispensing either 2.5, 5.0 or 10.0 mg/kd/day of Bosutinib or with pumps dispensing saline as a control for 8 weeks following tamoxifen activation of constitutive TBRI expression. Skin sections and lungs isolated from control and Bosutinib-treated animals (n=6 per group) were analyzed by histopathology following hematoxylin/eosin and Masson’s trichrome staining, measurement of tissue hydroxyproline content, and by evaluation of the expression of genes associated with tissue fibrosis, and myofibroblast differentiation and activation.

**Results:** Constitutive TGFβ-1 signaling in Col1a-expressing cells induced severe cutaneous and pulmonary tissue fibrosis in untreated mice. In contrast to mice receiving saline-containing pumps, a strong decrease in TGF-β-induced collagen deposition in the dermis and lungs was observed in response to Bosutinib treatment by histopathological analysis of these tissues. Quantitative assays for collagen content showed that control untreated mice displayed a 1.5 fold increase in hydroxyproline levels in skin and a 1.9 fold increase in the lung following tamoxifen administration. These increases were abrogated in a dose-dependent manner in mice receiving Bosutinib. The marked increase in expression of genes associated with tissue fibrosis and with transdifferentiation and activation of myofibroblasts observed following tamoxifen administration was also abrogated in a dose-dependent fashion in response to Bosutinib.

**Conclusion:** Cutaneous and pulmonary fibrosis induced in mice carrying an inducible constitutively active TBRI receptor transgene was abrogated in a dose-related manner following administration of the tyrosine kinase inhibitor Bosutinib as assessed by histopathology, measurements of tissue hydroxyproline content, and analysis of expression levels of profibrotic and myofibroblast activation-associated genes. These results demonstrate that the BCR/ABL and Src kinase inhibitor Bosutinib may be a potential therapeutic agent for tissue fibrosis in SSc and other fibroproliferative disorders.

**Disclosure:** P. J. Wermuth, None; S. A. Jimenez, None.


**Abstract Number:** 1721

**Long Noncoding RNA H19X Is a Key Regulator of Apoptosis and Proliferation of Fibroblasts in Systemic Sclerosis and Other TGFβ-Driven Fibrotic Diseases**

Elena Pachera¹, Adam Wunderlin¹, Shervin Assassi², Gloria Salazar², Mojca Frank Bertoncelj¹, Rucsandra Dobrota¹, Matthias Brock³, Carol A. Feghali-Bostwick⁴, Gerard Dijkstra⁵, Gerhard Rogler⁶, Tobias van Haaften
Background/Purpose: Long noncoding RNAs (lncRNAs) are a class of transcripts regulating gene expression. We have recently identified a novel lncRNA, H19X, which was upregulated in the skin of patients with SSc. We also demonstrated that TGFβ regulates H19X expression and is a key mediator of myofibroblast development and extracellular matrix synthesis. Here we aimed to assess whether (1) H19X is a general regulator of TGFβ-driven fibrotic diseases and (2) H19X upregulation in SSc dermal fibroblasts is anti-apoptotic and pro-proliferative thereby favoring fibrosis.

Methods: To study the function of H19X in apoptosis and proliferation of dermal fibroblasts we silenced H19X using locked nucleic acid oligonucleotides (LNA GapmeRs) followed by microarray analysis, qPCR, BrdU cell proliferation assay, Caspase 3/7 apoptosis assay and scratch assay. Cells were treated with 10 ng/ml TGFβ. Lung tissues were obtained from patients with SSc and idiopathic pulmonary fibrosis (IPF) undergoing organ transplantation, and from healthy controls (HC). Fibrotic gut tissues were obtained from patients with Crohn's disease undergoing gut resection. Expression of H19X was analyzed by qPCR.

Results: H19X expression was significantly increased in SSc interstitial lung disease and IPF patients versus HC (n=11 each, p<0.05). A significant H19X overexpression was also detected in fibrotic gut tissue from patients with Crohn's disease versus control (n=10 and 4 respectively; p<0.05). Furthermore, H19X was found to be increased in physiological wound healing tissue versus HC samples (n=11 and 8 respectively; p<0.05). Upregulation of H19X was paralleled by an upregulation of PAI-1, indicating TGFβ pathway activation in these tissues.

H19X knockdown followed by microarray analysis (n=5) showed that “FAS signaling pathway”, “cyclins and cell cycle regulation”, “regulation of cell cycle progression by Plk3”, and “free radical induced apoptosis” were among the pathways with the highest number of significantly enriched genes (p<0.005). Apoptosis markers like BCL2, IGFBP3 and FAF1 (n=5, p<0.05) were significantly downregulated in H19X-silenced fibroblasts. These results indicated that targeting H19X might have a pro-apoptotic effect on fibroblasts. Functional studies of apoptosis confirmed enhanced fibroblast apoptosis after H19X silencing and TGFβ stimulation (n=5, p<0.05). In addition to decreased apoptosis, increased fibroblast proliferation might also favor fibrosis. Indeed, H19X downregulation led to reduced fibroblast proliferation as measured by BrdU assay (n=5, p<0.05). Scratch assays (n=5) showed that H19X knockdown decreased TGFβ reduced wound healing.

Conclusion: H19X supports TGFβ-driven fibrosis by inducing proliferation and reducing apoptosis of fibroblasts. These effects are not limited to SSc, but also apply to a wider range of fibrotic diseases. Our results highlight the role of the novel lncRNA H19X as an important profibrotic mediator in TGFβ mediated processes.
Identification of a Sub-Population of Autoantibodies Targeting BICD2 Cross-Reacting with CENP-a Derived Peptides in Patients with Systemic Sclerosis

Michael Mahler¹, Chelsea Bentow¹, Jay Milo¹, May Choi², Mianbo Wang³, Petra Budde⁴, Murray Baron⁵, Marie Hudson⁶ and Marvin J. Fritzler⁷

¹Research and Development, Inova Diagnostics, San Diego, CA, ²University of Calgary, Calgary, AB, Canada, ³Lady Davis Institute for Medical Research, Montreal, QC, Canada, ⁴Protagen AG, Dortmund, Germany, ⁵Rheumatology, Jewish General Hospital, Montreal, QC, Canada, ⁶Division of Rheumatology, Jewish General Hospital, Lady David Institute for Medical Research, Montreal, QC, Canada, ⁷Medicine, University of Calgary, Calgary, AB, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Anti-nuclear antibodies (ANA) are present in approximately 90% of sera from systemic sclerosis (SSc) patients and play an important role in the diagnosis and prognosis of SSc. Recently, a novel autoantibody targeting the Cytoskeleton-Like Bicaudal D Protein Homolog 2 (BICD2) has been described in SSc. Studies to date on BICD2 show a significant overlap with anti-centromere antibodies. We aimed to analyze the B-cell epitopes of anti-BICD2 antibodies and to study the clinical associations of this antibody in SSc.

Methods:

Serum pools with (n=2) and without (n=1) anti-BICD2 antibodies, assayed by an addressable laser bead-based immunoassay (ALBIA) with recombinant BICD2, were used for epitope discovery with peptide arrays covering the
full-length amino acid sequences of CENP-A, CENP-B and BICD2. The identified candidate sequences were then utilized to synthesize synthetic, biotinylated, soluble peptides for ALBIA. The peptides were tested on five groups of patients [BICD2(+)/CENP-A(+) (n=15), BICD2(-)/CENP-A(+) (n=10), BICD2(+)/CENP-A(-) (n=5), BICD2(-)/CENP-A(-) (n=10), and healthy individuals (n=7)]. A total of 451 well characterized SSc patients were used to establish sero-clinical associations.

Results:

Epitope mapping revealed a serine/proline-rich nonapeptide SPSPGSSLPS comprising amino acids 606–614 localized to a non-coiled coil domain of BICD2 as the core epitope. This epitope had 29.6% identity and 55.6% similarity to a peptide in CENP-A (TGTPGSPSRGP) within which PGPSRR was previously identified as a key CENP-A epitope. Among the five groups of patients tested for reactivity with the BICD2 derived epitope, the highest reactivity was observed in BICD2(+)/CENP-A(+) sera followed by the BICD2(-)/CENP-A(+) group. In the BICD2(+)/CENP-A(-) group, one patient showed moderate reactivity. No reactivity was observed in the BICD2(-)/CENP-A(-) group or in HI. Next, we compared the reactivity to recombinant BICD2 (aa 606-821) with the BICD2 and the CENP-A derived peptides using spearman correlation. We observed a significant correlation between antibodies to the BICD2 and the CENP-A derived peptide (r=0.70; p<0.0001), to a lesser extent between CENP-A peptide and recombinant BICD2 (r=0.42; p<0.0001) and between recombinant BICD2 and the BICD2 peptide (r=0.59; p<0.0001). Inhibition experiments demonstrated that the anti-CENP-A peptide reactivity could be abolished with the BICD2 derived peptide and vice versa. However, some sera also had reactivity to the recombinant BICD2 protein that could not be inhibited by CENP-A peptide, indicating that there might be additional BICD2 specific epitopes. Anti-BICD2 antibody positive SSc patients (without other SSc specific antibodies) showed significantly higher prevalence of myositis (p=0.003) and less bacterial overgrowth (p=0.043).

Conclusion:

In the present study, we first describe a linear B-cell epitope on BICD2 which shows sequence homology and cross-reactivity with an epitope on CENP-A, which explains the strong serological overlap between anti-BICD2 and anti-centromere antibodies. Anti-BICD2 antibodies may have additional diagnostic and prognostic properties beyond currently known SSc-specific antibodies.

Disclosure: M. Mahler, Inova Diagnostics, Inc., 3; C. Bentow, Inova Diagnostics, Inc., 3; J. Milo, Inova Diagnostics, Inc., 3; M. Choi, None; M. Wang, None; P. Budde, Protagen, 3; M. Baron, None; M. Hudson, None; M. J. Fritzler, Inova Diagnostics, Inc., 5.


Abstract Number: 1723

**Nuclear Magnetic Resonance Based Metabolomics Study Identifies Highly Discriminatory Metabolites in 87 Systemic Sclerosis Patients**

Sakir Ahmed¹, Mohit Kumar Rai¹, Durgesh Dubey², Atul Rawat³, Dinesh Kumar³, Durga Prasanna Misra¹ and Vikas Agarwal¹, ¹Clinical Immunology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, ²Centre for Biomedical Research, PhD Student, Lucknow, India, ³Centre for Biomedical Research, Lucknow, India

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017
Background/Purpose:

Proton based Nuclear Magnetic Resonance ($^1$H NMR) can identify concentration of hundreds of small molecules in body fluids. A hypothesis-free approach was used to analyze metabolic perturbations in sera of Systemic Sclerosis (SSc) to identify potential biomarkers of the disease.

Methods:

Sera from 87 patients meeting ACR 1980 criteria for Systemic Sclerosis, and 40 age and sex similar controls, was analyzed using $^1$H NMR spectroscopy coupled with multivariate statistical analysis.

Results:

There was clear distinction between SSc and healthy controls on Partial Least Square-Discriminate Analysis (PLS-DA) [$R^2=0.98$]. Several metabolites of discriminatory relevance were identified, and further evaluated using analysis of variance (ANOVA) and Receiver Operator Curve (ROC) analysis. Methylamine, nitrosodimethylamine (NDMA), citrate and malonate were 4 metabolites that had maximum area under curve (AUC> 0.95) in distinguishing SSc from controls [Figure 2]. Methylamine and NDMA were uniformly elevated almost exclusively in SSc patients. Figure 3 shows Orthogonal PLS-DA of limited versus diffuse disease; or patients with or without interstitial lung disease (ILD).

Conclusion:

$^1$H NMR based metabolomics identified metabolites that have high discriminate value for SSc. The potential of these molecules as biomarkers, or their possible roles in disease pathogenesis need to be explored.
Figure 1: Representative 800 MHz $^1$H NMR spectra d(0.75-4.65) of serum from SSc and from controls

Dark blue rectangles show NDMA, malonate, and methylamine peaks in SSc spectra. Corresponding peaks absent in controls (light blue rectangles).

Univariate ROC curves of metabolites with AUC > 0.95
Disclosure: S. Ahmed, None; M. K. Rai, None; D. Dubey, None; A. Rawat, None; D. Kumar, None; D. P. Misra, None; V. Agarwal, None.


Abstract Number: 1724

Metabolic Regulation of Fibrosis in Systemic Sclerosis: The CD38-NAD+ Link

Bo Shi¹, Wenxia Wang¹, Jun Wei², Swati Bhattacharyya¹, Benjamin Korman³, Eduardo Chini⁴ and John Varga⁵, ¹Northwestern University, Chicago, IL, ²Northwestern University, Chicago, IL, ³Department of Rheumatology, Northwestern University, Feinberg School of Medicine Scleroderma Program, Chicago, IL, ⁴Kogod Center on Aging, Mayo Clinic, Rochester, MN, ⁵Rheumatology and Dermatology, Northwestern University, Feinberg School of Medicine Scleroderma Program, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The anti-aging deacetylase enzymes SIRT1 and SIRT3 show potent anti-fibrotic activity, and their expression and function are markedly deregulated in patients with systemic sclerosis (SSc). SIRT activity is exquisitely regulated by cellular metabolism and requires the ubiquitous cofactor nicotinamide adenine dinucleotide (NAD⁺). Cellular NAD⁺ levels must be maintained by balanced biosynthesis and degradation, the latter mediated by NADase enzyme CD38. Elevated CD38 levels in aging contribute to decline of NAD⁺ levels, resulting...
in mitochondrial dysfunction and metabolic abnormalities. We hypothesize that SSc-associated SIRT dysfunction might be linked to elevated CD38 expression and NAD⁺ catabolism, contributing to persistent fibroblast activation and unresolving fibrosis.

**Methods:** CD38 expression was measured in skin biopsies. Expression and regulation of CD38, collagen, aSMA and p300, and Smad and SITR and FAK activation were examined in normal and SSc fibroblasts treated with CD38 inhibitors and nicotinamide riboside (NR), an orally bioavailable NAD⁺ precursor.

**Results:** SSc skin biopsies showed elevated CD38 mRNA expression. A CD38 coexpression module of 194 genes was able to differentiate SSc from control biopsies. Levels of CD38 in the skin correlated with MRSS. Moreover, explanted SSc skin fibroblasts showed 3-fold increased CD38 expression compared to age-matched healthy controls. Recombinant human CD38 caused suppression of SIRT deacetylase activity, while augmenting TGF-b-induced fibrotic responses. In contrast, CD38 inhibition or genetic ablation resulted in reduced fibrotic responses. Supplementation of fibroblasts with NR increased cellular NAD⁺ level, and mitigated fibrotic responses induced by TGF-b. Moreover, NR supplementation markedly reduced Smad-dependent transcriptional activity via suppression of lysine acetylation mediated through coactivator p300. Modulation of age-dependent spontaneous and inducible fibrotic responses in mice by ablation of CD38 or NR supplementation, both of which augment NAD⁺ levels, is under investigation.

**Conclusion:** NAD⁺ levels appear to be critical in determining the amplitude/duration of tissue fibrosis through mechanisms that involve the SIRT deacetylases, and declining NAD⁺ plays a role in age-related tissue fibrosis. Elevated expression of the NAD⁺-consuming enzyme CD38 in lesional tissues in SSc is likely contributes to NAD⁺ depletion, impaired SIRT function and unchecked fibroblast activation in these patients. Boosting NAD⁺ levels using novel selective pharmacological CD38 inhibitors, NR supplementation, or augmented NAD⁺ biosynthesis via the salvage pathways, are promising novel approaches to the treatment of SSc.

**Disclosure:** B. Shi, None; W. Wang, None; J. Wei, None; S. Bhattacharyya, None; B. Korman, None; E. Chini, None; J. Varga, BMS, 2, Pfizer Inc, 2.


**Abstract Number:** 1725

## Insulin-like Growth Factor Binding Protein-4 Exerts Anti-Fibrotic Effects and Its Levels Are Reduced in SSc-Associated Lung Fibrosis

**Yunyun Su¹, Stanley Hoffman² and Carol A. Feghali-Bostwick³,¹** Medicine, Division of Rheumatology and Immunology, Medical University of South Carolina, Charleston, SC, ²Division of Rheumatology and Immunology, Medical University of South Carolina, Charleston, SC, ³Division of Rheumatology and Immunology, Division of Rheumatology and Immunology, Medical University of South Carolina, Charleston, SC, United States, Charleston, SC

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster II

**Session Type:** ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

The Insulin-like growth factor (IGF) system plays an important role in cellular growth, proliferation, differentiation, apoptosis and transformation; IGF binding proteins (IGFBP) exert cell and tissue-specific effects in an IGF-dependent and independent manner. For example, IGFBP-3 and -5 are increased in dermal and pulmonary fibrosis associated with systemic sclerosis (SSc), induce extracellular matrix (ECM) production, and promote fibrosis in vitro and in vivo. We sought to examine the effects of another member of the IGFBP family, IGFBP-4, on ECM production and fibrosis.

Methods:

Primary human fibroblasts were cultured from lung tissues of patients with SSc-associated lung fibrosis and from normal donors. Lung fibrosis was induced in C57BL/6J mice using bleomycin. Quantitative real time PCR was used to measure mRNAs levels in lung tissues of patients with SSc and normal donors. Immunoblotting was used to examine proteins levels. Suppression of IGFBP-4 in primary fibroblasts using gene-specific siRNA was used to examine the effects of loss of function. A replication-deficient adenovirus expressing IGFBP-4 was used for gain of function studies.

Results:

IGFBP-4 mRNA levels were significantly decreased in pulmonary fibroblasts of patients with SSc compared to those of normal donors. Production of ECM components including fibronectin, collagen and tenasin C, was significantly reduced by endogenous expression of IGFBP-4 and exogenous recombinant IGFBP-4 in a dose-dependent manner. The anti-fibrotic activity of IGFBP-4 also blocked TGFβ-induced ECM production. Expression of IGFBP-4 inhibited ECM production ex vivo in human lung and skin in organ culture. In vivo, IGFBP-4 reduced bleomycin-induced collagen production and histologic evidence of fibrosis. Silencing IGFBP-4 expression to mimic levels observed in SSc lung fibroblasts resulted in increased ECM production. Gene expression array analysis of IGFBP-4-treated primary human lung fibroblasts showed a reduction in the levels of the chemokine receptor CXCR4 and the pro-fibrotic factor CTGF. IGFBP-4 also reduced CXCR4 and CTGF protein levels.

Conclusion:

IGFBP-4 exerts anti-fibrotic effects by reducing the levels of the chemokine receptor CXCR4 and the levels of the pro-fibrotic factor CTGF. Thus reduced IGFBP-4 levels in SSc lung fibroblasts may contribute to the fibrotic phenotype via loss of IGFBP-4 anti-fibrotic activity. Our findings suggest that IGFBP-4 is an anti-fibrotic factor whose effects can be harnessed for the development of therapies to reduce fibrosis in SSc.

Disclosure: Y. Su, None; S. Hoffman, None; C. A. Feghali-Bostwick, None.


Abstract Number: 1726

Human Skin in Organ Culture As an Ex Vivo Model for Assessing the Fibrotic Effects of Bleomycin

Tomoya Watanabe¹, Logan Mlakar², Jonathan Heywood³, Maya Malaab² and Carol A. Feghali-Bostwick⁴, ¹Rheumatology, Medical University of South Carolina, Charleston, SC, ²Medical University of South Carolina, Charleston, SC, ³Rheumataology, Medical University of South Carolina, Chareston, SC, ⁴Division of Rheumatology
SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Systemic sclerosis (SSc) is a connective tissue disease of unknown etiology. Using human skin as an ex vivo organ model of fibrosis is an attractive tool to examine mechanisms underlying fibrosis and assess the potential effect of anti-fibrotic therapies. We have previously shown that a single injection of TGF-β induced dermal fibrosis in human skin ex vivo. In this study, we examined the effect of Bleomycin (BLM).

Methods: Human skin was stimulated with BLM using two different methods: injection and immersion. For the injection method, normal human skin was obtained from residual tissue following plastic surgery. Subcutaneous fat tissue was removed and skin tissue was cut into 1.5 cm x 1.5 cm sections. Skin tissues were injected intradermally with a total volume of 100 μl of 1×PBS: BLM (1 or 10 mU/ml) or 1× PBS as a vehicle control. Skin samples were cultured in an air-liquid interface with the epidermal side up. The culture medium was replaced after 72h. After 7 days, skin tissue corresponding to an area with 8-mm diameter centered around the injection site was harvested with a disposable 3 mm punch. For the immersion method, normal human skin was cut with a disposable 3 mm punch, and punches were cultured in medium containing BLM (1 or 10 mU/ml) or 1× PBS as a vehicle control. Skin tissues were harvested after 48 hours or 7 days post-treatment for real-time PCR and hydroxyproline assay, respectively.

Results: BLM significantly increased hydroxyproline levels and dermal thickness in a dose-dependent manner 7 days after injection. BLM had a similar effect on skin punches immersed in media for the same duration. The increase in hydroxyproline was paralleled by increased dermal thickness and Masson Trichrome staining. qRT-PCR analysis revealed that the expression levels of fibrosis-related genes, collagen 1A1, fibronectin, CTGF, and TGFb1, were significantly increased in BLM-treated skin compared with control skin.

Conclusion:

Our findings show that BLM induces fibrosis in human skin and higher doses of BLM are more effective at inducing significant increases in collagen content, expression of fibrosis-associated genes, and dermal thickness. Moreover, immersing skin in medium containing BLM is more effective at inducing dermal fibrosis than intradermal BLM injections. BLM treatment using the immersion method may be an attractive tool for the functional analysis of skin fibrosis in human skin in organ culture, providing a tool with direct relevance to human fibrotic skin disease.

Disclosure: T. Watanabe, None; L. Mlakar, None; J. Heywood, None; M. Malaab, None; C. A. Feghali-Bostwick, None.


Abstract Number: 1727
Genome-Wide DNA Methylation Analysis in Systemic Sclerosis Reveals Hypomethylation of Interferon-Associated Genes in CD4+ and CD8+ T Cells

Weilin Pu1, Weifeng Ding2, Lei Wang3, Shuai Jiang4, Wenzhen Tu3, Shicheng Guo5, Qingmei Liu6, Yanyun Ma4, Sidi Chen7, Wenyu Wu6, Xiaodong Zhou8, Maureen D. Mayes9, Shervin Assassi9, John D. Reveille9, Li Jin10 and Jiucun Wang10, 1State Key Laboratory of Genetic Engineering, Collaborative Innovation Center for Genetics and Development, School of Life Sciences, School of Life Sciences and Institutes of Biomedical Sciences, Fudan University, Shanghai, China, Shanghai, China, 2Medical Laboratory Center, Medical Laboratory Center, Affiliated Hospital of Nantong University, Nantong, Jiangsu Province, China, Nantong, China, 3Division of Rheumatology, Division of Rheumatology, Shanghai TCM-integrated Hospital, Shanghai, China, Shanghai, China, 4Ministry of Education Key Laboratory of Contemporary Anthropology, School of Life Sciences, Ministry of Education Key Laboratory of Contemporary Anthropology, School of Life Sciences, Fudan University, Shanghai, China, Shanghai, China, 5Department of Bioengineering, Department of Bioengineering, University of California at San Diego, CA, USA, San Diego, CA, 6Department of Dermatology, Department of Dermatology, Huashan Hospital, Fudan University, Shanghai, China, Shanghai, China, 7State Key Laboratory of Genetic Engineering, Collaborative Innovation Center for Genetics and Development, School of Life Sciences and Institutes of Biomedical Sciences, State Key Laboratory of Genetic Engineering, Collaborative Innovation Center for Genetics and Development, School of Life Sciences and Institutes of Biomedical Sciences, Fudan University, Shanghai, China, Shanghai, China, 8Internal Medicine-Rheumatology, University of Texas McGovern Medical School, Houston, TX, 9University of Texas McGovern Medical School, Houston, TX, 10State Key Laboratory of Genetic Engineering, Collaborative Innovation Center for Genetics and Development, School of Life Sciences and Institutes of Biomedical Sciences, State Key Laboratory of Genetic Engineering, Collaborative Innovation Center for Genetics and Development, School of Life Sciences and Institutes of Biomedical Sciences, Fudan University, Shanghai, China, Shanghai, China

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a complex systemic autoimmune disease caused by complicated interaction between genetic, epigenetic and environmental risk factors. Evidence showed epigenetic modifications, including DNA methylation, play an important part in the regulation of gene expression and the pathogenesis of a large number of autoimmune diseases such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). However, variations of DNA methylation in SSc have not been comprehensively investigated, especially for subtypes of the immune cells separately. To examine the methylation status in CD4+ and CD8+ T cells of SSc, we performed genome-wide DNA methylation microarray study in Chinese SSc patients and matched controls.

Methods: CD4+ and CD8+ T cells were obtained from SSc patients (n =24) and from age- and sex-matched healthy controls (n =24). All patients met the 2013 criteria for SSc established by the ACR/EULAR. Illumina Infinium HumanMethylation450 BeadChip was utilized for DNA quantification. The significantly differentially methylated sites (DMS) were validated using targeted bisulfite sequencing in an extended cohort consisting of 43 SSc patients and 41 controls (including 12 cases and 12 controls from the initial group). The expression profiles of the differentially methylated genes were measured by RT-PCR. In addition, the serum level of type I interferon-alpha/beta in SSc patients and controls was also quantified by ELISA.
**Results:** In the discovery stage, type I interferon (IFN)-associated genes were significantly hypomethylated and type I IFN signaling pathway was most significantly enriched in both CD4+ and CD8+ T cells of SSc patients compared to controls, suggesting an abnormality of the type I IFN pathway in SSc patients (Fig 1-A, B). In the second stage, the significantly hypomethylation status of five type I IFN-associated genes (*EIF2AK2, IFI44L, IFITM1, MX1, PARP9*) was validated (by targeted bisulfite sequencing). Moreover, the upregulation of these genes was also shown in both CD4+ CD8+ T cells of SSc patients (by RT-PCR) (Fig 1-C, D). Further, the serum levels of type I IFN-alpha/beta were also elevated in SSc patients over controls (by ELISA) (Fig 1-E, F). The significant correlations between gene expression, DNA methylation and serum level of type I IFN-alpha/beta were also confirmed, though showing different patterns between CD4+ and CD8+ T cells.

**Conclusion:** Hypomethylation and upregulation of type I IFN-associated genes were observed in both CD4+ and CD8+ T cells of SSc patients. The serum level of type I IFN-alpha/beta was elevated in SSc patients and correlated significantly with the methylation and expression of its associated genes. It is suggested that hypomethylation of type I IFN-associated genes may be involved in the pathogenesis of SSc.
Disclosure: W. Pu, None; W. Ding, None; L. Wang, None; S. Jiang, None; W. Tu, None; S. Guo, None; Q. Liu, None; Y. Ma, None; S. Chen, None; W. Wu, None; X. Zhou, None; M. D. Mayes, None; S. Assassi, None; J. D. Reveille, None; L. Jin, None; J. Wang, None.


Abstract Number: 1728
Interferon Gamma (IFN-γ) Subpopulations in Skin Homing T Cells of Localized Scleroderma

Claudia Macaubas¹, Emily Mirizio², Kaila Schollaert-Fitch³, Elizabeth D. Mellins⁴ and Kathryn S. Torok³,
¹Department of Pediatrics, Program in Immunology, Stanford University Med Ctr, Stanford, CA, ²Pediatric Rheumatology, Univ of Pittsburgh Med Ctr, Pittsburgh, PA, ³Pediatric Rheumatology, University of Pittsburgh Med Ctr, Pittsburgh, PA, ⁴Dept of Pediatrics CCSR, Stanford University Med Ctr, Stanford, CA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Localized scleroderma (LS) has both inflammatory and fibrotic components contributing to its effect on the skin and underlying tissue. The understanding of the pathophysiology driving this process is limited, though there is evidence supporting T cell involvement in both systemic sclerosis (SSc), its related disease, and LS. Recent studies in SSc have focused on skin homing T cells in the circulating peripheral blood which may be directly contributing to disease progression and skin inflammation with subsequent fibrosis (1). We aim to study this same concept in LS and investigate skin homing cells that may contribute to skin inflammation and reflect activity at lesion sites.

Methods:
PBMCs were isolated from 10 pediatric LS subjects with paired active/inactive blood specimens (20 samples total), and were analyzed at rest and after PMA/ionomycin stimulation. Flow cytometry was performed to characterize T cells using antibodies for T cell subsets (CD3, CD4, CD8, CD28), T memory cells (CD45RO), T trafficking and adhesion (CXCR3, CCR4, CCR6, CD62L), and skin homing cells (CCR10 and CLA). Selected intracellular T H1 and T H2 cytokines (IFN-γ, TNF-α, and IL-13) were also measured. Cell populations were compared between LS active and inactive disease states using paired Wilcoxon Signed-Ranks Test.

Results:
The proportion of CD4+ (T H) and CD8+ (T C) T cells among total PBMC were not significantly different between active and inactive disease states. However, there was a significant increase in the proportion of skin homing CCR10+ T C (Fig.1A) in samples collected during active disease. In addition, both CCR10+ T C and CCR10+ T H cells produced inflammatory cytokine populations, IFN-γ, that were significantly increased in the active disease state compared to the inactive disease state (Fig 1B).

Conclusion:
This is one of the first studies to examine circulating cell immunophenotypes in pediatric-onset localized scleroderma, with emphasis on examining the association of T skin homing cell subtypes with disease activity. These findings suggest increased skin homing (CCR10+) of inflammatory cytokine producing subpopulations of T C and T H cells in active disease (Fig 1). In adult SSc, IL-13+, and not IFN-γ+, CD8+CCR10+ cells appear to be the skin homing cell type that propagates disease (1), emphasizing possible biological differences in scleroderma phenotypes; more inflammatory, T H1/T C1 phenotype in LS and the more fibrotic, T H2/T C2 phenotype, in SSc.
Determining active disease status in patients with scleroderma may allow targeting of key immune components to prevent damage and disfigurement.

References:


Disclosure: C. Macaubas, None; E. Mirizio, None; K. Schollaert-Fitch, None; E. D. Mellins, None; K. S. Torok, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/interferon-gamma-ifn-%ce%b3-subpopulations-in-skin-homing-t-cells-of-localized-scleroderma

Abstract Number: 1729

**Increased Serum Levels of Micro-RNA 30d and Micro-RNA 423-5p in 2 Independent Cohorts of Patients with Morphea**

**Jorre S. Mertens**1,2, Wiola Marut1, Cornelis P.J. Bekker1, Elke M.G.J. de Jong3 and Timothy R.D.J. Radstake1,4,

1Rheumatology and Clinical Immunology, Laboratory of Translational Immunology, University Medical Center Utrecht, Utrecht, Netherlands, 2Department of Dermatology, Radboud University Medical Center, Nijmegen, Netherlands, 3Radboud University Medical Center, Nijmegen, Netherlands, 4Laboratory of Translational Immunology, University Medical Center Utrecht, Utrecht, Netherlands

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster II

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM
Background/Purpose:

Morphea, also known as localized scleroderma, encompasses a group of idiopathic sclerotic skin diseases. MicroRNAs (miRNAs) are a large family of highly conserved noncoding genes that play a fundamental role in biological processes by controlling protein expression by binding to protein-coding messenger RNAs, resulting in translational repression or mRNA degradation [REF]. Besides intracellularly, miRNAs are also found in several biological fluids, including serum. We aimed to investigate serum levels of miRNAs in morphea.

Methods:

Serum was collected from patients affected by morphea. Disease subtypes were classified according to Zulian and Laxer, with the addition of Eosinophilic Fasciitis (EF) as a distinct subtype. Two independent cohorts of patients were established. A discovery cohort, consisting of 22 morphea patients and 14 healthy controls (HCs), was used for miRNA profiling in serum, by TaqMan Real-time quantitative Polymerase Chain Reaction (RT-qPCR) on an OpenArray, which allowed simultaneous analysis of 758 miRNAs. The mean relative fold change (FC) was calculated for the group of morphea patients and HC, and compared between the two groups via Student’s t-test. A selection of 8 miRNAs were found to be differentially expressed between the patients and healthy controls (P<0.05; selection based on lowest P-values). These targets were selected for technical and biological validation, by miRNA-specific TaqMan RT-qPCR, in an independent cohort of 29 morphea patients and 9 HCs.

Results:

The mean FC of the individual miRNAs from the discovery cohort are displayed in figure 1. Technical validation was achieved for all selected 8 miRNAs; supporting the array results. Serum levels of miR-30d and miR-423-5p were significantly elevated in patients, compared to healthy controls in both the discovery cohort [miR-30d: mean FC 1.4, P 0.003; miR-423-5p: mean FC 1.659, p 0.001] and the independent validation cohort [miR-30d: mean FC 2.28, P < 0.001; miR-423-5p: mean FC 1.500, p 0.0103] (Figure 2). The remaining 6 targets did not show significantly altered levels in the validation cohort. Most interesting, both miR-30d and miR-423-5p were especially increased in patients affected by more severe subtypes, such as linear morphea and eosinophilic fasciitis.

Conclusion:

Serum levels of miR-30d and miR-423-5p were significantly higher in morphea compared to healthy controls in 2 independent cohorts. In addition, more severe subtypes such as linear morphea and EF showed increased levels of these 2 targets, as compared to milder subtypes.
Figure 1 Volcano Plot of discovery cohort. Mean fold changes (FC) of morphea group (n=22) versus healthy control samples (n=14). Mean FC are displayed on X-axis and corresponding P-values, on a log10-scale, are displayed on the y-axis. Targets depicted in red were selected for replication in an independent cohort of morphea patients.
IL-6 Mediates Activation of Macrophages in Patients with Systemic Sclerosis
Rajan Bhandari1, Michael Ball2, Viktor Martyanov3, Dillon Popovich4, Mary A. Carns5, Kathleen Aren5, Monique Hinchcliff6, Michael L. Whitfield7 and Patricia A. Pioli8, 1Geisel School of Medicine at Dartmouth, Lebanon, NH, 2Geisel School of Medicine at Dartmouth, Lebanon, NH, 3Department of Molecular and Systems Biology, Geisel School of Medicine at Dartmouth, Hanover, NH, 4Geisel School of Medicine at Dartmouth, Hanover, NH, 5Northwestern University, Feinberg School of Medicine Scleroderma Program, Chicago, IL, 6Rheumatology, Northwestern Medicine, Chicago, IL, 7Molecular and Systems Biology, Geisel School of Medicine at Dartmouth, Hanover, NH, 8Microbiology and Immunology, Geisel School of Medicine at Dartmouth, Hanover, NH

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics Poster II
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Activated macrophages (MØs) have been implicated as regulators of fibrosis in patients with systemic sclerosis (SSc), and we have shown that MØs from SSc patients are activated under basal conditions, releasing elevated levels of IL-6, CCL2, and TGF-β. Because MØs are plastic and may be modulated by local micro-environmental factors, it is likely that activation of MØs in SSc is regulated by the interplay of many factors. In this study, we identify a critical role for IL-6 in the regulation of human SSc MØ activation, and provide evidence for a molecular mechanism by which MØ and fibroblast-derived IL-6 supports the pro-fibrotic immuno-phenotype of these cells.

Methods:

Plasma and PBMCs were obtained from whole blood of 6 SSc patients (disease duration <5 years) and from 5 healthy age and gender-matched control subjects following informed written consent. CD14+ monocytes were isolated from PBMCs using magnetic bead selection, and were cultured with either autologous or allogeneic plasma for 7 days to differentiate the cells into MØs. To demonstrate specificity of IL-6-mediated effects on SSc MØ activation, MØ differentiation was performed in indicated cultures in the presence of anti-IL-6 neutralizing antibody or isotype control. For reciprocal activation studies, SSc MØs were co-cultured with fibroblasts using Transwells. RNA expression in MØs and fibroblasts was analyzed using genome-wide analysis and RT-PCR, and protein expression and secretion were monitored using flow cytometry and by ELISA.

Results: Healthy age and gender-matched control MØs differentiated in plasma from SSc patients recapitulate the immuno-phenotype of MØs derived from SSc patients. Intriguingly, when MØs from SSc patients are differentiated in healthy control plasma, the pro-fibrotic activation profile of these cells is abrogated, suggesting SSc MØ activation arises from soluble factors present in the local micro-environment. Analysis of signaling pathway activation in SSc MØs demonstrates constitutive phosphorylation of STAT3 in these cells, consistent with IL-6 activation. Differentiation of SSc MØs in the presence of anti-IL-6 neutralizing antibody results in loss of basal MØ activation—i.e. loss of CCL2 and IL-6 production. To identify the potential mechanism by which IL-6 mediates SSc MØ activation, we assessed expression of regulators of fibrosis and immune activation. We now show that IL-6 upregulates expression of IL-4Ra in SSc MØs, and that stimulation with IL-4/IL-13 results in enhanced production of CCL2 in an IL-6-dependent manner.

Conclusion: IL-6 mediates pro-fibrotic activation of SSc MØs, as blockade of IL-6 abrogates production of CCL2 and IL-6 in these cells. Our results suggest a potential mechanism by which IL-6 mediates these effects, as IL-6 upregulates expression of IL-4Ra, and stimulation of SSc MØs with IL-4/IL-13 results in enhanced CCL2 expression in an IL-6-dependent manner. These results implicate a role for IL-6 in the induction of the pro-fibrotic
activation profile of SSc MØs, and suggest targeted intervention against the signaling pathways that underlie MØ activation may be therapeutically beneficial in ameliorating SSc disease.

Disclosure: R. Bhandari, None; M. Ball, None; V. Martyanov, None; D. Popovich, None; M. A. Carns, None; K. Aren, None; M. Hinchcliff, None; M. L. Whitfield, Corbus, UCB, glaxosmithkline, 5; Celdara medical llc, 9; P. A. Pioli, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/il-6-mediates-activation-of-macrophages-in-patients-with-systemic-sclerosis

Abstract Number: 1731

Abnormal Responses of γδ T Cell Subsets to Stimulation with Cardiolipin and Zoledronate in Systemic Sclerosis

Ilan Bank1, Paul Fisch2, Jose Villacorta Hidalgo3, Alexandra Balbir-Gurman4, Yolanda Braun-Moscovici5 and Helena Migalovich Sheikhet6, 1Medicine, Maayenei Hayeshuah and Chaim Sheba Medical Center, Israel, Bnei Brak, Israel, 2Department of Clinical Pathology, University of Freiburg Medical Center, Freiburg, Germany, 3Department of Clinical Pathology, University of Freiburg Medical Center, Freiburg, Germany, 4Rheumatology Unit, Rambam Health Care Campus, Rappaport Faculty of Medicine, Technion, Haifa, Israel, Haifa, Israel, 5B Shne Department of Rheumatology, Rambam Health Care Campus,. Rappaport Faculty of Medicine, Technion, Haifa, Israel, 6Medicine, Laboratory of Immunoregulation, Chaim Sheba Medical Center, Ramat Gan, Israel

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: T Cell Biology and Targets in Autoimmune Disease Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic sclerosis (SSc) is an auto-immune disorder leading to destructive tissue fibrosis. Abnormal responses of SSc T cells to lipid antigens and low molecular weight phospho-antigens have been observed but not extensively explored. We determined how exposure to cardiolipin, a lipid auto antigen, and zoledronate (zol), an inducer of intracellular phospho-antigens (e.g isopentenyl pyrophosphate), affect cytokine secretion and activation of SSc T cells. We focused on non-conventional innate gd T cells since these: 1. Are oligoclonally expanded in SSc 2. infiltrate damaged organs, and 3. include lipid reactive Vdelta (d)1+ and phospho-antigen reactive Vgamma (g)9+ gammadelta (gd) T cells.

Methods: Peripheral blood mononuclear cells (PBMC) were isolated by ficoll hypaque density centrifugation from 12 SSc patients (SScp) and 13 healthy controls (HC). Expression of CD25, a marker of activation, on Vg9+, Vd1+ and total CD3+ T cells in PBMC cultured for at 2X10^6 cells/ml 96 hour in RPMI-1640 tissue culture medium supplemented with 10% fetal bovine serum, penicillin streptomycin, and glutamine, (TCM) containing 100 international units of interleukin (IL)-2 and added reagents as indicated, was measured by flow cytometry - as were cell surface binding of CD1d tetramers, and effects of monoclonal antibody (mAb) mediated blockade of CD1d. Intracellular production of anti fibrotic [interferon (IFN) g] and pro fibrotic [IL- 4] cytokines was measured by flow cytometry after overnight incubation of PBMC in medium with added reagents.
Results: Secretion of IFNg (but not IL-4) was suppressed in SSc relative to HC CD3+ and Vg9+, but not Vd1+ T cells cultured in TCM alone. However, both Vd1+ and Vg9+ T cell IFNg secretion in SSc were relatively reduced by adding cardiolipin (2.5 mg/ml), which, by contrast, augmented IL-4+ SSc Vg9+ T cells. Moreover, IFNg+ SSc Vg9+ T cells were relatively suppressed by zol (2mMol), consistent with subset restricted specific effects of cognate antigens. Conversely, %CD25+ CD3+ and Vd1+, and to a lesser degree Vg9+ T cells, were elevated significantly in 96 h cultured SSc PBMC compared to HC. Moreover, cardiolipin and zol respectively, significantly suppressed SSc but not HC %CD25+ Vg9+ and Vd1+ (but not total %CD25+CD3+) T cells suggesting antigen driven cross inhibitory effects by these gd T cell subsets. These effects could be partially reversed by culture with zol + cardiolipin, whereas this combination more strongly amplified both CD25+ gd T cell subsets of HC. Importantly, SSc and HC Vd1+ T cells > Vd1- T cells were highly reactive with lipid presenting CD1d – tetramers. Furthermore, a CD1d - blocking mAb decreased the zol + cardiolipin enhancement of %CD25+Vd1+ T cells in SSc PBMC cultures

Conclusion: SSc patient Vd1+ and Vg9+ T cell subsets exhibit disturbed and interactive responses to cardiolipin and zol in vitro, mediated in part by CD1d. Thus, the abnormal perception of cardiolipin and phospho-antigens by gd T cells may play a role in the immune pathology in SSc, notably that of pathological fibrosis, warranting further study.

Disclosure: I. Bank, None; P. Fisch, None; J. V. Hidalgo, None; A. Balbir-Gurman, None; Y. Braun-Moscovici, None; H. Migalovich Sheikhet, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/abnormal-responses-of-%ce%b3%ce%b4-t-cell-subsets-to-stimulation-with-cardiolipin-and-zoledronate-in-systemic-sclerosis

Abstract Number: 1732

The Characteristic T-Cell Receptor-Mediated Signaling of Peripheral Blood T Cells in Dermatomyositis and Polymyositis

Yasuhiro Shimojima1, Dai Kishida2 and Yoshiki Sekijima2, 1Department of Medicine (Neurology and Rheumatology), Shinshu University School of Medicine, Matsumoto, Japan, 2Department of Medicine (Neurology and Rheumatology), Shinshu University School of Medicine, Matsumoto, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: T Cell Biology and Targets in Autoimmune Disease Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: In dermatomyositis (DM) and polymyositis (PM), the characteristics of T cell expression in peripheral blood have been previously described; especially, decreased expression of interferon-γ (IFN-γ) and interleukin-17 (IL-17) producing CD4+ T cells was significantly demonstrated in the acute phase of DM. However, the mechanism underlying the decrease in circulating IFN-γ and IL-17 producing CD4+ T cell expression is still unknown. The purpose of this study was to investigate the T-cell receptor (TCR)-mediated intracellular signaling in peripheral blood T cells in DM and PM.
Methods: Peripheral blood T cells from 86 patients with DM (n = 57) and PM (n = 29), as well as from 28 healthy controls, were used for experimental investigations. T-cell subtypes and TCR-induced phosphorylated zeta-chain-associated protein kinase 70 (pZAP70) were analyzed by flow cytometry. Signal transducer and activator of transcription (STAT) and some inhibitory factors in T cells stimulated with anti-CD3/CD28 beads were also investigated by quantitative real-time polymerase chain reaction.

Results: Counts of CD3$^+$, CD4$^+$, and CD8$^+$ T cell were significantly lower in DM than in PM ($p < 0.0005$). Moreover, STAT and pZAP70 expression in CD4$^+$ T cells significantly decreased in DM ($p < 0.05$), whereas that in CD8$^+$ T cells significantly increased in PM ($p < 0.05$) (Fig. 1). Lower expression of forkhead box transcription factor (FoxP3) was also demonstrated in DM than in both PM and HC ($p < 0.005$). Especially in DM, a positive correlation between CD4$^+$ T cell counts and STAT expression was detected ($p < 0.05$). In addition, low CD4$^+$ T cell counts as well as reduced STAT expression were prominent in patients with interstitial lung disease ($p < 0.05$). STAT and pZAP70 expression significantly improved after clinical remission in both DM and PM ($p < 0.05$), although expression of FoxP3 remained suppressed. Besides, upregulation of suppressor of cytokine signaling-3 (SOCS3) and downregulation of interleukin 6 signal transducer (IL6ST) in CD4$^+$ T cells were observed in both DM and PM ($p < 0.05$); however, no significant improvements were detected after clinical remission.

Conclusion: STAT expression and TCR-proximal signaling in CD4$^+$ T cells were suppressed in DM, whereas those in CD8$^+$ T cells were induced in PM, suggesting that TCR-mediated signaling may be a key pathway to determine the characteristics of peripheral blood T cells in DM and PM. Furthermore, upregulation of SOCS3 and downregulation of IL6ST and FoxP3 in CD4$^+$ T cells cause an imbalance in intracellular signaling which may be associated with the development of DM.

Disclosure: Y. Shimojima, None; D. Kishida, None; Y. Sekijima, None.


Abstract Number: 1733

Increased Differentiation Resistance of Regulatory T Cells to Endoplasmic Reticulum Stress in Systemic Lupus Erythematosus Patients
Yunjung Choi1, Yu-Mi Lee2, Eun-Kyeong Lee3, Ji-Hyeon Jeong3, Myeung Su Lee4, Changhoon Lee5 and Wan-Hee Yoo2, 
1Division of Rheumatology, Department of Internal Medicine, Chonbuk National University Hospital, Jeonju, Korea, Republic of (South), 
2Division of Rheumatology, Department of Internal Medicine, Chonbuk National University Hospital, Jeonju, Korea, Republic of (South), 
3Research Institute of Clinical Medicine of Chonbuk National University-Biomedical Research Institute of Chonbuk National University Hospital, Jeonju, Korea, Republic of (South), 
4Department of Rheumatology, Wonkwang University Hospital, Iksan, Korea, Republic of (South), 
5Division of Rheumatology, Department of Internal Medicine, Wonkwang University Hospital, Iksan, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: T Cell Biology and Targets in Autoimmune Disease Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Defects of regulatory T cell (Tregs) mainly contribute to loss of tolerance to self-antigen which is significantly implicated in the pathogenesis of systemic lupus erythematosus (SLE). We investigated proportion of Tregs in the peripheral blood mononuclear cells (PBMCs) of patients with SLE and differentiation difference of induced Tregs in vitro under the presence or absence of endoplasmic reticulum (ER) stress, which is one of the causal factors triggering lupus flares, compared with that of healthy controls (HCs).

Methods: We isolated the PBMCs of 26 SLE patients and 26 HCs (Table 1). The percentage of CD4+CD25+FoxP3+ Tregs was analyzed using flow cytometry. The PBMCs were incubated with anti-CD3/CD28 beads, supplemented with transforming growth factor-¥â and interleukin-2 to induce differentiation of Tregs, with or without tunicamycin for 24 hours.

Results: The percentage of Tregs in the PBMCs of SLE patients was lower than that in the HCs (4.1 ± 1.0 versus 4.4 ± 1.5 %, p=0.5). The induced differentiation of Tregs increased in both groups, and the increased proportion was greater in the SLE group (327 ± 234 versus 221 ± 96%, p=0.04). Incubation with tunicamycin in the Tregs differentiation process also increased the proportion of Tregs in both groups (227 ± 186 versus 92 ± 57%, p=0.001), and the increased proportion was higher in the SLE group. We also compared the incremental differences between exposure of ER stress and no exposure of ER stress. In SLE patients, the smaller difference was observed (39 ± 46%) compared with HC group (73 ± 53%) with statistical significance (Figure 1).

Conclusion: The baseline percentage of Tregs was lower in SLE patients than in HCs. However, when Treg differentiation was induced, the differentiation was more increased in SLE group and incremental difference between under the condition of ER stress and absence of ER stress was also smaller in SLE group. The exaggerated differentiation of Tregs in SLE patients may reflect less susceptibility or more resistance to ER stress in SLE lymphocytes on the process of Tregs differentiation.

Table 1. Baseline Characteristics of SLE patients and HCs
Figure 1. Increased proportion and incremental difference of Induced Tregs in vitro with and without ER stress

<table>
<thead>
<tr>
<th></th>
<th>SLE (n=26)</th>
<th>HCs (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Mean (SD)</td>
<td>46.9 (11.0)</td>
<td>35.9 (5.7)</td>
</tr>
<tr>
<td>Gender Female/Male</td>
<td>19/7</td>
<td>19/7</td>
</tr>
<tr>
<td>Disease duration (years) Mean (SD)</td>
<td>6.5 (5.3)</td>
<td></td>
</tr>
<tr>
<td>SLEDAI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-5</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>6-10</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>&gt;11</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>6.0 (5.9)</td>
<td></td>
</tr>
<tr>
<td>C3 / C4 Mean (SD)</td>
<td>80.3 (33.0)/15.8 (12.7)</td>
<td></td>
</tr>
<tr>
<td>Anti-dsDNA antibody Mean (SD)</td>
<td>73.2 (82.6)</td>
<td></td>
</tr>
<tr>
<td>Immunosuppressants (number)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mycophenolate mofetil</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Azathioprine</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Methotrexate</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Steroid dose (mg) Mean (SD)</td>
<td>9.1 (11.3)</td>
<td></td>
</tr>
</tbody>
</table>

Disclosure: Y. Choi, None; Y. M. Lee, None; E. K. Lee, None; J. H. Jeong, None; M. S. Lee, None; C. Lee, None; W. H. Yoo, None.


Abstract Number: 1734
CXCR5+ CD4 T Cells Signature Differentiates Takayasu Arteritis from Giant Cell Arteritis

Anne-Claire Desbois1, Valentin Quiniou2, Patrick Bruneval3, Nicolas Derian2, Anna Maciejewski-Duval2, Marlène Garrido4, Cloé Comarmond5, Jacques Pouchot6, Michelle Rosenzwajg2, David Klatzmann2, Patrice Cacoub7 and David Saadoun8, 1Hôpital Pitié-Salpêtrière, Internal Medicine and Clinical Immunology, Paris, France, 2GHPS, Paris, France, 3HEGP, Paris, France, 4I3 laboratory, Pitié-Salpêtrière, Paris, France, 5DHU 2iB Internal Medicine Referral Center for Autoimmune diseases Pitie Hospital, Paris, France, 6Internal Medicine Department, European Hospital Georges Pompidou, Paris, France, 7Department of Internal Medicine and Clinical Immunology, Groupe Hospitalier Pitié-Salpêtrière, Paris, France, 8Sorbonne Universités, UPMC Univ Paris 06, UMR 7211, and Inflammation-Immunopathology-Biotherapy Department (DHU i2B), F-75005, Paris, France; INSERM, UMR_S 959, F-75013, Paris, France; CNRS, FRE3632, F-75005, Paris, France; AP-HP, Groupe Hospitalier, Paris, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: T Cell Biology and Targets in Autoimmune Disease Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: To compare microarray gene analysis of patients with Giant cell arteritis to patients with Takayasu arteritis.

Methods: We performed comparative microarray gene analysis of purified CD4+ T cells of TA (n=14) and GCA (n=15) patients.

Results: We found that purified CD4+ T cells of GCA and TA patients exhibit distinct RNA signatures. Sixty-seven genes were differentially expressed, among which CXCR5, CCR6 and CCL20 were shown to be significantly up-regulated in CD4+ T cells of TA patients as compared to those of GCA. Flow cytometry analysis confirmed that CXCR5+ CD4+ cells, defined as T Follicular Helper cells (TFH), were significantly higher in TA patients than in GCA patients [median proportion of CXCR5+ CD4+ T cells of 15.4 (10;30.8) in TA versus 5.3 (1.4; 12.2) in GCA (p<0.0001) and 9.7 (5.6; 12.5) in HD (p=0.0001)]. Among TFH subpopulations, TFH-17 (defined as CCR6+ CXCR5+ CD4+ T cells) was specifically increased in TA [4.52 (1.07; 13.35) in TA vs 0.69 (0.13; 2.16) in GCA (p=0.0001) and 2.3 (0.3; 4.2) in HD (p=0.02)]. The analysis of inflammatory aortic lesions revealed the presence of tertiary lymphoid structures, composed of CXCR5+, CD4+, PD-1 and CD-20 cells in TA whereas such organized inflammatory infiltrates were uncommon in GCA aortic lesions. We demonstrated an increased peripheral B cell immune response in TA, as the number of peripheral B cells is increased in TA compared to GCA. CXCR5+ CD4+ T cells in TA patients have specific characteristics of TFH, as they help B cells to differentiate into memory B cells, to proliferate and to secrete IgG.

Conclusion: Patients with TA differ from patients with GCA in microarray gene analysis of purified CD4+ T cells. Our data provide evidence of the critical role of TFH in pathogenesis of inflammatory lesions in TA and suggest the role of antigenic trigger.

Disclosure: A. C. Desbois, None; V. Quiniou, None; P. Bruneval, None; N. Derian, None; A. Maciejewski-Duval, None; M. Garrido, None; C. Comarmond, None; J. Pouchot, None; M. Rosenzwajg, None; D. Klatzmann, None; P. Cacoub, None; D. Saadoun, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/cxcr5-cd4-t-cells-signature-differentiates-takayasu-arteritis-from-giant-cell-arteritis
Brain Infiltrating CD4 T Cells Have a Pathogenic T Follicular Helper-Like Phenotype in Neuropsychiatric Lupus

Shweta Jain\textsuperscript{1}, Ariel Stock\textsuperscript{2}, Fernando Macian-Juan\textsuperscript{3} and Chaim Putterman\textsuperscript{4}, \textsuperscript{1}Department of Medicine, Albert Einstein College of Medicine, Div of Rheumatology, Bronx, NY, \textsuperscript{2}Albert Einstein College of Med, Bronx, NY, \textsuperscript{3}Albert Einstein College of Medicine, Bronx, NY, \textsuperscript{4}Division of Rheumatology, Albert Einstein College of Medicine, Bronx, NY, USA, Bronx, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: T Cell Biology and Targets in Autoimmune Disease Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The pathogenesis of neuropsychiatric systemic lupus erythematosus (NPSLE) is complex, yet incompletely understood. While the role of T cells is well defined in systemic disease, their involvement in NPSLE has not been carefully studied. Therefore, the aim of this study was to characterize the CD4 T cell populations present in the brain of MRL-lpr/lpr (MRL/lpr) mice, a spontaneous lupus mouse model which exhibits many parallels to human NPSLE.

Methods: T cells infiltrating the brain of female MRL/lpr mice with active neuropsychiatric disease (16-18 weeks of age) were characterized, and subset identification was done by multiparameter flow cytometry, PCR, and cell culture.

Results: We found extensive infiltration of T cells in the brain of female MRL/lpr mice, almost exclusively limited to the choroid plexus, the site of the brain-CSF barrier. MRL/lpr mice had significant CD4 T cell infiltration as compared to MRL/+ controls (10% of the total cells vs 0.1%, p<0.01). Most of the infiltrating CD4 T cells in MRL/lpr females had an activated phenotype. Specifically, infiltrating CD4 T cells constituted an effector phenotype (80% of CD4\textsuperscript{+} cells; p<0.01). Importantly, CD4 T cells displayed a T follicular helper cell (T\textsubscript{FH}) phenotype, as evidenced by their surface markers (CD4\textsuperscript{+}ICOS\textsuperscript{+}CXCR5\textsuperscript{+}PD1\textsuperscript{+}) and secretion of a signature cytokine, IL-21, \textit{in vitro} and \textit{in vivo}. Interestingly, CD4 T\textsubscript{FH} cells also secreted significant levels of IFN-\gamma and expressed Bcl-6, thereby conforming to a pathogenic T helper population that drives disease progression. On the other hand, the regulatory
axis comprising CD4 T regulatory cells and T follicular regulatory cells was downregulated in MRL/lpr choroid plexus.

Conclusion: These results imply that accumulation of pathogenic CD4 T follicular helper cells in the brain of MRL/lpr mice may contribute to the neuropsychiatric manifestations of SLE, and suggest this T cell subset as a novel therapeutic candidate.

Figure: T cells infiltrate the choroid plexus of MRL/lpr mice. (A) Single cell suspensions from choroid plexus of 16-18 week old female MRL/+ (n=4) and MRL/lpr (n=10) were stained for the presence of CD3, CD4 and CD8 T cells. (B) CD4 gated cells were characterized as effector (CD4 $T_{\text{Eff}}$; CD4$^{+}$CD44$^{+}$), naïve (CD4$^{+}$CD62L$^{+}$), and central memory phenotypes (CD4 $T_{\text{CM}}$; CD4$^{+}$CD44$^{+}$CD62L$^{+}$). Values indicate mean±SEM of cells per million and each dot represents one mouse. * $p<0.05$, ** $p<0.01$, ***$p<0.0001$

Disclosure: S. Jain, None; A. Stock, None; F. Macian-Juan, None; C. Putterman, None.
SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: T Cell Biology and Targets in Autoimmune Disease Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Pathogenic immune cell types and functions have not been identified yet in rheumatoid arthritis (RA). This is explained by the impact of disease heterogeneity on study power and by the limited number of immune markers tested so far. Our lack of understanding of RA pathophysiology results in practising trial and error medicine with the prescription of biologic drugs: 30% of patients fail to respond to the first drug prescribed. Using the world-wide largest prospective cohort of RA patients undergoing treatment with biologics, we aim to identify immunological signatures of RA endotypes using a T cell mass cytometry (CyTOF) panel to define treatment response groups at baseline.

Methods: Peripheral blood mononuclear cells (PBMCs) are isolated from patients enrolled in the Biologics in Rheumatoid Arthritis Genetics and Genomics Study Syndicate (BRAGGSS) prior to treatment with a biologic drug. One hundred RA patients with a DAS28 > 5.1 are enrolled prospectively each year in addition to healthy controls. Treatment response is assessed at 3, 6 and 12 months. PBMCs are stimulated for 4 hours using anti-CD3/anti-CD28 beads and stained with a 37-channel CyTOF panel which includes intracellular cytokines, transcription factors and co-stimulatory molecules to allow a detailed characterization of the function of T-cells (including Th1, Th2, Th17 and Treg). Data will be analysed using in house developed unbiased advanced computational strategies and clustering algorithms to define cellular clusters agnostically (Raychaudhuri’s lab). Our in house analytical pipeline (MASC: “Mixed model association of single cells”) will be compared with conventional biaxial gating and commercially available packages like CITRUS.

Results: Preliminary data on 10 healthy controls (HC) and 10 RA patients were available for analysis. Traditional biaxial gating showed large differences in the proportions of both Th1 cells (1-9 % in RA and 5-15 % in HC) and Th17 cells (0-9 %) within and between RA and HC. Depending on IFNγ and IL-17A expression in CD4+ T cells, individuals could be classified into 4 immunophenotypes: ‘Th1’, ‘Th17’, ‘double positive’, and ‘double negative’. CITRUS identified 3 clusters of cells which were significantly different in abundance between the HC and RA groups. As an example, one cluster was CD4+CD38+, had characteristics of regulatory T cells and was less abundant in RA. Preliminary analysis of the drug response data showed a strong increase in Th1 cells in responders seen only after in vitro stimulation, together with an increase of CD40L+CD4+ and CD40L+CD8+ T-cells.

Conclusion: These preliminary analyses show the potential of our study design to capture RA heterogeneity at the single cell level. Importantly, sample size needs to be increased and analytical algorithms further developed, which
An Abundance of Butyrate-Producing Bacterium in the Intestine and Increased Foxp3 Gene Expression of T Cells in Patients with Relapsing Polychondritis

Jun Shimizu, Takao Kubota and Noboru Suzuki, 1Department of Immunology and Medicine, St. Marianna University School of Medicine, Kawasaki, Japan, 2The Japan Self Defense Forces Central Hospital, Tokyo, Japan, 3Department of Immunology and medicine, St. Marianna University School of Medicine, Kawasaki-shi, 216-8511, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: T Cell Biology and Targets in Autoimmune Disease Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Helper T cell subsets including Th17 cells and regulatory T (Treg) cells play a role in the adaptive immune response. RORC and Foxp3 are master regulators of Th17 and Treg cells, respectively, and the gene expressions are suggested to be unstable in vivo. Th17 cells re-differentiated into unconventional Th1 cells (Th17/Th1 type cell conversion) and Treg cells converted into Th17 cells (Treg/Th17 type cell conversion) in experimental transplantation models. The converting T cells were more pathogenic in the lesions than conventional cells.

Recently, researchers found that gut microbes had close relationships with Th17 cell and Treg cell induction in the animals and humans. Intestinal colonization of segmented filamentous bacteria and short chain fatty acid (SCFA)-producing bacteria induce Th17 and Treg cells, respectively, and modulates the systemic inflammation of diseased mice. SCFAs in the intestine are important not only as Treg cell differentiators but also as major energy sources for the colonic wall.

We have reported characteristic features of gut microbiota and Th17/Th1 type T cell conversion shown in patients with Behcet's disease (PLoS One 2016;11:e0153746, Clin Rheumatol 2016;35:1857–63). The metagenomics suggested an intestinal depletion of SCFAs in the patients. We then analyzed fecal metagenomic and T cell gene expression data of patients with relapsing polychondritis (RP).

Methods: We explored fecal microbiota of 10 patients with RP and 16 normal individuals (NI) by sequencing of 16S rRNA gene. We calculated relative abundance of bacterial taxa using QIIME software. We stimulated peripheral
blood mononuclear cells of 9 RP patients and 10 NI with lectin and measured Th17/Treg cell-related gene expressions.

**Results:** The sequencing data showed that the family Ruminococcaceae and the species Faecalibacterium prausnitzii increased significantly in RP patients compared with NI. The species is one of the major butyrate (a SCFA)-producing bacteria of the human intestine. RP T cell gene expression analyses revealed that Foxp3 gene expression increased remarkably in RP patients compared with NI. We observed that RORC gene expression increased significantly with antigen stimulation in RP patients. Thus, RP T cells were suggested to demonstrate Treg/Th17 type cell conversion in the in vitro assay.

**Conclusion:** We consider that RP-specific gut microbes with the increased butyrate production may induce and maintain Treg cells in the intestine. The gut differentiated RP Treg cells may associated with subsequent inflammatory processes and their conversion into pathogenic Th17 cells in the absence of butyrate.

**Disclosure:** J. Shimizu, None; T. Kubota, None; N. Suzuki, None.


**Abstract Number: 1738**

**The Pattern of Proinflammatory Cytokine Expression By CD4+ T Lymphocytes Segregates the Clinical Response to Methotrexate in Recently Diagnosed Rheumatoid Arthritis Patients**

**Jorge Monserrat Sanz**, Ana Maria Gómez Lahoz, Cristina Bohórquez Heras, Maria Dolores Sosa Reina, Atusa Movasat, Ana Pérez Gómez, Lucía Ruiz Gutiérrez, Ana Sánchez Atrio, Eduardo Cuende Quintana, Maria José León, David Diaz, Fernando Albarrán Hernández and Melchor Alvarez-Mon. Laboratory of Immune System Diseases, Deparment of Medicine and Medical Specialties. IRYCIS. University of Alcalá. Madrid. Spain, Alcalá de Henares. Madrid, Spain, Laboratory of Immune System Diseases, Deparment of Medicine and Medical Specialties. IRYCIS. University of Alcalá. Madrid. Spain, Alcalá de Henares, Madrid, Spain, University Hospital Príncipe de Asturias, Immune System Diseases, Rheumatology Department, Alcalá de Henares, Madrid, Spain

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** T Cell Biology and Targets in Autoimmune Disease Poster I  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**
Mechanisms regulating the autoimmune response in rheumatoid arthritis (RA) are not well understood. However, it is known that T CD4+ lymphocytes play a pivotal role initiating and perpetuating the synovial and systemic chronic inflammation found in the disease. Methotrexate (MTX) is the most commonly used Disease-modifying antirheumatic drugs (DMARD) in RA patients. Regrettably, less than thirty percent of these patients do not respond to MTX and need to initiate additional treatments. The potential role of CD4+ T lymphocytes in the MTX clinical response in early RA remains unknown.
The objective of this study is to evaluate the relevance of the pattern of IFNγ, IL-4 and IL-17A production by naïve (T_N), central memory (T_CM), non-terminated effector memory (T_NTEM) and terminated effector memory (T_TEM) CD4+ T cells for the clinical response to MTX in recently diagnosed DMARD naïve RA patients.

Methods:

The number of IFNγ, IL-4, and IL-17A producing CD4+ T lymphocytes, and in their T_N, T_CM, T_NTEM and T_TEM subsets in forty DMARD naïve recently diagnosed RA patients were assayed using a multiparametric flow cytometry. The patients were treated with weekly MTX and the clinical response to the treatment was established after six month of MTX follow up. The patients were classified as responders or non-responders. We also studied twenty-five age and sex-matched healthy subjects as controls. Peripheral blood mononuclear cells (PBMC) were obtained and stimulated during six hour with phorbol-myristate-acetate and ionomycin. To study the intracellular cytokine production by CD4+ T lymphocyte subsets, we used monoclonal antibodies specific for the surface antigens CD3, CD4, CD45RA, CD27 and cells were fixed and permeabilized, and simultaneously stained with IFNγ, IL-4, and IL-17 intracellular cytokines. We acquired in a FacsAria-II flow cytometer and analyzed by FacsDiva and Flow-Jo software.

Results:

At basal pretreatment conditions, MTX non-responder RA patients showed a significant increased number of CD4+IL-17+T lymphocytes with respect to responder RA patients, explained by an expansion of the CD4+IL-17+T_N and CD4+IL-17+T_CM subsets. The number of CD4+IFNγ+ T lymphocytes was significantly increased in MTX non-responder RA patients with respect to that of responders. This elevated CD4+IFNγ+T lymphocyte number was due to an increase in the CD4+IFNγ+T_N, CD4+IFNγ+T_CM and CD4+IFNγ+T_NTEM subset numbers found in non-responder RA patients. There were not significant differences in the CD4+IL-4+T lymphocyte numbers between MTX responder and non-responder AR patients at basal conditions.

Conclusion:

Recently diagnosed DMARD naïve RA patients who eventually do not respond to MTX treatment show an abnormal increased numbers of the circulating IL-17A and IFNγ producing T_N and T_CM CD4+ lymphocytes with respect to MTX responder RA patients. These IL-17A and IFNg abnormalities in naïve T CD4 lymphocytes might be a good biomarker for the clinical response to MTX in DMARD naïve recently diagnosed RA patients.

Disclosure: J. Monserrat Sanz, None; A. M. Gómez Lahoz, None; C. Bohórquez Heras, None; M. D. Sosa Reina, None; A. Movasat, None; A. Pérez Gómez, None; L. Ruiz Gutiérrez, None; A. Sánchez Atrio, None; E. Cuende Quintana, None; M. J. León, None; D. Diaz, None; F. Albarrán Hernández, None; M. Alvarez-Mon, None.


Abstract Number: 1739

Vδ1, Vδ2, and Other γδT Cells in Blood and Synovium of Rheumatoid Arthritis and Other Autoimmune Arthritides

Anna Helena Jonsson1, Michael Gurish1, Lauren Henderson2, Peter Nigrovic1 and Michael Brenner3, 1Division of Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston,
Background/Purpose: Innate-like T cells comprise on average 10-15% of peripheral T cell and have T-cell receptors (TCRs) that engage ligands other than classic HLA class I or class II molecules displaying peptide. These cell types are characterized by a poised state at baseline, enabling rapid cytokine production upon stimulation. Innate-like T cells include natural killer T (NKT) cells, mucosal associated invariant T (MAIT) cells, and γδT cells, which in turn are divided into subsets based on their TCRδ gene expression (Vδ1, Vδ2, Vδ3, etc). The exact ligands for most γδTCR subsets are not clear, and there are indications that γδT cells can be activated independently of the TCR via NKG2D, which binds stress-induced ligands such as MICA and MICB, which are expressed in inflammatory synovium.

Methods: Synovial fluid mononuclear cells were collected from patients with clinical diagnoses of seropositive rheumatoid arthritis (RA), seronegative RA, spondyloarthritis (SpA), and juvenile idiopathic arthritis (JIA). Peripheral blood mononuclear cells were collected from patients with seropositive RA, seronegative RA, SpA, and JIA and from healthy controls (HC). We assessed the frequency and phenotypes of Vδ1, Vδ2, and other γδT cells using flow cytometry. We also stimulated synovial fluid mononuclear cells with CD3/CD28 beads or with phorbol myristate acetate (PMA) and ionomycin and measured cytokine production by Vδ1 and Vδ2 cells by intracellular cytokine staining. Statistics were performed by Kruskal-Wallis test.

Results: Vδ1 cells are enriched in synovial fluid from patients with JIA (7.61±4.07% vs 0.78±0.57% in HC blood, p<0.05), whereas non-Vδ1/Vδ2 γδT cells are elevated in synovial fluid from seropositive RA (7.20±4.05% vs 0.48±0.15% in seropositive RA blood, p<0.01). While a high frequency of all γδT cell subsets expressed NKG2D, other surface markers differed between γδT cell subsets and between blood and synovial fluid γδT cells. For example, CD69 was expressed at a high frequency on all three γδT cell subsets from synovial fluid from all four types of autoimmune arthritis but not from blood. CD25 is expressed at a higher rate among non-Vδ1/Vδ2 γδT cells from seropositive RA synovial fluid than from any of the other synovial fluid groups or from blood (36.7±16.4% vs 8.8±2.2% in seropositive RA blood, p<0.01). PD-1 was expressed by about half of Vδ1 and non-Vδ1/Vδ2 γδT cells from blood and was upregulated mainly on non-Vδ1/Vδ2 γδT cells in synovial fluid. Vδ2 cells, in contrast, expressed PD-1 at a low frequency in both blood and synovial fluid. Upon stimulation with PMA and ionomycin, both Vδ1 and Vδ2 cells from synovial fluid of all four types of autoimmune arthritis produced IFNγ and TNF at robust frequencies. However, only Vδ1 cells produced IL17A, with a frequency similar to CD4 T cells.

Conclusion: These findings suggest that Vδ1, Vδ2, and non-Vδ1/Vδ2 γδT cells represent cell populations with distinct functions in the blood and synovial fluid from patients with autoimmune arthritis. Additional studies are needed to further elucidate their roles in RA pathogenesis.

Disclosure: A. H. Jonsson, None; M. Gurish, None; L. Henderson, None; P. Nigrovic, None; M. Brenner, None.
Fc-Derived Immunodominant Peptides Stimulate Natural Regulatory T Cells: A New Avenue to Overcome Defects in the Fc Antigen Processing and Restore Immune Regulation in Rheumatic Diseases

Alessandra Franco, Pediatrics, University of California San Diego School of Medicine, La Jolla, CA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: T Cell Biology and Targets in Autoimmune Disease Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
The mechanisms of action of intravenous purified immunoglobulins (IVIG) in acute Kawasaki disease (KD) have been investigated in our laboratory and have led to a surprising revelation about the antiinflammatory effects of the constant region (Fc) of the IgG1 molecule: the expansion of Fc-specific natural (n) regulatory T cells (nTreg). This is the most relevant effferent arm of the immune response induced by IVIG in these patients as the development of arterial complications (CAA) correlates with lack of Fc-specific nTreg after therapy. We previously identified 16 Fc-derived peptides (15 amino acids long) that expand nTreg in vitro from KD patients after IVIG and healthy adult controls and determined their HLA binding affinity. Here we studied the response in vitro to the 16 most immunogenic Fc peptides in PBMC from KD subjects after IVIG, adult rheumatoid arthritis (RA) subjects and healthy adult donors to rank their immunodominance for pre-clinical development.

Methods:
The immunogenicity of Fc peptides was tested in vitro by stimulating PBMC with individual Fc peptides and Fc protein as a control (4x10^5 cells /w in 96 flat bottomed plate) and by screening at day 4 for nTreg expansion with two analyses: 1) FACS staining to enumerate CD4+ CD25high T cells and 2) measurement of IL-10 by ELISA in culture supernatants.

Results:
nTreg from KD and RA patients responded poorly to the whole Fc protein but did respond to Fc peptides. KD subjects after IVIG, and healthy donors showed a similar pattern of nTreg response to Fc peptides. Fc 181-195 that binds multiple class II HLA alleles was immunodominant in the three cohorts. After IVIG, the large majority of KD patients recognize Fc 51-65 and Fc 56-70, which are promiscuous for HLA binding. Fc 21-35, with a monogamous HLA restriction to a common allele in the general population, was also immunodominant in the three cohorts. In the KD cohort, peptide-specific nTreg responses were documented even in children who developed CAA and whose PBMC failed to respond to the intact Fc after IVIG treatment.

Conclusion:
KD subjects prior to IVIG and RA subjects showed poor nTreg response to the intact Fc, but an excellent response to Fc peptides. These results highlight a possible defect in the antigen processing that jeopardizes immune regulation in rheumatic diseases that can be restored by immunodominant pan-HLA Fc peptides.

Disclosure: A. Franco, None;
Abstract Number: 1741

Tolerance and Efficiency of Anti-Programmed Death 1 Antibodies in Patients with Cancer and Preexisting Autoimmune or Inflammatory Diseases

Francois-Xavier Danlos¹, Anne-Laure Voisin², Valérie Dyevre³, Jean-Marie Michot¹, Emilie Routier⁴, Laurent Taillade³, Stéphane Champiat¹, Sandrine Aspeslagh¹, Julien Haroche⁶, Laurence Albige⁷, Christophe Massard¹, Nicolas Girard⁸, Stéphane Dalle⁹, Benjamin Besse⁷, Salim Laghouati², Jean-Charles Soria¹, Christine Mateus⁴, Caroline Robert⁴, Emilie Lanoy³, Aurélien Marabelle¹,²,¹⁰ and Olivier Lambotte¹¹,¹ Drug Development Department, Gustave Roussy Institut, Villejuif, France, ²Unité Fonctionnelle de Pharmacovigilance, Gustave Roussy Institut, Villejuif, France, ³Service de biostatistique et d’épidémiologie, Gustave Roussy Institut, Villejuif, France, ⁴Department of dermatology, Gustave Roussy Institut, Villejuif, France, ⁵Department of medical oncology, Pitié Salpêtrière Hospital, Paris, France, ⁶Internal Medicine 2. Referal center for SLE/APS, Hôpital Pitié-Salpêtrière, AP-HP, UPMC Univ Paris 06 & French National Reference Center For Systemic Lupus and Antiphospholipid Syndrome, Paris, France, ⁷Department of medical oncology, Gustave Roussy Institut, Villejuif, France, ⁸Department of Respiratory Medicine, National Expert Centre for Thymic Malignancies, Hôpital Louis Pradel, Hospices Civils de Lyon, Lyon, France, ⁹Department of dermatology, Centre Hospitalier Lyon Sud, Hospices Civils de Lyon, Lyon, France, ¹⁰Immunotherapy program, Gustave Roussy Institut, Villejuif, France, ¹¹Internal Medicine, Hospital Kremlin Bicêtre, Kremlin Bicêtre, France

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: T Cell Biology and Targets in Autoimmune Disease Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

Patients with auto-immune or inflammatory diseases (AID) treated by immune check-points inhibitors (ICI) are intrinsically susceptible to develop immune related adverse events (irAE). We conducted this study to describe and analyze the tolerance and efficiency of anti-PD-1 antibodies in AID patients and to look for a clinical association between these preexisting immune conditions and patient’s outcome.

Methods:

We described patients with AID treated by ICI and conducted a prospective study in patients receiving anti-PD-1 antibody included in the registry REISAMIC (“Registry of Severe Adverse Events of Immunomodulating Monoclonal Antibodies in Oncology”) between 1st June 2014 and 31th December 2016. We analyzed the association between preexisting autoimmune disorder and irAE-free survival and overall survival.

Results:

We described 54 AID patients treated by ICI (mainly anti-PD-1 antibodies) including 45 AID patients which were analyzed and compared to non-AID patients among 397 patients from the registry REISAMIC. Cancer diagnoses included melanoma in 40 cases (74,1%), NSCLC in 10 cases (22,2%) and other cancers in 4 cases (2 renal cell
carcinoma and urothelial carcinoma). Preexisting autoimmune or inflammatory diseases were vitiligo (n=17, 31.5%), cutaneous psoriasis (n=13, 32.5%), auto-immune thyroiditis (n=8, 20%), Sjögren syndrome (n=4, 10%), rheumatoid arthritis (n=4, 10%), auto-immune cytopenia (n=3, 17.5%), spondyloarthritis (n=2, 5%), multiple sclerosis (n=2, 5%) hidradenitis suppurativa (n=2, 5%), and in one case each: myasthenia gravis, polymyalgia rheumatica, polyarteritis nodosa, sarcoidosis, chronic cutaneous lupus, type 1 diabetes, primary nephrotic syndrome, acute tubulo-interstitial nephritis and aseptic abscesses syndrome. 10 patients had two concomitant different AID (18.5%). In 23 cases (42.6%), patient presented at least one grade 2 CTCAE irAE. Among them, 13 irAE (57%) were associated with a preexisting AID: increase of cutaneous psoriasis, development of psoriatic arthritis and pustular psoriasis, extension of vitiligo, hyperthyroidism, exacerbation of Sjögren’s syndrome, myasthenia crisis, polyarthritis or mesenteric abscesses leading to death. Eleven patients developed irAE which were not associated with the AID. 33 patients (61.1%) were alive at the last follow-up with a median time of 6.3 months (range 4.1-9.7 months). 19 patients (35.2%) pursued anti-PD-1 treatments at last follow-up with a median time of 4.9 months (range 3.4-7 months).

The irAE free survival was shorter in AID patients (median=5.4 months) as compared with non-AID patients (median=13 months, p=2,1.10^-4). Overall survival in AID patients did not differ to the one observed in non-AID patients (p= 0.38).

Conclusion:
In patients treated by anti-PD-1 antibodies, autoimmune and inflammatory diseases was associated with a higher risk of immune related adverse events and particularly flares which could be severe and fatal. AID and non-AID patient’s overall survival were not different. These points increase the importance of networks of collaborations between oncologists, organs specialists, and clinical immunologists to improve patients care.

Disclosure: F. X. Danlos, None; A. L. Voisin, None; V. Dyevre, None; J. M. Michot, BMS, 4; E. Routier, BMS, Roche, Novartis, Merk, Amgen, 4; L. Taillade, None; S. Champiat, AstraZeneca, BMS, Janssen, MSD, Roche, 4; S. Aspeslagh, None; J. Haroche, None; L. Albiges, None; C. Massard, Amgen, Astellas, Astra Zeneca, Bayer, Celgene, Genentech, Ipsen, Jansen, Lilly, Novartis, Pfizer, Roche, Sanofi Orion, 4; N. Girard, BMS MSD, AstraZeneca, OSE, Merck, Serono and Roche, 4; S. Dalle, Roche, Amgen, MSD, Merck, BMS, 4; B. Besse, None; S. Laghouati, None; J. C. Soria, None; C. Mateus, Merck, BMS, Pfizer, 4; C. Robert, Roche, BMS, MSD, merck, Amgen, Novartis, 5; E. Lanoy, None; A. Marabelle, None; O. Lambotte, MSD, Genzyme, 5.


Abstract Number: 1742

Involvement of T Helper 17 Cells in Inflammatory Arthritis Depends on the Host Intestinal Microbiota

Heather Evans-Marin1, Rebecca Rogier2, Jose U. Scher3, Debbie M. Roeleveld2, Marijke I. Koenders4 and Shahla Abdollahi-Roodsaz5,6,

1Division of Rheumatology, New York University School of Medicine, New York, NY, 2Experimental Rheumatology, Radboud University Medical Center, Nijmegen, Netherlands, 3New York University School of Medicine, New York, NY, 4Experimental Rheumatology, Radboud university medical center, Nijmegen, Netherlands, 5Department of Medicine, Division of Rheumatology, New York University School of Medicine, New York, NY, 6Rheumatology, Radboud University Medical Center, Nijmegen, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
**Session Date:** Monday, November 6, 2017  
**Session Title:** T Cell Biology and Targets in Autoimmune Disease Poster I  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The intestinal microbiota has been associated with psoriatic and rheumatoid arthritis. One of the major effects of microbiota is the induction of mucosal T helper 17 (Th17) cells. We therefore reasoned that the efficacy of Th17-targeted therapies in arthritis may depend on the host microbiota. Previous studies focused on the role of the cytokine interleukin-17A (IL-17), rather than Th17 cells, by using IL-17 inhibitors or IL-17-deficient mice. Therefore, the role of Th17 cells, which produce multiple pro-inflammatory mediators in addition to IL-17, is not yet fully understood. The aim of this study was to determine the role of Th17 cells, beyond the cytokine IL-17, in arthritis, and to investigate whether Th17 cells are differentially involved in arthritis depending on the microbiota present.

**Methods:** We established conditional Th17-deficient mice, which exhibit a CD4-Cre-induced floxing of a part of the Rorc allele that encodes the Th17 master regulator RORγt. We compared the development of collagen-induced arthritis in Th17-deficient (CD4-Cre+ Rorc^flox/flox^) littermate mice, either colonized with known Th17 cell inducers segmented filamentous bacteria (SFB) or harboring the SFB-free Jackson microbiota. The abundance of Th1 and Th17 cells and the production of IL-17, IFNγ and GM-CSF were quantified by flow cytometry and multiplex cytokine assay.

**Results:** CD4-Cre^+ T cells and Gr1^+ neutrophils being the main alternative sources of IL-17. Despite this increased total IL-17 levels, conditional Th17-deficient mice developed a less severe arthritis compared with Th17-sufficient mice when intestinal microbiota comprised SFB. This suggests a role for Th17 cells in inflammatory arthritis distinct from IL-17. Accordingly, synovial inflammation, cartilage destruction and proteoglycan depletion were reduced in SFB-colonized Th17-deficient mice. While the production of IL-17 by joint-draining lymph node cells stimulated with PMA and ionomycin was similar between Th17-sufficient and –deficient mice, cells from the latter group produced significantly less IL-17 upon antigen-specific stimulation with type II collagen. Furthermore, the production of GM-CSF, another Th17 cell-derived cytokine, was significantly lower in the lymph nodes of Th17-deficient mice, an effect associated with the protection against arthritis. Importantly, substitution of the intestinal microbiota with SFB-free Jackson microbiota resulted in the loss of Th17 cell dependency of arthritis as Th17-sufficient and –deficient mice showed similar disease progression under this condition.

**Conclusion:** These data suggest that Th17 cells may mediate inflammatory arthritis partly through IL-17-independent mechanisms. Our observations also suggest that the involvement of Th17 cells in arthritis depends on the composition of the microbiota present in the host. Therefore, a microbiome-guided stratification of rheumatoid or psoriatic arthritis patients might improve the efficacy of Th17 (or IL-17)-targeted therapies.

**Disclosure:** H. Evans-Marin, None; R. Rogier, None; J. U. Scher, NIAMS-NIH, 2; D. M. Roeleveld, None; M. I. Koenders, None; S. Abdollahi-Roodsaz, None.


**Abstract Number:** 1743

**Serine Arginine/Rich Splicing Factor 1 (SRSF1) Increases IL-2 Production in T Cells By Increasing the Expression of NFAT and c-Fos**

Takayuki Katsuyama¹, Michael W. Mosho¹, George C. Tsokos¹ and Vaishali R. Moulton², ¹Division of Rheumatology, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston,
Background/Purpose: T cells from patients with systemic lupus erythematosus (SLE) produce insufficient amounts of the vital cytokine IL-2, and the molecular mechanisms leading to this defect are not fully known. IL-2 deficiency is critical in autoimmunity, because it is not only important for T cell responses but also for the maintenance and function of regulatory T cells (Tregs). We previously identified a novel role of the multifunctional protein serine arginine-rich splicing factor 1 (SRSF1) in the regulation of IL-2. We showed that SRSF1 is decreased in T cells from SLE patients, and associates with severe disease activity. Importantly, force expression of SRSF1 into SLE T cells rescues IL-2 production. We showed that SRSF1 enhances IL-2 production via transcriptional activation, however the molecular mechanisms underlying this regulation are not fully known. SLE T cells exhibit aberrant expression/function of the IL-2 regulating transcription factors NFκB, c-jun/c-fos (AP1) and NFAT. Here we asked whether SRSF1 controls IL-2 through the regulation of these factors.

Methods: T cells were isolated by negative selection from peripheral blood from healthy donors. SRSF1 was overexpressed in human T cells by transient transfection. T cell-restricted conditional Srsf1-cko mice were generated by crossing Srsf1-flox mice with d.Lck.Cre mice. Expression levels of NFAT, c-fos, and NFκB were assessed by quantitative RT-PCR and western blotting. To determine the recruitment of transcription factors to the IL-2 promoter, reporter-chromatin immunoprecipitation (R-ChIP) assays were performed in human T cells by transfection of an IL-2-promoter luciferase construct and SRSF1 overexpression. Cross-linked DNA-protein complexes were immunoprecipitated with appropriate antibodies, and purified DNA was amplified by quantitative PCR. T cells were stimulated with anti-CD3/CD28 or PMA and Ionomycin, and IL-2 production measured by intracellular cytokine staining and ELISA.

Results: Overexpression of SRSF1 enhanced IL-2 expression in human T cells. Further, SRSF1 overexpression led to increased mRNA and protein levels of NFAT and c-fos but not NFκB. In parallel, T cells from Srsf1-cko mice produced lower amounts of IL-2 and showed decreased expression levels of NFAT after stimulation with anti-CD3/CD28. To ask if SRSF1 affects the recruitment of NFAT and c-fos to the IL-2 promoter, R-ChIP assays were performed using SRSF1-transfected human T cells. An increased recruitment of NFAT and c-fos to the IL-2 promoter was observed in SRSF1-transfected compared to control-transfected cells. These results indicate that SRSF1 increases expression of NFAT and c-fos and their recruitment to the IL-2 promoter to increase transcriptional activity of IL-2.

Conclusion: SRSF1 increases the expression of NFAT and c-fos transcription factors to activate IL-2 production. These results suggest that decreased SRSF1 represents an important molecular defect which contributes to the IL-2 deficiency in SLE.

Disclosure: T. Katsuyama, None; M. W. Mosho, None; G. C. Tsokos, GSK, 5; V. R. Moulton, None.

Abstract Number: 1744
Transcriptome Profile of Inflammation Inducted Circulating Effector and Regulatory T Cells Is Dominated By HLA-DR Pivoted Functional Networks in Active Juvenile Idiopathic Arthritis Patients

Jing Yao Leong1, Salvatore Albani2, Pavanish Kumar2, Joo Guan Yeo3, Phyllis Chen1, Sharifah Nur Hazirah2, Camillus Chua2, Suzan Saidin2, Justin Hung Tiong Tan3, Thaschawee Arkachaisri3, Alberto Martini4, Marco Gattorno5 and Alessandro Consolaro6, 1Singhealth Translational Immunology and Inflammation Centre (STIIC), Duke-NUS Medical School, Singapore, Singapore, 2SingHealth Translational Immunology and Inflammation Centre (STIIC), Duke-NUS Medical School, Singapore, Singapore, 3Rheumatology and Immunology Service, KK Women's and Children's Hospital, Singapore, Singapore, 4PRINTO Coordinating Centre, Genoa, Italy, 5Pediatric Rheumatology, G. Gaslini Institute, Genoa, Italy, 6Pediatria II, Reumatologia, Istituto Giannina Gaslini, Genoa, Italy

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: T Cell Biology and Targets in Autoimmune Disease Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
We have previously identified two dichotomous CD4 pathogenic subsets in both T effector (CPLs: Circulating pathogenic like lymphocytes) and T regulatory (iaTreg: inflammation associated Treg) compartments that are both HLA-DR+, antigen experienced, pro-inflammatory, correlating with disease activity and sharing strong TCR sequence oligoclonality with synovial T cells from JIA patients. Despite being two functionally disparate T cell subsets, their phenotype and association with clinical fate suggests that these functionally discordant subsets may originate from a common precursor. To elucidate the common pathogenic gene drivers and their associated network of pathways within these two pathogenic subsets, we decided to perform next generation RNA sequencing on sorted CPLs and iaTregs and their conventional Teff/Treg counterparts.

Methods:
CPLs were sorted as CD3+ CD4+ CD14- HLA-DR+ CD25/CD127 Teff gate, and iaTregs were sorted as CD3+ CD4+ CD14- HLA-DR+ CD25hi/CD127low Treg gate with FACs Aria II from n=8 active JIA PBMCs. As a comparative control, similar HLA-DR- counterparts were respectively sorted from the same patients. Sorted cells were lysed and extracted for RNA, and cDNA libraries were ran on the Illumina HiSeq High output platform. RNA-Seq raw reads were mapped to human genome using STAR aligner with default options and reads were summarised at gene level by feature Count programme. Differential expression analyses were performed using edgeR package, and pathway enrichments under R statistical environment and Reactome.

Results:
Comparative gene expression analysis, between CPLs vs iaTreg and that of the common pool of Teff vs Treg, and phylogenetic association analysis suggests both CPLs and iaTregs are uncoupled and group separately from their conventional T cell compartments. TCR sequence oligoclonality in CPLs/iaTregs versus that of the common pipeline by feature Count programme. Differential expression analyses were performed using edgeR package, and pathway enrichments under R statistical environment and Reactome.
complement, and apoptosis. Transcription factors (TFs) gene regulatory network (TF-GRN) analysis identified the key regulatory molecules driving the convergence of pathogenic CPL and iaTreg populations. Global TF-GRN network analysis identified FOXP3, CEBP, SPI and E2F1 as key TFs driving the Teff, Treg to pathogenic iaTreg and CPLs, respectively.

**Conclusion:**

These mechanistic data strongly suggest shared pathogenic and developmental pathways for two T cell subsets and are strongly associated with clinical fate in autoimmune human arthritis. These pathways are probably shaped from a shared precursor in an inflammatory microenvironment.

**Disclosure:**

J. Y. Leong, None; S. Albani, None; P. Kumar, None; J. G. Yeo, None; P. Chen, None; S. Nur Hazirah, None; C. Chua, None; S. Saidin, None; J. H. T. Tan, None; T. Arkachaisri, None; A. Martini, None; M. Gattorno, None; A. Consolaro, None.


**Abstract Number:** 1745

**Autophagic Memory in Stress Experienced Human T Cells**

**Pavanish Kumar**1, Jorg van Loosdregt2, Suzan Saidin1, Bhairav Paleja1 and Salvatore Albani1, 1SingHealth Translational Immunology and Inflammation Centre (STIIC), Duke-NUS Medical School, Singapore, Singapore, 2Laboratory for Translational immunology, University Medical Center Utrecht, Utrecht, Netherlands

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** T Cell Biology and Targets in Autoimmune Disease Poster I

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Autophagy is central to many key immune related pathways, disregulation of which has been associated with rheumatoid arthritis (RA), cancer and neurodegenerative diseases. Autophagy is required for memory T cell generation and maintenance. Previous studies from our group showed higher levels of autophagy in CD4+ T cells from RA patients. Flow cytometry analysis of T cells from healthy individual indeed showed higher autophagy levels in memory CD4 and CD8 cells after activation, compared to naive T cells. However the basal level of autophagy was similar in both cell types, suggesting a memory for autophagy. Here, we hypothesise that T cells which experience immunological encounters and activation, attain, when compared to naive cells, heightened autophagic levels when a similar stimulus is encountered again, a phenomenon, which we term “autophagic memory” which may be pathogenically relevant.

**Methods:**

To dissect the molecular mechanisms of autophagic memory, we trained human T cells in low serum medium, to elicit stress-induced activation, for 5 days. The cells were then cultured in 10% serum media for 100 generations and
subjected to RNAseq and Methylome analyses at various time points. Primary cells from RA patients were sorted using flowcytometry followed by quantitative PCR analyses.

Results:

RNA-sequencing and methylome analysis of the trained and control cells at 5, 30,70 and 100 generations identified clusters of genes stably up or down regulated in trained cells compared to control cells until the 30th generation. These short term expression minor (STEM) gene expression profiles represented pathways related to stress, immunity and metabolism, all of which are critical contributors to the onset and modulation of the autophagic process. A transcription factor gene network reconstruction at the system level using ENCODE and HTrib data identified intersecting key regulatory genes for autophagic memory. Specifically, some key genes with roles in autophagy were also shown to be epigenetically modified in response to the starvation stimulus that was sustained over 30 generations suggesting a role for these genes in retention of autophagic memory. Importantly, gene expression analyses of primary CD4+T cells from RA patients recapitulated this observation, demonstrating a clinically relevant molecular signature that could contribute to autophagic memory in these cells.

Conclusion:

We describe here epigenetic and transcriptional elements which determine and control persistence of autophagic memory in experienced T cells. Based on our data which are reproducible both in healthy and diseases samples, we suggest that autophagic memory is an integral part of efficient activation of memory T cells, and it also contributes to persistence of T cell mediated inflammation in autoimmunity.

Disclosure: P. Kumar, None; J. van Loosdregt, None; S. Saidin, None; B. Paleja, None; S. Albani, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/autophagic-memory-in-stress-experienced-human-t-cells

Abstract Number: 1746

mTOR Pathway Activation in Takayasu Arteriti

Cloé Comarmond1, Aurélie Leroyer2, Zeidan Mohamad3, Jean-Pierre Foure4, Fabien Koskas5, Philippe Cluzel6, Anna Maciejewski-Duval7, Marlène Garrido8, Patrice Cacoub9 and David Saadoun10, 1DHU 2iB Internal Medicine Referral Center for Autoimmune diseases Pitie Hospital, Paris, France, 2Hopital de Marseille, Marseille, France, 3Hopital Neckar, Paris, France, 4Groupe Hospitalier Pitié-Salpêtrière, Paris, France, 5Department of vascular surgery, Assistance Publique-Hôpitaux de Paris (AP-HP), Paris, France, 6Department of cardiovascular imagery, Assistance Publique-Hôpitaux de Paris (AP-HP), Groupe Hospitalier Pitié Salpêtrière, 83 Boulevard de l'Hôpital, 75013, Paris, France., 7GHPS, Paris, France, 8I3 laboratory, Pitié-Salpêtrière, Paris, France, 9Department of Internal Medicine and Clinical Immunology, Groupe Hospitalier Pitié-Salpêtrière, Paris, France, 10Sorbonne Universités, UPMC Univ Paris 06, UMR 7211, and Inflammation-Immunopathology-Biotherapy Department (DHU i2B), F-75005, Paris, France; INSERM, UMR S 959, F-75013, Paris, France; CNRS, FRE3632, F-75005, Paris, France; AP-HP, Groupe Hospitalier, Paris, France

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: T Cell Biology and Targets in Autoimmune Disease Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM
**Background/Purpose:** mTORC1 drives the proinflammatory expansion of T helper (TH) type 1, TH17 cells and controls fibroblast proliferation, typical features of Takayasu arteritis (TA) pathogenesis. Molecular pathways involved in arterial lesions of TA are unknown.

**Methods:** We evaluate pathway activation in the mammalian target of rapamycin complex (mTORC) and the nature of cell proliferation in the vessels of patients with TA by using double immunostaining, western blot and flow cytometry.

**Results:** Proliferation of both endothelial cells and vascular smooth-muscle cells was shown in vascular lesions in TA. The vascular endothelium of proliferating aorta vessel from patients with TA showed indications of activation of the mTORC1 pathway. In cultured vascular endothelial cells, sera from patients with TA stimulated mTORC1 through the phosphatidylinositol 3-kinase (PI3K)–AKT pathway. Activation of mTORC was also found in Th1 and Th17 cells both systemically and in the blood vessels. Patients with TA exhibited a diminished AKT phosphorylation in Tregs. Inhibition of mTOR pathway with rapamycin increase Treg and decrease CD4+IFN+, CD4+IL17+ and CD4+IL21+ cells in patients with TA.

**Conclusion:** Our results suggest that the mTORC pathway is involved in the vascular lesions of Takayasu arteritis. Rapamycin could restore T cells homeostasis in patients with TA.

**Disclosure:** C. Comarmond, None; A. Leroyer, None; Z. Mohamad, None; J. P. Fourez, None; F. Koskas, None; P. Cluzel, None; A. Maciejewski-Duval, None; M. Garrido, None; P. Cacoub, None; D. Saadoun, None.

**Human C-C Chemokine Receptor-6 (CCR6)+ Th Memory Cells, Including Th17 and Th17.1 Cells, Change into Anti-Inflammatory Cells with Regulatory Capacity upon Exposure to Vitamin D**

Wendy Dankers1, Nadine Davelaar2, Jan Piet van Hamburg3, Patrick Asmawidjaja2, Hoyan Wen2, Johannes van Leeuwen4, Edgar Colin5 and Erik Lubberts2, 1Rheumatology, Erasmus MC, University Medical Center, Rotterdam, Netherlands, 2Rheumatology and Immunology, Erasmus MC, University Medical Center, Rotterdam, Netherlands, 3Rheumatology, Erasmus MC, Rotterdam, Netherlands, 4Internal Medicine, Erasmus MC, University Medical Center, Rotterdam, Netherlands, 5ZGT Almelo, Deventer, Netherlands

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017
**Session Title:** T Cell Biology and Targets in Autoimmune Disease Poster I
**Session Type:** ACR Poster Session B
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Autoimmune diseases such as RA are driven by an aberrantly activated immune system and an imbalance between pro- and anti-inflammatory cells, resulting in tissue damage and functional disability in patients. In the blood of treatment-naïve early RA patients, especially CCR6+ Th memory cells, including Th17 and Th17.1 cells, are
elevated and more activated compared to healthy controls. Therefore, blocking the full pathogenic potential of CCR6+ Th memory cells to restore the immunological balance in RA is an important challenge. The active vitamin D metabolite 1,25(OH)2D3 can inhibit the various pro-inflammatory cytokines produced by CCR6+ Th memory cells. However, whether 1,25(OH)2D3 also change the phenotype and functional properties of these CCR6+ Th memory cells is not fully elucidated and is the objective of this study.

Methods:

CCR6+ Th memory cells, excluding Tregs, from treatment-naïve early RA patients or healthy controls were sorted and cultured for three days with or without 1,25(OH)2D3 in the presence of anti-CD3 and anti-CD28. After that they were harvested for microarray analysis, RT-PCR, ELISA or flow cytometry. The cultured cells were also used in functional suppression assays, transwell migration assays and exposed to synovial fluid from active RA patients to test phenotype stability.

Results:

Microarray analysis of 1,25(OH)2D3-treated CCR6+ Th memory cells from treatment-naïve early RA patients showed that production of pro-inflammatory factors such as IL-17A, IL-17F, IFNg, IL-22, IL-26 and the Th17-related transcription factor RORC is inhibited. In contrast, anti-inflammatory factors such as IL-10 and CTLA4, but not FoxP3, are induced. To address whether these formerly pathogenic cells also have regulatory capacities, we evaluated their capacity to suppress proliferation of autologous CD3+ T cells. Interestingly, the 1,25(OH)2D3-treated CCR6+ Th memory cells were equally capable of suppressing proliferation of CD3+ T cells as classical Tregs. This confirms that the committed CCR6+ Th memory cells can change their phenotype from pro- to anti-inflammatory with regulatory capacity. Furthermore, we found that the shift in phenotype did not affect their potential to migrate towards the site of inflammation, since 1,25(OH)2D3-treated CCR6+ Th memory cells migrated equally well towards synovial fluid in a transwell migration assay compared to control-treated cells. Finally, we addressed the stability of the change in phenotype. When cells have been exposed to 1,25(OH)2D3 for three days, the anti-inflammatory phenotype is maintained for at least 7 days. Importantly, the cells retain this phenotype upon exposure to an inflammatory environment, modeled by synovial fluid.

Conclusion:

For the first time we show here that human committed pro-inflammatory CCR6+ Th memory cells can shift towards an anti-inflammatory cell with functional regulatory capacities. Furthermore, these cells can migrate towards synovial inflammation and keep their anti-inflammatory phenotype in this environment. Thereby, these 1,25(OH)2D3 treated CCR6+ Th memory cells can contribute to restoring the immunological balance and inhibiting synovial inflammation in RA.

Disclosure: W. Dankers, None; N. Davelaar, None; J. P. van Hamburg, None; P. Asmawidjaja, None; H. Wen, None; J. van Leeuwen, None; E. Colin, None; E. Lubberts, None.


Abstract Number: 1748

Cbl-b Associates with Bcl-6 and Is Differentially Expressed in Circulating Follicular T Helper Cells of Patients with Systemic Lupus Erythematosus
SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: T Cell Biology and Targets in Autoimmune Disease Poster I
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Activation of polyclonal CD4\(^+\) T cells and B cells is a hallmark of human and murine lupus, which suggests a global defect in the maintenance of T and B cell tolerance. Recent studies unveil a central role of T follicular helper (T\(_{FH}\)) cells that is critical in providing help to B cells in the overproduction of pathogenic auto-antibodies leading to tissue damage in systemic lupus erythematosus (SLE). Casitas B-lineage lymphoma proto-oncogene-b (Cbl-b) is an E3 ubiquitin ligase which has been shown to increase the activation threshold of immune cells. Bcl-6 is the master transcription regulator that controls the differentiation of naïve T cells into T\(_{FH}\) cells. A link between Cbl-b/ Bcl-6 and SLE has not been established.

Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from healthy subjects and patients with active or inactive SLE as determined by SLEDAI scores. CD4\(^+\) cells prepared from PBMCs were stained for CXCR5, ICOS, PD-1, and Cbl-b and mean fluorescent intensity (MFI) of Cbl-b was determined for positive cell populations. Additionally, immunoprecipitation (IP) was performed with PBMC lysates from healthy subjects with anti-human Bcl-6 monoclonal antibody, and then probed with rabbit anti-human Cbl-b.

Results: Flow cytometry analysis gating on CXCR5\(^+\), ICOS\(^+\), PD-1\(^+\) T\(_{FH}\) cells demonstrated significantly lower MFIs of Cbl-b in SLE patients relative to healthy controls (P < 0.05). Moreover, Cbl-b levels were lower in active SLE patients than those with less disease activity. At the molecular level, preliminary IP data show that Cbl-b forms a complex with Bcl-6 in human T\(_{FH}\) cells.

Conclusion: The association of Cbl-b and Bcl-6 suggests that Cbl-b could be the E3 ubiquitin ligase for Bcl-6. Down regulation of Cbl-b in the T\(_{FH}\) cells of patients with SLE may be the primary cause of heightened T\(_{FH}\) and germinal center B cells in lupus and the decreased expression of Cbl-b could serve as a biomarker for lupus flares. Ongoing studies examine Cbl-b expression prospectively in SLE patients who have a remitting relapsing disease course and the functional implication of down regulation of Cbl-b on human T\(_{FH}\) cells.
The Epidemiology of ANCA Associated Vasculitis in the U.S.: A 20 Year Population Based Study

Alvise Berti1, Divi Cornec2, Cynthia S. Crowson3, Ulrich Specks4 and Eric L. Matteson5, 1Division of Pulmonary and Critical Care Medicine, Mayo Clinic, Rochester, MN, 2Pulmonary and Critical Care Medicine, Mayo Clinic College of Medicine and Science, Rochester, MN, 3Health Sciences Research, Mayo Clinic College of Medicine and Science, Rochester, MN, 4Mayo Clinic College of Medicine, Rochester, MN, 5Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, MN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Vasculitis Poster II: ANCA-Associated Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: ANCA-associated vasculitis (AAV) is rare, with a worldwide reported annual incidence ranging from 1.2 to 2.0 cases per 100,000 individuals and a prevalence of 4.6-18.4 cases per 100,000 individuals. To date, precise data on AAV incidence, prevalence, and mortality are lacking in the United States (US). We aimed to estimate the incidence, prevalence and mortality rates of AAV and its subsets, granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA), in a US based adult population.

Methods:

All medical records of patients with a diagnosis or suspicion of AAV in a geographically defined region of the US from January 1, 1996 to December 31, 2015 were reviewed. Incidence and prevalence rates were calculated using population denominators for persons aged≥18 years from the US Census with age- and sex-adjustment to the 2010 US white population. Survival rates were compared with expected rates in the population.

Results:

Of 58 incident cases of AAV, 23 (40%) were GPA, 28 (48%) MPA, and 7 (12%) EGPA. Overall, 28 (48%) were women, 57 (98%) were Caucasian, with a mean (SD) age at diagnosis of 61.1 (16.5) years. ANCA was negative in 5 (9%) patients; 34 (61%) were MPO-ANCA and 17 (30%) were PR3-ANCA positive.

The annual incidence of AAV from 1996 through 2015 was 3.3/100,000 population (95%CI:2.4-4.1). GPA, MPA and EGPA incidence was 1.3 (95%CI:0.8-1.8), 1.6 (95%CI:1.0-2.2), and 0.4 (95%CI:0.1-0.6), respectively. Incidence rates by ANCA type were: 0.9 (95%CI: 0.5-1.4) for PR3-AAV, 2.0 (95%CI: 1.3-2.6) for MPO-AAV, and 0.3 (95%CI: 0.0–0.5) for ANCA-negative AAV.
There were 44 patients with prevalent AAV on January 1, 2015 for an overall prevalence rate of 42.1/100,000 (95%CI: 29.6-54.6). Prevalence by clinical diagnosis and ANCA type was: 21.8 (95%CI: 12.9-30.8) for GPA, 18.4 (95%CI: 10.1–26.7) for MPA, 1.8 (95%CI: 0.0–4.4) for EGPA, 19.0 (95%CI: 10.6 –27.3) for PR3-AAV, 19.2 (95%CI: 10.8–27.7) for MPO-AAV, and 2.8 (95%CI: 0.0–6.1) for ANCA-negative AAV.

Standardized mortality ratios (SMR) for AAV overall, and EGPA, MPA and MPO-AAV were increased (2.04, 16.6, 2.04 and 2.17 respectively, \( p < 0.05 \)); whereas mortality of GPA and PR3-AAV did not differ from general population (SMR 0.93 and 1.09, respectively). No death was recorded in ANCA-negative AAV.

**Conclusion:** The annual incidence of AAV in the US is 3.3/100,000, with a prevalence of 42/100,000, remarkably higher than previous reports. In contrast with most of the previous European studies, GPA and MPA have similar incidence rates, and MPO-AAV has a higher incidence than PR3-AAV. Mortality of MPA and EGPA, but not GPA is higher than the general population. The presence of MPO-ANCA is a marker of poor survival.

**Disclosure:** A. Berti, None; D. Cornec, None; C. S. Crowson, None; U. Specks, None; E. L. Matteson, None.


**Abstract Number:** 1750

**Risk of Cardiovascular and Thrombotic Disease Among Patients with Incident ANCA-Associated Vasculitis: A 20 Year Population Based Cohort Study**

**Alvise Berti**1,2, Eric L. Matteson3,4, Cynthia S. Crowson5,6, Ulrich Specks7 and Divi Cornec8,9, 1Department of Pulmonary and Critical Care Medicine, Mayo Clinic College of Medicine and Science, Rochester, MN, 2Department of Immunology, Rheumatology, Allergy and Rare Diseases, San Raffaele Scientific Institute, Milan, Italy, 3Division of Rheumatology, Department of Internal Medicine and Department of Health Sciences Research, Mayo Clinic, Rochester, MN, 4Department of Health Sciences Research, Division of Epidemiology, Rochester, MN, 5Health Sciences Research, Mayo Clinic College of Medicine and Science, Rochester, MN, 6Division of Biomedical Statistics and Informatics, Department of Health Sciences Research, Mayo Clinic, Rochester, MN, 7Mayo Clinic College of Medicine, Rochester, MN, 8Department of Rheumatology, Brest Teaching Hospital, Brest, France, 9Pulmonary and Critical Care Medicine, Mayo Clinic College of Medicine and Science, Rochester, MN

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Vasculitis Poster II: ANCA-Associated Vasculitis  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

ANCA-associated vasculitides (AAV) are characterized by inflammation and necrosis of small-sized vessels. Because cardiovascular disease (CVD) is a leading contributor to morbidity and mortality, we assessed the CVD and thrombotic disease risk among newly diagnosed patients with granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA) in a US based adult population.
Methods:

Patients with incident AAV in a geographically defined region of the US from January 1, 1996 to December 31, 2015 were previously identified by medical record review. For each incident AAV patient, 3 comparators of similar age and sex without AAV were randomly selected from the same population and assigned an index date corresponding to the AAV incidence date.

Medical records of cases and comparators were reviewed for CVD events which included coronary artery disease (CAD), heart failure (HF), atrial fibrillation (AF), cerebrovascular accident (CVA), peripheral vascular disease (PVD), and thrombotic non-cardiac vascular events, which included deep vein thrombosis (DVT), and pulmonary embolism (PE). CVD definitions were based on physician diagnosis. Data on baseline CVD risk factors, including smoking status, body mass index, diabetes mellitus, hypertension and dyslipidemia, were also collected. Cox models adjusted for age, sex and calendar year were used for comparisons between groups.

Results:

There were 58 incident cases of AAV (48%, women, 98% Caucasian, mean age 61.1 years) and 174 non-AAV comparators (48% women, 95% Caucasian, mean age 61.2 years). Among cases, 23 (40%) were GPA, 28 (48%) MPA, and 7 (12%) EGPA, mostly ANCA positive (MPO-ANCA 34 [61%), PR3-ANCA17 [30%]).

Baseline total cholesterol (median 179.0 mg/dL for AAV; 191.0 mg/dL for comparators; p=0.026) and current smoking (5% vs 19%; p=0.036) were lower in AAV than comparators, while the other CVD risk factors were not significantly different between the 2 groups. After adjustment for age and sex, hypertension was more frequent in MPA than GPA or EGPA patients at AAV diagnosis (79% vs 43% and 29%, p<0.05).

The prevalence of CVD and thrombotic events before the index date was not significantly different between the 2 groups. During median follow-up of 6.0 years for AAV and 6.7 years for comparators, CVD events developed in 14 AAV patients and 17 comparators corresponding to a >3 fold increased risk of CVD in AAV (hazard ratio [HR] 3.37, 95% confidence interval [CI]:1.64-6.91). By subtypes, risks were elevated for CVA (HR 8.16, 95%CI:2.45-27.15; p<0.001), cardiac events (CAD, HF or AF) (HR 2.95, 95%CI:1.42-6.12; p<0.005), but not PVD. The HR for non-cardiac vascular disease was 3.33 (95% CI: 0.86-12.86), significantly increased for DVT (HR 6.44, 95%CI:1.20-34.66) but not for PE (HR 1.33, 95%CI:0.23-7.60). Increased CVD risks compared to non-AAV were observed in MPA (HR 2.74, 95%CI:1.02-7.35) and MPO-AAV (HR 2.85, 95%CI:1.07- 7.57), but not in GPA or PR3-AAV.

Conclusion:

Despite a lower prevalence of some CVD risk factors at baseline, patients with AAV are at higher risk for incident CVD and DVT following AAV diagnosis.

Disclosure: A. Berti, None; E. L. Matteson, None; C. S. Crowson, None; U. Specks, None; D. Cornec, None.


Abstract Number: 1751

Association of a TNFSF4 Upstream Region Single Nucleotide Polymorphism with Susceptibility to Proteinase 3-ANCA Positive
Vasculitis in a Japanese Population

Yuka Iwahashi1, Aya Kawasaki1, Fumio Hirano2, Ken-ei Sada3, Daisuke Tsukui4, Yuya Kondo5, Shigeto Kobayashi6, Hidehiro Yamada7, Hiroshi Furukawa1, Kenji Nagasaki8, Takahiko Sugihara9, Kunihiro Yamagata10, Takayuki Sumida3, Shigeto Tohma11, Hajime Kono4, Shoichi Ozaki7, Seiichi Matsuo12, Hiroshi Hashimoto13, Hirofumi Makino14, Yoshihiro Arimura15, Masayoshi Harigai16 and Naoyuki Tsuchiya1, 1Molecular and Genetic Epidemiology Laboratory, University of Tsukuba, Faculty of Medicine, Tsukuba, Japan, 2Departments of Rheumatology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan, 3Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan, 4Department of Internal Medicine, Teikyo University School of Medicine, Tokyo, Japan, 5Department of Internal Medicine, University of Tsukuba, Faculty of Medicine, Tsukuba, Japan, 6Department of Internal Medicine, Juntendo University Koshigaya Hospital, Koshigaya, Japan, 7Department of Internal Medicine, St. Marianna University School of Medicine, Kawasaki, Japan, 8Department of Rheumatology, Ome Municipal General Hospital, Ome, Japan, 9Department of Medicine and Rheumatology, Tokyo Metropolitan Geriatric Hospital, Tokyo, Japan, 10Department of Nephrology, University of Tsukuba, Faculty of Medicine, Tsukuba, Japan, 11Clinical Research Center for Allergy and Rheumatology, Sagamihara Hospital, National Hospital Organization, Sagamihara, Japan, 12Department of Nephrology, Nagoya University Graduate School of Medicine, Nagoya, Japan, 13Juntendo University School of Medicine, Tokyo, Japan, 14Okayama University Hospital, Okayama, Japan, 15First Department of Internal Medicine, Kyorin University School of Medicine, Tokyo, Japan, 16Division of Epidemiology and Pharmacoepidemiology of Rheumatic Diseases, Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Vasculitis Poster II: ANCA-Associated Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

In the epidemiology of ANCA-associated vasculitis (AAV), an obvious difference between European and Asian populations has been reported. According to the clinical classification, granulomatosis with polyangiitis (GPA) is predominant in UK, while microscopic polyangiitis (MPA) is predominant in Japan. Based on the ANCA specificity, most of Japanese AAV are myeloperoxidase (MPO)-ANCA positive, whereas more than half of UK AAV patients are proteinase 3 (PR3)-ANCA positive. Differences in the genetic background between populations may play a role in such epidemiological differences. Thus far, HLA-DPB1*04:01, SERPINA1 and PRTN3 are associated with GPA in the Caucasian populations, while HLA-DRB1*09:01 haplotype with Japanese MPO-ANCA positive AAV.

TNFSF4 encodes OX40 ligand (OX40L), which is expressed on endothelial cells and antigen presenting cells and plays a role in T cell activation through OX40. A single nucleotide polymorphism (SNP) rs2205960 G>T, located upstream of TNFSF4, has been associated with upregulation of OX40L, and with susceptibility to systemic lupus erythematosus (SLE) in the British, Chinese, and Korean populations.

Based on substantial sharing of susceptibility genes among multiple autoimmune diseases, and potential role of OX40L-OX40 interaction between T cells and endothelial cells, we considered TNFSF4 as an attractive candidate for a susceptibility gene to AAV. No association study has been reported between AAV and TNFSF4. In this study, we conducted an association study of rs2205960 in Japanese AAV.

Methods:


Case-control association analysis was performed on 467 Japanese AAV patients and 1100 healthy controls under the allele model, using chi-square test. The P values were corrected for multiple testing using Bonferroni correction. The patients were classified into 285 MPA, 92 GPA, 56 eosinophilic granulomatosis with polyangiitis, and 34 were unclassifiable, according to the European Medicines Agency (EMEA) algorithm. With respect to ANCA specificity, PR3-ANCA were positive in 62 patients, and MPO-ANCA in 376 patients.

Results:

The results are shown in Table 1. Significant association was detected in PR3-ANCA positive (P=0.00583, \(P_{\text{Bonferroni}}=0.032\), odds ratio [OR]=1.75), but not in MPO-ANCA positive, patients. In addition, tendency towards association was detected in GPA (P=0.0507, OR=1.41). When the GPA patients were classified according to the ANCA specificity, association was preferentially detected in PR3-ANCA positive GPA (P=0.0213, OR=1.81) than in MPO-ANCA positive GPA (P=0.326, OR=1.32). The risk allele was T, which was the same as in SLE.

Conclusion:

Association of a \(TNFSF4\) upstream region SNP rs2205960T with PR3-AAV in a Japanese population was detected for the first time. This allele seemed to be more strongly associated with PR3-ANCA positivity than with the clinical classification of GPA.

Table 1. Allelic association of \(TNFSF4\) rs2205960 with AAV subsets in a Japanese population

<table>
<thead>
<tr>
<th>rs2205960 G&gt;T</th>
<th>n</th>
<th>MAF (%)</th>
<th>P</th>
<th>(P_{\text{Bonferroni}})</th>
<th>OR</th>
<th>95“CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPO-ANCA positive AAV</td>
<td>376</td>
<td>20.6</td>
<td>0.527</td>
<td>1.07</td>
<td>0.87-1.31</td>
<td></td>
</tr>
<tr>
<td>PR3-ANCA positive AAV</td>
<td>62</td>
<td>29.8</td>
<td>0.00538</td>
<td>0.032</td>
<td>1.75</td>
<td>1.17-2.61</td>
</tr>
<tr>
<td>MPA</td>
<td>285</td>
<td>20.5</td>
<td>0.600</td>
<td>1.06</td>
<td>0.85-1.34</td>
<td></td>
</tr>
<tr>
<td>GPA</td>
<td>92</td>
<td>25.5</td>
<td>0.0507</td>
<td>1.41</td>
<td>1.00-2.00</td>
<td></td>
</tr>
<tr>
<td>MPO positive GPA</td>
<td>35</td>
<td>24.3</td>
<td>0.326</td>
<td>1.32</td>
<td>0.76-2.30</td>
<td></td>
</tr>
<tr>
<td>PR3 positive GPA</td>
<td>36</td>
<td>30.6</td>
<td>0.0213</td>
<td>0.128</td>
<td>1.81</td>
<td>1.08-3.02</td>
</tr>
<tr>
<td>healthy controls</td>
<td>1100</td>
<td>19.5</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
<td></td>
</tr>
</tbody>
</table>

MAF: minor allele frequency, OR: odds ratio, CI: confidence interval


View Abstract and Citation Information Online - http://acrabstracts.org/abstract/association-of-a-tnfsf4-upstream-region-single-nucleotide-polymorphism-with-susceptibility-to-proteinase-3-anca-positive-vasculitis-in-a-
japanese-population
Pharmacokinetics of Rituximab and Clinical Outcomes in Patients with ANCA-Associated Vasculitis

Divi Cornec1, Brian Kabat1, John Mills1, Melissa Cheu2, Amber Hummel1, Darrell Schroeder1, Matthew Cascino3, Paul Brunetta3, David Murray1, Melissa Snyder1, Fernando Fervenza1, Gary S. Hoffman4, Cees G.M. Kallenberg5, Carol A. Langford6, Peter A. Merkel7, Paul A. Monach8, Philip Seo9, Robert F. Spiera10, E. William St Clair11, John H. Stone12, David Barnidge1 and Ulrich Specks13, 1Mayo Clinic, Rochester, MN, 2Genentech Inc., South San Francisco, CA, 3Genentech, Inc., South San Francisco, CA, 4Rheumatology, Cleveland Clinic, Cleveland, OH, 5Rheumatology and Clinical Immunology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, 6Rheumatic and Immunologic Diseases, Cleveland Clinic, Cleveland, OH, 7University of Pennsylvania, Philadelphia, MN, 8Boston University School of Medicine, Boston, MA, 9Medicine, Johns Hopkins University, Baltimore, MD, 10Rheumatology, Hospital for Special Surgery, New York, NY, 11Rheumatology, Duke University Medical Center, Durham, NC, 12Massachusetts General Hospital Rheumatology Unit, Harvard Medical School, Boston, MA, 13Mayo Clinic College of Medicine, Rochester, MN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Vasculitis Poster II: ANCA-Associated Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Response to rituximab (RTX) is variable in patients with ANCA-associated vasculitis (AAV), and predictors of treatment efficacy/relapse risk would be useful. Previous studies have shown that RTX pharmacokinetics (PK) is associated with treatment efficacy in patients with lymphoma. The objectives of this work were to study the determinants of RTX PK in patients treated for AAV and its association with clinical outcomes.

Methods:
This study included 88 patients from the RTX in ANCA-Associated Vasculitis (RAVE) trial who received the full dose of RTX (4 weekly 375 mg/m² infusions) and had available serum samples. RTX was quantified using two different assays: a traditional ELISA and a recently developed mass spectrometry-based assay (referred to as miRAMM). We analyzed week (W)2, W4, W8, W16 and W24 serum levels and the trapezoidal area under the curve (AUC) integrating baseline, W2, W4, and W8 levels. We explored potential determinants of RTX PK using univariate and multivariate analysis, and analyzed the association of RTX PK with clinical outcomes: achievement of complete remission at 6 months (defined by a BVAS/WG score of 0 with no prednisone), time to relapse in patients who achieved complete remission, and B-cell depletion duration.

Results:
RTX quantifications using ELISA and miRAMM were highly correlated, but miRAMM measured consistently higher serum levels, suggesting its ability to detect total serum RTX (including free and complexed rituximab). RTX PK was highly variable between patients, with W2 levels ranging between 43 and 259 μg/mL and AUC ranging between 2,668 and 17,513 μg/mL by miRAMM. W2 RTX levels and AUC were significantly lower in males and in newly-diagnosed patients, and were negatively correlated with body surface area, baseline B-cell count, and BVAS/WG. In multivariate analyses, the main determinants of RTX PK were sex and new diagnosis. Patients with a new diagnosis had higher baseline B-cell counts and BVAS/WG. Patients reaching complete remission at month 6 had similar mean RTX levels compared to patients who did not reach complete remission (W2 level by miRAMM: 136±44 vs 139±46, p=0.76; AUC: 8420±2875 vs 8558±3452, p=0.85). Patients with higher RTX levels generally experienced longer B-cell depletion durations, but RTX levels at the different time-points and AUC were not associated with time to any relapse or time to severe relapse. Similar results were observed when using rituximab quantification by miRAMM and by ELISA.

Conclusion:
Despite the body-surface-area-based dosing protocol, PK-RTX is highly variable among patients with AAV, its main determinants being sex and newly diagnosed disease. We did not observe any relevant association between PK-RTX and clinical outcomes. The monitoring of serum rituximab levels does not seem clinically useful in AAV.
Disclosure: D. Cornec, None; B. Kabat, None; J. Mills, None; M. Cheu, Genentech and Biogen IDEC Inc., 9; A. Hummel, None; D. Schroeder, None; M. Cacino, None; P. Brunetta, Genentech and Biogen IDEC Inc., 3; D. Murray, None; M. Snyder, None; F. Fervenza, None; G. S. Hoffman, None; C. G. M. Kallenberg, None; C. A. Langford, None; P. A. Merkel, None; P. A. Monach, Genentech and Biogen IDEC Inc., 2,GlaxoSmithKline, 2,Bristol-Myers Squibb, 2; P. Seo, GlaxoSmithKline, 5; R. F. Spiera, None; E. W. St Clair, None; J. H. Stone, Xencor, 2; D. Barnidge, None; U. Specks, None.


Abstract Number: 1753

“Recurrent Venous Thromboembolic Events in Granulomatosis with Polyangiitis Patients”

Alana Nevares1, William Messner2, Hiromichi Tamaki3, Yaseen Kinanah4 and Alexandra Villa-Forte5, 1Rheumatology, Cleveland Clinic Foundation, Cleveland, OH, 2Quantitative Health Sciences, Cleveland Clinic, Cleveland, OH, 3Rheumatology, Cleveland Clinic, Cleveland, OH, 4Internal Medicine, Cleveland Clinic Foundation, Cleveland, OH, 5Rheumatology, Clevand Clinic Foundation, Shaker Heights, OH

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Vasculitis Poster II: ANCA-Associated Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:

The incidence of first-time venous thromboembolic events (VTE) is high in granulomatosis with polyangiitis (GPA). The incidence of recurrent VTE in these patients has not been studied. The risk of VTE recurrence has been reported in other groups of patients and it is important as it affects recommendations for extended anticoagulation therapy. The aim of this study is to determine the incidence rate of recurrent VTE in GPA.

Methods:

A retrospective chart review was performed in patients with GPA and at least one VTE from a single Vasculitis Center from 2002 to 2016. Our inclusion criteria: 1) 1990 ACR criteria or 2012 Revised International Chapel Hill nomenclature for GPA, 2) ≥ 2 follow-up visits in our center, 3) ≥ 1 VTE documented during the study period, 4) VTE occurrence after diagnosis of GPA or within three months before GPA diagnosis. Kaplan-Meier was used to estimate second VTE event-free survival rates. Disease (GPA) activity was defined as BVAS/WG score of ≥ 1.

Results:

84 out of 137 patients with GPA and at least one VTE met inclusion criteria. Median age at the time of GPA and first VTE was 56 and 57 respectively. Majority were Caucasian (97.6%) and male gender (56%). Incidence rate for second VTE was 8.4 events per 100 patient years (95% CI 5.7-12.3) over a median duration of 2.4 years (0.6-5.5 years) observation period. The cumulative recurrence rates at 3, 6, 12 months, 3 and 5 years were 9.7%, 13.8%, 15.1%, 27.1 %, and 27.1% respectively. Median time-to-second event was 10.6 years, shorter for patients with BVAS at diagnosis ≥ 15 when compared to BVAS < 15 group (7.5 vs 11.3 years -p=0.0042 by Log-Rank test-). 89.3% of first VTE and 57.7% of second VTE occurred when disease was active (p< 0.001). Median BVAS at first event was 8.5 vs 4.0 at second event (p=0.030). Male and upper extremity deep vein thrombosis were associated with higher risk of recurrence (Odds ratios: 2.9 [95% CI: 1.1-8.0] and 6.0 [95%CI: 1.6-22.3] respectively). Lung involvement at GPA diagnosis was associated with lower risk for recurrence (odds ratio: 0.33 [95%CI: 0.12 – 0.95]). ANCA positivity was not associated with an increased risk of recurrence.

Conclusion:

GPA patients have a high rate of VTE recurrence compared to the general population with unprovoked VTE (8.4 vs 3.9 recurrent events per 100 patient years) (Kyrle PA, et al. Lancet. 2010). Recurrent events were not always related to clinically apparent active disease. Our results suggest that VTE in GPA is a recurrent disease, more so during the first three years after first event. Prospective studies are needed to address adequate duration of anticoagulation in this population.
Background/Purpose: ANCA-associated vasculitides (AAVs) are potentially life-threatening diseases rarely observed in childhood. Whether AAVs in children (cAAVs) differ from adult-onset AAVs (aAAVs) is still not known. This study was undertaken to investigate differences in clinical presentations and disease outcomes between cAAVs and matched aAAVs controls.

Methods: Demographic and clinical data and disease outcomes of consecutive patients (age <18 years at diagnosis) with cAAVs satisfying ACR, PRINTO/EULAR classification criteria and/or the revised Chapel Hill Nomenclature for Vasculitides were compared to a randomly selected sample of aAAV patients from the French Vasculitis Study Group (FVSG) registry. Cases and controls were matched for the following features: AAV (granulomatosis with polyangiitis [GPA], microscopic polyangiitis [MPA] or eosinophilic granulomatosis with polyangiitis [EGPA]), sex, year of enrollment and duration of follow-up after diagnosis. Prospectively collected information included medications, and disease activity and damage as assessed by the Birmingham Vasculitis Activity Score (BVAS) and the Vasculitis Damage Index (VDI), respectively. Relapses, survival rates and causes of death were analyzed. Kaplan–Meier curves and the log-rank test were used to analyze predefined-outcome differences between cases and controls. STROBE guidelines for reporting observational studies were applied.

Results: Thirty-five cAAV cases (25 GPA, 4 MPA, 6 EGPA) were compared with 151 aAAV controls (106 GPA, 17 MPA, 28 EGPA). Respective median ages (range) were 14 (2–17) vs. 53 (18–87) years, with median AAV follow-up durations of 71 and 64 months (P=0.49), respectively. At study entry, children had less frequent myalgias (P=0.005) and peripheral neuropathy (P<0.001) but were more frequently febrile (P<0.05). Their respective rates of renal involvement were comparable (13 (37%) vs. 73 (48%); P=0.31). Initial GPA-associated ischemic abdominal pain and nasal cartilage damage were more common in cAAVs than aAAVs (P<0.05). Their first relapse occurred at 17 (4–69) months vs. 24 (11–86) months (P=0.05). Children were treated with lower cumulative prednisolone equivalent doses (P=0.001) and had lower cumulative immunosuppressant doses (P<0.005). At last visit, children had accumulated more damage, mostly ENT sequelae (P=0.001), associated with longer maintenance therapy (P=0.03) than for aAAV controls. Four (11.4%) cAAV and 13 (8.6%) aAAV patients died (P=0.54).

Conclusion: cAAVs are severe diseases, characterized by a higher relapse rate, more accrued damage, mostly ENT sequelae, and longer maintenance therapy than aAAVs.
Safety of Methotrexate and Low-Dose Trimethoprim-Sulfamethoxazole in Patients with ANCA-Associated Vasculitis

Hiromichi Tamaki1, Robert Butler2 and Carol A. Langford3, 1Rheumatology, Cleveland Clinic, Cleveland, OH, 2Department of Quantitative Health Sciences, Cleveland Clinic, Cleveland, OH, 3Rheumatic and Immunologic Diseases, Cleveland Clinic, Cleveland, OH

Abstract Number: 1755

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Vasculitis Poster II: ANCA-Associated Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Low-dose trimethoprim-sulfamethoxazole (LDTS, 160mg-800mg 3x/week or 80mg-400mg/day) is effective for prevention of Pneumocystis jiroveci pneumonia (PCP), a serious opportunistic infection seen in patients with ANCA-associated vasculitis (AAV) receiving immunosuppression. There have been rare reports of profound cytopenias when therapeutic-dose TS (160mg-800mg 2x/day) was added to methotrexate (MTX), raising concern about whether LDTS could be given for PCP prophylaxis in AAV patients receiving MTX. This study sought to examine the safety of MTX+LDTS in a well characterized cohort of patients with AAV.

Methods:
A retrospective chart review was performed of AAV patients treated with MTX at our Center 2002-2017. Clinical variables and laboratory data were collected in RedCap. Kaplan-Meier curves were constructed of drug discontinuation by group with differences compared using the Log-rank test and Wilcoxon test. Side effects were compared using chi-square, Fisher’s exact test, or ANOVA.

Results:
130 patients were included: MTX only (N=33), MTX+LDTS (N=97). Demographics are summarized in Table 1. The rate of discontinuation for MTX was similar between the two groups (Figure 1), with no differences seen in the 5 identified reasons for discontinuation: side effects, infection, switching to another medication for active disease, MTX withdrawal after sustained remission, and patient discontinuation. The overall occurrence of side effects was similar (8.6% [MTX only] vs 7.1% [MTX+LDTS], P=0.32). Thrombocytopenia (3.8% [MTX only] vs 1.1% [MTX+LDTS], P<0.001) and gastrointestinal side effects (3.9% [MTX only] vs 1.6% [MTX+LDTS], P=0.005) occurred more frequently in those on MTX only but there was no difference in the frequency of leukopenia (0.8% [MTX only] vs 1.0% [MTX+LDTS], P=0.72), transaminitis (6.4% [MTX only] vs 6.2% [MTX+LDTS], P=0.88), hospitalization for suspected infection (2.5% [MTX only] vs 1.9% [MTX+LDTS], P=0.52). One patient on MTX 25mg/week + LDTS had Grade 4 neutropenia that occurred following rituximab and moderate renal insufficiency.

Conclusion:
In our AAV cohort, the frequency of MTX discontinuation and side effects was similar in patients treated with MTX alone or combined with LDTS. As this study only examined those receiving LDTS, these observations do not extend to those receiving higher doses of TS together with MTX. These results provide support that MTX can safely be combined with LDTS for PCP prophylaxis in AAV. As serious bone marrow suppression can occur with MTX use, with or without LDTS, close laboratory monitoring remains important.
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total (N=190)</th>
<th>MTX Only (N=82)</th>
<th>MTX+LDM (N=108)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>49.8±14.8</td>
<td>53.7±15.1</td>
<td>46.6±14.5</td>
<td>0.09*</td>
</tr>
<tr>
<td>Disease duration (months)</td>
<td>58.6±44.9</td>
<td>52.3±74.2</td>
<td>50.1±61.9</td>
<td>0.87*</td>
</tr>
<tr>
<td>Duration of follow up (years)</td>
<td>5.4±5.3</td>
<td>5.0±5.6</td>
<td>5.8±5.9</td>
<td>0.47</td>
</tr>
<tr>
<td>Methotrexate dosage</td>
<td>18.7±5.1</td>
<td>16.1±5.6</td>
<td>19.3±5.0</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td>0.62*</td>
</tr>
<tr>
<td>Male</td>
<td>56 (29)</td>
<td>13 (26)</td>
<td>43 (40)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>74 (71)</td>
<td>29 (64)</td>
<td>45 (42)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td>0.04*</td>
</tr>
<tr>
<td>White</td>
<td>123 (64)</td>
<td>69 (54)</td>
<td>54 (50)</td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>2 (1)</td>
<td>1 (1)</td>
<td>1 (1)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>5 (4)</td>
<td>2 (2)</td>
<td>3 (3)</td>
<td></td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
<td></td>
<td>0.55*</td>
</tr>
<tr>
<td>GPA</td>
<td>110 (58)</td>
<td>53 (65)</td>
<td>57 (53)</td>
<td></td>
</tr>
<tr>
<td>MPA</td>
<td>9 (5)</td>
<td>4 (5)</td>
<td>5 (5)</td>
<td></td>
</tr>
<tr>
<td>EGPA</td>
<td>9 (7)</td>
<td>4 (5)</td>
<td>5 (5)</td>
<td></td>
</tr>
<tr>
<td>GPA or MPA</td>
<td>3 (2)</td>
<td>1 (1)</td>
<td>2 (2)</td>
<td></td>
</tr>
<tr>
<td>IIF ANCA</td>
<td></td>
<td></td>
<td></td>
<td>0.09*</td>
</tr>
<tr>
<td>Perinuclear pattern (pANCA)</td>
<td>19 (11)</td>
<td>6 (11)</td>
<td>13 (12)</td>
<td></td>
</tr>
<tr>
<td>Cytoplasmic pattern (cANCA)</td>
<td>80 (44)</td>
<td>48 (58)</td>
<td>32 (30)</td>
<td></td>
</tr>
<tr>
<td>Both Negative</td>
<td>26 (15)</td>
<td>13 (16)</td>
<td>13 (12)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>5 (3)</td>
<td>2 (2)</td>
<td>3 (3)</td>
<td></td>
</tr>
<tr>
<td>ELISA ANCA</td>
<td></td>
<td></td>
<td></td>
<td>0.42*</td>
</tr>
<tr>
<td>PR3 ANCA</td>
<td>71 (38)</td>
<td>38 (46)</td>
<td>33 (31)</td>
<td></td>
</tr>
<tr>
<td>MPO ANCA</td>
<td>20 (11)</td>
<td>11 (13)</td>
<td>9 (9)</td>
<td></td>
</tr>
<tr>
<td>Both Negative</td>
<td>29 (16)</td>
<td>14 (17)</td>
<td>15 (14)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>10 (5)</td>
<td>5 (6)</td>
<td>5 (5)</td>
<td></td>
</tr>
<tr>
<td>Sites of organ involvement</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin</td>
<td>20 (27)</td>
<td>10 (12)</td>
<td>10 (10)</td>
<td>0.15*</td>
</tr>
<tr>
<td>Oral mucosa</td>
<td>18 (24)</td>
<td>11 (14)</td>
<td>7 (7)</td>
<td></td>
</tr>
<tr>
<td>Eyes</td>
<td>31 (42)</td>
<td>19 (23)</td>
<td>12 (11)</td>
<td>0.21*</td>
</tr>
<tr>
<td>ENT</td>
<td>114 (81)</td>
<td>59 (72)</td>
<td>55 (51)</td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td>6 (8)</td>
<td>4 (5)</td>
<td>2 (2)</td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>94 (72)</td>
<td>43 (52)</td>
<td>51 (48)</td>
<td>0.21*</td>
</tr>
<tr>
<td>Kidney</td>
<td>59 (45)</td>
<td>29 (36)</td>
<td>30 (28)</td>
<td></td>
</tr>
<tr>
<td>Neurologic</td>
<td>19 (15)</td>
<td>9 (11)</td>
<td>10 (10)</td>
<td>0.08*</td>
</tr>
<tr>
<td>Prior medication</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prednisone</td>
<td>121 (93)</td>
<td>62 (75)</td>
<td>59 (56)</td>
<td>0.14*</td>
</tr>
<tr>
<td>Intravenous cyclophosphamide</td>
<td>5 (4)</td>
<td>3 (4)</td>
<td>2 (2)</td>
<td>0.99*</td>
</tr>
<tr>
<td>Daily cyclophosphamide</td>
<td>77 (59)</td>
<td>48 (59)</td>
<td>29 (28)</td>
<td>0.01*</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>17 (13)</td>
<td>13 (16)</td>
<td>4 (4)</td>
<td></td>
</tr>
<tr>
<td>Methotrexate*</td>
<td>51 (37)</td>
<td>20 (24)</td>
<td>31 (29)</td>
<td>0.12*</td>
</tr>
<tr>
<td>Mycophenolate Mofetil</td>
<td>3 (2)</td>
<td>2 (2)</td>
<td>1 (1)</td>
<td></td>
</tr>
<tr>
<td>Etanercept</td>
<td>10 (7)</td>
<td>6 (7)</td>
<td>4 (4)</td>
<td>0.68*</td>
</tr>
<tr>
<td>Infliximab</td>
<td>5 (4)</td>
<td>3 (4)</td>
<td>2 (2)</td>
<td></td>
</tr>
<tr>
<td>Rituximab</td>
<td>7 (5)</td>
<td>4 (5)</td>
<td>3 (3)</td>
<td>0.60*</td>
</tr>
<tr>
<td>No prior treatment</td>
<td>8 (6)</td>
<td>3 (4)</td>
<td>5 (5)</td>
<td>0.48*</td>
</tr>
</tbody>
</table>

*Uncontrolled exposure prior to the last data collection visit.

Statistics presented as Mean±standard deviation or N (%).

P-values: ANOVA, or Pearson’s chi-square test, or Fisher’s Exact test.

Abbreviations:
ANCA: Anti-neutrophil cytoplasmic antibody, EGA: Eosinophilic granulomatosis with polyangitis, EUA: Enzyme-linked immunosorbent assay, GPA: Granulomatosis with polyangitis, IIF: Indirect immunofluorescence, MPA: Microscopic polyangitis; MPO: Myeloperoxidase, PR3: Proteinase 3
Interstitial Lung Disease in ANCA Associated Vasculitis: A Distinct or an Incomplete Subset in ANCA Vasculitis Patients?

Simone Barsotti¹,², Francesco Ferro¹, Elena Elefante¹, Rossella Neri³, Marta Mosca¹ and Chiara Baldini⁴, ¹Rheumatology Unit, University of Pisa, Pisa, Italy, ²Department of Medical Biotechnologies, University of Siena, Siena, Italy, ³Rheumatology Unit, University of Pisa, PISA, Italy, ⁴Internal Medicine, Rheumatology Unit, University of Pisa, Pisa, Italy

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Vasculitis Poster II: ANCA-Associated Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: ANCA-associated vasculitis (AAV) are heterogeneous disorders with a clinical presentation that may range from a full-blown disease to incomplete forms with isolated organ involvement. In particular, interstitial lung disease (ILD) may represent the only clinically evident involvement in some patients. Aim of our work was to describe AAV patients with isolated ILD focusing on their clinical characteristics, long-term outcome and clinical-serological associations.

Methods: In this single center study we collected epidemiologic, demographic, clinical, laboratory and serological data of AAV patients, excluding patients with diagnosis of EGPA. We recorded disease activity at the disease onset by Birmingham Vasculitis Activity Score (BVAS) and damage by using the Vasculitis Damage Index (VDI).

Results: Fifty-four patients with AAV (M:F=32:22, mean age at diagnosis 55.1±5.2 years) were enrolled. Twenty-nine patients were ANCA-MPO positive, while 25 were ANCA-PR3 positive. Eight ANCA positive patients (8/54, 14.8%) presented ILD as the main clinical feature of AAV (5 ILD as the only manifestation). The ILD pattern at lung CT was “non-specific interstitial pneumonia” (NSIP)-like in 2 patients and “usual interstitial pneumonia” (UIP)-like in 6 cases. Seven patients were ANCA-MPO positive while 1 was ANCA-PR3 positive. ILD patients presented a higher mean age at the disease onset compared to non-ILD subjects (65.63±7.36 vs 53.3±15.49 p=0.04), lower creatinine values (0.78 ±0.13 vs 1.77±2.1 p=0.018) and a lower BVAS at the disease onset (BVAS 3.75 ±2.49 vs 13.71±6.7 p=0.013). In the long-term follow-up (mean follow-up: 8.31±9.24 years), none of the ILD patients presented an end-
stage renal disease (vs 6 in non-ILD patients) or disease flares (vs 26 in non-ILD cases). The final VDI was lower in ILD patients when compared to non-ILD patients (VDI 2.12±0.83 vs 3.71±2.41 p=0.004). Moreover, no deaths were observed in the ILD group (vs 7 in non-ILD).

**Conclusion:** Patients with AAV presenting ILD seem to present a different phenotype compared to patients with a complete form of AAV. ILD patients presented lower disease activity at the onset, lower prevalence of complications, lower damage and an overall better prognosis compared to non-ILD patients. Further prospective studies in larger cohorts may clarify whether patients with isolated ILD should be classified as a distinct subset or an incomplete form of AAV.

**Disclosure:** S. Barsotti, None; F. Ferro, None; E. Elefante, None; R. Neri, None; M. Mosca, None; C. Baldini, None.

**Abstract Number:** 1757

**Rituximab for Induction and Maintenance Therapy of Granulomatosis with Polyangiitis: A Single-Center Cohort Study on 114 Patients**

Xavier Puéchal¹, Michele Iudici¹, Ana Luisa Calich², Alexandre Vivot³, Benjamin Terrier⁴, Alexis Regent¹, Pascal Cohen⁴, Claire Le Jeune⁴, Luc Mouton⁵, Philippe Ravaud⁶ and Loïc Guillemin for the French Vasculitis Study Group⁷, ¹National Referral Center for Rare Systemic Autoimmune Diseases, Hôpital Cochin, AP–HP, Université Paris Descartes, Paris, France, ²Universidade Federal de São Paulo, Hospital São Paulo, São Paulo, Brazil, ³Epidemiology, Hotel Dieu, Paris, France, ⁴Service de Médecine Interne, Hôpital Cochin, Centre de référence national pour les maladies systémiques autoimmunes rares d’Ille de France, DHU Authors, Assistance Publique-Hôpitaux de Paris (AP–HP), Paris, France, ⁵Service de Médecine Interne, Hôpital Cochin, Centre de référence national pour les maladies systémiques autoimmunes rares d’Ille de France, DHU Authors, Assistance Publique-Hôpitaux de Paris (AP–HP), Paris, France, ⁶Service de Médecine Interne, Hôpital Cochin, Paris, France, ⁷Service de Médecine Interne, Centre de Référence Maladies Auto-Immuènes et Auto-Inflammatoires Systémiques Rares, Hôpital Cochin, Paris, France

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Vasculitis Poster II: ANCA-Associated Vasculitis

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Randomized–controlled trials (RCTs) showed rituximab’s (RTX) noninferiority to cyclophosphamide for induction therapy of severe ANCA-associated vasculitides and significantly lower relapse rate than azathioprine maintenance. However, those RCTs enrolled granulomatosis with polyangiitis (GPA) and microscopic polyangiitis patients, who might need to be studied separately, and selected patients with low preexisting comorbidities that preclude generalization. This open-label, real-life, single-center cohort study was undertaken to assess efficacy of RTX induction-and-maintenance therapy for GPA patients.

**Methods:** All consecutive adults with GPA who received ≥1 RTX infusions for induction (April 2005–December 2016) at Cochin National Referral Center for Vasculitis were included. Patients had to satisfy the ACR classification criteria or revised Chapel Hill Nomenclature for GPA. Those enrolled in prospective trials were ineligible. After remission, preemptive low-dose RTX maintenance was given. Kaplan–Meier estimations of relapse-free survival were tested for significance with log-rank tests. Cox regression with time-dependent covariates was used to identify predictors of relapses, serious adverse events (SAEs) or serious infections.

**Results:** During the study, 114 patients, with relapsing (65%) or refractory/grumbling (22%) active GPA, received RTX induction therapy; 100 were given ≥1 RTX maintenance infusions and 90 received 500 mg every 6 months. The median (IQR) prednisone dose at first RTX infusion was 30 [20–50] mg/day. After the first RTX infusion, median follow-up was 3.6 [1.6–5.8] years; respective 1- and 2-year remission rates were 83.7% and 86.4%; respective 1-, 2-, and 3-year relapse-free survival rates were 93% (95% CI 88–98), 85% (78–92) and 82% (74–90); and the 2-year RTX-retention rate was 74% (SE 5%). Respective SAE or serious infection rates were 8.1 and 4.9 per 100-patient-years. Two patients died. Univariate analyses identified pure granulomatous disease (P=0.017), refractory/grumbling vs. new-onset/relapsing GPA (P<0.001), pachymeningitis (P=0.048) or estimated glomerular filtration rate >60 ml/min (P=0.005) as factors associated with less likely remission. Multivariate analyses retained subglottic stenosis (HR 4.88, 95% CI 1.79–13.25; P=0.002), ENT involvement (HR 2.91, 1.37–6.20; P=0.01), skin involvement (HR 5.20, 2.18–12.44; P=0.0003) and refractory/grumbling vs. new-onset/relapsing GPA (HR 4.73, 1.04–21.43; P=0.05) as independent predictors of relapse. Only the prednisone dose over time was associated with SAEs or serious infections (HR 1.03, 1.01–1.05 and HR 1.06, 1.02–1.09, respectively; both P<0.005).
Conclusion: Cohort studies and RCTs provide complementary information. The 2-year 74% RTX-retention rate with relatively low toxicity in this real-life setting has important implications. The glucocorticoid dose was the major factor associated with SAEs, even in this cohort whose median dose at inclusion was already lower than that used in the pivotal RCTs.

Disclosure: X. Puéchal, None; M. Judici, None; A. L. Calich, None; A. Vivot, None; B. Terrier, None; A. Regent, None; P. Cohen, None; C. Le Jeanne, None; L. Mouthon, None; P. Ravaud, None; L. Guillemin for the French Vasculitis Study Group, None.


Abstract Number: 1758

Risk of Serious Infection in Granulomatosis with Polyangiitis or Microscopic Polyangiitis: Long-Term Outcomes of 126 Wegent Trial Patients


First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Vasculitis Poster II: ANCA-Associated Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Adverse events, rather than active vasculitis, are the greatest threat to patients with ANCA-associated vasculitides (AAVs) during the first year of therapy but long-term data on the risk of serious infections are scarce. Results of the randomized–controlled WEGENT trial demonstrated that, after cyclophosphamide-induction therapy, methotrexate or azathioprine is a comparable option to maintain granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) remission but, at long-term follow-up, relapses and serious adverse events (SAEs) remain matters of concern.1,2

Methods: The long-term outcomes of 126 WEGENT trial patients were ascertained, including survival, immunosuppressant use and serious infections. Follow-up began at trial inclusion and continued until the last follow-up visit, death or 10 years postinclusion, whichever occurred first. Demographic, clinical and laboratory parameters at trial entry were evaluated as potential prognostic factors for serious infection in univariable and multivariable models. Analyses were adjusted to the length of follow-up.

Results: Among the 126 trial participants, long-term follow-up information was available for 124 (98.4%); 27 (21.4%) died before 10 years of follow-up and 14 (11.1%) were lost-to-follow-up. Median follow-up was 11.9 (95% confidence interval [95% CI] 11.3–12.5) years. At 10 years, 68 patients had had at least 1 serious adverse event (SAE), including 31 serious infections (requiring hospitalization) for 25 (20%), corresponding to a 2.5 per 100 patient-years incidence rate. At inclusion, mean (±standard deviation) age of the patients who would develop serious infections was 62.0 ± 13.1 vs. 57.6 ± 12.7 for those who did not (P=0.051). Median (Q1–Q3) time to infection was 2.3 (0.2–4.2) years postinclusion. The most frequent serious infections were 15 lung infections and 5 sepses. Infection led to 4 (3%) deaths (at mean age 74.5 ± 6.5 years), occurring a mean of 4.7 ± 3.4 years postinclusion. The 10-year overall survival rate was
77.5% [95% CI 70.4–85.4%] and the 10-year survival rate without SAE was 42.7% [95% CI 34.8–52.4%]. Univariable analysis variables significantly associated with serious infection at the 20% threshold were age, AAV entity, ANCA-negativity, pulmonary involvement, fewer pre-inclusion cyclophosphamide infusions and lower cumulative cyclophosphamide dose. Multivariable analyses retained AAV (incidence rate ratio GPA vs. MPA 3.60 [95% CI 1.05–12.3]; P=0.043) and previous cumulative cyclophosphamide dose (0.78 [95% CI 0.67–0.91]; P=0.002) as being significantly prognostic of serious infection.

**Conclusion:** The results of this long-term analysis confirm that serious infections are responsible for high morbidity and potential mortality during long-term AAV-patient follow-up. Serious infections represent nearly half of SAEs and led to the deaths of 3% of the patients. Further studies should examine newer strategies to prevent infections in AAV patients.


**Disclosure:** X. Puéchal, None; C. Pagnoux, None; E. Perrodeau, None; M. Hamidou, None; J. J. Boffa, None; X. Kyndt, None; F. Lifermann, None; T. Papo, None; D. Merrien, None; A. Smail, None; P. Delaval, None; C. Hanrotel-Saliou, None; B. Imbert, None; C. Khouatra, None; M. Lambert, None; C. Leské, None; K. H. Ly, None; E. Pertuiset, None; P. Roblot, None; M. Ruivard, None; J. F. Subra, None; J. F. Viallard, None; B. Terrier, None; P. Cohen, None; L. Mouthon, None; P. Ravaud, None; L. Guillevin for the French Vasculitis Study Group, None.

Economic Evaluation of Rituximab Versus Azathioprine for Maintenance Treatment of ANCA-Associated Vasculitis. a Prospective, Multicenter Study

Annalisa Montante1, Alicia Le Bras2, Benjamin Terrier3, Pascal Cohen3, Xavier Puéchal4, Alexandre Karras5, Philippe Ravaud6, Loïc Guillevin7 and Isabelle Durand-Zaleski8, 

1UNITÉ DE RECHERCHE ECONOMIQUE, UNIVERSITE PARIS DESCARTES, PARIS, France, 
2UNITÉ DE RECHERCHE ECONOMIQUE, UNIVERSITE PARIS DESCARTES, PARIS, France, 
3Service de Médecine Interne, Hôpital Cochin, Centre de référence national pour les maladies systémiques autoimmunes rares d’Île de France, DHU Authors, Assistance Publique-Hôpitaux de Paris (AP-HP), Paris, France, Paris, France, 
4Service de Médecine Interne, Centre de Référence Maladies Auto-Immunes et Auto-Inflammatoires Systémiques Rares, Hôpital Cochin, Paris, France, 
5Néphrologie, HEGP, Paris, France, 
6Hôpital Hôtel Dieu, Paris, France, 
7Internal medicine, Cochin University Hospital, paris, France, 
8UNITÉ DE RECHERCHE ECONOMIQUE, UNIVERSITE DE PARIS-CRETEIL, PARIS, France

First publication: September 18, 2017

**Session Information**
**Session Date:** Monday, November 6, 2017
**Session Title:** Vasculitis Poster II: ANCA-Associated Vasculitis
**Session Type:** ACR Poster Session B
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**
Rituximab was proven to be superior to azathioprine as maintenance therapy for ANCA-associated vasculitides (AAVs) at month 28 of MAINRITSAN-1–trial follow-up. Because of rituximab’s high cost, we conducted ancillary cost-utility and cost-effectiveness analyses.

**Methods:**
The multicenter, prospective, open-label randomized–controlled MAINRITSAN-1 trial included 115 patients in France between 2008 and 2012. We collected all hospital healthcare resources used: hospitalizations, consultations, drugs, tests. The costs of AAV-related inpatient and outpatient care were based on hospital codes. Quality of life was evaluated with the Medial Outcomes Study Short Form-36 questionnaire.

We calculated the incremental cost-utility (ICUR) and cost-effectiveness ratios (ICER) and their corresponding acceptability curves. Costs were assessed from the perspective of the French National Health Insurance, using 2016 reimbursement tariffs, expressed in euros. Deterministic sensitivity analyses assessed uncertainty over side effects and rituximab cost. Costs drivers were tested with a generalized linear model.
**Results:** Out of 115 patients enrolled in the trial, 3 were excluded from the economic study. The Table reports resource use and costs at trial month 28. Rituximab’s higher cost was partly offset by fewer relapses, side effects and follow-up expenses. The 28-month ICER was €13,092 per relapse avoided and the 28-month ICUR was €57,127/QALY. Relapses, side effects and renal impairment were major cost determinants.

<table>
<thead>
<tr>
<th></th>
<th><strong>Azathioprine</strong></th>
<th></th>
<th><strong>Rituximab</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean(SD)</td>
<td>Median[IQR]</td>
<td>Mean(SD)</td>
<td>Median[IQR]</td>
</tr>
<tr>
<td>Inpatient stays, n</td>
<td>1.9(2.6)</td>
<td>1[0–2]</td>
<td>1.7(2.9)</td>
<td>1[0–2]</td>
</tr>
<tr>
<td>Length of stay (days)</td>
<td>14.1(24.1)</td>
<td>7[1–16]</td>
<td>12.1(13.6)</td>
<td>7[5–14]</td>
</tr>
<tr>
<td>Outpatient visits, n</td>
<td>3.5(4.9)</td>
<td>1[0–5]</td>
<td>6.3(2.8)</td>
<td>6[5–7]</td>
</tr>
<tr>
<td>Cost (€/patient)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protocol drug</td>
<td>313(130)</td>
<td>337[264–391]</td>
<td>6,035(165)</td>
<td>6,057[6,057–6,057]</td>
</tr>
<tr>
<td>Its administration</td>
<td>0</td>
<td>0[0–0]</td>
<td>2,467(1,076)</td>
<td>2,020[1,830–2,875]</td>
</tr>
<tr>
<td>Maintenance therapy</td>
<td>633(1,808)</td>
<td>0[0–0]</td>
<td>2,020(1,076)</td>
<td>2,020[1,830–2,875]</td>
</tr>
<tr>
<td>Relapses</td>
<td>2,547(4,748)</td>
<td>0[0–4,737]</td>
<td>724(3,537)</td>
<td>0[0–0]</td>
</tr>
<tr>
<td>Side effects</td>
<td>2,869(6,946)</td>
<td>0[0–2,523]</td>
<td>1,983(4,908)</td>
<td>0[0–2,531]</td>
</tr>
<tr>
<td>Follow-up</td>
<td>3,126(7,183)</td>
<td>636[0–3,254]</td>
<td>1,713(3,809)</td>
<td>0[0–2,426]</td>
</tr>
<tr>
<td>Outpatient visits</td>
<td>988(407)</td>
<td>1,069[770–1,314]</td>
<td>748(285)</td>
<td>615[614–669]</td>
</tr>
<tr>
<td>Total cost</td>
<td>10,476(10,558)</td>
<td>6,049[2,140–14,501]</td>
<td>13,617(7,946)</td>
<td>10,942[9,103–14,197]</td>
</tr>
</tbody>
</table>

**Conclusion:** Rituximab maintenance therapy is cost-effective to prevent AAV relapses.

**Disclosure:** A. Montante, None; A. Le Bras, None; B. Terrier, None; P. Cohen, None; X. Puéchal, None; A. Karras, None; P. Ravaud, None; L. Guillemin, None; I. Durand-Zaleski, None.

**Abstract Number:** 1760

**Pulmonary Manifestations in Microscopic Polyangiitis and Granulomatosis with Polyangiitis: A Multicenter Cohort Analysis**

Saara M. Rawn¹, Gerard Cox¹, Christian Pagnoux², David Cuthbertson³, Simon Carette², Curry L. Koening⁴, Carol A. Langford⁵, Carol A. McAleen³, Paul A. Monach⁷, Larry W. Moreland⁸, Philip Seo⁹, Ulrich Specks¹⁰, Antoine G. Sreih¹¹, Steven R. Ytterberg¹², Renee Borchin¹³, Peter A. Merkel¹¹ and Nader A. Khalidi¹, ¹St. Joseph's Healthcare, McMaster University, Hamilton, ON, Canada, ²Division of Rheumatology, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada, ³Department of Biostatistics, University of South Florida, Tampa, FL, ⁴Rheumatology, University of Utah, Salt Lake City, UT, ⁵Rheumatic and Immunologic Diseases, Cleveland Clinic, Cleveland, OH, ⁶Division of Rheumatology, University of Pennsylvania, Philadelphia, PA, ⁷Rheumatology, Boston University, Boston, MA, ⁸Rheumatology & Clinical Immunology, University of Pittsburgh, Pittsburgh, PA, ⁹Division of Rheumatology, Johns Hopkins University, Baltimore, MD, ¹⁰Mayo Clinic, Rochester, MN, ¹¹Rheumatology, University of Pennsylvania, Philadelphia, PA, ¹²Division of Rheumatology, Mayo Clinic, Rochester, MN, ¹³University of South Florida, Tampa, FL

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Vasculitis Poster II: ANCA-Associated Vasculitis

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Pulmonary involvement in microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA) includes pulmonary nodules (PN), diffuse alveolar hemorrhage (DAH), and infiltrates attributed to vasculitis, each of which can co-exist.

The primary aim of this study was to determine the frequency of patients with both PN and DAH within the Vasculitis Clinical Research Consortium (VCRC) Longitudinal Study cohort. Additionally, it was determined whether patients with both PN and DAH had higher...
mortality or experienced a higher frequency of disease flares as compared to patients with only PN, only DAH, only infiltrates, or patients with GPA/MPA without these pulmonary manifestations.

Methods:

Data were extracted from the VCRC Longitudinal Study cohort. All patients in the cohort satisfied the modified ACR classification criteria for GPA or Chapel Hill Consensus definition of MPA. Pulmonary manifestations were classified as per assessment by site investigators and reported to the database via a standard protocol.

Results:

Of 736 patients with GPA/MPA in the cohort, 250 (34.0%) never developed pulmonary findings and 486 (66.0%) developed lung manifestations (Figure 1). If PN were not the first lung manifestation of the 343 patients to ever develop nodules, only 20 (5.8%) patients developed them at a later date. If patients had DAH as their initial manifestation, only 4 (2.2%) patients developed PN later in their disease course. PN and DAH were noted to be contemporaneous in 71 (14.6%) of patients. Nine patients (2.6%) with PN first went on to develop DAH, compared with 4 (2.4%) of patients who had infiltrates first.

Patients with GPA/MPA without pulmonary findings experienced 0.77 deaths/100 patient-years, which was comparable to patients with PN alone at 0.66/100 patient-years (p=0.79), DAH alone at 0.89/100 patient-years (p=0.78), and PN and DAH together at 0.69/100 patient-years (p=0.83). In patients with each of PN, DAH and infiltrates there were 1.84 deaths/100 patient-years, or 3 deaths out of 32 patients (p=0.25).

Patients without pulmonary findings had disease flares at a rate of 8.68/100 patient-years. PN alone had a flare rate of: 5.71/100 patient-years (p=0.07), DAH alone: 7.54/100 patient-years (p=0.92), PN and DAH: 7.96/100 patient-years (p=0.80). Those with each of PN, DAH and infiltrates had a flare-rate of 23.31/100 patient-years (p<0.01).

Conclusion:

Presentation with PN and DAH, but not infiltrates, occurs at a frequency of 10.5% in patients with GPA/MPA. Such patients have similar outcomes compared to patients without lung manifestations of vasculitis, those with only PN, or those with only DAH. However, those subjects who ever manifested each of PN, DAH and infiltrates during the course of their illness are at higher risk of flare.

Figure 1. Distribution of pulmonary nodules, diffuse alveolar hemorrhage and infiltrates in GPA and MPA. Azalea of intersection represent the number of patients who ever had pulmonary nodules and DAH (pANCA m112, pANCA m113); pulmonary nodules and infiltrates (pANCA m113); diffuse alveolar hemorrhage and infiltrates (pANCA m112); pulmonary nodules, DAH and infiltrates (pANCA m112, pANCA m113); other pulmonary findings are not shown. DAH = diffuse alveolar hemorrhage, pANCA = cytoplasmic antineutrophil cytoplasmic antibodies. protective antineutrophil cytoplasmic antibodies.

Disclosure: S. M. Rawn, None; G. Cox, None; C. Pagnoux, None; D. Cuthbertson, None; S. Carette, None; C. L. Koenig, None; C. A. Langford, None; C. A. McAlear, None; P. A. Monach, None; L. W. Moreland, None; P. Seo, None; U. Specks, None; A. G. Sreih, None; S. R. Ytterberg, None; R. Borchin, None; P. A. Merkel, None; N. A. Khalidi, None.

Abstract Number: 1761

Differential Characteristics of MPO-ANCA Positive and Negative Eosinophilic Granulomatosis with Polyangiitis
Shunsei Hirohata\textsuperscript{1}, Yu Matsueda\textsuperscript{2} and Yoshiyuki Arinuma\textsuperscript{2}, \textsuperscript{1}Kitasato University School of Medicine, Sagamihara, Japan, \textsuperscript{2}Rheumatology and Infectious Diseases, Kitasato University School of Medicine, Kanagawa, Japan

\textbf{First publication:} September 18, 2017

\section*{SESSION INFORMATION}

\textbf{Session Date:} Monday, November 6, 2017  
\textbf{Session Title:} Vasculitis Poster II: ANCA-Associated Vasculitis  
\textbf{Session Type:} ACR Poster Session B  
\textbf{Session Time:} 9:00AM-11:00AM

\textbf{Background/Purpose:} Eosinophilic granulomatosis with polyangiitis (EGPA) is characterized by the preceding history of type I allergic disorders, mostly bronchial asthma, followed by the development of vasculitis affecting mainly peripheral nervous system. Whereas MPO-ANCA is detected in approximately 60\% of patients with EGPA, its relationship with clinical manifestations remains unclear. We carried out a retrospective cohort study on patients in Tokyo metropolitan area to compare the clinical features between MPO-ANCA positive and negative EGPA.

\textbf{Methods:} All the patients fulfilled the diagnostic criteria for EGPA of the Japanese research committee of intractable vasculitis. Certificated medical records for application of medical subsidy between 2007 and 2010 were reviewed.

\textbf{Results:} A total of 131 patients were collected, aged 59.3 ± 15.9 years (Mean ± SD) (47 males, 84 females). The preceding allergic symptoms were bronchial asthma with or without allergic rhinitis in 96.9\%, and allergic rhinitis alone in 3.1\%. Peripheral neuropathy (mostly mononeuritis multiplex) was observed in 96.9\%. MPO-ANCA was positive in 53 patients (40.4\%). There were no significant differences in ages and gender between MPO-ANCA (+) patients and MPO-ANCA (-) patients. As to the vasculitic manifestations, arthritis and glomerulonephritis were more prevalent in MPO-ANCA (+) patients than in MPO-ANCA (-) patients (32.1\% vs 17.9\% [p=0.0612] and 24.5\% vs 2.6\% [p=0.0001], respectively, whereas there were no significant differences in frequencies of other manifestations, including purpura, fever, body weight loss, gastrointestinal bleeding, and cardiopulmonary involvement. Peripheral blood eosinophil counts and serum rheumatoid factors were significantly higher in MPO-ANCA (-) patients than in MPO-ANCA (+) patients, whereas there were no significant differences in white blood cell counts, platelet counts and serum IgE. Cyclophosphamide appeared to be administered more frequently in MPO-ANCA (+) patients than MPO-ANCA (-) patients (54.7\% vs 48.7\% [p=0.0710]), whereas there were no significant differences in the use of steroid pulse therapy (54.7\% vs 48.7\% [p=0.5937]).

\textbf{Conclusion:} The results underscore the differential features between MPO-ANCA (+) and MPO-ANCA (-) EGPA, especially the higher prevalence of arthritis and glomerulonephritis in the former. Thus, the data indicate that MPO-ANCA (+) EGPA has features comparable to microscopic polyangiitis, although further studies are needed to delineate the mechanisms of differences in eosinophil counts and rheumatoid factors.

\textbf{Disclosure:} S. Hirohata, None; Y. Matsueda, None; Y. Arinuma, None.

\textbf{View Abstract and Citation Information Online} - \url{http://acrabstracts.org/abstract/differential-characteristics-of-mpo-anca-positive-and-negative-eosinophilic-granulomatosis-with-polyangiitis}

\textbf{Abstract Number:} 1762

\section*{Association of ETS1 Polymorphism in 3’ Untranslated Region with Susceptibility to Granulomatosis with Polyangiitis and Proteinase 3-ANCA Positive Vasculitis in a Japanese Population}

Aya Kawasaki\textsuperscript{1}, Keita Yamashita\textsuperscript{2}, Fumio Hirano\textsuperscript{3}, Ken-ei Sada\textsuperscript{4}, Daisuke Tsukui\textsuperscript{5}, Yuya Kondo\textsuperscript{6}, Yoshitaka Kimura\textsuperscript{5}, Kurumi Asako\textsuperscript{5}, Shigeto Kobayashi\textsuperscript{7}, Hidehiro Yamada\textsuperscript{8}, Hiroshi Furukawa\textsuperscript{1}, Kenji Nagasaki\textsuperscript{9}, Takahiko Sugihara\textsuperscript{10}, Kunihiro Yamagata\textsuperscript{11}, Takayuki Sumida\textsuperscript{8}, Shigeto Tohma\textsuperscript{12}, Hajime Kono\textsuperscript{5}, Shoichi Ozaki\textsuperscript{8}, Seiichi Matsuo\textsuperscript{13}, Hiroshi Hashimoto\textsuperscript{14}, Hirofumi Makino\textsuperscript{15}, Yoshihiro Arimura\textsuperscript{16}, Masayoshi Harigai\textsuperscript{17} and Naoyuki Tsuchiya\textsuperscript{1}, \textsuperscript{1}Molecular and Genetic Epidemiology Laboratory, University of Tsukuba, Faculty of Medicine, Tsukuba, Japan, \textsuperscript{2}Molecular and Genetic Epidemiology, University of Tsukuba, Faculty of Medicine, Tsukuba, Japan, \textsuperscript{3}Departments of Rheumatology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan, \textsuperscript{4}Department of Rheumatology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan, \textsuperscript{5}Department of Internal Medicine, Teikyo University School of Medicine, Tokyo, Japan, \textsuperscript{6}Department of Internal Medicine, University of Tsukuba, Faculty of Medicine, Tsukuba, Japan, \textsuperscript{7}Department of Internal Medicine, Juntendo University Koshigaya Hospital, Koshigaya, Japan, \textsuperscript{8}Department of Internal Medicine, St.
Marianna University School of Medicine, Kawasaki, Japan, 9Department of Rheumatology, Ome Municipal General Hospital, Ome, Japan, 10Department of Medicine and Rheumatology, Tokyo Metropolitan Geriatric Hospital, Tokyo, Japan, 11Department of Nephrology, University of Tsukuba, Faculty of Medicine, Tsukuba, Japan, 12Clinical Research Center for Allergy and Rheumatology, Sagamihara Hospital, National Hospital Organization, Sagamihara, Japan, 13Department of Nephrology, Nagoya University Graduate School of Medicine, Nagoya, Japan, 14Juntendo University School of Medicine, Tokyo, Japan, 15Okayama University Hospital, Okayama, Japan, 16First Department of Internal Medicine, Kyorin University School of Medicine, Tokyo, Japan, 17Division of Epidemiology and Pharmacoepidemiology of Rheumatic Diseases, Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Vasculitis Poster II: ANCA-Associated Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: ETS Proto-oncogene 1, transcription factor (ETS1) is a transcription factor involved in immune responses. Genome-wide association studies on systemic lupus erythematosus (SLE) in Chinese populations identified the association of ETS1 polymorphism in 3' untranslated region, rs1128334 A allele, which was associated with lower ETS1 expression. Recent studies indicated that many susceptibility genes are shared by multiple autoimmune diseases. In this study, we examined whether ETS1 is associated with ANCA-associated vasculitis (AAV) in a Japanese population.

Methods: Association of rs1128334 was tested in 466 Japanese patients with AAV and 1099 healthy controls by logistic regression analysis under the additive model. AAV patients were classified into 285 microscopic polyangiitis (MPA), 92 granulomatosis with polyangiitis (GPA), 56 eosinophilic GPA, and 33 unclassifiable AAV, according to the European Medicines Agency (EMEA) algorithm. Among the patients, 376 were positive for MPO-ANCA and 62 for PR3-ANCA. Expression levels in ETS1 mRNA in the whole peripheral blood were compared between 8 AAV patients and 14 healthy controls.

Results: When the patients were classified according to the EMEA classification, rs1128334 A was significantly increased in GPA (P=0.0060, Pc=0.030, odds ratio [OR] 1.54, 95% confidence interval [CI] 1.13-2.10) when compared with healthy controls. With respect to the ANCA specificity, significant association was observed in PR3-ANCA positive AAV (P=0.0042, Pc=0.021, OR 1.72, 95% CI 1.19-2.49). Expression analysis indicated that ETS1 mRNA levels were decreased in AAV (P=0.0024).

Conclusion: ETS1 polymorphism was suggested to be associated with susceptibility to GPA and PR3-ANCA positive AAV in a Japanese population.

Table 1. Association of ETS1 polymorphism with AAV in a Japanese population.

<table>
<thead>
<tr>
<th>ETS1 rs1128334</th>
<th>A/A</th>
<th>A/G</th>
<th>G/G</th>
<th>A allele</th>
<th>P</th>
<th>Pc</th>
<th>OR(95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EMEA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>classification</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GPA(n=92)</td>
<td>20 (0.217)</td>
<td>50 (0.543)</td>
<td>22 (0.239)</td>
<td>90 (0.489)</td>
<td>0.0060</td>
<td>0.030</td>
<td>1.54 (1.13-2.10)</td>
</tr>
<tr>
<td>MPA(n=285)</td>
<td>53 (0.186)</td>
<td>138 (0.484)</td>
<td>94 (0.330)</td>
<td>244 (0.428)</td>
<td>0.072</td>
<td>0.36</td>
<td>1.19 (0.98-1.44)</td>
</tr>
<tr>
<td>EGPA(n=56)</td>
<td>7 (0.125)</td>
<td>30 (0.536)</td>
<td>19 (0.339)</td>
<td>44 (0.393)</td>
<td>0.90</td>
<td>1.0</td>
<td>1.03 (0.69-1.52)</td>
</tr>
<tr>
<td><strong>ANCA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>specificity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PR3-AAV(n=62)</td>
<td>17 (0.274)</td>
<td>30 (0.484)</td>
<td>15 (0.242)</td>
<td>64 (0.516)</td>
<td>0.0042</td>
<td>0.021</td>
<td>1.72 (1.19-2.49)</td>
</tr>
<tr>
<td>MPO-AAV(n=376)</td>
<td>68 (0.181)</td>
<td>188 (0.500)</td>
<td>120 (0.319)</td>
<td>324 (0.431)</td>
<td>0.032</td>
<td>0.16</td>
<td>1.20 (1.02-1.43)</td>
</tr>
<tr>
<td>Healthy controls(n=1099)</td>
<td>156 (0.142)</td>
<td>539 (0.490)</td>
<td>404 (0.368)</td>
<td>851 (0.387)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Disclosure: A. Kawasaki, None; K. Yamashita, None; F. Hirano, Chugai Pharmaceutical Co., Ltd.; Ono Pharmaceuticals; Mitsubishi Tanabe Pharma Co.; UCB Japan; CSL Behring; Towa Pharmaceutical Co., Ltd.; Abbvie Japan Co., Ltd.; Japan Blood Products
Abstract Number: 1763

**Time to Diagnosis of ANCA-Associated Vasculitides: Data from French Vasculitis Study Group Registry**

Caroline Morbieu, Maher Banjari, Benjamin Terrier, Pascal Cohen, Claire Le Jeune, Luc Mouthon, Xavier Puéchal andLoïc Guillemin for the French Vasculitis Study Group, National Referral Center for Rare Systemic Autoimmune Diseases, Hôpital Cochin, AP–HP, Université Paris Descartes, Paris, France

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017  
Session Title: Vasculitis Poster II: ANCA-Associated Vasculitis  
Session Type: ACR Poster Session B  
Session Time: 9:00AM-11:00AM  

Background/Purpose:

Diagnosing ANCA-associated vasculitides (AAVs) can be challenging. Their clinical presentations are numerous and the time to diagnosis may range from days to years.\(^1,2\) The impact of delayed diagnosis on AAV outcome has not been established. This study was conducted to assess the first-symptom-to-diagnosis times for patients with granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA).

Methods:

Adults diagnosed with new onset GPA or MPA between 2005 and 2015 and followed at Cochin National Referral Center for Vasculitides were selected from the French Vasculitis Study Group (FVSG) Registry. Patients were excluded when the date and first symptom were incomplete. First symptom (systemic vs ENT), clinical and laboratory findings, Birmingham Vasculitis Activity Score (BVAS) at diagnosis, time to diagnosis and Vasculitis Damage Index (VDI) at last visit were collected from the FVSG registry’s database and medical records. The first symptom had been systematically assessed by the treating physician at diagnosis. Data are expressed as median, interquartile range. Pearson and Mann–Whitney tests were used to analyze data.

Results:

Among 257 patients screened, 29 were excluded. The study population comprised 228 patients: 169 with GPA and 59 with MPA (median age at diagnosis 55 years [42–65]; M/F sex ratio 0.81). At diagnosis, their median BVAS was 12 [7–18], 44% had renal involvement and 22% had 2009 Five Factor Scores ≥1. The median time to diagnosis was 5.1 [2.1–16.2] (range 0.1–356) months, for which GPA and MPA did not differ significantly. Among AAV patients’ first symptoms, 174 (76%) were systemic and 54 (24%) were ENT, with longer times to diagnosis when ENT was the first symptom (8.65 vs 4.1 systemic; \(\text{P}<0.0001\)). The median time from first ENT to first systemic symptom was 6.1 [3.6–33] months. The time to diagnosis was significantly longer in women (6.1 vs 4.1 men; \(\text{P}<0.05\)) and in the absence of renal involvement (6.1 vs 3.2 renal involvement; \(\text{P}<0.01\)). No association was found between time to diagnosis and age, date of diagnosis, BVAS at diagnosis, or VDI at last visit. Thirty-nine (17%) patients, mostly with GPA (27, 69%), were diagnosed >24 months after the first symptom, which was mainly arthritis/arthralgias (n=9), retroorbital tumor (n=5), purpura/livedo (n=5), thoracic nodules (n=5), ENT (n=5) or others (n=10). Corticosteroids (4 patients) or immunosuppressants (3 patients) were prescribed before AAV diagnosis.
Conclusion:
The time to AAV diagnosis remains long, especially when the first symptom involves ENT. ANCA testing might shorten the time to diagnosis, and should be considered even in pauci-symptomatic patients.

References:
1 Yacyshyn E. Joint Bone Spine 2016;83:599.

Disclosure: C. Morbieu, None; M. Banjari, None; B. Terrier, None; P. Cohen, None; C. Le Jeunne, None; L. Mouton, None; X. Puéchal, None; L. Guillevin for the French Vasculitis Study Group, None.

Abstract Number: 1764

Small RNA Sequencing Shows Differential Plasma Microrna Expression in Patients with ANCA-Associated Vasculitis: A Pilot Study

Kevin Byram1, Joseph F. Solus1, Quanhui Sheng1, Yan Guo1, C Michael Stein1 and Michelle J. Ormseth2, 1Vanderbilt University Medical Center, Nashville, TN, 2Rheumatology, Vanderbilt Medical Center, Nashville, TN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Vasculitis Poster II: ANCA-Associated Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: MicroRNAs (miRNAs) are small RNA molecules (~22 nucleotides) that participate in post-transcriptional gene regulation. miRNAs have potential both as biomarkers for diagnosis and prognosis and as therapies. Few studies have examined plasma miRNA expression in patients with anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV); those that have focused on microarray and PCR-based analyses of a limited number of candidate miRNAs. Our objective was to determine which plasma miRNAs are altered in AAV compared to patients with inflammatory autoimmune disease and also control subjects using an unbiased approach: high throughput small RNA sequencing.

Methods: This pilot study included 10 patients with AAV, 13 controls with inflammatory disease (4 with rheumatoid arthritis and 9 with systemic lupus erythematosus), and 5 controls without inflammatory disease. Stored plasma was used to extract RNA and construct RNA sequencing libraries. Sequencing was done on Illumina NextSeq500. High quality reads were mapped to the human GRCh38 genome using Bowtie. MiRBase21.0 was used to quantify miRNAs. The abundance of miRNA expression was compared between AAV and both groups of control subjects by DESeq2 with 5% false discovery rate and adjustment for multiple comparisons by the Benjamini and Hochberg method. Potential miRNA pathway targets were explored with TargetScanHuman v7.1 and Ingenuity Pathway Analysis.

Results: Mean age was 64 years ± 11 years among patients with AAV, 43 ± 12 years among inflammatory disease controls, and 58 ± 13 years among control subjects. All groups were predominately Caucasian. Active disease was present in 60% of patients with AAV and 69% of inflammatory disease control subjects. Among patients with AAV, 100% were ANCA positive, 60% were positive for anti-proteinase 3 antibody and 40% were positive for anti-myeloperoxidase antibody. Of 209 reliably mapped miRNAs, 15 were significantly differentially expressed (≥2-fold) in patients with AAV compared to both control groups (Table). Of these, miR-21-5p and miR-17-5p are both predicted to target TGFBR2, a gene associated with various vascular phenotypes; and miR-146a-5p is predicted to target TLR9, a gene containing variants associated with AAV.

Conclusion: Several plasma miRNAs are differentially expressed in patients with AAV compared to patients with inflammatory autoimmune disease and controls. Further validation is necessary to confirm these findings.

Table. Significant differential microRNA expression in patients with ANCA-associated vasculitis compared to controls with and without inflammatory disease.
<table>
<thead>
<tr>
<th>miRNA</th>
<th>AAV vs Inflammatory Controls</th>
<th>AAV vs Noninflammatory Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fold Change</td>
<td>P-adj</td>
</tr>
<tr>
<td>miR-146b-5p</td>
<td>5.14</td>
<td>0.007</td>
</tr>
<tr>
<td>miR-320a</td>
<td>3.88</td>
<td>0.028</td>
</tr>
<tr>
<td>miR-98-5p</td>
<td>4.15</td>
<td>0.028</td>
</tr>
<tr>
<td>miR-146a-5p</td>
<td>3.54</td>
<td>0.028</td>
</tr>
<tr>
<td>miR-17-5p</td>
<td>4.15</td>
<td>0.028</td>
</tr>
<tr>
<td>miR-21-5p</td>
<td>3.64</td>
<td>0.028</td>
</tr>
<tr>
<td>let-7b-5p</td>
<td>3.83</td>
<td>0.032</td>
</tr>
<tr>
<td>miR-378a-3p</td>
<td>3.26</td>
<td>0.032</td>
</tr>
<tr>
<td>miR-148a-3p</td>
<td>3.19</td>
<td>0.032</td>
</tr>
<tr>
<td>miR-221-3p</td>
<td>3.32</td>
<td>0.032</td>
</tr>
<tr>
<td>miR-1307-3p</td>
<td>3.29</td>
<td>0.033</td>
</tr>
<tr>
<td>miR-155-5p</td>
<td>3.44</td>
<td>0.035</td>
</tr>
<tr>
<td>let-7a-5p</td>
<td>3.06</td>
<td>0.038</td>
</tr>
<tr>
<td>miR-421</td>
<td>3.14</td>
<td>0.038</td>
</tr>
<tr>
<td>miR-3168</td>
<td>2.96</td>
<td>0.041</td>
</tr>
</tbody>
</table>

Disclosure: K. Byram, None; J. F. Solus, None; Q. Sheng, None; Y. Guo, None; C. M. Stein, None; M. J. Ormseth, None.


**Validation of the ACR EULAR Provisional 2017 Classification Criteria of Granulomatosis with Polyangiitis (GPA) Amongst Patients with ANCA Associated Vasculitis**

Aman Sharma1, Adarsh MB2, Shankar Naidu3, Manish Rathi4, Benzeeta Pinto5, Varun Dhir6, Roshan Verma7, Kusum Sharma8, Ritambhara Nada9, Sanjay Jain5 and Ranjana Minz10

1 Internal Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh, India; 2 Internal Medicine, PGIMER, Chandigarh, India; 3 PGIMER, Chandigarh, India; 4 Department of Nephrology, PGIMER, Chandigarh, India; 5 PGIMER, Chandigarh, India; 6 Internal Medicine (Rheumatology Unit), PGIMER, Chandigarh, India; 7 PGIMER, Chandigarh, India; 8 Department of Medical Microbiology, PGIMER, Chandigarh, India; 9 Histopathology, Professor, Chandigarh, India; 10 Department of Immunopathology, PGIMER, Chandigarh, India

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017
**Session Title:** Vasculitis Poster II: ANCA-Associated Vasculitis
**Session Type:** ACR Poster Session B
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The purpose of this study was to validate the recently proposed ACR EULAR 2017 classification criteria of GPA in a real life cohort of ANCA associated vasculitis (AAV).

**Methods:** The proposed ACR EULAR 2017 criteria of GPA were applied to patients diagnosed to have AAV according to European Medicines Agency (EMA) algorithm. The level of agreement between the two criteria was assessed using Cohen’s kappa, and positive and negative percent agreement (PPA and NPA).
Results: 187 patients with mean age of 41.5±15.0 years were included. Female: male ratio was 1:0.8. ANCA by IIF was done in all patients and was positive in 142(cANCA -97, pANCA -45) . PR3/MPO ELISA was available in 118 patients(PR3-71, MPO- 31). Using EMA algorithm EGPA was diagnosed in 6, GPA in 148 and MPA in 33. With ACR 1990 criteria, GPA was diagnosed in 118 patients while with ACR/EULAR 2017 criteria 115 were classified as GPA. ACR/EULAR 2017 had better agreement with EMA (kappa-0.35, PPA-91.3 and NPA-40.2) than ACR criteria (kappa 0.15, PPA -68.6 and NPA -45.8). The sensitivity and specificity of ACR/EULAR 2017 against EMA GPA was 70.9% and 74.3% respectively. Ten out of thirty three MPA patients were reclassified as GPA by ACR/EULAR 2017 criteria. Out of 43 patients who were GPA by EMA algorithm but not by ACR EULAR 2017 criteria, 37 had lung and reninal involvement (DCVAS score 2), three had sinus and renal involvement (DCVAS score 3) and three had lung involvement with MPO positivity (DCVAS score 2). This resulted in low NPA of ACR EULAR 2017 criteria with EMA algorithm.

Conclusion: Within the limits of a retrospective design, the study showed fair agreement with high PPA but low NPA of ACR/EULAR 2017 criteria with EMA algorithm.

Table 1. Reclassification of various AAV patients (EMA and ACR 1990) by ACR EULAR 2017 provisional criteria of GPA

<table>
<thead>
<tr>
<th>ANCA associated vasculitis</th>
<th>No. of patients (n=187, %,)</th>
<th>Reclassified as GPA by ACR/EULAR 2017 criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACR 1990 GPA</td>
<td>118(63.1)</td>
<td>79</td>
</tr>
<tr>
<td>EMA GPA</td>
<td>148(79.1)</td>
<td>105</td>
</tr>
<tr>
<td>EMA MPA</td>
<td>33(17.6)</td>
<td>10</td>
</tr>
<tr>
<td>EMA EGPA</td>
<td>6(3.2)</td>
<td>0</td>
</tr>
</tbody>
</table>

Figure 1 – Showing different AAV according to various classification criteria

Disclosure: A. Sharma, None; A. MB, None; S. Naidu, None; M. Rathi, None; B. Pinto, None; V. Dhir, None; R. Verma, None; K. Sharma, None; R. Nada, None; S. Jain, None; R. Minz, None.


Abstract Number: 1766

Increased Renal Damage in Hypocomplementemic Patients with ANCA- Associated Vasculitis

Lucila Garcia¹, Claudia Elizabeth Pena², Mariana Pera³, Mercedes Garcia², Valeria Arturi³, Viviana Nagua¹, Rodrigo Aguila Maldonado², Ana Carolina Costi², Adriana Testi¹, Ariel Vulcano¹, Pierina Sansinanea¹, Martin Mamberti⁴, Maria Elena Bruzzone⁴, Carolina Barabani⁴ and Jimena Salomone⁴, ¹Rheumatology, HIGA General San Martin La Plata, la plata, Argentina, ²Rheumatology, HIGA General San Martin La Plata, La Plata, Argentina, ³HIGA General San Martin La Plata, La Plata, Argentina, ⁴Nephrology, HIGA General San Martin La Plata, la plata, Argentina
SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Vasculitis Poster II: ANCA-Associated Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: The pauci-immune nature of typical lesions in ANCA associated vasculitis (AAV) has led to the belief that complement does not play a role in the pathogenesis of this disease. Activation of the alternative complement pathway is necessary for the development of glomerulonephritis in murine models. The complement deposition in renal biopsies of patients with AAV was correlated with increased renal damage.

We hypothesized that there is greater morbidity, mortality and worse renal outcomes in hypocomplementemic patients with AAV compared to those who have normal complement values at the onset of the disease.

Our purpose was to compare clinical manifestations, laboratory values, histological type, renal prognosis and mortality in normal and hypocomplementemic patients with AAV.

Methods: Retrospective, observational, analytical study. Data from the medical records of patients over the age of 18 were evaluated between the years 2000-2017. Patients with diagnosis of AAV who met the criteria of ACR 1990 Classification or Chapel Hill Concensus Conference 2012 were included. Hypocomplementemia was defined as C3 values below 80 mg/dl or C4 below 15 mg/dl. Chi-square or Fisher's exact test was used for dichotomous variables as appropriate. P-value <0.05 was considered statistically significant. Logistic regression analysis was used to identify predictors of survival.

Results: We analyzed 87 patients with AAV (female 56.2%, mean follow-up 24 months, mean age at onset of the disease 49 years ± 14.9 SD). Most frequent type of vasculitis was Granulomatosis with polyangeitis (49.4%).

Hypocomplementemia was determined in 7/57 patients (12.28%) and was significantly associated with renal damage (p: 0.034 OR 12.8 CI95% 0.69-236) particularly with decreased glomerular filtrate (p: 0.045 OR: 8.2 CI 95% 0.92-74.0). A higher prevalence of proteinuria greater than 1 gr/24 hs was observed in hypocomplementemic patients 57% vs 25% (p: 0.068).

All renal biopsies were classified as pauci-immune glomerulonephritis. Average number of glomeruli affected was 13 [IQR 25-75% (7-17)], predominating the sclerosing type (44%). The degree of interstitial fibrosis, tubular atrophy (52%) and vascular damage (57%) was mild. In 3 samples we observed deposits of immunocomplexes (IgG+), complement (C3+) or fibrinogen by immunofluorescence. These patients showed creatinine values above 4 mg/dl. There were no statistically significant differences in renal histology between groups (p: 0.091).

There was no association between hypocomplementemia and other organic damage or laboratory values.

Mortality rate was 18% (16/87), without differences between groups (p: 0.300).

Conclusion: Hypocomplementemia was associated with increased renal damage: decreased glomerular filtrate and greater values of proteinuria; as reported in the literature. We did not find any other statistically significant difference between groups.

Disclosure: L. García, None; C. E. Pena, None; M. Pera, None; M. García, None; V. Arturi, None; V. Nagua, None; R. Aguila Maldonado, None; A. C. Costi, None; A. Testi, None; A. Vulcano, None; P. Sansinanea, None; M. Mamberti, None; M. E. Bruzzone, None; C. Barabani, None; J. Salomone, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/increased-renal-damage-in-hypocomplementemic-patients-withanca-associated-vasculitis

Abstract Number: 1767

The Effect on Health-Related Quality of Life of Treatment for Remission Maintenance in ANCA-Associated Vasculitis Beyond 18 Months

Gunnar Tomasson1, Antoine G. Sreih2, David Cuthbertson3, Simon Carette4, Nader A. Khalidi5, Curry L. Koening6, Carol A. Langford7, Carol A. McAlear8, Paul A. Monach9, Larry W. Moreland10, Philip Seo11, Ulrich Specks12, Steven R. Ytterberg13 and Peter A. Merkel14, 1University of Iceland, Faculty of Medicine, Reykjavik, IS, 2Rheumatology, University of Pennsylvania, Philadelphia, PA,
SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Vasculitis Poster II: ANCA-Associated Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Standard management of ANCA-associated vasculitis (AAV) involves treatment with immunosuppressive agents for at least 18 months. Treatment beyond 18 months reduces the rates of relapses but effect on health-related quality of life (HRQoL) is not known. The objective of this study was to assess the effect of treatment with immunosuppressive agents on HRQoL among patients with AAV that have had a sustained remission for at least 18 months.

Methods: Data from a multicenter longitudinal study of patients with AAV were used. Subjects came for quarterly- or annually-scheduled study visits. Disease activity was assessed by the Birmingham Vasculitis Activity Score for Wegener’s Granulomatosis (BVAS/WG), and medication use was recorded. Recording of ANCA status, previous disease flares, and a comprehensive cumulative list of disease manifestations was done at the initial study visit. Sustained remission was defined as enrollment in the cohort for 18 consecutive months without any detectable disease activity. Immunosuppressive medication use was defined as use of azathioprine, infliximab, methotrexate, mycophenolate mofetil, or rituximab. HRQoL was assessed with the physical component (PCS) and mental (MCS) summary scores of the Short Form 36 (SF-36) which have a normal distribution with a mean of 50 and standard deviation of 10 in the general population. The effect of immunosuppressive treatment was calculated with a linear regression model adjusted for age and sex, and additionally adjusted for ANCA type, organ involvement, and previous history of disease flare. General estimating equations were used to account for multiple visits from each subject.

Results: Data from 434 subjects that came for 1,679 study visits were used. At 979 visits (59%) subjects were receiving immunosuppressive agents. The median follow-up time was 1.84 years (Inter-Quartile Range 0.73 – 3.25). The mean age was 55.3 years (standard deviation 14.8) and 55% were women. The mean SF36 scores in were 43.8 and 50.3 for PCS and MCS, respectively. Use of immunosuppressive agents was associated with 2.17 (p=0.02) lower score for PCS and 0.43 (p=0.64) lower scores for MCS. Additional adjustment for ANCA type, organ involvement, and previous history of disease flare minimally affected the findings with 1.97 (p=0.03) and 0.28 (p=0.61) lower scores for PCS and MCS, respectively.

Conclusion: Among patients with AAV who have had sustained remission for 18 months long-term use of continued immunosuppressive medications is not associated with additional improvement in HRQoL.

Disclosure: G. Tomasson, None; A. G. Sreih, None; D. Cuthbertson, None; S. Carette, None; N. A. Khalidi, None; C. L. Koenig, None; C. A. Langford, None; C. A. McAlear, None; P. A. Monach, None; L. W. Moreland, None; P. Seo, None; U. Specks, None; S. R. Ytterberg, None; P. A. Merkel, None.


Abstract Number: 1768

Cocaine and ANCA Associated Vasculitis-like Syndromes – a Case Series

Sujith Subesinghe1, Sander van Leuven2, Leena Yalakki3, Shirish Sangle (Joint First Author)3 and David P. D'Cruz3, 1Rheumatology and Lupus, Guy's and St Thomas' Hospitals NHS Foundation Trust, London, United Kingdom, 2Rheumatology, Radboud University, Nijmegen, Netherlands, 3Louise Coote Lupus Unit, Rheumatology and Lupus, Guy's and St Thomas' Hospitals NHS Foundation Trust, London, United Kingdom

First publication: September 18, 2017
Background/Purpose:

Cocaine is a potent illicit stimulant and may trigger a ‘pseudovasculitis’ mimicking idiopathic ANCA vasculitis. We describe the clinical and serological manifestations of patients presenting with cocaine pseudovasculitis from the experience of a single tertiary rheumatology centre.

Methods:

The electronic patient record and clinic correspondence of 14 patients presenting consecutively between 2000 and 2017 to Guy’s and St. Thomas’ Hospitals London with cocaine pseudovasculitis were analysed. All patients disclosed a history of chronic habitual cocaine use. All patients had blood samples analysed for ANCA antibodies, inflammatory markers, haematology and biochemistry profiles. Eleven patients had CT sinus imaging, 8 had chest CT scans. Ten patients had tissue biopsies (renal, skin or nasal/sinus) during clinical work-up.

Results:

There were 10 male and 4 female patients, median age 39 years (range 25-52 years). The mean duration of cocaine use prior to presentation was 9.6 years (range 6-15). Twelve patients had significant sinus thickening or erosive nasal disease. Other multi-system manifestations included vasculitic rashes, pulmonary lesions and peripheral neuropathy. All patients had positive ANCA titres at presentation, persisting in 8 subjects despite clinical remission and drug cessation. Four patients had unusual ANCA patterns (P-ANCA, PR3 positive) with persistently positive ANCA on repeat assessment. Acute and chronic inflammatory changes were noted in all biopsy samples but no granulomas were visualised in the patients who underwent sinus or nasal biopsy. All patients were managed with corticosteroids +/- methotrexate and co-trimoxazole, 2 patients received cyclophosphamide.

The baseline demographics, laboratory assessments, serological status and clinical manifestations (including histological findings where available) are presented in the table. Four patients had positive urinary screens confirming recent cocaine exposure (patients 11 - 14).

Conclusion:

Cocaine induced vasculitis may be difficult to distinguish from idiopathic ANCA vasculitis. Cocaine induced disease is usually associated with localised rather than multi-system involvement. Advanced erosive nasal septal defects, atypical ANCA patterns, and urinary drug screen may be helpful to identify the cocaine induced pseudovasculitis. Complete drug cessation may negate the need for potent immunosuppressive agents. Early referral to drug rehabilitation services may be helpful.
<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age</th>
<th>Duration of cocaine use prior to presentation (years)</th>
<th>Serology</th>
<th>Creatinine (U/ml)</th>
<th>Pulmonary lesions</th>
<th>ENT lesions</th>
<th>Tissue histology</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>25</td>
<td>6</td>
<td>C-ANCA + PR3 57.5</td>
<td>64</td>
<td>+</td>
<td>None (X-ray)</td>
<td>Sinus biopsy: granulation tissue, no evidence of vasculitis</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>39</td>
<td>12</td>
<td>P-ANCA + MPO 22</td>
<td>74</td>
<td>+</td>
<td>None (CT)</td>
<td>Sinus biopsy: fibros acute and chronic inflammation. Necrosis at the surface with deeper, microscopic foci of stromal necrosis. Foci of acute venular inflammation no fibrinoid necrosis Polymorph inflammatory cell infiltrate. No granuloma seen.</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>39</td>
<td>60</td>
<td>P-ANCA + PR3/ MPO Ð</td>
<td>10</td>
<td>+</td>
<td>Solitary nodule and calcified granuloma (CT)</td>
<td>Maxillary antrum mucosal thickening. Thickening of osteomeatal complex.</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>43</td>
<td>99</td>
<td>P-ANCA + PR3/ MPO Ð</td>
<td>Unconfirmed</td>
<td>+</td>
<td>Calcification (CT)</td>
<td>Mucosal thickening of ethmoid sinuses. Polyploid thickening of</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Repeat ANCA -</td>
<td></td>
<td>right maxillary sinus. Thickened mucosa of middle and inferior turbinates. a venule. No granuloma.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>38</td>
<td>20</td>
<td>5</td>
<td>C-ANCA + PR3 381</td>
<td>59</td>
<td>15</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Repeat C-ANCA + PR3 8.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>39</td>
<td>10</td>
<td>1</td>
<td>P-ANCA + PR3/MPO +</td>
<td>99</td>
<td>Unconfirmed</td>
<td>+</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>41</td>
<td>5</td>
<td>25</td>
<td>C-ANCA + PR3/ MPO +</td>
<td>90</td>
<td>10</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Repeat ANCA -</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>53</td>
<td>5</td>
<td>5</td>
<td>C-ANCA + PR3/MPO +</td>
<td>91</td>
<td>10</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>45</td>
<td>18</td>
<td>10</td>
<td>P-ANCA + PR3 69</td>
<td>Repeat P-ANCA + PR3/MPO -</td>
<td>111</td>
<td>10</td>
</tr>
</tbody>
</table>
**Table 1: Demographics, serology and organ involvement of eleven patients with ANCA-associated vasculitis induced by cocaine**

| 14 | F | 32 | 32 | 15 | P-ANCA + PR3 + 18 MPO Ð Repeat P-ANCA + PR3 + 15, MPO - | 53 | 7 | - | + | - | None (X-Ray) | Sinonasal mucosal thickening, obstruction of left ostiomental complex. Bony erosion of the sphenoid sinus floor with bony sclerosis. | - |

ESR Ð Erythrocyte Sedimentation Rate, CRP Ð C-Reactive Protein, PNS Ð Peripheral Nervous System, ENT Ð Ear, Nose and Throat, C Ð Computerised Tomography, C-ANCA - cytoplasmic anti-neutrophil cytoplasmic antibody, P-ANCA - perinuclear anti-neutrophil cytoplasmic antibody, MPO Ð myeloperoxidase, PR3 Ð proteinase 3.

**Disclosure:** S. Subesinghe, None; S. van Leuven, None; L. Yalakki, None; S. Sangle (Joint First Author), None; D. P. D'Cruz, None.


**Abstract Number: 1769**

**Incidence, Predictors, and Outcome of Diffuse Alveolar Hemorrhage in Patients with MPO-ANCA Positive Microscopic Polyangiitis: A Multi-Center Retrospective Cohort Study**

Takashi Kida, Shunya Kaneshita, Takuya Inoue, Amane Nakabayashi, Yuji Kukida, Kazuki Fujioka, Hidetake Nagahara, Makoto Wada, Takahiro Seno, Masataka Kohno and Yutaka Kawahito, Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Vasculitis Poster II: ANCA-Associated Vasculitis

**Session Type:** ACR Poster Session B

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

In patients with microscopic polyangiitis (MPA), a variety of pulmonary lesions including diffuse alveolar hemorrhage (DAH), airways disease and interstitial lung disease (ILD) have been reported. Although DAH is a severe complication of MPA, its etiology and prognosis are poorly understood. The purpose of this study was to identify incidence and predictors of DAH and to evaluate its impact on clinical outcome in patients with MPA, focusing on the association of airways disease with DAH.

**Methods:**

We conducted a multi-center retrospective cohort study of patients with myeloperoxidase anti-neutrophil cytoplasmic antibody (MPO-ANCA) positive MPA at three institutes (Kyoto Prefectural University of Medicine, Japanese Red Cross Kyoto Daiichi Hospital, and Matsushita Memorial Hospital) from January 2006 to June 2015. All patients met the Chapel Hill Consensus Conference definition of MPA. DAH was diagnosed on the basis of bronchoscopy, CT findings, and hemoptyis. We evaluated chest CT images at the onset of MPA and examined the presence of airways disease and ILD. We assessed the associations of airways disease with DAH using odds ratio (OR) and 95% confidence interval (95% CI) estimated from logistic regression adjusted for other baseline characteristics, including age, sex, smoking history, antithrombotic drug use, ILD, rapidly progressive glomerulonephritis (RPGN), nerve involvement, gastrointestinal involvement, the five factor score (FFS), the Birmingham vasculitis activity score (BVAS), MPO-ANCA titer. We compared Kaplan-Meier survival curves between the 2 groups with or without DAH using the log-rank test and hazard ratio estimated by Cox proportional hazards model.
Results:

We included 123 consecutive patients with MPO-ANCA positive MPA. DAH was confirmed in 37 (30%) patients, and 33 of them presented DAH at the diagnosis of MPA. In the univariate analyses, airways diseases, absence of ILD, absence of nerve involvement, FFS and BVAS were associated with DAH (Figure 1). In the multivariate analysis, only airways disease (adjusted OR, 3.47; 95% CI, 1.29-9.37) was independently associated with DAH. Airways disease was found in 22 of 37 patients with DAH, and was already pointed out prior to the onset of MPA/DAH in 17 of them. The overall survival rates for patients with DAH were significantly lower than patients without DAH (HR, 3.45; 95% CI, 1.65-7.21) (Figure 2).

Conclusion:

DAH frequently occurred in patients with airways disease, and was associated with increased mortality. Airways disease may be involved in the cause of DAH.

Disclosure: T. Kida, None; S. Kaneshita, None; T. Inoue, None; A. Nakabayashi, None; Y. Kukida, None; K. Fujioka, None; H. Nagahara, None; M. Wada, None; T. Seno, None; M. Kohno, None; Y. Kawahito, None.


Abstract Number: 1770
ANCA-Associated Vasculitis (AAV) in Younger Vs Older Patients: Comparison of Clinical, Serologic and Outcome Differences and Their Implications for Management

Priya Chokshi1, Olufemi Aina2, Naveed Masani2, Melissa Fazzari3, Elise Belilos1, Kristina Belostocki1, Gary Rosenblum1, Tobin Abraham4, Daniil Shimonov4, Zinal Patel4 and Steven E. Carsons1, 1Rheumatology, NYU Winthrop Hospital, Mineola, NY, 2Nephrology, NYU Winthrop Hospital, Mineola, NY, 3Biostatistics, NYU Winthrop Hospital, Mineola, NY, 4Medicine, NYU Winthrop Hospital, Mineola, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Vasculitis Poster II: ANCA-Associated Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
ANCA-associated vasculitis (AAV) is a cause of multi-organ disease in all ages, but peaks at ages 65-74. Limited data is available on the characteristics of AAV in the elderly. Our aim is to compare clinical and serological presentations, treatment regimens, and survival outcomes between younger and older AAV patients.

Methods:
A retrospective review of patients younger and older than 65yrs [(<65grp); (≥65grp), respectively] diagnosed with AAV was conducted at our institution between 2005 and 2016. Data on demographics, organ system involvement, ANCA-MPO/PR3 serology, BVAS, Vasculitis Damage Index (VDI), 5 Factor Score (FFS) and treatment was recorded. Chi square tests of association and two-sample t-test for group mean differences were used to compare groups. Survival was assessed using Cox proportional hazard ratio and Kaplan-Meir estimates.

Results:
The cohort included 93 patients [52% (<65grp); 48% (≥65grp)]. The mean age at diagnosis was 59 ± 20 years (range 16-91). Specifically, the age of the ≤65grp was 43 ± 14 compared to 76 ± 7 for ≥65grp. Median follow-up was 4.6 years in the ≤65grp and 2.0 years in the 65grp. There were no significant differences in gender, race, BMI, or smoking status. At diagnosis, ≥65grp had 3 times as many comorbidities as <65grp (p <0.0001). The ≥65grp also had more renal involvement (73 vs 50%; p=0.02). The <65grp had more sinus (79 vs 44%; p=0.001) and skin (38 vs 18%; p=0.03) involvement. There were no differences in lung, ocular, neurologic, cardiovascular, gastrointestinal, musculoskeletal, constitutional, or hematologic/DVT findings. The elderly were also more likely to be MPO+ (69% MPO vs 31% PR3) whereas the younger were mostly PR3+ (17% MPO vs 83% PR3) (p <0.001).

Twenty percent of ≥65grp was hemodialyzed initially compared to 2 percent of <65grp (p=0.01). There was no difference in use of plasmapheresis, pulse steroids, cyclophosphamide (CYC) or rituximab (RTX). However, over the course of their illness, 21% of <65grp received both CYC and RTX vs none of the ≥65grp (p<0.001).

Although there was no significant difference between BVAS at presentation or VDI, the FFS at presentation was 2 times greater in the ≥65grp vs <65grp group (p<.0001). Interestingly, although both the mortality and FFS were increased in the ≥65grp, when this data was adjusted for age, the FFS did not have a significant association with the hazard of death (p=0.67) in the elderly. Although relapse was higher in the ≤65grp (56 vs 27%; p=0.0115), mortality was greater in the ≥65grp (98 vs 63%, p<0.001). There were no differences in complications.

Conclusion:
Our data indicate that clinical manifestations of AAV differ with age at presentation. There is also a striking age-related difference in distribution of ANCA subtype. While relapse was higher in younger patients, mortality was greater in the ≥65grp, possibly due to higher co-morbidity at presentation. A better understanding of the characteristic pattern of presentation between younger and older patients with AAV may have implications for appropriate management and help improve outcomes in this cohort of patients.

Disclosure: P. Chokshi, None; O. Aina, None; N. Masani, None; M. Fazzari, None; E. Belilos, None; K. Belostocki, None; G. Rosenblum, None; T. Abraham, None; D. Shimonov, None; Z. Patel, None; S. E. Carsons, None.

Prevalence and Prognostic Relevance of Cardiovascular Involvement in ANCA-Associated Vasculitis: A Retrospective Cohort Study

Qin Huang¹, Hao Ren¹, Yaping Zhan², Shenyi Yu² and Min Yang¹, ¹Department of Rheumatology, Nanfang Hospital, Southern Medical University, Guangzhou, China, ²Department of rheumatology, Nanfang Hospital, Southern Medical University, Guangzhou, China

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Vasculitis Poster II: ANCA-Associated Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Cardiovascular involvement in ANCA-associated vasculitis (AAV) including microscopic polyangiitis (MPA), eosinophilic granulomatosis with polyangiitis (EGPA) and granulomatosis with polyangiitis (GPA), has long been regarded as rare, yet a wide spectrum of abnormalities have been reported, with prevalence figures ranging from 5–60% of patients depending on the series and diagnostic methods applied. To investigate the prevalence and prognostic relevance of cardiovascular involvement in an AAV population of MPA, EGPA and GPA patients.

Methods: In a retrospective cohort study, 143 MPA, 46 GPA and 45 EGPA patients were analyzed. Birmingham vasculitis activity (BVA) score of all patients were calculated. Demographic and clinical characteristics of patients with and without AAV-related cardiovascular involvement were compared. Statistical analysis was done using SPSS version 22.0 for Windows.

Results: Within the cohort of 234 AAV patients, median follow-up times were 5.6 years for the MPA patients (age at diagnosis 55 ± 17, range 12–83years) and 5.2 years for the GPA patients (age 53± 16, range 12–82 years) and 4.8 years for the EGPA (age 48 ± 17, range 11–76 years). The percentages of cardiovascular involvement in patients with MPA, GPA and EGPA were 29.4%(42/143), 37.0% (17/46), and 35.6%(16/45), respectively. There is no significant difference among the three groups in terms of cardiovascular involvement. The common cardiovascular event in these 75 patients that can be observed is congestive heart failure (28/75), followed with valve disease (27/75), pericardial effusion (17/75), arrhythmia (17/75), cardiomyopathy (6/75) and angina (5/75). Univariate logistic regressions showed that age at diagnosis (P=0.002; 95% CI 2.922–12.221), sex (P=0.03; 95% CI 0.959-0.998), higher BVA score (P<0.001; 95% CI 3.063–6.429) and poor respiratory function at remission (P=0.013; 95% CI 1.282–8.595), respectively correlated with AAV patients with cardiovascular involvement. Mortality rate was 4.2% in AAV patients (10/243); 7 out of 10 death cases had cardiovascular involvement. There was a statistical significance of mortality between the patients with and without cardiovascular involvement.

Conclusion: In this retrospective study, the MPA, GPA and EGPA groups showed comparable mortality. AAV patients with cardiovascular involvement appeared at greater risk of premature death, with increased risk in males, elder age, higher BVA score and poor respiratory function at remission.

Disclosure: Q. Huang, None; H. Ren, None; Y. Zhan, None; S. Yu, None; M. Yang, None.


Abstract Number: 1772

Non-Protocolized Re-Biopsy in Patients with ANCA-Associated Glomerulonephritis: ¿Is It Necessary?

Valeria Scaglioni¹, Marina Scolnik², Florencia Pierini², Luis J. Catoggio³, Silvia Beatriz Christiansen⁴, Carlos Federico Varela⁵, Gustavo Greloni⁵, Guillermo Rosa-Diez⁵ and Enrique R Soriano⁶, ¹Rheumatology Unit, Internal Medicine Service. Hospital Italiano de Buenos Aires, CABA, Argentina, ²Rheumatology Unit, Internal Medicine Service, Hospital Italiano de Buenos Aires, CABA, Argentina, ³Rheumatology Unit, Internal Medicine Service. Hospital Italiano de Buenos Aires, Buenos Aires, Argentina, ⁴Pathology
SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Vasculitis Poster II: ANCA-Associated Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Protocolized and non-protocolized repeat renal biopsies are rarely performed in ANCA glomerulonephritis. Their role in predicting long term renal outcomes and aiding in clinical decisions have not been deeply analyzed. The aim of this study was to evaluate usefulness of renal re-biopsy in patients with ANCA glomerulonephritis in treatment decisions and the role of hematuria as a sign of active disease.

Methods: We included retrospectively all patients with biopsy-proven ANCA glomerulonephritis: granulomatosis with polyangiitis (GPA), granulomatosis with polyangiitis and eosinophilia (GPAE), microscopic polyangiitis (PAM) and renal limited vasculitis (RLV) between January 2002 and May 2017. We analysed patient’s baseline characteristics, induction and maintenance treatments, renal response after induction and time to renal relapse/rebiopsy. Histology of re-biopsies was reviewed and correlation with clinical findings (hematuria) and first biopsy histology was analyzed. Histological classification was made according to 2010 classification criteria for ANCA glomerulonephritis (four categories: focal, crescentic, mixed and sclerotic). Data of physicians' decisions after rebiopsy was collected.

Results: 60 patients (77% females) were included. Of those, 15 (25%) underwent renal re-biopsy during the follow up based on clinical manifestations. Mean time until re-biopsy was 38.4 months (SD 20.4). In the re-biopsy group, 73% of patients had new onset hematuria vs. 7.5% in the no-rebiopsy group (p=). New onset or worsening proteinuria was present in 73% of patients in the re-biopsy group (40% and 33% respectively) vs. only 2.5% in the no-rebiopsy group. Decline in the GFR was present in 60% of patients in the re-biopsy group vs. 2.5% in the other. When analysing histological changes in the repeat biopsy we didn’t find a correlation between active lesions (crescents, necrosis etc.) and hematuria. All patients that underwent repeat biopsy were considered to be active but renal histology showed progression in terms of chronicity and rare active histological lesions (table 1). Despite this lower percentage of active lesions, in 67% of patients, physicians made a treatment change, initiating a new induction therapy regimen and achieving renal response in 85% of patients.

Conclusion: Renal histology in repeat biopsies did not showed active lesions justifying clinical renal manifestations that lead to re-biopsy. In spite of this, physicians made a change in treatments in the majority of cases after rebiopsy. Patients who presented with new onset hematuria, proteinuria and worsening in the GFR had a good response to this new induction treatment achieving renal laboratory remission in 85% of patients. Role of histological findings in rebiopsies has to be further analyzed.

TABLE 1. Comparison of histological classification in the first and second renal biopsy

<table>
<thead>
<tr>
<th></th>
<th>FIRST BIOPTY*</th>
<th>SECOND BIOPTY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=15</td>
<td>N=15</td>
</tr>
<tr>
<td>Histological classification, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Focal</td>
<td>5 (33)</td>
<td>5 (33)</td>
</tr>
<tr>
<td>- Crescentic</td>
<td>6 (40)</td>
<td>1 (7)</td>
</tr>
<tr>
<td>- Mixed</td>
<td>4 (27)</td>
<td>5 (33)</td>
</tr>
<tr>
<td>- Sclerotic</td>
<td>0 (0)</td>
<td>4 (27)</td>
</tr>
</tbody>
</table>

*only patients who underwent a second biopsy

Disclosure: V. Scaglioni, None; M. Scolnik, None; F. Pierini, None; L. J. Catoggio, None; S. B. Christiansen, None; C. F. Varela, None; G. Greloni, None; G. Rosa-Diez, None; E. R. Soriano, AbbVie, Janssen, Novartis, Pfizer Inc, UCB, 2,AbbVie, Janssen, Novartis, Pfizer Inc, UCB, 5,AbbVie, Bristol-Myers Squibb, Janssen, Novartis, Pfizer Inc, Roche, UCB, 8.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/non-protocolized-re-biopsy-in-patients-with-anca-associated-glomerulonephritis-is-it-necessary

Abstract Number: 1773
New Use for an Old Drug: Hydroxychloroquine for the Treatment of ANCA Associated Vasculitis

Alina Casian1, Rachel Jones2, Ruzaiqa Cader3, Alan D. Salama4, Shirish Sangle5, David Jayne6 and David P. D'Cruz7, 1Lupus Unit, Guy's Hospital, London, United Kingdom, 2Nephrology, Addenbrooke's Hospital, Cambridge, United Kingdom, 3Nephrology, Norfolk and Norwich Hospitals, Norfolk, United Kingdom, 4Centre for Nephrology, University College London, London, United Kingdom, 5Louise Coote Lupus Unit, Guy's and St Thomas' Hospital, London, United Kingdom, 6Vasculitis and Lupus Clinic, Department of Medicine, University of Cambridge, Cambridge, United Kingdom, 7Louise Coote Lupus Unit, Rheumatology and Lupus, Guy's and St Thomas' Hospitals NHS Foundation Trust, London, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Vasculitis Poster II: ANCA-Associated Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
To assess retrospectively the efficacy and safety of hydroxychloroquine in patients with ANCA associated vasculitis.

There is an unmet need for a corticosteroid sparing, non-toxic therapy in ANCA vasculitis (AAV), as up to 50% of patients relapse by 5 years and 20% have sub-optimal disease control. Hydroxychloroquine (HCQ) has been effective and safe in autoimmune diseases such as systemic lupus erythematosus and rheumatoid arthritis but no systematic studies have been carried out to assess its role in vasculitis. There is mechanistic rationale for the effectiveness of HCQ in AAV, in view of its effect on immune mediators involved in vasculitis pathogenesis including Toll-like receptors, pro-inflammatory cytokines, autoreactive B and T lymphocytes.

Methods: Patients were identified by searching our departmental vasculitis databases and electronic clinical records. Thirty patients received HCQ +/- corticosteroids and immunosuppressants. We assessed the effect of HCQ on clinical symptoms and corticosteroid doses required.

Results: Thirty patients with ANCA+ vasculitis were treated with hydroxychloroquine (median dose 400 mg daily) for an average of 4.6 years. Median age was 56.5 years.

Fifteen patients had a diagnosis of granulomatosis with polyangiitis (GPA) with +PR3-ANCA, whilst 13 were diagnosed with microscopic polyangiitis (MPA) with +MPO-ANCA and 2 patients had eosinophilic granulomatosis with polyangiitis (eGPA) with +MPO-ANCA.

The systems involved were: joints (20 patients), kidneys (12), ear-nose-throat (11), skin (11), eyes (5), lungs (4), peripheral nerves (3) and gastrointestinal system (1). Twenty-nine out of 30 patients were treated with other maintenance immunomodulatory agents in addition to HCQ (See Table 1).

Twenty three out of 30 patients (76.7%) reported benefits attributed to HCQ ranging from amelioration of joint pains (n=17) to reduction of corticosteroid doses (4), frequency of vasculitic flares (3) and fatigue (1). The effects of HCQ were unclear in 6 patients and 1 reported no symptomatic improvement.

Two patients experienced transient gastrointestinal side effects with HCQ, 1 patient developed haemolysis associated with rise in bilirubin, 1 asymptomatic QT interval prolongation resulting in discontinuation of HCQ. No major other adverse events were reported.

Conclusion: The majority of patients reported symptomatic benefits associated with HCQ treatment, especially improvement of joint pains. Vasculitic relapses were less frequent in some patients, with a reduction in corticosteroid doses. HCQ was used mostly as adjunctive therapy in addition to other immunomodulatory agents and was usually well tolerated. Future randomized controlled clinical trials are needed to establish the role of HCQ in ANCA+ vasculitis.
<table>
<thead>
<tr>
<th>Concomitant Immunosuppressive therapy</th>
<th>Number of Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nil</td>
<td>1</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>16</td>
</tr>
<tr>
<td>Rituximab</td>
<td>9</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>7</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>6</td>
</tr>
<tr>
<td>Mycophenolate mofetil (MMF)</td>
<td>4</td>
</tr>
<tr>
<td>Tacrolimus + MMF (Renal transplant)</td>
<td>1</td>
</tr>
<tr>
<td>Mepacrine</td>
<td>1</td>
</tr>
</tbody>
</table>

**Disclosure:** A. Casian, None; R. Jones, None; R. Cader, None; A. D. Salama, None; S. Sangle, None; D. Jayne, None; D. P. D'Cruz, None.


**Abstract Number:** 1774

**Serum Periostin As a Biomarker in Eosinophilic Granulomatosis with Polyangiitis**

Rennie L. Rhee¹, Cecile TJ Holweg², David Cuthbertson³, Simon Carette⁴, Nader A. Khalidi⁵, Curry L. Koening⁶, Jeffrey Krischer⁷, Carol A. Langford⁸, Carol A. McAlear⁹, Paul A. Monach¹⁰, Larry W. Moreland¹¹, Christian Pagnoux⁴, Philip Seo¹², Ulrich Specks¹³, Antoine G. Sreih¹, Steven R. Ytterberg¹⁴ and Peter A. Merkel¹⁵. ¹Rheumatology, University of Pennsylvania, Philadelphia, PA, ²Genentech, Inc, South San Francisco, CA, ³Biostatistics and Informatics, Department of Pediatrics, University of South Florida, Tampa, FL, ⁴Division of Rheumatology, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada, ⁵Rheumatology, McMaster University, Hamilton, ON, Canada, ⁶Rheumatology, University of Utah, Salt Lake City, UT, ⁷University of South Florida, Tampa, FL, ⁸Rheumatic and Immunologic Diseases, Cleveland Clinic, Cleveland, OH, ⁹University of Pennsylvania, Philadelphia, PA, ¹⁰Boston University School of Medicine, Boston, MA, ¹¹Division of Rheumatology and Clinical Immunology, UPMC / University of Pittsburgh, Pittsburgh, PA, ¹²Medicine, Johns Hopkins University, Baltimore, MD, ¹³Mayo Clinic College of Medicine, Rochester, MN, ¹⁴Rheumatology, Mayo Clinic, Rochester, MN, ¹⁵Division of Rheumatology, University of Pennsylvania, Philadelphia, PA

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Monday, November 6, 2017  
**Session Title:** Vasculitis Poster II: ANCA-Associated Vasculitis  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**
Identification of a biomarker to predict relapse in eosinophilic granulomatosis with polyangiitis (EGPA; Churg-Strauss) would enhance the ability to personalize treatment options and improve outcomes. Periostin is a protein which facilitates eosinophil-mediated inflammation and fibrosis and is involved in other eosinophilic syndromes. This study examined the value of serum periostin in identifying disease relapse in patients with EGPA.

**Methods:**
Participants enrolled in a multicenter, prospective cohort of patients with EGPA who met the 1990 American College of Rheumatology classification criteria for Churg-Strauss syndrome were included in this study if they had a relapse (defined as BVAS > 0) during follow-up. Serum levels of periostin were measured, using the Elecsys®Periostin assay (Roche Diagnostics, Penzberg Germany), at relapse visit as well as 2 pre- and 2 post-relapse visits, if available. Periostin level between visits (pre- vs relapse, post- vs relapse, all remission vs relapse) were compared using Student’s t-test. Mixed-effect models were used to examine the association between periostin levels and
relapse, with the patient as the random effect to allow for assessment of changes within-patient, and adjusting for ANCA status (positive or negative ANCA), active asthma at visit, and time from relapse visit.

**Results:**

There were 49 patients included in the study: 14 (29%) were anti-myeloperoxidase-ANCA positive and 25 (51%) had experienced a relapse at some point prior to enrollment. Although there was no significant difference in periostin levels at relapse compared to all remission visits (60 vs 58 ng/ml, p = 0.41), the periostin levels were significantly higher in patients with EGPA compared to previously published levels using the same assay measured in healthy controls and patients with asthma (Figure 1). No significant difference was found comparing the periostin level between pre-visit vs relapse visit (p=0.59) or post-visit vs relapse visit (p=0.20). In the mixed-effect models, periostin level, change in periostin, and percent change in periostin were not associated with relapse (beta coefficient 0.007 [95% CI -0.07, 0.08] p=0.87, -6.1 [95% CI -13.9, 1.7] p=0.13, and -0.03 [95% CI -0.14, 0.07] p=0.55, respectively).

**Conclusion:**

Periostin levels in EGPA are higher than other previously studied cohorts, specifically healthy populations and patients with asthma, and are relatively stable over time. Serum periostin does not discriminate active from inactive disease in EGPA.

---

**Figure 1: Median Periostin Levels at All Visits of Patients with EGPA Compared to Controls**

![Graph showing median periostin levels at all visits](image)

Visit type for patients with EGPA

* P < 0.01 (compared to EGPA relapse visit)

---

**Disclosure:** R. L. Rhee, None; C. T. Holweg, Genentech, Inc, 3,Genentech, Inc, 1; D. Cuthbertson, None; S. Carette, None; N. A. Khalidi, None; C. L. Koening, None; J. Krischer, None; C. A. Langford, None; C. A. McAlear, None; P. A. Monach, None; L. W. Moreland, None; C. Pagnoux, None; P. Seo, None; U. Specks, None; A. G. Sreih, None; S. R. Ytterberg, None; P. A. Merkel, None.


Abstract Number: 1775

The Utility of the ACR/EULAR 2017 Provisional Classification Criteria for Granulomatosis with Polyangiitis in Korean Patients with Antineutrophil Cytoplasmic Antibody-Associated Vasculitis
**Juyoung Yoo**, Division of Rheumatology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea, Seoul, Korea, Republic of (South)

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Vasculitis Poster II: ANCA-Associated Vasculitis  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

We applied the ACR/ EULAR 2017 provisional classification criteria for granulomatosis with polyangiitis (GPA) to 150 Korean patients with previously diagnosed Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) and investigated how many patients with AAV were reclassified as GPA.

**Methods:**

We included patients with 30 GPA, 30 eosinophilic GPA (EGPA) and 90 microscopic polyangiitis (MPA) patients. Patients can be classified as GPA, when the sum of scores is more than 5.

**Results:**

The mean age of 150 patients with AAV was 60.1 years old, and 101 patients (67.3%) were women at diagnosis. Overall, 33 of 150 patients with AAV (22.0%) were classified as GPA according to the 2017 provisional criteria for GPA. The 2017 provisional criteria for GPA dropped 10.0% of previously diagnosed GPA patients and the major factor to drop 3 GPA patients was the deletion of 2 items of the 1990 criteria, urinary sediment and infiltrates on chest radiograph. Meanwhile, one of 30 patients with EGPA (3.3%) and 5 of 90 patients with MPA (5.6%) were newly classified as GPA based on the 2017 provisional criteria for GPA. Also we could find that items of the 2017 provisional criteria to contribute to reclassifying EGPA and MPA patients as GPA were PR3-ANCA, mass-like lung lesion and nasal congestion in Korean patients with AAV.

**Conclusion:** Use of the 2017 provisional criteria for GPA excluded 10.0% of previously classified GPA patients and newly classified 3.3% of EGPA patients and 5.6% of MPA patients as GPA in Korean patients with AAV.

**Disclosure:** J. Yoo, None;


**Abstract Number:** 1776

---

**Adverse Events for Discontinuation of Immunosuppressants and Outcome of Their Re-Administration in Patients with Antineutrophil Cytoplasmic Antibody-Associated Vasculitis: A Single Center Study in Japan**

**Takamasa Murosaki**, Takeo Sato, Yoichiro Akiyama, Katsuya Nagatani and Seiji Minota, Department of Internal Medicine, Division of Rheumatology/Clinical Immunology, Jichi Medical University, Shimotsuke, Japan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Vasculitis Poster II: ANCA-Associated Vasculitis  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The combination of immunosuppressants and glucocorticoid is recommended for the treatment of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). However, adverse events of immunosuppressants sometimes hamper the
Methods: The data of AAV-patients from 2005 to 2016 in our hospital were analyzed retrospectively. They included patients-demographics, ANCA subtype, use of immunosuppressants, the adverse events that caused their discontinuation, and the outcome of their re-administration.

Results: 162 patients were found to have AAV during that time; 132 were positive for myeloperoxidase-ANCA, 25 for proteinase 3-ANCA, and 5 for both. Among 162 patients, 93 (57.4%) were treated with both glucocorticoid and immunosuppressants. In 38 of 93 (40.9%), 44 immunosuppressants were discontinued due to adverse events; 3 patients received 2 immunosuppressants and 1 patient received 4 in the course of the treatment. Median (min.-max.) time from beginning to stopping immunosuppressants was 0.9 (0.3-96) months. 75.0% of the patients with kidney involvement and 38.6% of the patients without it discontinued immunosuppressants \( (p = 0.003, \text{Chi-square test}) \). The immunosuppressants discontinued were cyclophosphamide in 24 (54.4%), azathioprine in 6 (13.6%), mizoribine in 4 (9.1%), methotrexate in 3 (6.8%), rituximab in 2 (4.5%), and others in 5 times (11.6%). The adverse events were 21 infections (42.9%), 13 cytopenias (26.5%), 6 hepatotoxities (12.2%), and 9 others (28.4%); 7 patients experienced 2 adverse events and 1 patient experienced 5. The infection included reactivation of cytomegalovirus (42.9%), respiratory tract infections (33.3%), sepsis (9.5%), and others (8.7%). The incidence of adverse events of cyclophosphamide, azathioprine, mizoribine, methotrexate, and rituximab was 31.6%, 21.4%, 23.5%, 17.6%, and 20.0%, respectively \( (p = 0.75, \text{Fisher’s exact test}) \). The types of adverse events were different among immunosuppressants; infection and cytopenia, hepatotoxicity, and sepsis were most common in cyclophosphamide, azathioprine, and mizoribine, respectively. Among 38 patients who discontinued immunosuppressants, 11 were re-administered the same drugs (28.9%), 14 others (36.8%), and 13 none (34.2%). Median (min.-max.) time to re-administration was 2.0 (0-60) months.

Conclusion: The discontinuation of immunosuppressants due to adverse events was not rare in AAV-patients. One third of the patients who discontinued immunosuppressants were re-administered the same drugs without serious outcomes after recovery from adverse events. Kidney involvement was a risk of IS discontinuation and close monitoring of kidney involvement was mandatory in AAV-patients on immunosuppressants. Although no difference was observed in the incidence of adverse events, clinical presentation of adverse events was diverse among immunosuppressants.

Disclosure: T. Murosaki, None; T. Sato, None; Y. Akiyama, None; K. Nagatani, None; S. Minota, SHIONOGI & CO., LTD., 2,Mitsubishi Tanabe Pharma Corporation, 2,Pfizer Inc., 2,Chugai Pharmaceutical Co.,Ltd., 2,Asahi Kasei Pharma Corporation, 2.

Incidence and Prevalence of Granulomatosis with Polyangiitis and Microscopic Polyangiitis in a Health Management Organization: A 15-Year Study

Florence Pierini1, Marina Scolnik1, Valeria Scaglioni2, Florencia Beatriz Mollerach3 and Enrique R. Soriano1, 1Rheumatology Unit, Internal Medicine Service, Hospital Italiano de Buenos Aires, CABA, Argentina, 2Rheumatology Unit, Internal Medicine Service. Hospital Italiano de Buenos Aires, CABA, Argentina, 3Rheumatology Unit, Internal Medicine Service, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Vasculitis Poster II: ANCA-Associated Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: ANCA-associated vasculitides are rare diseases and epidemiological data on them is scarce. Our objective was to estimate incidence and prevalence rates of Granulomatosis with Polyangiitis (GPA) and Microscopic Polyangiitis (MPA) using data from a university hospital-based health management organization (HMO) in Latin America

Methods: Multiple methods for case finding were used to ensure complete ascertainment: (a) patients with diagnosis of vasculitis inHMO electronic medical records, (b) patients with an ANCA, proteinase-3 or myeloperoxidase positive test in laboratory database, (c) patients who consumed azathioprine, cyclophosphamide, methotrexate, mycophenolate or rituximab, from the administrative HMO
drugs database, (d) patients with a renal biopsy performed from pathology registry. GPA was diagnosed if fulfilling ACR 1990 criteria or a clinical diagnosis was made by an experienced rheumatologist; MPA if diagnosed by a rheumatologist in concordance with Chapel Hill 2012 consensus. Renal limited vasculitis (RLV) ANCA-P positive was considered along with MPA. Global, age-specific, and sex-specific incidence and prevalence rates were calculated for members of the HMO. Incidence study followed members with continuous affiliation ≥ 1 year from January 2000 to January 2015 until he/she voluntarily left the HMO, GPA or MPA were diagnosed, death, or study finalization. Prevalence was calculated on January 1, 2015 and only patients still on treatment at that time were considered for calculation

**Results:** 19 incident cases of GPA and 28 of MPA were identified from January 2000 to January 2015. Patients’ characteristics are shown in table 1. During this period, a total of 349,775 HMO persons contributed a total of 2,073,438 person-years. Incidence rates were measured as cases per 1,000,000 person-years. GPA and MPA overall incidence rate were 9 (CI 5–13) and 14 (CI 9-19) respectively. Incidence rates were greater in women [GPA 11 (CI 5-17) and MPA 17 (CI 10-24)] than in men [GPA 6 (CI 1-11) and MPA 8 (CI 2-14)]. Age-specific incidence rates in both female and male patients peaked in the seventh decades of life in our population. On January 1, 2015, 10 GPA and 7 MPA prevalent cases were identified from a denominator population of 135,750 HMO members. Prevalence rates were 7.4 per 100,000 (CI 2.8-12) for GPA and 5.2 per 100,000 (CI 1.3-9) for MPA. Prevalence rates were higher in ages over 70 for both sexes and both diseases

<table>
<thead>
<tr>
<th>Table 1. Incident cases of GPA and MPA characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Female, n (%)</strong></td>
</tr>
<tr>
<td>Granulomatosis with Polyangieitis (n=19)</td>
</tr>
<tr>
<td>Microscopic Polyangieitis (n=28)</td>
</tr>
<tr>
<td>14 (73.7)</td>
</tr>
<tr>
<td>21 (75)</td>
</tr>
<tr>
<td>Mean age at diagnosis, years (DS)</td>
</tr>
<tr>
<td>69.8 (11.3)</td>
</tr>
<tr>
<td>73.6 (13.2)</td>
</tr>
<tr>
<td>Global Incidence per 1,000,000 patients-year (CI 95%)</td>
</tr>
<tr>
<td>9 (5–13)</td>
</tr>
<tr>
<td>14 (9-19)</td>
</tr>
<tr>
<td>ANCA-C positive, % (CI 95%)</td>
</tr>
<tr>
<td>78.9 (52.7-92.7)</td>
</tr>
<tr>
<td>14.3 (5.1-33.9)</td>
</tr>
<tr>
<td>ANCA- P positive, % (CI 95%)</td>
</tr>
<tr>
<td>15.8 (4.6-42.2)</td>
</tr>
<tr>
<td>82.1 (62.1-92.8)</td>
</tr>
<tr>
<td>Clinical features, % (CI 95%)</td>
</tr>
<tr>
<td>Nasal /sino-nasal involvement</td>
</tr>
<tr>
<td>42.1 (21.1-66.5)</td>
</tr>
<tr>
<td>14.3 (5.1-34)</td>
</tr>
<tr>
<td>Hearingloss/reduction</td>
</tr>
<tr>
<td>52.6 (29.2-75)</td>
</tr>
<tr>
<td>10.7 (3.2-30)</td>
</tr>
<tr>
<td>Cartilagenousinvolvement</td>
</tr>
<tr>
<td>10.5 (2.3-37.1)</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>Red eye</td>
</tr>
<tr>
<td>15.8 (4.6-42.2)</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>Renal involvement</td>
</tr>
<tr>
<td>84.2 (57.8-95.4)</td>
</tr>
<tr>
<td>100</td>
</tr>
<tr>
<td>Nodules, mass or cavitation in chest CT</td>
</tr>
<tr>
<td>36.8 (17.3-62)</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>Interstitial Lung Disease</td>
</tr>
<tr>
<td>5.3 (0.1-26)</td>
</tr>
<tr>
<td>21.4(8.3-40.9)</td>
</tr>
<tr>
<td>Alveolar hemorrhage</td>
</tr>
<tr>
<td>15.8 (4.6-42.2)</td>
</tr>
<tr>
<td>10.7(3.2-30.1)</td>
</tr>
<tr>
<td>Skin vasculitis</td>
</tr>
<tr>
<td>15.8 (4.6-42.2)</td>
</tr>
<tr>
<td>10.7(3.2-30.1)</td>
</tr>
<tr>
<td>Arthritis</td>
</tr>
<tr>
<td>31.6 (13.7-57.3)</td>
</tr>
<tr>
<td>7.1 (1.6-26.3)</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
</tr>
<tr>
<td>15.8 (4.6-42.2)</td>
</tr>
<tr>
<td>3.6 (0.4-23.7)</td>
</tr>
<tr>
<td>Renal limited vasculitis</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>60.7 (40.6-78.5)</td>
</tr>
<tr>
<td>Fulfillment of ACR 1990 GPA criteria</td>
</tr>
<tr>
<td>42.1 (21.1-66.5)</td>
</tr>
<tr>
<td>NA</td>
</tr>
<tr>
<td>Fulfillment of GPA 2017 provisional criteria</td>
</tr>
<tr>
<td>89.5 (62.9-97.7)</td>
</tr>
<tr>
<td>NA</td>
</tr>
<tr>
<td>Follow-up time after diagnosis, years, median (RIC)</td>
</tr>
<tr>
<td>4.9 (2.4-7.8)</td>
</tr>
<tr>
<td>2.6 (0.7-6.1)</td>
</tr>
<tr>
<td>Mortality, n (%)</td>
</tr>
<tr>
<td>9 (47.4)</td>
</tr>
<tr>
<td>12 (42.9)</td>
</tr>
<tr>
<td>- Infections</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>6</td>
</tr>
<tr>
<td>- Cardiovascular</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>- Cancer</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>- Vasculitis</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>- Others</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>3</td>
</tr>
</tbody>
</table>
Conclusion: In this first study from Latin America, incidence and prevalence rates were in ranges of previous reports from other sites of the world. In our population GPA and MPA were more frequent in women and in older ages (over 70), and incidence of MPA was higher than GPA.

Disclosure: F. Pierini, None; M. Scolnik, None; V. Scaglioni, None; F. B. Mollerach, None; E. R. Soriano, Abbvie, BMS, Novartis, Janssen, Pfizer, Roche, UCB, 2, Abbvie, BMS, Novartis, Janssen, Pfizer, Roche, UCB, 5, Abbvie, BMS, Novartis, Janssen, Pfizer, Roche, UCB, 8.


Abstract Number: 1778

Prophylactic Treatment and Incidence of Pneumocystis Jiroveci Pneumonia in Japanese Patients with Antineutrophil Cytoplasmic Antibody-Associated Vasculitis

Izaya Nakaya1, Ken-ei Sada2, Jun Soma1, Yoshihiro Arimura3, Masayoshi Harigai4, Kunihiro Yamagata5, Hirofumi Makino6 and Seiichi Matsuo7, 1Department of Nephrology and Rheumatology, Iwate Prefectural Central Hospital, Morioka, Japan, 2Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan, 3First Department of Internal Medicine, Kyorin University School of Medicine, Tokyo, Japan, 4Division of Epidemiology and Pharmacoepidemiology of Rheumatic Diseases, Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan, 5Department of Nephrology, University of Tsukuba, Faculty of Medicine, Tsukuba, Japan, 6Okayama University Hospital, Okayama, Japan, 7Department of Nephrology, Nagoya University Graduate School of Medicine, Nagoya, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Vasculitis Poster II: ANCA-Associated Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose: Pneumocystis jiroveci pneumonia (PCP) is a fatal complication in antineutrophil cytoplasmic antibody-associated vasculitis (AAV). However, the current situation of prophylactic treatment of PCP and its effects on patients with AAV remain unknown. Therefore, we aimed to elucidate the current situation of prophylactic treatment and incidence of PCP in Japanese patients with AAV.

Methods: This study was conducted using the database of the RemIT-JAV-RPGN study. The current study included 321 patients who were registered from 53 tertiary care institutions in Japan and were newly diagnosed with AAV between April 2011 and March 2014. AAV was diagnosed based on the European Medicines Agency (EMA) algorithm. The exclusion criteria were as follows: age < 20 years, recurrent AAV, serological evidence of hepatitis B or C virus infection, and a history of malignancy. During the 2-year observation period, we examined the incidence of PCP, frequency of the usage and side effects of prophylactic drugs for PCP, and backgrounds of patients developing PCP.

Results: Of the 321 patients, 2 were excluded due to the lack of follow-up data. The mean age of the 319 patients was 69 ± 13 years, and 140 patients (44%) were males. Using the EMA algorithm, we identified 27 patients (8%) with eosinophilic granulomatosis with polyangiitis, 53 (17%) with granulomatosis with polyangiitis, 198 (62%) with microscopic polyangiitis/renal limited vasculitis, and 42 (13%) with unclassifiable disorders. The mean initial daily dose of prednisolone (PSL) was 40 ± 13 mg, and methylprednisolone (mPSL) pulse therapy was administered to 145 (45%) patients. Concomitant cyclophosphamide (CY) was administered during the initial 3 weeks of remission induction therapy in 105 (33%) patients. Most patients received prophylactic treatment of PCP along with immunosuppressive agents. Trimethoprim–sulfamethoxazole (TMP–SMX) and pentamidine were administered to 81% and 5% patients, respectively, during the initial 3 months. The percentage of patients treated with TMP–SMX and pentamidine gradually decreased. The following side effects of TMP–SMX were observed: cytopenia, 7 patients; drug eruption, hyponatremia, peripheral neuropathy, and liver function disorder, 2 patients each; and renal dysfunction, 1 patient. No side effect of pentamidine was recognized. During the 2-year observation period, 176 severe infections occurred in 111 (35%) of the 319 patients. Bacterial pneumonia was most frequently observed (134 times), followed by cytomegalovirus infection (28 times). However, PCP occurred only 9 times in 9 patients, and its incidence occupied only 5% of the total severe infections. However, of 26 patients who died, 13 patients died from infectious diseases, of which 4 were due to PCP. The median duration (min–max) to PCP onset was 96 (15–626) days. The mean initial daily dose of PSL was higher in patients in whom PCP occurred than in those in
whom it did not occur (54 ± 24 mg/day vs. 41 ± 12 mg/day). The rates of mPSL pulse and concomitant CY therapies were equal in both groups of patients.

**Conclusion:** Although the incidence of PCP onset is low in Japanese patients with AAV, the mortality rate is high.

**Disclosure:** I. Nakaya, None; K. E. Sada, None; J. Soma, None; Y. Arimura, None; M. Harigai, Eisai Ltd, Takeda Ltd, Teijin, 2,Eli Lilly and Company, BMS, Chugai, Janssen, 5; K. Yamagata, None; H. Makino, None; S. Matsuo, None.


**Abstract Number:** 1779

**Off-Label Use of Biological Therapies in Relapsing and/or Refractory Eosinophilic Granulomatosis with Polyangiitis (Churg–Strauss)**

Laure Denis¹, Maxime Samson², Francois Maurier³, Chaïhéra Khoutatra⁴, Vincent Germain⁵, Xavier Delbrel⁶, Philippe Bonniaud⁷, Alban Deroux⁸, Nicolas Girszyn⁹, Claire de Moreuil¹⁰, Dominique Chauveau¹¹, Anne Gondouin¹², Stephane Dominique¹³, Guillaume Le Guennoc¹⁴, Laurence Bouillet¹⁵, Bernard Bonnotte², Jean-Emmanuel Kahn¹⁶, Boris Bienvenu¹⁷, Bertrand Godeau¹⁸, Claire Le Jeune¹⁹, Xavier Puéchal²⁰, Loïc Guillevin for the French Vasculitis Study Group²⁰ and Benjamin Terrier¹⁹, 1Internal Medicine, CHU Estaing, Clermont-Ferrand, Clermont-Ferrand, France, 2Department of Internal Medicine and Clinical Immunology, Hôpital François Mitterrand, CHU de Dijon, Dijon, France, 3Internal Medicine, Sainte-Blandine de Metz Hospital, Metz, France, 4Lyon, Lyon, France, 5Rheumatology, CHU Pellegrin, Bordeaux, France, BORDEAUX, France, 6Internal Medicine, CH de Pau, PAU, France, 7Pulmonology, CHU de Dijon, Dijon, France, 8Internal Medicine, CHU de Grenoble, Grenoble, France, 9CHU de Rouen, Rouen, France, 10CHU de Brest, Brest, France, 1¹Nephrology, CHU de Toulouse, Toulouse, France, 12CH de Lons le Saunier, Lons le Saunier, France, 13Pulmonology, CHU de Rouen, Rouen, France, 14Internal Medicine department, Clermont-Ferrand, France, 15CHU, Grenoble, France, 16foch hospital, foch, France, 17Internal Medicine, Hôpital Saint Joseph, Marseille, France, 18Internal medicine, Hôpital Henri-Mondor, Créteil, France, 19Service de Médecine Interne, Hôpital Cochin, Centre de référence national pour les maladies systémiques autoimmunes rares d’Ile de France, DHU Authors, Assistance Publique-Hôpitaux de Paris (AP-HP), Paris, France, Paris, France, 20Service de Médecine Interne, Centre de Référence Maladies Auto-Immunes et Auto-Inflammatoires Systémiques Rares, Hôpital Cochin, Paris, France

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Vasculitis Poster II: ANCA-Associated Vasculitis  
**Session Type:** ACR Poster Session B  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Eosinophilic granulomatosis with polyangiitis (EGPA) (Churg–Strauss) is characterized by pulmonary and systemic small-vessel necrotizing vasculitis, vascular and/or extravascular granulomas, eosinophilia and tissue infiltration by eosinophils, occurring in individuals with asthma. Glucocorticoids (GCs) effectively control the disease, but relapses and/or GC-dependence are frequent, leading to immunosuppressant and/or biological therapy use. We examined off-label biological therapy use for relapsing and/or refractory EGPA.

**Methods:** This retrospective nationwide study included patients with EGPA meeting ACR criteria and/or Chapel Hill Consensus Conference definitions. Treatment efficacy and safety were recorded. Remission was defined as the absence of asthma and/or sinonasal exacerbations and vasculitis manifestations with a prednisone dose ≤7.5 mg/day, and partial response as requiring >7.5 mg of prednisone daily.

**Results:** Thirty-three patients (22 men, 11 women; median age 50 years) were included. Thirteen (39%) received rituximab (RTX) and 20 (61%) omalizumab (OMA). Previous treatments were: methylprednisolone infusions (54%), oral GCs (100%), IV cyclophosphamide (60%), azathiothrine (75%), methotrexate (24%), mycophenolate mofetil (6%), plasmapheresis (6%) and/or co-trimoxazole (33%). RTX was mainly prescribed for pulmonary involvement (92%), sinusitis (69%), peripheral neuropathy (61.5%) and cardiac involvement (46%). OMA was prescribed for pulmonary involvement (90%) and sinusitis (90%). At inclusion, median (range) BVAS for the RTX and OMA groups, respectively, were 4 (0–19) and 2 (0–9). After median follow-up of 20 months, remissions, partial responses and therapeutic failures, respectively, were 38%, 23% and 38% for RTX recipients, and 40%, 20% and 80% for the OMA group. Median
BVAS dropped to 0 for both groups. A GC-sparing effect was obtained for both groups but was greater for RTX recipients: median GC dose decreased from the baseline 16 mg/day to 15 at 3 months, 10 at 6 and 12 months and 7.5 at the last follow-up vs. 12.5 mg/day to 11.25 at 3 months, 12 at 6 months, 10 at 12 months and 9 at the last follow-up for the OMA group. Two patients stopped RTX because of severe asthma flares and another because of refractory disease. Eleven patients stopped OMA: 2 because of vasculitis relapses, 2 for severe asthma flares, 4 had refractory disease and 3 achieved remissions. The latter 3 patients then took azathioprine; no relapses occurred after discontinuing OMA. The only minor side effect, nausea, occurred in the RTX group.

**Conclusion:** The results of this study suggest that RTX and OMA may achieve GC-sparing in relapsing and/or refractory EGPA, but the latter remains frequent.

**Disclosure:** L. Denis, None; M. Samson, None; F. Maurier, None; C. Khouatra, None; V. Germain, None; X. Delbrel, None; P. Bonniaud, None; A. Deroux, None; N. Girszyn, None; C. de Moreuil, None; D. Chauveau, None; A. Gondouin, None; S. Dominique, None; G. Le Guenno, None; L. Bouillet, None; B. Bonnotte, None; J. E. Kahn, None; B. Bienvenu, None; B. Godeau, None; C. Le Jeunne, None; X. Puéchal, None; L. Guillemin for the French Vasculitis Study Group, None; B. Terrier, None.

**Abstract Number:** 1780

**Prognostic Factors in Patients with Granulomatosis with Polyangiitis Requiring Hospitalization- a 10 Year Nationwide Analysis**

Yumeng Wen1, Yiming Luo1 and Changchuan Jiang2, 1Department of Medicine, Mount Sinai St Luke's and Mount Sinai West Hospitals, Icahn School of Medicine at Mount Sinai, New York, NY, 2Department of Medicine, Mount Sinai St. Luke's West Hospitals. Icahn School of Medicine at Mount Sinai, New York, NY

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017
**Session Title:** Vasculitis Poster II: ANCA-Associated Vasculitis
**Session Type:** ACR Poster Session B
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Granulomatosis with Polyangiitis (GPA) is a form of systemic vasculitis with necrotizing granulomatous inflammation commonly involving upper and lower respiratory tracts, necrotizing glomerulonephritis and other organ systems. Limited literature has addressed the prognostic factors impacting on patients with GPA due to relative small sample size of previous studies. The aim of this study is to identify potential risk factors associated with overall in hospital mortality among patients diagnosed with GPA.

**Methods:**

This is a retrospective analysis based on the 2005-2014 National Inpatient Sample, the largest publicly available inpatient database in the United States. The database is composed of discharge-level data from approximately 8 million hospitalizations annually. The inclusion criteria were patients diagnosed with GPA. There were no exclusion criteria. The outcome of interest was in-hospital mortality. Multivariate logistic regression analysis adjusting for age, gender, race, comorbidities and specific system involvement was performed to evaluate for independent associations between variables of interest and in-hospital mortality. Diagnoses were identified using validated ICD-9-CM codes. Analysis was performed using STATA version 14.2.

**Results:**

A cohort of 103,701 patients diagnosed with GPA was included. The mean age was 60 years and the overall in hospital mortality rate was 4.69%. Our study revealed that older age (OR 1.04, p<0.001) was associated with increased in-hospital mortality among patients with GPA requiring hospitalization, while African-American race was associated with less mortality rates (OR 0.59, p=0.012) compared with Caucasian patients. Preexisting comorbidities or specific systemic involvements associated with increased in-hospital mortality were: congestive heart failure (OR 1.25, p=0.039), neutropenia (OR 1.69, p=0.043), coagulopathy (OR 2.02, p<0.001), acute kidney injury (OR 1.68, p<0.001), acute respiratory failure (OR 9.56, p<0.001), sepsis (3.51, p<0.001), gastrointestinal bleed (OR 1.90, p<0.001), intracranial hemorrhage (OR 7.96, p<0.001) and ischemic stroke (OR 2.75, p<0.001). However preexisting hypertension (OR 0.77, p=0.004), diabetes mellitus (OR 0.77, p=0.013), chronic lung disease (OR 0.75, p=0.004) and anemia (OR 0.64, p=0.001) were
associated with less in-hospital mortality. Other comorbidities that were not associated with in-hospital mortalities were: chronic kidney disease (OR 1.07, p=0.52) and chronic liver disease (OR 0.91, p=0.75).

Conclusion:

Clinical characteristics, preexisting comorbidities and major systemic involvements should be considered in the prognostication and risk stratification of patients diagnosed with GPA. Future prospective studies can be considered for further validation.

Disclosure: Y. Wen, None; Y. Luo, None; C. Jiang, None.


Abstract Number: 1781

**Pituitary Disease and Granulomatosis with Polyangiitis: A Collaborative Canadian Case Series and Review of the Literature**

Martha Decker1, Christian Pagnoux2, Constance Chik3, Nader A. Khalidi4, Derek Emery5 and Elaine Yacyshyn6, 1Division of Rheumatology, University of Alberta, Edmonton, AB, Canada, 2Division of Rheumatology, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada, 3Division of Endocrinology, University of Alberta, Edmonton, AB, Canada, 4Rheumatology, McMaster University, Hamilton, ON, Canada, 5Division of Radiology, University of Alberta, Edmonton, AB, Canada, 6Medicine, University of Alberta, Edmonton, AB, Canada

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017
Session Title: Vasculitis Poster II: ANCA-Associated Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

**Background/Purpose:** Pituitary involvement in granulomatosis with polyangiitis (GPA) is rare with an incidence of approximately 1%. Objectives were: (1) Describe ten new cases of pituitary involvement in GPA seen at Canadian healthcare institutions; (2) Perform a literature review of pituitary involvement in GPA and compare previously reported cases with our series.

**Methods:** We surveyed members of the Canadian Vasculitis Research Network (CanVasc; 18 centers across Canada) for patients with GPA and pituitary disease. Cases were defined based on: (1) Clinical characteristics consistent with GPA; (2) Pituitary MRI/pituitary histology consistent with GPA, with or without hormonal dysfunction; (3) Exclusion of alternative causes of pituitary disease. Clinical details were collected using a standardized record form. We performed a literature search of the following databases: Medline, Embase, Scopus, and Proquest, using “granulomatosis with polyangiitis” and “pituitary” as keywords.

**Results:**

Our case series included 10 patients (9 female, 1 male). Mean age at GPA diagnosis and presentation of pituitary disease were: 33.8 years (range 13 to 56) and 35.3 years (range 18 to 56), respectively. Five patients presented with pituitary disease at GPA diagnosis; mean time from GPA to pituitary disease diagnosis was 3.4 years for the remaining five. Nine patients were ANCA positive (PR3 for 8, MPO for 1). Diabetes insipidus (DI) was the most frequent hormonal dysfunction observed (n = 8). Hypogonadism and central hypothyroidism were seen in 3 and 2 patients, respectively. Pituitary hormone testing was normal in 2 patients (presenting with pituitary mass only). All patients had GPA involvement at other sites including ENT (n = 8), pulmonary (n = 6), and renal (n = 4). Eight patients received therapy including glucocorticoids alone (n = 1), with IV cyclophosphamide (CYC, n = 2), oral CYC (n = 3) or rituximab (n = 1), or a combination of mycophenolate mofetil and tacrolimus (n = 1). All patients had systemic disease remission on follow-up. Hormonal deficiencies were persistent after treatment in all patients with pituitary dysfunction at baseline. Our literature review yielded 67 other cases of pituitary involvement in GPA. The largest series included 9 patients. A limitation of our series, and previous case reports, is the lack of pituitary histology to definitively exclude an alternative cause for pituitary disease arising concurrently with GPA. Tissue is rarely obtained unless there is a surgical indication (e.g. compression of the optic chiasm) or a diagnostic dilemma exists, such as in isolated pituitary GPA.

**Conclusion:** This new and large case series of pituitary disease and GPA, together with previously reported cases, suggest: (1) Pituitary disease may be diagnosed concurrent to systemic GPA or later; (2) Pituitary disease is rarely isolated; (3) Posterior pituitary dysfunction...
is the most common disease manifestation; (4) Pituitary disease does not seem to negatively impact the global prognosis; (5) Pituitary
dysfunction and need for hormone supplementation are often irreversible.

Disclosure: M. Decker, None; C. Pagnoux, None; C. Chik, None; N. A. Khalidi, None; D. Emery, None; E. Yacyshyn, None.

Mycophenolic Acid Decreases IL-10 and IL-6 Production By B Cells of Granulomatosis with Polyangiitis Patients and Healthy Controls in Vitro

Anouk von Borstel1, Wayel H. Abdulahad2, Abraham Rutgers2, Judith Land2, Coen A. Stegeman1, Peter Heeringa3 and Jan-Stephan F. Sanders1, 1Internal Medicine, Division of Nephrology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, 2Rheumatology and Clinical Immunology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, 3Pathology and Medical Biology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Vasculitis Poster II: ANCA-Associated Vasculitis
Session Type: ACR Poster Session B
Session Time: 9:00AM-11:00AM

Background/Purpose:
Granulomatosis with polyangiitis (GPA) is a relapsing autoimmune disease affecting small- to medium-sized blood vessels. B cells are thought to play an important antibody-independent role in GPA patients. Immunosuppressants are used to induce remission at initial onset of disease, and subsequently used as maintenance treatment. Mycophenolate mofetil (MMF) was found to be effective for both induction and maintenance of remission in GPA; although, azathioprine (AZA) is superior as maintenance therapy compared to MMF. Little is known about the effect of these commonly used drugs on B cell cytokine production. We hypothesized that the differences in the efficacy of MMF and AZA could be the result of differential effects on B cell cytokine production. Therefore, we studied the effects of MMF and AZA on in vitro B cell cytokine production.

Methods:
We assessed the in vitro effect of the active compounds of MMF (MPA) and AZA (6-MP) on B cell cytokine production. PBMCs of twenty untreated GPA patients in remission and twenty age- and sex-matched healthy controls (HCs) were isolated. PBMCs were cultured with CpG and 3 uM MPA or 6-MP. After 3 days, PBMCs were restimulated with Ca-I and PMA for 5h in the presence of BFA, stained for intracellular IL-6 and IL-10 and measured by flow cytometry. In addition, to determine whether in vivo use of MMF or AZA influences in vitro B cell cytokine production, PBMCs from 14 patients in stable remission were cultured and stimulated as mentioned above. From each patient two samples were analyzed, one when patients were not treated and one when patients were receiving either MMF (n=4) or AZA (n=10). For comparison, PBMCs from 14 matched HCs were analyzed simultaneously.

Results:
MPA significantly decreased the frequency of IL-10+ and IL-6+ B cells in HCs and GPA patients, compared to CpG alone (p<0.001) and CpG+6-MP (p<0.001). PBMCs from GPA patients that were actively treated with MMF or AZA, tended to have a reduced IL-10+ B cell frequency compared to PBMCs from the same donors that did not receive treatment (p=0.1) or healthy controls (p=0.09). This reduction in IL-10+ B cells was only seen in MMF- and not in AZA-treated patients (p=0.09). In contrast, no effect of MMF or AZA was found on IL-6+ B cells (%).

Conclusion:
The decrease in *in vitro* B cell cytokine production in the presence of mycophenolic acid might explain why this agent is less effective as maintenance therapy in GPA. Further research is needed to elucidate whether this *in vitro* finding is clinically relevant.

Disclosure: A. von Borstel, None; W. H. Abdulahad, None; A. Rutgers, None; J. Land, None; C. A. Stegeman, None; P. Heeringa, None; J. S. F. Sanders, Dutch Kidney Foundation, 2, Netherlands Organization for Scientific Research, 2.


Abstract Number: 1783

**The Value of a Combination of Serum Proteins to Identify Response to Induction Therapy Among Patients with ANCA-Associated Vasculitis**

Sadao Jinno¹ ², S. Reza Jafarzadeh³, Roscoe Warner⁴, Ulrich Specks⁵, John H. Stone⁶, Gary S. Hoffman⁷, Cees G.M. Kallenberg⁸, Carol A. Langford⁹, Philip Seo¹⁰, Robert F. Spiera¹¹, E. William St Clair¹², Kent Johnson¹³, Peter A. Merkel¹⁴ and Paul A. Monach²

¹Rheumatology, Boston University School of Medicine, Boston, MA, ²Boston University School of Medicine, Boston, MA, ³Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA, ⁴University of Michigan Medical School, Ann Arbor, MI, ⁵Mayo Clinic College of Medicine, Rochester, MN, ⁶Massachusetts General Hospital Rheumatology Unit, Harvard Medical School, Boston, MA, ⁷Rheumatology, Cleveland Clinic, Cleveland, OH, ⁸Rheumatology and Clinical Immunology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, ⁹Rheumatic and Immunologic Diseases, Cleveland Clinic, Cleveland, OH, ¹⁰Medicine, Johns Hopkins University, Baltimore, MD, ¹¹Rheumatology, Hospital for Special Surgery, New York, NY, ¹²Rheumatology, Duke University Medical Center, Durham, NC, ¹³University of Michigan Medical School, Ann Arbor, MI, ¹⁴Division of Rheumatology, University of Pennsylvania; Perelman School of Medicine, Philadelphia, PA

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017

Session Title: Vasculitis Poster II: ANCA-Associated Vasculitis

Session Type: ACR Poster Session B

Session Time: 9:00AM-11:00AM

**Background/Purpose:** Most patients with anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) achieve clinical remission after induction therapy. However, even among patients who achieve remission, induction therapy sometimes must be changed or prolonged, or prednisone may be required to maintain remission. A decision support tool to better define patients with harder-to-control disease would help guide clinicians when starting therapy.

**Methods:** Twenty-eight serum proteins representing diverse aspects of the biology of AAV were measured at screening (during active disease) in 181 patients enrolled in the Rituximab in ANCA-Associated Vasculitis (RAVE) clinical trial. Two outcomes were used to test the ability of a combination of these biomarkers to predict optimal response to therapy: 1) “complete remission,” the primary endpoint of the RAVE trial, defined as remission (Birmingham Vasculitis Activity Score for Wegener’s granulomatosis [BVAS/WG]=0) at month 6, remaining in the assigned treatment arm, and off prednisone, with all other patients defined as non-responders; 2) remission (BVAS/WG=0) at month 6, with analysis limited to patients who remained in the trial through month 6 in their original treatment arm, and did or did not re-start prednisone at or before month 6. Demographic and clinical variables included age, sex, ANCA specificity (MPO or PR3), new diagnosis at entry, treatment (rituximab vs cyclophosphamide), and presence of renal disease. Models were developed using least absolute shrinkage and selection operator (lasso) regressions with leave-one-out cross-validation. Variables included all biomarkers in addition to demographic and clinical information.

**Results:** All subjects had severe active vasculitis (median BVAS/WG= 8) at screening. Sixty-two percent (112/181) achieved complete remission at month 6. A combination of 10 serum biomarkers and treatment with rituximab provided the best predictive ability for complete remission at 6-month (areas of under the curve [AUC] = 0.73), see Figure. Among 155 patients who remained on study protocol at month 6 in their original treatment group, 130 were in remission. A combination of 7 biomarkers, new diagnosis at entry, and rituximab treatment provided highest accuracy in predicting remission at month 6 (AUC = 0.85). Forcing additional demographic and clinical information did not improve accuracy in either model (AUC = 0.74 and 0.85).
Conclusion: A combination of several biomarkers during active disease could provide a useful tool to predict patients with AAV who will achieve optimal response to induction therapy. Further validation studies are needed to test the clinical utility of this panel of biomarkers.

Disclosure: S. Jinno, None; S. R. Jafarzadeh, None; R. Warner, None; U. Specks, None; J. H. Stone, Xencor, 2; G. S. Hoffman, None; C. G. M. Kallenberg, None; C. A. Langford, None; P. Seo, GlaxoSmithKline, 5; R. F. Spiera, Roche-Genetech, 2, GSK, 2, BMS, 2, Celgene, 2, Boehringer Ingelheim, 2, Cytori, 2, Chemocentryx, 2, Corbus Pharmaceuticals, 2, Primm, 2, Roche-Genetech, 5, GSK, 5, Boehringer Ingelheim, 5; E. W. St Clair, None; K. Johnson, None; P. A. Merkel, Actelion Pharmaceuticals US, Bristol-Myers Squibb, CaridianBCT, Celgene, Chemocentryx, Genentech/Roche, GlaxoSmithKline, Kypha, MedImmune/AZ, 2, American College of Rheumatology, European League Against Rheumatism, National Institutes of Health, US Food and Drug Administration, The Patient-Centered Outcomes Research Institute, The Vasculitis Foundation, 2, Actelion Pharmaceuticals US, Alexion, Boston Pharm, Bristol-Myers Squibb, Chemocentryx, Genzyme/Sanoji, GlaxoSmithKline, Genentech/Roche, InflRx, PrincipioBio, Proteon, Seattle Genetics, 5; P. A. Monach, Genentech and Biogen IDEC Inc., 2, GlaxoSmithKline, 2, Bristol-Myers Squibb, 2.

Abstract Number: 1784

The Novel Anti-CD40 Monoclonal Antibody CFZ533 Shows Beneficial Effects in Patients with Primary Sjögren’s Syndrome: A Phase IIa Double-Blind, Placebo-Controlled Randomized Trial

Benjamin Fisher1, Margit Zeher2, Wan-Fai Ng3, Michele Bombardieri4, Maximilian Posch5, Athena S Papas6, Arwa M Farag7, Thomas Daikeler7, Bettina Bannert8, Alan J. Kivitz7, Steven E. Carsons10, David A. Isenberg11, Francesca Barone12, Simon Bowman13, Pascal Espie14, Grazyna Wieczorek14, Pierre Moulin14, David Floch14, Cyrielle Dupuy14, Xiaohui Ren14, Petra Faerber14, Andrew M Wright15, Hans Ulrich Hacker15, Michael Rotte14, James S. Rush15 and Peter Gergely14,

1Rheumatology Research Group, Department of Rheumatology, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom, 2Division of Clinical Immunology, University of Debrecen, Debrecen, Hungary, 3Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, United Kingdom, 4Centre for Experimental Medicine and Rheumatology, William Harvey Research Institute, Queen Mary University of London, UK, London, United Kingdom, 5Charité Research Organisation GmbH, Berlin, Germany, 6Tufts University, Boston, MA, 7Rheumatology, University Hospital Basel, Basel, Switzerland, 8University Hospital Basel, Basel, Switzerland, 9Department of Rheumatology, Altoona Center for Clinical Research, Duncansville, PA, 10NYU Winthrop University Hospital, Department of Medicine, Mineola, NY, 11Centre for Rheumatology, Division of Medicine, University College London, London, United Kingdom, 12Institute of Inflammation and Ageing (IIA), University of Birmingham, Birmingham, United Kingdom, 13Department of Rheumatology, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK, Birmingham, United Kingdom, 14Novartis Institutes for Biomedical Research, Basel, Switzerland, 15Novartis Pharmaceuticals Corporation, Basel, Switzerland

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Plenary Session II
Session Type: ACR Plenary Session
**Background/Purpose:** Primary Sjögren’s syndrome (pSS) is a systemic, progressive autoimmune disease characterized by formation of ectopic germinal centers in exocrine glands and secretory gland dysfunction. A subset of patients also develops extraglandular manifestations. CFZ533 is a novel monoclonal antibody that potently and selectively blocks CD40, a co-stimulatory pathway receptor essential for germinal center reactions and other immune mediated functions implicated in pSS pathogenesis. We conducted a randomized, double–blind, placebo-controlled, multi-centric, partial cross-over Phase IIa Proof of Concept (PoC) study to evaluate the safety, tolerability and efficacy of CFZ533 in patients with pSS.

**Methods:** Clinically active (EULAR Sjögren’s Syndrome Disease Activity Index [ESSDAI]≥6) pSS patients were randomized to receive four doses of 3 mg/kg s.c. CFZ533 or placebo (2:1, Cohort 1) or 10 mg/kg i.v. CFZ533 or placebo (2:1, Cohort 2) over 12 weeks in Period 1. Four additional doses of 3 mg/kg s.c. CFZ533 or 10 mg/kg i.v. CFZ533, respectively, were administered in an open label extension (Period 2) for 12 weeks. Key outcomes included safety and efficacy as assessed by change in ESSDAI after 12 weeks treatment. In addition, measurements of pharmacokinetics and pharmacodynamics (PK/PD) of CFZ533, EULAR Sjögren’s Syndrome Patient Reported Index (ESSPRI), Multi-dimensional Fatigue Inventory (MFI), Physician’s Global Assessment, Patient’s Global Assessment, SF-36, and biomarkers of pSS were monitored.

**Results:** Forty-four patients were enrolled: 8 patients received 3 mg/kg s.c. CFZ533 and 4 placebo in Cohort 1 and 21 received 10 mg/kg i.v. CFZ533 and 11 placebo in Cohort 2. While PK/PD was as expected in the CFZ533 10 mg/kg i.v. cohort based on healthy volunteer data from the first in human trial, CFZ533 exposure appeared lower than expected in the 3 mg/kg s.c. cohort, likely due to target mediated disposition. Overall, CFZ533 was safe and well tolerated, and the majority of AEs were mild or moderate. There was a single serious AE (bacterial conjunctivitis) in the 3 mg/kg s.c. cohort that was not related to study drug. In Cohort 1, ESSDAI was observed to improve by approximately 2 points from mean baseline scores of approximately 12 in both placebo and 3 mg/kg s.c. groups, with therefore no evidence of treatment difference (ΔESSDAI=0.68, 95% CI = -4.71 – 6.46). However in Cohort 2, the improvement in ESSDAI from mean baselines of approximately 11 was observed to be 6.35 in the 10 mg/kg i.v. group compared to 1.27 in the placebo group, with the modelled difference between groups of ΔESSDAI=5.64 (95% CI=1.02 – 10.58) strongly favoring the CFZ533 i.v. treatment. Improvements in other measures such as ESSPRI, MFI, Physician’s Global Assessment, and Patient’s Global Assessment and decreases in the germinal center-related serum biomarker CXCL13 were also observed in the 10 mg/kg i.v. CFZ533 group.

**Conclusion:** In this proof of concept study, testing a blocking, non-depleting anti-CD40 antibody for the first time in primary Sjögren’s syndrome, results suggest that CFZ533 may offer a new treatment modality in clinically active pSS.

**Disclosure:** B. Fisher, Novartis, Roche, Virtualscopics, 5; M. Zeher, None; W. F. Ng, Pfizer, UCB, MedImmune, Takeda and Sanofi, 5; M. Bombardieri, GSK, Amgen/MedImmune and UCB, 5; M. Posch, None; A. S. Papas, None; A. M. Farag, None; T. Daikeler, None; B. Bannert, None; A. J. Kivitz, Sanofi, Pfizer, Roche, and UCB, 5; S. E. Carsons, None; D. A. Isenberg, EMD Serono, Inc, 5; F. Barone, None; S. Bowman, AstraZeneca/Medimmune, BMS, Celgene, Eli Lilly, Glenmark, GSK, MTPharma, Novartis, Ono, Takeda, UCB, XLT Bio., 5; P. Espie, Novartis Pharmaceutical Corporation, 3; G. Wieczorek, Novartis Pharmaceutical Corporation, 3; P. Moulin, Novartis Pharmaceutical Corporation, 3; D. Floch, Novartis Pharmaceutical Corporation, 3; C. Dupuy, Novartis Pharmaceutical Corporation, 3; X. Ren, Novartis Pharmaceutical Corporation, 3; P. Faerber, Novartis Pharmaceutical Corporation, 3; A. M. Wright, Novartis Pharmaceutical Corporation, 3; H. U. Hockey, Novartis Pharmaceutical Corporation, 3; M. Rotte, Novartis Pharmaceutical Corporation, 3; J. S. Rush, Novartis Pharmaceutical Corporation, 3; P. Gergely, Novartis Pharmaceutical Corporation, 3.

**Abstract Number:** 1785

**Serious or Opportunistic Infections in Infants Born to Pregnant Women with Rheumatoid Arthritis and Treated with a Biologic Medication**

Christina D Chambers¹, Diana L Johnson², Yunjun Luo³, Ronghui Xu⁴ and Kenneth L Jones³, ¹Pediatrics and Family Medicine and Public Health, University of California San Diego, La Jolla, CA, ²Department of Pediatrics, University of California, San Diego, La Jolla, CA, ³Pediatrics, University of California San Diego, La Jolla, CA, ⁴Department of Family Medicine and Public Health, University of California, San Diego, La Jolla, CA

**First publication:** September 18, 2017
**Background/Purpose:** Use of biologic therapies for rheumatoid arthritis (RA) in pregnancy is common. There is theoretical concern that these medications could interfere with postnatal immune function in the infant.

**Methods:** The Organization of Teratology Information Specialists (OTIS) Autoimmune Diseases in Pregnancy Project enrolled pregnant women from U.S. or Canada with or without RA in a prospective observational cohort study. Women were followed with 3-4 telephone interviews; medical records were abstracted from the delivery hospital, obstetric and specialty providers; follow-up data were obtained from the pediatrician through 1 year of age. Maternal use of biologic medications including start/stop dates was captured, and questions were asked about serious/opportunistic infections in the infant. These were defined as an infection requiring hospitalization or any of the following: neonatal sepsis, invasive fungal infection, x-ray proven pneumonia, meningitis, bacteremia, pneumocystis, septic arthritis, osteomyelitis, tuberculosis, herpes, listeria, legionella, mycobacteria, systemic cytomegalovirus, or abscess. We estimated relative risks (RR) and 95% confidence intervals (CI) using generalized estimating equations. We further stratified comparisons by gestational timing of last dose of the biologic after 24 and 32 weeks gestation, respectively.

**Results:** Between 2004-2016, 1,184 pregnancies ending in live born infants, including 73 infants of twin pregnancies, were followed to 1 year postpartum (252 with RA treated with a biologic in pregnancy, 463 with RA but no treatment with a biologic in pregnancy, and 469 with no chronic diseases). Of those in the RA biologic group, 97 (38.4%) took their last dose in the 1st or 2nd trimester and 155 (61.5%) received their last dose in the 3rd trimester (Figure). Serious or opportunistic infections were reported in 7/252 (2.8%) of infants born to women with RA treated with a biologic, 18/463 (3.9%) of infants born to women with RA not treated with a biologic (RR 0.71, 95% CI 0.30, 1.71), and 12/469 (2.6%) of those infants whose mothers had no chronic diseases (RR 1.09, 95% CI 0.43, 2.72). Restricting the group treated with a biologic to women whose last dose was sometime after 24 weeks gestation, 6/155 (3.9%) reported infant infections in the biologics group compared to 18/463 (3.9%) in the RA untreated group (RR 1.00, 95% CI 0.40, 2.48). Further stratification at 32 weeks gestation resulted in infections reported in 5/143 (3.5%) in the RA biologics group compared to 3.9% in the RA untreated group (RR 0.90, 95% CI 0.34, 2.39).

**Conclusion:** We found no evidence of increased risk of serious/opportunistic infections in infants in this sample. These data are reassuring for pregnant women who require treatment with a biologic medication. However, it is possible that less serious infections occur more frequently, and further research is needed.

**Disclosure:**

C. D. Chambers, AbbVie, 2,Amgen, 2,Bristol Myers Squibb, 2,Celgene, 2,Janssen Pharmaceutica Product, L.P., 2,Pfizer Inc, 2,Roche Pharmaceuticals, 2,Sequira, 2,SK, 2,UCB, 2,Sanofi-Aventis Pharmaceutical, 2; D. L. Johnson, None; Y. Luo, None; R. Xu, Amgen, 2,AbbVie, 2,Celgene, 2,Janssen Pharmaceutica Product, L.P, 2,Bristol Myers Squibb, 2,SK, 2,Sequira, 2,Pfizer Inc, 2,Sanofi-Aventis Pharmaceutical, 2,Roche Pharmaceuticals, 2,UCB, 2; K. L. Jones, AbbVie, 2,Amgen, 2,Bristol Myers Squibb, 2, Roche Pharmaceuticals, 2,Janssen Pharmaceutica Product, L.P, 2,Celgene, 2,Pfizer Inc, 2,UCB, 2,Sanofi-Aventis Pharmaceutical, 2,SK, 2,Sequira, 2.


**Abstract Number:** 1786

**Lupus Nephritis Is Linked to Immunity to an Intestinal Commensal Lachnospiraceae Species**
Gregg J. Silverman1, Doua F. Azzouz2, Hanane El Bannoudi2, Aidana Omarbekova3, Brad H. Rovin4, Roberto Caricchio5, Alexander Alekseyenko6 and Jill P. Buyon2, 1Department of Medicine, New York University School of Medicine, New York, NY, 2Medicine, New York University School of Medicine, New York, NY, 3New York University School of Medicine, New York, NY, 4Ohio State University Medical Center, Columbus, OH, 5Medicine/Rheumatology, Temple University, Philadelphia, PA, 6Medical University of South Carolina, Charleston, SC

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Plenary Session II
Session Type: ACR Plenary Session
Session Time: 11:00AM-12:30PM

Background/Purpose: A transmissible agent has long been suspected in the pathogenesis of SLE, yet the potential contribution of members of the intestinal microbiome to the immune abnormalities in active SLE has not previously been investigated. We therefore characterized the gut microbiota of patients with SLE, with special interest in those with Lupus nephritis (LN), a clinical feature too commonly associated with great morbidity and early mortality.

Methods: Blood and fecal samples from SLE patients were obtained, with the exclusion of patients with selective IgA deficiency, or history of prior cytotoxic drugs, or antibiotics within four months. Fecal 16S rRNA next generation sequencing was performed. Sera samples were profiled for autoantibodies. In addition, sera from two independent lupus cohorts were studied for validation.

Results: Compared to controls, the intestinal microbiome from SLE patients (N=61) showed decreased species richness diversity. The microbiota of patients in clinical remission (based on SLEDAI) were most similar to healthy controls, while reductions in taxonomic complexity were most pronounced in those with high disease activity. Notably, SLE patients had an overall 5-fold greater representation of a particular species in the Blautia genus of the Lachnospiraceae family of obligate anaerobic Gram-positive cocci. There were reciprocal significant contractions of two other commensal species with putative protective properties. Abundance of the Lachnospiraceae species significantly correlated with serum IgG to a cell wall moiety from a strain of this same species (P=0.002, N=61, Spearman) but not with 7 other strains. There was also a significant correlation between the distribution of SLEDAI scores and levels of these circulating anti-strain IgG antibodies (P=0.02, N=48). Using bacterial antigen treated with DNase/protease K, levels of IgG anti-strain antibodies were significantly higher in those with active nephritis at time of sampling compared to SLE without renal activity (Cohort 1 P=0.01 N=48; Cohort 2 P=0.006, N=28, Mann-Whitney). Levels of anti-strain antibodies also significantly correlated with high-titer serum IgG to native DNA (P<0.0001, N=27), and inversely correlated with C3 and C4 (each P<0.01, N=61). High titers of these anti-bacterial antibodies were found in patients with active Class III, IV and V LN (Cohort 3).

Conclusion: These findings suggest a novel paradigm for the pathogenesis of LN in which specific strains of common intestinal commensal bacteria contribute to the immune-complex mediated disease process responsible for glomerulonephritis (GN). This is reminiscent of poststreptococcal GN, although in LN the postulated intestinal bacterial dysbioses and microbial expansion appear to occur without outward signs and symptoms of clinical infection.

Disclosure: G. J. Silverman, None; D. F. Azzouz, None; H. El Bannoudi, None; A. Omarbekova, None; B. H. Rovin, None; R. Caricchio, None; A. Alekseyenko, None; J. P. Buyon, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/lupus-nephritis-is-linked-to-immunity-to-an-intestinal-commensal-lachnospiraceae-species

Abstract Number: 1787

Efficacy and Safety of Continuing Versus Withdrawing Adalimumab in Maintaining Remission in Patients with Non-Radiographic Axial Spondyloarthritis

Robert B.M. Landewé1, Joachim Sieper2, Philip J Mease3, Robert D Inman4, Xin Wang5, Mei Li5, Aileen L. Pangan5 and Jaclyn K. Anderson5, 1University of Amsterdam, Amsterdam, Netherlands, 2Charité Universitätsmedizin Berlin, Berlin, Germany, 3Swedish Medical Center and University of Washington, Seattle, WA, 4Department of Immunology, University of Toronto, Toronto, ON, Canada, 5AbbVie Inc., North Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION
Background/Purpose: It is not known whether TNF blockers can be stopped in non-radiographic (nr-axSpA) patients who are in remission. In ABILITY-1, adalimumab (ADA) significantly improved clinical response vs placebo (PBO) in patients (pts) with nr-axSpA. ABILITY-3 (NCT01808118), reported here, assessed if ADA can be discontinued or should be continued in nr-axSpA pts in sustained remission after a 28-wk open-label period.

Methods: ABILITY-3 enrolled adult pts diagnosed with nr-axSpA, fulfilling ASAS criteria but NOT modified New York criteria who had objective evidence of active MRI inflammation in the SI joints or spine or elevated high-sensitivity CRP at screening, active disease at baseline (ASDAS ≥2.1, BASDAI ≥4, total back pain ≥4), and inadequate response to ≥2 NSAIDs. Pts who achieved ASDAS inactive disease (ASDAS <1.3) with open-label ADA 40 mg every other wk at wk 16, 20, 24, and 28 were randomized to 40-wk, double-blind PBO (withdrawal) or ADA (continuation) in period 2. The primary efficacy endpoint was the proportion of patients who did not experience a flare (ASDAS ≥2.1 at 2 consecutive study visits) during period 2. Secondary endpoints were also assessed up to wk 68 (nonresponder imputation).

Results: Of 673 enrolled pts, 305 (45%) were randomized to double-blind treatment (Table). A significantly greater proportion of patients treated with ADA vs PBO had no flares (70% vs 47%; *P*<0.001) at wk 68; the relative risk of flare with treatment withdrawal was 1.77. Time to flare analysis showed significantly lower risk of flare for ADA vs PBO (Figure). At wk 68, significantly greater proportions of ADA vs PBO patients achieved secondary endpoints, except for HAQ-S (Table). Among pts who received ADA at any time, 77% reported adverse events (AEs) and 4% reported a serious AE; nasopharyngitis (17%), upper respiratory tract infection (12%), worsening of axSpA (9%), headache (8%), and diarrhea (6%) were the most common. During period 2, incidence of AEs was similar for ADA and PBO (65% vs 69%), incidence of serious AEs was higher for PBO vs ADA (7% vs 1%), and the most common AEs in both the ADA and PBO groups were nasopharyngitis (16% vs 13%), upper respiratory tract infection (13% vs 8%), and worsening of axSpA (6% vs 14%; none serious).
Table. Baseline Characteristics and Efficacy Outcomes at Week 68

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adalimumab (40 mg EOW)</th>
<th>Placebo</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline, mean (SD)*</td>
<td>n=152</td>
<td>n=153</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>34.7 (10.3)</td>
<td>35.3 (10.2)</td>
<td>0.611</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>56 (37)</td>
<td>60 (39)</td>
<td>0.724</td>
</tr>
<tr>
<td>HLA-B27 positive, n (%)</td>
<td>132 (87)</td>
<td>134 (88)</td>
<td>0.866</td>
</tr>
<tr>
<td>SpA symptom duration, y</td>
<td>6.4 (6.9)</td>
<td>7.1 (6.8)</td>
<td>0.358</td>
</tr>
<tr>
<td>SpA duration from diagnosis, y</td>
<td>1.9 (2.9)</td>
<td>1.8 (2.9)</td>
<td>0.711</td>
</tr>
<tr>
<td>ASDAS</td>
<td>3.5 (0.9)</td>
<td>3.5 (0.8)</td>
<td>0.851</td>
</tr>
<tr>
<td>BASDAI</td>
<td>6.8 (1.4)</td>
<td>6.8 (1.5)</td>
<td>0.851</td>
</tr>
<tr>
<td>Total back pain</td>
<td>7.0 (1.7)</td>
<td>7.0 (1.8)</td>
<td>0.946</td>
</tr>
<tr>
<td>ASDAS, wk 28</td>
<td>0.7 (0.4)</td>
<td>0.6 (0.4)</td>
<td>0.355</td>
</tr>
<tr>
<td>Wk 68†, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No flare</td>
<td>106 (70)</td>
<td>72 (47)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ASDAS ID</td>
<td>87 (57)</td>
<td>51 (33)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ASDAS MI</td>
<td>89 (59)</td>
<td>49 (32)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ASDAS CII</td>
<td>102 (67)</td>
<td>69 (45)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ASAS20</td>
<td>107 (70)</td>
<td>72 (47)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ASAS40</td>
<td>100 (66)</td>
<td>70 (46)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ASAS 5/6</td>
<td>87 (57)</td>
<td>49 (32)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ASAS PR</td>
<td>64 (42)</td>
<td>41 (27)</td>
<td>0.005</td>
</tr>
<tr>
<td>BASDAI50</td>
<td>103 (68)</td>
<td>72 (47)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Change from baseline in BASFI‡, LSmean ± SE</td>
<td>−3.97±0.11, n=111</td>
<td>−3.51±0.13, n=77</td>
<td>0.007</td>
</tr>
<tr>
<td>Change from baseline in HAQ-S‡, LSmean ± SE</td>
<td>−0.68±0.04, n=112</td>
<td>−0.58±0.04, n=79</td>
<td>0.088</td>
</tr>
</tbody>
</table>

ASAS, Assessment of SpondyloArthritis international Society; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; CII, clinically important improvement; EOW, every other week; HAQ-S, Health Assessment Questionnaire for the Spondyloarthropathies; HLA-B27, human leukocyte antigen B27; ID, inactive disease; LS, least squares; MI, major improvement; PR, partial remission; SE, standard error; SpA, spondyloarthritis.

*Baseline characteristics at overall study baseline (wk 0) unless indicated otherwise.

†Nonresponder imputation for wk 68 values; only data prior to rescue included.

‡Mixed effect Model Repeat Measurement.

*P* value using analysis of variance (baseline) or 2-sided Pearson chi-square test (wk 68 vs lead-in open-label baseline). *P* value for HAQ-S and BASFI change from baseline using analysis from 2-sided repeated measures model with fixed effect of treatment.
Conclusion: In pts with nr-axSpA who achieved sustained remission with ADA, continued therapy was associated with significantly more patients maintaining remission and lower disease activity than treatment withdrawal. These results support the continuation of ADA therapy after achievement of sustained remission. Safety findings were consistent with the established safety profile of ADA.

Disclosure: R. B. M. Landewé, Abbott/AbbVie, Ablynx, Amgen, Astra-Zeneca, Bristol Myers Squibb, Celgene, Janssen (formerly Centocor), Galapagos, GlaxoSmithKline, Novartis, Novo-Nordisk, Merck, Pfizer, Roche, Schering-Plough, Tigenix, UCB, and Wyeth, 5,Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, and Wyeth, 2,Abbott/AbbVie, Amgen, Bristol Myers Squibb, Janssen (formerly Centocor), Merck, Pfizer, Roche, Schering-Plough, UCB, and Wyeth, 8; J. Sieper, AbbVie, Janssen, Lilly, Merck, Novartis, Pfizer, Sun Pharma and UCB, 5,AbbVie, Janssen, Lilly, Merck, Novartis, and Pfizer, 8; P. J. Mease, Celgene, Novartis, AbbVie, Amgen, BMS, Lilly, Pfizer and UCB, 2,Cellgene, Corrona, Novartis, AbbVie, Amgen, BMS, Crescendo, Genentech, Janssen, Lilly, Merck, Pfizer and UCB, 5,AbbVie, Janssen, Lilly, Merck, Novartis, and Pfizer, 8; R. D. Inman, AbbVie, Amgen, Janssen, Novartis, 5; X. Wang, Abbvie, 3,Abbvie, 1; M. Li, AbbVie, 3,Abbvie, 1; A. L. Pangan, AbbVie, 1,AbbVie, 3; J. K. Anderson, Abbvie, 3,Abbvie, 1.


Abstract Number: 1788

Dose Intra-Articular Injection of Corticosteroids Increase the Risk of Knee Osteoarthritis Progression? Data from the Osteoarthritis Initiative

Guang-hua Lei1, Chao Zeng1, Jie Wei2,3, Yi-lun Wang1 and Dong-xing Xie1, 1Department of orthopaedics, Xiangya Hospital, Central South University, Changsha, China, 2Health Management Center, Xiangya Hospital, Central South University, Changsha, China, 3Department of Epidemiology and Health Statistics, Xiangya School of Public Health, Central South University, Changsha, China

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Plenary Session II
Session Type: ACR Plenary Session
Session Time: 11:00AM-12:30PM

Background/Purpose: Although intra-articular injection of corticosteroids (IAIC) has been one of the modalities of treatment for symptomatic knee OA, the recommendations for its use are inconsistent. Recently, a randomized clinical trial (RCT) reported that IAIC didn’t significantly improve pain, but instead resulted in greater cartilage volume loss compared with saline injections. To examine this unexpected finding in a real-life non-trial setting, we investigated IAIC in relation to knee radiographic osteoarthritis (ROA) progression in a prospective cohort study.
Methods: We conducted a propensity score matched cohort study to examine the effect of IAIC on the risk of knee ROA progression using data collected from the Osteoarthritis Initiative up to 8 years follow-up. Eligible subjects consisted of those who had at least one knee with a K/L grade of 2 or 3 and did not have IAIC at baseline. We identified subjects with incident knee IAIC during the study period. Knee ROA progression was defined as K/L grade worsening or knee replacement therapy during the follow-up. We used logistic regression model to calculate propensity scores for IAIC within each 1-year time block. The predictors for IAIC in the logistic regression model included age, sex, BMI, education, WOMAC pain score, knee injury history, physical activity level, NSAIDs use and K/L grade. Up to four knees without IAIC were propensity score matched to a knee with incident IAIC within each 1-year accrual block. Subjects were followed to the date of ROA progression, lost to follow-up, death or end of the follow-up, whichever came first. We plotted cumulative risk of ROA progression using Kaplan-Meier curves for each cohort accounting for competing risk. We fitted a Cox proportional-hazards model to examine the relation of IAIC to the risk of ROA progression.

Results: Baseline characteristics were well-balanced between IAIC and non-IAIC cohorts (Table 1). Risk of ROA progression was higher among knees with IAIC (60.86 per 1000 person-years) than those without IAIC (38.02 per 1000 person-years) during the follow-up (Figure 1). Compared with knees without IAIC, the hazard ratio of ROA progression for knees with IAIC was 1.60 (95%CI: 1.21 to 2.12). The associations appeared stronger among women (HR=1.71, 95%CI: 1.22 to 2.40) than men (HR=1.38, 95%CI: 0.84 to 2.28) although the effect estimate in men was not statistically significant owing to relatively small sample size (Table 1).

Conclusion: We found that knees with IAIC experienced higher risk of knee ROA progression than those without IAIC in a real-life setting, consistent with the recent RCT results.

Table 1. Hazard ratios for the risk of knee osteoarthritis progression associated with intra-articular corticosteroids injection

<table>
<thead>
<tr>
<th>Injection (n=134)*</th>
<th>No Injection (n=499)**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
</tr>
<tr>
<td>All patients³</td>
<td>58</td>
</tr>
<tr>
<td>By sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>17</td>
</tr>
<tr>
<td>Female</td>
<td>41</td>
</tr>
</tbody>
</table>

*mean age=62.7±8.9, female ratio=65.7%, body mass index=29.8±5.5.
**mean age=63.2±8.8, female ratio=67.9%, body mass index=29.9±4.8.
³Baseline characteristics (age, sex, body mass index, activity level, WOMAC pain score, education level, knee injury history, NSAIDs use, radiceline K/L grade and K/L grade when accepting the injection) were well-balanced between injection and non-injection cohorts (all P values>0.05).
Figure 1: Cumulative incidence of knee osteoarthritis progression in the propensity score-matched cohorts of injection subjects versus non-injection subjects.

Disclosure: G. H. Lei, None; C. Zeng, None; J. Wei, None; Y. L. Wang, None; D. X. Xie, None.


Abstract Number: 1789

Improved Survival with Transplantation in Granulomatosis with Polyangiitis in the United States: Data from the US Renal Data System

Zachary S. Wallace1, Rachel Wallwork2, Leo Lu3, John H. Stone4, Yuqing Zhang5 and Hyon K. Choi6, 1Division of Rheumatology, Allergy and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, 2Department of Medicine, Massachusetts General Hospital, Boston, MA, 3Allergy, Immunology, and Rheumatology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, 4Massachusetts General Hospital Rheumatology Unit, Harvard Medical School, Boston, MA, 5Department of Rheumatology, Allergy and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, 6Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
**Improved Survival with Transplantation in Granulomatosis with Polyangiitis in the United States: Data from the US Renal Data System**

**Background/Purpose:**

Granulomatosis with polyangiitis (GPA) is a common cause of glomerulonephritis and leads to end-stage renal disease (ESRD) in approximately 25% of patients. GPA is an accepted indication for transplantation and has comparable outcomes when compared to patients with ESRD due to other immune-mediated conditions. However, transplantation is a limited resource and the survival benefit of transplantation compared to remaining waitlisted has not been previously evaluated.

**Methods:**

We identified all incident cases of ESRD due to GPA (ICD9=446.4) in the United States Renal Data System (USRDS) who were waitlisted for a renal transplant between 1995 and 2014. The USRDS captures nearly all patients with ESRD in the US and requires that nephrologists report the ESRD cause (ICD-9 code). The USRDS includes details regarding demographics, comorbidities, and waitlist and transplant dates and statuses. It also includes details on date and cause of death. All patients were followed until death or January 1, 2016. We restricted our analysis to patients waitlisted for transplant to limit the potential bias of confounding by indication. We used a pooled logistic regression with transplantation as a time-varying covariate to estimate the relative risk (RR) and 95% confidence intervals (CIs) of death among those transplanted compared to those who remained on the waitlist. We adjusted for sociodemographic covariates (e.g., age, gender) as well as comorbidities (e.g., diabetes, cardiovascular disease (CVD)). We assessed differences in cause of death using cause-specific hazard models to estimate hazard ratios (HRs) and 95% CIs.

**Results:**

During the study period, 1,556 patients with ESRD due to GPA were waitlisted for a renal transplant and 977 (63%) of these patients received a transplant. The majority were male (60%) and white (84%). Average age at ESRD onset, waitlisting, and transplant were 47.3 ±16.5 years, 49.3 ±16.4 years, and 47.8 ±17.2 years, respectively. The average time from ESRD diagnosis to being waitlisted was 1.5 ±2.2 years. Total follow up time was 6.8 ±4.7 years. Overall, 444 deaths occurred. In fully-adjusted analyses, transplanted patients had a 59% lower risk of death compared to those who remained on the waitlist (RR 0.41, 95% CI 0.34-0.49). In fully adjusted cause-specific analyses, patients transplanted had a lower risk of cause-specific death from CVD (HR 0.06, 95% CI 0.03-0.1) and infection (HR 0.3 95% CI 0.2-0.6). There was no difference in the risk of cause-specific death from cancer (HR 0.5 95% CI 0.2-1.2).

**Conclusion:**

In this nationwide study of ESRD due to GPA, renal transplantation was associated with a significantly reduced risk of death compared to remaining on the waitlist. Our findings highlight the importance of identifying barriers to transplantation in this patient population. Additionally, evaluating management strategies to reduce the risk of CVD and infection in patients on the waitlist will likely improve survival.

**Disclosure:** Z. S. Wallace, None; R. Wallwork, None; L. Lu, None; J. H. Stone, Xencor, 2; Y. Zhang, None; H. K. Choi, None.


**Abstract Number:** 1790

**Sphingosine -1 Phosphate Receptor-1-Mediated Endothelial Cell Barrier Function Protects Against Immune Complex-Induced Vascular Injury: A Potential Novel Therapeutic Target for SLE**

**Nathalie Burg**¹, Steven Swendeman², Stefan Worgall³, Timothy Hla² and Jane E. Salmon¹, ¹Rheumatology, Hospital for Special Surgery, New York, NY, ²Boston Children's Hospital, Boston, MA, ³Pediatrics/ Pulmonary, Weill Cornell Medical Center, New York, NY

**First publication:** September 18, 2017
Sphingosine 1-phosphate (S1P), a bioactive lysophospholipid, is important for vascular homeostasis via signaling through S1P receptors. HDL-bound apolipoprotein M (ApoM) is a physiological S1P carrier that activates endothelial S1P₁ receptors, thereby increasing barrier function. ApoM-S1P also limits endothelial cell expression of adhesion molecules and activation of NF-κB in response to TNF-α. We tested a novel biologic S1P₁ receptor agonist, ApoM-Fc loaded with S1P, for its ability to protect the endothelial barrier in response to immune complex (IC) and neutrophil (PMN)-mediated injury in vitro and in vivo.

Methods:
Barrier function of human umbilical vein endothelial cells (HUVECs) in response to IC and C5a activated PMNs +/- ApoM-Fc was assessed by Electric Cell-substrate Impedance Sensing (ECIS). Phosphorylation of myosin light chain2 (p-MLC2) and VE-Cadherin staining in HUVECs after treatment with activated PMNs +/- ApoM-Fc was assessed by immunofluorescence (IF). The reverse arthus reaction (RAR) was performed in skin in mice treated locally with S1P₁ agonists and antagonists. Lung RAR was performed in WT and Apom⁻/⁻ mice and mice with an inducible endothelial cell deletion of S1P₁ (ECKO). ApoM-Fc (100 μg, IP) or PBS was administered to WT mice 2 hrs before lung RAR. PMNs and red blood cells in bronchoalveolar lavage fluid (BALF) were quantified. Lung weights and Evans blue (EB) were measured.

Results:
Activated PMNs decreased HUVEC resistance in ECIS and increased p-MLC2 and VE-Cadherin junction disassembly as assessed by IF. ApoM-Fc prevented the loss of barrier function (mean increase 224±28 Ohms, n=4) in a sustained manner (>8 hrs) and markedly reduced PMN-induced p-MLC2 and loss of VE-Cadherin. In contrast, a mutated ApoM-Fc construct that does not bind S1P was not protective. S1P also attenuated IC-mediated injury in vivo. S1P₁ agonist CYM-5442 decreased EB leak and skin weights after RAR compared to PBS treated controls (20 vs 27 mg, n=15-20, p <0.0001) and W146, a S1P₁ antagonist, increased EB leak and skin weights after RAR (24 vs 21 mg, n=12; p= 0.02). S1P₁ ECKO mice showed markedly increased lung RAR compared to controls: EB extravasation (157 vs 95 μg/g, n=3-5 mice; p=0.04), BAL WBCs (1.0 vs 0.6 X10⁵/μl, n=8-11; p=0.03), and lung mass (330 vs 265 mg, n=5-6; p=0.0007). Apom⁻/⁻ treated with local administration of W146 to partially block S1P₁ also showed more intense lung RAR than WT controls treated with W146, consistent with increased vascular vulnerability to injury. Importantly, delivery of S1P in vivo with ApoM-Fc was able to limit lung RAR with reduction in BALF WBCs and RBCs and decreased extravasated EB compared to PBS treated controls.

Conclusion:
These data demonstrate that stimulation of endothelial S1P₁ receptor by ApoM-HDL-S1P protects barrier integrity of the microvessels when challenged by IC-mediated vascular injury. S1P₁ receptor agonism represents a novel target to limit inflammation-induced injury in SLE and other IC mediated diseases. Moreover, because ApoM-Fc does not induce lymphopenia, unlike most other S1P₁ agonists, it could be used concomitantly with immunosuppressive therapies.

Disclosure: N. Burg, None; S. Swendeman, None; S. Worgall, None; T. Hla, None; J. E. Salmon, None.
SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis: Unexpected Effects from "Well-Known" Molecules
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:
Activated macrophages are found in the inflamed and hyperplastic synovial RA tissue. Macrophages are the main producers of high levels of pro-inflammatory cytokines such as TNFa and IL6. However, the mechanisms of TNFa overexpression are still unknown. Recent findings showed that the 5-methylcytosine (5-mC) modification of DNA can be converted to 5-hydroxymethylcytosine (5-hmC) through the activation of the family of Ten-Eleven-Translocation (TET1-3) enzymes. In the current study, we investigated the 5-hmC modification in macrophages stimulated with lipopolysaccharide (LPS) and characterized the function of TET1-3 enzymes during inflammation.

Methods:
The leukemic monocytic cell line THP-1 was differentiated into macrophages in the presence of 50nM phorbol myristate acetate (PMA). THP-1 derived macrophages were stimulated with 10 ng/ml LPS at different time points (0h, 2h, 4h, 6h, 24h). The global 5-hmC levels were quantified by DNA dot blot assay. Hydroxymethylated DNA immunoprecipitation (hMeDIP) and chromatin immunoprecipitation assays for TET1 were applied to analyze the levels of 5-hmC in the TNFa promoter. THP-1 derived macrophages were transfected with TET1,2,3 siRNA and then stimulated with 10ng/ml LPS for 2 hours. TNFa and IL6 levels were measured in the supernatants by ELISA.

Results:
The undifferentiated monocytes (THP-1) had the lowest basal levels of 5-hmC. The highest levels of 5-hmC was observed after 24 hours of PMA stimulation after which the monocytes had differentiated into macrophages. Furthermore, we searched for changes in 5-hmC at the promoter of TNFa and found a significant increase in THP-1 derived macrophages (n=3, p<0.05).

THP-1 derived macrophages were stronger responders to LPS than the monocytes for all inflammatory cytokines tested. For each stimulation time point, we measured the 5-hmC modification by hMeDIP and found a time depend increase in the level of 5hmC at the TNFa promoter. The 5-hmC enrichment of the TNFa promoter was significantly higher in THP-1 derived macrophages than THP-1 monocytes (n=3, p<0.05).

Then, we knocked down TET1 in THP-1 derived macrophages before stimulating the cells with LPS. Most importantly, TET1 inhibition reduced the stimulatory capacity of macrophages as shown by the significantly reduced mRNA and protein levels of pro-inflammatory cytokines (TNFa, IL-6, n=3, p<0.05). In contrast, siTET2 and siTET3 did not reduce the expression levels of TNFa and IL-6.

Since the function of TET1 enzymes is to hydroxymethylate the cytosine residues in gene enhancers and promoters, we measured the levels of 5-hmC at the promoter of TNFa and IL6 by hMeDIP. siTET1 transfected macrophages had significantly lower 5-hmC enrichment in comparison to control cells upon LPS stimulation (n=3, p<0.05). Furthermore, we found direct binding of TET1 at the promoter of TNFa by TET1 ChIP assay (2.5 TET1 fold enrichment versus IgG control, n=3).

Conclusion:
For the first time, we showed that TET1 contributes to the sustained activation of macrophages through the regulation of 5-hydroxymethylation in the promoter of TNFa. The TET1 enzyme could be a promising target to study in macrophages from RA patients.

Disclosure: E. Karouzakis, EU Horizon Reprogram, 2; F. Sun, None; A. Pajak, EU Horizon Reprogram, 2; S. Ye, Continent Pharmaceutical Company (China), 2; S. Gay, None; O. Distler, Abbvie,GSK,Mepha, MSD and UCB, 5,Abbvie,GSK,Mepha, MSD and UCB, 2; M. Neidhart, EU Horizon Reprogram, 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/tet1-is-an-important-transcriptional-activator-of-the-tnfa-locus-in-macrophages
Distinct and Overlapping Activities of IL-17A and TNF on the Expression of Proinflammatory Cytokines and MMPs in Psoriatic Arthritis: Rationale for Anti-IL-17A/Anti-Tnfalpha Combination Therapy?

Xiaofei Xu1, Nadine Davelaar2, Anne-Marie Otten-Mus3, Patrick Asmawidjaja2, J.M.W. Hazes4, Dominique Baeten5, Marijn Vis6, Radjesh Bisoendial1 and Erik Lubberts2, 1Rheumatology, Erasmus MC, Rotterdam, Netherlands, 2Rheumatology and Immunology, Erasmus MC, University Medical Center, Rotterdam, Netherlands, 3Immunology, Erasmus MC, University Medical Center, Rotterdam, Netherlands, 4Department of Rheumatology, Erasmus University Medical Centre, Rotterdam, Netherlands, 5Clinical Immunology and Rheumatology/Experimental immunology, Academic Medical Center/University of Amsterdam, Amsterdam, Netherlands, 6Rheumatology, Erasmus Medical Centre, Rotterdam, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis: Unexpected Effects from “Well-Known” Molecules
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:
TNF and IL-17A are proinflammatory cytokines critically involved in the pathogenesis of psoriatic arthritis (PsA). Currently, targeting TNF is the first choice of a biologic disease-modifying antirheumatic drug (bDMARD) in PsA. However, up to 30% of patients receiving anti-TNF monotherapy fail to respond and require switching to a second TNF-inhibitor or bDMARD with a different mode of action. Strategies targeted at neutralizing IL-17A have been shown to have beneficial effects on skin, enthesitis, dactylitis and joint inflammation. Here, we explore the effect of neutralizing IL-17A versus anti-TNF on the expression of proinflammatory cytokines and metalloproteinases (MMPs) and whether dual-therapy targeting TNF and IL-17A may have superior activity than treatment with either agent alone.

Methods:
An allogeneic co-culture system was used comprising synovial fluid T helper (Th) memory cells and synovial fibroblasts (SF), derived from patients with active PsA. Anti-CD3/CD28 stimulation was used during culture, and anti-IL-17A antibody (Secukinumab), anti-TNFalpha antibody (Adalimumab), or the combination were added. PsA unstimulated synovial Th memory cells co-cultured with PsA SF were included as a control group as well as an isotype antibody control group. After 72 hours, supernatants were harvested for ELISA and cells were lysed for qPCR analysis.

Results:
Anti-TNF Ab treatment had no effect on IL-17A levels and neutralization of IL-17A did not influence the TNF production in the co-culture system. Both anti-TNF and anti-IL-17A single treatment significantly inhibited the production of IL-8 and reduced the mRNA expression of IL-1beta. Interestingly, neutralizing IL-17A resulted in a significant suppression of IL-6 levels which was not reduced by anti-TNF. Anti-TNF inhibited the production of MMP-3 and only the combination of anti-TNF and anti-IL-17A resulted in a significant suppression of MMP-1 levels and MMP-9 mRNA expression. MMP-13 mRNA expression was significantly suppressed by anti-TNF but not by anti-IL-17A, however, neutralizing both IL-17A and TNF showed a significant improvement in downregulating MMP-13 mRNA expression compared to single cytokine treatment. Moreover, anti-IL-17A reduced RANK mRNA expression that was significantly more suppressed compared to anti-TNF alone. However, no additive effect was noted for the combination blocking. Interestingly, only neutralizing both IL-17A and TNF significantly reduced the mRNA expression of RANKL. OPG mRNA expression was not influenced by anti-IL-17A and/or anti-TNF treatment.

Conclusion:
Neutralizing IL-17A or TNF in the PsA synovial T cell – SF co-culture system resulted in overlapping but also distinct effects on proinflammatory cytokine expression. TNF inhibition markedly suppress different MMPs with mostly an additional effect upon neutralization of IL17A. Neutralization both IL-17A and TNF is needed to downregulate RANKL expression which changes the RANKL/OPG balance. Together, these preliminary data suggest that dual therapy targeting IL-17A and TNF may be superior in their activity to protect against erosive arthropathy in PsA than treatment with either agent alone.
Interleukin-17 Is Not a Determinant for the Pro- or Anti-Inflammatory Character of Interleukin-22 in Experimental Arthritis

Debbie M. Roeleveld, Loreto Parga Vidal, Monique M. Helsen, Birgitte Walgreen, Bianka Marklein, Karl Skriner, Martin Hegen, Peter L. van Lent, Fons A.J. van de Loo, Wim B. van den Berg, Peter M. van der Kraan and Marije I. Koenders

1 Experimental Rheumatology, Radboud University Medical Center, Nijmegen, Netherlands, 2 Experimental Rheumatology, Radboud university medical center, Nijmegen, Netherlands, 3 Experimental, Radboud university medical center, Nijmegen, Netherlands, 4 Humboldt University and Free University, Berlin, Germany, 5 Department of Rheumatology and Clinical Immunology, Charité - University Medicine Berlin, Free University and Humboldt University Berlin, Berlin, Germany, 6 Inflammation and Immunology Research Unit, Pfizer, Cambridge, MA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis: Unexpected Effects from "Well-Known" Molecules
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: High interleukin-22 (IL-22) levels are detected in serum and synovial fluid of rheumatoid arthritis (RA) patients and have been shown to positively correlate with disease activity markers and more erosive disease. The role of IL-22 in autoimmunity and inflammation appears to be greatly contradictory, being both pro- and anti-inflammatory. Previous work in other disease models suggested that the presence of IL-17 determines the inflammatory effect of IL-22, being protective in the absence and pathogenic in the presence of IL-17. The purpose of our study was to further unravel the role of IL-22 during experimental arthritis, in particular focusing on the cytokine interactions within the inflammatory environment.

Methods: To investigate the potential of IL-22 to drive joint inflammation and destruction, IL-22 was overexpressed in murine knee joints using an adenoviral construct (AdIL-22), and synovial biopsies and whole joints were collected for mRNA/protein expression analysis and histological scoring of joint pathology. To study the interaction of IL-22 within the disease cytokine network, AdIL-22 was injected intra-articularly as single cytokine, or combined with a second vector overexpressing TNFα, IL-17 or IL-1β. Furthermore, we studied the effect of local IL-22 overexpression on two experimental arthritis models: SCW and K/BxN serum transfer arthritis. To study the interaction of IL-22 within the disease cytokine network, AdIL-22 was used to overexpress cytokines in a variety of combinations.

Results: Despite the significantly enhanced synovial mRNA expression of pro-inflammatory and pro-destructive genes like IL-6, KC, S100A8 and RANKL, surprisingly IL-22 overexpression did not result in any sign of joint pathology in the knee joints of naïve mice. Furthermore, IL-22 neither aggravated disease severity during both models of innate immune-driven experimental arthritis, nor did it affect IL-17-, IL-1β-, or TNFα-induced joint inflammation when overexpressed in combination with other cytokines. Interestingly, in comparison to the spontaneous arthritis development in classical IL-1Ra−/− mice, the absence of IL-22 significantly reduced disease incidence and severity in this model. While the arthritis incidence in regular IL-1Ra−/− mice reached up to 95% at the age of 15 weeks, IL-22−/− x IL-1Ra−/− mice only showed 50% disease onset. In line with suppressed disease severity, anti-hnRNP autoantibodies were lowered in IL-22−/− x IL-1Ra−/− mice. No effects were observed on T cell responses. Remarkably, in the absence of IL-22 the therapeutic efficacy of anti-IL-17 treatment on arthritis progression in these mice was lost.

Conclusion: This study not only confirms the pro-inflammatory role of IL-22 in the development and progression of experimental arthritis, it also demonstrates a novel role in the formation of anti-hnRNP antibodies. Finally, we demonstrated that IL-17 is not a determinant for the pro- or anti-inflammatory character of IL-22 in experimental arthritis.
Disclosure: D. M. Roeleveld, None; L. Parga Vidal, None; M. M. Helsen, None; B. Walgreen, None; B. Marklein, None; K. Skriner, None; M. Hegen, Pfizer Inc, 3; P. L. van Lent, None; F. A. J. van de Loo, None; W. B. van den Berg, None; P. M. van der Kraan, None; M. I. Koenders, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/interleukin-17-is-not-a-determinant-for-the-pro-or-anti-inflammatory-character-of-interleukin-22-in-experimental-arthritis

Abstract Number: 1794

Overexpression of Interleukin-22 Induces Expression of the Negative Immune-Regulator SOCS3 and Potently Reduces Collagen-Induced Arthritis in Mice

Debbie M. Roeleveld1, Monique M. Helsen2, Birgitte Walgreen3, Elly Vitters2, Fons A.J. van de Loo2, Peter L. van Lent2, Wim B. van den Berg2, Peter M. van der Kraan2 and Marije I. Koenders2, 1Experimental Rheumatology, Radboud University Medical Center, Nijmegen, Netherlands, 2Experimental Rheumatology, Radboud university medical center, Nijmegen, Netherlands, 3Experimental, Radboud university medical center, Nijmegen, Netherlands

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis: Unexpected Effects from "Well-Known" Molecules
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: High interleukin-22 (IL-22) levels are detected in serum and synovial fluid of rheumatoid arthritis (RA) patients and have been shown to positively correlate with disease activity markers and more erosive disease. The role of IL-22 in autoimmunity and inflammation appears to be greatly contradictory, being both pro- and anti-inflammatory. Especially the anti-inflammatory properties of IL-22 are not well understood. The purpose of our study was to investigate the anti-inflammatory and immune-suppressive effect of IL-22 during experimental arthritis.

Methods: Collagen-induced arthritis was induced in DBA-1 mice by immunization and booster with bovine collagen type II (CII). After booster, but before arthritis onset, IL-22 was overexpressed either locally or systemically using an adenoviral construct (AdIL-22) or Luciferase as control (AdLuc). 1x107 plaque-forming units (PFU) of the adenoviruses were injected intra-articularly (i.a.) for local overexpression, or 3x108 PFU of adenoviruses were injected intravenously (i.v.) for systemic overexpression in immunized mice without clinical signs of CIA, and mice were sacrificed 10 days later. Macroscopic scoring and histological analysis was performed, and mRNA expression and protein production of various pro- and anti-inflammatory mediators was determined in synovial tissue, spleen, and serum.

Results: Local overexpression of IL-22 by injection of AdIL-22 in the knee joint of CII-immunized mice resulted in an unaltered arthritis incidence and severity as compared to the control virus AdLuc. Accordingly, no changes in mRNA expression or protein production were observed in mice locally overexpressing IL-22. In contrast, systemic overexpression of IL-22 potently reduced disease incidence and severity, which was also confirmed by histological analysis (See Figure 1). Mice overexpressing IL-22 systemically showed significantly lower mRNA levels of IFNγ and SOCS3, and protein levels of IFNγ, TNFα, MIP1α, and IL-10.
Conclusion: With this study, we revealed clear anti-inflammatory effects of IL-22 overexpression during collagen-induced arthritis, which are completely dependent on the systemic route of administration. Additionally, we were the first to show that this protective effect of IL-22 during experimental arthritis is likely orchestrated via up-regulation of the negative regulator SOCS3.

Disclosure: D. M. Roeleveld, None; M. M. Helsen, None; B. Walgreen, None; E. Vitters, None; F. A. J. van de Loo, None; P. L. van Lent, None; W. B. van den Berg, None; P. M. van der Kraan, None; M. I. Koenders, None.


Abstract Number: 1795

**IL-7 in Primary Sjogren Syndrome (pSS) Is Secreted By Salivary Gland Epithelial Cells after IFN Stimulation and Is Associated with B-Cell Activation**

Alexandre Virone1, Juliette Pascaud2, Elodie Rivière1, Jacques-Eric Gottenberg3, Véronique Le Guern4, Xavier Mariette1 and Gaetane Nocturne5, 1Université Paris Sud, Paris, France, 2U1184 IMVA, Université Paris Sud, Le Kremlin-Bicêtre Cedex, France, 3CNRS, Immunopathologie et Chimie Thérapeutique/Laboratory of Excellence Medalis, Institut de Biologie Moléculaire et Cellulaire, Strasbourg, France, 4Internal Medicine Department, Cochin Hospital, “René-Descartes Paris V” University, Paris, France, 5INSERM U1184, IMVA, Paris Sud University,LabEx LERMIT, Le Kremlin Bicêtre, France

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017
**Session Title:** Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis: Unexpected Effects from "Well-Known" Molecules
**Session Type:** ACR Concurrent Abstract Session
**Session Time:** 2:30PM-4:00PM

**Background/Purpose:**

pSS is characterized by a strong IFN signature, ectopic germinal centers formation and a chronic blood lymphopenia. IL-7 plays a central part in T cells homeostasis and in lymphoid structures organization. We aimed to assess the role of IL-7 in pSS pathogenesis.

**Methods:**

IL-7 serum level was assessed in 372 pSS patients and 73 paired controls. Primary cultures of salivary gland epithelial cells (SGEC) from patients and controls were stimulated by Poly I:C 30 ng/ml, IFN-α 600UI/ml, IFN-γ 5ng/ml and IFN-λ (IL-28) 25ng/ml for 72 hours. IL-7 secretion was tested in culture supernatant by ELISA. IL-7 expression after 24 hours stimulation was assessed by
quantitative RT-PCR. IL-7 and its receptor’s expressions were evaluated in RNA-Seq analysis from cells form salivary glands biopsies (SGB) and PBMC.

**Results:**

pSS patients had higher serum IL-7 levels than controls: 7.56 ng/ml ± 8.52 (mean ± SD) versus 4.86 ng/ml ± 5.59; p<0.0001. A positive correlation with B cells activation markers, IFN-induced chemokines and disease activity markers was observed. In multivariate analysis, serum IL-7 level was associated with CXCL13, anti-SSA, RF, κ light-chain and low C4.

SGEC stimulation with Poly I:C, IFN-α, -γ and -λ induced IL-7 protein secretion in the supernatant (p=0.002, p=0.004, p=0.007, p=0.004 respectively) (Figure 1). A trend for a greater IL-7 production in pSS patients compared to controls was observed. IL-7 expression was confirmed by quantitative RT-PCR. Among cell subsets purified ex vivo from SGB and PBMC, RNA-Seq analysis showed a greater expression of IL-7 by epithelial cells of patients compared to controls (p=0.03). No difference was observed regarding T and B cells either from biopsies or PBMC. IL-7 receptor expression was equivalent between patients and controls. Analysis of T cells exhaustion profile and IL-7 intracellular signaling are on-going.

**Conclusion:**

Our data demonstrate that IL-7 is secreted within the target tissue of pSS by SGEC after stimulation by IFNs. This IFN/IL-7 pathway can be involved in the organization of ectopic germinal centers found in pSS. But more importantly, since IL-7 is one of the major controller of homeostasis of T cells, this IFN/IL-7 pathway could be involved in the persistent lymphopenia which is a hallmark of the disease, either by favoring exhaustion of T cells or by an impaired function of the IL-7 intracellular signaling. Both mechanisms are currently explored and will be presented.

**Disclosure:** A. Virone, None; J. Pascaud, None; E. Rivière, None; J. E. Gottenberg, BMS, Gilead, Medimune,Pfzer Sanofi-Aventis, Ucb, 2; V. Le Guern, None; X. Mariette, None; G. Nocturne, None.


**Abstract Number:** 1796

**Benefits and Sustainability of a Learning Collaborative for Implementation of Treat to Target in Rheumatoid Arthritis: Results of Phase II of a Cluster Randomized Controlled Trial**

**Daniel H. Solomon**1, Liana Fraenkel2, Zhi Yu3, Bing Lu4, Asaf Bitton5, Agnes Zak6, Cassandra Corrigan7, Jen Agosti8, Leslie R Harrold9, Josef S. Smolen10, Jeffrey N. Katz11 and Elena Losina12. 1Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 2Rheumatology, Rheumatology, Yale University School of Medicine, New Haven, CT, New Haven, CT, 3Rheumatology Immunology & Allergy, Brigham and Women's Hospital, Boston, MA, 4Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 5Medicine, Brigham and Women's Hospital, Boston, MA, 6Brigham and Women's Hospital, Boston, MA, 7Rheumatology, Brigham and Women's Hospital, Boston, MA, 8JRA Consulting, Andover, MA, 9University of Massachusetts Medical School, Worcester, MA, 10Medical University Vienna, Division of Rheumatology, Department of
Background/Purpose: Treat to target (TTT) is a recommended strategy in the management of rheumatoid arthritis (RA), but its uptake in routine rheumatologic care in the US is sub-optimal. We carried out an RCT of a Learning Collaborative (LC) to facilitate implementation of TTT. In the first phase, TTT implementation increased 46% in the intervention group. Herein, we report on the second phase in which the Phase I intervention sites were observed without intervention and additional sites received intervention.

Methods: We recruited 11 rheumatology sites (49 providers) from the US and randomized them into 2 groups: 5 sites received the LC intervention over the first 9 months (Phase I) and the other 6 sites received the intervention over the subsequent 9 months (Phase II). The LC included a face-to-face meeting, 8 learning sessions via webinar, use of a web-based tool for sharing results of plan-do-study-act cycles, and monthly collection of improvement measures. The primary outcome was the change in TTT implementation over 9 months, measured using a chart review before the intervention and then again after. TTT implementation included 4 items: shared-decision making, choice of a target, use of a disease activity measure (DAM), and changing treatments based on the target and DAM. It was scored on a 0-100% scale based on the presence/absence of these items. Phase II analyses allowed us to examine: 1) the sustainability of improvement in TTT among the Phase I intervention teams, and 2) predictors of TTT improvement across the 11 teams. Analyses accounted for clustering within site using Generalized Estimating Equations.

Results: The chart review included 636 RA patients seen by teams during the Phase I or II intervention periods. These patients had mean age 61, 81% were female, and 79% seropositive. At baseline, mean TTT implementation score was 11% in the Phase I intervention arm and 13% in the Phase II intervention arm (see Table 1). After the intervention, TTT implementation improved in the Phase I intervention arm to 57% and to 58% in the Phase II intervention arm (both P-values < 0.001). TTT implementation among the five Phase I intervention teams decreased slightly from 57% to 52% (P = 0.1). Predictors of greater improvement in TTT included not having NP/PA at site, the RA provider being a trainee, and academic affiliation of the site (see Table 2).

Conclusion: Improvement in TTT remained relatively stable over a 9-month post-intervention period. Several predictors of improvement in TTT implementation were identified at the site and provider level that might be used to guide interventions.
<table>
<thead>
<tr>
<th></th>
<th>Phase I Intervention</th>
<th>Phase II Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Month 0</td>
<td>Month 9</td>
</tr>
<tr>
<td>Primary Outcome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Implementation score</td>
<td>11.1%</td>
<td>57.1%</td>
</tr>
<tr>
<td>Visits with components present</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment target</td>
<td>0.6%</td>
<td>45.6%</td>
</tr>
<tr>
<td>Disease activity measure</td>
<td>20.0%</td>
<td>89.1%</td>
</tr>
<tr>
<td>Shared decision-making†</td>
<td>51.3%</td>
<td>85.9%</td>
</tr>
<tr>
<td>Treatment decision‡</td>
<td>0.6%</td>
<td>27.8%</td>
</tr>
</tbody>
</table>

The number of visits included differed by Phase and by month of assessment. For Phase I, there were 320 visits at month 0 and at month 9, and 300 visits at month 18. For Phase II, there were 321 visits at month 0, and 316 visits at month 9 and 18.† The shared decision-making criteria did not apply to all visits when no decisions were being made about changing targets or changing treatments. The number of visits when shared decision-making applied for the Phase I intervention group: 115 at month 0, 184 at month 9, and 99 at month 18. For the Phase II intervention group: 102 at month 0, 94 at month 9, and 112 at month 18.‡ Treatment decision based on target and disease activity measure.
Table 2: Adjusted Mean Improvement in TTT Implementation Score over 9 months by Site Level and Provider Level Factors

<table>
<thead>
<tr>
<th>Site level factors</th>
<th>Univariate*</th>
<th>P-value</th>
<th>Multivariable</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase I</td>
<td>42.0 (33.8,</td>
<td>0.71</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>50.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase II</td>
<td>44.6 (34.1,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>55.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Academic affiliation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>47.2 (39.6,</td>
<td>0.12</td>
<td>52.9 (45.3, 60.5)</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>54.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>35.7 (23.3,</td>
<td></td>
<td>37.9 (24.5, 51.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>48.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fellows at site</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>47.3 (38.9,</td>
<td>0.20</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>55.6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>38.5 (27.8,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>49.2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NP/PA at site</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>33.9 (25.8,</td>
<td>0.002</td>
<td>37.0 (25.2, 48.8)</td>
<td>0.006</td>
</tr>
<tr>
<td></td>
<td>42.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>53.1 (43.7,</td>
<td></td>
<td>53.9 (44.6, 63.1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>62.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Provider level factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease activity measure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDAI</td>
<td>42.1 (32.8,</td>
<td>0.47</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>51.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rapid 3</td>
<td>47.4 (36.3,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>58.5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>33.0 (25.8,</td>
<td>0.03</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>40.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male sex of provider</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>39.5 (29.1,</td>
<td>0.31</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>49.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>46.5 (37.8,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>55.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Provider type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physician</td>
<td>44.3 (37.4,</td>
<td>0.46</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>51.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-physician</td>
<td>34.7 (10.2,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>59.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trainee</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>58.1 (42.1,</td>
<td>0.05</td>
<td>52.3 (37.2, 67.4)</td>
<td>0.09</td>
</tr>
<tr>
<td></td>
<td>74.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>40.3 (33.3,</td>
<td></td>
<td>38.5 (31.6, 45.5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>47.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Adjusted least square means generated using Generalized Estimating Equation, accounting for clustering of patients within providers. Multivariable analyses include the three variables with P values < 0.2 on univariate screen and account for clustering.

Disclosure: D. H. Solomon, None; L. Fraenkel, None; Z. Yu, None; B. Lu, None; A. Bitton, None; A. Zak, None; C. Corrigan, None; J. Agosti, None; L. R. Harrold, Corrona, 1,Pfizer Inc, 2,Roche Pharmaceuticals, 5,Corrona, 3; J. S. Smolen, AbbVie, Eli Lilly, Janssen, MSD, Pfizer Inc, Roche, 2,AbbVie, Amgen, AstraZeneca, Astro, Celgene, Celtrion, Eli Lilly, GSK, ILTOO, Janssen, MedImmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, UCB, 5,AbbVie, Amgen, AstraZeneca, Astro, Celgene, Celtrion, Eli Lilly, GSK, ILTOO, Janssen, MedImmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, UCB, 8; J. N. Katz, None; E. Losina, None.
Insights from Treating to Target in Rheumatoid Arthritis at an Academic Medical Center

Malithi Jayasundara¹, Ryan Jessee², Jason Weiner³, Tayseer Haroun⁴, Stephanie Giattino⁵, Atul Kapila⁴, Jenelle Hall⁴, Lisa Carnago⁴ and Lisa Criscione-Schreiber⁶, ¹Rheumatology, Duke University, Durham, NC, ²Department of Medicine, Division of Rheumatology and Immunology, Duke University, Durham, NC, ³Department of Medicine, Division of Rheumatology and Immunology, Duke University Medical Center, Durham, NC, ⁴Duke University, Durham, NC, ⁵Rheumatology, Duke University Medical Center, Durham, NC, ⁶Internal Medicine, Duke University Medical Center, Durham, NC

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Measures and Measurement of Healthcare Quality
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:
Current RA guidelines recommend treating to a target of remission or low disease activity (RM/LDA) state. In a prior quality improvement (QI) project, our practice increased documentation of Rapid3 in provider notes to 92%. This QI project was developed to improve the percentage of our RA patients in RM/LDA, as measured by Rapid3. We also aimed to understand providers’ attitudes and use of the Rapid3 in practice.

Methods:
We reviewed charts of established (>1 prior visit) RA patients over an 8-month period to assess use of Rapid3 in decision-making. We recorded Rapid3 presence and value, relevant co-morbidities (FM, OA and mood disorders) and whether a change in therapy was made. Using Plan-Do-Study-Act (PDSA) methodology, we introduced the following interventions to improve utilization: education through Grand Rounds, modification of electronic medical record templates and reminder emails to providers. Charts were analyzed at baseline, between interventions and at the conclusion of all interventions. We surveyed providers at baseline and at project completion regarding habits and attitudes towards Rapid3 in clinical practice.

Results:
Of 539 patient encounters with established RA, Rapid3 was documented in 501 encounters (93%). About 55% had at least 1 relevant co-morbid condition (182 patients with OA, 79 with FM, 74 with mood disorders); 295 had 1 co-morbidity, 34 had 2 co-morbidities and 6 had 3 co-morbidities. At baseline 38/139 (27%) were in RM/LDA. Our interventions resulted in 123/362 (34%) patients in RM/LDA (Figure 1). At almost every time point, percent of patients achieving RM/LDA was highest in patients with RA and no co-morbidities (Figure 1). Our survey of 18 providers found only 17% felt Rapid3 accurately reflected RA disease activity most of the time; 78% agreed Rapid3 changed their clinical management <10% of the time. Providers indicated the greatest challenges in using of Rapid3 were “score does not represent RA activity” and “other co-morbidities.”

Conclusion:
We sustained documentation rates of Rapid3 above 90%. The percent of patients in RM/LDA slightly improved, but this intervention was limited by short duration. We found very low provider confidence that the Rapid3 reflected RA activity, and it was infrequently used as a treatment target. The presence of any selected co-morbidities demonstrated a lower likelihood of achieving RM/LDA by Rapid3; FM and mood disorder had the greatest impact. Rapid3 may be most useful in patients without these co-morbidities. In the future, a “correction factor” for co-morbidities in scoring of Rapid3 may improve accuracy and provider use.
Effective Implementation and Evaluation of Quality Improvement Initiatives in a Safety Net Hospital Rheumatology Clinic

Alfredo Aguirre1, Laura Trupin2, Mary Margaretten3, Sarah Goglin4 and Jinoos Yazdany2, 1Internal Medicine, University of California, San Francisco, SAN FRANCISCO, CA, 2Medicine/Rheumatology, University of California San Francisco, San Francisco, CA, 3Medicine, University of California San Francisco, San Francisco, CA, 4Medicine/Rheumatology, University of California, San Francisco, San Francisco, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Measures and Measurement of Healthcare Quality
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Vulnerable populations with autoimmune rheumatic diseases are at higher risk for disparities in care. To address these health inequalities we developed and evaluated 2 initiatives at an adult rheumatology clinic, which is the safety net for a diverse, urban population. We used the Institute for Healthcare Improvement (IHI) Model for Improvement to implement and assess pneumococcal (PCV13) vaccination among patients receiving immunosuppression and rheumatoid arthritis (RA) disease activity measurement.

Methods: Performance on the PCV13 vaccine was calculated as the proportion of patients receiving immunosuppression who were vaccinated. The RA disease activity measurement was the percentage of patients with outpatient RA encounters who received a clinical disease activity index (CDAI) score. For PCV13 vaccination, our clinic team utilized an interdisciplinary conference and nurse-led physician chart reminders (starting 2/2016). For RA disease activity, we reconfigured the electronic health record and utilized quarterly physician performance feedback (starting 6/2016). Control charts were used to examine performance of these measures over time. Vertical lines indicate time points of quality initiatives as described above. A series of at least 8 data points over the control limit (horizontal line) was indicative of significant improvement.

Results: The patient population studied had a median age of 58; 73% were women and 89% were racial/ethnic minorities. Over a 27-month period, PCV13 vaccination rates increased from 0.6% to 85% (Figure 1). Over a 12-month period, documentation of CDAI measurement at clinic visits increased from 45% to 91% (Figure 2).

Conclusion: Both quality initiatives were successful in significantly increasing pneumococcal vaccination rates and RA disease activity documentation. Using the IHI Model for Improvement and an intraprofessional team approach, we were able to dramatically improve performance on two important measures of health care quality for patients with rheumatic diseases.
Time to First Appointment Among Young Adults Transitioning from Pediatric to Adult Rheumatologic Care in a Safety Net Population

Nicole Bitencourt\textsuperscript{1}, Una E. Makris\textsuperscript{1,2}, Tracey Wright\textsuperscript{3,4} and E. Blair Solow\textsuperscript{1}. \textsuperscript{1}UT Southwestern Medical Center, Dallas, TX, \textsuperscript{2}Department of Medicine, VA North Texas Health Care System, Dallas, TX, \textsuperscript{3}Pediatrics/Rheumatology, UT Southwestern Medical Center, Dallas, TX, \textsuperscript{4}Texas Scottish Rite Hospital for Children, Dallas, TX

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Measures and Measurement of Healthcare Quality
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:
For young adults with a chronic rheumatic illness transitioning from pediatric to adult care, the transfer to new system can be daunting; these challenges are heightened in a socioeconomically at-risk population. As part of a quality improvement project, we characterized the time from referral to first clinic visit with adult rheumatology in a large public safety net healthcare system. Further, we sought to describe factors that may influence time to first visit.

Methods:
A chart review was performed which identified 65 patients between ages 17 and 21 who were transitioning into adult care between 3/2014 and 4/2017. Data regarding time from referral to first scheduled appointment with adult rheumatology, as well as time from last pediatric visit to first adult visit was extracted and examined. Variables potentially related to time to first visit were also obtained and compared using the two-tailed t-test, including information as it related to referral patterns, medication adherence, and no-show rates.

Results:
Refer to Table 1 for demographic information. The average time from first referral to first scheduled appointment with adult rheumatology was 193 days, while time to the first actual visit was 221 days. Nearly half (45%) were seen more than 180 days following their last visit with pediatric rheumatology (Figure 1). Time to adult rheumatology visit was significantly longer if someone other than a pediatric rheumatologist placed the referral to adult rheumatology. Lengthier time between appointments was seen in patients with documented medication non-adherence at the first appointment. Young adults who no-showed to their first adult rheumatology visit were more likely to have had a lapse in coverage compared to those who came to their first scheduled appointment (Figure 2).

**Conclusion:**

Patients transitioning into adult rheumatologic care in a large public safety net system experience significant delays to their first adult visit, which may adversely impact medication adherence and show rates. We plan to shorten the time to first appointment by blocking slots for transitioning patients. Further, we will disseminate information on how to acquire medical coverage and navigate our safety net system in a timely, coordinated fashion.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Description</th>
<th>Number (percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Female</td>
<td>47 (72)</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>18 (28)</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td>Asian</td>
<td>2 (3)</td>
</tr>
<tr>
<td></td>
<td>Black</td>
<td>7 (11)</td>
</tr>
<tr>
<td></td>
<td>Hispanic</td>
<td>48 (74)</td>
</tr>
<tr>
<td></td>
<td>White</td>
<td>8 (12)</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Connective Tissue Disease</td>
<td>32 (49)</td>
</tr>
<tr>
<td></td>
<td>Juvenile Idiopathic Arthritis</td>
<td>32 (49)</td>
</tr>
<tr>
<td>Referring Clinician</td>
<td>Pediatric Rheumatologist</td>
<td>48 (74)</td>
</tr>
<tr>
<td></td>
<td>Non-Pediatric Rheumatologist</td>
<td>17 (26)</td>
</tr>
</tbody>
</table>

![Fig 1A: Time from First Referral to First Appointment](image)

![Fig 1B: Time from Last Pediatric Appointment to First Actual Visit](image)
Disclosure: N. Bitencourt, None; U. E. Makris, None; T. Wright, None; E. B. Solow, None.


Abstract Number: 1800

Do Patient Reported Outcome Measurement Information System (PROMIS) Computer Adaptive Tests Correlate with Disease Activity in Juvenile Idiopathic Arthritis?

Rebecca Trachtman1, Elizabeth T. Murray2, Jackie Szymonifka3, Alexa Adams4, Nancy Pan4, Sarah Taber4, Thomas J. A. Lehman4, Karen Onel4 and Lisa A. Mandl5, 1Pediatric Rheumatology, Hospital for Special Surgery Weill Cornell Medical College, NY, NY, 2Hospital for Special Surgery, New York, NY, 3Rheumatology, Hospital for Special Surgery, New York, NY, 4Pediatric Rheumatology, Hospital for Special Surgery Weill Cornell Medical College, New York, NY, 5Rheumatology, Hospital for Special Surgery Weill Cornell Medical College, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Measures and Measurement of Healthcare Quality
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: The importance of patient-reported outcomes is increasingly recognized both in clinical care and in research. PROMIS is an NIH-supported collection of patient-reported outcome measures, covering a variety of domains that are designed without disease specificity. While ‘short forms’ have been studied in juvenile idiopathic arthritis (JIA), PROMIS computer adaptive tests (CATs) have not. This study evaluates whether PROMIS CATs correlate with disease activity in patients with JIA.

Methods: A convenience sample of patients with JIA (N = 21) were recruited from a single center. Patients aged 10-17 years completed all available pediatric PROMIS CATs, and parents of patients aged 2-9 years completed all available parent proxy PROMIS CATs (fatigue, pain interference, peer relations, anxiety, depressive symptoms, and mobility). Correlation of the CATs t-scores with disease activity, as measured by the Juvenile Disease Activity Score-71 (JADAS-71), (0-101, higher being worse) was evaluated using Spearman correlation coefficients.

Results: All families approached completed the PROMIS CATs: 13 patients and 8 parents (Table 1). Median age was 12.7 years (range 1.3 – 18.6 years), and mean JADAS-71 score was 9.58 (SD 2.07). 69% of patients completed PROMIS CATs remotely via smartphone.
Anxiety ($r = 0.74$, $p = 0.006$), depressive symptoms ($r = 0.84$, $p < 0.001$), and pain interference ($r = 0.64$, $p = 0.018$) CATs correlated strongly with JIA disease activity (Table 2). Among parent proxy CATs, only anxiety correlated with disease activity ($r = 0.71$); however the association was not statistically significant.

**Conclusion:** Our results demonstrate that the PROMIS CATs are feasible to administer in an outpatient pediatric rheumatology setting. Anxiety, depressive symptoms, and pain interference were significantly correlated with disease activity, even though mean disease activity was relatively low. This underscores the negative effect on quality of life of even mild disease. Parent proxy CATs showed poor correlations with disease activity, suggesting parents are inaccurate in assessing important aspects of their child’s health. Larger prospective studies are needed to evaluate the sensitivity of PROMIS CATs to change in disease activity over time.

**Table 1. Patient characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N=26 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, median</td>
<td>12.7</td>
</tr>
<tr>
<td>[interquartile range]</td>
<td>[6.0, 14.5]</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>8 (30.8%)</td>
</tr>
<tr>
<td>Female</td>
<td>18 (69.2%)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White or Caucasian</td>
<td>20 (76.9%)</td>
</tr>
<tr>
<td>Black or African American</td>
<td>1 (3.9%)</td>
</tr>
<tr>
<td>American Indian or Alaska Native</td>
<td>1 (3.9%)</td>
</tr>
<tr>
<td>Asian</td>
<td>4 (15.4%)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>4 (15.4%)</td>
</tr>
<tr>
<td>Non-hispanic</td>
<td>22 (84.6%)</td>
</tr>
<tr>
<td>Insurance</td>
<td></td>
</tr>
<tr>
<td>Medicaid</td>
<td>6 (23.1%)</td>
</tr>
<tr>
<td>Private insurance</td>
<td>20 (76.9%)</td>
</tr>
<tr>
<td>Device</td>
<td></td>
</tr>
<tr>
<td>Smartphone</td>
<td>18 (69.2%)</td>
</tr>
<tr>
<td>iPad</td>
<td>3 (11.5%)</td>
</tr>
<tr>
<td>Computer</td>
<td>5 (19.2%)</td>
</tr>
<tr>
<td>Location</td>
<td></td>
</tr>
<tr>
<td>In hospital</td>
<td>8 (30.8%)</td>
</tr>
<tr>
<td>Remotely</td>
<td>18 (69.2%)</td>
</tr>
</tbody>
</table>

**Table 2. Spearman correlation coefficients for PROMIS domains and JADAS71 score**

<table>
<thead>
<tr>
<th>PROMIS domain</th>
<th>JADAS71 score Spearman correlation coefficient</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PATIENT SCORES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue T-score</td>
<td>0.488</td>
<td>0.090</td>
</tr>
<tr>
<td>Pain Interference T-score</td>
<td><strong>0.640</strong></td>
<td><strong>0.018</strong></td>
</tr>
<tr>
<td>Peer Relations T-score</td>
<td>-0.345</td>
<td>0.248</td>
</tr>
<tr>
<td>Anxiety T-score</td>
<td><strong>0.738</strong></td>
<td><strong>0.006</strong></td>
</tr>
<tr>
<td>Depressive Symptoms T-score</td>
<td><strong>0.840</strong></td>
<td>&lt;<strong>0.001</strong></td>
</tr>
<tr>
<td>Mobility T-score</td>
<td>-0.671</td>
<td>0.017</td>
</tr>
<tr>
<td><strong>PARENT PROXY SCORES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue T-score</td>
<td>-0.024</td>
<td>0.955</td>
</tr>
<tr>
<td>Pain Interference T-score</td>
<td>0.048</td>
<td>0.911</td>
</tr>
<tr>
<td>Peer Relations T-score</td>
<td>0.037</td>
<td>0.937</td>
</tr>
<tr>
<td>Anxiety T-score</td>
<td>0.714</td>
<td>0.071</td>
</tr>
<tr>
<td>Depressive Symptoms T-score</td>
<td>0.074</td>
<td>0.875</td>
</tr>
<tr>
<td>Mobility T-score</td>
<td>-0.464</td>
<td>0.294</td>
</tr>
</tbody>
</table>
Quantifying Clinical and Economic Outcomes Associated with Chronic Corticosteroid Exposure in a US Population

J. Bradford Rice\textsuperscript{1}, Alan White\textsuperscript{1}, Andrea Lopez\textsuperscript{1}, Aneesha Wagh\textsuperscript{1}, Yimin Qin\textsuperscript{2}, Ghaith Mitri\textsuperscript{2}, Laura Bartels-Peculis\textsuperscript{2}, Gosia Ciepielewskia\textsuperscript{2} and Winnie Nelson\textsuperscript{3}, \textsuperscript{1}Analysis Group, Inc., Boston, MA, \textsuperscript{2}Mallinckrodt Pharmaceuticals, Hampton, NJ, \textsuperscript{3}Health Economics and Outcomes Research, Mallinckrodt Pharmaceuticals, Hampton, NJ

Abstract Number: 1801

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Measures and Measurement of Healthcare Quality
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Corticosteroids (CS) are commonly used for rheumatologic conditions, and known to cause systemic adverse events (AEs), particularly when used at high doses for prolonged periods. The burden, the incidence of AEs, and associated costs were assessed across varying levels of CS exposure.

Methods: Patients with a diagnosis of select autoimmune and inflammatory diseases between 1/1/2006 and 9/30/2015 were selected from a de-identified claims database. Patients with \( \geq \)60 days of continuous CS use were stratified into three prednisone-equivalent dose cohorts: \( \leq \)7.5 mg/day ("low dose"), >7.5-\( \leq \)15 mg/day ("medium dose"), or >15 mg/day ("high dose"). These groups were compared with patients with <60 days of CS use. Outcomes were assessed from the first day of a patient's highest dose episode until the earliest of 30 days after the end of continuous use, plan disenrollment, or end of study period. The incidence of AEs and costs during follow up were compared across cohorts.

Results: Among the 167,165 included patients, one-third had <60 days of CS use, 4% had low, 5% had medium, and 4% had high dose use of \( \geq \)60 days. High and medium-dose CS use varied among the conditions: PM/DM (37%), lupus (19%), and RA (19%) (Exhibit 1). Compared to patients in the <60 days cohort, risks of AEs (new cases) were several folds higher in the high-dose cohort: myocardial infarction (incidence rate ratio [IRR] 3.8), pneumonia (IRR 4.1), glaucoma (IRR 2.3), and hypertension (IRR 2.4). Most AEs had increasing incidence with higher-dose use (Examples shown in Exhibit 2). Across the three \( \geq \)60-day cohorts, AEs occurred at an average of 2.3-6.7 months after the initiation of the CS episodes; AEs developed more quickly for patients with high-dose than medium- or low-dose CS use. All treatment cohorts had higher AE-related medical costs than disease-related medical costs (Exhibit 3). AE-related medical costs accounted for approximately 30\% of the mean annualized total healthcare costs (27\% for <60 day patients, 33\% for high-dose patients).

Conclusion: This study quantified and demonstrated a dose-relationship for the risks of and time to AEs as well as the costs of prolonged CS use. Among patients who are exposed to high-doses, considerations to reduce their reliance on CS may provide clinical and economic benefits.
Exhibit 1. Treatment cohorts

Exhibit 2. Adverse event incidence rate during the follow-up period

Exhibit 3. Annualized patient healthcare costs

<table>
<thead>
<tr>
<th></th>
<th>High dose</th>
<th>Medium dose</th>
<th>Low dose</th>
<th>&lt;60 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total all-cause healthcare costs (including medical and prescription drug costs)</td>
<td>$68,408</td>
<td>$35,498</td>
<td>$31,900</td>
<td>$32,690</td>
</tr>
<tr>
<td>Adverse event-related medical costs</td>
<td>$22,807</td>
<td>$10,632</td>
<td>$9,342</td>
<td>$8,947</td>
</tr>
<tr>
<td>Disease-related medical costs</td>
<td>$16,151</td>
<td>$6,846</td>
<td>$5,399</td>
<td>$4,133</td>
</tr>
<tr>
<td>Disease-related prescription drug costs</td>
<td>$2,066</td>
<td>$3,491</td>
<td>$3,749</td>
<td>$1,507</td>
</tr>
<tr>
<td>Non-adverse event or disease-related healthcare costs</td>
<td>$59,434</td>
<td>$27,160</td>
<td>$23,910</td>
<td>$28,132</td>
</tr>
</tbody>
</table>

Disclosure: J. B. Rice, None; A. White, None; A. Lopez, None; A. Wagh, None; Y. Qin, Mallinckrodt Pharmaceuticals, 3; Mallinckrodt Pharmaceuticals, 1; G. Mitri, Mallinckrodt Pharmaceuticals, 3; L. Bartels-Peculis, None; G. Ciepielewska, None; W. Nelson, Mallinckrodt Pharmaceuticals, 1, Mallinckrodt Pharmaceuticals, 3.

Detection of Flare over the Past 3 Months in Rheumatoid Arthritis: Cross-Cultural Equivalence of the Self-Report Flare-RA Questionnaire

Francis Guillemin 1, Marie-Line Erpelding 2, Annette de Thurah 3,4,5,6, Elena Myasoedova 7, Emilie E Schneeberger 8, Cynthia S. Crowson 9, Thomas Maribo 10, Gustavo Citera 11, Eric L. Matteson 12 and Bruno Fautrel 13, 1University of Lorraine, Nancy, France, Nancy, France, 2CIC 1433 Clinical Epidemiology, Inserm, Nancy, France, 3Department of Rheumatology, Aarhus University Hospital, Århus C, Denmark, 4Department of Rheumatology, Aarhus University Hospital, Aarhus, DK, Aarhus, Denmark, 5Department of Clinical Medicine, Aarhus University, Aarhus, Denmark, 6Department of Clinical Medicine, Aarhus University, Aarhus, DK, Aarhus N, Denmark, 7Rheumatology, Mayo Clinic, Rochester, MN, 8Section of Rheumatology, Instituto de Rehabilitación Psicofísica, Buenos Aires, Argentina, Buenos Aires, Argentina, 9Health Sciences Research, Mayo Clinic College of Medicine and Science, Rochester, MN, 10DEFACTUM, Central Region Denmark, Aarhus, Denmark, 11Section of Rheumatology, Instituto de Rehabilitación Psicofísica, Buenos Aires, Argentina, Buenos Aires, Argentina, 12Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, MN, 13UPMC University Paris 06, Pitié-Salpêtrière Hospital, Paris, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes I
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:
The Flare-RA questionnaire was developed and validated in French (1) for assessing the occurrence of a flare of rheumatoid arthritis (RA) during a 3-month period, and cross-culturally adapted for the English, Spanish and Danish languages. The objective was to assess its cross-cultural equivalence in dimensionality and scale calibration, conditioning its validity.

Methods:
Patients included in studies in each of 4 countries (2 cohort studies and 2 clinical trials) were age 18+ years, had RA according to 2010 ACR criteria, were in routine care in three studies and attended a tele-health consultation in one study. Flare occurrence during the most recent 3 months was assessed at baseline and at 3 months of follow-up using the Flare-RA 11-item questionnaire. Flare was measured in two dimensions, namely arthritis-related (5 items) and general (6 items) subscales scoring from 0 (no flare) to 10 (maximum flare). Statistical analysis used exploratory and confirmatory factor analyses to determine dimensionality. Rasch modelling for scale calibration was used to search for differential item functioning (DIF) for countries, sex, and flare anchor (yes/no) using RUMM 2030®.

Results:
Overall, 571 patients (by center: 75, 105, 138 and 253) with mean±SD age 56.9±13.5 years and 75.3% female were included. Self-perception of a flare was reported by 39.9% of patients. Baseline RA disease activity varied by center. Mean DAS28 scores for each center were 2.1±0.8, 2.5±1.2, 2.9±1.2 and 3.6±1.4. Flare-RA items did not show any ceiling effect; mean score was 2.9±2.7 for arthritis-related and 2.5±2.6 for general subscales.

Principal component analysis showed a consistent first factor (65.7% variance), and demonstrated a strong bi-dimensional structure (75.8% variance)(figure). This dimensionality was stable over time and across countries in confirmatory analysis.

The Rasch partial credit model for subscales showed no local dependency, good person separation index (range 0.76–0.87) and good ordering of scale modalities. Only one item on “pain killer intake” performed less well, with less balanced ordering. Two items presented some misfit (fit residual>|2.5|) for each subscale. It was decided to keep them for clinical relevance. Finally, there was some significant but moderate DIF for countries in 7 items, all being uniform DIF. No interaction (DIF) was seen by sex, and only 2 minor DIF with flare anchor.

Conclusion:
This international effort confirms the solid bi-dimensional structure of the Flare-RA questionnaire, with arthritis-related and general subscales, and its good scale measurement properties. There was a slight DIF that might be investigated in larger samples, but it nevertheless can be used as a quantitative scale. These findings demonstrate that the Flare-RA questionnaire has validity for measurement and for international comparison across cohorts and clinical trials.
Disclosure: F. Guillemin, None; M. L. Erpelding, None; A. de Thurah, None; E. Myasoedova, None; E. E. Schneeberger, None; C. S. Crowson, None; T. Maribo, None; G. Citera, Novartis, Pfizer Inc, 2,AbbVie, Bristol-Myers Squibb, Janssen, Novartis, Pfizer Inc, 5; E. L. Matteson, Centocor, 2,Genentech and Biogen IDEC Inc., 2,UCB, 2,NIH, 2,Mesoblast, 2,Novartis Pharmaceutical Corporation, 2,Up-To-Date, 7,Janssen Pharmaceutica Product, L.P., 2,Amgen, 2,Bristol Myers Squibb, 2; B. Fautrel, AbbVie, Biogen, BMS, Celgene, Hospira, Janssen, Eli Lilly and Company, Novartis, Pfizer, Roche, SOBI Pharma, UCB, 5.


Abstract Number: 1803

A Cluster Analysis Approach to Patient-Physician Discordance in Rheumatoid Arthritis Activity Evaluations Optimally Differentiates and Predicts Clinical, Functional and Quality of Life Outcomes

George Karpouzas and Sarah Ormseth, 1 Division of Rheumatology, Harbor-UCLA Medical Center, Torrance, CA, 2 Rheumatology, Harbor-UCLA Medical Center, Torrance, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes I
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Patients and physicians commonly differ in their evaluations of rheumatoid arthritis (RA) activity. However, clinically meaningful thresholds for such discordance or validation of their ability to optimally predict clinical and functional outcomes are lacking. We used an unbiased clustering approach to classify cases based on patient (PGA) and physician/evaluator (EGA) global assessments of RA activity. We first examined whether such an approach could generate distinct patient groupings with diverse clinical phenotypes. We subsequently explored whether this approach could explain a higher variance in clinical and functional parameters of interest compared to traditional discordance definitions.

Methods: We performed latent class cluster (LCC) analysis in 538 patients with established RA to identify patient subgroups based on PGA and EGA ratings (measured on 10-cm visual analogue scales). Conventional discordance definitions included a continuous score (PGA-EGA) as well as a threshold-based one; with the latter, patients were classified into three groups: concordant (PGA-EGA within ± 3cm), positively discordant (PGA-EGA ≥ 3cm) and negatively discordant (PGA-EGA ≤ -3cm). We used $R^2$ values to compare the explanatory power of regression models using LCC-generated solution or conventional discordance definitions to predict outcomes of interest.

Results: LCC analysis yielded a five-group solution (Fig 1A). Groups were distinct and reflected different pairings of PGA and EGA scores: (1) Low PGA/Low EGA (33%); (2) Moderate PGA/Low EGA (21%); (3) High PGA/Low EGA (19%); (4) High PGA/High EGA (10%); and (5) Low PGA/High EGA (17%). Classification accuracy was 98.3%. ANCOVA confirmed differences in...
characteristics among LCC groups (Table 1). The High PGA/High EGA group fared worst overall, with patient outcomes similar or worse than the High PGA/Low EGA group and clinician-evaluated indices comparable to or worse than the Low PGA/High EGA group. The explanatory power of the LCC-based solution significantly outperformed conventional discordance definitions predicting all measured outcomes (Fig 1B).

Conclusion: Our findings highlight the validity and advantages of an LCC approach in quantifying the relationship between patient-physician global activity assessments, based on two simple measures collected in routine practice. LCC-generated groups differed significantly across clinical, functional and quality of life outcomes, and identified patients in greatest need of adjunctive treatments targeting pain, fatigue and psychological distress.

Table 1. Clinical, functional, quality of life and work outcomes among LCC-generated groups

<table>
<thead>
<tr>
<th></th>
<th>PGA Low/ EGA Low</th>
<th>PGA Moderate/ EGA Low</th>
<th>PGA High/ EGA Low</th>
<th>PGA High/ EGA High</th>
<th>PGA Low/ EGA High</th>
</tr>
</thead>
<tbody>
<tr>
<td>PGA</td>
<td>1.46 (0.11)</td>
<td>4.75 (0.12)</td>
<td>7.70 (0.12)</td>
<td>8.04 (0.16)</td>
<td>3.77 (0.13)</td>
</tr>
<tr>
<td>EGA</td>
<td>1.11 (0.13)</td>
<td>1.56 (0.15)</td>
<td>2.16 (0.16)</td>
<td>8.15 (0.20)</td>
<td>7.30 (0.16)</td>
</tr>
<tr>
<td>PGA/EGA discrepancy</td>
<td>0.34 (0.16)</td>
<td>3.19 (0.18)</td>
<td>5.55 (0.19)</td>
<td>-0.11 (0.24)</td>
<td>-3.63 (0.20)</td>
</tr>
<tr>
<td>Tender joint count</td>
<td>1.23 (0.37)</td>
<td>2.19 (0.42)</td>
<td>3.24 (0.44)</td>
<td>12.63 (0.56)</td>
<td>9.17 (0.47)</td>
</tr>
<tr>
<td>Swollen joint count</td>
<td>1.22 (0.28)</td>
<td>1.33 (0.31)</td>
<td>2.02 (0.33)</td>
<td>9.65 (0.42)</td>
<td>9.12 (0.34)</td>
</tr>
<tr>
<td>ESR</td>
<td>30.35 (1.90)</td>
<td>29.40 (2.16)</td>
<td>35.66 (2.25)</td>
<td>52.30 (2.88)</td>
<td>46.83 (2.37)</td>
</tr>
<tr>
<td>CRP</td>
<td>0.69 (0.11)</td>
<td>0.82 (0.13)</td>
<td>1.13 (0.13)</td>
<td>2.11 (0.17)</td>
<td>1.83 (0.14)</td>
</tr>
<tr>
<td>DAS28-4 (ESR)</td>
<td>2.98 (0.08)</td>
<td>3.73 (0.09)</td>
<td>4.54 (0.09)</td>
<td>6.52 (0.12)</td>
<td>5.50 (0.10)</td>
</tr>
<tr>
<td>CDAI</td>
<td>5.02 (0.62)</td>
<td>9.84 (0.71)</td>
<td>15.12 (0.74)</td>
<td>38.47 (0.94)</td>
<td>29.36 (0.78)</td>
</tr>
<tr>
<td>Pain VAS</td>
<td>2.07 (0.18)</td>
<td>4.56 (0.20)</td>
<td>6.95 (0.21)</td>
<td>7.11 (0.27)</td>
<td>4.22 (0.22)</td>
</tr>
<tr>
<td>Fatigue VAS</td>
<td>1.64 (0.22)</td>
<td>4.30 (0.24)</td>
<td>6.53 (0.25)</td>
<td>6.83 (0.33)</td>
<td>3.67 (0.27)</td>
</tr>
<tr>
<td>PHQ-9</td>
<td>3.53 (0.49)</td>
<td>6.06 (0.59)</td>
<td>10.64 (0.58)</td>
<td>12.33 (0.74)</td>
<td>5.22 (0.61)</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>0.79 (0.05)</td>
<td>1.28 (0.07)</td>
<td>1.67 (0.07)</td>
<td>1.97 (0.09)</td>
<td>1.39 (0.07)</td>
</tr>
<tr>
<td>SF-12 PCS</td>
<td>35.90 (0.49)</td>
<td>31.20 (0.56)</td>
<td>27.81 (0.58)</td>
<td>27.10 (0.75)</td>
<td>30.72 (0.61)</td>
</tr>
<tr>
<td>SF-12 MCS</td>
<td>43.10 (0.77)</td>
<td>36.20 (0.87)</td>
<td>30.83 (0.91)</td>
<td>29.35 (1.16)</td>
<td>37.83 (0.95)</td>
</tr>
<tr>
<td>Absenteeism</td>
<td>0.06 (0.02)</td>
<td>0.11 (0.03)</td>
<td>0.14 (0.04)</td>
<td>0.22 (0.04)</td>
<td>0.08 (0.03)</td>
</tr>
<tr>
<td>Presenteeism</td>
<td>0.17 (0.04)</td>
<td>0.41 (0.05)</td>
<td>0.63 (0.07)</td>
<td>1.24 (0.07)</td>
<td>0.38 (0.05)</td>
</tr>
<tr>
<td>Work productivity loss</td>
<td>0.19 (0.04)</td>
<td>0.44 (0.06)</td>
<td>0.65 (0.07)</td>
<td>0.70 (0.07)</td>
<td>0.39 (0.05)</td>
</tr>
<tr>
<td>Activity impairment</td>
<td>0.25 (0.02)</td>
<td>0.49 (0.02)</td>
<td>0.71 (0.03)</td>
<td>0.78 (0.03)</td>
<td>0.50 (0.03)</td>
</tr>
</tbody>
</table>

Omnibus F statistic for between cluster group differences was significant for all listed outcomes (p < 0.001). Values represent estimated marginal means after adjusting for disease duration, rheumatoid factor positivity, irreversible arthritic damage, fibromyalgia diagnosis, prednisone use, and disease-modifying antirheumatic drug use. All pairwise comparisons within a row are Bonferroni-Hochberg-corrected; values in a row with different subscripts denote groups whose averages differ significantly (p < 0.05).

Disclosure: G. Karpouzas, None; S. Ormseth, None.

Patient-Reported Outcomes and Damage Predict Mortality in Lupus

Desiree R Azizoddin¹, Meenakshi Jolly², Patricia P. Katz³ and Edward H. Yelin⁴, ¹Department of Psychology, Loma Linda University, Loma Linda, CA, ²Rush, Chicago, IL, ³Medicine/Rheumatology, University of California, San Francisco, San Francisco, CA, ⁴Medicine/Rheumatology, University of California San Francisco, San Francisco, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes I
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Physician-assessed disease activity and damage predict mortality in systemic lupus erythematosus (SLE). Patient-reported outcomes (PROs) are known predictors of mortality in other chronic diseases, but this relationship has not been examined in SLE. This analysis assessed whether PROs predict mortality in patients with SLE.

Methods:
Data from 728 participants in the UCSF Lupus Outcomes Study were evaluated to determine if PROs at one point in time (“baseline”, 2007) would predict subsequent mortality. Mortality was determined as of December 2015. PROs included the 8 subscales of the SF-36 (Physical Function, Role Physical, Pain, General Health, Vitality, Social Function, Role Emotional, and Mental Health), and depressive symptoms measured with the Center for Epidemiologic Studies Depression scale (CESD). Covariates were age, gender, race/ethnicity, poverty, disease duration, self-reported disease activity (Systemic Lupus Activity Questionnaire, SLAQ), and self-reported disease damage (Brief Index of Lupus Damage, BILD). BILD has previously shown good correspondence with physician-assessed disease damage. Univariate Cox regression analyses first examined each PRO as a predictor of subsequent mortality. Multivariate Cox regression analyses including covariates were then conducted for each PRO separately.

Results: Mean (SD) age was 50.6 (12.6) years; 671 (92.2%) participants were women. Ethnic composition was 68.5% Caucasian, 9.2% Hispanic, 7.3% African American, and 9.5% Asian. Baseline demographics, disease and PROs are shown in Table 1A. Mean (SD) follow up was 74.6 (23.2) months. There were 71 (9.1%) deaths. In univariate analyses, all PROs except the SF-36 Mental Health subscale and CESD were associated with mortality. In multivariate analysis, patient-reported physical function at initial screening independently predicted mortality after controlling for all other covariates (Table 1B), such that the odds of death were 3.5% lower for every increased point rating in physical health on the SF-36 Physical Function score[Hazard Ration (HR) 0.97, 95%CI (0.94,0.99) p < 0.01].

Conclusion: Self-reported physical function was independently predictive of mortality in SLE, even after adjusting for demographics (including poverty) and disease (duration, activity and damage). Tracking PROs, particularly patient-reported function, in clinical settings may add important information to improve patient long-term outcomes.
Table 1. A. Demographics and general characteristics (n=728) B. Multivariate Cox Proportional hazard regression analysis of mortality at 8 years

<table>
<thead>
<tr>
<th></th>
<th>M</th>
<th>SD</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A.</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>671</td>
<td>92.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>50.6</td>
<td>12.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>499</td>
<td>68.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>67</td>
<td>9.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>53</td>
<td>7.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>69</td>
<td>9.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>40</td>
<td>5.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Below Poverty</td>
<td>80</td>
<td>11.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>26.8</td>
<td>6.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease activity</td>
<td>4.2</td>
<td>2.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease duration</td>
<td>16.7</td>
<td>8.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease damage</td>
<td>2.3</td>
<td>2.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deceased</td>
<td>71</td>
<td>9.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SF36 Physical Function</td>
<td>39.4</td>
<td>12.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>B.</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Predictor</td>
<td>Hazard Ratio</td>
<td>95% CI</td>
<td>p</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>2.51</td>
<td>1.18, 5.35</td>
<td>.02</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>1.04</td>
<td>1.02, 1.07</td>
<td>.00</td>
<td></td>
</tr>
<tr>
<td>Below Poverty</td>
<td>086</td>
<td>.40, 1.84</td>
<td>.69</td>
<td></td>
</tr>
<tr>
<td>Disease Duration</td>
<td>1.02</td>
<td>.99, 1.04</td>
<td>.28</td>
<td></td>
</tr>
<tr>
<td>Disease Activity</td>
<td>.10</td>
<td>.89, 1.12</td>
<td>.98</td>
<td></td>
</tr>
<tr>
<td>Disease Damage</td>
<td>1.23</td>
<td>1.12, 1.36</td>
<td>.00</td>
<td></td>
</tr>
<tr>
<td>SF-36 Physical Function</td>
<td>.97</td>
<td>.94, .99</td>
<td>.01</td>
<td></td>
</tr>
</tbody>
</table>

Note: A. Relates to demographics and general characteristics. B. Relates to Multivariate Cox Proportional hazard regression analysis of mortality at 8 years. SLE disease activity is rated as 10-point Likert scale of patient rated disease activity; Disease damage is rated on the Brief Index of Lupus Damage (BILD); Below poverty calculated by US federal government guidelines; 36-Item Short Form Survey (SF-36) including only physical function domain. All scores were
Deceased status was evaluated throughout 8-year study progression. HR = Hazard Ratio. 95% CI = 95% Confidence Interval. SLE disease activity is rated as 10-point Likert scale of patient rated disease activity; Disease damage is rated on the Brief Index of Lupus Damage (BILD); Below poverty calculated by US federal government guidelines; 36-Item Short Form Survey (SF-36) including only physical function domain. All scores were rates at T1.

Disclosure: D. R. Azizoddin, None; M. Jolly, Pfizer Inc, 2,Medimmune, celgene, boehringer ingelheim, aurinia,, 7; P. P. Katz, None; E. H. Yelin, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/patient-reported-outcomes-and-damage-predict-mortality-in-lupus

Abstract Number: 1805

Construct Validity of RAPID3 for Measurement of Disease Activity in Psoriatic Arthritis

Jessica A. Walsh¹, Christine Willinger², M. Elaine Husni³, Soumya M. Reddy⁴, Jose U. Scher⁵ and Alexis Ogdie⁶, ¹Division of Rheumatology, University of Utah, Salt Lake City, UT, ²University of Pennsylvania, Philadelphia, PA, ³Cleveland Clinic, Cleveland, OH, ⁴Department of Medicine, Division of Rheumatology *contributed equally, New York University School of Medicine, New York, NY, ⁵New York University School of Medicine, New York, NY, ⁶Medicine/Rheumatology and Epidemiology, University of Pennsylvania, Philadelphia, PA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes I
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: The Routine Assessment of Patient Index Data (RAPID3) was developed and validated for rheumatoid arthritis (RA). Little data exist on the use of RAPID3 in psoriatic arthritis (PsA). The objective of this study was to assess the construct validity (the ability of an instrument to measure the concepts it attempts to measure) of RAPID3 through investigation of its correlation with other validated measures of disease activity, physical function, and life impact among patients with PsA.

Methods: Patients with PsA were enrolled in the Psoriatic Arthritis Research Consortium (PARC) between 2015-2016. PARC is a longitudinal observational cohort study conducted at four institutions: University of Pennsylvania, Cleveland Clinic, New York University, and University of Utah. Standardized data are collected and entered into a Research Electronic Data Capture database. All sites collected RAPID3 and provider-assessed outcomes, including tender and swollen joint counts, provider global assessment of overall health, and provider global assessment of arthritis. Three sites administered the Short Form 12 (SF12), and two sites collected the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue scale, Psoriatic Arthritis Quality of Life (PsAQoL) index, Dermatology Life Quality Index (DLQI), Work Limitations Questionnaire (WLQ), and Work Productivity and Activity Impairment (WPAI) questionnaire. Licenses have been obtained for the use of the SF-12 and the WLQ. Only baseline data were included in this cross-sectional analysis. Construct validity was assessed with Spearman's correlation coefficients between RAPID3, other PROs, and provider-assessed disease activity measures.

Results: Among 401 PARC participants with RAPID3 scores, 275 had SF12 scores, and 208 had full set of surveys. Of those with complete surveys, the mean age was 51.5 and 57% were female. The RAPID3 was highly correlated with the PSAID9 (r=0.90) and BASDAI (0.89) (Table). RAPID3 was also correlated with the SF12 physical component score (r=-0.73), the FACIT-F (r=0.75), the work limitations questionnaire (r=0.70), tender joint count (r=0.43), and swollen joint count (r=0.43).

Conclusion: RAPID3 has good construct validity in PsA and measures disease impact more broadly than physical function and pain. RAPID3 scores strongly correlated with the PSAID, a PRO with specific questions addressing many facets of life impact (e.g., pain,
function, fatigue, sleep, coping, anxiety and depression). The moderate correlations between RAPID3 and provider-assessed outcomes demonstrated that patients interpreted their disease states differently than their providers.

<table>
<thead>
<tr>
<th>Table. Correlations between instruments in a cross-sectional setting of PsA patients.</th>
<th>RAPID3</th>
<th>PSSAS</th>
<th>PsAQol</th>
<th>SF-12 PCS</th>
<th>BASDAI</th>
<th>FACIT-F</th>
<th>WLM</th>
<th>Physician Global</th>
<th>Physician Arthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSAID*</td>
<td>0.60</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PsAQol</td>
<td>0.77</td>
<td>0.78</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SF-12 PCS</td>
<td>0.73</td>
<td>0.71</td>
<td>0.71</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BASDAI</td>
<td>0.69</td>
<td>0.68</td>
<td>0.73</td>
<td>-0.68</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FACIT-Fatigue</td>
<td>-0.75</td>
<td>-0.82</td>
<td>0.83</td>
<td>0.68</td>
<td>-0.76</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WLM*</td>
<td>0.70</td>
<td>0.70</td>
<td>0.80</td>
<td>-0.63</td>
<td>0.68</td>
<td>0.77</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Provider Global</td>
<td>0.59</td>
<td>0.60</td>
<td>0.42</td>
<td>-0.41</td>
<td>0.53</td>
<td>-0.41</td>
<td>0.42</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Provider Arthritis</td>
<td>0.58</td>
<td>0.55</td>
<td>0.35</td>
<td>-0.38</td>
<td>0.48</td>
<td>-0.34</td>
<td>0.37</td>
<td>0.80</td>
<td></td>
</tr>
<tr>
<td>Swollen Joint Count</td>
<td>0.43</td>
<td>0.38</td>
<td>0.29</td>
<td>-0.25</td>
<td>0.35</td>
<td>-0.24</td>
<td>0.27</td>
<td>0.53</td>
<td>0.71</td>
</tr>
<tr>
<td>Tender Joint Count</td>
<td>0.42</td>
<td>0.38</td>
<td>0.30</td>
<td>-0.29</td>
<td>0.37</td>
<td>-0.25</td>
<td>0.28</td>
<td>0.51</td>
<td>0.61</td>
</tr>
<tr>
<td>Pain</td>
<td>0.92*</td>
<td>0.89</td>
<td>0.87</td>
<td>-0.65</td>
<td>0.89</td>
<td>-0.66</td>
<td>0.84</td>
<td>0.81</td>
<td>0.60</td>
</tr>
<tr>
<td>Patient Global</td>
<td>0.95*</td>
<td>0.82</td>
<td>0.82</td>
<td>-0.64</td>
<td>0.84</td>
<td>-0.70</td>
<td>0.85</td>
<td>0.54</td>
<td>0.56</td>
</tr>
</tbody>
</table>

**Sparsen’s correlation coefficients are shown in this table. Yellow indicates a strong correlation (r = 0.8-1.0) and blue a good correlation (r = 0.6-0.79).**

**-PSSAS is presented but the results were nearly identical for PSAID1.**

**-Note that pain and global assessment are part of the RAPID3 so the correlation is expected to be high.**

**-The productivity score of the Work Limitations Questionnaire is shown here. The WLQ index had nearly identical coefficients.**

**-Additional Abbreviations: PSAID=Psoriatic Arthritis Impact of Disease; PsAQol=Psoriatic Arthritis Quality of Life; SF-12 PCS = Short Form 12 Physical Component Score; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; Physician global and Physician arthritis refer to the physician global assessment for overall health and arthritis respectively.**

**Disclosure:** J. A. Walsh, Novartis, 5; C. Willinger, None; M. E. Husni, Celgene, AbbVie, Genentech, Bristol-Myers Squibb, Pfizer, Novartis, and Janssen, 9; S. M. Reddy, Eli Lilly and Company, 5; J. U. Scher, NIAMS-NIH, 2; A. Ogdie, Pfizer, Novartis, 2, Takeda, Pfizer, Novartis, 5.


**Abstract Number:** 1806

**Performance of the Brief Index of Lupus Damage (BILD) in a Multi-Ethnic Population-Based Systemic Lupus Erythematosus (SLE) Cohort**

**Patricia P. Katz**¹, Maria Dal'Era², Laura Trupin³, Stephanie Rush⁴, Charles G. Helmick⁵, Lindsey A. Criswell⁴ and Jinoos Yazdany³,

¹Medicine, University of California, San Francisco, San Francisco, CA, ²Medicine/Rheumatology, University of California, San Francisco, San Francisco, CA, ³Medicine/Rheumatology, University of California San Francisco, San Francisco, CA, ⁴University of California, San Francisco, San Francisco, CA, ⁵Centers for Disease Control and Prevention, Atlanta, GA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Patient Outcomes, Preferences, and Attitudes I

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 2:30PM-4:00PM

**Background/Purpose:** The BILD¹² was developed and validated as a measure of SLE organ damage for use in epidemiologic studies in which administration of the SLICC Damage Index (SDI) by physicians is not feasible. This analysis examines the criterion validity and other performance characteristics of the BILD in 4 racial/ethnic groups.

**Methods:** Data were from the California Lupus Epidemiology Study (CLUES), a population-based, multi-ethnic SLE cohort. Subjects participated in a research clinic visit during which the SDI was completed by a physician and completed a structured interview administered by a trained interviewer in which BILD was administered. Race and ethnicity were self-reported. Prevalence-adjusted
Bias-adjusted kappa (PABAK) coefficients were calculated to determine item-by-item agreement between physicians and subjects. Spearman correlation coefficients examined relationships between BILD and SDI scores. Construct validity was evaluated by examining relationships of sociodemographic, disease-specific, general health, and health care utilization factors with BILD scores. BILD scores are not normally distributed, so were divided into rough quartiles for these analyses and differences tested using analysis of variance or chi-square analysis. All analyses were performed separately for each of 4 racial/ethnic groups: white (W), Hispanic (H), African American (AA), and Asian (AS).

Results: The sample (n=281) was 29% W, 23% H, 11% AA, and 37% AS; 89% female; mean age 45 (±14) years; 22% with education <high school; 12% with poverty-level income; mean disease duration 16 (±10) years. 85% of interviews were completed in English. Correlations with SDI ranged from 0.45 for AA subjects to 0.80 for AS subjects (Table). All PABAK coefficients were >0.75, with the exception of 1 item for H subjects. For each racial/ethnic group, individuals with higher BILD scores had disease of longer duration; were less likely to be working; had poorer self-rated health, physical functioning and pain interference; reported more physician visits during the previous year; and were more likely to have been hospitalized in the previous year. No differences were seen by education or health literacy. Among H and AS groups, no differences were seen in BILD performance by language of administration.

Conclusion: The BILD functioned reasonably well in all 4 racial/ethnic groups, regardless of language of administration. Correspondence with physician-completed SDI was moderate to good; correlations were lower for AA and H patients where sample size was smaller. Future research will examine the source of discrepancies (patient or physician reports). Results provide further support the use of the BILD in observational and epidemiologic research, including among racial/ethnic minorities.

1Yazdany, et al., *Arthritis Care Res* 2011; 63:1170


Table. Descriptive information of BILD and SLICC Damage Index score overall and by racial/ethnic group

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Scores &gt; 0</th>
<th>Mean</th>
<th>Median</th>
<th>IQR</th>
<th>Maximum</th>
<th>Correlation with SDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>281</td>
<td>199 (71%)</td>
<td>1.8</td>
<td>1</td>
<td>0 -- 3</td>
<td>12</td>
<td>0.65</td>
</tr>
<tr>
<td>BILD</td>
<td>144</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLICC DI</td>
<td>144</td>
<td>144 (51%)</td>
<td>1.2</td>
<td>1</td>
<td>0 -- 2</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>White (W)</td>
<td>82</td>
<td>56 (68%)</td>
<td>1.8</td>
<td>1</td>
<td>0 -- 3</td>
<td>9</td>
<td>0.73</td>
</tr>
<tr>
<td>BILD</td>
<td>56</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLICC DI</td>
<td>56</td>
<td>35 (44%)</td>
<td>1.1</td>
<td>0</td>
<td>0 -- 2</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Hispanic (H)</td>
<td>65</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BILD</td>
<td>65</td>
<td>47 (72%)</td>
<td>2.1</td>
<td>1</td>
<td>0 -- 4</td>
<td>12</td>
<td>0.57</td>
</tr>
<tr>
<td>SLICC DI</td>
<td>65</td>
<td>30 (46%)</td>
<td>1.2</td>
<td>0</td>
<td>0 -- 2</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>African-American (AA)</td>
<td>31</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BILD</td>
<td>31</td>
<td>26 (84%)</td>
<td>2.1</td>
<td>1</td>
<td>0 -- 3</td>
<td>9</td>
<td>0.45</td>
</tr>
<tr>
<td>SLICC DI</td>
<td>31</td>
<td>22 (71%)</td>
<td>1.6</td>
<td>1</td>
<td>0 -- 2</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Asian (AS)</td>
<td>103</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BILD</td>
<td>103</td>
<td>70 (68%)</td>
<td>1.5</td>
<td>1</td>
<td>0 -- 2</td>
<td>7</td>
<td>0.80</td>
</tr>
<tr>
<td>SLICC DI</td>
<td>103</td>
<td>70 (51%)</td>
<td>1.0</td>
<td>1</td>
<td>0 -- 1</td>
<td>6</td>
<td></td>
</tr>
</tbody>
</table>

Disclosure: P. P. Katz, Bristol-Myers Squibb, 2; M. Dall'Era, None; L. Trupin, None; S. Rush, None; C. G. Helmick, None; L. A. Criswell, None; J. Yazdany, None.
Abstract Number: 1807

Psychometric Evaluation of the Arthritis Research UK Musculoskeletal Health Questionnaire (MSK-HQ) in Inflammatory Arthritis

Sam Norton¹, Benjamin Ellis²,³, Beatriz Santana Suárez⁴, Fowzia Ibrahim⁵, Andrew Price⁶, Ray Fitzpatrick⁶ and James Galloway⁷,¹
¹Academic Rheumatology, King’s College London, London, United Kingdom, ²Arthritis Research UK, Chesterfield, United Kingdom, ³Imperial College Healthcare NHS Trust, London, United Kingdom, ⁴Academic Rheumatology, King's College London, London, United Kingdom, ⁵Academic Rheumatology Dept, King's College London, London, United Kingdom, ⁶University of Oxford, Oxford, United Kingdom, ⁷King's College, and King’s College Hospital, London, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes I
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: The Arthritis Research UK Musculoskeletal Health Questionnaire (MSK-HQ) is a recently developed patient reported outcome measure (PROM) for use across patients with different musculoskeletal conditions. The initial development included a detailed scoping exercise and qualitative development phase involving both patients and clinicians. This study provides the first validation of the MSK-HQ in inflammatory arthritis.

Methods: 287 adults with an established diagnosis of inflammatory arthritis were recruited from six centres in England. Patients completed the MSK-HQ and other PROMs at baseline and again after 3 months. The MSK-HQ consists of 14 items relating to facets of musculoskeletal health including pain, fatigue, physical function, symptom interference, sleep, self-efficacy and psychological well-being rated using a four point ordinal scale from ‘not at all’ to ‘extremely’. Construct validity was assessed using item response theory (IRT) methods. Specifically, a graded response model examined the functioning of each item with respect to underlying musculoskeletal health. Concurrent validity of the MSK-HQ total score was considered in relation to the Health Assessment Questionnaire (HAQ), as well as Rheumatoid Arthritis (RA) and Psoriatic Arthritis (PsA) Impact of Disease Scales in disease subgroups (RAID & PsAID). Test-retest reliability was considered over three months.

Results: The MSK-HQ was approximately normally distributed with no evidence of floor or ceiling effects. A unidimensional structure was confirmed though two items (understanding & self-efficacy) were less weakly related to the overall construct. Reliability across the range of responses was high (alpha 0.93). The total scale score correlated highly with the HAQ in all patients (r=-0.81), RAID in those with RA or undifferentiated patients (n=218, r=-0.88), and PsAID in PsA patients (n=43, r=-0.88). Test-retest reliability over three months was good in those with stable disease (intraclass correlation=0.73).

Conclusion: In this study, we have provided further support for the validity and reliability of a new musculoskeletal health PROM in people with inflammatory arthritis. The tool compares well to existing PROMs, with the added advantage of lacking the floor effect of HAQ. The major advantage of the MSK-HQ is it is not disease specific and has high content validity in rheumatological conditions. The MSK-HQ score will be of value in clinical rheumatology practice, providing a measure which can be used across disease areas.

Disclosure: S. Norton, None; B. Ellis, None; B. Santana Suárez, None; F. Ibrahim, None; A. Price, None; R. Fitzpatrick, None; J. Galloway, MSD, 5,UCB, 5,Bristol Myers Squibb, 5,Pfizer Inc, 5,Celgene, 5.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/psychometric-evaluation-of-the-arthritis-research-uk-musculoskeletal-health-questionnaire-msk-hq-in-inflammatory-arthritis

Abstract Number: 1808

Long-Term Immunogenicity of a Quadrivalent Human Papillomavirus Vaccine in Patients with Systemic Lupus Erythematosus
Chi Chiu Mok¹, Ling Yin Ho², Lai Shan Fong¹ and Chi Hung To³, ¹Medicine, Tuen Mun Hospital, Hong Kong, Hong Kong, ²Dept of Medicine, Tuen Mun Hospital, Hong Kong SAR, Hong Kong, ³Medicine, Pok Oi Hospital, Hong Kong, Hong Kong

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Reproductive Issues in Rheumatic Disorders
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:
To report the 5-year immunogenicity of a quadrivalent human papillomavirus (HPV) vaccine (GARDASIL) in patients with systemic lupus erythematosus (SLE).

Methods:
Female SLE patients and healthy controls, aged 18-35 years, who received GARDASIL in the year 2011 and sero-converted 12 months post-vaccination were followed for the persistence of immunogenicity at 5 years. Antibodies to HPV serotypes 6,11,16,18 were repeated at 5 years using an IgG immunoassay developed on a Luminex microsphere platform (total IgG LIA; Merck Research Laboratory). The rate of sero-reversion was compared between patients and controls. Factors associated with sero-reversion of the anti-HPV antibodies were studied by statistical analyses.

Results:
50 SLE patients (age 25.8±3.9 years) and 50 controls (25.8±3.9 years) were vaccinated with Gardasil in 2011. The sero-conversion rates of anti-HPV serotypes 6,11,16 and 18 in patients and controls were 82%, 89%, 95%, 76%, and 98%, 98%, 98%, 80%, respectively, at month 12 post-vaccination. Among those subjects who sero-converted and were available for follow-up, persistence of the antibodies to HPV serotypes 6,11,16 and 18 at 5 years was present in 24/27 (89%), 26/31 (84%), 32/34 (94%), 24/25 (96%) of the SLE patients and 32/33 (97%), 32/33 (97%), 32/32 (100%) and 23/24 (96%) of the controls, respectively. Moreover, antibody titers to HPV serotypes 6 and 16 at 5 years were significantly lower in SLE patients than controls. Seven (21%) SLE patients had sero-reversion of any one of the four anti-HPV antibodies (6,11,16 or 18) at year 5 post-vaccination. Patients who sero-reverted had received a significantly higher cumulative dose of prednisolone (13.0±5.34 vs 4.63±4.59 grams; p=0.002), mycophenolate mofetil (1050±1180 vs 238±49.5 grams; p=0.007) and tacrolimus (375±580 vs 268±1180 mg; p=0.03) during the 5-year follow-up than those with persistence of immunogenicity. These sero-reverted patients had also received a non-significantly higher cumulative dose of cyclophosphamide (1.97±5.22 vs 0.43±2.24 grams; p=0.27). In addition, sero-reverted patients had more SLE flares in the 5-year follow-up period compared to those with persistence of immunogenicity (3.14±1.21 vs 1.89±1.28; p=0.03). Among 64 flares in patients with persistent anti-HPV antibodies and 26 flares in those with sero-reversion, renal flares occurred more frequently in the latter group of patients (16% vs 38%; p=0.02).

Conclusion:
Immunogenicity of the quadrivalent HPV vaccine was retained in 79% of SLE patients at 5 year post-vaccination. Antibody titers to HPV serotypes 6 and 16 were significantly lower in SLE patients than controls. Patients who had more SLE flares, especially renal flares, and had received higher cumulative doses of glucocorticoids, mycophenolate mofetil and tacrolimus were more likely to have sero-reversion of one or more anti-HPV antibodies.

Disclosure: C. C. Mok, None; L. Y. Ho, None; L. S. Fong, None; C. H. To, None.


Abstract Number: 1809

Lack of Placental Transfer of Certolizumab Pegol during Pregnancy: Results from a Prospective, Postmarketing, Multicenter, Pharmacokinetic Study

Eliza Chakravarty¹, Frauke Förger², Bincy Abraham³, Ann Flynn⁴, Anna Moltó⁵, René-Marc Flipo⁶, Astrid van Tubergen⁷, Laura Shaughnessy⁸, Jeff Simpson⁸, Marie Teil⁹, Eric Helmer¹⁰, Maggie Wang⁸ and Xavier Mariette¹¹, ¹Arthritis and Clinical Immunology
Background/Purpose: There is a need for effective and safe treatment during pregnancy in women affected by chronic active inflammatory diseases such as rheumatoid arthritis. Adequate disease control is crucial to ensure the best fetal and maternal health, and to reduce the risk of adverse pregnancy outcomes. Anti-TNFs are an effective therapeutic option, but because most cross the placenta they are often stopped during pregnancy. Certolizumab pegol (CZP), due to its Fc-free molecular structure, is not expected to undergo active placental transfer compared to other antibody-based anti-TNFs. This study aimed to accurately measure the level of placental transfer of CZP from mothers to infants using a highly sensitive CZP-specific assay.

Methods: CRIB (NCT02019602) was a pharmacokinetic (PK) study of pregnant women (≥30 weeks [wks] gestation) receiving commercial CZP (maintenance dose) for an approved indication; the last dose was given within 35 days prior to delivery. Blood samples were collected from mothers, umbilical cords, and infants at delivery, and infants again at Wks 4 and 8 post-delivery. CZP concentration was measured with a highly sensitive, CZP-specific electrochemiluminescence immunoassay validated in plasma (lower limit of quantification [LLOQ]=0.032 μg/mL; >10-fold lower than assays used in prior CZP PK studies).

Results: Of 21 CZP-treated pregnant women screened, 16 entered the study (Table A). Maternal CZP plasma levels at delivery were within the expected therapeutic range (median [range]=24.4 [5.0–49.4] μg/mL). Of the 16 infants, 2 were excluded from the per-protocol set: 1 due to missing data at birth, and 1 due to implausible PK data (inconsistent with a pediatric CZP PK model). Of the remaining 14 infants, 13 had no quantifiable CZP level at birth (<0.032 μg/mL) and 1 had a minimal CZP level of 0.042 μg/mL (infant/mother plasma ratio=0.0009); no infants had quantifiable levels at Wks 4 and 8 (Figure). Of the 16 umbilical cord samples, 1 was excluded due to missing data; 3/15 had quantifiable CZP levels (max=0.048 μg/mL). No anti-CZP antibodies were detected in mothers, umbilical cords, or infants. The infants of CZP-exposed mothers had a safety profile consistent with that of unexposed, similar-age infants (Table B).

Conclusion: Using a highly sensitive assay, CZP levels were below LLOQ in 13/14 infant blood samples at birth, and all samples at Wks 4 and 8. This indicates no to minimal placental transfer of CZP from mothers to infants, suggesting lack of in utero fetal exposure during the third trimester. These results support continuation of CZP treatment during pregnancy, if anti-TNF therapy is considered necessary.
A Systematic Review of the Impact of Anti-Rheumatic Drugs upon Male Fertility and Paternal Exposure Peri-Conception
SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Reproductive Issues in Rheumatic Disorders
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:

There is limited evidence relating to the impact of disease modifying anti-rheumatic drugs (DMARDs) upon male fertility and on pregnancies conceived by men with rheumatic disease. Safety concerns of reduced fertility and increased risk of adverse pregnancy outcomes frequently limits the prescription of these drugs in men wishing to conceive. These concerns however, arise based mainly from animal or in vitro experimental data and should be weighed against the beneficial effects of DMARD treatment in controlling active inflammatory disease that itself increases the chance of conception. Given that human in-vivo data pertaining to fertility and peri-conception safety is limited we conducted a systematic review of available evidence to update information on this subject and guide counselling in this situation.

Methods:

A systematic search of PubMed and Embase was carried out in September 2016 to find relevant peer-reviewed papers, using keywords for fertility / spermatogenesis / conception, men, and disease modifying or biologic drugs commonly prescribed in patients with rheumatic disease. Exclusion criteria included review articles, abstracts, animal and in-vitro studies, studies of cancer chemotherapy or pre/peri-pubertal exposure only, and non-English language papers. The search yielded 644 papers, and the titles/abstracts were screened independently by MM and JF, duplicates removed and 174 potentially relevant papers selected for full text review.

Results:

A total of 74 papers were included in the final analysis. Papers included 19 case reports, 15 case series, 2 mechanistic studies, 36 cohort studies, 1 RCT and 1 meta-analysis and covered the impact on fertility of over 553 male exposures to relevant drugs, and over 948 pregnancies conceived during paternal exposure to these drugs. Only 26 papers had a comparator group. Results for the individual drugs are shown in table 1. Overall there was no firm evidence of harm to fertility or pregnancy outcomes with paternal exposure to anti TNF, azathioprine, cyclosporine A, hydroxychloroquine, leflunomide, methotrexate, mycophenolate mofetil or rituximab. The quality of evidence for all drugs (using the GRADE approach) is ‘low’ or ‘very low’. There was no evidence found pertaining to the effects of male exposure to IVIG, tacrolimus, golimumab or abatacept on fertility or pregnancy outcomes. Many papers noted a correlation between active inflammatory disease and poor sperm quality, with seminal parameters improving when disease was well controlled.

Conclusion:

These results present provide further reassurance as to the safety of DMARDs, in particular methotrexate, for men trying to conceive and will be useful when counselling men about risks of anti-rheumatic drugs to fertility and pregnancies, and following accidental conception.

Table 1: Results of Systematic Study of Paternal Exposure in men trying to conceive.
<table>
<thead>
<tr>
<th>Drug</th>
<th>No. studies of fertility / conception (total male exposures)</th>
<th>No. studies of pregnancy outcomes (total pregnancies exposed)</th>
<th>Outcome / conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-TNF: adalimumab</td>
<td>6 (30)</td>
<td>2 (&gt;6)</td>
<td>Improved control of inflammatory disease with anti-TNF therapy was generally associated with improved semen parameters. There were 2 case reports noting a co-incident decrease in sperm quality with anti-TNF therapy, and 2 small studies (total 13 exposures) suggesting a possible non-significant link between infliximab and reduced sperm motility or abnormal morphology, but there were multiple confounding factors and limitations to these studies.</td>
</tr>
<tr>
<td>Anti TNF: certolizumab</td>
<td>0</td>
<td>2 (&gt;33)</td>
<td>This paper was all too small to draw firm conclusions about safety in pregnancy, but none reported rates of adverse pregnancy outcomes that were significantly higher than would be expected.</td>
</tr>
<tr>
<td>Anti TNF: etanercept</td>
<td>5 (9)</td>
<td>4 (&gt;45)</td>
<td>The majority of papers were reassuring about the effect of azathioprine on semen parameters. The majority of papers do not raise a concern regarding pregnancy outcomes; only 1 paper reported a slightly higher malformation rate in exposed vs unexposed pregnancies. However, even in this paper, none of the 19 exposures that had occurred within 3 months of conception resulted in a malformation.</td>
</tr>
<tr>
<td>Anti TNF: infliximab</td>
<td>6 (78)</td>
<td>8 (&gt;39)</td>
<td>Universal reporting of reduced sperm counts and fertility which improves on stopping cyclophosphamide in most cases. Pregnancy data is inconclusive with only one paper reporting 5 positive conceptions, 7 pregnancy losses and 2 live births, but this was a survey and likely susceptible to selection and recall bias.</td>
</tr>
<tr>
<td>Anti TNF: combined</td>
<td>1 (110)</td>
<td></td>
<td>The very limited available evidence did not suggest an effect of Cyclosporin A on fertility. There was only a case report of one successful pregnancy and birth.</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>7 (&gt;28)</td>
<td>7 (&gt;331)</td>
<td>There was only one case report of the effect of HCQ on fertility, with multiple confounders. A national registry cohort study reported malformations in 1/12 babies with paternal exposure to HCQ &lt;3 months prior to conception, lower than the western population malformation rate of 2-4%.</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>10 (&gt;103)</td>
<td>2 (&gt;15)</td>
<td>In one case report the father was on leflunomide for 6 months prior to conception and during the pregnancy with no barrier protection used. One healthy baby was born. The second report was inconclusive.</td>
</tr>
<tr>
<td>Cyclosporin A</td>
<td>2 (&gt;2)</td>
<td>1 (1)</td>
<td>Aside from 2 case reports of oligospermia, the other 5 larger studies concluded that there was no impact of MTX on fertility. There is also now a reasonable body of reassuring evidence relating to paternal MTX exposure: only one small cohort study reported a major malformation amongst the 3 paternal exposures to MTX, whereas the other 11 papers (299 exposures) reported no link with adverse pregnancy outcomes or congenital malformations.</td>
</tr>
<tr>
<td>Hydroxychloroquine (HCQ)</td>
<td>1 (1)</td>
<td>1 (12)</td>
<td>There was only one cohort study of men with SLE, including 4 MMF exposures. This suggested a link between impaired fertility and active SLE, but not MMF exposure.</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>2 (2)</td>
<td></td>
<td>Pregnancy outcome data is limited but reassuring: Of the 11 reported exposures (2 weeks-1year prior to conception), there were 2 miscarriages, 7 live births and 2 ongoing pregnancies at the time of publication.</td>
</tr>
<tr>
<td>Methotrexate (MTX)</td>
<td>7 (48)</td>
<td>12 (302)</td>
<td>The vast majority of data comes from inflammatory bowel disease patients. Almost all studies noted poor sperm parameters in patients treated with sulfasalazine, but in most cases these resolved on stopping treatment. It must also be noted that infertility is not universal and most papers reported no adverse pregnancy outcomes attributed to sulfasalazine exposure.</td>
</tr>
<tr>
<td>Mycophenolate mofetil (MMF)</td>
<td>1 (4)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Rituximab</td>
<td>0</td>
<td>1 (11)</td>
<td></td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>29 (250)</td>
<td>9 (&gt;151)</td>
<td></td>
</tr>
</tbody>
</table>

Disclosure: J. D. Flint, None; M. Mouyis, None; I. Giles, None.
Abstract Number: 1811

Lupus Patients, and Their Sisters, Have Higher Miscarriage Rates Than Healthy Women

Eliza Chakravarty1, David Miklos2, Nathan Pezant3, Fang Wu2, Indra Adrianto4, R. Hal Scofield3, Joel M. Guthridge5, Courtney Montgomery4 and Judith A. James4, 1Arthritis and Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, 2Hematology, Stanford University, Stanford, CA, 3Oklahoma Medical Research Foundation, Oklahoma City, OK, 4Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 5Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, OKC, OK

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Reproductive Issues in Rheumatic Disorders
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that primarily affects women during the childbearing years. Among its protean manifestation, pregnancy complications including premature delivery and preeclampsia are common. Most studies of pregnancy outcomes in women with SLE focus on complications occurring in the second half of pregnancy rather than evaluating spontaneous abortions (Sab, or miscarriage) that generally occur before 14 weeks of gestational age. While Sab occurs in up to 20% of all pregnancies and sporadic Sab is often attributed to karyotypic or genetic anomalies, it is possible that women with SLE experience higher rates of Sab than healthy women, and this may have an immunologic basis. The presence of the antiphospholipid antibody syndrome is the most commonly recognized risk factor for pregnancy morbidity; as late pregnancy morbidity or >3 consecutive Sab itself meets criteria for the syndrome. We sought to understand the incidence of Sab in a large cohort of SLE women, their unaffected sisters, and unrelated unaffected women.

Methods: Clinical data and stored sera from the Lupus Family Registry and Repository of 1608 parous women between ages 20-45 including SLE patients (by ACR criteria, n=832), sisters of SLE patients (n=337), and unaffected, unrelated women (n=439) were utilized. Complete reproductive history, including gestational age and outcome of all pregnancies, was available as was standardized SLE serologies. Additional autoantibodies, related to exposure to paternal antigens, included antibodies against HLA class I and II, and antibodies directed at minor histocompatibility antigens on the Y-chromosome and their X-homologues were assessed. Ratios of the number of Sab to the total numbers of pregnancies were compared between the three groups. Regression models were developed to better understand the role of auto- or allo-immunization and risk of Sab. Analyses were repeated using the subset of 1050 women who were APL negative.

Results: Both women with SLE and their unaffected sisters had higher Sab to total pregnancy ratios than healthy women in a dose-dependent fashion: Odds Ratio (OR)=1.43 (p=0.000049) for SLE and OR=1.28, (p=0.019) for sisters. Preliminary multivariate regression analyses found that only group and +APL antibodies were significantly associated with increased Sab, neither other standard SLE antibodies nor antibodies against HLA, HY, or HX were significant.

When women with +APL were removed from the analyses the Sab ratio remained significantly different for SLE (OR=1.37, p=0.0156), but not for sisters (OR=1.11, p=0.4029) compared to healthy women. Prevalence of autoantibodies did not modify the result in multivariate models.

Conclusion: SLE women have higher rates of Sab than healthy women, and sisters of SLE patients have intermediate rates. Autoantibodies do no explain these differences.

Table
<table>
<thead>
<tr>
<th>Variable</th>
<th>SLE</th>
<th>Sisters</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>1396</td>
<td>580</td>
<td>564</td>
</tr>
<tr>
<td>age (mean, SD)</td>
<td>38.8 (7.2)*</td>
<td>40.17**</td>
<td>37.7 (7.6)</td>
</tr>
<tr>
<td># pregnancies</td>
<td>2.8 (1.7)</td>
<td>3.0 (1.8)</td>
<td>2.8 (1.6)</td>
</tr>
<tr>
<td># live births</td>
<td>1.8 (1.2)**</td>
<td>2.2 (1.3)</td>
<td>2.1 (1.2)</td>
</tr>
<tr>
<td>% with any Sab</td>
<td>39*</td>
<td>37</td>
<td>32</td>
</tr>
<tr>
<td>Sab: total pregnancy ratio</td>
<td>0.22**</td>
<td>0.17</td>
<td>0.15</td>
</tr>
<tr>
<td>% with +APL</td>
<td>40**</td>
<td>26</td>
<td>22</td>
</tr>
<tr>
<td>% with +ANA</td>
<td>90**</td>
<td>39**</td>
<td>21</td>
</tr>
<tr>
<td>% with ANA&gt; 1:360</td>
<td>72**</td>
<td>17**</td>
<td>4</td>
</tr>
<tr>
<td>% with +dsDNA</td>
<td>27**</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Women with -APL

| n                                | 471   | 224     | 335      |
| age (mean, SD)                   | 38.9 (7.4)** | 40.1 (7.2)** | 37.6 (7.5) |
| # pregnancies                    | 2.8 (1.5) | 2.9 (1.9) | 2.8 (1.5) |
| # live births                    | 1.8 (1.2)* | 2.1 (1.3) | 2.1 (1.2) |
| % with any Sab                   | 38     | 34      | 34       |
| Sab: total pregnancy ratio       | 0.19   | 0.16    | 0.16     |

* p<0.05, ** p<0.001 compared to controls by ANOVA

Disclosure: E. Chakravarty, None; D. Miklos, None; N. Pezant, None; F. Wu, None; I. Adrianto, None; R. H. Scofield, None; J. M. Guthridge, None; C. Montgomery, None; J. A. James, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/lupus-patients-and-their-sisters-have-higher-miscarriage-rates-than-healthy-women

Abstract Number: 1812

**Preeclampsia and Incident Cardiovascular Disease in SLE Pregnancy**

**Julia F Simard**¹, Marios Rossides², Elizabeth V. Arkema³, Elisabet Svenungsson⁴, Anna-Karin Wikstrom⁵, Murray Mittleman⁶ and Jane E. Salmon⁷, ¹Division of Epidemiology, Health Research and Policy Department, Stanford School of Medicine, Stanford, CA, ²Medicine Solna, Clinical Epidemiology Unit, Karolinska Institutet, Stockholm, Sweden, ³Clinical Epidemiology Unit, Department of Medicine, Karolinska Institutet, Stockholm, Sweden, ⁴Department of Medicine Solna, Rheumatology Unit, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, Stockholm, Sweden, ⁵Clinical Epidemiology Unit, Department of Medicine, Karolinska Institute, Stockholm, Sweden, ⁶Epidemiology, Harvard T. H. Chan School of Public Health, Boston, MA, ⁷Medicine/Rheumatology, Hospital of Special Surgery, New York, NY

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017
Session Title: Reproductive Issues in Rheumatic Disorders
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

**Background/Purpose:**

Pre-pregnancy cardiovascular health has been associated with preeclampsia during pregnancy, as well as future cardiovascular disease (CVD). Preeclampsia is related to endothelial dysfunction, hypertension, permanent vascular damage and increased arterial stiffness in the mother, factors associated with future CVD. It is unclear whether pregnancy unmasks endothelial vulnerability to injury which manifests as preeclampsia or whether the preeclampsia itself causes damage leading to CVD. Patients with SLE are at increased risk for...
preeclampsia as well as CVD and stroke. However, the relationship between these conditions has not been thoroughly examined among women with SLE.

Methods:

Using a population-based Swedish register linkage, we identified all singleton pregnancies in the Medical Birth Register (1987-2012) among mothers with prevalent SLE and a large general population comparator (non-SLE). SLE was defined as ≥2 SLE ICD-coded visits (inpatient, outpatient non-primary care, or both) with at least 1 visit coded by specialist who manages SLE. Primary CVD outcomes included any recorded MI or stroke based on ICD10 codes in the Patient or Death Register. Power permitting, stroke and MI were considered separately. Multivariable-adjusted stratified Cox models estimated hazard ratios and 95% confidence intervals (HR, 95% CI) among all deliveries, using robust variance estimators to account for autocorrelation (multiple pregnancies), time-varying covariates, and calendar year as the stratification variable. Preeclampsia and maternal hypertensive disorders were time-varying, such that once a woman was exposed to a preeclampsia-complicated pregnancy, she remained exposed. Sensitivity analysis restricted to first births only. HRs and 95% CIs estimated the association between preeclampsia and CVD in SLE vs non-SLE. We calculated the relative excess risk due to interaction (RERI) to assess for non-additivity.

Results:

Among 1207 SLE pregnancies, 19.4% were preeclampsia-exposed compared to 6.9% of the 18784 non-SLE pregnancies. SLE mothers were more likely to have pregestational hypertension and diabetes, renal disease, and DVT/pulmonary embolism. Among women with SLE, these pregestational comorbidities were more common in those with preeclampsia (renal disease history in 37% vs. 9% among normotensives). Any preeclampsia was associated with a 2.7-fold increased rate of CVD in both women with SLE and from the general population (RERI=18.8 (-5.3 to 42.9)). We found a significant interaction on the additive scale for stroke as the outcome (RERI=35.2 (1.1, 69.5); preeclampsia was associated with a roughly 4.5-fold increased rate of stroke in SLE but not associated with stroke in non-SLE.

Conclusion:

We confirmed that women with preeclampsia are at increased risk of future CVD, regardless of whether they had SLE during pregnancy or not. There was an excess risk of stroke specifically among women with SLE when compared to women from the general population.

Disclosure: J. F. Simard, None; M. Rossides, None; E. V. Arkema, None; E. Svenungsson, None; A. K. Wikstrom, None; M. Mittleman, None; J. E. Salmon, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/preeclampsia-and-incident-cardiovascular-disease-in-sle-pregnancy

Abstract Number: 1813

Rates of Contraceptive Use and Unintended Pregnancy in Teen Girls Prescribed Teratogenic Medications

Kimberly Hays1, Kit Simpson1, David Bundy1, Elizabeth Wallis1 and Natasha M. Ruth2, 1Pediatrics, Medical University of South Carolina, Charleston, SC, 2Rheumatology, Medical University of South Carolina, Charleston, SC

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Reproductive Issues in Rheumatic Disorders
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Reproductive aged women with rheumatic diseases are often prescribed teratogenic medications. These medications pose a serious threat to the mother and fetus. Rates of contraceptive use and unintended pregnancy among teen girls taking teratogenic medications are not well described.

Methods: Medicaid claims data from 12 de-identified US states, between 2013-2015, was used to create an inception cohort of teen girls aged 15-19 prescribed teratogenic medications. Teens received a prescription for at least 1 of 8 teratogenic medications used in the management of pediatric rheumatic disease. Teratogenic medications were defined as FDA category D or X. We identified teratogenic medications commonly prescribed to teens for a variety of conditions: cyclophosphamide, enalapril, leflunomide, lisinopril, losartan,
methotrexate and mycophenolate. Cyclosporine was also included (category C). Teens entered the cohort upon receiving a teratogenic medication prescription and were followed for 12 months or until the end of 2015. Outcome of interest was pregnancy. Covariate of interest was contraceptive use, which was evaluated by prescription claims for any type of prescription contraceptive. We identified a sub-group of teens with rheumatic diseases, as determined by outpatient visits with at least two diagnostic codes consistent with a rheumatic disease. Data were analyzed using SAS version 9.4.

Results: 4853 teen girls aged 15-19 met criteria for inclusion, 36.6% Black, 4.8% Hispanic, 13.6% other and 45.1% White. There were 368 pregnancies comprising 7.5% of the cohort, 26 resulted in abortion. Pregnancy by race was statistically significant (7.6% Blacks, 9.1% Hispanics, 4.7% other, and 8.3% Whites, p=0.0185). Of the total pregnancies, 50% occurred in girls aged 15-17, with 19 year olds having the most pregnancies. In pregnant teens, exposure days to teratogenic medications ranged from 117 days to 326 days, with 19 year olds having the shortest time on teratogenic medications prior to pregnancy. In this cohort, 52% were prescribed contraception during the analysis period. Contraception by race was statistically significant (50.5% Blacks, 37.9% Hispanics, 44.8% other, and 58.1% of Whites, p=0.001). In teens with unintended pregnancies, 75% did not receive a prescription for contraception prior to pregnancy. Approximately 10% of this cohort was identified as having a rheumatic disease, with SLE being the largest percentage (70%).

Conclusion: Contraceptive prescriptions in teens on teratogenic medications were low and a significant number of teens had unintended pregnancies. While only 10% of the individuals were identified as having a rheumatic disease based on ICD-9 coding, this number is likely higher as we were very specific in the ICD-9 codes chosen. Teen pregnancy is a serious population health risk especially in patients with chronic rheumatic disease on teratogenic medications. Future analyses will compare contraception and pregnancy rates in our cohort to teens not on teratogenic medications. This analysis highlights the importance of reproductive health education including improved access to contraception for patients on teratogenic medications.

Disclosure: K. Hays, None; K. Simpson, None; D. Bundy, None; E. Wallis, None; N. M. Ruth, None.


Abstract Number: 1814

Time Trends over a Decade Show Earlier Intensified Medication Strategies and Improved Outcomes in Canadians with Early Inflammatory Arthritis

Orit Schieir1, Marie-France Valois2, Susan J. Bartlett3,4, Carol A Hitchon5, Janet E. Pope6, Gilles Boire7, Boulos Haraoui8, Diane Tin9, Carter Thorne10, Edward C. Keystone11,12 and Vivian P. Bykerk13,14, 1Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada, 2McGill University, Montreal, QC, Canada, 3Department of Medicine, Division of ClinEpi, Rheumatology, Respiratory, McGill University, Montreal, QC, Canada, 4Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, 5University of Manitoba, Winnipeg, MB, Canada, 6Department of Medicine, Division of Rheumatology, University of Western Ontario, St Joseph's Health Care, London, ON, Canada, 7Rheumatology Division, Centre Hospitalier Universitaire de Sherbrooke and Universite de Sherbrooke, Sherbrooke, QC, Canada, 8Institut de Rheumatologie, Montreal, QC, Canada, 9The Arthritis Program, Southlake Regional Health Centre, Newmarket, ON, Canada, 10University of Toronto, Newmarket, ON, Canada, 11University of Toronto, Toronto, ON, Canada, 12Rheumatology, Mount Sinai Hospital, Toronto, ON, Canada, 13Mount Sinai Hospital, Toronto, ON, Canada, 14Division of Rheumatology, Hospital for Special Surgery, New York, NY

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects II: Treatment Patterns
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Treatment recommendations aim to improve outcomes in rheumatoid arthritis (RA) through early identification and a treat-to-target approach. We examined recent trends over the past decade including patient characteristics, treatment strategies and disease activity in the first year of follow-up in a large Canadian early inflammatory arthritis (EIA) cohort.
**Methods:** Data were from individuals with EIA (RA or probably RA <1-year of symptom duration) enrolled in an ongoing prospective multi-center cohort study between 2007 and 2016 and had complete DAS28 measures at 6 and 12-months. Protocolized visits include clinical assessments, questionnaires, and laboratory investigations every 3 months for the first year. Treatment is at the discretion of the treating rheumatologist, and cohort investigators met annually to discuss means to improve outcomes. We examined trends in patient characteristics, early treatment strategies with conventional(cs) and biologic(b) DMARDs and disease activity outcomes over 12-months (12M). Multivariable logistic regression was used to identify predictors of failure to achieve low disease activity (LDA) or remission (REM) by 12M.

**Results:** Over 10 years, 2822 EIA patients were enrolled who were mostly female (70%) and Caucasian (80%). At study entry, 86% met 1987 or 2010 ACR/ EULAR RA criteria; mean(sd) age was 54(15), symptom duration was 6(3) months. Most were treated with csDMARDs (92%), often with MTX, as monotherapy or in combination with csDMARDs (77%); 29% were prescribed oral steroids and 27% IA or IM steroids. Baseline patient characteristics changed slightly over time with increases in age, male sex, education, income, and declines in current smoking (all p’s <0.01). Baseline obesity rates, comorbidities and RA characteristics (serology, inflammatory markers, joint counts and disease activity indices) remained stable. Most (87%) entered in moderate or high disease activity (MDA or HDA), and disease activity at 6 and 12M markedly improved over calendar time (Figure 1). DAS28 REM at 12M increased by over 30% (range 39% to 73%, p<0.0001), and 20% more achieved LDA or REM by 6M (range 48% to 68%, p<0.0001) (Figure 1). Time trends in treatment showed earlier titration of MTX dosing to 20mg+, increases in subcut vs. oral MTX, earlier MTX combo therapies and more rapid escalation to bDMARDs all p’s <0.05). Older age, female sex, lower education, non-white, overweight/obese BMI, and more comorbidities were associated with an inadequate response (persistent MDA or HDA) at 12 months (all p’s<0.05).

**Conclusion:** This study of Canadian EIA patients over time suggests that earlier, more intensified treatment promoted in practice recommendations has resulted in lower disease activity and a greater proportion of patients reaching the target of therapy. Nevertheless 25-30% of patients still did not achieve LDA or REM by 12M.

**Disclosure:** O. Schieir, None; M. F. Valois, None; S. J. Bartlett, PROMIS, 6,Pfizer Inc, UCB, Lilly, 5; C. A. Hitchon, None; J. E. Pope, AbbVie, Amgen, Bayer, BMS, Celtrion, Eli Lilly and Company, Merck, Novartis, Pfizer, Roche, UCB, 5,Amgen, Bayer, BMS, GSK, Merck, Novartis, Pfizer, Roche, UCB, 2; G. Boire, None; B. Haraoui, AbbVie, Amgen, BMS, Celgene, Eli Lilly, Janssen, Merck, Pfizer, Roche, Sandoz, 6,AbbVie, Amgen, BMS, Janssen, Pfizer, Roche, and UCB:, 2,Pfizer, and UCB, 8; D. Tin, None; C. Thorne, AbbVie, Amgen, Celgene, Lilly, Novartis, Pfizer, Sanofi, and UCB; has served as a consultant for AbbVie, Amgen, Celgene, Centocor, Genzyme, Hospira, Janssen, Lilly, Medexus/Medac, Merck, Novartis, Pfizer, Sanofi, and UCB, 2,Medexus/Medac, 8; E. C. Keystone, Abbott Laboratories, Amgen Inc., AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb, F. Hoffmann-La Roche Inc, Janssen Inc, Lilly Pharmaceuticals, Novartis Pharmaceuticals, Pfizer Pharmaceuticals, Sanofi-Aventis, UCB, 2,Abbott Laboratories, AstraZeneca Pharma, Biotest, Bristol-Myers Squibb Company, Crescendo Bioscience, F. Hoffmann-La Roche Inc, Genentech Inc, Janssen Inc, Lilly Pharmaceuticals, Merck, Pfizer Pharmaceuticals, UCB, 5,Amgen, Abbott Laboratories, AstraZeneca LP, Bristol-Myers Squibb Canada, F. Hoffmann-La Roche Inc., Janssen Inc., Pfizer Pharmaceuticals, Sanofi Genzyme UCB, 8; V. P. Bykerk, Amgen, Bristol-Myers Squibb Company, Gilead, Sanofi-Genzyme/Regeneron, Pfizer Pharmaceuticals, UCB, 5.

Patterns of Methotrexate Use and Discontinuation in a U.S. Rheumatoid Arthritis Registry

Jeffrey R. Curtis, Gene Wallenstein, Liza Takiya, David Gruben, Connie Chen, Ying Shan, Taylor Blachley, Kimberly J Dandreo and Joel Kremer. 1 University of Alabama at Birmingham, Birmingham, AL, 2 Pfizer Inc, Groton, CT, 3 Pfizer Inc, Collegeville, PA, 4 Pfizer Inc, New York, NY, 5 Corrona, LLC, Southborough, MA, 6 Albany Medical College and The Center for Rheumatology, Albany, NY

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects II: Treatment Patterns
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Methotrexate (MTX) remains a cornerstone therapy in the management of rheumatoid arthritis (RA), but patterns of adherence, intolerance, and inadequate response are not well characterized in real-world settings. We compared the characteristics and reasons for MTX discontinuation in patients (pts) with RA who received MTX either as monotherapy or in combination with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs).

Methods: This analysis included pts enrolled in a US RA registry initiating MTX, who were naïve to targeted immune modulators (TIMs; biologics and small molecules). Cox proportional hazards models estimated the hazard ratio (HR) associated with MTX discontinuation and, in a separate analysis, TIM initiation, adjusting for potentially confounding factors. The reasons for MTX continuation were summarized descriptively, conditional on non-missing data.

Results: A total of 2144 RA pts initiated MTX (monotherapy: 69%; csDMARD users: 31%). csDMARD users were more likely to be Caucasian, non-Hispanic, have higher education, be employed full time, and have commercial insurance. Compared with MTX monotherapy, csDMARD users had lower Clinical Disease Activity Index (CDAI) scores (19.6 vs 16.9, p<0.0001), less disability as measured by the modified Health Assessment Questionnaire (mHAQ <0.5; 59% vs 70%, p<0.0001), longer duration of RA (3.8 vs 5.4 years, p<0.0001), and were less likely to be on a higher dose of prednisone (≥10 mg/day; 33% vs 22%, p<0.0001). The proportion of MTX monotherapy pts that discontinued MTX was 24% (1 year), 37% (2 years), and 46% (3 years), and was not significantly different from csDMARD users. The hazard of MTX discontinuation decreased as age at RA onset, duration of disease, and baseline CDAI increased (Table). After adjusting for potential confounding variables, an increased hazard of MTX discontinuation was associated with being disabled, retired, or regular alcohol use. MTX discontinuation was less likely in pts with older age, longer duration of RA, or higher baseline CDAI (Table). At 12 months, 27% of MTX monotherapy and 18% of csDMARD users had initiated a TIM. MTX monotherapy users were 39% more likely to have initiated a TIM by Month 12 compared with csDMARD users (HR 1.39; 95% CI 1.19, 1.59). However, after multivariable adjustment, the association between MTX monotherapy and TIM initiation was attenuated (HR 1.15; 95% CI 0.94, 1.41). The most common reasons reported for discontinuing MTX were safety/tolerability (48%) and other reasons (29%), rather than lack of efficacy (15%).

Conclusion: Despite the well-recognized role of MTX in RA management, approximately 30% of pts with RA discontinue MTX within 1–2 years after initiation. Strategies are required to better identify pts with suboptimal adherence to MTX and predict those most likely to not tolerate MTX, in order to optimize overall RA treatment.
Table. Patient characteristics associated with MTX discontinuation/TIM initiation

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adjusted HR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combination csDMARDs + MTX</td>
<td>0.95 (0.79, 1.14)</td>
</tr>
<tr>
<td>(relative to MTX monotherapy)</td>
<td></td>
</tr>
<tr>
<td>Age at RA onset (per 5 years)</td>
<td>0.94 (0.91, 0.97)</td>
</tr>
<tr>
<td>Duration of RA (per 5 years)</td>
<td>0.92 (0.87, 0.97)</td>
</tr>
<tr>
<td>Baseline CDAI (per 6-unit increment)</td>
<td>0.96 (0.92, 0.99)</td>
</tr>
<tr>
<td>Disabled (relative to full-time employment)</td>
<td>1.33 (1.01, 1.75)</td>
</tr>
<tr>
<td>Retired (relative to full-time employment)</td>
<td>1.27 (1.11, 1.69)</td>
</tr>
<tr>
<td>Alcohol (relative to none)</td>
<td></td>
</tr>
<tr>
<td>1–3 units/week</td>
<td>1.22 (1.00, 1.47)</td>
</tr>
<tr>
<td>1–2 units/day</td>
<td>1.53 (1.14, 2.05)</td>
</tr>
<tr>
<td>3+ per day</td>
<td>2.03 (1.14, 3.63)</td>
</tr>
</tbody>
</table>

*Also adjusted for mono/no therapy, baseline patient-reported pain, baseline mHAQ, ethnicity, insurance, baseline history of csDMARD use, and baseline prednisone use/day.

CDAI, clinical disease activity index; CI, confidence interval; csDMARD, conventional synthetic disease-modifying antirheumatic drug; HR, hazard ratio; mHAQ, modified Health Assessment Questionnaire; MTX, methotrexate.

Disclosure: J. R. Curtis, Amgen, Pfizer, Crescendo Bio, Corrona, 2,AbbVie, Roche/Genentech, BMS, UCB, Myriad, Amgen, Janssen, Pfizer, Corrona, 5; G. Wallenstein, Pfizer, Inc., 1,Pfizer, Inc., 3; L. Takiya, Pfizer, Inc, 1,Pfizer, Inc, 3; D. Gruben, Pfizer Inc, 1,Pfizer, Inc, 3; C. Chen, Pfizer, Inc, 1,Pfizer, Inc, 3; Y. Shan, Corrona, LLC, 3; T. Blachley, Corrona, LLC, 3; K. J. Dandreo, Corrona, LLC, 3; J. Kremer, Corrona, LLC, 1,Corrona, LLC, 3,AbbVie, Amgen, BMS, Genentech, Lilly, Regeneron, Sanofi, Pfizer, 5,AbbVie, Genentech, Lilly, Novartis, Pfizer, 2.


Abstract Number: 1816

Sex Differences in Orthopedic Surgery Among Patients with Rheumatoid Arthritis

Michael Richter¹, Cynthia S. Crowson², Eric L. Matteson³ and Ashima Makol³, ¹Internal Medicine, Mayo Clinic, Rochester, MN, ²Health Sciences Research, Mayo Clinic College of Medicine and Science, Rochester, MN, ³Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, MN

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects II: Treatment Patterns
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Despite a decline in the incidence of orthopedic surgeries for rheumatoid arthritis (RA) in recent years, joint replacement remains an option for patients with treatment refractory disease seeking symptomatic relief and functional improvement. Although multiple factors influence the need for joint surgery in RA, it is unclear if there are sex differences in the incidence and trends of large versus small joint surgery rates in RA over time.

Methods: A retrospective medical record review was performed of all orthopedic surgeries following first fulfillment of 1987 ACR criteria for adult-onset RA in 1980-2013 among residents of a geographically defined area with follow up until death, migration or July 1, 2016. Surgeries were classified as small (wrist, hand, foot) or large (shoulder, elbow, hip, knee, ankle) joint. Trends in incidence of joint surgeries over time by sex were examined using Poisson regression models.
Results: The study included 739 women and 338 men with RA (mean age at incidence ±SD) 55.9±15.6 years). During a median follow-up of 10.7 years, 90 women and 22 men underwent at least one small joint surgery (SJS) and 141 women and 63 men underwent at least one large joint surgery (LJS). The cumulative incidence of SJS was significantly higher in women (14.4% by 15 years after RA incidence; 95% confidence interval [CI]: 11.3-17.4%) than men (7.6% at 15 years; 95% CI: 4.3-10.8%; p=0.008), but no sex differences were noted in the cumulative incidence of LJS (20.2% at 15 years among women; 95% CI: 16.8-23.6% and 18.8% among men; 95% CI: 13.8-23.5%; p=0.55). The rates of small joint surgery declined in both sexes from 2000 onward (Figure 1; p=0.002), with no differences in trends between women and men (p=0.73). LJS rates were similar among both sexes (Figure 2; p=0.85) and there was no evidence of a trend over time among both sexes combined (p=0.87).

Conclusion: Women with RA had a higher rate of SJS compared to men, although there is a declining trend in SJS rates over time in both sexes. There were no sex differences in rates of LJS, which is in contrast to higher rates of hip and knee arthroplasties seen in women compared to men in the general population\(^1\,\!\!)\(^2\). This study also confirmed an absence of increase in rates of LJS among patients with RA during the study period.

References:


Abatacept Shows Better Sustainability Than TNF Inhibitors When Used Following
Initial Biologic DMARD Failure in the Treatment of RA: 8 Years of Real-World
Observations from the Rhumadata® Clinical Database and Registry

Denis Choquette, L Bessette, Alemao, B Harauoi, F Massicotte, M Mtibaa, E Muratti, Jean-Pierre Pelletier, R Postema, Jean-Pierre Raynauld, M-A Rémillard, D Sauvageau, A Turcotte, É Villeneuve, and L Coupal, \textsuperscript{1}Rheumatology, Institut de Recherche en Rhumatologie de Montréal (IRRM), Montréal, QC, Canada, \textsuperscript{2}Centre d'ostéoporose et de rhumatologie de Québec (CORQ), Québec, QC, Canada, \textsuperscript{3}Bristol-Myers Squibb, Princeton, NJ, \textsuperscript{4}Institut de Recherche en Rhumatologie de Montréal (IRRM), Montréal, QC, Canada, \textsuperscript{5}Bristol-Myers Squibb, Montréal, QC, Canada, \textsuperscript{6}Bristol-Myers Squibb, Uxbridge, United Kingdom,
SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects II: Treatment Patterns
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: In the absence of biomarkers predicting response to a specific therapy, the choice of second biologic is based mostly on habit and availability of an alternative agent. Traditionally, a second anti-TNF was the preferred option, but recent registry data point to better responses and retention if a drug with a different mode of action is prescribed. The aim of this study was to assess the long-term retention of abatacept and TNF inhibitor (TNFi) following first biologic (b)DMARD inadequate response in RHUMADATA® registry patients with RA.

Methods: Data from RHUMADATA® patients with RA prescribed either abatacept or TNFi as the second bDMARD after January 1, 2006 were analyzed. Patients were followed until treatment discontinuation or January 9, 2017 cut-off. Patient characteristics were compared using descriptive statistics, bDMARD discontinuation rates using Kaplan–Meier methods, and proportional hazard models were used to identify predictors of treatment discontinuation.

Results: Data for 92 and 194 patients prescribed abatacept or a TNFi, respectively, as second-line treatment were extracted. No clinically significant differences in baseline characteristics were noted between treatment groups. Most patients were women (76.2%), average age (SD) was 45.1 (13.3) years at diagnosis and disease duration 10.8 (9.0) years. Most patients were stopping an anti-TNF agent: 83% of those who were switched to abatacept and 97% of those who were prescribed a second anti-TNF. Overall, 77.6% of patients stopped their first bDMARD after >6 months of treatment (secondary failure). Significant differences in retention between abatacept and TNFi groups (logrank p=0.0002) were observed (Table, Figure). Results remained unchanged for patients treated with TNFi only in first line, and primary/secondary failure of the first bDMARD did not affect sustainability of the second agent. Lack of efficacy (57.7%) and AEs (16.5%) were the most commonly cited reasons for treatment discontinuation.

Conclusion: Abatacept has better sustainability over a second line TNFi in RA patients having failed one prior bDMARD.

Original abstract © EULAR/BMJ. First presented at EULAR 2017 and published in Ann Rheum Dis 2017;76 (Suppl 2):AB0397. Any reprints, promotional options, education material etc have to be done through the original source (ARD/BMJ).
Table. First bDMARD Failure and Retention Characteristics of the Second bDMARD

<table>
<thead>
<tr>
<th>Second bDMARD</th>
<th>Abatacept</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First bDMARD</strong></td>
<td><strong>Failure type</strong></td>
</tr>
<tr>
<td><strong>failed</strong></td>
<td>Primary</td>
</tr>
<tr>
<td>TNFi, n, %</td>
<td>41, 25.5%</td>
</tr>
<tr>
<td>Other mode of action</td>
<td>6, 18.2%</td>
</tr>
<tr>
<td>Total</td>
<td>47, 24.2%</td>
</tr>
</tbody>
</table>

**Second bDMARD retention probability at:**

- 6 months: 64.68% (3.45)
- 12 months: 50.54% (3.61)
- 24 months: 39.77% (3.59)
- 60 months: 22.26% (3.53)
- 96 months: 13.22% (3.62)

**Biologic retention time (years)**

- Mean (SE): 2.71 (0.25)
- Lower quartile (95% CI): 0.36 (0.28, 0.44)
- Median (95% CI): 1.08 (0.71, 1.60)
- Upper quartile (95% CI): 4.26 (3.25, 6.64)

*% survival (SE of % survival) bDMARD=biologic DMARD; SE=standard error; TNFi=TNF inhibitor

Disclosure: D. Choquette, Bristol-Myers Squibb, 5; Bristol-Myers Squibb, 8; L. Bessette, Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, 2; Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Celgene, Lilly, Novartis, 5; E. Alemao, Stocks, stock options, or bond holdings in a for-profit corporation or self-directed pension plan for BMS, 1; Bristol-Myers Squibb, 3; B. Haraoui, BMS, Janssen, Roche Speakers bureau: Pfizer, UCB, 2; AbbVie, Amgen, BMS, Celgene, Janssen, Merck, Pfizer, Roche, Sandoz, UCB, 5; F. Massicotte, None; M. Mtibaa, Bristol-Myers Squibb, 9; Bristol-Myers Squibb, 3; E. Muratti, Sandoz Biopharmaceuticals Canada, 3; J. P. Pelletier, AbbVie, 5; R. Postema, Bristol-Myers Squibb, 1; Bristol-Myers Squibb, 3; J. P. Raynauld, AbbVie, Amgen, BMS, Janssen, Pfizer, Roche, Sanofi, Novartis, UCB, 8; M. A. Rémillard, None; D. Sauvageau, None; A. Turcotte, Amgen, Abbvie, Janssen, 8; Amgen, AbbVie, Celgene, Janssen, Pfizer, Lilly, Novartis, Merck, Sanofi, 5; É. Villeneuve, AbbVie, Roche, BMS, Pfizer, 8; Celgene, UCB, Pfizer, AbbVie, Roche, Amgen, BMS, Novartis, 5; L. Coupal, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/abatacept-shows-better-sustainability-than-tnf-inhibitors-when-used-following-initial-biologic-dmard-failure-in-the-treatment-of-ra-8-years-of-real-world-observations-from-the-
Development of Abatacept- and Adalimumab-Specific Predictive Models of Response to Therapy in RA Using Data from a Head-to-Head Study

S Bandyopadhyay\(^1\), MA Maldonado\(^1\), R Ammar\(^1\), Michael Schiff\(^2\), Michael Weinblatt\(^3\), Roy Fleischmann\(^4\) and SE Connolly\(^1\),  
\(^1\)Bristol-Myers Squibb, Princeton, NJ, \(^2\)University of Colorado, Denver, CO, \(^3\)Brigham and Women’s Hospital, Boston, MA, \(^4\)University of Texas Southwestern Medical Centre, Dallas, TX  

First publication: September 18, 2017

SESSION INFORMATION  
Session Date: Monday, November 6, 2017  
Session Title: Rheumatoid Arthritis – Clinical Aspects II: Treatment Patterns  
Session Type: ACR Concurrent Abstract Session  
Session Time: 2:30PM-4:00PM

Background/Purpose: Highly effective, targeted DMARD therapies with different mechanisms of action are available for RA. Translating precision medicine into clinical practice requires treatment-specific predictive models, with a goal of individualized, targeted therapy. Therefore, we created separate predictive models for response to abatacept (ABA) or adalimumab (ADA), using baseline biomarker (BM) data from the head-to-head AMPLE study.\(^1\)

Methods: Predictive models were built using demographic data, baseline disease characteristics and several BMs, including RF, cyclic citrullinated peptide-2 (CCP2) and BMs from the multi-biomarker disease activity test as predictor variables and ‘polar’ clinical responses as the response variables. The polar responses were defined as patients (pts) who, after 1 year of treatment, achieved an ACR70 response or failed to achieve an ACR20 response. The elastic net method\(^2\) was used to build separate predictive models for ABA and ADA responders using their respective clinical data with 6-fold cross-validation (CV) repeated 10 times. Parameter tuning for model selection was based on a fixed alpha of 0.95 and varying levels of lambda. The final model was selected based on the lambda with maximum mean area under the curve (AUC) across all folds of CV. Glmnet\(^3\) and caret\(^4\) packages in R were used for model-building purposes.

Results: Predictive models generated included 13 variables for ABA and 11 for ADA. Of all the variables, resistin, vascular cell adhesion molecule-1, sex, CCP2 and pt-reported disease activity were unique to the ABA predictor, whereas matrix metalloproteinase-1, physician-reported disease activity and disease duration were unique to the ADA predictor. The variables common to both models showed the same association (positive or negative) but differing magnitude with response. AUC by receiver operating characteristic curves were used to assess the performance of the predictive models. The performance (AUC) of the ABA model on the ABA and ADA arms was 0.855 and 0.530, respectively (Figure a, b). The performance (AUC) of the ADA model on the ADA and ABA arms was 0.860 and 0.631, respectively (Figure c, d). This indicates that the models are very specific for their respective treatment and not for the other treatment.

Conclusion: Response-to-treatment predictive models were generated using baseline data from AMPLE that were highly specific to their respective treatment. This suggests that treatment-specific response predictors could be developed and should be considered, and highlights the value of head-to-head studies in predictive biomarker generation. Further testing on validation datasets is warranted.

Delay of Diagnosis and Treatment in Seronegative Rheumatoid Arthritis: Missing the Window of Opportunity

Caitrin Coffey¹, Cynthia S. Crowson², Elena Myasoedova³, Eric L. Matteson⁴ and John M. Davis III⁵, ¹Internal Medicine, Mayo Clinic, Rochester, MN, ²Health Sciences Research, Mayo Clinic College of Medicine and Science, Rochester, MN, ³Rheumatology, Mayo Clinic, Rochester, MN, ⁴Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, MN, ⁵Division of Rheumatology, Mayo Clinic, Rochester, MN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects II: Treatment Patterns
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Disclosure: S. Bandyopadhyay, Bristol-Myers Squibb, 1,Bristol-Myers Squibb, 3; M. Maldonado, Bristol-Myers Squibb, 1,Bristol-Myers Squibb, 3; R. Ammar, Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1; M. Schiff, AbbVie, BMS, Eli Lilly, JNJ, UCB, 5,AbbVie, BMS, 8; M. Weinblatt, Amgen, BMS, Crescendo Bioscience, UCB, DxtTerity, Sanofi, 2,Amgen, BMS, Crescendo Bioscience, UCB, AbbVie, Lilly, Pfizer, Roche, 5; R. Fleischmann, AbbVie, Amgen, Astellas, AstraZeneca, BMS, Celgene, EMD-Serano, Janssen, Eli Lilly, Merck, Novartis, Pfizer, Roche, Sanofi-Genzyme, UCB, 2,AbbVie, Amgen, BMS, Celgene, GSK, Janssen, Eli Lilly, Novartis, Pfizer, Roche, Sanofi-Genzyme, UCB, 5; S. Connolly, Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1.


Abstract Number: 1819
Evidence supports a therapeutic window of opportunity in early rheumatoid arthritis (RA), during which DMARD therapy most effectively improves clinical outcomes. The 2010 ACR/EULAR classification criteria for RA require that seronegative (i.e., RF- and ACPA-) patients have more joint involvement at diagnosis than patients who are seropositive (i.e., RF+ and/or ACPA+). We hypothesized that seronegative patients experience a delay in diagnosis and, thus, a delay in treatment initiation when compared with seropositive patients, potentially causing them to miss the therapeutic window of opportunity.

Methods:

A retrospective study was performed of a population-based cohort of patients with incident RA between 2009-2013 who fulfilled either the 1987 or 2010 classification criteria. A trained nurse abstractor unaware of the hypothesis collected data from the complete medical records. Patients were classified as either seronegative or seropositive as above. Time to fulfillment of both 1987 and 2010 classification criteria, first treatment with DMARD, and first remission were calculated from the time of first documented joint swelling. Health Assessment Questionnaire (HAQ), Disease Activity Score 28 (DAS28-CRP), and Simplified Disease Activity Index (SDAI) were compared between the groups. Remission was defined according to the 2011 ACR/EULAR Boolean-based definition.

Results:

156 patients were included; 113 were seropositive and 43 seronegative. Age, sex, smoking status, and obesity did not differ between groups. Median time from first documented joint swelling to fulfillment of the 1987 (100 vs. 3 days, p=0.003) and 2010 (58 vs. 0 days, p=0.011) criteria was significantly longer in seronegative than seropositive patients. The median time from first documented joint swelling to first DMARD was also significantly longer in seronegative patients (129.5 vs. 16 days, p=0.003). Methotrexate was the first DMARD for 97 patients (62%), with no significant differences between groups.

Patients were followed for a median of 4.9 years, during which disease activity measures were available for a median of 7 visits per patient, with no significant differences between groups. Time to first biologic DMARD was similar between the groups. Seronegative patients experienced persistently higher DAS28-CRP (mean difference: 0.46, p=0.027), SDAI (mean difference: 4.9, p=0.009), and HAQ disability index (mean difference: 0.25, p=0.020) over time, adjusting for age, sex and time from fulfillment of 2010 criteria. Time to first remission was later in seronegative than seropositive patients (hazard ratio: 0.47, 95% CI 0.24, 0.94). At 5 years after fulfillment of 2010 criteria, fewer seronegative than seropositive patients achieved ≥1 remission (32 vs. 50%, p=0.034).

Conclusion:

Patients with seronegative RA experience delay in diagnosis, according to both the 1987 and 2010 classification criteria, and delay in initiation of DMARD therapy. Patients with seronegative RA also experience persistently higher disease activity and delayed remission, suggesting that these patients miss the therapeutic window of opportunity more frequently than patients with seropositive RA.

Disclosure: C. Coffey, None; C. S. Crowson, None; E. Myasoedova, None; E. L. Matteson, None; J. M. Davis III, None.


Abstract Number: 1820

Sustained Effectiveness after Remission Induction with Methotrexate and Step-Down Glucocorticoids in Patients with Early Rheumatoid Arthritis Following a Treat-to-Target Strategy after 2 Years

Veerle Stouten1, Johan Joly2, Diederik De Cock1, Sofia Pazmino1, Kristien Van der Elst2,3, René Westhovens1,2 and Patrick Verschuuren1,2, 1KU Leuven Department of Development and Regeneration, Skeletal Biology and Engineering Research Center, Leuven, Belgium, 2University Hospitals Leuven on behalf of the CareRA Study Group, Leuven, Belgium, 3KU Leuven, Department of Public Health and Primary Care, Skeletal Biology and Engineering Research Center, Leuven, Belgium

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy I: Outcomes Therapy
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM
**Background/Purpose:**

Remission induction with methotrexate (MTX) and a moderate-dose, step-down scheme of Glucocorticoids (GC), (COBRA Slim strategy), showed equally high remission rates at year 1 and a more favourable safety profile compared to DMARD combinations, even at a higher step-down GC dosage, in patients with early Rheumatoid Arthritis (eRA). Objectives were to compare response rates, disease activity states and medication use, 2 years after induction with different intensive combination strategies, focusing on the high-risk population from CareRA.

**Methods:** CareRA is a two-year prospective investigator-initiated multicentre RCT. csDMARD naïve eRA patients were stratified into a high- or low-risk group based on classical prognostic markers. High-risk patients (n=289) were randomized to 1/3 arms: 1) COBRA Classic: MTX+ Sulphasalazine +60mg prednisone tapered over 6 weeks to 7.5mg daily; 2) COBRA Slim: MTX+30mg prednisone tapered over 5 weeks to 5 mg daily; 3) COBRA Avant-Garde: MTX+Leflunomide+30mg prednisone tapered over 5 weeks to 5 mg daily. From week 28, GC were tapered and stopped at week 34. From week 40, DMARD monotherapy was aimed for. A treat-to-target approach was applied per protocol until year 1 and afterwards at the discretion of the rheumatologist. Co-primary endpoint was proportion with DAS28-CRP<2.6 (“remission”), other efficacy measures were HAQ=0, DAS28-CRP change, ACR20/50/70 and clinically meaningful HAQ response (ITT analysis). Adverse events related to therapy (AEs) were registered, as well as RA medication use. Missing data were imputed by last observation carried forward.

**Results:** The proportion of high-risk patients with DAS28-CRP<2.6 at year 2 remained high and did not differ between the Classic (65.3%), Slim (73.5%) and Avant-garde (73.1%) group (p=0.369). Of patients with a DAS28-CRP<2.6 at year 1, 54.7% in Classic, 67.8% in Slim and 70.2% in Avant-Garde retained a DAS28-CRP<2.6 at every trimonthly evaluation until year 2. Persistently high and comparable ACR50 response rates were achieved in all groups. The total numbers of AEs related to study therapy, were 209 in 72 Classic patients, 164 in 69 Slim patients and 208 in 74 Avant-Garde patients (p=0.029). During the CareRA study, biologicals were started in 44 high-risk patients (15.2%): 18 Classic, 11 Slim and 15 Avant-Garde patients. At year 2, most patients were on MTX monotherapy: 67% in Classic, 63% in Slim and 49% in Avant-Garde. Only 14% of the high-risk population was taking oral GCs at year 2 at an average dose of 6.4mg prednisone equivalent.

**Conclusion:** All groups showed persistently high response rates and favourable disease activity states, 2 years after remission induction with csDMARDs and GCs in a treat to target setting. COBRA Slim showed comparable efficacy and ability to achieve sustained disease control with less adverse events, compared to DMARD combinations with GC at moderate or high induction dosages.

### Table

<table>
<thead>
<tr>
<th></th>
<th>COBRA Classic</th>
<th>COBRA Slim [high-risk]</th>
<th>COBRA Avant-Garde</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAS28-CRP change 6-12 month</td>
<td>2.6±1.4</td>
<td>2.6±1.3</td>
<td>2.6±1.6</td>
<td>0.966</td>
</tr>
<tr>
<td>DAS28-CRP change 12-24 month</td>
<td>0.0±1.0</td>
<td>0.2±1.0</td>
<td>0.3±1.1</td>
<td>0.412</td>
</tr>
<tr>
<td>DAS28-CRP &lt;2.6 (“remission”) year 1</td>
<td>65.3%</td>
<td>60.2%</td>
<td>61.3%</td>
<td>0.741</td>
</tr>
<tr>
<td>DAS28-CRP &lt;2.6 (“remission”) year 2</td>
<td>65.3%</td>
<td>73.5%</td>
<td>71.1%</td>
<td>0.189</td>
</tr>
<tr>
<td>ACR50 improvement year 2</td>
<td>74.5%</td>
<td>78.6%</td>
<td>75.9%</td>
<td>0.797</td>
</tr>
<tr>
<td>ACR70 improvement year 2</td>
<td>56.1%</td>
<td>60.2%</td>
<td>59.1%</td>
<td>0.635</td>
</tr>
<tr>
<td>Clinically meaningful HAQ change</td>
<td>41.8%</td>
<td>36.7%</td>
<td>44.1%</td>
<td>0.568</td>
</tr>
<tr>
<td>HAQ &lt; 0.1</td>
<td>70.4%</td>
<td>65.2%</td>
<td>70.7%</td>
<td>0.863</td>
</tr>
<tr>
<td>HAQ decrease</td>
<td>39.6%</td>
<td>37.8%</td>
<td>38.7%</td>
<td>0.908</td>
</tr>
</tbody>
</table>

*DAS28-CRP* = 28 joint disease activity score calculated with C-reactive protein; “remission” = DAS28-CRP<2.6; ACR improvement to the 20, 50 or 70% level; improvement in 28 tender and 28 swollen joint count; AND in 3/5 of pain visual analog scale (VAS); patient global assessment VAS; physician global assessment VAS; CRP and HAQ; HAQ<0.1 health assessment questionnaire; clinically meaningful HAQ change = HAQ change >0.22.

**Disclosure:** V. Stouten, None; J. Joly, None; D. De Cock, None; S. Pazmino, None; K. Van der Elst, None; R. Westhovens, None; P. Verschueren, Patrick Verschueren, 2, Patrick Verschueren, 9.

Dose Reduction of Baricitinib in Patients with Rheumatoid Arthritis Achieving Sustained Disease Control: Results of a Prospective Study

Tsutomu Takeuchi1, Mark C. Genovese2, Boulos Haraoui3, Zhanguo Li4, Li Xie5, Rena Klar6, Ana Pinto Correia5, Li Xie5, Rena Klar6, Ana Pinto Correia5, Pedro Lopez-Romero7, Inmaculada de la Torre5, Terence P. Rooney5 and Josef S. Smolen8, 1Keio University School of Medicine, Tokyo, Japan, 2Stanford University Medical Center, Palo Alto, CA, 3Institut de Rhumatologie de Montreal, Montreal, QC, Canada, 4Peking University People's Hospital, Beijing, China, 5Eli Lilly and Company, Indianapolis, IN, 6Quintiles IMS Holdings, Inc., Durham, NC, 7Europe Research Center, Eli Lilly and Company, Madrid, Spain, 8Medical University of Vienna, Vienna, Austria

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy I: Outcomes Therapy
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: In patients (pts) with active RA and inadequate response (IR) to DMARDs, phase 3 studies demonstrated efficacy of baricitinib (2-mg and 4-mg). Larger, more rapid treatment effects were observed with baricitinib 4-mg. The objective of this study was to investigate the effects of baricitinib dose step-down in patients who achieved sustained disease control with baricitinib 4-mg.

Methods: Pts with RA who completed a baricitinib phase 3 study could enter a long-term extension (LTE) study. In the LTE, pts who received baricitinib 4-mg for ≥15 months and who achieved sustained low disease activity ([LDA] - CDAI score ≤10 for pts from RA-BUILD, RA-BEAM, RA-BEACON) or remission (CDAI ≤2.8 for DMARD-naïve pts from RA-BEGIN) at 2 consecutive visits ≥3 months apart were re-randomized in a blinded manner to either continue baricitinib 4-mg or step down to 2-mg. Pts could be rescued (to baricitinib 4-mg) if CDAI >10, or > 2.8 for pts from RA-BEGIN. Efficacy and safety were assessed through 48 weeks following re-randomization.

Results: The majority of pts in both groups maintained the state of LDA or remission over the 48-week period. However, dose reduction to 2-mg resulted in significant increases in disease activity at 12, 24, and 48 weeks. Dose reduction also resulted in a more rapid time to relapse (defined as loss of step-down eligibility criteria) with significantly more pts relapsing over 48 weeks compared to the 4-mg group. Rescue rates were 9.6% for baricitinib 4-mg, and 18.3% for baricitinib 2-mg. Most rescued pts could regain LDA or remission with the 4-mg dose. Dose reduction was associated with a numerically lower rate of non-serious infections; rates of serious adverse events and adverse events leading to discontinuation were similar across groups.

Conclusion: These data indicate disease control was better maintained on the 4-mg dose than 2-mg. Nonetheless, most stepped-down pts could maintain LDA or remission, or recapture control with return to the 4-mg dose if needed. Stepping down to a dose of 2-mg daily may be a reasonable consideration for some pts after having achieved sustained LDA or remission on the 4-mg dose.
### Patients originating from RA-BEAM, RA-BUILD, RA-BEACON Combined†

<table>
<thead>
<tr>
<th></th>
<th>Week 12</th>
<th>Week 24</th>
<th>Week 48</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Continued bari 4-mg</td>
<td>Stepped down to bari 2-mg</td>
<td>Continued bari 4-mg</td>
</tr>
<tr>
<td><strong>Efficacy measure</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(93.5)</td>
<td>(82.9)**</td>
<td>(86.9)</td>
</tr>
<tr>
<td>CDAI remission ≤2.8</td>
<td>101/245</td>
<td>94/245</td>
<td>108/245</td>
</tr>
<tr>
<td></td>
<td>(41.2)</td>
<td>(38.4)</td>
<td>(44.1)</td>
</tr>
</tbody>
</table>

**NRI only for missing data (observed data used after rescue)**

| CDAI LDA ≤10     | 229/245 | 203/245 | 218/245 | 200/245 | 212/245 | 196/7. |
|                  | (93.5)  | (82.9)** | (89.0)  | (81.6)* | (86.5)  | (80.   )|
| CDAI remission ≤2.8 | 101/245 | 94/245  | 109/245 | 96/245  | 103/245 | 90/2   |
|                  | (41.2)  | (38.4)  | (44.5)  | (39.2)  | (42.0)  | (36.   )|

### Safety measure

<table>
<thead>
<tr>
<th>n [EAIR]</th>
<th>Weeks 0-48</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Continued bari 4-mg</td>
</tr>
<tr>
<td></td>
<td>N=245</td>
</tr>
<tr>
<td>SDEAE</td>
<td>149 [67.4]</td>
</tr>
<tr>
<td>Infection</td>
<td>65 [29.4]</td>
</tr>
<tr>
<td>SAE</td>
<td>17 [7.7]</td>
</tr>
<tr>
<td>Serious infection</td>
<td>5 [2.3]</td>
</tr>
<tr>
<td>AE ® discontinuation</td>
<td>7 [3.2]</td>
</tr>
</tbody>
</table>

Efficacy and safety data are n/N (%), and n [EAIR], respectively. †RA-BEAM=MTX-IR pts; RA-BUILD=csDMARD-IR pts; RA-BEACON=bDMARD-IR pts; AE=adverse event; bari=baricitinib; CDAI=Clinical Disease Activity Index; EAIR=exposure-adjusted incidence rate; LDA=low disease activity; n=number of responders; N=the number of patients re-randomized to the step down period at least 48 weeks prior to the data cut-off date (September 1, 2016); NRI=nonresponder imputation; SAE=serious adverse event; SDEAE=step-down emergen adverse event; *p≤0.05; **p≤0.01, ***p≤0.001 vs. continued bari 4-mg.

### Time to loss of step-down eligibility criteria

The figure represents patients who have completed 48 weeks in the step-down period, or would have completed 48 weeks if not discontinued. Relapse defined as loss of step-down eligibility criteria, or CDAI ≥ 10 for patients originating from RA-BUILD, RA-BEAM, or RA-BEACON; CDAI ≥ 2.8 for patients originating from RA-BEGIN. The p-value was computed using the Wilcoxon test.

The Effect of Sarilumab in Combination with Dmards on Fasting Glucose and Glycosylated Hemoglobin in Patients with Rheumatoid Arthritis with and without Diabetes

Mark C. Genovese1, Roy Fleischmann2, Owen Hagino3, Chih-Chi Hu4, Claudia Pena-Rossi3, Jonathan Sadeh3, Neil M.H. Graham5, Erin K. Mangan5, Hubert van Hoogstraten4 and Thomas Mandrup-Poulsen6, 1Stanford University Medical Center, Palo Alto, CA, 2Metroplex Clinical Research Center, University of Texas Southwestern Medical Center, Dallas, TX, 3Sanofi, Bridgewater, NJ, 4Sanofi Genzyme, Bridgewater, NJ, 5Regeneron Pharmaceuticals, Inc., Tarrytown, NY, 6University of Copenhagen, Copenhagen, Denmark

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy I: Outcomes Therapy
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: IL-6 involvement has been reported in glucose metabolism.1-4 Sarilumab, a human mAb blocking the IL-6Rα, was evaluated for treatment of RA in 3 clinical trials: MOBILITY, TARGET, and MONARCH. This analysis examined effects of sarilumab or placebo (Pbo), plus DMARDs, on fasting glucose and glycosylated hemoglobin (HbA1c) in patients with RA, with and without diabetes.

Methods: Fasting glucose and HbA1c data were collected during 2 Pbo-controlled studies of sarilumab plus DMARDs: MOBILITY and TARGET. Studies excluded patients with HbA1c ≥9.0%. Patients with baseline (BL) and ≥1 post-BL sample were included in post hoc pooled analyses and categorized as diabetic (DIAB) or non-DIAB based on medical history of diabetes or prior use of antidiabetic medication. Changes from BL in fasting glucose, HbA1c and weight were analyzed with a linear regression model. Spearman rank correlation coefficient was calculated for changes in glucose, HbA1c, and high-sensitivity (hs)-CRP. Changes in these parameters were stratified by clinical response. Clinical meaningfulness was based on comparison with results of clinical trials with antidiabetic medications.5

Results: The DIAB group (n=179) compared with the non-DIAB group (n=1803) had higher BL body weight (mean ± SD, kg: 84.8 ± 21.4 vs 74.6 ± 18.8) and a larger proportion of patients with BMI ≥30 kg/m² (56.7% vs 31.9%). Mean fasting glucose and HbA1c at BL were similar across treatment groups (Pbo, and sarilumab 150 and 200 mg every 2 wks [q2w]) but higher in the DIAB group than in the non-DIAB group (Table). Patients in the DIAB group had a greater reduction in fasting glucose at wk 24 compared with those in the non-DIAB group. Decreases in HbA1c occurred in non-DIAB and DIAB sarilumab-treated groups but not with Pbo. The treatment effect was largest in the DIAB group. At wk 24, the change in HbA1c was -0.43% in the DIAB (sarilumab 200 mg q2w) group and +0.17% in the DIAB (Pbo) group (-0.69% mean difference; P<0.001). Reductions in fasting glucose and HbA1c were observed in sarilumab-treated DIAB subgroups independently of changes in hs-CRP, ACR50, or DAS28-CRP remission status, and despite increases in mean body weight. The overall safety of sarilumab did not differ between DIAB and non-DIAB patients with RA.
Conclusion: Sarilumab + DMARDs reduced fasting glucose and HbA1c in DIAB and HbA1c in non-DIAB patients with RA, independent of changes in body weight, hs-CRP, ACR50, or DAS28-CRP remission status at wk 24. In DIAB patients, the difference in HbA1c reduction between sarilumab 200 mg q2w and Pbo was clinically meaningful.

References:

Disclosure: M. C. Genovese, Roche, Sanofi, GlaxoSmithKline, R-Pharm, and Bird Rock Bio, 2,Roche, Sanofi, GlaxoSmithKline, R-Pharm, and Bird Rock Bio, 5; *R. Fleischmann*, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, EMD Serono, Genentech, GlaxoSmithKline, Janssen, Eli Lilly, Pfizer, Roche, Sanofi, and UCB, 2,AbbVie, Akros Pharma, Amgen, Bristol-Myers Squibb, Genentech, GlaxoSmithKline, Janssen, Eli Lilly, Pfizer, Roche, Sanofi, and UCB, 5; *O. Hagino*, Sanofi, 1,Sanofi, 3; *C. C. Hu*, Sanofi-Genzyme, 1,Sanofi Genzyme, 3; *C. Penna-Rossi*, Sanofi, 1,Sanofi, 3; *J. Sadeh*, Sanofi, 1,Sanofi, 3; *N. M. H. Graham*, Regeneron Pharmaceuticals, Inc., 1,Regeneron Pharmaceuticals, Inc., 1,Regeneron Pharmaceuticals, Inc., 3; *H. van Hoogstraten*, Sanofi Genzyme, 3,Sanofi Genzyme, 1; *T. Mandrup-Poulsen*, Sanofi, 5.


**Abstract Number:** 1823

**Methotrexate Requires High Serum BAFF Levels to Prevent Immunization Against TNF-α Inhibitors**

Samuel Bitoun1, Pierre Donnès2, Aline Doublet3, Kimberly Florence4, Agnes Hincelin-Mery5, Gaëtan Nocturne6, Mattieu Allez7, N Ruperto8, Marc Pallardy9 and Xavier Mariette10, 1INSERM U1184, IMVA, Paris Sud University,LabEx LERMIT, Le Kremlin Bicêtre, France, 2SciCross AB, Skövde, Sweden, 3Department of Rheumatology, Kremlin-Bicêtre hospital INSERM U1184, Le Kremlin Bicêtre, France, 4Immunogenetics and Clinical Immunology, GlaxoSmithKline, King of Prussia, PA, 5Sanofi, Chilly-Mazarin, France, 6INSERM U1184, IMVA, Paris Sud University,LabEx LERMIT, Le Kremlin Bicêtre, France, 7Department of Gastroenterology, Hopital Saint-Louis, APHP, Paris, France, 8PRINTO Coordinating Centre, Genoa, Italy, 9Inflammation, Chimiokines et Immunopathologie, INSERM UMR 996, Faculté de Pharmacie, Chatenay Mallabry, France, 10Université Paris Sud, Paris, France

First publication: September 18, 2017
**Background/Purpose:** Immunization against TNF Inhibitors (TNFi) is observed in 30-50% of patients with inflammatory rheumatic diseases. With most TNFi, anti-drug antibodies (ADA) lead to rapid decrease of drug concentration that cause relapses. One of the identified factors of prevention of ADA is the co-prescription of methotrexate (MTX). In preliminary data from animal models, MTX is dramatically more efficient in preventing TNFi immunogenicity in B-cell Activating Factor (BAFF) overexpressing mice. The mechanism of interaction between MTX and BAFF could be an increase of the ectoenzyme CD73 expression induced by BAFF which may favor the transformation of AMP (released from the cell by MTX) in adenosine, a powerful immune-regulatory mediator. The goal of this study is to investigate in the clinics a possible interaction between MTX and BAFF to prevent ADA against TNFi.

**Methods:** Patients from the ABIRISK study, which is designed to prospectively identify risk factors of ADA against TNFi were included in this study. Patient’s underlying disease was Rheumatoid Arthritis, (RA) Inflammatory Bowel Disease (IBD) or Juvenile Inflammatory Arthritis (JIA). Patients were considered treated by MTX when this treatment was concomitantly administered with the newly introduced TNFi. Baseline serum was used for BAFF assay. Free BAFF serum levels were quantified using a new highly sensitive Errena immunoassay system based on single molecule counting. ADA were screened at 3, 6, 12 and 24 months post TNFi therapy using a modified Theradiag© assay. Patients with at least one time point with ADA detection were considered immunized (ADA+). Comparisons of BAFF levels among different subsets of patients were performed using Welch’ test.

**Results:** Serum BAFF quantification was performed in 383 patients (191 RA, 173 IBD and 19 JIA) who had undergone at least one dosage of ADA. In the 103 patients (91 RA and 12 IBD) treated with MTX, 9 (8.7%) developed ADA versus 28 (13.5%) in the non-MTX treated patients. In the 103 MTX-treated patients, the level of BAFF was significantly lower (0.49ng/mL) in ADA+ patients than in ADA-patients (0.69ng/mL p=0.02, Fig 1A). The removing of 3 patients with a low level of ADA against etanercept reinforces the association between low serum BAFF level and ADA (p=0.006). Conversely, in the 208 non-MTX treated patients, there was no significant difference in the serum level of BAFF between ADA+ and ADA- patients (p=0.65 Fig 1B).

**Conclusion:** These clinical data support the preliminary findings we have got in mice on an interaction between MTX and BAFF for preventing ADA formation. Patients treated with TNFi and MTX who do not develop ADA have a higher serum BAFF level than patients who develop ADA. Conversely, serum BAFF level has no influence on ADA formation in non MTX-treated patients. Thus, MTX might require high BAFF levels to prevent immunization against TNFi.

**Disclosure:** S. Bitoun, None; P. Dönnes, Sci Cross, 3; A. Doublet, None; K. Florence, GlaxoSmithKline, 3; A. Hincelin-Mery, Sanofi-Aventis Pharmaceutical, 3; G. Nocturne, None; M. Allez, None; N. Ruperto, None; M. Pallardy, None; X. Mariette, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/methotrexate-requires-high-serum-baff-levels-to-prevent-immunization-against-tnf-%ce%b1-inhibitors](http://acrabstracts.org/abstract/methotrexate-requires-high-serum-baff-levels-to-prevent-immunization-against-tnf-%ce%b1-inhibitors)

**Abstract Number: 1824**

**Evaluation of Pneumococcal and Tetanus Vaccine Responses in Patients with Rheumatoid Arthritis Receiving Baricitinib: Results from a Long-Term Extension Trial Substudy**
Kevin Winthrop1, Clifton O. Bingham III2, John D. Bradley3, Maher Issa3, Rena Klar4 and Cynthia E. Kartman3, 1Oregon Health and Sciences University, Portland, OR, 2Rheumatology, Johns Hopkins University, Baltimore, MD, 3Eli Lilly and Company, Indianapolis, IN, 4Quintiles IMS Holdings, Inc., Durham, NC

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy I: Outcomes Therapy
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Clinical guidelines recommend pneumococcal and tetanus vaccinations in patients (pts) with RA.1 Baricitinib (biri) is an oral, selective Janus kinase (JAK) 1/JAK 2 inhibitor and is approved in the EU for the treatment of moderately to severely active RA in adults. The objective of this substudy was to evaluate pneumococcal conjugate and tetanus toxoid vaccine responses in pts with RA receiving bari. These vaccines elucidate predominantly T-cell-dependent humoral antibody responses.2

Methods: Eligible RA pts in a Phase 3 long-term extension (LTE) trial (RA-BEYOND) in US/Puerto Rico receiving bari 2 or 4 mg with or without concomitant MTX were enrolled. Baseline antibody titers were measured and pts were vaccinated with Prevnar 13® (Pneumococcal 13-valent Conjugate Vaccine [Diphtheria CRM197 Protein]; Wyeth; PCV13) and Boostrix® (Tetanus Toxoid Vaccine, Reduced Diphtheria Toxoid, and Acellular Pertussis Vaccine, Adsorbed; GlaxoSmithKline Biologicals; Tdap). The primary endpoints were the proportion of pts achieving a satisfactory humoral response defined as 1) a ≥2-fold increase in anti-pneumococcal antibody titers in ≥6/13 serotypes and 2) a ≥4-fold increase in anti-tetanus titers at 5 wks post-vaccination.

Results: Of the 106 pts, 80% were female, 32 (30.2%) were taking glucocorticoids, with a mean age of ~55 yrs and a mean duration of RA ~12 yrs; 89% (N=94) were taking bari+MTX and 11% (N=12) were taking bari without MTX. Most pts (97% PCV13/96% Tdap) completed the evaluations (Table 1). The small size of the bari without MTX group precluded subgroup analysis; response in the overall group is reported here. Over two-thirds of pts (68.0%; 95% CI, 58.4, 76.2) achieved a positive response in ≥6/13 PCV13 serotypes (Table 1). Forty-three percent (43.1%; 34.0, 52.8) achieved a ≥4-fold increase in anti-tetanus titers and 73.5% (64.2, 81.1) achieved a ≥2-fold increase (Table 1). Through 12 weeks post-vaccination, 7 pts (6.6%) reported injection site events possibly related to vaccination. Two pts reported moderate pain. There were no serious adverse events (AE) related to the vaccine. (AE monitoring in the LTE trial was on-going.)

Conclusion: The proportions of pts on long-term bari (89% were on concomitant MTX) who achieved satisfactory humoral response five weeks post-vaccination were 68% for pneumococcal conjugate vaccine and 43% for tetanus toxoid vaccine (a ≥4-fold increase). These responses are broadly in line with responses to PCV13,3 23-valent pneumococcal polysaccharide vaccine (PPSV23),4,5 and tetanus toxoid vaccines2,5 described for other contemporary RA therapies.

References:
Table 1. Satisfactory Humoral Responses 5 Wks Post-vaccination for Overall Baricitinib

<table>
<thead>
<tr>
<th>Overall baricitinib</th>
<th>N=106</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of pts immunized with PCV13, n (%)</td>
<td>100 (100)</td>
</tr>
<tr>
<td>No. of pts with a baseline and Wks 5 PCV13 titer, N-obs (%)</td>
<td>103 (97.2)</td>
</tr>
<tr>
<td>No. of pts immunized with Tdap, n (%)</td>
<td>105 (99.1)</td>
</tr>
<tr>
<td>No. of pts with a baseline and Wks 5 Tdap titer, N-obs (%)</td>
<td>102 (96.2)</td>
</tr>
<tr>
<td>No. of pts with ≥2-fold increase in anti-pneumococcal IgG antibody titer in ≥2 pneumococcal serotypes, n (%) [95% CI]</td>
<td>70 (68.0) [58.4, 76.2]</td>
</tr>
<tr>
<td>No. of pts with ≥2-fold increase in anti-tetanus IgG antibody titer in pts with baseline anti-tetanus IgG titer ≥0.1 IU/ml, n (%) [95% CI]</td>
<td>44 (43.1) [34.0, 52.8]</td>
</tr>
<tr>
<td>No. of pts with ≥2-fold increase in anti-tetanus IgG antibody titer in pts with baseline anti-tetanus IgG titer ≥0.1 IU/ml, n (%) [95% CI]</td>
<td>75 (73.5) [64.2, 81.1]</td>
</tr>
</tbody>
</table>

aPCV13 serotypes are 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F.

b95% CI calculations based on the Wilson score method without continuity correction.

C-O. Bingham III, Pfizer, 5; K. Winthrop, Eli Lilly and Company, 5, Pfizer, BMS, 2; C. O. Bingham III, Eli Lilly and Company, 5; J. D. Bradley, Eli Lilly and Company, 1, Eli Lilly and Company, 3; M. Issa, Eli Lilly and Company, 1, Eli Lilly and Company, 3; R. Klar, Quintiles IMS Holdings, Inc., 3; C. E. Kartman, Eli Lilly and Company, 1, Eli Lilly and Company, 3.

Abstract Number: 1825

Comparative Analysis of Achievement of Individual Important Response Measured By DAS28dcrit in a Randomized Head-to-Head Trial of Tocilizumab Vs. Adalimumab in Active Rheumatoid Arthritis

Michaela Koehm1, Michael Hofmann2, Rasmus Lüthje2, Matthew McIntosh3, Varghese Abraham4, Cem Gabay4, Arthur Kavanaugh5, Harald Burkhardt6 and Frank Behrens6, 1Division of Rheumatology and Fraunhofer IME-Project-Group Translational Medicine and Pharmacology, Goethe University, Frankfurt/Main, Germany, 2Rheumatology, Chugai Pharma Europe Ltd., Frankfurt, Germany, 3Genentech, San Francisco, CA, 4SCQM, Geneva, Switzerland, Genev, Switzerland, 5Medicine, University of California, San Diego, La Jolla, CA, 6Division of Rheumatology and Fraunhofer IME-Project-Group Translational Medicine and Pharmacology, Goethe University, Frankfurt, Germany

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy I: Outcomes Therapy
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:

Fluctuations in disease activity due to short-term situational effects and measurement errors are important considerations for evaluation of individual clinically meaningful therapeutic response in daily practice in patients with rheumatoid arthritis (RA). To address this aspect, we established a statistical approach to determine a critical difference (dcrit) that defines valid criterion for response as assessed by the Disease Activity Score-28 joints (DAS28-ESR)1. In this analysis, DAS28dcrit response was evaluated post-hoc from a RCT (ADACTA2) comparing Tocilizumab (TCZ) to Adalimumab (ADA) treatment.

Methods:

Patient population was derived from AADACTA2 with active RA treated with monotherapy of TCZ (8mg/kg) and ADA (40 mg e.o.w.). 325 patients were analyzed. DAS28dcrit response of 1.8 was used as cut off for an individual important improvement of DAS28 derived from the established statistical approach on validation of DAS28dcrit response1. The cohort was used to calculate the proportion...
achieving DAS28\textsubscript{dcrit} response at every study visit (BL up to week 24). DAS28 \textsubscript{dcrit} response was compared to standard disease activity measurements. Achievement of DAS28\textsubscript{dcrit} response at multiple visits in individual patients (not consecutive) was evaluated.

**Results:**

Patient population of both treatment arms was comparable in disease activity at baseline, balance of gender and pretreatment. In the TCZ group, 53.8% of the patients achieved DAS28\textsubscript{dcrit} response at week 4, 75.2% at week 8, 82.7% at week 12, 84.5% at week 16, 89.5% at week 20 and 90.1% at week 24. In the ADA group, 36.6% achieved DAS28\textsubscript{dcrit} response at week 4, and 44.8% at week 8, 48.6% at week 12, 51.4% at week 16, 63.0% at week 20 and 59.1% at week 24 (Table 1). In the TCZ group, 88.3% of patients achieved DAS28\textsubscript{dcrit} response at least at 3 visits, 77.9% at least at 4, 65.5% at least at 5 and 37.2% at least at 6 visits; for the ADA group, 67.8% at least at 3, 53.0% at least at 4, 40.9% at least at 5 and 22.6% at least at 6 visits.

**Conclusion:**

The established critical differences for DAS28 (DAS28\textsubscript{dcrit}) of 1.8 was confirmed in an independent cohort of ADA-treated patients\textsuperscript{1}. In the RCT ADACTA\textsuperscript{2}, for the cut-off of 1.8, high percentages of patients achieved this level of response even early after initiation of TCZ-treatment (week 4 and 8) compared to ADA treatment. Stability of TCZ treatment effect was shown by approx. 78% of the patients (compared to 53.0% for ADA) with at least 4 visits out of 6 with DAS28\textsubscript{dcrit} response.

**References:**


**Disclosure:** M. Koehm, Pfizer Inc, 2; M. Hofmann, Chugai, 3; R. Lüthje, Chugai, 3; M. McIntosh, Genentech and Biogen IDEC Inc., 3; V. Abraham, Genentech and Biogen IDEC Inc., 3; C. Gabay, Roche, Pfizer, AB2 Bio, 2, Sanofi, AB2 Bio, AbbVie, Pfizer, BMS, MSD, Roche, Novartis, 5; A. Kavanaugh, Pfizer, AbbVie, Amgen, Janssen, UCB, Novartis, Eli Lilly, 5, AbbVie, Amgen, Janssen, UCB, Eli Lilly, Novartis, Pfizer, 2; H. Burkhardt, Pfizer Inc, 2; F. Behrens, Chugai, Abbvie, 2, Chugai, Abbvie, 8.


**Abstract Number:** 1826

**Secukinumab Achievement of Psoriatic Arthritis Disease Activity Score (PASDAS) Related Remission: 2-Year Results from a Phase 3 Study**

Laura C Coates\textsuperscript{1}, Dafna D Gladman\textsuperscript{2}, Peter Nash\textsuperscript{3}, Oliver FitzGerald\textsuperscript{4}, Arthur Kavanaugh\textsuperscript{5}, Lawrence Rasouliyan\textsuperscript{6}, Luminita Pricop\textsuperscript{7}, Kevin Ding\textsuperscript{7} and Corine Gailliez\textsuperscript{8}, \textsuperscript{1}Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, United Kingdom, \textsuperscript{2}Toronto Western Hospital, Toronto, ON, Canada, \textsuperscript{3}University of Queensland, Brisbane, Australia, \textsuperscript{4}St Vincent's University Hospital, Dublin, Ireland, \textsuperscript{5}UC San Diego School of Medicine, La Jolla, CA, \textsuperscript{6}RTI Health Solutions, Barcelona, Spain, \textsuperscript{7}Novartis Pharmaceuticals Corporation, East Hanover, NJ, \textsuperscript{8}Novartis Pharma AG, Basel, Switzerland

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment II  
**Session Type:** ACR Concurrent Abstract Session  
**Session Time:** 2:30PM-4:00PM
Background/Purpose: Psoriatic arthritis (PsA) disease activity score (PASDAS) assessing multiple facets of PsA was demonstrated to distinguish treatment effect, perform better in statistical terms than traditional joint-only indices and could be used as a treatment target in clinical trials in PsA. Secukinumab significantly improved the signs and symptoms of PsA over 104 weeks (wks) in the FUTURE 2 study. This post-hoc analysis assessed the ability of secukinumab to achieve low disease activity (LDA) or remission (REM) using PASDAS through 104 wks in the FUTURE 2 study.

Methods: FUTURE 2 study design has been previously published. PASDAS index is derived from physician’s global VAS, patient’s global VAS, SF-36 PCS, tender and swollen joint counts, Leeds enthesitis count, dactylitis count and CRP level with validated cut-points for high disease activity (HDA ≥5.4), moderate disease activity (3.2< MoDA <5.4), 1.9< LDA ≤3.2 and REM ≤1.9. PASDAS was assessed in the overall population and in patients (pts) stratified by prior anti-TNF use (naïve vs inadequate response [IR]) and disease duration (<2 years vs >2 years since first PsA diagnosis) and reported using mutually exclusive categories at group level and as observed analysis.

Results: PASDAS score at baseline was similar across the three treatment groups. In the overall population at Wk 16, PASDAS REM, LDA, and MoDA were achieved in: 15.6%, 22.9%, and 49.0% of pts, respectively; treated with secukinumab 300 mg; 15.2%, 19.2%, and 42.4%, respectively, with secukinumab 150 mg group vs. 2.3%, 13.8%, and 44.8%, respectively with placebo (PBO). At Wk 104, REM was achieved in 22.9% and 14.3% pts treated with secukinumab 300 and 150 mg, respectively. The proportion of pts achieving PASDAS derived criteria at Wks 16 and 104 by anti-TNF status is reported in the figure. The proportion of pts achieving PASDAS REM/LDA at Wks 16 and 104 was similar, irrespective of time since first diagnosis, for both secukinumab doses. Secukinumab treated pts achieving PASDAS REM had significantly greater improvements in function, physical and mental health quality of life, and fatigue compared to HDA through Wk 104.

Conclusion: PASDAS REM and LDA were achieved in 38.5% and 34.4% pts treated with secukinumab 300 and 150 mg, respectively, vs 16.1% in placebo group at Wk 16, with approximately 50% pts achieving PASDAS REM and LDA in both secukinumab groups at Wk 104. A higher proportion of anti-TNF-naïve pts treated with secukinumab achieved PASDAS REM or LDA than anti-TNF-IR through Wk 104. Secukinumab treated pts achieving PASDAS REM had significantly greater improvements in function, quality of life, and fatigue.


Disclosure: L. C. Coates, Abbvie, Janssen, 2, Abbvie, BMS, Celgene, Pfizer, UCB, MSD, Boehringer Ingelheim, Novartis, Lilly, Janssen, 5; D. D. Gladman, Amgen, AbbVie, BMS, Celgene, Eli Lilly, Janssen, Novartis, Pfizer and UCB., 2; P. Nash, Novartis, Abbvie, Roche, Pfizer, BMS, Janssen, and Celgene, 2, Novartis, Abbvie, Roche, Pfizer, BMS, Janssen, and Celgene, 5, Novartis, Abbvie, Roche, Pfizer, BMS, Janssen, and Celgene, 8; O. FitzGerald, Bristol-Myers Squibb, Roche, Abbott Laboratories, Pfizer Inc, UCB Pharma Ltd, 5; A. Kavanaugh, Navartis, 5; L. Rasouliyan, Novartis, 5, RTI Health Solutions, 3; L. Pricop, Novartis Pharmaceutical Corporation, 1, Novartis Pharmaceutical Corporation, 3; K. Ding, Novartis Pharmaceuticals Corporation, 1, Novartis Pharmaceuticals Corporation, 3; C. Gaillez, Novartis Pharma AG, BMS, 1, Novartis Pharma AG, 3.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/secukinumab-achievement-of-psoriatic-arthritis-disease-activity-score-pasdas-related-remission-2-year-results-from-a-phase-3-study
Comparison of Ixekizumab and Ustekinumab Efficacy in the Treatment of Nail Lesions of Patients with Moderate-to-Severe Plaque Psoriasis: 24-Week Data from a Phase 3 Trial

Pierre-Dominique Ghislain¹, Curdin Conrad², Yves Dutronc³, Carsten Henneges³, David Sandoval Calderon³, Myriam Vincent³, Liesbet Ghys³, Jolien de Gruijter³, and Peter C M van de Kerkhof¹, Cliniques Universitaires Saint-Luc, Brussels, Belgium; 2Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland; 3Eli Lilly and Company, Indianapolis, IN; 4Department of Dermatology, Radboud University Nijmegen Medical Center, Nijmegen, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment II
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Nails are frequently involved in psoriasis and represent one of the most difficult to treat manifestations of the disease. This study evaluated the comparative efficacy of ixekizumab (IXE) and ustekinumab (UST) in the treatment of nail lesions during a head-to-head trial, IXORA-S.

Methods: In this Phase 3b, multicenter, randomized, double-blinded, parallel-group trial (IXORA-S, NCT02561806), patients with moderate-to-severe plaque psoriasis were randomized (1:1) to receive either IXE (160-mg starting dose, then 80 mg every 2 weeks for 12 weeks followed by 80 mg every 4 weeks; N=136) or UST (45 mg/90 mg weight-based dosing at Weeks 0, 4 and every 12 weeks thereafter per label; N=166). The primary endpoint was to determine if IXE was superior to UST, as measured by the proportion of patients achieving ≥ 90% improvement in Psoriasis Area and Severity Index (PASI 90) after 12 weeks of treatment. Nail Psoriasis Severity Index (NAPSI) was used to assess fingernail psoriasis for all patients presenting with nail involvement at baseline (NAPSI>0), and these patients were included in the present analysis. Each fingernail was scored for bed and matrix psoriasis, then scores were added to obtain total NAPSI fingernail scores ranging from 0 (no nail psoriasis) to 80 (severe nail psoriasis). Categorical data were assessed using logistic regression with weight and geographic region as factors at Weeks 12 and 24 and Fisher’s exact test at other time points. Missing data were imputed using non-responder imputation. Least squares (LS) means (95% CI) were calculated for NAPSI and treatment groups compared using covariance analysis with weight, geographic region, and baseline NAPSI score as factors.

Results: At week 12, a significantly higher proportion of patients treated with IXE achieved PASI 90 relative to UST (72.8% [n=99] vs 42.2% [n=70], p<0.001, respectively), thereby achieving the primary endpoint of IXORA-S.¹ At baseline, 84 IXE-treated (61.8%) and 105 UST-treated (63.3%) patients in IXORA-S had nail psoriasis. Mean NAPSI score at baseline was 28.3 (standard deviation [SD]: 22.3) for IXE-treated and 24.6 (SD: 20.1) for UST-treated patients. Statistically significant differences in percentage of patients achieving NAPSI=0 were first seen at Week 16, with 26 (31.0%) IXE-treated patients and 18 (17.1%) UST-treated patients reaching complete resolution of nail psoriasis (p=0.037). At Week 24, LS mean change from baseline NAPSI was -19.9 (-22.3, -17.5) and -13.2 (-15.4, -11.0) for IXE-treated and UST, respectively (p<0.001), and 41 (48.8%) patients treated with IXE achieved NAPSI=0 compared to 24 (22.9%) patients treated with UST (p=0.012).

Conclusion: Complete resolution of nail psoriasis was seen in significantly greater percentages of patients treated with IXE compared to UST at Week 24, even though improvement was observed in both groups over 24 weeks. Twenty-four weeks may be too early for full evaluation of nail psoriasis, and continued improvement can be expected through one year.


Disclosure: P. D. Ghislain, Schering-Plough, Abbott/Abbvie, Janssen-Cilag, Leo, Novartis, Celgene, Eli Lilly and Company, Wyeth/Pfizer, 5,Wyeth/Pfizer, Schering-Plough, Abbott/Abbvie, Janssen-Cilag, Leo, Galderma, BMS, 8,Wyeth/Pfizer, Schering-Plough, Abbott/Abbvie, Janssen-Cilag, Novartis, Celgene, Eli Lilly and Company, Galderma, 9,Wyeth/Pfizer, Schering-Plough, Abbott/Abbvie, Janssen-Cilag, 2; C. Conrad, None; Y. Dutronc, Eli Lilly and Company, 1,Eli Lilly and Company, 3; C. Henneges, Eli Lilly and Company, 1,Eli Lilly and Company, 3; D. S. Calderon, Eli Lilly and Company, 1,Eli Lilly and Company, 3; M. Vincent, Eli Lilly and Company, 1,Eli Lilly and Company, 1,Eli Lilly and Company, 1,Eli Lilly and Company, 1,Eli Lilly and Company, 1,Eli Lilly and Company, 1,Eli Lilly and Company, 1,Eli Lilly and Company, 1,Eli Lilly and Company, 1; J. de Gruijter, Eli Lilly and Company, 1,Eli Lilly and Company, 3; P. C. M. van de Kerkhof, Celgene, Centocor, Allmiral, Amgen, Pfizer, Abbott, Eli Lilly and Company, Galderma, Novartis, Jansen, Cilag, Leo Pharma, Sandoz, Mitsubishi, Sandoz, 5,Basilea, Pfizer, Eli Lilly and Company, Amgen, Abbvie, Philips Lighting, Jansen Cilag, Leo Pharma, 9.
Secukinumab Provides Sustained Improvements in the Signs and Symptoms of Active Ankylosing Spondylitis: 2-Year Results from a Phase 3 Study

Karel Pavelka¹, Alan J. Kivitz², Eva Dokoupilova³, Ricardo Blanco⁴, Marco Maradiaga⁵, Hasan Tahir⁶, Alan Slade⁷, Yi Wang⁷, Susanne Rohrer⁸ and Brian Porter⁷, ¹Institute of Rheumatology, Prague, Czech Republic, Prague, Czech Republic, ²Altoona Center for Clinical Research, Duncansville, PA, ³MEDICAL PLUS s.r.o., Uherske Hradiste, Czech Republic, ⁴Hospital Universitario Marqués de Valdecilla, Santander, Spain, ⁵Centro de Investigación de Tratamientos Innovadores de Sinaloa, Culiacán, Mexico, ⁶Barts Health NHS Trust, London, United Kingdom, ⁷Novartis Pharmaceuticals Corporation, East Hanover, NJ, ⁸Novartis Pharma AG, Basel, Switzerland

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment II
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Secukinumab (SEC) improved the signs and symptoms of AS in 2 Phase 3 studies (MEASURE 1 and 2).¹,² Here, we present interim results through 104 weeks (wks) from the MEASURE 3 study (NCT02008916), the first Phase 3 study assessing efficacy and safety of subcutaneous (SC) maintenance therapy with 300 or 150 mg SEC following intravenous (IV) loading.

Methods: 226 patients (pts) were randomized to IV SEC 10 mg/kg (baseline, Wks 2 and 4) followed by SC SEC 300 or 150 mg every 4 wks (IV→300/150 mg), or matched placebo (PBO). At Wk 16, PBO pts were re-randomized to SC SEC 300 or 150 mg. Primary endpoint was ASAS20 response rate at Wk 16. Secondary endpoints included ASAS40, hsCRP, ASAS 5/6, BASDAI and ASAS partial remission (PR). Non-responder imputation through Wk 16 and multiple imputation for binary variables and mixed-effect model for continuous variables were used. Analyses by prior anti-TNF therapy use (anti–TNF-naïve and -inadequate response or intolerance [IR]) were pre-specified and reported as observed at Wk 104. Efficacy results at Wk 104 are reported for pts originally randomized to SEC. Safety analyses included all pts who received ≥1 dose of SEC.

Results: 84.2% (64/76; SEC IV→300 mg) and 77.0% (57/74; SEC IV→150 mg) pts completed 104 wks of treatment. ASAS20 response rate was significantly greater at Wk 16 (primary endpoint) in SEC IV→300 mg and IV→150 mg groups vs PBO. All secondary endpoints were met at Wk 16. Secondary endpoints included ASAS20, hsCRP, ASAS 5/6, BASDAI and ASAS partial remission (PR). Non-responder imputation through Wk 16 and multiple imputation for binary variables and mixed-effect model for continuous variables were used. Analyses by prior anti-TNF therapy use (anti–TNF-naïve and -inadequate response or intolerance [IR]) were pre-specified and reported as observed at Wk 104. Efficacy results at Wk 104 are reported for pts originally randomized to SEC. Safety analyses included all pts who received ≥1 dose of SEC.

Conclusion: SEC (300 and 150 mg) provided rapid and significant improvements in the signs and symptoms of active AS, with responses sustained through 104 wks. SEC was well-tolerated with a safety profile consistent with previous reports.

Table: Summary of Efficacy Results at Weeks 16 and 104

By overall population

<table>
<thead>
<tr>
<th>Variable</th>
<th>Week</th>
<th>Secukinumab 10 mg/kg IV→300 mg SC (N=70)</th>
<th>Secukinumab 16 mg/kg IV→150 mg SC (N=74)</th>
<th>Placebo (N=76)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASAS20*, n (%)</td>
<td>16</td>
<td>40 (60.6)**</td>
<td>43 (59.1)**</td>
<td>28 (38.8)</td>
</tr>
<tr>
<td></td>
<td>104</td>
<td>55 (72.1)</td>
<td>54 (73.0)</td>
<td>-</td>
</tr>
<tr>
<td>ASAS40*, n (%)</td>
<td>16</td>
<td>32 (42.1)**</td>
<td>30 (40.5)**</td>
<td>10 (21.1)</td>
</tr>
<tr>
<td></td>
<td>104</td>
<td>42 (55.7)</td>
<td>35 (49.2)</td>
<td>-</td>
</tr>
<tr>
<td>hsCRP (post-baseline/baseline ratio), mean change from baseline ± SE</td>
<td>16</td>
<td>0.48 ± 1.3**</td>
<td>0.65 ± 1.1*</td>
<td>1.06 ± 1.1</td>
</tr>
<tr>
<td></td>
<td>104</td>
<td>0.60 ± 1.1</td>
<td>0.59 ± 1.1</td>
<td>-</td>
</tr>
<tr>
<td>ASASE6*, n (%)</td>
<td>16</td>
<td>30 (39.5)**</td>
<td>31 (41.2)**</td>
<td>11 (14.5)</td>
</tr>
<tr>
<td></td>
<td>104</td>
<td>42 (54.9)</td>
<td>37 (59.0)</td>
<td>-</td>
</tr>
<tr>
<td>BASDAI4, mean change from baseline ± SE</td>
<td>16</td>
<td>-0.7 ± 0.3</td>
<td>-0.5 ± 0.3</td>
<td>-1.5 ± 0.3</td>
</tr>
<tr>
<td></td>
<td>104</td>
<td>-3.3 ± 0.3</td>
<td>-3.0 ± 0.3</td>
<td>-</td>
</tr>
<tr>
<td>ASAS partial remission, n (%)</td>
<td>16</td>
<td>16 (21.1)**</td>
<td>7 (9.6)</td>
<td>1 (1.3)</td>
</tr>
<tr>
<td></td>
<td>104</td>
<td>20 (25.7)</td>
<td>13 (17.2)</td>
<td>-</td>
</tr>
</tbody>
</table>

By anti-TNF status

<table>
<thead>
<tr>
<th>Variable</th>
<th>% responders</th>
<th>Week</th>
<th>Secukinumab 10 mg/kg IV→300 mg SC (N=57)</th>
<th>Placebo (N=59)</th>
<th>Secukinumab 16 mg/kg IV→150 mg SC (N=19)</th>
<th>Placebo (N=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASAS20</td>
<td>16</td>
<td>64 (89.7)</td>
<td>39 (64.1)</td>
<td>47.4</td>
<td>41.2</td>
<td>29.4</td>
</tr>
<tr>
<td></td>
<td>104</td>
<td>78.4</td>
<td>62.0</td>
<td>-</td>
<td>84.6</td>
<td>54.6</td>
</tr>
<tr>
<td>ASAS40</td>
<td>16</td>
<td>43.5**</td>
<td>45.7**</td>
<td>23.7</td>
<td>38.9</td>
<td>29.4</td>
</tr>
<tr>
<td></td>
<td>104</td>
<td>84.7</td>
<td>58.6</td>
<td>-</td>
<td>61.5</td>
<td>27.3</td>
</tr>
<tr>
<td>ASAS partial remission</td>
<td>16</td>
<td>21.1**</td>
<td>10.5</td>
<td>1.7</td>
<td>21.1</td>
<td>5.8</td>
</tr>
<tr>
<td></td>
<td>104</td>
<td>31.4</td>
<td>25.1</td>
<td>-</td>
<td>23.1</td>
<td>0</td>
</tr>
</tbody>
</table>

Figure: ASAS20/40 Response Rates through Week 104

*P < 0.0001, **P < 0.01, ***P < 0.05 versus placebo (P-values at week 16 were adjusted for multiplicity) Non-responder imputation through Week 16 and multiple imputation through Week 104

Disclosure: K. Pavelka, MSD, AbbVie, Roche, UCB, Amgen, Hospira, Egis, Pfizer, Medac, BMS, 8; A. J. Kivitz, AbbVie, Pfizer, Genentech, UCB, Sanofi/Regeneron and Celgene, 5; Celgene, Pfizer, Sanofi/Regeneron and Genentech, 8; E. Dokoupilova, None; R. Blanco, AbbVie, MSD, and Roche; 2, AbbVie, Pfizer, Roche, Bristol-Myers, Janssen, and MSD, 5, AbbVie, Pfizer, Roche, Bristol-Myers, Janssen, and MSD, 8; M. Maradiaga, None; H. Tahir, Novartis, Eli Lilly, and AbbVie, 8; A. Slade, Novartis Pharmaceutical Corporation, 3; Y. Wang, Novartis Pharmaceutical Corporation, 3; S. Rohrer, Novartis Pharma AG, 1, Novartis Pharma AG, 3; B. Porter, Novartis Pharma AG, 1, Novartis Pharma AG, 3.
Patterns and Predictors of Progression of Sacroiliitis in Psoriatic Arthritis and Its Relationship with Human Leukocyte Antigen (HLA) Alleles. Results from the Toronto Cohort

Musaab Elmamoun1, Justine (Yang) Ye2, Richard J. Cook3, Vinod Chandran4 and Dafna D Gladman5, 1Rheumatology, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, 2University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, 3Statistics and Actuarial Science, University of Waterloo, Waterloo, ON, Canada, 4Medicine, Krembil Research Institute, Toronto Western Hospital, University of Toronto, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment II
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:
Psoriatic arthritis (PsA) is clinically heterogeneous, with broad phenotypes of musculoskeletal (MSK) involvement including peripheral arthritis, enthesitis, dactylitis, and axial involvement. Sacroiliitis (SI) in PsA can be unilateral or bilateral in contrast with ankylosing spondylitis which appears to be commonly bilateral. It has been suggested that specific Human Leukocyte Antigen (HLA) allele can present with either unilateral or bilateral sacroilitis in PsA, HLA-B*27 with symmetrical SI, HLA-B*08 with unilateral or asymmetrical SI.

Our objectives were a) to determine the pattern of progression of sacroiliac joint involvement in PsA (unilateral versus bilateral; b) to determine the predictors of progression of sacroiliac joint involvement (symmetrical versus asymmetrical)

Methods:
A retrospective cohort analysis was conducted in patients followed in a large PsA clinic from 1978 to 2016. The participants were assessed at 6 to 12-month intervals according to a standard protocol. The collected information included demographics, medical history, radiological results, HLA allele, and PsA-related outcomes. Radiographs were performed at 2-year intervals. A statistical model was developed to assess for development of SI. Polychotomous logistic regression was used to assess the effect of HLA alleles.

Results:
A total of 1431 PsA patients were analysed. Three hundred and eight patients had SI (23%); 125 (9%) patients with unilateral SI; 17% of patients were HLA-B*27 positive, table 1. On analysis of the radiological result based on HLA alleles; 85 patients had bilateral asymmetrical SI, 29 (34%) were HLA-B*27 positive. 176 patients had symmetrical SI, 33 (22%) were HLA-B*27 positive. HLA-B*08 had similar proportion of patients in each category. In the bilateral SI group (20% in asymmetric, 16% in symmetric), 18% in the unilateral group. Interestingly, HLA-C*07 which has not been reported before accounted for more SI both in the unilateral and bilateral group, table 2.

Using polychotomous logistic regression, controlling for gender, HLA-B*27 positive patients had significantly higher odds of bilateral involvement compared to no sacroiliac joint involvement (OR = 2.42, 95% CI: 1.05, 5.56; p=0.038)

Conclusion:
HLA-B*27 is associated with bilateral sacroiliac joint involvement in PsA. Patients with HLA-C*07 are found to have more axial disease compared to the other HLA alleles.

References
Table 1: Patients characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall (N=1431)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>53.8 (14.8)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>634 (44%)</td>
</tr>
<tr>
<td>Age at diagnosed, psoriasis</td>
<td>28.8 (14.7)</td>
</tr>
<tr>
<td>Age at diagnosis, psoriatic arthritis</td>
<td>38.0 (13.6)</td>
</tr>
<tr>
<td>Swollen joint count</td>
<td>3.4 (4.9)</td>
</tr>
<tr>
<td>Tender joint count</td>
<td>7.1 (8.7)</td>
</tr>
<tr>
<td>Total clinical damaged joint count</td>
<td>2.6 (6.7)</td>
</tr>
<tr>
<td>Body mass index (BMI)</td>
<td>28.2 (7.8)</td>
</tr>
<tr>
<td>Psoriasis area and severity index (PASI)</td>
<td>3.8 (7.0)</td>
</tr>
<tr>
<td>Modified Steinbroker score</td>
<td>10.1 (22.9)</td>
</tr>
<tr>
<td>Number of X-ray, median (min, max)</td>
<td>2.0 (1.0, 17.0)</td>
</tr>
<tr>
<td>Number of visit, median (min, max)</td>
<td>6.0 (1.0, 66.0)</td>
</tr>
<tr>
<td>Inflammatory back pain, n (%)</td>
<td>214 (15%)</td>
</tr>
<tr>
<td>Damaged joints, n (%)</td>
<td>484 (34%)</td>
</tr>
<tr>
<td>Dactylitis, n (%)</td>
<td>403 (28%)</td>
</tr>
<tr>
<td>Enthesitis, n (%)</td>
<td>239 (17%)</td>
</tr>
<tr>
<td>Nail lesion, n (%)</td>
<td>949 (75%)</td>
</tr>
<tr>
<td>HLA-B27 positive, n (%)</td>
<td>188 (17%)</td>
</tr>
<tr>
<td>Sacroilitis, n (%)</td>
<td>308 (23%)</td>
</tr>
<tr>
<td>Radiographic unilateral &gt;=2, n (%)</td>
<td>125 (9%)</td>
</tr>
<tr>
<td>Radiographic bilateral &gt;=2, n (%)</td>
<td>274 (19%)</td>
</tr>
<tr>
<td>Radiographic damage, n (%)</td>
<td>724 (54%)</td>
</tr>
</tbody>
</table>
Bone Marrow Edema in Sacroiliac Joints of Young Athletes Is Common and Shows Most Frequently in the Posterior Lower Ilium

Ulrich Weber1, Anne Grethe Jurik2, Anna Zejden3, Ejnar Larsen4, Steen Hylgaard Jørgensen5, Kaspar Rufibach6, Christian Schioldan7 and Søren Schmidt-Olsen8. 1Department of Research, King Christian 10th Hospital for Rheumatic Diseases, Graaesten, Denmark, 2Dept. of Radiology, Aarhus University Hospital, Aarhus, Denmark, 3Radiology, Aarhus University Hospital, Aarhus, Denmark, 4Radiology, North Denmark Regional Hospital, Hjørring, Denmark, 5Rheumatology and Sports Medicine, North Denmark Regional Hospital, Hjørring, Denmark, 6Biostatistics, F. Hoffmann-La Roche, Basel, Switzerland, Basel, Switzerland, 7Physiotherapy, Clinic Benefit, Frederikshavn, Denmark

Disclosure: M. Elmamoun, None; J. Ye, None; R. J. Cook, None; V. Chandran, None; D. D. Gladman, None.

Background/Purpose: Low grade bone marrow edema (BME) was reported in the sacroiliac joints (SIJ) of up to 25% of healthy individuals and mechanical back pain patients, challenging the imaging discrimination from early spondyloarthritis (SpA) [1]. Potential explanations range from mechanical stress lesions to vascular signals and anatomical SIJ variants. There is little evidence as to whether physical strain, e.g. sports, heavy labour work, or multiparity may trigger SIJ BME. The goal of this study was to determine BME frequency and anatomical distribution in 8 SIJ regions in hobby and professional athletes.

Methods: The sample consisted of 2 cohorts of 20 healthy hobby runners (HR) before and after running and 22 professional ice hockey players (IP) from the Danish premier league: HR/IP 40%/100% men; mean age (SD) 27.2 (5.4)/25.9 (4.6) years; mean BMI (SD) 22.6 (1.5)/25.7 (1.6) kg/m². Semicoronal MRI scans of the SIJ with T1SE and STIR sequences were obtained in HR before and 24 hours after a running competition over 6.2 km (mean duration 35.4 minutes, mean speed 10.4 km/h), and in IP at the end of the competitive season. The scans were assessed for BME independently by 3 blinded readers (AGJ, AZ, UW) according to the quadrant based MORPHO module (www.carearthritis.com). Paired images of HR were read blinded to timepoint. 7 MRI scans (2 paired images) of SpA patients under TNF treatment served to mask readers. A pre-test reader calibration used MRI scans from 11 patients with active sacroiliitis and 9 healthy volunteers. Reader agreement was assessed by ICC (3, 1). Descriptive analysis comprised mean frequency of SIJ quadrants with BME and their distribution in 8 anatomical SIJ regions: upper/lower ilium and sacrum, subdivided in anterior and posterior slices, as concordantly recorded by the majority (≥2/3) of readers.

Results: Agreement among 3 readers for SIJ BME was excellent in calibration (ICC 0.93) and moderate in athletes (ICC 0.59) due to low frequency of BME. The mean number (SD) of SIJ quadrants showing BME was 3.1 (4.2)/3.1 (4.5) in HR before/after running, and 3.6 (3.0) in IP. The posterior lower ilium was the single most affected region, followed by the anterior upper sacrum, consistently across 2 cohorts of athletes.

Table 1. Frequency and anatomical distribution of SIJ quadrants with BME in 2 cohorts of athletes. Abbreviations. n (%) with ≥1/2/3/4 SIJ Q: number of subjects (%) with ≥1/2/3/4 SIJ quadrants with BME as reported by ≥2/3 readers.
<table>
<thead>
<tr>
<th>Cohort</th>
<th>SIJ quadrants</th>
<th>Lower Ilium</th>
<th>Lower Sacrum</th>
<th>All subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR before</td>
<td>Mean SIJ Q (SD)</td>
<td>Anterior</td>
<td>Posterior</td>
<td>Anterior</td>
</tr>
<tr>
<td>n (%) with ≥1 SIJ Q</td>
<td>3 (15.0)</td>
<td>0</td>
<td>1 (5.0)</td>
<td>8 (40.0)</td>
</tr>
<tr>
<td>n (%) with ≥2 SIJ Q</td>
<td>0</td>
<td>0</td>
<td>1 (5.0)</td>
<td>6 (30.0)</td>
</tr>
<tr>
<td>n (%) with ≥3 SIJ Q</td>
<td>0</td>
<td>0</td>
<td>1 (5.0)</td>
<td>2 (10.0)</td>
</tr>
<tr>
<td>n (%) with ≥4 SIJ Q</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (5.0)</td>
</tr>
</tbody>
</table>

| HR after | Mean SIJ Q (SD) | Anterior | Posterior | Anterior | Posterior | Anterior | Posterior | Anterior | Posterior |
| n (%) with ≥1 SIJ Q | 2 (10.0) | 0 | 2 (10.0) | 9 (45.0) | 3 (15.0) | 2 (10.0) | 3 (15.0) | 1 (5.0) | 16 (80.0) |
| n (%) with ≥2 SIJ Q | 0 | 0 | 1 (5.0) | 6 (30.0) | 2 (10.0) | 1 (5.0) | 0 | 1 (5.0) | 14 (70.0) |
| n (%) with ≥3 SIJ Q | 0 | 0 | 1 (5.0) | 3 (15.0) | 2 (10.0) | 0 | 0 | 1 (5.0) | 8 (40.0) |
| n (%) with ≥4 SIJ Q | 0 | 0 | 1 (5.0) | 1 (5.0) | 0 | 0 | 0 | 1 (5.0) | 5 (25.0) |

| IP | Mean SIJ Q (SD) | Anterior | Posterior | Anterior | Posterior | Anterior | Posterior | Anterior | Posterior |
| n (%) with ≥1 SIJ Q | 0 | 1 (4.5) | 7 (31.8) | 13 (59.1) | 3 (13.6) | 0 | 3 (13.6) | 0 | 20 (90.9) |
| n (%) with ≥2 SIJ Q | 0 | 0 | 4 (18.2) | 11 (50.0) | 2 (9.1) | 0 | 1 (4.5) | 0 | 15 (68.2) |
| n (%) with ≥3 SIJ Q | 0 | 0 | 0 | 6 (27.3) | 2 (9.1) | 0 | 0 | 0 | 12 (54.5) |
| n (%) with ≥4 SIJ Q | 0 | 0 | 0 | 3 (13.6) | 1 (4.5) | 0 | 0 | 0 | 11 (50.0) |

Conclusion:
In hobby and professional athletes, BME showed on average in 3-4 SIJ quadrants. The posterior lower ilium was the single most affected SIJ region, followed by the anterior upper sacrum. These findings in healthy controls help refine thresholds for a positive SIJ MRI in early SpA.


Disclosure: U. Weber, None; A. G. Jurik, None; A. Zeijden, None; E. Larsen, None; S. H. Jorgensen, None; K. Rufibach, None; C. Schioldan, None; S. Schmidt-Olsen, None.
A Positive MRI of the Sacroiliac Joints Is Not Specific for Axial Spondyloarthritis but Frequently Occurs in Healthy Individuals

Janneke de Winter¹, Manouk de Hooge², Marleen van de Sande¹, Lonneke van Hoeven³, Jet de Jong¹, Anoek de Koning², Inger Jorid Berg⁴, Roberta Ramonda⁵, Dominique Baeten¹,⁶, Désirée van der Heijde⁷, Angelique Weel⁸ and Robert B.M. Landewé⁹, ¹Clinical Immunology and Rheumatology, Amsterdam Rheumatology and immunology Center, Academic Medical Center/University of Amsterdam, Amsterdam, Netherlands, ²Rheumatology, Leiden University Medical Center, Leiden, Netherlands, ³Rheumatology, Maasstad Hospital, Rotterdam, Netherlands, ⁴Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, ⁵Rheumatology Unit, Department of Medicine DIMED, University of Padova, Padova, Italy, ⁶UCB Pharma, Slough, United Kingdom, ⁷Leiden University Medical Center, Leiden, Netherlands, ⁸Department of Rheumatology, Maasstad Hospital, Rotterdam, Netherlands, ⁹Amsterdam Rheumatology & Immunology Center, Academic Medical Center, Amsterdam, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment II
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:
Inflammation shown on MRI of the sacroiliac joint (MRI-SI) is prevalent in axSpA (±30%) but the specificity is not well known, hence we compared MRI-SI of healthy individuals and those with known mechanical strain acting upon SIJ.

Methods:
Three trained, blinded readers randomly scored MRI-SI of 172 subjects: 47 healthy individuals (1); 47 age- and gender-matched axSpA patients (with a confirmed positive MRI by central readers) from the SPondyloArthritis Caught Early (SPACE) cohort; 47 age- and gender-matched CBP patients (irrespective of MRI results) from the SPACE cohort; 7 women with postpartum back pain; and 24 frequent runners. The readers scored MRIs according to the ASAS/OMERACT and SPARCC definitions. MRIs were considered positive when at least two of the three readers agreed. SPARCC scores are the mean SPARCC scores of all three readers. MRI scores were considered positive when at least two of the three readers agreed. SPARCC scores are the mean SPARCC scores of all three readers.

Results:
The three reader pairs agreed in 75.6-79.9% of the cases on the presence/absence of BME (Cohen’s κ 0.48-0.59), SPARCC scores correlated well (ICCs 0.824-0.964). Of the healthy volunteers, 11 out of 47 (23.4%) had a positive MRI-SI, compared to 43 out of 47 (91.5%) of the positive axSpA patients and 3 out of 47 (6.4%) CBP patients. Of the runners, 3 out of 24 (12.5%) -and of the women with postpartum back pain 4 out of 7 (57.1%)- had a positive MRI-SI. The mean (SD) SPARCC scores were 1.7 (2.4) (healthy individuals), 20.9 (13.7) (positive axSpA patients), 0.8 (1.4) (CBP patients), 0.8 (1.1) (frequent runners) and 4.5 (6.3) (postpartum patients) (Figure 1). When a SPARCC score ≥2 was used as a cut-off for positivity, 12 out of 47 healthy volunteers (25.5%), 46 out of 47 positive axSpA patients (97.9%), 5 out of 47 CBP patients (10.6%), 4 out of 24 runners (16.7%) and 4 out of 7 women with postpartum back pain (57.1%) were declared positive. When a SPARCC score ≥5 was used as a cut-off score, these figures were 4 out of 47 healthy volunteers (8.5%), 40 out of 47 positive axSpA patients (87.2%), 1 out of 47 CBP patients (2.1%), 0 out of 24 runners and 2 out of 7 women with postpartum back pain (28.6%). 'Deep' BME-lesions (increase in signal ≥1 cm from the articular surface) were not found in healthy volunteers, CBP patients and runners, but in 38 out of the 47 positive axSpA patients (80.9%) and in one out of 7 women with postpartum back pain (14.3%).

Conclusion:
A substantial proportion of healthy individuals has a positive MRI-SI according to the ASAS/OMERACT definition. High SPARCC scores (≥5) rarely occur in healthy individuals, CBP patients and runners. 'Deep' (extensive) lesions seem exclusive of sacroiliitis in axSpA patients.

Figure 1. Percentage of positive MRI-SI and total SPARCC scores, each dot represents one individual.
References


Disclosure: J. de Winter, None; M. de Hooge, None; M. van de Sande, Takeda, Tillots, MSD, Abbvie, novartis, boeringer ingelheim, 5; Takeda, Tillots, MSD, Abbvie, novartis, boeringer ingelheim, 8; Takeda, Tillots, MSD, Abbvie, novartis, boeringer ingelheim, 5; L. van Hoeven, None; J. de Jong, None; A. de Koning, None; I. J. Berg, None; R. Ramonda, None; D. Baeten, UCB, 3; D. van der Heijde, AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, Glaxo-Smith-Kline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB, 5; Imaging Rheumatology bv., 9; A. Weel, None; R. B. M. Landewé, ASAS, 9.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/a-positive-mri-of-the-sacroiliac-joints-is-not-specific-for-axial-spondyloarthritis-but-frequently-occurs-in-healthy-individuals

**Gut Dysbiosis Contributes to Autoimmune Pathogenesis in Lupus-Prone Mice**

Seung Chul Choi¹, Josephine Brown¹, Mansour Mohamadzadeh², Byron Cocker¹ and Laurence Morel³, ¹Pathology, University of Florida, Gainesville, FL, ²Infectious Diseases & Pathology, University of Florida, Gainesville, FL, ³Pathology, Immunology, and Laboratory Medicine, University of Florida, Gainesville, FL

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Animal Models
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Multiple studies have demonstrated that commensal bacteria play an immunoregulatory role and that gut dysbiosis is associated with inflammatory diseases. This study was conducted to test the hypothesis that gut dysbiosis plays a role in SLE. We have used a congenic model of lupus, the B6.Sle1.Sle2.Sle3 (TC) mice, which share >95% of their genome with B6 controls to ask if differences in microbiota could synergize with lupus susceptibility genes to modulate autoimmune pathology.

Methods: The 16S rDNA sequences of fecal bacteria were compared between the two strains. Global fecal and serum metabolomic profiles were obtained using high-resolution mass spectrometry (Thermo Q-Exactive) coupled with ultra-high performance liquid chromatography. Tryptophan (Trp) metabolites were quantified with the same instruments relative to internal standards. Germ-free (GF) B6 mice were populated with fecal contents from either B6 or TC mice, and evaluated 4 weeks later. TC and B6 mice were treated with an antibiotic cocktail starting at 6 weeks of age and evaluated after 6 months of treatment. B6 and TC mice were either housed separately or co-housed in a mixed strains environment at weaning and evaluated 6 months later. B6 and TC mice were fed with Trp-deficient, Trp-supplemented (1%) and control chow starting at 2 months of age and evaluated 7 months later. Immunophenotypes were evaluated by flow cytometry. Serum and fecal antibodies were measured by ELISA. Kidney and gut pathology was evaluated by histology.
Results: TC and B6 mice have a different distribution of gut bacteria based on 16S rDNA sequencing. The colon and duodenum of aged TC mice showed a significant amount of immune cell infiltrate, which correlated with the severity of renal pathology. TC fecal transfers to GF B6 mice showed that microbiota from aged TC mice was sufficient to induce the production of serum anti-dsDNA IgG. TC microbiota also expanded germinal center (GC)-like organization in Peyser’s patches and follicular helper T (TFH) cells in the mesenteric lymph node. These changes were not observed with microbiota from young pre-disease TC mice. Treatment of TC mice with antibiotic cocktail significantly delayed anti-dsDNA IgG induction and expanded Treg and follicular regulatory T (TFR) cells. Co-housing TC and B6 mice revealed significant interactions between susceptibility genes and microbiota. Remarkably, the frequency of TFH cells was decreased in co-housed TC mice, corresponding to a drastic reduction of autoantibodies and amelioration of renal disease. Co-housed TC and B6 mice showed a similar fecal metabolome profile, which was significantly different from those of independently housed mice. Trp metabolites were among the metabolites found at different levels between TC and B6 stools. Similarly to what has been reported by others in SLE patients, TC mice have increased levels of serum and fecal kynurenine, one of Trp metabolites, as compared to B6. Accordingly, a Trp-supplemented chow accelerated autoimmune pathology in TC mice.

Conclusion: Overall, our results show that a dysregulated gut microbiota amplifies lupus pathogenesis in mice, and suggest that this is mediated at least in part by bacteria modifying Trp metabolism.

Disclosure: S. C. Choi, None; J. Brown, None; M. Mohamadzadeh, None; B. Croker, None; L. Morel, None.

Abstract Number: 1833

iRhom2 Deficiency Protects Fcgr2b-/− Lupus-Prone Mice from Kidney Damage By Modulating ADAM17-Dependent Shedding of TNF-α and EGFR Ligand

Xiaoping Qing1, Yuri Chinenov2, Patricia M. Redecha3, Michael Madaio4, Priya Issuree5, David McIlwain6, Tak Mak7, Carl Blobel5 and Jane E. Salmon8, 1Program in Inflammation and Autoimmunity, Hospital for Special Surgery, New York, NY, 2Arthritis & Tissue Degeneration Program, Hospital for Special Surgery, New York, NY, 3Autoimmunity & Inflammation, Hospital for Special Surgery, New York, NY, 4Medicine, Medical College of Georgia, Augusta, GA, 5Arthritis and Tissue Degeneration Program, Hospital for Special Surgery, New York, NY, 6Department of Microbiology and Immunology, Stanford University, Stanford, CA, 7Campbell Family Institute for Breast Cancer Research, Princess Margaret Cancer Center, Toronto, ON, Canada, 8Medicine/Rheumatology, Hospital of Special Surgery, New York, NY

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Animal Models
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: A disintegrin and metalloprotease 17 (ADAM17) controls ecto-domain shedding of TNFα and epithelial-growth factor ligands (EGFR) such as heparin-binding EGF (HB-EGF). TNFα and HB-EGF have both been implicated in kidney injury of systemic lupus erythematosus (SLE), yet targeting ADAM17 is limited by its essential role in protecting the skin and intestinal barrier. In contrast, mice lacking the inactive Rhomboid 2 (iRhom2), a key regulator of ADAM17 in myeloid cells, have normal development but are protected from TNFα-dependent septic shock and Rheumatoid Arthritis. iRhom2-deficient mice appear normal because the related iRhom1 supports ADAM17-dependent skin and intestinal barrier protection. Here, we sought to determine whether iRhom2/ADAM17 pathway contributes to the pathogenesis of lupus nephritis (LN).

Methods: iRhom2 (gene name Rhbd2) deficient mice were crossed with Fcgr2b-/− lupus-prone mice. Development of anti-dsDNA Abs and kidney injury was monitored by assessing proteinuria, BUN, kidney inflammatory cell infiltration, renal deposition of immune complexes and complement and histology. Molecular mechanism of renal damage was studied using RNA-sequencing analysis. Activation of iRhom2, ADAM17 and EGFR signaling was determined by qPCR and western-blot. To corroborate the contribution of both TNFα and EGFR signaling to renal injury, we treated Fcgr2b-/− mice with murine p75TNFRII-Fc or an EGFR tyrosine kinase inhibitor.

Results: Deficiency of iRhom2 almost completely protected Fcgr2b-/− mice from mortality (Fig. 1A). Development of severe proteinuria and elevated blood urea nitrogen (BUN) in aged Fcgr2b-/− (F2b-/-) mice were ameliorated by iRhom2 deficiency (iR2-/-) (Fig. 1B, C). Glomerular and tubulo-interstitial damage and inflammatory cell infiltrates (neutrophils, monocytes and T cells) in Fcgr2b-/− kidneys were markedly and significantly reduced in the absence of iRhom2, while anti-dsDNA Ab production and renal
deposition of IgG and C3 were minimally affected. These data suggest that iRhom2 targets the effector arm in SLE, rather than preventing development of autoimmunity. Strikingly, transcriptome profiling of mouse kidneys identified epithelial-mesenchymal-transition (EMT) and TNF signaling as top pathways activated in Fcgr2b−/− kidneys, along with marked upregulation of Tnf and Hbegf transcripts in these kidneys. This is confirmed by findings that kidney damage in Fcgr2b−/− mice was associated with increased renal expression of phospho-EGFR and phospho-ERK1/2, which was significantly diminished in the absence of iRhom2. Finally, blockade of TNF-α or EGFR in protected Fcgr2b−/− mice from kidney injury.

**Conclusion:** Our findings provide the first evidence that iRhom2, a major regulator of ADAM17, plays a critical role in the pathogenesis of LN, most likely by processing TNFα and EGFR ligands in the diseased kidneys.

**Figure 1**

**A**

- WT
- IR2−/−
- F2b−/−
- F2b−/−IR2−/−

**B**

- WT
- IR2−/−
- F2b−/−
- F2b−/−IR2−/−

**C**

- WT
- IR2−/−
- F2b−/−
- F2b−/−IR2−/−

*** P<0.0001
**** P<0.0005
** P<0.005

Disclosure: X. Qing, None; Y. Chinenov, None; P. M. Redecha, None; M. Madaio, None; P. Issuree, None; D. McIlwain, None; T. Mak, None; C. Blobel, None; J. E. Salmon, None.


Abstract Number: 1834

**Selective Inhibitors of Nuclear Export Prevent Lupus Progression By Targeting Germinal Center Formation and Autoreactive Antibody Secreting Cells**

Javier Rangel-Moreno1, Jennifer Barnard2, Shelton Cochran3, Margaret Lee3, Sharon Tamir3 and Jennifer H. Anolik4, 1Medicine-Allergy, Immunology, and Rheumatology, University of Rochester Medical Center, Rochester, NY, 2Medicine-Allergy, Immunology and Rheumatology, University of Rochester Medical Center, Rochester, NY, 3Karyopharm Therapeutics, Newton, MA, 4Medicine-Allergy, Immunology and Rheumatology, University of Rochester Medical Center, Rochester, NY

First publication: September 18, 2017

SESSION INFORMATION

**Session Date:** Monday, November 6, 2017

**Session Title:** Systemic Lupus Erythematosus – Animal Models

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 2:30PM-4:00PM
Background/Purpose: There is great interest in developing new treatment approaches for systemic lupus erythematosus (SLE), but the biologic therapies under investigation over the past several years have yielded variable results. Recently the nuclear export protein Exportin 1 (XPO1, also known as CRM1) has surfaced as an attractive target for the treatment of malignancies and autoimmune disorders. Selective Inhibitor of Nuclear Export (SINE) compounds are potent, orally available and well tolerated XPO1 inhibitors that have shown potent activity in human phase I/II clinical trials against various hematologic malignancies. SINE compounds exert apoptotic and anti-inflammatory effects by mediating nuclear retention of important XPO1 cargos like the NFκB pathway regulatory protein, IκB. Based on the central role of NFκB signaling in the activation of immune cells in SLE, we evaluated the therapeutic efficacy of SINE compounds in murine SLE.

Methods:
Cohorts of nephritic NZB/W F1 lupus-prone female mice, with established disease (elevated anti-dsDNA antibody titer and proteinuria) were treated with low or high dose KPT-350 (5 or 7.5 mg/kg, respectively) or a vehicle control three times per week for 8 weeks (n=8 per group). Proteinuria was monitored and kidney histology assessed. Spleen, bone marrow (BM), and kidney cells were harvested and analyzed by flow cytometry. Antibody secreting cells (ASCs) and germinal centers (GCs) were enumerated and measured by ELISpot and immunofluorescent staining. Serum samples and RNA were collected for Luminex assay and qPCR.

Results: Treatment with SINE compounds significantly prevented increases in proteinuria (proteinuria scores: Control: 2.12±1.12; SINE (5 mg/kg): 1.06±0.49; SINE (7.5 mg/kg): 0.85±0.55) and drastically decreased IgG deposition and kidney pathology. Prevention of kidney damage was associated with a remarkable disruption of splenic GC, a significant reduction in the number of auto-reactive ASC, and a decrease in the accumulation of auto-reactive ASC in the inflamed kidney. Reduced numbers of plasma cells (PCs) in the inflamed kidney are likely due to the drastic decrease in the expression of molecules critical for PC attraction (CCL2, CXCL9, CXCL10, CXCL11) and survival (BAFF, APRIL). The potent effect of SINE compounds on GC and auto-reactive ASC is noticeable as early as 1 week after starting therapy. However, kinetics studies showed that a more pronounced elimination of GC and auto-reactive ASC is achieved after 8 weeks. Although SINE therapy has a drastic impact on spleen architecture, recovery experiments showed that complete recovery of immune cells in spleen occurred by 4 weeks. The reversible impact of SINE compounds on SLE provides a potential window of time for immunization of lupus patients.

Conclusion: SINE compounds have demonstrated efficacy in a murine model of SLE by reducing generation, survival and function of auto-reactive immune cells. It is likely that inhibition of the canonical NFκB pathway underlies KPT-350’s inhibitory effect. Together, our findings suggest the potential of SINE compounds to have a significant impact on disease progression in SLE.

Disclosure: J. Rangel-Moreno, None; J. Barnard, None; S. Cochran, Karyopharm Therapeutics, 3; M. Lee, Karyopharm Therapeutics, 1,Karyopharm Therapeutics, 3; S. Tamir, Karyopharm Therapeutics, 1,Karyopharm Therapeutics, 3; J. H. Anolik, None.


Abstract Number: 1835

Microglial Defects Contribute to Neuropsychiatric Symptoms of Systemic Lupus Erythematosus

Hadijat Makinde1, Philip J. Homan2, Harris Perlman2 and Carla Cuda2, 1Northwestern University, Chicago, IL, 2Department of Medicine Division of Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Animal Models
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Neuropsychiatric symptoms of systemic lupus erythematosus (NP-SLE), including headaches, cognitive dysfunction and psychiatric disorders, appear in up to 75% of SLE patients and may be among the earliest signs of SLE. However, these non-specific symptoms make diagnosis/treatment of NP-SLE problematic. Microglia are the resident innate immune cells in the brain and accumulating evidence points to this population as a source of neurotoxic factors that drive pathology of multiple neurodegenerative diseases. However, relatively little is known about microglia in the context of NP-SLE. We have shown that CD11c-specific deletion of caspase 8, an enzyme in the Fas pathway classically linked to apoptosis initiation and necroptosis suppression, induces a SLE-like
disease that originates in part from heightened dendritic cell activation. We find that caspase 8 deletion extends to microglia, as these cells can express CD11c. To this end, we examined the neurological consequences of microglial caspase 8 deletion.

**Methods:** Mice with caspase 8 flanked by loxP sites (Casp8fl/fl, WT) were bred to mice expressing Cre under control of the CD11c gene promoter (CreCD11c) to generate CreCD11cCasp8fl/fl mice. Mice were subjected to a battery of tasks at Northwestern University’s Behavioral Phenotyping Core. MRI was performed at Northwestern University’s Center for Translational Imaging. Cellular infiltration into the brain was assessed using 10-color flow cytometric analysis. RNAseq analysis was performed on sorted microglia.

**Results:** With age, CreCD11cCasp8fl/fl mice develop an inflammatory disease reminiscent of both classic murine models of SLE and human SLE. Strikingly, CreCD11cCasp8fl/fl mice also exhibit neurological deficits during the Morris water maze, pre-pulse inhibition, contextual fear conditioning and rotarod tasks that indicate hippocampal and cerebellar abnormalities. Increased vascular permeability in CreCD11cCasp8fl/fl mice, as evidenced by Dynamic Intravascular Contrast Agent MRI, correlates with increased leukocyte infiltration seen by flow cytometric analysis. This infiltration resembles that of an acute model of traumatic brain injury, wherein physical damage to the brain promotes leakage of the blood-brain barrier. However, in our case, this breach is the direct result of CD11c-specific caspase-8 deletion and chronic systemic inflammation. GO analysis of differentially expressed genes reveals that transcriptional profiles of young caspase 8-deficient microglia are enriched for genes involved in amyloid precursor protein metabolic and catabolic processes and Notch receptor processing, while profiles of 10-12 month old caspase 8-deficient microglia are enriched for genes involved in inflammatory and immune responses.

**Conclusion:** These data substantiate a novel mechanism whereby caspase-8 controls microglial function at both early and late stages of SLE to prevent NP-SLE manifestations and highlight microglial defects as a potential mechanism underlying the pathogenesis of NP-SLE. We intend to leverage our transcriptional data to further interrogate how defective microglial function incites NP-SLE.

**Disclosure:** H. Makinde, None; P. J. Homan, None; H. Perlman, None; C. Cuda, None.


**Abstract Number:** 1836

**Amelioration of Neuropsychiatric Systemic Lupus Erythematosus By Fingolimod-Mediated Sphingosine-1-Phosphate Receptor Modulation**

Elise Mike¹, Ariel Stock¹ and Chaim Putterman², ¹Microbiology and Immunology, Albert Einstein College of Medicine, Bronx, NY, ²Division of Rheumatology, Albert Einstein College of Medicine, Bronx, NY, USA, Bronx, NY

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Systemic Lupus Erythematosus – Animal Models

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 2:30PM-4:00PM

**Background/Purpose:** While the pathogenesis of neuropsychiatric SLE (NPSLE) is not fully understood, critical aspects of disease development include neuroinflammation and loss of brain barrier integrity. Fingolimod, a sphingosine-1-phosphate (S1P) receptor modulator, is approved for the treatment of multiple sclerosis. Through functional antagonism of S1P receptors, fingolimod prevents lymphocyte egress from lymphoid organs. In addition to reducing CNS infiltration by peripheral lymphocytes, fingolimod also exhibits direct neuroprotective effects such as preserving brain barrier integrity and decreasing pro-inflammatory cytokine secretion by astrocytes and microglia. Given these effects, we hypothesized that fingolimod would attenuate neurobehavioral deficits in MRL-lpr/lpr mice, a validated NPSLE model.

**Methods:** Ten-week-old female MRL-lpr/lpr mice were treated thrice weekly with fingolimod (3 mg/kg) or vehicle alone (n=16/group) by intraperitoneal injection. After 4 weeks of treatment, mice were assessed for alterations in cognitive function or emotionality. The object placement and object recognition tests were performed to assess visuospatial and recognition memory. The swim test was used to assess despair-like immobility. Brains were paraffin-embedded for histological analysis and immunohistochemical staining.

**Results:** Fingolimod-treated mice exhibited significantly improved preference for novel object placement when compared with control-treated mice (67±5% vs. 51±4.8%, p=0.024), demonstrating maintenance of visuospatial memory. Moreover, fingolimod-treated mice displayed less despair-induced immobility (57±2.7% vs. 45±4.2%, p=0.019), indicating that fingolimod mitigates the depression-like...
phenotype. Immunofluorescent staining revealed a significant reduction in B and T cell infiltration of the choroid plexus in fingolimod-treated mice (Figure 1). Finally, fingolimod reduced perivascular and periventricular leakage of serum albumin, supporting improved barrier functionality. Systemic effects of fingolimod included a significant decrease in splenomegaly and lymphadenopathy, but surprisingly without a change in circulating anti-DNA titers.

**Conclusion:** Fingolimod treatment ameliorates cognitive dysfunction and depressive-like behavior in MRL-lpr/lpr mice, and reduces CNS lymphocytic infiltration and brain barrier leakiness. Our results highlight a novel role of S1P in the pathogenesis of NPSLE and point to S1P receptor modulation as a potential therapeutic target.

**Disclosure:** E. Mike, None; A. Stock, None; C. Putterman, None.


**Abstract Number:** 1837

**Development of Murine SLE in the Absence of BAFF**

**William Stohl**¹, Ning Yu¹, Samantha Chalmers², Chaim Putterman³ and Chaim O. Jacob¹, ¹Division of Rheumatology, Keck School of Medicine of University of Southern California, Los Angeles, CA, ²Division of Rheumatology, Albert Einstein College of Medicine, Bronx, NY, ³Division of Rheumatology, Albert Einstein College of Medicine, Bronx, NY, USA, Bronx, NY

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Systemic Lupus Erythematosus – Animal Models

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 2:30PM-4:00PM

**Background/Purpose:** BAFF is a vital survival and differentiation factor for B cells. In human SLE, clinical efficacy with any of 4 different BAFF antagonists is modest at best. This limited ability of BAFF antagonists to control disease activity in human SLE points to a substantial BAFF-independent component. In stark contrast to this substantial BAFF-independent component to human SLE, disease in currently utilized murine SLE models is highly BAFF-dependent. To investigate the *in vivo* BAFF-independent component to SLE, we generated a murine model in which *SLE clinical disease* develops in the absence of BAFF.
Methods: Starting with C57BL/6 mice that express a human Bcl2 transgene (Tg) in their B cells (thereby permitting B cell survival even in the absence of BAFF), we introgressed this Tg into NZM 2328 (NZM) mice genetically deficient in BAFF (NZM.Baff-/-) to generate NZM.Baff-/- .Bcl2Tg mice. Expression of human BCL2 and lymphocyte profiles were assessed by FACS; serologic profiles were assessed by ELISA; renal immunopathology was assessed by immunofluorescence and histology; and clinical disease was assessed by testing for severe proteinuria and death. To determine whether NZM.Baff-/- .Bcl2Tg mice are sensitive to restoration of BAFF, NZM.Baff-/- .Bcl2Tg mice were crossed with NZM wild-type (WT) mice to yield BAFF-expressing NZM.Baff+/- .Bcl2Tg mice.

Results: Since SLE in NZM WT mice (and in humans) is predominantly a disease of females, only female mice were studied. In comparison to their NZM.Baff+/- littermates and to age-matched NZM WT mice, NZM.Baff-/- .Bcl2Tg mice selectively over-expressed BCL2 in their B cells. Whereas NZM.Baff+/- mice harbored decreased percentages and numbers of total B cells, follicular B cells, marginal zone (MZ) B cells, and plasma cells in comparison to NZM WT mice, these (other than MZ B cells) were restored in NZM.Baff-/- .Bcl2Tg mice to at least WT levels. NZM.Baff+/- .Bcl2Tg mice developed increased serum levels of IgG autoantibodies (anti-chromatin and anti-dsDNA), increased glomerular deposition of IgG and C3, and increased glomerular and tubulointerstitial pathology, culminating in severe proteinuria and death. The time course for development of SLE features in NZM.Baff-/- .Bcl2Tg mice was even more rapid than that in NZM WT mice. Whereas NZM WT mice start to develop severe proteinuria at 5-6 months of age, with 50% being affected by 7 months, NZM.Baff-/- .Bcl2Tg mice develop severe proteinuria as early as 3 months of age, with 50% of the mice being affected by 4 months. Whereas NZM WT mice begin dying at 6 months of age, with 50% mortality at 7.8 months, NZM.Baff-/- .Bcl2Tg mice die as early as 3 months of age, with 50% mortality at 4.5 months. SLE disease in NZM.Baff+/- .Bcl2Tg mice is even more severe, with 100% mortality at 5 months, thereby pointing to both BAFF-dependent and BAFF-independent components to disease in NZM.Baff+/- .Bcl2Tg mice.

Conclusion: BAFF may be dispensable to development of disease as long as B cell survival is preserved via a BAFF-independent pathway. This may help explain the limited and variable clinical success with BAFF antagonists in human SLE. In addition, NZM.Baff-/- .Bcl2Tg mice should serve as a powerful murine model for the study of BAFF-independent SLE.

Disclosure: W. Stohl, Janssen Research and Development, 5,Amgen, 5,GlaxoSmithKline, 2; N. Yu, None; S. Chalmers, None; C. Puttermann, None; C. O. Jacob, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/development-of-murine-sle-in-the-absence-of-baff

Abstract Number: 1838

Estimating Duration of Response in Systemic Lupus Erythematosus (SLE) Trials

Mimi Kim1, Joan T. Merrill2, Kenneth C. Kalunian3, Leslie Hanrahan4 and Peter M. Izmirly5, 1Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, NY, 2Oklahoma Medical Research Foundation, Oklahoma City, OK, 3Division of Rheumatology, Allergy and Immunology, UCSD School of Medicine, La Jolla, CA, 4Lupus Foundation of America, Washington DC, DC, 5Rheumatology, New York University School of Medicine, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment II: Clinical Trial Design and Outcome Measures
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: The primary endpoint in SLE trials is usually response to therapy at a landmark visit. However, during a trial, patients may alternate between response and non-response states. Duration of response would therefore be important to assess, but the optimal approach for estimating response duration has not been determined. Analyzing response duration only among responders at a landmark visit can result in selection bias. Drop-outs and missed visits further complicate estimation of response duration. We addressed these issues with a multi-state Markov ( MSM) model that was fit to quantify response duration and assess baseline predictors of transitions into and out of response in SLE patients receiving standard of care (SoC).

Methods: Data on 759 SLE patients with active disease (SLEDAI ≥ 6 at entry) randomized to SoC in 52 week trials was obtained from the Collective Data Analysis Initiative (CDAI) database of the Lupus Foundation of America. The following monthly response endpoints (without medication stipulations) were analyzed: SRI-4, SRI-5, SRI-6, and BICLA. A MSM model allowing for bidirectional transitions between response and non-response states was fit to estimate the probability of being in response at 52 weeks,
average duration of response (sojourn time) and mean total time in response. Predictors of attainment and loss of SRI-5 response were also identified.

**Results:** Based on the MSM model, the probability of being in response at 52 weeks ranged from 42% (SRI-6) to 61% (SRI-4), higher than conventional 52 week landmark response rates that assume non-response for missing data. The estimated mean duration of response ranged from 20.4 weeks (BICLA) to 31.5 weeks (SRI-4). Mean total time in response over 52 weeks based on all patients was 16.4 - 24.8 weeks. After adjusting for baseline SLEDAI score, patients with lower anti-dsDNA titers were more likely to achieve and maintain SRI-5 response (p < 0.001). Younger age (p < 0.001) and higher protein/creatinine ratio (p < 0.001) were associated with higher frequency of SRI-5 response but also shorter response duration. Response duration was also shorter in patients who were non-White (p < 0.001), had longer history of disease (p = 0.03), and lower lymphocyte count (p = 0.001) at baseline.

**Conclusion:** Factors associated with greater disease severity were consistently associated with shorter response duration on SoC, despite exhibiting variable effects on the probability of achieving response at a given time. Response duration might therefore provide a more discriminating measure to distinguish effective investigational treatments from background SoC, although this remains to be tested. Multi-state models make better use of complex longitudinal clinical trial data and provide a more comprehensive view of the response profile and the role of patient characteristics in different aspects of response.

**Disclosure:** M. Kim, None; J. T. Merrill, None; K. C. Kalunian, Eli Lilly and Company, S; L. Hanrahan, None; P. M. Izmirly, None.


**Abstract Number:** 1839

**Development and Validation of a Novel Evidence-Based Lupus Multivariable Outcome Score for Clinical Trials**

Michal Abrahamowicz¹, John M. Esdaile², Rosalind Ramsey-Goldman³, Lee S. Simon⁴, Vibeke Strand⁵ and Peter E. Lipsky⁶,

¹Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montreal, QC, Canada, ²Arthritis Research Canada, Richmond, BC, Canada, ³FSM, Northwestern University, Chicago, IL, ⁴SDG LLC Consulting, West Newton, MA, ⁵Stanford University, Palo Alto, CA, ⁶AMEL BioSolutions, LLC, Charlottesville, VA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment II: Clinical Trial Design and Outcome Measures

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 2:30PM-4:00PM

**Background/Purpose:** Randomized controlled trials (RCTs) of new SLE treatments are hampered by the lack of effective outcome measures that are responsive to change and clinically relevant. To address this, we developed a new Multivariable Lupus Outcome Score (LuMOS) from raw data from a previous RCT and validated it using data from an independent trial.

**Methods:**

The new LuMOS formula was developed by analyzing raw data of two pivotal RCTs: BLISS-52 and BLISS-76, the basis for approval of belimumab for treatment of SLE. Using data from BLISS-76 as the learning dataset, we optimized discrimination between outcomes for patients treated with 10mg/kg belimumab (BM-10mg) versus placebo over the first 52 weeks of follow-up. LuMOS was developed through multivariable logistic regression analyses that combined *a priori* inclusion of some variables, such as change in SLEDAI ≥4
points, with forward selection of others. The final model was selected using the Akaike Information Criterion. Performance of LuMOS was assessed using an independent validation dataset from the BLISS-52 RCT. For each belimumab trial, we tested significance of the differences in the mean LuMOS in the Active Treatment versus Placebo groups. To compare discriminatory ability of LuMOS with the conventional SLE Response Index (SRI-4), used as the primary outcome measure in both BLISS trials, we relied on Effect Size (ES = Cohen’s d = mean difference divided by within-group standard deviation).

Results:

The final LuMOS model incorporated reduction in SELENA-SLEDAI ≥4 points, increase in C4 concentration, decrease in anti-dsDNA Ab titer, and changes in BILAG organ system manifestations: no new symptoms or no worsening in renal and improvements in mucocutaneous components. Decreases in prednisone doses and increases in C3 concentration, included based on clinical considerations, had very minor impacts on total LuMOS. In all analyses of BLISS-76 and BLISS-52 RCTs, mean LuMOS were significantly higher (p < 0.0001) for BM-10mg and BM-1mg treatment groups than placebo. LuMOS also found significant differences between active treatment and placebo when SRI did not, as for BM 1mg in BLISS-76. The ES were consistently and significantly much higher, and p-values systematically much lower with LuMOS compared with SRI (Table 1).

Conclusion:

The proposed evidenced-based LuMOS developed with data from BLISS-76 and validated with data from BLISS-52 exhibits superior capacity to discriminate responders from nonresponders, compared to the SRI-4. Use of LuMOS may improve the efficiency and power of analyses in future lupus trials.

Disclosure: M. Abrahamowicz, None; J. M. Esdaile, None; R. Ramsey-Goldman, None; L. S. Simon, None; V. Strand, None; P. E. Lipsky, None.

Abstract Number: 1840

Comparison of Different Definitions of Remission in Systemic Lupus Erythematosus (SLE) – a Study Based on the BLISS-76 Clinical Trial

Sharzad Emanikia1, Cidem Gentline1, Elizabeth V. Arkema2, Laurent Arnaud3, Katerina Chatzidionysiou1,4 and Ronald F van Vollenhoven5,6, 1Department of Medicine, (ClinTRID), Karolinska Institute, Stockholm, Sweden, 2Clinical Epidemiology Unit, Department of Medicine, Karolinska University Hospital and Karolinska Institutet, Stockholm, Sweden, 3Department of Rheumatology, Université de Strasbourg, Strasbourg, France, 4On behalf of the SRQ/ARTIS registry, Stockholm, Sweden, 5Department of Medicine, (ClinTRID), Karolinska Institute, Solna, Sweden, 6AMC, F4-214, Amsterdam Rheumatology and Immunology Center, Amsterdam, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment II: Clinical Trial Design and Outcome Measures
Background/Purpose: Remission in SLE is a desirable target, however there is no gold standard for the definition of remission. An international task force agreed on various definitions of remission in SLE (DORIS) [1]. Our aim was to apply these definitions on a clinical trial.

Methods: This is a post-hoc analysis of a prospective randomized controlled trial (RCT) in SLE, the BLISS-76 clinical trial [2]. We have applied two DORIS definitions (Table 1) at three time points, week (wk) 24, 52 and 76. The patient could be in remission on or off treatment. Remission on treatment allowed maintenance anti-malarials, low dose glucocorticoids (GCs) (prednisone ≤ 5 mg/day or equivalent), maintenance immunsuppressives and maintenance biologics. Remission off treatment allowed maintenance anti-malarials only. Additionally, we applied each definition where the remission on treatment allowed a GC dose ≤ 10 mg/day (not a part of the original DORIS-definitions).

Results: There were 819 patients enrolled in BLISS-76. The baseline characteristics are shown in Table 2. The proportions of patients that fulfilled remission according to the above definitions are shown in Table 3. The highest point prevalence (9.5%) was when definition 1a on treatment was applied at wk 76. As expected, even more patients fulfilled definition 1a when a GC dose ≤ 10 mg/day was allowed at wk 76 (13.8%). More patients fulfilled the remission criteria when clinical SLEDAI was used compared to when BILAG was used. When serology (anti-DNA antibodies and complement) was taken into consideration (definitions 1b and 3b), less patients fulfilled remission. Very low numbers of patients (≤1%) fulfilled remission off treatment.

Conclusion: Overall, few patients fulfilled remission according to these definitions. More patients fulfilled the definitions when serology was excluded and when a higher dose of GCs was allowed.

References

Table 1. DORIS definitions of remission in SLE

<table>
<thead>
<tr>
<th>Definition</th>
<th>1a</th>
<th>1b</th>
<th>2a</th>
<th>3b</th>
</tr>
</thead>
<tbody>
<tr>
<td>cSLEDAI=0</td>
<td>v</td>
<td>v</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>P/H/AG=0.5</td>
<td>v</td>
<td>v</td>
<td>v</td>
<td>v</td>
</tr>
<tr>
<td>Serology</td>
<td>Regardless</td>
<td>Normal</td>
<td>Regardless</td>
<td>Normal</td>
</tr>
<tr>
<td>BILAG D/E only</td>
<td>-</td>
<td>-</td>
<td>v</td>
<td>v</td>
</tr>
</tbody>
</table>

cSLEDAI: clinical Systemic Lupus Erythematosus Disease Activity Index; P/H/AG: Physician Global Assessment; BILAG: British Isles Lupus Assessment Group.
Note: anti-double stranded DNA and complement (C3 and C9) is included in serology. These definitions were first tested (a) regardless of serology and then (b) normal serology (negative anti-DNA antibodies AND normal complement).
Table 2. Baseline characteristics of patients who started the BLISS-76 trial (n=613) who were in remission at week 24, weeks 50, and weeks 78 using different definitions

<table>
<thead>
<tr>
<th>Definition</th>
<th>Remission at Week 24</th>
<th>Remission at Week 50</th>
<th>Remission at Week 78</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remission A</td>
<td>4.3 (29)</td>
<td>6 (38)</td>
<td>6 (38)</td>
</tr>
<tr>
<td>Remission B</td>
<td>3.7 (22)</td>
<td>6 (38)</td>
<td>6 (38)</td>
</tr>
<tr>
<td>Remission C</td>
<td>3.7 (22)</td>
<td>6 (38)</td>
<td>6 (38)</td>
</tr>
</tbody>
</table>

Definition A: cSLEDAI-2K ≤5 and oral corticosteroids ≤10 mg/day. Definition B: cSLEDAI-2K ≤5 and oral corticosteroids ≤2.5 mg/day. Definition C: cSLEDAI-2K ≤5 and oral corticosteroids ≤1 mg/day.

Disclosure: S. Emamikia, None; C. Gentline, None; E. V. Arkema, None; L. Arnaud, Amgen, Astra-Zeneca, GSK, Lilly, Pfizer, Roche, 5; K. Chatzidionysiou, Lilly, AbbVie, Pfizer, Roche, Sandoz, 5; R. F. van Vollenhoven, AbbVie, Amgen, Biotest, BMS, Celgene, Crescendo, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, UCB, and Vertex; 2, AbbVie, Amgen, Biotest, BMS, Celgene, Crescendo, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, UCB, and Vertex; 5, AbbVie, Amgen, Biotest, BMS, Celgene, Crescendo, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, UCB, and Vertex; 9.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/comparison-of-different-definitions-of-remission-in-systemic-lupus-erythematosus-sle-a-study-based-on-the-bliss-76-clinical-trial

Abstract Number: 1841

Can Systemic Lupus (SLE) Disease Activity be Consistently Scored and Interpreted with Simple, Rapid Outcome Measures?

Aikaterini Thanou1, Stan Kamp2, Stavros Stavakis3, Cristina Arriens4, Teresa Aberle2, Eliza Chakravarty5, Joe Rawdon2, Judith A. James6, Joan T. Merrill7, and Anca Askanase8, 1Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 2Arthritis and Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, 3University of Oklahoma Health Sciences Center, Ok, OK, 4Arthritis & Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, 5Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation, Oklahoma City,
SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment II: Clinical Trial Design and Outcome Measures
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Clinical trial evaluations in SLE have been problematic, in part due to glossary-based outcome measures that provide imperfect thresholds for grading flares or improvement. Visual analogue scales (VAS) allow refined scaling of change in disease severity, grounded in real world clinical observation, but have been inconsistent in practice when used over time or by different raters. The SELENA SLEDAI Physician's Global Assessment (SSPGA) is a VAS with severity anchors and a simple but specific protocol for scoring designed to improve inter-and intra-rater consistency. The Rapid Evaluation of Activity in Lupus (LFA-REAL™) extends the SSPGA structure by providing separate scales for each active symptom, supporting evaluation of patient progress in individual symptoms, organs, or total disease activity. We compared performance of SS PGA and LFA-REAL™ to accepted SLE trial outcome measures during an ongoing trial in SLE.

Methods: Disease activity (SLEDAI, BILAG 2004, SS PGA and LFA-REAL™) was evaluated at consecutive monthly visits in an investigator-initiated, double-blind, placebo controlled trial of abatacept (trial results pending). Validation of total scores and change in SSPGA and REAL vs SLEDAI and BILAG were examined by Spearman Correlation. ROC curve analysis (SAS) was applied to compare changes in SSPGA and LFA-REAL™ to frequently used dichotomous SLE trial endpoints, SRI-4 and BICLA.

Results: 50 patients [47 female, mean age (SD) 45 (11.6) years] were assessed at 528 visits. Changes in disease activity compared to baseline were examined in 478 visit pairs. Total SSPGA and REAL scores strongly correlated to each other (r=0.936), as well as to total SLEDAI and BILAG [SS PGA: r= 0.742 (SLEDAI), r=0.776 (BILAG). REAL: r=0.778 (SLEDAI), r=0.813 (BILAG); all p<0.0001]. Changes in SS PGA and LFA-REAL™ at each visit compared to screening correlated to each other (r= 0.857) as well as to changes in SLEDAI and BILAG [Delta SS PGA: r=0.678 (Delta SLEDAI), r= 0.624 (Delta BILAG); Delta LFA-REAL™: r=0.686 (Delta SLEDAI), and 0.700 (Delta BILAG); all p<0.0001]. Changes in SS PGA and LFA-REAL™ were very strongly related to the dichotomous SRI-4 and BICLA endpoints by ROC analysis (p<0.0001 for all) (Table 1). Mean (95% CI) improvement in SS PGA reflecting SRI-4 was 37.3mm (35.4 to 39.3mm) and for LFA-REAL™ 52mm (48.9 to 55.1mm). Unlike SS PGA, LFA-REAL™ could be correlated to BILAG individual organ scores with musculoskeletal scores r=0.842 and mucocutaneous r=0.826 (p<0.0001 for both).

Conclusion: When scored by protocol standards, both the SS PGA and LFA-REAL™ are reliable surrogates of commonly used endpoints in SLE trials. Both instruments are easy to score and understand, and could be employed as continuous or dichotomous endpoints. The LFA-REAL™ provides an advantage of individualized scoring at the symptom or organ level.

Table 1. AUC of changes in LFA-REAL™ and PGA in relation to SRI-4 and BICLA.

<table>
<thead>
<tr>
<th></th>
<th>SRI-4</th>
<th>BICLA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Δ LFA-REAL™</td>
<td>0.8758</td>
<td>0.8517</td>
</tr>
<tr>
<td>Δ SS PGA</td>
<td>0.8946</td>
<td>0.9126</td>
</tr>
</tbody>
</table>

Disclosure: A. Thanou, None; S. Kamp, None; S. Stavrakis, None; C. Arriens, None; T. Aberle, None; E. Chakravarty, None; J. Rawdon, None; J. A. James, None; J. T. Merrill, Anthera Pharmaceuticals, Lilly, EMD Serono, GlaxoSmithKline and Biogen., 5; A. Askanase, Exagen, 2.


Abstract Number: 1842

Subsetting Systemic Lupus Erythematosus By Interferon Gene Signatures and Serologies (anti-dsDNA and Low Complement) Uncovers Significant Clinical Diversity
Background/Purpose: Personalized therapy in systemic lupus erythematosus (SLE) will require identifying SLE subsets that will benefit from different targeted therapies. Belimumab, for example, has the highest response rates in those with low complement and high anti-DNA, whereas anifrolumab (anti-interferon receptor alpha) has the highest response rates in those with the interferon alpha gene signature.

Methods: Objective molecular and biochemical baseline parameters were obtained to characterize SLE patients in two large multinational trials (n=2262 patients). Patients were categorized with three dichotomous baseline parameters: IFN gene signature, anti-dsDNA, and C3/C4.

Results: Table 1 shows the different subgroups of those with or without interferon gene signature grouped by serologies. Table 2 contains the p-values.

Table 1.

<table>
<thead>
<tr>
<th>Subgroup Criteria</th>
<th>IFN Positive Groups</th>
<th>IFN Negative Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SLE Group 1</td>
<td>SLE Group 2</td>
</tr>
<tr>
<td>IFN (+)</td>
<td>(+)</td>
<td>(+)</td>
</tr>
<tr>
<td>Anti-dsDNA (+)</td>
<td>(+)</td>
<td>(-)</td>
</tr>
<tr>
<td>Low C3 or C4 (+)</td>
<td>(+)</td>
<td>(-)</td>
</tr>
<tr>
<td>n=536</td>
<td>n=351</td>
<td>n=316</td>
</tr>
</tbody>
</table>

Baseline SLEDAI
- SLEDAI (mean): 12.4, 8.9, 10.1, 10.7, 10.1, 11.1, 9.8, 8.3, 9.2
- SLEDAI ≥ 10 (%): 80.2, 37.3, 54.4, 67.8, 63.5, 80.4, 65.6, 27.9, 45.0

Baseline Concomitant Medications
- Corticosteroids (%): 89.4, 67.2, 75.3, 75.7, 68.3, 82.6, 53.2, 49.0, 57.6
- Antimalarials (%): 64.6, 65.0, 68.4, 72.2, 66.4, 67.4, 75.0, 72.1, 70.4
- Immunosuppressants (%): 47.2, 40.7, 40.2, 52.2, 42.3, 34.8, 34.4, 31.2, 34.5
- Azathioprine (%): 22.2, 16.0, 20.9, 25.2, 19.2, 17.4, 21.9, 10.5, 14.2
- MTX (%): 10.1, 15.1, 11.7, 20.0, 8.7, 6.5, 6.3, 15.4, 12.1
- MMF (%): 12.7, 7.4, 7.0, 10.4, 11.5, 8.7, 3.1, 3.6, 6.1

Baseline Organ Involvement (SLEDAI)
- CNS (%): 0.8, 2.6, 2.9, 1.7, 1.0, 0.0, 0.0, 3.2, 2.1
- Vascular (%): 10.3, 7.4, 6.0, 10.4, 5.8, 4.4, 3.1, 2.4, 3.5
- Musculoskeletal (%): 79.7, 94.3, 87.0, 87.0, 90.4, 87.0, 90.6, 95.2, 92.8
- Renal (%): 15.1, 3.7, 6.0, 6.1, 10.6, 6.5, 3.1, 4.5, 6.1
- Mucocutaneous (%): 87.9, 96.9, 89.2, 94.8, 84.6, 82.6, 90.6, 96.0, 91.4
- CV/Respiratory (%): 10.3, 6.3, 5.7, 7.0, 6.7, 8.7, 6.3, 9.3, 8.4
- Immunologic (%): 99.8, 12.0, 99.4, 99.1, 100.0, 100.0, 96.9, 5.3, 45.2
- Constitutional (%): 1.7, 2.0, 2.2, 3.5, 1.0, 2.2, 0.0, 8.0, 0.9
- Hematologic (%): 13.4, 6.0, 9.8, 13.0, 2.9, 8.7, 3.1, 1.6, 2.8

* Combination of Groups 5-8.
### Table

<table>
<thead>
<tr>
<th></th>
<th>P-values IFN (-) Combined Groups versus</th>
<th>P-values Group 2 versus Group 1</th>
<th>Group 3</th>
<th>Group 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFN</td>
<td>(+)</td>
<td>(+)</td>
<td>(+)</td>
<td>(+)</td>
</tr>
<tr>
<td>Anti-dsDNA</td>
<td>(+)</td>
<td>(+)</td>
<td>(+)</td>
<td>(+)</td>
</tr>
<tr>
<td>Low C3 or C4</td>
<td>(+)</td>
<td>(+)</td>
<td>(+)</td>
<td>(+)</td>
</tr>
</tbody>
</table>

**Baseline SLEDAI**

- **SLEDAI (mean)**: <0.0001, 0.3378, 0.0006, <0.0001, <0.0001, <0.0001, <0.0001
- **SLEDAI ≥ 10 (%)**: <0.0001, 0.0370, 0.0108, <0.0001, <0.0001, <0.0001, <0.0001

**Baseline Concomitant Medications**

- **Corticosteroids (%)**: <0.0001, 0.0057, <0.0001, 0.0004, <0.0001, 0.0216, 0.0894
- **Antimalarials (%)**: 0.0548, 0.1054, 0.5496, 0.7097, 0.9018, 0.3531, 0.1540
- **Immunosuppressants (%)**: <0.0001, 0.0729, 0.1116, 0.0005, 0.0584, 0.8849, 0.0319
- **Azathioprine (%)**: 0.0016, 0.4995, 0.0168, 0.0048, 0.0222, 0.1000, 0.0256
- **MTX (%)**: 0.3123, 0.2253, 0.8638, 0.0295, 0.0246, 0.2006, 0.2170
- **MMF (%)**: 0.0006, 0.4531, 0.6204, 0.1022, 0.0125, 0.8241, 0.3032

**Baseline Organ Involvement (SLEDAI)**

- **CNS (%)**: 0.0703, 0.6662, 0.5099, 0.5012, 0.0276, 0.8212, 0.6130
- **Vascular (%)**: <0.0001, 0.0149, 0.1039, 0.0023, 0.1491, 0.4733, 0.3023
- **Musculoskeletal (%)**: <0.0001, 0.3904, 0.0087, 0.0465, <0.0001, 0.0111, 0.0095
- **Renal (%)**: <0.0001, 0.1330, 0.9783, 0.9916, <0.0001, 0.1636, 0.2738
- **Mucocutaneous (%)**: 0.0787, 0.0015, 0.3267, 0.2291, <0.0001, <0.0001, 0.3010
- **CV/Respiratory (%)**: 0.3234, 0.2607, 0.1608, 0.6162, 0.0389, 0.7562, 0.7940
- **Immunologic (%)**: <0.0001, <0.0001, <0.0001, <0.0001, <0.0001, <0.0001, <0.0001
- **Constitutional (%)**: 0.3174, 0.2108, 0.1514, 0.044, 0.7302, 0.8425, 0.3630
- **Hematologic (%)**: <0.0001, 0.0279, <0.0001, <0.0001, 0.0004, 0.0657, 0.0138

*p-values are from pairwise tests

Comparing negative interferon gene signature with the four interferon gene signature positive groups showed that interferon gene signature negative patients were more likely to have musculoskeletal activity than interferon gene signature positive Groups 1, 3, and 4; and more likely to have mucocutaneous activity than Group 2. Comparing Group 2 (interferon gene signature alone with no serologies) versus the other three interferon gene signature positive groups showed that the other groups had more activity and required more treatment. However, Group 2 was more likely than the other interferon gene signature groups to have musculoskeletal and mucocutaneous activity.

**Conclusion:** Subsetting SLE by BOTH interferon alpha gene signature AND serologies is much more informative than just the interferon alpha gene signature alone. There is tremendous, highly statistically significant clinical diversity within the interferon positive subgroups. This suggests that results for clinical trials of interferon targeted therapy should include such subset analyses.

**Disclosure:** M. Petri, Anthera Inc, 5,GlaxoSmithKline, 5,EMD Serono, 5,Eli Lilly and Company, 5,Bristol Meyer Squibb, 5,Amen, 5,United Rheumatology, 5,Global Academy, 5,Exagen, 2, S. Watts, Eli Lilly and Company, 1,Eli Lilly and Company, 3; R. Higgs, Eli Lilly and Company, 1,Eli Lilly and Company, 3; M. Morgan-Cox, Eli Lilly and Company, 1,Eli Lilly and Company, 3; M. D. Linnik, Eli Lilly and Company, 1,Eli Lilly and Company, 3.


**Abstract Number:** 1843

### Serum Albumin at 12 Months Post Biopsy Has Excellent Sensitivity and Specificity for Favorable 4 Year Renal Outcome in Lupus Nephritis (LN)

**Vinicius Domingues**¹, Nicole Bornkamp¹, Benjamin A. Levinson², Judith D. Goldberg², Jill P. Buyon¹ and H. Michael Belmont¹, ¹Medicine, New York University School of Medicine, New York, NY, ²Population Health, New York University School of Medicine, New York, NY

**First publication:** September 18, 2017
Background/Purpose: LN is a common, deleterious manifestation of systemic lupus erythematosus (SLE) and despite recent advances in treatment remains the most significant end organ injury contributing to morbidity and mortality. Recent studies suggest at the 12-month mark post initial treatment, proteinuria <0.7g/day is predictive of favorable long term renal outcome. Using a large multi-ethnic SLE cohort, we assessed if the level of serum albumin and urine protein-to-creatinine ratio (uPCR) at 12-month mark was predictive of long-term renal outcome.

Methods: Data were obtained from the NYU SAMPLE biorepository/registry of 750 patients fulfilling SLE criteria, 249 with renal involvement. 83 met inclusion criteria of renal bx with at least 4 years of yearly f/u serum and urine data. Adverse renal outcome (ARO) was defined as doubling of creatinine (or final creatinine >4 if initial creatinine >2.5), ESRD or need for transplantation. Included patients had to be ARO free for the first year (±1 month). Spearman correlation coefficient(S) was estimated between albumin and uPCR at 12 months and Kaplan-Meier curves and Cox models used to evaluate the predictive role of each in ARO-free survival. ROC curves were constructed to generate optimal cutoff points for sensitivity and specificity (based on Youden indices) for albumin and uPCR at 12 months. P-values of ≤ 0.05, 2-side were considered statistically significant.

Results: Of the 83 subjects, 78% were female; median age 37.0±0.9, 10% white, 35% black, 14% Asian, 41% Hispanic. ISN/RPS Class represented: 42% V, 53% III&IV, 5% II. Median albumin and uPCR were 3.9 (Range: 2.1-4.9) and 0.86 (Range: 0.06-5.96). Albumin and uPCR values at 12 months were negatively correlated (S=-0.4, p=0.0002). There were 14 AROs in the 36 months follow-up period, with a 21% cumulative ARO rate. Univariate Cox models found albumin (hazard ratio (HR)=0.15) and uPCR at 12 months (HR=1.43) as significant predictors of ARO. When evaluated jointly, only albumin at 12 months was significant (HR=0.14). The ROC of albumin alone generated an area under the curve (AUC) of 0.92 with an optimal 12-month albumin cutoff of 3.7, predicting ARO-free at 48 months post-bx with a sensitivity of 91% and specificity of 85%.

Conclusion: Serum albumin at 1 year predicted ARO-free status with high sensitivity and specificity 4 years after induction treatment, outperforming uPCR. uPCR sensitivity and specificity in our analysis contrasts with other reports as the definition of ARO is more clinically relevant for avoiding renal replacement risk and has a shorter interval of follow-up. It remains to be determined if preservation of serum albumin, despite proteinuria, reflects a non-inflammatory state, if selectivity for non-albumin proteinuria represents less glomerular injury, or if non-albumin proteins are less injurious to the tubulointerstium.

Disclosure: V. Domingues, None; N. Bornkamp, None; B. A. Levinson, None; J. D. Goldberg, None; J. P. Buyon, None; H. M. Belmont, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/serum-albumin-at-12-months-post-biopsy-has-excellent-sensitivity-and-specificity-for-favorable-4-year-renal-outcome-in-lupus-nephritis-ln

Abstract Number: 1844
Circulating Cytokine Profiles Reflect ANCA Specificity in Patients with ANCA-Associated Vasculitis

Alvise Berti1, Roscoe Warner2, Kent Johnson3, Divi Cornec4, Darrell Schroder5, Brian Kabat5, Peter A. Merkel6, Carol A. Langford7, Gary S. Hoffman8, Cees G.M. Kallenberg9, Philip Seo10, Robert F. Spiera11, Eugene St. Clair12, John H. Stone13, Ulrich Specks14 and Paul A. Monach15

1Division of Pulmonary and Critical Care Medicine, Mayo Clinic, Rochester, MN, 2University of Michigan Medical School, Ann Arbor, MI, 3University of Michigan Medical School, Ann Arbor, MI, 4Pulmonary and Critical Care Medicine, Mayo Clinic College of Medicine and Science, Rochester, MN, 5Mayo Clinic, Rochester, MN, 6Division of Rheumatology, University of Pennsylvania; Perelman School of Medicine, Philadelphia, PA, 7Rheumatic and Immunologic Diseases, Cleveland Clinic, Cleveland, OH, 8Rheumatology, Cleveland Clinic, Cleveland, OH, 9Rheumatology and Clinical Immunology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, 10Medicine, Johns Hopkins University, Baltimore, MD, 11Rheumatology, Hospital for Special Surgery, New York, NY, 12Department of Medicine, Duke University Medical Center, Durham, NC, 13Massachusetts General Hospital Rheumatology Unit, Harvard Medical School, Boston, MA, 14Mayo Clinic College of Medicine, Rochester, MN, 15Boston University School of Medicine, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Vasculitis II: Biomarkers and Disease Activity
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: To evaluate serum cytokine and chemokine profiles in patients with ANCA-associated vasculitis (AAV) classified by ANCA specificity (proteinase 3 (PR3)-ANCA versus myeloperoxidase (MPO)-ANCA) or by clinical diagnosis (granulomatosis with polyangiitis (GPA) versus microscopic polyangiitis (MPA)).

Methods: A panel of 29 soluble mediators involved in the pathogenesis of AAV was tested in active AAV patients at inclusion in a large randomized clinical trial. The levels of each biomarker were compared between groups within each classification system, ANCA type (PR3-AAV vs MPO-AAV) and clinical diagnosis (GPA vs MPA). Multivariable analyses corrected for age, sex, and renal insufficiency (eGFR<60ml/min/1.73m²) were also performed, with each biomarker as the dependent variable and ANCA type/clinical diagnosis as the explanatory variables of interest.

Results: The 186 subjects included 92 male and 94 female patients with median age 52 (IQR 44-66; range 15-92), all of whom had severe disease: median BVAS/WG 8 (IQR 5-10, range 3-23). Among these patients, 140 had been diagnosed with GPA and 46 with MPA; 124 were positive for anti-PR3 and 62 for anti-MPO. In each pair of groups (AAV clinical diagnosis, ANCA type) median BVAS/WG levels and number of patients on steroid or immune-suppressive treatment were not significantly different (p>0.05 in all comparisons). Levels of 9 mediators were significantly higher in PR3-AAV (IL-6, GM-CSF, IL-15, IL-8, TARC, IL-18Bb, sIL-2Ra, NGFb; p<0.05), compared to 4 cytokines that were higher in MPO-AAV (sIL6R, sTNFR II, NGAL, ICAM-1; p<0.05). In contrast, only 6 cytokines (IL-6, GM-CSF, IL-15, IL-18, sIL-2Ra, NGFb; p<0.05) were higher in GPA than MPA, and 3 (Osteopontin, sTNFR II, NGAL; p<0.05) were higher in MPA than GPA. Although not formally compared, for nearly all biomarkers the difference between PR3-AAV/MPO-AAV was larger than that between GPA/MPA (Figure). The multivariate analysis showed that 8 soluble mediators (IL-6, GM-CSF, IL-15, IL-18, sIL-2Ra, NGFb, sTNFR II, NGAL; p<0.05) distinguished with more accuracy AAV patients when grouped for ANCA type rather than for clinical diagnosis.

Conclusion: According to serum biomarkers, ANCA specificity better discriminates distinct subsets of patients when compared to clinical diagnosis, suggesting important differences in underlying pathophysiology and justifying stratification of patients by ANCA specificity for treatment trials. Moreover, these findings suggest that expression of certain combination of cytokines and chemokines may be driven by and/or potentially impact pathways more active in PR3-AAV than in GPA, MPA and MPO-AAV, irrespective of severity of the disease.

Figure. Serum biomarkers’ association with ANCA type and AAV clinical diagnosis groups (PR3-AAV vs MPO-AAV and GPA vs MPA).
Disclosure: A. Berti, None; R. Warner, None; K. Johnson, None; D. Corne, None; D. Schroeder, None; B. Kabat, None; P. A. Merkel, None; C. A. Langford, None; G. S. Hoffman, None; C. G. M. Kalenberg, None; P. Seo, GlaxoSmithKline, 5; R. F. Spiera, None; E. St. Clair, Bristol-Myers Squibb, 2; Bristol-Myers Squibb, 5; AbbVie, 5; UpToDate, 7; J. H. Stone, Xencor, 2; U. Specks, None; P. A. Monach, Genentech and Biogen IDEC Inc., 2; GlaxoSmithKline, 2; Bristol-Myers Squibb, 2.


Abstract Number: 1845

**Comparison of Magnetic Resonance Angiography (MRA) and 18f-Fluorodeoxyglucose Positron Emission Tomography (PET) in Large Vessel Vasculitis**

Kaitlin A. Quinn1,2, Ashkan Malayeri3, Mark Ahlman3, Armin Bagheri4, Robert Evers5, Ali Cahid Civelek3, Elaine Novakovich6 and Peter C. Grayson7, 1Rheumatology, MedStar Georgetown University Hospital, Washington, DC, 2NIAMS/NIH, Bethesda, MD, 3Radiology and Imaging Sciences, National Institutes of Health, Bethesda, MD, 4Vasculitis Translational Research Program, NIAMS, NIH, Bethesda, MD, 5NIH, Bethesda, MD, 6NIH, Bethesda, MD, 7Systemic Autoimmunity Branch, NIAMS, National Institutes of Health, Bethesda, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Vasculitis II: Biomarkers and Disease Activity
Session Type: ACR Concurrent Abstract Session
Background/Purpose:
Magnetic resonance imaging (MRI) and $^{18}$F-fluorodeoxyglucose positron emission tomography (PET) may provide unique or redundant information in large vessel vasculitis (LVV). The study objective was 1) to assess agreement between interpretation of MRA and PET for disease activity and disease extent and 2) to determine MRA features associated with PET activity.

Methods:
An observational cohort of patients with giant cell arteritis (GCA) or Takayasu’s arteritis (TAK) were prospectively recruited, along with a comparator group (patients with vasculopathy or healthy controls). Subjects underwent clinical assessment, MRA, and PET within 24 hours. Imaging and clinical assessments were performed blinded to each other. A radiologist and two nuclear medicine physicians with vascular imaging expertise evaluated the MRA and PET studies for evidence of active vasculitis. To evaluate disease extent, the aorta and primary branches were divided into 15 vascular territories. Vascular involvement within each territory was defined on MRI as presence of wall thickness (black blood sequences), edema (STIR sequences), stenosis, occlusion, or aneurysm. Vascular involvement on PET was defined as visual FDG uptake in each arterial territory > liver. Agreement was assessed by percent overall agreement, Cohen’s kappa, and McNemar’s test. Multivariable logistic regression was used to test which factors on MRA were associated with PET interpretation of disease activity.

Results:
68 patients (GCA=26; TAK=24; Comparator=18) contributed 115 paired PET/MRA studies. A total of 1398 vascular territories were evaluated. Scans were interpreted as active disease in 76 PETs and 77 MRAs. 80 studies showed agreement (70%, Cohen’s kappa=0.32) between PET and MRA. In 35 studies with disagreement, PET demonstrated disease activity in 17 studies and MRA in 18 studies (McNemar’s p=1.00). Clinical disease status was associated with PET scan interpretation (p=0.01) but not MRA interpretation (p=0.52). More comparators were interpreted as active vasculitis by MRA versus PET (50% vs 11%, p=0.03). 782 territories showed agreement (56%, Cohen’s kappa=0.17) for disease extent between PET and MRA. Of the 608 territories with disagreement, MRA demonstrated disease in more territories than PET (513 vs 95, McNemar’s p=0.01). Territories with PET disease activity were positively associated with edema (OR=1.36, 95%CI=1.10-1.70, p<0.01) and wall thickness (OR=1.17, 95%CI=1.01-1.37, p=0.04) but not associated with stenosis (OR=0.07, 95%CI=0.33-0.96, p=0.33).

Conclusion:
There was fair agreement in the interpretation of PET and MRA findings for disease activity, but PET interpretation, and not MRA interpretation, was associated with clinical assessment. MRA detects disease activity and damage, thus identifying a greater extent of vascular involvement compared to PET. These data suggest that PET and MRA provide complementary information in LVV. In situations where PET is not available, increasing number of arterial territories with edema and wall thickness on MRA could be a surrogate for PET scan activity.

Disclosure: K. A. Quinn, None; A. Malayeri, None; M. Ahlman, None; A. Bagheri, None; R. Evers, None; A. C. Civelek, None; E. Novakovich, None; P. C. Grayson, None.


Abstract Number: 1846

Increased CD38hiCD27+ Plasmablast Frequency in Remission Predicts Relapsing Disease in Granulomatosis with Polyangiitis Patients

Anouk von Borstel1, Wayel H. Abdulahad2, Abraham Rutgers2, Judith Land2, Coen A. Stegeman1, Peter Heeringa3 and Jan-Stephan F. Sanders1, 1Internal Medicine, Division of Nephrology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, 2Rheumatology and Clinical Immunology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, 3Pathology and Medical Biology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands

First publication: September 18, 2017
Patients with granulomatosis with polyangiitis (GPA) are prone to disease relapse. Changes in anti-neutrophil cytoplasmic autoantibodies (ANCA) levels can predict relapses in individual patients to some extent. Plasmablasts are considered precursors of ANCA-producing plasma cells and are therefore expected to be involved in GPA. This study aimed to determine whether patients at risk for relapse could be distinguished based on increased plasmablast frequency during remission.

Methods:

90 proteinase 3 (PR3)-ANCA positive GPA patients in remission were monitored for relapses for up to 6.3 years. Moreover, 48 healthy controls (HCs) were included. The B cell phenotype was determined at inclusion by flow cytometry, serum ANCA levels were measured with both indirect immunofluorescence and the Phadia ImmunoCAP 250 analyzer. Spontaneous and stimulated \textit{in vitro} PR3-ANCA production by isolated PBMCs, after 12-day stimulation with or without CpG-ODN, BAFF and IL-21 was measured with Phadia ImmunoCAP 250 analyzer. The frequency of plasmablasts at inclusion of future-relapsing (F-R) and non-relapsing patients (N-R) was compared and the median frequency of plasmablasts was related to relapse-free survival.

Results:

27 of the 90 patients (30%) relapsed after on average 1.64 years (median: 1.75; range: 0.07-3.78) since inclusion. The median frequency of circulating plasmablasts was significantly increased in F-R patients (median: 2.39%, range: 0.6-16.3%) compared to N-R patients (p=0.0014, median: 1.03%, range: 0.1-12.5%) and HCs (p=0.0208, median: 1.33%, range: 0.5-7.6%). The actuarial survival analysis showed a higher percentage of plasmablasts at inclusion was related to decreased relapse-free survival during follow-up (p=0.0001). 70% of the patients with $\geq 2.39\%$ plasmablasts eventually experienced a relapse during study follow-up compared to 19% in the $<2.39\%$ plasmablast group. At inclusion, no significant correlation was found between plasmablast frequency and ANCA titer, serum PR3-ANCA or \textit{in vitro} PR3-ANCA production.

Conclusion:

Our data suggest that an increased plasmablast frequency during remission is related to a higher frequency of disease relapses in GPA patients. However no correlation with ANCA levels was found. In conclusion, plasmablast frequency might be a helpful biomarker to identify patients in remission at risk for relapse.

 Disclosure: A. von Borstel, None; W. H. Abdulahad, None; A. Rutgers, None; J. Land, None; C. A. Stegeman, None; P. Heeringa, None; J. S. F. Sanders, Dutch Kidney Foundation, 2, Netherlands Organization for Scientific Research, 2.
Background/Purpose: Granulomatosis with Polyangiitis (GPA) is characterized by vasculitis in lungs, kidneys and the ear, nose and throat region. Regular monitoring and treatment adjustments are needed, as disease activity tends to fluctuate over time. Unfortunately, good markers for disease activity are lacking, leading to over- and undertreatment. Immunoglobulin G4 positive (IgG4+) B-cells and plasma cells are implicated in the pathogenesis of GPA. Recently, we developed a test that indirectly measures the presence of IgG4+ B-cells/plasma cells in blood by measuring the IgG4:IgG RNA ratio\(^1\). We hypothesized that this test could serve as a disease activity marker in GPA. Here we test the IgG4:IgG RNA ratio in peripheral blood as a disease activity marker in GPA.

Methods: 29 PR3-ANCA positive GPA patients were included. Mean age was 53 years, 55% were female, and 41% had active disease. For each patient ESR, CRP, BVAS, and PR3-ANCA-titre was measured. Active disease was defined as BVAS $\geq 3$. We also included 10 healthy controls (HC) and 63 patients with other immune mediated inflammatory diseases (systemic lupus erythematosus (SLE) (n = 24), rheumatoid arthritis (RA) (n = 19), primary sclerosing cholangitis (PSC) (n = 20)). The IgG4:IgG RNA ratio in peripheral blood samples was measured using a validated qPCR test\(^1\).

Results: The median IgG4:IgG RNA ratio was significantly higher in the GPA cohort (6.0; IQR 2.7-19.8) compared to all controls: 1.2 in SLE (0.7-3.3; p=0.0001), 2.5 in RA (IQR 0.7-4.1; p<0.05), 1.6 in PSC (IQR 1.0-2.8; p<0.01) and 1.3 in HC (IQR 0.6-1.8, p<0.001). In addition, the median IgG4:IgG RNA ratio was significantly higher in active disease (20.7; IQR 14-28.5) compared to remission (3.5; IQR 1.9–5.5) (p<0.0001). An IgG4:IgG RNA ratio of 9.3 differentiated perfectly between active disease and remission (AUC 1.000). The IgG4:IgG RNA ratio (p<0.0001) outperformed other disease activity parameters such as ESR (p<0.05), CRP (p<0.01) and PR3-ANCA titre (ns) in detecting active disease. The height of the IgG4:IgG RNA ratio significantly correlated with height of the BVAS (Spearman r=0.78, p<0.0001).

Conclusion: The IgG4:IgG RNA ratio distinguishes active GPA from GPA in remission with excellent specificity and sensitivity. Moreover, the ratio shows a significant correlation with disease severity and outperforms other disease activity parameters. Retesting in a prospective study is indicated to validate the IgG4:IgG ratio as a novel marker of disease activity in GPA.

Abstract Number: 1848

**NMR-Based Serum Metabolomics of Patients with Takayasu Arteritis (TA) and Relationship with Disease Activity**

**Ramnath Misra**¹, Avinash Jain², Dinesh Kumar³, Durga Prasanna Misra⁴, Anupam Guleria⁵, Sandeep Kumar⁶, Atul Rawat³, Smriti Chaurasia⁴, Umesh Kumar⁶, Abhishek Zanwar⁴, Durgesh Dubey⁵, Ruchika Goel⁸, Debashish Danda⁹ and Paul Bacon¹⁰,

¹Clinical Immunology, Sanjay Gandhi Postgraduate of Medical Sciences, Lucknow, India, ²Clinical Immunology, Senior Resident, Lucknow, India, ³Centre for Biomedical Research, Lucknow, India, ⁴Clinical Immunology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, ⁵Centre for Biomedical Research, DST-INSPIRE Faculty, Lucknow, India, ⁶Centre for Biomedical Research, Research Scholar, Lucknow, India, ⁷Centre for Biomedical Research, PhD Student, Lucknow, India, ⁸Rheumatology, Christian Medical College, Vellore Tamilnadu, India, ⁹Clinical Immunology & Rheumatology, Christian Medical College, Vellore, India, Vellore, India, ¹⁰Rheumatology, Emeritus Professor, Birmingham, United Kingdom

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Vasculitis II: Biomarkers and Disease Activity  
**Session Type:** ACR Concurrent Abstract Session  
**Session Time:** 2:30PM-4:00PM

**Background/Purpose:** Takayasu arteritis (TA) is a large vessel vasculitis of unknown pathogenesis. The current serological and radiological parameters used to assess disease activity are not highly specific and there is a need for a relevant biomarker. In our previous study [1], NMR based serum metabolomics had revealed distinctive metabolic signatures in patients with TA compared to age/sex matched healthy controls and SLE [2]. In this study we investigate whether these distinctive metabolites correlate with disease activity.

**Methods:** Patients with TA fulfilling ACR criteria were assessed for disease activity using ITAS A (ESR), with a score of ≥4, considered as active. The serum metabolic profiles of active and inactive TA patients obtained with an 800 MHZ NMR spectrometer were compared using multivariate orthogonal partial least-squares discriminant analysis (OPLS-DA) to identify metabolites that related to disease activity [based on PLS-DA VIP(variable importance on projection) score >1.5 and permutation test, p-value < 0.01].
Results: 98 patients were categorized into active (45) and inactive (53) groups - median age 27 years in both groups and female to male ratio 3.5:1 and 4.9:1 respectively. The majority had class V disease. Mean duration of illness was $8.8 \pm 1.3$ years in active TA and $5.2 \pm 5.6$ years in inactive TA group. An exquisite separation in OPLS-DA score plot showed metabolic differences between active and inactive TA patients (Fig. 1A). The key metabolites with highest discriminatory potential (VIP score > 1.5) which were elevated in active TA were glutamate, N-acetyl glycoprotein (NAG), glucose, phosphoglyceride, glycerol, leucine whereas lactate, choline, low/very-low density lipoproteins (LDL/VLDL) were decreased. Receiver operating characteristic (ROC) curve analysis revealed glutamate and NAG had the highest potential to discriminate active from inactive TA (area under the curve 0.775 and 0.769 respectively (p-value<0.0001) (Fig. 1B, 1C). The spectra did not correlate with current therapy but did alter when disease activity changed on follow-up.

Conclusion: This large cohort of patients revealed metabolic profiles discriminating between clinically active and inactive TA patients. It suggests glutamate and NAG have strong potential as biomarkers for disease activity in TA and may serve as a guide to therapy. We are now working to further validate these results in longitudinal studies.

References


Disclosure: R. Misra, None; A. Jain, None; D. Kumar, None; D. P. Misra, None; A. Guleria, None; S. Kumar, None; A. Rawat, None; S. Chaurasia, None; U. Kumar, None; A. Zanwar, None; D. Dubey, None; R. Goel, None; D. Danda, None; P. Bacon, None.


Abstract Number: 1849

Urinary Epidermal Growth Factor and Monocyte Chemoattractant Protein-1 As Biomarkers of Renal Involvement in ANCA-Associated Vasculitis

Catherine E. Najem1, Wenjun Ju2, Viji Nair2, David Cuthbertson3, Rennie L. Rhee1, Laura Mariani4, Simon Carette5, Nader A. Khalidi6, Curry L. Koening7, Carol A. Langford8, Carol A. McAleer9, Paul A. Monach10, Larry W. Moreland11, Christian Pagnoux5, Philip Seo12, Ulrich Specks13, Antoine G. Sreih1, Steven R. Ytterberg14, Jeffrey Krischer15, Matthias Kretzler4 and Peter A. Merkel16,

1Rheumatology, University of Pennsylvania, Philadelphia, PA, 2University of Michigan, Ann Arbor, MI, 3Biostatistics and Informatics, Department of Pediatrics, University of South Florida, Tampa, FL, 4Division of Nephrology, University of Michigan, Ann Arbor, MI, 5Division of Rheumatology, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada, 6Rheumatology, McMaster University, Hamilton, ON, Canada, 7Rheumatology, University of Utah, Salt Lake City, UT, 8Rheumatic and Immunologic Diseases, Cleveland Clinic, Cleveland, OH, 9University of Pennsylvania, Philadelphia, PA, 10Boston University School of Medicine, Boston, MA, 11Rheumatology & Clinical Immunology, University of Pittsburgh, Pittsburgh, PA, 12Medicine, Johns Hopkins University, Baltimore, MD, 13Mayo Clinic College of Medicine, Rochester, MN, 14Rheumatology, Mayo Clinic, Rochester, MN, 15University of South Florida, Tampa, FL, 16Biostatistics, Epidemiology, and Informatics, University of Pennsylvania, Philadelphia, PA

First publication: September 18, 2017

SESSION INFORMATION
Background/Purpose:

Epidermal growth factor (EGF) mediates distal tubular epithelial cell function and regeneration. Monocyte chemoattractant protein-1 (MCP-1) participates in recruitment of leukocytes to areas of inflammation. Urinary EGF (uEGF) and MCP-1 (uMCP-1) predict active and chronic renal disease in primary glomerulopathies. This study examined the utility of uEGF and uMCP-1 as biomarkers of renal disease in patients with ANCA-associated vasculitis (AAV).

Methods:

Data from patients with AAV enrolled in a prospective multicenter cohort were included. uEGF and uMCP-1 were measured at baseline, an active renal disease visit (index), 1-2 visits prior to and after the index visit, and at 1 year follow-up. Chronic kidney disease (CKD) was defined as eGFR< 60 mL/min/1.73 m2 for >3 months. Index was defined as the first visit with a new/worse BVAS/WG renal item since prior visit. uEGF and uMCP1 were converted to log2 uEGF/urinary creatinine and log2 uMCP1/urinary creatinine ratios for all analyses. To assess the association of each biomarker with disease activity, a mixed effect model was used, adjusting for ANCA type (MPO or PR-3), albumin/creatinine ratio, eGFR, and visit type. To assess time to CKD outcome, a Cox proportional hazard model was used, adjusting for sex, age, race, ANCA type, albumin/creatinine, and eGFR.

Results:

At baseline, 165 of 544 (30%) patients had CKD. For each unit increase in baseline uEGF/Cr there was a lower risk of CKD [HR=0.62, (0.43, 0.88), p=0.01]. After adjusting for sex, age, race, ANCA type, eGFR, and albumin/Cr, the percentage of patients surviving without CKD was significantly lower (p<0.01) in patients with lower uEGF at baseline (Quartile 1) compared to patients with higher levels of uEGF at baseline (Quartile 4) (Figure 1). Higher baseline uMCP-1/Cr didn’t predict risk of CKD [HR=1.14, (0.88, 1.48), p=0.33]. In the same adjusted model, the percentage of patients surviving without CKD was not significantly different (p=0.06) in patients with lower uMCP1 at baseline (Quartile 1) compared to patients with higher levels of uMCP1 (Quartile 4) (Figure 2).

112 patients had active renal disease. uEGF/Cr levels did not significantly differ between pre-, post-, and index visits. Compared to index visit, uMCP-1/Cr was lower at pre- and post-index visits (p=0.04 and p<0.01, respectively) after adjusting for the mixed effect model variables.

Conclusion:

In patients with AAV, uEGF predicts progression to CKD independently of urine albumin/creatinine and eGFR. uMCP-1, but not uEGF, is associated with renal disease activity. uEGF and uMCP-1 are useful biomarkers in AAV.
Efficacy of Zoledronic Acid and Denosumab in the Treatment of Patients with Low Back Pain and Modic Changes: A Proof of Principle Trial

Guoqi Cai¹, Laura Laslett¹, Dawn Aitken², Andrew Halliday³, Feng Pan², Petr Otahal¹, Deb Speden⁴, Tania Winzenberg¹ and Graeme Jones², ¹Menzies Institute for Medical Research, University of Tasmania, Hobart, Australia, ²Musculoskeletal Unit, Menzies Institute for Medical Research, University of Tasmania, Hobart, Australia, ³Radiology, Royal Hobart Hospital, Hobart, Australia, ⁴Royal Hobart Hospital, Hobart, Australia
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: ACR/ARHP Combined: Orthopedics and Rehabilitation Science
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Low back pain (LBP) is a common and debilitating problem. There are currently very limited pharmacological treatments for LBP. Vertebral endplate subchondral bone abnormalities (Modic abnormalities (MC)) are consistently associated with LBP and could be a potential treatment target. Previous research suggests that bone active agents, such as zoledronic acid (ZA) may be effective for knee bone marrow lesions and back pain. No evidence is available for denosumab (DN). This study aims to compare the effects of ZA and DN on LBP in patients with MC.

Methods: Adults aged ≥40 years with significant LBP (>6 months) and MC (type 1, 2 or mixed) were randomised to receive either ZA (5mg/100ml) or DN (60mg), or placebo. The chief outcomes were change in pain assessed by Visual Analogue Scale (VAS, 0-100) and size of MC measured on MRIs of T12-S1 vertebrae over 6 months. Other outcomes included: change in pain assessed by the LBP Rating Scale (RS, 0-30), disability by the Roland-Morris Disability Questionnaire (RMDQ, 0-24), and quality of life by Assessment of Quality of Life (AQoL, 0-48) after 3 and 6 months. Repeated measures regression was performed to analyse the change in outcomes.
Results: 103 participants (39% females, mean age 59.8 yrs) were enrolled. At baseline, mean (SD) VAS, and RS scores were 57.1 (18.3) and 17.6 (5.0), and the median total MC area was 538 mm². Subjects were generally well matched at baseline. Table 1 presents the findings for the chief and other outcomes. Compared to placebo, VAS scores decreased by clinically significant amounts in both the ZA and DN groups after 6 months, but the change was not statistically significant (p=0.13 and 0.06 respectively). There was little reduction in areal MC size and no difference between groups. LBP RS scores were significantly reduced compared to placebo in the ZA group after 3 (-3.5, 95%CI -6.2 to -0.8) and 6 months (-3.3, 95%CI -5.9 to -0.7), and in the DN group after 6 months (-3.0, 95%CI -5.7 to -0.3). Improvements in disability (RMDQ) occurred in the ZA group after 3 months (-2.1, 95%CI -4.0 to -0.2). Time course analysis suggested ZA treated patients had lower VAS pain scores after one month and DN after 2 months. Both therapies were more effective for VAS pain after 6 months in those with smaller Modic area and milder disc degeneration as classified at screening, and DN was more effective for VAS pain in patients with type 1 MC (Fig 1). Adverse events were more frequent in the ZA group; primarily flu-like symptoms and headaches.

Conclusion: These pilot findings suggest that both ZA and DN may reduce LBP associated with MC but do not change MC size over 6 months.

Table 1. Study outcomes over 3 and 6 months among ZA, DN and placebo groups 5

<table>
<thead>
<tr>
<th></th>
<th>ZA (n=35)</th>
<th>DN (n=33)</th>
<th>Placebo (n=37)</th>
<th>ZA - Placebo</th>
<th>DN - Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 Months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LBP VAS, 0-200</td>
<td>17.3(-19.4 to -9.7)</td>
<td>13.0(-23.1 to -9.8)</td>
<td>7.8(-10.3 to -1.1)</td>
<td>-9.5(-20.3 to 1.3)</td>
<td>-7.2(-18.4 to 4.0)</td>
</tr>
<tr>
<td>LBP RS, 0-30</td>
<td>-6.4(-7.3 to -5.5)</td>
<td>-4.3(-5.3 to -2.3)</td>
<td>-1.9(-3.9 to 0)</td>
<td>-3.5(-4.6 to -2.4)</td>
<td>-2.3(-5.1 to 0.5)</td>
</tr>
<tr>
<td>RVICOL, 0-24</td>
<td>-3.5(-4.9 to -2.2)</td>
<td>-1.2(-2.5 to 0.2)</td>
<td>-1.4(-2.8 to -0.0)</td>
<td>-2.3(-4.0 to -0.7)</td>
<td>0.3(-1.7 to 2.1)</td>
</tr>
<tr>
<td>AQOL, 0-60</td>
<td>-2.2(-3.1 to -0.4)</td>
<td>-0.2(-1.3 to 0.7)</td>
<td>-0.5(-1.4 to 0.4)</td>
<td>-0.8(-2.0 to 0.5)</td>
<td>0.3(-0.9 to 1.6)</td>
</tr>
<tr>
<td>6 Months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total area, mm²</td>
<td>-0.8(-1.8 to 0.2)</td>
<td>-2.9(-3.3 to 0.5)</td>
<td>5.8(-1.7 to 23.3)</td>
<td>-6.6(-11.4 to 7.8)</td>
<td>-8.9(-19.2 to 16.7)</td>
</tr>
<tr>
<td>LBP VAS, 0-100</td>
<td>-2.6(-29.1 to -0.8)</td>
<td>-24.0(-32.1 to -16.0)</td>
<td>-13.9(-20.8 to -6.8)</td>
<td>-8.2(-18.8 to 2.4)</td>
<td>-10.7(-22.7 to 0.3)</td>
</tr>
<tr>
<td>LBP RS, 0-30</td>
<td>-6.3(-8.2 to -4.4)</td>
<td>-3.0(-3.8 to -0.2)</td>
<td>-3.0(-4.9 to -1.1)</td>
<td>-3.3(-5.9 to -0.7)</td>
<td>-3.0(-5.7 to -0.3)</td>
</tr>
<tr>
<td>RVICOL, 0-24</td>
<td>-2.0(-4.3 to -1.9)</td>
<td>-1.6(-3.0 to -0.2)</td>
<td>-1.8(-3.1 to 0.5)</td>
<td>-1.4(-3.2 to 0.5)</td>
<td>0.2(-1.7 to 2.1)</td>
</tr>
<tr>
<td>AQOL, 0-60</td>
<td>-1.5(-2.4 to -0.7)</td>
<td>-0.4(-1.3 to 0.5)</td>
<td>-0.8(-1.7 to 0.0)</td>
<td>-0.7(-2.9 to 0.5)</td>
<td>0.5(-0.8 to 1.7)</td>
</tr>
</tbody>
</table>

1 Changes from baseline to 3 months and 6 months among the three groups were compared using multilevel mixed-effects linear regression.
2 Total area meant the sum of the maximum area of each Modic lesion from the upper endplate of T12 down to the upper endplate of S1.

Figure 1. Change in low back pain (VAS) among the ZA, DN and placebo groups in: a) All participants; b) Participants with type 1 MC at screening; c) Participants without severe disc degeneration (level 5, by Pfirrmann Grading System) at screening; and d) Participants with screening Modic area below the median. P values indicate the between-group differences at 6 months.

Disclosure: G. Cai, None; L. Laslett, None; D. Aitken, None; A. Halliday, None; F. Pan, None; P. Otahal, None; D. Speden, None; T. Winzenberg, None; G. Jones, None.


Abstract Number: 1851

Improving Walking Ability in Degenerative Lumbar Spinal Stenosis: A Randomized Trial Comparing 2 Self-Management Training Programs
Background/Purpose: Degenerative lumbar spinal stenosis (DLSS) is a leading cause of pain, disability and loss of independence in older adults. It is caused by age related osteoarthritic changes to the lumbar spine resulting in spinal canal narrowing and compression to the spinal nerves. Neurogenic claudication is the clinical syndrome caused by DLSS and reduced walking ability is its hallmark feature. Effective non-surgical approaches for DLSS are unknown. The main objective of this study is to compare the ability of 2 self-management training programs to improve walking capacity in DLSS.

Methods: Eligible consenting participants with neurogenic claudication with DLSS and limited walking ability (<30 minutes) were randomized to a 6-week (w) comprehensive self-management training program or a self-directed self-management training program with a single educational session. Both groups received a pedometer, an exercise manual and video with instructions on daily home exercises and self-management strategies recommended to be followed for life. The primary outcomes were objective continuous walking distance in meters (m) in 30 minutes assessed by the Self-Paced Walk Test (SPWT) at 8w, 3, 6 and 12 months following randomization; and the proportion of participants achieving at least 30% improvement (minimal clinically important difference, MCID) in the SPWT. Secondary outcomes included the Zurich Claudication Questionnaire (ZCQ), the Oswestry Disability Index and the Numeric Pain Scale for low back and leg pain. Intention-to-treat analysis was performed for all outcomes.

Results: Fifty-one participants were randomized to the comprehensive and 53 to the self-directed group. At 8w, the mean improvement in walking distance was 502m in the comprehensive group and 211m in the self-directed group, with an adjusted mean treatment effect of 345.4m; 95% confidence interval [CI], 150 to 660.6; P=0.0006. At 12 months the mean improvement in walking distance from baseline was 675m in the comprehensive group and 201m in the self-directed group with a between-group adjusted mean difference of 473.2m; 95% CI, 203.9 to 742.4; P = 0.0007. At 8w, 85% versus 61%, adjusted relative risk (RR), 1.4; 95% CI, 1.1 to 1.8; P= 0.008, and at 12 months, 81% versus 59%, adjusted RR, 1.4; 95% CI, 1.1 to 1.8; P= 0.018, of participants achieved the MCID in the SPWT in the comprehensiveverses the self-directed group respectively. At 12 months all secondary outcomes showed significant improvement from baseline in both groups with the comprehensive group demonstrating significantly greater improvement in the ZCQ functional scale, adjusted mean difference of -0.48; 95% CI, -0.90 to -0.06 compared to the self-directed group.

Conclusion: Both self-management training programs showed significant improvement in walking distance with the comprehensive program demonstrating superior improvement in walking distance and proportion of participants meeting the MCID at each follow-up. The large improvement in walking distance in comprehensive group was sustained at 12 months without additional interventions beyond the initial comprehensive training program.

Disclosure: C. Ammendolia, None; P. Côté, None; D. Southerst, None; M. Schneider, None; B. Budgell, None; C. Bombardier, None; G. Hawker, None; Y. R. Rampersaud, None.


Abstract Number: 1852

Validating Patient Reported Outcomes in Older Veterans with Chronic Back Pain

Rabih Nayfe1, Matthieu Chansard2, Thiru Annaswamy3, Katharine McCallister2, Liana Fraenkel4, Eric Mortensen5 and Una E. Makris6. 1Department of Medicine, UT Southwestern Medical Center, Dallas, TX, 2Clinical Sciences, UT Southwestern Medical Center, Dallas, TX, 3Physical Medicine & Rehabilitation., VA North Texas Health Care System, Dallas, TX, 4Rheumatology,
Background/Purpose: Chronic back pain is the second most common reason for a physician’s visit and results in significant physical and psychosocial consequences in older adults. Identifying appropriate, efficient and reliable patient reported outcome measures is critical for research and clinical purposes. The NIH’s Patient Reported Outcomes Measurement Information System (PROMIS) instruments provide robust patient-reported outcome measures; however, these have not been compared to validated “legacy” instruments in older adults with chronic back pain. This study aims to evaluate convergent validity and time to completion (TTC) of PROMIS as compared to “legacy” instruments (both self-reported).

Methods: We enrolled older Veterans (age 60+) with chronic back pain with/without leg pain (≥3 months) scheduled for lumbar epidural steroid injections. Participants completed PROMIS computer adaptive test (CAT) item banks and corresponding “legacy” instruments in the following domains: pain interference, behavior and intensity; functional status; depression and anxiety; fatigue; sleep and social functioning. Convergent validity between PROMIS and “legacy” instruments was evaluated using Pearson correlation coefficients in a correlation matrix. Paired sample t-tests compared average TTC between both instruments.

Results: Participants included 71 Veterans who were on average 67 years old, 94% men, 73% non-Hispanic white, 16.9% African American. Over half were obese with mean BMI 32, 25% reported multi-site pain and 59% were diagnosed with depression, anxiety and/or PTSD. The majority (69%) reported pain duration ≥5 years with ~ 93% reporting associated radiculopathy. Pearson correlations between PROMIS and “legacy” instruments are listed in Table 1 and show moderate to strong convergent validity, with the exception of social functioning domains. PROMIS items had significantly shorter TTC than “legacy” items across all domains (Table 2).

Conclusion: PROMIS measures, especially for depression, anxiety, fatigue and sleep domains, have strong convergent validity in older Veterans with chronic back (and associated leg) pain. Moreover, PROMIS measures require less time to complete. Given time efficiency of using PROMIS, along with strong convergent validity, PROMIS instruments are a valid and practical choice for both research and clinical purposes.
Table 2: TIME TO COMPLETE (TTC) – PROMIS VS LEGACY INSTRUMENTS
(minutes:seconds)

<table>
<thead>
<tr>
<th>COMPARISON</th>
<th>PROMIS TTC (mean)</th>
<th>LEGACY TTC (mean)</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain Interference vs BPI</td>
<td>1:37</td>
<td>3:26</td>
<td>-7.87</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Pain Interference vs SF-36 Bodily</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>1:58</td>
<td>6:22</td>
<td>-10.59</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Pain Behavior vs PCS</td>
<td>0:43</td>
<td>2:31</td>
<td>-14.47</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Pain Behavior vs FABQ</td>
<td>0:43</td>
<td>6:51</td>
<td>-19.23</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Physical Function vs Roland Morris</td>
<td>0:53</td>
<td>2:21</td>
<td>-13.75</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Depression vs PHQ4-Depression</td>
<td>0:37</td>
<td>0:18</td>
<td>5.89</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Anxiety vs PHQ4-Anxiety</td>
<td>1:05</td>
<td>0:22</td>
<td>4.64</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Fatigue vs FACIT – Fatigue Subscale</td>
<td>0:37</td>
<td>1:25</td>
<td>-12.10</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Sleep Disturbance vs MOS Sleep</td>
<td>0:45</td>
<td>3:13</td>
<td>-14.35</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Social Isolation vs MOS SSI</td>
<td>0:49</td>
<td>2:16</td>
<td>-6.97</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Social Satisfaction vs MOS SSI</td>
<td>0:50</td>
<td>2:17</td>
<td>-5.18</td>
<td>P &lt; 0.001</td>
</tr>
</tbody>
</table>

BPI = Brief Pain Inventory, PCS = Pain Catastrophizing Scale, FABQ = Fear Avoidance Belief Questionnaire, FACIT = Functional Assessment of Chronic Illness Therapy, MOS Sleep = Medical Outcomes Study Sleep Scale, MOS SSI = Medical Outcomes Study Social Support Survey

Disclosure: R. Nayfe, None; M. Chansard, None; T. Annaswamy, None; K. McCallister, None; L. Fraenkel, None; E. Mortensen, None; U. E. Makris, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/validating-patient-reported-outcomes-in-older-veterans-with-chronic-back-pain

Abstract Number: 1853

Exercise and Adherence over Two Years: Beliefs of Adults with Knee Osteoarthritis

Aileen Ledingham¹, Ellen Cohn², Kristin Baker³ and Julie Keyser¹, ¹Physical Therapy, Boston University, Boston, MA, ²Occupational Therapy, Boston University, Boston, MA, ³Physical Therapy, Boston University Sargent College, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: ACR/ARHP Combined: Orthopedics and Rehabilitation Science
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Exercise is an established treatment to improve pain and physical function in adults with knee osteoarthritis (KOA), which is a leading cause of disability affecting 14 million adults. Most adults with KOA do not adhere to long-term exercise, abating benefits. The literature lacks well-controlled studies evaluating approaches to improve long-term exercise adherence. We conducted a randomized controlled trial (RCT) in people with KOA where both groups received the same evidence based exercise protocol and differed only in adherence interventions. Two-year adherence was the primary outcome. The intervention group received theoretically informed automated interactive telephone calls to coach and motivate subjects to adhere to the exercise protocol; both control and intervention arms received recorded telephone reminders to continue with the exercise protocol. Here we report on an ancillary study to this RCT that explored experiences, feelings and perspectives of subjects related to long-term adherence to exercise and use of technology.

Methods: Qualitative design informed by grounded theory using semi-structured interviews. Consecutive participants of the RCT were purposely recruited and enrolled. Participants were >50 years with knee pain, self-report doctor diagnosed KOA, and not strength training for previous 6 months. Data collection: Post the RCT final assessment, 1-1 interviews were conducted (n=25, mean age 67 and BMI 31, 77% female) using guiding questions to elicit participants’ views on exercise experiences and impressions of technology to foster adherence to exercise. Participants were categorized into low-, or high- adherence groups according to a self-assessment questionnaire. Data analysis: constant comparative methods. Initial coding related to participants' experiences on adherence to exercise.
and use of technology. Focus coding explored the meaning of data represented in the initial codes that more deeply reflected participants' experiences regarding motivation toward exercise and home exercise abilities. Third level of coding compared high-adherence data to low-adherence at 2 years, and intervention compared to control groups.

**Results:** Three themes were identified: monitoring, knowledge of exercise, and beliefs about benefits of exercise. Participants with high-adherence appeared self-determined with a sense of self-efficacy. Participants with low-adherence expressed ambivalence about the benefits of exercise and desired more social support. Figure 1 provides more details. These results were independent of group assignment.

**Conclusion:** This study provides new evidence that promoting self-determination may improve long-term exercise adherence among adults with KOA. In addition, subjects valued monitoring provided by the group exercise approach and automated telephone technology.

**Disclosure:** A. Ledingham, None; E. Cohn, None; K. Baker, None; J. Keysor, None.


**Abstract Number:** 1854

**Identifying Vulnerable Patient Populations Based on Age and Physical Function on Clinical Outcomes Following Total Knee Arthroplasty**

**Jesse Christensen**1, Andrew Kittelson2, Brian Loyd3, Jackie Del Giorno4, Brian Burnikel5 and Jennifer Stevens-Lapsley6, 1University of Utah, SLC, UT, 2Rehabilitation Science PhD Program, University of Colorado Anschutz Medical Campus, Aurora, CO, 3University of Colorado Anschutz Medical Campus, Aurora, CO, 4ATI Physical Therapy, Greenville, SC, 5Steadman Hawkins Clinic of the Carolinas, Greenville Health Systems, Greenville, SC, 6Universtiy of Colorado, Anschutz Medical Campus, Aurora, CO

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Monday, November 6, 2017
**Session Title:** ACR/ARHP Combined: Orthopedics and Rehabilitation Science
**Session Type:** ACR Concurrent Abstract Session
**Session Time:** 2:30PM-4:00PM
Background/Purpose: Total knee arthroplasty (TKA) has historically been viewed as a surgical procedure of last resort for older adults suffering with chronic arthritis. However, rates of TKA in younger, more medically complex patients have increased over the last several decades. A growing body of literature indicates that younger patients are less satisfied with their functional ability relative to older counterparts. The purpose of this study was to characterize this problematic subpopulation by examining whether a younger, poorer functioning subgroup differs in preoperative characteristics of health status, psychological status, or knee function, compared to others undergoing the procedure.

Methods: We conducted a retrospective analysis of clinically-collected data from 181 patients (57% female, mean age 64.8 yrs. + 8.9, mean BMI 33.3 + 7.1 kg/m²) undergoing TKA and subsequent rehabilitation between January 2013 and August 2015. Using these data, we constructed a categorical variable to represent age and function, by dichotomizing age (younger than 65 vs older than 65) and postoperative (6-week) Timed Up and Go (TUG) time (median split at 8.65 seconds). This resulted in 4 subgroups: younger/poorer TUG (n=36), younger/better TUG (n=42), older/poorer TUG (n=46), older/better TUG (n=39). Analysis of Covariance was then performed to compare subgroups, with the younger/poorer group as the reference group. The following preoperative measures were examined across groups: health status (comorbidity score, body mass index), psychological status (depression, pain catastrophizing) and knee function (quadriceps strength, surgical knee range of motion).

Results: After controlling for sex, the younger/poorer function subgroup demonstrated significantly worse quadriceps strength and pain catastrophizing scores relative to both young and old high-functioning subgroups. This subgroup also demonstrated worse depression scores relative to the older/better TUG subgroup relative to the younger/better TUG subgroup. No significant differences were seen in knee range of motion or comorbidity scores between any of the subgroups.

Conclusion: A clinical picture emerges of a subgroup that is relatively young and poor functioning following surgery. Preoperative characteristics of this subgroup included poorer psychological status (worse pain catastrophizing and depression scores) and reduced quadriceps strength. These factors could be incorporated into treatment strategies to maximize outcomes in this problematic, but growing patient demographic.

Disclosure: J. Christensen, None; A. Kittelson, None; B. Loyd, None; J. Del Giorno, None; B. Burnikel, None; J. Stevens-Lapsley, None.

Feasibility and Preliminary Effects of a Novel Rehabilitation Strategy to Improve Hand and Arm Function in Systemic Sclerosis

Susan L. Murphy1, Mary Barber2, Kristen Homer3, Carole Dodge2 and Dinesh Khanna4, 1Physical Medicine & Rehabilitation, University of Michigan, Ann Arbor, MI, 2Physical Medicine and Rehabilitation, University of Michigan, Ann Arbor, MI, 3Department of Internal Medicine, Rheumatology Division, University of Michigan, Ann Arbor, MI, 4University of Michigan, Ann Arbor, MI
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: ACR/ARHP Combined: Orthopedics and Rehabilitation Science
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Individuals with systemic sclerosis (SSc) suffer from limited arm and hand function due to skin thickening and contractures. Evidence-based medical rehabilitation strategies for these issues remain limited. Standard treatments of heat massage, and exercise are recommended but are primarily focused on the hand, not taking into account wrist, elbow, and shoulder contractures. In addition the rehabilitation treatments do not often target the skin scarring that underlies contracture formation. The purpose of this study was to determine the feasibility and preliminary effects of a novel treatment approach to improve arm and hand function in patients with scleroderma with both arm and hand contractures.

Methods: Participants with early SSc with arm and hand contractures were recruited from our Scleroderma Clinic. The intervention involved eight in-person weekly sessions with an occupational therapist and involved heat, mobility and range of motion exercises, and the use of the Physiotouch®, a negative pressure device that is commonly used at our center in other patient populations for mobilizing tissue with positive effects on the lymphatic system and skin mobilization. Feasibility was assessed by determining participant flow.
through the trial including the number of people enrolled who were eligible, and the number of people that adhered to the entire treatment protocol. A secondary goal was to examine preliminary effects on arm and hand function using the QuickDASH disability measure. Primary outcomes were measured at baseline and 8 weeks with an intermediate assessment at 4 weeks post baseline.

**Results:** The sample (N = 16) had a mean age of 46 (range 22-67), was 88% female, and 44% indicated being from racial minority group. The sample are diffuse scleroderma subset with a mean Rodnan skin score of 17.9 (+/- 10.1), and a mean QuickDASH score was 53.4 (+/- 22.7), which is almost three standard deviations above the population mean. Of those screened in-person, 95% were eligible, and 90% were enrolled. 50% have currently adhered to the entire protocol. 50% of our sample who have so far completed treatment at 8 weeks had improvements on the QuickDASH (n = 8) which ranged between 6-13 points, the mean improvement was statistically significant (t=6.6, df=7, p = .0001). Participants reported positive outcomes of the treatment such as improved coordination, fluidity of movement, not dropping things, and pain improvement.

**Conclusion:** This intervention is feasible despite the burden of traveling to the center for 8 in-person visits and led to improvements in half of the participants. This study would benefit from bolstering home rehabilitation components and future work will need to compare those who receive this treatment to a control group.

**Disclosure:** S. L. Murphy, None; M. Barber, None; K. Homer, None; C. Dodge, None; D. Khanna, Actelion, Bayer, BoehringerIngelheim, Chemomab, Corbus, Covis, Cytori,Eicos, EMD Serono, Genentech/Roche, Gilead, GSK, Sanofi-Aventis,UCB Pharma, 5,NIH/NIAMS, NIH/NIAID,Bayer, BMS, Genentech/Roche, Pfizer, 2,Eicos, 4.

**Abstract Number:** 1856

**Patient and Physician Perspectives on Content Value for Educational Material Regarding Rare Rheumatic Diseases**

Chris Hatzis¹, Elizabeth Soto-Cardona², Jessica K. Gordon² and Robert F. Spiera², ¹Medicine, Hospital for Special Surgery, New York, NY, ²Rheumatology, Hospital for Special Surgery, New York, NY

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017
**Session Title:** ARHP Education/Community Programs
**Session Type:** ARHP Concurrent Abstract Session
**Session Time:** 4:30PM-6:00PM

**Background/Purpose:** Internet-based information is important for patients and their caregivers. For the past 4 years, our academic medical center’s Center for Scleroderma, Vasculitis & Myositis (SVM) has produced monthly email NewsBlasts to provide information to our patients and their caregivers. The Newsblasts are distributed by email free of charge to subscribers. We conducted a survey evaluating what information is most important to our subscribers, and we compared responses from patients and caregivers. Additionally, we queried caregivers as to what they thought patients would perceive as most valuable, and compared those responses to patient's self-reported perceptions.

**Methods:** All SVM NewsBlasts were placed into 2 broad categories, and then into 1 of 6 sub-categories. NewsBlasts were categorized as Disease-Focused or Psychosocial-Focused. Within the Disease-Focused category were the following sub-categories: Organ System Complications & Mechanisms of Disease, Treatment, and Disease-Related Research. Within the Psychosocial-Focused category were the following sub-categories: Healthcare Access & Delivery, Patient Support, and Self Help / Lifestyle. A survey was created, in which users ranked the sub-categories from 1 (most important) to 6 (least important). Also, all caregivers – rheumatologists, nurses, social workers, and friends and family – were required to rank how important they thought each sub-category was to their patients or relative. The rankings submitted by patients and those submitted by Physicians were compared using Wilcoxon tests.

**Results:** The survey was sent via email to our 476 subscribers. A total of 177 (37%) recipients opened the email, and 77 (44% of opens, 16% overall) clicked the survey link. Of those recipients that opened the link, 53 responses were complete and included in the analysis. The respondent demographics are as follows: 32/53 (60%) patients; 13/53 (25%) rheumatologists; 3/53 (6%) nurses and social workers; 5/53 (9%) friends and family.

On average, patients assigned the Disease-Focused category a rank of 2.75±0.75, compared to a rank of 4.25±0.75 for the Psychosocial-Focused category (p <0.0001). However, rheumatologists predicted that patients would rank Psychosocial-Focused information as more...
important than Disease-Focused information (3.33±0.62 vs. 3.67±0.62, p=0.05). Rheumatologists predicted that patients would assign the Disease-Focused category a rank of 3.67±0.62, while patients themselves assigned the Disease-Focused category a rank of 2.75±0.75 (p=0.002). Caregivers overall, when including nurses, social workers, friends and family in addition to rheumatologists, lacked consensus when ranking the relative importance of Disease-Focused and Psychosocial-Focused information. No single sub-category was ranked as significantly more or less important by respondents.

**Conclusion:** Patients found Disease-Focused information to be most important. Rheumatologists wrongly thought that patients would rank Psychosocial-Focused information as most important. These results emphasize the importance of patient feedback regarding what information is deemed of most value when selecting and developing content for future patient education materials.

**Disclosure:** C. Hatzis, None; E. Soto-Cardona, None; J. K. Gordon, None; R. F. Spiera, None.


---

**If Mobile Advertising Is the Future, the Future Is Now: Productivity of Digital Ads By Terminology and Delivery Device.**

**Teresa J. Brady**¹ and Kamil E. Barbour², ¹Arthritis Program, Centers for Disease Control and Prevention, Atlanta, GA, ²Centers for Disease Control and Prevention, Atlanta, GA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** ARHP Education/Community Programs  
**Session Type:** ARHP Concurrent Abstract Session  
**Session Time:** 4:30PM-6:00PM

**Background/Purpose:**

CDC is pilot-testing a multi-modal marketing campaign to promote self-management education (SME) as a chronic disease management strategy. The campaign targets adults ages 45-75 with any chronic condition, including arthritis. The campaign includes both earned and paid media (i.e., radio, out-of-home, print, and digital advertising) with a call-to-action to visit [www.cdc.gov/LearnMoreFeelBetter](http://www.cdc.gov/LearnMoreFeelBetter) to learn more about SME.

Formative audience research indicated that consumers preferred “ongoing” over “chronic” to describe their health condition, but paradoxically, they used “chronic” when describing their condition.

One element of the paid media campaign strategy is the presentation of digital ads (similar to pop-up ads) to desktop computers, tablets, and smart phones to consumers likely to have chronic conditions. Digital ads were used in the first 9 weeks of the campaign pilot-test (January 23-March 26, 2017).

The purposes of this observational study are to determine whether: 1) “ongoing” or “chronic” terminology in ads is more productive, and 2) ads presented via desktop computer or mobile device (tablet, smartphone) are more productive.

**Methods:**

Two versions of the digital ads were produced; ads were identical except for the use of “ongoing” or “chronic.”

A commercial vendor distributed the digital ads to consumers likely to have a chronic disease using a proprietary algorithm that used demographic and consumer spending data to identify consumers likely to have chronic conditions.

Ad productivity was defined as visits to the campaign home page and data was collected using Site Catalyst, a web analytics software program.

Productivity was measured in 3 ways:

1. Click thru Rate: Percentage of people who clicked on the ad out of all exposed to ad;
2. Cost per Click: Total costs to run ad to the device divided by number of clicks;

3. Minutes on Site: Average number of minutes spent on the site by those who clicked through from ad to campaign website.

Results:

A total of 8,887 visits (from all sources) were made to the campaign home page during the first flight of digital ads. The following table reports productivity of digital ads by Click-Thru Rate, Cost per Click and Minutes on Site for ads using “ongoing” or “chronic” terminology.

<table>
<thead>
<tr>
<th></th>
<th>Mobile</th>
<th>Desktop</th>
<th>Mobile</th>
<th>Desktop</th>
<th>Mobile</th>
<th>Desktop</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Chronic”</td>
<td>0.36%</td>
<td>0.13%</td>
<td>$0.87</td>
<td>$3.08</td>
<td>6.36</td>
<td>2.12</td>
</tr>
<tr>
<td>“Ongoing”</td>
<td>0.34%</td>
<td>0.13%</td>
<td>$0.90</td>
<td>$3.04</td>
<td>6.06</td>
<td>2.03</td>
</tr>
</tbody>
</table>

Conclusion:

Results were consistent across all 3 measures of productivity. Although audience research suggested that consumers prefer “ongoing” to “chronic” in describing their health condition, ads using either term were similarly productive in prompting consumers to visit the campaign home page. Ads can use either “ongoing” or “chronic” to describe long-term health conditions with equal effectiveness.

However, ads appearing on mobile devices were nearly 3 times as productive as ads appearing on desktop computers across all 3 measures. If dollars are limited, placing digital ads on mobile devices, rather than desktop computers, will be a better investment.

Disclosure: T. J. Brady, None; K. E. Barbour, None.


Abstract Number: 1858

Utilizing Needs Assessment Data to Establish Foundational Training for Adult and Pediatric Nurse Practitioners (NP) and Physician Assistants (PA) Entering Rheumatology Practice

Barbara Slusher1,2, Jeanne Scott3, Christine A. Stamatos4, Benjamin J Smith5,6,7, Elizabeth A. Schlenk8, Heather Benham9, Daniel Schaffer10 and Karen L. Smart11, 1Physician Assistant Studies, University of Texas Medical Branch, Galveston, TX, 2Rheumatology, University of Texas Medical Branch, Galveston, TX, 3Rheumatology, Cheshire Medical Clinic, Keene, NH, 4Rheumatology, Northwell Health, Great Neck, NY, 5Rheumatology, Florida State University, Tallahassee, FL, 6Rheumatology, McIntosh Clinic, P.C., Thomasville, GA, 7School of Physician Assistant Practice, Florida State University College of Medicine, Tallahassee, FL, 8School of Nursing Room 415, University of Pittsburgh, Pittsburgh, PA, 9Pediatric Rheumatology, Texas Scottish Rite Hospital for Children, Dallas, TX, 10Rheumatology, Mayo Clinic, Rochester, MN, 11Rheumatology Research, Harry S Truman Memorial VA Hospital, Columbia, MO

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: ARHP Education/Community Programs
Session Type: ARHP Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose:

Rheumatology is a cognitive specialty requiring years of clinical exposure and hands-on training to manage complex patients. However, there is no current standardized training model or understanding of the educational needs of an NP/PA entering rheumatology. An ACR-
Association of Rheumatology Health Professionals (ARHP) task force (TF) was created to identify how best to prepare and train NP/PAs for rheumatology practice. A needs assessment was conducted to obtain data from experienced NP/PAs to inform the development of a curriculum for NP/PAs in their first year of rheumatology practice.

**Methods:**

A Survey Monkey invitation was sent to current ARHP NP/PA members (n=317) by ARHP staff. The survey consisted of four multiple choice demographic questions to include years of experience in rheumatology, diseases treated, and practice setting(s). Five open ended questions were: best practices for learning joint injection technique, knowledge, skills, attitudes, and resources needed in the first year of rheumatology practice. An initial invitation was followed by a reminder one week later.

**Results:**

Response rate was 27% (87 responses). Regarding rheumatology years of experience, most respondents (45%) reported practicing < 5 years and 23% reported practicing > 15 years. Top ten rheumatic diseases that NP/PAs reported treating, in rank order, were RA, PsA, SLE, CTD, OA, gout, PMR, AS, FM and myositis. Most respondents worked in an outpatient setting (80%); treated new (74%) and follow-up (98%) patients; and treated adults (84%). Respondents also reported having research (36%) and teaching (37%) duties. Most respondents reported prescribing traditional (98%) and biologic (93%) DMARDs while a majority (69%) prescribe opioid analgesics. Elements deemed most important for a new rheumatology NP/PA were: **KNOWLEDGE** - disease states, recognizing disease presentation, and differential diagnoses; **SKILLS** - musculoskeletal physical examination and joint injection; **ATTITUDE** - openness to learning, knowing limitations and willingness to ask questions. The most impactful resource that contributed to NP/PA success was a physician preceptor and access to educational resources.

**Conclusion:**

The NP/PA needs assessment demonstrated the depth and breadth to which NP/PAs are utilized in rheumatology practices and provides the underpinnings of training elements needed to ensure successful assimilation of NP/PAs into rheumatology practice. To meet the educational needs of NP/PAs new to rheumatology, educators need to focus on adequately preparing NP/PAs to: treat many diseases predominate in rheumatology; see inpatients and outpatients; maintain a varied clinical workload, to include new patients; ensure training in musculoskeletal exam and joint injections; establish a mentoring relationship with a rheumatologist; and offer adequate clinical resources. These aspects should be included in any rheumatology curriculum for NP/PAs.

**Disclosure:** B. Slusher, None; J. Scott, None; C. A. Stamatos, None; B. J. Smith, American Board of Internal Medicine, 5,American College of Rheumatology, Association of Rheumatology Health Professionals, 5; E. A. Schlenk, None; H. Benham, None; D. Schaffer, None; K. L. Smarr, None.


Abstract Number: 1859

**Meeting the Needs of Rheumatology Health Professional Learners: the Success of the American College of Rheumatology (ACR) and Association of Rheumatology Health Professionals (ARHP) Online Educational Products**

Benjamin J Smith1, Katelyn Graves2, Thomas Morgan2, Debra Bancroft Rizzo3, Geri Neuberger4, Kori Dewing5, Atul A. Deodhar6 and Ramona Hilliard7, 1School of Physician Assistant Practice, Florida State University College of Medicine School of Physician Assistant Practice, Tallahassee, FL, 2Florida State University College of Medicine School of Physician Assistant Practice, Tallahassee, FL, 3Department of Medicine [Division of Rheumatology], University of Michigan, Ann Arbor, MI, 4School of Nursing MS 4043, Univ of Kansas Medical Ctr, Kansas City, KS, 5Rheumatology, Virginia Mason Medical Center, Seattle, WA, 6Oregon Health & Science University, Portland, OR, 7ARHP, American College of Rheumatology, Atlanta, GA

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** ARHP Education/Community Programs  
**Session Type:** ARHP Concurrent Abstract Session  
**Session Time:** 4:30PM-6:00PM
Background/Purpose: Rheumatic diseases are complex conditions often affecting multiple organ systems needing treatment by expert health care providers. These providers function in multi-disciplinary teams for the most optimal patient outcomes. Significant rheumatology workforce shortages are prevalent and are expected to increase over the next decade. While rheumatologists receive rheumatology specific post-graduate training during fellowships, other health professionals have no formalized training pathway in rheumatology after completing their formal education. The ACR and the ARHP have recognized the need to provide rheumatology specific educational opportunities for health professionals who participate in the care of persons with rheumatic disease by creating online educational products. These online educational products are the Advanced Rheumatology Course (ARC), the Fundamentals of Rheumatology Course (FRC), and Rheumatology e-Bytes. These module based educational activities are intended to provide foundational, intermediate and advanced levels of content to meet the needs of health professionals with varying educational and career experience. The aim of this study is to describe the utilization of these educational products and summarize the feedback obtained from the ARC and FRC participants.

Methods: Data from ARC and FRC utilization and evaluations were obtained. Analyses of the available information were conducted. ARC participant data from December 2008 to December 2015 were reviewed. FRC participant data from October 2012 to December 2015 were reviewed. Rheumatology e-Byte data were not evaluated due to its recent release in January 2017.

Results: Since their debut, both the ARC and FRC have been highly utilized as evidenced by the geographic, gender, and profession diversity of learners. (Table 1) Those who have completed ARC and FRC modules have rated their participation in these activities as formative, aiding in their increase of confidence in assessing, managing, and evaluating persons with rheumatic disease. (Table 2) International rheumatology health professionals have also taken advantage of these quality educational tools.

Conclusion: The ACR and ARHP have capitalized on the advances in technology to provide enhanced learning opportunities to the rheumatology community. The ACR and ARHP online educational products have been successful in educating nurses, nurse practitioners, physician assistants and other health professionals.

Disclosure: B. J. Smith, None; K. Graves, None; T. Morgan, None; D. Bancroft Rizzo, None; G. Neuberger, None; K. Dewing, None; A. A. Deodhar, None; R. Hilliard, None.

Abstract Number: 1860

A Trial Testing Strategies to Enhance Patient Understanding of Drug Information: Experience Recruiting Subjects through an Online Patient Community

Susan J. Blalock1, Elizabeth Solow2, W. Benjamin Nowell3, Steven Woloshin4, Lisa Schwartz4, Delesha M. Carpenter2, Jeffrey R. Curtis6, Larry W. Moreland7, Caprice Hunt1, Genevieve Hickey1 and Valerie Reyna8, 1Eshelman School of Pharmacy, University of North Carolina at Chapel Hill, Chapel Hill, NC, 2Internal Medicine, University of Texas Southwestern Medical Center, Dallas, TX, 3CreakyJoints/Global Health Living Foundation, Upper Nyack, NY, 4Geisel School of Medicine, Dartmouth, Hanover, NH, 5Eshelman School of Pharmacy, University of North Carolina at Chapel Hill, Asheville, NC, 6Division of Clinical Immunology and Rheumatology,
SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: ARHP Education/Community Programs
Session Type: ARHP Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Current guidelines for the treatment of rheumatoid arthritis (RA) underscore the importance of an early and targeted approach to control inflammation. We describe initial experiences in recruiting RA patients (target n=300) from clinic sites versus an online patient support network into a randomized trial comparing the effectiveness of two educational interventions designed to enhance informed decision-making.

Methods: Participants are recruited from four clinic sites and CreakyJoints, an online patient support network. Eligibility criteria include: physician-diagnosed RA, moderate/high disease activity per the RAPID3, eligible for treatment escalation per provider, and internet access. Two interventions are being evaluated: (1) DrugFactsBoxes, which provide quantitative information concerning potential medication benefits and harms, and (2) Gist Reasoning Training, which is designed to help patients develop the skills needed to process complex information (e.g., the nature of scientific uncertainty). Data are collected by telephone interviews and on-line questionnaires. Because data collection is currently underway, this presentation focuses on the results of recruitment efforts.

Results: CreakyJoints sent 3,094 emails to their online community from January through March 2017, inviting members to participate in the study. Of these, 979 (31.6%) emails were opened and 269 (8.6%) people clicked a link in the email taking them to the study website. A total of 156 (58.0%) of the CreakyJoints members who visited the website emailed study staff expressing interest in participating, 139 met study eligibility criteria, and 96 have completed baseline data collection. During this same time period, 34 participants were recruited via the four clinic sites and completed baseline data collection. Compared to participants recruited via clinic sites, those recruited via CreakyJoints are less likely to be African-American (7% versus 22%, p = 0.02) or Hispanic (3% versus 14%, p = 0.02) and have greater RA knowledge (Means: 85.1 versus 75.4, p <0.0001) and higher health literacy as assessed by the Newest Vital Sign (Means: 83.5 versus 73.7, p = 0.02). Participants recruited via CreakyJoints, versus clinic sites, were equally likely to be women (95% versus 91%, p=0.46), have completed college (55% versus 61%, p=0.59), and be using a DMARD (12% versus 6%, p=0.28).

Conclusion: Recruitment from an online support community is feasible and efficient. Online participants may differ from clinic participants in some sociodemographic characteristics. Better understanding of these differences is needed to improve the generalizability of results generated from online communities and clinic sites to maximize the external validity of research findings.

Disclosure: S. J. Blalock, None; E. Solow, None; W. B. Nowell, Global Healthy Living Foundation, 3; S. Woloshin, None; L. Schwartz, None; D. M. Carpenter, None; J. R. Curtis, None; L. W. Moreland, None; C. Hunt, None; G. Hickey, None; V. Reyna, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/a-trial-testing-strategies-to-enhance-patient-understanding-of-drug-information-experience-recruiting-subjects-through-an-online-patient-community

Abstract Number: 1861

Evaluation of a Longstanding Telephone Peer Counseling Service on People with Systemic Lupus Erythematosus and Their Loved Ones

Priscilla Toral1, Melissa T. Flores1, Roberta Horton1 and Jillian Rose2, 1Social Work Programs, Hospital for Special Surgery, New York, NY, 2Hospital for Special Surgery, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: ARHP Education/Community Programs
Session Type: ARHP Concurrent Abstract Session
Session Time: 4:30PM-6:00PM
Background/Purpose:

Studies show telephone peer support has been used to address a range of health concerns in people living with chronic illness. A phone evaluation was conducted with participants of a national toll-free phone peer counseling service. Ongoing since 1988, this service provides emotional support for people with SLE and their loved ones, by trained volunteers living with SLE. The evolution of this program has been presented at prior ACR/ARHP, including the impact of a revised curriculum on a new cohort of peer volunteers staffing the service.

Methods:

A 60-item survey, with Likert scale & open-ended questions was administered to callers who were matched with a peer-counselor between 2015-2017. The survey captured demographics, satisfaction with the screening process & their peer counselors, SLE management/ coping & overall service impact. Surveys were completed by phone interviews with a volunteer not directly connected to program.

Results:

Of the 32 users outreached to 23 (72%) completed the survey. The majority (89%) of respondents were female, 47% identified as Black/African-American, 35% White, 31% Hispanic &18% some other race. Callers’ ages ranged from 30-80, with 67% ages 40-59. Most respondents were unemployed (43%) & 39% employed part/full time. Almost half of the callers (47%) were married, 94% had SLE & diagnosed for > 12 years. When asked about their initial reasons for calling 68% indicated emotional support & SLE education & resources (63 %). Most participants were satisfied (90%) with the screening call with the social worker. When asked about initial expectations of their first call, callers shared, “I wanted to know more about SLE” & “have someone to listen & guide me.” Most callers indicated their expectations were met (95%). Callers shared that having someone knowledgeable about SLE (72%) was the most valuable aspect of the call. Most callers (52%) had > 12 calls with their peer counselor & 95% were satisfied (77% very; 18% moderately) with their match.

In relation to coping, 85% indicated that they have coped better with their SLE since being matched & 81% agreed they had a better understanding of SLE. 88% respectively attributed this to utilization of the program. When asked about depression 66% reported feeling less depressed since starting the service with a majority of callers (78%) crediting the service for this change. Callers also reported feeling less isolated (71 %) with 73% indicating this was also a result of the service. One caller shared, “I feel less alone.”

When asked if their communication & or relationship with their doctor improved since using the service 58% said yes & 100% indicated that the program was responsible for this. When asked about the single most helpful part of using the service responses included, “you know you can call the line & there is someone to listen” & “knowing support is a phone call away.” Most (94%) indicated they would recommend the service to others.

Conclusion:

Despite limitations due to a small sample size, results indicate continued satisfaction & positive impact, with slight increases since last evaluation. Results point to the continued relevance of a phone support service that is easily accessible & can connect people with SLE & their loved ones to support & resources.

Disclosure: P. Toral, None; M. T. Flores, None; R. Horton, None; J. Rose, None.


Abstract Number: 1862

Association between Hydroxychloroquine Nonadherence and Adverse Outcomes Among Patients with Systemic Lupus Erythematous

Candace H. Feldman¹, Zhi Zhang², Rishi J. Desai³, Tzu-Chieh Lin⁴, Jamie E. Collins⁵, S.V. Subramanian⁶, Ichiro Kawachi⁷, Daniel H. Solomon⁸ and Karen H. Costenbader⁴, ¹Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA, ²Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA, ³PharmacoEpidemiology & PharmacoEconomics, Brigham & Women's Hospital, Boston, MA, ⁴Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ⁵Orthopaedic and Arthritis Center for Outcomes Research, Department of Orthopedic Surgery, Brigham & Women's Hospital, Boston, MA, ⁶Social and Behavioral Sciences, Harvard T.H. Chan School of Public Health, Boston, MA, ⁷Social and Behavioral Sciences, Harvard T. H. Chan School of Public Health, Boston, MA, ⁸Brigham and Women's Hospital and Harvard Medical School, Boston, MA
Background/Purpose: Prior observational studies suggest that SLE patients receiving hydroxychloroquine (HCQ) may have reduced risk of infections, cardiovascular disease and end-stage renal disease (ESRD). However, adherence to HCQ was not assessed. HCQ is the standard of care for SLE, and therefore randomized trials comparing outcomes among users vs. nonusers are not feasible. We implemented inverse probability weighting within a marginal structural modeling framework to assess whether SLE patients who adhered to HCQ (vs. nonadherers) had reduced risks of disease-related adverse outcomes, adjusting for time-varying confounding and healthy adherer effects.

Methods: We identified Medicaid beneficiaries (2000-2010) from 28 states with SLE, defined by ≥2 SLE ICD-9 codes, who initiated HCQ (index date) and had no use in the prior 6 months (baseline period). We examined 3 outcomes: ESRD, serious infections requiring hospitalization, and myocardial infarction/cerebrovascular accident (MI/CVA), excluding these outcomes during the baseline period. For our primary analyses, we updated monthly adherence (80% of days/month covered = adherent), and used inverse probability weights to account for prior adherence, time-varying confounders (comorbidities, medications), and censoring (death, disenrollment, retinal toxicity). We constructed marginal structural pooled logistic models for each outcome. In secondary analyses, we adjusted only for baseline, time-fixed covariates using Fine and Gray proportional hazards models accounting for the competing risk of death, to examine the association between adherence 90-days post index date (proportion of days covered (PDC) ≥80% = adherent), and outcomes after this period. We also assessed the relationship between adherence and motor vehicle accidents (MVAs), a control outcome; no association would support potential biologic effects in our main models.

Results: We identified >20,000 HCQ initiators with SLE with mean (± SD) follow-up of >4 (± 3) years. For all cohorts, the mean (± SD) PDC during the 90-days post index date was 62% (± 26); 31% had PDC≥80%. In our marginal structural models, comparing adherers vs. nonadherers, we observed reduced risks of ESRD (OR 0.73, 95% CI 0.61-0.89) and serious infections (OR 0.84, 95% CI 0.79-0.90), and borderline reduced risk of MI/CVA (OR 0.92 95% CI 0.85-1.00) (Table). There was no association between adherence and MVAs, our negative control (OR 0.95 95% CI 0.75-1.19). In secondary analyses adjusted only for baseline covariates, results were similar but attenuated for ESRD and serious infections.

Conclusion: We observed modestly reduced risks of ESRD, serious infections and MI/CVA among HCQ adherers vs. nonadherers. Our analyses are limited by lack of data on reasons for HCQ discontinuation and the challenge of distinguishing between the biologic effects of HCQ vs. unmeasurable healthy adherer effects.

Table. Association of hydroxychloroquine (HCQ) adherence vs. nonadherence with adverse outcomes among patients with SLE

<table>
<thead>
<tr>
<th></th>
<th>End-stage renal disease</th>
<th>Serious infections</th>
<th>Myocardial infarction and cerebrovascular accident (MI/CVA)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td># of events</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Marginal Structural Models*</td>
<td>21,390</td>
<td>649</td>
<td><strong>0.73</strong></td>
</tr>
</tbody>
</table>
| *Marginal structural models (accounting for time-varying adherence and time-varying and baseline time-fixed confounding) adjusted for baseline covariates: age, sex, race/ethnicity, index date calendar year, region, zip code median household income, lupus nephritis, comorbidities, SLE risk-adjustment index, number of other medications, immunosuppressant use, corticosteroid use and dose, number of SLE-related lab tests, healthcare utilization and preventive care to address healthy adherer effect (vaccinations, PCP prophylaxis, mammograms, colonoscopy, general wellness outpatient visits, pap test). Time-varying confounders updated every 30 days included: prior HCQ adherence, lupus nephritis, diabetes mellitus, healthcare utilization, number of medications, corticosteroid dose, SLE risk adjustment index, antidepressant medication use and ESRD (for infection and MI/CVA analyses). Adherence was updated every 30 days as >90% of patients received 30-day HCQ prescriptions. Ns differ slightly between cohorts because individuals with events during the baseline period were excluded from the corresponding analysis. For bolded values, p≤0.05, *p=0.05
Inflammatory Dietary Pattern and Risk of Developing Rheumatoid Arthritis in Women

Bing Lu¹, Jeffrey A. Sparks¹, Susan Malspeis¹, Medha Barbhaiya¹, Sara K. Tedeschi², Karen H. Costenbader³ and Elizabeth Karlson³,
¹Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ²Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ³Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: ACR/ARHP Combined: Epidemiology and Public Health: Prevention, Recognition, and Treatment
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: The preclinical period of rheumatoid arthritis (RA) is characterized by elevated inflammatory biomarkers but it is unclear whether inflammatory diet may contribute to RA risk. We aimed to examine whether a dietary pattern associated with inflammatory biomarkers predicts subsequent risk of RA using the Nurses’ Health Study (NHS) and NHS II.

Methods: We prospectively followed 79,988 women in NHS aged 38-63 years at 1984 and 93,585 women in NHS II aged 27-44 years at 1991, who were free from RA or other connective tissue diseases. Lifestyle, environmental, and anthropometric information were collected at baseline and updated biennially. Dietary data were obtained from validated food frequency questionnaires at baseline and approximately every 4 years during follow-up. RA cases were self-reported and confirmed by a connective tissue disease screening questionnaire and medical record review according to the 1987 ACR criteria. Seropositive RA was defined as positive rheumatoid factor or anti-citrullinated peptide antibody and was determined by medical record review. The inflammatory dietary pattern was measured by the Empirical Dietary Inflammatory Index (EDII), a weighted score including 9 pro- and anti-inflammatory food groups, which was predictive of 3 plasma inflammatory biomarkers (CRP, IL-6 and sTNFR2). Higher (more positive) scores indicate more pro-inflammatory diets and lower (more negative) scores indicate anti-inflammatory diets. We pooled the data from both cohorts to examine the association between cumulative averaged EDII and risk of RA among younger (≤55 years) and older age groups (>55 years) since diet has been shown to have different effects on RA risk according to age of onset in previous studies. The EDII was categorized according to baseline quartile cutoffs. Time-varying Cox regression models were used to calculate the hazard ratios and 95% confidence intervals (CI) after adjusting for potential confounding factors.

Results: During 34 years of follow-up, we identified 1,188 incident RA cases. Among women ≤55 years old, a higher EDII was associated with a higher RA risk: HRs (95% CI) across increasing quartiles of EDII score were 1.00 (reference), 1.16 (0.87 to 1.53), 1.38 (1.05 to 1.81) and 1.43 (1.08 to 1.89) (p-trend 0.007). After additional adjustment for BMI, the observed results were attenuated. When further stratifying by serostatus, the significant association was observed only for seropositive RA (p-trend: 0.028) (Table). There was no significant association for RA among women aged >55 years (p for EDII-age interaction <0.01).

Conclusion: In these two large prospective cohort studies, inflammatory dietary pattern was associated with increased risk of developing RA among young and middle-aged women. The observed association may be partially mediated through BMI.
<table>
<thead>
<tr>
<th>Age ≤55 years</th>
<th>Empirical Dietary Inflammatory Index (EDII) quartiles</th>
<th>Q1 (least inflammatory)</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4 (most inflammatory)</th>
<th>p-trend ‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case/person-years</td>
<td>All RA (n=488 cases)</td>
<td>84/456,054</td>
<td>122/610,940</td>
<td>144/630,777</td>
<td>138/598,524</td>
<td></td>
</tr>
<tr>
<td>Multivariable model 1 (main)*</td>
<td>1.00 (Ref)</td>
<td>1.16(0.87 to 1.53)</td>
<td>1.38(1.05 to 1.81)</td>
<td>1.43(1.08 to 1.89)</td>
<td>0.007</td>
<td></td>
</tr>
<tr>
<td>Multivariable model 2†</td>
<td>1.00 (Ref)</td>
<td>1.12(0.85 to 1.49)</td>
<td>1.30(0.99 to 1.72)</td>
<td>1.29(0.97 to 1.71)</td>
<td>0.055</td>
<td></td>
</tr>
<tr>
<td>Multivariable model 2†</td>
<td>1.00 (Ref)</td>
<td>1.13(0.79 to 1.61)</td>
<td>1.49(1.06 to 2.09)</td>
<td>1.22(0.85 to 1.75)</td>
<td>0.172</td>
<td></td>
</tr>
<tr>
<td>Seropositive RA (n=317 cases)</td>
<td>Multivariable model 1 (main)*</td>
<td>1.00</td>
<td>1.17(0.82 to 1.67)</td>
<td>1.61(1.15 to 2.26)</td>
<td>1.40(0.98 to 2.00)</td>
<td>0.028</td>
</tr>
<tr>
<td>Multivariable model 2†</td>
<td>1.00</td>
<td>1.13(0.79 to 1.61)</td>
<td>1.49(1.06 to 2.09)</td>
<td>1.22(0.85 to 1.75)</td>
<td>0.172</td>
<td></td>
</tr>
<tr>
<td>Seronegative RA (n=171 cases)</td>
<td>Multivariable model 1 (main)*</td>
<td>1.00</td>
<td>1.14(0.72 to 1.80)</td>
<td>1.02(0.63 to 1.63)</td>
<td>1.48(0.94 to 2.33)</td>
<td>0.107</td>
</tr>
<tr>
<td>Multivariable model 2†</td>
<td>1.00</td>
<td>1.12(0.71 to 1.77)</td>
<td>0.98(0.61 to 1.57)</td>
<td>1.41(0.89 to 2.23)</td>
<td>0.173</td>
<td></td>
</tr>
<tr>
<td>Age &gt;55 years</td>
<td>Multivariable model 1 (main)*</td>
<td>1.00</td>
<td>1.09(0.89 to 1.32)</td>
<td>0.97(0.79 to 1.20)</td>
<td>0.90(0.70 to 1.16)</td>
<td>0.341</td>
</tr>
<tr>
<td>Multivariable model 2†</td>
<td>1.00</td>
<td>1.08(0.88 to 1.31)</td>
<td>0.96(0.78 to 1.19)</td>
<td>0.90(0.69 to 1.16)</td>
<td>0.343</td>
<td></td>
</tr>
<tr>
<td>Seropositive RA (n=426 cases)</td>
<td>Multivariable model 1 (main)*</td>
<td>1.00</td>
<td>1.17(0.90 to 1.50)</td>
<td>1.08(0.82 to 1.41)</td>
<td>0.82(0.58 to 1.15)</td>
<td>0.322</td>
</tr>
<tr>
<td>Multivariable model 2†</td>
<td>1.00</td>
<td>1.17(0.90 to 1.50)</td>
<td>1.08(0.83 to 1.42)</td>
<td>0.83(0.59 to 1.17)</td>
<td>0.374</td>
<td></td>
</tr>
<tr>
<td>Seronegative RA (n=274 cases)</td>
<td>Multivariable model 1 (main)*</td>
<td>1.00</td>
<td>0.97(0.71 to 1.33)</td>
<td>0.83(0.59 to 1.17)</td>
<td>1.03(0.70 to 1.50)</td>
<td>0.780</td>
</tr>
<tr>
<td>Multivariable model 2†</td>
<td>1.00</td>
<td>0.94(0.69 to 1.30)</td>
<td>0.80(0.56 to 1.13)</td>
<td>0.98(0.67 to 1.44)</td>
<td>0.612</td>
<td></td>
</tr>
</tbody>
</table>

Hazard ratios were calculated using time-varying Cox proportional hazards models

* Adjustment for age, cohort, questionnaire period, household income, smoking (never, past, current 1-14 cigarettes/d, current ≥15 cigarettes/d), age at menarche (<12, 12, >12 years), parity and breast feeding (nulliparous, parous/no breastfeeding, parous/1-12 months breastfeeding, parous/ >12 months breastfeeding), hormone use (pre-menopausal, post-menopausal with never use, current use and past use) and total energy (quintiles)

† Additional adjustment for BMI (<20, 20-22.9, 23-24.9, 25-29.9, ≥30kg/m²)

‡ p for trend was derived from tests of linear trend across categories of EDII using the median value of each category as a continuous variable

Disclosure: B. Lu, None; J. A. Sparks, None; S. Malspeis, None; M. Barbhaiya, None; S. K. Tedeschi, None; K. H. Costenbader, Glaxo Smith Kline, 5,Merck Pharmaceuticals, 2,Biogen Idec, 5,AstraZeneca, 5; E. Karlson, None.


Abstract Number: 1864
Longitudinal Changes in Serum Uric Acid Levels and Associated Risk of Cardiometabolic Events and Renal Insufficiency in Gout Patients

Rishi J. Desai1, Jessica Franklin2, Julia Spoendlin2, Goodarz Danaei3, Daniel H. Solomon4 and Seoyoung C. Kim5,
1PharmacoEpidemiology & PharmacoEconomics, Brigham & Women’s Hospital, Boston, MA, 2Brigham & Women's Hospital, Boston, MA, 3Harvard School of Public Health, Boston, MA, 4Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 5Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: ACR/ARHP Combined: Epidemiology and Public Health: Prevention, Recognition, and Treatment
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Gout patients have an increased risk of type 2 diabetes mellitus (T2DM), cardiovascular disease (CVD), and chronic kidney disease (CKD); however, it is not known whether this risk is modifiable by reducing levels of serum uric acid (SUA). Therefore, we aimed to evaluate the association between changes in SUA levels over time and the risk of incident T2DM, CVD, and renal function insufficiency in gout patients.

Methods: We designed an observational cohort study among gout patients aged > 40 years using data from Optum Clinformatics database with available laboratory results (2004-2015). Index date was defined as the first SUA measurement ≥6.8 mg/dl after 6 months of continuous health plan coverage, ≥1 gout diagnosis and no use of urate lowering treatment during this time. The exposure of interest was change in SUA level, which measured as a cumulative variable updated monthly. Three separate outcomes were assessed during the post-index period: 1) incident T2DM, 2) incident CVD (a composite endpoint of myocardial infarction, stroke, or coronary revascularization), 3) renal insufficiency (reduction in the estimated glomerular filtration rate of ≥ 30% from baseline). Hazard ratios (HR) and 95% confidence intervals (CI) were derived using marginal structural models with stabilized inverse probability treatment weights accounting for baseline confounders including age, gender, hyperlipidemia, hypertension, and >20 other medical conditions and medication use as well as >10 time-varying confounders including serum creatinine, blood urea nitrogen, glycated hemoglobin, and urate lowering drugs.

Results: Among 26,341 patients with gout, the average age was 62 and 75% were men. The median baseline SUA was 8.6 mg/dl (interquartile range (IQR) 7.7 to 9.5) and the median level of SUA reduction over an average follow-up of 33 months was 1 mg/dl (IQR: 0 to 2.7). The incidence rates/100 person-years (95% CI) were 1.63 (1.51-1.75) for T2DM, 0.77 (0.70-0.84) for CVD, and 4.32 (4.14-4.49) for renal insufficiency. The HR (95% CI) per 3 mg/dl reduction in SUA was 1.07 (0.91-1.24) for T2DM, 1.01 (0.81-1.27) for CVD, and 0.89 (0.81-0.98) for renal insufficiency.

Conclusion: Reduction in SUA in patients with gout may be associated with a reduced risk of renal insufficiency, but we did not find an association with T2DM or CAD. These findings suggest that aggressive SUA lowering approaches may slow renal disease progression but it is less clear whether such approaches will reduce the risk of T2DM or CAD in gout patients.

Table- Association between cumulative changes in uric acid over time and outcome events of interest in gout patients, Optum Clinformatics data 2004-2015
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Event counts and incidence rates</th>
<th>Hazard ratio (95% confidence interval) for 3 mg/dl reduction in serum uric acid during the follow-up period</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of events</td>
<td>Total person years of follow-up</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>749</td>
<td>45,972</td>
</tr>
<tr>
<td>Composite cardiovascular endpoint(^1)</td>
<td>470</td>
<td>60,910</td>
</tr>
<tr>
<td>Renal insufficiency(^2)</td>
<td>2,373</td>
<td>54,981</td>
</tr>
</tbody>
</table>

\(^1\) Myocardial infarction, Ischemic stroke, revascularization
\(^2\) 30% reduction in glomerular filtration rate from baseline

**Disclosure:** R. J. Desai, None; J. Franklin, None; J. Spoendlin, None; G. Danaei, None; D. H. Solomon, None; S. C. Kim, AstraZeneca, 2,Pfizer Inc, 2,Roche Pharmaceuticals, 2,Bristol-Myers Squibb, 2,Merck Human Health, 2.


**Abstract Number:** 1865

**Novel Approach to Arthritis Surveillance Suggests a Much Higher Prevalence of Arthritis Among US Adults Than Previous Estimate**

S. Reza Jafarzadeh and David T. Felson, Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** ACR/ARHP Combined: Epidemiology and Public Health: Prevention, Recognition, and Treatment

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 4:30PM-6:00PM

**Background/Purpose:** Current national estimates of arthritis prevalence in the United States rely on a single survey question about doctor-diagnosed arthritis from the National Health Interview Survey (NHIS) without using survey information on joint symptoms. In a validation study of these NHIS questions, some persons with only joint symptoms were found to have arthritis when examined by trained rheumatology nurses who excluded those with asymptomatic findings. The validation study suggested that the current surveillance definition of doctor-diagnosed arthritis had only 53% sensitivity among adults between 45-64 years of age resulting in missing nearly half of arthritis cases in that age group. The substantial misclassification as a result of the current imperfect surveillance definition would result in a marked underestimation of prevalence. We aimed to estimate arthritis prevalence, using the term 'true' to represent estimates that are adjusted for the imperfect sensitivity and specificity of the current surveillance definition, and the term 'apparent' to represent ordinary proportion estimates which fail to so adjust.

**Methods:** Using the 2015 NHIS, we developed a Bayesian multinomial latent class model for arthritis surveillance criteria based on NHIS questions on joint symptoms and whether symptom duration exceeded three months in addition to a question about doctor-diagnosed arthritis. The NHIS questions explicitly ask subjects to exclude back and neck pain from the reports of joint pain or arthritis.
Our Bayesian approach accounted for the imperfect (i.e. <100%) sensitivity and specificity of each criterion in addition to accounting for the correlation between chronic joint symptoms and doctor-diagnosed arthritis in the survey.

**Results:** Of 33,672 participants in the 2015 NHIS, 19.3% (2,242/11,597) of men and 16.7% (2,294/13,697) of women between 18-64 years of age reported joint symptoms without doctor-diagnosed arthritis; estimates were 15.7% (545/3,474) and 13.5% (660/4,904), respectively, for those ≥65 years old. Bayesian posterior estimates and the corresponding 95% probability intervals (PI) for the ‘true’ prevalences in the 4 sub-populations stratified by age and sex are presented in the Table. Based on our estimates of ‘true’ prevalence, arthritis affected 91.2 (of 247.7; 36.8%) million adults in the US in 2015, which included 61.1 (of 199.9; 30.6%) million persons between 18-64 years of age. Our estimate for arthritis prevalence in 2015 is 68% higher than that previously reported based on the doctor-diagnosed arthritis question of 54.4 (22.7%) million adults.

**Conclusion:** Arthritis prevalence in the US population has been substantially underestimated, especially among adults <65. Our results may partially explain recent surge in arthritis-related healthcare utilizations such as total knee replacement, especially among younger adults.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age (Years)</th>
<th>'Apparent' Prevalence of Doctor-Diagnosed Arthritis in NHIS (Individuals)</th>
<th>'True' Prevalence of Arthritis (95% Bayesian Probability Interval)</th>
<th>US Adults with Arthritis Based on 'True' Prevalence (Millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>18-64</td>
<td>15.0% (1,740/11,597)</td>
<td>29.9% (23.4%, 42.3%)</td>
<td>29.8 (of 99.6)</td>
</tr>
<tr>
<td>Women</td>
<td>18-64</td>
<td>20.0% (2,734/13,697)</td>
<td>31.2% (25.8%, 44.1%)</td>
<td>31.3 (of 100.0)</td>
</tr>
<tr>
<td>Men</td>
<td>≥65</td>
<td>43.5% (1,511/3,474)</td>
<td>55.8% (49.9%, 70.4%)</td>
<td>11.8 (of 21.1)</td>
</tr>
<tr>
<td>Women</td>
<td>≥65</td>
<td>55.1% (2,704/4,904)</td>
<td>68.7% (62.1%, 79.9%)</td>
<td>18.3 (of 26.7)</td>
</tr>
</tbody>
</table>

Disclosure: S. R. Jafarzadeh, None; D. T. Felson, None.


Abstract Number: 1866

**Use of Aromatase Inhibitors and Risk of Arthritis and Musculoskeletal Problems Among Taiwanese Women with Breast Cancer: A Nationwide Claims Analysis**

**Hsu-Chih Chien**1,2,3, Wei-Hsuan Lo-Ciganic4, C. Kent Kwoh5 and Yea-Huei Kao Yang6,1, Department of Medicine, University of Arizona, Tucson, AZ, Division of Rheumatology, Tucson, AZ,2 College of Medicine and Health Outcome Research Center, National Cheng Kung University, Tainan, Taiwan, Institute of Clinical Pharmacy and Pharmaceutical Sciences, Tainan, Taiwan,3 University of Arizona Arthritis Center, Tucson, AZ,4 Department of Pharmacy, Practice and Science, College of Pharmacy, University of Arizona, Associate professor, TUCSON, AZ, 5 University of Arizona, Tucson, AZ,6 College of Medicine, National Cheng Kung University, Institute of Clinical Pharmacy and Pharmaceutical Science, Tainan, Taiwan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** ACR/ARHP Combined: Epidemiology and Public Health: Prevention, Recognition, and Treatment

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 4:30PM-6:00PM

**Background/Purpose:** Asian women accounted for more than 40% of incident breast cancer (BC) worldwide. While aromatase inhibitors (AIs) significantly reduce recurrence of breast cancer (BC) and improve disease-free survival in post-menopausal women with hormone receptor-presenting BC, over one-third of AI users in randomized controlled trials developed arthralgia. Little is known about the risk of AI-induced arthralgia among Asian women with BC in real-world settings. Our objective was to compare the risk of AI-induced arthritis/musculoskeletal problems (A/MSK) between use of AIs vs. tamoxifen in a large Taiwan administrative claims dataset having >99% national coverage and ~23 million enrollees. **Methods:** In a retrospective cohort study using Taiwan Catastrophic Illness Patient Datasets and Taiwan National Health Insurance Research Datasets, we identified BC women (ICD-9 code: 174) that newly initiated AIs (anatrazole, exemestane and letrozole) or tamoxifen (TAM) from 2007 to 2012. We examined three A/MSK -related outcomes of interest within a year after therapy initiation, including women having 1) prescription pain relievers (i.e., non-steroidal anti-inflammatory drugs [NSAIDs], acetaminophen and opioids), 2) diagnosis of any type of arthritis (ICD-9: 710-719), or 3) carpal tunnel syndrome (CTS) or trigger fingers (TF; ICD-9: 354.0, 727.03). Individuals having outcome episodes that occurred within 3 months prior to AI/TAM initiation were excluded. We applied Greedy methods to match AI users with up to 5 TAM users on age and prior use
of taxane therapy. To ensure the robustness of our results, we estimated the association between A/MSK risk and AI use compared to TAM use using conditional logistic regression, cause-specific Cox regression and competing risk regression models. **Results:** Among 40,761 BC women initiating endocrine therapy from 2007 to 2012, 15.5% were AI users and 84.5% were TAM users. The mean age was 54.1 (SD±12.1) years and 19.6% had history of taxane exposure prior to AI/TAM initiation. There were significant differences (p <0.0001) in the crude rates of pain reliever use (68.7% vs. 65.0%), diagnosed arthritis (16.8% vs. 11.7%) and CTS/TF (2.6% vs. 1.1%) within a year after AIs or TAM initiation. After matching, AI users had higher odds of receiving pain relievers (OR: 1.13, 95%CI: 1.02-1.24), having a diagnosis of arthritis (OR: 1.09, 95%CI: 1.00-1.18) and a diagnosis of CTS/TF (OR: 2.19, 95%CI: 1.76-2.74) compared to TAM users (Table 1). Similar findings were seen using cause-specific Cox regression and competing risk regression (Table 1).

**Conclusion:** We found that AI users have a higher risk of A/MSK within the first year of treatment compared with TAM users among Taiwanese BC women. Timely pain management and close follow-up for AI-induced A/MSK is suggested to prevent poor adherence or discontinuation of AI therapy.

<table>
<thead>
<tr>
<th>Outcomes of interest</th>
<th>Using pain relievers</th>
<th>Arthritis</th>
<th>CTS/TF</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AI users</td>
<td>TAM users</td>
<td>AI users</td>
</tr>
<tr>
<td>Unmatched cohort</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. for eligible patients for each outcome</td>
<td>2,967</td>
<td>16,329</td>
<td>5,845</td>
</tr>
<tr>
<td>Event No.</td>
<td>2,039</td>
<td>10,619</td>
<td>983</td>
</tr>
<tr>
<td>Crude Incidence (%)</td>
<td>68.7</td>
<td>65.0</td>
<td>16.8</td>
</tr>
<tr>
<td>Matched cohort</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. for eligible patients</td>
<td>2,727</td>
<td>8,743</td>
<td>5,365</td>
</tr>
<tr>
<td>Event No.</td>
<td>1,869</td>
<td>5,764</td>
<td>891</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>1.13 (1.02-1.24)</td>
<td>1.09 (1.00-1.18)</td>
<td>2.19 (1.76-2.74)</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>1.13 (1.06-1.20)</td>
<td>1.11 (1.02-1.20)</td>
<td>2.20 (1.76-2.75)</td>
</tr>
<tr>
<td>sHR (95% CI)</td>
<td>1.11 (1.05-1.16)</td>
<td>1.08 (1.01-1.15)</td>
<td>2.15 (1.80-2.57)</td>
</tr>
</tbody>
</table>

**Table 1. Crude incidence and the risk of arthralgia among Taiwanese women with breast cancer that received aromatase inhibitor vs. tamoxifen therapy.**

| Abbreviations: AIs: aromatase inhibitors; CTS: carpal tunnel syndrome; HR: hazard ratio, estimated by Cox regression; sHR: subdistributional hazard ratio, estimated by competing risk regression model; TF: trigger fingers, OR: odds ratio, estimated by conditional logistic regression.|

**Disclosure:** H. C. Chien, None; W. H. Lo-Ciganic, None; C. K. Kwoh, NIH/NIAMS, 2,EMD Serono, 2,Abbvie, 2; Y. H. Kao Yang, None.

**Abstract Number:** 1867

**Can Vs. Do: Using Walking Speed and Moderate-to-Vigorous Physical Activity to Predict Incident Low Health-Related Quality of Life and Disability**

**Louise Thoma**¹, Hiral Master¹, Meredith Christiansen¹, Dana Mathews² and Daniel White³, ¹Physical Therapy and Biomechanics and Movement Science, University of Delaware, Newark, DE, ²Physical Therapy, Biomechanics and Movement Science, University of Delaware, Newark, DE, ³Department of Physical Therapy, University of Delaware, Newark, DE

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** ACR/ARHP Combined: Epidemiology and Public Health: Prevention, Recognition, and Treatment

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 4:30PM-6:00PM

**Background/Purpose:**
Walking speed is a measure of performance, i.e., what people “can” do, and is a known predictor of future health, disability, and mortality in older adults. Time in moderate-to-vigorous physical activity (MVPA), is a complementary measure of the frequency of behavior at given intensity, i.e., what people actually “do”, and is also associated with future health and mortality. However, it is unclear how both walking speed and MVPA are jointly associated with future health. The purpose of this study was to examine the associations of combined walking speed (what people “can” do) and MVPA (what people “do”) categories with health-related quality of life (HR-QoL) and disability in adults with or at risk of knee osteoarthritis (OA).

Methods:
We used data from the Osteoarthritis Initiative, a large cohort study of people with or at risk for knee OA. Walking speed and MVPA were collected at the 48-month visit. Walking speed was calculated from a 20-m walk test. MVPA was measured with an accelerometer (Actigraph GT1M) worn at the hip for ≥10 hrs/day for ≥4 days, and defined as ≥2020 counts/min. We classified people as Fast-Active (>1.2 m/s and MVPA >11 min/day, median value of the sample), Fast-Inactive (>1.2 m/s and MVPA <11 min/day), Slow-Active (<1.2 m/s and MVPA >11 min/day), and Slow-Inactive (<1.2 m/s and MVPA <11 min/day). Study outcomes were incident low HR-QoL measured with the Short-Form 12 Physical Component Score (SF-12 PCS, Score <40 indicating low HR-QoL) and incident disability measured with the Late Life Disability Instrument (Limitation Score [LLDI-L] <50 and Frequency Score [LLDI-F] <70 indicating disability) measured 4 years later. We calculated risk ratios and 95% confidence intervals adjusting for potential confounders at baseline.

Results:
Of 1876 people with baseline walking speed and MVPA data (55% women, age 65.1±9.1 years, BMI 28.4±4.8 kg/m²), 1419, 1250, and 1413 people were free of the outcome at baseline and had 4-year follow-up data for the PCS, LLDI-L, and LLDI-F, respectively. At the 4-year follow up, 11-15% of the analytic sample developed low HR-QoL and disability (Table 1). The Fast-Inactive and Slow-Inactive groups had greater risk of incident low HR-QoL compared to the Fast-Active group; the Slow-Active group had similar risk. The Slow-Inactive group had greater risk for incident disability (LLDI-F) compared to the Fast-Active group; otherwise the groups had similar risk.

Conclusion:
Compared to people who were fast and active, those who were slow and active were at similar risk, those who were fast and inactive had greater risk of HR-QoL, and those who were slow and inactive had greater risk of developing low HR-QoL and disability. Advising patients to “do”, i.e. spend more time in MVPA (e.g. a brisk walk), may be as or more important than ensuring that they “can” do, i.e. walk fast enough for community ambulation, to prevent the development of future low HR-QoL.

Table 1. Descriptive statistics and risk ratios (95% Confidence Interval) for the incident outcomes by exposure group

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Baseline</th>
<th>Incident Outcome</th>
<th>Unadjusted RR</th>
<th>Adjusted RR*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(Mean ± SD)</td>
<td>Proportion (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SF-12 PCS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fast-Active</td>
<td>53.0 ± 5.2</td>
<td>61/731 (8.6)</td>
<td>REF</td>
<td>REF</td>
</tr>
<tr>
<td>Fast-Inactive</td>
<td>51.7 ± 5.9</td>
<td>74/407 (18.8)</td>
<td>2.2 (1.6 - 3.0)</td>
<td>1.6 (1.1 - 2.2)</td>
</tr>
<tr>
<td>Slow-Active</td>
<td>51.0 ± 5.6</td>
<td>15/98 (15.8)</td>
<td>1.8 (1.1 - 3.1)</td>
<td>1.3 (0.8 - 2.3)</td>
</tr>
<tr>
<td>Slow-Inactive</td>
<td>49.8 ± 5.4</td>
<td>55/230 (24.9)</td>
<td>2.9 (2.1 - 4.0)</td>
<td>1.7 (1.1 - 2.6)</td>
</tr>
<tr>
<td><strong>LLDI - Limitations</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fast-Active</td>
<td>89.9 ± 10.7</td>
<td>69/627 (11.4)</td>
<td>REF</td>
<td>REF</td>
</tr>
<tr>
<td>Fast-Inactive</td>
<td>87.5 ± 11.4</td>
<td>59/355 (17.2)</td>
<td>1.5 (1.1 - 2.1)</td>
<td>1.1 (0.8 - 1.6)</td>
</tr>
<tr>
<td>Slow-Active</td>
<td>87.6 ± 11.4</td>
<td>8/88 (9.2)</td>
<td>0.8 (0.4 - 1.6)</td>
<td>0.6 (0.3 - 1.2)</td>
</tr>
<tr>
<td>Slow-Inactive</td>
<td>85.8 ± 11.5</td>
<td>56/221 (26.4)</td>
<td>2.3 (1.7 - 3.2)</td>
<td>1.3 (0.9 - 2.0)</td>
</tr>
<tr>
<td><strong>LLDI - Frequency</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fast-Active</td>
<td>57.1 ± 5.6</td>
<td>57/666 (8.8)</td>
<td>REF</td>
<td>REF</td>
</tr>
<tr>
<td>Fast-Inactive</td>
<td>56.9 ± 5.1</td>
<td>40/415 (10.0)</td>
<td>1.1 (0.8 - 1.7)</td>
<td>1.1 (0.8 - 1.7)</td>
</tr>
<tr>
<td>Slow-Active</td>
<td>55.9 ± 4.7</td>
<td>11/97 (11.6)</td>
<td>1.3 (0.7 - 2.4)</td>
<td>1.3 (0.7 - 2.4)</td>
</tr>
<tr>
<td>Slow-Inactive</td>
<td>56.6 ± 4.9</td>
<td>46/281 (17.0)</td>
<td>1.9 (1.4 - 2.8)</td>
<td>1.8 (1.2 - 2.7)</td>
</tr>
</tbody>
</table>

Disclosure: L. Thoma, None; H. Master, None; M. Christiansen, None; D. Mathews, None; D. White, None.
Association between Brain-Derived Neurotrophic Factor Gene Polymorphisms and Fibromyalgia in a Korean Population: A Multi-Center Study

Ji-Hyoun Kang¹, Kyung-Eun Lee², Dong-Jin Park¹, Seong-Ho Kim³, Seong-Su Nah⁴, Ji Hyun Lee⁵, Seong-Kyu Kim⁶, Yeon-Ah Lee⁷, Seung-Jae Hong⁸, Hyun-Sook Kim⁹, Hye-Soon Lee¹⁰, Hyou-Ah Kim¹¹, Chung-II Joung¹², Sang-Hyon Kim¹³ and Shin-Seok Lee¹,²

¹Rheumatology, Chonnam National University Medical School and Hospital, Gwangju, Korea, Republic of (South), ²Chonnam National University Medical School and Hospital, Gwangju, Korea, Republic of (South), ³Inje University Haeundae Paik Hospital, Busan, Korea, Republic of (South), ⁴Soochunhyang University, College of Medicine, Cheonan, Korea, Republic of (South), ⁵Maryknoll Medical Center, Busan, Korea, Republic of (South), ⁶Rheumatology, Catholic University of Daegu School of Medicine, Daegu, Korea, Republic of (South), ⁷Rheumatology, Kyung Hee University Hospital, Seoul, Korea, Republic of (South), ⁸Dept. of Rheumatology, #1 Hoeg, KyungHee University Medical Center, SEOUL, Korea, Republic of (South), ⁹Soochunhyang university school of medicine, Seoul, Korea, Republic of (South), ¹⁰Hanyang University Guri Hospital, Gyeonggi-do, Korea, Republic of (South), ¹¹Ajou University Hospital, Suwon, Korea, Republic of (South), ¹²Konyang University Medical School, Daejeon, Korea, Republic of (South), ¹³Division of Rheumatology, Department of Internal Medicine, Keimyung University Dongsan Medical Center, Keimyung University School of Medicine, Daegu, Republic of Korea, Daegu, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Several lines of evidence suggest that brain-derived neurotrophic factor (BDNF) is involved in the pathophysiology of fibromyalgia (FM) and studies have found that FM patients have altered serum and plasma BDNF levels. However, it is not known whether polymorphisms of the BDNF gene are associated with FM. In this study, we explored the association between polymorphisms of the BDNF gene with FM susceptibility and the severity of symptoms.

Methods: The study enrolled 409 patients with FM and 423 controls from 10 medical centers that participated in the Korean nationwide FM survey study. Alleles at 10 positions in the BDNF gene were genotyped: rs2883187 (C>T), rs7103873 (G>C), rs7103411(C>T), rs10835210 (C>A), rs11030104 (A>G), rs12273539 (C>T), rs11030102(C>G), rs11030101 (A>T), rs6265 (G>A), and rs7124442(C>T).

Results: The allele and genotype frequencies of BDNF rs11030104 differed significantly between the FM patients and controls (P=0.031). The GG genotype of rs11030104 had a protective role against FM (P=0.016) and the G allele of rs11030104 was negatively associated with the presence of FM compared with the A allele (P=0.013). In comparison, although the allele and genotype frequencies of BDNF rs12273539 did not differ between the FM patients and controls, the TT genotype of BDNF rs12273539 was associated with susceptibility to FM (P=0.038). Haplotype analyses suggested that some BDNF haplotypes have a protective role against FM. Finally, we found that that some genotypes and haplotypes of the BDNF gene contribute to the specific symptoms of FM.

Conclusion: This study is the first to evaluate the associations of BDNF gene polymorphisms with FM. Our results suggest that some BDNF single-nucleotide polymorphisms and haplotypes are associated with susceptibility to, and contribute to the symptoms of, FM.

Disclosure: J. H. Kang, None; K. E. Lee, None; D. J. Park, None; S. H. Kim, None; S. S. Nah, None; J. H. Lee, None; S. K. Kim, None; Y. A. Lee, None; S. J. Hong, None; H. S. Kim, None; H. S. Lee, None; H. A. Kim, None; C. I. Joung, None; S. H. Kim, None; S. S. Lee, None.


Abstract Number: 1869
Effects of Add-on Transcranial Direct Current Stimulation on Pain in Korean Patients with Fibromyalgia

Ji-Hyoun Kang, Kyung-Eun Lee, Dong-Jin Park and Shin-Seok Lee, 1Rheumatology, Chonnam National University Medical School and Hospital, Gwangju, Korea, Republic of (South), 2Chonnam National University Medical School and Hospital, Gwangju, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Despite promising preliminary results of transcranial direct current stimulation (tDCS) treatment in patients with fibromyalgia (FM), several issues need to be addressed, including its limited efficacy, low response rate, and poor tolerability. We investigated the efficacy and safety of tDCS as an add-on treatment for chronic widespread pain in Korean patients with FM.

Methods: This study enrolled 38 patients, who were refractory to pain medications, seen at Chonnam National University Hospital from May 2016 to December 2016. A conventional tDCS device was used to supply 2 mA of current for 20 minutes on 5 consecutive days. The anode was placed over the primary motor cortex (M1) and the cathode was located contralateral supraorbital area. The primary end point was a change in visual analogue scale (VAS) pain score at the end of treatment and secondary end points included changes in Fibromyalgia Impact Questionnaire (FIQ), Brief Pain Inventory (BPI), Brief Fatigue Inventory (BFI), Beck Depression Inventory (BDI), State-Trait Anxiety Inventory (STAI), and Medical Outcomes Study Sleep Scale scores.

Results: After tDCS, 38 patients showed clinical improvements in the VAS pain score on days 6, 13 and 36 compared with day 0 ($p < 0.001$). However, improvement of FIQ scores was only seen at day 36. The BPI and BDI were significantly decreased on days 6 and 13, while BFI and STAI-I were significantly improved only at day 6. The most of improved indices were not maintained until day 36. There were no significant improvements in Sleep Scale scores after tDCS at days 6, 13, and 36. No serious adverse event was observed.

Conclusion: Our results suggest that tDCS has the potential to produce significant pain relief in FM patients, and may constitute an effective add-on treatment for these patients.

Disclosure: J. H. Kang, None; K. E. Lee, None; D. J. Park, None; S. S. Lee, None.


Abstract Number: 1870

Validation of an Electronic Version of the Michigan Body Map

Chad M. Brummett, David Kohms, Rishi Bakshi, Jenna Goesling, Stephanie Moser, Jennifer Pierce, David Williams, Daniel J. Clauw, Afton L. Hassett and Erin Spencer, 1Anesthesiology, University of Michigan, Ann Arbor, MI, 2University of Michigan, Ann Arbor, MI, 3Physical Medicine Rehabilitation, University of Michigan, Ann Arbor, MI, 4Department of Anesthesiology, University of Michigan, Ann Arbor, MI, 5Chronic Pain & Fatigue Research Center, University of Michigan, Ann Arbor, MI

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose:
We previously validated the Michigan Body Map (MBM) to accurately assess widespread body pain and as a means of administering the Widespread Pain Index for the 2011 Fibromyalgia Survey Criteria. Given the increased use of electronic platforms for patient reported outcomes, this study aimed to validate an electronic version of the MBM, including a version allowing for the rating of pain in different body zones.

**Methods:**

Patients (n = 68; M_{age} = 51.7, SD = 15.1; 57.4% female; 85.3% White) were recruited from a pain clinic. For Aim 1, participants completed the MBM in paper (MBM-P) and electronic (MBM-E) forms in randomized order, as well as completed a structured interview to assess their experience and to verbally affirm pain locations. For Aim 2, participants also completed the Brief Pain Inventory (BPI) and a modified version of the MBM assessing pain zone severity. Data were analyzed using StataIC 13.

**Results:**

There were no differences between MBM-E or MBM-P in preference, ease of completion, ability to show painful areas, or ability to distinguish right and left sides of the body (Figure 1). Of the 2,380 possible regions (35 body areas/participant), 46 (1.9%) body areas on the MBM-P and 38 (1.6%) body areas on the MBM-E were discrepant when compared to verbal report as the gold standard (McNemar’s χ² = 0.76, p = 0.38). There were no differences in accuracy between the MBM-E and MBM-P in each of the body zones with the exception of a small improvement in accuracy of the back region for the MBM-E (McNemar’s χ² = 7.36, p = .01). There were no associations between age or comfort using electronic screens and discrepancies on the MBM-P or the MBM-E. Participants did not believe the MBM-E looked different from the MBM-P or have difficulty marking areas of pain on the MBM-E (Table 1). Participants did report some issues with reading or sizing on the MBM-E. For Aim 2, participants indicated they preferred the MBM-E and the MBM-E with pain zones more than the BPI as a way to best describe their pain (Figure 2).

**Conclusion:**

The present study demonstrates the utility, reliability and construct validity of an electronic version of the MBM. Moreover, the new MBM-E with pain zones allows patients to rate pain intensity and was preferred to the classic 0-10 scales from the BPI to describe their pain.

Table 1
Problems with Electronic MBM

<table>
<thead>
<tr>
<th>Problem Description</th>
<th>No</th>
<th>Yes</th>
<th>$\chi^2$</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did they look different?</td>
<td>55</td>
<td>11</td>
<td>1.83</td>
<td>.18</td>
</tr>
<tr>
<td>Did you have any issues with reading or sizing of</td>
<td>53</td>
<td>15</td>
<td>3.31</td>
<td>.07</td>
</tr>
<tr>
<td>the body map or labels?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Did you have any trouble or difficulty marking</td>
<td>58</td>
<td>10</td>
<td>1.47</td>
<td>.23</td>
</tr>
<tr>
<td>areas of pain?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Preferred Method for Describing Pain

![Graph showing Preferred Method for Describing Pain](image)

Figure 2. Most preferred method for describing pain. Participants preferred the MBM-E (Original) and the MBM-E (Zones) more than the BPI. There was no significant difference in preference between MBM-E (Original) and MBM-E (Zones).

Disclosure: C. M. Brummett, MDHHS (Sub K Michigan OPEN); NIH-DHHS (P90 AR070600-05 CORT) UM MICHIGAN Genomics Initiative, 2; NIDA (ntralized Pain Opiod Non-Responsiveness RO1 DA03826-05); Neuros Medical, Inc. (research funding only), 2; Peripheral Perineural Dexmedetomidine Patent, 7; D. Kohns, None; R. Bakshi, None; J. Goesling, NIH Project #1K23DA038718-01A1, 2; S. Moser, None; J. Pierce, None; D. Williams, American Pain Society, 6; Pfizer Inc, 6; Community Health Focus, Inc., 5; D. J. Clauw, Abbott Pharmaceuticals, 5; Aptinyx, 5; Cerephex, 5; Daiichi Sankyo, 5; Pfizer Inc, 5; Samumed, 5; Theravance, 5; Tonix, 5; University of Michigan, 3; Abbott Pharmaceuticals, 6; Astellas, 6; Cerephex, 6; Pfizer Inc, 6; Zynerba, 6; A. L. Hassett, Association of Rheumatology Health Professionals, 6; NIH 1R01NR017096-01A1, 2; E. Spencer, None.


Abstract Number: 1871

**Identifying Pain Sites Highly Associated with the Fibromyalgia (FM) Phenotype**

Louis Lu\(^1\), Stephanie Moser\(^2\), Chad M. Brummett\(^2\) and Daniel J. Clauw\(^3\), \(^1\)Anesthesiology & Perioperative Care, UC Irvine, Orange, CA, \(^2\)Anesthesiology, University of Michigan, Ann Arbor, MI, \(^3\)Chronic Pain & Fatigue Research Center, University of Michigan, Ann Arbor, MI

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017

Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes

Session Type: ACR Concurrent Abstract Session

Session Time: 4:30PM-6:00PM
**Background/Purpose:** Fibromyalgia is challenging to diagnose given its overlapping symptoms with other chronic pain conditions. The most characteristic feature of FM is widespread pain, operationalized by the 2016 FM Survey Criteria as involving at least 4 out of 5 body regions (axial region and limbs). We hypothesized that certain pain locations may be virtually pathognomonic of FM, because these pain sites occur commonly in FM patients but are very uncommon in individuals without FM.

**Methods:** This is a single center retrospective observational study of patients recruited prior to elective surgery to be in an institutional biorepository. Patients completed the Michigan Body Map to assess the presence or absence of pain in 35 body sites, as well as the 2011 FM symptom (FS) scores were calculated by adding the widespread pain index (WPI) and symptom severity (SS) scale. Based on the 2016 Modified FM Criteria, patients were diagnosed with FM if they reported pain in 4+ body regions and their FS scores were 12+. Controls were patients that did not meet the criteria. Univariate differences were assessed via t-tests and chi-square tests. Multivariate linear regression accounted for age and gender.

**Results:** 891 patients (5.5%) out of 16,273 patients were diagnosed with FM. Median age for FM patients was 53 vs 54 (p = 0.62) and 72% female vs 52% (p < 0.0001). Pain sites with the highest odds ratios between FM patients and controls were the left upper arm (23.9), left lower arm (23.4), right upper arm (22.6), right lower arm (21.8), left shoulder (21.6), and right shoulder (18.7). Upon multivariate analysis, statistically significant sites were the head (p = 0.006), face (p = 0.04), left upper arm (p = 0.004), left lower arm (p = 0.0001), left wrist/hand (p = 0.02), left knee (p < 0.0001), left lower leg (p = 0.002), left ankle/foot (p = 0.007), right jaw (p = 0.01), right upper arm (p = 0.006), right elbow (p < 0.0001), right lower arm (p < 0.0001), right wrist/hand (p < 0.0001), right knee (p < 0.0001), and right lower leg (p = 0.001). See **Table 1** for the results of all queried body sites.

**Conclusion:** Pain in non-joint regions of all four limbs, in addition to the head, face and jaw, were all statistically more significantly seen in individuals with FM and unusual in non-FM patients. Though other regions of pain were also commonly seen in FM, because they were also seen in non-FM patients, they would not be helpful in differentiating a chronic pain patient with FM vs. one with a different underlying cause.

**Table 1:**
<table>
<thead>
<tr>
<th>Site</th>
<th>FM Patients</th>
<th>Controls</th>
<th>Odds Ratio</th>
<th>Multivariate Analysis p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head</td>
<td>41.6%</td>
<td>8.7%</td>
<td>7.5 (6.5 - 8.7)</td>
<td>0.006</td>
</tr>
<tr>
<td>Face</td>
<td>10.2%</td>
<td>2.5%</td>
<td>4.4 (3.4 - 5.6)</td>
<td>0.04</td>
</tr>
<tr>
<td>Neck</td>
<td>66.4%</td>
<td>13.8%</td>
<td>12.4 (10.7 - 14.4)</td>
<td>0.08</td>
</tr>
<tr>
<td>Upper Back</td>
<td>53.2%</td>
<td>7.4%</td>
<td>5.7 (4.9 - 6.6)</td>
<td>0.04</td>
</tr>
<tr>
<td>Head</td>
<td>41.6%</td>
<td>8.7%</td>
<td>7.5 (6.5 - 8.7)</td>
<td>0.006</td>
</tr>
<tr>
<td>Lower Back</td>
<td>84.5%</td>
<td>30.0%</td>
<td>4.9 (4.1 - 5.6)</td>
<td>0.04</td>
</tr>
<tr>
<td>Pelvis</td>
<td>27.6%</td>
<td>7.3%</td>
<td>8.0 (6.6 - 9.6)</td>
<td>0.04</td>
</tr>
<tr>
<td>Lower Back</td>
<td>84.5%</td>
<td>30.0%</td>
<td>4.9 (4.1 - 5.6)</td>
<td>0.04</td>
</tr>
<tr>
<td>Pelvis</td>
<td>27.6%</td>
<td>7.3%</td>
<td>8.0 (6.6 - 9.6)</td>
<td>0.04</td>
</tr>
<tr>
<td>Left Jaw</td>
<td>20.2%</td>
<td>3.1%</td>
<td>21.6 (18.5 - 25.3)</td>
<td>0.04</td>
</tr>
<tr>
<td>Left Shoulder</td>
<td>71.4%</td>
<td>10.3%</td>
<td>23.9 (20.0 - 28.7)</td>
<td>0.004</td>
</tr>
<tr>
<td>Left Upper Arm</td>
<td>34.0%</td>
<td>2.1%</td>
<td>16.0 (13.4 - 19.1)</td>
<td>0.11</td>
</tr>
<tr>
<td>Left Elbow</td>
<td>31.0%</td>
<td>2.7%</td>
<td>23.4 (19.3 - 28.4)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Left Lower Arm</td>
<td>29.0%</td>
<td>1.7%</td>
<td>13.9 (12.0 - 16.0)</td>
<td>0.02</td>
</tr>
<tr>
<td>Left Wrist/Hand</td>
<td>59.6%</td>
<td>9.6%</td>
<td>8.0 (6.6 - 9.6)</td>
<td>0.04</td>
</tr>
<tr>
<td>Left Buttocks</td>
<td>20.1%</td>
<td>3.1%</td>
<td>7.6 (6.2 - 9.4)</td>
<td>0.04</td>
</tr>
<tr>
<td>Left Chest/Breast</td>
<td>16.5%</td>
<td>2.5%</td>
<td>15.8 (13.6 - 18.4)</td>
<td>0.04</td>
</tr>
<tr>
<td>Left Hip</td>
<td>66.4%</td>
<td>11.1%</td>
<td>4.5 (3.6 - 5.5)</td>
<td>0.04</td>
</tr>
<tr>
<td>Left Groin</td>
<td>15.3%</td>
<td>3.9%</td>
<td>12.2 (10.4 - 14.2)</td>
<td>0.04</td>
</tr>
<tr>
<td>Left Upper Leg</td>
<td>40.2%</td>
<td>5.2%</td>
<td>7.4 (6.4 - 9.6)</td>
<td>0.04</td>
</tr>
<tr>
<td>Left Knee</td>
<td>59.6%</td>
<td>16.6%</td>
<td>14.1 (12.2 - 16.4)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Left Lower Leg</td>
<td>46.7%</td>
<td>5.8%</td>
<td>9.8 (8.5 - 11.4)</td>
<td>0.0007</td>
</tr>
<tr>
<td>Left Ankle/Foot</td>
<td>57.6%</td>
<td>12.1%</td>
<td>8.8 (7.3 - 10.6)</td>
<td>0.01</td>
</tr>
<tr>
<td>Right Jaw</td>
<td>21.8%</td>
<td>3.1%</td>
<td>18.7 (16.0 - 21.8)</td>
<td>0.18</td>
</tr>
<tr>
<td>Right Shoulder</td>
<td>70.8%</td>
<td>11.5%</td>
<td>22.6 (18.9 - 27.1)</td>
<td>0.006</td>
</tr>
<tr>
<td>Right Upper Arm</td>
<td>33.6%</td>
<td>2.2%</td>
<td>13.6 (11.4 - 16.2)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Right Elbow</td>
<td>29.9%</td>
<td>3.0%</td>
<td>21.8 (17.9 - 26.5)</td>
<td>0.0000</td>
</tr>
<tr>
<td>Right Lower Arm</td>
<td>27.3%</td>
<td>1.7%</td>
<td>14.4 (12.5 - 16.7)</td>
<td>0.0000</td>
</tr>
<tr>
<td>Right Wrist/Hand</td>
<td>61.6%</td>
<td>10.0%</td>
<td>7.5 (6.2 - 9.1)</td>
<td>0.01</td>
</tr>
<tr>
<td>Right Buttocks</td>
<td>19.5%</td>
<td>3.1%</td>
<td>7.5 (6.1 - 9.3)</td>
<td>0.01</td>
</tr>
<tr>
<td>Right Chest/Breast</td>
<td>16.2%</td>
<td>2.5%</td>
<td>14.6 (12.6 - 17.0)</td>
<td>0.01</td>
</tr>
<tr>
<td>Right Hip</td>
<td>64.9%</td>
<td>11.2%</td>
<td>14.6 (12.6 - 17.0)</td>
<td>0.01</td>
</tr>
<tr>
<td>Body Part</td>
<td>Percentage</td>
<td>Error</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>------------------</td>
<td>------------</td>
<td>-------</td>
<td>------</td>
<td>----</td>
</tr>
<tr>
<td>Right Groin</td>
<td>16.3%</td>
<td>0.09</td>
<td>4.6</td>
<td>0.75</td>
</tr>
<tr>
<td>Right Upper Leg</td>
<td>41.0%</td>
<td>0.30</td>
<td>12.5</td>
<td>1.46</td>
</tr>
<tr>
<td>Right Knee</td>
<td>61.1%</td>
<td>0.0000</td>
<td>7.8</td>
<td>0.80</td>
</tr>
<tr>
<td>Right Lower Leg</td>
<td>47.0%</td>
<td>0.001</td>
<td>15.0</td>
<td>1.75</td>
</tr>
<tr>
<td>Ankle/Foot</td>
<td>57.8%</td>
<td>0.10</td>
<td>9.6</td>
<td>1.11</td>
</tr>
</tbody>
</table>

**Disclosure:** L. Lu, None; S. Moser, None; C. M. Brummett, MDHHS (Sub K Michigan OPEN); NIH-DHHS (P90 AR070600-05 CORT) UM MICHIGAN Genomics Initiative, 2,NIH-DHHS (ntralized Pain Opioid Non-Responsiveness RO1 DA03826-05); Neuros Medical, Inc. (research funding only), 2,Peripheral Perineural Dexmedetomidine Patent, 7,NIH-DHHS-US (K23 DA038718-04) Chronic Pain through Individualized Opioid Cessation, 2,NIH-DHHS (P50 AR070600-05 CORT), 2,UM Michigan Genomics Initiative, 2,Neuros Medical, Inc. (research funding only), 2; D. J. Clauw, Abbott Pharmaceutical, 5,Apinix, 5,Astellas Pharmaceutical, 5,Cerephex, 5,Daiichi Sankyo, 5,Pfizer Inc, 5,Pierre Fabre, 8,Samumed, 5,Teravance, 5,Tonix, 5.


**Abstract Number:** 1872

**The Effect of EEG-Amygdala-Related-Neurofeedback on REM Latency in Patients with Fibromyalgia**

Noam Goldway, Haggai Sharon, Eti Ben Simon, Libat Weizman, Ayam Greental, Omer Lubin, Marc Cavazza, Fred Charles, Talma Hendler and Jacob N. Ablin. 1Functional Brain Center, Wohl Institute for Advanced Imaging, Tel-Aviv Sourasky Medical Centre, Tel Aviv, Israel, 2School of Computing, Teesside University, United Kingdom, Middlesbrough, United Kingdom, 3Department of Creative Technology, Bournemouth University, Bournemouth, United Kingdom, 4Rheumatology, Rheumatology Institute, Tel Aviv, Tel Aviv, Israel

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes  
**Session Type:** ACR Concurrent Abstract Session  
**Session Time:** 4:30PM-6:00PM

**Background/Purpose:**

Fibromyalgia syndrome (FMS) is a condition characterized by widespread pain, sleep disturbance and chronic fatigue, and mood disorder. FMS was suggested to represent a prototype of central nervous system hypersensitivity (central sensitivity-CS). While the mechanisms underlying CS remain incompletely understood, a role for limbic and sleep related dysregulation has been argued. The aim of the current study was to examine the feasibility of fMRI-inspired *Electrical Finger Print (EFP)* of the amygdala as a probe for NeuroFeedback (amyEFP NF) training for FM patients. We expected to find improved sleep quality among trainees successful in downregulating amygdala activity.

**Methods:**

Thirty four FMS patients (3M:31F, average age 35.6 SD=11.82) underwent 10 sessions of amyEFP-NF, targeting down-regulation of the amygdala. Nine patients received rewarding sham NF and served as a control group. The 24 patients that received real feedback were divided into successful (succ+) (N=13) and unsuccessful (succ-) (N=12) feedback learners. Two interfaces were used to give the feedback: Auditory feedback and multi-modal virtual reality feedback. An objective outcome measure of sleep quality was taken using the WatchPAT device before and after NF training.

**Results:** Repeated measures ANOVA for feedback learning provided significant results (F=3.23 p=0.05), indicating that succ+ subjects displayed improved ability to regulate their amyEFP signal following treatment, in comparison to succ- and sham participants. The three groups also differed in REM latency improvement: repeated measures ANOVA for REM latency was significant (F=3.557 p=0.04),
indicating that only succ+ subjects displayed longer REM latency following amyEFP-NF. Furthermore, the change in REM latency was
correlated with feedback learning only in the succ+ group (R=0.497 p=0.05)

Conclusion:
In order to improve the sleep quality of patients suffering from central sensitivity disorder we targeted the amygdala, a limbic hub that is
known to be affected by sleep impairment. We show feedback-specific effect of improved REM latency, a well-known marker for mood
disorder. This study provides novel evidence of neurofeedback specific effect on objective sleep measures in FMS patients.

Disclosure: N. Goldway, None; H. Sharon, None; E. Ben Simon, None; L. Weizman, None; A. Greental, None; O. Lubin, None;
M. Cavazza, None; F. Charles, None; T. Hendler, None; J. N. Ablin, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-effect-of-eeg-amygdala-related-neurofeedback-
on-rem-latency-in-patients-with-fibromyalgia

Abstract Number: 1873

Evaluating Pain Related Disability in Fibromyalgia: A Comparison of the Fibromyalgia Impact Questionnaire and the Polysymptomatic Distress Scale

Nilamba Jhala1, Yaseen Kinana2, Sahar Kaouk3, Deb Bork4, Sara Davin5, Sarah Rispinto5, William Wilke4 and Carmen E. Gota4,
1Internal Medicine, Cleveland Clinic, Cleveland, OH, 2Internal Medicine, Cleveland Clinic Foundation, Cleveland, OH, 3John Carroll
University, University Heights, OH, 4Orthopedic and Rheumatologic Institute, Cleveland Clinic, Cleveland, OH, 5Neurologic Institute,
Cleveland Clinic, Cleveland, OH
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose:
Both the fibromyalgia impact questionnaire (FIQ) and the polysymptomatic distress scale (PSD) have been proposed as measures of FM
impact and severity. It is not known how they related to each other and to what extent they relate to FM process items such as pain,
depression, anxiety, and catastrophizing.

We set to compare the correlation between FIQ and PSD, and their correlates with depression, anxiety, and catastrophizing, and to
determine the individual impact of FIQ and PSD on pain disability index as a measure of the extent to which fibromyalgia pain
interferes with a patient’s ability to engage in essential life activities. In this study we considered pain disability index as a surrogate for
FM severity.

Methods:
The PSD is the sum of two variables used in the 2010 preliminary American College of Rheumatology fibromyalgia criteria, the
widespread pain index (WPI) and symptom severity scale (SS). The FiQ, captures the total spectrum of problems related to FM and has
been used as a measure of fibromyalgia severity.

The pain disability index measures the impact of chronic pain on seven essential life activities, family, recreational, social, occupational,
sexual, self care, and life support. and is the sum of the scores (0 - 10) of all life activities divided by the number of activities rated. We
measured the patient health questionnaire (PHQ-9) for depression, the general anxiety disorder scale (GAD-7), and the pain
catastrophizing scale.

Results:
Patients diagnosed clinically with FM were included:n 555, 85.5% female, 79.5% white, age 44.3 (12), 87.2% met ACR 2010 FM
criteria, PHQ-9 13.7 (6.5), GAD-7 8.6 (6.6), pain catastrophizing scale 22.6 (13.4), PSD 21 (10.6), FIQ 57.9 (20.4), pain disability index
5.3 (2.3).
FIQ correlated with PSD $r = 0.465$, GAD-7 $r = 0.368$, PHQ-9 $r = 0.476$, pain catastrophizing scale $r = 0.262$, pain disability index $r = 0.602$; PSD score correlated with GAD-7 $r = 0.233$, PHQ-9 $r = 0.371$, pain catastrophizing scale $r = 0.262$, pain disability index $r = 0.377$. All correlations were significant at $p<0.001$.

Linear regression was calculated to predict FIQ based on GAD-7, PHQ-9 and pain catastrophizing scale. A significant regression equation was found $F(1, 120)=42.064$, $P<0.001$, $R^2 = 0.513$ of FIQ. Depression and catastrophizing scores remaining independent predictors of FIQ. A similar model significantly predicts the PSD score, $F(1,130)=26.849$, $P<0.001$, $R^2 = 0.383$ of PSD; only depression measured by PHQ-9 remained an independent predictor of PSD. To measure the individual contribution of FIQ and PSD score on pain disability index we performed a linear regression model. A significant regression equation was found $F(2,165)=154.619$, $R^2 = 0.652$ of PDI. In this model, FIQ but not PSD remained independent predictor of pain disability index.

**Conclusion:**

Our data suggests that the FIQ and the PSD show only a moderate degree of correlation. Also, the FIQ has stronger associations with FM process measures including depression, anxiety, pain catastrophizing and pain disability index, compared to the PSD. This may explain why the FIQ, but not the PSD remains an independent predictor of pain disability score.

**Disclosure:** N. Jhala, None; Y. Kinanah, None; S. Kaouk, None; D. Bork, None; S. Davin, None; S. Rispinto, None; W. Wilke, None; C. F. Gota, None.

lesions that had the highest PPV were: PD at the enthesis (PD grade greater than 2 (100%) and PD grade greater than 1 (97%)), erosions (89%) and bone proliferation (87%). In general, the sensitivity of was much lower ranging from 0.1% to 27%. No significant differences were found in the frequencies of calcifications or bursitis between PsA patients and controls.

**Conclusion:** We identified elemental ultrasonographic abnormalities that could distinguish PsA and controls. This information will contribute to the development of a new sonographic score for assessment of enthesitis in patients with PsA that could be used for diagnostic purposes and contribute to new understanding and clinical application of ultrasonographic enthesitis at the bedside.

### Table 1: The Frequencies, Sensitivities, Specificities and Positive Predictive Values of Enthesal Lesions

<table>
<thead>
<tr>
<th>Enthesal structural abnormality</th>
<th>PsA (%)</th>
<th>Control (%)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Enthesophyte</td>
<td>27</td>
<td>18</td>
<td>27</td>
<td>82</td>
<td>60</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Enthesophyte-grade&gt;1</td>
<td>13</td>
<td>6</td>
<td>13</td>
<td>94</td>
<td>67</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Enthesophytes – grade &gt;2</td>
<td>6</td>
<td>3</td>
<td>6</td>
<td>97</td>
<td>65</td>
<td>0.003</td>
</tr>
<tr>
<td>Non-traction enthesophytes</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>98</td>
<td>66</td>
<td>0.03</td>
</tr>
<tr>
<td>Bony proliferation</td>
<td>3</td>
<td>0.5</td>
<td>3</td>
<td>100</td>
<td>87</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Any erosion</td>
<td>8</td>
<td>1</td>
<td>8</td>
<td>99</td>
<td>89</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Any PD signal</td>
<td>9</td>
<td>1</td>
<td>9</td>
<td>99</td>
<td>87</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PD signal – grade=1</td>
<td>4</td>
<td>0.2</td>
<td>4</td>
<td>100</td>
<td>96</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PD signal – grade&gt;2</td>
<td>0.8</td>
<td>0.09</td>
<td>0.8</td>
<td>100</td>
<td>90</td>
<td>0.03</td>
</tr>
<tr>
<td>Any PD close to enthesitis</td>
<td>7</td>
<td>1</td>
<td>7</td>
<td>99</td>
<td>87</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PD signal – grade=1 close to enthesitis</td>
<td>3</td>
<td>0.1</td>
<td>3</td>
<td>100</td>
<td>97</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PD signal – grade&gt;2 close to enthesitis</td>
<td>0.8</td>
<td>0</td>
<td>0.1</td>
<td>100</td>
<td>100</td>
<td>0.008</td>
</tr>
<tr>
<td>Calcification</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>97</td>
<td>54</td>
<td>0.578</td>
</tr>
<tr>
<td>Bursitis</td>
<td>1.8</td>
<td>1</td>
<td>2</td>
<td>99</td>
<td>65</td>
<td>0.148</td>
</tr>
</tbody>
</table>

Disclosure: S. Tom, None; Y. Zhong, None; R. J. Cook, None; S. Z. Aydin, None; G. S. Kaeley, None; L. Eder, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/development-of-an-ultrasonographic-enthesitis-score-for-psoriatic-arthritis-patients](http://acrabstracts.org/abstract/development-of-an-ultrasonographic-enthesitis-score-for-psoriatic-arthritis-patients)

**Abstract Number:** 1875

**Assessment of Structural Damage of the Thumb Base in Patients with Hand Osteoarthritis: Comparing the Newly Developed Omeract Magnetic Resonance Imaging Scoring System with Standard Radiography**

S. van Beest¹, F.P.B. Kroon¹, W. Damman¹, R. Liu¹, H.M. Kroon² and M. Kloppenburg³, ¹Rheumatology, Leiden University Medical Center, Leiden, Netherlands, ²Radiology, Leiden University Medical Center, Leiden, Netherlands, ³Rheumatology and Clinical Epidemiology, Leiden University Medical Center, Leiden, Netherlands

**First publication:** September 18, 2017

**SESSION INFORMATION**
Background/Purpose: Thumb base osteoarthritis (OA) is characterized by structural damage, most commonly evaluated by radiography. However radiography is insensitive. Magnetic resonance (MR) imaging could be a valuable alternative, however a standardized scoring method for thumb base MR images did not exist until recently OMERACT developed the thumb base OA MRI scoring system (TOMS). Our aim was to investigate the validity of the new TOMS by comparing TOMS scores with radiographic scores.

Methods: Two hundred patients (83.5% women, median age 60.5 years) with primary hand OA (90.5% fulfilling ACR classification criteria) from the rheumatology outpatient clinic, who had dorsopalmar radiographs and MR scans of the right thumb base, were studied. T1- and fat suppressed T2-turbo spin weighte sequences were obtained on a 1.5 Tesla scanner. Radiographs of the first carpometacarpal (CMC1) and scaphotrapeziotrapezoid (STT) joints were scored using the OARSI atlas (osteoophytes and joint space narrowing [JSN] in CMC1: 0-3 and STT: absent/present) in consensus by two readers with good intra-reader reliability. MR images were scored using TOMS (osteoophytes in CMC1: 0-6 and STT: 0-9; cartilage space loss [CSL] for both joints: 0-3) by two readers, with good intra- and inter-reader reliability. For analysis we used the average of both readers. Readers were blinded for clinical and other imaging data. To study validity, the distribution of the TOMS scores for osteophytes and CSL were described stratified for the different radiographic stages for osteophytes and JSN, respectively.

Results: On MR images osteophytes were detected in the vast majority of thumb bases (CMC1 n=172; STT n=102). The score of TOMS increased with more severe radiographic stages (see figures). However, the number of patients without any osteophytes in both CMC1 and STT was considerably lower for TOMS (n=19) than for the OARSI (n=105) scoring. A similar difference was apparent for absence of CSL (n=82) versus JSN (n=107) in both CMC1 and STT. Patients with isolated STT osteophytes were quite rare for both TOMS (n=9) and the OARSI (n=1) scoring. The most prominent discrepancy between TOMS and OARSI sensitivity was found for osteophytes: an additional 170 joints (CMC1 n=79; STT n=91) were found positive with TOMS, while only 1 OARSI-positive CMC1 scored negative with TOMS.

Conclusion: Scores of OA features assessed on MR images by TOMS were correlated with radiographic scores, indicating good validity of the TOMS. Furthermore, the frequencies of positive features assessed on MR images were higher compared to those on radiographs, suggesting high sensitivity for the TOMS.

Disclosure: S. van Beest, Innovative Medicines Initiative: Approach, 2; F. P. B. Kroon, None; W. Damman, None; R. Liu, None; H. M. Kroon, None; M. Kloppenburg, Pfizer, 2,AbbVie, GlaxoSmithKline, Merck, Levicept, 5,Dutch Arthritis Fund, 2,Innovative Medicines Initiative: APPROACH, 2.

A Non-Invasive Ultrasound Surface Wave Elastography Technique for Assessing Interstitial Lung Disease

Thomas Osborn¹, Xiaoming Zhang², Sanjay Kalra³, Boran Zhou⁴ and Brian Bartholmai⁵, ¹Rheumatology, Mayo Clinic, Rochester, MN, ²Mayo Clinic college of Medicine, Rochester, MN, ³Pulmonary and Critical Care Medicine, Mayo Clinic, Rochester, MN, ⁴Radiology, Mayo Clinic, Rochester, MN, ⁵Thoracic Radiology, Mayo Clinic, Rochester, MN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Imaging of Rheumatic Diseases I: Novel Imaging and Scoring Systems
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Surface wave elastography is an ultrasound based noninvasive technique to measure tissue viscoelasticity (“stiffness”). Preliminary studies in assessing scleroderma associated skin thickening have been promising. Ultrasonography is not widely used in clinic for lung assessment. Lung tissue is normally filled with air, and the difference in acoustic impedance between air and tissue is large. Most of the energy of an ultrasound wave is reflected from the lung surface and ultrasound cannot image deep lung tissue. In this abstract, we present a novel technique, lung ultrasound surface wave elastography, for measuring the elastic properties of superficial lung tissue. The lung changes in many interstitial lung diseases (ILD), including scleroderma associated ILD, are peripheral/superficial and have fibrosis-related “stiffening.”

Methods: A handheld vibrator was used to generate a small, local, and 0.1 second harmonic vibration on the chest of a subject. A Versonics ultrasound probe (L11-4/central frequency of 6.4 MHz) was used to measure the resulting surface wave speed on the lung. In a large clinical study of ILD patients, we measure both lungs through six intercostal spaces for patients and controls. Patients were selected from the Adult Pulmonary and Rheumatology outpatient clinics. Clinical and CT diagnosis of interstitial lung disease, either idiopathic or associated with a connective tissue disease/autoimmune inflammatory arthritis. Controls were never-smoking, asymptomatic adults with no history of cardiorespiratory disease. We compared 91 ILD patients to 30 normal controls. The 91 ILD patients’ diagnoses included: Scleroderma (39), rheumatoid arthritis (12), overlap CTD (10), idiopathic ILD (10), antisynthetase (7), myositis (7), Sjögren’s (5), and SLE (1).

Results: The surface wave speed was measured at 100 Hz, 150 Hz, and 200 Hz. The surface wave speeds at 100 Hz, were 2.26 ± 0.4 m/s and 2.87 ± 0.53 m/s, respectively, for 30 healthy subjects and 91 patients with ILD at the lower right lungs The surface wave speeds were significantly higher in ILD patients than that in healthy subjects (p<0.001) at each intercostal space and at each frequency.

Conclusion: Lung ultrasound surface wave elastography may prove to be a useful noninvasive and nonionizing technique to measure the elastic properties of superficial lung tissue. Significant differences of wave speed between healthy subjects and patients with peripherally distributed interstitial fibrosis were found. Lung ultrasound surface wave elastography has potential utility in assessing ILDs.

Disclosure: T. Osborn, None; X. Zhang, None; S. Kalra, None; B. Zhou, None; B. Bartholmai, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/a-non-invasive-ultrasound-surface-wave-elastography-technique-for-assessing-interstitial-lung-disease

The Performance of MRI Using the 3D Volumetric Interpolated Breath-Hold Sequence (VIBE) Technique to Detect Structural Changes in Patients with Early Axial Spondyloarthritis in Comparison to Conventional Radiography and Computed Tomography
Background/Purpose: Magnetic resonance imaging (MRI) is the gold standard for detection of inflammation in the sacroiliac joints (SIJ) of patients (pts) with axial spondyloarthritis (axSpA), while for chronic, structural changes (erosions, sclerosis and ankylosis) conventional radiographs (CR) and computed tomography (CT) are often preferred. The 3D volumetric interpolated breath-hold sequence (VIBE) is an MRI technique, easy to acquire in daily practice, that can visualize cartilage especially well because of its good contrast to synovial tissue. Here we compare the ability of the VIBE technique to detect structural changes in comparison to CR and CT in SIJs of axSpA patients in relation to symptom duration and age.

Methods: Complete sets of MRI (T1 and VIBE techniques), CT and CR of SIJs of 109 AS patients were available. Two readers evaluated all images independently, blinded to demographic data and in separate sessions for each technique. The assessment of lesions was performed based on SIJ-quadrants (SQ) to score erosions, sclerosis and ankylosis (SIJ-halves). Lesions were counted as positive if both readers were in agreement. Comparisons between MRI techniques were performed by Wilcoxon-test. Linear regression analysis was used to evaluate the influence of age and disease duration on the occurrence of different structural lesions by modeling the differences in the number of lesions in different imaging techniques as dependent variable.

Results:

The mean age ± standard deviation was 45.3±13.9 years (y), 55 pts (50.5%) were aged ≤45y, 67.9% male, 82.3% HLA-B27+, 58 pts (53.2%) had a disease duration ≤3y. Agreement for positive and negative findings between MRI and CT was generally high (>80% of SQs in all subgroups) and agreement between readers for all techniques and lesion types was excellent (ICC=0.979-0.997).

Overall, MRI detected significantly more SQ with erosions in pts ≤45y (n=134) and in pts with disease duration ≤3y (n=125) as compared to CT (n=91, p=0.002 and n=90, p=0.003, respectively) and in pts with age ≤45y (n=61, p<0.001) as compared to CR, while there were no differences between MRI and CT in pts. >45y or disease duration >3y. Linear regression analysis showed that MRI was superior in the detection of erosions in younger ages as compared to CT (B=0.032, p=0.001).

However, CT detected significantly more SIJ halves with ankylosis in all subgroups and more SQ with sclerosis in pts with disease duration ≤3y (n=64 vs. n=37, respectively, p=0.006), and it also detected more SQ with sclerosis in pts >45y (n=67 vs. n=38, p=0.001) and disease duration >3y (n=64 vs. n=40, p=0.003) as compared to MRI, while no differences were found in the assessment of ankylosis.

Conclusion: MRI in the T1 and VIBE technique is more sensitive in the detection of erosions as compared to CT and CR in axSpA pts with short disease duration and younger age. This is due to its ability to identify structural damage in the SIJ cartilage that has not yet extended to the underlying bone. These differences are not found in pts with longer disease duration or older age. This data suggests a more prominent role for MRI also for the early detection of structural changes in the SIJ of axSpA pts..

Disclosure: X. Baraliakos, None; F. Hoffmann, None; X. Deng, None; Y. Wang, None; F. Huang, None; J. Braun, Abbott, BMS, Celgene, Celltrion, Chugai, Johnson & Johnson, MSD, Novartis, Pfizer, Roche, UCB Pharma, 5,Abbott, BMS, Celgene, Celltrion, Chugai, Johnson & Johnson, MSD, Novartis, Pfizer, Roche, UCB Pharma, 2.


Abstract Number: 1878

The Utility of the Omeract Ultrasound Tenosynovitis Scoring System in Multicenter Clinical Trials
Session Date: Monday, November 6, 2017
Session Title: Imaging of Rheumatic Diseases I: Novel Imaging and Scoring Systems
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Tenosynovitis is very common in patients with RA and is associated with lower physical function. Several studies have confirmed the limitations of clinical examination for detection of tenosynovitis in comparison with ultrasound (US) and a highly validated and reliable US scoring system is therefore needed if implementing US-tenosynovitis as an outcome measure in clinical trials. The OMERACT US group’s tenosynovitis scoring system has a good single and multicenter intra- and inter-observer agreement, whereas the sensitivity to change in a multicenter design has never been tested.

Furthermore, it is unknown whether low grade synovial hypertrophy without Doppler signal represents true inflammation, i.e. can be eliminated by anti-inflammatory therapy and is sensitive to change.

The aim of this study was to test the sensitivity to change of the OMERACT US scoring system for tenosynovitis, including minimal signs of tenosynovitis, in a multicenter design in order to validate it as an outcome measure in RA multicenter clinical trials. Furthermore, to assess the association between US and HAQ and DAS28.

Methods: Forty-nine patients with established RA (duration ≥1 year) and 18 early RA patients (<1 year) with US-verified tenosynovitis were recruited from six rheumatology outpatient clinics in four different countries, if they were scheduled for treatment intensification with synthetic and/or biological DMARD. Tenosynovitis was assessed at baseline, and at three and six months’ follow-up, by GS and Doppler, using the semi-quantitative OMERACT scoring system. Furthermore, HAQ and DAS28 were assessed.

Results: At baseline tenosynovitis was most frequently found at the extensor carpi ulnaris and tibialis posterior tendons (70.7% and 44.4%, respectively). The overall GS score showed a statistically significant decrease from baseline median 5 (25th;75th percentile: 2;7) to 6 months 0 (0;3) and the overall Doppler score decreased statistically significant from baseline 3 (2;6) to 6 months 0 (0;1), both with a p<0.01. Both GS and Doppler showed high responsiveness (SRM>0.9), as did HAQ and DAS28 (table 1). Among tendons with grey scale (GS)=1/Doppler=0, 36 of 39 (92.3%) showed therapy-induced improvements. Changes in US-scores were statistically significantly associated with DAS28 (p=0.02), but not with HAQ.

Conclusion: In conclusion, this RA multicenter study documented a high sensitivity to change of both GS and Doppler US tenosynovitis scores, indicating utility of the OMERACT US scoring system for diagnosing and monitoring tenosynovitis in multicenter trials. Secondly, synovial hypertrophy without Doppler signal, do respond to therapy, suggesting it reflects true inflammation. Finally, changes in US tenosynovitis scores are associated with changes in DAS28.
<table>
<thead>
<tr>
<th>All Sites - Imaging modality</th>
<th>Baseline</th>
<th>Δ 0-3 month</th>
<th>p</th>
<th>SRM Δ 3-6 month</th>
<th>p</th>
<th>Δ 0-6 month</th>
<th>SRM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grey scale</td>
<td>Median [25p;75p]</td>
<td>4 [2;7]</td>
<td>-2 [3;-0] &lt;0.01</td>
<td>0.8</td>
<td>-1.0 [-2;0] &lt;0.01</td>
<td>0.4</td>
<td>-2 [-5;-5] &lt;0.01</td>
</tr>
<tr>
<td>Mean ±SD</td>
<td>5.0 ±3.4</td>
<td>-2.4 ±2.9</td>
<td>-0.9 ±2.4</td>
<td>-3.3 ±3.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doppler</td>
<td>Median [25p;75p]</td>
<td>3 [2;6]</td>
<td>-2 [-4;-1] &lt;0.01</td>
<td>0.8</td>
<td>0 [-2;0] &lt;0.01</td>
<td>0.3</td>
<td>-3 [-5;2] &lt;0.01</td>
</tr>
<tr>
<td>Mean ±SD</td>
<td>1.2 ±0.66</td>
<td>-0.8 ±0.6</td>
<td>0 ±0.2</td>
<td>-0.7 ±0.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DAS28</td>
<td>Median [25p;75p]</td>
<td>4.6[3.7;5.3]</td>
<td>-1.4 [-48;-2] &lt;0.01</td>
<td>0.9</td>
<td>-0.4[-1.3;0.1] &lt;0.01</td>
<td>0.3</td>
<td>-1.6[-3.2;-0.7] &lt;0.01</td>
</tr>
<tr>
<td>Mean ±SD</td>
<td>4.4 ±1.3</td>
<td>-1.4 ±1.5</td>
<td>-0.5 ±1.5</td>
<td>-1.8 ±1.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HAQ</td>
<td>Median [25p;75p]</td>
<td>1.0[0.5;1.5]</td>
<td>-0.25[-0.75;0] &lt;0.01</td>
<td>0.8</td>
<td>0 [-0.25;0] 0.02</td>
<td>0.3</td>
<td>-0.375[-0.875;0] &lt;0.01</td>
</tr>
<tr>
<td>Mean ±SD</td>
<td>1.0 ±0.6</td>
<td>-0.4 ±0.4</td>
<td>-0.1 ±0.3</td>
<td>-0.5 ±0.5</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

P, p-value for Wilcoxon’s test for change of paired data between 2 time points; N, number of patients; SRM, standardized response mean.

Disclosure: M. Ammitzbøll-Danielsen, None; M. Østergaard, AbbVie, BMS, Celgene, Crescendo Bioscience, Janssen, Merck, 2,Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Centocor, GSK, Hospira, Janssen, Merck, Novartis, Orion, Pfizer, Regeneron, Roche, Takeda, and UCB, 5; E. Naredo, Abbvie, Roche, BMS, Pfizer, UCB, Novartis, Lilly, Janssen, 5; A. Iagnocco, None; I. Moller, None; M. A. D’Agostino, None; P. Gandjbakhch, None; L. Terslev, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-utility-of-the-omeract-ultrasound-tenosynovitis-scoring-system-in-multicenter-clinical-trials

Abstract Number: 1879

Majority of Rheumatoid Arthritis Patients in Clinical Remission As Defined By DAS-28, CDAI, SDAI and RAPID-3 Have No Signal on Ultrasound Power Doppler

Allen P. Anandarajah1, Andreea Coca2 and Ralf G. Thiele3, 1Dept of Rheumatology, Univ of Rochester Medical Ctr, Rochester, NY, 2University of Rochester Medical Center, Rochester, NY, 3Medicine, University of Rochester Medical Center, Rochester, NY
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Imaging of Rheumatic Diseases I: Novel Imaging and Scoring Systems
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Remission in rheumatoid arthritis (RA) is often assessed using the following indices: disease activity scores (DAS-28), clinical disease activity index (CDAI), Simplified Disease Activity Index (SDAI) and Routine Assessment of Patient Index Data (RAPID-3). There is increasing literature supporting the benefits of using imaging modalities to better define remission in RA. Musculoskeletal ultrasound (MUS) allows for direct visualization of diverse pathologic features such as cortical bone erosions, synovial thickening, and synovial vascularity in the joints affected by RA with high sensitivity, specificity, and accuracy. The purpose of this study was to investigate the association between clinical outcome measures and ultrasound score of the dominant hand in RA patients.

Methods: This was a single center study of patients from the RA clinic at the University of Rochester seen between July 2015 and April 2017. The DAS-28, CDAI, SDAI are collected as standard of care in the RA clinic. Patients are also offered the option of doing the RAPID-3 and getting MUS evaluations as part of their assessment. All clinical measures were collected by AA and AC. MUS exams were done by RT, who was blinded to the clinical scores, using a GE Logiq E9 (2014 model). MSK evaluations were done, using frequencies of 15-18 MHz for gray scale (GS). The following joints were assessed: dorsal wrist, 2nd, 3rd, 4th and 5th MCPs and the 2nd, 3rd, 4th and 5th PIP. MCP joints 2-5 were scanned from a dorsal aspect, and PIP joints 2-5 were scanned from a volar aspect. The scans were retrospectively scored for presence of synovitis on GS and Power Doppler (PD) (0=none; 1=mild; 2=moderate and 3=severe) for each joint. A total score was calculated by adding GS and PD scores and compared to clinical measures.
Results: A total of 113 patients volunteered for MUS but complete data were available in only 67. The median age of the group was 61 years and comprised 41 females and 26 males, with 62 being sero-positive and 38 with erosive disease. A total of 26 patients were in remission by DAS-28(CRP), 12 by CDAI, 14 by SDAI and 9 by RAPID-3, criteria. Low disease activity was seen in 11 by DAS-28, 17 by CDAI, 22 by SDAI and 9 by RAPID-3 criteria while 25, 24, 19 and 18 patients were with moderate disease activity and 5, 14, 12 and 31 had high disease activity, respectively. The median scores on MUS GS and PD for each category of disease activity are shown in Table 1. Interestingly, the median score on PD was 0 for remission by all outcome measures. MUS scores were associated with disease activity scores and a positive correlation was detected between MUS (GS and PD) scores and DAS-28 scores.

Conclusion: Most patients in clinical remission as assessed by DAS-28, CDAL, SDAI and RAPID-3 had no activity on PD and low scores on GS MUS evaluations. MUS of the dominant hand, using a simple scoring system, can be as effective in defining remission.

<table>
<thead>
<tr>
<th></th>
<th>DAS-28 (CRP)</th>
<th>CDAI</th>
<th>SDAI</th>
<th>RAPID-3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GS</td>
<td>PD</td>
<td>GS</td>
<td>PD</td>
</tr>
<tr>
<td>Remission</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Low-disease activity</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Moderate disease activity</td>
<td>5</td>
<td>4</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>High disease activity</td>
<td>7</td>
<td>4</td>
<td>10</td>
<td>4.5</td>
</tr>
</tbody>
</table>

Table 1: Ultrasound scores (GS and PD) for each category of clinical disease activity

Disclosure: A. P. Anandarajah, None; A. Coca, None; R. G. Thiele, Amgen, 8,AbbVie, 8,BioClinica, 5,Fujifilm SonoSite, 9.


Abstract Number: 1880

Cancer Immunotherapy in Patients with Preexisting Rheumatologic Disease: The Mayo Clinic Experience

Michael Richter¹, Olga Pinkston², Lisa Kottschade³, Heidi Finnes³, Svetomir N. Markovic⁴ and Uma Thanarajasingam⁵, ¹Internal Medicine, Mayo Clinic, Rochester, MN, ²Rheumatology, Mayo Clinic Florida, Jacksonville, FL, ³Oncology, Mayo Clinic, Rochester, MN, ⁴Department of Medicine and Oncology, Mayo Clinic, Rochester, MN, ⁵Division of Rheumatology, Mayo Clinic, Rochester, MN

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases I
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Immune checkpoint inhibitors have revolutionized the treatment of advanced malignancies. By blocking T-cell inhibition these drugs result in immune targeting of tumor cells and normal tissue. As such, their main toxicity is inducing immune-mediated tissue damage. Patients with preexisting rheumatologic diseases were excluded from the clinical trials for these agents, and little is known about the safety, efficacy, or risk for disease flares in these patients.

Methods: A retrospective medical record review was performed to identify all patients who received checkpoint inhibitor therapy at Mayo Clinic, Rochester between 2011 and 2016. Those with preexisting rheumatologic disease were identified using specific diagnostic codes.

Results: There were 16 patients identified (81% female, mean age 68.3). The most common rheumatologic diseases were rheumatoid arthritis (5), polymyalgia rheumatica (5), Sjogren’s syndrome (2), and systemic lupus erythematosus (2). Seven patients were receiving treatment with immunosuppressive therapy upon starting a checkpoint inhibitor. The primary malignancies were melanoma (10), pulmonary (4), or hematologic (2). In most cases checkpoint inhibitors were offered only after failure of several other therapies.
Immune-related adverse events (IRAE) occurred in 6 patients and all were treated successfully with corticosteroids and discontinuation of therapy. Survival was significantly prolonged in patients with an IRAE (17 months vs. 1.4 months [p=0.003]). There were no significant differences in time from cancer diagnosis to immunotherapy, duration of immunotherapy, age, or sex between these groups.

**Conclusion:** To our knowledge, this represents the largest single-center cohort of patients with rheumatologic diseases who were exposed to cancer immunotherapy. Only a minority of these patients experienced a flare of their preexisting rheumatologic disease or any other IRAE. The presence of an IRAE was associated with significantly prolonged survival.

<table>
<thead>
<tr>
<th>Table 1. Baseline Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (%)</td>
</tr>
<tr>
<td>(n=16)</td>
</tr>
<tr>
<td><strong>Demographics and malignancy characteristics</strong></td>
</tr>
<tr>
<td>Age, median (range)</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Metastatic disease</td>
</tr>
<tr>
<td>Chemotherapy prior to immunotherapy</td>
</tr>
<tr>
<td><strong>Primary malignancy type</strong></td>
</tr>
<tr>
<td>Melanoma</td>
</tr>
<tr>
<td>Pulmonary</td>
</tr>
<tr>
<td>Hematologic</td>
</tr>
<tr>
<td><strong>Rheumatologic condition</strong></td>
</tr>
<tr>
<td>Polymyalgia rheumatica</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
</tr>
<tr>
<td>Giant cell arthritis</td>
</tr>
<tr>
<td>Sjogren's syndrome</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
</tr>
<tr>
<td>Ankylosing spondylitis</td>
</tr>
<tr>
<td>Idiopathic enteritis</td>
</tr>
<tr>
<td>Sarcoidosis</td>
</tr>
<tr>
<td>Unicausal vasculitis</td>
</tr>
<tr>
<td><strong>Treatment at immunotherapy initiation</strong></td>
</tr>
<tr>
<td>DMARD</td>
</tr>
<tr>
<td>Glucocorticoid</td>
</tr>
<tr>
<td>DMARD plus glucocorticoid</td>
</tr>
<tr>
<td>Prior treatment with DMARDs</td>
</tr>
</tbody>
</table>

**Disclosure:** M. Richter, None; O. Pinkston, None; L. Kottschade, None; H. Finnes, None; S. N. Markovic, None; U. Thanarajasingam, None.
The Utility of Autoimmune Serologies in Recurrent and Chronic Inflammatory Eye Disease

Alexander Wu1, Sulaiman Mapara2, William Messner3, Sunil Srivastava4, Careen Lowder4 and Rula A Hajj-Ali5,

1 Internal Medicine, Cleveland Clinic, Cleveland, OH, 2 Hospital Medicine, Cleveland Clinic, Akron, OH, 3 Quantitative Health Sciences, Cleveland Clinic, Cleveland, OH, 4 Cole Eye Institute, Cleveland Clinic, Cleveland, OH, 5 Rheumatic and Immunologic Disease, Cleveland Clinic, Cleveland, OH

First publication: September 18, 2017

Methods:
We performed a retrospective review of patients seen at Cleveland Clinic between 2013 and 2014 by the ophthalmology department with a diagnosis of uveitis or scleritis based on ICD 9 and 10 codes. Subjects were included if they had recurrent or chronic uveitis or scleritis based on 2005 SUN working group nomenclature and no diagnosis of SAD prior to the inflammatory eye disease. Charts were further reviewed for any subsequent development of SAD. Sensitivity and specificity analysis was performed based on the following tests ANA, ACE, RF, CCP and ANCA and the associated SAD.

Results:
2351 patients were identified with uveitis or scleritis, of which 545 patients were recurrent or chronic and were included in the analysis. Eighty-five patients (15.6%) were subsequently diagnosed with a systemic autoimmune disease: sarcoidosis (54%), spondyloarthritis (22%), rheumatoid arthritis (13%), systemic lupus erythematosus (7%), and anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis (3.5%). Sensitivities of the screening tests are shown below.

<table>
<thead>
<tr>
<th>screening test</th>
<th>Number of unique patients with screening test ordered at least once (n=545)</th>
<th>Number of patients diagnosed with SAD</th>
<th>Sensitivity of serologies for diagnosis of SAD in patients with scleritis or uveitis (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANA</td>
<td>232</td>
<td>6 SLE</td>
<td>*</td>
</tr>
<tr>
<td>ACE</td>
<td>262</td>
<td>46 Sarcoidosis</td>
<td>0.59 (0.41-0.77)</td>
</tr>
<tr>
<td>RF</td>
<td>165</td>
<td>11 Rheumatoid Arthritis</td>
<td>0.5 (0.19-0.81)</td>
</tr>
<tr>
<td>CCP</td>
<td>118</td>
<td>11 Rheumatoid Arthritis</td>
<td>0.5 (0.19-0.81)</td>
</tr>
<tr>
<td>HLA-B27</td>
<td>175</td>
<td>19 Spondyloarthritis</td>
<td>0.55 (0.25-0.84)</td>
</tr>
<tr>
<td>C-ANCA</td>
<td>120</td>
<td>3 ANCA Vasculitis</td>
<td>*</td>
</tr>
<tr>
<td>P-ANCA</td>
<td>120</td>
<td>3 ANCA Vasculitis</td>
<td>*</td>
</tr>
</tbody>
</table>

*Due to small sample size, sensitivity was not calculated.

Conclusion:
15% of patients diagnosed with chronic or recurrent autoimmune uveitis or scleritis subsequently developed a systemic autoimmune disease. Laboratory testing such as ANA for SLE, HLA-B27 for spondyloarthritis, RF and CCP for rheumatoid arthritis, C-ANCA and P-ANCA for ANCA associated vasculitis and ACE level for sarcoidosis were not sensitive for screening tests. Therefore, it is inadequate to use laboratory testing alone to guide referral for evaluation of systemic autoimmune disease in patients with chronic or recurrent uveitis or scleritis. Other aspects, such as characteristics of the eye findings and patient symptoms should be evaluated to improve sensitivity.

Disclosure: A. Wu, None; S. Mapara, None; W. Messner, None; S. Srivastava, None; C. Lowder, None; R. A. Hajj-Ali, Abbvie, 8,Novartis Pharmaceutical Corporation, 5.


Abstract Number: 1882

Thymus and Activation-Regulated Chemokine (TARC) As Biomarker for IgG4-Related Disease

Masataka Umeda1,2, Tomoki Origuchi3, Shinya Kawashiri1,4, Tomohiro Koga1,5, Kunihiro Ichinose1, Yushiro Endo1, Sousuke Tsuji1, Ayuko Takatan1, Takashi Igawa1, Toshimas Shimizu1, Shoichi Fukui1,4, Remi Sumiyoshi1, Ayako Nishino1,6, Naoki Iwamoto1, Mami Tamai1, Hideki Nakamura1 and Atsushi Kawakami1,1 Department of Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, 2Medical Education Development Center, Nagasaki University Hospital, Nagasaki, Japan, 3Department of Rehabilitation Sciences, Nagasaki University, Nagasaki, Japan, 4Departments of Community Medicine, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, 5Center for Bioinformatics and Molecular Medicine, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki City, Japan, 6Center for Comprehensive Community Care Education, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases I
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: TARC, also known as chemokine ligand 17 (CCR17), is expressed in the thymus and is produced by dendritic cells, endothelial cells, keratinocytes and fibroblasts. TARC has affinity as a ligand for CCR4 and CCR8, which are predominantly expressed by Th2 cells. High serum concentration of TARC is determined in allergic diseases such as atopic dermatitis and bronchial asthma. Several studies have reported frequent atopic symptoms among patients with IgG4-related disease (IgG4-RD). We investigated the role of TARC as a biomarker in IgG4-RD, in which Th2 cytokines associate in disease states.

Methods: We evaluated the serum concentration of TARC from 26 IgG4-RD patients, 22 healthy controls (HC) by ELISA. We also analyzed the correlations between TARC concentration and clinical parameters. To investigate the biological effect of TARC toward pathogenesis in IgG4-RD, in vitro induction of plasmablasts from peripheral blood mononuclear cells (PBMCs) in patients with IgG4-RD by TARC was evaluated.

Results: We found that the serum concentration of TARC in the IgG4-RD was significantly higher than HC (IgG4-RD mean 493.9 ng/mlHC mean 262.0 ng/mlCp<0.001). ROC curve for TARC distinguish IgG4-RD from HC, the cutoff value 296.5 ng/ml (sensitivity 80.8%, specificity 72.7%). Serum concentration of TARC from IgG4-RD positively correlated with number of organ involvement (Fig. 1) whereas showed the correlation neither with serum IgG nor eosinophil number in peripheral blood. In addition, no difference in TARC concentration was found among IgG4-RD patients with or without atopic symptoms. TARC in vitro clearly induced the formation of plasmablasts from patients with IgG4-RD (Fig. 2).

Conclusion: Collectively, our data suggest that TARC is an essential Th2 cytokine in patients with IgD4-RD. TARC may be involved in the development of IgG4-RD through an aberrant induction of plasmablasts.
Abstract Number: 1883

Patterns of Osteoarticular Involvement in SAPHO Syndrome: A Cluster Analysis Based on Whole Body Bone Scintigraphy in 157 Patients

Yihan Cao1, Chen Li2, Ping Xu1, Yueting Li1, Qiao Yang1 and Xiaochuan Sun1, 1Peking Union Medical College, Beijing, China, 2Peking Union Medical College Hospital, Beijing, China

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases I
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: The aim was to explore patterns of osteoarticular involvement in SAPHO syndrome using cluster analysis of lesions revealed by whole body bone scintigraphy.

Methods: Data on whole body bone scintigraphy was collected in 157 patients enrolled in a single center cohort study1 who fulfill the Kahn and Khan’s criteria for SAPHO syndrome2. Twelve characteristic or most frequently involved osteoarticular sites in SAPHO syndrome revealed by whole body bone scintigraphy were analyzed by hierarchical cluster analysis with the Ward minimum-variance method.

Results: Three major subtypes with distinct patterns of osteoarticular involvement were identified: (A) the sternoclavicular type (52 patients), with predominant involvement of bilateral sternoclavicular joints, characterized by the classic “bull’s head” sign; (B) the costal type (35 patients), with predominant lesions in the anterior ribs, particularly the first ribs; and (C) the spinal type (70 patients), with significantly higher frequency of lesions in the thoracic, lumbar and sacral spine. Interestingly, a significant increase in age at onset of skin lesions was observed in spinal type (40.1 ± 11.2 years) than sternoclavicular type (34.6 ± 10.5 years, p = 0.036) and costal type (35.0 ± 10.0 years, p = 0.035). On the other hand, the duration of disease was significantly higher in sternoclavicular type (93.2 ± 120.4 months) compared with costal type (27.6 ± 32.2 months, p = 0.001) and spinal type (29.0 ± 37.1 months, p < 0.001).

Conclusion: The osteoarticular involvement in SAPHO syndrome can be clustered into three distinct patterns with different clinical pictures. The costal involvement in SAPHO syndrome, which was less well recognized previously, may define a separate type of the disease.

REFERENCES


Table 1: Identified lesions revealed by whole body bone scintigraphy of the 42 patients with ALHDS syndrome

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cluster A (n = 32)</th>
<th>Cluster B (n = 34)</th>
<th>Cluster C (n = 36)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone Scintigraphy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sternum</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>0.934</td>
</tr>
<tr>
<td>Pelvis</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>1.000</td>
</tr>
<tr>
<td>Clavicle</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>1.000</td>
</tr>
<tr>
<td>Ribs</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>1.000</td>
</tr>
<tr>
<td>Thoracic spines</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>1.000</td>
</tr>
<tr>
<td>Lumbar spine</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>1.000</td>
</tr>
<tr>
<td>Occipital bone</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>1.000</td>
</tr>
<tr>
<td>Pelvic bone</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>1.000</td>
</tr>
<tr>
<td>Metacarpal bone</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>1.000</td>
</tr>
<tr>
<td>Carpals</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>1.000</td>
</tr>
</tbody>
</table>

Data are presented as n (%) * Asterisk indicates a significant bone scintigraphic lesion and small nuclei.

Figure 1: Three clusters of patients identified by cluster analysis of lesions revealed by whole body bone scintigraphy

Table 2: Lesions revealed by bone scintigraphy and baseline clinical characteristics according to patient clusters.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cluster A (n = 32)</th>
<th>Cluster B (n = 34)</th>
<th>Cluster C (n = 36)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone Scintigraphy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sternum</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>0.934</td>
</tr>
<tr>
<td>Pelvis</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>1.000</td>
</tr>
<tr>
<td>Clavicle</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>1.000</td>
</tr>
<tr>
<td>Ribs</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>1.000</td>
</tr>
<tr>
<td>Thoracic spines</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>1.000</td>
</tr>
<tr>
<td>Lumbar spine</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>1.000</td>
</tr>
<tr>
<td>Occipital bone</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>1.000</td>
</tr>
<tr>
<td>Pelvic bone</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>1.000</td>
</tr>
<tr>
<td>Metacarpal bone</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>1.000</td>
</tr>
<tr>
<td>Carpals</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>1.000</td>
</tr>
</tbody>
</table>

Note: Only qualitative characteristics with significant differences among clusters are shown. For bone lesions revealed by bone scintigraphy, the size depth of each lesion was not analyzed due to the percentage of patients with the specific lesion.
Mepolizumab for the Treatment of Patients with Eosinophilic Granulomatosis with Polyangiitis: Post-Hoc Results of a Phase III Randomized, Placebo-Controlled Trial

Jonathan Steinfeld1, Eric S Bradford2, Judith Brown3, Stephen Mallett4, Steven W Yansey2 and Michael E Wechsler5, 1Respiratory TAU & Flexible Discovery Unit, GSK, Philadelphia, PA, USA, Philadelphia, PA, 2Respiratory Therapeutic Area, GSK, Research Triangle Park, NC, USA, Research Triangle Park, NC, 3Research and Development, Immuno-Inflammation TAU, GSK, Stockley Park West, Uxbridge, Middlesex, UK, Uxbridge, United Kingdom, 4Research & Development, Statistics, GSK, Stockley Park West, Uxbridge, Middlesex, UK, Uxbridge, United Kingdom, 5Department of Medicine, National Jewish Health, Denver, CO

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases I
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose:
In a recent Phase III study (NCT02020889) in patients with Eosinophilic Granulomatosis with Polyangiitis (EGPA) the anti-interleukin-5 monoclonal antibody mepolizumab showed significant benefit when compared to placebo for both primary endpoints and all secondary endpoints. As not all subjects treated with mepolizumab were able to achieve remission, we investigated post-hoc the benefit in terms of not only remission, but also oral corticosteroid reduction, and/or relapses.

Methods: We conducted a Phase III, randomized, placebo-controlled, double-blind, parallel-group, multi-center study in patients with EGPA and a history of relapsing or refractory disease on stable therapy with prednisolone/prednisone ≥7.5–≤50mg/day with or without additional immunosuppressive therapy for ≥4 weeks. Patients were randomized 1:1 to receive mepolizumab 300mg or placebo subcutaneously, in addition to standard of care, every 4 weeks for 52 weeks. Remission was defined with both the stringent definition utilized in the primary endpoint (Birmingham Vasculitis Activity Score [BVAS]=0, corticosteroid dose ≤4mg/day) as well as the European League Against Rheumatism (EULAR) definition (BVAS=0, corticosteroid dose ≤7.5mg/day). Oral corticosteroid reduction was defined post-hoc as ≥50% reduction from baseline in average prednisolone/prednisone dose during Weeks 48-52. Benefit in relapse was defined post-hoc if a subject was relapse free throughout the 52 week treatment period. We also summarized specific sub-populations of clinical interest: baseline blood eosinophil count <150 cells/μL, oral corticosteroid dose >20 mg/day, and weight >85 kg.

Results: 136 patients received at least one dose of study medication (mepolizumab n=68, placebo n=68). With the primary endpoint definition of remission the results showed that 53 (78%) subjects in the mepolizumab group received clinical benefit in terms of remission and/or a 50% reduction in oral corticosteroid dose and/or having no relapses during the study treatment period, compared with 22 (32%) subjects in the placebo group. For the EULAR definition of remission 59 (87%) subjects in the mepolizumab group received clinical benefit compared with 36 (53%) subjects in the placebo group. In all of the sub-populations described, clinical benefit was seen in greater percentages of subjects treated with mepolizumab compared to placebo.

Conclusion: Using a broader yet clinically relevant definition of response that includes remission, absence of relapse, and/or steroid reduction, a significantly greater proportion of mepolizumab treated patients experienced clinical benefit when compared to placebo. In addition, more subjects in sub-populations of interest experienced clinical benefit with mepolizumab treatment compared to placebo. (Funded by GSK [Study 115921] in collaboration with NIAID [U01 AI097073] and the Division of Intramural Research, NIAID, NIH).
Epidemiology of Hospitalized Adult Onset Still’s Disease in United States

Bella Y. Mehta¹, William Briggs² and Petros Efthimiou³, ¹Rheumatology, Hospital for Special Surgery/Weill Cornell Medicine/Mailman School of Public Health, New York, NY, ²New York Presbyterian/ Brooklyn Methodist Hospital, New York, NY, ³Medicine/Rheumatology, New York University School of Medicine/NYU Langone Health, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases I
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: There is a dearth of epidemiological studies on Adult Onset Still’s Disease (AOSD) and no consensus on its incidence and prevalence. Most studies report a majority of patients below the age of 35 [Sakata et al, Rheumatol Int 2016]. Our objective is to describe the demographics, complications and mortality of hospitalized patients with AOSD in USA.

Methods: Adult (>18 years) hospitalized patients between 2009 and 2013 from a nationwide inpatient sample (NIS) database were captured. AOSD patients were identified using the ICD-9 code 714.2 that was in use before 2015. Patients also coded for RA, SLE, Myositis, PMR, AS and Psoriatic Arthritis were excluded. This was done in order to capture patients with strictly AOSD. NIS is the largest all-payer inpatient care database in the United States with approximately 8 million hospitalizations each year. Discharge weights were used to enable nationwide estimates. Descriptive statistics were represented as means/medians for continuous and as frequencies (%) for categorical variables.

Results: Between 2009 and 2013, 5,820 AOSD patients were hospitalized (Table 1). AOSD patients had a mean age of 53.6 (SE – 0.6) years and 3817 (70.4%) were females. The racial/ethnic distribution showed that 56% white, 15% African American, 11.7% Hispanic and 3% Asian patients were affected. 37.6% of patients were hospitalized in urban teaching hospitals. The Mid-Atlantic census division had the highest number of patients (Figure 1). 100 (1.7%) developed Macrophage Activating Syndrome (MAS), 66 (1.1%) patients had disseminated intravascular coagulation (DIC) and 25(0.4%) had thrombotic thrombocytopenic purpura (TTP). The mean length of stay was 6.9 (SE- 0.3) days. There were 154 inpatient deaths in 5 years (mortality 2.6%) (Table 2). The patients who died during hospitalization were more likely to be older, mean age of 62.4 (SE- 3.1) years, women (69.2%) and/or Asian (13.9%).

Conclusion: In hospitalized US AOSD patients, the average age was higher than previously described in cross sectional studies. This may indicate an aging population with a higher number of comorbidities that prompt hospitalization. Mortality increased with age and was higher among women and Asians. To our knowledge, this is the largest epidemiological study of AOSD today in the USA.
Table 1: Characteristics of the Hospitalized Adult Onset Still’s Disease over 5 years.

<table>
<thead>
<tr>
<th>Year</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>846</td>
<td>995</td>
<td>1,434</td>
<td>1,280</td>
<td>1,265</td>
<td>5,820</td>
</tr>
</tbody>
</table>

**Age in Years, Mean (SE)**
- 2009: 53.4 (1.3)
- 2010: 52.3 (1.6)
- 2011: 54.9 (1.1)
- 2012: 52.8 (1.2)
- 2013: 53.9 (1.1)
- Total: 53.6 (0.6)

**Female**
- 2009: 520 (61.4%)
- 2010: 645 (64.8%)
- 2011: 870 (68%) 890 (70.4%)
- 2012: 890 (70.4%)
- 2013: 3817 (65.6%)

**Race**
- White
  - 2009: 437 (51.6%)
  - 2010: 515 (51.8%)
  - 2011: 819 (57.1%)
  - 2012: 760 (59.4%)
  - 2013: 730 (57.7%)
- Black
  - 2009: 117 (13.9%)
  - 2010: 168 (16.9%)
  - 2011: 243 (16.9%)
  - 2012: 180 (14.1%)
  - 2013: 165 (13%)
- Asian
  - 2009: 25 (3%) 47 (4.7%)
  - 2010: 47 (4.7%)
  - 2011: 29 (2%)
  - 2012: 25 (2%)
  - 2013: 50 (4%)

**Expected primary payer**
- Medicare
  - 2009: 311 (36.7%)
  - 2010: 338 (34%)
  - 2011: 589 (41.1%)
  - 2012: 525 (41%)
  - 2013: 570 (45.1%)
- Medicaid
  - 2009: 104 (12.3%)
  - 2010: 157 (15.7%)
  - 2011: 170 (11.8%)
  - 2012: 145 (11.3%)
  - 2013: 160 (12.6%)
- Private including HMO
  - 2009: 351 (41.5%)
  - 2010: 373 (37.5%)
  - 2011: 474 (33.1%)
  - 2012: 475 (37.1%)
  - 2013: 375 (29.6%)
- Self-pay
  - 2009: 60 (7.1%)
  - 2010: 79 (7.9%)
  - 2011: 95 (6.6%)
  - 2012: 85 (6.6%)
  - 2013: 80 (6.3%)

**Median household income national quartiles for patient's ZIP Code**
- $1 - $38999
  - 2009: 205 (24.2%)
  - 2010: 276 (27.7%)
  - 2011: 294 (20.5%)
  - 2012: 340 (26.6%)
  - 2013: 315 (24.9%)
- $39000 - $47999
  - 2009: 217 (25.7%)
  - 2010: 222 (22.3%)
  - 2011: 275 (17.6%)
  - 2012: 325 (25.4%)
  - 2013: 315 (24.9%)
- $48000 - $62999
  - 2009: 166 (19.6%)
  - 2010: 275 (27.7%)
  - 2011: 370 (25.8%)
  - 2012: 325 (25.4%)
  - 2013: 315 (24.9%)
- $63000+
  - 2009: 236 (27.9%)
  - 2010: 188 (18.9%)
  - 2011: 498 (34.7%)
  - 2012: 335 (26.2%)
  - 2013: 315 (24.9%)

**Bed size of the hospital**
- Small
  - 2009: 51 (6%)
  - 2010: 78 (7.8%)
  - 2011: 123 (8.5%)
  - 2012: 140 (13.7%)
  - 2013: 566 (9.7%)
- Medium
  - 2009: 169 (20%)
  - 2010: 222 (20.5%)
  - 2011: 253 (15.9%)
  - 2012: 305 (16.1%)
  - 2013: 1133 (19.5%)
- Large
  - 2009: 341 (40.3%)
  - 2010: 384 (38.5%)
  - 2011: 462 (38.5%)
  - 2012: 640 (50%)
  - 2013: 2436 (41.9%)

**Location / teaching status of hospital**
- Rural
  - 2009: 60 (7.1%)
  - 2010: 93 (9.4%)
  - 2011: 88 (6.2%)
  - 2012: 65 (5.1%)
  - 2013: 100 (7.9%)
- Urban non-teaching
  - 2009: 233 (27.6%)
  - 2010: 240 (24.2%)
  - 2011: 379 (26.4%)
  - 2012: 345 (26.9%)
  - 2013: 340 (26.4%)
- Urban teaching
  - 2009: 267 (31.6%)
  - 2010: 286 (24.2%)
  - 2011: 347 (24.2%)
  - 2012: 710 (55.5%)
  - 2013: 2191 (37.6%)
- Transferred in from a different hospital/ facility
  - 2009: 71 (8.4%)
  - 2010: 72 (7.2%)
  - 2011: 138 (9.6%)
  - 2012: 125 (10.2%)
  - 2013: 535 (9.9%)

**In-Hospital death**
- 2009: 16 (1.9%)
- 2010: 35 (3.6%)
- 2011: 27 (1.9%)
- 2012: 40 (3.1%)
- 2013: 35 (2.8%)
- Total: 154 (2.6%)

**Length of Stay in days, Mean (SE)**
- 2009: 6.1 (0.5)
- 2010: 8.7 (1.1)
- 2011: 7 (0.4)
- 2012: 6.6 (0.4)
- 2013: 6.3 (0.4)

**Cost of hospitalization in USD, Mean (SE)**
- 2009: $33,152
- 2010: $25,501
- 2011: $29,633
- 2012: $32,080
- 2013: $31,367
- Total: $30,857

*The values are presented as Number (%) unless indicated otherwise.*
**Table 2: Description of patients who died in the hospital**

<table>
<thead>
<tr>
<th>N</th>
<th>154</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age in yrs, Mean (SE)</strong></td>
<td>62.4 (3.1)</td>
</tr>
<tr>
<td><strong>Age Distribution</strong></td>
<td></td>
</tr>
<tr>
<td>18 - 39 yrs</td>
<td>21 (13.4%)</td>
</tr>
<tr>
<td>39 - 54 yrs</td>
<td>15 (9.9%)</td>
</tr>
<tr>
<td>54 - 67 yrs</td>
<td>50 (32.5%)</td>
</tr>
<tr>
<td>67 - 90 yrs</td>
<td>68 (44.3%)</td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td>106 (69.2%)</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>81 (52.8%)</td>
</tr>
<tr>
<td>Asian</td>
<td>21 (13.9%)</td>
</tr>
<tr>
<td>Others</td>
<td>26 (19.8%)</td>
</tr>
<tr>
<td><strong>Expected primary payer</strong></td>
<td></td>
</tr>
<tr>
<td>Medicare</td>
<td>92 (59.6%)</td>
</tr>
<tr>
<td>Medicaid</td>
<td>21 (13.4%)</td>
</tr>
<tr>
<td>Private insurance / Self-pay</td>
<td>41 (26.9%)</td>
</tr>
<tr>
<td><strong>Median household income - national quartiles</strong></td>
<td></td>
</tr>
<tr>
<td>for patient's ZIP Code</td>
<td></td>
</tr>
<tr>
<td>$1 - $38,999</td>
<td>15 (9.9%)</td>
</tr>
<tr>
<td>$39,000 - $47,999</td>
<td>35 (23.1%)</td>
</tr>
<tr>
<td>$48,000 - $62,999</td>
<td>36 (23.5%)</td>
</tr>
<tr>
<td>$63,000+</td>
<td>61 (40%)</td>
</tr>
<tr>
<td><strong>Bed size of the hospital</strong></td>
<td></td>
</tr>
<tr>
<td>Small</td>
<td>16 (10.6%)</td>
</tr>
<tr>
<td>Medium</td>
<td>45 (29.5%)</td>
</tr>
<tr>
<td>Large</td>
<td>50 (32.7%)</td>
</tr>
<tr>
<td><strong>Location/teaching status of hospital</strong></td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>20 (13.2%)</td>
</tr>
<tr>
<td>Urban non-teaching</td>
<td>15 (9.8%)</td>
</tr>
<tr>
<td>Urban teaching</td>
<td>77 (49.8%)</td>
</tr>
<tr>
<td><strong>Transferred in from a different hospital/facility</strong></td>
<td>22 (14.6%)</td>
</tr>
<tr>
<td><strong>Length of Stay in days, Mean (SE)</strong></td>
<td>13.4(4.4)</td>
</tr>
<tr>
<td><strong>Total Charges during hospitalization in USD (SE)</strong></td>
<td>$66,083 (18,346)</td>
</tr>
</tbody>
</table>

*The values are presented as Number (%) unless indicated otherwise.*

**Disclosure:** B. Y. Mehta, None; W. Briggs, None; P. Efthimiou, Abbvie, novartis, BMS, Myriad, medac, janssen, pfizer, mnk, celgene, 5.


**Abstract Number:** 1886
Continued Fracture Risk Reduction after 12 Months of Romosozumab Followed By Denosumab through 36 Months in the Extension of the Phase 3 Fracture Study in Postmenopausal Women with Osteoporosis

E Michael Lewiecki\textsuperscript{1}, Rajani V Dinavahi\textsuperscript{2}, Marise Lazaretti-Castro\textsuperscript{3}, Peter R Ebeling\textsuperscript{4}, J Adachi\textsuperscript{5}, Akimitsu Miyauchi\textsuperscript{6}, Evelien Gielen\textsuperscript{7}, Cassandra E Milmont\textsuperscript{2}, Cesar Libanati\textsuperscript{8} and Andreas Grauer\textsuperscript{2}, \textsuperscript{1}New Mexico Clinical Research & Osteoporosis Center, Albuquerque, NM, \textsuperscript{2}Amgen Inc., Thousand Oaks, CA, \textsuperscript{3}Federal University of São Paulo, São Paulo, Brazil, \textsuperscript{4}Monash University, Melbourne, Australia, \textsuperscript{5}McMaster University, Hamilton, ON, Canada, \textsuperscript{6}Miyauchi Medical Center, Osaka, Japan, \textsuperscript{7}University Hospitals Leuven, Leuven, Belgium, \textsuperscript{8}UCB Pharma, Brussels, Belgium

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Romosozumab (Romo) is a monoclonal antibody that binds sclerostin with a dual effect, increasing bone formation and decreasing bone resorption. In the primary analysis of the multicenter, double-blind, FRActure study in postmenopausal woMen with ostEoporosis (FRAME) (NCT01575834), women aged 55–90 (T-score ≤–2.5 at total hip [TH] or femoral neck), Romo significantly reduced vertebral and clinical fracture risk vs placebo (Pbo) at 12 months (M).\textsuperscript{1} A continued 75% new vertebral fracture and 33% clinical fracture relative risk reduction was observed at 24M in patients who initially received Romo, despite all patients receiving denosumab (DMAb) after 12M. BMD showed rapid and robust increases with Romo at the spine and hip, and these increases continued on transition to DMAb.\textsuperscript{1}

Methods: In FRAME, patients received Pbo or Romo SC monthly for 12M, followed by open-label DMAb SC every 6M for 12M. Here, we report results through 36M after a further 12M of open-label DMAb. Key endpoints included patient incidence of new vertebral, clinical (nonvertebral plus symptomatic vertebral), and nonvertebral fracture, and BMD.

Results: Of the 7180 women enrolled, 5743 (80%) completed the 36M study (2892 Pbo followed by DMAb; 2851 Romo followed by DMAb). Through 36M, fracture risk reduction was observed for new vertebral, clinical, nonvertebral, and other predefined fracture endpoints in patients who received Romo followed by 24M of DMAb vs Pbo followed by 24M of DMAb (Table). At 36M, BMD continued to increase in the Romo followed by DMAb group to 18.1% (lumbar spine) and 9.4% (TH) (Figure). The mean differences in BMD in patients who received Romo in the first 12M compared with those initially on Pbo remained significant over the entire 36M (P<0.001). Adverse events were generally balanced between groups; no additional positively adjudicated cases of atypical femoral fracture or osteonecrosis of the jaw were reported since reporting the 24M data.\textsuperscript{1}

Conclusion: In postmenopausal women with osteoporosis, Romo followed by DMAb was well tolerated and reduced new vertebral, clinical, and nonvertebral fracture risk vs Pbo followed by DMAb for 24M. BMD continued to increase in both groups. BMD in patients treated with Romo in the first 12M remained significantly higher than in those who initially received Pbo despite all patients receiving DMAb for 24M, underscoring the important foundational effect of Romo. The sequence of Romo followed by DMAb will be a promising treatment regimen for postmenopausal women with osteoporosis.

\textsuperscript{1}Cosman \textit{NEJM} 2016

<table>
<thead>
<tr>
<th>Fracture Category</th>
<th>Pbo/DMAb N = 3591</th>
<th>Romo/DMAb N = 3591</th>
<th>RRR (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>New vertebral fracture</td>
<td>94 (2.6)</td>
<td>32 (0.9)</td>
<td>0.908</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clinical fracture</td>
<td>196 (5.5)</td>
<td>143 (4.0)</td>
<td>0.904</td>
<td></td>
</tr>
<tr>
<td>Nonvertebral fracture</td>
<td>176 (4.9)</td>
<td>136 (3.9)</td>
<td>0.939</td>
<td></td>
</tr>
<tr>
<td>Major nonvertebral fracture</td>
<td>136 (3.9)</td>
<td>103 (2.9)</td>
<td>0.915</td>
<td></td>
</tr>
<tr>
<td>Major osteoporotic fracture</td>
<td>147 (4.1)</td>
<td>103 (2.9)</td>
<td>0.906</td>
<td></td>
</tr>
<tr>
<td>Multiple new or worsening vertebral fracture</td>
<td>20 (0.6)</td>
<td>2 (0.0)</td>
<td>0.01</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>New or worsening vertebral fracture</td>
<td>94 (2.6)</td>
<td>33 (0.9)</td>
<td>0.901</td>
<td></td>
</tr>
<tr>
<td>Clinical new or worsening vertebral fracture</td>
<td>26 (0.7)</td>
<td>5 (0.1)</td>
<td>0.01</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hip fracture</td>
<td>315 (8.9)</td>
<td>183 (5.6)</td>
<td>0.41</td>
<td>0.071</td>
</tr>
</tbody>
</table>

\textsuperscript{1}Number of patients randomized; n/N = number of patients with fractures/number of patients in the analysis set.

DMAb = denosumab; Pbo = placebo; RRR = relative risk reduction; Romo = romosozumab.
Ten-Year Continued Nonvertebral Fracture Reduction in Postmenopausal Osteoporosis with Denosumab Treatment

S Ferrari¹, PW Butler², DL Kendler³, Paul D Miller⁴, C Roux⁵, AT Wang², Rachel B. Wagman² and EM Lewiecki⁶, ¹Geneva University Hospital, Geneva, Switzerland, ²Amgen Inc., Thousand Oaks, CA, ³University of British Columbia, Vancouver, BC, Canada, ⁴Colorado Center for Bone Research, Lakewood, CO, ⁵Paris Descartes University, Paris, France, ⁶New Mexico Clinical Research & Osteoporosis Center, Albuquerque, NM

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Treatment with denosumab (DMAb) for 3 years significantly reduces the incidence of nonvertebral fractures (NVFx; Cummings NEJM 2009). While there are limited data describing the benefit/risk of long-term reduction in bone remodeling, recent findings show that subjects receiving DMAb for up to 7 years experience further decreases in NVFx risk (Ferrari OI 2015). To better characterize this observation, we evaluated the reproducibility of the 7-year findings in the FREEDOM Extension (EXT) crossover (XO) group and assessed long-term fracture rates with 10 years of DMAb treatment in the EXT long-term (LT) group.

Methods: During FREEDOM, subjects were randomized to placebo or DMAb 60 mg every 6 months (Q6M) for 3 years. Subjects who missed ≤ 1 dose could enroll in the 7-year EXT, when all subjects were to receive open-label DMAb 60 mg Q6M; LT subjects could receive up to 10 years of DMAb and XO subjects could receive up to 7 years of DMAb. The NVFx rate in the first 3 years of DMAb was compared with 1) years 4-7 in LT and XO groups separately and combined, and 2) years 4-10 in the LT group. Adjusted rate ratios (RR, 95% confidence intervals [CIs]) between observational periods were computed by generalized estimating equation Poisson regression.

Results: Of 5,928 subjects eligible for the EXT, 4,550 (77%) enrolled (N = 2,343 LT; N = 2,207 XO). Baseline characteristics at FREEDOM and EXT and percent of subjects who completed the EXT were balanced between groups. The NFVx rate (95% CI) in the LT group was 1.98 (1.67-2.34) per 100 subject-years during the first 3 years of DMAb treatment and 1.54 (1.29-1.83) during years 4-7 (RR 0.79, p = 0.046; Table). To confirm this observation, the NVFx rate in the XO group was 2.37 (1.97-2.84) during the first 3 years of DMAb treatment and 1.52 (1.24-1.87) during years 4-7 (RR 0.65, p = 0.002). The NVFx rate in the combined LT + XO group was 2.15...
(1.90-2.43) during the first 3 years and 1.53 (1.34-1.75) during years 4-7 (RR 0.72, p < 0.001). The LT group showed a NVFx rate of 1.44 (1.24-1.66) during years 4-10 (RR 0.74, p = 0.008). For 6,089 subjects exposed to DMAb in FREEDOM or the EXT, the rate of bone safety events (ONJ or AFF) was 4.2 per 10,000 subject-years.

**Conclusion:** Compared with the first 3 years of DMAb treatment, a longer duration of DMAb therapy was associated with a further decrease in NVFx rate through 10 years. Long-term reduction in bone remodeling is not only associated with continued increases in BMD (Bone ASBMR 2016), but also with a favorable benefit/risk profile for bone.

**Table. Comparison of Nonvertebral Fracture Rates up to 10 Years of Denosumab Treatment**

<table>
<thead>
<tr>
<th></th>
<th>First 3 Years of DMAb Treatment</th>
<th>Years 4-7 of DMAb Treatment</th>
<th>Years 4–10 of DMAb Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Long-term Subjects</strong> (N = 2343)</td>
<td>140 Fractures</td>
<td>126 Fractures</td>
<td>184 Fractures</td>
</tr>
<tr>
<td>Fracture Rate (95% CI)</td>
<td>1.98 (1.67–2.34)</td>
<td>1.54 (1.29–1.83)</td>
<td>1.44 (1.24–1.66)</td>
</tr>
<tr>
<td>Rate Ratio (95% CI)</td>
<td>[Referent]</td>
<td>0.79 (0.62–1.00)</td>
<td>0.74 (0.60–0.93)</td>
</tr>
<tr>
<td>p-value</td>
<td>[Referent]</td>
<td>p = 0.046</td>
<td>p = 0.008</td>
</tr>
<tr>
<td><strong>Cross-over Subjects</strong> (N = 1731)</td>
<td>123 Fractures</td>
<td>91 Fractures</td>
<td>--</td>
</tr>
<tr>
<td>Fracture Rate (95% CI)</td>
<td>2.37 (1.97–2.84)</td>
<td>1.52 (1.24–1.87)</td>
<td>--</td>
</tr>
<tr>
<td>Rate Ratio (95% CI)</td>
<td>[Referent]</td>
<td>0.65 (0.50–0.86)</td>
<td>--</td>
</tr>
<tr>
<td>p-value</td>
<td>[Referent]</td>
<td>p = 0.002</td>
<td>--</td>
</tr>
<tr>
<td><strong>Long-term and Cross-over Subjects Combined</strong> (N = 4074)</td>
<td>263 Fractures</td>
<td>217 Fractures</td>
<td>--</td>
</tr>
<tr>
<td>Fracture Rate (95% CI)</td>
<td>2.15 (1.90–2.43)</td>
<td>1.53 (1.34–1.75)</td>
<td>--</td>
</tr>
<tr>
<td>Rate Ratio (95% CI)</td>
<td>[Referent]</td>
<td>0.72 (0.61–0.86)</td>
<td>--</td>
</tr>
<tr>
<td>p-value</td>
<td>[Referent]</td>
<td>p &lt; 0.001</td>
<td>--</td>
</tr>
</tbody>
</table>

N = number of subjects who completed FREEDOM (ie, completed their 3-year visit and did not discontinue IP), did not miss >1 dose of IP in FREEDOM, and who enrolled in the Extension. In addition, cross-over subjects completed 3 years of the extension and did not miss >1 dose of DMAb during the first 3 years of the Extension. Fracture rates and rate ratios were obtained using generalized estimating equation Poisson models; fracture rates are per 100 subject-years. Rate ratios relative to the first 3 years of DMAb treatment were adjusted for age, total hip BMD T-score, weight, and history of nonvertebral fracture. In addition, the treatment group variable was included in the model for the combined analysis only.

**Disclosure:** S. Ferrari, MSD, UCB Pharma, 2, Agnovos, Amgen, Labatec, UCB Pharma, 5, Amgen, Sandoz, UCB Pharma, 8, Novartis Pharmaceutical Corporation, 9; P. Butler, Amgen Inc., 1, Amgen Inc., 3; D. Kendler, Amgen, Astellas, AstraZenica, Eli Lilly, 2, Amgen, Eli Lilly, Pfizer, 5, Amgen, Eli Lilly, Pfizer, 8; P. D. Miller, Amgen, Lilly, Merck, Radius Health, Ultragenyx, 2, Amgen, Alexion, Merck, Lilly, Radius Health, Ultragenyx, 5; C. Roux, Ultragenyx, 2, Alexion, Amgen, Eli Lilly, UCB Pharma, 5; A. Wang, Amgen, 1, Amgen, 3; R. B. Wagman, Amgen, 1, Amgen, 3; E. Lewiecki, Amgen, 2, Amgen, Radius, 5.


Abstract Number: 1888

**Effect of Denosumab Compared with Risedronate on Percentage Change in Lumbar Spine Bone Mineral Density at 12 Months in Subgroups of Glucocorticoid-Treated Individuals**
Glucocorticoid (GC)-induced osteoporosis (GIOP) remains the most common secondary cause of osteoporosis. We previously demonstrated that denosumab (DMAb) significantly increased lumbar spine (LS) BMD more than risedronate (RIS) at 12 mos in GC-treated individuals. Here, we explored the effects of DMAb and RIS on LS BMD in predefined subgroups to determine whether these factors affected the treatment effect.

Methods: This was a phase 3, randomized, double-blind, double-dummy, active-controlled study to evaluate DMAb vs. RIS in GC-treated individuals for 24 mos. Eligible subjects were women and men ≥18 yrs receiving GC therapy at a dose ≥7.5 mg prednisone daily or its equivalent for ≥3 mos or <3 mos prior to screening (GC-continuing [GC-C] and GC-initiating [GC-I], respectively). All subjects <50 yrs were required to have a history of osteoporotic fracture. GC-C subjects ≥50 yrs were required to have a LS, total hip, or femoral neck T-score ≤‒2.0; or a T-score ≤‒1.0 with a history of osteoporotic fracture. Subjects were randomized 1:1 to SC DMAb 60 mg every 6 mos or oral RIS 5 mg daily for 24 mos. Subjects were to receive daily calcium (≥1000 mg) and vitamin D (≥800 IU). Effect of DMAb vs. RIS with respect to percentage change from baseline in LS BMD at 12 mos was determined in the GC-C and GC-I subpopulations and in 7 predefined subgroups that may influence treatment effect (gender, race, age group, baseline BMD T-score, geographic region, menopausal status, and baseline GC daily dose).

Results: A total of 795 subjects (505 GC-C and 290 GC-I) enrolled in the study. Baseline characteristics were balanced between treatment groups. As previously shown (Saag, ACR 2016), DMAb resulted in greater gains in LS BMD at 12 mos compared with RIS for both the GC-C and GC-I subpopulations (Table). Results from all of the subgroups consistently demonstrated a greater increase in LS BMD at mo 12 with DMAb compared with RIS. A significant quantitative interaction was observed only in the gender analysis in the GC-I subpopulation. However, non-significant qualitative interaction testing indicated that there was no evidence that the direction of the DMAb effect differed by gender in this subpopulation.

Conclusion: DMAb consistently increased BMD more than RIS at the LS at 12 mos across 7 different subgroups of GC-treated individuals. DMAb has the potential to become a better treatment option for patients newly initiating or continuing GC who are at increased risk for fracture.

Table. Difference in Lumbar Spine BMD Percentage Change From Baseline at Month 12 (GC-C and GC-I Subpopulations)
<table>
<thead>
<tr>
<th>Subpopulation</th>
<th>GC-C Subpopulation (N = 230 RIS / 228 DMAb)</th>
<th>GC-I Subpopulation (N = 133 RIS / 128 DMAb)</th>
<th>Interaction</th>
<th>P value</th>
<th>Quantitative Difference (DMAb – RIS)</th>
<th>Quantitative Interaction (Qualitative)</th>
<th>Quantitative Interaction (DMAb – RIS)</th>
<th>Quantitative Interaction (Qualitative)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>2.2 (1.4, 3.0)*</td>
<td>2.9 (2.0, 3.9)*</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td>Female</td>
<td>2.4 (1.5, 3.3)*</td>
<td>3.7 (2.5, 4.9)*</td>
<td>0.018</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Male</td>
<td>1.3 (–0.3, 2.9)</td>
<td>1.2 (–0.4, 2.8)</td>
<td>(0.50)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td>Caucasian</td>
<td>2.1 (1.2, 2.9)*</td>
<td>2.9 (1.9, 3.8)*</td>
<td>0.68</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Not Caucasian</td>
<td>2.5 (0.2, 4.8)*</td>
<td>3.0 (–0.4, 6.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age Group</td>
<td></td>
<td></td>
<td>&lt; 60 years</td>
<td>1.9 (0.8, 3.1)*</td>
<td>2.7 (0.6, 4.8)*</td>
<td>0.57</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>≥ 60 years</td>
<td>2.3 (1.2, 3.5)*</td>
<td>3.1 (2.0, 4.2)*</td>
<td>0.57</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline LS T-score</td>
<td></td>
<td></td>
<td>≤ –2.5</td>
<td>2.4 (0.9, 3.9)*</td>
<td>3.8 (1.5, 6.0)*</td>
<td>0.081</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt; –2.5</td>
<td>2.0 (1.1, 2.9)*</td>
<td>2.5 (1.5, 3.5)*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline LS T-score</td>
<td></td>
<td></td>
<td>≤ –1.0</td>
<td>2.2 (1.3, 3.2)*</td>
<td>3.5 (2.2, 4.9)*</td>
<td>0.18</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt; –1.0</td>
<td>1.3 (–0.2, 2.9)</td>
<td>2.0 (0.7, 3.2)*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Geographic Region</td>
<td></td>
<td></td>
<td>Europe</td>
<td>2.0 (1.0, 3.0)*</td>
<td>3.2 (2.1, 4.3)*</td>
<td>0.60</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Non-Europe</td>
<td>2.5 (1.1, 3.8)*</td>
<td>2.6 (0.8, 4.3)*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Menopausal Status</td>
<td></td>
<td></td>
<td>Premenopausal</td>
<td>1.7 (–0.7, 4.1)</td>
<td>6.3 (1.9, 10.7)*</td>
<td>0.37</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Postmenopausal</td>
<td>2.4 (1.4, 3.4)*</td>
<td>3.5 (2.2, 4.8)*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline GC Daily Prednisone-equivalent Dose</td>
<td></td>
<td></td>
<td>7.5 - &lt; 10 mg</td>
<td>2.9 (1.7, 4.1)*</td>
<td>3.1 (0.9, 5.4)*</td>
<td>0.98</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>≥ 10 mg</td>
<td>2.0 (1.0, 3.1)*</td>
<td>2.9 (1.8, 4.0)*</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

N = Number of randomized subjects with a baseline and ≥ 1 postbaseline lumbar spine BMD measurement. *DMAb compared with RIS p < 0.05

Disclosure: K. Saag, Amgen, Merck, 2,Amgen, Merck, Radius, 5; N. Pannacciulli, Amgen Inc., 1,Amgen Inc., 3; P. Geusens, Abbott, Amgen, BMS, Eli Lilly, MSD, Novartis, Pfizer, Roche, UCB Pharma, Will, 2,Amgen, Eli Lilly, UCB Pharma, 8; J. Adachi, Amgen, Eli Lilly, Merck, 2,Amgen, Eli Lilly, Merck, 5,International Osteoporosis Foundation Board of Directors, Scientific Advisor; Osteoporosis Canada Past-President, 6,Amgen, 8; E. Lespessailles, Amgen, Eli Lilly, MSD, UCB Pharma, 2,Amgen, Eli Lilly, Expanscience, MSD, UCB Pharma, 5; J. Malouf, None; O. Messina, None; A. Wang, Amgen, 1,Amgen, 3; R. B. Wagman, Amgen Inc., 1,Amgen Inc., 3; W. Lems, Amgen, Eli Lilly, MSD, 5,Amgen, Eli Lilly, 8.


Abstract Number: 1889

Safety and Efficacy of Denosumab Among Subjects with Mild-to-Moderate Chronic Kidney Disease (CKD) in the “Fracture Reduction Evaluation of Denosumab in Osteoporosis Every 6 Months” Extension Study

Aaron Broadwell1, Peter R Ebeling2, Edward Franek3, Stefan Goemaere4, Rachel B. Wagman5, Xiang Yin5, Susan Yue5 and Paul D Miller6, 1Rheumatology and Osteoporosis Specialists, Shreveport, LA, 2Monash University, Clayton, Australia, 3Mossakowski Medical
Background/Purpose: As renal function may decline with age, it is important to understand the safety and efficacy of therapeutic agents for postmenopausal osteoporosis (PMO) and the effect these agents may have on intrinsic renal function in patients with age-related renal insufficiency. We assessed the safety and efficacy of denosumab among subjects with mild-to-moderate renal insufficiency who participated in the “Fracture REDuction Evaluation of Denosumab in Osteoporosis every 6 Months” (FREEDOM) extension study.

Methods: Subjects were grouped based on baseline estimated glomerular filtration rate (eGFR) normalized to body surface area and calculated using the MDRD study equation. Change in eGFR from baseline to last on-study visit for each subject was assessed and summarized. The annualized rates of new vertebral fractures (VFx), non-VFx, and adverse events (AEs) were assessed for the subgroups of subjects with normal renal function (eGFR ≥ 90 mL/min), mild renal insufficiency (eGFR = 60-89 mL/min; CKD stage 2), or moderate renal insufficiency (eGFR = 30-59 mL/min; CKD stage 3). These outcomes were evaluated for the long-term arm (up to 10 years of denosumab treatment) and the crossover arm (up to 7 years of denosumab treatment).

Results: The majority of subjects in the long-term arm (1969/2343; 84%) and crossover arm (1781/2206; 81%) had mild or moderate renal insufficiency (CKD stage 2 or 3) prior to receiving denosumab. Few subjects (n = 4 long-term arm; n = 5 crossover arm) had an eGFR = 15-29 mL/min (CKD stage 4) at baseline, and none had CKD stage 5. Most subjects (1325/1969 [67%] long-term arm; 1216/1781 [68%] crossover arm) with baseline CKD stage 2 or 3 had relatively stable renal function, remaining within the same CKD subgroup at the last on-study visit. Less than 1% of subjects progressed from CKD stage 2 or 3 to CKD stage 4, and no subjects initiated renal replacement therapy. The incidence of new VFx was similar among subjects with normal eGFR or CKD stage 2 or 3 in both the long-term arm (Figure) and crossover arm (data not shown). The percentage of subjects reporting serious AEs was similar among the renal subgroups for both the long-term arm (54% normal GFR; 52% CKD stage 2; 57% CKD stage 3) and crossover arm (43% normal GFR; 42% CKD stage 2; 45% CKD stage 3).

Conclusion: The safety and efficacy of denosumab did not substantially differ among subjects with mild-to-moderate renal insufficiency. Furthermore, long-term exposure to denosumab does not appear to have a meaningful effect on renal function in women with PMO.

Figure. Annualized Incidence Rate of New VFx for the Long-Term Treatment Arm

Disclosure: A. Broadwell, AbbVie, Janssen, 5,AbbVie, Amgen, Celgene, Janssen, Mallinckrodt, Pfizer, UCB Pharma, 8; P. R. Ebeling, Amgen, Eli Lilly, UCB Pharma, 5,Amgen, Eli Lilly, 8; E. Franek, Amgen, MSD, 8; S. Goemaere, Amgen, 8; R. B. Wagman, Amgen Inc., 1,Amgen Inc., 3; X. Yin, Amgen Inc., 1,Amgen Inc., 3; S. Yue, Amgen Inc., 1,Amgen Inc., 3; P. D. Miller, Amgen, Lilly, Merck, Radius Health, Ultragenyx, 2,Amgen, Alexion, Merck, Lilly, Radius Health, Ultragenyx, 5.
Abstract Number: 1890

Persistent Fracture Reduction with Abaloparatide-SC (TYMLOS™) Followed By 24 Months of Alendronate

Kenneth Saag¹, Paul D Miller², Felicia Cosman³,⁴, Lorraine A Fitzpatrick⁵, Gary Hattersley⁶, Robert Gut⁶, Bruce Mitlak⁶, John P Bilezikian⁴ and Robin K Dore⁷, ¹Department of Medicine, University of Alabama at Birmingham, Birmingham, AL, ²Colorado Center for Bone Research, Lakewood, CO, ³Helen Hayes Hospital, West Haverstraw, NY, ⁴Columbia University College of Physicians and Surgeons, New York, NY, ⁵Chief Medical Officer, Radius Health, Inc., Waltham, MA, ⁶Radius Health, Inc., Waltham, MA, ⁷Robin K Dore, MD, Inc., Tustin, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: In the ACTIVE phase III trial, postmenopausal women with osteoporosis were randomized 1:1:1 to abaloparatide (ABL; n=824), blinded placebo (PBO; n=821), or open-label teriparatide (n=818). During ACTIVE, ABL increased BMD and reduced vertebral, nonvertebral, clinical, and major osteoporotic fractures compared to PBO. Women who completed ABL or PBO treatment in ACTIVE were eligible to enroll in an extension study (ACTIVExtend) to receive up to 24 months of open-label alendronate (ALN). The objectives of ACTIVExtend were to provide additional safety information and to evaluate vertebral and nonvertebral fracture endpoints.

Methods: The ACTIVExtend study enrolled 558 women from the original ABL group and 581 from the PBO group of the ACTIVE study (92% of women who completed ABL or PBO treatment in ACTIVE). Pre-specified endpoints, including vertebral, nonvertebral, clinical, and major osteoporotic fractures, were assessed over the 43-month period from ACTIVE baseline to the end of ACTIVExtend (18 months of ABL or PBO treatment, 1 month for reconsent, and 24 months of ALN treatment). Nonvertebral fracture endpoints were assessed using the Kaplan-Meier (KM) method, proportional hazard model, and logrank test for patients enrolled in ACTIVExtend and for the full ITT population randomized to ABL or PBO treatment in ACTIVE.

Results: During the 43-month period, 5.6% (n=32) of evaluable women sustained a new morphometric vertebral fracture in the PBO followed by ALN (PBO/ALN) group compared to 0.9% (n=5) in the ABL/ALN group, an 84% relative risk reduction (p<0.0001).

The Table shows the KM rates of nonvertebral fracture endpoints over 43 months from ACTIVE baseline through the end of ACTIVExtend for both the ACTIVExtend cohorts as well as the full ACTIVE ITT population.

The incidence of adverse events (AEs) including severe and serious AEs during ALN treatment period was similar for both study groups. The most common AEs were arthralgia, URI, and back pain. No cases of atypical femoral fracture or osteonecrosis of the jaw were reported.

Conclusion: In the ACTIVExtend study, administration of ABL for 18 months followed by ALN for 24 months resulted in sustained vertebral and nonvertebral fracture reduction compared to PBO followed by ALN. In the full randomized ACTIVE ITT population, over 43 months, in the ABL + ABL/ALN groups, there was a significant reduction in the incidence of vertebral and non-vertebral fractures as well as hip fractures compared to the PBO + PBO/ALN groups.

Table. Kaplan-Meier rates of nonvertebral fracture endpoints during the 43-month analysis period (from ACTIVE baseline through the end of ACTIVExtend).
Disclosure: K. Saag, Amgen, Eli Lilly, Radius Health, 5; Amgen, Eli Lilly, Radius Health, 9; P. D. Miller, Alexion, Amgen, Boehringer-Ingelheim, Daiichi-Sankyo, Eli Lilly, Immunodiagnostics, Merck, Merck Serono, National Bone Health Alliance, Novartis, Radius Health, Regeneron, Roche Diagnostics, Ultragenyx, 9; AgNovos, Amgen, Eli Lilly, Merck, Radius Health, Roche, Ultragenyx, 9; Allergan, Grunenthal Group, 9; F. Cosman, Eli Lilly, Amgen, Tarsa, 5; Eli Lilly, Amgen, 8; Eli Lilly, Amgen, Radius Health, Merck, 9; Eli Lilly, Amgen, 2; L. A. Fitzpatrick, Radius Health, 3; Radius Health, 3; G. Hattersley, Radius Health Inc, 3; R. Gut, Radius Health, 3; Radius Health, 1; B. Mitlak, Radius Health, 3; Radius Health, 1; R. K. Dore, Eli Lilly, Amgen, Pfizer, Abbvie, Biogen, Gilead, Novartis, 9; Eli Lilly, Amgen, Novartis, 5; Eli Lilly, Amgen, Pfizer, Abbvie, Radius, UCB, Novartis, 8.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/persistent-fracture-reduction-with-abaloparatide-extend-followed-by-24-months-of-alendronate

Abstract Number: 1891

Low Alkaline Phosphatase Levels: Could It be Hypophosphatasia?

C. Tornero1, P. Aguado1, S. Garcia-Carazo1, J.A. Tenorio2, P. Lapunzina2, K. Heath2, A. Buño3, J.M. Iturzaeta3, Irene Monjo4, C. Plasencia1 and Alejandro Balsa1, 1Rheumatology, Rheumatology. La Paz University Hospital, Spain.; Madrid, Spain, 2Institute of Medical and Molecular Genetics (INGEMM), Institute of Medical and Molecular Genetics (INGEMM). La Paz University Hospital, Spain., Madrid, Spain, 3Laboratory medicine, Laboratory medicine. La Paz University Hospital, Spain., Madrid, Spain, 4Rheumatology, Rheumatology. La Paz University Hospital, Spain., MADRID, Spain

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Hypophosphatasia (HPP) is a rare inherited disorder caused by mutations in ALPL (alkaline phosphatase liver type ALPL gene). Clinical presentation is variable and adult forms of the disease are usually milder than those affecting infants and children. It can be easily overlooked or misdiagnosed as chondrocalcinosis or osteoporosis, which can lead to erroneous therapeutic decisions. The primary objectives were to estimate the prevalence of patients with adult forms of HPP, to analyze their clinical and functional characteristics and to compare these findings between the patients with or without mutations. Methods: In this cross-sectional study, 1,536,711 ALP measurements from 386,356 patients were evaluated between 2009 and 2015. Those having at least two values below 35 IU/l and none above 45 IU/l constituted the study population, a total of 427 patients were included. Among them, 31 were excluded because of secondary hypophosphatasemia and 13 were lost on follow-up. 108 patients were contacted by phone to fulfill a questionnaire about clinical manifestations and health assessment. Patients were divided into two groups according to whether or not they presented a positive (HPP GT+) or negative (HPP GT-) genetic test. Results: Demographic and clinical characteristics are shown in Table 1. Of the 108 patients evaluated, genetic results were available for 85: 47% (40/85) were found to have pathogenic mutations, five previously unreported with the remaining having variants of unknown significance. We identified compound heterozygous mutations in an adult patient diagnosed with infantile HPP and the rest were in heterozygosity and associated with a less severe phenotype. Nine patients carried mutations associated with odonthohypophosphatasia. A significantly higher proportion of patients in the HPP GT+ group presented bone pain (80 v 46.7%, p=0.001), dental abnormalities (35 v 13.3%, p=0.01), premature dental loss (17.5 v 2.2%, p=0.02), and stress fractures (10.2 v 0%, p=0.047). Furthermore, there was a non-significant trend to present orthopedic surgery, chondrocalcinosis and peripheral fractures in this group. No significant differences were found in muscle weakness, vertebral fractures,
Calcific periarthritis, renal disease or necessity of analgesic medication. In terms of biochemical tests, an elevation of serum phosphate was found in the HPP GT+ group (4.1 ± 0.8 v 3.6 ± 0.6, p=0.01). No differences were observed in pain assessment (Visual Analogue Scale-VAS) and the health assessment questionnaire (HAQ-DI). **Conclusion:** The diagnosis of HPP can be difficult and is often missed or delayed, particularly in adults. The prevalence of HPP in patients with low ALP values is high and although clinical presentation is milder in adults, it often presents with bone pain, dental abnormalities, premature loss and fractures. These data should promote a proactive attitude towards detection of adult HPP.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>HPP GT + group N=40</th>
<th>HPP GT - group N=45</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age ± DS</td>
<td>50.58 ± 15.17</td>
<td>44.53 ± 10.47</td>
<td>p&lt;0.04</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Male</td>
<td>16/40 (40%)</td>
<td>7/45 (15.6%)</td>
<td>p=0.01</td>
</tr>
<tr>
<td>- Female</td>
<td>24/40 (60%)</td>
<td>38/45 (84.4%)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Caucasian</td>
<td>38/40 (95.4%)</td>
<td>45/45 (100%)</td>
<td>NS</td>
</tr>
<tr>
<td>- Hispanic</td>
<td>1/40 (2.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Black</td>
<td>1/40 (2.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Clinical characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic bone pain, n/N (%)</td>
<td>32/40 (80.6%)</td>
<td>21/45 (46.7%)</td>
<td>P=0.001</td>
</tr>
<tr>
<td>Muscle weakness, n/N (%)</td>
<td>6/40 (15%)</td>
<td>3/45 (6.7%)</td>
<td>NS</td>
</tr>
<tr>
<td>Calcific periarthritis, n/N (%)</td>
<td>5/40 (12.5%)</td>
<td>3/45 (6.7%)</td>
<td>NS</td>
</tr>
<tr>
<td>Chondrocalcinosis, n/N (%)</td>
<td>2/39 (5.12%)</td>
<td>0/45 (0%)</td>
<td>P&lt;0.13</td>
</tr>
<tr>
<td>Peripheral fractures, n/N (%)</td>
<td>18/39 (46.2%)</td>
<td>13/43 (30.2%)</td>
<td>P=0.14</td>
</tr>
<tr>
<td>Stress fractures, n/N (%)</td>
<td>9/39 (23.1%)</td>
<td>0/45 (0%)</td>
<td>P=0.047</td>
</tr>
<tr>
<td>Vertebral fractures, n/N (%)</td>
<td>3/37 (8.1%)</td>
<td>1/45 (2.2%)</td>
<td>NS</td>
</tr>
<tr>
<td>Dental abnormalities, n/N (%)</td>
<td>14/40 (35%)</td>
<td>6/45 (13.3%)</td>
<td>P=0.04</td>
</tr>
<tr>
<td><strong>Teeth loss, n/N (%)</strong></td>
<td>7/40 (17.5%)</td>
<td>1/45 (2.2%)</td>
<td>P=0.02</td>
</tr>
<tr>
<td>History of orthopedic surgery</td>
<td>7/40 (17.5%)</td>
<td>2/45 (4.4%)</td>
<td>P=0.01</td>
</tr>
<tr>
<td>Use of analgesic medication for pain, n/N (%)</td>
<td>23/40 (62.5%)</td>
<td>23/45 (51.1%)</td>
<td>NS</td>
</tr>
<tr>
<td>History of kidney disease</td>
<td>5/39 (12.8%)</td>
<td>2/39 (5.12%)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Biochemical data</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alkaline phosphatase ± DS</td>
<td>21.6 ± 6.7</td>
<td>29.69 ± 3.44</td>
<td>P=0.0001</td>
</tr>
<tr>
<td>Serum calcium ± DS</td>
<td>9.43 ± 0.4</td>
<td>9.27 ± 0.3</td>
<td>P=0.15</td>
</tr>
<tr>
<td>Urine calcium ± DS</td>
<td>68.2 ± 44.1</td>
<td>122</td>
<td>NS</td>
</tr>
<tr>
<td>Serum phosphorus ± DS</td>
<td>4.11 ± 0.78</td>
<td>3.57 ± 0.62</td>
<td>P=0.01</td>
</tr>
<tr>
<td>Urine phosphorus ± DS</td>
<td>235.5 ± 354</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Quality of life assessment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visual analog scale (VAS pain) ± DS</td>
<td>3.32 ± 2.3</td>
<td>2.34 ± 2.72</td>
<td>P=0.08</td>
</tr>
<tr>
<td>Health assessment disability (HAQ-DI) ± DS</td>
<td>0.18 ± 0.14</td>
<td>0.18 ± 0.37</td>
<td>NS</td>
</tr>
</tbody>
</table>

**Disclosure:** C. Tornero, Alexion Pharmaceuticals, Inc., 9; P. Aguado, Alexion Pharmaceuticals, Inc., 9; S. García-Carazo, Alexion Pharmaceuticals, Inc., 9; J. A. Tenorio, Alexion Pharmaceuticals, Inc., 2; P. Lapunzina, None; K. Heath, None; A. Buño, None; J. M. Iturzaeta, None; I. Monjo, Alexion Pharmaceuticals, Inc., 9; C. Plasencia, Alexion Pharmaceuticals, Inc., 9; A. Balsa, Alexion Pharmaceuticals, Inc., 9.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/low-alkaline-phosphatase-levels-could-it-be-hypophosphatasia](http://acrabstracts.org/abstract/low-alkaline-phosphatase-levels-could-it-be-hypophosphatasia)

**Abstract Number:** 1892

**A20 Haploinsufficiency: Clinical Phenotypes and Disease Course of Patients with This Newly Recognized Autoinflammatory Disease**
Background/Purpose: Haploinsufficiency of A20 (HA20) is a newly discovered autoinflammatory disease caused by mutations in TNFAIP3. A20 is a protein with a crucial role in the negative regulation of inflammation and immunity. This study aimed at describing the clinical phenotypes and disease course of patients with HA20.

Methods: All cases from the initial publication were reviewed (1), additional cases were identified through the group who described the disease. Standardized data collection forms were used to collect demographic, clinical, laboratory, imaging and histologic features, disease course and treatment regimens.

Results: A total of 17 patients (82% female) from 7 families with a genetic diagnosis of HA20 were included. Behçet disease, followed by SLE and JIA were the most frequent diagnoses prior to confirmation of HA20. Clinical phenotypes were heterogeneous between and within families. First symptoms commonly occurred in early childhood, disease onset ranged from the 1st week of life to 29 years of age. Most common presenting symptoms were recurrent oral and/or genital ulcers in 59% of patients. During disease course, symptoms and disease severity varied highly. Recurrent painful oral, genital and/or gastrointestinal ulcers were the hallmark feature in all patients. Ulcers recurred frequently (monthly to every few months), isolated or in combination with other symptoms such as fever. Singular or multiple ulcers lasted 7-10 days and some healed with scarring. Other symptoms commonly observed during disease course are shown in Table 1. Most patients had a relapsing-remitting disease course, one patient died. Laboratory features included elevated acute phase reactants, especially during relapses, and the fluctuating presence of various autoantibodies such as antinuclear antibodies (4/10 patients tested) and anti-dsDNA (2/5 patients). Lupus anticoagulant was positive in 6/7, anticardiolipin antibodies in 2/5 patients tested. Tissue biopsy of different sites was performed in 9/17 patients (53%) and revealed non-specific chronic inflammation in 6, findings consistent with class V lupus nephritis in 1 and normal results in 2 patients. There was no standardized treatment: 15/17 (88%) patients received various immunosuppressive therapies, seven of them also biologic agents. More recently, therapeutic approaches were based on functional cytokine studies.

Conclusion: Early-onset recurrent oral, genital and/or gastrointestinal ulcers are the hallmark feature of HA20. Other signs and symptoms and disease course varied considerably with an overall high morbidity and mortality. Treatment regimens should be based on disease severity, cytokine inhibitors are often required to control relapses.


Table 1.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent ulcers (oral, genital, gastrointestinal)</td>
<td>17 (100)</td>
</tr>
<tr>
<td>Musculoskeletal manifestations</td>
<td>9 (53)</td>
</tr>
<tr>
<td>Arthritis</td>
<td>6 (35)</td>
</tr>
<tr>
<td>Gastrointestinal manifestations</td>
<td>9 (53)</td>
</tr>
<tr>
<td>(Bloody) Diarrhea</td>
<td>5 (29)</td>
</tr>
<tr>
<td>Cutaneous manifestations</td>
<td>8 (47)</td>
</tr>
<tr>
<td>Recurrent fever</td>
<td>7 (41)</td>
</tr>
<tr>
<td>Recurrent respiratory tract / otorhinolaryngologic infections</td>
<td>7 (41)</td>
</tr>
<tr>
<td>Ocular manifestations</td>
<td>3 (18)</td>
</tr>
<tr>
<td>Cardiovascular manifestations</td>
<td>3 (18)</td>
</tr>
<tr>
<td>Pericarditis</td>
<td>2 (12)</td>
</tr>
</tbody>
</table>

Disclosure: F. A. Aeschlimann, None; E. D. Batu, None; E. Go, None; A. Gül, None; P. M. Hoffmann, None; H. L. Leavis, Shire and Thermo Phisher, Shire/Baxalta, 9; S. Ozen, Novartis, R-Pharm, Roche, 5; A. van Royen-Kerkof, None; D. Schwartz, None; D. L. Stone, None; I. Aksentijevich, None; D. L. Kastner, None; R. Laxer, Abbvie, Novartis, Sobi, Lilly, Sanofi, 9.


Abstract Number: 1893

**Pharmacokinetics (PK), Pharmacodynamics (PD), and Proposed Dosing of Oral Janus Kinase (JAK)1 and JAK2 Inhibitor Baricitinib in Patients with IFN-Mediated Autoinflammatory Diseases (AIDs)**

Hanna Kim1, Kristina M. Brooks2, Paul Wakim3, Mary Blake4, Stephen R. Brooks5, Gina A. Montealegre Sanchez6, Adriana Almeida de Jesus6, Yan Huang6, Wanxia Li Tsai7, Massimo G. Gadina4, Parag Kumar2 and Raphaela Goldbach-Mansky6, 1Pediatric Translational Research Branch, NIAMS/NIH, Bethesda, MD, 2Clinical Pharmacokinetics Research Unit, Pharmacy Department, NIH Clinical Center, Bethesda, MD, 3Biostatistics and Clinical Epidemiology Service, NIH Clinical Center, Bethesda, MD, 4Translational Immunology Section, Office of Science and Technology, NIAMS/NIH, Bethesda, MD, 5Biodata Mining and Discovery Section, Office of Science and Technology, NIAID/NIH, Bethesda, MD, 6Translational Autoinflammatory Disease Studies (TADS), Laboratory of Clinical Investigation and Microbiology (LCIM), NIAID/NIH, Bethesda, MD, 7Translational Immunology, Office of Science and Technology, NIAMS/NIH, Bethesda, MD

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects I: Autoinflammatory Diseases
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: JAK inhibitors reduce IFN-signaling ex vivo. We evaluated the PK and PD of the oral JAK1 and JAK2 inhibitor, baricitinib, from data collected in a compassionate use program in patients with Chronic Atypical Neutrophilic Dermatosis with Lipodystrophy and Elevated temperature (CANDLE) (1), STING Associated Vasculopathy with onset during Infancy (SAVI) (2), and other presumed IFN-driven AIDs with the goal to support a clinically derived dosing regimen for pediatric and young adult patients with CANDLE, SAVI, and other rare IFN-mediated diseases.
Methods: Baricitinib dosing was titrated based on clinical response and safety measures, with PK assessments following dose escalations in a compassionate use program (NCT01724580). Population pharmacokinetic (PopPK) modeling was applied to assess the PK profile of baricitinib. The effect of baricitinib treatment on STAT-1 phosphorylation, IFN-response gene expression (25-gene IFN score), and serum IP-10 levels, was assessed.

Results: A total of 18 patients received between 0.1 to 17 mg of baricitinib daily for up to 53 months. Weight and renal function significantly influenced PK parameters volume of distribution and clearance, respectively. The half-life of baricitinib, particularly in patients less than or equal to 40 kg, was considerably shorter than in adult patients with rheumatoid arthritis (RA), resulting in the need for dosing up to 4 times daily. On effective therapeutic doses (ranging from 6 to 13 mg/day), the daily drug exposure or mean area-under-the-concentration-versus-time curve over a 24-hour period (AUC$_{24,SS}$) at the final PK assessment was 2388 nM*hr, which is 1.83-fold higher than the mean exposures obtained in adult RA patients receiving baricitinib 4 mg once-daily in phase 3 studies (Table 1). IFN-alpha stimulated STAT-1 phosphorylation (pSTAT-1) in immune cells from CANDLE and SAVI patients negatively correlated with plasma baricitinib levels. A 25-gene IFN score and serum IP-10 levels, both markers of IFN signaling, significantly decrease with increased drug exposure. A subset of CANDLE patients normalized the 25-gene IFN score at AUC$_{24,SS}$ values between ~1500-2000 nM*hr, but higher exposures were required in patients with more severe disease.

Conclusion: Baricitinib blocks IFN signaling in patients with CANDLE, SAVI, and other interferonopathies. PK/PD data suggest that pediatric patients with rare interferonopathies require treatment with higher daily doses and more frequent dosing versus adult RA patients. PopPK and PD data support an empirically derived dosing regimen based on body weight and estimated glomerular filtration rate (eGFR) to guide initial dosing of baricitinib in patients with rare interferonopathies.

Funding: The Intramural Research Program of NIH, NIAID, NIAMS, CC and Eli Lilly and Company.

Refs.

<table>
<thead>
<tr>
<th>Table 1. Summary of Predicted PK Parameters by Body Function at Final PK Visit (Exclude Subject 1003)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Weight Category</strong></td>
</tr>
<tr>
<td><strong>Height</strong></td>
</tr>
<tr>
<td><strong>Age</strong></td>
</tr>
<tr>
<td><strong>Weight</strong></td>
</tr>
<tr>
<td><strong>BMI</strong></td>
</tr>
<tr>
<td><strong>eGFR</strong></td>
</tr>
<tr>
<td><strong>AUC$_{24,SS}$ (nM*hr)</strong></td>
</tr>
<tr>
<td><strong>AUC$_{24,SS}$ (nM*hr)</strong></td>
</tr>
<tr>
<td><strong>PK Parameters</strong></td>
</tr>
</tbody>
</table>

Disclosure: H. Kim, None; K. M. Brooks, None; P. Wakim, None; M. Blake, None; S. R. Brooks, None; G. A. Montealegre Sanchez, Eli Lilly and Company, 9; A. Almeida de Jesus, None; Y. Huang, None; W. L. Tsai, None; M. G. Gadina, None; P. Kumar, None; R. Goldbach-Mansky, Eli Lilly and Company, 9;SOBI, 9,Regeneron, 9,Novartis Pharmaceutical Corporation, 9.

Genetic Phenotypes Impacting Efficacy and Safety of Canakinumab in Patients with Colchicine-Resistant FMF, TRAPS and Hids/Mkd: Results from Cluster Study

Fabrizio De Benedetti1, Paivi Miettunen2, Tilmann Kallinch3, Gerd Horneff4, Riva Brik5, Alberto Tomassini6, Takahiro Yasumi7, Sinisa Savic8, Ivan Foeldvari9, Liora Harel10, Romina Gallizzi11, Antonio Speziale12, Guido Junge12 and Marco Gattorno13, 1Division of Rheumatology, IRCCS Bambino Gesù Children's Hospital, Rome, Rome, Italy, 2Alberta Children's Hospital Research Institute/University of Calgary, Calgary, AB, Canada, 3Charité, Humboldt University Medicine Berlin, Berlin, Germany, 4Asklepios Kliniken GmbH, Hamburg, Germany, 5Pediatrics, Rambam Medical Center, Haifa, Israel, 6Institute for Maternal and Child Health-IRCCS “Burlo Garofolo”, Trieste, Italy, 7Department of Pediatrics, Kyoto University Graduate School of Medicine, Kyoto, Japan, 8University of Leeds, Leeds, United Kingdom, 9Hamburger Zentrum für Kinder-und Jugend Rheumatologie, Hamburg, Germany, 10Schneider Children's Medical Center of Israel, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel, 11Department of Pediatrics, University of Messina, Messina, Italy, 12Novartis Pharma AG, Basel, Switzerland, 13Pediatric Rheumatology, G. Gaslini Institute, Genoa, Italy

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects I: Autoinflammatory Diseases
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Familial Mediterranean fever (FMF), Hyper IgD Syndrome (HIDS)/mevalonate kinase deficiency (MKD) and TNF-receptor associated periodic syndrome (TRAPS) are monogenic auto-inflammatory diseases caused by mutations in the MEFV, MVK and TNFRSF1A genes, respectively.1 We analyzed responses to canakinumab (CAN), a fully human anti-IL-1β monoclonal antibody, in the pivotal, controlled CLUSTER trial in patients with colchicine-resistant FMF (crFMF), HIDS/MKD and TRAPS, according to MEFV, MVK and TNFRSF1A genes.

Methods: Inclusion criteria were: age ≥2 years with a baseline flare, fulfillment of Tel Hashomer criteria, at least one known MEFV exon 10 gene mutation, ≥1 documented flare/month on colchicine (crFMF); genetic or enzymatic diagnosis of HIDS/MKD and ≥3 documented flares in 6 months (HIDS/MKD); TNFRSF1A gene mutation and chronic or recurrent (>6 flares/year) disease (TRAPS). The study design has been reported previously.2 Overall, 63 crFMF, 72 HIDS/MKD, and 46 TRAPS patients were randomized 1:1, to receive CAN 150 mg or placebo q4w. Patients (pts) were eligible for blinded escape until Day 29 if the baseline flare did not resolve and received 1 add-on injection of CAN 150 mg. We analyzed the proportion of patients showing complete response (resolution of the baseline flare and no new flare until Week 16) from those pts initially randomized to CAN (31 crFMF, 37 HIDS/MKD, 22 TRAPS).

Results: The primary outcome of complete response was achieved by more pts randomized to CAN than to placebo (p<0.001 for each disease cohort).2 Among the crFMF pts randomized to CAN, no significant difference in complete response were observed between 25 pts homozygous for M694V and six pts heterozygous for exon 10 mutations (Table). In HIDS/MKD pts, the proportion of CAN responders was higher in pts carrying at least one V377I mutation, compared to those carrying other mutations. Most of the TRAPS pts with classic pathogenic mutations achieved complete response.

Table. Proportion of patients randomized to canakinumab attaining the primary outcome at week 16 according to the genotypes.
Responders including 150 mg q4w to 300 mg q4w before Day 29

<table>
<thead>
<tr>
<th>n/M (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>crFMF</td>
</tr>
<tr>
<td>Patients with M694V/M694V</td>
</tr>
<tr>
<td>Patients heterozygous for M694V or M694I or M680I</td>
</tr>
<tr>
<td>HIDS/MKD</td>
</tr>
<tr>
<td>Patients with atleast one V377I mutation</td>
</tr>
<tr>
<td>Patients with mutations other than V377I and/or mutations classically associated to mevalonic aciduria</td>
</tr>
<tr>
<td>TRAPS</td>
</tr>
<tr>
<td>Patients with classic pathogenic mutations (N65I, H105P or T50M) including cysteine mutation</td>
</tr>
<tr>
<td>Patients with P46L or R92Q or mutation</td>
</tr>
</tbody>
</table>

1 p<0.05 versus patients with Non V377I/non V377I and patients with 1 mutation associated with mevalonic aciduria

2 p<0.001 versus patients with R92Q or P46L

**Conclusion:** Homozygous and heterozygous patients with crFMF showed no difference in CAN responses. Among HIDS/MKD pts, the proportion of CAN responders was higher among those carrying at least one V377I mutation. Among TRAPS pts, all pts carrying mutations associated with classical TRAPS responded to CAN; the poor response rate of pts carrying R92Q or P46L variants shows that the disease associated with these variants differs from classic TRAPS, not only in clinical features, but also in the role that IL-1β production plays in the pathogenesis.


Study Number: NCT02059291

**Disclosure:** F. De Benedetti, Novartis, Roche, Pfizer, SOBI, AbbVie, Novimmune, BMS, Sanofi, 2; P. Miettunen, None; T. Kallinich, None; G. Horneff, AbbVie, Pfizer, Novartis, and Roche, 2,AbbVie, Novartis, Sobi, Pfizer, and Roche, 9; R. Brik, None; A. Tomassini, None; T. Yasumi, None; S. Savic, None; I. Foeldvari, AbbVie and Novartis, 9; L. Harel, Novartis, 2; R. Gallizzi, AbbVie, 5; A. Speziale, Novartis, 3; G. Junge, Novartis, 3; M. Gattorno, Novartis, SOBI, 2,Novartis, SOBI, 8,Novartis, SOBI, 5.


Abstract Number: 1895

**Serum Interleukin 18 As a Biomarker for Systemic Juvenile Idiopathic Arthritis and Macrophage Activation Syndrome and Use of Recombinant Human IL-18 BP in a Patient with Refractory Disease**

Shima Yasin1, Rachel Brown1, Ndate Fall2, Krista Solomon1, Scott Canna3, Charlotte Girard4, Cem Gabay5, Eduardo Schiffrin6, Andrew Sleight6, Alexei A. Grom7 and Grant Schulert8, 1Pediatric Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 2Division of Rheumatology, Cincinnati Children's Hospital, Cincinnati, OH, 3NIAMS, National Institutes of Health, Bethesda, MD, 4Division of Rheumatology, Department of Internal Medicine Specialties, University Hospital of Geneva, Geneva, Switzerland, 5SCQM, Geneva, Switzerland, Geneva, Switzerland, 6AB2 Bio, Lausanne, Switzerland, 7Division of Pediatric Rheumatology, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH, United States Minor Outlying Islands, 8Pediatric Rheumatology, Division of Pediatric Rheumatology, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH

First publication: September 18, 2017

SESSION INFORMATION

**Session Date:** Monday, November 6, 2017
**Session Title:** Pediatric Rheumatology – Clinical and Therapeutic Aspects I: Autoinflammatory Diseases  
**Session Type:** ACR Concurrent Abstract Session  
**Session Time:** 4:30PM-6:00PM

**Background/Purpose:** Systemic juvenile idiopathic arthritis is an autoinflammatory childhood arthritis with prominent innate immune activity. Macrophage activation syndrome is a severe and potentially fatal complication of sJIA. IL-18 is felt to play a key role in pathogenesis of sJIA and in particular MAS; possibly through IFN-g activation. IL-18 binding protein (IL-18BP) is an endogenous inhibitor that binds IL-18 tightly. However, clinical effects of blocking IL-18 in sJIA are still unknown.

**Objective:** To examine serum IL-18 levels in sJIA patients with regards to disease activity, MAS features, and other novel MAS biomarkers. Additionally, we report the use of recombinant IL-18 BP (rIL-18BP) in a patient with severe, refractory sJIA and MAS.

**Methods:** Serum samples obtained from 20 established sJIA patients. Total IL-18, CXCL9 and S100 protein were measured. In addition, in one patient serial free IL-18 levels were determined. We compared IL-18 levels in patients with active vs inactive disease as well as with history of MAS vs no MAS.

**Results:**

Serum IL-18 levels were higher in patients with active sJIA (mean 52537 pg/ml ± 24442, N=10), but were still persistently elevated (2733 ± 889, N=10, upper limit of normal 540) in majority of patients with inactive disease (p=0.07). Patients with history of MAS had significantly higher IL-18 levels (63170 ± 29586, N=8) as compared to those without MAS history (3945 ± 1708, N=12, p=0.03). Only patients with fever had significantly higher IL-18 levels compared to their counter parts (P=0.03), while arthritis and elevated ESR or CRP showed no difference (p=0.1 and 0.08 respectively). We observed a weak but significant correlation between total IL-18 and CXCL9 (correlation coefficient of 0.4 (p=0.03)) but not for S100A8/A9. Given these findings by us and others, we utilized Tadekinig alfa (rhIL-18BP) in a 5 year old male with sJIA and persistently elevated free IL-18 levels. His course was complicated by recurrent MAS, failure of all prior biologic treatments, chronic high dose steroids with flare of sJIA and MAS upon attempts to wean steroids. He was started on rhIL-18BP 2mg/kg/dose subcutaneous every 48h in addition to continuous IL-1 inhibition attempting to control disease and prevent MAS. His initial total and free serum IL-18 levels were high at 117356 pg/ml and 46.8 pg/ml respectively. Although his total IL-18 remained elevated after start of rhIL-18BP, free IL-18 was undetectable. In addition, since initiation of Tadekinig alfa, steroid dose was decreased by more than 50% with increase in linear growth. While on Tadekinig alfa, he developed two MAS episodes (triggered by parainfluenza and acute gastroenteritis), but both were mild and easily controlled.

**Conclusion:**

Total serum IL-18 levels were elevated in the majority of sJIA patients regardless of disease activity, with higher levels in patients with active disease and those with history of MAS. This indicates that IL-18 might be an important driver of sJIA and MAS. Use of rIL-18 BP improved patient disease course with less frequent and easily controlled MAS episodes. This response raises optimism about use of rIL-18 BP in patients with IL-18 driven disease preventing life-threatening MAS.

**Disclosure:** S. Yasin, None; R. Brown, None; N. Fall, None; K. Solomon, None; S. Canna, AB2Bio Ltd, 5; C. Girard, None; C. Gabay, Roche, Pfizer, AB2 Bio, 2, Sanofi, AB2 Bio, AbbVie, Pfizer, BMS, MSD, Roche, Novartis, 5; E. Schiffrin, AB2bio Ltd, 3; A. Sleight, Ab2 bio, 3; A. A. Grom, NovImmune, 2, Ab2 Bio, 2, Novartis Pharmaceutical Corporation, 5, Juno, 5; G. Schulert, Novartis Pharmaceutical Corporation, 5.


Abstract Number: 1896

**IL-18 As a Diagnostic Biomarker, Differentiating Systemic JIA from Acute Leukaemia, Severe Bacterial Infections and Other Auto-Immune Disorders**

Arjen Leek1, Nienke Ter Haar2, Valerie De Haas3, Ayman El Idrissi1, Judith Wienke1, Sytze de Roock4, Dirk Holzinger5, Wilco de Jager6, Jorg van Loosdregt7 and Sebastiaan Vaster14,8 1Pediatric Rheumatology and Immunology, University Medical Center Utrecht, Utrecht, Netherlands, 2Department of Pediatric Rheumatology and Immunology, University Medical Center Utrecht, Utrecht, Netherlands, 3DCOG Laboratory, SKION, Den Haag, Netherlands, 4Laboratory of Translational Immunology, University Medical Center Utrecht, Utrecht, Netherlands, 5Department of Pediatric Rheumatology and Immunology, University Medical Center Utrecht, Utrecht, Netherlands, 6Division of Pediatric Rheumatology, University Medical Center Utrecht, Utrecht, Netherlands, 7Division of Pediatric Rheumatology, University Medical Center Utrecht, Utrecht, Netherlands
Systemic onset Juvenile Idiopathic Arthritis (sJIA) is a disease characterized by systemic inflammation in addition to arthritis and it’s diagnosis currently still depends on the clinical ILAR classification criteria of 2003, with arthritis as a required criterium. A significant portion of patients however exhibit inflammatory symptoms weeks, sometimes even months before showing signs of any joint involvement, making the diagnosis of sJIA challenging for the treating clinician due to the broad differential diagnosis of systemic inflammation. Recent insights in the underlying auto-inflammatory disease mechanisms in sJIA have proposed several candidate biomarkers aiding in the diagnostic process, including interleukin-18 (IL-18), a member of the IL-1 family. Here, we compare peripheral blood serum levels of IL-18 in sJIA at disease onset with several important differential diagnoses.

Here, we tested the value of IL-18 as a diagnostic biomarker aiding in diagnosing sJIA and differentiating sJIA from children with systemic infection (INF), acute lymphatic leukaemia (ALL) and auto-immune conditions like vasculitis.

Methods: A cohort was assembled retrospectively consisting of patients with sJIA at disease onset (n=39, presenting initially with and without arthritis, ultimately diagnosed according to ILAR criteria), oligo- and polyarticular JIA(n=28), ALL(n=18), various auto-immune diseases including vasculitis (n=14) and healthy controls(HC, n=30). Clinical and laboratory data were extracted from patient files. Peripheral blood serum IL-18 measurements were performed using a multiplex immunoassay based on Luminex technology.

Results: Of all sJIA patients(n=39), 97.1% experienced fever on the day of sampling. A cutaneous rash was seen in 82.9% of patients and 40% of patients suffered from lymphadenopathy at disease onset. 68.6% of patients showed overt arthritis (median joint count 1.5, IQR 0-3) and 77.1% suffered from arthralgia (median joint count 2, IQR 1-4). At time of sampling, 57.1% of patients were being treated with NSAID.

IL-18 values (pg/ml, median, IQR) were evidently elevated in sJIA (5465, 1962-13428) and differed significantly from the levels measured in the other disease groups (oligo JIA (274, 172-378), poly JIA (177, 121-342), ALL (542, 315-869), other auto-immune diseases including vasculitis (64, 36-131)) and healthy controls (228, 175-327). The IL-18 levels in the serum of children with systemic infections are currently being measured.

We evaluated different cut-off values for IL-18 using an ROC curve. A value of 1500pg/ml performed best, with a specificity of 0.976 and a sensitivity of 0.800.

Conclusion: Here we show the potential value of IL-18 as a diagnostic biomarker for sJIA in the process of differential diagnosis. When sJIA is suspected in a patient with symptoms of systemic inflammation with or without arthritis, an IL-18 level of 1500 or higher seems clearly suggestive of sJIA. In patients with suspected sJIA but IL-18 levels below 1500, we recommend additional diagnostic modalities, including for example PET scan or bone marrow biopsy where indicated, to rule out other diagnoses like childhood malignancy.

Disclosure: A. Leek, None; N. Ter Haar, None; V. De Haas, None; A. El Idrissi, None; J. Wienke, None; S. de Roock, None; D. Holzinger, None; W. de Jager, None; J. van Loosdregt, None; S. Vastert, None.


Abstract Number: 1897

the Ferritin to ESR Ratio: A Simple Measure to Distinguish Macrophage Activation Syndrome from Systemic Arthritis Flare

Esraa M. A. Eloseily1,2, Francesca Minoia3, Timothy Beukelman2, Angelo Ravelli4 and Randy Q. Cron2, 1Pediatrics, Assiut University, Assiut, Egypt, 2Pediatric Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 3Istituto Giannina Gaslini, Genoa, Italy, 4University of Genova, Genova, Italy

First publication: September 18, 2017
Background/Purpose:

Macrophage activation syndrome (MAS) is a life threatening complication of systemic juvenile idiopathic arthritis (sJIA). As MAS often shares clinical and laboratory features with sJIA disease flare, it can be difficult to distinguish. For new sJIA diagnoses, MAS associated with sJIA (sJIA-MAS) also has to be discerned from infection. A previous study suggested a serum ferritin to erythrocyte sedimentation rate (ESR) ratio of >80 could identify MAS among a small cohort of children with new-onset sJIA (J Rheumatol. 2013;40:1191). As a simple and quick tool, the ferritin to ESR ratio was explored to differentiate sJIA-MAS from active sJIA without MAS (flare), and from hospitalized febrile patients with systemic infections (SI).

Methods:

Data was reviewed from a multinational study of patients with sJIA-MAS (n=362), sJIA flare (n=404), and SI (n=345) (Arthritis Rheumatol. 2014;66:3160). Patients without documented ESR or ferritin were excluded, leaving 262 sJIA-MAS, 262 sJIA flare, and 93 SI. Receiver operating characteristic curves for ferritin/ESR were constructed, and areas under the curves (AUC) were calculated with 95% confidence intervals. The Youden index was used to determine the optimal ferritin/ESR cut-point.

Results:

For the ferritin/ESR ratio, comparing sJIA-MAS vs. sJIA flare, a cut off value of 21.5 had a sensitivity of 0.82 and specificity of 0.78 (AUC: 0.87 [0.84-0.90]). Comparing the ratio in sJIA-MAS cases vs. SI, a cut off value of 11.3 had a sensitivity of 0.91 and specificity of 0.93 (AUC: 0.95 [0.92-0.97]). Comparing sJIA-MAS cases vs. all others (sJIA flare & SI combined), a cut off value of 21.5 had a sensitivity of 0.82 and specificity of 0.83. (AUC: 0.89 [0.87-0.92]).

Conclusion:

The ferritin/ESR ratio with a cut off value of 21.5 accurately distinguishes sJIA-MAS from sJIA flare. This discriminatory ratio performs comparably to and is less complicated than the recent MAS in sJIA classification criteria (Ann Rheum Dis. 2016;75:481). In distinguishing sJIA-MAS from hospitalized infection, a ferritin/ESR ratio of 11.3 was a powerful tool with high sensitivity and specificity. The ferritin/ESR ratio is a quick and simple measure for distinguishing sJIA-MAS from sJIA flare and infection. Future studies should explore the measure in different MAS cohorts.
Disclosure: E. M. A. Eloseily, None; F. Minoia, None; T. Beukelman, UCB, 5, Novartis Pharmaceutical Corporation, 5; A. Ravelli, None; R. Q. Cron, SOBI, 5.


Abstract Number: 1898

**Overweight/Obesity Affect Histological Features of Synovial Membrane of Rheumatoid Arthritis Patients from Disease Onset to Stable Remission Achievement**

Stefano Alivernini1, Barbara Tolusso1, Maria Rita Gigante1, Laura Bui2, Clara Di Mario1, Luca Petricca1, Gabriele Di Sante1, Roberta Benvenuto2, Anna Laura Fedele1, Francesco Federico2, Gianfranco Ferraccioli3 and Elisa Gremese1, 1Institute of Rheumatology, Fondazione Policlinico Universitario A. Gemelli - Catholic University of the Sacred Heart, Rome, Italy, 2Institute of Pathology, Fondazione Policlinico Universitario A. Gemelli - Catholic University of the Sacred Heart, Rome, Italy, 3Institute of Rheumatology, Università Cattolica - Fondazione Policlinico Universitario A. Gemelli, Rome, Italy

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017

Session Title: Rheumatoid Arthritis – Clinical Aspects III: Obesity and Other Comorbidities

Session Type: ACR Concurrent Abstract Session

Session Time: 4:30PM-6:00PM

**Background/Purpose:** Despite animal models, little is known about synovial tissue (ST) composition of overweight/obese Rheumatoid Arthritis patients. The aim of the study was to investigate the impact of high Body Mass Index (BMI) on ST inflammation of RA patients from disease onset to stable remission achievement.

**Methods:** One-hundred twenty five RA patients [(57 DMARDs naïve, 43 Methotrexate inadequate responder (MTX-IR) and 25 in stable clinical (DAS<1.6) and ultrasound remission under MTX+TNF-i respectively] were enrolled and underwent ST biopsy. At study entry RA patients were divided based on BMI (kg/m^2) in normal weight (BMI<25), overweight (BMI>25) and obese (BMI>30) respectively. Immunohistochemistry for CD68⁺, CD21⁺, CD20⁺ and CD3⁺ cells was performed. Each naïve RA patient was treated according to the treat to target (T2T) strategy and followed for 12 months.

**Results:** Among the whole RA cohort, naïve RA were younger (53.5 ± 15.4 years) than MTX-IR RA (59.5 ± 13.8 years) and RA patients in stable remission (57.2 ± 15.0; p=0.02 using ANOVA test), whereas there were no significant differences in terms of other demographic, immunological and clinical characteristics comparing naïve to treatment and MTX-IR RA patients. The overweight/obesity rate was comparable between the 3 subgroups [34(59.6%) naïve RA vs 25(58.2%) MTX-IR RA vs 14(56.0%) RA in stable remission were overweight/obese, p>0.05]. However, naïve RA patients with BMI>30 kg/m² showed more likely follicular synovitis (78.6%) than normal weight naïve RA (39.1%; p=0.02). Particularly, naïve RA with BMI>35 kg/m² showed higher histological...
scores for CD68+ (p=0.03 and p=0.01 for lining and sublining), sublining CD20+ (p=0.005), CD21+ (p<0.001 and p=0.003 for lining and sublining) and sublining CD3+ cells (p=0.003) than normal weight naïve RA. Moreover, BMI directly correlated with synovial aggregate grade (R=0.311; p=0.02) and histological scores of CD21+ (R=0.344; p=0.01), CD20+ (R=0.295; p=0.03) and CD3+ cells (R=0.256; p=0.05) in naïve RA. Conversely, MTX-IR RA patients showed similar synovial inflammation degree based on different BMI categories. Regardless of the synovial inflammatory pattern (follicular vs diffuse), naïve overweight/obese RA patients showed a worse clinical response to T2T strategy compared to normal weight naïve RA at 6 and 12 months follow-up respectively (p<0.05 for both). Finally, despite RA in stable remission showed lower disease activity index (DAS) and inflammatory markers (ESR and CRP) than naïve RA (p<0.001 for each comparison), overweight/obese RA in stable remission showed higher degree of residual synovial inflammation in terms of sublining CD68+ cells (p=0.001), lining CD20+ cells (p=0.04), and lining and sublining CD3+ cells (p=0.04 and p=0.05 respectively) compared to normal weight RA patients in stable remission.

Conclusion: Overweight and obesity are associated with higher degree of histologically proven synovitis in RA patients from the time of disease onset to the achievement of stable remission influencing the response rate to T2T regimen. These findings suggest that BMI control should be a key target during the whole disease course in RA patients.

Disclosure: S. Alivererni, None; B. Toulusso, None; M. R. Gigante, None; L. Bui, None; C. Di Mario, None; L. Petrica, None; G. Di Sante, None; R. Benvenuto, None; A. L. Fedele, None; F. Federico, None; G. Ferraccioli, None; E. Gremese, None.


Abstract Number: 1899

Osteopontin and Leptin Are Associated with Erosive Disease in an Inception Cohort of Rheumatoid Arthritis Treated-to-Target with Combination Conventional DMARD Therapy

Mihir D. Wechalekar1,2,3, Susan Lester4, Sunil Nagpal5, Suzanne Cole6, Jessica Peters7, Anuk Das8, Pravin Hissaria9, Tania Crotti10, Catherine Hill1,11,12, Sudha Raghunath13, Llew Spargo14, Jennifer G Walker13,14,15, Malcolm D. Smith2 and Susanna Proudman1,10,
1Rheumatology Unit, Royal Adelaide Hospital, Adelaide, Australia, 2Flinders University, Adelaide, Australia, 3Rheumatology Unit, Repatriation General Hospital, Adelaide, Australia, 4Queen Elizabeth Hospital, Adelaide, Australia, 5Immunology, Janssen Research & Development, Spring House, PA, 6Immunology, Janssen Research and Development, Spring House, PA, 7Janssen Research & Development, Spring House, PA, 8Janssen R&D, Berwyn, PA, 9Immunology, SA Pathology, Adelaide, Australia, 10University of Adelaide, Adelaide, Australia, 11Medicine, The University of Adelaide, Adelaide, Australia, 12The Queen Elizabeth Hospital, Adelaide, Australia, 13 Repatriation General Hospital, Adelaide, Australia, 14Rheumatology Unit, Royal Adelaide Hospital, South Australia, Adelaide, Australia, 15Flinders University of South Australia, Adelaide, Australia

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects III: Obesity and Other Comorbidities
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: We sought to identify biomarkers associated with erosive disease and bone loss in an inception rheumatoid arthritis (RA) cohort receiving treat-to-target combination DMARD therapy without oral corticosteroids. Markers of osteoclast activation (RANKL) and inhibition [osteoprotegerin (OPG)], osteoblast inhibition [Dickkopf-1 (Dkk-1), sclerostin (SOST), osteopontin (OPN)], were serially tested. The degree of inflammation (TNFa, IL6, IL1b, ACTH), adipose tissue activity (leptin, insulin) and markers of bone turnover/damage [osteocalcin (OC), parathyroid hormone (PTH), fibroblast growth factor-23 (FGF23)], were also tested.

Methods: Patients with early RA (< 1 year; fulfilling ACR 1987 and/or 2010 classification criteria) received triple therapy (methotrexate, sulfasalazine, hydroxychloroquine) escalated to achieve DAS28 remission. Serum biomarkers were analysed using human bone panel LumineX kits in patients (n=112) at 0, 6, 12 months, and controls (n=33). Responses to treatment were analysed by mixed model regression. Principal component analysis (PCA) was performed on the within-individual correlations between treatment responses. Erosion and femoral neck bone density (BMD) data were available at 0, 1, 2, 3 years, and were analysed using the biomarker
log(mean) as a predictor, adjusted for baseline covariates. Erosion progression was analysed using a zero inflated Poisson regression model.

**Results:** 53% of the cohort were anti-CCP (cyclic-citrullinated peptide) positive; mean (SD) age was 58(14) years, DAS28 5.5(1.3), 73% females, 60% current/past smokers and 20% had erosive disease. Table 1 summarises results. Nine biomarkers changed following therapy: IL6, TNFa, IL1b, RANKL levels were decreased, whereas leptin, SOST, PTH, OC, OPG were increased. IL6 and TNFa represented two different axes of the treatment response (PCA analysis, Figure 1). Anti-CCP positivity (p = 0.009), higher disease activity (p<0.001), OPN (p<0.001), and lower leptin levels (p=0.002) were associated with higher erosion counts, and older age (p<0.001) and higher TNFa (p = 0.022) were associated with a lower probability of remaining erosion-free. Higher TNFa (p=0.003) and lower leptin (p = 0.029) levels were associated with lower BMD.

**Conclusion:** Biomarkers from both treatment response axes (Figure 1) are associated with erosive disease and bone loss in RA. Low leptin (Component 1) may be a new biomarker for erosive disease and bone loss in RA, and its improvement with treatment was correlated with suppression of IL-6. OPN, which was invariant to treatment, may be a novel biomarker for active erosive disease.

<table>
<thead>
<tr>
<th>Marker</th>
<th>RA vs Controls</th>
<th>Within RA Patients</th>
<th>Age</th>
<th>BMI</th>
<th>Females</th>
<th>antiCCP</th>
<th>Treatment</th>
<th>Erosions</th>
<th>BMD</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAS28 (ESR)</td>
<td>NA</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RANKL</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IL6</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TNFalpha</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IL1beta</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LEPTIN</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SOST</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OPN</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FGF23</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dkk1</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACTH</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>INSULIN</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTH</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OC</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OPG</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Component loadings

**Disclosure:** M. D. Wechalekar, Janssen, 2; S. Lester, None; S. Nagpal, Janssen, 3; S. Cole, Janssen, 3; J. Peters, Janssen, 9; A. Das, Janssen, 3; P. Hisaria, None; T. Crotti, None; C. Hill, None; S. Raghunath, None; L. Spargo, None; J. G. Walker, None; M. D. Smith, Janssen, 5; S. Proudman, Actelion Pharmaceuticals US, 2,GlaxoSmithKline, 2.


Abstract Number: 1900
Effect of Age and Body Mass Index (BMI) on Multi-Biomarker Disease Activity (MBDA) Score in Patients with Rheumatoid Arthritis

Kerri Ford¹, David Chernoff¹, Xingbin Wang¹, Eric H. Sasso¹, Carol J. Etzel²,³ and Dimitrios A. Pappas³,⁴, ¹Crescendo Bioscience Inc., South San Francisco, CA, ²Departments of Epidemiology and Biostatistics, University of Texas School of Public Health, Houston, TX, ³Corrona, LLC, Southborough, MA, ⁴Columbia University, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects III: Obesity and Other Comorbidities
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: We evaluated the associations between MBDA score and age and between MBDA score and BMI in patients with rheumatoid arthritis (RA). These relationships may be important to patient management and clinical decision-making.

Methods: Data in this retrospective study are from CORRONA, a longitudinal RA registry comprising >625 US rheumatologists in 40 states. Patients included must have had an MBDA test performed between 1 month before to 7 days after a CORRONA visit, which was the source of patient characteristics and clinical data. MBDA scores were categorized as low (<30), moderate (30-44), and high (>44). Age was categorized by decade (<40, 40-49, 50-59, 60-69, 70-79, and >80 years). BMI was categorized as ≤25, >25-30, >30-<35, ≥35 kg/m². Associations between age or BMI and MBDA score were evaluated using the Chi-square and trend tests.

Results: 878 patients were included: 77.9% were female with mean age 60.9 years, mean weight of 177.6 lbs, and mean RA disease duration of 10.7 years. Approximately half of patients (54%) were using methotrexate or other conventional DMARDs (21%), and nearly half (45%) were using a biologic (Table 1). Mean MBDA score was 42.6, with 18% in the low, 38% moderate and 44% high MBDA categories. The distribution of patients across the low, moderate and high MBDA categories was significantly associated with age by decade (Figure 1) both by chi-square test (p=0.001) and trend test (p<0.0001). MBDA category was also significantly associated with BMI (chi-square p=0.001; trend test p<0.0001) (Table 1). Low MBDA scores were observed in 135 of 545 (24.8%) patients with BMI ≤30 and 6 of 142 (4.2%) with MBDA scores ≥35 (Table 1). Conversely, high MBDA scores were observed in 196 of 545 (36.0%) of patients with BMI ≤30 and in 91 of 142 (64.1%) with BMI ≥35 (Table 1).

Conclusion: Age and BMI were each found to have a significant association with the MBDA score. These data suggest inflammatory biomarkers in RA may be affected by non-RA related factors. The magnitude of these effects deserves further evaluation in order to provide guidance on the interpretation of MBDA scores in older patients and those with very high BMI (≥35).
Unfavorable Body Composition Already at the Onset of Clinical Arthritis

Samina A. Turk1,2, Dirkjan van Schaardenburg3,4, Maarten Boers4,5, Sylvia de Boer1, Cindy Fokker1, Willem F. Lems4,5 and Michael Nurmohamed1,5, 1Rheumatology, Amsterdam Rheumatology and Immunology Center | Reade, Amsterdam, Netherlands, 2Rheumatology, Amsterdam Rheumatology and Immunology Center | Academic Medical Center, Amsterdam, Netherlands, 3Amsterdam Rheumatology and Immunology Center | Academic Medical Center, Amsterdam, Netherlands, 4Amsterdam Rheumatology and Immunology Center | Reade, Amsterdam, Netherlands, 5Rheumatology, Amsterdam Rheumatology and Immunology Center | VU University Medical Center, Amsterdam, Netherlands
Background/Purpose:

An unfavorable body composition is often present in chronic arthritis patients. This unfavorable composition is a loss of muscle mass (sarcopenia), with a stable or increased (abdominal) fat mass (sarcopenic obesity). Since it is unknown when this unfavorable composition develops, we compared body composition in disease-modifying antirheumatic drugs (DMARD)-naive early arthritis patients with non-arthritis controls and explored the association, in early arthritis patients, with disease activity and traditional cardiovascular risk factors.

Methods:

317 consecutive early arthritis patients (84% rheumatoid arthritis according to 2010 ACR/EULAR criteria) and 1268 age-/gender-/ethnicity-matched non-arthritis controls underwent a Dual-energy X-ray absorptiometry scan to assess fat percentage, fat mass index, fat mass distribution and lean (muscle) mass index. Additionally, disease activity, acute phase proteins, lipid profile and blood pressure were evaluated.

Results:

Sarcopenia and sarcopenic obesity was 4-5 times more common in early arthritis patients, with a significantly lower mean lean mass index (females 6% and males 7% lower, p<0.01). Patients had more fat distributed to the trunk (females p<0.01, males p=0.07) and females had a 4% higher mean fat mass index (p<0.01). An unfavorable body composition was associated with a higher blood pressure and an atherogenic lipid profile. There was no relationship with disease activity, physical function or acute phase proteins.

Conclusion:

Sarcopenia and sarcopenic obesity is 4-5 times more common in early arthritis patients, and is in early arthritis patients associated with a higher blood pressure and an atherogenic lipid profile. Therefore, cardiovascular risk is already increased at the clinical onset of arthritis making cardiovascular risk management necessary in early arthritis patients.

Figure. Prevalence of sarcopenia and sarcopenic obesity in early arthritis patients compared with non-arthritis controls.
Table. Body composition of early arthritis patients and non-arthritis controls stratified for gender.
### Table

<table>
<thead>
<tr>
<th></th>
<th>Mean values for control females (n=880)</th>
<th>Differences for female arthritis patients (n=220), B or OR and (CI) p-value</th>
<th>Mean values for control males (n=388)</th>
<th>Differences for male arthritis patients (n=97), B or OR and (CI) p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BMI</strong></td>
<td>27.1 (4.7) 1.0</td>
<td>(0.26-1.70) 0.008*</td>
<td>27.4 (3.7) (-1.11-0.61)</td>
<td>0.573</td>
</tr>
<tr>
<td><strong>LMI</strong></td>
<td>7.0 (0.8) -0.3</td>
<td>(-0.44 -0.19) &lt;0.001*</td>
<td>8.6 (1.0) (-0.83 -0.39)</td>
<td>0.001*</td>
</tr>
<tr>
<td><strong>FMI</strong></td>
<td>26.6 (4.6) 1.1</td>
<td>(0.38-1.78) 0.003*</td>
<td>27.4 (3.6) (-1.45-0.23)</td>
<td>0.154</td>
</tr>
<tr>
<td>Android to gynoid fat mass ratio</td>
<td>0.5 (0.2) &lt;0.1</td>
<td>(-0.04-0.00) 0.102</td>
<td>0.8 (0.2) (-0.09 -0.01)</td>
<td>0.029</td>
</tr>
<tr>
<td>Body fat%</td>
<td>39.8 (6.4) 0.9</td>
<td>(-0.05-1.92) 0.062</td>
<td>30.7 (5.5) (-2.07-0.47)</td>
<td>0.216</td>
</tr>
<tr>
<td>% of fat distributed to the trunk</td>
<td>49.4 (6.5) 2.8</td>
<td>(1.83-3.75) &lt;0.001*</td>
<td>57.6 (5.6) (-0.11-2.47)</td>
<td>0.074</td>
</tr>
<tr>
<td>Obese</td>
<td>38.4</td>
<td>(0.98-1.78) 0.068</td>
<td>58</td>
<td>(0.51-1.25) 0.324</td>
</tr>
<tr>
<td>Sarcopenic</td>
<td>1.3</td>
<td>(1.78-9.72) 0.001*</td>
<td>1.5</td>
<td>(1.94-16.91) 0.002*</td>
</tr>
<tr>
<td>Sarcopenic obesity</td>
<td>0.2</td>
<td>(0.56-28.52) 0.167</td>
<td>0.8</td>
<td>(1.22-25.17) 0.027</td>
</tr>
</tbody>
</table>

Results are expressed as mean (SD) or percentages and as beta (B) or odds ratio (OR) with a 95%-confidence interval (CI) and a p-value.

BMI: body mass index, FMI: fat mass index, LMI: lean mass index, n=number, RA: rheumatoid arthritis, SD: standard deviation

*significant results at the 0.05 false discovery rate for 18 tests, between arthritis patients and non-arthritis controls.

---

**Disclosure:** S. A. Turk, None; D. van Schaardenburg, None; M. Boers, None; S. de Boer, None; C. Fokker, None; W. F. Lems, None; M. Nurmohamed, None.


**Abstract Number:** 1902

**A Pattern of Higher Serum Levels of IL-10 and MMP-3, Along with Lower IL-6R, Identify RA Patients with Interstitial Lung Disease**
SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects III: Obesity and Other Comorbidities
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: The pathogenesis and prediction of RA-associated interstitial lung disease (ILD), an extra-articular manifestation with high morbidity and mortality, is poorly understood. We explored the associations of serum levels of inflammatory mediators with radiographic ILD in RA.

Methods: RA patients participating in a study of subclinical cardiovascular disease underwent computed tomography (CT) of the chest with interpretation by a pulmonary radiologist for CT-ILD features. A panel of 28 cytokines, chemokines, proteases, and other immune mediators was measured from serum using various optimized methods at the time of CT scanning. Generalized linear models were constructed to model the serum biomarkers associated with CT-ILD. A weighted biomarker score was constructed for each patient based on the biomarker level and its MV regression coefficient and modeled on CT-ILD, adjusting for pertinent confounders.

Results: A total of 156 RA patients [60% female, mean age 59 years, median RA duration=8 years, 76% seropositive for RF or anti-CCP, median DAS28=3.6] had both CT scanning and serum biomarkers measured. Any CT-ILD was found in 47 (30%) with a pattern of ground glass opacification (GGO) in 18 (44% of those with ILD) and reticulation, traction bronchiectasis, or honeycombing (R/TB/HC) in 23 (56% of those with ILD). In multivariable (MV) modeling, serum IL-10 and MMP-3 were significantly positively associated with any CT-ILD, while IL-6R was significantly inversely associated, even after adjusting for relevant confounders (listed in Fig). The association of the weighted biomarker score based on these 3 factors with ILD was not linear, as there was a markedly stronger association among patients with a score above the median (adjOR=3.99; p=0.003), translating to an adjusted prevalence of ILD of 40% for those with a higher biomarker score vs. only 14% among those with a lower score (Fig A). The association of the biomarker score was stronger for predicting R/TB/HC than GGO (Fig B), and was only significant among those with a history of smoking (Fig C). The area under the receiver operator curve (AUC-ROC) for predicting any CT-ILD with the biomarker score alone was 0.654 (95%CI 0.573-0.734) which increased to 0.834 with the additional covariates added to the model. The AUC-ROC for the biomarker score alone for predicting CT-ILD among ever smokers was 0.726 (95%CI 0.632-0.819). Interestingly, those with a higher biomarker score did not differ from those with a lower score on demographics or RA disease activity, severity, or treatment characteristics.

Conclusion: Both IL-10 and MMP-3 have been implicated in lung fibrosis in non-RA diseases. These findings suggest further evaluation of IL-10, MMP-3, and IL-6R levels are merited to determine if these biomarkers have utility in predicting ILD in some patients with RA, particularly among those with a history of smoking.

Disclosure: J. T. Giles, None; C. Johnson, None; E. J. Bernstein, None; E. Darrah, None; F. Andrade, None; S. K. Danoff, None.
Abstract Number: 1903

**Can Achieving Sustained DAS Remission Prevent Arterial Stiffness Progression in Early Rheumatoid Arthritis – a Post-Hoc Analysis of a Randomized Controlled Study**

Lydia Ho Pui Tam¹, Qing SHANG², Edmund Li³, Priscilla WONG³, Kitty Y Kwok⁴, Emily W Kun⁵, Issac C Yim⁶, Violet KL Lee⁷, Ronald ML Yip⁸, Steve H Pang⁸, Virginia W Lao⁸, Queenie Mak¹, Tsz Ho CHENG¹, Xerox Lau¹, Tena K. Li⁹, Tracy Y. ZHU¹⁰, PW Alex LEE¹ and Lai-Shan Tam², ¹Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong, Hong Kong, ²Department of Medicine & Therapeutics, The Chinese University of Hong Kong, Hong Kong, Hong Kong, ³Department of Medicine & Therapeutics, The Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong, Hong Kong, ⁴Department of Medicine, Queen Elizabeth Hospital, Hong Kong, Hong Kong, ⁵Alice Ho Miu Ling Nethersole Hospital, Hong Kong, Hong Kong, ⁶Department of Medicine, Tseung Kwan O Hospital, Hong Kong, Hong Kong, ⁷Department of Medicine, Pamela Youde Nethersole Eastern Hospital, Hong Kong, Hong Kong, ⁸Department of Medicine, Kwong Wah Hospital, Hong Kong, Hong Kong, ⁹Department of Medicine & Therapeutics, The Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong, China, ¹⁰Bone Quality and Health Center of the Department of Orthopedics & Traumatology, The Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong, Hong Kong

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Monday, November 6, 2017

Session Title: Rheumatoid Arthritis – Clinical Aspects III: Obesity and Other Comorbidities

Session Type: ACR Concurrent Abstract Session

Session Time: 4:30PM-6:00PM

**Background/Purpose:** Patients with rheumatoid arthritis (RA) have a higher incidence of cardiovascular disease (CVD) and prevalence of arterial stiffness (AS) due to chronic inflammation. AS in RA correlates not only with traditional CV risk factors, but also with current inflammation. Increased number and duration of flares over time and cumulative RA disease activity contribute to risk of CVD. While achieving Disease Activity Score in 28 joints (DAS) remission was associated with significant benefits in articular disease, its effect on co-morbidities such as CVD risk is uncertain. A more rigorous and sustained control of inflammation might be associated with a more favourable CV outcome in RA patients. The objective of this study was to investigate the effect of achieving sustained remission (DAS28 <2.6) on progression of arterial stiffness in early RA patients.

**Methods:** This is a post-hoc analysis of a prospective, randomized, controlled trial. 110 early RA patients received 1-year treatment based on a treat-to-target, tight-control protocol. Pulse wave velocity (PWV) and augmentation index (AIx) were measured at baseline and 12 months. Changes in AIx and PWV over 1-year was compared between patients who achieved sustained DAS remission (at 6, 9 and 12 months) (SDR group) and those who did not (non-SDR group).

**Results:** Sustained DAS remission was achieved in 37 (34%) patients. Baseline clinical characteristics and cardiovascular risk factors between the two groups were similar, except the symptom duration in the SDR group was significantly shorter. After 12 months, the change in PWV was significantly different between the two groups (SDR group: -67.0 [-153.0 to -43.5] cm/s vs non-SDR group: 14.0 [-68.0 to 14.5] cm/s, p=0.007). The change in AIx was similar between the two groups. Using multivariate regression analysis, independent predictors for PWV reduction included achieving sustained DAS remission (£\(\alpha\) = -73, 95% CI: -150.1 to -9.1, p = 0.027) and a shorter symptom duration (£\(\alpha\)= 6.3, 95% CI: 0.6 to 12.0, p = 0.032).

**Conclusion:** A significantly greater improvement in PWV was observed in patients who achieved sustained DAS remission compared to those who did not, indirectly supporting the notion that remission in RA confers diminished cardiovascular morbidity.

We would like to acknowledge the Health and Medical Research Fund (HMRF) for funding support (HMRF Project No.10110071)
Figure - Change in pulse wave velocity (PWV) between subject with sustained remission (SDR group) and without sustained remission (non-SDR group)

Disclosure: L. H. P. Tam, None; Q. SHANG, None; E. Li, None; P. WONG, None; K. Y. Kwok, None; E. W. Kun, None; I. C. Yim, None; V. K. Lee, None; R. M. Yip, None; S. H. Pang, None; V. W. Lao, None; Q. Mak, None; T. H. CHENG, None; X. Lau, None; T. K. Li, None; T. Y. ZHU, None; P. A. LEE, None; L. S. Tam, None.


Abstract Number: 1904

A Phase 3 Randomized, Placebo-Controlled, Double-Blind Study of Upadacitinib (ABT-494), a Selective JAK-1 Inhibitor, in Patients with Active Rheumatoid Arthritis with Inadequate Response to Conventional Synthetic DMards

Gerd R. Burmester1, Joel Kremer2, Filip van Den Bosch3, Yihan Li4, Yijie Zhou4, Ahmed A. Othman5, Aileen L. Pangan4 and Heidi S. Camp5, 1Department of Rheumatology and Clinical Immunology, Charité - University Medicine Berlin, Free University and Humboldt University Berlin, Berlin, Germany, 2Albany Medical College, Albany, NY, 3Rheumatology, Ghent University Hospital, Gent, Belgium, 4AbbVie Inc., North Chicago, IL, 5AbbVie, North Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy II: Trials Therapy
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Upadacitinib (UPA) is an oral, selective JAK-1 inhibitor in development for the treatment of patients (pts) with moderate to severe rheumatoid arthritis (RA) and other immune-mediated diseases.

Methods: This Phase 3 study in pts with inadequate response (IR) to csDMARDs included a double-blind placebo (PBO)-controlled period (Period 1, reported here), during which pts were randomized 1:1:1 to receive once-daily (QD) extended-release formulation of UPA at 15 mg or 30 mg, or PBO for 12 weeks (wks). The primary efficacy endpoints were the proportion of pts who achieved an ACR20 response and the proportion who achieved DAS28-CRP low disease activity (LDA, ≤3.2) at Wk 12, using non-responder imputation (NRI).
Results:

Of 661 pts who were randomized, all received study drug, and 618 (93.5%) completed Period 1. At baseline, demographics and disease characteristics were similar across arms. The study met all primary and key secondary endpoints with p values < 0.001 for both doses. At Wk 12, significantly more pts receiving UPA 15 mg and 30 mg QD vs PBO achieved an ACR20 response (63.8% and 66.2% vs 35.7%, p<.001), and DAS28-CRP LDA (48.4% and 47.9% vs 17.2%, p<.001) (Table 1). Onset of action was rapid with significantly more pts in both UPA arms achieving ACR20 at Wk 1 vs PBO. At Wk 12, significantly more pts met ACR50 and ACR70 in the UPA 15 mg (38% and 20.8%) and 30 mg QD arms (43.4% and 26.5%) vs PBO (14.9% and 5.9%). Significantly more patients receiving UPA 15 mg and 30 mg QD vs PBO achieved DAS28-CRP <2.6 (30.8% and 28.3% vs 10%, p<.001]) and CDAI-LDA (40.3% and 42% vs 19%, p<.001), and pts receiving UPA at both doses experienced significantly greater improvements in DAS28-CRP, HAQ-DI, morning stiffness and FACIT-F vs PBO (p<.001).

Adverse events (AEs) and serious AEs were numerically higher with UPA than PBO (Table 2). The overall incidence of infection was higher for UPA 15 mg and 30 mg QD vs PBO, but few were serious infections. There were 4 cases of herpes zoster/Varicella Zoster Virus infection (1 on PBO). Asymptomatic CPK elevations were only reported for patients on UPA. Two malignancies and 3 adjudicated cardiovascular events were reported. There were no deaths, cases of TB or GI perforations. Types and frequency of laboratory abnormalities were similar to findings in Phase 2 studies with UPA.

Conclusion: The efficacy of UPA at 15 mg and 30 mg QD vs PBO was demonstrated in this csDMARD-IR study population. The most notable responses were observed in the more stringent endpoints of LDA (by either DAS28-CRP or CDAI) and ACR70. The safety and tolerability profile was consistent with observations in the Phase 2 studies with UPA.

| Table 1. Efficacy Endpoints at Week 12# |
|-----------------|-----------------|-----------------|
| Endpoint        | Placebo         | Upadacitinib    | Upadacitinib    |
|                 | N=221           | 15 mg QD N=221  | 30 mg QD N=219  |
| Primary Endpoints |                 |                 |                 |
| ACR20 (%)       | 35.7            | 63.8 ***        | 66.2 ***        |
| DAS28-CRP LDA (%) | 17.2            | 48.4 ***        | 47.9 ***        |
| Key Secondary Endpoints |                 |                 |                 |
| ACR20 at Week 1 (%) | 8.6             | 22.2 ***        | 28.3 ***        |
| ACR50 (%)       | 14.9            | 38.0 ***        | 43.4 ***        |
| ACR70 (%)       | 5.9             | 20.8 ***        | 26.5 ***        |
| DAS28-CRP <2.6 (%) | 10.0            | 30.8 ***        | 28.3 ***        |
| CDAI LDA (%)    | 19.0            | 40.3 ***        | 42.0 ***        |
| Δ DAS28-CRP    | -1.02           | -2.20 ***       | -2.34 ***       |
| Δ HAQ-DI       | -0.25           | -0.59 ***       | -0.54 ***       |
| Δ SF-36 PCS    | 3.03            | 7.58 ***        | 8.01 ***        |
| Δ Morning Stiffness Duration (min.) | -34.27          | -85.28 ***      | -85.13 ***      |
| Δ FACIT-F      | 2.96            | 7.91 ***        | 7.74 ***        |

Values are LS mean unless otherwise specified. Δ, Change from baseline; QD, once daily; ACR20/50/70, 20/50 or 70% improvement in ACR criteria; DAS28-CRP, 28-joint disease activity score using C-reactive protein; HAQ-DI, health assessment questionnaire disability index; SF-36 PCS, short form 36- physical component score; LDA, low disease activity; FACIT-F, functional assessment of chronic illness therapy-fatigue (FACIT-F)

#Results for binary endpoints are based on NRI analysis. Results for DAS28-CRP and HAQ-DI are based on Multiple Imputation analysis. Results for other continuous endpoints are based on MMRM (Mixed Effect Model Repeat Measurement) analysis.

*** p<.001
**Table 2. Adverse Events Summary**

<table>
<thead>
<tr>
<th>n (%)</th>
<th>Placebo N=221</th>
<th>Upadacitinib 15 mg QD N=221</th>
<th>Upadacitinib 30 mg QD N=219</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Adverse Event (AE)</td>
<td>108 (48.9)</td>
<td>125 (56.6)</td>
<td>118 (53.9)</td>
</tr>
<tr>
<td>Serious AE</td>
<td>5 (2.3)</td>
<td>9 (4.1)</td>
<td>6 (2.7)</td>
</tr>
<tr>
<td>AE Leading To Discontinuation Of Study Drug</td>
<td>7 (3.2)</td>
<td>7 (3.2)</td>
<td>13 (5.9)</td>
</tr>
<tr>
<td>Severe AE</td>
<td>5 (2.3)</td>
<td>8 (3.6)</td>
<td>7 (3.2)</td>
</tr>
</tbody>
</table>

**AE of Special Interest**

<table>
<thead>
<tr>
<th>Infection</th>
<th>Placebo N=221</th>
<th>Upadacitinib 15 mg QD N=221</th>
<th>Upadacitinib 30 mg QD N=219</th>
</tr>
</thead>
<tbody>
<tr>
<td>-Serious Infection</td>
<td>47 (21.3)</td>
<td>64 (29.0)</td>
<td>69 (31.5)</td>
</tr>
<tr>
<td>-Opportunistic Infection</td>
<td>1 (0.5)</td>
<td>0</td>
<td>3 (1.4)</td>
</tr>
<tr>
<td>Anemia</td>
<td>3 (1.4)</td>
<td>0</td>
<td>3 (1.4)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>1 (0.5)</td>
<td>4 (1.8)</td>
<td>8 (3.7)</td>
</tr>
<tr>
<td>Herpes Zoster</td>
<td>1 (0.5)</td>
<td>1 (0.5)</td>
<td>2 (0.9)</td>
</tr>
<tr>
<td>Hepatic disorder</td>
<td>5 (2.3)</td>
<td>4 (1.8)</td>
<td>6 (2.7)</td>
</tr>
<tr>
<td>CPK elevation</td>
<td>0</td>
<td>5 (2.3)</td>
<td>6 (2.7)</td>
</tr>
<tr>
<td>Malignancy (including NMSC)</td>
<td>0</td>
<td>0</td>
<td>2 (0.9)</td>
</tr>
<tr>
<td>Cardiovascular event (adjudicated)</td>
<td>0</td>
<td>2 (0.9)</td>
<td>1 (0.5)</td>
</tr>
</tbody>
</table>

AE, adverse event; CPK, creatine phosphokinase; NMSC, non-melanoma skin cancer

- Serious Infection events: PBO: pneumonia; UPA 15 mg: enterocolitis infection; UPA 30 mg: 1 varicella zoster, 1 viral upper respiratory tract infection, 1 staphylococcal wound infection
- Opportunistic infection events: PBO: oral candidiasis; UPA 30 mg: 2 oral candidiasis, 1 varicella zoster pneumonia
- 1 pt on UPA 30 mg was exposed to chicken pox and had primary varicella infection.
- Malignancies: UPA 30 mg: 1 case of basal cell carcinoma in pt with history of skin cancer, 1 case of chronic lymphocytic leukemia/small lymphocytic lymphoma. Both were deemed unrelated to study drug by the investigator.
- Cardiovascular events (adjudicated): UPA 15 mg: 1 congestive cardiac failure, 1 stent placed in pt with prior history of angina, coronary artery disease and transient ischemic attack; UPA 30 mg: ischemic stroke in pt with history of hypertension

**Disclosure:**
- **G. R. Burmester,** AbbVie Inc., Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB., 5, AbbVie Inc., Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB., 8; **J. Kremer,** Corrona, 1, Corrona, 3, AbbVie, 2, BMS, Genentech, Gilead, GSK, Eli Lilly and Pfizer, 5; **F. van Den Bosch,** AbbVie Inc., Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer and UCB, 5, AbbVie Inc., Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer and UCB, 8; **Y. Li,** AbbVie, 1, AbbVie, 3; **Y. Zhou,** Abbvie, 1, AbbVie, 3; **A. A. Othman,** AbbVie, 1, AbbVie, 3; **A. L. Pangan,** AbbVie, 1, AbbVie, 3; **H. S. Camp,** AbbVie, 1, AbbVie, 3.

Sustained Response Following Discontinuation of Methotrexate in Patients with Rheumatoid Arthritis Treated with Subcutaneous Tocilizumab: Results from a Randomized Controlled Trial

Joel Kremer1, William F C Rigby2, Nora Singer3, Christine Birchwood4, Darcy Gill4, William Reiss4, Jinglan Pei4 and Margaret Michalska4
1Albany Medical College, Albany, NY, 2Geisel School of Medicine at Dartmouth, Lebanon, NH, 3Case Western Reserve University School of Medicine, Cleveland, OH, 4Genentech, Inc., South San Francisco, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy II: Trials Therapy
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Although methotrexate (MTX) is often administered in combination with biologics for the treatment of rheumatoid arthritis (RA), it may be discontinued due to intolerance or to reduce medication burden. This study evaluated whether tocilizumab-monotherapy (TCZ-MONO) is non-inferior to TCZ + MTX in maintaining clinical response in patients who achieve low disease activity with TCZ + MTX in the COMP-ACT trial.

Methods: US patients with RA who were inadequate responders to MTX initially received MTX (≥ 15 mg/week orally) plus TCZ 162 mg subcutaneous (SC) either weekly (patients ≥ 100 kg) or every 2 weeks (patients < 100 kg). Patients who had not achieved low disease activity (DAS28 ≤ 3.2) at week 12 could escalate from q2w to qw dosing. Patients who achieved DAS28-ESR ≤ 3.2 at week 24 were randomized 1:1 to receive TCZ-MONO or TCZ + MTX until week 52 (double-blind). The primary outcome measured was the comparison of mean change in DAS28-ESR score from weeks 24 to 40 between the TCZ-MONO and TCZ + MTX arms (non-inferiority margin of 0.6). Secondary outcomes included the proportion of patients achieving DAS28 < 2.6, DAS28 ≤ 3.2 and American College of Rheumatology 20%/50%/70% (ACR20/50/70) responses at weeks 40 and 52, and safety. Trial registration number: NCT01855789.

Results: Of 718 patients enrolled, 296 were randomized at week 24 (TCZ-MONO, n = 148; TCZ + MTX, n = 148). Early discontinuation in the randomized cohort occurred in 12.2% of patients in the TCZ-MONO group and 10.2% in the TCZ + MTX group. Baseline characteristics were balanced between treatment groups (mean age, 55.5 years; 74.8% female; mean RA duration, 6.8 years; mean DAS28-ESR, 6.3). At week 24, DAS28 scores were similar in both groups, but ACR responses were ≈8% to 11% lower in the TCZ-MONO group prior to MTX withdrawal (randomization). The mean change in DAS28 was similar between the randomized treatment groups (Table 1). For the primary efficacy analysis, the mean changes in DAS28 from weeks 24 to 40 were 0.46 and 0.14 in the TCZ-MONO and TCZ + MTX groups, respectively (95% CI, 0.045-0.592). This study met the primary endpoint by demonstrating that discontinuing MTX in TCZ responders was noninferior to continuing MTX. The safety of TCZ-SC in this study was consistent with the known safety profile, with no new safety signals observed (Table 2). The most common SAE was infection, occurring in 4.1% of patients. TCZ + MTX had greater frequency of AEs, SAEs and serious infections than TCZ-MONO.

Conclusion: These results demonstrate that patients receiving TCZ + MTX who achieve low disease activity can discontinue MTX and maintain disease control.
Table 1. Efficacy of TCZ as Monotherapy and in Combination With MTX

<table>
<thead>
<tr>
<th></th>
<th>TCZ-MONO (n = 147)</th>
<th>TCZ + MTX (n = 147)</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>TCZ-MONO minus</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TCZ + MTX</td>
</tr>
<tr>
<td>ADAS28-ESR, mean (SEM)*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 24 to week 40</td>
<td>0.46 (0.123)</td>
<td>0.14 (0.126)</td>
<td>0.318 (0.045, 0.592)</td>
</tr>
<tr>
<td>Week 24 to week 52</td>
<td>0.43 (0.136)</td>
<td>0.20 (0.139)</td>
<td>0.232 (−0.068, 0.532)</td>
</tr>
<tr>
<td>Response at Week 40, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DAS28 ≤ 3.2</td>
<td>94 (63.9)</td>
<td>113 (76.9)</td>
<td>−12.9 (−23.3, −2.6)</td>
</tr>
<tr>
<td>DAS28 &lt; 2.6</td>
<td>74 (50.3)</td>
<td>87 (59.2)</td>
<td>−8.8 (−20.2, 2.5)</td>
</tr>
<tr>
<td>ACR20</td>
<td>103 (70.1)</td>
<td>116 (78.9)</td>
<td>−8.8 (−18.8, 1.1)</td>
</tr>
<tr>
<td>ACR50</td>
<td>76 (51.7)</td>
<td>94 (63.9)</td>
<td>−12.2 (−23.4, −1.0)</td>
</tr>
<tr>
<td>ACR70</td>
<td>51 (34.7)</td>
<td>62 (42.2)</td>
<td>−7.5 (−18.6, 3.6)</td>
</tr>
<tr>
<td>DAS28 Worsening ≥ 1.2, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 24 to week 40</td>
<td>42 (28.6)</td>
<td>31 (21.1)</td>
<td>7.5 (−2.4, 17.3)</td>
</tr>
</tbody>
</table>

ACR, American College of Rheumatology criteria; AE, adverse event; DDAS28-ESR, change in Disease Activity Score-28 joints erythrocyte sedimentation rate; MTX, methotrexate; SAE, serious adverse events; SEM, standard error of the mean; TCZ, tocilizumab; TCZ+MTX, TCZ plus MTX; TCZ-MONO, TCZ monotherapy.

* Adjusted means from ANCOVA model include week 24 DAS28 as a covariate, treatment group and the randomization stratification factors: DAS28 remission status at week 24 (< 2.6; ≥ 2.6 to ≤ 3.2), patient anti-TNF exposure (Yes/No), baseline weight-by-dosing group (< 80 kg q2w; < 80 kg qw; 80 to < 100 kg q2w; 80 to < 100 kg qw, ≥ 100 kg qw). Last observation carried forward (LOCF) was used to impute missing data at week 40 only.

Table 2. Safety of TCZ as Monotherapy and in Combination With MTX

<table>
<thead>
<tr>
<th>Rate, per 100 PY (95% CI)</th>
<th>Total* N = 713 700.60 PY</th>
<th>TCZ-MONO† n = 144 92.44 PY</th>
<th>TCZ + MTX† n = 139 90.56 PY</th>
</tr>
</thead>
<tbody>
<tr>
<td>AEs</td>
<td>377.1 (362.9, 391.8)</td>
<td>238.0 (207.6, 271.6)</td>
<td>308.1 (273.0, 346.4)</td>
</tr>
<tr>
<td>SAEs</td>
<td>17.0 (14.1, 20.3)</td>
<td>8.7 (3.7, 17.1)</td>
<td>14.4 (7.6, 24.6)</td>
</tr>
<tr>
<td>Serious infections</td>
<td>5.0 (3.5, 7.0)</td>
<td>3.3 (0.7, 9.5)</td>
<td>4.4 (1.2, 11.3)</td>
</tr>
</tbody>
</table>

AE, adverse event; MTX, methotrexate; PBO, placebo; PY, patient-year; SAE, serious adverse event; TCZ, tocilizumab; TCZ+MTX, TCZ plus MTX; TCZ-MONO, TCZ monotherapy.

* Safety population from baseline to end of study.
† Includes all randomized patients who were administered TCZ+MTX or TCZ+PBO from week 24 to end of study.
Tofacitinib with and without Methotrexate Versus Adalimumab with Methotrexate for the Treatment of Rheumatoid Arthritis: Patient-Reported Outcomes from a Phase 3b/4 Randomized Trial

Vibeke Strand1, Eduardo Mysler2, Robert J Moots3, Gene Wallenstein4, Ryan DeMasi5, Zhen Luo6, Koshika Soma4, Noriko Iikuni7 and Roy Fleischmann8, 1Division of Immunology/Rheumatology, Stanford University, Palo Alto, CA, 2Organización Médica de Investigación, Buenos Aires, Argentina, 3Institute of Ageing and Chronic Disease, University of Liverpool, Liverpool, United Kingdom, 4Pfizer Inc, Groton, CT, 5Pfizer Inc, Collegeville, PA, 6Pfizer Inc, Shanghai, China, 7Pfizer Inc, New York, NY, 8Metroplex Clinical Research Center and University of Texas Southwestern Medical Center, Dallas, TX

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy II: Trials Therapy
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). We compared patient-reported outcomes (PROs) among patients receiving tofacitinib monotherapy, tofacitinib + methotrexate (MTX), and adalimumab (ADA) + MTX, in a head-to-head trial of patients with RA and inadequate responses to MTX (MTX-IR).

Methods: ORAL Strategy (NCT02187055) was a Phase 3b/4, 1-year, triple dummy, active randomized controlled trial (RCT). Patients were randomized 1:1:1 to receive tofacitinib 5 mg twice daily (BID; tofa mono), tofacitinib 5 mg BID + MTX (tofa+MTX) or subcutaneous ADA 40 mg every other week + MTX (ADA+MTX); MTX doses were 15–25 mg/wk. PROs (secondary endpoints in this RCT) assessed at Months (Mos) 6 and 12 included mean changes from baseline in: patient global assessment of disease activity (visual analog scale [VAS]); arthritis pain (VAS); Health Assessment Questionnaire-Disability Index (HAQ-DI); Short Form-36 Health Survey; EuroQol 5-dimensions Questionnaire; Work Productivity and Activity Impairment Questionnaire; Functional Assessment of Chronic Illness Therapy-Fatigue; and the proportion of patients reporting improvements in HAQ-DI ≥ minimum clinically important difference (MCID; -0.22). Nominal p values were calculated with no adjustment for multiple comparisons.

Results: Among 1146 patients treated (tofa mono: n=384; tofa+MTX: n=376; ADA+MTX: n=386), baseline demographics and disease characteristics were comparable. At Mos 6 and 12, improvements in all PROs were similar for tofa+MTX and ADA+MTX (there were essentially no differences based on nominal p values) and numerically greater than with tofacitinib monotherapy (Table). Mean changes from baseline in HAQ-DI scores were similar in each treatment group at Mos 6 and 12; similar proportions reported improvements ≥MCID.

Conclusion: MTX-IR patients with RA reported PRO improvements with all 3 treatment regimens that were clinically meaningful, comparable for tofacitinib + MTX and adalimumab + MTX, and numerically higher with combination therapy than with tofacitinib monotherapy. Nominal p values should be interpreted with caution as they were not controlled for Type 1 error.
Disclosure: V. Strand, AbbVie, Amgen, Bristol Myers Squibb, CORRONA, Eli Lilly, Janssen, Novartis, Pfizer Inc, UCB, 5; E. Mysler, AbbVie, Bristol Myers Squibb, Eli Lilly, Janssen, Medimmune, Pfizer Inc, and Roche, 2; AbbVie, Bristol Myers Squibb, Eli Lilly, Janssen, Medimmune, Pfizer Inc, and Roche, 5; AbbVie, Bristol Myers Squibb, Eli Lilly, Janssen, Medimmune, Pfizer Inc, and Roche, 8; R. J. Moots, Biogen, Bristol-Myers Squibb, Chugai, Novartis, Pfizer, Roche, Sandoz, UCB Pharma, 2; Biogen, Bristol-Myers Squibb, Chugai, Novartis, Pfizer, Roche, Sandoz, UCB Pharma, 5; Biogen, Bristol-Myers Squibb, Chugai, Novartis, Pfizer, Roche, Sandoz, UCB Pharma, 8; G. Wallenstein, Pfizer Inc, 1; Pfizer Inc, 3; R. DeMasi, Pfizer Inc, 1; Pfizer Inc, 3; Z. Luo, Pfizer Inc, 1; Pfizer Inc, 3; K. Soma, Pfizer Inc, 1; Pfizer Inc, 3; N. Iikuni, Pfizer Inc, 1; Pfizer Inc, 3; R. Fleischmann, Pfizer, UCB, AbbVie, 2; Pfizer, UCB, AbbVie, 5.


Abstract Number: 1907

Safety, Pharmacokinetics, and Efficacy of E6011, an Anti-Fractalkine Monoclonal Antibody, in a First-In-Patient Phase 1/2 Study on Rheumatoid Arthritis: 52-Week Results

Yoshiya Tanaka1, Tsutomu Takeuchi2, Hisanori Umehara3, Toshihiro Nanki4, Nobuyuki Yasuda5, Fumitoshi Tago6, Makoto Kawakubo6, Yasumi Kitahara6, Seiichiro Hojo6, Tetsu Kawano7 and Toshio Imai7, 1The First Department of Internal Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan, 2Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, 3Division of Rheumatology and Immunology, Nagahama City Hospital, Shiga, Japan, 4Division of Rheumatology, Department of Internal Medicine, Toho University School of Medicine, Tokyo, Japan, 5KAN Research Institute, Inc., Tokyo, Japan, 6Eisai Co., Ltd., Tokyo, Japan, 7KAN Research Institute, Inc., Kobe, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy II: Trials Therapy
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Fractalkine (CX3C1/FKN) is a chemokine that regulates chemotaxis and adhesion of CX3C chemokine receptor 1 (CX3CR1)-expressing inflammatory cells. We previously presented the interim results of a 12-week treatment phase during phase 1/2, open-label, multiple dose clinical study of E6011, a novel humanized anti-FKN monoclonal antibody, in Japanese
active rheumatoid arthritis (RA) patients\(^1\). This is the first report of the 52-week safety, pharmacokinetics and efficacy of this clinical trial (NCT02196558).

**Methods:** Japanese patients with active RA who have shown inadequate responses or intolerance to methotrexate (MTX) or TNF inhibitor received E6011 at week 0, 1, 2, and then every 2 weeks for up to week 10 during the Treatment Phase. If no safety concerns were raised, subjects who showed a ≥ 20% improvement in both tender and swollen joint counts were given the option to receive 20 additional biweekly administrations at the same dose in the Extension Phase; 52 weeks in total.

**Results:** Twelve, 15, and 10 subjects were enrolled in the 100, 200, and 400 mg cohorts, respectively. Of these subjects, a total of 28 subjects were entered in the Extension Phase with 11, 11 and 6 subjects in the 100, 200, and 400 mg cohorts, respectively. As a result, repeated dose of E6011 was found safe and well tolerated during the Extension Phase. The incidence of AE, treatment-related AE and SAE was 83.8%, 48.6% and 13.5%, respectively. There were no severe AE or deaths, and no significant differences were observed in the incidence or severity of AE across the cohorts. After starting multiple dose administration of E6011, the steady state was achieved at week 2, and was held up to week 52. ACR 20 response rates at Week 12 and 52 (LOCF) were 75.0% and 58.3%, 80.0% and 73.3%, and 70.0% and 60.0% in the 100, 200, and 400 mg cohort respectively.

**Conclusion:** E6011 was safe and well tolerated, and demonstrated durable efficacy for 52-week in active RA with an inadequate response or intolerance to MTX or TNF inhibitor therapies. These results support the continuation of E6011 clinical study in phase 2 trials during which an optimal clinical dose and further safety and efficacy thresholds should be confirmed in a placebo controlled double-blinded manner.

**Reference:**

1. 2015 ACR/ARHP Annual Meeting. Abstract Number: 13L


**Abstract Number:** 1908

**Long-Term Efficacy and Safety Results of a Global Phase 3 Trial of Sirukumab, an Anti–IL-6 Cytokine Monoclonal Antibody, in Patients with Active Rheumatoid Arthritis Despite Disease-Modifying Anti-Rheumatic Drug Treatment**
Carter Thorne1, Tsutomu Takeuchi2, George Karpuzas3, Shihong Sheng4, Regina Kurrasch5, Kaiyin Fei4 and Benjamin Hsu4,  
1University of Toronto, Newmarket, ON, Canada, 2Keio University Hospital School of Medicine, Tokyo, Japan, 3Division of Rheumatology, Harbor-UCLA Medical Center, Torrance, CA, 4Janssen Research & Development, LLC, Spring House, PA, 5GlaxoSmithKline, Collegeville, PA  
First publication: September 18, 2017  
SESSION INFORMATION  
Session Date: Monday, November 6, 2017  
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy II: Trials Therapy  
Session Type: ACR Concurrent Abstract Session  
Session Time: 4:30PM-6:00PM  
Background/Purpose: In patients (pts) with active rheumatoid arthritis (RA) despite DMARD treatment, sirukumab, a human monoclonal antibody that selectively binds to the IL-6 cytokine with high affinity, significantly reduced signs and symptoms and inhibited radiographic progression vs placebo at 52 wks in SIRROUND-D. Long-term efficacy (Wk 104) and safety (Wk 120) results are presented.  
Methods: In this Phase 3 study, 1670 pts with moderate to severe active RA refractory to DMARDs (≥6/66 swollen and ≥6/68 tender joints and minimum CRP ≥8.0 mg/L) were randomized (1:1:1) to SC sirukumab 50mg q4w, sirukumab 100mg q2w, or placebo q2w. Pts in the placebo group with <20% improvement in swollen/tender joints at Wks 18 or 40 or still taking placebo at Wk 52 were re-randomized to sirukumab. Pts received blinded sirukumab in an active-controlled period from Wk 52 to 104, followed by a 16-wk safety phase to Wk 120. Efficacy endpoints, ACR20/50/70/90 responses, DAS28(CRP) remission, Short Form-36 (SF-36) Health Survey mental and physical component summary (MCS, PCS) scores, and HAQ-DI, were analyzed for pts on study treatment at Wk 52. Pts with data missing or who terminated study treatment were considered ACR20/50/70/90 non-responders and not achieving DAS28(CRP) remission. Missing MCS, PCS, and HAQ-DI scores were imputed using the non-missing score at Wk 52 or 76, whichever was the last prior visit. Treatment-emergent adverse events (AEs) and serious AEs were assessed for all pts who received ≥1 dose of study drug.  
Results: Of 1114 pts originally randomized to sirukumab and 556 to placebo, 944 and 458 were receiving sirukumab at Wk 52 for a total of 1402 pts in efficacy analyses from Wk 52 to 104. Of pts originally randomized to sirukumab, the proportions of pts achieving ACR20/50/70/90 responses and DAS28(CRP) remission were consistent at Wks 52 and 104 (Table); among those who achieved ACR20 and ACR50 responses at Wk 52, 90% and 79%, respectively, in each sirukumab dose group maintained them at Wk 104. Improvements from baseline in MCS and PCS scores and HAQ-DI were comparable for each outcome at Wks 52 and 104. Among pts originally randomized to placebo who crossed over to sirukumab, Wk 104 responses were similar to those for pts originally randomized to sirukumab. Through Wk 120 for all pts in the study, incidences of AEs and serious AEs, respectively, were similar with sirukumab 50mg q4w (84.0% and 17.7%) and 100mg q2w (86.7% and 16.5%). The most common AEs with sirukumab (≥10% in either group) were elevated liver enzymes, upper respiratory tract infection, nasopharyngitis, and injection site erythema. Serious AEs with the highest incidence were infections and infestations.  
Conclusion: In this 2-year Phase 3 study of sirukumab in pts with active RA despite DMARDs, improvements in signs and symptoms of RA and health-related physical and emotional well-being were maintained. No new safety signals were reported through Wk 120.
Long Term Safety of Filgotinib in the Treatment of Rheumatoid Arthritis: Week 84 Data from a Phase 2b Open-Label Extension Study

Mark C. Genovese1, Arthur Kavanaugh2, Kevin Winthrop3, Maria Greenwald4, Lucia Ponce5, Favio Enriquez Sosa6, Mykola Stanislavchuk7, Minadora Mazur8, Alberto Spindler9, Regina Cseuz10, Natalya Nikulenkova11, Maria Glowacka-Kulesz12, Istvan Szombati13, Anna Dudek14, Neelufar Mozaffarian15, Joy Greer15, Xiao Ding15, Pille Harrison16, Annegret Van der Aa16, René Westhovens17, and Rieke Alten18, 1Stanford University Medical Center, Palo Alto, CA, 2Medicine, University of California, San Diego, 3Oregon Health Sciences University, Portland, OR, 4Desert Medical Advances, Palm Desert, CA, 5Consulta Privada Dra. Lucia Ponce, Temuco, Chile, 6Clinistile SA de CV, Col., Mexico City, Mexico, 7Vinnitsa Regional Clinical Hospital, Vinnitsa, Ukraine, 8IMSP Inst. de Cardiologie, Chisinau, Moldova, The Republic of, 9Centro Médico Privado de Reumatologia, Centro Médico Privado de Reumatología, Argentina, 10Revita Reumatologiai Rendelo, Budapest, Hungary, 11Vladimir Reg Clin Hosp, Vladimir, Russian Federation, 12Silesiana Centrum Medyczne, Wroclaw, Poland, 13QUALICLINIC Kft., Budapest, Hungary, 14Centrum Medyczne AMED Warszawa Targówek, Warszawa, Poland, 15Gilead Sciences, Inc, Foster City, CA, 16Galapagos NV, Mechelen, Belgium, 17KU Leuven Department of Development and Regeneration, Skeletal Biology and Engineering Research Center, Leuven, Belgium, 18Internal Medicine, Rheumatology & Clinical Immunology, Schlosspark-Klinik, University Medicine Berlin, Berlin, Germany

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy II: Trials Therapy
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Filgotinib is an orally administered, selective inhibitor of Janus Kinase 1 (JAK1) currently in Phase 3 development for the treatment of rheumatoid arthritis (RA).

Methods: Previously, two 24-week Phase 2b studies were conducted in subjects with moderately to severely active RA (DARWIN 1, DARWIN 2; Ref 1, 2). Upon completing one of these studies, subjects could receive open-label filgotinib in the DARWIN 3 long-term follow-up study, given as 200 mg QD (100 mg QD for males in the US) or 100 mg BID. This report summarizes safety data from the first dose of filgotinib in DARWIN 1, 2 or 3 until the time that the last subject completed 84 weeks of filgotinib dosing. Efficacy is summarized for all subjects through Week 84 of DARWIN 3.

Results: Ninety percent of subjects (790 of 877) completed the Phase 2b studies, and 739 (84%) enrolled in DARWIN 3; 603 (82%) were female and the mean age was 53 years; 560 completed 84 weeks of filgotinib dosing. When the last subject completed 84 weeks in DARWIN 3, 520 (70.4%) subjects remained on study and 219 (29.6%) had discontinued. Most frequent reasons for discontinuation were positive/indeterminate QuantiFERON (10.3%; no active tuberculosis), protocol specified adverse event (AE) stopping rules (6.8%) and withdrawal of consent (5.8%). Cumulative patient years of exposure (PYE) were 1708 with a median time on study drug of 917 days (range 64 to 1329 days). A summary of safety events and laboratory abnormalities are summarized below. Based on ‘observed
case analysis, 86%, 69%, and 47% of 560 subjects achieved ACR20/50/70, respectively, and 71% (386/543) achieved DAS28-CRP ≤3.2.

Conclusion: Filgotinib long-term follow-up data demonstrate a favorable safety and durable efficacy profile in subjects with RA, consistent with prior reports.

Table 1: Summary of Exposure and Safety Outcomes Per 100 PYE

<table>
<thead>
<tr>
<th>Filgotinib + MTX</th>
<th>Filgotinib Monotherapy</th>
<th>Total (N=739)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 mg BID (N=251)</td>
<td>100 mg QD* (N=9)</td>
<td>200 mg QD (N=251)</td>
</tr>
<tr>
<td>Total FIL patient years of exposure (PYE)</td>
<td>593.5</td>
<td>21.8</td>
</tr>
<tr>
<td>Median FIL exposure (days)</td>
<td>936</td>
<td>896</td>
</tr>
<tr>
<td>TEAEs/100PYE#</td>
<td>153.3</td>
<td>77.9</td>
</tr>
<tr>
<td>Serious TEAEs/100PYE#</td>
<td>6.2</td>
<td>0</td>
</tr>
<tr>
<td>TEAEs for Infections/100PYE</td>
<td>44.5</td>
<td>9.2</td>
</tr>
<tr>
<td>Serious TEAEs for Infections/100PYE</td>
<td>1.5</td>
<td>0</td>
</tr>
<tr>
<td>Malignancy (excluding NMSC†)/100PYE</td>
<td>0.7</td>
<td>0</td>
</tr>
</tbody>
</table>

*Treatment group is comprised of male subjects located in the US only
†Non-melanoma skin cancer

Table 2: Treatment Emergent Laboratory Abnormalities Per 100 PYE

<table>
<thead>
<tr>
<th>Filgotinib + Methotrexate</th>
<th>Filgotinib Monotherapy</th>
<th>Total (N=739)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 mg BID (N=251)</td>
<td>100 mg QD* (N=9)</td>
<td>200 mg QD (N=251)</td>
</tr>
<tr>
<td>Hemoglobin/100 PYE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 2</td>
<td>4.4</td>
<td>0</td>
</tr>
<tr>
<td>Grade 3</td>
<td>0.5</td>
<td>0</td>
</tr>
<tr>
<td>Grade 4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Lymphocytes/100 PYE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 2</td>
<td>9.1</td>
<td>0</td>
</tr>
<tr>
<td>Grade 3</td>
<td>1.0</td>
<td>0</td>
</tr>
<tr>
<td>Grade 4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Neutrophils/100 PYE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 2</td>
<td>1.2</td>
<td>0</td>
</tr>
<tr>
<td>Grade 3</td>
<td>0.2</td>
<td>0</td>
</tr>
<tr>
<td>Grade 4</td>
<td>0.2</td>
<td>0</td>
</tr>
<tr>
<td>Platelets/ 100 PYE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 2</td>
<td>0.2</td>
<td>0</td>
</tr>
<tr>
<td>Grade 3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Grade 4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>ALT/100PYE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 2</td>
<td>2.9</td>
<td>0</td>
</tr>
<tr>
<td>Grade 3</td>
<td>0.3</td>
<td>0</td>
</tr>
<tr>
<td>Grade 4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Creatinine/100PYE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Grade 3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Grade 4</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Toxicity Grading Scale Used: CTCAE Version 3.0

*Treatment group includes male subjects located in the US only
Table 3: Treatment Emergent Laboratory Abnormalities for Lipids Per 100 PYE

<table>
<thead>
<tr>
<th></th>
<th>Filgotinib + Methotrexate</th>
<th>Filgotinib Monotherapy</th>
<th>Total (N=739)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>100 mg BID (N=251)</td>
<td>100 mg QD* (N=9)</td>
<td>200 mg QD (N=251)</td>
</tr>
<tr>
<td>LDL/100 PYE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100 – 129 mg/dL</td>
<td>42.8</td>
<td>114.5</td>
<td>54.1</td>
</tr>
<tr>
<td>130 - 159 mg/dL</td>
<td>51.2</td>
<td>22.9</td>
<td>45.8</td>
</tr>
<tr>
<td>160 - 189 mg/dL</td>
<td>28.6</td>
<td>0</td>
<td>32.2</td>
</tr>
<tr>
<td>≥ 190 mg/dL</td>
<td>18.0</td>
<td>0</td>
<td>5.7</td>
</tr>
<tr>
<td>HDL/100 PYE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;40 mg/dL</td>
<td>5.7</td>
<td>41.2</td>
<td>7.6</td>
</tr>
<tr>
<td>40 – 60 mg/dL</td>
<td>23.8</td>
<td>41.2</td>
<td>17.1</td>
</tr>
<tr>
<td>Total Cholesterol/100 PYE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>200 - 239 mg/dL</td>
<td>78.5</td>
<td>87.0</td>
<td>79.3</td>
</tr>
<tr>
<td>≥ 240 mg/dL</td>
<td>61.0</td>
<td>0</td>
<td>64.3</td>
</tr>
</tbody>
</table>

Grading based on ATPIII Classification

*Treatment group includes male subjects located in the US only

References


Disclosure: M. C. Genovese, Gilead, 5,Galapagos NV, 5,AbbVie, 5,Eli Lilly and Company, 5; A. Kavanaugh, Gilead Sciences, Inc, 5,Galapagos NV, 5,Pfizer Inc, 5,AbbVie, 5,Eli Lilly and Company, 5; K. Winthrop, Galapagos NV, 5,Pfizer Inc, 5,AbbVie, 5,Eli Lilly and Company, 5; M. Greenwald, Pfizer Inc, 5,Eli Lilly and Company, 5; L. Ponce, None; F. Enriquez Sosa, None; M. Stanislawchuk, None; M. Mazur, None; A. Spindler, None; R. Cseuz, None; N. Nikulenkova, None; M. Glowacka-Kulesz, None; I. Szombati, None; A. Dudek, None; N. Mozaffarian, Gilead Sciences, Inc, 1,Gilead Sciences, Inc, 3,Eli Lilly and Company, 1; J. Greer, Gilead Sciences, Inc, 1,Acteta Pharma, 1,Gilead Sciences, Inc, 3; X. Ding, Gilead Sciences, Inc, 1,Gilead Sciences, Inc, 3; P. Harrison, Galapagos NV, 1,Galapagos NV, 3; A. Van der Aa, Galapagos NV, 1,Galapagos NV, 3; R. Westhovens, Bristol-Myers Squibb, 2,Roche Pharmaceuticals, 2,CellTrion, 5,Galapagos NV, 5; R. Alten, Galapagos NV, 2.


Abstract Number: 1910

**ERAP1 Deficiency Implicates Long Peptides in Protection from HLA-B27-Induced Experimental Spondyloarthritis**

Tri Tran1, Tejpal Gill1, Joshua R. Bennett1, Vance Holt1, Sohee Hong2, Joel Taurog3 and Robert Colbert1, 1National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, 2National Institutes of Arthritis and Musculoskeletal and skin diseases, National Institutes of Health, Bethesda, MD, 3Dept Int Med-Rheum Dis Div, University of Texas Southwestern Medical Center, Dallas, TX

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 4:30PM-6:00PM

**Background/Purpose:** Common endoplasmic reticulum (ER) aminopeptidase 1 (*ERAP1*) haplotypes influence the risk of developing axial spondyloarthritis (SpA) in HLA-B27-positive individuals, with loss-of-function and reduced expression conferring protection.
ERAP1 increases the pool of short peptides, which are thought to be optimal for binding to most HLA class I molecules. The role of B27 in this model is not clearly defined, although misfolding and expression of cell surface dimers have both been implicated, while CD8+ T cells appear to be dispensible. Thus, the role of peptides in axial SpA remains unclear. We investigated the interaction between ERAP1 and HLA-B27 in the rat model of SpA.

**Methods:** ERAP1-deficient rats generated by genome editing were crossed with disease prone HLA-B27 transgenic (B27 Tg) rats (33-3 Tg locus), and B7 Tg rats as controls. The phenotype was monitored for up to 6 months. Colitis was assessed by stool and histology scores. Bone marrow-derived macrophages (BMM) were used to examine HLA class I by FACS and immunoprecipitation with conformation-specific antibodies. ER stress was assessed by quantitative PCR.

**Results:** ERAP1 deficiency reduced the prevalence of arthritis and orchitis by 64% and 58%, respectively (p<0.05), in male B27 Tg rats. Clinical colitis was unaffected, while histology scores were slightly increased in rats lacking ERAP1 (p<0.05). Wild type and B7 Tg rats with and without ERAP1 remained healthy. BMM from B27 Tg ERAP1-/- rats exhibited a 12-fold increase in cell surface B27 displaying long peptides (MARB4), a 40% and 50% increase in free heavy chains (FHC) and FHC dimers of B27, respectively (p<0.05), while folded complexes (ME1) were increased 25% (NS). Immunoprecipitation of total cellular folded and FHC revealed that ERAP1 deficiency reduced the pool of B27 FHC by 30%, including a 50% reduction in misfolded disulfide-linked and BiP-bound dimers, and increased the ratio of folded/free HC by 56% (p<0.05 for each). In contrast, for B7, total cellular FHC were increased 3-fold (p<0.05) by ERAP1 deficiency, and the ratio of folded/free HC was reduced by 60% (p<0.05). B27 upregulation results in the accumulation of misfolded, disulfide-linked dimers. ERAP1-deficiency resulted in a significant reduction in the accumulation of misfolded and BiP-bound B27 during upregulation. This was associated with attenuated activation of the unfolded protein response, with upregulation of Hsp5a and Ddit3 reduced by up to 50%, and attenuated Xbp1 splicing (p<0.05).

**Conclusion:** ERAP1-deficiency protects B27 Tg line 33-3 rats from arthritis and orchitis, without reducing the severity of gut inflammation. We demonstrate that ERAP1 deficiency promotes B27 folding and reduces misfolding and its consequences, while increasing the expression of cell surface dimers and aberrant long peptide complexes. Interestingly, ERAP1 deficiency impairs the formation of folded B7 complexes, consistent with the importance of short peptides for most other HLA alleles. Together, these results suggest that the preservation of long peptides in the absence of ERAP1 may rescue B27 from misfolding, and identify ERAP1 as a potential target for therapeutic intervention in SpA.

**Disclosure:** T. Tran, None; T. Gill, None; J. R. Bennett, None; V. Holt, None; S. Hong, None; J. Taurog, Abbvie; Anges; Inc; Celgene; S. Hong, None; J. Taurog, Abbvie; Anges; Inc; Celgene; 5. R. Colbert, None.


**Abstract Number:** 1911

**Impaired Control of Autoreactive T Cell Expansion Is Coupled with Type-1 Regulatory T Cell Deficiency in BALB/c ZAP70W163C Mutant Mice**

M. Arifur Rahman1, Daphne Montizaan2, Zaied Ahmed Bhuyan3, Linda Rehaume3 and Ranjeny Thomas4, 1The University of Queensland Diamantina Institute, The University of Queensland, Brisbane, Australia, 2The University of Groningen, Groningen, Netherlands, 3The University of Queensland Diamantina Institute, Translational Research Institute, Brisbane, Australia, 4Dendright Pty Ltd, Brisbane, Australia

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Spondyloarthopathies and Psoriatic Arthritis – Pathogenesis, Etiology

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 4:30PM-6:00PM

**Background/Purpose:** In the context of reduced TCR signaling in the BALB/c ZAP70W163C mutant (SKG) mouse, development of arthritis, psoriasis-like skin inflammation and ileitis after intra-peritoneal injection of microbial β-glucan (curdlan), is characterized by an overwhelming increase of autoreactive CD4+ T cells in the peripheral organs. Inflammatory disease in SKG mice is observed within 7 days in the intervertebral joint of the upper tail, sacroiliac joints and Achilles tendon. However, curdlan-triggered arthritis in BALB/c mice is mild to absent. The mechanism by which systemic microbial-derived adjuvant promotes T-cell-mediated tissue inflammation in SKG mice but not in BALB/c mice is poorly understood. Here, we studied the role of peripheral Type-1 regulatory T (Tr1) cells in regulating activation and proliferation of autoreactive T cells in the genetically predisposed mice model of Spondyloarthritis (SpA).
**Methods:** To elucidate the dynamics of post-curdlan CD4+ T cell expansion and regulation, syngeneic luciferase-expressing CD4+ T cells were magnetically sorted from SKG.luc+ mice, adoptively transferred, and tracked in vivo post-curdlan in SKG and BALB/c mice using in vivo bioluminescence imaging. Development of arthritis was monitored in these mice by measuring width of the ankles, wrists and footpads using calipers. Flow cytometry was used to phenotypically characterize effector and regulatory T cell populations. Tr1 cells were generated from naïve CD4+ T cells in vitro using anti-CD3/anti-CD28 and IL-27.

**Results:** After transfer of SKG.luc+ CD4+ T cells to SKG hosts, bioluminescent images showed CD4+ T cell accumulation in spleen and inguinal lymph nodes 3 days after curdlan, and traffic to joints, tail, and ears at day 7. Subsequently the signal continued to expand as arthritis increased in severity. After transfer of SKG.luc+ CD4+ T cells to BALB/c hosts, signals increased in spleen and inguinal lymph nodes 7 days after curdlan, but subsequently disappeared within 1 week. Furthermore, T cells expanding in SKG mice were significantly more likely to produce IL-17 than in BALB/c mice. In addition, the frequency of CD4+Foxp3+ regulatory T (Treg) cells were significantly higher in SKG mice, both in naïve and after curdlan, compared to BALB/c mice. In contrast, the frequency of CD4+Foxp3-IL-10+IFN-γ+ Tr1 regulatory T cells was significantly lower in SKG than BALB/c mice. Differentiation of naïve SKG or BALB/c CD4+ T cells to Tr1 cells in vitro in the presence of IL-27 was comparable.

**Conclusion:** These data indicate that autoreactive Th17 cells first expand as a result of autoantigen presented in inguinal lymph nodes in SKG and BALB/c mice. While they are tightly regulated in BALB/c hosts, they expand and rapidly infiltrate joints and skin in SKG hosts, despite increased frequencies of Foxp3+ Treg cells. In contrast, Tr1 cell differentiation is deficient in SKG mice in vivo but can be restored in vitro with addition of IL-27. The data suggest that while IL-27 signaling is intact in ZAP70W163C mutant T cells, IL-27 production is reduced and contributes to the lack of peripheral tolerance in SKG hosts.

**Disclosure:** M. A. Rahman, None; D. Montizaan, None; Z. A. Bhuyan, None; L. Rehaume, None; R. Thomas, None.


**Abstract Number:** 1912

### Broad Immunophenotyping Results: CCR10 Expressing CD8 T Cells Distinguish Psoriatic Arthritis from Psoriasis Limited to Skin Involvement

**Emmerik F.A. Leijten**1,2, Tessa S. van Kempen1,2, Michel A.M. Olde Nordkamp1,2, Fleurieke H. Verhagen2,3, Sanne Hiddingh2,3, Jonas J.W. Kuiper2,3, Marianne L. Boes2,4 and Timothy R.D.J. Radstake1,2, 1Department of Rheumatology & Clinical Immunology, University Medical Center Utrecht, Utrecht, Netherlands, 2Laboratory of Translational Immunology, University Medical Center Utrecht, Utrecht, Netherlands, 3Ophthalmology, University Medical Center Utrecht, Utrecht, Netherlands, 4Department of Pediatrics, University Medical Center Utrecht, Utrecht, Netherlands

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017  
**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology  
**Session Type:** ACR Concurrent Abstract Session  
**Session Time:** 4:30PM-6:00PM

**Background/Purpose:** Studies that compare the immune cell phenotype or function from patients with psoriatic arthritis (PsA) to patients with psoriasis limited to cutaneous involvement (Pso) are exceedingly scarce, particularly in patients without immunomodulatory medications that confound results. A head-to-head comparison of the immune cell composition in PsA and Pso is an essential step to understand the development of rheumatic manifestations in patients with psoriasis.

**Methods:** Blood samples and clinical parameters were collected from 23 healthy controls (HC), 21 patients with psoriasis in whom psoriatic arthritis was excluded by a rheumatologist (Pso), 21 patients with psoriatic arthritis meeting CASPAR criteria (PsA) and 16 patients with ankylosing spondylitis meeting ASAS criteria but without psoriasis (AS). The Pso and PsA cohorts were matched for age, gender, CRP, ESR, psoriasis duration and psoriasis skin severity. All patients were free from biological or conventional DMARD therapy. Using a highly standardized flow-cytometric protocol the peripheral blood mononuclear cells (PBMCs) from patients and controls underwent extensive extracellular and intracellular immunophenotyping capable of detecting over 110 different myeloid and lymphoid cell subsets / populations. In synovial fluid (SF) samples from patients with psoriatic arthritis the level of CCL27 was determined using Luminex Technology and the presence of CCR10+ CD8 T cells was evaluated by flow-cytometry.
**Results:** The overall phenotype and immune cell composition showed remarkable overlap in PsA and Pso, with both cohorts characterized by an increase in the frequency of regulatory T cells, an increase in IL-17A & IL-22 co-producing CD4 and CD8 T cells, a decrease in plasmacytoid dendritic cells, and a decrease in mucosal-associated invariant T (MAIT)-like cells. Only one specific cell population differentiated the PsA from Pso cohort: CCR10+ CD8 T cells, being enriched in PsA as compared to Pso (Figure 1). These CCR10+ CD8 T cells had an effector memory status, were CXCR3-CCR6- and predominantly co-expressed CCR4. While the CCR4+ CD8 T cell frequencies were positively correlated to psoriasis skin severity, the CCR10+ CD8 T cell frequencies were not related to skin severity. Analysis of SF samples from psoriatic arthritis patients confirmed the presence of CCL27, the ligand for CCR10 receptor, and the expression of CCR10 on SF CD8 T cells.

**Conclusion:** A broad immunophenotyping strategy has revealed a potentially novel role for CD8 T cells expressing CCR10 to mediate the progression from cutaneous disease to joint disease in psoriatic arthritis. Further functional studies are needed to investigate the role these cells play in the different compartments affected by the disease.

**CD8 T cells expressing CCR10**

![Graph showing the frequency of memory CD8 T cells expressing CCR10](image)

*Figure 1:*

The frequency of memory CD8 T cells that expressed CCR10 was elevated in PsA as compared to Pso (p=0.01) and HC (p<0.001), with a trend towards higher levels in PsA as compared to AS (p=0.05). The frequency of memory CD8 T cells expressing CCR10 was also significantly higher in PsA compared to Pso and HC when calculated as % of total CD8 T cells (data not shown).

**Disclosure:** E. F. A. Leijten, None; T. S. van Kempen, None; M. A. M. Olde Nordkamp, None; F. H. Verhagen, None; S. Hiddingh, None; J. J. W. Kuiper, None; M. L. Boes, None; T. R. D. J. Radstake, None.


**Abstract Number:** 1913

**Inter-Omic Analysis Reveals Functional Relationship between Diverse Gut Microbiota and Dysregulated Host Immune Response in HLA-B27-Mediated Experimental Spondyloarthritis**

Tejpal Gill¹, Stephen R. Brooks², Mark Asquith³, James T. Rosenbaum⁴ and Robert Colbert⁵, ¹National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, ²Biodata Mining and Discovery Section, Office of
SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: HLA-B27 has been hypothesized to alter gut microbiota and host-microbe interactions to promote spondyloarthritis (SpA). In HLA-B27 transgenic (HLA-B27 Tg) rats with experimental SpA, we have reported that HLA-B27 effects on gut microbiota diverge on different genetic backgrounds despite common patterns of immune dysregulation. Using an integrative analysis of gut microbiome and host transcriptome (inter-omics), we asked which microbes correlate with immune dysregulation on different genetic backgrounds, and whether they have similar functional implications.

Methods: We correlated the relative frequency of gut microbes determined by 16S rRNA gene sequencing, with host gene expression determined by RNAseq, for cecum and colon samples derived from 193 HLA-B27 Tg and wild type (WT) rats from Dark Agouti (DA), Lewis (LEW) and Fischer (F344) backgrounds. Microbes with a relative abundance of >0.1% in at least one sample, and genes with expression values (reads per kilobase million; RPKM) >1 in at least one sample and a coefficient of variation >0.8 across the dataset were included. Significant correlation coefficients (r) between the microbial relative frequency and transcript RPKM value (p<0.05) were used to identify relevant relationships. PICRUSt was used to predict microbial functions based on metagenomic profiles, which were then correlated with disease severity (histology scores), and significant metabolic perturbations associated with inflammation were identified (q<0.05 based on FDR-corrected p-values was used).

Results: Inter-omic analysis revealed several microbes associated with dysregulated cytokines driving inflammatory response pathways (e.g. IL-23, IL-17, IL-12, IFN-γ, TNF) in both cecum and colon. While some microbes were differentially abundant on both LEW and F344 backgrounds (Clostridium, Ruminococcus), other differences were unique to either LEW (Prevotella, Dehalobacterium, Sutterella) or F344 (Akkermansia, rc4-4, Coprococcus, Blautia). Interestingly, many microbes that were strongly correlated with immune dysregulation (e.g. Granulicatella, Staphylococcus and members of family Lachnospiraceae) were not identified by analyzing effects of HLA-B27 alone. Metabolic functions of microbes determined by PICRUSt revealed involvement of similar pathways (e.g. fatty acid and glycan biosynthesis, steroid biosynthesis) in both HLA-B27 Tg LEW and HLA-B27 Tg F344 rats, despite dramatic differences in microbial dysbiosis.

Conclusion: Inter-omic analysis of gut microbiota and the host immune response in experimental SpA provides an unprecedented view of the complexity of microbial dysbiosis associated with HLA-B27 and gut inflammation. Perturbation of common metabolic pathways by divergent gut microbiota on different genetic backgrounds during inflammation suggests important functional overlaps that may be key to evoking similar host immune dysregulation. These results suggest that effects of HLA-B27 in the human population will depend on other genetic factors, and that microbial communities and their function may be more important than individual microbes.

Disclosure: T. Gill, None; S. R. Brooks, None; M. Asquith, None; J. T. Rosenbaum, AbbVie, UCB, XOMA, Santen, Novartis, Gilead, Mallinckrodt, Eyevensys, Theravance, Cavtherx, Portage, Topivert, Regeneron, Allergan, and Sanofi, 5,Alcon Research Institute, 2; R. Colbert, None.


Abstract Number: 1914

Discovery of a Novel CD8+ T Cell Population in Ankylosing Spondylitis Implicates Gut-Joint Trafficking in the Disease

Zoya Qaiyum1,2, Eric Gracey3,4, Yuchen Yao3,4 and Robert D Inman5, 1Genetics and Development, Krembil Research Institute, Toronto Western Hospital, Toronto, ON, Canada, 2Department of Immunology, University of Toronto, Toronto, ON, Canada, 3Krembil Research Institute, Toronto Western Hospital, Toronto, ON, Canada, 4University of Toronto, Toronto, ON, Canada, 5Immunology and Institute of Medical Science, Toronto Western Hospital, University of Toronto, Toronto, ON, Canada

First publication: September 18, 2017
Background/Purpose: Ankylosing spondylitis (AS) has a strong connection with gut inflammation: 10% of AS patients have inflammatory bowel disease (IBD) and 60% have subclinical ileal inflammation. Further, there is strong overlap between genetic susceptibility to IBD and to AS. This suggests that immune events in the gut may impact on joint inflammation but what directs cells in the gut-joint axis is undefined. For this reason, we are examining trafficking molecule expression on immune cells. Identification of trafficking molecules at a single-cell level has been possible through flow cytometry, but spectral overlap limits the number of parameters that can be tested simultaneously. Advances in single-cell mass cytometry have led to platforms such as Cytometry by Time-of-flight (CyTOF) that utilize stable lanthanide metal-conjugated antibodies bound to cells. This eliminates spectral overlap, thereby allowing for analysis of >30 parameters/cell. Our objectives are 1) to assess differential expression patterns of trafficking molecules between AS patients and controls, and 2) to generate tissue-specific cellular signatures.

Methods: Male subjects under 40 years of age fulfilling the mNY criteria were recruited from a longitudinal AS cohort. The following cells were surface stained using a 36-marker antibody panel: (i) Peripheral blood mononuclear cells (PBMC) from 30 AS patients, 20 healthy controls and 18 rheumatoid arthritis (RA) patients; (ii) Synovial fluid mononuclear cells (SFMC) from 10 AS patients and 4 RA patients. After acquiring on CyTOF2, data were subjected to SPADE and viSNE analysis for data visualization and Citrus and FlowJo for statistical analysis.

Results: Few differences were detected in PBMC trafficking marker expression between patients and controls. In AS SFMC mature CD4+ T cells, CXCR4 was reduced but CCR2, CCR5 and CD49a median expression was elevated (FDR<0.05). Furthermore, CCR2, CCR5 and CD49a were co-expressed in CD4+CD45RO+ cells. Mature CD8+ T cells were increased in frequency in AS SFMC, with significant changes in their phenotype: β7+, CD103+, CD18+, CD29+ and CD49a+ integrin expression was increased in CD8+CD45RO+ cells in AS SFMC vs paired AS PBMC (mean 9.05% vs 0.97%, p=0.0061), whereas similar comparison of RA SFMC vs RA PBMC showed less significant differences (mean 4.5% vs 0.63%, p=0.0578).

Conclusion: Analysis using mass cytometry revealed disease- and tissue-specific alterations in trafficking marker expression on AS patient T cells. We identified a novel integrin manifesting CD8+ mature T cell subset (CD49a+CD103+β7+CD29+CD18+) with some specificity for AS. Further experiments to determine similar expression profile on gut tissue biopsies from AS patients, as well as murine gut and joint tissues from experimental AS, are in progress to examine the arthritogenic potential of these cells. CyTOF represents an innovative new technology which can provide new insights into the immune mechanisms linking inflammation in the AS gut and the joint. These insights could lay the groundwork for innovative immunotherapy for AS in the future.

Disclosure: Z. Qaiyum, None; E. Gracey, None; Y. Yao, None; R. D. Inman, None.


Abstract Number: 1915

Gut-Derived TNF As Risk Factor for the Development of Sacroiliac Inflammation

Karlijn Debusschere1, Heleen Cypers2, Peggy Jacques3, Filip van Den Bosch4, Thomas Renson5, Don Souza6, Martha Brown6, Gerald Nabozny7, Devin Dove6, Alexander Klimowicz8 and Dirk Elewaut9, 1Ghent University - VIB, Ghent, Belgium, 2Laboratory for Molecular Immunology and Inflammation, Department of Rheumatology, VIB, Ghent University and Ghent University Hospital, Ghent, Belgium, 3Ghent University Hospital, Ghent, Belgium, 4Rheumatology, Ghent University Hospital, Gent, Belgium, 5Rheumatology, Ghent University Hospital, GENT, Belgium, 6Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT, 7gerald.nabozny@boehringer-ingelheim.com, Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT, 8Department of Immunology and respiratory discovery research, Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT, 9VIB Inflammation Research Center, University of Ghent, Ghent, Belgium

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose:

An intriguing link exists between gut and joint inflammation in spondyloarthritis (SpA). About 50% of patients has subclinical (eg. microscopic) gut inflammation, which represents a risk factor for development of Crohn's disease, sacroiliac inflammation and evolution in to Ankylosing Spondylitis. However, the underlying mechanisms are still relatively poorly understood. Our goal was to examine the relationship between TNF, microscopic gut inflammation and axial inflammation using human samples and a novel mouse model. We speculated that TNF in the gut represents an important risk factor for disease severity and progression in SpA.

Methods:

We examined in situ expression of TNF, TNFR1 and TNFR2 using triple in situ hybridisation in gut biopsies of human SpA patients. Furthermore, we generated intestinal specific human TNF transgenic mice, in which hTNF is under control of a rat iFABP (fatty acid binding protein) promoter, generating a mouse-model over-expressing human TNF in the ileum. These mice, together with wild type littersmates, were evaluated for the development of arthritis up until the age of 13 weeks after which they were euthanized and ankle and sacroiliac joints as well as ileum were processed for histology.

Results:

There was a marked upregulation of TNF in inflamed versus non- inflamed gut biopsies of human SpA patients. We also noted a predominant upregulation of TNFR1 on intestinal epithelium and TNFR2 in lamina propria respectively. Of interest, IL-17 and IL-23 were also markedly increased while IL-22 was most abundant in chronically inflamed samples. In line with this, we found that patients with gut inflammation had a higher need for anti-TNF therapy and their degree of clinical response after anti-TNF was also markedly higher. Our transgenic mice exhibited a runt phenotype and hallmarks of inflammatory bowel disease, including increased intestinal permeability and inflammation compared to their wild-type littersmates. While in peripheral joints no clear signs of arthritis were observed, the sacroiliac joints in transgenic mice, by contrast, showed marked signs of inflammation as well as bone erosion and destruction.

Conclusion:

These data propose a new paradigm that gut-derived TNF is sufficient to trigger sacroiliitis and provide an alternate explanation on the relationship between gut inflammation, evolution to inflammatory bowel disease and axial inflammation in SpA.

Disclosure: K. Debusschere, None; H. Cypers, None; P. Jacques, None; F. van Den Bosch, AbbVie Inc., Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer and UCB, 5,AbbVie Inc., Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer and UCB, 8; T. Renson, None; D. Souza, Boehringer Ingelheim, 3; M. Brown, Boehringer Ingelheim, 3; G. Nabozny, Boehringer Ingelheim, 3; D. Dove, Boehringer Ingelheim, 3; A. Klimowicz, Boehringer Ingelheim Pharmaceuticals Inc, 3; D. Elewaut, Scientific Research Flanders; Research Council Ghent University; Interuniversity Attraction Pole., 2,Boehringer Ingelheim; Pfizer; UCB; Merck; Novartis; Janssen; Abbvie, 5.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/gut-derived-tnf-as-risk-factor-for-the-development-of-sacroiliac-inflammation

Abstract Number: 1916

The Interferon Gamma Release Assay Is a Novel Predictor of Disease Activity in Systemic Lupus Erythematosus

Jenna Thomason¹, Christian Lood² and Grant Hughes³, ¹Medicine, University of Washington, Seattle, WA, ²Division of Rheumatology, Division of Rheumatology, Department of Medicine, University of Washington, Seattle, WA, ³Medicine/Rheumatology, University of Washington, Seattle, WA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment III: Biomarkers
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM
**Background/Purpose:** Interferon gamma (IFN-G) is a critical cytokine for defense against intracellular pathogens; it is also involved in the pathogenesis of systemic lupus erythematosus (SLE). The IFN-G release assay (IGRA) estimates probability of latent tuberculosis (TB) infection (LTBI) based on whole-blood IFN-G release upon exposure to TB antigen, mitogen (IGRA-MT) or no stimulation (IGRA-NL). We previously observed that elevated IGRA-NL values (representing spontaneous IFN-G release, SIR) are associated with a limited set of diagnoses, including LTBI and SLE. Here, we examine the clinical and immunologic correlates of SIR in a cohort of SLE patients undergoing IGRA testing. We hypothesize that SIR is associated with active SLE and select disease manifestations.

**Methods:** We queried a clinical data repository (2010–2016) from a U.S. academic medical center for subjects with a diagnosis of SLE, a positive ANA and at least one IGRA result (n=167). SLE classification by SLICC criteria was confirmed by chart review (n=99). Of these 99, 53 had sufficient data to calculate a complete SELENA-SLEDAI (SLEDAI) score at the time of IGRA testing. We then assessed relationships between IGRA-NL, IGRA-NL/MT ratios, SLEDAI and related clinical/immunologic variables using univariate (Fisher’s Exact, Kruskal-Wallis, Mann Whitney tests) and multivariate (linear regression) analyses.

**Results:** The cohort of 99 patients was 85% female, 71% non-white, with a median (range) age of 36 years (18–84) and disease duration of 3.9 years (0–39). Median (range) for SLEDAI (n = 53) was 12 (0–33). Compared to subjects without SLEDAI scores, subjects with SLEDAI scores had significantly shorter disease duration and higher IGRA-NL/MT ratios. Linear regression analysis revealed a significant positive association between IGRA-NL/MT ratios and SLEDAI (r = 0.53, p < 0.0001) that was stronger than that of IGRA-NL (r = 0.21, p = 0.0616) or anti-dsDNA (r = 0.32, p = 0.0107). The linear association between IGRA-NL/MT and SLEDAI remained significant (p = 0.031) after controlling for all non-SLEDAI variables significantly associated with upper-half IGRA-NL/MT ratios (history of APLA/lupus inhibitor, low complement, Coomb’s positivity, current prednisone 5-20 mg/d, current/past hydroxychloroquine use). SLEDAI features positively associated with upper-half IGRA-NL/MT were proteinuria (p = 0.0028), rash (p=0.0394) and fever (p=0.0030). Using a 50th percentile cutoff, IGRA-NL/MT could predict active disease (SLEDAI > 6) with a sensitivity of 77.5% and a specificity of 61.5% (p=0.0128), which was superior to either anti-dsDNA or IGRA-NL (neither statistically significant).

**Conclusion:** In our cohort of SLE patients undergoing IGRA testing, IGRA-NL/MT ratios correlated with and predicted active disease better than either anti-dsDNA or IGRA-NL. Correlation between IGRA-NL/MT and select disease features supports a pathogenic role for IFN-G activation in renal, dermatologic and systemic manifestations of SLE. Thus, the IGRA test may represent a readily available assay with unique biomarker potential in SLE.

**Disclosure:** J. Thomason, None; C. Lood, None; G. Hughes, None.

**Abstract Number:** 1917

**A Novel Type I Interferon Biomarker on B Cell Predicts with Disease Activity in SLE and Can be Measured By Cell Surface Tetherin (CD317)**

Yasser M El-Sherbiny1,2,3, Md Yusaiful Md Yuso1, Antonios Psarras1, Elizabeth M.A. Hensor1, Kumba Kabba1, Alaa Mohamed1,4, Miriam Wittmann5, Paul Emery5,6 and Edward M Vital1,5,7, 1Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom, 2NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals, NHS Trust, Leeds, United Kingdom, 3Clinical Pathology dept., School of Medicine, Mansoura University, Mansoura, Egypt, 4Faculty of Medicine, Assiut University, Department of Rheumatology and Rehabilitation, Assiut, Egypt, 5NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom, 6University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom, 7University of Leeds, Leeds, United Kingdom

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment III: Biomarkers

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 4:30PM-6:00PM

**Background/Purpose:**
SLE is an IFN-I-mediated disease with dysregulated handling of self-nuclear antigens triggering anti-viral immune mechanisms. The level of IFN-I activity appears to stratify for disease severity and therapy response but existing studies using IFN-stimulated gene (ISG) expression signatures weakly correlates with clinical features. ISG expression influenced by cellular composition of sample and individual cell responses. CD317/Tetherin is a cell surface protein encoded by the interferon-stimulated gene BST2. So we aimed to develop a fast, convenient assay to measure cell-specific IFN-I suitable for analysis of large cohorts of patients using flow cytometry correlates with disease activity and predicts clinical flare.

**Methods:**

We developed a flow cytometric assay for cell-specific IFN-I response using tetherin, as well as ISG gene expression score derived from 18 well known. FACS sorting was used to evaluate cell-specific interferon response by both assays. IFN-I biomarkers were then evaluated against diagnosis, disease activity in a discovery cohort of 156 SLE patients with 30 ACPA+ANA- RA (DAS28>3.2) and 22 healthy controls. A longitudinal validation cohort of 80 patients with monitoring of tetherin in an independent routine diagnostic laboratory was recruited to confirm findings and test prediction of flares.

**Results:**

*In vitro*, ISG expression score predominantly reflected monocyte signal and many ISGs responded to both IFN-α and IFN-γ. Flow cytometric analysis of tetherin (BST2) accurately determined cell-specific response to IFN-I in a dose-responsive manner and was more selective for IFN-I.

In the discovery cohort, B cell tetherin was associated with diagnosis and clinical disease activity equally or more closely than gene expression score or monocyte tetherin. Memory B cell tetherin was increased with renal (p=0.005) or haematological (p=0.005) activity with no differences in ISG score for these domains (p=0.152, p=0.989 respectively). The validation cohort confirmed the relationship between B cell tetherin and disease activity and also, showed that higher B cell tetherin predicted increased risk of future clinical flares. (Fig 2)
Conclusion:

The B cell response to IFN-I predicts clinical features of SLE, and tetherin provides a convenient, validated method to analyse this pathway in routine clinical practice. Tetherin is also a tool for future research in cell-specific IFN-I response in a broad spectrum of other diseases.

Disclosure: Y. M. El-Sherbiny, None; M. Y. Md Yusof, None; A. Psarras, None; E. M. A. Hensor, None; K. Kabba, None; A. Mohamed, None; M. Wittmann, None; P. Emery, See notes, 5; E. M. Vital, Roche, GSK and AstraZeneca., 2.

Abstract Number: 1918

**Blood Levels of Complement Split Product iC3b and C3 Outperform Traditional Biochemical Measures of SLE Disease Activity in Associating with Active and Clinically Meaningful Changes**

Alfred Kim¹, Deepali Sen², Vibeke Strand³, Qiang John Fu⁴, Nancy Mathis¹, Martin Schmidt⁵, Robin Bruchas⁶, Nick Staten⁶, Paul Olson⁶, Chad Stiening⁶ and John Atkinson¹,².¹Rheumatology, Washington University School of Medicine, Saint Louis, MO, ²Division of Rheumatology, Washington University School of Medicine, St. Louis, MO, ³Stanford University, Palo Alto, CA, ⁴Biostatistics, Saint Louis University, Saint Louis, MO, ⁵Kypha, Inc., St. Louis, MO, ⁶Kypha, Inc., Saint Louis, MO

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment III: Biomarkers
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: A major unmet need in SLE is the identification of a biomarker that consistently tracks with disease activity. One current approach is measuring complement activation by evaluating consumption of serum C3 and C4. However, since they are acute phase reactants, interpretation of these levels is challenging as serum levels may not decrease until late in a disease flare. iC3b is a proteolytically derived molecule of C3b, and increases with complement activation. iC3b/C3 ratio measures complement consumption relative to production, which may provide for a more accurate assessment of complement activation. We hypothesize that blood iC3b and iC3b/C3 levels will provide a more specific and reliable marker of complement activation and disease activity in SLE.

Methods: 159 adult SLE patients were enrolled in this prospective, longitudinal, observational study. 83 patients with 3-7 study visits were used for this longitudinal analysis. C3 and C4 were measured by nephelometry; iC3b by a lateral flow assay using an investigational medical device. SLE disease activity was measured using the SLEDAI 2K Responder Index-50 instrument. Statistical analyses were performed using SAS v9.4. Multilevel regression models examined associations for SLE disease activity. Ordinal logistic
regression models with generalized estimating equation modeling (GEE) examined associations for clinically meaningful changes since the outcome variable is ordinal. Odds ratios and 95% confidence intervals were estimated using Proc GLIMMIX and Proc GENMOD. Receiver operator curves and areas under the curve were performed using iC3b/C3 ratios, C3, C4, and dsDNA levels.

Results: Blood levels of iC3b, C3, iC3b/C3 ratio, C4, dsDNA, and prednisone use each correlated with SLE disease activity (Figure 1A). Multilevel multiple logistic regression analysis revealed only iC3b/C3 ratio, dsDNA levels, and prednisone use were significant predictors of disease activity (Figure 1B). To determine whether iC3b/C3 ratio can predict clinically meaningful changes in SLE disease activity, we evaluated the interpatient longitudinal associations between clinical deterioration, stability, and improvement and iC3b/C3 ratios. Only iC3b/C3 ratio significantly predicted clinically meaningful changes in disease activity in multivariate regression analysis. iC3b/C3 ratio also discriminated for active versus inactive disease (AUC=0.657, 95% CI=0.604-0.710).

Conclusion: In this prospective, longitudinal study, blood iC3b/C3 ratios are more strongly associated with active SLE disease compared to other traditional biomarkers of disease activity. Likewise, iC3b/C3 ratio is predictive of clinical meaningful changes in SLE disease activity. Finally, iC3b/C3 ratio discriminated for active SLE. These data suggest iC3b/C3 ratio may provide clinical utility as a biomarker for SLE disease activity.

Figure 1: iC3b/C3 ratio correlated with active SLE disease

Disclosure: A. Kim, Kypha, Inc., 2,Exagen Diagnostics, 5,NIH/NIAMS, 2,Department of Defense, 2,Rheumatology Research Foundation, 2,Doris Duke Foundation, 2,Midwest Strategic Pharma-Academic Research Consortium, 2; D. Sen, None; V. Strand, AbbVie, Amgen, AstraZeneca, BMS, Celgene, Genentech, GSK, Janssen, Lilly, Novartis, Pfizer, Regeneron, Sanofi, and UCB, 5,AbbVie, Amgen, AstraZeneca, BMS, Celgene, Genentech, GSK, Janssen, Lilly, Novartis, Pfizer, Regeneron, Sanofi, and UCB, 9; D. Sen, None; V. Strand, AbbVie, Amgen, AstraZeneca, BMS, Celgene, Genentech, GSK, Janssen, Lilly, Novartis, Pfizer, Regeneron, Sanofi, and UCB, 5,AbbVie, Amgen, AstraZeneca, BMS, Celgene, Genentech, GSK, Janssen, Lilly, Novartis, Pfizer, Regeneron, Sanofi, and UCB, 9; Q. J. Fu, None; N. Mathis, None; M. Schmidt, Kypha, Inc., 3; R. Bruchas, Kypha, Inc., 3; N. Staten, Kypha, Inc., 3; P. Olson, Kypha, Inc., 3; C. Stiening, Kypha, Inc., 3; J. Atkinson, NIH/NIGMS, 2,Midwest Strategic Pharma-Academic Research Consortium, 2,Kypha, Inc., 5,Gemini Therapeutics, Inc., 5,Compliment Corporation, 5,Cellxide Therapeutics, 5,CLInical Pharmacy Services, CDMI, 5,OMeros, 5,Achillion Pharmaceuticals, Inc., 5,TRUE North Therapeutics, Inc., 5,biomarin Pharmaceutical Inc., 5,Annexon Biosciences, 5.


Abstract Number: 1919

The SLE-Key Test Detects an SLE Serologic Signature That Persists over Time and Is Independent of Disease Activity

Chaim Putterman1, Michelle Petri2, Roberto Caricchio2, Jim C. Oates4, Pennina Safer5, Keren Jakobi-Brook5, Rachel Sorek5, Ilana Gluzman5, Steve Wallace6 and Irun R. Cohen6, 1Division of Rheumatology, Albert Einstein College of Medicine, Bronx, NY, USA, Bronx, NY, 2Medicine (Rheumatology), Division of Rheumatology, Johns Hopkins University School of Medicine, MD, USA, Baltimore, MD, 3Temple Lupus Clinic, Temple University, Philadelphia, PA, USA, Philadelphia, PA, 4Division of Rheumatology & Immunology, Department of Medicine, Medical University of South Carolina, Charleston, SC, 5ImmunArray Ltd., Rehovot, Israel, Rehovot, Israel, 6ImmunArray Inc., VA, USA, Richmond, VA, 7Weizmann Institute of Science, Rehovot, Israel, Rehovot, Israel

First publication: September 18, 2017

SESSION INFORMATION
Background/Purpose: We have developed the iCHIP\textsuperscript{1,2} to profile repertoires of serum autoantibodies. The first iCHIP application was the SLE-key RuleOut test\textsuperscript{3,4}, to rule out a diagnosis of SLE with 94% sensitivity, 75% specificity, and 93% negative predictive value (NPV). In current study we asked whether the SLE-key test results are stable over time, and whether the test results can be used as a serologic signature of lupus which is independent of treatment and/or disease activity.

Methods: We determined the SLE-key scores for 197 paired serum samples submitted by 4 independent academic lupus centers. SLEDAI scores at the time of blood draw ranged from 0 to 22. The mean absolute SLEDAI difference between the paired samples was 6.2±3.4; 60% of pairs manifested a decrease in SLEDAI score at time point 2 (T2) relative to time point 1 (T1), and 40% showed an increase. T2-T1 time interval ranged from several weeks to 12 years (mean 1.5 ± 2.3 years). The sensitivity of the SLE-key score between T1 and T2 to technical variability was determined independently. Subjects exhibiting score changes of more than 2SD were defined as “changers”, and within 2SD were classified as “stable” (Figure 1).

Results: The SLE-Key test identifies an SLE-specific serologic signature based on a profile of IgG and IgM autoantibodies to a combination of two nucleic acids (complex ssDNA and a defined oligonucleotide) and three nuclear antigens (u1snRNP, Smith, and histone). This signature was found to be stable (within 95% confidence) in 71.6% (141/197) of subjects. Moreover, 84% (47/56) of the “changers” had no resultant change in their SLE-key RuleOut status (i.e. “Ruled Out” or “Not Ruled Out”). Of the remaining 9 patients, 7 changed from Not Ruled Out at T1 to Ruled Out at T2, and 2 subjects changed from SLE Ruled Out at T1 to Not Ruled Out at T2. The stability of the signature was independent of age, race, and time post diagnosis or between sampling. Furthermore, the signature was also independent of SLEDAI score.

Conclusion: The SLE-key RuleOut test detects a serologic signature which remains stable, irrespective of time or SLEDAI in >70% of subjects. This signature may therefore be helpful clinically to confirm a historical diagnosis of SLE in patients that currently have low disease activity. Even among the “changers”, the large majority had no change in their SLE-key RuleOut status. The stability of this signature over time indicates that it functions as a biomarker of SLE, but may not reflect disease activity. We are currently studying the possible reasons for a changing score in the remaining 30% of subjects, and the differences between the “changers” and the “stable” subjects.

References

\textsuperscript{1} Fattal et al; Immunology 2010 \textsuperscript{2}Cohen IR, LOA 2016 \textsuperscript{3}Putterman et al; J Immunol Methods, 2016 \textsuperscript{4}Massenburg et al; LOA 2017

Acknowledgements: authors wish to acknowledge Cohen-Gindi O, Lerner M, Tarnapolski O, Blumenstein Y, Javaherian A, Pitts J, Barton M and Wong E
Tacrolimus Induces Remission in Refractory and Relapsing Lupus Nephritis By Decreasing P-Glycoprotein Expression and Function on Peripheral Blood Lymphocytes

Vikas Gupta, Sukesh Edavalath, Mohit Kumar Rai, Harshit Singh, Saurabh Chaturvedi and Vikas Agarwal, Clinical Immunology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment III: Biomarkers
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose:
About 15-30% of Lupus Nephritis (LN) patients do not respond to first-line immunosuppressive therapy. P-glycoprotein (P-gp) mediated efflux of corticosteroids (CS) may contribute to the treatment unresponsiveness. Tacrolimus is a P-gp inhibitor and hence, may overcome this resistance. We, therefore, aimed to study the response to Tacrolimus, along with the expression and function of P-gp on peripheral blood lymphocytes (PBL) in patients with refractory and relapsing proliferative (ISN/RPS Class III/IV) Lupus Nephritis.

Methods:
We enrolled 12 refractory/relapsing LN patients (6 patients refractory to CYC based regimens and 6 patients with renal relapse) and treated them with CS + Tacrolimus (2-3 mg/day) for 6 months. Expression and function of P-gp on PBL was measured by flow cytometry (as relative fluorescence index, RFI) before and 3 months after Tacrolimus therapy. P-gp expression and function, before Tacrolimus therapy, was also compared with that in 16 LN patients who were naive to immunosuppressive drugs and CS (treatment-naive LN patients). Renal response was assessed according to ACR response criteria after 3 and 6 months of Tacrolimus therapy. Renal disease activity was measured by renal SLEDAI (rSLEDAI). The data (median and IQR) was analysed using non-parametric tests.

Results:
P-gp expression and function on PBL of refractory/relapsing LN patients before Tacrolimus therapy was significantly increased as compared to the treatment-naive LN patients (p < 0.01 and p < 0.001 respectively). 8 out of 12 refractory/relapsing LN patients achieved renal response (5 partial response, PR and 3 complete response, CR) as early as 3 months after start of Tacrolimus therapy, and 11 patients achieved renal response (7 PR and 4 CR) at 6 months from start of Tacrolimus therapy. Proteinuria decreased from median urine protein creatinine ratio (UPCR) of 2.80 (2.00-3.40) at baseline to 1.20 (0.66-1.73) at 3 months (p < 0.001) and to 0.80 (0.19-1.30) at 6 months (p < 0.01). Median rSLEDAI decreased from 8 (8-12) at baseline to 4 (3-5) at 3 months (p < 0.01) and to 4 (0-4) at 6 months (p < 0.01). There was significant decrease both in P-gp expression [RFI, 3.33 (2.87-4.97) vs 2.03 (1.25-3.86), p < 0.05] and P-gp function (RFI, 55.7 (29.7-84.1) vs 26.8 (16.1-37.0), p < 0.01) after 3 months of Tacrolimus therapy. None of the patients developed any adverse effects except one who developed rise in serum creatinine after 4 months of therapy.

Conclusion:
Tacrolimus achieves renal response in refractory/relapsing proliferative LN patients by overcoming P-glycoprotein mediated treatment unresponsiveness.
Background/Purpose: The goal of this study is to investigate how urinary angiostatin, VCAM-1 and established measures of renal function relate to specific histologic findings in paired kidney biopsy samples from patients with lupus nephritis (LN).

Methods: Patients fulfilling the ACR classification for SLE were recruited into the study. Urine samples were collected from 54 lupus nephritis patients together with concurrent kidney biopsy samples and examined for urinary angiostatin and vascular cell adhesion molecule 1 (VCAM-1) protein levels. SLE disease activity was assessed using the SLEDAI, renal disease activity was assessed by the renal SLEDAI (range 0-16; 0= inactive LN, ≥ 8= active renal). The ISN/RPS criteria were used to assess the histologic features of LN. Our patients were categorized into two groups; active proliferative (ISN/RPS classes III/IV) and non-proliferative (classes I/II/V). Biopsy activity and chronicity indices (BAI, BCI respectively) were used for biopsy assessment according to the standards of NIH for LN, the BAI score (range 0-24; 0= inactive LN) and BCI score (range 0-12; 0= no LN chronicity), with BAI and BCI scores of ≥7 and ≥4 respectively considered as risk factors for poor LN outcomes. Nonparametric tests were used to examine the association of both urinary biomarkers and established traditional laboratory markers of renal function with nine specific renal histologic features seen in LN using concurrent renal biopsies.

Results: 54 active LN patients (94.4% women, age 33.3±9.7 years) and 20 healthy controls were studied. Unlike conventional laboratory measures, urinary angiostatin and VCAM-1 levels normalized to Cr were significantly higher in patients with active proliferative LN than non-proliferative LN (angiostatin 21900±3.43 vs 2200±0.79 pg/ng; P<0.0001; VCAM-1 1249±3.93 vs 166±42.5 pg/ng; P<0.0001). A significant correlation was found between urine VCAM-1 and SLEDAI (r = 0.324, P <0.05), as well as renal SLEDAI (r = 0.319, P <0.05). Urinary angiostatin correlated significantly with renal SLEDAI (r = 0.327, P < 0.05). Urinary angiostatin and VCAM-1 strongly correlated with the renal biopsy activity index in concurrent biopsies (r = 0.929, P < 0.001 and r = 0.97, P < 0.001 respectively), but not with the chronicity index. Both angiostatin and VCAM-1 showed an outstanding ability (AUC 0.97, 0.98...
respectively) to predict concurrent renal biopsy activity index score ≥ 7, compared to conventional measures such as sCr, eGFR and uPCR. Whereas urine VCAM-1 was most significantly associated with fibrous crescents, urine angiostatin was most significantly associated with endocapillary proliferation, cellular crescents, fibrinoid necrosis and fibrous crescents in concurrent renal biopsies.

**Conclusion:** Urinary angiostatin and VCAM-1 are associated with specific histologic features of LN activity and chronicity in concurrent renal biopsies. Further longitudinal studies are necessary to delineate the utility of these two urinary proteins in tracking renal pathology changes in SLE patients, and predicting long-term patient and renal mortality in LN.

**Disclosure:** S. Soliman, None; F. Mohamed, None; F. Ismail, None; R. Saxena, None; C. Mohan, None.


**Abstract Number:** 1922

**Cell Type Specific Gene Expression Analysis of Early Systemic Sclerosis Skin Shows a Prominent Activation Pattern of Innate and Adaptive Immune System in the Prospective Registry for Early Systemic Sclerosis (PRESS) Cohort**

**Shervin Assassi**1, Dinesh Khanna2, Monique Hinchcliff3, Virginia D. Steen4, Faye Hant5, Jessica K. Gordon6, Ami A. Shah7, Jun Ying8, William Swindell9, Wenjin Zheng10, Lisha Zhu10, Victoria K. Shanmugam11, Robyn T. Domsic12, Flavia V. Castelino13, Elana J. Bernstein14 and Tracy M. Frech15, 1University of Texas McGovern Medical School, Houston, TX, 2University of Michigan, Ann Arbor, MI, 3Rheumatology, Northwestern Medicine, Chicago, IL, 4Rheumatology, MedStar Georgetown University Hospital, Washington, DC, 5Medicine/Rheumatology & Immunology, Medical University of South Carolina, Charleston, SC, 6Rheumatology, Hospital for Special Surgery, New York, NY, 7Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, 8Department of Internal Medicine - Rheumatology, University of Texas McGovern Medical School, Houston, TX, 9Dermatology, University of Michigan - Ann Arbor, Ann Arbor, MI, 10University of Texas - School of Biomedical Informatics, Houston, TX, 11Rheumatology, The George Washington University, Washington, DC, 12Rheumatology, University of Pittsburgh, Pittsburgh, PA, 13Rheumatology, Harvard Medical School, Boston, MA, 14Rheumatology, Columbia University, New York, NY, 15Division of Rheumatology, University of Utah, Salt Lake City, UT

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics I

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 4:30PM-6:00PM

**Background/Purpose:**

To examine the global gene expression profile in patients with very early diffuse systemic sclerosis (SSc).

**Methods:**

Skin biopsies were obtained from patients enrolled in the Prospective Registry for Early Systemic Sclerosis (PRESS). All patients had diffuse cutaneous involvement and disease duration < 2 years. Fifty-seven patients and 33 age-, gender-matched controls were examined by nextGen RNA Sequencing (Depth: 50 million reads, 75 bp length) on Illumina HiSeq 3000 platform. Cell type-specific signature scores were calculated for each patient sample compared to the average score in controls as previously described (Assassi et al. Arthritis Rheum 2015). Gene signatures for 15 cell types present in skin were calculated including: Fibroblasts, keratinocytes, CD4+ and DC8+ T-cells, NK cells, dendritic cells, M1 and M2 macrophages, and B-cells.

**Results:**

The median disease duration was only 1.1 years while median mRSS score was 22. In comparison to controls, 2537 transcripts were differentially expressed (FDR <5%).

An Ingenuity Pathway Analysis revealed that the following top over-represented pathways: Hepatic fibrosis (p= 3.85x10^{-39}), granulocyte adhesion and diapedesis (p=3.11x10^{-19}), leukocyte extravasation signaling (p=2.79x10^{-16}), Th1 and Th2 activation pathway.
(p=1.44x10^{-15}), agranulocyte adhesion and diapedesis (p=6.56x10^{-14}). The cell-type specific signature score analysis revealed a prominent up-regulation of innate and adaptive immune cell types. The three most frequent activated cell-type signatures were M2 Macrophage (present in 96% of patient samples), fibroblast (93%), and microvascular endothelial cells (91%). Interestingly, the proportion of patient samples with an adaptive immune system signature was much higher than the frequencies observed in our previously published data set (61 SSc patients with mean disease duration of 7.7 years and 36 matched controls). Specifically, CD8+ T cell, CD4+ T cell, and B-cell signatures were present in 67%, 61%, and 67% of samples in the present study whereas those signatures were present in less than 25% of SSc samples with established disease in the previous data set. Figure shows the distribution of signature scores for adaptive immune cell types in the present data set (early diffuse SSc) and previously published study (established SSc).

Conclusion:

Skin samples of patients with early diffuse involvement have a prominent adaptive immune signature which is not present in established disease. This finding can have important implications for clinical trials targeting adaptive immune system.

Disclosure: S. Assassi, Bayer Healthcare, 2.Biogen Idec, 2.Reata, 5.Boehringer Ingelheim, 5; D. Khanna, Actelion, Bayer, BoehringerIngelheim, Chemonab, Corbus, Covis, Cytori,Eicos, EMD Serono, Genentech/Roche, Gilead, GSK, Sanofi-Aventis,UCB Pharma, 5,NIH/NIAMS, NIH/NIAID,Bayer, BMS, Genentech/Roche, Pfizer, 2,Eicos, 4; M. Hinchcliff, None; V. D. Steen, None; F. Hant, None; J. K. Gordon, Corbus Pharmaceuticals, 2,Cumberland Pharmaceuticals, 2,Bayer Pharmaceuticals, 2; A. A. Shah, None; J. Ying, None; W. Swindell, None; W. Zheng, None; L. Zhu, None; V. K. Shanmugam, Multiple, 9; R. T. Domsic, None; F. V. Castelino, None; E. J. Bernstein, None; T. M. Frech, None.

Abstract Number: 1923

Single Cell RNA Sequencing Reveals a Signature of Endothelial Injury in Scleroderma Skin

Sokratis Apostolidis¹, Giuseppina Stifano², Tracy Tabib³, Lisa Rice², Christina Morse³, Bashar Kahaleh⁴ and Robert A. Lafyatis³, ¹Medicine, University of Pittsburgh Medical Center, Pittsburgh, PA, ²Boston University School of Medicine, Boston, MA, ³Medicine, Rheumatology, University of Pittsburgh Medical Center, Pittsburgh, PA, ⁴Medicine/Rheumatology, University of Toledo, Toledo, OH First publication: September 18, 2017

SESSION INFORMATION
Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics I
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose:
Vascular injury is a hallmark event in the pathogenesis of Systemic Sclerosis (SSc). Endothelial dysfunction happens early in the course of the disease and drives some of the most prominent clinical manifestations of scleroderma, including Raynaud’s phenomenon, telangiectasias and gastric antral vascular ectasias, pulmonary arterial hypertension and scleroderma renal crisis. The exact mechanisms that lead to endothelial cell injury and propagate the vasculopathy in scleroderma are not well understood. Single cell RNA sequencing provides a robust platform for cellular identification, allows gene expression analysis at the single cell level and accounts for cellular heterogeneity.
Methods:
The study was completed in the Scleroderma Center of UPMC in collaboration with the Scleroderma Research Center of Boston University and the Broad Institute of Boston. We implemented single cell sorting and subsequent RNA sequencing of cells isolated from scleroderma and healthy control skin. The analysis was performed using R software. We used t-distributed stochastic neighbor embedding (t-SNE) with k-means clustering to identify the various cell types. We performed pathway analysis using Gene Set Enrichment Analysis (GSEA) and Ingenuity Pathway Analysis (IPA). Finally, we independently verified distinct markers using immunohistochemistry on skin biopsies and qPCR in primary endothelial cells isolated from skin of scleroderma patients and healthy controls.

Results:
In order to visualize and ultimately define the various cell subsets in the single cell RNA sequencing dataset, we used t-SNE analysis, a method of unsupervised learning for dimensionality reduction. 2D projection of the t-SNE coupled with k-means clustering effectively reduced the dimensionality of the data. By combining the t-SNE analysis with the expression of known endothelial cell markers, including VWF, PECAM1 and CDH5, we were able to positively identify the endothelial cells among the sorted single cells from healthy and scleroderma skin. Subsequently, we analyzed the differential expression profile between the endothelial cells from healthy and scleroderma skin. Using GSEA and IPA analysis, we were able to demonstrate that the SSc endothelial cell expression profile is enriched in processes associated with extracellular matrix generation, negative regulation of angiogenesis and epithelial-to-mesenchymal transition. Finally, two of the top differentially expressed genes, HSPG2 and APLNR, were independently verified. Primary endothelial cells isolated from scleroderma skin expressed higher levels of APLNR mRNA compared to endothelial cells isolated from healthy skin. Immunohistochemistry studies of skin biopsies revealed that HSPG2 showed increased expression in the perivascular area of scleroderma skin compared to healthy skin.

Conclusion:
Using single cell RNA sequencing we were able to identify an endothelial cell gene signature in scleroderma skin. Differential gene expression and pathway analysis revealed that endothelial cells from scleroderma patients exhibit a pattern of endothelial injury and activation as well as increased extracellular matrix generation and negative regulation of angiogenesis.

Disclosure: S. Apostolidis, None; G. Stifano, None; T. Tabib, None; L. Rice, None; C. Morse, None; B. Kahaleh, None; R. A. Lafyatis, None.

The Nuclear Receptor ROR-Alpha As a Key Checkpoint of Tissue Repair

Rosebeth Kagwiria¹, Ruifang Liang², Chih-Wei Chen³, Thomas Burris⁴, Georg Schett⁵ and Jörg Distler⁶, ¹Department of Internal Medicine 3 and Institute for Clinical Immunology, Friedrich-Alexander-University of Erlangen-Nuremberg and University Hospital Erlangen, Erlangen, Germany, ²Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, Department of Internal Medicine 3 and Institute for Clinical Immunology, Friedrich-Alexander-University of Erlangen-Nuremberg and University Hospital Erlangen, Erlangen, Germany, ³Department of Internal Medicine 3 – Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Erlangen, Germany, ⁴Department of pharmacology and physiology, Saint Luis University-school of medicine, Florida, USA, St. Louis, Missouri, MO, ⁵Department of Internal Medicine 3 – Rheumatology and Immunology, Department of Internal Medicine 3 and Institute for Clinical Immunology, Friedrich-Alexander-University of Erlangen-Nuremberg and University Hospital Erlangen, Erlangen, Germany, ⁶Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Erlangen, Germany

First publication: September 18, 2017
**Background/Purpose:** The Retinoic-acid related Orphan Receptor-alpha (RORα) is a member of the nuclear receptor superfamily and a ligand-dependent transcription factor implicated in a wide range of physiological and pathological processes. The key objective for this study is to evaluate the role of RORα in tissue repair and to elucidate antifibrotic effects of targeting RORα in preclinical models of fibrosis.

**Methods:** The expression was analysed by qPCR, Western blot and immunofluorescence staining. The expression of RORα was modulated via genetic abrogation or adenoviral overexpression. RORα was also targeted pharmaceutically using the small molecule inhibitor SR3335. The role of RORα in fibrosis was evaluated in TGF-β receptor I (TBRI) and bleomycin-induced murine models.

**Results:** The expression of RORα was increased in fibroblasts in both human and murine fibrotic lung and liver. Activation of canonical Wnt/β-catenin signalling mimicked the upregulation of RORα in fibrosis and potently induced RORα expression. Consistently, reporter-assays showed that canonical Wnt ligands induced the promoter activity of RORα target gene BMla1. Overexpression of RORα in fibroblasts induced fibroblast-to-myofibroblast transition and collagen release. Inactivation of RORα signalling, either by knockout of RORα or by treatment with SR3335 inhibited WNT- and TGF-β-dependent fibroblast activation and blocked extracellular matrix secretion. Inhibition of RORα also demonstrated potent antifibrotic effects in the mouse models of bleomycin- and TBRI-induced fibrosis. Mice treated with SR3335 demonstrated reduced dermal thickening, decreased hydroxyproline content and impaired myofibroblast differentiation as compared to vehicle-treated mice.

**Conclusion:** Our study identifies RORα as a key checkpoint of TGF-β- and WNT-induced fibroblast activation. RORα is induced in fibrotic diseases in a WNT-dependent manner to promote TGF-β- and WNT-induced fibroblast activation and tissue fibrosis. Targeting of RORα simultaneously interferes with TGF-β- and WNT-signalling as two core profibrotic pathways, which translates into potent antifibrotic effects.

**Disclosure:** R. Kagwiria, None; R. Liang, None; C. W. Chen, None; T. Burris, None; G. Schett, None; J. Distler, 4D Science, 1,Anamar Medical, Active Biotech, Array Biopma, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, GSK, Novartis, Sanofi-Aventis, UCB, 2,Aetelion Pharmaceuticals US, Active Biotech, Anamar, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi, UCB, 5.

**View Abstract and Citation Information Online** - [http://acrabstracts.org/abstract/the-nuclear-receptor-ror-alpha-as-a-key-checkpoint-of-tissue-repair/](http://acrabstracts.org/abstract/the-nuclear-receptor-ror-alpha-as-a-key-checkpoint-of-tissue-repair/)

**Abstract Number:** 1925

**TGFβ Promotes Fibrosis By MYST1-Dependent Epigenetic Regulation of Autophagy**

Ariella Zehender1, Neng-Yu Lin2, Adrian Stefanica3, Chih-Wei Chen4, Alina Soare5, Thomas Wohlfahrt6, Simon Rauber6, Christina Bergmann7, Andreas Ramming8, Oliver Distler9, Georg Schett10 and Jörg Distler10, 1Department of Internal Medicine 3 – Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Erlangen, Germany, 2Department of Internal Medicine III and Institute for Clinical Immunology, University of Erlangen-Nuremberg, Erlangen, Germany, 3Department of Internal Medicine 3 – Rheumatology and Immunology, University of Erlangen, Erlangen, Germany, 4Department of Internal Medicine 3 – Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Erlangen, Germany, 5Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätssklinikum Erlangen, Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Erlangen, Germany, 6Department of Internal Medicine 3, Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Erlangen, Germany, 7Department of Internal Medicine 3 and Institute for Clinical Immunology, Friedrich-Alexander-University of Erlangen-Nuremberg and University Hospital Erlangen, Erlangen, Germany, 8Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Erlangen, Germany, 9Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland, 10Department of Internal Medicine 3 – Rheumatology and Immunology, Department of Internal Medicine 3 and Institute for Clinical Immunology, Friedrich-Alexander-University of Erlangen-Nuremberg and University Hospital Erlangen, Erlangen, Germany

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Monday, November 6, 2017

**Session Title:** Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics I

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 4:30PM-6:00PM
Background/Purpose:

Autophagy (Atg) is catabolic process allowing cells to degrade unnecessary or dysfunctional cellular organelles. Aberrant activation of Atg has been implicated into the pathogenesis of various diseases.

Methods:

We generated Atg7fl/fl Col1a2;CreER mice with selective inactivation of Atg in fibroblasts. The role of the Atg was investigated in the model of bleomycin- and TβRIact-induced dermal and pulmonary fibrosis. Overexpression of Myst1 and Beclin1 was achieved by adenoviral overexpression. ChIP and reporter assays were performed to study physical and functional interactions between MYST1 and SMAD3.

Results:

Atg is strongly activated in fibroblasts from SSc skin and also in experimental dermal and pulmonary fibrosis as compared to respective non-fibrotic control tissue with overexpression of ATG7 and of BECLIN, downregulation of the autophagy substrate p62 and activation of autophagy-dependent reporter activity. The aberrant activation of Atg has profound stimulatory effects on fibroblasts. Activation of Atg by forced expression of BECLIN1 promoted fibroblast-to-myofibroblast transition and stimulates the collagen release in vitro and in vivo. Moreover, inactivation of autophagy by fibroblast-specific knockout of Atg7 prevented myofibroblast differentiation and ameliorated fibrosis, demonstrating that activation of Atg is both, sufficient and required, for fibroblast activation and tissue fibrosis. We also provide evidence that TGFβ activates Atg by an epigenetic mechanism to amplify its profibrotic effects. TGFβ induces Atg in fibrotic diseases by SMAD3-dependent downregulation of the H4K16-histoneacetyltransferase MYST1, which controls the expression of core components of the Atg machinery such as ATG7 and BECLIN1. Forced expression of MYST1 abrogates the stimulatory effects of TGFβ on Atg and re-establishes the epigenetic control of autophagy in fibrotic conditions. Overexpression of MYST1 prevents the aberrant activation of Atg, inhibits TGFβ-induced fibroblast activation and ameliorates experimental dermal and pulmonary fibrosis.

Conclusion:

We demonstrate that the epigenetic control of Atg is disturbed by a TGFβ-dependent downregulation of MYST1 in SSc. The resulting uncontrolled activation of Atg promotes fibroblast-to-myofibroblast transition and tissue fibrosis. Restoration of the epigenetic control of autophagy limits the profibrotic effects of TGFβ and ameliorates experimental fibrosis. These findings link uncontrolled TGFβ signaling to aberrant autophagy and altered epigenetics in fibrotic diseases.

Disclosure: A. Zehender, None; N. Y. Lin, None; A. Stefanica, None; C. W. Chen, None; A. Soare, None; T. Wohlfahrt, None; S. Rauber, None; C. Bergmann, None; A. Ramming, None; O. Distler, 4 D Science, Actelion, Active Biotec, Bayer, Biogen Idec, Boehringer Ingelheim Pharma, BMS, ChemomAb, EpiPharm, Ergonex, espeRare foundation, GSK, Roche-Genentech, Inventiva, Lilly, medac, MedImmune, Mitsubishi Tanabe, Pharmacies, Pfizer, Sanofi, Seroda, 2; G. Schett, None; J. Distler, 4D Science, Anamar Medical, Active Biotech, Array Biopma, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, GSK, Novartis, Sanofi-Aventis, UCB, 2, Actelion Pharmaceuticals US, Active Biotech, Anamar, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi, UCB, 5.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/tgf%ce%b2-promotes-fibrosis-by-myst1-dependent-epigenetic-regulation-of-autophagy

Abstract Number: 1926

Cardiac Remodeling in Systemic Sclerosis: TGF-β/Fra2-Dependent Autophagy As a Novel Target for Heart Fibrosis

Mara Stellato1, Michal Rudnik1, Florian Renoux1, Elena Pachera1, Karl Sotlar2, Karin Klingel3, Joerg C. Henes4, Przemyslaw Blyszczuk1,5, Oliver Distler1 and Gabriela Kania1, 1Department of Rheumatology, Center of Experimental Rheumatology, University Hospital Zurich, Zurich, Switzerland, 2Institute of Pathology, Ludwig Maximilians University, Munich, Germany, 3Department of Molecular Pathology, University Hospital Tuebingen, Tuebingen, Germany, 4Department of Internal Medicine II, Division of Rheumatology, University Hospital Tuebingen, Tuebingen, Germany, 5Department of Clinical Immunology, Jagiellonian University Medical College, Krakow, Poland

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Monday, November 6, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics I
**Background/Purpose:**

SSc patients frequently suffer from primary cardiac involvement. The main histological feature is fibrosis, but the mechanisms responsible for the heart failure remain unclear. It is known that cellular progenitors, including stromal cells, differentiate into myofibroblasts and autophagy may favor fibrosis through enhanced differentiation of cardiac stromal cells. Here we describe the role of Fos-related antigen 2 (fra-2)/autophagy crosstalk in TGFβ-dependent myocardial fibrosis in SSc.

**Methods:**

Immunohistochemistry (IHC) and immunofluorescence (IF) were performed on endomyocardial biopsies (EMBs) from SSc patients and hearts from fra-2tg SSc mouse model and WT mice. Myocardial stromal Ter119CD45CD31 (Lin) gp38+ stromal cells were sorted for in vitro culture. The cellular phenotype was assessed by qPCR, IF, stress fiber staining, SIRCOL and contraction assay on sorted cells. The antisense oligonucleotide GapmeR was used to knock-down fra-2.

**Results:**

Fibrosis, collagen deposition and αSMA+ myofibroblasts were increased in the myocardium of SSc patients (n=10). Fra-2 and autophagy markers such as LC3B, Beclin-1 and Atg5 were expressed in fibrotic cardiac tissues. In parallel, the myocardium of fra-2tg mice showed higher expression of the profibrotic markers αSMA, vimentin and collagen I compared to WT mice (n=5), as well the expression of LC3B and Beclin-1 in fibrotic regions. Among cardiac stromal cells (Lin), the frequency of gp38+ cells was significantly higher in fra2tg myocardium compared to WT mice (n=8, p=0.02). Lin/gp38+ cells co-expressed αSMA, vimentin and collagen I together with LC3B and Beclin-1 (n=3). Following TGFβ stimulation, WT Lin/gp38+ cells entered fibroblast-to-myofibroblast transition characterized by increased mRNA and protein levels of αSMA, collagen I, fibronectin (n=3-6), formation of αSMA+ fibers and stress fibers (n=3), increased cell proliferation (n=5; p=0.04), contraction capability (n=5; p<0.05) and collagen secretion (n=5; p=0.04). TGFβ stimulation of WT Lin/gp38+ cells induced the expression of LC3B, Beclin-1 and Atg5 at mRNA and protein level (n=3-5). Accordingly, TGFβ inhibition caused the downregulation of these markers (n=3). In contrast to WT cells, fra-2tg Lin/gp38+ cells showed the presence of αSMA+ fibers, stress fibers and an increased contraction capability even without TGFβ stimulation. Finally, fra-2 silencing resulted in decreased Lin/gp38+ cell differentiation and autophagy activity as following: levels of αSMA and collagen I (n=5; p=0.007), secreted collagens (n=5; p<0.05) and αSMA fibers (n=3) were significantly downregulated in addition to a significant decrease of mRNA and protein expression of LC3B, Beclin-1 and Atg5 (n=3).

**Conclusion:**

The TGFβ/fra-2 axis regulates the autophagy process, leading in turn to stromal-to-myofibroblast transition. Therefore, targeting autophagy might ameliorate the fibrotic process during heart remodeling in SSc.

**Disclosure:** M. Stellato, None; M. Rudnik, None; F. Renoux, None; E. Pachera, None; K. Sotlar, None; K. Klingel, None; J. C. Henes, None; P. Blyszczuk, None; O. Distler, Actelion, Bayer, BiogenIdec, Boehringer Ingelheim, ChemomAb, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Novartis, Pfizer, Sanofi, Sinoxa and UCB, 2,Actelion, Bayer, BiogenIdec, Boehringer Ingelheim, ChemomAb, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Novartis, Pfizer, Sanofi, Sinoxa and UCB, 5,mir-29 for the treatment of systemic sclerosis, 9; G. Kania, Bayer, 2.


Abstract Number: 1927

**Anti-Fibrotic Mechanisms of Endostatin-Derived Peptide Are the Result of Reduction in Pro-Fibrotic Mediators and Promotion of Extracellular Matrix Degradation**

Tomoya Watanabe1, Tetsuya Nishimoto2, Takahisa Takihara3, Logan Mlakar4, Yunyun Su5 and Carol A. Feghali-Bostwick6,

1Rheumatology, Medical University of South Carolina, Charleston, SC, 2Division of Rheumatology and Immunology, Medical University of South Carolina, Charleston, SC, 3Division of Pulmonary Medicine, Tokai University School of Medicine, Isehara, Japan,
Fibrotic disorders such as systemic sclerosis (SSc) result in end-stage organ failure and loss of function, consequently causing high morbidity and mortality. We recently demonstrated that the C-terminal domain of endostatin, known as E4, prevented and reversed both dermal and pulmonary fibrosis. In this study, we investigated the mechanism by which E4 exerts anti-fibrotic effects using pre-clinical models of SSc.

Methods:

To assess the effects of E4, lung fibroblasts were treated with TGF-β with vehicle or E4. The expression levels and activity of matrix metalloproteases (MMP)-1 and MMP-3 were evaluated by using real-time PCR, immunoblotting (IB), and collagen and casein zymography, respectively. Furthermore, the mRNA and protein levels of the pro-fibrotic proteins, connective tissue growth factor (CTGF) and insulin-like growth factor binding protein (IGFBP)-3, were measured using real-time PCR and IB, respectively. In vivo, bleomycin with vehicle or E4 was administered intratracheally to 6 to 8-week-old C57BL/6J male mice to induce lung fibrosis. Lung and bronchoalveolar lavage fluid (BALF) were collected 7 days post-treatment, and the levels and activity of hepatocyte growth factor (HGF) were measured using real-time PCR and immunoblotting.

Results:

The mRNA levels of MMP-1 and MMP-3 were increased by E4. Similarly, secreted MMP-1 and MMP-3 protein levels were upregulated in culture supernatants. Furthermore, MMP-1 and MMP-3 activity was increased as assessed by zymography. TGF-β increased the expression levels of CTGF and IGFBP-3 in primary human fibroblasts, and E4 abrogated these effects. In vivo, bleomycin reduced HGF levels in BALF and lung tissues. E4 peptide partially blocked these effects.

Conclusion:

Our results demonstrate that E4 increased MMP-1 and MMP-3 levels and activity. The ability of E4 to reverse fibrosis can thus be explained, in part, by its increase of MMP, thus promoting extracellular matrix (ECM) degradation. In addition, E4 reduced levels of the pro-fibrotic mediators CTGF and IGFBP-3 while increasing levels of the anti-fibrotic and anti-inflammatory factor HGF. Our findings suggest that the anti-fibrotic effects of E4 peptide are multi-pronged and include decreasing levels of essential pro-fibrotic mediators, increasing levels of an anti-fibrotic mediator, and promoting ECM degradation.
Background/Purpose:

The pathophysiology of osteoarthritis (OA) involves wear and tear, and a state of low-grade inflammation. Wear and tear leads to tissue degradation followed by tissue repair responses including TGFβ-induced myofibroblast production of extracellular matrix (ECM). Fibronectins are an essential part of the ECM, and injection of fibronectin fragments into rabbit joints is an established animal model of OA. Recently, alternatively spliced fibronectin containing the ED-A domain (ED-A FN) has been shown to activate Toll-like receptor 4. In this study, we hypothesize that FN fragments containing the ED-A domain could be one mechanism transducing mechanical events into inflammatory signals in OA.

Methods:

Samples of synovial membrane and cartilage were obtained from patients with knee OA undergoing joint replacement surgery. Immunostaining was performed on synovial membranes. Fibroblast-like synovial cells (FLS) isolated by enzymatic digestion of remnant synovial membrane were stimulated with TGFβ, TNFα, lipopolysaccharide, IL-6, OA synovial fluid from two different donors, or chondrocyte lysate, and culture supernatants were analyzed for ED-A FN by immunofluorescence staining. ED-A FN fragments were obtained by plasmin digestion of cellular FN. Synovial cells isolated by enzymatic digestion and human monocyte-derived macrophages (MDM) were incubated with recombinant ED-A FN, plasmin, cellular FN, or cellular FN digested with plasmin; and culture supernatants were analyzed for MCP-1 and TNFα.

Results:

We hypothesized that ED-A FN is produced by OA FLS in response to products reflecting tear and wear in OA. Indeed, the production of ED-A FN by OA FLS was increased by TGFβ, OA synovial fluid, and lysed chondrocytes in all experiments (n=3, see figure). ED-A FN co-localized with the myofibroblast marker αSMA in both the OA FLS (n=3) and in the OA synovial membranes (n=8). We further hypothesized that ED-A FN expression is associated with inflammation in OA. ED-A FN staining was associated with both number of lining layer cells (rho=0.85 and p=0.011) and infiltrating sublining cells (rho=0.88 and p=0.007) in the OA synovium (n=8), and co-localized with both MCP-1 and TNFα (n=5). Recombinant ED-A FN increased the production of both MCP-1 and TNFα by MDM (n=3) and OA FLS (n=3). Finally, we demonstrated that the FN fragments containing the ED-A domain generated the same production of both MCP-1 and TNFα as recombinant ED-A FN.

Conclusion:

The disease process in OA shares features with the chronic wound healing response including myofibroblast differentiation and that humoral mediators found in the joint can promote myofibroblast production of ED-A FN. We additionally show that recombinant and plasmin-derived ED-A fragments can induce generation of pro-inflammatory mediators from FLS and MDM. This study supports targeting the formation of ED-A FN or the enzymatic fragmentation of FN to reduce pro-inflammatory responses in OA.

Disclosure: T. W. Kragstrup, None; D. H. Sohn, None; C. Lepus, None; K. Onuma, None; Q. Wang, None; W. H. Robinson, None; J. Sokolove, None.
Sustained Efficacy of Intra-Articular SB-061, a Novel Matrix Regulator Inspired By Aggrecan, in a Rat Model of Osteoarthritis

Kate Stuart, Julia Chen, Sharmi Saha, Harsha Kabra, Athene Chan, Kamal Egodoge, Jennifer Oskins, Chaohua Lin, Morten Karsdal, Mark Chambers and John Paderi
Symic Bio, Emeryville, CA, Lilly Research Laboratories, Indianapolis, IN, Biomarkers and Research, Nordic Bioscience, Herlev, Denmark

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Biology and Pathology of Bone and Joint Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
No therapy for osteoarthritis (OA) has yet to deliver both structural and symptomatic benefits. Symic is approaching this unmet clinical need with a novel matrix regulator, SB-061, inspired by aggrecan. Aggrecan is a critical component for cartilage structure and plays a key role as part of the protective molecules shielding collagen from degradation. Native aggrecan is lost early in the progression of OA and restoring the function of aggrecan in the joint is hypothesized to reduce OA progression. SB-061 was designed as a novel functional mimic of aggrecan, and was evaluated in a standard rodent model of OA.

Methods:
SB-061 was synthesized by linking the glycosaminoglycan chondroitin sulfate (CS) with peptides known to bind to hyaluronic acid (HA). An ELISA assay was developed by immobilizing HA on a plate and using an antibody to the SB-061 molecule to confirm the concentration dependent binding of SB-061 to HA. In vivo experiments were performed to assess the pain reducing effect of SB-061. Rats received a medial meniscal tear in their right hind-limbs, and SB-061 was injected into the injured joint beginning 1 week after surgery and weekly throughout the study. Incapacitance testing was performed to detect differences in pain related responses (load bearing on the injured joint) throughout the duration of the 6-week study.

Results:
SB-061 demonstrates high affinity binding to HA (EC50 = 10nM) and produces a robust, dose related reduction in pain responses following intra-articular injection in a rat model of OA. The timecourse and magnitude of SB-061 mediated analgesic effects in the rat OA model were comparable across 4 independent studies with a maximum pain reduction of approximately 30% at week 4 of treatment. Continued weekly dosing of SB-061 resulted in a sustained reduction of pain throughout the course of the study, whereas termination of SB-061 dosing resulted in a diminishment of the pain relief effect over a two week period. These results are superior to historical data with a clinically relevant dose of an NSAID administered at similar times following the meniscal tear surgery. We hypothesize that SB-061 acts as a matrix regulator via its aggrecan-like properties to produce a sustained pain relieving effect in this model.

Conclusion:
We have demonstrated that SB-061 functionally mimics aggrecan with respect to binding to HA, and significantly reduces pain related responses in a sustained manner in an industry standard animal model of OA. These data suggest that SB-061 may exhibit clinical efficacy in human OA via a similar mechanism. Additional studies are underway to elucidate the mechanism of action of SB-061 within the joint and its potential for disease modification.

Interleukin 1β Decreases Capacity for Repair Human Cartilage Lesions By Mesenchymal Stromal Cells on Collagen/Proteoglycan Scaffolds

Clara Sanjurjo-Rodríguez1, ROCÍO CASTRO-VIÑUELAS2, Tamara Hermida-Gómez3, ISAAC FUENTES BOQUETE4, Francisco Javier De Toro Santos5, Francisco J Blanco6 and SILVIA MARIA DÍAZ-PRADO1, 1of Biomedical Sciences, Medicine and Physiotherapy., Cell Therapy and Regenerative Medicine Group. Universidade da Coruña. INIBIC. CIBER-BBN., A CORUÑA, Spain, 2Biomedical Sciences. Medicine and Physiotherapy, Cell Therapy and Regenerative Medicine Group. Universidade da Coruña. INIBIC., A CORUÑA, Spain, 3Rheumatology, INIBIC. Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas. CIBER-BBN., A Coruña, Spain, 4Biomedical Sciences, Medicine and Physiotherapy, Cell Therapy and Regenerative Medicine Group. Universidade da Coruña. INIBIC. CIBER-BBN. Complejo Hospitalario Universitario A Coruña (SERGAS), La Coruña, Spain, 5Servicio de Reumatología. Area Genomica. Instituto de Investigación Biomédica de A Coruña (INIBIC). Complejo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidade da Coruña (UDC), A Coruña, Spain

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Biology and Pathology of Bone and Joint Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: There is controversy about the effect of catabolic cytokines in regenerative medicine. The purpose of this study was to evaluate the effect of interleukin 1β (IL1β) in the repair capacity of bone marrow mesenchymal stromal cells (BMSCs) seeded on collagen (Col)/proteoglycan (PG) scaffolds, in an in vitro cartilage lesion model.

Methods: Samples were obtained from hips (BMSCs and cartilage) and knees (only cartilage) of patients who underwent total joint replacement. 3 mm-diameter lesions were made in cartilage biopsies using a dental drill. Injured biopsies were pre-treated with 10 ng/ml of IL1β for 24 hours. 2x10^5 BMSCs were seeded on type I and II Col with heparan sulfate (C1C2HS), and C1C2 with chondroitin sulfate (C1C2CHS) scaffolds. Resulting constructs were introduced inside the lesion and cultured for 60 days in chondrogenic medium. Controls without IL1β pre-treatment were performed. Histological analyses were made and repaired tissue was evaluated using the International Cartilage Research Society scale II (ICRSII) [1].

Results: In the IL1β pre-treated model, Hematoxilin-Eosin staining (HE, Figure) showed neotissue formation within the lesion with fewer rounded cells than in the non pre-treated model. Staining with Masson’s Trichrome (MT, Figure) showed the presence of Col in the extracellular matrix (ECM) of all the constructs. The presence of PGs detected by Safranin O (SO, Figure) staining was more metachromatic in non pre-treated C1C2HS (52.426±4.877) and C1C2 with chondroitin sulfate (C1C2CHS) scaffolds. Resulting constructs were introduced inside the lesion and cultured for 60 days in chondrogenic medium. Controls without IL1β pre-treatment were performed. Histological analyses were made and repaired tissue was evaluated using the International Cartilage Research Society scale II (ICRSII) [1].

By ICRS II assessment of the non-pretreated model, the repair score for C1C2HS was 46% (fibrocartilage neotissue), and 73% (mixed fibrocartilage and hyaline cartilage) for C1C2HS constructs. In the IL1β pre-treated model, morphological changes with the loss of ECM components observed by SO and MT staining resulted in lowering of the ICRSII scores.

Targeting Cartilage Aging As Osteoarthritis Therapeutics By Drug Repurposing


First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Biology and Pathology of Bone and Joint Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Background: Effective treatments for Osteoarthritis (OA) are not available. In aging-related diseases, including OA, failure of cellular homeostasis mechanisms, such as autophagy can cause extracellular matrix destruction and cell death. Chondrocytes are essential for the maintenance of cartilage integrity. With aging, chondrocyte function is diminished, contributing to a cellular senescence phenotype often observed in OA chondrocytes. In addition, a defect in autophagy is observed in both aging and cartilage degeneration. The objective of this study was to identify anti-senescence and pro-autophagy molecules by a cell-based high-throughput screening (HTS) in human chondrocytes.

Methods:

Methods: To induce cellular senescence or reduced autophagy, immortalized human chondrocytes, TC28a2 were seeded in 384 well plates, and treated with IL-6 (20ng/ml) for 72 or 18 hours, respectively. Then, chondrocytes were incubated with Prestwick Chemical Library (1120 approved drugs) at 10μM for 72 hours. To identify anti-senescence hits, nuclei was stained with Hoechst 33342 (2,5μg/ml), while β–galactosidase subcellular structures was stained by using ImaGene Green C12FDG substrate (30μM). To evaluate autophagic flux, a reporter cell line was generated by lentiviral transfection of pBABE-mCherry-EGFP-LC3 plasmid in TC28a2 chondrocytes. Plates were imaged by using Operetta® High Content Screening (HCS) System. Relative intensity of C12FDG in cytoplasm and relative spot intensity of cytoplasm were determined to quantitate β–galactosidase activity and autophagic flux respectively. For compound validation, senescence markers, autophagic flux, inflammation and apoptosis were evaluated in human chondrocytes. Moreover, cartilage degradation and autophagy were evaluated by safranin O staining and immunohistochemistry in human cartilage explants.

Results:

Results: A primary screening was performed to identify anti-senescence compounds by measurement of senescence-associated β-galactosidase activity. 252 compounds with anti-senescence effects were identified. The anti-senescence hits were analyzed by
monitoring autophagic flux. 26 compounds with both anti-senescence and pro-autophagy effects were selected. Then, one compound was selected for further validation. The compound reduced senescence (p <0.001) and increased autophagic flux (p <0.0001) in response to IL-6. Western Blot analysis showed protective effect against defective autophagy, senescence and inflammation. Interestingly, this protective effect was partially mediated by mTOR inhibition, a proposed mechanism to prevent cartilage aging. Moreover, the selected compound conferred protection against cell death by apoptosis and reduced nitric oxide (NO) production into supernatants (p < 0.05) and cartilage degradation in response to IL-1β.

Conclusion:

Conclusions: These observations provide a unique opportunity to study cartilage aging with the objective to explore the therapeutic potential of pharmacological prevention of chondrocyte senescence and autophagy as a strategy to slow or reverse aging-associated changes, prevent the onset of OA and provide benefits for its clinical management.

Disclosure: B. Carames, None; U. Nogueira-Recalde, None; M. I. Loza, None; F. J. Blanco, None; E. Dominguez, None.

A2A Adenosine Receptor (A2AR) Stimulation Modulates NR4A2 Orphan Receptor Expression during Osteoclast Differentiation

Carmen Corciulo1, Tuere Wilder1 and Bruce Cronstein2, 1Department of Medicine, Division of Rheumatology, NYU School of Medicine, New York, NY, 2Rheumatology, New York University School of Medicine, Division of Rheumatology, New York, NY

First publication: September 18, 2017

Methods: Immunohistochemistry of articular bone was used to determine NR4A2 expression in bone. Osteoclast precursors were isolated from primary bone marrow cells and, along with the murine macrophage cell line RAW 264.7 cells, were induced to differentiate into osteoclasts following treatment with M-CSF and RANKL (30ng/ml). NR4A2 expression was measured in vitro by RT-PCR and Western Blot.

Results: NR4A2 is expressed in articular bone (osteoclasts, osteoblasts and osteocytes) but not articular chondrocytes. During osteoclast differentiation induced by RANKL treatment of primary osteoclast precursors there is a marked reduction of NR4A2 mRNA expression (75% of control, p<0.01). Similarly, RANKL induction of osteoclast differentiation by RAW 264.7 cells is also associated with diminished NR4A2 mRNA expression (Day 3, 99.8% reduction, p<0.01). Moreover immunofluorescence and western blotting data show cytosolic and nuclear NR4A2 negatively correlates with expression of cathepsin-K, consistent with reduced NR4A2 expression during osteoclast differentiation (nuclear NR4A2 is decreased by 27% and 49% at days 3 and 6 of osteoclast differentiation, respectively). Interestingly treatment of osteoclast precursors with CGS21680 (1 uM), a selective A2AR agonist, reverses this expression pattern, significantly increasing NR4A2 mRNA expression in both primary macrophages (2 fold increase vs control; p<0.05) and RAW 264.7 cells (51 fold increase vs control; p<0.01).

Conclusion: Reduced expression of NR4A2 is characteristic of osteoclast differentiation and stimulation of A2AR receptors on osteoclast precursors reverses both the reduction in NR4A2 expression and osteoclast differentiation.
Mitochondrial ROS Activate the p38-MAPK/AP1 Pathway to Induce the Expression of Matrix Metalloproteases and IL-6 in Human Chondrocytes

Mohammad Y. Ansari and Tariq M Haqqi, Anatomy & Neurobiology, Northeast Ohio Medical University, Rootstown, OH

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Biology and Pathology of Bone and Joint Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Mitochondria not only ‘power’ the cell, but are also essential for maintaining physiological levels of prooxidants (ROS) which is critical for homeostasis. Damaged and dysfunctional mitochondria are hallmarks of aging-related diseases including osteoarthritis (OA) but how they contribute to the pathogenesis of OA is not clear. Here we investigated the mechanism of mitochondrial dysfunction-induced expression of IL-6 and MMP-3, -9 and -13 in human normal and OA chondrocytes.

Methods:

OA cartilage samples were obtained from donors who underwent total joint replacement surgery at Crystal Clinic, Akron, OH. Normal knee cartilage samples were from post mortem donors via NDRI. Mitochondrial dysfunction in chondrocytes was induced by treatment with IL-1β or CCCP (Carbonyl cyanide m-chlorophenyl hydrazone). JC-1 staining of chondrocytes was used to measure the loss of mitochondrial membrane potential. Mitochondrial ROS levels were analyzed by MitoSOX probe. Chondrocytes treated to induce mitochondrial damage were harvested and (1) RNA was prepared for measuring gene expression by TaqMan assays; and (2) total lysate was prepared for protein expression analysis by immunoblotting for OA signature genes. Culture supernatants were used to determine the levels of secreted IL-6 and MMP-13 protein by ELISA. ATP levels in normal and OA chondrocytes treated with CCCP or IL-1β were measured by Mitochondrial ToxGlo Assay. Activation of p38-MAPK and cFos was determined by Western immunoblotting using antibodies validated for the total and phosphorylated proteins. Activation of the NF-kB and AP1 signaling pathways was analyzed by reporter assays, immunoblotting for IkBα degradation and nuclear translocation of cFos using immunofluorescence staining. Nucleofection was used to transfect chondrocytes.

Results:

IL-1β or CCCP treatment caused a significant loss of mitochondrial membrane potential and production of mitochondrial ROS in chondrocytes as measured by JC-1 and MitoSOX staining respectively. OA chondrocytes compared to normal chondrocytes had significantly low ATP levels and treatment with IL-1β or CCCP resulted in reduced production of ATP in normal chondrocytes. Both normal and OA chondrocytes with damaged mitochondria showed increased mRNA expression of IL-6 and MMP-3, -9 and -13 and the phosphorylation of p38MAPK, cFos and nuclear translocation of cFos. In normal or OA chondrocytes treated with CCCP or H2O2, activation of NFkB as determined by immunoblotting for IkBα degradation, was not observed. Also, in normal or OA chondrocytes transfected with either AP1 or NFkB activity reporter vectors and then treated with CCCP, activation of AP1 but not of NF-kB was observed. Treatment of chondrocytes with damaged/dysfunctional mitochondria with mitochondrial ROS inhibitor Mito-TEMPO, inhibited the AP1 activation and suppressed the expression of IL-6, MMP-3 -9 and -13 mRNA and protein.

Conclusion: Here we show for the first time that mitochondrial damage/dysfunction contributes to the pathogenesis of OA via p38 MAPK/AP1 activation and not through the activation of NF-kB pathway. This knowledge may help in designing novel therapies for the management of OA.

Supported by USPHS/NIH grants

Disclosure: M. Y. Ansari, None; T. M. Haqqi, None.
Chondrocytes Derived from Mesenchymal Stem Cells Differentiated in the Presence of Plasma-Derived Extracellular Vesicles from Osteoarthritic Patients Express Disease-Related Genes

Bartijn C.H. Pieters1, Onno J. Arntz1, Arjen B. Blom2, Peter M. van der Kraan2, and Fons A.J. van de Loo2, 1Experimental Rheumatology, Radboudumc, Nijmegen, Netherlands, 2Experimental Rheumatology, Radboud university medical center, Nijmegen, Netherlands
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Biology and Pathology of Bone and Joint Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Osteoarthritis (OA) is an age-related musculoskeletal disease and the most common form of arthritis characterized by low grade synovial inflammation and articular cartilage degeneration. Many different cell types have been implicated in the pathogenesis of OA and interplay between these cells contribute to the dynamic events associated with disease. Recently, extracellular vesicles (EVs) have emerged as mediators of intercellular communication. Being carriers of proteins, genetic information and metalloproteinases, their involvement in many diseases has now been established. There is however very little known about the pathophysiological role of EVs in musculoskeletal diseases. In this study, we investigated the effect of plasma EVs from OA patients during chondrogenic differentiation of mesenchymal stem cells (MSCs).

Methods: Plasma-derived extracellular vesicles (pEVs) were isolated from plasma of OA patients and age-matched healthy controls using size-exclusion chromatography. EV containing fractions were characterized according to ISEV guidelines [1]. Pelleted MSCs were stimulated with TGF-β and BMP-2 to induce chondrogenic differentiation, either in the presence of pEVs isolated from OA patients or healthy controls. After 8 days, RNA was isolated and RT-qPCR was performed to determine the gene expression profiles.

Results: No significant difference was observed in particle concentration, size or protein concentration between OA patients and age-matched healthy controls. In the presence of pEVs from OA patients MSC-derived chondrocytes showed a significant increase in the expression of MMP13 (6.1-fold), RUNX2 (1.9-fold) and RANKL (2.3-fold), compared to pEVs from healthy controls. A trend towards higher ADAMTS5 expression (2.5-fold, p=0.0685) with OA pEVs was also observed. Additionally, we found significantly higher expression of WISP1 (24-fold), suggesting activation of Wnt signaling. All other proinflammatory genes tested were not significantly different between the two groups.

Conclusion: A previous study [2] has shown that EVs released from IL-1β stimulated synovial fibroblasts can induce osteoarthritic changes in articular chondrocytes. Here, we show direct evidence that circulating pEVs from OA patients can enhance OA-related genes, like MMP13, in MSC-derived chondrocytes. The expression profile found suggest the presence of Wnt-proteins on pEVs from OA patients, which are known to be involved in cartilage development and we previously have shown that WISP-1 expression is a feature of experimental and human OA [3].

Disclosure: B. C. H. Pieters, None; O. J. Arntz, None; A. B. Blom, None; P. M. van der Kraan, Contract research UCB, 2; F. A. J. van de Loo, None.

Influence of Adipokines on the Differentiation of Spongiosa-Derived Mesenchymal Stromal Cells from Osteoporosis and Osteoarthritis Patients

Lali Tsiklauri¹, Janina Werner², Klaus W. Frommer¹, Rosel Engel³, Stefan Rehart⁴, Sabine Wenisch², Ulf Müller-Ladner⁵ and Elena Neumann¹, ¹Justus-Liebig-University Giessen, Department of Internal Medicine and Rheumatology, Kerkhoff-Klinik, Bad Nauheim, Germany, Bad Nauheim, Germany, ²Justus-Liebig-University Giessen, Institute of Veterinary-Anatomy, -Histology and –Embryology, Clinic of Small Animals, Giessen Germany, Giessen, Germany, ³Justus-Liebig-University Giessen, Department of Internal Medicine and Rheumatology, Kerkhoff-Klinik, Bad Nauheim, Germany, Bad nauheim, Germany, ⁴Orthopedic & Trauma Surgery, Agaplesion Markus-Hospital, Frankfurt, Frankfurt, Germany, ⁵Justus-Liebig-University Giessen, Department of Internal Medicine and Rheumatology, Kerkhoff-Klinik, Bad Nauheim, Germany, Bad-Nauheim, Germany

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Biology and Pathology of Bone and Joint Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Osteoporosis predominantly affects elderly people and is characterized by bone loss, increased fracture risk and reduced regeneration ability. An inverse relationship between bone marrow adipose tissue and bone mineral density in osteoporosis and during aging is well documented, but the role of fat–bone interactions in the pathogenesis of osteoporosis is poorly understood. Adipose tissue is metabolically highly active. Adipokines (e.g. visfatin, resistin and leptin) are adipocyte-derived factors with immunomodulatory properties and they might influence the differentiation of bone marrow-derived mesenchymal stem cells (MSC) into osteoblasts and adipocytes. Thus, the presence of adipokines in bone tissue of femoral heads and their effects on MSC differentiation were analyzed.

Methods:
RNA and MSC were isolated from spongiosa of femoral heads derived from hip replacement surgery of osteoarthritis patients or after osteoporotic femoral neck fracture. Adipogenic as well as osteogenic MSC differentiation was performed with and without adipokines. For the transfer and differentiation of MSC on cancellous bone, bone fragments were purified and sterilized. Gene expression was evaluated by Realtime PCR. Matrix mineralization was assayed using Alizarin red S staining and proinflammatory factors were measured by ELISA.

Results:
Higher levels of visfatin (FF mean 7.77±1.86, n=11; OA 2.25±0.36, n=13) and leptin (FF mean 21.98±5.41, n=11; OA 15.86±3.93, n=12) could be detected in osteoporotic (FF) bone compared to non-osteoporotic (OA) bone, however resistin was reduced in FF (FF mean 7.73±2.95, n=9; OA 34.28±9.27, n=12). Visfatin induced the secretion of proinflammatory factors (IL-6, IL-8, MCP-1 and GRO-a) during both, osteogenic and adipogenic differentiation. Significantly increased matrix mineralization (visfatin: 82%±28%, control: 3.9%±1.8%; n=3) and downregulated collagen type 1 expression (e.g. d21: -4.6-fold, n=7) were detected in osteogenically differentiated cells after visfatin stimulation. In contrast to leptin and resistin, visfatin reduced the expression of MMP2, MMP13, TIMP1 and TIMP2 (e.g. d21: -2.4-fold / -3.18-fold / -3.2-fold / -4.3 fold, respectively) during osteogenetic differentiation. The expression of MMP13 (e.g. d21: -104-fold, n=9) and MMP2 (e.g. d21: 5.1-fold, n=9) was significantly enhanced after stimulation with visfatin during adipogenic differentiation under standard cell culture conditions, however visfatin-mediated MMP13 expression (e.g. d21: 13.8-fold, n=7) as well as induction of IL-6 and IL-8 release was markedly reduced during differentiation on purified autologous cancellous bone.

Conclusion: The results support the hypothesis that adipokines, especially the visfatin-mediated increase of matrix mineralization and reduction of collagen type 1 expression might lead to enhanced bone fragility and contribute to the pathogenesis of osteoporosis. Moreover visfatin-induced release of proinflammatory cytokines and dysregulated expression of MMPs and TIMPs during MSC-differentiation might influence bone turnover at the adipose tissue/bone interface

Disclosure: L. Tsiklauri, None; J. Werner, None; K. W. Frommer, None; R. Engel, None; S. Rehart, None; S. Wenisch, None; U. Müller-Ladner, None; E. Neumann, None.

Bimekizumab Blocks T Cell-Mediated Osteogenic Differentiation of Periosteal Stem Cells: Coupling Pathological Bone Formation to IL-17A and IL-17F Signaling

Mittal Shah1,2, Ash Maroof1, Rawiya Al-Hosni2, Panagiotis Gikas3, Neil Gozzard1, Stevan Shaw1 and Scott Roberts1, 2, UCB Pharma, Slough, United Kingdom, 2University College London, London, United Kingdom, 3The Royal National Orthopaedic Hospital, London, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Biology and Pathology of Bone and Joint Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Structural tissue damage, as a result of pathological bone formation, is a major cause of disability in spondyloarthritis (SpA). A paucity of in vitro models that faithfully replicate human skeletal biology has impeded research into the cellular and molecular triggers for this osteoimmunologic phenomenon. Nevertheless, clinical and animal studies have defined IL-17 signaling as a key regulator of SpA disease; however, the role of IL-17 in bone pathology is poorly understood. IL-17-producing γδ-T cells have a critical function in periosteal bone formation for fracture repair,1 the periosteum has also been implicated in pathological bone formation in SpA disease progression.2 This study aimed to investigate IL-17 signaling in the context of pathological bone formation using a biomimetic human periosteum derived stem cell (hPDSC) model of osteogenic differentiation.

Methods: hPDSCs were obtained through enzymatic digestion of periosteal biopsies from patients undergoing orthopedic surgery. Expanded cultures were treated with recombinant human IL-17A, IL-17F, or both over 96h and expression of gene markers evaluated. hPDSCs were also stimulated using a biomimetic protocol in combination with IL-17A and IL-17F, or human Th17 and γδ-T-cell supernatants (SNs) (as a surrogate disease-like inflammatory milieu). Antibodies with strong-affinity to IL-17A, IL-17F, or bimekizumab (a humanized monoclonal IgG1 antibody with strong affinity for both IL-17A and IL-17F) were used to define the role of these cytokines in the SNs. Expression of osteogenic markers and matrix mineralization was assessed to define in vitro bone formation.

Results: Under basal conditions IL-17A and IL-17F significantly up-regulated IL-6 expression and transiently enhanced the expression of the osteogenic transcription factor RUNX-2. When IL-17 cytokines were combined in a biomimetic protocol, both IL-17A and IL-17F promoted osteogenic differentiation. Following 9 days’ exposure, IL-17F enhanced the expression of most osteogenic markers to a greater extent than IL-17A alone. Conversely, IL-17A treatment resulted in elevated in vitro mineralization vs IL-17F. The SNs potently enhanced hPDSC osteogenic differentiation and mineralization. While IL-6 expression and in vitro bone formation were blocked by neutralization of IL-17A or IL-17F individually, dual neutralization with bimekizumab exhibited the greatest effect on most of the tested parameters.

Conclusion: These data show that both IL-17A and IL-17F enhance in vitro osteogenic differentiation and bone formation from hPDSCs. The source of these cytokines has not been established but may, for example, involve enthesal resident γδ-T cells. We propose that IL-17A and IL-17F drive pathological bone formation resulting in enthesophytes at the enthesis/periosteum interface. Current therapeutics display limited efficacy in blocking enthesisphymate formation, hence inhibition of both IL-17A and IL-17F with bimekizumab offers an attractive therapeutic strategy to prevent this debilitating feature of SpA.

References:


Disclosure: M. Shah, UCB Pharma, 3, UCB Pharma, 2; A. Maroof, UCB Pharma, 3, UCB Pharma, 9; R. Al-Hosni, None; P. Gikas, None; N. Gozzard, UCB Pharma, 3; S. Shaw, UCB Pharma, 3, UCB Pharma, 9; S. Roberts, UCB Pharma, 3.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/bimekizumab-blocks-t-cell-mediated-osteogenic-differentiation-of-periosteal-stem-cells-coupling-pathological-bone-formation-to-il-17a-and-il-17f-signaling

Abstract Number: 1936
Abaloparatide, an Osteoanabolic PTHrP Analog, Increased Bone Mineral Density in Rabbits with Glucocorticoid Induced Osteopenia

Heidi Chandler1, Allen Pierce2, Jeffery Brown2, Michael Ominsky2 and Gary Hattersley3, 1Research, Radius Health Inc, Waltham, MA, 2Radius Health Inc, Waltham, MA, 3Radius Health, Inc., Waltham, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Biology and Pathology of Bone and Joint Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Estrogen deficiency and glucocorticoid (GC) therapy are the main causes of postmenopausal and secondary osteoporosis, respectively. Bone loss in both states relate to a negative bone balance (bone resorption exceeding formation), driven primarily by increased bone resorption in the case of estrogen deficiency, and by decreased bone formation with GC therapy.1 Both conditions increase in the risk of fragility fractures, including vertebral fractures.1 Abaloparatide (ABL), an anabolic PTHrP analog, increased bone formation and reduced the risk of new vertebral and nonvertebral fracture in women with postmenopausal osteoporosis at high risk of fracture.2 In estrogen-deficient ovariectomized (OVX) rats, ABL increased bone formation, bone mineral density (BMD) and bone strength without increasing bone resorption.3, 4 The current study assessed effect of ABL on BMD in a rabbit bone loss model that combines increased bone resorption via OVX5 plus impaired bone formation via GC therapy.6

Methods: 32 6-month-old female New Zealand White rabbits underwent OVX, 24 of which received the GC methylprednisolone (OVX + GC; daily, SC) starting 1 day after OVX. Another 8 rabbits had sham surgery and did not receive GC (Sham). After a 6-week bone depletion period, OVX + GC rabbits continued to receive GC and treatment began with daily SC vehicle (VEH) or ABL at 5 μg/kg (ABL5) or 25 μg/kg (ABL25) (all n = 8). The remaining OVX and Sham controls received VEH. Lumbar vertebra areal BMD (LV BMD) was assessed before surgery and at treatment week 0, 4, 8 and 12 by dual X-ray absorptiometry (DXA). Animals were sacrificed after 12 weeks of treatment.

Results: The OVX + GC VEH group showed an absolute reduction in LV BMD of 30.4% between the start and end of the bone depletion, indicating osteopenia prior to treatment initiation. LV BMD in the OVX + GC VEH group was significantly lower vs OVX controls at the end of the bone depletion period, demonstrating a significant independent contribution of GC to osteopenia. Progressive bone loss continued in the OVX + GC VEH group throughout the treatment period; by treatment week 12 their LV BMD was 49.8% lower than before the bone depletion period, 47.2% lower than Sham controls, and 36.6% lower than OVX VEH controls. ABL dose-dependently increased LV BMD, and by treatment week 8 the effect of ABL25 on LV BMD was significant compared with OVX + GC VEH controls (P < 0.05). By treatment week 12, LV BMD in the ABL25 group was increased by 15.7% vs treatment week 0, whereas LV BMD in the OVX + GC VEH controls decreased by 27.8% over that time (P = 0.0001).

Conclusion: These data indicate that ABL robustly increased BMD in rabbits rendered severely osteopenic by the combined effects of OVX plus GC therapy. These findings also provide preclinical support for investigating the potential of ABL for increasing BMD in patients with bone loss caused by GC therapy.


View Abstract and Citation Information Online - http://acrabstracts.org/abstract/abaloparatide-an-osteoanabolic-PTHrP-analog-increased-bone-mineral-density-in-rabbits-with-glucocorticoid-induced-osteopenia

Abstract Number: 1938

TGFB1 Governs Osteoblast Differentiation in Ankylosing Spondylitis Via Modulating BMP2
Sungsin Jo\textsuperscript{1}, Seung Hyun Choi\textsuperscript{2}, Il-Hoon Sung\textsuperscript{3}, Ye-Soo Park\textsuperscript{4} and Tae-Hwan Kim\textsuperscript{1}, 1Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), 2Choate Rosemary Hall, Wallingford, CT, 3Orthopaedic, Hanyang University Seoul Hospital, Seoul, Korea, Republic of (South), 4Orthopaedic, Hanyang University Guri Hospital, Guri, Korea, Republic of (South)

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** Biology and Pathology of Bone and Joint Poster II  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Ankylosing spondylitis (AS) is characterized by inflammation, high osteoblastic activity, leading to ankyloses. Transforming growth factor beta 1 (TGFB1) has been known to be a proinflammatory cytokine in inflammatory disorder and is expressed in AS. This study was undertaken to investigate the role of TGFB1 on osteoblast differentiation, to determine where TGFB1 can stimulate the osteoblast-induced bone formation that is a hallmark of AS.

**Methods:** All experimental and clinical samples were male. Serum from 26 patients with AS, 23 patients with rheumatoid arthritis (RA), and 28 healthy controls (HC) were collected. Bone tissues were obtained at surgery from facet joints of 10 patients with AS and 26 patients with noninflammatory spinal disease from traffic trauma or spinal compression disease, who served as controls. Expression of TGFB1 in patient serum and bone tissues with AS was confirmed by ELISA and immunohistochemistry, respectively. Primary osteoprogenitor cells were cultured to assess osteoblastic activity, using intracellular alkaline phosphatase (ALP) activity and staining, calcium deposit, and hydroxyapatite staining. Additionally, we observed the effect of TGFB1 on the expression of BMP2 which was evaluated by qPCR, promoter assay, immunostaining, immunoblotting, and Chromatin Immunoprecipitation (ChIP) assay.

**Results:** Serum and bone tissues of AS patients exhibited higher level of TGFB1 than those of RA and controls. Moreover, treatment of TGFB1 with primary osteoprogenitor cells showed an increase in phos-smad2 and phos-smad3 proteins, intercellular ALP activity, and BMP2 transcript under non-osteoblastic stimuli. TGFB1 also activated phos-smad2 protein directly binds to proximal region at Smad protein biding element (SBE) in BMP2 promoter. Interestingly, a slight stimulation of TGFB1 in immature stage promises more rapid differentiation toward mature stage under osteogenic stimuli.

**Conclusion:** TGFB1 was highly expressed in AS patients, which were considered to promote osteoblastic activity and osteoblast differentiation by a direct activation of BMP2 signaling pathway. These findings suggest that activation of TGFB1 contribute to the pathogenesis of new bone formation and TGFB1 appears to be a novel therapeutic target in preventing progression of AS.

**Figure:** TGFB1 is highly activated in AS. A, serum level of TGFB1 in AS and RA patients and healthy control as determined by ELISA assay. B, Immunohistochemical staining for TGFB1 in AS and normal bone.

**Disclosure:** S. Jo, None; S. H. Choi, None; I. H. Sung, None; Y. S. Park, None; T. H. Kim, None.


**Abstract Number:** 1939

**Dipyridamole, an Ent-1 Adenosine Transporter Inhibitor, Reverts De Osteoclastic Phenotype Induced By Tenofovir**
Background/Purpose: Adenosine, generated from the catabolism of adenine nucleotides, modulates cell function by interacting with specific cell-surface receptors (A<sub>1</sub>R, A<sub>2A</sub>R, A<sub>2B</sub>R, A<sub>3</sub>R). Inhibition of osteoclast formation via adenosine A2A receptor stimulation or increasing local adenosine concentration stimulates new bone formation as well as rhBMP-2. Bone alterations have been observed in HIV (Human Immunodeficiency Virus) disease for nearly two decades, in particular a higher risk of low bone mineral density (BMD) and fragility fractures. Treatment with Tenofovir leads to changes in bone catabolism markers and significant reductions in BMD in children and young adults. Tenofovir is taken up by cells and phosphorylated and inhibits HIV-reverse transcriptase by mimicking AMP. We have recently found that Tenofovir inhibits Pannexin-1/Connexin-43-mediated ATP release from cells and decreases extracellular adenosine levels and fibrosis in murine models. Here we determined if Tenofovir directly affects bone and if Dipyridamole, may be a useful treatment to counteract the effects.

Methods: M-CSF/RANKL-induced osteoclast (OC) were studied in primary murine bone marrow culture as the number of TRAP-positive cells after challenge with Tenofovir (1nM-100μM) alone or in combination with Dipyridamole (1nM-100μM). OC differentiation markers were study by RT-PCR. Male C57Bl/6 mice were divided into four groups: saline 0.9% (control), Tenofovir 75mg/Kg/day, Dipyridamole 25mg/Kg/day, combination Tenofovir/Dipyridamole for 4 weeks (n=10 each). Double labelling of bone with calcein /Alizarin Red was performed to analyzed bone formation and long bones prepared for microCT and histology.

Results: Tenofovir produced a dose-dependent increase in OC differentiation (EC50=44.5nM) that was reversed by Dipyridamole (IC50=0.3μM). Tenofovir increases Cathepsin K and NFATc1 mRNA levels during OC differentiation, and the effect was reverted by Dipyridamole. In vivo, mice treated with Tenofovir lost nearly 10% of body weight (p<0.001) and DXA analysis revealed a decrease in % fat (p<0.05), effect reverted by Dipyridamole. Tenofovir reduced bone formation in vivo (19±2µm bone apposition vs 35±4µm in control, p<0.05) and this effect was reverted by Dipyridamole (30±3µm, p<0.05 vs Tenofovir alone). microCT analysis revealed decrease BMD and altered trabecular bone in Tenofovir-treated mice, been reverted in the presence of Dipyridamole. TRAP-staining showed increased OC in vivo in Tenofovir-treated mice (88±31 vs 27±1 OC/hpf in control, p<0.005) that was reverted inn the presence of Dipyridamole (30±2OC/hpf, p<0.05 vs Tenofovir alone). Similar results were obtained for Cathepsin K and CD68. RANKL-positive cells were increased in the presence of Tenofovir meanwhile OPG positive cells decreases, and both effets were reverted in the presence of Dipyridamole.

Conclusion: These results indicate that Tenofovir enhances osteoclast differentiation and inhibits osteoblast differentiation by an adenosine-ATP-dependent mechanism and suggests that treatment with agents that increase local adenosine concentrations, like Dipyridamole, might prevent bone loss following Tenofovir treatment.

Disclosure: F. M. Conesa-Buendia, None; P. Llamas, None; T. Wilder, None; P. Atencio, None; A. Cabello, None; M. Gorgolas, None; B. Cronstein, NIH grant, 2,Arthritis foundation grant, 2,AstraZeneca, 2,Celgene, 2,Eli Lilly & Co., 5,AstraZeneca, 5,Canfite Biopharma, 1; R. Largo, None; G. Herrero-Beaumont, None; A. Mediero, Instituto de Salud Carlos III y Fondos FEDER, 2,Lead Discovery Center, 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/dipyridamole-an-ent-l-adenosine-transporter-inhibitor-reverts-de-osteoclastic-phenotype-induced-by-tenofovir

Abstract Number: 1940

Immunologic Synovitis Score: A New Score for Synovial Membrane Characterization in Inflammatory and Non-Inflammatory Arthritis
Aurélie Najm1,2, Benoît Le Goff MD PhD2,3, Frédéric Blanchard1, Jérôme Amiaud4, Céline Charrier5 and Veit Krenn6, 1INSERM U1238 University of medicine, PHY-OS Laboratory, Nantes, France, 2Rheumatology, Nantes University Hospital, Nantes, France, 3UNR1238 University of medicine, PHY-OS Laboratory, Nantes, France, 4UMR1238 University of medicine, PHY-OS Laboratory, Nantes, France, 5UNMR1238 University of medicine, PHY-OS Laboratory, Nantes, France, 6Zytologie und Molekulare Diagnostik, MVZ-Zentrum für Histologie, Trier, Germany

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Biology and Pathology of Bone and Joint Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
General Synovitis score (GSS) has been developed by Krenn et al in order to discriminate inflammatory arthritis (IA) and non-inflammatory arthritis (NIA) (1). This score allow to quantify inflammation by scoring 3 major components of synovitis: lining layer hyperplasia, activation of resident cells (stroma) and inflammatory infiltrate. All components are graded semi-quantitatively from 0 to 3 and the total score is on 9. High-grade synovitis is highly associated with IA and is defined by a score above 5 with a sensitivity of 61.7% and a specificity of 96.1%. As immunohistochemistry (IHC) is frequently used to better characterize synovitis, we propose to create a new IMmunologic SYnovitis SCore (IMSYC) adding 5 components to the GSS: CD68, CD3, CD20, CD31 and Ki67 immunostaining.

Our work aimed to evaluate the diagnostic performance of this new score including IHC, to define the best cut off for inflammatory arthritis recognition, and to compare its diagnostic performance with the GSS.

Methods:
Synovial samples from patients were obtained during surgical procedure (arthroplasty or synovectomy). All patients gave written consent prior surgery. Samples were cut and Hematoxylin and eosin stained. CD68, CD3, CD20, CD31 and Ki67 IHC were performed. GSS was assessed for each slide and semi-quantitative 4 scale scores (0-3) were given for each immunostaining, in a blind manner. The score is calculated on 24 (GSS 0-9 points, and 0-3 score for each of the 5 immunostaining).

The 2 readers met and scored a representative amount of slides with a spearman correlation coefficient of 0.95 (p<0.0005). They then defined a consensual and reproducible scoring atlas.

Results:
53 patients were included. 25 were females (47,2%), mean age was 62.1 years (standard deviation (SD) 13.2 years). 36 had IA reparsed as follows: 28 Rheumatoid arthritis (RA), 5 had Psoriatic arthritis (Psa), 3 had Undifferentiated arthritis (UA). “Non inflammatory” arthritis group included 10 patients with Osteoarthritis (OA) and 7 with ligaments or meniscus injuries (post traumatic arthritis (PtA).

Mean Synovitis Score was significantly superior in the IA group 5.70 [SD 0.321] vs.3.51 [SD 0.351] ; p<0.001). Mean IMSYC was significantly superior in the IA group 14.94 [SD 0.747] vs. 8.50 [SD 0.639]; p<0.001). In univariate analysis by logistic regression, GSS (Odd Ratio (OR) 2.27; p<0.001), CD3 (OR 4.3; p=0.002), CD68 (OR 4.5; p=0.002), Ki67 (OR 11.8; p<0.001), CD31 scores (OR 6.5; p=0.001) and were significantly associated with IA, however CD20 score was not (OR 0.9; p=0.34).

ROC curve analysis of diagnostic performances determined the score of 10.5 out of 24 as the best cut off for discrimination between IA and non-IA with a sensitivity of 74.3% and specificity of 100%. The area under ROC curves (AUC) were nearly statistically different between GSS (0.81) and IMSYC (0.93) (p=0.05).

Conclusion: We hereby propose a new synovitis score including IHC. This score has a better sensitivity and specificity than the Synovitis score for discrimination between inflammatory and non-inflammatory arthritis. Moreover, IMSYC accurately describes synovial membrane immunophenotype and could therefore give a basis for tissue driven therapies in rheumatic diseases, especially in RA.

Disclosure: A. Najm, None; B. Le Goff MD PhD, None; F. Blanchard, None; J. Amiaud, None; C. Charrier, None; V. Krenn, None.

Microenvironmental and Systematic Evaluation of the Immunome in Osteoarthritis

Bhairav Paleja1, Ying Ying Leung2, Pavanish Kumar1, Suzan Saidin1, Ahmad Lajam2, Liyun Lai1 and Salvatore Albani1, 1SingHealth Translational Immunology and Inflammation Centre (STIIC), Duke-NUS Medical School, Singapore, Singapore, 2Singapore General Hospital, Singapore, Singapore

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Biology and Pathology of Bone and Joint Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Osteoarthritis is the most common joint disease and involves whole joint, including degeneration of articular cartilage and surrounding tissues. Although widely prevalent, the exact mechanisms involved in pathogenesis of OA are not well understood. Increasing body of data suggest role of low-grade, subclinical, in pathogenesis of OA. However the role of immune cell subsets in OA is poorly investigated. In present study we have applied a combination of single cell mass cytometry for analysis of the peripheral immunome and next generation RNA-sequencing on cell pellet from knee joint fluid to characterise immune cells and pathways.

Methods:
Patients samples were taken from a randomized controlled trial on treatment of symptomatic knee OA using colchicine for 16 weeks (1) (2). Patients were grouped as having ≥30% improvement in WOMAC (improvement group) and improvement of WOMAC not reaching 30%(Worsening group) at study end regardless of treatment arms. For RNA sequencing analysis 16 paired patient samples, from baseline and study end, were used. For mass cytometry analysis, 37 marker panel was designed to aid in identification of major peripheral blood mononuclear cell (PBMCs) subsets. Unsupervised clustering of mass cytometry data was performed using in-house developed analysis software MARVIS. This software combines dimension reduction and clustering steps to identify all possible cellular subsets from high dimension data. Further, custom R scripts helped in identifying nodes that were differentially expressed between the study groups and also phenotype of these nodes.

Results:
Differential gene expression analysis comparing baseline vs week 16 from worsening group revealed changes in 696 genes and in improvement group 89 genes were identified. Estimation of cell type abundances, using Cibersort algorithm, showed increased frequency of M2 macrophages, follicular helper T cells and activated NK cells in worsening group and increased memory CD4 T cells in improvement group. Mass cytometry analysis of PBMCs showed increase in inflammatory Tbet+ ILC subsets in worsening group (n=6) and an increase in Th2 like GATA3+ CD4 T cells in improvement group (n=6) at baseline.

Conclusion:
Our systematic multi dimensional approach reveals differences in the alteration of immune cells in knee OA patients with/ without symptoms improvement, both at synovial fluid level and systemic blood level. Further analysis may provide insights into mechanistic pathways involved in pathogenesis of OA, the interaction between tissue and systemic circulation and for advent of novel OA therapies.

Disclosure: B. Paleja, None; Y. Y. Leung, None; P. Kumar, None; S. Saidin, None; A. Lajam, None; L. Lai, None; S. Albani, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/microenvironmental-and-systematic-evaluation-of-the-immunome-in-osteoarthritis

Abstract Number: 1942

CTLA4-Ig Directly Inhibits Osteoclast Generation from Human Peripheral Monocytes and Tumor Necrosis Factor α-Treated Inflammatory Monocytes
Katsuhiro Oi1, Tadahiro Tokunaga1, Tatsuomi Kuranobu1, Yusuke Yoshida2, Shintaro Hirata1, Takaki Nojima3 and Eiji Sugiyama2,
1Clinical Immunology and Rheumatology, Hiroshima University Hospital, Hiroshima, Japan, 2Department of Clinical Immunology and
Rheumatology, Hiroshima University Hospital, Hiroshima, Japan, 3Clinical Immunology and Rheumatolog, Graduate School of
Medicine, Kyoto University, Kyoto, Japan
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Biology and Pathology of Bone and Joint Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: CTLA-4 is a surface protein on T lymphocytes, which negatively regulates the co-stimulation process between
antigen-presenting cells and T cells. CTLA-4 binds to monocytes via CD80/CD86, which are precursor of osteoclast. In addition,
CTLA-4 has been shown to directly inhibit osteoclast formation. However, little is known about the effect of CTLA-4 on osteoclast
generation from human monocytes and monocytes exposed to inflammatory cytokines. The aim of this study was to evaluate the effect
of a CTLA4-Ig (Abatacept) on osteoclastogenesis in human peripheral monocytes and TNFα-treated inflammatory monocytes.

Methods: Peripheral blood mononuclear cells are separated by Ficoll-Paque gradient centrifugation. Highly purified monocytes are
prepared from prepared mononuclear cells using MACS microbeads (Pan Monocyte Isolation kit). In this study, more than 92 % of
obtained cells are CD14-positive, as determined by flow cytometric analysis. Cultures were maintained in α-minimal essential medium
for 7-14 days with both or either of M-CSF, RANKL and/or TNFα in the presence or absence of CTLA4-Ig. Osteoclasts were identified
by TRAP staining and bone resorptive activity using the osteo assay surface multiwell plate. The expressions of CD80/CD86 on resting
and TNFα-pretreated monocyte were determined by flow cytometric analysis.

Results: Peripheral monocytes from healthy donors were incubated with M-CSF (50 ng/ml) and RANKL (100 ng/ml) in the presence of
increasing doses of CTLA4-Ig for 5~7 days. After the culture, generated osteoclasts were determined by TRAP staining and bone
resorptive activity. CTLA-4 inhibited the osteoclast generation in a dose-dependent manner (in the range of 0 to 500 μg/ml). To examine
the effect of CTLA4-Ig on monocytes exposed to inflammatory cytokines, peripheral monocytes were preincubated with TNFα for 24
hours, and then cultured with RANKL. When the expression of CD80/CD86 antigens on peripheral monocytes was analysed, CD80 was
only expressed on resting monocytes. Interestingly, TNFα pretreatment potently induced the expression of CD80, suggesting
modification of action of CTLA-4. CTLA4-Ig more potently inhibited osteoclast generation from TNFα-treated monocytes than those
from resting monocytes.

Conclusion: CTLA4-Ig directly inhibits osteoclast generation from human peripheral monocytes. In addition, the inhibitory effect
of CTLA4-Ig is more potent in TNFα-treated inflammatory monocytes than resting monocytes, suggesting that CTLA4-Ig could inhibit
osteoclast generation in inflammatory monocytes at inflamed joints of RA.

Disclosure: K. Oi, None; T. Tokunaga, None; T. Kuranobu, None; Y. Yoshida, None; S. Hirata, None; T. Nojima, None; E.
Sugiyama, Bristol-Myers Squibb, 2,Chugai, 2,Pfizer Inc, 2,Abbvie GK, 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/ctla4-ig-directly-inhibits-osteoclast-generation-
from-human-peripheral-monocytes-and-tumor-necrosis-factor-%ce%b1-treated-inflammatory-monocytes

Abstract Number: 1943

Adipocytokines in an Osteoarthritis Mouse Model

Marie-Lisa Hülser1, Carina Schreiyäck1, Yubin Luo2, Aline Bozec2, Georg Schett3, Elena Neumann4 and Ulf Müller-Ladner5,
1Department of Internal Medicine and Rheumatology, Justus-Liebig-University Giessen, Department of Internal Medicine and
Rheumatology, Kerckhoff-Klinik, Bad Nauheim, Germany, Bad Nauheim, Germany, 2Department Clinic of Medicine 3 - Immunology
und Rheumatology, University of Erlangen-Nürnberg, Department Clinic of Medicine 3 - Immunology and Rheumatology, Erlangen,
Germany, Erlangen, Germany, 3Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Department of Internal Medicine 3 –
Rheumatology and Immunology, Universitätsklinikum Erlangen, Erlangen, Germany., Erlangen, Germany, 4Justus-Liebig-University
Giessen, Department of Internal Medicine and Rheumatology, Kerckhoff-Klinik, Bad Nauheim, Germany, Bad Nauheim, Germany,
5Justus-Liebig-University Giessen, Department of Internal Medicine and Rheumatology, Kerckhoff-Klinik, Bad Nauheim, Germany,
Bad-Nauheim, Germany
First publication: September 18, 2017
Background/Purpose:

In the Western society adiposity and metabolic syndrome are an increasing field of medical research. Both entities influence the expression of adipokines such as adiponectin, visfatin or leptin, which also modulate the progress of osteoarthritis (OA).

To evaluate these comorbidities together, we combined a high-fat diet (HFD) with the DMM mouse model (destabilization of the medial meniscus). The serologic and local effects of HFD at different states of OA development were correlated to local/systemic adipokine expression.

Methods:

HFD and ND (normal diet) as control were fed to male C57Bl/6 mice for 3 months followed by surgical DMM (time point 0). Joints, organs and sera were collected 4, 6, and 8 weeks after surgery. Concentrations of the adipocytokines leptin, visfatin, adiponectin and IL-6 in the sera were measured by ELISA. Liver fat was scored to show metabolic changes. Arthritis progression was scored and quantified using histologic stainings of the joints (H/E, safranin O, Pappenheim and Masson-Goldner’s trichrome). Immunohistochemical stainings of the mouse joints were performed to evaluate the local distribution of adipokines. Adipokine levels were correlated to arthritis scores, fatty liver score and bodyweight.

Results:

At all time points, OA was significantly induced, especially by HFD compared to ND (e.g.: OA score at 6 weeks HFD 3.7 vs. ND 1.4). Systemically, leptin levels were significantly higher in HFD compared to ND, but DMM decreased leptin levels at all time points independent from diet (e.g. 4 weeks: HFD healthy 18.4 ng/ml vs. HFD DMM 3.7ng/ml). Systemic leptin levels correlate with liver fat content. Interestingly, the systemic changes of adiponectin by DMM were only present at week 8 (HFD healthy 5176ng/ml vs. HFD DMM 6149ng/ml). The combination of HFD and DMM did not show significant effects on serum levels of adiponectin, visfatin or IL-6 in this experimental setting. Local adipokine expression in the joints was independent from systemic adipokine levels.

Conclusion:

The data show that similar to the human setting, OA in the DMM model is deteriorated by HFD. This is serologically reflected by reduced protective leptin levels but not increased proinflammatory visfatin or adiponectin supporting the idea of a prominent local rather than systemic pathophysiology.

Disclosure: M. L. Hülsen, None; C. Schreiyäck, None; Y. Luo, None; A. Bozec, None; G. Schett, None; E. Neumann, None; U. Müller-Ladner, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/adipocytokines-in-an-osteoarthritis-mouse-model

Abstract Number: 1944

A Dual Role for IL-23 Receptor Signaling in Normal Bone Remodeling Versus Inflammation-Mediated Bone Damage during Arthritis

Wida Razawy1, Marijke Koedam2, Patrick Asmawidjaja3, Anne-Marie Otten-Mus4, Bram van der Eerden2 and Erik Lubberts3,
1Rheumatology and Immunology, Erasmus MC, Rotterdam, Netherlands, 2Internal Medicine, Erasmus MC, Rotterdam, Netherlands, 3Rheumatology and Immunology, Erasmus MC, University Medical Center, Rotterdam, Netherlands, 4Immunology, Erasmus MC, University Medical Center, Rotterdam, Netherlands
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Biology and Pathology of Bone and Joint Poster II
Session Type: ACR Poster Session C
Background/Purpose:

The interleukin (IL)-23/IL-17A immune pathway is critical for the development of autoimmune arthritis. Systemic exposure of IL-23 induced chronic arthritis, increased osteoclast differentiation and systemic bone loss in mice. However, the role of IL-23 on normal and pathologic bone remodeling is not fully elucidated. Here we examined the role of IL-23R signaling on bone remodeling in steady state and on bone damage during a T cell-mediated inflammatory arthritis using wild type (WT) and IL-23RKO mice.

Methods:

Femurs of naïve WT and IL-23RKO mice were used for MicroCT analysis of the bone and a three-point bending test for bone strength. Bone marrow cells (BM) were cultured towards osteoclasts with MCSF, RANKL and +/- IL-17 and assessed for osteoclast-like cells using tartrate-resistant acid phosphatase (TRAP) staining and bone resorption assay.

For antigen-induced arthritis (AIA), WT and IL-23RKO mice were immunized with methylated bovine serum albumin (mBSA) supplemented in Complete Freund’s Adjuvant. After 7 days mice were injected in the knee joints with mBSA. Mice were macroscopically scored at given time points and knees were used for histological analysis of joint inflammation and bone erosion.

Results:

MicroCT data revealed a low bone mass phenotype in naïve IL-23RKO mice compared to WT mice, with lower trabecular bone volume fraction, thickness and number as well as lower cortical volume and thickness. Three-point bending data show significantly reduced maximum force in IL-23RKO femurs. However, IL-17 stimulation of both WT and IL-23RKO BM cells increased osteoclast bone resorption activity in vitro.

In contrast, histological analysis revealed significantly less inflammation-mediated bone damage in knees of IL-23RKO versus WT mice during AIA. This was accompanied with significantly less severe joint inflammation, although the onset of arthritis was not prevented in IL-23RKO mice.

Conclusion:

IL-23R signaling is important for the maintenance of bone mass under steady state conditions. However, although the effect of IL-17A on bone resorption is independent of IL-23R signaling, T cell driven inflammatory bone erosion during arthritis is IL-23R signaling dependent.

Disclosure: W. Razawy, None; M. Koedam, None; P. Asmawidjaja, None; A. M. Otten-Mus, None; B. van der Eerden, None; E. Lubberts, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/a-dual-role-for-il-23-receptor-signaling-in-normal-bone-remodeling-versus-inflammation-mediated-bone-damage-during-arthritis

Abstract Number: 1945

Repositioning Suramin As a Cartilage-Protective Drug

Laura-An Guns1, Silvia Monteagudo1, Maryna Kvasnytsia1, Greet Kerckhofs1, Jennifer Vandooren2, Ghislain Opdenakker2, Frederic Cailotto1,3 and Rik Lories4, 1Skeletal Biology and Engineering Research Center, KU Leuven, Leuven, Belgium, 2Rega Institute, KU Leuven, Leuven, Belgium, 3University of Lorraine, Nancy, France, 4Rheumatology, UZ Leuven, Leuven, Belgium

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Biology and Pathology of Bone and Joint Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Drug repositioning is a recent pharmaceutical strategy to discover new uses for market-approved drugs with known safety profiles that can provide quick transition from the laboratory bench to bedside. Suramin is a poly-sulfonated molecule, used for the treatment of African sleeping sickness. Suramin has been used in vitro to isolate MMPs and tissue inhibitor of
Metalloproteinase 3 (TIMP3) from the rat uterus. Here, we investigated therapeutic repositioning of suramin to protect the joint against the development of osteoarthritis, hypothesizing that suramin interacts with cartilage extracellular matrix (ECM) proteins.

**Methods:** *In vitro* ECM deposition in the presence or absence of suramin was studied in murine chondrogenic ATDC5 cells or in human articular chondrocytes from osteoarthritis and control patients, by gene expression and protein analysis, colorimetric staining and immunohistochemistry. To study the effect of suramin *in vivo*, the drug was injected intra-articularly in the papain-model of osteoarthritis in wild-type C57/Bl6 mice. Disease severity was analyzed by histology, immunohistochemistry and contrast-enhanced nanofocus computed tomography.

**Results:** In ATDC5 micromass cultures, suramin treatment increased tissue inhibitor of metalloproteinase-3 (TIMP3) levels and decreased the activity of matrix metalloproteinases (MMPs) and aggrecanases. Suramin treatment thus resulted in increased glycosaminoglycan content. This effect on the cartilage ECM was prevented by co-culture with anti-TIMP3 antibody. Mice treated intra-articularly with repetitive suramin injections in the disease model of osteoarthritis, showed reduced cartilage damage compared to controls, with increased TIMP3, and decreased MMP and aggrecanase activity. Translational validation in human chondrocytes confirmed increased TIMP3 function and reduced cartilage breakdown after suramin treatment.

**Conclusion:** Suramin prevented the development of osteoarthritis in a mouse model of direct cartilage damage. Mechanistically, the effects of suramin appear to be mediated by a functional increase of TIMP3, and a subsequent decrease in the activity of catabolic enzymes.

**Disclosure:** L. A. Guns, None; S. Monteagudo, None; M. Kvasnytsia, None; G. Kerckhofs, None; J. Vandooren, None; G. Opdenakker, None; F. Cailotto, None; R. Lories, None.

**Abstract Number:** 1946

**Development of a Multi-Component 3D Arthritic Joint Model**

**Alexandra Damerau**1,2, Lisa Ehlers1,2, Moritz Pfiefenberger1,2, Igor Ponomarev3, Frank Buttgereit2,4, Timo Gaber4,5 and Annemarie Lang1,2, 1Rheumatologie und klinische Immunologie, Charité-Universitätsmedizin Berlin, Berlin, Germany, 2Deutsches Rheuma-Forschungszentrum Berlin, Berlin, Germany, 3Research Center of Medical Technology and Biotechnology, Bad Langensalza, Germany, 4Rheumatologie und klinische Immunologie, Charité Universitätsmedizin Berlin, Berlin, Germany, 5German Rheumatism Research Center (DRFZ) Berlin, Berlin, Germany

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Tuesday, November 7, 2017
**Session Title:** Biology and Pathology of Bone and Joint Poster II
**Session Type:** ACR Poster Session C
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Our goal is to develop an *in vitro* 3D joint model to simulate the immune mediated pathogenesis of arthritides in order to present an alternative experimental setup for traditional animal models. There are currently no appropriate *in vitro* models capable of simulating an arthritic joint in such a comprehensive way that all relevant humoral and cellular factors as well as the different tissue types are involved. Therefore, we work to establish an *in vitro* 3D healthy joint model, followed by the simulation of an arthritic joint. The *in vitro* 3D joint model is planned to consist of an (1) osteogenic part and (2) a chondrogenic part, (3) the joint space with synovial fluid, and (4) the synovial membrane.

Development of the first two components of our *in vitro* 3D joint model, namely (1) the osteogenic and (2) the chondrogenic part.

**Methods:**

We used β-tricalcium phosphate (TCP) with 60% porosity as the mineral part of our osteogenic model. This substrate was populated with human bone marrow derived mesenchymal stromal cells (hMSC) predifferentiated towards the osteoblastic lineage and then cultured for up to 21 days under normoxic conditions (37 °C, 18% O2). The adhesion of the cells and their structural integrity were evaluated by Scanning Electron Microscopy and Laser Scanning Microscopy. To confirm cell attachment and biocompatibility of β-TCP particles, cellular release of LDH (after 1 d) was assessed, and LIVE/DEAD staining was applied (1, 7, 14, 21 d). Osteogenic
differentiation was verified on gene expression level using qRT-PCR. The chondrogenic model, a scaffold-free 3D cartilage construct (fzmb GmbH), was generated using native hMSC. Chondrogenic differentiation was performed under hypoxia (37 °C, 1% O₂) with intermittent mechanical stimulation and analyzed by histology (HE staining) and immunohistology (Col1a1, Col2a1, Alcian Blue).

Results:

We have been able to successfully develop an in vitro 3D bone model by seeding predifferentiated hMSC (after 24-hour preincubation with osteogenic medium) on a β-TCP scaffold. The analysis of cell viability via LDH detection did not show any toxic effects during cultivation of the cells seeded. Histological and immunofluorescence analyses demonstrated good cell attachment, cell integrity and metabolic activity of the β-TCP scaffold until day 21, demonstrating the good suitability of both the scaffold and the cultivation method. mRNA expression of bone-related genes such as RUNX2, SPP1 and COL1A1 confirmed phenotypic changes as induced during osteogenic differentiation. The development of a cartilage phenotype from the accordingly differentiated hMSC was confirmed by HE and Alcian Blue staining as well as by Col1a1 and Col2a1 expression. Histological analyses performed after 21 d of co-cultivation showed successful colonization, connectivity and initial calcification implying a functional transitional bridging area.

Conclusion: These initial results from our in vitro 3D models confirm good cell vitality indicating successful progression of developing our model. This 3D multi-component joint model should enable us to simulate arthritis and to study the efficacy of drug treatment in vitro.

Disclosure: A. Damerau, None; L. Ehlers, None; M. Pfeiffenberger, None; I. Ponomarev, None; F.Buttgereit, None; T. Gaber, None; A. Lang, None.

Thy1 Is a Positive Regulator of Osteoblast Differentiation and Modulates Bone Homeostasis in Obese Mice

Ananta Paine1, Collynn Woeller2, Nelson Huertas1, Maria de la Luz Garcia-Hernandez3, Richard Phipps2 and Christopher T. Ritchlin4,

1Department of Medicine, Division of Allergy, Immunology and Rheumatology, School of Medicine and Dentistry, University of Rochester, Rochester, New York, USA, Rochester, NY, 2Department of Environmental Medicine, School of Medicine and Dentistry, Department of Environmental Medicine, School of Medicine and Dentistry, University of Rochester, Rochester, New York, USA, Rochester, NY, 3Department of Medicine, Division of Allergy, Immunology and Rheumatology, School of Medicine and Dentistry, University of Rochester, Rochester, New York, USA, Rochester, NY, 4Division of Allergy, Immunology and Rheumatology, School of Medicine and Dentistry, Division of Allergy, Immunology and Rheumatology, School of Medicine and Dentistry, University of Rochester, Rochester, New York, USA, Rochester, NY

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Biology and Pathology of Bone and Joint Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Thy1 (CD90) is a glycosylated, glycophosphatidylinositol (GPI)-anchored membrane protein originally identified as a marker for mouse T cells but subsequent reports noted expression on stem cells, osteoblasts and fibroblasts. Thy1 is abundantly expressed by mesenchymal stem cells and inhibits adipogenesis. We examined the contribution of Thy1 to osteoblastogenesis and bone homeostasis.

Methods: A pre-osteoblastic MC3T3 cell line, and primary bone marrow derived mesenchymal stem cells from wild type (WT) C57BL/6 mice were cultured in osteogenic conditions for up to 21 days. Messenger RNA (mRNA) and protein expression of Thy1 and the OB differentiation markers RUNX2, BGLAP, COL1A1, were analyzed by real-time PCR and western blot. Similarly, mouse embryonic fibroblasts (MEFs) isolated from WT and Thy1 knockout (KO) mice were cultured in osteogenic media. Mineralized matrix and calcium deposition were examined with alizarin red staining. To study the impact of Thy1 depletion on bone quality in the normal and obese mice, 2 month old C57BL/6 WT and Thy1 KO mice were fed a normal or high fat diet for 2 months and long bones were analyzed with micro-CT to compare changes in bone architecture and overall bone quality.
Results: *In vitro* assays revealed that osteogenic conditions transiently increased Thy1 expression during OB differentiation. *In vitro* experiments with WT and Thy1 KO mesenchymal cells and MEFs further revealed that in the absence of Thy1, osteoblastogenesis was delayed as noted by alizarin red staining. Micro CT analysis of long bones in WT and Thy1 KO mice revealed that when Thy1 KO and WT mice were fed a high fat diet, bone quality at 4 months differed significantly between WT and KO mice. In particular, a significant reduction in trabecular bone quality was noted in Thy1 KO mice. The most significant differences were seen in tibial trabecular bone volume/total volume (BV/TV): 0.12 ± 0.02 in WT vs 0.09 ± 0.01 in Thy1 KO, (p < 0.03), femoral BV/TV: 0.37 ± 0.15 in WT vs. 0.19 ± 0.03 in Thy1 KO femur, (p < 0.03) and tibial trabecular bone connectivity density: 50.01 ± 10.85 in WT vs 28.29 ± 6.72 in Thy1 KO, (p < 0.01), and femoral trabecular bone connectivity density: 42.03 ± 14.42 in WT vs. 22.17 ± 7.79 in Thy1 KO femur, (p < 0.019); overall more than a 40% decrease. Interestingly, significant differences were not detected in WT and Thy1 KO mice fed a normal diet.

Conclusion: We find that Thy1 is required for differentiation of OB based on our *in vitro* experiments. Absence or decreased expression of Thy1 was associated with reduced bone quality. Of note, higher levels of Thy1 mRNA and protein levels were reported in osteoarthritis patients, a disease characterized by osteophyte formation with higher prevalence in obese individuals. Thus, Thy1 may serve as an important mechanistic link between bone formation and obesity.

Disclosure: A. Paine, None; C. Woeller, None; N. Huertas, None; M. D. L. L. Garcia-Hernandez, None; R. Phipps, None; C. T. Ritchlin, UCB, 2, Abbvie, 2, Amgen, 2, Amgen, 5, Abbvie, 5, Janssen Pharmaceutica Product, L.P., 5, Novartis Pharmaceutical Corporation, 5, Pfizer Inc, 5.
the level of TNFR1 decreased during OC differentiation. Blockade of TNFR1 negated the inhibitory capacity of simultaneous TNF-α whilst blockade of TNFR2 reverted the enhancing capacity of TNF-α. Inhibition of IKK-β revealed that the TNFR1-driven inhibitory signal was dependent on the canonical NF-κB pathway. At a molecular level, TNF-α signalling in CD14+ monocytes blocked the M-CSF-driven up-regulation of RANK transcript.

In comparison to CD14+ monocytes, pre-DCs differentiated quicker and more efficiently into OCs under M-CSF and RANK-L stimulation. Interestingly, pre-DCs were found to express less TNFR1 than CD14+ monocytes and TNF-α failed to inhibit RANK expression and thus their differentiation into functional OCs.

**Conclusion:** We have shown that the hierarchy between TNF-α and RANK-L is crucial for driving the differentiation of CD14+ monocytes into either macrophage or osteoclasts. In comparison, this axis does not influence the ability of pre-DCs to differentiate down the OC lineage. This study provides new insight in the contribution of different circulating myeloid precursors to bone destruction in a TNF-α rich environment.

**Disclosure:** C. Ansalone, None; F. Sunzini, None; C. Duncan, None; S. Chilaka, None; I. B. McInnes, None; C. S. Goodyear, None.


**Abstract Number:** 1949

**Anti-Inflammatory Effects of Standardized Platelet-Rich Plasma Releasates in Knee and Hip OA Chondrocytes**

Lucia Gato-Calvo1, Ángela Vela-Anero2, Elena F. Burguera1 and Francisco J Blanco3, 1Servicio de Reumatología. Instituto de Investigación Biomédica de A Coruña (INIBIC). Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidade de A Coruña (UDC), A Coruña, Spain, 2Cell Therapy and Regenerative Medicine Group, Department of Medicine, University of A Coruña, A Coruña, Spain, 3Proteomics Group, Rheumatology Division, ProteoRed, PRB2-ISCIII. INIBIC-Hospital Universitario A Coruña, 15006 A Coruña-Spain, A Coruña, Spain

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Biology and Pathology of Bone and Joint Poster II

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** There is a need to standardize platelet-rich plasma (PRP)-derived products and their dosage to evaluate efficacy for each intended indication. Our purpose here was to test the anti-inflammatory effects of PRP releasates (PRP-rs) from PRP with standardized (absolute) platelet concentrations in OA knee and hip chondrocytes stimulated with IL-1B.

**Methods:** Blood was obtained from healthy volunteers after informed consent. PRPs with different platelet concentrations (0, 0.25, 0.5, 0.75, 1.5, 3, 6 and 15x10^5 platelets/uL) were prepared by first, separating platelets and platelet poor plasma (PPP), and then re-suspending platelets in known absolute numbers. PRPs were then clotted with CaCl2 to obtain their PRP-rs. Human chondrocytes (hCH) were isolated from OA hip and knee joints after informed consent. Co-stimulation of hCH with IL-1B and the different PRP-rs (10% in DMEM) was used to test their anti-inflammatory effect. We assessed the expression of relevant inflammatory markers with qRT-PCR, ELISA and immunocytochemistry. GraphPad Prism software was used for data analysis with both parametric (ANOVA + Bonferroni’s post hoc test) and non-parametric (Kruskal-Wallis + Dunn’s test) approaches.

**Results:** Inflammatory stimulation with IL-1B sharply increased the expression of iNOS, COX-2, PTGES, MMP-13 and IL-6. All PRP-rs showed a significant anti-inflammatory effect in knee OA hCH for all markers, ranging from 80% for COX_2 to 99% for iNOS (Fig.1a-c). Remarkably, this reduction was not dependent on platelet dose; even PPP showed maximum anti-inflammatory effect. As for hip OA hCH, only the lower platelet doses of 0 - 0.75x10^5/uL reduced the expression of COX-2 (~90%), PTGES and MMP-13 (~90%) significantly (Fig.1f-g). Increasing platelet doses (except for iNOS, Fig.1e) resulted in a progressive loss of this anti-inflammatory effect in hip OA hCH. ELISA quantitation of MMP-13 protein corroborated these trends on knee and hip hCH: all PRP_rs (except 6 and 15x10^5/uL) reduced MMP-13 to approximately basal levels (Fig 1d, h). Immunocytochemistry of iNOS and COX-2 in knee hCH were concordant with qRT-PCR results as well (Fig 2).
Conclusion: PRP-r can exert anti-inflammatory effects in OA hCH but platelet enrichment is not needed for knee OA hCH, and it is detrimental in hip OA. In this case, only doses below peripheral blood platelet concentration (< 1.5x10^5 platelet/μL) were effective. Therefore, platelet dosages in PRP need to be standardized to evaluate efficacy and might need to be adjusted for different indications.

Disclosure: L. Gato-Calvo, None; Á. Vela-Anero, None; E. F. Burguera, None; F. J. Blanco, None.

Cross-Sectional Analysis of Foot Osteoarthritis Frequency and Associated Factors: The Johnston County Osteoarthritis Project

Portia Flowers¹, Amanda Nelson², Howard J. Hillstrom³, Jordan B. Renner⁴, Joanne M. Jordan⁵ and Yvonne M. Golightly⁶, ¹Thurston Arthritis Research Center, University of North Carolina - Chapel Hill, Chapel Hill, NC, ²Division of Rheumatology, Allergy, and Immunology and Thurston Arthritis Research Center, University of North Carolina at Chapel Hill, Chapel Hill, NC, ³Rehabilitation, Hospital Special Surgery (HSS), New York, NY, ⁴UNC School of Medicine, University of North Carolina, Chapel Hill, NC, ⁵Thurston Arthritis Research Center, University of North Carolina at Chapel Hill, Chapel Hill, NC, ⁶Epidemiology, University of North Carolina at Chapel Hill, Chapel Hill, NC

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Epidemiology and Public Health Poster III: Rheumatic Disease Risk and Outcomes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The rising number of adults with arthritis and associated activity limitations present a serious public health problem. Although studies have explored lower limb osteoarthritis (OA) at the knee and hip, few have focused on the foot. Therefore, the purpose of this study is to determine the frequency of foot OA and identify potential associated risk factors.
Methods: Participants were from the Johnston County OA Project, a community-based study of individuals in rural North Carolina with and without OA. Weight-bearing anteroposterior and lateral radiographic images of the foot were obtained. Based on the La Trobe radiographic atlas, foot radiographic OA (rOA) was defined as a score of 2 or more for osteophytes or joint space narrowing in at least one of the following 5 joint sites: 1st metatarsophalangeal joint, 1st & 2nd cuneo-metatarsal joints, navicular-1st cuneiform joint, and talo-navicular joint. Foot symptoms were assessed via questionnaire by answering the question: “On most days of any one month in the last 12 months did you have pain, aching or stiffness in your [left/right] foot?” Symptomatic OA (sxOA) was defined as symptoms in the presence of foot rOA. At the joint level, separate logistic regression models with generalized estimating equations (GEE) to account for intra-person correlations were performed to examine discrete associations (odds ratios [OR]) of foot rOA or sxOA with age, body mass index (BMI), sex (women/men), race (African-American/Caucasian), history of foot injury (yes/no), and foot symptoms ([yes/no], rOA models only). Next, multiple logistic regression models with GEE were performed for foot rOA or sxOA outcomes adjusting for all factors (foot symptoms: rOA models only).

Results: Of the 864 participants with available data (mean age 71 yrs, mean BMI 30.8 kg/m\(^2\), 68.2% women, 33.4% African American), 22.1% had rOA, 20.4% had foot symptoms, 5.3% had sxOA, and 3.8% reported prior foot injury. In adjusted models, symptoms vs. no symptoms were associated with 1.48 times the odds of rOA (Table 1). Compared to non-obese (BMI<30) participants, obese (BMI≥30) individuals had 1.74 times the odds of rOA (Table 1) and 3.30 times the odds of sxOA (Table 2). African Americans vs. Caucasians had 1.49 times the odds of rOA; the association was not statistically significant in the adjusted model (Table 1).

Conclusion: In this community-based cohort, 1 out of 5 older adults had foot rOA and 1 out of 20 had foot sxOA. Obesity was linked with foot OA, even when considering other factors, suggesting that weight reduction may be an important strategy, especially for individuals with sxOA.

Table 1 – Odds ratios (OR) and 95% confidence intervals (CI) for associations of participant characteristics with foot radiographic osteoarthritis (rOA, N=864, feet=1728).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall</th>
<th>Foot rOA</th>
<th>No Foot rOA</th>
<th>OR* (95% CI)</th>
<th>Adjusted** OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: 70-94 years, n/N (%)</td>
<td>473/864 (54.8)</td>
<td>111/191 (58.1)</td>
<td>362/673 (53.8)</td>
<td>1.11 (0.81, 1.53)</td>
<td>1.30 (0.93, 1.80)</td>
</tr>
<tr>
<td>Age: 55-&lt;70 years</td>
<td>391/864 (45.3)</td>
<td>80/191 (41.9)</td>
<td>311/673 (46.2)</td>
<td>referent</td>
<td>referent</td>
</tr>
<tr>
<td>BMI: ≥ 30 kg/m(^2), n/N (%)</td>
<td>435/864 (50.4)</td>
<td>118/191 (61.8)</td>
<td>317/673 (47.1)</td>
<td>1.79 (1.30, 2.48)</td>
<td>1.74 (1.25, 2.41)</td>
</tr>
<tr>
<td>BMI: &lt;30 kg/m(^2), n/N (%)</td>
<td>429/864 (49.7)</td>
<td>73/191 (38.2)</td>
<td>356/673 (52.9)</td>
<td>referent</td>
<td>referent</td>
</tr>
<tr>
<td>Women, n/N (%)</td>
<td>589/864(68.2)</td>
<td>134/191 (70.2)</td>
<td>455/673 (67.6)</td>
<td>1.23 (0.87, 1.73)</td>
<td>1.12 (0.79, 1.59)</td>
</tr>
<tr>
<td>Men, n/N (%)</td>
<td>275/864 (31.8)</td>
<td>57/191 (29.8)</td>
<td>218/673 (32.4)</td>
<td>referent</td>
<td>referent</td>
</tr>
<tr>
<td>African American, n/N (%)</td>
<td>289/864 (33.4)</td>
<td>78/191 (40.8)</td>
<td>211/673 (31.4)</td>
<td>1.49 (1.09, 2.06)</td>
<td>1.39 (0.99, 1.97)</td>
</tr>
<tr>
<td>Caucasian, n/N (%)</td>
<td>575/864 (66.6)</td>
<td>113/191 (59.2)</td>
<td>462/673 (68.6)</td>
<td>referent</td>
<td>referent</td>
</tr>
<tr>
<td>Foot injury, n/N (%)</td>
<td>33/864 (3.8)</td>
<td>9/190 (4.7)</td>
<td>24/672 (3.6)</td>
<td>1.34 (0.53, 3.39)</td>
<td>1.44 (0.57, 3.66)</td>
</tr>
<tr>
<td>No foot injury, n/N (%)</td>
<td>829/862 (96.2)</td>
<td>181/190 (95.3)</td>
<td>648/672 (96.4)</td>
<td>referent</td>
<td>referent3.39</td>
</tr>
<tr>
<td>Foot symptoms, n/N (%)</td>
<td>176/863 (20.4)</td>
<td>51/191 (26.7)</td>
<td>125/672 (18.6)</td>
<td>1.46 (1.01, 2.12)</td>
<td>1.48 (1.02, 2.16)</td>
</tr>
<tr>
<td>No foot symptoms, n/N (%)</td>
<td>687/863 (79.6)</td>
<td>140/191 (73.3)</td>
<td>547/672 (81.4)</td>
<td>referent</td>
<td>referent</td>
</tr>
</tbody>
</table>

* adjusted only for intra-person correlation using generalized estimating equations

**adjusted for intra-person correlation and all other listed covariates
Table 2 – Odds ratios (OR) and 95% confidence intervals (CI) for associations of participant characteristics with foot symptomatic osteoarthritis (sxOA, N=863, feet=1726).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall N=863</th>
<th>Foot sxOA N=46 (5.3%)</th>
<th>No Foot sxOA N=817 (94.7%)</th>
<th>OR* (95% CI)</th>
<th>Adjusted** OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: 70-94 years, n/N (%)</td>
<td>472/863 (54.7)</td>
<td>23/46 (50.0)</td>
<td>449/817 (55.0)</td>
<td>0.94 (0.51, 1.75)</td>
<td>1.10 (0.58, 2.11)</td>
</tr>
<tr>
<td>Age: 55-&lt;70 years, n/N (%)</td>
<td>391/863 (45.3)</td>
<td>23/46 (50.0)</td>
<td>368/817 (45.0)</td>
<td>referent</td>
<td>referent</td>
</tr>
<tr>
<td>BMI: ≥ 30 kg/m², n/N (%)</td>
<td>435/863 (50.4)</td>
<td>34/46 (73.9)</td>
<td>401/817 (49.1)</td>
<td>3.19 (1.59, 6.40)</td>
<td>3.30 (1.60, 6.83)</td>
</tr>
<tr>
<td>BMI: &lt;30 kg/m², n/N (%)</td>
<td>428/863 (49.6)</td>
<td>12/46 (26.1)</td>
<td>416/817 (50.9)</td>
<td>referent</td>
<td>referent</td>
</tr>
<tr>
<td>Women, n/N (%)</td>
<td>588/863 (68.1)</td>
<td>35/46 (76.1)</td>
<td>553/817 (67.7)</td>
<td>1.49 (0.72, 3.06)</td>
<td>1.49 (0.67, 3.30)</td>
</tr>
<tr>
<td>Men, n/N (%)</td>
<td>275/863 (31.9)</td>
<td>11/46 (23.9)</td>
<td>264/817 (32.3)</td>
<td>referent</td>
<td>referent</td>
</tr>
<tr>
<td>African American, n/N (%)</td>
<td>289/863 (33.5)</td>
<td>15/46 (32.6)</td>
<td>274/817 (33.5)</td>
<td>0.97 (0.50, 1.88)</td>
<td>0.77 (0.37, 1.62)</td>
</tr>
<tr>
<td>Caucasian, n/N (%)</td>
<td>574/863 (66.5)</td>
<td>31/46 (67.4)</td>
<td>543/817 (66.5)</td>
<td>referent</td>
<td>referent</td>
</tr>
<tr>
<td>Foot injury, n/N (%)</td>
<td>33/861 (3.8)</td>
<td>4/46 (8.7)</td>
<td>29/815 (3.6)</td>
<td>2.82 (0.72, 11.06)</td>
<td>2.89 (0.69, 12.10)</td>
</tr>
<tr>
<td>No foot injury, n/N (%)</td>
<td>828/861 (96.2)</td>
<td>42/46 (91.3)</td>
<td>786/815 (96.4)</td>
<td>referent</td>
<td>referent</td>
</tr>
</tbody>
</table>

* adjusted only for intra-person correlation using generalized estimating equations
**adjusted for intra-person correlation and all other listed covariates

Disclosure: P. Flowers, None; A. Nelson, QuantiaMD, 9,NIAMS-NIH, 2,RRF, 2; H. J. Hillstrom, None; J. B. Renner, None; J. M. Jordan, None; Y. M. Golightly, None.


Abstract Number: 1951

Effect of Initiating Metformin Vs. Sulfonylureas on the Risk of Total Knee Arthroplasty

Yuqing Zhang¹, Christine Peloquin², Na Lu³, Tuhina Neogi³ and David T. Felson³, ¹School Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, ²Boston University School of Medicine, Boston, MA, ³Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Epidemiology and Public Health Poster III: Rheumatic Disease Risk and Outcomes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM
**Background/Purpose:** Metformin is the most widely used first-line therapy for type 2 diabetes. Studies have suggested that metformin reduces inflammation and lowers levels of PGE2, IL-1β, IL-6 and TNFα in macrophages through its effects on AMPK and the NF-κB pathway. Further, by activating AMPK, metformin may suppress chondrocyte matrix catabolic responses to inflammatory cytokines. However, few studies have assessed the effect of metformin on the risk of end-stage knee OA.

**Methods:** We carried out 2 studies to examine the effect of metformin on the risk of total knee arthroplasty (TKA). Subjects, drawn from The Health Improvement Network (THIN) in the United Kingdom, were between 40-90 years old (year 2000-2014) and had clinical OA with no history of renal disease or TKA. In the first cohort study, each metformin initiator was propensity-score matched to a sulfonylurea initiator within 12-month accrual block. Subjects were followed to the date of TKA, disenrollment from THIN, or 12/31/2014. We plotted cumulative risk of TKA for each cohort accounting for competing risk and examined the relation of metformin to the risk of TKA using Cox proportional hazards model. In the second case-control study conducted among metformin initiators only, we randomly selected up-to four controls from a risk set matched to each TKA case by age, sex, and year of metformin initiation. We estimated the odds ratio (OR) of TKA according to recency of use (i.e., remote: stopped metformin prescription ≥12 months prior to TKA; recent: stopped metformin prescription between >15 days -<12 months prior to TKA; and current use: metformin use within 15 days prior to TKA) and duration of use among the current users (i.e., <1 year, 1-<2 years, 2-<4 years, and 4+ years) using conditional logistic regression model adjusting for BMI, NSAIDs use, OA duration, GP visits prior to metformin use, Townsend deprivation score, comorbidities and other oral antidiabetics.

**Results:** The baseline characteristics were well balanced in the two comparison cohorts (n=1,387 in each cohort) in the first study. Over 15,871 person-years of follow-up, 75 TKA cases (incidence rate: 9.04/1000 person-years) in the metformin cohort and 63 (incidence rate: 8.31/1000 person-years) in the sulfonylureas cohort had TKA. No difference in the risk of TKA was observed between the cohorts (p> 0.65, Figure 1). Compared with sulfonylurea initiators the hazard ratio of TKA for metformin initiators was 1.08 (95% CI: 0.77-1.51). The ORs of TKA for recent and current use of metformin were 0.88 (95% CI: 0.61-1.27) and 1.12 (95% CI: 0.84-1.49), respectively, compared with remote use. There was no dose–response relationship between duration of metformin: ORs of TKA were 1.04, 1.14, 1.22 and 1.05 for use <1 year, 1-<2 years, 2-<4 years and 4+ years, respectively, compared with remote use.

**Conclusion:** Our findings suggest that in persons with OA, metformin use does not lower the risk for TKA.

**Trend of Arthrocentesis Utilization Among Inpatients over 10 Years – Data from National Inpatient Sample**
Background/Purpose:
Arthrocentesis (AC) is a common and simple yet invasive procedure with potential of serious complications. There are no studies evaluating how often this procedure is utilized among hospitalized patients and if the outcomes are different when the procedure occurs. We explored the same using a large inpatient US database.

Methods:
Using the largest inpatient National Inpatient Sample (NIS) data from 2004-2013, we identified adults with AC related discharges based on ICD-9 procedure codes. We calculated the proportion/rate of AC by sex, racial groups and arthritis categories; and outcomes (mean LOS and mortality). Analysis was done using STATA and Joinpoint Regression software. SVY commands were used to derive national estimation. Annual Percentage Changes (APC) were calculated to check the significance of changing trend (p<0.05) unless specified.

Results:
Our study included 686,538 discharges with AC as a procedure during hospitalization from 2004-2013. There was an overall increasing trend in total number (APC=2.26) and rate of arthrocentesis (APC=2.73) (Fig-1). However, the use of AC showed decreasing trends for crystal disease, OA, RA, infective and hemarthrotic/traumatic arthropathy (Fig-2). Interestingly, LOS among discharges with AC had decreasing trend compared to those without, while mortality rate remained same throughout (Fig-3). All sex and race categories showed increasing trend of AC utilization during inpatient stays.

Conclusion:
There was an increasing trend of utilizing arthrocentesis among hospitalized patients from 2004-2013 with a concurrent decreasing trend of LOS and stable mortality rate among those patients. This highlights the improvement in quality of this procedure performed in the hospitals of US. The reducing trends among etiologic categories such as crystal disease, RA, OA and infective arthritis might indicate better outpatient management of these patients with improved disease control and thus requiring less invasive procedures like AC.

Figure-1:Trend of total and rate of discharges with arthrocentesis -2004-2013
Dietary Quality and Risk of SLE in the Nurses’ Health Studies

Medha Barbhaiya¹, Bing Lu¹, Sara K. Tedeschi², Susan Malspeis³, Jeffrey A. Sparks⁴, Walter C. Willett⁵,⁶, Elizabeth Karlson⁷ and Karen H. Costenbader⁷, ¹Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ²Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ³Division of Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ⁴Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ⁵Channing Division of Network Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ⁶Department of
Background/Purpose: Prior studies suggest that high intake of antioxidants, fish, olive oil, and nuts may decrease risk of chronic inflammatory diseases and reduce inflammatory biomarkers. Current knowledge remains scarce regarding a potential association of dietary factors and incident SLE. We aimed to prospectively evaluate the association between the Alternate Healthy Eating Index 2010 (AHEI-2010), a dietary quality index that measures how well Americans’ diets conform to the Dietary Guidelines for Americans, and risk of incident SLE and its subtypes of dsDNA positive (+) versus negative (-) SLE.

Methods: We included 79,939 female nurses in NHS (1984-2012) and 93,554 in NHSII (1991-2013). Lifestyle, environmental, and medical data were collected through biennial questionnaires. Dietary data were obtained from validated food frequency questionnaires at baseline and approximately every 4 years during follow-up. Incident SLE was confirmed by medical record review. Time-varying Cox regression models estimated pooled hazard ratios (HRs [95% confidence intervals]) of SLE risk, overall and by dsDNA subtype, in association with cumulative average AHEI-2010 (in quartiles, with higher AHEI-2010 quartiles corresponding to a ‘healthier’ diet) through the 2-year cycle prior to diagnosis, controlling for potential confounders. Individual AHEI-2010 components and SLE risk were assessed separately.

Results: We identified 183 SLE cases (88 dsDNA+ and 95 dsDNA-) during nearly 20 years of follow-up from 1984 to 2013 in NHS/NHSII. In multivariable-adjusted models, we found that greater adherence to the highest, or ‘healthiest’ quartile of AHEI-2010 (vs. lowest quartile, reference) was not associated with SLE risk overall (HR 0.93 [95% CI 0.59-1.44]) or after stratification by dsDNA+ (HR 0.85 [95% CI 0.44-1.60]) or dsDNA- (HR 0.99 [95% CI 0.54-1.83]) subtypes (Table). However, women in the highest quartile of nut/legume intake had a decreased risk of developing SLE (HR 0.77 [95% CI 0.62-0.97], p-trend 0.02) compared to women in the lowest quartile. No association was demonstrated with other individual AHEI-2010 components and SLE risk.

Conclusion: Healthy diet as quantified by the AHEI-2010 was not associated with SLE risk overall or by dsDNA subtype among women. We did however observe a potential 23% reduction in overall SLE risk with high nut/legume intake, known to be a rich source of anti-inflammatory polyunsaturated fats. This finding suggesting a link between a dietary component and SLE risk is hypothesis generating and warrants further investigation.

Table. Hazard ratios (95% CI) for incident SLE, overall and stratified by double stranded DNA (dsDNA) subtype, according to cumulative Alternate Healthy Eating Index (AHEI-2010) in Nurses’ Health Study and Nurses’ Health Study II.

<table>
<thead>
<tr>
<th>Alternate Healthy Eating Index-2010 quartiles</th>
<th>Case/person-years</th>
<th>Age adjusted model</th>
<th>Multivariable-model</th>
<th>P-trend</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SLE</strong></td>
<td>Q1</td>
<td>Q2</td>
<td>Q3</td>
<td>Q4</td>
</tr>
<tr>
<td>47,900,845</td>
<td>47,900,845</td>
<td>57,983,921</td>
<td>39,984,479</td>
<td>40,985,155</td>
</tr>
<tr>
<td>Age adjusted model</td>
<td>1.0 (ref)</td>
<td>1.0 (ref)</td>
<td>1.0 (ref)</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>Multivariable-model</td>
<td>1.2 (0.87-1.90)</td>
<td>0.87 (0.57-1.33)</td>
<td>0.93 (0.61-1.42)</td>
<td>0.93 (0.59-1.44)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>dsDNA positive SLE</th>
<th>P-trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case/person-years</td>
<td>22,972,075</td>
</tr>
<tr>
<td>Age adjusted model</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>Multivariable-model</td>
<td>1.14 (0.94-1.03)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>dsDNA negative SLE</th>
<th>P-trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case/person-years</td>
<td>23,975,008</td>
</tr>
<tr>
<td>Age adjusted model</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>Multivariable-model</td>
<td>1.37 (0.82-2.35)</td>
</tr>
</tbody>
</table>

Disclosure: M. Barbhaiya, None; B. Lu, None; S. K. Tedeschi, None; S. Malspeis, None; J. A. Sparks, None; W. C. Willett, None; E. Karlson, None; K. H. Costenbader, None.
Association of CRP with BMI in Males and Females

Taik Kim1, Stephen J. Ganocy2, Maria Antonelli3, Douglas Einstadter4 and Stanley Ballou1, 1Rheumatology, Case Western Reserve University/MetroHealth Medical Center, Cleveland, OH, 2Case Western Reserve University, Cleveland, OH, 3Department of Medicine/Division of Rheumatology, Case Western Reserve University School of Medicine, MetroHealth Medical Center, Cleveland, OH, 4Case Western Reserve University at MetroHealth Medical Center, Cleveland, OH

First publication: September 18, 2017

C-reactive Protein (CRP) is an inflammatory marker commonly used to help aid in diagnosis, assess disease activity or monitor response to therapy. It is well established that many factors alter the serum CRP level, excluding infectious, malignancy, or rheumatologic causes. Obesity has been demonstrated to be a risk factor that contributes to elevated CRP levels. There is evidence that adiposity influences CRP levels and not vice versa (1). The proposed mechanism is that human adipose tissue expresses and releases the pro-inflammatory cytokine interleukin-6, inducing low-grade systemic inflammation in individuals with excess body fat (2).

The widely accepted reference range of CRP in healthy individuals is <1.0 mg/dL. The objective of our study was to quantify the association between obesity and CRP in order to establish an upper reference limit CRP for a given body mass index (BMI) in a healthy adult population.

Methods:

The NHANES (National Health and Nutrition Examination Survey) data from 2000 to 2010 was analyzed. Age was limited to 21 years and above to represent the adult population. BMI was limited to ≤50 kg/m^2 and CRP limited to ≤5 mg/dL to exclude extreme values. The total number of analyzed subjects was 37303.

Quantile regression analysis was used to determine the median (CRP50) and 95th percentile CRP (CRP95) at various BMI levels. CRP95 was accepted as the upper reference limit of CRP.

Subgroup analysis was done comparing a younger population (21 to 45 years old) and older population (50 years old and above) and all analyses were based on gender.

Results:

Both CRP50 and CRP95 increase with increase in BMI.

The slope estimate of CRP95 was higher in females compared to males (0.0761 vs 0.0455 (P<0.001), respectively).
From these results we derived a simple calculation to approximate the CRP95, or reference upper limit of CRP, for a given BMI:

Males: \[ \text{CRP} \leq 1.0 + \frac{\text{BMI}-25}{25} \]

Females: \[ \text{CRP} \leq 1.0 + \frac{\text{BMI}-25}{12.5} \]

Subgroup analyses showed that the younger female subgroup had the highest increase in CRP95 (slope estimate=0.089) and the older male group showed almost no increase in CRP95 with increase in BMI (slope estimate=0.002).

**Conclusion:**

Serum CRP levels increase with BMI increase in adults, and are higher in females than males at all elevated levels of BMI. BMI seems to influence the 95\textsuperscript{th} percentile CRP of younger females most and older males least.

We propose a practical calculation that can predict the upper reference limit of CRP for a given BMI.

Reference

1. Int J Obes (Lond) 2011 Feb ; 35(2): 300–308
2. JAMA 1999 Dec 8;282(22):2131-5

**Disclosure:** T. Kim, None; S. J. Ganocy, None; M. Antonelli, None; D. Einstadter, None; S. Ballou, None.

Abstract Number: 1955

Health Care Provider Advice for Weight Loss Among US Adults with Arthritis, National Health Interview Survey, 2014

Jennifer M. Hootman1, Miriam G. Cisternas2, Louise Murphy3 and Teresa J. Brady4, 1Centers for Disease Control and Prevention, Kennesaw, GA, 2MGC Data Services, Carlsbad, CA, 3Division of Population Health, Centers for Disease Control and Prevention, Atlanta, GA, 4Arthritis Program, Centers for Disease Control and Prevention, Atlanta, GA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Epidemiology and Public Health Poster III: Rheumatic Disease Risk and Outcomes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Most clinical practice guidelines for the management of osteoarthritis recommend weight loss for adults with arthritis who are overweight or obese. A health care provider’s (HCP) advice for weight loss is strongly associated with weight loss attempts. The purpose of this study is to estimate the prevalence and characteristics of adults with arthritis reporting a HCP’s advice to lose weight among overweight and obese adults with arthritis.

Methods:

The National Health Interview Survey, conducted annually, targets the civilian, non-institutionalized population and gathers data on a variety of health topics. We used data from 2014 (sample size 36,697). Doctor-diagnosed arthritis was defined as a ‘yes’ to: “Have you ever been told by a doctor or other health care professional that you have arthritis, rheumatoid arthritis, gout, lupus or fibromyalgia?” HCP advice for weight loss was defined as a ‘yes’ response to “Has a doctor or other health professional EVER suggested losing weight to help your arthritis or joint symptoms?” Age-standardized prevalence (%) and 95% confidence intervals (CI) of HCP advice for weight loss was calculated using statistical weights to account for the complex survey design. Prevalence was calculated by sociodemographic characteristics (age, sex, race/ethnicity, and education) and health-related characteristics (arthritis-related activity limitation (AAAL), self-rated health (excellent/very good, good, fair/poor), body mass index (BMI; 25.0–<30 overweight and 30.0+ obese), smoking status (current, former, never), physical activity level (inactive, insufficient, meets recommendations) and having a primary care provider (yes, no). Low rates of HCP advice for weight loss was defined as < 45%.

Results:

Age-standardized prevalence of HCP advice for weight loss among overweight/obese adults with arthritis was 45.8% (CI 43.3-48.2%). Subgroups with low rates of HCP advice for weight loss included males (41.2%), Non-Hispanic Others (25.6%), < high school education (41.9%), university degree (44.7%), work status ‘other’ (42.4%), none to mild joint pain (41.0%), excellent/very good health (37.9%), current smokers (40.4%) and those meeting physical activity recommendations (42.9%). Prevalence rates of HCP advice for weight loss increased as overweight/obesity increased (Figure). Subgroups with the highest rates (>55.0%) were extreme obesity (80.3%), Obese Class II (65.3%), Non-Hispanic Asian (57.6%), unable to work/disabled (55.6%), and those with fair/poor health (55.0%).

Conclusion:

Less than half of overweight/obese adults with arthritis report having been advised by a health care provider to lose weight. Additional health care professional education/training and system improvements like electronic reminders may help increase rates of recommended provider advice and weight loss attempts.

Disclosure: J. M. Hootman, None; M. G. Cisternas, None; L. Murphy, None; T. J. Brady, None.


Abstract Number: 1956
An Approach to Linkage of Registry Data to Medicare Claims Using Multiple Non-Unique Identifiers

Fenglong Xie¹, Lang Chen¹, Huifeng Yun², Jeffrey D Greenberg³ and Jeffrey R. Curtis⁴, ¹Division of Clinical Immunology & Rheumatology, University of Alabama at Birmingham, Birmingham, AL, ²University of Alabama at Birmingham, Birmingham, AL, ³NYU School of Medicine, New York, NY, ⁴Rheumatology & Immunology, University of Alabama at Birmingham, Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Epidemiology and Public Health Poster III: Rheumatic Disease Risk and Outcomes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Registries and claims data can complement each other to facilitate observational studies. However, methods to link on multiple non-unique identifiers (MNUI) are limited and therefore, there is a need to develop and test an approach to link registry data to Medicare claims using multiple non-unique identifiers.

Methods: Social security numbers (SSN) from participants in the Corrona registry with at least one registry visit in 2014 or prior were linked by CMS to Medicare fee-for-service (FFS) data. Using CMS created crosswalk file between Corrona ID (CID) and Medicare ID (MID), birth date (DOB) and sex, we established the SSN linkage as a gold standard. Using full DOB, sex, visit dates in registry and CMS data, and Corrona physician NPI, we developed an approach for linkage using MNUI based on 1) sex; 2) DOB elements (day, month and year, with year at most +-1 year), 3) number of visit dates matching exactly between Corrona and Medicare data, where the Medicare provider NPI matched the Corrona physician. These features were each included in a logistic regression model to evaluate the likelihood of a successful match using SSN+sex+DOB as the gold standard.

Results: The SSN linkage with sex and DOB confirmation resulted in 2,527 linked patients with any type of Medicare coverage. Among these, 1,854 had at least one month of Medicare FFS coverage in which a Corrona visit occurred. The initial match result in 565,856 potential pairings of CID and MID. The C-index for the model was 0.996. Choosing 0.06 as cut-points of predicted probability to achieve a PPV greater than 0.90, the algorithm predicted 1,858 matches; among then 1,732 were consistent with the SSN linkage. Keeping only the pairs with highest predicted probability result in 1,846 matches; among these, 1,731 were correct matches. Sensitivity of the approach was 0.93 (1,731/1,854), 95% CI: 0.92-0.95. The Positive predicted value (PPV) was 0.94 (1,731/1846), 95% CI: 0.93-0.95.

Conclusion: Linkage of an outpatient registry with administrative claims data using multiple non-unique identifiers is both technically feasible and accurate and yields high sensitivity and PPV

Disclosure: F. Xie, None; L. Chen, None; H. Yun, Bristol-Myers Squibb, 2; J. D. Greenberg, corrona, LLC, 1,Corrona, LLC, 3,Genentech, Janssen, Novartis, Pfizer, Eli Lilly, 5; J. R. Curtis, AbbVie, Roche/Genentech, BMS, UCB, Myra, Lilly, Amgen, Janssen, Pfizer, Corrona, 5,Amgen, Pfizer, Crescendo Bio, Corrona, 9.

Impact of Maternal Systemic Autoimmune Rheumatic Diseases on Neonatal Outcomes: A Population-Level Analysis

Stephanie Keeling¹, Anamaria Savu² and Padmaja Kaul³, ¹Department of Medicine, University of Alberta, Division of Rheumatology, Edmonton, AB, Canada, ²Canadian Vigour Center, Edmonton, AB, Canada, ³Cardiology, University of Alberta, Edmonton, AB, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Epidemiology and Public Health Poster III: Rheumatic Disease Risk and Outcomes

Abstract Number: 1957

Impact of Maternal Systemic Autoimmune Rheumatic Diseases on Neonatal Outcomes: A Population-Level Analysis

Stephanie Keeling¹, Anamaria Savu² and Padmaja Kaul³, ¹Department of Medicine, University of Alberta, Division of Rheumatology, Edmonton, AB, Canada, ²Canadian Vigour Center, Edmonton, AB, Canada, ³Cardiology, University of Alberta, Edmonton, AB, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Epidemiology and Public Health Poster III: Rheumatic Disease Risk and Outcomes
**Background/Purpose:** The impact of systemic autoimmune rheumatic diseases (SARDS) on peripartum outcomes is not well described at a population level despite the potential for active disease in this period.

**Methods:** The patient population consisted of women giving birth between January 1, 2005 to December 31, 2014 (n=312,081). For women with multiple gestations during the period, one birth event was randomly selected. Women with SARDS included any of the following: systemic lupus erythematosus, systemic sclerosis, myositis and sjogren’s syndrome, diagnoses based on the presence of International Classification of Disease version 9/10 codes in outpatient or inpatient records. Baseline characteristics, comorbidities, medication use (available for all births after January 1, 2009), and neonatal outcomes among women with and without SARDS were compared.

**Results:** Compared to women with no SARDS (n=311,755), women with SARDS (n=326, 0.1%) were slightly older (SARDs 31.3 vs No SARDs 29.3 years (p<0.01)) but did not differ in terms of rural residence, ethnicity, median household income or nulliparity. However, rates of pre-term delivery, emergent cesarean section, induction, hypertensive disorders/eclampsia and mortality were higher among women with SARDS than those with no SARDS (Table 1). Offspring of women with SARDS had lower birth weights, were more likely small for gestational age (SGA), and had longer stays in neonatal ICU (Table 1). Among women with SARDS, prescription rates in the 270 days prior to delivery were highest for anti-malarials (Table 2). After multivariable adjustment, both NSAIDS use (OR(95% CI): 5.24 (1.57, 17.52), p<0.01) and steroid use (OR(95% CI): 3.15 (1.31, 7.59), p<0.01) were significantly associated with a higher risk of preterm delivery.

**Conclusion:** Women with SARDS are at an increased risk of adverse outcomes during pregnancy. The association between corticosteroid and NSAID use and preterm delivery requires further investigation. Our findings suggest the need for closer monitoring and coordinated care with obstetrics and perinatology in these high risk women.

<table>
<thead>
<tr>
<th>OUTCOME</th>
<th>Mothers</th>
<th>NO SARDs # (%)</th>
<th>SARDs # (%)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-term Delivery</td>
<td>22205 (7.1)</td>
<td>58 (17.8)</td>
<td>&lt; 0.01</td>
<td></td>
</tr>
<tr>
<td>C-section (Emergent)</td>
<td>51132 (16.4)</td>
<td>82 (25.2)</td>
<td>&lt; 0.01</td>
<td></td>
</tr>
<tr>
<td>Hypertensive Disorders</td>
<td>20029 (6.4)</td>
<td>47 (14.4)</td>
<td>&lt; 0.01</td>
<td></td>
</tr>
<tr>
<td>Small for Gestational Age</td>
<td>35047 (11.2)</td>
<td>68 (20.9)</td>
<td>&lt; 0.01</td>
<td></td>
</tr>
<tr>
<td>Congenital Anomaly</td>
<td>5810 (1.9)</td>
<td>11 (3.4)</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>Mean days in Neonatal ICU</td>
<td>0.8 (5.0)</td>
<td>2.3 (9.6)</td>
<td>&lt; 0.01</td>
<td></td>
</tr>
</tbody>
</table>

*Sensitive analysis utilizing primiparous SARDs vs NonSARDs women confirmed similar results

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Steroids</th>
<th>Nonsteroidal Anti-Inflammatories</th>
<th>Antimalarials</th>
</tr>
</thead>
<tbody>
<tr>
<td>SGA [OR (95% CI)]</td>
<td>2.06 (0.91, 4.67)</td>
<td>1.08 (0.29, 4.12)</td>
<td>1.54 (0.74, 3.20)</td>
</tr>
<tr>
<td>Gestational Diabetes [OR (95% CI)]</td>
<td>1.67 (0.51, 5.47)</td>
<td>N/A</td>
<td>0.91 (0.28, 2.93)</td>
</tr>
<tr>
<td>Preterm Delivery [OR (95% CI)]</td>
<td>3.84 (1.66, 8.89)**</td>
<td>4.96 (1.55, 15.85)**</td>
<td>1.82 (0.83, 4.00)</td>
</tr>
<tr>
<td>C-section [OR (95% CI)]</td>
<td>0.88 (0.41, 1.90)</td>
<td>0.98 (0.31, 3.11)</td>
<td>0.57 (0.29, 1.13)</td>
</tr>
<tr>
<td>Hypertensive Disorders of Pregnancy [OR (95% CI)]</td>
<td>3.67 (1.51, 8.93)**</td>
<td>0.50 (0.06, 4.03)</td>
<td>1.23 (0.51, 2.99)</td>
</tr>
</tbody>
</table>

**Disclosure:** S. Keeling, None; A. Savu, None; P. Kaul, None.


**Abstract Number:** 1958

**Burden of Rheumatic Disease Among Korean Women in Childbearing Years Based on the National Health Insurance Service-National Sample Cohort**

Min Kyung Chung⁵, Jisoo Lee⁵, Eun-Hee Ha² and Ji-Young Shin², ¹Division of Rheumatology, Department of Internal Medicine, Ewha Womans University School of Medicine, Seoul, Korea, Republic of (South), ²Department of Occupational and Environmental Medicine, Ewha Womans University School of Medicine, Seoul, Korea, Republic of (South)
SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Epidemiology and Public Health Poster III: Rheumatic Disease Risk and Outcomes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Many rheumatic diseases predominantly affect women in their reproductive years, and have a significant impact on childbearing, but its burden remains incompletely understood. The study aimed to identify the prevalence and incidence of rheumatic diseases among Korean women in childbearing years, and the effect of the diseases on prevalence of comorbidities, and pregnancy rate.

Methods: From National Health Insurance Service-National Sample Cohort (NHIS-NSC) data during 2010-2013, we identified 210,328 women aged between 20-44 years. Among these women, we estimated the prevalence and incidence of rheumatic diseases including rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and ankylosing spondylitis (AS). Prevalence of chronic diseases such as cancer (Ca), hypertension (HT), hyperlipidemia (HLD), and diabetes mellitus (DM) was compared in women with or without rheumatic diseases. We also investigated pregnancy rate in women with rheumatic or chronic diseases, and control subjects without rheumatic or chronic diseases.

Results: Total prevalence of rheumatic diseases in childbearing years during 2010-2013 was 0.43%. Total incidence during 2010-2013 was 9.37 cases per 10,000 person-years. Women with rheumatic diseases had significantly higher association with chronic diseases compared with those without (28.38% vs 10.19%, p=<0.001), and had increased risk for HT (OR 3.24, p<0.001) and HLD (OR 3.25, p<0.001). Pregnancy rate was significantly lower in women with rheumatic diseases compared with the control (12.60% vs 18.69%, p<0.001). Among women with rheumatic diseases, women with RA (OR 0.44, p<0.001) were less likely to become pregnant, whereas women with SLE and AS had comparable rate of pregnancy compared with the normal control. Likelihood of becoming pregnant in women with RA is comparable with women with Ca (OR 0.49, p<0.001), HT (OR 0.76, p<0.001), and HLD (OR 0.48, p<0.001).

Conclusion: Rheumatic diseases are a significant burden for women in childbearing years causing increased co-morbidities and reduced pregnancy rate.

Disclosure: M. K. Chung, None; J. Lee, None; E. H. Ha, None; J. Y. Shin, None.


Abstract Number: 1959

Multimorbidity in Patients with Sarcoidosis: A Population-Based Cohort Study

Patompong Ungprasert1, Eric L. Matteson2 and Cynthia S. Crowson3, 1Rheumatology, Mayo Clinic, Rochester, MN, 2Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, MN, 3Department of Medicine, Division of Rheumatology, Mayo Clinic, Rochester, MN

First publication: September 18, 2017
Multimorbidity in Patients with Sarcoidosis: A Population-Based Cohort Study

Background/Purpose: Recent studies have suggested an increased risk of comorbidity in patients with sarcoidosis. However, whether sarcoidosis is associated with increased incidence of multimorbidity is not known.

Methods: 345 patients (50% female; 90% Caucasian, 5% African-American; mean age 45.6 years) with incident sarcoidosis in 1976-2013 in a geographically well-defined population were identified from a comprehensive medical record linkage system. Diagnosis of sarcoidosis was confirmed by individual medical record review which required diagnosis of sarcoidosis by physician supported by histopathology, compatible clinical presentation, and exclusion of other granulomatous diseases. A total of 345 sex and age-matched comparators (50% female; 95% Caucasian, 1% African-American; mean age 45.4 years) were also identified from the same underlying population. Cases and comparators were then reviewed for 18 common chronic comorbidities at index date and after index date. Aalen-Johansen methods were used to estimate the cumulative incidence of multimorbidity (defined as presence or at least 2 chronic comorbidities) adjusted for the competing risk of death. Cox proportional hazards models with adjustment for age, sex, and calendar year were used to compare the rate of development of multimorbidity between cases and comparators.

Results: At index date, 111 patients with sarcoidosis and 110 comparators without sarcoidosis had multimorbidity (p value 1.0). The mean number of comorbidities was 1.2 in both groups. During a median follow-up of 12.9 years among patients with sarcoidosis and 15.6 years among comparators, 156 patients with sarcoidosis developed multimorbidity compared to 142 comparators, corresponding to an adjusted hazard ratio of 1.60 (95% confidence interval, 1.07 – 1.69). The percentage of patients developing multimorbidity by years since sarcoidosis incidence/index date is shown in the figure. Analysis by specific comorbidity revealed significantly increased incidence of congestive heart failure, coronary artery disease, arrhythmia, cerebrovascular accident, arthritis, asthma, depression, diabetes and osteoporotic fracture after the index date among patients with sarcoidosis. The most common combination of comorbidities was hypertension and hyperlipidemia, although these were not significantly increased in sarcoidosis relative to comparators.

Conclusion: This first ever population-based evaluation of multimorbidity in sarcoidosis revealed that patients have a significantly increased incidence of multimorbidity after the diagnosis of sarcoidosis.

Figure. Probability of developing 2,3,4, 5+ comorbidities according to years since sarcoidosis incidence/ index date for patients with sarcoidosis (S) and comparators (C).

Disclosure: P. Ungprasert, None; E. L. Matteson, None; C. S. Crowson, None.

National Survey of Childhood-Onset Rheumatic Diseases Followed up in the Clinical Pediatric Facilities in Japan

Masaaki Mori1, Syuji Takei2, Yasuhiro Itoh3, Ichiro Kobayashi4, Minako Tomiita5, Nami Okamoto6 and Kazuko Yamazaki7,

1Department of Lifetime Clinical Immunology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan, 2Department of Pediatrics, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima, Japan, 3Department of Pediatrics, Nippon Medical School, Tokyo, Japan, 4Department of Allergy and Rheumatology, Chiba Children's Hospital, Sapporo, Japan, 5Department of Allergy and Rheumatology, Chiba Children's Hospital, Chiba, Japan, 6Pediatrics, Graduate School of Medicine, Osaka Medical College, Takatsuki, Japan, 7Department of Pediatrics, Saitama Medical Center, Saitama Medical University, Kawagoe, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Epidemiology and Public Health Poster III: Rheumatic Disease Risk and Outcomes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: We did not grasp how many and where pediatric rheumatic patients exist in Japan quite exactly until now. About juvenile idiopathic arthritis (JIA), child-onset systemic lupus erythematosus (SLE), juvenile dermatomyositis (JDM), child-onset Sjögren's syndrome (SS), we would like to know the actual situation of follow-up in clinical pediatric facilities in Japan.

Methods: For 519 clinical pediatric training institutes in Japan Pediatric Society, we performed the questionary survey for grasping the number of patients < 16 and ≥16 years about the above diseases with letter form. The answer period was from May 1 to December 31, 2016.

Results: As for the answer from 474 institutes (91.3%), the number of patients < 16 and ≥16 years were as follows; JIA: 1,704 vs 750, SLE: 404 vs 525, JDM: 268 vs 113, SS: 148 vs 126, individually. As results of statistical analysis, we could recognize that the number of JIA was approximately 2,700, that of SLE 1,000, that of JDM 400 and that of SS 300 in the whole Japan. Because the population of 2016 of Japan < 16 years was 16,954,000, the prevalence of each disease < 16 years was 11.0, 2.6, 1.7, 1.0 per 100,000 persons. We also reported the detail of the medical actual situation such as the enforcement systems of the transition medicine in the childhood-onset rheumatic diseases, based on 1) number of patients at 47 prefectures in Japan (Table), 2) distribution of pediatric rheumatic specialists, 3) cooperation with the core institutions for pediatric rheumatology in each medical area.

Conclusion: This is the first accurate report about of national survey of childhood-onset rheumatic diseases followed up in the clinical pediatric facilities in Japan. We are convinced that these results build the foundation to plan the cooperation with patient and family society, the choice of the clinical trial facilities of the new medicine, and the construction of both domestic and international pediatric rheumatic disease-registry in future.
Disclosure: M. Mori, None; S. Takei, Chugai, Eisai, Takeda, Bristol-Myers Squibb, 2,Chugai, Mitsubishi-Tanabe, Pfizer, Ayumi, 8; Y. Itoh, None; I. Kobayashi, None; M. Tomiita, None; N. Okamoto, None; K. Yamazaki, None.


Abstract Number: 1961

Risk Factors for Low Muscle MASS in Community-Dwelling Older Women: A Population-Based Prospective Cohort Study in Brazil. the São Paulo Ageing & Health Study

Ketty Machado1, Diogo S Domiciano2, Luana G Machado3, Jaqueline B Lopes4, Camille P Figueiredo5, Valéria F. Caparbo3, Liliam Takayama3, Paulo Menezes6 and Rosa M R Pereira2, 1Rheumatology, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, 2Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, Brazil, 3Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, 4Rheumatology Division, Rheumatology Division, Faculdade de Medicina da USP, São Paulo, Brazil, 5Rheumatology Division, Faculdade de Medicina da USP, São Paulo, Brazil, 6Preventive medicine, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Epidemiology and Public Health Poster III: Rheumatic Disease Risk and Outcomes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Sarcopenia is a syndrome characterized by progressive loss of skeletal muscle mass, which results in decreased muscle strength and impairment of functional capacity. Moreover, sarcopenia is an important clinical problem in older people with some adverse outcomes including an increased risk of death. Despite the increasing frequency of this clinical condition, prospective data
Methods: A total of 408 women aged 65 years and older from the São Paulo Ageing & Health study (SPAH) was evaluated with clinical data, laboratory bone tests, BMD and body composition by DXA. All risk factors were performed at baseline (2005-2007). Along with the Foundation for the National Institutes of Health (FNIH) criteria, low muscle mass was defined when appendicular lean mass divided by body mass index (ALM/BMI) is less than 0.512 (value for female). After a mean follow-up of 4.3±0.8 years, subjects were classified according to the appendicular muscle mass obtained by DXA. Logistic regression models were used to identify independent risk factors for low muscle mass.

Results: 116 women (28.4%; 95% CI: 24.0-32.7) had low muscle mass at the end of follow-up. Age averages were 73.3±4.9 years and 72.5±4.5 years, in the low muscle mass group and in the normal muscle mass group, respectively (p=0.11). Mean BMI was 30.6±5.2 kg/m² in low muscle mass group and 28.1±4.7 kg/m² in normal group (p<0.001). In multivariate analyses, predictors of low muscle mass were: number of falls (OR = 1.14, 95% CI 1.02-1.27, p = 0.016), TSH levels (OR = 1.08, 95% CI 1.01-1.15, p = 0.018, per each 1 μUI/L-increase), serum creatinine (OR = 11.11, 95% CI 2.78-33.33, p < 0.001, per each 1 mg/dL-decrease) and visceral adipose tissue (VAT) mass (OR = 1.17, 95% CI 1.07-1.27, p < 0.001, per each 100g-increase).

Conclusion: Falls, higher TSH, lower creatinine and higher VAT were risk factors for low muscle mass in community-dwelling older women. These results reinforced that visceral fat, which is associated with metabolic syndrome and chronic inflammation, is related to muscle mass consumption and fragility in elderly. Taken together, these findings support the notion that more attention should be paid to these factors in clinical practice, since they are potentially reversible with adequate therapeutic intervention.

Disclosure: K. Machado, None; D. S. Domiciano, None; L. G. Machado, None; J. B. Lopes, None; C. P. Figueiredo, None; V. F. Caparbo, None; L. Takayama, None; P. Menezes, None; R. M. R. Pereira, None.


Abstract Number: 1962

Rates of Malignancy Associated with Anti-TNF Agents and Subsequent Biologic Use after Malignancy Using U.S. SEER Registry Data

HuiFeng YUN1, Fenglong XIE2, Shuo Yang2, Lang Chen1 and Jeffrey R. Curtis3, 1University of Alabama at Birmingham, Birmingham, AL, 2Division of Clinical Immunology & Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 3Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Epidemiology and Public Health Poster III: Rheumatic Disease Risk and Outcomes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Biologic disease-modifying anti-rheumatic drugs (DMARDs) have been widely used for treatment of rheumatoid arthritis (RA) in United States. However, it is not clear whether biologics are associated with elevated cancer risk. We estimated cancer incidence rates (IRs) among anti-TNF users and evaluated biologic use after cancer diagnosis among RA patients, using validated cancer outcomes from the U.S. SEER program.

Methods: Using 2006-2013 SEER-Medicare linked data and a 5% non-cancer sample, we identified new anti-TNF users (etanercept, adalimumab, certolizumab, golimumab, infliximab) among RA patients, identified using algorithms that required ≥ 1 rheumatologist diagnosis code for RA at any time before specific drug use. New users were defined specific to each drug as no use of that therapy in the ‘baseline’ period. Eligible subjects were continuously enrolled in Medicare Parts A, B and D in baseline and throughout follow up. Patients with history of cancer were excluded. We identified all cancers reported to SEER nationally, as confirmed nationally by trained
tumor registrars. Follow up started from the drug initiation date and ended at the earliest date of: malignancy, a 90-day gap in current exposure, death, switch to another biologic, or loss of Medicare coverage. We calculated the number of cancer events in both SEER and 5% non-cancer sample, and then calculated the weighted national IRs of cancer for each drug, along with 95% confidence interval, by multiplying the observed person years for non-cancer patients with 20. Subgroup analyses based on the concurrent use of methotrexate (MTX) were conducted. We also evaluated patients’ subsequent biologic use after their cancer diagnosis.

**Results:** We identified 1,374 new anti-TNF users in SEER-Medicare linked cancer registry and 5% non-cancer sample. Of these, 36.5% used infliximab, 25.9% adalimumab, 20.3% etanercept, 11.0% certolizumab, and 6.1% golimumab. During follow-up, we identified 231 cancers yielding a weighted IR from a low of 0.8 (golimumab) to a high of 1.9 (certolizumab) per 1000 person years across different anti-TNFs. IRs with concurrent MTX use were greater than those without MTX (table). After cancer diagnosis, 60-70% of patients resumed the same anti-TNF, 15-25% discontinued all biologic use, and the remainder switched to non-biologic DMARDs or other biologics. This pattern was consistent across different anti-TNFs.

**Conclusion:** Crude incidence rates of cancer among RA patients were comparable between users of different anti-TNF users. Concurrent MTX use was associated with higher cancer risk, although ongoing work is evaluating potential confounding.

<table>
<thead>
<tr>
<th>Anti-TNFs</th>
<th>MTX</th>
<th>Validated Cancer Events, n</th>
<th>Weighted Average Follow-up time†</th>
<th>Weighted cancer incidence rate (95% CI) per 1000 person years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adalimumab</td>
<td>No</td>
<td>18</td>
<td>2332</td>
<td>0.77 (0.49-1.23)</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>34</td>
<td>2944</td>
<td>1.15 (0.83-1.62)</td>
</tr>
<tr>
<td>Certolizumab</td>
<td>No</td>
<td>9</td>
<td>1353</td>
<td>0.66 (0.35-1.28)</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>10</td>
<td>1017</td>
<td>0.98 (0.53-1.83)</td>
</tr>
<tr>
<td>Etanercept</td>
<td>No</td>
<td>19</td>
<td>2658</td>
<td>0.71 (0.46-1.12)</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>28</td>
<td>2074</td>
<td>1.35 (0.93-1.96)</td>
</tr>
<tr>
<td>Golimumab</td>
<td>No</td>
<td>5</td>
<td>574</td>
<td>0.87 (0.36-2.09)</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>2</td>
<td>410</td>
<td>0.49 (0.12-1.95)</td>
</tr>
<tr>
<td>Infliximab</td>
<td>No</td>
<td>40</td>
<td>4415</td>
<td>0.91 (0.66-1.24)</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>66</td>
<td>4962</td>
<td>1.33 (1.05-1.69)</td>
</tr>
</tbody>
</table>

MTX: Methotrexate

† calculated by multiplying 20 and observed patient years among non-cancer sample, and then adding the observed patient years for cancer patients.

**Disclosure:** H. Yun, BMS, 2; F. Xie, None; S. Yang, None; L. Chen, None; J. R. Curtis, UCB Pharma, Janssen-Cilag, Amgen, Roche, Myriad Genetics, Lilly, Novartis, BMS, Pfizer, 2, UCB Pharma, Janssen-Cilag, Amgen, Roche, Myriad Genetics, Lilly, Novartis, BMS, Pfizer, 5.


**Abstract Number:** 1963

**Association of Corticosteroid Exposure with Ophthalmologic Complications and Systemic Adverse Events in Non-Infectious Uveitis Patients Using Administrative Claims in the United States**

Nisha Acharya1, Keith A. Betts2, Oscar Patterson-Lomba2, Arijit Ganguli3, Sophie Schonfeld2 and Jenny Griffith3, 1University of California San Francisco, San Francisco, CA, 2Analysis Group, Inc., Boston, MA, 3AbbVie Inc., North Chicago, IL

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017
Session Title: Epidemiology and Public Health Poster III: Rheumatic Disease Risk and Outcomes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Noninfectious uveitis (NIU) is a collection of intraocular inflammatory disorders associated with significant visual impairment. Corticosteroids (CS) are typically the first-line drug therapy for NIU. Despite a general awareness that patients with long-term CS exposure can suffer from serious ocular and systemic adverse events (AEs), a clear understanding of the relationship between CS exposure and the occurrence of AEs, especially in a real-world setting, is lacking. This study estimates the associations between CS exposure and the risks of developing certain ophthalmologic-related complications and systemic AEs using a large, retrospective, administrative claims database.

Methods: This analysis used data from the Truven Health MarketScan Commercial Claims Encounters database from Q1 2011 – Q1 2016, which collects data from approximately 100 different insurance companies representing about 93 million covered lives. NIU patients were included if they were older than 18 years, had two or more CS prescription fills after an NIU diagnosis, and continuous enrollment for at least 8 months (6 months prior to first CS fill and at least 2 months after). CS exposure was captured via time-dependent cumulative treatment duration (in months), cumulative daily dose of systemic CS fills, and cumulative number of topical CS fills (including eye drops and CS injections). The outcomes of interest were time to ophthalmologic-related complications (glaucoma, blindness and cataract) and time to systemic AEs (osteoporosis, cardiac failure and infections). Multivariate Cox regression models were developed to assess the relationship of CS exposure with the risk of each outcome, controlling for baseline covariates, i.e., age, gender, various comorbidities, use of immunosuppressants and biologic therapies.

Results: Among the 56,782 patients with NIU eligible for the study, 60% were female and the average age was 56 years. The cumulative number of topical CS fills was associated with a significant increase in the risk of developing all ophthalmologic-related complications (hazard ratios [HR] of 1.10, 1.06, 1.04 for glaucoma, blindness and cataract, respectively), all p-values <0.001. The cumulative systemic CS duration was associated with a significant increase in the risk of all systemic AEs (HR of 1.03, 1.02 and 1.01 for osteoporosis, cardiac failure and infections, respectively), all p-values <0.001, while the cumulative systemic CS daily dose had no substantial impact on any outcome. Immunosuppressant therapies were associated with a significant increase in the risk of blindness (HR=1.40), cataract (HR=1.20) and osteoporosis (HR=1.47), all p-values <0.05. Biologic therapies were not associated with a significant increased risk of developing any of the outcomes.

Conclusion: Increased exposure to topical CS was associated with a significant increase in the risk of developing ophthalmologic-related complications, and longer duration of systemic CS was associated with a significant increase in the risk of CS-related AEs. These findings suggest that therapies alternative to corticosteroids could be beneficial in minimizing ophthalmologic complications and AEs among patients with NIU.

Disclosure: N. Acharya, AbbVie Inc., 5, AbbVie Inc., 2; K. A. Betts, AbbVie, 5; O. Patterson-Lomba, Abbvie Inc., 5; A. Ganguli, AbbVie, 3, AbbVie, 1; S. Schonfeld, AbbVie Inc., 5; J. Griffith, AbbVie, 1, AbbVie, 3.


Abstract Number: 1964

The Risk of Hydroxychloroquine Toxic Retinopathy and Its Risk Factors in the Treatment of Rheumatic Diseases: A Systematic Review

April Jorge1, Sharan K. Rai2 and Hyon K. Choi2, 1Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, 2Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Epidemiology and Public Health Poster III: Rheumatic Disease Risk and Outcomes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Hydroxychloroquine (HCQ) is widely used in the treatment of systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and other rheumatic diseases. While generally well-tolerated and regarded as one of the safest treatment options for these conditions, the major long-term risk is vision-threatening retinopathy. The risk of retinopathy has been shown to vary by amount of HCQ exposure. However, the true risk of HCQ retinopathy remains unclear, and clinical consensus may be lacking between US and European rheumatology and ophthalmology societies regarding the safe dosing of HCQ. Our objective was to systematically review and appraise current evidence of the risk of HCQ retinopathy and its purported risk factors.

Methods:
We conducted a systematic search of MEDLINE and EMBASE databases through June 2017. Inclusion criteria were: 1) study sample including individuals treated with HCQ; 2) study design of either retrospective or prospective study with a comparator group; and 3) retinopathy outcomes reported. The primary outcome was HCQ retinopathy incidence and/or prevalence, and other data of interest included measures of HCQ exposure (e.g., mean daily dose, mean cumulative dose, and mean duration of HCQ use), method of HCQ retinopathy ascertainment, risk factors for HCQ retinopathy, and rheumatologic diagnosis.

Results:
We identified 3,236 unique citations. Of these, 28 studies were ultimately included in the systematic review. Ten studies (all published in 2014 or later) reported current standard-of-care screening modalities (e.g., Humphreys visual fields (VF) and spectral domain-optical coherence tomography (SD-OCT)). Eleven studies reported the use of only older screening modalities (e.g., funduscopic, visual acuity, and color vision assessments), 5 studies used ophthalmologist reports of toxicity, and 2 studies did not describe a method of retinopathy ascertainment. Of the 10 recent studies, HCQ retinopathy risk estimates ranged from 2.9-30.5%, with 2 studies reporting a risk of 10% or higher. Of the 18 older studies, HCQ retinopathy risk estimates ranged from 0.5%-21%, with 2 studies reporting a risk over 5%. Twelve studies examined predictors of retinopathy. Of these, 3 found age and 1 found CKD to be predictors of retinopathy. Duration of HCQ use, cumulative dose of HCQ, and daily dose of HCQ were associated with HCQ retinopathy risk in 5, 4, and 2 studies, respectively. Underlying rheumatologic disease (e.g., SLE versus RA) did not impact retinopathy risk. The mean daily HCQ doses varied from 3.1mg/kg/day to 8.4mg/kg/day for the overall cohorts exposed to HCQ, with some studies reporting dose per ideal body weight and others reporting actual body weight.

Conclusion:
This is the first systematic review on the risk of toxic retinopathy secondary to HCQ. The risk estimate of HCQ retinopathy varies considerably in the published literature, with increased risk estimates reported in recent studies. More recent ophthalmologic screening methods including SD-OCT have increased sensitivity to detect earlier stages of retinopathy. Prospective studies are urgently needed to accurately characterize the risk and risk factors of HCQ retinopathy.

Disclosure: A. Jorge, None; S. K. Rai, None; H. K. Choi, Selecta, Horizon, 5,AstraZeneca, 2.


Abstract Number: 1965

Evolution of Anti-Citrullinated Protein Antibodies in Post-Chikungunya Arthritis Patient in Dominican Republic

E Tejada-Reyes, I Mercedes-Núñez, Y Cruz-Rojas, E Rodriguez-Bautista, V Rosario, R Peña-Blanco, R Muñoz-Louis, T Valdez-Lorie and R Alba-Fériz, Rheumatology, Hospital Docente Padre Billini (HDPB), Santo Domingo, Dominican Republic

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Epidemiology and Public Health Poster III: Rheumatic Disease Risk and Outcomes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Chikungunya (CKV) is a disease caused by an alphavirus, transmitted by mosquitoes of the genus Aedes. It is characterized by arthralgia, myalgia, arthritis and tenosynovitis. Anticyclic citrullinated peptide antibodies (ACPA) are considered specific markers of rheumatoid arthritis (RA). However, ACPA have also been detected in patients with other types of chronic inflammatory rheumatism. The objective of this study is to investigate the positivity of ACPA in post-chikungunya arthritis.

Methods:
This was an ambispective study, cross-sectional, with patients who were taken from the group comprised a total of 514 patients from the register of patients with musculoskeletal post-chikungunya infections in the rheumatology department of the Hospital Docente Padre Billini, from December 2013 to June 2017, patients who met the classification criteria for reactive arthritis.

Results:
Of a total of 514 patients, 41 patients met the criteria. 90.2% (37) was female, 46-64 years was the most frequent age range. 70.7% (29) had synovitis, of these 29 patients, 75.8% (22) had chronic stage synovitis. At the start of the study 9.7% (4) had positive ACPA and in time seroconversion to 34.1% (14). 24.3% (10) had positive rheumatoid factor (RF). 19.5% (8) had RA according to the 2012 American College of Rheumatology classification criteria for RA. Of these 8 patients, the 87.5% (7) had ACPA positive. 2.4% (1) developed an undifferentiated polyarthritis and 2.4% (1) met criteria for spondyloarthritis with axial and peripheral HLAB27 positive. 14.6% (6) increase C reactive protein and 46.3% (19) increase erythrosedimentation rate. 12.1% (5) were smokers.

Conclusion:
34.1% (14) of 41 patients had ACPA positive over time, of these 14 patients, 57.1% (8) developed ACPA positive RA and 42.8% (6) had positive RF. This demonstrates a relationship between CKV infection arthritis clinics for the first time with musculoskeletal manifestation secondary arthritis and ACPA positivity over time, together with a high risk of developing RA.

References
2. Caterbi, S. Bistoni, O. Alunno, A. et al. Anticyclic Citrullinated Peptide Antibodies in Patients with Rheumatic Diseases other than Rheumatoid Arthritis: Clinical or Pathogenic Significance? J Rheumatol 2015;42;1063-1064

Disclosure: E. Tejada-Reyes, None; I. Mercedes-Núñez, None; Y. Cruz-Rojas, None; E. Rodriguez-Bautista, None; V. Rosario, None; R. Peña-Blanco, None; R. Muñoz-Louis, None; T. Valdez-Lorie, None; R. Alba-Fériz, None.


Abstract Number: 1966

Risk of Tuberculosis in Biologic Users for Rheumatic Diseases: Results from the South African Biologies Registry

Clive Pettipher and Romela Benitha, Rheumatology, Private Practice, Stellenbosch, South Africa

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Epidemiology and Public Health Poster III: Rheumatic Disease Risk and Outcomes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM
Background/Purpose:

To evaluate the rate of tuberculosis (TB) in biologic users for rheumatic diseases in South Africa, a TB endemic country, the effectiveness of our latent TB (LTB) screening program, risk factors and clinical outcome.

Methods:

Documented cases of TB were collected from the South African biologics registry (SABIO), practicing rheumatologists and pharmaceutical companies. Data on demographics, LTB screening tests and prophylaxis, biologic and DMARD therapies, TB diagnosis and treatment outcomes were recorded. A matched control arm evaluated the risk of TB in non-biologics users.

Results:

96 TB cases were collected from June 1999 to June 2017 (RA=55 (57%), AS=27 (28%), PsA=4 (4%), JIA=10 (10%)). The rate of TB was 1,240/100,000 person-years for all biologic users (n=96) compared to the control arm of 0/100,000 years (n=0) with an incidence rate difference of 0.0124 (95% CI 0.007 to 0.018, p<0.0001). Of these, 60/96 (62.5%) had pulmonary and 36/96 (37.5%) had extra-pulmonary disease. Reactivation TB occurred in 45/96 (51%) cases, despite a vigilant LTB screening program; new TB in 49/96 (47%) cases and 2 were undetermined. TB occurred in all 7 biologics licenced for use in SA (adalimumab 48, infliximab 15, golimumab 3, etanercept 19, tocilizumab 2, abatacept 5 and rituximab 4) with the majority from monoclonal TNF inhibitors (1,683/100 000 person-years) compared to etanercept (861/100,000 years) and non-TNF inhibitors (681/100,000 years). The incidence rate ratio (IRR) for monoclonal inhibitors compared to etanercept was 1.96 (95% CI 1.16 to 3.45, p=0.005) and 2.47 (95% CI 1.29 to 5.19, p=0.002) compared to non-TNF inhibitors. There was no significant difference between non-TNF inhibitors and etanercept (IRR 0.79; 95% CI 0.34 to 1.75, p=0.336). From registry data, it was extrapolated that 625 from 4830 patients (12.9%) screened LTB positive and were treated, yet 14 still developed TB (9 reactivation and 5 new onset TB). The majority (77) of TB cases, screened negative and screening was not done in 5. Steroid use, methotrexate use and male gender were significantly associated with acquiring TB (OR = 6.12; p<0.001, OR=7.5; p<0,001 and OR = 1.82; p=0.005 respectively), while the underlying rheumatic condition, race and geographic region were not. Two drug resistant TB cases and 6 deaths were recorded.

Conclusion:

TB poses a significant risk to all biologics users, including non-anti TNF’s in SA, a TB endemic country, despite our screening program. Concomitant methotrexate and steroid use further increase this risk.

Comparison of TB rates in biologic users across registries

<table>
<thead>
<tr>
<th></th>
<th>SABIO (RSA)</th>
<th>BSRBR (British)</th>
<th>BADBADASER (Spanish)</th>
<th>RATIO (French)</th>
<th>US National bank</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of TB cases</td>
<td>96</td>
<td>40</td>
<td>15</td>
<td>69</td>
<td>4</td>
</tr>
<tr>
<td>Number of patients</td>
<td>4 830</td>
<td>10 712</td>
<td>5 198</td>
<td>Not reported</td>
<td>6 460</td>
</tr>
<tr>
<td>TB rate using anti TNF per 100 000 person-years</td>
<td>1 387</td>
<td>106</td>
<td>172</td>
<td>116</td>
<td>52</td>
</tr>
<tr>
<td>TB rate using non-anti TNF per 100 000 person-years</td>
<td>681</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TB rates of individual biologic agents (SABIO)</th>
<th>Sum of biologic exposure (years)</th>
<th>TB cases per drug (n=96)TB rate per 100 000 person-years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adalimumab</td>
<td>2,954</td>
<td>48</td>
</tr>
<tr>
<td>Infliximab</td>
<td>694</td>
<td>15</td>
</tr>
<tr>
<td>Golimumab</td>
<td>273</td>
<td>3</td>
</tr>
<tr>
<td>Etanercept</td>
<td>2,207</td>
<td>19</td>
</tr>
<tr>
<td>Abatacept</td>
<td>546</td>
<td>5</td>
</tr>
<tr>
<td>Rituximab</td>
<td>803</td>
<td>4</td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>265</td>
<td>2</td>
</tr>
</tbody>
</table>

Disclosure: C. Pettipher, Have been awarded a research grant by Pfizer, 2; R. Benitha, Research grant from Pfizer, 2.


Abstract Number: 1967
Strongyloides Screening in Immunocompromised Immigrant Rheumatology Patients

Sahitya Mallipeddi1, Christina Coyle2 and Beverly Johnson1, 1Rheumatology, Albert Einstein College of Medicine, Bronx, NY, 2Infectious Diseases, Albert Einstein College of Medicine, Bronx, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Epidemiology and Public Health Poster III: Rheumatic Disease Risk and Outcomes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Strongyloides Stercoralis is a helminthic infection that is usually chronic and asymptomatic and may persist undiagnosed for decades. Patients from strongyloides endemic areas (tropics and subtropics) on immunosuppression are at risk for disseminated disease that carries a high morbidity and mortality. Our aim is to prospectively evaluate the prevalence of Strongyloides infection in immunocompromised immigrant patients with rheumatic diseases.

Methods: A single center, prospective, pilot study was conducted at an urban safety net hospital caring for a large immigrant population from September 2016 to June 2017. Inclusion criteria included subjects with rheumatologic diagnosis who are from strongyloides endemic areas on immunosuppressant drugs. A strongyloides screening questionnaire was developed in collaboration with the infectious disease division. Patients were interviewed to obtain medical history, demographic, and social variables. Strongyloides serology was performed with ELISA at the medical center. If there was a positive or indeterminate test, treatment protocol was initiated in parasitology clinic. Statistical analysis was performed using SPSS. Institutional IRB approval was obtained.

Results: A total of 101 patients were screened. The most frequent diagnosis was lupus (39%) followed by rheumatoid arthritis (32%). Most of the patients immigrated from South America (62.6%) and rest of the population was from Asia and Africa. The majority of the patients were female (83.8%). A total of 88 patients completed strongyloides screening and out of which four (4.5%) had positive tests and three (3.4%) had an indeterminate tests. In terms of the socioeconomic conditions, 90.7 % had a bathroom in the house in their home country, 86.6% had running water in the house, 36.1% responded that they swam in fresh water and 43.3% had their home situated in the country side. Over half (56.3%) of the patients were on steroids, (9% on prednisone 15 mg and above), 15.4% of the patients were on biologic DMARDS and 72.5% were on non-biologic DMARDs.

Conclusion: We found 7.95% of patients were strongyloides positive or indeterminate. This is likely an underestimate of the true prevalence of strongyloides infection in this population as our population may be representing a higher socioeconomic status (SES) than the general immigrant population as over 90.7% of patients had bathrooms in their home country and 86.6% had running water which is a surrogate marker of higher SES. Further investigation into larger cohorts may be required to quantify the true incidence and prevalence of strongyloides in this population. Given the magnitude of the morbidity and mortality that strongyloides can cause in immunocompromised patients, health care providers should consider strongyloides screening in their immunocompromised patients. As the exposure may be remote and patients are asymptomatic, increased awareness among physicians is critical in identifying and treating high risk populations to prevent the occurrence of severe strongyloides infection. To our knowledge, this is one of the few studies to evaluate prospectively for strongyloides infection in high risk individuals and the only one in patients with rheumatic disease.

Disclosure: S. Mallipeddi, None; C. Coyle, None; B. Johnson, Johnson & Johnson, 1,TREG, 5.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/strongyloides-screening-in-immunocompromised-immigrant-rheumatology-patients

Abstract Number: 1968

Occurrence of Rheumatic Diseases in a National Cohort of Hospitalizations for Progressive Multifocal Leukoencephalopathy

Liudmila Kastssianok1, Prabha Ranganathan2, Seth Eisen3 and Xinliang Huang4, 1Rheumatology, Washington University in Saint Louis, School of Medicine, St Louis, MO, 2Washington University in Saint Louis, School of Medicine, Saint Louis, MO, 3Internal Medicine-Rheumatology, Washington University in Saint Louis, School of Medicine, Saint Louis, MO, 4Washington University in Saint Louis, School of Medicine, St Louis, MO

First publication: September 18, 2017
Background/Purpose: Progressive multifocal leukoencephalopathy (PML), a rare, usually fatal, central nervous system demyelinating disorder that occurs in immunocompromised hosts, results from reactivation of the JC virus. We undertook this study to determine the frequency of rheumatic and other diseases associated with an immunocompromised state in a national cohort of PML hospitalizations derived from the Nationwide Inpatient Sample (NIS).

Methods: The NIS, established as part of the Healthcare Cost and Utilization Project, is a 20% sample of all US hospital discharges weighted to represent the entire US population. Data collected and analyzed from January 1 1998 until December 31 2011. A NIS sampling design change in 2012 precluded reliably including the data from 2012 to 2014. International Classification of the Diseases, Ninth Revision, Clinical Modification codes were used to identify the total number of hospitalizations for PML and diseases of interest (rheumatic diseases, multiple sclerosis (MS), human immunodeficiency virus (HIV) infection, hematologic and solid organ malignancies, and bone marrow and solid organ transplants). Information on demographics and hospital characteristics (region and type of hospital) was also collected. All analyses were performed using SAS enterprise guide, version 7.13 (SAS Institute, Cary, NC).

Results: A total of 17,268 hospitalizations for PML was identified over the 14 year period. The frequency of hospitalizations for PML among the diseases of interest is presented in Table 1. Details of demographics and hospital characteristics are presented in Table 2. Among the rheumatic diseases, there were 145 (0.84%) PML hospitalizations with SLE, 103 (0.60%) PML hospitalizations with RA, 11 (0.06%) PML hospitalizations with granulomatosis with polyangiitis, and no PML hospitalizations with microscopic polyangiitis. Hospitalization rates for PML per 100,000 hospitalizations among patients with rheumatic diseases are presented in Table 3.

Conclusion: PML is a rare complication even among diseases at high risk for JC virus reactivation. The frequency of PML hospitalizations among rheumatic diseases was reassuringly low. Only among rheumatic disease patients with HIV, MS, or a hematologic malignancy did the rate of PML hospitalizations increase substantially.

### Table 1: Frequency of hospitalizations for PML among diseases of interest 1998 through 2011

<table>
<thead>
<tr>
<th>Diseases</th>
<th>Hospitalization for PML, N (Percent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>12,383 (71.71)</td>
</tr>
<tr>
<td>Hematologic malignancies</td>
<td>864 (5.00)</td>
</tr>
<tr>
<td>Multiple sclerosis</td>
<td>351 (2.03)</td>
</tr>
<tr>
<td>Solid organ malignancies</td>
<td>324 (1.88)</td>
</tr>
<tr>
<td>Rheumatic diseases</td>
<td>246 (1.42)</td>
</tr>
<tr>
<td>Bone marrow and organ transplants</td>
<td>108 (0.63)</td>
</tr>
<tr>
<td>All other diseases</td>
<td>2,992 (17.33)</td>
</tr>
<tr>
<td>Total</td>
<td>17,268 (100.00)</td>
</tr>
</tbody>
</table>
### Table 2: Demographics and hospital characteristics and type

<table>
<thead>
<tr>
<th>Weighted frequency</th>
<th>HIV</th>
<th>Hematologic malignancies</th>
<th>Multiple sclerosis</th>
<th>Solid organ malignancies</th>
<th>Rheumatic diseases</th>
<th>Transplants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (Total)</td>
<td>12384</td>
<td>864</td>
<td>351</td>
<td>324</td>
<td>246</td>
<td>108</td>
</tr>
<tr>
<td>Male</td>
<td>8956</td>
<td>425</td>
<td>104</td>
<td>133</td>
<td>87</td>
<td>54</td>
</tr>
<tr>
<td>Female</td>
<td>3403</td>
<td>439</td>
<td>247</td>
<td>191</td>
<td>159</td>
<td>54</td>
</tr>
<tr>
<td>Missing Value</td>
<td>25</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Race (Total)</td>
<td>12384</td>
<td>864</td>
<td>351</td>
<td>324</td>
<td>246</td>
<td>108</td>
</tr>
<tr>
<td>White</td>
<td>3659</td>
<td>613</td>
<td>248</td>
<td>235</td>
<td>171</td>
<td>65</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1160</td>
<td>28</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Asian or Pacific</td>
<td>51</td>
<td>X</td>
<td>0</td>
<td>X</td>
<td>0</td>
<td>19</td>
</tr>
<tr>
<td>Native American</td>
<td>38</td>
<td>15</td>
<td>24</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>339</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Missing Value</td>
<td>2013</td>
<td>189</td>
<td>28</td>
<td>60</td>
<td>28</td>
<td>16</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>42.10</td>
<td>60.3 (1.39)</td>
<td>46.68 (1.63)</td>
<td>63.52 (1.71)</td>
<td>57.22 (2.46)</td>
<td>55.41 (2.76)</td>
</tr>
<tr>
<td>Age groups (Total)</td>
<td>12384</td>
<td>864</td>
<td>351</td>
<td>324</td>
<td>246</td>
<td>108</td>
</tr>
<tr>
<td>&lt;=18</td>
<td>100</td>
<td>15</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>0</td>
</tr>
<tr>
<td>19-29</td>
<td>746</td>
<td>45</td>
<td>25</td>
<td>X</td>
<td>14</td>
<td>X</td>
</tr>
<tr>
<td>30-39</td>
<td>4022</td>
<td>49</td>
<td>84</td>
<td>X</td>
<td>32</td>
<td>X</td>
</tr>
<tr>
<td>40-49</td>
<td>4969</td>
<td>65</td>
<td>101</td>
<td>41</td>
<td>X</td>
<td>17</td>
</tr>
<tr>
<td>50-59</td>
<td>2073</td>
<td>156</td>
<td>92</td>
<td>45</td>
<td>69</td>
<td>28</td>
</tr>
<tr>
<td>60-69</td>
<td>413</td>
<td>261</td>
<td>44</td>
<td>110</td>
<td>72</td>
<td>52</td>
</tr>
<tr>
<td>&gt;=70</td>
<td>61</td>
<td>273</td>
<td>X</td>
<td>114</td>
<td>48</td>
<td>0</td>
</tr>
<tr>
<td>Hospital region (Total)</td>
<td>12383</td>
<td>864</td>
<td>351</td>
<td>324</td>
<td>246</td>
<td>108</td>
</tr>
<tr>
<td>Northeast</td>
<td>3639</td>
<td>257</td>
<td>61</td>
<td>50</td>
<td>49</td>
<td>24</td>
</tr>
<tr>
<td>Midwest</td>
<td>1728</td>
<td>210</td>
<td>77</td>
<td>95</td>
<td>35</td>
<td>44</td>
</tr>
<tr>
<td>South</td>
<td>5089</td>
<td>227</td>
<td>155</td>
<td>119</td>
<td>120</td>
<td>15</td>
</tr>
<tr>
<td>West</td>
<td>1927</td>
<td>170</td>
<td>58</td>
<td>60</td>
<td>41</td>
<td>25</td>
</tr>
<tr>
<td>Hospital type (Total)</td>
<td>12383</td>
<td>864</td>
<td>351</td>
<td>324</td>
<td>246</td>
<td>108</td>
</tr>
<tr>
<td>Rural</td>
<td>276</td>
<td>X</td>
<td>24</td>
<td>X</td>
<td>X</td>
<td>0</td>
</tr>
<tr>
<td>Urban nonacademic</td>
<td>3036</td>
<td>213</td>
<td>97</td>
<td>107</td>
<td>93</td>
<td>15</td>
</tr>
<tr>
<td>Urban academic</td>
<td>9058</td>
<td>587</td>
<td>230</td>
<td>194</td>
<td>147</td>
<td>93</td>
</tr>
<tr>
<td>Missing Value</td>
<td>13</td>
<td>X</td>
<td>0</td>
<td>X</td>
<td>X</td>
<td>0</td>
</tr>
</tbody>
</table>

X - values less than 11 are not presented because of risk of patient re-identification

### Table 3: Hospitalization rates for PML with a rheumatic disease alone and with an additional disease associated with an immunocompromised state 1998 through 2011

<table>
<thead>
<tr>
<th>PML hospitalizations with any rheumatic disease and:</th>
<th>Total PML cases</th>
<th>Disease hospitalization rates per 100,000 hospitalizations</th>
</tr>
</thead>
<tbody>
<tr>
<td>No additional disease associated with an immunocompromised state</td>
<td>246</td>
<td>2.87</td>
</tr>
<tr>
<td>HIV</td>
<td>147</td>
<td>622.59</td>
</tr>
<tr>
<td>MS</td>
<td>15</td>
<td>39.43</td>
</tr>
<tr>
<td>A hematologic malignancy</td>
<td>20</td>
<td>14.04</td>
</tr>
<tr>
<td>A solid organ malignancy</td>
<td>19</td>
<td>2.45</td>
</tr>
<tr>
<td>A bone marrow or solid organ transplant</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Disclosure: L. Kastianok, None; P. Ranganathan, None; S. Eisen, None; X. Huang, None.
Prevalence and Predictive Value over 16 Years of Serum Rheumatoid Factor and Anti-Cyclic Citrullinated Peptide Antibodies in the General Population

Elena Generali, Natasa Isailovic, Maria De Santis, Angela Ceribelli, Fausto Alborghetti, Guido Colloredo, Luisa Porrati, Torsten Matthias, Alberto Zucchi, Giacomo Maria Guidelli, Marta Caprioli, Carlo Selmi

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Epidemiology and Public Health Poster III: Rheumatic Disease Risk and Outcomes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The prevalence of Rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) antibodies in the general population may vary widely, as RF is present in 0-5% and anti-CCP in 0-9% of healthy controls, but the clinical significance in the general population remains unclear. We determined the prevalence of RF and anti-CCP antibodies in a large sample of the general population and their predictive value over developing rheumatoid arthritis (RA) over 16 years.

Methods: We took advantage of a randomly selected sample of a general population study initiated in 1998 (Isola I, originally including 2,828 subjects; 53% women, age 43±13 years) from a well-defined Northern Italian area. Serum RF and anti-CCP were tested in recent years by ELISA on 2,690 samples and data collected in 2017 (Isola II: 50% women, age 58±13 years). Administrative databases were searched for RA diagnoses occurring between enrollment and May 31st 2017. The risk ratio (RR) was calculated for incident RA cases between subjects exposed and not exposed to RF and anti-CCP antibodies.

Results: RF was positive in 276 (10.2%), while anti-CCP were found in 127 (4.7%) subjects, with the latter at medium-high titer (>30 U/mL) in 25 (0.9%) subjects. Twelve (0.4%) cases of RA were found over 16 years, of which 3 (25%) positive for RF and 5 (41.7%) positive for anti-CCP antibodies, mostly at medium-high titer (4/5, 80%). Only one (8.3%) case of RA was positive both for RF and anti-CCP antibodies. We observed two cases of Sjögren’s syndrome, both positive for RF, while one was positive also for anti-CCP. The risk ratio (RR) of developing RA over 16 years is 3.08 (95% confidence interval – CI – 0.82-11.56, p=0.07) for RF positive subjects and 20.13 (95% CI 5.09-79-52, p<0.001), for anti-CCP antibodies positive subjects, and it increases up to 67.46 (95%CI 16.36-253.98; p<0.001) for medium-high titer anti-CCP antibodies.

Conclusion: We report a high prevalence of RF and anti-CCP in the general population of a Northern Italian region, but only anti-CCP are associated with a significantly increased risk of RA over 16 years.

Disclosure: E. Generali, None; N. Isailovic, None; M. De Santis, None; A. Ceribelli, None; F. Alborghetti, None; G. Colloredo, None; L. Porrati, None; T. Matthias, Aesku Diagnostics, 3; A. Zucchi, None; G. M. Guidelli, None; M. Caprioli, None; C. Selmi, None.
Sang Hyun Joo 1, Eun Hye Park 2, Joongyub Lee 3 and Yeong Wook Song 4, 1Division of Rheumatology, Department of Internal Medicine, Jungang Medical Foundation, Jeju, Korea, Republic of (South), 2Division of Rheumatology, Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea, Republic of (South), 3Division of Clinical Epidemiology Medical Research Collaborating Center Biomedical Research Institution, Seoul National University Hospital, Seoul, Korea, Republic of (South), 4Department of Molecular Medicine and Biopharmaceutical Sciences, Graduate School of Convergence Science and Technology, Seoul National University, Seoul, Korea., Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Epidemiology and Public Health Poster III: Rheumatic Disease Risk and Outcomes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Allergy and autoimmune disease are related to the immune system. It was not clear in the previous studies whether allergic disease (e.g., asthma, allergic rhinitis, and atopic dermatitis) are associated with rheumatoid arthritis (RA).

Methods:
We analyzed RA, allergic disease (asthma, allergic rhinitis, and atopic dermatitis) and the serum immunoglobulin E (IgE) against inhalant antigen (total IgE, IgE Dermatophagoides farina (df), IgE cockroach and IgE dog) from the data of KNHANES (N=8958, estimated population size=47933924). We analyzed the prevalence of RA and allergic diseases using general linear model and logistic regression with complex sample design method adjusted by age and sex and evaluated the association between RA and allergic diseases including serum IgE levels.

Results:
The prevalence of RA was 2.22 % [95% CI; 1.46-3.38]. The prevalence of allergic diseases was 22.89% [95% CI: 20.61-25.35]. The prevalence of RA with allergic disease (2.63 % [95% CI; 1.68-4.10]) were significantly increased compared with that of RA without allergic diseases (1.91 % [95% CI; 0.99-3.67]) (p =0.02). Asthma (adjusted odds ratio (OR): 2.60 [1.89-3.58], p<0.001) and atopic dermatitis (adjusted OR: 2.22 [1.81-2.73], p<0.001) were positively associated with RA.

Total IgE levels were increased in RA patients (RA vs. control: 561.99 ± 286.98 kU/L vs. 269.17 ± 16.37 kU/L, p=0.04). But serum IgE df were decreased in RA patients (RA vs. control: 1.39 ± 0.63 kU/L vs. 5.09 ± 0.43 kU/L, p<0.01). Serum IgE cockroach level (RA vs. control: 1.39 ± 0.87 kU/L vs. 0.52 ± 0.05 kU/L, p=0.06) and serum IgE dog levels (RA vs. control: 0.10 ± 0.04 kU/L vs. 0.34 ± 0.12 kU/L, p=0.15) were not different.

Conclusion:
We showed increased prevalence of RA patients in the individuals with the allergic diseases than those without allergic diseases. Serum total IgE levels was increased in RA patients of the KNHANES data of Korean populations.

Disclosure: S. H. Joo, None; E. H. Park, None; J. Lee, None; Y. W. Song, None.


Abstract Number: 1971

Association between Genetic Variants and the Presence of Rheumatoid Arthritis-Related Autoimmunity and Progression to Classified Rheumatoid Arthritis in an at-Risk Population

Rachael Sawaya1, Elizabeth A. Bemis1, Ryan W. Gan2, Jill M. Norris3, Jeffrey A. Sparks4, Elizabeth Karlson5, M. Kristen Demoruelle6, Kevin D. Deane7, V. Michael Holers8, Marie L. Feser7, Laurie Moss7, Jane H. Buckner9, Richard M. Keating10, Peter Gregersen11, Michael Weisman12, Ted R. Mikuls13 and James R. O'Dell14, 1Epidemiology, Colorado School of Public Health, Aurora,
CO, 2Colorado School of Public Health, University of Colorado Denver, Aurora, CO, 3Department of Epidemiology, Colorado School of Public Health, Aurora, CO, 4Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 5Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 61775 Aurora Ct, 1775 Aurora Ct, Aurora, CO, 7Division of Rheumatology, University of Colorado School of Medicine, Aurora, CO, 8Rheumatology Division, University of Colorado School of Medicine, Aurora, CO, 9Benaroya Research Institute at Virginia Mason, Seattle, WA, 10Division of Rheumatology, Scripps Clinic, La Jolla, CA, 11The Feinstein Institute for Medical Research, Northwell Health, Manhasset, NY, 12Cedars-Sinai Medical Center Division of Rheumatology, Los Angeles, CA, 13Internal Medicine, Division of Rheumatology, University of Nebraska Medical Center, Omaha, NE, 14Department of Internal Medicine, University of Nebraska Medical Center, Omaha, NE

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Epidemiology and Public Health Poster III: Rheumatic Disease Risk and Outcomes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is an autoimmune disease characterized by the presence of RA-related autoantibodies prior to the development of clinical disease. While HLA-shared epitope (SE) is the strongest genetic factor for RA, genome-wide association scans (GWAS) have identified additional single nucleotide polymorphisms (SNPs) associated with RA. We investigated whether these SNPs were associated with the presence of anti-cyclic citrullinated peptide autoantibodies (CCP) in RA-free At-Risk individuals, and/or with progression to classified RA in CCP positive (CCP+) individuals.

Methods: We tested 1066 RA-free first degree relatives (FDRs) of RA patients for CCP2 and CCP3.1 as part of the Studies of the Etiology of RA (SERA); 124 ever tested CCP+ at baseline or during follow-up. We examined associations between 41 GWAS-identified SNPs and ever CCP+ using logistic regression in additive models. We also assessed SE, age, and sex as effect modifiers. When a significant interaction was found, results were stratified. Of the CCP+ FDRs, 84 were followed over time and 10 developed classified RA. We examined whether the SNPs were associated with development of RA in CCP+ FDRs using Cox proportional hazards; effect modification was not tested due to small numbers. As each SNP was of interest due to the known association with RA, we did not adjust for multiple comparisons in this exploratory analysis.

Results: FDRs who were ever CCP+ were less likely to be ≥50 years old than CCP- FDRs (Table 1). Significant SNP and CCP+ associations and their interactions are presented in table 2. For some SNPs, associations differed by SE, age, and sex. In longitudinal analyses, CCP+ FDRs who developed RA were less likely to be non-Hispanic White (NHW) and more likely to be SE+ than CCP+ FDRs that did not develop RA (Table 1). In CCP+ FDRs, progression to RA was associated with different SNPs than those associated with CCP+ (Table 2).

Conclusion: These findings indicate that some RA-associated SNPs may play a role in the early development of serum CCP+ in absence of RA, and others may play a role in the progression from CCP+ without RA to classifiable disease. Moreover, associations between SNPs and autoimmunity differ by SE, age, and sex, suggesting disease heterogeneity. The effect modification by SE that we observed may suggest that GWAS SNPs may have a more influential effect when the individual does not have SE to promote disease. These findings need further exploration to inform disease mechanisms, prediction and therapeutic/prevention studies.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>CCP + (n=124)</th>
<th>CCP - (n=942)</th>
<th>p-value</th>
<th>Developed RA (n=10)</th>
<th>Did not develop RA (n=74)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: N (% ≥ 50)</td>
<td>54%</td>
<td>65%</td>
<td>0.02</td>
<td>40%</td>
<td>53%</td>
<td>0.52</td>
</tr>
<tr>
<td>Race/Ethnicity: N (% NHW)</td>
<td>77%</td>
<td>75%</td>
<td>0.62</td>
<td>50%</td>
<td>85%</td>
<td>0.02</td>
</tr>
<tr>
<td>Sex: N (% female)</td>
<td>90%</td>
<td>90%</td>
<td>0.95</td>
<td>80%</td>
<td>89%</td>
<td>0.34</td>
</tr>
<tr>
<td>Education: N (% &gt; high school)</td>
<td>26%</td>
<td>28%</td>
<td>0.58</td>
<td>40%</td>
<td>30%</td>
<td>0.72</td>
</tr>
<tr>
<td>Income: N (% ≥ 40K)</td>
<td>90%</td>
<td>90%</td>
<td>0.90</td>
<td>90%</td>
<td>86%</td>
<td>1.00</td>
</tr>
<tr>
<td>Shared Epitope: N (% positive)</td>
<td>55%</td>
<td>53%</td>
<td>0.73</td>
<td>90%</td>
<td>51%</td>
<td>0.04</td>
</tr>
<tr>
<td>Pack Years: N (% &gt; 10)</td>
<td>15%</td>
<td>15%</td>
<td>0.98</td>
<td>0%</td>
<td>15%</td>
<td>0.35</td>
</tr>
</tbody>
</table>

Table 1: Demographic characteristics at first CCP+ visit (or last study visit in CCP-subjects) by the two study outcomes
Table 2: Significant associations between RA GWAS SNPs and CCP positivity in RA-free FDRs, and for progression from CCP+ to RA in FDRs

<table>
<thead>
<tr>
<th>Gene name (SNP)</th>
<th>Odds Ratio (95% CI)</th>
<th>Interaction p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DNASE1L3-ABHD6-PXK (rs73081554)</td>
<td>0.21 (0.08-0.57)</td>
<td>ns</td>
</tr>
<tr>
<td>CFLAR-CASP8 (rs6715284)</td>
<td></td>
<td>0.03</td>
</tr>
<tr>
<td>SE-</td>
<td>0.39 (0.18-0.87)</td>
<td></td>
</tr>
<tr>
<td>SE+</td>
<td>1.15 (0.67-1.97)</td>
<td></td>
</tr>
<tr>
<td>TPDS2 (rs998731)</td>
<td>0.59 (0.40-0.88)</td>
<td>0.02</td>
</tr>
<tr>
<td>SE-</td>
<td>1.20 (0.84-1.73)</td>
<td></td>
</tr>
<tr>
<td>SE+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CCL21 (rs11574914)</td>
<td></td>
<td>0.04</td>
</tr>
<tr>
<td>Age &lt; 50 first CCP+ visit or last visit CCP-</td>
<td>1.84 (1.21-2.80)</td>
<td></td>
</tr>
<tr>
<td>Age ≥ 50 first CCP+ visit or last visit CCP-</td>
<td>0.97 (0.66-1.49)</td>
<td></td>
</tr>
<tr>
<td>PADI4 (rs2301888)</td>
<td></td>
<td>0.002</td>
</tr>
<tr>
<td>Age &lt; 50 first CCP+ visit or last visit CCP-</td>
<td>1.42 (0.94-2.14)</td>
<td></td>
</tr>
<tr>
<td>Age ≥ 50 first CCP+ visit or last visit CCP-</td>
<td>0.50 (0.30-0.83)</td>
<td></td>
</tr>
<tr>
<td>CCK6 (rs4272)</td>
<td></td>
<td>0.03</td>
</tr>
<tr>
<td>Female</td>
<td>1.13 (0.81-1.58)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>0.20 (0.04-0.92)</td>
<td></td>
</tr>
<tr>
<td>COG6 (rs9603616)</td>
<td></td>
<td>0.02</td>
</tr>
<tr>
<td>Female</td>
<td>0.93 (0.69-1.26)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2.97 (1.21-7.24)</td>
<td></td>
</tr>
<tr>
<td>LBH (rs10175798)</td>
<td></td>
<td>0.04</td>
</tr>
<tr>
<td>Female</td>
<td>1.06 (0.80-1.39)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2.41 (1.16-4.95)</td>
<td></td>
</tr>
</tbody>
</table>

Outcome = Progression to 2010 or 1987 RA in CCP+ FDRs‡ (Nanalyzed=84)

<table>
<thead>
<tr>
<th>Gene name (SNP)</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAD51B (rs1950897)</td>
<td>3.40 (1.08-10.69)</td>
</tr>
<tr>
<td>SPRED2 (rs1858037)</td>
<td>2.77 (1.02-7.50)</td>
</tr>
<tr>
<td>IL2RA (rs706778)</td>
<td>5.06 (1.51-16.96)</td>
</tr>
<tr>
<td>AFF3 (rs9653442)</td>
<td>0.18 (0.04-0.83)</td>
</tr>
<tr>
<td>RUNX1 (rs9979383)</td>
<td>5.77 (1.49-22.40)</td>
</tr>
</tbody>
</table>

†Separate models are run for each SNP, and are adjusted for race, age ≥ 50, and account for familial correlation. Odds ratios represent the increase (or decrease) in risk associated with an additional minor allele of the SNP.

‡Separate models are run for each SNP, and are adjusted for race, age ≥ 50, SE, and account for familial correlation. Hazard ratios represent the increase (or decrease) in risk associated with an additional minor allele of the SNP.

Disclosure: R. Sawaya, None; E. A. Bemis, None; R. W. Gan, None; J. M. Norris, None; J. A. Sparks, None; E. Karlson, None; M. K. Demoruelle, None; K. D. Deane, Inova Diagnostics, Inc., 5; V. M. Holers, None; M. L. Feser, None; L. Moss, None; J. H. Buckner, None; R. M. Keating, None; P. Gregersen, None; M. Weisman, None; T. R. Mikuls, BMS, 2, Ironwood Pharm, 2, Pfizer Inc, 5, NIH, VA, 2; J. R. O’Dell, Medac, 5, Coherus, 5.


Abstract Number: 1972
Causes of Death in 350 Patients with Systemic Autoimmune Rheumatic Diseases

Juan Gabriel Ovalles-Bonilla1,2, Olaia Fernández-Berrizbeitia3, Julia Martínez-Barrio1, Larissa Valor1, Diana Hernández1, Justina Janta1, Belen Serrano1, Claudia Saez1, Roberto Gonzalez1, Maria Correyyero1, Leticia Garcia1, Ana López-Cerón1, Alicia Silva1, Juan Carlos Nieto1, Carlos González1,4, Indalecio Montaegudo1 and Francisco Javier López Longo1,4. 1Rheumatology, Hospital General Universitario Gregorio Marañón, Madrid, Spain, 2Instituto de Investigación Sanitaria Gregorio Marañón, Madrid, Spain, 3Rheumatology, Hospital Universitario Basurto, Bilbao, Spain, 4Facultad de Medicina, Universidad Complutense de Madrid, Madrid, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Epidemiology and Public Health Poster III: Rheumatic Disease Risk and Outcomes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The major SARD have an increased mortality compared to the general population. It is well known that the main causes of death in Systemic Lupus Erythematosus (SLE) are infections (INF), cardiovascular events (CV), neoplasia (NEO) and disease activity. However, the compared mortality of Mixed Connective Tissue Disease (MCTD), Systemic Sclerosis (SSc), Poly/Dermatomyositis (PM/DM), overlap syndromes (OS), Sjögren's syndrome (SS), Antiphospholipid syndrome (APS), systemic vasculitis (SV), and undifferentiated or incomplete Connective Tissue Disease (UCTD) is poorly described. To analyze the causes of death and the autoantibodies (AAB) profile among the SARD.

Methods: This was a single center, prospective and observational study. Mortality by all causes and relationship with AAB profile were analyzed in patients diagnosed of SLE, MCTD, SSc, PM/DM, OS (simultaneous or sequential criteria of 2 or more SARD), SS, APS, SV and UCTD or incomplete SARD (at least one clinical criterion of the classification criteria and a related antibody of any of the SARD). Data were obtained from the “Systemic Autoimmune Rheumatic Diseases Registry” of a tertiary referral hospital from 1986 to 2016. Patients with rheumatoid arthritis were excluded. The SARD registry counts with the institutional review board approval.

Results: 1750 patients were included, of whom 1453 (83%) were women. Five hundred fifty six SLE, 125 SSc, 111 PM/DM, 91 OS, 90 MCTD, 250 SS, 211 SV, 117 UCTD and 128 losses to follow-up, the global follow up rate was 92.7%. A global mortality of 350 (20%) cases was observed: 101 INF (28%,8%), 89 CV (25,4%), 51 NEO (14,5%), 45 due to disease activity (12,8%), 41 other causes (11,7%) and 23 from unknown causes (6,5%). Table 1 shows detailed mortality causes compared by diseases. A higher mortality was associated (p<0,05) with older patients (71 years, 20-96), SV (OR 3,65), male patients (OR 1,95), SSC/PM/DM (OR 1,76), MCTD (OR 1,6) and OS (OR 1,43). AAB to pANCA (OR 4,43), anti-topoisomerase I (OR 3,64), myositis-specific AAB (OR 3.0), cANCA (OR 2,19) and anticardiolipin (OR 1,89) were associated with poorer survival. A higher survival rate was observed in patients with SLE (OR 1,7), SS (OR 1,69) and UCTD (OR 15,57) (p<0,05).

Conclusion: The main causes of death among SARD patients are CV (MCTD, SLE, and SSC), severe infections (OS, SV, and PM/DM), disease activity (APS) and neoplasia (SS). A higher mortality is observed among ANCA positive SV, anti-topoisomerase I positive SSC, MCTD, OS, anticardiolipin and myositis-specific positive patients.

<table>
<thead>
<tr>
<th>CAUSES</th>
<th>SLE %</th>
<th>SSc %</th>
<th>MCTD %</th>
<th>SV %</th>
<th>PM/DM %</th>
<th>OS %</th>
<th>SS %</th>
<th>APS %</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV</td>
<td>30,86</td>
<td>27,02</td>
<td>42,3</td>
<td>25,55</td>
<td>18,18</td>
<td>16,12</td>
<td>17,64</td>
<td>21,4</td>
</tr>
<tr>
<td>INF</td>
<td>27,16</td>
<td>21,62</td>
<td>3,84</td>
<td>36,66</td>
<td>33,33</td>
<td>45,16</td>
<td>23,52</td>
<td>21,4</td>
</tr>
<tr>
<td>NEO</td>
<td>14,81</td>
<td>13,51</td>
<td>15,38</td>
<td>8,88</td>
<td>18,18</td>
<td>9,67</td>
<td>26,47</td>
<td>14,28</td>
</tr>
<tr>
<td>ACTIVITY</td>
<td>9,87</td>
<td>18,91</td>
<td>19,23</td>
<td>11,11</td>
<td>12,12</td>
<td>19,35</td>
<td>11,76</td>
<td>28,57</td>
</tr>
<tr>
<td>OTHER</td>
<td>8,64</td>
<td>13,51</td>
<td>11,53</td>
<td>15,55</td>
<td>9,09</td>
<td>3,22</td>
<td>8,82</td>
<td>0,00</td>
</tr>
<tr>
<td>UNKNOWN</td>
<td>8,64</td>
<td>5,40</td>
<td>7,69</td>
<td>2,22</td>
<td>9,09</td>
<td>6,45</td>
<td>11,76</td>
<td>14,28</td>
</tr>
</tbody>
</table>
MORTALITY RISK FACTORS

<table>
<thead>
<tr>
<th>FACTORS</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>SYSTEMIC VASCULITIS</td>
<td>3.65</td>
</tr>
<tr>
<td>MALE SEX</td>
<td>1.95</td>
</tr>
<tr>
<td>SLE OR PM/DM</td>
<td>1.76</td>
</tr>
<tr>
<td>MCTD</td>
<td>1.60</td>
</tr>
<tr>
<td>OS</td>
<td>1.43</td>
</tr>
<tr>
<td>P-ANCA</td>
<td>4.43</td>
</tr>
<tr>
<td>ANTI SCL-70</td>
<td>3.64</td>
</tr>
<tr>
<td>MYOSITIS AAB</td>
<td>3.00</td>
</tr>
<tr>
<td>C-ANCA</td>
<td>2.19</td>
</tr>
<tr>
<td>ANTI-CARDIOLIPIN</td>
<td>1.89</td>
</tr>
</tbody>
</table>

Disclosure: J. G. Ovalles-Bonilla, None; O. Fernández-Berrizbeitia, None; J. Martínez-Barrio, None; L. Valor, None; D. Hernández, None; I. Janta, None; B. Serrano, None; C. Saez, None; R. Gonzalez, None; M. Correjero, None; L. García, None; A. López-Cerón, None; A. Silva, None; J. C. Nieto, None; C. González, None; I. Monteagudo, None; F. J. López Longo, None.


Abstract Number: 1973

Fibromyalgia in Real Life a National French Web-Based Survey in 4516 Patients

Francoise Laroche¹, julien Guerin², deborah Azoulay³, joel Coste⁴ and serge Perrot³, ¹Pain and Palliative care, APHP Hospital, Paris, France, ²CETD, APHP Hospital, Paris, France, ³CETD, Paris, France, ⁴Biostatistics in university Hospital, Paris, France

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Fibromyalgia (FM) is the most frequent widespread chronic pain disorder (1.6% of the French population) (1). The medical and socioeconomic burden is high and severity depends on medical status and symptoms as defined by the OMERACT criteria (2). Most of the studies are performed in specialized centers, recruiting the most severe patients, but very few data exist on its real impact on daily life.

Methods:

A large internet-based national survey of people suffering from FM was developed by a national patient association (Fibromyalgie-SOS Association) on their website, in France in 2014. The survey included 103 qualitative and quantitative questions that were developed by 3 medical experts (including rheumatologists) and patients.

Results:
The questionnaire was completed by 4516 people. Respondents were predominantly middle-aged (48 yrs) females (93%), most of whom had FM symptoms duration for 12 years and a diagnosis for 5 years. Diagnosis was made by a rheumatologist in 54% of the cases. The symptoms were concordant with the OMERACT domains (chronic pain, fatigue stiffness and other FM-associated symptoms) as previously published by Bennett in 2007 (3). The mean FIQ (Fibromyalgia Impact Questionnaire) score was 51 (0-100). 55% were currently working but 65% of them have been on sick leave in the 12 previous months. FIQ was mostly impacted by injustice feeling (+4.5), part time job (+2.4) and low income - less than 1000 euros monthly (+2.3) (linear regression).

Somatic comorbidities were mostly osteoarthritis (49%). Psychological comorbidities were injustice feeling (77%), cognitive symptoms (62%), anxiety (52%) and depression (48%). Initiating factors were reported by 73% of them: physical (50%) and/or psychological (76%). Aggravating factors included excess of activities, conflicts, traumatism and displacement. Treatments were provided by general practitioner (85%), physiotherapist (63%), rheumatologist (54%) and osteopathic manual practitioner (41%). Treatment was prescribed in 76.6% of the patients, including paracetamol alone (51.4%), paracetamol and weak opioids (64%), strong opioids (20.1%), antidepressants (81.5%), antiepileptic agents (54.5%), nonsteroids NSAIDs (53.8%), anxiolytics (52.4%) and steroids (12.8%).

Conclusion:
This unique descriptive survey in a large population provides data on symptoms, emotional distress, prescribing habits and impact of FM on daily life and work. Results show that FM is altered by emotional (including injustice feeling) and socio-economic factors.

Disclosure: F. Laroche, None; J. Guerin, None; D. Azoulay, None; J. Coste, None; S. Perrot, None.


Efficacy and Safety of Pregabalin for Fibromyalgia in a Population of Chinese Patients: A Phase 3, Randomized, Double-Blind, Placebo-Controlled Trial

Xiao Zhang1, Huji Xu2, Zhiyi Zhang3, Yang Li4, Lynne Pauer5, Shanmei Liao6, Gaiping Xu7 and Fengchun Zhang8, 1Guangdong General Hospital, Guangdong, China, Guangdong, China, 2Department of Rheumatology and Immunology, Shanghai Changzheng Hospital, Second Military Medical University, Shanghai, China, 3The First Affiliated Hospital of Harbin Medical University, Harbin, China, Harbin, China, 4The Second Affiliated Hospital of Harbin Medical University, Harbin, China, Harbin, China, 5Pfizer, Groton, CT, USA, Groton, CT, 6Pfizer (China) Statistics Department, Global Innovative Pharma Business, Shanghai, China, Shanghai, China, 7Pfizer (China) Clinical Development, Global Innovative Pharma Business, Beijing, China, Beijing, China, 8Peking Union Medical College Hospital, Beijing, China

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017

Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster II

Session Type: ACR Poster Session C

Session Time: 9:00AM-11:00AM

Background/Purpose: Global trial data demonstrate the efficacy of pregabalin for the treatment of pain associated with fibromyalgia (FM), but there are currently no approved medical treatments for FM-related pain in China.

Methods: A phase 3, 14-week, multicenter, randomized, double-blind, flexible-dose, parallel-group, placebo-controlled trial was conducted in China (Feb 2012–Oct 2016) to assess the efficacy and safety of pregabalin in Chinese patients with FM. Eligible patients were aged ≥18 years, met the American College of Rheumatology 1990 criteria for FM, and had a mean numeric daily pain rating scale score of ≥4 (0=‘no pain’ to 10=‘worst possible pain’, 24-hr recall period) over a 7 day baseline period. Patients were randomized (1:1) to receive pregabalin (dosed twice daily) or matching placebo as follows: 1-week screening/placebo run-in, 2-week dose titration (150 mg/day titrated to 300–450 mg/day, based on efficacy and tolerability), 12-week fixed dose, and 1-week taper. Treatment allocation used a computer-generated pseudorandom code and the random permuted blocks method. The primary endpoint was change from baseline to endpoint (Week 14) in mean pain score analyzed using a mixed-model repeated measures (MMRM) approach; weekly mean pain scores were also evaluated using MMRM. Secondary endpoints included the percentage of patients with ≥30% and ≥50% reduction in endpoint mean pain score, Patient Global Impression of Change (PGIC), Fibromyalgia Impact Questionnaire (FIQ) total score, and measures of sleep. Adverse events (AEs) were also reported.
Trial registration: ClinicalTrials.gov Identifier: NCT01387607

Results: In total, 343 patients were randomized and 334 (86% female; average age 44 years) were treated (170 pregabalin, 164 placebo). Reduction in mean pain score was significantly greater with pregabalin than placebo at endpoint (least square mean difference [95% confidence interval], –0.73 [–1.10, –0.36]; P=0.0001) and at every week during the study (P<0.05) (Fig 1). Pregabalin treatment improved the percentage of patients achieving ≥30% (P=0.0044) and ≥50% (P=0.0189) reduction in pain score over placebo at endpoint. Pregabalin, compared with placebo, also significantly improved sleep interference score (P<0.0001). There was no statistically significant improvement in PGIC, FIQ total score and the Medical Outcomes Study–Sleep Scale sleep disturbance score at endpoint with pregabalin versus placebo. The most commonly reported AEs in the pregabalin vs placebo groups were dizziness (41.8% vs 18.3%), somnolence (17.6% vs 7.9%), headache (5.9% vs 6.1%) and upper respiratory tract infection (5.9% vs 4.3%), consistent with the safety profile of pregabalin.

Conclusion:

Pregabalin was effective in reducing pain compared with placebo and is well tolerated in Chinese patients with FM.

This study was sponsored by Pfizer.

Disclosure: X. Zhang, Roche, Abbvie, Xian Janssen, 8; H. Xu, Pfizer Inc., Xian Janssen, 8; Z. Zhang, Pfizer Inc, 5,Pfizer Inc, 8; Y. Li, Roche, Simcere, 8; L. Pauer, Pfizer Inc, 1,Pfizer Inc, 3; S. Liao, Pfizer Inc, 1,Pfizer Inc, 3; G. Xu, Pfizer Inc, 1,Pfizer Inc, 3; F. Zhang, Xian Janssen, 8.


Abstract Number: 1975

Association of the 16519 Polymorphism in Patients with Fibromyalgia. Case-Control Study
Background/Purpose: More than 20% of the general population suffer from functional syndromes. It has been reported that the mitochondrial polymorphism at position 16519 is associated with functional syndromes, such as migraine, cycling vomiting syndrome, irritable bowel syndrome, non-specific abdominal pain, chronic fatigue syndrome and complex regional pain syndrome. The aim of this study was to evaluate the association of polymorphism 16519 in patients with fibromyalgia (FM).

Methods: Patients with fibromyalgia according to the 1990 or 2010 ACR criteria and be able to provide informed consent and healthy controls were recruited for this study. Inclusion criteria were: age ≥ 18 years old, diagnosis of FM, and as exclusion criteria: patients with another rheumatic comorbidity. The protocol was approved by the Ethics Committee of the Hospital Central Dr. Ignacio Morones Prieto, San Luis Potosi, México. Statistical analysis was performed with $X^2$ test.

Results: We included 40 FM patients and 36 controls, all patients were women. Mean age were 49.1 years (SD 11 years) in the group of FM and 43.2 years (SD 11.9 years) in the control group. The demographic characteristics of both groups are in table 1. In the FM group the average number of positive tender points was 10 (SD 5), with average Widespread Pain Index (WPI) of 10 (SD 5), average symptom Severity Score 7 (SD 2.7) and the Fibromyalgia Impact Questionnaire (FIQ) 52.8 (SD 19.3). The presence of the polymorphism 16519 in the group of FM was observed in 21/40 (53%) vs 29/36 (80.6%) of control group, with a $p$ value of 0.010, OR 0.27 (IC 95% 0.080 – 0.82). We did not find association between the polymorphism and the severity score.

Conclusion: The polymorphism at position 16519 has been reported previously as a genetic factor predisposing individuals to develop functional syndrome; our results showed a negative association between this polymorphism and patients with fibromyalgia.
Table 1. Demographic characteristics of patients with fibromyalgia and control group

<table>
<thead>
<tr>
<th>Variable</th>
<th>Fibromyalgia (n=40)</th>
<th>Control (n=36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>16519 polymorphism</td>
<td>21 (52.5%)</td>
<td>29 (80.6%)</td>
</tr>
<tr>
<td>Females</td>
<td>40 (100%)</td>
<td>36 (100%)</td>
</tr>
<tr>
<td>Age (SD)</td>
<td>49.1 (SD 11)</td>
<td>43.2 (SD 11.9)</td>
</tr>
<tr>
<td>Weight (SD)</td>
<td>66.1 (SD 10.2)</td>
<td>65 (SD 8.5)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>156.2 (SD 5.8)</td>
<td>157.2 (SD 6.1)</td>
</tr>
<tr>
<td>Body Mass Index (kg/m²)</td>
<td>26.9 (SD 5.8)</td>
<td>26.3 (SD 3.5)</td>
</tr>
<tr>
<td>Years with Fibromyalgia disease</td>
<td>3.1 (SD 2.4)</td>
<td>NA</td>
</tr>
<tr>
<td>Number of tender points</td>
<td>10 (SD 5)</td>
<td>NA</td>
</tr>
<tr>
<td>Widespread Pain Index (WPI)</td>
<td>10 (SD 5)</td>
<td>NA</td>
</tr>
<tr>
<td>Symptom Severity Score (SS)</td>
<td>7 (SD 2.7)</td>
<td>NA</td>
</tr>
<tr>
<td>Fibromyalgia Impact Questionnaire (FIQ)</td>
<td>52.8 (SD 19.3)</td>
<td>NA</td>
</tr>
<tr>
<td>Fatigue</td>
<td>31 (77.5%)</td>
<td>NA</td>
</tr>
<tr>
<td>Sleep disorder</td>
<td>33 (82.5%)</td>
<td>NA</td>
</tr>
<tr>
<td>Cognitive disorder</td>
<td>22 (55%)</td>
<td>NA</td>
</tr>
<tr>
<td>Somatic disorder</td>
<td>27 (67.5%)</td>
<td>NA</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>11 (27.5%)</td>
<td>NA</td>
</tr>
<tr>
<td>Depression</td>
<td>22 (55%)</td>
<td>NA</td>
</tr>
<tr>
<td>Anxiety</td>
<td>16 (40%)</td>
<td>NA</td>
</tr>
</tbody>
</table>

Figure 1. Percentage of association of 16519 polymorphism in the Fibromyalgia and control group.

Disclosure: G. Martínez-Flores, None; M. U. Martínez-Martínez, None; V. M. Saavedra Alanis, None; T. A. Luna-Zúñiga, None; G. Aguilara Barragán-Pickens, None; D. Ramos-Bello, None; A. J. Pedro Martínez, None; E. S. Acevedo-Castañeda, None; D. Herrera Van Oostdam, None; A. A. Vazquez Castillo, None; M. A. Islas Aguilar, None; C. Abud-Mendoza, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/association-of-the-16519-polymorphism-in-patients-with-fibromyalgia-case-control-study

Abstract Number: 1976

High and Low Widespread Pain Index Fibromyalgia Patient Groups, Same, or Different?

Sahar Kaouk1, Yaseen Kinanah2, Nilamba Jhala3, Deb Bork4, Sarah Rispinto5, Sara Davin5, William Wilke4 and Carmen E. Gota4,6, 1John Carroll University, University Heights, OH, 2Internal Medicine, Cleveland Clinic Foundation, Cleveland, OH, 3Internal Medicine, Cleveland Clinic, Cleveland, OH, 4Orthopedic and Rheumatologic Institute, Cleveland Clinic, Cleveland, OH, 5Neurologic Institute, Cleveland Clinic, Cleveland, OH, 6The Cleveland Clinic Rheum, The Cleveland Clinic Desk A50, Cleveland, OH

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster II
Background/Purpose:

The ACR 2010 preliminary criteria for fibromyalgia (FM) classifies patients in high WPI group, widespread pain index (WPI) ≥7, symptom severity scale (SS) ≥5, and low WPI group, WPI 3-6, SS ≥9.

It is not clear why some FM patients have less pain. Low WPI FM have lower disability scores, lower pain and global severity than high WPI group. Are there differences in the characteristics of low WPI and high WPI FM patients with regards to depressive, anxiety symptoms, pain and global FM severity and catastrophizing scores?

Methods:

Consecutive clinically diagnosed FM patients were classified in low WPI or high WPI groups, demographic and clinical data was compared. Questionnaires used: patient health questionnaire (PHQ-9), general anxiety disorder questionnaire (GAD-7), health assessment questionnaire disability index (HAQ-DI), fibromyalgia impact questionnaire (FIQ), pain disability index, pain catastrophizing scale, polysymptomatic distress scale (PSD), as the sum of WPI and SS.

Results:

Of 552 patients diagnosed clinically with FM, age 44.3 (12), 79.5% white, 85.5% female, 4% met the low WPI and 82.1% met the high WPI criteria.

Only SS, WPI and PSD, were each significantly different between low and high WPI groups (Table 1). To understand why, we looked at the individual correlations of WPI and SS (Table 2). In linear regression model, PHQ-9, GAD-7, Pain disability index, Pain catastrophizing, HAQ-DI and FIQ significantly predict WPI, F(6,98)=4.904, P<0.0001, R2 0.184; FIQ remains an independent predictor of WPI. The same model predicts SS, F(6, 98)=17.932, P<0.0001, R2 0.523; FIQ, pain catastrophizing score, PHQ-9 remain independent predictors of SS.

| Table 1. Fibromyalgia and severity measures according to criteria categories. Values are mean (SD) unless specified. Low WPI and high WPI group are statistically significant different from each other at p <0.05 if flagged with asterisks; * p<0.05; ** P<0.001 |
|-----------------|------------------|------------------|
|                | All              | WPI 3-6 and SS ≥9 | WPI ≥7 and SS ≥5 |
| N               | 475              | 22               | 453               |
| Age, yrs        | 43.9 (11.7)      | 40.9 (12.9)      | 44.1 (11.6)       |
| Female, %       | 86.7%            | 90.9%            | 86.5%             |
| Race white %    | 79.8%            | 81.8%            | 79.7%             |
| Employed full time % | 36.4%         | 36.4%            | 36.4%             |
| WPI             | 12.6 (3.7)       | 4.6 (1.0)        | 12.9 (3.4)**     |
| SS              | 9.3 (1.9)        | 10.4 (1.1)       | 9.2 (1.9)*       |
| PSD             | 21.9 (4.5)       | 15 (1.4)         | 22.2 (4.3)**     |
| FIQ             | 60.6 (19.4)      | 47.5 (13.7)      | 60.9 (7.2)       |
| PHQ-9           | 13.3 (6.0)       | 12.4 (5.3)       | 13.3 (6.1)       |
| GAD-7           | 9.5 (7.1)        | 8.8 (6.2)        | 9.5 (7.2)        |
| HAQ-DI          | 1.2 (1.6)        | 1.2 (1.9)        | 1.2 (1.5)        |
| Pain catastrophizing | 23.9 (13.2)    | 20.3 (14)        | 24 (13.3)        |
| Pain disability index | 5.6 (2.1)       | 4.9 (2.4)        | 5.7 (2.1)        |
Table 2. WPI and SS correlations with pain disability index, FIQ, HAQ-DI, PHQ-9, GAD7 and PSD. Unless specified by * all correlations were significant at p<0.0001,* P<0.05

<table>
<thead>
<tr>
<th></th>
<th>WPI</th>
<th>SS</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSD</td>
<td>0.911</td>
<td>0.541</td>
</tr>
<tr>
<td>SS</td>
<td>0.175</td>
<td></td>
</tr>
<tr>
<td>Pain disability index</td>
<td>0.301</td>
<td>0.421</td>
</tr>
<tr>
<td>FIQ</td>
<td>0.352</td>
<td>0.569</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>0.293</td>
<td>0.316</td>
</tr>
<tr>
<td>PHQ-9</td>
<td>0.271</td>
<td>0.516</td>
</tr>
<tr>
<td>GAD-7</td>
<td>0.170</td>
<td>0.344</td>
</tr>
<tr>
<td>Pain catastrophizing</td>
<td>0.205*</td>
<td>0.338</td>
</tr>
</tbody>
</table>

Conclusion:

No differences were found between high and low WPI groups, except for significantly higher PSD scores, despite many variables trending higher in the high WPI group, possibly due to the low number of patients in the low WPI group. We found that WPI and SS differ in their strength of association with core FM domains, which suggests they contribute differently to FM diagnosis.

Disclosure: S. Kaouk, None; Y. Kinanah, None; N. Jhala, None; D. Bork, None; S. Rispinto, None; S. Davin, None; W. Wilke, None; C. E. Gota, None.

Abstract Number: 1977

Elevated Levels of Eotaxin-2 in Serum of Fibromyalgia Patients

Victoria Furer¹, Eyal Hazan², Adi Mor³, Michal Segal³, Avi Katav³, Valerie Alouš⁴, Ori Elhayam⁴, Jacob George³,⁵ and Jacob N. Ablin⁶,⁷, ¹Rheumatology, Tel Aviv Sourasky Medical Center and the Sackler Faculty of Medicine, Tel Aviv University, Tel-Aviv, Israel, ²Internal Medicine D, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, ³ChemomAb Ltd. Israel, Tel Aviv, Israel, ⁴Rheumatology, Tel Aviv Sourasky Medical Center and the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel, ⁵Heart Institute, Kaplan Medical Center, Rehovot, Israel, ⁶Internal Medicine H, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, ⁷Rheumatology, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Fibromyalgia is a widespread chronic pain syndrome (FMS) the pathogenesis of which remains incompletely understood. FMS patients demonstrate an altered profile of chemokines relative to healthy controls (HC).(1) An interplay between glial and neuro-glial cells involving an extensive cytokines/chemokines network has been suggested as a potential key mechanism underlying chronic pain.(2,3) Eotaxin-2 is a potent chemoattractant for eosinophils, basophils and lymphocytes, distributed in a variety of tissues, including human brain.(4)

The aim of the current study was to compare serum levels of eotaxin-2 between FMS patients and HC and to examine a potential correlation between eotaxin-2 levels and clinical parameters of FMS.
**Methods:** 50 patients fulfilling ACR 2010 diagnostic criteria for FMS and 15 HC were recruited. Patients filled out questionnaires to assess and document severity of symptoms of FMS and depression, including the widespread pain index (WPI), the symptom severity scale (SSS), the fibromyalgia impact questionnaire (FIQ), and the Beck depression inventory (BDI). Serum levels of Eotaxin-2 (ELISA) were determined in all participants. High sensitive CRP (hs-CRP) was measured in the FMS group. Data were statistically analyzed with SPSS (version 20) and the significance level was set to P value of 0.05.

**Results:** The FMS cohort included predominantly females (84%), mean age 49 yo, mean disease duration of 6 years, with the following characteristics (means): WPI 12.5 (±4.2), SSS 9.1 (±1.9), FIQ 63.9 (±16.9), BDI 20 (±11). FMS patients exhibited significantly higher eotaxin-2 serum levels (pg/ml) vs HC: 833 (±384) vs 622 (±149), *p*-value 0.04, respectively. (Figure 1)

Mean hsCRP levels among FMS patients were 4.8±6 mg/dl, a value not indicative of acute inflammation, and no correlation was found between the eotaxin-2 and hs-CRP levels. Further, no correlation was found between Eotaxin-2 /hs-CRP levels and severity measures of FMS or depression.

**Conclusion:** Significantly increased levels of Eotaxin-2 were demonstrated in FMS compared with HC, with no correlation observed between Eotaxin-2 and hsCRP levels. Further, no correlation was found between FMS activity and Eotaxin-2 levels. Thus, Eotaxin-2 does not appear to be a candidate for a disease activity biomarker. Further research is warranted into the role of this chemokine in the pathophysiology of the FMS.

Figure 1. Serum concentration of eotaxin-2 in patients with FMS vs controls

![Figure 1](image_url)

**References:**


**Disclosure:** V. Furer, None; E. Hazan, None; A. Mor, None; M. Segal, None; A. Katav, None; V. Aloush, None; O. Elkayam, None; J. George, ChemomAb Ltd Israel, 2; J. N. Ablin, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/elevated-levels-of-eotaxin-2-in-serum-of-fibromyalgia-patients](http://acrabstracts.org/abstract/elevated-levels-of-eotaxin-2-in-serum-of-fibromyalgia-patients)

**Abstract Number:** 1978

**Employment Status in Fibromyalgia: Comparison of Employed and Unemployed Patients and Predictors of Unemployed Status**

**Yaseen Kinanah¹, Nilamba Jhala², Sahar Kaouk³, Deb Bork⁴, Sara Davin⁵, Sarah Rispinto⁵, William Wilke⁴ and Carmen E. Gota⁴, ¹Internal Medicine, Cleveland Clinic Foundation, Cleveland, OH, ²Internal Medicine, Cleveland Clinic, Cleveland, OH, ³John Carroll University, University Heights, OH, ⁴Orthopedic and Rheumatologic Institute, Cleveland Clinic, Cleveland, OH, ⁵Neurologic Institute, Cleveland Clinic, Cleveland, OH**
Background/Purpose:
Disabled status in fibromyalgia (FM) was found to be associated with lower education, higher FM symptom burden, and lower functional status. Less is known about the characteristics of unemployed FM patients who are not receiving any form of disability benefits.

Methods:
Patients diagnosed clinically with fibromyalgia were enrolled and classified according to employment status and compared. Questionnaires used: patient health questionnaire (PHQ-9), general anxiety disorder -7 questionnaire (GAD-7), health assessment questionnaire disability index (HAQ-DI), fibromyalgia impact questionnaire (FIQ), pain disability index, pain catastrophizing scale, polysymptomatic distress scale (PSD) as the sum of widespread pain index (WPI), and the symptom severity scale (SS).

Results:
Of 555 FM patients, 87.2% met the ACR 2010 preliminary FM criteria, 38.4% working full time, 13.3% part time, 11.7% receiving disability, 27.9% unemployed 2.7% students and 5.9% retired. We compared patients who were employed either full or part time and/or student, with unemployed FM patients (Table 1).

Binomial logistic regression was performed to ascertain the effects of BMI, education level, PHQ-9, GAD-7, HAQ-DI, pain related disability, FIQ, pain catastrophizing score, and PSD on the likelihood that FM patients were unemployed. The model explained 49.2% (Nagelkerke R2) of the variance in unemployed status, and correctly classified 82.8% of the cases, sensitivity 77.1%, specificity 86.5%, positive predictive value 79.4%, negative predictive value 84.9% Of the nine predictor variables only three were statistically significant: FIQ, pain catastrophizing score and the pain disability index. Increasing FIQ, pain disability index, and pain catastrophizing were each significantly associated with increasing likelihood of being unemployed.

We also compared unemployed to disabled FM patients, and the only significant difference observed was that more disabled FM were recipients of Medicare 25.5% vs 4% p=0.001.

Conclusion:
Compared to employed fibromyalgia patients, those who are unemployed have higher BMI, are more depressed and experience higher physical and pain related disability. They also have higher FM severity and distress, measured by FIQ and PSD.

Increasing fibromyalgia severity, pain related disability, and catastrophizing predict unemployment status in patients with FM. This information suggests that in order to prevent unemployment, we need to identify early the subset of FM patients with severe FM, who catastrophize and have high pain related disability scores. This subset of FM patients, may need intensive multidisciplinary interventions that include physical and occupational therapy and psychological interventions that can modify patients’ maladaptive responses to pain.
Table 1: Characteristics of employed and unemployed patients with fibromyalgia. Values are the mean (standard deviation) or percentages.

<table>
<thead>
<tr>
<th></th>
<th>EMPLOYED</th>
<th>UNEMPLOYED</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>N, %</td>
<td>302</td>
<td>150</td>
<td></td>
</tr>
<tr>
<td></td>
<td>66.8%</td>
<td>33.2%</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>41.8 (11.1)</td>
<td>42.9 (10.0)</td>
<td>0.389</td>
</tr>
<tr>
<td>Female sex, %</td>
<td>82.8% female</td>
<td>92% female</td>
<td>0.021</td>
</tr>
<tr>
<td>Ethnicity white %</td>
<td>79.8%</td>
<td>78%</td>
<td>0.774</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td>0.222</td>
</tr>
<tr>
<td>Married %</td>
<td>54.6%</td>
<td>60%</td>
<td></td>
</tr>
<tr>
<td>Divorced %</td>
<td>15.9%</td>
<td>18.7%</td>
<td></td>
</tr>
<tr>
<td>Living with partner %</td>
<td>1.3%</td>
<td>1.3%</td>
<td></td>
</tr>
<tr>
<td>Single %</td>
<td>23.8%</td>
<td>19.3%</td>
<td></td>
</tr>
<tr>
<td>Widowed %</td>
<td>2%</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>Education level</td>
<td></td>
<td></td>
<td>0.655</td>
</tr>
<tr>
<td>Less than 12th grade</td>
<td>3.3%</td>
<td>5.3%</td>
<td></td>
</tr>
<tr>
<td>High school graduate</td>
<td>14.6%</td>
<td>16.7%</td>
<td></td>
</tr>
<tr>
<td>Some college</td>
<td>19.5%</td>
<td>23.3%</td>
<td></td>
</tr>
<tr>
<td>College graduate</td>
<td>31.1%</td>
<td>30%</td>
<td></td>
</tr>
<tr>
<td>Post graduate</td>
<td>14.9%</td>
<td>6.7%</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>29.4 (6.9)</td>
<td>31.7 (9.7)</td>
<td>0.008</td>
</tr>
<tr>
<td>PHQ-9</td>
<td>11.6 (6.1)</td>
<td>14 (6.2)</td>
<td>0.0001</td>
</tr>
<tr>
<td>GAD-7</td>
<td>8.4 (6.8)</td>
<td>9.3 (6.3)</td>
<td>0.213</td>
</tr>
<tr>
<td>WPI</td>
<td>10.8 (4.5)</td>
<td>13.7 (15.5)</td>
<td>0.004</td>
</tr>
<tr>
<td>SS</td>
<td>8.6 (2.3)</td>
<td>9.3 (2)</td>
<td>0.002</td>
</tr>
<tr>
<td>PSD</td>
<td>19.5 (5.8)</td>
<td>23.9 (17.6)</td>
<td>0.002</td>
</tr>
<tr>
<td>Pain catastrophizing score</td>
<td>22 (13.8)</td>
<td>23.3 (12.6)</td>
<td>0.613</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>0.8 (1.0)</td>
<td>1.3 (0.9)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Pain disability index</td>
<td>4.6 (2.2)</td>
<td>6.5 (1.9)</td>
<td>0.0001</td>
</tr>
<tr>
<td>FIQ total</td>
<td>52.0 (20.1)</td>
<td>68.4 (17.1)</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Disclosure: Y. Kinanah, None; N. Jhala, None; S. Kaouk, None; D. Bork, None; S. Davin, None; S. Rispinto, None; W. Wilke, None; C. E. Gota, None.


Abstract Number: 1979

Relationship between Religiosity /Spirituality and Physical and Mental Outcomes in Fibromyalgia Patients
**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster II  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Similar to other chronic disorders, Fibromyalgia syndrome (FMS) poses a major challenge for patients coping capacities and extracts a far-reaching cost on functioning and quality of life. Various aspects of resilience are utilized by individuals coping with chronic health disorders and previous research points to the positive effects of faith, religiosity and spirituality as tools for coping with illness. However, the role played by these factors in coping with chronic pain such as FMS has not previously been studied. The purpose of the current study was to evaluate the link between religiosity and spirituality and the outcomes of FMS.

**Methods:**

Fifty five FMS patients (ACR criteria) attending a tertiary rheumatology clinic were recruited. Demographic data was registered. Level of spirituality/religiosity was estimated by the validated Hebrew version of the Spiritual and Religious Attitudes in Dealing with Illness (SpREUK) Questionnaire for Religiosity, Spirituality and Health, which contains 5 domains. Locus of control (LOC) was evaluated by the Locus of control questionnaire. FMS related outcome measures included the Fibromyalgia Impact Questionnaire (FIQ) (Validated Hebrew version), the SF-36, and the Beck Depression Index (BDI), assessing depression and anxiety.

**Results:**

A significant negative correlation was found between two domains of the SpREUK ("search for meaningful support" and "trust in higher guidance") and domains of the SF-36: "Role limitation due to physical health" and "Role limitation due to emotional health" (p<0.05). When comparing patients on basis of religious sector (secular, conservative, religious) secular patients showed significantly higher scores on SF-36 domains of "Role limitation due to emotional health" and "General health" compared with other sectors (p<0.05).

No significant correlation was found between LOC (internal versus external) and FMS outcome measures. No significant correlation was found between SpREUK domains and the BDI.

**Conclusion:**

In the current study, higher levels of religiosity/spirituality appeared to be inversely correlated with specific outcome measures of FMS. Unlike other chronic medical conditions, FMS patients do not appear to gain benefit from high levels of religiosity or spirituality; conversely, more severe FMS patients may be more prone to turn to religiosity/spirituality for support, so it is not possible to determine the direction of a casual relation. Chronic pain may pose a unique challenge for the faith of religious individuals who are obliged to cope with their suffering in context of a religious frame of beliefs. Physicians treating FMS patients should be aware of the impact of religious belief and spirituality on the physical and mental health in these patients.

**Disclosure:** V. Aloush, None; E. Hazan, None; R. Shorer, None; V. Furer, None; O. Elkayam, None; J. N. Ablin, None.


**Abstract Number:** 1980

**Impact of Whole-Body Cryotherapy on Gene Expression of Peripheral Blood Cells in Patients with Fibromyalgia and Association with Patient-Reported Outcomes**
Whole-body cryotherapy (WBCT) has been demonstrated in several studies as being effective in the reduction of inflammatory symptoms and in providing pain relief. It is recommended for the treatment of arthritis, fibromyalgia (FMS) and ankylosing spondylitis. The mode of action of this therapy, which consists of a brief exposure to temperatures between -110 and -160°C in special cryochambers, has not been fully elucidated.

The aim of this study was to investigate the changes in the gene expression of selected genes (CCL4, TGFBR3, CD69, MAP2K3, and IL-8) going through a series of three exposures to WBCT within three days and to analyse the association with patient reported outcomes.

Methods:
Twenty six patients with fibromyalgia (24 female/2 male, age 51.8±8.9 years (mean±SD) were included in the study and underwent 3 exposures to WBCT in a cryochamber system (Zimmer MedizinSysteme GmbH, Germany) with 3 chambers (10 seconds at -10°C, 10 seconds at -60°C and for a maximum of 3 minutes at -110°C) on 3 consecutive days. During the study patients did not change their medication. Patients were asked to complete a questionnaire of 11 questions (including pain, restlessness, physical function, and headache). Blood was collected immediately prior to (baseline) and directly after the first exposure to WBCT and after the third exposure using PAXgene RNA tubes. Total RNA was extracted with the PAXgene Blood RNA kit. Gene expression levels of MAP2K3, CCL4, TGFBR3, CD69, and IL-8 were analysed by real-time PCR.

Results:
All 26 patients tolerated the application of the WBCT well. The VAS pain reduced significantly from 6.0±0.3 at baseline to 4.1±0.3 after the third cold exposure (p<0.001). In 15 patients an improvement by at least 20% of the patient reported outcomes was found.

The gene expression levels of CCL4, CD69 and TGFbR3 decreased significantly (p<0.001, p<0.01, and p<0.05, resp.) In contrast, the expression of MAP2K3 was found to be significantly up-regulated (p<0.05). No significant change was observed regarding the IL-8 expression.

Changes of the expression levels were not found to be associated with improvements of VAS pain, headache, restlessness, or physical function.

Conclusion:
The results of our study indicate that the whole-body cryotherapy may cause subtle but significant changes in gene expression levels of CCL4, CD69, MAP2K3, and TGFbR3 in immune cells of peripheral blood. The MAP2K3 expression is known to be regulated by environmental stress, which is in accordance with the observed up-regulation of MAP2K3 expression. The down-regulation of the CD69, a marker for T-cell activation and the chemokine CCL4 that is produced by T-cells, indicate that the exposure to WBCT has an effect on peripheral T-cells. This effect seems to be independent from the patients’ response.

Further studies are necessary to elucidate the molecular mechanisms associated with the therapeutic effect of the WBCT.

Disclosure: S. Drynda, None; O. Mika, None; J. Kekow, None.
The Etiology of Fibromyalgia May be Related to Increased Muscle Pressure

Robert S. Katz1, Jessica L. Polyak2, Alexandra Katz Small3, Ben J Small4 and Frank Leavitt1, 1Rush University Medical Center, Chicago, IL, 2Rheumatology Associates S.C., Chicago, IL, 3University of Illinois College of Medicine, Chicago, IL, 4Rheumatology, University of Illinois at Chicago Medical School, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

The Etiology of Fibromyalgia May be Related to Increased Muscle Pressure

Background/Purpose: The muscles are tender in fibromyalgia syndrome (FMS) patients, and the location of pain is generally over the muscles, as seen in body diagrams shaded in by patients with fibromyalgia. Previous research also showed a reduced lordotic curve of the cervical spine on lateral-view radiographs, suggesting a muscular etiology and possible increased muscle tension. We measured muscle pressure directly in patients with FMS and controls.

Methods: Fibromyalgia patients meeting the 2010 ACR criteria for the diagnosis were evaluated using a pressure gauge attached to a No. 22 needle, and 0.3 cc of saline was injected into the mid portion of the trapezius muscle of patients with fibromyalgia, and also into normal controls. The pressure in mm Hg was determined using this device. In addition, patients and controls had dolorimetry testing and manual compression of the trapezius muscles to determine the amount of tenderness.

Results: 103 FMS patients were evaluated, 88 females and 15 males. The mean age was 52 y o for females and 47.5 y o for males. The mean dolorimetry score in the FMS patients was 8.1mmHg (0-30). The muscle pressure in fibromyalgia patients averaged 33mmHg (22-43). The mean pain scale on a 1-10 visual analog scale, with 10 being the worst, was 7 in these FMS patients. In 16 fibromyalgia patients with mild muscle tenderness, the mean dolorimetry reading was 11.8, mean muscle pressure reading was 28.7 mmHg, and the mean pain scale rating was 5. In the 52 FMS patients with moderate tenderness over the trapezius muscle, the mean dolorimetry reading was 7.9, the mean muscle pressure score was 33.9 mmHg, and the mean pain score was 6. In the FMS group with extreme muscle tenderness (30 patients with fibromyalgia), the mean dolorimetry score was 6.6, the mean muscle pressure reading was 35.5 mmHg, and the mean pain scale rating was 8. In the controls, 7 males and 18 females, the diagnoses included 15 with RA, 6 with SLE, and 4 healthy office personnel. The mean dolorimetry score in this group was 21.2 (0-30). The mean muscle pressure was 12.2 mmHg (8.0-18.0). The mean pain VAS scale score was 2. Mild muscle tenderness was noted in 1 patient.

Conclusion: Patients with fibromyalgia, compared to controls, have significantly increased intramuscular pressure. Muscles were also tender and dolorimetry scores were low indicating decreased tolerance for manually applied pressure. The amount of muscle tenderness correlated with the muscle pressure. The pain in fibromyalgia may be related to increased muscle pressure and tension. Fibromyalgia patients may be unconsciously tightening their muscles. Though pain centers in the brain light up quickly (central sensitization) in fibromyalgia patients when pressure is applied to the muscles, this finding may be due to increased muscle tenderness and elevated muscle pressure in fibromyalgia patients.

Disclosure: R. S. Katz, None; J. L. Polyak, None; A. Katz Small, None; B. J. Small, None; F. Leavitt, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-etiology-of-fibromyalgia-may-be-related-to-increased-muscle-pressure
Abstract Number: 1982

Leptin, a Hypothalamic Signaling Hormone, Is Elevated in Fibromyalgia Patients

Robert S. Katz, Rush University Medical Center, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Leptin, a 16 kDa protein, acts on receptors in brain neurons, especially in the hypothalamus. It could affect the hypothalamic-pituitary axis and be involved in the stress response. We analyzed leptin levels in the serum of patients with fibromyalgia and rheumatoid arthritis.

Methods: Leptin levels were assessed in 27 fibromyalgia syndrome patients and six rheumatoid arthritis patients followed in a rheumatology office practice. Leptin was measured by the University of Miami Immunology Laboratory.

Results: Leptin levels varied between 1.7 and 70.7 ng/ml (mean 28.0) in FMS patients and 0.6 to 33.0 ng/ml (mean 10.1) in rheumatoid arthritis patients. The mean leptin/BMI ratio for 20 FMS pts was 1.0. The mean leptin/BMI for RA was 0.50.

Conclusion: Leptin levels appear to be elevated in fibromyalgia patients and could provide a link between chronic stress, the hypothalamic-pituitary axis, and fibromyalgia. Leptin might be a potential therapeutic target in fibromyalgia.

Disclosure: R. S. Katz, None;

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/leptin-a-hypothalamic-signaling-hormone-is-elevated-in-fibromyalgia-patients

Abstract Number: 1983

The Types of Stress That Appear to Aggravate the Symptoms of Fibromyalgia

Robert S. Katz, Rush University Medical Center, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The types of stresses evaluated include financial stress (i.e., decreased income, unexpected expenses or outgoings); employment stress (i.e. job promotion, relocation, increased workload or travel, etc.); family/spouse stress (i.e. medical illness or addiction, unemployment); psychological/emotional stress (i.e. death of a loved one, divorce); physical stress (i.e. motor vehicle accident, pregnancy/childbirth, personal medical illness), and patients were asked if they had no obvious stress at the time of flare-ups or at the onset of their symptoms.

Methods: Patients with fibromyalgia and rheumatic disease controls filled out a questionnaire, including questions regarding the type of stress they experienced and its effect on their pain. Financial stress, employment stress, Family/spouse stress, psychological/emotional stress, physical stress was all listed as possible stresses that have an effect on the patient’s pain.

Results: Fibromyalgia patients meeting the 2011 ACR criteria for the diagnosis and non-FMS rheumatic disease controls filled out a questionnaire on the types of stresses affecting their pain. The questionnaire used a 1-10 visual analog scale (VAS- 0-10; 10= an extreme effect on pain).

Family Stress- 98 FMS patients, the mean VAS score was 5.1; In 161 controls, the mean VAS was 4.3 (P>.03)
Financial Stress- 100 FMS patients, the mean VAS score was 4.3; In 161 controls, the mean VAS was 3.7. (n/s)
Job Stress- 88 FMS patients, the mean VAS score 5.5; In 149 control patients the mean VAS was 4.2. (P>.002)
Health Stress- 97 FMS patients, the mean VAS score was 6.9; In 162 controls, the mean VAS score was 5.0. (P>.001)
Marital Stress- 88 FMS patients, the mean VAS score was 3.0; In 145 controls, the mean VAS score was 2.7. (n/s)

Conclusion: Reduction of stress should be an important goal especially for fibromyalgia patients. These patients appear to have a more
significant effect on their illness due to stress. It seems that all types of stress—financial, job, emotional, health issues, physical, and family/marital stress—have a greater effect on the pain in fibromyalgia than in rheumatic disease controls. Participation by psychologists and psychiatrists in the treatment of the patient’s stress may be important. And the rheumatologist, primary care physician, and office nurse may also help with stress reduction techniques and medications. Interdisciplinary programs may be helpful for some patients and these may include cognitive behavioral therapy, biofeedback, individual therapy, massage, meditation and other relaxation therapies, and yoga.

Disclosure: R. S. Katz, None;

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-types-of-stress-that-appear-to-aggravate-the-symptoms-of-fibromyalgia

Abstract Number: 1984

The Cervical Spine in Fibromyalgia Patients: Loss of Lordotic Curve Is Characteristic of Fibromyalgia and Can Assist in the Diagnosis

Robert S. Katz¹, Alexandra Katz Small², Ben J Small³ and Anthony Farkasch⁴, ¹Rush University Medical Center, Chicago, IL, ²University of Illinois College of Medicine, Chicago, IL, ³Rheumatology, University of Illinois at Chicago Medical School, Chicago, IL, ⁴Rheumatology Associates S.C., Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Patients with fibromyalgia have widespread pain. We have found that a lateral view of a cervical spine radiograph frequently identifies a loss of the lordotic curve but otherwise normal architecture. We asked rheumatology nurse professionals to evaluate visually whether the cervical spine was straight on the lateral view in fibromyalgia and non-fibromyalgia rheumatic disease patients.

Methods: 121 cervical spine radiographs were reviewed by a rheumatology nurse without knowledge of the patient’s diagnosis. Only the lateral view of the cervical spine was visualized to determine whether it was straight. A straight cervical spine is seen in fibromyalgia patients and may assist in the diagnosis. Other abnormalities of the cervical spine including disc space narrowing, osteophytes, spondylolisthesis, and reactive bony changes were also noted if present.

Results: Of the 121 cervical spine radiographs reviewed the rheumatology nurse, there were 84 patients with fibromyalgia, and 37 non-fibromyalgia rheumatic disease controls. Without being told the patients diagnosis, the nurse was able to correctly diagnosis 66 (75.5%) of the 84 fibromyalgia patients, and was able to accurately say that 29) of the control patients did not in fact have fibromyalgia.
Conclusion: A straight cervical spine can be used to assist in the diagnosis of fibromyalgia. The loss of lordotic curve without other radiographic abnormalities (disc space narrowing, reactive bony changes, etc.) is present in the majority of fibromyalgia patients and not in the non-fibromyalgia rheumatic disease patients. A straight cervical spine is further evidence of increased muscle tension in fibromyalgia.

Disclosure: R. S. Katz, None; A. Katz Small, None; B. J. Small, None; A. Farkasch, None.


Abstract Number: 1985

Cervical Spine Radiographs in Fibromyalgia Patients Show Reduced Cobb Angle and Suggest the Presence of Increased Muscle Pressure As a Cause of the Illness

Robert S. Katz1, Ben J Small2, Alexandra Katz Small3 and Anthony Farkasch4, 1Rush University Medical Center, Chicago, IL, 2Rheumatology, University of Illinois at Chicago Medical School, Chicago, IL, 3University of Illinois College of Medicine, Chicago, IL, 4Rheumatology Associates S.C., Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Fibromyalgia patients are reported to have a straight neck on lateral x-ray views of the cervical spine. We measured the Cobb angle in fibromyalgia and non-fibromyalgia rheumatic disease patients in a rheumatology office practice.

Methods: The Cobb angle between the bottom of C2 and the top of C7 was measured in rheumatic disease patients without knowledge of the diagnosis.

Results: 121 patients, (84 fibromyalgia with a mean age of 45.3 and 37 non-fibromyalgia rheumatic disease controls with a mean age of 52.7), had radiographs of their cervical spine, which the Cobb angle was measured. We found that the cervical spine becomes noted as a “straight neck” at the 7° mark and below. There were 50 FMS and 13 controls with a cervical Cobb of 7° or below. Between 8° and 10° is where the cervical spine “straightness” becomes more prominent; there were 10 FMS and 1 control with a Cobb between 8° and 10°. There were 24 FMS and 23 control patients with a cervical Cobb angle of 11° or higher.
Conclusion: The Cobb angle between C2 and C7 was less than 10 degrees in fibromyalgia patients and greater than 10 degrees in rheumatic disease patients without fibromyalgia. The straight neck is present in fibromyalgia and may assist in the diagnosis. The cutoff point of 10 degrees may help to determine the presence of a significant loss of lordotic curve in future studies of fibromyalgia.

Disclosure: R. S. Katz, None; B. J. Small, None; A. Katz Small, None; A. Farkasch, None.


Abstract Number: 1986

Using the BILAG to Assess the Activity of Lupus in Patients with Fibromyalgia

Robert S. Katz1, Jessica L. Polyak2 and Frank Leavitt1, 1Rush University Medical Center, Chicago, IL, 2Rheumatology Associates S.C., Chicago, IL
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The BILAG is often used to assess the efficacy of lupus treatments, and is a commonly used tool in lupus drug trials. But the BILAG contains many symptoms, which are also present in fibromyalgia, and the presence of concomitant fibromyalgia in lupus patients may nullify the results of clinical drug trials. Fibromyalgia patients may not respond well to the treatment and also have more drug side effects.

Methods: Fibromyalgia patients, meeting the 2011 ACR criteria for the diagnosis, took an in-office survey listing some of the British Isles Lupus Activity Group (BILAG) lupus symptoms. The symptoms asked of fibromyalgia and non-fibromyalgia patients included anemia; mouth or nasal sources; numbness and tingling; persistent headache; chest pain; skin rash; hair loss; cognitive changes; arthritis; and colitis. They were asked to score the above symptoms using the following scale: 1, improving; 2, same; 3, worse; and 4, new.

Results: The following symptoms frequently represented by fibromyalgia patients and are among those that are part of BILAG Lupus Activity Index: Anemia, Headache, Rash, “Arthritis”, Oral Ulcers, Chest Pain, Hair Loss, Colitis, Numbness, and Cognitive
**Conclusion:** Many fibromyalgia patients reported that certain symptoms that are listed in the BILAG were present including mouth and oral ulcers; hair loss; numbness and tingling; cognitive changes; headaches; arthritis; and chest pain.

Concomitant lupus and fibromyalgia can nullify the results of lupus clinical drug trials and interfere with the accurate assessment of lupus. Many fibromyalgia patients report some of the symptoms listed in the BILAG, which is considered a reliable instrument for assessing lupus disease activity, but if the presence of concomitant fibromyalgia is not assessed, the results of the BILAG may be invalid. Using the 2010 ACR criteria guidelines and a simple one-page form for assessing the presence of fibromyalgia, concomitant fibromyalgia can be determined in lupus patients. This would make the BILAG a more accurate assessment tool if used for pure lupus.

**Disclosure:** R. S. Katz, None; J. L. Polyak, None; F. Leavitt, None.


**Abstract Number:** 1987

**Exercise in Fibromyalgia Patients**

**Robert S. Katz**¹, Jessica L. Polyak² and Frank Leavitt¹, ¹Rush University Medical Center, Chicago, IL, ²Rheumatology Associates S.C., Chicago, IL

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes Poster II

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** It has been reported that aerobic exercise may be beneficial for fibromyalgia patients. Stamina and energy, sense of well-being, and increased mental relaxation can be achieved with an exercise program. We asked fibromyalgia patients whether exercise had a beneficial effect on their illness.

**Methods:** An office questionnaire was given to rheumatic disease patients in a rheumatology office practice. The patients were asked about the effect of aerobic exercise, muscle strengthening exercise, stretching, and yoga and whether they made their symptoms better or worse and whether it affected their level of pain.

The patients were divided into Fibromyalgia Syndrome (FMS) patients and non-FMS rheumatic disease controls.

**Results:** 78 FMS patients and 167 non-FMS rheumatic disease pts were compared. The mean number of days which 78 Fibromyalgia Syndrome patients reported exercising was 3.4, compared to 3.6 days for non-FMS rheumatic disease controls (n/s). The time devoted by FMS patients per exercise session was 32.6 min, compared to 44.7 min for controls (P <.001)

Using a 0-10 visual analogue scale with 10 being the worst score (makes pain much worse), fibromyalgia patients reported a mean of 7.0 for aerobic exercise, where controls reported a mean of 4.3 (P <.001). The mean for muscle strengthening for FMS was 5.4, and
controls 4.2 (P<.001). Stretching exercises, mean for FMS patients was 4.1, compared to 3.1 for non-FMS patients (P<.001). Yoga exercises seemed to be preferred among fibromyalgia patients, the mean was 4.0, controls 3.5 (n/s).

Fibromyalgia patients exercise approximately the same number of days as non-FMS rheumatic disease patients. Aerobic and also muscle strengthening and stretching exercises were found to make FMS patients’ symptoms worse. There was no significant difference between groups for yoga.

![Image of a table showing exercise days and mean values]

**Conclusion:** Assuming one objective is to get FMS patients to do aerobic exercise on a regular basis, the exercises would need to be modified in a way that patients are able to perform them without a significant increase in symptoms. We initiated a program in which patients are asked to do 10 minutes of aerobic exercise (huffing and puffing) daily on a stationary bike. Preliminary anecdotal observations suggest that patients exercising daily on the stationary bike, appear to be doing better.

If the studies are correct that regular aerobic exercise may benefit fibromyalgia, the fact that these patients tend to feel worse is an obstacle. It is interesting that yoga, a relaxation technique, was more helpful than other forms of exercise evaluated.

Whether achievable aerobic exercise, such as 10 minutes on a stationary bike daily, or a focus on relaxing activities such as yoga will have a greater positive effect on the symptoms of fibromyalgia, is unclear, but more research needs to be done to help fibromyalgia patients overcome the levels of fatigue and pain and poor general function in order to try regular, brief exercise.

**Disclosure:** R. S. Katz, None; J. L. Polyak, None; F. Leavitt, None.

**View Abstract and Citation Information Online** - [http://acrabstracts.org/abstract/exercise-in-fibromyalgia-patients](http://acrabstracts.org/abstract/exercise-in-fibromyalgia-patients)

**Abstract Number:** 1988

**Most Fibromyalgia Patients in a Rheumatology Office Practice Accept the Diagnosis of Fibromyalgia**

Robert S. Katz1, Jessica L. Polyak2 and Frank Leavitt1, 1Rush University Medical Center, Chicago, IL, 2Rheumatology Associates S.C., Chicago, IL

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** ARHP Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** In the community, many comments are made about fibromyalgia that are not accurate, such as, it is a made-up illness; a ‘garbage’ diagnosis; everything else needs to be excluded to diagnose someone with fibromyalgia; it is an unscientific term; or it is a name used for autoimmune conditions, such as lupus, when the doctor is uncertain. We asked patients with fibromyalgia in a rheumatology office practice what they thought when they were given the diagnosis of fibromyalgia by a rheumatologist.
Methods: 37 patients with clinically diagnosed fibromyalgia were given an in-office questionnaire. The questions included whether fibromyalgia was a diagnosis that made them feel good and that the doctor understood that was the cause of their symptoms; whether they felt that the diagnosis was not accurate; whether they felt that fibromyalgia is a made-up, unscientific term; whether they felt that they really had lupus or some other disorder; and whether they felt that fibromyalgia was not a real diagnosis.

Results: Patients generally accept the diagnosis of fibromyalgia but are concerned that physicians and non-physicians may think that it is “all in their heads”. See table.

<table>
<thead>
<tr>
<th>Questions</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>What do you think when you received it?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A. Felt good about diagnosis was made.</td>
<td>3</td>
<td>25</td>
</tr>
<tr>
<td>B. Felt that this is not my true diagnosis.</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>C. Felt that fibromyalgia is a made-up diag.</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>D. Felt that I really have Lupus or some other disorder</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>E. Felt that fibromyalgia is not a real diag.</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>I don't like the diagnosis of fibromyalgia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A. Doctors and other think it's all &quot;in your head&quot;</td>
<td>2</td>
<td>16</td>
</tr>
<tr>
<td>B. It's not a real diagnosis</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>C. It's a diagnosis used when everything else is ruled out</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>D. Other</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>I do like and accept the diagnosis of fibromyalgia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A. It could have been a life threatening condition</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>B. I am glad to have gotten a diagnosis</td>
<td>2</td>
<td>16</td>
</tr>
<tr>
<td>C. I know that it is not a progressive or crippling</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>D. Other</td>
<td>0</td>
<td>6</td>
</tr>
</tbody>
</table>

Conclusion: The great majority of fibromyalgia patients in a rheumatology office practice felt good that a diagnosis was made to explain their symptoms. Only a minority thought that the diagnosis was either inaccurate or that the term “fibromyalgia” was an unscientific one and not a real diagnosis.

The biggest problem accepting the diagnosis is that many patients think that doctors and others feel that the symptoms are ‘all in your head’.

The word is spreading about fibromyalgia, such that many patients now accept the diagnosis and feel more comfortable that something more serious and progressive is not present. Though fibromyalgia can be challenging to treat, at least in a rheumatology office practice patients do feel more comfortable given that diagnosis.

A few patients will push back, and these can be a source of stress for the patient and for medical practitioners. The ACR 2010 guidelines for the diagnosis, which can be summarized in a one-page sheet that the patient and practitioner fill out, can assist in verifying the diagnosis. Through scientific research, and also advertising FDA approved drugs to patients, the diagnosis of fibromyalgia appears to be generally accepted.

Disclosure: R. S. Katz, None; J. L. Polyak, None; F. Leavitt, None.


Abstract Number: 1989

**Improving Sleep in Fibromyalgia Patients Ameliorates Their Pain**

Robert S. Katz, Rush University Medical Center, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017

Session Title: ARHP Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes

Session Type: ACR Poster Session C

Session Time: 9:00AM-11:00AM
**Background/Purpose:** Fibromyalgia patients complain of poor sleep. We assessed whether patients with fibromyalgia who were able to significantly improve their sleep, including sleeping uninterrupted through the night, had less pain. It is possible that solid rest at night can lead to muscle relaxation and central nervous system rest and result in improvement in fibromyalgia symptoms.

**Methods:** 37 patients were given the opportunity to participate in this rheumatology office trial. Patients with diagnosed fibromyalgia according to the 2010 ACR criteria who had poor sleep were given amitriptyline, doxepin, or trazodone in gradually increasing dosages, enough for them to sleep through the night. Those who completed at least two weeks of medication therapy in doses enough to make them sleep well were further evaluated for a response in terms of pain level and fatigue.

**Results:** See graph below

<table>
<thead>
<tr>
<th>Medication</th>
<th># of patients taking</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline</td>
<td>22 (19.4%)</td>
</tr>
<tr>
<td>Doxepin</td>
<td>9 (24.3%)</td>
</tr>
<tr>
<td>Trazodone</td>
<td>6 (16.3%)</td>
</tr>
</tbody>
</table>

**Conclusion:** In this open label, uncontrolled study, we found that many patients who are able to sleep through the night by using amitriptyline, doxepin, or trazodone had an improvement in pain and global scores for Fibromyalgia. Starting with low dosage given early in the evening, generally 7 PM, and titrating upward until uninterrupted sleep was achieved. Good sustained sleep maybe therapeutic in this illness, but to achieve that may require a significant step-wise increase in these medications until uninterrupted sleep is achieved.

**Disclosure:** R. S. Katz, None;

*View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/improving-sleep-in-fibromyalgia-patients-ameliorates-their-pain-2](http://acrabstracts.org/abstract/improving-sleep-in-fibromyalgia-patients-ameliorates-their-pain-2)*

**Abstract Number:** 1990

**Effectiveness and Durability of a Brief Multidisciplinary Treatment Program for Patients with Fibromyalgia**

**Jessica Gehin**1, Andy Abril2, Fernando Rivera3, Benjamin Wang4, Ronald Butendieck2, Florentina Berianu2, Kenneth Calamia2, Madeleine Allman1, Isabel Abril1 and Barbara Bruce1,1Department of Psychiatry and Psychology, Mayo Clinic Florida, Jacksonville, FL,2Division of Rheumatology, Mayo Clinic Florida, Jacksonville, FL, 3Division of Consultative and Diagnostic Medicine, Mayo Clinic Florida, Jacksonville, FL, 4Rheumatology, Mayo Clinic Florida, Jacksonville, FL

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** ARHP Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Fibromyalgia (FM) effects upwards of 60 million adults in the US alone. The disability and psychological distress often observed in these patients has been documented. Despite a recent update of diagnostic criteria for FM by the American College of Rheumatology (ACR) and the availability of demonstrated effective interventions for the treatment of FM, patients continue to be misunderstood, misdiagnosed and often left untreated. The purpose of this study is to examine the effectiveness and durability of a brief multidisciplinary intervention for patients with FM provided in a tertiary care setting in improving functioning and psychological distress.

**Methods:** Four hundred and twenty two (422) patients who participated in the Fibromyalgia Treatment Program between August 2015 and August 2016 were subjects in this study. The patients in the study were referred to a tertiary medical center for evaluation of fibromyalgia symptoms and were subsequently diagnosed with FM by meeting the 2010 ACR criteria. The patients were then enrolled
in a 2-day multidisciplinary treatment program. Patients completed the Fibromyalgia Impact Questionnaire – Revised (FIQR), the Center for Epidemiological Studies of Depression Scale (CES-D), and the Pain Catastrophizing Scale (PCS) at the time of admission to the program and at 3-month and 6-month follow-up. The treatment program targeted Cognitive Behavioral Therapy (CBT) skills of evidence-based education regarding FM, chronic fatigue and central sensitization in addition to activity pacing, exercise, relaxation strategies, sleep hygiene, and moderation.

Results: The average age of patients was 48 years with a range of 19-79. The majority was female (90%). Duration of fibromyalgia symptoms on average was 10 years at the time of referral. At the time of admission to the program, patients were functionally impaired and psychologically distressed. The FIQR results on admission showed an average score of 60.0 which is in the severe level of impairment range. The average CES-D score on admission was 25.4 suggesting significant depression. The PCS scores on admission were on average 25 suggesting elevated levels of pain catastrophizing. At 3-month follow-up, the scores on all three measures were significantly decreased and the improvement observed across all scores were maintained or further improved at 6 month follow-up.

Conclusion: A brief multidisciplinary treatment program for patients with Fibromyalgia appears to be effective at decreasing functional impairment and psychological distress and the improvements are maintained or further improved at 3 and 6 month follow-up.

Disclosure: J. Gehin, None; A. Abril, None; F. Rivera, None; B. Wang, None; R. Butendieck, None; F. Berianu, None; K. Calamia, None; M. Allman, None; I. Abril, None; B. Bruce, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/effectiveness-and-durability-of-a-brief-multidisciplinary-treatment-program-for-patients-with-fibromyalgia

Abstract Number: 1991

Fibromyalgia in Russian Refugees: Translation and Validation of the Revised Symptom Impact Questionnaire

Kim Jones1, Robert M. Bennett1, Ronald Friend2 and Neema Mohammad Nader2, 1Schools of Nursing and Medicine, Oregon Health & Science University, Portland, OR, 2School of Nursing, Oregon Health & Science University, Portland, OR
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: ARHP Fibromyalgia, Soft Tissue Disorders, Regional and Specific Clinical Pain Syndromes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
The Revised Symptom Impact Questionnaire (SIQR) is an updated version of the Revised Fibromyalgia Impact Questionnaire (FIQR) that can be used in both fibromyalgia and non-fibromyalgia patients (FM). The SIQR has been translated into 8 other languages but no Russian version is currently available, even though Russian asylum seekers are the fast-growing segment of North America. Unrelenting stress endured by refugees and immigrants put them at increased risk for multiple health related problems, including FM. However, no tool currently exists to monitor FM in Russian speakers of the former Soviet bloc. This project describes the process of creating a culturally appropriate scale to assess FM severity in Russian speaking people.

Methods:
We used the Mapi Research Trust process to translate a validated questionnaire to Russian. The SIQR is a 21-item scale consisting of 3 subscales which assess physical functioning, common symptoms experienced in fibromyalgia, and global impact. The process of translation and validation of the SIQR involved: conceptual analysis of source questionnaire, forward/backward translation, committee review, pretesting, and revision.

Results:
The author (NMN) and 2 Russian interpreters translated the English version of the SIQR. A certified translator with formal education in the Russia Federation evaluated the translation. These 3 bilingual individuals back-translated the questionnaire. Committee review of the back translation was done by the original developers (RMB, RF & KDJ). 12 Russian speakers completed the pretest questionnaire. As expected, there were some challenges creating equivalent questionnaire items, mostly involving the physical function items. For example, some subjects endorsed the words “ходить в магазин” (go to a store), while others preferred “ходить за покупками” (go
Changes in Clinical Disease Activity Are Associated with Changes in the Total MRI Inflammation Score in Rheumatoid Arthritis Patients Who Are Escalating Therapy in a Treat-to-Target (T2T) Regimen

Fiona M. McQueen¹, Peter T. Chapman², Terina Pollock³, Dena D'Souza⁴, Arier Lee⁵, Nicola Dalbeth⁶, Lisa K. Stamp⁷, Karen Lindsay⁸ and Anthony Doyle³,⁹, ¹Molecular Medicine, Univ of Auckland Sch of Med, Auckland, New Zealand, ²Christchurch Hospital, Christchurch, New Zealand, ³Radiology, Auckland District Health Board, Auckland, New Zealand, ⁴Rheumatology, University of Auckland, Auckland, New Zealand, ⁵Biostatistics and Epidemiology, University of Auckland, Auckland, New Zealand, ⁶University of Auckland, Auckland, New Zealand, ⁷University of Otago, Christchurch, New Zealand, ⁸Rheumatology, Auckland District Health Board, Auckland, New Zealand, ⁹Anatomy with Radiology, University of Auckland, Auckland, New Zealand

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Imaging of Rheumatic Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
RA patients are managed using treat-to-target (T2T) regimens often utilizing the DAS28CRP as an outcome measure. In this study we compared clinical changes in RA disease activity with changes in MRI inflammation on T2T escalation.

Methods:
80 seropositive rheumatoid arthritis (RA) patients on conventional disease-modifying anti-rheumatic drugs (cDMARDs) were enrolled if they had DAS28CRP > 3.2: Group A escalated to another cDMARD combination, Group B to anti-TNF therapy/cDMARDs. Contrast-enhanced 3T-MRI wrist scans were obtained before (V1) and 4 months after (V2) regimen change. Scan pairs were scored by one experienced radiologist reader for synovitis, osteitis and tenosynovitis, summed as MRI inflammation (MRI(i)) score, plus erosions. Associations between DAS28CRP and MRI(i) were investigated.

Results:
58 patients were enrolled in Group A (42 female, 16 male) and 22 in Group B (18, 4). 66 scan pairs were available for analysis including 8 pairs from 4 patients who were sequentially enrolled into Group A then Group B. Intra-reader reliability was high: ICC(average) 0.89 (0.56 - 0.97). DAS28CRP and disease duration (months) were lower in Group A than B: 4.22 vs 5.16 (p = 0.001) and 30 vs 77 (p = 0.01). Change in DAS28CRP (median (range)) Group A: -0.92 (-3.30, 1.61), Group B: -1.38 (-3.59, 0.26) (p = 0.31). Change in MRI(i) Group A, 0 (-25, 7) and Group B, 0 (-7, 28) (p =0.37). Combining groups, change in MRI(i) correlated with change in DAS28CRP (Spearman's ρ = 0.36, P = 0.003). Using multiple linear regression analysis adjusting for age, gender, duration, anti-CCP titer and MRI erosion score (V1), change in DAS28CRP was associated with change in MRI(i) so that for every unit increase in change in DAS28CRP there was a 1.83U increase in change in MRI(i), p = 0.052. The components of MRI(i) were analyzed and only MRI tendonitis correlated with change in DAS28CRP (Spearman's ρ = 0.33, P = 0.007). There was no significant difference between groups for change in MRI(i) although the fall in score was numerically greater for Group A (- 3.61) than Group B (- 0.73) , p = 0.18. Change in MRI(i) was associated with the MRI erosion score (V1) (p = 0.0054).
Conclusion:
We report the first study investigating the link between clinical and imaging inflammation on T2T escalation in a real world RA cohort. The association was surprisingly weak, especially in those escalating to anti-TNFs where chronic inflammation associated with longer disease duration may have been less amenable to intervention. Given the efficacy of T2T regimens using clinical targets, the use of MRI targets cannot be advocated as yet. Further studies are needed to investigate the long-term implications of persisting MRI inflammation in clinically normal joints.

Figure 1. Change in MRI inflammation score vs change in DAS28CRP on T2T escalation on therapy in Group A and Group B

Disclosure: F. M. McQueen, None; P. T. Chapman, None; T. Pollock, None; D. D'Souza, None; A. Lee, None; N. Dalbeth, Abbott Laboratories, 8; L. K. Stamp, None; K. Lindsay, None; A. Doyle, None.


Abstract Number: 1993

Are MRI-Detected Erosions Specific for RA? a Large Explorative Cross-Sectional Study

Debbie M. Boeters1, Wouter P. Nieuwenhuis1, Hanna W van Steenbergen1, M. Reijnierse2, Robert B.M. Landewé3 and Annette H.M. van der Helm-van Mil1, 1Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, 2Department of Radiology, Leiden University Medical Center, Leiden, Netherlands, 3University of Amsterdam and Atrium Medical Center, Amsterdam, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Imaging of Rheumatic Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Magnetic resonance imaging (MRI) is recommended in the diagnostic process of rheumatoid arthritis (RA), as it can detect joint damage early. However MRI-detected erosions are also present in symptom-free controls, especially at older age. It is unclear how RA-specific erosions on MRI can be distinguished from physiological erosions in symptom-free individuals. Therefore this study compared MRI-detected erosions between RA-patients and healthy controls, including evaluation of the effect of age.

Methods: 589 newly-presenting early arthritis patients (284 RA, 305 other arthritides) and 193 symptom-free controls underwent contrast-enhanced MRI of unilateral metacarpophalangeal(MCP)- and metatarsophalangeal(MTP)-joints. Total erosion score according to the RAMRIS method, number, severity, location of erosions and simultaneous presence of MRI-detected inflammation (synovitis and/or bone marrow edema) were compared between groups; participants were categorized in three age-groups (<40, 40-59, ≥60).

Results: RA-patients had higher total erosion scores than controls but there was large overlap of MRI-erosion scores between RA-patients and controls, as visually no separate clustering of groups was observed (Figure). Severe erosions (grade≥2) and MTP5-erosions were specific for RA (specificity 98-100% and 90-98% for different age-groups). MTP1-erosions were only specific if aged<40
(specificity 98%) and erosions with inflammation if aged<60 (specificity 91-100%). ≥1 of the mentioned erosions characteristics were present in 28% of RA-patients. Comparing RA-patients with other arthritides revealed that severe erosions and MTP5-erosions remained specific for RA (specificity ≥90%) as well as MTP1-erosions if aged<40 (specificity 92%), in contrast to erosions combined with inflammation (specificity 49-86%).

**Conclusion:** Whilst RA-patients at disease presentation had significantly higher erosion-scores than controls, scores of individuals were largely overlapping. Erosion characteristics specific for RA were identified, but were present in a minority of RA-patients.

![Figure: Predicted probabilities of having RA (probability of 0 indicates 0% chance of having RA and probability of 1 indicates 100% chance of having RA), obtained from logistic regression. The total MRI-detected erosion score was used to predict whether a patient had RA.](image)

**Disclosure:** D. M. Boeters, None; W. P. Nieuwenhuis, None; H. W. van Steenbergen, None; M. Reijnierse, None; R. B. M. Landewé, None; A. H. M. van der Helm-van Mil, None.

**Abstract Number:** 1994

**Erosion Depth Predicts Erosion Progression in Patients with Early RA: A Longitudinal Analysis Using HR-pQCT**

**Jiang YUE**¹, James F Griffith², Fan XIAO³, Jiankun XU⁴, Ling Qin⁵ and Lai-Shan Tam⁶, ¹Department of Medicine & Therapeutics, The Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong, Hong Kong, ²Department of Imaging and Interventional Radiology, The Prince of Wales Hospital, The Chinese University of Hong Kong, HONGKONG, Hong Kong, ³Department of Imaging and Interventional Radiology, The Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong, Hong Kong, ⁴Department of Orthopedics & Traumatology, The Chinese University of Hong Kong, Hong Kong, Hong Kong, ⁵Bone Quality and Health Centre of the Department of Orthopaedics and Traumatology, The Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong, Hong Kong, ⁶Department of Medicine & Therapeutics, The Chinese University of Hong Kong, Hong Kong, China.

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Tuesday, November 7, 2017
**Session Title:** Imaging of Rheumatic Diseases Poster II
**Session Type:** ACR Poster Session C
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

---

1. **Disclosures**: Information is not provided for this section.
To ascertain the predictors of erosion progression in patients with early RA using high-resolution peripheral quantitative computed tomography (HR-pQCT).

**Methods:**

In this prospective study, 80 ERA patients were treated with a tight-control protocol aiming at remission using csDMARDs. HR-pQCT examinations were performed at baseline and after one year post-baseline. Erosion number and volume and the bone density of the surrounding bone were quantified. Erosion progression was defined as an erosion showing both (a) an increase in erosion volume exceeding the smallest detectable change (SDC) and (b) a decrease in bone density surrounding the erosion exceeding the SDC.

**Results:**

45% ERA patients showed erosion progression. Logistic regression analysis showed that greater erosion depth (p=0.043) and higher damage joint count (p=0.035) at baseline were independent predictors of erosion progression at 12 months. Erosion depth discriminated ERA patients with erosion progression from those without progression with an area under receiver operating characteristic curve of 0.798 (95% CI: [0.650, 0.946]; p =0.002). An erosion depth at baseline of ≥1.225 mm predicted erosion progression with a sensitivity of 81.3%, specificity of 71.4% and a Youden index of 0.527.

**Conclusion:**

Erosion depth at baseline is an indicator of erosion progression in ERA patients treated with csDMARDs. Deeper erosions are more likely to progress than shallower erosions.

**Disclosure:** J. YUE, None; J. F. Griffith, None; F. XIAO, None; J. XU, None; L. Qin, None; L. S. Tam, None.


**Abstract Number:** 1995

**Analysis of Erosion Volume of the Distal Radius By HR-pQCT in Patients with Rheumatoid Arthritis**

**Ko Chiba**1, Naoki Iwamoto2, Makoto Osaki1 and Atsushi Kawakami2, 1Department of Orthopedic Surgery, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, 2Department of Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** Imaging of Rheumatic Diseases Poster II  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

HR-pQCT is a high resolution CT dedicated to human extremities. It has been used mainly for osteoporosis, while in more recent years it has been applied to research in rheumatoid arthritis (RA).

The purpose of this study is to develop a method to quantify the erosion volume of distal radius in patients with RA semiautomatically using second generation HR-pQCT.

**Methods:**

Ten patients with RA (ave. 66 years, 7 female, 3 male) participated in this study. The wrist joint was scanned using HR-pQCT (XtremeCT II, Scanco Medical, Switzerland) at the voxel size of 61 um.

The erosion volume was measured semiautomatically using the dedicated software (TRI/3D-BON, Ratoc System Engineering, Tokyo).
All concave regions on the bone surface around the distal radius were extracted automatically by subtracting the bone region from the smoothed bone model. Erosions were selected manually by a medical doctor based on certain criteria. The volume of the erosions were measured by voxel counting.

Results:

16 erosions were detected by HR-pQCT, mainly located on the palmar side of the distal radius (palmar: 12, dorsal: 3, radial: 1). The average volume of the erosions was 5.5 mm$^3$, minimum 0.3 mm$^3$, and maximum 20.0 mm$^3$.

Conclusion:

The semiautomatic method to quantify the erosion volume of distal radius in RA patients by HR-pQCT was developed. The opinion as to whether concave regions are pathological erosion or physiological concave, vascular channel or recess of osteophyte is difficult and should be performed by an experienced tester.
Changes in Cartilage Matrix Measured By MR T1ρ Are Correlated with Changes in Bone Erosion Volume Measured By HR-pQCT Three Months after MTX and Anti-TNF Treatment in Patients with Rheumatoid Arthritis: A Multi-Modality Imaging Study

Tomohiro Shimizu1,2,3, Kenji Mamoto1, Ursula Heilmeier1, Matthew Tanaka1, Andrew J Burghardt1, Thomas Link1, Jonathan Graf4, John B. Imboden Jr.5 and Xiaojuan Li6, 1Department of Radiology & Biomedical Imaging, Musculoskeletal Quantitative Imaging Research, University of California, San Francisco, San Francisco, CA, 2Department of Orthopaedic Surgery, University of California, San Francisco, San Francisco, CA, 3Department of Orthopaedic Surgery, Hokkaido University, Sapporo, Japan, 4Department of Medicine, Division of Rheumatology Zuckerber San Francisco General Hospital, University of California, San Francisco, San Francisco, CA, 5Medicine, University of California, San Francisco, San Francisco, CA, 6Radiology & Biomedical Imaging, Department of Radiology and Biomedical Imaging, University of California San Francisco, San Francisco, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Imaging of Rheumatic Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: MR-based T1rho relaxation time mapping allows non-invasive quantification of early cartilage deterioration, while high-resolution peripheral quantitative computed tomography (HR-pQCT) can detect early changes in bone erosion volume. It is unknown whether changes of cartilage T1ρ values are associated with concomitant bone erosion changes and reflect treatment response. Therefore, we used 3T MRI and HR-pQCT to investigate the changes of bone and cartilage damage in RA patients receiving methotrexate (MTX) and anti-tumor necrosis factor alpha (TNFa) therapy.

Methods: Twenty RA patients receiving MTX treatment were recruited into either a low DAS group (n=9, DAS28≤3.2) or a high DAS group (n=11, DAS28>3.2). At baseline, the high DAS group initiated supplemental anti-TNFα treatment in addition to ongoing MTX. All patients underwent MRI wrist scans and HR-pQCT scans of the MCP and wrist at BL and after 3 months (3M). DAS28 CRP was assessed at BL and 3M. Lunar, scaphoid and radius and global cartilage T1rho values were measured. HR-pQCT-derived erosion volume at lunate, radius, scaphoid, MCP2 and MCP3 were semi-quantitatively measured. Longitudinal changes and associations were evaluated either via paired t-test or Pearson’s correlations.

Results: Anti-TNFα therapy in the high-DAS group resulted in a significant decrease of DAS28 CRP score (p<0.001), which was accompanied by decreases in mean T1f/I values (reached significance in scaphoid T1rho, P=0.031) and erosion volumes (reached significance in MCP3 and global) at all measurement sites (Table.1). The low DAS group in contrast, displayed an increasing trend in T1ρ values and erosion volumes (reached significance in radius and global) despite low disease activity (Table.1) Changes in T1ρ values and bone erosion volume were significantly positively correlated, and both were significantly correlated with changes in DAS28 CRP score (Figure 1).

Conclusion: Anti-TNFα therapy seems to simultaneously prevent bone and cartilage from further destruction and might even partially repair preexisting cartilage deterioration and bone erosions within first 3 months of therapy as indicated by our observed decrease in T1ρ values and erosion volumes in our cohort. Our observation that early changes in cartilage T1ρ values are associated with changes in clinical disease activity and erosion volume, recommends a more extensive investigation of T1ρ as a predictor of disease progression. Our data illustrate the powerful potential of multimodal imaging with MRI and HR-pQCT to evaluate early response to treatment in RA.
Table 1: Longitudinal changes of MRI and HR-pQCT data

<table>
<thead>
<tr>
<th></th>
<th>Low disease activity (N=5)</th>
<th>High disease activity (N=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td># Baseline</td>
<td>3 Month</td>
</tr>
<tr>
<td><strong>T1p values (ms)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radius</td>
<td>37.9±4.0</td>
<td>36.8±4.7</td>
</tr>
<tr>
<td>Lunate</td>
<td>36.5±3.2</td>
<td>36.9±3.9</td>
</tr>
<tr>
<td>Scaphoid</td>
<td>40.1±4.6</td>
<td>40.5±6.7</td>
</tr>
<tr>
<td>Global</td>
<td>38.1±2.9</td>
<td>39.2±4.6</td>
</tr>
<tr>
<td><strong>Bone erosion (mm²)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radius</td>
<td>18.17±26.4</td>
<td>18.2±26.8</td>
</tr>
<tr>
<td>Lunate</td>
<td>19.10±6.8</td>
<td>10.8±6.0</td>
</tr>
<tr>
<td>Scaphoid</td>
<td>4.7±1.5</td>
<td>4.9±1.2</td>
</tr>
<tr>
<td>MCP2</td>
<td>7.2±2.9</td>
<td>3.5±3.7</td>
</tr>
<tr>
<td>MCP3</td>
<td>7.2±1.8</td>
<td>2.7±2.6</td>
</tr>
<tr>
<td>Global</td>
<td>55.33±24.5</td>
<td>32.9±26.4</td>
</tr>
</tbody>
</table>

Figure 1: Pearson correlations in overall cohort assessing associations between 3 months' changes in cartilage T1p, changes in clinical DAS 28 CRP scores and bone erosion volumes, respectively.

Disclosure: T. Shimizu, None; K. Mamoto, None; U. Heilmeier, None; M. Tanaka, None; A. J. Burghardt, None; T. Link, None; J. Graf, None; J. B. Imboden Jr., None; X. Li, None.


Abstract Number: 1997

Detection of Progression of Radiographic Damage Despite Early and Targeted Therapy in Inflammatory Arthritis Using High-Resolution Peripheral Quantitative Computed Tomography

Sarah Manske¹,², Stephanie Finzel³, Steven K. Boyd⁴ and Cheryl Barnabe⁵, ¹Department of Radiology, University of Calgary, Calgary, AB, Canada, ²McCaig Institute for Bone and Joint Health, University of Calgary, Calgary, AB, Canada, ³Department of Rheumatology and Clinical Immunology, Medical Center University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany, ⁴Cumming School of Medicine, University of Calgary, Calgary, AB, Canada, ⁵Division of Rheumatology, University of Calgary, Calgary, AB, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Imaging of Rheumatic Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Early initiation of DMARDs and targeted therapy to achieve remission are said to offer the best opportunity to prevent radiographic damage in early inflammatory arthritis (EIA). High-resolution peripheral quantitative computed tomography (HR-pQCT) provides superior resolution of bone compared to x-ray, and reliable quantification of joint space [1] and erosions [2]. We used HR-pQCT to quantify changes in joint space, erosion number and size, and bone microarchitecture in EIA patients during the first year of therapy.
Methods: We recruited 47 EIA subjects and performed HR-pQCT (XtremeCT I, Scanco Medical AG, Switzerland) scans of the 2nd and 3rd MCPs of their dominant hand at diagnosis and 1 year later and collected sociodemographic and disease characteristics and disease activity at both timepoints. Erosion number and size were assessed from HR-pQCT images by applying the erosion definition and margin landmarks proposed by SPECTRA [2]. Mean, maximum, and minimum joint space width as well as joint space volume were assessed in 3D [1]. Total bone mineral density (Tt.BMD) was assessed in the distal 12% of the 2nd and 3rd metacarpal heads.

Results: At baseline, 34 met classification criteria for RA [3] and 13 had undifferentiated arthritis. After 1 year several individuals were reclassified: 1 had adult onset Still’s disease, 1 had Psoriatic Arthritis, and 3 had a self-limited arthritis. The majority received DMARD therapy (89%) and 27% progressed to biologic use. The mean DAS28 improved from 5.4 (SD 1.2) to 2.4 (SD 1.1), and the HAQ decreased from 1.20 (SD 0.72) to 0.41 (SD 0.51). Erosions by HR-pQCT were found in 34% (19) of subjects at baseline, with 32 erosions detected (mean axial width 1.2 (SD 0.7) mm, axial depth 1.8 (SD 1.1) mm, perpendicular width 1.4 (SD 0.9) mm, perpendicular depth 1.8 (SD 1.1) mm. This increased to 40 erosions at 1 year, with 23 subjects remaining free of erosions, 12 having a stable number and 8 having an increased number of erosions. However, only 3 erosions had a depth increase that exceeded the smallest detectable change. At the 3rd MCP, mean and minimum joint space width (mm) decreased by 0.06 (SD 0.11) and 0.082 (SD 0.20), respectively. In contrast there were no significant changes in joint space width or volume at the 2nd MCP joint. There were no significant changes in Tt.BMD in the 2nd or 3rd MC. Type of therapy, CCP, RF, or 1-year remission status did not influence change in Tt.BMD or joint space.

Conclusion: Joint space narrowing progressed and the number of erosions increased despite rheumatologic intervention. HR-pQCT provides greater sensitivity for detection of changes in joint space, erosions and bone microarchitecture.

Figure 1. Change in erosion over 1-year follow-up evaluated with HR-pQCT after registration and alignment with baseline image.


Disclosure: S. Manske, None; S. Finzel, None; S. K. Boyd, None; C. Barnabe, None.


Abstract Number: 1998

The Value of Dynamic Contrast-Enhanced MRI and Delayed Gadolinium Enhanced MRI of the Cartilage in Patients with Early Rheumatoid Arthritis: Leads Local Hyperperfusion to Cartilage Loss?

Philipp Sewerin1, Anja Mueller-Lutz2, Christoph Schleich3, Florian Fichter4, Markus Eichner5, Ruben Sengewein6, Lien Le7, Hans-Jörg Wittsack8, Matthias Schneider9 and Benedikt Ostendorf1,10

1Department and Hiller-Research-Unit for Rheumatology, Heinrich-Heine University, Düsseldorf, Germany, 2Dep. for diagnostic and interventional Radiology, Heinrich-Heine-University, Düsseldorf, Germany, 3Dep. for diagnostic and interventional Radiology, Heinrich-Heine University, Duesseldorf, Germany, 4Dep. for interventional and diagnostic radiology, Heinrich-Heine University, Düsseldorf, Germany, 5Dep. for interventional and diagnostic radiology, Heinrich-Heine University, Duesseldorf, Germany, 6Department and Hiller Research Unit for Rheumatology, Heinrich-Heine University, Düsseldorf, Germany, 7Ludwig-Maximilian University, Munich, Germany, 8Dep. for diagnostic and interventional radiology, Heinrich-Heine University, Düsseldorf, Germany, 9Policlinic for Rheumatology & Hiller Research Centre for Rheumatology, Heinrich-Heine-University Duesseldorf, Duesseldorf, Germany, 10Department of Rheumatology, Univ. Duesseldorf, Düsseldorf, Germany

First publication: September 18, 2017
Background/Purpose: To investigate the local inflammatory activity by using dynamic magnetic resonance imaging (MRI) and cartilage biochemical composition of the metacarpophalangeal joints (MCP) digits 2 and 3 by using Delayed Gadolinium-Enhanced MRI (dGEMRIC) in patients with early rheumatoid arthritis (eRA) treated with Methotrexat (MTX).

Methods: MCP joints of the index and middle finger of 28 patients with eRA from the AthroMark cohort were examined prior to MTX-therapy (baseline) as well as 3 and 6 months after initiation of MTX-therapy (follow up). Perfusion parameters and dGEMRIC index were calculated. OMERACT RA MRI score, including synovitis, edema and erosion subscores, and clinical parameters (CRP and DAS28) were registered at all time points.

Results: In follow-up measurements, the local perfusion in dynamic MRI decreased significantly between months 0 and 3 and between months 0 and 6. Decreasing of local perfusion correlates significantly with the DAS28 improvement at 3 months (p < 0.05). The extent of local inflammation (MCP II or MCP III) was significantly correlated with dGEMRIC values at all time points (p < 0.05). Furthermore, local inflammation and cartilage composite measurements showed significant correlation with edema subscore in follow up after 3 months and with RAMRIS and erosion subscore in follow up after 6 months (p < 0.05).

Conclusion: In patients with eRA synovial local hyperperfusion measured by dynamic MRI correlated significantly with the local cartilage composite and decreased significantly after 3 and 6 months after initiating MTX-therapy. Dynamic MRI seems to be a useful parameter of therapy success, since DAS28, RAMRIS and edema/erosion

Disclosure: P. Sewerin, None; A. Mueller-Lutz, None; C. Schleich, None; F. Fichter, None; M. Eichner, None; R. Sengewein, None; L. Le, None; H. J. Wittsack, None; M. Schneider, None; B. Ostendorf, None.

Magnetic Resonance Imaging of Skeletal Muscles in Patients with Dermatomyositis and Polymyositis: Novel and Distinctive Characteristic Findings

Taro Ukichi1, Ken Yoshida1, Satoshi Matsushima2, Go Kawakami2, Kentaro Noda1, Kazuhiro Furuya1 and Daitaro Kurosaka1,
1Division of Rheumatology, Department of Internal Medicine, Jikei University School of Medicine, Tokyo, Japan, 2Department of Radiology, Jikei University School of Medicine, Tokyo, Japan

First publication: September 18, 2017
muscle); distributions of HSI areas in muscle (diffuse, patchy, peripheral); patterns of HSI in muscle (honeycomb, foggy, strong high signal intensity [SHSI]).

**Results:** Among the 79 patients with abnormal MRI findings, 48 were diagnosed with DM and 31 were diagnosed with PM. Of these, Gd-T1WI was performed in 45 patients with DM and 27 patients with PM. Table 1 shows the differences in the percentage appearances of MRI findings between DM and PM patients. On STIR and Gd-T1WI images, the percentage appearances of the following characteristics were higher in DM patients than in PM patients: subcutaneous HSI, fascial HSI, peripheral distribution in muscle, honeycomb pattern in muscle. Patchy distribution and foggy pattern in muscle were higher in PM patients than in DM patients. There were no significant differences between the groups for diffuse distribution and SHSI pattern in muscle. Table 2 shows the differences in the percentage appearances of MRI findings between the autoantibody-positive and autoantibody-negative PM groups. The percentage appearances of subcutaneous and fascial HSI on STIR and Gd-T1WI images were higher in autoantibody-positive PM patients than in autoantibody-negative PM patients. Patchy distribution in muscle on Gd-T1WI was higher in autoantibody-negative PM patients than in autoantibody-positive PM patients.

**Conclusion:** Subcutaneous and fascial HSI, peripheral distribution in muscle, and honeycomb pattern in muscle are characteristic MRI findings in patients with DM, whereas patchy distribution and foggy pattern in muscle are characteristic MRI findings in patients with PM. MRI could be a useful tool for diagnosing DM and PM.

**Table 1:** Percentage appearances of characteristic findings on MRI in patients with DM or PM

<table>
<thead>
<tr>
<th>STIR</th>
<th>DM (n = 48)</th>
<th>PM (n = 31)</th>
<th>p-value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>subcutaneous HSI</td>
<td>34 (70.8)</td>
<td>9 (29.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>fascial HSI</td>
<td>41 (85.4)</td>
<td>13 (41.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>peripheral distribution</td>
<td>43 (89.6)</td>
<td>14 (45.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>diffuse distribution</td>
<td>23 (47.9)</td>
<td>14 (45.2)</td>
<td>0.81</td>
</tr>
<tr>
<td>patchy distribution</td>
<td>12 (22.9)</td>
<td>15 (48.4)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>honeycomb pattern</td>
<td>34 (70.8)</td>
<td>11 (35.5)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>foggy pattern</td>
<td>3 (6.3)</td>
<td>17 (54.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SHSI pattern</td>
<td>9 (18.8)</td>
<td>2 (6.5)</td>
<td>0.12</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gd-T1WI</th>
<th>DM (n = 45)</th>
<th>PM (n = 27)</th>
<th>p-value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>subcutaneous HSI</td>
<td>31 (68.9)</td>
<td>8 (29.6)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>fascial HSI</td>
<td>37 (82.2)</td>
<td>10 (37.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>peripheral distribution</td>
<td>40 (88.9)</td>
<td>12 (44.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>diffuse distribution</td>
<td>20 (44.4)</td>
<td>9 (33.3)</td>
<td>0.35</td>
</tr>
<tr>
<td>patchy distribution</td>
<td>10 (22.2)</td>
<td>16 (59.3)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>honeycomb pattern</td>
<td>34 (75.6)</td>
<td>7 (25.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>foggy pattern</td>
<td>3 (6.7)</td>
<td>13 (48.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SHSI pattern</td>
<td>6 (13.3)</td>
<td>2 (7.4)</td>
<td>0.44</td>
</tr>
</tbody>
</table>

* Values are the number (%).

† Statistical analysis was performed by Pearson’s chi-square test.
Table 2: Percentage appearances of characteristic findings on MRI in autoantibody-positive and autoantibody-negative PM groups*

<table>
<thead>
<tr>
<th></th>
<th>AA (+) ( n = 18 )</th>
<th>AA (-) ( n = 13 )</th>
<th>p-value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>STIR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>subcutaneous HSI</td>
<td>8 (44.4)</td>
<td>1 (7.7)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>fascial HSI</td>
<td>13 (72.2)</td>
<td>0 (0.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>peripheral distribution</td>
<td>8 (44.4)</td>
<td>5 (38.5)</td>
<td>1.00</td>
</tr>
<tr>
<td>diffuse distribution</td>
<td>8 (44.4)</td>
<td>6 (46.2)</td>
<td>1.00</td>
</tr>
<tr>
<td>patchy distribution</td>
<td>6 (33.3)</td>
<td>9 (69.2)</td>
<td>0.073</td>
</tr>
<tr>
<td>honeycomb pattern</td>
<td>9 (50.0)</td>
<td>2 (15.4)</td>
<td>0.066</td>
</tr>
<tr>
<td>foggy pattern</td>
<td>7 (38.9)</td>
<td>10 (76.9)</td>
<td>0.067</td>
</tr>
<tr>
<td>SHSI pattern</td>
<td>1 (5.6)</td>
<td>1 (7.7)</td>
<td>1.00</td>
</tr>
<tr>
<td>Gd-T1WI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>subcutaneous HSI</td>
<td>7 (46.7)</td>
<td>1 (8.3)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>fascial HSI</td>
<td>10 (66.7)</td>
<td>0 (0.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>peripheral distribution</td>
<td>7 (46.7)</td>
<td>5 (41.7)</td>
<td>1.00</td>
</tr>
<tr>
<td>diffuse distribution</td>
<td>6 (40.0)</td>
<td>3 (25.0)</td>
<td>0.68</td>
</tr>
<tr>
<td>patchy distribution</td>
<td>6 (40.0)</td>
<td>10 (83.3)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>honeycomb pattern</td>
<td>6 (40.0)</td>
<td>1 (8.3)</td>
<td>0.091</td>
</tr>
<tr>
<td>foggy pattern</td>
<td>5 (33.3)</td>
<td>8 (66.7)</td>
<td>0.13</td>
</tr>
<tr>
<td>SHSI pattern</td>
<td>1 (6.7)</td>
<td>1 (8.3)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

* Values are the number (%). AA (+) = an autoantibody-positive PM group, containing patients with myositis-specific autoantibodies, myositis-associated autoantibodies, and/or other connective tissue disease-specific autoantibodies; AA (-) = an autoantibody-negative PM group, containing patients without these autoantibodies.

† Statistical analysis was performed by Fisher’s exact test.

Disclosure: T. Ukichi, None; K. Yoshida, None; S. Matsushima, None; G. Kawakami, None; K. Noda, None; K. Furuya, None; D. Kurosaka, None.


Abstract Number: 2000

MRI Contributes to Accurate and Early Diagnosis of Non-Radiographic HLA-B27 Negative Axial Spondyloarthritis

Chun-Chi Lu, Guo-Shu Hunag, Tony Szu-Hsien Lee, En Chao, Hsiang-Cheng Chen, Shi-Jye Chu, Feng-Cheng Liu, San-Yuan Kao, Tsung-Yun Hou, Chen-Hung Chen, Sin-Yi Lyu and Deh-Ming Chang, 1University of Washington; Tri-Service General
Background/Purpose: According to the ASAS classification criteria for axial spondyloarthritis (SpA), the presence of structure changes of sacroiliac (SI) joints such as sclerosis, bone erosion, joint space widening or ankyloses can’t be adopted to confirm active sacroilitis on magnetic resonance imaging (MRI) in the absence of bone marrow edema (BME). Previous data indicated less than half Asian patients with axial SpA were characterized by BME. For patients with early phase of SpA, HLA-B27 is associated with early diagnosis and axial inflammation of SI joints on MRI, while serum c reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are incapable of predicting early sacroilitis. Nonetheless, HLA-B27 is not associated with structural lesions of SI joints. All factors contribute to difficult defining early Asian SpA patients in the absence of serum HLA-B27 and obvious imaging inflammation. This study aims to define the prevalence of structure changes of SI joints on MRI in Taiwanese patients with non-radiographic axial SpA and identify how to confirm an early diagnosis of HLA-B27 negative axial spondyloarthritis.

Methods: Eighty patients with inflammatory back pain and morning stiffness and high disease activity (BASDAI≥4) who had to be either serum HLA-B27 positive (27 patients) with ≥1 SpA-feature or HLA-B27 negative with ≥2 SpA-features (53 patients) were included in this prospective study. All patients were tested for X-rays of the pelvis before MRI examination and did not meet the definition for a positive radiograph according to the modified New York criteria. MRI of sacroiliac joints (MRI-SIJ) was performed with multiple sequence (Coronal and axial T1-weighted spin echo, coronal and axial short-tau inversion recovery). SI joints were evaluated for the prevalence of subchondral BME and structure changes, including sclerosis, bone erosion, joint space widening and ankylosis. All MRI-SIJ were scored according to the SPARCC score. All patients were tested for serum levels of ESR and CRP. Correlation analysis was performed among the different collected variables.

Results: Subchondral BME was present in 12 of 57 patients with HLA-B27 serum negative SpA (21.1 %), while 15 of 23 (65.2 %) HLA-B27 serum positive SpA patients had active BME on MRI (p = 0.02). Patients with SpA and positive HLA-B27 were characterized by higher SPARCC scores, compared to serum negative patients (p = 0.001). Structural changes of SIJ, including sclerosis, bone erosion and joint space widening were identified in 20 (86.9 %), 27 (100 %) and 10 (43.5 %) SpA patients with positive HLA-B27, respectively. These structural changes of SIJ on MRI were less common in HLA-B27 serum negative patients, as 30 (52.6 %), 50 (87.7 %) and 9 (15.8 %) of 23 patients, respectively. Among patients with high serum ESR or CRP, joint space widening developed accompanied with higher SPARCC scores (p = 0.024 and 0.019, respectively).

Conclusion: MRI is able to detect active sacroilitis and structure changes of SI joints for patients with non-radiographic axial spondyloarthritis in the absence of serum HLA-B27. Structure changes on MRI-SIJ could be used alternatively for early diagnosis of SpA in Asian people whom are characteristic by less bone marrow edema.

Disclosure: C. C. Lu, None; G. S. Hunag, None; T. S. H. Lee, None; E. Chao, None; H. C. Chen, None; S. J. Chu, None; F. C. Liu, None; S. Y. Kao, None; T. Y. Hou, None; C. H. Chen, None; S. Y. Lyu, None; D. M. Chang, None.


Abstract Number: 2001

Prevalence of Inflammatory Posterior Arch Abnormalities on Lumbar Spine MRI in Spondyloarthritis Patients Compared to Low Back Pain Patients

Helene Braun1, Clement Geniez1, Yannick Degboe2, Arnaud Constantin3, Alain Cantagrel4, Delphine Nigon5, Marie Faruch-Bilfeld1 and Adeline Ruyssen-Witrand4, 1Purpan Hospital, Toulouse, France, 2Department of Rheumatology, Purpan Hospital, Toulouse III University, Toulouse, France, 3Toulouse Hospital, toulouse, France, 4Purpan Hospital, Toulouse III University, Toulouse, France, 5CHU Purpan, Toulouse, France
SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Imaging of Rheumatic Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: To compare the prevalence of inflammatory posterior arch abnormalities (IPAA) on lumbar spine MRI between spondyloarthritis patients (SpA) and low back pain patients (LBP).

Methods: Design : Monocentric cross-sectional case-controlled study. Patients : SpA patients fulfilling the 2009 ASAS criteria who had a lumbar spine MRI were retrospectively selected from medical files. Chronic LBP patients with a lumbar spine MRI planned in the Toulouse Hospital Radiology Center were prospectively selected if they had no argument for a symptomatic back pain (e.g. tumor, infection,...). MRI : STIR and T1 sagittal images from 3 and 1.5 Tesla MRI going up to T8-T9 stages were reviewed by two experienced rheumatologists, blinded from the diagnosis and clinical data. IPAA (i.e.: pedicle edema, transverse and spinous process edema, interspinous process edema, costo-transverse or zygapophyseal joint arthritis) were collected in the two groups. Analyses : The prevalence of IPAA between SpA and LBP patients were compared by Chi2 or Fisher's exact test. Clinical data (age, sex, disease duration, BASDAI, CRP, BASFI) were compared in the SpA group according to the presence/absence of IPAA by Chi2 or Wilcoxon tests.

Results: Ninety-five patients were included in each group. Inter and intra-observer agreement was excellent (κ=0.938). The prevalence of all IPAA was not significantly different between SpA and LBP groups (55.9% in SpA group versus 69.5% in LBP group, p = 0.97). On the other hand, there was a significant difference in the prevalence of costo-transverse joint arthritis, pedicle edema, transverse and spinous process edema between the two groups (prevalence of these anomalies in SpA group: 27% versus 8% in LBP group, p = 0.006). Costo-transverse joint arthritis and transverse process edema have a specificity and a positive predictive value of 100% for the diagnosis of SpA, with sensitivity of 17% and 3.2% respectively. Patients with IPAA in SpA group had a longer disease duration (11 years versus 8 years, p=0.02), higher CRP level (medians : 11 versus 3, p=0.0002), more often a MRI sacroiliitis (84% versus 47%, p=0.001), more often psoriasis (27% versus 10.2%, p=0.04) but received less NSAIDs (42% versus 69%, p=0.01) compared to patients without IPAA.

Conclusion: Costo-transverse joint arthritis, pedicle edema and transverse process edema are more frequent and specific for the diagnosis of SpA. IPAA are frequently associated with biological inflammation and MRI sacroiliitis.

Disclosure: H. Braun, None; C. Geniez, None; Y. Degboe, None; A. Constantin, None; A. Cantagrel, None; D. Nigon, None; M. Faruch-Bilfeld, None; A. Ruyssen-Witrand, None.

Baseline 18F Sodium Fluoride Uptake of Vertebral Bodies but Not Vertebral Corners on Positron Emission Tomography Is Associated with Changes in Bone Mineral Density at Lumbar Vertebrae in Ankylosing Spondylitis: A 1-Year Longitudinal Study

Seung-Geun Lee1, Keunyoung Kim2, Seong-Min Kweon3, Eun-Kyoung Park4, Yun-Kyung Kim5 and Geun-Tae Kim6, 1Internal Medicine, Pusan National University School of Medicine, Pusan National University Hospital, Busan, Korea, Republic of (South), 2Department of Nuclear Medicine and Biomedical Research Institute, Pusan National University Hospital, Busan, Korea, Republic of (South), 3Internal Medicine, Pusan National University School of Medicine, Pusan National University Hospital, Busan, South Korea, Busan, Korea, Republic of (South), 4Division of Rheumatology, Department of Internal Medicine, Pusan National University School of Medicine, Busan, Korea, Republic of (South), 5Internal Medicine, Kosin University College of Medicine, Busan, South Korea, Busan, Korea, Republic of (South), 6Kosin University College of Medicine, Busan, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Imaging of Rheumatic Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: 18F sodium fluoride (NaF) positron emission tomography (PET) allows quantitative assessment of osteoblastic bone synthesis in specific skeletal sites. Previous studies showed that increased 18F NaF uptake at vertebral corners was linked with syndesmophytes formation in patients with ankylosing spondylitis (AS), but the association between bone metabolism measured by 18F NaF PET and bone mineral density (BMD) has not been studied. Thus, we investigated whether baseline 18F NaF uptake of vertebral bodies or vertebral corners on PET is associated with changes in BMD at the corresponding lumbar vertebrae in AS.

Methods: In 12 male AS patients, 18F NaF PET/computed tomography (CT) was performed at baseline and dual energy X ray absorptiometry (DEXA) was performed at baseline and the 1-year follow-up. The maximum standardized uptake value (SUVmax) of the vertebral body and both upper and lower vertebral corners from the L1 to L4 were measured in the mid-sagittal plane of the 18F NaF PET/CT image. By using the squared region of interest (ROI), the SUVmax of the vertebral body was acquired (Figure 1a). For the SUVmax of the corners, we used the arithmetic mean SUVmax of the upper and lower vertebral corners which were evaluated with 1cm-sized circular ROIs (Figure 1b). The BMD of the L1 to L4 were calculated from conventional DEXA. The association of the SUVmax of the vertebral bodies or corners with the changes in BMD during 1-year follow-up was analyzed at the lumbar vertebral level using generalized estimating equations (GEE) to adjust within-patient correlation for a total number of lumbar vertebrae.

Results: We analyzed 48 lumbar vertebrae in 12 AS patients. At the lumbar vertebral level, the mean (SD) baseline SUVmax of the vertebral body and the median (IQR) baseline SUVmax of the vertebral corners were 6.7(1.8) and 6.5(5.3-7.1), respectively. The mean (SD) BMD of each vertebra at baseline and 1-year follow-up were 1.18 (0.21) g/cm² and 1.19 (0.19) g/cm², respectively. In correlation analyses, changes in BMD at lumbar vertebrae was positively correlated with the baseline SUVmax of the vertebral bodies \(r=0.39, \ p=0.036\) but not with that of the vertebral corners \(r=-0.07, \ p=0.657\). In multivariable GEE analysis, the baseline SUVmax of the vertebral bodies was significantly associated with changes in BMD at the lumbar vertebrae \(B(SE)=0.009(0.004), \ p=0.017\), but that of vertebral corners did not showed this association \(B(SE)=-0.003(0.002), \ p=0.174\). The baseline BMD of the vertebra also showed significant associations with changes in BMD.

Conclusion: Baseline 18F NaF uptake of the vertebral bodies but not that of the vertebral corners on PET was associated with 1-year changes in BMD at the lumbar vertebrae in AS patients. Our data suggests different mechanisms of bone metabolism between the vertebral bodies and corners that have separate effects on BMD in AS.
Disclosure: S. G. Lee, None; K. Kim, None; S. M. Kweon, None; E. K. Park, None; Y. K. Kim, None; G. T. Kim, None.


Abstract Number: 2003

18 FDG PET/CT Predicts Decline in Functional Respiratory TESTS in Systemic Sclerosis Patients but NOT in Rheumatoid Arthritis Patients

Jorge Juan Fragio Gil1, Jose Ivorra Cortes1, Manuela Martinez Frances2, Jose Luis Loaiza Gongora3, Juan José Alegre4, Marta Garijo Buñón5, Susana Herrera Lara6, Inmaculada Chalmeta Verdejo1, Luis Gonzalez Puig1, Rosa Negueroles Albueche1, Cristina Alcañiz Escandell1, Karla Arevalo Ruales1, Ines Canovas Olmos1, Carlos Feced Olmos1, Roxana Gonzalez Mazarlo1, Elena Grau Garcia1, Eztizen Labrador Sanchez1, Isabel Martinez Cordellat1, Carmen Najera Herranz1, Jose Eloy Oller Rodriguez1, Francisco Miguel Ortiz-Sanjuán1, Elvira Vicens Bernabeu1, Marta De la Rubia Navarro1, David Hervás Marín7 and Jose Andres Roman Ivorra1,

1Rheumatology Department. Hospital Universitario y Politecnico La Fe, Valencia, Spain, 2Pneumology Department. Hospital Universitario y Politecnico La Fe, Valencia, Spain, 3Nuclear Medicine Department. HUP La Fe, Valencia, Spain, 4Sección de Reumatología Hospital Universitario Dr Peset Valencia, Valencia, Spain, 5Rheumatology Unit. Hospital de León, León, Spain, 6Pneumology Department. Hospital Dr. Peset, Valencia, Spain, 7Biostatistics Unit. IIS La Fe, Valencia, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Imaging of Rheumatic Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Interstitial lung diseases (ILD) are a group of illnesses that often complicate connective tissue diseases (CTD) such as rheumatoid arthritis (RA) or systemic sclerosis (SS), but the lung is the only affected organ in the idiopathic pulmonary fibrosis (IPF). Nonspecific interstitial pneumonia (NSIP) is the more frequent form in SS while usual interstitial pneumonia (UIP) predominates in RA patients and in the IPF form. ILD are one of the most important causes of mortality in CTD, but evaluating their prognosis remains difficult. Some studies suggested that 18-FDG-PET/CT could help to detect zones of activity in lung tissue in IPF and this in turn could predict the progress of the disease, but the results are inconclusive. Moreover, little is known about the value of 18-FDG PET uptake in ILD associated to RA or SS. The purpose of this study is to evaluate the predictive value of 18 FDG-PET/CT scan images in functional pulmonary progression of ILD associated to RA or SS.

Methods:
We conducted a 12 month prospective observational study on patients diagnosed with ILD associated to SS or RA between January 2015 and May 2017. ILD diagnosis was based on clinical assessment, pulmonary function tests (PFTs) and expert HRCT evaluation. This study was approved by the ethic research committee of our institution, and a formal written consent was obtained by all patients.

We performed three visits: basal, 6 month and 12 month visits. On all visits a general exploration, forced vital capacity (FVC) and diffusing capacity of the lungs for carbon monoxide (DLCO) were carried out. On basal and 6 month visits a 18 FDG-PET/TC were performed within a period of three months from the PFTs.

The patients selected continued with their treatment (corticosteroids, DMARDs or immunosuppressants).

The nuclear medicine physician identified the maximum and mean standardized uptake value (SUVmax and SUVmean) in the three areas with the most FDG uptake, and adenopathies uptake.

PET/CT images were reviewed by 2 combined radiologist/nuclear medicine physicians in consensus.

**Results:** We included 17 patients, 10 had UIP associated with RA and 7 NSIP related to SS. It appeared that RA patients had longer lung illness evolution and worse FVC than SS patients (table), in spite of not having found statistical differences. We detected significant statistical relation between the highest SUVmax and FVC (p=0.009) or DLCO progression (p=0.006) in SS patients, independently of the basal FVC and DLCO, and duration of lung illness in a multivariable linear mixed model. We didn’t find any relation between SUVmax and FVC or DLCO progression in RA patients.

<table>
<thead>
<tr>
<th></th>
<th>Rheumatoid arthritis (n=10)</th>
<th>Systemic Sclerosis (n=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex (female)</strong></td>
<td>6 (60%)</td>
<td>6 (86%)</td>
</tr>
<tr>
<td><strong>Age at visit(years)</strong></td>
<td>61 (52-67)</td>
<td>53 (50-62)</td>
</tr>
<tr>
<td><strong>Duration of disease (months)</strong></td>
<td>64(10-102)</td>
<td>28 (17-176)</td>
</tr>
<tr>
<td><strong>Duration of ILD (months)</strong></td>
<td>40 (29-56)</td>
<td>16 (12-25)</td>
</tr>
<tr>
<td><strong>FVC (L)</strong></td>
<td>2.4 (2.3-12)</td>
<td>2.4 (1.2-2.67)</td>
</tr>
<tr>
<td><strong>FVC (% predicted)</strong></td>
<td>74% (68-97%)</td>
<td>96% (70-106%)</td>
</tr>
<tr>
<td><strong>DLCO (% predicted)</strong></td>
<td>54% (41-70%)</td>
<td>52% (44-75%)</td>
</tr>
<tr>
<td><strong>SUVmax</strong></td>
<td>2.95 (2.5-3.5)</td>
<td>2.5 (1.85-3.05)</td>
</tr>
<tr>
<td><strong>Corticosteroids</strong></td>
<td>8 (80%)</td>
<td>3 (43%)</td>
</tr>
<tr>
<td><strong>DMARDs</strong></td>
<td>6 (60%)</td>
<td>4 (57%)</td>
</tr>
<tr>
<td><strong>Immunosuppresants</strong></td>
<td>3 (30%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

**Conclusion:**

In our cohort of patients with SS, 18 FDG PET/TAC can aid in predicting the progression of ILD associated disease, which does not occur in RA patients.

**Disclosure:** J. J. Fragio Gil, None; J. Ivorra Cortes, None; M. Martinez Frances, None; J. L. Loaiza Gongora, None; J. J. Alegre, None; M. Garijo Bufort, None; S. Herrera Lara, None; I. Chalmeta Verdejo, None; L. Gonzalez Puig, None; R. Negueroles Albuixech, None; C. Alcañiz Escandell, None; K. Arevalo Ruales, None; I. Canovas Olmos, None; C. Feced Olmos, None; R. Gonzalez Mazario, None; E. Grau Garcia, None; E. Labrador Sanchez, None; I. Martinez Cordellat, None; C. Najera Herranz, None; J. E. Oller Rodriguez, None; F. M. Ortiz-Sanjuán, None; E. Vicens Bernabeu, None; M. De la Rubia Navarro, None; D. Hervás Marín, None; J. A. Roman Ivorra, None.


**Abstract Number:** 2004

**Simplified Assessment in Capillaroscopy**

Virginia Durigan¹, Anastasia Secco², Felix Enrique Romanini³, Virginia Ortiz⁴, Marta Mamani⁴ and Leticia Sormani de Fonseca⁴, ¹Reumatology, Hospital Bernardino Rivadavia, CABA, Argentina, ²Reumatology, Hospital Bernardino Rivadavia, Buenos Aires, Argentina, ³Hospital Bernardino Rivadavia, CABA, Argentina

**First publication:** September 18, 2017
Background/Purpose: Nailfold Capillaroscopy is a non-invasive diagnostic technique designed to evaluate small vessels of the microcirculation. The most important indication for capillaroscopy is Raynaud’s phenomenon. The complexity and meticulous evaluation of the eight fingers is difficult to apply in daily practice given the limited availability of time to perform. For this reason it is necessary to develop simple and abbreviated techniques, to achieve an optimal and rapid evaluation of the patient. The objective of this study is determine the performance of the method of the 4° finger for the diagnosis of SD pattern in patients with Raynaud's phenomenon taking the eight finger pattern as a gold standard.

Methods: Cross-sectional study with blinded and independent measurements. Nailfold Capillaroscopy was performed on the four fingers of each hand, except thumbs. Another observer evaluated the 4th finger of the hands. The interobserver agreement was made before carrying out the study and was 100%. The 8-finger method (gold standard) was considered positive when at least one finger has SD pattern and the 4° finger method was considered positive when at least one of them presents the SD pattern. We included patients older than 18 years with a diagnosis of Raynaud Phenomenon and suspected autoimmune disease. Patients with thickening of the skin in the nailfold, digital lesion that made it difficult to assess (trauma, amputation, burns, etc.) and patients who did not consent to the procedure were excluded.

Results: We included 78 patients, 90% was female. The mean age was 53 years (+/- 13.5). Sixty-three patients had a score of eight fingers positive (cases) and 15 had a score of eight fingers negative (controls). The sensitivity of the 4° finger evaluation method was 89% (95% CI: 82-96%) and 93% specificity (95% CI: 88-99%). The positive predictive value of this method was 98% (95% CI: 95-100%) and the negative predictive value was 67% (95% CI: 56-77%). The positive likelihood ratio was 13 (95% CI: 2-89).

Conclusion: The simplified method of the 4° finger showed good performance for the diagnosis of SD pattern compared to the standard method of evaluation of the 8 fingers.

Disclosure: V. Durigan, None; A. Secco, None; F. E. Romanini, None; V. Ortiz, None; M. Mamani, None; L. Sormani de Fonseca, None.

Abstract Number: 2005

Nailfold Capillaroscopy in Systemic Sclerosis: How Many Fingers Should be Examined to Detect Abnormality?

Graham Dinsdale1, Tonia Moore2, Neil O’Leary3, Michael Berks4, Chris Roberts3, Joanne Manning2, John Allen5, Marina E Anderson6, Maurizio Cuto10, Roger Hesselstrand8, Kevin Howell9, Carmen Pizzorni7, Vanessa Smith10, Alberto Sulli11, Marie Wildi8, Christopher Taylor4, Andrea Murray1 and Ariane L. Herrick1,12, 1Division of Musculoskeletal & Dermatological Sciences, University of Manchester, Salford Royal Hospital NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, UK, Manchester, United Kingdom, 2Salford Royal Hospital NHS Foundation Trust, Salford, UK, Salford, United Kingdom, 3Centre for Biostatistics, Division of Population Health, Health Services Research & Primary Care, University of Manchester, Manchester, UK, Manchester, United Kingdom, 4Centre for Imaging Sciences, Division of Informatics, Imaging & Data Sciences, University of Manchester, Manchester, UK, Manchester, United Kingdom, 5Microvascular Diagnostics, Northern Medical Physics and Clinical Engineering, Freeman Hospital, Newcastle upon Tyne, UK, Newcastle upon Tyne, United Kingdom, 6Institute of Ageing and Chronic Disease, University of Liverpool, Liverpool, UK, Liverpool, United Kingdom, 7Research Laboratory and Academic Unit of Clinical Rheumatology, Department of Internal Medicine, University of Genova, Genova, Italy, Genova, Italy, 8Department of Clinical Sciences, Section of Rheumatology, Lund University, Lund, Sweden, Lund, Sweden, 9Institute of Immunity and Transplantation, University College London, Royal Free Campus, London, UK, London, United Kingdom, 10Department of Rheumatology, Ghent University Hospital, Faculty of Internal Medicine, Ghent University, Ghent, Belgium, Ghent, Belgium, 11Research Laboratory and Academic Unit of Clinical Rheumatology, Department of Internal Medicine, University of Genova, Genova, Italy, Genoa, Italy, 12NIHR Manchester Musculoskeletal Biomedical Research Unit, Central Manchester NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, UK, Manchester, United Kingdom

First publication: September 18, 2017
SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Imaging of Rheumatic Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Nailfold capillaroscopy plays an important role in diagnosing systemic sclerosis (SSc), with abnormal nailfold capillary appearance being included in the 2013 ACR/EULAR diagnostic criteria [1]. Common queries from clinicians who assess patients with suspected SSc are: which finger(s) should be imaged, and how many digits in total, given that assessing 8 fingers (excluding thumbs) takes time in a busy clinical practice? Our aim was to demonstrate the sensitivity of assessing different (combinations of) fingers for the presence of two markers of capillary abnormality: (1) presence of giant capillaries, and (2) overall image grade, compared to assessment of all 8 fingers.

Methods:
Nailfold images (all fingers from each of 101 patients with SSc) and subsequent multi-observer assessments from a large study of quantitative capillaroscopy [2] were characterised by digit. Using custom software, observers counted giant vessels and graded the image overall (including normal/early/active/late). Patients were defined as “true case” for each of 2 parameters (giants, and image grade) if at least one of 8 fingers tested positive for the parameter (i.e. ≥ 1 giant vessels in one or more fingers, or one or more fingers given an ‘abnormal’ [early/active/late] grade). Seven single-finger, or finger combinations (derived from the middle and ring fingers), were then tested for sensitivity of achieving the correct result against the 8-finger “gold standard” true cases.

Results:
For each of seven combinations of finger(s), sensitivity percentages for the two parameters are shown in Table 1. For the 8-finger “gold standard”, sensitivity against the diagnostic criteria was 53.0% (71 +ve cases from 134 assessments) and 73.1% (98 +ve cases from 134 assessments) for presence of giants and image grade, respectively. Pairs of fingers have higher sensitivity than single fingers in all cases, and the 4-finger combination shows a sensitivity of 85.9% and 91.8% for giants and image grade, respectively.

Conclusion:
1. Assessing only middle and ring fingers on both hands detects abnormality in 85-90% of cases of established SSc (halving imaging time).

2. Assessing only ring fingers (sensitivity 73-80%) brings a 75% reduction in imaging time.

3. Some cases of abnormality will be missed by not examining all fingers.

References

Table 1. Sensitivity values for two nailfold capillary parameters (presence of giants, and image grade).

<table>
<thead>
<tr>
<th>Finger(s)</th>
<th>Presence of giant capillaries (71 assessments from 42 patients)</th>
<th>Abnormal image grade (98 assessments from 58 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Frequency (%)</td>
<td></td>
</tr>
<tr>
<td>Ring Left</td>
<td>40</td>
<td>56.3</td>
</tr>
<tr>
<td>Ring Right</td>
<td>32</td>
<td>45.1</td>
</tr>
<tr>
<td>Either Ring</td>
<td>52</td>
<td>73.2</td>
</tr>
<tr>
<td>Middle Left</td>
<td>32</td>
<td>45.1</td>
</tr>
<tr>
<td>Middle Right</td>
<td>23</td>
<td>32.4</td>
</tr>
<tr>
<td>Either Middle</td>
<td>40</td>
<td>56.3</td>
</tr>
<tr>
<td>Any Middle or Ring</td>
<td>61</td>
<td>85.9</td>
</tr>
</tbody>
</table>

Disclosure: G. Dinsdale, None; T. Moore, None; N. O’Leary, None; M. Berks, None; C. Roberts, None; J. Manning, None; J. Allen, None; M. E. Anderson, None; M. Cutolo, None; R. Hesselstrand, None; K. Howell, None; C. Pizzorni, None; V. Smith, None; A. Sulli, None; M. Wildt, None; C. Taylor, None; A. Murray, None; A. L. Herrick, None.
Altered Microcirculation As a Proxy for Inflammation in Hand Osteoarthritis Can Reliably be Assessed Using Fluorescence Optical Imaging

Ida K. Haugen¹, Sigrid Hestetun¹, Benedict Drude², Gerd R. Burmester³, Tore K Kvien⁴ and Sarah Ohndorf², ¹Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, ²Rheumatology and Clinical Immunology, Charité-University Medicine Berlin, Berlin, Germany, ³Rheumatology and Clinical Immunology, Charité - University Medicine Berlin, Free University and Humboldt University Berlin, Berlin, Germany, ⁴Diakonhjemmet Hospital, Oslo, Norway

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Imaging of Rheumatic Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Previous studies in systemic inflammatory joint diseases have suggested that Fluorescence Optical Imaging (FOI) is a reliable and sensitive tool for the detection of altered microcirculation as a proxy for inflammation. Inflammation is commonly present in hand osteoarthritis (OA), and plays a role for symptoms and disease progression. Feasible, sensitive and reliable tools to evaluate inflammation are important in hand OA trials. Our aim was to explore the inter-reader reliability of FOI in hand OA, which has not been assessed in any previous trials.

Methods: Hand OA patients with no systemic inflammatory joint disease or psoriasis were included in the Nor-Hand study. A fluorescence dye was administered intravenously (ICG-pulsion, 0.1 mg/kg body weight), and one image was obtained every second for 6 minutes using the Xiralite scanner. Two readers independently scored the FOI scans from 21 patients (19 women, mean (standard deviation) age 63.9 (5.6) years). Fluorescence enhancement in 32 joints including the bilateral distal (DIP), proximal interphalangeal (PIP), metacarpophalangeal (MCP), first carpometacarpal (CMC1) and wrist joints was scored on 0-3 scales. The readers evaluated three different phases (phase 1-3) based on the wash-in and wash-out of the dye and the prima vista mode (PVM; a composite of the 240 first images). We assessed the agreement between the two readers by calculating weighted kappa values at joint level as well as intraclass correlation coefficients (ICC) and smallest detectable difference (SDD) values for sum scores when using the two readers' average scores (=1.96*standard deviation of the difference between readers/Â²).

Results: Fluorescence enhancement was most commonly seen in phase 2 of the examination. Enhancement in phase 3 and especially phase 1, which is thought to represent active inflammation, was uncommon (Table). In phase 2, the readers agreed upon enhancement in 152/210 (72.3%) PIP and 83/168 (49.4%) DIP joints, but only 3/41 (7.3%) wrist joints. No enhancement was found in the CMC1 joints in any of the phases. The inter-reader ICC values were very good for the PVM and phase 2-3. In these phases, the inter-reader kappa values were good/very good for PIP joints and good for DIP joints. The reliability was lower for MCP and wrist joints. Fluorescence enhancement in phase 1 could not be reliably assessed.
<table>
<thead>
<tr>
<th></th>
<th>PVM</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reader 1:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>15.0 (10.5, 19.5)</td>
<td>0.0 (0.0, 0.5)</td>
<td>23.0 (19.0, 27.5)</td>
<td>4.0 (0.5, 10.5)</td>
</tr>
<tr>
<td>Reader 2:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>12.0 (9.5, 18.0)</td>
<td>2.0 (0.0, 4.5)</td>
<td>24.0 (19.5, 30.5)</td>
<td>6.0 (2.0, 11.0)</td>
</tr>
<tr>
<td>ICC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.89 (0.72, 0.96)</td>
<td>0.10 (-0.32, 0.50)</td>
<td>0.87 (0.72, 0.95)</td>
<td>0.89 (0.75, 0.95)</td>
</tr>
<tr>
<td>SDD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.6</td>
<td>6.1</td>
<td>6.8</td>
<td>3.9</td>
</tr>
</tbody>
</table>

**Weighted kappa values across joint groups**

<table>
<thead>
<tr>
<th>Joint Group</th>
<th>Reader 1</th>
<th>Reader 2</th>
<th>Reader 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>DIP 2-5</td>
<td>0.63</td>
<td>0.84</td>
<td>0.62</td>
</tr>
<tr>
<td>PIP 1-5</td>
<td>0.55</td>
<td>0.59</td>
<td>0.55</td>
</tr>
<tr>
<td>MCP 1-5</td>
<td>0.55</td>
<td>0.59</td>
<td>0.55</td>
</tr>
<tr>
<td>CMC1</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Wrist</td>
<td>0.55</td>
<td>0.59</td>
<td>0.07</td>
</tr>
</tbody>
</table>

PVM=Prima Vista Mode; IQR=Interquartile range; ICC=Intraclass Correlation Coefficients; SDD=Smallest Detectable Difference; DIP=distal interphalangeal; PIP=proximal interphalangeal; MCP=metacarpophalangeal; CMC=carpometacarpal; NA=Not appropriate due to grade 0 in all joints.

**Conclusion:** In hand OA, signal alterations by FOI as a proxy for inflammation were most commonly found in DIP and PIP joints. FOI seemed insensitive for the detection of inflammation in CMC1 joints. The inter-reader reliability was good for all phases, except phase 1.

**Disclosure:** I. K. Haugen, None; S. Hestetun, None; B. Drude, None; G. R. Burmester, Pfizer Inc, 2, Pfizer Inc, 5; T. K. Kvien, AbbVie, 2, Pfizer Inc, 2, Roche Pharmaceuticals, 2, UCB, 2, BMS, 2, MSD, 2, AbbVie, 5, Pfizer Inc, 5, BMS, 8, MSD, 8, Roche Pharmaceuticals, 8, UCB, 8, AbbVie, 8; S. Ohrndorf, None.

**Abstract Number:** 2007

**Disturbances of the Acral Perfusion Detected By Fluorescence Optical Imaging Are Associated with the Development of Ischemic Complications in Patients with Systemic Sclerosis**

**Stefanie Friedrich**1,2, Susanne Lueders3, Stephanie Werner3,4, Anne-Marie Glimm5, Gabriela Schmittar5, Gerd R. Burmester6, Gabriela Riemekasten7, Marina Backhaus8 and Sarah Ohrndorf9, 1Department of of Rheumatology and Clinical Immunology, Department of Rheumatology and Clinical Immunology, Charité University Hospital Berlin, Germany, Berlin, Germany, 2Department of Radiology, Department of Radiology, Charité University Hospital, Berlin; Germany, Berlin, Germany, 3Department of Rheumatology and Clinical Immunology, Department of Rheumatology and Clinical Immunology, Charité University Hospital, Berlin; Germany, Berlin, Germany, 4Department of Rheumatology and Clinical Immunology, Department of Rheumatology and Clinical Immunology, Charité University Medicine Berlin, Berlin, Germany, 5Department of Rheumatology and Clinical Immunology, Charité - University Medicine Berlin, Free University and Humboldt University Berlin, Berlin, Germany, 6Department of Rheumatology, Universitätsklinikum Schleswig-Holstein, Lubeck, Germany, 8Rheumatology, Park-Klinik Weissensee, Berlin, Germany, 9Rheumatology and Clinical Immunology, Charité-University Medicine Berlin, Berlin, Germany

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017
Background/Purpose:
Systemic sclerosis (SSc) is a condition causing impaired microcirculation with the risk of ischemic complications such as digital ulcers and pitting scars (DU/PS). Fluorescence optical imaging (FOI) is an imaging method that detects enhanced microcirculation as a sign of joint inflammation in both hands of patients with rheumatoid arthritis and other arthritides [1, 2]. FOI’s impact to record disturbed microcirculation in the hands of patients with systemic sclerosis has not yet been sufficiently investigated [3]. The aim of this study is to find associations of disturbed microcirculation initially detected by FOI and the development of new DU/PS throughout a follow-up of 12 months.

Methods:
Sixty-three patients with SSc were included and received FOI examination following the Xiralite-System guidelines (ICG 0.1mg/kg BW i.v.; 6 minute duration) as well as capillaroscopy at baseline. After a mean follow-up time of 12 months (min-max: 8-20 months), all participants were followed regarding the development of new ulcers and pitting scars.

Results:
A disruption of microcirculation in FOI was defined as a lack of a sufficient fluorescent signal in at least one fingertip over the entire course of the examination and was found in 11 of 63 SSc patients. All of these patients had a history of DU/PS and frequently presented with a late pattern capillaroscopy (9 of 11) at baseline. Fingers with a disrupted microcirculation also showed a reduced capillary density to a greater extend (96.0%) than fingers with a sufficient signal in FOI (76.0%; p=0.0241).

30 of 60 patients developed digital ulcers or pitting scars during follow up (3 drop outs due to death [n=2] or withdrawal). 81.8% of patients with a disrupted microcirculation in FOI developed these complications during follow-up compared with 42.9% of patients without a disruption in FOI (p=0.0419; OR=6.0 [95%CI 1.2 - 30.7]). A disruption of microcirculation especially increased the risk of developing DU/PS in the same finger: 20.1% of fingers with normal, but 65.4% with a missing FOI signal in the fingertip presented with an ischemic complication during follow-up (p<0.0001; OR=7.5 [95%CI 3.3 - 17.3]).

Conclusion:
Fluorescence optical imaging can reveal an impaired microcirculation in patients with systemic sclerosis, which is associated with microangiopathic changes as seen in capillaroscopy as well as the subsequent development of digital ulcers and pitting scars. Therefore, FOI might help to identify patients at risk for these complications.

Disclosure: S. Friedrich, None; S. Lueders, None; S. Werner, None; A. M. Glimm, None; G. Schmittat, None; G. R. Burmester, AbbVie, BMS, MSD, Pfizer, Roche, and UCB, 5; G. Riemekasten, CellTrend, 4; M. Backhaus, None; S. Ohrndorf, None.


Abstract Number: 2008

“Intrathoracic Manifestations of Connective Tissue Diseases on High Resolution Computed Tomography”

Diego Baenas1, Maira Orozco2, María Eugenia Olmos3, Luis Lasca4, Paula Riba5, Patricio Muszinsky5, Juan Pablo Pirola6, Verónica Saurit7, Alejandro Alvarellos7, Ana C. Alvarez8, Soledad Retamozo9,10, Nadia Riscannevo7,11, Janet Flores12, Ariel Blu3, Ana María López13, Gustavo Muñoz14, Santiago Orozco15 and Francisco Caeiro16, 1Rheumatology Unit, Hospital Privado Universitario de Córdoba, Postgraduate Career of Rheumatology Catholic University of Córdoba, Cordoba, Argentina, 2Radiology, Radiology Unit, Hospital Privado Universitario de Córdoba, Cordoba, Argentina, 3Pulmonary, Pulmonary Unit, Hospital Privado Universitario de Córdoba, Cordoba, Argentina, 4Radiology Unit, Oulton Institute, Cordoba, Argentina, 5Radiology, Radiology Unit, Oulton Institute, Cordoba, Argentina, 6Rheumatology, Rheumatology Unit, Hospital Privado Universitario de Córdoba, Cordoba, Argentina, 7Rheumatology, Rheumatology Unit, Hospital Privado Universitario de Córdoba, Cordoba, Argentina, 8Rheumatology, Rheumatology Unit, Hospital Privado Universitario de Córdoba, Cordoba, Argentina, 9Instituto de Investigaciones en Ciencias de la Salud, Universidad Nacional de Córdoba, Consejo Nacional de Investigaciones Científicas y Técnicas (INICSA-UNC-CONICET), Cordoba, Argentina, 10Hospital Privado Centro Médico de Córdoba, Cordoba, Argentina, 11Rheumatology Unit, Hospital Privado Universitario
SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Imaging of Rheumatic Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Connective tissue diseases (CTD) can cause intrathoracic involvement, increasing patients morbidity and mortality. High-resolution computed tomography (HRCT) is a key method for evaluation of these manifestations. The aim of this study is to describe clinical features and to evaluate intrathoracic HRCT findings in patients with CTD.

Methods:
Retrospective descriptive study, from January 2010 to December 2016. We evaluated HRCT findings in patients with CTD. We excluded patients under 18 years of age, pregnant, diagnosis of vasculitis, respiratory infections, drug toxicity, and previous thoracic surgery or radiotherapy. Data were analyzed using SPSS 17.0 software.

Results:
Out of 199 patients, 96 had rheumatoid arthritis (RA), 29 systemic lupus erythematosus (SLE), 26 systemic sclerosis (SSc), 23 inflammatory myopathies (IM), 22 primary Sjögren’s syndrome (pSS) and 3 mixed connective tissue disease (MCTD). The baseline characteristics of patients are shown in table 1.

Table 1. Baselines features.
<table>
<thead>
<tr>
<th>Features</th>
<th>RA (n=96)</th>
<th>SLE (n=29)</th>
<th>SSc (n=26)</th>
<th>IM (n=23)</th>
<th>pSS (n=22)</th>
<th>MCTD (n=3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (x years ± SD),</td>
<td>62.4 ±13.1</td>
<td>45±15.3</td>
<td>50.5±16.9</td>
<td>58.3±14.9</td>
<td>64± 9.4</td>
<td>43.3± 7.4</td>
</tr>
<tr>
<td>Sex (female), n (%)</td>
<td>68 (70.8)</td>
<td>27 (93.1)</td>
<td>23 (88.5)</td>
<td>17 (73.9)</td>
<td>20 (90.9)</td>
<td>3 (100)</td>
</tr>
<tr>
<td>Disease duration (x years ± SD)</td>
<td>11.2 ± 7.5</td>
<td>8 ± 8.5</td>
<td>7.3 ± 6.5</td>
<td>6.4 ± 7</td>
<td>8.2 ± 5.5</td>
<td>5 ± 3</td>
</tr>
<tr>
<td>Tabaquism, n (%)</td>
<td>24 (25)</td>
<td>9 (31)</td>
<td>5 (19.2)</td>
<td>5 (21.7)</td>
<td>2 (9.1)</td>
<td>1 (33.3)</td>
</tr>
<tr>
<td>Smokers</td>
<td>30 (31.3)</td>
<td>4 (13.8)</td>
<td>5 (19.2)</td>
<td>1 (4.3)</td>
<td>4 (18.2)</td>
<td>-</td>
</tr>
<tr>
<td>Former smokers</td>
<td>42 (43.7)</td>
<td>16 (55.2)</td>
<td>16 (61.5)</td>
<td>17 (73.9)</td>
<td>16 (72.7)</td>
<td>-</td>
</tr>
<tr>
<td>Never smokers</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pleuropulmonary involvement as first manifestation of CTD, n (%)</td>
<td>6 (6.3)</td>
<td>2 (6.9)</td>
<td>4 (15.4)</td>
<td>2 (8.7)</td>
<td>5 (22.7)</td>
<td>-</td>
</tr>
<tr>
<td>Symptoms, n (%)</td>
<td>38 (39.6)</td>
<td>8 (27.6)</td>
<td>14 (53.8)</td>
<td>8 (34.8)</td>
<td>9 (40.9)</td>
<td>1 (33.3)</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>36 (37.5)</td>
<td>12 (41.4)</td>
<td>13 (50)</td>
<td>9 (39.1)</td>
<td>13 (59.1)</td>
<td>1 (33.3)</td>
</tr>
<tr>
<td>Cough</td>
<td>12 (12.5)</td>
<td>1 (3.4)</td>
<td>1 (3.8)</td>
<td>1 (4.3)</td>
<td>2 (9.1)</td>
<td>-</td>
</tr>
<tr>
<td>Sputum production</td>
<td>8 (8.3)</td>
<td>4 (13.8)</td>
<td>-</td>
<td>-</td>
<td>1 (4.5)</td>
<td>-</td>
</tr>
<tr>
<td>Chest pain</td>
<td>12 (12.5)</td>
<td>7 (24.1)</td>
<td>1 (3.8)</td>
<td>1 (4.3)</td>
<td>2 (9.1)</td>
<td>2 (66.7)</td>
</tr>
<tr>
<td>Fever</td>
<td>10 (34.5)</td>
<td>23 (88.5)*</td>
<td>4 (17.4)</td>
<td>2 (9.1)</td>
<td>2 (66.7)</td>
<td></td>
</tr>
<tr>
<td>Laboratory</td>
<td>41±31.5</td>
<td>39.6±28.5</td>
<td>50.5±16.9</td>
<td>38.4±30</td>
<td>32.8±30</td>
<td>38±25.5</td>
</tr>
<tr>
<td>ESR (x mm/h ± SD)</td>
<td>2.3±3.7</td>
<td>2.3±2.7</td>
<td>1.7± 2.8</td>
<td>4.2±7.5</td>
<td>3.7±5.7</td>
<td>1.2±0.8</td>
</tr>
<tr>
<td>RCP (x ± SD)</td>
<td>3(3.1)</td>
<td>20 (69)*</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Hypocomplementemia, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HRCT findings, n (%)</td>
<td>28 (29.2)*</td>
<td>1 (3.4)</td>
<td>4 (15.4)</td>
<td>4 (17.4)</td>
<td>4 (18.2)</td>
<td>1 (33.3)</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>18 (18.8)</td>
<td>2 (6.9)</td>
<td>4 (15.4)</td>
<td>2 (8.7)</td>
<td>3 (13.6)</td>
<td>1 (33.3)</td>
</tr>
<tr>
<td>Bronchiolitis</td>
<td>8 (8.3)</td>
<td>10 (34.5)*</td>
<td>-</td>
<td>1 (4.3)</td>
<td>1 (4.5)</td>
<td>-</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>9.9 4</td>
<td>2 (7.7)</td>
<td>2 (8.7)</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Pleural thickening</td>
<td>8 (8.3)</td>
<td>4 (13.8)</td>
<td>4 (15.4)</td>
<td>3 (13)</td>
<td>2 (9.1)</td>
<td>-</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>2 (2.1)</td>
<td>5 (17.3)</td>
<td>1 (3.8)</td>
<td>1 (4.3)</td>
<td>1 (4.5)</td>
<td>-</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>-</td>
<td>6 (20.7)</td>
<td>18 (69.2)*</td>
<td>2 (8.7)</td>
<td>5 (22.7)</td>
<td>2 (66.7)</td>
</tr>
<tr>
<td>Esophageal dilatation</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1 (4.5)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Diaphragmatic elevation</td>
<td>12 (12.5)</td>
<td>8 (27.6)</td>
<td>12 (46.2)*</td>
<td>4 (17.4)</td>
<td>2 (9.1)</td>
<td>2 (66.7)</td>
</tr>
<tr>
<td>PAH</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autoantibodies, n (%)</td>
<td>83 (86.5)*</td>
<td>7 (24)</td>
<td>2 (7.7)</td>
<td>3 (13)</td>
<td>7 (31.8)</td>
<td>-</td>
</tr>
<tr>
<td>RF</td>
<td>5 (5.2)</td>
<td>29 (100)*</td>
<td>26 (100)*</td>
<td>13 (56.5)</td>
<td>11 (50)</td>
<td>-</td>
</tr>
</tbody>
</table>
The mean age was 58 years (range 18-84, SD ± 15.5) with a female predominance in all groups. In 10% of cases pleuropulmonary involvement was the first manifestation of CTD. HRCT findings and ILD patterns are shown in table 1 and 2 respectively.

Table 2. HRCT findings in CTD.
Interstitial lung disease (ILD) was observed in 55.3% of patients.

There was a higher frequency of bronchiectasis in RA, esophageal dilation in SSc and pleural effusion in SLE (p <0.05).

Pleurale involvement was the most frequent manifestation in SLE (48.3%) and esophageal involvement in SSc (69.2%).

In RA we observed bronchial involvement in 47.9% of patients and pleural in 17.7%. 43.8% of the patients with RA presented ILD; usual interstitial pneumonia (UIP) was the most frequent pattern in 52.4% followed by non-specific interstitial pneumonia (NSIP) in 40.5% and cryptogenic Organizing Pneumonia (COP) in 7.1%. All patients with RA and ILD in our sample had positive rheumatoid factor (RF). Only 2 patients with RA had rheumatoid nodules.

NSIP was the most frequent pattern of ILD in the remaining CTD (37.9% in SLE, 34.6% in SSc, 65.2% in IM, 45.5% pSS and 33.3% in MCTD).

Tomographic signs of pulmonary arterial hypertension (PAH) were evidenced in 40 patients, 30% with RA and 30% SSc. A statistically significant association was found between PAH and SSc (p = 0.0) and among the findings of PAH in HRCT and SD pattern in capillaroscopy (p = 0.01).

Conclusion:

Intrathoracic manifestations are common in patients with CTD. A comprehensive knowledge of the pleuropulmonary involvement in CTD is important, because the prognosis and optimal therapy differ for each presentation.

Disclosure: D. Baenas, None; M. Orozco, None; M. E. Olmos, None; L. Lasca, None; P. Riba, None; P. Muszinsky, None; J. P. Pirola, None; V. Saurit, None; A. Alvarellos, None; A. C. Alvarez, None; S. Retamozo, None; N. Riscanevo, None; J. Flores, None; A. Blu, None; A. M. López, None; G. Muño, None; S. Orozco, None; F. Caeiro, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/intrathoracic-manifestations-of-connective-tissue-diseases-on-high-resolution-computed-tomography

Abstract Number: 2009

Quantitative Radiographic Analysis of Interstitial Lung Disease Associated with Rheumatoid Arthritis

Jeong Seok Lee1, Hyun J. Grace Kim2, Jonathan Goldin3, Wonho Lee1, You-Jung Ha4, Eun Ha Kang4, Yun Jong Lee5, Yeong Wook Song6 and Eun Young Lee7, 1Division of Rheumatology, Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea, Republic of (South), 2Department of Radiology, David Geffen School of Medicine at UCLA, Los Angeles, CA, 3University of
SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Imaging of Rheumatic Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Quantitative analysis of fibrotic patterns provides an objective measurement of treatment efficacy in interstitial lung disease (ILD). We aimed to measure the extent of ILD in rheumatoid arthritis (RA) patients by computer-aided analysis of high-resolution chest CT (HRCT), and to identify correlation with the visual assessment by radiologist and results of pulmonary function test (PFT).

Methods: Twenty-six RA patients with ILD who had two HRCTs with matched PFT result within 3 months were enrolled in this retrospective study. Demographic, clinical, laboratory information were obtained through a medical chart review. Quantitative analysis of HRCT image was conducted by the Radiology Core at University of California at Los Angeles. Quantitation was expressed as parameters in detail such as ground-glass opacity (QGG), lung fibrosis (QLF), honeycombing (QHC), and their summation (QILD).

Results: Baseline demographics and clinical characteristics of the patients with rheumatoid arthritis-associated interstitial lung disease were not different when analyzed by interval progression evaluated by radiologist, except for body mass index (progressive group 20.0±3.7; non-progressive group 25.5±3.6 kg/m², P = 0.001), time interval between HRCTs (progressive group 2.0±1.2; non-progressive group 1.1±0.6 years, P = 0.047), and all-cause mortality (progressive group 50.0%; non-progressive group 7.1%, P = 0.031). Negative correlation between PFT results and QILD scores at whole lung or zone of maximal involvement were significant (Fig. 1). Correlation between the evaluation of radiologist and QILD scores at whole lung was significant on QLF score (progressive group 3.38±4.15; non-progressive group -1.01±2.64, P = 0.004) (Fig. 2). More involvement of ILD on upper and middle zone of lung (versus lower zone) would predict progression of ILD (Fig. 3).

Conclusion: QILD score provides reliable estimate of ILD status and prognosis in RA patients when compared to PFT and assessment of radiologist.
Figure 1. Correlation between PFT results and QILD scores at whole lung (WL) and zone of maximal involvement (ZMI) (p: Spearman's rho)

(A) p=0.478, P=0.014
(B) p=0.268, P=0.140
(C) p=0.523, P=0.006
(D) p=0.433, P=0.027
(E) p=0.567, P=0.002
(F) p=0.442, P=0.024
(G) p=0.667, P<0.001
(H) p=0.634, P=0.001

Figure 2. Correlation between the evaluation of radiologist and QILD scores at whole lung (P: progressive, NP: nonprogressive, Mann-Whitney test)

(A) P=0.106
(B) P=0.004
Does PET CT Matter in Assessing Extent of Disease in Relapsing Polychondritis – a Single Center Pilot Study

Aman Sharma¹, Adarsh MB², Shankar Naidu³, Varun Dhir⁴, Roshan Verma⁵, Rajender Bashier⁵, Anish Bhattacharya⁶, Sanjay Jain⁷ and B R Mittal⁶, ¹Internal Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh, India, ²Internal Medicine, PGIMER, Chandigarh, India, ³PGIMER, cHANDIGARH, India, ⁴Internal Medicine (Rheumatology Unit), Postgraduate Institute of Medical Education and Research, Chandigarh, India, ⁵PGIMER, Chandigarh, India, ⁶Nuclear Medicine, PGIMER, Chandigarh, India, ⁷PGIMER, CHANDIGARH, India

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Imaging of Rheumatic Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Relapsing polychondritis(RP) is a rare rheumatic disease involving cartilaginous and proteoglycan rich structures. Clinical examination and radiological investigations have limitations in assessing the extent of disease. The study was done to evaluate the role of 18F-FDG PET CT in RP.

Methods:

Thirteen patients who underwent PET CT examination for evaluation of the extent of the disease were included. The diagnosis of RP was made according to Damiani and Levine’s modification of McAdam’s criteria. PET CT was done at the time of diagnosis in 11 patients and at disease relapse in two. The FDG uptake along with CT findings were recorded. A follow up PET was done in 3 patients.
Results:

The details of findings are given in Table 1. Mean age was 36.8±12.9 yrs with a Male:Female ratio of 6:7. Out of 12 patients with aural pain/tenderness 5 had increased FDG uptake (SUV max 1.2-8.0) and it was bilateral in all. This gap between clinical findings and FDG uptake may be due to initiation of immunosuppressive therapy before the PET CT as necessitated by the clinical presentation. Non FDG avid thickening of ear was noted in one. Eustachian tube was involved in two patients. Of 8 patients with nasal pain/tenderness only 5 had increased uptake. Of the 4 patients with saddle nose deformity, only one had increased PET uptake in nasal cartilage. Increased FDG uptake was noted in tracheal cartilage in 2 and main bronchus in 4(SUV max 1.6-4.8). Out of four patients with increased FDG uptake in bronchi, three were symptomatic with stridor and breathlessness. Three patients had non FDG avid bronchial thickening on CT. One patient had asymptomatic involvement of aorta, superior mesenteric artery and renal arteries. Two patients with scleritis showed increased uptake in three or more sites. All the three patients on follow up PET showed a response to treatment with all showing persistent thickening with no uptake in involved sites.

Conclusion:

FDG PET is useful in assessing disease extent and picking up involvement in areas not accessible to clinical examination like airways and internal blood vessels. It is also useful in assessing treatment response in these patients

Table 1: showing the clinical characteristics, PET CT abnormalities and treatment outcomes in patients with relapsing polychondritis
<table>
<thead>
<tr>
<th>No</th>
<th>Age</th>
<th>Sex</th>
<th>Clinical symptoms and examination findings</th>
<th>PET abnormalities (SUV)</th>
<th>CT finding</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ear nose throat</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Airway</td>
<td>Other areas</td>
</tr>
<tr>
<td>1</td>
<td>46</td>
<td>F</td>
<td>Collapsed nasal bridge, ear pain and tenderness, laryngeal tenderness, Stridor</td>
<td>None</td>
<td>Trachea(2.3), both main bronchi (1.6)</td>
</tr>
<tr>
<td>2</td>
<td>45</td>
<td>M</td>
<td>Ear pain, scleritis, nasal pain, joint pain, ear tenderness, nasal bridge collapse</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>3</td>
<td>26</td>
<td>F</td>
<td>Ear and nasal pain, cough, ear tenderness, laryngeal tenderness</td>
<td>Both ear(1.2 and 1.4), nasal(1.8)</td>
<td>None</td>
</tr>
<tr>
<td>4</td>
<td>33</td>
<td>F</td>
<td>Ear pain, joint pain, ear tenderness, nasal pain and tenderness</td>
<td>Nasal(3.5)</td>
<td>None</td>
</tr>
<tr>
<td>5</td>
<td>58</td>
<td>M</td>
<td>Ear pain, ear tenderness, nasal pain and tenderness</td>
<td>Both ear(4.4 and 4.4), nasal(4.0)</td>
<td>None</td>
</tr>
<tr>
<td>6</td>
<td>21</td>
<td>F</td>
<td>Ear, nasal pain and tenderness, nasal bridge collapse, joint pain, tracheal tenderness, scleritis</td>
<td>Nasal(4.1)</td>
<td>Trachea (3.3), bronchii (4.4)</td>
</tr>
<tr>
<td>7</td>
<td>37</td>
<td>F</td>
<td>Ear and nasal pain, joint pain, ear and laryngeal tenderness, SNHL</td>
<td>Left Eustachian tube(3.8)</td>
<td>Main bronchi (2.7)</td>
</tr>
<tr>
<td>8</td>
<td>32</td>
<td>F</td>
<td>Ear and nasal pain, stridor, cough, ear and laryngeal tenderness, SNHL</td>
<td>Left eustachian tube (5.9)</td>
<td>Right bronchus (4.3)</td>
</tr>
<tr>
<td>9</td>
<td>28</td>
<td>M</td>
<td>Ear pain and tenderness</td>
<td>Both ears (1.2 and 1.1)</td>
<td>None</td>
</tr>
<tr>
<td>10</td>
<td>24</td>
<td>M</td>
<td>Ear pain and tenderness</td>
<td>Both ears (1.3, 1.2), cricoid (3.2)</td>
<td>None</td>
</tr>
<tr>
<td>11</td>
<td>55</td>
<td>F</td>
<td>Stridor on follow up</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>12</td>
<td>52</td>
<td>M</td>
<td>SNHL, vertigo,</td>
<td>Nasal(3.5)</td>
<td>None</td>
</tr>
<tr>
<td>#</td>
<td>Sex</td>
<td>Ear, splenic infarcts</td>
<td>None</td>
<td>None</td>
<td>Normal</td>
</tr>
<tr>
<td>----</td>
<td>------</td>
<td>-----------------------</td>
<td>------</td>
<td>------</td>
<td>--------</td>
</tr>
<tr>
<td>13</td>
<td>M</td>
<td>Ear pain, nasal pain redness, hoarseness of voice, dermatomyositis</td>
<td>Ear(8.0), vocal cord(13.0)</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

M= Male, F= Female, SNHL= Sensorineural hearing loss

Disclosure: A. Sharma, None; A. MB, None; S. Naidu, None; V. Dhir, None; R. Verma, None; R. Basher, None; A. Bhattacharya, None; S. Jain, None; B. R. Mittal, None.


**Assessment of Methods to Quantitatively Evaluate Global Synovitis Activity with FDG-PET/CT**

William Y. Raynor¹, Venkata S. Jonnakuti¹, Kaiyuan Zheng¹, Poul Flemming Høiland-Carlsen², Abass Alavi³ and Joshua Baker⁴, ¹Radiology, University of Pennsylvania, Philadelphia, PA, ²Nuclear Medicine, Odense University Hospital, Odense, Denmark, ³Department of Radiology/Division of Nuclear Medicine, University of Pennsylvania, Philadelphia, PA, ⁴Rheumatology, University of Pennsylvania, Philadelphia, PA

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Imaging of Rheumatic Diseases Poster II

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**
Fluorodeoxyglucose (FDG)-positron emission tomography (PET) allows more direct assessment of inflammation than other imaging modalities by portraying metabolic activity. No standards exist for objective quantification of joint activity using PET, and many techniques rely on subjective initial assessments and use of a sample of voxels such as SUVmax or SUVpeak to characterize an entire region. The aim of this study was to compare the accuracy and reliability of novel methods of assessing global synovitis activity in patients with rheumatoid arthritis (RA) and healthy controls.

**Methods:**

FDG-PET/CT scans were performed on 19 RA patients and compared to 19 asymptomatic age- and sex-matched control subjects using similar acquisition methods. Several methods of quantification were performed. Method A used a traditional subjective approach to only measure ÒactiveÓ joints and an adaptive thresholding algorithm with a lower threshold defined as 40% of the SUVmax in selected joints. Methods B utilized the average SUVmax in control subjects as a lower threshold to exclude only the expected background uptake (separately for each joint type). For both methods, the sum of the partial volume-corrected mean metabolic volume product (cMVPmean) for all ROIs represented the global synovitis score for each subject. RA patients were compared to controls and correlations with clinical indicators of disease activity were assessed among RA patients.

**Results:**

Method B demonstrated superior inter-reader reliability ($r = 0.982$) compared to method A ($r = 0.636$). Patients with RA had much higher PET global activity scores than controls regardless of method (Figure). Method B correlated strongly with more objective clinical measures of systemic inflammation and disease activity. Method B also generally correlated more strongly with modified disease activity (M-DAS28) scores that exclude subjective components, compared to traditional disease activity scores (Table).
Conclusion:

For quantification of synovial inflammation by PET/CT, a method of thresholding that eliminates calculated background activity is more accurate and reliable than methods that depend on the assessment of subjectively active joints using focal measurements. Further studies are needed to determine how these methods of quantification perform in longitudinal assessments to assess course of the disease and the effects of various interventions.

Table 1: Correlation of PET quantification methods with clinical and laboratory features of disease activity and inflammation.

<table>
<thead>
<tr>
<th>Method A</th>
<th>Method B</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP</td>
<td>0.16</td>
</tr>
<tr>
<td>ESR</td>
<td>0.17</td>
</tr>
<tr>
<td>Swollen Joints</td>
<td>0.17</td>
</tr>
<tr>
<td>Tender Joints</td>
<td>0.17</td>
</tr>
<tr>
<td>Patient Global</td>
<td>-0.23</td>
</tr>
<tr>
<td>Evaluator Global</td>
<td>-0.032</td>
</tr>
<tr>
<td>IL-6 Levels</td>
<td>0.073</td>
</tr>
<tr>
<td>TNF-levels</td>
<td>-0.31</td>
</tr>
<tr>
<td>IL-1 levels</td>
<td>0.34</td>
</tr>
<tr>
<td>Disease Activity</td>
<td>0.15</td>
</tr>
<tr>
<td>DAS28(CRP)</td>
<td>0.27</td>
</tr>
<tr>
<td>M-DAS</td>
<td>0.076</td>
</tr>
</tbody>
</table>

*p<0.10; **p<0.05

Disclosure: W. Y. Raynor, None; V. S. Jonnakuti, None; K. Zheng, None; P. F. Høilund-Carlsen, None; A. Alavi, None; J. Baker, None.


Abstract Number: 2012
First Description of Tenosynovitis Prevalence in a Large Cohort of ACPA-Positive Patients

Gisela Eugénio1,2,3, Kulveer Mankia3,4, Peta Pentony2,3, Jackie L. Nam2,3, Laura Hunt2,3, Hanna Gul2,3, Richard J. Wakefield2,3 and Paul Emery3,5

1Rheumatology, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal, 2Leeds Teaching Hospitals NHS Trust, NIHR Leeds Musculoskeletal Biomedical Research Unit, Leeds, United Kingdom, 3University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom, 4Rheumatology, Leeds Teaching Hospitals NHS Trust, NIHR Leeds Musculoskeletal Biomedical Research Unit, Leeds, United Kingdom, 5NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Imaging of Rheumatic Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Tenosynovitis has been regarded as a feature of RA, although its true prevalence in early stages has not been firmly established. The aim of this work was to evaluate US findings of tenosynovitis in a cohort of ACPA+ patients.

Methods:

Consecutive ACPA+ patients, without clinical synovitis (CS), underwent US of 9-paired tendons and 24-paired joints. Baseline assessment included: 1) demographic/clinical characteristics, 2) extensor carpi ulnaris and flexor tendons gray-scale (GS) and power-doppler (PD), 3) joint GS, PD and erosions. US findings were assessed with the OMERACT semi-quantitative score. χ²/Fisher’s exact test for categorical and Student-t test/Mann-Whitney for continuous variables, were used to identify differences regarding the prevalence of US tenosynovitis, synovitis or progression to CS.

Results:

A total of 146 individuals were included (71% women, mean(SD) age of 50(14) years) with 17 (11.6%) progressing to CS (all RA). This was predicted by the duration of early morning stiffness (p<.01), presence of shared epitope (p=.02) and high titres of RF(p<.01) and anti-CCP (p<.01) (table 1). The median (IQR) time to progression of CS was 6.5 (4.3-10.5) months.

Twenty subjects (13.7%) had changes of GS and/or PD tenosynovitis, the majority classified as GS=1. A positive trend was found towards the progression to CS [OR (95%)=3.2 (1.0-10.2), p=.06]. The same association was seen between US synovitis and CS, with higher OR when PD was ≥2 [OR(95%)=4.2 (0.7-24.7), p=.15] (table 2).

Of those 20 individuals, 7 had concomitant US synovitis in the respective anatomical joints. Even though a correlation between significant US synovitis (GS≥2 and/or PD≥1) and tenosynovitis (any finding) was not found, an association was seen for the subgroup of patients who presented only with PD synovitis [OR (95%CI)=4.5 (1.4-14.0), p=.01]. This was reinforced when only PD≥2 synovitis was considered [OR (95%CI)=15.5 (2.6-91.5), p<.01]. Tenosynovitis was anatomically separate to synovitis with one exception.

Finally, tenosynovitis was not significantly associated with any of the demographic or clinical characteristics.

Conclusion:

To our knowledge this is the first study to assess tenosynovitis in a large cohort of ACPA+ patients; a low prevalence and a positive trend towards the progression to CS were found. The low prevalence of progression to CS and the absence of its association with US synovitis may suggest that this could represent the earliest stage of disease. Further studies with larger samples and with other methods (e.g. MRI) are warranted to confirm these results.
Table 1. Baseline demographic and clinical characteristics of ACPA+ individuals and those with progression to CS

<table>
<thead>
<tr>
<th></th>
<th>Total patients (n=146)</th>
<th>Patients with progression to CS (n=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Years (mean (SD))</td>
<td>49.94 (14.12)</td>
<td>55.15 (16.03)</td>
</tr>
<tr>
<td>Gender</td>
<td>Female 71.2% (104/146)</td>
<td>58.8% (10/17)</td>
</tr>
<tr>
<td>Symptom duration Months (median (IQR))</td>
<td>14.33 (7.42-60.23)</td>
<td>12.43 (5.33-59.90)</td>
</tr>
<tr>
<td>Sudden symptom onset Yes</td>
<td>38.1% (51/134)</td>
<td>41.2% (7/17)</td>
</tr>
<tr>
<td>EMS Minutes (median (IQR))</td>
<td>0.00 (0.00-52.50)</td>
<td>60.00 (2.50-120.00)</td>
</tr>
<tr>
<td>FDR with RA Yes</td>
<td>20.5% (30/146)</td>
<td>29.4% (5/17)</td>
</tr>
<tr>
<td>BMI Kg/m² (mean (SD))</td>
<td>28.99 (6.05)</td>
<td>29.11 (7.22)</td>
</tr>
<tr>
<td>Smoker Ever</td>
<td>60.2% (80/133)</td>
<td>76.5% (13/17)</td>
</tr>
<tr>
<td>Alcohol consumer Yes</td>
<td>60.0% (78/130)</td>
<td>76.5% (13/17)</td>
</tr>
<tr>
<td>No. of painful joints 0 to 18 (median (IQR))</td>
<td>4 (2-8)</td>
<td>5 (3-8)</td>
</tr>
<tr>
<td>Localization of patient-reported joint symptoms</td>
<td>None 9.6% (13/136)</td>
<td>11.8% (2/17)</td>
</tr>
<tr>
<td></td>
<td>Small joints only 16.9% (23/136)</td>
<td>23.5% (4/17)</td>
</tr>
<tr>
<td></td>
<td>Large joints only 11.0% (15/136)</td>
<td>0% (0/17)</td>
</tr>
<tr>
<td></td>
<td>Small and large joints 62.5% (85/136)</td>
<td>65.7% (11/17)</td>
</tr>
<tr>
<td>Localization of patient-reported joint symptoms in extremities</td>
<td>None 9.6% (13/136)</td>
<td>11.8% (2/17)</td>
</tr>
<tr>
<td></td>
<td>Upper only 14.7% (20/136)</td>
<td>11.8% (2/17)</td>
</tr>
<tr>
<td></td>
<td>Lower only 12.5% (17/136)</td>
<td>0% (0/17)</td>
</tr>
<tr>
<td></td>
<td>Upper and lower 63.2% (86/136)</td>
<td>76.5% (13/17)</td>
</tr>
<tr>
<td>Symmetry of patient-reported joint symptoms</td>
<td>None 9.6% (13/136)</td>
<td>11.8% (2/17)</td>
</tr>
<tr>
<td></td>
<td>Symmetrical 65.4% (89/136)</td>
<td>64.7% (11/17)</td>
</tr>
<tr>
<td></td>
<td>Asymmetrical 25.0% (34/136)</td>
<td>23.5% (4/17)</td>
</tr>
<tr>
<td>No. of tender joints TJC28 (median (IQR))</td>
<td>0 (0-2)</td>
<td>1 (0-4)</td>
</tr>
<tr>
<td></td>
<td>RAI (median (IQR))</td>
<td>0 (0-3)</td>
</tr>
<tr>
<td>Localization of clinical joint tenderness</td>
<td>None 46.2% (66/143)</td>
<td>29.4% (5/17)</td>
</tr>
<tr>
<td></td>
<td>Small joints only 29.4% (42/143)</td>
<td>47.1% (8/17)</td>
</tr>
<tr>
<td></td>
<td>Large joints only 10.5% (15/143)</td>
<td>0% (0/17)</td>
</tr>
<tr>
<td></td>
<td>Small and large joints 14.0% (20/143)</td>
<td>23.5% (4/17)</td>
</tr>
<tr>
<td>Localization of clinical joint tenderness in extremities</td>
<td>None 46.2% (66/143)</td>
<td>29.4% (5/17)</td>
</tr>
<tr>
<td></td>
<td>Upper only 21.0% (30/143)</td>
<td>23.5% (4/17)</td>
</tr>
<tr>
<td></td>
<td>Lower only 11.2% (16/143)</td>
<td>5.9% (1/17)</td>
</tr>
<tr>
<td></td>
<td>Upper and lower</td>
<td>Symmetry of clinical joint tenderness</td>
</tr>
<tr>
<td>--------------------------</td>
<td>----------------</td>
<td>--------------------------------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Symmetrical</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Asymmetrical</td>
</tr>
<tr>
<td></td>
<td></td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td>One copy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Two copies</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Low positive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High positive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Low positive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High positive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td>One copy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Two copies</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Low positive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High positive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td>One copy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Two copies</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Low positive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High positive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td>One copy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Two copies</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Low positive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High positive</td>
</tr>
</tbody>
</table>

CS: clinical synovitis; EMS: early morning stiffness; FDR: first degree relative; RA: Rheumatoid Arthritis; BMI: body mass index; RF: rheumatoid factor; hsCRP: high sensitivity C-reactive protein; ESR: erythrocyte sedimentation rate; VAS: visual analogue scale; PGA-GH: patient global assessment; HAQ-DI: health assessment questionnaire disability index. The status of high-level RF or anti-CCP was defined according to the American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) 2010 criteria by a cut-off level of > 3 timed the upper limit of normal. hsCRP was performed and levels ≥ 2mg/l, which have been associated with disease activity in RA, were considered positive.
Table 2. Tendon and joint US findings at baseline regarding individual and tendon/joint-level evaluation

<table>
<thead>
<tr>
<th>Tendon US findings according to individual-level n=146</th>
<th>Tendon US findings according to tendon-level n= 2628</th>
</tr>
</thead>
<tbody>
<tr>
<td>All tendons included in maximum score - n(%)</td>
<td>All tendons included- n(%)</td>
</tr>
<tr>
<td>GS=0</td>
<td>GS=0</td>
</tr>
<tr>
<td>126 (86.30%)</td>
<td>2581 (98.21%)</td>
</tr>
<tr>
<td>GS=1</td>
<td>GS=1</td>
</tr>
<tr>
<td>18 (12.33%)</td>
<td>42 (1.60%)</td>
</tr>
<tr>
<td>GS≥2</td>
<td>GS≥2</td>
</tr>
<tr>
<td>2 (1.37%)</td>
<td>5 (0.19%)</td>
</tr>
<tr>
<td>PD=0</td>
<td>PD=0</td>
</tr>
<tr>
<td>142 (97.26%)</td>
<td>2616 (99.54%)</td>
</tr>
<tr>
<td>PD=1</td>
<td>PD=1</td>
</tr>
<tr>
<td>2 (1.37%)</td>
<td>10 (0.38%)</td>
</tr>
<tr>
<td>PD=2</td>
<td>PD=2</td>
</tr>
<tr>
<td>2 (1.37%)</td>
<td>2 (0.08%)</td>
</tr>
<tr>
<td>Joint US findings according to individual-level n=146</td>
<td>Joint US findings according to joint-level n= 7008</td>
</tr>
<tr>
<td>All joints included in maximum score - n(%)</td>
<td>All joints included- n(%)</td>
</tr>
<tr>
<td>GS=0</td>
<td>GS=0</td>
</tr>
<tr>
<td>8 (5.48%)</td>
<td>6111 (87.20%)</td>
</tr>
<tr>
<td>GS=1</td>
<td>GS=1</td>
</tr>
<tr>
<td>39 (26.71%)</td>
<td>535 (7.63%)</td>
</tr>
<tr>
<td>GS≥2</td>
<td>GS≥2</td>
</tr>
<tr>
<td>99 (67.81%)</td>
<td>362 (5.17%)</td>
</tr>
<tr>
<td>PD=0</td>
<td>PD=0</td>
</tr>
<tr>
<td>128 (87.67%)</td>
<td>6972 (99.49%)</td>
</tr>
<tr>
<td>PD=1</td>
<td>PD=1</td>
</tr>
<tr>
<td>11 (7.53%)</td>
<td>20 (0.29%)</td>
</tr>
<tr>
<td>PD=2</td>
<td>PD=2</td>
</tr>
<tr>
<td>7 (4.79%)</td>
<td>16 (0.23%)</td>
</tr>
<tr>
<td>ERO=0</td>
<td>ERO=0</td>
</tr>
<tr>
<td>138 (94.52%)</td>
<td>6996 (99.83%)</td>
</tr>
<tr>
<td>ERO=1</td>
<td>ERO=1</td>
</tr>
<tr>
<td>8 (5.48%)</td>
<td>12 (0.17%)</td>
</tr>
<tr>
<td>MTPs excluded from maximum score- n(%)</td>
<td>MTPs excluded- n(%)</td>
</tr>
<tr>
<td>GS=0</td>
<td>GS=0</td>
</tr>
<tr>
<td>31 (21.23%)</td>
<td>5036 (90.77%)</td>
</tr>
<tr>
<td>GS=1</td>
<td>GS=1</td>
</tr>
<tr>
<td>71 (48.63%)</td>
<td>398 (7.17%)</td>
</tr>
<tr>
<td>GS≥2</td>
<td>GS≥2</td>
</tr>
<tr>
<td>44 (30.14%)</td>
<td>114 (2.05%)</td>
</tr>
<tr>
<td>PD=0</td>
<td>PD=0</td>
</tr>
<tr>
<td>132 (90.41%)</td>
<td>5519 (99.48%)</td>
</tr>
<tr>
<td>PD=1</td>
<td>PD=1</td>
</tr>
<tr>
<td>8 (5.48%)</td>
<td>14 (0.25%)</td>
</tr>
<tr>
<td>PD=2</td>
<td>PD=2</td>
</tr>
<tr>
<td>6 (4.11%)</td>
<td>15 (0.27%)</td>
</tr>
<tr>
<td>ERO=0</td>
<td>ERO=0</td>
</tr>
<tr>
<td>140 (95.89%)</td>
<td>5540 (99.86%)</td>
</tr>
<tr>
<td>ERO=1</td>
<td>ERO=1</td>
</tr>
<tr>
<td>6 (4.11%)</td>
<td>8 (0.14%)</td>
</tr>
</tbody>
</table>


Disclosure: G. Eugénio, None; K. Mankia, None; P. Pentony, None; J. L. Nam, None; L. Hunt, None; H. Gul, None; R. J. Wakefield, None; P. Emery, None.

Abstract Number: 2013

Physician Experience and Patient’s Disease Activity Affect the Impact of Musculoskeletal Ultrasound on the Treatment Decision in Rheumatoid Arthritis Patients

César Sifuentes-Cantú 1, Irazu Contreras-Yañez 2, Marvin Gutierrez 3 and Virginia Pascual-Ramos 4, 1Department of Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, 2Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico, Mexico, 3Rheumatology, Instituto Nacional de Rehabilitación, Mexico City, Mexico, 4Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Imaging of Rheumatic Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
In a real clinical setting of RA outpatients, we previously showed that musculoskeletal ultrasound (MUS) added to clinical evaluation impacted the treatment decision in 20% of the clinical scenarios evaluated; the impact was greater for the trainee in rheumatology (TR) than for the senior rheumatologist (SR). The aim of the present study was to explore if the results could be generalized to a higher number of physicians.

Methods:
The population of physicians consisted of 10 SR (mean age: 46.2± 12.7 years, 3 of them with 2-5 years of experience, 4 with 6-14 years and 3 >15 years) and 12 TR (median age: 30.8±1.3 years); 94% and 16.7% of the TR and the SR, respectively, referred theoretical MUS training.

10 clinical vignettes included data abstracted from 10 RA outpatients, randomly selected from an ongoing cohort. Each vignette was shared with 6 TR and 6 SR, who were asked to give a first treatment recommendation based on “traditional rheumatic assessments” and in a second step, to confirm or not their previous recommendation after MUS findings were incorporated to the rheumatic assessments.

Each vignette included the following data: in the first sheet, patient socio-demographic characteristics, comorbidities, extended disease activity evaluation, previous RA treatment, comorbid conditions treatment and a space for the first treatment recommendation; in the second sheet, MUS information and a space for eventual RA specific treatment changes (Figure).

Results:
Patients were middle-aged females (41.9±7 years old) with (mean±SD) disease duration of 7.5±3.4 years. Six of them had DAS28-ESR remission.

MUS added to the clinical evaluation induced a treatment modification in 26% of the 96 clinical scenarios evaluated, with similar percentage in TR (29.2%) and SR (22.9%), (p=0.64). Within SR, the lesser experienced rheumatologist (<15 years) changed their treatment proposal after MUS finding more frequently (44%) than those with ≥15 years of experience (0%, p=0.002); training in MUS did not impact treatment modifications.

MUS induced more treatment modifications in those clinical scenarios with DAS28-ESR active disease vs. remission patients 68% vs 32%, p=0.005. There was a higher (albeit not significant) percentage of disagreement in disease activity level between DAS28 and MUS in active vs. remission patients: 75% vs. 32.8%, p=0.51). Then, we identified 48 clinical scenarios (50%) with disagreement in disease activity as per DAS28 and per MUS; of them 18 (37.5%) were in DAS28-ESR remission and 30 had active disease; there were a higher percentage of treatment modifications after MUS information was incorporated to clinical data in active clinical scenarios vs. remission clinical scenarios: 43.3% vs. 11.1%, p=0.026.

Conclusion:
The impact of adding MUS to clinical evaluations in the treatment decision of RA patients is affected by physician experience and disease activity status.

**Disclosure:**
C. Sifuentes-Cantú, None; I. Contreras-Yañez, None; M. Gutierrez, None; V. Pascual-Ramos, None.


**Abstract Number:** 2014

**Reliability of 8-Joint Ultrasonography Scores in Follow up of Biological Therapy in Patients with Rheumatoid Arthritis**

Ying-Chou Chen Sr., Division of Allergy, Immunology and Rheumatology, Chang Gung Memorial Hospital, Kaohsiung, Taiwan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Imaging of Rheumatic Diseases Poster II

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

The use of biological agents, or biologics, has revolutionized the treatment of rheumatoid arthritis (RA). Using power Doppler ultrasound, this study to evaluate the comparative efficacy of biologics for refractory RA patients has been a trend. However, there were no standard exam to follow up on rheumatoid arthritis therapy. The primary objectives were to explore the associations between a comprehensive ultrasonographic (US) assessment of joints, tendons and bursae and previously described reduced joint counts (8-, 7-, 12-, 28) as well as to assess the sensitivity to change of these different US joint combinations during biological treatment.

**Methods:**

8-joint (bilateral elbow, wrist, MCP II and III) were involved in this study. 49 patients with rheumatoid arthritis (RA) were examined by US (B-mode (BM) and power Doppler (PD)) with use of a semi-quantitative (0 to 3) score of 34 joints, tendons/tendon groups at baseline and 1, 3, 6 and 12 months after initiating treatment with biological therapy. BM and PD scores for the different joint combinations were generated.

**Results:** The reduced 8-joint scores had high correlation coefficients with the 28-joint score at all examinations (range 0.87 to 0.94 for BM and 0.69 to 0.93 for PD, each P < 0.001) and sum BM and PD scores of all the different joint combinations improved significantly during follow-up (P ≤ 0.05 to 0.001).
Conclusion:

The reduced joint combinations were highly associated to the 28-joint score. Furthermore, all the joint combinations presently explored responded well to biological treatment. This indicates that an approach focusing on few joints and tendons gives equivalent information about the inflammatory activity in RA patients as a comprehensive US examination. The optimal combination of joints and tendons for a valid, reliable and feasible US measurement should be further explored to define a US score for follow-up of RA patients on biological treatment.

Table 1. Correlation coefficients between sum scores B mode (BM) of the different joint combinations

<table>
<thead>
<tr>
<th>BM 7-joint score</th>
<th>BM 12-joint score</th>
<th>BM 28-joint score</th>
</tr>
</thead>
<tbody>
<tr>
<td>BM 8-joint score</td>
<td>0.872/0.809</td>
<td>0.891/0.870</td>
</tr>
<tr>
<td>BM 7-joint score</td>
<td>0.873/0.845</td>
<td>0.908/0.886</td>
</tr>
<tr>
<td>BM 12-joint score</td>
<td></td>
<td>0.937/0.926</td>
</tr>
</tbody>
</table>

Table 2. Correlation coefficients between sum scores power Doppler (PD) of the different joint combinations

<table>
<thead>
<tr>
<th>PD 7-joint score</th>
<th>PD 12-joint score</th>
<th>PD 28-joint score</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD 8-joint score</td>
<td>0.883/0.696</td>
<td>0.921/0.811</td>
</tr>
<tr>
<td>PD 7-joint score</td>
<td>0.931/0.711</td>
<td>0.947/0.820</td>
</tr>
<tr>
<td>PD 12-joint score</td>
<td></td>
<td>0.956/0.896</td>
</tr>
</tbody>
</table>

Disclosure: Y. C. Chen Sr., None;


Abstract Number: 2015

Ultrasonographic Evaluation of Metacarpophalangeal Joints Can be Useful in the Differential Diagnosis of Early Rheumatoid Arthritis and Early Spondyloarthritis. A Monocentric Preliminary Study

Alberto Batticciotto¹, Giada Prato², Marco Antivalle², Maria Chiara Ditto¹, Maria Chiara Gerardi², Rossella Talotta², Federica Rigamonti², Fabiola Atzeni¹ and Piercarlo Sarzi-Puttini². ¹Rheumatology Unit, ASST Fatebenefratelli - Sacco, L.Sacco University Hospital, Milano, Italy, ²Rheumatology Unit, ASST Fatebenefratelli - Sacco, L. Sacco University Hospital, Milano, Italy

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Imaging of Rheumatic Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: A number of studies have demonstrated that musculoskeletal ultrasonography (MSUS) is more sensitive in diagnosing arthritis than clinical examination although, as underlined in a recent review, it remains controversial whether it can substantially improve discrimination in the setting of early arthritis (EA). In 2011, Gutierrez et al. published preliminary data showing a
The high frequency of peritenon extensor tendon inflammation in patients with psoriatic arthritis (PsA), thus suggesting the potentially important role of US in the differential diagnosis of rheumatoid arthritis (RA) and PsA at metacarpophalangeal (MCP) joint level, and recommending additional research in order to confirm these data. Aim was to compare MSUS findings at MCP joint level in patients with early RA and early spondyloarthritis (SpA).

Methods: We retrospectively selected 35 patients who had been definitely diagnosed as having RA (2010 ACR/EULAR criteria) or axial/peripheral SpA (2009 ASAS criteria) within one year of their first visit from a consenting cohort of EA patients attending our Rheumatology Department between November 2012 and July 2016. Their demographic, clinical data and baseline MCP/wrist MSUS assessment data were recorded during the patients’ first visit to our EA clinic by an experienced rheumatologist and a blinded experienced sonographer. All of the patients were scanned using an ESAOTE MyLAB 70 equipped with a 6-18 MHz linear array transducer, and the findings were scored in accordance with the OMERACT guidelines.

Results:
The MSUS data of 20 RA patients (17 females and three males; median age 59 years, range 35-83 years; median time to a definite diagnosis 2.4 months, range 1-11 months) and 15 SpA patients (nine females and six males; median age 53 years range, 18-78 years; median time to definite diagnosis 1.7 months, range 1-8 months) were retrospectively analysed. At the time of their first visit at the EA clinic, all of the patients had at least one MCP joint with synovial fluid and/or synovial hypertrophy with a grey scale (GS) score of >1, and there were no statistically significant differences in the percentages of patients presenting at least one power Doppler(PD)-positive joint (55% of RA and 53% of SpA patients; p= 0.92) and PD-positive tenosynovitis of the flexor tendons in at least one finger (10% of RA and 33% of SpA patients; p= 0.08). There was a statistically significant difference in the percentage of patients with erosion in at least one MCP (25% of RA and 0% of SpA patients; p=0.036) and in the percentage of patients with PD-positive paratenonitis of the extensor tendons in at least one finger (30% of RA and 80% of SpA patients; p= 0.003).

Conclusion: The patients with early RA showed a statistically higher percentage of erosions at the MCP MSUS evaluation of their first visit to the EA clinic than the patients with early SpA, who presented a higher percentage of PD-positive paratenonitis at the level of the extensor tendons than the patients with early RA. Larger studies are required to confirm the potential role of MCP MSUS in the differential diagnosis of early RA and early SpA.

Disclosure: A. Batticciotto, None; G. Prato, None; M. Antivalle, None; M. C. Ditto, None; M. C. Gerardi, None; R. Talotta, None; F. Rigamonti, None; F. Atzeni, None; P. Sarzi-Puttini, None.


Abstract Number: 2016

**Favourable Changes in Power Doppler Scores in the Feet over 1-Year in an Early Rheumatoid Arthritis Cohort: The Role of Rheumatoid Factor and Anti–Citrullinated Protein Antibody**

Karen A. Beatte1, Hanyan Zou2, George Ioannidis3 and Maggie Larche1, 1Medicine, McMaster University, Hamilton, ON, Canada, 2McMaster University, Hamilton, ON, Canada, 3St Joseph's Healthcare Hamilton, Hamilton, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Imaging of Rheumatic Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

MTP joints are seldom examined in routine clinical visits. As such, it is important to understand how the standard treatment of patients with early RA and their serological RF and ACPA status may affect active inflammation in the MTP joints. This study aimed to characterize 1) 1-year changes in power Doppler (PD) scores of patients with early RA treated as per standard of care, and 2) changes in PD scores based on serological RF and ACPA status.
Methods:

Patients with early RA (ACR criteria) were examined at baseline, 6 weeks, 3 months, 6 months and 1 year. At baseline, all patients were DMARD naïve and treated as per standard of care. Except in a few cases, initial treatment involved mainly MTX and occasionally LEF. For the purpose of this study, subgroup analyses were conducted for patients who were characterized as being seronegative for both RF and ACPA (-/-), or seropositive for both RF and ACPA (+/+). At each visit, a rheumatologist imaged the 2nd-5th MTP joints of both feet using US, and graded PD semiquantitatively (score 0-3 per joint, max. score=24/patient). Paired t-tests compared baseline and 1-year PD, and PD between serology groups.

Results:

Forty patients were enrolled [mean (SD) age=52.1(10.4) years, n=32 female]. At baseline, PD scores ranged from 0 to 17; at 1-year PD scores ranged from 0 to 5. Mean (SD) PD scores were significantly lower at 1-year [0.5 (1.1)] than baseline [2.3 (4.2)], p<0.05. Changes in the level of active inflammation developed rapidly: within 6 weeks, 8 patients improved (decreased PD≥2) and 5 patients worsened markedly (increased PD≥2). All except 1 of the patients who worsened improved by 3 months (patient stopped medication at 3 months, and improved once restarted). The mean baseline PD (SD) was significantly higher for +/+ patients [n=14, 5.3 (5.8)], than -/- patients [n=20, 0.5 (0.9)], p<0.05. Of all patients who maintained PD=0 at all visits (n=12), 8 were -/- and 3 were +/+. Of 14 patients who had PD≥5 at any visit, 9 were +/- and 1 was -/. In 20 patients who either maintained a low PD baseline score (±2 at each visit) or improved, serology was split (n=10 -/-, n=9 +/-). Patients who worsened (increased PD≥2) after baseline (n=6) were split on serology as well (n=2 +/-, n=2 +/+). The two groups of patients followed similar courses of treatment, and their responses were both favourable: 39 patients had inflammation controlled (PD≤3) at 1 year.

Conclusion:

Patients with early RA seropositive for RF and ACPA had, on average, more severe inflammation at baseline. However, serotype did not appear to affect patient response to standard initial treatment. Patients with severe inflammation at baseline and 6 weeks all improved by 3-6 months, and patients with low initial inflammation did not generally worsen, regardless of serology, and without considerable changes to treatment.

Disclosure: K. A. Beattie, None; H. Zou, None; G. Ioannidis, None; M. Larche, None.


Abstract Number: 2017
Prospective Study of Bio-Free Remission Maintenance Using Ultrasonography in Rheumatoid Arthritis Patients: 52-Week Result

Koichi Amano1, Kazutoshi Aoki2, Yoshiaki Kuga3, Koji Nishimura4, Hayato Nagasawa5, Takuma Tsuzuki Wada6, Kenji Takagi7, Junji Hayashi8, Motohide Kaneko9, Ryota Sakai10, Akiko Shibata11, Kentaro Chino11, Shuntaro Saito11, Ayumi Okuyama12, Tsunoo Kondo12, Hirofumi Takei12 and Toshihide Mimura13, 1Department of Rheumatology and Clinical Immunology, Saitama Medical Center, Saitama Medical University, Saitama, Japan, 2Aoki Clinic, Saitama, Japan, 3Wakaba Hospital, Sakado, Japan, 4internal medicine, Saitama Medical Center, Japan Community Health care Organization, Saitama, Japan, 5Nagasawa Clinic, Kawagoe, Japan, 6Department of Rheumatology and Applied Immunology, Faculty of Medicine, Saitama Medical University, Saitama, Japan, 7Rheumatology and Clinical Immunology, Higashi-Omiya General Hospital, Saitama, Japan, 8Orthopedic Surgery, Niizashiki Chuo General Hospital, Niiza, Japan, 9Kaneko Clinic, Kawaguchi, Japan, 10Microbiology and Immunology, Keio University School of Medicine, Tokyo, Japan, 11Rheumatology and Clinical Immunology, Saitama Medical Center, Saitama Medical University, Kawagoe, Japan, 12Department of Rheumatology and Clinical Immunology, Saitama Medical Center, Saitama Medical University, Saitama, Japan, 13Department of Rheumatology and Applied Immunology, Faculty of Medicine, Saitama Medical University, Saitama, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Imaging of Rheumatic Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Recently, a significant number of rheumatoid arthritis (RA) patients can reach low disease activity (LDA) by using biologics such as adalimumab. However biologics therapy can sometimes cause serious side-effects and is expensive. Therefore, it could be expedient to discontinue biologics after achieving sustained remission or LDA. Ultrasonography seems to be a good predictor of relapse in this respect in several studies. The PRIMULA (Prospective study of Remission Induction & Maintenance using ULtrasongraphy in rheumatoid Arthritis) study, is a multicenter prospective study to investigate if ultrasonography (US)-based evaluation could provide an additive value to composite measure-based evaluation for clinical relapse and radiological progression in RA patients who discontinued adalimumab after obtaining sustained LDA.

Methods: Thirty-one RA patients in sustained LDA (DAS28-CRP < 3.2 for more than 6 months) who had been receiving adalimumab plus MTX enrolled in the PRIMULA study were evaluated in this study. All patients underwent US evaluation of synovial hypertrophy (SH) and power Doppler (PD) signal presence. The joints were graded on grayscale (GS; 0-3) and power Doppler (PD; 0-3). Nineteen patients agreed to discontinue adalimumab and 12 continued. Trial visits were performed at week 13, 26, and 52. Modified total Sharp score (mTSS) was also evaluated at the enrollment and the end of study (at week 52). Relapse was defined when DAS28-CRP score elevated more than 3.2. The relationship between the integral value of each disease activity score (ESR, CRP, DAS28, SDAI, and US-SH and -PD score, etc.) and ΔmTSS (0-52w) was analysed.

Results:

Among the 19 discontinuation group patients, 8 cases relapsed during 1-year study period. There was no significant difference between the relapse group (n=8) and non-relapse group (n=11) in the baseline clinical composite measure (DAS28-CRP 1.3 vs. 1.3; p=0.68) and US score (GS and PD total score 3.4 vs. 3.5; p=0.64) (table 1). Only the integral value (0-52w) of CRP significantly correlated with ΔmTSS (0-52w) (r=0.617, p=0.006) (table 2).

Conclusion: In this study, US provided limited additional value as a tool to predict patients’ prognosis according to clinical disease activity and radiographic progression, after discontinuation of adalimumab in RA patients who achieved sustained LDA with adalimumab plus MTX.

Table 1. demographic and clinical characteristics at discontinuation
demographic and clinical characteristics | Discontinuation group | Wilcoxon rank sum test
---|---|---
age (years) | | 
n | mean | SD | n | mean | SD | 
---|---|---
n | 56.0 | 18.2 | 8 | 61.4 | 9.8 | 0.408

Disease duration (years) | | 
n | mean | SD | n | mean | SD | 
---|---|---|---|---|---|---|---|---
n | 9.4 | 12.9 | 8 | 8.5 | 6.6 | 0.386

MTX dose (mg/wk) | | 
n | mean | SD | n | mean | SD | 
---|---|---|---|---|---|---|---|---
n | 8.2 | 1.1 | 8 | 7.8 | 2.7 | 0.567

ESR (mm/hr) | | 
n | mean | SD | n | mean | SD | 
---|---|---|---|---|---|---|---|---
n | 13.1 | 9.0 | 8 | 13.6 | 6.9 | 0.620

CRP (mg/dl) | | 
n | mean | SD | n | mean | SD | 
---|---|---|---|---|---|---|---|---
n | 0.14 | 0.36 | 8 | 0.05 | 0.07 | 0.655

DAS28/4 ESR | | 
n | mean | SD | n | mean | SD | 
---|---|---|---|---|---|---|---|---
n | 1.7 | 0.6 | 8 | 1.9 | 0.4 | 0.364

DAS28/4 CRP | | 
n | mean | SD | n | mean | SD | 
---|---|---|---|---|---|---|---|---
n | 1.3 | 0.3 | 8 | 1.3 | 0.2 | 0.679

SDAI | | 
n | mean | SD | n | mean | SD | 
---|---|---|---|---|---|---|---|---
n | 1.2 | 0.6 | 8 | 2.1 | 1.3 | 0.230

CDAI | | 
n | mean | SD | n | mean | SD | 
---|---|---|---|---|---|---|---|---
n | 1.1 | 0.7 | 8 | 2.0 | 1.3 | 0.159

US total | | 
n | mean | SD | n | mean | SD | 
---|---|---|---|---|---|---|---|---
n | 3.5 | 3.5 | 8 | 3.4 | 4.7 | 0.643

US GS | | 
n | mean | SD | n | mean | SD | 
---|---|---|---|---|---|---|---|---
n | 2.0 | 1.9 | 8 | 2.0 | 3.0 | 0.583

US DP | | 
n | mean | SD | n | mean | SD | 
---|---|---|---|---|---|---|---|---
n | 1.5 | 1.8 | 8 | 1.4 | 1.7 | 0.863

MMP-3 (ng/ml) | | 
n | mean | SD | n | mean | SD | 
---|---|---|---|---|---|---|---|---
n | 85.5 | 106.5 | 8 | 42.0 | 13.1 | 0.591

RF | | 
n | mean | SD | n | mean | SD | 
---|---|---|---|---|---|---|---|---
n | 72.7 | 101.8 | 2 | 84.5 | 21.9 | 0.317

body weight (kg) | | 
n | mean | SD | n | mean | SD | 
---|---|---|---|---|---|---|---|---
n | 50.9 | 7.3 | 8 | 51.9 | 5.3 | 0.755

Erosion | | 
n | mean | SD | n | mean | SD | 
---|---|---|---|---|---|---|---|---
n | 28.1 | 67.3 | 4 | 15.4 | 12.5 | 0.084

JSN | | 
n | mean | SD | n | mean | SD | 
---|---|---|---|---|---|---|---|---
n | 21.5 | 45.9 | 4 | 12.9 | 10.3 | 0.392

mTSS | | 
n | mean | SD | n | mean | SD | 
---|---|---|---|---|---|---|---|---
n | 49.6 | 113.2 | 4 | 28.2 | 22.4 | 0.201

Table 2. Correlation between each integral value and △TSS

<table>
<thead>
<tr>
<th>N</th>
<th>Pearson's correlation R</th>
<th>Prob.</th>
</tr>
</thead>
<tbody>
<tr>
<td>US total</td>
<td>17</td>
<td>0.392</td>
</tr>
<tr>
<td>US GS</td>
<td>17</td>
<td>0.272</td>
</tr>
<tr>
<td>US PD</td>
<td>17</td>
<td>0.385</td>
</tr>
<tr>
<td>ESR</td>
<td>18</td>
<td>0.204</td>
</tr>
<tr>
<td>CRP</td>
<td>18</td>
<td>0.617</td>
</tr>
<tr>
<td>DAS28ESR</td>
<td>18</td>
<td>0.009</td>
</tr>
<tr>
<td>DAS28CRP</td>
<td>18</td>
<td>0.256</td>
</tr>
<tr>
<td>SDAI</td>
<td>18</td>
<td>0.274</td>
</tr>
<tr>
<td>CDAI</td>
<td>18</td>
<td>0.028</td>
</tr>
</tbody>
</table>

Disclosure: K. Amano, Abbvie, 5, Pfizer Inc, 5, Tanabe-Mitsubishi Pharma, 5, Astellas, 5, Janssen Pharmaceutica Product, L.P., 5, Daiichi-Sankyo, 5, Chugai, 5; K. Aoki, Abbvie, 5; Y. Kuga, Abbvie, 5; K. Nishimura, None; H. Nagasawa, None; T. T. Wada, None; K. Takagi, None; J. Hayashi, None; M. Kaneko, None; R. Sakai, None; A. Shibata, None; K. Chino, None; S. Saito, None; A. Okuyama, None; T. Kondo, None; H. Takei, None; T. Mimura, Abbvie, 5, Astellas, 5, Eisai, 5, Janssen Pharmaceutica Product, L.P., 5, Novartis Pharmaceutical Corporation, 5, Ono Pharma, 5, Pfizer Inc, 5, Sanofi-Aventis Pharmaceutical, 5, Takeda Pharmaceutical, 5, Tanabe-Mitsubishi Pharma, 5.


Abstract Number: 2018

A Novel Ultrasound Scoring System for the Pediatric Knee

Tracy Ting1, Patricia Vega-Fernandez2, Edward Oberle3, Deirdre De Ranieri3, Hulya Bukulmez5 and Johannes Roth6,
1Rheumatology/MLC 4010, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 2Pediatrics, Emory University School of
SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Imaging of Rheumatic Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Musculoskeletal ultrasound (MSUS) is increasingly being utilized in children. In order to provide objective assessments of arthritis, reliable scoring systems are needed. Yet, given the unique pediatric anatomy, adult scoring systems cannot simply be adapted for children. The aim of this study was to develop and assess reliability of a B-Mode and Doppler scoring system for arthritis in the pediatric knee.

Methods: As part of the Childhood Arthritis and Rheumatology Research Alliance (CARRA) ultrasound group, six pediatric rheumatologists developed a set of standard views of the knee relevant for the assessment of arthritis in children. This was done through a comprehensive literature review followed by a practical exercise and consensus process. Similarly, a B-mode and Doppler scoring system was developed through both literature review and consensus process and subsequently validated by several practical exercises on images that were obtained based on the previously agreed standard views. Agreement between raters was determined using two-way single score intraclass correlation coefficients (ICC).

Results: A total of 21 possible views/images to assess the presence of arthritis in children were identified. After evaluation of the proposed views during a practical exercise, a total of 3 views were chosen for each B-mode and Doppler in a subsequent consensus process, all at 30 degrees of flexion: a suprapatellar view, a medial and a lateral parapatellar view. An initial scoring exercise included 218 images. ICC for all B-mode images was 0.66 (CI 0.58-0.73). ICC for all Doppler images was 0.53 (CI 0.37-0.67). There was excellent agreement for B-mode on suprapatellar images with ICC 0.78 (CI 0.70-0.85) and fair to good agreement for parapatellar images: medial ICC 0.52 (CI 0.37-0.67), lateral ICC 0.60 (CI 0.46-0.73). The ICC for Doppler was fair at 0.39 (CI 0.22-0.58), 0.57 (CI 0.38-0.75) and 0.54 (CI 0.32-0.73) for suprapatellar, medial and lateral parapatellar views respectively. After revision of the scoring system, 90 images were assessed in a second round. Results improved with the ICC for B-mode in the suprapatellar view now at 0.82 (CI 0.70-0.91, excellent). The ICC for Doppler on the suprapatellar view improved to 0.49 (CI 0.25-0.78 fair/good) and on the lateral parapatellar view to 0.64 (CI 0.37-0.87, good).

Conclusion: A novel B-Mode and Doppler scoring system for assessing arthritis of the pediatric knee was successfully developed through a consensus process. Preliminary results from practical exercises indicate overall good reliability but also illustrate the challenges in certain views especially with regards to Doppler scoring. With further refinement and validation, this scoring system could serve as a clinical tool and outcome measure for scientific purposes.

Disclosure: T. Ting, None; P. Vega-Fernandez, None; E. Oberle, None; D. De Ranieri, None; H. Bukulmez, None; J. Roth, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/a-novel-ultrasound-scoring-system-for-the-pediatric-knee

Abstract Number: 2019

Structural Abnormalities in the Knee Detected By MRI in Middle-Aged Subjects without Radiographic Knee Osteoarthritis

Jaanika Kumm1, Aleksandra Turkiewicz2, Fan Zhang2 and Martin Englund2, 1Department of Radiology, University of Tartu, Tartu, Estonia, 2Clinical Sciences Lund, Orthopedics, Clinical Epidemiology Unit, Lund University, Lund, Sweden

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Imaging of Rheumatic Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Early OA is a complex, poorly understood and still largely an unchartered “entity”. Thus, our purpose was evaluate the prevalence of findings suggestive of knee OA by MRI in middle-aged subjects without evidence of radiographic OA but with or without risk factors for OA.

Methods:

We selected 340 subjects from the Osteoarthritis Initiative, aged 45-55 years (51% women) with Kellgren Lawrence grade 0 in both knees, who had 3T knee MR images. Among them, 294 subjects had OA risk factors and 46 individuals were without risk factors (Table 1). Right knee MR images were assessed by one radiologist for osteophytes, cartilage damage, bone marrow lesions (BMLs), meniscal damage, synovitis-effusion and Hoffa synovitis using the MOAKS scoring system. Meniscal body extrusion was measured in mm, and we considered ≥3 mm as meniscal extrusion.

Results:

At least one MR-detected feature was found in 96% (281/294) of the subjects with OA risk factors and in 87% (40/46) of those without. Cartilage damage (82%), BMLs (60%), osteophytes (45%), meniscal body extrusion (32%), synovitis-effusion (29%) were the most common findings in subjects with OA risk factors, while cartilage damage (67%), osteophytes (46%), meniscal body extrusion (37%) and BMLs (35%) in subjects without. The prevalence of any abnormality was significantly higher in subjects with OA risk factors than in subjects without (prevalence ratio adjusted for age and sex 1.34 [95% CI 1.11, 1.62]), so was prevalence of subchondral cysts 2.11 (1.16, 3.84); BMLs 1.73 (1.15, 2.59), and cartilage lesions 1.22 (1.00, 1.50). Osteophytes, BMLs and subchondral cysts were observed more frequently in the patellofemoral joint than in the tibiofemoral compartments (Table 2).

Conclusion:

Our findings highlight the challenge to distinguish pathological features of knee OA from ‘normal’ ageing of the joint. Still, BMLs and cysts in particular were more frequently found in subjects having multiple OA risk factors than those without.

Table 1. Characteristics of the study participants.

<table>
<thead>
<tr>
<th></th>
<th>Subjects with OA risk factors (n=294)</th>
<th>Reference cohort (n=46)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean (SD)</td>
<td>50.4 (2.9)</td>
<td>50.3 (3.3)</td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>146 (49.7)</td>
<td>27 (58.7)</td>
</tr>
<tr>
<td>BMI, kg/m2, mean (SD)</td>
<td>104 (35.4)</td>
<td>26 (56.5)</td>
</tr>
<tr>
<td>&lt;25</td>
<td>114 (38.8)</td>
<td>20 (43.5)</td>
</tr>
<tr>
<td>25-29</td>
<td>70 (23.8)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Table 2. Prevalence of structural abnormalities on MRI in the right knees of the study subjects with and without knee OA risk factors; data are numbers and percentages in parentheses.
<table>
<thead>
<tr>
<th>MRI feature</th>
<th>Subjects with OA risk factors (n=294)</th>
<th>Reference cohort (n=46)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cartilage damage</td>
<td>240 (82)</td>
<td>31 (67)</td>
</tr>
<tr>
<td>Tibiofemoral</td>
<td>189 (64)</td>
<td>21 (46)</td>
</tr>
<tr>
<td>Patellofemoral</td>
<td>199 (68)</td>
<td>26 (57)</td>
</tr>
<tr>
<td>Osteophytes</td>
<td>131 (45)</td>
<td>21 (46)</td>
</tr>
<tr>
<td>Tibiofemoral</td>
<td>56 (19)</td>
<td>5 (11)</td>
</tr>
<tr>
<td>Patellofemoral</td>
<td>124 (42)</td>
<td>20 (43)</td>
</tr>
<tr>
<td>Bone marrow lesions</td>
<td>176 (60)</td>
<td>16 (35)</td>
</tr>
<tr>
<td>Tibiofemoral</td>
<td>91 (31)</td>
<td>5 (11)</td>
</tr>
<tr>
<td>Patellofemoral</td>
<td>138 (47)</td>
<td>14 (30)</td>
</tr>
<tr>
<td>Subchondral cysts</td>
<td>119 (40)</td>
<td>9 (20)</td>
</tr>
<tr>
<td>Tibiofemoral</td>
<td>51 (17)</td>
<td>3 (7)</td>
</tr>
<tr>
<td>Patellofemoral</td>
<td>93 (32)</td>
<td>6 (13)</td>
</tr>
<tr>
<td>Meniscal damage</td>
<td>55 (19)</td>
<td>5 (11)</td>
</tr>
<tr>
<td>Meniscal extrusion</td>
<td>68 (23)</td>
<td>10 (22)</td>
</tr>
<tr>
<td>Synovitis effusion</td>
<td>86 (29)</td>
<td>8 (17)</td>
</tr>
<tr>
<td>Hoffa synovitis</td>
<td>130 (44)</td>
<td>14 (30)</td>
</tr>
<tr>
<td>Popliteal cysts</td>
<td>83 (28)</td>
<td>12 (26)</td>
</tr>
</tbody>
</table>

Disclosure: J. Kumm, None; A. Turkiewicz, None; F. Zhang, None; M. Englund, None.


Abstract Number: 2020

**Definition and Standardization of Inflammatory Pathology in Hand Osteoarthritis Assessed By Ultrasound: Results from a Delphi Process and Reliability Testing in the Omeract Ultrasonographer Group in Hand Osteoarthritis**

Alexander Mathiesen1, Hilde B Hammer1, Lene Terslev2, George A. W. Bruyn3, Maria Antonietta D'Agostino4, Georgios Filippou5, Emilio Filippucci6, Ida Kristin Haugen7, Marion Kortekaas8, Luana Mancarella9, Peter Mandl10, Ingrid Moller11, Mohamed Atia Mortada12, Esperanza Naredo13, Andrea Delle Sedie14, Ruth Wittoek15, Annamaria Iagnocco16 and Karen Ellegaard17, 1Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, 2Copenhagen University Hospital at Glostrup, Copenhagen, Denmark, 3Rheumatology, MC Groep, Loenga, Netherlands, 4Department of Rheumatology, Assistance publique-Hôpitaux de Paris Ambroise Paré Hospital, Boulogne-Billancourt , Université Versailles Saint Quentin en Yvelines, Paris, France, 5University of Siena, Siena, Italy, 6Rheumatology Unit, Università Politecnica delle Marche, Jesi, Italy, 7Diakonhjemmet Hospital, Oslo, Norway, 8Dept. of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, 9Rheumatology Unit, Rizzoli Orthopaedic Institute, Bologna, Italy, 10Department of Internal Medicine III; Division of Rheumatology, Medical University Vienna, Vienna, Austria, 11Instituto Poal de Reumatologia, Barcelona, Spain, 12Dept. of Rheumatology, Zagazig University, Zagazig, Egypt, 13Rheumatology Department, Hospital Gregorio Marañón, Madrid, Spain, 14University of Pisa, Rheumatology Unit, Pisa, Italy, 15Rheumatology, Ghent University Hospital, Ghent, Belgium, 16Academic Rheumatology Unit, Università degli Studi di Torino, Torino, Italy, 17Dept. of Rheumatology, The Parker Institute, Copenhagen, Denmark

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Tuesday, November 7, 2017
Session Title: Imaging of Rheumatic Diseases Poster II
Session Type: ACR Poster Session C  
Session Time: 9:00AM-11:00AM

Background/Purpose:
The introduction of MRI and ultrasound (US) atlases has improved reliability in rheumatoid arthritis. With an increased interest in the role of inflammation in osteoarthritis (OA), a similar US reference atlas could be useful for hand OA. Recent US studies of hand OA either apply a preliminary hand OA scoring system without image examples or an US atlas developed for RA patients. Hence, our aim was to standardize and explore the reliability of US assessments of inflammatory pathologies in patients with hand OA.

Methods:
The OMERACT (Outcome Measures in Rheumatology) US group in hand OA performed a Delphi exercise to agree on US-detected inflammatory pathologies including synovitis, effusion and power Doppler signals in hand OA finger joints. Still-images of interphalangeal joints with different grades of pathology were acquired and a set of 99 images was distributed in a web-based reliability exercise, with re-reading of 40 images after a week. Finally, the definitions were tested in a patient-based reliability exercise, where 6 experienced sonographers examined 12 patients with hand OA using GE Logic E9 machines. The 2nd–5th proximal and distal interphalangeal joints of the right hand were scored 0-3 for synovial hypertrophy and effusion (dorsal and volar side) and for Doppler activity (dorsal side). An US atlas was available during the exercise. Intraclass correlation coefficient (ICC) values were calculated with average-measure for inter-reader and single-measure for intra-reader reliability, defined as poor (<0.5), moderate (0.5–0.75), good (0.75–0.9) and excellent (>0.90).

Results:
US atlases of elementary lesions were developed (figure). The web-based reliability exercise (completed by 12 sonographers) showed excellent inter-reader and good to excellent intra-reader reliability for all variables (table). The patient-based reliability exercise showed moderate to good inter-reader and intra-reader reliability for all pathologies (table), with slightly better agreement for dorsal assessment of hypertrophy and effusion.

Conclusion:
Following a Delphi process, a semiquantitative scoring system with a complementary US atlas showed moderate to excellent reliability for sonographic assessments of inflammatory features in finger joints of hand OA patients. Our study demonstrates that ultrasound is a reliable tool for evaluating inflammation in hand OA patients.

Figure

Table
<table>
<thead>
<tr>
<th>Lesion</th>
<th>Reader ICC (95% CI)*</th>
<th>Intra-reader ICC mean (range)</th>
<th>Reader ICC (95% CI)*</th>
<th>Intra-reader ICC mean (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertrophy dorsal</td>
<td>0.98 (0.95–0.99)</td>
<td>0.84 (0.55, 0.97)</td>
<td>0.76 (0.48–0.92)</td>
<td>0.73 (0.48, 0.87)</td>
</tr>
<tr>
<td>Hypertrophy palmar</td>
<td>0.96 (0.93–0.98)</td>
<td>0.69 (0.17, 0.93)</td>
<td>0.64 (0.28–0.87)</td>
<td>0.56 (0.16, 0.76)</td>
</tr>
<tr>
<td>Effusion dorsal</td>
<td>0.98 (0.95–0.99)</td>
<td>0.79 (0.35, 0.95)</td>
<td>0.88 (0.63–0.96)</td>
<td>0.83 (0.54, 0.97)</td>
</tr>
<tr>
<td>Effusion palmar</td>
<td>0.97 (0.93–0.99)</td>
<td>0.80 (0.54, 1.00)</td>
<td>0.74 (0.44–0.91)</td>
<td>0.59 (0.28, 0.81)</td>
</tr>
<tr>
<td>Doppler dorsal</td>
<td>0.99 (0.99–1.00)</td>
<td>0.98 (0.92, 1.00)</td>
<td>0.82 (0.60–0.94)</td>
<td>0.51 (0.29, 0.86)</td>
</tr>
</tbody>
</table>

* Highest result in round 1 and 2.

Disclosure: A. Mathiessen, None; H. B. Hammer, None; L. Terslev, None; G. A. W. Bruyn, None; M. A. D’Agostino, None; G. Filippou, None; F. Filippucci, None; I. K. Haugen, None; M. Kortekaas, None; L. Mancarella, None; P. Mandl, None; I. Moller, None; M. A. Mortada, None; E. Naredo, None; A. Delle Sedie, None; R. Wittoek, None; A. Iagnocco, None; K. Ellegaard, None.

Abstract Number: 2021

**Reliability of Ultrasound Elementary Lesions in Gout: Results from an Inter- and Intra-Reading International Multicenter Exercise By 62 Sonographers**

Tomas Cazenave1, María Victoria Martire2, Christian A. Waimann3, Ana Bertoli4, Anthony Reginato5, Andy Abri6, Eliana Natali Ayala Ledesma7, Maximiliano Bravo8, César Cefferino9, Carla Airoldi10, Carla Saucedo11, Carlos Pineda12, Gustavo Rodriguez Gil13, Cecilia Urquíola14, Cesar Graf15, Clarisa Sandoval16, M. Concepción Castillo Gallego17, Cristian Trotiño18, Cristina Hernandez-Diaz19, David Navarta20, Diana Peiteado21, MARIO DIAZ22, Diego Saabibi23, Henry Julio Colon Castillo24, Marwin Gutierrez25, Ana Laura Alvarez del Castillo Araujo26, Oscar Sedano27, Edith Alarcón28, Erika Catay29, Claudia Mora29, Eugenio De Miguel30, Félix Fernández Castillo31, Florencia Marenco32, Gabriel Aguilar33, Irene Monjo34, Javier Rosa35, José Francisco Diaz Coto36, Jorge Saavedra Muñoz37, Josefina Marín38, Lida Santiago39, Magali Alva40, Manuela Lima Gomes Ochtop41, Maria Guinsburg42, Mariana Benegas43, María Julia Santa Cruz44, Paula Kohan45, Natalia Estrella46, Mariana Pera47, Patricia Tate48, Priscila Marcaida49, Guillermo Py50, RICARDO PAVAO51, R Munoz-Louis52, Roser Arey Micas53, Rodolfo Arape54, Santiago Ruta55, María Soledad Gálvez Elkin55, Lorena Urioste56, Lina Saldarriaga Rivera57, OSCAR VEGA-HINOJOSA58, Lucio Ventura59, Walter J. Spindler60, Yvonne Rengel61, Maritza Quintero62 and Marcos G. Rosemffet63, 1Instituto de Rehabilitación Psicofísica, Buenos Aires, Argentina, 2Instituto Médico Patense, La Plata, Argentina, 3Hospital Dr. Hector Cura, Olavarria, Argentina, 4Instituto Reumatológico Strusberg, Córdoba, Argentina, 5Rhode Island Hospital, The Warren Alpert School of Medicine at Brown University, Providence, RI, 6Rheumatology, Mayo Clinic Florida, Jacksonville, FL, 7Hospital Nacional Arzobispo Loayza, Lima, Peru, 8Consultorios Moreno, Formosa, Argentina, 9HOSPITAL NACIONAL DOS DE MAYO, Lima, Peru, 10Hospital Provincial, Rosario, Argentina, 11Hospital Aníta Elicagary, Adolfo Gonzales Chaves, Argentina, 12Instituto Nacional de Rehabilitación, Mexico, Mexico, 13Hospital Municipal de Aguadu "Dr Leónidas Lucero", Bahía Blanca, Argentina, 14Hospital Municipal Dr. Leónidas Lucero, Bahia Blanca, Argentina, 15Centro...
Methods: We conducted a cross-sectional study. Sixty-two sonographers from several countries and different degree of experience took part in an US reading exercise. All observers evaluated 50 ultrasound videos from patients with gout diagnoses. In addition, a group of 15 videos was displayed twice to assess intra-reader reliability. We evaluated the presence of the four elementary lesions described by OMERACT US Gout Task Force: double contour (DC), tophus, aggregates and erosion. Intra and Inter-reader reliability was calculated by the Cohen’s kappa coefficient and classified according to Landis and Koch criteria. Sonographers were stratified according to US experience (defining High experience as at least ≥5 years of experience, ≥100 US assessments/month and ≥10 US in gout patients/month), evaluating differences in intra, inter – reader reliability and overall agreement. Bias-adjusted and prevalence-adjusted kappa (PABAK) was calculated to overcome prevalence bias in kappa estimates.

Results: A total of 3100 US assessment were performed. Prevalence of lesions were: Tophus (34%), Aggregates (29%), Erosions (22%) and DC (20%). The mean intra-reader values were good to excellent in all lesions (table 1). Mean Kappa inter-reader correlation coefficients, were fair for aggregates, moderate for tophus and erosions, and good for DC (Table 1). Adjusting for low-prevalence using PABAK estimates, inter-rater reliability increased to 0.42 (moderate), 0.49 (moderate), 0.69 (good) and 0.79 (good); respectively. There was not significant difference between experience and non-experience sonographers regarding to agreement and inter-rater reliability. Experience sonographers showed better intra-rater reliability for the detection of erosions (table 1).

Conclusion: The inter-rater reliability of the OMERACT US elementary lesions for gout is still a concern, especially in others than Double Contour. This results should be taken into account in the design of future multicenter studies.
<table>
<thead>
<tr>
<th>Group</th>
<th>US experience [median, (p25-75)]</th>
<th>US assessment per months [median, (p25-75)]</th>
<th>US assessment in gout patients per months, (median, (p25-75))</th>
<th>Reliability assessment (Intra or Inter rater)</th>
<th>Aggregates</th>
<th>DC</th>
<th>Tophus</th>
<th>Erosions</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Examiners (n=62)</td>
<td>8 (4-10)</td>
<td>65 (43-130)</td>
<td>5 (2-8)</td>
<td>Inter</td>
<td>71%</td>
<td>0.31</td>
<td>89%</td>
<td>0.67</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Intra</td>
<td>83%</td>
<td>0.62</td>
<td>95%</td>
<td>0.85</td>
</tr>
<tr>
<td>High experience (n=9)</td>
<td>10 (8-12)</td>
<td>130 (130-174)</td>
<td>15 (10-20)</td>
<td>Inter</td>
<td>68%</td>
<td>0.27</td>
<td>93%</td>
<td>0.73</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Intra</td>
<td>83%</td>
<td>0.64</td>
<td>95%</td>
<td>0.84</td>
</tr>
<tr>
<td>Low experience (n=53)</td>
<td>8 (4-10)</td>
<td>52 (43-130)</td>
<td>4 (1-5)</td>
<td>Inter</td>
<td>71%</td>
<td>0.31</td>
<td>89%</td>
<td>0.67</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Intra</td>
<td>83%</td>
<td>0.62</td>
<td>95%</td>
<td>0.85</td>
</tr>
</tbody>
</table>

Abbreviations: p25-75 – percentile 25 and 75; DC – double contour; k – Light’s kappa; % - proportion of observed agreement.

Disclosure: T. Cazenave, None; M. V. Martire, None; C. A. Waimann, None; A. Bertoli, None; A. Reginato, None; A. Abril, None; E. N. Ayala Ledesma, None; M. Bravo, None; C. Cefferino, None; C. Airoldi, None; C. Saucedo, None; C. Pineda, None; G. Rodriguez Gil, None; C. Urquiola, None; C. Graf, None; C. Sandoval, None; M. C. Castillo Gallego, None; C. Troitiño, None; C. Hernandez-Diaz, None; D. Navarta, None; D. Peiteado, None; M. DIAZ, None; D. Saaihi, None; H. J. Colon Castillo, None; M. Gutierrez, None; A. L. Alvarez del Castillo Arajao, None; O. Sedano, None; E. Alarcón, None; E. Catay, None; C. Mora, None; E. De Miguel, None; F. Fernandez Castillo, None; F. Marenco, None; G. Aguilar, None; I. Monjo, None; J. Rosa, None; J. F. Diaz Coto, None; J. S. Muñoz, None; J. Marin, None; L. Santiago, None; M. Alva, None; M. Lima Gomes Ochtop, None; M. Guinsburg, None; M. Benegas, None; M. J. Santa Cruz, None; P. Kohan, None; N. Estrella, None; M. Pera, None; P. Tate, None; P. Marcaida, None; G. Py, None; R. PAVAO, None; R. Munoz-Louis, None; R. Areny Micas, None; R. Arape, None; S. Ruta, None; M. S. Gálvez Elkin, None; L. Urioste, None; L. Salzbarriaga Rivera, None; O. VEGA-HINOJOSA, None; L. Ventura, None; W. J. Spindler, None; Y. Rengel, None; M. Quintero, None; M. G. Rossemffet, None.


Abstract Number: 2022

Diagnostic and Prognostic VALUE of Salivary GLAND Ultrasonography in Primary Sjögren’s Syndrome: a Preliminary Study

Maria Pascual¹, Mercè López¹, Joan Miquel Nolla², Javier Narváez³, helena borrell¹ and Carmen Moragues⁴, ¹DEPARMENT OF RHEUMATOLOGY, HOSPITAL UNIVERSITARI DE BELLVITGE, BARCELONA, Spain, ²Rheumatology, Hospital Universitario de Bellvitge, Barcelona, Spain, ³Rheumatology Department, Hospital de Bellvitge. Barcelona. Spain, L’Hospitalet de Llobregat, Spain, ⁴DEPARMENT OF RHEUMATOLOGY, HOSPITAL UNIVERSITARI DE BELLVITGE, barc+, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Imaging of Rheumatic Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
In recent years, salivary gland ultrasonography (SGUS) has emerged as a promising tool for the diagnosis and prognostic stratification of patients with primary Sjögren’s syndrome. However, more studies are needed to demonstrate its diagnostic usefulness before it can be used in daily clinical practice. Our objective is to evaluate the diagnostic and prognostic value of salivary gland ultrasonography (SGUS) in primary Sjögren’s syndrome (pSS).

Methods:

Patients with primary SS (fulfilling the American-European Consensus Group criteria of 2002) and controls with secondary SS or sicca syndrome are evaluated using a simplified SGUS scoring system.

Parotid and submandibular glands on both sides were assessed for parenchymal inhomogeneity, which was performed by the same ecographist. Echographic alterations of the salivary glands were graded from 0 to 3, with grades 0 (normal) and 1 (mild inhomogeneity) being interpreted as normal, and grades 2 and 3 as primary SS typical lesions. Associations between SGUS and clinical and laboratory disease were analyzed. Moreover, to test the accuracy for diagnosis of SGUS, we calculated sensitivity, specificity, PPV, NPV and positive/negative likelihood ratio.

Results:

Thus far, twenty-five patients have been included, thirteen with pSS and twelve with secondary SS/sicca syndrome. The hypoechoic lesions (score 2 or 3) were found in 76.9% of primary SS patients and in none of controls (p <0.001). Specificity and positive predictive value of abnormal SGUS was 100%, sensitivity and negative predictive values were 76.9% and 80%, respectively. The negative likelihood ratio was 0.23 and the positive likelihood ratio was > 10, which means that typical SS lesions would improve the probability of having primary SS. However, if the SGUS results negative, another diagnostic test are needed in order to avoid patient misclassification.

Patients with parenchymal heterogeneity, more frequently, had positivity for anti-Ro/SSA (p=0.022), anti-La/SSB (p=0.005) and rheumatoid factor (p=0.007). Moreover, the presence of hypergammaglobulinemia, (p=0.001), leucolymphopenia (p<0.001), and elevated ESR (p<0.001) was associated with typical pathologic SGUS. Consequently, the EULAR Sjögren’s syndrome disease activity index (ESSDAI) was higher in patients with abnormal SGUS (p=0.025). We could not detect an association with age, disease duration, ANA positivity, complement level, anemia and, suprisingly, extraglandular involvement.

Conclusion:

In our preliminary study, assessment of parenchyma dyshomogeneity with SGUS is highly specific in differentiating primary SS from idiopathic sicca syndrome or Secondary SS. Moreover, this technic can provide prognostic stratification in patients with primary SS.

Disclosure: M. Pascual, None; M. López, None; J. M. Nolla, None; J. Narváez, None; H. borrell, None; C. Moragues, None.

Abstract Number: 2023

Diagnostic Value of the Non-Observation of the Frontal Branch of the Temporal Arteries By Ultrasonography in the Diagnostic of Giant Cell Arteritis (GCA)

Natacha Cambray1 and Artur J de Brum-Fernandes2, 1Rheumatology Division, Université de Sherbrooke, Sherbrooke, QC, Canada, 2Rheumatology Division, Université de Sherbrooke, Rheumatology Division, Canada, Sherbrooke, QC, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Imaging of Rheumatic Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

The absence of the parietal branch of the temporal artery during an ultrasound evaluation may be due to a variance of the normal anatomy or to technical difficulties due to interference of hair. However, the significance of a complete absence of the frontal branch
without any obvious stenosis or sudden occlusion is not known. The objective of the present study was to determine if the non-observation of the frontal branch of the temporal arteries by ultrasonography had any diagnostic value in patients with a clinically suspected GCA, as defined by biopsy or the ACR classification criteria.

Methods:

From May 2011 to February 2017, 102 patients underwent an US evaluation of the temporal arteries for suspected GCA. US of the common, parietal and frontal branches of the TA were done with a MyLab70 device and Color Doppler technique, bilaterally. A definitive stenosis was diagnosed when the frontal branch had its diameter decreased or the blood flow increased by at least twofold; obstruction was diagnosed by the sudden loss of a proximally well-identified artery. Non-observation was defined when at least one of the frontal branches of the temporal arteries was not observed at all.

Results:

102 patients were included in the study: 71.6% of them were women and the average age was of 72 years; 49% of the patients presented at least 3 ACR criteria for GCA. 18 patients underwent a temporal artery biopsy, 4 with positive results. A definitive stenosis or occlusion on US examination was found in 11 of our patients. In 12 other patients the frontal branch of one of the temporal arteries could not be identified during US examination.

Compared to the ACR criteria, the presence of a definite stenosis had a sensibility of 18.6%, a specificity of 93.6 %, a PPV of 72.7% and a NPV of 55.7%. The non-identification of at least one frontal branch had a very similar predictive value: sensitivity of 14%, specificity of 90.4%, PPV of 58.3% and NPV of 52.2%. Compared to the biopsy, the presence of a definite stenosis or occlusion had a sensibility of 100%, a specificity of 84.6%, a PPV of 33.3% and a NPV of 100%, while the non-observation of the frontal branch of the TA showed 75%, 85.7%, 60% et 92.3%, respectively.

Conclusion:

In our cohort the non-observation of the frontal branch of the temporal arteries was highly predictive of GCA whether the disease was defined by ACR criteria or by biopsy. Its predictive values were very close to those found for stenosis or occlusion, suggesting that it may be a manifestation of the same phenomenon.

Disclosure: N. Cambray, None; A. J. de Brum-Fernandes, None.


Abstract Number: 2024

**Prediction of Response to Certolizumab-Pegol in Rheumatoid Arthritis By Functional MRI of the Brain – an Interim Analysis of an Ongoing Investigator Initiated Phase III Trial**

Hannah Schenker¹, Andreas Hess², Laura Konerth², Marina Sergeeva², Jutta Prade², Arnd Kleyer¹, Michaela Reiser¹, Axel J. Hueber¹, Matthias Englbrecht¹, Eugen Feist³, Reinhard Volz⁴, Bettina Bannert⁴, C Baerwald⁵, Julie Rösch⁶, Arnd Dörrler⁷, José António P. da Silva⁸, Nemanja Damjanov⁹, Georg Schett¹ and Juergen Rech¹, ¹Department of Medicine 3, Rheumatology and Immunology, University of Erlangen-Nuremberg, Erlangen, Germany, ²Institute of Pharmacology and Toxicology, University of Erlangen-Nuremberg, Erlangen, Germany, ³Department of Rheumatology and Clinical Immunology, Charité, Berlin, Berlin, Germany, ⁴Clinic for Rheumatology and Clinical Immunology, Medical University of Freiburg, Germany, Freiburg, Germany, ⁵Department of Rheumatology, University of Leipzig, Germany, Leipzig, Germany, ⁶Department of Neuroradiology, University of Erlangen-Nuremberg, Germany, Erlangen, Germany, ⁷Department of Neuroradiology, University of Erlangen-Nuremberg, Germany, e, Germany, ⁸Rheumatology, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal, ⁹Institute of Rheumatology, Belgrade University School of Medicine, Belgrade, Serbia

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Imaging of Rheumatic Diseases Poster II
Session Type: ACR Poster Session C
Tumor necrosis factor inhibitors (TNFi) signify a major advance in the treatment of rheumatoid arthritis (RA). However, treatment success initially remains uncertain as one third of patients do not respond adequately to TNFi. We investigated whether brain activity associated to arthritis measured by functional magnetic resonance imaging (fMRI) can function as a predictor of response to TNFi in RA patients.

Methods:

This is an interim analysis of the first 50 patients of the PreCePRA trial, a multi-center, randomized, double-blind, placebo-controlled fMRI trial on patients with RA. [1] [2] Active RA patients failing csDMARDs with a DAS28-ESR>3.2 and at least three tender and/or swollen joints received a brain BOLD (blood-oxygen-level dependent) fMRI scan upon joint compression at screening. Patients were then randomized into a 12-week double-blinded treatment phase with 200mg Certolizumab-Pegol every two weeks (arm 1: fMRI BOLD signal >2000 voxel, i.e. 2 cm$^3$; arm 2: fMRI BOLD signal <2000 voxel) or placebo (arm 3) or. DAS28-ESR low disease activity at 12 weeks was assigned as primary endpoint. A 12-week follow-up phase in which patients were switched from the placebo to the treatment arm followed the blinded phase. fMRI was carried out at screening as well as after 12 and 24 weeks of receiving Certolizumab-Pegol or placebo.

Results:

In responders screening signal volume, i.e. sum of significantly coupled voxels after FDR thresholding, was higher compared to non-responders allowing discrimination between the two groups prior to treatment. In responders we detected a persistent decrease of BOLD volume at week 12 and 24 compared to screening ($r^2=0.561$) whereas BOLD volume in non-responders persistently increased ($r^2=0.589$).

Conclusion: Based on this interim analysis we conclude that high BOLD volumes in fMRI indicating high-level brain representation of pain in arthritis predict response to TNFi. These data represent the first encouraging results of the PreCePRA brain fMRI study supporting the concept that increased RA-related brain activity correlates with response to TNFi.

References:


Disclosure: H. Schenker, None; A. Hess, None; L. Konerth, None; M. Sergeeva, None; J. Prade, None; A. Kleyer, None; M. Reiser, None; A. J. Hueber, None; M. Englbrecht, None; E. Feist, None; R. Voll, None; B. Bannert, None; C. Baerwald, None; J. Rösch, None; A. Dörfler, None; J. A. P. da Silva, None; N. Damjanov, None; G. Schett, None; J. Rech, None.

Potential Clinical Utility of Manu-Scan, the Novel Optical Molecular Imaging, in Patients with Hand Rheumatoid Arthritis

Dong Jin Go1, Sang Jin Lee1,2, Sang Hyun Joo3, Eun Hye Park4, Gi Jeong Cheon5, Sung Hwan Hong6 and Yeong Wook Song1,4

1Department of Molecular Medicine and Biopharmaceutical Sciences, Graduate School of Convergence Science and Technology, and College of Medicine, Seoul National University, Seoul, Korea, Republic of (South), 2Division of Rheumatology, Department of Internal Medicine, Kyungpook National University Hospital, Seoul, Korea, Republic of (South), 3Division of Rheumatology, Department of Internal Medicine, Jungang Medical Foundation, Jeju, Korea, Republic of (South), 4Division of Rheumatology, Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea, Republic of (South), 5Department of Nuclear Medicine, Seoul National University Hospital, Seoul, Korea, Republic of (South), 6Department of Radiology, Seoul National University Hospital, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: ARHP Imaging of Rheumatic Diseases Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Recently, optical molecular imaging is expected to serve as the new technique for early diagnosis and treatment monitoring of rheumatoid arthritis (RA). "Manu-Scan" is the diffuse optical tomography detecting near infrared ray (wavelength 0.7-1.4um) beamed into patient's joint. This pilot study was aimed to assess the clinical utility of Manu-Scan in patients with hand RA.

Methods: In 14 RA patients and 3 healthy controls, Manu-Scan was performed twice with a one-week interval to detect repetitive error, targeting metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints. Enrolled subjects also underwent joint physical exam, magnetic resonance imaging (MRI), bone scan (BS), and single photon emission computed tomography (SPECT) at the same time. Manu-Scan score was measured by contrast ratio between maximum and minimum scattering factors inside the joint.

Results: Among 215 hand joints assessed using Manu-Scan, 166 (77%) joints within repetitive error less than 20% (137 in RA patients and 29 in healthy controls) were valid for evaluation. Manu-Scan scores in RA joints were significantly lower than those in control joints (median 2.05 vs 2.80, p < 0.001). Manu-Scan scores were also lower in RA joints without tenderness or swelling (n = 44) compared with control joints (p = 0.002). In RA patients, Manu-Scan scores were negatively correlated with MRI grades (rho -0.502, p < 0.001), BS grades (rho - 0.516, p < 0.001), and SPECT scores (rho -0.178, p = 0.038). Moreover, even if RA joints were lesion-free on MRI (n = 69), Manu-Scan had moderate to good discriminatory ability between RA and control, based on ROC curve analysis (AUC 0.763 95% CI [0.661, 0.864]).

Conclusion: Manu scan could be utilized as a novel imaging modality reflecting synovial inflammation without exposure to radiation in RA patients. Further large-scale trial is needed to confirm this finding.

Disclosure: D. J. Go, None; S. J. Lee, None; S. H. Joo, None; E. H. Park, None; G. J. Cheon, None; S. H. Hong, None; Y. W. Song, None.


Abstract Number: 2026

Pneumococcal Vaccination Rates: Improving Safety in Immunocompromised Patients

Shanley O'Brien and Paul Schmidt, Department of Internal Medicine, Division of Allergy, Clinical Immunology, & Rheumatology, Kansas University Medical Center, Kansas City, KS

First publication: September 18, 2017

SESSION INFORMATION
Streptococcus pneumoniae is the most common cause of bacterial pneumonia. Invasive pneumococcal infections carry a 10% mortality rate, which is higher in the immunosuppressed. The Infectious Diseases Society of America recommends pneumococcal vaccination in patients planning to start or already on immunosuppression. This project’s purpose is to improve the pneumococcal vaccination rate of patients on immunosuppression with the goal of decreasing morbidity and mortality from invasive pneumococcal disease.

Methods: In an adult rheumatology clinic in a tertiary care center, a best practice alert (BPA) was created within the electronic medical record (EMR). The BPA is triggered for patients taking an immunosuppressive medication who have not received both the pneumococcal conjugate vaccine and the pneumococcal polysaccharide vaccine within the last 5 years. Options within BPA include: a link to the Centers for Disease Control and Prevention website, an option to order either vaccine, and a link to document the vaccine if historically given. Educational sessions on vaccine guidelines were held periodically with both the clinic physicians and nursing staff. A survey of clinic physicians was conducted both prior to and after initiation of the BPA. Baseline data was collected prior to initiation of the BPA and quarterly thereafter to determine the rate of patients who had received 1, 2 or 3 vaccines. Fisher’s exact test was utilized.

Results: Baseline data from January to March 2016 found that of 741 patients, 335 (45.2 percent) had received 0 pneumococcal vaccines, 205 (27.6 percent) had received 1 pneumococcal vaccine, 168 (22.6 percent) had received 2 pneumococcal vaccines and 33 (4.4 percent) had received 3 pneumococcal vaccines. The BPA was implemented in May 2016. Repeat data from January to March 2017 showed that of 741 patients, 224 (30.2 percent) had received 0 pneumococcal vaccines, 219 (29.5 percent) had received 1 pneumococcal vaccine, 247 (33.3 percent) had received 2 pneumococcal vaccines and 51 (6.8 percent) had received 3 pneumococcal vaccines. The total number who had received at least 1 pneumococcal vaccine improved significantly after the intervention [406 (54.7 percent) to 517 (69.7 percent); (p = <0.0001)]. The rate of physicians surveyed who “usually” or “always” discussed vaccines with patients on immunosuppression improved from 50% (4/8) to 88.8% (8/9).

Conclusion: A BPA within the EMR was successful in significantly improving pneumococcal vaccination rates for patients on immunosuppression. A limitation of this study is that it was conducted in a tertiary care center and may not be generalizable to all care settings. Obtaining vaccination history was a challenge throughout the project. Future directions for this project include adding a patient education arm or expanding the BPA for use in other specialty clinics or additional vaccine types.

References:

Disclosure: S. O'Brien, None; P. Schmidt, None.

Abstract Number: 2027

Pre-Visit Planning Improves Pneumococcal Vaccination in Patients with Childhood-Onset Systemic Lupus Erythematosus

Kelly Wise, Fatima Barbar-Smiley, Stephanie Lemle, Darby MacDonald, Ohoud AlAhmed, Evan Mulvihill, William Cotton, Monica Ardura, Cagri Yildirim-Toruner and Vidya Sivaraman

Pharmacy/Rheumatology, Nationwide Children's Hospital, Columbus, OH, Nationwide Children's Hospital, Columbus, OH, Pediatrics, Nationwide Children's Hospital, Columbus, OH, Pediatrics and Rheumatology, Nationwide Children's Hospital and The Ohio State University, Columbus, OH, Rheumatology, Nationwide Children's Hospital, Columbus, OH, Pediatric Rheumatology, Nationwide Children's Hospital, Columbus, OH, Pediatrics, The Ohio State University, COLUMBUS, OH

First publication: September 18, 2017
SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Patients with Systemic Lupus Erythematosus (SLE) lupus are up to 13 times more likely to develop invasive pneumococcal infections, resulting in increased morbidity and mortality. Vaccination against S. pneumoniae is therefore recommended in all patients with SLE, however, vaccination rates in routine rheumatology care remain low. Barriers to vaccination are lack of provider recommendation, concerns about vaccine efficacy and safety, lack of vaccine supply, incomplete immunization records and time. The aim of this study was to increase pneumococcal vaccination rates in patients with Childhood-onset SLE (c-SLE) from 3.6% to 50% in 1 year and 80% by the following year. This report describes the interim results at 9-months from the initiation of the project.

Methods:
Patients with childhood-onset SLE followed in the pediatric rheumatology clinic at Nationwide Children's Hospital from 1/1/2015 to 8/31/2016 were included for the baseline analysis. Newly diagnosed patients with c-SLE were included for the ongoing study. A letter was sent to these patients and their primary care providers requesting an updated immunization record. An age-based algorithm was developed for pneumococcal conjugate (PCV13) and pneumococcal polysaccharide (PPSV23) vaccination based on current ACIP guidelines, followed by an education session for rheumatology providers and clinic staff. Pre-visit planning included: 1) Generating a weekly report of upcoming appointments for c-SLE patients, 2) Entering updated immunization records with the help of the clinical pharmacist in the electronic health record (EHR), identifying candidates for vaccination, and notifying the rheumatology team of vaccination opportunities on a weekly basis, and 3) Weekly monitoring by clinic nurses to ensure adequate vaccine stock.

Results:
83 patients with c-SLE were seen in the pediatric rheumatology clinic in the baseline period, with a median age of 18.3 years (range 7-24). An additional 8 newly diagnosed patients were included in this analysis, with a total of 91 patients. Over the study period, the number of patients with updated vaccine records in the EHR increased from 25.6% to 65.1%. Vaccination rates for PCV13 increased from 8.4% to 49.4% (p<0.0001) and PPSV-23 rates increased from 24.1% to 32.9%. A total of 20/91 (21.9%) were appropriately immunized with both vaccines, compared with 3.6% at baseline (p<0.0001). Notably, 60.4% of patients had received at least 1 dose of pneumococcal vaccine as compared to 28.9% at the start of the study (p<0.0001).

Conclusion:
This study highlights the benefits of pre-visit planning in improving pneumococcal vaccination in patients with c-SLE. Access to updated immunization records in the EHR at the time of the visit facilitated timely decision making. Targeted vaccine recommendations prior to the visit minimized the time burden on providers and served as a reminder to order the vaccine. Future efforts will be directed at building clinical decision support in the EHR for vaccinations in high-risk individuals, evaluating vaccine immunogenicity and expanding the service to patients with other pediatric rheumatic diseases.

Disclosure: K. Wise, None; F. Barbar-Smiley, None; S. Lemle, None; D. MacDonald, None; O. AlAhmed, None; E. Mulvihill, None; W. Cotton, None; M. Ardura, None; C. Yildirim-Toruner, None; V. Sivaraman, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/pre-visit-planning-improves-pneumococcal-vaccination-in-patients-with-childhood-onset-systemic-lupus-erythematosus

Abstract Number: 2028

Compliance with Pneumococcal Vaccination in Rheumatic Disease Patients on Immunosuppressive Medications

Zainab Shahnawaz1, Fatme Allam2 and Andras Perl3, 1Medicine/Rheumatology, SUNY Upstate Medical University, Syracuse, NY, 2SUNY Upstate Medical University, Syracuse, NY, 3Medicine, SUNY Upstate Medical University, Syracuse, NY
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Background/Purpose:

The 2012 recommendations of the Centers for Disease Control (CDC) advise that adults aged ≥19 years with immunocompromising conditions including patients on iatrogenic immunosuppression should receive a dose of Pneumococcal Conjugate Vaccine (PCV13) first, followed by a dose of Pneumococcal Polysaccharide Vaccine (PPSV23) at least 8 weeks later (1). A second PPSV23 dose is recommended 5 years after the first PPSV23 dose for patients aged 19–64. Additionally, those who received PPSV23 before age 65 years for any indication should receive another dose at age of 65 years, or later if at least 5 years have elapsed since their previous PPSV23 dose. The preceding, 2008 recommendations suggested to vaccinate with PPSV23 alone (2). This project was initiated to evaluate compliance with the 2012 and 2008 guidelines at the Veteran’s Affairs (VA) Medical Center in Syracuse, New York.

Methods:

This study included patients with the diagnoses of rheumatoid arthritis, systemic lupus erythematosus, or granulomatosis with polyangiitis who were treated with methotrexate, azathioprine, adalimumab, tofacitinib, apremilast, rituximab, mycophenolate mofetil, anakinra, etanercept, seukinumab, ustekinumab, certolizumab or cyclophosphamide. Compliance rate in our cohort was compared to previously published studies with chi-square test using GraphPad software (San Diego, CA). Two-tailed p <0.05 was considered significant.

Results:

The records of 3095 cases between 1/1/2014-1/1/2017 were examined. 414 of 3095 cases were treated with immunosuppressants. Only 138/414 (33%) of the patients were immunized appropriately following the 2012 guidelines (1). 155/414 patients (37%) received PPSV23 alone, which follows the 2008 guidelines (2). 271/414 patients (65%) received PCV13 alone, while 288/414 patients (70%) received PCV13 or PPSV23. As reference points for our study, we were unable to find publications that evaluated compliance with 2012 CDC recommendations. However, we found three studies that assessed pneumococcal vaccination in similar cohorts (Table 1). Compliance with 2008 CDC guidelines was significantly lower in study No. 1 but greater in studies No. 2 and 3 as compared to our cohort at 37%.

Table 1. Compliance rate of 37% at the Syracuse VA with 2008 CDC guidelines (2) is compared to three studies documented in the literature.

<table>
<thead>
<tr>
<th>Study No.</th>
<th>Reference</th>
<th>Vaccinated</th>
<th>Not Vaccinated</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Arthritis Rheum. 2009; 61:1505-10.</td>
<td>99 (19%)</td>
<td>420</td>
<td>519</td>
</tr>
<tr>
<td>2</td>
<td>Rheumatology 2011; 50:366-372.</td>
<td>1491 (54%)</td>
<td>1272</td>
<td>2763</td>
</tr>
<tr>
<td>3</td>
<td>Open Forum Infect Dis. 2015; 2: ofv119.</td>
<td>1449 (50%)</td>
<td>2898</td>
<td>4347</td>
</tr>
</tbody>
</table>

P value vs 37% |<0.0001 |<0.0001 |<0.0001

Conclusion:

This study demonstrates that the 66% majority of rheumatic disease patients on immunosuppressants at the Syracuse VA were not receiving adequate pneumococcal vaccination as recommended by the CDC (1). Therefore, quality improvement is necessary to enhance compliance with current CDC recommendations. Follow-up studies are warranted given the significant morbidity and burden to society inflicted by non-compliance with pneumococcal vaccination guidelines.

References:


Disclosure: Z. Shahnawaz, None; F. Allam, None; A. Perl, None.

Abstract Number: 2029
Improved Provider Awareness and Delivery of Zoster Vaccination in Patients with Rheumatoid Arthritis Contemplating Biologic Therapy: Need to Target Eligible Patients Prescribed for Vaccination Post-Clinic

Gina Prakash¹, Kenneth O'Rourke² and Stephen Mullis³, ¹Department of Internal medicine, Section on Rheumatology and Immunology, Wake Forest School of Medicine, Winston Salem, NC, ²Department of Internal Medicine, Section on Rheumatology and Immunology, Wake Forest School of Medicine, Winston-Salem, NC, ³Department of Internal Medicine, Section on Rheumatology and Immunology, Wake Forest School of Medicine, Winston Salem, NC

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Vaccination against herpes zoster (shingles) can reduce the frequency of infection, the severity of shingles should it occur, and the frequency of post-herpetic neuralgia. As active biologic therapy is currently considered a contraindication to vaccination against shingles with a live virus zoster vaccine (LVZV), provider awareness of this situation may promote vaccination rates in eligible patients for whom biologic therapy is contemplated. Factors such as determining vaccine cost may limit point-of-care (POC) vaccination in eligible patients.

Methods:
In patients with a coded diagnosis of rheumatoid arthritis (RA) chart documentation assessed how frequently LVZV was addressed prior to initiation of biologic therapy. Following an educational intervention, a reminder and documentation system was implemented using a sheet given to all patients at the time of clinic intake, including a decision tree for providers to determine the need for vaccination based on age, prior vaccine status, diagnosis, and potential contraindications. A senior rheumatology fellow reviewed all charts. Pre-intervention consecutive charts from patients attending the rheumatology outpatient clinics in 2016 from 5/1 thru 5/31 were retrospectively reviewed. Inclusion criteria were patients coded with RA, age >50 years, and on biologic therapy. Exclusion criteria included patients already on biologics prior to established care in our clinic, or contraindication to LVZV per CDC guidelines. The post-intervention study prospectively reviewed charts on the same eligible consecutive patients seen in 2017 from 5/10 thru 5/26.

Results:
Of 168 consecutive charts retrospectively reviewed pre-intervention, only 76 met eligibility criteria. In 0 charts was there provider documentation about the need for vaccination. Although nursing and/or medication documentation noted LVZV was appropriately given in 19%, there was no provider documentation as to why or if it actually was given. The percentage of vaccinated patients being seen solely by attendings were slightly higher compared to those seen by fellows.

All patients representing the 116 consecutive charts, which were reviewed post-intervention, were screened with the reminder sheet: only 16 met eligibility criteria for LVZV. Only 2 of the eligible patients received LVZV or a prescription for it accompanied by documentation by the provider in the record that the vaccine was given. 8 of the eligible patients were given a prescription for LVZV vaccination (4 seen by attendings, 4 by fellows), but there has been no documentation of the provider subsequently receiving confirmation that patients so prescribed actually received the vaccine. 6 of the eligible patients already had received LVZV previously as recorded in the clinic reminder sheet, but in only 4 patients was subsequent chart documentation found.

Conclusion:
In eligible RA patients the documentation of completed LVZV remains low. The majority of eligible patients required a prescription for vaccination after POC, but there has been no confirmation that any received it. Efforts at increasing vaccination rates should be directed at providing a system to report back successful receipt of vaccination post-visit.

Disclosure: G. Prakash, None; K. O'Rourke, ACR Curriculum Subcommittee, 6; S. Mullis, None.

Patient Motivation in Inflammatory Arthritis: The Use of Ultrasound-Guided Patient Education to Endorse Medication Adherence and Facilitate Cost-Effective Targeted Management

Yasser M. El Miedany1,2, Maha El Gaafary3, Nadia El Aroussy1, Sally Youssef4 and Deborah Palmer5, 1Rheumatology and Rehabilitation, Ain Shams University, Cairo, Egypt, 2Rheumatology, Darent Valley Hospital, Dartford, United Kingdom, 3Community, Environmental and Occupational Medicine, Ain Shams University, Abbassia, Egypt, 4Rheumatology & Rehabilitation, Ain Shams University, Cairo, Egypt, 5Rheumatology, North Middlesex University Hospital, London, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: To assess the value of sharing the real-time ultrasound (US) images of the inflamed joints/ tendons with inflammatory arthritis patients and its impact on: 1. patient motivation; 3. medication adherence; 3. Control of disease activity; and 4. Patient cost-benefit decision.

Methods: Observational longitudinal study which included 121 patients, diagnosed to have active RA (62-patients, DAS-28 >3.2), or psoriatic arthritis (59-patients) who were treated according to Treat-to-Target approach. At baseline, 3-, 6- and 12-month every patient completed: A. PROMs questionnaire [1]; B. Beliefs about Medicines Questionnaire (BMQ) [2] to assess the cost-benefit analysis made by patients regarding the necessity versus concern of medication; C. Patient Motivation Measure [3]; D. Compliance Questionnaire-Rheumatology (CQR) [4] to measure medication adherence. US joint/ soft tissue examination was carried out based on patient reported joint/ enthesitis tenderness. All the US findings which were explained through direct clinician-patient interaction. Scores of US disease activity were recorded semi-quantitatively.

Control group: 118 of age and sex matched group of patients living with inflammatory arthritis (61 RA and 57 Psoriatic arthritis) treated per Treat-to-Target in standard outpatient setting. The patients were subjected to the same clinical assessment and completed the same questionnaires at the same time intervals. However, they were not subjected to US guided education.

Appropriate tests of significance were used to compare the study statistics. Pearson correlation coefficients were used to test the relationship between patient beliefs and medication adherence.

Results: Incorporation of US-guided patient education improved patient motivation and adherence to therapy. Patient motivation scores showed the highest significant changes in response to the US-guided education at 3-, 6-, and 12-months of follow up (p< 0.001). This was paralleled by similar significant improvement in the DAS-28 score (P < 0.01) at both 3- and 6-months of follow up.

Patient cost-benefit decisions shifted positively in the group who had US guided education. The shift was in favour of “belief in the necessity” of medication with a mean ± SD cost-benefit ratio at 3-month of 2.72±3.41 which increased at 6-month to 4.92±4.84, whereas at 12-month 9.83±4.62, P = 0.01. Similar improvement was noted in the CQR score as well as functional disability and quality of life measures.

Conclusion: US-guided patient education helped to improve the patient motivation and those patients with better understanding of the treatment benefits were more inclined to accept risks in the pursuit of successful disease control. Results highlighted that inflammatory arthritis patients who were well informed about the risks and benefits of medication showed better cost-benefit analyses. The patients would be more adherent to medication if they visualized the necessity of medication outweighed concerns about adverse effects.

References:
Background/Purpose: As part of passage of the Affordable Care Act in 2010, Meaningful Use Core Measures were outlined to improve electronic medical record (EMR) systems. One of these such measures is enabling patients to electronically view laboratory results. Allowing patients to view and track their labs can improve patient engagement in their medical care. However whether increased electronic patient engagement results in better clinical outcomes is not yet known. We reviewed whether viewing labs amongst rheumatoid arthritis patients resulted in improvement in laboratory results over an 18 month period.

Methods: Data was obtained from a retrospective chart review of rheumatoid patients seen at the Ohio State University Rheumatology Clinics. The cohort included patients who had an ICD-9 or ICD-10 diagnosis consistent with rheumatoid arthritis. The most recent sedimentation rate (ESR) and an ESR 18 months prior were recorded as the two outcome measures. Patients were divided into a group who had viewed their labs online and a group that did not, which could be determined from our EMR tracking system. The difference between the ESR over the 18 months was calculated and a one tailed t test was done between the 2 groups.

Results: 173 patients were included in the study with 111 of the patients not viewing their labs online (Non-viewers) and 62 having viewed the labs online (Viewers). 138 of the patients were female (79.8%), with a mean age of 56.6 ±12.4 years. Baseline ESR were similar between both groups. At 18 months there was a statistically significant difference (p=0.039) in the ESR of 31.68 ±27.12 mm/hour in Non-viewers compared to 23.87 ±19.61 mm/hour in Viewers. However the degree of change in the ESR over the 2 data points was not statistically significant (p=0.29). The change in ESR over 18 months in the Non-viewers was -6.16 ±22.42 mm/hour compared to -8.16 ±23.93 mm/hour in Viewers.

Conclusion: To our knowledge this is the first study evaluating whether patient viewing of labs online results in a change in laboratory results overtime in rheumatoid arthritis patients. After 18 months the ESR did improve in both populations, however the degree of change in ESR over the course of 18 months in those who viewed labs online and those who did not was not statistically significant.

Table 1. Patient Demographics
<table>
<thead>
<tr>
<th></th>
<th>Non-Viewers</th>
<th>Viewers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>111</td>
<td>62</td>
</tr>
<tr>
<td>Age (years)</td>
<td>57.22 (±12.68)</td>
<td>55.5 (±11.83)</td>
</tr>
<tr>
<td>Female (%)</td>
<td>81.08%</td>
<td>77.40%</td>
</tr>
<tr>
<td>Race (n)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>59</td>
<td>52</td>
</tr>
<tr>
<td>African American</td>
<td>39</td>
<td>6</td>
</tr>
<tr>
<td>Hispanic</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Mexican</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Asian</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Middle Eastern</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Asian-Indian</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Laotian</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Bengali</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Somali</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 2. Sedimentation Rate (ESR) For Non-viewers and Viewers

<table>
<thead>
<tr>
<th></th>
<th>Non-Viewers</th>
<th>Viewers</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESR at start</td>
<td>37.98 (±31.46)</td>
<td>34.48 (±24.03)</td>
</tr>
<tr>
<td>ESR at 18 months</td>
<td>31.68 (±27.12)</td>
<td>23.87 (±19.61)</td>
</tr>
<tr>
<td>Change in ESR</td>
<td>-6.16 (±22.42)</td>
<td>-8.16 (±23.93)</td>
</tr>
</tbody>
</table>

Disclosure: S. Mascarenhas, None; S. Roy, None; A. Pinto, None; P. Gupta, None.


Abstract Number: 2032

Evaluation of RA Outcome Measures between Users and Non-Users of the Patient Portal

Sheryl Mascarenhas1, Shuvro Roy2, April Pinto2 and Preeta Gupta2, 1Rheumatology, The Ohio State University, Columbus, OH, 2The Ohio State University, Columbus, OH
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Patient engagement has become a growing focus in healthcare, catalyzed with the passage of the Affordable Care Act in 2010. Stage 2 of the Meaningful Use has criteria dependent on a patient portal, however whether electronic patient engagement translates into better clinical outcomes is yet to be determined. To begin an evaluation into this we reviewed outcomes in rheumatoid arthritis patients who had signed up for the patient portal compared to those who did not.

Methods: Data was obtained from a retrospective chart review of rheumatoid patients seen at the Ohio State University Rheumatology Clinics. The cohort included patients who had an ICD-9 or ICD-10 diagnosis consistent with rheumatoid arthritis. Patient outcome measures including the most recent sedimentation rate (ESR), Rapid 3, and swollen joint count were recorded along with demographic data. Two tailed t tests for these outcomes were done between each the group who had signed up for the patient portal compared to those who did not.

Results: 132 patients were included with 66 having signed up for the patient portal (Users) and 66 not signed up for the patient portal (Non-users). 103 (78.0%) of patients were female, with a mean age of 55 with a standard deviation of 13.79 years. Outcome measures
between the patients who signed up for the patient portal compared to those who had not 14.77 ±7.57 compared to 13.48 ±7.73 (p=0.33) for Rapid 3 scores, 1.97 ±2.25 compared to 2.86 ±4.06 (p=0.16) for swollen joint count, and 39.88 ±29.76 mm/hour compared to 30.61 ±22.04 mm/hour (p=0.04) for ESR.

**Conclusion:** To our knowledge this is the first study to examine whether electronic patient engagement is associated with a change in clinical outcomes in rheumatoid arthritis. This initial study cohort does not demonstrate any clinically significant change in several key outcome measures in rheumatoid arthritis, particularly Rapid 3 scores, swollen joint counts. However there was a statistical difference between the ESR, with more favorable values in patients using the patient portal. This data suggests further study is needed to better understand if electronic patient engagement does have an effect on clinical outcomes in RA.

### Table 1. Patient Demographics

<table>
<thead>
<tr>
<th>Race (n)</th>
<th>Non-Users</th>
<th>Users</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>41</td>
<td>53</td>
</tr>
<tr>
<td>African American</td>
<td>16</td>
<td>7</td>
</tr>
<tr>
<td>Hispanic</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Laotian</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Bengali</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Asian Indian</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Mexican</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Asian</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Middle Eastern</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Pakistani</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Unknown</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 2. Outcome Measures between Users and Non-Users of the Patient Portal

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Non-Users</th>
<th>Users</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESR</td>
<td>39.88 (±29.76)</td>
<td>30.61 (±22.04)</td>
<td>0.04</td>
</tr>
<tr>
<td>Swollen joint count</td>
<td>1.97 (±2.25)</td>
<td>2.86 (±4.06)</td>
<td>0.16</td>
</tr>
<tr>
<td>Rapid 3</td>
<td>14.77 (±7.57)</td>
<td>13.48 (±7.73)</td>
<td>0.33</td>
</tr>
</tbody>
</table>

**Disclosure:** S. Mascarenhas, None; S. Roy, None; A. Pinto, None; P. Gupta, None.


**Abstract Number:** 2033

**Low Health Literacy Does Not Impact Adherence to Hydroxychloroquine in Patients with Systemic Lupus**

Alexandra Perel-Winkler¹, Kayla Neville², Samantha Nguyen¹, Miya Okado¹, James Miceli¹, Jon T. Giles³ and Anca Askanase¹,

¹Rheumatology, Columbia University College of Physicians & Surgeons, New York, NY, ²Columbia University College of Physicians & Surgeons, New York, NY, ³Division of Rheumatology, Columbia University College of Physicians & Surgeons, New York, NY

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Measures and Measurement of Healthcare Quality Poster II

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM
**Background/Purpose:** Low health literacy has been associated with poor health outcomes and increased hospital admissions. Adherence to medication has been shown to significantly impact mortality, morbidity, and health care utilization in SLE. The relationship between medication adherence and health literacy has not been evaluated in SLE. Accordingly, the current study aims to assess the relationship between health literacy and adherence to HCQ in a multiethnic, urban SLE population.

**Methods:** SLE patients from the Columbia Lupus Center meeting ACR/SLICC criteria, treated with HCQ for >6 months, that had self-reported adherence, were included in study. Health literacy was assessed in English or Spanish using the validated Pfizer Health Literacy Questionnaire (HLQ), OneVest Vital Signs. Limited health literacy is defined as an HLQ score of 0-3, and adequate health literacy as a score of 4-6. HCQ testing was done by high performance liquid chromatography on whole blood by Exagen Laboratory. Adherence was defined as a HCQ level of >/= 500ng/ml. We evaluated the relationship between HLQ score, patient demographics, disease characteristics, and HCQ levels. A significant association was considered at \( p \leq 0.05 \).

**Results:** The study included 67 lupus patients, average age 37 (range 19-66)91% female, 58% Hispanic, and average SLEDAI of 4.5 (range 0-15). 60% (n=40) of the population had limited health literacy, with HLQ scores of 0-3. Limited health literacy was significantly associated with Hispanic ethnicity, being Spanish speaking only (language barrier), having a household income below the poverty line, and less than high school education (Table 1). Younger patients and those with longer disease duration were more likely to have adequate health literacy. HCQ adherence, disease activity scores and SLE disease characteristics, such as organ involvement or current/recent use of steroids, were not associated with health literacy (Table 2).

**Conclusion:** Limited health literacy is significantly associated with markers of low socioeconomic status (SES) such as low level of education, language barrier, and poverty. There was no association between health literacy and medication adherence or disease activity. These data suggest that in an urban, multiethnic SLE population alternative factors affect compliance. Further study into these alternative factors is likely to help improve adherence.

**Disclosure:** A. Perel-Winkler, None; K. Neville, None; S. Nguyen, None; M. Okado, None; J. Miceli, None; J. T. Giles, None; A. Askanase, Exagen, 2.


**Abstract Number:** 2034

**New Guidelines on Hydroxychloroquine Dosage – Where Are We?**

Shriyanka Jain\(^1\) and John Waterman\(^2\), \(^1\)Division of Rheumatology, University of Connecticut, School of Medicine, Farmington, CT, \(^2\)Rheumatology, Connecticut VA Healthcare System, Newington, CT

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017
Background/Purpose:

Hydroxychloroquine (HCQ) is a widely-used medication in many rheumatologic conditions. The most worrisome toxicity is irreversible damage to retinal pigment epithelium which can lead to blindness. The most recent 2016 guidelines from the American Academy of Ophthalmology (AAO) recommend the dose of HCQ ≤5 mg/kg real body weight to minimize toxicity. According to these new guidelines, the risk of HCQ retinopathy is less than 1% in the first year of therapy and less than 2% up to 10 years of therapy. There is an increased risk of HCQ retinopathy with increase in the cumulative dose. Per the prior 2011 AAO guidelines the recommended maximum dose to minimize HCQ retinal toxicity was 6.5 mg/kg based on ideal body weight. The advantage of the real body weight formula is that it distributes the risk evenly on a broad range of body habitus.

Methods:

We identified, patients on HCQ in year 2016 at VA Connecticut Health Care System. Primary outcome was to identify patients whose dose exceeded the maximum recommended dose as per the 2016 guidelines. Data on indications for medication use, dose, ideal weight, real weight, duration of therapy and adherence to the last 3 years screening ophthalmologic exams were obtained. We also looked at the number of patients who were discontinued from HCQ use due to retinal toxicity.

Results:

There were 102 patients who were prescribed HCQ in the year 2016. 89 patients were actively on HCQ. The average age was 64.7; (69/89) were male. 46/89 had RA. 12/89 had SLE. Other diseases included ScLE, MCTD, UCTD, Sjogren’s syndrome, hepatitis C related arthritis. 45/77 of patients had 3 ophthalmology screening in past 3 years for toxicity. The average duration of HCQ use varied from <1 year to 20 years. There were 19/89 (21.3%) patients who were receiving more than 5 mg/kg/day of HCQ. HCQ was discontinued in one patient due to HCQ retinal toxicity during the observation period. He had been on HCQ for 13 years.

Conclusion:

Our study revealed, 19/89 (21.3%) patients who were receiving more than currently recommended daily doses of HCQ based on the 2016 AAO guidelines potentially placing them at increased risk for HCQ retinal toxicity. With the new guidelines for HCQ dosing it becomes imperative for rheumatologists to assess the weight of their patients and adjust the dose of HCQ downward if the patient weights <80 kg.

References:


Disclosure: S. Jain, None; J. Waterman, None.

Clinical Audit of Hydroxychloroquine Dosing and Toxicity Screening in Patients with Inflammatory Arthritis and Connective Tissue Diseases

Sahil Koppikar¹ and Henry Averns², ¹Department of Rheumatology, University of Toronto, Toronto, ON, Canada, ²Private Practice, Kingston, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Background/Purpose: Hydroxychloroquine (HCQ) is used widely for the treatment of inflammatory arthritides and systemic lupus erythematosus. Recent publications have shown that HCQ toxicity is not as rare as previously thought among long-term users of the drug, with overall prevalence in a large demographic study around 7.5%. The risk of toxicity was greatly dependent on daily dose. Furthermore, HCQ retinopathy is not reversible and cellular damage may progress even after the drugs are stopped. The purpose of our study was to determine whether appropriate HCQ dosing and toxicity screening is elicited during regular clinical encounters for patients with inflammatory arthritis and connective tissue diseases.

Methods: A prospective clinical audit was conducted at nine Canadian rheumatology practices in eastern Ontario. Audit standards were based on the American College of Rheumatology (ACR) and American Academy of Ophthalmology (AAO) recommendations. Best practice standards included appropriate weight based dosing of hydroxychloroquine and subsequent monitoring for toxicity. We audited 100 appropriate patient encounters, spread out over nine practices using a standardized screening form.

Results: Among the 100 patients enrolled in the study, 80% were female with an average age of 58 years. Patients were on hydroxychloroquine for an average duration of 73 months, with rheumatoid arthritis (61%) and systemic lupus erythematosus (23%) being the most common diagnoses as per the ACR classification criteria. A total of 62 patients were considered high risk for retinal toxicity based on AAO criteria including age, duration of use, renal or liver dysfunction and pre-existing retinal disease.

Three out of four audit standards were not met. No patients in our audit had hydroxychloroquine retinopathy and therefore, the last standard could not be assessed. Only 70% of patients were being appropriately dosed based on body weight. Furthermore, 17% of patients were on a prescription dose that was greater than 10% of the recommended dosage. Only 87% of patients had a baseline ophthalmologic exam in the first year of treatment, while guidelines suggest all patients should have one. Within the hydroxychloroquine retinopathy high-risk cohort, only 91% of patients were getting yearly eye exams.

Conclusion: Our guideline-based standards of appropriately dosing hydroxychloroquine and monitoring for retinopathy are not being met in typical patient encounters. The current system can be improved and the next step is to provide clinicians with a weight-based dosing chart that includes monitoring requirements. This intervention will be applied over three months and a re-audit will be conducted. The results will be compared to pre-intervention outcomes.

Disclosure: S. Koppikar, None; H. Averns, None.


Abstract Number: 2036

Rheumatologists’ Compliance with Screening for Viral Hepatitis B and C Prior to Initiation of Methotrexate Treatment Needs Quality Improvement

Farheen Jaffari1, Andras Perl2 and Fatme Allam3, 1Rheumatology, SUNY Upstate, Syracuse, NY, 2Medicine, SUNY Upstate Medical University, Syracuse, NY, 3SUNY Upstate Medical University, Syracuse, NY

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

The risk of viral hepatitis reactivation in patients undergoing immunomodulating therapy is being increasingly recognized. The American College of Rheumatology guidelines recommends screening for hepatitis B virus (HBV) and hepatitis C virus (HCV) infections prior to initiation of Methotrexate (Arthritis Rheum. 2003; 49: 843–845; Arthritis Rheum. 2008; 59: 762–784). In this Quality Improvement (QI) study, we evaluated screening practices at the Veterans Affairs (VA) Medical Center in Syracuse, New York.
Methods:

To perform quality assessment as the first step of the Plan-Do-Study-Act QI methodology (BMJ Qual Saf. 2014; 23: 290–8), we extracted records of 299 patients receiving methotrexate for rheumatologic diseases at the Syracuse VA between 2011-2016. The patient records were then retrospectively examined to assess if they had undergone screening for HBV and HCV infections prior to initiation of methotrexate. The inclusion criteria were defined as: 1) age > 30 years; 2) initiation of methotrexate within the 5 years preceding the study period; and 3) methotrexate dosages < 30 mg per week. Compliance rate from the current study at the Syracuse VA was compared to two previously published studies with chi-square test using GraphPad software (San Diego, CA). Two-tailed p <0.05 was considered significant.

Results:

From a total of 299 patients treated with methotrexate at the Syracuse VA, only 104 (34%) were screened for both HBV and HCV infections prior to therapy initiation. In comparison to peer-reviewed literature, there was considerable variability in screening rates.

Table 1: HBV and HCV screening at the Syracuse VA and its comparison to the literature.

<table>
<thead>
<tr>
<th>Study</th>
<th>Tested</th>
<th>Not tested</th>
<th>Compliance</th>
<th>Chi-square p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Syracuse VA</td>
<td>104</td>
<td>195</td>
<td>34.7%</td>
<td>-</td>
</tr>
<tr>
<td>Clin Rheumatol 2014; 33: 1823</td>
<td>6</td>
<td>79</td>
<td>7%</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Clin Exp Rheumatol. 2016; 34:473-9</td>
<td>861</td>
<td>475</td>
<td>64.4%</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

Conclusion:

Our study clearly indicates that QI aimed at increasing compliance with ACR guidelines among rheumatologists regarding the risks of viral hepatitis reactivation in patients treated with immunosuppressant medications is warranted. We propose a QI initiative that testing for HBV and HCV should be prompted when electronically ordering methotrexate in patients with rheumatic diseases.

Disclosure: F. Jaffari, None; A. Perl, None; F. Allam, None.


Abstract Number: 2037

HLA-B27 Testing in Patients >= 45 Years of Age and Subsequent Diagnosis of Late Onset Spondyloarthritis

Marc W. Nolan1,2, Morgan M. Brown3 and Elie Gertner1,2, 1Section of Rheumatology, Regions Hospital, St. Paul, MN, 2Division of Rheumatology, University of Minnesota Medical School, Minneapolis, MN, 3HealthPartners Institute, St. Paul, MN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

In 2015, the Canadian Rheumatology Association published their Choosing Wisely recommendations regarding HLA-B27 testing. One of the criteria that triggers testing is inflammatory back pain in patients < 45 years old (y/o). This was chosen based on ASAS criteria for axial and peripheral SpA which were validated in patients under 45 y/o. However, studies have indicated that 3-10.6% of patients with SpA diagnosis occur in patients >= 45 y/o, hinting at a “late onset” SpA group. We sought to assess the utility of HLA-B27 testing in patients >= 45 y/o to determine how many were eventually diagnosed with SpA.

Methods:
Retrospective analysis of all patients $\geq 45$ y/o who had HLA-B27 testing by a non-rheumatology provider (PCP, Ophthalmology, Orthopedics) at Regions Hospital/ Health Partners, a large academic vertically and horizontally integrated health care system, from 1/1/2014 - 7/1/2015. Chart review identified features of SpA (defined as inflammatory back pain $> 3$ months with onset $< 45$ y/o, peripheral synovitis, enthesitis, dactylitis, psoriasis, or uveitis) that were present at the time of HLA-B27 testing. We assessed if imaging (Xray, CT, or MRI) identifying sacroiliitis +/- 6 months from HLA-B27 order was present, the presence of inflammatory markers (ESR or CRP) +/- 1 month from the HLA-B27 order, and if an eventual diagnosis of SpA was made. Data were analyzed to generate descriptive information regarding frequency, and logistic regression was used to identify which features of SpA and SpA subsets are identified in HLA-B27 tested patients $\geq 45$ y/o.

Results:

Over the 18 months, 291 HLA-B27 tests were ordered by non-rheumatologists. The age ranged from 1 to 92 years. 141/291 tests were in individuals $\geq 45$ y/o [63 tests $> 50$ y/o, 44 tests $> 55$ y/o]. Diagnosis of a SpA was made in 11/141 (7.8%) (8 AS, 3 PsA) whereas 32 total diagnoses of SpA were made in the entire group (regardless of age). Thus, 11/32 (34.4%) of SpA diagnosis occurred in patients $\geq 45$ y/o. At a 95% confidence level, psoriasis (OR 14.66) and back pain (OR 13.98) were the significant predictors for SpA in the group $\geq 45$ y/o (Table 1). There were insufficient numbers to evaluate the predictive value of the other symptoms in the group $\geq 45$ y/o. In the entire group, back pain was also the most significant predictive factor (OR 28.5) for a diagnosis of SpA. Thus inflammatory back pain can trigger evaluation for SpA regardless of age.

Conclusion:

In this study, of the 291 non-rheumatologist ordered HLA-B27 tests, 11/141 (7.8%) of patients $\geq 45$ y/o eventually received a SpA diagnosis which represents 1/3 of the eventual SpA diagnoses. This significant amount of late onset SpA combined with the highest OR being back pain emphasizes the importance of being aware of late onset SpA as well as considering inflammatory back pain regardless of age as a feature for SpA.

| Table 1. Demographics, HLA-B27 results, SpA diagnoses and features in a large integrated healthcare system. |
|---------------------------------------------------------------|---------------------------------------------------------------|---------------------------------------------------------------|---------------------------------------------------------------|---------------------------------------------------------------|
|                                                                                                           | N (%),< 45                                                  | N (%),$\geq 45$                                              | N (% of total)                                               | OR (p) for $\geq 45$ group with SpA diagnosis |
| Male                                                         |                                                                                                           |                                                             |                                                             | |
| Male                                                         |                                                                                                           |                                                             |                                                             | |
| Female                                                       |                                                                                                           |                                                             |                                                             | |
| HLA-B27 Positive                                            | 37 (24.67%)                                                 | 25 (17.73%)                                                | 62 (21.31%)                                                 | 21.75 (0.0017)                                             |
| HLA-B27 Negative                                            | 113 (75.33%)                                                | 116 (82.27%)                                               | 229 (78.69%)                                                |                                                           |
| SpA Diagnosis                                                | 21 (14.00%)                                                 | 11 (7.80%)                                                 | 32 (11.00%)                                                 |                                                           |
| No SpA Diagnosis                                             | 129 (86.00%)                                                | 130 (92.20%)                                               | 259 (89.00%)                                                |                                                           |
| AS                                                           | 11 (7.33%)                                                  | 8 (5.67%)                                                  | 19 (6.53%)                                                  |                                                           |
| PsA                                                          | 5 (3.33%)                                                   | 3 (2.13%)                                                  | 8 (2.75%)                                                   |                                                           |
| IBD                                                          | 3 (2.00%)                                                   | 0 (0.00%)                                                  | 3 (1.03%)                                                   |                                                           |
| Reactive                                                     | 2 (1.33%)                                                   | 0 (0.00%)                                                  | 2 (0.69%)                                                   |                                                           |
| Inflammatory Back Pain                                      | 38 (25.33%)                                                 | 17 (12.06%)                                                | 55 (18.90%)                                                 | 13.98 (0.0036)                                            |
| Peripheral Synovitis                                        | 16 (10.67%)                                                 | 8 (5.67%)                                                  | 24 (8.25%)                                                  | 2.34 (0.5446)                                             |
| Enthesitis                                                   | 4 (2.67%)                                                   | 2 (1.42%)                                                  | 6 (2.06%)                                                   | 0 (0.9977)                                                |
| Dactylitis                                                   | 3 (2.00%)                                                   | 3 (2.13%)                                                  | 6 (2.06%)                                                   | 0 (0.9966)                                                |
| Psoriasis                                                    | 8 (5.33%)                                                   | 13 (9.22%)                                                 | 21 (7.22%)                                                  | 14.66 (0.0191)                                            |
| Uveitis                                                      | 32 (21.33%)                                                 | 44 (31.21%)                                                | 76 (26.17%)                                                 | 0.85 (0.8713)                                             |

Disclosure: M. W. Nolan, None; M. M. Brown, None; E. Gertner, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/hla-b27-testing-in-patients-45-years-of-age-and-subsequent-diagnosis-of-late-onset-spondyloarthritis

Abstract Number: 2038

Radiological Changes Measured By MRI and High-Resolution Peripheral Quantitative Computed Tomography (HR-pQCT) Show Correlation with Michigan
Hand Outcome Questionnaire (MHQ) in Rheumatoid Arthritis Patients

Ana Cruz1, Tomohiro Shimizu2, Matthew Tanaka3, Kenji Mamoto3, Andrew J Burghardt3, Ursula Heilmeier3, Thomas Link3, Jonathan Graf4, John B. Imboden Jr.5 and Xiaojuan Li6, 1University of California, San Francisco, San Francisco, CA, 2Department of Radiology & Biomedical Imaging, Musculoskeletal Quantitative Imaging Research, University of California, San Francisco, SAN FRANCISCO, CA, 3Department of Radiology & Biomedical Imaging, Musculoskeletal Quantitative Imaging Research, University of California, San Francisco, San Francisco, CA, 4Department of Medicine, Division of Rheumatology Zuckerberg San Francisco General Hospital, University of California, San Francisco, San Francisco, CA, 5Department of Medicine, University of California, San Francisco, San Francisco, CA, 6Radiology & Biomedical Imaging, Department of Radiology and Biomedical Imaging, University of California San Francisco, San Francisco, CA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Disease progression and therapy response in patients with rheumatoid arthritis (RA) is currently evaluated using clinical and functional assessments that include subjective measurements such as DAS28, HAQ, and the Michigan Hand Outcome Questionnaire (MHQ). Studies have been conducted to determine potential associations between radiological imaging, DAS28, and HAQ. There are limited studies that investigate the connection with MHQ. Our study aims to explore if radiological studies using magnetic resonance imaging (MRI) and high-resolution peripheral quantitative computed tomography (HR-pQCT) demonstrate any association with the more hand-focused MHQ score.

Methods: Patients were screened and separated into two groups based on their disease activity determined by DAS28: Group I: low disease activity (DAS28 ≤3.2) and Group II: high disease activity (DAS28 >3.2). Following current guidelines set by the American College of Rheumatology (ACR); group I continued their current treatment using methotrexate, while group II were initiated on an anti-TNFα. At baseline (immediately before anti-TNFα initiation for group II) and 3-months, each patient underwent clinical (DAS28), functional (MHQ and HAQ), and structural (imaging of dominant hands/wrists via 3 Tesla MRI and HR-pQCT) assessments. Bone marrow edema pattern, synovitis, and erosion were graded using the RA MRI score (RAMRIS) system. Bone erosion volumes were calculated using HR-pQCT images. Measures at baseline and 3-months were compared using paired t-test. The association between changes in MHQ and imaging measures from baseline to 3-months were evaluated using Pearson’s correlation coefficient.

Results: Twenty patients were studied (9 group I and 11 group II, Table 1). Significant increases in MHQ (suggesting improvement) and significant decreases of DAS and erosion volumes from baseline to 3-months were observed in group II (Table 1); while significant increases in DAS28-CRP and erosion volumes were observed in group I. 3-month changes in bone erosion volume and edema had a significant correlation with changes in MHQ score (Figure 1 top). Significant correlations with 3-month changes in MHQ and DAS28 and HAQ were also found (Figure 1 bottom).

Conclusion: Advanced imaging measures such as bone erosion volume and bone marrow edema show great potential to serve as biomarkers to determine disease progression, therapy response, and specific hand functions in patients with RA. The study is recruiting more patients and will follow up patients at 12-months to evaluate potential imaging markers that may predict hand functional outcomes.

<table>
<thead>
<tr>
<th>Table 1: Patient Demographic and Clinical Information</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group I</strong></td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>61.6 (13.1)</td>
</tr>
<tr>
<td>Female, %</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
</tr>
<tr>
<td>MHQ</td>
</tr>
<tr>
<td>79.8 (20.2)</td>
</tr>
<tr>
<td>HAQ</td>
</tr>
<tr>
<td>1.0 (0.8)</td>
</tr>
<tr>
<td>1.9 (0.7)</td>
</tr>
<tr>
<td>DAS28-CRP</td>
</tr>
<tr>
<td>1.8 (0.6)</td>
</tr>
<tr>
<td>3.5 (1.1)</td>
</tr>
<tr>
<td>DAS28-ESR</td>
</tr>
<tr>
<td>1.9 (0.9)</td>
</tr>
<tr>
<td>3.5 (1.2)</td>
</tr>
<tr>
<td>HR-pQCT total erosion volume (mm³)</td>
</tr>
<tr>
<td>24.9 (24.5)</td>
</tr>
<tr>
<td>184.2 (318.2)</td>
</tr>
<tr>
<td>RAMRIS Synovitis</td>
</tr>
<tr>
<td>3.4 (2.1)</td>
</tr>
<tr>
<td>8.1 (8.1)</td>
</tr>
<tr>
<td>RAMRIS Bone erosion</td>
</tr>
<tr>
<td>2.6 (2.3)</td>
</tr>
<tr>
<td>39.4 (33.2)</td>
</tr>
<tr>
<td>RAMRIS Bone edema</td>
</tr>
<tr>
<td>5.5 (3.8)</td>
</tr>
<tr>
<td>9.3 (6.9)</td>
</tr>
</tbody>
</table>

Data presented in mean (SD); *Significant paired t-test compared to baseline (p<0.05)
Validity of the WPAI-SHP in Psoriatic Arthritis and Estimation of the Minimally Important Difference

William Tillett¹,², Gavin Shaddick³, Bashaar Boyce⁴ and Neil J. McHugh⁵, ¹Pharmacy and Pharmacology, University of Bath, Bath, United Kingdom, ²Royal National Hospital for Rheumatic Diseases and University of Bath, Bath, United Kingdom, ³Centre for Data Science and Statistics, University of Exeter, Bath, United Kingdom, ⁴Royal National Hospital for Rheumatic Diseases, Bath, United Kingdom, ⁵Royal National Hospital for Rheumatic Diseases, Bath, UK, Bath, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Participation, including work disability, is an important patient centred outcome and is in the middle ring of the Outcome Measures in Rheumatology (OMERACT) psoriatic arthritis core set of domains. The Work Productivity and Activity Index Specific Health Problem (WPAI-SHP) is a feasible, patient reported measure of work disability but there is little data on the validity of the WPAI-SHP in PsA. We set out to determine the validity of the WPAI-SHP and the minimally important difference (MID) for improvement in PsA.

Methods:
LOPAS II is a UK multicentre observational study of work disability in PsA. Working patients were included for analysis. Construct validity was determined by correlation with other clinical and patient reported outcomes using spearman correlation coefficients. Responsiveness was calculated using the standard error of the mean (SEM). The MID was determined by the health based anchor method (mean change in score amongst patients who improved) and the receiver operating characteristic curve (ROC) method.

Results:
Analyses were undertaken on 177 of 229(77.3%) working participants with complete data at baseline and three months follow up. The mean age was 48 years and median disease duration 6.0 years (IQR 2.0 – 12.0). The mean change of presenteeism was -7.9 (sd30.0), SEM 16.2 and SRM -0.26. Correlations with other outcomes are reported in table 1. Amongst 105 (59.3%) patients who reported no change between baseline and follow up the mean change in WPAI was; absenteeism 2.9 (sd30.7), presenteeism 4 (22.4), productivity loss 7.7 (22.4), activity impairment 1.9 (24.4). The MID for improvement amongst 72 (40.7) patients who reported improvement was; absenteeism -6.1 (26.2), presenteeism -20.8 (28.2), productivity loss -21.7 (30.8) and activity impairment -27.2 (29.5). The MID using the ROC method for presenteeism, productivity loss and activity impairment was -5.0 (AUC 0.75), -11.3 (AUC 0.76) and -25.0 (AUC 0.79) respectively (Figure 1).
Conclusion:

We report data on the validity of the WPAI-SHP in PsA and an estimate of the MID for improvement. Presenteeism and productivity loss are moderately correlated with clinical measures. Responsiveness was small to moderate amongst the group as a whole.

Table 1 Spearman correlation coefficients of the WPAI-SHP and clinical, composite and patient reported outcomes at baseline.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>WPAI absenteeism</th>
<th>WPAI presenteeism</th>
<th>WPAI productivity loss</th>
<th>WPAI activity impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAPSA</td>
<td>0.20</td>
<td>0.34</td>
<td>0.39</td>
<td>0.45</td>
</tr>
<tr>
<td>RAPID3</td>
<td>0.32</td>
<td>0.54</td>
<td>0.62</td>
<td>0.77</td>
</tr>
<tr>
<td>HAQ</td>
<td>0.31</td>
<td>0.42</td>
<td>0.51</td>
<td>0.61</td>
</tr>
<tr>
<td>EQ5D</td>
<td>-0.29</td>
<td>-0.42</td>
<td>-0.44</td>
<td>-0.59</td>
</tr>
<tr>
<td>FACIT fatigue</td>
<td>-0.40</td>
<td>-0.44</td>
<td>-0.53</td>
<td>-0.61</td>
</tr>
<tr>
<td>Global VAS</td>
<td>0.26</td>
<td>0.47</td>
<td>0.52</td>
<td>0.70</td>
</tr>
<tr>
<td>Pain VAS</td>
<td>0.26</td>
<td>0.51</td>
<td>0.57</td>
<td>0.65</td>
</tr>
</tbody>
</table>

Disclosure: W. Tillett, Sonya Abraham, MRCP, PhD, 2,Sonya Abraham, MRCP, PhD, 5,Sonya Abraham, MRCP, PhD, 9; G. Shaddick, None; B. Boyce, None; N. J. McHugh, None.


Abstract Number: 2040

Improving Quality of Care for Rheumatoid Arthritis Patients in an Underserved Area

Qingying Lai¹ and Beverly Johnson², ¹Internal Medicine, Jacobi Medical Center, Bronx, NY, ²Department of Rheumatology, Jacobi Medical Center, Bronx, NY

First publication: September 18, 2017
Background/Purpose:

The American College of Rheumatology (ACR) has endorsed a set of quality measurements for patients with rheumatoid arthritis (RA). Our patient population was at two city hospitals which serve a large underserved population. This study is aimed to use these ACR quality measurements to assess the quality of care of RA patients in this population.

Methods:

This is a retrospective study conducted by chart review of patients with an ICD-9 or ICD-10 diagnosis code of RA that visited rheumatology clinic of two public hospitals in an underserved area between July 1st, 2015-July 1st, 2016. All patients met ACR criteria for RA. We measured five ACR endorsed quality measurements (see Table 1) and compared between patients of different socioeconomic status (SES) and different provider type (trainees and attendings).

Results:

240 patients were seen in rheumatology clinic of the two public hospitals during the targeted time period, 89% of whom were of low SES defined as having Medicare/Medicaid or no insurance. Almost all patients were on DMARD (95.8%) during the index clinic visit and 35% were on biological DMARD. The majority of the patients (7/11) not on DMARD were of low SES and were not on DMARD due to documented non-compliance and poor follow-up. All patients (83/84) with increased disease activity had changes in regimen except for one who refused changes. Among the 28 patients who were started on biological DMARD during the targeted year, 25% (7/28) had no tuberculosis (TB) screening documented within the prior 12 months (3 had TB screening more than 12 months prior, 2 were documented after initiation of biological DMARD and 2 had no documentation). Less than half of the patients (43%) had Clinical Disease Activity Index (CDAI) documented in >=50% of the clinic encounters. Attendings had a slightly better percentage of CDAI documentation than trainees (49% vs 40%) but the difference was not statistically significant (chi-square test, p=0.206). Only 7% of patients were on prednisone > 10mg daily for more than 3 months and most of them (10/13) had a documented glucocorticoid taper plan.

Conclusion:

Providing high quality of care to patients with rheumatoid arthritis in an underserved area is challenging. Our providers did a good job of initiating DMARD, escalating treatment in the face of high disease activity and decreasing high prednisone doses. In these areas, the main limitation was low SES with medication non-compliance. Areas for improvement are reaching 100% screening for TB prior to starting biologics and to achieve higher disease activity documentation rate. Based upon this study, a prospective intervention will be started in the clinics to improve TB screening and documentation of disease activity as an ongoing divisional QI project.

Table 1: ACR Endorsed Quality Measurement

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Percentage of patients with diagnosis of RA who were prescribed DMARD therapy within 12 months</td>
</tr>
<tr>
<td>2</td>
<td>Percentage of patients with increased disease activity have changes in regimen (e.g. Change DMARD/glucocorticoid dose, add additional DMARD et al.)</td>
</tr>
<tr>
<td>3</td>
<td>Percentage of patients who have TB screening documented within 12 months prior to receiving first course of biological DMARD</td>
</tr>
<tr>
<td>4</td>
<td>Percentage of patients have &gt;=50% total number of outpatient encounters with disease activity assessment</td>
</tr>
<tr>
<td>5</td>
<td>Percentage of patients being on prolonged doses of prednisone &gt; 10mg daily have documented glucocorticoid management plan</td>
</tr>
</tbody>
</table>

Disclosure: Q. Lai, None; B. Johnson, Johnson & Johnson, 1,TREG, 5.
Abstract Number: 2041

**Practice Improvement Utilizing Six Sigma and Health Informatics in an Academic Setting**

Puneet Bajaj1, Shilu Varghese2, Allison Sunleaf2, Paul Padilla2, Shannon Scielzo2, Sherene Philip2, Justin Haridas2, Claire Wang2, Vaishnavi Kannan2, Jeffrey Lewis2, Deepa Bhat2, Jacqueline Mutz2, Duwayne Willett2, Jason Fish2 and David Karp2, 1Rheumatology, UT Southwestern Medical Center, Dallas, TX, 2UT Southwestern Medical Center, Dallas, TX

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** Measures and Measurement of Healthcare Quality Poster II  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

For projects such as the ACR Rheumatology Informatics System for Effectiveness (RISE) to succeed for quality improvement, practice benchmarking, & research, the data included must be high fidelity and represent the majority of patients in participating practices. To prepare a large academic practice for RISE participation, we synergistically harnessed the power of institutional informatics coupled with systems engineering. We focused on two Rheumatoid Arthritis (RA) assessments: Routine Assessment of Patient Index Data (RAPID3) & Clinical Disease Activity Index (CDAI). Baseline data was extremely low (13% & 27% respectively). The aim was to improve compliance for these instruments in the Rheumatology clinics to > 75% by December 2016.

**Methods:**

High quality data was extracted from our RA registry established in April 2015. Inclusion criteria: RA patients seen by a rheumatology provider twice in the last 24 months & at least once in last 12 months. By Feb 2017, the registry had 543 patients. The project team utilized Six Sigma DMAIC (Define, Measure, Analyze, Improve & Control) data-driven improvement cycle for problem-solving & process improvement. Tools & techniques included brainstorming, project charter, process maps, fishbone diagrams, Pareto chart, & feedback communications. Interventions were aimed towards standardization of clinic work flow, and motivating better EMR documentation practices.

**Results:**

We examined growth of compliance (proportion of completed assessments) over time. We found very strong effect sizes \( r > .90, p < .001 \) for both completion of the Rapid3 & CDAI (average growth rates over 3% a month). Their compliance was also highly related; but Rapid3 compliance was not the sole explanatory variable for CDAI compliance as demonstrated by mediational analyses.

We have created modified control charts (Tables 1 & 2). Given our goal to demonstrate differences over time, the standard error of difference (SED; \((σ/N)^{*\sqrt(2)}*1.96\)) within month was calculated and used to create the bounds around the observed compliance rates. Any month’s proportion rate outside of other months’ SED bounds is statistically different at \( α = .05 \).

**Conclusion:**

Combining the power of informatics & systems engineering led to impressive improvements in provider behaviors. This methodology helped to identify opportunities to overcome barriers & to motivate providers. High quality processes facilitated high quality data, and vice versa. Performance expectations were clear, improvements were sustained, and we have believable long-term RA outcomes data that can be used to improve outcomes at the practice level.
Disclosure: P. Bajaj, None; S. Varghese, None; A. Sunleaf, None; P. Padilla, None; S. Scielzo, None; S. Philip, None; J. Haridas, None; C. Wang, None; V. Kannan, None; J. Lewis, None; D. Bhat, None; J. Mutz, None; D. Willett, None; J. Fish, None; D. Karp, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/practice-improvement-utilizing-six-sigma-and-health-informatics-in-an-academic-setting

Abstract Number: 2042

Referral Criteria to an Early Arthritis Clinic: Poor Agreement between Referring Physicians and Rheumatologists
Rheumatology, Centro Hospitalar do Baixo Vouga, E.P.E., Aveiro, Portugal, 2Rheumatology, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal, 3Centre for Social Studies, Universidade de Coimbra, Coimbra, Portugal, 4Faculty of Medicine, Universidade de Coimbra, Coimbra, Portugal

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Prompt identification and referral of patients with suspected inflammatory arthritis to a rheumatology clinic are crucial for early diagnosis and treatment. In the referral letter to our Early Arthritis Clinic (EAC), the physician should refer, out from seven possible criteria, the ones motivating the referral. The objectives of our study were: 1) to assess the level of agreement between the referring physician and the rheumatologist, regarding the presence of referral criteria; 2) to identify the set of criteria that best predicts the presence of inflammatory arthritis.

Methods: Unicentric retrospective observational study, including patients observed in the EAC until May/2016. Subjects were excluded if they had been referred to the EAC by a rheumatologist and if we couldn’t access the referral letter or the medical records from the first visit to the EAC. Demographic data, provenience, referral criteria and the final diagnosis were retrieved from individual clinical files and the Portuguese Registry of Rheumatic Patients – Reuma.pt. For the referral criteria, the agreement between the referring physician and the rheumatologist in the first EAC visit, was assessed using the Cohen’s Kappa. In the second step, we created four new variables, each one corresponding to a set of criteria, as indicated by the referring physician. ROC curves were drawn by a nonparametric method in order to identify the set that best predicts the presence of inflammatory arthritis.

Results: We included 132 patients, 66% females, mean age 52±17 years; Referred from primary care (72%), emergency department (17%) and other hospital specialties (11%). An inflammatory arthritis was diagnosed in 73% of the cases. Table 1 shows the level of agreement between the referring physician and the rheumatologist, regarding the presence of each of the referral criteria. Table 2 shows the area under the curve for each set of criteria.

Conclusion: Among the clinical criteria, there was poor agreement regarding the presence of arthritis and no significant agreement regarding the characterization of the arthralgia as inflammatory, the morning stiffness and the squeeze test. The weak performance of all sets of criteria in predicting inflammatory arthritis is probably due to deficient recognition of each criterium. These results suggest the need for improving education among the physicians referring patients to the EAC.

Table 1: Agreement between the referring physician and the rheumatologist, regarding the presence of each of seven criteria.

<table>
<thead>
<tr>
<th>Referral criteria</th>
<th>N Ref/Rheum</th>
<th>kappa</th>
<th>CI 95%</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthritis (N=122)</td>
<td>83/82</td>
<td>0.23</td>
<td>0.05-0.41</td>
<td>0.01</td>
</tr>
<tr>
<td>Squeeze (N=80)</td>
<td>23/36</td>
<td>0.03</td>
<td>-0.17-0.24</td>
<td>0.75</td>
</tr>
<tr>
<td>Inflammatory arthralgia (N=131)</td>
<td>95/112</td>
<td>-0.01</td>
<td>-0.17-0.15</td>
<td>0.90</td>
</tr>
<tr>
<td>Morning stiffness &gt; 30' (N=107)</td>
<td>51/80</td>
<td>0.01</td>
<td>-0.02-0.30</td>
<td>0.09</td>
</tr>
<tr>
<td>Rheumatoid Factors (N=117)</td>
<td>31/27</td>
<td>0.59</td>
<td>0.42-0.76</td>
<td>0.00</td>
</tr>
<tr>
<td>Elevated Erythrocyte Sedimentation Rate (N=125)</td>
<td>63/65</td>
<td>0.33</td>
<td>0.16-0.49</td>
<td>0.00</td>
</tr>
<tr>
<td>Elevated C reactive Protein (N=124)</td>
<td>60/74</td>
<td>0.30</td>
<td>0.13-0.46</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Table 2: Area under the curve for each set of criteria, as indicated by the referring physician.

<table>
<thead>
<tr>
<th>Set of criteria</th>
<th>AUC</th>
<th>CI 95%</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>All_Criteria</td>
<td>0.577</td>
<td>0.478 – 0.677</td>
<td>0.177</td>
</tr>
<tr>
<td>Clinical_Criteria</td>
<td>0.465</td>
<td>0.356 – 0.574</td>
<td>0.543</td>
</tr>
<tr>
<td>Clinical+ESR+CRP_Criteria</td>
<td>0.544</td>
<td>0.442 – 0.647</td>
<td>0.439</td>
</tr>
<tr>
<td>Arthritis+Lab_Criteria</td>
<td>0.677</td>
<td>0.583 – 0.771</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Disclosure: F. Farinha, None; G. Eugénio, None; M. Marques, None; F. Freitas, None; J. A. P. da Silva, None; C. Duarte, None.

Abstract Number: 2043

Adherence to American College of Rheumatology Guidelines for Prevention of Glucocorticoid-Induced Osteoporosis in Patients with Polymyalgia Rheumatica

Brittany Frankel¹, Angela Christensen² and Monica Guma³, ¹Internal Medicine, University of California, San Diego, San Diego, CA, ²Rheumatology, University of California, San Diego, San Diego, CA, ³University of California, San Diego, San Diego, CA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
American College of Rheumatology (ACR) 2010 guidelines recommend that any patient initiating glucocorticoid therapy with an anticipated duration of ≥3 months should receive a baseline assessment of bone mineral density (BMD), assessment of osteoporosis risk factors, vitamin D supplementation, and counseling on calcium intake and lifestyle modification. Prior studies suggest that implementation of glucocorticoid-induced osteoporosis (GIOP) prevention measures is often suboptimal. Polymyalgia rheumatica (PMR) is a common rheumatologic condition for which most patients receive >3 months of prednisone. As such, we utilized this population to investigate compliance with GIOP prevention measures within our healthcare system’s rheumatology clinics.

Methods:
A retrospective review of the electronic health record (EHR) was conducted to identify patients with a documented diagnosis of PMR and at least 2 rheumatology clinic encounters. A total of 170 patient charts were reviewed. 55 patients met inclusion criteria, which required presence of a new diagnosis of PMR at the time of any rheumatology clinic visit, PMR diagnosis no earlier than November 2010 (date of 2010 ACR GIOP guideline publication), and absence of osteoporosis at the time of PMR diagnosis. The EHR was reviewed directly to obtain data.

Results:
Mean age was 69.5 years, 55% were male, 76% were Caucasian, and mean BMI was 26.9. 64% had a primary care provider within our healthcare system. All patients were treated with ≥3 months of prednisone. Median duration of prednisone use was 20 months (range 4 to 75 months). Median initial dose of prednisone was 20mg/day (range 5 to 80mg/day). Per 2010 ACR guidelines, a baseline dual-energy X-ray absorptiometry (DXA) scan was indicated in all patients. Only 24% of patients had a documented DXA scan between 5 years before and 3 months after PMR diagnosis, although DXA scans obtained outside of our health system may not have been available for review. Among DXA scans ordered within 3 months of diagnosis, 20% were recommended by a rheumatologist, and the rest were ordered by a primary care provider. Recommendations for calcium intake were documented in 42% of patients. Vitamin D supplementation was documented in 55% of patients. Per 2010 ACR guidelines, prophylactic antiresorptive therapy was indicated in at least 96% of patients. However, only 18% were treated with a bisphosphonate at any point after PMR diagnosis. A repeat DXA 1 year or more after PMR diagnosis was obtained in 29% of patients. 20% of these patients developed osteoporosis by T score definition. Although bisphosphonates were indicated at the time of steroid initiation in all patients who developed osteoporosis, none were started on bisphosphonates until 1 year after PMR diagnosis.

Conclusion:
Rates of implementation of GIOP preventative and treatment measures among patients with PMR are suboptimal in our healthcare system. The authors plan to implement an EHR template to remind rheumatology providers to order a DXA and counsel on GIOP prevention. We are also investigating the feasibility of an EHR pop-up to prompt providers to order a baseline DXA when glucocorticoids are ordered for >3 months for patients who do not have a baseline DXA on file.

Disclosure: B. Frankel, None; A. Christensen, None; M. Guma, None.


Abstract Number: 2044
Secondary Prevention of Cardiovascular Disease Is Incomplete in a Systemic Lupus Erythematosus Population-Based Cohort

Suzana John¹, Cristina Drenkard², Gaobin Bao² and S. Sam Lim², ¹Rheumatology, Emory University, Atlanta, GA, ²Division of Rheumatology, Emory University School of Medicine, Atlanta, GA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Cardiovascular disease (CVD) is a common cause of morbidity and mortality in systemic lupus erythematosus (SLE). We know that a combination of traditional cardiovascular disease (CVD) risk factors and dysregulation of the immune system play a role in the pathogenesis. Strict adherence to established preventive measures in these patients is important. This study evaluated secondary prevention of CVD in a large population-based SLE cohort.

Methods:
Georgians Organized Against Lupus (GOAL) is a population-based cohort of patients with validated SLE surveyed annually and matched to the Georgia Hospital Discharge Database to capture all hospitalizations throughout the state. Those with CVD were identified from responses to the validated Self-Administered Brief Index of Lupus Damage. CVD related hospitalizations were identified based on the first 3 admission codes.

Results:
164 out of 685 respondents had CVD. Patients with CVD were more often older, black, poor, unemployed and on Medicare/Medicaid. Blood pressure was monitored very well. Most but not all received an annual check-up and cholesterol monitoring. Measures that were met the least included not smoking, adequate physical activity, and aspirin adherence. Smokers were more often on Medicare/Medicaid than non-smokers (p=0.015).

Conclusion:
SLE patients with known CVD are at high risk for recurrent cardiovascular events and mortality, making prevention a crucial and cost effective priority. There continues to be significant room for improvement in many preventive measures. Further study may direct education and resources to improve performance in these areas.

Table 1: Socio-demographic description of the GOAL Cohort
<table>
<thead>
<tr>
<th>Descriptors</th>
<th>GOAL Cohort (N=685)</th>
<th>CVD status Non-CVD (N=519)</th>
<th>CVD (N=164)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± SD)</td>
<td>48.1 ± 13.2</td>
<td>46.5 ± 12.7</td>
<td>53.1 ± 13.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>40 (5.8)</td>
<td>26 (5.0)</td>
<td>14 (8.5)</td>
<td>0.094</td>
</tr>
<tr>
<td>Female</td>
<td>645 (94.2)</td>
<td>493 (95.0)</td>
<td>150 (91.5)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>529 (77.2)</td>
<td>392 (75.5)</td>
<td>135 (82.3)</td>
<td>0.17</td>
</tr>
<tr>
<td>White</td>
<td>144 (21.0)</td>
<td>118 (22.7)</td>
<td>26 (15.9)</td>
<td></td>
</tr>
<tr>
<td>Living below poverty level</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>256 (37.3)</td>
<td>183 (35.2)</td>
<td>72 (44.0)</td>
<td>0.019</td>
</tr>
<tr>
<td>White</td>
<td>356 (52.0)</td>
<td>231 (44.5)</td>
<td>124 (75.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Unemployed or disabled</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>125 (18.2)</td>
<td>99 (19.1)</td>
<td>25 (15.2)</td>
<td>0.27</td>
</tr>
</tbody>
</table>

Table 2: Meeting secondary and other preventive measures in the GOAL Cohort with known CVD within the past year

<table>
<thead>
<tr>
<th>Measures</th>
<th>GOAL Cohort with CVD(N=164)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Met N (%)</td>
</tr>
<tr>
<td>Blood pressure monitoring</td>
<td>157 (96.9)</td>
</tr>
<tr>
<td>Annual check up</td>
<td>132 (84.6)</td>
</tr>
<tr>
<td>Cholesterol monitoring</td>
<td>130 (80.2)</td>
</tr>
<tr>
<td>Not smoking</td>
<td>107 (69.0)</td>
</tr>
<tr>
<td>Flu vaccination</td>
<td>103 (63.6)</td>
</tr>
<tr>
<td>Aspirin adherence</td>
<td>96 (60.4)</td>
</tr>
<tr>
<td>Cardiology visit</td>
<td>84 (58.3)</td>
</tr>
<tr>
<td>Adequate physical activity</td>
<td>90 (56.3)</td>
</tr>
</tbody>
</table>

Physical activity: any exercise within the past month other than regular job

Disclosure: S. John, None; C. Drenkard, None; G. Bao, None; S. S. Lim, None.


Abstract Number: 2045

**Prophylaxis of Ischemic Disease in Giant Cell Arteritis Patients: An Application of a “Big Data” Tracking Tool in the Electronic Health Record in an University-Based Medical Center**
Meera Subash1, Zunera Tahir2 and Arthur Kavanaugh3, 1Internal Medicine, University of California, San Diego, San Diego, CA, 2Internal Medicine, Div of Rheumatology, Allergy, and Immunology, University of California, San Diego, San Diego, CA, 3Medicine, University of California, San Diego, La Jolla, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The primary objective of this study was to better characterize the prescribed rates of aspirin prophylaxis for ischemic considerations in patients diagnosed with Giant Cell Arteritis (GCA). Secondary objectives included utilizing this functionality of the electronic health record to further characterize rates of biopsy-proven diagnoses, initial and alternative therapies offered, and incidence of ischemic events in patients diagnosed with GCA.

Methods: This study utilized the SlicerDicer capability of the Epic electronic health record at the University of California, San Diego. Encounters were reviewed individually to determine if patients met ACR criteria for the diagnosis of GCA. The above objectives were accomplished by reviewing all documentation regarding the indication of aspirin use in these patients, whether related to GCA or for other indications.

Results: 92 patients were identified through the overall query of the tracking tool for GCA of which 40 met ACR criteria for diagnosis of GCA. We found 52.5% (21 of 40) patients were identified to be prescribed aspirin with only 5 patient charts with distinct documentation for the indication of GCA. Two additional patients were on other forms of anticoagulation. Five patients suffered either strokes or transient ischemic attacks, of which 4 of 5 were before or the presenting feature of GCA. One was secondary to inappropriately stopping anticoagulation for atrial fibrillation. Only three of the four were prescribed aspirin prior to the documented event. Of note, two patients were noted to have either active or history of gastrointestinal bleeds with aspirin started after a prolonged period. Lastly, 22.5% of patients failed prednisone as the initial therapy and required alternative treatments.

Conclusion: Our data demonstrated that 52.5% of patients who met ACR criteria for GCA were on ischemic prophylaxis therapy with aspirin and only 12.5% of these patients had documentation for why or why not aspirin was recommended. The majority of cerebral ischemic events preceded or served as a presenting manifestation of GCA in this cohort. Our data indicates that we have opportunity to improve the number of patients on prophylaxis with aspirin for ischemic disease in GCA.

Disclosures: M. Subash, None; Z. Tahir, None; A. Kavanaugh, Pfizer, AbbVie, Amgen, Janssen, UCB, Novartis, Eli Lilly, 5,AbbVie, Amgen, Janssen, UCB, Eli Lilly, Novartis, Pfizer, 2.

Development and Validation of a Rheumatologist Satisfaction with Practice Scale – “the Rheumatologist Satisfaction Scale” (RSS)

Khushboo Sheth\textsuperscript{1}, Antonia Valenzuela\textsuperscript{2}, Stanford Shoor\textsuperscript{3}, Philip L. Ritter\textsuperscript{3} and Kate Lorig\textsuperscript{4}, \textsuperscript{1}Immunology & Rheumatology, Stanford University, Stanford, CA, \textsuperscript{2}Immunology and Rheumatology, Stanford University, Palo Alto, CA, \textsuperscript{3}Immunology & Rheumatology, Stanford University, Palo Alto, CA, \textsuperscript{4}Stanford University, Palo Alto, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Measures and Measurement of Healthcare Quality Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Practice improvement research routinely measures patient satisfaction and disease-specific outcomes but seldom considers the satisfaction of physicians who deliver the care. Studies suggest that physician dissatisfaction may pose a barrier to implementing quality improvement efforts. There is a paucity of succinct measures of physician satisfaction. As part of a Performance Improvement Project, in an academic rheumatology practice and an affiliated practice, we developed and piloted a simple questionnaire.

Methods: Thirty five rheumatologists in the academic or private setting were sent opened-ended questions to determine the factors that made them satisfied or dissatisfied with respect to their rheumatology practice. From the responses we formed a 14 questions 0 to 10 scale centering on satisfaction and dissatisfaction. We then administered the questionnaires to a small pilot of 30 rheumatologists in academic and/or private setting.

Results: Our sample included 30 rheumatologists, from whom 60\% were faculty members, 27\% were fellows, 53\% (N=16) were males and the majority (77\%) were salaried. Racial distribution was 57\% white, and 40\% Asian, with 7\% Hispanic/Latino ethnicity. The most common practice setting was academic medicine (80\%, N=24), followed by multi-specialty group (10\%, N=3), private practice (7\%, N=2), and rheumatology group (3\%, N=1). Forty percent (N=12) and 37\% (N=11) had been in practice <5 and >30 years, respectively. Coefficient Alpha for each factor was 0.54 (raw) 0.66 (standardized) for satisfaction and 0.60 (raw) and 0.60 (standardized) for dissatisfaction. Based on the results of this survey, mean satisfaction factor in rheumatologists was high (8.6±0.99). 91.3\% of rheumatologists (N=21) had mean satisfaction factor >8 (range 5.5-9.9). The ability to make a difference in patient’s life and having the opportunity to work with great colleagues were the strongest contributors to physicians' satisfaction (mean 9.2±1.1 and 9.4±0.8, respectively). Time spent on documentation and getting inappropriate referrals that are not in the scope of practice were among the strongest contributors to physicians' dissatisfaction (mean 3± 1.9 and 3.9±1.3, respectively). None of the items were highly correlated with each other.

Conclusion: A simple and practical questionnaire to measure physician satisfaction was developed and successfully piloted on a predominately academic sample of rheumatologists. The strongest correlates of physician satisfaction were the “ability to make a difference in a patient’s life” and to “work with great colleagues” whereas the greatest correlates of dissatisfaction were “time spent on documentation” and “inappropriate referrals.” It is hoped that with further testing on a larger sample, this scale will serve as a means to identifying potential barriers to the implementation of performance improvement projects in the practice of Rheumatology.

Disclosure: K. Sheth, None; A. Valenzuela, None; S. Shoor, None; P. L. Ritter, None; K. Lorig, None.


Abstract Number: 2047

Development and Implementation of a “Data-in-Once” Model for a Pediatric Rheumatology Learning Health System

Tzielan Lee\textsuperscript{1}, Sharon Bout-Tabaku\textsuperscript{2}, Joshua Conkle\textsuperscript{3}, Karan Iyer\textsuperscript{4}, Chris Servick\textsuperscript{2} and Esi Morgan\textsuperscript{3}, \textsuperscript{1}Pediatric Rheumatology, Stanford University, Palo Alto, CA, \textsuperscript{2}Nationwide Children's Hospital, Columbus, OH, \textsuperscript{3}Cincinnati Children's Hospital, Cincinnati, OH, \textsuperscript{4}Stanford University, Stanford, CA

Abstract Number: 2047

Development and Implementation of a “Data-in-Once” Model for a Pediatric Rheumatology Learning Health System

Tzielan Lee\textsuperscript{1}, Sharon Bout-Tabaku\textsuperscript{2}, Joshua Conkle\textsuperscript{3}, Karan Iyer\textsuperscript{4}, Chris Servick\textsuperscript{2} and Esi Morgan\textsuperscript{3}, \textsuperscript{1}Pediatric Rheumatology, Stanford University, Palo Alto, CA, \textsuperscript{2}Nationwide Children's Hospital, Columbus, OH, \textsuperscript{3}Cincinnati Children's Hospital, Cincinnati, OH, \textsuperscript{4}Stanford University, Stanford, CA
Background/Purpose:

Medical institutions are adopting electronic health records (EHR) in accordance with Meaningful Use making it possible to standardize and capture patient data for registries that serve Learning Health Systems (LHS). LHS leverage clinical data to generate new evidence and knowledge improving clinical practice; ensuring quality, safety, and value; and driving innovation in health care.

The Pediatric Rheumatology Care and Outcomes Improvement Network (PR-COIN) is an 18 center learning network designed to improve the outcomes of rheumatic disease care. Teams collect and analyze point of care data on process and outcomes that guide improvement activities. Currently for most centers, data collection and entry is manual and duplicative: (1) patients and providers fill out paper forms; (2) providers document clinical visits in multiple areas within the EHR; (3) staff complete paper case report forms (CRF); and (4) staff enter data from CRFs into the registry database. This time and resource consuming process increases the risk for data entry errors, is very expensive, and delays optimal evidence based care.

We describe a PR-COIN and EHR vendor (Epic Systems Corporation) collaboration to design, build, and implement a technical architecture to make clinical documentation efficient, standardize data collection, enhance data display and access, to improve patient care and facilitate research.

Methods:

Development entailed direct interaction of the EHR vendor with three institutions’ information systems departments. Over a course of two years, twice monthly meetings occurred to discuss collection form and note template builds, data element standardization, and process workflows. Our goals were: (1) to support a “data-in-once” strategy for registry data collection while integrating data capture into routine patient clinical visit documentation; (2) to develop automated pre-visit planning reports within the EHR that support evidence based chronic care patient management.

Results:

Components of the “data-in-once” build included: (1) point of care seamless discrete standardized data exchange between the clinical documentation and PR-COIN registry data collection elements within the EHR; (2) capability for ongoing electronic transfer of the EHR PR-COIN registry data to the external PR-COIN registry. Automated pre-visit planning reports are strategically localized in the EHR for ease of access and use. Three institutions are piloting system implementation with subsequent roll-out planned to other users in the learning network.

Conclusion:

Learning health systems can be the foundation for improved quality of clinical care and patient outcomes. Successful implementation and utilization of registries rely on integration into the clinical process and a coordinated effort to analyze workflows and define build requirements. Using the EHR platform to obtain registry data directly from the patient care process, we developed a method to efficiently and unobtrusively collect patient data. This effectively accelerates the rate of useful data accumulation for analysis and provides visually enhanced presentation of clinically meaningful data to users.

Disclosure: T. Lee, None; S. Bout-Tabaku, None; J. Conkle, None; K. Iyer, None; C. Servick, None; E. Morgan, None.


Abstract Number: 2048

the Impact of Diagnostic Misregistration of Rheumatoid Arthritis on the Establishment of a Value Based Healthcare System
Background/Purpose: Value based health care has gained worldwide attention due to the refocusing vision of creating value around and for patients. The latter is obtained by measuring healthcare outcomes/quality relative to the cost. Besides measuring these parameters, another crucial element in the evaluation of value-based reimbursement decisions depends on adequate registration. Therefore, in this study we aimed to objectify the degree of misregistration by comparing the received diagnosis of rheumatoid arthritis from a rheumatologist-driven, scientific (ACR/EULAR-2010 criteria for RA), and financial (ICD-10) perspective.

Methods: All patients who received the diagnosis Rheumatoid Arthritis (RA) between 2000-2016 within our hospital, were identified according to the Diagnosis Treatment Code (DTC) RA, which is a financial instrument that corresponds to the ICD-10 system (corresponding codes for RA: ICD-10 M05.79/M05.89/M06.09/M06.89). Clinical and demographic data were extracted from digital patient records in which 10% of the data were randomly cross-checked. The collected variables at time of RA diagnosis included number and type of swollen/painful joints, inflammatory markers, rheumatoid factor (RF), ACPA, disease duration and patients primary/secondary/tertiary diagnosis according to the rheumatologist. Additionally, patients were classified according to the ACR/EULAR 2010 criteria for RA. The degree of discordance was determined by descriptive statistics.

Results: A total number of 1641 patients were identified by DTC RA. The majority of the population was female (73%) with a mean age of 55 at time of RA diagnosis. According to the rheumatologist 371(23%) patients did not had RA. From the remaining 1270 patients who received the diagnosis RA according to the rheumatologist, 272(17%) did not fulfill the ACR/EULAR 2010 criteria (Figure 1). The patients who did not fulfill the ACR/EULAR 2010 criteria had less inflammation, were more often RF and/or ACPA negative, and had less involved joints, in terms of patient characteristics there was no significant difference within the groups. Approximately 10% of the data were missing at random.

Conclusion: For the measurement of healthcare quality and outcomes within a VBHC system, the patient population needs to be clearly defined and identified from hospital data sources. ICD-10 allows for baseline stratification. In this study we compared the financial DTC-RA registration, clinical diagnosis and ACR/EULAR classification criteria, and found a total discrepancy of 40%. Unfortunately from these descriptive analyses, it can be concluded that the ICD-10/DTC-RA codes are not the most reliable source of information on which the patient selection should be based. It is expected that this degree of misregistration for RA will have an impact on the value-based driven reimbursement system which we are currently investigating.

Erin L. Merz1, Linda Kwakkenbos2,3,4, Marie-Eve Carrier2, Shadi Gholizadeh5, Sarah D. Mills6, Rina S. Fox7, Lisa Jewett2,8, Heidi Williamson9, Diana Harcourt9, Shervin Assassi10, Daniel E. Furst11, Karen Gottesman12, Maureen D Mayes13, Tim Moss9, Brett D. Thoms2,3 and Vanessa L. Malarne6,14, 1Department of Psychology, California State University, Dominguez Hills, Carson, CA, 2McGill University, Montreal, QC, Canada; 3Lady Davis Institute for Medical Research, Jewish General Hospital, Montreal, QC, Canada, 4Radboud University, Nijmegen, Netherlands, 5Psychoogy, SDSU/UC San Diego Joint Doctoral Program in Clinical Psychology, San Diego, CA, 6SDSU/UC San Diego Joint Doctoral Program in Clinical Psychology, San Diego, CA, 7Northwestern University Feinberg School of Medicine, Chicago, IL, 8Jewish General Hospital, Montreal, QC, Canada, 9University of the West of England, Bristol, United Kingdom, 10University of Texas McGovern Medical School, Houston, TX, 11Department of Internal Medicine and Rheumarology, University of California Los Angeles, David Geffen School of Medicine, Division of Rheumatology; University of Washington, Seattle, Washington; University of Florence, Florence, Italy, Los Angeles, CA, 12Scleroderma Foundation, Los Angeles, CA, 13Department of Internal Medicine - Rheumatology, University of Texas-McGovern Medical School, Houston, TX, 14Psychology, San Diego State University, San Diego, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: ARHP Measures and Measurement of Healthcare Quality Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Valid measures of appearance concern are needed in systemic sclerosis, a rare, disfiguring rheumatologic disease. The Derriford Appearance Scale-24 (DAS-24) is a self-report measure that assesses appearance-related distress related to visible differences. There is uncertainty regarding the DAS-24 factor structure, possibly due to its scoring method of the 14 items with a “not applicable” response option.

Methods: Patients with systemic sclerosis (N = 950) completed self-report measures at enrollment to the Scleroderma Patient-centered Intervention Network (SPIN) Cohort Study. DAS-24 items marked “not applicable” were scored two ways: (1) “not applicable” scored as 0, per standard DAS-24 scoring; (2) “not applicable” treated as missing. Internal consistency reliability was evaluated using Cronbach’s alpha. The one-factor DAS-24 model was evaluated using confirmatory factor analysis. Convergent validity was evaluated using bivariate correlations with social interaction anxiety, depressive symptomatology, fear of negative evaluation, and satisfaction with appearance.

Results: Internal consistency reliability was high (α = .92). When items marked by respondents as “not applicable” were scored as 0, the one-factor model fit poorly (CFI = .896, RMSEA = .096). When items marked by respondents as “not applicable” were treated as missing data, the one-factor model fit well (CFI = .958, RMSEA = .065). Convergent validity analyses revealed strong correlations that were similar across scoring methods (Standard rs: .44-.68; Missing rs: .47-.72).

Conclusion: Treating “not applicable” responses as missing improved the measurement model, but did not yield substantively different relationships with theoretically related constructs. It is unlikely that using standard DAS-24 scoring greatly impacts the practical interpretation of scores. Indications of item redundancy and poorly performing items suggest that the DAS-24 could be improved and potentially shortened.

Disclosure: Erin L. Merz, None; L. Kwakkenbos, None; M. E. Carrier, None; S. Gholizadeh, None; S. D. Mills, None; R. S. Fox, None; L. Jewett, None; H. Williamson, None; D. Harcourt, None; S. Assassi, None; D. E. Furst, None; K. Gottesman, None; M. D. Mayes, None; T. Moss, Derriford Appearance Scale, 4; B. D. Thoms, None; V. L. Malarne, None.
Analysis of Data Collected from Right and Left Limbs: Accounting for Dependence and Improving Statistical Efficiency in Musculoskeletal Research

Sarah Stewart¹, Janet Pearson², Keith Rome³, Nicola Dalbeth⁴ and Alain Vandal⁵, ¹School of Podiatry, Auckland University of Technology, Auckland, New Zealand, ²Auckland University of Technology, Auckland, Niger, ³School of Clinical Science, Health & Rehabilitation Research Institute, AUT University, Auckland, New Zealand, ⁴University of Auckland, Auckland, New Zealand, ⁵Counties Manukau District Health Board, Auckland, New Zealand

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: ARHP Measures and Measurement of Healthcare Quality Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Statistical techniques used in musculoskeletal research often inefficiently account for paired-limb measurements or the relationship between measurements taken from multiple sites within limbs. This study compared three commonly used analysis methods with a multivariate mixed-effects model which accounts for the association between limbs, sites, and trials and that utilises all information available from repeated trials.

Methods: Four analysis models were applied to an existing data set containing peak plantar pressure data, a continuous variable. The original study compared pressure during barefoot walking in people with gout (n = 25) or people with asymptomatic hyperuricaemia (n = 27) with normouricaemic controls (n = 34). Pressure data was collected for both feet over three walking trials. Peak pressure was calculated for each of 7 masked regions of the plantar foot (heel, midfoot, 1st metatarsal, 2nd metatarsal, metatarsals 3 to 4, hallux and lesser toes). The data set was analysed using the following 4 approaches: Model 1 analysed right foot data; Model 2 analysed data from a randomly selected foot; Model 3 averaged right and left foot data; Model 4 used all available data in a mixed-effects regression model which accounted for repeated measures taken for each foot, foot site and trial. Two comparisons were considered for all analyses: gout vs. normouricaemic control and asymptomatic hyperuricaemic vs. normouricaemic control. Age and body mass index were included in all analyses as covariates. For the purpose of model comparison, confidence interval widths for the mean differences between groups for each foot site were used as a criteria for statistical efficiency.

Results: Estimated mean differences in peak pressure between diagnostic groups for Analysis Models 1 to 3, were similar across all analysis methods, while the confidence interval widths for the mean differences were consistently smaller for Analysis Model 4 (Figure 1). The mean peak pressure estimates for each diagnostic group, for Analysis Models 1 to 3, were also similar across analysis methods, while confidence interval widths were again consistently lowest in Analysis Model 4. Model 4 also revealed significant between-group differences which were not detected in Models 1-3.

Conclusion: Adoption of a multivariate mixed-effects linear regression model efficiently addresses the issue of between-limb dependence in musculoskeletal research through retaining individual side and trial data, and utilising the relationship between site measurements on the same foot. The improved efficiency and power generated from this model produces more precise estimates compared to alternative approaches which discard or average data to take into account the paired nature of the data, and which model site measurements independently.
The Lasso Selection Model in Rheumatology Epidemiologic Studies

Sofia Pedro, Bella Mehta, Gulsen Ozen, and Kaleb Michaud

1National Data Bank for Rheumatic Diseases, Wichita, KS, 2Rheumatology, Hospital of Special Surgery, New York, NY, 3Rheumatology, Marmara University, School of Medicine, Rheumatology, Istanbul, Turkey, 4Department of Rheumatology, University of Nebraska Medical Center, Omaha, NE, 5University of Nebraska Medical Center, Omaha, NE

First publication: September 18, 2017

Abstract Number: 2051

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: ARHP Measures and Measurement of Healthcare Quality Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Selecting the best model in an epidemiologic analysis is challenging as it addresses problems like confounding and allows the estimation of unbiased results. Stepwise selection is the most commonly used method but also the most criticized, as it relies on an arbitrary threshold, the probability of removal, to decide which variables will be included in the model. Modern shrinkage techniques such as the Least Absolute Shrinkage and Selection Operator (LASSO) may address this issue. Using a rheumatology patient registry, we compared the LASSO method with traditional regression model techniques including stepwise and change-in-estimate.

Methods:

LASSO can be used with several statistical models including generalized linear models and proportional hazards models. In the latter, it maximizes the partial likelihood of regression coefficients subject to a constraint imposed on the sum of the absolute value of all regression coefficients. It excludes variables without formal statistical testing by correcting the extremes in the distribution and shrinking unstable estimates to zero. The constraint can be estimated via cross-validation. We illustrate this technique in a sample of patients enrolled in the National Data Bank for Rheumatic Diseases from 2001 to 2016. We applied survival methods to assess the risk of serious infections (SI) in patients with RA compared to non-inflammatory rheumatic disease (NIRD) controls. Variables included demographics, clinical status, disease severity and prednisone use.
Results:

20,361 RA and 6176 NIRD patients contributed to 81,499 and 20,665 patient-years of exposure, having had 1600 (7.9%) and 276 (4.5%) SI, respectively (incidence rate ratio: 1.5 [1.3-1.7]). Baseline characteristics by disease (RA:NIRD) were age (58:63 yrs), female sex (79:80%) and HAQ (1.11: 1.10). The LASSO HR of SI comparing RA vs NIRD was 1.15 (0.99 – 1.32), being prednisone, vaccination, and prior infections the variables with the highest impact (Figure). Similar results were obtained with stepwise, selecting almost the same covariates. However, when using different thresholds, slightly different models were obtained (Table).

Conclusion:

Identical estimates were obtained across methods, not imposing arbitrary thresholds with LASSO. Although LASSO has many positive attributes, such as being very powerful when variables exceed observations, it is still rarely applied in epidemiologic studies. It is a valid alternative to the popular stepwise, as it is less variable and yields interpretable models.

Table. Best Cox models selected for serious infections accordingly to several selection techniques.

<table>
<thead>
<tr>
<th>Method</th>
<th>HR (RA vs NIRD)</th>
<th>Other variables selected</th>
</tr>
</thead>
<tbody>
<tr>
<td>LASSO</td>
<td>1.15 (0.99-1.32)</td>
<td>Ethnicity (white vs. other), sex, smoking status, age, disease duration, residency (urban vs. rural), prior infections, RD comorbidity index, HAQ, pain, education, prednisone, vaccination, diabetes</td>
</tr>
<tr>
<td>Change-in-estimate</td>
<td>1.13 (0.98-1.30)</td>
<td>Prednisone</td>
</tr>
<tr>
<td>(10% change)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change-in-estimate</td>
<td>1.17 (1.01-1.34)</td>
<td>Prednisone, pain, age, education</td>
</tr>
<tr>
<td>(2% change)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stepwise (20% removal probability)</td>
<td>1.14 (1.0-1.31)</td>
<td>Ethnicity (white vs. other), sex, smoking status, age, disease duration, residency (urban vs. rural), prior infections, RD comorbidity index, HAQ, pain, education, prednisone, vaccination, diabetes</td>
</tr>
<tr>
<td>Stepwise (10% removal probability)</td>
<td>1.15 (1.0-1.32)</td>
<td>Ethnicity (white vs. other), sex, smoking status, age, disease duration, prior infections, RD comorbidity index, HAQ, pain, education, prednisone, vaccination, diabetes</td>
</tr>
</tbody>
</table>
Figure. LASSO coefficients estimates by the regularization term.

Disclosure: S. Pedro, National Data Bank for Rheumatic Diseases, 3; B. Mehta, None; G. Ozen, None; K. Michaud, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-lasso-selection-model-in-rheumatology-epidemiologic-studies

Abstract Number: 2052

Apply Musculoskeletal Ultrasonography to Predict Chronic Gouty Arthritis in Patients with Chronic Kidney Diseases

Zheng-Hao Huang1, Chi-Ching Chang2, En Chao3, Hui-Hsun Chiang4, Shu-Yi Lin5, Kun-Lin Wu6, Hsiang-Cheng Chen5, Shi-Jye Chu5, San-Yuan Kao5, Tsung-Yun Hou5, Feng-Cheng Liu5, Chen-Hung Chen7, Deh-Ming Chang8 and Chun-Chi Lu9, 1Division of Rheumatology, Immunology and Allergy, Department of Internal Medicine, Kaohsiung Armed Forces General Hospital; Tri-service general hospital, National Defense Medical Center, Taipei, Taiwan, 2Taipei Medical University Hospital, Taipei, Taiwan, 3Tri-Service General Hospital Songsshan Branch, Taipei, Taiwan, 4School of Nursing, National Defense Medical Center, Taipei, Taiwan, 5Tri-Service General Hospital, Taipei, Taiwan, 6Armed Forces Taoyuan General Hospital, Taipei, Taiwan, 7Taipei Tzu Chi hospital, Taipei, Taiwan, 8Taipei Veterans General Hospital, Taipei, Taiwan, 9University of Washington; Tri-Service General Hospital, National Defense Medical Center, Seattle, WA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Metabolic and Crystal Arthropathies Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Gouty arthritis, caused by the deposition of monosodium urate (MSU) monohydrate crystals at joints, is comprised of multiple inflammatory processes in synovium, tendons, cartilages and bone. In addition to traditional serum tests including C reaction protein (CRP), erythrocyte sedimentation rate (ESR), uric acid and blood white cell counts, musculoskeletal ultrasonography (MSKUS) is a convenient, costless and straightforward tool to identify anatomical location and severity of inflammation, which guided clinicians appropriate treatment. Here, we retrospectively investigated how rheumatologists applied MSKUS in detecting and treating acute and chronic tophaceous gouty arthritis. We further analysed serum inflammatory markers, biochemistric results and blood cell counts and compared MSKUS manifestations to identify whether renal insufficiency influenced uric acid deposition at joints of patients with gouty arthritis.

Methods: This is a retrospective review of clinical and ultrasonographic findings in 280 patients with gouty arthritis from August 2004 to May 2017. All patients met the criteria of 2015 American College of Rheumatology/European League Against Rheumatism.
Ultrasonographic manifestations include joint effusion, synovial proliferation, tenosynovitis, Baker's cyst, double contour sign (DCS), and tophi-like lesion (TLL). Patients received blood tests including serum white blood cell count (WCC), serum uric acid, CRP, ESR, estimated glomerular filtration rate (eGFR) and we collected synovial fluid WCC from arthritis sites. Differences were analysed by independent \( t \) tests, phi coefficient, Pearson correlation coefficient and Cramer's V Coefficient.

**Results:** Joint effusion, synovial proliferation, tenosynovitis, Baker's cyst, DCS, and TLL were detected in 75.7%, 45.3%, 20.0%, 9.2%, 42.8% and 23.9% of joints, respectively. Patients with acute gouty arthritis and leucocytosis would have higher serum CRP \((p < 0.01)\). Patients with synovial proliferation, tenosynovitis, or DCS had lower synovial fluid WCC \((p = 0.04, 0.04, \text{ and } < 0.01, \text{ respectively})\). Patients with TLL had lower serum UA \((p =0.013)\). Patients with renal insufficiency \((\text{eGFR}< 90)\) were characterized by higher prevalence of Baker's cyst \((p =0.02)\).

**Conclusion:** We would recognize Baker's cyst, DCS, and TLL as MSKUS manifestations of chronic gout. Synovial proliferation and tenosynovitis can exist in both acute or chronic gouty arthritis. Synovial proliferation was considered as a transformational change between acute and chronic gout. Patients with chronic kidney disease have an increasing risk of development of Baker's cyst. Early treatment of patients with gouty arthritis and chronic kidney disease help prevent development of chronic joints destructions.

**Disclosure:** Z. H. Huang, None; C. C. Chang, None; E. Chao, None; H. H. Chiang, None; S. Y. Lin, None; K. L. Wu, None; H. C. Chen, None; S. J. Chu, None; S. Y. Kao, None; T. Y. Hou, None; F. C. Liu, None; C. H. Chen, None; D. M. Chang, None; C. C. Lu, None.

**Computed Tomography Dependent Diagnosis of Crowned Dens Syndrome; A Cervical Manifestation of Patients with Calcium Pyrophosphate Dihydrate Crystal Deposition Disease**

Ammar Haikal1, Brian Everist2, Pim Jetanalin3 and Mehrdad Maz3, 1Department Internal Medicine, Department of Internal Medicine, University of Kansas Medical Center, Kansas City, KS, 2Department of Radiology (MSK), Department of Radiology (MSK), University of Kansas Medical Center, Kansas City, KS, 3Allergy, Clinical Immunology, and Rheumatology, Division of Allergy, Clinical Immunology and Rheumatology, Department of Internal Medicine, University of Kansas Medical Center, Kansas City, KS

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** Metabolic and Crystal Arthropathies Poster II  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Crowned Dens Syndrome (CDS), a variation of Calcium Pyrophosphate Deposition Disease (CPPD), is a radiologic-clinical entity defined by the association of radiological calcifications around the odontoid process and periodic cervico-occipital pain. The true incidence and prevalence of CDS in the general population or in those with CPPD remain unknown. Here, we discuss 34 patients as one of the largest reported series.

**Methods:** This is a retrospective chart and radiology registry imaging study review from a single tertiary medical center from 11/1/2005-10/31/2015. 191 patients with a diagnosis of CPPD and/or CDS were identified. Terms used in the search included pseudogout, CPPD, CDS, chondrocalcinosis and calcification. 57 patients had at least one c-spine CT performed for a variety of indications. The CTs were analyzed by a musculoskeletal radiologist for the presence of periodontoid calcifications.

**Results:** Of the 191 patients with CPPD, 57 had c-spine CTs obtained; 34 of whom (34/57, 59.64%) had periodontoid calcifications. Only 12/34 patients were formally diagnosed with CDS by rheumatologists. The others (22/34) were either not seen by a rheumatologist or were not diagnosed with CDS if seen by other specialists. The median age of diagnosis was 78.5 years, with majority (73.52 %) over 70 y/o and 24/34 (70.58%) were female. 17/34 patients (50%) were symptomatic; defined as presence of acute to sub-acute neck pain within 6 weeks of performing the c-spine CT. The majority of the patients (82.35%, 28/34) had additional sites of chondrocalcinosis on joint radiographs; 8 patients (28.57%) had 3 or more sites of chondrocalcinosis in typical CPPD locations. Six patients did not have any joint radiographs. 16/34 patients (47.05%) who had CDS and chondrocalcinosis elsewhere, also carried...
metabolic diseases, including: hyperparathyroidism (2), hypothyroidism (10), hypomagnesemia (2) and hypophosphatemia (2). None of the patients had a documented history of hemochromatosis or evidence of iron overload based on laboratory tests.

**Conclusion:** Crowned Dens Syndrome is an under-recognized entity, which should be considered in elderly patients with neck pain in the setting of CPPD. Our data demonstrates a high percentage (about 60%) of patients with CPPD who had c-spine CT findings consistent with CDS. This underscores the importance of performing c-spine CTs when evaluating patients with neck pain and CPPD or chondrocalcinosis in other joints, as radiographs and MRI may not be diagnostic of CDS.

Periodontoid curvilinear calcifications on noncontrast c-spine CT of the transverse ligament seen in both sagittal (A) and axial (B) planes.

**Disclosure:** A. Haikal, None; B. Everist, None; P. Jetanalin, None; M. Maz, None.

**Rapid Tophus Resolution in Chronic Refractory Gout Patients Treated with Pegloticase**

Brian F. Mandell¹, Herbert S. B. Baraf², Anthony Yeo³ and Peter E. Lipsky⁴, ¹Rheumatology, Cleveland Clinic, Cleveland, OH, ²The Center for Rheumatology and Bone Research, Wheaton, MD, ³Horizon Pharma, Lake Forest, IL, ⁴AMPEL BioSolutions, LLC, Charlottesville, VA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017
**Session Title:** Metabolic and Crystal Arthropathies Poster II
**Session Type:** ACR Poster Session C
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** It has been suggested that the velocity of resolution of tophi in chronic tophaceous gout is related to serum uric acid (sUA) levels.¹ However, few subjects with a persistent sUA <4.0 mg/dL have been studied. Pegloticase is a recombinant uricase conjugated to polyethylene glycol approved in the U.S. for chronic refractory gout that profoundly decreases sUA in responders to <1 mg/dL.² The results from the pegloticase randomized clinical trials (RCTs) permitted determination of the impact of persistent, very low sUA levels on the velocity of tophus resolution.

**Methods:** This analysis used results from two RCTs of 6-months duration.²,³ Photographs were taken of hands, feet and up to 2 other locations. Serial standardized digital images of tophi were analyzed by a blinded reader using computer-assisted quantitative measurement software. Subjects were defined as responders and non-responders (NRs) based upon persistent sUA lowering.²
Results: A total of 952 tophi were analyzed in 87 subjects; 341 in 30 responders; 361 in 36 NRs receiving pegloticase infusions; and 250 in 21 subjects receiving placebo infusions. At baseline, the mean tophus areas were $644.7 \pm 789.2 \text{ mm}^2$ (mean ± SD) in responders, $820.0 \pm 1349 \text{ mm}^2$ in NRs, and $777.2 \pm 1056.0 \text{ mm}^2$ in placebo-treated subjects (3 group comparison, not significantly different). Achievement of tophus resolution in the three groups is summarized in Figure 1. By regression analysis, the velocity of tophus reduction over 6 months of treatment was 66.4 mm$^2$/mo in responders ($P<0.0001$ comparing all visits). The mean time for complete resolution of tophi in responders was 9.7 mo (range 5.2 to 23.1 mo). By contrast, in NRs, the velocity of resolution was $-74.9 \text{ mm}^2$/mo from dose 1 to dose 7 ($P<0.0001$) and $+23.5 \text{ mm}^2$/mo from dose 7 to the final dose ($P>0.05$), reflecting the loss of urate lowering effect in the NRs during the latter 3 months. The sUA AUC during the 6 months of the RCT was calculated for all subjects. There was a significant negative correlation between the velocity of tophus resolution and sUA AUC ($r=-0.31$, $P=0.0032$) Figure 2. Baseline age, BMI, gender, race, total tophus area and tophus location did not significantly influence velocity of tophus resolution.

Conclusion: Pegloticase treatment causes a rapid resolution of tophi in responders. However, there is considerable heterogeneity in the velocity of tophus reduction.

Disclosure: B. F. Mandell, Horizon Pharma, 2, Horizon Pharma, 5; H. S. B. Baraf, Takeda, Horizon Pharma, 2, Takeda, Horizon Pharma, 2, Horizon Pharma, 5; A. Yeo, Horizon Pharma, 5; P. E. Lipsky, Horizon Pharma, 5.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/rapid-tophus-resolution-in-chronic-refractory-gout-patients-treated-with-pegloticase

Abstract Number: 2055

Omeract Ultrasonographic Criteria for the Diagnosis of Calcium Pyrophosphate Deposition Disease at the Metacarpal-Phalangeal, Wrist, Acromion-Clavicular and Hip Joints: An Inter-Observer and Intra-Observer Reliability Study

Pascal Zufferey1, Georgios Filippou2, Carlo Alberto Scirè3, Nemanja Damjanov4, MA D'Agostino5, George A. W. Bruyn6, Antonella Adinolfi2, Greta Carrara7, Valentina Di Sabatino8, Andrea Delle Sedie9, Tomas Cazenave10, Carlos Pineda11, Francesco Porta12, Daryl K. MacCarter13, Emilio Filippucci14, Frédérique Gandjbakhch15, Ingrid Moller16, Anthony Reginato17, Mihaela Cosmina Micu18, Mohamed Mortada19, Gaël Mouterde20, Lena Terslev21, Esperanza Naredo22, Valentina Picerno2, Mohamed Mortada, 1

First publication: September 18, 2017

SESSION INFORMATION
Background/Purpose:

The OMERACT US subtask force “US in CPPD” has recently created the definitions for US identification of crystal deposits in joints and tested the reliability between different observers[1]. Those criteria were however validated only at the knee. The Objectives were to assess the inter- and intra-observer reliability of US on detecting CPPD in the triangular fibrocartilage complex (TFCC) of the wrists, fibrocartilage of the acromio-clavicular (AC) joint and hip labrum (HL) and hyaline cartilage (HC) of the metacarpal heads (MC) and femoral head.

Methods: The OMERACT US criteria for identification of CPPD have been used for this exercise[2] using a two steps approach. First, a panel of US experts gave a dichotomous score (presence/absence of CPPD) of 120 images of sites under investigation using a web based platform. The assessment was carried out twice in order to calculate both the inter and intra-observer reliability. In the second step, the experts met for a patient based assessment of CPPD in a workshop. Bilateral evaluation of TFCC, AC joints, HL and HC of the hip and HC of the II and III MC of 8 patients was carried out twice in the same day by 18 US experts. Eight US machines (3 GE, 1 Samsung and 4 Esaote) equipped with high resolution linear probes were used for the workshop.

Results:

Reliability values of the web based exercise (both intra and inter) were high demonstrating that definitions were clear for all participants for all sites. The results of the patient based exercise are presented in table 1. The TFCC of the wrist demonstrated to be the most reliable site for the assessment of CPPD followed by the AC joint. Other sites demonstrated lower kappa values and thus are not considered reliable for assessment of CPPD.

<table>
<thead>
<tr>
<th>Section</th>
<th>Mean prevalence</th>
<th>Mean observed agreement</th>
<th>Mean kappa</th>
<th>Pabak*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inter-Reader Agreement</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1) ALL</td>
<td>48,2</td>
<td>0,71</td>
<td>0,43</td>
<td>0,42</td>
</tr>
<tr>
<td>2) Fibrocartilage</td>
<td>72,7</td>
<td>0,75</td>
<td>0,39</td>
<td>0,51</td>
</tr>
<tr>
<td>3) Hyaline cartilage</td>
<td>23,7</td>
<td>0,67</td>
<td>0,09</td>
<td>0,34</td>
</tr>
<tr>
<td>4) Hand</td>
<td>22,6</td>
<td>0,69</td>
<td>0,12</td>
<td>0,38</td>
</tr>
<tr>
<td>5) Wrist Fibrocartilage</td>
<td>95,1</td>
<td>0,91</td>
<td>0,01</td>
<td>0,82</td>
</tr>
<tr>
<td>6) Acromion-Clavicular Joint</td>
<td>61,1</td>
<td>0,75</td>
<td>0,51</td>
<td>0,51</td>
</tr>
<tr>
<td>7) Hip</td>
<td>43,7</td>
<td>0,61</td>
<td>0,23</td>
<td>0,23</td>
</tr>
<tr>
<td>7a) Hip Labrum</td>
<td>61,8</td>
<td>0,6</td>
<td>0,16</td>
<td>0,19</td>
</tr>
<tr>
<td>7b) Hip Cartilage</td>
<td>25,7</td>
<td>0,63</td>
<td>0,04</td>
<td>0,26</td>
</tr>
<tr>
<td><strong>Intra-Reader Agreement</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1) ALL</td>
<td>48,3</td>
<td>0,85</td>
<td>0,69</td>
<td>0,71</td>
</tr>
<tr>
<td>2) Fibrocartilage</td>
<td>73,1</td>
<td>0,85</td>
<td>0,57</td>
<td>0,71</td>
</tr>
<tr>
<td>3) Hyaline cartilage</td>
<td>23,4</td>
<td>0,86</td>
<td>0,53</td>
<td>0,73</td>
</tr>
<tr>
<td>4) Hand</td>
<td>23</td>
<td>0,84</td>
<td>0,48</td>
<td>0,69</td>
</tr>
<tr>
<td>5) Wrist Fibrocartilage</td>
<td>95,1</td>
<td>0,93</td>
<td>0,66</td>
<td>0,87</td>
</tr>
<tr>
<td>6) Acromion-Clavicular Joint</td>
<td>62,5</td>
<td>0,88</td>
<td>0,68</td>
<td>0,76</td>
</tr>
<tr>
<td>7) Hip</td>
<td>42,9</td>
<td>0,82</td>
<td>0,58</td>
<td>0,66</td>
</tr>
<tr>
<td>7a) Hip Labrum</td>
<td>61,7</td>
<td>0,73</td>
<td>0,32</td>
<td>0,47</td>
</tr>
<tr>
<td>7b) Hip Cartilage</td>
<td>23,9</td>
<td>0,91</td>
<td>0,67</td>
<td>0,83</td>
</tr>
</tbody>
</table>

Strength of agreement: < 0.20 Poor. 0.21 - 0.40 Fair. 0.41 - 0.60 Moderate. 0.61 - 0.80 Substantial. 0.81 - 1.00 Excellent

*Pabak: Prevalence-Adjusted Bias-Adjusted Kappa

Conclusion:

the TFCC of the wrist is the most reliable site for assessing CPPD. By adding these results to the previous exercise[2], we can confirm that the new OMERACT US definitions for assessing CPPD can be applied reliably at the knee (meniscus and HC), TFCC of the wrist...
and AC joints. These peripheral sites are the most frequently involved in CPPD. The next step of the OMERACT “US in CPPD” subtask force, will be to test the value of these findings in a longitudinal observational study.

Disclosure: P. Zufferey, None; G. Filippou, None; C. A. Scirè, None; N. Damjanov, None; M. D'Agostino, BMS, AbbVie, Novartis, 8; G. A. W. Bruyn, None; A. Adinolfi, None; G. Carrara, None; V. Di Sabatino, None; A. Delle Sedie, None; T. Cazenave, None; C. Pineda, None; F. Porta, None; D. K. MacCarter, None; E. Filippucci, None; F. Gandjbakhch, None; I. Moller, None; A. Reginato, None; M. C. Micu, None; M. Mortada, None; G. Mouterde, None; L. Terslev, None; E. Naredo, Abbvie, Roche, BMS, Pfizer, UCB, Novartis, Lilly, Janssen, 5; V. Picerno, None; W. A. Schmidt, Roche Pharmaceuticals, 8, Roche Pharmaceuticals, 5, Roche Pharmaceuticals, 2, GlaxoSmithKline, 2, GlaxoSmithKline, 5, Bristol-Myers Squibb, 5, Bristol-Myers Squibb, 8; V. Vlad, None; F. Ananu Vreju, None; A. Iagnocco, None.


Abstract Number: 2056

Performance and Validity of Musculoskeletal Ultrasound in the Assessment of Synovial Inflammation in Experimental Acute Gout

Raquel Largo1, Juan Pablo Medina2, Sandra Perez-Baos2, Victor Najera-Aleson2, Aranzazu Mediero2, Gabriel Herrero-Beaumont1 and Esperanza Naredo3, 1Bone and Joint Research Unit, IIS-Fundacion Jimenez Diaz UAM, Madrid, Spain, 2Joint and Bone Research Unit, IIS-Fundacion Jimenez Diaz UAM, Madrid, Spain, 3Rheumatology, Joint and Bone Research Unit, IIS-FJD, Hospital Universitario Fundación Jiménez Diaz., Madrid, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Metabolic and Crystal Arthropathies Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Musculoskeletal ultrasound (MS-US) has not been validated as a reliable technique to evaluate joint inflammation in an acute gout rabbit model. Rabbit has been used to accurately reproduce human acute gout. Thus, validating ultrasonographic imaging in this animal model would be important to use this technique for sequential evaluation of synovium damage, synovial fluid effusion, crystal deposits, and the efficacy of new pharmacological options.

Methods:
Monosodium urate (MSU) crystals were used to induce acute gout in 10 New Zealand white rabbits through bilateral intra-articular injections, while 3 controls received vehicle injection. Both rabbit knees were assessed by B-mode and power Doppler (PD) US blindly to the type of injection, both 24 and 72 h after the injections. All US examinations were carried out with a commercially available real-time scanner (LOGIQ e R7, GE Medical Systems) equipped with a 22 MHz linear transducer (6-15 MHz). B-mode and PD machine settings were optimised as follows: B-mode gain of 47 dB, dynamic range 72 dB, Doppler frequency of 14.3 MHz, Doppler gain of 28 dB, low-wall filters, and pulse repetition frequency of 700 Hz. B-mode global distension (GD), synovial fluid (SF) and synovial thickening (Sth); and PD-detected synovial blood flow (PD) were semiquantitatively scored (0-3) at the lateral recess of the knees. Additionally, the presence of MS-US features of MSU crystal deposit was investigated. Progression of joint swelling was followed by knee perimeter measurements. After 72 h, all rabbits were euthanized, and synovial membranes were fixed and embedded in paraffin for histological and immunohistochemical evaluation, and processed for protein expression studies.

Results:
We showed that MS-US was able to discriminate between the MSU crystal injected group and the control vehicle injected group for the different inflammatory findings both at 24 and 72 h (p<0.05). A statistically significant positive correlation was found between the increment in knee perimeter and GD MS-US at 24h (Spearman’s correlation coefficient r=0.579, p=0.0019). Sth MS-US score also showed a significant correlation with the global histopathological score in synovium paraffin sections measured by Krenn’s score (Spearman’s correlation coefficient r=0.466, p=0.018). Furthermore, PD intra-synovial US signal significantly correlated with the
synovial tissue vascularization measured by % CD31 immunohistochemical positive staining (r=0.463, p=0.017). Additionally, we observed that GD MS-US significantly correlated with the protein levels of IL1β in the synovial membranes measured by western-blot studies (Spearman’s correlation coefficient r=0.529, p=0.0078).

Conclusion:

Our results indicate that MS-US imaging measurements correlate with joint swelling, histological inflammation and vascularization of the synovium. Furthermore, MS-US could also serve as an indicator of the inflammatory degree in relation to the level of some pro-inflammatory cytokines, such as IL-1β, involved in the pathogenesis of gout. Therefore, ultrasonography analysis can be considered a feasible valid method for assessing the evolution of synovial inflammation in experimental gouty arthritis in rabbits.

Disclosure: R. Largo, None; J. P. Medina, None; S. Perez-Baos, None; V. Najera-Aleson, None; A. Mediero, None; G. Herrero-Beaumont, None; E. Naredo, Abbvie, Roche, BMS, Pfizer, UCB, Novartis, Lilly, Janssen, 5.


Identification of Urate Deposits in Patients with Asymptomatic Hyperuricemia Using a Dual-Energy CT Scan

Penny Wang1, Stacy Smith2, Rajesh Garg3, Fengxin Lu1, Alyssa Wohlhaft1, Anarosa Campos1, Kathleen Vanni4, Zhi Yu5, Daniel H. Solomon1 and Seoyoung C. Kim1, 1Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA, 2Radiology, Division of Musculoskeletal Imaging and Intervention, Brigham and Women's Hospital, Boston, MA, 3Division of Endocrinology, Diabetes & Hypertension, Brigham and Women's Hospital, Boston, MA, 4Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA, 5Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Metabolic and Crystal Arthropathies Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Serum uric acid (sUA) is a useful indicator of the risk of developing gout. However, most patients with elevated sUA levels do not have gout. Dual-energy computed tomography (DECT) scan is a relatively sensitive and specific imaging tool used to measure and visualize urate deposits in the joints. Prior research shows presence of subclinical urate deposits in nearly one-quarter of patients with severe hyperuricemia (i.e., sUA >9 mg/dl) without gout. We conducted a cross-sectional study to identify urate deposits using DECT and examine whether an association exists between sUA levels and total volume of urate deposits in patients with asymptomatic hyperuricemia.

Methods: We recruited adults aged ≥40 years with sUA levels ≥6.5 mg/dl and metabolic syndrome according to the National Cholesterol Education Program–Adult Treatment Panel III criteria. We excluded patients with gout, end-stage renal disease, renal replacement therapy, active malignancy, and use of xanthine oxidase inhibitors, colchicine or probenecid. All patients underwent a measurement of sUA level and DECT scan of a foot. A fellowship trained MSK radiologist processed and reviewed the DECT images and determined total volume of urate deposits. We used logistic regression to assess the association between sUA and presence of urate deposits and linear regression to examine the association between sUA and total volume of urate deposits.

Results: A total of 46 subjects participated in this study. The mean age was 62 (±8) years, 41% were male and mean sUA level was 7.8 (±1.0) mg/dl. Seven of 46 (15%) patients had urate deposits in the feet. The mean total volume of urate deposits was 0.13 (±0.14) cm³. On univariable analysis, age had significant association with presence of urate deposits but sUA, male sex, body mass index, presence of diabetes, and renal function did not (Table). sUA had a modest linear association (β coefficient=0.11, p=0.09), albeit statistically not significant, with total volume of urate deposits (Figure).

Conclusion: In this cross-sectional study, 15% of patients with elevated sUA but no known gout had urate deposits in the foot DECT scan. There were no clear patient factors other than older age associated with presence of urate deposits on DECT scans. While the clinical significance of these urate deposits is unclear, it is possible that these patients may develop gouty arthritis or they may have
“resistance” to reacting against urate deposits. Further research on why certain patients with hyperuricemia develop gout may present important clues to gout prevention.

| Disclosure: P. Wang, None; S. Smith, None; R. Garg, None; F. Lu, None; A. Wohlfahrt, None; A. Campos, None; K. Vanni, None; Z. Yu, None; D. H. Solomon, AstraZeneca, 2,Bristol-Myers Squibb, 2,Pfizer Inc, 2,Roche Pharmaceuticals, 2; S. C. Kim, AstraZeneca, 2,Pfizer Inc, 2,Roche Pharmaceuticals, 2,Bristol-Myers Squibb, 2,Merck Human Health, 2. |  


Abstract Number: 2058

A Study on Febuxostat Prescribing Practices for Patients with Chronic Gout Previously Managed with Allopurinol at the Veterans Affairs Puget Sound

Percy Balderia and Elizabeth R. Wahl, Rheumatology, University of Washington School of Medicine, Seattle, WA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Metabolic and Crystal Arthropathies Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: American College of Rheumatology (ACR) guidelines recommend use of either allopurinol or febuxostat as first-line approaches to urate lowering therapy in gout. Prior studies of managed care cohorts have shown that patients are commonly switched to febuxostat before their allopurinol dose has been optimized. While each is effective, their cost differential (8 cents/pill compared to 5 dollars/pill at our facility) suggests there may be good reason to favor allopurinol use within a health system. To identify potential areas for improvement for allopurinol and febuxostat use, we sought to better understand current febuxostat prescribing practices at our facility among patients with chronic gout who were initially on allopurinol.

| Table. Association between clinical characteristics and presence of urate deposits on DECT scans among patients with asymptomatic hyperuricemia (n=48) |  

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Univariable OR (95% CI)</th>
<th>SUA-adjusted OR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum uric acid (SUA)</td>
<td>1.30 (0.63-2.59)</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>1.20 (0.53-1.39)</td>
<td>1.51 (1.03-2.12)</td>
</tr>
<tr>
<td>Male sex</td>
<td>1.08 (0.21-5.49)</td>
<td>1.04 (0.21-5.46)</td>
</tr>
<tr>
<td>Body mass index</td>
<td>0.97 (0.85-1.11)</td>
<td>0.94 (0.81-1.10)</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>0.97 (0.19-4.93)</td>
<td>0.87 (0.16-4.98)</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>0.02 (0.08-11.19)</td>
<td>0.50 (0.04-8.22)</td>
</tr>
<tr>
<td>High-sensitivity C-reactive protein</td>
<td>1.00 (0.94-1.06)</td>
<td>1.00 (0.94-1.06)</td>
</tr>
</tbody>
</table>

Figure. Association between suA level and total volume of urate deposits measured with DECT.

β=0.11, p=0.09
**Methods:** Data were extracted from the local pharmacy prescription database to identify all patients ≥ 18 years of age, seen at our facility, and prescribed febuxostat between 1/1/13 and 8/31/16. We conducted a retrospective chart review to identify the daily dose of allopurinol before febuxostat prescription. Additionally, the type of prescribing physician (rheumatologist, non-rheumatologist), reason for prescribing febuxostat (inadequate response to other medications, kidney dysfunction, allopurinol hypersensitivity), uric acid level, estimated glomerular filtration rate (GFR) at time of switch, presence of tophi, and demographic data were recorded.

**Results:** Sixty-four patients with chronic gout were switched from allopurinol to febuxostat. Forty-two patients were switched due to adverse drug events (most commonly rash, n = 17 or gastrointestinal symptoms, n = 8) and 22 due to inadequate response.

**Table 1.** Characteristics of Patients Switched to Febuxostat Due to Inadequate Response to Allopurinol

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in y: median (IQR)</td>
<td>63 (9.3)</td>
</tr>
<tr>
<td>Male: n (%)</td>
<td>21 (95.5)%</td>
</tr>
<tr>
<td>Tophaceous gout: n (%)</td>
<td>6 (27.3)%</td>
</tr>
<tr>
<td>Allopurinol duration in months: median (IQR)</td>
<td>49 (41.5)</td>
</tr>
<tr>
<td>Documented trial of probenecid: n (%)</td>
<td>3 (13.6)</td>
</tr>
<tr>
<td>Uric acid level in mg/dL: median (IQR)</td>
<td>9.2 (3.3)</td>
</tr>
</tbody>
</table>

**Table 2.** Allopurinol Dosing Prior to Switching to Febuxostat According to Estimated Glomerular Filtration Rate

<table>
<thead>
<tr>
<th>Estimated GFR in mg/dL/m²: range (n)</th>
<th>Daily Dose in mg: median (IQR), range</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤30 (10)</td>
<td>300 (175), 100-450</td>
</tr>
<tr>
<td>&gt;30 - ≤60 (8)</td>
<td>300 (100), 50-825</td>
</tr>
<tr>
<td>&gt;60 (4)</td>
<td>600 (100), 600-800</td>
</tr>
</tbody>
</table>

**Conclusion:** In our facility, most of the patients were prescribed febuxostat due to adverse effects from allopurinol. Among those switched due to inadequate response, almost two-thirds had a dose of 300 mg/day or less.

**Disclosure:** P. Balderia, None; E. R. Wahl, None.


**Abstract Number:** 2059

**Allopurinol Dose-Titration Patterns Relative to Serum Uric Acid Levels in Gout Patients: US Electronic Health Record Data**

An-Chen Fu, Douglas C.A. Taylor and David S. Reasner, Ironwood Pharmaceuticals, Inc., Cambridge, MA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Metabolic and Crystal Arthropathies Poster II

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM
Background/Purpose: Gout is the most common form of inflammatory arthritis and is caused by elevated serum uric acid (sUA). Allopurinol is a first-line urate-lowering therapy for patients with gout and the American College of Rheumatology guidelines recommend allopurinol dose titration to lower and maintain sUA levels <6 mg/dL. Understanding the gap between treatment guidelines and real-world dose titration patterns in patients with gout may ultimately lead to better disease management and control. Hence, the aim of this study was to understand real-world allopurinol dose-titration patterns relative to sUA levels.

Methods: This was a retrospective study using de-identified Humedica electronic medical record data from 2007 to 2015. The study cohort included gout patients (International Classification of Disease, Ninth Revision, Clinical Modification [ICD-9-CM: 274.xx]), aged ≥18 years on the first gout diagnosis, with at least 1 sUA result and 2 allopurinol prescriptions. An sUA episode within the study cohort was defined as allopurinol initial dosage (ID) prior to (closest) and titrated dosage (TD) after (within 30 days of) an sUA test. Study measurements included dosage (strength/day) by imputing allopurinol strength, and dose frequency, dose titration was categorized as up-titration, down-titration, or no-dosage-change by comparing ID and TD for each episode (up-titration: ID < TD; down-titration: ID > TD, no-dose-change: ID = TD). Uncontrolled episodes were defined as episodes with sUA levels ≥6 mg/dL. Prescriber’s specialty was identified from the TD prescription. Descriptive episode-level and patient-level analyses were performed.

Results: All sUA episodes (n=64,609) selected in this analysis were from 40,143 unique patients (mean age of 64 years, 73% male, and 82% Caucasian). Of all sUA episodes, 57% were uncontrolled (sUA ≥6 mg/dL). A total of 71% uncontrolled episodes had no-dosage-change (n=26,123), 21% had up-titration (n=7,823), and 7% had down-titration (n=2,704). Among no-dosage-change sUA episodes, episodes with lower dosages were uncontrolled at higher rates. Seventy-eight percent of dosage-change episodes were uncontrolled, of which 100 to 300 mg/day was the most frequent (39%) dose titration. Overall, the most frequent TD was 300 mg/day (52%) followed by 100 mg/day (36%), >100 & <300 mg/day (3%), and <100 mg/day (5%). Prescriber specialty at the time of a TD prescription was mostly primary care (77%), followed by rheumatology (13%), others/unknown (9%), and nephrology (2%). Among uncontrolled episodes, rheumatologists dose-titrated allopurinol more often than other specialists (rheumatologists [46%], nephrologists [29%], others/unknown [29%], and primary care physicians [26%]).

Conclusion: Contrary to current guidelines from the American College of Rheumatology, allopurinol dose was generally not titrated, regardless of sUA levels. This current lack of titration suggests a need for more active management of patients with gout and uncontrolled sUA, including consideration of new treatment options in addition to allopurinol.

Disclosure: A. C. Fu, Ironwood Pharmaceuticals, 1, Ironwood Pharmaceuticals, 3; D. C. A. Taylor, Ironwood Pharmaceuticals, 1, Ironwood Pharmaceuticals, 3; D. S. Reasner, Ironwood Pharmaceuticals, 3.

Pseudogout Among Patients Fulfilling a Billing Code Algorithm for Calcium Pyrophosphate Deposition Disease (CPPD)

Sara K. Tedeschi, Daniel H. Solomon and Katherine P. Liao, Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Metabolic and Crystal Arthropathies Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Calcium pyrophosphate deposition disease (CPPD) has a spectrum of manifestations, of which pseudogout is the most acute inflammatory phenotype. Studies focusing on pseudogout are limited by a paucity of algorithms to identify this condition in large datasets. To our knowledge, there is only one published algorithm for CPPD, developed at a Veterans’ Administration Medical Center to identify “definite or probable CPPD” per Ryan and McCarty’s diagnostic criteria.1 The algorithm includes ≥1 ICD-9 code 275.49 (other disorders of calcium metabolism) or 712.1-712.39 (chondrocalcinosis due to dicalcium phosphate crystals, pyrophosphate crystals, or cause unspecified). We examined characteristics of patients fulfilling this algorithm at a tertiary care academic medical center, with a focus on subjects clinically manifesting as pseudogout.

Methods: Following the published methods, we applied the algorithm to patients with ≥1 encounter at our center over 2 years (1/1/15-12/31/16). 100 patients were randomly selected for medical record review from date of 1st qualifying ICD-9 code through present. We...
evaluated each record for 2 phenotypes: 1) “definite or probable CPPD”, defined as joint pain, and either synovial fluid with calcium pyrophosphate crystals or radiographic chondrocalcinosis in any joint, or both; 2) pseudogout, defined as synovitis and synovial fluid aspirate with calcium pyrophosphate crystals. We recorded information on demographics, healthcare utilization, musculoskeletal diagnoses, and evaluation and treatment.

**Results:** 68% of patients had one or both phenotypes; 32% met neither definition (Table). 18 patients (18%) had pseudogout, all of whom also met the definition of “definite or probable CPPD”. 50 patients (50%) had “definite or probable CPPD” but not pseudogout. Overall 73% had osteoarthritis per x-ray reports or notes, with the highest frequency (90%) among “definite or probable CPPD” only, compared to 72% of pseudogout patients. Synovial fluid aspiration was performed in 25% of patients and was positive in all with crystal-proven pseudogout by definition, but not positive in any others. Among 92 patients with x-rays, chondrocalcinosis was noted in 61% and in 100% of patients with “definite or probable CPPD” only. Chondrocalcinosis was present in <1/3 of patients with both x-rays and crystal-proven pseudogout; among these, it was present in <20% of symptomatic joints.

**Conclusion:** Among subjects identified using a published CPPD algorithm, 18% had crystal-proven pseudogout, of whom <20% had x-ray chondrocalcinosis in the affected joint. These findings highlight a need for improved understanding of pseudogout and improved approaches to identify this acute phenotype of CPPD.

Characteristics of 100 patients meeting a CPPD billing code algorithm,* by clinical phenotype

<table>
<thead>
<tr>
<th>Phenotype according to medical record review</th>
<th>Definite or probable CPPD† (n=68)</th>
<th>Not meeting CPPD§ or pseudogout ** definition (n=32)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Crystal-proven pseudogout ** and definite/probable</td>
<td>Definite/probable</td>
</tr>
<tr>
<td>Number</td>
<td>All CPPD only</td>
<td>32</td>
</tr>
<tr>
<td>Mean age (standard deviation), years</td>
<td>70.4 (12.0) 66.7 (14.4)</td>
<td>71.7 (10.9) 64.8</td>
</tr>
<tr>
<td>Female</td>
<td>55.9</td>
<td>53.1</td>
</tr>
<tr>
<td>White</td>
<td>79.4</td>
<td>87.5</td>
</tr>
<tr>
<td>Billing location</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inpatient</td>
<td>8.8</td>
<td>25.0</td>
</tr>
<tr>
<td>Outpatient</td>
<td>73.5</td>
<td>62.5</td>
</tr>
<tr>
<td>Emergency or urgent care</td>
<td>17.7</td>
<td>12.5</td>
</tr>
<tr>
<td>Billing provider type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary care</td>
<td>8.8</td>
<td>15.6</td>
</tr>
<tr>
<td>Rheumatologist</td>
<td>32.4</td>
<td>21.9</td>
</tr>
<tr>
<td>Orthopedic surgeon</td>
<td>35.4</td>
<td>15.6</td>
</tr>
<tr>
<td>Other</td>
<td>23.5</td>
<td>46.9</td>
</tr>
<tr>
<td>Rheumatology or ortho evaluation</td>
<td>86.8</td>
<td>71.2</td>
</tr>
<tr>
<td>Rheumatology or ortho diagnosis(es)††</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pseudogout (possible, probable, or definite)</td>
<td>37.3 (22/59)</td>
<td>43.5 (10/23)</td>
</tr>
<tr>
<td>CPPD</td>
<td>93.8 (15/16) 16.3 (7/43)</td>
<td></td>
</tr>
<tr>
<td>osteoarthritis</td>
<td>6.8 (4/59) 6.3 (1/16)</td>
<td>17.4 (4/23)</td>
</tr>
<tr>
<td>gout</td>
<td>49.2 (29/59)</td>
<td>8.7 (2/23)</td>
</tr>
<tr>
<td>other</td>
<td>5.1 (3/59) 6.3 (1/16)</td>
<td>8.7 (2/23)</td>
</tr>
<tr>
<td>Osteoarthritis on x-ray or in notes</td>
<td>13.6 (8/59) 6.3 (1/16)</td>
<td>43.5 (10/23)</td>
</tr>
<tr>
<td>Joint pain</td>
<td>85.3</td>
<td>46.9</td>
</tr>
<tr>
<td>Synovitis (pain, swelling &amp; tenderness)</td>
<td>98.5</td>
<td>59.4</td>
</tr>
<tr>
<td>Joint(s) with pain or synovitis</td>
<td>36.8</td>
<td>28.2</td>
</tr>
<tr>
<td>Shoulder</td>
<td>8.8</td>
<td>6.3</td>
</tr>
<tr>
<td>Wrist</td>
<td>19.1</td>
<td>18.8</td>
</tr>
<tr>
<td>MCP</td>
<td>4.4</td>
<td>9.4</td>
</tr>
<tr>
<td>Knee</td>
<td>83.8</td>
<td>28.1</td>
</tr>
<tr>
<td>Ankle</td>
<td>5.9</td>
<td>15.6</td>
</tr>
<tr>
<td>Other</td>
<td>19.1</td>
<td>34.4</td>
</tr>
<tr>
<td>Synovial fluid aspiration</td>
<td>30.9</td>
<td>12.5</td>
</tr>
<tr>
<td>CPP crystals present</td>
<td>85.7 (18/21)</td>
<td>0 (0/4)</td>
</tr>
<tr>
<td>X-ray of any joint performed</td>
<td>97.1</td>
<td>81.3</td>
</tr>
<tr>
<td>Chondrocalcinosis in any joint</td>
<td>83.3 (55/66)</td>
<td>3.8 (1/26)</td>
</tr>
<tr>
<td>Chondrocalcinosis in affected joint</td>
<td>74.2 (49/66)</td>
<td>3.8 (1/26)</td>
</tr>
<tr>
<td>Treatment(s) for initial episode</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSAID</td>
<td>22.1</td>
<td>18.8</td>
</tr>
<tr>
<td>Colchicine</td>
<td>7.4</td>
<td>9.4</td>
</tr>
</tbody>
</table>
Oral glucocorticoids 16.2 38.9 8.0 6.3
Intra-articular glucocorticoids 11.8 27.8 6.0 3.1

Presented as % unless specified otherwise. Abbreviations: CPPD: calcium pyrophosphate deposition disease  CPP: calcium pyrophosphate

* At the time of fulfilling a published ICD-9 code algorithm for definite or probable CPPD

+ Definite or probable CPPD: joint pain, and either synovial fluid with CPP crystals or radiographic chondrocalcinosis in any joint, or both

** Crystal-proven pseudogout: synovitis and synovial fluid with CPP crystals

++ Diagnoses to explain the patient’s chief complaint. >1 diagnosis per patient possible

Disclosure: S. K. Tedeschi, None; D. H. Solomon, None; K. P. Liao, None.

Abstract Number: 2061

Population-Specific Factors Associated with Fractional Excretion of Uric Acid

Zoe Vincent¹, Amanda Phipps-Green², Lisa K. Stamp³, Tony R. Merriman⁴ and Nicola Dalbeth¹, ¹University of Auckland, Auckland, New Zealand, ²University of Otago, Dunedin, New Zealand, ³University of Otago, Christchurch, New Zealand, ⁴Biochemistry Dept, PO Box 56, University of Otago, Dunedin, New Zealand

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Metabolic and Crystal Arthropathies Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: For most people with gout, reduced renal clearance of uric acid is a key contributor to hyperuricemia. It is increasingly recognized that gout has a genetic basis, and that renal clearance of uric acid is also genetically determined. However, the factors that contribute most to reduced renal clearance of uric acid are unknown. The aim of this study was to examine clinical and genetic factors associated with fractional excretion of uric acid (FEUA), including in the New Zealand Maori and Pacific population which has high prevalence of hyperuricemia and gout.

Methods: New Zealand Maori, Pacific and European participants in the Genetics of Gout in Aotearoa study with available genotyping and FEUA data were included in this analysis (n=1713, 896 with gout and 817 without gout). All participants completed a study visit which included clinical assessment and collection of blood and urine for urate and creatinine testing. FEUA was calculated as the urate clearance/creatinine clearance, expressed as a percentage. Participants with chronic kidney disease stage 5 were excluded from the analysis. Associations with FEUA were tested using linear regression models. The top 10 loci previously associated with FEUA in a European population by GWAS (Kottgen, Nature Genetics 2013) were analysed. For genetic analysis, P for experiment-wide significance was 0.005.

Results: The mean (SD) FEUA in the entire study group was 5.5 (2.7)%. Maori or Pacific participants had lower FEUA compared to European participants (mean (SD) FEUA 5.0 (2.6)% vs. 5.9 (2.7)%, P for difference=2x10-12). The number of SLC2A9 rs11942223 risk alleles was associated with FEUA in European participants (age and sex-adjusted P=3 x 10-8). Most (89%) Maori or Pacific participants had two SLC2A9 rs11942223 risk alleles, and no association between SLC2A9 and FEUA was observed in Maori or Pacific participants (age and sex-adjusted P=0.15). No other tested loci met experiment-wide significance for association with FEUA. In European participants, gout status, diuretic use, male sex, body mass index, and number of SLC2A9 risk alleles were independently
associated with FEUA, and these five variables accounted for 37% of the variance of FEUA in the regression model (Table). In contrast, in Maori or Pacific participants, these variables contributed to 19% of the variance of FEUA in the regression models (Table).

**Conclusion**: Both genetic and non-genetic factors contribute to renal clearance of uric acid. \( SLC2A9 \) exerts population-specific effects on FEUA, with effects observed in European, but not Maori or Pacific people.

### Table: Predictors of FEUA in linear regression analysis.

<table>
<thead>
<tr>
<th>Variable</th>
<th>European participants (n=948)</th>
<th>Maori or Pacific participants (n=765)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Standardised beta</td>
<td>P</td>
</tr>
<tr>
<td>Gout status</td>
<td>-0.25</td>
<td>2x10⁻⁷</td>
</tr>
<tr>
<td>Diuretic use</td>
<td>-0.19</td>
<td>3x10⁻⁵</td>
</tr>
<tr>
<td>Male sex</td>
<td>-0.24</td>
<td>2x10⁻⁸</td>
</tr>
<tr>
<td>Body mass index</td>
<td>-0.20</td>
<td>4x10⁻⁵</td>
</tr>
<tr>
<td>Number of ( SLC2A9 ) risk alleles</td>
<td>-0.17</td>
<td>6x10⁻⁶</td>
</tr>
</tbody>
</table>

**Disclosure**: Z. Vincent, None; A. Phipps-Green, None; L. K. Stamp, Amgen, 8; T. R. Merriman, Ardea Biosciences, 2; N. Dalbeth, Takeda, AstraZeneca, Abbvie, 9.


**Abstract Number**: 2062

**Flow-Mediated Dilation As a Marker of Endothelial Dysfunction in Gout**

**Enrique Calvo Aranda**¹, Ofelia Carrion², Afnan Abdelkader², Jorge Juan González Martín³, Francisco Aramburu³, Marta Valero⁴, Silvia Rodríguez⁴, Carolina Marin³, Irene Ami³, Felipe Sainz² and Paloma Garcia De La Peña³, ¹RHEUMATOLOGY, Hospital Madrid Norte Sanchinarro, Madrid, Spain, ²Vascular Surgery Department, Hospital Madrid Norte Sanchinarro, Madrid, Spain, ³Rheumatology, Hospital Madrid Norte Sanchinarro, Madrid, Spain, ⁴Rheumatology, Hospital Madrid Norte Sanchinarro, MADRID, Spain, ⁵Vascular Surgery, Hospital Madrid Norte Sanchinarro, MADRID, Spain  

**First publication**: September 18, 2017

**SESSION INFORMATION**  
Session Date: Tuesday, November 7, 2017  
Session Title: Metabolic and Crystal Arthropathies Poster II  
Session Type: ACR Poster Session C  
Session Time: 9:00AM-11:00AM

**Background/Purpose**: Several studies have shown the relationship between gout and increased cardiovascular risk and mortality. Hyperuricemia and crystal-induced synovitis are associated with endothelial dysfunction and patients with gout may be at increased risk of early atherosclerosis. Many reports have indicated that endothelial dysfunction plays a key role in affecting cardiovascular and renal function. The flow-mediated dilation (FMD) test is the most commonly used non-invasive assessment of vascular endothelial function and is associated with an increased risk of vascular events. There is a lack of studies with FMD assessment in patients with gout.

**Methods**: Prospective cohort study with collection of demographic and clinical data and cardiovascular treatments received. BMI, serum uric acid, ESR, high-sensitivity CRP [hsCRP], ferritin, cholesterol, triglycerides, vitamin D and homocysteine were measured.
Patients were referred to Vascular Surgery Department for flow-mediated dilation assessment with high-resolution two-dimensional ultrasound imaging of the brachial artery. Endothelial dysfunction was defined as pathological values of FMD below 10 (severe if less than 5). All patients met the ACR classification criteria for gout.

**Results:** One hundred and fifty patients, 97% men and 3% women. Average age: at time of study 56 (23-92); at diagnosis 47 years (15-79); at symptoms onset 45 years (15-77). 22.5% had tophi, 11.3% urate kidney stones, 42% gout family history, 41% cardiovascular disease family history. Hypertension 47.3%; diabetes mellitus 4.6%; dyslipidemia 56.7%; smokers 20.6%, quitters 37.6%; 75% overweight obesity, mean BMI 28 (19-40). One patient had suffered stroke; 4 thrombosis; 17 ischemic heart disease (11 angina, 6 myocardial infarction). Analytical parameters: ESR 10 mm/h (1-68), hs-CRP 2.7 mg/dL (0.1-57.7); serum uric acid 6.9 mg/dL (2.4-23.6; 29% <20); homocysteine 24.7 mmol/L (4-40; 32% >15 mmol/L). FMD was assessed in 147 patients with a mean value of -0.60 ± 0.52. The 81% of subjects showed pathological values indicating endothelial dysfunction, severe in 52%. In the multivariate analysis, the only analytical determinant of endothelial dysfunction was the serum vitamin D concentration, which showed a negative correlation with FMD.

**Conclusion:** There is a high prevalence of traditional cardiovascular risk factors and cardiovascular diseases in our cohort. Most of our patients with gout have endothelial dysfunction measured by FMD, and that is severe in more than a half of them. Vitamin D deficiency is common and correlates with pathological values of FMD in gout. Cardiovascular risk should be periodically assessed in gout and we will continue studying the potential value of FMD as a marker of endothelial dysfunction in patients with this rheumatic disease.

**Disclosure:** E. Calvo Aranda, Fundación Española de Reumatología, 2; O. Carrion, None; A. Abdelkader, None; J. J. González Martín, None; F. Aramburu, None; M. Valero, None; S. Rodriguez, None; C. Marin, None; I. Amil, None; F. Sainz, None; P. García De La Peña, Fundación Española de Reumatología, 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/flow-mediated-dilation-as-a-marker-of-endothelial-dysfunction-in-gout

**Abstract Number:** 2063

**Relation of Serum Urate and Gout Duration to Tophi, Urate Deposition, and Inflammation**

Ana Beatriz Vargas-Santos1, S. Reza Jafarzadeh2, Geraldo Castelar-Pinheiro1, Nicola Dalbeth3, William J. Taylor4, Jaap Fransen5, Tim L. Jansen6, H. Ralph Schumacher7 and Tuhina Neogi2, 1Internal Medicine - Rheumatology, State University of Rio de Janeiro, Rio de Janeiro, Brazil, 2Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA, 3University of Auckland, Auckland, New Zealand, 4Department of Medicine, University of Otago, Wellington, New Zealand, 5Department of Rheumatology, Radboud University Medical Center, Nijmegen, Netherlands, 6Rheumatology, Radboud University Medical Center, Nijmegen, Netherlands, 7Medicine, Rheumatology, U Penn & VA Med Ctr, Philadelphia, PA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Metabolic and Crystal Arthropathies Poster II

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Gout duration and serum urate (SU) levels are thought to influence development of tophi and chronic inflammatory gouty arthropathy, but the extent to which either one or both contribute to their development is not clear. We evaluated the relation of SU and of gout duration to the presence of tophus, urate deposition, and inflammation in a large cohort of crystal-proven gout subjects.

**Methods:** We used data from the 509 crystal-proven gout subjects in the Study for Updated Gout Classification Criteria (SUGAR) cohort to evaluate the effect of highest-ever recorded SU and gout duration (years since 1st flare) separately, as well as in combination to examine their joint effects on tophi, urate deposition, and inflammation. Subjects were enrolled irrespective of flare status. Radiographs of the hands and feet, and ultrasound (US) of a clinically affected joint were obtained. Tophi were evaluated as clinically evident tophi, as well as imaging evidence of tophus (based on X-ray or US). Urate deposition was determined based on US evidence of urate deposition (double-contour sign), and inflammation was assessed as power Doppler signal on US indicative of synovitis. We assessed
the relation of highest SU, gout duration, and their combination using logistic regression, adjusting for age, sex, and ethnicity. Relative Excess Risk due to Interaction (RERI) was assessed using a linear additive risk-ratio model.

**Results:** Study sample included ~87% males, ~66% Caucasians, mean age of 60 years. Highest SU ranged from 2.6-19.2 mg/dL, and gout duration from 0-54 yrs. Higher levels of SU and longer duration of gout were significantly associated with clinical tophus, imaging evidence of tophus and double-contour sign, but not with power Doppler signal (Table 1A). The combination of higher SU and longer gout duration had the strongest association with the 4 outcomes, followed by longer disease duration regardless of highest SU for tophi and urate deposition, while for synovitis effects were similar regardless of the combination of SU with gout duration compared with low SU and shorter gout duration (Table 1B). However, we did not find any evidence of an additive interaction (Table 1C).

**Conclusion:** Both gout duration and highest-ever recorded SU levels were each associated with clinical and imaging evidence of tophus and with US-evidence of urate deposition, but not clearly with evidence of synovitis (power Doppler). The combination of high SU and longer gout duration resulted in the highest risk of tophaceous disease, but there not appeared to be a potentiation of individual effects. These data highlight the importance of managing the hyperuricemia of gout to minimize the adverse clinical features of the disease.

**Disclosure:** A. B. Vargas-Santos, None; S. R. Jafarzadeh, None; G. Castelar-Pinheiro, None; N. Dalbeth, Takeda, AstraZeneca, Abbvie, 9; W. J. Taylor, Pfizer Inc, 5; J. Fransen, None; T. L. Jansen, None; H. R. Schumacher, None; T. Neogi, None.


**Abstract Number:** 2064

**The Nomenclature of Gout: A Content Analysis of Contemporary Medical Journals**

David Bursill\(^1,2\), William J. Taylor\(^3\), Robert Terkeltaub\(^4\) and Nicola Dalbeth\(^5\), \(^1\)Medicine, University of Auckland, Auckland, New Zealand, \(^2\)School of Medicine, University of Adelaide, Adelaide, Australia, \(^3\)University of Otago, Wellington, New Zealand, \(^4\)Rheumatology, VA San Diego Healthcare System, San Diego, CA, \(^5\)University of Auckland, Auckland, New Zealand

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Metabolic and Crystal Arthropathies Poster II

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Gout has been recognized and described since antiquity. However, the terms used to describe the disease lack standardization. The aim of this study was to identify and categorise the labels used for the basic disease elements of gout in...
contemporary medical literature.

Methods: We analysed articles from the ten highest ranked general rheumatology and five highest ranked general internal medicine journals according to 2015 Thomson-Reuters Journal Citation Reports for the period January 2012 to January 2017. For each journal, relevant articles were identified by the search terms ‘gout’ and/or ‘hyperuricemia’ using MEDLINE. No exclusion criteria were applied. Labels were extracted from each article and categorised according to the descriptions given to the basic disease elements as shown in table 1. A label was determined to be ‘unique’ if it used different words or phrases to describe an element.

Results: There were 549 articles from 15 journals over the five-year period. A total of 3,220 labels were identified, of which 342 were unique. Table 1 shows the number of unique labels identified for each element, and the most commonly used label. For a few elements, there was consistency in the label used; for example, 99.0% of articles describing ‘an elevated circulating level of the final enzymatic product generated by xanthine oxidase in purine metabolism in humans’ used the label ‘hyperuric(a)emia’, and 92.5% of articles describing ‘a discrete collection of pathogenic crystals with associated host-response tissue’ used the label ‘tophus’. However, for most elements, a wide range of labels was used with no dominantly used label (Table 1). The element ‘an episode of acute inflammation triggered by the presence of pathogenic crystals’ had the largest number of unique labels; 162 unique labels were identified, and 33.6% articles used at least 4 unique labels for this element. For ‘the circulating form of the final enzymatic product generated by xanthine oxidase in purine metabolism in humans’, there were two widely used labels; ‘uric acid’ (63.0% articles) and ‘urate’ (62.5% articles); with both labels used interchangeably in 25.9% articles.

Conclusion: The existing nomenclature of gout disease elements is imprecise and inconsistent. This imprecision may be a barrier to effective communication in both clinical and research settings. Consensus regarding the nomenclature of disease elements is required.

Table 1 – Unique labels identified for the basic disease elements of gout in 549 disease-relevant articles
<table>
<thead>
<tr>
<th>Disease Element</th>
<th>Number of Unique Labels Identified</th>
<th>Most frequently used label (% articles)</th>
</tr>
</thead>
<tbody>
<tr>
<td>The pathogenic crystals in gout</td>
<td>28</td>
<td>Monosodium urate crystals (73.1%)</td>
</tr>
<tr>
<td>The circulating form of the final enzymatic product generated by xanthine oxidase in purine metabolism in humans</td>
<td>9</td>
<td>Uric acid (63.0%)</td>
</tr>
<tr>
<td>An elevated circulating level of the final enzymatic product generated by xanthine oxidase in purine metabolism in humans</td>
<td>7</td>
<td>Hyperuric(a)emia (99.0%)</td>
</tr>
<tr>
<td>A discrete collection of pathogenic crystals with associated host-response tissue</td>
<td>18</td>
<td>Tophus (92.5%)</td>
</tr>
<tr>
<td>A discrete collection of pathogenic crystals with associated host-response tissue, detectable on physical examination</td>
<td>27</td>
<td>Subcutaneous tophus (44.1%)</td>
</tr>
<tr>
<td>An episode of acute inflammation triggered by pathogenic crystals</td>
<td>162</td>
<td>Acute gout (33.6%)</td>
</tr>
<tr>
<td>The condition in which there is an absence of clinically evident inflammation after or between episodes of acute inflammation</td>
<td>16</td>
<td>Intercritical period (42.1%)</td>
</tr>
<tr>
<td>Persistent inflammation induced by pathogenic crystals</td>
<td>34</td>
<td>Chronic gout (58.4%)</td>
</tr>
<tr>
<td>The presence of pathogenic crystal deposition on imaging</td>
<td>11</td>
<td>Urate deposition (63.3%)</td>
</tr>
<tr>
<td>The presence of structural bone damage due to gout</td>
<td>30</td>
<td>Erosion (54.0%)</td>
</tr>
</tbody>
</table>

**Disclosure:** D. Bursill, None; W. J. Taylor, Pfizer Inc, 5; R. Terkeltaub, VAMC/UCSD location, 3, ARDEA/Astra-Zeneca, 2, SOBI, Selecta, Horizon, Cymabay, Aequus, 5; N. Dalbeth, Takeda, AstraZeneca, Abbvie, 9.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/the-nomenclature-of-gout-a-content-analysis-of-contemporary-medical-journals](http://acrabstracts.org/abstract/the-nomenclature-of-gout-a-content-analysis-of-contemporary-medical-journals)

**Abstract Number:** 2065

**Higher Urate Volume Measured By Dual Energy Computed Tomography Is Associated with Unfavourable Cardiovascular Risks in Patients with Gout**
Hyperuricemia and gout are associated with increased risk of cardiovascular disease. The aim of the study was to evaluate the correlation between cardiovascular risk and total urate volumes measured by dual energy computed tomography (DECT).

Methods:
DECT datasets from 91 crystal-proven gout patients were analyzed retrospectively. The total volumes of uric acid deposition were quantified using automated volume assessment software. The 10-year cardiovascular risk using Framingham risk score (FRS) and metabolic syndrome (MS) based on National Cholesterol Education Program were estimated.

Results:
Fifty five patients with positive results on DECT and 36 patients with negative results on DECT were assessed. Patients with positive DECT showed significant higher systolic blood pressure, diastolic blood pressure, and fasting glucose and higher prevalence of chronic kidney disease, compared with those with negative DECT. The total urate volumes were significantly correlated with FRS and the number of component of metabolic syndrome (r = 0.22, P = 0.036 and r = 0.373, P < 0.001, respectively).

Conclusion:
This study demonstrated the correlation between total urate volumes on DECT and cardiovascular risk. Higher urate burden could affect unfavorable cardiovascular outcomes.

Disclosure: S. H. Lee, None; H. R. Kim, None; K. A. Lee, None; J. W. Hur, None.


Mediation Analysis to Understand Genetic Relationships between Habitual Coffee Intake and Gout

Joseph Hutton1, Tanya Major2, Ruth Topless3, Tony R. Merriman4 and Nicola Dalbeth1, 1University of Auckland, Auckland, New Zealand, 2Biochemistry, University of Otago, Dunedin, New Zealand, 3University of Otago, Dunedin, New Zealand, 4Biochemistry Dept, PO Box 56, University of Otago, Dunedin, New Zealand

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Metabolic and Crystal Arthropathies Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM
Background/Purpose: Increased coffee intake is associated with reduced serum urate concentrations and lower risk of gout. Recent genome wide association studies (GWAS) have shown that genetic variants influence both coffee intake and serum urate. Specific alleles of SNPs in the ABCG2, GCKR, MLXIPL and CYP1A2 genes have been associated with reduced coffee intake and increased serum urate in separate GWAS. The aim of this study was to determine whether these SNPs influence the risk of gout through their effects on coffee consumption.

Methods: This research was conducted using the UK Biobank Resource (approval number 12611). Data, including genome-wide genotypes, were available for 130,966 European participants, aged 40-69 years. A validated case definition of ‘self-reported gout or urate-lowering therapy use’ was used to determine gout status. Gout status and coffee intake (cups per day) were tested for association with four SNPs: ABCG2 (rs2231142), GCKR (rs1260326), MLXIPL (rs1178977) and CYP1A2 (rs2472297) using regression models, adjusted for age, sex, body mass index, hypertension, kidney disease, diabetes mellitus, and intake of additional dietary factors. Total, direct or indirect standardized effect estimates of the causal association with gout were calculated and Sobel’s test was used to determine whether the indirect effect of each SNP on gout risk, mediated through coffee consumption, was significant.

Results: Coffee consumption was inversely associated with gout (multivariate adjusted odds ratio (95% CI) per cup consumed per day 0.85 (0.82 - 0.87), p = 9x10^{-32}). The urate-increasing ABCG2, GCKR, MLXIPL and CYP1A2 alleles were associated with reduced daily coffee consumption, with the strongest associations for CYP1A2 (beta -0.35, p=8x10^{-40}), and MLXIPL (beta -0.23, p=3x10^{-8}), and weaker associations for ABCG2 (beta -0.11, p=2x10^{-9}) and GCKR (beta -0.10, p=3x10^{-10}). ABCG2 and GCKR were associated with gout at genome-wide significance (multivariate adjusted p<5x10^{-8} for both), but the association of MLXIPL and CYP1A2 did not achieve experiment-wide significance (multivariate adjusted p>0.0125 for both). In mediation analysis, the direct effects of ABCG2 and GCKR accounted for most of the total effect on gout risk, with much smaller indirect effects mediated by coffee consumption (Figure).

Conclusion: Lower coffee consumption is associated with gout. Although alleles at several SNPs associate with both lower coffee consumption and higher risk of gout, these SNPs largely influence gout risk directly, rather than indirectly through effects on coffee consumption.

Figure. Mediation analysis of A. ABCG2 and B. GCKR with gout, mediated by coffee consumption. Multivariate-adjusted standardised path coefficients are shown. The direction of the path analysis from SNP to gout risk was pre-specified.

Disclosure: J. Hutton, None; T. Major, None; R. Topless, None; T. R. Merriman, Ardea Biosciences, 2; N. Dalbeth, Takeda, AstraZeneca, Abbvie, 9.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/mediation-analysis-to-understand-genetic-relationships-between-habitual-coffee-intake-and-gout

Abstract Number: 2067

Treatment with Pegloticase Significantly Decreases Mean Arterial Blood Pressure in Patients with Chronic Gout
Hyon K. Choi¹, Richard Johnson², Anthony Yeo³ and Peter E. Lipsky⁴, ¹Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, ²Medicine, University of Colorado Denver, Aurora, CO, ³Horizon Pharma, Lake Forest, IL, ⁴AMPEL BioSolutions, LLC, Charlottesville, VA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Metabolic and Crystal Arthropathies Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: There are significant correlations between serum uric acid (sUA) and blood pressure (BP) in individuals with and without gout.¹ Limited data suggest that lowering sUA may decrease BP², but a metaanalysis suggests no consistent effect³. Pegloticase is a recombinant uricase conjugated to polyethylene glycol approved for chronic refractory gout that decreases sUA to <1 mg/dL.⁴ The results from the pegloticase randomized clinical trials (RCTs) permitted determination of the impact of persistent, very low sUA levels on BP in subjects with chronic refractory gout.

Methods: This analysis used results from 2 6-month RCTs in which subjects were treated with 8 mg pegloticase every 2 or 4 weeks (q2 or q4) or placebo.⁴ sUA responders maintained sUA <6 mg/dL.⁴ Sitting BP was measured at each visit and estimated glomerular filtration rate (eGFR) was determined at baseline and after 3 and 6 months.

Results: Serial blood pressure measures were obtained in 173 subjects during the course of the RCTs. Significant reductions in mean MAP from baseline to 6 months were noted in q2 responders (P=0.0029) (Figure 1), whereas reductions in mean MAP in other groups were not significant. Notably, 18/29 (62.1%) of q2 sUA responders experienced persistent reductions in MAP (p=0.01 compared to other groups). Of the q2 sUA responders exhibiting persistent decreases in MAP, there were no significant differences in baseline age, gender, race, BMI, history of hypertension, gout duration, MAP, sUA, cholesterol, eGFR or urinary UA /creatinine ratio compared with those who did not lower MAP. There were no significant changes in eGFR in sUA responders to pegloticase treatment over the course of the study (Figure 2) and there was no significant correlation between change from baseline MAP and eGFR in these subjects (r= -0.16, P=0.43) (Figure 3).

Conclusion: sUA responders to pegloticase experienced significant reductions in MAP that were independent of changes in renal function.

Figure 1. MAP over study visits in all treatment groups

Figure 2. eGFR measurements in q2 responders (each line is an individual subject)
Figure 3. Relationship between changes from baseline in MAP and eGFR for q2 responders
Disclosure: H. K. Choi, Selecta, Horizon, 5; AstraZeneca, 2; R. Johnson, None; A. Yeo, Horizon Pharma, 5; P. E. Lipsky, Horizon Pharma, 5.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/treatment-with-pegloticase-significantly-decreases-mean-arterial-blood-pressure-in-patients-with-chronic-gout

Abstract Number: 2068

Previous Prescription of Allopurinol Reduces the Risk of NSAIDs-Related Acute Kidney Injury in Patients with Gout

Fernando Perez-Ruiz1 and Sandra Chinchilla2, 1BioCrues Health Research Institute, Barakaldo, Spain, 2Rheumatology Division, Hospital Universitario Cruces, Baracaldo, Spain
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Metabolic and Crystal Arthropathies Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: untreated or undertreated gout is characterized by recurrent episodes of acute inflammation of joint structures, called gout flares, and flares are commonly treated with non-steroidal anti-inflammatory drugs (NSAIDs). To evaluate risk factors associated with acute kidney injury (AKI) attributed to NSAIDs in a cohort of patients who were exposed to NSAIDs to treat gout flares gout prior to urate-lowering therapy.

Methods: retrospective analysis of a nested prospective cohort of 983 gout patients in whom general variables (age, gender, renal function, ethanol intake, hypertension, hyperlipidemia, diabetes, vascular events, diuretic use) and also variables related to gout and severity of gout (serum urate levels, number for flares per year, presence of tophi, joint distribution, X-ray involvement, previous prescription of urate-lowering therapy) are available for analysis. Outcomes considered were loss of renal function attributed to NSAIDs prescription following the KDIGO AKI Work Group and staging. Variables associated to increased risk in Kaplan-Meier survival analysis were tested with multivariate Cox survival analysis, using time from onset of gout to the event as time exposed to NSAIDs.

Results: 55/983 patients (5.59%, 0.82 per 100 patient-yr) experienced an episode of AKI: 31, 13, and 11 patients showed Grade 1, Grade 2, and Grade 3 AKI. Among the gout-related variables, the number of flares in the year previous to the renal event and polyarticular joint distribution were associated with higher risk of renal events. Other general variables previously described in the literature, as the presence of previous chronic renal disease, the use of diuretics, and prevalent vascular events were also independently associated to increased risk of AKI. Interestingly, patients who had been previously prescribed allopurinol (other medications were uncommonly prescribed) showed a lower risk of acute renal events (Table).

<table>
<thead>
<tr>
<th>Variable</th>
<th>AKI uncorrected</th>
<th>AKI corrected</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>1.127 (0.611-2.078)</td>
<td>0.996 (0.541-1.831)</td>
<td>0.996</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>1.003(0.977-1.030)</td>
<td>1.002 (0.976-1.029)</td>
<td>0.876</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>0.551 (0.190-1.601)</td>
<td>0.593 (0.205-1.761)</td>
<td>0.335</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.396 (0.621-3.141)</td>
<td>1.448 (0.663-3.163)</td>
<td>0.353</td>
</tr>
<tr>
<td>Diuretic use</td>
<td>1.963 (0.988-3.898)</td>
<td>2.168 (1.130-4.161)</td>
<td>0.020</td>
</tr>
<tr>
<td>CKD 3-4</td>
<td>2.755 (1.435-5.286)</td>
<td>2.695 (1.404-5.172)</td>
<td>0.003</td>
</tr>
<tr>
<td>Previous vascular event</td>
<td>2.173 (1.708-4.383)</td>
<td>2.453 (1.259-4.782)</td>
<td>0.008</td>
</tr>
<tr>
<td>Polyarticular gout</td>
<td>3.560 (1.233-10.282)</td>
<td>3.90 (1.358-11.216)</td>
<td>0.011</td>
</tr>
<tr>
<td>Flares (&gt;2 per year)</td>
<td>2.489 1.194-5.187)</td>
<td>2.723 (1.030-5.693)</td>
<td>0.008</td>
</tr>
<tr>
<td>Not on allopurinol</td>
<td>3.634 (1.880-7.022)</td>
<td>3.921 (2.056-7.476)</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Conclusion: the number of flares and extensive joint distribution, variables related to gout clinical severity and surrogates for NSAID prescription, were associated with higher risk for renal injury in patients with gout, while previous prescription of allopurinol was...
associated with lower risk. We are uncertain if this finding is related to the use of allopurinol or a signal of better standard of healthcare that may reduce the risk of events indirectly.

Disclosure: F. Perez-Ruiz, Asociacion de reumatologos de Cruces, 2,Grünenthal, 5,Grünenthal, 8,Menarini, 5,Menarini, 8; S. Chinchilla, None.


Abstract Number: 2069

Gout Is More Frequent in Sickle Cell Disease Than the General Population

Richard Akintayo1, Olufemi Adelowo2, Adindu Chijioke1, Timothy Olanrewaju1, Kehinde Olufemi-Aworinde3 and Foluke Akintayo4, 1Internal Medicine, University of Ilorin Teaching Hospital, Ilorin, Nigeria, 2Arthrimed Specialist Clinic:The Arthritis Centre, Lagos, Nigeria, 3Haematology, Bowen University Teaching Hospital, Ogbomosho, Nigeria, 4Family Medicine, Ladoke Akintola University of Technology Teaching Hospital, Ogbomosho, Nigeria

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Metabolic and Crystal Arthropathies Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Despite the well known risk of hyperuricaemia in Sickle Cell Disease (SCD), it has not been determined if these patients are more prone to gout than the general populace. We studied the frequencies of gout between patients with SCD and controls with haemoglobin AA genotype and determined the factors associated with gout in SCD.

Methods: A prospective study of 104 patients with haemoglobin SS or SC and 104 age and sex-matched control participants with haemoglobin AA was conducted at the University of Ilorin Teaching Hospital, Nigeria. Clinical and demographic information were obtained from each participant and 10 ml of venous blood was taken for determination of haemoglobin genotype, serum uric acid and creatinine. Joint aspiration was done in all individuals presenting with articular pain and swelling. This sample was examined by polarized microscopy for monosodium urate crystals.

Results: The mean age of the patients was 27.4±8.3 years. Eight (7.7%) of the patients had genotype SC while the remaining 96 (92.3%) had SS. Hyperuricaemia was found in 28 (26.9%) and 2 (1.9%) individuals with SCD and controls respectively (p=0.001). Six (5.8%) cases of gout were found among the SCD patients and none among the controls (p=0.029). None of the gouty individuals had ever been diagnosed with gout before and they all had serum uric acid in the hyperuricaemic range. Four (66.7%) of them were males giving a male-female ratio of 2:1. The pattern of articular involvement was monoarticular in 2 (33.3%), oligoarticular in 3 (50%) and polyarticular in 1 (16.7%). The knee was the most frequently affected joint seen in 4 patients. Five (66.7%) individuals reported having painful and swollen joints on more than two occasions in the past while only one (16.7%) reported a single previous episode. One (16.7%) patient had subcutaneous tophi. Factors associated with gout in SCD were age, hyperuricaemia, more than two SCD crises in the past year and more than two hospital admissions in the past year (p 0.05 in each case).

Conclusion: Gout is more frequent in SCD than in individuals with HbAA genotype and many episodes of gouty attacks may have been mistaken for vaso-occlusive crises thereby delaying correct diagnosis and leading to mounting morbidities.

Characteristics of the patients with gout
### Patients with gout among patients with SCD

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Patients with gout N=6 (%)</th>
<th>Patients without gout N=98 (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SS</td>
<td>5 (83.3)</td>
<td>91 (92.8)</td>
<td>0.389</td>
</tr>
<tr>
<td>SC</td>
<td>1 (16.7)</td>
<td>7 (7.1)</td>
<td></td>
</tr>
</tbody>
</table>

### Age

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Patients with gout</th>
<th>Patients without gout</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-27</td>
<td>0 (0.0)</td>
<td>59 (60.2)</td>
<td>0.001</td>
</tr>
<tr>
<td>28-37</td>
<td>2 (33.3)</td>
<td>32 (32.7)</td>
<td></td>
</tr>
<tr>
<td>38-47</td>
<td>3 (50.0)</td>
<td>6 (6.1)</td>
<td></td>
</tr>
<tr>
<td>48-57</td>
<td>1 (16.7)</td>
<td>1 (1.0)</td>
<td></td>
</tr>
</tbody>
</table>

### Sex

<table>
<thead>
<tr>
<th>Sex</th>
<th>Patients with gout N=6 (%)</th>
<th>Patients without gout N=98 (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>4 (66.7)</td>
<td>52 (53.1)</td>
<td>0.684</td>
</tr>
</tbody>
</table>

### BMI

<table>
<thead>
<tr>
<th>BMI Category</th>
<th>Patients with gout</th>
<th>Patients without gout</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>1 (16.7)</td>
<td>28 (28.6)</td>
<td>0.753</td>
</tr>
<tr>
<td>Normal weight</td>
<td>5 (83.3)</td>
<td>68 (69.4)</td>
<td></td>
</tr>
<tr>
<td>Overweight</td>
<td>0 (0.0)</td>
<td>2 (2.0)</td>
<td></td>
</tr>
</tbody>
</table>

### Hyperuricaemia

<table>
<thead>
<tr>
<th>Patients with gout N=6 (%)</th>
<th>Patients without gout N=98 (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 (100.0)</td>
<td>22 (22.5)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

### Seafood consumption

<table>
<thead>
<tr>
<th>Patients with gout N=6 (%)</th>
<th>Patients without gout N=98 (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 (100.0)</td>
<td>92 (93.9)</td>
<td>0.532</td>
</tr>
</tbody>
</table>

### Animal innards consumption

<table>
<thead>
<tr>
<th>Patients with gout N=6 (%)</th>
<th>Patients without gout N=98 (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 (100.0)</td>
<td>91 (92.9)</td>
<td>0.498</td>
</tr>
</tbody>
</table>

### Sweetened beverage consumption

<table>
<thead>
<tr>
<th>Patients with gout N=6 (%)</th>
<th>Patients without gout N=98 (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 (66.7)</td>
<td>89 (90.8)</td>
<td>0.121</td>
</tr>
</tbody>
</table>

### Alcohol Consumption

<table>
<thead>
<tr>
<th>Patients with gout N=6 (%)</th>
<th>Patients without gout N=98 (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (0.0)</td>
<td>5 (5.1)</td>
<td>0.738</td>
</tr>
</tbody>
</table>

### Smoking

<table>
<thead>
<tr>
<th>Patients with gout N=6 (%)</th>
<th>Patients without gout N=98 (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (0.0)</td>
<td>2 (2.0)</td>
<td>0.724</td>
</tr>
</tbody>
</table>

### Frequency of SCD Crises

<table>
<thead>
<tr>
<th>Patients with gout N=6 (%)</th>
<th>Patients without gout N=98 (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 (83.3)</td>
<td>18 (18.7)</td>
<td>0.002</td>
</tr>
<tr>
<td>1 (16.7)</td>
<td>80 (81.6)</td>
<td></td>
</tr>
</tbody>
</table>

### Frequency of Admissions

<table>
<thead>
<tr>
<th>Patients with gout N=6 (%)</th>
<th>Patients without gout N=98 (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 (83.3)</td>
<td>18 (18.7)</td>
<td>0.002</td>
</tr>
<tr>
<td>1 (16.7)</td>
<td>80 (81.6)</td>
<td></td>
</tr>
</tbody>
</table>

### Routine folic acid use

<table>
<thead>
<tr>
<th>Patients with gout N=6 (%)</th>
<th>Patients without gout N=98 (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 (6.1)</td>
<td>93 (93.9)</td>
<td>0.738</td>
</tr>
</tbody>
</table>

SUA=Serum Uric Acid; BMI=Body Mass Index; Lt.=Left; Rt.=Right; MTP1=1st metatarsophalangeal joints
Evidence-Based Development of Criteria for Complete Response in Patients with Chronic Refractory Gout

Naomi Schlesinger¹, Puja Khanna², Anthony Yeo³ and Peter E. Lipsky⁴, ¹Medicine, Rutgers-Robert Wood Johnson Medical School, New Brunswick, NJ, ²Rheumatology, University of Michigan, Ann Arbor, MI, ³Horizon Pharma, Lake Forest, IL, ⁴AMPEL BioSolutions, LLC, Charlottesville, VA

First publication: September 18, 2017

Session Date: Tuesday, November 7, 2017
Session Title: Metabolic and Crystal Arthropathies Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: A Delphi exercise reached consensus on a definition for gout remission that included serum uric acid (sUA) <6 mg/dL, no flares, resolution of all tophi, limited pain, and low disease impact by patient global assessment (PGA). The frequency with which these criteria are achieved in response to treatment has not been assessed. Our study evaluated these criteria using results from patients with chronic refractory gout who received pegloticase (8 mg every 2 weeks), a mammalian recombinant uricase conjugated to polyethylene glycol approved for treatment of adults with chronic gout refractory to oral urate lowering therapy.

Methods: The results from two identical randomized controlled trials (RCTs) of pegloticase were analyzed. Patients received 6 months of treatment with 8 mg of pegloticase or placebo, and responders were defined as those with persistent urate lowering. Overall, 42% (n=36) of the patients who received pegloticase 8 mg every 2 weeks were responders in the RCTs and 34 continued in the open-label extension. Initially, individual patient data was reviewed to establish the frequency with which pegloticase responders met the proposed remission criteria. Subsequently, using mixed modelling, we determined the best criteria for a “complete response” (CR) using a repeated-measures, mixed-effects model to relate the time when a patient's response was noted, assessed by patient global assessment (PGA), SF-36 bodily pain scores, visual analog scale pain levels, numbers of tender and swollen joints, number of flares, and the degree of tophus resolution controlling for repeated measures. Variables were eliminated by dropping the least statistically significant item. All components of the final model were statistically significant.

Results: Of 34 pegloticase responders, 29 (85.3%) met the published criteria for remission. However, comparison of various components of the composite criteria indicated weak or absent correlations. Mixed effects modelling defined the following criteria for a CR: sUA <6 mg/dL, resolution of all measured tophi, PGA ≤1, swollen joint count ≤1, and tender joint count ≤1. The mean time from the beginning of the RCT to reach CR criteria was 11.5 months. All patients who achieved a CR maintained it until the end of follow-up. The mean duration of CR was 507.4 days and there was a significant inverse relationship between the time to CR and the duration of the response (P=0.0008).

Conclusion: These results defined criteria for a CR in individuals with chronic refractory gout treated with pegloticase, suggesting that, the majority of patients who persistently lower sUA, reach criteria for CR, and do so within 1 year from the initiation of therapy. CR persisted for the length of treatment.

This composite CR index can serve as an evidence-based target goal for a “Treat to Target” strategy in clinical practice and in future clinical trials.

A Novel Selective URAT1 Inhibitor, Tei-a, with Potent Uricosuric Property

Johji Nomura¹, Yoshimasa Takahashi², Kumiko Aoki², Naoki Hase² and Tsunefumi Kobayashi², ¹Teijin Institute for Bio-medical Research, TEIJIN PHARMA LIMITED, Tokyo, Japan, ²TEIJIN PHARMA LIMITED, Tokyo, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Metabolic and Crystal Arthropathies Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Hyperuricemia, abnormally elevated level of serum uric acid, is associated with gout as well as other diseases including metabolic syndrome, hypertension, diabetic kidney disease. In particular, hyperuricemia has causative link with gout, a metabolic disease characterized by deposition of sodium urate crystals in the joints and recurrent attacks of painful inflammatory arthritis. The therapeutic options for hyperuricemia/gout include xanthine oxidase inhibitors and uricosurics. Benzbromarone, probenecid and lesinurad are clinically available uricosurics, which increase the renal urate excretion by inhibiting URAT1, the transporter responsible for urate reabsorption. However, they are not widely used due to safety concern. In this study, we describe a novel URAT1 inhibitor, TEI-A, with a potent and highly selective properties.

Methods: Human URAT1overexpressing cells were treated with TEI-A, benzbromarone or lesinurad, and the uptake amounts of the specific substrates were measured to determine the inhibitory activities against the transporters. To determine the selectivity of TEI-A to URAT1, OAT1, OAT3 or OAT4-overexpressing cells, or ABCG2-overexpressing vesicles were treated with TEI-A, and the uptake amounts of the specific substrates were measured. Male tufted capuchin monkeys were administrated once orally with TEI-A (0.1-10 mg/kg), benzbromarone (3-30 mg/kg) and lesinurad (30 and 100 mg/kg). The fractional excretion of uric acid and serum uric acid level up to 24 hours after dosing were measured to determine uricosuric effects.

Results: In in vitro assays, TEI-A showed concentration-dependent inhibition of human URAT1-specific uptake of uric acid with IC₅₀ value of 14.3 ± 0.5 nmol/L. Inhibitory activity of TEI-A against URAT1 was 18-fold and 1600-fold stronger than those of benzbromarone and lesinurad, respectively. In addition, TEI-A showed highly selective to URAT1 over OAT1, 3, 4 and ABCG2. In tufted capuchin monkeys, TEI-A dose-dependently increased fractional excretion of uric acid up to 24 hours after dosing. Uricosuric effects of TEI-A were significantly stronger than those of benzbromarone and lesinurad. TEI-A also lowered serum uric acid level in tufted capuchin monkeys.

Conclusion: TEI-A is a potent and highly selective URAT1 inhibitor, and has greater uricosuric effects than benzbromarone and lesinurad in monkeys. TEI-A is a promising candidate for the treatment of patients with hyperuricemia and gout.

Disclosure: J. Nomura, TEIJIN PHARMA LIMITED, 3; Y. Takahashi, TEIJIN PHARMA LIMITED, 3; K. Aoki, TEIJIN PHARMA LIMITED, 3; N. Hase, TEIJIN PHARMA LIMITED, 3; T. Kobayashi, TEIJIN PHARMA LIMITED, 3.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/a-novel-selective-urat1-inhibitor-tei-a-with-potent-uricosuric-property

A Pharmacokinetic and Pharmacodynamic Evaluation of URC102, a Potent and Selective Inhibitor of URAT1, after Single and Multiple Oral Administrations in Healthy Volunteers

Disclosure: J. Nomura, TEIJIN PHARMA LIMITED, 3; Y. Takahashi, TEIJIN PHARMA LIMITED, 3; K. Aoki, TEIJIN PHARMA LIMITED, 3; N. Hase, TEIJIN PHARMA LIMITED, 3; T. Kobayashi, TEIJIN PHARMA LIMITED, 3.


Abstract Number: 2072

A Pharmacokinetic and Pharmacodynamic Evaluation of URC102, a Potent and Selective Inhibitor of URAT1, after Single and Multiple Oral Administrations in Healthy Volunteers
Background/Purpose:
URC102, a novel and potent inhibitor of human uric acid transporter 1 (hURAT1), is currently under clinical development to treat patients with gout. In preclinical studies, URC102 inhibited URAT1 more selectively leading to more potent uricosuric and hypouricemic effects than conventional uricosuric agents such as benzbromarone. A phase I study was performed to evaluate the pharmacokinetics (PK), pharmacodynamics (PD), safety and tolerability profiles of URC102 after single and multiple oral administrations.

Methods:
A randomized, double-blind, placebo-controlled, single and multiple dose-escalation study was conducted in healthy male volunteers. Thirty-one healthy Koreans randomly received a single oral dose of placebo or URC102 1, 3, 10 or 30 mg and twenty-four Caucasian received 1, 3 and 10 mg in the fasting state. Furthermore, 44 healthy Koreans received repeated doses of placebo or URC102 1, 3, 5, 7 or 10 mg for 7 consecutive days. Blood and urine samples were collected up to 168 hours post-dose in the single ascending dose study, and up to 312 (blood) and 168 (urine) hours post-dose in the multiple dose study. Serum uric acid, urinary uric acid output, and fractional excretion of uric acid were the PD variables. Safety and tolerability were also evaluated based on monitoring of physical conditions, vital signs, electrocardiograms, and clinical laboratory tests.

Results:
The maximum plasma concentration (C max) and the area under the plasma concentration-time curve up to the last measurable time (AUC last) increased as the dose increased in both single (1 to 30 mg) and multiple ascending dose (1 to 10 mg) studies. URC102 was rapidly absorbed after single and repeated doses (time to reach C max or T max less than 2 and 1 to 6 hours, respectively). Blood or urine PK characteristics of URC102 were not significantly different between Koreans and Caucasians. The serum uric acid levels were rapidly reduced after single and repeated administrations of URC102. The maximum mean decrease in serum uric acid from baseline was more than 70% after repeated oral doses of URC102 at 5 to 10 mg. No serious AE was reported, and all AEs were resolved.

Conclusion:
Orally administered URC102 was well tolerated over the dose range of 1 to 10 mg after single and multiple once-daily administrations for 7 days, and showed a linear PK profile in the ranges of 1 to 30 mg (single dose) and 1 to 10 mg (multiple doses). URC102 was effective in lowering serum uric acid levels.

Disclosure: H. A. Lee, None; S. I. Park, None; S. Yoon, None; M. Onohara, Chugai Pharmaceutical Co., Ltd., 3; J. Choi, JW Pharmaceutical Corporation, 3; K. S. Yu, None; H. Lee, None.
Background/Purpose: Gout is the most common form of arthritis worldwide. Hyperuricemia is a crucial risk factor resulting in accumulation of uric acid (s-UA) crystals in tissues and in a subset development of clinical gout. The relative importance of other risk factors, some of which are associated with s-UA levels, is slightly more controversial. The aim of this preliminary analysis, were to identify such predictors for clinical gout in a population survey, the Malmö Preventive Project (MPP)- a large-scale screening and case-finding program for cardiovascular risk factors, alcohol abuse and breast cancer in the city of Malmö, Sweden.

Methods: Overall, 33,346 individuals (67% male, mean age 45.7 years at inclusion, mean follow up 28.2 years) participated. The study population was screened between 1974 and 1992. A baseline health screening included: 1. Questionnaire with 260 questions (socioeconomic factors, alcohol consumption, smoking, physical activity, dietary habits, history of gout and other co-morbidities) 2. Physical examination (including weight, height, BMI, and blood pressure) and 3. Laboratory tests (serum urate, fasting glucose, s-creatinine). Endpoint was defined as the date of first gout diagnosis, death, moving from the area, or December 31st 2014. In order to identify all gout diagnoses (using ICD-codes) given at visits to physicians in primary care, in specialized in-patient (from 1974) and out-patient specialized care (from 2001); MPP cohort was linked to regional health care register and to the national patient register, respectively. Individuals with a history of gout before the inclusion in MPP (n=11) were excluded from the analysis. Possible baseline predictors of developing gout were analysed using Cox-regression model.

Results: Of 33,346 individuals participating in MPP project, 1275 (3.8%) were diagnosed with clinically gout over 30 years follow up. Subjects with higher s-UA at baseline (age- and sex-adjusted) had a significantly increased risk of developing gout. In addition, results from the multivariate analysis identified higher age, male sex, higher baseline BMI, systolic blood pressure, current smoking for ≥ 10 years and daily alcohol drinking as independent predictors of incident gout (Table).

Conclusion: In addition to hyperuricemia, increased age, male sex, hypertriglyceridemia, concomitant hypertension, smoking and daily drinking were independent predictors for development of gout in this large cohort of middle-aged individuals.

Table: Baseline predictors of development of gout over 30 years

<table>
<thead>
<tr>
<th></th>
<th>Mean (SD)</th>
<th>HR (95% CI) (age/sex adjusted)</th>
<th>HR (95% CI)* (multivariate analysis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>45.7 (7.4)</td>
<td>1.5 (1.4-1.6)</td>
<td>1.4 (1.3-1.6)</td>
</tr>
<tr>
<td>s-UA (µmol/L)</td>
<td>300.8 (70.1)</td>
<td>2.0 (1.9-2.0)</td>
<td>1.8 (1.8-1.9)</td>
</tr>
<tr>
<td>s-creatinine (µmol/L)</td>
<td>87.6 (18.7)</td>
<td>1.1 (1.0-1.1)</td>
<td>1.0 (1.0-1.1)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.6 (3.6)</td>
<td>1.5 (1.4-1.6)</td>
<td>1.3 (1.2-1.3)</td>
</tr>
<tr>
<td>s-glucose (mmol/L)</td>
<td>4.97 (1.0)</td>
<td>1.1 (1.1-1.2)</td>
<td>0.8 (0.7-0.9)</td>
</tr>
<tr>
<td>s-cholesterol (mmol/L)</td>
<td>5.7 (1.1)</td>
<td>1.2 (1.1-1.2)</td>
<td>1.1 (1.0-1.1)</td>
</tr>
<tr>
<td>s-triglycerides(mmol/L)</td>
<td>1.4 (0.9)</td>
<td>1.1 (1.1-1.2)</td>
<td>1.1 (1.0-1.1)</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>129.8 (17.1)</td>
<td>1.3 (1.3-1.4)</td>
<td>1.2 (1.1-1.2)</td>
</tr>
<tr>
<td>Sex (% male)</td>
<td>67.3%</td>
<td>1.7 (1.4-1.9)</td>
<td>1.4 (1.2-1.7)</td>
</tr>
<tr>
<td>Daily alcohol drinking (yes/no)</td>
<td>0.7%</td>
<td>1.8 (1.1-3.1)</td>
<td>1.4 (1.1-1.9)</td>
</tr>
<tr>
<td>Smoking for &gt;10 years (yes/no)</td>
<td>53.1%</td>
<td>1.3 (1.1-1.4)</td>
<td>1.3 (1.2-1.5)</td>
</tr>
<tr>
<td>Treatment for hypertension (yes/no)</td>
<td>2.2%</td>
<td>1.9 (1.4-2.6)</td>
<td>1.1 (0.9-1.4)</td>
</tr>
<tr>
<td>Treatment with diuretics (yes/no)</td>
<td>0.6%</td>
<td>1.4 (0.8-2.7)</td>
<td>0.8 (0.6-1.2)</td>
</tr>
</tbody>
</table>
HR is calculated per 1 SD or for dichotomous covariates (yes vs. no).


**Abstract Number: 2074**

**A Series of Double-Blind, Placebo-Controlled, Randomized, Multicenter, Phase 2 Studies to Evaluate the Efficacy, Safety, and Dose-Response Relationship of Orally Administered URC102, a Novel URAT1 Inhibitor, in Korean Patients with Gout**

**Jae-Bum Jun**1, Howard Lee2, Chang-Hee Suh3, Chang Keun Lee4, Dong Wook Kim5, Jung-Yoon Choe6, Sang-Heon Lee7, Sang-Hyon Kim8, Seung-Jae Hong9, So-Young Bang10, Sung Jae Choi11, Yong-Beom Park12, Makoto Onohara13, Jeongeun Choi14, Jung Soo Song15 and Won Park16. 1Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), 2Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Hospital, Seoul, Korea, Republic of (South), 3Ajou University School of Medicine, Suwon, Korea, Republic of (South), 4Division of Rheumatology, Department of Internal Medicine, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea, Republic of (South), 5Division of Rheumatology, Department of Internal Medicine, Inje University College of Medicine, Busan, Korea, Republic of (South), 6Division of Rheumatology, Department of Internal Medicine, Catholic University of Daegu School of Medicine, Daegu, Korea, Republic of (South), 7Division of Rheumatology, Department of Internal Medicine, Konkuk University School of Medicine, Seoul, Korea, Republic of (South), 8Division of Rheumatology, Department of Internal Medicine, Keimyung University Dongsan Medical Center, Keimyung University School of Medicine, Daegu, Republic of Korea, Daegu, Korea, Republic of (South), 9Department of Rheumatology, Kyung Hee University Medical Center, Seoul, Korea, Republic of (South), 10Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), 11Internal Medicine, Korea University Medical Center, Seoul, Korea, Republic of (South), 12Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea, Republic of (South), 13Science and Strategy, Translational Clinical Research, Chugai Pharmaceutical Co., Ltd, Tokyo, Japan, 14JW Pharmaceutical Corporation, Seoul, Korea, Republic of (South), 15Rheumatology, Chung-Ang University College of Medicine, Seoul, Korea, Republic of (South), 16Medicine/Rheumatology, Inha University Hospital, Incheon, Korea, Republic of (South)

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** Metabolic and Crystal Arthropathies Poster II  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

URC102 is a novel URAT1 inhibitor under clinical development for the treatment of hyperuricemia with gout. A series of double-blind, placebo-controlled, randomized, multicenter, phase 2 studies investigated the efficacy, safety, and dose-response relationship of URC102 in patients with gout (NCT02290210 and NCT02557126).

**Methods:**

Korean male patients aged ≥20 and <70 years with gout and serum uric acid (sUA) levels ≥7.0 mg/dL and ≤10.0 mg/dL at screening were randomized to orally (QD) receive placebo or URC102 at 0.25 mg, 0.5 mg, 1 mg, and 2 mg (first study with low-dose URC102) and placebo or URC102 at 3 mg, 5 mg, 7 mg, and 10 mg (second study with high-dose URC102) for 14 days. Efficacy was evaluated by analyzing the trend of sUA reduction, defined as percentage changes of sUA for 2 weeks with reference to baseline, after administration of URC102. Safety was assessed with adverse events (AEs), physical examinations, and laboratory findings throughout the studies.

**Results:**

Sixty-four (first study) and 76 (second study) patients with gout were randomized. The mean percentage changes (± standard deviation) of sUA on Day 15 was -3.96 (±15.77)%, -3.28 (±10.39)%, -10.63 (±10.09)%, -13.15 (±20.30)%, and -29.52 (±8.45)% in the placebo,
URC102 decreased sUA levels in a dose-dependent manner in Korean patients with gout. All doses of orally administered URC102 for 14 days were well tolerated. Further long-term clinical studies in larger populations are warranted to evaluate the effectiveness of URC102, which could be a new effective treatment option as a urate-lowering therapy.

Conclusion:

Disclosure: J. B. Jun, None; H. Lee, None; C. H. Suh, None; C. K. Lee, None; D. W. Kim, None; J. Y. Choe, None; S. H. Lee, None; S. H. Kim, None; S. J. Hong, None; S. Y. Bang, None; S. J. Choi, None; Y. B. Park, None; M. Onohara, Chugai Pharmaceutical Co., Ltd., 3; J. Choi, JW Pharmaceutical Corporation, 3; J. S. Song, None; W. Park, None.

Abstract Number: 2075

The Effect of Uric Acid Lowering Treatment on the Microbiome in Gout Patients

Hye Won Kim1, Eun-Jeong Yoon2, Seok Hoon Jeong2 and Min-Chan Park1, 1Division of Rheumatology, Department of Internal Medicine, Yonsei University College of Medicine,Gangnam Severance Hospital, Seoul, Korea, Republic of (South), 2Department of Laboratory Medicine, Severance Hospital, Research Institute of Bacterial Resistance, Yonsei University College of Medicine, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Metabolic and Crystal Arthropathies Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Accumulating evidence indicates that gut microbiota interact with gout but it is still unknown how the uric acid lowering treatment (ULT) affects to the gut microbiome. This study was performed to investigate the effect of ULT on gut microbiome composition.

Methods: Stool samples from asymptomatic hyperuricemic patients (asHU, n = 3) and three groups of gout patients, i.e. a group of acute gout patients before ULT (noULT, n = 14), a group of gout patients after the 30-day-ULT (30ULT, n = 9) and a group of chronic gout patients having the > 6-month-ULT (cULT, n = 18), were collected and analyzed using 16S rRNA gene-based pyrosequencing. The composition of gut microbiota and the abundant phylogenetic types were evaluated.

Results: Firmicutes/Bacteroidetes ratio in the cULT group was higher compared to those in noULT and 30ULT groups. We identified four robust enterotypes, which was affected by ULT. For the 30ULT group, proportion of patients with Bacteroidaceae dominant gut type were reduced and we observed enhanced prevalence of Ruminococcaceae-Prevotellaceae dominant gut type than in the noULT group. Ruminococcaceae-Prevotellaceae dominant gut type in the cULT group was not enriched as in the 30ULT group. In any group of gout patients, notable bacterial families presented significantly differed proportions: Veillonellaceae, Pedospheara_f, GQ396871_f, Polyangiaceae, EU335275_f, Natronincola_f, FQ032818_f,Fucaceae in family level and Bradyrhizobium, Natronincola_f uc_s, Lactobacillus casei group and DQ905770_s in species level.

Conclusion: This study suggest that fecal microbiome may change after ULT in gout patients. Further research is warranted to uncover the potential links between the specific microbes and uric acid processing in human intestine.
Comparative Effectiveness of Allopurinol Versus Febuxostat in Preventing Incident Dementia in the Elderly

Jasvinder A. Singh\(^1\) and John Cleveland\(^2\), \(^1\)Rheumatology, University of Alabama at Birmingham, Birmingham, AL, \(^2\)Rheumatology, University of Alabama at Birmingham (UAB), Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Metabolic and Crystal Arthropathies Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Previous studies of hyperuricemia and dementia have provided contradictory findings, ranging from reduced to increased risk. Our objective was to assess the comparative effectiveness of allopurinol vs. febuxostat for preventing incident dementia in elderly.

Methods: In a retrospective cohort study using Medicare claims data, we included patients newly treated with allopurinol or febuxostat (baseline period of 365 days without either medication). We used 1:5 propensity-matched Cox regression analyses to compare the hazard ratio (HR) of incident dementia with allopurinol vs. febuxostat, assessing use, dose and duration.

Results: We found 42,704 new allopurinol or febuxostat treatment episodes in 35,030 patients, of which 2,591 ended in incident dementia. Crude rates of incident dementia per 100,000 person-days were lower with higher daily dose: allopurinol <200, 200-299 and \(\geq 300\) mg/day with 12, 9 and 8; and febuxostat 40 mg and 80 mg/day with 9 and 8, respectively. In propensity-matched analyses, compared to allopurinol <200 mg/day, higher allopurinol doses (200-299 mg/day and \(\geq 300\) mg/day) and febuxostat 40 mg/day dose were associated with lower HR of dementia, 0.80 (95% CI, 0.64, 0.98), 0.59 (95% CI, 0.50, 0.71) and 0.64 (95% CI, 0.47, 0.86), respectively;
febuxostat 80 mg/day was not associated, 0.66 (95% CI, 0.36, 1.19). Compared to allopurinol use for 1-180 days, longer febuxostat or allopurinol use durations were not significantly associated with differences in HR of dementia, ranging 0.76 to 1.14.

**Conclusion:** Higher allopurinol dose and febuxostat were more effective than low-dose allopurinol in preventing dementia in elderly patients. Future studies need to examine the mechanism of this benefit of febuxostat and higher-dose allopurinol.

**Keywords:** Allopurinol; Febuxostat; Dementia; Elderly; Medicare

Comparative Effectiveness of Allopurinol versus Febuxostat in preventing Incident Dementia in the Elderly

**Disclosure:** J. A. Singh, Takeda and Savient, 2,Savient, Takeda, Regeneron, Merz, Iroko, Bioiberica, Crealta/ Horizon and Allergan pharmaceuticals, WebMD, UBM LLC and the American College of Rheumatology., 5,JAS serves as the principal investigator for an investigator-initiated study funded by Horizon pharmaceuticals through a grant to DINORA, Inc., a 501 (c)(3) entity., 9,JAS is a member of the executive of OMERACT, an organization that develops outcome measures in rheumatology and receives arms-length funding from 36 companies., 9,JAS is the editor and the Director of the UAB Cochrane Musculoskeletal Group Satellite Center on Network Meta-analysis., 9,Jas is a member of the American College of Rheumatology's (ACR) Annual Meeting Planning Committee (AMPC); Chair of the ACR Meet-the-Professor, Workshop and Study Group Subcommittee., 9,a member of the Veterans Affairs Rheumatology Field Advisory Committee, 9; J. Cleveland, None.


**Abstract Number:** 2077

**Statin Use and Mortality in Gout: A General Population-Based Cohort Study**

Sarah Keller\(^1\), Sharan K. Rai\(^2\), Na Lu\(^1\), Amar Oza\(^3\), Yuqing Zhang\(^4\) and Hyon K. Choi\(^2\), \(^1\)Rheumatology, Allergy and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, \(^2\)Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, \(^3\)Allergy, Immunology, and Rheumatology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, \(^4\)School Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Metabolic and Crystal Arthropathies Poster II

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

Background/Purpose: Although the cardinal feature of gout is inflammatory arthritis, it is also a metabolic condition closely associated with an elevated uric acid burden and insulin resistance. Thus, gout and hyperuricemia are associated with major cardiovascular (CV)-metabolic-renal comorbidities and their sequelae. Statins confer both CV and survival benefits in both individuals with and without CVD; however, the impact of statins in gout remains unknown. We examined the potential survival benefit of statin use among gout patients in a general population context.

**Methods:** We performed an incident user cohort study with time-stratified propensity score matching using an electronic medical record database representative of the UK general population. The study population included individuals aged ≥20 years who had a diagnosis of gout between January 1999 and December 2014. To account for potential confounders, we compared propensity score-matched cohorts of statin initiators and non-initiators within 1-year cohort accrual blocks. The variables used to create the propensity score model included disease duration, body mass index, lifestyle factors, duration of gout, CV comorbidities, and medication use, including anti-gout medications. We estimated the mortality hazard ratio of statin initiation using Cox proportional hazard models and the mortality rate difference using an additive hazard model.

**Results:** After propensity score matching, the baseline characteristics were well-matched between the two groups. Among 17,018 statin initiators, 2,503 deaths occurred during the follow-up period (mean=5.0 years), resulting in an all-cause mortality rate of 23.97/1000 person-years (PY). The corresponding number of deaths and all-cause mortality rate among the 17,018 matched comparators during the follow-up period (mean=4.6 years) were 2,025 and 31.67/1000 PY, respectively. As such, all-cause mortality during the follow-up period was lower among the statin initiators than among the comparators (see Figure). Compared with non-initiators, statin initiators experienced a 16% lower relative rate of all-cause mortality (HR=0.84, 95% CI 0.79 to 0.89) and a rate difference of 7.7 (95% CI 6.1 to 9.3) fewer deaths per 1000 PY. The protective association between statin initiation and all-cause mortality persisted across subgroups,
including age (age <60, HR=0.85; age 60-70, HR=0.81; age >70, HR=0.85), sex (males, HR=0.82; women, HR=0.88), and socioeconomic status (low, HR=0.82; high, HR=0.86).

**Conclusion:** In this general population-based cohort study, we found that statin initiation is associated with a lower risk of mortality among gout patients. The magnitude of this inverse association (i.e., a 16% reduction) appears at least comparable to or greater than that found in the general population where statins are used for primary prevention.

**Disclosure:** S. Keller, None; S. K. Rai, None; N. Lu, None; A. Oza, None; Y. Zhang, None; H. K. Choi, Selecta, Horizon, 5, AstraZeneca, 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/statin-use-and-mortality-in-gout-a-general-population-based-cohort-study

Abstract Number: 2078

**Hypersensitivity Reactions with Allopurinol and Febuxostat in Adults 65 Years or Older: A Study Using the Medicare Claims Data**

**Jasvinder A. Singh**¹ and John Cleveland², ¹Rheumatology, University of Alabama at Birmingham, Birmingham, AL, ²Rheumatology, University of Alabama at Birmingham (UAB), Birmingham, AL

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Metabolic and Crystal Arthropathies Poster II

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Clinicians using allopurinol are always concerned about the risk of rare hypersensitivity reaction. Allopurinol and febuxostat are the two most common urate-lowering agents used for the treatment of hyperuricemia in gout. Population-based studies to estimate the risk of hypersensitivity reactions with allopurinol and febuxostat have not been done. Our objective was to describe the risk of hypersensitivity reactions with allopurinol and febuxostat.

**Methods:** We used the 5% Medicare Beneficiary sample (≥65 years) from 2006-2012 to identify people with a new filled prescription for allopurinol or febuxostat or colchicine, with a baseline period of 365 days without either medication. We used Cox regression analyses to compare the hazard ratio (HR) of incident hypersensitivity reactions with allopurinol or febuxostat vs. colchicine use.

**Results:** Of the 68,230 new medication exposure episodes, 363 ended in a hypersensitivity reaction. Crude incidence rates of hypersensitivity reactions were as follows: allopurinol, 23.7; febuxostat, 30.7; and colchicine, 25.6 per 1,000 person-years. Incidence of hypersensitivity reactions was highest in the first 30 days of exposure to allopurinol or febuxostat, with a progressive reduction later. In multivariable-adjusted analyses, compared to colchicine, allopurinol, febuxostat and febuxostat + colchicine combination were associated with significantly higher hazard ratios of hypersensitivity reactions, 1.32 (95% CI, 1.10, 1.60) and 1.54 (95% CI, 1.12, 2.12)
and 2.17 (95% CI, 1.18, 3.99), respectively. In multivariable-adjusted analyses limited to allopurinol users, compared to allopurinol start dose of <200 mg/day, allopurinol start dose of ≥300 mg/day and diabetes were associated with significantly higher hazard of hypersensitivity reactions, 1.27 (95% CI, 1.12, 1.44), and 1.21 (95% CI, 1.00, 1.45).

**Conclusion:** In people 65 years or older, allopurinol and febuxostat increased the risk of hypersensitivity reactions. In allopurinol users, allopurinol start dose and diabetes increased this risk. Future studies need to examine as to why a higher start dose increases hypersensitivity risk.

**Disclosure:** J. A. Singh, Takeda and Savient, 2; Savient, Takeda, Regeneron, Merz, Iroko, Bioiberica, Crealta/ Horizon and Allergan pharmaceuticals, WebMD, UBM LLC and the American College of Rheumatology., 5, JAS serves as the principal investigator for an investigator-initiated study funded by Horizon pharmaceuticals through a grant to DINORA, Inc., a 501 (c)(3) entity., 9, JAS is a member of the executive of OMERACT, an organization that develops outcome measures in rheumatology and receives arms-length funding from 36 companies., 9, JAS is the editor and the Director of the UAB Cochrane Musculoskeletal Group Satellite Center on Network Meta-analysis., 9, JAS is a member of the American College of Rheumatology's (ACR) Annual Meeting Planning Committee (AMPC); Chair of the ACR Meet-the-Professor, Workshop and Study Group Subcommittee., 9, a member of the Veterans Affairs Rheumatology Field Advisory Committee, 9; J. Cleveland, None.


**Abstract Number:** 2079

**Rotator Cuff Calcific Tendinopathy: Chondrocyte-like Cells Surrounding Calcific Deposits Express TNAP and ENPP1, Two Key Enzymes of the Mineralization Process.**

*Christelle Darrieutort-Laffite*¹,², *Aurélie Najm*¹,³, *Thomas Garraud*¹,², *Pierre Layrolle*², *Frédéric Blanchard*³ and *Benoit Le Goff*¹,²,

¹Rheumatology, Nantes University Hospital, Nantes, France, ²INSERM U1238, PHY-OS Laboratory, Nantes, France, ³INSERM U1238 University of medicine, PHY-OS Laboratory, Nantes, France

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** Metabolic and Crystal Arthropathies Poster II  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**  
Calcific tendinopathy represents 10 to 42% of chronic painful shoulders. These calcium deposits are composed of carbonated apatite. Although the disease is frequent, its origin stays still largely unknown. Molecular and cellular mechanisms involved in this pathological mineralization process are not currently identified. The objective of the study was to analyze calcified tendon samples to understand the organization of the deposits and to characterize the cells potentially involved in their formation.

**Methods:**  
Samples were collected from cadaveric subjects. Ultrasound was first used to detect calcified tendons. Then, tendons were collected and fixed in formalin 4% during 48h. Samples were then decalcified in EDTA, dehydrated and embedded in paraffin. Some samples were not decalcified to allow a better characterization of the calcific deposits. Hematoxylin and eosin (HE), Safranin O/Fast Green (SO/FG) and Von Kossa (no decalcified samples) staining were performed. Immunohistochemistry using anti-Runx2, anti-Sox9, anti-Collagen II and X, anti-CD31 and CD68 has been performed to characterize the cells and tissue around the calcifications. We used also used anti-TNAP (Tissue Nonspecific Alkaline Phosphatase) and ENPP1 (Ectonucleotide Pyrophosphatase/Phosphodiesterase 1) antibodies. Indeed, these two enzymes are essential in the physiological mineralization: extracellular inorganic pyrophosphates are provided by ENPP1 then hydrolyzed by TNAP to promote mineralization.

**Results:**  
Six samples were collected (1 normal and 5 calcified). On HE staining, voluminous calcium deposits were encapsulated by a fibrocartilaginous tissue. In one sample, we observed an intra-tendinous osseous metaplasia. This fibrocartilaginous area presented a red
coloration (proteoglycan specific) on SO/FG staining but was collagen II negative whereas the fibrocartilage at the tendon attachment was strongly positive. Within this area, cells with round nuclei and pericellular lacunae and different from tenocytes were observed as previously described (Uhthoff, 1975). These cells expressed Runx2 and Sox9 suggesting a chondrocyte differentiation but only a small number of them expressed type X collagen, hypertrophic chondrocytes-specific marker. These cells also expressed ENPP1 and TNAP. Interestingly, extracellular TNAP deposits were also present at the periphery of the deposits. We identified vessels surrounding the deposits on 4 of the 5 calcified samples. Finally, no CD68 positive cells were detected around the deposits.

Conclusion:

Histological analyses of whole calcified tendon tissues showed a fibrocartilaginous area surrounding the calcium deposits. Chondrocyte-like cells present within this area expressed ENPP1 and TNAP suggesting their crucial role in the deposition of apatite crystals. An osseous metaplasia was seen in one sample but probably does not represent the main mineralization process involved in the disease. Further analyses are necessary to understand the origin of these cells and the regulatory factors involved in their differentiation.


Disclosure: C. Darrieutort-Laffite, None; A. Najm, None; T. Garraud, None; P. Layrolle, None; F. Blanchard, None; B. Le Goff, None.


Abstract Number: 2080

Serum Uric Acid and Incident Dementia: A Population Based Study

Lieke E.J.M. Scheepers¹, Mats Dehlin¹, Lennart TH Jacobsson¹, Lena Johansson² and Ingmar Skoog², ¹Department of Rheumatology and Inflammation Research, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, ²Department of Psychiatry and Neurochemistry, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Metabolic and Crystal Arthropathies Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Elevated serum uric acid (sUA) is an established risk factor for gout. Its role in the development of dementia is controversial, low levels of sUA has been suggested to increase the risk for dementia because of its reduction impairs antioxidants capacity, on the other hand, high levels of sUA are associated with increased cardiovascular risk which might increase the risk for vascular dementia (VaD). We therefore examined the possible association of sUA with the risk of Alzheimer’s disease (AD) and VaD in a population-based cohort of women.

Methods: Longitudinal analyses were conducted in the Prospective Population Study of Women in Gothenburg, Sweden. In 1968, 1462 women 38–60 years old randomly selected from the population census, were examined with a wide range of possible predictors for dementia. Re-examination occurred in 1974, 1980, 1992, 2000, 2005, 2009, and 2012 (with sUA being collected only in 1968 and 1992). Subjects with dementia or stroke before baseline were excluded (n=38). Follow-up was defined from baseline to either the date of developing dementia, date of death, or end of data collection (31st of December 2012), whichever came first. Dementia was diagnosed according to Diagnostic and Statistical Manual (DSM – III) of Mental Disorders criteria based on information from neuropsychiatric examinations, informant interviews, hospital records and registry data. Multivariate proportional-hazards analyses were used to assess sUA in a time-dependent fashion as a predictor for AD and VaD in separate models, since the effect may differ between dementia subtypes. Analyses were adjusted for socioeconomic status and level of education at baseline and for age, body mass index (BMI), alcohol consumption, smoking status, triglycerides, cholesterol and hypertension in a time-dependent fashion.

Results: At baseline, women were on average 46.8 (SD 6.2) years old and had a mean sUA of 234.5 µmol/L (SD 75.5). During the 44-year follow-up, 153 women developed AD and 48 developed VaD. Women in higher sUA tertiles (compared to lower) were older and had a worse metabolic profile, with a higher BMI, blood pressure, cholesterol and triglycerides concentration. Table 1 shows the results of the age and fully adjusted analyses. In fully adjusted analyses, an increase in sUA concentration (per SD) was associated with a
decreased risk for AD (HR 0.78; 95% Confidence Interval (CI) 0.63 to 0.96). For VaD, women in the lowest and highest tertiles had an increased risk for VaD (HR 3.41; CI 1.36 to 8.54) and (HR 2.61; CI 1.00 to 6.88), respectively, compared to women in the middle tertile.

**Conclusion:** In a population-based cohort study we found that a lower sUA level was associated with an increased risk for developing AD in women. For VaD, we found an increased risk among women with low and high sUA levels. If these findings are confirmed in men and other populations the inverse association between AD and sUA should be addressed in treatment of hyperuricemia.

<table>
<thead>
<tr>
<th>Table 1. Time-dependent cox-proportional hazard ratios for incidence dementia per 1 SD increase in serum uric acid and according to tertiles.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Per SD increase in uric acid</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>1st tertile</td>
</tr>
<tr>
<td>2nd tertile</td>
</tr>
<tr>
<td>3rd tertile</td>
</tr>
</tbody>
</table>

Serum uric acid (μmol/L): low: ≤197; medium: 198 – 257; high: ≥258 tertile.

Model 1: age adjusted

Model 2: Age, body mass index, alcohol consumption (none, low, medium, high), smoking, triglycerides, cholesterol, hypertension (SBP > 160 mmHg, DBP > 100 mmHg, or use of antihypertensive) at baseline and follow-up. Socioeconomic status and level of education at baseline.

# Patients with a previous stroke were deleted (n = 38).

**Disclosure:** E. J. M. Scheepers, None; M. Dehlin, None; L. T. Jacobsson, Abbvie, Celegen, MSD, Novartis and UCB, 5; L. Johansson, None; I. Skoog, None.


**Abstract Number:** 2081

**Synovial Fluid Leukocyte Count and Its Association with Crystal Deposition in Asymptomatic Hyperuricemia**

**Mariano Andrés**1,2, José Antonio Bernal3, María Dolores Arenas4 and Eliseo Pascual1,5, 1Sección de Reumatología, Hospital General Universitario de Alicante, Alicante, Spain, 2Departamento de Medicina Clínica, Universidad Miguel Hernández, Alicante, Spain, 3Reumatología, Hospital Universitario del Vinalopó, Elche, Spain, 4Unidad de Nefrología, Hospital Vithas Perpetuo Socorro, Alicante, Spain, 5Emeritus Professor, Universidad Miguel Hernández, Elche, Spain

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Metabolic and Crystal Arthropathies Poster II

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM
**Background/Purpose:** Articular and periarticular deposits of monosodium urate (MSU) crystals in asymptomatic hyperuricemia (AH) may associate with more severe forms of atherosclerosis [Andrés 2016]. This likely relates with crystal-driven subclinical inflammation, a phenomenon well described in gout [2] but to date not assessed in AH. The aim of the present study was to assess the synovial fluid (SF) leukocytes count in patients with AH depending on the presence of crystals.

**Methods:** Consecutive patients with AH were selected from nephrology clinics. Hyperuricemia threshold was established at serum uric acid (SUA) >7mg/dL; those on current urate-lowering therapy were excluded. Ultrasound (US) of knees, ankles and first metatarsophalangeal joints was performed blinded to clinical and laboratory data, to perform US-guided aspiration and obtain SF samples. Samples were jointly analyzed in fresh by two observers, using a compensated polarized light microscope equipped with two viewing stations. The second observer was also unaware of US findings. The presence of leukocytes and crystals was established by consensus. SF leukocyte count was performed using a Neubauer counting camera. Mann-Whitney’s U and Kruskal-Wallis’ H were used for comparisons between groups.

**Results:** A total of 30 patients have been assessed, with SF samples available from 27 (three showed no joint effusion at US). Median age was 70 years (p25-75 59.8-75.5), and 16 of them (60%) were males. Median (p25-75) SUA and estimated glomerular filtration rate were 8.1 mg/dL (7.6-8.5) and 37.0 mL/min (31.0-47.5), respectively. Seven (25%) were on diuretics. After microscopy evaluation, MSU crystals were found in four patients (14.8%), calcium pyrophosphate (CPP) crystals in five (18.5%), and no crystals in 18 (66.7%). Groups were similar in SUA levels and renal function. Figure shows median leukocytes count according to crystal group: 200/mm3 (138-540) in MSU group; 60/mm3 (50-235) in CPP group; and 30/mm3 (10-53) in those with no crystal at SF. A statistically significant difference was found between the three groups (p=0.001), and comparing MSU crystals and no crystals groups (p<0.001); no difference was found between MSU and CPP groups, nor between CPP and no crystals groups.

**Conclusion:** MSU crystal deposition in patients with AH leads to higher SF leukocyte count, indicating low-grade inflammation. Despite low numbers, this significant finding adds evidence to the potential deleterious role of silent crystal deposits in AH patients.

**Disclosure:** M. Andrés, Grunenthal, 5; J. A. Bernal, None; M. D. Arenas, None; E. Pascual, AstraZeneca, 5,Grunenthal, 5.


**Abstract Number:** 2082

**Clinical Presentation, Management, and Prognosis of Pseudogout in Prosthetic Joint Implant Patients: A Retrospective Study**

Merit P. George1, Floranne C. Ernste2, Aaron J. Tande3, Douglas R. Osmon3, Tad M. Mabry4 and Elie F. Berbari3, 1Mayo Clinic School of Medicine, Rochester, MN, 2Division of Rheumatology, Mayo Clinic Rochester, Rochester, MN, 3Division of Infectious Diseases, Mayo Clinic Rochester, Rochester, MN, 4Division of Orthopedic Surgery, Mayo Clinic Rochester, Rochester, MN

**First publication:** September 18, 2017
Background/Purpose: The prevalence of total knee arthroplasty (TKA) and total hip arthroplasty (THA) has risen considerably in the U.S. There has been a relative lack of investigation into the incidence of post-implant CPDD (pseudogout) at prosthetic joint sites. We retrospectively reviewed cases of post-implant pseudogout treated at our tertiary care center. All patients met the ACR criteria for pseudogout. Our goal was to describe the demographics, clinical presentation, management, and outcomes of this cohort.

Methods: All patients >18 y.o with post-implant pseudogout at a prosthesis site, who were evaluated at our medical center between January 1, 2000 and June 30, 2016, were identified. Implant associated pseudogout was defined as CPPD crystals found in synovial fluid aspirates taken from periprosthetic fluid. Variables pertaining to patient demographics, presentation, management, and outcomes were abstracted and aggregated.

Results: There were 22 patients (15 male, 7 female) who met inclusion criteria. The average age for this cohort was 71 (Range: 51-84). Nine patients had concomitant negative joint fluid cultures, while 13 patients had concomitant positive joint fluid cultures. The most common implant was TKA, accounting for 13 (59.1%) of all cases of pseudogout. The most common indication for prosthetic placement was degenerative joint disease.

Clinical presentation for patients without concomitant infection included pain (100%), swelling at the joint (88.9%), redness (33.3%), fever (22.2%), and decreased joint range of motion (100%). Findings were mostly similar for patients with evidence of concomitant infection, however none of the patients without concomitant infection exhibited tachycardia or drainage from the prosthesis site. Various management steps and findings for the cohort are summarized in the table below.

Ten patients in the overall cohort (45.5%) had either relapse or continuation of symptoms after treatment. Of the 7 patients who received subsequent surgical intervention at the affected joint, 6 had evidence of concomitant infection.

Conclusion: Our study suggests strong resemblance in presentation between post-implant pseudogout and commonly encountered PJI, based on similar exam and lab findings (pain, swelling, redness, decreased ROM, elevated ESR/CRP/PMN%). Tachycardia and purulent drainage might hold some utility in distinguishing between the two conditions. Still, more conclusive tests including synovial fluid aspiration with crystal and culture analyses are needed for this. Unfortunately, many patients receive antibiotics prior to establishment of an etiologic diagnosis, as seen in more than half of our pseudogout patients with negative synovial fluid cultures. Future research should explore paired comparisons between post-implant patients with pure pseudogout & PJI, matched on the basis of variables such as age, gender, and implant site.
<table>
<thead>
<tr>
<th></th>
<th>Entire Cohort (n= 22)</th>
<th>Patients with concomitant positive synovial fluid cultures (n=13)</th>
<th>Patients with concomitant negative synovial fluid cultures (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Time from symptom onset to CPPD finding (days)</strong></td>
<td>2.5 [0-96]</td>
<td>1 [0-11]</td>
<td>7 [1-96]</td>
</tr>
<tr>
<td><strong>Initial blood culture completed</strong></td>
<td>16 (72.7)</td>
<td>10 (76.9)</td>
<td>6 (66.7)</td>
</tr>
<tr>
<td>- Positive result</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td><strong>Initial imaging obtained</strong></td>
<td>21 (95.5)</td>
<td>12 (92.3)</td>
<td>9 (100)</td>
</tr>
<tr>
<td><strong>CRP (mg/L)</strong></td>
<td>141 ± 99</td>
<td>180 ± 103</td>
<td>83 ± 58</td>
</tr>
<tr>
<td><strong>ESR (mm/hr)</strong></td>
<td>58 ± 32</td>
<td>50 ± 24</td>
<td>71 ± 40</td>
</tr>
<tr>
<td><strong>Leukocyte count</strong> (x 10^3/µL)</td>
<td>10 ± 4</td>
<td>11 ± 4</td>
<td>9 ± 3</td>
</tr>
<tr>
<td><strong>Neutrophil count</strong> (x 10^3/µL)</td>
<td>8 ± 3</td>
<td>8 ± 4</td>
<td>7 ± 2</td>
</tr>
<tr>
<td><strong>Serum sodium (mmol/L)</strong></td>
<td>136 ± 4</td>
<td>134 ± 3</td>
<td>138 ± 4</td>
</tr>
<tr>
<td><strong>Serum potassium (mmol/L)</strong></td>
<td>4 ± 0.6</td>
<td>4 ± 0.5</td>
<td>4 ± 0.7</td>
</tr>
<tr>
<td><strong>Primary synovial fluid appearance</strong></td>
<td>8 (36.4)</td>
<td>5 (38.4)</td>
<td>3 (33.3)</td>
</tr>
<tr>
<td>- Cloudy</td>
<td>12 (54.5)</td>
<td>6 (46.2)</td>
<td>6 (66.7)</td>
</tr>
<tr>
<td>- Bloody</td>
<td>2 (9.1)</td>
<td>2 (15.4)</td>
<td>0 (0)</td>
</tr>
<tr>
<td><strong>Synovial fluid total nucleated cells (cell/µL)</strong></td>
<td>49635 ± 67098</td>
<td>70226 ± 80149</td>
<td>19892 ± 22318</td>
</tr>
<tr>
<td><strong>Synovial fluid PMN%</strong></td>
<td>88 ± 16</td>
<td>93 ± 6</td>
<td>80 ± 23</td>
</tr>
<tr>
<td><strong>Antibiotics received prior/at time</strong></td>
<td>17 (77.3)</td>
<td>10 (76.9)</td>
<td>7 (77.8)</td>
</tr>
</tbody>
</table>
The Inflammation Induced By Four Types of Calcium Pyrophosphate Crystals Depends on Their Capacity to Stimulate NF-κb and MAPK Pathways

Félix Renaudin¹, Laure Campillo-Gimenez², Pierre Gras³, Christèle Combes⁴, Martine Cohen-Solal¹, Frederic Liote⁵ and Hang-Korng Ea¹, ¹INSERM UMR1132, Paris Diderot University, Paris, France, ²Inserm UMR1132 Bioscar, Paris, France, ³CIRIMAT, INPT-UPS-CNRS, Toulouse, France, ⁴ENSIACET, CIRIMAT, INPT-UPS-CNRS, Toulouse, France, ⁵University Paris Diderot, Paris, France

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Metabolic and Crystal Arthropathies Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

 Calcium pyrophosphate (CPP) crystal-induced inflammation is mainly driven by interleukin (IL)-1β. IL-1β production involves a two-step process including the formation of pro-IL-1β through NF-κB activation and its' maturation through NLRP3 inflammasome activation. Two CPP crystal phases, namely monoclinic and triclinic CPP dehydrated (m- and tCPPD) crystals are identified in synovial fluids. They display different inflammatory potentials.

We aimed to assess the inflammatory properties of different CPP crystal phases and the intracellular pathways involved in CPP crystal-induced IL-1β production

Methods:

 Four synthesized and pyrogen-free CPP crystals (aCPP (amorphous), mCPPD or tetrahydrated (mCPPT) and tCPPD) (Gras P et al. 2014) and monosodium urate crystals (MSU) were used, in vitro, to stimulate THP-1 cell line or mouse bone marrow-derived
macrophages (BMDM) in the presence or not of pharmacological inhibitors: Bay-117085 (Bay, NF-κB inhibitor); SB203580 (SB, MAPK p38 inhibitor); SP600125 (SP, JNK inhibitor) and PD98059 (PD, p42/44 MAPK inhibitor). The expression of pro- and anti-inflammatory cytokine genes was assessed by qRT-PCR, IL-1β and IL-8 production by ELISA and MAPK activation by immunoblot. NF-κB activation was assessed in THP-1 cell line containing a gene reporter plasmid. In vivo, we used air pouch model to assess the effects of NF-κB inhibition in CPP crystal-mediated inflammation.

Results:

In vitro mCPPD crystals were the most inflammatory CPP crystals and induced a higher production of mature IL-1b and IL-8 and a higher expression of inflammatory cytokine genes (IL-1β, IL-6, IL-8, IL-33, TNF, COX-2) than tCPPD, mCPPT and MSU crystals. aCPP crystals did not have inflammatory property. Similarly, mCPPD crystals induced a higher activation of NF-κB, a higher production of NLRP3 inflammaome and a stronger phosphorylation of p38, p42/44 and JNK MAPKs. Inhibition of NF-κB with Bay completely abrogated mature IL-1β and IL-8 secretion and pro-IL-1β synthesis induced by all CPP crystals. Inhibition of JNK and p42/44 MAPK with SP and PD, respectively, decreased both IL-1β secretion and NF-κB activation induced by CPP crystals. In vivo IL-1β and IL-8 production and neutrophil infiltration induced by mCPPD crystals were dramatically decreased by NF-κB inhibitor.

Conclusion:

Our results suggested that the inflammatory potential of different CPP crystals relied on their capacity to activate MAPK pathways and NF-κB. Studies are ongoing to investigate the underlying mechanisms.

Disclosure: F. Renaudin, None; L. Campillo-Gimenez, None; P. Gras, None; C. Combes, None; M. Cohen-Solal, None; F. Liote, None; H. K. Ea, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-inflammation-induced-by-four-types-of-calcium-pyrophosphate-crystals-depends-on-their-capacity-to-stimulate-nf-%ce%bab-and-mapk-pathways

Abstract Number: 2084

Patients with Early Onset Gout Develop Earlier Severe Joint Involvement and Metabolic Comorbid Conditions

Tristan Pascart1, Laurène Norberciak2, Hang-Korng Ea3, Sabine Lanz4, Charles Lambert5, Pascal Guggenbuhl6 and Frederic Liote7, 1Rheumatology, Lille Catholic University, Lille, France, 2Lille Catholic University, Lille, France, 3INSERM UMR1132, Paris Diderot University, Paris, France, 4Laboratoire Mayoli Spindler, Chatou, France, 5Laboratoire Ipsen Pharma, Bouologne, France, 6Rennes University, Rennes, France, 7University Paris Diderot, Paris, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Metabolic and Crystal Arthropathies Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Patients with Early Onset Gout develop Earlier Severe Joint Involvement and Metabolic Comorbid Conditions

Background/Purpose:

Early onset gout might encompass more severe cases along with genetic defects, leading to early management as pointed out by recent guidance from the US or Europe. The objective of this study was to compare disease characteristics and comorbidities of patients suffering from gout with early onset (EOG) before the age of 40 to the general population of gouty patients.

Methods:

Patients from the cross-sectional national GOSPEL cohort having suffered from the first symptoms of gout before the age of 40 were included in the EOG group and compared to those with an onset after 40 included in the common gout (CG) group.
Results:

A total of 120 (12.2%) patients was included in the EOG group (aged 49.5 (±11.9) years) and 865 patients in the CG group (aged 64.4 (±10.1) years). Patients with EOG presented with a higher prevalence of polyarticular flares (p<0.01), but had similar proportions of patients having had at least 2 flares over the past year (p=0.16), similar prevalence of gout arthropathy (p=0.79) and tophi (p=0.53). A total of 68.9% among EOG patients were treated with urate lowering therapy (ULT) compared to 67.9% in the CG group (p=0.91), but only 19.1% in the EOG had an SUA level below 6.0mg/dL versus 29.8% in the CG group (p<0.05). More patients of the CG group where suffering from moderate to severe CKD (p<0.01). A similar proportion of patients suffered from diabetes mellitus in the EOG (12%) and CG (15.5%) groups (p=0.38) and prevalence of each item composing the metabolic syndrome did not differ significantly between groups. However, in EOG patients, cardiovascular comorbidities were present before gout onset (figure 1).

Conclusion:

In this large French cohort, EOG patients develop similar joint involvement and comorbid disorders than CG patients, but earlier in life.

Figure 1: Time to diagnosis of cardiovascular comorbidities from the first manifestations of gout in early and common gout groups. *p<0.05

Disclosure: T. Pascart, Ipsen Pharma and Mayoli Spindler, 5; L. Norberciak, None; H. K. Ea, None; S. Lanz, Mayoli Spindler, 3; C. Lambert, Ipsen Pharma, 3; P. Guggenbuhl, Menarini and Ipsen Pharma, 5; F. Liote, Astra-Zeneca, Grunenthal, Ipsen Pharma, Menarini France and Global, Mayoly-Spindler, Novartis France, Novartis Global, 5.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/patients-with-early-onset-gout-develop-earlier-severe-joint-involvement-and-metabolic-comorbid-conditions

Abstract Number: 2085

Relationship between Gout and Asthma: A National Database Analysis

Yiming Luo1, Jiehui Xu2, Yumeng Wen1, Alvaro Ramos-Rodriguez3, Changchuan Jiang1, Shuyang Fang1, Mustafa Kagalwalla1 and Neha Ohri4, 1Department of Medicine, Mount Sinai St Luke's and Mount Sinai West Hospitals, Icahn School of Medicine at Mount Sinai, New York, NY, 2Department of Biostatistics, Mailman School of Public Health, Columbia University Medical Center, New York, NY, 3Mount Sinai St Luke's and Mount Sinai West Hospitals, Icahn School of Medicine at Mount Sinai, New York, NY, 4Division of Rheumatology, Department of Medicine, Mount Sinai St Luke's and Mount Sinai West Hospitals, Icahn School of Medicine at Mount Sinai, New York, NY

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Metabolic and Crystal Arthropathies Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Gout is an inflammatory disorder related to hyperuricemia and abnormal deposition of monosodium urate crystals in joints or other tissues. The relationship between serum uric acid and asthma is controversial in the literature. While some studies found it an initiator and amplifier of asthma, others had the opposite results. Most previous studies involved either animal models or small patient samples. In our study, we analyzed the association of asthma and gout in hospitalized patients.

**Methods:**

We conducted a cross-sectional study using data from National Inpatient Sample (NIS) for the year of 2014. Diagnosis for asthma, subtypes of asthma (i.e. allergic asthma, non-allergic asthma, exercise-induced bronchospasm and cough variant asthma) and gout were identified using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes. STATA software package was used for statistical analyses. Multivariate logistic regression models were created to adjust for potential confounders such as age, gender, race, insurance type, current tobacco abuse and obesity. Patients younger than 18 years old were excluded from the study. For asthma exacerbations, we also studied exacerbations related to acute respiratory infections (ARI) and status asthmaticus.

**Results:**

A total of 858,750 hospitalizations with a diagnosis of gout and 2,331,616 hospitalizations with a diagnosis of asthma were included in the study. Compared with those without gout, asthma patients with gout are more likely to be older (mean age 67.6 vs 54.9), male (50.5% vs 29.2%), more African American and less Hispanic (26.8% and 5.0% vs 21.3% and 10.2%), less smoker (10.3% vs 19.1%) and more obesity (33.8% vs 23.7%). The adjusted OR for all types of asthma and gout was 1.15 (95% CI 1.13 - 1.17, p < 0.001). For asthma subtypes, the adjusted OR was statistically significant only for allergic asthma (OR 1.16, 95% CI 1.01 - 1.35, p = 0.035). There was no difference for non-allergic asthma (OR 0.78, 95% CI 0.47 - 1.32, p = 0.363), exercise-induced bronchospasm (OR 0.93, 95% CI 0.55 - 1.56 p = 0.776), and cough variant asthma (OR 1.43, 95% CI 0.89 - 2.29, p = 0.136) in patients with gout. For patients with asthma exacerbations, gout was associated with a lower risk of overall exacerbations (OR 0.87, 95% CI 0.83 - 0.91, p < 0.001), ARI-related exacerbations (OR 0.78, 95% CI 0.66 - 0.92, p = 0.003) and status asthmaticus (OR 0.59, 95% CI 0.46 - 0.77, p<0.001). There was no difference for exacerbations from allergic asthma (OR 0.76, 95% CI 0.52 - 1.10, p = 0.142) in patients with gout.

**Conclusion:**

Our study suggested that gout is a risk factor only for allergic subtypes of asthma, and that it may be a protective factor for asthma exacerbations except for the allergic subtype. This unexpected finding may be due to the unique biochemical properties of uric acid, being both pro-inflammatory and anti-oxidant and also the heterogeneity for different subtypes of asthma. However, we also cannot rule out the effects of systemic steroid, which is one of the short-term treatment for acute gouty arthritis, as a possible confounder. Whether a target level of uric acid in gout patients with allergic and non-allergic asthma needs to be individualized warrants further investigations.

**Disclosure:** Y. Luo, None; J. Xu, None; Y. Wen, None; A. Ramos-Rodriguez, None; C. Jiang, None; S. Fang, None; M. Kagalwalla, None; N. Ohri, None.


**Abstract Number:** 2086

**Calcium Pyrophosphate Crystal Size, Shape and Appearance Variability**

Monica Zell1, Ann Rosenthal2, Thanda Aung3, Marian Kaldas3 and John Fitzgerald4, 1Albert Einstein College of Medicine, New York, NY, 2Division of Rheumatology, Medical College of Wisconsin, Milwaukee, WI, 3UCLA, Los Angeles, CA, 4Rheumatology, UCLA, Los Angeles, CA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Metabolic and Crystal Arthropathies Poster II

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** To better understand the variation in calcium pyrophosphate (CPP) crystal, size, shape and appearance under compensated polarized microscope, synovial fluid crystals were examined by 4 independent raters.
Methods: Over a 4-month period, synovial fluid samples were de-identified and collected from the university clinical laboratory when found to be positive for CPP crystals. All samples were centrifuged for 5 minutes (prior to clinical lab examination) and stored at 4°C. For this research effort, slides were dry mounted for enhanced stability.

Two experienced raters and two novice raters were trained using an atlas with sample CPP crystal images and a standardized protocol for describing each crystal’s shape, birefringence strength, color, and the raters’ certainty that the object was a CPP crystal. Raters examined each slide until a minimum of 10 CPP suspected crystals were identified and photographed with 100x objective, or a maximum of 30 minutes was reached.

For the purpose of crystal measurement, Adobe Photoshop CS6 was used to apply a high pass linear light filter to digital images to provide enhanced resolution and line discrimination. Crystal area (μm²), length (μm), and width (μm) (for rods), and diagonals (μm) (for rhomboids) were measured. Crystals rated with low certainty (1 on 1-3 scale) or crystals that had atypical shape or uncharacteristically bright birefringence were excluded. All remaining crystals were reviewed by a national CPP crystal expert (AR) for final inclusion in the dataset.

Results: Synovial fluid from 16 joint aspirates was reviewed by 4 raters. Of the 564 potential crystals identified by the 4 raters, the expert rater confirmed 293 (52%) were definite CPP crystals. Crystals that were rejected were more likely to be smaller, rhomboid, yellow rather than blue, and have weaker or no birefringence. After the brief training session, there were few differences in either the number of definite crystals or accuracy of crystal identification between the more experienced and lesser experienced raters.

Of the 293 definite crystals, 185 (63%) were categorized as rods with median area of 3.8 mm², (range, 1.0 – 22.9 mm²), and 108 rhomboids (37%) with median area of 5.8 mm², (range, 0.9 – 27.0 mm²), p <0.005. The expected frequency of color distribution ought to be 50:50; however, 60% of confirmed crystals were blue (suggesting that the yellow-orange crystals were not as easily identified). Compared to rhomboids, rods were more likely to be scored as having low birefringence (35% vs. 9%). Only 4 (1.4%) non-birefringent confirmed crystals were identified. Rod median length was 3.8 mm (range, 1.0 – 14.3 mm), median length to width ratio 3.4 (range, 1.1 – 13). Rhomboid median (maximum) diagonal length, 3.6 mm (range, 1.0 – 9.0 mm), median (minimum) diagonal length, 2.6 mm (0.9 – 7.0 mm) and median acute angle of 74º (range, 41º to 90º).

Conclusion: After a brief training session, less experienced raters performed similarly to more experienced raters. CPPD crystals that are smaller, show weaker birefringent or are aligned perpendicular to the short-axis of polarization are harder to identify. There is significant variation in crystal size, shape and appearance under polarized microscopy.

Disclosure: M. Zell, None; A. Rosenthal, None; T. Aung, None; M. Kaldas, None; J. Fitzgerald, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/calcium-pyrophosphate-crystal-size-shape-and-appearance-variability

Abstract Number: 2087

Allelic Variants of ABCG2 and Gout Risk

Blanka Stiburkova1,2, Katerina Pavelcova2,3, Jakub Zavada2, Lenka Petru2,3, Marketa Pavlikova2,4, Hirotaka Matsuo5, Tony R. Merriman6 and Karel Pavelka7, 1Institute of Inherited Metabolic Disorders, First Faculty of Medicine, Charles University, Prague, Czech Republic, 2Institute of Rheumatology, Prague, Czech Republic, 3Department of Rheumatology, First Faculty of Medicine, Charles University, Prague, Czech Republic, 4Department of probability and mathematical statistics, Faculty of Mathematics and Physics, Charles University, Prague, Czech Republic, 5Department of Integrative Physiology and Bio-Nano Medicine, National Defense Medical College, Tokorozawa, Japan, 6Department of Biochemistry, University of Otago, Dunedin, New Zealand, 7Institute of Rheumatology, Praha, Czech Republic

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Metabolic and Crystal Arthropathies Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Common dysfunctional variants of ABCG2, a high-capacity urate transporter gene, that result in decreased urate excretion, are major causes of hyperuricemia and gout. In the present study, we describe the first detailed analysis of disease-relevant functional allelic variants in the \textit{ABCG2} gene.

\textbf{Methods:}

The main cohort recruited from the Czech Republic consisted of 155 gout patients, 115 normouricemic controls were used for comparison. We amplified, directly sequenced, and analyzed 15 \textit{ABCG2} exons. The associations between genetic variants and clinical phenotype were analyzed using the t-test, Fisher exact test and logistic and linear regression approach. Data from a NZ Polynesian sample set and the UK Biobank were included for the p.V12M analysis.

\textbf{Results:}

In the \textit{ABCG2} gene, 18 intronic (one dysfunctional splicing) and 12 exonic variants were detected: 10 were non-synonymous (two common, eight rare including one novel): p.V12M, p.Q141K, p.R147W, p.T153M, p.F373C, p.T434M, p.S476P, p.S572R, p.D620N, and p.K360del. The p.Q141K (rs2231142) variant had a significantly higher minor allele frequency (0.23) in the gout patients compared to the European-origin population (0.09) and was significantly more common among gout patients than among normouricemic controls (OR = 3.15, p<0.0001). Patients with non-synonymous allelic variants had an earlier onset of gout (41.5 vs. 48 years, p=0.0478) and a greater likelihood of a familial history of gout (42% vs. 26%, OR = 2.02, p=0.043). In a meta-analysis p.V12M exerted a protective effect from gout (p<0.0001).

\textbf{Conclusion:}

Genetic variants of ABCG2, common and rare, increased the risk of gout. Non-synonymous allelic variants of ABCG2 had a significant effect on earlier onset of gout and the presence of a familial gout history. ABCG2 should thus be considered a common and significant risk factor for gout.

\textbf{References}


This study was supported by the grants from the Czech Republic Ministry of Health AZV 15-26693A.

\textbf{Disclosure:} B. Stiburkova, None; K. Pavelcova, None; J. Zavada, None; L. Petru, None; M. Pavlikova, None; H. Matsuo, None; T. R. Merriman, Ardea Biosciences, 2; K. Pavelka, None.

View Abstract and Citation Information Online - \url{http://acrabstracts.org/abstract/allelic-variants-of-abcg2-and-gout-risk}

\textbf{Abstract Number: 2088}

\section*{Clinical Significance of Urate Deposition in Tendon: A Dual-Energy CT Study}

\textbf{In Young Kim}\textsuperscript{1}, Yeonghee Eun\textsuperscript{2}, Ji young Chi\textsuperscript{3}, Chan Hong Jeon\textsuperscript{4}, Jinsok Kim\textsuperscript{5}, Hyungjin Kim\textsuperscript{2}, Jaejoon Lee\textsuperscript{1}, Eun-Mi Koh\textsuperscript{2} and Hoon-Suk Cha\textsuperscript{6}, \textsuperscript{1}Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, Republic of (South), \textsuperscript{2}Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, Republic of (South), \textsuperscript{3}Department of Rheumatology, Bundang Jesaeng Hospital, Seongnam, Korea, Republic of (South), \textsuperscript{4}Department of Internal Medicine, Soonchunhyang University College of Medicine, Bucheon, Korea, Republic of (South), \textsuperscript{5}Department of Internal Medicine, Jeju National University Hospital, Jeju National University School of Medicine, Jeju, Korea, Republic of (South), \textsuperscript{6}Department of Medicine, Division of Rheumatology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, Republic of (South)

\textbf{First publication:} September 18, 2017

\textbf{SESSION INFORMATION}

\textbf{Session Date:} Tuesday, November 7, 2017

\textbf{Session Title:} Metabolic and Crystal Arthropathies Poster II

\textbf{Session Type:} ACR Poster Session C

\textbf{Session Time:} 9:00AM-11:00AM
Background/Purpose:

Dual-energy computed tomography (DECT) is advanced imaging modality that shows the deposition of monosodium urate (MSU) crystal in tissue as a color signal. In the 2015 American College of Rheumatology/European League Against Rheumatism gout classification criteria, DECT was included as one of the imaging modalities for diagnosis. The MSU crystal deposit around the symptomatic joint is considered as a positive finding, but the clinical significance of urate deposition around the tendon is still unclear.

The aim of this study was to compare the clinical characteristics and DECT findings in people with MSU crystal deposition in the joints and people with urate deposition only in the tendons.

Methods:

DECT was performed in 71 patients who complained of recurrent painful swelling of the foot and/or ankle joints, and 35 of them showed MSU crystal deposition in the joints on DECT. The patients were divided into two groups according to the location of uric acid deposition on DECT. We analyzed the differences in clinical features and imaging findings between the two groups.

Results:

The mean age of the patients was 50 ± 14 years, and 67 patients (94%) were male. All of patients who had shown the deposition of uric acid crystals in joints on DECT had a history of typical gout attacks, but 29 (81%) of those only in tendons on DECT had experienced typical gout attacks (p=0.011). The overall mean uric acid level in all patients was as high as 7.5 ± 2.2 mg/dL. The uric acid level was found to be higher in patients with joint involvement, but this difference was not statistically significant. The concordance rate between the symptomatic sites and the urate deposition sites was 91% in patients with joint deposition, but the rate was only 6% in patients without joint deposition (p<0.001). There were 4 patients (11%) who showed gouty erosion without MSU crystal deposition in joints on DECT.

Conclusion:

The MSU crystal deposition in the tendon was not correlated well with clinical features. However, in some patients, MSU crystal deposition may be observed only in the tendon, even with gouty erosion in joints. Therefore, careful interpretation of the DECT is necessary.

Disclosure: I. Y. Kim, None; Y. Eun, None; J. Y. Chai, None; C. H. Jeon, None; J. Kim, None; H. Kim, None; J. Lee, None; E. M. Koh, None; H. S. Cha, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/clinical-significance-of-urate-deposition-in-tendon-a-dual-energy-ct-study

Abstract Number: 2089

Arhalofenate Acid Inhibits Urate Crystal-Induced Inflammatory Responses through Activation of AMP-Activated Protein Kinase (AMPK) Signaling

Charles McWherter¹, Robert Terkeltaub²,³ and Ru Liu-Bryan³,⁴ ¹CymaBay Therapeutics, Inc., Newark, CA, ²Rheumatology, VA San Diego Healthcare System, San Diego, CA, ³Medicine-Rheumatology, University of California, San Diego, La Jolla, CA, ⁴VA San Diego Healthcare System, San Diego, CA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Metabolic and Crystal Arthropathies Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Arhalofenate is an investigational drug with dual uricosuric and anti-inflammatory properties. Arhalofenate reduced the risk of acute flare while lowering serum urate levels in gout patients in a phase II trial. Previous studies demonstrated that arhalofenate (or its active acid form) suppresses the production of IL-1β in response to urate crystals in macrophages in vitro and in a mouse air pouch model in vivo. In this study, we characterized the molecular mechanism of action of arhalofenate acid, studying urate crystal-induced inflammatory responses in macrophages in vitro.
Methods: Bone marrow derived macrophages (BMDMs) were stimulated with urate crystals in the presence or absence of arhalofenate acid. IL-1b release was measured from conditioned media by ELISA analysis. Western blot was carried out to examine expression of NLRP3, pro-caspase-1 and cleaved caspase-1 (for NLRP3 inflammasome activation); phosphorylation and expression of the nutritional biosensor AMPKα (AMP-activated protein kinase), the NAD⁺-dependent protein deacetylase SIRT1, the PPARγ co-activator and master regulator of mitochondrial biogenesis PGC-1a, the nuclear-encoded mitochondrial transcription factor A TFAM, cytosolic thioredoxin 1 (TXN1), nuclear thioredoxin 2 (TXN2), thioredoxin-interacting protein (TXNIP) involved in NLRP3 inflammasome activation; microtubule-associated protein 1 light-chain 3 (LC3) and p62 (an adaptor contributing to autophagic degradation of ubiquitinated substrates and damaged organelle such as damaged mitochondria) for autophagy.

Results: Arhalofenate acid attenuated urate crystal-induced IL-1b production in BMDMs via inhibition of NLRP3 inflammasome activation, evidenced by inhibition of protein expression of NLRP3 and cleaved caspase-1 (p10). In addition, arhalofenate acid dose-dependently increased phosphorylation of AMPKα, as well as expression of SIRT1 that was dependent on AMPK, since arhalofenate acid failed to increase SIRT1 expression in AMPKα1 knockout (KO) BMDMs. Arhalofenate acid was also unable to significantly inhibit urate crystal-induced IL-1b production in AMPKα1 KO, compared to WT BMDMs, indicating that AMPK mediates inhibitory effect of arhalofenate acid. Moreover, urate crystals concurrently reduced phosphorylation of AMPKα, expression of SIRT1, PGC-1a, TFAM, TXN1, TXN2, but induced expression of TXNIP, all of which were reversed by arhalofenate acid in BMDMs, implicating a role for arhalofenate acid in maintaining mitochondrial function, limiting oxidative stress and preventing TXNIP-mediated inflammasome activation. Furthermore, arhalofenate acid was able to not only promote induction of autophagy but also accelerate autophagic flux.

Conclusion: Arhalofenate acid, the active form of arhalofenate, is anti-inflammatory via activation of AMPK and downstream signaling in macrophages, thereby increasing cellular resistance to stresses induced by urate crystals, mediated by maintaining mitochondrial integrity and cellular quality control through autophagy. These effects likely contribute to gout flare risk reduction by arhalofenate.

Disclosure: C. McWherter, CymaBay Therapeutics, Inc., 3; R. Terkeltaub, VAMC/UCSD location, 3, ARDEA/Astra-Zeneca, 2, SOBI, Selecta, Horizon, Cymabay, Aequus, 5; R. Liu-Bryan, None.

Utility of Anakinra in Acute Crystalline Diseases: A Retrospective Study Comparing a University Hospital with Veterans Affairs Medical Center

Julianna Desmarais¹ and Cong-Qiu Chu², ¹Department of Arthritis and Rheumatic Diseases, Oregon Health & Science University, Portland, OR, ²Rheumatology, Oregon Health & Science University, Portland, OR

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Metabolic and Crystal Arthropathies Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Anakinra is an IL-1 blocking medication used off label to relieve acute inflammation from gout and pseudogout. The efficacy and safety of this treatment in the inpatient setting have not been well evaluated.

Methods: Patients with crystal-induced arthritis who were hospitalized at Oregon Health & Science University (OHSU) Hospital and the VA Portland Health Care System (VA) since 2008 were included. Patient characteristics, comorbidities, medications prior to anakinra use, reason for anakinra use, number of doses of anakinra (one dose was 100 mg subcutaneous injection), adverse events, and response to treatment were analyzed. A response to treatment was defined as a pain score improvement of 2 on a 0-10 pain scale, functional improvement such as ability to bear weight on affected limb when unable to initially, or a documented clinical response such as “great improvement.” For pain improvement, a student’s t test was used to calculate significance.

Results: A total of 79 gout patients were identified who had 101 flares. There were 11 patients with pseudogout who had 14 flares. Three patients had both processes on joint aspiration. The average patient age was 64 (61 at OHSU, 69 at the VA), with an average of 3.9 joints flaring. At both OHSU and the VA around half of all patients had comorbidities such as diabetes, congestive heart failure, and chronic kidney disease that affected the choice of their crystal induced arthritis treatment. At OHSU each patient received an average of 4.6 doses of anakinra, while at the VA the average number of doses of anakinra was 3.3. All of the patients except two had a response to
anakinra. Ninety percent of the patients responded within 2 days after initiation of anakinra at both hospitals when evaluating function, pain, and/or clinical response. Anakinra was well tolerated. No adverse reactions to anakinra were reported.

**Conclusion:** Anakinra is an effective and safe medication for the use of gout and pseudogout in hospitalized patients in the academic and VA settings who have acute crystal induced arthritis, particularly in those who have comorbidities that would limit the use of other acute gout medications.

**Disclosure:** J. Desmarais, None; C. Q. Chu, None.


**Abstract Number:** 2091

**Initial Phase 2 Clinical Data of SEL-212 in Symptomatic Gout Patients: Monthly Dosing of a Pegylated Uricase (Pegsiticase) with Svp-Rapamycin Enables Sustained Reduction of Serum Uric Acid Levels By Mitigating Formation of Anti-Drug Antibodies**

Earl Sands\(^1\), Alan J. Kivitz\(^2\), Wesley DeHaan Ph.D.\(^1\), Lloyd Johnston\(^1\) and Takashi Kei Kishimoto\(^1\), \(^1\)Selecta Biosciences, Watertown, MA, \(^2\)Department of Rheumatology, Altoona Center for Clinical Research, Duncansville, PA

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Tuesday, November 7, 2017
**Session Title:** Metabolic and Crystal Arthropathies Poster II
**Session Type:** ACR Poster Session C
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Pegylated uricases are promising therapies for the treatment of severe chronic gout, particularly for the rapid resolution of tophi. However uricases are limited by the induction of anti-drug antibodies (ADAs) that can compromise efficacy and safety. We have developed SEL-212, a novel combination product consisting of pegsiticase co-administered with synthetic vaccine particles encapsulating rapamycin (SVP-R). Preclinical studies have shown the ability of SVP-R to induce durable, antigen-specific immune tolerance to a range of co-administered biologic drugs. A Phase 1 study of SEL-212 demonstrated mitigation of ADAs and sustained control of serum uric acid (sUA) for at least 30 days after a single dose. Here we report initial data on the safety, tolerability, and effects on sUA, ADAs, and gout fares of repeated monthly doses of SEL-212 from an ongoing Phase 2 clinical study in symptomatic gout patients.

**Methods:**
Patients with symptomatic gout (≥1 tophus, gout flare within 6 months, and/or gouty arthropathy) and elevated sUA (sUA ≥6mg/dL) were enrolled in SEL-212 treatment cohorts (N=6-10 patients/cohorts) of fixed doses of pegsiticase (0.2mg/kg or 0.4mg/kg) alone or co-administered with SVP-R (0.05, 0.08, or 0.1mg/kg). SEL-212 was infused in 28-day cycles x3 doses followed by challenge with pegsiticase alone on 28-day cycles x2 doses. Safety, tolerability, sUA, and ADAs were monitored, and clinical data were collected.

**Results:**
As of 12 June 2017, 60 patients had been dosed. A dose range matrix of pegsiticase and SVP-R enabled the identification of the minimum effective monthly dose (MED) as 0.4mg/kg pegsiticase+0.08mg/kg SVP-R. At the MED, 5/6 initial evaluable patients demonstrated sustained sUA levels <0.1 mg/dL with no or low ADA titers through 5 monthly doses, including two challenges with pegsiticase alone, and 4/6 demonstrated evidence of immune tolerance induction (Figure 1). In contrast, all patients treated with 0.4 mg/kg pegsiticase alone developed ADAs after the first dose and lost control of sUA by 14-21 days. Flare rates in the first 3 months were low for patients treated with SEL-212 (22%) versus those treated with pegsiticase alone (50%). SEL-212 was generally well tolerated at the clinically active doses. Of 7 observed serious infusion reactions, 4 were associated with patients receiving pegsiticase alone or the lowest dose of SEL-212, as expected, and two were related to dosing errors.

**Conclusion:**
SEL-212 has been well-tolerated, and, unlike pegylated uricases alone, has mitigated immunogenicity, reduced flare rate and enabled repeated monthly dosing with sustained control of sUA levels in gout patients.

Figure 1. SEL-212 control of sUA (green) and ADAs (blue)

Disclosure: E. Sands, Selecta Biosciences, 1,Selecta Biosciences, 3; A. J. Kivitz, Sanofi, Pfizer, Roche, and UCB, 5; W. DeHaan Ph.D., Selecta Biosciences, 1,Selecta Biosciences, 3; L. Johnston, Selecta Biosciences, 1,Selecta Biosciences, 3; T. K. Kishimoto, Selecta Biosciences, 1,Selecta Biosciences, 3.


Abstract Number: 2092

Pilot Clinical Study of a Novel Unobtrusive Carpal Tunnel Tissue Manipulation Device in Reducing Symptoms of Carpal Tunnel Syndrome

Pauline Luong1,2, Frank King3, Zong-Ming Li2,4, Matt Dickason5, Matthew Diamond6 and Jae Son1,2, 1Pressure Profile Systems, Los Angeles, CA, 2Sohn Inc, Los Angeles, CA, 3Mission Pain and Spine Institute, Mission Viejo, CA, 4Biomedical Engineering, Orthopaedic Surgery, and Physical Medicine & Rehabilitation, Cleveland Clinic, Cleveland, OH, 5Renaissance Associates, Newport Beach, CA, 6Rusk Institute of Rehabilitation Medicine, NYU School of Medicine, San Francisco, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Carpal tunnel syndrome (CTS) is the most common peripheral entrapment neuropathy and has been associated with systemic conditions such as rheumatoid arthritis, hypothyroidism, and obesity, as well as occupational tasks involving repetitive manual activities. The most common treatments for CTS have several drawbacks, such as invasiveness (surgery), lack of long-term efficacy (corticosteroid injections), or low compliance (braces). To overcome these shortcomings, an unobtrusive and non-invasive device was developed to treat CTS by relieving pressure on the median nerve. This carpal tunnel tissue manipulation device (CTMD) is
attached to the volar aspect of the wrist and applies a consistent level of tension to the underlying tissue. A pilot clinical trial was performed to investigate the feasibility, safety and efficacy of the CTMD to relieve symptoms of and potentially treat CTS.

**Methods:** Subjects with mild to severe unilateral or bilateral CTS, confirmed using electrodiagnostic testing and AANEM criteria, were enrolled into the study. Subjects with concomitant ulnar or radial neuropathies, diabetes, thyroid disease, or connective tissue diseases were excluded. The CTMD was worn on the affected wrist(s) for 8-10 hours daily for 28 days, followed by 8 weeks of no CTS treatment. The primary outcome measure was the Symptom Severity Scale (SSS) score of the Boston Carpal Tunnel Questionnaire (BCTQ). The BCTQ was administered at 0, 2, and 4 weeks into treatment, and 8 weeks post-treatment. Data for bilateral subjects were evaluated only for the wrist with higher CTS severity and higher BCTQ score.

**Results:** Eleven (11) subjects were enrolled: mean age 51.4 years (+11.1), 64% female, 7 treated for unilateral CTS and 4 for bilateral CTS. Subjects’ average SSS score reduced from baseline by 0.63 ± 0.56 points at 2 weeks and by 0.59 ± 0.68 points at 4 weeks (p<0.05). Subjects’ scores continued to improve 8 weeks post-treatment, resulting in an overall improvement in SSS of 0.79 ± 0.74 points (p<0.01). Although a history of connective tissue disorders was an exclusion criteria, it was later found that two subjects had or possibly had arthritis. One subject had wrist arthritis and unilateral CTS but showed improvement of 0.91 points 8 weeks post-treatment. In contrast, the other subject had unconfirmed RA and bilateral CTS and experienced a 0.46 point degradation 8-weeks post-treatment. Unilateral CTS subjects’ average SSS score improved more than bilateral subjects at each timepoint and most significantly at 8 weeks post-treatment (1.2 ± 0.5 points vs. 0.09 ± 0.41 points).

**Conclusion:** At least 4 weeks of daily wear of the CTMD improved severity of CTS symptoms in patients with unilateral CTS. These results suggest that the CTMD may have a lasting effect up to 8 weeks post-treatment. Bilateral CTS patients may respond differently to treatment than unilateral CTS patients. An extended, randomized, placebo-controlled study is proposed to investigate long-term effects.

**Disclosure:** P. Luong, Sohn Inc, 1,Pressure Profile Systems, 3; F. King, Sohn Inc, 1; Z. M. Li, Sohn Inc, 6,Sohn Inc, 4; M. Dickason, Sohn Inc, 1; M. Diamond, Sohn Inc, 4; J. Son, Sohn Inc, 4,Pressure Profile Systems, 4.

Conclusion: The present findings suggest that eosinophilia, and high serum levels of IgE and IgG4 are common features in IgG4-RD patients regardless of allergy, although there may be some clinical differences according to the concomitant allergic conditions that are present.

Disclosure: T. Saeki, None; T. Ito, None; M. Tamura, None; S. Yoshikawa, None; H. Yamazaki, None.

Prevalence of Organ Involvement in Mixed Connective Tissue Disease

Javier Narváez1, Maria Pascual2, Gloria Albert Espi3, Milena Millan4, Mercè López de Recalde5, Juan José Alegre6, Ivan Castellví7, Carmen Gomez Vaquero5 and Joan Miquel Nolla8, 1Rheumatology Department, Hospital de Bellvitge. Barcelona. Spain, L'Hospitalet de Llobregat, Spain, 2Rheumatology, Hospital Universitari de Bellvitge, Barcelona, Spain, 3Rheumatology Department, Hospital Universitario Doctor Peset, Valencia, Spain, 4Rheumatology, Hospital de Sant Pau, Barcelona, Spain, 5Department of Rheumatology, Hospital Universitari de Bellvitge, Barcelona, Spain, 6Sección de Reumatología Hospital Universitario Dr Peset Valencia, Valencia, Spain, 7Rheumatology, Hospital Universitari de la Santa Creu i Sant Pau, Barcelona, Spain, 8Rheumatology, Hospital Universitario de Bellvitge, Barcelona, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Mixed connective tissue disease (MCTD) is characterized by overlapping features of SLE, SSc, PM/DM and rheumatoid arthritis together with the presence of high-titre of anti-RNP antibodies. Its most common clinical manifestations are Raynaud’s phenomenon, arthritis, sclerodactyly, edema in the hands and myositis. However, organ involvement is more extensive than first descriptions reported. The disease can be serious with development of pulmonary, kidney, cardiovascular, gastrointestinal and neurological manifestations. The objective of the present study was to evaluate the frequency and the different types of organ damage in a well characterized cohort of patients with MCTD.

Methods: Ambispective study of 42 MTCD patients, all of them fulfilling the diagnostic criteria proposed by Alarcon-Segovia (J Rheumatol 1989;16:328-34), with a minimal follow-up after the first clinical presentation of at least 2 yr. The endpoint of patient follow-up was the date of the last clinic visit.

Results: At the end of the follow-up period (median ± SD: 117.3 ± 63.1 months; minimum, maximum: 28-432 months), 69% of patients (29/42) had 1 or more organ involvement.

Esophageal dysmotility and reflux disease was the most prevalent complication, being observed in 43% (18/42) of cases. Pulmonary abnormalities were also common, being found in 38% of patients (16/42). The most frequent lung manifestations were diffuse interstitial lung disease in 24% (10/42) of patients (including 6 cases of nonspecific interstitial pneumonitis, 3 cases of usual interstitial pneumonitis and 1 case of lymphocytic interstitial pneumonia), and pleuritis in 19% (8/42). Other pulmonary complications include primary pulmonary hypertension in 12% of patients (5/42) and shrinking lung syndrome in 2% (1/42).

Neurological disease was observed in 19% (8/42) of patients (including 4 cases of trigeminal neuropathy, 1 with dyskinesias, 1 with sensory peripheral neuropathy, 1 case of intracranial haemorrhage, and 1 with CNS vasculitis), cardiac involvement in 12% (5/42) (4 cases of pericarditis which was usually mild, and 1 case of myocarditis), and renal involvement in 10% (4/42), (2 mesangial glomerulonephritis [GN], 1 focal proliferative GN, and 1 diffuse proliferative GN).

Conclusion: MCTD is a well-defined entity with a wide spectrum of clinical manifestations. Long-term follow-up reveal that some patients may have mild self-limited disease, whereas others may develop severe major organ involvement which does not always have a good prognosis.

Disclosure: J. Narváez, None; M. Pascual, None; G. Albert Espi, None; M. Millan, None; M. López de Recalde, None; J. J. Alegre, None; I. Castellví, None; C. Gomez Vaquero, None; J. M. Nolla, None.
Traditional Disease Modifying Anti-Rheumatic Drugs (tDMARDs), Hydroxychloroquine (HCQ) and/or Sulfasalazine (SSZ), Are Rapidly Effective in Immune Checkpoint Inhibitors-Induced Inflammatory Arthritis

Jessie Alperin, Jeffrey Sarazin, Leslie Fecher, Christopher Lao, Seetha Monrad, David Fox and Elena Schiopu

1University of Michigan Medical System, Ann Arbor, MI, 2Rheumatology, University of Michigan Medical System, Ann Arbor, MI, 3Oncology, University of Michigan Medical System, Ann Arbor, MI, 4Internal Medicine/Rheumatology, University of Michigan Medical System, Ann Arbor, MI, 5Internal Medicine, University of Michigan Medical System, Ann Arbor, MI

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Immune checkpoint inhibitor (ICI) therapy is widely used in the treatment of metastatic melanoma and non-small cell lung cancer and it is under investigation for multiple other cancers (lymphoma, head and neck cancers, renal cell carcinoma, urothelial carcinoma, and breast cancer). ICIs can cause a variety of immune-related adverse events, including inflammatory arthritis (IA), which is an increasingly recognized complication. A variety of interventions directed at ICI-induced IA, including corticosteroids and biologic DMARDs, have already been published with variable efficacy, but the long term side effects of glucocorticoids and malignancy risk are important challenges in this population.

Methods: We performed a retrospective chart review of all the cases of ICI-induced inflammatory arthritis referred to the Rheumatology service in a single academic center from January 2015 through May 2017 who have had at least one follow-up visit after treatment initiation. We abstracted demographic data, type of ICI used, swollen and tender joint counts, imaging (radiographic and/or high power Doppler ultrasound), laboratory data (C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)), serological data (Rheumatoid Factor (RF), anti-nuclear antibody (ANA) and anti-CCP antibodies), side effects from DMARDs and patterns of rheumatic treatment.

Results: Six patients who had a 2-month follow up were identified: age 63 ± 3.8 years, BMI of 31 ±7.3 kg/m², 5 males and 1 female, all Caucasian with stage IV metastatic melanoma (see Table); four patients developed IA after <5 months of exposure to ICI (7.8 ± 5.6 months); 2 patients developed IA 15 months after initiation of ICI with ulnar styloid erosions seen on radiographs. All patients received combinations of ipilimumab (Ipi) and/or nivolumab (Nivo) or Pembrolizumab (Pembro) prior to developing IA. At the time of our analysis, 4 patients had stopped ICIs. None of the patients had evidence of other immune/inflammatory disorders. ANA, RF and CCP were negative. Five patients received HCQ (6.5 mg/kg) and SSZ (maximum dose of 2 grams/day), and one received HCQ monotherapy; 4 patients required steroids at maximum dose of 30 mg daily; five patients completely tapered steroids by the second follow up visit; one patient had rash with SSZ. One patient achieved partial remission and 5 patients achieved complete remission of IA within 2 months.
Patient | Age(y) | Gender | ICI | Time ICIàIA (months) | Ongoing(Y/N) | tDMARD | Erosions | Pre-DMARD | Post-DMARD |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>66</td>
<td>M</td>
<td>Pembro, Ipi</td>
<td>5</td>
<td>Y</td>
<td>PLQ+SFSZ</td>
<td>N</td>
<td>2</td>
<td>L</td>
</tr>
<tr>
<td>2</td>
<td>61</td>
<td>M</td>
<td>Nivo, Ipi</td>
<td>5</td>
<td>N</td>
<td>PLQ+SFSZ</td>
<td>N</td>
<td>&gt;10</td>
<td>S+L</td>
</tr>
<tr>
<td>3</td>
<td>59</td>
<td>M</td>
<td>Ipi, Pembro</td>
<td>15</td>
<td>N</td>
<td>PLQ+SFSZ</td>
<td>Y</td>
<td>4</td>
<td>S+L</td>
</tr>
<tr>
<td>4</td>
<td>65</td>
<td>M</td>
<td>Ipi+Nivo</td>
<td>2</td>
<td>Y</td>
<td>PLQ+SFSZ</td>
<td>N</td>
<td>6</td>
<td>S+L</td>
</tr>
<tr>
<td>5</td>
<td>59</td>
<td>F</td>
<td>Nivo</td>
<td>15</td>
<td>N</td>
<td>PLQ+SFSZ</td>
<td>N</td>
<td>2</td>
<td>L</td>
</tr>
<tr>
<td>6</td>
<td>68</td>
<td>M</td>
<td>Ipi+Nivo</td>
<td>5</td>
<td>N</td>
<td>PLQ</td>
<td>Y</td>
<td>&gt;10</td>
<td>S+L</td>
</tr>
</tbody>
</table>

M=male; F=female; S=small; L=large

**Conclusion:** Combination non-immunosuppressive tDMARDs is a valid alternative in managing ICI-related IA, and it is rapidly effective and well tolerated. Our small series suggests a potential risk for erosive IA in patients managed on corticosteroids alone. Prospective registries are needed to stratify the risk for developing ICI-induced IA and to assess comparative effectiveness among traditional and biologic DMARD regimens.

**Disclosure:** J. Alperin, None; J. Sarazin, None; L. Fecher, None; C. Lao, None; S. Monrad, None; D. Fox, None; E. Schiopu, None.

**Abstract Number:** 2096

**Nailfold Capillaroscopy Is an Opportunity for Telerheumatology**

**Jacob R. Stever**, 1 Nicholas Lebedoff, 2 Tracy M. Frech, 3 Lesley A. Saketkoo 4 and Marcus Snow, 5, 1Salt Lake City VA Medical Center and University of Utah, Salt Lake City, UT, 2Internal Medicine, University of Utah, Salt Lake City, UT, 3Division of Rheumatology, University of Utah, Salt Lake City, UT, 4Rheumatology, Tulane University School of Medicine, New Orleans, LA, 5Internal Medicine, University of Nebraska, Omaha, NE

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Miscellaneous Rheumatic and Inflammatory Diseases Poster II

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The 2013 classification criteria for systemic sclerosis (SSc) provide 2 points (towards a 9 point diagnosis) for patients who have abnormal capillaroscopy. In the United States (U.S.), formal capillaroscopy training programs do not exist as part of fellowship training for assessment of patients complaining of Raynaud’s phenomenon. There is an effort in the European Union League Against Rheumatism (EULAR) microcirculation group to introduce training and certification for capillaroscopy in the United States (U.S.). The purpose of this project was to assess if U.S. trainees at a single center could effectively use nailfold videocapillaroscopy (NVC) with non-formal educational training provided by a local expert and through remote store-it-forward telehealth send images for additional teaching at other U.S. SSc centers. Additionally, the quality of dermatoscope images were compared to NVC to assess the role of this device for image capture.
Methods: Two trainees (JS and NL) had health related training in capillaroscopy, which involved observation and then hands-on performance of nailfold video capillaroscopy (NVC, Optilia®) and dermatoscope (Dermalite®) capillaroscopy on SSc registry patients. Subsequently 20 SSc patients had two NVC (Optilia®) and dermatoscope (Dermalite®) capillaroscopy on 8 digits obtained (Figure 1). These 153 images (2 patients had multiple auto-amputation) were interpreted by the two trainees and then sent to 2 U.S. members of the EULAR microcirculation group to determine whether normal versus abnormal could be effectively obtained and determined by dermatoscope, and whether trainees could identify abnormal features of NVC.

Results: The inter-rater reliability of the 153 NVC images was 0.82. Based on the NVC images all 20 patients would have been appropriately referred to a SSc center for further evaluation, but 29 images had additional abnormality features (micro-hemorrhage and neo-angiogenesis) found by the expert reviewers. Dermatoscope was able to recognize abnormal capillaroscopy in 13 of the 20 patients (65% of the time; Figure 1).

Conclusion: Store-it-forward capillaroscopy image capture with expert read is a potential modality to integrate nailfold capillaroscopy into U.S. fellowship training programs. While NVC is the gold-standard device for capillaroscopy, dermatoscope can be effectively used to evaluate the complaint of Raynaud’s phenomenon. This pilot suggests that nailfold capillaroscopy is an opportunity to integrate telehealth technology into rheumatology practice and educational curriculums.

Disclosure: J. R. Stever, None; N. Lebedoff, None; T. M. Frech, None; L. A. Saketkoo, None; M. Snow, None.
function test, and interstitial lung abnormalities (ILA) using chest computed tomography (CT). Patients were subclassified according to ILA score: 0 for no ILD, 1 for indeterminate ILD, 2 for mild ILD, and 3 for advanced ILD based on chest CT scans.

Results: In all, 29 patients had radiologically advanced ILD, 18 had mild ILD, 18 had indeterminate ILD, and 15 had no ILD. A higher ILA score was associated with more severe dyspnea, and decreased volume and percent of functional vital capacity, forced expiratory volume in 1 s, and diffusion capacity of carbon monoxide. As clinical manifestations, a higher ILA score was associated with a higher GAP index but not with the parameters of disease activity. A higher ILA score was associated with higher levels of KL-6 and SP-D and a higher percentage of subjects with abnormal levels, and this was more pronounced in SLE, SSc, and SS than in RA.

Conclusion: Serum levels of KL-6 and SP-D are associated with the radiological severity of ILD. Hence, these can serve as markers for ILD severity, especially in SLE, SSc, and SS.

Disclosure: K. E. Lee, None; J. H. Kang, None; D. J. Park, None; S. S. Lee, None.

Abstract Number: 2098

Systemic Treatment for ACUTE Anterior Uveitis (SYNTHETIC AND BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS): A Systematic Literature Review

Alejandro Gómez-Gómez,1 Estibaliz Loza,2 Maria P Rosario,3 Gerard Espinosa,4 Jose M Ruiz de Morales,5 Jose M Herreras,6 Santiago Muñoz7 and Miguel Cordero-Coma,8 1Hospital Universitario Infanta Sofía, Madrid, Spain, 2Instituto de Salud Musculoesquelética (InMusc), Madrid, Spain, 3Instituto de Salud Musculoesquelética, Madrid, Spain, 4Autoimmune Diseases Department. Hospital Clínico de Barcelona, Barcelona, Spain, 5Complejo Asistencial Universitario de León, León, Spain, 6Ophthalmology, Hospital Universitario, IOBA, Valladolid, Spain, 7Rheumatology, Hospital Infanta Sofía, Madrid, Spain, 8Ophthalmology, Hospital de León. Spain, León, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Acute anterior uveitis (AAU) is the most common form of uveitis. One third of AAU patients may present recurrences, some requiring systemic disease-modifying antirheumatic drugs (DMARDs). The aim of this study was to perform a systematic and critical literature review on the use of synthetic and biologic DMARDs in AU.

Methods: A systematic literature review was performed. Studies were identified by sensitive search strategies in the main bibliographic databases (Medline, Embase and Cochrane Library) up to July 2016. Mesh terms and text word were used. We selected articles that analyzed, in AAU patients, the efficacy or safety of DMARDs and biologic therapies including: flares, time to flare, visual acuity, corticoid sparing (CS) effect, etc. Any type of study except case series or case reports with less than 10 patients was eligible. Two reviewers (AG and EL) screened the titles and abstracts of the retrieved articles independently. Both reviewed the selected articles in detail and collected data from the studies by using ad hoc standard forms. A hand search was completed by reviewing the references of the included studies. Quality was graded using the Jadad scale and the Oxford Centre for Evidence-based Medicine Levels of Evidence. Evidence and results tables were produced.

Results: A total of 14 articles included, 2 randomized controlled trials and 12 observational studies, with low or moderate quality. The mean duration/follow-up, number (n) and patients characteristics were highly variable. The definition of the anatomic classification of AUs was generally not clear. Systemic DMARDs were used, including Methotrexate (MTX), Azathioprine (AZA), Cyclosporine A (CsA) and anti-TNFα (Adalimumab (ADA), Golimumab (GLM)), at usual dosage prescription. Number of flares, disease activity and corticoid sparing (CS) effect were the most common outcomes, with big differences between studies in variables included and their definitions. MTX showed efficacy in disease remission, n of flares, time between flares, lower activity and CS effect. SSZ showed lower
n of flares and improvement in visual acuity (VA) in AS-associated AAU patients. AZA (low quality RCT) showed no differences in VA, Tyndall, flares or IOP. A prospective OS showed lower activity and CS effect. CsA (moderate quality OS) showed efficacy improving activity and as CS agent (mid/long term). Anti-TNFα: ADA, (2 OSs) with SpA-associated AU patients lowered n of flares (mid/long term), can improve VA, Tyndall and be used as CS agent. GLM in AU patients refractory to DMARDs (some to other biologics), showed CS effect in 2 studies. One showed improvement in VA and Tyndall, but not in OCT or n of flares. Adverse events recorded were those usually registered for all these drugs.

**Conclusion:** MTX showed efficacy in idiopathic and systemic disease-associated (SDA) AU.(EL 2c; RG B), SSZ showed efficacy in idiopathic and SDA AU.(EL 3a; RG B-C), AZA seems to be effective in naïve and DMARDs-refractory AU (EL 3a; RG C), CsA showed efficacy in idiopathic and SDA AU (EL 2c; RG B-C), ADA showed efficacy in idiopathic and SDA AU, naïve or DMARDs-refractory AU (LE 2c; RG B), GLM showed efficacy in DMARD-refractory AU (2nd line and further) and other biologic therapies (EL 3a; RG B-C).

**Disclosure:** A. Gómez-Gómez, None; E. Loza, None; M. P. Rosario, None; G. Espinosa, None; J. M. Ruiz de Morales, None; J. M. Herreras, None; S. Muñoz, None; M. Cordero-Coma, None.

**Abstract Number:** 2099

**Elderly – Onset Sarcoidosis: a Single Center Comparative Study**

Senol Kobak1, Fidan Yildiz2, Huseyin Semiz3 and Mehmet Orman4, 1Rheumatology, Istinye University Faculty of Medicine, Istanbul, Turkey, 2Chest Diseases, Medicalpark Hospital, Izmir, Turkey, 3Internal Medicine, Ege University Faculty of Medicine, Izmir, Turkey, 4Statistics, Ege University Faculty of Medicine, Izmir, Turkey

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Miscellaneous Rheumatic and Inflammatory Diseases Poster II

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Sarcoidosis is a chronic granulomatous inflammatory disease characterized with non-caseified granuloma formation. It is rarely affects patients older than 65 years old. The purpose of this study is to compare and evaluate the demographic, clinical and laboratory features of elderly-onset(EOS) and young-onset sarcoidosis(YOS) patients.

**Methods:**

One hundred and thirty one patients diagnosed with sarcoidosis according to clinical, radiologic and histopathological evaluation were included in this study. The patients with initial symptoms started after age 65 were accepted as EOS. Demographic, clinic, radiologic, and laboratory data and the medication which the patients received were recorded and retrospectively evaluated.

**Results:**

Twenty (15.3%) of 131 patients were diagnosed as EOS, and 111 (84.7%) patients were evaluated as YOS. Fifteen of 20 EOS patients were female and 5 of them were male. Average duration of the disease was determined as 38.4 months for YOS and 22.5 months for EOS (p = 0.556). Delay of the diagnosis was 12 months for YOS while it was 3 months for EOS (p = 0.001). Higher rates of fatigue, comorbid diseases and more Hydroxychloroquine (HQ) use were detected in EOS patients comparing to YOS (p = 0.010, p = 0.003 and p = 0.039 respectively). There was obviously more disease modifying anti-rheumatic drugs (DMARDs) use by YOS group but statistical difference wasn’t significant. The 3-year survival rate after diagnosis of sarcoidosis was %95 in the EOS group, compared with %100 in the YOS group.

**Conclusion:**

In this study we showed that YOS and EOS patients may be presented with different clinical, and laboratory features. EOS patients are characterized with higher rates of fatigue and comorbid diseases, less inflammatory sign and delayed diagnosis, and less DMARDS.
An International Consensus Exercise to Develop Candidate Items for Classification Criteria in Relapsing Polychondritis


First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

There are no validated classification criteria for relapsing polychondritis (RP). Given that some manifestations of RP are organ- or life-threatening, it is imperative that classification criteria in RP have adequate sensitivity to identify cases early during the disease. The objective of this study was to use consensus procedures to select a set of items with potential utility to classify RP, focusing on items related to disease activity and organ damage.

Methods:

An international, multidisciplinary group of physicians with experience managing RP was formed. Based on a systematic review of publications reporting on observational cohorts, case series, and case reports data in RP, combined with clinical experience, a list of potential candidate items for classification criteria was generated. All group members were invited to participate in an online Delphi exercise for item reduction. Survey participants rated each potential candidate item on a scale of 1-10 (ranging from 1=completely inappropriate to 10=completely appropriate for inclusion as a potential classification criteria item in RP). Items with a median response score of ≤4 were eliminated from further consideration. Items with a median score of ≥7 were retained. Items with a median score >4 and <7 were termed indeterminate and will be subject to 1-2 additional Delphi rounds.

Results:
A list of 142 candidate items was generated related to patient-reported symptoms, physician-observed findings, laboratory, and imaging assessments in RP. The first round of the Delphi survey led to a response rate within 16 days of 81% (25/31). Respondents were from 6 countries (United States=15; France=3; Japan=3; Canada=2; United Kingdom=1; India=1) representing multiple subspecialties (Otolaryngology=4; Pulmonology=3; Adult Rheumatology=14; Pediatric Rheumatology=4). Based on survey responses, 49 items were retained, 34 were eliminated, and 59 were indeterminate. Most retained items were related to the respiratory, head/eyes/ears/nose/throat, and musculoskeletal systems (Figure). Items related to damage (e.g. deformed ear, tracheomalacia) were consistently rated higher than features of active disease (but non-damage) (e.g. red ear, anterior neck tenderness). The only laboratory items retained were a negative test for anti-neutrophil cytoplasmic antibody and a positive test for anti-collagen II antibody.

**Conclusion:**

This consensus exercise generated a preliminary set of candidate items for use in developing classification criteria for RP through prospective data collection. The final rounds of the Delphi will help refine what will be an extensive set of candidate items related to disease activity or damage. Development of classification criteria that represent the broad spectrum of clinical presentations in RP will facilitate the design and implementation of clinical trials in this complex disease.

![Figure](image_url)

**Disclosure:** M. A. Ferrada, None; P. A. Merkel, Actelion, Alexion, Boston Pharm., Bristol-Myers Squibb, ChemoCentryx, Genzyme/Sanofi, GlaxoSmithKline, Genentech/Roche, InflaRx, PrincipioBio, Proteon, Seattle Genetics, 5,Actelion, Bristol-Myers Squibb, CaridianBCT, Celgene, ChemoCentryx, Genentech/Roche, GlaxoSmithKline, Kypha, MedImmune/AstraZeneca, 2,-American College of Rheumatology European League Against Rheumatism National Institutes of Health: NHLBI, NIAMS, NIAID, NCATS, ORDR US Food and Drug Administration The Patient-Centered Outcomes Research Institute The Vasculitis Foundation, 2; K. A. Sikora, None; R. Colbert, None; C. Terao, None; H. Yoshifuji, None; T. Nakajima, None; A. Sharma, None; S. Sangle, None; D. Rumsey, None; C. Pagnoux, None; L. Young, None; C. K. Correll, None; F. Maldonado, None; R. Lebovics, None; A. Gelbard, None; P. Zapata, None; A. Clint, None; O. Rickman, None; N. Seam, None; G. Moulin, None; N. Costedoat-Chalumeau, None; C. J. Michet Jr., None; J. D. Katz, None; P. C. Grayson, None.

**Abstract Number:** 2101

**The Clinical Characteristics of IgG4 Related Disease in China: With 346 Cases Reported**

Panpan Zhang, Wen Zhang, Jizhi Zhao, Mu Wang, Ruie Feng, Xiaowei Liu, Xuelei Li, Yamin Lai, Xuejun Zeng, Juhong Shi, Huijuan Zhu, Huadai Xue, Wei Zhang, Hua Chen, Yunyun Fei, Linyi Peng, Xiaofeng Zeng, and Fengchun Zhang.

**Disclosure:** 1. Department of Rheumatology, Peking Union Medical College Hospital, Beijing, China
2. Rheumatology, Peking Union Medical College Hospital, Beijing, China
3. Peking Union Medical College Hospital, Beijing, China
4. Rheumatology, Peking Union Medical College Hospital, Beijing, China
5. Rheumatology, Peking Union Medical College and Chinese Academy of Medical Sciences, Peking Union Medical College Hospital, Beijing, China

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017
Background/Purpose: To study the clinical characteristics of IgG4-RD patients in China

Methods: Patients were recruited from a prospective cohort study of IgG4-RD in Peking Union Medical College Hospital between 2011 and 2016, who were followed-up for more than 6 months. The demographic characteristics, organ involvements, the laboratory examinations and treatment were analyzed

Results: A total number of 346 patients were enrolled, including male 230 (66.5%), female 116 (33.5%). The age of disease onset was 53.8 ± 14.2 years old. The mostly common related organ onset was lymphadenopathy (56.4%), submandibular glands (52.6%). Other affected organs included: swelling of the lacrimal glands (46.5%), autoimmune pancreatitis (38.4%), pulmonary involvement (28.0%), sclerosing cholangitis (25.4%), naso-sinusitis (23.4%), salivary swelling were (21.7%), retroperitoneal fibrosis (19.9%), large arteries involvement (9.5%), kidney involvement (6.9%), skin lesions (6.4%). Rarely involved organs were thyroid glands, pituitary glands, gastrointestinal tract, pachymeningitis, pericardium, sclerosing mediastinitis and orchid. The majority of patients had multi-organ involvement, 74.3% of patients with 3 and more organs involvement 18.2% and 7.5% of patients with 2 and single organ involvement respectively. The average IgG4-RD responder index (IgG4-RD RI) was 13.21±5.7. History of allergy was found in 172(49.7%) patients. Of the laboratory tests, elevated serum IgG4 levels were found in 285(94.1%) patients, and positively correlated with IgG4-RD RI. Of treatment, 33.5% patients received treatment of glucocorticoids, 52.6% patients were treated with glucocorticoids combined with immunosuppressors, 3.2% patients were treated with immunosuppressors, and 9.0% patients received no drugs at baseline evaluation. Most patients improved after regular drug treatment.

Conclusion: IgG4-RD is a systemic fibro-inflammatory disease with multiple organs involvement. The mostly common related organs respectively were lymph node, submandibular glands, and pancreas. Glucocorticoids and immunosuppressors were effective treatment strategies of IgG4-RD.

Disclosure: P. Zhang, None; W. Zhang, None; J. Zhao, None; M. Wang, None; R. Feng, None; X. Liu, None; X. Li, None; Y. Lai, None; X. Zeng, None; J. Shi, None; H. Zhu, None; H. Xue, None; W. Zhang, None; H. Chen, None; Y. Fei, None; L. Peng, None; X. Zeng, None; F. Zhang, Xian Janssen, 8.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-clinical-characteristics-of-igg4-related-disease-in-china-with-346-cases-reported

Abstract Number: 2102

The Difference between International Criteria for BD (ICBD) and the BD Criteria of International Study Group (ISG) in Our Behcet’s Disease (BD) Patients Who Fulfilled Japanese BD Criteria

Tsuyoshi Kobashigawa, Yuki Nanke, Hisashi Yamanaka and Shigeru Kotake, Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: In Japan, we have a criteria for BD since 1988. (International Journal of Tissue Reactions. 1988: 10; 59-65.) In Japanese patients diagnosed according to this Japanese BD criteria, the recent number of patients with the ocular lesions decreased compared with those with of the passed time; however, those the intestinal lesions increased. Moreover, a new international criteria for Behcet’s disease (ICBD) was proposed in 2006. (Clinical and Experimental Rheumatology. 2006: 24; S13, S14-15.) In ICBD the intestinal lesions were excluded as well as the criteria of international study group (ISG) in 1990 (Lancet. 1990: 335; 1078-80.). The purposes of this study are to analyze the clinical features of BD with comparison among four 5-year-patient groups, and to search which criteria was useful for Japanese BD patients between ISG and ICBD.
Methods: We enrolled our 264 (67.2%) BD patients out of 393. We diagnosed the patients having BD with Japanese BD criteria. We divided our patients to four groups with ones arriving period of 5 years: 49 BD patients were arrived at our clinic and started following until 2000, 70 patients from 2001 to 2005, 77 from 2006 to 2010, and 69 from 2011 to 2015, and compared symptoms of BD among four groups. We then analyzed the escape rate of our Japanese BD patients when we evaluated between ISG and ICBD. Moreover, we compared each rate, which criteria will be more usefull for Japanese BD patients comparing escape rate with chi square test.

Results: The characteristics of our 264 BD patients were as described below: 264 recurrent oral aphthous ulcers (100.0%), 206 genital ulcers (78.0%), 103 ocular manifestations (39.0%), 246 skin manifestations (93.2%), 161 arthritis (61.0%), 7 pathergy tests (2.7%), 71 intestinal lesions (26.9%), 23 neural lesions (8.7%), 22 vascular (8.3%), 11 epidemiditis (4.20%), 86 HLA-B5 (32.6%), 16 HLA-A26 (6.1%). There was no significant differentiations among periods. The escape rate of our BD patients using ISG was 12.9% (n=34) and that using ICBD was 23.4% (n=15), and statistical analyses showed that ICBD may be useful criteria for Japanese BD patient (chi’s P<0.005: p=0.0044).

Conclusion: The clinical features of our BD patients did not change among four 5-year periods. In our BD patients diagnosed with Japanese BD criteria, the diagnosing criteria for BD called ICBD was better item than ISG.

Disclosure: T. Kobashigawa, None; Y. Nanke, None; H. Yamanaka, MSD, Astellas, AbbVie, BMS, Kaken, UCB, Ono, Ayumi, Eisai, Daiichi-Sankyo, Takeda, Tanabe-Mitsubishi, Chugai, Teijin, Torii, Nipponshinyaku, and Pfizer, 2,Pfizer, YL biologics, Takeda, Teijin, BMS, Nipponkayaku, Chugai, Tanabe-Mitsubishi, Daiichi-Sankyo and Astellas, 5; S. Kotake, None.

Abstract Number: 2103

Problems in the Diagnosis of Familial Mediterranean Fever in Turkey

Mustafa Erdogan1, Yesim Ozugler1, Elif Dincses2, Sinem Nihal Esatoglu1, Gul Guzelant1, Guzin Karatemiz1, Serdal Ugurlu2, Gulen Hatemi1, Huri Ozdogan1, Hasan Yazici1 and Emire Seyahi1, 1Istanbul University, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey, 2Istanbul University, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey, 3Rheumatology, Istanbul University, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

PROBLEMS IN THE DIAGNOSIS OF FAMILIAL MEDITERRANEAN FEVER (FMF) IN TURKEY

Background/Purpose: The diagnosis of FMF can be missed or delayed even in a country like Turkey, an endemic region for FMF (1). We compared the duration of delay in diagnosis before and after year 2000, and assessed the problems related to a late diagnosis of FMF.

Methods: We studied 177 (104 F, 73 M) consecutive patients with FMF seen at our rheumatology outpatient clinic. Patients completed a self-administered questionnaire that assessed initial symptoms, previous diagnoses and treatments received before a formal diagnosis of FMF. Patients were divided in 2: Group 1, which included 128 patients seen for the first time by a physician before 2000 and Group 2, which included 49 patients seen in or after year 2000.

Results: The median age of the patients was 33 years [IQR:26-43]. The initial symptom was abdominal pain in the majority (n = 156, 88 %), followed by fever (n=139, 79%), arthritis (n=123, 69%) and pleuritic pain (n=53, 30%).

The median age at initial symptom was 8 years (IQR:5-14). The median delay in diagnosis was 11 years (IQR:4-18). This was significantly shorter in Group 2 (med. 4 years) than that observed in Group 1 (med. 15 years) as shown in Table.

A total of 146 patients (82 %) were diagnosed with one or more diseases other than FMF. These were appendicitis (n=79, 45 %), acute rheumatic fever (n=65, 37 %), gastro-intestinal diseases (n= 42, 23 %), inflammatory arthritis (n=28, 16 %), kidney stones (n=18, 10
%, gynecological diseases (n=15, 8 %) and others (n=14, 8 %). As shown in Table, the frequency of patients with misdiagnosis, was lower in Group 2 (76 %) compared to Group 1 (85 %).

A total of 88 patients (50 %) received other long-term treatments, mainly monthly penicillin (n=48), prior to colchicine. There were 53 surgical interventions in 48 patients (27 %), before the diagnosis of FMF, the most common being appendectomy in 45, followed by gastrointestinal tract surgeries (2 gastrectomies, 2 cholecystectomies, 2 intestinal herniation operations) in 6. It was noted that, the frequency of surgical operations was somewhat less in Group 2 (22 %) compared to Group 1 (30 %) (Table).

The presence or absence of MEFV mutations was assessed in 69 patients (39 %) before the diagnosis or after to confirm the diagnosis. As expected, this was significantly more frequent in Group 2 (51 %) compared to Group 1 (34 %) (Table).

73 patients (41 %) were diagnosed as FMF only after it was found out someone else in the family or a friend had a similar diagnosis. The frequency of these patients was similar when Group 1 and 2 were compared.

### Table: Demographic and clinical characteristics of patients

<table>
<thead>
<tr>
<th></th>
<th>Group 1, (n=128)</th>
<th>Group 2, (n=49)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/Female</td>
<td>48/80</td>
<td>25/24</td>
<td>Non-significant</td>
</tr>
<tr>
<td>Current age, med [IQR]</td>
<td>40[31-51.5]</td>
<td>32[24.5-38]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Delay in dx, med [IQR]</td>
<td>15 [8-22]</td>
<td>4 [1-9]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Misdiagnosed, n (%)</td>
<td>109 (85)</td>
<td>37 (76)</td>
<td>0.013</td>
</tr>
<tr>
<td>Appendicitis, n (%)</td>
<td>59 (46)</td>
<td>20 (41)</td>
<td></td>
</tr>
<tr>
<td>ARF, n (%)</td>
<td>54 (42)</td>
<td>11 (9)</td>
<td></td>
</tr>
<tr>
<td>Gastro-intestinal diseases, n (%)</td>
<td>30 (23)</td>
<td>12 (9)</td>
<td></td>
</tr>
<tr>
<td>Inflammatory arthritis, n (%)</td>
<td>22 (17)</td>
<td>6 (12)</td>
<td></td>
</tr>
<tr>
<td>Kidney stones, n (%)</td>
<td>15 (12)</td>
<td>3 (6)</td>
<td></td>
</tr>
<tr>
<td>Gynecological diseases, n (%)</td>
<td>11 (9)</td>
<td>4 (8)</td>
<td></td>
</tr>
<tr>
<td>Others, n (%)</td>
<td>14 (11)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Surgery before dx, n (%)</td>
<td>37 (30)</td>
<td>11 (22)</td>
<td>0.3</td>
</tr>
<tr>
<td>Appendectomy</td>
<td>34 (27)</td>
<td>11 (22)</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal Surgery</td>
<td>6</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Gynecological surgeries</td>
<td>1</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>1</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Penicilin treatment, n (%)</td>
<td>43 (34)</td>
<td>5 (10)</td>
<td>0.002</td>
</tr>
<tr>
<td>Dx’ed after seeing another person’s dx, n (%)</td>
<td>50 (39)</td>
<td>23 (47)</td>
<td>0.5</td>
</tr>
<tr>
<td>MEFV Gene analyses available</td>
<td>44 (34)</td>
<td>25 (51)</td>
<td>0.035</td>
</tr>
</tbody>
</table>

### Conclusion:
Although there is considerable decrease in delayed diagnosis of FMF, there is still a significant amount of misdiagnoses after the year 2000, even in a geography where FMF is highly prevalent.

### Reference:

### Disclosure:
M. Erdogan, None; Y. Ozguler, None; E. Dincses, None; S. N. Esatoglu, None; G. Guzelant, None; G. Karatemiz, None; S. Ugurlu, None; G. Hatemi, None; H. Ozdogan, None; H. Yazici, None; E. Seyahi, None.

Exposure to Fine Particle Air Pollution and Anti-Nuclear Antibodies (ANA) in a Large Population-Based Sample

Sasha Bernatsky1, Audrey Smargiassi2, Lawrence Joseph3, Patrick Belisle3 and Marvin J. Fritzler4, 1Divisions of Rheumatology and Clinical Epidemiology, Research Institute of the McGill University Health Centre, Montreal, QC, Canada, 2Université de Montreal, Montreal, QC, Canada, 3Research Institute of the McGill University Health Centre, Montreal, QC, Canada, 4Medicine, University of Calgary, Calgary, AB, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Fine particle air pollution (PM2.5) has been associated with many conditions including systemic autoimmune rheumatic diseases. Our work has previously suggested an association between estimates of exposure to industrial emissions of PM2.5 and anti-Cyclic Citrullinated Peptide (CCP), but no one to date has assessed anti-nuclear antibodies (ANA). Our purpose was to determine the association of ANA with estimates of exposure to PM2.5 (industrial emissions recorded by Environment Canada, and estimates from satellite imagery).

Methods: We assessed 2304 subjects from a large general population cohort, drawn from four census metropolitan areas in the province of Quebec, Canada. Within these 2304 patients, we performed multivariable logistic regression models for the outcome of positive ANA, assessing for independent effects of PM2.5 exposure (PM2.5 emissions and PM2.5 satellite estimates), adjusting for age, sex, smoking, and self-reported French Canadian ancestry. Exposures were determined from baseline six digit postal code of residence, to industrial PM2.5 emitters, estimated using Environment Canada's National Pollutant Release Inventory. Our analyses assessed tons of PM2.5 annual industrial emissions, distance to major industrial emitters (industry emitting more than an average of 100 tons of PM2.5) and regional satellite PM2.

Results: In multivariate analyses, the only variable convincingly associated with ANA positivity was older age (1.020, 95% CI 1.007, 1.033). Our primary multivariate estimate of the odds ratio (OR) related to ANA positivity was 1.001 (95% CI 1.000, 1.002) for PM2.5 emissions. No clear association was seen with distance to emitters in any of our models, nor with PM2.5 from satellite images, though many of our estimates being relatively imprecise and did not preclude an effect of air pollution on ANA positivity.

Conclusion: In these preliminary analyses, we did not see strong associations of ANA positivity with PM2.5 exposure. We are currently exploring additional models and considering the effects of other air pollution exposures, including nitrogen dioxide (NO2) and ultrafine particles, in a larger sample.

Disclosure: S. Bernatsky, None; A. Smargiassi, None; L. Joseph, None; P. Belisle, None; M. J. Fritzler, Inova Diagnostics, Inc., 5.


Abstract Number: 2105

Epidemiology of Interstitial Pneumonia with Autoimmune Features

Robert Mango1, Ashima Makol2, Cynthia S. Crowson3, Jay H. Ryu4 and Eric L. Matteson2, 1Internal Medicine, Division of Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, MN, MN, 2Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, MN, 3Health Sciences Research, Mayo Clinic College of Medicine and Science, Rochester, MN, 4Division of Pulmonary and Critical Care Medicine, Mayo Clinic College of Medicine and Science, Rochester, MN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster II
**Background/Purpose:**Interstitial pneumonia with autoimmune features (IPAF) is a subset of interstitial lung disease (ILD) with clinical features suggestive of, but not sufficient for, a diagnosis of a connective tissue disease (CTD). Previous reports suggest it has a prognosis intermediate between that of idiopathic pulmonary fibrosis (IPF) and that of CTD related ILD (CTD-ILD). The epidemiology and progression of IPAF in a population based cohort has not been defined.

**Methods:** All residents of a geographically-defined area who first met the Fischer criteria for IPAF (Eur Respir J 2015; 46; 976-987) in 2000-2015 were identified. Manual chart review of all patients with ILD with abnormal serologies listed in the IPAF criteria, or with at least one rheumatology evaluation was performed. Those with a diagnosis of a CTD prior to or within 6 months after ILD diagnosis were excluded. Baseline serologies, clinical characteristics, comorbidities, ILD subtype, pulmonary function tests, and echocardiograms were collected. Incidence rates were calculated and adjusted to the US white 2010 population. Mortality was estimated by Kaplan-Meier methods. The performance of GAP and ILD-GAP prognostic models was assessed using standardized incidence ratios (SIR).

**Results:** We identified 17 cases meeting classification criteria for IPAF (7 [41%] female; mean age: 72.5 years; range 35-89), with an estimated incidence of 1.2 per 100,000 (95% CI 0.6 – 1.8). The incidence increased over time (p=0.024), perhaps reflecting increasing surveillance for CTD-ILD. Based on high resolution chest CT, there were 10 (59%) with nonspecific interstitial pneumonia (NSIP), 6 (35%) with usual interstitial pneumonia (UIP), and 1 with organizing pneumonia. Seven patients (41%) were never seen by a rheumatologist but met criteria based on serologies. Antinuclear antibodies were positive in 8 patients (73%). Six patients (40%) had a DLCO < 40% or were too ill to perform DLCO at the time of meeting IPAF criteria, and these were over-represented in the UIP group (p = 0.036). Only 4 patients (24%) had pulmonary hypertension. None of the patients progressed to a diagnosis of a CTD. During a median of 2.6 years of follow-up, 10 patients died (5 year survival rate: 36%; 95% CI 18- 71; median: 1.5 years). Both the GAP and ILD-GAP models underestimated mortality (SIR for GAP: 2.16; 95% CI: 1.12-4.15; SIR for ILD-GAP: 4.79; 95% CI: 2.49-9.21). In subgroup analysis, this appeared to be due to underestimation for patients with UIP.

**Conclusion:** The incidence of patients with ILD meeting criteria for IPAF in this first ever population based study was 1.2 per 100,000, although it may be increasing over time. Patients are generally older, with mean age at the time of meeting IPAF criteria of 72.5 years. Mortality in this population-based cohort was higher than previously published estimates for IPF or CTD-ILD. The GAP and ILD-GAP prognostic models underestimated mortality, particularly in patients with a UIP pattern. Overall, outcomes in this population-based cohort were significantly worse than those previously reported for IPAF cohorts at tertiary care centers.

**Disclosure:** R. Mango, None; A. Makol, None; C. S. Crowson, None; J. H. Ryu, None; E. L. Matteson, None.

Methods: We performed a retrospective chart review of all patients treated for cancer with anti-PD1 (pembrolizumab or nivolumab) or anti-CTLA4 (ipilimumab) at the University of Iowa Hospitals and Clinics between January 2014 to April 2016. Demographic data, cancer type and stage, autoimmune diagnosis and symptoms, and drug treatment information were extracted. IrAEs included any new autoimmune disorder (i.e. inflammatory arthritis) or disease flare of pre-existing autoimmune disorder that occurred after start of ICI treatment.

Results: We identified 220 patients prescribed pembrolizumab, nivolumab, or ipilimumab. Fifteen percent (33/220) developed IrAE, 16 with anti-CTLA4 (Table 1) and 17 with anti-PD1 (Table 2). Two patients on anti-PD1 developed new onset inflammatory arthritis and were successfully treated with corticosteroids and methotrexate. Twelve patients were diagnosed with colitis, 9 with thyroid disorder or worsening of previously stable thyroid disease, 4 with pneumonitis, 2 with hypophysitis, 1 with myasthenia gravis flare, 1 with optic neuritis, 1 with psoriasis flare, and 1 with adrenal crisis. The severity of IrAEs required discontinuation of cancer therapy in 39% of those with IrAEs and 5.9% of all ICIs-treated patients.

Conclusion: Gastrointestinal and thyroid IrAEs were by far the most common, accounting for nearly two-thirds of all IrAEs. Only 2 patients developed inflammatory arthritis, and corticosteroids and methotrexate controlled symptoms in both. Additional studies are needed to determine whether one can maintain more patients on ICI treatment by earlier referral to specialist for appropriate intervention of IrAEs.

Table 1. Patient demographics, cancer type and stage, IrAE reported, and its treatment while on anti-CTLA4

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender</th>
<th>Age</th>
<th>Medication Received</th>
<th>Cancer Type</th>
<th>Stage</th>
<th>IRAE Reported</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>34</td>
<td>Ipilimumab</td>
<td>Melanoma</td>
<td>IV</td>
<td>Hypothyroidism</td>
<td>Levothyroxine</td>
</tr>
<tr>
<td>2</td>
<td>Male</td>
<td>62</td>
<td>Ipilimumab</td>
<td>Melanoma</td>
<td>IV</td>
<td>Hypothyroidism</td>
<td>Levothyroxine</td>
</tr>
<tr>
<td>3</td>
<td>Female</td>
<td>63</td>
<td>Ipilimumab</td>
<td>Melanoma</td>
<td>IIIC</td>
<td>Hypothyroidism</td>
<td>Levothyroxine</td>
</tr>
<tr>
<td>4</td>
<td>Female</td>
<td>29</td>
<td>Ipilimumab</td>
<td>Melanoma</td>
<td>IIIC</td>
<td>Hypothyroidism</td>
<td>Levothyroxine</td>
</tr>
<tr>
<td>5</td>
<td>Female</td>
<td>53</td>
<td>Ipilimumab</td>
<td>Melanoma</td>
<td>IV</td>
<td>Hypophysitis</td>
<td>Corticosteroids, endocrine consult</td>
</tr>
<tr>
<td>6</td>
<td>Male</td>
<td>64</td>
<td>Ipilimumab</td>
<td>Melanoma</td>
<td>IV</td>
<td>Hypophysitis</td>
<td>Endocrine consult, levothyroxine, systemic steroids</td>
</tr>
<tr>
<td>7</td>
<td>Male</td>
<td>65</td>
<td>Ipilimumab</td>
<td>Melanoma</td>
<td>IV</td>
<td>Adrenal crisis</td>
<td>Corticosteroids</td>
</tr>
<tr>
<td>8</td>
<td>Male</td>
<td>52</td>
<td>Ipilimumab</td>
<td>Melanoma</td>
<td>IIIC</td>
<td>Colitis</td>
<td>Corticosteroids, ipilimumab discontinued</td>
</tr>
<tr>
<td>9</td>
<td>Male</td>
<td>69</td>
<td>Ipilimumab</td>
<td>Melanoma</td>
<td>IV</td>
<td>Colitis</td>
<td>Corticosteroids, ipilimumab discontinued</td>
</tr>
<tr>
<td>10</td>
<td>Male</td>
<td>63</td>
<td>Ipilimumab</td>
<td>Melanoma</td>
<td>IV</td>
<td>Colitis</td>
<td>Corticosteroids, ipilimumab discontinued</td>
</tr>
<tr>
<td>11</td>
<td>Male</td>
<td>64</td>
<td>Ipilimumab</td>
<td>Melanoma</td>
<td>IV</td>
<td>Colitis</td>
<td>Corticosteroids</td>
</tr>
<tr>
<td>12</td>
<td>Male</td>
<td>58</td>
<td>Ipilimumab</td>
<td>Melanoma</td>
<td>IV</td>
<td>Colitis</td>
<td>Corticosteroids</td>
</tr>
<tr>
<td>13</td>
<td>Female</td>
<td>76</td>
<td>Ipilimumab</td>
<td>Melanoma</td>
<td>IV</td>
<td>Colitis</td>
<td>Corticosteroids</td>
</tr>
<tr>
<td>14</td>
<td>Male</td>
<td>57</td>
<td>Ipilimumab</td>
<td>Melanoma</td>
<td>IIIC</td>
<td>Colitis</td>
<td>Prednisone, ipilimumab discontinued</td>
</tr>
<tr>
<td>15</td>
<td>Male</td>
<td>82</td>
<td>Ipilimumab</td>
<td>Melanoma</td>
<td>IV</td>
<td>Pneumonitis</td>
<td>Corticosteroids, ipilimumab discontinued</td>
</tr>
<tr>
<td>16</td>
<td>Female</td>
<td>27</td>
<td>Ipilimumab</td>
<td>Melanoma</td>
<td>IV</td>
<td>Optic neuritis</td>
<td>Corticosteroids</td>
</tr>
</tbody>
</table>

Table 2. Patient demographics, cancer type and stage, IrAE reported, and its treatment while on anti-PD1
<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender</th>
<th>Age</th>
<th>Medication Received</th>
<th>Cancer Type</th>
<th>Stage</th>
<th>IRAE Reported</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>71</td>
<td>Nivolumab</td>
<td>Renal</td>
<td>IV</td>
<td>Inflammatory arthritis</td>
<td>Corticosteroids, Methotrexate</td>
</tr>
<tr>
<td>2</td>
<td>Female</td>
<td>67</td>
<td>Pembrolizumab</td>
<td>Melanoma</td>
<td>IV</td>
<td>Inflammatory arthritis</td>
<td>Prednisone, Methotrexate</td>
</tr>
<tr>
<td>3</td>
<td>Male</td>
<td>67</td>
<td>Pembrolizumab</td>
<td>Melanoma</td>
<td>IV</td>
<td>Psoriasis flare</td>
<td>Dexamethasone</td>
</tr>
<tr>
<td>4</td>
<td>Male</td>
<td>69</td>
<td>Pembrolizumab</td>
<td>Melanoma</td>
<td>IIIC</td>
<td>Hypothyroidism</td>
<td>Levothyroxine</td>
</tr>
<tr>
<td>5</td>
<td>Male</td>
<td>50</td>
<td>Pembrolizumab</td>
<td>Melanoma</td>
<td>IV</td>
<td>Hypothyroidism</td>
<td>Levothyroxine</td>
</tr>
<tr>
<td>6</td>
<td>Female</td>
<td>71</td>
<td>Nivolumab</td>
<td>Renal</td>
<td>IV</td>
<td>Hypothyroidism</td>
<td>Levothyroxine</td>
</tr>
<tr>
<td>7</td>
<td>Female</td>
<td>66</td>
<td>Nivolumab</td>
<td>Lung adenocarcinoma</td>
<td>IV</td>
<td>Autoimmune thyroiditis</td>
<td>Endocrine consult, nivolumab stopped.</td>
</tr>
<tr>
<td>8</td>
<td>Male</td>
<td>47</td>
<td>Pembrolizumab</td>
<td>Clear cell sarcoma</td>
<td>IV</td>
<td>Autoimmune thyroiditis</td>
<td>Levothyroxine, endocrine consult</td>
</tr>
<tr>
<td>9</td>
<td>Male</td>
<td>76</td>
<td>Pembrolizumab</td>
<td>Melanoma</td>
<td>IV</td>
<td>Myasthenia gravis flare</td>
<td>Corticosteroids, plasmapheresis, pembrolizumab discontinued</td>
</tr>
<tr>
<td>10</td>
<td>Male</td>
<td>57</td>
<td>Pembrolizumab</td>
<td>Melanoma</td>
<td>IV</td>
<td>Colitis</td>
<td>GI consult, budesonide, pembrolizumab continued.</td>
</tr>
<tr>
<td>11</td>
<td>Female</td>
<td>45</td>
<td>Nivolumab</td>
<td>Bladder</td>
<td>IV</td>
<td>Colitis</td>
<td>Corticosteroids</td>
</tr>
<tr>
<td>12</td>
<td>Female</td>
<td>73</td>
<td>Nivolumab</td>
<td>Melanoma</td>
<td>IV</td>
<td>Colitis</td>
<td>Corticosteroids, budesonide</td>
</tr>
<tr>
<td>13</td>
<td>Female</td>
<td>77</td>
<td>Nivolumab</td>
<td>Melanoma</td>
<td>IV</td>
<td>Ulcerative colitis flare</td>
<td>Corticosteroids, nivolumab discontinued after 2nd flare</td>
</tr>
<tr>
<td>14</td>
<td>Male</td>
<td>63</td>
<td>Nivolumab</td>
<td>Melanoma</td>
<td>IV</td>
<td>Colitis</td>
<td>Corticosteroids, nivolumab discontinued</td>
</tr>
<tr>
<td>15</td>
<td>Male</td>
<td>65</td>
<td>Nivolumab</td>
<td>Lung adenocarcinoma</td>
<td>IIIA</td>
<td>Pneumonitis</td>
<td>Corticosteroids, nivolumab continued. Nivolumab discontinued after 2nd flare</td>
</tr>
<tr>
<td>16</td>
<td>Female</td>
<td>51</td>
<td>Nivolumab</td>
<td>NSCLC</td>
<td>IV</td>
<td>Pneumonitis</td>
<td>Corticosteroids, nivolumab discontinued</td>
</tr>
<tr>
<td>17</td>
<td>Male</td>
<td>60</td>
<td>Nivolumab</td>
<td>Renal</td>
<td>IV</td>
<td>Pneumonitis</td>
<td>Corticosteroids, nivolumab discontinued</td>
</tr>
</tbody>
</table>

Disclosure: T. Doberstein, None; A. Kaur, None; E. Field, None; N. Singh, None.


Abstract Number: 2107

**Therapeutic Response to Prednisone in Relation to Age in Polymyalgia Rheumatica: A Controlled Study**
Polymyalgia rheumatica (PMR) is an inflammatory rheumatic disorder which usually affect patients over 65 years old. Different poor prognostic factors are involved in prednisone response including rapid decrease of prednisone dose or female sex. To date, there is no data relating the impact of the age on therapeutic response in PMR. The aim of this study was to compare, in case of PMR, the response to prednisone in patients younger than 60 to patients over 65 years old.

Methods:

This was a retrospective, monocentric study. We included patients with PMR, meeting ACR 2012 criteria. Patients were classified into two groups, one group with patients less than 60 years, and one group with patients over 65 years. We registered demographic, clinical, biological, and imaging data as well as therapeutic response profile. The local inflammation was evaluated with PET scan, by studying each anatomical site usually affected by PMR. Then, the rate of inflammation was scored from 0 to 3, according to the intensity of uptake compared to liver. The treatment was standardized. The initial dose of prednisone was of 0.3mg/kg/j during the two first weeks, then, the dose was slowly decreased by 10% each month. The main endpoint was a steroid dependence defined by the recurrence of PMR symptoms and/or the increase of CRP at two times during the decrease of prednisone.

Results:

We included 14 patients younger than 60 years old (average age 54 +/- 0.8 years) and 28 patients older than 65 years old (average age 75.8 +/- 1.5 years). The population younger than 60 years was mainly male (60% VS 27 %, p<0.05). Both groups were similar in terms of morning stiffness (2.1 ± 0.4 VS 1.9 ± 0.3 hours; p>0.05), disease duration (4.2 ± 0.8 VS 4.1 ± 0.6 months; p>0.05), leukocytes rate (8.3 ± 1.37 VS 8 ± 0.7 G/L; p=0.05) and percentage of antinuclear antibodies rate over 1/320 (20 % VS 10%; p>0.05). However, regarding to local inflammation, the intensity of FDG uptake highlighted by the PET scan was lower among young patients (score of 16.9 ± 1.7 VS 26.5 ± 3.0; p<0.05). Furthermore, we observed a significant difference concerning therapeutic response according to the age: 60% of the young patients developed a steroid dependence compared to 20% in group of old patients (p<0.05). Moreover, the introduction of methotrexate was necessary for 35% of the young patients against 6.5% (p<0.05).

Conclusion:

Our study is the first to show the age as a bad prognosis factor in case of PMR. This difference is independent to the systemic and local inflammation (assessed by the PET score) is more important in elderly people. Young patients with PMR are mostly men and are more dependent on steroids. Thus, methotrexate could be straightaway proposed, particularly in patient younger than 60 years old.
Background/Purpose: Familial Mediterranean fever (FMF) is an autoinflammatory disease. Colchicine is used in FMF patients for preventing attacks and amyloidosis. There were conflicting reports as to existence of proarrhythmic electrocardiographic (ECG) findings in FMF(1,2). Furthermore, studies showed that colchicine might be protective in non FMF patients against atrial fibrillation(3). Besides, its effect on FMF patients was not evaluated. In the present study, in order to evaluate effect of colchicine treatment on arrhythmia risk in FMF patients, we assessed ECG of the new diagnosed FMF patients for arrhythmatogenic anomalies at baseline and after one year of colchicine treatment.

Methods: Twenty eight new diagnosed FMF patients who fulfilled Modified Tel-hashomer criteria were recruited to study. After baseline measurements, colchicine treatment was started. ECG, laboratory parameters, demographic and disease related parameters of the patients were obtained at the first visit and after one year of treatment. We evaluated the risk of atrial arrhythmia with P dispersion and risk of ventricular arrhythmia with Tp-E, Tp-E/Qt, Tp-E/Qtc (2). P dispersion ≥ 40 ms was accepted as arrhythmatogenic anomaly for atrial arrhythmias(2).

Results: Demographic, laboratory and disease related characteristics of the patients at baseline were shown in Table 1. There was no statistical difference between the number of patient with arrhythmatogenic P dispersion at baseline and after one year of treatment. Furthermore, Tp-E, Tp-E/Qt values decreased with treatment (Table 2).
<table>
<thead>
<tr>
<th>Patients (n=28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (M/F)</td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Age at first attack</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
</tr>
<tr>
<td>Smoking (%)</td>
</tr>
<tr>
<td>Co-morbid illnesses* (%)</td>
</tr>
<tr>
<td>Frequency of attacks (/year)</td>
</tr>
<tr>
<td>Duration of attacks (day)</td>
</tr>
<tr>
<td>Main FMF symptom</td>
</tr>
<tr>
<td>Peritonitis (%)</td>
</tr>
<tr>
<td>Fever (%)</td>
</tr>
<tr>
<td>Musculoskeletal symptoms (%)</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
</tr>
<tr>
<td>ALT (IU/L)</td>
</tr>
<tr>
<td>AST(IU/L)</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
</tr>
<tr>
<td>Sedimentation rate (mm/h)</td>
</tr>
<tr>
<td>Spot urine protein/creatinine</td>
</tr>
<tr>
<td>WBC (/mcL)</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
</tr>
<tr>
<td>Platelet (x10⁶/mcL)</td>
</tr>
<tr>
<td>Documented tachycardia (%)</td>
</tr>
</tbody>
</table>

BMI: Body mass index; ALT: Alanin aminotransferase; AST: Aspartate aminotransferase; CRP: C-reactive protein; WBC: White blood cell

*Hypertension, hypothyroidism, hyperthyroidism cardiovascular diseases, coronary artery diseases, cerebrovascular diseases, chronic renal disease, chronic obstructive pulmonary disease, diabetes mellitus

Table 2. Electrocardiographic findings and disease parameters of the patients at baseline and after one year of colchicine treatment

<table>
<thead>
<tr>
<th>Pretreatment ( n=28)</th>
<th>Treatment* (n=28)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tp-E interval (ms)</td>
<td>69.93±14.68</td>
<td>66.21±14.35</td>
</tr>
<tr>
<td>Tp-E/Qt ratio</td>
<td>0.21±0.04</td>
<td>0.19±0.03</td>
</tr>
<tr>
<td>Tp-E/Qt coefficient</td>
<td>0.17±0.37</td>
<td>0.16±0.03</td>
</tr>
<tr>
<td>P dispersion</td>
<td>31.64±11.67</td>
<td>32.93±10.33</td>
</tr>
<tr>
<td>P dispersion ≥ 40 ms</td>
<td>7 (25.0%)</td>
<td>10 (35.7%)</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>19.17±31.97</td>
<td>9.46±17.12</td>
</tr>
<tr>
<td>Sedimentation rate</td>
<td>23.75±16.60</td>
<td>16.79±14.93</td>
</tr>
<tr>
<td>Frequency of attacks</td>
<td>10.60±7.00</td>
<td>0.80±1.24</td>
</tr>
<tr>
<td>Colchicine dosage</td>
<td>1.23±0.31</td>
<td></td>
</tr>
</tbody>
</table>

* Electrocardiographic measurements and disease parameters of the patients evaluated after one year of colchicine treatment

**Actual colchicines dosage at the first year of the treatment

p<0.05 shown with bold numbers
Conclusion: We found that colchicine treatment may have no effect on atrial arrhythmia risk. Furthermore, it might have favorable effect on ventricular repolarization indices and might be protective against ventricular arrhythmias and sudden death in FMF patients.

References:


Disclosure: A. Gozek Ocal, None; L. Ocal, None; M. E. Tezcan, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/colchicine-treatment-may-be-protective-against-ventricular-arrhythmias-in-fmf-patients

Abstract Number: 2109

Hyperferritinemic Syndrome in a General Hospital

Ignacio Javier Gandino1, Florencia Pierini2, Jose Maximiliano Martinez P2, Santiago Ruta2, Marina Scolnik2 and Enrique R Soriano4, 1Reumatologia, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina, 2Rheumatology Unit, Internal Medicine Service, Hospital Italiano de Buenos Aires, CABA, Argentina, 3Rheumatology, Internal Medicine Service, Rheumatology Unit, Internal Medicine Service, Hospital Italiano de Buenos Aires, Instituto Universitario Hospital Italiano de Buenos Aires, and Fundacion PM Catoggio, Buenos Aires, Argentina, 4Argentina, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Hyperferritinemia is associated with inflammatory conditions, such as rheumatologic diseases. Objectives: To determine which diseases are associated with hyperferritinemia in a tertiary hospital; to compare ferritin levels between these different entities and to evaluate relationship between levels of ferritin and mortality in these patients.

Methods: A retrospective study was carried out in which all patients over 18 years with at least one determination of serum ferritin equal to or greater than 1000 ng/ml were identified in the laboratory database of our hospital between 2006 and 2016. Corresponding electronic medical records were reviewed and demographic data and clinical data were collected. Mortality was assessed at the end of follow-up. A descriptive statistical analysis and logistic regression analysis were performed in order to identify variables associated with mortality.

Results: 1979 patients were included, 1235 men with a mean age of 63.2 years (SD 17.2). Only 36 patients (1.8%) presented a rheumatologic diagnosis as the only cause of high levels of ferritin. Still's disease and systemic Vasculitis being the main diagnoses. Table 1 shows patients’ characteristics grouped according to whether the elevation of ferritin was associated with a rheumatic disease or not. Median serum ferritin and transferrin saturation in both groups were similar. Mortality was lower for rheumatologic causes (5.9% vs 37.2%, p <0.001). Variables that were associated with mortality in multivariable logistic regression analysis were: maximum ferritin value (OR 1.0004, 95% CI 1.0003-1.0004, p <0.001) and age (OR 1.03, 95%CI 1.02-1.04, p <0.001), whereas rheumatologic diagnosis was a protective factor for mortality (OR 0.11, 95% CI 0.03-0.47, p = 0.003 ). ROC curve for ferritin and mortality showed an area under the curve of 0.59 (95%CI 0.58-0.62). Ferritin levels greater than 3000 ng/ml showed a specificity of 89.2% and a sensitivity of 19.7% for mortality, regardless of cause.

Conclusion: rheumatologic diseases, although representing a smaller percentage of the causes of elevation of ferritin above 1000 ng / ml, were associated with lower mortality than the non rheumatologic causes of hyperferritinemia. Serum ferritin levels were significantly associated with increased mortality regardless of the underlying cause.

Table1 Patients’ characteristics grouped by cause of Hyperferritinemia
<table>
<thead>
<tr>
<th></th>
<th>Only rheumatologic disease (n=35)</th>
<th>Other causes of ferritin elevation (n=1944)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%)</td>
<td>13 (37.1)</td>
<td>731 (37.6)</td>
<td>0.96</td>
</tr>
<tr>
<td>Mean age, years (DS)</td>
<td>62.5 (17.1)</td>
<td>52.4 (21.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diagnostic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
<td>4</td>
<td>Solid cancer</td>
<td>497</td>
</tr>
<tr>
<td>SLE</td>
<td>3</td>
<td>Onco-hematologic disease</td>
<td>302</td>
</tr>
<tr>
<td>Vasculitis</td>
<td>9</td>
<td>Chronic renal insufficiency</td>
<td>236</td>
</tr>
<tr>
<td>Still’s disease</td>
<td>8</td>
<td>Sepsis</td>
<td>46</td>
</tr>
<tr>
<td>Gout</td>
<td>2</td>
<td>Infections</td>
<td>336</td>
</tr>
<tr>
<td>Seronegative arthritis and psoriatic arthritis</td>
<td>3</td>
<td>Hepatic disease</td>
<td>188</td>
</tr>
<tr>
<td>IgG4</td>
<td>1</td>
<td>Hematologic disease</td>
<td>128</td>
</tr>
<tr>
<td>Juvenile idiopathic arthritis</td>
<td>1</td>
<td>Cardiovascular</td>
<td>57</td>
</tr>
<tr>
<td>Myositis</td>
<td>1</td>
<td>Iron overload</td>
<td>2</td>
</tr>
<tr>
<td>Others</td>
<td>3</td>
<td>Others</td>
<td>152</td>
</tr>
<tr>
<td>Serum ferritin, median (IQR)</td>
<td>1622 (1264-3639)</td>
<td>1460 (1200-2140)</td>
<td>0.07</td>
</tr>
<tr>
<td>Transferrin saturation, %, median (IQR)</td>
<td>38 (19-50)</td>
<td>33 (18-55)</td>
<td>0.83</td>
</tr>
<tr>
<td>Follow-up time, years, median (IQR)</td>
<td>5.2 (1.2-10.2)</td>
<td>5.7 (1.2-8.9)</td>
<td>0.97</td>
</tr>
<tr>
<td>Mortality, n (%)</td>
<td>2 (5.9)</td>
<td>698 (37.2)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Disclosure:** I. J. Gandino, None; F. Pierini, None; J. M. Martinez P, None; S. Ruta, None; M. Scolnik, None; E. R. Soriano, Abbvie, Janssen, Novartis, Pfizer Inc, UCB, 2, Abbvie, Janssen, Novartis, Pfifer Inc, UCB, 5, Abbvie, Bristol-Myers Squibb, Janssen, Novartis, Pfifer Inc, Roche, UCB, 8.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/hyperferritinemic-syndrome-in-a-general-hospital](http://acrabstracts.org/abstract/hyperferritinemic-syndrome-in-a-general-hospital)

**Abstract Number: 2110**

**Blood Group ”a“ Was Increased in FMF Patients and Blood Group ”0“ May be Associated with Colchicine Resistance**

Abdulsamet Erden¹, Ezgi Deniz Batu², Berkan Armagan³, Hafize Emine Sonmez⁴, Alper Sari⁵, Selcan Demir⁶, Emre Bilgin⁷, Esra Firat⁸, Levent Kilic¹, Yelda Bilginer⁹, Omer Karadag¹, Umut Kalyoncu¹ and Sedat Kiraz¹, ¹Department of Internal Medicine, Division of Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Turkey, ²Department of Pediatrics, Division of Rheumatology, Hacettepe University Faculty of Medicine, ANKARA, Turkey, ³Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Turkey, ⁴Department of Pediatrics, Division of Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Turkey, ⁵Department of Internal Medicine, Hacettepe University Faculty of Medicine, Ankara, Turkey, ⁶Department of Pediatrics, Division of Rheumatology, Hacettepe University Faculty of Medicine, ANKARA, Turkey.
Background/Purpose: Colchicine is the main therapy for familial Mediterranean fever (FMF). However, about 5-10% of FMF patients are colchicine-resistant (1). The reason for colchicine resistance in FMF patients remains obscure. ABO genes are distributed differently among socioeconomic groups, and socioeconomic status is one of the risk factors for disease severity in FMF. To date, no report has evaluated this relation. Our aim was to investigate the association between blood groups and colchicine resistance in FMF patients.

Methods: This is a single-center, cross-sectional study. Between January and December 2016 385 FMF patients were assessed by the Adult and Pediatric Rheumatology outpatient clinics and 297 patients had blood groups (ABO and Rh) results. The blood groups in 1000 volunteer donors who admitted to the Turkish Red Crescent Blood Service in Ankara in 2015 were enrolled as healthy control group. Demographic and clinical data collected for each patient. Response to colchicine was evaluated by two experts (YB and UK). The patients were grouped into two groups: colchicine-responsive patients (Group CR) and colchicine-unresponsive patients (Group CUR).

Results: 297 patients were included in the study. As expected, the acute phase reactants were higher and arthralgia/arthritis, pleuritic chest pain, and erysipelas-like erythema were more frequent in group CUR (p<0.05). FMF patients had frequently blood group “A” than healthy controls (152/297 (51.2%) vs 420/1000 (42.0%), p=0.006). Patients with blood group “A” had 1.5 folds higher FMF compared to “non-A” blood group [OR 1.50 (95% CI 1.11-1.87)], particularly having “A” Rh (+) blood group [OR 1.47 (95% CI 1.13-1.91)]. Furthermore, patients with blood group “A” had a better response to colchicine treatment than “non-A” blood group OR 2.21 (95% CI 1.15-4.27). On the contrary, patients with blood group “0” had prominently associated with unresponsive to colchicine (Table 1).

Table 1. Comparison of blood groups between colchicine unresponsive and responsive familial Mediterranean fever (FMF)a patients

<table>
<thead>
<tr>
<th>ABO / Rh blood group</th>
<th>Colchicine unresponsive FMF patients (n=46)</th>
<th>Colchicine responsive FMF patients (n=251)</th>
<th>Odds ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>O</td>
<td>21 (45.7)</td>
<td>71 (28.3)</td>
<td>2.12 (1.12-4.04)</td>
<td>0.019</td>
</tr>
<tr>
<td>Non- O</td>
<td>25 (54.3)</td>
<td>180 (71.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>O Rh (-)</td>
<td>6 (13.0)</td>
<td>7 (2.8)</td>
<td>5.31 (1.69-16.62)</td>
<td>0.002</td>
</tr>
<tr>
<td>Non- O Rh(-)</td>
<td>40 (87.0)</td>
<td>244 (97.2)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: It is well known that blood group A is associated with some of the Cancer such as stomach (2). It may also be related to inflammatory diseases (3). Our results may support associations of blood groups and inflammatory diseases. We demonstrated the blood subgroups and colchicine responses, as well. ABO blood group phenogroups may be used in combination with other risk factors to identify FMF patients at high risk for colchicine resistance.

References


Disclosure: A. Erden, None; E. D. Batu, None; B. Armagan, None; H. E. Sonmez, None; A. Sari, None; S. Demir, None; E. Bilgin, None; E. Firat, None; L. Kilic, None; Y. Bilginer, None; O. Karadag, None; U. Kalyoncu, None; S. Kiraz, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/blood-group-a-was-increased-in-fmf-patients-and-blood-group-0-may-be-associated-with-colchicine-resistance](http://acrabstracts.org/abstract/blood-group-a-was-increased-in-fmf-patients-and-blood-group-0-may-be-associated-with-colchicine-resistance)

Abstract Number: 2111
Anti-N-Methyl-D-Aspartate Receptor Encephalitis – Expanding Our Understanding of the Clinical Needs of Pediatric Patients with This Complex Disorder

Katherine A. Battisti1, Tobias J. Tsai2, Angela Pickersgill3 and Sheetal S. Vora4, 1Emergency Medicine, Nationwide Children's Hospital, Columbus, OH, 2Physical Medicine and Rehabilitation, Levine Children's Hospital/Carolinas Medical Center, Charlotte, NC, 3Pediatrics, Levine Children's Hospital, Charlotte, NC, 4Pediatric Rheumatology, Levine Children's Hospital, Charlotte, NC

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Although recognized only 10 years ago, anti-N-Methyl-D-Aspartate receptor encephalitis (anti-NMDAR encephalitis) has become a leading cause of encephalitis with an identifiable etiology in pediatric patients1. The clinical presentation of patients with this disorder is quite variable but typically involves acute onset of symptoms with a characteristic progression including movement disorders, psychiatric symptoms, autonomic instability and seizures2. Despite efforts to fully understand this disorder, there continue to be gaps in our knowledge.

Methods: This was a retrospective chart review of patients admitted to a mid-sized tertiary pediatric hospital for medical or rehabilitative services with a diagnosis of anti-NMDAR encephalitis over a 41 month period. Only patients with laboratory evidence of anti-NMDAR encephalitis between the ages of 24 months and 18 years were included in this study.

Results: 12 patients met our inclusion criteria ranging in age from 2 years to 17 years of age with a median age of 9. These patients represent 12.5% of the patients with a diagnosis of encephalitis at our hospital during this time frame. 58% were female. Multiple ethnicities and socioeconomic backgrounds were represented. All but one patient presented with sudden onset of unexplained behavioral change from baseline. Mean time to diagnosis was 17 days. Eleven out of twelve patients had a minimum of 3 of the 8 characteristic symptoms noted in 90% of patients3. One patient died of overwhelming sepsis while immunosuppressed. Only one patient was found to have an associated tumor. 41% of patients required a PICU admission. All of the patients required inpatient rehabilitation. 75% of patients required gastrostomy tube placement. 25% of patients have returned to baseline and another 16% demonstrated functional gains by the most recent follow up. Many are still in the initial 12-24 months of recovery so their outcomes are still undetermined. 3 of the 12 patients in our study had pre-existing cognitive deficits or propensity for them; these patients were noted to all have incomplete recovery.

Conclusion: Though previously described, anti-NMDAR encephalitis may be more common than we recognize. In this study we present 12 cases of anti-NMDAR encephalitis treated at a single center pediatric tertiary care institution. We found no correlation of time to diagnosis with ethnicity or socioeconomic status. Our series corroborates the current literature with most patients presenting with acute unexplained behavioral change. Many patients required intensive care management. Their recovery is prolonged and almost invariably requires inpatient rehabilitation and often gastrostomy tubes. This suggests that management at a tertiary care center and early physical medicine and rehabilitation consultation is recommended. Recovery for these patients is mixed, and though our study is too small to reach statistical significance, we did note a trend in patients with pre-existing cognitive deficits or propensity for them who seem to have diminished recovery compared to patients with no prior history suggesting the need for further research in this area.

Disclosure: K. A. Battisti, None; T. J. Tsai, None; A. Pickersgill, None; S. S. Vora, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/anti-n-methyl-d-aspartate-receptor-encephalitis-expanding-our-understanding-of-the-clinical-needs-of-pediatric-patients-with-this-complex-disorder

Abstract Number: 2112

Anti-TNFα Versus Rituximab in Refractory Peripheral Ulcerative Keratitis Associated to Rheumatic Diseases. Multicenter Study of 24 Patients

Lucia C. Domínguez-Casas1, Vanesa Calvo-Rio1, Olga Maiz-Alonso2, Ana Blanco3, Emma Beltran4, Lucía Martínez Acosta5, María Concepcion Alvarez de Buergo6, Esteban Rubio-Romero7, David Diaz-Valle8, R López-González9, Angel Garcia-Aparicio10, Antonio Juan Mas11, Enar Pons1, Rosalia Demetrio12, Nuria Vegas-Revenga1, José Luis Martín-Varillas1, Belén Atienza-Mateo1, Carlos
Peripheral ulcerative keratitis (PUK) is a severe inflammation of the outer portions of the cornea that may lead to perforation. It may be associated with rheumatic diseases. The treatment is based on systemic corticosteroids and conventional immunosuppressive drugs. In refractory cases, biological therapy may be needed.

Our aim was to compare anti-TNFα vs Rituximab (RTX) in refractory PUK.

**Methods:**

Multicenter study of 24 patients with PUK. All of them presented inadequate response to corticosteroids and at least 1 systemic traditional immunosuppressive drug.

Anti-TNFα were used in 17 patients: Adalimumab (n=9) 40 mg/sc every 1-2 weeks, infliximab (IFX) (n=7) 3-5 mg/kg iv/4-6 weeks, etanercept (n=1) 50 mg/week. RTX was used in 7 patients 1-2 g i.v. every 6 or 12 months.

The main outcomes were Best Corrected Visual Acuity (BCVA), signs of inflammation (scleritis and episcleritis), progression to corneal thinning, central keratolysis, and ocular perforation.

Comparisons were made between baseline and 1st month, 6th month, and 1st year (STATISTICA, StatSoft Inc. Tulsa, Oklahoma, USA). Quantitative variables were expressed as mean±SD or median [IQR], accordingly to its distribution. They were compared with the Student t or the Mann-Whitney U test respectively. Dichotomous variables were expressed as percentages and compared by the chi-square test.

**Results:**

We studied 24 patients/32 affected eyes. The underlying diseases in the anti-TNFα group were Rheumatoid Arthritis (RA) (n=14), Psoriatic Arthritis (n=2) and Behçet Disease (n=1); and in the RTX group: RA (n=5), granulomatous polyangiitis (n=1) and microscopic polyangiitis (n=1).

At baseline there were no significant differences between both groups in general features or in ocular involvement (TABLE). Before biological therapy they had received the following systemic drugs (anti-TNFα vs RTX) i.v. metilprednisolone (2 vs 4), doxycycline (7 vs 1), ascorbic acid (2 vs 0), MTX (11 vs 4), AZA (1 vs 2) and others (7 vs 3). In addition, 10 patients, in both groups, had to be undergoing to surgery: amniotic membrane (n=5), penetrating keratoplasty (n=2), conjunctival resection (n=2), tissue adhesives (n=2), conjunctival flap (n=1) and lamellar keratoplasty (n=1).

Once the treatment was initiated the ocular evolution was similar (TABLE).

After a men follow-up of 22.53±22.60 (anti-TNFα) and 22.28±8.28 months with RTX the following severe side effects were observed: supraventricular tachycardia (n=1) with RTX and pulmonary Tuberculosis (n=1) with IFX.

**Conclusion:**

In this study, anti-TNFα therapy and RTX seem to be equally effective for the treatment of peripheral ulcerative keratits associated to rheumatic diseases refractory to conventional treatment.
TABLE. Evolution of ocular parameters with antiTNFα and RTX

<table>
<thead>
<tr>
<th></th>
<th>anti-TNFα</th>
<th>RTX</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=17</td>
<td>n=7</td>
<td></td>
</tr>
<tr>
<td>General features</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex (♂/♀)</td>
<td>4/2</td>
<td>13/5</td>
<td>0.79</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>59.1±18.3</td>
<td>54.28±10.7</td>
<td>0.49</td>
</tr>
<tr>
<td>Ocular bilateral</td>
<td>23.53</td>
<td>57.14</td>
<td>0.13</td>
</tr>
<tr>
<td>involvement #</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of underlying</td>
<td>183.06±18.3</td>
<td>138.85±77.68</td>
<td>0.59</td>
</tr>
<tr>
<td>diseases (days)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BCVA*</td>
<td>0.58±0.38</td>
<td>0.56±0.34</td>
<td>0.68</td>
</tr>
<tr>
<td>Peripheral thinning #</td>
<td>18</td>
<td>9</td>
<td>0.77</td>
</tr>
<tr>
<td>Central keratolysis #*</td>
<td>4</td>
<td>1</td>
<td>0.59</td>
</tr>
<tr>
<td>Ocular perforation #</td>
<td>2</td>
<td>1</td>
<td>0.89</td>
</tr>
<tr>
<td>Scleritis #</td>
<td>3</td>
<td>8</td>
<td>0.001</td>
</tr>
<tr>
<td>Episcleritis #</td>
<td>3</td>
<td>4</td>
<td>0.15</td>
</tr>
<tr>
<td>Uveitis #</td>
<td>3</td>
<td>2</td>
<td>0.77</td>
</tr>
<tr>
<td>1st month</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BCVA *</td>
<td>0.67±0.31</td>
<td>0.56±0.27</td>
<td>0.67</td>
</tr>
<tr>
<td>Peripheral thinning #</td>
<td>5</td>
<td>6</td>
<td>0.032</td>
</tr>
<tr>
<td>Central keratolysis #*</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ocular perforation #</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Scleritis #</td>
<td>1</td>
<td>1</td>
<td>0.54</td>
</tr>
<tr>
<td>Episcleritis #</td>
<td>1</td>
<td>0</td>
<td>0.45</td>
</tr>
<tr>
<td>Uveitis #</td>
<td>1</td>
<td>2</td>
<td>0.23</td>
</tr>
<tr>
<td>6th month</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BCVA *</td>
<td>0.7±0.25</td>
<td>0.73±0.29</td>
<td>0.67</td>
</tr>
<tr>
<td>Peripheral thinning #</td>
<td>9</td>
<td>3</td>
<td>0.14</td>
</tr>
<tr>
<td>Central keratolysis #*</td>
<td>0</td>
<td>3</td>
<td>0.028</td>
</tr>
<tr>
<td>Ocular perforation #</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Scleritis #</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Episcleritis #</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Uveitis #</td>
<td>1</td>
<td>0</td>
<td>0.38</td>
</tr>
<tr>
<td>1st year</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BCVA *</td>
<td>0.75±0.22</td>
<td>0.70±0.24</td>
<td>0.77</td>
</tr>
<tr>
<td>Peripheral thinning #</td>
<td>7</td>
<td>3</td>
<td>0.25</td>
</tr>
<tr>
<td>Central keratolysis #*</td>
<td>1</td>
<td>1</td>
<td>0.89</td>
</tr>
<tr>
<td>Ocular perforation #</td>
<td>0</td>
<td>1</td>
<td>0.30</td>
</tr>
<tr>
<td>Scleritis #</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Episcleritis #</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Uveitis #</td>
<td>1</td>
<td>0</td>
<td>0.35</td>
</tr>
</tbody>
</table>

* Results are expressed as mean±SD; # Results are expressed as %

Disclosure: L. C. Domínguez-Casas, None; V. Calvo-Río, None; O. Maiz-Alonso, None; A. Blanco, None; E. Beltran, None; L. Martínez Acosta, None; M. C. Álvarez de Buergo, None; E. Rubio-Romero, None; D. Diaz-Valle, None; R. López-González, None; A. García-Aparicio, None; A. J. Mas, None; E. Pons, None; R. Demetrio, None; N. Vegas-Revenga, None; J. L. Martín-Varillas, None; B. Atienza-Mateo, None; C. Fernández-Díaz, None; J. L. Hernández, None; M. A. González-Gay, None; R. Blanco, None.
Familial Mediterranean Fever in Chinese Adult Patients

Di Wu and Min Shen, Rheumatology, Peking Union Medical College Hospital, Beijing, China

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Familial Mediterranean fever (FMF) is the most common monogenic autoinflammatory disease (AUID) worldwide. There have been hardly any cases reported in Chinese population. We aimed to describe the first cohort of adult FMF patients in Chinese population.

Methods:
We prospectively evaluated clinical and genetic features of adult patients suspected of FMF at the our adult AUID center from April 2015 through April 2017. Patients were diagnosed clinically according to Tel-Hashomer criteria. Whole exome sequencing by Next Generation Sequencing was performed in every patient.

Results:
During the study period, a total of 11 adult patients were diagnosed as FMF. The male to female ration is 8:3. The median age at disease onset was 31 years. All patients were of Chinese Han ethnicity without positive family history. All patients had intermittent self-limiting febrile episodes. Two patients had fever duration of less than 3 days, 7 patients had fever duration of 3 to 7 days. The interval between attacks ranged from weeks to years. During attacks, 7 patients developed generalized abdominal pain; 3 patients experienced chest pain with clear evidence of pleuritis, 2 of which also have evidence of pericarditis; 4 patients had arthritis involving large joints; none of the patients reported erysipelas-like skin lesion. Other manifestations included: pharyngitis, headache, aphthous stomatitis, unilateral conjunctivitis, bilateral sacroiliitis, ulcers in the stomach and small intestines. No patient had evidence of amyloidosis. Every patient carried at least one mutation in MEFV gene (1 homozygous, 6 heterozygous, 4 compound heterozygous). Allelic frequencies were E148Q (22.7%), R202Q (22.7%), G304R (18.2%), P369S/R408Q (9.1%), E148V (4.5%), M694V (4.5%). All patients had good response to low to moderate dose of colchicine, whereas the response to low to moderate dose of glucocorticoid varied considerably.

Conclusion:
Our registry suggested for the first time that FMF could be identified among adult Chinese patients suffered from intermittent fever of unknown cause. The incomplete or atypical clinical manifestations of our patients compared to patients with Mediterranean origins may be related to low-penetrance and heterozygous mutations.

References:

Table 1. Summary of the clinical and genetic characteristics of our patients.

<table>
<thead>
<tr>
<th>No.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
</tr>
</thead>
</table>

Disclosure: D. Wu, None; M. Shen, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/familial-mediterranean-fever-in-chinese-adult-patients](http://acrabstracts.org/abstract/familial-mediterranean-fever-in-chinese-adult-patients)

Abstract Number: 2114

**Interstitial Pneumonia with Autoimmune Features (IPAF): Are There Definable Subsets?**

Sepehr Mesdaghinia¹, Julio Arturo Huapaya², Brainerd Ewarie² and Virginia D. Steen¹, ¹Rheumatology, MedStar Georgetown University Hospital, Washington, DC, ²Medicine, MedStar Georgetown University Hospital, Washington, DC

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

- **Background/Purpose:**
  Interstitial lung disease (ILD) can be an early manifestation of an occult connective tissue disease (CTD). It is important to separate these patients from Idiopathic pulmonary fibrosis (IPF), since the outcome and treatment are different. Recently, an international task force proposed criteria for patients with ILD and at least one feature from clinical, serologic or morphologic domains, calling it ‘Interstitial Pneumonia with Autoimmune Features (IPAF)’ (Fischer, 2015). We carefully reviewed ILD patients seen since 2008 to see if they had features suggestive of CTDs and also a possible flavor to help define subsets.

- **Methods:**
  We identified 374 patients with ILD who were seen at rheumatology and pulmonary clinics. Patients with clear IPF or a definable CTD were excluded (n=276) and the remaining 98 patients were thoroughly reviewed for the demographic, clinical, laboratory, and radiographic features. Those featured were entered in Excel database and analyzed from different aspects.

- **Results:**
  Of these 98 patients with ILD, 66 met criteria for IPAF, 14 patients met criteria for a CTD, 3 patients had IPF and 15 patients did not meet criteria for IPAF primarily due to lack of rheumatologic evaluation or complete serologic testing. Among 15 patients without IPAF, 4 patients had elevated CPK and aldolase that could not be used towards IPAF criteria. In comparison with IPF, our IPAF patients were younger (mean age 60.7). There were more women and African Americans (74% and 46% respectively) and smoking history did not seem to be a major contributing factor (only 32%), (Table 1). Table 2 describes the features (domains) that led to the diagnosis of IPAF. Among these IPAF patients, 77% had features suggestive of a specific CTD with scleroderma the most frequent at 41% (Table 3). Some patients did not have enough features to suggest a possible CTD (23%).
Conclusion:
IPAF is an important subgroup of patients who need to be better characterized. These patients are more commonly female and have serologic abnormalities. Further consideration may be helpful to include some other features in the criteria (e.g. elevated muscle enzymes). A large portion of patients with IPAF (77%) appeared to fit into a CTD subgroup which could be helpful in determining the best treatment.

Table 1. Characteristics of IPAF patients in our study in comparison to IPF from literature

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>IPAF (%)</th>
<th>IPF %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (years)</td>
<td>60.7</td>
<td>60</td>
</tr>
<tr>
<td>Female</td>
<td>49 (74)</td>
<td>40</td>
</tr>
<tr>
<td>Male</td>
<td>17 (26)</td>
<td>60</td>
</tr>
<tr>
<td>White</td>
<td>22 (33.3)</td>
<td>N/A</td>
</tr>
<tr>
<td>African American</td>
<td>31 (47)</td>
<td>N/A</td>
</tr>
<tr>
<td>Asian</td>
<td>4 (6)</td>
<td>N/A</td>
</tr>
<tr>
<td>Hispanic</td>
<td>5 (8)</td>
<td>N/A</td>
</tr>
<tr>
<td>Never Smoker</td>
<td>45 (68)</td>
<td>38</td>
</tr>
<tr>
<td>Former Smoker</td>
<td>20 (30)</td>
<td>72</td>
</tr>
<tr>
<td>Active smoker</td>
<td>1 (1.8)</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 2. IPAF features seen in our patients

<table>
<thead>
<tr>
<th>Domains</th>
<th>Total (n=66)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical</td>
<td>48</td>
</tr>
<tr>
<td>Serologic</td>
<td>61</td>
</tr>
<tr>
<td>Morphologic</td>
<td>65</td>
</tr>
<tr>
<td>Clinical and Serologic</td>
<td>45</td>
</tr>
<tr>
<td>Clinical and Morphologic</td>
<td>47</td>
</tr>
<tr>
<td>Serologic and Morphologic</td>
<td>60</td>
</tr>
<tr>
<td>All three domains</td>
<td>42</td>
</tr>
<tr>
<td>Total</td>
<td>66</td>
</tr>
</tbody>
</table>

Table 3. Possible CTD subsets of IPAF patients based on clinical and laboratory features

<table>
<thead>
<tr>
<th>Possible CTD subset</th>
<th>Frequency</th>
<th>Percent (%)</th>
<th>Clinical and Laboratory Features (Number)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLE like</td>
<td>9</td>
<td>13</td>
<td>Rash (3), malar rash (1), arthritis (3), alopecia (2), ANA (1), ds-DNA (5)</td>
</tr>
<tr>
<td>RA like</td>
<td>6</td>
<td>9</td>
<td>Polyarthritis (6), morning stiffness (4), RF (2), CCP (2)</td>
</tr>
<tr>
<td>Sjogren’s like</td>
<td>5</td>
<td>7</td>
<td>Joint symptoms (2), parotid swelling (1), hypergammaglobulinemia (1), SSA (4), SSQ (2), SSA and SSQ (2)</td>
</tr>
<tr>
<td>Scleroderma like</td>
<td>27</td>
<td>41</td>
<td>Raynaud’s (4), swollen fingers (6), telangiectases (5), digital ulcers (1), abnormal nailfold capillaroscopy (5), ANA (25), nuclear ANA (11), Scl-70 (9), Centromere (1)</td>
</tr>
<tr>
<td>Myositis like</td>
<td>4</td>
<td>6</td>
<td>Muscle weakness (4), Gottron’s (2), mechanic’s hands (1), elevated CPK (2), elevated aldolase (1), Jo-1 (2), PR3-ACL (1)</td>
</tr>
<tr>
<td>No definable subset</td>
<td>15</td>
<td>23</td>
<td>Raynaud’s (6), arthritis (2), morning stiffness (3), muscle weakness (1), CPK (2), aldolase (2), ESR (3), CRP (1), ANA (11), RNP (1), RF (2), SSA (3), SSQ (1)</td>
</tr>
</tbody>
</table>

Disclosure: S. Mesdaghinia, None; J. A. Huapaya, None; B. Ewarien, None; V. D. Steen, None.
Mast Cell Activation Features in Ehlers-Danlos/Joint Hypermobility Patients: A Retrospective Analysis in Light of an Emerging Disease Cluster

Dave Lee1 and Eric Mueller2, 1Arthritis Northwest, PLLC, Spokane, WA, 2Discus Analytics LLC., Spokane, WA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Mast cells are immune cells often residing in connective tissue, best known for their role in allergic and anaphylactic responses1. Mast cell activation syndrome (MCAS) is a relatively newly recognized group of immune disorders in which patients have a normal number of “hyperresponsive,” mast cells which degranulate inappropriately and excessively. Clinical presentations of MCAS include: flushing, physical/cholinergic urticaria, angioedema, hypotension, diarrhea, and rhinitis1.

Several investigators have recently noted a possible link between MCAS and Ehlers-Danlos (EDS)/joint hypermobility syndrome1,2. Cheung et al. surveyed patients with both postural orthostatic tachycardia syndrome and hypermobility, and found 66% had MCAS symptoms. We aimed to evaluate the incidence of MCAS in hypermobile patients seen at our clinic over a 6-month period.

Methods:
The study sample consisted of hypermobility patients seen by an individual provider at a rheumatology clinic in Spokane, WA over a 6 month period (Nov, 2016 to May, 2017). A cohort of 36 hypermobile patients with MCAS were identified through a search of the electronic health record system for a cross-section between: 1) Hypermobility/EDS (ICD-10 M35.7, M24.80, and Q79.6); and 2) idiopathic MCAS (ICD D89.42).

A second cohort (from the same 6-month period) of non-hypermobile patients with possible MCAS features of MCAS were found using an expanded set of ICD diagnosis codes for features associated with MCAS, as described by Seneviratne et al.1: D89.42 (idiopathic MCAS), I95.1 (Orthostatic hypotension), J30.9 (Allergic rhinitis), J45.909 (Asthma), K12.0 (Aphthous stomatitis), K21.0 (GERD), L29.8 (Pruritis), L50.X (Urticaria), R00.0 (Tachycardia), R10.9 (Unspecified abdominal pain), R14.0 (Bloating), R19.7 (Diarrhea), and R55 (Syncope).

Results:
During this 6-month period, the provider saw a total of 1010 distinct patients. The first cohort was comprised of 36 patients (3.6% of total, 45.6% of hypermobile patients) with both hypermobility and possible MCAS. 33/36 (91.7%) were female, median age 48. A total of 79 patients – including the first cohort – met criteria for hypermobility with a Beighton score of ≥5/9 on exam.

The second cohort of non-hypermobility patients with possible MCAS found 118 distinct patients (12.7% of non-hypermobile patients) who had one of the ICD codes associated with MCAS. Only 5 (0.5%) patients had been diagnosed with MCAS without meeting criteria for hypermobility.

Conclusion:
Our preliminary data demonstrate a higher incidence rate of MCAS features in our patients with joint hypermobility compared to the non-hypermobile population. This suggests a positive correlation between MCAS and joint hypermobility. Many hypermobile patients tend to be referred to rheumatology, and if a correlation between hypermobility and MCAS exists, MCAS may be an under-recognized phenomenon in our practices.

References:
Evaluation of Connective Tissue Diseases in Patients Presenting with Interstitial Lung Disease in a Referral Center in Santiago, Chile

Verónica Wolff1,2, Matias Florenzano1, Angela Rivera3, Carolina Cuellar4, Juan Maya5, Mauricio Salinas1,6, Cristian Ibarra1, Angélica Bello7 and Daniela Soto8,
1Rheumatic Lung diseases Unit, Instituto Nacional del Tórax, Santiago, Chile, 2Rheumatology Unit, Hospital del Salvador, Facultad de Medicina, Universidad de Chile, Santiago, Chile, 3Rheumatology Unit, Hospital Del Salvador, Facultad de Medicina, Universidad de Chile, Santiago, Chile, 4Rheumatology unit, Hospital Del Salvador, Facultad de Medicina, Universidad de Chile, SANTIAGO, Chile, 5Rheumatology Unit, Hospital del Salvador. Facultad de Medicina. Universidad de Chile, Santiago, Chile, 6Facultad de Medicina, Universidad de Chile, Santiago, Chile, 7Instituto Nacional del Tórax - Universidad de Chile, SANTIAGO, Chile, 8Instituto Nacional del Tórax - Universidad de Chile, Santiago, Chile

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Type: Miscellaneous Rheumatic and Inflammatory Diseases Poster II
Session Time: 9:00AM-11:00AM

Background/Purpose: Connective tissue diseases (CTDs) are systemic autoimmune disorders that can compromise the lung. Interstitial lung disease (ILD) is one of the major forms of lung involvement in CTDs. Main CTDs with lung involvement are Rheumatoid Arthritis (RA), Systemic Sclerosis (SSc) and Idiopathic Inflammatory Myopathies (IIM) spectrum. ILD can be the first or the only manifestation of a CTD. Some ILD patients who don’t meet specific CTD classification criteria but have autoimmune findings have been classified as interstitial pneumonias with autoimmune features (IPAF). CTD related ILD (CTD-ILD) have the same patterns than idiopathic ILD, with predominance of non-specific interstitial pneumonia (NSIP). Response to immunosuppressive (IS) therapy and prognosis of CTD-ILD can be better than idiopathic ILD and it may be necessary to treat extra-thoracic disease, so oportune diagnosis of an underlying CTD is essential. The aim of this study is to describe the clinical and radiological features of a historical cohort of patients with CTD-ILD in a specialized pneumo-rheumatology clinic.

Methods: The study was conducted at the Instituto Nacional del Tórax in Santiago, Chile, a national referral center for ILD. It is a retrospective study of a historical cohort started in 2012 by the authors. All patients were evaluated in a multidisciplinary team. Descriptive statistics were done. For comparison alfa 0,05 two tails was used; for multiple comparisons Bonferroni correction was used. Analysis was done in Stata 14.0

Results: 219 patients were included in the study. Their main clinical and radiological characteristics are summarized on Table 1. All patients are hispanic, with female predominance (84.5%). Main CTDs were RA, SSc and IIM. 15 patients (6.8%) met IPAF criteria. NSIP was the overall predominant ILD pattern (Table 1, Graphic 1). In 34.7 % of patients diagnosis of ILD was done before CTD, in 27.4 % diagnosis of CTD/ILD was concomitant and in 38 % ILD was diagnosed after CTD. Mean FVC and DLCO at ILD diagnosis were 75% and 47.7% respectively. 49 patients (22%) didn’t get IS therapy due to mild and stable lung disease. 20 patients (9.1%) died in the period of observation. Main first line IS were Azathioprine, Mycophenolate or Cyclophosphamide.

Conclusion: Our cohort show the same kind of CTDs with lung involvement and related ILD patterns described in other series and worldwide literature. There might be an increase in ILD patients meeting IPAF criteria in the future.
TABLE 1  Baseline characteristics of study population  N = 219

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at CTD-ILD diagnosis (years)</td>
<td>57.5 +/- 13.6</td>
</tr>
<tr>
<td>Female</td>
<td>185 (84.5%)</td>
</tr>
<tr>
<td>Radiologic ILD pattern (HRCT)</td>
<td></td>
</tr>
<tr>
<td>UIP</td>
<td>55 (25.1%)</td>
</tr>
<tr>
<td>NSIP</td>
<td>90 (41.1%)</td>
</tr>
<tr>
<td>OP</td>
<td>22 (10%)</td>
</tr>
<tr>
<td>NSIP/OP</td>
<td>32 (14.6%)</td>
</tr>
<tr>
<td>LIP</td>
<td>6 (2.7%)</td>
</tr>
<tr>
<td>AIP</td>
<td>2 (0.9%)</td>
</tr>
<tr>
<td>Bronchiolar disease</td>
<td>5 (2.3%)</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>1 (0.5%)</td>
</tr>
<tr>
<td>Unspecific</td>
<td>6 (2.7%)</td>
</tr>
<tr>
<td>CTD</td>
<td></td>
</tr>
<tr>
<td>RA</td>
<td>51 (23.3%)</td>
</tr>
<tr>
<td>IIM (other than AS)</td>
<td>19 (8.7%)</td>
</tr>
<tr>
<td>AS</td>
<td>50 (22.8%)</td>
</tr>
<tr>
<td>SSc</td>
<td>52 (23.7%)</td>
</tr>
<tr>
<td>SLE</td>
<td>5 (2.3%)</td>
</tr>
<tr>
<td>pSS</td>
<td>7 (3.2%)</td>
</tr>
<tr>
<td>MCTD</td>
<td>3 (1.4%)</td>
</tr>
<tr>
<td>IIM/SSc overlap</td>
<td>8 (3.7%)</td>
</tr>
<tr>
<td>UCTD</td>
<td>7 (3.2%)</td>
</tr>
<tr>
<td>AAV</td>
<td>2 (0.9%)</td>
</tr>
<tr>
<td>IPAF</td>
<td>15 (6.8%)</td>
</tr>
<tr>
<td>Pulmonary function at ILD diagnosis (average)</td>
<td></td>
</tr>
<tr>
<td>FVC (%)</td>
<td>75 (139 – 28)</td>
</tr>
<tr>
<td>DLCO (%)</td>
<td>47.7 (122 – 23)</td>
</tr>
<tr>
<td>Diagnosis timing</td>
<td></td>
</tr>
<tr>
<td>Previous ILD</td>
<td>76 (34.7%)</td>
</tr>
<tr>
<td>Concomitant CTD/ILD</td>
<td>60 (27.4%)</td>
</tr>
<tr>
<td>Previous CTD</td>
<td>83 (38%)</td>
</tr>
<tr>
<td>First Line Immunosuppressive therapy</td>
<td></td>
</tr>
</tbody>
</table>
**C-Reactive Protein and Serum Amyloid a in Sepsis, Acute Appendicitis and Familial Mediterranean Fever**

Oguzhan Selvi\(^1\), Serdal Ugurlu\(^2\), Murat Bolayirli\(^3\), Kenan Barut\(^4\), Sezgin Sahin\(^4\), Amra Adrovic\(^4\), Mustafa Akker\(^5\), Bilgesu Ergezen\(^6\), Osman Simsek\(^7\), Ozgur Kasapcopur\(^4,8\) and Huri Ozdogan\(^1\), \(^1\)Istanbul University, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey, \(^2\)Rheumatology, Istanbul University, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey, \(^3\)Istanbul University, Cerrahpasa Medical Faculty, Department of Biochemistry, Istanbul, Turkey, \(^4\)Pediatric Rheumatology, Istanbul University, Cerrahpasa Medical School, Department of Pediatric Rheumatology, Istanbul, Turkey, \(^5\)Department of Anesthesiology, Sisli Hamidiye Training and Research Hospital, Istanbul, Turkey, \(^6\)Division of Rheumatology, Department of Internal Medicine, Cerrahpasa Medical Faculty, University of Istanbul, Istanbul, Turkey, \(^7\)Istanbul University, Cerrahpasa Medical Faculty, Department of General Surgery, Istanbul, Turkey, \(^8\)Istituto Giannina Gaslini - Pediatria II, Reumatologia - PRINTO, Genoa, Italy

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Miscellaneous Rheumatic and Inflammatory Diseases Poster II

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Familial Mediterranean Fever (FMF) is an autoinflammatory disease characterized by recurrent inflammatory attacks. Attacks are accompanied by substantial increase in acute phase reactants such as C-reactive protein (CRP) and serum amyloid A (SAA) which usually decrease once the attack subsides. CRP and SAA have been considered as the most sensitive acute phase markers. We aimed to compare the behaviour of SAA and CRP in four different clinical conditions, in order to evaluate their role and possible differences during the course of FMF. Here we report our preliminary results on SAA and CRP response in a group of patients with FMF, sepsis, appendicitis and healthy controls.
Methods:

Our study has a prospective design and is performed in a single institution. Blood samples were drawn from 15 FMF patients during attacks and control samples were obtained once the attacks subsided. We also included 17 patients with acute appendicitis and samples were drawn before and after the appendectomy. We also included 43 cases with sepsis. Among these 43, serial blood testing was performed for 19 cases. We also included 20 healthy controls without a proven medical condition. Serum CRP levels were measured via Enzyme Immunoassay (ELISA) method. Cut-off level was determined as 8 mg/L. Results were given as x-folds of normal. Serum Amyloid A levels were measured by using nephelometric method. Cut-off level was determined as 6.8 mg/L.

Results: During the FMF attack, mean SAA level was 50±34.96, whereas it was 0.92±1.10 during the attack-free period (p<0.01). CRP was also decreased from 26.32 ± 13.9 to 3.61 ± 2.67 once the attacks subsided (p<0.01). For the group with acute appendicitis, preoperative and postoperative mean SAA levels were 51.70 ± 63.09 and 0.82 ± 0.89, respectively (p<0.001). For this group, mean CRP was also decreased following the operation from 21.75 ± 12.47 to 3.31 ± 3.40 (p<0.01). In sepsis group mean SAA and CRP levels were 43.42 ± 40.92 and 27.92 ± 12.23, respectively. Whereas in healthy controls mean SAA level was 0.63 ± 0.25, while mean CRP level was 0.53 ± 0.2. With regards to the correlation between SAA and CRP, analysis was performed for each setting. In FMF group, SAA and CRP were correlated both during and after the attacks (r=0.806, p<0.001). Also in acute appendicitis group, CRP and SAA were positively correlated (r=0.877, p<0.001) both preoperatively and postoperatively. In addition to the finding that CRP and SAA were also positively correlated in sepsis group (r=0.278, p=0.012), for the 19 sepsis cases in which serial measures were performed, this correlation was sustained for three consecutive days (r=0.610, p=0.009; r=0.596, p=0.012; r=0.574, p=0.016; day 1, 2 and 3, respectively).

Conclusion: We report that, SAA and CRP levels were correlated in various disease settings. Given the fact that, none of our patients had higher than normal SAA levels despite normal CRP, these two markers seem to have, if any, only minute behavioural differences when it comes to following an FMF case in clinical practice. Although our results are grounded on our preliminary data, both CRP and SAA seem to be effective and efficient to follow a case with FMF.

Disclosure: O. Selvi, None; S. Ugurlu, None; M. Bolayirli, None; K. Barut, None; S. Sahin, None; A. Adrovic, None; M. Akker, None; B. Ergezen, None; O. Simsek, None; O. Kasapcopur, Novartis Pharmaceutical Corporation, 8, Roche Pharmaceuticals, 8; H. Ozdogan, None.
Serum level of malondialdehyde (MDA), and adiponectin were measured by ELISA. The morphologic changes of flexor digitorum tendons were assessed by ultrasonography. Serum samples were obtained from all the enrollee at the time point of ultrasonography study. The study was carried out at the diabetes clinic of Bucheon St. Mary’s Hospital, Catholic University of Korea, from March 2014 to April 2015. All subjects were informed and gave their written consent.

**Results:** Fifty-three (67%) patients with type 2 diabetes showed pathologic changes of flexor digitorum tendon, whereas only 4 (10%) subjects in control group did. The duration of diabetes tended to be longer in patients with flexor digitorum tendinopathy (FDT) compared with those without FDT. Body mass index (BMI) was significantly higher in patients with FDT than those without FDT. There was no difference in prevalence of macrovascular and microvascular complications, cholesterol profiles, HOMA-IR, and QUICKI between the the patients with FDT and those without FDT. Serum levels of adiponectin in type 2 diabetes patients with FDT were significantly lower than those of control group, but not in type 2 diabetes patients without FDT. Serum MDA levels were higher both in diabetes patients with FDT and those without FDT than controls. But, there was no difference in serum MDA level between the patients with FDT and those without FDT. Logistic regression analysis revealed that BMI, disease duration and abdominal obesity are predictor of morphologic changes of flexor digitorum tendons.

**Conclusion:** The morphologic changes of flexor digitorum tendons were first studied. Morphologic changes of flexor tendons in patients with type 2 diabetes might reflect the chronic burden of oxidative stress in tendons due to hyperglycemia.

**Disclosure:** K. M. Ko, None; J. K. Min, None; S. J. Moon, None.


**Abstract Number: 2119**

**Rheumatological Immune Related Adverse Events in Malignancy Patients Treated with Anti-Programmed Cell Death (PD) 1 Antibodies**

**Emma Mitchell**1, Peter Lau2, Chloe Khoo2, Kortneye Smith2, Benjamin Brady2, Mark Shackleton2, Grant McArthur2, Ian Wicks1,3,4 and Shahnene Sandhu2,3Rheumatology, Royal Melbourne Hospital, Melbourne, Australia,2Cancer Medicine, Peter MacCallum Cancer Centre, Melbourne, Australia,3Medicine, University of Melbourne, Melbourne, Australia,4Wicks Lab, Walter and Eliza Hall Institute, Melbourne, Australia

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** Miscellaneous Rheumatic and Inflammatory Diseases Poster II  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Immune checkpoint inhibitors (ICIs), including anti-programmed cell death 1 (anti-PD 1) antibodies, are established therapies for advanced malignancies, including melanoma, and non-small cell lung cancer (NSCLC). The adverse event (AE) profile of anti-PD 1 antibodies includes immune-related adverse events (irAEs) spanning several organ systems, many of which have defined management pathways. However, no consensus exists for the management of rheumatological (Rh) irAEs, including inflammatory arthritis, PMR and myositis, which affect 5-10% of patients receiving anti-PD 1 antibodies. Equally, there is a paucity of data presenting management options for flares of pre-existing rheumatic disease whilst undertaking anti-PD 1 therapy.

**Methods:**

We conducted a single centre retrospective study of patients treated with anti-PD 1 antibodies pembrolizumab (P) and nivolumab (N), who developed Rh irAEs, experienced flares of existing rheumatic disease, or experienced stability of existing rheumatic disease. Clinical and demographic data were obtained, including anti-PD 1 response (timing, durability and reason for cessation), rheumatologic presentation (including temporal relationship to anti-PD 1 therapy), rheumatologic treatment and response.

**Results:**

Eighteen patients (12 male, 6 female; median age 71.5 years) were included. All had metastatic malignancy (14 melanoma, 2 NSCLC, 2 head and neck squamous cell carcinoma). Anti-PD1 monotherapy (P or N) was used in 17 patients, 1 of whom had previously received
the anti-cytotoxic T-lymphocyte-associated protein 4 (anti-CTLA4) antibody ipilimumab (I). One patient received combination N-I.

Thirteen patients developed de novo Rh irAEs (7 inflammatory arthritis, 1 PMR, 4 myositis, 1 fasciitis). Three experienced flare of Rh disease (all PMR). Two patients had no flare of their existing Rh disease (1 PMR, 1 with JIA/SSc). The median time to Rh irAE was 10.9 weeks (range 0.7-113). All myositis cases manifested within 4 weeks.

Twelve of the 16 irAEs required prednisone, all at doses ≥10mg/day. DMARDs were used in 5 cases, including HCQ in 4, MTX in 1, and SSZ in 1. One case received intravenous immunoglobulin.

Of the 18 patients, 7 completely responded to anti-PD 1, 7 partially responded, 3 had stable disease, and 1 progressive disease. Responses have been maintained despite Rheumatologic therapy. Median duration of response has not been reached.

Conclusion:
Rh irAEs to anti-PD 1 therapy present a new challenge for Rheumatologists and Oncologists. Both de novo disease, and flare, can occur. Our cohort demonstrated a high rate of response to anti-PD 1 therapy, including when Rheumatologic therapy was initiated. Prospective analysis is required to further characterise this set of diseases.

Disclosure: E. Mitchell, None; P. Lau, None; C. Khoo, None; K. Smith, None; B. Brady, None; M. Shackleton, None; G. McArthur, None; I. Wicks, None; S. Sandhu, None.

Quality, Content and Readability Assessment of Patient Education Websites Relating to Ehlers-Danlos Syndrome

Ahmed Omar1,2, Laura Passalent3, Leslie Soever4, Medha Soowamber5 and Simon Carette6, 1Rheumatology, Toronto Western Hospital, University of Toronto, Toronto, ON, Canada, 2Rheumatology, Mount Sinai Hospital, Toronto, ON, Canada, 3Allied Health, Toronto Western Hospital, Toronto, ON, Canada, 4Toronto General Hospital, Toronto, ON, Canada, 5University Health Network, Toronto, ON, Canada, 6Division of Rheumatology, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Ehlers-Danlos Syndrome (EDS) is a heritable connective tissue disease that presents in myriad ways. Education is an essential component in managing this complex condition. Patients are increasingly relying on the internet to obtain health information. There is a lack of data looking at the quality of EDS patient education websites. In this study, we aimed to address this gap by assessing the quality, content and readability of existing websites specific to EDS.

Methods: The term “Ehlers Danlos Syndrome” was searched in Google.com and Bing.com. 60 results were retrieved from each search engine. Duplicates were removed and physician, commercial, news and video specific websites were excluded. Two independent readers analyzed the websites for website quality using two validated tools (DISCERN quality assessment instrument and The Health on the Net (HON) foundation certification). Web site content was scored by a self-developed content analysis tool based on established evidence and EDS standards of practice. Website Readability was assessed via the Flesch-Kincaid Reading Grade Level (FKGL) and Flesch Reading Ease Score (FRES).

Results: Of the 120 websites identified, 29 websites remained after the exclusion criteria were applied. Inter-observer reliability between the two readers was substantial, with ICC scores of 0.76 (95% CI=0.50, 0.89) and 0.71 (95% CI=0.40, 0.86) for total content and DISCERN scoring respectively. The mean content score was low at 3.55 out of a total of 80 (SD=17.92). Although most websites reported symptoms and diagnosis information, treatment content scores were generally lower. Only 37.93% mentioned self-management approach. The psychological component was especially neglected with 65.52% of websites failing to address this topic. The mean DISCERN score was poor at 36.21 out of a total of 80 (SD=11.71). 65.50% of websites had poor DISCERN scores, and only 6.90% reached the good to excellent range. Only 24.14% of the websites had the HON foundation certification seal. Regarding readability, the average FKGL was high at 11.42 (SD=0.91), with none of the website achieving the recommended FKGL scores of ≤6. The FRES was
Conclusion: Although most of the websites studied provided a general description of EDS, most failed to achieve the required quality, this is especially so for treatment advice. Readability scores also did not meet the recommended standards. Future online patient education endeavours specific to EDS need to address these shortcomings and include more treatment advice, especially as self-management is an essential component of EDS care.

Disclosure: A. Omar, None; L. Passalent, None; L. Soever, None; M. Soowamber, None; S. Carette, None.


Abstract Number: 2121

Autoantibodies As Biomarkers for the Identification of Pre-Clinical Stages of Autoimmune Diseases: Demonstration of Inflammatory and Fibrotic Activity in the Liver of Asymptomatic and Biochemically Normal Individuals with Anti-Mitochondria Antibodies

Danielle Baldo¹, Alessandra Dellavance¹, Maria Lucia Ferraz² and Luis Eduardo C. Andrade³,⁴

¹Research and Development Department, Fleury Medicine and Health Laboratories, São Paulo, Brazil, ²Gastroenterology Division, Escola Paulista de Medicina, Universidade Federal de São Paulo, São Paulo, Brazil, ³Rheumatology Division, Universidade Federal de São Paulo, São Paulo, Brazil, ⁴Immunology Division, Fleury Medicine and Health, São Paulo, Brazil

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Circulating autoantibodies precede clinical onset of several autoimmune diseases. The characteristics of the so-called pre-clinical stage of autoimmune diseases are poorly understood. Anti-mitochondria autoantibodies (AMA) occur in >95% Primary Biliary Cholangitis (PBC) patients. AMA-positive subjects with normal liver enzymes are occasionally suspected in the indirect immunofluorescence (IIF) assay on HEP-2 cells and further confirmed on specific AMA assays. The liver histological status in biochemically normal (BN) AMA-positive individuals (BN/AMA) is not determined. The Enhanced Liver Fibrosis (ELF) score is a surrogate marker for assessing liver fibrosis state. We prospectively followed-up the autoantibody response, serum liver enzymes and ELF score in AMA/BN and PBC patients along a 7-year period.

Methods: 327 samples from 35 PBC patients and 59 BN/AMA were prospectively obtained along an average interval of 4.09 (range: 0.50–7.10) and 3.59 (0.50–7.40) years, respectively. Samples were tested by IIF on rat kidney (IIF-AMA), western blot with rat liver (WB-AMA) and ELISA for PBC-associated autoantibodies against pyruvate dehydrogenase (anti-PDC-E2), nuclear envelope protein gp210, protein sp100, and centromeric proteins CENP-A/B. Anti-PDC-E2 avidity was determined by 6M urea-elution modified ELISA. Alkaline phosphatase (ALP), gamma glutamyl transferase (γGT) and ELF score were measured by automated methods.

Results: PBC patients had higher ELF score (p<0.001), ALP (p <0.001), γGT (p<0.001), and anti-PDC-E2 (p<0.001) serum levels, as well as higher anti-PDC-E2 avidity (p=0.022) than BN/AMA. Along the follow-up, there was an increase in anti-PDC-E2 (p<0.001) and IIF-AMA (p<0.001) serum levels in BN/AMA, but not in PBC patients. There was increase in anti-PDC-E2 avidity (p<0.001) and ELF score (p<0.001) in both groups. There was a positive temporal correlation between: 1) ELF score and anti-PDC-E2 levels in BN/AMA (r=0.239; p<0.001) and in PBC patients (r=0.268; p=0.004); 2) ELF score and IIF-AMA in BN/AMA (r=0.465; p<0.001); and 3) ELF score and anti-PDC-E2 avidity in PBC (r=0.341; p<0.001). Along time, there was an increase in the number of recognized autoantigen targets in 39% BN and 49% PBC patients. BN/AMA depicted four divergent patterns of longitudinal behavior regarding anti-PDC-E2 serum levels and ELF score: ascending, descending, stable and erratic.

Conclusion: Along time, AMA/BN asymptomatic individuals undergo progressive expansion and intensification in the humoral autoimmune response. This process correlates with increase in serum liver fibrosis biomarkers indicating an ongoing silent inflammatory process in the liver. This represents an opportunity case for early therapeutic intervention and prevention of development of autoimmune diseases. However, there is heterogeneity in the longitudinal behavior among AMA/BN individuals, and not all AMA/BN individuals may evolve to overt PBC.
Association of Retroperitoneal Fibrosis with Malignancy

Sang Jin Lee¹, Jung Su Eun¹, Na Ri Kim², Eon Jeong Nam¹, Yeong Wook Song³ and Young Mo Kang⁴, ¹Division of Rheumatology, Department of Internal Medicine, Kyungpook National University School of Medicine, Daegu, Korea, Republic of (South), ²Internal Medicine (Rheumatology), Kyungpook National University School of Medicine, Daegu, Korea, Republic of (South), ³Internal Medicine, Seoul National University College of Medicine, Seoul, Korea, Republic of (South), ⁴Division of Rheumatology, Department of Internal Medicine, Kyungpook National University School of Medicine, Daegu, Republic of Korea, Daegu, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Retroperitoneal fibrosis (RPF) is a periaortic sclerotic disease that encases adjacent structures, particularly the ureters. Because it is unclear whether RPF is associated with malignancy, we examined standardized incidence ratios (SIRs) of cancers in patients with RPF compared with age- and sex-matched general population. Subsequently, the characteristics of patients with RPF accompanied by malignancy were analyzed.

Methods:
Medical records of 111 patients diagnosed as having RPF by computed tomography, positron emission tomography (PET), and/or histological evaluation were reviewed. Forty one cases of cancers, which were confirmed by biopsies, were identified in 35 patients with RPF. Cancer incidence rates were calculated and compared with that observed in the Korean general population, computing the standardized incidence ratios (SIRs), which were then stratified according to RPF-cancer intervals.

Results:
The mean ± SD age at RPF diagnosis was 59.2 ± 15.0 years, and 69.4% of the patients were male. Ninety two cases (82.9%) showed peri-aortitis, and 65 cases (58.6%) presented with hydrenephrosis. The cancer SIR (95% confidence intervals) in patients with RPF relative to age- and sex-matched individuals in the general population was 3.18 (2.23-4.41) [2.65 (1.70 - 3.94) in men; 5.34 (2.76 - 9.32) in women]. The most frequent cancer was unspecified urinary organ cancers with SIR of 733 (238 – 1711). SIRs of multiple myeloma [27.6 (3.34 – 99.6)], renal cell cancers [9.53, (1.15-34.4)] and adenocarcinoma of unknown primary cancers [16.9, (2.05 - 61.1)] were also significantly higher than in the general population. When stratified by RPF-cancer intervals, SIR was 10.4 (6.59 - 15.60) within 1 year of RPF diagnosis, while no significant increase in SIR was found out of 1 year around RPF diagnosis. Among malignancies (n=23) within 1 year of RPF diagnosis (RPF with concurrent cancers), predominant cellular origin was epithelial cells, such as transitional cell carcinoma (n=4) and adenocarcinoma (n=13). Although RPF patients with concurrent cancers were significantly older at the diagnosis of RPF than RPF patients without concurrent cancers (65.6 ± 12.3 vs 57.5 ± 15.2 years, respectively; p=0.017), there was no significant differences in the laboratory findings including erythrocyte sedimentation rate, C-reactive protein, and immunoglobulin G4. Moreover, the maximum standardized uptake values at RPF measured by PET were not significantly different between RPF patients with concurrent cancers (n=3) and those without (n=16) (5.17 ± 0.40 vs 4.93 ± 2.14, respectively).

Conclusion:
RPF was strongly associated with cancers within 1 year of RPF diagnosis. Our results indicate that cancer screening should be performed in patients with RPF, particularly in the aged patients.

Disclosure: S. J. Lee, None; J. S. Eun, None; N. R. Kim, None; E. J. Nam, None; Y. W. Song, None; Y. M. Kang, None.
Abstract Number: 2123

Protein-Losing Enteropathy in Patients with Systemic Autoimmune Diseases: Characterization of 263 Cases (GEAS-SEMI Spanish Cohort)

Alejandra Flores-Chavez1,2,3, Soledad Retamozo4,5,6, Angel Robles7, Guadalupe Fraile Rodriguez8, Sofia Arteaga9,10, Celeste Galceran-Chaves11, Roberto Pérez-Alvarez12, Marta Pérez de Lis12, Belchín Kostov13, Manuel Ramos-Casals14,15 and Pilar Brito-Zerón14,16

1 Department of Autoimmune Diseases, ICMiD, Hospital Clinic Barcelona, Spain., Barcelona, Spain, 2 Unidad de Investigación Biomédica 02 (Unidad de Investigación en Epidemiología Clínica), UMAE, Hospital de Especialidades, Centro Médico Nacional de Occidente, Instituto Mexicano del Seguro Social, Jalisco, Mexico, 3 Programa de Doctorado en Ciencias Médicas, Centro Universitario de Investigaciones Biomédicas (CUIB), Universidad de Colima, Colima, Mexico, Mexico, Mexico, 4 Instituto de Investigaciones en Ciencias de la Salud, Universidad Nacional de Córdoba, Consejo Nacional de Investigaciones Científicas y Técnicas (INICSA-UNC-CONICET), Cordoba, Argentina, 5 Laboratory of Systemic Autoimmune Diseases “Josep Font”, CELLEX, Institut d’Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Department of Systemic Autoimmune Diseases, ICMiD, Hospital Clinic, Barcelona, Barcelona, Spain, 6 Rheumatology Unit, Hospital Privado Universitario de Córdoba, Institute University of Biomedical Sciences University of Córdoba (IUCBC), Cordoba, Argentina, 7 Department of Internal Medicine, Hospital La Paz, Madrid, Madrid, Spain, 8 Internal Medicine, Hospital Ramón y Cajal, Madrid, Madrid, Spain, 9 Department of Autoimmune Diseases, ICMiD, Hospital Clinic Barcelona, Barcelona, Spain, 10 Universidad de Antioquia, Medellin, Colombia, Medellin, Colombia, 11 Neuroscience Clinical Institute, Hospital Clinic Barcelona, Barcelona, Spain, 12 Department of Internal Medicine, Hospital Alvaro Cunqueiro, Vigo, Vigo, Spain, 13 Primary Care Research Group, IDIBAPS, Centre d’Assistència Primària ABS Les Corts, CAPSE, Barcelona, Barcelona, Spain, 14 Laboratory of Systemic Autoimmune Diseases “Josep Font”, CELLEX, Institut d’Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Department of Systemic Autoimmune Diseases, ICMiD, Hospital Clinic Barcelona, Barcelona, Spain, 15 Department of Medicine, University of Barcelona, Barcelona, Spain, Barcelona, Spain, 16 Autoimmune Diseases Unit, Department of Medicine, Hospital CIMA- Sanitas, Barcelona., Barcelona, Spain

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Protein-losing enteropathy (PLE) is a rare condition characterized by a loss of serum protein into the gastrointestinal tract resulting in hypoproteinemia, which can be complicated by edema, ascites, pleural and pericardial effusions, and malnutrition. Although rare, PLE may complicate a variety of diseases, most commonly cardiac or gastrointestinal conditions, and less infrequently, systemic autoimmune diseases (SAD).

Methods: In January 2016, we created a retrospective multicenter collection of cases of PLE reported in patients with SAD through the Spanish Autoimmune Diseases Study Group (GEAS-SEMI), and we carried out a systematic literature review. PLE was clinically diagnosed in patients presenting with hypoalbuminemia due to gastrointestinal loss after discarding urinary protein loss and reduced protein synthesis (malnutrition, liver disease, etc). Patients in whom evidence of protein leakage from the gastrointestinal tract as detected by 99 m Tc-HSA scintigraphy were classified as definite PLE, and those patients in which this examination was not performed were classified as probable PLE.

Results: A total of 263 patients with SAD-related PLE (6 patients from the Registry and 210 from the literature review) were included (80% were women, with a mean age at diagnosis of disease of 41.1 years, range 16-79 years); 226 (86%) of cases were reported from Asian countries (64% from China), 24 from European countries and 13 from America (7 from US). The main underlying SAD was systemic lupus erythematosus (SLE) in 202 (77%) cases, followed by Sjögren syndrome in 18 (7%) and sarcoidosis in 15 (6%). The main signs and symptoms at presentation were peripheral edema in 192 (85%) patients, pleural effusion in 129 (57%), ascites in 120 (53%) and diarrhea in 96 (43%) patients. Internal organ involvement CNS (in 8 (16%), pulmonary in 23 (46%) and renal in 15 (30%). The main analytical markers consisted of hypercholesterolemia (90%), hypertriglyceridemia (85%) and positive alpha1-antitrypsin in stool (68%). The main gastrointestinal endoscopic finding consisted of edematous mucosa either in upper endoscopy (67/129, 52%) and lower endoscopy (74/139, 53%). One hundred and eighty-two (69%) patients were classified as definite PLE and 81 (31%) were classified as probable PLE. Therapies included corticosteroids in 162 patients and immunosuppressive agents in 171 (mainly
cyclophosphamide and azathioprine); biological agents were used in 5 patients (rituximab in 4, infliximab in 1). After a mean follow-up of 15 months, 77% of patients had a complete response, 6% developed a disease relapse, and 4% died.

**Conclusion:** A very specific epidemiological and clinical profile was observed for protein-losing enteropathy associated with systemic autoimmune diseases, with nearly 90% of cases reported from Asian countries (two out of three cases from China), and nearly 80% reported in patients with underlying SLE. Patients were overwhelmingly treated with corticosteroids and immunosuppressive agents with a complete response of nearly 80% of cases and a global mortality of less than 5%.

**Disclosure:** A. Flores-Chavez, None; S. Retamozo, None; A. Robles, None; G. Fraile Rodriguez, None; S. Arteaga, None; C. Galceran-Chaves, None; R. Pérez-Alvarez, None; M. Pérez de Lis, None; B. Kostov, None; M. Ramos-Casals, None; P. Brito-Zerón, None.

**Abstract Number:** 2124

**Mixed Connective Tissue Disorder Has Higher Prevalence of Arthritis and Use of Methotrexate Than Systemic Lupus Erythematosus**

**Gunasekaran Sambandam**¹², Dr. Varun Dhir³, Dr. Mahesh Prakash⁴, Ranjana Minz⁵, Shefali Sharma⁶ and Aman Sharma⁷, ¹Internal Medicine, Post Graduate Institute of Medical Education and Research (PGIMER), chandigarh, India, ²Internal medicine, Post graduate Institute of medical education and research, chandigarh, India, ³Internal Medicine ( Clinical Rheumatology), Post Graduate Institute of Medical Education and Research, chandigarh, India, ⁴Radio Diagnosis, Post Graduate Institute of Medical Education and Research, chandigarh, India, ⁵Department of Immunopathology,, PGIMER,, Chandigarh, India, ⁶Department of Medicine, All India Institute of Medical Sciences, New Delhi, New Delhi, India, ⁷Internal Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh, India

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** Miscellaneous Rheumatic and Inflammatory Diseases Poster II  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Mixed connective disease is a multi-system disorder with overlapping features of SLE, rheumatoid arthritis, scleroderma and polymyositis/dermatomyositis with high titres of U1 RNP. Arthritis is a common manifestation that can be erosive and deforming. However, it is unclear whether clinical arthritis in MCTD is more common than SLE and there is little data comparing detection of synovitis by ultrasound in the two diseases.

**Methods:** In this cross-sectional study, we used the Kasukawa criteria for the diagnosis of MCTD and SLICC criteria for SLE patients. Patients were matched for gender and disease duration. U1-RNP was done in MCTD patients by Fluorescence Enzyme Immuno Assay in a 1:10 dilution and ANA by ELISA with a 1:200 dilution of sera. History of arthralgia/arthritis and clinical evaluation for swelling, tenderness, limitation of movements and deformities was done. Functional disability was assessed using the Indian Health assessment questionnaire.Hand radiographs of patients were assessed by for erosions. In addition, ultrasound (9-14 Mhz linear probe) of the non-dominant wrist, metacarpal joints for synovitis and teno-synovitis of flexor and extensor wrist compartments was assessed using the OMERACT definition.

**Results:** Forty patients were recruited in both groups, with similar gender distribution (F:M=38/2, 38/2), disease duration (3.7±2.3, 4.7±3.1, p=0.1) but slightly younger in age (31.8±13.3, 36±10.2, p=0.01) in MCTD than SLE. ANA was positive in all patients in both groups, and U1RNP was positive in all MCTD patients. History suggestive of inflammatory arthralgia/arthritis (100 vs 75%, p = 0.001) and current arthritis on examination (65 vs 37.5%, p=0.03) was significantly higher in MCTD than SLE (Table 1). PIP (30 vs 10%, p=0.025) and wrist (61.8vs 32.5%, p =0.007) involvement were significantly more in the MCTD. (Table 1) Use of methotrexate was also significantly more in the MCTD group(20% vs 5% p=0.043). However, on Ultrasound there was no significant difference in presence of synovitis (p=0.32) or teno-synovitis (p=0.51) and there was no difference in the functional disability measured by Indian Health assessment questionnaire (0.73 vs 0.74, p=0.7).Deformity was more common in MCTD (10 vs 0%), however, erosions were uncommon in both.Rheumatoid factor was positive more in patients with MCTD than SLE (34.4 vs 6.3%, p=0.005)
Conclusion: In this study we observed clinical arthritis to be significantly higher in MCTD patients in comparison with SLE, however, an equally high presence of synovitis on Ultrasound.

Table 1: clinical arthritis

<table>
<thead>
<tr>
<th>Joints/ arthritis</th>
<th>MCTD (%)</th>
<th>SLE (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atleast one tender joint</td>
<td>65</td>
<td>37.5</td>
<td>0.014</td>
</tr>
<tr>
<td>Atleast one swollen joint</td>
<td>47.5</td>
<td>15</td>
<td>0.002</td>
</tr>
<tr>
<td>PIP</td>
<td>27.5</td>
<td>42.5</td>
<td>0.16</td>
</tr>
<tr>
<td>DIP</td>
<td>10</td>
<td>30</td>
<td>0.025</td>
</tr>
<tr>
<td>MCP</td>
<td>0</td>
<td>2.5</td>
<td>0.314</td>
</tr>
<tr>
<td>Wrist</td>
<td>32.5</td>
<td>61.8</td>
<td>0.007</td>
</tr>
<tr>
<td>Elbow</td>
<td>12.5</td>
<td>22.5</td>
<td>0.239</td>
</tr>
<tr>
<td>Shoulder</td>
<td>20</td>
<td>27.5</td>
<td>0.431</td>
</tr>
<tr>
<td>Hip</td>
<td>0</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Knee</td>
<td>15</td>
<td>10</td>
<td>0.499</td>
</tr>
<tr>
<td>Ankle</td>
<td>12.5</td>
<td>12.5</td>
<td>1.0</td>
</tr>
<tr>
<td>MTP</td>
<td>5</td>
<td>7.5</td>
<td>0.644</td>
</tr>
<tr>
<td>IP</td>
<td>0</td>
<td>0</td>
<td>-</td>
</tr>
</tbody>
</table>

Disclosure: G. Sambandam, None; D. V. Dhir, None; D. M. Prakash, None; R. Minz, None; S. Sharma, None; A. Sharma, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/mixed-connective-tissue-disorder-has-higher-prevalence-of-arthritis-and-use-of-methotrexate-than-systemic-lupus-erythematosus

Abstract Number: 2125

Identification of Long-Term Prognostic Factors for Relapse or Exacerbation in Patients with Pulmonary Sarcoidosis: A Single Center Long-Term Observational Cohort Study

Okinori Murata1, Atsuko Kudo2 and Katsuya Suzuki3, 1Department of Pulmonary medicine, Hachinohe Red Cross Hospital, Hachinohe, Japan, 2Hachinohe Red Cross Hospital, Hachinohe, Japan, 3Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Sarcoidosis is a systemic granulomatous disease that can affect multiple organs, and in particular lung involvements are common and found in more than 90% of the patients [1]. Spontaneous remission is often observed within 2 years [2] and chest radiographic stage, skin involvements, over 40 years old or smoking history are reported as poor prognostic factors in pulmonary salcoidosis [3, 4]. However, there were no comprehensive reports of factors of relapse or exacerbation and characteristics of favorable patients without treatment in the long-term period more than 2 years. Aim of study is to identify prognostic factors for relapse or exacerbation in patients with pulmonary sarcoidosis in the long-term period.

Methods: Ninety-three patients who had visited at our division of Hachinohe Red Cross Hospital between January 2007 and December 2016 and clinically diagnosed as pulmonary sarcoidosis, were enrolled. They were divided into two groups, which presented relapse or exacerbation, and spontaneous remission. Clinical, laboratory and imaging data were collected from medical records and statistically analyzed.
Results: In 93 patients, 77% were women and mean age at diagnosis was 50.1 ± 16.6 years old. Mean observation period was 9.9 ± 8.8 years. Numbers of patients who had previously reported short-term prognostic factors are following: chest radiographic stage (Stage 0: n=3, Stage I: n=29, Stage II: n=36, Stage III: n=15, Stage IV: n=10), skin involvement (n=9), age over 40 years old (n=66), and smoking history (n=31). Overall relapse or exacerbation rate was 18.3% (n=17) and mean period to relapse or exacerbation was 8.5 ± 8.4 years. Then, we purified 64 patients who were observed for more than 5 years, and relapse or exacerbation was found in 7 patients. When compared characteristics at diagnosis between two groups, decrease of peripheral number of lymphocytes, frequency of bilateral hilar lymphadenopathy, or less than 3.5 in the ratio of CD4/CD8 in bronchoalveolar lavage fluid (BALF) were significantly highlighted in relapse or exacerbation group (P=0.019, 0.042, and 0.018, respectively).

Conclusion: Our long-term observational cohort study identified incidence rate and unique pronostic factors of relapse or exacerbation in patients with pulmonary sarcoidosis. This information could contribute to more appropriate medical administration in long term period.


Disclosure: O. Murata, None; A. Kudo, None; K. Suzuki, None.


Abstract Number: 2126

Safety of Immune Checkpoint Inhibitors for the Treatment of Melanoma, Bronchopulmonary and Urologic Neoplasms in Patients with Preexisting Autoimmune Disease

Alice Tison1, Gilles Quere1, Laurent Misery1, Thierry Lesimple2, Marie Marcq3, Stephanie Martinez4, Florence Brunet-Possenti5, Sandrine Mansard6, Nathalie Beneton7, Mickaël Lambert8, Christophe Roge8, Ouidad Zehou9, François Aubin10, Sarah Maanaoui11, Camille Scalbert11, damien giaccheri12, Nora Kramkimel13, François Skowron14, Anne Pham-Ledard15, Divi Cornee1 and Marie Kostine15.

1CHU Brest, Brest, France, 2Centre Eugène Marquis, Rennes, France, 3CH Vendee, La Roche-sur-Yon, France, 4CH Aix-en-Provence, Aix-en-Provence, France, 5CHU Bichat, Paris, France, 6CHU Clermont-Ferrand, Clermont-Ferrand, France, 7CH Le Mans, Le Mans, France, 8CH Morlaix, Morlaix, France, 9Hôpital Henri Mondor, Creteil, France, 10CHU Besancon, Besancon, France, 11CHU Lille, Lille, France, 12Centre Antoine Lacassagne, Nice, France, 13CHU Cochin, Paris, France, 14CH Valence, Valence, France, 15CHU Bordeaux, Bordeaux, France

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Immune checkpoint inhibitors (ICIs), by inhibiting immunosuppressive molecules overexpressed in the tumoral environment such as CTLA-4 or PD1, increase the anti-tumor immune response and have been approved for an increasing number of cancers. However, they are responsible for immune related adverse effects (IRAEs), and patients with preexisting autoimmune diseases (PAD) have been excluded from clinical trials evaluating those molecules. The aim of this study was to evaluate their safety in routine practice in patients with PAD and the anti-tumoral response in this population.

Methods: Three national expert networks, focusing respectively on skin cancers, thoracic cancers, and inflammatory diseases, participated in the study. All patients who received an ICI despite a PAD were included in this nationwide retrospective study.

Results: 31 patients were included in the study (19 men (61%), median age of 66). Most frequent PADs were rheumatoid arthritis (n=9; 29%), psoriasis (n=6; 19%), lupus (n=4; 13%), ulcerative colitis (n=3; 10%), and spondyloarthritis (n=3; 10%). Eleven patients were receiving an immunosuppressive therapy when the ICI was initiated, and 10 had an active disease at that time. Neoplasm types were melanoma (n=16; 52%), non-small-cell lung carcinoma (n=12; 39%), and urologic neoplasms (n=3; 9%), with a median disease duration of 19 months. The majority of the patients (30/31) received an anti-PD1 drug, for a median duration of 4 months. PAD flares were frequent (n=18; 58%) but mostly mild: CTCAE grade 1-2 (n=12; 67%), grade 3-4 (n=3; 17%). 14 patients (78%) received
corticosteroids or NSAIDs, and 3 (17%) methotrexate or acitretine for the treatment of these flares. IRAEs not associated with PAD appeared in 10 patients (32%): arthralgia (n=5), colitis (n=2), thyroiditis (n=2), vitiligo (n=2) with mild severity. None of the patients received TNF blockers, neither for a flare nor for an IRAE. 5 patients discontinued the immunotherapy because of an adverse effect. Regarding the cancer response rate, 4 patients over 11 who were taking an immunosuppressive treatment were responders (36%), versus 12 over the 20 other patients (60%).

Conclusion: PAD flares are frequent during ICI therapy and other IRAEs are also possible, usually easily managed with corticosteroids only. Anti-tumor response could be reduced when an immunosuppressor is ongoing at the beginning of the ICI, within the limit of the number of patients analyzed so far. Overall, the tolerance of ICIs in patients with PAD seems acceptable, but a multidisciplinary follow-up with the PAD referral physician is appropriate to manage frequent PAD flares and/or IRAEs.

Disclosure: A. Tison, None; G. Quere, None; L. Misery, None; T. Lesimple, None; M. Marcq, None; S. Martinez, None; F. Brunet-Possenti, None; S. Mansard, None; N. Beneton, None; M. Lambert, None; C. Roge, None; O. Zehou, None; F. Aubin, None; S. Maanaoui, None; C. Scalbert, None; D. giacchero, None; N. Kramkimel, None; F. Skowron, None; A. Pham-Ledard, None; D. Cornee, None; M. Kostine, None.


Abstract Number: 2127

Tumor Necrosis Factor Inhibitors for Sarcoidosis

Stefanie Wade\textsuperscript{1} and Mollie Carruthers\textsuperscript{2}, \textsuperscript{1}Medicine, University of Connecticut Health Center, Farmington, CT, \textsuperscript{2}Rheumatology, University of British Columbia, Vancouver, BC, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Patients with sarcoidosis refractory to standard treatment are a therapeutic challenge and are often managed by a variety of specialists due to the heterogeneity of disease manifestations. Treatment options for symptomatic sarcoidosis have improved in recent years and we are now using tumor necrosis factor (TNF) inhibitors for moderate or severe disease. Currently treatment response in pulmonary sarcoidosis is assessed via pulmonary function, chest imaging, and quality of life measures. Our objective was to evaluate the safety and efficacy of TNF inhibitors in multi-system sarcoidosis.

Methods: A systematic English literature review and meta-analysis using PubMed was performed on published studies and case series. Search strategy involved screening for articles between 1996 and 2017 which reported use of TNF inhibitors (etanercept (ETN), adalimumab (ADA), infliximab (INF), golimumab or certolizumab) for the treatment of biopsy proven sarcoidosis. We selected studies that directly assessed the effects of TNF inhibitors on treatment outcomes in systemic sarcoidosis. We excluded case reports, sarcoidosis that developed while on a TNFi, and disease limited to cutaneous involvement. Data regarding disease phenotype, past therapies, treatment outcomes, and adverse events were extracted by two reviewers and is undergoing assessment to be pooled in a meta-analysis.

Results: There were 470 abstracts identified. Selection was made of 102 original articles using TNF inhibitors in sarcoidosis. Fourteen studies were evaluated: five comparative trials and nine observational. The most robust studies were comparative trials in patients with pulmonary sarcoidosis. 450 cases of biopsy proven sarcoidosis underwent treatment with TNF inhibitors. Variation in objective results (including pulmonary function tests) was seen. Adverse events leading to discontinuation were infrequent. Observational studies assessed patients with more wide ranging phenotypes including cutaneous, ocular, central nervous system (CNS), cardiac, pulmonary, liver, and musculoskeletal manifestations. Clear benefit with INF in neurosarcoidosis (when used with mycophenolate) and in multi-system sarcoidosis was seen. Both INF and ADA led to improved outcomes in uveitis. In one open label study, INF led to improvement in FDG PET in a majority of patients and improvement in FVC by 6.6%. ADA improved or stabilized FVC in all patients with severe, symptomatic pulmonary sarcoid and led to improved 6MWT, Borg dyspnea score, and both patient and physician global assessment. An open label study with ETN for stage II and III pulmonary sarcoid was terminated early due to frequency of treatment failure. Case series support use in a wide range of extra-pulmonary organ systems, most notably neurosarcoidosis.

Conclusion: Current results from randomized and open label studies appear to support use of monoclonal antibody TNF inhibitors, for use in extra-pulmonary sarcoïd disease, with particularly compelling evidence for use in uveitis and neurosarcoidosis.
A Systematic Review of the Management of Patients with Preexisting Rheumatologic Diseases Receiving Checkpoint Inhibitors for Cancer

Noha Abdel-Wahab¹,², Mohsin Shah¹, Maria A. Lopez-Olivo¹ and Maria Suarez-Almazor¹, ¹Section of Rheumatology and Clinical Immunology, Department of General Internal Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA, Houston, TX, ²Rheumatology and Rehabilitation Department, Assiut University Hospitals, Assiut, Egypt, Assiut, Egypt

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The incidence and management of rheumatologic immune-related adverse events (irAEs) as a consequence of the checkpoint inhibitor (CPI) therapy in patients with cancer has been investigated, but no studies have synthetized the management of preexisting rheumatologic diseases in patients receiving CPI. We systematically review all reported cases describing the use of CPI in patients with a preexisting rheumatologic disease.

Methods: We searched 5 electronic databases through November 2016 and handsearched the references of relevant articles. We collected data on the specific CPI received, disease activity and anti-rheumatic modifying drugs while receiving CPI, and development and management of irAEs.

Results: Eleven publications met inclusion criteria, reporting on 30 cases (18 rheumatoid arthritis (RA)/inflammatory arthritis (IA); 3 seronegative spondyloarthropathy (2 psoriatic and 1 reactive arthritis); 3 sarcoidosis; 2 systemic erythematosus lupus (SLE); 2 vasculitis; 1 rheumatic fever; 1 Sjögren's syndrome). Age of the cases ranged from 30 to 84 years. All had melanoma. Of the 18 patients with RA/IA, 16 received ipilimumab, 1 nivolumab, and 1 pembrolizumab. Sixteen patients had active arthritis before starting CPI and 6 were kept on treatment (steroids, hydroxychloroquine, or leflunomide) while receiving CPI. Fifteen of 18 had irAEs (8 flare, 2 colitis, 1 autoimmune thyroiditis, 4 flare plus colitis or hypophysitis). Nonsteroidal anti-inflammatory drugs or steroids were used to treat all irAEs which resulted in improvement. However, infliximab and surgical resection were required for a patient with exacerbation of colitis after steroids tapering and CPI discontinuation was recommended in 5 patients. One patient with inactive RA was maintained on methotrexate and prednisolone, with no irAEs. Of the 3 patients with seronegative spondyloarthropathy, all received ipilimumab. Two patients with psoriatic arthritis had active disease, and one was maintained on methotrexate with no irAEs reported. The other patient stopped methotrexate prior to receiving the CPI and had worsening of plaques and de novo colitis that required steroids. No irAEs were reported in the 3 patients with seronegative spondyloarthropathy, all received ipilimumab. Two patients with psoriatic arthritis had active disease, and one was maintained on methotrexate with no irAEs reported. The other patient stopped methotrexate prior to receiving the CPI and had worsening of plaques and de novo colitis that required steroids. No irAEs were reported in the 3 patients with sarcoidosis, all received ipilimumab. Only one had active disease and was maintained on steroids while receiving CPI. All had irAEs (2 flare and 1 glaucoma) and improved with increasing steroids dose. The 2 patients with SLE, received ipilimumab. One had active disease, and both were maintained on hydroxychloroquine and/or steroids. None developed adverse events. irAEs were reported in one patient each with Behcet, eosinophilic granulomatous with polyangiitis, and Sjögren's, but none for the rheumatic fever.

Conclusion: Flares and irAEs in patients with rheumatologic disease receiving CPI can be managed, often not requiring therapy discontinuation. No difference was noted in the occurrence of irAEs in patients with active versus non-active preexisting diseases. CPI can be offered to these patients considering risk-benefit ratios and patient preferences.
Evaluation of Suppurative Hidradenitis in Patients with Chronic Arthritis Treated with Full and Tapered Biological Disease-Modifying Antirheumatic Drugs

Larissa Valor\textsuperscript{1}, Diana Hernández-Flórez\textsuperscript{2}, Tamara del Río\textsuperscript{2}, Juan Gabriel Ovalles-Bonilla\textsuperscript{3}, Julia Martínez-Barrio\textsuperscript{4}, Justina Janta\textsuperscript{1}, Belen Serrano\textsuperscript{5}, Juan Carlos Nieto\textsuperscript{1}, María Corre耶ro\textsuperscript{1}, Leticia Garcia Montoya\textsuperscript{6}, Carlos M Gonzalez\textsuperscript{1}, Indalecio Monteagudo\textsuperscript{1} and Francisco Javier López Longo\textsuperscript{7}, \textsuperscript{1}Rheumatology, Hospital General Universitario Gregorio Marañón, Madrid, Spain, \textsuperscript{2}Rheumatology, Hospital General Universitario Gregorio Marañón, Madrid, Spain, \textsuperscript{3}Instituto de Investigación Sanitaria Gregorio Marañón, Madrid, Spain, \textsuperscript{4}Rheumatology, Hospital General Universitario Gregorio Marañón, Madrid, Spain, \textsuperscript{5}Rheumatology, Hospital General Universitario Gregorio Marañón, Genoa, Italy, \textsuperscript{6}Facultad de Medicina, Universidad Complutense de Madrid, Madrid, Spain

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Suppurative Hidradenitis (SH) is an inflammatory skin disease with often disappointing response to treatment. It is a disorder of apocrine glands (axillary, inguinal and anogenital regions) with infection and multiple inflamed nodules, cysts, abscesses and sinus tracts. It has been associated in a 1-4% with spondyloarthropathies and inflammatory bowel disease, possibly due to an innate immune system deregulation. The use of biological disease-modifying antirheumatic drugs (bDMARD) specifically tumor necrosis factor inhibitors has been described as a therapeutic alternative achieving good clinical results in these patients. Objective: To evaluate the prevalence of SH using the SH-questionnaire in patients diagnosed with chronic arthritis treated with bDMARD.

Methods:
This cross-sectional study included 325 patients with a diagnosis of chronic arthritis. Those were recruited from Biological Therapy Unit at the Hospital General Universitario Gregorio Marañón and consecutively attended from January to March of 2015. All patients were treated with full or tapered bDMARD for at least 1 year. The bDMARD dosage tapering had been made in patients with a maintained remission according to their attending rheumatologist and the patient approval. None of patients had a previous SH diagnosis. All patients self-completed the validated SH-questionnaire (Esmann S, et al. Br J Dermatol. 2010 Jul;163(1):102-6, it was considered positive with an affirmative answer and lesions in >1 anatomical location. Patients were classified in peripheral arthritis (PerAR) [rheumatoid arthritis (RA)], psoriatic arthritis (PsA) and peripheral spondyloarthropathies (PerSpA) and axial spondyloarthopathies (AxSpA). The clinical evaluation was always performed by the same observer. Demographic, clinical and laboratory variables were collected and clinical indices related to each pathology were calculated (DAS28-ESR, DAS28-CRP, SDAI, CDAI, BASDAI, BASFI, ASDAS-CRP).

Results:
SH-positive was observed in 25/325 (7.7% vs. 92.3%) patients. Of these 25 patients, 12 (48%) were female and 13 (52%) were male. The mean age was 52 years (SD ± 12.9) and mean time since diagnosis was 14 years (SD ± 9.3). Twenty-four out of 25 patients had anti-TNF treatment (ETN=10, GOL=7, ADL=6, CTZ= 1). We found that 84% of patients had full and 16% had tapered bDMARD dosage. According to pathology, 13 had PerAR and 12 had AxSpA diagnosis (5.8% vs. 11.8%, p=0.062). Comparing the subtypes of PerAR, we found that 6 patients had PsA and 5 had RA. Evaluating the clinical activity disease, we found 9/13 patients in the PerAR group with clinical remission according to DAS28-ESR and CDAI (p=0.02 for both). Additionally, we found only 4/12 patients in remission in the AxSpA group by BASDAI, BASFI and ASDAS-PCR (p=0.006, p=0.005, p=0.004, respectively).

Conclusion:
We found more SH-positivity in the AxSpA than in the PerAR group, which is consistent with published data. A bDMARD tapered dosage was related to SH-positivity which might be linked to persistent and undetectable inflammation.

Disclosure: L. Valor, None; D. Hernández-Flórez, None; T. del Río, None; J. G. Ovalles-Bonilla, None; J. Martínez-Barrio, None; I. Janta, None; B. Serrano, None; J. C. Nieto, None; M. Corre耶ro, None; L. Garcia Montoya, None; C. M. Gonzalez, MSD, Celgene, Novartis, Abbvie, Janssen, 5,MSD, Celgene, Novartis, Janssen, UCB Pharma, 8; I. Monteagudo, None; F. J. López Longo, None.
Joint Manifestations in Patients Diagnosed with Idiopathic Inflammatory Myopathy: Multicenter Registry on Inflammatory Myositis from the Rheumatology Society in Madrid, Spain


Rheumatology, Hospital General Universitario Gregorio Marañón, Madrid, Spain, Rheumatology, Gregorio Marañón University General Hospital, Madrid, Spain, Servicio de Reumatología, Hospital General Universitario Gregorio Marañón, Madrid, Spain, Rheumatology, Hospital Universitario 12 de Octubre, Madrid, Spain, Servicio de Reumatología, Hospital Universitario La Paz, Madrid, Spain, Hospital Gregorio Marañón, Madrid, Spain, Rheumatology, H.U. La Princesa, Madrid, Spain, Hospital Universitario Puerta de Hierro, Madrid, Spain, Rheumatology, Hospital Madrid Norte Sanchinarro, Madrid, Spain, Pediatric Rheumatology Unit, University Children's Hospital Niño Jesús, Madrid, Spain, University Hospital Príncipe de Asturias, Immune System Diseases, Rheumatology department, Alcalá de Henares, Madrid, Spain, Hospital Universitario Reina Sofia, Universidad Europea de Madrid, Madrid, Spain, Rheumatology Unit, Hospital Universitario Fundación Alcorcón, Madrid, Spain, Rheumatology, Hospital Universitario La Paz, Spain, Instituto for Musculoskeletal Health, Madrid, Spain, Facultad de Medicina, Universidad Complutense de Madrid, Madrid, Spain

First publication: September 18, 2017

SESSION INFORMATION

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Muscle Biology, Myositis and Myopathies Poster

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

Background/Purpose: Idiopathic inflammatory myopathies (IIM) comprise a heterogeneous group of autoimmune conditions characterized by muscle non-suppurative inflammation, progressive muscle weakness and a variety of extra-muscular manifestations. Joint involvement can be considered to be part of the IIM systemic manifestations, together with a possible gastrointestinal, cardiovascular and/or pulmonary involvement. Although articular involvement in the IIM, including inflammatory arthralgia and arthritis, has been described as variable and non-specific with a chronic course it might be an early symptom of dermatomyositis in up to 30% of cases and in those patients with overlap syndromes. We aim to evaluate and to identify joint manifestations in IIM patients.

Methods: We evaluated a cohort of 479 patients that included 12 hospitals in the Community of Madrid belonging to the IIM registry of the Society of Rheumatology of Madrid (SORCOM-REMICAM) with diagnosis from January 1980 to December 2014. All patients were diagnosed of IIM according to Bohan and Peter criteria (Bohan A, Peter JB. N Engl J Med 1975 Feb 13;292(7):344-7). The presence of arthralgia and arthritis was considered. IIM were classified as dermatomyositis (primary and secondary dermatomyositis) (DM) and polymyositis (PM) including the rest of the patients (classification I). Also, IIM were classified (II) as primary polymyositis (PPM), primary dermatomyositis (PDM), overlap syndrome (OsD), juvenile myopathies (JM), cancer-associated myopathies (CAM), autoimmune necrotizing myopathy and inclusion body myositis (these were grouped as other myositis; OM).

Results: We found 70 (18%) patients with acute arthritis (<6 weeks), 74 (19%) patients with chronic arthritis (>6 weeks) and 245 (65%) patients without any joint manifestations. Using the Tanimoto et al. criteria (1), the presence of erosive arthritis was observed in 149/479 (38.3%) of the patients. When comparing the joint manifestations in the PM and DM groups (n=250, 52.2% vs. n=229, 47.8%) no statistically significant differences were observed. However, assessing joint manifestations according to classification II, we observed that the highest prevalence was found in the OsD group, followed by the PDM group (p=0.0001). The group with less joint manifestations was JM compared to OsD and PDM (45% vs. 90% and 71%, respectively).

Conclusion: The presence of joint manifestations associated with IIM in our cohort is higher compared to other studies described in the literature so far and emphasize the importance of an accurate joint examination in these patients. The OsD group showed more joint manifestations which might be explained by the coexistence of SLE and MCTD patients in this group. Currently, no association between the clinical subtypes of IIM, overall, these results are encouraging and suggest that joint assessment in follow up may be helpful in differentiating subtypes of IIM.
Longitudinal Cohort Study of Anti-PM/Scl Myositis Patients: Mild Muscle and Lung Involvement with Prominent Perivascular Inflammation

Rebecca De Lorenzo1, Iago Pinal-Fernandez2, Maria Casal-Dominguez2, Wilson Huang2, Jose Cesar Milisenda1, Cassie Parks2, Katherine Pak3, Cheilonda Johnson4, Eleni Tiniakou5, Jemima Albyaida6, Julie J. Paik6, Sonye K. Danoff7, Lisa Christopher-Stine7, Andrea Corse8 and Andrew Mammen3,9, 1Muscle Disease Unit, NIAMS, NIH, Bethesda, MD, 2NIAMS, NIH, Bethesda, MD, 3National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, 4Medicine/Pulmonology, Johns Hopkins University School of Medicine, Baltimore, MD, 5Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, 6Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, 7Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, 8Neurology, Johns Hopkins University, Baltimore, MD, 9Neurology, Johns Hopkins University School of Medicine, Baltimore, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Muscle Biology, Myositis and Myopathies Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: To describe the clinical and serologic features, as well as the disease course and response to therapy of anti-PM/Scl patients.

Methods: All Johns Hopkins Myositis Center patients positive for anti-PM/Scl autoantibodies from 2002 to 2016 were included in the study and compared with other autoantibody-positive patients of the cohort. We studied the presence and rate of development of clinical features, the intensity of muscle and lung involvement, and the serologic and biopsy characteristics of these patients.

Results: 41 anti-PM/Scl patients were compared with 445 patients positive for other myositis autoantibodies. Muscle weakness was responsive to first-line immunosuppressants, similar in severity to that of patients with antisynthetase syndrome (AS) and dermatomyositis (DM) autoantibodies, and milder than in patients with immune-mediated necrotizing myopathy autoantibodies. Distal and deltoid weakness was more common in anti-PM/Scl patients than in other myositis subgroups. Muscle biopsies showed marked perivascular inflammation (79%) with scarce perifascicular atrophy (26%). ILD was detected in 61% of anti-PM/Scl patients, more frequently than in DM (13%) and less than in AS (80%), but was milder compared to AS. Extramuscular involvement was common and heterogeneous, with marked skin involvement. No major differences were detected between patients positive for both anti-PM/Scl-75 and anti-PM/Scl-100 and those positive for just one. The nucleolar ANA pattern was effective as a screening technique (sensitivity=94%, specificity=92%) to detect anti-PM/Scl autoantibodies in myositis patients. No increased cancer or mortality rates were detected in these patients.

Conclusion: Anti-PM/Scl myositis is characterized by a particular pattern of weakness, mild lung and muscle involvement, and marked extramuscular features.
Angiogenesis and VEGF-Expressing Cells Are Identified Predominantly in the Fascia Rather Than the Muscle in the Early Phase of Dermatomyositis

Ken Yoshida1,2, Haruyasu Ito1, Kazuhiro Furuya1, Taro Ukichi1, Kentaro Noda1 and Daitaro Kurosaka1, 1Division of Rheumatology, Department of Internal Medicine, Jikei University School of Medicine, Tokyo, Japan, 2Internal Medicine, Jikei University School of Medicine, Tokyo, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Muscle Biology, Myositis and Myopathies Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: We previously showed that fasciitis is a frequent manifestation of the disease in dermatomyositis (DM) but not in polymyositis (PM) and that DM-associated fasciitis is detected, as the result of the increased vascularity in the fascia, by power Doppler ultrasonography. We examined whether angiogenesis and vascular endothelial growth factor (VEGF)-expressing cells in the fascia are histologically identified in the early phase of DM, and whether inflammation is involved in angiogenesis and an increased number of VEGF-expressing cells.

Methods: We prospectively evaluated en bloc biopsy specimens obtained from 22 patients with DM and 11 patients with PM before treatment. Immunohistochemical staining for CD31, VEGF, and TNF-α were performed. The total vascular inflammation score (TVIS) was defined as the total number of aggregates of ≥50 perivascular inflammatory cells per 4-mm² area in the 3 fields with the most remarkable infiltration of perivascular inflammatory cells to quantify the degree of inflammation. The angiogenesis score (AS) was defined as the total number of CD31-positive blood vessels in 3 high-power fields (200×) that showed the most remarkable proliferation of the vessels. The numbers of VEGF- and TNF-α-expressing cells were counted in the 3 high-power fields (400×) that showed the largest accumulation of these cells. The TVIS, AS, and numbers of VEGF- and TNF-α-expressing cells were statistically analyzed in the fascia and muscle tissues.

Results: The AS, the number of VEGF-expressing cells, and the TVIS in the fascia of patients with DM were significantly higher compared with those of patients with PM; no significant difference was found in the muscle of patients with DM and PM. The number of VEGF-expressing cells in the fascia was correlated with the AS of patients with DM. In the early phase (the period from the onset of muscle symptoms until the biopsy <2months) of DM, the AS, the number of VEGF-expressing cells, and the TVIS in the fascia were significantly greater compared with the muscle. However, no significant differences were observed between the muscle and fascia in the late phase (the period ≥2) of DM. In patients with DM, the TVIS was correlated with the AS in the fascia, while the number of TNF-α-expressing cells was correlated with the TVIS and the number of VEGF-expressing cells in the fascia.

Conclusion: Angiogenesis, the number of VEGF-expressing cells, and the TVIS were higher in the fascia of patients with DM in comparison to patients with PM, and were increased predominantly in the fascia rather than the muscle in early-phase DM. Our data suggest that the angiogenesis induced by VEGF may progress from the fascia into the muscle in patients with DM. The degree of inflammation was correlated with that of angiogenesis in the fascia of patients with DM. These data suggest that the fascia can be a primary site of inflammation and angiogenesis in the pathogenesis of DM.

Disclosure: K. Yoshida, None; H. Ito, None; K. Furuya, None; T. Ukichi, None; K. Noda, None; D. Kurosaka, None.

Abstract Number: 2132

Clinical Characteristics of the Patients with Recurrent Myositis in Polymyositis and Dermatomyositis: A Retrospective Study

Akira Nishino, Yasuhiro Katsumata, Hidenaga Kawasumi, Yasushi Kawaguchi and Hisashi Yamanaka, Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan

First publication: September 18, 2017
Background/Purpose: Patients with polymyositis (PM) and dermatomyositis (DM) often experience relapse–remitting courses and recurrent myositis. However, only a few studies focused on this issue, and most of them were reported more than 10 years ago. We aimed to study the characteristics of PM/DM patients with recurrent myositis and to identify its risk factors.

Methods: We retrospectively reviewed the medical records of patients who were diagnosed as PM/DM between 1993 and 2016. All patients satisfied Bohan and Peter classification criteria for PM/DM. Patients with clinically amyopathic DM were excluded. Recurrent myositis was defined as a sustained elevation in serum creatine kinase (CK) levels, which required intensification of immunosuppressive treatment. Myositis-specific autoantibodies were thoroughly evaluated by immunoprecipitation and enzyme-linked immunosorbent assays. The baseline clinical characteristics were compared between patients with and without recurrent myositis. Univariate and multivariate logistic regression analyses were performed to identify the risk factors for recurrent myositis in patients with PM/DM.

Results: Of the 120 patients included in the present study, 56, 42, and 22 patients were PM, DM, and PM/DM associated with another connective tissue disease, respectively. Initially, glucocorticoids were administered to all the patients, and other immunosuppressants were concomitantly used in 76 patients, which led to the normalization of CK level in all the patients. Myositis recurred in 35 patients (29%) during the observation periods (median 2.4 years). Among these, 29 (83%) were treated with glucocorticoids alone at the time of the recurrence: median dosage was 10 mg/day as prednisolone. Table 1 shows the baseline characteristics of the patients with and without recurrent myositis. Baseline CK levels in patients with recurrent myositis were significantly higher than those without (p < 0.01), and the ROC curve analysis determined the cutoff value for baseline CK level as ≥ 2477 U/l. By univariate analyses, baseline CK level ≥ 2477 U/l, positive anti-signal recognition particle (anti-SRP) antibody, and initial treatment without calcineurin inhibitor, namely tacrolimus and cyclosporine were associated with myositis recurrence (p < 0.01). Multivariate analysis identified anti-SRP antibody (odds ratio [OR], 7.7; 95% confidence interval [CI], 1.6 to 38) as a positive risk factor, whereas initial treatment with calcineurin inhibitor (OR, 0.2; 95% CI, 0.1 to 0.7) as a negative risk factor for myositis recurrence.

Conclusion: The present study suggested that anti-SRP antibody is a risk for myositis recurrence and that initial treatment with calcineurin inhibitor is protective against myositis recurrence in patients with PM/DM. In addition, most of the patients with recurrent myositis were treated with glucocorticoids alone at the time of the recurrence.

Table 1 Baseline characteristics of patients with and without myositis recurrence

<table>
<thead>
<tr>
<th></th>
<th>Patients with myositis recurrence (n = 35)</th>
<th>Patients without myositis recurrence (n = 85)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>48 (28 to 76)</td>
<td>47 (19 to 80)</td>
<td>0.53</td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>36 (66%)</td>
<td>64 (79%)</td>
<td>0.23</td>
</tr>
<tr>
<td>PM/DM/Overlap myositis, n</td>
<td>18/16/6</td>
<td>37/32/16</td>
<td>0.56</td>
</tr>
<tr>
<td>Intestinal lung disease, n (%)</td>
<td>28 (80%)</td>
<td>58 (68%)</td>
<td>0.27</td>
</tr>
<tr>
<td>CK level, U/l</td>
<td>2986 (576 to 13380)</td>
<td>1266 (105 to 2917)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>CK level ≥ 2477 U/l, n (%)</td>
<td>21 (60%)</td>
<td>25 (20%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Myositis-specific autoantibodies</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-ARS antibody, n (%)</td>
<td>12 (34%)</td>
<td>39 (40%)</td>
<td>0.31</td>
</tr>
<tr>
<td>Anti-1 antibody, n (%)</td>
<td>7 (20%)</td>
<td>21 (25%)</td>
<td>0.64</td>
</tr>
<tr>
<td>Anti-SRP antibody, n (%)</td>
<td>5 (30%)</td>
<td>3 (4%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Anti-Mi-2 antibody, n (%)</td>
<td>1 (3%)</td>
<td>3 (4%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Anti-NXP-2 antibody, n (%)</td>
<td>1 (3%)</td>
<td>3 (4%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Anti-TIF1-γ antibody, n (%)</td>
<td>0 (0%)</td>
<td>4 (5%)</td>
<td>0.32</td>
</tr>
<tr>
<td>Anti-MDA5 antibody, n (%)</td>
<td>0 (0%)</td>
<td>5 (6%)</td>
<td>0.32</td>
</tr>
<tr>
<td>Initial treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prednisolone dosage, mg/day</td>
<td>50 (25 to 100)</td>
<td>51 (20 to 60)</td>
<td>0.81</td>
</tr>
<tr>
<td>Steroid pulse therapy, n (%)</td>
<td>6 (23%)</td>
<td>16 (19%)</td>
<td>0.80</td>
</tr>
<tr>
<td>Methylprednisolone, n (%)</td>
<td>4 (10%)</td>
<td>10 (12%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Calcineurin inhibitor, n (%)</td>
<td>4 (10%)</td>
<td>34 (40%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Intravenous cyclophosphamide, n (%)</td>
<td>9 (30%)</td>
<td>21 (25%)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

*Unless otherwise noted, data are described as median (range).

* p-values were determined by Fisher’s exact test or Mann-Whitney U test.

* Anti-1 antibody was included.

Disclosure: A. Nishino, None; Y. Katsumata, Chugai Pharmaceutical Co., Ltd., Astellas Pharma Inc., Takeda Pharmaceutical Company Limited., Bayer Yakuhin, Ltd., AYUMI Pharmaceutical Corporation, 5; H. Kawasumi, None; Y. Kawaguchi, None; H. Yamanaka, MSD, Astellas, AbbVie, BMS, Kaken, UCB, Ono, Ayumi, Eisai, Daiichi-Sankyo, Takeda, Tanabe-Mitsubishi, Chugai,
Identification of Multiple Cancer Associated Myositis Specific Antibodies in Idiopathic Inflammatory Myopathies: A Large Longitudinal Cohort Study

Hanbo Yang¹, Qinglin Peng², Liguo Yin¹, Shanshan Li¹, Jingli Shi¹, Yamei Zhang¹, Xin Lu¹, Xiaoming Shu¹, Sigong Zhang³ and Guochun Wang⁴,
¹Rheumatology, China-Japan Friendship Hospital, Beijing, China, ²Rheumatology, China-Japan Friendship Hospital, Beijing, China, ³Rheumatology, Lanzhou University Second Hospital, Lanzhou, China, ⁴China-Japan Friendship Hospital, Beijing, China
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Muscle Biology, Myositis and Myopathies Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Paraneoplastic myositis provide an exceptional opportunity for cancer triggered autoimmunity. Myositis specific antibodies (MSAs) show great clinical utility in IIM diagnosis and classification. However, cancer-associated MSAs has not been systematically identified, which may help for targeted cancer screening and provide clues to study cancer-immune system interactions. The objective of the study was to systematically evaluate the association between MSAs and cancer-associated myositis (CAM).

Methods: Sera from 627 idiopathic inflammatory myopathies (IIMs) patients were tested for MSAs. The cancer risk with different MSAs was estimated by standardized incidence ratio (SIR). The temporal relationship between myositis onset and cancer diagnoses, as well as the correlation between the clinical course of myositis and cancer in patients with IIM were evaluated.

Results: Compared with the general Chinese population, IIM patients with anti-TIF1-γ antibodies (SIR=17.28, 95% CI: 11.94 to 24.14); anti-NXP2 antibodies (SIR=8.14, 95% CI: 1.63 to 23.86); or anti-SAE1 antibodies (SIR=12.92, 95% CI: 3.23 to 32.94), or who were MSAs-negative (SIR=3.99, 95% CI: 1.96 to 7.14) faced an increased risk for cancer (Table 1). There was no association between specific MSAs subtypes and certain types of cancer. A close temporal relationship between the onset of myositis and cancer diagnoses was identified in the patients carrying anti-TIF1-γ, as well as other MSAs. In addition, a parallel between clinical course of myositis and cancer was observed in patients from various MSAs, such as anti-Jo-1 and anti-PL-12. There were no prognostic differences among the CAM patients from different MSA subgroups. However, patients with cancer developing within 1.5 year of myositis onset had a shorter survival time than those suffered from cancer beyond 1.5 year of myositis (17.0 vs. 45.0 months, p=0.004).

Conclusion: Our study demonstrates, in what is to our knowledge the largest population examined to date, that multiple myositis specific autoantibodies (anti-TIF1-γ, anti-NXP2, and anti-SAE1) are associated with cancer in IIM patients. Moreover, our data suggest that in some cases, anti-Jo-1 and anti-PL-12 antibody production might also be driven by malignancy. This can aid in the etiologic research of paraneoplastic myositis and clinical management.

Disclosure: H. Yang, None; Q. Peng, None; L. Yin, None; S. Li, None; J. Shi, None; Y. Zhang, None; X. Lu, None; X. Shu, None; S. Zhang, None; G. Wang, None.

ADAM-17 Is Expressed in the Inflammatory Myopathy, and Is Involved with Interstitial Lung Disease
Background/Purpose: A disintegrin and metalloprotesase (ADAM) family is protease that is thought to have an important role in tissue destruction and inflammatory reaction. ADAMs are also involved in the amputation from the cell surface of inflammatory cytokines. ADAM-17 is one of the ADAM family, and is first described as the protease responsible for tumor necrosis factor (TNF)-α shedding. However, the function of ADAM-17 in myositis is unclear. Here, we have shown the expression of ADAM-17 in inflammatory myopathy and demonstrated the role of inflammation in interstitial lung diseases (ILD).

Methods: The serum were collected from the patients who were diagnosed with inflammatory myopathy in Showa University Hospital from 2003 to 2015. Twenty-six patients were diagnosed with polymyositis (PM), 34 patients were diagnosed with dermatomyositis (DM), and 10 patients were diagnosed clinically amyopathic dermatomyositis (CADM). Clinical manifestations and clinical data were also collected. The levels of ADAM-17 in the serum samples were measured using enzyme-linked immunosorbent assay (ELISA). ADAM-17 expression was determined in muscle tissues from DM using immunohistological staining. To determine that the role of lung fibrosis in inflammatory myopathy with ILD, we used human lung fibroblasts (HLF). ADAM-17 expression on HLF was also demonstrated by immunohistogical staining.

Results: ADAM-17 in inflammatory myopathy was significantly higher than in healthy control (n=19) (mean ± SEM; 1048 ± 312 pg/ml and 36 ± 18 pg/ml, respectively, p<0.05). ADAM-17 in corticosteroid and/or immunosuppressant treatment patient serum was also significantly decreased compared with in pre treatment patient serum (1465 ± 562 pg/ml and 1059 ± 503 pg/ml, respectively, p<0.01). ADAM-17 was significantly positive correlated with fractalkine/CX3CL1 in serum (r=0.27, p<0.05). In addition, ADAM-17 in inflammatory myopathy with ILD patients (n=46) was significantly higher than in non-ILD patients (n=24) (1379 ± 454 pg/ml and 413 ± 226 pg/ml, respectively, p<0.05). Finally, we found the expression of ADAM-17 in muscle biopsy tissue. Hence, ADAM-17 on HLF was expressed by immunohistochemistry. ADAM-17 in IL-6 and IL-6R stimulated HLF was significantly higher compared with non-stimulated HLF (48 ± 6 pg/ml and 0 ± 0 pg/ml, respectively, p<0.05).

Conclusion: ADAM-17 is expressed in inflammatory myopathies especially with ILD and expressed on HLF, suggesting that ADAM-17 may play the role in lung fibrosis. ADAM-17 may be a potential target in inflammatory myopathies with ILD.

Disclosure: A. Nishimi, None; T. Isozaki, None; S. Nishimi, None; S. Ishii, None; T. Tokunaga, None; H. Furuya, None; K. Wakabayashi, None; T. Kasama, None.

Abstract Number: 2136

Association of HLA-DQA1*05 with the Presence of Interstitial Lung Disease Independent of Autoantibody Status in Caucasian Patients with Polymyositis and Dermatomyositis

Adam Schiffenbauer1, Sara Faghihi-Kashani2, Terrance P. O'Hanlon1, Willy Flegel3, Sharon Adams3, Ira N. Targoff4, Chester V. Oddis5,6, Rohit Aggarwal7,8, Lisa G Rider1, Steven R. Ytterberg9, Lisa Christopher-Stine10, Sonye K. Danoff11, Paul F. Dellaripa12,13, Ejaz Shamim14, Andrew Mammen15 and Frederick W Miller16, 1Environmental Autoimmunity Group, NIEHS, NIH, Bethesda, MD, 2Environmental Autoimmunity Group, National Institute of Environmental Health, Bethesda, MD, 3Department of Transfusion Medicine, National Institutes of Health, Bethesda, MD, 4VA Medical Center, University of Oklahoma Health Sciences Center, Oklahoma Medical Research Foundation, Oklahoma City, OK, 5Rheumatology/Clinical Immunology, University of Pittsburgh/University of Pittsburgh Medical Center, Pittsburgh, PA, 6Rheumatology/Clinical Immunology, University of Pittsburgh, Pittsburgh, PA, 7Pediatra II, Reumatologia, PRINTO, Istituto Giannina Gaslini, Genoa, Italy, 8Department of Medicine / Rheumatology, University of Pittsburgh Medical Center, Pittsburgh, PA, 9Rheumatology, Mayo Clinic, Rochester, MN, 10Medicine, Johns Hopkins University
Interstitial lung disease (ILD) is a frequent complication and a major contributor to mortality and morbidity in polymyositis and dermatomyositis (PM/DM). Prior studies have linked the presence of anti-synthetase autoantibodies (ASA) and part of the HLA 8.1 ancestral haplotype (AH8.1) to ILD in PM/DM patients. This study aimed to evaluate the contribution of HLA-DQA1*05 to the presence of ILD in Caucasian PM/DM independent of ASA.

Methods:

A total of 82 Caucasian patients with adult-onset PM/DM per Bohan and Peter criteria and with HLA class I (A, B and C) and class II (DRB1 and DQA1) evaluated by sequence-specific oligonucleotide probe hybridization and priming techniques or sequencing methods were included. ILD status was determined by retrospective chart review based on imaging results, lung biopsy, and/or pulmonary function tests. ASA were determined by standard immunoprecipitation methods. AH8.1 was defined as the presence of HLA-A*01, B*08, C*07, DRB1*0301, and DQA1*05. Pearson chi-square (or Fischer exact when appropriate), multiple logistic regression tests and forward stepwise logistic methods were applied. P < 0.05 was considered statistically significant.

Results:

Overall, 27 (33%) had ILD, 29 (35%) were positive for ASA and 29 (35%) carried the AH8.1. ILD was associated with ASA (OR=8.0, 95%CI: 2.83-22.58, P<0.001) and with the AH8.1 (OR=3.66, 95%CI: 1.38-9.67, P=0.009) as expected. Of the five AH8.1 alleles, HLA-DQA1*05 was the only locus significantly associated with ILD after adjusting for the presence of ASA (OR=5.95, 95%CI: 1.47-24.05, P=0.012). This association remained significant after adjusting for the presence of the other alleles of the AH8.1 and ASA status (OR=12.31, 95% CI: 1.81-83.81, P=0.010). Chi squared tables, categorizing the cohort based on the presence or absence of each AH 8.1 allele, were used to assess the independent effect of HLA-DQA1*05 on risk of ILD conditioned on ASA status and the frequency of ILD was higher in DQA1*05 carriers, however, due to limited power, not all comparisons met statistical significance. Additionally, forward stepwise logistic analysis, while keeping ASA in the model regardless of step, showed that DQA1*05 was the only HLA allele that remained in the best fit model for risk of ILD (OR=5.95, 95% CI: 1.47-24.05, P=0.012). Figure 1 shows the risk of ILD in Caucasian PM and DM patients based on the ASA and DQA1*05 status.

Conclusion:

HLA-DQA1*05 is associated with an increased risk of ILD in Caucasian PM and DM patients, independent of ASA and other AH8.1 alleles, implying that HLA-DQA1*05 impacts the risk of ILD independently from ASA in Caucasian PM/DM. Thus, HLA-DQA1*05 may be a useful screening test for evaluating the risk of ILD in ASA negative PM/DM patients and may have diagnostic, prognostic and pathogenic implications for myositis-associated ILD that should be further assessed in additional cohorts.
Abstract Number: 2137

Clinical Factors Associated with Long-Term Damage and Calcinosi

Vladislav Tsaltyskan1, Annette Aldous2, Sam Serafi1, Heidi Sami1, Gulnara Mamyrova1, Frederick W Miller3, Sam Simmons2, Rodolfo Curiei1, Olay Y. Jones4 and Lisa G Rider3, 1Department of Rheumatology, George Washington University, Washington, DC, 2Department of Epidemiology and Biostatistics, George Washington University Milken Institute School of Public Health, Washington, DC, 3Environmental Autoimmunity Group, National Institute of Environmental Health Sciences, National Institutes of Health, Bethesda, MD, 4Department of Pediatrics, Walter Reed National Military Medical Center, Bethesda, MD

First publication: September 18, 2017
Background/Purpose: Juvenile idiopathic inflammatory myopathies (JIIM) are rare, autoimmune chronic muscle diseases of childhood with significant potential long-term morbidity. In this study we investigate associations of clinical and demographic factors with long-term outcomes in a referral population of patients with JIIM who are currently adults.

Methods: Adults with JIIM were assessed at two referral centers between 1994 and 2016. Bivariate analysis was used to test for associations of 94 clinical, demographic, and laboratory factors with two long-term outcomes: a higher Myositis Damage Index (MDI) and the presence of calcinosis on last evaluation. A multivariable regression model for MDI used backwards selection on factors with statistically significant associations (p < .15) in bivariate analysis.

Results: Forty-nine patients with probable or definite JIIM (37 dermatomyositis, 5 polymyositis, 7 overlapping myositis) had a median age of 24 years [IQR 19, 28], and median follow-up period of 12 years after diagnosis [IQR 5, 20]; 59% were Caucasian and 82% were female; 63% had a chronic, 31% a polycyclic, and 6% a monocyclic illness course. Damage was present in 96%, with a median MDI score of 6 [IQR 3, 9]. Cutaneous (80%) and muscle (78%) damage were most frequent and most severe (median score 2 [IQR 1, 3] for both) among the MDI organ systems. Calcinosis was present in 55% of patients. Of the 94 potential predictors, 17 were significantly (p < 0.15) associated with total MDI score and 11 were significantly (p < 0.05) associated with the presence of calcinosis (Table). All selected variables in the multivariable model were independently associated with a higher MDI score: erythroderma, shawl sign, disease duration, worst ACR functional class, and heliotrope rash. Several factors were strongly associated with calcinosis in bivariate analysis including disease duration, younger age at diagnosis, falling episodes, Gottron’s papules, clinical subgroup JDM, constipation, periungual capillary changes, lipodystrophy, and contractures (Table). The multivariable logistic regression model for calcinosis did not converge due to the small sample size.

Conclusion: This is one of the largest cohorts of patients with JIIM evaluated for long-term outcomes into adulthood. We were able to identify multiple clinical factors associated with long-term damage and calcinosis when JIIM patients become of adult age, which included specific cutaneous and musculoskeletal features.

Table 1: Top factors associated with Myositis Damage Index (MDI) score and calcinosis at last evaluation (N = 49).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Predictors of MDI score</th>
<th>Predictors of Calcinosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bivariate Analysis</td>
<td>Multivariable Regression</td>
</tr>
<tr>
<td></td>
<td>Corr. Coef, p</td>
<td>Est (B), SE, P, OR (95% CI), P</td>
</tr>
<tr>
<td>Erythroderma (ever)</td>
<td>0.42 (.003)</td>
<td>3.94 (1.50, 0.01)</td>
</tr>
<tr>
<td>Shoulder sign (ever)</td>
<td>0.35 (.01)</td>
<td>2.71 (9.94, 0.006)</td>
</tr>
<tr>
<td>Wheezing (ever)</td>
<td>0.33 (.03)</td>
<td>1.48 (0.04, 0.04)</td>
</tr>
<tr>
<td>Disease duration (per year)</td>
<td>0.31 (.03)</td>
<td>1.12 (1.03-1.24), .006</td>
</tr>
<tr>
<td>Age at diagnosis (per year)</td>
<td>0.30 (.04)</td>
<td>0.81 (0.70-0.95), .008</td>
</tr>
<tr>
<td>Falling episodes (ever)</td>
<td>0.34 (.04)</td>
<td>5.89 (1.38-25.33), .03</td>
</tr>
<tr>
<td>Gottron’s papules (ever)</td>
<td>0.29 (.04)</td>
<td>3.88 (.05)</td>
</tr>
<tr>
<td>Clinical subgroup (JDM, JPM, KMTH)</td>
<td>NA (.04)</td>
<td>5 (.01)</td>
</tr>
<tr>
<td>Worst ACR functional class (per level)</td>
<td>0.28 (.05)</td>
<td>1.33 (1.37, .001)</td>
</tr>
<tr>
<td>Azathioprine use (ever)</td>
<td>0.28 (.05)</td>
<td></td>
</tr>
<tr>
<td>Disease course</td>
<td>NA (.05)</td>
<td></td>
</tr>
<tr>
<td>Ulceration (ever)</td>
<td>0.25 (.09)</td>
<td></td>
</tr>
<tr>
<td>Malar rash (ever)</td>
<td>0.23 (.11)</td>
<td></td>
</tr>
<tr>
<td>Antistreptolob antibody</td>
<td>0.26 (.11)</td>
<td></td>
</tr>
<tr>
<td>Cuticular overgrowth (ever)</td>
<td>0.22 (.13)</td>
<td></td>
</tr>
<tr>
<td>Heliotrope rash (ever)</td>
<td>0.22 (.13)</td>
<td>2.69 (1.01, 0.05)</td>
</tr>
<tr>
<td>Number of DMARDs used</td>
<td>0.21 (.14)</td>
<td></td>
</tr>
<tr>
<td>Constipation (ever)</td>
<td>3 (.006)</td>
<td></td>
</tr>
<tr>
<td>Periungual capillary changes (ever)</td>
<td>8.65 (1.63-46.08), .007</td>
<td></td>
</tr>
<tr>
<td>Lipodystrophy (ever)</td>
<td>5.97 (1.22-21.28), .02</td>
<td></td>
</tr>
<tr>
<td>Contracture (ever)</td>
<td>3.98 (1.00-13.55), .04</td>
<td></td>
</tr>
</tbody>
</table>

1 Dichotomous variables: point-biserial correlation coefficients; ordinal or continuous variables: Spearman correlation coefficient; categorical with 3 levels not available based on analysis of variance (ANOVA).
2 Due to missing data, these variables were not included in multivariable model.
3 Odds ratio could not be calculated.

Disclosure: V. Tsai, None; A. Aldous, None; S. Serafi, None; H. Sami, None; G. Mamyrrova, Cure JM, 2; F. W. Miller, None; S. Simmons, None; R. Curiel, Cure JM, 2,BMS, 2; O. Y. Jones, None; L. G. Rider, None.


Abstract Number: 2138
Predictive Factors for Achievement of Sustained Remission with Polymyositis/Dermatomyositis: A Retrospective Single Center Cohort Study in Japan

Eri Watanabe1, Takahisa gono1, Shinji Watanabe1, Hiroki Yabe1, Masataka Kuwana2 and Chihiro Terai1, 1Department of Rheumatology, Saitama Medical Center, Jichi Medical University, Saitama, Japan, 2Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Muscle Biology, Myositis and Myopathies Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Polymyositis (PM), dermatomyositis (DM), and clinically amyopathic DM (CADM) are systemic inflammatory diseases that affect skeletal muscle, skin, and other organs, such as lungs, heart, and joints. Several complications, such as interstitial lung disease (ILD), cardiomyopathy, and malignancy, are associated with poor prognosis for patients with PM/DM/CADM. Previous studies have highlighted the mortality and prognostic factors in PM/DM. Recently, myositis-specific autoantibodies (MSAs) have been used to predict clinical features, treatment response, and prognosis in patients with PM/DM/CADM. However, disease status after the treatment of adult patients with PM/DM/CADM, such as persistent existing disease activity or sustained remission, remains unclear in daily practice. Therefore, we investigated the disease status after treatment and clarified the predictive factors for sustained remission in adult patients with PM/DM/CADM using clinical data, including MSAs.

Methods: A total of 161 adult patients with PM/DM/CADM who visited our hospital from January 2001 to January 2017 were enrolled in this study. We retrospectively compiled clinical data, including age, gender, disease duration, organ involvement, MSAs, treatment history, and disease activity after treatment. Sustained remission was defined as following: any of active skin rash, such as Gottron's papules/sign, heliotrope rash, and erythema, myositis, and ILD requiring treatment intensification were not revealed continuously for more than six months after one year since initiation of induction therapy for PM/DM/CADM.

Results: The number of patients with PM, DM, and CADM was 47, 85, and 29, respectively. The median duration of follow-up was 4 years. MSAs were identified in 102 patients. The prevalence of MSAs was as follows: anti-ARS antibody (Ab) in 40 (39%), anti-MDA5 Ab in 15 (15%), anti-TIF1-γ Ab in 12 (12%), anti-SRP Ab in 4 (4%), anti-NXP2 Ab in 4 (4%), and anti-SAE Ab in 2 (2%) patients. MSAs were negative in 25 (24%) patients. The total sustained remission rate was 58%. In patients with anti-ARS, anti-MDA5, anti-TIF1-γ, or anti-SRP Abs, the sustained remission rate was 50%, whereas in those without any of these 4 MSAs, the sustained remission rate was 87%. Multivariate analysis revealed that the achievement of sustained remission was associated with absence of anti-ARS, anti-MDA5, anti-TIF1-γ, or anti-SRP Abs (Odds ratio = 6.7, 95% confidence interval (CI) = 1.7–33.0, P = 0.0045) and no complication of severe muscle weakness requiring assistance at the time of diagnosis (Odds ratio = 23.6, 95% CI = 2.6–618.2, P = 0.003).

Conclusion: The absence of anti-ARS, anti-MDA5, anti-TIF1-γ, and anti-SRP Abs and no complication of severe muscle weakness before initiation of treatment predict achieving sustained remission after treatment in adult patients with PM/DM/CADM.

Disclosure: E. Watanabe, None; T. gono, Astellas, Japan Blood Products Organization, 8; S. Watanabe, None; H. Yabe, None; M. Kuwana, Astellas, 2, Medical & Biological Laboratories, Co., Ltd, 7, Astellas, Medical & Biological Laboratories, Co., Ltd, Japan Blood Products Organization, 8; C. Terai, None.


Abstract Number: 2139

Analysis of Required Dose of Corticosteroid As Maintenance Therapy and Related Factors in Patients with Polymyositis/Dermatomyositis

Eri Watanabe1, Takahisa gono1, Shinji Watanabe1, Hiroki Yabe1, Masataka Kuwana2 and Chihiro Terai1, 1Department of Rheumatology, Saitama Medical Center, Jichi Medical University, Saitama, Japan, 2Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan
First publication: September 18, 2017
Background/Purpose: PM and DM are inflammatory myopathies, sometimes complicated by interstitial lung disease (ILD), myocarditis, arthritis, and malignancies. The intensity of immunosuppressive therapies depends on the severity of muscle weakness and organ complications associated with PM/DM in individual patients. Corticosteroids remain the mainstay of treatment for PDM, although immunosuppressive agents have also been administered to better control disease activity and taper the dose of prednisolone (PSL) as much as possible. Long-term usage of PSL could cause a wide range of complications such as steroid myopathy, infection, osteoporosis, and diabetes mellitus. However, in daily clinical practice, it is difficult for some patients with PM/DM to taper PSL dose because of disease activity or repetitive recurrence despite combination therapy with immunosuppressants. Therefore, we clarified the required dose of PSL as maintenance therapy and investigated factors associated with the maintenance PSL dose in patients with PM/DM.

Methods: A total of 133 patients with PM/DM, who visited our hospital from January 2001 to January 2017 and had been treated for more than one year after initiation of therapies for PM/DM, were enrolled in this study. We retrospectively compiled clinical data, including age, gender, muscle strength, organ complications, laboratory data, including myositis-specific autoantibodies (MSAs), and treatment content. We investigated factors associated with the requirement of >5 mg/day of PSL, using multiple logistic regression analysis.

Results: The number of patients with PM, DM, and clinically amyopathic DM was 41, 69, and 23, respectively. The median follow-up duration was 4 years. ILD was observed in 76 (57%), dysphagia in 23 (17%), and malignancies in 29 (22%) patients. The median initial PSL dose was 50 mg/day. Methyl-PSL pulse therapy was performed in 45 (34%) patients. Immunosuppressants, including MTX, AZA, cyclophosphamide, and calcineurin inhibitors, and IVIG were administrated in 94 (71%) and 19 (14%) patients, respectively. The median maintenance PSL dose was 5 mg/day (interquartile range: 2–8 mg/day). The requirement of >5 mg/day of PSL as maintenance therapy was found in 52 patients (39%). In multivariate analysis choosing age, gender, disease duration, myositis type, MSAs, treatment content, and follow-up period as explanatory variables, the presence of anti-ARS antibody (Ab) was a significant factor associated with the requirement of >5 mg/day of PSL (Odds ratio = 6.3, 95% confidence interval = 1.5–33.1, P = 0.01). There were no other statistically significant factors. The requirement of >5 mg/day of PSL was found in 23 (59%) patients with anti-ARS Ab, but only in 13 (24%) patients without anti-ARS Ab (P < 0.001).

Conclusion: In most patients without anti-ARS Ab, it is possible to decrease the maintenance PSL dose to ≤5 mg/day. The presence of anti-ARS Ab is associated with difficulty of tapering PSL dose to 5 mg/day despite combination therapy with PSL and immunosuppressants.

Disclosure: E. Watanabe, None; T. gono, Astellas, Japan Blood Products Organization, 8; S. Watanabe, None; H. Yabe, None; M. Kuwana, Astellas, 2, Medical & Biological Laboratories, Co., Ltd, 7, Astellas, Medical & Biological Laboratories, Co., Ltd, Japan Blood Products Organization, 8; C. Terai, None.

Infections and Medications Associated with Onset of Myositis in Myovision, a National Myositis Patient Registry

Lisa G Rider1, Payam Noroozi Farhadi1, Nastaran Bayat1, Jesse Wilkerson2, Abdullah Faiq1, John McGrath2, Hermine I. Brunner3, Bob Goldberg4 and Frederick W Miller1, 1Environmental Autoimmunity Group, National Institute of Environmental Health Sciences, National Institutes of Health, Bethesda, MD, 2Social and Scientific Systems, Inc., Durham, NC, 3Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 4The Myositis Association, Alexandria, VA

First publication: September 18, 2017
Background/Purpose: Myositis is a rare systemic autoimmune disease with suspected environmental and genetic risk factors, but little is known about specific infections and medications that might be triggers.

Methods: Myositis patients (362 dermatomyositis [DM], 250 polymyositis [PM], 256 inclusion body myositis [IBM] enrolled in MYOVISION, diagnosed after January 1, 2002, and who met Bohan and Peter or Griggs criteria were included. Infections and medications received within the 12 months prior to diagnosis were queried. Significant univariable results were examined in multivariable logistic regression. Odds ratio point estimates with 95% confidence intervals and p-values were reported for each subtype pairwise comparison, after adjusting for age, gender, race, and year of diagnosis. Interactions of the effects between any infection and any medication, antibiotics, or NSAIDS were tested, after adjusting for age gender, race, and year of diagnosis.

Results: Overall, infections in the 12 months prior to diagnosis were reported more frequently in DM (OR 1.86: 95% CI 1.19-2.92, p ≤0.01) and PM (OR 1.61: 95% CI 1.01-2.55, p ≤0.05) than in IBM. Similar relationships were seen for gastroenteritis (OR 3.45:1.44-8.25 DM vs. IBM, OR 3.39:1.40-8.20 PM vs. IBM, p ≤0.01), respiratory infections, including upper respiratory infections (OR 1.76:1.07-2.89 DM vs. IBM, OR 1.82: 1.10-3.02 PM vs. IBM, p ≤0.05), and febrile illnesses (OR 3.18: 1.26-8.05 DM vs. IBM, OR 3.49: 1.37-8.90, PM vs. IBM, p≤0.05). The same infections were increased in the year prior to diagnosis in patients with an anti-synthetase phenotype with lung disease and arthritis or fever compared to those without. In addition, pneumonia (OR 5.31: 95% CI 2.67-10.6, p≤0.0001) was increased only in patients with an anti-synthetase phenotype. Hepatitis, urinary tract and skin infections were reported in ≤10% of patients in each subgroup and did not differ among subgroups. Among medications, statins were used more frequently in DM and PM than IBM (OR 2.22: 95%CI 1.33-3.70 DM vs. IBM, OR 2.13: 1.26-3.58 PM vs. IBM, p ≤0.005) in the year prior to diagnosis. Diabetes medications (OR 3.35: 95%CI 1.36-8.23, p =0.008) and levothyroxine (OR 2.20: 1.03-4.71, p=0.042) were also used more frequently in PM than IBM. Antibiotics (OR 1.76: 95% CI 1.18-2.63, p<0.01) and NSAIDs (OR 1.73: 1.17-2.57, p<0.01) were used more frequently in patients with the anti-synthetase phenotype. Use of blood pressure medicines, other lipid lowering agents, and oral contraceptives did not differ by subgroup. In examining the interaction of any infection with antibiotics, no interaction was detected by clinical subgroups (p=0.14 – 0.84), or within the anti-synthetase phenotype (p=0.45).

Conclusion: Variations among myositis subgroups in reported infections and medications received within the 12 months prior to diagnosis suggest possible risk factors for myositis phenotypes. Certain infections, particularly gastrointestinal and respiratory, are increased in DM and PM patients relative to IBM. A history of pneumonia and antibiotic usage are increased in patients with lung disease. Controlled studies examining these factors may be helpful in elucidating their role in disease development.

Disclosure: L. G. Rider, None; P. Noroozi Farhadi, None; N. Bayat, None; J. Wilkerson, None; A. Faiq, None; J. McGrath, None; H. I. Brunner, None; B. Goldberg, None; F. W. Miller, None.

Quantitative Nailfold Video Capillaroscopy Parameters Correlate with Dermatomyositis Activity and Damage

Hans Prakash1, Diego Song1, Daniel Lichy1, Pranay Rao2, Mina Jain3, Joseph Shrader2, Frederick W Miller4, Adam Schiffenbauer5, Alexander Gorbach1 and Lisa G Rider1, 1National Institute of Biomedical Imaging and Bioengineering, National Institutes of Health, Bethesda, MD, 2National Institute of Biomedical Imaging and Bioengineering, National Institutes of Health, Bethesda, MD, 3Rehabilitation Medicine Department, National Institutes of Health, Bethesda, MD, 4Environmental Autoimmunity Group, National Institute of Environmental Health Sciences, National Institutes of Health, Bethesda, MD, 5Environmental Autoimmunity Grp, National Institute of Environmental Health Sciences, National Institutes of Health, Bethesda, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Muscle Biology, Myositis and Myopathies Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM
Background/Purpose:

To assess microvascular structure and function in patients with adult dermatomyositis (DM) and juvenile dermatomyositis (JDM), we have designed and built a mobile, high-resolution Nailfold Video Capillaroscopy (NFVC) installation for clinical use, and correlated the results with both laboratory and clinical measures in patients.

Methods:

We quantified nailfold capillary features in patients with DM (n=28) and JDM (n=17) with median age of 16.1 yrs (IQR 10.5 – 42.8) and median disease duration of 2.95 yrs (IQR 1.1 - 10.2) (74% females and 59% Caucasian) and healthy control subjects (n=18) with similar demographics. Capillary structural markers, including capillary density, tortuosity, interlimb distance, and functional markers, including local blood velocity in arterial (BVA) and venous (BVV) segments of capillaries, were measured. Left ring finger imaging of the nailfold area was performed with a motorized stereomicroscope (Leica M205C) equipped with a video camera (Hamamatsu ORCA-Flash4.0) at 25x overall magnification, providing 1 µm resolution and up to 100 Hz acquisition rate. Spearman rank correlation coefficients and p-values were calculated to determine correlations between NFVC markers and clinical data.

Results:

Capillary density (p<0.01), BVA (p < 0.05), and BVV (p < 0.05) are significantly lower in patients with DM and JDM than healthy subjects. Interlimb distance and capillary tortuosity were higher in DM or JDM than healthy controls (p<0.01). Capillary density and capillary interlimb distance (r=-0.65, p <0.001) correlated inversely, and BVA and BVV strongly correlated (r=0.95, p <0.001). There were no significant differences in any of these NFVC parameters between DM and JDM. NFVC markers correlated with myositis activity and damage measures and laboratory data from the combined DM/JDM group. Skin disease activity scores (DAS skin) negatively correlated with capillary density (r= -0.46, p <0.01) and positively with capillary interlimb distance (r=0.48, p<0.01). Extramuscular Myositis Disease Activity Assessment Tool (MDAAT) correlated with capillary tortuosity (r=0.35, p<0.05). Gastrointestinal (GI) MDAAT scores correlated negatively with BVA and BVV (r = -0.62 - 0.58, p<0.01), whereas manual muscle testing correlated with BVA and BVV (r=0.50-0.53, p<0.05). Among laboratory measures, ESR correlated with interlimb distances (r=0.41, p < 0.05) and negatively correlated with BVA and BVV (r= -0.47 - -0.48, p<0.05), and white blood cell count correlated with capillary tortuosity (r=0.55, p <0.001). Muscle enzymes and von Willebrand factor related antigen levels did not correlate with NFVC parameters. Among damage measures, MD global damage and muscular and skeletal damage in the Myositis Damage Index (MDI) correlated with capillary tortuosity (r=0.36 - 0.37, p<0.05), and GI MDI scores correlated negatively with BVA and BVV (r= -0.57 – -0.63, p<0.05).

Conclusion:

Structural and functional NFVC markers correlate with disease activity and damage measures in muscle and extramuscular organs in children and adults with DM. Functional parameters of NFVC, including tortuosity and blood velocity, reveal new dimensions of the utility of NFVC in myositis assessment.

Disclosure: H. Prakash, None; D. Song, None; D. Lichy, None; P. Rao, None; M. Jain, None; J. Shrader, None; F. W. Miller, None; A. Schiffenbauer, None; A. Gorbach, None; L. G. Rider, None.


Abstract Number: 2142

Autoantibodies Recognizing Cytosolic 5’-Nucleotidase 1A Are Associated with More Severe Disease in Patients with Juvenile Myositis

Richard Yeker1, Iago Pinal-Fernandez2, Takayuki Kishi3, Ira N. Targoff4, Frederick W Miller3, Lisa G Rider3 and Andrew Mammen5, 1National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, 2NIAMS, NIH, Bethesda, MD, 3Environmental Autoimmunity Group, National Institute of Environmental Health Sciences, National Institutes of Health, Bethesda, MD, 4VA Medical Center, University of Oklahoma Health Sciences Center, Oklahoma Medical Research Foundation, Oklahoma City, OK, 5Muscle Diseases Unit, National Institute of Arthritis and Musculoskeletal and Skin Diseases. National Institutes of Health, Bethesda, MD

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Background/Purpose: Autoantibodies recognizing cytosolic 5’-nucleotidase 1A (NT5C1A) are present in the sera of adults with myositis and other autoimmune diseases. They are especially prevalent in adults with inclusion body myositis (IBM), where they are associated with more severe weakness. This study was undertaken to define the prevalence and clinical features associated with anti-NT5C1A autoantibodies in juvenile myositis.

Methods: We screened sera from 380 juvenile myositis patients, 30 patients with juvenile idiopathic arthritis (JIA), and 92 healthy control children for anti-NT5C1A. Clinical characteristics were compared between myositis patients with and without anti-NT5C1A.

Results: Anti-NT5C1A autoantibodies were present in the sera of 102 of 380 (27%) patients with juvenile myositis, 11 of 92 (12%) healthy control children (p=0.002) and 27% of children with JIA (p=0.05 vs. controls). Eighty-three of 307 (27%) juvenile dermatomyositis and 16 of 46 (35%) juvenile overlap myositis patients’ sera were anti-NT5C1A positive (p<0.01 vs. controls for each). Only 3 of 27 (11%) juvenile polymyositis patients were anti-NT5C1A positive. Juvenile myositis patients with and without anti-NT5C1A autoantibodies had similar phenotypes. However, anti-NT5C1A positive myositis patients had more frequent hospitalizations (p=0.007), required more medications (p<0.001), and had higher early total, skin and lung symptom scores (p≤0.05) (Table 1). The HLA alleles DRB1*07 (21% vs. 9%, p=0.04) and DQA1*0201 (22% vs. 6%, p=0.005) were more frequent in anti-NT5C1A negative patients.

Conclusion: Anti-NT5C1A autoantibodies are present in 27% of children with myositis, as is the case for JIA. As in adults with IBM, juvenile myositis patients with anti-NT5C1A autoantibodies have more severe disease.

Table 1. Disease outcomes and medications received per anti-NT5C1A status.
<table>
<thead>
<tr>
<th>Disease Course</th>
<th>NT5C1A (n=102)</th>
<th>NT5C1A multivariate (n=278)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monocyclic course</td>
<td>16% (12/76)</td>
<td>23% (53/229)</td>
<td>0.2</td>
</tr>
<tr>
<td>Polycyclic course</td>
<td>18% (14/76)</td>
<td>24% (56/229)</td>
<td>0.3</td>
</tr>
<tr>
<td>Chronic continuous course</td>
<td>66% (50/76)</td>
<td>52% (120/229)</td>
<td>0.07</td>
</tr>
<tr>
<td>Steinbrocker functional class at final assessment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Functional class 1</td>
<td>64% (65/102)</td>
<td>72% (198/274)</td>
<td>0.06</td>
</tr>
<tr>
<td>Functional class 2</td>
<td>29% (30/102)</td>
<td>18% (50/274)</td>
<td>0.01</td>
</tr>
<tr>
<td>Functional class 3</td>
<td>2% (2/102)</td>
<td>4% (11/274)</td>
<td>0.3</td>
</tr>
<tr>
<td>Functional class 4</td>
<td>5% (5/102)</td>
<td>5% (15/274)</td>
<td>0.9</td>
</tr>
<tr>
<td>Muscle enzymes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak creatine kinase</td>
<td>1010 (296-3971)</td>
<td>672 (252-5460)</td>
<td>0.6</td>
</tr>
<tr>
<td>Peak aldolase</td>
<td>16.9 (23.9)</td>
<td>20.8 (37.2)</td>
<td>0.9</td>
</tr>
<tr>
<td>Severity at onset</td>
<td>2.1 (1.4)</td>
<td>2.2 (0.9)</td>
<td>0.3</td>
</tr>
<tr>
<td>Early total symptom score</td>
<td>0.27 (0.12)</td>
<td>0.23 (0.11)</td>
<td>0.02</td>
</tr>
<tr>
<td>Early muscle score</td>
<td>0.38 (0.19)</td>
<td>0.38 (0.20)</td>
<td>0.6</td>
</tr>
<tr>
<td>Early joint score</td>
<td>0.52 (0.41)</td>
<td>0.43 (0.42)</td>
<td>0.1</td>
</tr>
<tr>
<td>Early skin score</td>
<td>0.29 (0.15)</td>
<td>0.24 (0.13)</td>
<td>0.05</td>
</tr>
<tr>
<td>Early gastrointestinal score</td>
<td>0.09 (0.13)</td>
<td>0.07 (0.10)</td>
<td>0.09</td>
</tr>
<tr>
<td>Early lung score</td>
<td>0.13 (0.17)</td>
<td>0.15 (0.15)</td>
<td>0.003</td>
</tr>
<tr>
<td>Early cardiac score</td>
<td>0.03 (0.08)</td>
<td>0.08 (0.08)</td>
<td>0.9</td>
</tr>
<tr>
<td>Early constitutional symptoms score</td>
<td>0.41 (0.26)</td>
<td>0.39 (0.27)</td>
<td>0.4</td>
</tr>
<tr>
<td>Mortality</td>
<td>4% (4/102)</td>
<td>9% (278)</td>
<td>0.6</td>
</tr>
<tr>
<td>Hospitalized</td>
<td>65% (62/96)</td>
<td>55% (148/268)</td>
<td>0.1</td>
</tr>
<tr>
<td>Number of hospitalizations</td>
<td>1.6 (2.3)</td>
<td>1.1 (1.7)</td>
<td>0.007</td>
</tr>
<tr>
<td>Need for wheelchair</td>
<td>21% (21/100)</td>
<td>18% (47/268)</td>
<td>0.07</td>
</tr>
<tr>
<td>Response to treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete clinical response</td>
<td>22% (19/87)</td>
<td>33% (74/225)</td>
<td>0.1</td>
</tr>
<tr>
<td>Remission</td>
<td>15% (13/88)</td>
<td>27% (63/232)</td>
<td>0.2</td>
</tr>
<tr>
<td>Total number of medications used</td>
<td>4.8 (2.0)</td>
<td>3.6 (2.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>p-value</td>
<td></td>
</tr>
<tr>
<td>--------------------------------</td>
<td>-----------</td>
<td>---------</td>
<td></td>
</tr>
<tr>
<td>Treatment trials per year</td>
<td>3.0 (2.7)</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>Medications received</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral steroids</td>
<td>99%</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>Intravenous pulsed steroids</td>
<td>78%</td>
<td>&lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>Methotrexate</td>
<td>67%</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>Intravenous immunoglobulin</td>
<td>33%</td>
<td>&lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>Other DMARDs</td>
<td>99%</td>
<td>0.01</td>
<td></td>
</tr>
</tbody>
</table>

Dichotomous variables were represented as percentage (count/total), continuous variables as mean (SD) and the creatine kinase was presented as median (Q1-Q3). Multivariate analysis used linear or logistic regression adjusted for time of follow-up, autoantibodies and clinical groups. Creatine kinase was log-transformed prior to statistical analysis.

Disclosure: R. Yeker, None; I. Pinal-Fernandez, None; T. Kishi, The Myositis Association, 2; I. N. Targoff, Oklahoma Medical Research Foundation Clinical Immunology Laboratory, 6; F. W. Miller, None; L. G. Rider, None; A. Mammen, None.


Abstract Number: 2143

**Circulating Endothelial Cells and Endothelial Activation Markers As Disease Activity Measures in Idiopathic Inflammatory Myopathies**

Takayuki Kishi1, Jonathan Chipman1, Maryalice Stetler-Stevenson2, Khanh Nghiem3, Melvina Evereklian1, Margaret E. Rick3, Frederick W Miller1 and Lisa G Rider1, 1Environmental Autoimmunity Group, National Institute of Environmental Health Sciences, National Institutes of Health, Bethesda, MD, 2Laboratory of Pathology, National Cancer Institute, National Institutes of Health, Bethesda, MD, 3Coagulation Laboratory, Clinical Center, National Institutes of Health, Bethesda, MD

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017

Session Title: Muscle Biology, Myositis and Myopathies Poster

Session Type: ACR Poster Session C

Session Time: 9:00AM-11:00AM

Background/Purpose: The idiopathic inflammatory myopathies (IIM) are systemic autoimmune diseases with chronic muscle inflammation and microvascularopathy of muscle and skin capillaries. Circulating endothelial cells (CECs), von Willebrand Factor antigen (vWF), P-selectin, and thrombomodulin are released from damaged endothelium. Loss of function of endothelial progenitor cells (EPCs) has been associated with poor vascular outcomes in other autoimmune diseases. These endothelial markers may be part of the pathogenic changes of IIM and we hypothesized they may be indicators of disease activity.

Methods: We assessed endothelial biomarkers in 24 probable or definite IIM patients (20 juvenile dermatomyositis (DM), 2 adult DM, 1 each with juvenile and adult polymyositis) with a median age of 12.6 yrs [IQR 9.8-16.4] and 67% female, and in 29 healthy controls with similar ages and genders. CECs and EPCs in peripheral blood were quantitated by flow cytometry. EPC markers included CD34+/133+, KDR+/133+, and CXCR4+/133+. Plasma vWF antigen (Ag) was measured in an immunoassay, vWF activity in a Ristocetin cofactor assay, and Factor VIII (FVIII) in a one-stage clotting assay based on activated partial thromboplastin time. Thrombomodulin and P-selectin were measured by ELISA. IMACS and PRINTO myositis disease activity and damage measures were assessed and periungual nailfold capillary (NFC) morphology and density were quantified using digital photographs in IIM patients. Group differences were evaluated by Wilcoxon-rank sum test, and Spearman’s rank correlations assessed relationships between variables.
Multiple Serum Cytokine and Chemokine Profiling to Identify Combinational Biomarkers Toward Patients of Polymyositis/Dermatomyositis Complicated with Rapidly Progressive Interstitial Lung Disease

Toshimasa Shimizu1, Tomohiro Koga1,2, Yoshiro Horai3, Keita Fujikawa4, Yushiro Endo1, Sousuke Tsuji1, Ayuko Takatani1, Masataka Umeda1, Shoichi Fukui1, Remi Sunimiyoshi4, Ayako Nishino1, Shinya Kawashiri1, Naoki Iwamoto1, Takashi Igawa1, Kunihiro Ichinose1, Mami Tamai1, Norihiro Sakamoto2, Hideki Nakamura1, Tomoki Oriuchi6, Hiroshi Mukae1, Masataka Kuwana7 and Atsushi Kawakami1, 1Department of Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, 2Center for Bioinformatics and Molecular Medicine, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, 3Department of Rheumatology, National Hospital Nagasaki Medical Center, Nagasaki, Japan, 4Japan Community Health care Organization Ishaya General Hospital, Nagasaki, Japan, 5Department of Respiratory Medicine, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, 6Department of Rehabilitation Sciences, Nagasaki University, Nagasaki, Japan, 7Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Muscle Biology, Myositis and Myopathies Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Polymyositis (PM)/dermatomyositis (DM) is a chronic inflammatory disorders involved in skeletal muscles. Interstitial lung disease (ILD) complicated with PM/DM patients is often developed as rapidly progressive ILD (RPILD), which can be treatment resistant and life threatening. However, serum biomarkers of PM/DM with RPILD still remain to be obscure. This study was aimed to identify the specific biomarkers to assess PM/DM complicated with RPILD.

Methods: Forty-six patients with PM/DM-ILD, in either RPILD (n = 20) or chronic ILD (n = 26), were enrolled from Nagasaki University Hospital and related institutions. They gave their informed consent to be subjected to the protocol that was approved by the Institutional Review Board of Nagasaki University. Using medical records, we analyzed the patient's demographics and clinical characteristics. Serum levels of 42 cytokines/chemokines were measured by multi-suspension cytokine array. Serum levels of anti-melanoma differentiation-associated gene 5 (MDA5) antibody, ferritin and interferon-alpha (IFN- alpha) were measured by enzyme linked immunosorbent assay. These serum variables were ranked by their importance by a multivariate classification algorithm termed...
random forest analysis. We performed a logistic regression analysis to determine a set of specific biomarkers for distinguishing patients with RPILD from patients with chronic ILD.

**Results:** Patients with RPILD had significantly higher age, mortality, the frequency of clinically amyopathic DM (CADM), the prevalence of mediastinal emphysema, periungual erythema and mechanic's hand than patients with chronic ILD. Twenty-four out of 42 cytokines/chemokines, anti-MDA5 antibody, ferritin and IFN- alpha were available for further analyses. Patients with RPILD had significantly higher serum levels of 5 cytokines (IL-15, IL-6, CCL7, CXCL10 and VCAM-1), anti-MDA5 antibody and ferritin than patients with chronic ILD patients whereas CCL-22 was significantly low in RPILD patients. We found that IL15 was most significant cytokine to distinguish patients with RPILD from patients with chronic ILD using random forest analysis (Fig. 1). Additionally, we found that anti-MDA5 antibody, IL-15, TNF- alpha, CXCL-8, CCL-22 and IL-RA were the best combination to distinguish patients with RPILD from patients with chronic ILD (sensitivity: 95%, specificity: 88.5%, accuracy: 91.3%).

**Conclusion:** Our data for the first time identify the combinational serum biomarkers to predict PM/DM patients complicated with RPILD.

![Random forest analysis to distinguish PM/DM patients with RPILD from chronic ILD](image_url)

**Disclosure:** T. Shimizu, None; T. Koga, None; Y. Horai, None; K. Fujikawa, None; Y. Endo, None; S. Tsuji, None; A. Takatani, None; M. Umeda, None; S. Fukui, None; R. Sumiyoshi, None; A. Nishino, None; S. Kawashiri, None; N. Iwamoto, None; T. Igawa, None; K. Ichinose, None; M. Tamai, None; N. Sakamoto, None; H. Nakamura, None; T. Origuchi, None; H. Mukae, None; M. Kuwana, Medical & Biological Laboratories, Co., Ltd, 7; A. Kawakami, None.


**Abstract Number:** 2145

**Anti-CXCR3 Antibody Suppresses Inflammation in C Protein-Induced Myositis Model**

Ji Yong Choi, Joo Youn Lee, Ji Soo Park, Sehui Shon, Kathleen Phillips, Eun Young Lee, Eun Bong Lee and Yeong Wook Song

1Division of Rheumatology, Department of Internal Medicine, Seoul National University, Seoul, Korea, Republic of (South), 2Department of Molecular medicine and biopharmaceutical science, Seoul National University, seoul, Korea, Republic of (South), 3Department of Molecular medicine and biopharmaceutical science, Seoul National University, Seoul, Korea, Republic of (South), 4Pfizer Inc. Cambridge, MA, USA, Cambridge, MA, 5Division of Rheumatology, Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Tuesday, November 7, 2017

Session Title: Muscle Biology, Myositis and Myopathies Poster
**Background/Purpose:** CXCR3 is a chemokine receptor that plays an important role in T cell chemotaxis in human autoimmune diseases. CXCR3, which is activated by ligand interferon gamma-inducible protein 10 (CXCL10, IP-10), was reported to be increased in muscle tissue in polymyositis. We investigated the effect of CXCR3 blockade in C protein-induced myositis (CIM) animal model.

**Methods:** CIM was induced with human skeletal C protein in 7 week old female C57BL/6 mice. Mice were treated with anti-CXCR3 antibody or control IgG at day 8 and day 15 after induction with C protein. Mouse muscle tissue was evaluated on day 21. H&E stain of muscle was performed to evaluate infiltrated inflammatory cells. CXCR3 expressing cells from mouse splenocytes and lymph node cells were analyzed by flow cytometry.

**Results:** Flow cytometric analysis demonstrated decreased CXCR3+CD8+memory T cells and CXCR3+pDC cells in lymph nodes of the anti-CXCR3 antibody treated group compared to that of the control IgG treated group (36.583 ± 9.39 % vs 31.266 ± 7.78 % ; p = 0.06, 40.6 ± 5.622 % vs 56.1 ± 5.72 % ; p = 0.012, respectively). In addition, CD8+IFN-γ+CXCR3+ cells in lymph nodes significantly decreased in the anti-CXCR3 antibody group compared to that of the vehicle group (9.725 ± 0.67 % vs 17.05 ± 4.69 % ; p < 0.01). Anti-CXCR3 antibody group showed lower inflammation score in muscle compared to that of the vehicle group (p = 0.032).

**Conclusion:** CXCR3 blockade suppressed inflammation in muscle and CXCR3 expression in lymph node cells in CIM model. These results suggest a therapeutic effect of anti-CXCR3 antibody in inflammatory myopathy.

**Conflicts of Interest (COI) declaration:** Anti-CXCR3 antibody and control IgG antibody were provided by Pfizer through collaboration with Charles MacKay and Remy Robert at Monash University, Melbourne, Australia.

**Disclosure:** J. Y. Choi, None; J. Y. Lee, None; J. S. Park, None; S. Shon, None; K. Phillips, Pfizer Inc, 4; E. Y. Lee, None; E. B. Lee, None; Y. W. Song, None.

individual disease progress were analyzed. Cytokine expression of isolated CD4+CXCR4+ T cell and co-cultured fibroblast proliferation was measured.

**Results:**

The percentages of peripheral CD4+CXCR4+ T cells are significantly elevated in IIM-ILD patients compared to controls (p<0.01 Figure 1), correlate with HRCT scores (r=0.5820) and pulmonary function impairments (FVC, DLCO/VA). They are associated with anti-MDA5 autoantibodies and the amyopathic dermatomyositis (ADM) phenotype. In IIM-ILD, percentages of CD4+CXCR4+ T cells ≥ 45% revealed a 6-month mortality over 50% (Figure 2). CD4+CXCR4+ T cells from ADM-ILD patients express high levels of IL-21. In vitro blockade of IL-21 signaling by neutralization of IL-21 or JAK inhibitor could abolish the fibroblast proliferation (Figure 3).

**Conclusion:**

CD4+CXCR4+ T cells appear to be a potentially valuable novel biomarker associated with the severity and prognosis of IIM-ILD. They promote pulmonary fibroblast proliferation via IL-21, which may herald future targeted treatments for this severe disease.

---

**Disclosure:** K. Wang, None; J. Zhao, None; Z. Chen, None; T. Li, None; X. Tan, None; Y. Zheng, None; L. Gu, None; L. Guo, None; F. Sun, None; H. Wang, None; J. Li, None; X. Wang, None; G. Riemekasten, None; S. Ye, Continent Pharmaceutical Company, 2.


**Abstract Number:** 2147

**Dysphagia in Inflammatory Myositis: A Study of the Structural and Physiologic Changes Resulting in Disordered Swallowing**
Background/Purpose:

The prevalence of dysphagia in patients with inflammatory myopathies has been reported to be as high as 60% (1). Aspiration pneumonia is one of the main causes of mortality in patients affected by immune mediated myositis, especially in those with chronic deterioration(2). The goal of this study was to characterize the pathophysiologic changes in swallowing of myositis patients by examining videofluoroscopic swallow studies (VFSS) for kinematic, temporal, and functional measures of swallowing.

Methods:

VFSS of 23 myositis patients (IBM= 7, Necrotizing= 2, DM= 13, PM =1, age range= 21-81) complaining of dysphagia were collected, and frame by frame analysis of temporal and kinematic measures were performed. The swallows of each subjects were rated by MBSImP® and Penetration-Aspiration Scale. Swallowing measures from patients were compared to those from 64 healthy subjects (ages range= 18-90) by Wilcoxon rank-sum tests.

Results:

In patients with myositis, food entered the pharynx earlier relative to the initiation of swallowing than in healthy participants (p<0.0001). Myositis patients had a significantly shorter duration of upper esophageal sphincter (UES) opening and laryngeal vestibule closure than healthy subjects (p<0.0001). There were no statistically significant differences in AP diameter of the UES between healthy subjects and myositis patients (p=0.9). In myositis patients, several MBSImP® component scores indicated impairment, particularly those related to residue after swallowing, base of tongue movement, and posterior pharyngeal wall movement. Aspiration was observed in 26% of the patients.

Conclusion:

Swallowing pathophysiology in myositis appears to be related to reduced muscle strength and endurance. Tongue weakness resulted in premature entrance of bolus into the pharynx prior to airway closure. Diminished pharyngeal stripping wave and tongue retraction contributes to poor bolus clearance. Decreased duration of UES opening with preserved extent of anteroposterior diameter suggest conserved ability to open the UES but reduced endurance in the submental musculature to sustain opening. Strength and endurance exercises of the tongue and submental muscles are potential therapeutic targets for preservation of swallowing function in myositis patients.


Disclosure: A. Azola, None; T. Chung, None; R. Mulheren, None; G. McKeon, None; L. Christopher-Stine, OptionCare, 5, Mallinckrodt, 5, Inova Diagnostics, Inc., 7; J. Palmer, None.


Abstract Number: 2148

Association of the Paraoxonase 1 Q192R Genetic Polymorphism with Disease Activity in Dermatomyositis

Sangmee Bae¹, Buzand Oganesian², Tyler Dowd³, Ilana Golub¹, Ani Shahbazian⁴, Jennifer Wang³, Srinivasa T. Reddy⁵ and Christina Charles-Schoeman¹, ¹University of California, Los Angeles, Los Angeles, CA, ²Medicine-Rheumatology, University of California, Los Angeles, Los Angeles, CA, ³UCLA, Los Angeles, CA, ⁴Medicine-Rheumatology, UCLA David Geffen School of Medicine, Los Angeles, CA, ⁵Medicine-Cardiology, University of California, Los Angeles, Los Angeles, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Muscle Biology, Myositis and Myopathies Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Injury to the vascular endothelium is implicated in the pathogenesis of dermatomyositis (DM). Normal high density lipoprotein (HDL) protects the vascular endothelium from damage due to oxidized phospholipids, which accumulate under conditions of oxidative stress
and are metabolized by the HDL-associated enzyme, paraoxonase 1 (PON1). The current work evaluates the relationship of the PON1Q192R genetic polymorphism and PON1 activity to disease activity and damage in DM pts.

Methods:

In a cross-sectional cohort of 118 DM pts, the relationships between PON1 activity, PON1 genotype (for the functional polymorphism at position 192), and myositis disease activity and damage were assessed using physician global 5 point Likert and 100 mm visual analogue scales (VAS), CPK levels, and pulmonary function tests (PFTs) in pts with myositis–associated interstitial lung disease (ILD). Plasma PON1 activity was measured using paraoxon as the substrate and the PON1 Q192R genotype was determined as described previously (A&R 2013,65(11) 2765). Lipoprotein cholesterol levels were assessed by standard assays and traditional CV risk factors and myositis disease characteristics were assessed by questionnaire and chart review.

Results:

PON1 activity was highest in DM patients with the RR genotype, intermediate for the QR genotype, and lowest for the QQ genotype (Table). Pts with the QQ genotype had trends for lower levels of systemic inflammation, higher HDL cholesterol (HDL-C), and significantly lower global disease activity/damage scales compared to QR or RR genotypes (Table). In patients with ILD who had available PFTs (n=30), the % predicted DLCO was significantly higher in the QQ group compared to the QR group; this relationship remained in multivariate (MV) analysis controlling for age and sex. A significant association of the QQ genotype with lower global disease activity (VAS) also remained in MV analysis controlling for demographic characteristics, medication use, disease duration, and HDL-C levels. Higher HDL-C levels were significantly associated with lower disease activity in this analysis.

Conclusion:

In a large cross-sectional cohort of DM pts, the PON1Q192R QQ genotype was associated with a more favorable disease activity profile including lower global disease activity assessments and higher DLCO in patients with myositis-associated ILD. Because DM is a systemic vascular disease and the PONQ192R polymorphism has previously been associated with vascular outcomes, further investigation and validation of these findings is warranted.
<table>
<thead>
<tr>
<th></th>
<th>QQ Genotype (n=42)</th>
<th>QR Genotype (n=62)</th>
<th>RR Genotype (n=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PON1 activity (nmoles/minute/ml)</td>
<td>86 ± 61</td>
<td>162 ± 84*</td>
<td>202 ± 103*</td>
</tr>
<tr>
<td>Age (years)</td>
<td>49 ± 15</td>
<td>46 ± 14</td>
<td>51 ± 14</td>
</tr>
<tr>
<td>Sex (% female)</td>
<td>76</td>
<td>77</td>
<td>78</td>
</tr>
<tr>
<td>Race (% caucasian)</td>
<td>93</td>
<td>78</td>
<td>79</td>
</tr>
<tr>
<td>Ethnicity (% hispanic)</td>
<td>12</td>
<td>25</td>
<td>36</td>
</tr>
<tr>
<td>Body Mass Index (kg/m²)</td>
<td>28 ± 7</td>
<td>28 ± 7</td>
<td>28 ± 5</td>
</tr>
<tr>
<td>Disease Duration (years)</td>
<td>5.7 ± 9.3</td>
<td>3.3 ± 6.3</td>
<td>5.8 ± 9.4</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL)</td>
<td>201 ± 38</td>
<td>207 ± 55</td>
<td>197 ± 42</td>
</tr>
<tr>
<td>LDL Cholesterol (mg/dL)</td>
<td>115 ± 34</td>
<td>121 ± 47</td>
<td>117 ± 35</td>
</tr>
<tr>
<td>HDL Cholesterol (mg/dL)</td>
<td>61 ± 19</td>
<td>56 ± 20</td>
<td>49 ± 15</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>144 ± 81</td>
<td>175 ± 119</td>
<td>171 ± 118</td>
</tr>
<tr>
<td>ESR (mm/hr)</td>
<td>24 ± 23</td>
<td>31 ± 28</td>
<td>39 ± 39</td>
</tr>
<tr>
<td>HS-CRP (mg/L)</td>
<td>6.2 ± 10.1</td>
<td>6.8 ± 11.1</td>
<td>9.1 ± 13.4</td>
</tr>
<tr>
<td>CPK</td>
<td>262 ± 825</td>
<td>409 ± 1097</td>
<td>224 ± 269</td>
</tr>
<tr>
<td>Prednisone Use (% yes)</td>
<td>71</td>
<td>70</td>
<td>57</td>
</tr>
<tr>
<td>Prednisone daily dose (mg)</td>
<td>14 ± 17</td>
<td>19 ± 20</td>
<td>9 ± 15</td>
</tr>
<tr>
<td>Methotrexate (% yes)</td>
<td>29</td>
<td>33</td>
<td>21</td>
</tr>
<tr>
<td>Mycophenolate Mofetil (% yes)</td>
<td>25</td>
<td>25</td>
<td>21</td>
</tr>
<tr>
<td>Azathioprine (% yes)</td>
<td>18</td>
<td>8</td>
<td>14</td>
</tr>
<tr>
<td>IVIG (% yes)</td>
<td>22</td>
<td>23</td>
<td>14</td>
</tr>
<tr>
<td>Diabetes (% yes)</td>
<td>10</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Current smoking (% yes)</td>
<td>5</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Hypertension (% yes)</td>
<td>33</td>
<td>18</td>
<td>29</td>
</tr>
<tr>
<td>Hydroxychloroquine (% yes)</td>
<td>22</td>
<td>28</td>
<td>21</td>
</tr>
<tr>
<td>Physician Global Activity-VAS</td>
<td>34 ± 19</td>
<td>46 ± 18*</td>
<td>39 ± 21</td>
</tr>
<tr>
<td>Physician Global Activity-Likert</td>
<td>1.5 ± 0.7</td>
<td>2.0 ± 0.8*</td>
<td>1.7 ± 0.7</td>
</tr>
<tr>
<td>Physician Global Damage-VAS</td>
<td>26 ± 21</td>
<td>35 ± 26</td>
<td>37 ± 19*</td>
</tr>
<tr>
<td>Physician Global Damage-Likert</td>
<td>1.1 ± 0.9</td>
<td>1.6 ± 1.1*</td>
<td>1.7 ± 0.8*</td>
</tr>
<tr>
<td>% of patients with ILD</td>
<td>29</td>
<td>35</td>
<td>79*</td>
</tr>
<tr>
<td>FVC % Predicted (in ILD pts)</td>
<td>71 ± 18</td>
<td>60 ± 25</td>
<td>65 ± 19</td>
</tr>
<tr>
<td>DLCO % Predicted (in ILD pts)</td>
<td>74 ± 19</td>
<td>49 ± 24*</td>
<td>55 ± 20</td>
</tr>
</tbody>
</table>

*P<0.05 compared to QQ genotype. ESR=erythrocyte sedimentation rate, HSCRP=high sensitivity C-reactive protein, ILD=interstitial lung disease, FVC=forced vital capacity, DLCO=diffusing capacity for carbon monoxide. VAS= Visual analogue scale (0-100 mm scale), Likert= 0-4 scale. PFT data presented for 30 ILD patients with PFTs available (QQ: n=7, QR: n= 13, RR: n= 10).

Disclosure: S. Bae, None; B. Oganesian, None; T. Dowd, None; I. Golub, None; A. Shahbazian, None; J. Wang, None; S. T. Reddy, None; C. Charles-Schoeman, None.

Statin Use in a Longitudinal Cohort of Patients with Idiopathic Inflammatory Myopathies

Sangmee Bae1, Ilana Golub1, Buzand Oganesian2 and Christina Charles-Schoeman1, 1University of California, Los Angeles, Los Angeles, CA, 2University of California, Los Angeles, Los angeles, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Muscle Biology, Myositis and Myopathies Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Patients(pts) with idiopathic inflammatory myopathies (IIM) have an increased risk of cardiovascular (CV) disease. Statins reduce CV risk but have been associated with myalgias, myositis, and rhabdomyolysis. We describe the use of statins in a longitudinal cohort of pts with IIM.

Methods: A retrospective review was conducted of 189 IIM pts (127 DM, 51 PM, 13 IBM, 3 HMGCR+ IMNM) enrolled in a longitudinal IIM cohort. All pts on statins were identified. Physician global myositis disease activity(DA) and damage(DD) assessments (100 mm visual analogue scales(VAS) and 5 point Likert scales) were performed at 3 visits: 1) visit prior to statin initiation, 2) visit immediately after statin initiation, and 3) most recent follow-up. For pts without visits prior to statin initiation, the initial study visit and two longitudinal visits were evaluated. All assessments were performed by the same myositis physician who was blinded to the statin use/non-use at the visits. Laboratory data and adverse events were gathered by chart review.

Results: 22 pts taking a statin were identified including 6 pts who were not on a statin at time of study enrollment and were started during the follow-up period. The 3 HMGCR ab+ IMNM pts in the cohort were historically on a statin but discontinued by the time of study enrollment and so not included in this analysis. Mean (SD) age was 53 (34) years and most were female (n=14, 64%). Thirteen pts had myositis antibody testing available: Ro (n=5), MDA5 (n=2), Jo1 (n=1), U1RNP(n=1), Ku(n=1) and MJ (n=1). Types of statins used included atorvastatin 10-40mg (n=12), rosuvastatin 5-20mg (n=7), simvastatin 40-80mg (n=2), pravastatin 20mg (n=2) and lovastatin 40mg (n=1). Mean (range) duration of observed statin use was 34 (0-90) months.

Among pts that were on a statin at study enrollment, 19/22 remained on a statin during the follow-up period. Of the remaining 3/22 pts: Pt #1 had a history of statin intolerance before onset of DM and remained intolerant to statins after DM diagnosis despite multiple agents tried; Pt #2 presented with rapidly progressive MDA5 + ILD, which was fatal within 1 month; Pt #3 had the statin discontinued by her primary care provider for unclear reasons (disease activity score remained low before (VAS DA=12) and after statin discontinuation (VAS DA=8) without note of intolerance). For the 6 pts started on statins during the study period, there was no worsening in disease activity measures between visit 1 (pre-statin) and visit 2 (post statin) (Table). Mean (SD) follow-up between visits 1 and 2 = 2.2(0.9) months. 3/6 IIM pts were started on a statin in the setting of active disease including cardiac muscle involvement (mean(SD) VAS DA= 49(9) n=3).

Conclusion: Statins were well tolerated in a relatively large longitudinal cohort of IIM patients. Use may be considered in IIM patients without HMGCR ab when clinically indicated for CV risk reduction.
Visit prior to statin initiation | Visit after statin initiation
--- | ---
CK, U/L | 450 (49-1842) | 330 (45-1369)
Aldolase, U/L | 8.9 (4.6-23.3) | 7.1 (3.7-15.3)
ESR, mm/hr | 33 (16-65) | 32 (9-60)
CRP, mg/dL | 1.6 (<0.3-2.7) | 0.6(<0.3-1.7)
Physician global Disease activity | 30 (10-58) | 24 (5-50)
VAS(0-100) Likert (0-4) | 1.5 (1-2) | 1.3 (1-2)
Physician global Disease damage | 47 (0-75) | 47 (0-75)
VAS(0-100) Likert (0-4) | 2 (0-3) | 2 (0-3)

Disclosure: S. Bae, None; I. Golub, None; B. Oganesian, None; C. Charles-Schoeman, None.

Abstract Number: 2150

**Serum Microrna-1 Can be a Predictive Marker for Disease Activity of Polymyositis/Dermatomyositis-Associated Interstitial Lung Disease**

Yumiko Sugiyama, Ryusuke Yoshimi, Yosuke Kunishita, Daiga Kishimoto, Yohei Kirino and Hideaki Nakajima, Department of Stem Cell and Immune Regulation, Yokohama City University Graduate School of Medicine, Yokohama, Japan

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Tuesday, November 7, 2017
Session Title: Muscle Biology, Myositis and Myopathies Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

**Background/Purpose:** Although intensive immunosuppressive treatment are necessary for the severe cases with polymyositis (PM)/dermatomyositis (DM), the prognostic factors or disease activity indices for PM/DM have not established yet. On the other hand, microRNAs are small non-coding RNAs, some of which have a certain function such as a transcriptional regulation. MicroRNA-1 (miR-1) has been shown to be associated with myocyte differentiation, decreased in muscle biopsy sample from patients with inflammatory myopathies, and induced by type I interferon. Here we investigated the association between serum miR-1 level and clinical course of PM/DM patients.

**Methods:** We retrospectively analyzed clinical features, and laboratory data at baseline in patients with PM/DM patients who had received initial treatment at Yokohama City University Hospital from 2008 to 2017. We also investigated initial therapeutic regimens, clinical outcomes, and episodes of serious infection. The serum samples from PM/DM were collected before and after starting treatment and those from healthy controls were recruited from the biobank institution in the hospital. The serum miR-1 levels were measured by quantitative real-time PCR.

**Results:** Twenty-two patients (PM 4, DM 11, clinically amyopathic DM (CADM) 7) were recruited. The mean age was 63.5 ± 8.5 years, 13 (59%) were female, and 14 patients (64%) had interstitial lung disease. Among the patients, 3 patients died and 9 had infections which needed antibiotic therapy within 6 months from diagnosis. The serum miR-1 level was significantly elevated in PM/DM patients as compared to healthy control (p = 0.008; Figure 1). In PM/DM patients, the serum miR-1 level was significantly decreased by treatment (p = 0.03). There was a correlation between serum CK and miR-1 levels in PM/DM patients (p = 0.005, r = 0.58), although there was no correlation between the improvement rate of serum CK and miR-1 levels in PM/DM patients. We identified the cutoff value of serum miR-1 level from the two standard deviations in healthy controls, and divided all the PM/DM patients or PM/DM patients with interstitial lung disease (PM/DM-ILD) into two groups by the serum miR-1 level at baseline,
respectively. There were no significant differences in clinical data, outcomes, and treatment regimens in PM/DM patients. However, in
the PM/DM-ILD patients, although there was no significant differences in clinical data at baseline and the initial dose of prednisolone
(PSL), the higher miR-1 group needed longer time to be tapered to the half of initial PSL dose ($p = 0.021$) as compared to lower miR-1
group. The higher miR-1 group also tended to be complicated by infection within 6 months from starting treatment more frequently ($p = 0.008$).

**Conclusion:** This is the first report showing the elevated serum miR-1 level in PM/DM patients. miR-1 can be a predictive marker for
response to immunosuppressive therapy for PM/DM-ILD.

**Abstract Number:** 2151

**The Predictive Risk Factors for Opportunistic Infection during Treatment for Polymyositis/Dermatomyositis-Associated Interstitial Lung Disease**

Yumikoo Sugiyama$^{1,2}$, Ryusuke Yoshimi$^{1,2}$, Maasa Tamura$^{2,3}$, Naoki Hamada$^{1,2}$, Hideto Nagai$^{1,2}$, Naomi Tsuchida$^{1,4}$, Yosuke
Kunishita$^{1,2}$, Yutaro Soejima$^{1,2}$, Daiga Kishimoto$^{1,2}$, Reikou Kamiyama$^{1,2}$, Kaoru Minegishi$^{1,5}$, Yohei Kirino$^{1,2}$, Shigeru Ohno$^{1,6}$ and
Hideaki Nakajima$^{2}$, 1Y-CURD Study Group, Yokohama, Japan, 2Department of Stem Cell and Immune Regulation, Yokohama City
University Graduate School of Medicine, Yokohama, Japan, 3Y-CURD Study Group, Yokohama, Japan, 4Department of Hematology and
Clinical Immunology, Yokohama City University Graduate School of Medicine, Yokohama, Japan, 5Rheumatic Disease Center,
Yokohama City University Medical Center, Yokohama, Japan, 6Center for Rheumatic Disease, Yokohama City University Medical
Center, Yokohama, Japan

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Tuesday, November 7, 2017
**Session Title:** Muscle Biology, Myositis and Myopathies Poster
**Session Type:** ACR Poster Session C
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Although concomitant infectious diseases are the predominant causes of death in patients with polymyositis
(PM)/dermatomyositis (DM)-associated interstitial lung disease (ILD), intensive immunosuppressive treatment are necessary for severe
cases. We have already reported that high initial dose of glucocorticoid for induction therapy, high serum LDH and KL-6 levels at the
baseline were independent risk factors for infection. Here we investigated the predictive risk factors for opportunistic infection during
treatment for PM/DM-ILD by assessing cytomegarovirus (CMV) antigen test as a barometer for immunocompromised status.
Methods: We retrospectively analyzed clinical features, laboratory data and high-resolution computed tomography (HRCT) findings at baseline in the patients with PM/DM-ILD who had received initial treatment at six hospitals affiliated to Yokohama City University from 2003 to 2016. We also investigated initial therapeutic regimens and clinical outcomes including CMV antigenemia as a complication. We conducted univariate and multivariate analyses to extract risk factors for CMV antigenemia.

Results: One hundred sixteen patients (PM 22, DM 51, and clinically amyopathic DM (CADM) 43) were recruited. The mean age was 56 ± 15 years and 83 (71.6%) were female. As initial therapies, oral prednisolone (PSL) was prescribed in all patients. Methylprednisolone (mPSL) pulse, intravenous cyclophosphamide (IVCY), and oral calcineurin inhibitor therapies were performed in 78 (67%), 48 (41%) and 81 (70%), respectively. Forty patients (34%) received combination therapy with IVCY and a calcineurin inhibitor. Forty-two patients (36%) had CMV antigenemia within 6 months from initiation of immunosuppressants. Low serum albumin and PaCO$_2$ levels ($p = 0.001$ and $p = 0.004$, respectively), high serum ferritin levels ($p = 0.007$), ILD region existing in the upper lung field ($p = 0.008$), high initial PSL dose ($p = 0.006$), mPSL pulse ($p = 0.001$), IVCY ($p < 0.001$), and combination therapy ($p < 0.001$) were extracted as risk factors for CMV antigenemia by univariate analyses (Table 1). There were no association between the cumulative PSL dose and CMV antigenemia. A multivariate logistic regression analyses revealed that low PaCO$_2$ ($p = 0.044$, OR 4.96), above 0.6 mg/kg/day of initial PSL dose ($p = 0.027$, OR 3.56) and the treatment with oral calcineurin inhibitor ($p = 0.007$, OR 21.23) were independent risk factors for CMV antigenemia. Of 27 patients who died during the observation period 13 (48%) had CMV antigenemia.

Conclusion: Although rapid and intensive therapies are required for PM/DM-ILD, appropriate monitoring, prophylaxis and early treatment for opportunistic infection are important, especially in patients who receive high initial dose of glucocorticoid or calcineurin inhibitor and who show low PaCO$_2$ level.

Table 1. Comparison between the PM/DM-ILD patients complicated by CMV antigenemia and those without CMV antigenemia

<table>
<thead>
<tr>
<th>Variable</th>
<th>CMV positive ($n = 42$)</th>
<th>CMV negative ($n = 74$)</th>
<th>$p$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of disease</td>
<td>PM 4, DM 28, CADM 10</td>
<td>PM 7, DM 47, CADM 26</td>
<td>0.007*</td>
</tr>
<tr>
<td>Age (years)</td>
<td>56 ± 15.3</td>
<td>56 ± 15.3</td>
<td>0.310</td>
</tr>
<tr>
<td>Female (%)</td>
<td>83 (71.6%)</td>
<td>57 (76.7%)</td>
<td>0.650</td>
</tr>
<tr>
<td>Follow-up period (days)</td>
<td>98 ± 155.9</td>
<td>96 ± 109.8</td>
<td>0.763</td>
</tr>
<tr>
<td>CR (UI)</td>
<td>309 (109-737)</td>
<td>327 (121-708)</td>
<td>0.033</td>
</tr>
<tr>
<td>LDH (UI)</td>
<td>271 (100-609)</td>
<td>244 (90-609)</td>
<td>0.495</td>
</tr>
<tr>
<td>RL (G/dl)</td>
<td>511 (486-648)</td>
<td>511 (486-648)</td>
<td>0.995</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>4.3 (0.02-432)</td>
<td>4.4 (0.02-432)</td>
<td>0.554</td>
</tr>
<tr>
<td>Baseline data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alkalinephosphate (mg/dl)</td>
<td>3.5 ± 0.22</td>
<td>3.6 ± 0.23</td>
<td>0.061</td>
</tr>
<tr>
<td>PaCO$_2$ (mmHg)</td>
<td>37.3 (31.6-42.8)</td>
<td>38.5 (31.6-42.8)</td>
<td>0.641</td>
</tr>
<tr>
<td>Ferritin (ng/ml)</td>
<td>310 (104-600)</td>
<td>300 (104-600)</td>
<td>0.007*</td>
</tr>
<tr>
<td>IgG 100 (111-210)</td>
<td>100 (111-210)</td>
<td>100 (111-210)</td>
<td>0.963</td>
</tr>
<tr>
<td>Antibodies</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-Jo-1 Ab</td>
<td>8 (19.5%)</td>
<td>11/68 (17%)</td>
<td>0.271</td>
</tr>
<tr>
<td>Anti-Scl Ab</td>
<td>6/34 (25%)</td>
<td>3/21 (14%)</td>
<td>0.460</td>
</tr>
<tr>
<td>Anti-RO 50 Ab</td>
<td>71 (34%)</td>
<td>3/11 (33%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Rheumatoid Factor (%)</td>
<td>94/236 (40%)</td>
<td>253/464 (40%)</td>
<td>0.671</td>
</tr>
<tr>
<td>Malignancy (%)</td>
<td>7/40 (18%)</td>
<td>14/46 (27%)</td>
<td>0.442</td>
</tr>
<tr>
<td>PSL (mg/kg)</td>
<td>1.53 ± 0.20</td>
<td>0.76 ± 0.32</td>
<td>0.003*</td>
</tr>
<tr>
<td>Amiodarone (mg/kg)</td>
<td>16.2 ± 1.22</td>
<td>6.3 ± 2.32</td>
<td>0.270</td>
</tr>
<tr>
<td>Imatinib (mg/kg)</td>
<td>31.1 ± 12.68</td>
<td>8.3 ± 2.68</td>
<td>0.224</td>
</tr>
<tr>
<td>mPSL pulse (mg/kg)</td>
<td>36 (60%)</td>
<td>37 (55%)</td>
<td>0.611</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VCY (mg)</td>
<td>22 (50%)</td>
<td>16 (39%)</td>
<td>0.091</td>
</tr>
<tr>
<td>Calcineurin inhibitor (%)</td>
<td>30 (65%)</td>
<td>31 (55%)</td>
<td>0.611</td>
</tr>
<tr>
<td>Combination (n)</td>
<td>27 (64%)</td>
<td>11 (15%)</td>
<td>0.021*</td>
</tr>
</tbody>
</table>

* The odds ratio (OR) = exp(coefficient)

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-predictive-risk-factors-for-opportunistic-infection-during-treatment-for-polymyositisdermatomyositis-associated-interstitial-lung-disease

Disclosure: Y. Sugiyama, None; R. Yoshimi, None; M. Tamura, None; N. Hamada, None; H. Nagai, None; N. Tsuchida, None; Y. Kunishita, None; Y. Soejima, None; D. Kishimoto, None; R. Kamiyama, None; K. Minegishi, None; Y. Kirino, None; S. Ohno, None; H. Nakajima, None.

Abstract Number: 2152

Mycophenolate Mofetil Treatment with or without a Calcineurin Inhibitor in Resistant Inflammatory Myopathy

Hironari Hanaoka, Harunobu Iida, Tomofumi Kiyowaka, Yukiko Takakuwa and Kimito Kawahata, Division of Rheumatology and Allergology, Department of Internal Medicine, St. Marianna University School of Medicine, Kawasaki, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Muscle Biology, Myositis and Myopathies Poster
Session Type: ACR Poster Session C  
Session Time: 9:00AM-11:00AM

Background/Purpose: Patients with polymyositis (PM) and dermatomyositis (DM) refractory to glucocorticoid therapy have been treated with a variety of immunosuppressants including mycophenolate mofetil (MMF) and calcineurin inhibitors (CNIs). Although therapeutic effect of the each agent has been partially evaluated, its combination therapy has been poorly investigated. In this study, we evaluated the efficacy and tolerability of MMF with or without CNIs in patients with inflammatory myopathy taking prednisolone (PSL), but refractory to conventional immunosuppressive therapy.

Methods: The records of patients with inflammatory myopathy who had previously failed treatment with at least one immunosuppressant were retrospectively evaluated. We selected patients treated with MMF and divided them into two groups depending on whether or not there was concomitant use of CNIs. We investigated the efficacy by changes in creatine kinase (CK) levels, forced vital capacity (%FVC), and PSL dose. Deterioration was defined as death or drug change due to treatment failure.

Results: We identified 19 patients (14 for DM and 5 for PM) on MMF treatment. There were seven (36.8%) patients on MMF and CNIs, including five on cyclosporine and two on tacrolimus. Average observational periods were 18.6 (SD: 20.5) months in those with the MMF and CNIs and 14.3 (SD: 13.7) months in patients with MMF (P = 0.29). At baseline no significant difference in clinical features including the prevalence of interstitial lung disease (ILD) was seen in between patients taking or not taking CNIs (Table 1). Improvement in CK was seen in patients treated with CNIs (P = 0.04) but not in those without (P = 0.39). No significant improvement in %FVC was found in patients with ILD in either group, and patients with CNIs had a slightly better result than those without in deterioration rate but no differences was seen (P = 0.62) (Figure 1).

Conclusion: The combination of CNIs and MMF might be more effective for decreasing CK levels than MMF alone. Neither treatment arm had a beneficial effect on ILD or deterioration rate over a short-term observation.
Disclosure: H. Hanaoka, None; H. Iida, None; T. Kiyokawa, None; Y. Takakuwa, None; K. Kawahata, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/mycophenolate-mofetil-treatment-with-or-without-a-calcineurin-inhibitor-in-resistant-inflammatory-myopathy

Abstract Number: 2153

**Decreased Lean Body Mass and Bone Mineral Density but Increased Body Fat in Myositis Patients Are Associated with Disease Duration, Inflammatory Status, Skeletal Muscle Involvement and Physical Activity**

Sabina Oreska, Maja Spiritovic, Petr Cesak, Ondrej Marecek, Hana Storkanova, Katerina Kubinova, Martin Klein, Lucia Vernerova, Olga Ruzickova, Radim Beecar, Karel Pavelka, Herman F. Mann, Jiri Vencovsky, and Michal Tomcik

Institute of Rheumatology, Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, Prague, Czech Republic

First publication: September 18, 2017
Methods: 54 patients with IIM (45 females/9 males; mean age 57.3; disease duration 5.8 years; polymyositis (PM, 22)/dermatomyositis (DM, 25)/necrotizing myopathy (IMNM, 7)) and 30 age-/sex-matched HC (25 females/5 males, mean age 54.9) without rheumatic/tumor diseases or manifest cardiovascular event were included. PM/DM patients fulfilled Bohan/Peter criteria for PM/DM. Anthropometric parameters and body composition were assessed (by densitometry-iDXA Lunar, and by bioelectric impedance-BIA2000-M), and physical activity was evaluated using Human Activity Profile (HAP) questionnaire. Routine biochemistry analysis was performed after 8 hours of fasting. Muscle involvement was evaluated by manual muscle test (MMT-8). Data are presented as mean±SD.

Results: Compared to HC, patients with IIM had significantly increased body fat % as assessed by iDXA (BF%: 38.7±6.7 vs. 42.5±7.1%, p=0.015), but decreased lean body mass as assessed both by iDXA (LBM: 45.7±6.6 vs. 40.3±7.0 kg, p=0.0005) and BIA (LBM: 53.2±8.5 vs. 48.7±9.0 kg, p=0.0295), and increased extracellular mass/body cell mass (ECM/BCM) ratio (1.00±0.12 vs. 1.43±0.42, p<0.0001), which reflects worse muscle predispositions for physical exercise, aerobic fitness/performance, and also increases with deteriorating nutritional status. Compared to HC, IIM patients had significantly lower bone mineral density (BMD: 1.16±0.10 vs. 1.05±0.11 g/cm², p=0.0010), and were currently able to perform less energetically demanding physical activities according to HAP score (86.3±5.9 vs. 49.0±20.2, p<0.0001). Disease duration negatively correlated with BMD (r=-0.392, p=0.004) and LBM-BIA (r=-0.272, p=0.047). CRP was positively associated with BF% assessed both by DEXA (r=0.276, p=0.035) and BIA (r=0.306, p=0.025). MMT-8 score negatively correlated with ECM/BCM ratio (r=-0.385, p=0.006), and physical activity (HAP) negatively correlated with BF%-DEXA (r=-0.292, p=0.032).

Conclusion: Compared to healthy age-/sex-matched individuals we found significant negative changes in body composition of our IIM patients, which are associated with their disease duration, inflammatory status, skeletal muscle involvement, and physical activity, and could reflect their impaired nutritional status and predispositions for physical exercise, aerobic fitness and performance.

Acknowledgement: Supported by AZV-16-33574A, GAUK-214615.

Disclosure: S. Oreska, None; M. Spiritovic, None; P. Cesak, None; O. Marecek, None; H. Storkanova, None; K. Kubinova, None; M. Klein, None; L. Vernerova, None; O. Ruzickova, None; R. Becvar, None; K. Pavelka, None; L. Senolt, None; H. F. Mann, None; J. Vencovsky, Samsung Bioepis Co., Ltd., Biogen, 5; M. Tomcik, None.

Abstract Number: 2154

Efficacy of an Intensive 24-Week Physiotherapy Programme in Patients with Idiopathic Inflammatory Myopathies – Preliminary Data from a Single-Center Controlled Study

Maja Spiritovic1,2, Sabina Oreska1, Hana Storkanova1, Petr Cesak2, Adela Rathouska1, Katerina Kubinova1, Martin Klein1, Lucia Vernerova1, Olga Ruzickova1, Herman F Mann1, Karel Pavelka1, Ladislav Senolt1, Jiri Vencovsky1 and Michal Tomcik1, 1Institute of Rheumatology, Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, Prague, Czech Republic, 2Faculty of Physical Education and Sport, Charles University, Prague, Czech Republic, Prague, Czech Republic

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Muscle Biology, Myositis and Myopathies Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Involvement of musculoskeletal system (inflammation, atrophy and permanent damage to the muscle) in idiopathic inflammatory myopathies (IIM) leads to impaired function, reduced muscle strength, endurance and aerobic capacity, decreasing quality of life. Data on efficacy of non-pharmacologic care in IIM is very limited due to variety in studied interventions/outcomes. The aim of our study was to address the limitations of existing studies, and evaluate the effect of a controlled, long-term (24-week intervention, 24-week follow-up), intensive (1h physiotherapy twice weekly, and home-exercise for 1h 5x weekly), tailored physiotherapy program to improve muscle strength, endurance and deep stabilizer system, and quality of life/disability in cohorts with a substantial number of IIM patients.
Methods: All patients fulfilled the Bohan and Peter 1975 diagnostic criteria for dermatomyositis (DM) or polymyositis (PM), had skeletal muscle involvement, and were consecutively recruited from 2014 to 2016 at the Institute of Rheumatology in Prague. Both groups received educational materials and instructions for home exercise at baseline, however, only intervention group underwent the intensive physiotherapy programme. At months 0,3,6,12 all patients were assessed by a physician (physical examination, MITAX, MYOACT, and MDI), and a physiotherapist blinded to intervention (standardized tests evaluating the level of muscle strength MMT-8), and endurance (FI-2), patients filled out patient reported outcomes (PRO)/questionnaires [HAQ, SF-36, Beck’s depression inventory-II (BDI-II), PROs assessing nutrition and fatigue], body composition was analyzed using densitometry (iDXA Lunar) and bioelectric impedance (BIA2000-M), and patients provided blood for routine laboratory analysis and biobanking. Normality of data was tested and inter-group analysis performed with 2-way ANOVA and intra-group analysis by Friedman’s test with Dunn’s post hoc test.

Results: 27 IIM patients (22 female / 5 male, 10 DM / 12 PM / 5 IMNM (immune mediated necrotizing myopathy), median of age 58.0 and disease duration 7.0 years) were recruited into the intervention group (IG) and 27 patients into the control group (CG) (24 female / 3 male, 13 DM / 12 PM / 2 IMNM, median of age 56.5 and disease duration 4.7 years). Compared to observed statistically significant deterioration in CG over the period of months 0-6, we found statistically significant improvement in FI-2, MMT8, HAQ, BDI-II (Table 1). Only numerical improvement in IG compared to numerical deterioration in CG, which has not reached statistical significance, was observed in SF-36 and fatigue PROs.

Conclusion: Our intensive 24-week physiotherapy programme led to a significant improvement in muscle strength, endurance, function and depression, which was clinically meaningful in a substantial proportion of patients.

Acknowledgement: Supported by AZV-16-33574A.

<table>
<thead>
<tr>
<th>Parameter (unit)</th>
<th>Intervention group</th>
<th>Control group</th>
<th>Intra-group analysis (Friedman+Dunn)</th>
<th>Inter-group analysis (2WA)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SEM</td>
<td>Mean ± SEM</td>
<td>Intervention gr.</td>
<td>Control group</td>
</tr>
<tr>
<td>MMT-8</td>
<td>m0: 54.7 ± 2.6</td>
<td>m0: 64.2 ± 2.3</td>
<td>m0-m3: p&lt;0.001</td>
<td>m0-m3: p=0.01</td>
</tr>
<tr>
<td></td>
<td>m3: 60.7 ± 2.4</td>
<td>m3: 58.4 ± 2.0</td>
<td>m3-m6: p&lt;0.01</td>
<td>m3-m6: p=NS</td>
</tr>
<tr>
<td></td>
<td>m6: 69.1 ± 1.9</td>
<td>m6: 55.3 ± 2.0</td>
<td>m6-m0: p&lt;0.001</td>
<td>m0-m6: p=0.001</td>
</tr>
<tr>
<td>FI-2 (%)</td>
<td>m0: 30.0 ± 4.4</td>
<td>m0: 40.2 ± 5.9</td>
<td>m0-m3: p&lt;0.001</td>
<td>m0-m3: p=NS</td>
</tr>
<tr>
<td></td>
<td>m3: 46.9 ± 4.7</td>
<td>m3: 30.8 ± 4.9</td>
<td>m3-m6: p&lt;0.001</td>
<td>m3-m6: p=NS</td>
</tr>
<tr>
<td></td>
<td>m6: 70.6 ± 4.9</td>
<td>m6: 28.7 ± 4.5</td>
<td>m6-m0: p&lt;0.001</td>
<td>m0-m6: p=0.01</td>
</tr>
<tr>
<td>HAQ</td>
<td>m0: 0.91 ± 0.16</td>
<td>m0: 1.25 ± 0.17</td>
<td>m0-m3: p=NS</td>
<td>m0-m3: p=NS</td>
</tr>
<tr>
<td></td>
<td>m3: 0.69 ± 0.14</td>
<td>m3: 1.33 ± 0.18</td>
<td>m3-m6: p=NS</td>
<td>m3-m6: p=NS</td>
</tr>
<tr>
<td></td>
<td>m6: 0.56 ± 0.11</td>
<td>m6: 1.27 ± 0.19</td>
<td>m6-m0: p&lt;0.001</td>
<td>m0-m6: p=NS</td>
</tr>
<tr>
<td>BDI-II</td>
<td>m0: 11.9 ± 2.1</td>
<td>m0: 13.3 ± 1.5</td>
<td>m0-m3: p=NS</td>
<td>m0-m3: p=NS</td>
</tr>
<tr>
<td></td>
<td>m3: 10.7 ± 1.7</td>
<td>m3: 15.2 ± 1.8</td>
<td>m3-m6: p=NS</td>
<td>m3-m6: p=NS</td>
</tr>
<tr>
<td></td>
<td>m6: 8.9 ± 1.5</td>
<td>m6: 14.6 ± 1.4</td>
<td>m6-m0: p&lt;0.05</td>
<td>m0-m6: p=NS</td>
</tr>
</tbody>
</table>

Acronyms: SEM, standard error of the mean; Friedman, Friedman’s test; Dunn, Dunn’s post hoc test; 2WA, two way ANOVA, MMT-8, Manual muscle test-8; FI-2, Functional index-2; HAQ, Health assessment questionnaire; BDI-II, Beck’s depression inventory-II; m0, month 0 (= at the baseline); m3, month 3 (= in the middle of intervention period); m6, month 6 (= at the end of intervention); p, p-value; NS, not significant

Disclosure: M. Spiritovic, None; S. Oreska, None; H. Storkanova, None; P. Cesak, None; A. Rathouska, None; K. Kubinova, None; M. Klein, None; L. Vernerova, None; O. Ruzickova, None; H. F. Mann, None; K. Pavelka, None; L. Senolt, None; J. Vencovsky, Samsung Bioepis Co., Ltd., Biogen, 5; M. Tomcik, None.
Background/Purpose: Immune checkpoint inhibitor therapy (ICI) has surfaced as a successful and robust treatment option in the fight to end cancer. As we gain more insight, immunotoxicity and autoimmunity as a result of ICI exposure have shown to affect every organ system of the human body in the form of immune related adverse events. In this novel case series, we report nine patients on ICI therapy that presented with either de novo myositis or with pre-existing dermatomyositis.

Methods: Patients with myositis in context of ICI therapy were identified from all institutional databases using ICD 9 & 10 diagnostic codes for myositis from January 2004 until September 2016. We included cases with de novo myositis occurring within 3 months of last treatment with one or more diagnostic codes that could not be present within a 6-month window before treatment. We defined de novo myositis in those cases including initial creatinine kinase levels at least three times the normal limit along with persistent elevation at the end of the following 7 days, a rheumatologist or neurologist diagnosing myositis, as well as muscle pains and weakness after starting ICI. Pre-existing dermatomyositis cases were defined as those that had a rheumatologist note diagnosing them prior to initiation of ICI. Clinical data was extracted retrospectively from time prior to starting checkpoint inhibitor therapy until 3 months.

Results: Nine patients with myositis were identified. Six patients developed de novo myositis as a result of ICI while 3 had pre-existing dermatomyositis out of which 1 flared post treatment. Mean age was 67.1 years (standard deviation=10.2) and 66.6% were males. Cancer types included melanoma, bladder cancer, and squamous cell carcinoma of the lung, acute myeloid leukemia, prostate cancer, and renal cell carcinoma. ICI regimens included nivolumab (n=2), ipilimumab (n=1), pembrolizumab (n=3; one patient received nivolumab followed by pembrolizumab 18 months later), and atezolizumab (n=1) as monotherapy or as a combination of nivolumab and ipilimumab (n=3). Other immune related adverse events included: pneumonitis, migratory joint pain, rash, and increase in transaminases as well as hypo and hyperthyroidism and severe rhabdomyolysis. Patients were treated with corticosteroids ranging from 1 to 2mg/kg with variable response rates, except for one patient who received non-steroidal anti-inflammatory drugs to manage his myalgias. Two out of 6 patients died with de novo myositis whereas 2 out of 3 died with pre-existing dermatomyositis. All patients with de novo myositis had elevated levels of creatinine kinase ranging from 514 to 13,010 U/L. Median time to development of de novo myositis from first infusion was 1.25 months (range=0.5-4.0).

Conclusion: We found evidence of de novo myositis in addition to patients with pre-existing dermatomyositis who flared following ICI therapy. This preliminary data warrants further investigation into determining the risk of developing myositis in the cancer patient population undergoing ICI which may help understand and treat the underlying etiology and prevent occurrence.

Disclosure: M. Shah, None; J. Tayar, None; N. Abdel-Wahab, None; M. Suarez-Almazor, Bristol-Myers Squibb, 5.

Abstract Number: 2156

Comparison of Patients with Dermatomyositis in a Specialty Clinic Versus Clinical Trial with Anabasum (JBT-101), a Cannabinoid Receptor Type 2 Agonist

Disclosure: M. Shah, None; J. Tayar, None; N. Abdel-Wahab, None; M. Suarez-Almazor, Bristol-Myers Squibb, 5.
Background/Purpose: There are limited treatment options and no published double-blind randomized placebo-controlled trials for the treatment of skin manifestations of dermatomyositis (DM). There is no information about patients enrolled in trials to study efficacy of treatments of skin involvement in DM. Anabasum is a non-immunosuppressive, synthetic, preferential CB2 agonist that resolves inflammation in animal and human models of innate immune responses and reduces cytokine production by isolated mononuclear cells from DM patients.

Methods: A double-blind randomized placebo-controlled Phase 2 trial (JBT101-DM-001) with NIH as a collaborator was designed to test efficacy and safety of anabasum in adults with DM and refractory skin involvement. The trial is done at a clinic specializing in skin involvement in DM which allows comparison of trial subjects to the general DM population at the same clinic.

Results: Selection criteria included Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) activity score of ≥ 14, minimal active muscle involvement, failure or intolerance to hydroxychloroquine, and stable DM medications including immunosuppressive drugs. Trial subjects (N = 22) and the general clinic population (N = 221) were predominantly middle-aged white, non-Hispanic women (Table 1). Trial subjects had high skin disease activity compared to the clinic population and widespread use of immunosuppressive drugs (86%), including second-line immunosuppressive drugs (64%), with the mostly commonly used immunosuppressive drugs being antimalarial drugs (45%), mycophenolate (32%), methotrexate (23%), and systemic corticosteroids (23%).

Table 1. Comparison of demographics and disease characteristics between trial and overall DM population
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>JBT101-DM-001 (N = 22)</th>
<th>General DM Clinic (N = 221)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range)</td>
<td>53 (36-69)</td>
<td>57 (23-88)</td>
</tr>
<tr>
<td>Sex, % female</td>
<td>95%</td>
<td>85%</td>
</tr>
<tr>
<td>Race, % white</td>
<td>95%</td>
<td>90%</td>
</tr>
<tr>
<td>Ethnicity, % not Hispanic or Latino</td>
<td>86%</td>
<td>97%</td>
</tr>
<tr>
<td>DM subset</td>
<td></td>
<td></td>
</tr>
<tr>
<td>· Classic</td>
<td>41%</td>
<td>38%</td>
</tr>
<tr>
<td>· Clinically amyopathic</td>
<td>59%</td>
<td>62%</td>
</tr>
<tr>
<td>CDASI activity score, final visit, median (range)</td>
<td>33 (22-57)</td>
<td>13 (0-71)</td>
</tr>
<tr>
<td>CDASI damage score, final visit, median (range)</td>
<td>2 (0-13)</td>
<td>2 (0-14)</td>
</tr>
<tr>
<td>Physician Global Assessment, median, range</td>
<td>4.7 (2.6 – 8.3)</td>
<td>1 (0-9.4)</td>
</tr>
<tr>
<td>Patient Global Assessment, median, range</td>
<td>5.4 (0.4 – 9.7)</td>
<td>4 (0-10)</td>
</tr>
<tr>
<td>Skinindex-29, median (range)</td>
<td>48.6 (17-77)</td>
<td>35.7 (0-96.4)</td>
</tr>
<tr>
<td>· Symptoms</td>
<td>37.8 (4-78)</td>
<td>30.0 (0-100)</td>
</tr>
<tr>
<td>· Emotions</td>
<td>24.2 (0-67)</td>
<td>12.5 (0-100)</td>
</tr>
<tr>
<td>· Functioning</td>
<td>40 (0-80)</td>
<td>50 (0-100)</td>
</tr>
<tr>
<td>· Photosensitivity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 1 immunosuppressive drug including antimalarials</td>
<td>86%</td>
<td>40%</td>
</tr>
<tr>
<td>≥ 1 immunosuppressive drug excluding antimalarials</td>
<td>64%</td>
<td>19%</td>
</tr>
<tr>
<td>IVIG</td>
<td>0%</td>
<td>10%</td>
</tr>
</tbody>
</table>

**Conclusion:** This is the first report of subject demographics and disease characteristics in a clinical trial focused on safety and efficacy in skin-predominant dermatomyositis. Trial subjects had similar demographics to the overall DM clinic population. However, skin disease activity and patient-reported skin symptoms were greater in the trial subjects than in the overall DM clinic population, despite much higher use of second-line immunosuppressive medications. Disease activity in trial subjects was much higher than required by inclusion criteria. Combined, these data show that subjects enrolled in trials of treatment of skin involvement in DM may have disease that is more active and more difficult to control than the general population of patients, reminiscent of early efficacy trials in other systemic autoimmune diseases.

**Disclosure:** V. P. Werth, None; E. Hejazi, None; S. M. Pena, None; J. S. Haber, None; J. Okawa, None; R. Feng, None; K. Gabre, None; J. Concha, None; S. Constantine, Corbus Pharmaceuticals, Inc., 1,Corbus Pharmaceuticals, Inc., 3; B. White, Corbus Pharmaceuticals, 1,Corbus Pharmaceuticals, 3.


**Abstract Number:** 2157

**Factors Associated with Clinical Remission of Skin Disease in Dermatomyositis**

Paige Wolstencroft¹, Lorinda Chung², Shufeng Li¹, Livia Casciola-Rosen³ and David Fiorentino⁴, ¹Dermatology, Stanford University School of Medicine, Stanford, CA, ²Division of Immunology and Rheumatology, Stanford University School of Medicine, Stanford,
Quantitative estimates of the duration and severity of cutaneous disease are lacking for adult dermatomyositis (DM) patients. The Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) is a validated instrument that quantifies cutaneous disease activity (CDASI-a), and allows for objective assessments of disease severity. Our aims were to estimate the percentage of DM patients with clinically significant skin inflammation who achieve clinical remission (CR) of skin disease during a 3-year follow-up period and to examine the relationship between skin disease course and selected clinical variables.

Methods:
Adult DM patients (age >18 years) seen at our outpatient clinic between May 15, 2007 and October 28, 2016 were considered for this study. DM was diagnosed using Bohan/Peter criteria, or, for clinically amyopathic patients, Sontheimer criteria. Patients were included if their initial CDASI-a score was greater than or equal to 12, and they had a minimum of 2 scores recorded 3 or more months apart. CR was defined as a CDASI-a less than or equal to 5 with no individual erythema score >1 and no ulcerations. Univariable and multivariable logistic regression analysis was performed using age, race, gender, amyopathic status, DM-associated malignancy, baseline CDASI-a, disease duration at baseline, time until first systemic therapy, autoantibody phenotype (Mi-2, TIF-1gamma, SAE1, MDA5, NXP2 or Ro52), and medication exposure as covariates. For selected variables, Kaplan-Meier plots were created and log-rank analysis used to compare curves.

Results:
In total 74 patients met our inclusion criteria. The median duration of follow-up was 17.5 (11-28) months, with a median of 4 (3-6) months between CDASI scores. Overall, 36% of patients were treated with mycophenolate mofetil (MMF), 38% with antimalarials, 39% with methotrexate and 24% with IVIG. Twenty-eight patients (38%) entered CR within 3 years, and the overall probability of CR was 0.43 after 36 months (Figure 1A). The probability of CR was significantly higher for patients without anti-MDA5 antibodies (Figure 1B) as 0/10 anti-MDA5 patients entered CR. Increased age (OR 1.07, 95% CI 1.02-1.12; \(P=0.01\)), DM-associated malignancy (OR 14.46, 95% CI 2.18-96.07; \(P=0.006\)) and MMF (OR 6.00, 95% CI 1.66-21.78; \(P=0.0064\)) were significantly associated with CR in multivariable regression analysis.

Conclusion:
CR was relatively uncommon in our population, and even less common among anti-MDA5 patients, despite the use of aggressive systemic therapy. The positive association between MMF and CR suggests that MMF should be considered a first line agent for DM skin disease, while our overall results highlight the need for new therapies to more effectively treat skin disease in DM. Increased age and DM-associated malignancy were both associated with positive cutaneous outcomes, which has important prognostic significance.

Disclosure: P. Wolstencroft, None; L. Chung, None; S. Li, None; L. Casciola-Rosen, None; D. Fiorentino, None.
Abstract Number: 2158

HLA-DRB1*04:03/*04:06 As the Genetic Susceptibility to Dermatomyositis Positive for Anti-Transcriptional Intermediary Factor 1-γ Antibody in Japanese Population

Yukie Yamaguchi1, Masataka Kuwana2, Miwa Kanaoka1, Tomoya Watanabe1, Naoko Okiyama3, Takahisa Gono2, Masanari Kodera4, Takeshi Kambara5, Yasuhiyo Hamaguchi6, Mariko Seishima7, Kazuhiko Takehara6, Manabu Fujimoto3 and Michiko Aihara1,
1Department of Environmental Immuno-Dermatology, Yokohama City University Graduate School of Medicine, Yokohama, Japan, 2Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan, 3Department of Dermatology, University of Tsukuba, Tsukuba, Japan, 4Department of Dermatology, Japan Community Health care Organization Chukyo Hospital, Nagoya, Japan, 5Department of Dermatology, Yokohama City University Medical Center, Yokohama, Japan, 6Department of Dermatology, Kanazawa University, Kanazawa, Japan, 7Department of Dermatology, Gifu University Graduate School of Medicine, Gifu, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Muscle Biology, Myositis and Myopathies Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Dermatomyositis (DM) is characterized by inflammation of the skin and skeletal muscle, and is occasionally complicated by interstitial lung disease or concomitant malignancy. It has been recognized that myositis-specific autoantibodies (MSAs) are correlated with unique sets of clinical manifestations. The mechanisms underlying production of MSAs still remain uncertain, but genetic factors, such as human leukocyte antigen (HLA) class II genes, are reported to play some roles. Anti-Jo-1 and anti-melanoma differentiation-associated gene 5 (MDA5) antibodies are associated with HLA-DRB1*04:05 in Japanese population, but there is no information on the HLA-DRB1 association with anti-transcriptional intermediary factor 1-γ (TIF1-γ) antibody.

Methods: We enrolled 36 DM patients with anti-TIF1-γ antibody, 24 DM patients without anti-TIF1-γ antibody, and 161 ethnicity-matched healthy controls, who were recruited form 7 medical centers across Japan. Eighteen patients with anti-TIF1-γ antibody had concomitant malignancy which was defined by the diagnosis within 2 years before or after DM diagnosis. HLA typing was performed by next-generation sequencing method. Strength of associations was estimated by odds ratios (OR) and 95% confidence intervals (CI) and frequencies were compared using the Fisher’s exact test. P values were corrected by multiplying the number of alleles detected in Japanese.

Results: Although there is no statistically significant difference in distribution of HLA-DRB1 alleles among 3 groups, we found a trend toward increased frequencies of DRB1*04:03 and DRB1*04:06 in DM patients with anti-TIF1-γ, in comparison with DM patients without anti-TIF1-γ or healthy controls (19% versus 4% or 7%, 19% versus 0% or 8%, respectively). Interestingly, DRB1*04:03 and DRB1*04:06 alleles are evolutionally close and commonly have unique amino acid sequence (LLEQRRAE at positions 67-74) in the third hypervariable region of the HLA-DRB1. The frequency of having either DRB1*04:03 or DRB1*04:06 in DM patients with anti-TIF1-γ was significantly higher than the frequency in DM patients without anti-TIF1-γ (39% versus 4%; OR = 14.6, 95%CI 1.8-121, corrected P = 0.04) and tended to be higher than the frequency in healthy controls (39% versus 16%; OR = 3.3, 95%CI 1.5-7.3, corrected P = 0.09). No significant difference was observed in the frequency of DRB1 alleles between anti-TIF1-γ-positive patients with and without concomitant malignancy.

Conclusion: In Japanese population, anti–TIF1-γ antibody is associated with rare HLA–DRB1*04:03/*04:06 alleles, which are distinct from the DRB1 allele associated with other MSAs, including anti-Jo-1 and anti-MDA5 antibodies.

Disclosure: Y. Yamaguchi, None; M. Kuwana, None; M. Kanaoka, None; T. Watanabe, None; N. Okiyama, None; T. Gono, Astellas, Japan Blood Products Organization, 8; M. Kodaera, None; T. Kambara, None; Y. Hamaguchi, None; M. Seishima, None; K. Takehara, None; M. Fujimoto, None; M. Aihara, None.

Dermatomyositis Acute Onset/Flares Following Ingestion of IsaLean® Herbal Supplement: Clinical and Immunostimulatory Findings

Majid Zeidi¹,², Peter B Chansky¹,² and Victoria P Werth³,⁴, ¹Department of Dermatology, Corporal Michael J. Crescenz VAMC, PHILADELPHIA, PA, ²Department of Dermatology, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, ³University of Pennsylvania and the VA Medical Center, Philadelphia, PA, ⁴Department of Dermatology, Corporal Michael J. Crescenz VAMC, Philadelphia, PA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Muscle Biology, Myositis and Myopathies Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The use of complementary and alternative medicine (CAM) has gained popularity in the United States over the last few decades. Herbal supplements have adverse medical effects. We observed two patients with acute onset/flare of their classic dermatomyositis after the ingestion of IsaLean®, an herb-based weight-loss product. The purpose of this study was to investigate and characterize the immunostimulatory properties of the herbal and dietary supplement IsaLean® underlying the acute onset/flare of dermatomyositis in two patients.

Methods: Peripheral blood mononuclear cells were isolated from 5 dermatomyositis patients and 5 control patients stimulated with increasing concentrations of IsaLean®: 0, 0.05, 0.5, and 5 µg/ml to evaluate the cellular production of tumor necrosis factor alpha (TNFα), interferon alpha (IFN-α), and interferon beta (IFN-β), key pathogenic cytokines in dermatomyositis. The cells were also incubated with IsaLean® and lipopolysaccharide (LPS), and the effect of neutralizing anti-TLR4, quinacrine (QC), and hydroxychloroquine (HCQ) on the cellular production of TNFα was examined. Cytokine production was measured by enzyme-linked immunosorbent assay. The One-way analysis of variance (ANOVA) with Dunnett's multiple comparison test was used to compare the level of TNF-α, IFN-α, and IFN-β after stimulation with Isalean and treatment with Anti-TLR4, QC, and HCQ.

Results: The IsaLean® stimulated cells secreted mean (standard error) TNFα levels of 1.78 (0.38), 339.5 (39), 1188 (125.5) and 2224 (488.7) pg/ml at 0, 0.05, 0.5, and 5 µg/ml concentrations of IsaLean®, respectively. IsaLean® increased cellular secretion of TNFα at 0.5 µg/ml (p<0.01) and 5 µg/ml (p<0. 001) (Figure 1). Anti-TLR4 suppressed cellular secretion of TNFα from IsaLean® (p<0.001) and LPS-stimulated cells (p<0.05) (Figure 2). QC significantly reduced the production of TNFα from IsaLean® (p<0.001) and LPS-stimulated (p<0.05) compared to HCQ (Figure 3).

Conclusion: IsaLean®, an herb-based weight-loss product, induced secretion of TNFα, IFN-α, and IFN- β from immune cells of dermatomyositis patients in vitro. These cytokines are thought to be key immunostimulatory cytokines causing cutaneous dermatomyositis. These studies demonstrate that the pro-stimulatory effects of IsaLean® are mediated through TLR4.
Disclosure: M. Zeidi, None; P. B. Chansky, None; V. P. Werth, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/dermatomyositis-acute-onset-flares-following-ingestion-of-isalean-herbal-supplement-clinical-and-immunostimulatory-findings

Abstract Number: 2160

Clinical Significance of Anti-Aminoacyl tRNA Synthetase Antibodies Which Are Positive By ELISA but Not By Immunoprecipitation – the Variations of Antigen Recognition and the Association with Interstitial Lung Diseases but Not Myositis –

Yuki Ishikawa¹,², Ran Nakashima¹, Takaki Nojima³,⁴, Takuya Isayama⁵, Nobuo Kuramoto¹, Kosaku Murakami¹, Hajime Yoshifuji¹, Koichiro Ohmura¹ and Tsuneyo Mimori¹, ¹Clinical Immunology and Rheumatology, Graduate School of Medicine, Kyoto University, Kyoto, Japan, ²One Joslin Place, Joslin Diabetes Center, Harvard Medical School, Boston, MA, ³Clinical Immunology and Rheumatolog, Graduate School of Medicine, Kyoto University, Kyoto, Japan, ⁴Nojima Internal Medicine Clinic, Hiroshima, Japan, ⁵Medical & Biological Laboratories CO., LTD., Nagoya, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Muscle Biology, Myositis and Myopathies Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM
**Background/Purpose:** Anti-aminoacyl tRNA synthetase (ARS) antibodies are associated with common clinical characters, which are fever, polyarthritis, interstitial lung disease (ILD), Raynaud’s phenomenon, mechanic’s hand and myositis, and the constellation of these symptoms in patients with anti-ARS antibody is called anti-synthetase syndromes (ASS). So far, anti-ARS antibodies have been screened by RNA/protein immunoprecipitation (IP) or line blot. Recently, an enzyme-linked immunosorbent assay (ELISA), in which the mixture of 5 ARS antigens are coated on the plate, has been established, and growing number of blood samples has been examined in daily clinical practices. However, we often encounter such patients that are positive for anti-ARS antibody by ELISA but negative by IP. Thus, we analyzed the discrepancy between the ELISA and IP precisely to elucidate the underlying mechanism and the clinical meaning of the discrepant results.

**Methods:** We screened anti-ARS antibodies both by RNA-IP using HeLa cells and ELISA (MESACUP™ anti-ARS test, MBL CO., LTD., Nagoya, Japan) for sera obtained from patients who visited to our department with suspicion of rheumatic diseases from January 2014 to March 2017. The sera which showed discrepant results between two methods were further analyzed by individual antigen-specific ELISA, immunoblotting, and protein-IP. Obtained results were compared to see the discordance among different methods. The clinical features of the patients were also characterized.

**Results:** Eleven patients (6 females and 5 males with mean age of 67.3±12.4 years-old) were found to be positive for anti-ARS by the ELISA but negative by RNA-IP. The clinical diagnoses were 2 RA, 2 SSc, 1 SS, 1 DLE, 1 PM with SS, 1 DM and 3 unclassified ILD. Within these 11 patients, anti-Jo-1 antibody was detected by specific ELISA in 9 patients, but only in 5 and 1 by protein-IP and immunoblot, respectively. On the other hand, anti-EJ antibody was detected in 5 patients by immunoblot, and some of these sera were considered to cross-react to Jo-1 antigen by absorption ELISA using each antigen. Ten (91%) patients presented ILD, which responded to glucocorticoids without recurrence, while, numbers of patients presented other ASS symptoms were as follows; 3 (27%) mild myositis, 4 (36%) polyarthritis, 5 (45%) Raynaud’s phenomenon, 1 (9%) mechanic’s hand, and 0 (0%) fever.

**Conclusion:** Positivity of anti-ARS antibodies sometimes shows discrepancy between ELISA and IP, and it may be due to the recognition of denatured or cryptic ARS epitopes by the antibodies. In such cases, anti-ARS antibodies can be associated more strongly with ILD than with myositis. However, we need to further follow up these patients to investigate whether epitope spreading may occur, which leads to the onset of established myositis with positive anti-ARS antibodies not only by ELISA but also by IP.

**Disclosure:** Y. Ishikawa, None; R. Nakashima, None; T. Nojima, None; T. Isayama, None; N. Kuramoto, None; K. Murakami, None; H. Yoshifuji, None; K. Ohmura, None; T. Mimori, None.

Methods: This was a retrospective, observational cross-sectional study of 96 patients (62 African American (AA) and 34 Caucasian) with PM/DM seen in an academic rheumatology clinic from 1994 - 2016. Clinical characteristics were compared, and they included demographics, clinical and laboratory data at initial presentation to the clinic, and development of interstitial lung disease (ILD) (Table 1). Treatment medications (immunosuppressives (IS) and steroids), mean creatine kinase values (CK) in the last year of follow-up, and frequency of achieving stable disease state on or off medications (IS and steroids) in the last year of follow-up were compared between the groups to study treatment response (Table 2). Multivariate linear and logistic regression analysis was performed to determine factors that were associated with initial CK, presence of ILD and achievement of stable disease state during follow-up.

Results: Median CK was higher and rash was seen more frequently in AA patients at presentation than in Caucasians. The disease duration prior to the initial presentation was longer in AA patients. The AA and Caucasian patients did not differ in terms of frequency of dysphagia, autoantibodies at presentation, presence of ILD or age at diagnosis (Table 1). In a multivariable model, age at diagnosis was associated with initial CK ($P = 0.0142$) but other parameters including race did not correlate. During follow-up, the two groups were similar in terms of the number of IS used, and frequency of achieving stable disease state on or off medications in the last year of follow-up (Table 2). In a multivariable analysis, anti-Jo1 (OR 8.90, $P = 0.00104$) and SSA antibodies (OR 5.60, $P = 0.00795$) were associated with development of ILD. Presence of rash (OR 0.25, $P = 0.00996$), ILD (OR 0.24, $P = 0.00738$) and the number of IS used (OR 0.40, $p=0.01199$) were negatively associated with achieving stable disease state on or off medications in the last year of follow-up. Race was not a significant factor in either model.

Conclusion: The AA and Caucasian patients did not differ in terms of development of ILD or achieving stable disease state. Other parameters including presence of autoantibodies, rash and ILD and higher number of immunosuppressants used were associated with worse outcome. To our knowledge, this study included one of the largest AA PM/DM patient cohort to date.
Table 1: Comparison of clinical characteristics between African American (AA) and Caucasian patients with polymyositis and dermatomyositis.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Caucasian (n = 34)</th>
<th>AA (n = 62)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age at diagnosis, years</td>
<td>48.7 ±13.8</td>
<td>46.6 ±16.1</td>
<td>0.5173</td>
</tr>
<tr>
<td>Number of females</td>
<td>21 (61.8 %)</td>
<td>54 (87.1 %)</td>
<td>0.0085</td>
</tr>
<tr>
<td>Never smoked^a</td>
<td>24 (70.6 %)</td>
<td>42 (67.7 %)</td>
<td>0.3829</td>
</tr>
<tr>
<td>Active smoking at diagnosis</td>
<td>0 (0 %)</td>
<td>11 (17.7 %)</td>
<td>0.0071</td>
</tr>
<tr>
<td>Median CK (U/L) (interquartile range)^a</td>
<td>825 (268 – 2433)</td>
<td>2610 (932 – 5323)</td>
<td>0.0037</td>
</tr>
<tr>
<td>Rash^a</td>
<td>12 (35.3 %)</td>
<td>42 (67.7 %)</td>
<td>0.0023</td>
</tr>
<tr>
<td>Dysphagia^a</td>
<td>7 (20.6 %)</td>
<td>8 (12.9 %)</td>
<td>0.3825</td>
</tr>
<tr>
<td>ANA^a</td>
<td>25 (73.5 %)</td>
<td>43 (69%)</td>
<td>0.2537</td>
</tr>
<tr>
<td>Jo1^a</td>
<td>13 (38.2 %)</td>
<td>14 (22.5%)</td>
<td>0.1546</td>
</tr>
<tr>
<td>SSA^a</td>
<td>7 (20.6 %)</td>
<td>17 (27.4%)</td>
<td>0.6229</td>
</tr>
<tr>
<td>ILD development^b</td>
<td>17 (50 %)</td>
<td>27 (43.5 %)</td>
<td>0.6689</td>
</tr>
<tr>
<td>Early ILD</td>
<td>13</td>
<td>20</td>
<td>1</td>
</tr>
<tr>
<td>Honeycombing</td>
<td>5</td>
<td>4</td>
<td>0.2747</td>
</tr>
<tr>
<td>Median income ($)</td>
<td>68090</td>
<td>37342</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

^a These variables were present at initial presentation to the rheumatology clinic

^b Interstitial lung disease (ILD) development during follow-up. Early ILD defined as development of ILD within 6 months of initial presentation
<table>
<thead>
<tr>
<th>Variables</th>
<th>Caucasian (n = 34)</th>
<th>AA (n = 62)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease duration, years (interquartile range)</td>
<td>4.5 (2.25 – 8)</td>
<td>9 (5 – 12)</td>
<td>0.0056</td>
</tr>
<tr>
<td>Prednisone 7.5 mg/day or greater(^a)</td>
<td>10 (29.4 %)</td>
<td>20 (32.2 %)</td>
<td>0.8216</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>21 (61.8 %)</td>
<td>47 (75.8 %)</td>
<td>0.1653</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>16 (47.0 %)</td>
<td>40 (64.5 %)</td>
<td>0.1301</td>
</tr>
<tr>
<td>Mycophenolate mofetil</td>
<td>18 (52.9 %)</td>
<td>18 (29.0 %)</td>
<td>0.0278</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>3 (8.8 %)</td>
<td>3 (4.8 %)</td>
<td>N/A</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>13 (38.2 %)</td>
<td>27 (43.5 %)</td>
<td>0.6691</td>
</tr>
<tr>
<td>Rituximab</td>
<td>15 (44.1 %)</td>
<td>27 (43.5 %)</td>
<td>1</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>3 (8.8 %)</td>
<td>3 (4.8 %)</td>
<td>N/A</td>
</tr>
<tr>
<td>Median number of immunosuppressives (interquartile range)(^b)</td>
<td>1 (1 – 2)</td>
<td>2 (1 – 2)</td>
<td>0.5832</td>
</tr>
<tr>
<td>Median CK (U/L) at follow-up (interquartile range)(^c)</td>
<td>106 (61 – 168)</td>
<td>204 (109 – 413)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Stable disease state(^d)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>On medications</td>
<td>19 (55.9 %)</td>
<td>33 (53.2 %)</td>
<td>0.8334</td>
</tr>
<tr>
<td>Off medications</td>
<td>3 (8.8 %)</td>
<td>5 (8.1 %)</td>
<td>1</td>
</tr>
</tbody>
</table>

\(^a\) In the last year of follow-up

\(^b\) They include azathioprine, methotrexate, mycophenolate, leflunomide and tacrolimus

\(^c\) Median of the mean CK of each subject in the last year of follow-up

\(^d\) Stable disease state defined as stable disease with no change in immunosuppressives or steroids (prednisone less than 7.5 mg/day) or completely off of...
Nailfold Videocapillaroscopy in Idiopathic Inflammatory Myopathies

Elvira Bangert1, Marie Hudson2,3, Evelyne Vinet4, Mianbo Wang5 and Genevieve Gyger6, 1Department of Medicine, Division of Rheumatology, Queen's University, Kingston, ON, Canada, 2Division of Rheumatology, Jewish General Hospital, Lady David Institute for Medical Research, Montreal, QC, Canada, 3McGill University, Montreal, QC, Canada, 4Divisions of Rheumatology and Clinical Epidemiology, McGill University Health Centre, Montreal, QC, Canada, 5Lady Davis Institute for Medical Research, Montreal, QC, Canada, 6Department of Medicine, Jewish General Hospital, McGill University, Montreal, QC, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Muscle Biology, Myositis and Myopathies Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
In systemic sclerosis, a scleroderma pattern on nailfold videocapillaroscopy (NVC) (SSc) is well recognized. In idiopathic inflammatory myopathies (IIM), a scleroderma-like pattern, including giant-ramified capillaries, has been proposed. The aim of our study was to describe nailfold capillary abnormalities in IIM subsetted using newly proposed integrative criteria [1,2].

Methods:
We studied IIM subjects in the Canadian Inflammatory Myopathy Study (CIMS), a cohort of subjects with early onset disease followed prospectively. NVC images were acquired using the DS MEDICA Videocap (X200 magnification). The nailfolds of the second, third, fourth and fifth fingers of both hands were photographed and scored by an experienced rheumatologist. Microhemorrhages, giant capillaries, ectasias and ramified capillaries were scored using a standardized semi-quantitative scale (0 = no, 1 = ≤33%, 2 = 33–66%, and 3 = >66% abnormalities per linear millimeter). Capillary density was scored both semi-quantitatively (0 if ≥7, 1 if 4–6, or 2 if ≤3 capillaries/mm) and quantitatively (mean number of capillaries/mm). Each NVC parameter, as well as disorganization and giant-ramified capillaries, were also scored as present or absent. Finally, the proportion of subjects with scleroderma-like, scleroderma (SSc), non-specific, and normal patterns were compared.

Results:
38 IIM subjects were included: 18 with DM (of which 9 had myositis specific antibodies and 9 were seronegative) and 20 with OM (of which 8 had anti-synthetase syndrome). Baseline characteristics of the subjects and NVC features and patterns are presented in Tables 1-3. Capillary density was lower than normal in both DM (mean 5.5/mm) and OM (mean 6.1/mm). Giant-ramified capillaries were present in 22.2 % of DM and 25% of OM subjects. SSc-like pattern was more common in DM (50%) than OM (25%), whereas active- or late-SSc pattern was more common in OM than DM (25% vs 5.6%).

Conclusion:
This is the first study of NVC using integrative criteria for IIM. We found differences in NVC features and patterns between DM and OM subsets. NVC may be an additional diagnostic tool in IIM. A larger study is ongoing to confirm these findings.
Clinical Utilization Patterns and Performance of Commercial Myositis Autoantibody Panels in Routine Practice

Prateek C. Gandiga1, Junqian Zhang2, Preethi Thomas1, Victoria P. Werth2,3, Sapna Sangani1, Sharon L. Kolasinski1 and Michael D. George1, 1Division of Rheumatology, University of Pennsylvania, Philadelphia, PA, 2Department of Dermatology, University of Pennsylvania, Philadelphia, PA, 3Corporal Michael J. Crescenz VA Medical Center, Philadelphia, PA

First publication: September 18, 2017

Disclosure: E. Bangert, None; M. Hudson, None; E. Vinet, None; M. Wang, None; G. Gyger, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/nailfold-videocapillaroscopy-in-idiopathic-inflammatory-myopathies

Abstract Number: 2163

Clinical Utilization Patterns and Performance of Commercial Myositis Autoantibody Panels in Routine Practice
SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Muscle Biology, Myositis and Myopathies Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Myositis autoantibody testing is now widely commercially available, with an evolving role in routine clinical care. However, the use and performance of commercial "myositis panels" in usual practice have been poorly studied. We examined commercial myositis autoantibody panel ordering patterns and testing results in a large tertiary-care health system.

Methods:
We conducted a retrospective observational study of all adult patients with a commercial myositis autoantibody panel ordered at all outpatient and two inpatient locations of the University of Pennsylvania between January 2011 and March 2016. We abstracted information about patient demographics, myositis panel orders [specialty of the ordering provider, symptoms/signs which prompted the order (indication), performing commercial vendor, autoantibodies tested], and relevant clinical, laboratory, radiographic, and histopathologic data. For each subject, clinical diagnosis was assigned considering all available information except autoantibody profile. Bohan and Peter's and Sontheimer's criteria were used for PM/DM and clinically amyopathic dermatomyositis (CADM), with positive skin biopsy required for definite CADM. Equivocal cases were resolved by consensus among all investigators.

Results:
378 patients were included (66% women, mean age 55 ± 15 years). Myositis panels were ordered most often by rheumatology (39%), pulmonology (23%), dermatology (18%), and inpatient medicine (12%). ARUP Laboratories performed 72% of testing. The number of myositis panels ordered markedly increased over the study period for all indications (Figure) and departments. 10.3% of subjects had positive myositis specific autoantibodies (MSA); 19.6% had positive myositis associated autoantibodies (MAA). The rate of positive MSA was similar for all indications [p=0.47]. Only 11 of 76 (14.5%) of patients with probable/definite PM, DM, or CADM had positive MSA (Table). A comparable rate of positive MSA occurred in patients with ILD without myositis [10/102 (9.8%); p=0.34]. Patterns for MAA followed similar trends.

Conclusion:
Commercial myositis autoantibody panel testing has dramatically increased for expanding clinical indications by rheumatologists and non-rheumatologists alike. Clinicians must be aware that negative MSA testing with these assays was common, even in patients with clinically affirmed disease. MSA were found at a similar rate in patients with isolated ILD, and may provide important information for this population. Continued study of the performance of commercial myositis autoantibody testing is required as the role of these assays further develops.
Prognostic Factors in Polymyositis/Dermatomyositis Patients with Anti-Synthetase Antibodies

Masashi Taniguchi\textsuperscript{1}, Ran Nakashima\textsuperscript{1}, Nobuo Kuramoto\textsuperscript{1}, Kosaku Murakami\textsuperscript{1}, Motomu Hashimoto\textsuperscript{2}, Hajime Yoshifuji\textsuperscript{1}, Masao Tanaka\textsuperscript{2}, Koichiro Ohmura\textsuperscript{1} and Tsuneyo Mimori\textsuperscript{1}, \textsuperscript{1}Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University, Kyoto, Japan, \textsuperscript{2}Department of Advanced Medicine for Rheumatic Diseases, Graduate School of Medicine, Kyoto University, Kyoto, Japan

\textbf{First publication: September 18, 2017}

\textbf{SESSION INFORMATION}
\textbf{Session Date:} Tuesday, November 7, 2017
\textbf{Session Title:} Muscle Biology, Myositis and Myopathies Poster
\textbf{Session Type:} ACR Poster Session C
\textbf{Session Time:} 9:00AM-11:00AM

\textbf{Background/Purpose:} Anti-aminocarboxyl-tRNA synthetase antibodies (Abs), which mainly consists of anti-Jo1, PL-7, PL-12, EJ, OJ and KS, are the most common myositis-specific autoantibodies (MSAs). It has been recognized that anti-synthetase Abs are associated with characteristic clinical phenotype, chronic disease course, good response to initial glucocorticoid therapy and relatively good prognosis. However, we sometimes encounter such patients that are resistant to immunosuppressive therapies and have poor prognosis. Therefore, we retrospectively analyzed prognostic factors in polymyositis (PM)/dermatomyositis (DM) patients with anti-synthetase Abs.

\textbf{Methods:} We retrospectively examined medical records of 121 PM/DM patients with anti-synthetase Abs who had been treated in our hospital from April 2001 to December 2016 (32 with Jo-1, 26 with PL-7, 25 with EJ, 21 with PL-12, 11 with OJ, 4 with KS, 1 with PL7 and PL12, 1 with Jo-1 and PL12). Anti-ARS Abs were examined with RNA immunoprecipitation using Hela cells. We analyzed the prognostic factors with univariate cox proportional hazards regression analysis. Next, we analyzed each of them with multivariate analysis. Comparison of survival time among each anti-synthetase Abs, we used Kaplan-Meier method.

\textbf{Results:} The 10-year survival of whole anti-synthetase Abs-positive PM/DM patients was 74.7%. 21 patients died of interstitial pneumonia (n=8), infection (n=2), malignancy (n=4), thrombotic thrombocytopenic purpura (TTP) (n=1), alveolar hemorrhage (n=2), subarachnoid hemorrhage (n=1), unknown cause (n=3). In univariate analysis, old age at onset, male, anti-PL-7, high values of lactate dehydrogenase, high dose of maintenance glucocorticoid, no use of immunosuppressant were found to be significant poor prognostic factors. Multivariate analysis revealed 5 significant poor prognostic factor, anti-PL-7 Ab, old age at onset, male, high dose of maintenance glucocorticoid, no use of immunosuppressant. In Kaplan-Meier analysis, it was suggested that anti-EJ-positive patients may have poor prognosis after more than 15 years follow-up as well as anti-PL-7-positive patients.

\textbf{Conclusion:} The poor prognostic factors in anti-ARS-positive patients were anti-PL-7 Ab, old age at onset, male, high dose of maintenance glucocorticoid, no use of immunosuppressant. Moreover, anti-EJ have poorest survival after more than 15 years follow-up as well as anti-PL-7.
Easily Obtainable Myositis Autoantibody Panel Predictive Factors

**Jason Weiner**¹, Ryan Jessee², Amanda M. Eudy³, Robert T. Keenan⁴, Michael Datto⁵ and Lisa Criscione-Schreiber⁶, ¹Department of Medicine, Division of Rheumatology and Immunology, Duke University Medical Center, Durham, NC, ²Department of Medicine, Division of Rheumatology and Immunology, Duke University, Durham, NC, ³Duke University Medical Center, Chapel Hill, NC, ⁴Rheumatology, NYU-HJD, New York, NY, ⁵Department of Pathology, Duke University, Durham, NC, ⁶Internal Medicine, Duke University Medical Center, Durham, NC

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Tuesday, November 7, 2017
**Session Title:** Muscle Biology, Myositis and Myopathies Poster
**Session Type:** ACR Poster Session C
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**
Myositis autoantibodies have diagnostic, therapeutic and prognostic implications, but their utility in clinical practice is unclear. We aimed to describe our institution’s ordering practices and positivity rate in an undiagnosed population of patients to improve utilization.

**Methods:**
We included all Duke University Health System patients who had a myositis autoantibody panel (including anti-Jo-1, PL-7, PL-12, EJ, OJ, Mi-2, SRP, PM/Scl, Ku and U2-snRNP) ordered between October 2014 and December 2015. We recorded autoantibody positivity, demographics, past medical history, family history, review of systems items (ROS) and physical examination (PE) findings. Fisher’s exact and t-tests were performed for statistical significance.

**Results:**
Of 373 ordered tests, there were 75 (20%) positive autoantibodies. Significant demographic factors were older age and African American race or Hispanic ethnicity (Table 1). Positivity rates among African Americans (30%) and Hispanic/Latinos (50%) were significantly greater than white patients (15%).

---

**Disclosure:** M. Taniguchi, None; R. Nakashima, None; N. Kuramoto, None; K. Murakami, None; M. Hashimoto, None; H. Yoshifuji, None; M. Tanaka, None; K. Ohmura, None; T. Mimori, None.
higher than in Caucasians (15%; 71% of the tested population). A recorded past medical history of RA, SLE or connective tissue disease were associated with positive autoantibodies, while use of statins, antibiotics or chronic steroids had a negative association. The only statistically significant ROS factor was photosensitivity. Important ROS elements were infrequently documented prior to testing in this cohort. Specifically, <50% of tested patients were asked about myalgias, 20% about photosensitivity, 13% about voice changes and 3% about nasal regurgitation. Of recorded PE findings symmetric muscle weakness, sclerodermoid skin changes and arthritis were significantly associated with a positive antibody test.

Conclusion:

Myositis autoantibodies were positive in more than 30% of African American and Hispanic individuals tested. History of an autoimmune disease, photosensitivity and expected IIM PE findings were associated with a positive panel. While many easily obtainable factors may be associated with positive myositis autoantibodies, these history, PE and ROS elements are incompletely recorded. In our large academic multispecialty practice, the myositis autoantibody panel appears to be largely used as a screening test. Future efforts will include cohort characterization and provider education to guide testing.

Disclosure: J. Weiner, None; R. Jessee, None; A. M. Eudy, None; R. T. Keenan, Horizon, 5,AstraZeneca, 5,Ironwood, 5; M. Datto, None; L. Criscione-Schreiber, None.
Background/Purpose:
Despite the absence of specific guidelines or trials on intravenous immunoglobulins (IvIg) in patients with idiopathic inflammatory myopathies (IIM), the treatment is considered effective in refractory IIMs. The aim of our study is to evaluate the efficacy of IvIg in patients with IIM followed in 3 third level centers and to identify predictive factors correlated to their efficacy.

Methods:
retrospective study of IIM pts classified according to Bohan and Peter criteria treated with IvIg (2gr/kg/month). At baseline and after treatment the following data were collected: muscle necrosis enzymes, myositis specific autoantibodies; muscle strength (manual muscle test-MMT), clinical symptoms (skin lesions, dysphagia severity according to patient’s VAS, dyspnea, loss of strength) and clinical response according to physician judgment. We analyzed indications to treatment, major organ involvement, previous therapies.

Results:
92 pts were included (30 M, 62 F), 34 affected by PM, 48 DM, 3 IBM and 7 IIM overlap (3 Sjögren syndrome, 4 SSc); 12 were affected by cancer associated MII. Mean age at the start of IVIG therapy was 57.4±15 years, mean disease duration was 39±88 months.

Main indications to the treatment were: loss of strength (74), dysphagia (42), lung involvement (6), DM rash (27), arthritis (3).

IvIg were started in all pts for refractory disease to treatment with corticosteroids (CS). CS were used alone (22 pts) or associated with immunosuppressive drugs (70 pts). In 19/22 pts treated with cs alone, immunosuppressive drugs were contraindicated for neoplasia (9), recurrent infections (9), pregnancy (1).

The treatment was suspended after an average duration of 14 months; at the treatment suspension, muscle necrosis enzyme CK, LDH, GOT and GPT decreased significantly (p<0.001) and the mean MMT value increased (102.3±24.37 vs 125.0±23.16 p<0.001); mean dysphagia VAS decreased from 40.5±36.8 to 11.7±21.7 (p<0.001). The mean weekly corticosteroid dose decreased from 152.5±126.3 mg to 71.2±63.3 p<0.001.

According to physician judgment, 71 pts were classified as responder to IVIG (77.1%); 41 pts responded after six months of treatment and 30 pts after more than 6 months of treatment (mean 26.3±29.3 months).

Responders had a shorter disease duration (p<0.001), higher CK levels at baseline (2038±2479 vs 626±736 p<0.001), higher prevalence of dysphagia (p=0.012) and lower prevalence of Raynaud phenomenon (p=0.031) compared to non responders.

Conclusion:
Despite their high cost, IvIg confirmed their efficacy in refractory IIM pts, particularly in muscular and oesophageal manifestations. A shorter disease duration, higher CK levels and specific clinical features are associated to a better response.

Disclosure: S. Barsotti, None; I. Cavazzana, None; R. Neri, None; F. Locatelli, None; M. Taraborelli, None; E. Cioffi, None; I. Chiapparoli, None; A. Tincani, None; F. Franceschini, None; M. Mosca, None.

Efficacy and Safety of Rituximab in Anti-Synthetase Positive and Negative Patients with Idiopathic Inflammatory Myopathy– a Registry-Based Study

Valérie Leclair, Maryam Dastmalchi, Angeles Shunashy Galindo-Feria and Ingrid E. Lundberg, Department of Medicine, Rheumatology Unit, Karolinska University Hospital, Karolinska Institutet, Stockholm, Sweden
First publication: September 18, 2017
Background/Purpose:
Rituximab (RTX) in idiopathic inflammatory myopathies (IIM) failed to show efficacy in the placebo-controlled Rituximab in Myositis (RIM) trial. However, post hoc analyses indicated that patients with specific auto-antibodies may benefit from RTX treatment. The aim of this study was to evaluate the efficacy and safety of RTX in IIM subjects in relation to their auto-antibody profile.

Methods:
Adult IIM subjects registered in the Swedish Quality Registry (SRQ) who received ≥1 dose of RTX were enrolled. Clinical data were extracted from SRQ or medical records including myositis autoantibodies status (anti-aminoacyl-tRNA synthetase (ARS), anti-MDA5, anti-Mi2, anti-NXP2, anti-SAE, anti-SRP, and anti-TIF1-gamma antibodies). Efficacy was based on measures endorsed by the International Myositis Assessment and Clinical Studies group taken at baseline, after first and last RTX cycle. Safety assessment included serious infections, infusion reactions and death during study period. Comparisons between groups based on anti-ARS status were done using the Student’s t-test or Mann-Whitney U test for continuous variables, and Chi square or Fisher exact test for categorical variables.

Results:
Sixty-five subjects were included and 68% had a follow-up visit within 6 to 10 months (Table 1). At baseline, efficacy measures were similar except for higher HAQ score in the anti-ARS negative subjects (1.69 vs 0.75, p=0.003) (Table 2). After one cycle, the anti-ARS positive group had significantly lower patient global assessment (33.8 vs 51.4, p=0.042) and extra-muscular activity (9.9 vs 21.3, p=0.009) on visual analog scales (0-100) compared to the anti-ARS negative group. A steroid-sparing effect was only seen in the anti-ARS positive group (median steroid dosage 20 to 10mg, p <0.001). After several cycles, anti-ARS positive (n=19) compared to anti-ARS negative subjects (n=10) showed a faster decrease in disease activity, moreover, they had lower HAQ (0.5 vs 1.75, p=0.003), patient global assessment (mean 30.1 vs 57.8, p=0.011) and steroid doses (4.37 vs. 10mg, p=0.04). In the anti-ARS positive group, 3 deaths, 2 infusion reactions and 3 severe infections were recorded compared to 1 death, 1 infusion reaction and 2 severe infections in the negative group.

Conclusion:
In this observational study, we confirmed the benefit of RTX in anti-ARS positive patients who showed a significant decrease in several disease activity measures including patient-reported measure (ex: HAQ), in addition to a significant steroid-sparing effect. The effect was less dramatic in the anti-ARS negative group. These findings support the role of B cell in IIM pathogenesis.
Table 1 – Characteristics of subjects included in the efficacy analysis prior to their first rituximab infusion

<table>
<thead>
<tr>
<th></th>
<th>Anti-ARS positive (n=27)</th>
<th>Anti-ARS negative (n=17)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female (n, %)</td>
<td>20 (74)</td>
<td>11 (65)</td>
<td>0.507</td>
</tr>
<tr>
<td>Age (mean (sd))</td>
<td>56.6 (10.2)</td>
<td>56.5 (18.17)</td>
<td>0.975</td>
</tr>
<tr>
<td>Disease duration in months before RTX introduction (median (IQR))</td>
<td>15 (4-52)</td>
<td>67 (14.5-151)</td>
<td>0.042</td>
</tr>
<tr>
<td>Cancer (n, %)</td>
<td>4 (14,8)</td>
<td>8 (47)</td>
<td>0.150</td>
</tr>
<tr>
<td>Clinical features (n, %)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscle weakness</td>
<td>18 (66,7)</td>
<td>14 (82,4)</td>
<td>0.315</td>
</tr>
<tr>
<td>Raynaud phenomenon</td>
<td>12 (44,4)</td>
<td>4 (23,5)</td>
<td>0.208</td>
</tr>
<tr>
<td>V-sign</td>
<td>1 (3,7)</td>
<td>4 (23,5)</td>
<td>0.065</td>
</tr>
<tr>
<td>Heliotrope rash</td>
<td>2 (7,4)</td>
<td>5 (29,4)</td>
<td>0.089</td>
</tr>
<tr>
<td>Gottron’s papule</td>
<td>3 (11,1)</td>
<td>5 (29,4)</td>
<td>0.227</td>
</tr>
<tr>
<td>Mechanic’s hands</td>
<td>12 (44,4)</td>
<td>6 (35,3)</td>
<td>0.548</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>5 (18,5)</td>
<td>10 (58,8)</td>
<td>0.006</td>
</tr>
<tr>
<td>Calcinosis</td>
<td>0</td>
<td>1 (5,8)</td>
<td>0.386</td>
</tr>
<tr>
<td>Arthritis</td>
<td>15 (55,6)</td>
<td>10 (58,8)</td>
<td>0.831</td>
</tr>
<tr>
<td>Interstitial Lung Disease</td>
<td>23 (85,2)</td>
<td>7 (41)</td>
<td>0.002</td>
</tr>
<tr>
<td>Number of RTX infusions (median (IQR))</td>
<td>4 (3-4)</td>
<td>4 (2-5)</td>
<td>0.873</td>
</tr>
<tr>
<td>Number of RTX cycles (median (IQR))</td>
<td>3 (2-3)</td>
<td>2 (1-3.5)</td>
<td>0.449</td>
</tr>
<tr>
<td>Cumulative RTX dose (g) (median (IQR))</td>
<td>3.5 (3-4)</td>
<td>4 (2-5)</td>
<td>0.883</td>
</tr>
<tr>
<td>Discontinuation (n, %)</td>
<td>9 (33,3)</td>
<td>12 (70,6)</td>
<td>0.016</td>
</tr>
<tr>
<td>Low disease activity / remission</td>
<td>4 (14,8)</td>
<td>3 (17,6)</td>
<td>1.0</td>
</tr>
<tr>
<td>No effect</td>
<td>0</td>
<td>5 (29,4)</td>
<td>0.006</td>
</tr>
<tr>
<td>Death</td>
<td>3 (11,1)</td>
<td>1 (5,8)</td>
<td>1.0</td>
</tr>
<tr>
<td>Side effect</td>
<td>2 (7,4)</td>
<td>3 (17,6)</td>
<td>0.549</td>
</tr>
<tr>
<td>Previous treatment (n, %)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 immunosuppressor*</td>
<td>10 (37)</td>
<td>5 (29,4)</td>
<td>0.603</td>
</tr>
<tr>
<td>2 immunosuppressors*</td>
<td>12 (44,4)</td>
<td>5 (29,4)</td>
<td>0.319</td>
</tr>
<tr>
<td>≥ 3 immunosuppressors*</td>
<td>4 (14,8)</td>
<td>3 (17,6)</td>
<td>1.00</td>
</tr>
<tr>
<td>Concomitant treatment (n, %)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prednisone</td>
<td>21 (77,8)</td>
<td>13 (76,5)</td>
<td>1.0</td>
</tr>
<tr>
<td>1 immunosuppressor*</td>
<td>18 (66,7)</td>
<td>11 (64,7)</td>
<td>0.894</td>
</tr>
<tr>
<td>2 immunosuppressors*</td>
<td>5 (18,5)</td>
<td>2 (11,8)</td>
<td>0.689</td>
</tr>
<tr>
<td>≥ 3 immunosuppressors*</td>
<td>0</td>
<td>1 (5,8)</td>
<td>0.386</td>
</tr>
</tbody>
</table>
**immunosuppressors***

ARS, aminoacyl-tRNA synthetase; Jo1, histidyl t-RNA synthetase; PL-7, threonyl t-RNA synthetase; PL-12, alanyl t-RNA synthetase; TIF1-g, transcriptional intermediary factor 1-gamma; Mi2, chromatin remodeling enzyme; MDA5, melanoma differentiation-associated gene 5; SD, standard deviation; IQR interquartile range; RTX, rituximab.

*excluding prednisone

Table 2 – Comparison of core set disease activity measures between anti-ARS positive and negative groups before treatment with rituximab, after the 1st cycle and after multiple cycles

<table>
<thead>
<tr>
<th></th>
<th>MMT8 Median (IQR)</th>
<th>Extra-muscular (VAS 0-100) Mean (sd)</th>
<th>Ph Global (VAS 0-100) Mean (sd)</th>
<th>Pt Global (VAS 0-100) Mean (sd)</th>
<th>HAQ Median (IQR)</th>
<th>CK levels Median (IQR)</th>
<th>Prednisone doses Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anti-ARS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>1 cycle (n=44)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before treatment</td>
<td>78.5 (73-80)</td>
<td>37 (18.2)</td>
<td>43.4 (17.7)</td>
<td>43.5 (28.1)</td>
<td>0.75* (0.32-1.32)</td>
<td>1.69* (1.38-1.97)</td>
<td>1.2 (0.8-2.6)</td>
</tr>
<tr>
<td></td>
<td>75 (60-77)</td>
<td>38.6 (20.5)</td>
<td>40.8 (18.3)</td>
<td>59.4 (28.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>After 1st cycle</td>
<td>79 (77-80)</td>
<td>21.3* (12.5)</td>
<td>21.8 (10.8)</td>
<td>51.4* (26.1)</td>
<td>0.38* (0.13-0.94)</td>
<td>1.5* (0.88-1.88)</td>
<td>1.3 (0.8-3.6)</td>
</tr>
<tr>
<td></td>
<td>77.5 (59-80)</td>
<td>21.4* (12.5)</td>
<td>33.8* (23.5)</td>
<td>1.5* (0.88-1.88)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>9.9* (9)</td>
<td>14 (14)</td>
<td>1.5* (0.88-1.88)</td>
<td>1.3 (0.8-3.6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Several cycles (n=29)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before treatment</td>
<td>79* (76-80)</td>
<td>33.9 (19.2)</td>
<td>40.3 (20.5)</td>
<td>51.7* (29.6)</td>
<td>0.63* (0.13-1.38)</td>
<td>1.69* (1.14-1.94)</td>
<td>1.2 (0.7-8.1)</td>
</tr>
<tr>
<td></td>
<td>73.5* (52-80)</td>
<td>37.2 (21.4)</td>
<td>37.7* (23.5)</td>
<td>61.7* (29.6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>39.5 (21.4)</td>
<td>40.3 (20.5)</td>
<td>51.7* (29.6)</td>
<td>61.7* (29.6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>9.9* (9)</td>
<td>14 (14)</td>
<td>1.5* (0.88-1.88)</td>
<td>1.3 (0.8-3.6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>1 cycle</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before treatment</td>
<td>80 (78-80)</td>
<td>10.3* (8.9)</td>
<td>13.2* (13.2)</td>
<td>1.5* (1-1.88)</td>
<td>1.2 (1-2.3)</td>
<td>1.3 (0.6-18.1)</td>
<td>8.75 (3.75-10)</td>
</tr>
<tr>
<td></td>
<td>73.5 (52-80)</td>
<td>12.6* (12.6)</td>
<td>33.8* (23.4)</td>
<td>1.5* (1-1.88)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10.3* (8.9)</td>
<td>13.2* (13.2)</td>
<td>33.8* (23.4)</td>
<td>1.5* (1-1.88)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>9.9* (9)</td>
<td>14 (14)</td>
<td>1.5* (1-1.88)</td>
<td>1.3 (0.6-18.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Last cycle</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before treatment</td>
<td>79 (74-80)</td>
<td>9.4 (9.3)</td>
<td>12.4 (11)</td>
<td>57.8* (24.5)</td>
<td>0.5* (0.94)</td>
<td>1.75* (1.07-1.82)</td>
<td>1.4 (0.1-3.2)</td>
</tr>
<tr>
<td></td>
<td>73.5 (65-80)</td>
<td>11 (9.7)</td>
<td>15.8 (11.2)</td>
<td>0.5* (0.94)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>9.4 (9.3)</td>
<td>12.4 (11)</td>
<td>15.8 (11.2)</td>
<td>0.5* (0.94)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10.3* (8.9)</td>
<td>11.2* (9.7)</td>
<td>30.1* (18.2)</td>
<td>1.75* (1.07-1.82)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>9.9* (9)</td>
<td>14 (14)</td>
<td>1.75* (1.07-1.82)</td>
<td>1.4 (0.1-3.2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ARS, aminoacyl-tRNA synthetase; MMT8, manual muscle testing (0-80); VAS, visual analog scale; Ph, physician; Pt, patient; HAQ, Health Assessment Questionnaire; CK, creatinine kinase; SD standard deviation; IQR, interquartile range

*p <0.05, comparison between anti-ARS positive and negative groups for each core set activity measure
Dissociation of FVC and DLco in Patients with Dermatomyositis and Polymyositis

Eun Hye Park¹, Woo Chang Hwang², Eun Young Lee¹, Eun Bong Lee¹, Yeong Wook Song³ and Jin Kyun Park¹, ¹Division of Rheumatology, Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea, Republic of (South), ²Department of Statistics, Data Science for Knowledge Creation Research Center, Seoul National University, Seoul, Korea, Republic of (South), ³Division of Rheumatology, Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
- Session Date: Tuesday, November 7, 2017
- Session Title: Muscle Biology, Myositis and Myopathies Poster
- Session Type: ACR Poster Session C
- Session Time: 9:00AM-11:00AM

Background/Purpose:
Interstitial lung disease in patients with polymyositis (PM) and dermatomyositis (DM) is characterized by decrease in both lung compliance and pulmonary vascularity, leading to decreased forced vital capacity (FVC) and diffusing capacity for carbon monoxide (DLCO). However, since DLCO is also influenced by the pulmonary circulation, additional pulmonary vascular disease would disproportionately decrease DLCO. This study was aimed to investigate the changes in FVC and DLCO over time in patients with DM and PM and to identify factors associated with disproportional decline in DLCO.

Methods:
A total of 89 DM and 14 PM patients who had been cared at the Rheumatology Clinic of Seoul National University Hospital, a tertiary referral center, from January 2004 to June 2016, with 2 or more pulmonary function tests (PFTs) during follow-up duration, were retrospectively evaluated. FVC and DLCO were expressed as the percentage of values predicted on the basis of patient age, sex, height and weight. Regression was calculated using mixed model with random effect.

Results:
Total of 103 patients with DM and PM were included. The study population was predominantly female (72.8%), with the mean age at diagnosis of 49.9 ± 12.9 years. The mean duration of follow-up was 4.4 ± 3.2 years. There was a strong correlation between FVC and DLCO at baseline (r= 0.618, p<0.001). In 85 (82.5%) of 103 patients, DLCO was lower than FVC by 9.8±14.2% at baseline. There was disproportional change in DLCO relative to FVC over time. Patients with worse decline of DLCO than the change of FVC over time had a higher frequency of Raynaud’s phenomenon (35.1% vs 9.7%, p= 0.021) and positive antinuclear antibody (ANA) (78.4% vs. 48.4%, p=0.012) compared to the patients with better improvement of DLCO relative to FVC over time. There was no significant difference in other clinical and laboratory parameters according to disproportional decline in DLCO relative to FVC. Patients with Raynaud’s phenomenon had significantly higher decline of DLCO from the baseline than those without Raynaud’s phenomenon (-5.6 ± 16 vs 4.4 ± 18.4, p=0.016) and the observed changes of DLCO per year (-9.0 ± 28.3 vs 4.9 ± 29.4 p=0.040).

Conclusion:
In patients with DM and PM, Raynaud’s phenomenon and positive ANA are associated with disproportional decline in DLCO relative FVC. Further prospective studies are needed to determine whether improving pulmonary circulation adds any therapeutic benefit in those idiopathic inflammatory myopathy patients with disproportional decline in DLCO.
A Two-Center Experience with Rituximab in Patients with Primary Idiopathic Myositis and Overlap Myositis: A Retrospective Observational Study

Kimberly A. Rehberg, Morgan M. Brown, Anna K. Shmagel, Elie Gertner and Jerry A. Molitor

Rheumatic & Autoimmune Diseases, University of Minnesota, Minneapolis, MN, HealthPartners Institute, St. Paul, MN, Section of Rheumatology, Regions Hospital, St. Paul, MN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Muscle Biology, Myositis and Myopathies Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Recent studies have suggested the possible benefit of the anti-CD20 agent Rituximab (RTX) in autoimmune myositis (AIM). As AIM is a rare and heterogeneous condition, no randomized controlled trial results are available to validate these findings. We present a two-center experience with the use of RTX in AIM.

Methods:
Adult patients (pts) with AIM treated with RTX between years 2005-2016 were identified by electronic medical record inquiry from two large urban multispecialty care systems in the Twin Cities, Minnesota. Charts were reviewed by two trained rheumatologists to confirm the correct diagnosis and treatment. 28 cases were identified, of them 16 pts were classified as primary idiopathic myositis (PIM) by accepted diagnostic criteria and 12 pts were classified as overlap myositis (OM) by criteria for their respective connective tissue disease (CTD) and clinically demonstrated inflammatory myositis. RTX was used for disease refractory to initial treatment, severe initial onset, and the presence of interstitial lung disease (ILD). Outcomes data for up to the first 3 RTX courses were obtained from clinical records, up to 4 months prior to each RTX and 4-6 months post RTX, and included prednisone dose, serum creatinine kinase (CK), serum C-reactive protein (CRP), forced vital capacity (FVC), and hip flexion strength (HFS). Paired sample T-tests were used for analysis.

Results:
For pts with PIM, mean age was 43 ± 16 y, 8 were female (50%), and mean disease duration was 33 ± 48 mo, with subgroups of 7 with dermatomyositis, 6 with polymyositis, and 3 with necrotizing autoimmune myopathy. For pts with OM, mean age was 53 ± 13 y, 11 were female (92%), and mean disease duration was 47 ± 54 mo, with subgroups of 7 with systemic lupus erythematosus, 2 with systemic sclerosis, 2 with Sjogren’s syndrome, and 1 with mixed CTD. The average number of non-corticosteroid medications used prior to the first RTX for pts with PIM was 2.2 ± 1.6 and for OM was 3.5 ± 1.7.

After one RTX course, pts with PIM but not OM had a significant reduction in prednisone dose from 44.38 ± 23.58 mg/day to 14.34 ± 15.27 mg/day (p=0.0002). After one RTX course, pts with PIM but not OM had a significant reduction in CRP from 25.57 ± 22.56 mg/dL to 9.61 ± 6.31 mg/dL (p=0.029). Among AIM pts with concomitant ILD, there was also a statistically significant improvement in % predicted FVC after one RTX course by 9.2 ± 8.69 % (p=0.045). There was no observed statistically significant change in CK or HFS.

Conclusion:
In 28 AIM pts treated with RTX, we observed a significant improvement in prednisone dose and serum CRP levels following the first treatment cycle for pts with PIM but not OM. There was also a modest improvement in % predicted FVC among patients with concomitant ILD, but no significant change in CK levels or HFS.

Disclosure: K. A. Rehberg, None; M. M. Brown, None; A. K. Shmagel, None; E. Gertner, None; J. A. Molitor, Shire Human Genetic Therapies Inc., 5.


Abstract Number: 2169
Near Patient Detection of Anti-MDA5 Antibodies Using Photonic Ring Immunoassays

Makoto Miyara¹, Rémi Chieze², Yurdagul Uzunhan³, Jean-Luc Charuel⁴, Pascale Ghillani-Dalbin⁴, Sasi Mudumba⁵, Alice Wu⁵, Hilario Nunes³, Zahir Amoura⁶, Rufus Burlingame⁶ and Lucile Musset¹, ¹Department of Immunology, Pitié-Salpêtrière Hospital (AP-HP), Paris, France, ²Department of Immunology, Pitié-Salpêtrière Hospital (AP-HP), Paris, France, ³Pulmonary diseases department, Avicenne Hospital (AP-HP), Bobigny, France, ⁴Department of Immunology, Pitié-Salpêtrière Hospital (AP-HP), Paris, France, ⁵Genalyte Inc., San Diego, CA, ⁶Hôpital Pitié-Salpêtrière, AP-HP, UPMC Univ Paris 06 & French National Reference Center For Systemic Lupus and Antiphospholipid Syndrome, Paris, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Muscle Biology, Myositis and Myopathies Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

The presence of anti-MDA5 antibody is associated with amyopathic dermatomyositis and/or rapidly progressive interstitial lung disease that can be fatal. In the latter case, it is mandatory to confirm the diagnosis as soon as possible in order to initiate aggressive treatments and the presence of anti-MDA5 autoantibodies is an important part of the differential diagnosis. The immunoassay using photonic microrings is a new sensitive technology that enables rapid results in less than 15 minutes. The aim of our study was to evaluate this technology for the detection of anti-MDA5 antibodies in sera with known positivity.

Methods:
The system is based on immobilizing the antigenic target, MDA5, above the photonic rings in a silicon chip. We analyzed a total of 72 sera drawn from 40 patients known to be positive for anti-MDA5 antibody in our laboratory using immunoblotting assays and 4 negative controls. For some patients, several samples drawn during the follow-up could be analyzed.

Results:

Using the photonic ring immunoassay, we could confirm the presence of anti-MDA5 antibody in all samples known as positive for anti-MDA5 antibody by other techniques. No false positive or false negative results were found. Moreover, high levels of MDA-5 antibodies measured at diagnosis are associated with interstitial lung disease with respiratory functional impairment at presentation. Interstingly, we observed a decrease in anti-MDA5 antibodies titers in followed-up patients.

Conclusion:
The photonic ring immunoassay is a fast and reliable technology for the detection of anti-MDA5 antibodies.

Disclosure: M. Miyara, Genalyte, 5; R. Chieze, None; Y. Uzunhan, None; J. L. Charuel, None; P. Ghillani-Dalbin, None; S. Mudumba, None; A. Wu, Genalyte, 3; H. Nunes, None; Z. Amoura, None; R. Burlingame, None; L. Musset, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/near-patient-detection-of-anti-mda5-antibodies-using-photonic-ring-immunoassays

Abstract Number: 2171

Functional Measures and Patient Home Self-Assessments in the Idiopathic Inflammatory Myopathies

Amanda Kocoloski¹, Courtney Ward², Diane Koontz², Chester V. Oddis³ and Rohit Aggarwal⁴, ¹Internal Medicine, Division of Rheumatology, University of Pittsburgh Medical Center, Pittsburgh, PA, ²Internal Medicine Division of Rheumatology, University of Pittsburgh, Pittsburgh, PA, ³Rheumatology/Clinical Immunology, University of Pittsburgh/University of Pittsburgh Medical Center, Pittsburgh, PA, ⁴Medicine / Rheumatology, University of Pittsburgh/University of Pittsburgh Medical Center, Pittsburgh, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Muscle Biology, Myositis and Myopathies Poster
Background/Purpose: Myositis leads to significant morbidity and loss of function. Currently, simple objective measures of patient functional outcomes are lacking. Our aims were to a) test functional measures (sit to stand [STS], timed up and go [TUG], and 6-minute walk distance [6MWD]) in myositis patients against established myositis core set measures, and b) evaluate reliability of the same measures self-performed by patients at home.

Methods: We collected data on the 6 validated myositis core measures (manual muscle testing [MMT], physician global disease activity, patient global disease activity, extra-muscular global disease activity, HAQ and muscle enzymes) as well as performed 3 functional measures in clinic (STS, TUG, and 6MWD) on patients with DM, PM and necrotizing myopathy at baseline, 3 and 6 months. STS is number of times a patient can stand from a seated position and sit back down, as many times in 30 seconds. TUG is the time needed to rise from a chair, walk 3 meters, return to the chair and sit down. 6MWD is the maximum distance patient can walk in 6 minutes. We instructed patients on conducting these functional measures at home, and they reported performance results at home within a week of clinic evaluation. To assess validity we compared functional measures against all core set measures at baseline and MMT longitudinally. We examined test-retest reliability of home assessments with in clinic assessments. We use Spearman correlations with rho >0.5 considered strong, 0.35-0.5 moderate, and 0.2-0.35 weak.

Results: Data from 31 patients [58% females, 90% Caucasians, mean age 48 (±16)] from an ongoing observational study were included in this analysis. As shown in table 1, at baseline, STS correlated strongly with MMT, patient/physician global assessment, and muscle enzymes, and had moderate correlation with HAQ, and no correlation with extra-muscular global. Similarly, at baseline, TUG showed moderate correlation with physician/patient global and muscle enzymes, but only weak association with MMT, HAQ and extra-muscular global. The 6MWD showed strong correlation with MMT, moderate with patient global and HAQ, and weak with physician global and muscle enzymes. Longitudinally, 6MWD showed strong association with MMT, where as STS and TUG showed moderate and weak associations with MMT respectively. Home assessments of STS (rho: 0.91), TUG (rho: 0.94) and 6MWD (rho: 0.86) showed high test-retest reliability compared to clinic assessment (P<0.01 for all 3).

Conclusion: Preliminary data suggests strong cross sectional correlation of STS and 6MWD with MMT and moderate to strong correlation with MMT longitudinally. All tests were reliable when self-performed by patients at home. This suggests these simple measures may provide objective functional assessment of patient-centric outcomes in myositis in clinic as well as at home.

Table 1. Baseline and Longitudinal Comparisons of Core and Functional Measures in Myositis

<table>
<thead>
<tr>
<th></th>
<th>Sit to Stand</th>
<th>Timed Up and Go</th>
<th>6-Minute Walk Distance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manual Muscle Testing</td>
<td>Rho: 0.63; p= &lt;0.01</td>
<td>Rho: -0.30; p=0.11</td>
<td>Rho: 0.58; p=&lt;0.01</td>
</tr>
<tr>
<td>Physician Global</td>
<td>Rho: -0.56; p= &lt;0.01</td>
<td>Rho: 0.46; p=0.01</td>
<td>Rho: -0.29; p=0.13</td>
</tr>
<tr>
<td>Patient Global</td>
<td>Rho: -0.52; p= &lt;0.01</td>
<td>Rho: 0.48; p=0.01</td>
<td>Rho: -0.37; p=0.05</td>
</tr>
<tr>
<td>Extra-Muscular Global</td>
<td>Rho: -0.02; p=0.93</td>
<td>Rho: 0.22; p=0.25</td>
<td>Rho: 0.01; p=0.96</td>
</tr>
<tr>
<td>Health Assessment Questionnaire</td>
<td>Rho: -0.40; p=0.03</td>
<td>Rho: 0.20; p=0.32</td>
<td>Rho: -0.48; p=0.01</td>
</tr>
<tr>
<td>Muscle Enzymes</td>
<td>Rho: -0.52; p=0.01</td>
<td>Rho: 0.39; p=0.06</td>
<td>Rho: -0.28; p=0.24</td>
</tr>
<tr>
<td><strong>Longitudinal</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manual Muscle Testing</td>
<td>Rho: 0.36; p=0.08</td>
<td>Rho: -0.31; p=0.19</td>
<td>Rho: 0.61; p=&lt;0.01</td>
</tr>
</tbody>
</table>

Disclosure: A. Kocoloski, None; C. Ward, None; D. Koontz, None; C. V. Oddis, None; R. Aggarwal, Pfizer Inc, 2,Bristol-Myers Squibb, 2,Mallinckrodt, 2,Genentech and Biogen IDEC Inc., 2,Momenta, 2,Bristol-Myers Squibb, 5,Octapharma, 5,Mallinckrodt, 5.


Abstract Number: 2172
Clinical Significance of Serum Levels of Anti-Transcriptional Intermediary Factor 1-γ Antibody in Patients with Dermatomyositis

Nobuaki Ikeda, Yukie Yamaguchi, Miwa Kanaoka, Yasushi Ototake, Eriko Takebayashi and Michiko Aihara, Department of Environmental Immuno-Dermatology, Yokohama City University Graduate School of Medicine, Yokohama, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Muscle Biology, Myositis and Myopathies Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Dermatomyositis (DM) is an autoimmune inflammatory disease characterized by skin eruptions and myositis, which is occasionally complicated by interstitial lung disease (ILD) or concomitant malignancy. It has been recognized that myositis-specific autoantibodies (MSAs) are correlated with unique sets of clinical manifestations. Anti–transcriptional intermediary factor 1-γ (TIF1-γ) antibody is one of the most frequently detected MSAs both in juvenile and adult DM, and adult DM positive for anti-TIF1-γ have a markedly higher rate of malignancy. In Japan, an individual measurement of anti-TIF1-γ by enzyme-linked immunosorbent assay (ELISA) is now covered by insurance. However, little is known about clinical utility of quantitative ELISA index of anti-TIF1-γ in association with disease activity.

Methods: We studied 26 Japanese adult DM patients positive for anti-TIF1-γ antibody detected by ELISA, who had been under treatment in our department. All patients were confirmed negative for anti-Mi-2 antibody concomitantly measured by ELISA. Seventeen patients with anti-TIF1-γ antibody (65.4%) had concomitant malignancy which was defined by the diagnosis within 2 years before or after DM diagnosis. Sequential serum samples were obtained in 16 patients. Clinical utility of quantitative anti-TIF1-γ index was analyzed in association with patient’s characteristics and disease severity.

Results: Anti-TIF1-γ-positive patients frequently had facial erythema (84.6%) including heliotrope rash (73.0%), Gottron’s papules (69.2%), erythema of the trunk (61.5%), and dysphagia (46.2%). Three patients were classified as clinically amyopathic DM (11.1%) and 5 patients had ILD (18.5%). Although maximum levels of serum creatine kinase (CK) was significantly higher in patients with malignancy compared to those without (mean ± SD IU/L, 2494.1 ± 5326.9, 392.3 ± 423.3, respectively, P < 0.05), there was no significant difference on anti-TIF1-γ index between patients with and without malignancy (105.4 ± 38.0, 113.0 ± 39.2, respectively, P = 0.32). No positive correlation was found between levels of serum CK and anti-TIF1-γ (r = 0.32, P = 0.17). In sequential analysis (n=16), anti-TIF1-γ level in patients without malignancy was decreased by more than 30% or turned negative after treatment for DM. However, antibody titer tended to be sustained in patients with malignancy at stage IV. Interestingly, re-increase of antibody titer was observed at a recurrence of malignancy (n=1) or increase of DM activity (n=3). Two patients had completely succeeded treatments for their malignancy, then anti-TIF1-γ level turned negative as loss of DM activity.

Conclusion: Higher index of anti-TIF1-γ may not directly indicate the presence of malignancy or higher activity of DM. However, longitudinal change of anti-TIF1-γ index in individual patients may partially reflect activities both of DM and malignancy. Close monitoring may be suggested if patients have sustained antibody titer despite no malignancy and loss of DM activity.

Disclosure: N. Ikeda, None; Y. Yamaguchi, None; M. Kanaoka, None; Y. Ototake, None; E. Takebayashi, None; M. Aihara, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/clinical-significance-of-serum-levels-of-anti-transcriptional-intermediary-factor-1-%ce%b3-antibody-in-patients-with-dermatomyositis

Abstract Number: 2173

Characteristics Unique to MDA5 and Anti-Ro/SSA-52 Kda Dual Antibody Positive Patients with Inflammatory Myopathies

Juan J Maya, Olga Pinkston, Florentina Berianu, Benjamin Wang and Andy Abril, Rheumatology, Mayo Clinic Florida, Jacksonville, FL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Background/Purpose: The anti-melanoma differentiation-associated gene 5 antibody (MDA5) was recently classified as a myositis-specific antibody (MSA), and has been associated with rapidly progressive interstitial lung disease (ILD), amyopathic dermatomyositis (aDM), mechanic’s hands, ulcerations, inflammatory arthritis, and increased mortality. This study sought to distinguish the clinical characteristics of MDA5-positive patients with and without additional MSAs.

Methods: We retrospectively identified all MDA5 positive patients who were evaluated at our center from 2015 to 2017 with suspected myositis and had myositis-associated autoantibodies tested using a commercial panel (Myomarker Panel 3, RDL Reference Laboratories). For all patients who were positive for MDA5, we collected clinical information on the presence of myopathy, skin involvement and ILD, data on the autoantibody profile, PFTs and high resolution CT pattern.

Results: In our sampling period, 62 patients were positive for 1 or more MSA, of which 13 were positive for MDA5 (20.9%). Two MDA5 positive patients had incomplete clinical data and were not included in the analysis. Of the remaining 11 patients, 7 were females and 4 were males, with mean age 56.6 years (SD 10.9). Six MDA5 positive patients also had high titers of anti-Ro/SSA-52 kDa (46.1%) (mean Ab level by ELISA 120.5, SD 52). Five of the dual-positive patients had ILD (83.3%), versus 2 of MDA5-only patients (40%) (p=0.39). Of the dual-positive patients with ILD all had nonspecific interstitial pneumonitis (NSIP), 3 of which also had organizing pneumonia (67%), while in the MDA5-only group, one had fatal acute interstitial pneumonitis (20%) and the other one had UIP (20%). All of the dual-positive patients demonstrated improvement with immunosuppressive treatment as determined by CT, PFTs and clinical evaluation (100%), while only 2 patients from the MDA5-only group did (40%) (p=0.12). Three of the 6 dual-positive patients had EMG and/or MRI evidence of myopathy (50%) compared to 2 of 5 of the MDA5-only patients (40%). Two patients in the dual-antibody group had mechanic hands while only one in the MDA-only group had it.

Conclusion: Anti-Ro/SSA-52 kDa was frequently encountered in patients with MDA5-positive myopathic disease. In these dual-positive patients, ILD and NSIP were more common compared to patients that were positive for MDA5-only. A definite trend for response to immunosuppressive treatment was seen in the dual-positive group than in the MDA5-only group. As it has been reported previously, there was a high incidence of mechanic’s hands and aDM in patients positive for MDA5. This preliminary study indicates that certain autoantibody profiles in myositis are related to pulmonary and cutaneous manifestations, and may be predictive of response to treatment. These data highlight the importance of screening for these markers. Further study is ongoing to further elucidate the association of MSA and the clinical manifestations and response to treatment response of patients with inflammatory myopathies.

Disclosure: J. J. Maya, None; O. Pinkston, None; F. Berianu, None; B. Wang, None; A. Abril, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/characteristics-unique-to-mda5-and-anti-rossa-52-kda-dual-antibody-positive-patients-with-inflammatory-myopathies

Investigating Exercise- and Crossfit-Induced Rhabdomyolysis: Data from a Community Healthcare System

Sneha Sundaram¹, Michelle Meyer², Richard Shaw³ and Ingeborg Schafhalter-Zoppoth¹, ¹Internal Medicine, California Pacific Medical Center, San Francisco, CA, ²Pediatrics, UCSF Benioff Children's Hospital Oakland, Oakland, CA, ³California Pacific Medical Center, San Francisco, CA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Muscle Biology, Myositis and Myopathies Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
The work-up of elevated muscle enzymes is a common reason for rheumatology consults. The differential diagnosis of rhabdomyolysis includes trauma, exertion, hereditary myopathies, drugs, toxins and infections. Especially exertional rhabdomyolysis can be underdiagnosed as its prevalence in civilians is unclear and its clinical course is mostly described by case reports. We studied the
prevalence, nature, and consequences of exertional rhabdomyolysis in patients younger than 55 years. We especially focused on CrossFit-induced rhabdomyolysis as data of its involvement in rhabdomyolysis are controversial. CrossFit is a conditioning program involving high-intensity exercises performed in rapid repetition with minimal recovery time.

**Methods:** We conducted a retrospective chart review of all encounters with a diagnosis of rhabdomyolysis within all acute and ambulatory Sutter locations in Northern California between January 2004 and February 2016. Patients older than 55 years or with Medicare insurance were excluded. We reviewed the records and identified cases of rhabdomyolysis caused by exercise. Extracted data included age, gender, BMI, types of exercises performed, symptoms, sites of injury, location of presentation, creatinine and CPK levels at initial presentation and at follow-up, treatment administered, and hospitalization or discharge. Statistical analyses included Chi-square, Fisher’s exact tests, t-tests, and linear regression.

**Results:** We identified 1,277 patients with rhabdomyolysis. Exercise-induced rhabdomyolysis was diagnosed in 297 patients, with 42 of these cases caused by CrossFit. Mean age of all patients with exercise-induced rhabdomyolysis was 31 years (range: 12 to 53), with a gender composition of 70% males and 30% females. The majority of patients (51%) presented to the emergency department. Mean CPK at presentation was 36,120 U/L (range: 213 to 522,040), mean creatinine was 1.14 mg/dl (range: 0.37 to 29.00). Higher levels of CPK and creatinine were associated with hospitalization (p<0.0001 and p=0.004, respectively) and with longer hospital stays (p=0.025 and p<0.0001, respectively). Average hospital stay was 4 days (range 1-12 days). Patients with CrossFit relate rhabdomyolysis had lower creatinine levels at presentation (0.82 vs 1.19 mg/dl, p=0.008), were more likely to have IV fluids administered (86% vs 73%, p=0.048), and a shorter hospital stay (3.5 vs 4.4 days, p=0.029).

**Conclusion:**

This is the first large-scale study to investigate exercise- and CrossFit-induced rhabdomyolysis. The prevalence of exertional rhabdomyolysis is significant, with a notable proportion of these cases attributable to CrossFit. As patients with muscle pain and elevated muscle enzymes are referred to the rheumatologist it is important to know about this disease. There is often a delay in diagnosis and treatment, therefore education to physicians and athletes about exertional rhabdomyolysis for primary prevention and for early diagnosis is necessary.

**Disclosure:** S. Sundaram, None; M. Meyer, None; R. Shaw, None; I. Schafhalter-Zoppoth, None.


**Abstract Number:** 2175

**Novel Assessment of Interstitial Lung Disease Using the “Computer-Aided Lung Informatics for Pathology Evaluation and Rating” Software System in Idiopathic Inflammatory Myopathies**

Patompong Ungprasert¹, Katelynn Wilton², *Floranne C. Ernste³*, Sanjay Kalra⁴, Cynthia S. Crowson⁵, Srinivasan Rajagopalan⁶ and Brian Bartholmai⁷, ¹Rheumatology, Mayo Clinic, Rochester, MN, ²Immunology, Mayo Clinic, Rochester, MN, ³Division of Rheumatology, Mayo Clinic Rochester, Rochester, MN, ⁴Pulmonary and Critical Care Medicine, Mayo Clinic, Rochester, MN, ⁵Health Sciences Research, Mayo Clinic College of Medicine and Science, Rochester, MN, ⁶Mayo Clinic, Rochester, MN, ⁷Thoracic Radiology, Mayo Clinic, Rochester, MN

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Muscle Biology, Myositis and Myopathies Poster

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The idiopathic inflammatory myopathies (IIM) are often associated with interstitial lung diseases (ILD). Yet, pulmonary function testing (PFT) results can be confounded by patient effort, mixed obstructive/restrictive disease and pulmonary hypertension. Our purpose was to evaluate the correlation between measurements from quantitative thoracic high-resolution CT (HRCT) analysis with Computer-Aided Lung Informatics for Pathology Evaluation and Rating (CALIPER) software and PFTs in patients with IIM-associated ILD.
Methods: A cohort of patients with IIM-associated ILD seen at a single institution was identified from medical record review in 2003-2011. Retrospective analysis of HRCT data and PFTs at baseline and 1 year was performed. The abnormalities in HRCT were quantified using CALIPER software. Correlation between baseline CALIPER measurements and PFT measurements as well as correlation between changes of CALIPER measurements and PFT measurements at one year (compared with baseline) were assessed using Spearman correlation coefficients.

Results: A total of 110 patients were identified. At baseline, total interstitial abnormalities as measured by CALIPER, both by absolute volume and by percentage of total lung volume, had a significant negative correlation with diffusing capacity for carbon monoxide (DLCO), total lung capacity (TLC) and oxygen saturation (Table). Analysis by subtype of interstitial abnormality revealed significant negative correlations between ground glass opacities (GGO) and reticular density (RD) with DLCO (p<0.001) and TLC (p<0.001).

At one year, changes of total interstitial abnormalities compared with baseline had a significant negative correlation with changes of TLC and oxygen saturation (p = 0.015; p < 0.01). Figure 1 demonstrates a sample of CALIPER analysis of a lung affected by progressive nonspecific interstitial pneumonia, 2009-2012.

Conclusion: This study provides evidence of the utility of CALIPER software, as it is the first study to demonstrate the correlation between CALIPER measurements and functional measurements in patients with IIM-associated ILD.

Table: Correlation between CALIPER measurements and PFT measurement at baseline

<table>
<thead>
<tr>
<th>CALIPER measurements</th>
<th>TLC (n=87)</th>
<th>DLCO (n=104)</th>
<th>FEV1/FVC (n=110)</th>
<th>Oxygen saturation at rest (n=90)</th>
<th>Oxygen saturation during exercise (n=68)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>p-value</td>
<td>r</td>
<td>p-value</td>
<td>r</td>
</tr>
<tr>
<td>LAA</td>
<td>0.529</td>
<td>&lt;0.001</td>
<td>0.491</td>
<td>&lt;0.001</td>
<td>0.232</td>
</tr>
<tr>
<td></td>
<td>0.486</td>
<td>&lt;0.001</td>
<td>0.461</td>
<td>&lt;0.001</td>
<td>0.202</td>
</tr>
<tr>
<td>GGO</td>
<td>-0.235</td>
<td>0.029</td>
<td>-0.351</td>
<td>&lt;0.001</td>
<td>0.205</td>
</tr>
<tr>
<td></td>
<td>-0.346</td>
<td>0.001</td>
<td>-0.455</td>
<td>&lt;0.001</td>
<td>0.248</td>
</tr>
<tr>
<td>HC</td>
<td>0.288</td>
<td>0.007</td>
<td>0.207</td>
<td>0.034</td>
<td>-0.057</td>
</tr>
<tr>
<td></td>
<td>0.259</td>
<td>0.015</td>
<td>0.168</td>
<td>0.088</td>
<td>-0.035</td>
</tr>
<tr>
<td>RD</td>
<td>-0.112</td>
<td>0.303</td>
<td>-0.252</td>
<td>0.010</td>
<td>0.011</td>
</tr>
<tr>
<td></td>
<td>-0.304</td>
<td>0.004</td>
<td>-0.397</td>
<td>&lt;0.001</td>
<td>0.090</td>
</tr>
<tr>
<td>Total interstitial abnormality</td>
<td>-0.231</td>
<td>0.031</td>
<td>-0.376</td>
<td>&lt;0.001</td>
<td>0.154</td>
</tr>
<tr>
<td></td>
<td>-0.397</td>
<td>&lt;0.001</td>
<td>-0.513</td>
<td>&lt;0.001</td>
<td>0.222</td>
</tr>
</tbody>
</table>
Clusterin Is Upregulated in Muscle Tissue and Serum in Idiopathic Inflammatory Myopathies and Is Associated with Clinical Disease Activity

Tereza Lennerova1,2, Lucia Vernerova1, Martin Klein1, Veronika Hruskova1,3, Lucie Andres Cerezo1, Barbora Sumova1,2, Michal Tomcik1,2, Sabina Oreska1,2, Herman F Mann1,2, Josef Zamecnik4, Karel Pavelka1,2, Jiri Vencovsky1,2 and Ladislav Senolt1,2

1Institute of Rheumatology, Prague, Czech Republic, Prague, Czech Republic, 2Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, Prague, Czech Republic, 3Faculty of Science, Charles University, Prague, Czech Republic, Prague, Czech Republic, 4Department of Pathology and Molecular Medicine, 2nd Medical School and University Hospital Motol, Charles University, Prague, Czech Republic, Prague, Czech Republic

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Muscle Biology, Myositis and Myopathies Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Clusterin (also known as apolipoprotein J) is a molecular chaperone that participates in a number of biological processes, such as inflammation and apoptosis. Recent data suggest its possible role in the development of chronic autoimmune diseases. The aim of this study was to analyse skeletal muscle expression and serum levels of clusterin in patients with idiopathic inflammatory myopathies (IIM) and in healthy individuals, and to investigate their potential association with clinical disease activity.

Methods: Protein expression of clusterin in muscle tissues was determined by immunohistochemistry in 5 patients with polymyositis (PM), 5 patients with dermatomyositis (DM) and in 5 control subjects. Clusterin mRNA expression in skeletal muscle samples was analysed in 10 patients with IIM and 10 healthy donors by qPCR. Clusterin serum levels were measured by commercial ELISA kit (BioVendor) in 65 IIM patients (28 PM, 27 DM, 10 immune-mediated necrotizing myopathy (IMNM)) and 65 age-/sex-matched healthy individuals. Patients with PM and DM fulfilled Bohan and Peter diagnostic criteria. IMNM was diagnosed according to ENMC 2003 criteria. Disease activity was assessed using myositis disease activity assessment visual analogue scales (MYOACT), myositis intention to treat index (MITAX), health assessment questionnaire (HAQ) and global disease assessment evaluated by patient and doctor. Data are presented as mean ± SD.
**Results:** Clusterin mRNA expression in muscle tissues was significantly increased in patients with IIM compared to healthy donors (p=0.029). Clusterin protein was found to be accumulated in the cytoplasm of regenerating muscle fibers in patients with PM/DM. Serum clusterin levels were significantly higher in all IIM patients than in healthy subjects (87.1 ± 22.8 vs 66.9 ± 11.9, p<0.0001) and also in individual subsets of patients in comparison to the control group (PM: 86.1 ± 23.2, DM: 87.7 ± 24.7, IMNM: 88.15 ± 18.0, p<0.0001 for all). Clusterin levels in all patients with IIM positively correlated with MYOACT (r=0.337, p=0.008), MITAX (r=0.357, p=0.004) and global disease assessment evaluated by a doctor (r=0.309, p=0.015). In patients with DM, positive correlations with MYOACT (r=0.499, p=0.009), MITAX (r=0.491, p=0.009), HAQ (r=0.470, p=0.014) and global disease assessment evaluated by a doctor (r=0.559, p=0.004) were found. No such associations were observed in PM or IMNM subsets.

**Conclusion:** We demonstrate increased local and systemic expression of clusterin in IIM patients compared to healthy individuals and its association with clinical disease activity, especially in patients with DM.

**Acknowledgement:** This study was supported by the project of MHCR for conceptual development of research organization 00023728, project NV16-33746A and project GAUK No. 534217.

**Disclosure:** T. Lennerova, None; L. Vernerova, None; M. Klein, None; V. Hruskova, None; L. Andres Cerezo, None; B. Sumova, None; M. Tomcik, None; S. Oreska, None; H. F. Mann, None; J. Zamecnik, None; K. Pavelka, None; J. Vencovsky, Samsung Bioepis Co., Ltd., Biogen, 5; L. Senolt, None.


**Abstract Number:** 2177

**The Medial Shift of the Tibial Articular Surface Is One Factor of Medial Osteoarthritis of the Knee**

**Ryuji Nagamine,** Artificial joint and rheumatism, Fukuoka Tokushukai Medical Center, Kasuga, Japan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Varus alignment is one factor of medial osteoarthritis (OA) of the knee. According to the concept of the constitutional varus, the bone growth disturbance at the medial proximal metaphysis of the tibia results in proximal tibia vara. In this situation, the tibia is bent at the proximal metaphysis. Therefore, the tibial articular surface (TAS) tilts in varus position and shifts medially. The medial shift of TAS may influence the value of the Hip-knee-ankle (HKA) angle because the ankle joint shifts laterally relative to the TAS. The purpose of this study was to assess the extent of the medial shift of TAS in knees with medial OA, and to assess the effect of this medial shift of TAS on the value of HKA angle, and to discuss the importance of the medial shift of TAS for the onset of medial OA of the knee.

**Methods:** This study consisted of 116 knees with medial OA. The mean age was 75.3 years old. The mean standing femorotibial angle (FTA: lateral angle between femoral and tibial anatomical axes) was 183.6˚. On the anteroposterior view radiograph of the tibia, an anatomical axis (AA), a mechanical axis (MA) and a tibial plateau tangent were drawn. AA was the central line of the tibial shaft. MA is the line between the center of the tibial spines notch and the center of the tibial plafond (ankle joint). Two angle parameters and two distance parameters were measured. Those were angle between AA and MA (Angle A-M) (the value was positive when MA located medial to AA), angle between the tibial plateau tangent and the line perpendicular to AA (Angle plateau), distance from AA to MA on the tibial plateau (Distance A-M) (the value was positive when MA located medial to AA), and the length of MA.

**Results:** The mean (±SD) Angle A-M and Angle plateau was 1.0˚ ± 0.6˚ (range, -0.1˚ to 3.0˚) and 8.2˚ ± 2.9˚ (1.0˚ to 17.0˚), respectively. The mean Distance A-M and length of MA was 5.6mm ± 3.4mm (-1.4mm to 16.1mm) and 347.3mm ± 3.4mm (300.7mm to 408.2mm), respectively. The correlation coefficient between Angle Plateau and Distance A-M was 0.62. The more proximal tibia had varus deformity, the more TAS shifted medially. The maximum Distance A-M was 16.1mm. In this case, HKA angle underestimated varus deformity up to 3˚. The coronal alignment of the lower extremity is expressed in the two-dimensional coordinate system. HKA angle is constructed by three points (hip, knee and ankle) in the system on condition that AA and MA match on the tibia. The difference between MA and AA cannot be assessed by HKA angle. The medial shift of the TAS would increase the mechanical loading in the medial side of the knee.
Conclusion: The knees with proximal tibia vara have medial shift of the tibial articular surface. HKA angle under-estimates varus deformity in such knees. The medial shift of the tibial articular surface should be taken into account for one factor of the medial OA of the knee, and for the treatment of the medial OA.

Disclosure: R. Nagamine, None;


Abstract Number: 2178

Metabolic Osteoarthritis: Relation of Cardiovascular Disease and Diabetes to Knee Osteoarthritis

Laura Kuusalo1, David T. Felson2, Carrie Brown3, Cora E. Lewis4, James Torner5 and Tuhina Neogi2, 1University of Turku and Turku University Hospital, Turku, Finland, 2Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA, 3Boston University School of Public Health, Boston, MA, 4University of Alabama Birmingham, Birmingham, AL, 5University of Iowa, Iowa City, IA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Metabolic changes or low-grade inflammation related to cardiovascular disease (CVD) and diabetes have been hypothesized to contribute to the development of OA. Prior studies have demonstrated an association between diabetes and OA, and recognized OA as a risk factor for incident CVD. However, it remains unclear whether these associations are truly causal as they have not been confirmed in longitudinal cohort studies and may be explained by shared risk factors. The aim of the current study was therefore to examine the associations of pre-existing CVD and diabetes to prevalent and incident ROA and SxOA.

Methods: The study sample consisted of Multicenter Osteoarthritis (MOST) Study participants. We used a self-administered modified Charlson comorbidity questionnaire to assess pre-existing CVD (heart attack, stroke, transient ischemic attack, heart or leg bypass surgery, treatment for heart failure) and diabetes in the participants at baseline. We assessed radiographic (ROA) and symptomatic (SxOA) knee OA at baseline and at 60-months follow-up. We defined ROA as Kellgren-Lawrence grade ≥ 2 on the knee radiograph, and SxOA as ROA and frequent knee pain in the same knee. While we primarily aimed to evaluate the effect of CVD and diabetes on development of knee OA, we recognize that such comorbidities are often chronic and their effects on OA may have already occurred in these older study subjects prior to their study entry. This could result in depletion of susceptibles in a study of their effects on incident knee OA. Therefore, we evaluated both the cross-sectional and longitudinal relation of CVD and diabetes to prevalent and incident ROA and SxOA using logistic regression. We adjusted the models for age, sex, body mass index (BMI), history of knee injury/surgery, physical activity, and correlation between knees within each participant.

Results: We included 5929 knees of 3014 participants in the baseline cross-sectional analyses (mean±SD age 62.5±8.1, mean BMI 30.8±6.0, 60% Caucasian) and 2317 knees of 1181 participants free of knee OA at baseline in the longitudinal analyses (mean±SD age 60.7±7.7, mean±SD BMI 29.1±4.7, 59% Caucasian). In cross-sectional analyses, CVD and diabetes were not associated with ROA and SxOA (Table). In longitudinal analyses, we also found no association of CVD or diabetes with incident ROA or SxOA (Table).

Conclusion: Self-reported CVD and diabetes were not associated with prevalent or incident knee ROA or SxOA after adjustment for potential confounders. Although some of our analyses had limited precision, our results suggest that that these common comorbidities do not appear to contribute to development of knee OA. Specific factors that may contribute to a metabolic OA phenotype require...
Comparing Observed with Expected Assessments of Osteoarthritic Pain over Time: Application of Successive Prediction to Data from the Osteoarthritis Initiative

Steven Mongin¹, Naoko Onizuka², Lisa Langsetmo³ and Anna Shmagel⁴, ¹Biostatistics, University of Minnesota School of Public Health, Minneapolis, MN, ²Medicine, University of Minnesota, Minneapolis, MN, ³University of Minnesota School of Public Health, Minneapolis, MN, ⁴Rheumatic & Autoimmune Diseases, University of Minnesota, Minneapolis, MN

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: High variability in patient-reported outcome scores presents a major challenge in the design and interpretation of clinical studies in osteoarthritis (OA). We present a novel successive prediction algorithm that forecasts individual WOMAC scores based on known clinical parameters and identifies risk factors for deviations between observed and predicted scores.

Methods: Participants from the Osteoarthritis Initiative progression cohort with a baseline Kellgren-Lawrence grade ≥2 for either knee were selected for analysis (N = 1,122). Demographic data, history of pain and depression, BMI, and physical activity parameters at baseline and eight subsequent annual observation times were processed to maximize the number of complete records. WOMAC scores were predicted for study years four through eight, using a mixed effects regression model applied to data up to, but not including, each study year. The predictive model adjusted for continuous time trends for individual subjects as well as the overall cohort, yielding an expected WOMAC score for each participant. To identify subgroups with excessive residual WOMAC scores, subject-specific residuals were analyzed by a separate multivariable regression at each time point.

Results: We were able to accurately model WOMAC scores and to use the fitted models to predict individual scores for each successive year. The predictive model for each visit showed significant overall fit (p < 0.0001 at all targeted study years). The succession of fitted models adapted to new information gained over time, and adjusted predictions to minimize residuals (Figure 1). Factors associated with lower than expected WOMAC scores on more than one successive visit were long-standing history of knee pain and history of hip pain, with mean residual WOMAC (95% confidence interval) ranging from −3.3 (−5.5, −1.7) to −7.7 (−13.2, −2.3). The factor associated with higher than expected WOMAC scores was high performance on the 20-meter walk test, with mean residual WOMAC ranging from +3.3 (+0.5, +6.0) to +4.5 (+1.7, +7.2).
Conclusion: A successive prediction model closely predicted WOMAC scores based on traditional OA risk factors and prior clinical assessments. Subjects with long-standing histories of knee pain and associated hip pain, as well as subjects with good physical performance displayed unexpected WOMAC scores over time.

Disclosure: S. Mongin, None; N. Onizuka, None; L. Langsetmo, None; A. Shmagel, None.

Metabolic Syndrome Does Not Modify the Association between Obesity and Hip Osteoarthritis

Karen Cheng¹, Scott Ball¹, Simon Schenk¹, Elsa Strotmeyer², John Schousboe³, Marcia Stefanick⁴, Elizabeth Barrett-Connor⁵, Deborah Kado⁵, Michael Nevitt⁶, Nancy E. Lane⁷, Eric Orwoll⁸ and Jan M. Hughes-Austin⁹, ¹Orthopaedic Surgery, University of California, San Diego, San Diego, CA, ²Department of Epidemiology, University of Pittsburgh, Pittsburgh, PA, ³University of Minnesota, Minneapolis, MN, ⁴Stanford University, Stanford, CA, ⁵University of California, San Diego, San Diego, CA, ⁶Department of Epidemiology & Biostatistics, University of California San Francisco School of Medicine, San Francisco, CA, ⁷Center for Musculoskeletal Health, University of California at Davis, Hillsborough, CA, ⁸OHSU, Portland, OR, ⁹Orthopaedic Surgery, University of California, San Diego, La Jolla, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Obesity and metabolic syndrome (MetS) are the strongest modifiable risk factors of knee OA, and frequently affect the same individual. The reported associations in hip OA are less consistent. Weight reduction alone has not been shown to prevent the progression of hip OA, which led us to consider the metabolic effects of obesity. This study tests the interaction between obesity and MetS on hip OA in older men and women, to determine whether odds of hip OA were higher among individuals with both MetS and obesity as compared to those with only one or neither of these conditions.

Methods: Cross-sectional analysis was performed on two groups: 4871 women from the Study of Osteoporotic Fractures (SOF) and 3567 men from the Osteoporotic Fractures in Men Study (MrOS) cohorts. Participants were included if they had available hip...
radiographs, documented hip exam, and measurements of body mass index (BMI), systolic blood pressure, triglycerides, high density lipoprotein, and fasting glucose. Clinical hip OA was defined as a modified Croft Score ≥2 or THR by radiographic review, and either hip pain or limited hip range of motion. The odds ratio for hip OA in obese (BMI≥30) as compared to non-obese and in MetS as compared to non-MetS participants was estimated using multivariable logistic regression, adjusting for covariates (Table). An interaction term was then included to determine whether MetS modified associations between obesity and hip OA. In SOF, serum measurements required to evaluate MetS were only available for 401 participants. Compared to the 4871 SOF participants, these 401 women were 0.6 years older, less educated, had 2.6% more DM; and were similar in prevalent hip OA and anthropometry.

**Results:** The prevalence of obesity was 21.4% in men and 19.3% in women. Fifty percent of women and 60.2% of men met the definition for MetS. In men, there was a 70% higher odds of hip OA in obese as compared to non-obese individuals in fully adjusted analysis (95% CI: 1.03-2.84). Among women, no significant association between obesity and hip OA was found in fully adjusted analysis (Table 1). There was no significant association between MetS and hip OA (Table 1) or interactive effect (data not shown) between MetS and obesity on hip OA in either women (p=0.996) or men (p=0.394).

**Conclusion:** Obesity, but not MetS, conferred a higher odds of hip OA in a population of community-dwelling older men, suggesting that mechanical load has a more significant role in hip OA pathogenesis than the metabolic effects of increased adiposity. Neither obesity nor MetS were associated with hip OA in the women studied. Given the small sample size, future studies are needed to evaluate MetS and hip OA in women.

Table 1. Odds ratios (and 95% Confidence Intervals) for associations of obesity (BMI≥30 kg/m²) and metabolic syndrome (2 of 4 NCEP-ATPIII criteria, excluding waist circumference) with clinical hip osteoarthritis in SOF and MrOS.

<table>
<thead>
<tr>
<th>Prevalent Clinical Hip Osteoarthritis</th>
<th>Women in SOF</th>
<th>Men in MrOS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%) positive</td>
<td>N</td>
</tr>
<tr>
<td>Obesity</td>
<td>940 (19.3)</td>
<td>762 (21.4)</td>
</tr>
<tr>
<td>Unadjusted</td>
<td>4871</td>
<td>3567</td>
</tr>
<tr>
<td>Demographic adjusted</td>
<td>4855</td>
<td>3567</td>
</tr>
<tr>
<td>Fully adjusted*</td>
<td>4731</td>
<td>1458</td>
</tr>
<tr>
<td>Metabolic Syndrome</td>
<td>260 (50.0)</td>
<td>2149 (60.2)</td>
</tr>
<tr>
<td>Unadjusted</td>
<td>401</td>
<td>3567</td>
</tr>
<tr>
<td>Demographic adjusted</td>
<td>400</td>
<td>3567</td>
</tr>
<tr>
<td>Fully adjusted*</td>
<td>394</td>
<td>1458</td>
</tr>
<tr>
<td>p-value for interaction</td>
<td>0.996</td>
<td>0.394</td>
</tr>
</tbody>
</table>

*Fully adjusted for demographics (age, white race, high school education), medical comorbidities (DM, MI), medication use (NSAID, corticosteroid, bisphosphonate), bone mineral density, vitamin D level.

²Not available in SOF

Disclosure: K. Cheng, None; S. Ball, None; S. Schenk, None; E. Strotmeyer, None; J. Schousboe, None; M. Stefanick, None; E. Barrett-Connor, None; D. Kado, None; M. Nevitt, None; N. E. Lane, None; E. Orwoll, None; J. M. Hughes-Austin, None.
Is a Decrease in MRI-Defined Inflammation Associated with a Decrease in Pain in Patients with Hand Osteoarthritis? a Two-Year Follow-up Study

S. van Beest¹, W. Damman¹, R. Liu¹ and M. Kloppenburg², ¹Rheumatology, Leiden University Medical Center, Leiden, Netherlands, ²Rheumatology and Clinical Epidemiology, Leiden University Medical Center, Leiden, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Joint pain in hand osteoarthritis (OA) is associated with synovitis in cross-sectional studies. Therefore we hypothesized that synovitis could be a target for treatment. Our aim was to investigate the longitudinal associations between inflammatory features on MRI and joint tenderness in patients with primary hand OA over a two-year period.

Methods: Eighty-five consecutively included patients (81.2% women, median age 58.7 years) with primary hand OA (89.4% fulfilling ACR classification criteria) from a rheumatology outpatient clinic, who received contrast-enhanced MRI and physical examination of the right hand at baseline and at follow-up two years later, were studied. Fat suppressed T2-turbo spin weighted and pre- and post-gadolinium injection T1-weighted sequences were performed in axial and coronal planes on a 1.5 Tesla extremity MR unit. Baseline and follow-up images were scored paired in unknown time order, blinded for clinical data, by one reader according to the Hand OA MRI scoring system (HOAMRIS). Joint tenderness was assessed by trained research nurses. Odds ratios were calculated on joint level (n=680; 8 interphalangeal joints of right digits 2-5 per patient), using generalized estimating equations to account for the within patient effects. Additional adjustments were made for gender, baseline status of MRI-defined osteophytes, synovitis and BML, and change in MRI-defined osteophytes, synovitis/BML and erosions, when appropriate.

Results: Out of 116 joints with baseline tenderness, 73 had loss of tenderness at follow-up. Decrease in synovitis was seen in 21 joints, and decrease in BMLs only in 13. Loss of tenderness was associated in adjusted analyses with a decrease in synovitis, but not in BMLs (Table 1). However, when stratifying for change in synovitis, a decrease in BMLs showed an additive effect (Table 2). Out of 564 joints without baseline tenderness, 103 had incident tenderness at follow-up. Incident tenderness was associated with an increase in synovitis and, to a lesser extent, BMLs. After adjusting for each other it became apparent that synovitis was the main effect modifier and BMLs only had an additive effect (data not shown).

Conclusion: A decrease in inflammatory MRI features is associated with loss of joint tenderness, supporting targeting MRI-defined synovitis in hand OA.
Disclosure: S. van Beest, Innovative Medicines Initiative: Approach, 2; W. Damman, None; R. Liu, None; M. Kloppenburg, Pfizer, 2, AbbVie, GlaxoSmithKline, Merck, Levicept, 5, Dutch Arthritis Fund, 2, Innovative Medicines Initiative: APPROACH, 2.


Abstract Number: 2182

Cardiovascular Events in Patients with Diffuse Idiopathic Skeletal Hyperostosis. a 10 Years Follow-up Study

Karina Glick1, Irina Novofastovski2, Naama Schwartz3 and Reuven Mader2, 1Medicine C, Emek Medical Center, Afula, Israel, Afula, Israel, 2Rheumatology, Emek Medical Center, Afula, Israel, Afula, Israel, 3Biostatistics, Emek Medical Center, Afula, Israel, Afula, Israel

First publication: September 18, 2017

SEASON INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: DISH has been reported to be associated with constitutional and metabolic derangement. In particular, patients with DISH were reported to bear a higher cardiovascular risk. The outcome of these CV risks has never been evaluated. The aim of the study was to explore if patients with DISH develop, over time, a significant cardio-vascular morbidity in a real life scenario.

Methods: This is a follow-up study on a group of patients without cardiovascular diseases. The patients' characteristics and their CV risk factors, their prevalence of MS and their Framingham risk score has been already described. The medical records were reviewed, and the data about their current diagnoses, medical treatments, hospitalizations and mortality were re-collected. The statistical analysis compared the data with the historical data of the same groups (DISH vs non-DISH) as well as changes within the same group (DISH or non-DISH).

Results: There were 49 patients in the DISH group and 48 in the NDISH group. In this cohort, patients with DISH were significantly more often affected by type 2 diabetes, obesity, insulin resistance. They also had a significant higher risk for the development of cardiovascular events. The mean follow-up time was approximately 10 years for both groups. No differences for gender, age, age at diagnosis were observed. Patients with DISH were more often admitted to the department of medicine, the difference though did not reach statistical significance (p=0.07). More DISH patients developed acute MI (12 vs 2 p=0.0044), and were affected by hypertension and DM (60% vs 86% p=0.0049; 17% vs 54% p=0.001 respectively). The crude odds ratios for DISH patients to develop myocardial infarction during the follow-up and after adjustment for diabetes, hypertension and obesity were 7.46 (95%CI 1.57-35.44) and 5.65 (95%CI 1.08-29.43) respectively. The Framingham CV risk score under estimated the occurrence of cardiac events in particular in the DISH group. No differences were detected between the groups in the prevalence of TIA's, CVA's or PVD. The mortality rate between the groups was nearly equal (8.33 vs 10%). Significantly more patients in the DISH group developed de novo DM, and were prescribed ACE inhibitors, compared with the NDISH group. Increased hypertension prevalence, between the first assessment and at 10 years, was similar between the groups.

Conclusion: The incidence of MI is significantly higher in patients with DISH compared with age and sex matched NDISH patients. The increased CV risk attributed to patients with DISH is evidenced at ten years with a significant increase in myocardial infarction events during that period of time. The Framingham score under estimated the risk in patients with DISH. On the other hand, the prevalence of vascular morbidities such as TIA's, CVA's or PVD's was similar between the groups. More studies are needed to determine if these findings depend only on the association of DISH with traditional CV risk factors, or, if there is a contribution of the musculoskeletal condition per se.

<table>
<thead>
<tr>
<th>Bone marrow lesions</th>
<th>Synovitis No change/increase Decrease</th>
<th>Synovitis No change/increase Decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>No change/increase</td>
<td>1.0 (0.00 to 10.0)</td>
<td>0.80 (0.00 to 3.32)</td>
</tr>
<tr>
<td>Decrease</td>
<td>0.80 (0.00 to 3.32)</td>
<td>0.80 (0.00 to 3.32)</td>
</tr>
</tbody>
</table>

Table 2 The odds ratios for loss of joint tenderness (in joints with tenderness at baseline) when stratified for change in both synovitis and bone marrow lesions.
Disclosure: K. Glick, None; I. Novofastovski, None; N. Schwartz, None; R. Mader, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/cardiovascular-events-in-patients-with-diffuse-idiopathic-skeletal-hyperostosis-a-10-years-follow-up-study

Abstract Number: 2183

Two-Year Changes in Knee Osteoarthritis Symptoms: Comparing Clinical Relevance of Patient-Reported Outcomes By Anchoring to Knee Replacement

C. Kent Kwoh¹, Hans Guehring², Erin Ashbeck³, Michael J Hannon⁴ and Aida Aydemir⁵, ¹University of Arizona Arthritis Center, Tuscan, AZ, ²Merck KGaA, Darmstadt, Germany, ³The University of Arizona Arthritis Center, Tucson, AZ, ⁴Medicine, University of Pittsburgh, Pittsburgh, PA, ⁵EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Randomized controlled trials (RCTs) of interventions for knee OA (KOA) may include a patient-reported outcome (PRO) measure as a primary endpoint. Several measures of KOA symptoms are potential candidates, although their comparative performance is unclear. The objectives of this study were to 1) estimate clinically important differences in 2-year changes in symptoms by anchoring change scores to a clinically important outcome, that is, future knee replacement (KR), and 2) compare 2-year changes in symptom scores with respect to their ability to discriminate knees that underwent KR over 7 years of follow-up.

Methods: OA Initiative knees were selected for analysis, based on eligibility criteria typical of a disease-modifying osteoarthritis drug (DMOAD) RCT for KOA, including Kellgren-Lawrence grade of 2 or 3, medial minimum joint space width ≥2.5 mm, knee pain at worst in the past 30 days from 4 to 9 on a 10-point numerical rating scale (NRS) or 0 to 3 if pain medication was taken for joint pain, excluding those with malalignment of >5º. KOA symptoms were assessed over 2 years, including knee pain severity over the past 30 days on a NRS, and over the past 7 days on a NRS, as well as WOMAC subscales, Knee injury and OA Outcome Score (KOOS) subscales, and the 12-item short-form health survey (SF-12). Scores were scaled 0–100, with 100 as the worst possible score. To characterize clinically relevant change, 2-year change in symptom scores was anchored to KR up to 7 years of follow-up and difference in mean change was estimated. To evaluate the ability of 2-year change in symptom scores to discriminate knees that went on to future KR, area under the receiver operating characteristic curve (AUC) was estimated and compared.

Results: The sample included 1,181 knees, with median follow-up of 5.8 years after the initial 2-year assessment, and 131 underwent KR. Two-year changes in WOMAC total, KOOS NRS 7 days, KOOS symptoms score, and NRS 30 days had similar discrimination for future KR (Table 1). When compared directly, the AUC for NRS 30 days was significantly better than other measures such as NRS 7 days (AUC difference = 0.05, CI = 0.01–0.10), total WOMAC (AUC difference = 0.06, CI = 0.01–0.11), and KOOS symptoms (AUC difference = 0.06, CI = 0.002–0.12).

Conclusion: Among knees that met typical eligibility criteria for a DMOAD RCT, 2-year change in WOMAC total, KOOS symptoms score, KOOS pain frequency, and KOOS pain severity NRS 7 days performed similarly, although the NRS 30 days was marginally better at discriminating future KR up to 7 years of follow-up. Investigators conducting RCTs of KOA interventions may consider each of these PRO measures as potential primary endpoints. Overall performance was modest, and additional work is needed to develop more responsive measures.
Relation of Gait Speed to Incident Knee Replacement: The Multicenter Osteoarthritis Study

Joshua Stefanik1, Jodie McClelland2, Carrie Brown3, Michael P. LaValley3, James Torner4, Michael Nevitt5, Cora E. Lewis6 and Tuhina Neogi1, 1Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA, 2Lawrope University, Melbourne, Australia, 3Boston University School of Public Health, Boston, MA, 4University of Iowa, Iowa City, IA, 5Department of Epidemiology & Biostatistics, University of California San Francisco School of Medicine, San Francisco, CA, 6University of Alabama Birmingham, Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: For some individuals with knee osteoarthritis (OA), the failure of conservative management can often lead to knee replacement (KR). Identifying who will progress to KR may allow efficient dedication of resources towards this group with interventions that may delay or prevent the need for surgery. To date, self-reported pain severity and function has not provided sufficient prediction of KR. The speed of a person’s gait is a powerful predictor of significant health events in older adults. Gait speed may encapsulate a range of functional limitations and impairments that could precipitate the need for KR and may therefore be an appropriate measure that predicts the need for KR in patients with knee OA. At the same time, because KRs occur in older individuals, observational studies need to properly account for competing risk of death and study withdrawal to obtain valid estimates of risk of KR. The aim of this study was to investigate the relation of gait speed to incident KR in older individuals with or at risk for knee OA.

Methods: The MOST Study is a NIH-funded cohort of persons with or at risk of knee OA. MOST participants completed baseline, 30-, 60-, and 84-month clinic visits. Gait speed at the baseline clinic visit was calculated from the time taken to complete the 20-meter walk test (meters(m)/second(s)). Date of first KR was confirmed. Participants without a KR were censored at their last attended clinic visit. We examined the relation of gait speed to KR using a Cox proportional hazards model accounting for competing events. Participants without a KR were censored at their 84-month visit, and death and early withdrawals were considered competing events. In separate models, we dichotomized gait speed at values related to functional limitation and community walking speed (1.0 and 1.2 m/s, respectively), and also into tertiles. Analyses were adjusted for age, sex, BMI, clinic site, baseline knee pain severity (visual analog scale 0-100 in the most painful knee) and baseline Kellgren-Lawrence (KL) score (maximum of right and left).
Results: 2774 participants were included: mean±SD age, BMI, and gait speed were 62.3±8.0, 30.6±6.0, and 1.20±0.2, respectively; 60% were female. 47% and 15% of participants walked at 1.0 and 1.2 m/s at baseline, respectively. While lower gait speeds were associated with higher risk of KR in the crude model, once we accounted for the confounding effects of pain severity and the competing risk of death and study withdrawal, lower gait speeds were no longer associated with incident KR (Table). Compared with the highest gait speed tertile, those in the lowest had 1.2 (0.9, 1.6) times the risk of KR.

Conclusion: Gait speed was not a strong predictor of KR once we accounted for the confounding effects of pain and competing risk of death and study withdrawal.

<table>
<thead>
<tr>
<th>Hazard Ratio (95% CI) for KR (n=2774)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>20-m walk &lt;1.0 m/s</td>
</tr>
<tr>
<td>20-m walk &lt;1.2 m/s</td>
</tr>
<tr>
<td>20-m walk (range)</td>
</tr>
<tr>
<td>Lowest Tertile (0.2-1.13)</td>
</tr>
<tr>
<td>Middle Tertile (1.14-1.29)</td>
</tr>
<tr>
<td>Highest Tertile (1.3-1.9)</td>
</tr>
</tbody>
</table>

Disclosure: J. Stefanik, None; J. McClelland, None; C. Brown, None; M. P. LaValley, None; J. Torner, None; M. Nevitt, None; C. E. Lewis, None; T. Neogi, None.

Abstract Number: 2185

Relation of Foot Pronation to Medial Knee Load in Persons with Medial Knee Osteoarthritis

K. Douglas Gross¹, Richard Jones², David T. Felson³, Salinda Chong⁴ and Howard J. Hillstrom⁵, ¹Physical Therapy, MGH Institute of Health Professions, Boston, MA, ²School of Health Sciences, University of Salford, Manchester, United Kingdom, ³Arthritis Research UK Centre for Epidemiology, Institute of Inflammation and Repair, University of Manchester, Manchester, United Kingdom, ⁴MGH Institute of Health Professions, Boston, MA, ⁵Rehabilitation, Hospital Special Surgery (HSS), New York, NY

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The knee adduction moment (KAM) estimates medial knee load during gait, with high KAM fueling worsening OA. Understanding how foot mechanics contribute to KAM would inform the development of more effective footwear and insoles to prevent worsening knee OA. During the initial and early stance phases, a neutrally aligned foot with adequate pronation could dissipate impact loads, reduce varus thrust, and minimize KAM as it rises to an initial peak. Yet, excessive pronation in late stance redistributes load medially, possibly increasing KAM as it reaches a second peak. In persons with medial knee OA, we assessed: 1) the relation of foot pronation during the initial and early stance phases to 1st peak KAM; and 2) the relation of foot pronation during late stance to 2nd peak KAM. Given possible effects of both diminished and excessive pronation, we assessed both linear and u-shaped trends.
Methods: The Effectiveness of Shoes and Insoles on Loading at the Knee (SILK) Study included adults aged 45-70 yrs with medial knee OA. Plantar pressure profiles of the index limb were acquired during 5 trials of self-paced barefoot walking using an Emed-X platform. From these, we measured foot pronation during the initial, early, and late stance phases using the Pronation-Supination Index (PSI) as described by Motooka et al., where lower PSI values indicate greater pronation (retest ICC 0.46-0.90). Concurrently, a Qualisys motion capture system with AMTI force plates measured 1st and 2nd peak KAM in Newton-meters per kg of body weight (retest ICC= 0.86). In tertiles of increasing pronation (decreasing PSI), generalized linear models estimated mean 1st and 2nd peak KAM while adjusting for age, sex, body mass, and walking velocity. Tests for linear and u-shaped trend identified dose-response relationships.

Results: In 70 SILK participants (mean age 60.3 ± 9.6 yrs, body mass 87.3 ± 18.5 kg, walking velocity 1.12 ± 0.23 m/sec, 61.4% female), mean 1st and 2nd peak KAM was 0.36 and 0.32 Nm/kg, respectively. At initial contact, feet with diminished (PSI ≥ 58.14) or increased (PSI ≤ 55.09) pronation in comparison to the middle PSI tertile (PSI 55.10, 58.13) had increased 1st peak KAM (mean difference = 0.07 and 0.10 Nm/kg, respectively), resulting in a significant u-shaped trend (p for trend = 0.02). During early stance, 1st peak KAM was greatest among feet with the least pronation and declined linearly across tertiles of increasing pronation (p for trend = 0.06). There was no association between foot pronation in late stance and 2nd peak KAM (see table).

Conclusion: In adults with medial knee OA, feet with diminished or excessive pronation at initial contact, and feet with reduced pronation during the early stance phase of walking, experience increased peak medial knee loads. These findings could inform efforts to refine more effective footwear or insole interventions to minimize loads for persons with medial knee OA.

Table. Medial knee load, as measured by 1st or 2nd peak knee adduction moment (KAM), in tertiles of increasing foot pronation (PSI) during the initial, early, and late stance phases of walking:

<table>
<thead>
<tr>
<th>Initial Contact</th>
<th>Foot Pronation</th>
<th>PSI (high)</th>
<th>increasing</th>
<th>PSI (low)</th>
<th>p for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSI range</td>
<td>p-linear</td>
<td>p-u-shaped</td>
<td>p-linear</td>
<td>p-u-shaped</td>
<td></td>
</tr>
<tr>
<td>Mean* 1st peak KAM</td>
<td>0.38</td>
<td>0.31</td>
<td>0.41</td>
<td>0.44</td>
<td>0.02</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.32, 0.44</td>
<td>0.25, 0.37</td>
<td>0.35, 0.47</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Early Stance</th>
<th>Foot Pronation</th>
<th>PSI (high)</th>
<th>increasing</th>
<th>PSI (low)</th>
<th>p for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSI range</td>
<td>p-linear</td>
<td>p-u-shaped</td>
<td>p-linear</td>
<td>p-u-shaped</td>
<td></td>
</tr>
<tr>
<td>Mean* 1st peak KAM</td>
<td>0.40</td>
<td>0.38</td>
<td>0.32</td>
<td>0.06</td>
<td>0.70</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.34, 0.47</td>
<td>0.31, 0.44</td>
<td>0.26, 0.38</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Late Stance</th>
<th>Foot Pronation</th>
<th>PSI (high)</th>
<th>increasing</th>
<th>PSI (low)</th>
<th>p for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSI range</td>
<td>p-linear</td>
<td>p-u-shaped</td>
<td>p-linear</td>
<td>p-u-shaped</td>
<td></td>
</tr>
<tr>
<td>Mean* 2nd peak KAM</td>
<td>0.32</td>
<td>0.28</td>
<td>0.36</td>
<td>0.40</td>
<td>0.13</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.26, 0.38</td>
<td>0.23, 0.34</td>
<td>0.20, 0.41</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Means adjusted for age, sex, body mass and walking velocity.

Disclosure: K. D. Gross, None; R. Jones, None; D. T. Felson, None; S. Chong, None; H. J. Hillstrom, None.


Abstract Number: 2186

The Role of Hip Injury in Pain Exacerbation in Hip Osteoarthritis: an Internet-Based Case-Crossover Study

Kai Fu1, Joanna Makovey2, Ben Metcalf3, Kim Bennell3, Yuqing Zhang4, Rebecca Asher5, Sarah Meneses2, Leticia Deveza2 and David Hunter2, 1Rheumatology, Institute of Bone and Joint Research, Kolling Institute, University of Sydney, Sydney, Australia, 2Rheumatology, Institute of Bone and Joint Research, Kolling Institute, University of Sydney, Sydney, Australia, 3Centre for Health, Exercise and Sports Medicine, Department of Physiotherapy, University of Melbourne, Melbourne, Australia, 4School Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, 5NHMRC Clinical Trials Centre, University of Sydney, Sydney, Australia

First publication: September 18, 2017
Background/Purpose: Pain is the main symptom in hip osteoarthritis (OA) and many patients experience recurrent pain exacerbations. The purpose of this study is to evaluate the association between hip injury and hip pain exacerbations in persons with symptomatic hip OA.

Methods: We conducted an internet-based case-crossover study to assess potential risk factors, including hip injury, for hip pain exacerbation. Eligible participants with symptomatic hip OA were followed for 90 days and asked to complete online questionnaires at 10-day intervals (control periods). They also logged on to the study website to complete questionnaires in the episode of a hip pain exacerbation (case periods) defined as an increase of 2 points in pain intensity compared with baseline on numeric rating scale (0-10). Participants were asked whether they had hip injury that limited usual activities (such as falls, sports injuries, etc.) during the last 7 days and whether they experienced any episodes of hip "giving way" in the last 2 days at both control and case periods. The relationship of hip injury and “giving way” to the risk of pain exacerbation was examined using conditional logistic regression.

Results: Of 249 patients recruited 133 (53%) and 132 (53%) with both control periods and case periods were included in the analysis of injury and “giving way” respectively. Hip injury during the last 7 days increased the risk of pain exacerbations (odds ratio [OR] 2.74, 95% CI 1.62, 4.62) compared with no injury to the hip. Hip “giving way” during the last 2 days was also associated with an increased risk of hip pain exacerbation (OR 2.50, 95% CI 1.68, 3.73), and showed a significant dose-response relationship between the number of hip “giving way” events and risk of hip pain exacerbations during the last 2 days (≥ 6 vs. 0 episodes; OR 7.86, 95% CI 2.74, 22.55).

Conclusion: The findings of this study indicate that hip injury and episodes of hip “giving way” are significantly related to pain exacerbation in persons with symptomatic hip OA. Reducing and avoiding such episodes may decrease the risk of hip pain exacerbations and improve the pain situation in persons with hip OA.

Tables

Table 1. Association of hip injury and hip pain exacerbation (132 subjects)

<table>
<thead>
<tr>
<th>Hip injury</th>
<th>Case periods (n=304)</th>
<th>Control periods (n=807)</th>
<th>OR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>253 (83%)</td>
<td>760 (94%)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Yes</td>
<td>51 (17%)</td>
<td>47 (6%)</td>
<td>2.74 (1.62, 4.62)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 2. Association of hip “giving way” and hip pain exacerbation (133 subjects)

<table>
<thead>
<tr>
<th>Hip “giving way”</th>
<th>Case periods (n=347)</th>
<th>Control periods (n=905)</th>
<th>OR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>288 (83%)</td>
<td>843 (93%)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Yes</td>
<td>59 (17%)</td>
<td>62 (7%)</td>
<td>2.50 (1.68, 3.73)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 3. Association of the number of hip “giving way” events and hip pain exacerbations
<table>
<thead>
<tr>
<th>Number of hip “giving way” events in the past 2 days</th>
<th>Case periods (n=347)</th>
<th>Control periods (n=905)</th>
<th>OR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>215 (62%)</td>
<td>718 (79%)</td>
<td>1.86 (1.14, 3.04)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1</td>
<td>43 (12%)</td>
<td>87 (10%)</td>
<td>4.53 (2.00, 5.75)</td>
<td></td>
</tr>
<tr>
<td>2-5</td>
<td>64 (18%)</td>
<td>92 (10%)</td>
<td>7.86 (2.74, 22.55)</td>
<td></td>
</tr>
<tr>
<td>≥6</td>
<td>25 (7%)</td>
<td>8 (1%)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**Disclosure:** K. Fu, China Scholarship Council (CSC), 9; J. Makovey, None; B. Metcalf, None; K. Bennell, None; Y. Zhang, None; R. Asher, None; S. Meneses, None; L. Deveza, None; D. Hunter, Flexion, Merck Serono, Tissuegene, 5, DJO, 7.


**Abstract Number:** 2187

**Association of Circulating microRNAs with Prevalent and Incident Osteoarthritis in Women: The Ofely Study**

Jean-Charles Rousseau¹, Marjorie Millet¹, Martine Croset¹, Elisabeth Sornay-Rendu², Olivier Borel² and Roland Chapurlat³, ¹INSERM 1033, Lyon, France, ²INSERM 1033, E. Herriot Hospital, Hospices Civils de Lyon, Lyon, France, ³INSERM 1033, University of Lyon, E. Herriot Hospital, Hospices Civils de Lyon, Lyon, France

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Sensitive and specific blood biomarkers to detect the initial stages of osteoarthritis (OA) and to predict the future development of the disease are not available in clinical routine. Consequently, there is a considerable interest in the identification of new markers. The small non-coding microRNAs (miRs) are endogenous regulators of gene expression by binding to complementary sequence on target messenger RNA transcripts that results in translational repression or target degradation. The remarkable miR stability in biofluids has suggested their utility as non-invasive disease biomarkers. Thus the levels of 19 circulating miRs has been assessed in subjects with and without OA in the OFELY cohort.

**Methods:**

The study group for the measurement of serum miR expression included French postmenopausal women belonging to the population-based cohort OFELY (Os des Femmes de LYon, n= 610). Firstly, we randomly selected 43 women with a prevalent knee OA (Kellgren & Lawrence score of 2 and 3; early and intermediate knee OA) with or without OA at others sites (lumbar spine, hip, hand) (age: 68.3 ± 6.6 years, body mass index (BMI): 26.6 ± 4.4 kg/m²) and 43 healthy women without OA at any site matched for age and BMI. Secondly, we randomly selected 23 women with incident knee OA over the next 4 years (age: 68.4 ± 8 years, BMI: 25.2 ± 4 kg/m²) and 25 healthy subjects without incident OA matched for age and BMI. We have selected 19 candidate miRs (let-7c-5p; 16-5p; 29a-3p, 29b-3p; 29c-3p; 93-5p; 126-3p; 132-3p; 139-5p; 146a-5p; 184; 186-5p; 195-5p; 199a-3p; 200a-3p, 345-5p; 375; 885-5p; 1299) for real-time PCR analysis on the basis of our previous Next Generation Sequencing study measuring all circulating miRs and on literature data. Total RNA was extracted from 200 µl of serum (RNA isolation biofluids, EXIQON). MiRs were reverse-transcribed and PCR was performed with custom TaqMan array microRNA cards on a QuantStudio 7 flex (Applied Biosystems). The expression levels were
Results:

When considered as a continuous variable, miR-146a-5p was significantly increased in the group of prevalent OA compared with healthy subjects (RQ: relative quantification; median [IQR]: 1.12 [0.73; 1.46] RQ vs 0.85 [0.62; 1.03] RQ, p=0.015 respectively). Using logistic regression analysis, the risk of OA prevalence was significantly increased (odds-ratio [95% CI]: 1.83 [1.21-2.77], p=0.004) for each quartile increase in serum miR-146a-5p. Moreover, there was a significant association between baseline miR-186 levels and the risk of incident knee OA for each quartile increase (odds-ratio [95% CI]: 1.71 [1.00-2.95], p=0.049).

Conclusion:

We have shown that miR-146a-5p is increased in women suffering from mild to moderate OA compared to healthy women. Importantly, miR-186 is also increased in those women who will develop radiographic knee OA over the next 4 years, therefore with the potential to detect preclinical knee OA.

Disclosure: J. C. Rousseau, None; M. Millet, None; M. Croset, None; E. Sornay-Rendu, None; O. Borel, None; R. Chapurlat, None.

Risk of Disability in Underweight Persons with or at Increased Risk of Knee Osteoarthritis

Nilasha Ghosh, Joan S. Chmiel, Orit Almagor, Karen W. Hayes, Kirsten C. Moisio, Alison H. Chang, Julie Szymaszek and Leena Sharma, Northwestern University, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: US studies have revealed a U-shaped relationship between BMI and poor outcomes (function, mortality); both underweight and overweight/obese persons have greater risk. In knee OA, effects of overweight/obesity have been studied, but the impact of being underweight is unknown. We hypothesized that, in persons with or at higher risk for knee OA, underweight persons are at higher risk for incident and worsening disability.

Methods: A cohort study of persons 45-79 yrs with or at higher risk of knee OA, the OAI began ADL/IADL collection at 48m (analysis baseline). 48m BMI was stratified as underweight (<20 kg/m²), healthy weight (≥20 to <25), overweight (≥25 to <30), or obese (≥30), and disability levels were: none (no ADL/IADL limitation), mild (only IADL), moderate (1-2 basic ADL), or severe (≥3 basic ADL). Incident disability was defined as 96m IADL or basic ADL disability in persons without 48m disability, and worsening disability as 48m-96m level worsening. Logistic regression was used to assess associations between BMI group (vs. healthy weight) and outcomes. Multivariable models included BMI and variables with univariate p≤0.20; backward selection (removing variables with adjusted p>0.20) was used for final models.

Results: Of 2795 persons eligible (57% female, mean age 64.7, BMI 28.5), 754 (27%) developed incident disability. Of 3054 persons (57% female, age 64.8, BMI 28.6), 360 (12%) had worsening disability. Each BMI group had increased odds for both outcomes, not statistically significant for underweight, vs. healthy (Table, Fig). In final models, age, comorbidity, depressive symptoms, knee symptoms, hip pain, ankle pain, and physical activity were associated with both outcomes; sex, with incident disability only; and injury, confidence, and falls with worsening disability only.
Conclusion: In persons with or at increased risk for knee OA, being underweight may result in an increased risk for incident and worsening disability. The lack of significance may be due to the small number (60) of underweight persons in the OAI, which was enriched for higher BMI. These findings suggest the importance of targeting a healthy BMI range and identify a subgroup who may be at risk for poor outcome.

<table>
<thead>
<tr>
<th>Independent Variable</th>
<th>Incident Disability (n = 2790)</th>
<th>Worsening of Disability (n = 2082)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>1.03 (1.02, 1.04)</td>
<td>1.02 (1.01, 1.04)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>0.91 (0.86, 0.96)</td>
<td>0.86 (0.80, 0.93)</td>
</tr>
<tr>
<td>BMI groups, kg/m² (category)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20 (underweight)</td>
<td>1.46 (0.74, 2.90)</td>
<td>1.69 (0.93, 2.97)</td>
</tr>
<tr>
<td>≥20 to &lt;30 (overweight)</td>
<td>1.39 (0.53, 4.07)</td>
<td>1.67 (0.46, 2.96)</td>
</tr>
<tr>
<td>≥30 (obese)</td>
<td>1.47 (1.14, 1.98)</td>
<td>2.18 (7.24, 2.55)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Caucasian</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>1.29 (0.97, 1.71)</td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>1.44 (1.06, 1.92)</td>
<td>1.82 (1.33, 2.50)</td>
</tr>
<tr>
<td>Education levels</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>0.91 (0.69, 1.22)</td>
<td>n/a</td>
</tr>
<tr>
<td>1</td>
<td>0.95 (0.77, 1.20)</td>
<td>n/a</td>
</tr>
<tr>
<td>2</td>
<td>0.99 (0.79, 1.26)</td>
<td>n/a</td>
</tr>
<tr>
<td>Knee symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.18 (1.05, 1.34)</td>
<td>1.74 (1.67, 2.16)</td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hip pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.44 (1.06, 1.92)</td>
<td>1.82 (1.33, 2.50)</td>
</tr>
<tr>
<td>No</td>
<td>0.91 (0.69, 1.22)</td>
<td>n/a</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>1.44 (1.06, 1.92)</td>
<td>1.82 (1.33, 2.50)</td>
</tr>
<tr>
<td>Black</td>
<td>1.44 (1.06, 1.92)</td>
<td>1.82 (1.33, 2.50)</td>
</tr>
<tr>
<td>Education levels</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>0.91 (0.69, 1.22)</td>
<td>n/a</td>
</tr>
<tr>
<td>1</td>
<td>0.95 (0.77, 1.20)</td>
<td>n/a</td>
</tr>
<tr>
<td>2</td>
<td>0.99 (0.79, 1.26)</td>
<td>n/a</td>
</tr>
<tr>
<td>Knee injury</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.44 (1.06, 1.92)</td>
<td>1.82 (1.33, 2.50)</td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical activity (PA)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PA (metabolic score)</td>
<td>0.90 (0.80, 1.00)</td>
<td>0.90 (0.80, 0.99)</td>
</tr>
</tbody>
</table>

OR, odds ratio; CI, confidence interval.

Table. Results from Multivariable Logistic Regression Models for Incident Disability and Worsening of Disability 4-Year Outcomes After Baseline. Results are adjusted for other variables in the column (other than those marked n/a). Statistical significance corresponds to a 95% CI that excludes 1. Significant results are bolded in the table.
Disclosure: N. Ghosh, None; J. S. Chmiel, None; O. Almagor, None; K. W. Hayes, None; K. C. Moisio, None; A. H. Chang, None; J. Szymaszek, None; L. Sharma, None.


Abstract Number: 2189

Metabolic Syndrome Influences the Radiographic Progression of Knee Osteoarthritis and Condition the Risk of Erosive Hand OA


First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
The contribution of metabolic factors in the development of OA has not been fully elucidated. The aim of this work is to analyze the influence of metabolic syndrome (MetS) in the rate of radiographic progression of knee osteoarthritis, as well as in the prevalence of radiographic hand OA.

Methods:
For this work we used data from the Spanish cohort PROCOAC (PROspective Cohort of OsteoArthritis A Coruña). This cohort consists of subjects that visited the Rheumatology consultations at different time points and comprises 984 subjects at baseline including radiographic knee and hip KL grade, radiographic hand OA status (129 of them with an erosive phenotype), demographic and clinical data as well as the necessary information to assess the MetS at baseline, that is, abdominal circumference (in cm) in addition to at least two of the following parameters: triglycerides above 200mg/dL, low HDL (<35 mg/dL), hypertension and glucose blood levels (>110 mg/dL). To assess the severity of the disease, the number of affected joints was coded as 0-1 and 2-3, according to the radiographic information of hands, knees and hips. Appropriate statistical analyses including regression models adjusting for the confounder variables of gender, age and BM, and chi-square contingency tables, were performed with SPSS v24.

Results:
MetS appeared as a significant risk factor (HR=2.651;95CI:1.224-5.744;p-value=0.0013) in those OA patients that experienced radiographic knee OA progression over time (any KL increase from KL>=2 at baseline) (Figure 1).

MetS is also a risk factor for OA occurrence if BMI is not taken into account (HR=1.716;95CI:1.069-2.754;p-value=0.025); however, when BMI is considered, the effect of MetS in OA is lost.

MetS was not associated with radiographic hand OA presence (HR=1.063;95CI:0.573-1.976;p-value=0.847). In relation to each of the components of MetS, only hypertension was borderline statistically significantly associated with radiographic hand OA (HR=1.584;95CI:0.986-2.546;p-value=0.057). When considered the subgroup of patients with the erosive phenotype, MetS significantly associates with an increased risk (HR=1.821;95CI:1.023-3.241;p-value=0.042)

In terms of severity, MetS associates with an increased number of affected joints (OR=1.735;95%CI=1.102-2.731;p=0.016).

Conclusion:
MetS condition the progression of knee osteoarthritis and is also a risk factor for erosive hand OA; however, its impact in the occurrence of the knee OA is dependent of BMI. The possible role played by hypertension in radiographic hand OA requires further investigation.
War and Arthritis

Rohan Sharma1, Casey Cooper2, Kaustubh Chaudhari3, Sixia Chen4 and R. Hal Scofield5, 1Medicine and Public Health, Univeristy of Oklahoma Health Sciences Center, Oklahoma City, OK, 2Public Health, University of Oklahoma Health Sciences Center, Oklahoma City, OK, 3Medicine, Department of Veterans Affairs Medical Center, Oklahoma City, OK, 4Biostatistics and Epidemiology, University of Oklahoma Health Sciences Center, Oklahoma City, OK, 5Arthritis & Clinical Immunology Program, Oklahoma Medical Research Foundation; Department of Medicine, University of Oklahoma Health Sciences Center; US Department of Veterans Affairs Medical Center, Oklahoma City, OK

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Veterans have increased predilection for multiple health conditions. We undertook this study to investigate the possible association of participation in active military duty in veterans with osteoarthritis.

Since the year 2000, the United States has been involved in two major military conflicts in Afghanistan and Iraq (Operation Enduring Freedom and Operation Iraqi Freedom). The number of troops that have taken part in these interventions is around 2.5 million. There has also been an increase in deployment for female veterans since 2000, with women comprising of over eleven percent of troops deployed. Veterans have a higher predisposition for several health conditions including arthritis. There are however limited data regarding active military duty and its effects on the risk for developing arthritis.

Methods: We analyzed Center for Disease Control and Prevention (CDC) Behavioral Risk Factor Surveillance System (BRFSS) survey data for the years 2000 and 2015 to understand the changes in arthritis prevalence in the veteran population following the two major military conflicts. We compared the prevalence odds ratio for arthritis in the year 2000 versus 2015 amongst male and female veterans as compared to the general population in United States. The data was stratified by sex (Male and Female) and age (18-29, 30-49, 50-69 and over 70) and a weighted analysis was done using Statistical Analysis System (SAS) software.

Results: We found that the odds ratio for arthritis in female veterans for age 18-29 were significantly higher in the year 2015 as compared to the year 2000 (difference in OR=1.54, p=0.008,
95% CI= 2.69 to 0.39). The 2015 odds ratio was also higher in 18-29 male veterans compared to the 2000 odds ratio (difference in OR=0.96, p=0.012, 95% CI= 1.72 to 0.2). The odds ratio for male veterans age 50-69 was also marginally higher as compared to the general population in 2015 (difference in OR=0.4, p= less than 0.001, 95% CI= 0.57 to 0.26). The odds ratios for other age groups for both male and female veterans as compared to the general population between 2000 and 2015 were not significantly different.

**Conclusion:** The prevalence odds ratio for male and female veterans in age 18-29 years have increased significantly from 2000 to 2015 following the two major military interventions.

**Disclosure:** R. Sharma, None; C. Cooper, None; K. Chaudhari, None; S. Chen, None; R. H. Scofield, None.

**Abstract Number:** 2191

**Widespread Regulation of Gene Expression By Glucocorticoids in Chondrocytes from OA Patients As Determined By NGS-Based Genome Wide Expression Analysis**

Antti Pemmari, Erja-Leena Paukkeri, Mari Hämäläinen, Tiina Leppänen and Eeva Moilanen, The Immunopharmacology Research Group, Faculty of Medicine and Life Sciences, University of Tampere and Tampere University Hospital, Tampere, Finland, Tampere, Finland

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** In osteoarthritis (OA), chondrocytes display marked changes in their gene expression profile. Some of these are thought to be protective [e.g. increased synthesis of extracellular matrix (ECM) components] and some harmful (e.g. secretion of proteolytic enzymes and proinflammatory factors). Glucocorticoids (GCs) can counteract many of those harmful changes. Accordingly, intra-articular GC injections are widely used as a symptomatic treatment for OA. However, there are also concerns about their potentially harmful effects, and their comprehensive effect on chondrocyte phenotype remains poorly understood. We studied the effects of GCs on gene expression in OA chondrocytes with genome wide expression analysis based on next generation sequencing (NGS).

**Methods:** Chondrocytes were isolated from cartilage obtained from ten OA patients undergoing knee replacement surgery. The cells were cultured with or without the GC dexamethasone for 24 h. Total mRNA was isolated and sequenced with Illumina HiSeq2500 at the Institute for Molecular Medicine Finland. Functional analysis was performed against the GO (Gene Ontology) database. We also separately investigated the 54 genes linked to OA in recent genome-wide association (GWAS) studies (Loughlin 2015, Wang et al. 2016), as well as those 19 genes previously found to be differentially expressed in OA affected vs. preserved cartilage in a genome wide expression analysis (the RAAK study, Ramos et al. 2014).

**Results:** In dexamethasone-treated chondrocytes, 896 genes were down- and 685 upregulated in a statistically significant manner with a fold change of more than 2.0. Several genes associated with lipid and glucose metabolism as well as those involved in inflammation were among the most strongly affected genes. In the GO analysis, genes involved in ECM organization, cell proliferation and adhesion, and both collagen catabolism and anabolism were enriched among the significantly affected genes. Of note was the downregulation of several matrix degrading enzymes (e.g. MMP1, MMP13 and ADAMTS1) and pro-inflammatory factors (e.g. COX-2, MCP-1 and TNFSF15) but also cartilage-specific collagens (including COL2A1, COL9A1 and COL11A1). Conversely, several anti-inflammatory (e.g. DUSP1, DUSP4) and antioxidative (e.g. KLF9, FOXO3) genes were upregulated. Notably, 11 (COL11A1, FILIP1L, VEGFA, DIO2, COX-2, IGFBP3, VDR, ADAM12, ASPN, GDF5 and IL16) of the 54 genes linked to OA in GWAS studies (Loughlin 2015, Wang et al. 2016), as well as those 19 genes previously found to be differentially expressed in OA affected vs. preserved cartilage in a genome wide expression analysis (the RAAK study, Ramos et al. 2014).

**Conclusion:** The results indicate that GCs regulate the expression of a wide range of genes in OA chondrocytes. In addition to clear anti-inflammatory and antitabatic effects, CGs affect lipid and glucose metabolism in chondrocytes, an observation that might be particularly important in the metabolic phenotype of OA. Further studies are needed to confirm the long-term net effects of these wide-range changes in chondrocyte pathophysiology, as they are induced by a widely used pharmacological treatment.

**Disclosure:** A. Pemmari, None; E. L. Paukkeri, None; M. Hämäläinen, None; T. Leppänen, None; E. Moilanen, None.
Abstract Number: 2192

Association between Mitochondrial DNA (mtDNA) Haplogroups and Bone Marrow Lesions at 24 Months in Osteoarthritis Subjects: Subjects from the Osteoarthritis Initiative

Ignacio Rego-Pérez1, Jean-Pierre Pelletier2, François Abram3, Natividad Oreiro4, Carlos Fernandez-Lopez1, Ana Cecilia Raga1, Francisco J Blanco1 and Johanne Martel-Pelletier2, 1Servicio de Reumatología. Instituto de Investigación Biomédica de A Coruña (INIBIC), Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidad da Coruña (UDC). As Xubias, 15006. A Coruña. España, A Coruña, Spain, 2Osteoarthritis Research Unit, University of Montreal Hospital Research Centre (CRCHUM), Montreal, QC, Canada, 3Medical Imaging Research & Development, ArthroLab Inc., Montreal, QC, Canada, 4Servicio de Reumatología. Instituto de Investigación Biomédica de A Coruña (INIBIC), Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidad da Coruña (UDC). As Xubias, 15006. A Coruña. España, A Coruña, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Bone marrow lesions (BMLs) have been consistently associated with the development of osteoarthritis (OA); however the extent to which they are genetically driven by mitochondrial genetic background is unknown. Since specific mtDNA haplogroups have been associated with decreased risk of incident knee OA, the aim of this work was to examine the associations between mtDNA haplogroups and MRI-detected BMLs.

Methods: Knees that did not develop either incident OA or radiographic progression during 48 months follow-up were identified from 1030 Osteoarthritis Initiative (OAI) subjects. The most common Caucasian mtDNA haplogroups (H, Uk, J, T and Others) were assigned to all participants using the single base extension (SBE) assay. BML measurements from MR images acquired using IW-TSE sequence with sagittal slices in different knee regions were obtained annually between baseline and 24 months using an automated system, and were expressed as % of the bone region. Logistic regression with generalized estimating equations and multinomial logistic regression models were used to evaluate the association between mtDNA haplogroups and i) large BMLs, present at any point between baseline and 24 months and defined as ≥33% of the subregional bone volume, as well as ii) the progression of BMLs at 24 months according to an increase of ±1% volume between baseline and final visit. Both models were adjusted by confounder variables of gender, age and BMI. Participants with haplogroup H served as the reference group.

Results: Participants included in this study had a mean age of 62.43 (sd 9.2), with a percentage of females of 54.1%. Haplogroups for the 1030 participants included H (n=419, 40.7%), J (n=88, 8.5%), T (109, 10.6%), Uk (n=236, 22.9%) and the less common haplogroups “others” (n=178, 17.3%).

Knees of participants with haplogroup J had significantly lower risk of large BMLs in lateral femur (OR=0.545;95%CI:0.299–0.996;p=0.048); in contrast, participants with haplogroup T had significantly increased risk of large BMLs in global tibia (OR=1.500;95%CI:1.020–2.206;p=0.039) and lateral plateau (OR=1.525;95%CI:1.003–2.320;p=0.048). No evidence of a protective or risk effect of any other haplogroup in the odds of large BMLs was detected in the rest of the knee compartments.

In terms of BMLs progression, participants with haplogroup J showed a lower risk of BML progression over time and an increased rate of no change in global femur compartment (OR=0.549;95%CI:0.309–0.977;p=0.041); participants with haplogroup T showed an increased rate of BML regression over time in global knee (OR=2.534;95%CI:1.236–5.195;p=0.011) as well as in medial plateau (OR=1.987;95%CI:1.006–3.925;p=0.048). No other haplogroup was associated with the risk of BML progression for either knee region.

Conclusion: mtDNA haplogroup J appeared to be OA protective, as it is associated with lower risk of large BMLs in lateral femur as well as a lower rate of BML progression over time in global femur. Interestingly, haplogroup T, despite its association with an increased risk of large BMLs, was significantly associated with BML regression rates in the whole knee. Both haplogroups J and T slow down the progression of BMLs.
Physical Activity and Disease Progression in Persons with or at Higher Risk for Knee Osteoarthritis

Prakash Jayabalan1,2, Gerald W. Rouleau1, Masha Kocherginsky1, Dorothy D. Dunlop1, Julia (Jungwha) Lee1, Rowland W. Chang1 and Leena Sharma1, 1Northwestern University, Chicago, IL, 2Shirley Ryan AbilityLab, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The benefits of physical activity in the general population and among persons with knee osteoarthritis (OA) are well-established. However, it remains unclear if inactivity or heavy activity accelerate structural progression of knee OA disease. We tested the hypothesis that objectively measured physical activity is associated with greater risk of radiographic worsening of knee OA.

Methods: In Osteoarthritis Initiative (OAI) participants with or at higher risk for knee OA enrolled in an accelerometer substudy at 48m (analysis baseline), physical activity was measured by a uniaxial accelerometer (ActiGraph GT1M). Radiographic progression was defined primarily as any 48m-96m KL grade worsening. All analyses were knee-level; we used multivariable logistic regression with GEE, adjusting for key covariates.

Results: 1206 persons [mean age 64 yrs (SD 9), 631 (52%) women, BMI 28 (5), sedentary activity 602 minutes (86), light activity 284 minutes (75), moderate-vigorous activity 20 minutes (20)] contributed 1978 knees (at 48m, 57% KL0, 28% KL1, 10% KL2, 5% KL3) to the analysis sample, of which 267 (14%) had KL worsening. As shown in the Table, average daily accelerometer counts were not associated with worsening, nor was any type of physical activity examined in separate models. When sedentary, light, and moderate-vigorous activity were included in the same model, age, sex, BMI, and pain, but no type of activity, were associated with worsening: sedentary, adjusted OR 1.00, 95% CI 0.98, 1.02; light, adjusted OR 1.01, 95% CI 0.99, 1.04; moderate-vigorous, adjusted OR 1.01, 95% CI 0.93, 1.10. In analyses of the sample with full-limb alignment data, findings were similar and further adjustment for alignment had minimal impact. Inclusion of a quadratic term in these models did not reveal any evidence of a U-shaped relationship.

Conclusion: In persons with or at higher risk for knee OA, age, sex, BMI, and pain – but not average daily accelerometer counts or minutes of sedentary, light, or moderate-vigorous activity – were associated with subsequent worsening of KL grade. In this sample, most knees had no or only mild radiographic OA, and time spent in moderate-vigorous activity was relatively low. Whether findings differ in persons with more severe knee OA and/or engaged more frequently in moderate-vigorous activity should be examined in future studies.
Abstract Number: 2194

The Relationship between the Number of Prescription Medications and Physical Activity Amongst Patients with or at High Risk for Knee Osteoarthritis

Nivaas Thanoo1, Abigail Gilbert2, Jing Song3, Dorothy D. Dunlop4 and Rowland W. Chang5, 1Feinberg School of Medicine, Chicago, IL, 2Division of Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL, 3Center for Healthcare Studies, Northwestern University Feinberg School of Medicine, Chicago, IL, 4Inst Hlthcare Studies, Northwestern Univ/ Feinberg, Chicago, IL, 5Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM
**Background/Purpose:** Physical activity amongst individuals with knee osteoarthritis (KOA) has been linked to improved pain, functional status, and less disability. It is important to understand possible barriers to physical activity within this population in order to minimize less favorable health outcomes associated with low levels of physical activity. One possible risk factor for lower physical activity is taking a large number of prescription medications, the side effects of which may reduce physical activity. This study evaluated the relationship between the number of prescription medications taken and moderate-vigorous physical activity.

**Methods:** Adults with or at high risk for KOA from an Osteoarthritis Initiative (OAI) substudy had physical activity assessed by accelerometer monitoring. We used a hierarchical median quantile regression analysis to determine the relationship between the number of prescription medications taken in the 30-days prior to the visit and the median daily minutes of moderate-vigorous (MV) physical activity. Model 1 of the analysis controlled for demographic factors known to affect physical activity (age, gender, race, BMI), model 2 controlled for model 1 variables and disease confounders (Kellgren and Lawrence grade, WOMAC pain), and model 3 additionally controlled for comorbidity confounders (Charlson comorbidity index and high depressive symptoms defined as Center for Epidemiological Studies Depression Scale ≥16).

**Results:** Valid physical activity data and prescription medication data at the 4-year visit were available for 1889 men and women; mean age 65, 55.5% female, 83.9% white, non-Hispanic. A total of 278 (14.7%) participants reported not taking any prescription medications in the 30 days prior to the visit, 1265 (67%) reported 1-5 prescription medications, and 346 (18.3%) reported 6 or more prescription medications. Controlling for demographic factors, we found a decrease of 0.58 minutes in the median daily moderate-vigorous physical activity per additional prescription medication (95% CI -0.87, -0.29; p<0.001). This decrease persisted when additionally controlling for disease confounders (0.53 minutes/prescription medication, 95% CI -0.83, -0.23; p=0.001) and comorbidity confounders (0.52 minutes/prescription medication, 95% CI -0.85, -0.19; p=0.002).

**Conclusion:** Participants taking more prescription medications had lower levels of moderate-vigorous physical activity independent of OA severity and comorbidities. These results show that polypharmacy might be a risk factor for lower physical activity. Future research should explore the relationship between certain medication classes common to KOA patients (e.g. narcotic analgesics, psychotropics, beta-blockers, statins, antihistamines) and physical activity.

**Disclosure:** N. Thanoo, None; A. Gilbert, None; J. Song, None; D. D. Dunlop, None; R. W. Chang, None.


**Abstract Number:** 2195

**The Relationship between Self-Reported Restless Sleep and Objectively Measured Physical Activity**

Abigail Gilbert¹, Julia (Jungwha) Lee², Jing Song³, Pamela Semanik⁴, Linda S. Ehrlich-Jones⁵, C. Kent Kwoh⁶, Dorothy D. Dunlop³ and Rowland W. Chang⁷,⁸, ¹Division of Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL, ²Preventive Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, ³Center for Healthcare Studies, Northwestern University Feinberg School of Medicine, Chicago, IL, ⁴College of Nursing, Rush University, Chicago, IL, ⁵Research CROR, Shirley Ryan AbilityLab, Chicago, IL, ⁶University of Arizona, Tucson, AZ, ⁷Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL, ⁸Preventive Medicine, Medicine, and Physical Medicine & Rehabilitation, Northwestern University Feinberg School of Medicine, Chicago, IL

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Title:** The Relationship between Self-reported Restless Sleep and Objectively Measured Physical Activity

**Background/Purpose:** Despite many health benefits of physical activity, inactivity is endemic among adults, especially those with knee osteoarthritis (KOA). Attempts to sustain long-term increases in physical activity in adults with KOA show limited success. Poor sleep is a potentially powerful modifiable risk factor but is under-investigated as a determinant of physical activity. Sleep may be a novel target to improve physical activity. However the relationship between sleep and physical activity in individuals with KOA remains unknown. We evaluated if participants with greater self-reported restless sleep were more likely to have decreased physical activity.
Methods: The Osteoarthritis Initiative (OAI) enrolled adults with or at high risk for radiographic KOA. Clinical data and physical activity data by accelerometer monitoring were collected at the 4 year follow-up visit. We evaluated weekly minutes of moderate-vigorous activity stratified by responses to the Center for Epidemiological Studies-Depression (CES-D) question on frequency of restless sleep in the past week. Due to skewed distribution, weekly moderate-vigorous physical activity was log-transformed. We repeated the analysis adjusting for potential confounders including age, gender, BMI, KOA severity, Charlson comorbidity score and depressive symptoms (CES-D>16).

Results: Complete data were available for 1900 OAI participants. A total of 169 (9%) reported they experienced restless sleep much of the time (3-4 days in the past week), and 132 (7%) reported restless sleep most or all of the time (5-7 days in the past week). Participants who reported 3-4 days and 5-7 days of restless sleep had 11.1% and 23.8% less weekly minutes of moderate-vigorous activity, respectively, compared to participants reporting restless sleep rarely or none of the time. These results were similar when adjusted for potential confounders with 8.4% and 19.1% less moderate-vigorous activity for restless sleep reported 3-4 days and 5-7 days, respectively, compared to those who rarely reported restless sleep (p for trend 0.0330).

Conclusion: Participants who reported restless sleep much or most of the time performed less moderate-vigorous physical activity than those who rarely reported restless sleep. Some of this effect might be mediated by depression. Future research could focus on characterizing the mechanisms of how poor sleep might result in less physical activity and the possibility of a bidirectional relationship.

Table. Difference* in weekly moderate-vigorous physical activity minutes compared to restless sleep rarely or none of the time

<table>
<thead>
<tr>
<th></th>
<th>Rarely/None of the time (&lt;1 day in the past week)</th>
<th>Some of the time (1-2 days in the past week)</th>
<th>Much of the time (3-4 days in the past week)</th>
<th>Most/all of the time (5-7 days in the past week)</th>
<th>p for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Average weekly activity minutes</strong></td>
<td>130.2</td>
<td>126.1</td>
<td>122.5</td>
<td>96.6</td>
<td></td>
</tr>
<tr>
<td><strong>Unadjusted model</strong></td>
<td>Reference</td>
<td>-1.4% (1.1, 11.6)</td>
<td>-11.1% (34.3, 10.8)</td>
<td>-23.8% (-52.2, -2.2)</td>
<td>0.022</td>
</tr>
<tr>
<td><strong>Adjusted model</strong></td>
<td>Reference</td>
<td>2.3% (8.6, 13.3)</td>
<td>-8.4% (27.8, 10.2)</td>
<td>-19.1% (-42.9, 0.5)</td>
<td>0.033</td>
</tr>
</tbody>
</table>

*Percent difference for each restless sleep category compared to rarely or none of the time.

 Disclosure: A. Gilbert, None; J. Lee, None; J. Song, NIH funding, 2; P. Semanik, NIH funding, 2; L. S. Ehrlich-Jones, None; C. K. Kwoh, NIH/NIAMS, 2, EMD Serono, 2, Abbvie, 2; D. D. Dunlop, NIH funding, 2; R. W. Chang, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-relationship-between-self-reported-restless-sleep-and-objectively-measured-physical-activity

Abstract Number: 2196

An Exploratory Analysis of Physical Activity Levels and the Presence of Bone Marrow Lesions in Adults with Knee Osteoarthritis: Data from the Osteoarthritis Initiative

Amanda R. Canavatchel, Lori Lyn Price, Jeffrey B. Driban, Ming Zhang, Grace H. Lo, and Timothy E. McAlindon, 1Tufts Medical Center, Boston, MA, 2Tufts Clinical and Translational Science Institute, Tufts University, Boston, MA, 3Rheumatology, Tufts Medical Center, Boston, MA, 4Immunology, Allergy, Rheumatology, Baylor College of Medicine, Houston, TX, 5Division of Rheumatology, Tufts Medical Center, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Many people with knee OA have bone marrow lesions (BMLs). BMLs are related with structural pathology and pain. Some investigators have found an association between strenuous physical activity and increased BML volume, leading to a potential increase in pain. Because of the health benefits of exercise, it is important to determine if physical activity could affect pain
levels in patients who have knee OA. The purpose of this study was to determine if physical activity influences the existing relationship between BMLs and pain.

**Methods:** To determine if exercise has an effect on the relationship between BMLs and pain, we performed an exploratory analysis on a sample of 85 knees with BMLs from the Osteoarthritis Initiative (OAI). To determine the presence of a BML, one reader (AC), used customized software to segment the BML volume (patella, tibiofemoral; intraclass correlation coefficient ≥ 0.96) on paired baseline and 24-month MRIs. All MRI scans and measurements were assessed for quality with another reader (JD). To measure physical activity, we used the Physical Activity Scale for the Elderly (PASE). The questions on walking, light sport/recreation, moderate sport/recreation, and strenuous sport/recreation of the Physical Activity Scale for the Elderly (PASE) were used to calculate exercise hours per week. To get a more accurate picture of typical physical activity in our sample, we took the average of 0, 12-, and 24-month exercise hours. To measure pain, we used the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain subscale (range 0-20). A change of 2 points was considered clinically meaningful. We assessed two exercise categories: any vs. none. Spearman correlations were calculated. Ordinal logistic regression was used to assess the relationship between change in WOMAC pain (improved, no change, worsened) and exercise category. We adjusted for age, sex, and BMI.

**Results:** The study population was mostly white (81%), female (58%), and had KL grades 2 (38%) or 3 (53%) at baseline. 63 participants (74%) exercised. Of those who exercised, 96.5% walked, 27.1% participated in light recreation, 38.8% participated in moderate recreation, and 49.4% participated in strenuous recreation for at least one time point. There was no significant difference in the change in WOMAC pain between those who did or did not exercise (p=0.59) (Table 1). In the group that exercised, there was a weak positive correlation (r= 0.27, p=0.037) between total BML at baseline and change in WOMAC pain scores. In the group that did not exercise, there was a weak negative correlation (r= -0.19, p=0.44) between total BML at baseline and change in WOMAC pain score.

**Conclusion:** When adjusted, BMLs are associated with pain, but only among those who exercise. As our population was relatively sedentary, this study may not be generalizable to a population that regularly participates in vigorous exercise.

**Table 1. Frequencies and Odds Ratios between Change in WOMAC Pain Score and Exercise Category**

<table>
<thead>
<tr>
<th>Patient Group^</th>
<th>WOMAC Pain Score Improved by 2 points (%)</th>
<th>No Change in WOMAC pain score (%)</th>
<th>WOMAC Pain Score Worsened by 2 points (%)</th>
<th>Adjusted OR* (CL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise (n=63)</td>
<td>24</td>
<td>37</td>
<td>40</td>
<td>1.2 (0.8, 1.9)</td>
</tr>
<tr>
<td>No Exercise (n=22)</td>
<td>36</td>
<td>32</td>
<td>32</td>
<td>(reference group)</td>
</tr>
</tbody>
</table>

^ All participants had the presence of a BML

*adjusted for age, sex, and BMI

Disclosure: A. R. Canavatchel, None; L. L. Price, None; J. B. Driban, NIAMS-NIH, 2,AXSOME Therapeutics, Inc., 5; M. Zhang, None; G. H. Lo, None; T. E. McAlindon, None.


Abstract Number: 2197

**Systemic Inflammation and Physical Function in Knee Osteoarthritis**

Devyani Misra1, Carrie Brown2, Roger A. Fielding3, Tuhina Neogi4, Michael C. Nevitt5, Cora E. Lewis6, James Torner7 and David T. Felson4, 1Medicine, Section of, Boston University School of Medicine, Boston, MA, 2Boston University School of Public Health, Boston, MA, 3Nutrition, Exercise Physiology and Sarcopenia Laboratory, Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, Boston, MA, 4Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA, 5Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, CA, 6University of Alabama Birmingham, Birmingham, AL, 7University of Iowa, Iowa City, IA
Background/Purpose: Knee osteoarthritis (OA) is a leading cause of functional limitation and disability in older adults. But why some knee OA patients develop functional limitation but not others, is unclear. Systemic inflammation is a strong risk factor for aging-related muscle impairment which can contribute to functional limitation. Modest elevations in measures of systemic inflammation are present in persons with knee OA. We hypothesized that this inflammation might play a role in contributing to OA-related function limitation. We examined the relation of serum TNF-α level (marker of systemic inflammation) with 20 meter walk time and timed chair stands (measures of physical function) in community-dwelling older adults, with and without knee OA.

Methods: We included a subset of participants from the Multicenter Osteoarthritis (MOST) study, a NIH-funded longitudinal cohort of persons with or at risk of knee OA who had assessments of serum TNF-α, knee radiographs, 20m walk time (time to walk 20 meters) and timed chair stands (time to perform chair stands X 5) assessed at baseline visit. Persons with whole knee radiographic OA (ROA, yes/no) were defined by the presence of tibiofemoral (KL grade ≥2) or patellofemoral (osteophytes ≥ 2 or joint space narrowing score (JSN) ≥1 or JSN plus any osteophyte) OA in either or both knees. Persons with symptomatic knee OA (SOA, yes/no) were defined by presence of pain plus ROA in the same knee. To examine the association of serum TNF-α with 20 m walk time and timed chair stands (separate analyses), we performed linear regression, adjusting for age, sex, BMI, physical activity score (PASE) and site, stratified by ROA and SOA status.

Results: Among 953 subjects (55% women, mean± SD age 62 ± 7.7, mean± SD BMI 30 ± 5.4), 494 subjects had ROA (52%) and 276 (30%) had SOA at baseline. We found higher serum TNF-α levels were significantly associated with slower 20 m walk time (Std. β 0.15 ± 0.04) and slower chair stands (Std. β 0.08 ± 0.04), among those with ROA but not in persons without ROA (walk time Std. β 0.02 ± 0.05; chair stands Std. β 0.01 ± 0.05) (Table). Similar significant association between higher serum TNF-α level and slower walk time was found in those with SOA but not those without SOA (Table). Serum TNF-α was not associated with timed chair stands, irrespective of SOA status (Table).

Conclusion: In this large cross-sectional study of community-dwelling older adults, a systemic inflammatory marker was significantly associated with measures of physical function in those with knee OA but not in those without knee OA. Future longitudinal studies are warranted to evaluate whether presence of systemic inflammation leads to development of functional limitation in knee OA.

Table: Cross-sectional association of serum TNF-α with 20 m walk time and timed chair stands by radiographic and symptomatic knee OA status

<table>
<thead>
<tr>
<th>Radiographic OA</th>
<th>N</th>
<th>20m Walk Time</th>
<th>5 Chair Stands</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Std.β ± SE*</td>
<td>p-value</td>
<td>Std.β ± SE*</td>
<td>p-value</td>
</tr>
<tr>
<td>Yes</td>
<td>494</td>
<td>0.15 ± 0.04</td>
<td>0.08 ± 0.04</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>No</td>
<td>459</td>
<td>0.02 ± 0.05</td>
<td>0.01 ± 0.05</td>
<td>0.69</td>
</tr>
<tr>
<td>Symptomatic OA</td>
<td>276</td>
<td>0.25 ± 0.07</td>
<td>0.09 ± 0.09</td>
<td>0.0002</td>
</tr>
<tr>
<td>Yes</td>
<td>258</td>
<td>0.09 ± 0.09</td>
<td>0.31</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>669</td>
<td>0.09 ± 0.07</td>
<td>0.21</td>
<td></td>
</tr>
</tbody>
</table>

*Standardized β co-efficient from linear regression models, adjusted for age, sex, BMI, physical activity and clinic site

Disclosure: D. Misra, None; C. Brown, None; R. A. Fielding, None; T. Neogi, None; M. C. Nevitt, None; C. E. Lewis, None; J. Torner, None; D. T. Felson, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/systemic-inflammation-and-physical-function-in-knee-osteoarthritis

Abstract Number: 2198

Combinatorial Peripheral Blood Inflammatory and MRI-Based Biomarkers Predict Radiographic Joint Space Narrowing in Knee OA
Background/Purpose: Inflammation contributes to OA disease pathogenesis. Subsets of knee OA patients with peripheral blood leukocyte (PBL) detected inflammatory gene expression profiles exhibit more rapid radiographic joint space narrowing (JSN). Bone marrow lesions (BMLs) on baseline knee MRI also predict JSN. We investigated whether the combination of the PBL inflammatory transcriptome(s) together with medial BML enhanced the ability of either alone to predict radiographic knee OA progression.

Methods: PBL inflammatory gene expression (IL-1, TNFα, COX-2) and 3T knee MRI were assessed in 111 patients with symptomatic medial knee OA and BMI<33. At baseline and 24 months, subjects underwent standardized fixed-flexion knee radiographs, scored for joint space width (JSW) by a musculoskeletal radiologist blinded to subject data; a separate, also blinded radiologist scored MRIs for BMLs using the whole-organ MRI scoring method scoring system. JSN was determined as medial JSW change over the study period. Radiographic progressors were defined by various cut-points of JSN (JSN>0.0mm, >0.2mm, and >0.5mm) and were compared to non-progressors (JSN ≤0.0 mm). Logistic regression model was fit with 10-fold cross validation and repeated 100 times. Models were evaluated by area under the receiver operating characteristic curve (AUC) on test data. P values were obtained from DeLong test comparing models’ AUC to 0.5.

Results: Progressors by any JSN cut-point had significantly higher baseline medial BML scores (1.42±2.11, 1.45±2.13 and 1.78±2.23 for JSN>0.0mm, >0.2mm, and >0.5mm, respectively; p=0.025, 0.021, and 0.003) than non-progressors (0.59±1.14). Baseline medial BML scores distinguished progressors by any level of JSN, from non-progressors in multivariate analyses (Table1; AUC 0.61, p=0.025; AUC 0.61, p=0.023, AUC 0.66, p=0.004, for JSN>0.0mm, >0.2mm, and >0.5mm, respectively). Elevated baseline PBL inflammatory gene expression also predicted JSN at all levels of progression, with COX-2 being the strongest predictor (Table 1). The combination of baseline medial BML scores with PBL inflammatory transcriptome markers, especially that of BML and PBL COX-2 expression (AUC 0.78, p<0.001 for JSN >0.5mm), yielded improved predictive power than any of the individual biomarkers alone (Table 1).

Conclusion: The combination of PBL-based inflammatory transcriptome and MRI-based medial BML biomarkers improves the prognostic utility to predict knee OA radiographic progression.
Disclosure: S. Krasnokutsky Samuels, None; H. Zhou, None; M. Attur, None; J. Samuels, None; G. Chang, None; J. Bencardino, None; S. Ma, None; L. Rybak, None; S. B. Abramson, None.


Abstract Number: 2199

Feasibility of a Novel Approach to Studying Early Knee Osteoarthritis: An Offspring Study

Grace H. Lo1, Jane A. Cauley2, Michael T. Strayhorn3, Mary Jansen4, Michael J Hannon5, Donna White6, Stephanie Green7 and C. Kent Kwoh8,9,11 Immunology, Allergy, Rheumatology, Baylor College of Medicine, Houston, TX, 2Department of Epidemiology, Univ of Pittsburgh, Pittsburgh, PA, 3VA HSR&D Center for Innovations in Quality, Effectiveness and Safety; Department of Medicine, Michael E. DeBakey VA Medical Center, Baylor College of Medicine, Houston, TX, 4University of Pittsburgh, Pittsburgh, PA, 5Medicine, University of Pittsburgh, Pittsburgh, PA, 6Baylor College of Medicine, Houston, TX, 7University of Pittsburgh, Houston, PA, 8University of Arizona, Tucson, AZ, 91501 N. Campbell Avenue, Room 8303, The University of Arizona Arthritis Center, Tucson, AZ

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Much of osteoarthritis (OA) research has focused on identifying treatments for late stage disease. However, interventions in early disease may be most effective. Capitalizing on the heritability of knee OA, we assessed the feasibility of using the phenotype of a proband to study risk factors in their offspring. The objectives of this study were: 1) to establish feasibility of deploying such an offspring study within the Osteoarthritis Initiative (OAI) where the proband phenotype is well-characterized, 2) to assess whether this offspring design can detect known risk factors of medial compartment knee OA, and 3) to evaluate exploratory risk factors.
Methods: We selected two groups of proband OAI participants from the University of Pittsburgh site: medial tibiofemoral OA group and no OA group. To preferentially include those more likely to have a heritable etiology of their phenotype, we recruited probands with the same OA phenotype in both knees. The case probands had bilateral medial tibiofemoral OA; control probands had no radiographic evidence of OA in either knee. We only included biological offspring who were ≥18 years old. We approached current OAI participants from the Pittsburgh site who met our eligibility criteria. We developed a privacy-sensitive method of contacting the proband’s offspring to invite them to participate. Willing offspring completed an online survey that assessed OA symptoms and diagnoses as well as known and exploratory risk factors. We calculated the percentage of probands with OA in each strata of the risk factors. To see if OA risk factors in offspring are associated with proband OA status, we used logistic regression models conducted with generalized estimating equations to account for the correlation among offspring related to a given proband.

Results: We established contact with 269/413 (65.1%) potential probands. Most (227/269, 84.4%) had ≥1 eligible biological offspring, with 213/227 (93.8%) willing to share information about the study with their offspring. Our online survey was completed by 185 offspring from 109 probands. Offspring age ranged from 21 – 67 years old (mean=42.9), with 64.9% female, 84.3% White/Caucasian, and mean BMI=23.7 kg/m². Median time to complete survey =14.1 minutes.

Table. Associations of risk factors between offspring and proband OA status.

<table>
<thead>
<tr>
<th>Known OA Risk Factors in the Offspring</th>
<th>% of Probands with bilateral medial TF knee OA</th>
<th>p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heberden’s Nodes Present</td>
<td>13/15 (87%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Heberden’s Nodes Absent</td>
<td>92/170 (54%)</td>
<td></td>
</tr>
<tr>
<td>Overweight</td>
<td>19/61 (69%)</td>
<td>0.07</td>
</tr>
<tr>
<td>Not Overweight</td>
<td>63/124 (51%)</td>
<td></td>
</tr>
<tr>
<td>Obese</td>
<td>20/28 (72%)</td>
<td>0.1</td>
</tr>
<tr>
<td>Not Obese</td>
<td>85/157 (54%)</td>
<td></td>
</tr>
<tr>
<td>Knee Injury</td>
<td>31/51 (61%)</td>
<td>0.5</td>
</tr>
<tr>
<td>No Knee Injury</td>
<td>74/134 (55%)</td>
<td></td>
</tr>
</tbody>
</table>

Exploratory OA Risk Factors in the Offspring

| Regular Cigarette Smoker              | 24/37 (65%)                                | 0.6      |
| Never Regular Cigarette Smoker        | 77/141 (55%)                               |          |
| Diabetes Present                      | 4/7 (57%)                                  | 1.0      |
| Diabetes Absent                       | 99/176 (56%)                               |          |
| Hypertension Present                  | 20/25 (80%)                                | 0.03     |
| Hypertension Absent                   | 84/158 (53%)                               |          |
| Hyperlipidemia Present                | 16/27 (59%)                                | 0.8      |
| Hyperlipidemia Absent                 | 88/157 (56%)                               |          |

Conclusion: Our pilot study establishes feasibility of deploying an offspring study within the OAI using an online survey. Using this design, we detected significant associations between offspring presence of Heberden’s nodes and hypertension, and presence of parental OA. Our findings show good proof of concept for performing an offspring study based out of the OAI.
History of Walking for Exercise Is Not Associated with More Symptomatic Knee Osteoarthritis: Data from the Osteoarthritis Initiative

Grace H. Lo1, Jeffrey B. Driban2, Andrea Kriska3, Timothy E. McAlindon4, Richard Souza5, Nancy J. Petersen6, Bonny Jane Rockette-Wagner7, Charles Eaton8, Marc Hochberg9, Rebecca D. Jackson10, C. Kent Kwoh11, Michael C. Nevitt12 and Maria Suarez-Almazor13, 1Immunology, Allergy, Rheumatology, Baylor College of Medicine, Houston, TX, 2Rheumatology, Tufts Medical Center, Boston, MA, 3University of Pittsburgh, Pittsburgh, PA, 4Division of Rheumatology, Tufts Medical Center, Boston, MA, 5University of California, San Francisco, San Francisco, CA, 6Medicine, Baylor College of Medicine, Houston, TX, 7University of Pittsburgh Medical Center, Pittsburgh, PA, 8Family Medicine and Epidemiology, Warren Alpert Medical School, School of Public Health, Brown University, Providence, RI, 9Department of Medicine, University of Maryland School of Medicine, Baltimore, MD, 10Ohio State University, Columbus, OH, 11University of Arizona, Tucson, AZ, 12Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, CA, 13Section of Rheumatology and Clinical Immunology, Department of General Internal Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA, Houston, TX

First publication: September 18, 2017

SESSION INFORMATION
Walking is recommended for those with knee OA (KOA). However, few studies have explored the association between walking and symptomatic OA, and conflicting data exists whether walking is beneficial or harmful to knee structure. Walking is a weight-bearing exercise and chronic mechanical overloading could physically damage knee structures. Alternatively, people who walk are likely to have a lower body mass index (BMI), which is protective of KOA. Therefore, we evaluated the relationship of history of walking with symptomatic KOA in the Osteoarthritis Initiative (OAI).

Methods:

This is a cross-sectional study of OAI participants with knee x-rays, symptom assessments, and lifetime physical activity. At the 96-month visit, a modified version of the Lifetime Physical Activity Questionnaire (LPAQ) asked participants about the number of times they walked for exercise from ages 12 – 18, 19 – 34, 35 – 49 and >50 years old. This information was used to create biologically meaningful groups based on walking history. The lowest group were people who did not walk for exercise. The highest group included the top one or two levels of walking. We pooled the number of times people walked from all time periods. PA semi-flexed knee radiographs were obtained at OAI 48-month visit and scored for Kellgren-Lawrence (KL) grade (0-4). Radiographic OA (ROA) was defined as KL ≥ 2. Frequent knee pain within a person required at least one knee have frequent knee pain at the OAI 48-month visit. Symptomatic radiographic OA (SOA) required that at least one knee had both ROA and frequent knee pain. Anyone with a total knee replacement was classified as having SOA. We performed logistic regression with the predictor of groups based walking history over a lifetime and in the specific age ranges. The outcomes were ROA, frequent knee pain, and SOA; adjusted analyses included covariates age, sex, and BMI at the 48-month visit and injury up to the 48-month visit.

Results:

2637 participants were included, 44% were male, mean age was 64.3 (8.9) years and BMI was 28.4 (4.9) kg/m² at the 48 month visit. Walking for exercise increased with increasing age. The percentage of obesity by lifetime walker group (never walker to high level walker) was: 41%, 39%, 33%, and 30% respectively. Findings for frequent knee pain and ROA were similar for SOA.
Table. Odds Ratios of Prevalent Symptomatic OA By Walking Level (lowest to highest).

<table>
<thead>
<tr>
<th>Walking Time Period</th>
<th>Prev. of Frequent SOA</th>
<th>Unadjusted Odds Ratios</th>
<th>Adjusted Odds Ratios*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walking over a lifetime</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-walker (n = 493)</td>
<td>31.2%</td>
<td>Referent</td>
<td>Referent</td>
</tr>
<tr>
<td>Low (n = 694)</td>
<td>26.7%</td>
<td>0.80 (0.62-1.03)</td>
<td>0.85 (0.65-1.10)</td>
</tr>
<tr>
<td>Middle (n = 711)</td>
<td>29.8%</td>
<td>0.94 (0.72-1.20)</td>
<td>1.03 (0.79-1.34)</td>
</tr>
<tr>
<td>High (n = 708)</td>
<td>23.2%</td>
<td>0.66 (0.51-0.86)</td>
<td>0.74 (0.57-0.97)</td>
</tr>
<tr>
<td>p for trend=0.01</td>
<td></td>
<td>p for trend=0.11</td>
<td></td>
</tr>
</tbody>
</table>

| Ages 12 – 18 years old |                       |                        |                       |
| Non-walker (n = 1512) | 28.4%                 | Referent               | Referent              |
| Low (n = 434)         | 27.7%                 | 0.97 (0.76-1.22)       | 1.00 (0.78-1.28)      |
| High (n = 660)        | 25.2%                 | 0.85 (0.69-1.05)       | 0.85 (0.69-1.06)      |
| p for trend=0.13      |                       | p for trend=0.16       |                       |

| Ages 19 – 34 years old |                       |                        |                       |
| Non-walker (n=1369)   | 27.9%                 | Referent               | Referent              |
| Low (n = 355)         | 27.0%                 | 0.96 (0.74-1.25)       | 1.00 (0.76-1.32)      |
| Middle (n = 412)      | 27.7%                 | 0.99 (0.77-1.26)       | 1.02 (0.79-1.32)      |
| High (n = 470)        | 26.1%                 | 0.92 (0.72-1.16)       | 0.94 (0.74-1.21)      |
| p for trend=0.5       |                       | p for trend=0.7        |                       |

| Ages 35 – 49 years old |                       |                        |                       |
| Non-walker (n=1102)   | 30.0%                 | Referent               | Referent              |
| Low (n = 470)         | 28.9%                 | 0.95 (0.75-1.20)       | 1.02 (0.80-1.32)      |
| Middle (n = 415)      | 25.3%                 | 0.79 (0.61-1.02)       | 0.84 (0.64-1.10)      |
| High (n = 619)        | 23.1%                 | 0.70 (0.56-0.88)       | 0.76 (0.60-0.96)      |
| p for trend=0.001     |                       | p for trend=0.01       |                       |

| Ages > 50 years old   |                       |                        |                       |
| Non-walker (n = 693)  | 32.9%                 | Referent               | Referent              |
| Low (n = 651)         | 25.4%                 | 0.69 (0.55-0.88)       | 0.75 (0.58-0.96)      |
| Middle (n = 596)      | 26.0%                 | 0.72 (0.56-0.91)       | 0.81 (0.63-1.04)      |
| High (n = 666)        | 25.1%                 | 0.68 (0.54-0.86)       | 0.79 (0.62-1.01)      |
| p for trend=0.003     |                       | p for trend=0.09       |                       |

*Adjusted for age, sex, BMI, and prior knee injury.

Conclusion:

Our findings suggest walking for exercise at any time in life is not associated with a higher odds of prevalent ROA, knee pain, and SOA later in life. Walking for exercise may be beneficial but this may be obscured due to confounding by indication. Because people self-select whether they walk, they may stop the activity because of knee symptoms. Walking for exercise was more common with increasing age and was inversely associated with obesity. Walking for exercise does not appear detrimental, and may be protective of SOA.

Disclosure: G. H. Lo, None; J. B. Driban, None; A. Kriska, None; T. E. McAlindon, None; R. Souza, None; N. J. Petersen, None; B. J. Rockette-Wagner, None; C. Eaton, None; M. Hochberg, None; R. D. Jackson, None; C. K. Kwoh, None; M. C. Nevitt, None; M. Suarez-Almazor, None.


Abstract Number: 2201
Baseline Periarticular Tibial Knee Bone Mineral Density Is Associated with Change in Static Alignment

Grace H. Lo1, Jeffrey B. Driban2, Michael T. Strayhorn3, Lori Lyn Price4, Charles Eaton5 and Timothy E. McAlindon6, 1Immunology, Allergy, Rheumatology, Baylor College of Medicine, Houston, TX, 2Rheumatology, Tufts Medical Center, Boston, MA, 3VA HSR&D Center for Innovations in Quality, Effectiveness and Safety; Department of Medicine, Michael E. DeBakey VA Medical Center, Baylor College of Medicine, Houston, TX, 4Tufts Clinical and Translational Science Institute, Tufts University, Boston, MA, 5Family Medicine and Epidemiology, Warren Alpert Medical School, School of Public Health, Brown University, Providence, RI, 6Division of Rheumatology, Tufts Medical Center, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Relative local knee periarticular bone mineral density (paBMD) as measured by dual x-ray absorptiometry (DXA) has been associated with static alignment cross-sectionally, but not longitudinally; we postulated that there would be an association. We evaluated the association of paBMD with femur-tibial angle (FTA) within the Osteoarthritis Initiative (OAI).

Methods:
We performed a longitudinal study of a subgroup of the incidence subcohort of the OAI who had right knee DXA scans from both the 72-month and 96-month visits, generating knee medial:lateral paBMD ratios focused on the tibial plateau. Also, participants had to have radiographs read for FTA at the 72- and 96- month visits (negative value = greater varus) and 48-month readings of Kellgren and Lawrence (KL) grade, where grade ≥ 2 was considered as having ROA. Stratified by ROA status, we performed Spearman’s correlations of: 72- month paBMD ratio and FTA, as well as the 72- to 96- month change in paBMD ratio and FTA.

Results: 400 participants, 54% female, were included with a mean age of 65.0 (8.2) years and BMI of 28.3 (4.9) kg/m^2.

Among those with no ROA based on the 48 month radiographs, n = 168, mean 72- month paBMD ratio was 1.09 (0.09) and FTA was -5.26 (1.66) (varus). Mean change from 72- to 96- month paBMD ratio was 0.00 (0.05) and FTA was -0.04 (0.83) (varus). Spearman correlations are presented in table 1.

Among those with ROA based on the 48 month radiographs, n = 232, mean 72- month paBMD ratio was 1.12 (0.13) and FTA was -5.43 (2.77) (varus). Mean change from 72- to 96- month paBMD ratio was 0.00 (0.06) and FTA was -0.04 (0.80) (varus). Spearman correlations are presented in table 2.

Table. Spearman’s Correlations of paBMD and Static Alignment
<table>
<thead>
<tr>
<th></th>
<th>paBMD Ratio</th>
<th>FTA</th>
<th>paBMD Ratio Difference</th>
<th>FTA Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>No ROA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>paBMD Ratio</td>
<td>1.00</td>
<td>-0.22</td>
<td>-0.016</td>
<td>0.25</td>
</tr>
<tr>
<td>FTA</td>
<td>1.00</td>
<td>0.08</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>paBMD Ratio Difference</td>
<td>1.00</td>
<td>-0.05</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FTA Difference</td>
<td>1.00</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ROA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>paBMD Ratio</td>
<td>1.00</td>
<td>-0.60</td>
<td>-0.11</td>
<td>0.23</td>
</tr>
<tr>
<td>FTA</td>
<td>1.00</td>
<td>0.10</td>
<td>-0.10</td>
<td></td>
</tr>
<tr>
<td>paBMD Ratio Difference</td>
<td>1.00</td>
<td>-0.06</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FTA Difference</td>
<td>1.00</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

For each cell correlation coefficients are provided with the p-values below.

**Conclusion:** Baseline paBMD was associated with change in static alignment in those without and with OA. However, baseline static alignment was not associated with change in paBMD and change in paBMD was not associated with change in static alignment. Perhaps this is evidence that change in paBMD precedes altered static alignment in the natural history of OA. These findings support the idea that paBMD changes occur early in the natural history of OA and holds the promise of being a good marker for early disease.

**Disclosure:** G. H. Lo, None; J. B. Driban, None; M. T. Strayhorn, None; L. L. Price, None; C. Eaton, None; T. E. McAlindon, None.


**Abstract Number:** 2202


Young Bin Joo¹, Joo-Hyun Lee², Minkyung Han³, Seong-Ryul Kwon⁴, Won Park⁵, Kyung-Su Park⁶, Bo Young Yoon⁷ and Kyong-Hee Jung⁸, ¹Internal Medicine, Department of Rheumatology, St. Vincent's Hospital, The Catholic University of Korea, Suwon, Gyeonggido, Korea, Republic of (South), ²Rheumatology, Inje University Ilsan Paik Hospital, Goyang, Korea, Republic of (South), ³Public health, Yonsei University graduate school, Seoul, Korea, Republic of (South), ⁴Rheumatology, Inha University, Incheon, Korea, Republic of (South), ⁵Medicine/Rheumatology, Inha University Hospital, Incheon, Korea, Republic of (South), ⁶Internal Medicine, St. Vincent's Hospital, The Catholic University of Korea, Suwon, Korea, Republic of (South), ⁷Rheumatology/Internal medicine, Inje University Ilsan Paik Hospital, Goyang, Korea, Republic of (South)

**First publication:** September 18, 2017

**SESSION INFORMATION**
*Session Date:* Tuesday, November 7, 2017
*Session Title:* Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies
*Session Type:* ACR Poster Session C
*Session Time:* 9:00AM-11:00AM

**Background/Purpose:**
Osteoarthritis (OA) is the most common form of arthritis, caused by a combination of systemic and local factors. Its multi-factorial etiology includes oxidative stress and the overproduction of reactive oxygen species (ROS). Previous researchers tried to investigate the role of ROS pathway to reveal the pathogenesis of OA. Oxidative balance score (OBS), which is based on the summed intake of various pro-oxidants and anti-oxidants, is well known to reflect oxidative stress in an individual. Recent studies have investigated the
associations between OBS and several chronic diseases, including prostate cancer, colorectal cancer, and the risk of cardiovascular disease and end-stage renal diseases. However, the association between OBS and OA has not been studied. This study aimed to investigate the association between OBS and OA and between OBS and quality of life in patients with OA.

Methods:

Using the Korea National Health and Nutrition Examination Survey (KNHANES) VI (2014–2015) program, OBS was calculated by combining 10 pro- (polyunsaturated fatty acid, omega-6, smoking, alcohol, BMI) and anti-oxidant (carotene, retinol, vitamin C, omega-3, physical activity) factors through baseline nutritional and lifestyle assessment. OBS was divided into quartiles (Q1–Q4), considering the lowest quartile, Q1 (predominance of pro-oxidants), as a reference. Multivariable logistic regression was used to estimate adjusted odds ratios (ORs) for OA and EuroQol five dimensions questionnaire (EQ-5D) in patients with OA after adjusting for demographic factors and comorbidities.

Results:

Among the 14,930 participants, 296 patients with OA and 1,309 controls were included in the analysis. Patients with OA had lower OBS than that of controls (17.04 ± 0.22 and 17.08 ± 0.12, respectively), although there was no statistically significant difference between the groups. Especially, patients with OA had significantly lower anti-oxidant OBS than that of controls (p<0.01). The OR of dietary anti-oxidant OBS was 0.92 (95% confidence interval 0.87–0.97) and that of non-dietary lifestyle anti-oxidant (physical activity) OBS was 0.82 (0.71–0.94). In a logistic regression model to assess the association of OBS with OA, the adjusted OR for EA was 0.95 (0.91–1.00). Moreover, the adjusted OR for higher EQ5D was 1.17 (1.06–1.30) in patients with OA.

Conclusion:

Higher OBS was associated with a lower risk of OA. Among the OBS items, lower physical activity had the greatest contribution to the risk of OA. In addition, higher OBS was associated with better quality of life in patients with OA.

Disclosure: Y. B. Joo, None; J. H. Lee, None; M. Han, None; S. R. Kwon, None; W. Park, Celltrion Inc., 5; K. S. Park, None; B. Y. Yoon, None; K. H. Jung, None.


Abstract Number: 2203

Association of Hip Bone Geometry and Volumetric Density with Hip Osteoarthritis

Johann Grapinet1, Jean-Baptiste Pialat1, mathilde Proriol1, Pawel Szulc2, Eric Lespessailles3 and Roland Chapurlat4, 1INSERM UMR 1033, LON, France, 2Epidemiology of Osteoporosis, INSERM UMR 1033, Lyon, France, 3University Orleans, Orleans, France, 4INSERM 1033, University of Lyon, E. Herriot Hospital, Hospices Civils de Lyon, Lyon, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Hip osteoarthritis (OA) is a major public health concern. It is associated with hip pain, functional decline and possibly increased cardiovascular mortality. The determinants of hip OA, however, are not as well understood as those of other OA sites, such as the knee. Therefore, we sought whether hip geometry, bone mineral density and microarchitecture were associated with hip OA.

Methods:

We have studied 1537 post-menopausal women from the QUALYOR prospective cohort. At baseline, we measured areal BMD by DXA at the lumbar spine and the hip, volumetric BMD and geometry by hip quantitative computerized tomography (QCT) scan using the Bone Investigational Toolkit (BIT) software, and microarchitecture at the distal radius and tibia by high resolution peripheral quantitative tomography (HRpQCT). We built a hip OA score (CT OA score) with images from the hip CT, based on the depiction of the
four major signs of osteoarthritis: increased density of the subchondral bone, joint space narrowing, osteophytes and subchondral cysts. The severity of each of these four signs was graded as absent, light, moderate or severe (semi-quantitative score ranging from 0 to 3 for each sign thus 0 to 12 in total). Women with and without hip OA were compared by way of analysis of variance and multivariable modeling.

Results:

The mean age was 65.9 and the mean body mass index was 24.6. Among these 1537 women, 670 had a OA score of 0, 710 between 1 and 4 (mild OA) and 157 greater than 4 (severe OA). Women with severe osteoarthritis had significantly higher areal BMD at the lumbar spine (0.866 vs 0.875, p <0.05) and the femoral neck (0.656 vs 0.671, p <0.005); significantly higher area (30.74 vs 31.95, p <0.001) and volume (85.58 vs 89.90, p <0.001) of the hip and lower trabecular hip BMD (128.1 vs 123, p<0.001). Cortical hip BMD did not differ between women with and without hip OA (964.5 vs 969, p =0.45). The BIT analysis showed higher parameters of bone resistance (CSA with 8.36 vs 8.91, CSMI with 5.68 vs 6.51 and Z polar with 7.66 vs 8.4, p <0.001) at the OA femoral neck, more important trochanter, femoral and global width and hip axis length, and a significantly lower cortical thickness. In multivariable analysis, parameters most strongly related to severe OA were the trabecular and cortical volumes of the femoral neck, in the dominant and non-dominant hip. No difference was observed in peripheral bone microarchitecture between hip OA patients and non OA individuals.

Conclusion:

Women with hip OA have a bigger femoral neck, suggesting a sizeable role of bone geometry in the pathophysiology of hip OA.

Disclosure: J. Grapinet, None; J. B. Pialat, None; M. Proriol, None; P. Szulc, None; E. Lespessailles, None; R. Chapurlat, None.


Abstract Number: 2204

Neuropathic Pain in Patients with Knee Osteoarthritis and Related Factors: A Multicenter Longitudinal Study-Preliminary Report

Ece Kaptanoglu¹, Ozlem Şahin², Tiraje Tuncer³, Sami Hizmetli¹, Lale Altan⁴, Figen Ayhan⁵, Ajda Bal⁶, Meral Bilgilosoy⁷, Gulnur Boybas⁸, Lale Cerrahoglu⁹, Remzi Cevik¹⁰, Tuncay Duruoz¹¹, Deniz Dulgeroglu⁶, Gulcan Gurur¹², Savas Gursoy¹³, Simin Hepguler¹⁴, Cahit Kacar¹⁵, Tacisier Kaya¹⁶, Meltem Melikoglu¹⁷, Kemal Nas¹⁸, Suheda Ozczakir¹⁹, Senay Ozdolap⁰, merih Saridogan²¹, Selda Sarikaya⁰, Dilsad Sindel²², Omer F Şendur⁸, Canan Tikiz²³ and Hatice Ugurlu²⁴, ¹Department of Physical Medicine and Rehabilitation, Division of Rheumatology, Cumhuriyet University School of Medicine, Sivas, Turkey, ²Department of Physical Medicine and Rehabilitation, Cumhuriyet University School of Medicine, Sivas, Turkey, ³Department of Physical Medicine and Rehabilitation, Akdeniz University School of Medicine, Antalya, Turkey, ⁴Department of Physical Medicine and Rehabilitation, Division of Rheumatology, Uludag University School of Medicine, Bursa, Turkey, ⁵Department of Physical Medicine and Rehabilitation, University of Health Ankara Training and Research Hospital, Ankara, Turkey, ⁶Department of Physical Medicine and Rehabilitation, University of Health Sciences Diskapi Yildirim Beyazit Training and Research Hospital, Ankara, Turkey, ⁷Department of Physical Medicine and Rehabilitation, University of Health Sciences Antalya Training and Research Hospital, Antalya, Turkey, ⁸Department of Physical Medicine and Rehabilitation, Adnan Menderes University School of Medicine, Aydin, Turkey, ⁹Department of Physical Medicine and Rehabilitation, Celal Bayar University School of Medicine, Manisa, Turkey, ¹⁰Department of Physical Medicine and Rehabilitation, Dicle University School of Medicine, Diyarbakir, Turkey, ¹¹Department of Physical Medicine and Rehabilitation, Division of Rheumatology, Marmara University School of Medicine, Istanbul, Turkey, ¹²Department of Physical Medicine and Rehabilitation, Division of Rheumatology, Adnan Menderes University School of Medicine, Aydin, Turkey, ¹³Department of Physical Medicine and Rehabilitation, Gaziantep University School of Medicine, Gaziantep, Turkey, ¹⁴Department of Physical Medicine and Rehabilitation, Ege University School of Medicine, Izmir, Turkey, ¹⁵Department of Physical Medicine and Rehabilitation, Division of Rheumatology, Akdeniz University School of Medicine, Antalya, Turkey, ¹⁶Department of Physical Medicine and Rehabilitation, University of Health Sciences Izmir Bozyaka Training and Research Hospital, Izmir, Turkey, ¹⁷Department of Physical Medicine and Rehabilitation, Division of Rheumatology, Ataturk University School of Medicine, Erzurum, Turkey, ¹⁸Department of Physical Medicine and Rehabilitation, Sakarya University School of Medicine, Sakarya, Turkey, ¹⁹Department of Physical Medicine and Rehabilitation, Uludag University School of Medicine, Bursa, Turkey, ²⁰Department of Physical Medicine and Rehabilitation, Bulent Ecevit University School of Medicine, Zonguldak, Turkey, ²¹Department of Physical Medicine and Rehabilitation, Istanbul University Cerrahpasa School of Medicine, Istanbul, Turkey, ²²Department of Physical Medicine and Rehabilitation, Istanbul University Istanbul
Background/Purpose:

Neuropathic pain (NP) was accused for increased pain and reduced functional capacity in knee osteoarthritis (KO). Here we aimed to find out the prevalence of neuropathic pain and its relationship with gender, age, body mass index (BMI), pain, symptom duration and functional status in patients with KO.

Methods:

713 patients with KO were included in the study from the multicenter national cohort conducted by the Turkish League Against Rheumatism-Osteoarthritis Study Group. Sociodemographic variables, BMI, and duration of symptoms were recorded. Pain severity was measured by visual analog scale (VAS), neuropathic pain was assessed by PainDETECT questionnaire and Western Ontario and McMaster Universities Arthritis Index (WOMAC) questionnaire and timed up and go test were used for functional evaluation, and somatosensory dysfunction and characteristics of pain (night pain, relief of pain on rest, pain on motion, aggravation of symptoms with cold) were also questioned.

Results:

The mean age of the patients with KO were 63.29± 9.53 and 83.9 % were female, 16.1% were male, mean duration of symptoms was 80.73±86.59 months (1-720 months), and BMI was 31.5±5.4. NP was found in 20.9 % of the patients and 19.2% of the patients were in the unclear range according to PainDETECT. The age, gender and symptom duration of patients were comparable in patients with or without NP. BMI (31.2±5.4 vs 32.0±5.4, p= 0.016), pain severity (6.35±0.12 vs 6.77±0.29, p=0.004), WOMAC function [31 (3-80) vs 43 (5-106), p=0.036] and WOMAC stiffness [3 (0-16) vs 4 (0-8), p=0.014] scores, night pain (68.4% vs 31.5%, p=0.001) and aggravation of symptoms by cold (70.4% vs 29.5%, p=0.032) were higher in KO patients with NP. There was no difference between the WOMAC total, WOMAC pain and timed up and go test scores, somatosensory dysfunction, relief of pain on rest and pain on motion of the patients with or without NP.

Conclusion:

BMI and pain severity were higher in KO patients with NP and may probably provoke neuropathic pain which in turn decreases functional capacity. Night pain and aggravation of symptoms with cold may also be related to neuropathic pain.

Disclosure: E. Kaptanoglu, None; O. Şahin, None; T. Tuncer, None; S. Hizmetli, None; L. Altan, Amgen, MSD; Roche, Abvie,UCB, Pfizer, 9; F. Ayhan, None; A. Bal, None; M. Bilgilişoy, None; G. Bozbas, None; L. Cerrahoglu, None; R. Cevik, None; T. Duruoz, AbbVie, Sanovel, 9; D. Dulgeroglu, None; G. Gurer, None; S. Gursoy, None; S. Hizmetli, None; L. Kaya, None; M. Melikoglu, None; K. Nas, None; S. Ozcaikir, None; S. Ozdolap, None; M. Saridogan, None; S. Sarikaya, None; D. Sindel, Amgen, Novartis and Sandoz, Lilly, 9; O. F. Şendur, None; C. Tikiz, None; H. Ugurlu, None.

Trajectories of Knee Bone Shape Change Are Associated with Sex and Osteoarthritis

Barton L Wise1, Jingbo Niu2, Yuqing Zhang3, Felix Liu4, Joyce Pang5, John A. Lynch6 and Nancy E. Lane7, 1Orthopaedics, Internal Medicine, University of California, Davis School of Medicine, Sacramento, CA, 2Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA, 3School Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, 4Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, CA, 5University of Nevada, Reno, Reno, NV, 6Department of Epidemiology and Biostatistics, University of California, San
Knee osteoarthritis (OA) is more common in women than men; however, the biological mechanisms for sex difference in knee OA are not well understood. Bone shape is a strong risk factor for hip OA, and studies have found a relation with knee OA. The purpose of the present study was to describe knee bone shape changes over time and to examine whether sex is associated with change of bone shape.

Methods: We used data collected from the NIH-funded Osteoarthritis Initiative (OAI), a cohort of persons aged 45-79 at baseline who either had symptomatic knee OA or were at high risk of it. We selected a random sample of 473 knees with radiographs present at baseline, 2 years and 4 years at follow-up visits regardless of OA status. We outlined distal femur and proximal tibia shape on radiographs at all three time points using Statistical Shape Modeling. Group-based trajectory modeling was employed to identify distinctive patterns of bone shape change for each mode. We examined the association between sex and radiographic OA at baseline with trajectories of each bone shape mode using multivariable polytomous regression model while adjusting for age, BMI, race, and results for the first modes for femur and tibia are presented here.

Results: The mean age was 59.9 years (±9.3 SD) for the subjects; the proportion of women was 53.8%. Thirteen modes were derived for proximal tibial shape and for distal femoral shape, accounting for 95.5% of the total variance. In all modes, three distinct trajectory groups were derived with the mean posterior probabilities ranging from 84.3% to 98.8%, indicating excellent model fitting. For the majority of both femoral and tibial modes, the slopes of change were mostly similar within each mode but the intercepts for the 3 trajectory subgroups were different. For femur mode 1, which explained the greatest amount of variance of shape, subgroup mode values decreased slightly over time (see figure); compared with group 1, trajectory subgroup 3 was more likely to include a knee from a woman (OR=28.8, 95% CI: 12.4, 67.1) as was subgroup 2 (OR=4.6, 95%CI: 2.7, 7.9); subgroup 3 was less likely to include knees with OA (OR=0.66; 95%CI 0.56, 0.80), as was subgroup 2 (OR=0.8; 95%CI: 0.7, 0.9). For mode 1 in the tibia, subgroup mode values remained constant over time; compared with group 1, trajectory subgroup 3 was less likely to include womens’ knees (OR=0.6; 95% CI 0.3, 1.1; NS), as was subgroup 2 (OR=0.5; 95%CI 0.3, 0.9); knees with OA were more likely in group 3 (OR=1.3; 95%CI: 1.3, 1.6), but no difference was observed in trajectory membership between groups 2 and 1 for knees with OA.

Conclusion: The shapes of the distal femur and proximal tibia change little over time but do divide into separate trajectory groups largely due to baseline differences that propagate across the years. The trajectory subgroups are associated with both sex and knee OA.
Healthy Weight Loss Is Associated with Improved Pain and Function over 8 Years in Overweight Subjects with Knee Osteoarthritis: Data from the Osteoarthritis Initiative

Naoko Onizuka¹ and Anna K. Shmagel², ¹Medicine, University of Minnesota, Minneapolis, MN, ²Rheumatic & Autoimmune Diseases, University of Minnesota, Minneapolis, MN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: In clinical trials, weight loss was associated with improvement in knee osteoarthritis (OA) pain and function up to 18 months of follow up. However, clinical trials are performed under highly controlled conditions, and may not be representative of long-term effects in community settings. The aim of this study was to investigate the effects of healthy weight loss on knee pain and function over long-term follow up in a pragmatic cohort setting.

Methods: Participants from the Osteoarthritis Initiative progression cohort with a baseline Kellgren-Lawrence grade ≥2 in either knee, and baseline BMI≥25 were selected. Weight and WOMAC scores were followed for up to 8 years, along with demographic data, depression scores, physical activity indicators, pain medication use, and pain in other joints. Weight loss modality was reported retrospectively at 8 years by participants who lost weight during the study period; subjects who reported unhealthy weight loss were excluded. Linear mixed effects models were used for analyses.

Results: Nine hundred and fifty six patients were enrolled. Over 8 years, weight was stable (within 5% margin) in 60% of subjects, 17% of subjects lost ≥5% of weight, and 24% of subjects gained ≥5% of weight. Weight change trends were gradual and linear for both weight loss and gain. Those who lost ≥5% of their weight had improved WOMAC scores over 8 years compared with the weight stable group: -4.2 points in an unadjusted model (p=0.006), and -3.9 in a fully adjusted model (adjusted for age, gender, race, depression score, baseline BMI, pain medication use, PASE, and pain in other joints, p=0.01). Within the weight loss group, there was no statistically significant difference in WOMAC in ≥10% weight loss vs 5-10% weight loss: -4.8 points in unadjusted model (p=0.2) and -4.4 (p=0.24) in fully adjusted model.

Conclusion: In overweight community adults, healthy, gradual weight loss of ≥5% was associated with improved knee pain and function over 8 years. There was no added benefit for losing ≥10% of weight.

Disclosure: N. Onizuka, None; A. K. Shmagel, None.


Abstract Number: 2207

Urine CTX-II, CTX-I, Osteocalcin, and Radiographic Severity of Multiple OA Knee Joints: Does CTX-II Originate from Bone or Cartilage?

Asger R. Bihlet¹, Inger Byrjalsen², Anne C. Bay-Jensen³, Jeppe Andersen⁴, Claus Christiansen¹, Bente J. Riis¹ and Morten Asser Karsdal³, ¹Nordic Bioscience, Clinical Development, Herlev, Denmark, ²Nordic Bioscience, Herlev, Denmark, ³Rheumatology, Nordic Bioscience, Herlev, Denmark, ⁴Clinical Development, Nordic Bioscience, Herlev, Denmark

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM
Background/Purpose: Excessive cartilage degradation is a known characteristic of osteoarthritis (OA), and several methods of quantification of cartilage degradation exist. Biomarkers such as urinary C-telopeptide fragments resulting from inflammatory destruction of collagen type II (uCTX-II) have been shown to be associated with disease severity and pain in OA, yet the tissue-origin of uCTX-II has been disputed.

The purpose of this analysis was to investigate the potential association between OA in single and multiple joints at different radiographic stages on circulating levels of uCTX-II and biomarkers of bone resorption and bone formation; serum and urine C-telopeptide of collagen type I, CTX-I, and serum osteocalcin, respectively.

Methods: Pooled, pre-treatment baseline data of two phase III randomized clinical trials (NCT00486434 and NCT00704847) in patients with radiographic OA of at least one knee joint were analyzed post-hoc. Key inclusion criteria were knee OA with a Kellgren and Lawrence (KL) score of 2 or 3, and pain of at least 150 mm out of 500 mm using the WOMAC pain subscore, of at least one knee. A subgroup with available urine samples (N=1200) was analyzed for this report. Baseline levels of serum and urine CTX-I, urine CTX-II and serum osteocalcin were analysed using validated enzyme-linked immunosorbent assays and analyzed for associations with combined KL-scores for both knees, and cumulative KL-scores to assess the individual biomarker contribution of joints at different disease stages using multiple pairwise comparisons. KL score of 0 was defined as absence of OA, while all knees with KL scores of ≥ 1 were defined as OA joints.

Results: Unilateral knee OA was present in 4.1 % of patients in the study. 63.1 % of patients had bilateral, early OA, 10.1 % had bilateral late OA, and 22.0 % had bilateral OA of mixed stages. No patients had unilateral OA with late stage disease. Patients with bilateral, late-stage OA had significantly higher levels of uCTX-II compared to patients with earlier OA. The presence of at least one KL-4 joint appeared to markedly increase the level of CTX-II regardless of the KL-score of the contralateral knee joint. Levels of CTX-I and osteocalcin were not significantly different between KL-grades.

Conclusion: These results confirm that levels of uCTX-II are associated with radiographic severity of OA, while biomarkers of bone turnover was not. Multiple joints appear to contribute to uCTX-II levels in an incremental manner according to radiographic severity of individual joints.

Figure 1

Association between geometric mean concentration of uCTX-II, sCTX-I and osteocalcin and Kellgren-Lawrence radiographic stage in the knees of 1200 OA patients. Asterisks indicate statistically significant (p<0.05) difference to the group of subjects with the lowest cumulative KL-score, i.e. a KL-grade of 0 in one knee and 2 in the other (“0-2”).

Disclosure: A. R. Bihlet, Nordic Bioscience Diagnostic, 3; I. Byrjalsen, Nordic Bioscience Diagnostic, 3; A. C. Bay-Jensen, Nordic Bioscience Diagnostic, 3; J. Andersen, Nordic Bioscience Diagnostic, 3; C. Christiansen, Nordic Bioscience Diagnostic, 3; B. J. Riis, Nordic Bioscience Diagnostic, 3; M. A. Karsdal, Nordic Bioscience Diagnostic, 3.

A Novel Omeract MRI Scoring System Providing Insights in the Association of MRI Synovitis and Bone Marrow Lesions with Pain in Thumb Base Osteoarthritis

F.P.B. Kroon, S. van Beest, W. Damman, R. Liu, J.L. Bloem, M. Reijnierse and M. Kloppenburg, 1 Rheumatology, Leiden University Medical Center, Leiden, Netherlands, 2 Radiology, Leiden University Medical Center, Leiden, Netherlands, 3 Clinical Epidemiology, Leiden University Medical Center, Leiden, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Osteoarthritis (OA) in the thumb base joints (first carpometacarpal [CMC1] and scaphotrapeziotrapezoid [STT]) is highly prevalent and disabling, however much is still unknown about its pathophysiology, and focussed studies on thumb base OA are rarely performed. We took advantage of the newly developed OMERACT thumb base OA MRI scoring system (TOMS) to investigate the prevalence of MRI synovitis and bone marrow lesions (BMLs) in the thumb base, and their association with pain, in addition to radiographic features.

Methods: Two readers scored MRIs of the right thumb base for synovitis and BMLs in CMC1 and STT (grade 0-3) in consecutive patients diagnosed by their treating rheumatologist with primary hand OA from the Hand OSTeoArthritis in Secondary care (HOSTAS) study. BMLs were evaluated in proximal and distal joint parts separately, resulting in 0-6 and 0-9 sum scores for CMC1 and STT, respectively. Synovitis and BML scores were both aggregated into dichotomous thumb base scores (0-1 in both joints versus ≥2 in at least one joint). Trained nurses assessed thumb base tenderness on palpation. Osteophyte presence (according to OARSI atlas) in CMC1 and STT was assessed on radiographs. Associations between MRI synovitis or BMLs and thumb base tenderness were analysed using logistic regression, stratified for absence/presence of osteophytes.

Results: 85 of 202 hand OA patients (84% women, mean age 60.1 years, 90% fulfilling ACR criteria) reported thumb base tenderness on palpation. Synovitis was seen in both thumb base joints (CMC1 42%, STT 37%), although prevalence of grade 2-3 synovitis was low in both the CMC1 (16%) and STT (14%). BMLs were present in CMC1 and STT in 54 and 53%, respectively, with 18 and 21% having a sum score of 2-3, and 16 and 7% a sum score ≥4. In absence of radiographic osteophytes, presence of synovitis or BMLs in either thumb base joint was not statistically significantly associated with thumb base tenderness (odds ratio (OR) 1.9 [95% confidence interval 0.6-6.4] and 1.5 [0.5-4.3]). However, in absence of severe synovitis or BMLs, radiographic osteophytes and pain were associated, with increasing ORs when synovitis or BMLs were additionally present (Table). Similar results were found for self-reported thumb base pain (not shown).

Conclusion: Synovitis and BMLs are present in thumb base OA, although severe synovitis or BMLs were uncommon. Osteophytes seemed more important in predicting thumb base tenderness than synovitis or BMLs alone. Combined presence of osteophytes and synovitis or BMLs had a small additive effect. These findings differ from interphalangeal OA studies, supporting thumb base OA as a distinct subset. It might also explain why trials investigating intra-articular corticosteroids in thumb base OA produced equivocal results.

Table. Associations (odds ratios with 95% confidence intervals) of MRI synovitis or BMLs and radiographic osteophytes with pain on palpation in thumb base osteoarthritis (n=196*)

<table>
<thead>
<tr>
<th>Synovitis</th>
<th>Osteophyte CMC-1 or STT</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absent</td>
<td>Present</td>
<td></td>
</tr>
<tr>
<td></td>
<td>n=106</td>
<td>n=90</td>
<td></td>
</tr>
<tr>
<td>CMC1 and STT grade 0-1</td>
<td>1</td>
<td>4.2 (2.0-8.6)</td>
<td></td>
</tr>
<tr>
<td>n=145</td>
<td>n=93</td>
<td>n=52</td>
<td></td>
</tr>
<tr>
<td>CMC1 or STT grade ≥ 2</td>
<td>1.9 (0.6-6.4)</td>
<td>5.9 (2.6-13.3)</td>
<td></td>
</tr>
<tr>
<td>n=51</td>
<td>n=13</td>
<td>n=38</td>
<td></td>
</tr>
<tr>
<td>BML</td>
<td>CMC1 and STT grade 0-1</td>
<td>1</td>
<td>4.3 (1.7-11.0)</td>
</tr>
<tr>
<td></td>
<td>n=109</td>
<td>n=85</td>
<td>n=24</td>
</tr>
<tr>
<td>CMC1 or STT grade ≥ 2</td>
<td>1.5 (0.5-4.3)</td>
<td>5.3 (2.6-10.8)</td>
<td></td>
</tr>
<tr>
<td>n=87</td>
<td>n=21</td>
<td>n=66</td>
<td></td>
</tr>
</tbody>
</table>

BML, bone marrow lesion; CMC1, first carpometacarpal; MRI, magnetic resonance imaging; STT, scaphotrapeziotrapezoid.

*n=196 patients with available radiographs and evaluable MRI for synovitis and BMLs.

Disclosure: F. P. B. Kroon, Dutch Arthritis Fund, 2; S. van Beest, Dutch Arthritis Fund, 2,IMI APPROACH, 2; W. Damman, Dutch Arthritis Fund, 2; R. Liu, Dutch Arthritis Fund, 2; J. L. Bloem, None; M. Reijnierse, None; M. Kloppenburg, Pfizer, 2,AbbVie, GlaxoSmithKline, Merck, Leviecept, 5,Dutch Arthritis Fund, 2.


Abstract Number: 2209

Leptin and Adiponectin Mediate the Association between Body Mass Index and Hand and Knee Osteoarthritis

F.P.B. Kroon¹, A. Veenbrink¹, R. de Mutsert², A.W. Visser¹, Saskia le Cessie³, F.R. Rosendaal² and M. Kloppenburg¹,², ¹Rheumatology, Leiden University Medical Center, Leiden, Netherlands, ²Clinical Epidemiology, Leiden University Medical Center, Leiden, Netherlands, ³Medical Statistics and Bioinformatics, Leiden University Medical Center, Leiden, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Associations between obesity and osteoarthritis (OA) in non-weight bearing joints suggest that systemic influences also contribute to OA. Systemically active substances secreted by adipose tissue, including adipokines, are hypothesized to
play a role in OA. We examined whether two adipokines, leptin and adiponectin, mediate the association between body mass index (BMI) and hand and knee OA.

**Methods:** Participants of a cross-sectional population-based study completed questionnaires and underwent standardized physical examination of hands and knees to define OA according to clinical ACR criteria. Fasting serum leptin and adiponectin were measured with immunoassays. Potential mediation was investigated using the Baron and Kenny framework. Four assumptions were investigated: associations between (1) BMI and OA (pathway C), (2) BMI and adipokines (pathway A), (3) adipokines and OA (pathway B), and (4) attenuation of the association between BMI and OA after including adipokines (pathway C'). No exposure-mediator interaction and mediator-outcome confounding was assumed. Assumptions were investigated using logistic and linear regression analyses as appropriate. Odds Ratios (ORs) were calculated per standard deviation (SD) in BMI, and per 10 and 5 units in leptin and adiponectin. Percentage mediation with 95% confidence intervals (CIs) was estimated when all four assumptions were fulfilled, using causal mediation analyses in Stata (*medeff*). Models were adjusted for age, ethnicity and education, and stratified by sex.

**Results:** In 6462 participants (56% women, median age 56 years (range 45-65), mean BMI 26.3 kg/m^2^), prevalence of hand OA, knee OA and combined hand and knee OA were 8%, 10% and 4%, respectively. Median leptin and adiponectin concentrations were 7.1 ug/L (range 0.9-60.9) and 6.0 mg/L (0.5-23.7) in men, and 19.1 ug/L (0.5-262.0) and 10.5 mg/L (0.5-98.6) in women. BMI was positively associated with OA presence and serum leptin in both men and women (Table). A negative association was observed between BMI and serum adiponectin (-0.73 mg/L per SD BMI, 95% CI -0.55;-0.91). Leptin was positively associated with most OA types, except knee OA in men. Leptin partially mediated the association of BMI with hand OA in men (9% mediation, 95% CI 5;17) and women (30%, 13;198), and the association of BMI with knee OA in women (15%, 12;21). Similar analyses for adiponectin revealed a negative association of adiponectin with hand OA in men and partial mediation of the association of BMI with hand OA in men (19%, 12;37), whereas mediation was absent in other subgroups.

**Conclusion:** Leptin partially mediated the association of BMI and hand OA in both men and women, as did adiponectin in men. Moreover, mediation by leptin for the association of BMI and knee OA was demonstrated in women. These findings suggest that systemic mediators contribute to hand OA, and to a lesser extent to knee OA.
<table>
<thead>
<tr>
<th>Pathway A</th>
<th>Pathway B</th>
<th>Pathway C</th>
<th>Pathway C'</th>
<th>Mediation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MEN</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>BMI – log leptin</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SD BMI:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.72</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hand OA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.70 (1.64 – 1.77)</td>
<td>1.30 (1.13 – 1.50)</td>
<td>1.39 (1.18 – 1.64)</td>
<td>1.34 (1.06 – 1.70)</td>
<td>8.6 (5.4 – 17.2)</td>
</tr>
<tr>
<td><strong>Knee OA</strong></td>
<td>1.14 (0.98 – 1.43)</td>
<td>1.25 (1.06 – 1.48)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hand and knee OA</strong></td>
<td>1.28 (1.07 – 1.52)</td>
<td>1.59 (1.31 – 1.93)</td>
<td>1.82 (1.39 – 2.39)</td>
<td></td>
</tr>
<tr>
<td><strong>WOMEN</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>BMI – log leptin</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SD BMI:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.88</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hand OA</strong></td>
<td>1.08 (1.01 – 1.15)</td>
<td>1.18 (1.01 – 1.37)</td>
<td>1.12 (0.89 – 1.40)</td>
<td>30.3 (13.3 – 198.2)</td>
</tr>
<tr>
<td><strong>Knee OA</strong></td>
<td>1.21 (1.14 – 1.29)</td>
<td>1.62 (1.42 – 1.85)</td>
<td>1.50 (1.25 – 1.81)</td>
<td>15.4 (11.7 – 21.3)</td>
</tr>
<tr>
<td><strong>Hand and knee OA</strong></td>
<td>1.13 (1.05 – 1.22)</td>
<td>1.48 (1.26 – 1.74)</td>
<td>1.55 (1.25 – 1.93)</td>
<td></td>
</tr>
</tbody>
</table>

BMI, body mass index; CI, confidence interval; OA, osteoarthritis; OR, Odds Ratio; SD, standard deviation. Adjusted for age, ethnicity and education.

*logarithmic transformation performed to obtain normal distribution. ^Mediation not calculated (no association within pathway B). ‡Mediation not calculated (no attenuation of the total association of BMI and OA after including leptin in the model).
**Background/Purpose:** Osteoarthritis (OA) in the first carpometacarpal (CMC1) joint in the thumb base is frequent and has a large contribution in hand pain and disability. Previous ultrasonography (US) studies of hand OA have focussed on interphalangeal joints, showing inflammatory features that associate with clinical signs and symptoms. Until now, US studies specifically addressing the CMC1 joint have not been performed. We investigated the associations between inflammatory features, structural damage and pain in CMC1 OA.

**Methods:** Cross-sectional data of 87 hand OA patients according to ACR criteria who participated in the EChography in Hand OA (n=63) and the Etanercept in Hand OA (n=24) study at the Leiden University Medical Center were used in this analysis. Both CMC1 joints were assessed with US for synovial thickening, effusion and power Doppler signal (PDS) on a 0-3 scale by experienced ultrasonographers. Presence of pain upon palpation of the thumb base was assessed by trained research nurses on the same day as the US. Hand radiographs were scored blinded for clinical and US features, according to the Osteoarthritis Research Society International atlas for osteophytes (0-3), joint space narrowing (JSN, 0-3), sclerosis (0-1) and malalignment (0-1) in the CMC1 joint. Risk ratios (RRs) with 95% confidence intervals (CIs) were calculated using generalized estimating equations to investigate associations between US or radiographic features and thumb base pain on joint level.

**Results:** Of 87 patients (mean age 60.3 years, 82% women, mean BMI 27.2 kg/m$^2$) 174 CMC1 joints were assessed, of which 54 (31%) were painful. The US features synovial thickening, effusion and PDS were found in 26%, 33% and 25% of the joints, respectively. Radiographic features were present in 55% (osteophytes), 79% (JSN), 20% (sclerosis) and 12% (malalignment) of the joints. No associations were seen between inflammatory US features and pain upon palpation of the thumb base (Table). However, osteophytes and sclerosis were associated with more pain (RR 2.5 [95% CI 1.4 to 4.6] for osteophytes grade 3 versus no osteophytes, and RR 2.0 [95% CI 1.3 to 3.2] for presence of sclerosis). Other radiographic features (JSN, malalignment) showed a trend for increased risk of pain on palpation, and for osteophytes and JSN a dose-response relation was apparent.

**Conclusion:** Radiographic features, especially osteophytes and JSN, were prevalent and more frequently present than US inflammatory features in the CMC1 joints of hand OA patients. In contrast to what is known from studies in interphalangeal joints, the presence of inflammatory US features was not associated with pain in the thumb base, but structural damage was. These results suggest differences in aetiology of pain in thumb base compared to interphalangeal OA, with a larger role for structural damage in thumb base OA.
**Table.** Associations of US and radiographic features with tenderness in the thumb base in hand OA patients (n=171 joints*)

<table>
<thead>
<tr>
<th></th>
<th>Tenderness yes/no, n</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>US features</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Synovial thickening</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>40/85</td>
<td>1</td>
</tr>
<tr>
<td>Grade 1</td>
<td>10/22</td>
<td>1.1 (0.6-1.8)</td>
</tr>
<tr>
<td>Grade 2/3</td>
<td>4/10</td>
<td>0.9 (0.4-2.4)</td>
</tr>
<tr>
<td>Effusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>35/79</td>
<td>1</td>
</tr>
<tr>
<td>Grade 1</td>
<td>13/25</td>
<td>0.8 (0.4-1.5)</td>
</tr>
<tr>
<td>Grade 2/3</td>
<td>6/13</td>
<td>0.8 (0.3-2.0)</td>
</tr>
<tr>
<td>Power doppler signal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>41/86</td>
<td>1</td>
</tr>
<tr>
<td>Grade 1</td>
<td>8/24</td>
<td>0.9 (0.5-1.6)</td>
</tr>
<tr>
<td>Grade 2/3</td>
<td>5/7</td>
<td>1.2 (0.7-2.0)</td>
</tr>
<tr>
<td><strong>Radiographic features</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osteophytes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>18/58</td>
<td>1</td>
</tr>
<tr>
<td>Grade 1</td>
<td>16/40</td>
<td>1.2 (0.7-2.2)</td>
</tr>
<tr>
<td>Grade 2</td>
<td>11/13</td>
<td>1.5 (0.7-2.9)</td>
</tr>
<tr>
<td>Grade 3</td>
<td>9/6</td>
<td>2.5 (1.4-4.6)</td>
</tr>
<tr>
<td>Joint space narrowing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>8/27</td>
<td>1</td>
</tr>
<tr>
<td>Grade 1</td>
<td>36/77</td>
<td>1.6 (0.8-3.3)</td>
</tr>
<tr>
<td>Grade 2</td>
<td>7/9</td>
<td>2.1 (0.8-5.3)</td>
</tr>
<tr>
<td>Grade 3</td>
<td>3/4</td>
<td>2.5 (0.9-7.0)</td>
</tr>
<tr>
<td>Sclerosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>38/104</td>
<td>1</td>
</tr>
<tr>
<td>Present</td>
<td>16/13</td>
<td>2.0 (1.3-3.2)</td>
</tr>
<tr>
<td>Malalignment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>44/107</td>
<td>1</td>
</tr>
<tr>
<td>Present</td>
<td>10/10</td>
<td>1.4 (0.7-2.7)</td>
</tr>
</tbody>
</table>

*3 joints no information on tenderness. CI, confidence interval; n, number; OA, osteoarthritis; RR, risk ratio; US, ultrasound.
Abstract Number: 2211

Investigation of Self-Reported Painful Joint Count As an Outcome Measure in Hand Osteoarthritis

F.P.B. Kroon¹, J.L. van der Plas¹, S. van Beest¹, W. Damman¹ and M. Kloppenburg¹,², ¹Rheumatology, Leiden University Medical Center, Leiden, Netherlands, ²Clinical Epidemiology, Leiden University Medical Center, Leiden, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Hand osteoarthritis (OA) research is in need of disease-specific validated instruments to measure patient-reported outcomes. Self-reported painful joint count (PJC) could be useful to assess pain, including information about the distribution of tender joints, while being less time-consuming than assessor-reported PJC. We investigated metric properties of self-reported PJC compared to assessor-reported PJC to measure pain.

Methods: Symptomatic hand OA patients from the Hand OSTeoArthritis in Secondary care (HOSTAS) study marked which joints were painful on standardized hand diagrams. Pain upon palpation was scored on similar diagrams by trained nurses, who were unaware of patients’ scores. Self- and assessor-reported PJCs were calculated as the sum of painful joints of both hands (range 0-30). Patients also rated pain on visual analogue scale and completed Australian/Canadian Hand Osteoarthritis index pain subscale, Short Form-36 Mental/Physical Component Summary scales, and Hospital Anxiety and Depression Scale. Radiographs were scored according to Kellgren-Lawrence. MRIs of the right distal and proximal interphalangeal joints (DIPs/PIPs) were evaluated for bone marrow lesions and synovitis. Validity was investigated by assessing correlations between self- and assessor-reported PJC, and of both PJCs with other outcome measures. Absolute agreement between PJCs on joint level, and patient level intra-class correlation coefficients (ICCs) were calculated.

Results: Of 524 hand OA patients (86% women, mean age 61, 90% fulfilling ACR criteria), 506 (96.9%) reported ³1 painful joint (median PJC 8 [interquartile range (IQR) 4-13]), while nurses reported ³1 painful joint in 426 (81.3%) patients (PJC 3 [1-7]). Patients and assessors both reported pain most often in DIP 2-3, PIP 2-3 and the thumb base, and least often in metacarpophalangeal joints (MCPs) 2-5. Correlation between self- and assessor-reported PJC was 0.38. Correlations of both PJCs with other measures were comparable, ranging from 0.11 to 0.37 (Table). Absolute agreement was highest in MCPs 2-5 and lowest for thumb base, DIP 2-3 and PIP 2-3 (range 61%-89%). ICC between PJCs was 0.28 (95% confidence interval 0.08-0.14).

Conclusion: Hand OA patients reported more painful joints than assessors. Self-reported PJC correlated weakly with assessor-reported PJC, and other instruments measuring pain and physical health. Divergent correlations with mental health and imaging scores were even lower. Agreement between patients and assessors was highest in joints with low prevalence of pain, but overall agreement was low. Despite apparent advantages, these results suggest that self-reported and assessor-reported PJCs cannot be used interchangeably, and further study of PJC as an outcome measure in hand OA is warranted.
Table. Correlation coefficients for painful joint counts (PJC) and selected clinical and imaging outcomes.

<table>
<thead>
<tr>
<th></th>
<th>Self-reported PJC</th>
<th>Assessor-reported PJC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-reported PJC</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Assessor-reported PJC</td>
<td>0.38**</td>
<td>-</td>
</tr>
<tr>
<td>VAS pain</td>
<td>0.37**</td>
<td>0.37**</td>
</tr>
<tr>
<td>AUSCAN pain</td>
<td>0.36**</td>
<td>0.36**</td>
</tr>
<tr>
<td>SF-36 PCS</td>
<td>-0.30**</td>
<td>-0.27**</td>
</tr>
<tr>
<td>SF-36 MCS</td>
<td>-0.12**</td>
<td>-0.11**</td>
</tr>
<tr>
<td>HADS depression scale</td>
<td>0.14**</td>
<td>0.15**</td>
</tr>
<tr>
<td>Kellgren-Lawrence score</td>
<td>0.08</td>
<td>0.04</td>
</tr>
<tr>
<td>MRI synovitis†</td>
<td>0.22*</td>
<td>0.21*</td>
</tr>
<tr>
<td>MRI BML†</td>
<td>0.14</td>
<td>0.22*</td>
</tr>
</tbody>
</table>

AUSCAN, Australian/Canadian osteoarthritis hand index; BML, bone marrow lesion; HADS, Hospital Anxiety and Depression Scale; MCS, mental component summary; MRI, magnetic resonance imaging; PCS, physical component summary; PJC, painful joint count; SF-36, Short Form 36; VAS, visual analogue scale. *p<0.05; **p<0.01; †PJC of DIP and PIP joints of right hand (n=92) was used (range 0-8).
A Metabolite of C-Reactive Protein, a Marker of Disease Activity, Is Prognostic of Radiographic Knee OA

**Anne C. Bay-Jensen**¹, Asger R. Bihlet², Inger Byrjalsen³, Jeppe Andersen⁴, Yi He⁵, Anne Sofie Siebuhr¹, Christian S. Thudium⁶, Bente J. Riis², Claus Christiansen² and Morten Asser Karsdal¹, ¹Rheumatology, Nordic Bioscience, Herlev, Denmark, ²Nordic Bioscience, Clinical Development, Herlev, Denmark, ³Nordic Bioscience, Herlev, Denmark, ⁴Clinical Development, Nordic Bioscience, Herlev, Denmark, ⁵Rheumatology, Nordic Bioscience, Biomarkers and Research, Herlev, Denmark, ⁶Biomarkers and Research, Nordic Bioscience, Herlev, Denmark

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** There are two major needs in clinical DMOAD development: Identifying a population with an active and progressive disease to demonstrate significant improvements by an efficacious intervention; Phenotyping patients and linking them to a corresponding treatment mode-of-action (e.g., anti-inflammatory). CRPM is a metabolite of CRP. It is released from the inflamed tissue when CRP is degraded by proteases such as MMPs. The purpose of this study was to translate the use of the blood-based marker CRPM to OA, from rheumatoid arthritis (RA), where it has been extensively tested. Furthermore, to test whether it is predictive of radiographic progression in OA.

**Methods:** The placebo arms of two phase III OA trial (NCT00486434/NCT00704847), a phase III RA study (the LITHE study, N=490), which included patients with active, moderate-severe RA (NCT00106535), and in an early RA cohort (N=92) were used.
Subjects with symptomatic and radiographic knee OA: WOMAC pain ≥150mm and/or WOMAC function ≥510mm, and KL grade 2 or 3. KLG were scored for both knees at baseline and year 2 (Y2). Serum CRPM and CRP were measured at baseline. The association between serum CRPM levels and disease activity score (DAS28) and CRP was investigated by Spearman’s correlations. Quartile ranges of CRPM in the early RA cohort were used to define the cut-off between inflammatory OA and non-inflammatory OA. OA knees were divided into cases and controls based on a terminology proposed by the FNIH-OAI consortium; knees with KLG≥2 at BL were excluded, and incidence OA at Y2 was defined KLG≥2. Logistic regression was used to compare cases and controls.

Results: There was a significant correlation between disease activity measures and CRPM in both RA studies. Seventy-five percent of the LITHE patients had high or very high levels of CRPM at BL, which was changed to a pattern similar to early RA after treatment (table). Mean CRPM levels were significantly lower in OA (8.5 [8.3-8.8]) compared to the RA patients (15.6 [9.5-21.6]); however, a significant subset of OA patients (41%-31% in SMC2301/02) had CRPM levels ≥9ng/mL, as 75% of patients with early RA. Patients with BL or Y2 CRPM levels ≥9ng/mL were more likely to develop knee OA than patients with low level of CRPM. Overall, moderate to very high levels of CRPM at BL and Y2 were predictive of incidence OA with odds ratio of 4.6 [1.2-17] and 2.5 [1.2-4.8].

Conclusion: CRPM is associated with disease activity and modulated in response to anti-inflammatory treatment in RA. A subset of OA patients, up to 41%, appear to have tissue inflammation comparable to that of RA, reflected by the level of CRPM. Furthermore, high CRPM levels was prognostic of incident knee OA.

Disclosure: A. C. Bay-Jensen, Nordic Bioscience Diagnostic, 3; A. R. Bihlet, Nordic Bioscience Diagnostic, 3; I. Byrjalsen, Nordic Bioscience Diagnostic, 3; J. Andersen, Nordic Bioscience Diagnostic, 3; Y. He, Nordic Bioscience Diagnostic, 3; A. S. Siebuhr, Nordic Bioscience Diagnostic, 3; C. S. Thudium, Nordic Bioscience Diagnostic, 3; B. J. Riis, Nordic Bioscience Diagnostic, 3; C. Christiansen, Nordic Bioscience Diagnostic, 3; M. A. Karsdal, Nordic Bioscience Diagnostic, 3.


Abstract Number: 2213

“Generalized Osteoarthritis”: Update to a Systematic Review

Terese R. Gullo1,2 and Amanda Nelson3, 1Thurston Arthritis Research Center, Chapel Hill, NC, 2Ohio State University College of Medicine, Columbus, OH, 3Thurston Arthritis Research Center, University of North Carolina at Chapel Hill, Chapel Hill, NC

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: To perform a systematic review of the definitions of generalized osteoarthritis (GOA). An initial systematic review of the literature for GOA was published in 2014 (PMID 24461078); this review is an update to the definitions analyzed in the original work.

Methods: We performed a systematic review in Medline using the terms osteoarthritis, generalized, polyarticular, multiple joint, multi-joint, and others to obtain articles related to GOA, following PRISMA guidelines. The search was performed 4/18/17 by a professional librarian. The initial searches produced 216 articles for title and abstract review (performed by AEN and TRG), after which 75 underwent full text review (AEN and TRG). Of these, 39, along with 3 identified through bibliographic review, were included for data extraction (TRG) based on pre-specified criteria including the requirement for a clearly stated definition of OA (clinical, radiographic, or symptomatic) assessed at more than one body site.

Results: In the 42 included articles, 29 large cohorts (n~56,000) were represented along with 7 clinical series (n~28,000), 1 systematic review (n=79 studies) and 2 meta-analyses (n~980,000) across 14 countries and 5 years (2012-2017). The sites assessed, and OA definitions at each site, varied but most often included the hands, knees and hips. Five of the 42 studies explicitly stated a definition for...
GOA, and I gave an implicit definition. No two of these definitions were the same, however all required a minimal number of joints affected without regard to body region (Table). No definitions contained a supporting rationale. Estimates of the prevalence of GOA in these studies ranged from 7-13%.

Although the remaining 36 articles did not provide a definition for GOA, 11 studies did collect data for OA disease characteristics in multiple joints within the individual. For instance, one study tallied the number of painful joint regions to assess the extent of disabling OA at the person level (as opposed to the regional level). Another study listed Clinical OA - number of sites as a categorical variable. Finally, in at least 7 articles the authors used alternate terms to denote multiple joint involvement—among these polyarticular OA and multijoint OA.

**Conclusion:** As in 2014, when the initial systematic review was conducted, GOA remains a commonly used term in the literature despite its lack of a clear or widely agreed upon definition. Most studies that discuss GOA do not define it, and for those that do, still no consensus has been reached. Alternate terms have been used, such as multijoint OA, to describe symptoms and/or radiographic features manifested in more than 1 joint in the individual. However, the use of these terms has yet to improve precision in the definition of GOA. It remains appropriate for individual studies to clearly define any terms used to designate OA of multiple joints or joint groups.

<table>
<thead>
<tr>
<th>Author</th>
<th>No. joints or groups</th>
<th>Hand</th>
<th>Knee</th>
<th>Hip</th>
<th>Other specified sites</th>
<th>PMID</th>
</tr>
</thead>
<tbody>
<tr>
<td>Espinoza (2014)</td>
<td>In alphabetical and 10 symptoms</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Cervera (2013)</td>
<td>2 or 7 (symptomatic)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>12345123</td>
<td></td>
</tr>
<tr>
<td>Mint (2012)</td>
<td>5+</td>
<td>X</td>
<td>X</td>
<td>12312312</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kean (2012)</td>
<td>3+</td>
<td>X</td>
<td>X</td>
<td>12345123</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Park (2015)</td>
<td>In four related pairs</td>
<td>X</td>
<td>X</td>
<td>12345123</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verras (2015)</td>
<td>5+</td>
<td>X</td>
<td>X</td>
<td>12345123</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Disclosure:* T. R. Gullo, None; A. Nelson, None.


**Abstract Number:** 2214

**Contrary to Current Understanding of Osteoarthritis Pathogenesis, Only Gender and Radiographic Status Predict Progression: A Machine Learning Study of 9,254 Knees from the Osteoarthritis Initiative**

Michael A Bowes¹, Oras Alabas², Gwenael Guillard¹, Graham R. Vincent¹, Alan Brett³ and Philip G. Conaghan⁴, ¹Imorphics Ltd, Manchester, United Kingdom, ²Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, United Kingdom, Leeds, United Kingdom, ³Imorphics Ltd, MANCHESTER, United Kingdom, ⁴Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017
**Session Title:** Osteoarthritis – Clinical Aspects Poster II: Observational and Epidemiological Studies
**Session Type:** ACR Poster Session C
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Currently there are a large number of postulated predictors for OA progression, proposed on the basis of relatively small studies (100’s), and measurement approaches involving large error margins. Supervised machine learning techniques, allows the study of key pathologies without prior assumptions, and accurate quantified segmentation. Our aim was to evaluate predictors of cartilage loss in the entire OAI dataset.
Methods:

Automated cartilage segmentation was assessed for repeatability and accuracy and then applied to all knees from the OAI with baseline, 1 and 2-year images. Shape models were used to measure cartilage thickness in a consistent anatomical region of the medial tibiofemoral joint.

Multilevel modelling was used to consider the effects of previous postulated covariates at knee-level and subject-level at baseline and in longitudinal change. Gender, KL grade, race, knee alignment, height and weight, age, pain, physical activity, NSAID use, previous surgery, smoking and systolic blood pressure were used as covariates.

Results:

The segmentation method showed excellent accuracy; miss-n-out validation in a training set of 287 knees with varying radiographic OA, showed a mean point-to-surface accuracy of 0.12 mm, mean 95% error of 0.37mm (less than one voxel edge). 9,254 knees were included; mean age was 61.2 (SD 9.2); 58.5% were female. 24.8% used NSAIDs, 47.2% were smokers, 22.7% had previous surgery.

Gender and KL grade explained almost all the variability in cartilage thickness at baseline; for example, the adjusted pseudo-$r^2$ of femur and tibia models using only gender and KL grade were 38% and 40%, the full models were 40% and 43%, coefficients are provided in Table 1. A similar pattern was found in longitudinal analysis (Table 2); gender and KL grade accounted for almost all the variability in change in thickness.

Conclusion:

This is the first study to characterise the relationship of cartilage thickness, and its change, using a very large dataset. Two covariates explained almost all the variance in thickness: gender and radiographic disease, previously described factors such as weight and alignment (nor NSAIDS and smoking) had surprisingly little effect. This changes our concept of osteoarthritis progression, and potential interventions.

Disclosure: M. A. Bowes, None; O. Alabas, None; G. Guillard, Stryker Corp, 3; G. R. Vincent, Stryker Corp, 3; A. Brett, Stryker Corp, 3; P. G. Conaghan, AbbVie, BMS, Eli Lilly, Novartis, Pfizer, Roche, 5; AbbVie, BMS, Eli Lilly, Novartis, Pfizer, Roche, 8.

Abstract Number: 2215

Effect of Single 6 Ml Intraarticular Injection of Hylan G-F 20 in Patients with Knee Osteoarthritis: Results of a Single Centre Study

SUNIL KUMAR PANDEY and SAT PAL SINGH, 1ORTHOPEDIC DEPARTMENT, SAFDARJUNG HOSPITAL, VMMC, NEW DELHI, NEW DELHI, India, 2DEPARTMENT OF MEDICINE, SAFDARJUNG HOSPITAL, VMMC, NEW DELHI, NEW DELHI, India

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: ARHP Osteoarthritis – Clinical Aspects Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: To evaluate the effect of single 6ml intraarticular injection of hylan G-F 20 in patients with knee osteoarthritis.

Author: Dr. Pandey Sunil Kumar*, Dr. Singh Sat Pal*

*Safdarjung hospital, New Delhi

Objective: To evaluate efficacy and effect on analgesic requirement of 6 ml single injection of hylan G-F 20 in patients with primary knee osteoarthritis
Methods: In this prospective study, adult patients with primary knee osteoarthritis (grade II to IV) were treated with 6 ml single intra-articular injection of hylan G-F 20. Patients were followed at 6 and 12 months. Difference in WOMAC score from baseline to 6 and 12 months was evaluated by paired "t" test. Numbers and percentages of patients requiring analgesics on daily basis were recorded at all visits.

Results: A total of 352 patients [male 113 (32.10%); female 239 (67.90%)] [grade II 197(55.97%), grade III 119 (33.81%) and grade IV 36 (10.23%)] with mean age of 59.10 (4.39) years and mean body mass index 27.20 (3.81) kg/m$^2$ were included in the study. Mean weight and height of the study participants was 68.11 (7.40) kg and 159 (10) cm respectively. One hundred patients (28.41%) patients had varus deformity. Twenty five (7.10%) and 14 (3.98%) patients had effusion in the right and left knee respectively. The WOMAC score from reduced from 64.44(16.89) at baseline to 34.00(10.31) at 6 month and 36 (11.65) at 12 months respectively. The difference in the WOMAC score from baseline to 6 months and 12 months was statistically significant (P<0.001 for both). Number of patients requiring analgesics daily reduced from 28(7.95%)at baseline to 2(0.57%) at 6 months and 3(0.85%) at 12 months.

Conclusion: Single 6 ml injection of hylan G-F was effective and well tolerated in patients with knee osteoarthritis. Hylan G-F 20 also reduced the requirement of analgesics.

Key words: Efficacy, hylan G-F 20, knee osteoarthritis

Disclosure: S. K. PANDEY, None; S. P. SINGH, None.


Abstract Number: 2216

Are Adults with Arthritis Advised to Exercise By Their Health Care Providers? National Health Interview Survey, 2002 and 2014

Jennifer M. Hootman1, Louise Murphy2, Michael Boring3 and Teresa J. Brady3, 1Centers for Disease Control and Prevention, Kennesaw, GA, 2Division of Population Health, Centers for Disease Control and Prevention, Atlanta, GA, 3Arthritis Program, Centers for Disease Control and Prevention, Atlanta, GA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: ARHP Osteoarthritis – Clinical Aspects Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Most published clinical practice guidelines for the management of osteoarthritis recommend exercise as a primary self-management strategy. Despite this, less than one-third of primary care physicians provide exercise advice during office visits. This study’s purpose was, for 2002 and 2014, to: 1) estimate percentage of US adults with arthritis whose health care provider (HCP) advised them to exercise to manage their arthritis, and 2) describe sociodemographic and health-related subgroups with low prevalence of HCP exercise advice.

Methods:
The National Health Interview Survey (NHIS), is an ongoing survey of the civilian, non-institutionalized population and gathers data on a variety of health topics. We analyzed 2002 and 2014 data (sample sizes = 31,044 and 36,697, respectively). Doctor-diagnosed arthritis was defined as a ‘yes’ to: “Have you ever been told by a doctor or other health care professional that you have arthritis, rheumatoid arthritis, gout, lupus or fibromyalgia?” HCP advice for exercise was defined as a ‘yes’ to “Has a doctor or other health professional EVER suggested physical activity or exercise to help your arthritis or joint symptoms?” Age-standardized prevalence (%) and 95% confidence intervals (CI) of HCP advice for exercise was calculated overall and by sociodemographic characteristics (age, sex, race/ethnicity, and education) and health-related characteristics (arthritis-related activity limitation (AAAL), self-rated health (excellent/very good, good, fair/poor), body mass index (BMI, <25.0, 25.0-<30 and 30.0+), smoking status (current, former, never), physical activity level (inactive, insufficient, meets recommendations) and having a primary care provider (yes, no). All analyses
accounted for NHIS’ complex survey design. Prevalence of HCP advice for exercise was considered low if <50% in 2002 and <60% in 2014.

**Results:**

In 2002 and 2014, age-standardized prevalence of HCP advice for exercise among adults with arthritis was 51.9% (CI 49.9-53.8%) and 61.0% (CI 58.6-63.4%), respectively (a 17.5% increase). In 2002, groups with low age-standardized prevalence of HCP advice for exercise were: men; Non-Hispanic Others; those with less than a high school or high school/GED education; no AAAL; Excellent/very good health; those who were overweight or obese; current smokers; physically inactive; and had no primary care provider. In 2014, groups with low age-standardized prevalence of HCP advice for exercise were the same as in 2002 with the addition of those age 18-44 year old age. In 2002 and 2014, the prevalence of HCP for exercise among adults with arthritis who were physically inactive was 47.2% (CI 44.0-50.4%) and 56.7% (CI 52.3-61.0%), respectively (a20% increase).

**Conclusion:**

While prevalence rates of HCP advice for exercise have increased over more than a decade, there are still groups with high need that have persistently low prevalence. Incorporating prompts into electronic medical records and written exercise prescriptions are potential strategies that may lead to increased prevalence of HCP advice for exercise.

**Disclosure: J. M. Hootman, None; L. Murphy, None; M. Boring, None; T. J. Brady, None.**


Abstract Number: 2217

**Combined Impacts of Lifestyle Factors on Knee Osteoarthritis in the Osteoarthritis Initiative**

Zhaoli (Joy) Dai¹, Carrie Brown², Yuqing Zhang³ and David T. Felson⁴, ¹Boston University School of Medicine, Boston, MA, ²Boston University School of Public Health, Boston, MA, ³School Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, ⁴Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** ARHP Osteoarthritis – Clinical Aspects Poster  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Body mass index (BMI), healthy diet or components, physical activity, and tobacco smoking have been examined independently with risk of knee osteoarthritis (OA). Sleep quality has been shown to be related to chronic pain but its relation to knee OA is unclear. In this study, we evaluated the combined effects of lifestyle factors with or without BMI on risk of knee OA.

**Methods:** We used data from the Osteoarthritis Initiative (OAI), a prospective, multicenter study of 4,796 U.S. men (41.5%) and women [mean (SD) age: 61.2 (9.2) y and BMI: 28.6 (4.8) kg/m²] with or at risk of knee OA. Lifestyle factors assessed at baseline of the study including overall diet (assessed by Dietary Approaches to Stop Hypertension, DASH), physical activity (Physical Activity Scale for the Elderly, PASE), tobacco smoking (never, former and current smokers), and sleep quality (frequency of restless sleep in the Center for Epidemiologic Studies Depression Scale, CESD), and BMI (kg/m²) were examined separately for their relationship with risk of incident symptomatic (SxOA) and radiographic (ROA) knee OA. Because physical activity did not show a consistent relationship with knee OA, each participant was scored on all factors except PASE from least healthy (0 point) to healthiest (1 point) for each factor with a total score of 0 (least healthy) to 3 (healthiest) excluding BMI in the composite or a total score of 0 (least healthy) to 4 (healthiest) including BMI (see Table 1). Incident ROA was defined as a new onset of Kellgren and Lawrence grade ≥2 and incident SxOA was defined as new cases of both ROA and a painful knee on most days in past month. We applied Generalized Estimating Equations to account for correlations of both knees in each person in multivariable regression models to assess the association between the lifestyle composite and risk of knee OA using 0 (least healthy) as the referent group.
**Results:** Up to 96 months in OAI, we identified 1340 knees with incident SxOA among 7662 knees and 625 knees with incident ROA among 5861 knees after excluding knees with missing values of OA status or knees with prevalent OA. When BMI was excluded in the composite, a higher score was associated with a lower risk of SxOA (p-trend<0.0001), but no association was found with ROA. When BMI was included in the composite, there was a significant inverse relationship with risks of SxOA and ROA (p-trend<0.0001) (see Table 2).

**Conclusion:** Data from the OAI suggested that persons who lived a healthy lifestyle independent of BMI and physical activity had a lower risk of symptomatic knee OA, but the combined impacts of diet, sleep and tobacco smoking was not related to risk of radiographic knee OA.

<p>| Table 1. Lifestyle factors at baseline and their score criteria in the Osteoarthritis Initiative |
|-----------------------------------------------|------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Lifestyle factor</th>
<th>Score</th>
<th>Interpretation of score</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep</td>
<td>0</td>
<td>Restless sleep at least 1 day/week in CESD</td>
<td>58.7</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Restless sleep &lt;1 day/week in CESD</td>
<td></td>
</tr>
<tr>
<td>Smoking tobacco</td>
<td>0</td>
<td>Former or current smokers</td>
<td>21.0</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Never smokers</td>
<td></td>
</tr>
<tr>
<td>Diet quality-DASH</td>
<td>0</td>
<td>Lower 75%</td>
<td>75.0</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Upper 25%</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>0</td>
<td>≥25 (kg/m²)</td>
<td>76.2</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>&lt;25 and ≥18.5(kg/m²)</td>
<td></td>
</tr>
</tbody>
</table>

| Table 2. Combined impacts of lifestyle factors in relation to incident knee OA |
|-----------------------------------------------|------|-----------------|-----------------|
| Without BMI (range: 0-3) | Odds Ratio (95% CI)² | With BMI (range: 0-4) | Odds Ratio (95% CI)² |
| Incident SxOA | n/N #knee¹ | | n/N #knee | |
| 0         | 151/712 | 1.0 | 0 | 135/608 | 1.0 |
| 1         | 664/3386| 0.83 (0.61, 1.13) | 1 | 593/2671 | 0.91 (0.70, 1.17) |
| 2         | 429/2824| 0.63 (0.45, 0.88) | 2 | 146/1286 | 0.59 (0.45, 0.77) |
| 3         | 96/740  | 0.52 (0.34, 0.78) | 3 | 231/1724 | 0.39 (0.29, 0.53) |
| 4         | 18/261  | 0.52 (0.34, 0.78) | 4 | 18/261  | 0.23 (0.13, 0.38) |
| P-trend   | <0.0001 | |<0.0001|
| Incident ROA | | |
| 0         | 60/515  | 1.0 | 0 | 51/433 | 1.0 |
| 1         | 287/2588| 1.00 (0.65, 1.54) | 1 | 248/1978 | 0.98 (0.68, 1.41) |
| 2         | 225/2177| 0.96 (0.61, 1.53) | 2 | 238/2182 | 0.81 (0.56, 1.19) |
| 3         | 53/581  | 0.83 (0.48, 1.44) | 3 | 80/1040 | 0.55 (0.36, 0.85) |
| 4         | 4       | 0.83 (0.48, 1.44) | 4 | 8/228  | 0.22 (0.10, 0.48) |
| P-trend   | 0.38 | |<0.0001|

¹Number of knees of incident OA/total number of knees

²Model adjusted for age (years), sex (men vs. women), race (white vs. non-white), BMI (kg/m²) (for composite excluding BMI only), total energy intake (kcal/day), education level (college and above vs. below college), physical activity (PASE), and CESD without restless sleep.

**Disclosure:** Z. Dai, None; C. Brown, None; Y. Zhang, None; D. T. Felson, None.
Abstract Number: 2218

**Concurrent Change in Quadriceps Strength and Physical Function over 5 Years in the Multicenter Osteoarthritis Study**

*Kathryn Bacon¹, Neil Segal², BE Øiestad³, Cora E. Lewis⁴, Michael C. Nevitt⁵, Carrie Brown⁶ and David T. Felson⁷, ¹Clinical Epidemiology Research & Training Unit, Boston University School of Medicine, Boston, MA, ²University of Kansas, Shawnee, KS, ³Oslo and Akershus University College of Applied Sciences, Oslo, Norway, ⁴University of Alabama Birmingham, Birmingham, AL, ⁵Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, CA, ⁶Boston University School of Public Health, Boston, MA, ⁷Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA

**First publication:** September 18, 2017

**SESSION INFORMATION**

 Session Date: Tuesday, November 7, 2017
Session Title: ARHP Osteoarthritis – Clinical Aspects Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

**Background/Purpose:** Quadriceps weakness is associated with functional limitations and a target in the treatment of knee osteoarthritis (OA). There are limited data on the effect of modest strengthening on improvements in function. Our objective was to evaluate concurrent changes in quadriceps strength and physical function over 5 years.

**Methods:** We examined subjects in the Multicenter Osteoarthritis (MOST) study who had knee extensor strength measured using an isokinetic dynamometer at 60°/sec at baseline and 60-month visits. We excluded those with knee replacement after baseline, and those whose values at baseline, at 60 months or in change from baseline were in the most extreme 1%.

Based on studies using 15% change in a person’s strength as a clinically important cutoff (ArchPMR 88:626, 2007), we created a 3-category variable defined by whether, at 60 months, strength increased ≥15%, decreased ≥15%, or remained within 15% of baseline. Sensitivity analyses assessed 20% and 30% change in strength.

Physical function was measured with the Five-Times Sit-to-Stand-Test, 20-Meter Walk Test, and WOMAC physical function score. Generalized linear models were used to evaluate if a 15% change in strength was associated with a change in physical function over 60 months. Analyses were stratified by sex and adjusted for baseline age and weight. Based on cross-sectional analyses in MOST which suggested a threshold of strength for function in women, we stratified analyses at 56Nm at baseline to determine whether associations differed in weaker vs. stronger women.

**Results:** Of 1534 study participants (60.6% women; mean age 62 years, mean BMI 30) 44% of women and 43% of men had Kellgren-Lawrence grades ≥2. 89% had a walking speed of ≥1 m/s. Mean quadriceps strength in women (68±23Nm) was lower than in men (124±38Nm). 22% of men and 30% of women increased strength at least 15% at 60 months; 31% of men and 23% of women decreased strength at least 15%. Decreases of ≥15% strength were associated with slower walking and chair stand times and worse WOMAC scores.

Compared with women whose strength did not change by at least 15%, among weaker women (<56 Nm) at baseline (see table), a 15% increase in strength was associated with 1.0 second faster chair stands time, but there was no effect on 20-meter walking time or WOMAC scores. In stronger women (>56 Nm), a 15% increase in strength was associated with faster chair stands time of 0.6 seconds (p=0.06), but little improvement in walk time or WOMAC scores. A 15% increase in strength had no effect in men.

Sensitivity analyses of 20% and 30% change in strength showed similar results.

**Conclusion:** An increase in measured strength was associated with improved chair stand performance in women, but not improved walk time or self-reported functional limitations. Increase in strength was not associated with change in physical function in men. Modest improvements in strength may not affect physical function.
Table 1. Change in 20-meter walk time, chair stands time, and WOMAC Scores, stratified by strength, in women

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean Change in 20-meter walk time (seconds)</th>
<th>Mean Change in chair stands time (seconds)</th>
<th>Mean Change in WOMAC Score “walking”</th>
<th>Mean Change in WOMAC Score “stair climbing”</th>
<th>Mean Change in WOMAC Score “getting in/out of bed”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter</td>
<td>p-value</td>
<td>p-value</td>
<td>p-value</td>
<td>p-value</td>
<td>p-value</td>
</tr>
<tr>
<td>Change in strength</td>
<td>Decrease</td>
<td>0.09 (0.09)</td>
<td>0.06 (0.06)</td>
<td>0.09 (0.09)</td>
<td>0.06 (0.06)</td>
</tr>
<tr>
<td>Increase</td>
<td>0.10 (0.10)</td>
<td>0.08 (0.08)</td>
<td>0.10 (0.10)</td>
<td>0.08 (0.08)</td>
<td>0.10 (0.10)</td>
</tr>
<tr>
<td>Net change (&lt;15% change)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Disclosure: K. Bacon, None; N. Segal, None; B. Øiestad, None; C. E. Lewis, None; M. C. Nevitt, None; C. Brown, None; D. T. Felson, None.


Abstract Number: 2219

Remaining Pain in DMARD-Naive Rheumatoid Arthritis Patients Treated with Baricitinib and Methotrexate

Yvonne C. Lee1, Paul Emery2, John D. Bradley3, Baojin Zhu3, Carol L Gaich3, Zhihong Cai4, Amanda Quebe3, Anabela Cardoso3, Yun-Fei Chen3 and Roy Fleischmann5, 1Department of Medicine, Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA, 2Leeds Musculoskeletal Biomedical Research Unit, LTHT Leeds Institute of Rheumatic and Musculoskeletal Medicine University of Leeds, Leeds, United Kingdom, 3Eli Lilly and Company, Indianapolis, IN, 4Eli Lilly Japan K.K., Kobe, Japan, 5University of Texas Southwestern Medical Center, Dallas, TX

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Pain – Basic and Clinical Aspects Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Patient (pt)-reported pain is common in rheumatoid arthritis (RA), even in pts with good disease control1. This analysis evaluated pain control achieved by methotrexate (MTX), baricitinib (BARI), or combination of baricitinib+MTX (BARI+MTX) in DMARD-naive RA pts from a Phase 3 study, RA-BEGIN2.

Methods:

Pts were randomized and treated with MTX (N=210), BARI (4 mg QD, N=159), or BARI+MTX (N=215). Pain intensity was assessed on a 0-100 mm visual-analog scale (VAS). Percentage of pts reporting improvement in pain of ≥30%, ≥50%, and ≥70% was evaluated, and time to achieve these improvements was assessed with the cumulative incidence estimate3. Between-group comparisons of pain improvement (≥30%, ≥50%, and ≥70%) and percentage achieving low disease activity (LDA) and remission were made using logistic models. Pain improvement among pts achieving remission (CDAI ≤2.8) or LDA (CDAI ≤10) was assessed relative to thresholds for ‘remaining’ pain (pain VAS ≤10 mm, ≤20 mm, or ≤40 mm) at Week 24.

Results:

The mean (SD) baseline pain VAS for MTX, BARI, and BARI+MTX were 65.2 (24.1), 64.1 (21.6), and 62.6 (22.6), which improved to 35.2 (26.2), 24.2 (22.2), and 23.8 (23.0) at Week 24, respectively. BARI and BARI+MTX resulted in more pain improvement (–40.8
and -41.2, respectively, p<0.001) than MTX (-30.0). The percentage of pts reaching ≥70% pain improvement by Week 24 was 32.7% for MTX, 50.0% for BARI (p≤0.001 vs. MTX), and 50.5% for BARI+MTX (p≤0.001 vs. MTX). The time when 50% of pts achieved 70% pain improvement was 20 weeks for MTX, 12 weeks for BARI and 8 weeks for BARI+MTX, respectively. The cumulative incidence for achieving 70% improvement is shown (Fig). BARI and BARI+MTX demonstrated similar pain improvement responses. The percentage of pts achieving remission at Week 24 was higher for BARI (21%) and BARI+MTX (22%) compared to MTX (11%)\(^2\). Similarly, the percentage of pts achieving LDA was higher for BARI (60%) and BARI+MTX (59%) compared to MTX (39%).\(^2\) Mean pain VAS at Week 24 was 6.9 and 16.8, respectively, for pooled patients in remission and LDA. Across treatment groups, the percentage of pts achieving ≤10, ≤20 or ≤40 mm remaining pain by remission and LDA are presented in the Table.

Conclusion:

More pts treated with BARI or BARI+MTX had greater levels of pain improvement more rapidly compared to MTX. Pts treated with BARI or BARI+MTX were more likely to achieve remission and LDA. Patients achieving remission had less remaining pain than those in LDA.

References:

1 Altawil, et al *Arthritis Care Res* 2016

2 Fleischmann, et al *Arthritis Rheumatol* 2017

3 Gooley TA *Statist Med* 1999

![Figure. Cumulative Incidence of 70% Pain Improvement over 52 Weeks in RA-BEGIN](image-url)

Table. Percent of Patients with Pain VAS at or Below Each Threshold by Disease Activity at Week 24

<table>
<thead>
<tr>
<th>Percent of Patients with Pain VAS at or Below Each Threshold</th>
<th>Remission (CDAI ≤ 2.8) (n=105)</th>
<th>LDA (CDAHI 이상 n=303)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 10 mm</td>
<td>77.1</td>
<td>48.2</td>
</tr>
<tr>
<td>≤ 20 mm</td>
<td>88.6</td>
<td>66.7</td>
</tr>
<tr>
<td>≤ 40 mm</td>
<td>98.1</td>
<td>89.4</td>
</tr>
</tbody>
</table>

Missing data for pain VAS was imputed using modified last observation carried forward (mLOCF) and missing data for LDA and remission responders were based on nonresponder imputation (NRI)

Disclosure: Y. C. Lee, Express Scripts, 1,Pfizer Inc, 2; P. Emery, Pfizer, MSD, Abbvie, BMS, UCB, Roche, Novartis, Samsung, Sandoz, Eli Lilly and Company, 5; J. D. Bradley, Eli Lilly and Company, 1,Eli Lilly and Company, 3; B. Zhu, Eli Lilly and Company, 1,Eli Lilly and Company, 3; C. L. Gaich, Eli Lilly and Company, 1,Eli Lilly and Company, 3; Z. Cai, Eli Lilly and Company, 1,Eli Lilly and Company, 3; A. Quebe, Eli Lilly and Company, 1,Eli Lilly and Company, 3; A. Cardoso, Eli Lilly and Company, 1,Eli Lilly and Company, 3; Y. F. Chen, Eli Lilly and Company, 1,Eli Lilly and Company, 3; R. Fleischmann, Abbvie, Amgen, Astra Zeneca, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly and Company, Novartis, Roche, Sanofi-Aventis, Pfizer, UCB, 5.
Neuropathic-like Pain Affects the Tender Joint Count and Health-Related Quality of Life in Patients with Rheumatoid Arthritis

Kentaro Noda1, Miku Tajima2, Yosuke Oto3, Kazuhiro Otani3, Yoshiga Masayuki3, Haruyasu Ito1, Ken Yoshida1 and Daitaro Kurosaka1, 1Division of Rheumatology, Department of Internal Medicine, Jikei University School of Medicine, Tokyo, Japan, 2Division of Rheumatology, Department of Internal Medicine, Jikei University School of Medicine, Tokyo, Japan, 3Internal Medicine, Jikei University School of Medicine, Tokyo, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pain – Basic and Clinical Aspects Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Pain in rheumatoid arthritis (RA) has been thought to be due to nociceptive pain, but it was reported recently to include a mechanism associated with neuropathic pain as well. We therefore examined the frequency and clinical characteristics of RA patients with neuropathic-like pain.

Methods: Neuropathic-like pain in 145 outpatients (37 males, 108 females) with RA was evaluated from December 2015 to July 2016 using the PainDETECT Questionnaire (PDQ), a screening tool for evaluating neuropathic pain. The disease activity was evaluated using the disease activity score of 28 joint (DAS28), clinical disease activity index (CDAI), and simplified disease activity index (SDAI). The following parameters were evaluated: swollen joint count on 28 joints (SJC), tender joint count on 28 joints (TJC), patient global assessment (PGA), estimator global assessment (EGA), pain visual analogue scale (PainVAS), serum C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR). The physical function was evaluated using the mHAQ-DI. The quality of pain was evaluated using the short form of the McGill Pain Questionnaire (SF-MPQ). The health-related quality of life was evaluated using the short-form 36-item health survey (SF-36). We compared the clinical parameters between the patients with (PDQ≥13) and without (PDQ≤12) neuropathic-like pain.

Results: Thirty (20.7%) of the 145 patients with RA had neuropathic-like pain according to the PDQ. In patients with neuropathic-like pain, the sex, PGA, EGA, PainVAS, TJC, DAS28, CDAI, SDAI, SF-MPQ sensory and affective scores, HAQ-DI, mental component summary scores (MCS), and role-social component summary scores (RCS) in SF-36 were significantly higher than in those without neuropathic-like pain. There were no significant differences in the RA patients with and without neuropathic-like pain in SJC, CRP, or ESR. In a multinomial logistic regression analysis, significant differences were found in the TJC (p=0.015, OR 1.54), physical component summary (PCS) scores (p=0.041, OR 0.959), MCS scores (p=0.024, OR 0.940), and RCS scores (p=0.021, OR 0.959) in SF-36.

Conclusion: Neuropathic-like pain in RA patients was associated with subjective indicators, including TJC and the health-related quality of life, rather than objective indicators of the disease activity, including SJC, CRP, and ESR. Proper treatment of neuropathic-like pain in RA patients may improve the health-related quality of life.

Disclosure: K. Noda, None; M. Tajima, None; Y. Oto, None; K. Otani, None; Y. Masayuki, None; H. Ito, None; K. Yoshida, None; D. Kurosaka, None.

Eradication of Hepatitis C Among US Veterans: Examination of Changes in Pain Severity and Prescription Opioid Use Following Treatment

Abstract Number: 2221

Eradication of Hepatitis C Among US Veterans: Examination of Changes in Pain Severity and Prescription Opioid Use Following Treatment


Abstract Number: 2221

Eradication of Hepatitis C Among US Veterans: Examination of Changes in Pain Severity and Prescription Opioid Use Following Treatment

Hepatitis C virus (HCV) is associated with chronic widespread pain, fatigue, myalgia, arthritis, sicca symptoms and vasculitis. Data regarding prior interferon-based treatment of HCV on pain is conflicting and the impact of direct acting antivirals (DAA) on extrahepatic manifestations is unknown. The study objective is to assess the impact of DAA treatment on pain and opioid use among patients treated at a single VA medical center.

Methods:
Data was obtained from the VA electronic health record through retrospective administrative data abstraction and manual chart review. Inclusion criteria: Veterans with positive HCV antibody or HCV RNA or HCV genotype test or an ICD 9/ICD 10 code for HCV, seen in the rheumatology clinic at least once during the study period and treated with DAA without interferon between January 1, 2010 and December 31st 2016; exclusion criteria: deceased during study period. In addition to demographics, HCV status and HCV treatment, data abstracted included (1) numeric rating scale pain scores (0=“no pain” to 10=“Worst pain imaginable”) obtained with other vital signs during outpatient visits and (2) opioid dose for patients prescribed opioid therapy. Pain scores were averaged over two 6-month periods: 6 months leading up to HCV treatment and 6 months following completion of treatment. Opioid dose was converted to a morphine equivalent daily dose (MEDD) and averaged across the same two 6-month intervals. Generalized estimating equations were used to model the change in average pain and MEDD from pre- to post-HCV treatment.

Results:
A total of 126 patients completed HCV treatment with DAA, of which 121 (96%) achieved a sustained virologic response (SVR) and were included in the analysis. A majority (93%) were male, with a mean age of 59 (± 5.6) years. Average pre-treatment pain was 4.4 (SD 2.4). Among the 67 patients prescribed opioid therapy, average pre-treatment MEDD was 52.40mg. Both pain and MEDD decreased following SVR. The effect of time was associated with an average reduction in pain of 0.54 points (p=0.02, Cohen’s d=0.16). Of the 67 patients prescribed opioids in the pre-treatment period, average MEDD decreased by 8mg during the post-treatment period (p<0.01, Cohen’s d=0.24), and 67% of patients experienced an opioid dose reduction, with 12 patients discontinuing opioids entirely.

Conclusion:
Among US Veterans with HCV seen in a rheumatology clinic at a single center, subjective pain scores were reduced post-treatment. In addition, among those prescribed opioids pre-treatment, a majority had a reduction in opioid dose post-treatment. Further evaluation of change in musculoskeletal manifestations of HCV and utilization of rheumatology care with the advent of highly effective HCV treatment is warranted.
Comparative Risk of Respiratory Depression in Patients Treated with Opioids for Non-Malignant Pain

Meghna Jani, Kamilla Kopec-Harding, Mark Lunt and William G Dixon, Arthritis Research UK Centre for Epidemiology, The University of Manchester, Manchester, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pain – Basic and Clinical Aspects Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Opioid use for non-cancer pain has increased considerably over the last 30 years. The U.S. Food and Drug Administration announced several boxed warnings in 2016 to highlight serious opioid related risks in an effort to reduce fatal overdoses, 80% of which are unintentional. The most serious opioid related adverse event is respiratory depression (RD), which is potentially fatal. Few data exist on the incidence of RD in opioids users for non-malignant pain with no comparative data between drugs. The aim of this study was to assess the comparative risk of RD in new users of opioids for non-malignant pain using routinely collected electronic patient records (EPR).

Methods:

Opioid users from Salford hospital EPR were identified (26/9/14-31/5/16). Patients with prior malignancy were excluded using ICD-10 codes. Those with prior history of opioid use were excluded using keyword searches within the medicines reconciliation document. Administered medication was categorised as opioid monotherapy by drug or combination of opioids. Electronic National Early Warning Scores (regularly monitor vital signs during inpatient stays) were used to classify RD. An RD event was defined as any one of the following: respiratory rate (RR) ≤8/min, RR ≤10/min and oxygen saturations<94%, RR≤10/min and altered consciousness, or dispensed naloxone use. The primary analysis attributed RD to opioids during a risk window of ‘on drug + 1 day’, unless the patient switched to...
another opioid. Patients contributed follow up time for a particular drug from dispensed drug start date until day after discontinuation, first RD event, death or end of last hospital admission. Crude rates/1000 person years of follow up were calculated and Cox proportional hazards models were used to examine the comparative risk of administered opioids and RD, adjusted using propensity scores (PS) derived using inverse-probability of treatment weights.

Results:

7702 opioid users were included in the study, 3,839 female (50%) and a mean age (SD) of 52(21) years. There were 261 RD events observed on treatment, 130 with severe respiratory depression (RR<8/min), 135 requiring naloxone and 3 respiratory arrests. Patients on fentanyl, morphine, oxycodone and combination treatment had the highest crude rates (table). Patients on oxycodone had the highest proportion of comorbidities. In the propensity adjusted Cox-model, using codeine as the referent, patients on fentanyl, morphine, and combination opioids had the highest risk of RD (table). Compared to morphine, codeine had an adjusted HR of 0.64 (95% CI: 0.43, 0.95).

Conclusion:

Fentanyl and morphine monotherapy have a significantly higher risk of RD than codeine. Following PS adjustment the risk of RD on oxycodone no longer remained significant. The strengths of this study include real time physiological parameters to define RD and administered medication use (rather than prescribed) to define exposure.

<table>
<thead>
<tr>
<th>Opioid (no. of patients)</th>
<th>Codeine</th>
<th>Fentanyl</th>
<th>Morphine</th>
<th>Oxycodone</th>
<th>Combination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years, SD)</td>
<td>53</td>
<td>49</td>
<td>52</td>
<td>52</td>
<td>53</td>
</tr>
<tr>
<td>Gender (no. of patients)</td>
<td>80%</td>
<td>82%</td>
<td>83%</td>
<td>80%</td>
<td>82%</td>
</tr>
<tr>
<td>Respiratory depression</td>
<td>0.64</td>
<td>0.43</td>
<td>0.57</td>
<td>0.64</td>
<td>0.43</td>
</tr>
</tbody>
</table>

Disclosure: M. Jani, None; K. Kopeck-Harding, None; M. Lunt, None; W. G. Dixon, None.
Background/Purpose: Osteoarthritis (OA) is a common cause of pain and is associated with depression in older adults. Pain and depression are major burdens to people suffering from OA. Being physically active has broad health benefits for people with OA, including reduced pain and depressive symptoms. Increasing physical activity within a fixed 24-hour day requires trading time with other behaviors. Applying isotemporal substitution methods to observational data, we modeled the potential benefits in relation to pain and high depressive symptoms from trading time in one type of activity for another (e.g. replacing sedentary time with moderate physical activity).

Methods: This cross-sectional study examined data from the Accelerometer Sleep Substudy of Osteoarthritis Initiative. Participants wore two ActiGraph GT3X triaxial accelerometers for 24 hours over 7 days: one on non-dominant wrist to monitor sleep and one on waist to monitor physical activity (PA). Outcomes were the presence of WOMAC knee pain, report of pain interference with work, and presence of high depressive symptoms identified by Center for Epidemiologic Studies Depression scale >=16. Odds ratio (OR) and 95% confidence interval (CI) from logistic regression were presented for the isotemporal substitution of the same amount of time in one type of activity (sleep, sedentary behavior, light PA, moderate PA) for another in relation to the outcomes holding time in other activities constant. Isotemporal substitution models controlled for socioeconomics (age, sex, race, income) and health factors (knee OA, obesity, comorbidity).

Results: These 187 men and women had mean age 67 (SD 8.5), 50% were female, 41% obese and 60% had radiographic knee OA. On a daily basis, these adults on average spent 7 hours in sleep, 10 hours in sedentary behavior, 6 hours in light PA, and 27 minutes in moderate PA. Isotemporal analyses on WOMAC pain indicated substituting 10 minutes/day of moderate PA for either sleep (OR=0.82) or light PA (OR=0.83) was significantly (P≤0.05) associated with less frequent reports of knee pain. Similarly, substituting 10 minutes/day of moderate PA for sleep (OR=0.60), sedentary behavior (OR=0.62) or light PA (OR=0.62) was significantly associated with less frequent pain interference. Isotemporal analyses on high depressive symptoms indicated substituting 10 minutes/day of light PA for either sleep (OR=0.78) or sedentary behavior (OR=0.79) was significantly associated with less frequent report of high depressive symptoms.

Conclusion: Interventions promoting moderate activities may be beneficial to address pain while substituting light activity for sedentary behavior or sleep may be beneficial to address depressive symptoms.

Disclosure: J. Song, NIH funding, 2; D. D. Dunlop, NIH funding, 2; P. Semanik, NIH funding, 2; A. H. Chang, NIH funding, 2; R. D. Jackson, NIH funding, 2; R. W. Chang, NIH funding, 2; J. Lee, NIH funding, 2.


Abstract Number: 2224

Analgesic Potential of NEO6860, a Modality Selective TRPV1 Antagonist, in Osteoarthritis Knee Pain: Results of a Randomized, Controlled, Proof-of-Concept Trial
SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pain – Basic and Clinical Aspects Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Current treatments of osteoarthritis (OA) of the knee, such as NSAIDs, have significant limitations in both efficacy and safety. NEO6860 is a modality selective antagonist (shows full antagonism when activated by capsaicin, but little or no antagonism when activated by heat or low pH) at the cloned human transient receptor potential vanilloid subtype 1 (TRPV1) receptor. In a phase I study\(^1\), NEO6860 showed good bioavailability and demonstration of pharmacodynamic effect as well as a target engagement.

Methods: This proof-of-concept, randomized, double blinded, placebo controlled, 3-period crossover, phase II study compared alternately 1 day (2 doses): NEO6860 (500 mg bid), placebo, and naproxen (500 mg bid) in a random sequence in 54 patients with OA (mean age: 61; mean BMI 29 kg/m\(^2\); 35% with hypertension, 14% with dyslipidemia and 10% with diabetes).

Results: Pharmacokinetics (PK) data revealed that the exposure was approximately 1.6 times higher when compared with phase I at the same dose (\(C_{\text{max}} = 4337\text{ ng/mL and } 2770\text{ ng/mL, respectively}\). An analgesic effect of NEO6860 was shown using Numerical Rating Scale (NRS) post-exercise at 3 and 24h, using a mixed ANCOVA Model, controlling for Period, Sequence and Treatment as fixed effects and baseline by period as covariate:

<table>
<thead>
<tr>
<th></th>
<th>NEO6860 (N=52)</th>
<th>Naproxen (N=52)</th>
<th>Placebo (N=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in NRS from baseline to...</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 hours post-dose, Mean (95%CI)</td>
<td>-0.56 (-0.94 ; -0.19)</td>
<td>-0.7 (-1.09 ; -0.34)</td>
<td>-0.38 (-0.75 ; -0.00)</td>
</tr>
<tr>
<td>8 hours post-dose, Mean (95%CI)*</td>
<td>-0.57 (-0.95 ; -0.20)</td>
<td>-0.65 (-1.02 ; -0.27)</td>
<td>-0.83 (-1.20 ; -0.46)</td>
</tr>
<tr>
<td>24 hours post-dose, Mean (95%CI)</td>
<td>-0.67 (-1.09 ; -0.26)</td>
<td>-0.97**(-1.39 ; -0.55)</td>
<td>-0.29**(-0.71 ; 0.13)</td>
</tr>
</tbody>
</table>

*: 8 h post dose was the primary endpoint; **: p <0.05 comparing naproxen to placebo.

This pattern was confirmed on NRS pre-exercise, Patient’s Global Impression of Change (PGIC) and, to a lesser extent, the WOMAC; however, the observed effect was below the hypothesis used for power estimate, explaining in part the \(P\) values \(\geq 0.05\). The safety profile was comparable to that in the prior phase I study, taking into consideration the unexpectedly higher level of exposure, and the two severe adverse events (AEs) reported (feeling hot and headache, each reported by one patient) were resolved within one day. Importantly, no hyperthermia and no change in heat pain perception were reported.

Conclusion:

In patients with OA pain, an analgesic effect was observed with NEO6860 while not showing the two AEs previously observed with TRPV1 antagonist, consistent with its modality selective mode of action. Future investigations should emphasize on: 1- reducing the NEO6860 dose, which may maintain the analgesic effect with multiple dosing, and 2- testing NEO6860 in combination with NSAIDs to improve analgesia and potentially alleviate safety concerns of current treatments of OA.


Disclosure: P. Arsenault, NEOMED paid consulting fees, 5; R. Leff, NEOMED paid consulting fees, 5; N. Katz, NEOMED paid consulting fees, 5; P. Walker, NEOMED Institute, 3; D. Chiche, NEOMED Institute, 3.

Cntx-4975 (Trans-Capsaicin) Injection Provides Clinically Meaningful Pain Reduction in Subjects with Painful Intermetatarsal Neuroma (Morton’s Neuroma): An Open-Label, Ascending-Dose Study

Peter Hanson1, Ira Gottlieb2, Margaret Kelly3, James Campbell1, Robert Allen4 and Randall Stevens1, 1Centrexion Therapeutics, Boston, MA, 2Chesapeake Research Group, Pasadena, MD, 3Edirutop, Christiansburg, VA, 4Allen Medical LLC, Malvern, PA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pain – Basic and Clinical Aspects Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Morton’s neuroma (MN) is a painful condition of the third intermetatarsal space caused by distal common digital nerve compression. CNTX-4975, a highly purified, synthetic trans-capsaicin, targets the transient receptor potential vanilloid 1, producing analgesia via reversible desensitization of end terminals of primary afferent pain fibers. A prior double-blind randomized trial demonstrated efficacy of CNTX-4975 100 µg injected into the area surrounding the neuroma.* This phase 1b, open-label trial further evaluated dosing, safety (including sensory and motor examination), tolerability, efficacy, and duration of pain relief following injection of CNTX-4975.

Methods: Subjects with painful MN indicated their level of pain at baseline and up to 6 months following a single injection of CNTX-4975 200 µg or 600 µg using the Numeric Pain Rating Scale (NPRS; 0 [none]–10 [severe]). Clinically meaningful pain reduction was defined as ≥30% pain decrease versus baseline.

Results: Eleven subjects were enrolled (200 µg, n=5; 600 µg, n=6). The mean (SD) baseline pain score with walking was 5.7 (1.3). A substantial reduction in pain with walking was evident as early as 1 week in both dose groups (−3.0, 200 µg; −2.9, 600 µg). The mean (SD) change in pain with walking score at 8 weeks was −3.0 (3.8) in the 200-µg group and −4.3 (2.4) in the 600-µg group. At 6 months (only the 600-µg group was followed), the change in pain score was −3.8 (3.1). None of the subjects had a decrease in sensory or motor function compared with baseline. All 11 subjects reported procedure pain as tolerable.

Conclusion: A single injection of CNTX-4975 200 µg and 600 µg for MN provided a rapid and prolonged duration of clinically meaningful pain reduction with acceptable tolerability and safety. This study provides a basis for further randomized trials at these dose levels. *Campbell, et al, Pain, 2016.

Disclosure: P. Hanson, Centrexion Therapeutics, 3; I. Gottlieb, None; M. Kelly, None; J. Campbell, Centrexion Therapeutics, 3; R. Allen, None; R. Stevens, Centrexion Therapeutics, 3.


Abstract Number: 2226

Cntx-4975 (Trans-Capsaicin) Injection Provides Clinically Meaningful Pain Reduction in Subjects with Painful Intermetatarsal Neuroma (Morton’s Neuroma): A Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Study

James Campbell1, Randall Stevens1, Ira Gottlieb2, Kimberly Guedes1, Robin Burges1, Margaret Kelly3 and Peter Hanson1, 1Centrexion Therapeutics, Boston, MA, 2Chesapeake Research Group, Pasadena, MD, 3Edirutop, Christiansburg, VA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pain – Basic and Clinical Aspects Poster  
Session Type: ACR Poster Session C  
Session Time: 9:00AM-11:00AM

**Background/Purpose:** Morton’s neuroma (MN) is a painful condition of the third intermetatarsal space caused by distal common digital nerve compression. CNTX-4975 is a highly purified, synthetic, trans-capsaicin that targets the transient receptor potential vanilloid 1, producing analgesia via reversible desensitization of end terminals of primary afferent pain fibers. Prior trial data support the use of injectable CNTX-4975 to treat MN in subjects who fail conservative measures.*

**Methods:** The primary efficacy endpoint in this phase 2, 12-week randomized, double-blind, placebo-controlled trial was change from baseline to week 4 in the average diary scores for neuroma foot pain with walking using the Numeric Pain Rating Scale. Clinically meaningful pain reduction was defined as ≥30% pain reduction versus baseline. Safety and tolerability assessments included treatment-emergent adverse events (TEAEs) and sensory function examination.

**Results:** Subjects received a single, ultrasound-guided injection of placebo (n=39), CNTX-4975 200 µg (n=38), or CNTX-4975 600 µg (n=39) following ankle-block anesthesia. Although the primary endpoint did not reach statistical significance, both doses were numerically superior to placebo, with greater clinically meaningful reductions from baseline at weeks 4 and 12. One study site, identified as an outlier site before database lock, had a high placebo rate; in a post-hoc analysis excluding this site, results either achieved (weeks 5 and 12; P<0.05) or neared statistical significance despite a 34% decrease in the number of subjects. The cumulative responder analysis at week 12 showed >90% pain reduction versus baseline for 2% of the placebo group and 40% of the CNTX-4975 200-µg group. In total, 63% of subjects reported ≥1 TEAE (56%, placebo; 74%, CNTX-4975 200 µg; 56%, CNTX-4975 600 µg). No decline was observed in tactile sensibility following injection.

**Conclusion:** A single injection of CNTX-4975 200 µg or 600 µg for MN provided rapid and prolonged clinically meaningful pain reduction with good tolerability. *Campbell, et al., Pain, 2016.

Disclosure: J. Campbell, Centrexion Therapeutics, 3; R. Stevens, Centrexion Therapeutics, 3; I. Gottlieb, None; K. Guedes, Centrexion Therapeutics, 3; R. Burges, Centrexion Therapeutics, 3; M. Kelly, None; P. Hanson, Centrexion Therapeutics, 3.


**Abstract Number:** 2227

**S100A9 Induces a Pain Response during Experimentally Induced Acute Synovitis**

**Arjen B. Blom**¹, Edwin J. W. Geven¹, Martijn H. van den Bosch¹, Esmeralda N. Blaney Davidson¹, Peter M. van der Kraan¹ and Peter L. van Lent², ¹Experimental Rheumatology, Radboud university medical center, Nijmegen, Netherlands, ²Radboud University Nijmegen Medical Center, Rheumatology; Nijmegen, Netherlands  
**First publication:** September 18, 2017

**SESSION INFORMATION**  
**Session Date:** Tuesday, November 7, 2017  
**Session Title:** Pain – Basic and Clinical Aspects Poster  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Synovitis-associated pain is an important aspect of arthritis pathology. Several inflammatory mediators released by the synovium have been implicated in the regulation of pain, including S100A8 and S100A9 which may regulate pain either via direct stimulation of TLR4 on the nerve endings in the synovium or via stimulation of the dorsal root ganglia (DRG), thereby enabling an increased phagocyte infiltration. To investigate the role of S100A9 in the pain response after induction of an acute synovitis using streptococcal cell walls (SCW) as a trigger, comparing S100A9⁻/⁻ mice and their WT controls.

**Methods:**
Acute synovitis was induced by a single i.a. injection of SCW in the knee joint of C57Bl6 (WT) mice and S100A9−/− mice, control mice received an i.a. saline injection. Serum S100A8/A9 levels were investigated by ELISA and expression of S100A8 and S100A9 in synovium and DRG by immunohistochemistry. Joint swelling and cell influx was assessed by 99mTc accumulation and histology, respectively. Pain response were investigated Incapacitance Tester (weight bearing), Catwalk (gait analysis) and von Frey’s filaments (mechanical allodynia). Gene expression of inflammatory mediators and neuron activation markers in DRG were determined by q-PCR.

Results:

A single i.a. injection of SCW resulted in increased synovial expression of S100A8 and S100A9 and subsequent increased serum S100A8/A9 levels (2.6-fold, \(P < 0.001\)) 1 day p.i., which returned to basal levels at 7 days p.i. The increased expression of S100A9 did not contribute to the development of inflammation since joint swelling and cell influx were similar in WT and S100A9−/− mice 1 day p.i. Using the Incapacitance Tester, WT mice showed a marked and significant decrease in percentage of weight bearing on the SCW injected hindpaw (28%) compared to saline injection (47%, \(P < 0.001\)) 1 day p.i., whereas S100A9−/− mice did not. In addition, gait analysis showed that the stand-phase of the unaffected paws were significantly increased in WT mice 1 day p.i., which will reduce the load on the inflamed paw, while in S100A9−/− mice these parameters were not altered. No difference in mechanical allodynia was observed, both mouse strains showed a similar reduction of paw withdrawal threshold (4.2 and 4.5 fold decrease respectively). Analysis of DRG showed no increased phagocyte infiltration after SCW injection as determined by S100A8 and S100A9 immunohistochemistry and no change in gene expression of MCP-1, KC, IL-1β or TNF was measured. However, expression of neuron activation markers NAV1.7, ATF3 and GAP43 were significantly increased at 1 day after SCW injection in WT mice as determined by S100A8 and S100A9 immunohistochemistry and no change in gene expression of MCP-1, KC, IL-1β or TNF was measured. However, expression of neuron activation markers NAV1.7, ATF3 and GAP43 were significantly increased at 1 day after SCW injection in WT mice as compared to saline injected mice (\(P = 0.022, 0.004\) and 0.030, respectively) while SCW injection in S100A9−/− mice did not show increased expression, which is in line with the reduced pain response observed earlier in S100A9−/− mice.

Conclusion:

These findings show that S100A9, which is released from the synovium upon inflammation, is an important mediator of inflammatory pain response in the knee, and that during the acute phase of inflammation is likely regulated via direct activation of TLR4 on nerve endings in the synovium and not via increased infiltration of phagocytes in the DRG.
We performed a multimodal study in TrkA/C knock-in mice expressing a chimeric receptor formed by the native extracellular part of TrkA and the functional transmembrane and intracellular part of the tyrosine kinase type C receptor (TrkC) which binds neurotrophin 3 (NT3). We investigated nociceptive behavior such as mechanical allodynia and thermal hyperalgesia using von Frey and paw immersion test in CFA induced-arthritis model. In vivo cartilage and bone remodeling were assessed by scintigraphic imaging using $^{99m}$Tc-NTP 15-5 and $^{99m}$Tc-HMDP radiotracers, respectively. CD68 positive cell infiltration and CGRP positive nerve fibers sprouting were assessed in the joint as well as TrkA and ASIC3 expression in DRG cells bodies using an immunohistochemical approach. We are currently investigating the intracellular pathway potentially involved at the DRG level.

**Results:** Our results showed a specific lack of mechanical allodynia development while thermal hyperalgesia was unaffected in TrkA/C monoarthritic mice compared to WT littermates. This change in pain behavior was associated with a specific decrease of $^{99m}$Tc-HMDP in TrkA/C monoarthritic mice, suggesting a unique change in bone remodeling. Indeed, cartilage remodeling was similar between both genotypes. We also observed a decrease of CD68-positive cell infiltration as well as CGRP expression in the inflamed joint in TrkA/C mice compared to WT mice while the expression of TrkA and ASIC3 in the DRGs was unaffected between both genotypes following monoarthritis.

**Conclusion:**

The present study demonstrates a specific involvement of NGF/TrkA signaling in pain, especially mechanical hypersensitivity and also bone remodeling in inflammatory arthritis. We are now investigating the specific intracellular pathway involved.

**Disclosure:** L. Delay, None; J. Barbier, None; L. Boudieu, None; D. Ardid, None; A. Briat, None; P. Auzeloux, None; E. Moit-Noirault, None; A. Moqrich, None; F. Marchand, None.


**Abstract Number:** 2229

**The Effect of Intra-Articular Neurotoxin on Arthritis Pain and Substance P Expression in the Dorsal Root Ganglion: Results from Murine Arthritis Models**

**Hollis Krug**$^{1,2}$, Sandra Frizelle$^3$, Nicole Blanshan$^4$, Christopher W. Dorman$^3$ and Maren Mahowald$^{2,5}$, $^1$Medicine, Minneapolis VAHCS, Minneapolis, MN, $^2$Medicine, University of Minnesota Medical School, Minneapolis, MN, $^3$Research, Minneapolis VA Health Care System, Minneapolis, MN, $^4$Research, Minneapolis VAHCS, Minneapolis, MN, $^5$Rheumatology/ Dept of Medicine, Minneapolis VA and Univ MN Med School, SAINT PAUL, MN

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Pain – Basic and Clinical Aspects Poster

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Substance P (SP) release and binding to NK-1 produces pain transmission. Neurotoxins (NT) that prevent release of SP, such as onabotulinum toxin (BoNT/A), and those that deplete SP, such as vanilloids (VAN), produce analgesia in chronic murine arthritis. This study evaluated the relationship of dorsal root ganglion (DRG) SP expression to pain and analgesia in murine arthritis treated with these NTs.

**Methods:** C57Bl6 male mice received intra-articular (IA) carrageenan, Complete Freund’s Adjuvant (CFA) or Collagenase (COL) to produce acute inflammatory, chronic inflammatory or chronic noninflammatory arthritis respectively. IA therapies were given at appropriate intervals before examination. Twelve-week-old mice were examined after arthritis induction. Evoked and spontaneous pain was quantitated. DRGs were harvested for immunohistochemistry (IHC) after pain assessment. SP expression was measured as % DRG neurons expressing SP.

**Results:** Evoked pain in arthritic and naïve mice correlated with SP expression ($R^2=0.906, \beta=1.343$). IA vanilloid agonists and antagonist reduced SP expression in a dose dependent manner in chronic inflammatory arthritis (CFA). IA BoNT/A reduced SP expression in CFA arthritis but significantly increased SP expression in COL arthritis at 4 weeks after induction but not at 6 weeks. None of the neurotoxins altered SP expression in non-arthritic mice.
Conclusion: Both SP depletion and release inhibition are analgesic in chronic murine arthritis. SP expression varied with NT mechanism of action in COL arthritis at 4 weeks. BoNT/A had different effects on SP expression in 4 week COL and CFA arthritis but SP expression in 6 week COL treated with BoNT/A was similar to that seen in BoNT/A treated CFA. The effect of NT on SP expression may depend on pathophysiology of pain production and chronicity. Understanding the effect of NT treatment on NK-1 expression will be important.

Disclosure: H. Krug, None; S. Frizelle, None; N. Blanshan, None; C. W. Dorman, None; M. Mahowald, None.

Abstract: The effect of intra-articular neurotoxin on arthritis pain and substance P expression in the dorsal root ganglion results from murine arthritis models

Abstract Number: 2230

Use of Prescription Opioids Among Patients with Systemic Inflammatory Diseases (SID) Versus Patients with Hypertension but No SID

Sarah Chen1, Candace H. Feldman2, Gregory Brill3, Yvonne C. Lee4, Rishi J. Desai5 and Seoyoung C. Kim6, 1Brigham and Women's Hospital, Boston, MA, 2Rheumatology, Brigham & Women's Hospital, Boston, MA, 3Division of Pharmacoepidemiology and Pharmacoeconomics, Brigham and Women's Hospital/Harvard Medical School, Boston, MA, 4Rheumatology Immunology & Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 5Division of Pharmacoepidemiology and Pharmacoeconomics, Brigham and Women's Hospital, Boston, MA, 6Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pain – Basic and Clinical Aspects Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Opioid prescribing in the U.S. has increased at an alarming rate amid uncertainty over effectiveness and rising concerns over safety of this practice. Patients with systemic inflammatory diseases (SID) often suffer from chronic pain, and may be more likely to be prescribed opioids compared to those without SID. We investigated the rates of opioid prescribing in SID patients compared to age, sex and index date-matched patients with hypertension (HTN) but no SID.

Methods: We conducted a cohort study using insurance claims data from Truven MarketScan (2003-2014). We identified individuals aged >18 years with prevalent SID [i.e., rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), ankylosing spondylitis (AS), and psoriatic arthritis (PsA)] based on a combination of ≥2 diagnosis codes and ≥1 dispensing for disease-specific drug dispensing and defined the dispensing date of the disease-specific prescription as the index date. We matched each SID patient 1:1 by age, sex and index date to a HTN patients, identified using >2 diagnosis codes for HTN and >1 dispensing for antihypertensive medication. We excluded patients with any malignancy. All patients were required to have ≥1 year of continuous enrollment before and after the index date. We assessed prescription opioid use during the 1-year follow-up from the index date in the SID group compared to HTN group.

Results: We identified 181,922 RA (77% female, mean age 55), 45,879 SLE (91% female, mean age 47), 30,346 PsA (51% female, mean age 50) and 7,704 AS (39% female, mean age 45) patients, matched to HTN patients. At baseline, depression and fibromyalgia were more prevalent in SID cohort compared to matched HTN patients, while diabetes and cardiovascular disease were more common in HTN patients. Back pain was most prevalent among AS cohort (16%) compared to 4% in the matched HTN cohort (p<0.001). During
1 year follow-up, >1 opioid prescription was dispensed among 46% RA (vs. 32% HTN, p<0.001), 46% SLE (vs. 33% HTN, p<0.001), 41% PsA (vs. 31% HTN, p<0.001), and 50% AS (vs. 30% HTN, p<0.001) patients. Long-term opioid use (>90 days), and extended-acting opioid prescriptions also showed similar trends, with higher rates seen in SID cohorts compared to HTN, and highest use seen among AS patients (Table).

**Conclusion:** Nearly half of SID patients and approximately 30% of HTN patients used prescription opioids during a 1-year period. The highest percentage of opioid dispensing were seen among patients with AS. Compared to HTN patients, SID patients had more frequent use of any opioids, multiple types or long-acting opioids. Long-term use was also more common in SID patients.

<table>
<thead>
<tr>
<th>Table. Patient characteristics at baseline and their prescription opioid use patterns during 1-year followup</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RA SID</strong></td>
</tr>
<tr>
<td><strong>Baseline characteristics</strong></td>
</tr>
<tr>
<td>Age (SD)</td>
</tr>
<tr>
<td>% Female</td>
</tr>
<tr>
<td>Baseline opioid use</td>
</tr>
<tr>
<td>Substance use</td>
</tr>
<tr>
<td>Smoking</td>
</tr>
<tr>
<td>Depression</td>
</tr>
<tr>
<td>Fibromyalgia</td>
</tr>
<tr>
<td>Diabetes</td>
</tr>
<tr>
<td>Back pain</td>
</tr>
<tr>
<td>Migraine headache</td>
</tr>
<tr>
<td>Osteoarthritis</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
</tr>
<tr>
<td>NSAID use</td>
</tr>
<tr>
<td>Benzodiazepine use</td>
</tr>
<tr>
<td><strong>Outcome during 1-year follow-up</strong></td>
</tr>
<tr>
<td>% patients with &gt;1 opioid Rx</td>
</tr>
<tr>
<td>% patients with &gt;2 types of opioid Rx</td>
</tr>
<tr>
<td>% patients with immediate-acting opioid Rx</td>
</tr>
<tr>
<td>% patients with extended-acting opioid Rx</td>
</tr>
<tr>
<td>% patients with long-term opioid Rx (&gt;90 days)</td>
</tr>
</tbody>
</table>

Disclosure: S. Chen, None; C. H. Feldman, None; G. Brill, None; Y. C. Lee, Express Scripts, 1,Pfizer Inc, 2; R. J. Desai, None; S. C. Kim, AstraZeneca, 2,Pfizer Inc, 2,Roche Pharmaceuticals, 2,Bristol-Myers Squibb, 2,Merck Human Health, 2.


Abstract Number: 2231
MCC22, a Novel Compound That Targets Both CCR5 and Mu Opioid Receptors, Is Highly Effective in Treating Inflammatory Arthritis Pain

Raini Dutta¹, Mary Lunzer², Jennifer L. Auger³, Eyup Akgün², Philip Porthoghese² and Bryce A. Binstadt³. ¹Pediatrics, University of Minnesota, Minneapolis, MN, ²Department of Medicinal Chemistry, University of Minnesota, Minneapolis, MN, ³Center for Immunology and Department of Pediatrics, University of Minnesota, Minneapolis, MN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pain – Basic and Clinical Aspects Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The pain that accompanies rheumatoid arthritis and other chronic inflammatory conditions is difficult to manage. Although opioids provide potent analgesia, chronic opioid use is associated with tolerance and addiction. Recent studies have demonstrated functional interactions between chemokines and opioids in pain signaling pathways. Reported crosstalk and even heterodimerization between chemokine and opioid receptors led our group to develop bivalent compounds that can bind both types of receptors, with the goal of targeting opioids to sites of inflammation. MCC22 is novel bivalent compound comprising a CCR5 antagonist and a mu opioid receptor agonist, connected by a 22-atom linker. We evaluated the efficacy of MCC22 in the K/B.g7 T cell receptor transgenic mouse model of inflammatory arthritis.

Methods: MCC22 or morphine was administered intraperitoneally at varying doses to arthritic K/B.g7 mice or non-arthritic control mice. Mechanical pain hypersensitivity was measured each day before (baseline) and after drug administration, using the electronic von Frey test. The potency of MCC22 relative to morphine was calculated. Functional readouts of pain included grip strength and nesting behavior. A separate dosing regimen was used to determine whether the drugs induced pharmacologic tolerance.

Results: MCC22 provided ~3000-fold more potent analgesia than morphine in this model of inflammatory arthritis. Daily treatment with MCC22 also led to a cumulative analgesic effect, reducing the daily baseline pain level. MCC22 produced no observable analgesic effect in non-arthritic control mice. Importantly, repeated administration of MCC22 did not induce pharmacologic tolerance, whereas a similar regimen of morphine did. Both grip strength and nesting behaviors improved among arthritic mice treated with MCC22. Ankle thickness and arthritis scores were not affected by MCC22 administration. The analgesic effect of MCC22 was abolished in K/B.g7 mice genetically lacking CCR5, demonstrating the receptor specificity of the pharmacophore.

Conclusion: MCC22 is a novel bivalent compound that relies on a CCR5 antagonist to deliver an opioid agonist to sites of inflammatory pain. Our findings demonstrate that MCC22 provides highly potent analgesia and improved functional outcomes in a model of inflammatory arthritis, without inducing typical opioid tolerance. These findings suggest that MCC22 or similar compounds could be used to treat the pain associated with inflammatory arthritis and related conditions, while minimizing the risks typically associated with chronic opioid use.

Disclosure: R. Dutta, None; M. Lunzer, None; J. L. Auger, None; E. Akgün, None; P. Porthoghese, None; B. A. Binstadt, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/mcc22-a-novel-compound-that-targets-both-ccr5-and-mu-opioid-receptors-is-highly-effective-in-treating-inflammatory-arthritis-pain

Abstract Number: 2232

A Role for CCR2 in Chronic Behavioral and Neuroimmune Changes in the DMM Model of Osteoarthritis

Phuong Tran¹, Shingo Ishihara², Rachel E. Miller³, Richard J. Miller⁴ and Anne-Marie Malfait¹. ¹Rheumatology, Rush University Medical Center, Chicago, IL, ²Internal Medicine, Rush University Medical Center, Chicago, IL, ³Biochemistry, Rush University Medical Center, Chicago, IL, ⁴Pharmacology/Medical Humanities and Bioethics, Northwestern University, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017

Abstract Number: 2232

A Role for CCR2 in Chronic Behavioral and Neuroimmune Changes in the DMM Model of Osteoarthritis

Phuong Tran¹, Shingo Ishihara², Rachel E. Miller³, Richard J. Miller⁴ and Anne-Marie Malfait¹. ¹Rheumatology, Rush University Medical Center, Chicago, IL, ²Internal Medicine, Rush University Medical Center, Chicago, IL, ³Biochemistry, Rush University Medical Center, Chicago, IL, ⁴Pharmacology/Medical Humanities and Bioethics, Northwestern University, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Background/Purpose: The aim of this study was to explore pain-related behaviors and associated cellular changes in the pain pathway in experimental osteoarthritis (OA) induced by destabilization of the medial meniscus (DMM). In wild-type (WT) mice, DMM results in slowly progressive knee OA, associated with pain behaviors, including mechanical allodynia and decreased locomotion. We have previously reported that CCR2 signaling is a key mediator for persistence of pain after DMM. Specifically, 8 weeks after DMM, L3-L5 dorsal root ganglia (DRG) neurons show increased expression of CCR2 gene and protein. Ccr2 null mice develop initial mechanical allodynia following DMM, but the allodynia is not maintained (unlike in WT mice). WT and Ccr2null mice develop the same extent of joint damage after DMM.

Methods: DMM or sham surgery was performed in the right knees of 10-week old male WT or Ccr2 null C57BL/6 mice. The elevated plus maze was employed as a method for assessing anxiety-related responses (time spent grooming; time spent immobile) over a period of 5 minutes. To assess cellular changes in the peripheral and central nervous system, we quantified (1) macrophages in the L4 DRG, by immunostaining for F4/80 and (2) activated microglia in the L4 dorsal horn of the spinal cord, based on the morphology of Iba1-immunoreactive microglia, using established methods.

Results: Eight weeks after sham or DMM surgery, WT mice showed no behavioral changes in the elevated maze plus test. However, by 16 weeks after surgery, DMM (but not sham) operated mice showed behaviors indicative of anxiety, including increased periods of immobility (p=0.002, n=5-13) and increased time spent grooming (p=0.0073, n=6-15). These behaviors did not develop in Ccr2 null mice (p>0.9, n=8-14).

In WT mice, L4 DRG were strongly infiltrated with F4/80 expressing macrophages, 8 and 16 weeks after DMM. In contrast, in Ccr2 null mice, L4 DRG showed some macrophage infiltration at 8 weeks, but to a lesser extent than in WT mice. Furthermore, in Ccr2 null mice, F4/80 levels returned to baseline by week 16. The L4 dorsal horn in WT mice showed a clearly increased number of activated microglia 8 and 16 weeks after DMM but not sham surgery (wk 8: p=0.015; wk 16: p=0.039, n=3-6/group/time point). In Ccr2 null mice, activated microglia were increased 8 wks after DMM compared to baseline (p<0.05, n = 3-9/group/time point), but this returned to baseline by week 16.

Conclusion: We describe a novel behavior that specifically develops during the chronic stage of the DMM model: increased grooming, which is considered an indicator of anxiety. Increased grooming may be indicative of pain-related anxiety, since it coincides with the chronic pain phase of the disease. Ccr2 null mice did not develop this grooming behavior, confirming our previous findings that these mice do not develop chronic pain after DMM. Overall, these data support our previous work suggesting that CCR2 activation is important in the maintenance of chronic OA pain, perhaps by mediating neuro-immune interactions in both the DRG and the spinal cord. The fact that Ccr2 null mice developed initial macrophage infiltration and microgliosis that subsequently resolved suggests that these pathways may be targetable.

Disclosure: P. Tran, None; S. Ishihara, None; R. E. Miller, None; R. J. Miller, None; A. M. Malfait, Galapagos, Regeneron, 5,Ferring, 2,OARSI board of directors, 6.


Abstract Number: 2233

The Role of Life Purpose in Disability and Depression in Patients with Acute Low Back Pain

Elizabeth Salt¹, Leslie Crofford², Mary Kay Rayens³ and Suzanne Segerstrom⁴, ¹University of Kentucky, Lexington, KY, ²Vanderbilt University, Nashville, KY, ³College of Nursing, University of Kentucky, Lexington, KY, ⁴Psychology, University of Kentucky, Lexington, KY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: ARHP Pain – Clinical Aspects Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM
The Role of Life Purpose in Disability and Depression in Patients with Acute Low Back Pain

**Background/Purpose:** Life purpose (also termed purpose in life or meaning in life) has been defined as “believing one’s actions have a set place in the larger order of things and that one’s behavior fits naturally into the course of a larger, more important social whole.” Although there is a dearth of published research on the role of life purpose in patients with acute low back pain, research in chronic pain suggests that those with chronic pain who have increased life purpose had less depression among other important health outcomes.

**Methods:** We used linear regression models to describe the relationship of life purpose (Scale of Psychological Well-Being-Life Purpose subscale; range=14-84) with disability (total score, Roland Morris Disability Scale, range=0-24) and depression (total score, Center for Epidemiologic Studies Depression Scale, range=20-80) in persons with acute low back pain (healthcare provider diagnosed low back pain present for less than 3 months; N=37) participating in a randomized clinical trial to prevent transition to chronic low-back pain.

**Results:** In our predominantly female sample (81.8%) with a mean age of 53 years (standard deviation =11.6 years), 52% worked full-time. Controlling for current work status (working full-time versus not), the overall model was significant for disability (R² =.16, F[2,36]=3.17; p=.05), with an adjusted R² of 0.11. Predicted disability was lower by .38 points per 1-point higher score on life purpose (p=.02). Controlling for gender (rates of depression are higher in females), the overall model was significant for depression (R² =.26, F[2,36]=6.07; p=.006), with an adjusted R² of 0.22. Predicted depression score was lower by 0.52 points per 1-point higher score on life purpose (p=.002).

**Conclusion:** Findings from this study suggest that life purpose has a significant association with disability (controlling for work status) and depression (controlling for gender) in this sample of persons with acute low back pain which is previously undescribed in the identified published literature. A furthered understanding of the relationship between life purpose and depression and disability could improve these important health factors in this population.

**Disclosure:** E. Salt, None; L. Crofford, None; M. K. Rayens, None; S. Segerstrom, None.


**Abstract Number:** 2234

Disability in Acute Low Back Pain: The Role of Pain Severity, Pain Catastrophizing, Depression, and Exercise

Elizabeth Salt¹, Leslie J. Crofford², Mary Kay Rayens³ and Suzanne Segerstrom⁴, ¹University of Kentucky, Lexington, KY, ²Medicine, Vanderbilt University Medical Center, Nashville, TN, ³College of Nursing, University of Kentucky, Lexington, KY, ⁴Psychology, University of Kentucky, Lexington, KY

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Tuesday, November 7, 2017
**Session Title:** ARHP Pain – Clinical Aspects Poster
**Session Type:** ACR Poster Session C
**Session Time:** 9:00AM-11:00AM

**Disability in Acute Low Back Pain: The Role of Pain Severity, Pain Catastrophizing, Depression, and Exercise**

**Background/Purpose:** The effectiveness of cognitive treatments for low back pain, a prevalent and costly condition, are commonly based on the principles of the Vlaeyen Fear of Movement/(Re) Injury Model. In this model, persons with a painful injury/experience who also engage in pain catastrophizing are most likely to avoid activity leading to disability. The validation of this model in patients suffering from acute low back is limited. The purpose of this project is to describe whether level of disability is associated with variables identified in the Fear of Movement/(Re) Injury Model, including pain, pain catastrophizing, depression, and exercise in persons with acute low back pain.
Factors Associated with Opioid Use in End-Stage Knee, Hip and Spine Osteoarthritis

J. Denise Power, Anthony V. Perruccio, Rajiv Gandhi, Christian Veillette, J. Roderick Davey, Stephen J. Lewis, Khalid Syed, Nizar Mahomed and Y. Raja Rampersaud, 1Arthritis Program, Krembil Research Institute, University Health Network, Toronto, ON, Canada, 2Arthritis Program, Krembil Research Institute, University Health Network, Torotno, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: ARHP Pain – Clinical Aspects Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The use of prescription opioids has been under increasing scrutiny due to concerns about the potential for misuse, dependency and increased adverse events. The objectives of our study were to examine the rates of prescription opioid use among pre-surgical knee, hip and spine osteoarthritis (OA) patients as well as the association between use and a range of socio-demographic and health status characteristics.

Methods: Study participants were 1204 patients with knee (N=577), hip (N=459) and spine (N=168) OA scheduled for surgery at a tertiary care hospital in Toronto, Canada. In pre-surgery questionnaires, data were collected on current usage (never, sometimes, daily) of opioid pain medications, as well as other prescription (NSAIDs, anti-depressants, neuroleptics) and over-the-counter pain medications for arthritis/joint pain. Additional questionnaire variables included: socio-demographics (age, sex, education), body mass index, comorbidity, depressive symptoms (Hospital Anxiety and Depression Scale) and pain level (0-10 numeric rating scale for average pain in the past week). Rates of opioid use were calculated by sex, age (<65 and 65+) and surgical site. Multivariable logistic regression was used to examine the associations between current reported opioid use (outcome: sometimes/daily vs. never) and other study variables.

Results: Participants were of mean age 65.6 years; 55.5% were women. Overall, 15% of patients reported ‘sometimes’ using opioid and an additional 15% reported ‘daily’ use. Any reported use of opioid was highest among spine OA patients (40%) and similar among knee and hip patients (28% and 30%). Younger women (<65 years) reported the greatest use of opioid overall, and particularly among spine patients (61%). From multivariable logistic regression, greater likelihood of opioid use was significantly associated with spine OA (vs. knee OA; p=0.03), younger age (p=0.02), obesity (vs. underweight/normal; p<0.01), fibromyalgia (present vs. absent; p=0.02), greater depressive symptoms (p=0.01), greater pain (p<0.001) and current use of other prescription pain medication (p<0.001).

Conclusion: Nearly a third of pre-surgical knee, hip and spine OA patients reported using prescription opioid medication for their OA pain. The higher use among younger individuals and those with greater depressive symptoms may warrant attention given growing
concerns around adverse outcomes related to opioid use. While increased use of opioids among those with higher levels of current pain may be expected, this additionally raises questions as to whether these individuals are deriving intended clinical benefits. Further, available research suggests that opioid use in the surgical OA population may negatively impact outcomes. Consideration of pre-surgical opioid use screening, including potential dependency, may be warranted for patients undergoing surgery for OA.

Disclosure: J. D. Power, None; A. V. Perruccio, None; R. Gandhi, None; C. Veillette, None; J. R. Davey, None; S. J. Lewis, None; K. Syed, None; N. Mahomed, None; Y. R. Rampersaud, None.


Abstract Number: 2236

Neuropathic Pain in End-Stage Hip and Knee Osteoarthritis: Differences between Men and Women and Differential Associations with Pain at Rest and Pain on Activity

J. Denise Power, Anthony V. Perruccio, Rajiv Gandhi, Christian Veillette, J. Roderick Davey, Khalid Syed, Nizar Mahomed and Y. Raja Rampersaud, Arthritis Program, Krembil Research Institute, University Health Network, Toronto, ON, Canada, Arthritis Program, Krembil Research Institute, University Health Network, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: ARHP Pain – Clinical Aspects Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: There is increasing support in the literature for a neuropathic component to OA pain. Our primary objective was to determine whether pain at rest and pain on activity are differentially associated with neuropathic pain scores in individuals with end-stage hip and knee OA. In addition, we examined the associations of neuropathic pain scores with psychological factors, health status and sociodemographic characteristics. As there is evidence of sex specific effects on pain, we analysed men and women separately.

Methods: Study participants were 843 patients with hip or knee OA scheduled for total joint arthroplasty (TJA) in Toronto, Canada. In pre-surgery questionnaires, data were collected using the painDETECT scale for neuropathic pain, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain subscale (items split into pain at rest (sitting, night pain) and pain on activity (standing, up/down stairs, walking on flat ground) and summed), the Hospital Anxiety and Depression Scale (HADS; depression only) and the Pain Catastrophizing Scale (PCS). Data on socio-demographics, health status (body mass index (BMI), comorbidity count, possible neuropathic comorbidities, symptomatic joint count) and medication use were also collected. Multivariable linear regression models were estimated for men and women to examine associations with neuropathic pain scores (higher indicates greater likelihood of neuropathic pain) by entering variables in predetermined blocks.

Results: Participants were of mean age 65.1 years; 57.1% were women. 55.3% of men and 57.6% of women were scheduled for knee TJA. Mean painDETECT scores were significantly higher (p=0.0001) for women (11.2±6.6 out of 38) than men (9.3±7.0), with 35.6% of women and 27.7% of men meeting established cut-offs for possible (painDETECT scores: 13-18) or likely (painDETECT scores: 19+) neuropathic pain. In regression modeling, pain at rest explained the most variance in neuropathic pain scores (men: 23.4%; women: 13.9%). In the final regression model for women, surgical joint (knee>hip; p=0.04), joint count, pain at rest, pain on activity, depression and pain catastrophizing were significantly associated with neuropathic pain score. In the final model for men, pain at rest, depression, pain catastrophizing and use of narcotics were significantly associated with neuropathic pain score. For women, the coefficient for pain at rest was 1.6 times greater than that for pain on activity. For men, pain on activity was not significantly associated (p=0.47) with neuropathic pain score.

Conclusion: Findings support that likely neuropathic pain is experienced by a notable proportion of patients with end-stage hip and knee OA. A greater neuropathic pain score was more strongly associated with pain at rest than pain on activity, particularly in men. Clinically, the presentation of pain at rest may suggest that a more thorough evaluation for potential neuropathic pain is warranted and may have implications for appropriate pain management. Findings also suggest that use of the WOMAC pain subscale as a single measure of pain burden (i.e. combined pain at rest and pain on activity) may need to be revisited.

Disclosure: J. D. Power, None; A. V. Perruccio, None; R. Gandhi, None; C. Veillette, None; J. R. Davey, None; K. Syed, None; N. Mahomed, None; Y. R. Rampersaud, None.
Work Productivity and Activity Impairment in Primary Sjögren’s Syndrome

Marisel Bejarano1, Anastasia Secco1, Antonio Catalan Pellet2, Marta Mamani3, Silvia Papasidero4, Julia Demarchi5, Cecilia Asnal6, Catherine Crow7, Alejandro Nitsche8, Laura Encinas9, Francisco Caeiro10, Carla Gobbi11, Eduardo Albiero12, Andrea Gomez13, Juan Carlos Barreira14, Rodrigo Aguila Maldonado15, Mercedes Garcia16, Maria Gallardo17, Enrique R Soriano18, Laura Raiti19, Gabriela Salvatiera20 and Alicia Eimon21, 1Hospital Bernardino Rivadavia, CABA, Argentina, 2Rheumatology, Hospital Bernardino Rivadavia, Buenos Aires, Argentina, 3Rheumatology Department, Hospital Bernardino Rivadavia, Buenos Aires, Argentina, 4Section of Rheumatology, Hospital General de Aguados “Dr. E. Tornú”, Buenos Aires, Argentina, Buenos Aires, Argentina, 5Hospital General de Aguados “Dr. E. Tornú”, CABA, Argentina, 6Rheumatology, Hospital Alemán, Buenos Aires, Argentina, 7cathecrow@yahoo.com.ar, Hospital Alemán, Buenos Aires, Argentina, 8Hospital Alemán, CABA, Argentina, 9Hospital Privado Centro Médico de Córdoba, Córdoba, Argentina, 10Rheumatology, Hospital Privado Centro Médico de Córdoba, Córdoba, Argentina, 11Rheumatology, Hospital Córdoba, Córdoba, Argentina, 12Universidad Nacional de Córdoba, Rheumatology Unit Córdoba Hospital, Córdoba, Argentina, 13Hospital Británico de Buenos Aires, CABA, Argentina, 14Rheumatology Unit, Hospital Británico de Buenos Aires, CABA, Argentina, 15Rheumatology, HIGA General San Martin La Plata, La Plata, Argentina, 16Hospital San Martín de la Plata, La Plata, Argentina, 17Hospital Italiano de Buenos Aires, CABA, Argentina, 18Hospital Italiano de Buenos Aires, Buenos Aires, Argentina, 19Rheumatology Department, Clínica Bessone, Buenos Aires, Argentina, 20IPRI, Santiago del Estero, Argentina, 21CEMIC, Buenos Aires, Argentina

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: To describe the work productivity and activity impairment in adult patients diagnosed with primary Sjögren’s Syndrome (pSS). To evaluate the association between activity impairment and clinical manifestations, depression and anxiety. To compare the activity impairment according to educational level and site of care (public or private centers) as surrogates of socioeconomic status.

Methods: We included patients with diagnosis of pSS according to the American-European criteria (2002) treated in 11 private and public argentine rheumatologic centers between November 2013 and December 2016. All patients with another autoimmune rheumatic or chronic disease were excluded. The WPAI questionnaire was used. Design: observational, analytic, cross-sectional study. For the descriptive analysis, continuous variables were informed as mean and SD. Categorical variables were reported in percentage. A multiple linear regression model was performed, taking impaired activity due to health as the dependent variable, adjusted by potential confounders. The performance of the model was evaluated (assumptions, atypical observations, multicollinearity). If linearity and/or homoscedasticity was not fulfilled, transformation of variables or robust regression was performed, as appropriate.

Results: 252 patients were included, 98.38% were female, mean age of 52.64 years (+/-14.84). The mean percentage of working time lost due to health was 15.74% (+/-30.12.CI95%:9.58-21.90); disability work due to health was 27.18% (+/-30.19. CI95%:21.25-33.11), the total disability percentage due to health was 33.70% (+/-35.76.CI95%: 26.39-41.01) and impaired activity due to health was 34.17% (+/-30.94.CI95%:30.35-37.99). The following variables showed significantly and independent association in the multivariable analysis of robust regression: xerostomy (β coefficient: 0.25. CI 95%: 0.13-0.37), arthritis (β coefficient: 11.15.CI 95%:0.55-21.74), mild depression (β coefficient: 8.77. CI 95%: 1.43-16.12), moderate depression (β coefficient: 25.47. CI 95%: 13.84-37.10), moderately severe depression (β coefficient: 36.92. CI 95%: 26.91-46.93), severe depression (β coefficient: 32.12. CI 95%: 16.31- 48.10). The mean impaired activity due to health was 38.24% (+/-30.67) in patients treated in public centers vs 28.04% (+/-30.61) on private centers, being this difference statistically significant. No statistically significant differences were found between patients with full or higher secondary education ((32.96% (+/-31.03) vs patients with lower educational level ((35.73% (+/-31.08)).

Conclusion: We found a decrease in the score of all WPAI scales. Arthritis, xerostomy and depression were significantly and independently associated with impaired activity due to health. The patients treated in public centers presented a greater impaired activity. This could be an expression of the impact of the socio-economic status in these aspects.
Mapping PainDetect, a Neuropathic Pain Screening Tool, to Patient-Reported Outcomes Measurement Information System (PROMIS) 29 in Patients with Rheumatoid Arthritis: Developing a Neuropathic Pain Scale As a Measure of Treatment Outcome

Yong Gil Hwang1, Lei Zhu2, Ajay Wasan3 and Larry W. Moreland1, 1Rheumatology & Clinical Immunology, University of Pittsburgh, Pittsburgh, PA, 2University of Pittsburgh, Pittsburgh, PA, 3Departments of Anesthesiology and Psychiatry, University of Pittsburgh, Pittsburgh, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: To investigate relationships between painDETECT (PDQ), neuropathic pain screening tool, and patient-reported outcomes measurement information system (PROMIS) 29 in patients with rheumatoid arthritis (RA).

Methods: For rheumatoid arthritis (RA) subjects enrolled in the University of Pittsburgh Rheumatoid Arthritis Comparative Effectiveness Registry (RACER), a cross-sectional analysis was performed for all RACER patients who completed PDQ and PROMIS29 short form. Association between PDQ and PROMIS29 was evaluated by Spearman’s correlation coefficient. Multiple regression models were conducted for PROMIS29 domain scores, adjusting for age, gender, race, RA disease activity measured by clinical disease activity index (CDAI). Analysis of variance and pairwise comparisons for adjusted scores were performed among PDQ classifications and standardized mean differences were calculated to assess the magnitude of effect.

Results: For the 302 subjects analyzed, age was 63.8 +/- 12.4 (mean +/- SD) years with disease duration of 18.4 +/-11.9 years. PDQ score was moderately correlated with pain severity (current, average pain for the past week, and past month, rho =0.52, 0.60, 0.56, p <0.001, respectively). PROMIS29 scores showed poorer physical function, participation in social role and higher depression, anxiety, fatigue, and sleep disturbance across PDQ classifications from nociceptive (N=225, 74.7%) to transitional (45, 14.9%) to neuropathic pain group (N=31, 10.3%) (Figure 1 and 2). Pairwise comparisons of PDQ classifications for adjusted PROMIS29 domain scores showed significantly worse health status for neuropathic pain group relative to both nociceptive and transitional group (Table).

Conclusion: Mapping the relationships between PDQ and PROMIS29 domains showed classifications by PDQ of nociceptive, transitional and neuropathic pain are characterized by overall decremental health status measured by PROMIS29. These data support the PDQ score as a possible treatment outcome measure and its use in RA management.
<table>
<thead>
<tr>
<th>PROMIS Domain</th>
<th>PainDETECT classification</th>
<th>Nociceptive</th>
<th>Transitional</th>
<th>Neuropathic</th>
<th>NeP - Noci</th>
<th>NeP - Tr</th>
<th>Tr - Noci</th>
<th>NeP - Tr</th>
<th>Tr - Noci</th>
<th>NeP - Tr</th>
<th>Tr - Noci</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFA</td>
<td>43.13</td>
<td>37.18</td>
<td>32.79</td>
<td>NeP - Noci</td>
<td>-10.34</td>
<td>&lt;0.001</td>
<td>1.46</td>
<td>2.45</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANX</td>
<td>47.36</td>
<td>53.40</td>
<td>57.31</td>
<td>NeP - Noci</td>
<td>9.94</td>
<td>&lt;0.001</td>
<td>0.80</td>
<td>4.09</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DEP</td>
<td>46.92</td>
<td>52.19</td>
<td>55.58</td>
<td>NeP - Noci</td>
<td>8.66</td>
<td>&lt;0.001</td>
<td>1.02</td>
<td>3.72</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FTG</td>
<td>50.59</td>
<td>58.84</td>
<td>64.23</td>
<td>NeP - Noci</td>
<td>13.64</td>
<td>&lt;0.001</td>
<td>1.45</td>
<td>3.56</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLP</td>
<td>49.75</td>
<td>54.72</td>
<td>57.43</td>
<td>NeP - Noci</td>
<td>7.68</td>
<td>&lt;0.001</td>
<td>0.72</td>
<td>3.08</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SRP</td>
<td>51.27</td>
<td>44.77</td>
<td>40.33</td>
<td>NeP - Noci</td>
<td>-10.94</td>
<td>&lt;0.001</td>
<td>1.43</td>
<td>3.67</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PIN</td>
<td>54.22</td>
<td>62.17</td>
<td>67.85</td>
<td>NeP - Noci</td>
<td>-13.63</td>
<td>&lt;0.001</td>
<td>1.83</td>
<td>3.14</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table. Pairwise comparison of PROMIS29 domain scores across painDETECT classifications (Noci: Nociceptive, Tr: Transitional, NeP: Neuropathic, SMD: standardized mean difference, PFA: physical function, ANX: anxiety, DEP: depression, FTG: fatigue, SLP: sleep disturbance, SRP: Abilities to participate in social role, PIN: pain interference)

Figure 1. Correlation matrix between PainDETECT and PROMIS29 domains (PFA: physical function, ANX: anxiety, DEP: depression, FTG: fatigue, SLP: sleep disturbance, SRP: Abilities to participate in social role, PIN: pain interference)

Figure 2. Relationship between PainDETECT and PROMIS29 domains (A) Radar chart displaying PROMIS29 domain unadjusted scores across painDETECT classifications (B) Radar chart showing relative values of each domain across painDETECT classification (minimum value = 0%, maximum value = 100%) (PFA: physical function, ANX: anxiety, DEP: depression, FTG: fatigue, SLP: sleep disturbance, SRP: Abilities to participate in social role, PIN: pain interference)
Disclosure: Y. G. Hwang, Pfizer Inc, 2; L. Zhu, None; A. Wasan, None; L. W. Moreland, None.

Abstract Number: 2239

The Recall Program: Data from a Multicenter Educational Event on Patients with Rheumatoid Arthritis

Andrea Delle Sedie, Emilio Filippucci, Oscar Epis, Pierluigi Macchioni, Sebastiano Tropea, Carlo Bonali, Marco Canzoni and Annamaria Iagnocco, Department of Rheumatology, University of Pisa, Pisa, Italy; Rheumatology Unit, University Politecnica delle Marche, Jesi, Italy; Rheumatology Unit, Ospedale Niguarda, Milano, Italy; Arcispedale Santa Maria Nuova, Reggio Emilia, Italy; ASP7, Busacca Hospital, Ragusa, Italy; Rheumatology Unit, Ospedale San Paolo, Bari, Italy; Local Health Unit (ASL) Rome 1, Rome, Italy; Academic Rheumatology Unit, Università degli Studi di Torino, Torino, Italy

SEASON INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: ultrasound (US) is able to show subclinical synovitis in patients (pts) with rheumatoid arthritis (RA) who are in clinical remission (CR); this has been proposed as a predictive factor for both clinical flares and progression of the structural damage in CR pts. The aim of this work was to investigate the US characteristics of RA pts presenting either CR or low disease activity (LDA).

Methods: in 2015 and 2016 an educational event focus on the added value of US in RA pts was held in 22 rheumatology centers in Italy. After a brief presentation on the evidence of the added value of US for the clinician given by expert sonographers (rheumatologists with a special interest in US who were performing US as their usual activity since many years), in every center, the local rheumatologists provided RA pts to be examined by US. All of the US machine were identical both for type (Logiq E R7, General Electrics, with a 4.2-13 MHz linear probe) and settings (both for grey-scale and power Doppler (PD)). Pts signed an informed consent and a brief history of them was collected by the local rheumatologists (previous and current therapy, DAS28, HAQ score). The US examination was performed bilaterally on wrists, MCP and MTP joints, looking for synovitis (effusion, synovial proliferation and PD) and erosions. The positive findings were scored according to a 0-3 score for synovitis components and presence/absence for erosions; the number and dimensions of the largest erosion were also registered.

Results: demographic and descriptive data of the 1466 pts examined are reported in Table I. Pts were divided on the basis of the DAS28 result. A statistically significant difference in age was registered between the group in CR and the group with DAS28>3.2 (p=0.003), while no differences were found for HAQ or MTX use. Higher prevalence of findings (regardless the score) was present in LDA group with respect to the CR one for effusion, synovial proliferation, PD and erosions, with significant differences for effusion (global, wrist, MCP and MTP joints; p=0.001, 0.024, 0.001 and 0.000 respectively), synovial proliferation effusion (global, wrist and MTP joints; p=0.019, 0.005, and 0.029 respectively), PD positivity (global, wrist, MCP and MTP joints; p=0.000, 0.000, 0.001, and 0.000 respectively) and erosions (global and MCP joints; p=0.009 and 0.000 respectively).

Table 1: demographic data

<table>
<thead>
<tr>
<th>N (M:F)</th>
<th>DAS28 &lt;2.6</th>
<th>DAS28 2.6-3.2</th>
<th>DAS28&gt;3.2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean±SD; yy)</td>
<td>56.6±13.9</td>
<td>59.2±11.7</td>
<td>61.0±11.1</td>
</tr>
<tr>
<td>Disease duration (mean±SD; dd)</td>
<td>2619.08±2686.78 2850.47±2509.29</td>
<td>2046.39±1951.16</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: in this large group of RA pts, US showed frequent abnormalities both in the CR and in the LDA group. Our results are in line with previous studies and confirm that US is a useful imaging tool for the detection of subclinical joint abnormalities in RA.
Partnering in Research: Maximizing Benefits & Minimizing Risks in Patient-Researcher Relationships

Jenny Leese\(^1\), Graham Macdonald\(^2\), Bao Chau Tran\(^1\), Lianne Gulka\(^3\), Alison Hoens\(^3\), Sheila Kerr\(^3\), Wendy Lum\(^3\) and Linda Li\(^4\),
\(^1\)Physical Therapy, University of British Columbia, Vancouver, BC, Canada, \(^2\)Occupational Science and Occupational Therapy, University of British Columbia, Vancouver, BC, Canada, \(^3\)Arthritis Research Canada, Richmond, BC, Canada, \(^4\)Rheumatology, Arthritis Research Canada, Richmond, BC, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Patient engagement in research has become a key requirement of many research funding organizations in Western countries. The principle of justice is central to patient engagement, indicating an ethical imperative for people who may be affected by health research to have the right, if they choose, to a say in what and how research is undertaken. There is, however, little empirical evidence to better understand ethical issues encountered in the everyday practice of patient engagement, particularly from the perspectives of patients. Our objective is to explore benefits and risks within patient-researcher relationships from the perspectives of arthritis patients with experience engaging in the research process.

Methods: The project is jointly designed and conducted by researchers and patient partners. Participants were invited to take part in a one-hour in-depth interview, in-person or by phone. Eligible participants were current or past members of an arthritis patient advisory board in a research centre. A semi-structured topic guide was used with prompts and probes to elicit detail about relationships with researchers. An iterative thematic analysis was conducted using constant comparison methods. A lens of relational ethics was found to highlight benefits and risks originating in emergent themes. Key elements of an ethical relationship, according to a relational ethics framework, include mutuality (encompassing deep understanding of each other’s values), choice and consideration of context.

Results: In 2015-16, 22 participants (aged between 26 and 68 years old) were recruited. Twenty-one (95%) were female, and 14 (64%) had at least one university degree. Of the 21 participants who reported, 12 (55%) had inflammatory arthritis, 5 (23%) had osteoarthritis, and 4 (18%) had both. Time spent as a patient partner ranged from 1 month to 10 years. Benefits and risks in patient-researcher relationships emerged across 2 distinct but related themes: 1) “Being Heard”: Participants described being heard as a mutual benefit in respectful patient-researcher relationships. Being heard involved having patient and researcher perspectives taken seriously and acted upon in the research process, which required patients and researchers to value different ways of knowing (e.g., lived experience, objective fact); 2) “Being with Supportive People”: Participants valued researchers who actively supported them to manage (actual and potential) negative physical and emotional impacts (e.g., fatigue, stress, uncertainty) of engaging in research in the context of their daily lives.

Conclusion: Findings make visible important values and behaviours for developing and maintaining ethical patient-researcher relationships, from the perspectives of patients with varying experiences of engaging in arthritis research. These values and behaviours can serve as a guide for researchers and patients who have chronic illness to anticipate and address benefits and risks that may arise in their engagement with each other. Our findings are a critical step to fostering everyday ethical practices of patient engagement in research that are anchored in patients’ perspectives.
Patterns and Outcomes on Disease Activity in Patients with Ankylosing Spondylitis (AS) Using Smart System of Disease Management (SSDM): Analysis of T2T Pattern Shift and Influential Factors

Jing Xue1, Wenqiang Fan2, Hua Wei3, Jing Yang4, Hui Song5, Hongbin Li6, Hongzhi Wang7, Xinwang Duan8, Zhenchun Zhang9, Jianlin Huang10, Yasong Li11, Jian Ding12, Xiaofei Shi13, Miaojia Zhang14, Zhenbiao Wu15, Cundong Mi16, Fei Xiao17, Hui Xiao17, Yuhua Jia17, Rui Bai17, Yan Bu17 and Huaxiang Wu18, 188 Jiefang Road, The Second Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou, China, 2Department of rheumatology, Central Hospital of XinXiang, Henan, XinXiang, China, 3Department of rheumatology, Central Hospital of MianYang, Sichuan, Mian Yang, China, 4Beijing Jishuitian Hospital, Beijing, China, 5The Affiliated Hospital of Inner Mongolia Medical University, Hohhot, China, 6The First Hospital of Jiaxing, Jiaxing, China, 7Department of rheumatology, The Second Affiliated Hospital of Nanchang University, Nanchang, China, 8People's Hospital of Linyi, Shandong, Linyi, China, 9Department of rheumatology, The Sixth Hospital Affiliated to Sun yat-sen University, Guangzhou, China, 10Zhejiang Provincial People's Hospital, Hangzhou, China, 11Zhejiang University School of Medicine, Hangzhou, China, 12Ningbo City Medical Treatment Center Lihuili Hospital, Ningbo, China, 13The First Affiliated Hospital of Henan University of Science and Technology, Luoyang, China, 14Department of Rheumatology and Immunology, Jiangsu Province Hospital, Nanjing, China, 15The First Affiliated Hospital of The Fourth Military Medical University, Xi'an, China, 16The Second Affiliated Hospital of Guangxi Medical University, Nanning, China, 17Gothic Internet Technology Corporation, Shanghai, China, 18The Second Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou, China

First publication: September 18, 2017

SESION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: This study is to evaluate pattern shifts and outcome trends of treat-to-target (T2T) under standard of care in ankylosing spondylitis patients with interactive Smart System of Disease Management (SSDM).

Methods: Ankylosing Spondylitis Disease Activity Score (ASDAS) was adopted to evaluate the degree of disease activity and the inflammatory response in AS patients. ASDAS score ≤1.3 represents inactive disease (ID) status and achievement of T2T. SSDM is a set of disease management tool based on mobile internet. The patient’s terminal system includes self-evaluation (ASDAS, HAQ), lab test results and medication management. After data entry, patients can synchronize data to the mobile terminal of their authorized rheumatologist. Under the guidance of health professionals, patients downloaded SSDM and registered, then self-evaluated ASDAS and was required for repeated evaluation after leaving the hospital. Data were analyzed and processed by IBM SPSS 22.0. The one-way ANOVA was used to analyze the influential factors. The chi square test was adopted to compare rates between groups, with P<0.05 as the criterion for the significant differences.

Results: From January 2015 to June 2017, 4,668 AS patients from 251 hospitals registered on SSDM, with mean age of 33.63 ± 11.47 years and median disease duration of 20.47 (0.73 - 66.73) months. Among them, 3,311 patients performed ASDAS evaluation at least once, totally 5,433 times; 989 patients carried out repeated evaluation for 2,122 times (male 690, female 299) through >5 month follow-up.

Among patients repeated assess ASDAS, baseline rate of T2T was 23% (228/989), and the final rate of T2T was significantly increased to 34% (334/989) (χ² = 392.114, p <0.001) after median evaluation of 3 (2-16) times per patient. The mean score of ASDAS decreased from 2.13 ± 1.07 to 1.81 ± 0.58 (mean improvement -0.32 ± 0.58, p <0.001). Analysis of influential factors showed that: among T2T patients in baseline (228, 23%), 151/228 (66%) remained T2T and 77/228 (34%) relapsed at the end of follow-up, there was no difference in age, sex distribution and disease duration between maintaining T2T achiever and the relapser but the mean interval of ASDAS evaluation in maintaining T2T achiever was significantly shorter than that of the relapser (26 days vs. 40 days, p <0.05). Among patients failed to reach target in baseline (761/989, 77%), 183/761 (24%) patients achieved T2T and 578/761 (76%) patients remain failure of T2T. There were no significant difference in age, sex distribution and disease duration between T2T achievers and patients remaining failure of T2T, but the mean evaluation interval of the achievers was significantly shorter than that of the latter (30 days vs. 40 days, p <0.05).
Pattern and Influential Factors in Promoting Treat-to-Target (T2T) for Follow-up RA Patients with a Rheumatologist-Patient Interactive Smart System of Disease Management (SSDM): A Cohort Study from China

Rong Mu1, Jing Yang2, Hua Wei3, Wengiang Fan4, Jianlin Huang5, Hongzhi Wang6, Jinli Ru7, Yongfu Wang8, Jimeei Zou9, Jianling Dong2, Xinwang Duan9, Fang He10, Xiaofei Shi11, Xiaofei Xin12, Fei Xiao13, Hui Xiao13, Yuhua Jia13, Minjun Wang13, Lijun He13, Rui Bai13, Xiyao Huang13, Bing Wu13 and Zhanguo Li14. 1Department of Rheumatology and Immunology, Peking University People's Hospital, Beijing, China; 2Department of rheumatology, Central Hospital of MianYang, Sichuan, Mian Yang, China; 3No 98,Nantong West Rd,Yangzhou, Northern Jiangsu People's Hospital, Yangzhou, China; 4Department of rheumatology, Central Hospital of XinXiang, Henan, XinXiang, China; 5Department of rheumatology, The Sixth Hospital Affiliated to Sun yat-sen University, Guangzhou, China; 6The First Hospital of Jinjiang, Jinjiang, China; 7The 264th Hospital of the PLA, Taiyuan, China; 8The First Affiliated Hospital of BaoTou Medical College, Baotou, China; 9Department of rheumatology, The Second Affiliated Hospital of Nanchang University, Nanchang, China; 10Central Hospital of Suining, Sichuan, Suining, China; 11The First Affiliated Hospital of Henan University of Science and Technology, Luoyang, China; 12Ningbo First Hospital, Zhejiang, Ningbo, China; 13Gothic Internet Technology Corporation, Shanghai, China; 14Rheum/Immunology, Peking University People's Hospital, Beijing, China

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00 AM

Background/Purpose: Treat-to-Target (T2T), achieving a DAS28 lower than 2.6 (remission) or below 3.2 (low disease activity), is the main management strategy. The Smart System of Disease Management (SSDM) is an interactive mobile disease management tool, including the doctors’ and patients’ application system. The patients can perform self-evaluation, including DAS28, morning stiffness time (MST) and HAQ, and enter medical records (including medication and laboratory test results) through the mobile application. The data synchronizes to the mobiles of authorized rheumatologists through cloud data base and advices could be delivered. The purpose of this study is to evaluate the patterns of T2T and related influential factors among RA patients after applying SSDM in real world.

Methods: Patients were registered through downloading the SSDM application, then were trained to master SSDM by health professionals in clinics. The first assessment for DAS28 were performed as baseline. The patients were required to perform repeated assessments once a month after leaving hospital.

Results: From June 2014 to June 2017, 1,232 RA patients from 145 hospitals across China were followed up for more than 6 months through SSDM, and the results at baseline and in final follow up were shown in table 1. The rate of T2T achievers were 40% (491/1,232) at baseline, and improved significantly to 64% (793/1,232) after 6 month follow up. Among T2T achievers at baseline, 75% (369/491) maintained T2T, 25% (122/491) relapsed. Compared with relapers, T2T maintainers performed more self-evaluation (5.78 vs 4.73, P=0.0017), took medications at higher ratio on DEMARDs (69% vs 59%), lower ratio on NSAIDs (4% vs 13%, p<0.01) or glucocorticoid (3% vs 8%, p<0.01). Among patients failed to reach T2T at baseline, 57% (424/741) achieved T2T after 6 months. Comparing with 6 month failure (317/741), new T2T achievers got shorter the MST (16.77±27.12 vs 27.03±33.76, p<0.001), lower HAQ score (2.17 ± 3.36 vs 3.36 ± 4.05, p<0.001) at baseline, performed more times of self-evaluation (6.56 vs 5.35, P=0.007).

Conclusion: T2T rate of AS in daily care is low in China. Significant improvement is observed under applying SSDM through empowering patients. Regularly performing self-management with SSDM associates with the achievements of maintaining T2T pattern and converting the patterns from failure of T2T to T2T. SSDM warrant a further evaluation and clinical application.

Disclosure: J. Xue, None; W. Fan, None; H. Wei, None; J. Yang, None; H. Song, None; H. Li, None; H. Wang, None; X. Duan, None; Z. Zhang, None; J. Huang, None; Y. Li, None; J. Ding, None; X. Shi, None; M. Zhang, None; Z. Wu, None; C. Mi, None; F. Xiao, None; H. Xiao, None; Y. Jia, None; R. Bai, None; Y. Bu, None; H. Wu, None.
However, even in patients of 6 month failure, the MST and HAQ score improved significantly in final follow up comparing with those at baseline (16.59±28.76 vs 27.03±33.76, p<0.001; 2.77±3.52 vs 3.36±4.05, p<0.001, respectively).

**Conclusion:** After interactive disease management via SSDM for more than 6 months, the rate of T2T in RA patients increased significantly. More NSAIDs and glucocorticoid but less DMARDs were associated with higher probability of relapse. The patients perform more self-evaluations through SSDM had lower probability of relapse and higher T2T maintaining and achievement. SSDM is a valuable tool for long term RA follow-up through empowering patients. Future RCT of improving T2T outcome through intervention of above influential factors with SSDM is warranted.

**Disclosure:** R. Mu, None; J. Yang, None; H. Wei, None; W. Fan, None; J. Huang, None; H. Wang, None; J. Ru, None; Y. Wang, None; J. Zhou, None; J. Dong, None; X. Duan, None; F. He, None; X. Shi, None; X. Xin, None; F. Xiao, None; H. Xiao, None; Y. Jia, None; M. Wang, None; L. He, None; R. Bai, None; X. Huang, None; B. Wu, None; Z. Li, None.

---

**Abstract Number:** 2243

**Youtube Videos on Rheumatoid Arthritis: A Qualitative Analysis of Views and Content**

Mosaab Mohameden1, Baker Alkhairi2, Seba Issa3, Asmaa Mohameden4 and Candice Yuvienco5, 1Internal Medicine, University of California San Francisco - Fresno Medical Education Program, Fresno, CA, 2Internal Medicine, Blake Medical Center, Bradenton, FL, 3Pediatrics, American University of Beirut, Beirut, Lebanon, 4Internal Medicine, School of Medicine, AlMaarefa Colleges for Science and Technology, Ad Diriyah, Saudi Arabia, 5Internal Medicine, Division of Rheumatology Director, University of California San Francisco, Fresno Medical Education Program, Fresno, CA

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Patient Outcomes, Preferences, and Attitudes Poster III

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Rheumatoid arthritis is a chronic potentially disabling disease affecting about 1.3 million people in the U.S. and as much as 1% of the worldwide population. Patient education plays a paramount role in rheumatoid arthritis management. Patients use the internet, and particularly social media, to learn about their medical condition. Youtube is the second largest search engine after Google and the most visited social media site with more than two billion views every day. In our study, we aim to evaluate the quality of material available for rheumatoid arthritis patients on Youtube.
Methods: Youtube.com main page was queried for the search term “Rheumatoid Arthritis.” The resulting videos were evaluated for content, duration, source, and audience interaction: number of views, likes, and dislikes. Content was classified as useful, misleading or patient’s views/experience. Useful videos were further analyzed for content using the published DISCERN instrument with 16 questions each consists of 5-point scale for assessing the quality of health information.

Results: The search term “rheumatoid arthritis” retrieved about 160,000 videos sorted by default filter of “relevance.” The top 20 videos were analyzed as these are the videos that patients were likely to view by visitor statistics. On average, videos had 15:52 minute duration, 7605 views, 639 likes, and 23 dislikes. 40% of videos were from non-professional educational groups, 30% from individuals/patients, 20% from health care professionals, 5% from news agencies, and 5% from health care organizations. 50% of the videos were classified as useful, 30% were patient views/experience, and 20% were misleading. Useful videos scored an average of 3.1 out of 5 on the DISCERN scale indicating fair quality. 60% of the useful videos were from non-professional educational groups with average DISCERN score of 3.5 out of 5. 20% were from health care professionals with average score of 2.5 out of 5. 10% were from individual/patient experience with a score of 2 out of 5. 10 % were from news agency reports with a score of 3 out of 5.

Conclusion: Despite being the most visited social media site and the second largest search engine, Youtube lacks high quality education materials for patients with rheumatoid arthritis. Majority of videos were from non-professional educational groups with fair quality. Healthcare organizations and professionals contributed to only 20% of Youtube videos on rheumatoid arthritis. Rheumatologists and professional healthcare organizations are encouraged to engage in patient education using Youtube given the high utilization frequency of this site by patients, but the quality of education must be stringently overseen, and misleading views have to be corrected.

Disclosure: M. Mohamen, None; B. Alkhairi, None; S. Issa, None; A. Mohamen, None; C. Yuvienco, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/youtube-videos-on-rheumatoid-arthritis-a-qualitative-analysis-of-views-and-content

Abstract Number: 2244

Can Achieving Remission Improve Work Ability and Quality of Life in Early Rheumatoid Arthritis (RA) Patients? a Prospective Cohort Study

Ho Man Lam1, Tsz Ho CHENG2 and Lai-Shan Tam1, 1Department of Medicine & Therapeutics, The Chinese University of Hong Kong, Hong Kong, Hong Kong, 2Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong, Hong Kong
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: RA patients often suffer from impaired work ability and reduced health related quality of life (HRQoL). Whether achieving remission through tight-control treatment strategy using conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) can improve work ability and HRQoL remains unclear. The aim of this study was to ascertain whether achieving remission can improve work ability and quality of life in early RA patients.

Methods: Early RA patients with symptom onset <2 years were recruited. All patients satisfied the 2010 ACR-EULAR classification criteria for RA (>=6 points). Remission status was measured by Disease Activity Score 28 (DAS28) and Simple Disease Activity Index (SDAI) every 3 months. Work ability was evaluated by working ability index (WAI) compared to life time best (score from 0-10, with 10 as best). HRQoL was assessed by 36-Item Short Form Survey (SF-36), Health Assessment Questionnaire Disability Index (HAQ-DI), Functional Assessment of Chronic Illness Therapy (FACIT) and EuroQol five dimensions questionnaire (EQ-5D).

Results: A total of 199 (51]13 years old, 158[79.4%] female, 146[73.4%] employed) patients completed one year follow up. At baseline, unemployed patients have a higher physician global assessment score, more swollen joints, lower WAI, lower EQ-5D and higher HAQ-DI (Table1). Using multivariate linear regression, achieving DAS28 and SDAI remission at ≥ 2 visits are independent predictors for better WAI, HRQoL, HAQ, FACIT and EQ5D at one year after adjustment for other covariates (Table2). Achieving remission only once in the first year was not associated with improvement in WAI.
Conclusion: Achieving at least two time remissions is important in improving patients’ work ability and HRQoL.

Table 1: Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Unemployed n=59</th>
<th>Employed n=146</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>49.7±9.14</td>
<td>50.7±13.12</td>
<td>0.639</td>
</tr>
<tr>
<td>Symptom duration, month</td>
<td>7.51±3.11</td>
<td>2.68±1.90</td>
<td>0.001</td>
</tr>
<tr>
<td>ESRi, mm/h</td>
<td>47.7±25.69</td>
<td>72.0±29.89</td>
<td>0.005</td>
</tr>
<tr>
<td>VAS Pain Score, 0-100</td>
<td>5.6±2.61</td>
<td>4.3±2.20</td>
<td>0.042</td>
</tr>
<tr>
<td>VAS PASI Score, 0-10</td>
<td>56.8±25.29</td>
<td>50.0±23.17</td>
<td>0.021</td>
</tr>
<tr>
<td>VAS PGA score, 0-10</td>
<td>56.4±24.90</td>
<td>49.7±27.98</td>
<td>0.005</td>
</tr>
<tr>
<td>Tender Joints, 0-28</td>
<td>8.3±1.31</td>
<td>6.8±1.35</td>
<td>0.138</td>
</tr>
<tr>
<td>Swollen Joints, 0-28</td>
<td>5.4±1.59</td>
<td>3.7±1.61</td>
<td>0.082</td>
</tr>
<tr>
<td>DFI, mm</td>
<td>52.5±17.63</td>
<td>53.0±14.44</td>
<td>0.743</td>
</tr>
<tr>
<td>CRP, mg/L</td>
<td>17.2±22.43</td>
<td>16.8±2.25</td>
<td>0.795</td>
</tr>
<tr>
<td>ESR, mm/h</td>
<td>6.6±1.39</td>
<td>6.7±1.29</td>
<td>0.002</td>
</tr>
<tr>
<td>DDI</td>
<td>21.2±14.35</td>
<td>22.4±13.30</td>
<td>0.004</td>
</tr>
<tr>
<td>CoE0 (AUC)&gt;70, n</td>
<td>27 (46.40)</td>
<td>35 (60.43)</td>
<td>0.220</td>
</tr>
<tr>
<td>CoE0 (Percentile, n)</td>
<td>19 (75.86)</td>
<td>42 (29.21)</td>
<td>0.046</td>
</tr>
<tr>
<td>Co NSAI, n</td>
<td>39 (79.59)</td>
<td>85 (62.52)</td>
<td>0.187</td>
</tr>
<tr>
<td>VAS Activity, 0-10</td>
<td>4.3±2.54</td>
<td>5.6±2.17</td>
<td>0.005</td>
</tr>
<tr>
<td>HAPA, 0-3</td>
<td>0.97±1.27</td>
<td>0.93±1.55</td>
<td>0.603</td>
</tr>
<tr>
<td>HAPA (3-52)</td>
<td>30.8±11.45</td>
<td>38.1±9.64</td>
<td>0.071</td>
</tr>
<tr>
<td>HAPA (Knee arthritis)</td>
<td>0.21±0.19</td>
<td>0.14±0.67</td>
<td>0.821</td>
</tr>
<tr>
<td>HAPA (Depression, 0-21)</td>
<td>0.38±0.97</td>
<td>0.27±0.31</td>
<td>0.001</td>
</tr>
<tr>
<td>SF36 (Physical functioning), 3-100</td>
<td>52.19±22.80</td>
<td>61.36±24.68</td>
<td>0.024</td>
</tr>
<tr>
<td>SF36 (Energy/Fatigue)</td>
<td>0.106</td>
<td>0.87±2.19</td>
<td>0.957</td>
</tr>
<tr>
<td>SF36 (Mental wellbeing), 0-200</td>
<td>59.12±17.97</td>
<td>57.77±16.62</td>
<td>0.725</td>
</tr>
<tr>
<td>SF36 (Social functioning), 0-100</td>
<td>55.33±27.33</td>
<td>62.97±25.81</td>
<td>0.097</td>
</tr>
<tr>
<td>EQ5D-O, 0-100</td>
<td>0.64±0.18</td>
<td>0.69±0.15</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Table 2: Multivariate linear regression

<table>
<thead>
<tr>
<th></th>
<th>DAS remission: times = 1 Coefficient (95%CI)</th>
<th>p value</th>
<th>DAS remission: times = 2 Coefficient (95%CI)</th>
<th>p value</th>
<th>DAS remission: times = 3 Coefficient (95%CI)</th>
<th>p value</th>
<th>DAS remission: times = 4 Coefficient (95%CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESR</td>
<td>0.68 (0.96, 2.08)</td>
<td>0.002</td>
<td>0.91 (0.48, 2.09)</td>
<td>0.392</td>
<td>2.85 (0.88, 4.83)</td>
<td>0.008</td>
<td>2.83 (0.80, 5.13)</td>
<td>0.517</td>
</tr>
<tr>
<td>HAPA</td>
<td>0.45 (0.71, 0.25)</td>
<td>0.007</td>
<td>0.44 (0.40, 0.65)</td>
<td>0.005</td>
<td>0.36 (0.48, 0.21)</td>
<td>0.004</td>
<td>0.27 (0.45, 0.12)</td>
<td>0.003</td>
</tr>
<tr>
<td>VAS</td>
<td>0.71 (0.91, 0.51)</td>
<td>0.007</td>
<td>5.13 (2.12, 8.44)</td>
<td>0.001</td>
<td>5.12 (2.53, 8.01)</td>
<td>0.001</td>
<td>3.31 (0.64, 5.99)</td>
<td>0.053</td>
</tr>
<tr>
<td>SF36 (Physical functioning), 0-100</td>
<td>1.76 (1.28, 2.02)</td>
<td>0.001</td>
<td>0.16 (1.76, 18.46)</td>
<td>0.001</td>
<td>53.52 (0.64, 21.55)</td>
<td>0.001</td>
<td>54.17 (1.25, 18.35)</td>
<td>0.001</td>
</tr>
<tr>
<td>SF36 (Emotional wellbeing), 0-100</td>
<td>1.23 (1.65, 1.84)</td>
<td>0.001</td>
<td>0.57 (1.60, 17.19)</td>
<td>0.009</td>
<td>7.27 (0.73, 33.82)</td>
<td>0.000</td>
<td>5.21 (1.84, 50.39)</td>
<td>0.152</td>
</tr>
<tr>
<td>SF36 (Social functioning), 0-100</td>
<td>0.87 (2.89, 34.55)</td>
<td>0.001</td>
<td>0.71 (2.27, 17.17)</td>
<td>0.001</td>
<td>5.46 (4.35, 11.35)</td>
<td>0.075</td>
<td>5.73 (0.37, 52.73)</td>
<td>0.064</td>
</tr>
<tr>
<td>SF36 (General health), 0-100</td>
<td>0.16 (0.10, 0.25)</td>
<td>0.001</td>
<td>0.61 (0.10, 0.25)</td>
<td>0.001</td>
<td>0.16 (0.01, 0.06)</td>
<td>0.001</td>
<td>0.04 (0.03, 0.18)</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Disclosure: H. M. Lam, None; T. H. CHENG, None; L. S. Tam, None.


Abstract Number: 2245

The Effects of Structural Damage on Functional Disability in Psoriatic Arthritis

Andreas Kerschbaumer1, Gabriela Supp1, Josef S. Smolen1,2 and Daniel Aletaha1, 1Medical University Vienna, Division of Rheumatology, Department of Internal Medicine III, Vienna, Austria, 22nd Department of Medicine, Hietzing Hospital, Vienna, Austria

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017

Session Title: Patient Outcomes, Preferences, and Attitudes Poster III

Session Type: ACR Poster Session C

Session Time: 9:00AM-11:00AM

Background/Purpose:
Functional outcomes are central in patients with chronic inflammatory musculoskeletal diseases. In a secondary data analysis of the GO-REVEAL trial we investigated if structural damage is linked to functional impairment in patients with psoriatic arthritis (PsA).

**Methods:**

We analyzed data of patients enrolled in the GO-REVEAL trial including modified Sharp-van-der-Heijde X-ray -scores for PsA (mSVDHS) performed at weeks 0, 24, 52 and 104 (n=363). In longitudinal data analyses, all patients and patients in Disease Activity index for Psoriatic Arthritis (DAPSA) remission (n=117), utilising all remission visits (REM; DAPSA <4), we used the HAQ as dependent variable and total mSVDHS, joint space narrowing (JSN) and erosion (ERO) scores, respectively, as independent variables. To analyse effects of structural damage on the potential to improve physical function, we identified a subgroup of patients who had major functional limitations at baseline (HAQ≥1) and showed a major DAPSA-response. In this model we assessed the effect of mSVDHS on changes in HAQ (n=67). As validation cohort, we analyzed routine PsA patients from our clinic with complete cDAPSA (DAPSA without CRP) and mSVDHS (n=160).

**Results:**

As visualised in figure 1, mSVDHS (panel A) JSN and ERO (panel B+C) had significant effects on HAQ in all patients (ALL) and patients in REM.

In the second analysis (figure 2), in patients achieving DAPSA major response, results were significant for the association of mSVDHS and JSN with relative (REL) and absolute (ABS) HAQ changes (panel A). Additionally, higher estimates of JSN, compared with erosion scores could be observed, with absolute (B) and relative (C) HAQ change as outcome parameter.

These results could be confirmed in the validation cohort and in analyses using the SF-36 Physical Component Score instead of the HAQ as outcome variable in GO-REVEAL patients.

**Conclusion:**

Our results reveal that responsiveness of functional impairment decreases with increasing joint damage. They further suggest that JSN is functionally more important than erosions. Both, achievable HAQ levels and HAQ responses are negatively impacted by a high degree of structural damage. Consideration of these components is clinically and therapeutically relevant, as the HAQ component related to inflammation is expected to be reversible, while that related to damage is not.

**Figure 1.**

![Figure 1](image1)

**Figure 2.**

![Figure 2](image2)
Impact of Patient Education Tool to Increase Cardiovascular Risk Knowledge, Attitudes, and Behaviors in Patients with Rheumatoid Arthritis

Lisa Zickuhr¹, William Messner², Abby Abelson³ and M. Elaine Husni⁴, ¹Rheumatology, Cleveland Clinic Foundation, Cleveland, OH, ²Quantitative Health Sciences, Cleveland Clinic, Cleveland, OH, ³Department of Rheumatologic & Immunologic Disease, Cleveland Clinic Foundation, Cleveland, OH, ⁴Cleveland Clinic, Cleveland, OH

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Rheumatoid arthritis (RA) raises cardiovascular disease (CVD) risk, yet RA patients underestimate their personal risk. The principle of self-management posits patients will be self-motivated stewards of their health if they have the knowledge, resources, and support to influence their care. We assess how an education handout aimed at improving RA patients’ self-management of CVD risk changes their knowledge, attitudes, and behaviors. We hypothesize it will improve knowledge with little effect on attitudes and behaviors.

Methods: We prospectively recruited RA patients from an outpatient general rheumatology clinic to read a patient education handout and answer three surveys at time of enrollment (week 0), week 1, and week 8. We distributed education handouts after completion of the week 0 survey. Surveys at weeks 0 and 8 contained questions about behavioral risk factors from the Centers for Disease Control’s Behavioral Risk Factor Surveillance System, novel Likert scales ranking patients’ attitudes about CVD risk, and the Heart Disease Fact Questionnaire-Rheumatoid Arthritis (HDFQ-RA), a validated measurement of RA patients’ knowledge of general CVD and RA-specific CVD risk. The survey at week 1 was the HDFQ-RA. Wilcoxon signed-rank test (α=0.05) analyzed changes in HDFQ-RA scores and Likert rankings, while McNemar’s test (α=0.05) analyzed changes in behaviors.
**Results:** A total of 38 participants completed all surveys and read the handout. Most patients were female (89%), aged 61.5 (±11.9) years old with a mean RA duration of 15.3 (±13.3) years. Based on total HDFQ-RA scores, both general and RA-specific CVD knowledge significantly improved at week 1 and was sustained at week 8 (table 1).

<table>
<thead>
<tr>
<th>Survey</th>
<th>Mean Change</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Heart Disease Fact Questionnaire-Rheumatoid Arthritis (HDFQ-RA) Score (13 questions)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 0 vs Week 1</td>
<td>1.342</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Week 0 vs Week 8</td>
<td>1.421</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Week 1 vs Week 8</td>
<td>0.079</td>
<td>0.549</td>
</tr>
<tr>
<td>General Cardiovascular Disease (CVD) Risk Knowledge from HDFQ-RA Score (9 questions)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 0 vs Week 1</td>
<td>0.895</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Week 0 vs Week 8</td>
<td>0.816</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Week 1 vs Week 8</td>
<td>-0.079</td>
<td>0.407</td>
</tr>
<tr>
<td>Rheumatoid Arthritis-Specific CVD Risk Knowledge from HDFQ-RA Score (4 questions)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 0 vs Week 1</td>
<td>0.447</td>
<td>0.015</td>
</tr>
<tr>
<td>Week 0 vs Week 8</td>
<td>0.605</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Week 1 vs Week 8</td>
<td>0.158</td>
<td>0.041</td>
</tr>
</tbody>
</table>

Based on Likert scales, only attitudes regarding the influence of RA disease activity on CVD risk changed (p=0.012). A total of 23 of the 38 participants (73.7%) stated the handout motivated them to make lifestyle changes, and a significant change was noted in exercise at week 8 (p=0.016), but not in smoking cessation or diet (p>0.99).

**Conclusion:** A patient education handout improved RA patients’ self-management of CVD risk, not only enhancing knowledge but also improving lifestyle self-management, as patients increased their exercise habits over an 8-week period. Patients also believed that RA management is more important in mitigating their CVD risk after reading the handout. This data suggests a patient handout can effectively change patients’ understanding of CV risks and influence certain lifestyle factors, such as exercise. Further study is needed to review self-management strategies that may further augment knowledge, attitudes, and behaviors of CVD in RA patients and potentially improve CV risk factors.

**Disclosure:** L. Zickuhr, None; W. Messner, None; A. Abelson, None; M. E. Husni, Abbvie, Amgen, Bristol-Myers Squibb, Eli Lilly, Janssen, Novartis, Regeneron, UCB, 5, Pfizer Inc, 6, PASE Questionnaire, 7.


**Abstract Number:** 2247

**Secondary Fibromyalgia Is Not Associated with Higher Likelihood of Patient-Physician Discordance in Global Assessment in Patients with Osteoarthritis and Rheumatoid Arthritis**

**Isabel Castrejón,** Shakeel M. Jamal and Najia Shakoor, Division of Rheumatology, Rush University Medical Center, Chicago, IL

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Patient Outcomes, Preferences, and Attitudes Poster III

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Pain is the strongest driver of patient-physician discordance in global assessment in patients with rheumatoid arthritis (RA) and osteoarthritis (OA). Having secondary fibromyalgia (FM), a disorder with vague and nonspecific symptoms (e.g.,
widespread body pain or fatigue) may increase the likelihood of discordance. We aim to analyze if patients with RA and OA presenting with secondary FM have higher likelihood of discordance.

**Methods:** All patients complete a multidimensional health assessment questionnaire (MDHAQ) as part of their routine care which includes scores for physical function, pain, PATGL, fatigue, and demographic data. Rheumatologists complete a RheuMetric including 4 visual analogue scales: a physician global assessment (DOCGL) and three subscales for inflammation, damage, and distress/FM. A mean difference PATGL-DOCGL ≥2cm was considered a relevant discordance. Patients with a clinical diagnoses of OA or RA were classified into 3 categories: PATGL ≥ DOCGL by 2/10 units, PATGL = DOCGL, and DOCGL ≥ PATGL by 2 units. Secondary FM was evaluated using two criteria: 1) clinical diagnosis by the treating rheumatologist. 2) A score ≥6 in the VAS for distress/FM. The percentage of patients in each group was compared using chi-square.

**Results:** 243 OA and 216 RA patients were included. Patients with OA were older and showed higher scores for PATGL, pain, and fatigue (data not showed) and higher level of discordance (PATGL>DOCGL) in comparison with RA (34% vs 18%, p<0.001). A higher percentage of patients with OA showed secondary FM (15% versus 3%, p<0.001) and a VAS for distress ≥6 (12% versus 5%, p=0.01) in comparison with patients with RA. Patients with OA and secondary FM have *higher* level of concordance (PATGL=DOCGL) in comparison with patients with OA without secondary FM (Table). There were no significant differences in the RA patients group when comparing patients with and without secondary FM (Table).

**Table. Level of discordance/concordance in patients with or without secondary FM with OA or RA**

<table>
<thead>
<tr>
<th>Discordance groups, no. (%)</th>
<th>OSTEOARTHRITIS</th>
<th>RHEUMATOID ARTHRITIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>PATGL&gt;DOCGL</td>
<td>207 (85%)</td>
<td>210 (97%)</td>
</tr>
<tr>
<td>Secondary FM</td>
<td>36 (15%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>p</td>
<td>0.03</td>
<td>0.58</td>
</tr>
<tr>
<td>PATGL=DOCGL</td>
<td>110 (53%)</td>
<td>141 (67%)</td>
</tr>
<tr>
<td>Secondary FM</td>
<td>26 (72%)</td>
<td>3 (50%)</td>
</tr>
<tr>
<td>Distress VAS&lt;6</td>
<td>184 (88%)</td>
<td>188 (95%)</td>
</tr>
<tr>
<td>Distress VAS≥6</td>
<td>24 (12%)</td>
<td>9 (5%)</td>
</tr>
<tr>
<td>p</td>
<td>0.24</td>
<td>0.40</td>
</tr>
<tr>
<td>PATGL&lt;DOCGL</td>
<td>22 (12%)</td>
<td>30 (16%)</td>
</tr>
<tr>
<td>Secondary FM</td>
<td>2 (8%)</td>
<td>2 (22%)</td>
</tr>
</tbody>
</table>

**Conclusion:** Patient-physician discordance is more prevalent in patients with OA versus RA. FM is also more prevalent in OA versus RA but the presence of FM does not account for the higher discordance rate. In fact, those with OA and FM appear to have more concordant scores with their physicians. The dual diagnoses of FM may make the physicians more sensitive to the pain of their patients.

**Disclosure:** I. Castrejón, None; S. M. Jamal, None; N. Shakoor, None.


**Abstract Number:** 2248

**Function, Pain, Fatigue, and Participation Are the Primary Contributors to the Patient Global Assessment in Rheumatoid Arthritis**

Ethan Craig¹, Susan J. Bartlett², Jamie Perin³, Scott Zeger³ and Clifton O. Bingham III¹

¹Rheumatology, Johns Hopkins University, Baltimore, MD, ²Department of Medicine, Division of ClinEpi, Rheumatology, Respirology, McGill University, Montreal, QC, Canada, ³Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD

**First publication:** September 18, 2017

**SESSION INFORMATION**
Background/Purpose: The patient global assessment (PGA) is widely used in disease activity scores for RA, including the CDAI, SDAI, and DAS28. While pain has been shown to be a major component of this score, other specific contributors of the patient experience to this score remain less clear. We examined the contribution of multiple domains of health-related quality of life measured by Patient-Reported Outcomes Measurement Information System (PROMIS) computer adapted testing. These measures by nature have heavily correlated structures which may lead to erroneous results from regression. Here, a factor analysis was used to identify latent variables. Using these latent variables along with clinical characteristics, we developed a multivariable model to explain the relative contributions of these measures to the PGA.

Methods: We conducted a cross sectional analysis of a cohort of 196 patients with RA receiving guideline-based care in an academic rheumatology clinic. PROMIS computer-adapted tests, including domains of physical function, pain interference, social participation, fatigue, sleep disturbance, depression, and anxiety were used. Factor analysis was used to identify factor structures. A multivariable linear regression model was then developed to identify an optimal model including these factors and other clinical characteristics.

Results: Among 196 patients (mean age 54.8 +/- 13.4 years, 81% female, mean RA duration of 11 +/- 9.6 years, mean PGA 29). Most (69%) were well-controlled, in remission or low disease activity. Factor analysis revealed three major factors. The first, referred to as "function", had highest loading of physical function, followed by pain interference, fatigue, and social participation. The second, referred to as "emotional distress", had equal loading of depression and anxiety. A third had loading only on sleep disturbance. "Function" alone, in univariable analysis, explained 52% of the variance in PGA. A multiple linear regression including "function", sleep disturbance, swollen joint count, sex, BMI, and an interaction term of each of the three factors with one another explained 59% of the variance in PGA.

Conclusion: A single factor including fatigue, pain interference, physical function, and social participation explained most of the variance in the PGA in univariable regression. Emotional distress was not associated with the PGA when other factors were adjusted for. These data suggest that the PGA was primarily related to one latent variable related to "function", and was influenced by "emotional distress" only insofar as it modified other symptoms.

<table>
<thead>
<tr>
<th></th>
<th>Univariable</th>
<th>Multivariable – Adj R² = 0.59</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β</td>
<td>p-value</td>
</tr>
<tr>
<td>“Function”</td>
<td>20.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>“Emotional distress”</td>
<td>11.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>“Sleep disturbance”</td>
<td>23.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>“Function” x “Emotional”</td>
<td>0.8</td>
<td>0.68</td>
</tr>
<tr>
<td>“Function” x “Sleep”</td>
<td>1.9</td>
<td>0.44</td>
</tr>
<tr>
<td>“Sleep” x “Psych”</td>
<td>2.5</td>
<td>0.32</td>
</tr>
<tr>
<td>Swollen Joints</td>
<td>2.69</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BMI</td>
<td>0.55</td>
<td>0.04</td>
</tr>
<tr>
<td>Sex</td>
<td>0.44</td>
<td>0.93</td>
</tr>
</tbody>
</table>

Disclosure: E. Craig, None; S. J. Bartlett, None; J. Perin, None; S. Zeger, None; C. O. Bingham III, None.


Abstract Number: 2249

Influence of Large-Joint Involvement on Patient-Physician Discordance in Global Assessment of Rheumatoid Arthritis Disease Activity Analyzed By Novel Joint Index

Tetsuji Sawada¹, Mayu Tago¹, Susumu Nishiyama², Koichiro Tahara¹, Eri Kato³, Hiroaki Mori¹, Haeru Hayashi¹, Jinju Nishino⁴, Toshihiro Matsui⁵ and Shigeto Tohma⁶; ¹Rheumatology, Tokyo Medical University, Tokyo, Japan, ²Rheumatic Disease Center, Kurashiki Medical Center, Okayama, Japan, ³Rheumatology, Tokyo Medical University, Shinjuku Tokyo, Japan, ⁴Department of
Background/Purpose: The discordance between patient global assessment (PGA) and physician global assessment (PhGA) of rheumatoid arthritis (RA) disease activity may be problematic in clinical practice. The aim of this study was to identify determinants of this discordance using a nationwide RA database in Japan (NinJa) with special attention to large joint involvement.

Methods: We investigated 12,043 adults with RA and used a discordance cutoff of 3 cm. Large joint involvement was investigated using novel joint indices (x, y, z) and the large joint index (Nishiyama S et al. Rheumatol Int. 2012;32:2569), in which x and y were the indices for upper and lower joints, respectively, and z was for large joint predominance. Predictors of PGA-PhGA discordance and determinants of PGA and PhGA were analyzed by multivariate logistic and linear regression models, respectively. In logistic regression analysis, the odds ratio (OR) for positive discordance (PGA ≥ PhGA by 3 cm) was computed using a concordance (no discordance) group as reference.

Results: Multivariate logistic regression identified age (OR: 1.01 [95% confidence interval: 1.01–1.02]), pain (2.15 [2.08–2.22]) and modified Health Assessment Questionnaire score (1.56 [1.39–1.75]) as significant predictors of positive discordance. On the other hand, TJC (0.93 [0.91–0.94]), SJC (0.92 [0.90–0.94]), CRP (0.88 [0.83–0.93]), class 3-4 (0.63 [0.53–0.76]), Z (0.72 [0.59–0.88]), and the large joint index (0.59 [0.47–0.74]) predicted significantly against positive discordance. Linear regression analysis demonstrated that PGA was mainly determined by pain, whereas PhGA was determined by various factors, including the large joint index (Figure 1) and Z.

Conclusion: RA care providers should focus on pain, functional disability and the size of affected joints to decrease PGA-PhGA discordance and to share with patients a common recognition of disease activity.

Disclosure: T. Sawada, None; M. Tago, None; S. Nishiyama, None; K. Tahara, None; E. Kato, None; H. Mori, None; H. Hayashi, None; J. Nishino, None; T. Matsui, AbbVie GK, Ayumi Pharmaceutical Corporation, Chugai Pharmaceutical Co., Ltd., CSL Behring K.K., Japan Blood Products Organ, 2; S. Tohma, None.


Abstract Number: 2250

Linguistic Differences in Gout-Related Online Content: A Comparison of Professional Health Literature for Consumers Vs Patients’ Online Discussions of Gout

W. Benjamin Nowell¹, Kayla Jordan², Kelly Gavigan¹, Louis Tharp¹, Jeffrey R. Curtis³ and James Pennebaker⁴, ¹Global Healthy Living Foundation, Upper Nyack, NY, ²University of Texas at Austin, Austin, TX, ³Division of Clinical Immunology and
Non-adherence to gout medication is high. This may be due in part to patients’ belief that gout is primarily caused by overindulgence in certain foods and beverages and that it can therefore be alleviated by diet change alone. We sought to identify whether an incongruence existed between professional web-based content created for gout patients and patient’s online discussions.

Methods: Using word frequency analysis and NLP, we examined linguistic differences in a convenience sample of professional webpages and online patient discussions for gout, comparing content from three types of media: 1) consumer literature for patients posted on websites by health organizations (e.g. Gout and Uric Acid Education Society, WebMD, Mayo Clinic) and pharmaceutical companies (n=205 webpages with average of 330 words/page); 2) patient blogs (e.g. gout blogs on patient.com) (n=337 blogs average 641 words/post); and 3) social media (e.g. gout subreddit, a forum on the website Reddit where people can post thoughts or questions for comment) (n=687 original posts average 157 words/post and n=5274 comments average 70 words/comment), excluding posts or comments <20 words. Each unique page on a website relevant to gout was collected and saved into separate text files. After processing and cleaning, consumer sites, blogs, original and reply posts on Reddit were analyzed separately. Differences in psychological processes were identified using LIWC2015 (Pennebaker, Boyd, Jordan, & Blackburn, 2015), a text analysis program measuring a number of psychological dimensions.

Results: LIWC analysis yielded two main findings: 1) consumer sites had greater health focus, shown by use of words like doctor, pain, disease (d=1.34), while blogs/social media, had slightly greater focus on ingestion (i.e. food/drinks) indicated by words such as eat, sweet, feed (d=0.18); and 2) professional and health sites used more risk-oriented language (d=0.57) concerned with prevention and losses (e.g. words like lose, lack, worse), while blogs/social media were somewhat more reward-oriented (d=0.43) focused on potential benefits and gains of treatment and prevention (e.g. words like optimistic, success, and good). All differences between the two groups were significant (p<0.01) and showed comparable patterns across all three types of media. One commonality between sites is frequent discussion of symptoms (e.g. attacks and flares). Word clouds (Figure 1) showed the 30 most common words in each type of site based on basic frequency analysis methods.

Conclusion: People living with gout focus more on food and diet, whereas medical professionals emphasize medical causes and preventions/treatments. More research is needed to determine the most effective ways to encourage patients to seek treatment beyond diet and lifestyle changes.

Disclosures: W. B. Nowell, None; K. Jordan, None; K. Gavigan, None; L. Tharp, None; J. R. Curtis, Crescendo Biosciences, 2, Crescendo Biosciences, 5; J. Pennebaker, None.
Preferences for Physical Activity: A Discrete Choice Experiment in People with Chronic Knee Pain

Daniel Pinto1, Ulf Bockenholt2, Rowland W. Chang3,4, Julia (Jungwha) Lee5, Jane Holl6, Daniel Finn6, Leena Sharma7, Allen Heinemann8 and Paul Hansen9, 1Department of Physical Therapy & Human Movement Sciences, Northwestern University Feinberg School of Medicine, Chicago, IL, 2Department of Marketing, Kellogg School of Management, Northwestern University, Evanston, IL, 3Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL, 4Preventive Medicine, Medicine, and Physical Medicine & Rehabilitation, Northwestern University Feinberg School of Medicine, Chicago, IL, 5Preventive Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, 6Center for Healthcare Studies, Northwestern University Feinberg School of Medicine, Chicago, IL, 7Division of Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL, 8Center for Rehabilitation Outcomes Research, Shirley Ryan Ability Lab, Chicago, IL, 9Economics, University of Otago, Dundin, New Zealand

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Preferences For Physical Activity: A Discrete Choice Experiment In People With Chronic Knee Pain

Background/Purpose: Understanding preferences for physical activity (PA) can help guide patient consultations. The purpose of this study is to discover the relative importance of attributes associated with the decision to engage in PA for adults with knee pain and to identify whether clusters of adults with shared preferences exist.

Methods: A discrete choice experiment was conducted using the PAPRIKA method to determine the relative importance of six attributes: health benefit, enjoyment, convenience, financial cost, effort, and time cost. All participants completed health history questionnaires, patient reported outcomes, and standing knee radiographs. Cluster analysis was performed to identify clusters (subgroups) of adults who place similar importance on attributes. Differences in sample characteristics between clusters were assessed using chi-square for categorical variables and ANOVA with Bonferroni correction for continuous variables.

Results: The study sample included 150 adults; 47% were 65 years or older, 72% female, 47% white, non-Hispanic, and 41% black, non-Hispanic. The six attributes in decreasing order of importance (mean weights) were: health benefit (0.26), enjoyment (0.24), convenience (0.16), financial cost (0.13), effort (0.11) and time cost (0.10) (see Figure 1). Table 1 reports on socio-demographic and health outcomes of the full sample and by preference cluster. Three clusters are found in Table 1: Cluster 1 (n=33), for whom enjoyment (0.35) is twice as important as health benefit; Cluster 2 (n=63), health benefit (0.38) is most important; Cluster 3, all attributes are equally important. Cluster 1 was healthiest (e.g., best self-reported health, lowest BMI), Cluster 2 had greatest exercise self-efficacy, and Cluster 3 had greatest number of participants with ≥1 comorbidity.

Conclusion: In the full sample, health benefit and enjoyment are the most important attributes associated with the decision to engage in PA, whereas financial cost, effort and time are much less important. Distinct subgroups place different relative importance on the attributes. These findings may help to better target interventions to increase PA engagement.
Disclosure: D. Pinto, None; U. Bockenholt, None; R. W. Chang, None; J. Lee, None; J. Holl, None; D. Finn, None; L. Sharma, None; A. Heinemann, None; P. Hansen, None.

**Initial Validation of Patient-Reported Outcomes Measurement Information System (PROMIS®) in Children with Juvenile Myositis**

Kaveh Ardalan\(^1,2\), David Cella\(^3\), Lauren M. Pachman\(^4\), Elizabeth L. Gray\(^5\), Julia (Jungwha) Lee\(^5\), Kyle Fahey\(^6,7\), Madison Wolff\(^6,7\), Megan L. Curran\(^7,8\), Mariana C. Marques\(^6,7\) and Rowland W. Chang\(^9\), \(^1\)Departments of Pediatrics and Medical Social Sciences, Northwestern University Feinberg School of Medicine, Chicago, IL, \(^2\)Division of Rheumatology, Ann & Robert H. Lurie Children’s Hospital of Chicago, Chicago, IL, \(^3\)Medical Social Sciences, Northwestern University Feinberg School of Medicine, Chicago, IL, \(^4\)Cure JM Program of Excellence in Juvenile Myositis Research, Stanley Manne Children’s Research Institute, affiliated with Ann & Robert H. Lurie Children’s Hospital of Chicago, Chicago, IL, \(^5\)Preventive Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, \(^6\)Division of Rheumatology, Ann & Robert H. Lurie Children’s Hospital of Chicago, Chicago, IL, \(^7\)Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, IL, \(^8\)Division of Rheumatology, Ann and Robert H. Lurie Children’s Hospital of Chicago, Chicago, IL, \(^9\)Preventive Medicine, Medicine, and Physical Medicine & Rehabilitation, Northwestern University Feinberg School of Medicine, Chicago, IL

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** Patient Outcomes, Preferences, and Attitudes Poster III  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**
Juvenile myositis (JM) can worsen quality of life (QoL) via proximal weakness, rashes, and treatments side effects. QoL legacy instruments may be limited by floor effects, unresponsiveness, and cost, justifying the need for new approaches. We present cross-sectional data for initial validation of Patient-Reported Outcomes Measurement Information System (PROMIS) in JM.

**Methods:**
Children (5-17 yo) with JM and parents enrolled at routine clinic visits. Demographic/clinical data were recorded, e.g. Physician Global Assessment of Disease Activity (PGA); Disease Activity Score (DAS-Total, -Muscle, -Skin); Childhood Myositis Assessment Scale (CMAS); muscle enzymes; nailfold capillary end row loops (NFC-ERL); neopterin; absolute NK cell count; C4 level. Children (8-17 yo) and parents (of all patients 5-17yo) completed patient/parent-proxy versions of PedsQL-generic core scales and rheumatology module (PedsQL-GC, -RM) and PROMIS Pain Interference, Physical Function (Mobility, Upper Extremity), Fatigue, and Emotional Distress (Depressive Symptoms, Anxiety) fixed short forms. Interrater (i.e. patient-parent) reliability was assessed via intraclass correlation coefficients (ICCs). Concurrent and construct validity were assessed via Spearman’s correlation coefficients between PROMIS and PedsQL scales and between PROMIS domains and clinical/lab data respectively.

**Results:**
Table 1 lists descriptive data. Patient-Parent ICCs were highest for PedsQL-GC (>0.6 for all except Social domain [=0.48]) compared with PedsQL-RM and PROMIS (>0.4 for all but PedsQL-RM Worry/Communication domains). Patient/parent PROMIS domains demonstrated concurrent validity (Spearman’s >0.4) with related PedsQL-GC/-RM domains (Table 2). Pediatric PROMIS and PedsQL-GC/-RM did not correlate with clinical/lab data; parent-proxy PROMIS fatigue, physical function (mobility, upper extremity), and multiple PedsQL-GC/-RM domains correlated with DAS-muscle and CMAS (Table 3).
Conclusion:

PROMIS pediatric fixed short forms demonstrate similar evidence for reliability and validity compared with PedsQL-GC/-RM in children with JM. Patient and parent-proxy reports differ sufficiently to suggest both should be collected. PROMIS can be considered for clinical/research use in JM.

Table 2: Spearman's Correlations PROMIS and PedsQL-GC/-RM*

<table>
<thead>
<tr>
<th>PROMIS Domain</th>
<th>Physical</th>
<th>Emotional</th>
<th>Social</th>
<th>School</th>
<th>Psychological</th>
<th>Total</th>
<th>PedsQL-domain1</th>
<th>PedsQL-domain2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ancestry</td>
<td>0.42</td>
<td>-0.56</td>
<td>-0.48</td>
<td>-0.83</td>
<td>-0.51</td>
<td>-0.39</td>
<td>-0.22</td>
<td>-0.84</td>
</tr>
<tr>
<td>Depression</td>
<td>-0.52</td>
<td>0.60</td>
<td>0.45</td>
<td>0.82</td>
<td>-0.61</td>
<td>-0.04</td>
<td>0.39</td>
<td>0.42</td>
</tr>
<tr>
<td>Fatigue</td>
<td>-0.71</td>
<td>-0.58</td>
<td>0.53</td>
<td>0.84</td>
<td>-0.76</td>
<td>-0.43</td>
<td>0.33</td>
<td>0.47</td>
</tr>
<tr>
<td>Mobility</td>
<td>0.29</td>
<td>0.69</td>
<td>0.27</td>
<td>0.41</td>
<td>0.53</td>
<td>0.4</td>
<td>0.61</td>
<td>0.32</td>
</tr>
<tr>
<td>Pain interference</td>
<td>-0.62</td>
<td>-0.42</td>
<td>-0.48</td>
<td>-0.86</td>
<td>-0.61</td>
<td>-0.17</td>
<td>0.42</td>
<td>-0.35</td>
</tr>
<tr>
<td>Upper Extremity</td>
<td>0.98</td>
<td>0.3</td>
<td>0.23</td>
<td>0.38</td>
<td>0.89</td>
<td>0.06</td>
<td>0.28</td>
<td>0.27</td>
</tr>
<tr>
<td>Parent-proxy report</td>
<td>0.51</td>
<td>-0.80</td>
<td>-0.43</td>
<td>-0.66</td>
<td>-0.64</td>
<td>-0.35</td>
<td>-0.48</td>
<td>-0.61</td>
</tr>
<tr>
<td>Depression</td>
<td>-0.60</td>
<td>0.76</td>
<td>0.47</td>
<td>0.67</td>
<td>-0.56</td>
<td>-0.46</td>
<td>0.51</td>
<td>-0.69</td>
</tr>
<tr>
<td>Fatigue</td>
<td>-0.29</td>
<td>0.55</td>
<td>0.42</td>
<td>0.81</td>
<td>-0.63</td>
<td>-0.06</td>
<td>0.39</td>
<td>-0.48</td>
</tr>
<tr>
<td>Mobility</td>
<td>0.33</td>
<td>0.61</td>
<td>0.59</td>
<td>0.85</td>
<td>0.36</td>
<td>0.67</td>
<td>0.59</td>
<td>0.47</td>
</tr>
<tr>
<td>Pain interference</td>
<td>0.58</td>
<td>-0.38</td>
<td>-0.82</td>
<td>-0.64</td>
<td>-0.51</td>
<td>-0.35</td>
<td>0.56</td>
<td>-0.24</td>
</tr>
<tr>
<td>Upper Extremity</td>
<td>0.72</td>
<td>0.47</td>
<td>0.42</td>
<td>0.63</td>
<td>0.53</td>
<td>0.56</td>
<td>0.66</td>
<td>0.61</td>
</tr>
</tbody>
</table>

*All Spearman's correlation coefficients are shown except for those in bold which are <0.05.

Disclosure: K. Ardalan, None; D. Cella, None; L. M. Pachman, None; E. L. Gray, None; J. Lee, None; K. Fahey, None; M. Wolfe, None; M. L. Curran, None; M. C. Marques, None; R. W. Chang, None.
Abstract Number: 2253

Patient’s Self-Monitoring of Disease Activity of Rheumatic Diseases Via Webapp – Study Design, Patient’s Perspective and Recruitment in the First 16 Months of a Swiss Multicentre, Longitudinal Study

Veronika K. Jaeger¹, Anna Barmet¹, Pia Schiffer², Pascal Zufferey³, Andrea Badaracco⁴, Marcel Walder⁵, Jean Dudler⁶, Dieter Frey⁷, Franziska Müller¹, Lilian Pichler¹, Peter Voss¹, Lorenzo Bosia⁸ and Ulrich A. Walker¹,
¹Department of Rheumatology, University Hospital Basel, Basel, Switzerland, ²Praxis beim Rathaus, Zofingen, Switzerland, ³Department of Rheumatology, University Hospital Lausanne, Lausanne, Switzerland, ⁴Studio Medico Badaracco Cattaneo, Lugano, Switzerland, ⁵Praxis Walder, Dübendorf, Switzerland, ⁶Hôpital Cantonal Fribourg, Fribourg, Switzerland, ⁷Praxis Frey, Basel, Switzerland, ⁸Praxis Bosia, Locarno, Switzerland

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

The management of patients with rheumatic diseases is partly guided by the medical history at each clinic visit. Patients however often find it difficult to accurately remember the course of their symptoms between appointments. Regular App-based patients’ self-monitoring of disease between clinic visits might provide an innovative and feasible improvement. The COMPASS I study [1] demonstrated that RA patients’ self-assessments of disease activity via App correlate strongly with clinicians’ assessments.

The main aims of COMPASS II are to assess if continuous self-monitoring of the disease optimises disease management in rheumatic diseases, and to assess the fluctuation of disease activity between clinic visits. This abstract describes the set-up and recruitment of the COMPASS II study in the first 16 months.

Methods:

The COMPASS II App questionnaire consists of the RAPID3 score, a validated, commonly used PRO to self-assess disease activity. Additionally, patients are asked about their therapy compliance and cortisone dose. COMPASS II is embedded in the SCQM (Swiss Clinical Quality Management for Rheumatic Diseases) registry and hence allows the linkage of data obtained via the WebApp from the patients with routine clinical data collected in the SCQM. Interested SCQM patients with RA, axSpA or PsA are electronically randomized into 3 study arms (Figure). In arm 1 patients and rheumatologists are displayed the self-assessed disease activity over time, the patient directly via the App and the rheumatologists via SCQM. In arm 2 only patients are displayed their chart and in study arm 3 neither sees the recorded data. Patients are encouraged to fill in the App weekly.

Results:

The COMPASS II App went online in 02/2016. In the first 16 months, 329 patients were enrolled. 65% of patients used the App, 78% of those filled in the questionnaires for longer than a month; currently, the longest follow-up is 16 months. On average patients use the App every 2 weeks.
Patients using the App for longer than 6 months rated the user-friendliness/usability of the WebApp as very positive in terms of the ease of use (mean of 82 on the system usability scale, a score of 68 is considered average [2]) and indicated that they felt a benefit in terms of patient physician communication with a mean score of 58 on the 100-mm VAS.

**Conclusion:**

Patients are highly adherent in the App use, rate it as very user-friendly and feel a benefit in patient physician communication. The COmPASS II study will validate the utility of app-based patients’ self-assessments in enhancing disease control.

**References:**


**Acknowledgements:** COmPASS II is supported by an unrestricted grant from AbbVie.

**Figure 1. Design of the COmPASS II study.**

**Disclosure:** V. K. Jaeger, None; A. Barmet, None; P. Schiffer, None; P. Zufferey, None; A. Badaracco, None; M. Walder, None; J. Dudler, None; D. Frey, None; F. Müller, None; L. Pichler, None; P. Voss, None; L. Bosia, None; U. A. Walker, None.


**Abstract Number:** 2254

**Disability (HAQ) and Quality of Life (SF-12) As Related to Adherence and Health Literacyin Patients with Rheumatoid Arthritis – the Trace-Study**
Jens Gert Kuipers¹, Michael Koller², Florian Zeman², Karolina Mueller² and Jens Ulrich Rueffer³, ¹Department of Rheumatology, Red Cross Hospital Bremen, Bremen, Germany, ²University Hospital Regensburg, Center for Clinical Studies, Regensburg, Germany, ³German Fatigue Society, Cologne, Germany

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Disabilities in daily living and quality of life are key endpoints to evaluate the outcome of treatment for rheumatoid arthritis (RA). Among factors that may contribute to good outcome are adherence and health literacy.

Methods: The survey included a representative, nationwide sample of German physicians specialized in RA and patients with RA. The physician questionnaire included the disease activity score (DAS28) and medical prescriptions. The patient questionnaire included fatigue (EORTC QLQ-FA13), health assessment questionnaire (HAQ), quality of life (SF-12), health education literacy (HELP), and patients’ listings of their medications.

Adherence was operationalized in various ways: patient-reported (CQR5), behavioral (correspondence between physicians and patients listings of medications), physician-assessed (five-point rating scale ranging from 1=very adherent to 5=not at all adherent) and a combined measure of physician rating (1= very adherent, 0 = less adherent) and the match between physicians’ prescriptions and patients’ accounts of their medications (1 = perfect match, 0 = no perfect match), leading to three categories of adherence: high, medium and low. Linear regressions were calculated using HAQ and SF-12 (physical and psychological) as dependent variables and adherence, health literacy and the set of demographic and clinical variables as predictor variables.

Results: A total of 708 pairs of patient and physician questionnaires were analyzed. The mean age of the patients, of whom 73% were women, was 60 years (SD=12). All results are shown in the multiple regression analyses.

Conclusion: This study showed that HAQ and SF-12 were related to adherence and health literacy. This finding highlights the importance of patient education and counseling in order to increase both, medical understanding and adherence to therapy.

Table 1: Patient characteristics

<table>
<thead>
<tr>
<th>Sociodemographics</th>
<th>Prescribed medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>60 (SD 12)</td>
</tr>
<tr>
<td>Total number of prescribed</td>
<td>4.9 (SD .27)</td>
</tr>
<tr>
<td>medications</td>
<td></td>
</tr>
<tr>
<td>Sex, male</td>
<td>193 (27%)</td>
</tr>
<tr>
<td>MTX</td>
<td>411 (58%)</td>
</tr>
<tr>
<td>Relationship status, married</td>
<td>512 (72%)</td>
</tr>
<tr>
<td>DMARD, without MTX and Biologica</td>
<td>169 (24%)</td>
</tr>
<tr>
<td>Children, yes</td>
<td>449 (63%)</td>
</tr>
<tr>
<td>Biologica</td>
<td>301 (43%)</td>
</tr>
<tr>
<td>Education, matriculation standard</td>
<td>203 (29%)</td>
</tr>
<tr>
<td>Glucocorticoide</td>
<td>416 (59%)</td>
</tr>
<tr>
<td>Occupation, employed</td>
<td>286 (40%)</td>
</tr>
<tr>
<td>Insurance, compulsory health</td>
<td>644 (91%)</td>
</tr>
<tr>
<td>insurance</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Multiple linear regression models
<table>
<thead>
<tr>
<th>MLR model*</th>
<th>Predictor</th>
<th>HAQ*</th>
<th>SF-12 Physical</th>
<th>SF-12 Psychological</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1</td>
<td>All 4 rheumatism agents taken as prescribed</td>
<td>4.41 (.45, 8.38)</td>
<td>.029</td>
<td>2.39 (.51, 4.28)</td>
</tr>
<tr>
<td></td>
<td>Adherence by doctor (ref. medium or less adherence)</td>
<td>1.79 (-3.89, 7.45)</td>
<td>.534</td>
<td>3.14 (.43, 5.86)</td>
</tr>
<tr>
<td></td>
<td>adherent</td>
<td>3.14 (.43, 5.86)</td>
<td>.023</td>
<td>3.01 (-2.56, 8.58)</td>
</tr>
<tr>
<td></td>
<td>Very adherent</td>
<td>3.28 (.61, 5.95)</td>
<td>.016</td>
<td>2.39 (.51, 4.28)</td>
</tr>
<tr>
<td></td>
<td>Health education literacy*</td>
<td>.330 (.229, .431)</td>
<td>&lt;.001</td>
<td>.141 (.093, .189)</td>
</tr>
<tr>
<td>Model 2</td>
<td>All 4 rheumatism agents taken as prescribed</td>
<td>3.22 (-.87, 7.32)</td>
<td>.123</td>
<td>2.00 (.04, 3.96)</td>
</tr>
<tr>
<td></td>
<td>Adherence composite score (ref. low adherence)</td>
<td>2.22 (-1.16, 6.06)</td>
<td>.256</td>
<td>.67 (-1.17, 2.51)</td>
</tr>
<tr>
<td></td>
<td>medium adherence</td>
<td>5.06 (.62, 9.50)</td>
<td>.026</td>
<td>1.48 (-.65, 3.61)</td>
</tr>
<tr>
<td></td>
<td>high adherence</td>
<td>.323 (.222, .423)</td>
<td>&lt;.001</td>
<td>.141 (.093, .190)</td>
</tr>
</tbody>
</table>

All models are adjusted for sex, age, drinking alcohol (y/n), smoking status (y/n) and sport activities (y/n); B, regression coefficient; 95%-CI, 95%- confidence interval; *linearly transformed on a scale from 0 (negative/low) to 100 (positive/high).

Disclosure: J. G. Kuipers, None; M. Koller, None; F. Zeman, None; K. Mueller, None; J. U. Rueffer, None.


Abstract Number: 2255

Using PROs to Guide Patient-Centered Conversations and Care in Inflammatory Arthritis: The Patient Perspective

Clifton O. Bingham III1, Katherine Clegg Smith2, Elaine de Leon2, Michelle Jones3, Anna Kristina Gutierrez4, Allie Butanis5 and Susan J. Bartlett4, 1Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, 2Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, 3Johns Hopkins University School of Medicine, Baltimore, MD, 4Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, 5Rheumatology, Johns Hopkins School of Medicine, Baltimore, MD

First publication: September 18, 2017
Background/Purpose: Although optimal care is patient-centered and grounded in shared decision-making (SDM) between patients and providers, rheumatologists often have little insight into the day-to-day experiences of their patients with inflammatory arthritis. We hypothesized that the use of validated patient-reported outcomes (PROs) querying RA symptoms and impact would provide insight into patient priorities, values, and preferences and facilitate SDM around treatment choices.

Methods: Participants in an observational study at an academic arthritis center completed PROMIS fatigue, pain, physical function, sleep, and participation on a tablet in the waiting room. Reports of results in numerical and graphical formats were available during the visit for review and discussion with the rheumatologist. Within 48 hours of the clinic visit, patients completed surveys about the relevancy and impact on the clinical visit. In-depth interviews were conducted with a subset.

Results: Survey data are from 68 patients who were mostly white (85%), female (81%) with a mean age of 54 (13) and RA duration of 10 (9) years. Interviews with 15 participants provided additional support to themes identified in the survey. Almost all (94%) reported the PRO question addressed important aspects of their health:

- Addresses a wide range of issues, which is great
- It shows the impact my arthritis has on me, not just the pain
- Helps give a better overall picture of what’s going on

Most (82%) reported the discussion of results during the visit improved communication and made it easier to raise issues:

- I love seeing data and graphs -- it really helps me
- It focuses...discussion with your physician so you can address the most pressing, sort of prioritize, the issues you want to address
- Doctor referred to my answers during discussion

A few (3%) were unclear if PRO results had been reviewed, or whether care was impacted:

- I think my doctor [already] treats me well

Conclusion: Patients place high value on PRO information which gives insight into day-to-day life and unmet needs. Expanded PRO assessment with real time review of results provides an opportunity for more patient-centered RA care and SDM by guiding conversations and improving communication about disease-related symptoms and impacts that matter to patients.

Funding PCORI IP2-PI0000737, SC14-1402-10818.

Disclosure: C. O. Bingham III, None; K. Clegg Smith, None; E. de Leon, None; M. Jones, None; A. K. Gutierrez, None; A. Butanis, None; S. J. Bartlett, None.


Abstract Number: 2256
Temporal Increases in Side Effect Concerns of Osteoporosis Medications Among Women with Previous Fractures

Maria I. Danila1, Elizabeth J. Rahn2, Amy S. Mudano1, Ryan Outman3, Peng Li4, David T. Redden4, Fred A. Anderson5, Susan L. Greenspan6, Andrea Z. LaCroix7, Jeri W. Nieves8, Stuart L. Silverman9, E.S. Siris10, Nelson B. Watts11, Sigrid Ladores12, Karen Meneses12, Jeffrey R. Curtis13 and Kenneth Saag13, 1University of Alabama at Birmingham, Birmingham, AL, 2Department of Medicine, Division of Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 3Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 4Department of Biostatistics, University of Alabama at Birmingham, Birmingham, AL, 5University of Massachusetts Medical School, Worcester, MA, 6Medicine, University of Pittsburgh, Pittsburgh, PA, 7Group Health Cooperative, Seattle, WA, 8Helen Hayes, West Haverstraw, NY, 9Cedars-Sinai Medical Center, Los Angeles, CA, 10Columbia University Medical Center, New York, NY, 11University of Cincinnati, Cincinnati, OH, 12Nursing, University of Alabama at Birmingham, Birmingham, AL, 13Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: High-consequence, albeit rare, adverse side effects of osteoporosis medication raise patients’ risk perceptions and contribute to non-adherence. In the past decade, fears of osteonecrosis of the jaw (ONJ) and atypical femoral fractures (AFF) have been increasingly reported as barriers to both the initiation of and adherence to osteoporosis medications. We examined the temporal prevalence of self-reported concern about ONJ and AFF as reason for discontinuation of osteoporosis medication.

Methods: Activating Patients at Risk for OsteoPOroSis (APROPOS) enrolled US women from the Global Longitudinal Study of Osteoporosis (GLOW) with previous self-reported fractures and no current use of osteoporosis medication. Using mailed surveys in 2010 (T1), 2012 (T2) and 2013 (T3), women were asked whether they discontinued osteoporosis medication in the prior year because of concerns about ONJ at three time points (T1, T2, T3) and AFF at two time points (T2, T3). We calculated the proportion of women reporting fears of ONJ and AFF as reason for discontinuation of osteoporosis medication, and compared the proportions using chi-square tests.

Results: A total of 833 women discontinued osteoporosis treatment at three time points, T1 (N = 255), T2 (N = 471), and T3 (N= 107), respectively. There were no differences in the demographic characteristics between groups. The proportion of women reporting concerns of ONJ was 18.4% (T1), 26.7% (T2) and 64.5% (T3), while 23.5% (T2) and 60.7% (T3) reported fear of AFF as reason to discontinue osteoporosis treatment. These differences were statistically significant (p<0.0001) for all comparisons.

Conclusion: The proportion of women reporting concerns of ONJ and AFF increased over time among those women who discontinue osteoporosis medications. Strategies are needed to help patients balance risks and benefits given a significant and temporally growing concern of rare bisphosphonate side effects.

Disclosure: M. I. Danila, None; E. J. Rahn, None; A. S. Mudano, None; R. Outman, None; P. Li, None; D. T. Redden, None; F. A. Anderson, Millenium Pharmaceuticals, 5; S. L. Greenspan, Amgen, 2,Lilly, 2; A. Z. LaCroix, Amgen, Pfizer, Sermonix, 9; J. W. Nieves, None; S. L. Silverman, Amgen, Lilly, 2,Amgen, 5; E. S. Siris, None; N. B. Watts, OsteoDynamics, 1,Shire, 2,OsteoDynamics, 4,AbbVie, Amgen, Janssen, Merck, Radius, Sanofi, 5,Amgen, Shire, 9; S. Ladores, None; K. Meneses, None; J. R. Curtis, Amgen, 2,Amgen, 5; K. Saag, Amgen, Lilly, Merck, 5,Amgen, Lilly, Merck, 2.
Assessing the Impact of a Digital Health Coaching Program for Patients with Rheumatoid Arthritis

Imon Ghosh¹, Uma Srivastava², B Stephen Burton², Maria Antonia Garcia-Espinosa¹, Dhiren Patel³ and Mazi Rasulnia⁴

¹Strategic Partnerships, Pack Health, Birmingham, AL, ²Outcomes, Pack Health, Birmingham, AL, ³Pack Health, Cambridge, MA, ⁴Co-Founder / Strategic Partnerships, Pack Health, Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Despite considerable advancements in pharmacotherapy treatments, millions of people still suffer with Rheumatoid Arthritis (RA). This puts management in the hands of the patients, requiring lifestyle changes to improve symptoms associated with RA. This study of patients with RA examined the efficacy of behavior modification in reducing RA-inducing stressors (1,2) and increasing healthy behaviors proven to reduce symptoms, healthy eating (3,4) and exercise (5). We hypothesized that the program would increase healthy habits and decrease the negative effects of RA.

Methods: RA patients (n=127) were enrolled in a 12 week behavior modification program. Each patient was paired with a non-clinical health coach. The patients were contacted once a week by telephone and surveyed about their behaviors and condition. Information about mental and physical health were collected through PROMIS Global Health-10. The Patient Activity Scale-II (PAS-II) was used to determine symptom severity and disease activity.

Results: Results indicate significant improvements in BMI (decrease 0.54 kg/m²), weekly physical activity (increase of 73%), hours of sleep per night (increase of .4 hrs), and alcohol and tobacco consumption (decrease of 15% and 25%, respectively). The effect of behavior change was shown by significant increases in physical (PROMIS physical health domain, 24%) and mental health (PROMIS mental health domain, 17%) as well as higher motivation (6%). In addition, flare frequency dropped by 48% suggesting that improvement of healthy behaviors and the reduction of stressors were associated.

Conclusion: The results of the study indicate that behavior modification would improve healthy behaviors and decrease RA symptoms. Future studies should examine the impact of coaching in various segments of RA patients such as underserved, those with multiple comorbidities and those newly diagnosed versus patients living with RA for multiple years.

Disclosure: I. Ghosh, None; U. Srivastava, None; B. S. Burton, None; M. A. Garcia-Espinosa, None; D. Patel, None; M. Rasulnia, None.
Real-World Evidence Linking Health-Related Quality of Life to Work Outcomes in Patients with Rheumatoid Arthritis

Vibeke Strand\textsuperscript{1}, Mark Kosinski\textsuperscript{2}, Regina Rendas-Baum\textsuperscript{2}, David Brooks\textsuperscript{3} and Rita Ganguly\textsuperscript{4}, \textsuperscript{1}Division of Immunology/Rheumatology, Stanford University, Stanford, CA, \textsuperscript{2}Optum, Inc, Eden Prairie, MN, \textsuperscript{3}GlaxoSmithKline, Philadelphia, PA, \textsuperscript{4}GlaxoSmithKline, Collegeville, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Evaluating health-related quality of life (HRQoL) scores is a key component of the management of rheumatoid arthritis (RA) and evaluation of treatment efficacy. There is a need to further understand how observed differences in these scores translate into impact on work-related outcomes. The objective of these analyses was to establish a quantitative link between reported HRQoL and work outcomes of RA patients.

Methods: Patient data was obtained from 2 independent databases: QualityMetric’s 2009 PRO Norming Survey (QMPRONS) and the Medical Expenditure Panel Survey (MEPS). Physical and Mental Component Summary (PCS and MCS) scores of Short Form-12v2 Health Survey (SF-12v2; captured in MEPS) and Short Form-36v2 Health Survey (SF-36v2; captured in QMPRONS) assessed HRQoL. Work outcomes were evaluated using the following endpoints: inability to work due to disability, lost days of work/housework, self-rated job performance, and presence of serious cognitive difficulties. Logistic regression models analyzed binary outcomes (inability to work, self-rated job performance [low vs medium/high], and presence of cognitive difficulties). A zero-inflated Poisson model was used to analyze the relationship between HRQoL and lost days of work/housework. A 5-point difference was used to illustrate the impact of lower HRQoL on work outcomes.

Results: Lower PCS and MCS scores were significantly associated with inability to work due to health (lower PCS: odds ratio [OR], 2.42; 95% confidence interval [CI], 2.14-2.74; lower MCS: OR, 1.40; 95% CI, 1.28-1.52; both \( P <0.0001 \)). Furthermore, lower SF-12v2 summary scores were significantly associated with increased numbers of missed days of work/housework (lower PCS: 4.4 vs 1.3 missed days for scores of 40 vs 45, respectively; \( P <0.0001 \); lower MCS: 3.6 vs 1.6 missed days for scores of 40 vs 45, respectively; \( P = 0.0002 \)). For SF-36v2 MCS, a lower score was associated with greater odds of low job performance among employed patients (OR, 1.58; 95% CI, 1.34-1.85; \( P <0.0001 \)), although a lower PCS score did not significantly increase odds of reporting low job performance. Lower SF-12v2 scores were significantly associated with increased risks for serious cognitive difficulties in both employed and all patients (all \( P <0.0001 \); Figure).

Conclusion: Low physical and mental health is associated with an increased inability to work and increased number of missed days of work. These analyses demonstrate that lower scores significantly impact work outcomes and underscore the importance of both summary measures in terms of measuring the impact of RA.

Figure. Increase in the odds of presence of cognitive difficulties associated with a 5-point lower SF-12v2 score.
SF-12v2, Short Form-12v2 Health Survey; PCS, physical component summary; MCS, mental component summary; CI, confidence interval.

Disclosure: V. Strand, AbbVie, Amgen, AstraZeneca, Biogen Idec, Boehringer Ingelheim, Celltrion, Crescendo, Genentech/Roche, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sanofi, and UCB, 5; M. Kosinski, Optum, Inc, 3; R. Rendas-Baum, Optum, Inc, 3; D. Brooks, GlaxoSmithKline, 3,GlaxoSmithKline, 1; R. Ganguly, GlaxoSmithKline, 1,GlaxoSmithKline, 3.


Abstract Number: 2259

Quality of Life Evaluation in New Onset Juvenile Dermatomyositis Patients from the Printo Trial

Andressa Guariento1, Gabriella Giancane2, Elena Fueri1, Francesco Zulian3, Angelo Ravelli4, Bo Magnusson3, Tadej Avcin3, Fabrizia Corona3, Valeria Gerloni1, Claudia Bracaglia1, Rolando Cimaz1, Antonella Meini2, Silvana Martino3, Anne Pagnier1, Michel Rodiere3, Christine Soler3, Valda Stanevicha3, Rebecca ten Cate5, Jelena Vojinovic3, Simona Angioloni1, Luca Villa1, Michele Pesce1, Irene Gregorini1, Chiara Pallotti1, Alberto Martini6, Angela Pistorio3 and Nicola Ruperto3, 1Istituto Giannina Gaslini - Pediatrica II, Reumatologia - PRINTO, Genova, Italy, 2Pediatrica II, Reumatologia - PRINTO, Istituto Giannina Gaslini - Pediatrica II, Reumatologia - PRINTO, Genova, Italy, 3Istituto Giannina Gaslini - Pediatrica II, Reumatologia - PRINTO, Genoa, Italy, 4University of Genova, IRCCS Istituto Giannina Gaslini, Genova, Italy, 5Pediatric Rheumatology, Leiden University Medical Center, Leiden, Nethedlands, 6Istituto Giannina Gaslini, Genoa, Italy

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Juvenile dermatomyositis (JDM) is the most common clinical pediatric idiopathic inflammatory myopathy and it may severely compromise the quality of life of affected patients. Early adequate immunosuppressive treatment can improve the quality of life in JDM as in other rheumatic diseases like juvenile idiopathic arthritis (JIA).
Objective: To evaluate the HRQoL change over time in children with new-onset JDM patients enrolled in the PRINTO trial.

Methods: In the PRINTO JDM trial, children aged 18 years old or younger with newly diagnosed and untreated probable or definite JDM were enrolled. All patients received three daily pulses of intravenous methylprednisolone at onset, and then they were randomized to one of the following three different treatment groups: prednisone (PDN), prednisone plus ciclosporin (PDN+CSA) and prednisone plus methotrexate (PDN+MTX).

In our study, we considered patients who had a complete HRQoL assessment at onset through the Child Health Questionnaire (CHQ). We compared quality of life among the responders (PRINTO20-50-70) belonging to the three treatment groups, and between responder and not responder patients. Moreover we compared the affected patients to healthy children.

Results: Out of a total of 139 patients enrolled in the PRINTO JDM trial, 129 (92.8%) were retained for the analysis (41.9% males and 58.1% females; median age 7.4 years). At baseline, patients with JDM showed poorer scores in quality of life (PhS = 15.6 and PsS=40.0) than healthy children. In particular, “Physical Summary score” (PhS) turned out to be significantly lower than 2 standard deviations with respect to the mean value of the healthy children with no difference among the 3 treatment groups (PDN, PDN+MTX, PDN+CSA). Less compromised scores were observed for the PsychoSocial summary Scale, with values between 1 and 2 standard deviations below the mean values of healthy children. We found similar values between «responder 20» and «not responders». A statistically significant improvement was observed after 6 months of treatment both in the PhS and in the PsS subscales (P<0.0001) irrespective of the treatment group, and in all items of the CHQ with the exception of the GBE (Global behavior parameter). A significant improvement over time was observed regardless of the treatment group and the level of response (PRINTO 20, 50, 70). “Responder” patients showed PhS values significantly higher than “not responder”; on the contrary, PsS values did not reveal a significant difference between “responders” and “not responders”, despite an improvement over time.

Conclusion: Children with new-onset JDM, treated with PDN alone or in combination with other therapies, showed a significant improvement in quality of life during a two-year follow-up. According to the “PRINTO 20-50-70” criteria, “responder” patients showed a statistically significant improvement in the PhS score compared to the “not responders”.

References:


Disclosure: A. Guariento, None; G. Giancane, None; E. Fueri, None; F. Zulian, None; A. Ravelli, None; B. Magnusson, None; T. Avcin, None; F. Corona, None; V. Gerloni, None; C. Bracaglia, None; R. Cimaz, None; A. Meini, None; S. Martino, None; A. Pagnier, None; M. Rodiere, None; C. Soler, None; V. Stanevicha, None; R. ten Cate, None; J. Vojinovic, AbbVie, 8; S. Angioloni, None; L. Villa, None; M. Pesce, None; I. Gregorini, None; C. Pallotti, None; A. Martini, GASLINI Hospital, 3,Astellas, AstraZeneca, Bristol-Myers Squibb, Italfaraco, and MedImmune, 8,AbbVie Inc., AstraZeneca, Bristol-Myers Squibb, Janssen Biologies B.V., Eli Lilly and Co., “Francesco Angelini”, GlaxoSmithKline, Italfaraco, Novartis, Pfizer, Roche, Sanofi Aventis, Schwarz Biosciences GmbH, Xoma, and Wyeth Pharmaceuticals, 2; A. Pistorio, None; N. Ruperto, GASLINI Hospital, 3,Astellas, AstraZeneca, Bristol-Myers Squibb, Italfaraco, Janssen Biologies B.V., MedImmune, Roche, and Wyeth/Pfizer, 8.


Abstract Number: 2260

Communication Strategies Are Highly Important to Avoid Nocebo Effect When Performing Non-Medical Switch from Originator Product to
Biosimilar Product: Danish Results from Applying the Parker Model a Qualitative 3-Step Research Model

Tanja Schjødt Jørgensen¹, Marie Skougaard¹, Hans Christian Asmussen²,³, Anne Lee⁴, Peter C. Taylor⁵, Henrik Gudbergsen¹ and Lars Erik Kristensen¹, ¹The Parker Institute, Copenhagen University Hospital, Bispebjerg and Frederiksberg, Copenhagen F, Denmark, ²NATiON, Copenhagen, Denmark, ³Communication IKH, Roskilde University, Roskilde, Denmark, ⁴University of Southern Denmark, Odense, Denmark, ⁵University of Oxford Botnar Research Centre, Kennedy Institute of Rheumatology, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Introducing a non-medical switch from originator to a biosimilar product in the management of chronic arthritis, i.e. switching patients in remission or low disease activity, may generate economic advantages, but on the other hand jeopardize patient engagement and empowerment. To explore impact of performing a non-medical switch from etanercept originator to a biosimilar in Danish patients with a chronic arthritis, and to explore the economic impact.

Methods:
The Parker model, a 3-step qualitative research approach, was used to study the impact of switching from etanercept originator to a biosimilar in patients with remission or low disease activity. Concept mapping (CM), a structured group process focused on patient-relevant themes, was used to identify treatment-related issues and concerns. Subsequently, the retrieved information was utilized in a series of iterative participatory design (PD) sessions. Finally, these two methods were complemented by stakeholder evaluations (SE) based on semi-structured group and solo-interviews with a series of disease-management stakeholders.

Results:
The study included 10 rheumatoid arthritis (RA) patients, 5 spondyloarthritis patients (SpA), 1 ankylosing spondylitis (AS) patient, 2 doctors, 2 nurses, 1 medical secretary, and 4 key public stakeholders involved in the disease-management of the selected rheumatic diseases. Saturation was reached after 3 CM workshops, including patients switching from etanercept originator to a biosimilar, generating 122 statements, out of which 7 concepts were generated; information from doctors/nurses, concerns/side effects, effect of medication, etanercept biosimilar, economy, own perception of switch, and discomfort. In addition, 1 extra workshop was conducted including 5 RA patients switching from etanercept biosimilar back to originator or to a third biologic agent, generating 45 statements, from which 4 concepts were generated; patient experiences/concerns, information, meeting with healthcare professionals/therapists, and etanercept biosimilar. These data were used in the iterative PD sessions, resulting in 5 newly proposed personalized communication strategies. Finally, SE demonstrated that implementing a non-medical biological switch involves both dialogue and clear communication in relation to logistic and background information. Communication needs to be well prepared, allowing sufficient time for providing all involved with an opportunity to discuss relevant educational materials. Health economic analyses estimated that the annual savings are between approx. DKK 8,900 and DKK 64,600 per patient depending on type of administration.

Conclusion:
Patient participation in the 3-step qualitative Parker Model identified important aspects regarding communication strategies to consider when introducing a biosimilar to the market for the treatment and management of RA and SpA. The importance of systematic education and communication with all directly involved stakeholders was highlighted. The cost of implementing switching is very limited and savings incurred by the significantly lower prices of biosimilar compared to originator makes the switch instantly economically viable.

Disclosure: T. S. Jørgensen, Abbvie, Roche, Novartis, UCB, Biogen, 8; M. Skougaard, None; H. C. Asmussen, None; A. Lee, None; P. C. Taylor, Biogen, Sandoz, UCB, Pfizer, AbbVie, Janssen Pharmaceuticals, 5; H. Gudbergsen, MSD and Pfizer, 8; L. E. Kristensen, Pfizer, AbbVie, Amgen, UCB, Celgene, BMS, MSD, Novartis, Eli Lilly, Janssen Pharmaceuticals, Biogen, 8.


Abstract Number: 2261

Supporting Smoking Cessation in RA and SLE: Identifying Patient-Centered Outcomes

Aimée Wattiaux1, Laura Block2, Andrea Gilmore-Bykovskyi2, Edmond Ramly3, Jane Sadusky4, Megan Piper5, Brittany Bettendorf5, Ann Rosenthal7 and Christie M. Bartels8, 1Department of Medicine, University of Wisconsin School of Medicine and Public Health, Madison, WI, 2University of Wisconsin School of Nursing, Madison, WI, 3Industrial and Systems Engineering, University of Wisconsin College of Engineering, Madison, WI, 4Research Consultant, Madison, WI, 5University of Wisconsin Center for Tobacco Research and Intervention, Madison, WI, 6Rheumatology, Medical College of Wisconsin, Milwaukee, WI, 7Division of Rheumatology, Medical College of Wisconsin, Milwaukee, WI, 8Rheumatology/Medicine, University of Wisconsin - Madison, Madison, WI

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Patients with RA and SLE are at higher risk for premature cardiovascular disease (CVD) than peers. Smoking is a leading modifiable risk factor for CVD and exacerbates rheumatic disease symptoms. Despite this, our prior work showed that only 10% of rheumatology visits with patients who smoke document cessation counseling. To address this gap, we previously implemented a new rheumatology staff protocol that increased referrals to the tobacco quit line 20-fold. The objective of the current study was to engage RA and SLE patients who smoke in focus groups to 1) examine barriers and facilitators of smoking cessation to further inform the protocol, and 2) identify meaningful outcomes that are signs of progress towards smoking cessation.

Methods: Using targeted letters, we recruited 19 patients (12 RA and 7 SLE) from two health systems to participate in one of three focus groups about smoking cessation support. 89% of participants were female, 47% white, 42% black, and 11% unknown race/Hispanic ethnicity. Ages ranged from 33-72. Two expert facilitators led each one-hour focus group using a semi-structured interview guide. Focus groups were recorded and transcribed verbatim. We used directed content analysis to classify barriers, facilitators, and valued outcomes regarding smoking cessation support. Two trained coders reviewed and coded all data using NVivo software.
**Results:** Participants discussed common barriers to quitting, including viewing smoking as “a crutch,” “a comfort,” and “the one thing I still have control over” while dealing with the burden of rheumatic disease, socioeconomic and other stressors, or trauma (Table 1). The new protocol was well received. Participants endorsed flexible terms like “cutting down” as opposed to strictly “quitting,” and preferred to receive counseling from staff who had personal experience with smoking or quitting. The outcomes that participants said they would value most fell primarily within two categories: knowing why to quit and knowing how to quit. Few were aware of the physiological impact smoking has on rheumatic disease, and none had heard that smoking can reduce the efficacy of rheumatic disease medication. Participants reported that knowing more about the effects of smoking on rheumatic disease and treatment would be a key motivator to quit smoking. Many requested that rheumatology staff help them identify tangible, day-to-day strategies to overcome cravings and connect them with resources they can use to quit smoking.

**Conclusion:** Focus group findings identified two key facilitators of smoking cessation for those with RA and SLE: understanding the specific health risks of smoking in rheumatic disease and knowing tangible steps to take towards quitting. Emphasizing the why and the how of smoking cessation is essential when designing and evaluating outcomes of rheumatology smoking cessation interventions.

<table>
<thead>
<tr>
<th>Table 1. Barriers &amp; Facilitators of Smoking Cessation in RA &amp; SLE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Barriers</strong></td>
</tr>
<tr>
<td>---------------------------------</td>
</tr>
<tr>
<td>Maintaining Autonomy</td>
</tr>
<tr>
<td>Coping with Burden of Disease</td>
</tr>
<tr>
<td>Navigating the System</td>
</tr>
<tr>
<td>Knowing Why</td>
</tr>
<tr>
<td>Knowing How</td>
</tr>
</tbody>
</table>

**Disclosure:** A. Wattiaux, None; L. Block, None; A. Gilmore-Bykovskyi, None; E. Ramly, None; J. Sadusky, None; M. Piper, None; B. Bettendorf, None; A. Rosenthal, None; C. M. Bartels, Pfizer Inc, 2.


**Abstract Number:** 2262

**Knowledge, Beliefs and Concerns about Osteoporosis – a Qualitative Synthesis**

Jude des Bordes¹, Seema Prasad², Gregory Pratt³, Maria Suarez-Almazor¹ and Maria A. Lopez-Olivo¹, ¹Section of Rheumatology and Clinical Immunology, Department of General Internal Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA, Houston, TX, ²Gastroenterology Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA, Houston, TX, ³Research Medical Library, The University of Texas MD Anderson Cancer Center, Houston, TX, USA, Houston, TX

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Background/Purpose:** Educating patients with osteoporosis about bone health could increase their knowledge and self-efficacy. These can help them adopt healthy lifestyles to prevent osteoporosis-associated fractures. To undertake an effective bone health education for these patients, it is necessary to determine what the gaps in knowledge are. This study synthesized the evidence on perceptions about osteoporosis.

**Methods:** A comprehensive search of the literature was done in an electronic database (Ovid – Medline) from 1946 to 2016, to identify qualitative studies exploring knowledge, beliefs and concerns of patients about osteoporosis and related terms. We included any study reporting detail data on literacy, understanding, perceptions and/or learning needs about bone health, low bone density, and osteoporosis. Major themes were identified and organized by categories.

**Results:** Ninety-three records were identified. Eight studies comprising 5 qualitative and 3 mixed-methods studies were included and underwent analysis. Population included 1,475 participants (including men and women), 18-90 years, 21% with confirmed osteoporosis. Major areas of knowledge deficits included: i) risk factors, ii) causes, iii) treatment, and iv) prevention. Two major categories were identified when patients were asked their beliefs about osteoporosis: i) osteoporosis is a disease of the old, frail with collapsed back and associated with weak bones and fractures; and ii) some thought it was very painful and could be caused by circumstances beyond one’s control and stressful life situations. Patients also reported that osteoporosis was not perceived as a serious illness such as stroke or cancer and that long term medication safety or efficacy was limited. There were four categories identified as concerns: i) diagnosis and treatment could be a source of worry (especially in the absence of symptoms); ii) patients may be “labeled” with the condition; iii) side effects and costs of osteoporosis medications, and iv) living with fractures.

**Conclusion:** Areas of knowledge deficit were risk factors, causes, treatment and prevention. The most common themes regarding patients’ beliefs across studies were that osteoporosis is a condition associated with weak bones and is painful. Medication side effects were of most concern to patients. This information can be used to tailor education, communication, and service initiatives to increase bone health knowledge and self-efficacy in osteoporosis patients and decrease fracture risk.

**Disclosure:** J. des Bordes, None; S. Prasad, None; G. Pratt, None; M. Suarez-Almazor, None; M. A. Lopez-Olivo, None.

**View Abstract and Citation Information Online** - [http://acrabstracts.org/abstract/knowledge-beliefs-and-concerns-about-osteoporosis-a-qualitative-synthesis](http://acrabstracts.org/abstract/knowledge-beliefs-and-concerns-about-osteoporosis-a-qualitative-synthesis)

**Abstract Number:** 2263

---

**Obesity Independently Associates with Worse Patient Reported Outcomes in Women with Systemic Lupus Erythematosus**

**Sarah L. Patterson**¹, Gabriela Schmajuk², Kashif Jafri³, Katherine D. Wysham³ and Patricia P. Katz⁴, ¹Division of Rheumatology, University of California, San Francisco, San Francisco, CA, ²San Francisco VA Medical Center, University of California San Francisco, San Francisco, CA, ³University of California, San Francisco, San Francisco, CA, ⁴Medicine/Rheumatology, University of California, San Francisco, San Francisco, CA

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Tuesday, November 7, 2017
**Background/Purpose:** Obesity has been shown to exacerbate systemic inflammation in the general population and contributes to worse disease-related outcomes in rheumatoid arthritis. The impact of excess adiposity in systemic lupus erythematosus (SLE) has not been established despite obesity being a common comorbidity in SLE. We aimed to determine whether excess adiposity in women with SLE independently associates with worse patient reported outcomes (PROs).

**Methods:** Participants in this sample, drawn from the Arthritis Body Composition and Disability (ABCD) study, were at least 18 years old, female, and carried a diagnosis of SLE verified by medical record review. Body mass index (BMI) was calculated as weight (kg) divided by height (m$^2$), and fat mass index (FMI), a measure of total fat mass adjusted for height, was assessed using whole dual x-ray absorptiometry (DXA). Two established definitions for obesity were used: FMI $\geq 13$ kg/m$^2$ and BMI $\geq 30$ kg/m$^2$. Dependent variables included 4 validated PROs: disease activity via Systemic Lupus Activity Questionnaire (SLAQ), depressive symptoms via Center for Epidemiologic Studies Depression Scale (CES-D), pain via Short Form 36 Health Survey (SF-36) Pain Subscale, and fatigue via SF-36 Vitality Subscale. We used multivariable linear regression to evaluate the associations of obesity with PROs while controlling for potential confounders (age, race, education, income, smoking, disease duration, disease damage, and prednisone use). We then calculated adjusted means for each outcome based on the multivariable regression.

**Results:** The sample (n=148) was 65% white, 14% Asian, and 13% African American; mean age 48 (± 12.3) years; 17% with poverty-level income; 86% with education beyond high school; mean disease duration 16 (± 9) years; and 45% taking glucocorticoids. 32% and 30% of participants met criteria for obesity by the FMI and BMI definitions, respectively. In the multivariate regression model, obesity defined by FMI associated with worse scores on each PRO: greater disease activity, higher levels of depressive symptoms, more pain, and more fatigue (Table). The same relationship between obesity and each of the reported PROs was observed after repeating the analyses using the traditional BMI $\geq 30$ kg/m$^2$ cut-off.

**Conclusion:** In a representative sample of women with SLE, obesity (by FMI and BMI) independently associated with worse patient reported outcomes, including disease activity, depressive symptoms, and symptoms of pain and fatigue. Obesity may represent a modifiable target for improving outcomes in this patient population.
Table. Adjusted Means for Patient Reported Outcomes by Obesity Status

<table>
<thead>
<tr>
<th>Patient Reported Outcomes</th>
<th>Obese (^{b}) (95% CI)</th>
<th>Not Obese (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease Activity (SLAQ)</td>
<td>14.8 (12.7-16.9)</td>
<td>11.5 (10.1-12.9)</td>
<td>0.010</td>
</tr>
<tr>
<td>Depression (CES-D)</td>
<td>19.8 (16.1-23.4)</td>
<td>13.1 (10.6-15.6)</td>
<td>0.004</td>
</tr>
<tr>
<td>Pain (SF-36 Pain)</td>
<td>38.7 (35.7-41.7)</td>
<td>44.2 (42.2-46.3)</td>
<td>0.004</td>
</tr>
<tr>
<td>Fatigue (SF-36 Vitality)</td>
<td>39.6 (36.2-43.0)</td>
<td>45.2 (42.9-47.6)</td>
<td>0.010</td>
</tr>
</tbody>
</table>

\(^{a}\) Adjusted means calculated based on multivariate linear regression adjusted for age, race, education, income, smoking, disease duration, disease damage (Brief Index of Lupus Damage score), and prednisone use.

\(^{b}\) Obesity defined by fat mass index \(\geq 13 \text{ kg/m}^2\)

\(^{c}\) Higher scores reflect better status (less pain/fatigue)

SLAQ – Systemic Lupus Activity Questionnaire
CES-D – Center for Epidemiologic Studies Depression Scale
SF-36 – Short Form 36 Health Survey

Disclosure: S. L. Patterson, None; G. Schmajuk, None; K. Jafri, None; K. D. Wysham, None; P. P. Katz, None.


Abstract Number: 2264

**Low Educational Attainment Is Associated with Poor Patient Status in Rheumatoid Arthritis (RA) or Osteoarthritis (OA) at the Initial Rheumatology Visit, with Remarkably Similar Patterns in Either Diagnosis**

Juan Schmukler\(^1\), Jacquelin R. Chua\(^1\), Shakeel M. Jamal\(^1\), Isabel Castrejón\(^1\), Joel A Block\(^1\) and Theodore Pincus\(^2\), \(^1\)Division of Rheumatology, Rush University Medical Center, Chicago, IL, \(^2\)Rheumatology, Rush University Medical Center, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster III
Session Type: ACR Poster Session C
**Background/Purpose:** Low educational attainment is associated with higher prevalence, morbidity, and mortality of many diseases, including rheumatoid arthritis\(^1\) (RA) and osteoarthritis\(^2\) (OA). These associations often are attributed to limited access of disadvantaged people to medical services. We studied clinical status of patients with RA or OA, all of whom had access to rheumatology care, at their initial visit.

**Methods:** All patients seen at an academic rheumatology clinic complete a multidimensional health assessment questionnaire (MDHAQ) at each visit. MDHAQ is a patient self-report questionnaire that includes 3 0-10 scales for physical function (FN), pain (PN), and global assessment (PATGL), compiled into a 0-30 routine assessment of patient index data (RAPID3). We identified 132 new patients with a diagnosis of either RA (n=66) or OA (n=66) seen for an initial visit between May, 2011 and February, 2017, and for whom all data were available. Patient-reported FN, PN, PATGL and RAPID3 were compared in 3 groups according to completed years of schooling, < 12 years, 12 years, and > 12 years, using analysis of variance (ANOVA).

**Results:** Mean MDHAQ scores were remarkably similar in OA vs RA, and varied similarly according to education level (Table). Mean RAPID3 scores were 15.4 in OA vs and 15.3 in RA patients, 18.2 and 19.8 in OA vs RA patients with <12 years, 15.9 and 16.0 in OA and RA patients with 12 years, and 14.0 and 13.7 in OA vs RA patients with >12 years of education (p=0.11 for OA, p=0.04 for RA) (Table). FN scores were 2.9 for all patients in both OA and RA, 3.9 in both groups for <12, 3.3 in both groups for 12, and 2.3 and 2.4 in OA vs RA patients, respectively, for those with >12 years of education (comparisons by education level p=0.02 for OA, p=0.08 for RA). PN scores were 6.9 and 6.4 in all OA vs RA patients, 7.3 and 8.5 for OA vs RA patients with <12 years, 7.1 and 6.2 for OA vs RA patients with 12 years, and 6.7 and 5.9 for OA vs RA patients with >12 years of education (p=0.69 for OA, p=0.02 for RA). PATGL was 5.6 and 6.0 for all OA vs RA patients, 7.0 and 7.4 for OA vs RA patients with <12 years, 5.5 and 6.5 for OA vs RA patients with 12 years, and 5.1 and 5.4 in OA vs RA patients, with >12 years of education (p=0.14 for OA, p=0.12 for RA).

**Table:**

<table>
<thead>
<tr>
<th>OA</th>
<th>Total N=66</th>
<th>Groups by level of Education (years)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>&lt;12 (n=12)</td>
<td>12 (n=21)</td>
</tr>
<tr>
<td>MDHAQ-Function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MDHAQ-Pain</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MDHAQ-PATGL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAPID3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RA</td>
<td>Total N=66</td>
<td>Groups by level of Education (years)</td>
<td>p*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;12 (n=12)</td>
<td>12 (n=21)</td>
</tr>
<tr>
<td>MDHAQ-Function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MDHAQ-Pain</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MDHAQ-PATGL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAPID3</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** Low education was associated with RAPID3 and all measures both in RA and OA. Differences according to formal education level differed far more than differences by diagnosis, which were negligible. These variations do not appear attributable to differences in access to medical service.

**References:**
Abstract Number: 2265

Survey on Gout-Related Knowledge and Perception in Inpatient Setting on Hospitalized Patients with Gout

Roshanak Habibi¹, David T Liss², Sreelakshmi Panginikkod¹, Alvaro Altamirano Ufion³, Ehsan Rajabirostami¹ and Manish Jain⁴, ¹Internal Medicine, Presence Saint Francis Hospital, Evanston, IL, ²Northwestern University, Chicago, IL, ³Internal Medicine, Advocate Illinois Masonic Medical Center, Chicago, IL, ⁴Rheumatology, Presence Saint Francis Hospital, Evanston, IL

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

The increasing global burden of gout disease and its impact on the patient’s quality of life calls for new strategies in management. Even though gout is one of the most effectively treated of all rheumatic diseases, it is among the worst-managed diseases due in part to barriers in patient knowledge and perception about the disease. Our aim was to assess the disease-related knowledge and attitude among gout patients in inpatient setting and to identify the barriers to optimal management.

Methods:

A cross section survey of patients admitted to a community hospital for various reasons including acute gout flare from March 2016 through March 2017 was conducted using a 10-item gout related survey, previously used in the literature. Patients were identified for survey if they carried a diagnosis for gout based on American college of rheumatology classification criteria. Patient medication and demographic information was also collected. Patients were considered to have “good” knowledge if they answered 70% of the questions correctly. Gout survey performance was compared to demographic and medication data. In bivariate analysis, we examined differences in mean survey performance using 1-way analysis of variance (ANOVA). We obtained adjusted relative risks (RRs) of good knowledge by estimating a multivariable Poisson regression model with robust variance estimates, adjusted for covariates. Analyses were conducted using Stata, version 14.2.

Results:
Fifty-eight patients surveys were conducted. Most were aged 65 and older (60%) with equal number of males and females. Only 29% of respondents completed college or above and 24% were currently employed. Mean duration of gout in years was 11.8 years. Thirty-nine (81%) patients had at least one visit to the treating physician and thirty-five patients had at least 1 flare (60%) in last year. Most of the patients were taking allopurinol (69%). Good knowledge was demonstrated by 60% of the respondents. Knowledge strengths in terms of percentage of patients having correct answers included the majority of patients identifying that gout was related to elevated uric acid levels (86%); that pain with swelling in the joint as being a sign of acute flare (82%); and that hypertension was associated with gout (89%). Knowledge gaps included: uric acid goals (19%), treatment of acute flare (29%), prophylaxis of flare (37%), duration of ULT (42%), and life style modification (14%). In multivariable regression analysis, gout related knowledge was found to be higher among females (RR=1.5; P=0.03; 95% CI,1.04 to 2.28); patients with higher level of education (RR=3.4; P=0.04;95% CI,1.08 to 10.9) and in those patients using allopurinol (RR=1.9; P=0.05; 95% CI,0.97 to 4.00).

Conclusion:

We conclude that a large disease related knowledge gap is identified in our survey of gout patients in inpatient setting. Our data informed the areas of major knowledge gaps. We also identified certain demographic and medication factors influencing gout knowledge. To our knowledge this is the first patient education study in gout focusing on a hospitalized patient population, and we believe the inpatient setting may be a focus of opportunity for gout education.

Disclosure: R. Habibi, None; D. T. Liss, None; S. Panginikkod, None; A. Altamirano Ufion, None; E. Rajabiostami, None; M. Jain, None.

Patient Knowledge, Attitudes, and Beliefs Regarding Biologic Therapies in Ankylosing Spondylitis (AS): Insights from a Large-Scale Analysis of Social Media Platforms

Deeba Minhas1, Benjamin Noah2, Eldin Dzubur2, Christopher Almario3, Mariko Ishimori1, Corey Arnold4, Amber Howard2, Carine Khalil2, Alma Jusufagic2, Michelle Chen2, Jina Park5, Michael Weisman1 and Brennan Spiegel3, 1Cedars-Sinai Medical Center Division of Rheumatology, Los Angeles, CA, 2Cedars-Sinai Center for Outcomes Research and Education (CS-CORE), Los Angeles, CA, 3Cedars-Sinai Center for Outcomes Research and Education (CS-CORE), Cedars-Sinai Medical Center Division of Digestive and Liver Diseases, Los Angeles, CA, 4Medical Imaging Informatics, Department of Radiology, University of California Los Angeles, Los Angeles, CA, 5Novartis Pharmaceuticals Corporation, East Hanover, NJ

First publication: September 18, 2017
such as in clinical trials and clinic visits. In this study, we used social media data to examine AS patients’ knowledge, attitudes, and beliefs regarding biologic therapies.

**Methods:** We collected posts from 601 social media sites made between 1/1/06-4/26/17. Each post mentioned both an AS keyword and a biologic. To explore themes within the collection in an unsupervised manner, a latent Dirichlet allocation (LDA) topic model was fit to the dataset. Under LDA, each discovered topic is represented as a discrete distribution over the words in the collection, which may be thought of as a word cloud (i.e. words with more probability are larger in the cloud). The topics were manually reviewed to identify themes, which were then confirmed by reviewing relevant posts within each candidate topic.

**Results:** We examined 27,416 social media posts that focused on AS and biologics and found 112 themes. The majority of themes (60%, 67/112) focused on discussions surrounding AS treatment. Other themes including psychological impact of AS, reporting of medical literature, and AS disease consequences accounted for the remaining 40% (45/112) of topics (**Figure 1**). Within AS treatment discussions (**Figure 2**), most topics (61%) involved discussions about pharmacologic treatment (biologic and non-biologic options). The majority of biologic subthemes (78%) centered on side-effects related to its use (e.g. fatigue, allergic reactions), biologic attributes (e.g. dosing, frequency), and concerns with its use (e.g. increased cancer risk, reproductive concerns).

**Conclusion:** Social media reveals a dynamic range of themes governing AS patients’ experience and choice with biologics. The complexity of selecting among biologics and navigating their risk-benefit profiles suggests merit in creating online tailored decision-tools to support patients’ decision-making with AS biologic therapies.

---

**Figure 1. Primary Patient Discussion Themes Identified by Topic Modeling**

```
N=1
AS characteristics
N=1
Lab Test monitoring
N=2
AS comorbidities
N=2
AS etiology
N=2
AS history
N=3
AS diagnosis
N=4
Cost of biologics
N=5
AS disease consequences
N=6
AS disease consequences
N=7
Medical Literature
N=8
Interaction with rheumatologist
N=67
AS treatment
```

*Note: Size of individual boxes represents relative prevalence of theme.*

**Figure 2. Subthemes Within AS Treatment Identified by Topic Modeling**

```
N=11
Invasive intervention
N=7
Drug Dose Antiquity
N=8
Adjuvant Medicine
N=11
Pharmacologic Treatment
N=16
Complementary/Alternative Medicine
N=7
Medication Uncertainty
N=36
Biologic
N=9
Biologic Attributes
N=5
Biologic Concerns
N=14
Biologic Side Effects
N=1
Duration/Time
N=1
Personal Experience
N=1
Pre-Biologic Testing
N=2
Treatment Effect
```

*Note: Size of individual boxes represents relative prevalence of theme. Boxes in bold font emerged as predominant subthemes.*
Health Related Quality of Life in Lupus: Self-Management- a Modifiable Predictor

Kenneth Johnsen¹, Meenakshi Jolly² and Narender Annapureddy³, ¹Division of Rheumatology, Vanderbilt University Medical Center, Nashville, TN, ²Rush, Chicago, IL, ³Vanderbilt University Medical Center, Nashville, TN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Health Related Quality of Life in Lupus: Self-Management- a Modifiable Predictor.

Background/Purpose: Health related quality of life (HRQOL) is significantly effected in patients with Lupus. While mortality in Lupus patients has improved in the past few decades, these patients continue to have significant impairment in their health related quality of life. There are multiple complex factors which can influence health related quality of life in these patients.

Methods: A cross sectional study was done in 50 Patients in the Vanderbilt Lupus Center meeting the 1997 ACR classification criteria for SLE. LupusPRO, a disease-specific patient reported outcomes tool, was used to assess HRQOL and non HRQOL. Disease activity was assessed using the SLEDAI-2K. Data on following were collected: coping (BRIEF-COPE questionnaire), social support (ENRICHD Social Support Instrument (ESSI)), quality of patient-health care provider communication (Patient-Health Care Provider Communication Scale (PHCPCS)), self-management (Perceived Medical Condition Self-Management Scale (PMCSMS)), and patient-reported medication adherence (Medication Adherence Self-report Inventory (MASRI)). Correlational and multivariate linear regression analyses with HRQOL as the dependent variable were conducted. A p-value of <0.05 was considered significant on 2-sided t-test.

Results: Mean (SD) age was 40.3 (12.9) years; 94% of patients were women (Table 1). Mean (SD) HRQOL score was 68.0 (21.5). HRQOL correlated positively with PMCSMS (0.704, p <0.001), BRIEF-COPE (0.643, p<0.001), ESSI (0.299, p 0.041), PHCPCS (0.464, p 0.001), and SLEDAI (-0.320, p 0.027). On multivariate linear analysis regression, PMCSMS (beta= 2.079, 0.001) and BRIEF-COPE (1.969, p 0.036) were independent predictors of HRQOL (Table 2). Domains for coping, social support and satisfaction with care on the LupusPRO correlated with BRIEF-COPE, ESSI and PHCPCS respectively.

Conclusion: Self-management skills and coping mechanism, are both modifiable predictors of HRQOL in our lupus patients. Besides controlling for disease activity, strategies to intervene on self-management and coping need to be integrated into routine care of Lupus patients.
Table 1: Characteristics of the sample, n=50

<table>
<thead>
<tr>
<th></th>
<th>Mean ± SD</th>
<th>% (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years)</td>
<td>40.3 + 12.9</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>94 (47)</td>
<td></td>
</tr>
<tr>
<td>Duration of disease</td>
<td>13.5 + 8.1</td>
<td></td>
</tr>
<tr>
<td>Age at diagnosis (Years)</td>
<td>26.9 +11.7</td>
<td></td>
</tr>
<tr>
<td>SLEDAI 2K</td>
<td>2.0, 5.0 (median, IQR)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Correlation of HRQOL as assessed by LupusPRO

<table>
<thead>
<tr>
<th></th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>PMCMS</td>
<td>0.70 (&lt;0.001)</td>
<td>PMCSMS 2.08 (0.001)</td>
</tr>
<tr>
<td>BRIEF-COPE</td>
<td>0.64 (&lt;0.001)</td>
<td>BRIEF-COPE 1.97 (0.036)</td>
</tr>
<tr>
<td>ESSI</td>
<td>0.30 (0.041)</td>
<td></td>
</tr>
<tr>
<td>PHCPCS</td>
<td>0.46 (0.001)</td>
<td></td>
</tr>
<tr>
<td>SLEDAI</td>
<td>-0.32 (0.027)</td>
<td></td>
</tr>
</tbody>
</table>

In univariate analysis – correlation coefficient measured by spearman correlation (p-value)

In multivariate analysis – beta value (p-value) from multivariate linear regression analysis

Disclosure: K. Johnsen, None; M. Jolly, Pfizer Inc, 2,LupusPRO, 7; N. Annapureddy, None.


Abstract Number: 2268

Patient Perspectives from a Qualitative Study Predict Non-Adherence in Rheumatoid Arthritis

Valentin Ritschl1,2, Angelika Lackner3, Carina Boström4, Michael Kundi5, Michaela Lehner6, Paul Studenic7, Winfried Graninger8, Josef S. Smolen9 and Tanja Stamm10, 1Section for Outcomes Research, Center for Medical Statistics, Informatics, and Intelligent Systems, Medical University of Vienna, Vienna, Austria, Vienna, Austria, 2Section Occupational Therapy, Department Health Sciences, FH Campus Wien, Vienna, Austria, Vienna, Austria, 3Rheumatology and Immunology, Medical University Graz, Graz, Austria, Graz, Austria, 4Division of Physiotherapy, Department of Neurobiology, Karolinska Institutet, Huddinge, Sweden, Stockholm, Sweden, 5Center for Public Health, Department of Environmental Health, Medical University of Vienna, Vienna, Austria, Vienna, Austria, 6Division of Rheumatology, Department of Internal Medicine III, Medical University of Vienna, Vienna, Austria, 1090 Vienna, Austria, 7Medical University Vienna, Division of Rheumatology, Department of Internal Medicine III, Vienna, Austria,
SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: ARHP Patient Outcomes, Attitudes, and Preferences Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: In rheumatoid arthritis (RA), up to 80% of patients were found to be non-adherent to prescribed medication and non-pharmacological interventions. These patients do not reach optimal clinical outcomes. In the present study, we therefore explored predictors that may lead to non-adherence from the perspective of patients.

Methods: In a mixed-methods study, retrospective, observational data from patients with RA diagnosed according to the EULAR/ACR criteria with at least one DMARD therapy who failed to attend to the follow-up visits for at least 9 months (and were thus considered to be potentially non-adherent to recommended interventions) were selected from the databases of two rheumatology centers. Subsequently, we invited all these patients to take part in a qualitative semi-structured interview study with a meaning condensation data analysis. Based on the interviews, patients were assigned to the sub-groups ‘adherent’ (e.g. having regular rheumatology visits in another clinic) or ‘non-adherent’ (e.g. having stopped taking the prescribed medication and interventions). Possible predictors derived from the qualitative analysis and clinical variables obtained from the patient databases of the centers were tested in a logistic regression model.

Results: In total, data of 459 eligible patients (346 [75.4%] females; total mean age 63.0 [SD 14.8]) were identified. One hundred thirty one of these (109 [83.2%] females; total mean age 64.8 [SD 14.1]) agreed to participate in the qualitative interviews. In addition to already known themes, new issues important to patients emerged from the qualitative analysis (table 1): (i) the so-called “patient’s dogma” inhibited adherent behavior, in that patients felt that pain was an important part of life and attributed this to having had a high manual workload during life of which patients were proud; (ii) patients trusted physicians who were seeking support from other physicians less, because they appeared to be “young or unexperienced”; (iii) some patients did not feel properly understood if physicians only prescribed medication without offering advice on non-pharmacological aspects of treatment. Two clinical variables were also found to be predictors for non-adherent behavior: higher number of swollen joints (OR 0.9; CI 95% 0.8-1.0) are associated with a higher likelihood of non-adherence, whereas older patients (OR per decade 1.3; CI 95% 1.0-1.7) were more likely adherent.

Conclusion: The predictors for non-adherence may be used to improve patients’ counseling and to enhance patient adherence and improve clinical outcome in pharmacological and non-pharmacological interventions.

Table 1. Qualitative results.
Main Topics | Description/Examples
--- | ---
So-called “patient’s dogma” | “Patient’s dogma” which is defined as preconceived opinions of the patient trigger non-adherent behaviour. For example, some patients believed that rheumatologists’ decisions are influenced by the pharmaceutical industry and therefore they just prescribe medications instead of letting “natural” processes of inflammation occur (Participant No. 2, female, age 40).

Perceived “trustworthiness” of physicians/health professionals | Patients search for the best and most trustworthy physician/health professional. For Example, if two physicians disagree and have different opinions regarding recommendations (Participant No. 28, female, age 43), patients were likely not to adhere to the prescriptions.

Comprehensive medical advice including non-pharmacological methods | Patients were seeking comprehensive medical advice. If advice on non-pharmacological aspects of treatment e.g. strategies for daily routines, sports, limited evidence of diet and alternative medications, are not covered (Participant No. 182, female, age 34), patients were less likely to adhere.

**Disclosure:** V. Ritschl, None; A. Lackner, None; C. Boström, None; M. Kundi, None; M. Lehner, None; P. Studenic, None; W. Graninger, None; J. S. Smolen, AbbVie, Amgen, Astra-Zeneca, Astro, BMS, Celgene, Celltrion, Chugai, Gilead, Glaxo, ILTOO, Janssen, Eli Lilly and Company, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi-Aventis, UCB, 5,AbbVie, Janssen, Eli Lilly and Company, MSD, Pfizer, Roche, 2,AbbVie, Amgen, Astra-Zeneca, Astro, BMS, Celgene, Celltrion, Chugai, Gilead, Glaxo, ILTOO, Janssen, Eli Lilly and Company, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi-Aventis, UCB, 8; T. Stamm, AbbVie, 2,AbbVie, Janssen, MSD, Novartis, Roche, 9.


Abstract Number: 2269

**The Meaningful Patient Engagement in Research Framework – an Empirically Based Conceptual Framework**

Clayon Hamilton¹,², Alison Hoens¹,²,³, Catherine L. Backman⁴,⁵, Annette McKinnon⁶, Shanon McQuitty⁶, Kelly English⁶ and Linda Li⁴, ¹Physical Therapy, University of British Columbia, Vancouver, BC, Canada, ²Arthritis Research Canada, Richmond, BC, Canada, ³BC SUPPORT Unit, Vancouver, BC, Canada, ⁴Rheumatology, Arthritis Research Canada, Richmond, BC, Canada, ⁵Occupational Science & Occupational Therapy, The University of British Columbia, Vancouver, BC, Canada, ⁶Arthritis Patient Advisory Board, Arthritis Research Canada, Richmond, BC, Canada

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Tuesday, November 7, 2017

Session Title: ARHP Patient Outcomes, Attitudes, and Preferences Poster

Session Type: ACR Poster Session C

Session Time: 9:00AM-11:00AM
**Background/Purpose:** Patient engagement in research is promoted to improve the relevance and quality of health research, but has little conceptualization derived from empirical data. To address this issue, we sought to develop an empirically based conceptual framework for *meaningful* patient engagement in research founded on a patient perspective.

**Methods:**

We conducted a qualitative analysis of transcripts from one-on-one in-depth interviews with 18 patient research partners who are living with arthritis. The data analysis involved three phases: identifying the themes, developing a framework, and confirming the framework. Specifically, we coded and organized the data, and abstracted, illustrated, described, and explored the emergent themes using thematic analysis. Directed content analysis was conducted to derive concepts from 18 publications related to patient engagement in research to supplement, confirm or refute, and extend the emergent conceptual framework. The framework was critically reviewed by our entire research team, including four patient research partners with arthritis.

**Results:** The experiences the participants had when they worked with researchers were generally positive. Eight themes emerged: *Procedural Requirements, Convenience, Contributions, Support, Team Interactions, Research Environment, Feel Valued,* and *Benefits.* These themes were interconnected and formed a conceptual framework to explain the phenomenon of meaningful patient engagement in research from a patient perspective. For example, the contributions of patient research partners could be facilitated when researchers maintain certain procedural requirements, offer opportunities to engage in ways that patient research partners find convenient, and provide appropriate support, such that patient research partners feel valued and identify benefits from engaging with a research team.

**Conclusion:** The Meaningful Patient Engagement in Research (PEIR) Framework provides guidance regarding key aspects of meaningful patient engagement in research that could be operationalized by research teams. It could be particularly useful when patient-researcher partnerships are led by researchers with little experience of engaging patients in research.

**Disclosure:** C. Hamilton, None; A. Hoens, None; C. L. Backman, None; A. McKinnon, None; S. McQuitty, None; K. English, None; L. Li, None.

**Abstract Number:** 2270

**Identification of Optimal Subcutaneous Doses of Tocilizumab in Children with Polyarticular-Course Juvenile Idiopathic Arthritis**

**Hermine I. Brunner**1, Nicola Ruperto2, Alberto Martini2, Athimalaipet V. Ramanan3, Rubén Cuttica4, Jennifer E. Weiss5, Michael Henrickson1, Heinrike Schmeling6, Jordi Anton7, Kirsten Minden8, Joy Hsu9, Kamal Bharucha10, Sunethra Wimalasundera11, Alysha K. Kadva10, Ruchi Upmanyu11, Navita L. Mallalie19, Wendy Douglass11, Daniel J Lovell1 and Fabrizio De Benedetti12, 1Pediatric Rheumatology Collaborative Study Group (PRCSG), Cincinnati, OH, 2PRINTO Coordinating Centre, Genoa, Italy, 3Bristol Royal Hospital for Children, Bristol, United Kingdom, 4Hospital Gral de Niños Pedro Elizalde, Buenos Aires, Argentina, 5Hackensack University Medical Center, Hackensack, NJ, 6Alberta Children’s Hospital/University of Calgary, Calgary, AB, Canada, 7Hospital Sant Joan de Deu, Barcelona, Spain, 8Charité – University of Medicine Berlin, Berlin, Germany, 9Roche Innovation Center, New York, NY, 10Genentech, South San Francisco, CA, 11Roche Products, Ltd., Welwyn Garden City, United Kingdom, 12Istituto Giannina Gaslini - Pediatria II, Reumatologia - PRINTO, Genoa, Italy

**First publication:** September 18, 2017
Background/Purpose: The efficacy and safety of intravenous (IV) tocilizumab (TCZ), an interleukin-6 receptor-alpha inhibitor, have been demonstrated in patients with polyarticular-course juvenile idiopathic arthritis (pcJIA) (Brunner H I et al. *Ann Rheum Dis*. 2014;74:1110-7). This study investigated appropriate dosing regimens of subcutaneous (SC) TCZ in a similar population.

Methods: We enrolled patients aged 1-17 years with pcJIA who had inadequate response/intolerance to methotrexate and were TCZ naive or received TCZ IV with adequate disease control. TCZ SC was administered open label according to a body weight (BW)–based dosing regimen based on pharmacokinetic (PK) simulations aimed at obtaining TCZ trough exposures at or above those achieved by approved IV dosing in pcJIA patients. pcJIA patients weighing <30 kg received TCZ 162 mg every 3 weeks (Q3W) while those weighing ≥30 kg received TCZ 162 mg Q2W for 52 weeks. Adequacy of TCZ dosing was assessed by comparing model-estimated PK parameters (C\text{trough}, C\text{max}, area under the concentration-time curve) with the IV exposure data; safety and efficacy (exploratory; JADAS71) were also measured.

Results: Among the 52 patients (69% female) enrolled, 27 patients had <30 kg BW and 25 patients ≥30 kg BW. Median baseline age was 6.0 years for the <30 kg BW group and 15.0 years for the ≥30 kg BW group. In the <30 kg BW group 85% were TCZ naive, and in the ≥30 kg BW group 56% were TCZ naive. Given similarities in steady state PK of the naive vs non-naive patients, pooled data analyses are presented. Median C\text{trough} was similar between BW groups and higher than with TCZ IV in both BW categories, confirming adequate exposure from SC doses. C\text{max} and AUC\text{12weeks} were higher in the <30 kg BW than the ≥30 kg BW TCZ SC group. Consistent with SC vs IV administration, median C\text{max} from SC dosing was lower than with IV dosing in both BW groups. Changes in PD parameters for TCZ-naive patients were consistent with those previously observed for TCZ IV, suggesting adequate reduction of inflammation. JIA activity (JADAS-71) improved in both BW groups (Table), with trends consistent with those observed for TCZ IV. Infections were the most frequent adverse event (AE). Four serious AEs occurred in 3 patients (croup and varicella [same patient], anorexia, and arthralgia). Injection site reactions were more common in the ≥30 kg BW group (Table). No serious hypersensitivity, AE leading to withdrawal, opportunistic infection, serious hepatic AE, or death occurred. The overall rate of AEs was 7.9/100 patient-years, consistent with that for TCZ IV in pcJIA.

Conclusion: The BW-based TCZ SC dosing regimens for pcJIA provided adequate exposure to support efficacy comparable to that of TCZ IV, with an acceptable benefit-risk profile.

### Table. Results

<table>
<thead>
<tr>
<th></th>
<th>TCZ 162 mg SC Q3W BW &lt;30 kg (n = 27)</th>
<th>TCZ 162 mg SC Q2W BW ≥30 kg (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Model-computed steady state PK parameters, median [range]</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C\text{trough}, ng/mL</td>
<td>13.4 [0.2, 55.3]</td>
<td>12.7 [0.2, 23.8]</td>
</tr>
<tr>
<td>C\text{max}, ng/mL</td>
<td>62.4 [39.4, 121.1]</td>
<td>29.7 [7.6, 50.3]</td>
</tr>
</tbody>
</table>
| AUC\text{trough, mgL/}
| day                  | 2998 [1465, 7708]                     | 1933 [524, 3098]                     |

<table>
<thead>
<tr>
<th><strong>Change from baseline to week 52</strong> in observed levels of PD markers, median [range]; TCZ-naive patients</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-6, pg/mL</td>
<td>27.3 [3.5, 173.9]; n=11</td>
</tr>
<tr>
<td>sIL-6, ng/mL</td>
<td>612.1 [309.4, 808.4]; n=14</td>
</tr>
<tr>
<td>CRP, mg/L</td>
<td>-1.3 [-17.0, 0.5]; n=21</td>
</tr>
<tr>
<td>ESR, mm/h</td>
<td>-11.0 [-40.0, 0.0]; n=21</td>
</tr>
</tbody>
</table>

| **Efficacy at week 52, TCZ-naive patients** |                      |
| Change from baseline in JADAS-71                  | -16.8 [-40.3, -4.4]; n=21 | -12.9 [-48.1, -2.3]; n=12 |

<table>
<thead>
<tr>
<th>Safety over 52 weeks, all patients</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection AEs, n (%)</td>
<td>20 (74)</td>
</tr>
<tr>
<td>SAEs, n (%)</td>
<td>1 (4)</td>
</tr>
</tbody>
</table>

*Week 51 for Q3W group. AE, adverse event; AUC, area under the concentration curve; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; IL-6, interleukin-6; ISR, injection site reaction; JADAS-71, Juvenile Arthritis Disease Activity Score-71; SAE, serious adverse event; sIL-6, soluble IL-6 receptor.

Disclosure: H. I. Brunner, None; N. Ruperto, BMS, GlaxoSmithKline, Hoffmann-La Roche, Novartis, Pfizer, Sanofi Aventis, Schwarz Biosciences, Abbott, Francesco Angelini S.P.A., Sobi, Merck Serono, 5; A. Martini, AbbVie,
Safety of Adalimumab±Methotrexate for the Treatment of Polyarticular Juvenile Idiopathic Arthritis (pJIA)

Hermine I. Brunner1, Nicola Ruperto2, Kabita Nanda3, Mary Toth4, Ivan Foeldvari5, John F. Bohnsack6, Diana Milojevic7, C. Egla Rabinovich8, Daniel J Kingsbury9, Katherine Marzan10, Pierre Quartier11, Kirsten Minden12, Elizabeth Chalom1, Gerd Horneff13, Rolf M. Kuester14, Jason A Dare15, Mareike Bereswill16, Jasmina Kalabic16, Hartmut Kupper16, Daniel J Lovell1 and Alberto Martini2,

1 PRCSG, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH, 2 PRINTO-IRCCS Gaslini, Genova, Italy, 3 University of Washington School of Medicine and Seattle Children’s Hospital, Bayside, NY, 4 Akron Children's Hospital, Akron, OH, 5 Department of Pediatric Rheumatology, Hamburger Zentrum für Kinder und Jugendrheumatologie, Hamburg, Germany, 6 University of Utah, Department of Pediatrics, Salt Lake City, UT, 7 The Floating Hospital for Children at Tufts Medical Center, Boston, MA, 8 Duke University Medical Center, Durham, NJ, 9 Randall Children’s Hospital at Legacy Emanuel, Portland, OR, 10 Children's Hospital Los Angeles, Los Angeles, CA, 11 Hopital Necker-Enfants Malades, Paris, France, 12 Kinderklinik der Charite, Otto-Heubner Centrum, Berlin, Germany, 13 Asklepios Clinic Sankt Augustin, Sankt Augustin, Germany, 14 Orthopädiezentrum Altona, Hamburg, Germany, 15 Arkansas Children’s Hospital, Little Rock, AR, 16 AbbVie Deutschland GmbH & Co. KG, Ludwigshafen, Germany

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: JIA is the most common chronic inflammatory rheumatic disease of childhood. Due to their known safety and efficacy, TNF inhibitors are used for long-term control of pJIA disease. The purpose of this analysis was to evaluate the 7 year (y) safety of Adalimumab treatment with or without methotrexate (ADA±MTX) when used in current clinical practice for treatment of patients (pts) with active pJIA.

Methods: This is a 7 y interim analysis of an ongoing, multicenter, non-interventional, observational registry of pts with pJIA with up to 10 y safety follow-up. Included pts were treated with either ADA±MTX or MTX alone as comparison arm according to routine clinical care in US, EU, and Australia. MedDRA observational adverse events (AEs) were recorded from 1st day in the registry through last contact, irrespective of the duration of registry treatment.
**Results:** In January 2014, enrollment was complete. As of June 1, 2016 cut-off date, 838 pts (301- MTX arm and 537 - ADA±MTX arm) were treated in the registry. There were 39 pts who rolled over from MTX to the ADA±MTX arm. At registry entry mean pJIA disease duration was 1.3 y and 3.7 y and mean AJC71 was 5.8 and 5.2 for MTX and ADA±MTX arms, respectively. CHAQ disability index was 0.6 for both arms. The mean duration of study drug exposure in registry was 2.0 y (range: 0.0 – 7.1) and 2.5 y (range: 0.0 – 7.9) for MTX and ADA±MTX arms, respectively. The mean duration of observation in registry was 3.9 y (range: 0.0 – 7.2) and 3.5 y (range: 0.0 – 7.9) for MTX and ADA±MTX arms, respectively. Overall, 213 pts (70.8%) in MTX and 225 pts (41.9%) in ADA±MTX arms discontinued registry drug through 7 y. The main reasons for registry drug discontinuation for MTX arm: pts required additional therapy (32.6%), other (13.3%), lack of efficacy (11.6%), AEs (9.3%), or pts achieved JIA remission (8.6%), and for ADA±MTX arm: lack of efficacy (17.9%), other (7.3%), lost to follow-up (5.6%), AEs (5.4%), or pts achieved JIA remission (5.0%). Frequencies and rates of treatment-emergent AEs (from 1st dose date of registry drug in registry up to last dose + 70 days in registry, excluding AEs occurring during treatment interruption) were similar to those reported for observational AEs (from 1st day in registry up to last contact irrespective of drug treatment duration) (Table). The rate of serious infections was similar between MTX and ADA±MTX arms. One pt (0.2%) reported an event of opportunistic infection (fungal oesophagitis) in ADA±MTX arm. No reports of deaths, malignancies, active tuberculosis, oral candidiasis, demyelination, or congestive heart failure.

**Conclusion:** Overall, ADA±MTX was well-tolerated in these pts with pJIA with no new safety signals. The retention rate for registry drug was higher in ADA±MTX arm compared to MTX arm.

**Table. Overview of the Observational Adverse events**

<table>
<thead>
<tr>
<th></th>
<th>MTX</th>
<th>ADA±MTX</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ADA only</td>
<td>ADA + MTX #</td>
</tr>
<tr>
<td></td>
<td>N=301 n (%)</td>
<td>N=160 n (%)</td>
</tr>
<tr>
<td></td>
<td>PYs=1170.3 E (E/100 PYs)</td>
<td>PYs=517.0 E (E/100 PYs)</td>
</tr>
<tr>
<td>Any AE</td>
<td>157 (52.2)</td>
<td>66 (41.3)</td>
</tr>
<tr>
<td>AE at least “possibly drug related” per the investigator</td>
<td>87 (28.9)</td>
<td>30 (18.8)</td>
</tr>
<tr>
<td>Severe AE</td>
<td>17 (5.6)</td>
<td>14 (8.8)</td>
</tr>
<tr>
<td>Severe AE</td>
<td>32 (10.6)</td>
<td>21 (13.1)</td>
</tr>
<tr>
<td>AE leading to discontinuation of study drug or study</td>
<td>28 (9.3)</td>
<td>13 (8.1)</td>
</tr>
<tr>
<td>Infectious AE</td>
<td>87 (28.9)</td>
<td>38 (23.8)</td>
</tr>
<tr>
<td>Serious infectious AE</td>
<td>14 (4.7)</td>
<td>6 (3.8)</td>
</tr>
<tr>
<td>Injection site-related AE</td>
<td>6 (2.0)*</td>
<td>5 (3.1)</td>
</tr>
</tbody>
</table>

E, events; PYs, patient years (Observation time irrespectively of study drug treatment duration). *3 patients experienced injection site-related AEs with etanercept injections. During the registry, 52 (17.3%) pts in MTX arm and 45 (8.4%) pts in ADA arm started with a biologic DMARD. #MTX was used at any point of time during the course of the registry.

**Disclosure:** H. I. Brunner, AbbVie Inc., AstraZeneca, Centocor, Bristol-Myers Squibb, Boehringer-Ingelheim, Pfizer, Regeneron, Hoffman La-Roche, Novartis, Takeda, UCB, and Genentech, 5, AbbVie Inc., AstraZeneca, Centocor, Bristol-Myers Squibb, Boehringer-Ingelheim, Pfizer, Regeneron, Hoffman La-Roche, Novartis, Takeda, UCB, and Genentech, 9, Genentech Pharmaceuticals, 8; N. Ruperto, GASLINI Hospital, 3, Astellas, AstraZeneca, Bristol-Myers
Squibb, Italfarmaco, Janssen Biologies B.V., MedImmune, Roche, and Wyeth/Pfizer, 8; K. Nanda, Medac Pharma, Inc, 5; M. Toth, None; I. Foeldvari, Abbvie and Novartis, 9; J. F. Bohnsack, Novartis Pharmaceutical Corporation, 5; D. Milojevic, Genentech and Novartis, 5; C. E. Rabinovich, UCB Pharma, Janssen Research & Development, LLC, Hoffmann-La Roche Inc., and AbbVie, 9; D. J. Kingsbury, AbbVie, 9; K. Marzan, AbbVie, 2; P. Quartier, AbbVie, Novartis, Pfizer, BMS, Chugai-Roche, MedImmune, Servier, and Swedish Orphan Biovitrum, 2,AbbVie, Novartis, Pfizer, BMS, Chugai-Roche, MedImmune, Servier, and Swedish Orphan Biovitrum, 5,Sanofi trial., 9; K. Minden, from Pfizer, AbbVie and Roche/Chugai, 2,Pfizer, Genzyme, and Pharma-Allergan, 5,Pfizer, AbbVie, Genzyme, and Pharma-Allergan, 9; E. Chalom, Abbvie SPeaker's Bureau, 8; G. Horneff, AbbVie, Pfizer, Novartis, and Roche, 2,AbbVie, Novartis, Sobi, Pfizer, and Roche, 9; R. M. Kuester, AbbVie Inc. and Wyeth/Pfizer, 9; J. A. Dare, AbbVie, AstraZeneca, Bristol-Myers Squibb, Horizon Pharma, Medac, Pfizer, Roche, and UCB, 9; M. Bereswill, Abbvie, 3,Abbvie, 1; J. Kalabic, AbbVie Inc, 1,AbbVie Inc, 3; H. Kupper, AbbVie, 1,AbbVie, 3; D. J. Lovell, AbbVie Inc., AstraZeneca, Centocor, Bristol-Myers Squibb, Pfizer, Genzyme, and Hoffman La-Roche, Novartis, UBC, Xoma, and Genentech, 5,Wyeth Pharmaceuticals, 8,Amgen and Forest Research, 9; A. Martini, GASLINI Hospital, 3,Astellas, AstraZeneca, Bristol-Myers Squibb, Italfarmaco, and MedImmune, 8,AbbVie Inc., AstraZeneca, Bristol-Myers Squibb, Janssen Biologies B.V., Eli Lilly and Co., “Francesco Angelini”, GlaxoSmithKline, Italfarmaco, Novartis, Pfizer, Roche, Sanofi Aventis, Schwarz Biosciences GmbH, Xoma, and Wyeth Pharmaceuticals, 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/safety-of-adalimumab%2cmethotrexate-for-the-treatment-of-polyarticular-juvenile-idiopathic-arthritis-pjia

Abstract Number: 2272

Long-Term Effectiveness and Safety of Abatacept in Juvenile Idiopathic Arthritis: Ongoing Results from the Abatacept in JIA Registry

Daniel J Lovell1, N Ruperto2, N Tzaribachev3, A Zeft4, Rolando Cimaz5, V Stanevica6, Gerd Horneff7, John F. Bohnsack8, Thomas A. Griffin9, R Carrasco10, Maria Trachana11, Jason A Dare12, I Foeldvari13, Richard K Veh14, TA Simon15, Hermine I. Brunner16 and Alberto Martini2, 1Cincinnati Children’s Hosp. Medical Center, Cincinnati, OH, 2Istituto G. Gaslini Pediatria II Reumatologia, Genova, Italy, 3University Medical Center Schleswig-Holstein, Bad Bramstedt, Germany, 4Cleveland Clinic, Cleveland, OH, 5Azienda Ospedaliero-Universitaria Meyer, Florence, Italy, 6Riga Stradins University, Riga, Latvia, 7Asklepios Klinik Zentrum für Allgemeine Paediatrie und Neonatologie, Sankt Augustin, Germany, 8University of Utah School of Medicine, Salt Lake City, UT, 9Levine Children’s Hospital at Carolinas Medical Center, Charlotte, NC, 10Specially For Children, Austin, TX, 11Hippokration General Hospital, Thessaloniki, Greece, 12University of Arkansas for Medical Sciences, Little Rock, AR, 13Hamburg Centre for Pediatric Rheumatology, Hamburg, Germany, 14University of Minnesota, Minneapolis, MN, 15Bristol-Myers Squibb, Princeton, NJ, 16Cincinnati Children's Hospital Medical Center, Cincinnati, OH

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017

Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis

Session Type: ACR Poster Session C

Session Time: 9:00AM-11:00AM

Background/Purpose: Abatacept is an FDA- and EMA-approved biologic that is widely used in children with juvenile idiopathic arthritis (JIA). The purpose of this long-term ongoing registry is to describe the longitudinal effectiveness and safety of SC and IV abatacept in JIA patients (pts). Methods: Using a standardized protocol, clinical sites in the Pediatric Rheumatology Collaborative Study Group (PRCSG) and Paediatric Rheumatology International Trial Organization (PRINTO) enrolled pts with JIA currently on or starting abatacept in this longitudinal registry. Planned duration of follow-up is 10 years (yrs) and data shown are those collected through March 31, 2017 (up to 4 yrs’ follow-
**Results:** Overall, 354 pts with JIA were enrolled since January 2013, resulting in a total abatacept exposure of 364.5 pt-yrs (mean/median duration of abatacept treatment was 12.4/6.5 months), and 76 (22%) pts were new starters on abatacept (≤1 month of treatment), 76 (22%) had received abatacept for >1–≤6 months, 73 (20%) for >6–≤12 months and 129 (36%) for >12 months. SC abatacept was used in 80 (23%) pts and IV in 274 (77%); 4% of the pts were aged 2–5 yrs at enrollment.

**Baseline:** Of the 354 pts, 281 (79%) were female, mean/median age at enrollment was 13.0/13.6 yrs, and 15 (4%) were aged 2–5 yrs. JIA subtypes were: systemic (2%), oligoarticular (21%), polyarticular RF– (58%), polyarticular RF+ (9%), psoriatic (3%), enthesitis-related (3%) and undifferentiated (4%). At baseline, JIA duration was 5.4/4.4 yrs, mean/median active joint count was 2.9/0, a history of uveitis was recorded in 47 (13%) pts and 14 (4%) had active uveitis. Concomitant JIA medications were used by 81% of pts (58% MTX, 48% NSAIDs, 3% leflunomide, 4% hydroxychloroquine, 1% cyclosporine, 1% sulfasalazine).

**Follow-up outcomes & safety.** Clinical, functional and HRQoL scores are based on observed results for up to 4 yrs’ time in the registry (Table). In total, 23 serious AEs were reported (all single occurrences) in 23 pts (6% of study population), resulting in an overall serious AE rate per 100 pt-yrs on treatment of 6.3 (95% CI 4.1, 9.3). There were three events of special interest (ESI): acute uveitis, MRSA wound infection, infusion reaction; the ESI rate was 0.82/100 pt-yrs on treatment (95% CI 0.2, 2.2). No new autoimmune diseases, malignances or tuberculosis cases were reported. There was one death due to pre-existent cardiopulmonary disease considered unrelated to abatacept.

**Conclusion:** Abatacept was well tolerated and no new safety signals were observed. In this JIA cohort, abatacept demonstrated persistent effectiveness with low MD Global disease activity, low number of active joints and >30% of pts had clinical inactive disease.

**Table 1. Patient disposition at last registry visit**

<table>
<thead>
<tr>
<th>Endpoints</th>
<th>Baseline (n=354)</th>
<th>3 months (n=286)</th>
<th>6 months (n=252)</th>
<th>12 months (n=231)</th>
<th>24 months (n=81)</th>
<th>36 months (n=27)</th>
<th>42 months (n=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MD Global</td>
<td>1.9/1.0</td>
<td>1.5/1.0</td>
<td>1.5/0.5</td>
<td>1.2/0.5</td>
<td>0.75/0.5</td>
<td>1.5/0.5</td>
<td>1.1/0.5</td>
</tr>
<tr>
<td>CID, 1%</td>
<td>33</td>
<td>32</td>
<td>38</td>
<td>48</td>
<td>52</td>
<td>37</td>
<td>29</td>
</tr>
<tr>
<td>JAMAR Functional 2</td>
<td>6.3</td>
<td>5.2</td>
<td>5.3</td>
<td>4.5</td>
<td>2.9</td>
<td>3.7</td>
<td>4.2</td>
</tr>
<tr>
<td>JAMAR HRQoL</td>
<td>7.6</td>
<td>6.4</td>
<td>6.2</td>
<td>5.6</td>
<td>5.3</td>
<td>5.3</td>
<td>6.5</td>
</tr>
</tbody>
</table>

Data are mean/median unless otherwise indicated.

CID=clinical inactive disease (Wallace criteria); JAMAR Functional=Juvenile Arthritis Multidimensional Assessment Report Functionality Scale Child (range 0–15, 0 = no functional limitation); JAMAR HRQoL=Juvenile Arthritis Multidimensional Assessment Report Health-Related Quality of Life Scale Child (range 0–15, 0 = best possible HRQoL); MD Global=MD Global Assessment of JIA Activity (VAS 0–10; 0=inactive); VAS=visual analog scale


An Open-Label Extension Study to Assess the Long-Term Safety of Etanercept in Pediatric Patients with Extended Oligo, Enthesitis Related, and Psoriatic Juvenile Idiopathic Arthritis: 6-Year Data from the Clipper Studies

Ivan Foeldvari1, Tamas Constantin1, Jelena Vojinovic2, Gerd Horneff1, Jordana Susic1, Katarzyna Kobusinska1, Violeta Vladislava Panaviene1, Zbigniew Zuber1, Valda Stanevicha1, Vyacheslav Chasnyk1, Ronald Pedersen2, Jack F Bukowski4, Tina Hinnershitz5, Bonnie Vlahos6, Alberto Martini1 and Nicolino Ruperto1, 1Paediatric Rheumatology International Trials Organisation (PRINTO), Genoa, Italy, 2Paediatric Rheumatology International Trials Organisation (PRINTO), Genoa, Jersey, 3Department of Biostatistics, Pfizer, Collegeville, PA, 4Clinical Affairs, Pfizer, Collegeville, PA, 5Specialty Care MDG, Pfizer, Collegeville, PA, 6Clinical Sciences, Pfizer, Collegeville, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: A Phase 3b, open-label (OL), multicenter study (CLIPPER) has shown the safety of etanercept (ETN) in pediatric patients (pts) with extended oligoarticular (eo) juvenile idiopathic arthritis (JIA), enthesitis-related arthritis (ERA), and psoriatic arthritis (PsA). CLIPPER2 is an ongoing OL extension study assessing long-term safety and clinical benefits of ETN in this population. The objective of the current study was to describe the safety of 6 years (y) of ETN treatment in the CLIPPER (2-y) and CLIPPER2 (4-y) studies.

Methods: 127 pts with eoJIA (2-17 y), ERA, or PsA (each 12-17 y) who received ≥1 ETN dose (0.8 mg/kg QW [max, 50 mg]) in CLIPPER were eligible to enter CLIPPER2. Long-term safety of ETN treatment was assessed as the total incidence of events from CLIPPER baseline (BL) to month (m) 72, frequency of events per 100 patient-years (EP100PY), and frequency of events in each study year.

Results: 109/127 (86%) pts entered CLIPPER2. At m72, 39/127 (31%) were actively taking ETN, 6 (5%) had withdrawn from treatment due to low/inactive disease, 7 (6%) had re-started ETN following an earlier withdrawal from treatment, 36 (28%) had stopped ETN (but remained in the study under observation), and 37 (29%) had permanently discontinued from the CLIPPER studies. The safety of ETN treatment from BL to m72, including incidence of treatment-emergent adverse events (TEAEs) and infections, and patient withdrawals owing to these, is shown in Table 1. From BL to m72, the most frequently reported TEAEs were (N [EP100PY]), headache (28 [5.34]), arthralgia (24 [4.58]), pyrexia (20 [3.81]), diarrhea, and leukopenia (both 12 [2.29]). All 32 serious TEAEs occurred at a rate of ≤3 events each. In this study, only 1 case of malignancy (Hodgkin’s lymphoma) was reported (1 patient with eoJIA in y3 of the study). There were no cases of active tuberculosis or demyelinating disorders, and no deaths. The number and frequency (N [EP100PY]) of TEAEs (excluding infections/ISRs) decreased over the 6-y study period from 193
The number and frequency of TE infections and serious TE infections also decreased over the 6-y study period. The incidence of serious TEAEs, however, varied from a high of 10 [9.61] in y2 to a low of 0 in y4 with no clear trend of decrease with time.

**Conclusion:** OL ETN treatment to m72 was well tolerated. Frequency of TEAEs and TE infections decreased over time. **Trial Registration:** NCT00962741/NCT01421069

**Table 1. ETN safety summary (from CLIPPER BL to m72)**

<table>
<thead>
<tr>
<th></th>
<th>eoJIA EXP=245.607 PY</th>
<th>ERA EXP=158.888 PY</th>
<th>PsA EXP=119.945 PY</th>
<th>Total EXP=524.441 PY</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TEAEs</strong>*</td>
<td>244 (99.35)</td>
<td>151 (95.04)</td>
<td>90 (75.03)</td>
<td>485 (92.48)</td>
</tr>
<tr>
<td><strong>Serious TEAEs</strong>*</td>
<td>11 (4.48)</td>
<td>17 (10.70)</td>
<td>4 (3.33)</td>
<td>32 (6.10)</td>
</tr>
<tr>
<td><strong>TE infections</strong></td>
<td>351 (142.91)</td>
<td>93 (58.53)</td>
<td>117 (97.54)</td>
<td>561 (106.97)</td>
</tr>
<tr>
<td><strong>Serious TE infections</strong></td>
<td>5 (2.04)</td>
<td>4 (2.52)</td>
<td>4 (3.33)</td>
<td>13 (2.48)</td>
</tr>
<tr>
<td><strong>Opportunistic infections†</strong></td>
<td>0</td>
<td>1 (0.63)</td>
<td>1 (0.83)</td>
<td>2 (0.38)</td>
</tr>
<tr>
<td><strong>TEAEs</strong>* causing withdrawal, n (%)**</td>
<td>5 (2.04)</td>
<td>8 (5.03)</td>
<td>0</td>
<td>13 (2.48)</td>
</tr>
<tr>
<td><strong>TE infections causing withdrawal, n (%)</strong></td>
<td>2 (0.81)</td>
<td>0</td>
<td>1 (0.83)</td>
<td>3 (0.57)</td>
</tr>
</tbody>
</table>

Data from patients taking ETN (FAS)

*Excluding infections/ISRs

†All herpes zoster

EXP, exposure to ETN; FAS, full analysis set; ISRs, injection-site reactions; PY, patient-years; TE, treatment-emergent

**Disclosure:** I. Foeldvari, None; T. Constantin, None; J. Vojinovic, AbbVie, 8; G. Horneff, Pfizer Inc, 2; J. Dehoorne, AbbVie, 5,AbbVie, 8; G. Susic, Pfizer Inc, 2; K. Kobusinska, None; V. V. Panaviene, None; Z. Zuber,
Risk of Serious Events, Serious Infections, Uveitis, Crohn’s Disease, Colitis and Malignancies in Patients with Juvenile Idiopathic Arthritis on Continuous Treatment with Etanercept over Time: A Report from a Biologics Registry

Gerd Horneff1, Frank Weller-Heinemann2, Toni Hospach3, Prasad Oommen4, Gerd Ganser5, Johannes Peter Haas6, KMinden7 and Ariane Klein8, 1Asklepios Clinic, Sankt Augustin, Germany, 2PRINTO, Genoa, Italy, 3Pediatrics, Olgahospital, Klinikum Stuttgart, Stuttgart, Germany, 4University Duesseldorf, Duesseldorf, Germany, 5Pediatric Rheumatology, Sankt Josef Stift Sendenhorst, Sendenhorst, Germany, 6Centre for Pediatric Rheumatology Garmisch-Partenkirchen, Garmisch-Partenkirchen, Germany, 7Charité – University of Medicine Berlin, Berlin, Germany, 8Center of Pediatrics and Neonatology, Asklepios Clinic Sankt Augustin, Sankt Augustin, Germany

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: To investigate changes in the risk for adverse events of special interest in juvenile idiopathic arthritis (JIA) patients treated with Etanercept documented in the German BIKER registry.

Methods: This prospective cohort study included German JIA patients who began treatment with Etanercept 2000 to 2016 (n = 2,776, 11,772 patient years [PY]). Documentation began at the time of initiation visit and was continued irrespective of the withdrawal of medication. Adverse events (AE) were requested at every visit. AE of special internet included serious infections, uveitis events, diagnosis of chronic inflammatory bowel disease (CED) and malignancies. AE were attributed to Etanercept therapy if they occurred upon treatment or before 90 days of discontinuation. Malignancies were counted as ever exposed.

Results: In total there were 151 serious adverse events (0.054/pt.), 50 serious infections (0.018/pt.), 63 uveitis events (0.023/pat), 16 cases with CED (0.006/pat.) and 8 malignancies (0.003/pat.). The crude incidence rate ratios were 1.3/100 pt-years for all serious events, 0.4/100 pt-years for serious infections, 0.5/100 pt-years for uveitis events, 0.14/100 pt-years for CED and 0.06/100 pt-years for malignancies. The incidence of total serious events in the first year of 2.5/100 pt-years markedly decreased upon continuous treatment as well as the incidence of serious infections (first year 0.81/100PY), uveitis events (first year 1.09/100 PY) while no trend was observed with the rate of CED events (first year 0.20/100 patient years) or the rate for malignancies (0.08/100 patient years). Upon observation for more than 10 years, the yearly incidence markedly decreased for serious infections and uveitis events upon continuous treatment and remained stable for CED and malignancies (figure).
Conclusion: These results indicate significant decrease of the risk for several adverse events of special interest with continuous etanercept treatment over time; this may be explained by an evidence-based risk management for JIA patients given etanercept including the renouncement of steroids in the case of serious infections. Susceptible patients may be recognized early during the course of treatment. No increase of any of the risks was observed upon continuous treatment for up to 16 years.

Disclosure: G. Horneff, Pfizer Inc, 2; F. Weller-Heinemann, None; T. Hospach, None; P. Oommen, None; G. Ganser, Pfizer Inc, 2; J. P. Haas, None; K. Minden, Pfizer, Abbvie, Roche, 2, Abbvie, Pfizer, Pharm-Allergan, Roche, 5; A. Klein, None.


Abstract Number: 2275

Factors Related to Sustained Discontinuation of Medications for Well-Controlled JIA in the Childhood Arthritis & Rheumatology Research Alliance Registry

Daniel B. Horton1, Fenglong Xie2, Melissa L. Mannion3, Sarah Ringold4, Colleen K. Correll5, Anne C. Dennos6 and Timothy Beukelman7, 1Rutgers Biomedical and Health Sciences, New Brunswick, NJ, 2Division of Clinical Immunology & Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 3Pediatric rheumatology, University of Alabama at Birmingham, Birmingham, AL, 4Seattle Children's Hospital, Seattle, WA, 5Pediatrics, University of Minnesota, Minneapolis, MN, 6Duke Clinical Research Institute, Durham, NC, 7Pediatrics, University of Alabama at Birmingham, Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
**Session Title:** Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Stopping medications is a priority for many patients with well-controlled JIA, but few factors predict favorable outcomes after discontinuation. We examined factors associated with sustained discontinuation off disease-modifying drugs in a large pediatric registry.

**Methods:** We conducted a case-control study using the Childhood Arthritis & Rheumatology Research Alliance Registry of clinical data from >55 pediatric rheumatology clinics in the United States and Canada. The study included children with JIA who started at least 1 conventional or biologic DMARD and had at least 2 years of available subsequent data. Reasons for drug discontinuation were obtained from the medication log. Sustained discontinuers had at least 1 year of drug-free follow-up after discontinuation for well-controlled disease. Comparators included children who did not discontinue all DMARDs for well-controlled disease (never discontinuers) and those who stopped DMARDs for at least 30 days and restarted within 1 year (unsustained discontinuers). Children in each group may have stopped DMARDs for reasons besides well-controlled JIA. We compared characteristics of sustained discontinuers and comparators using descriptive statistics, excluding children with <1 year of follow-up off medicines without restarting DMARDs.

**Results:** There were 1194 children with JIA who started DMARDs, of whom 479 (40%) stopped all drugs due to well-controlled disease for at least 30 days after median 1.9 years of DMARD use (interquartile range [IQR] 1.1, 3.4). There were 175 sustained discontinuers (15%, group 1). Comparators included 268 unsustained discontinuers (22%, group 2) and 681 never discontinuers (57%, group 3) (Table). Only 24 children in group 2 subsequently stopped all DMARDs for at least 1 year. Compared with all children who started a DMARD (unsustained and never discontinuers), sustained discontinuers were younger at diagnosis and DMARD initiation, less likely to have polyarthritis, and less likely to have used a biologic DMARD. Compared with unsustained discontinuers, sustained discontinuers were less likely to have used biologics. No other factors were associated with sustained discontinuation among those who stopped DMARDs, including time to discontinuation and JIA category. A history of uveitis and radiographic joint damage were not associated with sustained discontinuation in either comparison.

**Conclusion:** In a large multicenter cohort of children with JIA who started DMARDs, only 1 in 6 children stopped DMARDs for well-controlled disease for at least 1 year. Younger age at DMARD initiation, oligoarticular disease course, and exclusive use of conventional DMARDs were independently associated with sustained discontinuation. The prognostic value of these factors should be considered when making decisions about stopping medicines for well-controlled JIA.
<table>
<thead>
<tr>
<th>Characteristic (N, % unless otherwise noted)</th>
<th>Group 1: off DMARDs ≥12 months(^1) (N=175)</th>
<th>Group 2: off DMARDs &lt;12 months(^1) (N=268)</th>
<th>Group 3: not off DMARDs(^1) (N=681)</th>
<th>P-value(^2) (1 vs 2+3)</th>
<th>P-value(^2) (1 vs 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at diagnosis (years), median (IQR)</td>
<td>4.0 (2.0, 8.0)</td>
<td>4.0 (2.0, 8.0)</td>
<td>6.0 (2.0, 11.0)</td>
<td>0.002</td>
<td>0.95</td>
</tr>
<tr>
<td>Age at start of DMARD (years), median (IQR)</td>
<td>5.5 (3.0, 8.9)</td>
<td>6.1 (3.1, 9.9)</td>
<td>8.3 (4.1, 12.3)</td>
<td>&lt;0.001</td>
<td>0.41</td>
</tr>
<tr>
<td>Time from start of DMARD to first DMARD discontinuation (years), median (IQR)</td>
<td>1.9 (1.2, 3.4)</td>
<td>1.9 (1.1, 3.4)</td>
<td>-</td>
<td>0.40</td>
<td>0.40</td>
</tr>
<tr>
<td>Time from start of first DMARD to end of follow-up (years), median (IQR)</td>
<td>6.0 (4.5, 8.8)</td>
<td>6.0 (4.0, 8.9)</td>
<td>4.1 (2.8, 6.6)</td>
<td>&lt;0.001</td>
<td>0.37</td>
</tr>
<tr>
<td>Female sex</td>
<td>126 (72%)</td>
<td>208 (78%)</td>
<td>522 (77%)</td>
<td>0.16</td>
<td>0.18</td>
</tr>
<tr>
<td>White race</td>
<td>141 (81%)</td>
<td>224 (84%)</td>
<td>550 (81%)</td>
<td>0.76</td>
<td>0.42</td>
</tr>
<tr>
<td>Latino ethnicity</td>
<td>22 (13%)</td>
<td>22 (8%)</td>
<td>83 (12%)</td>
<td>0.14</td>
<td>0.20</td>
</tr>
<tr>
<td>Residence in US</td>
<td>171 (98%)</td>
<td>259 (97%)</td>
<td>659 (97%)</td>
<td>0.95</td>
<td>0.72</td>
</tr>
<tr>
<td><strong>Clinical</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>JIA category</td>
<td></td>
<td></td>
<td></td>
<td>0.18</td>
<td>0.92</td>
</tr>
<tr>
<td>Systemic</td>
<td>29 (17%)</td>
<td>33 (12%)</td>
<td>93 (14%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oligoarticular, persistent</td>
<td>14 (8%)</td>
<td>26 (10%)</td>
<td>27 (4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oligoarticular, extended</td>
<td>23 (13%)</td>
<td>41 (15%)</td>
<td>53 (8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RF-polyarticular</td>
<td>84 (48%)</td>
<td>128 (48%)</td>
<td>338 (50%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RF+ polyarticular</td>
<td>9 (5%)</td>
<td>16 (6%)</td>
<td>78 (12%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psoriatic</td>
<td>7 (4%)</td>
<td>11 (4%)</td>
<td>40 (6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ERA</td>
<td>6 (3%)</td>
<td>7 (3%)</td>
<td>38 (6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undifferentiated</td>
<td>3 (2%)</td>
<td>6 (2%)</td>
<td>14 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥5 total joints affected</td>
<td>149 (85%)</td>
<td>245 (91%)</td>
<td>623 (91%)</td>
<td>0.006</td>
<td>0.11</td>
</tr>
<tr>
<td>Radiographic evidence of joint damage</td>
<td>33 (19%)</td>
<td>61 (23%)</td>
<td>136 (20%)</td>
<td>0.77</td>
<td>0.49</td>
</tr>
<tr>
<td>--------------------------------------</td>
<td>----------</td>
<td>----------</td>
<td>------------</td>
<td>------</td>
<td>------</td>
</tr>
<tr>
<td>ANA positive</td>
<td>78 (45%)</td>
<td>116 (43%)</td>
<td>277 (41%)</td>
<td>0.66</td>
<td>0.35</td>
</tr>
<tr>
<td>History of uveitis</td>
<td>15 (9%)</td>
<td>25 (9%)</td>
<td>72 (11%)</td>
<td>0.72</td>
<td>0.80</td>
</tr>
<tr>
<td>Any biologic DMARD use</td>
<td>69 (39%)</td>
<td>140 (52%)</td>
<td>599 (88%)</td>
<td>&lt;0.001</td>
<td>0.008</td>
</tr>
</tbody>
</table>

ANA, antinuclear antibody; DMARD, disease-modifying antirheumatic drug; RF, rheumatoid factor, ERA, enthesitis-related arthritis; IQR, interquartile range.

1 Refers to discontinuation from all DMARDs for at least 30 days for well-controlled JIA

2 P-values calculated by Wilcoxon rank sum testing for continuous variables and chi-square for categorical variables

Disclosure: D. B. Horton, None; F. Xie, None; M. L. Mannion, None; S. Ringold, Crescendo Bioscience, 2; C. K. Correll, None; A. C. Dennos, None; T. Beukelman, UCB, 5, Novartis Pharmaceutical Corporation, 5.


Abstract Number: 2276

**Etanercept (Enbrel®) Treatment Retention in the Sub-Population of Pediatric Patients from a Retrospective Cohort Study Using Canadian Claims-Level Data**

Majed M M Khraishi¹, Brad Millson², John Woolcott³, Heather Jones⁴ and Lisa Marshall⁴, ¹Faculty of Medicine, Memorial University of Newfoundland, St John's, NF, Canada, ²Health Access and Outcomes, QuintilesIMS, Kanata, ON, Canada, ³Inflammation & Immunology Global Outcomes & Evidence,, Pfizer, Inflammation & Immunology Global Outcomes & Evidence, Collegeville, PA, ⁴Inflammation & Immunology Global Medical Affairs, Pfizer, Collegeville, PA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Etanercept (ETN) was the first biologic approved for use in the treatment of patients with polyarticular-course juvenile idiopathic arthritis (JIA),¹ and is now indicated in other JIA subcategories.² Evidence from registry studies and real-world data suggest ETN is favored as a first-line biologic therapy in clinical practice in patients...
with JIA; however, the factors associated with long-term retention of ETN in this population have been little explored. **Objectives:** To evaluate retention rates up to 6 years in ETN-treated pediatric patients in Canada.

**Methods:** A retrospective cohort study was conducted using longitudinal prescription drug claims data from QuintilesIMS Private Drug Plan database (PDP), Ontario Public Drug Plan database (OPDP), and Quebec Public Drug Plan database. Between 07/2003 and 01/2011, biologic-naïve patients (ie, patients with no biologic treatment in the preceding 12 months) who initiated ETN, were identified and followed for 72 months. Disease indications were inferred through patient drug history. 12-month retention rates were evaluated in 1-year increments for all patients retained on therapy, and compared with the first-year retention rate. Exact 95% confidence intervals (CI) were calculated. McNemar's test was used to assess the difference between two correlated proportions, where these were based on the same sample of subjects, with reference to year-1 retention. This analysis assessed pediatric patients (ie, age 2-16 years at time of first prescription).

**Results:** The study identified 172 ETN-treated pediatric patients across Canada, who initiated therapy during the selection period. 67% were female; 94% were diagnosed with JIA. Private claims accounted for 69% of ETN-treated pediatric patients, and 49% of the patient population were from Ontario. Of the 152 patients covered by PDP and OPDP, 45% and 55% were aged 2-11 years and 12-16 years at initiation, respectively. 12-month ETN retention rates increased following their first year on therapy. 78% of patients were retained at year 1; 12-month retention rates through years 2-6 are shown in the Table. Retention rates for the corresponding periods in the adult population (>18 years) were: 66%, 79%, 82%, 84%, 83%, and 79%. 38% of pediatric patients remained on ETN treatment for the entire 72-months’ study. 66 patients switched treatments after discontinuing ETN, with 44% doing so more than once during the 6-year period.

**Conclusion:** Pediatric patients treated with ETN demonstrated significantly higher retention rates after the first year, with a considerable proportion of patients continuing for 6 years; many who discontinued ETN and subsequently switched treatment did not remain on their first-choice treatment. Further analysis of the reasons for ETN treatment discontinuation may assist in identifying measures to support patients in maintaining treatment to achieve sustained clinical benefit and quality of life.

<table>
<thead>
<tr>
<th>Year</th>
<th>Tracked Patients, n</th>
<th>Retained Patients, n</th>
<th>Yearly Retention Rate, % (95% CI)</th>
<th>Cumulative Retention Rate, % (95%, CI)</th>
<th>P-Value (Retention Rate Reference to Year 1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>172</td>
<td>135</td>
<td>76 (72, 84)</td>
<td>76 (72, 84)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>135</td>
<td>118</td>
<td>87 (81, 92)</td>
<td>69 (61, 75)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>3</td>
<td>118</td>
<td>101</td>
<td>86 (78, 91)</td>
<td>58 (51, 66)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>4</td>
<td>101</td>
<td>93</td>
<td>88 (81, 94)</td>
<td>52 (46, 60)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>5</td>
<td>90</td>
<td>81</td>
<td>90 (82, 95)</td>
<td>47 (39, 55)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>6</td>
<td>81</td>
<td>65</td>
<td>80 (70, 86)</td>
<td>38 (31, 45)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>


**Disclosure:** M. M. M. Khraishi, Pfizer Inc, 9,Novartis, Roche, 9; B. Millson, QuintilesIMS, 3; J. Woolcott, Pfizer Inc, 1,Pfizer Inc, 3; H. Jones, Pfizer Inc, 1,Pfizer Inc, 3; L. Marshall, Pfizer Inc, 1,Pfizer Inc, 3.


**Abstract Number:** 2277
Safety of Biologic Therapies for the Treatment of Juvenile Idiopathic Arthritis: Results from the Spanish Registry of Adverse Events with Biologic Therapies (BIOBADASER)

Juan José Bethencourt Baute1, Carlos Sánchez-Piedra2, Lorena Expósito Pérez1, M. Victoria Hernández3, Javier Manero4, Rosa Rosello5, Fernando Sánchez-Alonso6, Dolores Ruiz-Montesinos7, Eva Perez Pampín8, Carlos Rodriguez-Lozano9, Cristina Campos Fernandez10, Cristina Fernández-Carballedo11, Raquel Martín-Domenech11, Javier Del Pino-Montes12, Mercedes Freire13, Federico Díaz-González14, Juan J. Gomez-Reino15 and Sagrario Bustabad16,

1Servicio de Reumatología, Hospital Universitario de Canarias, Tenerife, Spain,
2Research Unit, Spanish Society of Rheumatology, Madrid, Spain,
3Hospital Clinic. Barcelona. Spain, Barcelona, Spain,
4Rheumatology, Hospital Miguel Servet, Zaragoza, Spain,
5Hospital San Jorge, Huesca, Spain,
6Unidad de Investigación, Spanish Society of Rheumatology, Madrid, Spain,
7Rheumatology, Hospital Virgen Macarena, Seville, Spain,
8Rheumatology, Complejo Hospitalario Universitario de Santiago, Santiago de Compostela, Spain,
9Hospital de Gran Canaria Dr. Negrín, Gran Canaria, Spain,
10Rheumatology, Hospital Universitario de Valencia., Valencia, Spain,
11Hospital General Universitario de Elda, Elda, Spain,
12Rheumatology, HOSPITAL CLÍNICO UNIVERSITARIO DE SALAMANCA, Salamanca, Spain,
13Servicio de Reumatología. Instituto de Investigación Biomédica de A Coruña (INIBIC). Complexo HospitalarioUniversitario de A Coruña (CHUAC), Sergas. Universidade da Coruña (UDC), A Coruña, Spain,
14Servicio de Reumatología. Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain,
15Fundacion Ramon Dominguez, Hospital Clinico Universitario, Santiago de Compostela, Spain,
16Rheumatology, Servicio de Reumatología. Hospital Universitario de Canarias, La Laguna, Tenerife, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in childhood. The treatment of JIA has been revolutionized by the use of biologic agents. Since studies on biologic therapy in young adults include relatively low numbers of patients and short trial durations, more evidence regarding safety issues is needed. Our aim is to evaluate the safety of biological therapy in JIA.

Methods: Multicenter prospective study. Information was obtained from BIOBADASER, a study based on routine clinical practice. All patients diagnosed before age 16 in our database between 2000 and 2015 were included in the analysis. JIA is classified into 7 subgroups: systemic, persistent or extended oligoarthritis, RF positive polyarthritis, RF negative polyarthritis, enthesitis-related arthritis, psoriatic arthritis, and undifferentiated arthritis. Due to the design of the registry, it was not possible to identify each of the JIA subgroups; thus, we classified them into systemic/oligo/polyarticular JIA, JIA related to enthesitis, and psoriatic JIA. Adverse event were coded using version 13.0 MedDRA (Medical Dictionary for Regulatory Activities).

Proportions, means and standard deviations (SD) were used to describe our population. Incidence rates and 95% confidence intervals were calculated to assess adverse events.

Results: A total of 469 patients were classified as systemic/oligo/polyarticular JIA (70.6%), JIA related to enthesitis (25%) and psoriatic JIA (4.5%). 46.1% of patients were women. Age at diagnosis was 9.4 (SD = 5.3) and years of disease evolution 24.1 (SD = 14.1). The age at biological treatment initiation was 23.9 years (SD= 13.9). Biologicals were used as monotherapy in the 42.4% of the treatments, while methotrexate was used in combination in 44.0% of the treatments. Table 1 shows incidence rates for adverse events. Serious adverse events had an incidence of 41.4 (35.2-48.7). Only in one case was a fatal adverse event (mycoplasma pneumonia during treatment with anakinra) recorded.
Conclusion: The most common incident adverse events were: infections, gastrointestinal disorders, skin and subcutaneous tissue disorders. There seemed to be little difference between the results for patients with JIA and those diagnosed with rheumatoid arthritis in BIOBADASER. Although this project allowed us to examine long-term drug safety in JIA, large registries that focus on such patients are needed to better understand rare adverse events.

Table 1. Incidence of adverse events recorded in patients with JIA by line of treatment.
<table>
<thead>
<tr>
<th>Incidence (CI95%) x 1,000 persons/year</th>
<th>First-line biologic</th>
<th>Second-line Biologic</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total adverse events</td>
<td>367.2 (342.8-393.3)</td>
<td>383.2 (351.3-417.9)</td>
<td>373.2 (353.6-393.8)</td>
</tr>
<tr>
<td>Severe adverse events</td>
<td>36.6 (29.4-45.5)</td>
<td>49.5 (38.9-63.0)</td>
<td>41.4 (35.2-48.7)</td>
</tr>
<tr>
<td>Fatal adverse events</td>
<td>-</td>
<td>0.7 (0.1-5.3)</td>
<td>0.3 (0.0-2.0)</td>
</tr>
</tbody>
</table>

By system / organ class

<table>
<thead>
<tr>
<th>System / Organ Class</th>
<th>First-line biologic</th>
<th>Second-line Biologic</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections and infestations</td>
<td>171.2 (154.8-189.3)</td>
<td>151.5 (131.9-173.9)</td>
<td>163.8 (151-177.6)</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>19 (14-25.7)</td>
<td>24.7 (17.6-34.8)</td>
<td>21.1 (16.9-26.5)</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>17.2 (12.5-23.6)</td>
<td>25.5 (18.2-35.7)</td>
<td>20.3 (16.1-25.6)</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>19.9 (14.8-26.7)</td>
<td>21 (14.5-30.4)</td>
<td>20.3 (16.1-25.6)</td>
</tr>
<tr>
<td>Eye disorders</td>
<td>13.5 (9.5-19.4)</td>
<td>19.5 (13.3-28.6)</td>
<td>15.8 (12.1-20.5)</td>
</tr>
<tr>
<td>Complementary explorations</td>
<td>15.4 (11-21.5)</td>
<td>15.7 (10.3-24.1)</td>
<td>15.5 (11.9-20.2)</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td>10.8 (7.3-16.2)</td>
<td>13.5 (8.5-21.4)</td>
<td>11.8 (8.7-16)</td>
</tr>
<tr>
<td>Surgical and medical procedures</td>
<td>9.5 (6.2-14.5)</td>
<td>14.2 (9.1-22.3)</td>
<td>11.3 (8.3-15.4)</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>11.3 (7.6-16.7)</td>
<td>11.2 (6.8-18.7)</td>
<td>11.3 (8.3-15.4)</td>
</tr>
<tr>
<td>Blood and lymphatic system disorders</td>
<td>8.6 (5.5-13.5)</td>
<td>10.5 (6.2-17.7)</td>
<td>9.3 (6.6-13.1)</td>
</tr>
<tr>
<td>Renal and urinary disorders</td>
<td>9.9 (6.5-15.1)</td>
<td>8.2 (4.6-14.9)</td>
<td>9.3 (6.6-13.1)</td>
</tr>
<tr>
<td>Reproductive system and breast disorders</td>
<td>8.1 (5.1-12.9)</td>
<td>9 (5.1-15.8)</td>
<td>8.5 (5.9-12.1)</td>
</tr>
<tr>
<td>Injury, poisoning and procedural complications</td>
<td>9 (5.8-14)</td>
<td>6.7 (3.5-13)</td>
<td>8.2 (5.7-11.8)</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>8.1 (5.1-12.9)</td>
<td>6 (3-12)</td>
<td>7.3 (5-10.8)</td>
</tr>
<tr>
<td>Neoplasms; benign, malignant and unspecified (including cysts and polyps)</td>
<td>6.3 (3.7-10.7)</td>
<td>3.7 (1.6-9)</td>
<td>5.4 (3.4-8.4)</td>
</tr>
<tr>
<td>Hepatobiliary disorders</td>
<td>5 (2.8-9)</td>
<td>5.2 (2.5-11)</td>
<td>5.1 (3.2-8.1)</td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td>4.5 (2.4-8.4)</td>
<td>5.2 (2.5-11)</td>
<td>4.8 (3.7-7)</td>
</tr>
<tr>
<td>Pregnancy, puerperium and perinatal conditions</td>
<td>1.4 (0.4-4.2)</td>
<td>9 (5.1-15.8)</td>
<td>4.2 (2.5-7)</td>
</tr>
<tr>
<td>Vascular disorders</td>
<td>3.6 (1.8-7.2)</td>
<td>4.5 (2-10)</td>
<td>3.9 (2.3-6.7)</td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td>3.6 (1.8-7.2)</td>
<td>4.5 (2-10)</td>
<td>3.9 (2.3-6.7)</td>
</tr>
<tr>
<td>Ear and labyrinth disorders</td>
<td>1.8 (0.7-4.8)</td>
<td>4.5 (2-10)</td>
<td>2.8 (1.5-5.2)</td>
</tr>
<tr>
<td>Immune system disorders</td>
<td>1.4 (0.4-4.2)</td>
<td>4.5 (2-10)</td>
<td>2.5 (1.3-4.9)</td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td>2.7 (1.2-6)</td>
<td>1.5 (0.4-6)</td>
<td>2.3 (1.1-4.5)</td>
</tr>
<tr>
<td>Endocrine disorders</td>
<td>1.8 (0.7-4.8)</td>
<td>1.5 (0.4-6)</td>
<td>1.7 (0.8-3.8)</td>
</tr>
<tr>
<td>Social circumstances</td>
<td>1.4 (0.4-4.2)</td>
<td>1.5 (0.4-6)</td>
<td>1.4 (0.6-3.4)</td>
</tr>
<tr>
<td>Congenital, familial and genetic disorders</td>
<td>2.3 (0.9-5.4)</td>
<td>0 (-)</td>
<td>1.4 (0.6-3.4)</td>
</tr>
</tbody>
</table>
Biologic Switching Among JIA Patients: A Cohort Study in the Childhood Arthritis and Rheumatology Research Alliance Registry

Melissa L. Mannion1, Fenglong Xie2, Daniel B. Horton3, Sarah Ringold4, Colleen K. Correll5, Anne C. Dennos6 and Timothy Beukelman7, 1Pediatric rheumatology, University of Alabama at Birmingham, Birmingham, AL, 2Division of Clinical Immunology & Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 3Pediatrics, Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, 4Seattle Children's Hospital, Seattle, WA, 5Pediatrics, University of Minnesota, Minneapolis, MN, 6Duke Clinical Research Institute, Durham, NC, 7Pediatric Rheumatology, University of Alabama at Birmingham, Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Biologic medications have allowed a significant proportion of JIA patients to achieve inactive disease. However, some patients will have ongoing moderate to high disease activity or will not tolerate the medication. Current treatment recommendations suggest changing biologic medications when inactive or low disease activity is not attained, but the switching patterns and reasons for switching in clinical practice in North America are not currently known.

Methods: We used the Childhood Arthritis & Rheumatology Research Alliance (CARRA) Registry of clinical data from >55 pediatric rheumatology clinics in the United States and Canada. Individuals with JIA and no prior biologic medication use were included if they newly started a biologic medication on or after enrollment in the registry and had a minimum of 6 months of observable time following medication start. Individuals with systemic JIA were excluded. Subjects were labelled switchers if they had subsequent use of any other biologic medication during the 6 month follow up time and labelled non-switchers if they did not. We compared characteristics of switchers and non-switchers using descriptive statistics and reported patterns of and reasons for switching.

Results: There were 134 biologic-naïve children with JIA who started a biologic medication after enrollment, of whom 14 (10%) switched to a different biologic medication within 6 months (Table). The median time before switching was 107.5 days (interquartile range (IQR) 75 - 133). The majority of patients had started on etanercept (102, 76%) and switched to adalimumab (9), abatacept (1), infliximab (1), and rituximab (1). One patient switched from adalimumab to etanercept, and 1 switched from infliximab to tocilizumab. Ineffectiveness was the most common reason for switch (6, 43%), 2 patients switched for intolerance of administration, 2 switched for adverse effects, and 1 each switched for financial cost, parental discretion, and not starting the first biologic. None of the individuals with persistent...
oligoarticular disease switched. There was no difference in methotrexate use or presence of uveitis between those who did and did not switch.

**Conclusion:** In a multicenter cohort of children with JIA who started a biologic, only 10% of children switched biologic medication in the 6 months after initiation of the first biologic. Etanercept was the most common first biologic medication and most patients who switched started another TNF inhibitor. Additional studies are needed to evaluate the clinical predictors of switching, the outcomes following biologic switching, to identify the optimal timing of switching and the preferred second-line agent.

<table>
<thead>
<tr>
<th>Table. Characteristics at time of biologic initiation among those who do and do not switch within 6 months (values are n (%) unless otherwise noted)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All biologic initiators</strong> n = 134</td>
</tr>
<tr>
<td>Age (years) median, IQR</td>
</tr>
<tr>
<td>Sex (F) n, %</td>
</tr>
<tr>
<td>White</td>
</tr>
<tr>
<td>Hispanic, Latino</td>
</tr>
<tr>
<td>Residence in US</td>
</tr>
<tr>
<td>JIA subtype: n, %</td>
</tr>
<tr>
<td>RF+ poly</td>
</tr>
<tr>
<td>RF- poly</td>
</tr>
<tr>
<td>Persistent Oligo</td>
</tr>
<tr>
<td>Extended oligo</td>
</tr>
<tr>
<td>ERA</td>
</tr>
<tr>
<td>psoriatic</td>
</tr>
<tr>
<td>undifferentiated</td>
</tr>
<tr>
<td>Uveitis n, %</td>
</tr>
<tr>
<td>Time from diagnosis to start biologic (days) median, IQR</td>
</tr>
<tr>
<td>MTX use (all) n, %</td>
</tr>
<tr>
<td>PO MTX n, %</td>
</tr>
<tr>
<td>SQ MTX n, %</td>
</tr>
<tr>
<td>First biologic: n, %</td>
</tr>
<tr>
<td>etanercept</td>
</tr>
<tr>
<td>adalimumab</td>
</tr>
<tr>
<td>infliximab</td>
</tr>
<tr>
<td>golimumab</td>
</tr>
<tr>
<td>abatacept</td>
</tr>
</tbody>
</table>

**Abbreviations:** IQR – interquartile range, JIA – juvenile idiopathic arthritis, RF – rheumatoid factor, poly – polyarticular, oligo – oligoarticular, ERA – enthesitis related arthritis, MTX – methotrexate, PO – oral, SQ - subcutaneous

**Disclosure:** M. L. Mannion, None; F. Xie, None; D. B. Horton, None; S. Ringold, Crescendo Bioscience, 2; C. K. Correll, None; A. C. Dennos, None; T. Beukelman, UCB, 5,Novartis Pharmaceutical Corporation, 5.
Abstract Number: 2279

**Dynamics of Concomitant Therapy in Children with Juvenile Idiopathic Arthritis Treated with Etanercept**

Ekaterina Alexeeva¹,², Tatiana Dvoryakovskaya¹,², Victor Gladkikh³,⁴, Andrei Moskalev⁴,⁵, Rina Denisova², Ksenia Isaeva², Olga Lomakina², Margarita Soloshenko² and Anna Karaseva², ¹Pediatrics, The Federal State Autonomous Educational Institution of Higher Education The First Moscow State Medical University named after I.M. Sechenov Ministry of Health of the Russian Federation (Sechenov University), Moscow, Russian Federation, ²Reumatology department, Federal State Autonomous Institution "National Scientific and Practical Center of Children's Health" Of the Ministry of Health of the Russian Federation, Moscow, Russian Federation, ³Department of Biostatistics, EOL Labs ltd, Novosibirsk, Russia, ⁴Laboratory of Computational Physics, Institute of Computational Mathematics and Mathematical Geophysics SB RAS, Novosibirsk, Russian Federation, ⁵Department of Biostatistics, EOL Labs ltd, Novosibirsk, Russian Federation

**First publication:** September 18, 2017

SESSION INFORMATION

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The effectiveness of target use of biological medications depends on how personalized they are to fit patient’s individual parameters with juvenile idiopathic arthritis (JIA). The proper selection of biologicals allows one to reach maximum effectiveness and reduce the dosage of concomitant therapy. Both the steroid- and NSAID-sparing effects of biological drugs are the key aspects of the dynamics of patient’s condition. Purpose: To study the dynamics of concomitant treatment with NSAIDs and corticosteroids during etanercept treatment in patients with JIA.

**Methods:**

This analysis was performed on 197 etanercept-naïve JIA patients (69.5% females) with median age of 7.25 years (IQR, 4–12 years). For each time point, as well as for the past medical history, the data on concomitant therapy were collected: the status of NSAID use, the fact of administration and dosage of oral glucocorticoids (orGC) and methotrexate (MTX). The effectiveness of primary therapy and the dynamics of concomitant therapy were analyzed after 3 months and every 6 months during the long-term follow-up (up to 4.5 years).

**Results:**

At the baseline, 162 (82.2%) patients received concomitant MTX; 10 (5.0%) patients, orGC; and 121 (61.4%) patients, NSAIDs. All patients with concomitant orGC received both ETA and MTX. No patients received intra-articular GK for the entire study period.

Within 1 year treatment with ETA, NSAIDs were discontinued in 114 (94.2%) patients, orGC were discontinued completely in 4 children (40%), and the dose of orGC was reduced in 1 patient (10%).

By the end of follow-up period, NSAIDs were withdrawn in 115 patients (95%), orGC were withdrawn in 4 (40%) patients, and were reduced in 4 (40%). Only one patient during the observation required an increase in dosage of orGC. During the entire period of observation, the appointment of NSAIDs or orGC was not required for any patient who had not previously received these drugs. There were no significant differences in the dynamics of withdrawal of NSAIDs in...
patients who received and did not receive MTX background therapy: the total withdrawal was 91 out of 96 (94.8%) patients in the MTX+ETA group vs 24 of 25 (96%) in the ETA group (p = 0.804). By the end of the follow-up period 36 (19.3%) of 187 patients who had any background therapy, could switch to ETA monotherapy.

Conclusion:

Our results demonstrate that long-term therapy with ETA makes it possible to reduce the dosage or completely discontinue most concomitant therapy agents (orGK, NSAIDS, MTX) in a significant percentage of patients. This reduces the risk of development of NSAID- and GC-associated pathological conditions, while the effectiveness of therapy of the underlying condition remains high.

Disclosure: E. Alexeeva, Roche Pharmaceuticals, 2; T. Dvoryakovskaya, Roche Pharmaceuticals, 2; V. Gladkikh, None; A. Moskalev, None; R. Denisova, None; K. Isaeva, None; O. Lomakina, None; M. Soloshenko, None; A. Karaseva, None.


Abstract Number: 2280

Effectiveness of Switching to Adalimumab As the Second- and Third-Line Biological Drug in Patients with Juvenile Idiopathic Arthritis

Ekaterina Alexeeva1, Tatiana Dvoryakovskaya2, Victor Gladkikh3,4, Andrei Moskalev4,5, Rina Denisova1, Ksenia Isaeva1, Olga Lomakina1, Margarita Soloshenko1 and Anna Karaseva1, 1Reumatology department, Federal State Autonomous Institution "National Scientific and Practical Center of Children's Health" Of the Ministry of Health of the Russian Federation, Moscow, Russian Federation, 2Pediatrics, The Federal State Autonomous Educational Institution of Higher Education The First Moscow State Medical University named after I.M. Sechenov Ministry of Health of the Russian Federation (Sechenov University), Moscow, Russian Federation, 3Department of Biostatistics, EOL Labs ltd, Novosibirsk, Rwanda, 4Laboratory of Computational Physics, Institute of Computational Mathematics and Mathematical Geophysics SB RAS, Novosibirsk, Russian Federation, 5Department of Biostatistics, EOL Labs ltd, Novosibirsk, Russian Federation

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

The range of biological drugs currently used in JIA therapy includes not only anti-TNF but also other varieties. However, despite the high effectiveness and good tolerability of biological agents, the first-line biological medication is discontinued in a certain cohort of children. The questions regarding effectiveness of switching to second-line and further biologics depending on the reasons for discontinuation of prior therapy and the acceptable number of drug switches still need to be solved. Purpose: To compare the effectiveness of adalimumab (ADA) therapy as the first-, second-, and third-line biological drug in children and adolescents with JIA.

Methods: A total of 214 juvenile patients were enrolled in this study: 120 ADA-naïve patients, 83 and 11 patients with a history of one and two drug switches, respectively. Response to therapy was assessed using the ACRPedi 30/50/70/90
criteria and the Wallace criteria. The treatment schedule and the reasons for discontinuation of prior biological medications were collected.

Results:

Eight patients received abatacept as the prior biological drug; 16 patients, etanercept; 64 patients, infliximab; 4 patients, rituximab; and 2 patients, tocilizumab. The predominant reasons for discontinuation of prior biological therapy were lack of primary effectiveness (16 (17%) patients) and partial ineffectiveness (39 (41.5%) patients); 14 patients (15%) had uveitis flare. In 8 patients (8.5%), therapy was discontinued because of adverse events; in 2 patients (2%), because of administrative reasons; and in 15 (16%) patients, because of stable remission. ADA therapy proved to be effective regardless of the number of prior biological drugs used. ACR90 was achieved by 75 (62.5%) ADA-naive patients and by 60 patients (63.8%) in the switching groups (p=0.841) within 1 year of treatment. Stable remission was achieved by 51 (42.5%) and 43 (45.7%) patients, respectively (p=0.635). However, the negative reasons for discontinuation of prior biological therapy are the risk factors for poor prognosis for response to therapy with different drugs. Among 57 children who discontinued the prior biological medication because of poor effectiveness, ADA was discontinued within the first year because of the same reason in 6 (10.5%) patients. Within this group, only 10 patients (17.5%) reached remission during the first year of ADA therapy and 32 patients (56.1%) reached ACR90.

Conclusion:

Adalimumab is highly effective as the first-, second-, and third-line biological drug in children with JIA. Discontinuation of prior drug because of poor effectiveness reduces the chances for reaching stable remission and improvement in ACR90 during the first year of ADA therapy.

Disclosure: E. Alexeeva, Roche Pharmaceuticals, 2; T. Dvoryakovskaya, Roche Pharmaceuticals, 2; V. Gladkikh, None; A. Moskaev, None; R. Denisova, None; K. Isaeva, None; O. Lomakina, None; M. Soloshenko, None; A. Karaseva, None.


Patterns of Medication Use in Non-Systemic Polyarthritis: Data from the Childhood Arthritis and Rheumatology Research Alliance Patient Registry

Sarah Ringold¹, Fenglong Xie², Daniel B. Horton³, Melissa L. Mannion⁴, Colleen K. Correll⁵, Anne C. Dennos⁶ and Timothy Beukelman⁷, ¹Seattle Children's Hospital, Seattle, WA, ²Division of Clinical Immunology & Rheumatology, University of Alabama at Birmingham, Birmingham, AL, ³Pediatrics, Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, ⁴Pediatric rheumatology, University of Alabama at Birmingham, Birmingham, AL, ⁵Pediatrics, University of Minnesota, Minneapolis, MN, ⁶Duke Clinical Research Institute, Durham, NC, ⁷Pediatric Rheumatology, University of Alabama at Birmingham, Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM
Background/Purpose: The Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry began enrolling children with juvenile idiopathic arthritis (JIA) in July 2015. The large number of children with prevalent JIA in the Registry and inclusion of medication logs which document medication use prior to enrollment provide a unique opportunity to describe patterns of medication use among children with JIA.

Methods: Participants were enrolled at >55 centers in the US and Canada. Children with polyarthritis, including the ILAR categories of extended oligoarticular JIA and polyarticular JIA (RF positive and negative), were included in these analyses if they had >12 months of data available since diagnosis. Data were obtained from Registry medication logs that contained the patient’s medication use history, including start and stop dates. Patient date of diagnosis and medication start and stop dates were imputed if month or day were missing. Longitudinal treatment maps were developed to visualize patient’s individual treatment courses and identify common usage patterns among them. To generate the treatment maps, each patient’s disease duration was divided into 60-day intervals over the first two years since diagnosis. Medication use for each interval was classified by the predominant medication usage pattern during that interval, including non-biologic and/or biologic DMARDs, or no treatment. Patients were sorted by initial and subsequent medication use to determine the most common patterns of medication use.

Results: 853 patients were included, the majority of whom had RF negative polyarticular JIA (71%; Table). 50% of children with RF negative polyarthritis 66% of children with RF positive polyarthritis received a biologic DMARD, most commonly a tumor necrosis factor alpha inhibitor (TNFi). Among children with extended oligoarticular JIA, 35% of children did not receive non-biologic or biologic DMARD treatment. The most common pattern of medication use in this group was methotrexate monotherapy (oral or subcutaneous). Among children with polyarticular JIA (RF positive or negative), the most common sequence was methotrexate monotherapy with addition of biologic DMARD, most commonly TNFi. Less common patterns were biologic DMARD monotherapy and initial therapy with biologic and non-biologic DMARDs. Use of a second or third TNFi and non-TNFi biologics was rare during the first 2 years of treatment.

Conclusion: Although there is variability in treatment approaches to non-systemic polyarthritis in children, patterns of early medication use can be identified by longitudinal mapping of individual patients' medication data. These data may be used to assess how treatment approaches change over time as new therapies become available.

| Table. Patient Characteristics and Medication Use During the First 24 Months After JIA Diagnosis |
|---------------------------------------------------------------|---------------------------------|---------------------------------|
| Extended Oligoarticular JIA (n=118) | Polyarticular JIA, RF positive (n=127) | Polyarticular JIA, RF negative (n=608) |
| Age at disease onset – years; median (IQR)* | 3 (2-5) | 11 (8-14) | 6 (2-10) |
| Female – n (%) | 99 (84) | 109 (86) | 462 (76) |
| White race – n (%) | 109 (92) | 72 (57) | 525 (86) |
| No non-biologic** or biologic DMARD- n (%) | 41 (35) | 17 (13) | 103 (17) |
| Non-biologic DMARD only - n (%) | 47 (40) | 26 (10) | 199 (33) |
| Any biologic- n (%) | 30 (25) | 84 (66) | 306 (50) |
| Any TNFi biologic – n (%) | 27 (23) | 81 (64) | 301 (50) |
| > 1 TNFi biologic – n(%) | 2 (2) | 9 (7) | 41 (7) |

*IQR: Interquartile range
The Childhood Arthritis and Rheumatology Research Alliance Start Time Optimization of Biologic Therapy in Polyarticular JIA Study: Interim Report of Baseline Patient Characteristics and Treatment Choices

Sarah Ringold1, George A. Tomlinson2, Pamela F. Weiss3, Laura E. Schanberg4, Brian M. Feldman5, Mary Ellen Riordan6, Anne C. Dennos7, Vincent Del Gaizo8, Katherine Murphy9 and Yukiko Kimura6, 1Seattle Children's Hospital, Seattle, WA, 2Medicine, Mount Sinai Hospital, Toronto, ON, Canada, 3Division of Rheumatology, Center for Pediatric Clinical Effectiveness, Children's Hospital of Philadelphia, Philadelphia, PA, 4Pediatrics, Duke University Medical Center, Durham, NC, 5Rheumatology, The Hospital for Sick Children, Toronto, ON, Canada, 6Hackensack University Medical Center, Hackensack, NJ, 7Duke Clinical Research Institute, Durham, NC, 8Parent Partner, Whitehouse Station, NJ, 9Parent Partner, San Francisco, CA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Despite the many available new and effective treatments for polyarticular JIA (P-JIA), there is significant variation in the timing of when biologic medications are started. Three consensus treatment plans (CTPs) reflecting the currently most commonly-used strategies for starting biologic treatment were developed by the Childhood Arthritis and Rheumatology Research Alliance (CARRA) using consensus methodology. The CARRA Start Time Optimization of Biologic Therapy in Polyarticular JIA (STOP-JIA) study aims to compare the effectiveness of the 3 CARRA P-JIA CTPs using a prospective, observational study design. This abstract describes interim baseline characteristics and CTP choices for the patients enrolled in STOP-JIA.

Methods: Untreated P-JIA patients were enrolled into the CARRA Registry. Providers and patients together chose one of the CTPs to follow: 1) Step-Up treatment (initial therapy with DMARD and biologic added after 3 months if needed); 2) Early Combination (initial therapy with both DMARD and biologic); and 3) Biologic First (initial treatment with biologic monotherapy). Providers had the option of prescribing glucocorticoids at baseline per their usual practice and were provided with tapering options. There is no randomization or blinding in this observational study.

Results: One hundred and eighty two patients were enrolled at 37 sites in the US and Canada between 1 Nov 15 and 31 May 17. Patient characteristics are summarized in Table 1. The most commonly chosen CTP was Step-Up (n=116; 64%). Early Combination CTP was the next most common choice (n=44; 24%). Forty eight (26%) of patients received oral steroids at baseline. To date, 491 follow up visits have been entered and 30 patients have completed their 12 month visit. Of the patients who have completed their 3 month visit, 10 patients were reported to have changed CTP. There
were 9 Serious Adverse Events (SAE) or Important Medical Events (IME): 1 each of septic shock (CTCAE Grade 3), influenza A (Grade 2), new onset uveitis (Grade 2), shingles (Grade 2), seizure (Grade 1), hepatitis (Grade 1), and 3 infections treated with IV antibiotics (Grades 1, 2, and 3).

**Conclusion:** To date, patients have been enrolled into all 3 CTP choices, with the Step-Up CTP being the most common. Ongoing, prospective data collection from these patients will allow for a comparison of the effectiveness of the strategies.

Table 1. Baseline Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total Cohort (n=182)</th>
<th>Step up (n=116)</th>
<th>Early Combination (n=44)</th>
<th>Biologic First (n=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Female N (%)</strong></td>
<td>134 (74%)</td>
<td>85 (76%)</td>
<td>31 (71%)</td>
<td>15 (68%)</td>
</tr>
<tr>
<td><strong>White N (%)</strong></td>
<td>118 (69%)</td>
<td>85 (73%)</td>
<td>28 (64%)</td>
<td>13 (59%)</td>
</tr>
<tr>
<td><strong>Age in yrs – median (IQR)</strong></td>
<td>11 (6, 14)</td>
<td>11 (6, 14)</td>
<td>11 (8, 14)</td>
<td>13 (7, 15)</td>
</tr>
<tr>
<td><strong>JIA Category</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>N (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extended Oligoarticular</td>
<td>2 (1)</td>
<td>2 (2)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Polyarticular</td>
<td>121 (67)</td>
<td>88 (76)</td>
<td>23 (52)</td>
<td>10 (46)</td>
</tr>
<tr>
<td>Polyarticular (RF-)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polyarticular (RF+)</td>
<td>27 (15)</td>
<td>14 (12)</td>
<td>12 (27)</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Psoriatic</td>
<td>9 (5)</td>
<td>4 (3)</td>
<td>2 (5)</td>
<td>3 (14)</td>
</tr>
<tr>
<td>Enthesitis-related</td>
<td>19 (10)</td>
<td>8 (7)</td>
<td>5 (11)</td>
<td>6 (27)</td>
</tr>
<tr>
<td>Undifferentiated</td>
<td>4 (2)</td>
<td>--</td>
<td>2 (5)</td>
<td>2 (9)</td>
</tr>
<tr>
<td><strong>Number of Active joints - median (IQR)</strong></td>
<td>9 (6, 17)</td>
<td>14 (8, 22)</td>
<td>8 (6, 13))</td>
<td>8 (6, 15)</td>
</tr>
<tr>
<td>Physician Global Assessment of Disease Activity - median (IQR)</td>
<td>5 (4, 7)</td>
<td>5 (4, 7)</td>
<td>7 (5, 8)</td>
<td>6 (5, 8)</td>
</tr>
<tr>
<td>Juvenile Arthritis Disease Activity Score - median (IQR)</td>
<td>18 (15, 22)</td>
<td>17 (14, 20)</td>
<td>21 (17, 23)</td>
<td>19 (17, 22)</td>
</tr>
<tr>
<td>CHAQ Score - median (IQR)</td>
<td>1 (0, 1.5)</td>
<td>0.6 (0.2, 1.2)</td>
<td>1 (0.6, 2.5)</td>
<td>0.9 (0.6, 2.1)</td>
</tr>
<tr>
<td>Oral steroids prescribed at baseline - N (%)</td>
<td>48 (26%)</td>
<td>31 (27)</td>
<td>15 (34)</td>
<td>2 (9)</td>
</tr>
</tbody>
</table>

* IQR: Interquartile Range

**Disclosure:** S. Ringold, Crescendo Bioscience, 2; G. A. Tomlinson, None; P. F. Weiss, Eli Lilly and Company, 5; L. E. Schanberg, Sanofi, Swedish Orphan Biovitrum, 9; B. M. Feldman, None; M. E. Riordan, None; A. C. Dennos, None; V. Del Gaizo, Sobi, 5; K. Murphy, None; Y. Kimura, None.


Abstract Number: 2283

**Adalimumab Therapy in Juvenile Idiopathic Arthritis: Addition of Lidocaine for Prevention of Injection Site Pain or Not? That Is the Question. a Comparison Study**
Background/Purpose: Up to 37% of patients prescribed adalimumab (AD) report significant injection-site pain (Registered Prescribing Information, 2016). For AD to be a stable pre-filled product, the pH is 5.2, which contributes to injection-site discomfort. Injection site pain is a major factor in patient willingness to initiate/continue AD. Literature reports less injection-site pain with older age, smaller volume, and use of autoinjectors. In 2008, we also reported that addition of lidocaine (LID) decreased discomfort by 80% and improved acceptance of AD. Incompatibility is not reported between AD and LID. AD and LID were combined at room temperature; no precipitation occurred. In our practice, when initiating AD, patients are offered the option of adding 0.2 ml of LID to AD.

To better understand the impact of LID added to AD, we evaluated two groups of JIA patients: those who used AD with LID, compared to those who did not. Our aim was to understand characteristics of the groups and to identify patients who might benefit by adding LID. We also sought to assess differences in disease control and adverse events that might occur when adding LID

Methods: Chart review of AD-treated JIA patients was performed. Age when instituting AD, sex, diagnoses, ESR, joint counts, and adverse events were reviewed. Results were compared between LID users (LID+) and non-users (LID-). Chi Square, T-Test and Z-score statistics assessed differences between groups.

Results: 98 JIA patients treated with AD from 2008 to May 2017 were included; 71 patients added LID, whereas 27 did not. JIA subtypes were: 28 ERA, 17 poly, 26 oligo, 23 psoriatic, 1 undifferentiated, 3 systemic; uveitis was present in 19 patients. No differences in LID use by diagnosis were found. Fewer males than females added LID (56% versus 78%) (p = 0.036). Mean age when AD was instituted and duration of use was similar: 12.2 years of age in LID+ group and 12.7 years in LID- group; AD taken for 16.2 mos ±14.2 in the LID- group and taken for 20.9 ± 20.6 mos in the LID+ group (both age and duration NS). JIA patients ≤ 10 yo did not add LID more often than those ≥ 11 yo. Further analysis by age showed that 91% of early adolescents aged 10-14 years added LID, compared to 59% children aged 1-9 years and 50% teens ≥15 years (p=0.002). In the LID+ group, joint counts and ESR improved significantly after taking AD (p =0.002 and p< 0.00001, respectively), but no improvement was seen in either metric in the LID- group. 11% of the total population reported mild adverse events. One patient in LID- group discontinued AD due to injection site pain.

Conclusion: In our cohort, adding LID to AD was preferred more by female and early adolescent patients. Adding LID produced no increased adverse events and did not impede response to AD, as shown by improved joint count/ESR in the LID+ group after starting AD. Interestingly, the LID- group demonstrated no such improvement. This may reflect non-adherence to AD in the latter group possibly due to painful injections and will need further study. Our previous work showed AD plus LID produced less injection-site pain; hence patients continued this treatment. We conclude that it is safe to add LID to AD and certain JIA patients prefer this addition, possibly with improved adherence and better disease control.

Disclosure: B. Ostrov, None; B. Groh, None; L. V. Scalzi, None; C. A. Bingham, None; N. Gaffney, None; M. Buckley, None; L. Robbins, None; R. Ayala, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/adalimumab-therapy-in-juvenile-idopathic-arthritis-addition-of-lidocaine-for-prevention-of-injection-site-pain-or-not-that-is-the-question-a-comparison-study
Use of Biological Therapies in Adult Patients Diagnosed with Juvenile Idiopathic Arthritis: Results from the Spanish Registry of Adverse Events with Biologic Therapies (BIOBADASER)

Carlos Sánchez-Piedra¹, Rosa Rosello², Javier Manero³, M. Victoria Hernández⁴, Fernando Sánchez-Alonso⁵, Eduardo Cuende⁶, Blanca García Magallón³, Ana M. Ortiz García⁷, Cesar Diaz-Torné⁸, Mercedes Freire⁹, Paloma Vela¹⁰, Raúl Menor Almagro¹¹, Agueda Prior¹², Federico Díaz-González¹³, Juan J. Gomez-Reino¹⁴ and Sagrario Bustabad¹⁵, ¹Research Unit, Spanish Society of Rheumatology, Madrid, Spain, ²Hospital San Jorge, Huesca, Spain, ³Rheumatology, Hospital Miguel Servet, Zaragoza, Spain, ⁴Rheumatology Service, Hospital Clinic de Barcelona, Barcelona, Spain, ⁵Unidad de Investigación, Spanish Society of Rheumatology, Madrid, Spain, ⁶University Hospital Príncipe de Asturias, Immune System Diseases, Rheumatology department, Alcalá de Henares, Madrid, Spain, ⁷Rheumatology, Rheumatology Service, Hospital Universitario de La Princesa, IIS-IP, Madrid, Spain, ⁸GEACSER, Madrid, Spain, ⁹Servicio de Reumatología. Instituto de Investigación Biomédica de A Coruña (INIBIC). Complejo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidade da Coruña (UDC), A Coruña, Spain, ¹⁰Reumatología, Hospital General Universitario de Alicant.e. Alicante. Spain, ¹¹Reumatología, Hospital Universitario Virgen del Rocío, Sevilla, Spain, ¹²Rheumatology, Hospital Universitari Germans Trias i Pujol, Barcelona, Spain, ¹³Servicio de Reumatología. Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain, ¹⁴Fundacion Ramon Dominguez, Hospital Clinico Universitario, Santiago de Compostela, Spain, ¹⁵Rheumatology, Servicio de Reumatología. Hospital Universitario de Canarias, La Laguna, Tenerife, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in childhood. The advent of new biological drugs has changed the prognosis and therapeutic approach to these patients. Our aim was to evaluate the use of biological therapy in JIA.

Methods:

Multicenter prospective study. Information was obtained from BIOBADASER. All patients diagnosed before age 16 in our database between 2000 and 2015 were included in the analysis. JIA is classified into 7 subgroups: systemic, persistent or extended oligoarthritis, RF positive polyarthritis, RF negative polyarthritis, enthesitis-related arthritis, psoriatic arthritis, and undifferentiated arthritis. Due to the design of the registry, it was not possible to identify each of the JIA subgroups; thus, we classified them into systemic/oligo/polyarticular JIA, JIA related to enthesitis, and psoriatic JIA.

Proportions, means and standard deviations (SD) were used to describe our population and the utilization of treatments. Survival rates were calculated until termination of treatment for any reason.

Results: A total of 469 patients were classified as systemic/oligo/polyarticular JIA (70.6%), JIA related to enthesitis (25%) and psoriatic JIA (4.5%). 46.1% of patients were women (n= 216). Age at diagnosis was 9.4 (SD= 5.3) and years of disease evolution 24.1 (SD= 14.1). The age at biological treatment initiation was 23.9 years (SD= 13.9). 42.4% of the biologics were used as monotherapy. Methotrexate was used in combination in 44.0% of the biological treatments. 12.4% of the patients received more than 3 biologicals (December 2015). The most commonly used drug was Etanercept (34.7%), followed by Infliximab (21.6%). Table 1 shows the biologic therapies used in our sample. 42.4% of
the treatments with Etanercept were in monotherapy. The median survival rate with the drug was over three years (Table 2).

**Conclusion:** TNFi were the most commonly used biologic therapies in JIA. Ineffectiveness was the main reason for discontinuation. Survival rates can be a crucial endpoint in JIA, with age at initiation of biological treatment of particular concern.

Table 1. Biological and concomitant drugs used in patients with JIA.

<table>
<thead>
<tr>
<th>Biologic drug</th>
<th>First-line Biologic n (%)</th>
<th>Second-line Biologic n (%)</th>
<th>All n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etanercept</td>
<td>204 (43.5)</td>
<td>119 (25.8)</td>
<td>323 (34.7)</td>
</tr>
<tr>
<td>Infliximab</td>
<td>143 (30.5)</td>
<td>58 (12.6)</td>
<td>201 (21.6)</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>89 (19.0)</td>
<td>108 (23.4)</td>
<td>197 (21.2)</td>
</tr>
<tr>
<td>Anakinra</td>
<td>8 (1.7)</td>
<td>15 (3.3)</td>
<td>23 (2.5)</td>
</tr>
<tr>
<td>Rituximab</td>
<td>0 (0.0)</td>
<td>72 (15.6)</td>
<td>72 (7.7)</td>
</tr>
<tr>
<td>Abatacept</td>
<td>5 (1.1)</td>
<td>28 (6.1)</td>
<td>33 (3.6)</td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>16 (3.4)</td>
<td>40 (8.7)</td>
<td>56 (6.0)</td>
</tr>
<tr>
<td>Golimumab</td>
<td>2 (0.4)</td>
<td>13 (2.8)</td>
<td>15 (1.6)</td>
</tr>
<tr>
<td>Certolizumab</td>
<td>2 (0.4)</td>
<td>5 (1.1)</td>
<td>7 (0.8)</td>
</tr>
<tr>
<td>Canakinumab</td>
<td>0 (0.0)</td>
<td>2 (0.4)</td>
<td>2 (0.2)</td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>0 (0.0)</td>
<td>1 (0.2)</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td>Concomitant drugs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Biological monotherapy</td>
<td>177 (37.7)</td>
<td>217 (47.1)</td>
<td>394 (42.4)</td>
</tr>
<tr>
<td>- Metotrexate</td>
<td>225 (48.0)</td>
<td>184 (39.9)</td>
<td>409 (44.0)</td>
</tr>
<tr>
<td>- Glucocorticoids</td>
<td>155 (33.1)</td>
<td>145 (31.5)</td>
<td>300 (32.3)</td>
</tr>
</tbody>
</table>

Table 2. Drug Survival Rates in patients with JIA in BIOBADASER Phase II. Discontinuation reasons.

<table>
<thead>
<tr>
<th>Supervivencia (IC(_{95}%))</th>
<th>First-line biologic</th>
<th>Second-line Biologic</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st year</td>
<td>0.809 (0.771-0.842)</td>
<td>0.723 (0.659-0.777)</td>
<td>0.797 (0.758-0.830)</td>
</tr>
<tr>
<td>2nd year</td>
<td>0.678 (0.634-0.719)</td>
<td>0.558 (0.493-0.618)</td>
<td>0.652 (0.609-0.691)</td>
</tr>
<tr>
<td>3rd year</td>
<td>0.586 (0.540-0.630)</td>
<td>0.418 (0.359-0.475)</td>
<td>0.542 (0.500-0.583)</td>
</tr>
<tr>
<td>4th year</td>
<td>0.516 (0.469-0.561)</td>
<td>0.352 (0.298-0.406)</td>
<td>0.462 (0.421-0.502)</td>
</tr>
<tr>
<td>5th year</td>
<td>0.482 (0.434-0.527)</td>
<td>0.274 (0.227-0.323)</td>
<td>0.397 (0.358-0.435)</td>
</tr>
<tr>
<td>6th year</td>
<td>0.434 (0.387-0.480)</td>
<td>0.210 (0.170-0.253)</td>
<td>0.341 (0.305-0.377)</td>
</tr>
<tr>
<td>7th year</td>
<td>0.393 (0.346-0.440)</td>
<td>0.169 (0.134-0.208)</td>
<td>0.286 (0.253-0.320)</td>
</tr>
<tr>
<td>8th year</td>
<td>0.369 (0.322-0.417)</td>
<td>0.134 (0.103-0.169)</td>
<td>0.243 (0.213-0.275)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Discontinuation reasons</th>
<th>n (%)</th>
<th>n (%)</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ineffectiveness or loss</td>
<td>106 (37.3)</td>
<td>126 (42.4)</td>
<td>232 (39.9)</td>
</tr>
<tr>
<td>Adverse event</td>
<td>80 (28.2)</td>
<td>61 (20.5)</td>
<td>141 (24.3)</td>
</tr>
<tr>
<td>Pregnancy or gestational desire</td>
<td>13 (4.6)</td>
<td>14 (4.7)</td>
<td>27 (4.7)</td>
</tr>
<tr>
<td>Loss of follow-up</td>
<td>24 (8.5)</td>
<td>8 (2.7)</td>
<td>32 (5.5)</td>
</tr>
<tr>
<td>Remission</td>
<td>35 (12.3)</td>
<td>9 (3.0)</td>
<td>44 (7.6)</td>
</tr>
<tr>
<td>Others</td>
<td>24 (8.5)</td>
<td>73 (24.6)</td>
<td>97 (16.7)</td>
</tr>
<tr>
<td>Unknown</td>
<td>2 (0.7)</td>
<td>6 (2.0)</td>
<td>8 (1.4)</td>
</tr>
<tr>
<td>Total</td>
<td>284</td>
<td>297</td>
<td>581</td>
</tr>
</tbody>
</table>
Treatment of Adult Juvenile Idiopathic Arthritis Patients with Biologic Agents. Data from the National Registry

Katerina Jarosova¹, Lenka Szczukova², Zlatuse Kristkov³ and Jiri Vencovsky⁴, ¹Institute of Rheumatology, Prague, Czech Republic, ²Institute of Biostatistics and Analyses. Faculty of Medicine, Masaryk University, Brno, Czech Republic, ³Institute of Biostatistics and Analyses, Faculty of Medicine, Masaryk University, Brno, Czech Republic, ⁴Institute of Rheumatology, Prague 2, Czech Republic

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: To analyze the efficacy and safety of biologic agents in adult patients with juvenile idiopathic arthritis (JIA).

Methods:

ATTRA is a Czech national registry of patients with different forms of chronic arthritis who are treated with biologics. We have used this registry to evaluate treatment with TNF antagonists and other biologics in adult patients with juvenile idiopathic arthritis. Patients were treated with doses recommended for rheumatoid arthritis patients. Those patients, who failed to improve in DAS28 by at least 1.2 after 3 months at 2 consecutive visits, who lost the response during the treatment, or who had to be discontinued due to adverse event, were switched to alternative TNF inhibitor or other biologic drug. Clinical efficacy was assessed by the improvement in DAS28 and by assessment of quality of life using standard questionnaires (HAQ, SF36). Survival on therapy with biologic agent was calculated. Safety assessments were done for all patients during the whole follow-up period in 3 months intervals.

Results:

There are 419 adult patients with JIA followed in the ATTRA registry. Seventy-four started the treatment with biologic before 16 year of age; the remaining 345 commenced biologics in adult age. Valid and complete data for analysis are available in 275 patients, who have begun treatment in adulthood.

At the start of the treatment with biologics the mean age was 27±9 years, duration of disease 16±10 years and 73.8% were females. Mean age at the diagnosis was 11±6 years.

Patients were of the following subtypes of JIA: JIA RF negative 28.3%, JIA RF+ 22.8%, enthesis related arthritis 18.9%, extended oligoarthritis 12.2%, psoriatic arthritis 7.2%, systemic onset 6.1% and persistent oligoarthritis 4.4%.
The first biologic was either infliximab (37.1%), or etanercept (26.2%), adalimumab (27.6%), golimumab (4.4%), certolizumab (2.5%), tocilizumab (1.5%), abatacept (0.4%) and rituximab (0.4%)

Efficacy of the first biologic (DAS28):

<table>
<thead>
<tr>
<th>DAS28</th>
<th>Before treatment</th>
<th>3 months</th>
<th>1 year</th>
<th>5 years</th>
<th>10 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean±SD</td>
<td>5.7±1.0</td>
<td>3.1±1.1</td>
<td>2.8±1.2</td>
<td>2.4±1.1</td>
<td>2.5±1.4</td>
</tr>
<tr>
<td>Median</td>
<td>5.7</td>
<td>3.0</td>
<td>2.7</td>
<td>2.2</td>
<td>2.1</td>
</tr>
<tr>
<td>5.; 95.perc</td>
<td>(4.0; 7.2)</td>
<td>(1.4; 5.2)</td>
<td>(1.2; 4.9)</td>
<td>(1.1; 4.5)</td>
<td>(1.2; 6.0)</td>
</tr>
<tr>
<td>Remission</td>
<td>2 (0.7%)</td>
<td>82 (34.2%)</td>
<td>91 (47.6%)</td>
<td>61 (64.2%)</td>
<td>23 (69.7%)</td>
</tr>
<tr>
<td>LDA</td>
<td>4 (1.5%)</td>
<td>56 (23.3%)</td>
<td>36 (18.8%)</td>
<td>15 (15.8%)</td>
<td>3 (9.1%)</td>
</tr>
<tr>
<td>Number of patients</td>
<td>275</td>
<td>240</td>
<td>191</td>
<td>95</td>
<td>33</td>
</tr>
</tbody>
</table>

Efficacy of long term treatment including switches (DAS28):

<table>
<thead>
<tr>
<th>DAS28</th>
<th>Before treatment</th>
<th>3 months</th>
<th>1 year</th>
<th>5 years</th>
<th>10 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean±SD</td>
<td>5.7±1.0</td>
<td>3.1±1.2</td>
<td>2.9±1.3</td>
<td>2.7±1.3</td>
<td>2.8±1.4</td>
</tr>
<tr>
<td>Median</td>
<td>5.7</td>
<td>3.1</td>
<td>2.8</td>
<td>2.5</td>
<td>2.4</td>
</tr>
<tr>
<td>5.; 95.perc</td>
<td>(4.0; 7.2)</td>
<td>(1.4; 5.2)</td>
<td>(1.2; 5.3)</td>
<td>(1.2; 5.4)</td>
<td>(1.2;6.0)</td>
</tr>
<tr>
<td>Remission</td>
<td>2 (0.7%)</td>
<td>83 (33.5%)</td>
<td>96 (45.1%)</td>
<td>86 (51.8%)</td>
<td>40 (53.3%)</td>
</tr>
<tr>
<td>LDA</td>
<td>4 (1.5%)</td>
<td>56 (22.6%)</td>
<td>42 (19.7%)</td>
<td>25 (15.1%)</td>
<td>13 (17.3%)</td>
</tr>
<tr>
<td>Number of patients</td>
<td>275</td>
<td>248</td>
<td>213</td>
<td>166</td>
<td>75</td>
</tr>
</tbody>
</table>

Conclusion:

A significant number of adult JIA patients benefit from long-term treatment with biological agents. DAS28 showed excellent and persistent improvement for patients maintaining first biologic up to 10 years. Treatment effect to second and other biologic agents was only slightly smaller and contributed to a very good persistence on the treatment. The effect on activity was mirrored also in the functional improvements assessed by HAQ.

Supported by Research Project from Ministry of Health in the Czech Republic No: 000 000 23728

Disclosure: K. Jarosova, None; L. Szczukova, None; Z. Kristkov, None; J. Vencovsky, None.


Abstract Number: 2286

Determinants of Anti-Tumor Necrosis Factor Drug Use in Juvenile Spondyloarthropathy and Impact on Clinical Disease Outcomes
Patients with juvenile spondyloarthropathy (JSpA) have lower clinical remission rates, report higher pain scores, worse functioning and lower quality of life compared to other juvenile arthritis subtypes. JSpA patients present with different clinical features, including enthesis, lower back pain, and sacroiliitis. Biologics, such as anti-tumor necrosis factor drug (TNFi), are increasingly being used for the treatment of pediatric inflammatory arthritis. In JSpA, TNFi are typically a second or third line treatment. We sought to evaluate the reasons for TNFi initiation in JSpA, identify specific measures of disease activity and disease progression associated with the TNFi start, and assess the effect of TNFi on JSpA disease activity.

Methods: A retrospective cohort study of JSpA patients with first-time use of a TNFi followed by the Pediatric Rheumatology Department at Stanford Children’s Health from January 1, 2007, to December 31, 2014, was conducted. Patients were identified using Stanford STRIDE, a clinical data review tool. Reasons for TNFi initiation and change in JSpA disease activity index (JSpADA) components were assessed. JSpADA components changes were compared at diagnosis, TNFi initiation, 6 months post-TNFi initiation and 12 months post-TNFi initiation, as well as by disease duration at TNFi start.

Results: A total of 86 patients with clinical documentation at the time of JSpA diagnosis, TNFi initiation, and 6 months post-TNFi initiation were included in the analysis. The median age at JSpA diagnosis was 13.4y (IQR 9.9-15.5y) and the median time from JSpA diagnosis to TNFi initiation was 0.5y (IQR 0.2-2.4y). The most common reason for the physician to initiate a TNFi was for physical exam findings consistent with active disease (61%). Pain was included as a reason for initiation in 24% of patients, but never as the only reason. After six months of TNFi therapy, patients on average had three fewer active joints and one fewer active enthesitis point. Patient-reported pain also improved from moderate/severe to mild pain. At 12 months post-TNFi initiation, 54% of TNFi initiators were still considered to have active disease. Comparisons with the total JSpADA scores were unable to be performed due to missing data.

Conclusion: This study provides insight into the relationship between TNFi initiation and clinical disease activity in the JSpA population. Physical exam findings of active disease were enough to escalate therapy with a TNFi for most JSpA patients. TNFi initiation for pain alone without any definitive signs of active disease was not found to be a reason for escalation. Six months after initiating a TNFi, there was an improvement in active joint and enthesitis counts as well as patient-reported pain. However, more than half of the patients still had active disease one year after TNFi initiation. The physician’s reason for starting a TNFi and the timing of TNFi initiation did not influence the clinical disease status after one year of TNFi therapy.

Disclosure: M. Oliver, None; J. F. Simard, None; D. Gerstbacher, None; T. Lee, None; C. Sandborg, None.


Abstract Number: 2287
Biosimilar Use in Children and Young People with Juvenile Idiopathic Arthritis in a Real-World Setting in the United Kingdom

Diederik De Cock1, Lianne Kearsley-Fleet1, Eileen Baildam2, Michael W. Beresford3,4, Helen E. Foster5, Taunton R. Southwood6, Wendy Thomson7,8 and Kimme L. Hyrich1,8, 1Arthritis Research UK Centre for Epidemiology, University of Manchester, Manchester Academic Health Science Centre, Manchester, United Kingdom, 2Clinical Academic Department of Paediatric Rheumatology, Alder Hey Children's NHS Foundation Trust, Liverpool, United Kingdom, 3Department of Paediatric Rheumatology, Alder Hey Children's NHS Foundation Trust Hospital, Liverpool, United Kingdom, 4Alder Hey Children's NHS Foundation Trust Hospital, Institute of Translational Medicine (Child Health), University of Liverpool, Liverpool, United Kingdom, 5Institute of Cellular Medicine and Paediatric Rheumatology, Newcastle University and Great North Children's Hospital, Newcastle Upon Tyne, United Kingdom, 6School of Immunity and Infection, Institute of Clinical Sciences, University of Birmingham, Birmingham, United Kingdom, 7Arthritis Research UK Centre for Genetics and Genomics, University of Manchester, Manchester Academic Health Science Centre, Manchester, United Kingdom, 8National Institute of Health Research Manchester Musculoskeletal Biomedical Research Centre, Central Manchester NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Despite their increasing use in adults, there is little to no data available on the use of biosimilar drugs in children with JIA, despite anecdotal evidence of their use in clinical practice. This analysis aims to describe the characteristics of children and young people (CYP) with JIA starting biosimilars in the UK over the first 2 years following their approval in the United Kingdom (UK) for adults with musculoskeletal diseases.

Methods: The Biologics for Children with Rheumatic diseases (BCRD) study, launched in 2010, is an ongoing prospective UK study of children with JIA starting biologic therapies other than etanercept (followed in a separate parallel study). Baseline information is collected via questionnaires completed by the treating physician or affiliated clinical research nurse. Follow-up data including disease activity measures and changes in drug therapy are collected at 6 months, 1 year and annually thereafter. Since 30/09/2015, data has been captured on 3 biosimilars available in the UK: infliximab (Inflectra and Remsima) and etanercept (Benepali).

Results: To 10/05/2017, 26 patients were identified in the BCRD study starting a biosimilar: 21 (81%) Remsima, 3 (12%) Inflectra and 2 (8%) Benepali. Of these, 9 (35%) started a biosimilar as their first biologic therapy. Only 1 patient starting Remsima switched directly from the originator product, Remicade. Sixteen (62%) switched from an alternative non-originator biologic (table). Reasons for switching from these alternative biologics were efficacy reasons (n=8, 50%), safety reason (n=5, 31%), efficacy and safety issues combined (n=2, 13%) and needle phobia (n=1, 6%). Six-month and 1 year follow-up data were available in 3 and 1 CYP respectively. No serious adverse events have been reported to date and all 4 CYP continue on their biosimilar drug.

Conclusion: This preliminary study gives a first overview of initial biosimilar use in CYP with JIA in the UK. It has shown that these drugs are used as both first-line and subsequent-line biologic therapy despite a lack of license for this indication. Unlike evidence from Rheumatoid Arthritis, where a majority of patients receiving biosimilars to date have switched from the originator, this initial experience in JIA suggests that biosimilars are being considered as front line therapeutic option instead of the originator, presumably as a cost-saving measure. Further follow-up of these children will assess the effectiveness and safety of these products in paediatric use.
Successful Treatment of Methotrexate Intolerance in Juvenile Idiopathic Arthritis Using Eye Movement Desensitization and Reprocessing (EMDR)

Lea Höfel, Bruno Eppler, Elisabeth Schnöbel-Müller, Johannes Peter Haas and Boris Hügle, German Center for Pediatric and Adolescent Rheumatology, Garmisch-Partenkirchen, Germany

First publication: September 18, 2017

SESSON INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Methotrexate (MTX) is commonly used in the treatment of children with juvenile idiopathic arthritis (JIA). It frequently has to be discontinued due to intolerance with anticipatory and associative gastrointestinal
Eye Movement Desensitization and Reprocessing (EMDR) is a therapy where non-processed and dysfunctional experiences and memories are reprocessed by intensive recall combined with eye movements. This leads to selective processing of the negative affect.

The objective of this study was to investigate effectiveness of EMDR in the treatment of MTX intolerance in JIA patients, with the underlying hypothesis that intolerance occurs due to dysfunctional memories and expectations.

Methods: An open prospective study on consecutive JIA patients with MTX intolerance was performed. Intolerance was determined using the Methotrexate Intolerance Severity Score (MISS) questionnaire, and health-related quality of live was determined using the PedsQL, at 3 time points: directly before and after treatment (after treatment: MISS only), as well as 4 months after treatment. Patients were treated using a standardized EMDR protocol with 8 sessions over a time period of 2 weeks. Changes in MISS and PedsQL were compared using descriptive and non-parametric methods.

Results: 14 patients with MTX intolerance (median MISS at inclusion: 13.5, range: 6-26) were included. Directly after treatment, all patients reported marked improvement of MTX intolerance symptoms (median MISS: 0.5, range: 0-3, p=0.001). After 4 months, lasting reduction of MTX intolerance symptoms was observed (n=5, median MISS: 5, range: 0-10, p=0.068). However, 2/5 patients (40%) showed renewed signs of MTX intolerance with MISS >6. The health-related quality of life showed a trend towards improvement 4 months after treatment (n=5, median pedsQL prior to treatment 84.4%, 4 months after treatment 92.4%, p=0.46).

Conclusion: MTX intolerance in children with JIA can effectively be treated using an EMDR protocol, with lasting improvement over a period of 4 months. This intervention could potentially increase quality of life in affected patients and enable continued treatment with MTX as an effective, economic and well-tolerated medication.

Disclosure: L. Höfel, None; B. Eppler, None; E. Schnöbel-Müller, None; J. P. Haas, None; B. Hügle, None.

Abstract Number: 2289

Individualized Prediction of Early Remission on Medication in Juvenile Idiopathic Arthritis

Jaime Guzman1, Andrew Henrey2, Thomas Loughin2, Kiem Oen3, Natalie J. Shiff4, Roberta Berard5, Roman Jurencak6, Adam Huber7, Kerstin Gerhold6, Susanne Benseler9, Ciarán M. Duffy10 and Lori Tucker1, 1BC Children's Hospital, Vancouver, BC, Canada, 2Statistics and Actuarial Science, Simon Fraser University, Burnaby, BC, Canada, 3Department of Pediatrics and Child Health University of Manitoba, Winnipeg, MB, Canada, 4University of Florida, Gainesville, FL, 5Pediatrics, Children's Hospital, London Health Sciences Centre, London, ON, Canada, 6University of Ottawa, Ottawa, ON, Canada, 7IWK Health Centre, Halifax, NS, Canada, 8Pediatrics, University of Manitoba, Winnipeg, MB, Canada, 9Pediatric Rheumatology, University of Calgary, Alberta Children's Hospital, Calgary, AB, Canada, 10Children's Hospital of Eastern Ontario and University of Ottawa, Ottawa, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM
**Background/Purpose:** The Research in Arthritis in Canadian Children emphasizing Outcomes cohort (ReACCh-Out) showed a 45% chance of attaining inactive disease within a year of diagnosis with conventional JIA treatments. Children who do not attain inactive disease may miss a window of opportunity to start aggressive treatment. Here, we used ReACCh-Out data to develop models to assign probability of early remission on medication (ERM) for each child with JIA at diagnosis.

**Methods:** ReACCh-Out recruited 1497 patients newly diagnosed with JIA in 2005-2010 and followed them for five years or until May 2012. Children were included in this study if they 1) were enrolled within 90 days of diagnosis, 2) received conventional treatment (no biologics or triple DMARD within 6 months of diagnosis) and 3) had enough follow-up to determine the outcome. Outcome (ERM): at least six months of inactive disease with the first inactive disease visit occurring within one year of diagnosis. Documentation of any of the following within that period meant ERM was not attained: an active joint, enthesitis, a physician global assessment of 1 or more in a 10cm scale, systemic JIA manifestations, active uveitis, corticosteroid eye drops, morning stiffness >15 min, ESR >20 mm/h, CRP >5 mg/L. Patients who discontinued treatment during that period and remained inactive were still counted as having attained ERM. Eligible subjects were randomly split into a training set to develop candidate models (75% of subjects) and a test set to determine their accuracy (25% of subjects). Missing data on predictors were imputed using multiple imputation (20 datasets). Data splitting and model fitting were repeated 10 times for each imputed dataset to assess model stability.

**Results:** We included 916 children enrolled a median of 2 days after JIA diagnosis, of whom 409 (44.7%) attained ERM. Among 50-plus assessed variables, 17 were positively or negatively associated with ERM (Table). A logistic regression model combining these variables had a c-index of 0.62 (95% CI 0.59, 0.66). Although predicted and observed frequencies of ERM paralleled each other (Figure), the model’s c-index was similar to using JIA category alone (c-index of 0.59; 95% CI 0.56, 0.63). C-index values >0.70 are considered helpful prediction.

**Conclusion:** In this cohort, many variables easily available at diagnosis were associated with ERM in children with JIA. However, a prediction model combining the variables was only marginally better than using JIA category alone. Novel biomarkers and modelling methods may be needed to improve prediction accuracy.
<table>
<thead>
<tr>
<th>Baseline variable</th>
<th>Univariable beta coefficient (95%CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician global assessment (0 to 10)</td>
<td>-0.16 (-0.23, -0.09)</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>JIA category at diagnosis:</td>
<td></td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Enthesitis related</td>
<td>-0.43 (-0.85, -0.01)</td>
<td></td>
</tr>
<tr>
<td>Oligoarthritis</td>
<td>0.20 (-0.03, 0.43)</td>
<td></td>
</tr>
<tr>
<td>RF-negative polyarthritis</td>
<td>-0.58 (-0.93, -0.24)</td>
<td></td>
</tr>
<tr>
<td>RF-positive polyarthritis</td>
<td>-1.43 (-2.34, -0.52)</td>
<td></td>
</tr>
<tr>
<td>Psoriatic</td>
<td>0.26 (-0.39, 0.90)</td>
<td></td>
</tr>
<tr>
<td>Systemic</td>
<td>0.04 (-0.54, 0.63)</td>
<td></td>
</tr>
<tr>
<td>Undifferentiated</td>
<td>-0.71 (-1.21, -0.21)</td>
<td></td>
</tr>
<tr>
<td>Juvenile Arthritis Quality of Life Questionnaire (1 to 7)</td>
<td>-0.28 (-0.40, -0.15)</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Symmetric joint involvement</td>
<td>-0.71 (-1.05, -0.38)</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Finger joint involvement</td>
<td>-0.78 (-1.14, -0.41)</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Pain intensity in last week (0 to 10)</td>
<td>-0.13 (-0.19, -0.07)</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Upper limb involvement</td>
<td>-0.61 (-0.95, -0.27)</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Active joint count</td>
<td>-0.04 (-0.06, -0.02)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CHAQ Disability Index (0 to 3)</td>
<td>-0.47 (-0.75, -0.19)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RF positive at least once</td>
<td>-1.18 (-2.01, -0.35)</td>
<td>0.003</td>
</tr>
<tr>
<td>Parent global assessment of wellbeing (0 to 10)</td>
<td>-0.10 (-0.17, -0.03)</td>
<td>0.004</td>
</tr>
<tr>
<td>Quality of my life scale (0 to 10)</td>
<td>0.09 (0.03, 0.16)</td>
<td>0.006</td>
</tr>
<tr>
<td>Wrist involvement</td>
<td>-0.49 (-0.87, -0.10)</td>
<td>0.01</td>
</tr>
<tr>
<td>C-reactive protein level in mg/l</td>
<td>-0.01 (-0.015, -0.002)</td>
<td>0.01</td>
</tr>
<tr>
<td>Subtalar joint involvement</td>
<td>-0.55 (-1.03, -0.06)</td>
<td>0.02</td>
</tr>
<tr>
<td>Presence of morning stiffness</td>
<td>-0.43 (-0.80, -0.06)</td>
<td>0.02</td>
</tr>
<tr>
<td>Jaw involvement</td>
<td>-0.98 (-1.92, -0.03)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

**Disclosure:** J. Guzman, None; A. Henrey, None; T. Loughin, None; K. Oen, None; N. J. Shiff, None; R. Berard, None; R. Jurencak, None; A. Huber, None; K. Gerhold, None; S. Benseler, None; C. M. Duffy, None; L. Tucker, None.
Abstract Number: 2290

Comparing Effectiveness of Early Initiation of Biologic Treatment for Newly Diagnosed Juvenile Idiopathic Arthritis Using a Novel Statistics Causal Inference Method Applied to Observational Data

Bin Huang¹, Esi Morgan², Chen Chen², Jinzhong Liu², Michelle Adams², Timothy Beukelman³, Hermine I. Brunner⁴ and Daniel J Lovell⁵, ¹Biostatistics and Epidemiology, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH, ²Cincinnati Children’s Hospital, Cincinnati, OH, ³Pediatric Rheumatology, University of Alabama at Birmingham, Birmingham, AL, ⁴Rheumatology, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH, ⁵PRCSG, Cincinnati, OH

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: We compare the effectiveness of two approaches to treat Juvenile idiopathic arthritis (JIA): early combination of biologic and non-biologic disease modifying anti rheumatic drugs (b+nbDMARDs) vs. non-biologic DMARDs (nbDMARDs) alone using a novel statistics causal inference method applied to an existing observational study. Other commonly used causal inference methods are also applied and the results are compared.

Methods: A study of health related quality of life (HRQoL) study enrolled 193 children age 2-16 with newly diagnosed (< 6 month) JIA treated at a large pediatric rheumatology clinic in United States between October 2008 and August 2012, and prospectively followed the participants at 6 and 12 months after enrollment. The current study retrospectively extracted medication prescriptions to the HRQoL participants from the date of diagnosis to the 12 month follow up visit. Patient with polyarticular forms of JIA (pJIA) and on DMARDs at the study baseline were eligible for the current study. The study endpoint was Juvenile Arthritis Disease Activity Score (JADAS) at the 6 months of follow up visit. Different statistics causal inference methods are considered, including propensity score sub-classification, inverse treatment probability weighting (IPTW), regression adjustment, and a newly proposed Bayesian Gaussian Process (GP) causal inference method that is designed to model outcome and while matched on pre-treatment factor simultaneously.

Results: At the baseline visit, 111 children were treated with DMARDs: 32 (29%) with b+nbDMARDs, 66 (59%) nbDMARD and 13 (12%) bDMARDs only. Table 1 provides the baseline characteristics of patients by treatment group. Patients on b+nbDMARDs had higher JADAS scores at the baseline, with mean±SD of 18.66±11.69 vs.11.46±8.54 (Student P value <.02), and higher rate of RF positive (28.1% vs. 10.6%, Chisq P<.05). Controlled for treatment selection bias, Bayesian GP method find children treated with b+nbDMARDs show 3.83 points improvement (95% confidence interval of 0.14-7.53) in JADAS than those treated with nbDMARDs at 6 month. Other causal inference methods suggested similar effectiveness but with more uncertainty.

Conclusion: The early initiation of b+nbDMARDs approach improves clinical outcomes at 6 months more effectively than the nbDMARDs alone strategy in children with newly onset of pJIA.

Table 1. Baseline Patient Characteristics by Treatment Group
<table>
<thead>
<tr>
<th>JIA Subtype*</th>
<th>nbDMARDs (N = 66)</th>
<th>b+nbDMARDs (N = 32)</th>
<th>bDMARDs (N = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Col%</td>
<td>Row%</td>
</tr>
<tr>
<td>Poly RF-</td>
<td>39</td>
<td>59.1</td>
<td>60.0</td>
</tr>
<tr>
<td>Poly RF+</td>
<td>7</td>
<td>10.6</td>
<td>43.8</td>
</tr>
<tr>
<td>Oligo</td>
<td>14</td>
<td>21.2</td>
<td>82.4</td>
</tr>
<tr>
<td>Other</td>
<td>6</td>
<td>9.1</td>
<td>46.2</td>
</tr>
<tr>
<td>White Race</td>
<td>60</td>
<td>90.9</td>
<td>57.7</td>
</tr>
<tr>
<td>Private Insurance</td>
<td>50</td>
<td>75.8</td>
<td>58.1</td>
</tr>
<tr>
<td>Mean</td>
<td>Std</td>
<td>Min</td>
<td>Max</td>
</tr>
<tr>
<td>biological age (year)</td>
<td>10.00</td>
<td>4.30</td>
<td>2</td>
</tr>
<tr>
<td>onset age (year)</td>
<td>8.92</td>
<td>4.37</td>
<td>1.3</td>
</tr>
<tr>
<td>diagnosis age (year)</td>
<td>9.80</td>
<td>4.32</td>
<td>1.8</td>
</tr>
<tr>
<td>MD Global**</td>
<td>2.87</td>
<td>2.49</td>
<td>0</td>
</tr>
<tr>
<td>Patient Wellbeing</td>
<td>2.65</td>
<td>2.65</td>
<td>0</td>
</tr>
<tr>
<td>Active Joint Count**</td>
<td>5.33</td>
<td>6.21</td>
<td>0</td>
</tr>
<tr>
<td>Lost Range of Motion</td>
<td>4.73</td>
<td>6.78</td>
<td>0</td>
</tr>
<tr>
<td>C-HAQ+</td>
<td>0.53</td>
<td>0.72</td>
<td>0</td>
</tr>
<tr>
<td>JADAS*</td>
<td>11.46</td>
<td>8.54</td>
<td>0</td>
</tr>
<tr>
<td>global pain rating</td>
<td>3.04</td>
<td>2.73</td>
<td>0</td>
</tr>
<tr>
<td>ANA</td>
<td>0.62</td>
<td>0.49</td>
<td>0</td>
</tr>
<tr>
<td>ESR+</td>
<td>16.33</td>
<td>17.87</td>
<td>2</td>
</tr>
</tbody>
</table>

Statistics comparisons performed for the b+nbDMARDs patients vs. the nbDMARDS only patients using Chi-square for categorical and student T for continuous measures: ** P value <.01; * P value <.05; † P value <.1.

Disclosure: B. Huang, None; E. Morgan, None; C. Chen, None; J. Liu, None; M. Adams, None; T. Beukelman, None; H. I. Brunner, None; D. J. Lovell, AbbVie Inc., AstraZeneca, Centocor, Bristol-Myers Squibb, Pfizer, Regeneron, Hoffman La-Roche, Novartis, UBC, Xoma, and Genentech, 5,Wyeth Pharmaceuticals, 8,Amgen and Forest Research, 9.


Abstract Number: 2291

Three Treatment Strategies in Recent Onset DMARD Naive Juvenile Idiopathic Arthritis: First Results of Clinical Outcome after 24 Months

Petra Hissink Muller1,2, Danielle Brinkman1,3, Dieneke Schonenberg-Meinema4, Yvonne Koopman-Keemink5, Wyts van den Bosch6, Isabel Brederije1, Peter Bekkering7, Taco Kuipers1, Marion van Rossum8, Lisette van Suijlekom-Smit2, J Merlijn van den Berg4, CF Allaart9 and Rebecca ten Cate1, 1Pediatric Rheumatology, Leiden University Medical Center, Leiden, Netherlands, 2Pediatric Rheumatology, Erasmus MC Sophia Children's Hospital, Rotterdam, Netherlands, 3Pediatrics, Alrijne Hospital, Leiderdorp, Netherlands, 4Department of Pediatric Hematology, Immunology, Rheumatology and Infectious Diseases, Emma Children's Hospital AMC, University of Amsterdam,
SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

The BeSt treatment strategy for children with juvenile idiopathic arthritis (JIA) has not been determined. The aim of the BeSt for Kids study was to investigate, which of three treatment strategies is most effective and safe, by direct comparison. The target was inactive disease in all arms was inactive disease by rapid reduction of disease activity and repeated monitoring and revision of therapy in case of insufficient response. We hypothesized that early treatment with etanercept and methotrexate (arm 3), compared to initial monotherapy (arm 1) or initial combination therapy with methotrexate and prednisone (arm 2), would lead to significantly earlier clinical inactive disease.

Methods:

We conducted a randomized, single blinded, multicenter, treatment strategy study with 24 months of follow up. Disease modifying anti rheumatic drug (DMARD)-naive JIA patients were randomized to 1. sequential DMARD-monotherapy (sulfasalazine (SSZ) or methotrexate (MTX), 2. combination therapy: MTX and prednisolone-bridging, 3. Combination-therapy MTX with etanercept. For all arms, the treatment protocol described a number of subsequent treatment steps in case medication failed. Missing data were imputed. Primary outcome was time to inactive disease and time to flare after tapering and stopping DMARD therapy calculated using Kaplan Meier plot with log rank test. Secondary outcomes are adjusted ACRPedi 30/50/70/90 scores and toxicity. Generalised Estimates Equations were used for longitudinal data analyses.

Results:

Ninety-four patients were randomised, 32 in arm 1, 32 in arm 2 and 30 in arm 3. Two patients received a different diagnosis during follow-up and were left out of all analysis. Two patient were lost to follow up but were analysed due to intention to treat principle. Overall baseline median (InterQuartileRange IQR) age was 9.1 (4.6-12.9) years. 37% were ANA positive, 11 patients had oligo-articular disease, 66 patients polyarticular JIA and 15 patients juvenile psoriatic (polyarticular) arthritis. Baseline median (IQR) ACRpedi-scores: VAS physician 50 (39-58) mm, VAS patient 54 (37-70) mm, ESR 6(2-14) mm/hr, active joint count 8 (5-12), limited joint count 2.5 (1-5), CHAQ score 0.9 (0.6-1.5). Inactive disease occurred overall after mean 9.8 months (8.5-11.1). Time to inactive disease was not significantly different in all three arms (log rank test p=0.23). Outcome measures after 24 months are summarised in the table.
<table>
<thead>
<tr>
<th></th>
<th>Arm 1</th>
<th>Arm 2</th>
<th>Arm 3</th>
<th>3 vs 1 p OR (CI)</th>
<th>2 vs 1 p OR (CI)</th>
<th>3 vs 2 p OR (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>aACRPEdi30% (CI)</td>
<td>92.2</td>
<td>84.4</td>
<td>96.6</td>
<td>0.14</td>
<td>1.7 (0.8-3.4)</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td>(82.1-102.4)</td>
<td>(71.2-97.5)</td>
<td>(89.8-103.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>aACRPEdi50% (CI)</td>
<td>85.5</td>
<td>83.8</td>
<td>93.1</td>
<td>0.3</td>
<td>1.4(0.7-2.8)</td>
<td>0.9</td>
</tr>
<tr>
<td></td>
<td>(72.4-98.6)</td>
<td>(70.1-97.4)</td>
<td>(83.7-102.4)</td>
<td></td>
<td></td>
<td>1.1(0.6-2.0)</td>
</tr>
<tr>
<td>aACRPEdi70% (CI)</td>
<td>69.0</td>
<td>68.8</td>
<td>82.8</td>
<td>0.07</td>
<td>1.8(1.0-3.3)</td>
<td>0.7</td>
</tr>
<tr>
<td></td>
<td>(52.1-85.9)</td>
<td>(51.6-85.9)</td>
<td>(68.8-96.8)</td>
<td></td>
<td></td>
<td>0.9(0.4-1.7)</td>
</tr>
<tr>
<td>aACRPEdi90% (CI)</td>
<td>58.4</td>
<td>55.3</td>
<td>69.0</td>
<td>0.34</td>
<td>1.4(0.7-2.6)</td>
<td>0.38</td>
</tr>
<tr>
<td></td>
<td>(40.6-76.1)</td>
<td>(37.3-73.3)</td>
<td>(51.8-86.1)</td>
<td></td>
<td></td>
<td>0.7(0.4-1.5)</td>
</tr>
<tr>
<td>Inactive disease (%</td>
<td>61.0</td>
<td>63.1</td>
<td>61</td>
<td>0.9</td>
<td>1.0(0.7-1.7)</td>
<td>0.1</td>
</tr>
<tr>
<td>(CI)</td>
<td>(39.7-82.3)</td>
<td>(43.6-82.7)</td>
<td>(40.9-81.2)</td>
<td></td>
<td></td>
<td>0.7(0.4-1.1)</td>
</tr>
<tr>
<td>JADAS-10 (CI)</td>
<td>2.6(1.4-3.8)</td>
<td>4.0(2.2-5.8)</td>
<td>3.0(1.6-4.4)</td>
<td>0.6</td>
<td>0.6(0.1-3.5)</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.6(0.1-3.5)</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Conclusion:

Although our study did not meet its primary end point, treat-to-target treatment in this cohort of children with recent onset JIA resulted in high frequencies of clinical inactive disease and adjusted ACRpedi30/50/70 scores in all three arms. In clinical trials inactive disease seems a feasible goal in juvenile idiopathic arthritis patients. Tight control seems to be more important than the agent(s) inducing it.

Disclosure: P. Hissink Muller, None; D. Brinkman, None; D. Schonenberg-Meinema, None; Y. Koopman-Keemink, None; W. van den Bosch, None; I. Brederije, None; P. Bekker, None; T. Kuijpers, None; M. van Rossum, None; L. van Suijlekom-Smit, None; J. M. van den Berg, None; C. Allaart, None; R. ten Cate, None.

Abstract Number: 2292

Effectiveness of Common Treatment Strategies for Juvenile Arthritis in Usual Practice: Results from the Research in Arthritis in Canadian Children Emphasizing Outcomes Cohort

Amieleena Chhabra1, Adam Huber2,3, Natalie J. Shiff4, Gilles Boire5, Kim Oen6 and Jaime Guzman1, 1BC Children's Hospital, Vancouver, BC, Canada, 2IWK Health Centre, Halifax, NS, Canada, 3Dalhousie University,
SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
The efficacy of medications in randomized trials may differ substantially from their effectiveness (degree of beneficial effect under “real world” clinical settings). Reliable estimates of actual observed effectiveness of medications in usual medical practice will help parents and physicians make better-informed treatment decisions. Therefore we sought to estimate the effectiveness of common treatment strategies observed in usual practice in JIA patients followed in a large prospective inception cohort.

Methods:
Data from the Research in Arthritis in Canadian Children emphasizing Outcomes (ReACCh-Out) cohort were used to describe the observed success rate of common JIA treatment strategies. Treatment changes in each child were conceptualized as a series of n-of-1 treatment trials and systematically analyzed. A treatment trial starts with a change in treatment and concludes with the next change in treatment. The start could also be the initial treatment. Success was defined as attainment of inactive disease, or as maintenance of inactive disease when tapering treatment. Inactive disease was defined as no active joints, no extra-articular manifestation and PGA <10mm according to criteria by Wallace et al. Success rates and 95% confidence intervals (CI) were calculated for trials observed in at least 25 patients.

Results:
2962 treatment trials were observed in 1275 children; 2151 (72.6%) were step-up trials. NSAID monotherapy (usually naproxen) was trialed in 606 children, mostly as first line treatment for oligoarthritis, at a mean of 1.1 years after disease onset and had a success rate of 62%. NSAID plus joint injection (JI) had a success rate of 74% (see Table). Adding a DMARD to NSAID ±JI was trialed in 445 children. Methotrexate plus NSAID was trialed in 385 children, many with polyarticular involvement, at a mean of 1.2 years since onset and had a success rate of 67%. In logistic regression analyses, the odds of success for NSAID ±JI were reduced by each additional active joint at the start of a trial (odds ratio OR 0.90, 95%CI 0.87-0.94) and by each additional year since onset (OR 0.90, 0.81-0.99). RF negative polyarthritis, ERA and undifferentiated JIA had decrease chances of DMARD success relative to oligoarticular JIA. After adjustment for time since disease onset, number of active joints and JIA category, ankle or wrist involvement were associated with a reduced NSAID success rate (OR for ankle 0.53, 0.38-0.74; for wrist 0.66, 0.42-1.0). Similar trends were observed for response to adding a DMARD to NSAID ±JI.

Table: Success rate of various treatment strategies:
<table>
<thead>
<tr>
<th>Treatment</th>
<th>Subgroup</th>
<th>Number of patients/trials</th>
<th>Success rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAID</td>
<td>All</td>
<td>606</td>
<td>62 (58-66)</td>
</tr>
<tr>
<td></td>
<td>Naproxen</td>
<td>514</td>
<td>62 (58-66)</td>
</tr>
<tr>
<td></td>
<td>Indomethacin</td>
<td>66</td>
<td>56 (42-66)</td>
</tr>
<tr>
<td></td>
<td>Ibuprofen</td>
<td>21</td>
<td>--*</td>
</tr>
<tr>
<td></td>
<td>&lt;5 active joints</td>
<td>501</td>
<td>67 (63-71)</td>
</tr>
<tr>
<td></td>
<td>5 or more</td>
<td>105</td>
<td>36 (26-46)</td>
</tr>
</tbody>
</table>

| NSAID+JI   | All               | 298                       | 74 (69-79)            |
|            | Naproxen+JI       | 260                       | 76 (71-82)            |
|            | Indomethacin+JI   | 21                        | --*                   |
|            | Ibuprofen+JI      | 16                        | --*                   |
|            | <5 active joints  | 271                       | 75 (70-80)            |
|            | 5 or more         | 27                        | 66 (47-86)            |

| Adding DMARD to NSAID ±JI | Methotrexate | 385 | 67 (62-72) |
|                          | <5 active joints | 182 | 75 (69-82) |
|                          | 5 or more         | 203 | 60 (53-66) |

|                          | Sulfasalazine     | 60  | 62 (49-74) |

*not estimated as number was <25.

Disclosure: A. Chhabra, None; A. Huber, None; N. J. Shiff, None; G. Boire, None; K. Oen, None; J. Guzman, None.


Abstract Number: 2293

**Can We Predict Achievement of Clinically Inactive Disease and Sustained Remission in Children with Juvenile Idiopathic Arthritis?**

Stephanie Shoop-Worrall1, Suzanne M Verstappen2, Janet E. McDonagh3, Wendy Thomson4 and Kimme L. Hyrich1,
1The University of Manchester, Arthritis Research UK Centre for Epidemiology, Manchester, United Kingdom, 2Centre for Musculoskeletal Research, Faculty of Biology, Medicine and Health, Manchester Academic Health Science Centre, The University of Manchester, Arthritis Research UK Centre for Epidemiology, Manchester, United Kingdom, 3Faculty of Medical and Human Sciences, Centre for MSK Research, Manchester, United Kingdom, 4Arthritis Research UK Centre for Genetics and Genomics, The University of Manchester, Manchester, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
**Background/Purpose:** Identifying predictors for clinically inactive disease (CID) and sustained remission would allow rapid escalation of therapies for children less likely to achieve these states. This analysis assessed predictors of achievement of CID and sustained remission states over the first five years following diagnosis in children with JIA.

**Methods:** Children and young people enrolled in the Childhood Arthritis Prospective Study (CAPS), a UK multicentre inception cohort, before January 2011, were selected if diagnosed with oligoarticular, RF-negative or RF-positive polyarticular JIA.

Components for CID and sustained remission according to i) Wallace’s preliminary criteria and ii) cJADAS10 were collected at annual follow-ups to five years according to CAPS protocol. Sustained remission was defined as two consecutive follow-ups in CID. Individual baseline core outcome variables (active joint count, limited joint count, physician’s global, parental global, functional ability (Childhood Health Assessment Questionnaire (CHAQ)) and ESR) were tested for predictive ability for i) CID at one year and ii) ever sustained remission within five years. Associations were tested in multivariable logistic regressions including all COVs, age and symptom duration at initial presentation, gender, ILAR subtype and recruiting centre. Multiple imputation accounted for missing predictor and outcome data.

**Results:** Of 832 children, 70% were female and the majority had oligoarticular JIA (68%). At one year, 31% had achieved CID according to Wallace’s preliminary criteria and 44% according to the cJADAS10 (26% CID on both). Within five years, 60% had ever achieved sustained remission on Wallace’s preliminary criteria and 66% on the cJADAS10 (52% sustained remission on both).

In multivariable analyses, an increase in 0.125 points (1 unit) on the CHAQ at baseline independently predicted 4% lower odds of CID on the cJADAS10 (95% CI 0.92, 0.99). No baseline COVs predicted CID on Wallace’s preliminary criteria. An increased year of age at initial presentation to paediatric rheumatology independently predicted 12% higher odds of sustained remission on Wallace’s preliminary criteria (95% CI 1.07, 1.17). In addition, one increased unit in CHAQ at baseline independently predicted 6% lower odds of sustained remission on both outcome measures (95% CI: Wallace: 0.91, 0.99; cJADAS10: 0.90, 0.98). Compared with oligoarticular JIA, children with RF-negative polyarticular and RF-positive polyarticular JIA had at least 49% and 68% lower odds of both sustained remission states, respectively. Gender and symptom duration to initial presentation were not independently associated with either outcome.

**Conclusion:** There were different predictors for CID on the cJADAS10 vs. Wallace’s preliminary criteria although similar predictors for sustained remission using either definition were identified. Children with poor functional ability, polyarticular JIA and younger age at initial presentation could be targeted with more aggressive treatment strategies than currently in practice to better control their disease.

**Disclosure:** S. Shoop-Worrall, None; S. M. Verstappen, None; J. E. McDonagh, None; W. Thomson, None; K. L. Hyrich, None.


**Abstract Number:** 2294

**Utilizing the Pediatric Rheumatology Care and Outcomes Improvement Network to Assess Practice Pattern Variation in Juvenile Idiopathic Arthritis**

Emily A. Smitherman¹, Janalee Taylor², Esi M. Morgan¹ and C. April Bingham³, ¹Pediatric Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, ²Division of Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, ³Pediatrics, Penn State College of Medicine, Hershey, PA
Background/Purpose: Despite modern treatment options for patients with juvenile idiopathic arthritis (JIA), rates of clinical inactive disease (CID) remain low. The Pediatric Rheumatology Care and Outcomes Improvement Network (PR-COIN) includes 18 centers that serve as a representative sample for current practice. Results from the PR-COIN registry have demonstrated marked center-to-center variability in the rate of CID. The objective of this study was to survey PR-COIN centers to assess JIA practice patterns that may account for CID variation.

Methods: A survey was distributed to PR-COIN centers in October 2016 that consisted of 23 Likert items with a 7-point scale ranging from “totally disagree” = 1 to “totally agree” = 7. Practice patterns were defined as “standard methods of how care is conducted” within the local rheumatology clinic or division. The items represented evidence and consensus-based factors both specific to JIA management and adapted from chronic illness models. All items were constructed using declarative statements in the positive direction. For the analysis, the 23 items were grouped into 7 domains, including prepared proactive team, self-management, multidisciplinary team, decision support, patient access and follow-up, medication management, and quality improvement (QI) engagement. Statistical analyses included descriptive statistics for the results across individual items and summarized within domains.

Results: A total of 10 PR-COIN centers completed the practice pattern survey with a single set of responses per center. The median and range of each item and domain were calculated (Table I). A diverging stacked bar chart was constructed to illustrate the frequency of Likert responses within each item (Figure 1). Overall, the results demonstrate substantial variation in responses both across items and within items. Two items demonstrated total agreement and 5 additional items demonstrated all positive responses. However, the remaining 16 items demonstrated a wide range of responses and 12 items included at least one center that answered “totally disagree”.

Conclusion: We identified wide variation in JIA practice patterns among centers that participate in the PR-COIN network. These initial results are critical for targeting future quality improvement interventions across the network as well as launching additional investigations into the specific practices that are associated with higher rates of CID. Next steps will include semi-structured interviews with the PR-COIN centers to better characterize modifiable factors and develop a best-practice JIA bundle.
Table 1: PR-COIN Practice Pattern Survey Responses

<table>
<thead>
<tr>
<th>Question</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. My site perform some form of pre-visit planning (PVP) at least 20% of the time.</td>
<td>6</td>
<td>5-7</td>
</tr>
<tr>
<td>2. We regularly use a population management tool to revivew patients with active disease.</td>
<td>2</td>
<td>1-7</td>
</tr>
<tr>
<td>3. We are trained to assess a team patients who have ongoing active diseases.</td>
<td>2.5</td>
<td>1-7</td>
</tr>
<tr>
<td>Summary</td>
<td>5.5</td>
<td>1-7</td>
</tr>
</tbody>
</table>

Self Management

4. We regularly use self-management tools with patients and families (e.g., self-management assessment tool, barriers check list, action plans). | 4      | 1-7   |
5. Team members including prescribing providers, nurses at my site have received training in self-management principles and behavior change counseling techniques. | 4      | 1-7   |
| Summary                                                                 | 5      | 1-7   |

Shared Experience Team

6. Our patients and families have easy access to OPI/P appointments. | 5      | 1-7   |
7. We have an OPI/P dedicated to pediatric rheumatology at our site. | 2      | 1-7   |
8. Our patients and families have easy access to OT, if needed. | 8      | 1-7   |
9. A social worker meets with all newly diagnosed JIA patients at our site. | 2.5    | 1-7   |
10. A child life specialist is available for patients, if needed. | 7      | 1-7   |
11. Nurses with pediatric rheumatology expertise are available in all clinics at the time. | 7      | 1-7   |
| Summary                                                                 | 6      | 1-7   |

Decision Support

12. We use and regularly update functional assessment tool results. | 5      | 1-7   |
13. We use algorithms to standardize treatment approaches for patients with active disease. | 5      | 1-7   |
| Summary                                                                 | 5      | 1-7   |

Patient Access and Follow-up

14. Our patients get a call back for a medical concern within 1 day by a nurse or physician. | 7      | 1-7   |
15. Appointment lists are available when needed. | 6.5    | 1-7   |
16. We have a system in place to keep track of patients who do not come back for follow up as recommended. | 3      | 1-7   |
17. Patients with active disease are seen within 1 week. | 6      | 1-7   |
| Summary                                                                 | 6      | 1-7   |

Medication Management

18. Joint injections are performed within 2 weeks of ordered need for all patients. | 9      | 3-7   |
19. Most prescribers provide my site generally initiate DMARDs within 2 months after diagnosing polyarticular or systemic JIA. | 7      | 1-7   |
20. Most prescribers provide my site initiate treatment within 3-4 months of patients who have active disease who are not responding to treatment. | 7      | 1-7   |
| Summary                                                                 | 7      | 3-7   |

QI Engagement

21. All prescribing providers at my site are PR-COIN. | 7      | 1-7   |
22. All prescribing providers at my site participate in PQB/PR-COIN improvement activities for JIA patients. | 7      | 1-7   |
| Summary                                                                 | 7      | 1-7   |

Figure 1. Diverging stacked bar chart showing responses across PR-COIN centers to JIA practice pattern survey with 7-point Likert scale.

Disclosure: E. A. Smitherman, None; J. Taylor, None; E. M. Morgan, None; C. A. Bingham, None.
Methotrexate As First Line Therapy in Juvenile Idiopathic Arthritis-Associated Uveitis: Myth or Reality

Jacopo Agnolucci¹, Maria Elisabetta Zannin¹, Giorgia Martini¹, Alessandra Meneghel² and Francesco Zulian², 
¹Department of Woman and Child Health, University of Padua, Padua, Italy, ²University of Padua, Department of Woman and Child Health, Padua, Italy

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Methotrexate (MTX) is the most used immunomodulatory drug in Juvenile Idiopathic Arthritis-associated uveitis (JIA-U) although its efficacy has been shown only in retrospective studies with limited number of subjects, short follow up and sometimes questionable methodology. The timing of MTX start in JIA-U as well as of switch from first and second-line therapy are still controversial. Aim of the present study was to evaluate the efficacy of MTX as first-line therapy in a monocentric inception cohort of patients with JIA-U.

Methods: Patients with JIA-U refractory to local eye drops treatment were managed by a standard protocol including MTX, at a standard dose of 10-15 mg/m²/week, as first line systemic treatment. Data, recorded every 3 months, included ocular flares and complications, drug-related adverse events (AE) and treatment change. The diagnosis of JIA was based upon the ILAR criteria¹ and the diagnosis of uveitis was made according to the SUN Criteria². Uveitis flare was defined as an increase of cells in the anterior chamber of 2+ or more as compared to the baseline. Clinical remission was defined as the absence of flares for more than 6 months on treatment, without or with minimal topical treatment (corticosteroid and/or mydriatic-cycloplegic eye drops ≤ 1/day). Data of patients treated for at least 1 year were analyzed using descriptive statistics.

Results: 84 consecutive JIA patients (71 F, 13 M), 82 oligoarticular, 2 polyarticular, treated with MTX for JIA-U and at least one year f/u entered the study. Mean age at MTX start was 5.7 years (1.8–21.6); mean f/u since MTX start 8.9 y (1–20 y). 68 patients started MTX primarily to treat uveitis (group A) (JIA duration 1.8 y), 16 patients introduced MTX for arthritis (group B) (JIA duration 0.54 y). The mean interval time between arthritis and uveitis onset was 0.8 y in group A and 2.1 y in group B (p<0.01). After treatment start, 25% relapsed with uveitis flare by 5 months, 50% by 9.7 mo and 75% by 36 mo. At the last evaluation, 40 pts (47.6%), 28 in group A and 12 in group B, needed anti-TNF therapy to control uveitis flares; 35 (41.7%) were in remission on medication and only 9 (10.7%) (all in group A) reached a complete remission at a mean f/u of 39.4 mo.

Conclusion: MTX loses its efficacy quite rapidly overtime and ensures clinical remission only in a minority of patients. When started before uveitis, MTX delays the uveitis onset but does not prevent its severe course.

References

Infliximab Use in JIA and Uveitis: Does Methotrexate Help or Hinder?

Ryan Funk¹, Valentina Shakhnovich², Leon van Haandel³ and Mara L Becker⁴, ¹University of Kansas Medical Center, Kansas City, KS, ²Gastroenterology and Clinical Pharmacology, Toxicology and Therapeutic Innovation, Children's Mercy Kansas City, Kansas City, MO, ³Clinical Pharmacology, Medical Toxicology, and Therapeutic Innovation, Children's Mercy Kansas City, Kansas City, MO, ⁴Rheumatology, Children's Mercy Kansas City, Kansas City, MO

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Infliximab (IFX) effectiveness is impacted in part by immunogenicity and the development of drug neutralizing anti-drug antibodies, thus methotrexate is commonly co-administered to minimize the immune response to IFX. However the mechanism by which MTX impacts IFX concentrations and anti-drug antibody formation is unknown. In adults with Rheumatoid Arthritis, higher concentrations of MTX polyglutamates (MTXGlu₃) were associated with lower drug antibody formation, suggesting that MTXGlu may impact IFX pharmacokinetics (1), however, little is known in children.

Methods: This is a cross-sectional study of patients receiving IFX at Children’s Mercy Kansas City (n=97) and included patients with Inflammatory Bowel Disease (IBD n= 73), Juvenile Idiopathic Arthritis (JIA n=16), and childhood uveitis (CU n=8). 35 patients were on concomitant MTX therapy (26% IBD, 75% JIA, 75% CU). Serum trough samples were analyzed for IFX and anti-IFX antibodies using a NF-κβ luciferase gene-reporter assay (ARUP Laboratories), and for erythrocyte MTXGluₙ levels by HPLC-MS/MS. Clinical data were collected by chart review. Statistical testing was conducted by Wilcoxon-rank sum or Spearman’s rank correlation analysis, and data were log transformed for regression analyses.

Results: Despite wide variations in dose, frequency, and trough IFX concentrations between groups, when normalized for variation in dose and frequency (NormIFX), troughs were not statistically different (median (IQR) in IBD: 3.5 (1.8, 5.2), JIA: 4.1 (2.3, 5.6), and CU: 4.4 (3.4, 5.6)). Only 3 IBD patients had anti-IFX Ab detected, and they had significantly lower median NormIFX concentrations (3.9 (2.2, 5.3) vs. 0 (0, 0) p<0.01), but no difference in MTXGluₙ concentrations, although only 1 patient was receiving MTX concurrently. When the JIA and CU patients were evaluated separately, there was a negative association between long chain MTXGlu₃₋₆ formation and NormIFX levels for JIA (ρ -0.81 p=0.005) and CU (ρ -0.94 p=0.005). This remained significant despite controlling for MTX dose and route in a linear regression model (JIA p=0.04, CU p= 0.04). In JIA patients, higher NormIFX levels were associated with lower cJADAS (ρ -0.72 p=0.009).

Conclusion: Anti-IFX Ab were rarely observed in this cohort of patients, and only seen in children whose trough IFX levels were undetectable. Once normalized for dose and frequency, trough IFX concentrations were not statistically significantly different between disease groups, although JIA and CU troughs were higher. In JIA and CU, but not IBD, MTXGluₙ accumulation negatively impacted NormIFX trough levels, suggesting mechanisms by which MTX enhances infliximab effectiveness may be independent of MTXGluₙ formation and may also be disease specific.
Golimumab Versus Tocilizumab in Uveitis Related to Refractory Juvenile Idiopathic Arthritis. National Multicenter Study of 33 Patients

Lucia C. Domínguez-Casas1, Vanesa Calvo-Río1, Inmaculada Calvo2, Mª Isabel González-Fernández3, Berta Lopez Montesinos3, Marina Mesquida4, Alfredo Adan4, M. Victoria Hernández4, Olga Maiz-Alonso5, Ana Blanco6, Antonio Atanes7, Beatriz Bravo8, Consuelo Modesto9, Gisela Diaz-Cordovés10, Miguel Cordero-Coma11, David Diaz-Valle12, Carlos Fernández-Cid13, Juan Cruz14, Oscar Ruiz Moreno15, MC Gonzalez-Vela16, Rosalía Demetrio-Pablo17, Nuria Vegas-Revenga1, Carlos Fernández-Diaz1, Jose L. Hernández18, Miguel Angel González-Gay1 and Ricardo Blanco1


First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Uveitis is a severe manifestation of Juvenile Idiopathic Arthritis (JIA). Systemic treatment is based on conventional immunosuppressants. Anti-TNFα are used in refractory cases, mainly adalimumab (ADA) or infliximab (IFX) (Levy-Clarke et al. Ophthalmology 2014). However, sometimes they are ineffective, contraindicated or non tolerated. The next...
therapeutic step is not defined. The main objective of this study was to compare Golimumab (GLM) vs Tocilizumab (TCZ) in uveitis related to JIA and refractory to conventional immunosuppressive drugs and anti-TNFα drugs.

Methods:

National multicenter study of 33 patients diagnosed with uveitis associated to JIA. The patients were refractory to conventional treatment with high dose of corticosteroids and at least a) 1 conventional immunosuppressive systemic treatment and b) 1 anti-TNFα. For this reason it was decided to initiate treatment with TCZ or GLM. TCZ was used in 25 patients: 8 mg/kg/4 w/iv (n=21), 8 mg/kg/2 w/iv (n=2); 8 mg/kg/8 w/iv (n=1) and 2.9 mg/kg sc/w (n=1). GLM was used in 8 patients (50 mg/sc/month). The main parameters assessed were the visual acuity (VA), degree of intraocular inflammation, vitreous inflammation and macular thickening (by OCT). Quantitative variables were expressed with mean±SD or median [IQR], according to its distribution. They were compared with the Student t or the Mann-Whitney U test, respectively. Dichotomous variables were expressed as percentages and compared by the chi-square test.

Results:

We studied 33 patients/61 affected eyes. There were no significant differences between both groups at baseline (TCZ vs GLM) in sex (♂/♀;4/21 vs 3/5; p=0.19), mean age (18.5±8.3 vs 19.9±8.7; p=0.55), positive ANA (95% vs 100%; p=0.7), uveitis duration before TCZ or GLM onset (116.4±93.6 vs 142.3±74.7 p=0.46), number of previous biological treatments (1.9±1.1 vs 2±1.4; p=0.84), VA (0.57±0.35 vs 0.5±0.37; p=0.42), combined immunosuppressive therapy (88% vs 75%; p=0.37), presence of cells in the anterior chamber (median [IQR] 1 [0-1] vs 1 [0.25-1.5]%; p=0.6), vitritis (0 [0-0] vs 0 [0-1]; p=0.7), macular thickening (358.7±92.2 vs 313.6±77.1; p=0.32).

Once the treatment was initiated there were no significant differences in the ocular parameters TABLE.

After a mean follow-up of 20.48±11.7 months with TCZ and 24.25±17 months with GLM the following side effects were observed; with TCZ: viral conjunctivitis + bullous impetigo (n=1), severe thrombocytopenia and pneumonia. This last patient showed hemolytic anemia, thrombocytopenia and splenomegaly, for this reason treatment with TCZ was discontinued. With GLM cutaneous reaction was observed in 2 patients.

Conclusion:

This study shows that both, TCZ and GLM, appear to be equally effective and safe for the treatment of uveitis associated to JIA refractory to conventional treatment and anti-TNFα. Further studies should be performed.

TABLE
<table>
<thead>
<tr>
<th></th>
<th>TCZ (n=25)</th>
<th>GLM (n=8)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Basal</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VA</td>
<td>0.57±0.35</td>
<td>0.5±0.36</td>
<td>0.43</td>
</tr>
<tr>
<td>Cells in the anterior chamber</td>
<td>0.92±0.81</td>
<td>2.79±4.82</td>
<td>0.63</td>
</tr>
<tr>
<td>Vitritis</td>
<td>0.43±0.91</td>
<td>0.33±0.5</td>
<td>0.78</td>
</tr>
<tr>
<td>OCT</td>
<td>358.69±92.17</td>
<td>313.60±77.05</td>
<td>0.31</td>
</tr>
<tr>
<td><strong>1st month</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VA</td>
<td>0.59±0.33</td>
<td>0.56±0.32</td>
<td>0.75</td>
</tr>
<tr>
<td>Cells in the anterior chamber</td>
<td>0.26±0.52</td>
<td>2.33±4.57</td>
<td>0.083</td>
</tr>
<tr>
<td>Vitritis</td>
<td>0.31±0.71</td>
<td>0±0</td>
<td>0.32</td>
</tr>
<tr>
<td>OCT</td>
<td>313.40±91.28</td>
<td>292.50±111.42</td>
<td>0.57</td>
</tr>
<tr>
<td><strong>6th month</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VA</td>
<td>0.63 ±0.32</td>
<td>0.62±0.33</td>
<td>0.85</td>
</tr>
<tr>
<td>Cells in the anterior chamber</td>
<td>0.1±0.34</td>
<td>0±3.28</td>
<td>0.43</td>
</tr>
<tr>
<td>Vitritis</td>
<td>0.07±0.33</td>
<td>0.25±0.62</td>
<td>0.62</td>
</tr>
<tr>
<td>OCT</td>
<td>274.91±101.32</td>
<td>261.37±75.15</td>
<td>0.94</td>
</tr>
<tr>
<td><strong>1st year</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VA</td>
<td>0.63 ±0.34</td>
<td>0.54 ±0.31</td>
<td>0.35</td>
</tr>
<tr>
<td>Cells in the anterior chamber</td>
<td>0±0.2</td>
<td>0±0</td>
<td>0.71</td>
</tr>
<tr>
<td>Vitritis</td>
<td>0.058±0.23</td>
<td>0±0</td>
<td>0.81</td>
</tr>
<tr>
<td>OCT</td>
<td>245.45±29.34</td>
<td>255±120.8</td>
<td>0.74</td>
</tr>
</tbody>
</table>
Results are expressed as mean±SD

**Disclosure:** L. C. Domínguez-Casas, None; V. Calvo-Río, None; I. Calvo, None; M. I. González-Fernández, None; B. Lopez Montesinos, None; M. Mesquida, None; A. Adan, AbbVie, Santen and Allergan, 9; M. V. Hernández, None; O. Maiz-Alonso, None; A. Blanco, None; A. Atanes, None; B. Bravo, None; C. Modesto, None; G. Díaz-Cordovés, None; M. Cordero-Coma, None; D. Diaz-Valle, None; C. Fernández-Cid, None; J. Cruz, None; O. Ruiz Moreno, None; M. Gonzalez-Vela, None; R. Demetrio-Pablo, None; N. Vegas-Revenga, None; C. Fernández-Díaz, None; J. L. Hernández, None; M. A. Gonzalez-Gay, None; R. Blanco, None.


Abstract Number: 2298

**Etanercept, Adalimumab and Methotexate Utilization By Juvenile Idopathic Arthritis Patients and the Occurrence of Uveitis**
SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Juvenile idiopathic arthritis (JIA) is a chronic arthritis with onset before 16 years of age, that persists for at least 6 weeks, and has an unknown etiology. Uveitis is a serious and common extra-articular manifestation of JIA, affecting 12-30% of patients (most commonly female patients with the antinuclear antibody-positive oligoarthritis subtype of JIA). First-line treatment for JIA-associated uveitis is usually topical corticosteroids and/or conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs), such as methotrexate (MTX). Biologic DMARDs (bDMARDs), such as the TNF inhibitors etanercept (ETN) and adalimumab (ADA), are used after failure of first-line treatments. However, it has been reported that ETN use is associated with uveitis flares or new-onset uveitis while a recent observational study reported similar uveitis flare rates for both ADA and ETN. The objective of this study was to analyze the occurrence of uveitis in patients with JIA treated with ETN, ADA, or MTX (as monotherapy and as part of combination therapy).

Methods: International Statistical Classification of Diseases (ICD)-9 diagnosis codes in a Truven MarketScan claims database were used to identify JIA patients diagnosed with uveitis over a 5-year interval. The analysis assessed the proportion of JIA patients (aged 0-19 years) treated with ETN, ADA, or MTX, as monotherapy or in combination. The percentage of patients diagnosed with uveitis and the time interval for uveitis diagnosis in JIA patients were determined.

Results: A total of 22,789 patients with JIA were included in this analysis. Mean age was 11.4 years, 69% of patients were female, and mean JIA disease duration was 3 years. This patient population included 19,814 patients with chronic, or not otherwise specified, polyarticular JIA. A total of 2581 (11.3%) patients (mean age 10.2 years, 73% female) were diagnosed with uveitis. There was no apparent difference in the percentage of JIA patients receiving ETN, ADA, or MTX who were diagnosed with uveitis. A total of 2.7-5.9% of patients receiving monotherapy were diagnosed with uveitis compared with 3.2-3.6% of patients receiving combination therapy (Figure). The vast majority of patients (2123 of 2581, 82.3%) with uveitis were diagnosed within a year of their JIA diagnosis.

Conclusion: In this patient database, a similar proportion of patients with JIA who were treated with ETN or ADA (either as monotherapy or in combination with MTX) received a subsequent diagnosis of uveitis.

References

Prospective outcomes of the management of aortic valve stenosis

 Disclosure: K. Roshak, Pfizer Inc, 3; J. M. Sopczynski, Pfizer Inc, 1,Pfizer Inc, 3; R. Suehiro, Pfizer Inc, 1,Pfizer Inc, 3; L. Marshall, Pfizer Inc, 1,Pfizer Inc, 3.


Abstract Number: 2299

Clinical Features and Characteristics of Juvenile Idiopathic Arthritis-Associated Uveitis in Japan: the First Report from the Pediatric Rheumatology Association of Japan (PRAJ)

Junko Yasumura1, Masato Yashiro2, Nami Okamoto3, Kosuke Shabana4, Hiroaki Umebayashi5, Naomi Iwata6, Tomohiro Kubota7, Mao Mizuta8, Kenichi Nishimura9, Yuka Okura10, Masaki Shimizu8, Minako Tomiita11, Syuji Takei7 and Masaaki Mori12, 1Department of Pediatrics, Hiroshima University Graduate School of Biomedical & Health Sciences, Hiroshima, Japan, 2Department of Pediatrics, Okayama University Hospital, Okayama, Japan, 3Pediatrics, Graduate School of Medicine, Osaka Medical College, Takatsuki, Japan, 4Department of Pediatrics, Graduate School of Medicine, Osaka Medical College, Takatsuki, Japan, 5Department of Rheumatics, Miyagi Children’s Hospital, Sendai, Japan, 6Department of Immunology and Infectious Diseases, Aichi Children’s Health and Medical Center, Obu, Japan, 7Department of Pediatrics, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima, Japan, 8Department of Pediatrics, Graduate School of Medical Sciences, Kanazawa University, Kanazawa, Japan, 9Department of Pediatrics, Yokohama City University Graduate School of Medicine, Yokohama, Japan, 10Department of Pediatrics, KKR Sapporo Medical Center, Sapporo, Japan, 11Department of Allergy and Rheumatology, Chiba Children's Hospital, Chiba, Japan, 12Department of Lifetime Clinical Immunology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Background/Purpose: Several reports examined ethnic differences of Juvenile Idiopathic Arthritis -associated uveitis (JIA-U), however, there were no information from Japan. Therefore, PRAJ underwent multi-center surveillance in Japan to clarify the clinical and epidemiologic characteristics of JIA-U.

Methods: Questionnaires were sent to pediatric rheumatologists in Japan to investigate clinical characteristics of JIA patients.

Results: Of 726 patients involved in this study, 44 (6.1%) had JIA-U during the whole disease course. Overall 682 non-uveitis JIA patients were compared with 44 JIA-U patients. Female ratio in non-uveitis vs JIA-U was 67.6% vs 70.5% ($P=0.7425$). Age at JIA diagnosis was 7.3 (4.5) vs 4.9 (4.0) (mean (SD)) years old ($P<0.0001$). The subtype of arthritis was shown in Table. There were no patients with uveitis in poly-RF positive and systemic type. Positivity for ANA was 57.5%, for RF was 2.5% and ACPA was 0% in JIA-U patients and that of ANA was significantly higher than non-uveitis JIA patients($P<0.0001$). There were no family histories of uveitis and episodes of infection before onset of uveitis. The mean age at diagnosis of uveitis was 5.5 (2.7) (mean(SD)) years old and the age under 8 years old were 82.5%. Uveitis occurred before the onset of arthritis in 5.0%, within the first 7 years after onset of arthritis in 97.5%. On the other hand, uveitis occurred during arthritis treatment in 35% and after off therapy in 20%. It occurred bilateral in 55.3% and 82.1% was anterior. 64.9% had no eye symptom, 36.8% had ocular complications (cataracts, posterior synechia of the iris, etc.), and 58% had active arthritis at the first diagnosis of uveitis. 39.5% had uveitis without arthritis at the last visit. There were no blindness, but eyes of 56.9% were not improved visual acuity at the last visit.

Conclusion: This is the first report of characteristics of JIA-U in Japan. Prevalence of JIA-U in Japan is lower than that of other country that were reported before. The reason may be because ratio of oligo-type JIA patients is lower in Japan than that of other country, though the risk factor of JIA-U of Japanese patients (oligo-type arthritis, ANA positive, early onset arthritis, RF negative) is similar that of reports from other country.

<table>
<thead>
<tr>
<th>JIA subtype</th>
<th>overall (N=726)</th>
<th>without uveitis (N=682)</th>
<th>with uveitis (N=44)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oligo persistent</td>
<td>184 (25.3%)</td>
<td>155 (22.7%)</td>
<td>29 (65.9%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Oligo extended</td>
<td>40 (5.5%)</td>
<td>33 (4.8%)</td>
<td>7 (15.9%)</td>
<td>0.0076</td>
</tr>
<tr>
<td>Poly RF(-)</td>
<td>95 (13.1%)</td>
<td>90 (13.2%)</td>
<td>5 (11.4%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Poly RF(+)</td>
<td>152 (20.9%)</td>
<td>152 (22.3%)</td>
<td>0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systemic</td>
<td>204 (28.1%)</td>
<td>204 (29.9%)</td>
<td>0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Psoriatic</td>
<td>4 (0.6%)</td>
<td>4 (0.6%)</td>
<td>0</td>
<td>1.000</td>
</tr>
<tr>
<td>Enthesitis related</td>
<td>37 (5.1%)</td>
<td>35 (5.1%)</td>
<td>2 (4.6%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Undifferentiated</td>
<td>10 (1.4%)</td>
<td>9 (1.3%)</td>
<td>1 (2.3%)</td>
<td>0.467</td>
</tr>
</tbody>
</table>

Fisher's exact test (two-tailed test)

Disclosure: J. Yasumura, None; M. Yashiro, None; N. Okamoto, None; K. Shabana, None; H. Umebayashi, None; N. Iwata, None; T. Kubota, None; M. Mizuta, None; K. Nishimura, None; Y. Okura, None; M. Shimizu, None; M. Tomiita, None; S. Takei, None; M. Mori, None.

Predictive Value of Magnetic Resonance Imaging in Patients with Juvenile Idiopathic Arthritis in Clinical Remission

Clara Malattia¹, Marta Mazzoni Sr.², Stefania Viola Sr.², Angela Pistorio³, Francesca Magnaguagno⁴, Alessia Urro Jr.², Angelo Ravelli⁵ and Alberto Martini⁶, ¹Pediatria2 Reumatologia, Istituto Giannina Gaslini, Genoa, Italy, ²Pediatria 2 Reumatologia, Istituto Giannina Gaslini, Genova, Italy, ³Istituto Giannina Gaslini - Pediatria II, Reumatologia - PRINTO, Genoa, Italy, ⁴UO Radiologia, Istituto Giannina Gaslini, Genoa, Italy, ⁵University of Genova, IRCCS Istituto Giannina Gaslini, Genova, Italy, ⁶Istituto Giannina Gaslini, Genoa, Italy

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
MRI studies on RA revealed that subclinical synovitis is common in patients in clinical remission and it is responsible for structural damage progression. MRI-detected synovitis in JIA patients with clinically inactive disease was also reported. Due to the lack of longitudinal studies in JIA, it is unclear whether this phenomenon entails an higher risk of joint damage progression and should affect treatment decisions.

Objectives: to assess the prevalence of MRI-detected synovitis in a cohort of JIA patients in clinical remission and to evaluate its association with disease flare and damage progression.

Methods:
all JIA patients who met the Wallace criteria for clinical remission and underwent contrast-enhanced MRI at the Study Unit between 2007 and 2015 were included. MRIs were scored by two independent readers according to the Outcome Measure in Arthritis Clinical Trials (OMERACT) Rheumatoid Arthritis Scoring System (RAMRIS). Joint damage progression was assessed by conventional radiography (CR) according to the adapted versions of the Sharp/van der Heijde score and to the Childhood Arthritis Radiographic Score of the Hip. The concordance between the readers was assessed using kappa statistics. Categorical data were analyzed using chi-squared test and Fisher’s exact test. Comparison of quantitative variables was performed by the non-parametric Mann–Whitney U-test. A logistic regression model was applied to perform multivariate analysis of the radiographic damage risk factors.

Results: a total of 90 patients (75 F; mean age 13.8 years; mean disease duration 8.5 years; mean follow-up duration 2.9 years) were included. Fourteen out of 90 patients (15.6%) were in remission off medication, while 76/90 patients (84.4%) were in remission on medication. Forty-five patients were assessed by MRI in the wrist, 30 in the hips, 13 in the ankle and 2 in the knee. Fifty-seven patients (63.3%) had evidence of synovitis on MRI. The inter-observer agreement for presence/absence of synovitis was good (k=0.74; 95% CI: 0.5-0.9). Forty-three out of 57 patients (75.4%) with synovitis experienced a disease flare versus 11 out of 33 patients (33.3%) who hadn't any synovial inflammation (P<0.0001). Radiographic progression was assessed in 54/90 patients for whom follow-up CRs were available and was detected in 19/54 patients (35.2%). A significant association between systemic JIA subtype and deterioration of joint damage was found (P=0.027). MRI-detected bone marrow oedema (BMO) and the baseline radiographic damage scores were also related to structural progression (P=0.002). The multivariable logistic regression analysis showed that only BMO score ≥3 independently contributed to explain radiographic damage progression (OR 4.82; 95% CI: 1.0-23.2; P=0.035).

Conclusion:
A sizeable proportion of patients in clinical remission has MRI evidence of persistent joint inflammation. Subclinical synovitis was significantly associated with disease flare, while BMO showed remarkable promise in predicting joint destruction. These findings support the utility of MRI for the assessment of JIA patients in clinical remission and may have important clinical implications for their management.

Disclosure: C. Malattia, None; M. Mazzoni Sr., None; S. Viola Sr., None; A. Pistorio, None; F. Magnaguagno, None; A. Urro Jr., None; A. Ravelli, None; A. Martini, GASLINI Hospital, 3,Astellas, AstraZeneca, Bristol-Myers Squibb, Italfarmaco, and MedImmune, 8,AbbVie Inc., AstraZeneca, Bristol-Myers Squibb, Janssen Biologies B.V., Eli Lilly and Co., “Francesco Angelini”, GlaxoSmithKline, Italfarmaco, Novartis, Pfizer, Roche, Sanofi Aventis, Schwarz Biosciences GmbH, Xoma, and Wyeth Pharmaceuticals, 2.


Abstract Number: 2301

Assessing the Utility and Impact of Musculoskeletal Ultrasound in a Large Pediatric Rheumatology Clinic

Onengiya Harry1, Jennifer L. Huggins2, Janalee Taylor3, Michael J. Holland4 and Tracy Ting5, 1Cincinnati Childrens' Hospital Medical Center, Cincinnati, OH, 2Pediatrics, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 3Division of Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 4Pediatric Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 5Rheumatology/MLC 4010, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Musculoskeletal ultrasound (MSUS) use in the care of pediatric rheumatology patients is increasing. Yet, despite the growing availability of MSUS, it remains unclear how best to utilize ultrasound within a busy pediatric rheumatology clinic - and how its results might affect patient care. A questionnaire was developed to assess the following: reasons for referral, correlation with clinical assessment, changes to management, and the patient/parent experience. The aim of this study is to evaluate physicians’ responses on the utility and impact of MSUS.

Methods: Beginning September 2016, pediatric rheumatology providers from a large tertiary care center with an established MSUS clinic were given a short questionnaire after the completion of a patient MSUS session. The questionnaire included 4 main outcome variables: normal or abnormal MSUS findings, consistency of MSUS results with clinical exam, family’s response to MSUS, and impact on management decisions. Secondary outcomes were: reasons for referral, how MSUS findings correlate to clinical exam (better, worse, or same), aid in family’s understanding of diagnosis, and influence on clinical management - (no change, maximize dose of medication, perform joint injection, or other). Descriptive analysis was performed on collected responses with frequency distribution reported for each variable.

Results: Survey responses were collected on 86 patients. The majority of referrals were placed to evaluate the extent of disease activity. Other reasons included the identification of active joint/tendon(s) for possible joint injection and in instances of discordance between clinical exam and patient symptoms. 80% of the MSUS results were abnormal; and 51% of the time, providers did not anticipate the results. While 51% of MSUS findings were consistent with clinical
exam, 41% identified more active joint/tendon(s). 66.3% of the time MSUS result had an impact on management decision. Of the 57 cases where MSUS influenced clinical management: 46% had medications maximized and 44% underwent joint injection. Providers reported that 97% of families found MSUS helpful in general; while 81% found it useful in their understanding of their child’s disease.

**Conclusion:** MSUS is a valuable tool to complement clinical examination in the care of children with rheumatologic disease. For a majority of referred patients, MSUS helped to assess disease activity and shape clinical management. MSUS can be an important screening tool in identifying worsening, or improving, disease than may be clinically apparent. This ongoing study suggests that there may be a role for MSUS in educating parents/children about their disease. A survey of families is needed to better clarify the impact of MSUS on their understanding of their disease.

**Disclosure:** O. Harry, None; J. L. Huggins, Pfizer Inc, 2; J. Taylor, None; M. J. Holland, None; T. Ting, None.


**Abstract Number:** 2302

**The Impact of JIA on Physician and Patient-Reported Outcomes over the First Five Years Following Diagnosis**

**Stephanie Shoop-Worrall**¹, Suzanne M Verstappen², Janet E. McDonagh³, Wendy Thomson⁴ and Kimme L. Hyrich⁴, ¹The University of Manchester, Arthritis Research UK Centre for Epidemiology, Manchester, United Kingdom, ²Arthritis Research UK Centre for Epidemiology, Centre for Musculoskeletal and Dermatology Research, Faculty of Medicine, Biology and Health, United Kingdom, University of Manchester, Manchester, United Kingdom, ³Faculty of Medical and Human Sciences, Centre for MSK Research, Manchester, United Kingdom, ⁴National Institute of Health Research Manchester Musculoskeletal Biomedical Research Centre, Central Manchester NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, United Kingdom

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Information regarding longer-term outcomes in JIA largely pre-date the introduction of biologic therapies and have been cross-sectional. The aim of this analysis was to assess physician and parent-reported outcomes over the first 5 years following initial presentation to paediatric rheumatology in young people diagnosed with JIA since 2001.

**Methods:** Young people with JIA of any disease subtype were selected if enrolled in the Childhood Arthritis Prospective Study (CAPS), a UK multicentre inception cohort, between October 2001 and January 2011. The following outcomes were assessed annually to five years and included in this analysis: Active joint count, limited joint count, physician’s global assessment (10cm visual analogue score (VAS)), parental global evaluation (10cm VAS), pain (10cm VAS), functional ability (Childhood Health Assessment Questionnaire (CHAQ) and psychosocial health (psychosocial scale on the Child Health Questionnaire (CHQ)).

Outcomes were assessed descriptively over time and differences between subtypes were assessed by applying multilevel (patient-level) zero-inflated negative binomial (CHAQ) and linear (all other outcomes) regression analyses, adjusting for age and disease duration at presentation, gender and hospital.
**Results:** Of 1087 young people, 67% were female and median age at initial presentation to paediatric rheumatology was 8 years (IQR 3, 12). The most common disease subtype was oligoarthritis (52%) and least common RF-positive polyarticular JIA (4%). Eighty four percent had ever been treated with NSAIDs, 74% corticosteroids, 55% with DMARDs and 21% with biologics within follow-up.

In the entire cohort, all outcomes were mild to moderate at baseline (median 2 active joints, 1 limited joint, physician’s global 2.9cm, patient global 2.2cm, pain 3.1cm, CHAQ 0.8 and CHQ psychosocial 50). Overall improvements were evident in all outcomes over the first year then remained stable with no further improvements at the cohort level to five years.

Compared with those with oligoarticular JIA, patients with both polyarthritis and systemic subtypes experienced significantly poorer outcomes across all variables. The most extreme point estimates were experienced in RF-positive polyarticular JIA, having 3 more active and limited joints (both 95% CI 2, 4), 1cm higher physician’s (95% CI 0.4, 1.2), parental (95% CI 0.5, 1.9) and pain (95% CI 0.3, 1.8) scores and 50% higher CHAQ scores (95% CI 1.2, 1.7). Young people with enthesitis-related, psoriatic and undifferentiated JIA experienced largely similar outcomes to those with oligoarthritis over follow-up.

**Conclusion:** On average, the largest improvement in physician and patient-reported outcomes occur in the first year following diagnosis, perhaps confirming the importance of early treat-to-target strategies. Patients with systemic and both polyarticular JIA subtypes have poorer parent and physician-reported outcomes than those with enthesitis-related, psoriatic, undifferentiated or oligoarthritis.

**Disclosure:** S. Shoop-Worrall, None; S. M. Verstappen, None; J. E. McDonagh, None; W. Thomson, None; K. L. Hyrich, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/the-impact-of-jia-on-physician-and-patient-reported-outcomes-over-the-first-five-years-following-diagnosis](http://acrabstracts.org/abstract/the-impact-of-jia-on-physician-and-patient-reported-outcomes-over-the-first-five-years-following-diagnosis)

Abstract Number: 2303

**Six Minute Walk Test in Children with Juvenile Idiopathic Arthritis: Normative Values, Prediction Equation, and Comparison to Healthy Children**

**Dax G. Rumsey**1,2, Michelle Roy1, Cara Kaup1, Lyne Bourassa3, Elham Khodayari Moez4, Olaf Verschuren5 and Lesley Pritchard-Wiart1,3; 1Glenrose Rehabilitation Hospital Edmonton, Edmonton, AB, Canada, 2Paediatrics, University of Alberta, Edmonton, AB, Canada, 3Physical Therapy, University of Alberta, Edmonton, AB, Canada, 4School of Public Health, University of Alberta, Edmonton, AB, Canada, 5Brain Center Rudolf Magnus and Center of Excellence for Rehabilitation Medicine, University Medical Centre Utrecht, Utrecht, Netherlands

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

The 6-minute walk test (6MWT) is a widely used measure of functional exercise capacity. It has not, however, been routinely used in pediatric rheumatology practice to date. There is little known about normative values for children with
rheumatic disease, including juvenile idiopathic arthritis (JIA). The objectives of this study were to: 1) describe normative values for patients with JIA; 2) investigate which characteristics best predict 6-minute walk distance (6MWD) in this population and establish a prediction equation; and 3) compare 6MWD in patients with JIA to published values for healthy children.

Methods:

At the Glenrose Rehabilitation Hospital in Edmonton, Canada, we have been administering the 6MWT to our JIA patients every 6 months since June 2013. We performed a retrospective chart review of 116 unique patients with a total of 272 6MWTs. Each 6 MWT was administered on a 25 m track by a therapy assistant. Sex, weight, height, date of birth, testing date, JIA subtype, and lower limb involvement (active and chronic) were recorded. A mixed effects model was used to analyze the data. Univariate modelling of outcome (6MWD) vs. potential predictors was conducted. Variables with p ≤ 0.2 were selected for inclusion in the final model (cross-sectional age, longitudinal age, height and weight). To address objective 3, predicted 6MWT distances were calculated according to established prediction equations for healthy children developed by Geiger et al. (2007) and Ben Saad et al. (2009). Percentage of predicted values were calculated using actual 6MWDs.

Results:

Normative values for children with JIA are presented in Table 1. The final prediction model for our population was 6MWD = 161.45 + cross-sectional age(years)*2.33 + longitudinal age *15.86 + height (m)*2.954 – weight (kg)*1.79; \( r^2 = 0.62 \). All other factors, including sex, lower limb involvement, and JIA subtype were not significant and therefore were excluded from the model. The 6MWDs of children with JIA were lower than reported for typically developing children (Geiger =84%, range 59%-109% of predicted; Ben Saad = 78%, range 53% -107% of predicted).

Conclusion:

This study provides normative values and a prediction equation for the 6MWT for children with JIA. Reference values are clinically relevant as they provide a user-friendly method for the interpretation and prediction of functional exercise capacity. The characterization of functional exercise capacity in children with JIA could provide the basis for an outcome measurement in this population. The difference in 6MWD between children who are typically developing and the children with JIA shows that children with JIA have impaired functional exercise capacity.

Table 1: 6 MWT Results by Age

<table>
<thead>
<tr>
<th>Age (years) (n)</th>
<th>Height, cm (mean,SD)</th>
<th>Weight, kg (mean,SD)</th>
<th>Mean 6MWD, m (mean,SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 (15)</td>
<td>120 (3)</td>
<td>24 (4)</td>
<td>478 (61)</td>
</tr>
<tr>
<td>7 (18)</td>
<td>126 (6)</td>
<td>28 (8)</td>
<td>494 (56)</td>
</tr>
<tr>
<td>8 (17)</td>
<td>128 (8)</td>
<td>28 (8)</td>
<td>496 (79)</td>
</tr>
<tr>
<td>9 (22)</td>
<td>135 (7)</td>
<td>34 (9)</td>
<td>550 (75)</td>
</tr>
<tr>
<td>10 (23)</td>
<td>140 (7)</td>
<td>37 (8)</td>
<td>539 (60)</td>
</tr>
<tr>
<td>11 (24)</td>
<td>148 (7)</td>
<td>44 (10)</td>
<td>540 (70)</td>
</tr>
<tr>
<td>12 (39)</td>
<td>154 (9)</td>
<td>52 (14)</td>
<td>585 (70)</td>
</tr>
<tr>
<td>13 (25)</td>
<td>157 (7)</td>
<td>57 (14)</td>
<td>556 (71)</td>
</tr>
<tr>
<td>14 (21)</td>
<td>164 (6)</td>
<td>58 (12)</td>
<td>534 (69)</td>
</tr>
<tr>
<td>15 (20)</td>
<td>163 (8)</td>
<td>61 (14)</td>
<td>567 (80)</td>
</tr>
<tr>
<td>16 (30)</td>
<td>166 (8)</td>
<td>64 (14)</td>
<td>569 (83)</td>
</tr>
<tr>
<td>&gt;16 (18)</td>
<td>166 (9)</td>
<td>65 (15)</td>
<td>602 (81)</td>
</tr>
</tbody>
</table>

Disclosure: D. G. Rumsey, None; M. Roy, None; C. Kaup, None; L. Bourassa, None; E. Khodayari Moez, None; O. Verschuren, None; L. Pritchard-Wiart, None.
Joint Injection Practices in Pediatric Rheumatology – Preliminary Data from an Ongoing Web Based Survey

Anita Dhanrajani¹ and Raju Khubchandani², ¹Rheumatology, Vasculitis Research Fellow - HSC, Toronto, ON, Canada, ²Department of Paediatrics, Jaslok Hospital and Research Center, Mumbai, India
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Corticosteroid joint injections are a routine procedure in pediatric rheumatology. The dearth of existing literature on current practices led the authors to conduct an online survey targeting pediatric rheumatologists in Europe and North America.

Methods: An electronic survey with 22 questions related to pre-procedural sedation, choice of anesthetic agent, dose and type of therapeutic agent, number of joints injected, use of ultrasound, and post procedure complications was designed with a web based survey engine – Survey Monkey. The survey was distributed via email to physicians registered in the PRINTO and CARRA/PRCSG networks.

Results: 187/213 respondents (Table 1) performed joint injections as a routine clinical practice, of which 110 (57.6%) had received formal training in the procedure. 51.1% procedures were performed as an outpatient, either in a procedure room, day care or minor operation room. 152/180 respondents (85.5%) injected multiple joints in one sitting. Less than half physicians (45%) resort to ultrasound guidance, most often for the hip joint. Ignoring availability, triamcinolone hexacetonide (TH) was the most preferred agent by 79.6% of respondents. Other agents were Triamcinolone acetonide, Methylprednisolone acetate, hydrocortisone acetate and betamethasone acetate, in order of frequency. Only 51.5% physicians said that TH was consistently available in their country. There was some consensus about the dose of steroid (TH equivalent) as 1 mg/kg for large joints (62.9%), but wide variation in the dose for smaller joints. 65.9% physicians resorted to local anesthesia, including EMLA cream, subcutaneous Lidocaine, Lidocaine spray, ethyl chloride spray or a combination. Intravenous sedation was used by more than half physicians (51.2%), oral sedation by 15.7%, long anesthesia by 2.4% and other methods by 30.7%

Most respondents experienced some procedural complications in their clinical experience, commonest being subcutaneous atrophy(Table 2). Most physicians recommended home ambulation for 24-48 hours after procedure, however some variations such as complete bed rest, splinting, immobilization, and rest for longer than 48 hours were observed. 48.2% respondents follow significantly different practices in 0-5 year age group, for either choice of anesthesia, setting of procedure, use of ultrasound guidance or number of joints injected.

Conclusion: Practices related to pediatric joint injection procedures are not uniform and methods to develop standardization of this extremely common procedure is the need of the hour.

Table 1:
<table>
<thead>
<tr>
<th>Geographical Location of training</th>
<th>Percentage (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europe</td>
<td>34.5(38)</td>
</tr>
<tr>
<td>UK *</td>
<td>8.2 (9)</td>
</tr>
<tr>
<td>Australia</td>
<td>1.8 (2)</td>
</tr>
<tr>
<td>Asia</td>
<td>1.8 (2)</td>
</tr>
<tr>
<td>India</td>
<td>0</td>
</tr>
<tr>
<td>USA **</td>
<td>37.3 (41)</td>
</tr>
<tr>
<td>Canada</td>
<td>16.4 (18)</td>
</tr>
<tr>
<td>Others</td>
<td>0</td>
</tr>
</tbody>
</table>

*UK – United Kingdom

**USA – United states of America

Table 2:

<table>
<thead>
<tr>
<th>Complication</th>
<th>Frequency (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subcutaneous atrophy</td>
<td>78.9 (131)</td>
</tr>
<tr>
<td>Iatrogenic infection</td>
<td>1.8 (3)</td>
</tr>
<tr>
<td>Anesthetic complications</td>
<td>4.8 (8)</td>
</tr>
<tr>
<td>Tendon rupture</td>
<td>1.2 (2)</td>
</tr>
<tr>
<td>Fat necrosis or calcification</td>
<td>24.7 (41)</td>
</tr>
<tr>
<td>Local bleeding</td>
<td>10.2 (17)</td>
</tr>
<tr>
<td>None</td>
<td>19.3 (32)</td>
</tr>
<tr>
<td>Other</td>
<td>9.0 (15)</td>
</tr>
</tbody>
</table>

Disclosure: A. Dhanrajani, None; R. Khubchandani, None.


Abstract Number: 2305

**Efficacy of Function-Based Exercise Program on Functional Ability, Pain and Quality of Life in Children with Juvenile Idiopathic Arthritis**

Ela Tarakci¹, Saime Nilay Baydogan¹, Sezgin Sahin², Amra Adrovic², Kenan Barut² and Ozgur Kasapcopur²,

¹Istanbul University, Faculty of Health Science, Division of Physiotherapy and Rehabilitation, Istanbul, Turkey,
²Pediatric Rheumatology, Istanbul University, Cerrahpasa Medical School, Department of Pediatric Rheumatology, Istanbul, Turkey

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Juvenile idiopathic arthritis (JIA) is one of the most common rheumatic diseases in childhood, affecting at least 1 in 1000 children. Children with JIA, experience joint inflammation and swelling, pain and tenderness, morning stiffness, limited mobility. Children with JIA complain pain and have lower functional ability and decreased quality of life compared with their peers. The objective of this study was to investigate the effects of a function-based exercise program on pain, functional ability and quality of life in children with JIA.

Methods:

32 children with JIA (19 female and 13 male), age range 5-16 years, participated in this study. Patient population consisted of 21 children with polyarticular, 9 children with oligoarticular, 1 children with systemic arthritis, and 1 children with psoriatic arthritis. All children and their parents were informed of about the study and the informed consent was obtained. The study was approved by Ethics Committee of Istanbul University.

Functional ability, pain, and quality of life were assessed with a Childhood Health Assessment Questionnaire (CHAQ), 11-point Numeric Analogue Scale (NRS) and the Pediatric Quality of Life Inventory (PedsQL), respectively. The children completed a 12-week individually planned function-based exercise program for thrice a week at the hospital in the supervised by the physical therapist. Function-based exercise program contained weight bearing to affected joint, squat, walking stair climbing and various activities for the upper limb (variable according to the needs of each patient).

Results:

The mean age and disease duration were 10.13±3.50 and 5.57±3.20 years, respectively. The mean of number of affected joint was 3.31±1.20. Baseline scores were NRS 30.31±24.81, CHAQ 0.73±0.68 and PedsQL 62.61±25.15. After the function-based exercise program, scores of NRS, CHAQ and PedsQL were 20.47±20.13, 0.23±0.38 and 84.46±13.67, respectively. Statistically significant improvements were found in all the outcome measures after the function-based exercise program \(p<0.001\). Also, it was found clinically relevant changes of CHAQ scores in a total of \%74.4 of the children with JIA after the treatment.

Conclusion:

The study demonstrated that a 12-week individually planned function-based exercise program could result in improved pain, independence of functional, quality of life in children with JIA. So, we suggest that an exercise program should be planned individually and focus function in children with JIA. Further research is needed to clarify the long-term effect of exercise in children with JIA.

References:


Disclosure: E. Tarakci, None; S. N. Baydogan, None; S. Sahin, None; A. Adrovic, None; K. Barut, None; O. Kasapcopur, Novartis Pharmaceutical Corporation, 8, Roche Pharmaceuticals, 8.
Abstract Number: 2306

Demographic and Clinical Characteristics of Hispanic Children with Juvenile Idiopathic Arthritis: An International, Multicenter Cross-Sectional Study

Martha Rodriguez⁴, Melissa Tesher¹, Deirdre De Ranieri¹, Linda Wagner-Weiner², Tamar Rubinstein³, Janet Orrock⁴, Christine Arango⁵, Angela Mosquera⁵, Carmen Tineo⁶, Romilda Salas⁷, Esthela Loyo⁸, Karen One³⁹ and Maria Alkureishi¹⁰

¹Pediatric Rheumatology, The University of Chicago Medicine, Chicago, IL, ²The University of Chicago Medicine, Chicago, IL, ³Albert Einstein College of Medicine, Children's Hospital at Montefiore, New York, NY, ⁴Pediatric Rheumatology, Albert Einstein College of Medicine, Children's Hospital at Montefiore, NY, Albania, ⁵Pediatric Rheumatology, Pediatric rheumatology post graduate program El Bosque University, Bogota, Colombia, ⁶Division of Rheumatology, Hospital Regional Universitario José Ma Cabral Baez, Santiago, Dominican Republic, ⁷Rheumatology, Hospital Regional Universitario José Ma Cabral Baez, Santiago, Dominican Republic, ⁸Departamento de Reumatología, Hospital Regional Universitario José Ma Cabral Baez, Santiago, Dominican Republic, ⁹Division of Pediatric Rheumatology, University of Chicago, Chicago, IL, ¹⁰Pediatrics, The University of Chicago Medicine, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Higher disease activity has been described in Hispanic patients with Juvenile Idiopathic Arthritis (JIA) living in the United States (US) vs non-Hispanics. There is no data available comparing JIA disease activity among Hispanics living in the US vs Latin America, or between Hispanic subgroups. We aim to describe the clinical characteristics of Hispanic children with JIA at several centers in the United States and in Latin America.

Methods: We analyzed preliminary data of 95 subjects from 4 centers (US: 2, Latin America:2) with a confirmed diagnosis of JIA based on the revised ILAR criteria with age of disease onset ≤16 years old. Subjects were grouped based on self-reported ethnicity and residency, with 52 Hispanics residing in Latin America (Colombia and Puerto Rico). In the US, 20 Hispanics and 23 non- Hispanic subjects were surveyed. Data collection is ongoing; we anticipate 240 subjects by completion of the study. We compared clinical characteristics, physician assessment of disease activity, parent/subject assessment of disease activity and pain, CHAQ score and presence/absence of imaging evidence of joint damage among the three groups.

Results: There was a significant difference in distribution of JIA subtypes between groups. Oligoarticular JIA was the most common among non-Hispanic US patients (27%) and polyarticular RF negative was the most common subtype in both Hispanic groups (35%). RF positive polyarticular JIA was more common in US Hispanics (25%) vs US non-Hispanics (13%), but lower in Hispanics residing in Latin America (12%). HLA B27 positivity was more frequent in US non-Hispanics (18% vs 5% in Hispanics in US and 15% in Hispanics in Latin America). Radiographic damage was significant more frequent among Latin American Hispanics (42%), compared to US Hispanics (35%) and US non-Hispanics (22%). Systemic steroid use was more frequent among Latin American Hispanics. Treatment with biologics was highest in US Hispanics (80%) vs US Non-Hispanics (70%); 54% of subjects in Latin America reported receiving biologics. Non-biologic DMARD use was similarly prevalent in the three groups: 90% in Latin American patients, 86% in US non-Hispanics, and 85% in US Hispanics. CHAQ scores were slightly higher in non-Hispanics; however physician global disease assessment was worse in Hispanics, particularly those residing in US.
**Conclusion:** Radiographic changes were significantly higher in all Hispanics which may reflect more aggressive disease as well as decreased use of biologic medications in Latin America. Systemic steroids are used more commonly among Latin American patients which likely reflects decreased availability of other medications, particularly biologics. In addition to treatment variation, genetics and environmental factors may contribute to the variable phenotypic expression of JIA found among Hispanic groups in this preliminary study. An improved understanding of the characteristics of JIA among Hispanic children is essential to guide disease management and better meet the needs of this population.

**Disclosure:** M. Rodriguez, None; M. Tesher, None; D. De Ranieri, None; L. Wagner-Weiner, None; T. Rubinstein, None; J. Orrock, None; C. Arango, None; A. Mosquera, None; C. Tineo, None; R. Salas, None; E. Loyo, None; K. Onel, None; M. Alkureishi, None.


**Abstract Number:** 2307

**Frequency of Comorbidities in Patients with Juvenile Ideopathic Arthritis – Results of an Observational Cohort Study**

**Jens Klotsche**¹, Nadine Betenstehl², Gerd Ganser³, Eva Seipel⁴, Stefanie Tatsis⁵, Heike-Franziska Weidemann⁶, Ivan Foeldvari⁷, Gerd Horneff⁸ and Kirsten Minden⁹, ¹Programme Area Epidemiology, German Rheumatism Research Center, a Leibniz institute, Berlin, Germany, ²Oberhavelkliniken Hennigsdorf, Hennigsdorf, Germany, ³Klinik für Kinder-und Jugendrheumatologie, Nordwestdeutsches Rheumazentrum, Sendenhorst, Germany, ⁴Rheumatologie und Klinische Immunologie, Immanuel Krankenhaus Berlin, Berlin, Germany, ⁵Geriatrie/Rheumatologie, Kath. Marienkrankenhaus Hamburg gGmbH, Hamburg, Germany, ⁶Internist.-Rheum. Praxis Dr. Weidemann, Hannover, Germany, ⁷Hamburger Zentrum für Kinder-und Jugend Rheumatologie, Hamburg, Germany, ⁸Arnold-Janssen-Strasse 29, Asklepios Klinik Sankt Augustin GmbH, Sankt Augustin, Germany, ⁹Epidemiology unit, German Rheumatism Research Center, Berlin, Germany

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Juvenile idiopathic arthritis (JIA) is a chronic inflammatory disease that often persists into adulthood. In addition to disability and poorer quality of life, JIA is associated with increased long-term morbidity and mortality. The long-term risk of comorbidities is uncertain and guidance on risk assessment is not currently available. The objective of this study was to determine the frequency of comorbid conditions in JIA patients.

**Methods:** Patients with JIA transferred from the biologic registry BIKER to the follow-up (FU) registry JuMBO were included in this analysis. All comorbidities, except for serious infections, prospectively recorded by physicians to BiKeR or JuMBO were considered. Comorbidity rates among the various JIA categories were assessed. The Medical Dictionary for Regulatory Activities (MedDRA) was used for disorder coding. Differences in the occurrence of comorbidities between JIA categories were analyzed by multinomial logistic regression.

**Results:** A total of 1,022 young adults (67% female) with JIA and a mean FU of 7.8 (SD=3.5) years (ys) were included in this analysis. The patients’ mean age was 23.1 ys (SD=3.7), and disease duration was 12.8 ys (SD=5.9) at last FU. The majority were classified as polyarticular-course JIA (53%) at BiKeR enrollment. Patients had received a mean of
2.9 (SD=1.3) DMARDs, 77% were ever treated with biologics. Comorbidities were reported for more than half of the patients (54%), 24.5% of the conditions were stated for the first time in adult age. Eye disorders were the most common comorbid condition group (16.9%), followed by Immune system disorders (12.3%), and psychiatric disorders (10.1%). The most frequently reported single diseases were uveitis in 15.9%, depression in 9.1%, hypertension in 8.5%, chronic secondary pain syndrome in 4.4%, and psoriasis in 3.3%. Females had significantly more often depression (11.8% versus 3.4%), pain syndromes (5.8% versus 1.6%), and autoimmune thyroiditis (3.3% vs. 0.9%) than males, whereas men had more often inflammatory bowel diseases than women (4.0% vs. 1.9%). The rate of comorbid conditions significantly differed across the various JIA categories, with the highest rates in patients with extended oligoarthritis, psoriatic arthritis and systemic arthritis. While extraarticular manifestations of JIA were the most common comorbid conditions in extended oligoarthritis and psoriatic arthritis, disease- or treatment-related complications were relevant comorbidities in systemic arthritis.

**Conclusion:** Young adults with JIA have a high rate of comorbidity overall, with extraarticular JIA manifestations being the most frequent comorbid conditions. Comorbidity rates vary among the various JIA categories. Patients with systemic JIA have the highest rate of cardiovascular risk factors and osteoporosis, while patients with extended OA have the highest rate of uveitis. An underreporting or unawareness of comorbidities by rheumatologists is possible, guidance on risk assessment in adults with JIA is needed.

**Disclosure:** J. Klotsche, None; N. Betenstehl, None; G. Ganser, None; E. Seipelt, None; S. Tatsis, None; H. F. Weidemann, None; I. Foeldvari, None; G. Horneff, AbbVie, Pfizer, Novartis, and Roche, 2, AbbVie, Novartis, Sobi, Pfizer, and Roche, 9; K. Minden, Pfizer, Abbvie, Roche, 2, Pfizer, Pharm-Allergan, and Roche, 5.


**Abstract Number:** 2308

**The Prevalence of Comorbidities in Pediatric Psoriasis and Juvenile Psoriatic Arthritis**

**Cuoghi Edens**, Angela Byun Robinson and Maria Antonelli, **1**Division of Pediatric Infectious Diseases and Rheumatology and Division of Rheumatology, Rainbow Babies and Children's Hospital and University Hospitals Cleveland Medical Center, Cleveland, OH, **2**Division of Pediatric Infectious Diseases and Rheumatology, Case Western Reserve University School of Medicine, Rainbow Babies and Children’s Hospital, Cleveland, OH, **3**Department of Medicine/Division of Rheumatology, Case Western Reserve University School of Medicine, MetroHealth Medical Center, Cleveland, OH

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Adult-onset psoriasis (PsO) and psoriatic arthritis (PsA) have been associated with increased rates of diabetes, obesity, and hypertension. We sought to evaluate the prevalence of these comorbidities in children with PsO and juvenile PsA (JPsA) in the United States.
Methods:

Utilizing a secure cloud-based platform, Explorys, we conducted a retrospective cross-sectional study of males and females ≤ 19 years of age from the United States with PsO and JPsA using pooled de-identified data from multiple United States healthcare systems, collected from 1999 to 2017. PsO subjects carried this diagnosis and also met exclusion criteria for any inflammatory arthritis or inflammatory bowel disease (IBD). Patients with both IBD and JPsA were included and analyzed separately. Comorbidities of interest included diabetes, hypertension, and obesity. Hypertension and diabetes was determined by the presence of their respective Systematized Nomenclature for Medicine-Clinical Terms (SNOMED-CT), as the Explorys database is ontology based. Subjects were considered obese if body mass index (BMI) was equal to or greater than the 95th percentile, based on CDC 2010 recommendations. Chi-squared test and odds ratio were calculated using Stata 10.0 software, Austin, Texas.

Results:

Of those ≤19 years of age, 6180 subjects with PsO were identified and 930 were identified with JPsA, 50 of those were also diagnosed with IBD. Of the PsO subjects, 54% were male versus 34% of total JPsA. Both cohorts were mostly Caucasian, with over three-fourths representation. Among children with PsO, 42% were obese compared to 52% of JPsA children. In this cohort, those with JPsA and IBD did not have concomitant diabetes or hypertension. JPsA patients were significantly more likely to have diabetes, hypertension, and obese than patients with purely skin disease. Having JPsA was associated with diabetes (OR 0.33, 0.23-0.48), hypertension (OR 0.41, 0.30-0.51), and obesity (OR 0.75, 0.65-0.86) compared to PsO. Table 1 summarizes the findings of each patient population at the time of data collection.

Conclusion:

Metabolic comorbidities are more prevalent in children with JPsA than PsO. Hypertension and diabetes diagnosed in childhood is more common in those with JPsA compared to those with skin disease only. Those diagnosed with PsO and JPsA in childhood have high rates of obesity, when determined by BMI percentile.

Table 1. Comorbidities in Pediatric Psoriasis and Juvenile Psoriatic Arthritis

<table>
<thead>
<tr>
<th></th>
<th>PsO N=6180</th>
<th>JPsA+IBD N=50</th>
<th>JPsA-IBD N=880</th>
<th>Total JPsA N=930</th>
<th>JPsA+IBD v JPsA-IBD p value</th>
<th>PsO v Total JPsA p value</th>
<th>PsO v Total JPsA OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>90 (1.5%)</td>
<td>0 (0)</td>
<td>40 (4.5%)</td>
<td>40 (4.3%)</td>
<td>-</td>
<td>p&lt; 0.0001</td>
<td>0.33 (0.23-0.48)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>170 (2.6%)</td>
<td>0 (0)</td>
<td>60 (6.8%)</td>
<td>60 (6.5%)</td>
<td>-</td>
<td>p&lt; 0.0001</td>
<td>0.41 (0.30-0.56)</td>
</tr>
<tr>
<td>Obese*</td>
<td>2490 (41.0)</td>
<td>40 (80.0)</td>
<td>440 (50.0)</td>
<td>480 (51.6)</td>
<td>&lt;0.0001</td>
<td>p&lt; 0.0005</td>
<td>0.75 (0.65-0.86)</td>
</tr>
</tbody>
</table>

Legend-Psoriasis (PsO), Juvenile Psoriatic arthritis (JPsA), Inflammatory bowel disease (IBD)

*Obese state determined as those ≥95th BMI percentile for age

Disclosure: C. Edens, None; A. Byun Robinson, None; M. Antonelli, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-prevalence-of-comorbidities-in-pediatric-psoriasis-and-juvenile-psoriatic-arthritis
Risk Factors for Arthritis and the Development of Comorbid Cardiovascular and Metabolic Disease in Children with Psoriasis

Cynthia K. Manos¹,², Rui Xiao³, Timothy G. Brandon¹, Alexis Ogdie⁴ and Pamela F. Weiss⁵,⁶, ¹Rheumatology, Children's Hospital of Philadelphia, Philadelphia, PA, ²Center for Clinical Epidemiology and Biostatistics, Perelman School of Medicine, Philadelphia, PA, ³Department of Pediatrics, Division of Biostatistics, Children's Hospital of Philadelphia, Philadelphia, PA, ⁴Rheumatology, Hospital of the University of Pennsylvania, Philadelphia, PA, ⁵Division of Rheumatology, Center for Pediatric Clinical Effectiveness, Children's Hospital of Philadelphia, Philadelphia, PA, ⁶Department of Pediatrics, Perelman School of Medicine, Philadelphia, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Relatively little is known about the epidemiology of juvenile psoriatic arthritis (PsA), including risk factors for development of PsA among children with psoriasis. It is also unknown whether children with PsA are at increased risk of cardiovascular and metabolic disease, similar to adults.

Methods: We conducted a retrospective cohort study of children with incident psoriasis and PsA using the Clinformatics TM DataMart (OptumInsight, Eden Prairie, MD), a de-identified administrative claims database. All incident psoriasis patients had ≥1 ICD-9 code for psoriasis and PsA patients had ≥ 1 ICD-9 code for PsA or psoriasis and arthritis. The index date was the date of the first ICD-9 code for the diagnosis of psoriasis or PsA. Patients were required to be continuously enrolled for 6 months before and 12 months after the index date. Controls were matched on age, sex, and date of psoriasis or arthritis diagnosis at a 10:1 ratio. Cox proportional hazard regression was performed to assess the risk of developing arthritis in children with psoriasis over time. Incidence rate ratios were used to compare the relative frequency of cardiovascular and metabolic co-morbid diagnoses.

Results: We identified 1,012 children with PsA, 14,610 with psoriasis, and 203,907 controls. The median time of continuous enrollment was 3.0 years (IQR 1.9-4.9). Median ages at the first diagnoses of PsA and psoriasis were 12 and 10 years, respectively. 56% and 53% of children with PsA and psoriasis were female. Amongst those children who had both psoriasis and arthritis, approximately 37% developed psoriasis first. Median time to development of arthritis after psoriasis diagnosis was 1.8 years (IQR 0.4-2.8). Older age was associated with a significantly increased risk of developing arthritis in children with psoriasis (Table 1). There was a trend towards increased risk of arthritis in psoriasis patients with ulcerative colitis and uveitis, albeit statistically insignificant. Children with psoriatic arthritis had a significantly increased incidence of hypertension, hyperlipidemia, and cerebrovascular disease compared to healthy controls (Table 2).

Conclusion: Older age was a risk factor for PsA among children with psoriasis. Similar to adults, PsA was associated with a higher risk of developing metabolic and cerebrovascular disease in children.
Disclosure: C. K. Manos, None; R. Xiao, None; T. G. Brandon, None; A. Ogdie, Pfizer, 2,AbbVie, Celgene and Pfizer, 2,Novartis, Takeda and Pfizer, 5; P. F. Weiss, None.


Abstract Number: 2310

Increased Risk of Extreme Obesity in Adults with History of Childhood Arthritis

Sangeeta Sule¹ and Kevin Fontaine², ¹Pediatrics, Johns Hopkins University, Baltimore, MD, ²Dept. of Health Behavior, Univ. of Alabama at Birmingham, Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION

Table 1: Risk Factors in the Development of Psoriatic Arthritis

<table>
<thead>
<tr>
<th></th>
<th>Univariate Analysis</th>
<th>Multivariate Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hazard Ratio (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>Age at psoriasis diagnosis</td>
<td>1.04 (1.02-1.06)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Male sex</td>
<td>0.97 (0.77-1.24)</td>
<td>0.83</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>0.69 (0.32-1.47)</td>
<td>0.34</td>
</tr>
<tr>
<td>Black</td>
<td>1.25 (0.52-1.92)</td>
<td>0.29</td>
</tr>
<tr>
<td>Hispanic ethnicity</td>
<td>0.62 (0.38-1.03)</td>
<td>0.07</td>
</tr>
<tr>
<td>Household income</td>
<td>1.04 (0.97-1.10)</td>
<td>0.31</td>
</tr>
<tr>
<td>Education level</td>
<td>1.05 (0.92-1.23)</td>
<td>0.43</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.29 (0.57-2.00)</td>
<td>0.54</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.75 (0.31-1.80)</td>
<td>0.80</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>1.84 (0.22-1.90)</td>
<td>0.16</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>0.99 (0.26-3.97)</td>
<td>0.99</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>2.07 (0.29-14.78)</td>
<td>0.47</td>
</tr>
<tr>
<td>Ulceritis</td>
<td>4.01 (1.00-15.12)</td>
<td>0.05</td>
</tr>
<tr>
<td>Gastroesophageal disease</td>
<td>1.50 (0.21-10.50)</td>
<td>0.69</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>3.92 (0.98-15.73)</td>
<td>0.05</td>
</tr>
<tr>
<td>Depression</td>
<td>1.48 (1.04-2.09)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Legend: Results of univariate and multivariate analysis of risk factors for development of PsA. Only those comorbidities diagnosed before psoriasis diagnosis were included in the analysis. Variables with a p-value <0.20 in univariate analysis were included in multivariate analysis. The likelihood-ratio test (p-value <0.05), Akaike information criterion, and link test were performed for final model selection in multivariate analysis.

Table 2: Incidence Rate Ratios of Comorbidities in Children with Psoriatic Arthritis and Psoriasis

<table>
<thead>
<tr>
<th></th>
<th>PsA IR, cases/1000 pyrs</th>
<th>Psoriasis IR, cases/1000 pyrs</th>
<th>Controls IR, cases/1000 pyrs</th>
<th>PsA/Psoriasis IRR (95% CI)</th>
<th>PsA/controls IRR (95% CI)</th>
<th>Psoriasis/controls IRR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>6.94</td>
<td>4.19</td>
<td>2.68</td>
<td>1.66 (1.06-2.59)</td>
<td>2.59 (1.09-6.31)</td>
<td>1.56 (1.35-1.81)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.83</td>
<td>1.15</td>
<td>0.75</td>
<td>1.83 (0.61-5.49)</td>
<td>2.41 (0.96-6.09)</td>
<td>1.52 (1.13-2.00)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>5.65</td>
<td>5.02</td>
<td>3.65</td>
<td>5.16 (1.81-12.16)</td>
<td>4.41 (1.67-11.35)</td>
<td>1.64 (1.44-1.85)</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>2.10</td>
<td>0.43</td>
<td>0.37</td>
<td>4.37 (1.08-11.48)</td>
<td>5.70 (2.44-11.30)</td>
<td>1.17 (0.71-1.92)</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>0.78</td>
<td>0.37</td>
<td>0.19</td>
<td>2.12 (0.40-7.28)</td>
<td>4.12 (0.84-12.29)</td>
<td>1.94 (1.12-3.37)</td>
</tr>
</tbody>
</table>

Legend: Patients were identified as having an incident comorbidity if the first ICD-9 code for that comorbidity occurred after the diagnosis of arthritis or psoriasis for cases or after the match date for controls. IR=incidence rate; IRR=incidence rate ratio; pyrs=person years.
Background/Purpose:
Over one-third of U.S. adults are obese, leading to major health conditions and increased costs. Identified risk factors that contribute to obesity include lifestyle, genetics and childhood diseases. Using data from the National Health and Nutrition Examination Survey (NHANES), we investigated whether the risk of obesity in adults associates with juvenile arthritis.

Methods:
We linked NHANES 2007-2014 datasets to assess the obesity status of respondents reporting any type of arthritis diagnosed prior to 18 years of age and compared them to a group of respondents with asthma diagnosed prior to 18 years of age (participants with both diseases were excluded from the analyses).

Body mass index (BMI), calculated as weight in kilograms divided by height in meters squared, and was used to characterize obesity status. Using federal BMI-defined obesity categories (normal weight (18.5-24.9 kg/m\(^2\)), overweight (25-29.9 kg/m\(^2\)), obese (≥30 kg/m\(^2\)) and extreme obesity (≥40 kg/m\(^2\)), we conducted logistic regression analyses controlling for age, gender and race, was used to estimate the odds ratio (OR) of obesity or extreme obesity, incorporating sample weight to account for the complex sampling design.

Results:
There were 294 respondents who reported being diagnosed with juvenile arthritis (JA) and 4232 who reported a diagnosis of childhood asthma. Participants with JA were older (45.9 vs. 37.2 years, p<0.01), female (59% vs. 45%, p<0.01), and Caucasian (74% vs. 53%, p<0.01) compared to those with childhood asthma. Adults with history of JA were shorter (168.4 vs. 170.5 cm, p=0.02) and had higher body weight (86.2 vs. 84.1 kg, p=0.04). There was also a trend towards higher BMI in the JA group (30.3 vs. 28.9 kg/m\(^2\), p =0.07). Unadjusted OR of obesity in the JA group were 1.2 (95% Confidence Interval (CI): 0.7-2.1) and adjusted OR was 0.9 (95% CI: 0.5-1.7). The odds of extreme obesity in the JA group compared to asthma group was almost double with unadjusted OR of 2.4 (95% CI: 1.2-4.8, p=0.02) and adjusted OR of 2.2 (95% CI: 0.9-5.7, p=0.09).

Conclusion:
A diagnosis of childhood arthritis independently associated with an increased risk of extreme obesity in adulthood. Our results may have been influenced by recall bias (i.e., misreporting age of diagnosed arthritis or asthma diagnosis). We were also unable to assess whether JA was still active in the adults. Nonetheless, our results suggest that factors related to having JA (e.g., inflammation, decreased physical activity, medical treatment) might contribute to developing extreme obesity in adulthood.

Disclosure: S. Sule, None; K. Fontaine, None.


Abstract Number: 2311

Prospective Validation of the Juvenile Spondyloarthritis Disease Activity Index and Its Comparison with Adult Spondyloarthritis Disease Activity Scores
Background/Purpose: Among JIA children with Enthesitis related arthritis (ERA) category have more pain, poorer health status and are less likely to achieve or maintain sustained remission. There has been paucity of instruments to measure disease activity in ERA and recently the Juvenile Spondyloarthritis Disease Activity Index (JSpDA) was developed. We planned to prospectively validate JSpDA and compare its performance with other disease activity scores used in children and adults.

Methods:

Children with ERA (ILAR criteria) less than 18 years of age were enrolled. Baseline characteristics and different disease activity measures (JSpDA, BASDAI, ASDAS-ESR, JADAS-10) and C-HAQ were recorded at baseline and on follow up after at least 3 months of follow up. At both visits physician global assessment and patient global assessment was recorded on the scale of 0-10. Construct validity was tested using JADAS-10, physician global assessment, patient global assessment and C-HAQ. Correlation of JSpDA and different disease activity scores was done. Internal consistency was evaluated using peripheral arthritis score. Discriminative validity was evaluated using the physician global assessment.

Results:

The mean age of 125 children (114 boys) was 14.2±2.23 years. The mean disease duration was 34.8±28.04 months. Eighty nine children had persistent disease while 31 had episodic disease and 5 children had less than 3 months of disease. Eighty eight of 102 (86%) children were HLA-B27 positive. Seventy seven (61.6%) children had inflammatory back pain ever and 43% had radiographic sacroiliitis. 113 had peripheral arthritis ever (90.4%) and eighty two (65%) at the time of recruitment.

Among 125 patients 91 were taking NSAIDs and 28 were taking synthetic DMARDs (Methotrexate=19, sulfasalazine=8, Leflunomide=1). Mean disease activity score were, JSpDA: 3.07±1.84, JADAS10: 12.43±8.58, BASDAI:3.06±2.3 ASDAS ESR: 3.01±1.24. Mean C-HAQ was 0.75 +0.65.

JSpDA showed high correlation with JADAS-10 (r=0.874) and PGA (r= 0.875) and moderate to high correlation with C-HAQ (r=0.733). Hence demonstrated good construct validity. Correlation between peripheral disease component and total score was 0.96, showing good internal consistency. The mean JSpDA scores for children with a physician global assessment (PGA) less than 0 (n=19) & >0 (n=105) were 0.31 and 3.6 respectively (p< 0.001) hence showing good discriminative validity.

37 children had a follow up visit at least 3 months later, disease activity increased in 21, decreased in 13 & did not change in 3. Mean change in JSpDA was significantly different among those who improved [+2.29±0.57] when compared to who worsened [-1.67±0.48; (p<0.001), showing good sensitivity to change.

JSpDA also showed highly correlation with other scores like JADAS10 (r=0.87) and BASDAI(r=0.83), ASDAS ESR(r=0.85). Adult score showed moderate to high correlation with PGA [ASDAS ESR(r=0.87), BASDAI (r=0.77)] and moderate with C-HAQ [ASDAS ESR(r=0.77), BASDAI (r=0.68)]

Conclusion: JSpDA is a valid score for measuring disease activity in ERA.

Disclosure: A. Zanwar, None; S. Phatak, None; A. Aggarwal, None.
Prevalence of Serum 14-3-3η (eta) in Juvenile Idiopathic Arthritis

Iris Reyhan1, Olga S. Zhukov2, Robert J. Lagier3, Robert Bridgforth4, Gary J Williams5, Joanna M. Popov2, Stanley J. Naides2 and Andreas Reiff6, 1Rheumatology, Children's Hospital of Los Angeles, Los Angeles, CA, 2Immunology, Quest Diagnostics Nichols Institute, San Juan Capistrano, CA, 3Research Support, Alameda, Quest Diagnostics Alameda, Alameda, CA, 4Quest Diagnostics Nichols Institute, clemente, CA, 5Quest Diagnostics Nichols Institute, San Juan Capistrano, CA, 6Children’s Hospital of Los Angeles, Los Angeles, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Juvenile idiopathic arthritis (JIA) is the most common pediatric rheumatic disease. Currently, diagnosis is based on clinical assessment defined by the International League of Associations for Rheumatology criteria. Disease specific laboratory biomarkers are limited to rheumatoid factor (RF) and cyclic citrullinated peptide (CCP) antibodies, which are associated with a poor JIA prognosis. Elevated serum levels of 14-3-3η (eta) biomarker have improved the diagnostic sensitivity of RF and CCP in adult RA and elevated 14-3-3η is associated with a more severe RA phenotype [1,2]. The objective of this study was to evaluate the prevalence and clinical significance of serum 14-3-3η in children with JIA.

Methods: One hundred fifty two patients from the Pediatric Rheumatology Core at Children’s Hospital of Los Angeles were divided into five groups: 39 with polyarticular JIA RF+ (PJIA RF+), 39 PJIA RF-, 36 oligoarticular JIA (OJIA), 20 with psoriatic arthritis (PsA) and 18 with enthesitis-related arthritis (ERA). OJIA patients served as a control group. RF, CCP, and 14-3-3η were measured via immunoturbidimetry, immunoassay, and ELISA, respectively. Based on adult onset RA, a 14-3-3η serum level of >0.2ng/mL was considered positive. Association of JIA with 14-3-3η positivity was performed by Fisher’s exact test. Disease activity was assessed by Juvenile Arthritis Disease Activity Score-10/71 (JADAS-10/71).

Results: RF, CCP, and 14-3-3η data are summarized in Table 1. Thirty five (23%) patients had a positive 14-3-3η. Twelve (8%) were single positive for 14-3-3η, 23 (15%) were positive for 14-3-3η and RF and/or CCP, and 17 (11%) were positive for all 3 markers. There was a positive correlation between 14-3-3η and PJIA RF+ vs. OJIA (p-value = 0.029) and PJIA RF+ vs. PsA (p-value = 0.012) and, but there was no correlation between presence and titer of 14-3-3η compared to JADAS-10/71.

Conclusion: All patient groups tested had levels of 14-3-3η above baseline. PJIA RF+ patients had the highest prevalence of 14-3-3η compared to all other groups. Of note, 14-3-3η was positive in other forms of JIA, especially OJIA where 22% of patients were positive. There was a positive correlation between 14-3-3η and positive RF and CCP, but none with disease activity. 14-3-3η might be a useful biomarker in the diagnosis, prognosis and in monitoring therapeutic response of children with PJIA RF+. However its role in other forms of JIA remains to be determined.

References:


Table 1: Prevalence of 14-3-3h, RF and CCP Across Patient Groups Compared to OligoJIA

<table>
<thead>
<tr>
<th></th>
<th>14-3-3η Positive</th>
<th>Odds Ratio</th>
<th>p-value</th>
<th>14-3-3η Positive RF &amp; CCP Negative</th>
<th>14-3-3η Positive RF or/&amp; CCP Positive</th>
<th>14-3-3η Positive RF &amp; CCP Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>PolyJIA RF+</td>
<td>19/39 (49%)*</td>
<td>3.27</td>
<td>0.029*</td>
<td>19/39 (49%)*</td>
<td>16/39 (41%)*</td>
<td></td>
</tr>
<tr>
<td>PolyJIA RF-</td>
<td>3/39 (8%)</td>
<td>0.30</td>
<td>0.105</td>
<td>1/39 (3%)</td>
<td>2/39 (5%)</td>
<td>-0-</td>
</tr>
<tr>
<td>OJIA</td>
<td>8/36 (22%)*</td>
<td>-NA-</td>
<td>-NA-</td>
<td>7/36 (19%)</td>
<td>1/36 (3%)</td>
<td>-0-</td>
</tr>
<tr>
<td>PsA</td>
<td>3/20 (15%)</td>
<td>1.61</td>
<td>0.728</td>
<td>2/20 (10%)</td>
<td>1/20 (5%)</td>
<td>1/20 (5%)</td>
</tr>
<tr>
<td>ERA</td>
<td>2/18 (11%)</td>
<td>0.44</td>
<td>0.466</td>
<td>2/18 (11%)</td>
<td>-0-</td>
<td>-0-</td>
</tr>
<tr>
<td>Total</td>
<td>35/152 (23%)</td>
<td>-NA-</td>
<td>-NA-</td>
<td>12/152 (8%)</td>
<td>23/152 (15%)</td>
<td>17/152 (11%)</td>
</tr>
</tbody>
</table>

*Indicates significant findings.

Disclosure: I. Reyhan, None; O. S. Zhukov, Quest Diagnostics, 3; R. J. Lagier, Quest Diagnostics, 1, Quest Diagnostics, 3; R. Bridgforth, Quest Diagnostics, 3; G. J. Williams, Quest Diagnostics, 1, Quest Diagnostics, 3; J. M. Popov, Quest Diagnostics, 1, Quest Diagnostics, 3; S. J. Naides, Quest Diagnostics, 3, Quest Diagnostics, 1; A. Reiff, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/prevalence-of-serum-14-3-3%ce%b7-eta-in-juvenile-idiopathic-arthritis

Abstract Number: 2313

Procalcitonin Differentiates Infection from Active Disease in Patients with Juvenile Idiopathic Arthritis

Rebecca Trachtman1, Elizabeth T. Murray2, Nancy Pan3, Sima S Toussi4, Marianne E Nellis5, Jackie Szyimonifka6, Sarah Taber3, Alexa Adams3, Thomas J. A. Lehman3, Karen Onel3 and Lisa A. Mandl7, 1Pediatric Rheumatology, Hospital for Special Surgery Weill Cornell Medical College, NY, NY, 2Hospital for Special Surgery, New York, NY, 3Pediatric Rheumatology, Hospital for Special Surgery Weill Cornell Medical College, New York, NY, 4Pediatric Rheumatology, Hospital for Special Surgery Weill Cornell Medical College, New York, NY, 5Pediatric Rheumatology, Hospital for Special Surgery Weill Cornell Medical College, New York, NY, 6Pediatric Rheumatology, Hospital for Special Surgery Weill Cornell Medical College, New York, NY, 7Pediatric Rheumatology, Hospital for Special Surgery Weill Cornell Medical College, New York, NY.
Background/Purpose: Patients with juvenile idiopathic arthritis (JIA) often present with signs and symptoms suggestive of infection. However, it is a diagnostic challenge to differentiate infectious from non-infectious presentation in routine clinical care. Procalcitonin (PCT) is a serum biomarker elevated in the setting of bacterial infection, but whether it can reliably differentiate infection from disease flare in patients with JIA is unknown.[1] We conducted a prospective cohort study to test the hypothesis that PCT levels will differ between active JIA, quiescent JIA, bacteremic patients and healthy controls.

Methods: From 10/16-4/17, consecutive children 6 months - 18 years with a) active untreated JIA (=>4 inflamed joints) b) quiescent JIA and c) healthy elective pre-surgical candidates were recruited from clinics at a musculoskeletal specialty hospital. JIA was defined according to ILAR criteria. Patients with active JIA despite treatment were excluded, to avoid confounding by treatment. Consecutive bacteremic patients were identified from an associated pediatric intensive care unit over the same period. No matching was performed. PCT as well as other common measures of inflammation were compared. Descriptive statistics and univariate logistic analyses were performed as appropriate. The study was IRB approved.

Results: Patient characteristics are summarized in Table 1. Bacteremic patients were younger (mean age 1.1 vs. 14.1 years) and had Staphylococcus aureus (80%) and Kingella kingae (20%) infections. PCT was elevated in bacteremic patients, and was undetectable in all other subjects (p-value <0.001; Table 2). There were trends towards higher ESR and CRP in bacteremic patients, but these were not statistically significant.

Conclusion: Serum PCT levels appear to be a reliable biomarker to distinguish infection vs. active JIA at presentation, and can aid in directing therapy. However, PCT does not appear to be a useful biomarker to assess disease activity in JIA. Further studies are needed to assess utility of serum PCT measurement in differentiating JIA flares from less severe infections.

**Table 1. Patient characteristics**
Table 2. Laboratory data

<table>
<thead>
<tr>
<th></th>
<th>All patients (N=40)</th>
<th>Active Untreated JIA (N=12)</th>
<th>Quiescent JIA (N=15)</th>
<th>Healthy Controls (N=15)</th>
<th>Bacteremic Patients (N=5)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong> (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(median, IQR range)</td>
<td>13.9 [7.3, 16.1]</td>
<td>9.0 [2.4, 12.8]</td>
<td>14.5 [9.9, 17.6]</td>
<td>14.4 [13.9, 16.6]</td>
<td>1.1 [0.8, 1.8]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.42</td>
</tr>
<tr>
<td>Male</td>
<td>17 (35.4%)</td>
<td>5 (41.7%)</td>
<td>3 (20.0%)</td>
<td>6 (37.5%)</td>
<td>3 (60.0%)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.28</td>
</tr>
<tr>
<td>Caucasian/White</td>
<td>35 (74.5%)</td>
<td>7 (58.3%)</td>
<td>14 (93.3%)</td>
<td>12 (75.0%)</td>
<td>2 (60.0%)</td>
<td></td>
</tr>
<tr>
<td>AA/Black</td>
<td>5 (10.6%)</td>
<td>1 (8.3%)</td>
<td>0 (0.0%)</td>
<td>3 (18.8%)</td>
<td>1 (26.0%)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>5 (10.6%)</td>
<td>3 (25.0%)</td>
<td>1 (6.7%)</td>
<td>8 (48.6%)</td>
<td>1 (26.0%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>2 (4.2%)</td>
<td>1 (8.3%)</td>
<td>0 (0.0%)</td>
<td>1 (6.3%)</td>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.82</td>
</tr>
<tr>
<td>Hispanic</td>
<td>6 (12.5%)</td>
<td>2 (16.7%)</td>
<td>2 (13.3%)</td>
<td>1 (6.3%)</td>
<td>1 (20.0%)</td>
<td></td>
</tr>
<tr>
<td>Insurance</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.15</td>
</tr>
<tr>
<td>Medicaid</td>
<td>9 (18.8%)</td>
<td>6 (48.7%)</td>
<td>1 (6.7%)</td>
<td>2 (12.5%)</td>
<td>1 (20.0%)</td>
<td></td>
</tr>
<tr>
<td>Private</td>
<td>39 (81.3%)</td>
<td>7 (51.3%)</td>
<td>14 (93.3%)</td>
<td>14 (87.5%)</td>
<td>4 (80.0%)</td>
<td></td>
</tr>
<tr>
<td><strong>BMI kg/m²</strong></td>
<td>15.4 [15.9, 23.0]</td>
<td>18.5 [17.2, 19.1]</td>
<td>20.0 [18.0, 23.0]</td>
<td>21.4 [18.0, 26.1]</td>
<td>15.1 [15.0, 19.8]</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Abstract Number: 2314

Monoarticular Juvenile Idiopathic Arthritis: A Unique Entity?

Caterina Politi1, Vanessa Cecchin1, Fabio Vittadello1, Alessandra Meneghel2, Giorgia Martini1 and Francesco Zulian2,
1 Department of Woman and Child Health, University of Padua, Padua, Italy, 2 University of Padua, Department of
Woman and Child Health, Padua, Italy
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Oligoarticular Juvenile Idiopathic Arthritis (oligoJIA) is the most common JIA subtype. According with the most recent classification criteria1, monoarticular JIA (monoJIA) is included in the oligoarticular subgroup. We investigated whether patients with persistent monoJIA have different clinical features and outcome as compared to those with oligoarticular disease.

Methods: We evaluated patients with oligoJIA followed at our Pediatric Rheumatology tertiary Center and at least one year of disease duration. MonoJIA we selected on the basis of the exclusive involvement of one single joint during the overall disease course. Each patients was followed with check visits, including ophthalmologic evaluation, every 3-4 months. For each patient, the following parameters were considered: sex, age at onset, presence of joint hypermobility (JH) according to Beighton’s criteria2, family history positive for JH, ANA (titer > 1/80 on Hep2 cells), presence and localization of active arthritis, presence of uveitis, treatment during the overall course of the disease and outcome. Treatment was grouped in four categories: intra-articular corticosteroid injection (IACs), non-steroidal anti-inflammatory drugs and/or oral corticosteroids (AIDs), MTX and other disease-modifying anti-rheumatic drugs (DMARDs), and biological agents (BAs). Outcome was defined according to Wallace criteria3 as: clinical remission (CR), clinical remission on medication (CRM) and active disease (A).

Results: 356 patients with oligoJIA, as defined by the ILAR criteria, entered the study. Among these, 23 were excluded for lack of complete data and 12 for follow-up shorter than 1 year. Among the remaining 321, followed for mean 7,6 years (1-21.7), 227 (70.7%) presented oligoJIA and 94 (29.3%) monoJIA. MonoJIA resulted significantly different from oligoJIA for the higher frequency of JH, positive family history for JH, lesser frequency of ANA+ and uveitis and for the less aggressive treatment and better long-term outcome. (Table 1)

Conclusion: MonoJIA seems to be a separate nosological entity from oligoJIA with less incidence of ANA, less uveitis and better long-term outcome. A different treatment approach should be therefore foreseen.

References
### Table

<table>
<thead>
<tr>
<th></th>
<th>Mono JIA (no.94)</th>
<th>Oligo JIA (no.227)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex (female)</strong></td>
<td>72 (76,6%)</td>
<td>189 (83,3%)</td>
<td>0,16</td>
</tr>
<tr>
<td><strong>Age at onset (years, months)</strong></td>
<td>5,7</td>
<td>4,7</td>
<td>0,06</td>
</tr>
<tr>
<td><strong>Joint Hypermobility (JH)</strong></td>
<td>68 (73,1%)</td>
<td>135 (61,4%)</td>
<td>0,04</td>
</tr>
<tr>
<td><strong>Positive family history of JH</strong></td>
<td>18 (56,3%)</td>
<td>29 (31,2%)</td>
<td>0,01</td>
</tr>
<tr>
<td><strong>ANA+</strong></td>
<td>72 (76,6%)</td>
<td>198 (87,2%)</td>
<td>0,02</td>
</tr>
<tr>
<td><strong>Uveitis</strong></td>
<td>19 (20,2%)</td>
<td>72 (31,7%)</td>
<td>0,03</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>1</td>
<td>1</td>
<td>0,000</td>
</tr>
<tr>
<td>IACs</td>
<td>86 (91,5%)</td>
<td>214 (94,3%)</td>
<td></td>
</tr>
<tr>
<td>AIDs</td>
<td>19 (20,2%)</td>
<td>137 (60,4%)</td>
<td></td>
</tr>
<tr>
<td>DMARDs</td>
<td>17 (18,1%)</td>
<td>165 (72,7%)</td>
<td></td>
</tr>
<tr>
<td>BAs</td>
<td>3 (3,2%)</td>
<td>57 (25,1%)</td>
<td></td>
</tr>
<tr>
<td><strong>Outcome</strong></td>
<td>1</td>
<td>1</td>
<td>0,000</td>
</tr>
<tr>
<td>CR</td>
<td>76 (80,9%)</td>
<td>73 (32,3%)</td>
<td></td>
</tr>
<tr>
<td>CRM</td>
<td>12 (12,8%)</td>
<td>98 (43,2%)</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>6 (6,4%)</td>
<td>56 (24,7%)</td>
<td></td>
</tr>
</tbody>
</table>

**Disclosure:** C. Politi, None; V. Cecchin, None; F. Vittadello, None; A. Meneghel, None; G. Martini, None; F. Zulian, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/monoarticular-juvenile-idiopathic-arthritis-a-unique-entity](http://acrabstracts.org/abstract/monoarticular-juvenile-idiopathic-arthritis-a-unique-entity)

Abstract Number: 2315

**Symptoms of Depression and Anxiety in Children with JIA: Relation to Other Domains of Health Related Quality of Life**

**Michael Miller**¹, Yufan Yan² and George Lales³, ¹Pediatrics, Feinberg School of Medicine, Northwestern University, Chicago, IL, ²Feinberg School of Medicine, Northwestern University, Chicago, IL, ³Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL

**First publication:** September 18, 2017

### SESSION INFORMATION

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Juvenile Idiopathic Arthritis (JIA) is associated with symptoms of anxiety and depression. We studied these symptoms and other health related quality of life (HRQOL) domains in JIA patients over a 3 year period, because associations between these domains have not been completely determined.

**Methods:** At each visit, all JIA patients meeting ACR classification criteria seen by M.L.M. receive Patient Reported Outcome Measurement Information System Short Form questionnaires v.1.0 (PROMIS) as part of routine care. Scores were calculated for mobility, anxiety, depressive symptoms, fatigue, peer relationships, pain interference domains. Data
extracted by optical mark recognition software was merged with EMR data, using Extract/Transform/Load software, for all visits March 2014 – February 2017, including active joint counts, visit age, ANA, RF, and B27 status.

**Results:** Data from 148 patients (114 females for 435 visits; 34 males for 118 visits; median 14.35 yrs, IQR 4.65) were analyzed, 70 oligo-JIA, 9 extended oligo-JIA, 19 ERA, 21 poly-RF- JIA, 5 poly-RF+ JIA, 11 undifferentiated arthritis, 3 psoriatic, 10 systemic arthritis. For all patients, by forward stepwise regression, depression scores were predicted by anxiety, pain interference, and peer relationship domains (p<0.001), but not other domains. Topological data modeling showed that patients endorsing depressive symptoms often reported anxiety and, less often, problems with peer relationships (figure). 31 patients (21%; 28 females, 3 males) had depression scores 60% or greater, with no predilection for subtype. However, per centile depression scores were comparable to normal reference scores (40.6, IQR 14.4); females had higher scores (43.5 IQR 14.4) than males (37.7 IQR 5.8)*. Anxiety scores, which correlated with depression scores (r=0.814), also were lower than norm scores for all patients (42.6 IQR 20.9), but higher for females (42.6 IQR 10.5 v. 39.5 IQR 13.7)* (*p<0.001 Mann-Whitney Rank Sum Test). There were no gender differences for other domains. No specific differences were distinguished by disease activity, JIA subset, laboratory results, or medications taken.

**Conclusion:** We found depressive symptoms related to anxiety, pain interference and peer relationship in JIA patients. While anxiety and depressive symptom scores were comparable to reference scores, PROMIS was effective in quickly identifying individual patients in need of additional support. PROMIS is effective in identifying the nature of HRQOL problems in JIA patients.

**Disclosure:** M. Miller, None; Y. Yan, None; G. Lales, None.


**Abstract Number:** 2316

**Barriers at School for Children with Juvenile Idiopathic Arthritis (JIA) – a Patient Reported Outcome**
SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Few studies in children with chronic illnesses/disability have reported challenges faced by patients at school. Therefore, the objective of this study is to identify barriers and their associated impact in Juvenile Idiopathic Arthritis (JIA).

Methods: A cross-sectional observational study of children aged 8 to 17 diagnosed with JIA followed at the Rheumatology Clinic/Alberta Children’s Hospital was performed between July and December 2016. Demographics, diagnosis and disease course were obtained from health records. A survey was administered to the child/caregiver to assess the barriers experienced by JIA patients at school. The survey collected information about school attendance/performance, impact of JIA symptoms (e.g. pain, fatigue), challenges and accommodations, communication, participation/peers, and school support. Descriptive statistics were used to analyze the data.

Results: A total of 80 children were recruited into the study. The median age of participants was 13 (range 8-17). The most common subtypes were rheumatoid factor negative polyarticular JIA (36%) and oligoarticular persistent JIA (33.7%) with a median disease duration of 5 years (range 0-15). The treatment included DMARDS (68.9%), NSAIDS (37.8%), biologics (36.7%), steroids (3.3%) and no medication (10%). Appointments, illness and JIA symptoms had a minor impact on school attendance and performance. However, physical challenges (e.g. gym, writing, sitting for long periods of time) at school were a barrier for 42.9% (sometimes 31.2%, often 9.1 %, almost always 2.6%). 25% recorded using accommodations (e.g. modified gym, accommodation letter, computer access). Patients were unable to participate in activities in class/outside with their peers (36.8%; sometimes 32.9%, almost always 3.9%) and in gym (41.4%; sometimes 35.7%, often 5.7%). Patients told their teachers/gym teacher about their disease (81%) but most patients did not continue to update their teachers. 9.5% of participants reported that their teachers did not understand their illness compared to 19.1% of gym teachers. 81.7% of participants told their friends about their illness and 41.9% told their classmates. Social concerns included being treated differently, being told they were faking their illness, and looking like they weren’t trying. The majority reported that the school was supportive of their illness (86%). Barriers tend to be reported more often by patients with active disease.

Conclusion:

JIA had a minor impact on school attendance and performance. However, many patients experienced some impacting physical challenges. Additional barriers included teacher understanding, participation and social anxiety.

Disclosure: K. Chomistek, None; N. Johnson, None; R. Stevenson, None; N. Luca, None; P. Miettunen, None; S. Benseler, None; D. Veeramreddy, None; H. Schmeling, None.


Abstract Number: 2317
Knowledge Translation in Juvenile Idiopathic Arthritis in Canada: A Focus on Parents of Children with JIA

Julia Wright1, Benjamin Rose-Davis2, Michelle Batthish3, Tania Cellucci4, Ciarán M. Duffy5, Lori Tucker6, Adam Huber7, Bianca Lang8, Deborah M. Levy9, Dax Rumsey10, Karen N Watanabe Duffy11, Janet Curran12 and Elizabeth Stringer13, 1Faculty of Medicine, Dalhousie University, Halifax, NS, Canada, 2Department of Computer Science, Health Informatics, Dalhousie University, Halifax, NS, Canada, 3Division of Pediatric Rheumatology, McMaster Children's Hospital, Hamilton, ON, Canada, 4McMaster University, Hamilton, ON, Canada, 5Children's Hospital of Eastern Ontario and University of Ottawa, Ottawa, ON, Canada, 6BC Children's Hospital, Vancouver, BC, Canada, 7IWK Health Centre, Halifax, NS, Canada, 8Pediatrics, IWK Health Centre, Halifax, NS, Canada, 9Division of Rheumatology, The Hospital for Sick Children, Toronto, ON, Canada, 10Stollery Children's Hospital, Edmonton, AB, Canada, 11Rheumatology, Children's Hospital of Eastern Ontario and University of Ottawa, Ottawa, ON, Canada, 12Department of Pediatrics, IWK Health Centre, Halifax, NS, Canada, 13Department of Rheumatology, IWK Health Centre, Halifax, NS, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects Poster III: Juvenile Arthritis
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The Research in Canadian Children with Childhood Arthritis Emphasizing Outcomes (ReACCh-Out) cohort (2005-2010) has characterized outcomes for Canadian children with Juvenile Idiopathic Arthritis (JIA). However, little is known about the uptake of this information, or JIA research findings in general, into clinical care. The aim of this study is to identify barriers and facilitators that influence the uptake and use of these findings by parents of children with JIA.

Methods: This descriptive exploratory study was conducted at 4 Canadian Centres (Halifax, Ottawa, Hamilton, Vancouver). Purposeful samples of parents were assembled based on duration and severity of JIA. Semi-structured focus group (FG) interviews were developed, focusing on perceptions about JIA research, how information from research was obtained/used, and what information was of greatest interest. Analysis comprised an open coding and general inductive approach.

Results: FG interviews were completed at the 4 sites (individual interviews supplemented low turnout at 2 sites). FG numbers ranged from 3-8 [22 parents (16 mothers); mean age 46 (32-59)]. None of the parents were aware of receiving information from the ReACCh-Out study as part of their child’s care, but subjects uniformly agreed on the importance of Canadian JIA research. They indicated a preference to receive information from their child’s health care providers and clinician endorsed organizations. Respondents conveyed a desire to have information at the time of diagnosis and when making decisions. Parents expressed a desire to have their interests taken into account when research questions are formulated. Sample quotes are shown in Table 1. Online or printed information was preferred.

Conclusion: Parents of children with JIA want up-to-date information from research translated and incorporated into clinical care and place trust in the health care team to deliver this information. Parents, however, were generally unaware of specific research findings on JIA. Critical time points when parents feel they need the most up-to-date information have been identified, however many barriers currently exist for parents who wish to access and use this information. Future work will incorporate findings from the other stakeholders in this study and will be directed at developing KT interventions that optimize delivery and utilization of research findings to improve the care of children with JIA.

Table 1: Barriers and Facilitators with Sample Quotes
<table>
<thead>
<tr>
<th>Identified Barriers</th>
<th>Sample Quote</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of awareness of JIA research</td>
<td>“I don’t know a lot about the individual studies going on, but I would trust that the practitioners and physicians here are the top notch and are doing the research that is needed.”</td>
</tr>
<tr>
<td>Parent’s don’t want new information when their child’s disease is stable</td>
<td>“Once things were stabilized, we were a bit saturated with all the information and once we were stabilized, we said, well we’re functioning.”</td>
</tr>
<tr>
<td>Parents are overwhelmed by the large volume of complex information</td>
<td>“I read the 30 pages of information on juvenile arthritis and it made me scared, I didn’t know how to interpret it, it was too much.”</td>
</tr>
<tr>
<td>Research questions misalign with parents’ interests</td>
<td>“I wish there were more information, more studies on whether or not these adjunct therapies would help [if] integrated into the treatment.”</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Identified Facilitators</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>New diagnosis of JIA</td>
<td>“When your child is diagnosed, you research and you try and find everything you can.”</td>
</tr>
<tr>
<td>Medication change</td>
<td>“…unless you go on new medication or there’s a reason for something specific, you don’t look for new research actively.”</td>
</tr>
</tbody>
</table>

Disclosure: J. Wright, None; B. Rose-Davis, None; M. Batthish, None; T. Cellucci, None; C. M. Duffy, None; L. Tucker, None; A. Huber, None; B. Lang, None; D. M. Levy, None; D. Rumsey, None; K. N. Watanabe Duffy, None; J. Curran, None; E. Stringer, None.


Abstract Number: 2318

**Measurement of Serum Infliximab and Antibody Levels As an Adjunct to Clinical Decision Making Regarding Infliximab Therapy**

Eileen Pagano\(^1\), Myriam Kline\(^2\) and B. Anne Eberhard\(^3\), \(^1\)Pediatric Rheumatology, Cohen Children's Medical Center of New York, New Hyde Park, NY, \(^2\)Biostatistics Unit, Feinstein Institute for Medical Research, Northwell Health, Manhasset, NY, \(^3\)Pediatric Rheumatology, Cohen Children's Medical Center of New York, Lake Success, NY

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** ARHP Pediatric Rheumatology – Clinical Aspects Poster
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Infliximab (IFX) is a chimeric monoclonal antibody against tumor necrosis factor alpha (TNF-a). It is known to be effective and often used in the treatment of juvenile idiopathic arthritis (JIA) and/or chronic iritis. It is known that children on IFX therapy may develop serum antibodies to IFX. The presence of serum IFX antibodies may potentially decrease effectiveness of IFX therapy and may be associated with severe systemic allergic reactions. The purpose of our study was to determine whether the regular monitoring of IFX serum and antibody levels may be a useful clinical tool in the management of JIA and iritis patients receiving IFX.

**Methods:**

The study was a single center retrospective chart review of 28 JIA and/or chronic iritis patients who received intravenous IFX from 3/15-5/17. Data was recorded prior to each infusion, which varied from one to a maximum of 17 infusions per patient, regarding diagnosis, age, IFX dose and frequency, IFX serum and antibody levels, methotrexate and/or leflunomide dose and route, active arthritis joint count, chronic iritis and/or worsening iritis, antinuclear antibody, rheumatoid factor, cyclic citrullinated peptide antibody, erythrocyte sedimentation rate, and c-reactive protein (CRP). A generalized linear mixed model for longitudinal binary data was used to predict the outcome variables.

**Results:**

A total of 19 female and 9 male patients were included in our sample, mean (SD) age was 15 (4.5). See Table I for characteristics of study patients. While patients with arthritis develop antibodies, it appears that the clinical effects of the antibodies are only seen in the iritis patients. Anti-IFX antibodies significantly predict active iritis (p=0.05) and worsening iritis (p=0.0079); with each one hundred unit increase in anti-infliximab antibodies, the odds of active iritis increase by 16% and the odds of worsening iritis increase by 29%. Increased CRP significantly predicted active iritis (p=0.03) and worsening iritis (p=0.014); with each increase in 0.5mg of CRP/L, the odds of active iritis and worsening iritis are increased by 36% and 48%, respectively. Advancing age significantly predicted decreased incidence of active iritis (p=0.0005) and worsening iritis (p=0.0028); with each one year increase in age, the odds of active iritis and worsening iritis are decreased by 15% and 19%, respectively.

**Conclusion:**

Monitoring anti-IFX antibodies during IFX therapy appears to be useful in the management of IFX therapy in pediatric patients with iritis. Our results indicate that younger age and rising CRP are associated with increased incidence of active iritis and may be a useful alert in managing patients with iritis. Future research with a larger sample and prospective design will be needed to confirm the relationships among the variables found herein.

**Table I – Characteristics of Study Group – N = 28**
<table>
<thead>
<tr>
<th>Diagnoses</th>
<th>RRR Reason for Infliximab Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Arthritis Only</td>
</tr>
<tr>
<td>Oligo Persistent JIA – N = 6 (21.4%)</td>
<td>2</td>
</tr>
<tr>
<td>Oligo Extended JIA – N = 5 (17.9%)</td>
<td>3</td>
</tr>
<tr>
<td>Polyarticular JIA, RF-Pos, - N = 1 (3.6%)</td>
<td>1</td>
</tr>
<tr>
<td>Polyarticular JIA, RF-Neg, - N = 8 (28.6%)</td>
<td>5</td>
</tr>
<tr>
<td>Psoriatic Arthritis – N = 3 (10.7%)</td>
<td>3</td>
</tr>
<tr>
<td>Systemic Onset JIA – N = 2 (7.1%)</td>
<td>2</td>
</tr>
<tr>
<td>Idiopathic Iritis – N = 1 (3.6%)</td>
<td>0</td>
</tr>
<tr>
<td>Granulomatous Iritis – N = 1 (3.6%)</td>
<td>0</td>
</tr>
<tr>
<td>Pars Planititis – N = 1 (3.6%)</td>
<td>0</td>
</tr>
</tbody>
</table>

Disclosure: E. Pagano, None; M. Kline, None; B. A. Eberhard, None.


Abstract Number: 2319

**Bradycardia after High-Dose Solu-Medrol**

Deirdre De Ranieri and Umesh Dyamenahalli, 1Pediatric Rheumatology, The University of Chicago Medicine, Chicago, IL, 2Pediatric Cardiology, University of Chicago, Chicago, IL

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** ARHP Pediatric Rheumatology – Clinical Aspects Poster

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Methylprednisolone (MP) in both high dose (2mg/kg or higher) and pulse dose (30mg/kg up to 1000mg) is often used to treat patients with connective tissue diseases, as these doses are more effective in controlling exacerbations than lower doses. We present 6 patients with SLE who experienced bradycardia after pulse-dose MP. Three of these patients had EKGs which revealed sinus bradycardia, with heart rates decreasing below 60 beats per minute, and occasionally as much as 40%-50% below baseline. There is scarce literature explaining this occurrence, so those who are unfamiliar with steroid induced bradycardia might order redundant lab tests and imaging to further evaluate this phenomenon.

**Methods:** Review of patient medical records and the literature on this topic.

**Results:** The mechanism for this dysrhythmia remains unclear. It could be multifactorial, however one theory is that steroids, through their effect on the potassium and sodium balance in the body, may cause acute electrolyte shifts across the myocardial cell membranes, and another theory suggests that a subsequent increase in intravascular volume may trigger a reflex bradycardia. In adults, there are reports of steroid-induced bradycardia in patients with a number of
different autoimmune conditions. In children, there is little literature on this topic. Herein, we report 6 children with SLE who experienced bradycardia subsequent to high dose or pulse MP infusions. However, contrary to what has been found before, in our review of the patients, the bradycardia occurred within 4 to 24 hours of receiving MP and resolved within 24 hours of discontinuation. During this time, the patients were not symptomatic, and EKG revealed sinus bradycardia.

**Conclusion:** It is reasonable to obtain a baseline EKG and electrolytes in patients being treated for connective tissue diseases who experience bradycardia as a side effect of treatment, as these diseases can affect the myocardium independent of medications. However, if patients are asymptomatic, their electrolytes are normal, they have no prior history of cardiac disease, and the EKG reveals only sinus bradycardia, these patients require only monitoring of rhythm and hemodynamics and might not require additional tests to identify the cause of bradycardia. Because of the lack of knowledge regarding this phenomenon in pediatrics, the bradycardia in this setting leads to major concerns among the treatment team, resulting in multiple studies. Despite most patients being asymptomatic, there are reports of symptomatic steroid induced bradycardia. It would be prudent in patients with or without known underlying cardiac problems to have cardiac monitoring during high dose/pulse steroid therapy. Risk factors for steroid induced bradycardia have not been evaluated to date.

**Disclosure:** D. De Ranieri, None; U. Dyamenahalli, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/bradycardia-after-high-dose-solu-medrol](http://acrabstracts.org/abstract/bradycardia-after-high-dose-solu-medrol)

Abstract Number: 2320

**Pediatric Rheumatology Infusion Center: Report on Therapeutic Protocols and Infusion Reactions over 4 Years**

**Annelle Reed**¹, Surabhi S. Vinod², Jamelle Maxwell³, Esraa M. A. Eloseily⁴,⁵, Matthew L. Stolt⁴ and Randy Q. Cron⁴, ¹Pediatric rheumatology, Childrens of Alabama, Birmingham, AL, ²University of Alabama at Birmingham, Birmingham, AL, ³Childrens of Alabama, Birmingham, AL, ⁴Pediatric Rheumatology, University of Alabama at Birmingham, Birmingham, AL, ⁵Pediatrics, Assiut University, Assiut, Egypt

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** ARHP Pediatric Rheumatology – Clinical Aspects Poster  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

The goals of this report are to describe various therapeutic protocols, volume of intravenous (IV) infusions, and associated adverse events at the University of Alabama at Birmingham (UAB) Pediatric Rheumatology Infusion Center from 2012 through 2015.

**Methods:**

This was an institutional review board (IRB) approved retrospective chart review of 7,585 IV infusions given to 398 patients from 2012-2015. Infusion medications included abatacept, belimumab, cyclophosphamide, immune globulin (IVIG), infliximab, methylprednisolone, N-acetylcysteine, pamidronate disodium, rituximab, and tocilizumab. For calendar year 2015, all adverse reactions were recorded along with management strategies and outcomes. Rates of adverse events were calculated per infusion medication.
Results:

During calendar year 2015, 234 patients received 2,181 infusions. Newer biologics (other than IVIG) represented 59% of the total IV infusions given. Of the 234 patients, 37 experienced 45 infusion reactions. The total adverse event rate for all infusions was 2%. Medications with infusion reactions were abatacept, infliximab, immune globulin, methylprednisolone, rituximab, and tocilizumab. Rituximab had the highest rate of adverse drug reactions with 11 patients experiencing reactions during 107 infusions (10%), mainly allergic in nature, while infliximab had the lowest rate of those with reactions with 7 adverse events occurring from 818 infusions (0.8%). All reactions were mild and resolved on slowing the infusion rate and treatment with antihistamines, corticosteroids, analgesics, anti-emetics, or epinephrine as needed.

Conclusion:

In recent years, the UAB Pediatric Rheumatology Infusion Center has treated a wide variety of diagnoses and given thousands of IV infusion. Adverse reactions were few and mostly mild and transient. The use of standardized infusion protocols, the experience of managing physicians and nurses, along with the safety of the medications themselves, allow for safe IV infusions for pediatric rheumatology patients, and provide examples for similar and future infusion centers. Of note, this study does not explore potential later events, such as cancer or tuberculosis, for example.

Table 1. Diagnoses Treated from 2012-2015

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Patients (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Juvenile Idiopathic Arthritis</td>
<td>174</td>
</tr>
<tr>
<td>Oligoarticular</td>
<td>36</td>
</tr>
<tr>
<td>Polyarticular RF+</td>
<td>50</td>
</tr>
<tr>
<td>Polyarticular RF-</td>
<td>6</td>
</tr>
<tr>
<td>Psoriatic</td>
<td>20</td>
</tr>
<tr>
<td>Enthesitis related arthritis</td>
<td>38</td>
</tr>
<tr>
<td>Systemic</td>
<td>16</td>
</tr>
<tr>
<td>Unspecified</td>
<td>8</td>
</tr>
<tr>
<td>Systemic Lupus Erythematous</td>
<td>64</td>
</tr>
<tr>
<td>Juvenile Dermatomyositis</td>
<td>26</td>
</tr>
<tr>
<td>Inflammatory Bowel Disease Related Arthritis</td>
<td>26</td>
</tr>
<tr>
<td>Crohn Disease</td>
<td>19</td>
</tr>
<tr>
<td>Ulcerative Colitis</td>
<td>7</td>
</tr>
<tr>
<td>Uveitis</td>
<td>20</td>
</tr>
<tr>
<td>Sjogren Syndrome</td>
<td>15</td>
</tr>
<tr>
<td>Granulomatosis with Polyangitis</td>
<td>11</td>
</tr>
<tr>
<td>Henoch-Schonlein Purpura</td>
<td>7</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>6</td>
</tr>
<tr>
<td>Common Variable Immunodeficiency</td>
<td>6</td>
</tr>
<tr>
<td>Mixed Connective Tissue Disease</td>
<td>5</td>
</tr>
<tr>
<td>Others</td>
<td>37</td>
</tr>
</tbody>
</table>

Table 2. Total Infusions given from 2012-2015 listed by medication
<table>
<thead>
<tr>
<th>Infusions 2012-2015</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infliximab</td>
<td>3,076</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>1,882</td>
</tr>
<tr>
<td>Immune globulin</td>
<td>842</td>
</tr>
<tr>
<td>Abatacept</td>
<td>699</td>
</tr>
<tr>
<td>Rituximab</td>
<td>370</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>359</td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>292</td>
</tr>
<tr>
<td>Belimumab</td>
<td>34</td>
</tr>
<tr>
<td>Pamidronate Disodium</td>
<td>25</td>
</tr>
<tr>
<td>N-acetylcysteine</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>7,585</td>
</tr>
</tbody>
</table>

Table 3. Number of infusion reactions in 2015

<table>
<thead>
<tr>
<th>Infusion Reaction (Infusion #)</th>
<th>Abatacept</th>
<th>IVIG</th>
<th>Infliximab</th>
<th>Methylprednisolone</th>
<th>Rituximab</th>
<th>Tocilizumab</th>
<th>Total Infusion Reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rash</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Nausea/Vomiting</td>
<td>3</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Cough</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td></td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Throat Tightness/Itching/Pain</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>5</td>
<td></td>
<td></td>
<td>10</td>
</tr>
<tr>
<td>Generalized Itching</td>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Chest Pain/Tightness</td>
<td></td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Headache</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>Swelling</td>
<td>2</td>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Wheezing</td>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Hives</td>
<td></td>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Blurry Vision</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Diminished Breath Sounds</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Total Events</td>
<td>5</td>
<td>12</td>
<td>7</td>
<td>8</td>
<td>11</td>
<td>2</td>
<td>45</td>
</tr>
</tbody>
</table>

Disclosure: A. Reed, None; S. S. Vinod, None; J. Maxwell, None; E. M. A. Eloseily, None; M. L. Stoll, Novartis Pharmaceutical Corporation, 5; R. Q. Cron, SOBI, 5.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/pediatric-rheumatology-infusion-center-report-on-therapeutic-protocols-and-infusion-reactions-over-4-years](http://acrabstracts.org/abstract/pediatric-rheumatology-infusion-center-report-on-therapeutic-protocols-and-infusion-reactions-over-4-years)

Abstract Number: 2321
Current Practices and New Directions in Occupational and Physical Therapy for Children with Rheumatic Diseases in the Biologic Era

Jill R. Blitz1 and Talitha Cox2, 1Rehabilitation Services, Children's Hospital Los Angeles, Los Angeles, CA, 2MS 56, Children's Hospital Los Angeles, Los Angeles, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: ARHP Pediatric Rheumatology – Clinical Aspects Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The development of targeted biologic therapy for rheumatic diseases, has led to improved patient outcomes and a change in the role of physical (PT) and occupational therapy (OT). The purpose of this study was to assess the current role of PTs and OTs nationally and internationally in the pediatric rheumatology population.

Methods: An internet survey was sent to pediatric PTs and OTs through 3 listservs: American Physical Therapy Association pediatric section listserv, rehab directors listserv, and pediatric rheumatology bulletin board list serve. Email links were also sent directly to colleagues working in the field. Demographic information was collected. The survey identified the presence of therapies in rheumatology clinics, diagnoses seen, treatments used, and changing PT and OT patient needs and clinical practice with the advent of biologic therapy.

Results: Eighty-five therapists (58 PT/ 27 OT) from more than 40 hospitals and 2 outpatient clinics completed the survey. The majority of respondents were from the US, with others from Canada, Australia and Germany. Sixty percent of respondents had over 10 years of experience. Thirty-eight percent had PT and OT presence in the rheumatology clinic. Thirty-eight percent saw children with rheumatic diagnoses 1-2x/month and 18% saw them >2x/week. Treatment sessions were evenly distributed between stretching (20%), active ROM (21%), strengthening (21%) and building endurance (19%). Twelve percent provided casting or splinting for contractures. Forty-eight percent noted a decreased need for PT and OT services since the advent of biologics. Facilitating patient involvement in community activities was specifically identified by 48% of respondents.

Discussion: While the advent of biologics has resulted in less need for traditional PT and OT services, there continues to be an important role in providing these therapies. In addition, PT and OT clinical practice may require an increased focus on getting children with rheumatic diseases involved in community sports and activities. PT and OT are in a unique position to identify underlying issues that may present as barriers to full participation in sports or other community activities, as well as provide guidance for safe participation in these activities.

Conclusion: Since the introduction of biologics, the role of PTs and OTs in the pediatric rheumatologic population has evolved to not only include traditional therapies but also the facilitation of wellness and participation in sports and community activities.

Disclosure: J. R. Blitz, None; T. Cox, None.


Abstract Number: 2322

Quantitative Proteomics Comparison of Children with Inactive and Active Uveitis
SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Pathogenesis and Genetics Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Children with chronic non-infectious uveitis are at high risk for sight-threatening complications and vision loss. No biomarker predicts uveitis development or treatment response. Aqueous humor has been studied but is not feasible to collect in children with JIA without eye disease. Tear proteomics is increasingly used for biomarker discovery in ocular and non-ocular diseases. Advantages of tear collection are easy accessibility, non-invasiveness and tolerance. We examined the tear profile of children with uveitis to identify potential markers for activity vs dormancy.

Methods: Tear samples were collected from children with chronic non-infectious uveitis (Table 1). A Schirmer strip was placed 6mm from the lateral canthus of the anesthetized eye for 2-5 minutes. Then, 50 ug of proteins were extracted for Tandem Mass Tag (TMT) labeling. The TMT pool was loaded onto an offline electrostatic repulsion interaction chromatography (ERLIC) fractionation HPLC system and 20 fractions were collected. LC-MS/MS analysis was done on all 20 fractions. Proteome Discoverer 2.1 (ThermoFisher Scientific, San Jose, CA) was used to search all the MS/MS spectra against a Uniprot human reference protein database (retrieved April 20, 2015; 90,411 target sequences) and TMT reporter quantitation was performed.

We compared children with 1) active vs inactive uveitis of all locations and 2) active vs. inactive anterior uveitis only (JIA-associated and idiopathic). Active uveitis was defined as anterior chamber cell grade of 0.5+ (1-5 cells/hpf) and greater. Inactive uveitis was grade 0.

Results: There were 19 children (29 eyes) examined. We quantified 1426 unique protein groups and found 34 and 39 statistically significant proteins, respectively for all uveitis and anterior uveitis only comparisons. Gene ontology showed pathways related to extracellular exosomes (adjusted p=10.6e-13 for all uveitis locations and p=1.23 e-14 for anterior uveitis only). In children with anterior uveitis only, there were pathways related to intracellular RNP complex (p=7.47 e-04), poly (A) RNA binding (p=0.002), and cadherin binding involved in cell-cell adhesion (p =0.012). These results suggest the homeostatic balance of translational and signaling machinery is disrupted during disease activity.

Conclusion: We identified potential biomarkers that may differentiate active ocular inflammation in children with uveitis. This may improve our understanding of the underlying mechanisms associated with ocular inflammation in children with JIA. Discovery of biomarkers in combination with clinical outcome measures may lead to better prediction of uveitis development and response to therapy.
Table 1. Demographics and Clinical Characteristics of Children with Chronic Non-infectious Uveitis, N (%)  

<table>
<thead>
<tr>
<th></th>
<th>ALL N = 19 children</th>
<th>Active N = 12 children</th>
<th>Inactive N = 7 children</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>29 eyes</td>
<td>10 eyes</td>
<td>19 eyes</td>
</tr>
<tr>
<td>Female</td>
<td>16 (84)</td>
<td>10 (83)</td>
<td>6 (86)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>13 (68)</td>
<td>6 (50)</td>
<td>7 (100)</td>
</tr>
<tr>
<td>African American</td>
<td>6 (32)</td>
<td>6 (50)</td>
<td>0</td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>17 (89)</td>
<td>10 (83)</td>
<td>7 (100)</td>
</tr>
<tr>
<td>Age at uveitis diagnosis</td>
<td>7.6 years</td>
<td>8.5 years</td>
<td>5.8 years</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>JIA-associated uveitis (oligo or poly RF negative)</td>
<td>9 (5)</td>
<td>5 (42)</td>
<td>4 (57)</td>
</tr>
<tr>
<td>Idiopathic chronic anterior uveitis</td>
<td>5 (26)</td>
<td>4 (33)</td>
<td>1 (14)</td>
</tr>
<tr>
<td>Idiopathic uveitis, not anterior in location</td>
<td>3 (16)</td>
<td>3 (25)</td>
<td>0</td>
</tr>
<tr>
<td>HLA-B27 associated</td>
<td>2 (10)</td>
<td>0</td>
<td>2 (28)</td>
</tr>
<tr>
<td>Uveitis location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>15 (79)</td>
<td>9 (75)</td>
<td>6 (86)</td>
</tr>
<tr>
<td>Anterior/Intermediate</td>
<td>1 (5)</td>
<td>0</td>
<td>1 (14)</td>
</tr>
<tr>
<td>Intermediate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate</td>
<td>2 (10)</td>
<td>2 (17)</td>
<td>0</td>
</tr>
<tr>
<td>Posterior</td>
<td>1 (5)</td>
<td>1 (8)</td>
<td>0</td>
</tr>
<tr>
<td>Bilateral</td>
<td>16 (84)</td>
<td>10 (83)</td>
<td>6 (85)</td>
</tr>
<tr>
<td>Medication use at time of collection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Topical steroids (prednisolone acetate or difluprednate)</td>
<td>12 (63)</td>
<td>10 (83)</td>
<td>2 (28)</td>
</tr>
<tr>
<td>Timolol</td>
<td>3 (16)</td>
<td>3 (25)</td>
<td>0</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>12 (63)</td>
<td>10 (83)</td>
<td>2 (28)</td>
</tr>
<tr>
<td>Mycophenolate</td>
<td>1 (5)</td>
<td>1 (4)</td>
<td>1 (14)</td>
</tr>
<tr>
<td>Lefunomide</td>
<td>2 (10)</td>
<td>1 (8)</td>
<td>1 (14)</td>
</tr>
<tr>
<td>Infliximab</td>
<td>6 (32)</td>
<td>3 (25)</td>
<td>3 (43)</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>3 (16)</td>
<td>2 (17)</td>
<td>1 (14)</td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>2 (10)</td>
<td>1 (8)</td>
<td>1 (14)</td>
</tr>
</tbody>
</table>

Disclosure: S. Angeles-Han, None; D. Duong, None; S. Yeh, None; P. Patel, None; V. Miraldi Utz, None; K. Jenkins, None; D. Lowe, None; S. Prahalad, None; G. Holland, None.


Abstract Number: 2323

Exploring HLA-DRB1 Risk Alleles in Non-Hispanic African American Children with Juvenile Idiopathic Arthritis and Chronic Anterior Uveitis

Lai Hin Kimi Chan¹, Courtney McCracken¹, Kirsten Jenkins², Steven Yeh³, Purnima Patel⁴, Sampath Prahalad⁵ and Sheila Angeles-Han⁶, ¹Pediatrics, Emory University School of Medicine, Atlanta, GA, ²Children's Healthcare of
Exploring HLA-DRB1 Risk Alleles in Non-Hispanic African American Children with Juvenile Idiopathic Arthritis and Chronic Anterior Uveitis

Background/Purpose:
HLA-DRB1*08, 11 and 13 are risk alleles associated with juvenile idiopathic arthritis (JIA). Carriage of DRB1*11 and *13 may increase the risk for uveitis in Non-Hispanic White children with oligoarticular and polyarticular rheumatoid factor (RF) negative JIA. HLA-B8, in linkage disequilibrium with DRB1*03, was reported in African American children with uveitis. Few studies investigate the role of HLA-DRB1 alleles in Non-Hispanic African American (NH AA) children with JIA or uveitis because they are rare conditions. Our aim is to explore the association of HLA-DRB1 alleles in NH AA children with JIA and chronic anterior uveitis (CAU).

Methods:
High-resolution HLA-DRB1 genotyping was performed to determine the frequency of HLA-DRB1*03, 08,11 and 13 alleles in our cohort of NH AA children with JIA and/or uveitis. Frequencies were compared among JIA and CAU (JIA-associated uveitis and idiopathic chronic anterior uveitis) groups using Chi-square tests and Exact tests. In addition, we compared the frequency of these alleles in our cohorts to 3734 AA healthy controls from the National Marrow Donor Program (NMDP) using two-sided Z-tests for proportions.

Results:
There were 58 NH AA children (43 JIA, 6 JIA-associated uveitis, and 9 idiopathic chronic anterior uveitis) who were mainly female (66%). Of those with JIA, 22 (45%) had extended or persistent oligoarticular JIA, and 27 (55%) had polyarticular RF negative JIA. Antinuclear antibody was positive in 17 (40%) JIA children and 3 (50%) JIA-associated uveitis (JIA-U) children.

Comparing children with JIA and CAU, there was a borderline significant difference in DRB1*03 (30.2% vs. 6.7%, p = 0.087) (Table 1).

Compared to AA controls, NH AA children with JIA alone had increased DRB1*03 (30.2% vs. 13.6%, p = 0.001), DRB1*08 (18.6% vs. 3.3%), and DRB1*11 (32.6% vs. 13.4%, p < 0.001). NH AA children with CAU (JIA-U and idiopathic chronic anterior uveitis) also had increased DRB1*08 (13.3% vs. 3.3%, p = 0.029) and DRB1*11 (46.7% vs. 13.4%, p < 0.001), which may be associated with the JIA diagnosis (Table 2).

Conclusion:
Carriage of HLA-DRB1*08 and 11 may increase the risk for JIA and uveitis in NH AA children. Carriage of DRB1*03 may also increase the risk for JIA in this cohort. Further studies including larger sample sizes of NH AA children should be conducted to investigate the role of HLA-DRB1 in children with JIA and uveitis.
Table 1. HLA-DRB1 alleles in Non-Hispanic African American Children with Polyarticular Rheumatoid Factor Negative or Oligoarticular JIA and Chronic Anterior Uveitis

<table>
<thead>
<tr>
<th>HLA configuration</th>
<th>JIA* N = 43</th>
<th>CAU* N = 15</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRB1*03</td>
<td>13 (30.2%)</td>
<td>1 (6.7%)</td>
<td>0.087</td>
</tr>
<tr>
<td>DRB1*08</td>
<td>8 (18.6%)</td>
<td>2 (13.3%)</td>
<td>0.719</td>
</tr>
<tr>
<td>DRB1*11</td>
<td>14 (32.6%)</td>
<td>7 (46.7%)</td>
<td>0.393</td>
</tr>
<tr>
<td>DRB1*13</td>
<td>8 (18.6%)</td>
<td>5 (33.3%)</td>
<td>0.288</td>
</tr>
</tbody>
</table>

*JIA: juvenile idiopathic arthritis; *CAU: chronic anterior uveitis (9 idiopathic chronic anterior uveitis, 6 JIA-associated uveitis)

Table 2. Comparison of Allele Frequencies in Our AA Cohort to the General AA Population

<table>
<thead>
<tr>
<th>N (%)</th>
<th>P-value vs. control</th>
<th>JIA* N = 43</th>
<th>CAU* (U-JIA-U) N = 15</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRB1*03</td>
<td>13.6%</td>
<td>13 (30.2%)</td>
<td>1 (6.7%)</td>
</tr>
<tr>
<td></td>
<td>P = 0.001**</td>
<td>P = 0.433</td>
<td>P = 0.029**</td>
</tr>
<tr>
<td>DRB1*08</td>
<td>3.3%</td>
<td>8 (18.6%)</td>
<td>2 (13.3%)</td>
</tr>
<tr>
<td></td>
<td>P &lt; 0.001**</td>
<td>P = 0.098</td>
<td>P &lt; 0.001**</td>
</tr>
<tr>
<td>DRB1*11</td>
<td>13.4%</td>
<td>14 (32.6%)</td>
<td>7 (46.7%)</td>
</tr>
<tr>
<td></td>
<td>P &lt; 0.001**</td>
<td>P = 0.098</td>
<td>P &lt; 0.001**</td>
</tr>
<tr>
<td>DRB1*13</td>
<td>17.2%</td>
<td>8 (18.6%)</td>
<td>5 (33.3%)</td>
</tr>
<tr>
<td></td>
<td>P = 0.810</td>
<td>P = 0.098</td>
<td>P = 0.098</td>
</tr>
</tbody>
</table>

Disclosure: L. H. K. Chan, None; C. McCracken, None; K. Jenkins, None; S. Yeh, None; P. Patel, None; S. Prahalad, None; S. Angeles-Han, None.


Abstract Number: 2324

**Single Cell RNA-sequencing of Bone Marrow Macrophages Identifies a Distinct Subpopulation in Systemic JIA with Features of Interferon Response, Endocytic Vesicles and Phagocytosis**

Grant Schulert¹, Nathan Salomonis², Sherry Thornton³ and Alexei A. Grom⁴, ¹Pediatric Rheumatology, Division of Pediatric Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, ²Division of Biomedical Informatics, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, ³Cincinnati Children's Hospital Medical Center, Cincinnati, OH, ⁴Division of Pediatric Rheumatology, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH, United States Minor Outlying Islands

First publication: September 18, 2017
Background/Purpose: Macrophage activation syndrome (MAS) is a life-threatening complication of systemic juvenile idiopathic arthritis (SJIA), characterized by activation and expansion of cytolytic lymphocytes and macrophages with hemophagocytic properties. Recent work has shown that emergence of MAS is associated with a surge in IFNg and IFN-induced chemokines; however, previous gene expression studies failed to demonstrate this IFN-induced signature in peripheral blood cells. However, these studies were limited by a failure to examine key myeloid effector cells, specifically activated macrophages which traffic to tissue including bone marrow during MAS.

Objective: Utilize single-cell RNA-sequencing to identify specific gene expression signatures of bone marrow macrophage populations in SJIA and MAS.

Methods: Macrophage single cell suspensions were obtained from unused portions of bone marrow aspirates using cell sorting for populations expressing the monocyte and macrophage surface markers CD14 and CD163 while excluding cells expression the granulocyte/monocyte marker CD15, prior to loading onto the Fluidigm C1 Single-Cell Auto Prep System. Extracted RNA was converted into cDNA and sequenced as a pooled library, and aligned to the human Ensembl transcriptome using Kallisto through AltAnalyze version 2.1.1.

Results: Three control samples yielded 180 single cells, and while there was substantial inter-individual variability, a core set of genes were identified that contributed to the heterogeneity of normal bone marrow macrophage population. Control macrophages formed at least three primary cellular clusters, which were distinguished based on expression of genes associated with proinflammatory receptors, GM-CSF signaling, and aurora B signaling. 61 single bone marrow macrophages were captured from a patient with newly diagnosed SJIA with active systemic features, arthritis, marked anemia, relative thrombocytopenia, but lacking other overt signs of MAS, but did have mild hemophagocytosis on diagnostic bone marrow aspiration. Expression profiles were broadly similar to control macrophages, and all macrophage clusters were represented. However, a distinct subpopulation of bone marrow macrophages from the SJIA patient was identified that exhibited markedly altered transcriptional profiles. Compared to other control and patient macrophages, this SJIA macrophage population showed alterations in gene pathways including cellular response to interferon gamma (p=1.35e-14), endocytic vesicle membranes (p=8.44E-14), phagosome (p=2.98e-9) and vesicle-mediated transport (p=1.05E-07). These cells showed a proinflammatory gene expression signature, including enrichment for genes regulated by NF-kB and STAT1.

Conclusion: We identify a distinct subpopulation of bone marrow macrophages in an SJIA patient with features associated with emergence of MAS, including interferon response, phagocytosis and vesicular transport. This validates a single-cell approach, and demonstrates the importance of studying these effector cells at the sites of inflammation, and suggests that tissue macrophages may be a key source of IFN-induced products during MAS.

Disclosure: G. Schulert, Novartis Pharmaceutical Corporation, 5; N. Salomonis, None; S. Thornton, None; A. A. Grom, NovImmune, Novartis Pharmaceutical Corporation, Roche Pharmaceuticals, 2.


Abstract Number: 2325

Extensive Serum Cytokine Analysis in Patients with Macrophage Activation Syndrome Complicating Systemic Juvenile Idiopathic Arthritis
The pathogenesis of Macrophage activation syndrome (MAS) complicating systemic juvenile idiopathic arthritis (s-JIA) is still unknown, but overproduction of proinflammatory cytokines from activated T lymphocytes and macrophages plays an important role to develop MAS. To understand the pathogenesis of MAS and to identify serum biomarker for the diagnosis of MAS, we employed an antibody array that simultaneously detects 174 serum cytokines.

Methods:

Twenty five patients with s-JIA and 4 healthy controls (HCs) were analyzed. Among 25 s-JIA patients, 15 patients including 5 patients receiving tocilizumab (TCZ) were complicated with MAS. Serum cytokine levels were quantified by Raybio Human Cytokine Antibody Array. Serum CXCL9 levels were quantified by enzyme-linked immunosorbent assay. The results were compared with the clinical features of MAS.

Results:

We identified fourteen cytokines whose levels increased in MAS compared to those in active phase of s-JIA. Of which, CXCL9, an interferon-γ induced chemokine, increased most significantly with the development of MAS. The cytokine profile during active phase of s-JIA was quite different between those in s-JIA patients with MAS and without MAS. Eighteen cytokines and 72 cytokines were lower in patients receiving TCZ compared to those in patients not receiving TCZ in active phase of s-JIA and in MAS, respectively. Serum CXCL9 levels were significantly elevated in MAS compared to those in the acute phase of s-JIA. Serum CXCL9 levels profoundly and rapidly increased as MAS developed and correlated positively with disease activity. Serum CXCL9 levels were significantly lower in patients receiving TCZ but those reflected disease activity.

Conclusion:

The elevated levels of CXCL9 and their correlation with disease activity of MAS indicate a pivotal role of IFN-γ in MAS. Monitoring of serum CXCL9 is useful for the evaluation of disease activity in s-JIA and MAS. The expression of many inflammatory cytokines decreased in patients receiving TCZ, suggesting suppress of many cytokines other than IL-6 by TCZ is closely related to masking of clinical symptoms of MAS and s-JIA during TCZ therapy.

Disclosure: M. Mizuta, None; M. Shimizu, None; N. Inoue, None; K. Kasai, None; Y. Nakagishi, None; A. Yachie, None.
Modeling Transcriptional Rewiring in Neutrophils through the Course of Treated Juvenile Idiopathic Arthritis

Zihua Hu¹, Kaiyu Jiang², Mark B. Frank³, Yanmin Chen² and James Jarvis⁴, ¹Center for Computational Research, University at Buffalo, Buffalo, NY, ²Pediatrics, University at Buffalo, Buffalo, NY, ³Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, ⁴Department of Genetics, Genomics & Bioinformatics, University at Buffalo, Buffalo, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Pathogenesis and Genetics Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: We have previously shown that neutrophils in children with polyarticular juvenile idiopathic arthritis (JIA) display abnormal transcriptional patterns linked to fundamental metabolic derangements. These transcriptional abnormalities include complex re-ordering of miRNA-RNA expression networks. In the current study, we sought to determine the effects of therapy of the reorganization of miRNA-RNA networks in polyarticular JIA.

Methods: In this cross-sectional analysis, we studied children with untreated, active JIA (ADU-n=35), 26 children with active disease on therapy with methotrexate + etanercept (ADT), and 14 children with inactive disease also on therapy (ID). We used Affymetrix exon and miRNA microarrays to identify expressed transcripts and compared results to findings from 35 healthy control (HC) children.

Results: Computational modeling demonstrated substantial re-ordering of miRNA-RNA networks after the initiation of therapy. Each of the 3 disease states, i.e., ADU, ADT, and ID, was associated with its own distinct transcriptional profile that showed only modest overlaps with the other 2. Gene ontology analysis corroborated this finding, as the genes showing differential expression between each of the disease states and HC were associated with different biological functions. Among the networks, the ADT state differed the most from HC while ID more strongly resembled HC. Computational modeling demonstrated complex interactions between transcription factors and miRNA that determine the gene expression signatures of each disease state.

Conclusion: Therapy for JIA induces substantial re-organization of neutrophil transcriptomes. It is interesting to note that each of the different treatment stages, which we derived from clinical observations (Wallace criteria), appear to be biologically distinct. These findings affirm the value of using the Wallace criteria for staging treatment response in JIA. Furthermore, these findings demonstrate that treatment response is not a linear process that results in gradual “normalization” of transcriptomes. Rather, treatment response occurs in distinct phases each with its own specific pattern of gene expression.

Disclosure: Z. Hu, None; K. Jiang, None; M. B. Frank, None; Y. Chen, None; J. Jarvis, None.


Abstract Number: 2327

14-3-3η (eta) Protein in Juvenile Idiopathic Arthritis (JIA) Patients

Austin M. Dalrymple¹, Paul Tuttle IV¹, Lance Feller², Olga S. Zhukov³, Robert J. Lagier⁴, Robert Bridgforth⁵, Gary J Williams⁵, Joanna M. Popov³, Stanley J. Naides³ and Terry Moore⁶, ¹Division of Adult & Pediatric Rheumatology,
Background/Purpose: 14-3-3 proteins are chaperonins found in all eukaryotic cells. There are multiple isoforms which are thought to be involved in intracellular signaling and transcription regulation. Recent work has implicated the η (eta) isoform as having diagnostic potential in inflammatory arthritides. Its utility in JIA has not been established. Our preliminary prior investigation indicated positivity in some JIA patients. In this study, we investigated a much larger cohort of patients with JIA and disease and healthy controls.

Methods: Measurement of 14-3-3η protein was evaluated in 29 rheumatoid factor (RF) positive (pos) polyarticular (poly) JIA patients, 29 RF negative (neg) poly patients, 34 oligoarticular (oligo) patients, 12 systemic-onset (SO) patients, 19 adult rheumatoid arthritis (RA) patients, 60 patients with systemic lupus (SLE), and 20 healthy controls by the assay established at Quest Diagnostics. Comparisons were made to CBC, ESR, CRP, RF and anti-CCP isotypes, and ANA positivity.

Results: 14-3-3η at 0.2 ng/ml or higher was considered positive; values of 0.5 ng/mL or greater have been considered prognostic of poor outcome in adults. Ten of 29 (34%) RF pos polys were positive for the 14-3-3η protein; 8 (28%) had values > 0.5 ng/mL. Nine of 29 (31%) RF neg polys were positive; 8/29 (28%) had values >0.5 ng/mL. Only 6/34 (18%) oligos were positive; 5/34 (15%) >0.5 ng/mL. Only 2/12 (16%) SO were positive; 1/12 (8%) >0.5 ng/mL. In the disease controls, 14/60 (23%) SLE were positive, but only 7/60 (12%) >0.5 ng/mL. 7/19 (37%) RA patients were positive, 4/19 (21%) >0.5 ng/mL. In the healthy controls, only 3/20 (15%) were positive, 1/20 (5%) > 0.5 ng/mL. The RF pos and RF neg polys positivity, especially at values >0.5 ng/mL compared favorably with the adult RA patient and were notable compared to disease and healthy controls. A weak correlation was noted between 14-3-3η positivity and CRP. Five of the 8 RF neg polys at original diagnosis that were 14-3-3η positive at >0.5 ng/mL have subsequently developed a positive RF and an anti-CCP antibody isotype. Also, the one SO positive for 14-3-3η >0.5 ng/mL also developed a positive RF.

Conclusion: Significant levels of 14-3-3η protein can be found in about 30% of RF pos and RF neg poly JIA patients. It may represent a new biomarker for RF neg poly JIA patients and a marker indicating the possibility of these patients becoming RF/anti-CCP antibody positive in the future. Further longitudinal studies are required to confirm these findings.

Disclosure: A. M. Dalrymple, None; P. Tuttle IV, None; L. Feller, None; O. S. Zhukov, Quest Diagnostics, 3; R. J. Lagier, Quest Diagnostics, 1, Quest Diagnostics, 3; R. Bridgforth, Quest Diagnostics, 3; G. J. Williams, Quest Diagnostics, 1, Quest Diagnostics, 3; J. M. Popov, Quest Diagnostics, 1, Quest Diagnostics, 3; S. J. Naides, Quest Diagnostics, 3, Quest Diagnostics, 1; T. Moore, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/14-3-3%ce%b7-eta-protein-in-juvenile-idiopathic-arthritis-jia-patients

Abstract Number: 2328
Characterisation of Lipid Mediator Profile and Immune Cells in Synovial Fluid of Juvenile Idiopathic Arthritis

Johannes Hendrick von Hegedus1, Q. S. R. Madari2, P.C.E. Hissink Muller3, M. Kloppenburg4, REM Toes4, Martin Giera5, TWJ Huizinga4, Rebecca ten Cate6 and A. Ioan-Facsinay4, 1Department of Rheumatology, LUMC, Leiden, Netherlands, 2LUMC, Leiden, Netherlands, 3Willem-Alexander Children's Hospital, LUMC, Leiden, Netherlands, 4Rheumatology, Leiden University Medical Center, Leiden, Netherlands, 5Center for Proteomics and Metabolomics, Leiden University Medical Center, Leiden, Netherlands, 6Leiden University Medical Center, Leiden, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Pathogenesis and Genetics Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Juvenile Idiopathic Arthritis (JIA) is often accompanied by inflammation of the joints. The mechanisms involved in the inflammation in JIA are incompletely understood. Several cells and soluble mediators, including lipid mediators regulate the course of inflammation. Lipid mediators such as prostaglandins and leukotrienes, derived from arachidonic acid have mostly pro-inflammatory properties, while specialized pro-resolving lipid mediators (SPM) derived from docosahexaenoic and eicosapentaenoic acid have anti-inflammatory/pro-resolving actions. Both types of lipid mediators are generated by cyclooxygenases and lipoxygenases. It is currently unknown which lipid pathways are present in synovial fluid (SF) of JIA.

The aim of this pilot study is to identify the lipid mediators present in the SF of JIA to gain a better understanding of the inflammatory process in the JIA joint.

Methods:
Ten anonymized JIA SF were obtained as leftover material from arthrocentesis from patients visiting the outpatient unit of the Pediatrics department in the LUMC. Clinical data such as diagnosis, age, gender and BMI were provided. Different immune cell populations in the SF were identified using flow cytometry. The presence of 60 different lipid mediators was determined in SF using liquid chromatography-mass spectrometry (LC-MS/MS) after hyaluronidase treatment, protein precipitation using methanol followed by enrichment for polar lipids by solid-phase extraction.

Results:
Major immune cell populations identified in SF were monocytes, neutrophils, T cells and B cells. In general, the abundance of these populations was comparable in all JIA samples, except for neutrophils, which were more prevalent in patients that showed enthesitis.

Using LC-MS/MS, we detected arachidonic acid and several of its derivatives in SF. Pro-inflammatory lipid mediators and their precursors derived from arachidonic acid and generated by cyclooxygenases (thromboxane B2, prostaglandin E2) and 5-lipoxygenase (5-HETE and leukotriene B4) were detected in most of the samples. Interestingly, precursors of arachidonic acid-derived anti-inflammatory lipids generated by 15-lipoxygenase (15-HETE) and 12-lipoxygenase (12-HETE) were also detected. However, despite the high levels of docosahexaenoic acid (a precursor of SPM) present in all SF, we did not detect any of its anti-inflammatory lipoxygenase derivatives or SPM. Moreover, only low levels of eicosapentaenoic acid (a precursor of SPM) were detected, but none of its derivatives.

Conclusion:
Our data suggests that the enzymatic pathways involved in both pro-inflammatory and anti-inflammatory lipid mediator production are active in JIA. However, they appear to preferentially handle arachidonic acid above docosahexaenoic and eicosapentaenoic acid to generate downstream metabolites.

**Disclosure:** J. H. von Hegedus, None; Q. S. R. Madari, None; P. C. E. Hisssink Muller, None; M. Kloppenburg, None; R. Toes, None; M. Giera, None; T. Huizinga, Abbott Laboratories, Biotest AG, Bristol-Myers Squibb, Crescendo Bioscience, Novartis Pharmaceuticals Corporation, Pfizer Inc, Roche, sanofi-aventis, Schering-Plough, UCB, Eli Lilly, 5,METEOR Board, 6,EU & Dutch Arthritis Foundation, 2,Abbott Laboratories, Biotest AG, Bristol-Myers Squibb, Novartis Pharmaceuticals Corporation, Pfizer Inc, Roche, sanofi-aventis, Schering-Plough, 8,Abbott Laboratories, Roche, 9; R. ten Cate, None; A. Ioan-Facsinay, None.


**Abstract Number:** 2329

**Monocytes from Patients with Enthesitis Related Arthritis Produce High Levels of Pro-Inflammatory Cytokines: Role of Endogenous Ligands**

Amita Aggarwal¹, Shruti Bhattacharya² and Ramnath Misra², ¹Department of Clinical Immunology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, ²Clinical Immunology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Tuesday, November 7, 2017
**Session Title:** Pediatric Rheumatology – Pathogenesis and Genetics Poster
**Session Type:** ACR Poster Session C
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** HLA B27 and gut bacteria are postulated to play a role in pathogenesis of Enthesitis Related Arthritis. Gut microbes can activate monocytes/macrophages by TLR pathway. However the mechanism of perpetuation of inflammation is not clear. Levels of endogenous ligands of TLR4 like myeloid Related Protein (MRP) 8/14 and Tenascin-C (TNC) are increased in patients with ERA. Thus we studied if monocytes from patients with ERA produce more pro-inflammatory cytokines in response to stimulation with TLR4 endogenous ligands (TNC and MRP8/14) as compared to healthy controls.

**Methods:** ERA patients satisfying ILAR criteria were enrolled. Whole blood was stimulated with TNC protein, MRP8/14 protein fragment, LPS or Proteoglycan for 24 hours and the culture supernatant was analyzed for IL-6 and TNF-alpha. Cytokine production was also measured by flow, cytometry after 6 hours culture and staining with antibodies against CD14, TNF-α and IL-6.

**Results:** 38 ERA patients (14.5 ± 3.6 years) with JSpADA score of (3.8 ± 1.15) and 23 healthy controls were enrolled. ERA patients showed significantly higher TNF-a production at baseline (18.4 ± 14.2 ng/ml for HC, 57.9 ± 53.21 ng/ml for ERA; p<0.05) as well as after stimulation by MRP8/14 (ERA-135.56 ± 165.51 ng/ml; p<0.05), Tenascin C (ERA- 89.03 ± 81.8 ng/ml), LPS (ERA-583.38 ± 212.59 ng/ml) and PG (ERA- 1104.43 ± 272.94 ng/ml) as compared to healthy subjects(p<0.05).

IL-6 production levels though not increased at baseline showed a significant increase after LPS (HC- 26.11 ± 7.62 pg/ml, ERA- 33.24 ± 6.49 pg/ml), PG (HC- 30.41 ± 10.63 pg/ml, ERA- 42.23 ± 6.35 pg/ml) and TNC (HC- 8.78 ± 7.39 pg/ml, ERA- 21.47 ± 9.43 pg/ml) stimulation (all p<0.01) as compared to healthy controls.
On flow cytometry also the ERA patients had higher frequency of TNF alpha producing monocytes as compared to healthy control (ERA-23.70 ± 12.0, p<0.01) at baseline. Stimulation with the endogenous ligands viz., MRP8 (HC-33.9 ± 6.9, ERA- 50.78 ± 15.74), TNC (HC- 22.4 ±10.2, ERA- 32.1 ± 15.16) and exogenous ligands viz., LPS (HC- 69.6 ±12.2, ERA- 85.75 ± 14.64) and PG (HC-70.2 ± 12.1,ERA- 89.27 ± 11.15) led to a significant increase in the frequency of TNF-α producing monocyte frequency in ERA patients compared to healthy controls (p <0.01). Similar trend was seen in frequency of IL-6 producing cells.

**Conclusion:** Patients with ERA have pre-activated monocytes in their peripheral blood. TLR4 endogenous ligands may be contributing to immune-inflammation by activating monocytes and leading to production of high levels of pro-inflammatory cytokines.

**Disclosure:** A. Aggarwal, None; S. Bhattacharya, None; R. Misra, None.

**View Abstract and Citation Information Online** - http://acrabstracts.org/abstract/monocytes-from-patients-with-enthesis-related-arthritis-produce-high-levels-of-pro-inflammatory-cytokines-role-of-endogenous-ligands

**Abstract Number:** 2330

**Evidence for Alternatively Activated (M2) Macrophage Activation in Patients with Enthesitis Related Arthritis Category of Juvenile Idiopathic Arthritis**

Amita Aggarwal¹, Priyanka Gaur² and Akhilesh Yadav³, ¹Clinical Immunology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, ²Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, ³Department of Clinical Immunology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017
**Session Title:** Pediatric Rheumatology – Pathogenesis and Genetics Poster
**Session Type:** ACR Poster Session C
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Among juvenile idiopathic arthritis (JIA), enthesitis related arthritis (ERA) category includes most children with juvenile onset spondyloarthropathy (SpA). Synovial fluid from patients with SpA causes more M2 polarization of peripheral blood monocytes than SF from patients with RA. Recently an increase in CD163+ macrophages was seen in ileal biopsies from patients with AS. A 6.5 fold higher expression of CD163 has been reported in SFMC gene expression as compared to PBMC of children with ERA. Thus we studied levels of sCD163 as a marker of activation of M2 macrophages in serum and synovial fluid of children with ERA.

**Methods:**

Serum samples from patients with ERA and healthy young adults were assayed for sCD163 using ELISA (R&D systems). In addition SF from children with ERA was also analyzed where available.

**Results:**

Sera from 85 patients and synovial fluid from 32 patients with ERA and serum from 46 young adults were analyzed. The average age of patients at inclusion was 16+3.24 years and age at onset was 11.2+2.79 years. 79 of them were boys
and HLA B27 was positive in 64/80 patients (data not available in 5)

The mean serum sCD163 levels were higher in patients as compared to healthy controls (1433.61 +1256.11 versus 907.35+726.56ng/ml; p<0.001). The synovial fluid levels were much higher than serum levels (4307.38+3363.92 ng/ml; p<0.003). Data on disease activity was available in 56 patients. The mean TJC was 3+2.7, SJC was 2.3+2.2, ESR was 74+34 mm and CRP was 6.98+5.4 mg/dl. The serum levels of sCD163 did not have any correlation with disease activity parameters.

Conclusion:

A higher levels of sCD163 in serum of patients with ERA and even higher levels in paired SF suggest that there is activation of alternatively activated macrophages in ERA. Lack of correlation with activity may suggest that they have immune regulatory role in patients with ERA.

Disclosure: A. Aggarwal, None; P. Gaur, None; A. Yadav, None.


Abstract Number: 2331

Next Generation Sequencing Analysis of Familial Haemophagocytic Lymphohistiocytosis (HLH) Related Genes in Macrophage Activation Syndrome (MAS) and Secondary HLH (sHLH)

Chiara Passarelli1, Manuela Pardeo2, Ivan Caiello3, Elisa Pisaneschi1, Antonio Novelli1, Fabrizio De Benedetti4 and Claudia Bracaglia2, 1Unit of Medical Genetics, Laboratory of Cytogenetics and Molecular Genetics, IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy, Rome, Italy, 2Division of Rheumatology, IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy, Rome, Italy, 3Division of Rheumatology, IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy, Rome, Italy, 4Division of Rheumatology, IRCCS Bambino Gesù Children's Hospital, Rome, Rome, Italy

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Pathogenesis and Genetics Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Macrophage activation syndrome (MAS) is a severe complication of rheumatic disease, particularly of systemic JIA (sJIA). It is currently classified among the secondary forms of HLH (sHLH). Primary HLH (pHLH) is caused by mutation of genes that code for proteins that are involved in cytotoxic functions. Mice carrying heterozygous mutations in more than 1 pHLH gene carry a higher risk to develop HLH following viral infection, suggesting that accumulation of partial genetic defects may be relevant in HLH.

Methods: Genes involved in pHLH were analysed, with next generation sequencing (NGS), in MAS in the context of different rheumatic diseases and in sHLH. A Targeted resequencing were performed on all patients using a panel including the 7 principal HLH-related genes (PRF1, UNC13d, STX11, STXBP2, RAB27a, XIAP, SH2D1A). Sequencing analysis were performed on the MiSeq® and NextSeq550® platforms (Illumina, San Diego, CA); all variants identified were confirmed by Sanger. The possible functional impact of variants was studied by in silico analysis using SIFT and PolyPhen softwares. We took into account only variants with anallelic frequency in the global population up to 1%, in
the dbSNP and Ensembl databases, with the exception of A91V variant in PRF1 gene, because of its conflicting interpretation of pathogenicity.

**Results:** Fifty patients, 29 MAS (23 developed this complication in the context of sJIA, and 6 developed MAS respectively in the context of systemic vasculitis, Crohn’s disease, systemic lupus erythematosus, anti-phospholipid syndrome, chronic recurrent multifocal osteomyelitis and Kawasaki disease) and 21 patients with HLH secondary to infections or without any demonstrable trigger, were analysed. At least 1 heterozygous variant was identified in one of the pHLH-associated genes in 24 patients (12/29 MAS, 12/21 sHLH) with a detection rate of 48%. Seventeen patients (34%) showed only 1 variant, while more than 1 variant were found in 7 patients (14%). Seven (24%) patients with MAS showed the A91V variant in PRF1 in an heterozygous state, and 5 (17%) patients showed an heterozygous variant in UNC13d gene. Four of the 29 MAS patients had mutations in two different genes: one of them had recurrent episodes of MAS with a severe disease and a prolonged ICU admission. Two MAS patients carried 2 heterozygous variants in the same gene. Three (14%) patients with sHLH showed a heterozygous mutation in RAB27a, 3 in UNC13d and 4 in PRF1 gene. Two patients carried more than a single heterozygous variant: one had variants in two different genes, while one patient showed 3 different variants in the same gene (PRF1). For two of these patients with variants in two different genes, one of them presented three episodes of HLH reactivation and the other one presented a severe disease with exitus.

**Conclusion:** Mutations of PRF1 and UNC13d genes were frequently observed in patients with MAS or secondary HLH; RAB27a variants seems to be more frequent in patients with sHLH. Re-occurrence and severity of disease tend to be more frequent and more severe in sHLH patients who carry mutations in two genes. The contribution of these variants to the risk of MAS or sHLH remains to be established in the context of a polygenic model of sHLH and MAS.

**Disclosure:** C. Passarelli, None; M. Pardeo, None; I. Caiello, None; E. Pisaneschi, None; A. Novelli, None; F. De Benedetti, Novartis, Roche, Pfizer, SOBI, AbbVie, Novimmune, BMS, Sanofi, 2; C. Bracaglia, None.


**Abstract Number:** 2332

**Biomarkers for the Diagnosis and the Identification of Risk of Macrophage Activation Syndrome (MAS) in Systemic Juvenile Idiopathic Arthritis (sJIA)**

**Claudia Bracaglia**¹, Denise Pires Marafon², Ivan Caiello³, Kathy de Graaf⁴, Maria Ballabio⁴, Walter Ferlin⁴, Sergio Davi⁵, Grant Schulert⁶, Angelo Ravelli⁷, Alexei A. Grom⁸, Robert Nelson⁴, Cristina de Min⁴ and Fabrizio De Benedetti², ¹Division of Rheumatology, IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy, ²Division of Rheumatology, IRCCS Bambino Gesù Children's Hospital, Rome, Rome, Italy, ³Division of Rheumatology, IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy, Rome, Italy, ⁴NovImmune S.A., Geneva, Switzerland, ⁵University of Genova, IRCCS Istituto Giannina Gaslini, Genoa, Italy, ⁶Pediatric Rheumatology, Division of Pediatric Rheumatology, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH, ⁷University of Genova, IRCCS Istituto Giannina Gaslini, Genova, Italy, ⁸Division of Pediatric Rheumatology, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH, United States Minor Outlying Islands

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Pediatric Rheumatology – Pathogenesis and Genetics Poster
Background/Purpose: We have recently reported high levels of IFNγ and of the IFNγ-related chemokines, (CXCL9 and CXCL10) in patients with MAS (1).

Methods: Circulating levels of IFNγ, CXCL9, CXCL10, IL-18, neopterin and sCD25 IFNγ, CXCL9, CXCL10, IL-18, neopterin and sCD25 were measured by Luminex assay in 57 samples obtained from 24 patients with active sJIA and in 37 samples from 20 MAS patients with variable degrees of disease severity and under different treatments at time of sampling. We evaluated if blood levels of these biomarkers may help to identify sJIA patients with the predisposition to develop MAS, and additionally if they may help clinicians to distinguish MAS from active sJIA.

Results: Levels of IFNγ, CXCL9, CXCL10, IL-18, neopterin and sCD25 were significantly elevated in MAS compared to active sJIA without MAS at sampling (p-values <0.0001, except for IL-18 p=0.012) and were significantly correlated with laboratory parameters of disease severity, except for IL-18, whose levels were available only for a portion of the samples. During active sJIA without MAS at sampling, levels of the IFNγ-induced chemokines (CXCL9 and CXCL10) were significantly higher in patients with a history of MAS as compared to those of patients without a history of MAS (Table 1). In order to verify if measurement of these biomarkers could help in distinguishing MAS from active sJIA, we analyzed sensitivity and specificity and the area under the curve (AUC) for each parameter. The highest AUC (=0.95) was found for neopterin levels >14.62 nmol/L (Sensitivity 85.3% Specificity 84.6%). AUC for IFNγ (>8.5 pg/ml), CXCL9 (>2677 pg/ml), CXCL10 (>725.5 pg/ml), IL-18 >(4309 pg/ml) and sCD25 (>211.65 pg/ml) were 0.77, 0.82, 0.82, 0.82 and 0.86, respectively.

Table 1. Cytokine levels in sJIA patients with active disease with or without history of MAS

<table>
<thead>
<tr>
<th></th>
<th>sJIA with history of MAS</th>
<th>sJIA without history of MAS</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N=17)</td>
<td>(N=40)</td>
<td></td>
</tr>
<tr>
<td>IFNγ (pg/ml)</td>
<td>5.6 (3.2-14.4)</td>
<td>5.3 (3.2-10)</td>
<td>0.74</td>
</tr>
<tr>
<td>CXCL9 (pg/ml)</td>
<td>3889 (965-7142)</td>
<td>519 (385-1168)</td>
<td>0.0015</td>
</tr>
<tr>
<td>CXCL10 (pg/ml)</td>
<td>764 (323-1259)</td>
<td>215 (152-470)</td>
<td>0.0003</td>
</tr>
<tr>
<td>IL-18 (pg/ml)</td>
<td>4405 (582-7122)</td>
<td>439 (312-824)</td>
<td>0.067</td>
</tr>
<tr>
<td>neopterin (nmol/L)</td>
<td>8.2 (6.5-13.9)</td>
<td>8.1 (6.6-8.8)</td>
<td>0.94</td>
</tr>
<tr>
<td>sCD25 (pg/ml)</td>
<td>80 (80-229)</td>
<td>80 (80-193)</td>
<td>1</td>
</tr>
</tbody>
</table>

Values are expressed as median (IQR)

Conclusion: Elevation of neopterin and CXCL9, both reflecting IFNγ production, and their correlation with laboratory parameters, supports the pathogenic role of IFNγ in MAS. Circulating levels of CXCL9 and CXCL10 (to a lesser extent of IL-18, though, not reaching statistical significance) are higher in patients with a history of MAS compared to patients without a history of MAS, suggesting subclinical activation of this pathway even in the absence of overt MAS and that CXCL9 and CXCL10 may identify patients at high risk for MAS; larger studies are needed. Regarding distinguishing MAS from active sJIA, levels of neopterin, IFNγ, CXCL9, CXCL10, sCD25, and IL-18 may be used and the possibility to integrate the currently available classification criteria with one or more of these biomarkers investigated in larger studies.


Disclosure: C. Bracaglia, None; D. Pires Marafon, None; I. Caiello, None; K. de Graaf, Novimmune, 3; M. Ballabio, Novimmune, 3; W. Ferlin, Novimmune, 3; S. Davi, None; G. Schultet, None; A. Ravelli, None; A. A.
**Adjudication of Infections from the Pharmacovigilance in Juvenile Idiopathic Arthritis Patients (PHARMACHILD) Treated with Biologic Agents and/or Methotrexate with a Focus on Opportunistic Infections**

**Joost Swart**¹, Gabriella Giancane¹,², Elio Castagnola¹, Andreas Groll¹, Gerd Horneff³, Hans-Iko Huppertz¹, Daniel J Lovell³, Tom Wolfs¹, Michaël Hofer¹, Ekaterina Alexeev¹, Violeta Vladislava Panaviene¹, Susan Nielsen¹, Jordi Anton¹, Florence Uettwiller¹, Valda Stanevicha¹, Maria Trachana¹, Fabrizio De Benedetti¹, Constantin Ailioaie¹, Elena Tsitsami¹, Sylvia S.M. Kamphuis¹, Troels Herlin¹, Pavla Dolezalová¹, Jordana Susic¹, Berit Flato¹, Flavio Sztajnbok¹, Elena Fueri⁴, Francesca Bovis⁵, Francesca Bagnasco¹, Angela Pistorio¹, Alberto Martini⁶, Nico Wulffraat⁷ and Nicolina Ruperto⁶, ¹Istituto Giannina Gaslini - Pediatria II, Reumatologia - PRINTO, Genoa, Italy, ²Pediatria II, Reumatologia - PRINTO, Genova, Italy, ³Rheumatology, PRCSG - Cincinnati Children's Hospital Medical Center, Cincinnati, OH, ⁴Istituto Giannina Gaslini - Pediatria II, Reumatologia - PRINTO, Genova, Italy, ⁵Università degli Studi di Genova, Genoa, Italy, ⁶Istituto Giannina Gaslini, Genoa, Italy, ⁷Pediatric rheumatology, Wilhelmina Children's Hospital/ UMC Utrecht, Utrecht, Netherlands

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** Pediatric Rheumatology – Pathogenesis and Genetics Poster  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Pharmachild is a pharmacovigilance registry on children with JIA treated mainly with biologics ± methotrexate (MTX). Little evidence exists in literature about the role of JIA or its immunosuppressive therapy in determining infections, especially caused by opportunistic pathogens.

**Methods:**

To provide an update on opportunistic infections (OI) revised by an independent Safety Adjudication Committee (SAC) (3 pediatric rheumatologists and 2 pediatric infectious disease specialists).

**Methods:** The participating centres were asked to report all infections encountered by their JIA patients. PRINTO and the medical monitor (MM) classified events based on MedDRA dictionary. Moderate/serious/severe/very severe infections were then revised blindly by the SAC, who were asked to answer 6 questions. The events with consensus of at least 3/5 experts on the first 3 questions (‘Is this an infection?’ , ‘Is it common?’ , ’Is it opportunistic?’) were retained for the analysis. With referral to the recommendations by Withrop et al.¹, for the first time a list of opportunistic infections in children with JIA on immunosuppressive therapy was elaborated and approved by consensus, through three Delphi steps.

**Results:** A total of 772 safety events related to 634 patients were submitted to the Safety Adjudication Committee. 689 (89.2%) events received consensus among the experts on the 3 questions and, of these, 682 (99.0%) were considered as infections, corresponding to 53 High Level Term (HLT) including 153 different Preferred Terms (PT), according to
MedDRA dictionary. Among the 682 infections, 603 (88.4%) were defined by the experts as common and 119 (17.4%) as opportunistic. For 92 (60%) of the 153 PT, the MM and SAC used the same PT, while the remaining 40% was adjudicated by a third examiner, who analyzed again the case reports and assigned the PT which was the most appropriate taking into account the experts’ opinion. A final number of 52 HLT emerged and, among them, herpes viral infections, tract respiratory infections and EBV were the most frequent (Table 1). Analyzing the infections by PT, 151 different PT resulted. Of them, the experts adjudicated: 22 as OI, 117 as not OI, 8 discordant and 4 not evaluable. Comparing the experts’ adjudication with the approved list of OI by PT, there was full agreement for the 22 PT classified as OI, while 26/117 (22.2%) PT resulted in the list, but were not classified as OI by the experts.

**Conclusion:** Our preliminary analysis showed a significant number of opportunistic infections in JIA patients on immunosuppressive therapy, which was mostly confirmed in the list of opportunistic infections approved by the experts. Further analysis on the correlation with medications is ongoing.


**Table 1. The most frequent HLT for the 682 infections with agreement of at least 3/5 experts on the first 3 questions. (N: number of infections)**

<table>
<thead>
<tr>
<th>HLT</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herpes viral infections</td>
<td>265</td>
<td>38.9</td>
</tr>
<tr>
<td>Lower respiratory tract and lung infections</td>
<td>49</td>
<td>7.2</td>
</tr>
<tr>
<td>Upper respiratory tract infections</td>
<td>44</td>
<td>6.5</td>
</tr>
<tr>
<td>Epstein-Barr viral infections</td>
<td>38</td>
<td>5.6</td>
</tr>
<tr>
<td>Abdominal and gastrointestinal infections</td>
<td>32</td>
<td>4.7</td>
</tr>
<tr>
<td>Tuberculous infections</td>
<td>29</td>
<td>4.3</td>
</tr>
<tr>
<td>Bacterial infections NEC</td>
<td>27</td>
<td>4</td>
</tr>
<tr>
<td>Infections NEC</td>
<td>19</td>
<td>2.8</td>
</tr>
<tr>
<td>Ear infections</td>
<td>18</td>
<td>2.6</td>
</tr>
<tr>
<td>Candida infections</td>
<td>17</td>
<td>2.5</td>
</tr>
<tr>
<td>Influenza viral infections</td>
<td>14</td>
<td>2.1</td>
</tr>
<tr>
<td>Streptococcal infections</td>
<td>14</td>
<td>2.1</td>
</tr>
<tr>
<td>Salmonella infections</td>
<td>9</td>
<td>1.3</td>
</tr>
<tr>
<td>Urinary tract infections</td>
<td>9</td>
<td>1.3</td>
</tr>
<tr>
<td>Cytomegaloviral infections</td>
<td>8</td>
<td>1.2</td>
</tr>
<tr>
<td>Molluscum contagiosum viral infections</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Papilloma viral infections</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Sepsis, bacteraemia, viraemia and fungaemia NEC</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Campylobacter infections</td>
<td>5</td>
<td>0.7</td>
</tr>
<tr>
<td>Staphylococcal infections</td>
<td>5</td>
<td>0.7</td>
</tr>
<tr>
<td>Viral infections NEC</td>
<td>5</td>
<td>0.7</td>
</tr>
<tr>
<td>Escherichia infections</td>
<td>4</td>
<td>0.6</td>
</tr>
<tr>
<td>Pneumocystis infections</td>
<td>4</td>
<td>0.6</td>
</tr>
<tr>
<td>Skin structures and soft tissue infections</td>
<td>4</td>
<td>0.6</td>
</tr>
</tbody>
</table>

**Disclosure:** J. Swart, None; G. Giancane, None; E. Castagnola, None; A. Groll, None; G. Horneff, AbbVie, Pfizer, Novartis, and Roche, 2, AbbVie, Novartis, Sobi, Pfizer, and Roche, 9; H. I. Huppertz, None; D. J. Lovell, AbbVie Inc., AstraZeneca, Centocor, Bristol-Myers Squibb, Pfizer, Regeneron, Hoffman La-Roche, Novartis, UBC, Xoma, and Genentech, 5, Wyeth Pharmaceuticals, 8, Amgen and Forest Research, 9; T. Wolfs, None; M. Hofer, Novartis and AbbVie, 5; E. Alexeeva, None; V. V. Panaviene, None; S. Nielsen, None; J. Anton, Roche Pharmaceuticals, 2; F.
Hypermethylation of NLRP3 Promoter Region Could be Responsible for Decreased Gene Expression, Inflammasome Malfunction and Gut Dysbiosis in Juvenile Spondyloarthritis Patients

Lovro Lamot1,2, Kristina Gotovac Jercic3, Antonela Blazekovic3, Mirta Lamot4, Mandica Vidovic4, Fran Borovecki3 and Miroslav Harjacek3,4, 1Department of Pediatrics, University of Zagreb School of Medicine, Zagreb, Croatia, 2Department of Pediatrics, Division of Clinical Immunology and Rheumatology, Clinical Hospital Center Sestre Milosrdnice, Zagreb, Croatia, 3University of Zagreb School of Medicine, Zagreb, Croatia, 4Clinical Hospital Center Sestre Milosrdnice, Zagreb, Croatia

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Pathogenesis and Genetics Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Juvenile spondyloarthritis (jSpA) is a complex disease with both genetic and environmental factors contributing to the etiology. Recently obtained gene signatures in jSpA patients revealed TLR4 and CXCR4 gene had increased, while NLRP3 and PTPN12 had decreased expression, though the mechanism(s) responsible for those alterations remained unknown. To elucidate the possible role of epigenetic modifications in the regulation of those genes, DNA methylation analysis was performed.

Methods:
DNA was isolated from PBMCs of 19 patients diagnosed with jSpA according to ILAR classification criteria for enthesitis related arthritis (ErA) and seven matched healthy children. None of the jSpA participant had symptoms for more than six months and all were untreated. Methylated DNA Immunoprecipitation (MeDIP) was performed in promotor region of differentially expressed genes (TLR4, CXCR4, NLRP3, PTPN12) using the Magmepid kit. Enrichment in MeDIP fraction was determined by quantitative RT-PCR using the AriaMx. MeDIP results were expressed as fold enrichment of immunoprecipitated DNA for each site.
Results:

Statistical analysis revealed significant hypermethylation of promoter sites in NLRP3 gene (p=0.0220). No significant alterations in methylation status were observed in promoter regions of other genes (Table 1).

Conclusion:

Our study indicates the hypermethylation of NLRP3 gene promoter is probably responsible for expression alterations in jSpA patients in the initial phase of the disease. The NLRP3 gene has a crucial role in assembly of NLRP3 inflammasome, innate immune sensor that regulates “danger” response upon various signals. While increased expression of this gene has been found in many autoinflammatory diseases, decreased expression has been associated with IBD in which the microbiota is believed to contribute to the intestinal inflammation. Therefore, it is not entirely surprising decreased expression has also been observed in jSpA, the disease that has clinical and genetic similarities with IBD and is often characterized by subclinical gut inflammation. The growing number of evidence shows any modification of gut microbiota can lead to dysbiosis with long-term consequences for the whole organism. Specifically, in jSpA this could result in increased influx of TLR4 ligands and increased expression of TLR4 gene, as well as in reduction of commensal bacteria with anti-inflammatory properties, namely bacteria Faecalibacterium prausnitzii that inhibits NF-κB signaling, leading to TNF-α abundancy characteristic for jSpA. Since inflammasomes have been shown to shape the microbiota, it is reasonable to assume these processes can at least partially be explained by reduced NLRP3 expression due to hypermethylation. Therefore, our findings could have important implications in understanding of the disease mechanisms and possible therapeutic options.

Table 1. Results of DNA promoter methylation and previously performed gene expression analysis in juvenile spondyloarthritis patients.

<table>
<thead>
<tr>
<th>GENES</th>
<th>Fold Enrichment of Immunoprecipitated DNA</th>
<th>Fold Change of Expression^{1}</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients</td>
<td>Controls</td>
</tr>
<tr>
<td>TLR4</td>
<td>0.213</td>
<td>0.153</td>
</tr>
<tr>
<td>NLRP3</td>
<td>11.24</td>
<td>5.412</td>
</tr>
<tr>
<td>CXCR4</td>
<td>0.372</td>
<td>0.182</td>
</tr>
<tr>
<td>PTPN12</td>
<td>0.338</td>
<td>0.202</td>
</tr>
</tbody>
</table>


Disclosure: L. Lamot, None; K. Gotovac Jercic, None; A. Blazekovic, None; M. Lamot, None; M. Vidovic, None; F. Borovecki, None; M. Harjacek, None.


Abstract Number: 2335

**Antiendothelial Cell Antibodies in Juvenile Dermatomyositis: A Proteomics-Based Approach**

Rie Karasawa^{1}, Mayumi Tamaki^{1}, Toshiko Sato^{1}, Megumi Tanaka^{1}, Kazuo Yudoh^{1} and James Jarvis^{2}, ^{1}Institute of Medical Science, St. Marianna University School of Medicine, Kawasaki, Japan, ^{2}Department of Genetics, Genomics & Bioinformatics, University at Buffalo, Buffalo, NY
Background/Purpose: Juvenile dermatomyositis (JDM) is a systemic disorder of childhood characterized by muscle inflammation and vasculopathy. The mechanisms of the blood vessel injury in JDM remain to be fully solved. Anti-endothelial cell antibodies (AECA) are detected in infectious, inflammatory diseases and autoimmune diseases such as vasculitis, and we have hypothesized that such antibodies may target the endothelium in JDM. In this study, we aimed to comprehensively detect endothelial target antigens in JDM using a proteomics approach. Methods: We extracted proteins from human aortic endothelial cells (HAEC), which were used as antigen sources. To comprehensively detect target antigens for AECA, we separated proteins extracted from HAEC by two-dimensional electrophoresis (2DE) and then transferred them onto membranes. Using standard western blotting techniques, membranes were probed with sera from children with JDM or healthy controls. Autoantigens that were positive only in sera from children with JDM but not healthy controls were then identified by mass spectrometry (MS). Enzyme-linked immunosorbent assay (ELISA) was then used to confirm presence of specific antibodies. Results: Five candidate protein spots as JDM-specific proteins were detected in 2DE-WB. From these spots, we successfully identified 34 proteins. 22 of the 34 identified antigens represented membrane proteins. Using Ingenuity Pathway Analysis, 27 of the 34 candidate target antigens for AECA in JDM were predicted to interact with chaperone proteins involved in antigen processing and presentation. Among the 8 chaperone or co-chaperone proteins were heat shock cognate 71 kDa protein (HSC70), heat shock protein HSP 90-bet (HS90B) and stress-induced-phosphoprotein 1 (STIP1), a protein that mediates the association of HSC70 and HSP90. By ELISA, IgG autoantibodies to HSC70 were detected in 23% of the patients with JDM (n=39). However, 50% of the untreated JDM patients with active disease (n=10) had anti-HSC70 antibodies, in contrast to 7% (p<0.05) of the patients with juvenile idiopathic arthritis (JIA) (n=15) and 5% (p<0.01) of control children (n=20). 13% of the treated JDM patients with active disease (n=15) and 14% of the inactive patients with JDM (n=14) had anti-HSC70 antibodies. IgG autoantibodies to HS90B were detected in 6% of the patients with JDM (n=31) and in 5% of control children, in contrast to 20% of the patients with JIA. Similarly, IgG autoantibodies to STIP1 were not detected patients with JDM, but were present in 5% of control children and 20% of the patients with JIA. Conclusion: IgG antibodies to chaperone proteins in the proteome of HAEC are present in the sera of children with JDM. The presence of AECA in JDM could implicate these antibodies in the disorders of immune system in JDM.

Disclosure: R. Karasawa, None; M. Tamaki, None; T. Sato, None; M. Tanaka, None; K. Yudoh, None; J. Jarvis, None.
Juvenile dermatomyositis (JDM) is a chronic autoimmune myopathy characterized by proximal muscle weakness and typical skin rashes. Type I interferon (IFN) gene expression in blood has been shown to correlate with muscle involvement in adult and juvenile dermatomyositis. Myxovirus-resistance protein A (MxA), a type I IFN-induced protein, is specifically regulated by type I IFN pathway. Since muscle is the major target of inflammation, the presence of MxA protein in muscles could be of greater relevance to direct mechanisms of tissue injury. This study aims to examine whether MxA protein expression in muscles correlates with disease activity in JDM.

Methods:

103 patients enrolled in the Juvenile Dermatomyositis Cohort and Biomarker Study (JDCBS) had muscle biopsies available, which were stained for MxA by immunohistochemistry. The expression of MxA in muscle fibres was scored semi-quantitatively. Scores range from 0 to 3 (0 = no MxA staining; 1 = weak; 2 = moderate; 3 = strong). Clinical and laboratory data at initial presentation including Childhood Myositis Assessment Scale (CMAS), Manual Muscle Testing of Eight Muscles (MMT8), physician’s global assessment (PGA) and muscle enzymes were collected. Kruskal-Wallis ANOVA with Bonferroni’s correction were tested to examine differences of MxA scoring data in muscle disease activity. Multiple linear regression analysis was performed to estimate the association between MxA expression on muscle fibres and muscle disease activity. The strength of the association was described by the standardised coefficient (β).

Results:

The median age at disease onset was 6.3 years and median duration from disease onset to muscle biopsy was 3.8 months. About 9% of patients had received corticosteroids at the time of biopsy. MxA expression was identified in 63 of 103 patients, with 57% of those showing strong MxA expression on myofibres. The distribution of MxA expression was observed in both perifascicular (46%) and scattered (53%) patterns. Comparing patients with varying MxA scores, there were no significant differences in age at onset, gender, and clinical features at first presentation, such as, the presence of calcinosis, nail fold capillary changes and PGA. There were statistical differences in duration from disease onset to muscle biopsy (p = 0.046), CMAS (p = 0.002) and MMT8 (p = 0.026). CMAS and MMT8 were significantly lower in the group of patients with strong MxA expression on myofibres. From post hoc analysis, there were significant differences in CMAS between patients with scores of 0 and 2 (p = 0.044), and scores of 0 and 3 (p = 0.001). Also, MMT8 in patients with scores of 0 and 3 were statistically significantly different (p = 0.013). Regression analysis confirmed that expression of MxA was significantly associated with CMAS (β = -0.433) and MMT8 (β = -0.368) at disease onset, after adjustment for time to biopsy.

Conclusion:

This study reveals an association between level of MxA expression on muscle fibres and clinical measures of muscular disease activity in JDM patients, CMAS and MMT8. This shows how immunohistochemical staining of MxA on muscle tissues has the potential of providing more insight into pathogenesis of JDM and may help develop more targeted therapies for JDM patients.

Disclosure: S. Soponkanaporn, None; C. Deakin, None; L. Marshall, None; C. Johnson, None; P. Schutz, None; L. R. Wedderburn, None.

Abstract Number: 2337

Novel Serum Broad-Based Proteomic Discovery Analysis Identifies Proteins and Pathways Dysregulated in Juvenile Dermatomyositis (JDM) and Myositis Autoantibody Groups

Hanna Kim¹, Angélique Biancotto², Foo Cheung³, Terrance P. O’Hanlon⁴, Ira N. Targoff⁵, Yan Huang⁶, Frederick W Miller⁴, Raphaëla Goldbach-Mansky⁶ and Lisa G Rider⁴, ¹Pediatric Translational Research Branch, NIAMS/NIH, Bethesda, MD, ²Center for Human Immunology, Autoimmunity and Inflammation (CHI), NHLBI, NIH, Bethesda, MD, ³Center for Human Immunology Autoimmunity and Inflammation (CHI), NHLBI, NIH, Bethesda, MD, ⁴Environmental Autoimmunity Group, NIEHS, NIH, Bethesda, MD, ⁵VA Medical Center, University of Oklahoma Health Sciences Center, Oklahoma Medical Research Foundation, Oklahoma City, OK, ⁶Translational Autoinflammatory Disease Studies (TADS), Laboratory of Clinical Investigation and Microbiology (LCIM), NIAID/NIH, Bethesda, MD

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Pathogenesis and Genetics Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Juvenile dermatomyositis (JDM) is a complex heterogeneous autoimmune disease. Myositis-specific autoantibodies (MSAs), present in up to 80% of JDM patients, help define distinct phenotypes within JDM and may indicate distinct pathogeneses. To define biomarkers and better understand JDM pathogenesis, aptamer-based proteomic technology was used to mine the serum proteome in a well-characterized JDM cohort.

Methods: Sera from 41 JDM patients (prevalent cases on variable treatment) were selected for relatively high disease activity (physician global activity or PGA median 4.0 (IQR 3.0-5.0)) with anti-TIF1 (n=21), NXP-2 (n=10), and MDA5 MSAs (n=10), and compared with 28 age- and gender-matched healthy controls (HC). Broad proteomic analysis of 1306 targets with a slow off-rate modified aptamer-based assay (SomaLogic, CO) generated simultaneous quantitative serum levels. Internal discovery/validation was done with 2 independently-analyzed groups each with JDM and HC sera, stratified to evenly distribute PGA, MSA, gender, oral steroid dose (median oral prednisone dose 0.40 mg/kg/day, IQR 0.17-0.73) and age. From proteins with Mann Whitney U FDR corrected p values of <0.10 (JDM vs. HC) common to both groups with expression ratio of >1.3, we performed Ingenuity Pathway Analysis (Qiagen, CA), as well as exploratory Spearman correlation of protein levels versus PGA, also among MSA groups, and protein levels vs. oral steroid dose (mg/kg/day).

Results: 166 proteins met significance criteria in both analysis groups of JDM versus HC sera, with 80 proteins upregulated and 86 downregulated (see Table). Pathway analysis revealed granulocyte/agranoocyte adhesion/diapedesis, interferon, remodeling/damage, Th1, and adipokines as top dysregulated pathway clusters in JDM, even after excluding 4 proteins that correlated with steroid dosage. We identified 13 proteins with serum levels positively correlated with PGA for JDM overall ($r_s$ = 0.31-0.41), 13 proteins in NXP2 Ab group ($r_s$ =0.65-0.89), 4 proteins in TIF1 Ab group ($r_s$ =0.45-0.54); none in MDA5 Ab group. Individual proteins within MSA groups had stronger correlation with PGA than in JDM overall, and some proteins were only identified in MSA groups (e.g. IFNB in NXP2 Ab group).

Conclusion: Broad quantitative proteomic analysis identified key differentiating pathway clusters in JDM versus HC, including some novel proteins. Several protein levels correlated with PGA, with stronger correlation within MSA groups and notable IFN-related proteins upregulated in the NXP2 MSA group. These proteins identified through a high-throughput screen bring to light pathways that may be important in JDM and potentially MSA-group specific pathogenesis.
Table 1: Top Dysregulated Proteins in JDM versus HC

<table>
<thead>
<tr>
<th>Target Full Name</th>
<th>JDMPC expression ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collagen-alpha 1-I chain</td>
<td>2.39</td>
</tr>
<tr>
<td>Desmin X-1</td>
<td>0.77</td>
</tr>
<tr>
<td>LANDR-1-1 protein (IDG 13)</td>
<td>0.30</td>
</tr>
<tr>
<td>ATP synthase (ATP5A1)</td>
<td>0.15</td>
</tr>
<tr>
<td>Mitochondrion (ATP5B)</td>
<td>0.15</td>
</tr>
<tr>
<td>Downregulated</td>
<td></td>
</tr>
<tr>
<td>Exocyst complex subunit 5</td>
<td>0.69</td>
</tr>
<tr>
<td>GTPase activating protein (AIP1)</td>
<td>0.67</td>
</tr>
<tr>
<td>Ras effector effector isoform 1</td>
<td>0.60</td>
</tr>
<tr>
<td>Ras GTPase activating protein</td>
<td>0.51</td>
</tr>
</tbody>
</table>

Disclosure: H. Kim, Cure JM Foundation, 2; A. Biancotto, None; F. Cheung, None; T. P. O’Hanlon, None; I. N. Targoff, None; Y. Huang, None; F. W. Miller, None; R. Goldbach-Mansky, None; L. G. Rider, None.


Abstract Number: 2338

Plasma Exosomes from Children with Juvenile Dermatomyositis Are Taken up By Human Aortic Endothelial Cells and Are Associated with Altered Gene Expression in Those Cells

Kaiyu Jiang¹, Zihua Hu², Rie Karasawa³, Yanmin Chen¹ and James Jarvis⁴, ¹Pediatrics, University at Buffalo, Buffalo, NY, ²Center for Computational Research, University at Buffalo, Buffalo, NY, ³Institute of Medical Science, St. Marianna University School of Medicine, Japan, Kawasaki, Japan, ⁴Department of Genetics, Genomics & Bioinformatics, University at Buffalo, Buffalo, NY

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Pathogenesis and Genetics Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The pathology of juvenile dermatomyositis (JDM) is characterized by prominent vessel wall and perivascular inflammation. This feature of the disease has remained unexplained and under-investigated. We have hypothesized that plasma exosomes, which play an important role in inter-cellular communication, may play a role in the vascular injury associated with JDM.

Methods: We purified exosomes from plasma samples of children with active, untreated JDM (n= 10) and healthy controls (n= 10) using the ExoQuick Precipitation method. We characterized the small RNA cargoes in JDM and control exosomes by RNA sequencing using the Illumina HiSeq 2500 platform. We incubated isolated exosomes from healthy controls and JDM patients with cultured human aortic endothelial cells (HAEC) for 24 hours. Fluorescence microscopy was used to confirm that both control and JDM exosomes were taken up by HAEC. RNA was then purified from HAEC that had been incubated with either control or JDM exosomes and sequenced on the Illumina platform. Differential expression of mRNAs from HAEC incubated with control or JDM exosomes was ascertained using standard computational methods. Finally, we assessed the degree to which differential gene expression in HAEC could
be attributed to the different small RNA cargoes in JDM vs control exosomes using conventional and novel analytic methods.

Results: We identified 10 small RNA molecules that showed differential abundance when we compared JDM and healthy control exosomes. Fluorescence microscopy of labeled exosomes confirmed that both JDM and control exosomes were taken up by HAEC. Differential gene expression analysis revealed 193 genes that showed differential expression between HAEC incubated with JDM exosomes vs HAEC incubated with exosomes from controls. Gene ontology analysis revealed that many of these differentially expressed genes (e.g., CXCL8/IL8) are associated with leukocyte migration and adherence. Analysis of the differentially expressed genes, however, failed to provide a strong link between the miRNA cargoes in the exosomes and patterns of gene expression.

Conclusion: Plasma exosomes from children with active, untreated JDM are taken up by HAEC and are associated with alterations in gene expression in those cells. However, we were unable to establish a strong link between transcriptional changes and the small RNA cargoes of JDM exosomes. This suggests that other exosome components are more likely to be involved.

Disclosure: K. Jiang, None; Z. Hu, None; R. Karasawa, None; Y. Chen, None; J. Jarvis, None.


Abstract Number: 2339

Expression of Type I and Type II Interferons Is Increased in Muscle Biopsies of Juvenile Dermatomyositis Patients and Related to Clinical and Histological Features

Rebecca Nicolai1, Gian Marco Moneta2, Silvia Rosina3, Chiara Fiorillo3, Denise Pires Marafon1, Margherita Verardo4, Luisa Bracci Laudiero5,6, Carlo Minetti3,7, Angelo Ravelli3,8 and Fabrizio De Benedetti1, 1Division of Rheumatology, IRCCS Bambino Gesù Children's Hospital, Rome, Rome, Italy, 2Division of Rheumatology, IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy, 3University of Genova, Genova, Italy, 4Unit of Neuromuscular and Neurodegenerative Disorders, Ospedale Pediatrico Bambino Gesù IRCCS, Roma, Roma, Italy, 5Division of Rheumatology, Ospedale Pediatrico Bambino Gesù IRCCS, Roma, Roma, Italy, 6Institute of Translational Pharmacology, CNR, Rome, Italy, 7Pediatric Neurology and Muscular Disorders, Giannina Gaslini Institute, Genova, Italy, 8Rheumatology, Giannina Gaslini Institute, Genova, Italy

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Pathogenesis and Genetics Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

There is growing evidence for an involvement of interferons (IFNs) in the chronic inflammation that characterizes juvenile dermatomyositis (JDM). The aim of this study was to investigate muscle expression of type I (IFNα/β) and type II (IFNγ) IFN inducible genes in muscle biopsies of JDM patients and their correlations with clinical and histological aspects of the disease.
**Methods:** In a retrospective cohort of patients diagnosed with JDM (n=35), expression of the six genes part of the so-called type I IFN score (IFI27, IFI44L, IFIT1, ISG15, RSAD2, SIGLEC1), as well as of IFNγ and of CXCL9, CXCL10, CXCL11, CIITA, were analyzed by real-time PCR on snap-frozen muscle biopsies and compared with biopsies from Duchenne muscular dystrophy (DMD) patients (n=24) and 4 healthy controls (HC). Expression levels of CXCL9, CIITA (genes specifically induced by IFNγ) and IFNγ itself were used to generate a type II IFN score. We also analyzed mRNA expression of the pro-inflammatory cytokines interleukin-1β (IL-1β), tumor necrosis factor-α (TNFα) and interleukin-6 (IL-6). Patient charts were reviewed to record clinical features at diagnosis and long term outcomes: physician’s global assessment of disease activity, serum levels of muscle enzymes, erythrocyte sedimentation rate, C-reactive protein level, antinuclear antibodies status, time to inactive disease and time to prednisone (or equivalent) dose 0.2 mg/kg/daily, and relapses. We furthermore evaluated typical histological aspects of JDM (inflammatory infiltrate, necrosis, perifascicular atrophy and fibrosis) on tissue sections of the muscle biopsies.

**Results:** JDM patients treated (n=12) with systemic glucocorticoids before biopsy were excluded from analysis, because expression levels of the studied genes were markedly reduced compared to untreated patients. The type I IFN score and type II IFN score were significantly higher in the muscle of untreated JDM patients (n=23) compared with controls (p<0.0001, p<0.001 respectively). Expression of TNFα, but not of IL-1β and IL-6, was significantly (p<0.05) higher in untreated JDM muscle biopsies compared with those of controls. Type I IFN score correlated with inflammatory infiltrate and necrosis, while the type II IFN score correlated with inflammatory infiltrate, perifascicular atrophy and fibrosis. Type I IFN score, type II IFN score and TNFα expression significantly correlated with physician’s global assessment at diagnosis (r=0.38, r=0.42, r=0.62, respectively). When analyzing correlations with long term outcomes, we found that patients with elevated type II IFN score reached clinically inactive disease significantly later than patients with low type II IFN score (log-rank chi square value=10.1, p<0.01).

**Conclusion:** IFN type I and type II scores in muscle biopsies of JDM patients correlate with clinical and histological features suggesting a pathogenic role of IFNs in muscle damage and inflammation in JDM. Noteworthily the type II score correlated with time to clinically inactive disease, suggesting a correlation with disease severity.

**Disclosure:** R. Nicolai, None; G. M. Moneta, None; S. Rosina, None; C. Fiorillo, None; D. Pires Marafon, None; M. Verardo, None; L. Bracci Laudiero, None; C. Minetti, None; A. Ravelli, None; F. De Benedetti, Novartis, Roche, Pfizer, SOBI, AbbVie, Novimmune, BMS, Sanofi, 2.


**Abstract Number:** 2340

**Correlation of Type I Interferon Score and CXCL10 (C-X-C Motif Chemokine Ligand 10) with Cutaneous and Muscular Disease Activity in Juvenile Dermatomyositis Patients**

Rebecca Nicolai1, Gian Marco Moneta2, Ivan Caiello3, Denise Pires Marafon1, Silvia Rosina4, Luisa Bracci Laudiero5,6, Angelo Ravelli4,7 and Fabrizio De Benedetti1,1Division of Rheumatology, IRCCS Bambino Gesù Children's Hospital, Rome, Rome, Italy, 2Division of Rheumatology, IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy, Roma, Italy, 3Division of Rheumatology, IRCCS Ospedale Pediatrico Bambino Gesù, Roma, Italy, 4University of Genova, Genova, Italy, 5Division of Rheumatology, Ospedale Pediatrico Bambino Gesù IRCCS, Roma, Roma, Italy, 6Institute of Translational Pharmacology, CNR, Rome, Italy, Rome, Italy, 7Rheumatology, Giannina Gaslini Institute, Genova, Italy.

**First publication:** September 18, 2017

**SESSION INFORMATION**
Background/Purpose: Interferons (IFNs) seem to be important contributors in the pathogenesis of juvenile dermatomyositis (JDM). Our group previously reported that expression of both type I and type II IFNs is increased in muscle biopsies of JDM patients and correlates with histological and clinical aspects of the disease, and other authors described up-regulation of interferon regulated genes (IRGs) in blood samples of JDM patients. The aim of this study was to investigate expression of IRGs (measured as type I IFN score) and serum levels of two type II IFN (IFNγ) induced chemokines (CXCL9, CXCL10) in peripheral blood of JDM patients. Furthermore, we wanted to evaluate possible correlations of type I IFN score, as well as of CXCL9 and CXCL10, with clinical and laboratory findings during disease course.

Methods: We collected 79 blood samples from 26 JDM patients at different times during the disease course. We measured expression of IRGs (IFI27, IFI44L, IFIT1, ISG15, RSAD2, SIGLEC1) by real-time PCR and calculated a type I IFN score; serum levels of CXCL9 and CXCL10 were analyzed by ELISA. The first blood sample was collected at the same time the patient underwent muscle biopsy in six patients. At each visit, the following clinical data were recorded: physician’s global assessment of disease activity VAS (Visual Analogue Scale), cutaneous VAS, Cutaneous Assessment Tool (CAT) activity and damage score, Childhood Myositis Assessment Score (CMAS), serum levels of creatine phosphokinase (CK, IU/l), prednisone (or equivalent) dose (mg/kg/daily), ongoing immunosuppressive medications.

Results: Blood expression levels of IRGs were up-regulated in untreated JDM patients at diagnosis compared to healthy controls. Type I IFN score progressively reduced after start of glucocorticoid and immunosuppressive therapy. CXCL9 and CXCL10 serum levels had a similar trend. These patients also showed an increased expression of IRGs, CXCL9 and CXCL10 in muscle biopsies obtained at diagnosis. We found that the type I IFN score correlates with cutaneous disease activity assessed by the CAT activity score ($p = 0.027$), whereas there was no significant correlation with cutaneous VAS ($p = 0.09$) or CAT damage score ($p = 0.88$). Serum levels of CXCL10 showed correlation with serum CK levels ($p = 0.042$) and muscular function assessed by CMAS ($p = 0.021$). None of the evaluated clinical features showed correlation with serum levels of CXCL9.

Conclusion: Our findings indicate that in addition to CXCL10, already suggested as potential biomarker in JDM, expression of IRGs measured as type I IFN score reflects disease activity in JDM.

Disclosure: R. Nicolai, None; G. M. Moneta, None; I. Caiello, None; D. Pires Marafon, None; S. Rosina, None; L. Bracci Laudiero, None; A. Ravelli, None; F. De Benedetti, Novartis, Roche, Pfizer, SOBI, AbbVie, Novimmune, BMS, Sanofi, 2.


Abstract Number: 2341

The Interaction between Genetic Risk Factors and Age of Disease Onset in Juvenile Dermatomyositis

Claire Deakin$^1$, John Bowes$^2$, Lucy Marshall$^1$, Cerise Johnson$^1$, Gulnara Mamyrova$^3$, Rodolfo Curiel$^4$, Kelly A. Rouster-Stevens$^5$, Heinrike Schmeling$^6$, Adam Huber$^7$, Brian M. Feldman$^8$, Ann M Reed$^9$, Lauren M. Pachman$^{10}$, Soumya Raychaudhuri$^{11}$, Stephen Eyre$^{12}$ and Lucy R Wedderburn$^1$, $^1$Infection, Immunity and Inflammation Programme, UCL Great Ormond Street Institute of Child Health, University College London, United Kingdom,
Juvenile dermatomyositis (JDM) is a rare, severe autoimmune disease characterized by muscle weakness and rash. Clinical features of JDM are heterogeneous, and can include serious complications such as calcinosis, ulceration, treatment-resistant rash and involvement of major organs, including gut, lungs and brain. While JDM and adult-onset dermatomyositis (DM) share similar clinical and biological features, there are differences in prevalence of clinical features. Cancer development is a major complication of DM, but not JDM. Conversely, calcinosis is a major cause of morbidity in JDM, but has a low occurrence in DM. The prevalence of myositis-specific autoantibodies (MSA), which are linked to different clinical features of disease, also differs between the adult and juvenile forms of the disease. These differences in the distribution of MSA and clinical features suggest an influential role for age of disease onset on the pathogenesis of disease.

Methods:

Caucasian JDM cases from the UK (n=312) were genotyped using the Illumina HumanCoreExome chip. Caucasian control data (n=2808) were obtained from the Wellcome Trust Case Control Consortium. Following quality control, classical human leukocyte antigen (HLA) alleles and HLA amino acids were imputed using SNP2HLA. Logistic, linear and Cox regression were performed using PLINK and R package GenABEL, with adjustment for the first two principal components. Genome-wide significant association was set at \( P < 5.0 \times 10^{-8} \) and suggestive association at \( P < 1.0 \times 10^{-5} \). We subsequently built an international consortium to create a replication cohort of Caucasian cases from North America (n=475).

Results:

Case-control analyses confirmed involvement of HLA including multiple loci within \( HLA-C \) \( (p = 1.35 \times 10^{-8}, \text{OR} = 2.49, 95\% \text{ CI} = 1.82 - 3.42) \) and \( HLA-DRB1 \) \( (p = 2.73 \times 10^{-8}, \text{OR} = 0.56, 95\% \text{ CI} = 0.46-0.69) \) at genome-wide levels of statistical significance. Outside the HLA region there was suggestive evidence of association at \( ZNF337 \) \( (p = 7.49 \times 10^{-6}, \text{OR} = 1.81, 95\% \text{ CI} = 1.40-2.34) \), a zinc finger protein of unknown function. Analyses of association with age of disease onset did not implicate HLA involvement, suggesting the associations between HLA and JDM/DM are not influenced by age. Analysis of age of onset as a quantitative trait revealed suggestive associations at \( PDE1A \) \( (p = 1.56 \times 10^{-6}, \beta = -1.61, 95\% \text{ CI} = -2.26- -0.97) \) and \( AGPAT3 \) \( (p = 2.26 \times 10^{-6}, \beta = 1.63, 95\% \text{ CI} = 0.97-2.30) \), genes involved in regulating intracellular cyclic nucleic acid concentrations and phospholipid biosynthesis/ Golgi-to-endoplasmic reticulum
retrograde transport, respectively. In addition, we now have a replication cohort via our international consortium to validate these findings.

**Conclusion:**

This study has confirmed findings from previously published GWAS and Immunochip studies of JDM and DM concerning HLA involvement. Additionally, analyses of associations with age of JDM onset identified novel loci, *PDE1A* and *AGPAT3*, which if validated could suggest novel processes involved in pathogenesis. These findings will be confirmed in an independent replication cohort. Together with these validation samples, this study will be the largest GWAS of JDM to date.

**Disclosure:**

C. Deakin, None; J. Bowes, None; L. Marshall, None; C. Johnson, None; G. Mamyrova, Cure JM, 2; R. Curiel, Cure JM, 2,BMS, 2; K. A. Rouster-Stevens, None; H. Schmeling, None; A. Huber, None; B. M. Feldman, None; A. M. Reed, None; L. M. Pachman, None; S. Raychaudhuri, Pfizer Inc, 2,Roche Pharmaceuticals, 2; S. Eyre, None; L. R. Wedderburn, None.


**Abstract Number:** 2342

**Transcriptomic Analysis Reveals Mitochondrial and Monocyte Dysfunctions Are Linked to the Interferonopathy of Juvenile Dermatomyositis**

*Claire Deakin*1, Elizabeth Rosser1, Lucy Marshall1, Meredyth Wilkinson2, Aziza Khabbush3, Stefania Simou1, Georg Otto3, Stefanie Dowle3, Daniel Kelberman3, Simon Yona2, Simon Eaton3 and Lucy R Wedderburn1, 1Infection, Immunity and Inflammation Programme, UCL Great Ormond Street Institute of Child Health, University College London, United Kingdom, London, United Kingdom, 2Division of Medicine, University College London, London, United Kingdom, 3Genetics and Genomic Medicine Programme, UCL Great Ormond Street Institute of Child Health, University College London, United Kingdom, London, United Kingdom

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** Pediatric Rheumatology – Pathogenesis and Genetics Poster  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Although type I interferon (IFN1) and endoplasmic reticulum (ER) stress have been implicated in pathogenesis of juvenile dermatomyositis (JDM), little else is known about additional biological processes that may be involved and perhaps upstream of these pathways, or about processes that remain abnormal even when inflammation is controlled. To identify novel pathways dysregulated in JDM, we performed RNASeq on sorted immune subtypes from JDM patients and healthy controls.

**Methods:**

Peripheral blood samples were obtained from patients enrolled in the Juvenile Dermatomyositis Cohort and Biomarker Study (JDCBS) at pre-treatment (n=13) and 11.8 [11.3-13.2] months follow-up, (n=13) including n=10 matched
samples, and age/sex-matched healthy controls (n=8). CD4⁺, CD8⁺, CD14⁺ and CD19⁺ cells were flow-sorted from PBMCs by flow cytometry and RNA was extracted and sequenced. Gene set enrichment analysis (GSEA) and gene ontology (GO) term enrichment analysis were performed.

Results:

A strong IFN1 signature was identified: “IFNα signaling” was the most strongly enriched gene set identified by GSEA in all cell types (normalized enrichment scores of 2.39 (p<0.001), 2.84 (p<0.001), 2.88 (p<0.001) and 3.41 (p<0.001) for CD4, CD8, CD19 and CD14 cells, respectively). Overall, a higher proportion of differentially expressed (DE) genes were identified in CD14⁺ monocytes compared to other cell subtypes. Interestingly, 1,594 genes were DE in on-treatment monocytes compared to controls when IFN1 was no longer abnormal, suggesting on-going abnormal function even after a year of treatment. GO analysis of these genes identified over-representation of GO terms involved in mitochondrial function. A mitochondrial score (comprising all 13 protein-coding mitochondrial genes) correlates negatively with an IFN1 score (15 representative IFN-stimulated genes) in baseline monocytes (R=-0.87, p=0.003), indicating reduced expression of mitochondrially-encoded genes is associated with increased IFN1 signature. Analysis of the 343 genes annotated by the “Mitochondrion” Gene Ontology term GO:0005739 showed 54 were DE in baseline monocytes compared to follow-up, 51 were DE in baseline monocytes compared to controls, and 59 were DE in follow-up monocytes compared to controls. Notably, a set of genes involved in mitochondrial function were abnormally expressed in both baseline and follow-up monocytes compared to controls, indicating that mitochondrial dysfunction is not fully corrected by current treatment. Functional studies to characterise dysfunctions of monocytes and mitochondria are ongoing.

Conclusion:

This transcriptomic study has identified abnormal gene expression in the monocyte compartment in particular, and a striking dysregulation of genes involved in mitochondrial function. Ongoing functional work to characterize these dysfunctions will explore the potential of mitochondrial dysfunction as a novel treatment target.

Disclosure: C. Deakin, None; E. Rosser, None; L. Marshall, None; M. Wilkinson, None; A. Khabbush, None; S. Simou, None; G. Otto, None; S. Dowle, None; D. Kelberman, None; S. Yona, None; S. Eaton, None; L. R. Wedderburn, None.


Abstract Number: 2343

A Genome-Wide Association Study Suggests the HLA Class II Region As the Major Susceptibility Locus for IgA Vasculitis

Raquel López-Mejías¹, Sara Remuzgo-Martínez¹, Fernanda Genre¹, Francisco David Carmona², Santos Castañeda³, Belén Sevilla Pérez⁴, Norberto Ortego Centeno⁵, Javier Llorca⁵, Begoña Ubiña¹, Veronica Mijares¹, Trinitario Pina⁶, Jose A. Miranda-Filloy⁷, Antonio Navas Parejo⁸, Diego Argila⁹, Maximiliano Aragüés¹⁰, Esteban Rubio-Romero¹¹, Manuel Leon Luque¹², Juan Maria Blanco Madrigal¹³, Eva Galindez-Agirregoikoa¹³, David Jayne¹⁴, Ricardo Blanco¹, Javier Martín¹⁵ and Miguel Angel González-Gay¹⁶, ¹Epidemiology, Genetics and Atherosclerosis Research Group on Systemic Inflammatory Diseases, Rheumatology Division, IDIVAL, Santander, Spain, ²Instituto de Parasitología y Biomedicina López-Neyra, IPBLN-CSIC, PTS-Granada, Departamento de Genética e Instituto de Biotecnología, University of Granada, Granada, Spain, ³Hospital Universitario La Princesa. IIS-IP. Madrid. Spain, Madrid, Spain, ⁴Medicine Department, Hospital Universitario San Cecilio, Granada, Spain, ⁵Department of Epidemiology and Computational Biology, School of Medicine, University of Cantabria, and CIBER Epidemiología y Salud Pública (CIBERESP), IDIVAL, Santander, Spain, ⁶Epidemiology, Genetics and Atherosclerosis Research Group on Systemic Inflammatory Diseases, IDIVAL, Santander, Spain, ⁷Rheumatology Division, Hospital Lucus Augusti, Lugo, Spain,
SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Pathogenesis and Genetics Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Immunoglobulin-A (IgA) vasculitis, also known as Henoch-Schöenlein purpura (HSP), is the most common type of primary small-sized blood vessel leukocytoclastic vasculitis in children, although it may also develop in adults [1]. IgA vasculitis has a multifactorial etiology in which both environmental and genetic factors seem to contribute to the predisposition and clinical phenotype of the disease [1,2]. However, the genetic component of this type of vasculitis remains poorly understood, as only a few candidate gene studies have been performed to date [3,4]. Taking these considerations into account, and to increase the current knowledge on the genetic component of this vasculitis, we performed the first genome-wide association study (GWAS) on this condition using the largest series of IgAV patients of European ancestry ever assessed for a genetic study.

Methods: 308 IgA vasculitis patients and 1,018 healthy controls from Spain were genotyped by Illumina HumanCore BeadChips. Imputation of GWAS data was performed using the 1000 Genomes Project Phase III dataset as reference panel [5]. After quality control filters and GWAS imputation, 285 patients and 1,006 controls remained in the datasets and were included in further analysis. Additionally, the human leukocyte antigen (HLA) region was comprehensively studied by imputing classical alleles and polymorphic amino acid positions [6].

Results: A linkage disequilibrium block of polymorphisms located in the HLA class II region surpassed the genome-wide level of significance (odds ratio = 0.56, 95% confidence intervals = 0.46-0.68). Although no polymorphic amino acid positions were associated at the genome-wide level of significance, P-values of potential relevance were observed for the positions 13 and 11 of HLA-DRB1 (P = 6.67E-05, P = 1.88E-05, respectively). Outside the HLA, potential associations were detected, but none of them were close to the statistical significance.

Conclusion: Our study suggests that IgA vasculitis is an archetypal HLA class II disease.


This study is supported by European Union FEDER funds and “Fondo de Investigaciones Sanitarias” (grant PI12/00193) from “Instituto de Salud Carlos III” (ISCIII, Health Ministry, Spain). RL-M is supported by the Miguel Servet I programme of the Spanish Ministry of Economy and Competitiveness through the grant CP16/00033. SR-M is supported by funds from the RETICS Program (RIER) (RD16/0012/0009). FG is recipient of a Sara Borrell postdoctoral fellowship from the “Instituto Carlos III de Salud” at the Spanish Ministry of Health (Spain) (CD15/00095). FDC is supported by the Ramón y Cajal programme of the Spanish Ministry of Economy and Competitiveness through the grant RYC-2014-16458.

Disclosure: R. López-Mejías, None; S. Remuzgo-Martínez, None; F. Genre, None; F. D. Carmona, None; S. Castañeda, None; B. Sevilla Pérez, None; N. Ortego Centeno, None; J. Llorca, None; B. Ubilla, None; V. Mijares,
Cell-Bound Complement Activation Products As Markers of Disease Flares in Childhood Onset Systemic Lupus Erythematosus

Yevgeniya Gartshteyn¹, Joyce Hui-Yuen², Miya Okado¹, Teja Kapoor¹, Thierry Dervieux³ and Anca Askanase⁴, ¹Rheumatology, Columbia University College of Physicians & Surgeons, New York, NY, ²Pediatric Rheumatology, Columbia University College of Physicians & Surgeons, New York, NY, ³3Exagen Diagnostics, Albuquerque, CA, ᴄDepartment of Medicine, Rheumatology, Columbia University College of Physicians & Surgeons, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Pathogenesis and Genetics Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Cell-bound complement activation products, CB-CAPs (C4d deposition on erythrocytes [EC4d], B lymphocytes [BC4d], reticulocytes [RC4d], platelets [PC4d], and C3d deposition on reticulocytes [RC3d]) are sensitive and specific markers for the diagnosis and evaluation of lupus. Cell-specific CB-CAPs may have a role as biomarkers of organ/systems involvement in SLE, such as the association of PC4d with cardiovascular events/presence of antiphospholipid antibodies, and EC4d with proteinuria. The current study investigated the role of CB-CAPs as markers of SLE flares, as well as their possible association with muco-cutaneous involvement.

Methods:
This was a longitudinal study of 33 patients with childhood onset SLE (cSLE, diagnosed at or before age 19) who fulfilled ACR SLE classification criteria and had up to 6 months of follow-up. Venous blood was collected every 3 months for CB-CAPs and results were reported as net mean fluorescence intensity index (MFI). Additionally, anti-dsDNA, complement levels (C3 and C4) and laboratory work needed for SLE Disease Activity Index (SLEDAI) scoring were also evaluated. Disease activity was assessed at each visit using SLEDAI. Lupus flares were identified using the Safety of Estrogens in Lupus Erythematosus: National Assessment (SELENA) SLEDAI flare index (SFI).

Results:
The study included 33 patients (19±4 years old, 79% female, 45% Hispanic, 33% African American). Patients met on average 5±1 ACR-SLE classification criteria; 97% had positive ANA titers, 88% had elevated dsDNA titers, and 21% tested positive for the antiphospholipid antibodies. Abnormal EC4d (>14 net MFI) levels were observed in 19, BC4d (>75 net MFI) in 20, and PC4d levels (> 20 net MFI) in 12 patients. All patients were treated with hydroxychloroquine, 55% with corticosteroids and 70% with immune-suppressants.

Twelve visits with SLE flares were identified, 7 of which were mild/moderate and 5 severe. Of these 12 flares, 5 patients had rashes, 4 arthritis, 4 nephritis (proteinuria) and 1 vasculitis.
SLE patients with flares (SLEDAI = 9 ± 3), as compared to SLE patients with stable disease (SLEDAI = 4 ± 3), had significantly higher PC4d values (18 [IQ 7-70] vs. 8 [IQ 3-15] net MFI; p=0.045). Among these patients with flares, two patients had normal complement levels and another one had stable/normal dsDNA levels but elevated PC4d. EC4d levels were numerically higher in patients with flares, 17 [IQ 14-29] vs 10 [IQ 6-26] net MFI, p=0.07. BC4d was not significantly different between the two groups, 81 [IQ 32-180] vs 77 [IQ 36-135] net MFI, p=0.91. In addition, within the cohort of 33 patients, 14 with rash had elevated RC3d and a trend toward elevated PC4d levels, with a median level of 4 [IQ 1-7] vs. 1 net MFI [IQ 1-4] (p=0.04) and 10 [IQ 5-36] vs. 8 [IQ 3-15] net MFI (p=0.09) respectively.

**Conclusion:**

These pilot findings suggest CB-CAPs as a potential biomarker to identify disease flares more consistently than low complement or high levels of anti-dsDNA in cSLE. The relatively shorter lifespan of platelets might allow for closer tracking of changes in disease activity associated with flare. Our data also suggest that reticulocyte bound CB-CAPs may play a role as a biomarker to predict muco-cutaneous involvement in cSLE patients.

**Disclosure:** Y. Gartshteyn, None; J. Hui-Yuen, None; M. Okado, None; T. Kapoor, None; T. Dervieux, Exagen, 3; A. Askanase, Exagen, 2.


**Abstract Number:** 2345

**Characterization of Adenosine Deaminase 2 Variants Identified in an International Pediatric Vasculitis Cohort**

Kristen Gibson1,2, David Cabral3,4, Britt Drogemoller5, Xiaohua Xhan5, Fudan Miao6, Kimberly Morishita7, Erin Gill8, Robert E. W. Hancock8, Colin Ross5,9, and Kelly Brown9,10, 1Medical Genetics, The University of British Columbia, Vancouver, BC, Canada, 2BC Children's Hospital Research Institute, Vancouver, BC, Canada, 3BC Children's Hospital, Vancouver, BC, Canada, 4University of British Columbia, Vancouver, BC, Canada, 5Pharmaceutical Sciences, The University of British Columbia, Vancouver, BC, Canada, 6The University of British Columbia, Vancouver, BC, Canada, 7BC Children's Hospital and University of British Columbia, Vancouver, BC, Canada, 8Microbiology and Immunology, The University of British Columbia, Vancouver, BC, Canada, 9BC Children's Hospital Research Institute, Vancouver, BC, Canada, 10Pediatrics, The University of British Columbia, Vancouver, BC, Canada

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Pediatric Rheumatology – Pathogenesis and Genetics Poster

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Deficiency of adenosine deaminase 2 (DADA2) is a recently recognized, autosomal recessive genetic disease. Patients present with various, early-onset systemic vascular and inflammatory manifestations, and often recurrent strokes. The clinical features and histological findings of DADA2 overlap with those of early childhood onset polyarteritis nodosa (PAN), a primary “idiopathic” systemic vasculitis, characterized by necrotizing inflammatory lesions of small and medium-sized vessels. Despite similar clinical presentation, individuals with PAN and DADA2 may benefit from
Different therapy. While treatment of primary chronic vasculitis is usually with toxic immunosuppressive drugs, there has been clinical indication that DADA2 patients respond better to less toxic IL-6 receptor antagonists and anti-TNFα therapy. We aimed to screen patients with PAN, cutaneous PAN, unclassifiable phenotype, or chronic vasculitis of any type with onset-age less than 5 years for variants in adenosine deaminase 2 (ADA2).

Methods:

Of the 493 pediatric patients included in our international, multi-ethnic cohort, ARChive (A Registry of Childhood Vasculitis), there were 99 patients who provided DNA samples, and 41 of these fulfilled screening criteria. We sequenced the coding exons of ADA2 in these 41 patients. Identified variants in ADA2 were characterized by quantifying their effect on ADA2 expression, secretion, and enzymatic activity by qPCR, standard ELISA, and kinetic colorimetric assays, respectively. RNA sequencing of whole blood was done to enable transcriptomic profiling of patients with DADA2 versus PAN and other types of chronic vasculitis.

Results:

We have identified variants in ADA2 with known and novel association with DADA2; four patients were found to be homozygous or compound heterozygous for rare (MAF < 0.01), predicted pathogenic variants. An additional two patients were found to be heterozygous for rare, missense variants; further analysis of expression and enzymatic activity may guide the identification of additional pathogenic variants that could contribute to the observed phenotype.

Conclusion:

At present, the gold standard for direct diagnosis of vasculitis is histopathological examination of biopsy specimens from involved organs. Screening ADA2 among patients with possible early-onset chronic vasculitis or PAN phenotype may identify and diagnose patients, perhaps without requirement for biopsy. Early diagnosis of DADA2 patients may spare them treatment with toxic systemic immunosuppressive drugs, and allow more effective intervention with targeted biologic and/or gene therapy.

This work was supported by a Canadian Institutes of Health Research grant for the PedVas Initiative [TR2-119188 to DAC].

Disclosure: K. Gibson, None; D. Cabral, None; B. Drogemoller, None; X. Xhan, None; F. Miao, None; K. Morishita, None; E. Gill, None; R. E. W. Hancock, None; C. Ross, None; K. Brown, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/characterization-of-adenosine-deaminase-2-variants-identified-in-an-international-pediatric-vasculitis-cohort

Abstract Number: 2346

Chemokine Ligand 9 (CXCL9) [Monokine Induced By Gamma Interferon (MIG)] As a Predictor of Active Disease Status in Localized Scleroderma

Kathryn S. Torok1, Qi Mi2, Emily Mirizio3, Kaila Schollaert-Fitch1, Mark Fritzler4 and Marvin J. Fritzler5, 1Pediatric Rheumatology, University of Pittsburgh Med Ctr, Pittsburgh, PA, 2Department of Sports Medicine and Nutrition, University of Pittsburgh, Pittsburgh, PA, 3Pediatric Rheumatology, University of Pittsburgh Med Ctr, Pittsburgh, PA, 4Eve Technologies, Calgary, AB, Canada, 5Medicine, University of Calgary, Calgary, AB, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Pathogenesis and Genetics Poster
Background/Purpose:

Localized scleroderma (LS) is a fibrotic autoimmune disease of the skin and underlying tissues which can lead to disfiguring sequelae, especially in childhood-onset. Untreated active disease is associated with long-term damage and disability; therefore accurate assessment of the active disease state is imperative, and a distinct activity biomarker would assist clinicians to intervene before disease progression. The purpose of this study was to investigate a wide variety of cytokine/chemokines, specifically within disease transition from active to inactive phases in individual patients, which correlate to established clinical measures of disease activity in LS.

Methods:

Plasma from 70 juvenile LS (jLS) patients with clinical data and longitudinal samples (average of 6 years follow-up), including at least one active and one inactive specimen (272 samples total), were evaluated by microarray to study a 60-analyte cytokine/chemokine panel. This included the study of T\textsubscript{H}1, T\textsubscript{H}2, and T\textsubscript{H}17 associated cytokines with an additional IFN-\gamma panel that emphasized CXCL9, CXCL11, and MIP-3β chemokines. Wilcoxon Signed-Ranks Test (p<0.05) was used to compare cytokine/chemokines between active and inactive disease subsets. Next, to focus on clinically significant cytokines, additional analyses included spearman’s correlation of analytes with the modified Localized Skin Severity Index (mLoSSI), a validated active disease variable, followed by multiple regression analyses of the significantly correlated cytokines using R language.

Results:

When dichotomizing the LS samples into active vs. inactive subjects, many reoccurring cytokines were significantly elevated (Table 1 – left column). Correlation of the 60 analyte panel resulted in moderate to strong correlation of IFN-\gamma and T\textsubscript{H}1-like associated cytokine/chemokines with the mLoSSI, including CXCL9 (MIG), MIP-3β, and IL-10 (Table 1 – right column). Of those that correlated strongly with the mLoSSI, IL-10 and CXCL9 were statistically significant predictors in multiple linear regression analyses (p = 0.002 and 0.001, respectively), with an adjusted R-squared of 0.71; meaning the change of IL-10 and CXCL9 are related to the change in mLoSSI, signifying change in disease activity status.

Conclusion:

This is a unique examination of circulating cytokines in jLS and further correlates the biological activity to clinical disease activity measures used for disease monitoring, the mLoSSI. The correlated chemokines indicate a strong IFN-\gamma associated environment. CXCL9 is a predominant IFN-\gamma inducible chemokine and is part of the IFN-\gamma family that contributes to the activation of the M1 phenotype and recruitment of T\textsubscript{H}1 cells, both of which induce further inflammatory cytokine response. Further analysis using the best-fit model is underway with the overall goal of finding the strongest core set of biomarkers that highly predicts the mLoSSI in LS patients, signifying degree of disease activity.
Table 1: Analyses of 60 cyto/chemokines in LS with focus on disease activity

<table>
<thead>
<tr>
<th>Active vs. Inactive LS</th>
<th>Correlation of the mLoSSI with the peripheral blood cyto/chemokines</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Peripheral Blood</strong></td>
<td><strong>Cyto/chemokine</strong></td>
</tr>
<tr>
<td>CXCL9 (MIG)</td>
<td>0.030</td>
</tr>
<tr>
<td>CXCL11 (I-TAC)</td>
<td>0.050</td>
</tr>
<tr>
<td>MIP-3β</td>
<td>0.001</td>
</tr>
<tr>
<td>IL-9</td>
<td>0.020</td>
</tr>
<tr>
<td>IL-2</td>
<td>0.020</td>
</tr>
<tr>
<td>CCL-1 (-309)</td>
<td>0.020</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Disclosure: K. S. Torok, None; Q. Mi, None; E. Mirizio, None; K. Schollaert-Fitch, None; M. Fritzler, Eve Technologies, 3; M. J. Fritzler, Inova Diagnostics, Inc., 5.


Abstract Number: 2347

**High Interferon (IFN) Signatures and Overlapping Clinical Features Characterize Subgroups of Patients with Presumed IFN-Mediated Autoinflammatory Diseases**

Adriana Almeida de Jesus1, Yanfeng Hou2, Louise Malle1, Scott Canna3, Stephen R. Brooks4, Hanna Kim5, Gina A. Montealegre Sanchez1, Rachel VanTries1, Angélique Biancotto6, Samantha Dill5, Dawn C. Chapelle5, Bernadette Marrero1, Yan Huang1 and Raphaela Goldbach-Mansky1, 1Translational Autoinflammatory Disease Studies (TADS), Laboratory of Clinical Investigation and Microbiology (LCIM), NIAID/NIH, Bethesda, MD, 2Department of Rheumatology, Shandong Provincial Qianfoshan Hospital, Shandong University, Shandong, China, 3Richard King Mellon Foundation Institute for Pediatric Research, Children's Hospital of Pittsburgh, Pittsburgh, PA, 4Biodata Mining and Discovery Section, Office of Science and Technology, NIAMS/NIH, Bethesda, MD, 5Pediatric Translational Research Branch, NIAMS/NIH, Bethesda, MD, 6Center for Human Immunology, Autoimmunity and Inflammation (CHI), NHLBI, NIH, Bethesda, MD

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017

Session Title: Pediatric Rheumatology – Pathogenesis and Genetics Poster

Session Type: ACR Poster Session C

Session Time: 9:00AM-11:00AM
Background/Purpose: Many pediatric patients (pts.) with early-onset autoinflammatory disease (AID) phenotypes are mutation-negative for genetically known AIDs. Recent data suggest a role for Type-I interferon (IFN) dysregulation in causing AID phenotypes with clinical features that are distinct from those found in pts. with IL-1 mediated AIDs. We screened pts. for the presence of IFN–response gene signatures (IRS) to characterize their clinical phenotypes, IFN-related biomarkers and genetic causes.

Methods: We assessed IRS from 63 consecutively evaluated patients (pts.) who were negative for known AID-causing mutations. Gene expression of 28 selected interferon response genes (IRG) was determined by Nanostring and an IFN-score was calculated. Serum levels of 48 cytokines were measured by a multiplex immunoassay. Pts. underwent clinical assessments and genetic analyses were performed by whole exome/genome sequencing (WES/WGS).

Results: Of 63 pts. tested, 36 had elevated IRS. Pts. with high IRS had higher serum levels (all in pg/ml) of: most pronounced in IP-10 (11169 ± 1849 vs 834 ± 117, p<0.0001), and MIG/CXCL9 (7133 ± 2450 vs 706 ± 61), MIP1α (195 ± 23 vs 153 ± 5.8), GROα (423 ± 95 vs 165 ± 14), all p<0.01 and MIP1β (301 ± 42 vs 220 ± 13), SCF (63 ± 15 vs 28 ± 4.8), with p<0.05, than those with negative IFN scores. Pts. with high IRS had significantly higher frequencies of panniculitis (58 vs 0%), basal ganglia calcifications (45 vs 0%), interstitial lung disease (ILD) (48 vs 4.8%), myositis (65 vs 15%), all with p<0.01 and skin vasculitis (29 vs 7.4%), and arterial hypertension (32 vs 3.7%), p<0.05, and lower frequency of aseptic osteomyelitis (0 vs 22%, p<0.01) than pts. without an IRS. Furthermore, anemia (33 vs 7.4%), lymphopenia (26 vs 0%) and positive ANA (42 vs 11%), all p<0.05, were more frequent in pts. with an IRS. Based on disease manifestations, patients could be assigned to 8 distinct groups. Pts. with ILD and macrophage activation syndrome (MAS) had very high IL-18 serum levels and a cytokine signature seen in other patients with MAS. Two pts. with lipodystrophy had novel LRBA mutations, 2 pts. with lymphohistiocytic panniculitis, ILD, cytopenias and white matter disease have de novo truncating mutations in SAMD9L, and with myositis and ILD had anti-MDA5 autoantibodies. One patient with “atypical CANDLE” had a novel PSMB8 mutation, and one pt. each had mutations in a novel proteasome gene, PSMG2, and a de novo somatic mutation in TREX1. IFI27 was the most upregulated gene in patients with SAVI, CANDLE and Aicardi-Goutières syndrome (AGS), but its expression in patients with LRBA and NEMO mediated disease was significantly lower.

Conclusion: The presence of an IFN signature is associated with distinct clinical and cytokine patterns, including pts. with ILD and high serum IL-18 and a predisposition to MAS. Our data suggest that IFN leads to a set of clinical features that combined with the assessment of an IFN response gene signature can identify patients and autoinflammatory interferonopathies and help define clinically distinct disease subsets. Whether IFN is the pathogenic cause of these diseases needs to be further investigated in treatment studies.

Disclosure: A. Almeida de Jesus, None; Y. Hou, None; L. Malle, None; S. Canna, AB2Bio Ltd, 5; S. R. Brooks, None; H. Kim, None; G. A. Montealegre Sanchez, Eli Lilly and Company, 9; R. VanTries, None; A. Biancotto, None; S. Dill, None; D. C. Chapelle, None; B. Marrero, None; Y. Huang, None; R. Goldbach-Mansky, Eli Lilly and Company, 9,SOBI, 9,Regeneron, 9,Novartis Pharmaceutical Corporation, 9.

A New Cause of Mendelian Lupus Due to IKZF1 Mutation Underlines the B Cell Landscape Heterogeneity in Monogenic Lupus

Alexandre Belot1,2, Cecile Frachette3, Omarjee Sulliman Ommar2, Anne-Laure Mathieu2, Thibault Andrieu2, Paul Mondier2, Gillian Rice4, Heloise Reumaux5, David Launay6,7, Marc Lambert8,9, Guillaume Lefevre10, Nicole Fabien11, Christophe Malcus12, Isabelle Rouvet13, Emilie Chopin13, Anne-Sophie Michallet14, Thierry De France14, Thierry Walzer14 and Yanick J Crow15, 1Pediatric Rheumatology Unit, HFME, Hospices Civils de Lyon, Bron, France,
Next generation sequencing (NGS) represents a revolution in the field of molecular medicine, and offers a new approach to deciphering the pathogenesis of complex diseases. One hypothesized that patients with early-onset lupus may be carrying genetic mutation responsible for the autoimmune condition. We have in the past described a B cell-related Mendelian form of lupus due to a deficiency of PKCδ. Here, we identified and characterized a new B cell-related Mendelian lupus secondary to \textit{IKZF1} mutation and compared this novel monogenic disease with PKCδ deficiency.

**Methods:**

We designed a NGS panel comprising 200 genes including proven disease-associated as well as prospective candidate genes, and analyzed 131 patients. We identified a family with three affected patients carrying a new mutation in \textit{IKZF1}. We set up functional assays including oligonucleotide pulldown assay, B cell phosphorylation and deep B cell immunophenotyping by mass cytometry.

**Results:**

We have identified a heterozygous missense mutation in \textit{IKZF1} c.359A>T in three affected patients in a single family. \textit{IKZF1} encodes IKAROS, a key transcriptional factor for B cell development. The patients did not display any recurrent infection and IgG level was normal. Functional assays showed that stability was not impaired, but DNA-binding was partially impacted for mutant IKAROS. We performed mass cytometry comparing SLE patients carrying \textit{PRKCD} and \textit{IKZF1} mutation. We identified B cell clusters and unsupervised analysis underlined the wide differences between two monogenic diseases leading to SLE.

**Conclusion:**

Ikaros deficiency reveals that monogenic lupus occurs under various B cell anomalies underlining that lupus should be considered as a syndrome more than a single homogenous disease.
Interferon Signature in Childhood Rheumatic Diseases

Hafize Emine Sonmez1, İ. Çağatay Karaaslan2, Ezgi Deniz Batu3, Banu Anlar4, Betul Sozeri5, Adriana Almeida de Jesus6, Raphaela Goldbach-Mansky7 and Seza Ozen8, 1Department of Pediatrics, Division of Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Turkey, 2Department of Molecular Biology, Hacettepe University, Ankara, Turkey, 3Pediatric Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Turkey, 4Department of Pediatrics, Division of Neurology, Hacettepe University Faculty of Medicine, Ankara, Turkey, 5Pediatric Rheumatology, Ümraniye Tranning and Research Hospital, İstanbul, Turkey, 6National Institute of Allergy and Infectious Diseases (NIAID), NIH, Bethesda, MD, 7Translational Autoinflammatory Disease Studies (TADS), Laboratory of Clinical Investigation and Microbiology (LCIM), NIAID/NIH, Bethesda, MD, 8Department of Pediatrics, Division of Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Turkey

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Pathogenesis and Genetics Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Several rheumatic diseases are characterized by overexpression of type I interferon(IFN)-inducible or viral response genes, termed the IFN signature. Recently this signature has been reported in a novel group of monogenic Type-I IFN mediated autoinflammatory diseases(AIDs) or autoinflammatory interferonopathies. We aimed to compare a set of clinical features previously associated with monogenic autoinflammatory AIDs and a blood IFN score with autoimmune (SLE, JDM) interferonopathies, and other disease controls.

Methods:

We identified 12 patients with probable interferonopathy and selected clinical features of IFN mediated AIDs based on literature review/expert opinion (Table 1). We compared the clinical criteria with 23 controls (8 healthy children, 6 oligoarticular juvenile idiopathic arthritis[oJIA] patients,4 systemic lupus erythematosus[SLE], 5 with DADA2). The expression of 28 IFN-related genes was quantified from RNA from whole blood using NanoString technology. Summary scores for IFN6/IFN28/ and a z-score for CXCL10(IP10) were calculated.

Results:

The mean clinical score was in the presumed IFNopathies(minimum-maximum) 5 (3-7). The median IFN6, IFN28, scores were significantly higher in the probable interferonopathy cases as compared to healthy controls and oJIA and DADA2 patients but did not differ from SLE patients. Interestingly, CXCL10(IP10) scores were higher (but not significant) in the probable interferonopathy group than the SLE and DADA2 groups.

Conclusion:
We suggest a set of clinical criteria combined with the 6 gene or 28gene IFN score in developing criteria for IFN-mediated AIDs. Development and validation of an appropriate criteria is ongoing.

**Table 1.** Preliminary clinical score to differentiate interferon(IFN)-mediated autoinflammatory diseases (AIDs) from interleukin-1(IL-1)-mediated AIDs
<table>
<thead>
<tr>
<th>Clinical preliminary criteria</th>
<th>Presumed IFN mediated AIDs</th>
<th>JIA (n=6)</th>
<th>SLE (n=4)</th>
<th>DADA2 (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Skin manifestations (nodular erythema, violaceous plaques in cold-sensitive acral areas)</td>
<td>12/12</td>
<td>0/6</td>
<td>0/4</td>
<td>1/5</td>
</tr>
<tr>
<td>2. Vasculopathy (chill-blain like rash, microangiopathic vasculopathy, gangrene/ulcers/infarcts in acral areas)</td>
<td>6/12</td>
<td>0/6</td>
<td>0/4</td>
<td>1/5</td>
</tr>
<tr>
<td>3. Lipodystrophy</td>
<td>2/12</td>
<td>0/6</td>
<td>0/4</td>
<td>0/5</td>
</tr>
<tr>
<td>4. Joint manifestations (contractures, non-erosive arthritis)</td>
<td>5/12</td>
<td>0/6</td>
<td>0/4</td>
<td>0/5</td>
</tr>
<tr>
<td>5. Myositis (patchy)</td>
<td>2/12</td>
<td>0/6</td>
<td>0/4</td>
<td>0/5</td>
</tr>
<tr>
<td>6. CNS manifestations (basal ganglia calcifications, leukoencephalopathy, white matter disease, L/P lymphocytic findings)</td>
<td>8/12</td>
<td>0/6</td>
<td>0/4</td>
<td>0/5</td>
</tr>
<tr>
<td>7. Pulmonary involvement (interstitial lung disease, pulmonary fibrosis, pulmonary hypertension)</td>
<td>2/12</td>
<td>0/6</td>
<td>0/4</td>
<td>0/5</td>
</tr>
<tr>
<td>8. Leukopenia/lymphopenia with flares</td>
<td>4/12</td>
<td>0/6</td>
<td>4/4</td>
<td>1/5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Median clinical score (STD)</th>
<th>5</th>
<th>0</th>
<th>1</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median 6-gene IFN score (minimum-maximum)</td>
<td>137.87 (0.251-380.09)</td>
<td>3.17 (-0.08-23.42)</td>
<td>159.66 (-0.22-381.69)</td>
<td>10.25 (2.86-36.37)</td>
</tr>
<tr>
<td>Median 28-gene IFN score (minimum-maximum)</td>
<td>324.01 (24.66-949.98)</td>
<td>18.64 (8.91-95.76)</td>
<td>236.45 (2.75-475.96)</td>
<td>60.39 (21.24-209.29)</td>
</tr>
</tbody>
</table>
Gastrointestinal Microbiota in New-Onset Juvenile Idiopathic Arthritis

Sriharsha Grevich1,2, Kyle Hager3, Mitchell Brittacher3, Hillary Hayden3, Sarah Ringold1,2, David Suskind1,2, Samuel Miller3 and Anne Stevens1,2, 1University of Washington, Department of Pediatrics, Seattle, WA, 2Seattle Children's Hospital, Seattle, WA, 3University of Washington, Department of Microbiology, Seattle, WA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Pathogenesis and Genetics Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Oral and gut microbes have been implicated in the pathogenesis of rheumatoid arthritis, spondyloarthropathy, and juvenile enthesitis-related arthritis (ERA). Pro-inflammatory microbes in the bacteroides phyla appear to be over-represented, while commensals in the firmicutes phyla are under-represented in inflammatory disease. The role of dysbiosis in the microbiota is not well-studied in new-onset juvenile idiopathic arthritis (JIA); individual variation secondary to diet, age, and other environmental factors makes such an analysis challenging. Previous studies demonstrated that healthy children derive most of their microbes from their mothers, and thus share similar microbial communities. We hypothesized that if the gut microbiota contributes to systemic inflammation, then children with JIA will have an altered microbiota compared to their mothers.

Methods:
Stool samples were collected from ten new-onset, treatment naive JIA patients aged 2-15 years (four oligoarticular, two polyarticular, three ERA, and one psoriatic), and their mothers in preservative-filled Omnigene-GUT cryovials designed to stabilize microbial communities. DNA was extracted from stool using the PowerSoil DNA Isolation Kit, and sequencing was performed on the Illumina HiSeq-2000 platform. Human DNA sequences, duplicate reads, sequence reads with ambiguous bases, and reads shorter than 80 bases were identified and removed from analysis. Taxonomic classification and relative species abundance of bacteria were obtained using MetaPhlAn2.

Results:
Compared to their mothers, 60% of JIA patients had lower fecal firmicutes populations. In 50%, higher bacteroidetes phyla were identified. Four of ten patients had both low firmicutes and increased bacteroidetes. The mean firmicutes:bacteroides ratio in patients was 7.2 (IQR 2.8-7.8) compared to 17.5 (IQR 9.6-24.9) in their mothers. The lowest ratio was detected in oligo JIA (mean 5.1, range 2.1-7.2), followed by poly JIA (6.7, range 1.3-12) and ERA (10, range 2.8-21). Of all of the patients, the three with the lowest ratios (1.3-2.8) all carried antinuclear antibodies.
Conclusion:
Consistent with previous results in adult RA and JIA, in new-onset JIA, fecal microbial communities were skewed toward bacteroides phyla, which can be pro-inflammatory. Whether this finding reflects a microbial trigger for JIA, or rather the coincident result of immune dysregulation, remains to be determined.

Disclosure: S. Grevich, Pfizer Inc, 2; K. Hager, None; M. Brittnacher, None; H. Hayden, None; S. Ringold, Crescendo Bioscience, 2; D. Suskind, None; S. Miller, None; A. Stevens, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/gastrointestinal-microbiota-in-new-onset-juvenile-idiopathic-arthritis

Are Sedentary Behavior and Reduced Physical Activity Associated with Long-Term Cardiovascular Risk in Individuals with Rheumatoid Arthritis?

Nevin Hammam1,2, Victor Ezeugwu1, Dax Rumsey3, Trish Manns4 and Lesley Pritchard-Wiart5,6, 1University of Alberta, Edmonton, AB, Canada, 2Rheumatology and Rehabilitation Department, University of Assiut, Assiut, Egypt, 3Stollery Children's Hospital, Edmonton, AB, Canada, 4University of Alberta, edmonton, AB, Canada, 5Glenrose Rehabilitation Hospital Edmonton, Edmonton, AB, Canada, 6Physical Therapy, University of Alberta, Edmonton, AB, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Patients with rheumatoid arthritis (RA) are at increased risk for cardiovascular disease (CVD) with subsequent morbidity and mortality1. It is well known that prolonged sedentary behaviour (SB) and reduced physical activity (PA) are risk factors for CVD. The purpose of this study was to examine the independent relationships between SB, very light (VLPA), light (LPA), and moderate to vigorous (MVPA) and 10-year CVD risk in a subsample of people with RA using the Framingham risk score (FRS), an accurate and widely used tool to assess 10 year CVD risk.2

Methods:
A subsample of individuals diagnosed with RA was extracted from the 2003–2006 National Health and Nutrition Examination Survey (NHANES) database, a population-representative US sample. Actigraphy, a uniaxial accelerometer ActiGraph 7164, was used to derive SB and PA volume and pattern. Raw actigraphy data were categorized into SB, VLPA, LPA, and MVPA expressed as mean minutes per day. Pattern variables, including number of breaks in sedentary time, length of sedentary time, and active bouts were calculated. Functional limitation was assessed by self-reported questionnaire. The 10-year CVD risk was determined based on the FRS. Descriptive statistics and multiple linear regression models were used in the analysis using Stata software version 14.

Results:
A total of 273 individuals with RA were included in the analysis. Mean age of participants was 62.7 ±13 years; 143 (52.4%) were women, and 167 (61.6%) had functional limitations. Participants spent an average of 9 hours/day in SB, 4 hours/day in VLPA, 1 hour/day in LPA, 23 minutes/day in MVPA.

Based on the FRS which considers age, sex, cholesterol (HDL-D and total), systolic blood pressure, diabetes and smoking, 35% of participants had higher than 20% 10 year CVD risk; 29% had 10-20% risk; and 36% had less than 10% risk.

Greater sedentary time (p= 0.019) and average length of sedentary bout (p<0.001) were associated with higher 10-year of CVD risk in patients with RA. Greater daily VLPA (p<0.001), LPA (p=0.001), MVPA (p=0.021), and total number of sedentary breaks (p<0.001) were negatively associated with 10-year CVD risk. The association between average length of activity bouts and 10-year CVD risk was not significant (p=0.068).

In the fully adjusted regression model (adjusted for wear time, body mass index, and waist circumference) the association between 10-year CVD risk and SB (R^2=0.26, p<0.001), VLPA (R^2=0.25, p<0.001), LPA (R^2=0.24, p=0.003), sedentary bout length (R^2=0.24, p=0.002), and breaks in sedentary time (R^2=0.23, p=0.026) remained significant.

While functional limitation was directly associated with higher 10-year CVD risk in the unadjusted model (p=0.006), this relationship was attenuated in the fully adjusted model (p=0.045).

**Conclusion:**

Given the increased cardiovascular risk in people with RA, high sedentary behaviour and low physical activity is concerning. Interventions aimed at decreasing SB and promoting PA may help to reduce long-term CVD risk.

References:


**Disclosure:** N. Hammam, None; V. Ezeugwu, None; D. Rumsey, None; T. Manns, None; L. Pritchard-Wiart, None.


**Abstract Number:** 2352

**Cardiovascular Safety during Treatment with Baricitinib in Rheumatoid Arthritis**

*M. Weinblatt*¹, Peter C. Taylor², Gerd R. Burmester³, Sarah Witt⁴, Chadi Saifan⁴, Chad Walls⁵, Terence P. Rooney⁴, Lei Chen⁴ and Tsutomu Takeuchi⁶, ¹Brigham and Women's Hospital, Boston, MA, ²NDORMS, University of Oxford, Oxford, United Kingdom, ³Department of Rheumatology and Clinical Immunology, Charité - University Medicine Berlin, Free University and Humboldt University Berlin, Berlin, Germany, ⁴Eli Lilly and Company, Indianapolis, IN, ⁵Eli Lilly and Company, Indianapolis, IN, ⁶Keio University School of Medicine, Tokyo, Japan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Background/Purpose: Baricitinib (BARI) is an oral selective inhibitor of Janus kinase (JAK)1 and JAK2 approved in the EU for the treatment of active RA. Patients (pts) with RA have increased cardiovascular risk, including for arterial and venous occlusive events. This abstract examines the effects of BARI on cardiovascular events in RA.

Methods: Data were pooled from 8 completed studies (1 Phase 1b, 3 Phase 2, 4 Phase 3) and 1 ongoing long term extension study (LTE) with data up to Sept. 1, 2016. The All BARI RA (All Exposure) analysis set included all pts exposed to any BARI dose. Comparisons with placebo (PBO) were based on 6 studies with BARI 4 mg once daily (QD) and PBO. Dose response was assessed based on 4 studies with BARI 2 and 4 mg QD, including data from the LTE (Extended 2 vs 4 mg set). Two studies contained active comparators (MTX and adalimumab [ADA]). Major adverse cardiovascular events (MACE) (composite of myocardial infarction, stroke and cardiovascular death) were blindly adjudicated by an independent panel for phase 3 studies and the LTE. Study database terms of “deep vein thrombosis” (DVT) / “pulmonary embolism” (PE) were analyzed without adjudication. Incidence rates (IR) per 100 pt-years [PY] of exposure were used.

Results: 3492 pts were exposed to BARI (6637 PY), 2723 pts (78.0%) for >1 year and 1867 (53.5%) for >2 years. In the 6-study PBO-controlled set (0-24 weeks), 2 cases of MACE were reported in the PBO group and 3 cases in the BARI 4 mg group (Figure 1). DVT/PE were reported for 0 pts in the PBO group and 5 in the BARI 4 mg group (Figure 2); 2 were serious, all had multiple risk factors, 1 occurred after discontinuing study drug, and 4 pts either continued or restarted BARI without worsening or occurrence of another event. In the Extended 2 vs. 4 mg set, IR for MACE and DVT/PE were comparable between doses. In the All BARI RA set, event rates were stable over time (Figure 3), with overall IR of 0.51 per 100 PY for MACE and 0.46 for DVT/PE (published RA DVT/PE rates 0.29 to 0.79 per 100 PY).

Conclusion: For MACE, IR were similar across analysis sets and did not increase with prolonged exposure. For DVT/PE, events were reported for BARI 4 mg but not PBO; IR were similar between doses, consistent over time, and comparable to published rates in RA.


Abstract Number: 2353
The Relationship between Disease Activity, VEGF and E-Selectin Levels with Arterial Stiffness in Rheumatic Patients Treated with Biological Agents

Taskin Senturk1, Huseyin Baygin1, Gokhan Sargin1, Hakan Akdam2 and Mustafa Yilmaz3, 1Rheumatology, Adnan Menderes University, Aydin, Turkey, 2Nephrology, Adnan Menderes University, Aydin, Turkey, 3Biochemistry, Adnan Menderes University, Aydin, Turkey

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Rheumatic diseases are chronic-inflammatory disease associated with endothelial damage, changes in vascular permeability and plaque formation. VEGF and E-selectin play an important role in chronic inflammation, therefore arterial stiffness is affected. Our aim was to evaluate association between disease activity, VEGF, E-selectin and arterial stiffness in patients with rheumatic diseases.

Methods: 41 patients with rheumatic disease (13 AS, 28 RA, 27 females and 14 males with mean age of 51,0±12,1 years) and 30 healthy controls (20 females and 10 males with mean age of 51,9±10,8 years) were enrolled to the study. Arterial stiffness, VEGF, E-selectin levels, BASDAI and DAS-28 scores were evaluated. VEGF and E-selectin were determined by ELISA, and arterial stiffness was measured by oscillometric method. Student's T Test, Mann-Whitney-U Test and Wilcoxon Test were performed as statistical analysis and p<0.05 was accepted as statistically significant.

Results: BASDAI, DAS-28, ESR and CRP levels were significantly decreased on the 3th month of treatment in all patients (p<0,001). Increased VEGF, E-selectin and decreased arterial stiffness parameters (PWV and Alx) was observed with treatment. These changes were not statistically significant. While the level of PWV was stable, Alx was decreased on the 3th months of non-TNF treatment in RA patients

Conclusion: Disease activity score, ESR and CRP were decreased in RA and AS patients with treatment resulting in reduced inflammation. Arterial stiffness and cardiovascular risk is expected to be reduced significantly ongoing treatment process. VEGF, E-selectin, arterial stiffness parameters (PWV and Alx) can be used as a marker of disease activity in RA and AS.

Disclosure: T. Senturk, None; H. Baygin, None; G. Sargin, None; H. Akdam, None; M. Yilmaz, None.


Abstract Number: 2354

Inflammatory Markers in Relation to Risk Factors for Cardiovascular Disease in the Pre-Symptomatic Phase of Rheumatoid Arthritis

Heidi Kokkonen1, Linda Johansson2, Hans Stenlund3 and Solbritt Rantapaa-Dahlqvist4, 1Public Health and Clinical Medicine/ Rheumatology, Umeå University, Umeå, Sweden, 2Public Health and Clinical Medicine/Rheumatology, Umeå University, Umeå, Sweden, 32Department of Public Health and Clinical Medicine, Epidemiology and Global
SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Individuals who later developed rheumatoid arthritis (RA) have increased levels and frequencies of risk factors for cardiovascular disease (CVD), years before onset of RA.

The relationships between CVD risk factors and inflammatory markers, i.e., cytokines and chemokines, were analysed in individuals prior to onset of symptoms and compared with controls.

Methods:

A case-control study was based on population surveys from The Västerbotten Intervention Programme (VIP) and the WHO Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) with data collected on socioeconomic and lifestyle factors, BMI, waist, blood pressure, and blood samples by a nurse. The register of patients with RA (ARA criteria) was co-analysed with the registers from the Medical Biobank and 469 pre-symptomatic individuals (median age 50.2 years; 67.8% women, median predating time 5.0 (IQR; 2.0-8.0) years), and 234 controls (median age 50.3 years; 67.1% women) were identified. CVD risk factors were defined as: hypertension (treatment or systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg), elevated ApoB/ApoA1 ratio (women ≥0.7, men ≥0.8, including lipid lowering treatment), BMI ≥25kg/m², diabetes, and ever being smoker. Concentrations of eotaxin, interferon gamma-induced protein (IP-10), monocyt-chemoattractant protein 1 (MCP1), macrophage derived chemokine (MDC), interleukin (IL) 2, IL-4, IL-6, IL-8, and IL-10, were analysed in plasma using R&D systems’ assays (Minneapolis, MN) according to the manufacturer’s instructions.

Results: Pre-symptomatic individuals had significantly higher levels of IL-6 compared with controls, both in women and men. IL-10 was significantly higher in pre-symptomatic men compared with controls. Cytokines/chemokines were significantly associated with the CVD risk factors in the cases e.g. IL-6 with each of the risk factors, eotaxin with smoking, IP-10 with increased BMI, being diabetes or having hypertension, whilst MDC was associated significantly with smoking and BMI≥25 kg/m². After adjustments for sex and age only eotaxin concentrations were significantly associated with being ever smoker. In women, MDC was significantly associated with smoking, BMI≥25 kg/m² and diabetes. Having the combination of several CVD risk factors was associated with significantly higher concentrations of MCP-1, MDC, and IL-6 in pre-symptomatic women. IL-6 increased further the relative risk in combinations with all CVD risk factors for the pre-symptomatic cases compared with controls.

Conclusion:

Increased concentrations of cytokines/chemokines were associated with CVD risk factors to a higher extent among the pre-symptomatic RA cases compared with controls. The pattern of association varied between the risk factors and the sex of the cases.

Disclosure: H. Kokkonen, None; L. Johansson, None; H. Stenlund, None; S. Rantapaa-Dahlqvist, None.
Arterial Wave Reflection and Subclinical Atherosclerosis in Rheumatoid Arthritis

Sule Gunter¹, Chanel Robinson¹, Angela Woodiwiss¹, Gavin Norton¹, Hon-Chun Hsu¹, Ahmed Solomon², Linda Tsang³, Aletta Millen¹ and Patrick Dessein⁴, ¹Physiology, University of Witwatersrand, Johannesburg, South Africa, ²Rheumatology, University of Witwatersrand, Johannesburg, South Africa, ³Rheumatology, Universitair Ziekenhuis Brussel, Brussels, Belgium, ⁴Rheumatology, Vrije Universiteit Brussel and Universitair Ziekenhuis Brussel, Brussels, Belgium

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Rheumatoid arthritis (RA) increases atherosclerotic cardiovascular disease risk. Wave reflection occurs at arterial branching points, which are particularly prone to atherosclerosis. We hypothesised that wave reflection as assessed in separation analysis, represents atherosclerosis in RA.

Methods: Confounder adjusted associations of SphygmoCor determined arterial stiffness (pulse wave velocity), wave reflection (augmentation index, reflected wave pressure and reflection magnitude) and pressure pulsatility (central systolic blood pressure, central pulse pressure, peripheral pulse pressure, pulse pressure amplification and forward wave pressure) with carotid plaque and intima-media thickness (c-IMT) on ultrasound were assessed in 163 RA patients (110 white, 31 Asian, 17 black and 5 of mixed ancestry) without cardiovascular disease. As age, sex, race, heart rate, body height, body weight and brachial mean blood pressure are established potential confounders in the present context, these characteristics were entered into each of the initial multivariable models (Table). Subsequently, other baseline characteristics that had bivariate associations with the arterial function variables were additionally entered as potential confounders in fully adjusted models on atherosclerosis (Table).

Results: One SD increase in reflected wave pressure (OR (95% CI) = 2.54 (1.41-4.44), p = 0.001), reflection magnitude (OR (95% CI) = 1.84 (1.17-2.89), p = 0.008), central pulse pressure (OR (95% CI) = 1.89 (1.12-3.22), p = 0.02) and peripheral pulse pressure (OR (95% CI) = 2.09 (1.23-3.57), p = 0.007) were independently associated with plaque (Table). The association of wave reflection with plaque was further independent of arterial stiffness and pressure pulsatility, and was present in both hypertensive and normotensive RA patients. In receiver operator characteristic curve analysis (Figure), the optimal cutoff value for reflected wave pressure in predicting plaque presence was 25 mm Hg with a sensitivity, specificity, positive predictive value and negative predictive value of 45.2%, 89.3%, 78.6% and 66.2%, respectively; a high reflected wave pressure increased the odds ratio for plaque 6.3 and 13.7 fold in univariate and adjusted analysis, respectively. Central systolic blood pressure (partial r = 0.161, p = 0.05) was independently related to c-IMT.

Conclusion: Increased wave reflection is associated with high risk atherosclerosis in RA. Consideration and therapeutic targeting of wave reflection may improve cardiovascular disease prevention in RA.
Figure: Receiver operator characteristic curve showing the accuracy of reflected wave pressure in predicting plaque presence among 163 patients with RA.

AUC (95% CI) = 0.658 p = 0.001

Table: Relationships of arterial function measures with C-MT and plaque in 163 RA patients

<table>
<thead>
<tr>
<th>Metric</th>
<th>Univariate Model</th>
<th>Known confounder adjusted model</th>
<th>Reflected wave adjusted model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>p</td>
<td>r</td>
</tr>
<tr>
<td>PWV</td>
<td>0.777</td>
<td>0.001</td>
<td>-0.051</td>
</tr>
<tr>
<td>AI</td>
<td>0.657</td>
<td>0.008</td>
<td>0.026</td>
</tr>
<tr>
<td>FFM</td>
<td>0.726</td>
<td>0.001</td>
<td>0.120</td>
</tr>
<tr>
<td>CBF</td>
<td>0.103</td>
<td>0.522</td>
<td>0.159</td>
</tr>
<tr>
<td>CPP</td>
<td>0.313</td>
<td>0.001</td>
<td>0.329</td>
</tr>
<tr>
<td>FPA</td>
<td>0.161</td>
<td>0.46</td>
<td>0.043</td>
</tr>
</tbody>
</table>

Disclosure: S. Gunter, None; C. Robinson, None; A. Woodiwiss, None; G. Norton, None; H. C. Hsu, None; A. Solomon, None; L. Tsang, None; A. Millen, None; P. Dessein, None.


Abstract Number: 2356

Disease Severity Impacts the Relationships of Apelin Concentrations with Arterial Function in Patients with Rheumatoid Arthritis
Patients with (RA) experience impaired inflammation induced arterial and endothelial function. Apelin can improve arterial function by enhancing the expression of endothelial nitric oxide synthase but this effect is dependent on endothelial integrity. We examined the potential effects of apelin on arterial function in RA.

Methods: Associations of apelin concentrations with SphygmoCor determined arterial stiffness (pulse wave velocity, wave reflection (augmentation index, reflected wave pressure and reflection magnitude) and pressure pulsatility (central systolic blood pressure (CSBP), central pulse pressure (CPP), peripheral pulse pressure (PPP), pulse pressure amplification (PPA) and forward wave pressure (FWP)) were identified in comprehensively adjusted multivariate regression models among 170 RA patients (112 white; 32 Asian; 22 black and 4 of mixed ancestry) without cardiovascular disease. Left ventricular stroke volume and ejection fraction were determined by echocardiography.

Results: Apelin concentrations were not independently associated with arterial function measures (p>=0.15) in all patients. Joint deformity counts impacted the apelin-CSBP, apelin-CPP, apelin-PPamp and apelin-FWP relations (interaction p = 0.004, 0.01, 0.01 and < 0.01, respectively); the Disease Activity Score in 28 joints (DAS28) and erythrocyte sedimentation rate (ESR) influenced the apelin-CSBP association (interaction p = 0.04 and 0.05, respectively). In stratified analysis, apelin was associated with CSBP (partial r=-0.33, p=0.01), CPP (partial r=-0.26, p=0.04), PPamp (partial r=-0.27, p=0.03) and FWP (partial r=-0.33, p=0.01) in patients without but not with joint deformities; apelin was related to CSBP (partial r=-0.24, p=0.05) in those with a DAS28 joint<2.8 (median value) (partial r=-0.24, p=0.05) but not >=2.8, and to CSBP (partial r=-0.30, p=0.01), CPP (partial r=-0.25, p=0.03), PPamp (partial r=-0.26, p=0.02) and FWP (partial r=-0.23, p=0.04) in those with an erythrocyte sedimentation rate<18 mm/hr (median value) but not >=18 mm/hr. Apelin concentrations were not related to left ventricular stroke volume and ejection fraction, and upon additional adjustment for systolic function, the relationships of apelin concentrations with pressure pulsatility were unaltered.

Conclusion: Apelin is associated with reduced pressure pulsatility in RA patients without but not with a high inflammatory burden. Apelin can additionally improve systolic function through enhancing myofilament sensitivity to intracellular calcium whereas pressure pulsatility is mediated by not only arterial properties but also the episodic nature of cardiac contractility. The apelin-pressure pulsatility relations were independent of systolic function in this study. A loss of apelin protective effects on arterial function may contribute to the link between heightened cardiovascular risk and RA severity.
Retinal Vessel Morphological Associations with Systemic Inflammation and Subclinical Atherosclerosis in Patients with Rheumatoid Arthritis

Panagiota Anyfanti\textsuperscript{1}, Areti Triantafyllou\textsuperscript{1}, Eugenia Gkaliagkousi\textsuperscript{1}, Xenophon Zabulis\textsuperscript{2}, Stella Douma\textsuperscript{1} and Spyros Aslanidis\textsuperscript{3}, \textsuperscript{1}3rd Department of Internal Medicine, Papageorgiou Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece, Thessaloniki, Greece, \textsuperscript{2}Institute of Computer Science, Foundation for Research and Technology-Hellas (FORTH), Heraklion, Greece, Heraklion, Greece, \textsuperscript{3}Rheumatology Department-2nd Propedeutic Department of Internal Medicine, Hippokration Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece, Thessaloniki, Greece

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Rheumatoid arthritis (RA) is associated with a chronic inflammatory state, accelerated atherosclerosis and excess cardiovascular risk. Quantification of morphological changes in the retinal microvasculature has emerged as a novel biomarker for cardiovascular health\textsuperscript{1}. These include narrower retinal arterioles, wider venules and a decrease in their ratio (retinal arteriovenous ratio, AVR), which represents an important parameter as it is widely used, can be objectively measured, and adjusts for both arterioles and venules. The present study examines retinal AVR for the first time in patients with RA, particularly in regard with systemic inflammation and subclinical atherosclerosis.

Methods:

Consecutive RA patients and age-, gender- and blood pressure-matched volunteers underwent nonmydriatic digital fundus photography with a NIDEK AFC-230/210 camera. Images were processed using a validated computerized semi-automated system, which measures vessel width in arterioles and venules, to obtain central retinal arteriolar equivalent (CRAE) and central retinal venular equivalent (CRVE), respectively, as well as their ratio (AVR)\textsuperscript{2}. Carotid ultrasound (Aloka Prosound A7) was used to assess subclinical atherosclerosis by measurement of carotid intima-media thickness (cIMT) in each common carotid artery.

Results:

A total of 129 individuals, 87 RA patients and 42 controls, with a mean age of 58.8±10.9 years, were studied. Patients exhibited narrower retinal arteriolar caliber (78.8±8.9 vs 93.9±8.0 μm, p<0.001), whereas retinal venular caliber did not differ compared to controls (115.0±14.8 vs 112.7±11.9 μm, p=0.381); accordingly, AVR was significantly decreased in RA patients (0.69±0.09 vs 0.84±0.09, p<0.001). Subclinical atherosclerosis was more pronounced in RA patients, who presented increased cIMT compared to controls [0.67 (0.60 – 0.77) vs 0.59 (0.55 – 0.67) mm, p=0.006]. In the univariate analysis, AVR inversely correlated with both C-reactive protein (CRP) (r=-0.449, p<0.001) and cIMT (r=-0.232, p=0.035) in the RA group. On the contrary, disease duration and activity appeared to have no effect on AVR in patients with RA. In the linear regression analysis accounting for age, sex, and hypertension, the association between AVR and cIMT was no longer significant (p=0.453), whereas CRP was identified as an independent prognostic factor of AVR (p=0.045).

Conclusion:

Quantitative evaluation of the retinal vessel morphology in our study revealed that patients with RA exhibit lower AVR compared to controls, mainly as a result of narrower arterioles. The heightened inflammatory state in these patients appears to be the biological link for the observed association between AVR and subclinical atherosclerosis.
Chest Pain and Angina Pectoris in Rheumatoid Arthritis: Frequency and Prediction of Cardiovascular Mortality

Jose Felix Restrepo¹, Inmaculada del Rincon¹, Carlos Lorenzo¹, Daniel Battafarano² and Agustin Escalante¹, ¹Internal Medicine-Rheumatology, University of Texas Health Science Center at San Antonio, San Antonio, TX, ²Rheumatology, San Antonio Military Medical Center (SAMMC), San Antonio, TX

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Despite increased cardiovascular (CV) risk in rheumatoid arthritis (RA), chest pain and angina have received little attention among RA patients. We examined the frequency of chest pain and angina, and their ability to predict CV mortality in an RA cohort, compared to controls from the general population.

Methods:
We recruited consecutive RA patients from public and private rheumatology practices. All patients underwent a comprehensive clinical and psychosocial assessment, and were followed prospectively over time until they died, or were lost to follow-up. Population-based controls were sampled from census tracks and recruited in their homes and followed prospectively as well. Patients and controls were interviewed by certified personnel for the presence of chest pain and angina pectoris using the Rose angina questionnaire, a standardized instrument designed for assessing the presence of angina pectoris in epidemiological studies. We ascertained deaths from family members, physician or hospital records, obituaries or public databases. We obtained certificates for all deaths. Deaths were attributed to CV causes using established criteria.

We used logistic regression to compare the baseline frequency of chest pain and angina between RA and controls, adjusting for age and sex. We used Cox proportional hazard models to examine the age- and sex-adjusted association of chest pain and angina with CV mortality in cases and controls.
Results:

We studied 1211 RA patients, of whom 906 were women (75%) and 5158 controls, of whom 2937 were women (56%). The mean follow-up time was 8745 person-years for RA cohort and 73,403 person-years for the control group. During this time there were 278 deaths in RA cohort, for a mortality rate 1.3 per 100 person-years, and 547 in the controls, for a mortality rate of 0.3 per 100 person-years.

Chest pain was more frequent in RA than in controls, with an age-sex adjusted frequency of 47% vs 31%, p < 0.0001, as was angina, age- and sex-adjusted frequencies of 11.7% vs 4.2%, p < 0.001, (Figure). Chest pain was a significant predictor of CV mortality in the RA patients (age-sex adjusted) HR 1.65, (95% CI 1.13-2.39), but not in the controls, adjusted HR 1.09 (95% CI 0.85, 1.41). Angina predicted CV mortality in both cohorts, adjusted HR 1.84(95% CI 1.0, 3.36) for RA and adjusted HR 1.77 (95% CI 1.15-2.72) for controls.

Conclusion:

These findings suggest that chest pain and angina are more frequent in RA than in controls, and that these symptoms are significant predictors of CV mortality. Clinicians should be aware that RA patients experiencing chest pain may be at high risk of death from CV causes.

Disclosure: J. F. Restrepo, None; I. del Rincon, None; C. Lorenzo, None; D. Battafarano, None; A. Escalante, None.


Abstract Number: 2359

Severity of Ischemic and Hemorrhagic Stroke in Patients with Rheumatoid Arthritis Compared with the General Population

Mei-Yun Hsieh¹, Chang-Fu Kuo², Kuang-Hui Yu², Shue-Fen Luo²,³ and Yen-Fu Chen², ¹Center for Big Data Analytics and Statistics, Chang Gung Memorial Hospital, Taoyuan, Taiwan, ²Division of Rheumatology, Allergy and Immunology, Chang Gung Memorial Hospital, Taoyuan, Taiwan, ³Chang Gung Memorial Hospital, Taoyuan, Taiwan
Rheumatoid arthritis (RA) patients are at higher risk of developing stroke but whether their risks for severe strokes are unknown.

Methods:
All patients with a diagnosis of RA who were registered in The National Health Insurance Research Database (NHIRD) of Taiwan from 1999 through 2005 were identified (N=23,820), and each patient was matched with one controls by age and gender. All those hospitalized for a first Ischemic stroke or hemorrhagic stroke were identified between the date of diagnosis of RA and December 31, 2015 or death. We used a claims-based stroke severity index (SSI) in patients with stroke to evaluate the risk in different severity (severe form: SSI > 12). Hazard ratios (HRs) and 95% confidence intervals (95% CI) were estimated using Cox proportional hazard regression models after adjusting for age, sex, Charlson comorbidity index (CCI) and co-medication.

Results:
We observed 1179 (4.95%) ischemic strokes and 14 (3.42%) hemorrhagic strokes in RA patients, compared to 1166 (4.90%) and 659 (2.77%) in the matched controls. The crude incidence rates (95% CI) of ischemic strokes and hemorrhagic strokes per 100 person years among 23,820 RA patients were 6.0 (5.6-6.3) and 4.1(3.9-4.4), respectively, compared to 5.85 (5.53-6.20) and 3.25(3.01-3.50) in matched controls. Multivariate HR (95% CI) were 1.09 (0.98-1.22) for ischemic stroke and 1.38(1.21-1.58) for hemorrhagic stroke. The HR (95% CI) was 1.05(0.93-1.19) for mild Ischemic stroke, 1.21 (0.98-1.49) for severe ischemic stroke, 1.25 (1.04-1.50) for mild Hemorrhagic stroke and 1.53 (1.26-1.86) for severe hemorrhagic stroke.

Conclusion:
RA patients have higher risks for severe strokes, particularly for hemorrhagic form.

Disclosure: M. Y. Hsieh, None; C. F. Kuo, None; K. H. Yu, None; S. F. Luo, None; Y. F. Chen, None.


Abstract Number: 2360

A Correlation Study between Expanded Cardiovascular Risk Prediction Score for Rheumatoid Arthritis and Nailfold Videocapillaroscopy

Tania Adriana Luna-Zúñiga1, Marco Ulises Martínez-Martínez2, Enrique Cuevas-Orta1, Georgina Martínez-Flores1, Georgina Aguilera Barragán-Pickens1, Angel Javier Pedro Martínez1, Dolores Ramos-Bello3, Homero López-Ferretis1, David Herrera Van Oostdam4 and Carlos Abud-Mendoza5, 1Unidad Regional de Reumatología y Osteoporosis Hospital Central "Dr. Ignacio Morones Prieto" y Facultad de Medicina de la UASLP, San Luis Potosí, Mexico, 2Unidad de Investigaciones Reumatológicas, Faculty of Medicine, Universidad Autónoma de San Luis Potosí and Hospital Central,
SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The most common cause of mortality in RA patients is the cardiovascular disease (CVD), with almost twice the risk for CVD events. Nailfold videocapillaroscopy (NVC) has emerged as an important tool for predicting severe organic disease in several rheumatic diseases. Although a correlation between NVC findings and CVD stratification risk has been poorly explored, NVC may be used as an early predictor for CVD risk. Our objective in this study was to evaluate the correlation between Expanded Cardiovascular Risk Prediction Score for Rheumatoid Arthritis (ESR-RA) scale and NVC morphological data.

Methods: This was cross-sectional study conducted in a single center; patients with RA according to the 2010 ACR/EULAR classification criteria were recruited. NVC was performed according to a standard method with a videocapillaroscope equipped with image analysis software (DinoCapture2.0). The following parameters were obtained: 1) demographic characteristics, 2) degree of enlarged capillaries, giant capillaries, tortuous capillaries, capillary density, disorganization of vascular array, meandering capillaries, ecstatic capillaries and ramified capillaries assessed by a semi-quantitative method 3) ESR-RA scale using the 10 years ERS-RA Risk Score Calculator for CVD risk. Correlation among individual capillaroscopy parameters with ESR-RA and RA disease duration was performed by Spearman’s rank correlation test.

Results: A total of 104 patients were analyzed (85.4% female; age 49.8±11.83 years). The mean disease duration was 7.4±6.67 years. Raynaud’s phenomenon was observed in 14.6%. The median ESR-RA score was 7.99% (IQR 1-54). A highest ESR-RA score correlated significantly with meandering capillaries (Rho 0.2459; p=0.012), disorganization of vascular array (Rho 0.1961; p=0.047), meandering capillaries (Rho 0.2844; p=0.0036), ecstatic capillaries (Rho 0.2192; p=0.027), disorganization of vascular array (Rho 0.3655; p<0.001) and tortuous capillaries (Rho 0.1935; p=0.05).

Conclusion: In this study, a correlation between the ESR-RA scale, longer disease duration and different capillaroscopic findings was demonstrated in patients with RA. Our findings suggest that capillaroscopy can be considered as a transcendent tool of the evaluation in patients with RA.

Disclosure: T. A. Luna-Zúñiga, None; M. U. Martínez-Martínez, None; E. Cuevas-Orta, None; G. Martínez-Flores, None; G. Aguilera Barragán-Pickens, None; A. J. Pedro Martínez, None; D. Ramos-Bello, None; H. López-Ferretis, None; D. Herrera Van Oostdam, None; C. Abud-Mendoza, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/a-correlation-study-between-expanded-cardiovascular-risk-prediction-score-for-rheumatoid-arthritis-and-nailfold-videocapillaroscopy

Abstract Number: 2361

Associated Factors of Hypertension and Hyperglycemia Related to Steroid Pulse in Autoimmune Diseases
Eduardo Saul Acevedo-Castañeda¹, Marco Ulises Martinez-Martinez², David Herrera Van Oostdam³, Carlos Abud-Mendoza⁴, Homero López-Ferretis⁵, Angel Javier Pedro Martínez⁵, Dolores Ramos-Bello⁶, Tania Adriana Luna-Zuñiga⁵, Georgina Aguilera Barragán-Pickens⁵ and Georgina Martínez-Flores⁵, ¹Medicina Interna, Unidad Regional de Reumatología y Osteoporosis Hospital Central "Dr. Ignacio Morones Prieto" y Facultad de Medicina de la UASLP, San Luis Potosi, Mexico, ²Unidad de Investigaciones Reumatológicas, Faculty of Medicine, Universidad Autónoma de San Luis Potosi and Hospital Central, San Luis Potosi, Mexico, ³Unidad de Investigaciones Reumatológicas, Hospital Central & Facultad de Medicina, Universidad Autónoma de San Luis Potosi, San Luis Potosi, Mexico, ⁴Unidad de Investigaciones Reumatológicas y Osteoporosis, Faculty of Medicine, Universidad Autónoma de San Luis Potosi and Hospital Central, San Luis Potosi, Mexico, ⁵Unidad Regional de Reumatologia y Osteoporosis Hospital Central "Dr. Ignacio Morones Prieto" y Facultad de Medicina de la UASLP, San Luis Potosi, Mexico, ⁶Reumatología, Unidad Regional de Reumatologia y Osteoporosis Hospital Central "Dr. Ignacio Morones Prieto" y Facultad de Medicina de la UASLP, San Luis Potosi, Mexico

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

-Background/Purpose: Steroid pulses are widely used in treatment for multiple inflammatory pathologies. The prevalence of hyperglycemia is 55-98%, and hypertension 5-52.5%. (1-2); safety profile could be different according glucocorticoid used and doses. Information at this topic is limited, and the development factors unknown.

-Methods: This was a retrospective cohort study, single-hospital. Participants were patients treated with steroid pulse in the last 10 years due to autoimmune diseases. Data was obtained from medical records: demographic data, capillary glycaemia and blood pressure. Data analysis were performed with R Commander V2.3-1. A bivariate analysis was performed between patients with and without hyperglycemia or hypertension for categorical variables test X²/ exact Fisher, for continuous variables parametric/no parametric tests as corresponded. In multivariate logistic regression model to assess independent factors for uncontrolled hypertension or blood glucose, as well as mixed models.

-Results: We included 171 patients, 156 received methylprednisolone and 15 dexamethasone. Logistic Regression identified previous diabetes (p = 0.0001) and use of fractional doses (p = 0.03), were factors associated with hyperglycemia. In hypertension male patients were less likely to develop this event (OR 0.43, IC95% 0.2-0.89, p 0.02). Patients who received methylprednisolone were less likely to develop diastolic hypertension (OR 0.28, 95% 0.06-1, p 0.03).

-Conclusion: The prevalence of hyperglycemia and hypertension was 53 and 42% respectively. Single-dose pulse therapy and methylprednisolone were protective factors. Age, female, prior diabetes mellitus or hypertension and creatinine level were associated as risk factors.

**Abstract Number: 2362**

**Novel Biomarkers for the Prediction of Subclinical Coronary Artery Atherosclerosis in Patients with Rheumatoid Arthritis**

Joan Bathon¹, Jenny Van Eyk², Nick Knowlton³, Ivan Ferraz-Amaro⁴, Jon T. Giles⁵, C. Michael Stein⁶, Mary Chester M. Wasko⁷ and Michael Centola⁸, ¹Division of Rheumatology, Columbia University, College of Physicians & Surgeons, New York, NY, ²Advanced Clinical BioSystems Research Institute, Cedars-Sinai Medical Center, Los Angeles, CA, ³Department of Arthritis and Clinical Rheumatology, Oklahoma Medical Research Foundation, Oklahoma, OK, ⁴Rheumatology, Hospital Universitario de Canarias, La Laguna, Tenerife, Spain, ⁵Division of Rheumatology, Columbia University College of Physicians & Surgeons, New York, NY, ⁶Medicine, Vanderbilt
SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Cardiovascular (CV) disease risk prediction models, that were originally developed for use in the general population, have been found to have suboptimal performance in patients with rheumatoid arthritis (RA) and to underestimate CV disease risk. The purpose of this study was to identify new protein biomarkers that could be added to the classic Framingham Risk Score model to improve capacity for coronary artery calcification (CAC) prediction. Our secondary aim was to quantify the improvement in the prediction of CAC with the assessment of these circulating biomarkers.

Methods: 561 patients with RA were included in this study. CAC by computed tomography was assessed using the Agatston method. 168 soluble protein-based potential candidate CV biomarkers were selected from literature screens and bioinformatics databases. 8 biomarkers were selected after algorithm training, 4 cytokines: Osteopontin, cartilage glycoprotein-39, cystatin C, chemokine (C-C motif) ligand 18; and 3 MRM (Spectroscopy Multiple Reaction Monitoring) biomarkers: SerD1_NFGYTLR PON1_IQNILTEEPK, Clusterin_IDSLLENDR. 6 models were designed: FRS (model 1); FRS + RA related factors (model 2); FRS + cytokines (model 3); FRS + RA related factors + cytokines (model 4); FRS + cytokines + MRM (model 5); FRS + RA related factors + cytokines + MRM (model 6). Increase in calibration between models was calculated through logistic regression using model 1 as the reference. Net reclassification index (NRI) and integrated discrimination improvement (IDI) and calibration of the models were calculated. Final reliability was performed using a 5-fold cross-validation of the final model.

Results: FRS score was statistically significantly associated with AUC values for both CAC >100 (0.784 [95% confidence interval -CI- 0.743-0.824]) and CAC >300 Agatston units (0.808 [95%CI 0.762-0.854]) categories. When FRS AUC was compared with the other 5 models, a statistically significant difference was found between model #3 vs. the FRS reference model (AUC 0.823 [95% CI 0.783-0.862] vs. 0.784 [95% CI 0.743-0.824], p=0.027) in the CAC >100 Agatston units subset. However, no differences were found between the other models or within the same model in the >300 Agatston units analysis. In the RA population with CAC higher than 300 Agatston units, model #3 (0.086 [95% CI 0.016-0.157], p=0.016), and model #4 (95% CI 0.093 [0.014-0.016], p=0.025), were found to have statistically significant NRIs. All models in the CAC > 100 Agatston units analysis disclosed a significantly higher integrated discrimination improvement (IDI) value when compared to the FRS reference model. Similarly, in the CAC > 300 Agatston units model, IDI was significantly higher in model #3, model #4 and model #5 when compared to the reference FRS model. Models calibrations were found to be optimal throughout the study. Internal cross-validation of model #4 through pseudo-R-squared was found to be optimal with a value of 0.237 and 0.218, respectively, for the prediction of CAC higher than 100 and higher than 300 Agatston units.

Conclusion: The addition of novel biomarkers related to RA and CV pathophysiological pathways to traditional CV risk scores might improve its prediction capacity.

Disclosure: J. Bathon, None; J. Van Eyk, None; N. Knowlton, None; I. Ferraz-Amaro, None; J. T. Giles, None; C. M. Stein, None; M. C. M. Wasko, None; M. Centola, None.


Abstract Number: 2363
Does Galectin-3 Have Utility As a Biomarker of Subclinical Cardiovascular Disease in RA Patients Independently of RA Disease Activity?

Amanda Nussdorf1, Isabelle Amigues2 and Joan Bathon3

1Columbia University Medical Center, New York, NY, 2Division of Rheumatology, Columbia University Medical Center, New York, NY, 3Division of Rheumatology, Columbia University, College of Physicians & Surgeons, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Galectin-3 is a beta-galactoside-binding lectin and is a marker of cardiovascular disease (CVD) in the general population. However, galectin-3 level is also elevated in RA sera and synovia. Thus, its utility as a biomarker of subclinical cardiac pathology in RA patients is not established. We investigated the association between galectin-3 levels and measures of cardiac structure and function in a cohort of patients with RA and no known clinical CVD.

Methods: RA patients (n=114) without clinical CVD participated in a prospective cohort study and underwent 3D echocardiography and cardiac (18F-fluorodeoxyglucose [FDG]) positron emission-computed tomography. FDG uptake in aorta and in myocardium, measured as standardized uptake values (SUV), was available in 88 and 97 participants respectively. Linear regression models were used to explore the associations of galectin-3 levels with RA patient characteristics, left ventricular mass index (LVMI), and SUVs.

Results: A total of 114 RA patients [mean age 56 years; 80% female; 36% White, 15% non-Hispanic Black, 44% Hispanic; Median RA duration 6.9 years; 77% RF or anti-CCP positive; Median CDAI 15.8; 51% treated with only conventional DMARD, 29% treated with conventional DMARD and biologic, 10% treated with biologic only, 10% treated with no DMARD; 38% on prednisone] were analyzed. Median galectin-3 level was 8.26 ng/mL. In univariate analyses, galectin-3 levels were significantly and positively correlated with age, Hispanic ethnicity, RA duration, IL-6 level, treatment with biologic only, prednisone use, diabetes, and aortic SUVmean, but not with LVMI or myocardial SUV. In an adjusted multivariable model (Model 2a), age (β=0.0107, p=0.002) and treatment with biologic only (β=0.4790, p=0.001) remained significantly associated with galectin-3 level. In an additional model adding aortic SUVmean (n=88) (Model 2b), prednisone use (β=0.3073, p=0.000) and aortic SUVmean (β=0.2803, p=0.0004) were significantly associated with galectin-3 level.

Conclusion: Age, treatment with biologic only, prednisone use, and aortic inflammation were associated with higher galectin-3 levels in RA patients without clinical CVD disease, while LVMI and myocardial inflammation were not. Galectin-3 was not an independent marker of higher LV mass (a precursor of heart failure) in this RA cohort, but additional measures of LV structure and function will be examined.
Disclosure: A. Nussdorf, None; I. Amigues, None; J. Bathon, None.


Abstract Number: 2364

Decrease in Cardiovascular Event Excess Risk in Rheumatoid Arthritis Since 2000: A Meta- Analysis of Controlled Studies

Elisabeth Filhol\textsuperscript{1}, Charlotte Hua\textsuperscript{2}, Anaiz Nutz\textsuperscript{3}, Françoise Flaisler\textsuperscript{1}, Cédric Lukas\textsuperscript{4}, Jacques Morel\textsuperscript{5}, Bernard Combe\textsuperscript{5} and Cécile Gaujoux-Viala\textsuperscript{6}, \textsuperscript{1}Rheumatology, Nîmes University Hospital, Nîmes, France, \textsuperscript{2}Reumatology, CHU Lapeyronie and Montpellier University, Montpellier, France, \textsuperscript{3}Rheumatology, Nîmes University Hospital and Montpellier University, Nîmes, France, \textsuperscript{4}Rheumatology, CHU Lapeyronie and EA2415, Montpellier University, University of Montpellier, France, \textsuperscript{5}Rheumatology, CHU Lapeyronie and Montpellier University, Montpellier, France, \textsuperscript{6}Rheumatology, Nîmes University Hospital and EA2415 Montpellier University, Nîmes, France

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM
Background/Purpose:

Compared with the general population, patients with rheumatoid arthritis (RA) have an increased risk of cardiovascular disease or events (CE): stroke, Myocardial Infarction (MI), Congestive Heart Failure (CHF) and Cardiovascular Mortality (CVM). Systemic inflammation is the cornerstone of both RA and atherosclerosis. Over the past fifteen years, new treatment strategies such as tight control, treat to target, methotrexate optimization, biologic DMARDs use has allowed a better control of this inflammation.

Objective: The aim of this systematic review was to assess the excess risk of presenting a CE in RA patients as compared to general population, for all studies and, before and after 2000.

Methods: We systematically searched literature (via Pubmed and Cochrane library) up to March 2016 for observational studies providing data about the occurrence of a CE (among stroke, MI, CHF, CVM) in patients with RA and in a control group. A meta-analysis of the relative risk (RR) concerning patients with RA in relation to the control group was performed for each cardiovascular event and for each period (before and after 2000).

Results:

Out of 5714 screened references, 28 studies were included. There was a significant increased risk for all CEs among people with RA relative to the general population.

For studies realized before 2000, a significant increased risk of CEs was observed in RA patients:

- RR=1.32 [1.24; 1.41], p<0.00001 for MI.
- RR=1.25 [1.14; 1.32], p<0.00001 for CHF
- RR=1.21 [1.15; 1.26], p<0.00001 for CVM
- RR=1.12, [95 % CI 1.04; 1.21], p<0.002 for stroke

For all studies realized after the year 2000, the excess risk of MI was significantly reduced in comparison with the period before 2000: RR=1.18 [1.14; 1.23], p<0.00001; the increased risk was not retrieved for CHF (RR= 1.17 [0.88; 1.56], p=0.27) and CVM (RR=1.07 [0.74; 1.56], p=0.71). The excess risk of stroke was stable: RR=1.23 [1.06; 1.43], p=0.006.

Discussion: This meta-analysis confirms an increased risk of CEs among people with RA relative to the general population. It also appears that this excess risk is less prevalent than prior to 2000s. This might have two explanations: a better management of the cardiovascular risk in patients with RA and a better control of chronic systemic inflammation thanks to new therapeutic strategies.

Conclusion: The cardiovascular excess risk of RA patients relative to the general population seems to be decreased since 2000, especially for MI and CVM. This suggests that the recent improvements in RA management may have a positive impact on cardiovascular comorbidities.

Disclosure: E. Filhol, None; C. Hua, Abbvie, BMS, Pfizer, 5; A. Nutz, Roche Pharmaceuticals, 5; F. Flaisler, Roche Pharmaceuticals, 5; C. Lukas, Abbvie, BMS, Celgene, Janssen, Medac, MSD, Nordic Pharma, Novartis, Pfizer, Sanofi, Schering, Roche-Chugai, UCB, 5; J. Morel, Abbvie, BMS, Celgene, Janssen, Medac, MSD, Nordic Pharma, Novartis, Pfizer, Sanofi, Schering, Roche-Chugai, UCB, 5; B. Combe, Pfizer, UCB, 2, BMS, Janssen, Lilly, MSD, Pfizer, Roche-Chugai, UCB, 8, Abbvie, BMS, Janssen, Lilly, MSD, Novartis, Pfizer, Roche-Chugai, UCB, 5; C. Gaujoux-Viala, Abbvie, BMS, Celgene, Janssen, Medac, MSD, Nordic Pharma, Novartis, Pfizer, Sanofi, Roche-Chugai, 5.


Abstract Number: 2365
Poor Cardiovascular Risk Management in Rheumatoid Arthritis Patients Despite an Explicit Cardiovascular Risk Management Program

Maaike Heslinga1, Inge van den Oever2, E. Griep3, Hanneke Griep-Wentink3, Yvo M. Smulders4, WF Lems5, Maarten Boers6, Alexandre Voskuyl7, Mike J.L. Peters4, Dirkjan van Schaardenburg2 and Michael Nurmohamed8, 1Amsterdam Rheumatology immunology Center | Reade, Amsterdam, Netherlands, 2Amsterdam Rheumatology and immunology Center | Reade, Amsterdam, Netherlands, 3Rheumatology, Antonius Hospital, Sneek, Netherlands, 4Internal Medicine, VU University Medical Center, Amsterdam, Netherlands, 5Amsterdam Rheumatology and immunology Center | VU University Medical Center, Amsterdam, Netherlands, Amsterdam, Netherlands, 6Epidemiology & Biostatistics, VU Univ Medical Center F-wing, Amsterdam, Netherlands, 7Department of Rheumatology, Amsterdam Rheumatology and immunology Center - location VU University Medical Center, Amsterdam, The Netherlands, Amsterdam, Netherlands, 8Rheumatology, Reade, Amsterdam Rheumatology and immunology Center, Amsterdam, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
In 2011, we started a cardiovascular (CV) risk management program for rheumatoid arthritis (RA) patients visiting Reade in the Netherlands. We previously reported the presence of under treatment of hypercholesterolemia and hypertension [1].

The aim of this study was to assess the effectiveness of our CV risk management program after one year.

Methods:
CV risk screening was performed at baseline and we informed the general practitioner (GP) about the results, including advices regarding the initiation of cardio preventive drugs. In high risk patients (i.e. a 10-year CV risk score ≥20%), antihypertensives were recommended when systolic blood pressure > 140 mm/Hg and statins were recommended when low-density lipoprotein >2.5 mmol/l. The decision to start preventive medication was left to the GP. CV risk screening was repeated after one year. Patients completed a questionnaire about the actions that were taken following the results of the initial screening.

Results:
Of the 266 patients 202 (76%) were female, the mean age was 58 ±11 years. After one year, 88 out of 134 patients who received inadequate or no treatment at baseline were still untreated or undertreated. Of the 188 (71%) patients who were at high CV risk and who did have an indication to start therapy, only 7.5% was contacted by their GP and another 6.8 % arranged an appointment themselves. While the 10-year CV risk did not decrease in the group as a whole, a risk reduction was found in the patients that started medication. Remarkably, 42% of patients reported lifestyle changes, including more exercise (20%), diet adaption (16%) and weight loss (9%).

Table 1. Cardiovascular risk factors at baseline and after one year
<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV disease history</td>
<td>20 (7.5)</td>
<td>23 (8.6)</td>
</tr>
<tr>
<td>CV risk &lt;10%</td>
<td>43</td>
<td>52 (19.5)*</td>
</tr>
<tr>
<td>(16.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CV risk 10-20%</td>
<td>60</td>
<td>62 (23.3)</td>
</tr>
<tr>
<td>(22.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CV risk &gt;20%</td>
<td>143</td>
<td>129</td>
</tr>
<tr>
<td>(53.8)</td>
<td></td>
<td>(48.5)*</td>
</tr>
<tr>
<td>SBP in mm/Hg</td>
<td>135 ±17</td>
<td>135 ±18</td>
</tr>
<tr>
<td>Body Mass Index in kg/m2</td>
<td>26.4</td>
<td>26.3 ±4.8</td>
</tr>
<tr>
<td>TC in mmol/l</td>
<td>5.5 ±1.0</td>
<td>5.2 ±1.0**</td>
</tr>
<tr>
<td>Triglycerides in mmol/l</td>
<td>1.4 ±0.8</td>
<td>1.4 ±0.8</td>
</tr>
<tr>
<td>LDL-cholesterol in mmol/l</td>
<td>3.2 ±0.9</td>
<td>3.0 ±0.9**</td>
</tr>
<tr>
<td>HDL-cholesterol in mmol/l</td>
<td>1.6 ±0.5</td>
<td>1.6 ±0.5</td>
</tr>
<tr>
<td>TC/HDL-ratio</td>
<td>3.7 ±1.2</td>
<td>3.7 ±1.2**</td>
</tr>
<tr>
<td>Current smokers</td>
<td>60</td>
<td>53 (20.1)</td>
</tr>
<tr>
<td>(22.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>12 (4.5)</td>
<td>12 (4.5)</td>
</tr>
<tr>
<td>SBP &gt;140 mm/Hg</td>
<td>95</td>
<td>96 (36.2)</td>
</tr>
<tr>
<td>(35.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL &gt; 2,5 mmol/l</td>
<td>208</td>
<td>180</td>
</tr>
<tr>
<td>(78.8)</td>
<td>(68.4)**</td>
<td></td>
</tr>
<tr>
<td>TC ≥ 6.5 mmol/l</td>
<td>37</td>
<td>26 (9.8)</td>
</tr>
<tr>
<td>(13.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antihypertensives</td>
<td>81</td>
<td>88 (33.1)</td>
</tr>
<tr>
<td>(30.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statins</td>
<td>38</td>
<td>57</td>
</tr>
<tr>
<td>(14.3)</td>
<td>(21.4)**</td>
<td></td>
</tr>
</tbody>
</table>

CV=Cardiovascular, HDL=high-density lipoprotein, LDL=low-density lipoprotein, TC=total cholesterol, SBP= Systolic blood pressure. Results are presented as mean ± standard deviation or n, (%). *p<0.05  
**p<0.01

**Conclusion:**

It is striking that one year after the introduction of our CV risk management program, only 14.3% patients with an indication for preventive treatment visited their GP and only 14% started with CV risk lowering drugs. This was mainly caused by the small percentage of high risk patients that contacted their GP. On the other hand, a high percentage reported the start of healthy lifestyle. These results underscore the need for a short-term follow-up, in close collaboration with primary care providers to ensure appropriate CV risk management. This is a future implementation project that will be initiated shortly.

**References:** 1. Ann Rheum Dis 2015;74:192
High Uric Acid As a Risk Factor for Cardiovascular Diseases in Rheumatoid Arthritis Patients

Adeeba Al-Herz1, Ali Aldei1, Khulood Saleh2, Adel Al-Awadhi3, Waleed Al-Kandari2, Eman Hasan4, Aqeel Ghanem5, Mohammad Hussain4, Ibrahim Nahar5, Fatemah Abutiban6, Ahmad Alenizi6, Yaser Ali5, Hebah Alhajeri5, Sawsan Hayat5, Ahmad Khadrway2, Ammad Fazal2, Khaled Mokaddem1, Agaz Zaman5, Ghada Mazloum5, Youssef Bartella1, Sally Hamed1, Ramia Alsouk6 and Ahmed Al-Saber7, 1Rheumatology, Al-Amiri Hospital, Kuwait city, Kuwait, 2Rheumatology, Farwania Hospital, Farwania, Kuwait, 3Faculty of Medicine, Kuwait, Kuwait, 4Al-Amiri Hospital, Kuwait city, Kuwait, 5Rheumatology, Mubarak Al-Kabeer Hospital, Hawally, Kuwait, 6Rheumatology, Jahra Hospital, Jahra, Kuwait, 7Department of Mathematics, Kuwait Technical College, Kuwait city, Kuwait

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Rheumatoid arthritis (RA) patients have an increased risk of cardiovascular diseases (CVD). It is unclear whether an elevated serum uric acid (UA) further increases that risk. We study CVD and their risk factors in association with UA in RA patients.

Methods: Adult patients who satisfied the ACR classification criteria for RA from The Kuwait Registry for Rheumatic Diseases (KRRD) from four major hospitals were evaluated from February 2013 through May 2017. Patients with recorded UA were identified and CVD and their risk factors were studied in those patients. To optimize classifier number and prediction accuracy, hierarchical cluster analyses for multiple factors were performed, which indicated nine possible independent CVD risk factors. A binary logistic regression was conducted to examine their significant association with CVD and the independence of UA as a risk factor.

Results: A total of 564 RA patients with available UA were identified, 353(62.6%) females. Mean age was 50.8+11.5 years and disease duration 10.5+2.9 years.

Mean UA was 271+78µmol/L. Of those patients, 31 (5.5%) were reported to have CVD. UA was significantly correlated to the presence of CVD ($\chi^2=6.49$, $p=0.011$). Logistic regression model indicated a 10% increase of CVD with every 10 µmol/L increase in UA (table). A correlation matrix between UA and other risk factors showed a significant association between high uric acid and a younger age at RA diagnosis ($r=-0.262$), hyperlipidemia ($r=0.191$) and diabetes mellitus ($r=0.244$).
### Conclusion:

Our study suggests that UA may be an independent risk factor for CVD and is associated with the presence of other risk factors. UA should be measured and carefully approached in RA patients.

---

**Disclosure:** A. Al-Herz, None; A. Aldei, None; K. Saleh, None; A. Al-Awadhi, None; W. Al-Kandari, None; E. Hasan, None; A. Ghanem, None; M. Hussain, None; I. Nahar, None; F. Abutiban, None; A. Alenizi, None; Y. Ali, None; H. Alhajeri, None; S. Hayat, None; A. Khadrawy, None; A. Fazal, None; K. Mokaddem, None; A. Zaman, None; G. Mazloum, None; Y. Bartella, None; S. Hamed, None; R. Alsouk, None; A. Al-Saber, None.


**Abstract Number:** 2367

### The Effect of Glucocorticoids on Bone Mineral Density in Patients with Rheumatoid Arthritis: a Systematic Review and Meta-Analysis

Anne-Birgitte Blavnsfeldt¹,², Malissa Dawn Thomsen³, Simon Tarp⁴, Bente Langdahl²,⁵, Ellen-Margrethe Hauge²,⁶ and Annette de Thurah⁷,⁸,¹ Rheumatology, Aarhus University Hospital, Aarhus C, Denmark, ²Department of Clinical Medicine, Aarhus University, Aarhus C, Denmark, ³Diagnostic Centre, Silkeborg Regional Hospital, Silkeborg, Denmark, ⁴The Parker Institute, Bispebjerg & Frederiksberg Hospital, Copenhagen, Denmark, ⁵Endocrinology, Aarhus University Hospital, Aarhus, Denmark, ⁶Aarhus University Hospital, Aarhus C, Denmark, ⁷Department of Rheumatology, Aarhus University Hospital, Aarhus, DK, Aarhus, Denmark, ⁸Department of Clinical Medicine, Aarhus University, Aarhus, Denmark

**First publication:** September 18, 2017

### SESSION INFORMATION

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

The role of glucocorticoids (GCs) in the treatment of rheumatoid arthritis (RA) is widely debated. GCs stimulate bone resorption and impair bone formation. Inflammatory cytokines also stimulate bone resorption, and patients with RA have a high risk of osteoporosis (OP) and fragility fractures. However, in patients with both RA and OP, impairment of bone formation by GCs may be counter-balanced by reduced systemic inflammation and increased physical activity.

---

<table>
<thead>
<tr>
<th></th>
<th>B</th>
<th>p-value</th>
<th>Odds Ratio</th>
<th>95% C.I. Lower</th>
<th>95% C.I. Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uric acid</td>
<td>0.011</td>
<td>&lt;0.001*</td>
<td>1.011</td>
<td>1.006</td>
<td>1.016</td>
</tr>
<tr>
<td>Smoking</td>
<td>-0.535</td>
<td>0.280</td>
<td>0.586</td>
<td>0.222</td>
<td>1.546</td>
</tr>
<tr>
<td>Anti-cyclic citrullinated peptide antibodies</td>
<td>-1.017</td>
<td>0.115</td>
<td>0.362</td>
<td>0.102</td>
<td>1.280</td>
</tr>
<tr>
<td>Rheumatoid factor</td>
<td>-0.717</td>
<td>0.337</td>
<td>0.488</td>
<td>0.113</td>
<td>2.111</td>
</tr>
<tr>
<td>Age at RA diagnosis</td>
<td>-0.071**</td>
<td>&lt;0.001*</td>
<td>0.931</td>
<td>0.896</td>
<td>0.968</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>2.220</td>
<td>0.001*</td>
<td>9.210</td>
<td>2.606</td>
<td>32.548</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.824</td>
<td>0.001*</td>
<td>6.199</td>
<td>2.470</td>
<td>15.556</td>
</tr>
<tr>
<td>Male gender</td>
<td>-1.097**</td>
<td>0.020*</td>
<td>0.334</td>
<td>0.132</td>
<td>0.844</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>2.619</td>
<td>&lt;0.001*</td>
<td>13.724</td>
<td>4.665</td>
<td>40.372</td>
</tr>
</tbody>
</table>
This systematic review aims to assess the effect of oral prednisolone and prednisone on bone mineral density (BMD) in patients with RA analyzed in randomized, controlled trials (RCT).

**Methods:**
We performed a systematic literature search and identified double-blinded RCTs. Prednisolone or prednisone was the intervention. BMD was measured by dual-energy absorptiometry at baseline and at least once thereafter. Two authors independently reviewed references, extracted data and assessed risk of bias. We used Cochrane’s risk of bias tool and assessed overall quality of evidence using the GRADE methodology. Primary outcomes were mean change in BMD over time. Secondary endpoints included RA disease activity and radiographic progression.

**Results:**
We identified 7 studies. Studies were comparable regarding study population and intervention. Risk of bias was considered low for BMD outcomes. Data completeness was low in some studies. Overall quality was rated high for BMD and disease activity outcomes and low for radiographic progression. Standard mean difference (SMD) in change in BMD from 0 to 24 months was -0.02 (95%CI -0.16, 0.12) at the lumbar spine and -0.11 (95% CI -0.25, 0.02) at the hip (Figures 1 and 2). Concomitant treatment of RA differed between studies, as did osteoporosis prophylaxis. However, sensitivity analyses excluding studies where anti-OP therapy was used yielded no difference in the estimate in the lumbar spine, but a small, not clinically relevant difference in the hip.

**Conclusion:**
In this group of RCT studies we found no difference in change in BMD in patients with RA who received GCs compared to placebo. The interpretation of this is difficult as it challenges the well-established fact that GCs negatively impact BMD through low calcium uptake and altered sex hormones. However, our findings suggest that in a population where BMD is affected by systemic inflammation, the dampening of the inflammation as well as increased physical activity may outweigh the inherent negative effects on bone when GCs are administered.

Figure 1: Meta-analysis of change in BMD at the lumbar spine

Figure 2: Meta-analysis of change in BMD at the hip

**Disclosure:** A. Blavnsfeldt, None; M. D. Thomsen, None; S. Tarp, None; B. Langdahl, UCB, Amgen, Eli Lily, 8, Amgen, Novo Nordisk, 2; E. M. Hauge, Novo Nordisk, Roche, 2; A. de Thurah, None.
Abstract Number: 2368

Global Circumferential Strain By Assessed a Feature Tracking Cardiac Magnetic Resonance (CMR) Imaging Was Associated with Myocardial Fibrosis in RA Patients

Yasuyuki Kobayashi¹, Hitomi Kobayashi², Isamu Yokoe³, Atsuma Nishiwaki⁴, Akiyuki Kotoku⁵ and Masami Takei⁴,
¹Advanced Biomedical Imaging Informatics, St.Marianna University School of Medicine, Kawasaki, Japan,
²Hematology and Rheumatology, Nihon University School of Medicine, Tokyo, Japan, ³Rheumatology, Kyoundo Hospital, Sasaki Institute, Tokyo, Japan, ⁴Division of Hematology and Rheumatology, Nihon University School of Medicine, Tokyo, Japan, ⁵Advanced Biomedical Imaging Informatics, St. Marianna University School of Medicine, Kawasaki, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Individuals with RA have a 1.5-2.0 fold higher risk of developing congestive heart failure (CHF) than the general population. It is important to understand more about subclinical left ventricular (LV) dysfunction, which can be a strong predictor of clinical CHF. There is an increasing interest in using noninvasive cardiac imaging biomarkers to diagnose subclinical myocardial dysfunction. Feature tracking cardiac magnetic resonance (CMR) imaging is a novel postprocessing technique increasingly being used to assess regional myocardial function. Especially, LV global longitudinal peak systolic strain (GLS) is a prognostic indicator of adverse cardiovascular outcomes in various patient populations, and global circumferential peak systolic strain (GCS) is a predictor of CHF in the general population. We previously reported that a high prevalence of myocardial abnormalities assessed by CMR were observed in patients with RA. Our current prospective study aimed to evaluate the association of regional function with myocardial abnormalities by using feature tracking CMR imaging in patients with RA without cardiac symptoms.

Methods: Patients with RA without cardiac symptoms were enrolled. Patients with RA and control subjects with no history and/or clinical findings of systemic and pulmonary hypertension, coronary artery disease, valvular heart disease, atrial fibrillation, diabetes mellitus, and dyslipidemia underwent contrast CMR imaging. Patients with RA received conventional synthetic DMARD (csDMARD) or biologic DMARD (bDMARD). All study subjects underwent evaluation of LV regional function, as measured by feature tracking CMR imaging. The GLS and GCS were calculated by the feature tracking of cine MRI in 6 segments of the mid-slice of the left ventricle. Late gadolinium enhancement (LGE) was obtained to assess myocardial fibrosis. Group comparisons were made using the Wilcoxon rank sum test, Fisher exact test, and Steel test, as appropriate. Multivariable linear regression analyses of the correlates were performed.

Results: We evaluated 70 patients with RA (88% women; mean age, 55.2±9.0 years); 30% of them had positive LGE. The GCS in the LGE positive group decreased more than that in the LGE negative group (p=0.001). However, the GLS tended to decrease in the LGE positive group compared to the LGE negative group. The GCS was associated with the LGE positive group (p=0.05). However, RA characteristics were not associated with the GCS. The GLS tended to be associated with the LGE positive group (p=0.07). The GCS was decreased more in the csDMARD group than in the bDMARD group (p=0.04). However, there were no differences in the GLS between the csDMARD and bDMARD groups. Results of multivariable analysis showed that the GCS was independently associated with positive LGE (area under the curve 0.75).
Conclusion: This is the first study to report an association between LV regional function and myocardial abnormalities in patients with RA. LV regional dysfunction may predict the myocardial abnormalities observed in patients with RA without cardiac symptoms. Longitudinal studies are required to determine whether the GCS predicts those who will develop clinical CHF.

Disclosure: Y. Kobayashi, None; H. Kobayashi, None; I. Yokoe, None; A. Nishiwaki, None; A. Kotoku, None; M. Takei, None.


Abstract Number: 2369

Relationship of Bone Mineral Density and Inflammatory Burden with Carotid Plaque Formation in Rheumatoid Arthritis: A 5-Year Prospective Study

Na Ri Kim, Jong Wan Kang, Jung Su Eun, Ji Hun Kim, Jin Young Kang, Gi Bum Bae, Sang Jin Lee, Eon Jeong Nam and Young Mo Kang, Division of Rheumatology, Department of Internal Medicine, Kyungpook National University School of Medicine, Daegu, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic and systemic inflammatory disease. The incidence of the cardiovascular (CV) disease is significantly increased in patients with RA compared with the general population, which is related to the fact that atherosclerosis has an inflammatory etiology. We previously have shown a synergistic interaction between inflammatory burden and conventional CV risk factors in the development of carotid atherosclerosis. In this study, we investigated the association between bone mineral density (BMD) and the formation of new carotid plaque in RA patients in a Kyungpook National University Hospital Atherosclerosis Risk in Rheumatoid Arthritis (KARRA) cohort study.

Methods: After a baseline evaluation for KARRA cohort enrollment, RA patients were prospectively followed up for 5 years or until deaths. We analyzed the demographic findings, conventional CV risk factors, RA disease activity, and BMD. Carotid ultrasounds at baseline and year 5 were performed for evaluation of the intima-medial thickness (IMT) and presence and progression of carotid plaques. BMD was measured at the lumbar spine (L-spine, L1-L4), femur neck (femoral neck), and distal forearm (radius).

Results: A total of 417 RA patients were included in the baseline KARRA cohort, and 325 patients with RA were followed for the 5 year period. New carotid plaque formation was found in 90 of 212 (42.5%) patients at year 5. New development of carotid plaques at year 5 in RA patients was associated with total and LDL cholesterols, ATP risk factor number, DAS28-ESR, DAS28-CRP, ESR area under the curve (AUC) and CRP AUC at year 5. The BMD in the L-spine, femur, and radius was significantly lower in patients with new carotid plaques (n = 77), compared to patients without new plaques (n = 111) (1.07 g/cm² ± 0.16 vs. 1.01 g/cm² ± 0.19, p = 0.012 for L-spine; 0.87 g/cm² ± 0.13 vs. 0.83 g/cm² ± 0.15, p = 0.034 for femur; and 0.61 g/cm² ± 0.11 vs. 0.55 g/cm² ± 0.13, p = 0.001 for radius, respectively). Multivariate logistic regression analysis revealed that age (OR 1.12 [95% CI 1.06 - 1.18; p < 0.001]),
LDL cholesterol (OR 1.02 [95% CI 1.00 - 1.03; p = 0.016]), DAS28-ESR at year 5 (OR 1.31 [95% CI 1.09 – 1.61; p = 0.030]), 5-year ESR AUC (OR 1.05 [95% CI 1.00 - 1.70; p = 0.036]), and BMD at radius (OR 2.07 [95% CI 1.08 – 2.66, p = 0.042]) were independent risk factors for new carotid plaque formation during the 5-year followed period. Correlation coefficients were calculated to analyze the relationship between 5-year ESR AUC and BMD. L-spine BMD (RR -0.206 [p < 0.001]), femur BMD (RR -0.297 [p < 0.001]), wrist BMD (RR -0.344 [p < 0.001]), and 5-year ESR AUC all showed the good correlation.

**Conclusion:** This study implicates that carotid plaque formation measured by ultrasound is associated with BMD as well as the conventional CV risk factors and inflammatory burden in RA patients, which supports further investigation of the linking processes between juxta-articular bone health and carotid atherosclerosis.

**Disclosure:** N. R. Kim, None; J. W. Kang, None; J. S. Eun, None; J. H. Kim, None; J. Y. Kang, None; G. B. Bae, None; S. J. Lee, None; E. J. Nam, None; Y. M. Kang, None.


**Abstract Number:** 2370

### Endothelial Nitric Oxide Synthase Gene Polymorphism As a Risk Factor of Hypertension in Patients with Rheumatoid Arthritis

Mykola Stanislavchuk¹,², Kateryna Zaichko² and Ayad Sulaiman², ¹Internal Medicine, VNMU n.a. M. Pirogov, Vinnytsia, Ukraine, ²Rheumatology, Vinnytsia Regional Clinical Hospital, Vinnytsia, Ukraine

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Rheumatoid arthritis (RA) and hypertension (HT) are multifactorial polygenic diseases. The incidence of hypertension in patients with RA is higher than in the general population, ranging from 20 to 60%. The role of genetic polymorphisms in the development of this comorbidity is investigated, but there is little information on the subject. So, potentially promising is the study of the prognostic value of gene promoter polymorphism of endothelial nitric oxide synthase NOS3 T-786C (rs2070744) in patients with RA. Additionally NOS3 plays an important role in the regulation of vascular tone, angiogenesis, osteogenesis, inflammation. The aim of the study was to investigate the prevalence of NOS3 T-786C (rs2070744) gene promoter polymorphism in patients with RA and RA associated with hypertension.

**Methods:** The study involved 148 patients with RA (100% women) aged 47.0 [42.8; 52.0] years, disease duration 78 [48; 120] months, moderate and high disease activity (DAS28> 3.2). The diagnosis of RA was established by ACR/EULAR (2010) criteria. Polymorphism of NOS3 T786C gene (rs2070744) was performed by PCR (Real-Time PCR, Bio-Rad iCycler IQ5) using a set of «SNP-express» (NPF "Lyteh", Russia). All studied polymorphism satisfied Hardy-Weinberg equilibrium ($\chi^2$ test, p> 0.05). The study was conducted in accordance with the Declaration of Helsinki of the World Medical Association "Ethical principles of medical research involving human subjects" (2000), the requirements of GCP, the applicable national legislation. Statistical analysis of the results was performed by methods of variation statistics in the application package SPSS22 (© SPSS Inc.).

**Results:** Among the patients with RA normotensive were 83 (56.1%) and 65 (43.9%) patients were hypertensive. In 44 (29.7%) patients with RA hypertension was registered after the onset of RA. In patients without hypertension (n = 83),
the frequency of genotypes was as follows: T/T - 43.3% (36 pts) T/C - 44.6% (37 pts), C/C - 12% (10 pts). In RA patients with hypertension (n = 65), the frequency of genotype C/C was significantly higher – 30.8% (20 pts); χ² = 8.44, p <0.01), and the frequency of genotype TT was conversely lower - 29.8%, than in RA patients without hypertension. Analysis of the common and recessive inheritance patterns showed that patients with RA, carriers of CC genotype, have 3 times higher risk of developing hypertension (OR = 3.24; 95% CI 1.39-7.55) compared to T/T and T/C genotype carriers. Analysis of the dominant inheritance model showed that patients with RA, presence of T/T genotype was characterized by tendency (χ² = 3.12; p = 0.08) to decrease the risk of hypertension compared to T/C and C/C genotype (OR = 0.54, 95% CI 0.27-1.07).

Conclusion: The association of T786C NOS3 (rs2070744) gene promoter polymorphism with the development of hypertension in patients with rheumatoid arthritis in the Ukrainian population was established. In RA patients the presence of genotype C/C increased risk of hypertension.

Disclosure: M. Stanislavchuk, None; K. Zaichko, None; A. Sulaiman, None.


Abstract Number: 2371

The Efficacy of Tofacitinib in Patients with Rheumatoid Arthritis Stratified By Baseline Body Mass Index

Ara Dikranian1, Miguel Angel Gonzalez-Gay2, Frank Wellborne3, Jose Maria Alvaro-Gracia4, Liza Takiya5, Lori Stocker5, Douglass Chapman6, Svitlana Tatulych7, Palle Dahl8 and Jeffrey R. Curtis9, 1Cabrillo Center for Rheumatic Disease, San Diego, CA, 2Hospital Universitario Marquês de Valdecilla, IDIVAL, Santander, Spain, 3Houston Institute for Clinical Research, Houston, TX, 4Hospital Universitario de La Princesa, IIS Princesa, Madrid, Spain, 5Pfizer Inc, Collegeville, PA, 6Pfizer Inc, New York, NY, 7Pfizer Inc, Groton, CT, 8Pfizer Inc, Ballerup, Denmark, 9University of Alabama at Birmingham, Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). This post-hoc analysis aims to explore the efficacy of tofacitinib in patients (pts) with RA based on their baseline (BL) body mass index (BMI).

Methods: Data were analyzed from Phase 3 studies for pts who were methotrexate-naïve (NCT01039688) or had an inadequate response to DMARDs (NCT00960440, NCT00847613, NCT00814307, NCT00856544, NCT00853385) who received ≥1 dose of tofacitinib 5 or 10 mg twice daily (BID) or placebo (PBO). Pts were stratified by BL BMI (<25, 25 to <30, ≥30). Efficacy endpoints (American College of Rheumatology [ACR]20/50/70 response rates at Month [M] 6; changes from baseline (Δ) in Health Assessment Questionnaire - Disability Index [HAQ-DI], Disease Activity Score in 28 joints by Erythrocyte Sedimentation Rate [DAS28-4(ESR)], and Clinical Disease Activity Index [CDAI] at M3 and M6) were assessed.

Results: Overall, 1589, 1611, and 681 pts received tofacitinib 5 and 10 mg BID and PBO, respectively, with 1690, 1173, and 1017 pts in the BMI <25, 25 to <30, and ≥30 categories, respectively. BL demographics were generally
similar between BMI categories with the exception of higher rates of diabetes (12.9–14.2 vs 3.5–9.8%), hypertension (53.2–58.9 vs 22.0–39.8%), and use of prior TNFi (23.7–46.8 vs 15.0–26.9%), and numerically higher tender (28.8–29.9 vs 23.5–26.9) and swollen joint counts (16.5–17.1 vs 14.5–16.3) and HAQ-DI scores (1.6 vs 1.4–1.5) in the BMI ≥30 group vs BMI <25 or 25 to <30. In general, ACR response rates were significantly higher (p<0.05) in the tofacitinib vs PBO groups, regardless of BMI category (Figure 1). There appeared to be a trend towards lower ACR20/50/70 response rates with increasing BMI at M6 in tofacitinib- and PBO-treated pts; however, confidence intervals (CI) overlap. A trend for smaller ΔHAQ-DI through M6 with increasing BMI was observed only in pts receiving tofacitinib 5 mg BID, with overlapping CI (Figure 2A). The ΔDAS28-4(ESR) and ΔCDAI scores were similar for tofacitinib- and PBO-treated pts regardless of BL BMI (Figure 2B–C). Generally similar trends were observed when stratified by weight.

**Conclusion:** Results of this post-hoc analysis suggest that tofacitinib is associated with improvements in RA outcomes compared with PBO regardless of BL BMI category. In both tofacitinib and PBO groups, similar trends in improvements were seen in most endpoints regardless of BMI category, implying that the effect of BL BMI is not specific to tofacitinib. Further investigation is needed to assess the degree of impact of BMI on tofacitinib efficacy.
Figure 1. ACR20/50/70 response rates at Month 6 for each treatment group stratified by BMI category (FAS, NRI)

A) ACR20 response rates

B) ACR50 response rates

C) ACR70 response rates

* p<0.05; ** p<0.01; *** p<0.0001 vs placebo
ACR, American College of Rheumatology; BID, twice daily; BMI, body mass index; CI, confidence interval; FAS, full analysis set; NRI, non-responder imputation
Disclosure: A. Dikranian, AbbVie, Mallinckrodt, Pfizer Inc, 5; AbbVie, Amgen, Celgene, Mallinckrodt, Pfizer Inc, 8; M. A. Gonzalez-Gay, Pfizer Inc, 5; F. Wellborne, AbbVie, Bristol-Myers Squibb, Eli Lilly, Genzyme, Pfizer Inc, Regnorn, Sanofi, 2; AbbVie, Bristol-Myers Squibb, Genzyme, Novartis, Pfizer Inc, Regnorn, Sanofi, 5; AbbVie, Bristol-Myers Squibb, Eli Lilly, Genzyme, Novartis, Pfizer Inc, Regnorn, Sanofi, 8; J. M. Alvaro-Gracia, None; L. Takiya, Pfizer Inc, 1, Pfizer Inc, 3; L. Stockert, Pfizer Inc, 1, Pfizer Inc, 3; D. Chapman, Pfizer Inc, 1, Pfizer Inc, 3; S. Tatulych, Pfizer Inc, 1, Pfizer Inc, 3; P. Dahl, Pfizer Inc, 1, Pfizer Inc, 3; J. R. Curtis, Amgen, Corrona, Crescendo Bio, Pfizer Inc, 2, AbbVie, Amgen, Bristol-Myers Squibb, Corrona, Eli Lilly, Janssen, Myriad, Pfizer Inc, Roche/Genentech, UCB, 5.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-efficacy-of-tofacitinib-in-patients-with-rheumatoid-arthritis-stratified-by-baseline-body-mass-index

Abstract Number: 2372

Obesity and the Impact on Treat to Target Goals and Functional Ability in RA. Results from Two Multi-Centre UK Inception Cohorts

Elena Nikiphorou1, Sam Norton2, Patrick Kiely3 and Adam Young4, 1Academic Rheumatology Department, King's College London, London, United Kingdom, 2Academic Rheumatology, King’s College London, London, United Kingdom, 3St George's Hospital, London, United Kingdom, 4University of Hertfordshire, Hertford, United Kingdom

First publication: September 18, 2017
Background/Purpose: The links between inflammation, obesity and joint dysfunction are well established. How these translate into clinical disease activity and functional disability in rheumatoid arthritis (RA) though, remains to be defined. This study explores associations between BMI and 1. The achievement of disease remission or low disease activity and 2. Functional ability, in RA.

Methods: Data from two consecutive UK multi-centre RA inception cohorts with similar design were used: the Early RA Study (ERAS) and Early RA Network (ERAN). Recruitment figures/median follow up for ERAS and ERAN were 1465/10 years (maximum 25 years), and 1236/6 years (maximum 10 years) respectively. Standard demographic and clinical variables were recorded at baseline and then annually until loss to follow-up or the end of study follow up. Multivariable logistic regression analysis was used with remission (R-DAS)/low disease activity status (L-DAS) and health assessment questionnaire (HAQ, <1 vs ≥1) as dependent categorical variables in models adjusted for patient, disease-related clinical variables and recruitment year. BMI was examined in separate models as both a continuous and categorical predictor variable according to WHO definitions.

Results: Baseline BMI data from 2420 patients (90%) indicated that 37.2% were overweight, 21.3% obese. Mean BMI at baseline was 25.5 in ERAS and 27.6 in ERAN and this increased over 5 years (Figure). In multilevel logistic models (table) adjusting for age, sex and year of recruitment among other, higher BMI was associated with reduced odds of achieving R-DAS (OR 0.97;95%CI 0.95, 0.99) and L-DAS, although the latter did not reach statistical significance (OR 0.98;95%CI 0.96, 1.00). Obesity was related to a significantly lower chance of R-DAS by 29% (OR 0.71;95%CI 0.55, 0.93) and L-DAS by 31% (OR 0.69;95%CI 0.55,0.87). Higher BMI was predictive of higher disability (OR 1.04;95%CI 1.01,1.06). More specifically, obesity increased the odds of higher disability by 63% (OR 1.63;95%CI 1.20,2.23) and in the same models, higher DAS was also strongly predictive of higher disability (OR 3.67;95%CI 3.41,3.95).

Conclusion: Higher BMI and in particular obesity was associated with lower remission and low disease activity states and higher disability. These findings argue strongly for the screening and management of obesity to become a central part of all treatment strategies in RA.
Low or High BMI Negatively Impacts RA Disease Activity in an Asian RA Cohort

Claire Teo\textsuperscript{1}, KP Leong\textsuperscript{2}, CM Woo\textsuperscript{3}, X Tang\textsuperscript{3}, J WL Tan\textsuperscript{4}, TY Lian\textsuperscript{4} and ET Koh\textsuperscript{2}, \textsuperscript{1}Rheumatology, Allergy and Immunology Department, Tan Tock Seng Hospital, Singapore, Singapore, \textsuperscript{2}Rheumatology/Allergy/Immunology, Tan Tock Seng Hospital, Singapore, Singapore, \textsuperscript{3}Clinical Research and Innovation Office, Tan Tock Seng Hospital, Singapore, Singapore, \textsuperscript{4}Department of Rheumatology, Allergy and Immunology, Tan Tock Seng Hospital, Singapore, Singapore

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
The association of body mass index (BMI) with the outcomes of rheumatoid arthritis (RA) has been inconsistent in the literature. It is postulated that high BMI or obesity may have a diverse influence on RA risk, clinical activity and treatment response. The aim of our study is to investigate the association of BMI with RA disease activity and severity in a multi-ethnic RA cohort in Singapore.

Methods:
We reviewed data that was collected from November 2013 to March 2017 in a tertiary rheumatology centre. There were 288 patients (83.68% Chinese, 5.9% Malay, 9.72% Indian, 0.69% others; 87.85% female, 12.15% male). All patients fulfilled the ACR 1987 criteria for RA. Based on the World Health Organization classification, patients were categorized into 3 groups: low, normal and high BMI [\(<18.5kg/m^2\) (underweight), 18.5-25kg/m\(^2\) (normal weight) and
Results:

The mean age of the cohort was 44.7±11.85 years, the median RA duration 197.5 months, with no statistical difference between the three groups. Patients with normal BMI were the most likely to attain remission (DAS28<2.6) among the three groups (58.14% vs 81.43% vs 76.24%, p=0.038). Patients with normal BMI had a significantly lower C-reactive protein (mg/L) compared with the two other groups (4.1 vs 3.2 vs 4.6, p=0.0214). The low BMI group had a higher physician’s assessment of disease activity, but this did not reach statistical significance (12.47±18.13 vs 7.45±15.82 vs 9.18±18.51, p=0.236). The obese patients had significantly lower physical functioning scores in SF-36 (85 vs 75 vs 70, p=0.0198). Not unexpectedly, obese patients were more likely to have hypertension (p=0.0001), low HDL (p=0.004) and high TG (p=0.0001) levels, but there was no statistically significant difference for diabetes mellitus, ischemic heart disease, cardiovascular accident, liver and renal disease in the three groups. The three groups did not differ in gender, smoking status, prevalence of rheumatoid factor and anti-citrullinated peptide antibody, number of deformed joints, health assessment questionnaire (HAQ) scores and treatment.

Conclusion:

In our multi-ethnic cohort, patients with normal BMI appear to have the best RA control. High BMI should be considered a modifiable risk factor for poor RA outcome. Future studies should be done to investigate the relation of BMI and adiposity, as well as influence of frailty and sarcopenia on RA disease activity.

Disclosure: C. Teo, None; K. Leong, None; C. Woo, None; X. Tang, None; J. W. Tan, None; T. Lian, None; E. Koh, None.

Abstract Number: 2374

Obesity Impacts ESR and Not Other Measures of Rheumatoid Arthritis Disease Activity

Ana Maheshwari1, Oumoul Barry1 and MJ Bergman2, 1Internal Medicine, Mercy Catholic Medical Center, Darby, PA, 2Medicine, Drexel University College of Medicine, Philadelphia, PA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Disease activity measurement is a cornerstone to treat to target strategy. The impact of body mass index (BMI) on disease activity in rheumatoid arthritis (RA) is not clear. We studied the impact of body mass index on various patient and physician variables in RA patients.

Methods: A retrospective observational study was done in a community based rheumatology clinic. Random visits from 155 patients with a diagnosis of RA who had documented DAS28-(ESR) (Disease Activity Score) and BMIs were
studied. Baseline patient demographics, DAS28, RAPID3, CDAI, SDAI, tender count, swollen count, physician global, pain scale, patient global, function, ESR, CRP, and BMI were collected. Obese was defined as: BMI < 29.9 (NON-OBSE) and BMI ≥ 30.0 (OBSE). A multiple regression analysis was done using a random set of patients. We used BMI and Obese as independent variables to determine the impact of BMI or Obesity on RA disease activity.

Results: Study population consisted of 155 patients of which 46% of the patients were obese with a mean BMI of 30. Patients had a mean DAS28 of 2.40, RAPID3 of 9.08, CDAI of 11.26, SDAI of 11.94. After controlling for age, sex, and duration of disease, higher BMIs were found to have a significantly increased ESR; obese patients had elevated ESR and DAS28, without changes in any other patient or physician reported measure. Additional results show that for every 10-point increase in BMI, ESR increases by 4.3mm/hour which leads to an increase in 1.02 points in the DAS28.

Table 1: Multiple regression for impact of Obesity on RA disease activity measures, controlling for age, sex, disease duration

<table>
<thead>
<tr>
<th>Variables</th>
<th>Coefficient</th>
<th>p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAS28</td>
<td>0.3856</td>
<td>0.029</td>
</tr>
<tr>
<td>RAPID3</td>
<td>0.1168</td>
<td>0.918</td>
</tr>
<tr>
<td>CDAI</td>
<td>0.9643</td>
<td>0.474</td>
</tr>
<tr>
<td>SDAI</td>
<td>1.1216</td>
<td>0.425</td>
</tr>
<tr>
<td>Tender Count</td>
<td>-0.3653</td>
<td>0.362</td>
</tr>
<tr>
<td>Swollen Count</td>
<td>1.2703</td>
<td>0.062</td>
</tr>
<tr>
<td>Physician Global</td>
<td>0.3587</td>
<td>0.222</td>
</tr>
<tr>
<td>Pain Scale</td>
<td>0.0926</td>
<td>0.848</td>
</tr>
<tr>
<td>Patient Global</td>
<td>-0.3430</td>
<td>0.450</td>
</tr>
<tr>
<td>Function</td>
<td>0.3151</td>
<td>0.285</td>
</tr>
<tr>
<td>ESR</td>
<td>5.598</td>
<td>0.046</td>
</tr>
<tr>
<td>CRP</td>
<td>0.6957</td>
<td>0.713</td>
</tr>
</tbody>
</table>

Conclusion: In this cohort, BMI was shown to significantly affect ESR, but no other objective or subjective measures of RA disease activity, suggesting that obesity in itself may increase the levels of inflammatory markers rather than the actual disease process. Using ESR may erroneously elevate DAS28 leading to misclassification of RA. This could lead to potential overtreatment in obese patients with RA. Further studies comparing the treatment groups and using larger number of patients are required to substantiate the results of this study.

Disclosure: A. Maheshwari, None; O. Barry, None; M. Bergman, Pfizer, JNJ, 1,Norvatis, AbbVie, Celgene, 8,AbbVie, BMS, Amgen, Celgene, Genentech, Pfizer, Janssen, GSK Horizon, 5.
Background/Purpose: Obesity has been proposed as a risk factor to develop rheumatoid arthritis (RA) and it has been associated with a worse response to several disease modifying anti-rheumatic drugs (DMARDs). Objective: To study the differences in baseline characteristics according to the body mass index (BMI) of patients in the PEARL (Princesa Early Arthritis Register Longitudinal) cohort.

Methods: A total of 432 patients (69.1% female) of the PEARL cohort were included for this study. The register protocol comprises the collection of sociodemographic, disease-related and treatment data in five visits (baseline, 6, 12, 24 and 60 months). The local ethics and clinical research committee approved the register protocol and all patients sign an informed consent prior to their inclusion. For this study it was analyzed the data of the baseline visit from the 304 (70.37%) patients that met ACR 1987 criteria for RA after 2 years of follow-up, as well as those considered undifferentiated arthritis (UA)since other diagnoses were excluded. The WHO definition for low weight, normal weight, overweight and obesity (BMI <18.5, 18.5-25, 25-30 or ≥30 kg/m2 respectively) was applied. ACPA were assessed by enzyme immunoassay (CCP2 Eurodiagnostica). HLA-DRB1 genotype was determined in 219 patients using specific HLADRB1 typing kits (Dynal RELI SSO). A multivariate logistic regression was performed to determine which factors may be related to ACPA positivity, including BMI, age, sex, smoking habit, number of SE alleles and study level as independent variables.

Results: Patients were 54.9 years old [44.2-67.5] (median [p25-p75]); disease duration was 5.3 months [3-8.4]. Differences in pain perception and dysability were related to BMI. Table 1 shows the main variables significantly associated to BMI. It was observed an inverse relationship between the presence of ACPA and BMI as well as a lower frequency of SE in patients with a higher BMI. The multivariate analysis, performed with the data of the 219 patients in whom the genetic study was available, showed, as previously described, that being smoker (everorcurrent) and carrying SE alleles is associated with the presence of ACPA. Moreover, adjusted by these variables, overweight and obesity were associated with a significantly lower probability of suffering an ACPA positive disease(OR 0.49, p = 0.027 and OR 0.39, p = 0.019 respectively).

Table 1 – Variables significantly different according to BMI

<table>
<thead>
<tr>
<th>BMI</th>
<th>Age (years)</th>
<th>Sex (W/M)</th>
<th>Level of studies (N/P/Se/U; %)</th>
<th>HAQ</th>
<th>VAS pain</th>
<th>TJC28</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low weight</td>
<td>52.3 [22.2-64]</td>
<td>7/0</td>
<td>0/14.3/42.9/42.9</td>
<td>1.25 [0.9-2.2]</td>
<td>50 [26-75]</td>
<td>7 [2-19]</td>
</tr>
<tr>
<td>Normal weight</td>
<td>50 [38.6-64]</td>
<td>145/24</td>
<td>1.2/21.4/35.1/42.3</td>
<td>0.87 [0.4-1.4]</td>
<td>41 [20-61]</td>
<td>3 [0-7]</td>
</tr>
<tr>
<td>Overweight</td>
<td>57.9 [47-69.6]</td>
<td>120/45</td>
<td>8.5/35.4/32.9/23.2</td>
<td>0.87 [0.5-1.6]</td>
<td>49 [20-62]</td>
<td>3 [0-9]</td>
</tr>
<tr>
<td>Obesity</td>
<td>59 [50.7-69.8]</td>
<td>68/23</td>
<td>12/38.5/26.5/22.9</td>
<td>1.3 [0.7-1.9]</td>
<td>50 [36-65]</td>
<td>5 [2-12]</td>
</tr>
</tbody>
</table>

*p≤0.001, p=0.01, p≤0.001, p=0.0018, p = 0.031, p=0.047

*W: women; M: men; N: no studies; P: primary studies; Se: secondary studies; U: universitary studies.

Conclusion: In our early arthritis registry, patients with a higher BMI have predominantly ACPA negative disease, a more intense perception of pain and higher disability. These findings should be validated in other populations.
Weight Histories Expose the Systematic Underestimation of the Risks of Obesity on Mortality in Rheumatoid Arthritis

Joshua Baker¹, Bryant R. England², Ted R. Mikuls³ and Kaleb Michaud⁴, ¹Medicine/Rheumatology, University of Pennsylvania, Philadelphia, PA, ²Division of Rheumatology & Immunology, Department of Internal Medicine, Nebraska-Western IA VA Health Care System & University of Nebraska Medical Center, Omaha, NE, ³Internal Medicine, Division of Rheumatology, University of Nebraska Medical Center, Omaha, NE, ⁴University of Nebraska Medical Center, Omaha, NE

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Emerging evidence suggests that long-term weight loss is an important confounder that results in an underestimation of the risks of obesity in chronic illness. Methodologies that consider weight earlier in life may help address this epidemiologic challenge. This study evaluated weight histories of patients with RA and their relationship to mortality.

Methods:
Patients with RA were active participants from 1999 to 2016 and of age ≥40 years in the National Data Bank for Rheumatic Diseases. Current and age-30 height and weight were self-reported at each semi-annual questionnaire. Body mass index (BMI) and percent weight change from age-30 were calculated and classified based on previously defined categories. Multivariable Cox proportional hazards models assessed the relationships between BMI at enrollment and age-30 with mortality. Estimates of risk were also assessed before and after adjusting for disability (HAQ) and comorbidity (Rheumatology Disease Comorbidity Index [RDCI])- factors hypothesized to be in the causal pathway.

Results:
Among 12,679 participants (80% female), the mean (SD) age and disease duration were 59.9 (10.5) and 13.9 (12.4) years, respectively. There were 1,520 deaths in 80,502 person-years of follow-up. Relationships between BMI categories and mortality were distinct by time of assessment (Figure). For example, at enrollment, low BMI was associated with a greater risk of death (Table). In contrast, those with low age-30 BMI were not at greater risk. While obesity at enrollment was modestly associated with mortality [HR 1.25 (1.10, 1.42) p=0.001], an obese age-30 BMI was associated with a pronounced increase in risk [HR 1.75 (1.45, 2.11) p<0.001]. Weight loss since age-30 was a strong and dose-dependent predictor of mortality independent of enrollment BMI. Compared to normal BMI, an obese age-30 BMI was associated with greater disability and comorbidity scores and greater odds of diabetes, hypertension, and work disability at enrollment after adjusting for sex, race, and age at enrollment. Adjustment for disability and comorbidity resulted in even further potential underestimation of risks of obesity at enrollment [HR 0.92 (0.80, 1.06) p=0.24] (Figure).
Conclusion:

Lifetime weight histories expose substantial underestimation of the risks of obesity on mortality in clinical studies in RA. Systematic underestimation of risk is due to the confounding effects of long-term unintentional weight loss often observed due to aging and chronic illness and to the over-adjustment for factors that are likely to be in the causal pathway.

<table>
<thead>
<tr>
<th>BMI Category</th>
<th>Enrollment BMI</th>
<th>Enrollment BMI + Weight Change Since Age 30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>1.56 (1.15, 2.14)</td>
<td>1.05 (0.76, 1.46)</td>
</tr>
<tr>
<td>Normal Weight</td>
<td>1 (reference)</td>
<td>1 (reference)</td>
</tr>
<tr>
<td>Overweight</td>
<td>0.97 (0.86, 1.09)</td>
<td>1.07 (0.94, 1.22)</td>
</tr>
<tr>
<td>Obese</td>
<td>1.25 (1.10, 1.42)</td>
<td>1.40 (1.20, &lt;0.001)</td>
</tr>
</tbody>
</table>

Weight Change Since Age 30

<table>
<thead>
<tr>
<th>Change Since Age 30</th>
<th>Enrollment BMI</th>
<th>Enrollment BMI + Weight Change Since Age 30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase 10%</td>
<td>--</td>
<td>0.86 (0.74, 0.99)</td>
</tr>
<tr>
<td>Increase 5%</td>
<td>--</td>
<td>0.81 (0.68, 0.98)</td>
</tr>
<tr>
<td>Stable</td>
<td>--</td>
<td>1 (reference)</td>
</tr>
<tr>
<td>Decrease 5%</td>
<td>--</td>
<td>1.30 (1.01, 1.66)</td>
</tr>
<tr>
<td>Decrease 10%</td>
<td>--</td>
<td>1.89 (1.52, &lt;0.001)</td>
</tr>
</tbody>
</table>

*All models adjusted for age, sex, white race, disease duration, and current smoking at enrollment.*
Disclosure: J. Baker, None; B. R. England, None; T. R. Mikuls, BMS, 2, Ironwood Pharm, 2, Pfizer Inc, 5, NIH, VA, 2; K. Michaud, None.


Abstract Number: 2377

**Impact of Body Mass Index and Weight Loss on Incident Disability in Patients with Rheumatoid Arthritis**

Joshua Baker¹, Ted R. Mikuls², Bryant R. England³, Michael D. George⁴, Grant Cannon⁵, Harlan Sayles⁶, Brian Sauer⁵, Liron Caplan⁷ and Kaleb Michaud⁶, ¹Medicine/Rheumatology, University of Pennsylvania, Philadelphia, PA, ²Internal Medicine, Division of Rheumatology, University of Nebraska Medical Center, Omaha, NE, ³Division of Rheumatology & Immunology, Department of Internal Medicine, Nebraska-Western IA VA Health Care System & University of Nebraska Medical Center, Omaha, NE, ⁴Division of Rheumatology, University of Pennsylvania, Philadelphia, PA, ⁵Salt Lake City VA Medical Center and University of Utah, Salt Lake City, UT, ⁶University of Nebraska Medical Center, Omaha, NE, ⁷Division of Rheumatology, University of Colorado School of Medicine, Aurora, CO

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Tuesday, November 7, 2017

Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities

Session Type: ACR Poster Session C

Session Time: 9:00AM-11:00AM

Background/Purpose:

Obese patients with rheumatoid arthritis (RA) have greater disability in cross-sectional studies. There are no long-term studies that assess trajectories of disability among individuals in different body mass index (BMI) categories. We evaluated associations between obesity, weight loss, and incident disability in two large longitudinal registries.

Methods:
This study included patients with RA and available data from the National Data Bank of Rheumatic Diseases (NDB) (N=22,432) and the Veterans Affairs RA (VARA) registry study (N=1580). Incident disability was defined as an increase of >0.2 on the Health Assessment Questionnaire (HAQ or MD-HAQ) (based on the MCID). Disability scores and BMI were recorded at routine clinical visits (VARA) or by questionnaire every 6 months (NDB). Patents from NDB were asked to estimate their weight at age 30. Multivariable Cox proportional hazards models evaluated associations between BMI and weight change and the risk of incident disability.

Results:

Disability was greater at enrollment in severely obese (BMI >35 kg/m\(^2\)) patients compared to normal weight (BMI 18.5-25 kg/m\(^2\)) after adjustment for demographics in NDB [B: 0.31 (0.28,0.34) p<0.001] and VARA [B: 0.19 (0.085,0.30) p<0.001]. Disability increased annually in both NDB [B: 0.011 (0.01, 0.012), p<0.001] and VARA [B: 0.022 (0.018, 0.027) p<0.001]. In multivariable models, severe obesity and greater comorbidity were associated with incident disability (Table). Associations for obesity were independent of disease duration, comorbidity, and time-varying CRP and swollen joint count (in VARA). In NDB, 5% weight loss from age 30 to enrollment (9.7% of patients) was associated with a greater risk of incident disability in similar models [HR: 1.13 (1.04,1.23) p=0.004] (Figure). Similarly in VARA, 5% weight loss from enrollment as a time-varying predictor (22.8% of observations) was associated with incident disability independent of time-varying BMI [HR 1.40 (1.15,1.71) p=0.004]. Figure 1 shows that survival without incident disability was shorter among severely obese patients in NDB and among those who lost 5% of weight since age 30.

Conclusion:

Obesity and comorbidity at enrollment predict greater and worsening disability scores in RA- an effect that is independent of disease activity. A direct effect of excess weight on disability over time represents an important confounder of these measures as RA outcomes. Interestingly, prior weight loss also predicts disability, possibly by identifying chronically ill individuals with unintentional weight loss.
Table: Cox proportional hazards models evaluating the risk of incident disability (HAQ or MD-HAQ increase >0.2).

<table>
<thead>
<tr>
<th></th>
<th>NDB (HAQ)</th>
<th>VARA (MD-HAQ)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>p</td>
</tr>
<tr>
<td>Model 1</td>
<td>N=22,432</td>
<td>N=1,580</td>
</tr>
<tr>
<td>Enrollment BMI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;18.5 kg/m²</td>
<td>0.91 (0.79, 1.06)</td>
<td>0.22</td>
</tr>
<tr>
<td>18.5-25 kg/m² (reference)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25-30 kg/m²</td>
<td>1.08 (1.03, 1.14)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>30-35 kg/m²</td>
<td>1.23 (1.17, 1.31)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt;35 kg/m²</td>
<td>1.36 (1.28, 1.45)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline HAQ/MD-HAQ</td>
<td>0.52 (0.51, 0.54)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Follow-up Time (per yr)</td>
<td>1.11 (1.09, 1.13)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age (per 10 yrs)</td>
<td>1.00 (0.98, 1.01)</td>
<td>0.80</td>
</tr>
<tr>
<td>Male</td>
<td>0.66 (0.63, 0.69)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Caucasian</td>
<td>0.87 (0.80, 0.94)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Comorbidity Score*</td>
<td>1.10 (1.09, 1.11)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Disease Duration (per yr)</td>
<td>1.03 (1.02, 1.05)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Current Smoking</td>
<td>1.13 (1.04, 1.22)</td>
<td>0.003</td>
</tr>
<tr>
<td>Time-varying factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Swollen Joints</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>CRP (per mg/dL)</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

*The comorbidity score is the Rheumatic Disease Comorbidity Index, range 0-9.

Abbreviations: VARA- VA Rheumatoid Arthritis; PY= Person-Years; HR= Hazard Ratio; HAQ= Health Assessment Questionnaire; MD-HAQ= Multidimensional Health Assessment
Body Mass Index and Persistence of Conventional Dmards and TNF Inhibitors in Rheumatoid Arthritis

Caroline McCulley\textsuperscript{1}, Ted R. Mikuls\textsuperscript{2}, Jennifer Barton\textsuperscript{3}, Grant Cannon\textsuperscript{4}, Brian C. Sauer, PhD\textsuperscript{5}, Liron Caplan\textsuperscript{6}, Bryant R. England\textsuperscript{7}, Chia-Chen Teng\textsuperscript{8} and Joshua Baker\textsuperscript{9}, \textsuperscript{1}Rheumatology, Oregon Health & Science University, Portland, OR, \textsuperscript{2}Internal Medicine, Division of Rheumatology, University of Nebraska Medical Center, Omaha, NE, \textsuperscript{3}VA Portland Health Care System, Portland, OR, \textsuperscript{4}Salt Lake City VA Medical Center and University of Utah, Salt Lake City, UT, \textsuperscript{5}Salt Lake City VA and University of Utah, Salt Lake City, UT, \textsuperscript{6}Division of Rheumatology, University of Colorado School of Medicine, Aurora, CO, \textsuperscript{7}Division of Rheumatology & Immunology, Department of Internal Medicine, Nebraska-Western IA VA Health Care System & University of Nebraska Medical Center, Omaha, NE, \textsuperscript{8}Rheumatology, University of Utah, Salt Lake City, UT, \textsuperscript{9}Rheumatology, University of Pennsylvania, Philadelphia, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Low body mass index (BMI) is associated with more destructive disease in rheumatoid arthritis (RA). Paradoxically, obese patients have been shown in studies to be more likely to discontinue therapy, suggesting a refractory phenotype. The purpose of this study was to examine the association between BMI and DMARD persistence, accounting for factors that may confound this relationship.

Methods:

VA administrative databases were used to define unique initial courses of methotrexate (MTX), self-injectable TNF inhibitors (TNFi), hydroxychloroquine (HCQ), sulfasalazine, and prednisone. Discontinuation was defined as a lapse in drug refill >90 days. The closest values for CRP and BMI within 30 days of treatment start date were linked. Multiple imputation was used to address missing laboratory values. Health factor data and diagnosis codes were linked to treatment courses. Multivariable Cox proportional hazards models were used to evaluate associations between BMI category and time to DMARD discontinuation. Covariates included age, sex, race (Black vs. White), calendar year (2005-2009 vs. 2010-2014), current smoking, CRP, disease duration >5 years, anti-CCP status, other DMARDs, diabetes, hypertension, CHF, history of malignancy, depression, and anxiety, and the Rheumatic Disease Comorbidity Index (RDCI).

Results:

There were 46,970 unique initial DMARD courses (88% male) with RA between 2003-2014. Patients in low (BMI <18.5) and normal (BMI 18.5-25) categories had the greatest likelihood of discontinuing MTX, HCQ, and TNFi (Figure). Severe obesity (BMI >35) was only associated with a greater likelihood of discontinuing prednisone compared to overweight BMI (BMI 25-30) [HR 1.09 (1.02, 1.16) p=0.004]. Factors associated with earlier MTX and/or TNFi discontinuation included female sex, black race, older age, greater comorbidity, and a history of depression, malignancy, CHF, active smoking, and recent calendar year (Table). Among TNFi users, concurrent MTX use was associated with a lower likelihood of discontinuation.

Conclusion:

Among US veterans with RA, obesity was not associated with reduced persistence of DMARDs and/or TNFi’s, except for prednisone. Conversely, low BMI was associated with reduced drug persistence; this finding may be explained by greater severity of RA and/or other co-morbidities and warrants further evaluation. These data are not consistent with the hypothesis that obesity is a biologic mediator of refractory disease, resulting in failure of drug therapy. In contrast, other co-morbidities are shown to be important predictors of drug persistence.
Figure. Risk of early discontinuation of therapy by drug class in fully adjusted models.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methotrexate (N=15,082)</td>
<td></td>
</tr>
<tr>
<td>TNF (N=8,412)</td>
<td></td>
</tr>
<tr>
<td>Hydroxychloroquine (N=7,490)</td>
<td></td>
</tr>
<tr>
<td>Sulfasalazine (N=4,359)</td>
<td></td>
</tr>
<tr>
<td>Prednisone (N=11,627)</td>
<td></td>
</tr>
</tbody>
</table>

BMI Category (Reference 25-30 kg/m²)

* p<0.05

Models adjusted for age, sex, race, EDCI, disease duration, CRP, CCP status, concurrent therapies, HTN, CHF, cancer, diabetes, anxiety, depression, current smoking.
Table 1: Risk factors associated with early discontinuation of methotrexate and TNFi.

<table>
<thead>
<tr>
<th></th>
<th>Methotrexate</th>
<th>TNFi</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;60 (reference)</td>
<td>(reference)</td>
<td>(reference)</td>
</tr>
<tr>
<td>60-70</td>
<td>0.87 (0.84, 0.91)*</td>
<td>0.93 (0.89, 0.98)*</td>
</tr>
<tr>
<td>70-80</td>
<td>0.97 (0.92, 1.01)</td>
<td>0.99 (0.92, 1.07)</td>
</tr>
<tr>
<td>&gt;80</td>
<td>1.09 (1.01, 1.17)*</td>
<td>1.26 (1.10, 1.44)*</td>
</tr>
<tr>
<td><strong>Male</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.90 (0.86, 0.95)*</td>
<td>0.80 (0.74, 0.85)*</td>
</tr>
<tr>
<td><strong>Black</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.10 (1.05, 1.16)*</td>
<td>1.05 (0.97, 1.12)</td>
</tr>
<tr>
<td><strong>Depression</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.07 (1.03, 1.12)*</td>
<td>1.14 (1.08, 1.19)*</td>
</tr>
<tr>
<td><strong>Anxiety</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.09 (1.03, 1.14)*</td>
<td>1.05 (0.99, 1.11)</td>
</tr>
<tr>
<td><strong>CHF</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.09 (1.03, 1.16)*</td>
<td>1.07 (0.97, 1.17)</td>
</tr>
<tr>
<td><strong>RDCI</strong>**</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.03 (1.01, 1.04)</td>
<td>1.03 (1.01, 1.05)*</td>
</tr>
<tr>
<td><strong>2010-2014 vs. 2005-2010</strong></td>
<td>1.32 (1.27, 1.38)</td>
<td>1.27 (1.20, 1.34)*</td>
</tr>
<tr>
<td><strong>Current Smoker</strong></td>
<td>1.08 (1.02, 1.04)</td>
<td>1.13 (1.06, 1.20)*</td>
</tr>
<tr>
<td><strong>Cancer</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.05 (0.99, 1.09)</td>
<td>1.08 (1.01, 1.17)*</td>
</tr>
<tr>
<td><strong>Anti-CCP Positive</strong></td>
<td>0.88 (0.85, 0.92)*</td>
<td>0.95 (0.88, 1.02)</td>
</tr>
<tr>
<td><strong>Concurrent Prednisone</strong></td>
<td>0.99 (0.95, 1.02)</td>
<td>1.12 (1.07, 1.18)*</td>
</tr>
<tr>
<td><strong>Concurrent MTX use</strong></td>
<td>n/a</td>
<td>0.93 (0.89, 0.97)*</td>
</tr>
<tr>
<td><strong>Initial Biologic</strong></td>
<td>n/a</td>
<td>0.81 (1.18, 1.66)*</td>
</tr>
</tbody>
</table>

*p<0.05

Included in the model but not shown: BMI category, CRP, disease duration >5 years, CCP positive, other DMARDs, diabetes, hypertension, anxiety

**RDCI (Rheumatic Disease Comorbidity Index)**

**Disclosure:** C. McCulley, None; T. R. Mikuls, BMS, 2,Ironwood Pharm, 2,Pfizer Inc, 5,NIH, VA, 2; J. Barton, None; G. Cannon, Amgen, 2; B. C. Sauer, PhD, Amgen, 2; L. Caplan, None; B. R. England, None; C. C. Teng, None; J. Baker, None.

Effect of DKK-1 and Osteoprotegerin on Bone Mass in Tightly Controlled Rheumatoid Arthritis

Javier Narváez1, Irene Martin-Esteve2, Andrea Zacarias3, Pedro Alia4, Estibaliz Loza5, Loreto Carmona5, Joan Miquel Nolla2 and Carmen Gomez Vaquero6, 1Rheumatology Department, Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Spain, 2Rheumatology, Hospital Universitari de Bellvitge, Barcelona, Spain, 3Hospital Universitari de Bellvitge, Barcelona, Spain, 4Clinical Laboratory Service, Hospital Universitari de Bellvitge - IDIBELL, Barcelona, Spain, 5Instituto de Salud Musculosquelética (InMusc), Madrid, Spain, 6Department of Rheumatology, Hospital Universitario de Bellvitge, Barcelona, Spain

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: To analyze the association between osteoprotegerin (OPG) and Dickkopf-related protein 1 (DKK-1) and the annual percent change (Δ%) in bone mineral density (BMD) in patients with tightly controlled rheumatoid arthritis (RA).

Methods: Observational mixed-study. RA patients followed-up with a tight-control strategy were included. Bone densitometries were performed at baseline (T0) and follow-up (T1) and OPG and DKK-1 were measured by ELISA also in T0 and T1; additional clinical variables included disease activity measures, and treatment for RA and osteoporosis. Descriptive bivariate and multivariate analyses, stratified by gender, were performed.

Results: We included 97 RA patients (70% female, with a mean age of 53 years, and 76% with low activity by DAS28); 95% were treated with DMARDs and 37% with anti-osteoporotic drugs. Mean lag-time between bone densitometries was 2.7 years. Most patients had their BMD improved. The mean Δ%BMD was +0.42% for lumbar spine, +0.15% for femoral neck and +0.91% for total femur. In men, baseline OPG was significantly associated with higher BMD loss (β coefficient -0.64) at femoral neck. In women, DKK-1 was associated with higher BMD loss at femoral neck (β coefficient -0.09), and total femur (β coefficient -0.11); however, DKK-1 was associated with lower BMD loss at lumbar spine (β coefficient 0.06).

Conclusion: In tightly controlled RA patients, we have found no evidence of bone loss. Other factors than OPG and DKK-1, namely smoking and ACPA, may have a larger effect on bone mass than these molecules.

Disclosure: J. Narváez, None; I. Martin-Esteve, None; A. Zacarias, None; P. Alia, None; E. Loza, None; L. Carmona, None; J. M. Nolla, None; C. Gomez Vaquero, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/effect-of-dkk-1-and-osteoprotegerin-on-bone-mass-in-tightly-controlled-rheumatoid-arthritis

Abstract Number: 2380

The Use of Fibroscan in Detecting Early Liver Fibrosis in RA Patients on Long Term MTX with Normal Liver Enzymes
FibroScan (FS) is a non-invasive investigation that allows assessment of possible liver fibrosis by measuring liver stiffness. There are studies which confirm that MTX-related liver fibrosis (LF) may not be associated with abnormal liver function tests (LFTs). The aim of this study was to investigate the incidence of possible LF detected by FS in RA patients taking MTX, who had never had abnormal LFTs since commencing MTX.

Methods:
This was a pilot, single-centre, prospective, cross-sectional cohort study. Patients were recruited from the rheumatology department at Wrexham Maelor Hospital, North Wales, UK, between September 2012 and July 2016. We included only patients with RA (seropositive and seronegative), who had never had abnormal LFTs since commencement of MTX, and who had been on MTX for 2 years or more. The hepatology team performed the FS in all patients. The FS score of an average of 10 readings was expressed in kilopascals (KPa). A FS result was considered abnormal if ≥ 8KPa. Patients with abnormal FS results were then assessed by the hepatology team for further clinical evaluation to establish the liver condition. Linear regression test was used to examine the relation between raised FS values and dose and duration of MTX use.

Results:
A total of 104 patients were recruited in this study. FS readings were invalid in 4 patients, and those patients were later excluded from the analysis. There were 65% females and 35% males in this cohort, reflecting the predominance of females in RA. The mean patient age was 65.1 years (SD 9.7). The mean MTX dose was 17.2mg (SD 5.2) weekly. The median duration of MTX treatment was 5.4 years (range 2-16 years) and this gave a total of 347 MTX- years. There were 41 patients on at least one other DMARD (SSZ, LEF, HCQ), and 17 patients on a biologic drug. The median FS score in this study was 4.7 KPa (range 0-14.5). Fifteen patients had abnormal FS readings with a median score of 9.1 (range 8.1-14.5). The incidence of an abnormal FS result was 15% in this cohort. The rate of abnormal FS score was 0.043/100 patient-years. We found no correlation between raised FS score and the dose or duration of MTX use - correlation coefficient F was 2.8 (p value 0.09) and 0.57 (p value 0.45) respectively. All patients with abnormal FS scores were clinically obese (BMI>30), and were diagnosed by the hepatologist as having fatty liver disease. None of these had MTX-induced liver fibrosis. Only 1 patient had non-alcoholic steatohepatitis with liver fibrosis confirmed on liver biopsy. This patient was advised to stop MTX, and all other patients were advised to lose weight and to continue taking MTX.

Conclusion:
We demonstrated in this study that subclinical MTX-induced LF in RA patients taking long-term MTX with normal LFTs is extremely low. The use of FS as part of routine monitoring for liver fibrosis in clinical practice is not necessary in patients with normal LFTs.

Disclosure: M. Alachkar, None; T. Mathialahan, None; S. Walsh, None; V. Lim, None.
Abstract Number: 2381

Hematologic Abnormalities during the Use of Low Dose Methotrexate for Rheumatoid Arthritis: A Systematic Review and Meta-Analysis

Kathleen Vanni¹, Zhi Zhang¹, Cassandra Corrigan² and Daniel H. Solomon³, ¹Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA, ²Rheumatology, Brigham and Women's Hospital, Boston, MA, ³Brigham and Women's Hospital and Harvard Medical School, Boston, MA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Methotrexate (MTX) is known to increase the risk of cytopenias, but the prevalence of hematologic abnormalities among patients taking low dose MTX is poorly defined. We conducted a systematic literature review and meta-analysis to estimate the prevalence of anemia, leukopenia, neutropenia, and thrombocytopenia associated with MTX plus folic acid supplementation among non-oncology patients.

Methods: We searched MEDLINE, PubMed, and Embase from inception to August 2016 for all randomized controlled clinical trials (RCTs) with a MTX monotherapy arm. We excluded RCTs for cancer and included only double-blind studies that reported on hematologic adverse events. Studies were excluded if patients did not receive folic acid or leucovorin supplementation. Most trials used MTX as the comparator arm against newer therapies. Full text articles were assessed by two independent reviewers. Risk of bias was assessed per Cochrane Risk of Bias guidelines including selection, performance, detection, attrition, and reporting bias. Pooled prevalence estimates were calculated using random-effects models. The heterogeneity across studies was tested using Cochran’s Q and I².

Results: Of 1601 studies identified, 30 (1.87%) were included that contained data from 3,858 patients with RA; no other rheumatologic conditions were represented. Seventeen trials reported on anemia (N=2,032), 17 reported on leukopenia (N=2,220), 16 reported on neutropenia (N=2,202), and 12 reported on thrombocytopenia (N=1,507). The mean dose of methotrexate was 15.4 (± 4.5) mg/week with a maximum dose of 30 mg/week, and 41.9% of subjects were using oral corticosteroids. Trial duration ranged from 12-62 weeks with a mean of 32 (±17) weeks. The pooled prevalence for anemia was 3.05% (95% CI 1.04-5.95%), leukopenia 1.67% (95% CI 0.55-3.31%), neutropenia 2.25% (95% CI 0.74-4.48%), and thrombocytopenia 0.67% (95% CI 0.18-1.42%) (Figure). Severe anemia was reported in 4 patients (0.20%), severe neutropenia was reported in 3 patients (0.14%), and no cases of severe leukopenia or thrombocytopenia were reported. The risk of bias assessment showed that most methodological limitations came from a failure to describe randomization procedures (N=23, 76.7%) and selective reporting of only severe hematologic adverse events (N=8, 26.7%). Significant statistical heterogeneity existed across studies for all cytopenias. The I² (percentage of variation due to heterogeneity rather than chance) was high: I² 89% for anemia, 81% for leukopenia, 86% for neutropenia, 42% for thrombocytopenia.

Conclusion: Cytopenias are an uncommon side effect of low-dose MTX with folic acid supplementation among RA patients. Randomized controlled clinical trials vary widely in their reporting of hematologic adverse events, with many failing to report mild and moderate cases. Further research is needed to reach a more precise estimate.
Reliability of the Biochemical Bone Markers CTX and P1NP during a TNF-Inhibitor Treatment Cycle in Patients with Rheumatoid Arthritis

Kim Holmsted1, Niklas Rye Jørgensen2 and Ole Rintek Madsen1, 1Center for Rheumatology and Spine Diseases & The DANBIO Registry, Copenhagen University Hospital Rigshospitalet Gentofte Glostrup, Copenhagen, Denmark, 2Dept. of Clinical Biochemistry, Rigshospitalet, Glostrup, Denmark

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Patients with rheumatoid arthritis (RA) have an increased risk of developing osteoporosis. Dual Energy X-ray Absorptiometry (DXA) with assessment of BMD is used for diagnosis and monitoring of treatment effect. The access to DXA may be limited and changes in BMD occur only slowly, however. Therefore, the use of biochemical bone turnover markers (BTMs) to control compliance and treatment effect is gaining ground in daily practice. According to the International Osteoporosis Foundation (IOF) the most promising markers for clinical use are s-P1NP (serum procollagen type 1 N-terminal propeptid, µg/L) and s-CTX (serum procollagen type 1 N-terminal propeptid, µg/L) reflecting the bone formation and resorption, respectively. When treating with bisphosphonates, the BTMs are expected to be suppressed already after a few months. However, analytic and biologic variation may influence the results. TNF-inhibitors reduce bone loss and reduce serum levels of P1NP and CTX. The use of BTMs in RA patients treated with anti-osteoarthritis agents is tempting, but there is no data on the reliability of BTM during TNF-inhibitor treatment cycles.
**Objective:**

To examine the reliability of CTX and P1NP in a group of stable RA patients during a cycle of TNF inhibitor treatment.

**Methods:**

27 RA patients with receiving TNF-inhibitor treatment were identified in the Danish Registry for biological treatment (DANBIO). None of the patients were treated with anti-osteoporotic agents. Measurements of fasting morning s-P1NP and s-CTX were performed 1-2 days before and after administration of the biological agent and in the middle of the treatment cycle. Analyses were performed according to standard procedures. Between-test differences were examined using Student’s t-test for paired data. Reliability was expressed as the coefficient of variation (CV) % calculated as \( 100 \times \sqrt{\frac{\sum s_i^2}{(n-1)}}/\text{mean} \) and as the corresponding minimal detectable difference (MDD) % calculated as \( 1.96 \times \sqrt{2 \times \text{CV} \%} \). The MDD is the difference between two measurements which would be statistically significant when applied to a reference group (level of significance 0.05).

**Results:**

Age was 61.6±12.6 years, DAS28 2.8±0.99 (mean±1SD). 57% of the patients were treated with adalimumab, 18% with certolizumab, 14% with etanercept, 11% with infliximab and 70% with a DMARD (methotrexate (n=17), azathioprine (n=2)). Results of P1NP and CTX measurements are shown in the Table.

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Before</th>
<th>After</th>
<th>Between</th>
</tr>
</thead>
<tbody>
<tr>
<td>s-CTX (µg/L)</td>
<td>0.41±0.23</td>
<td>0.41±0.22</td>
<td>0.40±0.22</td>
</tr>
<tr>
<td>s-P1NP (µg/L)</td>
<td>55.2±19.5</td>
<td>53.5±22.3</td>
<td>54.8±24.5</td>
</tr>
</tbody>
</table>

Significant differences between the time points were not found (p-value range 0.36-0.96)

The CV for P1NP was 18.7 % and the corresponding MDD 52.0 %. The CV for CTX was 20.3% and the MDD 56.3 %.

**Conclusion:**

The biochemical bone markers P1NP and CTX were stable on the group level during cycles of TNF-inhibitor treatment in patients with RA. CVs and MDDs were high, however. If treatment with anti-osteoporotic agents is initiated, changes in both P1NP and CTX below 50% in the individual patient may be due solely to measurement error and should therefore be interpreted with caution.

**Disclosure:** K. Holmsted, None; N. R. Jørgensen, None; O. Rintek Madsen, None.

**Abstract Number: 2383**

**Frailty and Risk of Fractures in Patients with Rheumatoid Arthritis: Data from the Ontario Best Practices Research Initiative (OBRI)**

Guowei Li¹, Xiuying Li², Angela Cesta³, Arthur Lau⁴, Claire Bombardier³ and J Adachi⁵, ¹Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, ON, Canada, ²University of Toronto, TORONTO, ON, Canada, ³Toronto General Hospital Research Institute, University Health Network, Toronto, ON, Canada, ⁴50 Charlton Avenue East, St Joseph's Healthcare Hamilton, Hamilton, ON, Canada, ⁵St Joseph's Healthcare Hamilton, Hamilton, ON, Canada
Background/Purpose:
Measuring the degree of frailty can help screen, quantify and predict future risk of adverse health outcomes at a clinical research level and at a healthcare policy level. The evidence assessing the relationship between frailty and risk of adverse health outcomes in rheumatoid arthritis (RA) patients remains limited and sparse in the literature. Therefore we aimed to assess the relationship between frailty and risk of fractures in patients with RA, using data from the Ontario Best Practices Research Initiative (a clinical registry of patients with RA in Ontario, Canada).

Methods:
Patients’ data were collected from the participating rheumatologists every 6 months, and from OBRI interviewers every 3 months in the first two years and every 6 months afterwards. The primary outcome was incident fractures during follow-up that led to a hospitalization or emergency room (ER) visit. Frailty was measured as a frailty index (FI) of deficit accumulation that included 32 health-related deficits consisting of 17 comorbidities, 16 symptoms and signs, and 9 activities of daily living. The FI ranged from 0 to 1, with a higher FI indicating higher frailty. Student’s t-test was used for comparison of FI between patients with and without a fracture during follow-up.

Results:
There were 3,153 patients (78% females, mean age 57.5 years) included for analyses. Patients’ mean FI at baseline was 0.21 (standard deviation [SD]: 0.17), and the age-invariant 99% upper limit was 0.52. During the mean follow-up of 3.7 years, there were 125 incident fractures reported. As shown in Table 1, patients experiencing a fracture were older, more likely to be females, and had a longer RA duration, compared to patients without a fracture. The FI was significantly higher in patients with a fracture compared to controls (0.25 vs. 0.21, p < 0.001).

Conclusion:
RA patients experiencing an incident fracture were significantly frailer than patients who did not experience a fracture. Measuring the grades of frailty may assist with the assessment and management of RA patients to predict and reduce their fracture risk.

Table 1. Comparison of baseline characteristics between RA patients with a fracture leading to hospitalization or ER visit and patients without fractures during follow-up
## Baseline characteristics

<table>
<thead>
<tr>
<th>Incident fracture that lead to a hospitalization or ER visit</th>
<th>Yes (n =125)</th>
<th>No (n = 3,028)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: mean (SD), years</td>
<td>61.9 (11.9)</td>
<td>57.3 (12.9)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Female: n (%)</td>
<td>109 (87%)</td>
<td>2,319 (78%)</td>
<td>0.013</td>
</tr>
<tr>
<td>RA duration: mean (SD), years</td>
<td>11.6 (11.4)</td>
<td>8.2 (9.7)</td>
<td>0.002</td>
</tr>
<tr>
<td>BMI: mean (SD), kg/m²</td>
<td>26.5 (5.0)</td>
<td>27.0 (5.6)</td>
<td>0.33</td>
</tr>
<tr>
<td>Family history of RA: n (%)</td>
<td>49 (39%)</td>
<td>970 (32%)</td>
<td>0.11</td>
</tr>
<tr>
<td>Smoking: n (%)</td>
<td>20 (16%)</td>
<td>504 (17%)</td>
<td>0.82</td>
</tr>
<tr>
<td>Alcohol drinking: n (%)</td>
<td>34 (27%)</td>
<td>828 (27%)</td>
<td>0.93</td>
</tr>
<tr>
<td>Osteoporosis medication use: n (%)</td>
<td>44 (35%)</td>
<td>826 (27%)</td>
<td>0.059</td>
</tr>
<tr>
<td>FI: mean (SD)</td>
<td>0.25 (0.12)</td>
<td>0.21 (0.12)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

ER = emergency room; SD = standard deviation; RA = rheumatoid arthritis; BMI = body mass index; FI = frailty index

**Disclosure:** G. Li, None; X. Li, None; A. Cesta, None; A. Lau, None; C. Bombardier, None; J. Adachi, Amgen, Eli Lilly, Merck, 2,Amgen, Eli Lilly, Merck, 5,International Osteoporosis Foundation Board of Directors, Scientific Advisor; Osteoporosis Canada Past-President, 6,Amgen, 8.


**Abstract Number:** 2384

### Incidence and Predictors of Dyspnea on Exertion in a Prospective Cohort of Patients with Rheumatoid Arthritis

**Jeffrey A. Sparks**¹, Tracy Doyle², Beatrice Pan³, Christine Iannaccone⁴, Michelle Frits³, Paul Dellaripa⁵, Ivan Rosas⁵, Bing Lu⁶, Michael Weinblatt⁶, Nancy A. Shadick⁷ and Elizabeth Karlson⁵, ¹Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ²Division of Pulmonary Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ³Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA, ⁴Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA, ⁵Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ⁶Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ⁷Rheumatology Immunology & Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Dyspnea on exertion symptoms often prompt clinical evaluation related to respiratory, cardiovascular, and functional status. However, the incidence and predictors of clinically significant dyspnea among
patients with rheumatoid arthritis (RA) has not been previously investigated.

**Methods**: We investigated dyspnea among RA patients using a single-center cohort of patients with RA and up to 12 years of prospective follow-up. We defined significant dyspnea on exertion using the Medical Research Council Dyspnea measure (³3 on 0-5 scale; unable to ambulate without breathlessness or worse, as previously validated), assessed at baseline and annually. We analyzed subjects with complete covariate data and no significant dyspnea at baseline and at least one year of follow-up. We determined the incidence rate (IR) of dyspnea during follow-up. Sociodemographics, lifestyles, clinical factors, and RA characteristics were considered as time-varying predictors assessed prior to the outcome. We used Cox regression to estimate the hazard ratios (HR) for dyspnea occurring one year after predictors were assessed throughout follow-up.

**Results**: We analyzed 991 patients with RA and no significant dyspnea at baseline during mean 5.1 (SD 3.8) years of follow-up. At baseline, mean age was 55.5 (SD 13.6) years and 66.0% were seropositive. During 5,041 person-years of follow-up, 142 (14.3%) subjects developed incident dyspnea (IR 52.5 per 100 person-years). The dyspnea IR was highest in the first year after baseline (IR 26.3 per 100 person-years, **Figure**). Independent predictors of clinically significant dyspnea were: older age (HR 1.03, 95%CI 1.01-1.05 per year, **Table**), female sex (HR 2.32, 95%CI 1.19-4.54), white race (HR 0.50, 95%CI 0.25-0.97 vs. non-white), obesity (HR 1.66, 95%CI 0.98-2.79 vs. normal), worsened functional status by MD-HAQ (HR 2.54, 95%CI 1.64-3.93 per unit), and mild dyspnea (HR 2.72, 95%CI 1.66-4.48 vs. no dyspnea). Biologic use was associated with dyspnea (HR 1.58, 95%CI 1.03-2.42 vs. non-use), but other RA characteristics including DAS28-CRP, seropositivity, duration, methotrexate use, and glucocorticoids were not associated with incident dyspnea.

**Conclusion**: In this long-term prospective study, the development of clinically significant dyspnea on exertion occurred in 14% of patients with RA. We identified sociodemographics (older age, white race, female sex), clinical factors (obesity, mild baseline dyspnea), and RA characteristics (MD-HAQ, biologic use) assessed prior to dyspnea development that inform intervention studies related to decreasing the respiratory and cardiovascular burden of RA.

![Figure](cumulative incidence rate per 100 person-years for development of clinically relevant dyspnea on exertion among patients with RA during 12 years of prospective follow-up (n=991).)

![Table](Predictors of clinically relevant dyspnea on exertion in RA assessed one year prior to development, in univariate and multivariable analyses (n=991).)

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Univariate HR (95%CI)</th>
<th>Multivariable HR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sociodemographics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (per year)</td>
<td>1.03 (1.01-1.06)</td>
<td>1.03 (1.01-1.08)</td>
</tr>
<tr>
<td>Female sex (vs. male)</td>
<td>1.92 (1.92-3.63)</td>
<td>2.32 (1.94-5.41)</td>
</tr>
<tr>
<td>White race (vs. non-white)</td>
<td>0.38 (0.30-0.54)</td>
<td>0.59 (0.39-0.90)</td>
</tr>
<tr>
<td>College education (vs. less education)</td>
<td>0.98 (0.77-1.25)</td>
<td>0.99 (0.82-1.24)</td>
</tr>
<tr>
<td><strong>Lifestyle and Clinical</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass index category</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underweight</td>
<td>1.00 (Ref)</td>
<td>1.00 (Ref)</td>
</tr>
<tr>
<td>Normal</td>
<td>1.00 (Ref)</td>
<td>1.00 (Ref)</td>
</tr>
<tr>
<td>Overweight</td>
<td>1.71 (1.08-2.65)</td>
<td>1.50 (0.90-2.44)</td>
</tr>
<tr>
<td>Obese</td>
<td>2.12 (1.31-3.45)</td>
<td>1.68 (0.58-5.79)</td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>1.00 (Ref)</td>
<td>1.00 (Ref)</td>
</tr>
<tr>
<td>Past</td>
<td>1.00 (Ref)</td>
<td>1.41 (0.33-6.14)</td>
</tr>
<tr>
<td>Current</td>
<td>1.34 (1.02-1.77)</td>
<td>0.99 (0.53-2.25)</td>
</tr>
<tr>
<td>Physical activity (per MET/day)</td>
<td>0.97 (0.94-1.01)</td>
<td>1.01 (0.97-1.05)</td>
</tr>
<tr>
<td>Pulmonary morbidity (vs. none)</td>
<td>2.97 (1.63-5.44)</td>
<td>1.56 (0.87-2.84)</td>
</tr>
<tr>
<td>Mild dyspnea, MD-HAQ score 1.2 vs. score of 0</td>
<td>2.95 (1.83-4.65)</td>
<td>2.72 (1.66-4.48)</td>
</tr>
<tr>
<td><strong>RA Characteristics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radiographic extension (vs. no extension)</td>
<td>1.98 (1.33-2.94)</td>
<td>1.07 (0.73-1.64)</td>
</tr>
<tr>
<td>RA duration (per year)</td>
<td>1.02 (1.00-1.04)</td>
<td>1.03 (0.99-1.07)</td>
</tr>
<tr>
<td>Severe disease (vs. none)</td>
<td>1.57 (0.59-3.55)</td>
<td>0.74 (0.47-1.17)</td>
</tr>
<tr>
<td>MD-HAQ (per unit)</td>
<td>3.98 (2.18-4.36)</td>
<td>2.94 (1.83-4.93)</td>
</tr>
<tr>
<td>Methotrexate use (vs. no)</td>
<td>0.78 (0.32-1.87)</td>
<td>0.68 (0.11-3.43)</td>
</tr>
<tr>
<td>Non-t-bio DMARD use (vs. no)</td>
<td>0.94 (0.53-1.63)</td>
<td>1.48 (0.83-2.65)</td>
</tr>
<tr>
<td>Biological DMARD use (vs. no)</td>
<td>3.86 (2.12-5.06)</td>
<td>1.58 (0.64-2.32)</td>
</tr>
<tr>
<td>Biologic use (vs. no)</td>
<td>1.57 (1.04-2.37)</td>
<td>1.14 (0.73-1.77)</td>
</tr>
</tbody>
</table>

Bold indicates p<0.05
*Pulmonary morbidity was a composite of asthma, chronic obstructive pulmonary disease, history of pneumoconiosis, or interstitial lung disease.
High Incidence of Hepatitis Related to HBV Reactivation in Rheumatoid Arthritis Patients with Resolved Hepatitis B Infection during Rituximab Treatment

Ming-Han Chen$^1$, Yen-Po Tsao$^2$, Yi-Hsiang Huang$^3$, Chung-Tei Chou$^4$ and Chang Youh Tsai$^2$,$^1$Division of Allergy-Immunology- Rheumatology, Department of Medicine, Division of Allergy- Immunology- Rheumatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan,$^2$Division of Allergy- Immunology- Rheumatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan,$^3$Division of Gastroenterology and Hepatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan,$^4$Faculty of Medicine, School of Medicine, National Yang-Ming University, Taipei, Taiwan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Abstract

Background/Purpose: Rituximab-based chemotherapy can induce hepatitis B virus (HBV) reactivation (HBVr) in patients with hematological malignancies who have been exposed to HBV infection. However, informative data regarding the risk of Rituximab on HBVr among patients with rheumatoid arthritis (RA) is unsettled.

Methods: We retrospectively reviewed RA patients in Taipei Veterans General Hospital and patients with available HBV markers before rituximab administration were enrolled. HBVr was defined as either an increase in HBV DNA $>1$ Log10 IU/ml compared with baseline or threefold increase in serum alanine aminotransferase (ALT) level accompanied with HBV DNA $>20,000$ IU/mL in cases without baseline HBV viral load, or hepatitis B surface antigen (HBsAg) reverse seroconversion in HBsAg-negative cases.

Results: Eighty-eight patients were enrolled; 83 (94.3%) were female and the mean age at diagnosis was 54.2 years (Table 1). They received a median of 9 cycles of RTX (range 1-20) without anti-HBV prophylaxis. Four patients were positive for hepatitis B surface antigen (HBsAg) before rituximab administration (Figure 1). In 84 HBsAg-negative patients, 46 were positive for anti-hepatitis B core antigen (anti-HBc), 19 were negative for anti-HBc, and 19 did not have anti-HBc data. Among 46 HBsAg-negative/anti-HBc-positive patients, 31 were hepatitis B surface antibody (anti-HBs)-positive, 6 were anti-HBs-negative, and 9 did not have anti-HBs data. During 10,877 person-months of follow-up, 5 (5.7%) patients developed HBVr. HBVr occurred in 2 (50.0%) of 4 HBsAg-positive patients and the time to HBVr was 40 and 74 months after the start of rituximab, respectively. Among 31 HBsAg-negative/anti-HBc-positive/anti-HBs-positive patients, a decrease in anti-HBs levels was observed in 21 (67.7%) cases after rituximab treatment and anti-HBs disappeared in 6 (19.4%) patients. Three (50.0%) of anti-HBs-disappear patients seroreverted to HBsAg-
positive and all of them developed HBVr later with the mean time from the start of rituximab to HBVr was 59.3 months (range 56-62months).

**Conclusion:** HBVr is common in HBsAg-positive RA patients under rituximab therapy. More importantly, rituximab may lead to high disappearance rate of anti-HBs in resolved HBV cases, resulting in high risk of HBVr. Monitor HBV status frequently is critical in RA patients who have been exposed to HBV infection during rituximab treatment.

Table 1 Characteristics of patients with RA on rituximab

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of diagnosis (years, mean ± SD)</td>
<td>54.2 ± 12.3</td>
</tr>
<tr>
<td>Female (n)</td>
<td>83 (94.3%)</td>
</tr>
<tr>
<td>Duration before rituximab use (years, mean ± SD)</td>
<td>5.4 ± 2.1</td>
</tr>
<tr>
<td><strong>Laboratory profile</strong></td>
<td></td>
</tr>
<tr>
<td>ESR (mm/hour)</td>
<td>56.1 ± 33.4</td>
</tr>
<tr>
<td>CRP (mg/dL)</td>
<td>2.6 ± 2.7</td>
</tr>
<tr>
<td>Rheumatoid factor positive</td>
<td>78/88 (88.6%)</td>
</tr>
<tr>
<td>Anti-CCP antibody positive</td>
<td>45/50 (90.0%)</td>
</tr>
<tr>
<td>DAS28 (ESR)</td>
<td>6.8 ± 0.8</td>
</tr>
<tr>
<td><strong>Comorbidity</strong></td>
<td></td>
</tr>
<tr>
<td>Sjogren’s syndrome</td>
<td>30 (34.1%)</td>
</tr>
<tr>
<td>SLE</td>
<td>7 (8.0%)</td>
</tr>
<tr>
<td>Interstitial lung disease</td>
<td>14 (15.9%)</td>
</tr>
<tr>
<td>Autoimmune hepatitis</td>
<td>1 (1.1%)</td>
</tr>
<tr>
<td>Pulmonary artery hypertension</td>
<td>2 (2.3%)</td>
</tr>
<tr>
<td>Follow up (years, mean ± SD)</td>
<td>10.3 ± 1.6</td>
</tr>
</tbody>
</table>

Disclosure: M. H. Chen, None; Y. P. Tsao, None; Y. H. Huang, None; C. T. Chou, None; C. Y. Tsai, None.


Abstract Number: 2386

The Risk Factors of Newly Developing/Worsening Pulmonary Abnormalities in Rheumatoid Arthritis
Rheumatoid arthritis (RA) is a systemic inflammatory disease that affects various organs including the lung. The pulmonary involvement is critical for prognosis of the patients and decision of the treatment. Moreover, the pulmonary involvement includes many pulmonary abnormalities such as interstitial lung disease (ILD), nodular lesions and airway disease (AD) and shows various patterns in the progression. Treatment of RA patients, according to the risk factors for the newly developing / worsening pulmonary abnormalities would be required. However, it is not fully identified what the risk factors are. The aim of this study is to identify the risk factors for newly developing pulmonary abnormalities in RA patients under the bDMARDs therapy.

Methods: Subjects were consecutive 208 RA patients started treatment with bDMARDs from 2004 to 2015 in our department and received HRCT scan before and after starting the therapy. Pulmonary abnormalities were classified into 4 categories (ILD, nodular lesions, AD and other) and 20 lesions such as ground-glass opacity, reticular pattern, bronchiolitis and bronchiectasis and were recorded in their existence and distribution. Based on the characteristics, clinical features and HR-CT findings, we identified risk factors for newly developing / worsening pulmonary abnormalities which were defined by HRCT findings. For this purpose, logistic regression analysis was conducted.

Results: Subjects were M/F; 64/144, mean age; 59.2 year-old and disease duration; 13.1 years. Pulmonary lesions were found in 146 (70.2%) of RA patients before bDMARDs. (ILD; 38.9%, nodular lesions; 21.6%. AD; 55.3%). AD was commonly found as a common pulmonary lesion in the most of patients with pulmonary abnormalities.

Sequential CT was conducted, the reasons for which were respiratory symptom such as cough in 40% and regular follow up of chest abnormalities in 60%. The intervals of the CT scans are 3.26±2.61 years. Newly developing/worsening pulmonary abnormalities were observed in 13.8 /100 person years. The incidence of ILD, nodular lesions, and AD were 8.5, 2.9 and 6.5 /100 person years, respectively.

The risk factors for newly developing / worsening pulmonary abnormalities were older age, older onset, and pre-existing pulmonary diseases (Odds 5.31), particularly AD (Odds 2.41). MTX was the protective factor (Odds 0.53). Multiple logistic analysis has shown that AD was the only an independent risk factor for newly developing/worsening pulmonary abnormalities(Odds 2.51).

Nine patients died of respiratory failure. The risk factors for fatal respiratory failure were pre-existing pulmonary lesions which were ILD (Odds 28.5) and AD (Odds 8.5), but not nodular lesions. Moreover, newly developing/worsening ILD was the risk factor (Odds 12.3), but not emerging nodular lesions or AD were. In addition, sero-positivity or treatment were not identified as risk factors.

Conclusion: Newly emerging/ worsening pulmonary abnormalities were observed in approximately 14/100 person-years under bDMARDs. The patients with pre-existing pulmonary lesions, particularly ILD and AD should be observed carefully for newly emerging/ worsening ILD.

Disclosure: A. Tanaka, None; K. Kurasawa, None; Y. Takamura, None; T. Miyao, None; R. Yamazaki, None; S. Arai, None; T. Owada, None; R. Maezawa, None; M. Arima, None.
Prevalence of Hepatitis C Virus Infection in Egyptian Patients with Rheumatoid Arthritis

Dahlia Abdel Mohsen, Sherin H. Hamza, Nashwa Aly Morshedy, F. DeWolfe Miller and Mahmoud S. Elzalabany

1Internal Medicine and Rheumatology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt, 2Department of Tropical Medicine, Medical Microbiology and Pharmacology, John A. Burns School of Medicine, University of Hawaii, Honolulu, HI, 3Internal Medicine Department, Ahmed Maher Teaching Hospital, Cairo, Egypt, 4Tahya Misr HCV Treatment Center, Luxor, Egypt

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
HCV is a major public health problem affecting approximately 2-3% of the world’s population with about 130-150 million people chronically infected worldwide. Egypt has the highest HCV prevalence in the world, estimated to be 15% in some studies. Despite this unique HCV epidemic, few studies were done to estimate the prevalence of HCV in Egyptian patients with rheumatoid arthritis (RA). The aim of the current study was to estimate this prevalence.

Methods:
This was a cross sectional study that included 300 Egyptian patients diagnosed with RA according to the ACR/ EULAR 2010 classification criteria. Patients were enrolled from the rheumatology outpatient clinics at Ain Shams University Hospitals and Ahmed Maher Teaching Hospital, Cairo, Egypt, from June 2015 till February 2017. Patients < 18 years old, with end stage renal disease on dialysis, or with other connective tissue diseases were excluded from the study. All participants were tested for HCV antibodies using 3rd generation ELISA and positive patients were tested for HCV RNA by Real Time PCR. DAS28 was used for assessment of RA disease activity.

Results:
HCV antibodies were detected in 15% of patients (45/300), of which 80% were positive for HCV RNA (36/45). The ratio of RNA to antibody is higher compared to general population (66%). Prevalence of HCV antibodies was higher in females than males (15.3% and 12.5%, respectively) and in patients living in rural areas than those living in urban areas (16.7% and 14.6%, respectively). HCV prevalence increased sharply with age to reach 50% in patients older than 60 years (12/24). There was a statistically highly significant increase (p<0.001) in the mean age and RA disease duration in the HCV antibodies positive group (51.1 vs. 41.2 and 11.7 vs. 5.2 years, respectively). According to DAS28; only 33 patients (11%) were in remission. The majority of patients (62.7%) had high disease activity. There was no statistically significant difference (p>0.05) in DAS28 between HCV antibodies positive and negative patients.

While the majority of the patients used a combination of different DMARDs, 14% used a single drug (42/300). The medications used for treatment of RA in the studied patients are shown in Table (1). There was a statistically highly significant decrease in the use of NSAIDs and methotrexate (p<0.001), while there was a statistically highly significant (p<0.001) increase in the use of sulfasalazine in patients positive for HCV antibodies.

Conclusion:
We estimated that the prevalence of HCV antibodies in Egyptian patients with RA is 15%. Given this exceptionally high prevalence, we recommend screening of all RA patients in Egypt for hepatitis C at diagnosis and before starting treatment. Our results also suggest that RA patients have a lower spontaneous clearance of the initial HCV infection.

Table (1): Characteristics of the total study population and HCV antibodies positive and negative patients:
<table>
<thead>
<tr>
<th></th>
<th>All patients (n=300)</th>
<th>HCV Antibodies positive group (n=45)</th>
<th>HCV Antibodies negative group (n=255)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>268 (89.3%)</td>
<td>41 (91.1%)</td>
<td>227 (89.0%)</td>
<td>0.68</td>
</tr>
<tr>
<td>Male</td>
<td>32 (10.7%)</td>
<td>4 (8.9%)</td>
<td>28 (11.0%)</td>
<td></td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Range</td>
<td>18 – 89</td>
<td>24–72</td>
<td>18 – 89</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>42.7 ± 12</td>
<td>51.1 ± 12.6</td>
<td>41.2 ± 11.5</td>
<td></td>
</tr>
<tr>
<td><strong>Address</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.69</td>
</tr>
<tr>
<td>Urban</td>
<td>240 (80%)</td>
<td>35 (77.8%)</td>
<td>205 (80.4%)</td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>60 (20%)</td>
<td>10 (22.2%)</td>
<td>50 (19.6%)</td>
<td></td>
</tr>
<tr>
<td><strong>RA disease duration (Years)</strong></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Range</td>
<td>1 – 45</td>
<td>0 – 45</td>
<td>0 – 25</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>6.2 ± 7.4</td>
<td>11.7 ± 12.8</td>
<td>5.2 ± 5.5</td>
<td></td>
</tr>
<tr>
<td><strong>DAS28 Score</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.26</td>
</tr>
<tr>
<td>Range</td>
<td>0.97 - 9.27</td>
<td>1.85 - 8.96</td>
<td>0.97 - 9.27</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>5.6 ± 2</td>
<td>5.3 ± 2.2</td>
<td>5.7 ± 2</td>
<td></td>
</tr>
<tr>
<td><strong>Medications</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSAIDs</td>
<td>186 (62%)</td>
<td>13 (28.9%)</td>
<td>173 (67.8%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>278 (92.7%)</td>
<td>43 (95.6%)</td>
<td>235 (92.2%)</td>
<td>0.42</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>170 (56.7%)</td>
<td>14 (31.1%)</td>
<td>156 (61.2%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>122 (40.7%)</td>
<td>19 (42.2%)</td>
<td>103 (40.4%)</td>
<td>0.82</td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>48 (16%)</td>
<td>18 (40.0%)</td>
<td>30 (11.8%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>264 (88%)</td>
<td>42 (93.3%)</td>
<td>222 (87.1%)</td>
<td>0.23</td>
</tr>
<tr>
<td>Biologic DMARDs</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td><strong>Rheumatoid Factor</strong></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Negative</td>
<td>122 (40.7%)</td>
<td>8 (17.8%)</td>
<td>114 (44.7%)</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>178 (59.3%)</td>
<td>37 (82.2%)</td>
<td>141 (55.3%)</td>
<td></td>
</tr>
<tr>
<td><strong>Anti-CCP (n=128)</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.80</td>
</tr>
<tr>
<td>Negative</td>
<td>70 (54.7%)</td>
<td>12 (57.1%)</td>
<td>58 (54.2%)</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>58 (45.3%)</td>
<td>9 (42.9%)</td>
<td>49 (45.8%)</td>
<td></td>
</tr>
<tr>
<td><strong>Other Laboratory tests</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin (mg/dl)</td>
<td>12 ± 1.5</td>
<td>12.5 ± 1.6</td>
<td>11.9 ± 1.5</td>
<td>0.015</td>
</tr>
<tr>
<td>WBCs (x10^3 cells/mm^3)</td>
<td>7.1 ± 2.44</td>
<td>7.6 ± 2.2</td>
<td>7.1 ± 2.5</td>
<td>0.19</td>
</tr>
<tr>
<td>PLT (x10^3 cells/mm^3)</td>
<td>301 ± 91.76</td>
<td>293 ± 111</td>
<td>302 ± 88</td>
<td>0.54</td>
</tr>
<tr>
<td>ESR (mm/hour)</td>
<td>45.8 ± 25.55</td>
<td>45.8 ± 24.4</td>
<td>45.8 ± 25.8</td>
<td>0.99</td>
</tr>
<tr>
<td>ALT (IU/ml)</td>
<td>21.1 ± 10</td>
<td>27.2 ± 17.7</td>
<td>20 ± 7.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AST (IU/ml)</td>
<td>21.2 ± 9.3</td>
<td>29 ± 16.2</td>
<td>19.9 ± 6.6</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Disclosure: D. Abdel Mohsen, None; S. H. Hamza, None; N. A. Morshedy, None; F. D. Miller, None; M. S. Elzalabany, None.


Abstract Number: 2388

**Women and Men with Rheumatoid Arthritis Present with Different Risks for Glucocorticoid-Related Comorbidities**

Dörte Huscher¹, Katinka Albrecht¹, Frank Buttgereit², Thorsten Eidner³, Stefan Kleinert⁴, Wolfgang Ochs⁵ and Angela Zink⁶, ¹Epidemiology Unit, German Rheumatism Research Centre (DRFZ), Berlin, Germany, ²Department of Rheumatology and Clinical Immunology, Charité Univeris, Berlin, Germany, ³Rheumatology/ Osteology, Friedrich-Schiller-University Jena, University Clinic, Jena, Germany, ⁴Rheumatologie, Praxisgemeinschaft Rheumatologie-Nephrologie, Rheumatologische Schwerpunktpraxis, Erlangen, Germany, ⁵Internistisch-rheumatologische Praxisgemeinschaft Bayreuth, Bayreuth, Germany, ⁶Epidemiology Unit / Rheumatology and Clinical Immunology, German Rheumatism Research Centre (DRFZ) / Charité University Hospital, Berlin, Germany

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Tuesday, November 7, 2017

Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities

Session Type: ACR Poster Session C

Session Time: 9:00AM-11:00AM

Background/Purpose: Osteoporosis, diabetes, hypertension and cardiovascular diseases are the most threatening glucocorticoid (GC)-related comorbidities in rheumatoid arthritis (RA), both from the patients and rheumatologists perspective¹. The aim of the study was to evaluate gender differences in the prevalence of GC-related comorbidities in patients with RA in the National Database of the German Collaborative Arthritis Centres.

Methods: Cross-sectional data of patients with RA with valid information on body mass index (BMI) and comorbidities (n=4,438) were analysed regarding the prevalence of osteoporosis, diabetes, cardiac disease and hypertension in women and men, stratified by age, BMI, disease activity (DAS28), education, smoking and GC use (no/≤5/>5-7.5/>7.5mg prednisone-equivalent per day). Gender differences were compared to those in the age-matched general population. Uni- and multivariable logistic regression analysis was applied to examine background risks in women and men.

Results: Data of 3,353 women and 1,085 men were available for analysis. Osteoporosis was more frequent in female (17.9% vs. 9.2%) while diabetes (10.3% vs. 15.9%), cardiac disease (9.4% vs. 18.3%) and hypertension (36.4% vs. 42.3%) were more often reported in male patients. Compared to the general population, the gender difference was 2.5 times higher for hypertension, 1.8-fold for diabetes, 1.2-fold for cardiac disease and 0.9-fold for osteoporosis. The differences persisted after stratification for GC use, disease activity, age BMI, smoking and education (Table 1). After controlling for these factors in multivariable analysis, women still had more osteoporosis (OR 2.06 [1.59-2.68]) and less diabetes (OR 0.65 [0.52-0.81]) or cardiac disease (OR 0.48 [0.38-0.61]).

Conclusion: After controlling for GC use and dosage, age, lifestyle and socioeconomic factors, gender was independently associated with comorbidities that may be GC-related. We found more cardiac diseases, hypertension and diabetes in men and more osteoporosis in women. Except for osteoporosis, the gender differences for these comorbidities were higher in RA patients than in the general population.

1 Van der Goes MC, Jacobs JW, Boers M, et al. Patient and rheumatologist perspectives on glucocorticoids: an exercise to improve the implementation of the European League Against Rheumatism (EULAR) recommendations on the

Table 1 Prevalence of comorbidities in female (F) and male (M) RA patients by categories of GC use, disease activity, age, BMI, smoking and educational status

<table>
<thead>
<tr>
<th>GCs, mg/d</th>
<th>Prevalence of GC-related comorbidities (%)</th>
<th>Osteoporosis</th>
<th>Diabetes</th>
<th>Hypertension</th>
<th>Cardiac disease</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F</td>
<td>M</td>
<td>F</td>
<td>M</td>
<td>F</td>
</tr>
<tr>
<td>none</td>
<td>14.5</td>
<td>6.5</td>
<td>9.6</td>
<td>16.1</td>
<td>33.0</td>
</tr>
<tr>
<td>≤5</td>
<td>22.5</td>
<td>12.6</td>
<td>10.7</td>
<td>13.8</td>
<td>40.6</td>
</tr>
<tr>
<td>&gt;5-7.5</td>
<td>17.9</td>
<td>9.1</td>
<td>11.4</td>
<td>24.2</td>
<td>40.8</td>
</tr>
<tr>
<td>&gt;7.5</td>
<td>18.7</td>
<td>11.1</td>
<td>13.4</td>
<td>16.0</td>
<td>36.9</td>
</tr>
<tr>
<td>DAS28 (ESR)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;3.2</td>
<td>15.8</td>
<td>7.3</td>
<td>8.1</td>
<td>13.6</td>
<td>31.5</td>
</tr>
<tr>
<td>3.2-5.1</td>
<td>20.1</td>
<td>13.3</td>
<td>13.5</td>
<td>21.9</td>
<td>43.8</td>
</tr>
<tr>
<td>&gt;5.1</td>
<td>19.7</td>
<td>9.9</td>
<td>14.8</td>
<td>11.8</td>
<td>44.3</td>
</tr>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;50</td>
<td>2.6</td>
<td>3.3</td>
<td>3.4</td>
<td>5.0</td>
<td>9.4</td>
</tr>
<tr>
<td>50-70</td>
<td>13.9</td>
<td>8.9</td>
<td>8.5</td>
<td>14.4</td>
<td>35.0</td>
</tr>
<tr>
<td>&gt;70</td>
<td>31.3</td>
<td>11.2</td>
<td>16.4</td>
<td>20.8</td>
<td>52.5</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;18.5</td>
<td>18.8</td>
<td>-</td>
<td>5.9</td>
<td>-</td>
<td>21.2</td>
</tr>
<tr>
<td>18.5-&lt;25</td>
<td>20.3</td>
<td>13.0</td>
<td>5.9</td>
<td>10.5</td>
<td>25.1</td>
</tr>
<tr>
<td>25-&lt;30</td>
<td>16.4</td>
<td>8.1</td>
<td>11.5</td>
<td>16.4</td>
<td>42.0</td>
</tr>
<tr>
<td>≥30</td>
<td>14.7</td>
<td>5.2</td>
<td>18.9</td>
<td>23.8</td>
<td>55.0</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>current</td>
<td>9.5</td>
<td>8.9</td>
<td>6.9</td>
<td>9.7</td>
<td>27.4</td>
</tr>
<tr>
<td>former</td>
<td>16.3</td>
<td>11.2</td>
<td>11.1</td>
<td>19.7</td>
<td>38.7</td>
</tr>
<tr>
<td>never</td>
<td>20.9</td>
<td>8.1</td>
<td>10.4</td>
<td>15.4</td>
<td>39.5</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;9 years</td>
<td>25.6</td>
<td>10.5</td>
<td>16.0</td>
<td>20.9</td>
<td>49.2</td>
</tr>
<tr>
<td>10-13 years</td>
<td>16.9</td>
<td>9.8</td>
<td>10.3</td>
<td>15.6</td>
<td>38.2</td>
</tr>
<tr>
<td>≥14 years</td>
<td>12.2</td>
<td>6.8</td>
<td>5.0</td>
<td>14.6</td>
<td>24.6</td>
</tr>
</tbody>
</table>

- Due to small case numbers (n<50) prevalence rates have been omitted.

Disclosure: D. Huscher, None; K. Albrecht, None; F. Buttgeret, None; T. Eidner, None; S. Kleinert, None; W. Ochs, None; A. Zink, AbbVie, BMS, MSD, Pfizer, Roche, UCB, 8.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/women-and-men-with-rheumatoid-arthritis-present-with-different-risks-for-glucocorticoid-related-comorbidities

Abstract Number: 2389

**Joint Surgery in Rheumatoid Arthritis 1980-2013: A Population-Based Study to Identify Risk Factors and Time Trends in Incidence**

Michael Richter¹, Cynthia S. Crowson², Eric L. Matteson³ and Ashima Makol³, ¹Internal Medicine, Mayo Clinic, Rochester, MN, ²Department of Medicine, Division of Rheumatology, Mayo Clinic, Rochester, MN, ³Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, MN

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Over the past two decades, the use of disease modifying anti-rheumatic drugs and treat-to-target strategies have dramatically improved the outcomes of patients with rheumatoid arthritis (RA). This has led to a decline in the rate of joint surgery, which is traditionally reserved for treatment of refractory patients aiming to improve function and quality of life. The goal of this study was to identify risk factors for joint surgery in RA and assess trends in surgery rates over time.

Methods: A retrospective medical record review was performed of all orthopedic surgeries following first fulfillment of 1987 ACR criteria for adult-onset RA in 1980-2013 among residents of a geographically defined area with follow up until death, migration or July 1, 2016. Surgeries were classified as small (wrist, hand, foot) or large (shoulder, elbow, hip, knee, ankle) joint. Risk factors were examined using Cox models adjusted for age, sex and calendar year of RA incidence.

Results: A total of 1077 patients with RA (mean age (±SD) 55.9±15.6 years, 69% female, 66% RF and/or ACPA positive) were followed for a median follow-up of 10.7 years during which 112 and 204 underwent at least one joint small and large joint surgery, respectively. Results of risk factor analysis for joint surgery at RA incidence and during follow up are shown in table 1. Advanced age (per 10 year increase) was associated with an increased risk for both small joint surgery (SJS) and large joint surgery (LJS). Other significant risk factors at the time of RA incidence included rheumatoid factor and anti-CCP antibody positivity for both SJS and LJS, and BMI≥30 kg/m² for LJS. Significant risk factors for SJS and LJS at any time during follow-up included the presence of radiographic erosions or destructive changes, large joint swelling, and methotrexate use. The use of glucocorticoids was associated with increased risk of LJS only. There was a decreased rate of SJS by calendar year of incidence (1994-2013 vs 1980-1993) (hazard ratio 0.53; p=0.001), and a significant decline in SJS incidence after 1995 with less than 1% of patients having surgery each year by the end of the study period (Figure). There were no significant trends in LJS over time.

Conclusion: There has been a significant decline in the incidence of SJS in RA but no change in the rate of LJS. Positive serologies, rheumatoid nodulosis, and radiographic erosions are strong predictors for SJS, but are also associated with increased risk for LJS. Increasing age and obesity are predictive of LJS, similar to the general population.

Table 1. Risk factors for joint surgery at RA incidence

<table>
<thead>
<tr>
<th>Characteristics at RA incidence</th>
<th>Small joint surgery</th>
<th>Large joint surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hazard ratio* (95% CI)</td>
<td>P value (95% CI)</td>
</tr>
<tr>
<td>Age (per 10 year increase)</td>
<td>0.84 (0.74, 0.96)</td>
<td>0.009</td>
</tr>
<tr>
<td>Sex, female</td>
<td>1.87 (1.17, 2.99)</td>
<td>0.008</td>
</tr>
<tr>
<td>Calendar year (1994-2013 vs 1980-1993)</td>
<td>0.53 (0.36, 0.78)</td>
<td>0.001</td>
</tr>
<tr>
<td>ESR at index (per 10 mm/1 hr)</td>
<td>1.02 (0.92, 1.13)</td>
<td>0.569</td>
</tr>
<tr>
<td>RF and/or CCP positive</td>
<td>2.47 (1.52, 4.01)</td>
<td>0.001</td>
</tr>
<tr>
<td>Current smoker</td>
<td>1.18 (0.77, 1.83)</td>
<td>0.168</td>
</tr>
<tr>
<td>Ever smoking</td>
<td>1.43 (0.97, 2.11)</td>
<td>0.069</td>
</tr>
<tr>
<td>Obesity (BMI≥30 kg/m²)</td>
<td>0.77 (0.49, 1.20)</td>
<td>0.254</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time-dependent Characteristics</th>
<th>Small joint surgery</th>
<th>Large joint surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid Nodules</td>
<td>3.32 (2.27, 4.87)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Erosions/ destructive changes</td>
<td>4.55 (2.93, 7.05)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Large joint swelling</td>
<td>1.61 (1.01, 2.58)</td>
<td>0.047</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>1.64 (1.08, 2.48)</td>
<td>0.019</td>
</tr>
<tr>
<td>Other DMARD</td>
<td>1.87 (1.18, 2.98)</td>
<td>0.008</td>
</tr>
<tr>
<td>Glucocorticoids</td>
<td>1.32 (0.87, 2.01)</td>
<td>0.196</td>
</tr>
</tbody>
</table>

*adjusted for age, sex and calendar year of RA incidence. p <0.05 considered statistically significant.
Trends and Predictors of Guideline Adherence for Glucocorticoid-Induced Osteoporosis Prevention in an Early Rheumatoid Arthritis Cohort

Stephanie Gottheil¹, Orit Schieir², Carter Thorne³, Carol A Hitchon⁴, Diane Tin⁵, Edward C. Keystone⁶, Gilles Boire⁷, Boulos Haraoui⁸, Susan J. Bartlen⁹, Vivian P. Bykerk¹⁰ and Janet E. Pope¹¹, ¹University of Western Ontario, LONDON, ON, Canada, ²McGill University, Montreal, ON, Canada, ³University of Toronto, Newmarket, ON, Canada, ⁴University of Manitoba, Winnipeg, MB, Canada, ⁵The Arthritis Program, Southlake Regional Health Centre, Newmarket, ON, Canada, ⁶Mt. Sinai Hospital, University of Toronto, Toronto, ON, Canada, ⁷Rheumatology Division, Centre Hospitalier Universitaire de Sherbrooke and Universite de Sherbrooke, Sherbrooke, QC, Canada, ⁸Institute de Rheumatologie, Montreal, QC, Canada, ⁹Department of Medicine, Division of ClinEpi, Rheumatology, Respirology, McGill University, Montreal, QC, Canada, ¹⁰2-005, Mt Sinai Hospital, Toronto, ON, Canada, ¹¹Department of Medicine, Division of Rheumatology, University of Western Ontario, St Joseph's Health Care, London, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
RA patients are at a high risk of osteoporosis and fracture, in part due to frequent glucocorticoid use. Despite recommendations from ACR guidelines on prevention of glucocorticoid-induced osteoporosis (GIOP), use of anti-
osteoporotic medication (AOM) in RA patients remains low. The current study aimed to analyze trends in AOM use over the past 10 years among early RA patients meeting guidelines for GIOP prevention, and to examine predictors of guideline adherence among this population.

Methods:

Data were obtained from a multi-center prospective cohort study of early RA patients. This analysis included participants over age 50, without a diagnosis of osteoporosis at baseline, with at least 6 months of follow up. GIOP guideline adherence was determined based on use of bisphosphonate or denosumab in patients receiving ≥ 7.5 mg prednisone daily for > 3 months. Logistic regression was used to determine predictors of guideline adherence adjusting for age, gender, ethnicity, comorbidities, BMI, average glucocorticoid dose, and baseline DAS28-ESR.

Results:

1468 patients were included with mean age 63 (9), 933 (64%) were female, and mean (sd) DAS28-ESR was 5.0 (1.4). 282 (19%) patients received ≥ 7.5 mg prednisone daily for > 3 months, and this number decreased over time (Figure 1A). Overall, only 54 (19%) eligible patients received AOM (Figure 1B), and 105 (37%) received Vitamin D. Chi square analyses showed a significantly higher likelihood of AOM and Vitamin D use in patients on chronic glucocorticoids. In logistic regression analyses, baseline DAS28 significantly predicted guideline adherence, while BMI and glucocorticoid dose showed trends towards significance.

Conclusion:

In this national early RA cohort, approximately 1 in 5 patients met criteria for GIOP prevention according to ACR guidelines. Chronic use of glucocorticoids did decrease over time, suggesting either less frequent use or faster tapering. Adherence to GIOP prevention guidelines was suboptimal and did not change over time. Higher disease activity was significantly associated with guideline adherence. Further research is needed to determine reasons for guideline nonadherence and to develop strategies to improve prevention of GIOP.
Incidence of Infections in Early Arthritis

Meriem Kerbachi¹, Louis Bessette², Cristiano S. Moura³, Sasha Bernatsky⁴, Orit Schieir⁵, Susan J. Bartlett⁶, Carol A Hitchon⁷, Janet E. Pope⁸, Gilles Boire⁹, Boulos Haraoui¹⁰, Edward C. Keystone¹¹, Diane Tin¹², Carter Thorne¹³ and Vivian P. Bykerk¹⁴, ¹McGill University, Montreal, QC, Canada, ²Centre d'ostéoporose et de rhumatologie de Québec.

Figure 1A. The percentage of patients on ≥7.5 mg prednisone daily for >3 months by year of enrollment. Dotted line represents the publication of ACR guideline on GIMP prevention (2010).

Figure 1B. The percentage of patients on ≥7.5 mg prednisone daily for >3 months by year of enrollment who also received prescription for bisphosphonate or denosumab.
SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Few studies have focused on analyzing infection risk in recent-onset rheumatoid arthritis (RA). The main objective of this study was to estimate the incidence of infections in patients with early RA, focusing on a multi-centre Canadian cohort of RA patients enrolled within 12 months of symptom onset.

Methods: All patients with early RA (<1 year) enrolled in the cohort were studied. Infections have been reported in a standardized manner by patients at yearly assessments. In each year, a patient was allowed to contribute more than one infection event, provided the event was a new or recurrent (not chronic) infection. From January 2007 to November 2015, we tabulated the total number of infections and generated incidence rates of infections with 95% confidence intervals (CI)

Results: A total of 1728 RA patients met study criteria and were followed for an average of 3.2 years. At the time of recruitment, mean (standard deviation, SD) age was 54.2 years (15.0), majority were Caucasian (N=1,419, 82.1%) and female (N= 1,245, 72.0%). Mean symptom duration at cohort entry was 5.8 months (3.0). The mean Disease Activity Score 28 was 5.1 (1.4), Simplified Disease Activity Index 28.6 (15.2) and Clinical Disease Activity Index 27.1 (14.4). One third (571, 33%) of these patients were on steroids at baseline and most (N= 1,566, 90.6%) were on DMARDs, with 1,262 (73.0%) patients having been exposed to MTX. Biologics were used only by 41 (2.37%) patients at the time of cohort entry.

Over the study interval, we recorded 452 infections over a total of 5,525 person-years (81.8 events per 1000 patient-years) and over a quarter of these (125 events) involved hospitalization. Eighty four (18%) of all infectious episodes were pneumonia (15.2 events per 1,000 patient years), with half of these pneumonias being associated with a hospitalization.

Conclusion: Reported infections in this Canadian cohort with early RA was not negligible. Half of reported pneumonia events in early RA involved hospitalization.

Disclosure: M. Kerbachi, None; L. Bessette, None; C. S. Moura, None; S. Bernatsky, None; O. Schieir, None; S. J. Bartlett, PROMIS, 6; Pfizer, UCB, Lilly, 5; C. A. Hitchen, ILAR, 2; J. E. Pope, AbbVie, Amgen, Bayer, BMS, Celtrion, Eli Lilly and Company, Merck, Novartis, Pfizer, Roche, UCB, 5, Amgen, Bayer, BMS, GSK, Merck, Novartis, Pfizer, Roche, UCB, 2; G. Boire, None; B. Harraoui, None; E. C. Keystone, Pfizer, Roche, Janssen, Amgen, BMS, Merck. Merck, Celltrion, Samsung Bioepis, 5; D. Tin, None; C. Thorne, AbbVie, Amgen, Celgene, Lilly, Novartis, Pfizer, Sanofi, and UCB; has served as a consultant for AbbVie, Amgen, Celgene, Centocor, Genzyme, Hospira, Janssen, Lilly, Medexus/Medac, Merck, Novartis, Pfizer, Sanofi, and UCB, 2, Medexus/Medac, 8; V. P. Bykerk, Amgen, Bristol-Myers Squibb Company, Gilead, Sanofi-Genzyme/Regeneron, Pfizer Pharmaceuticals, UCB, 5.
Impact of the Pattern of Interstitial Lung Disease on Mortality in Rheumatoid Arthritis: A Systematic Review and Meta-Analysis

Namrata Singh1, Jimmy Varghese2, Bryant R. England3, Joshua J. Solomon4, Kaleb Michaud5, Ted R. Mikuls6 and Marin Schweizer7, 1Internal Medicine, University of Iowa Hospitals and Clinics and Iowa City VA, Iowa City, IA, 2Internal Medicine, University of Iowa Hospitals and Clinics, Iowa City, IA, 3Division of Rheumatology & Immunology, Department of Internal Medicine, Nebraska-Western IA VA Health Care System & University of Nebraska Medical Center, Omaha, NE, 4Division of Pulmonary and Critical Care Medicine, National Jewish Health, Denver, CO, 5University of Nebraska Medical Center, Omaha, NE, 6Internal Medicine, Division of Rheumatology, University of Nebraska Medical Center, Omaha, NE, 7Internal Medicine, Iowa City VA, Iowa City, IA

First publication: September 18, 2017

SESSON INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

ABSTRACT

Impact of the Pattern of Interstitial Lung Disease on Mortality in Rheumatoid Arthritis: A systematic review and meta-analysis

Background/Purpose: Interstitial lung disease affects 10-15% of rheumatoid arthritis (RA) patients and carries poor prognosis with a median survival of less than 3 years following diagnosis. ILD can be classified into distinct patterns based on computed tomography or lung histopathology, with the usual interstitial pneumonia (UIP) pattern being the most common. While some studies have shown the UIP pattern to have a higher mortality risk, other studies have not found this association. The purpose of this study was to complete a systematic review and meta-analysis of the association between RA-ILD pattern and mortality risk.

Methods: Pubmed and Embase databases were searched for relevant, published articles from their inception to March 1st, 2017 using the PRISMA guidelines. The MeSH terms used for the search were “rheumatoid arthritis” and “interstitial lung disease”. Inclusion criteria were assessment of ILD pattern (either radiographically or based on histopathology) as a predictor of mortality in RA patients. Studies of connective tissue disease ILD without separate analysis of RA patients were excluded. No exclusions were made based on study design, quality of the study or duration of follow-up. Data was pooled using a random effects model with inverse variance weighting. Cochran’s Q statistic and $I^2$ test were used to test for heterogeneity among the studies. The Newcastle-Ottawa scale (NOS) was used to assess the risk of bias among the included studies.

Results: Five studies fulfilled inclusion and exclusion criteria. Two of the five studies found UIP pattern to be significantly associated with worse survival. In a meta-analytic approach, the UIP pattern was associated with a 2-fold increased risk of mortality (pooled risk ratio=2.03; 95% confidence interval=1.13, 3.66) (Figure 1). The results of the meta-analysis were heterogeneous, $I^2=67\%$ (p=0.02), with risk ratios for the UIP pattern ranging from 1.09 to 8.62. Three of the five studies were of high quality based on the NOS.
Conclusion: Using a meta-analytic approach, we found UIP pattern to be associated with higher mortality risk. However, there was substantial heterogeneity between studies and a limited number of studies investigating ILD pattern and mortality risk. Further study of mortality risk in RA-ILD is needed with standardized assessment of other RA and patient related factors such as age, gender, smoking history, autoantibody expression, disease activity and pulmonary function tests.

Figure 1. Pooled effect estimate of rheumatoid arthritis interstitial lung disease pattern and mortality risk.

Disclosure: N. Singh, None; J. Varghese, None; B. R. England, None; J. J. Solomon, None; K. Michaud, None; T. R. Mikuls, BMS, 2, Ironwood Pharm, 2, Pfizer Inc, 5, NIH, VA, 2; M. Schweizer, None.


Abstract Number: 2393

Evaluation of Live Zoster Vaccine in a Subset of Patients with Rheumatoid Arthritis Treated with Tofacitinib with or without Methotrexate, and Adalimumab with Methotrexate: Results from a Phase 3b/4 Randomized Trial

Leonard H. Calabrese1, Carlos Abud-Mendoza2, Stephen Lindsey3, Sang Heon Lee4, Liza Takiya5, Noriko Iikuni6, Koshika Soma7, Zhen Luo8 and Roy Fleischmann9, 1Cleveland Clinic Foundation, Cleveland, OH, 2Hospital Central, San Luis Potosi, Mexico, 3Ochsner Medical Center, Baton Rouge, LA, 4Konkuk University School of Medicine, Seoul, Korea, Republic of (South), 5Pfizer Inc, Collegeville, PA, 6Pfizer Inc, New York, NY, 7Pfizer Inc, Groton, CT, 8Pfizer Inc, Shanghai, China, 9Metroplex Clinical Research Center and University of Texas Southwestern Medical Center, Dallas, TX

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). Patients (pts) with RA are at increased risk for herpes zoster (HZ), which is further increased with tofacitinib treatment.1 In a subset of pts in the ORAL Strategy2 randomized controlled trial (RCT), we evaluated the effect of live zoster vaccination (LZV) on HZ rates in methotrexate inadequate responder (MTX-IR) pts with RA who received tofacitinib with or without MTX, or adalimumab (ADA) with MTX.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Log(Risk Ratio)</th>
<th>SE Weight</th>
<th>Risk Ratio</th>
<th>95% CI</th>
<th>Risk Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lee</td>
<td>1.3858185</td>
<td>1.395726</td>
<td>7.00 (4.45, 10.93)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Namul</td>
<td>0.605068</td>
<td>0.29764</td>
<td>2.22 (1.49, 3.26)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solomon</td>
<td>0.896402</td>
<td>0.34675</td>
<td>3.43 (2.51, 4.73)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tsutakawa</td>
<td>2.184165</td>
<td>0.664855</td>
<td>8.32 (3.34, 21.74)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zimmerman-Lopez</td>
<td>0.60665952</td>
<td>0.1002775</td>
<td>2.03 (1.13, 3.66)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Test for overall effect: Z = 2.35 (p = 0.02)

1Cleveland Clinic Foundation, Cleveland, OH, 2Hospital Central, San Luis Potosi, Mexico, 3Ochsner Medical Center, Baton Rouge, LA, 4Konkuk University School of Medicine, Seoul, Korea, Republic of (South), 5Pfizer Inc, Collegeville, PA, 6Pfizer Inc, New York, NY, 7Pfizer Inc, Groton, CT, 8Pfizer Inc, Shanghai, China, 9Metroplex Clinical Research Center and University of Texas Southwestern Medical Center, Dallas, TX

First publication: September 18, 2017
Methods: ORAL Strategy (NCT02187055) was a Phase 3b/4, 1-year, triple-dummy, active-comparator-controlled RCT. Pts were randomized 1:1:1 to receive tofacitinib 5 mg twice daily (BID; tofa mono), tofacitinib 5 mg BID + MTX (tofa+MTX), or subcutaneous ADA 40 mg every other week + MTX (ADA+MTX); target MTX dose was 15–25 mg/week. In countries where LZV was available, pts who were ≥50 years old received LZV at the investigator’s discretion, 28 days before the first dose of study drug. HZ incidence rates (IR; pts with events per 100 pt-years) and 95% confidence intervals (CI) were calculated for each treatment arm and for vaccinated vs non-vaccinated pts.

Results: Of 1146 pts who received study drug (mean age: 50.1 years old), 216 received LZV (proportion of pts who received LZV by treatment group: tofa mono: 18.0%; tofa+MTX: 19.9%; ADA+MTX: 18.7%) 28 days before randomization in this RCT; 30 pts self-reported prior vaccination (Table). No pts had zoster-like lesions within 42 days of vaccination; 1 pt had vaccination site erythema. In the overall study population, HZ IR was similar between tofa mono and ADA+MTX, and numerically higher (overlapping CIs) with tofa+MTX. IRs were generally similar for pts who received LZV (18.8% of pts were vaccinated) vs those who did not (81.2%) (Table). Overall, 18/1146 pts had HZ. Among vaccinated pts, 3 (1.4%) had HZ: no events were serious, and 1 (0.5%) event was multidermatomal (with tofa mono). Among pts not vaccinated, 15 (1.6%) had HZ: there were 2 (0.2%) serious HZ events (tofa+MTX: n=1; ADA+MTX: n=1) and 3 (0.3%) multidermatomal events (tofa mono: n=1; ADA+MTX: n=2).

Conclusion: In MTX-IR pts with RA, LZV was well-tolerated. HZ IR was numerically similar between tofa mono and ADA+MTX, and higher with tofa+MTX. HZ rates were generally similar in pts who received LZV vs those not vaccinated. LZV has shown efficacy in prevention of HZ in 51% (pts ≥60 years old) and 70% (50–59 years old) of immunocompetent adults. Efficacy of LZV could not be fully evaluated as a minority (<20%) of pts received LZV and not all geographic regions studied in other tofacitinib studies were represented.

References:

Disclosure: L. H. Calabrese, Celgene, Crescendo, 2,Celgene, Crescendo, 5,Celgene, Crescendo, 8; C. Abud-Mendoza, Bristol-Myers Squibb, Pfizer Inc, Roche, 5,Bristol-Myers Squibb, Merck-Serono, Pfizer Inc, Roche, UCB, 8; S. Lindsey, Pfizer Inc, 8; S. H. Lee, None; L. Takiya, Pfizer Inc, 1,Pfizer Inc, 3; N. Ikukuni, Pfizer Inc, 1,Pfizer Inc, 3; K. Soma, Pfizer Inc, 1,Pfizer Inc, 3; Z. Luo, Pfizer Inc, 1,Pfizer Inc, 3; R. Fleischmann, AbbVie, Pfizer Inc, UCB, 2,AbbVie, Pfizer Inc, UCB, 5.

Abstract Number: 2394

Differential Effect of Corticosteroids and Biological Dmards on Five-Year Radiographic Progression in Rheumatoid Arthritis: Results from a Weighted Cumulative Exposure Model Developed on the Espoir Cohort

Baptiste Louveau¹, Yann De Rycke¹, Alexandre Lafourcade¹, Alain Saraux², Francis Guillemin³, Florence Tubach⁴, Bruno Fautrel⁵ and David Hajage¹, ¹APHP, Pitié Salpêtrière Hospital, Département Biostatistics and Public health, Pharmacoépidémiology center (Cephepi), 75018 75013, Paris, France, Paris, France, ²Rheumatology Department, CHU de la Cavale Blanche, Brest, France, Brest Cedex, France, ³University of Lorraine, Nancy, France, Nancy, France, ⁴Université Pierre et Marie Curie (UPMC)-Paris 6; APHP, Pitié Salpêtrière Hospital, Département Biostatistics and Public health, Pharmacoépidémiology center (Cephepi), 75018 75013, Paris, France, Paris, France, ⁵UPMC University Paris 06, Pitié-Salpêtrière Hospital, Paris, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: In rheumatoid arthritis (RA), a strategic approach to achieve low-disease activity or remission is now recommended. Controlling joint damage is thus an important concern in daily clinical practice and models are needed to assess predictive variables associated with radiographic progression. Nevertheless, the role of treatments regarding to this event has rarely been questioned and none of models built so far have properly considered exposition to treatments. Therapeutic regimens have often been described as a binary variable or as a mean dose which do not represent correctly drug exposure. In RA, treatment is composed of two types of drugs undergoing multiple switches and dose adjustments: 1) DMARDs and 2) Corticosteroids. If the risk of radiographic progression is related to factors of severity at diagnosis, predictive models must consider variables reflecting the complexity of drug exposure.

This study aims to develop a predictive model of five-year radiographic progression considering both baseline characteristics and time-varying drug exposure to corticosteroids and DMARDs.

Methods: Our study population was composed of 403 patients of the ESPOIR cohort with radiographic data at inclusion and at five years of follow-up and classified as RA at the inclusion visit according to the 1987 ACR and 2010 ACR/EULAR criteria. Radiographic progression was defined at 5 years as a change in the Sharp/van der Heidje score (vSHS) ≥ 5. A predictive model considering baseline characteristics and treatments as weighted cumulative exposure (WCE) variables was built. A WCE variable represents drug exposure as the weighted sum of past doses and is able to model complex profile of therapeutic regimens. It allowed the estimation of risks associated to different profiles of drug exposure with adjustments on baseline characteristics.

Results: Radiographic progression occurred in 35.5% (143/403) patients. The multivariate model included ACPA status, ESR, swollen joint count and erosion score as baseline predictors and corticosteroids, MTX/LEF and biological DMARDs (bDMARDs) as WCE variables. These baseline characteristics were consistent with the literature. Thirty-six months exposure to bDMARDs had a significant protective effect on radiographic progression. On the other hand, a significant deleterious effect was described for recent cumulative exposure (3 months or less) to corticosteroids (Table 1).

Conclusion: The analysis of therapeutic regimens as WCE variables brought new insights on the role of DMARDs and corticosteroids on radiographic progression. If the significant protective effect of bDMARDs has been confirmed, considering corticosteroids as a WCE variable demonstrated their deleterious effect on radiographic progression.
Despite cautious consideration, these results contradict many clinical trials in which corticosteroids have been found protective.

**Disclosure:** B. Louveau, None; Y. De Rycke, None; A. Lafourcade, None; A. Sarau, None; F. Guillemin, None; F. Tubach, None; B. Fautrel, AbbVie, Biogen, BMS, Celgene, Hospira, Janssen, Eli Lilly and Company, Novartis, Pfizer, Roche, SOBI Pharma, UCB, 5; D. Hajage, None.


**Abstract Number:** 2395

**Recommendations on the Management of Rheumatoid Arthritis in Patients with Cancer: A Systematic Review of Clinical Practice Guidelines and Consensus Statements**

Maria A. Lopez-Olivo1, Ines Colmegna2, Aliza Matusevich1, Susan Ruyu Qi3, Natalia Zamora1, Robin Sharma1, Gregory Pratt4 and Maria Suarez-Almazor1, 1Section of Rheumatology and Clinical Immunology, Department of General Internal Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA, Houston, TX, 2Division of Rheumatology, Department of Medicine, Division of Experimental Medicine, McGill University, Montreal, Quebec, Canada, Montreal, QC, Canada, 3Faculty of Medicine, Université de Montréal, Montreal, Quebec, Canada, Montreal, QC, Canada, 4Research Medical Library, The University of Texas MD Anderson Cancer Center, Houston, TX, USA, Houston, TX

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** To compare the recommendations of clinical practice guidelines (CPGs) and consensus statements (CSs) regarding the management of rheumatoid arthritis (RA) in patients with cancer. We identified similarities, discrepancies, and areas not covered and summarized the key areas for future research.

**Methods:** We searched electronic databases, guideline registries and relevant websites for CPGs and CSs on the management of RA in patients with cancer. Two pairs of reviewers independently selected studies and appraised selected papers according to the 23-item Appraisal of Guidelines for Research and Evaluation (AGREE) II Instrument. Cancer-specific guidelines per drug, cancer type and time frame were extracted and compared.
Results: Of 2,980 citations, 51 guidelines were included from 17 countries and seven international collaborations. Of the 29 that reported funding sources, 15 were financed by the pharmaceutical industry, eight by national or international agencies and six by other means. Scores for the AGREE II domains ranged from 32% for 'Applicability' to 85% for 'Scope and Purpose' with the other domains scoring 41 to 66%. Recommendations were categorized as i) malignancy risk associated with RA disease modifying anti-rheumatic drugs (DMARDs), ii) management of RA in de novo malignancies, and iii) management of patients with RA and cancer history. Eleven guidelines discussed the risk of cancer associated with DMARDs and while most note no or unknown increased risk, some urged caution due to suspected increased risk of non-melanoma skin cancer, melanoma and lymphoma. Nine papers referred to the diagnosis of a new malignancy. All agreed that therapy must be re-evaluated: biologic DMARDs should unequivocally be ceased and, while some conventional DMARDs such as sulphasalazine, hydroxychloroquine and gold salts may be continued, cyclosporine, methotrexate and leflunomide must be reconsidered. Three guidelines also required reporting new cancers to pharmacovigilance units. All mentioned that decisions regarding resumption of treatment must be made on a case-by-case basis. Almost all guidelines (46/51) made some mention of past history of cancer. They differed in terms of the drugs evaluated, the cancer types included (solid tumors, skin cancers, lymphoproliferative and/or hematological diseases) as well as the time since treatment (not specified, less than 5 and/or 10 years). The consensus was that caution should be exercised, particularly in the first five years and it is best to consult with the treating specialist before coming to a decision with the patient. Tumor Necrosis Factor inhibitors (TNFi) and cyclosporine are contraindicated in all cases while some conventional DMARDs and non-TNFi agents, particularly rituximab can be used with caution within the five-year time frame.

Conclusion: The guidelines for treatment of RA reviewed often failed to meet expected methodologic criteria varying in quality as well as with respect to the question of how to treat RA in patients with cancer. Since there is a lack of evidence, research is needed focusing on the daily practice of healthcare providers or expert opinion to guide and standardize the management of these patients.

Disclosure: M. A. Lopez-Olivo, None; I. Colmegna, None; A. Matusevich, None; S. R. Qi, None; N. Zamora, None; R. Sharma, None; G. Pratt, None; M. Suarez-Almazor, Bristol-Myers Squibb, 5, Pfizer Inc, 5.


Abstract Number: 2396

Safety and Humoral and Cell-Mediated Immune Responses to Herpes Zoster Vaccine in Patients with Rheumatoid Arthritis

JungHee Koh1, Ji-Won Kim2, Seung-Ki Kwok3, Ji Hyeon Ju4 and Sung-Hwan Park5, 1Seochogu, Banpodaero, 222, Division of Rheumatology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea, Republic of (South), 2Division of Rheumatology, Department of Internal Medicine, Seoul St. Mary’s Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea, Republic of (South), 3seungki73@catholic.ac.kr, Division of Rheumatology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea, Republic of (South), 4Division of Rheumatology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea, Republic of (South), 5Kangnam St Mary's Hosp, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

**Background/Purpose:** To examine humoral and cellular immune responses induced by a live attenuated herpes zoster (HZ) vaccine in patients with rheumatoid arthritis (RA) compared with osteoarthritis (OA) patients.

**Methods:** we performed an observational study of a live attenuated HZ vaccine in 41 RA patients receiving conventional disease modifying anti-rheumatic drugs (DMARDs) and/or low-dose glucocorticoids (median 60 years-old, 92.7% female), 28 OA patients (median 62 years-old, 85.7% female). Blood samples were obtained before and at 12 weeks after HZ vaccination. Immunogenicity was assessed using varicella zoster virus (VZV)-specific interferon gamma (IFN-γ) enzyme-linked immunospot (ELISPOT) assays and an in-house enzyme-linked immunosorbent assay.

**Results:** No vaccinated patients developed HZ during the follow-up period (median, 1.6 years). The HZ vaccine induced a significant increase in the VZV-specific ELISPOT spot-forming units and anti-VZV immunoglobulin G antibodies in both RA and OA patients. The number of spot-forming units was lower in RA patients than in OA patients both at baseline and at 12 weeks after vaccination (Figure). The disease activity score 28 (DAS28) was similar at baseline and at 12 weeks after vaccination. However, six RA patients (15%) experienced a flare-up (increase in DAS28 > 1.2) during the 12 weeks. The HZ vaccine induced VZV-specific cellular and humoral responses in RA patients.

**Conclusion:** Although RA patients showed a weaker vaccine-induced VZV-specific cellular immune response than OA patients, the HZ vaccine may be considered in RA patients receiving conventional DMARDs and/or low dose glucocorticoids.

**Disclosure:** J. Koh, None; J. W. Kim, None; S. K. Kwok, None; J. H. Ju, None; S. H. Park, None.


**Abstract Number:** 2397

**Bilateral Femoral DXA Scan in Patients with Rheumatoid Arthritis**
Background/Purpose: RA is in independent risk factor for osteoporosis and fractures. The diagnosis of osteoporosis is based on T-score at lumbar spine or hip and conventionally femoral BMD is measured at left hip. RA could affect hip BMD results as a consequence of impaired mobility and gait abnormalities related to the disease itself. Since treatment decision in patient with RA is frequently based on the FRAX tool score and it relies on hip BMD results, measuring the left hip only we could miss some patient with low BMD worth to be started on treatment.

Our aim was to assess if measuring BMD at both hips could increase the number of RA patients diagnosed with osteoporosis/osteopenia and potentially to be started on treatment.

Methods: RA patients who underwent a DXA scan at Royal Lancaster Infirmary between June 2006 and October 2015, and had both hips scanned were included in our analysis. We compared the prevalence of osteoporosis/osteopenia pending on the results of each hip using simple statistics.

Results: 1527 patients were included in our analysis. 1207 (79%) were female, mean age was 64.3 (SD 11.6), BMD levels (neck and total hip) were 0.85 g/cm² (SD 0.15) and 0.90 g/cm² (SD 0.17 ) at the left hip and 0.85 g/cm² (SD 0.15) and 0.90 (SD 0.17) at the right hip.

According to left hip results (Neck or Total Hip) 198 patients (13%) were classified as osteoporotic and 621 (40.1%) as osteopenic, while according to right hip results 183 patients (12%) were classified as osteoporotic and 598 (39.2%) as osteopenic.

Overall 245/1527 (16%) patients could be diagnosed as osteoporotic with 136/245 patients having BMD levels in the osteoporotic range at both hips (55.5%), 62/245 patients (25.3%) at the left hip only and 47/245 patients (19.2%) at right hip only. No significant differences in terms of age, sex, BMI and steroid exposure were found among patients with discordant results between the two hips. Surprisingly a higher frequency of previous fragility fractures was observed in the group with osteoporosis at the right hip only compared to the one with osteoporosis at the left hip only (28/47 vs 23/62, p = 0.020).

Conclusion: Measuring BMD at both hips could increase the number of RA patients diagnosed with osteoporosis or osteopenia and consequently the number of patients started on bone sparing treatments. This strategy could eventually lead to a decrease of fragility fractures among patients with RA.

<table>
<thead>
<tr>
<th>OP L hip +/R hip -</th>
<th>OP L hip -/R hip +</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>62</td>
<td>47</td>
</tr>
<tr>
<td>Age (Mean +/- SD)</td>
<td>69 +/- 12</td>
<td>71 +/- 11</td>
</tr>
<tr>
<td>Sex (F)</td>
<td>83.8%</td>
<td>78.7%</td>
</tr>
<tr>
<td>BMI (Mean +/- SD)</td>
<td>25.7 +/- 5.3</td>
<td>25.9 +/- 5.1</td>
</tr>
<tr>
<td>Steroids</td>
<td>56.4%</td>
<td>51.1%</td>
</tr>
<tr>
<td>Previous fractures</td>
<td>37.1%</td>
<td>59.6%</td>
</tr>
</tbody>
</table>

Disclosure: M. Massarotti, None; M. Bukhari, None.
Abstract Number: 2398

A Population-Based Cohort Study of Chronic Obstructive Pulmonary Disease Among Patients with Rheumatoid Arthritis: Comorbidity and Mortality

Charlotte Hyldgaard¹, Elisabeth Bendstrup¹, Alma Becic Pedersen², Sinna Pilgaard Ulrichsen³, Anders Løkke¹, Ole Hilberg⁴ and Torkell Ellingsen⁵,⁶, ¹Pulmonology, Århus University Hospital, Århus, Denmark, ²Clinical Epidemiology, Århus University Hospital, Århus, Denmark, ³Clinical Epidemiology, Århus University Hospital, Århus, Denmark, ⁴Internal medicine, Vejle Hospital, Vejle, Denmark, ⁵Diagnostic Centre, Region Hospital Silkeborg, Silkeborg, Denmark, ⁶Department of Rheumatology, Odense University Hospital, Odense, DK, Odense, Denmark

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Only few studies have addressed the prognostic impact of chronic obstructive pulmonary disease (COPD) among patients with rheumatoid arthritis (RA), although both diseases are frequent, and smoking is a shared risk factor. The purpose is to estimate the burden of COPD among RA patients and the subsequent mortality.

Methods: We included patients who had been assigned a first-time diagnosis of RA in the Danish National Patient Registry between 2004 and 2016. RA patients with COPD were matched for birth year, gender, and age at RA diagnosis with RA patients without COPD. Vital status for all patients was obtained from the Civil Registration System. Mortality risks were assessed using Kaplan-Meier mortality curves. Adjusted hazard rate ratios (aHRRs) for death with 95% confidence intervals (CIs) were estimated using Cox regression models. Adjustment was made for seropositive RA and Charlson Comorbidity Index (CCI).

Results: The study population included 31,333 individuals with RA. 3,254 of those (10.4%) had a diagnosis of COPD and were matched to 9,706 RA patients without COPD. The mortality risks in RA patients with COPD and RA patients without COPD within 0-2 months were 3.2% and 0.5% (aHRR = 7.3, CI 4.9-11.0), 4.5% and 1.5% within 2-6 months (aHRR = 3.0, CI 2.3-3.9), and 59.3% and 39.8% within 0.5-10 years (aHRR = 2.1, CI 1.9-2.1).

Conclusion: The mortality risk in RA patients with COPD was significantly increased compared with matched RA patients without COPD. The relative mortality risk was most pronounced within the first two months after both diagnoses had been assigned.

Disclosure: C. Hyldgaard, None; E. Bendstrup, None; A. Becic Pedersen, None; S. Pilgaard Ulrichsen, None; A. Løkke, None; O. Hilberg, None; T. Ellingsen, None.
Rheumatoid Arthritis Have Lower Glomerular Filtration Rate Compared to Healthy Population: Role of Inflammation

Suad Hannawi1 and Issa Al Salmi2, 1Rheumatology, Asst.Prof, Dubai, United Arab Emirates, 2Prof, Muscat, Oman
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Rheumatoid Arthritis-(RA) is associated with subclinical kidney impairment which contributes to increase mortality and morbidity. The role of inflammation on kidney function in inflammatory arthritis is not well studied. The purpose of this study is to investigate associations between estimated-glomerular-filtration-rates(eGFR), traditional cardiovascular risk factors, and markers of inflammation in RA compared to healthy controls.

Methods:
Participants were recruited from a specialized rheumatology clinic at Ministry of Health and Prevention of UAE, from January 2013 to January 2016. Healthy subjects recruited from the community through brochure advertisement. The Modification-of-Diet-in-Renal Disease-Study-MDRD-formula was used to calculate the eGFR. ttest and compare laboratory values and kidney function parameters between two groups. Linear regression analysis used to look for the correlation between the eGFR and each of the traditional cardiovascular risk factors and inflammatory markers.

Results:
98 RA-patients and 82-controls were recruited. None of the participants has history of diabetes, atherosclerosis or kidney impairment. The mean age for total participants was 49 ±13 years (Min16 –Max 82). The mean eGFR of inflammatory arthritis patients was 118 ± 30 ml/min (range 60 - 227) and 128 ±37 ml/min (range 62 – 286) for the controls. Patients and control had no significant difference in Systolic-SBP and diastolic-blood-pressure-DBP.

Inflammatory arthritis patients had lower GFR, albumin (P<0.001), and total protein (p=0.03) levels, and had higher ESR (P<0.001), CRP (P<0.001), and uric acid level (p=0.01),

Negative linear relationships were found as follow: Among RA patients and controls; there was a negative linear relationship between GFR and each of: age of participants; (p<0.001, CI: -1.24, -0.40 for patients and p=0.01, CI: -1.82, -0.26 for controls, & SBP; (p= 0.04, CI: -0.61, -0.00 for patients and p=0.022, CI: -0.61, -0.05 for controls.

Among RA patients: GFR had a negative linear relationship with age of participants, age at RA onset (p=0.002, CI: -1.18, -0.29), dbp (p=-2.14, CI: -1.24, -0.05), ESR (p=0.04, CI: -0.24,-0.01), CRP (p=0.02, CI: -0.47, -0.04), uric acid (p<0.001, CI -0.18, -0.05), and total protein (p= 0.01, CI: -0.91, -0.16). There was a positive linear relationship between eGFR and albumin level (p=0.03, p= 0.14, 2.35),

Conclusion:
non-traditional CVD risk factors such as inflammatory markers are associated with sub-clinical kidney injury in patients with RA. Inflammation is involved in the early stages of impaired kidney function in RA patients. Hence, anti-inflammatory therapies may be effective in slowing down the deterioration of kidney function in the arthritis diseases.

Disclosure: S. Hannawi, None; I. Al Salmi, None.
In Rheumatoid Arthritis: Vitamin-D Deficiency Is an Outcome and a Cause of Subclinical Renal Impairment

Suad Hannawi, Issa Al Salmi

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Vitamin D deficiency is highly prevalent in patients with rheumatoid arthritis (RA), and it is linked to RA disease severity. Two steps of hydroxylation are required to activate vitamin-D, the first is carried out in the liver to be converted to 25-vitamin-D and then in the kidney to 1,25 vitamin-D; the active form. Subclinical kidney dysfunction is common in rheumatoid arthritis and might interfere with vitamin-D hydroxylation. This study investigates the relationship between vitamin-D level and kidney function in RA.

Methods:
Patient diagnosed by ACR 1988 criteria for RA. 25-vitamin D level was obtained. Estimated glomerular filtration rate (eGFR) calculated with Modification of Diet in Renal Disease (MDRD) formula. Univariate regression analysis was carried out to determine the relationship between 25-vitamin-D level and eGFR, other renal parameters, and the inflammatory markers.

Results:
55 rheumatoid arthritis patients were included for the study. The mean age was 45 ± 15 year for female and 46 ± 21 year for male. The mean 25-vitamin-D level was 39 ± 28 nmol/l (normal range: 50-80). Mean eGFR was 130 ±25 ml/min/m^2.

Univariate linear regression revealed a positive linear relationship between 25-vitamin-D level and weight of the patients (p=0.03, CI: 0.06, 1.04), body surface area (p=0.02, CI: 11-119), body mass index (BMI) (p=0.009, CI: 0.60, 4.00), and calcium level (p=0.02, CI: 7.25, 130). 25-vitamin-D level was negatively associated with eGFR (p=0.040, CI: -0.20, -0.01), microalbuminuria level (p=0.040, CI: -0.63, -0.01), CRP level (P=0.01, CI: -1.16, -0.16) and neutrophil count (p=p=0.03, CI: -1.67, -0.010).

Conclusion:
The negative linear relationship between 25-vitamin D level and the eGFR indicates high level of 25-vitamin-D due to kidney inefficiency in converting 25-vitamin-D to an active form; 1, 25 vitamin-D. Extrarenal activation of vitamin D require a high level of 25-vitamin-D of more than 78 nmol/l (30 ng/ml) for sufficient activation. Vitamin-D receptors are present in most cells in the body and in the T and B lymphocytes. The active form of vitamin-D (1, 25 vitamin-D) is one of the most potent modulator of the immune system. Hence, the negative relationship between 25-vitamin-D and CRP indicate 25-vitamin-D deficiency role in exacerbation of the inflammatory status, and possibly in a further renal
function deterioration. Screening for 25-vitamin-D deficiency might be an important step to detect subclinical renal insufficiency. Vitamin-D supplement might help in ameliorating the inflammation of rheumatoid arthritis.

Disclosure: S. Hannawi, None; I. Al Salmi, None.


Abstract Number: 2401

Rheumatoid Arthritis with Kidney Dysfunction Contributes to Higher Risk of Cardiovascular Disease Development

Suad Hannawi¹ and Issa Al Salmi², ¹Rheumatology, Asst.Prof, Dubai, United Arab Emirates, ²Prof, Muscat, Oman

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Reduced kidney function render patients with RA rheumatoid arthritis (RA), have an increased risk of cardiovascular disease (CVD), particulary ischemic heart disease (IHD). This higher risk is not related primarily to traditional cardiovascular/atherosclerosis risk factors but to the presence of high inflammation associated with RA. Also, subclinical decreased kidney function has been identified as an independent risk factor for CV events. The potential impact of impaired kidney function on atherosclerosis in RA requires more elucidation. This study assess the role of kidney parameters, alongside inflammation and traditional cardiovascular risk factors in predicting CVD; as manifested by carotid intima media thickness (cIMT) among RA population.

Methods:

68 patients with RA underwent measurement of cIMT and correlated it with kidney function parameters with adjustment for traditional CV risk factors and RA associated inflammation. Glomerular filtration rate (GFR) was estimated with the abbreviated Modification of Diet in Renal Disease formula. Linear regression determined the association between renal parameters and cIMT.

Results:

cIMT was positively associated with 1-demographic characteristics: age of the participants (p<0.001), & age at RA symptoms onset (p=0.001), 2-traditional cardiovascular risk factors such as systolic blood pressure (p<0.001), diastolic blood pressure (p=0.016), triglycerid level (p=0.016), and low densilty lipoprotein (LDL) (p=0.001), and negatively with high density lipoprotein (HDL)(p=0.037), 3-inflammatory markers such as erythrocytes sedimentation rate (ESR) (p=0.020) and c-reactive protein (CRP)(0.020), and 4-renal function parameters such as uric acid level (p=0.006), urine microalbumin level (p=0.030), and negatively with24 hours urine creatinine level (p=0.020) and glomerular filtration rate (p=0.008).

Conclusion:
Even subclinical kidney function in conjunction with tarditional and non-traditional CVD risk factors work synergistically to accelerate atherosclerosis in RA population.

Disclosure: S. Hannawi, None; I. Al Salmi, None.


Abstract Number: 2402

**Rituximab in Rheumatoid Arthritis with Interstitial Lung Disease: A Multicenter Study of 32 Patients**

Carlos Fernández-Díaz¹, Delia Reina², Paula Rubio-Muñoz³, Ana Urruticoechea-Arana⁴, Maria Carrasco-cubero⁵, María Martín-López⁶, Jose A. Miranda-Filloy⁷, Ignacio Villa-Blanco⁸, Ana Milena Millan⁹, Ivan Castellvi¹⁰, Olga Maiz-Alonso¹¹, Antonio Juan¹², Fátima Álvarez Reyes¹³, José Luis Martin-Varillas¹, Nuria Vegas-Revenga¹, Ricardo Blanco¹ and Miguel Angel González-Gay¹, ¹Rheumatology, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, ²Rheumatology, Hospital de Sant Joan Despí Moisès Broggi, Barcelona, Spain, ³Rheumatology, Hospital Universitario Germans Trias i Pujol, Badalona, Spain, ⁴Rheumatology Department. Hospital Can Misses, IBIZA, Spain, ⁵Hospital Infanta Cristina, Badajoz, Spain, ⁶Rheumatology, Hospital Universitario 12 de Octubre, Madrid, Spain, ⁷Rheumatology Division, Hospital Lucus Augusti, Lugo, Spain, ⁸Hospital de Sierrallana, Sierrallana, Spain, ⁹Unitat de Reumatologia. Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, ¹⁰Rheumatology, Hospital Universitari de la Santa Creu i Sant Pau, Barcelona, Spain, ¹¹Hospital Universitario Donostia. San Sebastian. Spain, Donostia, Spain, ¹²Hospital Universitario Son Llàtzer. Rheumatology, Palma de Mallorca, Spain, ¹³Rheumatology, University Hospital Ntra. Sra. de La Candelaria, Santa Cruz de Tenerife, Spain

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Anti-TNFα drugs and several conventional disease-modifying anti-rheumatic drugs (DMARDs) such as methotrexate (MTX) have been involved in the development of Interstitial Lung Disease (ILD).

Our aim was to assess the efficacy and safety of Rituximab (RTX) in RA patients with ILD.

**Methods:** Retrospective multicenter study of RA patients with ILD treated with RTX. ILD was diagnosed by high-resolution computed tomography (HRCT). RTX was used at standard dose (1 g x2 and premedication with 100mg iv Methylprednisolone for a six month interval. We assess the the following variables: a) 1-point change in the degree of dyspnea according to the Modified Medical Research Council (MMRC); b) Forced vital capacity (FVC) improvement ≥10%; and improvement ≥10% in DLCO; c) radiological changes in HRCT scan, and d) changes in the joint assessment measured by DAS28 score.

**Results:** We studied 32 patients (23 women /9 men) with ILD associated to RA. The mean age±SD was 63.7±10.1 years. The median [IQR] to progression of ILD previously RTX was 18 [6-43] months. They had received the following DMARDs previously; MTX (n=16), Leflunomide (LFN) (n=16) mycophenolate (MMF) (n=1) sulfasalazine (SSZ) (n=8), hydroxichloroquine (HCQ) (n=7), azathioprine (AZA) (n=3), gold salts (n=2), D-penicillamine (n=1),
cyclophosphamide (n=2). 14 patients had previously received biological drugs. Cyclic citrullinated peptide antibodies (CCPA) were positive in 29 cases (94%). Besides HRCT, the diagnosis of ILD was confirmed by biopsy in 12 patients. In 3 patients ILD was drug-related: MTX (n=3). RTX was prescribed as monotherapy (n=12) and combined with DMARDs (n=19). The DMARDs prescribed were: LFN (6), SSZ (2), MTX (7), HCQ (3), AZA (3) MMF (1). A significant improvement of the dyspnea was observed. FVC and HRCT showed an improvement in the period between 6 and 12 months. DLCO remained stable in the majority of the patients. DAS28 also improved.

### TABLE

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>3 months</th>
<th>6 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMRC, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- No change</td>
<td>22</td>
<td>24</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>- Improvement</td>
<td>14 (67)</td>
<td>14 (63)</td>
<td>15 (63)</td>
<td></td>
</tr>
<tr>
<td>- Worsening</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>FVC, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- No change</td>
<td>14 (70)</td>
<td>1 (100)</td>
<td>16 (77)</td>
<td></td>
</tr>
<tr>
<td>- Improvement</td>
<td>2 (10)</td>
<td>10</td>
<td>5 (23)</td>
<td></td>
</tr>
<tr>
<td>- Worsening</td>
<td>2 (20)</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>DLCO, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- No change</td>
<td>8 (83)</td>
<td>10 (33)</td>
<td>15 (66)</td>
<td></td>
</tr>
<tr>
<td>- Improvement</td>
<td>0</td>
<td>2 (67)</td>
<td>3 (17)</td>
<td></td>
</tr>
<tr>
<td>- Worsening</td>
<td>1 (17)</td>
<td>2</td>
<td>2 (17)</td>
<td></td>
</tr>
<tr>
<td>HRCT, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- No change</td>
<td>7 (86)</td>
<td>9 (76)</td>
<td>9 (64)</td>
<td></td>
</tr>
<tr>
<td>- Improvement</td>
<td>1 (14)</td>
<td>1 (8)</td>
<td>4 (39)</td>
<td></td>
</tr>
<tr>
<td>- Worsening</td>
<td>0</td>
<td>2 (16)</td>
<td>1 (7)</td>
<td></td>
</tr>
<tr>
<td>DAS28 CRP, - Mean</td>
<td>4.88±1.44</td>
<td>3.70±1.19</td>
<td>3.61±0.98</td>
<td>2.89±0.93</td>
</tr>
</tbody>
</table>

**Conclusion:** RTX seems to be an effective and relatively safe treatment in RA patients with ILD. However, these data should be verified in prospective and randomized studies.

**Disclosure:** C. Fernández-Díaz, None; D. Reina, None; P. Rubio-Muñoz, None; A. Urruticoechea-Arana, None; M. Carrasco-cubero, None; M. Martín-López, None; J. A. Miranda-Filloy, None; I. Villa-Blanco, None; A. M. Millan, None; I. Castellvi, None; O. Maiz-Alonso, None; A. Juan, None; F. Álvarez Reyes, None; J. L. Martín-Varillas, None; N. Vegas-Revenga, None; R. Blanco, None; M. A. González-Gay, None.


Abstract Number: 2403
Amylin in the Insulin Resistance of Patients with Rheumatoid Arthritis

Ivan Ferraz-Amaro¹, Beatriz-Segura Tejera², De Vera-González AM³, Alejandra González Delgado⁴, José Luis Hernandez⁵, Jose M Olmos⁶, Begoña Ubilla⁷, Raquel Lopez-Mejias⁸ and Miguel Angel González-Gay⁹,

¹Rheumatology, Hospital Universitario de Canarias, La Laguna, Tenerife, Spain, ²Rheumatology, Rheumatology Division, Hospital Universitario de Canarias, San Cristobal de La Laguna, Spain, ³Central Laboratory Division, University Hospital of Canary Islands, Tenerife, Spain, ⁴Central Laboratory Division. Hospital Universitario de Canarias, Tenerife, Spain., Tenerife, Spain, ⁵Division of Internal Medicine., Hospital Universitario Marqués de Valdecilla, IDIVAL., Santander, Spain, ⁶Division of Internal Medicine. Hospital Universitario Marqués de Valdecilla, IDIVAL.Universidad de Cantabria. RETICEF, Santander, Spain, ⁷Epidemiology, Genetics and Atherosclerosis Research Group on Systemic Inflammatory Diseases, IDIVAL, Santander, Spain, ⁸Department of Rheumatology, Hospital Marquez de Valdecilla, Santander, Spain, ⁹Rheumatology, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Amylin is a 37-amino acid peptide that is stored in pancreatic beta cells and is co-secreted with insulin. Amylin and insulin levels rise and fall in a synchronous manner. It is known that it is deficient in type 1 diabetes and relatively deficient in insulin-requiring type 2 diabetes. Similarly, chronic inflammation has been found to deteriorate insulin resistance (IR) and impair pancreatic beta cell function in rheumatoid arthritis (RA) patients. The aim of this study was to explore the role of amylin in the IR of RA patients.

Methods: Cross-sectional study that encompassed 361 non-diabetes individuals; 151 patients with RA and 210 age- and sex-matched controls. IR by homeostatic model assessment (HOMA2), insulin and C-peptide serum levels and amylin serum levels were assessed in patients and controls. A multivariable regression analysis, adjusted for IR related factors, was performed to evaluate the differences between patients and controls in amylin and how amylin is related to IR, disease activity and disease characteristics in RA patients. Fisher r-to-z transformation was used to compare Pearson’s r2 between patients and controls.

Results: HOMA2-IR indexes were higher in RA patients compared to controls. Similarly, insulin and C-peptide were superior in RA controls after multivariable analysis that included IR related factors and glucocorticoid intake. However, although amylin was found to be up regulated in the univariate analysis (1.36±8.81 vs. 1.79±1.51 ng/ml, p=0.011), this difference was lost after multivariate analysis (p=0.46). In RA patients, amylin showed a trend to be related with erythrocyte sedimentation rate (beta coef. 0.01 [95%CI -0.00-0.01], 0.07). Similarly, the presence of rheumatoid factor (beta coef. 0.90 [95%CI -0.23-1.56], p=0.009) and disease activity through SDAI was positively associated with amylin (0.01 [95%CI 0.00-0.03], p=0.034). This relation was not found with DAS28 or CDAI. The use of prednisone, methotrexate or anti-TNF therapies was not associated with amylin neither insulin nor C-peptide. Differences in the relation of insulin, C-peptide, amylin and HOMA2 indexes between each other and between populations were assessed. In this sense, relation between insulin and C-peptide (r² 0.817 vs. 0.947, p=<0.001), between C-peptide and HOMA2-IR (r² 0.831 vs. 0.948, p=<0.001), between insulin and HOMA2-%B-C peptide (r² 0.689 vs. 0.872, p=<0.001) and between C-peptide and HOMA2-%B-C peptide (r² 0.827 vs. 0.922, p=<0.001) were higher in controls compared to RA patients. Amylin had no relation with C peptide, insulin or HOMA2-IR and these relations were not different between patients and controls.

Conclusion: The mechanism that produces IR in RA patients may not be mediated by amylin.
Abstract Number: 2404

Use of Dmards after the Diagnosis of Cancers in Patients with RA

Young Bin Joo, Yune-Jung Park, Ki-Jo Kim and Kyung-Su Park, Internal Medicine, St. Vincent's Hospital, The Catholic University of Korea, Suwon, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Although there are many studies about the association of disease-modifying anti-rheumatic drugs (DMARDs) with cancers in patients with rheumatoid arthritis (RA), there are few reports about the use of DMARDs after the diagnosis of cancers. The aim of this study is to investigate use of DMARDs after the diagnosis of cancer in patients with RA.

Methods: We did retrospective chart review of 2,164 patients with RA who visited our rheumatology outpatient clinic between Jan 2008 and Feb 2017. We examined the use of DMARDs in RA patients who were diagnosed as having cancers after the onset of RA both at the time of the initial diagnosis of cancers and at the recent outpatient visit.

Results:

We found out 53 patients who were diagnosed with cancers after the onset of RA. At the time of initial diagnosis of cancer, the median age was 67 years (interquartile range; 53, 75) and disease duration was 4.5 years (2.7, 4.5). Female was 37 (70%), seropositive patients were 47 (89%), and those with joint erosions were 28 (53%).

The most frequent cancer was lung cancer (n=12), followed by stomach cancer (n=6) and cervical cancer (n=6). Twenty-five (47%) received surgery, 20 (38%) received chemotherapy, and 8 (15%) received conservative treatment.

At the time of initial diagnosis of cancers, DMARDs were stopped in 22 patients (42%), but resumed in 15 within mean 1.5 months. In 17 patients (32%), DMARDs was changed and 11 of the 17 patients received monotherapy, among which hydroxychloroquine was most frequently used (n=5). Fourteen patients (26%) received the same DMARDs used before the diagnosis of cancer.

At the recent outpatient visit (after the mean follow-up of 2.7 years), conventional DMARDs were used in 32 patients (60%) and biologics in 7 (13%). Fourteen patients (27%) were not on the DMARDs treatment. When it comes to conventional DMARDs, monotherapy was used in 12 patients and combination DMARDs in 20. Methotrexate monotherapy (n=6/32) and the combination of leflunomide and hydroxychloroquine (n=6/32) were the most prevalent DMARDs.

After adjusting for confounding factors, chemotherapy was associated with no DMARDs treatment at a recent outpatient visit (odds ratio 4.6, 95% confidence interval 1.1-19.9). Interestingly, all the RA patients diagnosed with hematologic cancer (n=2) were not on the DMARD treatment.
Conclusion: In RA patients with cancer, main treatment patterns at the initial diagnosis of cancer were discontinuation of DMARDs or change to monotherapy mainly hydroxychloroquine. After the mean follow-up of 2.7 years, methotrexate monotherapy, combination of leflunomide and hydroxychloroquine, and biologics were used with nearly equal frequencies. Chemotherapy was associated with no DMARDs treatment at a recent outpatient visit.

Disclosure: Y. B. Joo, None; Y. J. Park, None; K. J. Kim, None; K. S. Park, None.


Abstract Number: 2405

Biological Function Integrated Prediction of Severe Radiographic Progression in Rheumatoid Arthritis: A Nested Case Control Study

Young Bin Joo1, Yul Kim2, Youngho Park3, Kwangwoo Kim4, Jeong Ah Ryu5, Seunghun Lee6, So-Young Bang7, Hye-Soon Lee8, Gwan-Su Yi9 and Sang-Cheol Bae7,1 Internal Medicine, St. Vincent's Hospital, The Catholic University of Korea, Suwon, Korea, Republic of (South), 2 Bio and Brain Engineering, Korea Advanced Institute of Science and Technology, Daejeon, Korea, Republic of (South), 3 Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), 4 Department of Biology, Kyung Hee University, Seoul, Korea, Republic of (South), 5 Department of Radiology, Hanyang University Hospital, Seoul, Korea, Republic of (South), 6 17 Haengdang-Dong, Seongdong-G, Hanyang University Hospital, Seoul, Korea, Republic of (South), 7 Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), 8 Hanyang University Guri Hospital, Gyeonggi-do, Korea, Republic of (South), 9 Department of Bio and Brain Engineering, Korea Advanced Institute of Science and Technology, Daejeon, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Radiographic progression is reported to be highly heritable in rheumatoid arthritis (RA). However, previous study using genetic loci showed an insufficient accuracy of prediction for radiographic progression. The aim of this study is to identify a biologically relevant prediction model of radiographic progression in patients with RA using a genome-wide association study (GWAS) combined with bioinformatics analysis.

Methods: We obtained genome-wide single nucleotide polymorphism (SNP) data for 374 Korean patients with RA using Illumina HumanOmni2.5Exome-8 arrays. Radiographic progression was measured using the yearly Sharp/van der Heijde modified score rate, and categorized in no or severe progression. Significant SNPs for severe radiographic progression from GWAS were mapped on the functional genes and reprioritized by post-GWAS analysis. For robust prediction accuracy, 10-fold cross-validation using a support vector machine (SVM) classifier was conducted. Prediction accuracy of our model was compared with that of other models based on GWAS results and SPOT (one of the post-GWAS analyses). The reliability of our model was confirmed using GWAS data of Caucasian patients with RA.

Results: A total of 36,091 significant SNPs with a p-value <0.05 from GWAS were reprioritized using post-GWAS analysis and ~2700 were identified as SNPs related to RA biological features. The best average accuracy of 10 groups was 0.6015 with 85 SNPs, and this increased to 0.7481 when combined with clinical information. In comparisons of
Prediction accuracy, the 0.7872 AUC in our model was superior to that obtained with GWAS (AUC 0.6586, p-value 8.97 x 10^{-5}) or SPOT (AUC 0.7449, p-value 0.0423). Our model also showed superior prediction accuracy in Caucasian patients with RA compared with GWAS (p-value 0.0049) and SPOT (p-value 0.0151).

**Conclusion:** Using various biological functions of SNPs and repeated machine learning, our model could predict severe radiographic progression relevantly and robustly in patients with RA compared with models using only GWAS results or other post-GWAS tool.

**Disclosure:** Y. B. Joo, None; Y. Kim, None; Y. Park, None; K. Kim, None; J. A. Ryu, None; S. Lee, None; S. Y. Bang, None; H. S. Lee, None; G. S. Yi, None; S. C. Bae, None.


Abstract Number: 2406

**Increased Cartilage Damage in Metacarpophalangeal Joints of ACPA Positive Rheumatoid Arthritis (RA) Patients Using T2 Mapping in 3 Tesla Magnetresonance Imaging (MRI)**

Nina Renner¹, Arnd Kleyer², David Simon², Gerhard Krönke³, Juergen Rech², Georg Schett², Goetz Welsch⁴ and Milena L. Pachowsky¹, ¹Department of Trauma and Orthopedic Surgery, Friedrich-Alexander-University Erlangen-Nuremberg, Erlangen, Germany, Erlangen, Germany, ²Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, Erlangen, Germany, Erlangen, Germany, ³Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, Erlangen, Germany, Erlangen, Austria, ⁴UKE Athleticum, University Hospital Hamburg-Eppendorf, Hamburg, Germany

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM
**Background/Purpose:**

T2 mapping is a non-invasive MRI approach to measure cartilage quality, reflecting cartilage hydration and collagen integrity without using contrast enhancement. It has been demonstrated to be a sensitive tool to determine cartilage damage and is currently spreading into a broader clinical application.(1) The objective of this study was the qualitative and quantitative analysis of structural and biochemical changes in cartilage of MCP joints of patients with RA using T2 mapping in a 3 Tesla-MRI setting.

**Methods:**

Thirty RA patients fulfilling the 2010 ACR/EULAR criteria were recruited. ACPA positive patients were compared to ACPA negative patients. Imaging was performed with a 3 T whole body scanner (VERIO; SIEMENS Healthcare) of the 2nd and 3rd MCP joint, using two surface coils to perform high-resolution imaging and to enable parallel imaging techniques.(2) T2 maps were obtained using a pixel-wise, mono-exponential, non-negative least-squares-fit analysis. Region-of-interest (ROI) analysis was performed dividing the cartilage into medial, central and lateral phalangeal (med, cent, lat P) and metacarpal (MC) area. All results are provided as mean±standard deviation (SD). Statistical evaluation was performed by means of univariate ANOVA testing with random factors. A p-value <0.05 was considered statistically significant. The study protocol was approved by the local ethics commission and written informed consent was obtained from all patients.

**Results:**

Fourteen ACPA positive (3 male/11 female) and 16 ACPA negative patients (6 male/10 female) were included. Mean age, sex distribution and disease duration were comparable (age: 49.0 ± 15.1 years (ACPA+) vs. 56.1 ± 10.9 years (ACPA-), t=1.494, p=0.146; sex distribution: χ2 (1)= 0.918, p=0.338, disease duration: 7.9 ± 7.3 years (ACPA+) vs. 3.9 ± 3.8 years (ACPA-), U=69.0, Z=-1.799, p=0.072).

T2 values were significantly higher in the majority of the ROIs in ACPA-positive RA patients compared to ACPA negative patients with a statistical significance in most of the ROIs. Details are provided in Table 1.

**Conclusion:**

In our study we were able to demonstrate the feasibility of T2 mapping in MRI as a non-invasive tool for cartilage evaluation in MC joints in RA patients in a clinical setting. Interestingly, ACPA positive RA patients showed significantly increased T2 values compared to ACPA negative patients reflecting a more severe cartilage alteration despite comparable disease duration.

<table>
<thead>
<tr>
<th></th>
<th>ACPA pos.</th>
<th>ACPA neg.</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>14</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Male/Female N</td>
<td>3/11</td>
<td>6/10</td>
<td>0.338</td>
</tr>
<tr>
<td>Age (years)</td>
<td>49.0 ± 15.1</td>
<td>56.1 ± 10.9</td>
<td>0.146</td>
</tr>
<tr>
<td><strong>Disease specific characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>7.9 ± 7.3</td>
<td>3.9 ± 3.8</td>
<td>0.072</td>
</tr>
<tr>
<td><strong>MRI results (T2 values)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medial metacarpal area</td>
<td>41.3 ± 15.3</td>
<td>29.6 ± 7.4</td>
<td>0.010</td>
</tr>
<tr>
<td>Central metacarpal area</td>
<td>43.8 ± 14.6</td>
<td>28.4 ± 10.9</td>
<td>0.001</td>
</tr>
<tr>
<td>Lateral metacarpal area</td>
<td>45.6 ± 13.8</td>
<td>32.0 ± 8.6</td>
<td>0.008</td>
</tr>
<tr>
<td>Medial phalangeal area</td>
<td>30.3 ± 14.6</td>
<td>25.7 ± 14.0</td>
<td>0.169</td>
</tr>
<tr>
<td>Central phalangeal area</td>
<td>29.9 ± 13.0</td>
<td>22.5 ± 10.1</td>
<td>0.014</td>
</tr>
<tr>
<td>Lateral phalangeal area</td>
<td>37.0 ± 15.9</td>
<td>28.8 ± 12.6</td>
<td>0.039</td>
</tr>
</tbody>
</table>

1. Welsch, G.H., Apprich, S., Zbyn, S., et al., Biochemical (T2, T2* and magnetisation transfer ratio MRI of knee cartilage: feasibility at ultra-high field (7T) compared with high field (3T) strength. Eur

**Abstract Number: 2407**

**Clinical Significance of Elevated Anti-Cyclic Citrullinated Protein Antibody Titers in Patients with Pulmonary Hypertension**

Sarah Ifteqar1, Megan Krause2, Paul Schmidt3, Lewis Satterwhite4 and Mehrdad Maz5, 1Department of Medicine, Division of Allergy, Clinical Immunology and Rheumatology, University of Kansas Medical Center, Kansas City, KS, 2Department of Medicine, Division of Allergy, Clinical Immunology and Rheumatology, The University of Kansas Medical Center, Kansas City, KS, 3Department of Internal Medicine, Division of Allergy, Clinical Immunology, & Rheumatology, Kansas University Medical Center, Kansas City, KS, 4Department of Medicine, Division of Pulmonary and Critical Care, The University of Kansas Medical Center, Kansas City, KS, 5Allergy, Clinical Immunology, and Rheumatology, Division of Allergy, Clinical Immunology and Rheumatology, Department of Internal Medicine, University of Kansas Medical Center, Kansas City, KS

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Pulmonary hypertension (PH) is a disease entity characterized by elevated pulmonary artery pressure, which often results in right ventricular failure. As part of PH evaluation, anti-cyclic citrullinated protein antibody (ACPA) titers are intermittently checked. However, data regarding presence and clinical significance of elevated ACPA titers is unavailable.

**Methods:** A retrospective analysis of patients from 12/1/2006 to 12/31/2016 was completed at a single tertiary center. Patients with a diagnosis of PH, based on right heart catheterization and/or evaluation by a pulmonologist and consistent echocardiogram, in whom ACPA levels were obtained were included. Patients with RA and connective tissue disease (CTD), including SSc, SLE, MCTD, UCTD, PM, DM, Sjogren’s disease, Overlap and antisynthetase syndrome were identified based on a clinical diagnosis by a rheumatologist. P values were computed using Fishers exact test.

**Results:** A total of 263 charts were reviewed; 106 patients were confirmed to have PH and had ACPA measured. Of these patients, 21 (19.8%) were ACPA positive and 85 (80.2%) were ACPA negative.

Of the 21 patients who were ACPA positive, 15 (71%) had a concomitant diagnosis of RA and PH; the diagnosis of RA preceded the diagnosis of PH in 7 patients (46.7%); followed by PH preceding the diagnosis of RA in 5 (33.3%); and a
concurrent diagnosis was made in 3 (20%).

Similarly, of 85 ACPA negative patients, a concomitant diagnosis of RA and PH was made in 7 (8.2%); the diagnosis of RA preceded the diagnosis of PH in 3 (42.8%); a concurrent diagnosis of PH and RA was seen in 3 (42.8%), followed by a diagnosis of PH preceding the diagnosis of RA in 1 (14.4%).

In the 15 patients who were ACPA positive and had RA, 5 (33%) also had a diagnosis of interstitial lung disease (ILD). Of those who were ACPA negative and had RA, 3 of 7 (42.9%) had ILD (p=1).

Among ACPA positive patients (21) only 4 had a diagnosis of CTD along with RA as compared to the ACPA negative group of 85 patients of whom 44 (51.8%) had CTD alone and 3 had CTD with RA (47, 55.2%) (p=0.003).

The ACPA positive patients (7/21, 33.3%) had similar mortality compared to the ACPA negative patients (26/85, 30%) and ACPA positivity was not associated with an increased risk of death (p=0.79).

**Conclusion:** In a cohort of patients with PH who had ACPA levels obtained, 20% were positive. In majority of both ACPA positive and ACPA negative patients, the diagnosis of RA preceded or was made concurrently with the diagnosis of PH. However, the diagnosis of PH preceded that of RA in a relatively higher percentage of ACPA positive patients compared to ACPA negative patients. Interestingly, about 30% of ACPA positive patients with PH did not develop RA over the course of the follow-up. The link between positive ACPA and PH is not explained by ILD in isolation. Further data is required to understand the prognostic implications of the presence of ACPA in patients with PH.

**Disclosure:** S. Ifteqar, None; M. Krause, None; P. Schmidt, None; L. Satterwhite, None; M. Maz, None.


**Abstract Number:** 2408

**Early Frailty Syndrome in Rhematoid Arthritis: Screening Using the Frail Scale**
SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Frailty is defined as a syndrome of physiological decline in late life, characterized by marked vulnerability to adverse health outcomes. Frail adults are less able to adapt to stressors such as acute illness or trauma than non-frail adults. This increased vulnerability contributes to increased risk for multiple adverse outcomes, including procedural complications, falls, institutionalization, disability, and death.

The frailty syndrome requires at least three of the following five characteristics: Unintentional weight loss, as evidenced by a loss of at least 10 lbs or greater than 5% of body weight in the prior year, muscle weakness, as measured by reduced grip strength in the lowest 20% at baseline, adjusted for gender and BMI, physical slowness, based on measured time to walk a distance of 15 ft, poor endurance, as indicated by self-reported exhaustion and low physical activity, as scored using a standardized assessment questionnaire.

Rheumatoid arthritis (RA) is a chronic disabling disease, which leads to functional limitations and diminishes health-related quality of life. The presence of comorbidity and polypharmacy are both related to RA severity.

The aim of this study was to assess the prevalence of frailty in patients with RA using de Frail Scale.

Methods: We studied patients with RA (ACR criteria) that were seen at the outpatient clinic of the Rheumatology Service of a third level hospital. We applied the Frail Scale and registered data (demographic and disease related data) using a cross-sectional, observational, and descriptive study design.

Frail scale: Based on five items, reflecting performance, self-reports and common co-morbidities (Morley JE et al., J Nutr Health Aging. 2012;16(7):601-8).

FRAIL SCALE
Did you feel worn out? or Did you feel tired?
Ability to climb one flight of stairs
Ability to walk 100 m
Self-report of >5% weight loss
≤5 of: dementia; heart Disease; depression; arthritis; asthma; bronchitis/ emphysema; diabetes; hypertension; osteoporosis; stroke.

Results: 231 consecutive RA patients were included, 83.2 % were female. Mean age was 55.4 years and mean disease duration was 11.4 years.

Mean number of comorbidities was 1.48, with systemic hypertension and obesity as the most frequent ones (33.8 % and 26.4 %, respectively). Polypharmacy was found in 96.8 % and 64.7 % received more than five drugs simultaneously.

21.5 % met frailty criteria.

Conclusion: Prevalence of frailty in this study was high. Rheumatologists should make an early detection of signs of frailty.
Early detection of frailty can spur reforms to make routine care less hazardous, can focus on outcomes most relevant to patients and can aid in understanding effectiveness of health care interventions, including at the population level.

Disclosure: E. Trujillo, None; M. D. M. Trujillo, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/early-frailty-syndrome-in-rheumatoid-arthitis-screening-using-the-frail-scale

Abstract Number: 2409

Older Age and Male Gender Are Independent Predictors of Quantiferon Positivity Among Adult Rheumatic Patients in a Tertiary Care Center from a BCG Vaccinated Country: Hur-BIO Single Center Real Life Results

Emrah Seyhoglu1, Oguz Abdullah Uyaroglu1, Abdulsamet Erden2, Levent Kilic2, Berkan Armagan2, Alper Sari2, Omer Karadag2, Sule Apras Bilgen2, Ali Akdogan2, Ihsan Ertenli2, Umut Kalyoncu2 and Sedat Kiraz2, 1Internal Medicine, Hacettepe University Faculty of Medicine, Ankara, Turkey, 2Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Turkey
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

TNF-α inhibitors increase the risk of emergence of active tuberculosis (TB). Screening rheumatic patients for latent TB is a necessity before initiation of biological treatment. Population is vaccinated with BCG in Turkey and BCG vaccination decreases the specificity of tuberculin skin test (TST). QuantiFERON-TB Gold In-Tube Assay (QFT-GIT) is an option for latent TB screening in a BCG-vaccinated population. The aim of this study was to assess the factors affecting QFT-GIT test results before biological treatment.

Methods:

Hacettepe University Rheumatology Biologic Registry (HUR-BIO) is a single center biological registry since 2005. The study group is composed of patients registered in HUR-BIO. Only QFT-GIT is performed for latent TB screening before biological treatment since May 2011. Patients, who were screened with QFT-GIT for latent TB between May 2011 and August 2015, were included in the study. Demographical and clinical characteristics, QFT-GIT results of the patients were collected. Potential factors affecting QFT positivity were analyzed. Indeterminate results and diagnoses other than SpA and RA were excluded during the analysis.

Results:

1335 (58.2% female) patients were recruited. The mean age was 44.2 ± 12.9. Diagnoses were followed, 62.6 % SpA, 32.4 % RA, 5.0 % others. 94.2 % of patients declared that they had had BCG vaccination. QFT-GIT results were followed; 79.0 % negative, 19.3 % positive, 1.7 % indeterminate. On univariate analyses male gender (53.9% vs. 38.8%, p=0.001), mean age (50.6±12.4 vs. 42.8±12.5, p<0.001), ever-smoked (60.3% vs. 51.0%, p=0.008), diabetes mellitus (10.1% vs. 6.5%, p=0.05), educational level (high school, 47.3% vs. 57.5%, p=0.003), married patients (85.1%
vs. 77.1%, p=0.005) and RA diagnosis (39.5% vs. 32.4%, p=0.032) were significantly higher in QFT-GIT positive group compared to the negative group. There was no difference between positive and negative groups in terms of BCG vaccination, neither steroid nor other immunosuppressant use. On multivariate logistic analysis for QFT-GIT positivity, age≥ 45 years and male gender were identified as independent factors with adjusted odd ratios of respectively 3.91 (95% CI 2.71-5.63, p<0.001) and 2.62 (95% CI 1.83-3.75, p<0.001).

Conclusion:

The risk of QFT-GIT positivity increases with male gender and older age among rheumatic patients. The fact that males participate social life more actively in Turkey and the increased possibility of encountering tuberculosis bacillus with age can explain this situation. The use of steroids, other immunosuppressive drugs and BCG status in the rheumatic patient group does not affect QFT-GIT results.

Disclosure: E. Seyhoglu, None; O. A. Uyaroglu, None; A. Erden, None; L. Kilic, None; B. Armagan, None; A. Sari, None; O. Karadag, None; S. Apras Bilgen, None; A. Akdogan, None; I. Ertenli, None; U. Kalyoncu, Roche Pharmaceuticals, 5; S. Kiraz, None.


Abstract Number: 2410

Serious Infection Risk in Patients with Rheumatoid Arthritis Compared to Patients with Non-Inflammatory Rheumatic Diseases: A US National Cohort Study

Bella Y. Mehta1, Sofia Pedro2, Gulsen Ozen3 and Kaleb Michaud4, 1Rheumatology, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, 2National Data Bank for Rheumatic Diseases, Wichita, KS, 3Rheumatology, Marmara University, School of Medicine, Rheumatology, Istanbul, Turkey, 4University of Nebraska Medical Center, Omaha, NE

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Serious infections (SI) in patients with rheumatoid arthritis (RA) are a perpetual concern. We compared the risk by first and recurrent SIs in patients with RA compared to those with non-inflammatory rheumatic diseases (NIRD) in a real-world setting.

Methods: Participants had RA or NIRD from 1998 through 2016 in the National Data Bank for Rheumatic Diseases (NDB). NIRD included diagnoses such as osteoarthritis, back pain syndromes, tendonitis, etc; this comparator group helps minimize selection and reporting bias. SIs were defined as those requiring hospitalization or intravenous antibiotics, or leading to death. All SIs were described by etiology and location and were additionally categorized as opportunistic or herpes zoster when they occur. Survival analysis methods (Cox regression, time to first infection using time-varying covariates and Andersen-Gill multiple failures model) were applied, both in a univariate and multivariable manner. Confounders included demographics, comorbidities, disease severity measures and glucocorticoid (GC) use.
Results: There were 20,361 RA and 6,176 NIRD patients who contributed to 81,499 and 20,665 patient-years of exposure, having had 1,643 (7.9%) and 281 (4.5%) SIs, respectively. A higher proportion of RA patients with SI were younger, had worse HAQ scores, lower BMI, and a higher frequency of GC use and smoking compared to NIRD patients (Table 1). The most frequent SIs by etiology were bacterial and by location was respiratory in both groups. The incidence rate ratios (IRR) of the first and recurrent SIs for RA vs. NIRD were similar (1.5 [1.3 -1.7]). The IRRs for opportunistic infections and herpes zoster ranged between 2.2 - 3.3. The multivariable analysis showed a significant SI risk increase in RA patients compared to NIRD (HR 1.32 [1.15-1.52]). By etiology, the risk of bacterial infections was significantly higher in patients with RA than NIRD. Respiratory, bloodstream infections with sepsis, skin, bone and joint infections were also significantly increased in RA (Table 2).

Conclusion: The risk of SIs, particularly bacterial, respiratory, blood stream, skin and joint infections is increased in RA patients compared to NIRD patients. The increased risk could be explained by immune dysregulation caused by the disease itself, comorbid conditions or medications. A limitation of this study is that there was a significant proportion of SIs that were not categorized by type or location in medical records. Further studies collecting detailed SI information and the impact of medications would be needed to accurately describe the risk of SIs in RA.

| Table 1. Mean (SD) baseline characteristics of all RA and NIRD patients and by serious infections |
|----------------------------------------|--------|--------|--------|--------|--------|--------|--------|--------|
|                                      | All    | Serious Infections |
|                                      | RA     | NIRD   | P-value | RA     | NIRD   | P-value |
| N                                     | 20,361 | 6,176  |         | 1,643  | 281    |         |
| Age, yrs                               | 58.2 (13.7) | 62.8 (13.4) | <0.001 | 66.6 (12.0) | 71.7 (11.9) | <0.001 |
| Male, %                                | 20.3 | 19.6 | 0.223 | 25.1 | 22.1 | 0.279 |
| White, %                               | 94.3 | 96.6 | <0.001 | 94.6 | 95.7 | 0.449 |
| BMI, kg/m²                              | 28.9 (7.1) | 29.4 (7.4) | <0.001 | 28.4 (7.5) | 30.5 (8.4) | <0.001 |
| Urban vs Rural, %                       | 26.9 | 23.9 | <0.001 | 32.3 | 25.2 | 0.018 |
| Education, yrs                         | 13.6 (2.4) | 13.6 (2.4) | 0.210 | 13.3 (2.3) | 13.7 (2.3) | <0.001 |
| Smoking History, %                     | 41.5 | 34.9 | <0.001 | 50.6 | 40.6 | 0.002 |
| Disease duration, yrs                  | 14.1 (12.5) | 15.6 (13.5) | <0.001 | 19.7 (12.8) | 21.9 (15.1) | 0.010 |
| Comorbidity index (0-9)                | 1.8 (1.6) | 1.9 (1.6) | <0.001 | 2.5 (1.8) | 2.6 (1.6) | 0.650 |
| HAQ (0-3)                              | 1.1 (0.7) | 1.1 (0.7) | 0.300 | 1.3 (0.7) | 1.2 (0.7) | <0.001 |
| Pain (0-10)                            | 4.2 (2.9) | 4.2 (2.9) | 0.900 | 4.5 (2.8) | 4.7 (2.9) | 0.260 |
| Patient global (0-10)                  | 3.8 (2.6) | 3.8 (2.5) | 0.940 | 4.3 (2.5) | 4.1 (2.5) | 0.450 |
| Diabetes, %                            | 8.6 | 8.9 | 0.520 | 13.9 | 17.7 | 0.094 |
| Glucocorticoid use, %                  | 28.3 | 4.43 | <0.001 | 47.4 | 9.3 | <0.001 |
Table 2. Incidence Rate Ratio (IRR) and Multivariable Hazard Ratios (HR) (95%CI) of serious infections by Etiology location

<table>
<thead>
<tr>
<th>Infection</th>
<th>IRR first Infection</th>
<th>Multivariable HR first infection*</th>
<th>IRR recurrent Infection</th>
<th>Multivariable HR recurrent infection*</th>
</tr>
</thead>
<tbody>
<tr>
<td>All infections</td>
<td>1.5 (1.3-1.7)</td>
<td>1.3 (1.2-1.5)</td>
<td>1.5 (1.4-1.7)</td>
<td>1.3 (1.2-1.5)</td>
</tr>
<tr>
<td>Opportunistic infections</td>
<td>3.0 (1.4-7.7)</td>
<td>1.9 (0.8-4.2)</td>
<td>3.3 (1.5-8.4)</td>
<td>1.9 (0.9-4.3)</td>
</tr>
<tr>
<td>Herpes zoster</td>
<td>2.2 (0.9-6.2)</td>
<td>1.8 (0.7-4.4)</td>
<td>2.4 (1.0-6.8)</td>
<td>1.9 (0.8-4.7)</td>
</tr>
<tr>
<td>Bacterial infections</td>
<td>1.6 (1.3-2.0)</td>
<td>1.4 (1.2-1.8)</td>
<td>1.6 (1.4-1.9)</td>
<td>1.4 (1.1-1.6)</td>
</tr>
<tr>
<td>Viral infections</td>
<td>1.5 (0.9-2.6)</td>
<td>1.3 (0.7-2.2)</td>
<td>1.5 (0.9-2.5)</td>
<td>1.2 (0.7-2.0)</td>
</tr>
<tr>
<td>Fungal infections</td>
<td>5.1 (1.3-43.3)</td>
<td>3.0 (0.7-2.9)</td>
<td>5.4 (1.4-46.3)</td>
<td>2.9 (0.7-12.6)</td>
</tr>
<tr>
<td>Unknown cause</td>
<td>1.4 (1.2-1.7)</td>
<td>1.3 (1.1-1.5)</td>
<td>1.4 (1.2-1.7)</td>
<td>1.3 (1.1-1.5)</td>
</tr>
<tr>
<td>Respiratory</td>
<td>1.4 (1.2-1.7)</td>
<td>1.4 (1.1-1.6)</td>
<td>1.5 (1.3-1.7)</td>
<td>1.3 (1.1-1.6)</td>
</tr>
<tr>
<td>CNS</td>
<td>1.4 (0.4-7.5)</td>
<td>1.3 (0.4-5.0)</td>
<td>1.5 (0.4-7.9)</td>
<td>1.3 (0.4-4.8)</td>
</tr>
<tr>
<td>Abdominal</td>
<td>2.0 (1.0-4.3)</td>
<td>1.4 (0.7-2.8)</td>
<td>1.9 (1.0-3.9)</td>
<td>1.3 (0.7-2.6)</td>
</tr>
<tr>
<td>Urinary</td>
<td>0.8 (0.4-1.5)</td>
<td>0.7 (0.4-1.3)</td>
<td>0.9 (0.5-1.6)</td>
<td>0.7 (0.4-1.3)</td>
</tr>
<tr>
<td>Bloodstream infections</td>
<td>1.8 (1.3-2.5)</td>
<td>1.6 (1.1-2.2)</td>
<td>1.8 (1.4-2.5)</td>
<td>1.6 (1.2-2.2)</td>
</tr>
<tr>
<td>including sepsis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin, bone and joint infections</td>
<td>1.5 (1.2-1.9)</td>
<td>1.3 (1.0-1.7)</td>
<td>1.5 (1.2-1.8)</td>
<td>1.3 (1.0-1.6)</td>
</tr>
<tr>
<td>Unknown type</td>
<td>2.6 (1.2-6.2)</td>
<td>1.8 (0.8-3.8)</td>
<td>2.7 (1.3-6.6)</td>
<td>1.8 (0.9-3.9)</td>
</tr>
</tbody>
</table>

*Multivariable Cox proportional hazard model adjusted for age, sex, race, HAQ, pain scale, rheumatic diseases comorbidity index, education level, residency (urban vs rural), glucocorticoid use, prior serious infections and smoking status.

Disclosure: B. Y. Mehta, None; S. Pedro, None; G. Ozen, None; K. Michaud, None.


Abstract Number: 2411

**In-Hospital Risk of Asthma in Patients with Rheumatoid Arthritis: A Cross-Sectional Nationwide Analysis**

Yiming Luo¹, Jiehui Xu², Yumeng Wen¹, Alvaro Ramos-Rodriguez³, Changchuan Jiang¹, Shuyang Fang¹, Mustafa Kagalwalla¹ and Neha Ohri⁴, ¹Department of Medicine, Mount Sinai St Luke's and Mount Sinai West Hospitals, Icahn School of Medicine at Mount Sinai, New York, NY, ²Department of Biostatistics, Mailman School of Public Health, Columbia University Medical Center, New York, NY, ³Mount Sinai St Luke's and Mount Sinai West Hospitals, Icahn School of Medicine at Mount Sinai, New York, NY, ⁴Division of Rheumatology, Department of Medicine, Mount Sinai St Luke's and Mount Sinai West Hospitals, Icahn School of Medicine at Mount Sinai, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Background/Purpose:

Rheumatoid arthritis (RA) and asthma are both chronic inflammatory disorders. Lung pathology is a well-known extra-articular manifestation of RA and previous studies have shown an increased risk of asthma in patients with RA. Few studies have addressed the effects of RA on asthma exacerbations. We sought to explore the association of different asthma subtypes and asthma exacerbations in hospitalized adult patients with RA.

Methods:

We conducted a cross-sectional study using data from National Inpatient Sample (NIS) for the year of 2014. Diagnosis for asthma, subtypes of asthma (i.e. allergic asthma, non-allergic asthma, exercise-induced bronchospasm and cough variant asthma) and rheumatoid arthritis were identified using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes. STATA software package was used for statistical analyses. Multivariate logistic regression models were created to adjust for potential confounders such as age, gender, race, insurance type, current tobacco abuse and obesity. Patients younger than 18 years old were excluded from the study. For asthma exacerbations, we also studied exacerbations related to acute respiratory infections (ARI) and status asthmaticus.

Results:

A total of 102,805 hospitalizations with a diagnosis of RA and 2,331,616 hospitalizations with a diagnosis of asthma were included in our study. Compared those without RA, asthma patients with RA are more likely to be older (mean age 63.1 vs 55.0), more female (85.8% vs 69.6%), more Caucasian and less African American (68.4% and 17.8% vs 62.8% and 21.6%). The adjusted OR for all types of asthma and RA was 1.52 (95% CI 1.49 - 1.56, p < 0.001). For asthma subtypes, the adjusted OR was statistically significant only for allergic asthma (OR 1.43, 95% CI 1.23 - 1.66, p < 0.001). There was no difference for non-allergic asthma (OR 1.42, 95% CI 0.84 - 2.42, p=0.190), exercise-induced bronchospasm (OR 0.91, 95% CI 0.51 - 1.60, p = 0.732), and cough-variant asthma (OR 0.89, 95% CI 0.43 - 1.86, p=0.766) in hospitalized patients with RA. For asthma exacerbations, RA was associated with a higher risk of overall exacerbations (OR 1.26, 95% CI 1.21 - 1.33 p < 0.001), including both ARI-related exacerbations (OR 1.36, 95% CI 1.17 - 1.57, p < 0.001) and non-ARI related exacerbations (OR 1.21 95% CI 1.11 - 1.31, p < 0.001). There was no difference for status asthmaticus (OR 1.17, 95% CI 0.92 - 1.48, p=0.191) in patients with RA.

Conclusion:

Our study is consistent with previous studies that RA is associated with a higher risk of asthma in hospitalized adult population. However, our subgroup analysis showed that RA is only associated with allergic subtype of asthma, which may imply complex cross-link between Th1 and Th2 type autoimmunity. Furthermore, RA is associated with higher risk of both ARI and non-ARI related asthma exacerbations, despite that RA patients are more likely to take oral steroid, which is also a Global Initiative for Asthma (GINA) guideline recommended Step 5 asthma control medication. It suggests that increased infection risk secondary to immunosuppressive medications and systemic inflammation due to RA may both play a role in the pathophysiology of asthma exacerbation.

Disclosure: Y. Luo, None; J. Xu, None; Y. Wen, None; A. Ramos-Rodriguez, None; C. Jiang, None; S. Fang, None; M. Kagalwalla, None; N. Ohri, None.


Abstract Number: 2412
Mortality and Clinical Features in Rheumatoid Arthritis and Interstitial Lung Disease

Cristina Vadillo Font¹, Maria Asunción Nieto², Leticia Leon³, Luis Rodriguez-Rodriguez⁴, Judit Font Urgelles¹, Esperanza Pato Cour¹, Juan Angel Jover⁵ and Lydia A Alcazar⁶, ¹Rheumatology, Hospital Clínico San Carlos, Madrid, Spain, ²Pneumology. Hospital Clínico San Carlos, MD PhD, Madrid, Spain, ³Rheumatology, Department of Rheumatology, Hospital Clínico San Carlos, Madrid, Spain, ⁴Department of Rheumatology, Hospital Clínico San Carlos, Madrid, Spain, ⁵Rheumatology. Hospital Clínico San Carlos, MD PhD, Madrid, Spain, ⁶Rheumatology Department and Health Research Institute (IdISSC), Hospital Clínico San Carlos, Madrid, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Interstitial lung disease (ILD) is the most common extra-articular manifestation in Rheumatoid Arthritis (RA) generating higher mortality in these patients. The objective is to describe the mortality rate in a cohort of Rheumatoid Arthritis patients (RA) with Interstitial lung disease (ILD) over time, and to assess the influence of the ILD types on mortality risk.

Methods: The design was a longitudinal prospective study. A cohort of RA patients diagnosed of ILD since February 2007 until June 2017 were recruited and followed up in a multidisciplinary ILD, carried by a pneumologist and a rheumatologist in a Tertiary Hospital in Madrid, Spain. The main variable was death. Covariables: a) sociodemographic (age, sex), b) clinical (basal comorbidities, duration of RA disease, smoke, ILD type (non specific interstitial pneumonia [NSIP]; usual interstitial pneumonia [UIP]); c) pulmonary function tests (PTF ); d) laboratory tests (ESR, CRP, Rheumatoid factor) and therapy (concomitant corticoids, DMARDs and BA). Survival techniques were used to estimate the mortality rate (MR) in our cohort, expressed per 100 patient-years with their respective confidence interval [95 % CI]. They were follow-up until lost of follow-up, death or end of the study. Multivariable Cox proportional hazards model were run to evaluate the influence of ILD types on mortality.

Results: We included 37 patients, 67% were women with a mean lag time from RA diagnosis to ILD of 7.3±8 years and a mean age at diagnosis of ILD 69±1.6 years. 40% never smoked and the BMI was 27±4. Concomitant diseases were as follows: 62% hypertension, 13% cerebrovascular disease, 8% ischemic heart disease, 13% peripheral vascular disease 10% cancer, and 11% sleep apnea syndrome (SAS). Rheumatoid factor was positive in 92% of the patients, and the baseline ESR was 42±22. Regarding the ILD type, 32% had NSIP and 65.6% had UIP. The mean values of PTF parameters were 102%±16.8 for FVC and 68%±16.2 for DLCO. There were 7 deaths per 123.96 person-years at risk in the total cohort. The prevalence of deaths was 19%, and the most of them were due to respiratory cause (72%). The mean survival was 7.6 years and the MR was estimated in 5.6 [2.7-11.8] per 100 patient-years with their respective confidence interval [95 % CI]. They were follow-up until lost of follow-up, death or end of the study. Multivariable Cox proportional hazards model were run to evaluate the influence of ILD types on mortality.

Conclusion: 19% of the patients died, up to 72% were smokers and all of them positive to RF. The mortality rate in RA patients with ILD was 5.6% patient-years, with a mean survival time from diagnosis of ILD of 7.6 years. It seems that the type of ILD influence on mortality, showing that UIP patients have a poorer prognosis independently of the age and the sex.

Disclosure: C. Vadillo Font, None; M. A. Nieto, None; L. Leon, None; L. Rodriguez-Rodriguez, None; J. Font Urgelles, None; E. Pato Cour, None; J. A. Jover, None; L. A. Alcazar, None.
Abstract Number: 2413

**Assessment of the Most Distal Sensory Nerves in Patients with Rheumatoid Arthritis with Normal Value of Standard Nerve Conduction Studies**

Kyung Min Ko¹, Sun Im² and Su-Jin Moon³, ¹Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea, Republic of (South), ²Bucheon St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Bucheon, Korea, Republic of (South), ³Bucheon St. Mary's Hospital, Division of rheumatology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Bucheon, Korea, Republic of (South)

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Although it is generally accepted that peripheral neuropathy can occur in patients with rheumatoid arthritis (RA), most previous studies were conducted in RA patients with neurologic symptoms. We first evaluated the nerve conduction study (NCS) parameters of most distal sensory nerves of the lower extremities—namely the medial dorsal cutaneous (MDC), dorsal sural (DS), and medial plantar (MP) nerves as well as conventional nerves in RA patient, irrespective of neurologic symptoms.

**Methods:** Standard NCSs were performed on healthy controls (HC, n = 68), and RA group (n = 31). The bilateral NCS parameters of the MDC, DS, and MP nerves were investigated. The Toronto Clinical Scoring System (TCSS) was assessed.

**Results:** Age and BMI did not differ between the control and RA group. The mean TCSS scores of the RA and control groups were 5.8 ± 3.0 and 1.3 ± 0.9 respectively (p < 0.001). Although there were differences in NCS values of conventionally studied nerves (sural, superficial peroneal, median, and tibial nerves) between the two groups, the mean values of RA patients were within normal ranges. Interestingly, the RA group showed significant NCS differences in MDC, DS and MP nerves compared with the control group (p<0.001). The NCS parameters of most distal sensory nerves in RA group were not within normal values (mean ± 2 standard deviation). TCSS of RA patients showed significant associations with NCS values of most distal sensory nerves (onset amplitude of MP, sensory nerve action potential [SNAP] of MDC, peak amplitude of DS) (p < 0.05).

**Conclusion:** RA patients, despite of absence of evident neuropathic pain in most cases, showed axonal damage predominantly in most distal sensory large fiber. In patients with vague or equivocal neuropathic pain who showed normal findings on their routine NCS should be considered to evaluate whether they have early NCS changes in the most distal sensory large fiber such as MDC, DS and MP nerves.

**Disclosure:** K. M. Ko, None; S. Im, None; S. J. Moon, None.
Knowledge and Adherence to Current Immunization Recommendations in Patients with Rheumatoid Arthritis in Mexico

Andrea Sofia Cepeda-Perez1, Nina Tello Winniczuk2 and Alejandro Diaz-Borjon2, 1Internal Medicine, Hospital Angeles Lomas, Huixquilucan, Estado de Mexico, Mexico, 2Internal Medicine and Rheumatology, Hospital Angeles Lomas, Huixquilucan, Estado de Mexico, Mexico

First publication: September 18, 2017

Background/Purpose:

Patients with RA have a two to four-fold increased risk of developing infections than the general population. This is due to both, the disease itself and the therapy used to treat it. For this reason, the use of influenza and pneumococcal vaccines is recommended in all patients with AR, as well as shingles vaccine in patients older than 50 years. However, several studies have demonstrated a low prevalence of immunization and adherence to current recommendations by rheumatologists.

Our objective was to determine the knowledge and adherence to the current immunization recommendations in patients with RA by members of the Mexican College of Rheumatology (MCR) and to identify barriers in the application of these recommendations in patients with RA.

Methods:

A cross-sectional study was conducted through a survey sent by email to 577 rheumatologists from Mexico through the MCR database in January 2017.

The questions of this survey were aimed at evaluating the knowledge and adherence to current recommendations on vaccination in RA and to the clinical practice of rheumatologists in relation to these.

Results:

We obtained 122 responses, representing 21.14% of the 577 rheumatologists, of which 38.2% (n=47) were private practitioners, 19.67% (n=24) public practitioners and 41.8% (n=51) were both private and public practitioners.

Of those surveyed, 14.05% considered the responsibility for the update of vaccination schedules belonged to the family or general practitioner, 4.96% to the internist and 80.99% to the rheumatologist.

Moreover, 43.44% reported they did not collect the immunization history in the clinical record.

Also, 75.86% answered they did not recommend vaccines if the patient had contraindications for it, 20.69% did not recommend them because they gave priority to other aspects of the office visit and 3.45% responded they did not recommend it because of lack of time.

In terms of influenza vaccine, 9.84% reported recommending it to 0-25% of their patients, 12.3% to 26-50%, 27.05% to 51-75% and 50.82% to 76-100%. For pneumococcal vaccine, 19.67% reported recommending it to 0-25% of their patients, 20.49% to 26-50%, 23.77% to 51-75% and 36.07% to 76-100%.
Regarding the time of administration for influenza and pneumococcal vaccine, 13.11% administered it before starting treatment with DMARD. 22.13% administered it only before starting treatment with a biologic or tofacitinib, and 54.1% administered it indistinctly, before or during treatment with DMARD, tofacitinib or biologics and 10.66% responded they did not administer it routinely.

For Herpes Zoster vaccine, 69.67% answered they did not routinely recommend it to their patients. Only 6.56% recommended it before or during treatment with conventional DMARD and 23.77% recommended it before starting treatment with tofacitinib or biologics.

Conclusion:

According to the data obtained in this study, we conclude there is not yet adequate information on the importance of vaccination in patients with RA. It also shows us that the degree of adherence to the vaccine recommendations as well as the safety knowledge and optimal timing of vaccine administration are low in Mexico, this is most notable in Herpes Zoster immunization.

Disclosure: A. S. Cepeda-Perez, None; N. Tello Winniczuk, None; A. Diaz-Borjon, UCB Mexico, 8.


Abstract Number: 2415

Immunogenicity and Persistence of a Prime-Boost Re-Vaccination Strategy for Pneumococcal Vaccines (13-Valent Pneumococcal Conjugate Vaccine + 23-Valent Pneumococcal Polysaccharide Vaccine) in Patients with Rheumatoid Arthritis: A Pilot Study

Mathilde Bahuaud¹, Constance BEAUDOUIN², Anna Molto³, Odile Launay⁴, Frederic Batteux⁵ and Maxime Dougados⁶, ¹Université Paris Descartes, Sorbonne Paris Cité AP-HP, Département d’Immunologie Biologique, Groupe Hospitalier Cochin Broca Hôtel-Dieu, Paris, France; Paris, France, ²Cochin Hospital, APHP, Rheumatology B, Paris, France, ³Hôpital Cochin, Department of Rheumatology, Paris Descartes University, Paris, France; ⁴Université Paris Descartes, Sorbonne Paris Cité AP-HP, Groupe Hospitalier Cochin Broca Hôtel-Dieu, Fédération d'Infectiologie, Paris, France; Inserm, F-CRIN I-REIVAC., Paris, France, ⁵Immunology, APHP Hopital Cochin, Paris, France; ⁶Department of Rheumatology, Paris Descartes University, Hôpital Cochin, Paris, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Patients with rheumatoid arthritis (RA) are at an increased risk of some serious vaccine-preventable infections, like Pneumococcal infections. Since 2013, French vaccine recommendations committee considered as the best strategy for immune-suppressed patients, previously vaccinated by one dose of 23-valent pneumococcal polysaccharide vaccine (PPV23), a prime-boost revaccination strategy three years later. We evaluated in a pilot study the immunogenicity of the prime-boost revaccination strategy using PCV13 vaccination followed by PPV23 vaccination 8 weeks later in 24
patients with Rheumatoid Arthritis (RA) treated by Methotrexate (MTX) and anti-TNF. The persistence of a protective immunity for two years after revaccination was also evaluated in our population.

Methods:

Twenty-four patients with RA threatened by MTX + anti-TNF were included after having received one dose of PCV13 (Prevenar13; Pfizer) followed two months later by one dose of PPV23 (Pneumovax®, Merck) during routine-visits according to recommendations. All patients received a previous vaccination by the PPV23, at least three years before enrolment. Blood samples were obtained at baseline, 4 months, 12 months and 24 months following PCV13 immunization. Concentrations of IgG specific for 10 serotypes (7 common to both vaccines: 4, 6B, 9V, 14, 18C, 19F and 23F, and 3 uncommon, included only in the PPV23: 10A, 12F and 15B) were measured by standardized ELISA. Responders were defined as at least an IgG-concentration two fold increased from baseline by ELISA. An IgG-concentration ≥ 1.3µg/ml was used to defined long-term protection and Protected patients were those who fulfilled this criteria for at least 70% of the serotypes. Primary endpoint was the proportion of responders in ELISA for 70% of serotypes at four months.

Results:

Long term follow-up of antibody response to the vaccine shows a more severe decrease in the percentage of responders one and two years post immunization for the 7 common serotypes (from 33% responders at four months to 4% at 12 months and 3% at 24 months post immunization) compared to the 3 uncommon (from 47% responders at 4 months to 24% at 12 months and 23% at 24 months post immunization). As all patients received at least 3 years before enrolment one dose of PPV23, we found 33% (7 common serotypes) and 24% (3 uncommon serotypes) of patients considered protected at baseline. Similar percentages of protection were found at 4 months (63% vs. 65%), 12 months (54% vs. 59%) and 24 months (50% vs. 77%) for the 7 common and 3 uncommon serotypes.

Conclusion:

If the percentage of protection is quite equivalent for the seven common and the three uncommon serotypes, the more intense drop in antibody response for the seven common serotype compared to the three uncommon may suggest a negative impact of the PPV23 vaccine on the PCV13 response. The prime-boost strategy is recommended because of the poor immunogenicity of both type of pneumococcal vaccine in this case. Our results clearly question the advantage of the prime-boost strategy versus PPV23 or PCV13 alone as it highlight the possible hyporesponse induced by PPV23 against the immune response elicited by the primo-injection of the PCV13 vaccine.

Disclosure: M. Bahuaud, None; C. BEAUDOUIN, None; A. Molto, None; O. Launay, Pfizer Inc, 2; F. Batteux, None; M. Dougados, Abbvie, Pfizer, Eli Lilly and Company, Novartis, UCB, Merck, Roche, BMS UCB, 2,Abbvie, Pfizer, Eli Lilly and Company, Novartis, UCB, Merck, Roche, BMS, UCB, 5.

Histopathological Change Caused By Biological Treatment in Rheumatoid Arthritis Synovial Tissue

Ayako Kubota, Toru Suguro, Masayuki Sekiguchi and Kazuaki Tsuchiya, Toho University Omori Medical Center, Tokyo, Japan

First publication: September 18, 2017
Multiple studies addressing the effects of biologics on the synovial tissue in rheumatoid arthritis (RA) patients have been reported. There are, however, few studies comparing histopathological changes in the synovial tissue in the same RA patients between before and after biologics treatment. We examined biologics impacts on RA synovial tissues based on pathological findings in them collected during surgeries for the same patient before and after biological drug usage.

Methods:

Synovial tissues were collected from 28 RA joints before and after biologics. The average age and disease duration of the study subjects were 63.8 and 20.9, respectively. Histopathological changes in the synovial tissues were compared based on Rooney’s score, and presence or absence of fibrinoid degeneration, proliferation of villi and plasma cell infiltration in the subsynovial tissue. We examined correlation between pathological findings in RA synovium and disease activity under biologics. Disease activity was assessed by CDAI. Etanercept, Infliximab, Tocilizumab, Adalimumab and Abatacept was used as biological drug for 16, 5, 3, 2 and 2 joints respectively.

Results:

Rooney score between before and after biological drug usage improved from 28.4 to 12.3 showing significant difference. Significant improvement in Rooney score was observed in all items. Fibrinoid degeneration was observed in 25 cases (89.3%) and 5 cases (17.9%) before and after biologics treatment, respectively, demonstrating a significant reduction with biologics treatment. Proliferation of villi was observed in 27 cases (96.4%) and 10 (35.7%) before and after biologics treatment, respectively, demonstrating a significant reduction with biologics treatment. Plasma cell was observed in 24 cases (85.7%) and 15 (53.6%) before and after biologics treatment, respectively, demonstrating a significant reduction with biologics treatment. After biologics treatment, Rooney’s scores in the remission, low disease activity and moderate disease activity were 9.0, 10.2 and 15.6, respectively, showing a statistically significant difference. In addition, the moderate disease activity had significantly higher scores in perivascular lymphocytic infiltration, lymphoid follicle and lymphocyte infiltration compared to the remission and low disease activity.

Conclusion:

The study results demonstrated that biologics treatment significantly ameliorated inflammatory changes in the synovial lining layers and sublining layers. In addition, the results suggested that histopathological findings in the subsynovial tissue reflected disease activity.

Disclosure: A. Kubota, None; T. Suguro, None; M. Sekiguchi, None; K. Tsuchiya, None.
SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects Poster III: Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Patients with Rheumatoid Arthritis (RA) experience higher cardiovascular (CV) morbidity compared to controls. Coronary computed tomography angiography (CCTA) accurately detects plaque presence, burden and composition and independently predicts short and long-term incident cardiac events in general patients with unknown coronary artery disease (CAD). We evaluated, for the first time, the long-term prognostic role of CCTA in a cohort of established RA patients without symptoms or known cardiovascular disease.

Methods: One hundred and fifty participants from a single center underwent a baseline 64-slice CCTA for plaque evaluation between 3/2010-3/2011 and followed for a mean of 60±26 months. Patients were classified based on presence of normal coronaries, non-obstructive (<50%) and obstructive (>50%) lesions. Atherosclerosis burden was further evaluated with coronary plaque scores: SIS or segment involvement score, reflected number of segments with at least 1 plaque; SSS or segment stenosis score represented the overall plaque extent. The composite rates of ischemic CV events [cardiac death, non-fatal myocardial infarction (MI), ischemic stroke, peripheral arterial ischemia] were the study end-points. Cox regression analysis evaluated associations between CCTA parameters and outcomes; hazards ratios were generated in both raw and adjusted models. Event-free survival was assessed with Kaplan-Meier analysis and curves were compared using the log-rank test.

Results: Eleven patients suffered incident CV events (1.54/100PY): 8 were ischemic, including 1 cardiac death, 3 MI, 2 strokes, and 2 peripheral arterial ischemic events requiring emergent revascularizations; the 3 non-ischemic events were new onset, hospitalized, systolic heart failure. No ischemic events occurred in patients with normal coronaries (Figure 1); by contrast event-free survival was 97.5% and 63.3% in patients with non-obstructive and obstructive CAD respectively at 60 months (p=0.0001). Obstructive CAD was an independent predictor of ischemic events (HR=16.4, p=0.003, Table 1). Plaque burden was equally predictive; event-free survival was 97.1% vs. 54.4% in those with SIS=<5 vs. SIS>5 and 98.6% vs. 63% in patients with SSS=<5 vs. SSS>5, (both p<0.0001); 95% with CAC=<100 vs. 76% with CAC>100 experienced no events at 60 months (p<0.0001, Figure 1).

Conclusion: CCTA provided prognostic information in RA patients without symptoms or known CV disease; it showed excellent long-term prognosis when there was no evidence of atherosclerosis, and allowed risk stratification when CAD was present.
Disclosure: G. Karpouzas, None; J. Estis, None; J. Todd, None; M. Budoff, None.


Abstract Number: 2418
Tissue-Engineered Human Skeletal Muscle Model of Rheumatoid Arthritis

Catherine E. Oliver¹, Brittany N. Davis¹, James Hong¹, Kim M. Huffman² and George A. Truskey³
¹Duke University, Durham, NC, ²School of Medicine, Division of Rheumatology, Immunology and Molecular Physiology and Duram VA Medical Center, Duke University, Durham, NC, ³BME, Duke University, Durham, NC

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: In rheumatoid arthritis (RA) reduced muscle function clearly contributes to disability. Due to a lack of accurate in vitro RA models, the underlying mechanisms are not well understood. Moreover, current animal and cell culture systems are imperfect models of human disease, including RA, and do not recapitulate biologic and physiologic features of human skeletal muscle. Using engineered electrically responsive, contractile human skeletal muscle constructs (myobundles), we have established an in vitro 3D disease model of RA muscle to test the hypothesis that (1) myobundles derived from cells of RA patients show reduced capacity for repair and differentiation and reduced force production and (2) the overall decrement in function is due to select myokine (e.g. myostatin) and cytokine production.

Methods: Myobundles were fabricated using vastus lateralis skeletal muscle cells from RA patients and healthy controls. To block myostatin and subsequent downstream signaling events, LDN-193189 was added at the transition from myoblasts to myotubes, after myobundle fabrication. After a 1- to 2-week differentiation period, tissue function was assessed by measuring myobundle twitch and tetanic contraction using a custom force measurement system. Muscle maturation was assessed by immunostaining myobundles for maturation markers, myosin heavy chain (MHC) or sarcomeric α-actinin (SAA). 2D studies were also performed with RA cells and healthy controls to quantify myoblast purity and percent nuclei per SAA-positive fiber. Unpaired t-tests were used to compare differences.

Results: Compared to healthy controls (n=4 donors) at 2-weeks differentiation, myobundles generated from RA vastus lateralis cells (n=3 donors) exhibited reduced twitch and tetanus forces and myosin heavy chain staining. Treatment with 0.05 µM LDN-19318979 in 2D culture improved maturation (RA₂=47.5±1.5% % nuclei/SAA+ fiber versus Control₂=20.3±2.0%; Figure 1). Ten-day treatment of myobundles with 0.05 µM LDN-19318979 increased force production in RA myobundles (n=3 donors), but not in controls (n=3 donors).

Conclusion: Compared to healthy controls, RA myobundles exhibit reduced force production and MHC or SAA staining, indicative of reduced maturity and fiber formation. Treatment with LDN-19318979 increased RA myoblast fusion and myofiber formation in 2D and force production in 3D. RA muscle dysfunction may result from myostatin-mediated alterations in muscle remodeling.
Immunomodulatory Effects of Bone-Marrow Mesenchymal Stem Cells in Rheumatoid Arthritis: Influence of Disease Activity

Benjamín Fernández-Gutiérrez, Jose Ramon Lamas, Yaiza Lopiz, Cristina Lajas, Lydia A Alcazar and Luis Rodriguez-Rodriguez

1Department of Rheumatology, Hospital Clinico San Carlos, Madrid, Spain, 2Rheumatology, Instituto de Investigación Sanitaria San Carlos (IdISSC), Madrid, Spain, 3Cirugía Ortopédica y Traumatología, Hospital Clínico San Carlos, Madrid, Spain, 4Rheumatology Department, Hospital Clinical San Carlos, Madrid, Spain, 5Rheumatology Department and Heath Research Institute (IdISSC), Hospital Clinico San Carlos, Madrid, Spain, 6Department of Rheumatology, Hospital Clínico San Carlos, Madrid, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
To analyze the effect of demographic and clinical related characteristics of rheumatoid arthritis (RA) patients in the immunomodulatory effects of mesenchymal stem cells (MSCs). The proportion of CD69+, CD25+, and regulatory T cells (Treg) among CD4+ peripheral blood mononuclear cells (PBMCs) was used as surrogate markers of immunomodulation.
**Methods:**

**RA patients:** Consecutive patients diagnosed with RA according to the 2010 ACR/EULAR criteria attending from the Hospital Clínico San Carlos Rheumatology Outpatient Clinic. Demographic and clinical data was collected, including a Disease Activity Score of 28 joints (DAS28). PBMCs were isolated from fasting venous blood using density gradient centrifugation.

**MSCs donors:** MSCs were obtained from bone marrow aspirates from the iliac crests of 6 healthy donors. Cells in the fourth passage were used in the experiments.

**Co-cultures:** PBMCs were cultured alone or with MSCs (1 MSC:10 PBMCs) for 24h, 72h and 6 days. PBMCs were stimulated using CD3/CD28 coated beads (1 bead:4 PBMCs).

**T cell cytometry:** PBMCs were stained with anti CD4, anti CD25, anti CD69, and anti CD127 antibodies. The lymphocyte population was identified by side scatter/forward scatter. Treg cells were gated on the basis of CD4 expression, in combination with higher (bright) expression of CD25 and low/negative expression of CD127.

**Statistical analysis:** Influence of co-culture with MSCs and duration of culture in surface markers expression and Treg proportion was analyzed using repeated measures ANOVA (nested by RA patient) with the “lmerTest” R package. Coculture with BM-MSCs (yes/no) and time of culture (24h, 72h, 6 days) were the within-subject variables. An interaction between both was introduced in the analysis. Gender, age at inclusion, presence of RF, presence of ACPA, disease activity (DAS28-CRP: remission/low vs. moderate/high disease activity), current use of methotrexate, and current use of biological therapies were between subject variables. Triple interactions (adjusted by the BM-MSCs donor) among the within-subject variables and each between-subject variables were performed. P-values were adjusted using the FDR correction.

**Results:**

15 RA patients were collected. Interactions between co-culture and time were significant for CD69+, CD25+ and Treg proportion (p<0.0001 for each term). Only disease activity showed a significant interaction with time and co-culture in their influence in the proportion of CD69+ cells (p=0.003; Figure 1). In the post-hoc comparisons, patients in remission/low disease activity showed a higher expression of CD69 after 6 days of co-culture (p=0.017).

**Conclusion:**

The degree of disease activity could influence the effect of MSCs. In patients with lower disease activity could exert a greater immunomodulatory effect.
Mass Cytometry Analysis of CD4+ T Cells in Patients with Rheumatoid Arthritis

Laura Su\textsuperscript{1}, Daniel del Alcazar\textsuperscript{2} and Adam Marc\textsuperscript{2}, \textsuperscript{1}University of Pennsylvania, Philadelphia, PA, \textsuperscript{2}Medicine, University of Pennsylvania, Philadelphia, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: CD4+ T cells play a key role in the initiation and progression of RA. Past studies have identified impaired function and regulation of several CD4+ T cell lineages in RA patients. However, how diverse cellular subsets are maintained has not been comprehensively analyzed. Here, we utilized mass cytometry to
simultaneously assay expression of 36 markers to examine high-dimensional complexity of CD4+ T cells in RA patients.

**Methods:** Cryopreserved cells from 10 RA patients and 7 healthy controls were thawed, washed, and stimulated with 5ng/ml of PMA and 50ng/ml ionomycin in the presence of 2mM Monensin and 5ug/ml Brefeldin A at 37°C for 5 hours. After stimulation, cells were washed and incubated in 1uM cisplatin for 5 min, followed by staining with surface antibody cocktail for 30 min at room temperature. A panel of 36 metal conjugated antibodies was generated using the X8 Maxpar kit. For intracellular staining, cells were permeabilized and fixed using Foxp3 staining buffer set and incubated with the intracellular antibody cocktail for 1 hr at room temperature. After staining, cells were washed then resuspended in 2% paraformaldehyde with 125nM iridium intercalator for an overnight incubation at 4°C. The next day, cells were washed and resuspended in PBS containing normalization beads before acquisition on CyTOF 2.

**Results:** Our data show a prominent expansion of CD57+ CD4+ T cells in RA patients. CD57+ T cells express cytotoxic granules, perforin, granzymes A and B, and have been previously associated with more active and erosive disease in RA. Interestingly, we identified three distinct subsets of CD57+ CD4+ T cells and only those that co-express high levels of IFN-γ and TNF-α are increased in RA patients. In addition, patient derived samples showed a decrease in several populations of cytokine negative CD45RA+ naïve T cells.

**Conclusion:** Pilot analysis on a small numbers of samples from RA patients and healthy controls revealed cellular complexity in CD4+ T cells and suggested unique changes in RA patients. Extension of this analysis to a large cohort of RA patients with well annotated disease characteristics may uncover novel biomarkers for detection of early disease and provide new insights into the pathogenesis of RA.

**Disclosure:** L. Su, None; D. del Alcazar, None; A. Marc, None.


**Abstract Number: 2421**

**Aberrant Expression of CaMK4 in CD4 Positive T Cells Predicts Poor Response to Treatment in Patients with Active Rheumatoid Arthritis**

Tomohiro Koga1, Tomohito Sato1, Masataka Umeda2, Shoichi Fukui2, Ayako Nishino1, Shinya Kawashiri2, Naoki Iwamoto2, Kunihiro Ichinose2, Mami Tamai1, Tomoki Origuchi3, Hideki Nakamura2 and Atsushi Kawakami4,

1Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, 2Department of Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, 3Department of Rehabilitation Sciences, Nagasaki University, Nagasaki, Japan, 4Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki City, Japan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster III

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**
Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease arising from a breakdown of peripheral tolerance, which leads to aberrant Th1- or Th17-driven immune reaction. Although aberrant Calcium/calmodulin-dependent protein kinase IV (CaMK4) activation has been implicated in the development of Th17 driven autoimmune diseases, the roles of CaMK4 activation in CD4+ T cells in the development and the pathogenesis of RA remain to be elucidated.

Objectives:
We sought to determine the significance of CaMK4 in the pathological condition of RA and to clarify whether the expression of CaMK4 can be a prognostic predictor for the progression of RA in daily practice.

Methods:
We treated collagen-induced arthritis (CIA) mice with KN-93, an inhibitor of CaMK4 and evaluated the clinical score, in vivo micro-computed tomography (f-CT), and histological assessment. We examined the gene expression of Camk4 in CD4+ T cells from healthy controls (HC: n=20) and patients with active RA (n=21; median of DAS-ESR:5.14). We performed a multiple logistic regression analysis to explore the factors to predict poor response to treatment at 6 months.

Results:
Treatment of CIA mice with KN-93 results in a significant reduction of the clinical score of CIA severity and this is accompanied by decreased joint destruction evaluated by f-CT and histology analysis. The expression of Camk4 mRNA in CD4+ T cells displayed significantly higher in RA patients than HC. Of note, the multiple logistic regression analysis revealed that the independent variables to predict poor response to treatment were the expression level of Camk4 mRNA in CD4 positive T cells from RA patients at baseline (OR= 24.7, 95%CI 2.76-634) and DAS-ESR at baseline (1-unit increase OR=4.40, 95%CI 1.67-18.5).

Conclusion:
Our results indicate that CaMK4 expression associates with RA development and its inhibition represents a novel therapeutic strategy for the treatment of RA.

Acknowledgements:
This work was supported by grants from the Leading Initiative for Excellent Young Researchers of the Ministry of Education, Culture, Sports, Science and Technology (to T.K: no. 16810055) and the Uehara Memorial Foundation (to T.K: no 201510047).

Disclosure: T. Koga, None; T. Sato, None; M. Umeda, None; S. Fukui, None; A. Nishino, None; S. Kawashiri, None; N. Iwamoto, None; K. Ichinose, None; M. Tamai, None; T. Origuchi, None; H. Nakamura, None; A.
**Rheumatoid Arthritis (RA) Synovial Fluid Treg Cells Secrete IL-17 and at the Same Time Are Potent Suppressors of Tresp Cell Proliferation, TNF-α and Interferon γ Production**

Lorena Valdeolivas-De Opazo¹, Paula Fortea-Gordo¹, Marta Benito-Migue³¬², Alejandro Villalba¹, Gema Bonilla¹, Diana Peiteado¹, Alejandro Balsa¹, Pilar Aguado¹, Paloma Sanchez-Mateos³, Amaya Puig-Kröger⁴, Emilio Martín-Mola¹ and Maria Eugenia Miranda-Carus¹, ¹Rheumatology, Hospital La Paz-IdiPAZ, Madrid, Spain, ²Biochemistry, Centro de Ciencias de la Salud San Rafael. Universidad Antonio de Nebrija, Madrid, Spain, ³Immunology, Hospital Gregorio Marañón, Madrid, Spain, ⁴Immuno-oncology, Hospital Gregorio Marañón, Madrid, Spain

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster III

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** IL-17-expressing FoxP3 regulatory T cells have been described, and their suppressive capacity has been questioned. An inflammatory environment seems to favor IL-17 secretion by regulatory CD4+CD25+FoxP3+ T cells. Therefore, our objective was to assess the suppressive function and IL-17 producing capacity of CD4+CD25+CD127-FoxP3+ T cells in the synovial fluid of RA patients (RASFd).

**Methods:**

Synovial fluid was drawn from 35 patients with established RA who were receiving methotrexate and low-dose oral prednisone. The frequency of CD4+CD25+CD127-FoxP3+ T cells was assessed by flow cytometry. Total CD4+ T cells, CD4+CD25+CD127- T reg cells and CD4+CD25- Tresp cells were isolated by Ficoll-Hypaque gradient, followed by sorting. After isolation, cells were cultured for 5 days in flat-bottom 96-well plates coated with an anti-CD3 monoclonal antibody. Treg cell function was assessed using two different approaches: A. The regulatory function of natural proportions of Tregs was inferred by comparing the proliferative and cytokine responses of total CD4+ T cells (TCD4T) versus CD25+ depleted CD4+ T cells (CD4+CD25-T cells or Tresp cells); B. The per cell suppressor potency of Tregs was assessed in cocultures of isolated Tregs with Tresp, established at different Treg/Tresp ratios. Proliferation was determined by ³Hthymidine incorporation and CFSE dilution; cytokine secretion was measured by ELISA of culture supernatants.

**Results:**

A high proportion of CD4+CD25+CD127- T cells was present in RASFd (mean ± SD, 21.1%±6.2), which is significantly higher than reported frequencies of this cell population in the peripheral blood of both RA and healthy subjects. These RASFd CD4+CD25+CD127- T cells expressed FoxP3 but did not express CD69. The proliferation rate, TNFα and IFNγ secretion were significantly higher for isolated Tresp as compared with TCD4T cells, indicating that natural proportions of Treg cells present in the synovial fluid of RA are functionally suppressive. Surprisingly, TCD4T cells secreted higher amounts of IL-17 as compared with Tresp cells, although the difference did not reach statistical significance. On a per cell basis, RAPB Tregs were potent suppressors of Tresp proliferation, TNFα and IFNγ but not of...
IL-17 secretion; in fact IL-17 secretion did not decrease but was enhanced in the presence of increasing proportions of Treg cells. Isolated Treg cells did not proliferate or produce cytokines when cultured alone in anti-CD3 coated plates. However, in the presence of plate-bound anti-CD3 plus anti-CD28 and recombinant human IL-2, isolated Treg cells secreted significant amounts of IL-17 whereas no TNFα or IFNγ could be detected in supernatants.

Conclusion: CD4+CD27+CD127- FoxP3+ Treg cells present in the synovial fluid of RA patients are potent suppressors of Tresp cell proliferation, TNFα and IFNγ secretion, and at the same time produce significant amounts of IL-17.

Disclosure: L. Valdeolivas-De Opazo, None; P. Fortea-Gordo, None; M. Benito-Miguel, None; A. Villalba, None; G. Bonilla, None; D. Peiteado, None; A. Balsa, None; P. Aguado, None; P. Sanchez-Mateos, None; A. Puig-Kröger, None; E. Martín-Mola, None; M. E. Miranda-Carus, None.

Abstract Number: 2423

Patients with Active Rheumatoid Arthritis but Normal Levels of Acute Phase Proteins Have Altered Regulatory T Cell Function and Rapidly Progress to Biological Therapies

Claire Bradford¹, Shashank Ramakrishnan¹, Andrew Cole², Coziana Ciurtin³, Elizabeth Jury¹ and Jessica Manson⁴, ¹Division of Medicine, Centre for Rheumatology Research, University College London, London, United Kingdom, ²Centre for Rheumatology Research, University College London, London, United Kingdom, ³Rheumatology Department, University College London, London, United Kingdom, ⁴University College London Hospitals NHS Trust, London, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

An atypical subgroup of patients with seropositive rheumatoid arthritis (RA) was identified with active disease (confirmed by Power Doppler ultrasound (PDUS)) but normal levels of the acute phase protein C-reactive protein (CRP). We questioned whether this presentation was associated with altered response to treatment, risking worse disease outcome. Our objective was to investigate whether we could exploit the immunological and clinical phenotype of this patient subgroup to propose a more appropriate treatment algorithm.

Methods:

48 RA patients with active synovitis were recruited, defined by ≥1 joint with positive PDUS, 30 had normal (n)CRP (≤5mg/L) and 18 had high (h)CRP (>5mg/L) levels. Peripheral blood mononuclear cells (PBMC), serum and detailed clinical data were collected. 20 age- and sex-matched healthy donors were also analyzed. Multiparameter flow cytometry was used to perform in-depth PBMC immunophenotyping.
Results:

Pro-inflammatory cytokines IL-6, IL-1β, and TNF-α contribute to RA pathogenesis and are key in triggering CRP production. Despite normal measured CRP levels, all these cytokines were significantly elevated in both patient groups compared to HC (p=<0.001). CRP, SAA and IL-6 all correlated positively with pro-inflammatory cytokines in hCRP patients but not nCRP patients. Conversely, pro-inflammatory cytokine levels positively correlated with markers of disease severity in nCRP patients only. Interestingly, nCRP patients were able to mount a CRP response to infection. Thus the results point to an altered disease mechanism in nCRP compared to hCRP patients. In-depth phenotyping identified unique immune signatures in both patient groups compared to HCs and when compared to each other. Notably, nCRP patients had a significant increase in naïve regulatory T cells (Tregs) and in CD161 Tregs (known to correlate negatively with CRP levels and have increased suppressive capacity) compared to hCRP patients. Furthermore, Treg frequencies correlated significantly with markers of disease progression and serum lipids in the nCRP but not the hCRP patients suggesting that defects in Treg function and potentially lipid metabolism could play a role in disease pathogenesis in nCRP patients.

The immunological differences between the two groups were associated with an altered response to treatment. Disease activity was assessed ≥1 year post recruitment. In nCRP patients 50% still had active disease compared to only 10% in hCRP patients. Also, 50% of nCRP patients had treatment escalated to a biological (b)DMARD compared to only 10% of hCRP patients.

Conclusion:

This study stratifies distinct patient subgroups using detailed, clinical, immunophenotyping and proteomic signatures. We have identified altered immunopathological mechanisms in nCRP patients which could translate to improved patient-specific therapies. Provisional analysis suggested that nCRP patients were less responsive to treatment with conventional DMARDs, needing escalation to biologics earlier in their disease.

Disclosure: C. Bradford, None; S. Ramakrishnan, None; A. Cole, None; C. Ciurtin, None; E. Jury, None; J. Manson, None.

CD8-Positive Lymphocytes in Biopsy Specimens Predict Spontaneous Regression of Lymphoproliferative Disorders in Patients with Rheumatoid Arthritis Treated with Methotrexate

Tomohiro Kameda1, Hiroaki Dobashi1, Masayuki Inoo2, Ikuko Onishi2, Noriyuki Kurata2, Mikiya Kato1, Atsushi Kondo1, Risa Wakiya1, Hiromi Shimada1, Shusaku Nakashima1, Miharu Izumikawa1 and Norimitsu Kadowaki1,
1Internal Medicine Division of Hematology, Rheumatology, and Respiratory Medicine, Kagawa University, Kagawa, Japan, 2Utazu hospital, Kagawa, Japan
First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM
Background/Purpose: Patients with rheumatoid arthritis (RA) have a high risk of developing lymphoproliferative disorders (LPDs). LPDs that develop in patients treated with methotrexate (MTX) are known as MTX-associated LPDs (MTX-LPDs). We previously reported that MTX is an independent risk factor for LPD onset in Japanese patients with RA. The main characteristic of MTX-LPDs is that MTX withdrawal possibly results in spontaneous regression of the LPD. However, the predictive factors of spontaneous regression of MTX-LPDs remain unclear. Some reports have suggested that Epstein-Barr virus infection and increased peripheral lymphocytes after MTX discontinuation are related to spontaneous regression of MTX-LPDs. However, evidence of the relationships between these factors and spontaneous regression of MTX-LPDs is lacking. We investigated the predictive factors for spontaneous regression of MTX-LPDs in patients with RA.

Methods: We enrolled RA patients who developed MTX-LPDs in Kagawa Prefecture, Japan from June 2010 to March 2017. Patients were diagnosed according to the American College of Rheumatology 1987 classification criteria and treated with MTX. We divided the patients into those who were followed up after discontinuation of MTX alone (MTX withdrawal group) and those who underwent chemotherapy (CTx) ≥1 month after MTX discontinuation (CTx group). The following differences between the two groups were examined: 1) change in the peripheral lymphocyte count after MTX discontinuation, 2) subset of lymphocytes in a biopsy specimen from a lesion, and 3) histological findings of biopsied lesions using immunohistochemistry (IHC).

Results: We enrolled 45 patients with MTX-LPDs. The withdrawal group comprised 30 patients, and the CTx group comprised 15 patients. Between these two groups, 32 patients underwent analysis of the change in the peripheral lymphocyte count. Additionally, 22 patients (11 in the withdrawal group and 11 in the CTx group) underwent analysis of the subset of lymphocytes, and 12 (8 in the withdrawal group and 4 in the CTx group) underwent analysis of the IHC findings with a specimen from a lesion. In the withdrawal group, the peripheral lymphocyte count was significantly elevated after MTX discontinuation. With respect to the subset of lymphocytes and IHC findings, the number of CD8-positive lymphocytes increased by more in the CTx group than withdrawal group.

Conclusion: This study showed that the change in lymphocytes before and after MTX discontinuation and low levels of CD8-positive lymphocytes in biopsy lesions are associated with spontaneous regression of MTX-LPDs. We suggest that these factors may become predictive markers for MTX-LPD treatment strategies.

Disclosure: T. Kameda, None; H. Dobashi, None; M. Inoo, None; I. Onishi, None; N. Kurata, None; M. Kato, None; A. Kondo, None; R. Wakiya, None; H. Shimada, None; S. Nakashima, None; M. Izumikawa, None; N. Kadowaki, None.


Abstract Number: 2425

Decline in CD8+IFNγ+ Subset but Rise in CD8+IL17+ on Methotrexate Treatment in Rheumatoid Arthritis

Amit Sandhu1, Varun Dhir2, Shabeer Ahmad1, Prabhdeep Kaur1, Veena Dhawan3 and Archana Bhatnagar4, 1Internal Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh, India, 2Internal Medicine (Rheumatology Unit), Postgraduate Institute of Medical Education and Research, Chandigarh, India, 3Experimental Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh, India, 4Biochemistry, Panjab University, Chandigarh, India

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Background/Purpose: CD8 T cells comprise 40% of all T cells in the synovial compartment and are detectable in the preclinical stages as well. They have been shown to play an important role in rheumatoid arthritis pathogenesis. They can be divided by cytokine production into CD8+IFNγ+, CD8+IL4+ and CD8+IL17+. Methotrexate is the gold standard benchmark DMARD used in therapy of RA. The effect of methotrexate on these circulating CD8 T cell subsets has not been well described.

Methods: Patients who were 18 to 65 years of age and having active rheumatoid arthritis (fulfilling the ACR 1987 criteria) were treated with methotrexate for 24 weeks. Methotrexate was started at 15 mg per week, and escalated at 5 mg per month to a maximum of 25 mg per week. Disease activity was measured using the disease activity score and response to treatment assessed by EULAR criteria. At 0 (baseline) and 24 weeks (post methotrexate), PBMCs were isolated using density gradient centrifugation and stimulated with PMA/Ionomycin (with Brefeldin) for 5.5 hours. Surface staining was done using anti CD3/anti CD8 and intracellular cytokine staining with tagged antibodies to IFNγ, IL17 and IL4. 30,000 events were acquired and in CD3+ gate, frequencies of CD8+IFNγ+ cells, CD8+IL17+ and CD8+IL4+ were determined. Cytokine bead array was used to determine levels of IFNγ, IL-12, IL-10, IL-4 and IL-17 in plasma at 0 and 24 weeks. Cell frequencies and cytokine levels at baseline and 24 weeks were described by using median (IQR=interquartile range, 25th-75th percentile) and compared using non-parametric paired test (wilcoxon signed rank).

Results: This study included 67 patients (F:M=4:1) with rheumatoid arthritis, 57 (85%) being RF positive and 20 receiving prednisolone at baseline. The mean dose of methotrexate at 24 weeks was 22.9±3.0 mg per week. DAS28 declined from 5.9±1.1 to 4.8±1.0 (p<0.001). CD8+IFNγ+ cells declined from 37.2 (IQR 19.4-60.2) to 22.7% (IQR 8.5-49.7), p=0.04 and there was marginal increase in CD8+IL17+ cells from 0.3 (IQR 0.1-0.6) to 0.4 (IQR 0.2-1.2), p=0.006. In non-responders, there was a significant increase in CD8+IL17+ (p=0.01) that was not seen in responders. There was a significant decline in the circulating levels of IL-12 [519(IQR 40.4-2336.1), 124.7(IQR 23.5-771.9) pg/ml, p<0.001) and IL-17 but increase in IL-4 with treatment.

Conclusion: Methotrexate leads to changes in circulating CD8 subsets, predominantly decline of the CD8+IFNγ+ subset, that may be explained due to reduction in the polarising cytokine IL-12 and increase in IL-4. This may be one of the mechanisms responsible for the effect of methotrexate in RA.

Disclosure: A. Sandhu, None; V. Dhir, None; S. Ahmad, None; P. Kaur, None; V. Dhawan, None; A. Bhatnagar, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/decline-in-cd8ifn%ce%b3-subset-but-rise-in-cd8il17-on-methotrexate-treatment-in-rheumatoid-arthritis

Abstract Number: 2426

Altered Frequencies of Circulating Follicular T Helper Cell Counterparts and Their Subsets but Not of Peripheral Helper T Cells, Are Associated with Increased Circulating Plasmablasts in Seropositive Early RA Patients

Paula Fortea-Gordo1, Lorena Valdeolivas-De Opazo1, Laura Nuño2, Alejandro Villalba1, Paloma Sanchez-Mateos3, Amaya Puig-Kröger4, Alejandro Balsa1 and Maria Eugenia Miranda-Carus1, 1Rheumatology, Hospital La Paz-IdiPAZ, Madrid, Spain, 2Rheumatology, La Paz University Hospital, Madrid, Spain, 3Immunology, Hospital Gregorio Marañón, Madrid, Spain, 4Immuno-oncology, Hospital Gregorio Marañón, Madrid, Spain

First publication: September 18, 2017
Follicular T helper (Tfh) cells are typically located in lymphoid organs where they promote B cell differentiation and function. Circulating CD4 T cells expressing CXCR5 together with ICOS and/or PD-1 are considered as counterparts of Tfh and have B cell helper capacity (Simpson N et al, Arthritis Rheum 2010; Craft J, Nat Rev Rheumatol 2012). In addition, three subpopulations of circulating Tfh counterparts have been described: CXCR5+CXCR3+CCR6- (Tfh-Th1), CXCR5+CXCR3-CCR6+ (Tfh-Th17) and CXCR5+CXCR3-CCR6- (Tfh-Th2). Only Tfh-Th17 and Tfh-Th2, but not Tfh-Th1, display functional properties of Tfh cells (Morita et al., Immunity 2011). Altered numbers of these circulating Tfh counterparts (cTfh) and subpopulations have been associated with established RA but there are no reported studies on early RA (eRA). Furthermore, it has recently been published that CD4+CXCR5-PD-1hi cells ("peripheral helper T cells" or Tph) also have a Tfh-like function, and are increased in the peripheral blood of RA patients (Rao DA et al, Nature 2017). Therefore, our objective was to study the frequency of cTfh, cTfh cell subsets, Tph cells and circulating plasmablasts (CD19+CD20-CD27+CD38hi B cells), in patients with eRA.

Methods:

Peripheral blood was drawn from DMARD-naïve early RA patients (2010 ACR criteria) with a disease duration < 24 months (n=32), and healthy controls matched for age and gender (n=32). After isolation by Ficoll-Hypaque gradient, PBMCs were stained with antibodies to CD3, CD4, CXCR5, ICOS, PD-1, CCR6, CXCR3, CD19, CD20, CD27, and CD38, and examined by flow cytometry.

Results:

The frequency of circulating CXCR5+ cells gated for CD4+ T cells was not different among the studied groups. In contrast, eRA patients demonstrated an increased frequency of CD4+CXCR5+ICOShi, CD4+CXCR5+PD-1hi and CD4+CXCR5+ICOShiPD-1hi cells. Furthermore, in eRA patients, the frequency of Tfh-Th1 cells was significantly decreased and the frequency of Tfh-Th17 and Tfh-Th2 cells was significantly increased as compared with controls. Subsequently, the ratio (Tfh-Th17+Tfh-Th2)/Tfh-Th1 was increased in eRA. That is, eRA patients demonstrate a higher proportion of Tfh cell subsets bearing a phenotype associated with B cell helping capacity. When examining seropositive (RF+ and/or ACPA+, n=17) and seronegative eRA patients (RF- and ACPA-, n=15) separately, it was evident that the above described alterations were only apparent in seropositive eRA. At the same time, the frequency of circulating plasmablasts was increased in seropositive but not in seronegative eRA. However, the frequency of Tph cells in seropositive or seronegative eRA was not different from controls.

Conclusion:

Seropositive, but not seronegative eRA patients, demonstrate an increased frequency of circulating Tfh counterparts and altered proportions of circulating Tfh subpopulations, with overrepresentation of subsets bearing a phenotype associated with B cell helping capacity. At the same time, an increased proportion of circulating plasmablasts is apparent in seropositive eRA patients. However, the frequency of Tph cells in eRA is not different from controls.

Disclosure: P. Fortea-Gordo, None; L. Valdeolivas-De Opazo, None; L. Nuño, None; A. Villalba, None; P. Sanchez-Mateos, None; A. Puig-Kröger, None; A. Balsa, None; M. E. Miranda-Carus, None.

Exosomes Derived from T Lymphocytes Enhance Expression of CXCL10 Induced By IFN-γ in Rheumatoid Arthritis Synovial Fibroblasts Via Pattern Recognition Receptor, RIG-I

Kunihiko Umekita, Shunichi Miyauchi, Koshou Iwao, Mao Rikitake, Yuuki Rikitake, Chihiro Kawada, Ayako Aizawa, Yumi Kariya, Motohiro Matsuda, Takeshi Kagawuchi, Hajime Nomura, Ichiro Takajo and Akihiko Okayama, Department of Rheumatology, Infectious Diseases and Laboratory Medicine, University of Miyazaki, Miyazaki, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Exosomes have been recognized to have a function in cell-to-cell communication by transporting various factors including proteins and nucleic acids. These factors impact cell viability and cell differentiation, and are likely to play a prominent role in the pathophysiology of rheumatoid arthritis (RA); however, it is still not reveal that the roles of exosomes as inflammatory mediator in pathogenesis of RA. The purpose of this study is to investigate the role of T lymphocytes derived exosomes in the pathogenesis of RA.

Methods: Exosomes were isolated and purified from cultured medium of T lymphocytes cell line (JK). RA synovial fibroblasts (RASFs) were cultured with exosomes derived from JK with or without IFN-gamma for 24hours. Total RNA was extracted using TRIZOL methods. The expression of RIG-I, TLR3, IL-6 and CXCL10 mRNA in RASFs was measured using real-time quantitative PCR. The protein levels of RIG-I and TLR3 were determined by immune blotting. Silencing of RIG-I and TLR3 in RASF was performed by transfection of siRNA against these proteins.

Results: Treatment with PMA/Ionomycin increased the release of exosomes from JK. Large amount of RNA was detectable in exosomes derived from JK. Exosomes derived from JK increased the expression of IL-6 and CXCL10 mRNA in RASFs. When IFN-gamma is added to the culture medium of RASFs, increased expression of both RIG-I and TLR3 protein in RASF was observed in a dose dependent manner. IFN-gamma also induced the expression of CXCL10 mRNA, but not IL-6 mRNA, in RASF. Exosomes derived from JK significantly enhances the expression of CXCL10 mRNA, but not IL-6 mRNA, in RASF treated with IFN-gamma. Finally, silencing of RIG-I, but not TLR3, suppressed the expression of CXCL10 in RASF induced by co-stimulation of both exosomes and IFN-gamma.

Conclusion: The present study demonstrates that exosomes derived from JK enhance IFN-gamma induced expression of CXCL10 in RASF via pattern recognition receptor, RIG-I. The interaction between exosomes derived from T-cells and RIG-I can be a therapeutic target for RA.

Disclosure: K. Umekita, None; S. Miyauchi, None; K. Iwao, None; M. Rikitake, None; Y. Rikitake, None; C. Kawada, None; A. Aizawa, None; Y. Kariya, None; M. Matsuda, None; T. Kawaguchi, None; H. Nomura, None; I. Takajo, None; A. Okayama, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/exosomes-derived-from-t-lymphocytes-enhance-expression-of-cxcl10-induced-by-ifn-%ce%b3in-rheumatoid-arthritis-synovial-fibroblasts-via-pattern-recognition-receptor-rig-i

Abstract Number: 2428
Epstein-Barr Virus Infection and Epstein-Barr Virus Nuclear Antigen 1 Variants in the Synovial Tissue of Rheumatoid Arthritis

Shotaro Masuoka1, Natsuko Kusunoki1, Shinichi Kawai2 and Toshihiro Nanki1, 1Division of Rheumatology, Department of Internal Medicine, Toho University School of Medicine, Tokyo, Japan, 2Department of Inflammation and Pain Control Research, Toho University School of Medicine, Tokyo, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Epstein-Barr virus (EBV) infection causes various malignant tumors such as B cell lymphoma and epithelial cell cancer. Previous reports showed several variants in carboxyl-terminal region of EBV nuclear antigen 1 (EBNA-1), and the mutation was frequently detected in patients with nasopharyngeal carcinoma. The mutation of EBV gene may trigger development of the malignant cells. It was reported that titer of anti-EBV antibody was higher in rheumatoid arthritis (RA) compared to controls. Interestingly, the protein sequence of EBV gp110 glycoprotein resembles HLA DRB1 shared epitope (SE). These data suggest EBV infection may play a role of RA, however, underlying mechanisms remains unknown. Moreover, mutation of EBV in RA patients has not been examined. We then investigated EBNA-1 carboxy-terminal region in the synovial tissue of RA.

Methods: One hundred twenty-eight RA and 98 osteoarthritis (OA) patients undergoing joint surgery of the knee at the Toho University Omori Medical Center were enrolled in this study. Synovial tissues were collected during surgery under sterile condition. Informed consent was obtained from all the patients. DNA was extracted from the synovial tissues. The EBV gene was determined by nested PCR for amplifying EBNA-1 carboxy-terminal region, and then, the amplicons were detected by performing electrophoresis. Nucleotide sequence of the PCR product was determined. HLA DRB1 genotyping was also performed.

Results: EBV DNA was more frequently detected in synovial tissue from RA patients (32.8%; 42 of 128) than OA patient (15.3%; 15 of 98) (p<0.01, chi-squared test). The sequence of EBNA-1 carboxy-terminal revealed Japanese prototype (V-Val subtype) in 35 of the 42 RA (83.3%) and 13 of the 15 OA (86.7%) patients. Although four other subtypes were also detected in small number of patients, there were no significant differences between RA and OA. Frequency of HLA-DRB1*0405, *0410, *1001 (SE) was significantly higher in RA (55.5%) than OA (30.6%). Proportion of EBV-positive tended to be higher in SE-positive (39.4%; 28 of 71) than SE-negative (24.6%; 14 of 57), although it is not statistically significant.

Conclusion:
EBV infection might be an environmental risk factor for development or chronic synovitis of RA. However, nucleotide mutations of EBNA-1 may not contribute it.

Disclosure: S. Masuoka, None; N. Kusunoki, None; S. Kawai, None; T. Nanki, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/epstein-barr-virus-infection-and-epstein-barr-virus%e3%80%80nuclear-antigen-1-variants-in-the-synovial-tissue-of-rheumatoid-arthritis

Abstract Number: 2429
Towards Precision Medicine in Rheumatoid Arthritis (RA): Trans-Ethnic Analysis and Prioritization of SNPs in the AFF3 Locus

Vincent A. Laufer1, Maria I. Danila2, Richard J. Reynolds3, Leah C. Kottyan4, Kenneth Kaufman5, John B. Harley6, Carl D Langefeld7, Donna Arnett8 and S. Louis Bridges Jr.9, 1Division of Clinical Rheumatology and Immunology, University of Alabama at Birmingham, Birmingham, AL, 2University of Alabama at Birmingham, Birmingham, AL, 3Medicine, University of Alabama at Birmingham, Birmingham, AL, 4Center for Autoimmune Genomics and Etiology (CAGE), Division of Allergy and Immunology, Cincinnati Children's Hospital, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 5Center for Autoimmune Genomics and Etiology (CAGE), Cincinnati Children's Hospital Medical Center; US Department of Veterans Affairs Medical Center, Cincinnati, OH, 6Center for Autoimmune Genomics and Etiology (CAGE), Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 7Wake Forest University, Winston Salem, NC, 8University of Kentucky College of Public Health, Lexington, KY, 9Clinical Immunology & Rheum, Univ of Alabama, Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Genetic variants in AFF3 have been associated with RA, including in our GWAS and ImmunoChip analyses of African-Americans (610 RA; 1543 controls). Likewise, an AFF3 SNP (rs10865035) has been associated with response of RA to TNF inhibitors (TNFi) (Ann Rheum Dis. 2010 69:1029). AFF3 encodes LAF4, a tissue-restricted nuclear transcriptional activator expressed in cells such as monocytes and lymphocytes. Variants most strongly associated with RA are in the 5’ UTR; several are expression quantitative trait loci (eQTLs) for AFF3. We examined trans-ethnic associations of AFF3 with RA, prioritized candidate pathogenic variants using established algorithms, and compared this list to variants reported to influence the likelihood of response to TNFi in RA.

Methods: We aggregated our African American RA genetic data with publicly available GWAS data from >100,000 European and Asian RA patients and controls, using METASOFT meta-analysis software to assess overall trans-ethnic association strength ($p_{TE}$) and concordance of effects in each ethnicity (m-value). m>0.8 indicates high likelihood of existence of effect for a given population. We then used the PAINTOR3 algorithm (which incorporates multiple types of data) on data from all 3 ancestries to prioritize SNPs according to likelihood of being pathogenic. We compared this list to variants implicated in TNFi response.

Results: We found strong evidence (m>0.9) of trans-ethnic effect on RA for 91 AFF3 variants, mostly in the 5’ UTR. We confirmed the association of the AFF3 locus and the previously reported index variant (rs9653442) with RA in African-Americans ($p_{AFR} = 7.4*10^{-3}$, $m_{AFR} = 0.975$). rs9653442 has a robust trans-ethnic association with RA ($m_{EUR} = 1.000$; $m_{ASIAN} = 0.999$; $m_{AFR} = 0.975$; $p_{TE} = 1.14*10^{-15}$). We identified a set of 12 variants that together are >90% likely to include the pathogenic variant (the 90% ancestry informed credible set, see Table). rs10865035, which was previously associated with TNFi response in RA, was outside our 90% ancestry informed credible set.

Conclusion: We defined a set of 12 leading candidate pathogenic AFF3 variants, which may act to increase AFF3 expression in T cells or monocytes and influence RA susceptibility. Our study did not identify a likely pathogenic role for rs10865035 in RA susceptibility, but further studies are needed to establish whether rs10865035 underlies differences in TNFi response in RA. Our findings will guide selection of SNPs for future functional studies of susceptibility to RA.
Table – The 90% ancestry informed credible set for pathogenic AFF3 variants in RA and their characteristics. eQTL data are from the NESDA NTR Conditional eQTL Catalog (peripheral blood was used). Z.Afr, Z.Asn, Z.Eur are Z-statistics for each variant from each GWAS. Abbreviations: Alt – Alternate. CS – Chromatin State. HS – DNAse hypersensitive region. TFBS – transcription factor binding site.

Disclosure: V. A. Laufer, None; M. I. Danila, None; R. J. Reynolds, None; L. C. Kottyan, None; K. Kaufman, None; J. B. Harley, None; C. D. Langefeld, None; D. Arnett, None; S. L. Bridges Jr., None.


Abstract Number: 2430

For Each HLA-DRB1 Genotype, the Likelihood to Develop RA Correlates with the Probability of Binding at Least a Peptide from PAD4

Isabelle Auger1, Nathalie Balandraud2 and Jean Roudier3, 1INSERM UMRs 1097, Marseille, France, 2Rheumatology, APHM, Marseilles, France, 3Arthrites auto-immunes, INSERM UMRs 1097, Marseille, France
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

HLA-DRB1 genotypic risk to develop ACPA positive RA correlates with capability of encoded HLA-DRB1 chains to bind Peptidyl Arginyl Deiminase (PAD4) peptides, not citrullinated Fibrinogen peptides.

Background/Purpose: The risk to develop ACPA positive RA is controlled by HLA-DRB1 genotypes. This may be due to the binding of citrullinated peptides by HLA-DRB1 chains encoded by each genotype. Alternatively, we propose that binding of peptides from PAD4 by HLA-DRB1 allows to help the production of antibodies to citrullinated epitopes on any protein bound by PAD4.

Methods: We studied the binding of 65 overlapping peptides from PAD4 and 96 overlapping peptides from the Fibrinogen alpha and beta chains under their native or citrullinated form to purified HLA-DRB1*0401, *0404, *0101, *0402, *0701 by ELISA. We calculated a likelihood of binding at least one peptide from PAD4, native Fibrinogen or
citrullinated Fibrinogen by the two HLA-DRB1 chains encoded by each possible genotype and compared it with the risk carried by the same genotype to develop ACPA positive RA.

**Results:** HLA-DRB1 genotypic risks to develop RA correlate with likelyhood to bind PAD4 peptides (P=0.06, Pearson's), not citrullinated Fibrinogen peptides (p >0.6 and p>0.9) (Figure 1).

**Conclusion:** Comparison of binding properties of HLA-DRB1 molecules in each of 12 genotypes to PAD4 or native or citrullinated Fibrinogen peptides suggests restriction of PAD4 presentation may explain the association of HLA-DRB1 alleles with ACPA positive RA

---

**Disclosure:** I. Auger, None; N. Balandraud, None; J. Roudier, None.


**Abstract Number:** 2431

## Acquisition of Protective Alleles in Women with Rheumatoid Arthritis through Microchimerism

Sami B. Kanaan¹, Vijayakrishna K. Gadi¹,², Alexandra M. Forsyth¹, Christine Luu¹, Tessa Aydelotte¹ and J. Lee Nelson¹,³, ¹Clinical Research Division, Fred Hutchinson Cancer Research Center, SEATTLE, WA, ²Division of Oncology, University of Washington, SEATTLE, WA, ³Division of Rheumatology, University of Washington, SEATTLE, WA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster III  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM
Background/Purpose: As in many autoimmune diseases, rheumatoid arthritis (RA) has a female predominance and strong genetic susceptibility from the HLA region. The shared epitope (SE), motif of five amino-acids \(70Q\text{(or R)}-K\text{(or R)}-R-A-A\) on the third hypervariable region of DR\(\beta1\), accounts for the highest genetic risk. In contrast, \(HLA-DRB1\) alleles that express \(70D-E-R-A-A\) in the same positions are associated with protection from RA. Many RA patients do not carry the SE and, in women with RA, disease risk can be influenced by SE-positive alleles carried by their children (1). Two previous studies showed that, compared to healthy women, women with RA who are SE-negative more frequently harbor SE-positive microchimerism (Mc), a long-term legacy derived from feto-maternal exchange of cells during pregnancy (2, 3). In this study, we asked whether RA women who are DERAA-negative have less DERAA-positive Mc compared to healthy controls.

Methods: To detect and quantify Mc with DERAA-encoding alleles, a quantitative polymerase chain reaction (qPCR) assay was developed with primers and fluorogenic probes specific for the DERAA sequence and validated for specificity and sensitivity against an extensive panel of HLA well-characterized cell lines. We tested 53 female subjects who were genotypically negative for DERAA-encoding alleles, 26 RA patients and 27 healthy controls, similar for age, parity and gravidity. DERAA-Mc qPCR was conducted on DNA extracted from peripheral blood mononuclear cells (PBMC). Logistic regression modeled DERAA-Mc prevalence, and negative binomial regression modeled DERAA-Mc quantitative levels.

Results: DERAA-Mc was identified in 42.3% (11/26) of women with RA and in 7.4% (2/27) of healthy women \((P = 0.0041)\). The odds ratio for DERAA-negative RA patients of being DERAA-Mc positive was 9.2 \([1.8–47.9]\) (95% confidence interval \{CI\}). Quantitatively, DERAA-positive Mc was 313.8 \([38.3–2573.3]\) \(_{95\%CI}\) times more abundant in PBMC of RA patients compared to controls \((P < 0.0001)\). Among RA patients, DERAA-Mc levels increased 28.1 \([4.0–195.8]\) \(_{95\%CI}\) fold if genotype was SE+/+ compared to SE+/− or −/− \((P = 0.0008)\) and increased 3.3 \([1.6–6.8]\) \(_{95\%CI}\) fold with increasing parity \((P = 0.0014)\).

Conclusion: Unexpectedly, the presence of Mc carrying HLA alleles that encode RA-protective alleles was significantly increased in women with RA. This result aligns with a recent report that found increased RA risk in women who had a DERAA-positive child born prior to disease onset (also unexpectedly) (1). Furthermore, DERAA-Mc levels were especially high among RA women with a SE+/+ genotype. While the explanation for these observations is unknown, results support the concept that RA in women can be influenced by “reverse inheritance” from her children and suggest complexity in immunological interactions across generations (4).

References:


Funding: This work was supported by NIH grants HL117737 and AI 45659.

Disclosure: S. B. Kanaan, None; V. K. Gadi, None; A. M. Forsyth, None; C. Luu, None; T. Aydelotte, None; J. L. Nelson, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/acquisition-of-protective-alleles-in-women-with-rheumatoid-arthritis-through-microchimerism

Abstract Number: 2432

Longitudinal Changes in Gene Expression Associated with Disease Activity during Pregnancy and Post-Partum Among Women with Rheumatoid
Arthritis

Dana E. Goin1,2, Mette Smed3, Nicholas Jewell2, Lior Pachter2,4, J. Lee Nelson5,6, Hanne Kjaergaard3, Jørn Olsen7, Merete Lund Hetland8,9, Bent Ottesen3, Vibeke Zoffmann3 and Damini Jawaheer1,7,10, 1UCSF Benioff Children's Hospital Oakland/CHORI, Oakland, CA, 2University of California, Berkeley, Berkeley, CA, 3Juliane Marie Center, Copenhagen, Denmark, 4California Institute of Technology, Pasadena, CA, 5Fred Hutchinson Cancer Research Center, Seattle, WA, 6University of Washington, Seattle, WA, 7Aarhus University, Aarhus, Denmark, 8The DANBIO registry and the Danish Departments of Rheumatology, Glostrup, Denmark, 9University of Copenhagen, Copenhagen, Denmark, 10University of California, San Francisco, San Francisco, CA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Many women with rheumatoid arthritis (RA) experience an improvement in disease activity during pregnancy, and a predictable flare in the months after they give birth. The cause of these changes is unknown. We hypothesized that understanding biological changes (through gene expression) that occur from pre-pregnancy through the pregnancy and post-partum periods will contribute important evidence to our knowledge of the drivers of disease activity in RA during and after pregnancy.

Methods: We have established a prospective RA pregnancy cohort, with clinical data and blood samples collected at pre-pregnancy (T0), each trimester of pregnancy and every 3 months up to a year post-partum (up to 8 time points). Disease activity at each time point was assessed using disease activity scores (DAS28CRP4); women who showed an improvement during pregnancy were selected for analysis (n=9). Global gene expression profiles for each sample were generated using RNA-sequencing (RNA-seq). Raw reads were pseudo-aligned and quantified using kallisto. Random effects regression models were used to estimate the effects of changes in gene expression on disease activity (a) from T0 through the pregnancy period (P1), and (b) in the post-partum period (P2). The models were adjusted for age, medication status at baseline and batch effects. Significance was assessed using a threshold of q<0.05 (FDR-adjusted). Functional enrichment analysis was performed using WebGestalt.

Results: During pregnancy, 1,174 genes had expression patterns significantly associated with disease activity. While these were not significantly enriched in specific pathways, the genes whose increased expression was associated with the largest decrease (improvement) in disease activity during pregnancy were immune-related, and included ERAP1, CSNK2A1 and FAM175B. ERAP1 is involved in trimming peptides for presentation on MHC class I molecules; CSNK2A1 regulates cellular processes including cellular response to viral infection; FAM175B is involved in interferon-signaling. In the post-partum period, 4,693 genes had expression patterns significantly associated with disease activity. These were enriched (p<1x10^-6) in numerous immune-related pathways including MAPK signaling, T cell receptor signaling, osteoclast differentiation, hematopoietic cell lineage, B cell receptor signaling, Toll-like receptor signaling and leukocyte trans-endothelial migration, in addition to several pathways related to cancer. The genes whose increased expression were associated with larger increases in disease activity included EI24, CMTM7, PPP2CB and BFAR which are related to tumor suppression and/or regulation of apoptosis.

Conclusion: In this pilot RA pregnancy cohort study with longitudinal RNA-seq data, several candidate genes were identified as significantly associated with improvement in disease activity during pregnancy, and others were associated with post-partum flares. These results warrant further investigations into possible roles of these genes in modulating RA disease activity in a larger cohort.

Disclosure: D. E. Goin, None; M. Smed, None; N. Jewell, None; L. Pachter, None; J. L. Nelson, None; H. Kjaergaard, None; J. Olsen, None; M. Lund Hetland, None; B. Ottesen, None; V. Zoffmann, None; D. Jawaheer, None.
Transcriptome Analysis in Women with Rheumatoid Arthritis Who Improve or Worsen during Pregnancy

Dana E. Goin¹,², Mette Smed³, Lior Pachter²,⁴, Elizabeth Purdom², J. Lee Nelson⁵,⁶, Hanne Kjaergaard³, Jørn Olsen⁷, Merete Lund Hetland⁸,⁹, Bent Ottesen³, Vibeke Zoffmann³ and Damini Jawaheer¹,⁷,¹⁰ ¹UCSF Benioff Children's Hospital Oakland/CHORI, Oakland, CA, ²University of California, Berkeley, Berkeley, CA, ³Juliane Marie Center, Copenhagen, Denmark, ⁴California Institute of Technology, Pasadena, CA, ⁵Immunogenetics, Fred Hutchinson Cancer Resch, Seattle, WA, ⁶University of Washington, Seattle, WA, ⁷Aarhus University, Aarhus, Denmark, ⁸The DANBIO registry and the Danish Departments of Rheumatology, Glostrup, Denmark, ⁹University of Copenhagen, Copenhagen, Denmark, ¹⁰University of California, San Francisco, San Francisco, CA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Gene expression changes induced by pregnancy in women with rheumatoid arthritis (RA) and healthy women have not been examined. The few studies previously conducted did not have pre-pregnancy samples available as baseline. We have established a cohort of RA and healthy women followed prospectively from pre-pregnancy. In this study, we aimed to identify pregnancy-induced changes in gene expression among women with RA and healthy women, and to assess how those changes may differ between RA women who improve or worsen during pregnancy.

Methods: Clinical data and samples collected from a subset of 11 women with RA and 5 healthy women from our cohort before pregnancy (T0) and at the third trimester (T3) were analyzed. Disease activity scores were used to determine whether the RA women improved or worsened during pregnancy. Global gene expression profiles were generated by RNA sequencing (RNA-seq). The raw RNA-seq reads were pseudo-aligned to the reference transcriptome and expression levels were estimated with kallisto. Differential expression analysis of normalized expression levels was performed using edgeR to identify genes differentially expressed (DE) between each group of women (T3 vs T0), using a fold-change cut-off of 2 and a significance threshold of q<0.05 (FDR-adjusted). Functional enrichment analysis was performed using WebGestalt.

Results: Of the 11 women with RA, 8 showed an improvement in disease activity by T3 (RAimproved), while 3 worsened (RAWorsened). In the RAimproved group, a total of 161 genes were differentially expressed (DE) between T3 and T0. These included several genes whose expression have previously been associated with RA (e.g. S100A12, SLC14A1) as well as genes involved in the innate immune system (e.g. type I interferon-inducible genes). The majority of these genes (108 of 161) were also DE among healthy women. Of interest, most genes (30 of 31) that were significantly DE in both of the RA groups were also DE among healthy women (e.g. α-defensin genes). There were also differences between the RAimproved and RAWorsened groups. A set of IFN-inducible genes was over-expressed at T3 (vs T0) in the RAimproved but not the RAWorsened women. Additionally, some interesting candidate genes whose expression
have previously been associated with RA (e.g. MMP9, PADI4 and PGLYRP1) were over-expressed at T3 (vs. T0) among RA_{worsened} but not among RA_{improved} women.

**Conclusion:** Pregnancy-induced gene expression changes common between RA women who improved and those who worsened appeared to be normal pregnancy-related changes that were also observed among healthy women. Other genes that demonstrated different patterns of expression between the two RA groups are potential candidates that could be involved in the natural pregnancy-induced amelioration of RA.

**Disclosure:** D. E. Goin, None; M. Smed, None; L. Pachter, None; E. Purdom, None; J. L. Nelson, None; H. Kjaergaard, None; J. Olsen, None; M. Lund Hetland, None; B. Ottesen, None; V. Zoffmann, None; D. Jawaheer, None.

**Abstract Number:** 2434

**Baseline Expressions of Cellular microRNA-31 and microRNA-10a Predict Remission and Low Disease Activity in Patients with Early Rheumatoid Arthritis after Six and Twelve Months of Therapy**

Veronika Hruskova1,2, Klara Prajzlerova3, Martin Komarc4, Lucia Vernerova1, Herman F Mann3, Maria Fílková3, Karel Pavelka3, Jiri Vencovsky3 and Ladislav Senolt3, 1Institute of Rheumatology, Prague, Czech Republic, Prague, Czech Republic, 2Faculty of Science, Charles University, Prague, Czech Republic, Prague, Czech Republic, 3Institute of Rheumatology, Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, Prague, Czech Republic, 4Department of Anthropometrics and Methodology, Faculty of Physical Education and Sport, Charles University, Prague, Czech Republic, Prague, Czech Republic

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster III

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** MicroRNAs (miRNAs) post-transcriptionally regulate gene expression by targeting messenger RNAs. The expression of miRNAs was demonstrated to differ between patients with rheumatoid arthritis (RA) and healthy subjects. The aim of this study was to analyse cellular miRNAs from peripheral mononuclear cells (PBMCs) in order to determine their predictive value for achieving remission or low disease activity in patients with early RA.

**Methods:** At first, miRNAs were screened by TaqMan MicroRNA Array Cards in 4 treatment naïve patients with early RA (disease duration < 6 months) who achieved long-term remission (3 females; mean age 59 years; DAS28< 2.6) and 4 treatment naïve patients with early RA (disease duration < 6 months) with persistently high disease activity (3 females; mean age 63 years; DAS28> 5.1). Thirteen miRNAs with at least 2-fold difference between both groups were validated in a cohort of 60 patients (44 females; mean age 54 years) with early RA (baseline DAS28= 5.64, CRP= 22.72; DAS28 after 6 months= 2.80, CRP= 5.17); and 54 healthy controls (HC) (41 females; mean age 51 years). Total RNA was isolated from PBMCs in treatment naïve early RA patients at baseline and after the first and third month of conventional therapy. The expression of miRNAs was determined by quantitative PCR. Small nucleolar RNA RNU44 was used for normalization. Disease activity of RA patients was assessed according to the 28-Joint Count Disease Activity Score (DAS28) and the Simplified Disease Activity Index (SDAI). Area under the curve analysis was used to determine the predictive value of miRNAs to achieve remission or low disease activity.
**Results:** Cellular miRNA-31 expression was significantly lower in patients with early RA compared to HC (p= 0.002) and the therapy initiation contributed to its normalization over time. The expression of cellular miRNA-10a was also lower in patients with early RA compared to HC (p< 0.0001) however it has not significantly changed during the therapy. Although both miRNAs did not correlate with disease activity, higher baseline and also one-month miRNA-31 expression predicted achievement of remission after 6 months (DAS28: AUC= 0.713, p= 0.016; SDAI: AUC= 0.732, p= 0.011, and DAS28: AUC= 0.760, p= 0.003; SDAI: AUC= 0.734, p= 0.010; respectively). In addition, higher baseline expression of miRNA-10a predicted remission and low disease activity achievement after 12 months (DAS28: AUC= 0.750, p= 0.012; SDAI: AUC= 0.718, p= 0.038).

**Conclusion:** The expression of cellular miRNA-31 and miRNA-10a may represent potential biomarkers of treatment response in patients with early RA.

**Acknowledgement:** MHCR project no. 00023728, GAUK-367615 and SVV 260 373

**Disclosure:** V. Hruskova, None; K. Prajzlerova, None; M. Komarc, None; L. Vernerova, None; H. F. Mann, None; M. Filkova, None; K. Pavelka, None; J. Vencovsky, Samsung Bioepis Co., Ltd., Biogen, 5; L. Senolt, None.

**Circulating Mirnas As Potential Biomarkers of Cardiovascular Disease in Rheumatoid Arthritis Patients**

Chary Lopez-Pedrera¹, Nuria Barbarroja¹, Patricia Ruiz-Limon², Ivan Arias de la Rosa², Maria Carmen Abalos-Aguilera², Yolanda Jiménez-Gómez³, Rafaela Ortega-Castro¹, Eduardo Collantes-Estévez¹, Alejandro Escudero-Contreras², Raquel Lopez-Mejias³, Miguel Angel González-Gay³ and Carlos Perez-Sanchez¹, ¹Rheumatology service, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain, ²Rheumatology Service, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain, ³Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster III

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Extracellular microRNAs, circulating in the bloodstream and extracellular space, have been proposed as attractive candidates as both diagnostic and prognostic biomarkers in various diseases, including a spectrum of autoimmune and cardiovascular conditions. Yet, the contribution of circulating miRNAs to the cardiovascular pathogenesis of Rheumatoid Arthritis (RA) patients and their potential role as biomarkers are still unknown. Purpose: To identify circulating miRNAs as potential biomarkers for the presence of cardiovascular disease (CVD) in RA.

**Methods:** Plasma samples of 80 healthy donors (HDs) and 195 RA patients, including 90 RA patients with cardiovascular events (Ischemic heart disease, Heart failure, Cerebrovascular accident or Peripheral arterial disease) were collected. In the discovery phase, an array of 2,083 human miRNAs was performed by using HTG EdgeSeq miRNA Whole Transcriptome Assay (Next generation sequencing) in 9 plasma samples (3 HDs, 3 RA and 3 RA with
CVD). Then, differentially expressed miRNAs, were selected and validated by RT-PCR in the whole cohort of patients. Potential targets of the validated miRNAs, were identified by using Ingenuity Pathway Analysis (IPA) software and analyzed at protein levels (Multiplex Assay). Correlation and association studies of altered miRNAs with analytical and clinical variables such as the type of cardiovascular events, the presence of a pathologic carotid intima-media thickness (CIMT) and the autoimmune and inflammatory profile, were also performed.

**Results:** The miRNA whole Transcriptome assay showed that 360 miRNAs were differentially expressed in RA patients in relation to HDs, including 261 upregulated and 97 downregulated. Functional classification (IPA) demonstrated that deregulated miRNAs were mainly involved in processes such as inflammatory response, connective tissue development and function, haematological disease, tissue development and immunological disease. RA patients with CVD showed 17 differentially expressed plasma miRNAs in relation to RA patients, including 11 upregulated and 6 downregulated. In silico study identified that these CVD-associated miRNAs had potential targets related to cytokine signaling (TNF, TNFRSF, TNFSF, TRAF, IL1R, IL22, IL33, CCL21, CXCL12), atherosclerosis pathway (iNOS, VEGFA, LDL-R, COL1A1, COL10A1, COL5A3) and intracellular signal transduction (ERK and WNT). Furthermore, the altered levels of several miRNAs and target proteins were validated in the whole cohort of patients, and were linked to the clinical manifestations of the disease, such as the activity of the disease, the occurrence of cardiovascular events, presence of early atherosclerosis and endothelial dysfunction.

**Conclusion:** Circulating miRNAs levels in plasma of RA patients might be considered useful tools as biomarkers of cardiovascular disease in these patients. Acknowledgements: Supported by FIS (PI01333/2015) and CTS-7940.

**Disclosure:** C. Lopez-Pedrera, None; N. Barbarroja, None; P. Ruiz-Limon, None; I. Arias de la Rosa, None; M. C. Abalos-Aguilera, None; Y. Jiménez-Gómez, None; R. Ortega-Castro, None; E. Collantes-Estévez, None; A. Escudero-Contreras, None; R. Lopez-Meijas, None; M. A. González-Gay, None; C. Perez-Sanchez, None.


**Abstract Number:** 2436

**MiR-146a Upregulates the TLR4/NF-κb Signaling Pathway to Promote Cytokine Expression and Synovial Fibroblast Proliferation in Rheumatoid Arthritis**

**Yuan-hao Wu**¹,², Wei Liu¹, Lei Zhang³, Bin Xue³, Yi Wang³, Yao-ya Liu³, Yang Ji⁴, Ran Duan³, Yue Cai³ and Bo Zhang³, ¹Department of Rheumatology and Immunology, First Teaching Hospital of Tianjin University of Traditional Chinese Medicine, Tianjin, China, ²Institute of Basic Research in Clinical Medicine, China Academy of Chinese Medical Sciences, Beijing, China, ³First Teaching Hospital of Tianjin University of Traditional Chinese Medicine, Tianjin, China, ⁴The 272nd Hospital of Chinese People's Liberation Army, Tianjin, China

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Rheumatoid Arthritis – Human Etiology and Pathogenesis Poster III

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** To investigate the role of miR-146a in the activation of toll-like receptor-4 (TLR4)/ nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) signaling pathway, and the effect of miR-146a in cytokines expression and synoviocytes proliferation during rheumatoid arthritis (RA).
Methods: Synovial tissues were collected from RA patients who received arthroscopic synovectomy in the Department of Rheumatism at our hospital. Cells were categorized into a blank control group, a negative control group, a miR-146a mimics group and a miR-146a inhibitors group. The cholecystokinin (CCK)-8 assay was used to measure the inhibition on cell proliferation rate. TLR4 mRNA level, as well as the mRNA expressions of NF-κB, interleukin (IL)-1β, IL-6, IL-8, IL-17, cyclooxygenase (COX)-2, matrix metalloproteinase (MMP)-3, Seprase, and inducible nitric oxide synthase (iNOS) were detected by the reverse transcription-polymerase chain reaction (RT-PCR). Western blot was used to measure TLR4 and NF-κB proteins, and the expressions of IL-1β, IL-6, IL-8, IL-17, Seprase, MMP-3 and prostaglandin E2 (PGE2) were measured by enzyme linked immunosorbent assay (ELISA). The content of nitric oxide (NO) was measured by the Griess method.

Results: The CD3 and CD14 expression rate gradually decreased, and the CD90 expression rate gradually increased. After the third generation of cell culture, the CD90 expression rate (96.48%) was significantly higher than those of CD3 (1.17%) and CD14 (1.27%). After culturing for 48h and 72h, cell proliferation in the miR-146a mimics group was significantly increased (both \( P < 0.05 \)) as compared with the blank group, while that in the miR-146a inhibitors group significantly reduced (both \( P < 0.05 \)). With an extended time of cell culture, the change in cell proliferation was more significant, and differences were observed at each time point (all \( P < 0.05 \)). Compared with the blank group, the expressions of TLR4, NF-κB, IL-1, IL-6, IL-8, IL-17, COX-2, MMP-3, Seprase, iNOS and NO content in the miR-146a mimics group increased significantly (all \( P < 0.05 \)), but in the miR-146a inhibitors group, these values significantly reduced (all \( P < 0.05 \)).

Conclusion: The inhibition of miR-146a expression could block the TLR4/NF-κB signaling pathway, and inhibited synovial fibroblast proliferation and cytokine expressions in RA.

Disclosure: Y. H. Wu, None; W. Liu, None; L. Zhang, None; B. Xue, None; Y. Wang, None; X. Y. Liu, None; Y. Ji, None; R. Duan, None; Y. Cai, None; B. Zhang, None.

Abstract Number: 2437

Long-Term Effect of Sirukumab, an Anti–IL-6 Cytokine Monoclonal Antibody, on Radiographic Progression in Patients with Active Rheumatoid Arthritis Despite Disease-Modifying Anti-Rheumatic Drug Treatment: Results of a Global Phase 3 Trial

George Karpouzas1, Tsutomu Takeuchi2, Carter Thorne3, Shihong Sheng4, Regina Kur rasch5, Kaiyin Fei4 and Benjamin Hsu4, 1Division of Rheumatology, Harbor-UCLA Medical Center, Torrance, CA, 2Keio University School of Medicine, Tokyo, Japan, 3University of Toronto, Newmarket, ON, Canada, 4Janssen Research & Development, LLC, Spring House, PA, 5GlaxoSmithKline, Collegeville, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM
Background/Purpose: In the SIRROUND-D study, sirukumab (SIR), a human monoclonal antibody that selectively binds to the IL-6 cytokine with high affinity, significantly reduced radiographic progression after 52 wks compared with placebo (PBO) in patients (pts) with active rheumatoid arthritis (RA) despite DMARD treatment. Long-term data on radiographic progression after 104 wks of SIR treatment are presented.

Methods: In this Phase 3 study, 1,670 pts with moderate to severe active RA, defined as ≥6/66 swollen and ≥6/68 tender joints and a minimum CRP ≥8.0 mg/L, that was refractory to DMARDs were randomized (1:1:1) to SC SIR 50 mg q4w, SIR 100 mg q2w, or PBO q2w. Pts randomized to PBO who had <20% improvement in swollen/tender joints at Wks 18 or 40 or were still taking PBO at Wk 52 were re-randomized to SIR; blinded treatment lasted 104 wks. Images of the hands and feet were taken at baseline, Wks 18 (early escape [EE] criteria met), 24 (EE criteria not met), 52, and 104. For this analysis of radiographic change over the second year of SIRROUND-D, only images taken at baseline, Wk 52, and after Wk 52 (eg. Wk 104) were evaluated. The endpoints included changes from baseline at Wks 52 and 104 in the modified Sharp/van der Heijde score (SHS) for radiographic damage, erosion score, and joint space narrowing (JSN) score and the proportions of pts with radiographic progression (change >smallest detectable change [SDC]) and with a change of ≤0 from baseline in SHS. Analyses only included pts who were still on study treatment at Wk 52 and had non-missing SHS score at both baseline and Wk 52. All analyses were based on observed data unless noted.

Results: A high proportion of pts had readable images at baseline, Wk 52, and post-Wk 52, ranging from 94.5% to 97.1%. Of 1218 pts who had not terminated the study or study treatment early, 1176 had evaluable Wk 104 x-rays. The mean change from baseline in the SHS at Wk 104 generally increased slightly versus Wk 52; changes from baseline at Wks 52 and 104 remained below the SDC for SHS scoring for pts originally randomized to SIR (both doses; Table). Mean changes in the SHS from Wk 52 to Wk 104 were negligible across all treatment groups. Similar results were observed for the erosion and JSN scores (Table). At Wks 52 and 104, the proportions of pts with radiographic progression based on SHS were similar for both SIR doses among pts randomized to SIR and those randomized to PBO who crossed over to SIR. The proportions of pts with a change in SHS of ≤0 were generally comparable for both SIR doses among pts randomized to SIR and those randomized to PBO who crossed over to SIR at Wks 52 and 104.

Conclusion: Treatment with SIR 50 mg q4w and SIR 100 mg q2w in pts with active RA despite DMARD therapy resulted in minimal radiographic progression over 2 years, indicating that inhibition of joint damage by SIR demonstrated at Wk 52 was maintained through Wk 104 of this study.

Table. Radiographic Endpoints

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Placebo to sirukumab 50mg q4w (n=201)</th>
<th>Placebo to sirukumab 100mg q2w (n=301)</th>
<th>Sirukumab 50mg q4w (n=479)</th>
<th>Sirukumab 100mg q2w (n=444)</th>
<th>Placebo to sirukumab 50mg q4w (n=174)</th>
<th>Placebo to sirukumab 100mg q2w (n=304)</th>
<th>Sirukumab 50mg q4w (n=421)</th>
<th>Sirukumab 100mg q2w (n=412)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SHS, mean (SD) change from baseline</td>
<td>3.20 (5.74)</td>
<td>3.51 (6.00)</td>
<td>0.56 (2.79)</td>
<td>-0.1 (2.22)</td>
<td>3.79 (6.15)</td>
<td>3.32 (2.29)</td>
<td>1.23 (4.45)</td>
<td>0.76 (2.88)</td>
</tr>
<tr>
<td>SHS, mean (SD) change from Wk 52 to 104</td>
<td>0.48 (5.65)</td>
<td>0.28 (4.79)</td>
<td>0.70 (2.72)</td>
<td>0.43 (2.32)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erosion score, mean (SD) change from baseline</td>
<td>1.58 (3.11)</td>
<td>1.84 (5.85)</td>
<td>0.14 (1.00)</td>
<td>-0.13 (2.09)</td>
<td>1.85 (4.77)</td>
<td>1.49 (3.39)</td>
<td>0.37 (2.35)</td>
<td>-0.17 (2.65)</td>
</tr>
<tr>
<td>JSN, mean (SD) change from baseline</td>
<td>1.50 (3.70)</td>
<td>1.63 (4.40)</td>
<td>0.42 (1.35)</td>
<td>0.18 (1.77)</td>
<td>1.94 (3.14)</td>
<td>1.26 (2.27)</td>
<td>0.86 (2.27)</td>
<td>0.82 (2.50)</td>
</tr>
<tr>
<td>Proportion of patients, n (%) with radiographic progression</td>
<td>63 (31.0)</td>
<td>59 (29.1)</td>
<td>55 (31.1)</td>
<td>44 (26.9)</td>
<td>54 (26.3)</td>
<td>57 (21.9)</td>
<td>55 (31.4)</td>
<td>45 (21.4)</td>
</tr>
<tr>
<td>Proportion of patients, n (%) with change of ≥9 from baseline in SHS</td>
<td>75 (38.0)</td>
<td>77 (37.9)</td>
<td>244 (50.0)</td>
<td>278 (62.9)</td>
<td>70 (40.7)</td>
<td>68 (35.6)</td>
<td>196 (55.6)</td>
<td>234 (55.6)</td>
</tr>
</tbody>
</table>

Table: SHS, modified Sharp/van der Heijde score; SD, standard deviation; JSN, joint space narrowing.
*Score was based on observed data from active-controlled arms.
"SDC for change from baseline in SHS score at Week 52 = 2.82 and Week 104 = 3.61.

Abstract Number: 2438

Open Label Transitioning from Originator Etanercept to Biosimilar SB4 Compared to Continuing Treatment with Originator Etanercept in a Historical Cohort in Rheumatic Diseases in Daily Practice

L. Tweehuysen¹, V.J.B. Huiskes², B.J.F. Van den Bemt (PharmD, PhD)³, S. Teerenstra⁴, F.H.J. van den Hoogen⁵, C.H.M. van den Ende⁵ and A.A. Den Broeder⁵, ¹Rheumatology, Sint Maartenskliniek, Nijmegen, Netherlands, ²Pharmacy, Sint Maartenskliniek, Nijmegen, Netherlands, ³Pharmacy, Sint Maartenskliniek and Radboudumc, Nijmegen, Netherlands, ⁴Biostatistics, Radboudumc, Nijmegen, Netherlands, ⁵Rheumatology, Sint Maartenskliniek and Radboudumc, Nijmegen, Netherlands

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Blinded transitioning from originator infliximab (INX) to biosimilar CT-P13 was not inferior to continuing INX treatment.¹ Open label mandatory transitioning resulted in a slightly lower 1-year CT-P13 retention rate than for INX in a historical cohort.² However, non-mandatory transitioning might be preferred above mandatory. Therefore, we assessed the effects of open label non-mandatory transitioning from originator etanercept (ENB) to biosimilar SB4 on drug survival and effectiveness in rheumatic diseases in daily practice.

Methods: In 2016, 642 ENB treated patients were asked to transition to SB4 by a structured implementation strategy with opt-out option. Consenting patients were eligible for inclusion in our study [BIO-SPAN]. ENB treated patients in 2014 were recruited as historical cohort. The 6-months retention rate in the two cohorts was compared. Multivariable Cox regression analysis was used to calculate HR for discontinuation adjusted for baseline characteristics (age/gender/diagnosis/ENB treatment duration/ENB dose interval/csDMARD/CRP) and with a robust variance estimator to account for repeated subjects. Reasons for discontinuation and change in DAS28-CRP, BASDAI and CRP after 6 months were assessed.

Results: 635 (99%) patients agreed to transition to SB4 of whom 625 patients (433 RA, 128 PsA, 64 AS; 55% women; age 57 (14) years) were included in the transition cohort. 600 patients were included in the historical cohort. Crude 6-months retention rates of SB4 in the transition cohort and ENB in the historical cohort were: 90% (95%Ci 88%-93%) vs 92% (95%Ci 90%-94%). The transition cohort had a significantly higher relative risk of discontinuation than the historical cohort (adjusted HR 1.57, 95%Ci 1.05-2.36). Reasons for discontinuing SB4 (n=60, 10%) and ENB (n=46, 8%) were: lack of effect (43% vs 61%), adverse events (47% vs 28%), malignancy (3% vs 4%), pregnancy (4% vs 4%) and other (3% vs 3%). In the transition cohort, 17 patients restarted ENB, 32 patients switched to another biologic and
11 patients maintained biologic-free. DAS28-CRP, BASDAI and CRP were not statistically different between baseline and month 6 in the transition cohort. Due to a slightly lower baseline CRP (1 [0-5] vs 3 [1-5], p<0.001) and DAS28-CRP (1.9 [1.5-2.6] vs 2.1 [1.6-2.9], p<0.001) changes in CRP (0.5 (12) vs -1.5 (14), p=0.01) and DAS28-CRP (-0.01 (0.93) vs -0.26 (-0.99), p<0.001) at month 6 favored the historical cohort.

**Conclusion:** Open label non-mandatory transitioning from ENB to SB4 showed a statistically significantly but clinically not relevant lower retention rate compared to a historical cohort, similar to retention seen after mandatory INX transitioning. Non-mandatory transitioning, when executed optimally, might therefore be an attractive alternative to mandatory transitioning.

References: 1Jørgensen KK. Lancet 2017 2Glintborg B. Ann Rheum Dis 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Biosimilars, biopharmaceuticals assessed by regulatory agencies to have efficacy and safety similar to their reference products, were introduced to the UK market in February 2015 for rheumatoid arthritis (RA). Switching patients from originator to biosimilars could result in significant cost savings to the NHS but real world data about efficacy and safety of such a switch are lacking. This analysis describes the characteristics and initial follow-up of RA patients switching from the originator to biosimilars participating in the British Society for Rheumatology Biologics Register for Rheumatoid Arthritis (BSRBR-RA).

Methods: Since 03/08/2015, the BSRBR-RA has captured data on patients starting biosimilars available in the UK: infliximab (Inflectra and Remsima) and later in May 2016, etanercept (Benepali). At biosimilar start, information is captured from the hospital including demographic and clinical data, previous biologic exposure and, if switching therapies, the reason for switch (as a tick box and free text). Follow-up data (disease activity, occurrence of adverse events and changes to treatment) are captured 6-monthly for 3 years and annually thereafter. Descriptive data are presented.

Results: To 10/05/2017, 1,165 patients were recruited at point of starting a biosimilar. Of these, over half (59%, 691/1,165) switched directly from the originator product (74% Benepali, 9% Inflectra, 17% Remsima (table). By far the most frequent reason cited to switch was cost. These patients switched from originator after a median (IQR) time of 5.3 (2.7-8.8) years and the majority had low disease activity (median DAS28 2.7 (IQR 2.0-3.8). To date, follow-up data are available in 99 patients (61% Inflectra, 27% Remsima, 6% Benapali), primarily in those receiving infliximab biosimilars. After 6 months, 85% of these patients stayed on the baseline biosimilar, 7% switched back to their originator, 4% switched between infliximab biosimilars, 3% stopped treatment with a biosimilar and 1% switched to a biologic other than the originator. Reasons for switching back to the originator were inefficacy (n=3) and adverse events (n=2) with two reasons missing. A deterioration in DAS28 of >1.2 after 6 months was experienced by 17% (13/78) of patients. Only one serious adverse event (drug hypersensitivity reaction) was reported in a Remsima patient.

Conclusion: In the UK, RA patients are actively switched from originator to biosimilars mostly for cost reasons. Limited short-term follow up data seem to indicate a high retention on biosimilars, yet a minority of patients had a clinically significant deterioration of their disease activity and some were reported to switch back to the originator already after 6 months of treatment. Data capture will continue and updated reports from the BSRBR-RA will build on these early findings.
Long-Term Efficacy, Safety and Immunogenicity Results from a Randomized, Double-Blind, Phase III Confirmatory Efficacy and Safety Study Comparing GP2017, a Proposed Biosimilar, with Reference Adalimumab

Andrew Blauvelt1, Jean-Phillipe Lacour2, Joseph Fowler3, Ellen Schuck4, Julia Jauch-Lembach4, Alison Balfour4 and Craig Leonard5, 1Oregon Medical Research Center, Portland, OR, 2University of Nice Sophia Antipolis, Nice, France, 3Dermatology Specialists, Louisville, KY, 4Hexal AG, Holzkirchen, Germany, 5Central Dermatology, St. Louis, MO

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM
Background/Purpose: Based on the evaluation of physicochemical, biological, preclinical, and clinical data, a biosimilar may be approved for use in the same indications for which the reference medicine is approved. A prerequisite for this extrapolation is clinical confirmation of biosimilarity in a population sensitive enough to detect potential differences in efficacy, safety, or immunogenicity between the proposed biosimilar and the reference medicine. GP2017, a proposed biosimilar to adalimumab, was investigated in patients with moderate-to-severe chronic plaque psoriasis.

Methods: Eligible patients were randomized to receive an initial dose of 80 mg subcutaneous GP2017 or reference adalimumab, followed by 40 mg every other week, starting one week after the initial dose. To evaluate long-term effects and the impact of multiple switches between GP2017 and reference adalimumab, patients with ≥PASI 50 at Week 16 were re-randomized at Week 17 in a 2:1 ratio to either remain on their initial study treatment or undergo a sequence of three treatment switches between GP2017 and reference adalimumab until Week 35. Thereafter, patients were returned to their originally randomized treatment up to Week 51.

Results: Initially, 465 patients, including 98 (21.1%) with psoriatic arthritis, were randomized to GP2017 (n=231) or reference adalimumab (n=234). At Week 17, 379 patients were re-randomized to continue treatment with GP2017 (n=126) or reference adalimumab (n=127) or to switch between GP2017 and reference adalimumab, or vice versa (n=63 in each group). There were no clinically relevant differences in efficacy and safety between the continued and switched groups across the entire study duration (Table). At preferred term level, no severe/serious adverse events (AEs) were reported by more than one patient in a treatment group. Infections/infestations were the most common treatment-emergent AEs, with nasopharyngitis most frequently reported by 11.1% (reference adalimumab to GP2017), 12.6% (continued adalimumab), 12.7% (GP2017 to reference adalimumab) and 9.5% (continued GP2017) of patients. The incidence of injection site reactions was low and similar among the individual groups. Overall, from Week 1 to 51, differences in the frequency of antidrug antibody (ADA) detection were <11% among the individual groups; most ADA (75–100%) were neutralizing.

Conclusion: There were no clinically meaningful differences in long-term efficacy among patients who received continued GP2017 and reference adalimumab, or who switched between GP2017 and reference adalimumab multiple times. Switching treatments was well tolerated; overall safety profiles and immunogenicity rates were similar between the individual treatment groups. The data add to the totality of evidence suggesting GP2017 could be used as a biosimilar for the treatment of the same indications for which reference adalimumab is approved.
### Table. Summary of efficacy, safety and immunogenicity during entire study period

<table>
<thead>
<tr>
<th></th>
<th>Reference adalimumab to GP2017 (n=63)</th>
<th>Continued reference adalimumab (n=127)</th>
<th>GP2017 to reference adalimumab (n=63)</th>
<th>Continued GP2017 (n=126)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean reduction from baseline in PASI score, % (SD)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 17</td>
<td>86.58 (12.770)</td>
<td>82.39 (17.826)</td>
<td>84.87 (15.710)</td>
<td>84.82 (15.957)</td>
</tr>
<tr>
<td>Week 35</td>
<td>85.35 (17.456)</td>
<td>85.55 (16.681)</td>
<td>84.59 (21.033)</td>
<td>85.01 (19.739)</td>
</tr>
<tr>
<td>Week 51</td>
<td>85.01 (15.501)</td>
<td>84.71 (18.020)</td>
<td>83.91 (21.726)</td>
<td>86.84 (21.581)</td>
</tr>
<tr>
<td><strong>Overall TEAEs, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1 TEAE</td>
<td>42 (66.7)</td>
<td>86 (67.7)</td>
<td>47 (74.6)</td>
<td>85 (67.5)</td>
</tr>
<tr>
<td>≥1 severe TEAE</td>
<td>5 (7.9)</td>
<td>9 (7.1)</td>
<td>2 (3.2)</td>
<td>4 (3.2)</td>
</tr>
<tr>
<td>≥1 SAE</td>
<td>6 (9.5)</td>
<td>10 (7.9)</td>
<td>2 (3.2)</td>
<td>4 (3.2)</td>
</tr>
<tr>
<td>≥1 treatment-related TEAE</td>
<td>14 (22.2)</td>
<td>23 (18.1)</td>
<td>17 (27.0)</td>
<td>27 (21.4)</td>
</tr>
<tr>
<td>AE of special interest*</td>
<td>9 (14.3)</td>
<td>20 (15.7)</td>
<td>8 (12.7)</td>
<td>11 (8.7)</td>
</tr>
<tr>
<td>Drug interruption due to TEAE</td>
<td>9 (14.3)</td>
<td>8 (6.3)</td>
<td>5 (7.9)</td>
<td>16 (12.7)</td>
</tr>
<tr>
<td>Drug discontinuation due to TEAE</td>
<td>2 (3.2)</td>
<td>5 (3.9)</td>
<td>1 (1.6)</td>
<td>4 (3.2)</td>
</tr>
<tr>
<td>Deaths</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (0.8)†</td>
</tr>
<tr>
<td><strong>Patients with ISRs by maximum severity, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>3 (4.8)</td>
<td>9 (7.1)</td>
<td>5 (7.9)</td>
<td>8 (6.3)</td>
</tr>
<tr>
<td>Moderate</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (1.6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Severe</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (1.6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td><strong>ADA responses overall from Week 1, n/n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>24/61 (39.3)</td>
<td>55/122 (45.1)</td>
<td>28/60 (46.7)</td>
<td>44/123 (35.8)</td>
</tr>
<tr>
<td>Neutralizing</td>
<td>24/24 (100.0)</td>
<td>47/55 (85.5)</td>
<td>21/28 (75.0)</td>
<td>38/44 (86.4)</td>
</tr>
<tr>
<td>Transient</td>
<td>4/24 (16.7)</td>
<td>25/55 (45.5)</td>
<td>11/28 (39.3)</td>
<td>19/44 (43.2)</td>
</tr>
</tbody>
</table>

ADA, antidrug antibody; AE, adverse event; ISR, injection site reaction; PASI, psoriasis area severity index; SAE, serious AE; SD, standard deviation; TEAE, treatment-emergent AE; *Encompassing all special warnings and precautions given on the reference adalimumab label; †Suicide, not considered treatment-related

**Disclosure:** A. Blauvelt, None; J. P. Lacour, Sandoz, 2,Novartis Pharmaceutical Corporation, 2,Novartis Pharmaceutical Corporation, 5; J. Fowler, None; E. Schuck, Hexal AG, a Sandoz company, 3; J. Jauch-Lembach, Hexal AG, a Sandoz company, 3; A. Balfour, Hexal AG, a Sandoz company, 3; C. Leonardi, Sandoz, 5,Sandoz, 2,Novartis Pharmaceutical Corporation, 2,Novartis Pharmaceutical Corporation, 8.

A Phase III, Multicenter, Double-Blind, Randomized, Parallel-Group Study to Evaluate the Similarities between LBEC0101 and Etanercept Reference Product in Terms of Efficacy and Safety in Patients with Active Rheumatoid Arthritis Inadequately Responding to Methotrexate

Hiroaki Matsuno¹,², Masato Tomomitsu³, Atsushi Hagino³, Seonghye Shin⁴, Jiyoung Lee⁴ and Yeong Wook Song⁵,⁶,
¹Matsuno Clinic for Rheumatic Diseases, Toyama, Japan, ²Institute of Medical Science, Tokyo Medical University, Tokyo, Japan, ³Mochida Pharmaceutical Co., Ltd., Tokyo, Japan, ⁴Clinical Development, LG Chem, Ltd., Seoul, Korea, Republic of (South), ⁵Department of Molecular Medicine and Biopharmaceutical Sciences, Graduate School of Convergence Science and Technology, and College of Medicine, Seoul National University, Seoul, Korea, Republic of (South), ⁶Department of Molecular Medicine and Biopharmaceutical Sciences, Graduate School of Convergence Science and Technology, and College of Medicine, Medical Research Center, Seoul National University, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: LBEC0101 has been developed as a biosimilar to the etanercept reference product (ETN-RP). This study was to evaluate the similarities between LBEC0101 and ETN-RP as adjunctive therapy to methotrexate (MTX), in patients with active rheumatoid arthritis despite MTX treatment. In this abstract, not only the equivalence of the primary endpoint at Week 24 but also the results up to 52 weeks of the study comparing the long term efficacy, safety and immunogenicity between LBEC0101 and ETN-RP are reported.

Methods: This phase III, multicenter, randomized, double-blind, parallel-group, reference product-controlled study was conducted in Japan and Korea. Patients with active RA for ≥6 months who had an inadequate response to MTX were randomly assigned to receive weekly dose of 50 mg LBEC0101 or ETN-RP administered subcutaneously for 52 weeks. The primary efficacy endpoint was the mean change from baseline in the disease activity score in 28 joints based on erythrocyte sedimentation rate (DAS28-ESR) at Week 24. Efficacy, safety and immunogenicity outcomes were assessed up to Week 52.

Results: In total, 374 patients were randomized to LBEC0101 (N=187) or ETN-RP (N=187). The least square mean changes from baseline in DAS28-ESR score at Week 24 in the per-protocol set (PPS) were −3.009 in the LBEC0101 group and −2.859 in the ETN-RP group. The estimated treatment difference in change from baseline to Week 24 in DAS28-ESR between the two groups was −0.150 and the 95% confidence interval (CI) of the difference was −0.3768 to 0.0775, which was completely within the pre-specified equivalence margin of −0.6 to 0.6, indicating that equivalence in efficacy between LBEC0101 and ETN-RP was proved. As a secondary endpoint, ACR20 response rate was similar between the groups (93.3% for LBEC0101 and 86.7% for ETN-RP) at Weeks 24.

The incidence of AEas up to Week 54 was comparable, except for injection site reaction which was reported in the ETN-RP group (438 events in 64 subjects [34.2%]) and in the LBEC0101 group (77 events in 19 subjects [10.2%]), respectively.
Three (1.6%) and 18 (9.6%) patients in the LBEC0101 and ETN-RP groups, developed anti-drug antibody (ADA) up to 52 weeks, respectively.

**Conclusion:** The clinical efficacy of LBEC0101 was equivalent to that of ETN-RP. LBEC0101 was well tolerated and had a comparable safety profile to ETN-RP.


**Abstract Number:** 2442

**Biosimilar Candidate BI 695501 and Adalimumab Reference Product Have Similar Efficacy and Safety in Patients with Moderately-to-Severely Active Rheumatoid Arthritis (RA): 1-Year Results from a Phase III Study**

Stanley B Cohen1, Alberto Alonso-Ruiz2, Piotr A. Klimiuk3, Eric Lee4, Nuala Peter5, Niklas Czeloth5 and Girish Jayadeva5, 1Metroplex Clinical Research Center, Dallas, TX, 2Hospital de Cruces, Barakaldo, Spain, 3Medical University of Bialystok and Gabinet Internistyczno-Reumatologiczny, Bialystok, Poland, 4Inland Rheumatology, Upland, CA, 5Boehringer Ingelheim, Ingelheim a.R., Germany

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

Background/Purpose: Clinical equivalence has been shown for BI 695501 and the adalimumab reference product (RP) through similar ACR20 response at Weeks (wks) 12 and 24 in patients (pts) with moderately-to-severely active RA in the Phase III VOLTAIRE®-RA study (Cohen et al 2017. EULAR 2017. Abst FRI0189). Here we present the long-term safety, efficacy and immunogenicity data.

**Methods:** In this 58-wk, double-blind, multicenter, Phase III active-comparator study (NCT02137226), 645 adalimumab-naïve adults with moderately-to-severely active RA receiving stable treatment with methotrexate (prior exposure to one biologic allowed) were randomized (1:1) to BI 695501 or adalimumab RP 40 mg and treated every 2 wks up to Wk 24. At Wk 24, RP pts were re-randomized to switch to BI 695501 (SWITCH; n = 147 (full analysis set) /146 (safety analysis set [SAF])), or to continue RP (RP-CONT; n = 148) until Wk 48; BI 695501 pts were dummy re-randomized and continued BI 695501 (BI 695501-CONT; n = 298). Data from pts treated only with BI 695501 (N=324) or RP (N=175) for the entire 48 wks were also analysed. Efficacy data were collected until Wk 48. Safety follow-up was to Wk 58 for all pts who did not enter the open-label extension trial (VOLTAIRE®-RAext).
**Results:** Baseline demographics were balanced across treatment groups. ACR20/50/70 response rates were similar across the groups up to Wk 48 (Figure 1). At Wk 48, mean changes from baseline in DAS28-ESR were –2.71, –2.60, and –2.70 in the SWITCH, RP-CONT, and BI 695501-CONT groups, respectively. Safety findings were similar between continuous arms from Day 1 to Wk 58, and re-randomization groups from Wk 24 to Wk 58 (Table 1). Among serious adverse events (SAEs), infections and infestations was the most common system organ class (0.6% for BI 695501 vs 4.0% for RP). No deaths were reported during the study. Similar immunogenicity (anti-drug antibody [ADA] frequency and titers, neutralizing antibody [nAb] frequency) was detected up to Wk 48 in all re-randomized groups. The proportion of pts with positive ADA response at Wks 24 and 48 was 44.5% and 36.2% for the SWITCH group, 50.3% and 49.6% for RP-CONT, and 42.8% and 41.8% for BI 695501-CONT. Positive nAb response frequency at Wk 24 and 48 was 15.8% and 15.2% (SWITCH), 23.8% and 21.6% (RP-CONT), and 15.8% and 19.1% (BI 695501-CONT). The single transition from RP to BI 695501 had no impact on efficacy, safety, and immunogenicity.

**Conclusion:** These data confirm that BI 695501 and adalimumab RP have similar efficacy, safety, and immunogenicity in pts with RA over 48 wks of treatment. These findings also held true for pts switching from adalimumab RP to BI 695501 at Wk 24.

![Figure 1. ACR 20/50/70 response rates over 48 weeks](image)

<table>
<thead>
<tr>
<th></th>
<th>Overall (Day 1 to Week 58)</th>
<th>Re-randomization groups (Week 24 to Week 58)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BI 695501 (N = 324)</td>
<td>RP (N = 175)</td>
</tr>
<tr>
<td>≥1 AE</td>
<td>133 (41.0)</td>
<td>101 (58.0)</td>
</tr>
<tr>
<td>≥1 drug-related AE</td>
<td>62 (19.1)</td>
<td>40 (22.9)</td>
</tr>
<tr>
<td>≥1 serious AE</td>
<td>18 (5.6)</td>
<td>17 (9.7)</td>
</tr>
<tr>
<td>AE leading to study drug discontinuation</td>
<td>13 (4.0)</td>
<td>12 (6.9)</td>
</tr>
</tbody>
</table>

All = treatment-emergent adverse event.

**Acknowledgments:**

The authors would like to thank Deepak Assudani, Ivo Sonderegger, Michael Hug, Benjamin Lang, Susanne Buschke and Christina Grundt, who each provided substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work.
Disclosure: S. B. Cohen, Boehringer Ingelheim, Pfizer, Amgen, Colonis, 2,Sandoz, Pfizer, Amgen, Colonis, 5; A. Alonso-Ruiz, None; P. A. Klimiuk, None; E. Lee, None; N. Peter, Boehringer Ingelheim, 3; N. Czeloth, Boehringer Ingelheim, 3; G. Jayadeva, Boehringer Ingelheim, 3.


Abstract Number: 2443

Randomized, Double-Blind, Single-Dose, Three-Arm Parallel Trial to Determine the Pharmacokinetics and Safety of GP2017, EU- and US-Adalimumab in Healthy Male Subjects

Julia Jauch-Lembach1, Andrej Skerjanec1, Halimuniyazi Haliduola1, Nicole Hass1, Oliver von Richter1, Rainard Fuhr2 and Thomas Koernicke2. 1Hexal AG, Holzkirchen, Germany, 2PAREXEL International GmbH, Berlin, Germany

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: GP2017 is a proposed adalimumab biosimilar that has been shown to be similar to reference adalimumab at an analytical and preclinical level. The aim of this study was to determine the pharmacokinetics (PK), immunogenicity and safety of GP2017, EU-authorized adalimumab (EU-adalimumab) and US-licensed adalimumab (US-adalimumab) in healthy volunteers. As part of the global development program for GP2017, a further aim was to establish PK bridging data between EU- and US-adalimumab.

Methods: This was a randomized, double-blind, three-arm parallel study in healthy male volunteers aged 18 to 55 years, with a body mass index of 18.5 to 29 kg/m^2. Subjects were randomized to receive a single 40 mg/0.8 mL subcutaneous injection of either GP2017, EU- or US-adalimumab, with follow-up until Day 72. The primary objective was to demonstrate PK bioequivalence between GP2017 and EU-adalimumab, and between EU-adalimumab and US-adalimumab, by describing maximum observed serum concentration (C_{max}) and total area under the curve (AUC_{0-inf}). Secondary objectives included the assessment of AUC_{0-360h} and AUC_{0-last}, the comparison of PK parameters between GP2017 and US-adalimumab, and the evaluation of safety, tolerability and immunogenicity of all three products.

Results: A total of 318 subjects were randomized to GP2017 (n=107), EU-adalimumab (n=106) and US-adalimumab (n=105). Baseline characteristics, including body weight, were well balanced across treatment arms. For C_{max} and AUC_{0-inf} the 90% confidence interval (CI) for the ratio of geometric means was contained within prespecified bioequivalence limits of 0.8 to 1.25 for the primary analysis of GP2017 and EU-adalimumab, and EU- and US-adalimumab (Table). For the analysis of secondary objectives, 90% CI were contained within 0.8 to 1.25 for all pairwise comparisons of C_{max}, AUC_{0-inf}, AUC_{0-360h} and AUC_{0-last} (Table). The incidence of drug-related, treatment-emergent adverse events (TEAEs) was similar across the GP2017/EU-adalimumab/US-adalimumab treatment groups (57.9%/61.3%/58.1%) and all were mild or moderate in severity. Infections/infestations were the most common TEAEs. Injection site reactions were infrequent and mild. Overall, antidrug antibodies were detected in 57.9%/69.8%/69.5% of subjects in the GP2017/EU-adalimumab/US-adalimumab groups up to Day 72, which were neutralizing in 54.2%/ 64.2%/62.9% of subjects, respectively.
**Conclusion:** The results show that GP2017 is bioequivalent to EU- and US-adalimumab and EU-adalimumab is bioequivalent to US-adalimumab. There were no clinically relevant differences in safety, tolerability and immunogenicity among the three treatment arms in healthy subjects.

<table>
<thead>
<tr>
<th>Table. Summary statistical analysis of primary and secondary objectives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geometric least square means</td>
</tr>
<tr>
<td>PK parameter</td>
</tr>
<tr>
<td>C&lt;sub&gt;max&lt;/sub&gt;, ng/mL</td>
</tr>
<tr>
<td>AUC&lt;sub&gt;0-inf&lt;/sub&gt;, h×ng/mL</td>
</tr>
<tr>
<td>AUC&lt;sub&gt;0-360h&lt;/sub&gt;, h×ng/mL</td>
</tr>
<tr>
<td>AUC&lt;sub&gt;0-last&lt;/sub&gt;, hxng/mL</td>
</tr>
</tbody>
</table>

| Geometric least square means | Ratio EU/US-adalimumab; 90 % CI |
| PK parameter | EU-adalimumab n | US-adalimumab n | Estimate | Lower | Upper |
| C<sub>max</sub>, ng/mL | 3538.11 103 | 3715.28 99 | 0.95 | 0.90 | 1.01 |
| AUC<sub>0-inf</sub>, h×ng/mL | 2583873.09 85 | 2489573.33 82 | 1.04 | 0.96 | 1.13 |
| AUC<sub>0-360h</sub>, h×ng/mL | 1014666.89 102 | 1063027.38 99 | 0.95 | 0.90 | 1.01 |
| AUC<sub>0-last</sub>, hxng/mL | 2162943.25 103 | 2178039.09 99 | 0.99 | 0.91 | 1.08 |

| Geometric least square means | Ratio GP2017/US-adalimumab; 90 % CI |
| PK parameter | GP2017 n | US-adalimumab n | Estimate | Lower | Upper |
| C<sub>max</sub>, ng/mL | 3710.33 104 | 3715.28 99 | 1.00 | 0.94 | 1.06 |
| AUC<sub>0-inf</sub>, h×ng/mL | 2697410.33 81 | 2489573.33 82 | 1.08 | 1.00 | 1.18 |
| AUC<sub>0-360h</sub>, h×ng/mL | 1065832.23 101 | 1063027.38 99 | 1.00 | 0.94 | 1.06 |
| AUC<sub>0-last</sub>, hxng/mL | 2283589.70 104 | 2178039.09 99 | 1.05 | 0.96 | 1.14 |

**Disclosure:** J. Jauch-Lembach, Hexal AG, a Sandoz company, 3; A. Skerjanec, Hexal AG, a Sandoz company, 3; H. Haliduola, Hexal AG, a Sandoz company, 3; N. Hass, Hexal AG, a Sandoz company, 3; O. von Richter, Hexal AG, a Sandoz company, 3; R. Fuhr, PAREXEL International GmbH, 3; T. Koernicke, PAREXEL International GmbH, 3.

Effectiveness and Safety of CT-P13 in Patients with Rheumatoid Arthritis, Ankylosing Spondylitis, Psoriatic Arthritis and Plaque Psoriasis: Observational Study in Republic of Korea

Dong-Wook Kim1, Tae-Hwan Kim2, Seong Ryul Kwon3, Eun Young Lee4, Chang-Nam Son5, Yun Sung Kim6, Soung Hun Kim7, Yong-Beom Park8, Jin-Wuk Hur9, Hye-Soon Lee10, Sang Joon Lee11 and Jee Hye Suh12, 1Inje University Busan Paik Hospital, Busan, Korea, Republic of (South), 2Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), 3Inha University Hospital, Incheon, Korea, Republic of (South), 4Seoul National University College of Medicine, Seoul, Korea, Republic of (South), 5Keimyung University Dongsan Medical Center, Daegu, Korea, Republic of (South), 6Chosun University Hospital, Gwangju, Korea, Republic of (South), 7Gwangmyeong Saeum Hospital, Gyeonggi-do, Korea, Republic of (South), 8Yonsei University Severance Hospital, Seoul, Korea, Republic of (South), 9Eulji University Seoul Hospital, Seoul, Korea, Republic of (South), 10Hanyang University Guri Hospital, Gyeonggi-do, Korea, Republic of (South), 11CELLTRION, Inc., Incheon, Korea, Republic of (South), 12CELLTRION.Inc, Incheon, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: CT-P13 is approved as a biosimilar of innovator infliximab for marketing in 81 countries. After approval, observational study has been conducted in Republic of Korea in patients with Rheumatoid Arthritis (RA), Ankylosing Spondylitis (AS), Psoriatic Arthritis (PsA) and Plaque Psoriasis (PS). The objective of this study is to evaluate the effectiveness and safety of CT-P13 under routine care.

Methods: This study included both biologic naïve patients (Naïve group) and patients who switched from other anti-tumor necrosis factor (TNF)s such as infliximab, adalimumab, golimumab and etanercept to CT-P13 (Switch group). Effectiveness was evaluated based on remission (DAS28<=2.6 in RA, BASDAI<3 in AS and absence of swollen and tender joint counts in PsA) and response (BASDAI 20/50/70 in AS and PASI 50/75 in PS). Adverse events (AEs) were collected over 6 months.

Results: Total 940 patients (RA 400, AS 531, PsA 3 and PS 6) were registered and 338 (36.0%) patients (RA 108, AS 228, PS 2) who switched to CT-P13 were included.

The proportion of patients achieving remission was similar between Naïve and Switch groups in both RA and AS during post-baseline visits (Table 1). In RA, the proportion of patients achieving each disease activity category by DAS28 was similar between Naïve and Switch groups (Figure 1). The proportion of patients who achieved BASDAI 20/50/70 response gradually increased from week 6 to week 24 or 30 in AS Naïve group (Figure 1).

Fifty percent of 2 naïve patients in PsA achieved remission. The proportions of both PASI 50 and 75 response were 50% at Week 22 in Naïve and 100% and 50% in Switch group, respectively during post-baseline visits in PS.
 Throughout this study, treatment-emergent adverse events (TEAE) and treatment-emergent serious adverse events (TESAE) were reported as Table 2. Only 11% of patients experienced infection.

Table 1. Clinical remission in RA and AS
Table 2. Summary of safety results

<table>
<thead>
<tr>
<th></th>
<th>RA</th>
<th>AS</th>
<th>PsA</th>
<th>PS</th>
</tr>
</thead>
<tbody>
<tr>
<td>n/N (%)</td>
<td>198/400</td>
<td>183/531</td>
<td>1/3 (33.3)</td>
<td>3/6</td>
</tr>
<tr>
<td>TEAE related to</td>
<td>(49.5)</td>
<td>(34.5)</td>
<td>(0.0)</td>
<td>(50.0)</td>
</tr>
<tr>
<td>CT-P13</td>
<td>73/400</td>
<td>64/531</td>
<td>0/3 (0.0)</td>
<td>2/6</td>
</tr>
<tr>
<td>(18.3)</td>
<td>(12.1)</td>
<td>(33.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TESAE</td>
<td>52/400</td>
<td>14/531</td>
<td>0/3 (0.0)</td>
<td>1/6</td>
</tr>
<tr>
<td>(13.0)</td>
<td>(2.6)</td>
<td>(0.0)</td>
<td></td>
<td>(16.7)</td>
</tr>
<tr>
<td>TESAE related to</td>
<td>15/400</td>
<td>6/531</td>
<td>0/3 (0.0)</td>
<td>0/6 (0.0)</td>
</tr>
<tr>
<td>CT-P13</td>
<td>(3.8)</td>
<td>(1.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infusion-related</td>
<td>28/400</td>
<td>11/531</td>
<td>0/3 (0.0)</td>
<td>0/6 (0.0)</td>
</tr>
<tr>
<td>reactions</td>
<td>(7.0)</td>
<td>(2.1)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 1. Clinical responses in RA and Naïve AS Patients

Conclusion: CT-P13 is efficacious and well-tolerated in RA/AS/PsA/PS patients. Efficacy and safety results in patients treated with CT-P13 were clinically consistent to historical data [1][2][3]. Especially, Switch group results showed that CT-P13 provides a useful alternative to other anti-TNFs.


Abstract Number: 2445
Efficacy and Safety of Rituximab Biosimilar, CT-P10, after a Single Switch from Innovator Rituximabs in Patients with Rheumatoid Arthritis: Results from Phase 3 Randomized Controlled Trial over 72 Weeks

Seung-Cheol Shim1, Ljubinka Bozic Majstorovic2, Alfredo Berrocal Kasay3, Elias Chalouhi El-Khoury4, Fedra Irazoqu-Palazuelos5, Francisco Cons Molina6, Francisco G. Medina-Rodriguez7, Pedro Miranda8, Pavel Shesternya9, Jose Chavez Corrales10, Piotr Wiland11, Slawomir Jeka12, Olena Garmish13, Pawel Hrycaj14, Natalia Fomina15, Won Park16, Chang-Hee Suh17, Sang-Joon Lee18, Sung Young Lee19 and Dae-Hyun Yoo20, 1Department of Internal Medicine, Chungnam National University Hospital, Daejeon, Korea, Republic of (South), 2Clinical Centre Banja Luka, Bonja Luka, Bosnia and Herzegovina, 3ABK Reuma SRL – Medicentro Biociencias, Lima, Peru, 4Clinica Internacional, Lima, Peru, 5Centro de Investigacion y Tratamiento Reumatologico S.C, Mexico City, Mexico, 6Centro de Investigacion en Artritis y Osteoporosis, Mexicali, Mexico, 7Rheumatology, LaSalle University, Mexico City, Mexico, 8Centro De Estudios Reumatológicos, Santiago, Chile, 9Rheumatology Department, Krasnoyarsk State Medical University, Krasnoyarsk, Russia, 10Clinica San Borja, Lima, Peru, 11Department and Clinic of Rheumatology and Internal Medicine, Medical University, Wroclaw, Poland, 12nd University Hospital, CM UMK, Department of Rheumatology and Connective Tissue Diseases, Bydgoszcz, Poland, 13Institute of Cardiology named by M.D. Strazhskos NAMS of Ukraine, Kyiv, Ukraine, 14Department of Rheumatology and Clinical Immunology, Poznan University of Medical Sciences, Poznan, Poland, 15Kemerovo Regional Clinical Hospital, Kemerovo, Russian Federation, 16Medicine/Rheumatology, Inha University Hospital, Incheon, Korea, Republic of (South), 17Ajou University School of Medicine, Suwon, Korea, Republic of (South), 18CELLTRION, Inc., Incheon, Korea, Republic of (South), 19Clinical Planning Department, CELLTRION, Inc., Incheon, Korea, Republic of (South), 20Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Similarity of pharmacokinetic, efficacy and safety between CT-P10 and reference rituximab (RTX) were shown in the phase 3 randomized controlled trial (NCT02149121) up to 48 weeks in RA patients1,2,3. This is to investigate efficacy and safety of CT-P10 when used for long term and after switching from RTX in the extension phase of above study.

Methods: Patients who completed up to 48 weeks (Main Period), entered into the Extension Period. Patients who had received CT-P10 or EU-RTX in the Main Period received CT-P10 and patients who had received US-RTX randomly assigned in a 1:1 ratio to receive CT-P10 or US-RTX at Extension Weeks 0 and 2. Efficacy, pharmacodynamics (PD), safety and immunogenicity were evaluated for 24 weeks.

Results: A total of 295 patients (122 CT-P10 Maintenance, 64 US-RTX Maintenance, 62 CT-P10 Switched from US-RTX and 47 CT-P10 Switched from EU-RTX groups) were treated in the Extension Period.

The mean changes of DAS28 from baseline of Main Period and ACR response rate were comparable among the groups (Figures 1 and 2).

B-cell depletion after the 1st infusion was comparable and maintained until Extension Week 24 in all groups.
No remarkable changes in immunogenicity profile were observed following the drug switch. Two patients (1 patient each in the US-RTX Maintenance and CT-P10 Switched from US-RTX groups) had anti-drug antibody newly developed after Extension Week 0 infusion.

The safety profiles were also comparable among the groups (Table 1). All infusion related reactions were grade 1 or 2 intensity. Most frequent infections were upper respiratory and urinary tract infections. No malignancy, progressive multifocal leukoencephalopathy or death were reported.

**Conclusion:** Long term effectiveness and tolerability were achieved over 72-week treatment of CT-P10. The switched groups from RTX to CT-P10 were comparable to CT-P10 or US-RTX Maintenance groups in the efficacy, PD and safety profiles including immunogenicity.

**Reference**


**Figure 1. Improvement of DAS28**

**Figure 2. Proportion of Patients Achieving ACR**


Abstract Number: 2446

**Minimal and Comparable Radiographic Progression By Disease Activity States in Patients with Rheumatoid Arthritis Who Continued SB5 or Reference Adalimumab and Who Switched to SB5**

Michael Weinblatt¹, Asta Baranauskaite², Jeehoon Ghi³, Soo Yeon Cheong³ and Evelyn Hong³, ¹Brigham and Women’s Hospital, Boston, MA, ²Lithuanian University of Health Sciences, Kaunas, Lithuania, ³Samsung Bioepis Co., Ltd., Incheon, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017

Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars

Session Type: ACR Poster Session C

Session Time: 9:00AM-11:00AM

Background/Purpose : SB5 is a biologic agent developed as a biosimilar of the reference adalimumab (ADL). One year results including radiographic progression from the phase III equivalence study have been previously presented. This study further evaluates radiographic progression by different disease activity states by disease activity score by 28 joint count (DAS28) based on erythrocyte sedimentation rate (ESR), simplified disease activity index (SDAI) and clinical disease activity index (CDAI).

Methods : Patients with rheumatoid arthritis (RA) were randomized to receive 40 mg of either SB5 or ADL every other week. At week 24, patients receiving ADL were re-randomised to either switch to SB5 (ADL/SB5) or continue on ADL (ADL/ADL) up to 52 weeks. Patients receiving SB5 continued to receive SB5 (SB5/SB5). The proportion of patients achieving remission, low disease activity (LDA), moderate disease activity (MDA), or high disease activity (HDA) in terms of DAS28, SDAI, and CDAI was compared at weeks 12, 24, and 52. Radiographic progression was measured...
using the modified Total Sharp Score (mTSS) at weeks 0 and 52 and patients with mTSS ≥ 0 at week 52 were regarded as radiographic non-progressors.

Results: The proportion of patients with remission, LDA, MDA, or HDA was comparable across all treatment groups (SB5/SB5 vs. ADL overall vs. ADL/SB5 vs. ADL/ADL) in terms of DAS28 (Table 1) and also SDAI and CDAI (data not shown). The proportions of radiographic non-progressors by disease activity were comparable across treatment groups at week 12, 24 and 52 (Table 2). There was a general trend of higher radiographic progression (decreasing number of radiographic non-progressors and increasing change in mTSS) as disease activity worsened, but the overall radiographic progression was very low across all disease states in SB5 or ADL maintenance groups as well as in the ADL/SB5 switch group.

Conclusion: The proportion of patients in each disease state was comparable upon treatment with SB5 or ADL. The overall radiographic progression was very low across all treatment groups with the lowest progression generally seen in patients with remission and higher scores seen with increasing disease activity. These data further confirm similar effects on clinical and radiographic status with SB5 and ADL, even after switching occurs.

Disclosure: M. Weinblatt, Amgen, BMS, Crescendo Bioscience, UCB, DxtTerity, Sanofi, 2,Amgen, BMS, Crescendo Bioscience, UCB, AbbVie, Lilly, Pfizer, Roche, 5; A. Baranauskaitė, Samsung Bioepis Co., Ltd. Abbvie, 5; J. Ghil, Samsung Bioepis, 3; S. Y. Cheong, Samsung Bioepis Co., Ltd., 3; E. Hong, Samsung Bioepis Co., Ltd., 3.

Effectiveness and Tolerability of Benepali in Rheumatoid Arthritis Patients Switched from Enbrel

Sarah Dyball¹, Victoria Hoskins², Sharon Christy-Kilner² and Sahena Haque³, ¹Rheumatology, University Hospitals of South Manchester NHS Foundation Trust, Manchester, United Kingdom, ²University Hospitals of South Manchester NHS Foundation Trust, Manchester, United Kingdom, ³Rheumatology department, University Hospitals of South Manchester NHS Foundation Trust, Manchester, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Benepali, the etanercept biosimilar, is licenced in the UK for rheumatoid arthritis (RA) and costs less than Enbrel. This study aimed to evaluate the comparative effectiveness and tolerance of Benepali in RA patients that were switched from Enbrel.

Methods: A retrospective observational study design. Data collected from 38 patients with RA who had previously been established on Enbrel and were switched to Benepali with unchanged dosing regimens. Patient’s baseline characteristics, DAS-28, CRP, tender joints, swollen joints and global scores were collected before and after the switch from hospital records at a single centre.

Variables were analysed using the Bland-Altman 95% limits of agreement on the estimated mean bias between paired measurements ± 1.96SD. Student’s paired t-test was used to assess the significance of the mean difference.

Results: Patients had a mean age of 59.3 years, 69% were female and 88.5% were seropositive. There were 9/39 that had used a biologic prior to Enbrel.

| Table 1: Markers of disease activity in Enbrel and Benepali |
|---------------------------------|---------------|----------------|----------------|---------|
|                                | Enbrel average | Benepali average | Mean difference | P-value |
| DAS-28 (n=38)                  | 3.08           | 3.42            | +0.35           | 0.06    |
| CRP (n=38)                     | 7.00           | 6.95            | -0.05           | 0.98    |
| Tender joints (n=38)           | 3.10           | 3.84            | +0.74           | 0.15    |
| Swollen joints (n=38)          | 1.26           | 1.5             | +0.24           | 0.54    |
| Patient global health (n=38)   | 38.6           | 49.6            | +11             | 0.05    |

The mean difference in DAS-28, CRP, tender and swollen joints is not statistically significant (Table 1). There was an average increased global score of 11/100 (p=0.05) with Benepali. This suggests that the more objective scores were less likely to be affected by the switch to Benepali.
Bland-Altman analysis (Figure 1) shows wide limits of agreement (-1.86 to 2.56), with a small mean difference of 0.348 (95% CI -0.01, 0.71) in DAS-28 scores. This suggests that although majority of patients did not have a significant variation in their DAS-28, there were a number of patients that did significantly better or worse on the Benepali.

Benepali was discontinued 17% of patients (6/36); 4 stopped due to ineffectiveness (all of which were switched back to Enbrel) and 2 stopped due to adverse drug reactions (1 patient developed injection site reactions and switched back to Enbrel, and the other patient developed a rash and had a significant fall in neutrophils and was re-challenged with Benepali).

**Conclusion:** In this RA clinical cohort, objective measures of disease activity were not statistically different for Benepali compared with Enbrel. The switch to Benepali resulted in a drug cost saving of £26400 per annum.

**Disclosure:** S. Dyball, None; V. Hoskins, None; S. Christy-Kilner, None; S. Haque, None.


**Abstract Number:** 2448

**Increased Cumulative Exposure to Tumor Necrosis Factor Inhibitors Reduces Radiographic Progression in US Veterans with Rheumatoid Arthritis in Real World Clinical Practice**

**Grant Cannon**¹, Alan R. Erickson², Chia-Chen Teng, MS¹, Tina Huynh¹, Sally W. Wade³, Bradley S. Stolshek⁴, David Collier⁵, Alex Mutebi⁶ and Brian C. Sauer, PhD⁷, ¹Salt Lake City VA Medical Center and University of Utah, Salt Lake City, UT, ²Omaha VA Medical Center and University of Nebraska Medical Center, Omaha, NE, ³Wade Outcomes Research and Consulting, Salt Lake City, UT, ⁴Amgen, Inc., Thousand Oaks, CA, ⁵Amgen Inc., Thousand Oaks, CA, ⁶Global Health Economics, Amgen Inc., Thousand Oaks, CA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017
Background/Purpose: While tumor necrosis factor inhibitors (TNFi) have been proven to reduce progression of structural joint damage in rheumatoid arthritis (RA) in randomized clinical trials, this aspect of effectiveness has not been studied in real world clinical practice. We evaluated the relationship between cumulative exposure to TNFi therapy and progression of joint damage following initiation of TNFi therapy in US Veterans.

Methods: Veterans with RA who initiated TNFi use after at least six months of enrollment in Veterans Affairs (VA) health care were eligible for this study. Subjects were US Veterans with VA care between January 1, 2006 and June 30, 2016 with bilateral baseline hand x-rays during the interval between six months prior to and one month after TNFi initiation and follow-up bilateral hand x-rays taken between 10 and 18 months after TNFi initiation. Subjects with non-TNFi biologic drug exposure prior to TNFi initiation or between baseline and follow-up x-rays were excluded. Change in the modified Sharp Score (mSS) on hand radiographs that were interpreted by a single evaluator, blinded to TNFi history and sequence of x-rays, was assessed relative to cumulative TNFi exposure calculated from VA pharmacy data. A worsening of mSS of ≥5 points was considered clinically significant to account for reader variability. The population fraction with clinically significant change in mSS was explored using marginal structural models (MSM) with inverse probability of treatment weights (IPTW). Bootstrapping was used to compute 95% confidence intervals (CI). Baseline patient disease characteristics (e.g., age, seropositive status, smoking history, co-morbidities, concurrent medication, and baseline mSS) and time-varying covariates (ESR, C-reactive protein, and prednisone treatment) were deemed potential confounders and included as covariates in the MSM.

Results: There were 250 patients from 81 sites enrolled. The population’s baseline demographic features were: age 58 ±11 years, 81% male, 68% positive for rheumatoid factor, and 65% positive for anti-cyclic citrullinated peptide antibody (aCCP). Baseline mSS was 19.5±33.2 (median 8, range 0 to 214). The mean change in mSS was 0.5±4.6 (median 0, range -19 to 45). Increases in cumulative TNFi exposure were associated with decreases in mSS. In comparison to patients with less than one month of TNFi exposure, patients with 12-months of cumulative exposure exhibited less radiographic progression for weighted analysis.

Conclusion: While progression of radiographic changes as measured by mSS were small in the first year of use, increased cumulative TNFi exposure was associated with less progression of joint damage in US Veterans. These results demonstrate real-world effectiveness and support the findings of reduced radiographic progression with TNFi therapy reported in randomized clinical trials.

Disclosure: G. Cannon, Amgen, 2; A. R. Erickson, Amgen, 2; C. C. Teng, MS, Amgen, 2; T. Huynh, Amgen, 2; S. W. Wade, Amgen, 5; B. S. Stolshke, Amgen, 1,Amgen, 3; D. Collier, Amgen, 1,Amgen, 3; A. Mutebi, Amgen, 1,Amgen, 3; B. C. Sauer, PhD, Amgen, 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/increased-cumulative-exposure-to-tumor-necrosis-factor-inhibitors-reduces-radiographic-progression-in-us-veterans-with-rheumatoid-arthritis-in-real-
Abstract Number: 2449

Comparative Effectiveness of Tocilizumab (TCZ) Monotherapy with Tumor Necrosis Factor Inhibitors (TNFi) in Combination with Varying Doses of Methotrexate (MTX) in Patients with Rheumatoid Arthritis

Leslie R Harrold¹, George W. Reed¹, Jennie Best², Steve Zlotnick², Gioia Persuitte³ and Joel Kremer⁴, ¹University of Massachusetts Medical School, Worcester, MA, ²Genentech, Inc., South San Francisco, CA, ³Corrona, LLC, Southborough, MA, ⁴Albany Medical College and The Center for Rheumatology, Albany, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Clinical studies have shown that the efficacy of TCZ monotherapy (TCZ mono) is superior to that of TNFi monotherapy and comparable to that of TCZ in combination with MTX. The objective of this study was to compare the effectiveness of TCZ mono vs TNFi plus varying doses of MTX in patients with rheumatoid arthritis (RA) and prior exposure to TNFi in routine clinical practice.

Methods: Eligible participants were TCZ-naïve patients from the Corrona RA registry who had prior exposure to ≥ 1 TNFi, initiated TCZ mono or a TNFi + MTX between 2010 and 2016 and had a 6-month follow-up visit. The primary outcome was mean change from baseline in Clinical Disease Activity Index (CDAI) at 6 months. Secondary outcomes included achievement of low disease activity (LDA; CDAI ≤ 10) at 6 months. Patients initiating a TNFi + MTX were grouped by MTX dose (≤ 10 mg; > 10 to ≤ 15 mg; > 15 to ≤ 20 mg; > 20 mg); outcomes in each group were compared with those initiating TCZ mono using trimmed populations, excluding patients outside the propensity score (PS) distribution overlap (not on common support). The PS included age, sex, race, body mass index, smoking status, work status, disease duration, concomitant prednisone use/dose, prior biologic use, American College of Rheumatology functional class and baseline modified Health Assessment Questionnaire, CDAI and patient pain scores. As a sensitivity analysis, stratified-matched populations were created (stratified by 1 vs ≥ 2 prior biologics, then matched on PS). Linear and logistic regression models were estimated in the trimmed populations, adjusting for the same covariates as in the PS.

Results: Baseline demographics were generally comparable between the TNFi + MTX groups and their matched TCZ mono groups. Overall, the mean age was 54 to 59 years, and the mean disease duration was 10.5 to 15 years. A higher proportion of patients initiating TCZ mono had received ≥ 3 prior biologics compared with those initiating TNFi + MTX. Patients initiating TCZ mono had significantly longer mean disease duration than those initiating TNFi + MTX > 15 to ≤ 20 mg (13.0 vs 10.5 years) or TNFi + MTX > 20 mg (12.3 vs 9.3 years) and a higher mean baseline CDAI than those initiating TNFi + MTX ≤ 10 mg (28.1 vs 25.4). Patients in all groups had improvement in CDAI scores at 6 months. In adjusted models, improvement in CDAI and the likelihood of achieving LDA were similar between the TCZ mono group and all TNFi + MTX groups (Table 1). Similar results were observed in the PS-matched cohorts.

Conclusion: TCZ mono was as effective as TNFi + MTX, regardless of MTX dose, for improving disease activity in patients with prior TNFi exposure. These data suggest that TCZ mono is an effective treatment option for patients with RA who cannot tolerate or prefer not to use MTX.
Table 1. Disease activity outcomes at 6 months in patients who initiated TCZ mono compared with those who initiated TNFi + MTX.

<table>
<thead>
<tr>
<th></th>
<th>Change in CDAI</th>
<th></th>
<th>Achievement of LDA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted Mean (SD)</td>
<td>Adjusted β (95% CI)*</td>
<td>Unadjusted Response Rate, n (%)</td>
</tr>
<tr>
<td>TCZ mono</td>
<td>−9.7 (14.6)</td>
<td>—</td>
<td>82 (29)</td>
</tr>
<tr>
<td>(n = 283)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TNFi + MTX ≤ 10 mg</td>
<td>−7.8 (13.6)</td>
<td>−0.15 (−2.92 to 2.62)</td>
<td>33 (31)</td>
</tr>
<tr>
<td>(n = 108)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TCZ mono</td>
<td>−9.6 (14.5)</td>
<td>—</td>
<td>88 (29)</td>
</tr>
<tr>
<td>(n = 300)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TNFi + MTX &gt; 10 to ≤ 15 mg</td>
<td>−9.0 (14.2)</td>
<td>−0.3 (−2.83 to 2.22)</td>
<td>70 (38)</td>
</tr>
<tr>
<td>(n = 186)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TCZ mono</td>
<td>−9.6 (14.7)</td>
<td>—</td>
<td>85 (29)</td>
</tr>
<tr>
<td>(n = 292)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TNFi + MTX &gt; 15 to ≤ 20 mg</td>
<td>−6.9 (12.8)</td>
<td>−1.65 (−3.84 to 0.54)</td>
<td>73 (27)</td>
</tr>
<tr>
<td>(n = 273)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TCZ mono</td>
<td>−9.7 (14.7)</td>
<td>—</td>
<td>85 (30)</td>
</tr>
<tr>
<td>(n = 285)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TNFi + MTX &gt; 20 mg</td>
<td>−8.4 (15.0)</td>
<td>−1.43 (−5.12 to 2.25)</td>
<td>32 (30)</td>
</tr>
<tr>
<td>(n = 107)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CDAI, Clinical Disease Activity Index; LDA, low disease activity; MTX, methotrexate; OR, odds ratio; TCZ, tocilizumab; TNFi, tumor necrosis factor inhibitor.

*TZC compared with TNFi + MTX. Adjusted for sex, age, race (white vs nonwhite), disabled, retired, baseline CDAI, baseline modified Health Assessment Questionnaire, baseline patient pain scores, baseline prednisone use/dose, baseline body mass index, prior biologic use, prior TNFi use and American College of Rheumatology functional class.

Disclosure: L. R. Harrold, Corrona, LLC, 3,Corrona, LLC, 1,Pfizer Inc, 2,Roche Pharmaceuticals, 5; G. W. Reed, Corrona, LLC, 3,Corrona, LLC, 1; J. Best, Genentech, Inc, 3; S. Zlotnick, Genentech, Inc, 3; G. Persuitte, Corrona, LLC, 3; J. Kremer, Corrona, LLC, 3,Corrona, LLC, 1,AbbVie, Amgen, BMS, Genentech, GSK, Lilly, Pfizer, Regeneron, Sanofi, 5.


Abstract Number: 2450

Comparative Effectiveness of Abatacept Versus TNFi in Patients with RA Who Are CCP+ in the United States Corrona Registry

Leslie R Harrold1, Heather J. Litman2, SE Connolly3, E Alemao3, K Price3, S Kelly3, Sabrina Rebello4, W Hua2 and Joel Kremer5, 1University of Massachusetts, Worcester, MA, 2Corrona, Southborough, MA, 3Bristol-Myers Squibb, Princeton, NJ, 4Corrona, LLC, Southborough, MA, 5Albany Medical College and The Center for Rheumatology, Albany, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
**Background/Purpose:** Anti-cyclic citrullinated peptide positivity (CCP+) is associated with a better response to abatacept than anti-CCP negativity in patients with RA\(^1,2\); however, there are no head-to-head or comparative effectiveness research studies available evaluating responses to biologics in CCP+ patients in a real-world setting. The aim of this study was to compare the effectiveness of abatacept vs a TNF inhibitor (TNFi) in patients with RA who are CCP+. **Methods:** We identified adult patients with RA from a large observational US cohort (Dec 1, 2005–Aug 31, 2016) who initiated abatacept or a TNFi and who were CCP+ (≥20 U/mL) at or prior to initiation. Both groups had to have no prior exposure to other non-TNFi biologics or targeted synthetic DMARDs. TNFi initiators were excluded if they had prior use of abatacept. Using propensity score matching (1:1) stratified by prior TNFi use (0, 1 and 2+), effectiveness at 6 months after initiation was evaluated. Mean change in CDAI over 6 months following initiation was the primary outcome and secondary outcomes were: achievement of remission (CDAI ≤2.8), modified (m)ACR20, 50 and 70 responses and achievement of LDA/remission (CDAI ≤10) in those with moderate/high disease activity at initiation. A subset analysis was performed to consider separately patients who were biologic naïve and those who were biologic experienced at initiation.

**Results:** The 330 pairs of propensity score-matched abatacept and TNFi initiators had no substantial differences in baseline characteristics. Both treatment groups had similar mean change in CDAI at 6 months as well as achievement of LDA, remission and mACR20/50/70 responses (Table). Among the 97 matched biologic-naïve pairs, there was no significant difference in change in CDAI for abatacept initiators vs TNFi initiators (p=0.19). However, in the 233 matched biologic-experienced pairs, those initiating abatacept had a greater improvement in mean change in CDAI (p=0.033) and were more likely to achieve an mACR50 response (p=0.014).

**Conclusion:** Patients with RA who were CCP+ and received either abatacept or TNFi had a substantial improvement in clinical disease activity. In the overall propensity score-matched sample, similar outcomes were observed for both treatment groups. However, analysis of the biologic-experienced cohort found that abatacept initiators had a greater improvement in disease activity than TNFi initiators.


Original abstract © EULAR/BMJ. First presented at EULAR 2017 and published in *Ann Rheum Dis* 2017;76 (Suppl 2):AB0408. Any reprints, promotional options, education material etc have to be done through the original source (ARD/BMJ).

<table>
<thead>
<tr>
<th></th>
<th>Total population</th>
<th>CCP+ abatacept initiators n=330</th>
<th>CCP+ TNFi initiators n=330</th>
<th>p value(^a)</th>
<th>CCP+ abatacept initiators n=97</th>
<th>CCP+ TNFi initiators n=97</th>
<th>p value(^a)</th>
<th>CCP+ abatacept initiators n=233</th>
<th>CCP+ TNFi initiators n=233</th>
<th>p value(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcomes:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change in CDAI</td>
<td>Mean (95% CI)</td>
<td>−9.0 (−11.4)</td>
<td>−8.5 (−10.8)</td>
<td>0.24</td>
<td>−9.0 (−11.4)</td>
<td>−12.0 (−14.4)</td>
<td>0.19</td>
<td>−9.0 (−11.0)</td>
<td>−7.6 (−10.6)</td>
<td>0.033</td>
</tr>
<tr>
<td><strong>Secondary outcomes:</strong></td>
<td>Response rate (%)</td>
<td>51.3</td>
<td>16.9</td>
<td>0.69</td>
<td>16.9</td>
<td>17.6</td>
<td>0.72</td>
<td>16.9</td>
<td>16.6</td>
<td>0.71</td>
</tr>
<tr>
<td>LDA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Remission</td>
<td>Response rate (%)</td>
<td>18.9</td>
<td>7.2</td>
<td>0.27</td>
<td>18.9</td>
<td>7.2</td>
<td>0.27</td>
<td>18.9</td>
<td>7.2</td>
<td>0.27</td>
</tr>
<tr>
<td>mACR20</td>
<td>Response rate (%)</td>
<td>31.6</td>
<td>21.5</td>
<td>0.31</td>
<td>31.6</td>
<td>21.5</td>
<td>0.31</td>
<td>31.6</td>
<td>21.5</td>
<td>0.31</td>
</tr>
<tr>
<td>mACR50</td>
<td>Response rate (%)</td>
<td>59.4</td>
<td>29.3</td>
<td>0.48</td>
<td>59.4</td>
<td>29.3</td>
<td>0.48</td>
<td>59.4</td>
<td>29.3</td>
<td>0.48</td>
</tr>
<tr>
<td>mACR70</td>
<td>Response rate (%)</td>
<td>41.3</td>
<td>28.8</td>
<td>0.32</td>
<td>41.3</td>
<td>28.8</td>
<td>0.32</td>
<td>41.3</td>
<td>28.8</td>
<td>0.32</td>
</tr>
</tbody>
</table>

\(^a\)Fisher Exact test

CCP=anti-cyclic citrullinated peptide positivity, mACR=modified ACR, SD=standard error, TNFi=TNF inhibitor.

**Disclosure:** L. R. Harrold, Corrona, 1,Pfizer Inc, 2,Roche Pharmaceuticals, 5,Corrona, 3; H. J. Litman, Corrona, 3; S. Connolly, Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1; E. Alemao, Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1; K. Price, Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1; S. Kelly, Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1;
Rapid Onset of Response Observed with Certolizumab Pegol in Rheumatoid Arthritis Patients with Inadequate Response to Methotrexate: Efficacy and Safety Results of a Randomized, Double-Blind, Placebo-Controlled Phase 3 Study

LiQi Bi1, Yuhui Li2, Lan He3, Huji Xu4, Jieruo Gu5, Guochun Wang6, Zhiyi Zhang7, Yi Liu8, Marion Boehnlein9, Jochen Dunkel9, Jing Shao10, Kristina Harris11 and Zhanguo Li12, 1China-Japan Union Hospital of Jilin University*, Changchun, China, 2Peking University People’s Hospital*, Beijing, China, 3The First Affiliated Hospital of Xi’an Jiaotong University, Xi’an, China, 4Shanghai Changzheng Hospital, Shanghai, China, 5Sun Yat-sen University – The Third Affiliated Hospital, Guangzhou, China, 6China-Japan Friendship Hospital, Beijing, China, 7The First Affiliated Hospital of Harbin Medical University, Harbin, China, 8West China Hospital, Sichuan University, Chengdu, China, 9UCB Pharma, Monheim, Germany, 10UCB Pharma, Tokyo, Japan, 11UCB Pharma, Slough, United Kingdom, 12Peking University People's Hospital, Beijing, China

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Tuesday, November 7, 2017
**Session Title:** Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
**Session Type:** ACR Poster Session C
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**
There are unmet needs for patients (pts) suffering from rheumatoid arthritis (RA) in China, where a limited number of anti-TNFs are available.1, 2 Certolizumab pegol (CZP), with its demonstrated efficacy and safety, would provide an additional option for Chinese RA pts.3, 4 We report results from RAPID-C, which assessed the efficacy and safety of CZP in combination with methotrexate (MTX) in Chinese pts with active RA and an inadequate response to MTX.

**Methods:**
RAPID-C (NCT02151851) was a 24-week (wk), phase 3, double-blind, placebo-controlled study conducted in 30 centers across China. Pts with active RA were randomized 3:1 to receive CZP or placebo (PBO), together with MTX. Pts received either loading doses of CZP 400 mg or PBO at Wks 0, 2 and 4, followed by CZP 200 mg or PBO every 2 wks thereafter. The primary endpoint was ACR20 at Wk24, analyzed using logistic regression in the full analysis set (FAS) with non-responder imputation for missing data. Secondary endpoints were ACR50/70 responses and physical function as measured by change from baseline (CFB) in HAQ-DI at Wk24. ACR core components, CRP, DAS28(ESR) and fatigue (measured using BRAF-MDQ) were assessed at selected study visits. CFB in HAQ-DI and other continuous variables were analyzed in the FAS using analysis of covariance with last observation carried forward imputation for missing data. Incidence of treatment-emergent adverse events (TEAEs) and other safety parameters were monitored over the treatment period.
Results:

The FAS included 312 CZP+MTX pts and 113 PBO+MTX pts. The demographic and baseline disease characteristics were balanced between treatment arms. Compared with PBO+MTX, a significantly higher percentage of CZP+MTX pts achieved ACR20 response at Wk24 (54.8% vs 23.9%; odds ratio: 3.9, p<0.001). Greater improvements in HAQ-DI, higher ACR50/70 responses (Table A) and higher DAS28 remission rates were also observed in CZP+MTX pts at Wk24. Rapid onset of response was observed as early as Wk1 for most efficacy outcomes in CZP+MTX pts. The safety profile of CZP was in line with previous CZP studies (Table B).\textsuperscript{3, 4} No new safety signals were identified in this population of Chinese pts.

Conclusion:

CZP in combination with MTX has shown an acceptable safety profile, a rapid onset of action and sustained effects in reducing the signs and symptoms of RA and improving physical function in Chinese RA pts with an inadequate response to MTX.

*These authors contributed equally to this work.

References:

1. An Y. Clin Rheumatol 2017;36:35-43
2. Wang GY. Clin Rheumatol 2015;34:221-30
### Table A: Summary of Week 1 and Week 24 efficacy data (FAS population)

<table>
<thead>
<tr>
<th></th>
<th>Week 1</th>
<th></th>
<th>Week 24</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PBO+MTX (n=113)</td>
<td>CZP+MTX (n=312)</td>
<td>Odds ratio (95% CI)</td>
<td>PBO+MTX (n=113)</td>
</tr>
<tr>
<td>ACR20 (%) [e]</td>
<td>2.7</td>
<td>18.9</td>
<td>9.9 (3.0, 32.7)</td>
<td>23.9</td>
</tr>
<tr>
<td>ACR50 (%) [e]</td>
<td>0.9</td>
<td>3.6</td>
<td>4.4 (0.6, 34.8)</td>
<td>7.1</td>
</tr>
<tr>
<td>ACR70 (%) [e]</td>
<td>0.0</td>
<td>0.6</td>
<td>NE [b]</td>
<td>2.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>PBO+MTX (n=113)</td>
<td>CZP+MTX (n=312)</td>
<td>LS mean difference (SE)</td>
<td>PBO+MTX (n=113)</td>
</tr>
<tr>
<td>DAS28 (ESR) (median CFB) [f]</td>
<td>-0.10</td>
<td>-0.64</td>
<td>-</td>
<td>-0.51</td>
</tr>
<tr>
<td>CRP (LS mean RTB)</td>
<td>1.00</td>
<td>0.26</td>
<td>0.27 (0.22, 0.32)</td>
<td>0.90</td>
</tr>
<tr>
<td>TJC (66 joints) (LS mean CFB)</td>
<td>-0.23</td>
<td>-3.77</td>
<td>-3.48 (0.78)</td>
<td>-6.12</td>
</tr>
<tr>
<td>SJC (66 joints) (LS mean CFB)</td>
<td>-0.94</td>
<td>-3.50</td>
<td>-2.56 (0.57)</td>
<td>-4.77</td>
</tr>
<tr>
<td>PhGADA-VAS (LS mean CFB)</td>
<td>-4.07</td>
<td>-11.10</td>
<td>-7.03 (1.50)</td>
<td>-14.34</td>
</tr>
<tr>
<td>PAAP-VAS (LS mean CFB)</td>
<td>-1.15</td>
<td>-12.09</td>
<td>-10.94 (1.74)</td>
<td>-6.16</td>
</tr>
<tr>
<td>PGADA-VAS (LS mean CFB)</td>
<td>-2.62</td>
<td>-11.38</td>
<td>-8.76 (1.96)</td>
<td>-6.63</td>
</tr>
<tr>
<td>HAQ-DI (LS mean CFB)</td>
<td>-0.07</td>
<td>-0.15</td>
<td>-0.09 (0.04) [d]</td>
<td>-0.17</td>
</tr>
<tr>
<td>BAF-MDQ total score (LS mean CFB)</td>
<td>-0.76</td>
<td>-6.36</td>
<td>-5.59 (0.95)</td>
<td>-4.66</td>
</tr>
</tbody>
</table>

*p<0.001 for all outcomes and time points except: [a] p=0.16; [b] Odds ratio and p value not available due to lack of responders in the PBO+MTX group; [c] p=0.031; [d] p=0.029. All p values except for the primary endpoint are nominal. [e] Non-responder imputation. Last observation carried forward imputation used for all other outcomes. [f] Due to absence of normal distribution, Wilcoxon rank sum test was used to test the difference in median CFB between treatment arms. no LS mean difference was calculated. [g] Ratio of geometric mean calculated as CZP+MTX/PBO+MTX. Odds ratios were calculated as CZP+MTX/PBO+MTX; LS mean differences were calculated as CZP+MTX - PBO+MTX; PAAP-VAS was measured on a 0 (no pain) to 100 (most severe pain) scale; PhGADA-VAS and PGADA-VAS were measured on a 0 (no fatigue) to 70 (worst fatigue) scale. ACR: American College of Rheumatology; BAF-MDQ: Bristol Rheumatoid Arthritis Fatigue-Multidimensional Questionnaire; CRP: C-reactive protein; DAS28: 28-joint Disease Activity Score; ESR: erythrocyte sedimentation rate; HAQ-DI: Health Assessment Questionnaire – Disability Index; LS: last squared; NE: non-evaluable; PhGADA: Physician’s Global Assessment of Disease Activity; PAAP: Patient’s Assessment of Arthritis Pain; PGADA: Patient’s Global Assessment of Disease Activity; SJC: swollen joint count; RTB: ratio to baseline; TJC: tender joint count; VAS: visual analog scale.
Table B: Summary of TEAEs (safety set population)

<table>
<thead>
<tr>
<th></th>
<th>PBO+MTX (n=113)</th>
<th>CZP+MTX (n=318)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any TEAEs</td>
<td>82 (72.6) [415.1]</td>
<td>229 (72.5) [372.7]</td>
</tr>
<tr>
<td>Any SAEs</td>
<td>3 (2.7) [6.9]</td>
<td>20 (6.3) [14.9]</td>
</tr>
<tr>
<td>TEAEs leading to discontinuations</td>
<td>6 (5.3) [14.1]</td>
<td>28 (8.9) [21.1]</td>
</tr>
<tr>
<td>Drug-related TEAEs</td>
<td>48 (42.5)</td>
<td>145 (45.9)</td>
</tr>
<tr>
<td>Deaths</td>
<td>0</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>AEs of interest and other specific AEs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serious infections</td>
<td>0</td>
<td>6 (1.9) [4.4]</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>0</td>
<td>2 (0.6) [1.5]</td>
</tr>
<tr>
<td>Pulmonary TB</td>
<td>0</td>
<td>2 (0.6) [1.5]</td>
</tr>
<tr>
<td>Pericarditis TB</td>
<td>0</td>
<td>1 (0.3) [0.7]</td>
</tr>
<tr>
<td>TB pleurisy</td>
<td>0</td>
<td>1 (0.3) [0.7]</td>
</tr>
<tr>
<td>Serious hepatobiliary disorders</td>
<td>1 (0.9) [2.3]</td>
<td>2 (0.6) [1.5]</td>
</tr>
<tr>
<td>Liver injury</td>
<td>0</td>
<td>2 (0.6) [1.5]</td>
</tr>
<tr>
<td>MACE [a]</td>
<td>1 (0.9) [2.3]</td>
<td>0</td>
</tr>
<tr>
<td>Early systemic hypersensitivity reaction</td>
<td>0</td>
<td>4 (1.3) [2.9]</td>
</tr>
<tr>
<td>Hepatic disorders (SMQs)</td>
<td>19 (16.8) [49.1]</td>
<td>51 (19.3) [51.1]</td>
</tr>
<tr>
<td>Malignancies (SMQs)</td>
<td>0</td>
<td>1 (0.3) [0.7]</td>
</tr>
</tbody>
</table>

TEAEs were classified according to MedDRA version 15.1. [a] Sponsor-defined search criteria. IR: incidence rate per 100 patient-years. MACE: major adverse cardiovascular events; SAEs: serious TEAEs; SMQ: Standardized Medical Dictionary for Regulatory Activities Query; TB: tuberculosis.

Disclosure: L. Bi, None; Y. Li, None; L. He, None; H. Xu, None; J. Gu, None; G. Wang, None; Z. Zhang, None; Y. Liu, None; M. Boehnlein, UCB Pharma, 3; J. Dunkel, UCB Pharma, 3; J. Shao, UCB Pharma, 3; K. Harris, UCB Pharma, 3; Z. Li, None.


Abstract Number: 2452

**In Real-World Clinical Practice, Patients Switching from IV to SC Abatacept Maintain Clinical Efficacy after Switch**

Rieke Alten¹, HM Lorenz², X Mariette³, H Nüblein⁴, M Galeazzi⁵, F Navarro⁶, M Chartier⁷, J Heitzmann⁸, C Rauch⁹ and M Le Bars⁷, ¹Schloßpark-Klinik University Medicine, Berlin, Germany, ²University Hospital, Heidelberg, Germany, ³Université Paris-Sud, Paris, France, ⁴University of Erlangen-Nuremberg, Nuremberg, Germany, ⁵University of Siena, Siena, Italy, ⁶Hospital Universitario Virgen Macarena, Seville, Spain, ⁷Bristol-Myers Squibb, Rueilly-Malmaison, France, ⁸Excelya, Boulogne-Billancourt, France, ⁹Bristol-Myers Squibb, Munich, Germany

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
**Background/Purpose:** Patients (pts) with RA may be able to switch from IV to SC abatacept with no loss of efficacy or safety concerns, but data are inconclusive.\(^1\)\(^-\)\(^4\) ACTION (AbataCepT In rOutiNe clinical practice; NCT02109666) examined abatacept formulation switching and the impact on clinical efficacy over 2 years. **Methods:** ACTION is a 2-year, prospective, observational study of pts with moderate-to-severe RA who initiated IV abatacept in Europe and Canada between May 2008 and December 2013. Assessments in biologic-naïve and biologic-failure pts were: baseline characteristics, rates of/reasons for switching (IV to SC), re-switching to IV over 2 years and clinical efficacy outcomes in pts who switched. Descriptive data were generated: mean (SD) for continuous variables and n (%) for categorical variables. Rates of switching were estimated by Kaplan–Meier analysis. Owing to low numbers, cohorts were pooled to analyze further pts who switched.

**Results:** In total, 2350/2364 pts (99.4%) were evaluable for this analysis (673 [28.6%] biologic naïve, 1677 [71.4%] biologic failure); 728 (43.4%) biologic-failure pts had received 1, and 949 (56.6%) had received ≥2 previous biologics. Baseline characteristics in biologic-naïve and biologic-failure pts, respectively, were: mean (SD) age 59.9 (12.7) and 56.9 (12.5) years; mean (SD) RA duration 7.2 (8.22) and 12.1 (9.13) years; 496 (73.7%) and 1379 (82.2%) were women; 621 (92.3%) and 1552 (92.5%) had received prior MTX; and 533 (79.2%) and 1386 (82.6%) had received corticosteroids. Over 2 years, 195 pts switched from IV to SC abatacept (57 biologic naïve, 138 biologic failure; Figure). The primary reason for switch was pt wish (in 28/51 [54.9%] biologic-naïve and 75/121 [62.0%] biologic-failure pts with reason for switch available). Only 8 pts (4.1%) re-switched to IV abatacept (2 biologic naïve, 6 biologic failure). Reasons for re-switch were: pt wish (n=4), lack of efficacy (n=4), safety issue (n=1) and other (n=2). Clinical efficacy outcomes, stratified by prior treatment history, were generally similar at last follow-up before switching from IV to SC abatacept and at last follow-up on SC abatacept treatment (Table).

**Conclusion:** Over 2 years, in real-world clinical practice, of the pts who switched from IV to SC abatacept, less than 5% re-switched from SC abatacept to the IV formulation. No adverse clinical impact was observed following switching from IV to SC abatacept.

### Table. Efficacy of Abatacept at Last Follow-up Before Switching From IV to SC Formulation and at Last Follow-up Under SC Treatment (Overall Analysis Population)

<table>
<thead>
<tr>
<th></th>
<th>Last follow-up before switching from IV to SC</th>
<th>Last follow-up under SC treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Biologic-naïve cohort (n=51)</td>
<td>Biologic-failure cohort (n=122)</td>
</tr>
<tr>
<td>DAS28 (ESR), mean (SD)</td>
<td>3.0 (1.2) (n=42)</td>
<td>3.5 (1.2) (n=107)</td>
</tr>
<tr>
<td>DAS28 (ESR) remission, n (%)</td>
<td>17 (40.5) (n=42)</td>
<td>27 (25.2) (n=107)</td>
</tr>
<tr>
<td>DAS28 (CRP), mean (SD)</td>
<td>2.8 (1.1) (n=40)</td>
<td>3.2 (1.2) (n=105)</td>
</tr>
<tr>
<td>DAS28 (CRP) remission, n (%)</td>
<td>22 (55.0) (n=40)</td>
<td>35 (33.3) (n=105)</td>
</tr>
<tr>
<td>EULAR response (ESR/CRP) good or moderate, n (%)</td>
<td>38 (90.5) (n=42)</td>
<td>75 (70.1) (n=107)</td>
</tr>
<tr>
<td>CDAI, mean (SD)</td>
<td>8.0 (7.7) (n=39)</td>
<td>11.9 (9.5) (n=94)</td>
</tr>
<tr>
<td>CDAI LDA/remission, n (%)</td>
<td>26 (66.7) (n=39)</td>
<td>49 (52.1) (n=94)</td>
</tr>
<tr>
<td>SDAI, mean (SD)</td>
<td>9.5 (8.6) (n=33)</td>
<td>12.9 (9.8) (n=86)</td>
</tr>
<tr>
<td>SDAI LDA/remission, n (%)</td>
<td>22 (66.7) (n=33)</td>
<td>41 (47.7) (n=86)</td>
</tr>
<tr>
<td>Patient Global Assessment (mm), mean (SD)</td>
<td>28.9 (22.4) (n=49)</td>
<td>35.3 (23.8) (n=116)</td>
</tr>
<tr>
<td>HAQ-DI, mean (SD)</td>
<td>0.6 (0.6) (n=32)</td>
<td>1.0 (0.7) (n=87)</td>
</tr>
<tr>
<td>Boolean remission criterion, n (%)</td>
<td>10 (25.0) (n=40)</td>
<td>9 (8.6) (n=105)</td>
</tr>
</tbody>
</table>

**Disclosure:** R. Alten, Bristol-Myers Squibb, 2; H. Lorenz, AbbVie, Bristol-Myers Squibb, Roche-Chugai, UCB, MSD, GSK, SOBI, Medac, Novartis, Janssen-Cilag, AstraZeneca, Pfizer, Actelion, 5; X. Mariette, Bristol-Myers Squibb, LFB, Pfizer, GSK, UCB, 9, Biogen, Pfizer, UCB, 2; H. Nübbelein, AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, UCB, 5; M. Galeazzi, None; F. Navarro, Pfizer, MSD, AbbVie, Bristol-Myers Squibb, Roche, 2, Pfizer, MSD, Roche, UCB, AbbVie, Bristol-Myers Squibb, 8, Pfizer, MSD, Roche, UCB, AbbVie, Bristol-Myers Squibb, Janssen, Lilly, 5; M. Chartier, Bristol-Myers Squibb, 3; J. Heitzmann, Bristol-Myers
Methotrexate Discontinuation from Combination Therapy with Adalimumab Is Not Associated with Inferior Outcomes at 6 Months

Dimitrios A. Pappas1, Chitra Karki1, Ying Shan1, Jessica L. Suboticki2, Jenny Griffith3 and Joel Kremer4, 1Corrona, LLC, Southborough, MA, 2AbbVie Inc., Mettawa, IL, 3AbbVie Inc., North Chicago, IL, 4Albany Medical College and The Center for Rheumatology, Albany, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Methotrexate is frequently administered in combination with biologics for the therapy of Rheumatoid Arthritis (RA) as it leads to superior outcomes compared to biologic monotherapy. However, combination therapy may not be tolerated or may be associated with lower adherence.

Objective: To determine whether discontinuation of MTX from the combination regimen with adalimumab (ADA) will lead to inferior outcomes compared to continuation of both medications.

Methods: RA patients enrolled in the Corrona Registry who initiated ADA in combination with MTX were included in the analysis. Patients who discontinued MTX (MTX-DC) after at least three months of combination therapy with ADA were compared with patients who continued combination therapy (MTX-C). Baseline characteristics of both groups were described. Patients in the two groups were matched (1:3) using Propensity Scores (PS) on time from initiation to time to MTX discontinuation in the MTX-DC group and for a similar time point in the MTX-C group. Disease activity based on clinical disease activity index (CDAI) and patient reported outcomes (patient pain, fatigue, morning stiffness and disability index measured by modified health assessment questionnaire) were compared 6 months after the discontinuation of MTX and an equivalent time in the combination group. Multivariate regression was used to evaluate the aforementioned outcomes adjusted for statistically significant variables after PS matching.

Results: 137 MTX-DC patients were matched with 411 MTX-C patients. MTX-DC patients were more frequently females (82.5% vs 73.2%) and had shorter disease duration (mean±SD: 6.15±7.0 vs 8.03±8.84) compared to the MTX-C group, p<0.05. Baseline disease activity, rates of RF positivity, prior biologic use and concurrent steroid use did not differ between the two groups. Adjusted disease activity improvement outcomes at 6 months did not differ in the two groups; rates of achievement of low disease activity (CDAI≤10) were 39.7% vs 41.6% (p=0.7), minimal clinically important difference (MCID) for CDAI1 was achieved by 58.6% vs 61.6% (p=0.8) in MTX-C vs MTX-DC respectively. Methotrexate discontinuation was not significantly associated with change in CDAI (Beta-Coefficient, β (95% CI): 0.29 (-1.7 – 2.3). Adjusted patient reported outcomes were similar at 6 months for both groups (Table).

Conclusion: Methotrexate discontinuation after at least 3 months of combined therapy with adalimumab was not associated with inferior disease activity and patient reported outcomes after 6 months of discontinuation of MTX.
Table: Association of MTX discontinuation and change in patient reported outcomes at 6 months post-discontinuation

<table>
<thead>
<tr>
<th>Adjected models*</th>
<th>ΔmHAQ</th>
<th>ΔPain (VAS 0-100)</th>
<th>ΔFatigue (VAS 0-100)</th>
<th>ΔMorning stiffness [minutes]</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTX-DC**</td>
<td>0.06 [-0.03,0.14]</td>
<td>2.05 [-4.00,8.11]</td>
<td>4.43 [-4.06,12.93]</td>
<td>22.40 [-28.08,72.89]</td>
</tr>
</tbody>
</table>

References:


Disclosure: D. A. Pappas, Corrona, LLC, 3,Novartis Pharmaceutical Corporation, 9; C. Karki, Corrona, LLC, 3; Y. Shan, Corrona, LLC, 3; J. L. Suboticki, AbbVie, 1,AbbVie, 3; J. Griffith, AbbVie, 1,AbbVie, 3; J. Kremer, Corrona, LLC, 1,Corrona, LLC, 3,AbbVie, Amgen, BMS, Genentech, Lilly, Regeneron, Sanofi, Pfizer, 5,AbbVie, Genentech, Lilly, Novartis, Pfizer, 2.

Abstract Number: 2454

Real-World Consistency of Response to Adalimumab over Time in Patients with Rheumatoid Arthritis: Results from the Corrona Registry

Dimitrios A. Pappas1,2, George W. Reed2,3, Chitra Karki4, Jenny Griffith5, Martha Skup5, Vishvas Garg5 and Joel Kremer2,6, 1Columbia University, New York, NY, 2Corrona LLC, Southborough, MA, 3UMass Medical School, Worcester, MA, 4Corrona, LLC, Southborough, MA, 5AbbVie Inc., North Chicago, IL, 6Albany Medical College and The Center for Rheumatology, Albany, NY

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Adalimumab (ADA) was approved in the US in 2002 for rheumatoid arthritis (RA), and subsequently approved for the management of other inflammatory diseases such as Crohn’s disease, ulcerative colitis, plaque psoriasis, psoriatic arthritis, and ankylosing spondylitis. Expanded use of ADA has resulted in changes to manufacturing processes and production scale, making it important to examine the clinical response to ADA over time. This study aimed to assess the response rate to ADA in patients with RA over the years since its US approval.

Methods: Biologic-naïve patients with moderate to severe RA (Clinical Disease Activity Index [CDAI]>10) who initiated ADA during follow-up in the Corrona registry (2003–16) and had a 6-month registry visit (3–9 month window) were included in the study. Six groups were defined based on year of ADA initiation: 2003–05, 2006–07, 2008–09, 2010–11, 2012–13, and 2014–16. Patient characteristics at time of initiation were summarized by group year. Outcomes included percentage of patients with low disease activity (LDA)/remission (CDAI≤10) and modified American College of Rheumatology (mACR)20/50/70 (which do not include acute phase reactants) at 6-month follow-up. Non-response was imputed for patients switching to another biologic prior to 6 months. Chi-square tests were done.
to examine differences in response rates by group. Response rates were also compared among groups adjusting for covariates that differed at time of initiation using logistic regression models.

**Results:** Of 23,169 biologic-naïve patients, 1949 initiated ADA, 1056 had baseline CDAI>10, and 820 who had a 6-month follow-up visit were included. In earlier year groups, patients were younger at time of disease onset (44.5 years in 2003−05, 47.1 years in 2006−07, 46.5 years in 2008−09, 51.6 years in 2010−11, 48.3 years in 2012−13 and 51.1 years in 2014−16; \(P=.0001\)), but had longer disease duration (10.8 years in 2003−05, 8.0 years in 2006−07, 5.9 years in 2008−09, 3.7 years in 2010−11, 4.8 years in 2012−13 and 4.6 years in 2014−16; \(P<.0001\)) compared with later year groups. At least 2/3 of patients remained on ADA at 6-month follow-up (range: 66% in 2014−16 to 77% in 2003−05). In each group, 43%−52% of patients achieved LDA/remission (Table). No significant differences in mACR20/50/70 rates were seen across groups.

**Conclusion:** No differences in clinical response rates (CDAI and modified ACR20/50/70) to ADA were noted over time among patients with RA in a real-world setting. The findings of this study indicate a consistent clinical response to ADA in RA patients since the market launch of the drug.

### Table. Outcomes at 6-Month Follow-up

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>LDA/remission</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n) (%)</td>
<td>43 (46.7)</td>
<td>48 (42.9)</td>
<td>54 (52.4)</td>
<td>76 (48.1)</td>
<td>136 (50.0)</td>
<td>40 (48.2)</td>
</tr>
<tr>
<td>95% CI</td>
<td>(36.3, 57.4)</td>
<td>(33.6, 52.6)</td>
<td>(42.4, 62.4)</td>
<td>(40.1, 56.2)</td>
<td>(43.9, 56.1)</td>
<td>(37.1, 59.4)</td>
</tr>
<tr>
<td>OR (95% CI)(a)</td>
<td>ref</td>
<td>0.9 (0.5, 1.6)</td>
<td>1.2 (0.7, 2.2)</td>
<td>1.1 (0.6, 1.8)</td>
<td>1.1 (0.7, 1.8)</td>
<td>1.0 (0.5, 1.9)</td>
</tr>
<tr>
<td>mACR20</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n) (%)</td>
<td>32 (34.8)</td>
<td>41 (36.6)</td>
<td>41 (39.8)</td>
<td>54 (34.2)</td>
<td>103 (37.9)</td>
<td>28 (33.7)</td>
</tr>
<tr>
<td>95% CI</td>
<td>(25.2, 45.4)</td>
<td>(27.7, 46.2)</td>
<td>(30.3, 49.9)</td>
<td>(26.8, 42.1)</td>
<td>(32.1, 43.9)</td>
<td>(23.7, 45.0)</td>
</tr>
<tr>
<td>OR (95% CI)(a)</td>
<td>ref</td>
<td>1.0 (0.6, 1.8)</td>
<td>1.2 (0.7, 2.2)</td>
<td>0.9 (0.5, 1.6)</td>
<td>1.1 (0.7, 1.8)</td>
<td>0.9 (0.5, 1.8)</td>
</tr>
<tr>
<td>mACR50</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n) (%)</td>
<td>23 (25.0)</td>
<td>29 (25.9)</td>
<td>25 (24.3)</td>
<td>27 (17.1)</td>
<td>61 (22.4)</td>
<td>15 (18.1)</td>
</tr>
<tr>
<td>95% CI</td>
<td>(16.6, 35.1)</td>
<td>(18.1, 35.0)</td>
<td>(16.4, 33.7)</td>
<td>(11.6, 23.9)</td>
<td>(17.6, 27.9)</td>
<td>(10.5, 28.1)</td>
</tr>
<tr>
<td>OR (95% CI)(a)</td>
<td>ref</td>
<td>1.0 (0.5, 1.9)</td>
<td>0.9 (0.5, 1.8)</td>
<td>0.6 (0.3, 1.2)</td>
<td>0.8 (0.5, 1.5)</td>
<td>0.7 (0.3, 1.4)</td>
</tr>
<tr>
<td>mACR70</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n) (%)</td>
<td>12 (13.0)</td>
<td>11 (9.8)</td>
<td>18 (17.5)</td>
<td>12 (7.6)</td>
<td>27 (9.9)</td>
<td>5 (6.0)</td>
</tr>
<tr>
<td>95% CI</td>
<td>(6.9, 21.7)</td>
<td>(5.0, 16.9)</td>
<td>(10.7, 26.2)</td>
<td>(4.0, 12.9)</td>
<td>(6.6, 14.1)</td>
<td>(2.0, 13.5)</td>
</tr>
<tr>
<td>OR (95% CI)(a)</td>
<td>ref</td>
<td>0.7 (0.3, 1.7)</td>
<td>1.4 (0.6, 3.1)</td>
<td>0.5 (0.2, 1.3)</td>
<td>0.7 (0.3, 1.5)</td>
<td>0.4 (0.1, 1.3)</td>
</tr>
</tbody>
</table>

\(a\)Adjusted for baseline Clinical Disease Activity Index, duration of rheumatoid arthritis, initiation of mono versus combin therapy, prednisone use at initiation, age and sex.

CI, confidence interval; LDA, low disease activity; mACR, modified American College of Rheumatology; OR, odds ratio.
Efficacy of Etanercept in Elderly Patients with Rheumatoid Arthritis

Christopher J. Edwards¹, Katherine Roshak², Jack F Bukowski³, Ronald Pedersen⁴, Mazhar Thakur⁵, Lisa Marshall² and Heather Jones², ¹University Hospital Southampton, Southampton, United Kingdom, ²Inflammation & Immunology Global Medical Affairs, Pfizer, Collegeville, PA, ³Clinical Affairs, Pfizer, Collegeville, PA, ⁴Department of Biostatistics, Pfizer, Collegeville, PA, ⁵Pfizer Ltd, Sandwich, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Ageing is associated with declining immune cell function and age-related comorbidities.¹,² In the US, the prevalence of rheumatoid arthritis (RA) is ~2% in individuals ≥65 y.³ As life expectancy increases, there is a growing clinical need for data on the efficacy and safety of commonly used treatments in elderly patients with RA. The aim of this study was to compare the efficacy of etanercept (ETN) in patients with RA aged <65 y vs those aged ≥65 y.

Methods: In a post-hoc study, efficacy data from the open-label period of 3 ETN (50 mg QW) studies in patients with RA (Treat-to-Target in Emerging Market RA Patient Populations study [T2T], NCT01578850; PRESERVE, NCT00565409; PRIZE, NCT00913458) were analyzed in 2 cohorts: <65 y and ≥65 y. Descriptive statistics of 28-joint Disease Activity Score-Erythrocyte Sedimentation Rate (DAS28-ESR) scores, Health Assessment Questionnaire Disability Index (HAQ-DI), and modified total Sharp Scores (mTSS) in observed cases were collated. Least squares means were calculated and \( P \)-values were from F-tests from an analysis of covariance models testing the age group effect with baseline as covariate.

Results: Mean baseline DAS28-ESR and HAQ-DI scores were marginally higher in patients ≥65 y vs <65 y (Table 1). Mean changes from baseline (Table 2) in DAS28-ESR scores showed no consistent trend, i.e., both higher and lower changes were observed at different times in patients ≥65 y vs <65 y. Mean HAQ-DI scores were higher in patients ≥65 y vs <65 y, and the mean changes from baseline were either similar or marginally smaller in patients ≥65 y vs <65 y. mTSS were also found to be higher in patients ≥65 y vs <65 y, whereas the mean changes from baseline showed only marginal differences for patients ≥65 y vs <65 y. The smaller number of patients in the ≥65 y cohort compared with the <65 y cohort was a study limitation.

Conclusion: There were no substantial differences in efficacy for ETN-treated patients ≥65 y vs <65 y.

Table 1. Baseline DAS-28 ESR and HAQ-DI scores

<table>
<thead>
<tr>
<th>Study</th>
<th>Mean score (95% CI)</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DAS28-ESR</td>
<td>HAQ-DI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;65 y</td>
<td>≥65 y</td>
<td>&lt;65 y</td>
<td>≥65 y</td>
<td></td>
</tr>
<tr>
<td>T2T</td>
<td>6.36 (6.27, 6.46)</td>
<td>6.57 (6.22, 6.92)</td>
<td>1.52 (1.46, 1.58)</td>
<td>1.59 (1.35, 1.83)</td>
<td>n=416</td>
</tr>
<tr>
<td>PRESERVE</td>
<td>4.37 (4.34, 4.40)</td>
<td>4.46 (4.34, 4.58)</td>
<td>1.13 (1.09, 1.17)</td>
<td>1.32 (1.14, 1.50)</td>
<td>n=773</td>
</tr>
<tr>
<td>PRIZE</td>
<td>5.98 (5.86, 6.11)</td>
<td>6.11 (5.75, 6.47)</td>
<td>1.27 (1.19, 1.35)</td>
<td>1.27 (1.06, 1.48)</td>
<td>n=261</td>
</tr>
</tbody>
</table>

Table 2. Efficacy of ETN in patients with RA aged <65 y vs ≥65 y

<table>
<thead>
<tr>
<th>Study</th>
<th>LS mean change from baseline (95% CI)</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DAS28-ESR</td>
<td>HAQ-DI</td>
<td>mTSS</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;65 y</td>
<td>≥65 y</td>
<td>&lt;65 y</td>
<td>≥65 y</td>
<td></td>
</tr>
<tr>
<td>T2T</td>
<td>-1.60 (-169, -1.50)</td>
<td>-1.71 (-2.04, -1.39)</td>
<td>-0.45 (-0.50, -0.41)</td>
<td>-0.34 (-0.50, -0.19)</td>
<td>n=430</td>
</tr>
<tr>
<td></td>
<td>-3.34 (-3.44, -3.24)</td>
<td>-3.15 (-3.48, -2.81)</td>
<td>-0.81 (-0.87, -0.76)</td>
<td>-0.71 (-0.89, -0.53)</td>
<td>n=412</td>
</tr>
<tr>
<td>PRESERVE</td>
<td>-1.81 (-1.88, -1.74)</td>
<td>-1.64 (-1.90, -1.38)</td>
<td>-0.54 (-0.57, -0.50)</td>
<td>-0.43 (-0.56, -0.29)</td>
<td>n=725</td>
</tr>
<tr>
<td></td>
<td>-2.02 (-2.17, -1.88)</td>
<td>-1.89 (-2.27, -1.52)</td>
<td>-0.55 (-0.61, -0.49)</td>
<td>-0.34 (-0.49, -0.18)</td>
<td>n=253</td>
</tr>
<tr>
<td></td>
<td>-3.22 (-3.39, -3.06)</td>
<td>-3.15 (-3.55, -2.75)</td>
<td>-0.79 (-0.86, -0.72)</td>
<td>-0.69 (-0.85, -0.52)</td>
<td>n=235</td>
</tr>
<tr>
<td>PRIZE</td>
<td>0.33 (0.15, 0.51)</td>
<td>0.56 (-0.17, 1.29)</td>
<td>0.35 (-0.12, 0.81)</td>
<td>0.27 (-0.78, 1.33)</td>
<td>n=167</td>
</tr>
</tbody>
</table>

*Week 36 data. †Week 52 data. Week 4 and 24/26/28 data are shown in this table for comparison at similar visits across the different studies. There were significant differences (P<0.05) between the <65 y vs ≥65 y cohorts at some visits: PRESERVE, Week 4, 8, and 12 for DAS28-ESR and Week 12 for HAQ-DI; PRIZE, Week 2, 4, 13, 39, and 52 for HAQ-DI.
Disease Flares Among Early Rheumatoid Arthritis Patients Treated with Continued Methotrexate Either Alone or in Combination with Adalimumab (Humira)

Arthur Kavanaugh¹, Ronald F van Vollenhoven², Prashanth Sunkureddi³, Ying Zhang⁴, Jessica L. Suboticki⁵ and Josef S. Smolen⁶, ¹Division of Rheumatology, Allergy, and Immunology, University of California San Diego, La Jolla, CA, ²Amsterdam Rheumatology and Immunology Center ARC, Amsterdam, Netherlands, ³University of Texas Medical Branch, Galveston, TX, ⁴AbbVie Inc., North Chicago, IL, ⁵AbbVie Inc., Mettawa, IL, ⁶Division of Rheumatology, Department of Medicine, Medical University of Vienna, and Hietzing Hospital, Vienna, Austria

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Some rheumatoid arthritis (RA) patients (pts) may experience flares in their disease even after reaching stable low disease activity (sLDA), but the consequences of even temporary elevations in disease activity are poorly understood. The purpose of this analysis was to explore the rates of flares after reaching sLDA in pts treated to target with either methotrexate (MTX) monotherapy or adalimumab combination therapy (ADA+MTX).

Methods: This post hoc analysis included pts from the randomized, double-blind, double-period OPTIMA¹ trial achieving sLDA [DAS28(CRP) <3.2 at weeks (wks) 22 and 26] at the end of period 1 (P1). In P1, pts were randomized to receive ADA+MTX or placebo (PBO)+MTX for 26 wks. Pts on ADA+MTX achieving sLDA were randomized to receive PBO+MTX (ADA Withdrawal) or continue on ADA+MTX (ADA Continuation) for an additional 52 wks in period 2 (P2). Pts who achieved sLDA on PBO+MTX in P1 continued their treatment in P2 (MTX Continuation). Pts achieving sLDA in each treatment group were categorized based on whether they experienced a flare [change in DAS28(CRP) ≥0.6 at consecutive visits and DAS28(CRP) ≥3.2]; the proportion of pts experiencing flares and time to flare were assessed. For each group, mean change from wk 26 to wk 78 in disease activity [DAS28(CRP)], functional (HAQ-DI) and structural (mTSS) measures were analyzed.

Results: In pts achieving sLDA at the end of P1, flare rates in P2 differed based on initial treatment assignment (ADA Continuation: 11.7% [11/94]; MTX Continuation: 22.4% [22/98]). Interestingly, flare rates in pts randomized to withdraw ADA in P2 (ADA Withdrawal: 25% [22/88]) were numerically similar to the MTX Continuation group. The mean time to flare was 193, 191, and 177 days in the ADA Withdrawal, ADA Continuation, and MTX Continuation groups, respectively.
groups, respectively. During P2, the mean DAS28(CRP) scores were predictably higher in pts who flared compared with those who did not across treatment groups. In pts experiencing flares in P2, disease activity and functional measures worsened from wk 26 to wk 78 as compared with pts without flares (Table). Of the individual DAS28(CRP) components, pt global assessment of disease activity (PtGA) showed the greatest worsening. There were small differences in radiographic progression between pts experiencing flares compared with pts without flares.

Conclusion: In early RA pts achieving sLDA, flares were generally infrequent; however, they were more prevalent in pts receiving PBO+MTX compared with ADA+MTX. Flares were numerically associated with higher disease activity, functional deterioration, and higher PtGA, underscoring its impact on health-related quality of life and the importance of preventing flares as a therapeutic outcome.

Reference:


<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Visit Mean at Week 26</th>
<th>Mean Change (Δ) from Week 26 to Week 78</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Flare</td>
<td>No Flare</td>
</tr>
<tr>
<td>DAS28(CRP)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADA Withdrawal</td>
<td>2.2</td>
<td>2.0</td>
</tr>
<tr>
<td>ADA Continuation</td>
<td>2.1</td>
<td>2.0</td>
</tr>
<tr>
<td>MTX Continuation</td>
<td>2.2</td>
<td>2.1</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADA Withdrawal</td>
<td>0.4</td>
<td>0.2</td>
</tr>
<tr>
<td>ADA Continuation</td>
<td>0.5</td>
<td>0.3</td>
</tr>
<tr>
<td>MTX Continuation</td>
<td>0.4</td>
<td>0.3</td>
</tr>
<tr>
<td>mTSS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADA Withdrawal</td>
<td>8.4</td>
<td>11.5</td>
</tr>
<tr>
<td>ADA Continuation</td>
<td>6.9</td>
<td>12.7</td>
</tr>
<tr>
<td>MTX Continuation</td>
<td>10.5</td>
<td>9.2</td>
</tr>
</tbody>
</table>

*Flare was defined as change in DAS28(CRP) ≥0.6 at consecutive visits and DAS28(CRP) ≥3.2.

LDA = low disease activity; DAS28(CRP) = 28-joint disease activity score based on C-reactive protein; ADA = adalimumab; MTX = methotrexate; HAQ-DI = health assessment questionnaire disability index; mTSS = modified total Sharp score.

Disclosure: A. Kavanaugh, AbbVie, Amgen, AstraZeneca, BMS, Celgene, Centocor-Janssen, Pfizer, Roche, and UCB, 9; AbbVie, Amgen, AstraZeneca, BMS, Celgene, Centocor-Janssen, Pfizer, Roche, and UCB, 9; R. F. van Vollenhoven, AbbVie, Amgen, Biotech, BMS, Celgene, Crescendo, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, UCB, and Vertex, 2; AbbVie, Amgen, Biotech, BMS, Celgene, Crescendo, GlaxoSmithKline, Janssen, Lilly, Novartis, Pfizer, Roche, UCB, and Vertex, 5; AbbVie, Amgen, Biotech, BMS, Celgene, Crescendo, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, UCB, and Vertex, 9; P. Sunkureddi, Novartis, BMS, UCB, Pfizer, AbbVie Inc., and Takeda, 5; Novartis, BMS, UCB, Pfizer, AbbVie Inc., and Takeda, 8; Y. Zhang, AbbVie, 3; AbbVie, 1; J. L. Suboticki, AbbVie, 1; AbbVie, 3; J. S. Smolen, bbVie, Amgen, AstraZeneca, BMS, Celgene, Centocor-Janssen, Glaxo, Lilly, Pfizer, MSD, Novo Nordisk, Roche, Sandoz, and UCB, 2; AbbVie, Amgen, AstraZeneca, BMS, Celgene, Centocor-Janssen, Glaxo, Lilly, Pfizer, MSD, Novo Nordisk, Roche, Sandoz, and UCB, 5.


Abstract Number: 2457

Sarilumab for the Treatment of Active, Moderate-to-Severe Rheumatoid Arthritis (RA): An Analysis of Cost per Effectively Treated Patient
Background/Purpose: The MONARCH study (NCT02332590) evaluated monotherapy with sarilumab 200 mg subcutaneous (SC) + placebo every 2 weeks (Q2W) versus adalimumab 40 mg SC + placebo Q2W in RA patients who were either intolerant of, inadequate responders to, or considered inappropriate candidates for continued treatment with methotrexate. The dose regimen could be changed to once weekly (qw) administration of adalimumab or matching placebo in the sarilumab group. This analysis examined 24-week per-patient drug costs (2017 US, wholesale acquisition) associated with effective treatment, based on outcomes from MONARCH.

Methods: The endpoint of effective treatment at 24 weeks was defined on three outcomes: ACR20, ACR50, and EULAR Moderate/Good (DAS28-ESR 0.6+ improvement). Cost per responder for each outcome was calculated in addition to incremental cost per effectively treated patient (difference in 24-week drug cost multiplied by the number needed to treat [NNT]) for sarilumab compared with adalimumab, with adalimumab costs based on the Q2W 40mg dose. One-way sensitivity analyses were conducted by varying the odds ratio of response rates for sarilumab on the three outcomes to the upper and lower bounds of their 95% confidence intervals, by increasing and decreasing sarilumab costs by 10%, and by varying the adalimumab cost based on a weighted average of patient proportions with dosing adjustments.

Results: The ITT population included 184 and 185 patients in the sarilumab and adalimumab arms, respectively. Estimated NNTs for sarilumab on ACR20, ACR50 and EULAR DAS28-ESR were 7.5, 6.3 and 7.5, respectively. Based on 24-week drug costs of $18,000 for sarilumab 200mg SC Q2W and $26,647 for adalimumab 40 mg SC Q2W, costs per responder for sarilumab versus adalimumab, respectively, were $25,105 versus $45,629 on ACR20; $39,387 versus $89,722 on ACR50; and $21,378 versus $37,584 on EULAR DAS28-ESR. Sarilumab was consistently the more effective and cost-saving treatment on all outcomes of incremental cost per effectively treated patient.

Conclusion: Sarilumab versus adalimumab was the economically dominant treatment with respect to incremental cost per effectively treated patient. Given the higher levels of responses on ACR20, ACR50 and 0.6 EULAR DAS25-ESR, coupled with the lower 24-week drug costs, sarilumab across all analyses was the favourable treatment in terms of cost per responder. These results were maintained within the sensitivity analyses.

Figure 1: Percentage of patients achieving response and number needed to treat (NNT)
Disclosure: M. Fournier, Sanofi, 1, Sanofi, 3; C. I. Chen, Regeneron Pharmaceuticals, 3, Regeneron Pharmaceuticals, 1; A. Kuznik, Regeneron Pharmaceuticals, Inc., 1, Regeneron Pharmaceuticals, Inc., 3; C. Proudfoot, Sanofi, 3, Sanofi, 1; U. Mallya, Sanofi, 1, Sanofi, 3; K. Michaud, Pfizer, 2.

Tocilizumab Inhibits Progression of Erosive Joint Damage in Early Rheumatoid Arthritis More Effectively Than Step-up Methotrexate Therapy

Xavier M Teitsma1, Johannes WG Jacobs1, Paco MJ Welsing2, Attila Pethö-Schramm3, Michelle EA Borm4, Jacob M. van Laar5, Floris PJ Lafeber5 and Johannes W.J. Bijlsma2, 1Department of Rheumatology & Clinical Immunology, University Medical Center Utrecht, Utrecht, Netherlands, 2Rheumatology and Clinical Immunology, University Medical Center Utrecht, Utrecht, Netherlands, 3F. Hoffmann-La Roche, Basel, Switzerland, 4Beneluxlaan 2a, Roche Nederland BV, Woerden, Netherlands, 5Rheumatology & Clinical Immunology, University Medical Center Utrecht, Utrecht, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: In early rheumatoid arthritis (RA), starting therapy as soon as possible is important to reduce disease activity and preserve the joints. With application of biological disease modifying anti-rheumatic drugs (DMARDs), a remarkable gain is achieved in prevention of joint damage. Although with initiation of methotrexate (MTX) as only DMARD many patients achieve the treatment target of clinical remission, a large proportion (~30%) of them still shows radiographic progression as a result of ongoing subclinical inflammation. The aim of this study was to analyze whether tocilizumab (TCZ) in DMARD-naïve patients with early RA would result in significantly less joint damage when compared to a step-up methotrexate-based strategy and whether this would involve erosions and/or joint space narrowing (JSN) scores.

Methods: In U-Act-Early, patients initiated TCZ plus MTX, TCZ, or MTX therapy and were treated to target until sustained remission (defined as disease activity score assessing 28 joints (DAS28) <2.6 with ≤4 swollen joints for ≥24 weeks) was achieved. If no remission, hydroxychloroquine was added. Hereafter, if the target still was not achieved, the initial strategy ended and the subsequent strategy started; patients randomized to the TCZ or MTX arm switched to TCZ+MTX therapy. Those who initially started with this combination therapy switched to the standard of care (e.g. MTX combined with a tumor necrosis factor inhibitor). If sustained remission was achieved, medication was tapered and stopped. The Sharp-van der Heijde score (SHS) was used to evaluate radiographic progression; erosion and joint space narrowing (JSN) scores were also assessed separately. Furthermore, a computerized method was used to confirm the findings in JSN in the hand as evaluated by the SHS. Non-parametric testing was used to evaluate between-group differences as damage scores were not normally distributed.

Results: In total, 317 DMARD-naïve patients with early RA were randomized; 106 to the TCZ+MTX arm, 103 to the TCZ arm, and 108 to the MTX arm (Table). For changes from baseline in SHS, significantly lower scores when
compared to the MTX arm were found in the TCZ+MTX arm after 52 weeks (p=0.02); after 104 weeks the difference compared with the MTX arm was significant for both TCZ strategies (TCZ+MTX, p=0.02; TCZ, p=0.04). For erosions, significant between-group differences were noted after 104 weeks in favor of the TCZ strategies (TCZ+MTX vs. MTX, p=0.02; TCZ vs MTX, p=0.02). However, for JSN, no significant differences were found between the strategies during follow-up (p≥0.20), which was in accordance with the findings of the computerized method (p≥0.09) and data from literature.

**Conclusion:** Initiation of a tocilizumab-based strategy in DMARD-naïve patients with early RA results in significantly less progression of erosive radiographic joint damage when compared to a step-up methotrexate-based strategy, improving long-term clinical outcome.

| Table |
| Mean (SD)/median (IQR) change from baseline in radiographic joint scores. |
|---|---|---|---|
| | Tocilizumab plus methotrexate (n=106) | Tocilizumab (n=103) | Methotrexate (n=108) | Comparative tests, P-value |
| **Sharp-vanderHeijde** | | | | |
| Week 52 | 0.50 (1.50) / 0.00 (0.00-0.00) | 0.79 (3.24) / 0.00 (0.00-0.00) | 0.96 (2.87) / 0.00 (0.00-0.00) | TCZ+MTX vs MTX; p=0.016 |
| | | | | TCZ vs MTX; p=NS |
| | | | | TCZ+MTX vs TCZ; p=NS |
| Week 104 | 1.18 (3.92) / 0.00 (0.00-1.00) | 1.45 (4.27) / 0.00 (0.00-2.00) | 1.53 (2.42) / 0.00 (0.00-2.56) | TCZ+MTX vs MTX; p=0.021 |
| | | | | TCZ vs MTX; p=0.038 |
| | | | | TCZ+MTX vs TCZ; p=NS |
| **Joint Space Narrowing** | | | | |
| Week 52 | 0.10 (0.47) / 0.00 (0.00-0.00) | 0.24 (1.19) / 0.00 (0.00-0.00) | 0.21 (0.73) / 0.00 (0.00-0.00) | TCZ+MTX vs TCZ vs MTX; p≥0.20 |
| Week 104 | 0.18 (0.72) / 0.00 (0.00-0.00) | 0.77 (2.41) / 0.00 (0.00-0.00) | 0.53 (1.58) / 0.00 (0.00-0.00) | TCZ+MTX vs TCZ vs MTX; p≥0.25 |
| **Erosion** | | | | |
| Week 52 | 0.40 (1.35) / 0.00 (0.00-0.00) | 0.57 (2.38) / 0.00 (0.00-0.00) | 0.79 (3.00) / 0.00 (0.00-1.00) | TCZ+MTX vs TCZ vs MTX; p≥0.20 |
| Week 104 | 0.41 (1.25) / 0.00 (0.00-0.00) | 0.67 (2.58) / 0.00 (0.00-0.00) | 1.01 (1.68) / 0.00 (0.00-1.00) | TCZ+MTX vs MTX; p=0.016 |
| | | | | TCZ vs MTX; p=0.023 |
| | | | | TCZ+MTX vs TCZ; p=NS |

Data not normally distributed. SD = standard deviation; IQR = interquartile range; TCZ = tocilizumab; MTX = methotrexate; NS = not significant. Between-group comparisons were analyzed using a two-sided stratified non-parametric Mann-Whitney (Van Elteren) test, controlling for the two randomization stratification factors; baseline DAS28 (i.e. DAS28 <5.1 or ≥5.1) and center.

**Disclosure:** X. M. Teitsma, None; J. W. Jacobs, None; P. M. Welsing, None; A. Pethö-Schramm, F Hoffmann-La Roche, 3; M. E. Borm, Roche Nederland BV, 3; J. M. van Laar, MSD, Pfizer, Eli Lilly, and BMS, 5; F. P. Lafeber, Roche Nederland BV, 2; J. W. J. Bijlsma, Roche, AbbVie, Bristol-Myers Squibb, Merck Sharp & Dohme, Pfizer, and UCB, 2.
Incidence of Disease Worsening in Inflammatory Arthritis Patients on Long-Term Infliximab (Remicade®) Therapy

A Marilise Marrache1, Allen J Lehman1, Brendan Osborne1, Eliototis Psaradellis2, Julie Vaillancourt2, Emmanouil Rampakakis2 and Francois Nantel1, 1Medical Affairs, Janssen Inc., Toronto, ON, Canada, 2JSS Medical Research, Montreal, QC, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: A recent randomized controlled study in a single country reported rates of disease worsening over a one-year follow-up period for innovator infliximab (IFX) and a comparator in various diseases including AS and RA. After a mean duration of treatment of 6.7 years of IFX, rates for disease worsening post-one year follow-up were 39.5% in AS and 36.7% in RA1. Other such data reporting disease worsening rates are rare. Using data from a longitudinal database, the objective was to determine the incidence of disease worsening in AS and RA patients on long-term therapy with IFX. PsA patients were not included in this study due to low numbers (n=49).

Methods: BioTRAC is an ongoing, prospective registry of inflammatory arthritis patients initiating treatment with infliximab, golimumab or ustekinumab that has been ongoing since 2002 in Canada. We included AS and RA patients who had been on IFX therapy for at least two, four or six years. Disease worsening endpoint was defined as follows1: for AS patients; an increase in ASDAS ≥ 1.1 from baseline and a minimum score of 2.1. For RA patients; an increase in DAS28 ≥ 1.2 from baseline and a minimum score of 3.2.

Results: This analysis included a total of 196 AS and 425 RA patients. Among AS patients, 36.1% were female, 90.8% were bionaïve at IFX initiation and 50% were on concomitant NSAID(s) at the 2-year index. The mean (SD) ASDAS score was 2.17 (1.05). As for the RA patients, 75% were female, 88.5% were bio-naïve, and 93% were on concomitant DMARD(s) while 35% were on corticosteroids at the 2-year index. The mean (SD) DAS28 ESR and DAS 28 CRP were 3.37 (1.40) and 3.00 (1.24), respectively. As shown in table 1, the incidence of disease worsening in AS and RA patients on stable IFX for 2-6 years was low and varied from 2.7% to 11.5% at the subsequent 12 and 24 months visit.

Conclusion: In this prospective longitudinal cohort, patients on long-term IFX therapy show low rates of disease worsening of 2.7% to 11.5% at 1 and 2 years in AS and RA. Additional studies may elucidate the true rate of and reasons for disease worsening in rheumatologic populations.

Table 1. Incidence of disease worsening in AS and RA patients at the 2, 4, and 6-year index
<table>
<thead>
<tr>
<th>Disease</th>
<th>Outcome</th>
<th>Index date post IFX initiation</th>
<th>Disease worsening at subsequent visits</th>
<th>n/N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>12 months</td>
</tr>
<tr>
<td>AS</td>
<td>ASDAS</td>
<td>2 years</td>
<td></td>
<td>9/79 (11.4%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 years</td>
<td></td>
<td>2/42 (4.8%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6 years</td>
<td></td>
<td>1/25 (4.0%)</td>
</tr>
<tr>
<td>RA</td>
<td>DAS28 ESR</td>
<td>2 years</td>
<td></td>
<td>20/184 (10.9%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 years</td>
<td></td>
<td>9/121 (7.4%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6 years</td>
<td></td>
<td>8/73 (11.0%)</td>
</tr>
<tr>
<td></td>
<td>DAS28 CRP</td>
<td>2 years</td>
<td></td>
<td>16/160 (10.0%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 years</td>
<td></td>
<td>8/115 (7.0 %)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6 years</td>
<td></td>
<td>6/80 (7.5%)</td>
</tr>
</tbody>
</table>


Abstract Number: 2460

Patient-Reported Outcomes Following Discontinuation of Methotrexate in Patients with Rheumatoid Arthritis Treated with Subcutaneous Tocilizumab: Results from a Randomized Controlled Trial

Joel Kremer¹, William F C Rigby², Nora Singer³, Christine Birchwood⁴, Darcy Gill⁴, William Reiss⁴, Jennie Best⁴, Jinglan Pei⁴ and Margaret Michalska⁴, ¹Albany Medical College, Albany, NY, ²Geisel School of Medicine at Dartmouth, Lebanon, NH, ³Case Western Reserve University School of Medicine, Cleveland, OH, ⁴Genentech, Inc., South San Francisco, CA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Patients with rheumatoid arthritis (RA) often receive methotrexate (MTX) in combination with biologics; however, MTX may be discontinued due to intolerance or to reduce the medication burden once disease control is achieved. Whereas previous studies have established the efficacy of tocilizumab (TCZ) initiated as monotherapy (MONO) for the treatment of RA,¹² patient-reported outcomes (PROs) after MTX withdrawal in patients
achieving good clinical response to TCZ + MTX have not been evaluated. PROs are important measures when determining response to therapy in patients with RA with respect to health-related quality of life (HRQOL). This study evaluated PROs between patients with RA who achieved low disease activity with TCZ + MTX and then continued or discontinued MTX in the COMP-ACT trial (NCT01855789).

**Methods:** US patients with RA who were inadequate responders to MTX were enrolled; initial combination therapy included MTX (≥ 15 mg/week orally) plus TCZ 162 mg subcutaneous either weekly (qw) or every 2 weeks (q2w). Patients who achieved DAS28-ESR ≤ 3.2 at Week 24 were randomized 1:1 to receive TCZ-MONO or continue TCZ + MTX until week 52 (double-blind). Changes in PRO scores were measured between Week 24 and Weeks 40 and 52, and included patient global assessment of disease activity (PtGA; visual analog score [VAS], 0-100 mm), pain (VAS), Health Assessment Questionnaire Disability Index (HAQ-DI, 0-3) and Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue.

**Results:** Of the 296 randomized patients (TCZ + MTX, n = 148; TCZ-MONO, n = 148), 74.8% were women, mean age was 55.5 years, mean RA duration was 6.8 years and mean DAS28-ESR was 6.3 at baseline. At Week 24 (randomization), PRO scores were similar between the randomized treatment groups. The mean changes in PtGA, pain, HAQ-DI and FACIT-fatigue scores from Week 24 to Weeks 40 were similar between the TCZ + MTX and TCZ-MONO groups (Table). The proportion of patients with HAQ-DI < 0.5 was similar between the groups at Week 24 (randomization), and remained similar at Weeks 40 and 52.

**Conclusion:** Patients receiving TCZ who discontinue MTX appear to have similar PROs across multiple measures compared with patients continuing TCZ + MTX. Differences observed in clinical parameters between TCZ-MONO and TCZ + MTX did not appear to achieve a threshold that would be considered clinically meaningful. Similarities in PROs on both treatments were consistent with the clinical efficacy measures previously reported from COMP-ACT.

**References:**

<table>
<thead>
<tr>
<th>PRO Measure*</th>
<th>TCZ + MTX n = 147</th>
<th>TCZ-MONO n = 147</th>
<th>Difference (95% CI) (TCZ-MONO minus TCZ + MTX)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Δ PtGA, mean (SEM)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 24 to week 40</td>
<td>1.72 (1.79)</td>
<td>5.95 (1.75)</td>
<td>4.78 (-0.00, 9.56)</td>
</tr>
<tr>
<td>Week 24 to week 52</td>
<td>-0.33 (1.77)</td>
<td>3.58 (1.83)</td>
<td>4.14 (-0.56, 8.84)</td>
</tr>
<tr>
<td>Δ Pain, mean (SEM)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 24 to week 40</td>
<td>1.64 (1.74)</td>
<td>5.32 (1.61)</td>
<td>4.19 (-0.23, 8.61)</td>
</tr>
<tr>
<td>Week 24 to week 52</td>
<td>-0.05 (1.84)</td>
<td>4.26 (1.68)</td>
<td>4.69 (0.14, 9.24)</td>
</tr>
<tr>
<td>Δ HAQ-DI, mean (SEM)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 24 to week 40</td>
<td>0.01 (0.030)</td>
<td>0.04 (0.034)</td>
<td>0.03 (-0.05, 0.12)</td>
</tr>
<tr>
<td>Week 24 to week 52</td>
<td>0.01 (0.028)</td>
<td>0.02 (0.038)</td>
<td>0.01 (-0.08, 0.10)</td>
</tr>
<tr>
<td>Δ FACIT-Fatigue, mean (SEM)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 24 to week 40</td>
<td>1.57 (0.67)</td>
<td>-0.68 (0.64)</td>
<td>-1.68 (-3.39, 0.02)</td>
</tr>
<tr>
<td>Week 24 to week 52</td>
<td>1.30 (0.67)</td>
<td>-1.12 (0.75)</td>
<td>-1.82 (-3.69, 0.06)</td>
</tr>
<tr>
<td>HAQ-DI &lt; 0.5, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 24</td>
<td>64 (43.5)</td>
<td>56 (38.1)</td>
<td>-5.4 (-16.7, 5.8)</td>
</tr>
<tr>
<td>Week 40</td>
<td>60 (43.8)</td>
<td>54 (40.6)</td>
<td>-3.2 (-15.0, 8.6)</td>
</tr>
<tr>
<td>Week 52</td>
<td>60 (46.9)</td>
<td>53 (41.7)</td>
<td>-5.1 (-17.3, 7.0)</td>
</tr>
</tbody>
</table>

FACIT, Functional Assessment of Chronic Illness Therapy; HAQ-DI, Health Assessment Questionnaire Disability Index; PtGA, patient global assessment.

* A negative change in score represents an improvement in the respective PRO except for Fatigue.

† Estimated means from ANCOVA model includes Week 24 value as a covariate, treatment group, and the randomization stratification factors: DAS28 remission status at Week 24 (< 2.6, ≥ 2.6 to ≤ 3.2), baseline weight-by-dosing group (< 80 kg q2w, < 80 kg qw, 80 to < 100 kg q2w, 80 to < 100 kg qw, ≥ 100 kg qw), patient anti-TNF exposure (Yes or No).

Disclosure: J. Kremer, Corrona, LLC, 1,Corrona, LLC, 3,AbbVie, Amgen, BMS, Genentech, Lilly, Regeneron, Sanofi, Pfizer, 5,AbbVie, Genentech, Lilly, Novartis, Pfizer, 2; W. F. C. Rigby, Roche, 5; N. Singer, Merck, EMD Serono, 2,Pfizer Inc, 5; C. Birchwood, Genentech, Inc., 3; D. Gill, Genentech, Inc., 3; W. Reiss, Genentech, Inc., 3; J. Best, Genentech, Inc, 3; J. Pei, Genentech, Inc., 3; M. Michalska, Genentech, Inc, 3.


Abstract Number: 2461
Rituximab Is Effective in the Treatment of Rheumatoid Arthritis Irrespective of Body Mass Index; Up to 48 Weeks Results from Phase 3 Study

Dae-Hyun Yoo¹, Won Park², Chang-Hee Suh³, Seung-Cheol Shim⁴, Sang-Joon Lee⁵, Yun Ju Bae⁵, Chan Park⁵ and Noo Ri Han⁵, ¹Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), ²Medicine/Rheumatology, Inha University Hospital, Incheon, Korea, Republic of (South), ³Ajou University School of Medicine, Suwon, Korea, Republic of (South), ⁴Department of Internal Medicine, Chungnam National University Hospital, Daejeon, Korea, Republic of (South), ⁵CELLTRION, Inc., Incheon, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: High body mass index (BMI) is known to be associated with inadequate clinical response to anti-TNF agents in RA patients.¹ However, there are limited data on how high BMI affects the response to rituximab in RA patients with an inadequate response or intolerance to anti-TNF agents. The objective is to investigate the impact of BMI on clinical response in the post-hoc analysis of Phase 3 randomized controlled trial comparing CT-P10 and reference rituximab, RTX² (NCT02149121).

Methods: A total of 332 patients who received 2 cycles of either CT-P10 or RTX at weeks 0 and 24 were included in this analysis. Patients were classified into 3 groups; normal weight (<25kg/m²), overweight (25 kg/m²~30 kg/m²) and obesity (>=30 kg/m²) as per WHO BMI category. Improvement in disease activity by the DAS28-CRP, remission (<=2.6), low disease activity rate (LDA, <=3.2), ACR response at Week 24 and Week 48 and duration of sustained LDA (from the first LDA observed to the last LDA observed up to Week 48) were analysed by BMI categories in the each and combined group of CT-P10 and RTX.

Results: In the pooled group of CT-P10 and RTX, the mean weights were 59kg in normal weight, 73kg in overweight and 91kg in obesity subgroups. All other baseline characteristics were comparable among BMI groups including baseline disease activity based on DAS28; Moderate, 22.3% vs. 22.8% vs. 25.7%, respectively; High, 77.7% vs. 77.2% vs. 74.3%, respectively. Mean change of DAS28 from baseline (Figure 1), ACR response rate (Figure 2) and rate of remission and LDA for DAS28 (Figure 3) were comparable among BMI groups and there were no statistical significant difference (p>0.05). No association was shown between DAS28 improvement and BMI (p>0.05). Mean duration of sustained LDA (months) for DAS28 were also comparable among the groups (5.1 vs. 5.2 vs. 5.6, respectively). Additionally, similar trends in all analyses were observed in each treatment group; CT-P10 and RTX.

Conclusion: The impact of BMI on the clinical response to rituximab treatment was not significant in RA patients. Therefore, these results support that rituximab could be a reasonable therapeutic option for obese RA patients with inadequate response to anti-TNF agents.

References
Figure 1. DAS28 Improvement

Figure 2. ACR response rate
Tapering TNF Inhibitors in Rheumatoid Arthritis: A Retrospective Study

Ayse Hacioglu¹, Gulen Hatemi², Sinem Nihal Esatoglu², Yesim Ozguler², Serdal Ugurlu¹, Emire Seyahi², Melike Melikoglu², Izzet Fresko², Huri Ozdogan², Sebahattin Yurdakul² and Vedat Hamuryudan², ¹Rheumatology, Istanbul University, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey, ²Istanbul University, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Current guidelines on RA treatment recommend tapering of biologic DMARDs for patients in persistent remission.

Methods:
In this retrospective study we used the hospital administrative database to identify patients with a diagnosis of RA and a first time prescription of a biologic DMARD that was specifically limited to one of the 3 TNF inhibitors (etanercept, adalimumab, infliximab) between January 2012 and the end of December 2013. Patient demographics and information on treatment and outcome were retrieved from the medical charts.

**Results:**

Of the 125 patients identified at the database search, 104 were registered in our clinic and had available follow-up until June 2016. Seventy-nine (76%) were women and 25 (24%) were men. Their mean age was 47.7±13 SD years and their mean disease duration was 7.4±6.9 SD years. The distribution of the prescribed TNF inhibitors was: Etanercept = 60%, Adalimumab = 23% and Infliximab = 17%. After a mean duration of 14.0±7.6 SD months tapering of TNF inhibitors was made in 44 patients (42%). This was in the form of spacing in 39 patients (Etanercept = 16, Infliximab = 14, Adalimumab = 9) and dose reduction in 5 (all Etanercept). All of these were due to good clinical response except for 1 patient’s own request because of fear from possible adverse effects. Increased disease activity after tapering was seen in 16 patients (36%) mandating restoration of original dose schedule within a mean of 8.8±9.7 SD months with good response in all. On the other hand 28 patients (64%) preserved their good clinical response during a mean follow-up of 46.1±6.3 SD months which enabled further tapering in 20 of them. There was also reductions in the mean number of synthetic DMARD’s (1.4±0.8 SD at the initiation of TNF inhibitors and 0.7±0.8 SD at the end of follow-up) and in the percentage of patients using steroids (78% vs 33%). At the end of the follow-up, among the whole group of 104 patients, only 73 (70%) were using biologics (TNF inhibitors = 49, non-TNF biologics = 24). The reasons for stopping biologics in the remaining 31 patients were ongoing remission (16 patients; 15%), pregnancy (1 patient), non-compliance (4 patients), injection site reactions (3 patients), fear from adverse events (1 patient), decision for complementary medicine (1 patient) and other issues such as losing insurance and family issues (5 patients).

**Conclusion:**

Tapering of TNF inhibitors was possible in 40% of RA patients during follow-up. One third of the patients flared after tapering whereas the remaining two thirds maintained their good outcome allowing cessation in 15%. Further studies are needed to identify factors predicting successful tapering.

**Disclosure:**

A. Hacioglu, None; G. Hatemi, None; S. N. Esatoglu, None; Y. Ozguler, None; S. Ugurlu, None; E. Seyahi, None; M. Melikoglu, None; I. Fresko, None; H. Ozdogan, None; S. Yurdakul, None; V. Hamuryudan, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/tapering-tnf-inhibitors-in-rheumatoid-arthritis-a-retrospective-study](http://acrabstracts.org/abstract/tapering-tnf-inhibitors-in-rheumatoid-arthritis-a-retrospective-study)

Abstract Number: 2463

**Golimumab in Biologic-NaïVe Patients with Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA) or Ankylosing Spondylitis (AS) – Subanalysis from a Non-Interventional Evaluation in Germany**

Klaus Krüger1, Gerd R. Burmester2, Siegfried Wassenberg3, Martin Bohl-Buehler4 and Matthias H. Thomas5,

1Praxiszentrum St. Bonifatius München, München, Germany, 2Rheumatology and Clinical Immunology, Charité - University Medicine Berlin, Free University and Humboldt University Berlin, Berlin, Germany, 3Rheumazentrum Ratingen, Ratingen, Germany, 4Friedrich-Ebert-Str. 35, Rheumahaus, Potsdam, Germany, 5Medical Affairs, MSD Sharp & Dohme GmbH, Bünde, Germany

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Golimumab (GLM) has demonstrated efficacy and safety in several randomized clinical trials with biologic-naïve patients (pts.).

However, more data regarding the effectiveness and patient-reported outcomes (PROs) parameters in daily clinical practice in Germany are required and helpful.

The aim of this subanalysis is to assess Golimumab on the effectiveness and PROs in biologic-naïve pts. with established RA, PsA or AS.

Methods:

Subanalysis of the non-interventional, prospective, 24-month study GO-NICE with biologic-naïve pts. with established RA, PsA or AS starting with GLM 50mg SC once monthly in a real life setting in Germany. Endpoint measures: disease activity DAS28, PsARC and BASDAI. PROs included QoL (EQ-5D-3L), functionality (FFbH), and fatigue (FACIT-F).

Safety data were also collected.

Results:

RA-pts. (n=265): Mean age 54.5 yr, 82.1% of the pts. were female, 77.3% (n=204) were rheumatoid factor (RF) positive, and 76.4% (n=201) had anti ccp-antibodies at BL. The DAS28 score at BL was 5.0 and dropped significantly to 2.9 within 24 months (p<0.0001 v. BL). After 3 months of treatment, 45.2% of pts. had LDA (DAS28 ≤3.2). The amount of pts. increased to 50.8% after 6 month and 64.9% after 24 months.

PsA-pts. (n=247): Mean age 49.7 yr, 53.8% of the pts. were female, 42.1% (n=104) had a nail involvement, 25.5% (n=63) dactylitis and 13.8% (n=34) enthesitis at BL. The proportion of pts. achieving a response (mod PsARC) was 64%, 72.2% and 77.7% at 3, 6 and 24 months, respectively.

AS-pts. (n=246): Mean age 41.9 yr, 70.7% of the pts. were male, 80.5% (n=198) were HLAB27 positiv. Most common extra-articular manifestations were: enthesitis (12.6%), iritis (12.2%), IBD (3.7%), and dactylitis (2.8%) at BL. The BASDAI at BL was 5.0 and dropped significantly to 2.0 within 24 months (p<0.0001 vs. BL). The proportion of pts. achieving a response (BASDAI 50) was 62.2%, 66.9% and 76.9% at 3, 6 and 24 months, respectively. An improvement of quality of life (QoL) by EQ-5D-3L was seen after 6 months and was maintained over 24 months. The pts.’ health state today (EQ VAS) improved from 52.3 at BL to 64.9 (RA), from 49.0 to 66.3 (PsA) and from 49.2 to 70.6 (AS). The functional ability (FFbH) improved significantly (p<0.0001 vs. BL) from 73.1 to 80.4 points (RA), from 73.0 to 82.2 (PsA), and from 72.8 to 81.2 (AS). The mean Fatigue score (FACIT-F) increased from BL to visit 9 (month 24) 33.3 to 39.5 points (RA), from 31.6 to 38.4 points (PsA), and from 31.6 to 40.2 points (AS) (each p<0.001 vs BL). No new safety signals were detected.

Conclusion:

Across the three rheumatic diseases (RA, PsA, AS) in biologic-naïve pts. GLM SC once monthly showed remarkable improvements in clinical effectiveness, patient-reported quality of life, functionality, and fatigue parameters within 3 months.

These effects were maintained over 24 months: 64.9% of RA-pts. achieved LDA status, 77.7% of PsA-pts. a positive PsARC response and 76.9% of AS-pts. BASDAI 50. No new safety signals were detected.

Disclosure: K. Krüger, AbbVie, BMS, Celgene, Janssen Biologics, MSD, Pfizer, Roche, Sanofi-Aventis, 5; G. R. Burmester, AbbVie, BMS, MSD, Pfizer, Roche, and UCB, 5; S. Wassenberg, AbbVie, Chugai, Janssen Biologics, MSD, Novartis, Pfizer, Roche, and UCB, 5; M. Bohl-Buehler, AbbVie, Hexal, MSD, Roche, and UCB, 5; M. H. Thomas, MSD Sharp Dohme GmbH Germany, 3.
Similar Effectiveness of Both Formulations of Tocilizumab (TCZ) in Patients with Rheumatoid Arthritis (RA) Switching from Intravenous (IV) to Subcutaneous (SC) at 6 Months in Real Life

Jean Darloy1, René-Marc Flipo1, Nicolas Segaud2, Jean-Paul Eschard3, Vincent Goeb4, Jean-Hugues Salmon3, Eric Houvenagel5, Clément Chopin5, Samuel Gally6, David Pau7, Isabelle Idier8 and Guy Baudens9, 1Rheumatology, Rheumatology Department CHU Teaching Hospital Lille, Lille, France, 2Internal medicine, Internal Medicine Departement Armentières Hospital, Armentières, France, 3Rheumatology, Rheumatology Department CHU Teaching Hospital Reims, Reims, France, 4Rheumatologie, Rheumatology Department CHU Teaching Hospital Amiens, Amiens, France, 5Rheumatology, Groupe Hospitalier de l'Institut Catholique de Lille, Lomme, France, 6Clinical Operations, Roche SAS, Boulogne Billancourt, France, 7Statistics, Roche SAS, Boulogne Billancourt, France, 8Medical department, Chugai Pharma France, Paris La Defense, France, 9Rheumatology, Rheumatology Department CHR Valenciennes, Valenciennes, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
It has been proven, in a pivotal RCT, that SC TCZ was non-inferior to IV TCZ [1]. However, the effectiveness of the SC TCZ formulation has not been evaluated in “real life”.

The objective was to describe the effectiveness and the characteristics of RA patients switching from IV to SC TCZ formulation in current practice.

Methods:
We analysed all the RA patients of the shared medical file “RIC Nord de France” with at least 1 DAS 3 months before inclusion, treated with TCZ, switching or not from IV to SC TCZ, between April 30th 2015 and January 15th 2016. The primary efficacy endpoint was the proportion of patients remaining in their DAS28-ESR category remission/LDA or moving to an inferior DAS28-ESR category at 24 weeks (W24). DAS28-ESR was calculated at inclusion and at W24 for switch patients (IV-SC) and for non-switch patients (IV-IV). Permanent discontinuation of TCZ before W24 was considered as failure.

Results:
From the 263 patients included, 30% switched from IV to SC TCZ.

At baseline, there were 77.6% females, mean BMI was 27.46±6.40, and mean RA duration was 15.11±9.38 years in the whole population. Mean IV TCZ duration before inclusion was 35.2±24.3 months in switch and 24.7±22.1 months in
non-switch patients. 51.1% of the switch patients were treated in monotherapy, 49.1% in the non-switch group. Mean DAS28-ESR were 2.23±1.16 in the switch and 3.07±1.70 in the non-switch patients. 79.3% of the switch patients were in DAS28-ESR category remission or LDA, and 20.7% in MDA. 53.8% of the non-switch patients were in DAS28-ESR category remission or LDA, 33.3% in MDA, and 12.9% in HDA.

At W24, 73.9% (CI 95% = [63.4% - 82.7%]) of the switch patients, and 72% (CI 95% = [64.4% - 78.8%]) of the non-switch patients stayed in DAS28-ESR category remission/LDA or move to an inferior DAS28-ESR category (Table).

Table: DAS28-ESR at W24

<table>
<thead>
<tr>
<th></th>
<th>Switch N=92</th>
<th>No switch N=171</th>
<th>All N=263</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary criterion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>patients moving to a fewer DAS28 category (or staying in the category LDA/remission) with imputation *</td>
<td>N=249</td>
<td>N=468</td>
<td>N=717</td>
</tr>
<tr>
<td>No</td>
<td>88</td>
<td>161</td>
<td>249</td>
</tr>
<tr>
<td>Missing</td>
<td>4</td>
<td>10</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>23 (26.1%)</td>
<td>45 (28.0%)</td>
<td>68 (27.3%)</td>
</tr>
<tr>
<td></td>
<td>[17.3% - 36.6%]</td>
<td>[21.2% - 35.6%]</td>
<td>[21.9% - 33.3%]</td>
</tr>
<tr>
<td>Yes</td>
<td>65 (73.9%)</td>
<td>116 (72.0%)</td>
<td>181 (72.7%)</td>
</tr>
<tr>
<td></td>
<td>[63.4% - 82.7%]</td>
<td>[64.4% - 83.8%]</td>
<td>[66.7% - 85.1%]</td>
</tr>
</tbody>
</table>

*Permanent discontinuation of treatment was considered as failure

Conclusion:

In that “real life” population, the proportion of RA patients treated with TCZ in remission or LDA remains similar at W24 for switch patients (IV-SC) and for non-switch patients (IV-IV). Proportions of patients moving to an inferior DAS category were also comparable in both groups. Switch patients appear to have less active disease at baseline. Factors associated to switch will be investigated.

Reference:


Disclosure: J. Darloy, None; R. M. Flipo, Roche SAS, 5,Chugai Pharma France, 5; N. Segaud, None; J. P. Eschard, None; V. Goeb, Roche SAS, 5,Chugai Pharma France, 5; J. H. Salmon, None; E. Houvenagel, Roche SAS, 5; C. Chopin, None; S. Gally, Roche SAS, 3; D. Pau, Roche SAS, 3; I. Idier, Chugai Pharma France, 3; G. Baudens, Roche SAS, 5,Chugai Pharma France, 5.


Abstract Number: 2465

Association between Methotrexate Use and Effects of Treatment with a Second Biologic Agent in Rheumatoid Arthritis: A Multiple Imputation Approach

Yoshikazu Ogawa1, Nobunori Takahashi2, Naoki Ishiguro2 and Toshihisa Kojima2, 1Sakashita Hospital, Nakatsugawa, Japan, 2Orthopaedic Surgery, Nagoya University Graduate School of Medicine, Nagoya, Japan

First publication: September 18, 2017
Background/Purpose: Methotrexate (MTX) is recommended and widely prescribed as the first-line, evidence-based therapy for rheumatoid arthritis (RA) patients. Previous studies have demonstrated a significant effect of MTX on biologic therapy; however, these were mainly conducted on bio-naïve patients. The aim of the present study was to evaluate the association of the concomitant use of MTX with efficacy of biologics in RA patients who switched to second-line biologics in a real-world clinical practice setting.

Methods: This study included patients enrolled in the Tsurumai Biologic Communication Registry. RA first-time switchers were eligible for inclusion. To assess the working hypothesis that combination therapy is superior to biologic monotherapy, the primary outcome measure was defined as a change in DAS28-ESR at 24 weeks. Multiple linear regression analysis adjusted for covariates was employed. Additionally, multiple imputation analysis was performed to provide missing data. Excluding individuals with missing data, known as glistwise deletion, may yield biased estimates. All analyses were conducted in EZR version 1.35 and the package mice for the multiple imputation.

Results: Using linear multivariate regression models, we identified a significant association of the use of MTX with the treatment efficacy of second-line biologics (Table 1). This association did not differ between patients using TNF inhibitors and those using non-TNF inhibitors (Table 2). In the present study, the results from the multiple imputation analysis were consistent with those from the complete case analysis (Table 3).

Conclusion: In our multicenter study using a multiple imputation method, concomitant MTX was found to be associated with an improved second-line biologic therapy in a non-trial, real-world clinical practice setting.

Table 1 Complete-case analysis (n = 255)

<table>
<thead>
<tr>
<th></th>
<th>B coefficient (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTX use</td>
<td>0.49 (0.12, 0.87)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>PSL use</td>
<td>0.052 (-0.40, 0.30)</td>
<td>0.77</td>
</tr>
<tr>
<td>Age</td>
<td>-0.013 (-0.02, 0)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Female</td>
<td>-0.54 (-1.0, -0.09)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>DAS28ESR prior to switching</td>
<td>0.64 (0.53, 0.76)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>non-TNF as first bio</td>
<td>-0.054 (0.73, 0.62)</td>
<td>0.87</td>
</tr>
<tr>
<td>non-TNF as second bio</td>
<td>0.41 (0.01, 0.81)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Stage III, V (non-TNF as reference)</td>
<td>-0.003 (0.02, 0.01)</td>
<td>0.71</td>
</tr>
</tbody>
</table>

MTX: methotrexate, PSL: prednisolone, TNF: Tumor Necrosis Factor inhibitor

Table 2 TNF versus non-TNF

<table>
<thead>
<tr>
<th></th>
<th>TNF (n = 127) (95% CI)</th>
<th>non-TNF (n = 120) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTX use</td>
<td>0.47 (0.08, 1.0)</td>
<td>0.44 (-0.082, 0.96)</td>
</tr>
<tr>
<td>PSL use</td>
<td>0.1 (-0.35, 0.55)</td>
<td>-0.26 (-0.83, 0.30)</td>
</tr>
<tr>
<td>Age</td>
<td>-0.01 (-0.027, 0.010)</td>
<td>-0.014 (-0.033, -0.0004)</td>
</tr>
<tr>
<td>Female</td>
<td>-0.5 (-1.1, 0.10)</td>
<td>-0.5 (-1.2, 0.086)</td>
</tr>
<tr>
<td>DAS28ESR</td>
<td>0.64 (0.48, 0.79)</td>
<td>0.65 (0.40, 0.84)</td>
</tr>
<tr>
<td>non-TNF as first bio</td>
<td>0.065 (1.0, 0.83)</td>
<td>-0.19 (-1.2, 0.83)</td>
</tr>
<tr>
<td>Stage III, V</td>
<td>0.011 (0.0093, 0.033)</td>
<td>-0.018 (-0.043, 0.0061)</td>
</tr>
</tbody>
</table>

MTX: methotrexate, PSL: prednisolone, TNF: Tumor Necrosis Factor inhibitor
Radiographic Progression By Disease Activity States in Patients with Rheumatoid Arthritis Treated with SB2 or Reference Infliximab

Josef S. Smolen1, Jung-Yoon Choe2, Edward C. Keystone3, Young Hee Rho4, Younju Lee4 and Sora Lee4,
1Medical University Vienna, Division of Rheumatology, Department of Internal Medicine III, Vienna, Austria, 2Department of Internal Medicine, Catholic university of Daegu School of Medicine, Daegu, Korea, Republic of (South), 3Mt. Sinai Hospital, University of Toronto, Toronto, ON, Canada, 4Samsung Bioepis Co., Ltd., Incheon, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Based on the totality of evidence, SB2 has shown to be similar with reference infliximab (INF) and has been approved as a biosimilar by the European Medical Agency and U.S. Food and Drug Administration. It is, however, hitherto unknown, if SB2 also shares similar structural efficacy in the different disease activity states when compared with INF. The objective of this study is to evaluate the disease activity by simplified disease activity index (SDAI) and clinical disease activity index (CDAI) at weeks 14, 30 and 54 in patients with rheumatoid arthritis (RA) treated with SB2 or INF from a phase III study and to assess the radiographic progression at week 54 in patients by disease activity states (remission, low disease activity [LDA], moderate disease activity [MDA], or high disease activity [HDA]).

Methods: Patients with RA were randomized to receive either SB2 or INF 3 mg/kg at weeks 0, 2, 6, and then every 8 weeks thereafter until week 46 with background methotrexate. Dose increments were allowed after week 30 by 1.5 mg/kg up to a maximum dose of 7.5 mg/kg. Disease activities by SDAI, and CDAI were compared at weeks 14, 30, and 54. The radiographic progression was measured by modified Total Sharp Score (mTSS) at weeks 0 and 54.

Results: Up to week 54, comparable proportions of patients achieved ACR-EULAR-index remission between SB2 and INF (by SDAI: 13/279 [4.7%] vs. 13/283 [4.6%] at week 14; 24/250 [9.6%] vs. 29/263 [11.0%] at week 30; 34/226 [15.0%] vs. 24/224 [10.7%] at week 54; by CDAI: 12/279 [4.3%] vs. 12/283 [4.2%] at week 14; 22/253 [8.7%] vs.

Table 3 Multiple imputation (n = 762)

<table>
<thead>
<tr>
<th></th>
<th>B coefficient</th>
<th>(95% CI)</th>
<th>p_value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTX use</td>
<td>0.45</td>
<td>(0.12, 0.78)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>PSL use</td>
<td>-0.075</td>
<td>(0.44, 0.29)</td>
<td>0.65</td>
</tr>
<tr>
<td>Age</td>
<td>-0.01</td>
<td>(0.020, 0)</td>
<td>0.62</td>
</tr>
<tr>
<td>Female</td>
<td>-0.41</td>
<td>(0.60, 0.67)</td>
<td>0.886</td>
</tr>
<tr>
<td>DAS28ESR prior to switching</td>
<td>0.46</td>
<td>(0.28, 0.66)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>non-TNFα as first bio</td>
<td>0.15</td>
<td>(0.53, 0.52)</td>
<td>0.03</td>
</tr>
<tr>
<td>non-TNFα as second bio</td>
<td>0.56</td>
<td>(0.30, 0.83)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Stage II, IV (I, II as reference)</td>
<td>-0.0029</td>
<td>(0.019, 0.013)</td>
<td>0.7</td>
</tr>
</tbody>
</table>

MTX: methotrexate, PSL: prednisolone, TNFα: Tumor Necrosis Factor inhibitor
31/265 [11.7%] at week 30; 33/227 [14.5%] vs. 24/225 [10.7%] at week 54 in SB2 and INF, respectively). The proportions of radiographic non-progressors (defined as change in mTSS ≤ 0) by disease activity were comparable between SB2 and INF at week 14, 30 and 54 (Table 1). Patients treated with SB2 as well as INF also exhibited the lowest progression of radiographic damage in remission and the largest progression in HDA, but also very small increases in mTSS in LDA and MDA, in line with previous findings on INF.

### Table 1. The proportion of radiographic non-progressors (mTSS progression ≤ 0) and mean change from baseline in mTSS at week 54 by disease activity state at weeks 14, 30, and 54

<table>
<thead>
<tr>
<th>Disease activity state at each visit</th>
<th>SB2</th>
<th>INF</th>
<th>SB2</th>
<th>INF</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Radiographic non-progressors</td>
<td>Mean change</td>
<td>Radiographic non-progressors</td>
<td>Mean change</td>
</tr>
<tr>
<td>Week 14</td>
<td>43/62 (68.4)</td>
<td>0.44</td>
<td>42.59 (71.2)</td>
<td>0.61</td>
</tr>
<tr>
<td>HA</td>
<td>23/41 (56.1)</td>
<td>0.80</td>
<td>31.45 (68.9)</td>
<td>1.03</td>
</tr>
<tr>
<td>Week 30</td>
<td>54/86 (62.7)</td>
<td>0.32</td>
<td>57.82 (68.3)</td>
<td>0.64</td>
</tr>
<tr>
<td>MD</td>
<td>81/100 (81.0)</td>
<td>0.10</td>
<td>63.89 (70.8)</td>
<td>0.45</td>
</tr>
<tr>
<td>Week 54</td>
<td>43/76 (56.8)</td>
<td>0.54</td>
<td>49.58 (68.5)</td>
<td>0.38</td>
</tr>
<tr>
<td>LA</td>
<td>44.54 (69.9)</td>
<td>0.63</td>
<td>73.64 (63.6)</td>
<td>-0.27</td>
</tr>
<tr>
<td>Remission</td>
<td>7.6 (77.8)</td>
<td>1.04</td>
<td>7.6 (77.8)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

### Conclusion:

The proportion of patients achieving remission or LDA was comparable up to week 54 upon treatment with both SB2 and INF. Inhibition of radiographic progression was also comparable in each disease activity state. The proportion of radiographic non-progressors was also similarly high in patients achieving remission, and overall very low radiographic progression rates were seen even in LDA and MDA in both treatment arms. These data further confirm the comparability of SB2 and INF.

### Disclosure:

**J. S. Smolen**, AbbVie, Eli Lilly, Janssen, MSD, Pfizer Inc, Roche, 2,AbbVie, Amgen, AstraZeneca, Astro, Celgene, Celtrion, Eli Lilly, GSK, ILTOO, Janssen, MedImmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, UCB, 5,AbbVie, Amgen, AstraZeneca, Astro, Celgene, Celtrion, Eli Lilly, GSK, ILTOO, Janssen, MedImmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, UCB, 8; **J. Y. Choe**, None; **E. C. Keystone**, Pfizer, Roche, Janssen, Amgen, BMS, Merck, Merck, Celltrion, Samsung Bioepis, 5; **Y. H. Rho**, Samsung Bioepis, 3; **Y. Lee**, Samsung Bioepis, 3; **S. Lee**, Samsung Bioepis, 3.


### Abstract Number: 2467

**Evaluation of Radiographic Progression By Disease Activity States in Patients with Rheumatoid Arthritis Treated with SB4 or Reference Etanercept: Results from a Phase III Study**

**Paul Emery**, 1, Jiri Vencovsky2, Jeehoon Ghi3, Soo Yeon Cheong3 and Evelyn Hong3, 1NIHR-Leeds Musculoskeletal Biomedical Research Unit and Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom, 2Institute of Rheumatology, Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, 3Samsung Bioepis Co., Ltd., Incheon, Korea, Republic of (South)

**First publication**: September 18, 2017

**SESSION INFORMATION**
Background/Purpose: SB4 has been approved as a biosimilar of the reference etanercept by the European Commission. Results including one year radiographic progression from the pivotal phase III equivalence study have been previously presented. In this report, the radiographic progression will be further evaluated by different disease activity states in terms of disease activity score by 28 joint count (DAS28) based on erythrocyte sedimentation rate (ESR), simplified disease activity index (SDAI) and clinical disease activity index (CDAI).

Methods: Patients with rheumatoid arthritis (RA) were randomly assigned to receive weekly dose of 50 mg SB4 or ETN for 52 weeks. The proportions of patients achieving remission, low disease activity (LDA), moderate disease activity (MDA), or high disease activity (HDA) in terms of DAS28, SDAI, and CDAI were compared at weeks 12, 24, and 52. Radiographic progression was evaluated using the modified Total Sharp Score (mTSS) at weeks 0 and 52.

Results: The proportion of patients with remission, LDA, MDA, or HDA was generally comparable between SB4 and ETN at weeks 12, 24, and 52 for different disease activity indices (DAS28, SDAI, CDAI) (Table 1). The proportions of radiographic non-progressors (defined as change in mTSS ≤ 0) were comparable between SB4 and ETN in each disease activity state with a tendency to decrease as disease activity worsened. In a similar aspect, the radiographic progression evaluated by mTSS was lowest for patients in remission and largest in HDA, and the extent of progression was overall very low in patients with remission, LDA, and MDA (Table 2).

Conclusion: The proportions of patients achieving remission or LDA in the SB4 and ETN treatment groups were comparable at weeks 12, 24, and 52. The radiographic progression was also comparable in each disease activity state.

| Table 1. Proportion of patients in each disease activity state by DAS28, SDAI, and CDAI |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
|                                | DAS28                           | SDAI                           | CDAI                           |
| Time-point                      | Remission                       | ETN                            | Remission                       | ETN                            | Remission                       | ETN                            |
| Week 12                         | 4409 (45.6)                     | 32586 (41.6)                   | 33969 (41.5)                    | 39298 (46.2)                    | 33394 (41.2)                    | 32068 (41.4)                    |
| LDA                             | 12829 (11.9)                    | 27289 (9.6)                    | 109293 (13.1)                   | 71285 (25.9)                    | 95299 (32.3)                    | 95299 (32.3)                    |
| MDA                             | 127070 (45.6)                   | 162963 (61.6)                  | 107270 (36.5)                   | 137399 (48.9)                   | 90264 (30.6)                    | 119269 (42.1)                   |
| HDA                             | 70269 (22.9)                    | 61261 (23.3)                   | 53265 (18.1)                    | 45260 (7.5)                     | 76269 (25.9)                    | 75269 (27.1)                    |
| Week 24                         | 106920 (47.4)                   | 348272 (17.6)                  | 306792 (11.8)                   | 360792 (11.8)                   | 320992 (11.8)                   | 292972 (10.3)                   |
| LDA                             | 448020 (13.3)                   | 344072 (13.5)                  | 132286 (38.6)                   | 652772 (34.9)                   | 105298 (50.5)                   | 922972 (33.1)                   |
| MDA                             | 1260669 (47.2)                  | 334972 (61.7)                  | 952688 (34.4)                   | 351672 (46.5)                   | 1102821 (20.1)                  | 920217 (37.9)                   |
| HDA                             | 18692 (29.1)                    | 26792 (29.6)                   | 32288 (14.1)                    | 31272 (11.5)                    | 42828 (7.6)                     | 52272 (18.8)                    |
| Week 52                         | 693002 (20.5)                   | 472424 (18.1)                  | 629592 (23.8)                   | 560245 (25.4)                   | 542901 (22.3)                   | 482401 (19.5)                   |
| LDA                             | 620600 (11.4)                   | 302149 (15.9)                  | 93260 (35.8)                    | 92245 (7.6)                     | 93260 (35.8)                    | 83240 (33.3)                    |
| MDA                             | 1251059 (46.1)                  | 1031045 (60.7)                 | 80269 (30.8)                    | 842405 (47.3)                   | 78290 (30.6)                    | 88240 (35.8)                    |
| HDA                             | 103000 (11.5)                   | 289400 (11.1)                  | 25200 (9.5)                     | 19200 (7.4)                     | 31200 (16.6)                    | 28240 (11.1)                    |

Disease activity state defined as:
DAS28: remission: DAS28 ≤ 2.0; LDA: 2.0 < DAS28 ≤ 5.2; MDA: 5.2 < DAS28 ≤ 11.0; HDA: DAS28 > 11.0
LDA: remission: SDAI ≤ 3.3; LDA: 3.3 < SDAI ≤ 11.0; MDA: 11.0 < SDAI ≤ 23.0; HDA: SDAI > 23.0
CDAI: remission: CDAI ≤ 3.3; LDA: 3.3 < CDAI ≤ 9.0; MDA: 9.0 < CDAI ≤ 15.0; HDA: CDAI > 15.0

| Table 2. Proportion of radiographic non-progressors (≤ mTSS 0) and mean ± mTSS (week 02 baseline) by 13, 24, 52-week disease activity states |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
|                                | DAS28                           | SDAI                           | CDAI                           |
|                                | Radioactive non-progressors      | Mean change                    | Radioactive non-progressors     | Mean change                    | Radioactive non-progressors     | Mean change                    | Radioactive non-progressors     | Mean change                    |
| Remission                      | 254 (0.75)                      | -16                             | 275 (0.75)                      | -16                             | 277 (0.75)                      | -16                             |
| LDA                             | 251 (0.75)                      | -16                             | 275 (0.75)                      | -16                             | 277 (0.75)                      | -16                             |
| MDA                             | 12927 (46.1)                    | -16                             | 13292 (46.1)                    | -16                             | 13427 (46.1)                    | -16                             |
| HDA                             | 13292 (46.1)                    | -16                             | 13292 (46.1)                    | -16                             | 13292 (46.1)                    | -16                             |
| Remission                      | -27                             | 0.1                             | 0.1                             | 0.1                             | 0.1                             | 0.1                             |
| LDA                             | -27                             | 0.1                             | 0.1                             | 0.1                             | 0.1                             | 0.1                             |
| MDA                             | -27                             | 0.1                             | 0.1                             | 0.1                             | 0.1                             | 0.1                             |
| HDA                             | -27                             | 0.1                             | 0.1                             | 0.1                             | 0.1                             | 0.1                             |

Conclusion: The proportions of patients achieving remission or LDA in the SB4 and ETN treatment groups were comparable at weeks 12, 24, and 52. The radiographic progression was also comparable in each disease activity state.
with the rate of radiographic non-progressors being highest in patients achieving remission. The overall radiographic progression was very low even in patients with LDA and MDA but slightly higher in HDA.

Disclosure: P. Emery, Pfizer, MSD, Abbvie, BMS, UCB, Roche, Novartis, Samsung, Sandoz, Eli Lilly and Company, 5; J. Vencovsky, Samsung Bioepis Co., Ltd., Biogen, 5; J. Ghil, Samsung Bioepis, 3; S. Y. Cheong, Samsung Bioepis Co., Ltd., 3; E. Hong, Samsung Bioepis Co., Ltd., 3.


Abstract Number: 2468

Efficacy of Sarilumab in Patients with Rheumatoid Arthritis Who Previously Received Sarilumab or Tocilizumab

Paul Emery1, Hubert van Hoogstraten2, Shyamalie Jayawardena2, Erin K. Mangan3, Paula Cejas4 and Patrick Verschueren5, 1NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom, 2Sanofi Genzyme, Bridgewater, NJ, 3Regeneron Pharmaceuticals, Inc., Tarrytown, NY, 4Hospital Quirónsalud Infanta Luisa, Sevilla, Spain, 5Division of Rheumatology, University Hospital Leuven, Leuven, Belgium

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: ASCERTAIN (NCT01768572) was a 24-week, randomized, double-blind, double-dummy, parallel-group, 3-arm, safety study in patients with RA and inadequate response to or intolerance of TNF inhibitors receiving background conventional synthetic (cs)DMARDs. The purpose of this post hoc analysis was to examine outcomes for patients completing ASCERTAIN who were switched to sarilumab 200 mg every 2 weeks (q2w) subcutaneously (SC) in an open-label extension study (EXTEND, NCT01146652).

Methods: In ASCERTAIN, patients receiving background csDMARDs were randomized 1:1:2 to sarilumab 150 mg q2w SC, sarilumab 200 mg q2w SC, or tocilizumab every 4 weeks (q4w) intravenously (IV) starting at 4 mg/kg and increasing to 8 mg/kg if clinically indicated. Patients were eligible to enroll in EXTEND and receive open-label sarilumab 200 mg q2w after completing ASCERTAIN. Clinical endpoints were based on all available data as observed and were summarized through week 84 of EXTEND according to the original randomized treatment. Definitions used as cutoffs for remission and low disease activity (LDA) were DAS28-CRP <2.6 and <3.2 and clinical disease activity index (CDAI) ≤2.8 and ≤10.0, respectively. All patients who had not achieved individual parameters of remission, LDA, and ACR20/50/70 at enrollment into EXTEND were classified as nonresponders for that specific category.

Results: Of the 175 patients who completed ASCERTAIN, 93/96 from the tocilizumab group, 37/40 from the sarilumab 150 mg group, and 38/39 from the sarilumab 200 mg group entered EXTEND. Improvements observed in DAS28-CRP and CDAI in ASCERTAIN were maintained after the switch to open-label sarilumab in EXTEND through week 84 (data not shown). Regardless of initial treatment in ASCERTAIN, the proportions of patients who achieved ACR20/50/70 response, and DAS28-CRP and CDAI remission and LDA increased after switch to sarilumab 200 mg
q2w in EXTEND (Table). The greatest increase in patients meeting definitions of remission and LDA was observed in patients initially receiving tocilizumab. Generally, a greater proportion of nonresponders who switched from sarilumab 150 mg q2w to 200 mg q2w achieved ACR20/50/70 response, and DAS28-CRP and CDAI remission and LDA compared with nonresponders who were maintained on 200 mg q2w. The most common treatment-emergent adverse events observed in the EXTEND safety population, which included all patients enrolled from ASCERTAIN and 4 other sarilumab studies, were infections and neutropenia.

**Conclusion:** Efficacy was maintained or improved in patients rolling over from ASCERTAIN into EXTEND. Increased efficacy was seen in all nonresponder categories, with the largest increases occurring in those who initially received tocilizumab. Although based on a limited population, these findings suggest that switching tocilizumab nonresponders to sarilumab may have favorable efficacy outcomes.

**Table. Response Rates After 12 and 24 Weeks of Open-label Sarilumab Plus Background csDMARDs in Patients From ASCERTAIN Who Were Nonresponders* at Enrollment in EXTEND**

<table>
<thead>
<tr>
<th>Total enrolled patients</th>
<th>Tocilizumab 4/8 mg/kg</th>
<th>Sarilumab 150 mg q2w IV</th>
<th>Sarilumab 200 mg q2w SC</th>
<th>Sarilumab 200 mg q2w SC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total enrolled patients</td>
<td>N=93</td>
<td>N=37</td>
<td>N=38</td>
<td></td>
</tr>
<tr>
<td>DAS28-CRP ≥2.6, n (%)</td>
<td>53</td>
<td>23</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>DAS28-CRP &lt;2.6, wk 12, n (%)</td>
<td>21/59 (35.6)</td>
<td>10/22 (45.5)</td>
<td>5/20 (25.0)</td>
<td></td>
</tr>
<tr>
<td>DAS28-CRP &lt;3.2, wk 24, n (%)</td>
<td>22/57 (43.9)</td>
<td>8/22 (36.4)</td>
<td>5/21 (23.8)</td>
<td></td>
</tr>
<tr>
<td>CDAI ≥2.8, n (%)</td>
<td>77</td>
<td>32</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>CDAI ≥3.2, wk 12, n (%)</td>
<td>10/75 (13.3)</td>
<td>4/31 (12.9)</td>
<td>6/35 (17.1)</td>
<td></td>
</tr>
<tr>
<td>CDAI ≥3.2, wk 24, n (%)</td>
<td>14/71 (19.7)</td>
<td>6/30 (20.0)</td>
<td>3/34 (9.8)</td>
<td></td>
</tr>
<tr>
<td>CDAI ≥5.0, n (%)</td>
<td>51</td>
<td>16</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>CDAI ≥6.0, wk 12, n (%)</td>
<td>16/49 (32.7)</td>
<td>7/15 (46.7)</td>
<td>2/15 (13.3)</td>
<td></td>
</tr>
<tr>
<td>CDAI ≥6.0, wk 24, n (%)</td>
<td>20/45 (44.4)</td>
<td>7/15 (46.7)</td>
<td>5/14 (35.7)</td>
<td></td>
</tr>
<tr>
<td>No ACR70 response, n (%)</td>
<td>69</td>
<td>6</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>ACR20 response, wk 12, n (%)</td>
<td>4/16 (25.0)</td>
<td>2/5 (40.0)</td>
<td>3/3 (66.7)</td>
<td></td>
</tr>
<tr>
<td>ACR20 response, wk 24, n (%)</td>
<td>9/14 (64.3)</td>
<td>2/8 (25.0)</td>
<td>1/2 (62.5)</td>
<td></td>
</tr>
<tr>
<td>No ACR50 response, n (%)</td>
<td>67</td>
<td>19</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>ACR50 response, wk 12, n (%)</td>
<td>6/18 (33.3)</td>
<td>9/18 (50.0)</td>
<td>6/17 (47.1)</td>
<td></td>
</tr>
<tr>
<td>ACR50 response, wk 24, n (%)</td>
<td>18/45 (42.2)</td>
<td>7/18 (38.9)</td>
<td>12/16 (75.0)</td>
<td></td>
</tr>
<tr>
<td>No ACR70 response, n (%)</td>
<td>70</td>
<td>28</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>ACR70 response, wk 12, n (%)</td>
<td>16/58 (23.5)</td>
<td>9/27 (33.3)</td>
<td>8/39 (26.7)</td>
<td></td>
</tr>
<tr>
<td>ACR70 response, wk 24, n (%)</td>
<td>15/53 (28.6)</td>
<td>9/29 (31.0)</td>
<td>8/29 (31.0)</td>
<td></td>
</tr>
</tbody>
</table>

**Disclosure:** P. Emery, Abbott, AbbVie, Bristol-Myers Squibb, Pfizer, UCB, Merck Sharpe & Dohme, Roche, Novartis, Samsung, Takeda, Eli Lilly, Sanofi, and Regeneron Pharmaceuticals, Inc, 2, Abbott, AbbVie, Bristol-Myers Squibb, Pfizer, UCB, Merck Sharpe & Dohme, Roche, Novartis, Samsung, Takeda, Eli Lilly, Sanofi, and Regeneron Pharmaceuticals, Inc, 5; H. van Hoogstraten, Sanofi Genzyme, 3, Sanofi Genzyme, 1; S. Jayawardena, Sanofi Genzyme, 1, Sanofi Genzyme, 3; E. K. Mangan, Regeneron Pharmaceuticals, Inc., 1, Regeneron Pharmaceuticals, Inc., 3; P. Cejas, AbbVie, Bristol-Myers Squibb, Novartis, Pfizer, and Sun Pharma, 9; P. Verschueren, AbbVie, Bristol-Myers Squibb, Eli Lilly, Merck Sharpe & Dohme, Pfizer, Roche, Sanofi, and UCB, 5, Pfizer chair for early RA management at KU Leuven, 6.

**Abstract Number:** 2469

** Median Time to Lda Is Shorter in Tocilizumab Combination Therapy with CsDMARDs As Compared to Monotherapy in Patients with Active**
Rheumatoid Arthritis and Inadequate Responses to Csdmards and/or TNF Inhibitors: Sub-Analysis of the Swiss and Austrian Patients from the ACT-SURE Study

Ruediger Mueller1, Winfried Graninger2, Páris Sidiropoulos3, Christoph Goger4 and Johannes von Kempis5,
1Rheumatology, MD, St. Gallen, Switzerland, 2Rheumatology and Immunology, Medical University of Graz, Graz, Austria, 3F. Hoffmann-La Roche Ltd, South San Francisco, CA, 4Roche Austria GmbH, Vienna, Austria, 5Rheumatology, Kantonsspital St. Gallen, St. Gallen, Switzerland

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: To analyze efficacy and safety of tocilizumab in patients with rheumatoid arthritis (RA) and an inadequate response to conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) and/or tumor necrosis factor (TNF) inhibitors of the Swiss and Austrian patients from the ACT-SURE study.

Methods: Sub-analysis of RA patients from Switzerland and Austria, who participated in the international phase IIIb, open-label, ACT-SURE study. Patients with an inadequate response to csDMARDs or TNF antagonists receiving 8 mg/kg of IV tocilizumab every 4 weeks during a 24 week time period were included into the study Therapy with one or more csDMARDs could be continued as combination therapy with tocilizumab (Combo) or stopped, resulting in tocilizumab monotherapy (Mono), at the treating physician’s discretion. These two patient groups were analyzed in separate and compared.

Results: Overall, 107 (22 on Mono vs 85 on Combo) patients were treated with tocilizumab. The percentage of patients with at least one adverse event was significantly lower in the tocilizumab combination (58.8%) as compared to the monotherapy group (81.8%, p = 0.0458). No differences in ACR20/50/70/90 response rates were observed between both treatment groups at week 24 (Mono: 63.6%, 40.9%, 22.7%, and 18.2% vs. Combo: 61.2%, 43.5%, 25.9%, and 10.6%). The median time to low disease activity (LDA) was significantly shorter in patients treated with tocilizumab combination therapy Mono: 9.1, Combo 7.9 weeks, Log Rank p = 0.038).

Conclusion: In this post hoc regional sub-analysis of the ACT-SURE study no differences for disease activity were found comparing the two patient groups at week 24. However, median time to LDA was statistically shorter in patients treated with tocilizumab combination therapy as compared to tocilizumab monotherapy. Consequently, adding tocilizumab to csDMARD therapy rather than changing to tocilizumab monotherapy may be, in our opinion, the safest strategy to reach maximum effect in RA patients with active disease despite treatment with csDMARD. csDMARDs can be withdrawn either immediately due to adverse events or after at least low disease activity has been reached.

Disclosure: R. Mueller, None; W. Graninger, None; P. Sidiropoulos, Roche Pharmaceuticals, 3; C. Goger, Roche Pharmaceuticals, 3; J. von Kempis, None.


Abstract Number: 2470
Efficacy of Sarilumab in Combination with CsDMARDs in Patients with Rheumatoid Arthritis and Inadequate Response to TNF Inhibitors By Baseline Levels of Disease Activity

Roy Fleischmann1, Hubert van Hoogstraten2, Shyamalie Jayawardena2, Erin K. Mangan3, Daniel Ching4 and Gerd R. Burmester5, 1Metroplex Clinical Research Center, University of Texas Southwestern Medical Center, Dallas, TX, 2Sanofi Genzyme, Bridgewater, NJ, 3Regeneron Pharmaceuticals, Inc., Tarrytown, NY, 4Timaru Medical Specialists Ltd, Timaru, New Zealand, 5Rheumatology and Clinical Immunology, Charité - University Medicine Berlin, Free University and Humboldt University Berlin, Berlin, Germany

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Sarilumab is a human mAb blocking the IL-6Rα. In the phase 3 TARGET study (NCT01709578), sarilumab (150 or 200 mg subcutaneously every 2 weeks [q2w]) plus conventional synthetic (cs)DMARDs demonstrated efficacy in adults with active, moderate-to-severe RA and intolerance of or inadequate response to TNF inhibitors. The most common treatment-emergent adverse events in TARGET were infections, neutropenia, injection site reactions, increased lipids, and increased transaminases. It has been postulated that, in clinical trials, patients with higher baseline disease activity are more likely to show response than those with lower baseline disease activity.1 The objective of this post hoc analysis was to examine the efficacy of sarilumab in patient subgroups based on median baseline disease activity levels.

Methods: All patients in the TARGET study randomized to placebo (n=181), sarilumab 150 mg q2w (n=181), and sarilumab 200 mg q2w (n=184) were included. Disease activity at baseline was defined according to < or ≥ median levels (DAS28-CRP: 6.2, clinical disease activity index [CDAI]: 42.9, and CRP: 17.8). ACR20/50/70 response rates and changes in DAS28-CRP, CDAI, and CRP values were evaluated at week 24. Nominal P values were assessed using the Cochran-Mantel-Haenszel test for binary endpoints and mixed model with repeated measures for continuous endpoints.

Results: Regardless of disease activity at baseline, a higher percentage of patients treated with sarilumab vs placebo achieved ACR20/50/70 responses and had greater improvements in DAS28-CRP, CDAI, and CRP at week 24 (Table). Placebo-adjusted treatment effect with sarilumab was more pronounced in patients with higher baseline disease activity, with lower responses seen with placebo in these patients (data not shown). The odds ratio vs placebo for achieving an ACR20/50/70 response at week 24 was greater in sarilumab-treated patients with higher baseline disease activity than in those with lower baseline disease activity for each definition assessed. Likewise, change from baseline in DAS28-CRP, CDAI, and CRP at week 24 were greater in sarilumab-treated patients with higher baseline disease activity for each definition assessed.

Conclusion: Patients treated with sarilumab 150 and 200 mg q2w plus csDMARDs achieved greater clinical responses vs those treated with placebo, regardless of disease activity at baseline. The treatment effect of sarilumab was larger in patients with higher disease activity at baseline.

Reference:
| Table. Baseline Subgroup Efficacy of Sarilumab in Combination With csDMARDs at Week 24 |
|-----|------------------|------------------|------------------|------------------|------------------|
|     | 100 mg q4w + csDMARDs | More active disease, DAS28-CRP > median (n=94) |     | 100 mg q4w + csDMARDs | More active disease, DAS28-CRP > median (n=91) |
| ACR20 response, placebo adjusted, % | 14.5 (9.7, 25.3) | 13.1 (9.5, 18.9) | 15.5 (11.4, 20.5) | 13.9 (10.6, 17.9) |
| OR, 95% CI | 1.45 (0.76, 2.79) | 1.75 (1.04, 3.26) | 1.52 (0.90, 2.56) | 1.72 (1.04, 2.84) |
| ACR50 response, placebo adjusted, % | 15.0 (9.4, 22.3) | 15.0 (9.4, 22.3) | 15.0 (9.4, 22.3) | 15.0 (9.4, 22.3) |
| OR, 95% CI | 1.57 (0.96, 2.55) | 1.74 (1.04, 2.94) | 1.74 (1.04, 2.94) | 1.74 (1.04, 2.94) |
| ACR70 response, placebo adjusted, % | 15.0 (9.4, 22.3) | 15.0 (9.4, 22.3) | 15.0 (9.4, 22.3) | 15.0 (9.4, 22.3) |
| OR, 95% CI | 1.57 (0.96, 2.55) | 1.74 (1.04, 2.94) | 1.74 (1.04, 2.94) | 1.74 (1.04, 2.94) |

Disclosure: R. Fleischmann, AbbVie, Amgen, Ardea Biosciences, Bristol-Myers Squibb, Celgene, GlaxoSmithKline, Janssen, Eli Lilly, Novartis, Pfizer, Roche, Sanofi, and UCB; 2, AbbVie, Akros Pharma, Amgen, AstraZeneca, Bristol-Myers Squibb, GlaxoSmithKline, Janssen, Eli Lilly, Merck Serono, Novartis, Pfizer, Roche, Sanofi, and UCB; 5; H. van Hoogstraten, Sanofi Genzyme, 3, Sanofi Genzyme, 1; S. Jayawardena, Sanofi Genzyme, 1, Sanofi Genzyme, 3; E. K. Mangan, Regeneron Pharmaceuticals, Inc., 1; Regeneron Pharmaceuticals, Inc., 3; 3, D. Ching, AbbVie, Boehringer-Ingelheim, Celgene, Galapagos, Gilead, GlaxoSmithKline, Lilly, Merck Sharpe & Dhome, MedImmune, Pfizer, Roche, Sanofi, and UCB; 2, AbbVie, Boehringer-Ingelheim, Celgene, Galapagos, Gilead, GlaxoSmithKline, Lilly, Merck Sharpe & Dhome, MedImmune, Pfizer, Roche, Sanofi, and UCB; 5, AbbVie, 8; G. R. Burmester, AbbVie, Bristol-Myers Squibb, MedImmune, Merck, Pfizer, Roche, and UCB; 2, AbbVie, Bristol-Myers Squibb, MedImmune, Merck, Pfizer, Roche, and UCB; 5, AbbVie, Bristol-Myers Squibb, Merck, Pfizer, Roche, and UCB; 8.


Abstract Number: 2471

Sustained Response in a Phase 3 Study of Sarilumab Plus Nonbiologic Disease-Modifying Antirheumatic Drugs in Patients with Active,
Moderate-to-Severe Rheumatoid Arthritis and Inadequate Response or Intolerance to Tumor Necrosis Factor Inhibitors

Roy Fleischmann1, Greg St. John2, Toshio Kimura2, Melitza Iglesias-Rodriguez3, Itzhak Rosner4 and Gerd R. Burmester5,

1Metroplex Clinical Research Center, University of Texas Southwestern Medical Center, Dallas, TX,
2Regeneron Pharmaceuticals, Inc., Tarrytown, NY, 3Sanofi Genzyme, Cambridge, MA, 4Bnai-Zion Medical Center, Haifa, Israel, 5Department of Rheumatology and Clinical Immunology, Charité - University Medicine Berlin, Free University and Humboldt University Berlin, Berlin, Germany

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Sarilumab is a human mAb blocking the IL-6Rα. In the phase 3 TARGET study (NCT01709578), sarilumab (150 or 200 mg subcutaneously [SC] every 2 weeks [q2w]) plus conventional synthetic (cs)DMARDs demonstrated efficacy in adults with active, moderate-to-severe RA and inadequate response or intolerance to TNF inhibitors. Consistent with IL-6 inhibition and the safety profile of SC sarilumab, infections, neutropenia, injection site reactions, increased lipids, and increased transaminases were among the most common treatment-emergent adverse events. The objective of this analysis was to examine whether patients who achieved clinical response and improvements in physical function at week 12 in TARGET continued to sustain response up until the end of study at week 24.

Methods: A sustained response was defined as a response at week 12 (see below) with continuous response until the end of the study. An additional definition of a sustained response allowed for a single visit in between without a response, with the exception of the last 2 visits. Patients were seen at baseline and at weeks 2, 4, 8, 12, 16, 20, and 24 of the study. The sustainability of the response was measured for the following clinical efficacy endpoints: ACR20/50/70 response, HAQ–Disability Index (HAQ-DI; ≥0.22 units of improvement from baseline), clinical disease activity index (CDAI; ≤2.8 [remission], >2.8 to ≤10 [low disease activity; LDA]), simplified disease activity index (SDAI; ≤3.3 [remission], >3.3 to ≤11 [LDA]), and DAS28-CRP (<2.6, ≥2.6 to ≤3.2).

Results: A significantly higher percentage of patients treated with sarilumab + csDMARDs achieved ACR20/50/70 response (both doses) and HAQ-DI ≥0.22 units of improvement from baseline (200 mg q2w dose only) at week 12 in TARGET vs those treated with placebo + csDMARDs (Table). The majority of patients treated with sarilumab who achieved a response at week 12 sustained that response, or had up to 1 nonresponse, until the end of the study (Table). In contrast, there were fewer patients in the placebo + csDMARDs group who achieved and sustained a response from week 12 to the end of the study. These observations were similar regardless of whether a patient maintained a response at every visit after week 12 through the end of the study or had 1 nonresponse at a visit in between. A similar trend was also observed for CDAI and SDAI remission and LDA, and DAS28-CRP <2.6 and ≥2.6 to ≤3.2.

Conclusion: More patients with active, moderate-to-severe RA and inadequate response or intolerance to TNF inhibitors who were treated with sarilumab + csDMARDs achieved and sustained a clinically significant response compared with those treated with placebo + csDMARDs.
Integrated Phase 3 Safety Results of Sirukumab, an Anti–IL-6 Cytokine Monoclonal Antibody, in Patients with Active Rheumatoid Arthritis

Daniel Aletaha1, Carter Thorne2, Michael Schiff3, Masayoshi Harigai4, Prasheen Agarwal5, Ravi Rao6, Christopher Cohen7, Ben Cheng5, Kurt Brown7 and Benjamin Hsu5, 1Department of Medicine III, Division of Rheumatology, Medical University of Vienna, Vienna, Austria, 2University of Toronto, Newmarket, ON, Canada, 3University of Colorado School of Medicine, Aurora, CO, 4Division of Epidemiology and Pharmacoepidemiology of Rheumatic Diseases, Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan, 5Janssen Research & Development, LLC, Spring House, PA, 6GlaxoSmithKline, Stevenage, Hertfordshire, United Kingdom, 7GlaxoSmithKline, Collegeville, PA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
**Session Title:** Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Sirukumab (SIR), a human monoclonal antibody that selectively binds to the IL-6 cytokine with high affinity, is in development for rheumatoid arthritis (RA) in the global SIRROUND Phase 3 trial program. SIR significantly reduced signs/symptoms of RA and inhibited radiographic progression. SIR has been well tolerated in RA patients (pts) with a safety profile similar to that of other drugs targeting the IL-6 pathway. Pooled safety data from SIRROUND trials are presented.

**Methods:** Safety data through July 29, 2016 from 5 Phase 3 trials of SIR were analyzed. These trials included pts with moderate to severe active RA who were refractory or intolerant to conventional DMARDs (SIRROUND-D, M, H) or anti-TNF therapy (SIRROUND-T). SIRROUND-LTE is a long-term extension study for pts completing SIRROUND-D or T. SIR was administered SC at 50mg q4w or 100mg q2w. Safety analyses are presented by SIR treatment group for adverse events (AEs), serious AEs (SAEs), mortality, and AEs of special interest (serious infections, gastrointestinal [GI] perforations, major adverse cardiovascular events [MACE], and malignancies).

**Results:** In Phase 3 trials, 2926 pts received SIR. Pts were treated for up to 3.9 years (approximately 5300 patient-years of drug exposure), with a median exposure of 1.76 years. Similar proportions of pts had treatment-emergent AEs, discontinuations due to AEs, and SAEs in the 50mg and 100mg groups (Table). Incidences of common AEs were generally comparable across dose groups; however, injection site reactions (ISRs) occurred more frequently with more frequent dosing: 100-mg q2w (21.9%) versus 50-mg q4w (12.7%) dose, with erythema, pruritus, and swelling most frequently reported. Pneumonia (1.8%) and cellulitis (1.1%) were the only individual SAEs reported in ≥1% of all SIR-treated pts. No dose effect was observed for the incidence of serious infections. Rates of GI perforation and malignancies were low in both dose groups. MACE rates for SIR 50mg q4w were similar to those reported for other agents and RA in general and were numerically lower with SIR 100mg q2w. The overall mortality rates were similar for the 2 SIR doses and also consistent with those observed with other agents and RA.

**Conclusion:** In this pooled safety analysis of SIR in pts with active RA, no new safety signals were observed. Overall, no dose response was observed between SIR 50mg q4w and 100mg q2w for types and frequencies of AEs, with the exception of hypersensitivity and ISRs.

**Disclosure:** D. Aletaha, AbbVie, Pfizer, Grünenthal, Merck Medac, UCB, Mitsubishi/Tanabe, Janssen, and Roche, 5, AbbVie, Pfizer, Grünenthal, Merck Medac, UCB, Mitsubishi/Tanabe, Janssen, and Roche, 2; C. Thorne, AbbVie, Amgen, Celgene, Lilly, Novartis, Pfizer, Sanofi, and UCB, 2, Medexus/Medac, 8, AbbVie, Amgen, Celgene, Centocor, Genzyme, Hospira, Janssen, Lilly, Medexus/Medac, Merck, Novartis, Pfizer, Sanofi, and UCB, 5; M. Schiff, AbbVie,

---

**Table I. Treatment-emergent AEs in Phase 3 Trials Through Data Cut-off (July 29, 2016)**

<table>
<thead>
<tr>
<th>AEs, n (%)</th>
<th>Sirukumab 50mg q4w (n=1461)</th>
<th>Sirukumab 100mg q2w (n=1465)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AEs</td>
<td>1242 (85.0)</td>
<td>1267 (86.5)</td>
</tr>
<tr>
<td>AEs in &gt;10% of pts</td>
<td>235 (15.9)</td>
<td>262 (17.9)</td>
</tr>
<tr>
<td>Increased ALT</td>
<td>197 (13.5)</td>
<td>197 (13.4)</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>132 (9.0)</td>
<td>229 (15.6)</td>
</tr>
<tr>
<td>Injection site erythema</td>
<td>172 (11.8)</td>
<td>164 (11.2)</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>141 (9.7)</td>
<td>187 (12.8)</td>
</tr>
<tr>
<td>AEs leading to discontinuation</td>
<td>190 (13.0)</td>
<td>225 (15.4)</td>
</tr>
<tr>
<td>Hypersensitivity reactions</td>
<td>3 (0.2)</td>
<td>14 (1.0)</td>
</tr>
<tr>
<td>Incidence</td>
<td>0.11 (0.02, 0.33)</td>
<td>0.52 (0.29, 0.88)</td>
</tr>
<tr>
<td>SAEs</td>
<td>304 (20.8)</td>
<td>318 (21.7)</td>
</tr>
<tr>
<td>Serious infections</td>
<td>118 (81.1)</td>
<td>126 (81.8)</td>
</tr>
<tr>
<td>Incidence</td>
<td>4.59 (3.80, 5.50)</td>
<td>4.84 (4.03, 5.76)</td>
</tr>
<tr>
<td>GI perforations</td>
<td>8 (0.5)</td>
<td>11 (0.8)</td>
</tr>
<tr>
<td>Incidence</td>
<td>0.30 (0.13, 0.60)</td>
<td>0.41 (0.21, 0.74)</td>
</tr>
<tr>
<td>MACE</td>
<td>28 (1.9)</td>
<td>10 (0.7)</td>
</tr>
<tr>
<td>Incidence</td>
<td>1.07 (0.71, 1.54)</td>
<td>0.37 (0.18, 0.69)</td>
</tr>
<tr>
<td>Malignancies</td>
<td>24 (1.6)</td>
<td>28 (1.9)</td>
</tr>
<tr>
<td>Incidence</td>
<td>0.91 (0.59, 1.36)</td>
<td>1.05 (0.70, 1.52)</td>
</tr>
<tr>
<td>Deaths</td>
<td>18 (1.2)</td>
<td>19 (1.3)</td>
</tr>
<tr>
<td>Incidence</td>
<td>0.68 (0.40, 1.08)</td>
<td>0.71 (0.43, 1.11)</td>
</tr>
</tbody>
</table>

*Incidence per 100 patient-years (95% CI).*
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Sirukumab (SIR), a human monoclonal antibody that selectively binds to the IL-6 cytokine with high affinity, has demonstrated efficacy in rheumatoid arthritis (RA) using dose regimens of 50mg q4w and 100mg q2w. Maintenance of response throughout the dosing interval is beneficial, especially when treatment is given less frequently. A global Phase 3 study in patients (pts) with active RA refractory to conventional, synthetic, disease-modifying antirheumatic drugs (DMARDs; SIRROUND-D) demonstrated the efficacy and safety of both dose regimens of SIR. Post-hoc analyses of SIRROUND-D were performed to assess response maintenance with SIR 50mg q4w (less frequent dosing) and SIR 100mg q2w (more frequent dosing) over 2w and 4w intervals.

Methods: Pts (n=1,670) were randomized 1:1:1 to SC SIR 50 mg q4w, SIR 100mg q2w, or placebo q2w. The primary efficacy endpoint was ACR20 response at Wk 16. Additional efficacy outcomes evaluated included change from baseline (BL) in CDAI, DAS28(CRP), and CRP, evaluated every 2-4w. Serum samples for pharmacokinetics were collected and analyzed at BL up to 52w. Post hoc subgroup analyses of patients who were EULAR Good-Moderate responders at 12w assessed the % of pts with loss of response (improvement ≤1.2 from BL) over 2w and 4w dosing intervals and change from BL in DAS28(CRP) over 2w and 4w intervals by treatment group for study visits up to 52w to determine any change in response based on dosing regimen.

Results: Following multiple SC doses of SIR 50 mg q4w or 100 mg q2w, trough serum SIR concentrations reached steady state (SS) by approximately 12w and remained stable through 52w. ACR20 response and improvements from BL in CRP, CDAI, and DAS28(CRP) were achieved and maintained over 2w intervals from 16w to 20w (post-SS) and through 52w for both SIR dose groups (Fig 1). In pts with EULAR Good-Moderate response at 12w, there was no evidence of a change in mean DAS28(CRP) between Wks 16, 18, and 20 for either the 2w or 4w SIR dose. Furthermore, <3% of pts on SIR 50mg q4w and ≤5% of pts on SIR 100mg q2w lost response at any individual study visit from Wk 16 to 20w. Post hoc analysis showed no evidence of change in mean DAS28(CRP) between Wks 16, 18, and 20 for either the 2w or 4w SIR dose. Furthermore, <3% of pts on SIR 50mg q4w and ≤5% of pts on SIR 100mg q2w lost response at any individual study visit from Wk 16 to 20w. Post hoc analysis showed no evidence of change in mean DAS28(CRP) between Wks 16, 18, and 20 for either the 2w or 4w SIR dose.
visit between 16w and 52w. There was no increase in % of pts with loss of response over time, and 80% of pts with loss of response at a study visit had loss of response only at that visit or 1 other visit through 52w. The loss of response rates were similar for SIR 50mg q4w and SIR 100mg q2w.

**Conclusion:** In a SIR phase 3 clinical trial in RA pts refractory to DMARDs, trough serum SIR concentrations were stable during the time interval that efficacy was assessed in the majority of pts. The q4w and q2w dosing regimens were similar with respect to maintenance of response throughout the different dosing intervals, and the response was effectively maintained to 52w. These data demonstrate that sirukumab q4w dosing provides an effective treatment option for pts with RA.

Fig 1

![SIRROUND-D Change in CDAI](image)

**Disclosure:** D. M. Brooks, GlaxoSmithKline, 3,GlaxoSmithKline, 1; M. Plotnick, Johnson & Johnson, 1,Johnson & Johnson, 3; N. J. Williams, GlaxoSmithKline, 3,GlaxoSmithKline, 1; R. Kurrasch, GlaxoSmithKline, 1,GlaxoSmithKline, 3; Y. Zhuang, Johnson & Johnson, 3,Johnson & Johnson, 1; D. J. Tompson, GlaxoSmithKline, 3; B. Hsu, Johnson & Johnson, 1,Johnson & Johnson, 3; R. Rao, GlaxoSmithKline, 3,GlaxoSmithKline, 1.


Abstract Number: 2474

**Efficacy and Safety of Extending Tocilizumab Infusion Intervals from 4 Weeks to 6 Weeks in Patients with Rheumatoid Arthritis**

Hiroshi Uda1 and Osamu Saiki2, 1Rheumatology, Higashiosaka City Medical Center, Higashiosaka, Japan, 2Rheumatology, Higashiosaka City General Hospital, Higashiosaka, Japan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM
Background/Purpose: A period of 4 weeks (w) has been recommended for rheumatoid arthritis (RA) patients as the interval between tocilizumab (TCZ, 8mg/kg) infusions. However, a previous study has shown that the interval between successive TCZ infusions can be extended from 4 weeks to 6 weeks in more than 60% of patients suffering from RA who had previously shown good responses to TCZ infused at intervals of 4 weeks along with a constant low disease activity (LDA) for more than 2 years (1). Herein, we aimed to investigate the efficacy and safety of extending the interval from 4w to 6w.

Methods: The intervals between TCZ (8mg/kg) infusions were increased from 4 weeks to 6 weeks in patients responding favorably for more than 2 years. A retrospective observational study was conducted by enrolling patients in whom the intervals of TCZ infusions could be extended from 4w to 6w with an LDA for more than 2 years. We compared the efficacy and side effects of TCZ infusions at intervals of 4w and 6w in the same patients. We also examined serum levels of IL-6 and trough TCZ during the course of the study.

Results: A total of 125 patients were enrolled in this study, of which 78 patients showed a good response to TCZ infused at intervals of 6w. After extending the infusion intervals, the efficacy of the treatment was maintained, and the side effects decreased significantly. Parameters reflecting the disease activity such as serum CRP levels and DAS28-CRP scores were considerably low when the infusion interval was 4 weeks whereas they were slightly elevated when infusion interval was increased to 6 weeks, although within the LDA limit. During the course of the study, 11 patients who were administered TCZ at intervals of 4 weeks showed serious adverse events, whereas only 3 patients who were administered TCZ at intervals of 6 weeks showed similar adverse events. Common adverse events such as general fatigue, nausea, and dizziness were frequently observed in patients administered TCZ at intervals of 4 weeks. These common adverse events significantly decreased after the infusion interval was extended to 6 weeks. In addition, the levels of total cholesterol and triglyceride were returned to normal, and the serum trough levels of TCZ became undetectable.

Conclusion: We proved that intervals between TCZ infusions can be extended from 4w to 6w in more than 50% of RA patients along with a decrease in the side effects, thus suggesting the need to change the infusion intervals in suitable patients.

<table>
<thead>
<tr>
<th>Table 1 Clinical assessments before and after extension of TCZ intervals in 6w-responders (n = 78)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCZ interval</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
</tr>
<tr>
<td>DAS28-CRP</td>
</tr>
<tr>
<td>PtGA (mm)</td>
</tr>
<tr>
<td>PGA (mm)</td>
</tr>
<tr>
<td>Tender JC</td>
</tr>
<tr>
<td>Swollen JC</td>
</tr>
<tr>
<td>CDAI</td>
</tr>
</tbody>
</table>

Patients’ clinical assessments were examined before and after TCZ infusion. Values were given as mean ± SD. Seventy-eight patients were enrolled. JC: joint count, PtGA: visual analog scale (0 mm – 100 mm) of patient global assessment of disease activity, PGA: visual analog scale (0 mm – 100 mm) of physician global assessment of disease activity, CDAI: Clinical Disease Activity Index.
Clinical Remission in Subjects with Rheumatoid Arthritis Treated with Subcutaneous Tocilizumab As Monotherapy or in Combination with Methotrexate or Other Synthetic DMARDs: A Real-World Clinical Trial

Raimon Sanmartí1, Emilio Martín-Mola2, João E. Fonseca3, Douglas J. Veale4, Alejandro Escudero-Contreras5 and Carlos M Gonzalez6, 1Rheumatology Service, Hospital Clínic de Barcelona, Barcelona, Spain, 2Hospital La Paz, Madrid, Spain, 3Rheumatology Research Unit, Instituto de Medicina Molecular, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, Lisbon, Portugal, 4Rheumatology, St. Vincent's University Hospital, Dublin 4, Ireland, 5Rheumatology service, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain, 6Rheumatology, Hospital General Universitario Gregorio Marañón, Madrid, Spain

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: the primary objective of this study was to assess the 24-week efficacy and safety of subcutaneous (SC) tocilizumab (TCZ) 162 mg weekly (qw) as monotherapy or in combination with methotrexate (MTX) or other synthetic (s) DMARDs in patients with active rheumatoid arthritis (RA) in the real world setting. Secondary objectives included to evaluate whether increasing the dose interval from TCZ-SC 162 mg qw to TCZ-SC 162 mg every two weeks (q2w) would be associated with a sustained clinical remission up to week 48.

Methods: this multinational, multicenter, phase IIIb study was undertaken in subjects ≥18 years of age with active RA (DAS 28-ESR > 3.2) who have had inadequate response or intolerance to sDMARDs or to a first anti-TNF drug. The study comprised a phase 1 with open-label design in which patients received TCZ-SC 162 mg qw (+/- oral/SC MTX or

---

Table 2 Comparison of serious and common adverse events between at 4w and at 6w intervals

<table>
<thead>
<tr>
<th>Serious adverse events</th>
<th>Common adverse events</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=78</td>
<td>Total events</td>
</tr>
<tr>
<td></td>
<td>At 4w</td>
</tr>
<tr>
<td>Total events</td>
<td>3 (3.3%)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>1 (1.3%)</td>
</tr>
<tr>
<td>LCF</td>
<td>0</td>
</tr>
<tr>
<td>Pyelonephritis</td>
<td>1 (1.3%)</td>
</tr>
<tr>
<td>Herpes zoster</td>
<td>1 (1.3%)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>0</td>
</tr>
<tr>
<td>Enterocolitis</td>
<td>0</td>
</tr>
<tr>
<td>DFR</td>
<td>0</td>
</tr>
<tr>
<td>General Fatigue</td>
<td>4 (5.1%)</td>
</tr>
</tbody>
</table>

Serious and common adverse events were compared in the same patients for the last two years.
*These are suggested to be dependent on the concentration of IL-6. LCF: lumbar compression fracture, DFR: distal radius fracture, RTI: Respiratory tract infection, UTI: Urinary tract infection.
other sDMARDs) for 24-weeks and the main outcome was the percentage of patients achieving sustained clinical remission (DAS 28-ESR < 2.6) at Week 20 and Week 24 (primary outcome of the study); and a phase 2 where patients achieving sustained clinical remission during the phase 1 were randomized to receive TCZ-SC 162 mg qw or TCZ-SC 162 mg q2w (+/- oral/SC MTX or other sDMARDs) for an additional 24 weeks; the main outcome of the phase 2 was the percentage of patients who maintained the remission at week 48 (i.e. DAS 28-ESR<2.6).

**Results:** 401 patients were included in the phase 1, 74 patients received TCZ-SC monotherapy and 327 patients received TCZ-SC in combination with oral/SC MTX or other sDMARDs. Sustained clinical remission rates were comparable between the mono- and combination-therapy groups at 24 week (48.4% vs. 52.9%, p=0.523). Of the 179 patients who achieved sustained clinical remission during the phase 1, 89 were randomly assigned to receive TCZ-SC 162 mg qw and 90 to receive TCZ-SC 162 mg q2w. At the end of phase 2, the percentage of patients who maintained the remission at week 48 was 91.5% with TCZ-SC qw and 73.9% with TCZ-SC q2w (p=0.002). Main efficacy outcomes for both phases of the study are presented in the table. Rates of serious adverse events (AEs) and AEs leading to drug discontinuation were similar in patients treated with mono or combination therapy, and in patients treated with TCZ-SC qw or TCZ-SC q2w. At least one serious AE was reported in 3 (4.1 %) patients in the monotherapy group and in 10 (3.1%) patients in the combination therapy group (Phase 1); 2 (2.2%) patients in the TCZ-SC qw group and 1 (1.1%) patient in TCZ-SC q2w group reported at least one serious AE (Phase 2).

<table>
<thead>
<tr>
<th>Phase 1</th>
<th>Outcome</th>
<th>TCZ-SC monotherapy N=74</th>
<th>TCZ-SC Combination N=327</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sustained clinical remission, %</td>
<td>48.4</td>
<td>52.9</td>
<td>0.523</td>
<td></td>
</tr>
<tr>
<td>ACR20, %</td>
<td>79.7</td>
<td>83.3</td>
<td>0.495</td>
<td></td>
</tr>
<tr>
<td>ACR50, %</td>
<td>59.4</td>
<td>58.7</td>
<td>0.923</td>
<td></td>
</tr>
<tr>
<td>ACR70, %</td>
<td>40.6</td>
<td>37.7</td>
<td>0.666</td>
<td></td>
</tr>
<tr>
<td>ACR90, %</td>
<td>23.4</td>
<td>16.7</td>
<td>0.207</td>
<td></td>
</tr>
<tr>
<td>HAQ-DI (baseline/24 weeks), mean</td>
<td>1.49/0.85</td>
<td>1.36/0.82</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Phase 2</th>
<th>Outcome</th>
<th>TCZ-SC 162 mg qw N=89</th>
<th>TCZ-SC 162 mg q2w N=90</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical remission, %</td>
<td>91.5</td>
<td>73.9</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>ACR20, %</td>
<td>96.4</td>
<td>88.8</td>
<td>0.056</td>
<td></td>
</tr>
<tr>
<td>ACR50, %</td>
<td>88.1</td>
<td>79.8</td>
<td>0.766</td>
<td></td>
</tr>
<tr>
<td>ACR70, %</td>
<td>71.4</td>
<td>65.2</td>
<td>0.377</td>
<td></td>
</tr>
<tr>
<td>ACR90, %</td>
<td>45.2</td>
<td>32.6</td>
<td>0.088</td>
<td></td>
</tr>
<tr>
<td>Mean change in DAS28</td>
<td>-0.02</td>
<td>0.35</td>
<td>0.037</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** in the real world setting, treatment with TCZ-SC 162 mg weekly in patients with active RA is associated with rate of sustained clinical remission of approximately 50% regardless it is administered as monotherapy or in combination with a sDMARD. The proportion of patients who remained in clinical remission at week 48 was significantly higher with TCZ-SC qw than with TCZ-SC q2w.

**Disclosure:** R. Sanmartí, None; E. Martín-Mola, Pfizer Inc, Roche, 9; J. E. Fonseca, MSD, UCB, Pfizer, 2, MSD, Biogen, Pfizer, Roche, BMS, Abbvie, Janssen, 9; D. J. Veale, None; A. Escudero-Contreras, None; C. M. Gonzalez, MSD, Celgene, Novartis, Abbvie, Janssen, 5, MSD, Celgene, Novartis, Janssen, UCB Pharma, 8.

Assessment of Dose Dependent Effects of Vobarilizumab, an Anti-IL6 Receptor (IL-6R) Nanobody®, on Systemic Biomarkers in Patients with Moderate-to-Severe Rheumatoid Arthritis (RA): Results of Two Phase 2b Studies

Manuela Rinaldi1, Tom Van Bogaert2, Maarten Van Roy2, Lieselot Bontinck2, Andreas Hohlbaum2, Veerle Snoeck2, Evelyne Dombrecht2, Katrien Van Beneden2, Pieter Schoen2 and Hans Ulrichs2, 1Pharmacology, Ablynx, Zwijnaarde, Belgium, 2Ablynx, Zwijnaarde, Belgium

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Vobarilizumab is a Nanobody consisting of an anti-IL-6R domain and an anti-human serum albumin domain in development for treatment of rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). Main efficacy and safety results of both RA phase 2b studies with vobarilizumab when used in combination with methotrexate (ALX0061-C201) and as monotherapy (ALX0061-C202) were previously reported (ref 1 and 2).

The effect of vobarilizumab on different pharmacodynamic (PD), cartilage degradation and joint inflammation biomarkers was investigated in both studies.

Methods: In study ALX0061-C201, 345 patients were equally randomized to receive during a 24-week treatment period one of the four subcutaneous (s.c.) vobarilizumab dosing regimens (75 mg q4w, 150 mg q2w, 150 mg q4w, 225 mg q2w) or placebo q2w. In study ALX0061-C202, 251 patients were equally randomized to receive during a 12-week treatment period one of the three dosing regimens of s.c. vobarilizumab (150 mg q2w, 150 mg q4w, or 225 mg q2w). An open-label tocilizumab (TCZ) arm was included to obtain parallel descriptive information.

The effect of vobarilizumab and TCZ on the PD biomarkers soluble IL-6 receptor (sIL-6R), C-reactive protein (CRP), fibrinogen and erythrocyte sedimentation rate (ESR) was evaluated descriptively. In addition, matrix metalloproteinase-3 (MMP-3) was evaluated as a cartilage degradation biomarker and chemokine (C-X-C motif) ligand 13 (CXCL13) as a joint inflammation biomarker. Using validated assays, all biomarkers were measured at baseline and over time in serum, except for sIL-6R which was measured in plasma.

Results: As expected, based on vobarilizumab’s mechanism of action, mean plasma total sIL-6R concentrations increased following vobarilizumab administration and remained increased during the treatment period. A rapid decrease of the PD biomarkers CRP, fibrinogen and ESR was observed after the first administration of vobarilizumab. Over time, mean values of CRP and fibrinogen remained low for subjects in the 2 highest dosing regimens (i.e. 150 mg q2w and 225 mg q2w) (see Figure 1 for CRP results). ESR values remained low for all dosing regimens except for the 75 mg q4w dose used in ALX0061-C201 combination therapy study. Following administration of TCZ, comparable profiles were observed for the different PD biomarkers. Both vobarilizumab and TCZ also lead to a gradual decrease of MMP-3 and CXCL13. After vobarilizumab/TCZ treatment discontinuation, an increase of all biomarkers (except for sIL-6R) was observed.
**Conclusion:** The observed dose dependent PD biomarker responses and effects on cartilage degradation and joint inflammation biomarkers further support the strong potential for disease modifying activity of vobarilizumab in RA.

2. Dörner T. et al, EULAR 2017

Figure 1: Mean CRP ± SEM levels in ALX0061-C201 trial.

![Graph showing Mean CRP levels](image)

**Disclosure:** M. Rinaldi, Ablynx, 3; T. Van Bogaert, Ablynx, 3; M. Van Roy, Ablynx, 3; L. Bontinck, Ablynx, 3; A. Hohlbam, Ablynx, 3; V. Snoeck, Ablynx, 3; E. Dombrecht, Ablynx, 3; K. Van Beneden, Ablynx, 9; P. Schoen, Ablynx, 3; H. Ulrichs, Ablynx, 9.


Abstract Number: 2477

**Descriptive Patterns of Switches and Swaps in Patients with Rheumatoid Arthritis Initially Treated with Anti-TNF Agents in First Intention between 2000 and 2006, and 2007 and 2015 – Experience from a Real-World Database RHUMADATA®**

Denis Choquette¹, Louis Bessette², L Coupal³ and Kirsten Garces⁴, ¹University of Montreal Hospital Research Centre (CRCHUM), Notre Dame Hospital Montreal, Montreal, QC, Canada, ²Groupe de Recherche en Rhumatologie et Maladies Osseuses, Quebec, Quebec, QC, Canada, ³Institut de Recherche en Rhumatologie de Montréal (IRRM), Montréal, QC, Canada, ⁴Amgen Canada Inc., Mississauga, ON, Canada
SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Between 2000 and 2006, the only other treatment option for patients with rheumatoid arthritis (RA) first exposed to an anti-TNF agent was another anti-TNF agent. After 2006, agents with a different mode of action became available. The patterns of switches (anti-TNF to anti-TNF) and swaps (anti-TNF to another mode of action) have not been presented in detail. The real-world experience gathered since 2000 gives us a unique opportunity to examine change in prescribing patterns.

Methods: The data of biologic naïve RA patients starting a first anti-TNF [adalimumab (ADA), certolizumab (CER), etanercept (ETA), golimumab (GOL), infliximab (INF) or inflectra] between January 1, 2000 and December 31, 2006 (first era), and January 1, 2007 and December 2015 (second era) was extracted. Patients were followed until they stopped, changed their medication or were lost to follow-up. Switches or swaps could happen at any time. We analyzed the number of patients that stopped, switched or swapped in each treatment era and the time from initial treatment to second treatment or the cessation of treatment. Statistical analysis was performed using SAS version 9.4.

Results: The choice of a second biologic agent among patients having been prescribed their initial between Jan 1, 2000, and Dec 31, 2006, and Jan 1, 2007, and Dec 31, 2015, are presented Table 1. In the first era, switches accounted for 45.9% of cases, with most switching to ETN (42%), followed by ADA (30.6%), INF (19.7%), CER (3.8%), GOL (3.2%) and inflectra (0.6%). In the second era, switches accounted for 31.5% of cases, with most switching to ETN (31.7%), ADA (23.2%), CER (19.5%), GOL (15.9%), INF (7.3%) and inflectra (2.4%). Swaps accounted for 26.0% of cases in the first era. These swaps occurred towards abatacept (ABA), rituximab (RTX), tocilizumab (TOCI) and anakinra in 48.3%, 34.8%, 16.9% and 9.0% of cases. In the second era, the proportion of swaps increased to 38.8% and occurred towards ABA, RTX, TOCI and tofacitinib (TOFA) accounting for 42.6%, 26.7%, 24.8% and 5.9% of cases.

Conclusion: When switching occurs, most patients switched to a second anti-TNF in the first and second era. ETN was the anti-TNF more often selected for the in both eras. In the second era, there was an increased tendency to prescribe agents with a different mode of action after the first anti-TNF agent. This may be due to the availability of biologics with a different mode of action.

Table 1.
Disclosure: D. Choquette, Abbvie, Amgen, BMS, Celgene, Eli Lilly, Hospira, Merck, Novartis, Pfizer, Roche, Sanofi-Genzyme, UCB, Janssen, Sandoz, 8, Abbvie, Amgen, BMS, Celgene, Eli Lilly, Hospira, Merck, Novartis, Pfizer, Roche, Sanofi-Genzyme, UCB, Janssen, Sandoz, 5, Abbvie, Amgen, BMS, Celgene, Eli Lilly, Hospira, Merck, Novartis, Pfizer, Roche, Sanofi-Genzyme, UCB, Janssen, Sandoz, 2; L. Bessette, Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Lilly, Novartis, Sanofi, 8, Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Lilly, Novartis, Sanofi, 5, Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Lilly, Novartis, Sanofi, 2; L. Coupal, None; K. Garces, Amgen, 1, Amgen, 3.


Abstract Number: 2478

Retention on Adalimumab, Etanercept, Golimumab and Infliximab in Two Eras – Experience of Patients with Rheumatoid Arthritis from a Real-World Database RHUMADATA®

Denis Choquette1, Louis Bessette2, Louis Coupal3 and Kirsten Garces4, 1Osteoarthritis Research Unit, University of Montreal Hospital Research Centre (CRCHUM), Montreal, QC, Canada, 2Groupe de Recherche en Rhumatologie et Maladies Osseuses, Quebec, Quebec, QC, Canada, 3Institut de Recherche en Rhumatologie de Montréal (IRRM), Montréal, QC, Canada, 4Amgen Canada Inc., Mississauga, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Anti-TNFs have been used to treat RA since 2000. Since the availability of new agents with different mechanisms of action around 2007, the pattern of use has evolved. The long-term biologic retention rate is a good surrogate marker for effectiveness in the clinical setting. Randomized controlled trials and their open-label extension studies provide information on drug retention in a highly selected patient population. This information, however, is of limited use when prescribing biologics in a real-world setting. Real-world databases, such as RHUMADATA®, provides an excellent opportunity to examine the changes in retention rates over time.

Objectives: To assess the retention of the first-line anti-TNF and evaluate possible differences between two eras, early (2000-2006) and late (2007-2015).

Methods: Data of biologic naïve RA patients starting an anti-TNF [adalimumab (ADA), etanercept (ETA), golimumab (GOL) or infliximab (INF)] between Jan 1, 2000, and Dec 31, 2006 (early era), and Jan 1, 2007, and Dec 2015 (late era) was extracted. Patients were followed until they stopped, changed medication, or were lost to follow-up. Collected data included demographics, concomitant medication, comorbidities, laboratory variables, PROs, and disease activity measures. Infections occurring while on treatment, biologic status (ongoing or stopped) and the reasons for biologic cessation were also extracted. Overall retention was compared using Kaplan-Meier estimates (SAS 9.4). Cox proportional hazard models were used to adjust for differences between groups at baseline.

Results: Baseline variables were similar between the two eras, except that patients in the second era were older and had been diagnosed ~1 year sooner than first era patients. These patients were less exposed to corticosteroids, more
exposed to HCQ, and had lower ESR and CRP at treatment initiation. Over the entire period, ETN had a longest mean retention time of 6.32 years versus ADA (6.24y) and INF (5.6y). This difference was statistically significant between ETN and INF (p=0.026). When analyzed in the two eras, the mean retention times of all biologics were longer in the first era (6.72y) than the second (4.7y).

Conclusion: Patients treated in the first era appear to have more severe disease, greater exposure to corticosteroids and HCQ, and better retention rate compared to patients starting an anti-TNFi after 2006. More analysis should be done to understand these differences.

Disclosure: D. Choquette, Abbvie, Amgen, BMS, Celgene, Eli Lilly, Hospira, Merck, Novartis, Pfizer, Roche, Sanofi-Genzyme, UCB, Janssen, Sandoz, 8, Abbvie, Amgen, BMS, Celgene, Eli Lilly, Hospira, Merck, Novartis, Pfizer, Roche, Sanofi-Genzyme, UCB, Janssen, Sandoz, 5, Abbvie, Amgen, BMS, Celgene, Eli Lilly, Hospira, Merck, Novartis, Pfizer, Roche, Sanofi-Genzyme, UCB, Janssen, Sandoz, 2; L. Bessette, Amgen, BMS, Janssen, Roche, UCB, Abbvie, Pfizer, Merck, Celgene, Lilly, Novartis, Sanofi, 8, Amgen, BMS, Janssen, Roche, UCB, Abbvie, Pfizer, Merck, Celgene, Lilly, Novartis, Sanofi, 5, Amgen, BMS, Janssen, Roche, UCB, Abbvie, Pfizer, Merck, Celgene, Lilly, Novartis, Sanofi, 2; L. Coupal, None; K. Garces, Amgen, 1, Amgen, 3.


Abstract Number: 2479

Duration of Response in a Phase 3 Study of Sarilumab Plus Methotrexate in Patients with Active, Moderate-to-Severe Rheumatoid Arthritis

Mark C. Genovese1, Erin K. Mangan2, Toshib Kimura2, Melitza Iglesias-Rodriguez3 and Tom W.J. Huizinga4,

1Stanford University Medical Center, Palo Alto, CA, 2Regeneron Pharmaceuticals, Inc., Tarrytown, NY, 3Sanofi Genzyme, Cambridge, MA, 4Rheumatology, Leiden University Medical Center, Leiden, Netherlands

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
**Background/Purpose:** Sarilumab is a human mAb blocking the IL-6Rα. In the phase 3, 52-week MOBILITY study (NCT01061736), sarilumab (150 or 200 mg subcutaneously every 2 weeks [q2w]) + MTX demonstrated clinical and radiographic efficacy in adults with active, moderate-to-severe RA and inadequate response to MTX. The most common treatment-emergent adverse events were infections, neutropenia, injection site reactions, and increased transaminases. The objective of this analysis was to examine differences in the mean duration of response based on various definitions of response in MOBILITY.

**Methods:** Patients who achieved a response at any point during the study were considered responders and included in these analyses. If patients had a missing value or took rescue medication, they were considered nonresponders for those specific visits. Patients who did not respond at any visit were excluded from analysis. Five different definitions of duration of response were used: (1) *first response to loss of response* (time from initial response to loss of response); (2) *longest response* (all time segments of response were determined where each segment of response ended after first loss of response, and longest duration of response was selected); (3) *responder weeks* (cumulative number of weeks during which a patient was a responder, excluding nonresponder weeks in between responder weeks); (4) *responder weeks percent* (percentage of weeks during which a patient was a responder, excluding nonresponder weeks in between responder weeks); and (5) *sustained response* (binary analysis [yes/no] of whether the response was maintained until the end of the double-blind period). Duration of response was measured for ACR20, improvement in HAQ–Disability Index (HAQ-DI) of ≥0.3 units, clinical disease activity index (CDAI; ≤2.8), simplified disease activity index (SDAI; ≤3.3), and DAS28-CRP (<2.6).

**Results:** In patients achieving a response at any point in MOBILITY, those treated with sarilumab 150 or 200 mg q2w + MTX had significantly longer duration of response vs those treated with placebo + MTX regardless of definition of response used for ACR20, HAQ-DI, and DAS28-CRP (Table 1). Sarilumab-treated patients achieved significantly longer sustained response by both ACR20 and HAQ-DI, whether they achieved response at week 12 or 24 (Table 2).

**Conclusion:** This analysis examined 5 different definitions of clinical response. Regardless of definition of response used, patients treated with either dose of sarilumab + MTX experienced longer duration of response vs those treated with placebo + MTX.

**Reference:**

Table 1. Duration of Response by Various Definitions

<table>
<thead>
<tr>
<th>Definition of response, least squares mean (SE)</th>
<th>Placebo + MTX (N=398)</th>
<th>Sarilumab 150 mg q2w + MTX (N=400)</th>
<th>Sarilumab 200 mg q2w + MTX (N=399)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACR20</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First response to loss, wk</td>
<td>18.0 (1.2)</td>
<td>22.5 (1.0)*</td>
<td>25.5 (1.0)*</td>
</tr>
<tr>
<td>Longest response (first loss), wk</td>
<td>19.9 (1.0)</td>
<td>28.2 (0.9)*</td>
<td>30.6 (0.9)*</td>
</tr>
<tr>
<td>Responder weeks (first loss), wk</td>
<td>23.4 (1.0)</td>
<td>31.8 (0.9)*</td>
<td>33.9 (0.9)*</td>
</tr>
<tr>
<td>Responder weeks percent (first loss), %</td>
<td>44.8 (1.9)</td>
<td>61.0 (1.7)*</td>
<td>65.0 (1.6)*</td>
</tr>
<tr>
<td><strong>Improvement in HAQ-DI (≥0.3 units)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First response to loss, wk</td>
<td>15.5 (1.2)</td>
<td>22.5 (1.1)*</td>
<td>23.7 (1.1)*</td>
</tr>
<tr>
<td>Longest response (first loss), wk</td>
<td>20.3 (1.1)</td>
<td>27.4 (1.0)*</td>
<td>26.2 (1.0)*</td>
</tr>
<tr>
<td>Responder weeks (first loss), wk</td>
<td>23.2 (1.1)</td>
<td>30.2 (1.0)*</td>
<td>31.2 (1.0)*</td>
</tr>
<tr>
<td>Responder weeks percent (first loss), %</td>
<td>44.4 (2.1)</td>
<td>57.8 (1.9)*</td>
<td>59.7 (1.9)*</td>
</tr>
<tr>
<td><strong>CDAI (≤2.8)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First response to loss, wk</td>
<td>11.3 (1.7)</td>
<td>11.4 (1.2)</td>
<td>13.5 (1.2)</td>
</tr>
<tr>
<td>Longest response (first loss), wk</td>
<td>12.9 (1.7)</td>
<td>14.7 (1.2)</td>
<td>15.8 (1.2)</td>
</tr>
<tr>
<td>Responder weeks (first loss), wk</td>
<td>14.2 (1.8)</td>
<td>17.4 (1.3)</td>
<td>18.2 (1.2)</td>
</tr>
<tr>
<td>Responder weeks percent (first loss), %</td>
<td>27.2 (3.5)</td>
<td>33.3 (2.6)</td>
<td>34.8 (2.4)</td>
</tr>
<tr>
<td><strong>SDAI (≤3.3)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First response to loss, wk</td>
<td>11.2 (1.8)</td>
<td>11.1 (1.2)</td>
<td>13.2 (1.1)</td>
</tr>
<tr>
<td>Longest response (first loss), wk</td>
<td>12.2 (1.8)</td>
<td>14.3 (1.2)</td>
<td>15.6 (1.1)</td>
</tr>
<tr>
<td>Responder weeks (first loss), wk</td>
<td>13.6 (1.9)</td>
<td>17.1 (1.3)</td>
<td>17.8 (1.2)</td>
</tr>
<tr>
<td>Responder weeks percent (first loss), %</td>
<td>28.0 (3.8)</td>
<td>32.8 (2.6)</td>
<td>34.1 (2.2)</td>
</tr>
<tr>
<td><strong>DAS28-CRP (≤2.6)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First response to loss, wk</td>
<td>10.6 (1.5)</td>
<td>15.5 (1.0)*</td>
<td>16.4 (1.0)*</td>
</tr>
<tr>
<td>Longest response (first loss), wk</td>
<td>13.1 (1.4)</td>
<td>20.1 (1.0)*</td>
<td>22.0 (1.0)*</td>
</tr>
<tr>
<td>Responder weeks (first loss), wk</td>
<td>15.4 (1.5)</td>
<td>23.2 (1.0)*</td>
<td>25.8 (1.0)*</td>
</tr>
<tr>
<td>Responder weeks percent (first loss), %</td>
<td>29.4 (2.6)</td>
<td>44.5 (2.0)*</td>
<td>49.4 (1.9)*</td>
</tr>
</tbody>
</table>

CDAI, clinical disease activity index; HAQ-DI, HAQ-Disability Index; q2w, every 2 weeks; SDAI, simplified disease activity index; SE, standard error.  
*P<0.0001, †P<0.001, ‡P<0.01, *P<0.05.  
*Indicates patients who were responders at some point during the study period.

Table 2. Duration of Sustained Response for Patients Achieving Response at 12 and 24 Weeks

<table>
<thead>
<tr>
<th>Sustained response, %</th>
<th>Placebo + MTX (N=398)</th>
<th>Sarilumab 150 mg q2w + MTX (N=400)</th>
<th>Sarilumab 200 mg q2w + MTX (N=399)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACR20</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 12</td>
<td>42 (30.4)</td>
<td>108 (50.0)*</td>
<td>141 (54.4)*</td>
</tr>
<tr>
<td>Week 24</td>
<td>64 (48.1)</td>
<td>150 (64.7)*</td>
<td>164 (69.4)*</td>
</tr>
<tr>
<td><strong>Improvement in HAQ-DI (≥0.3 units)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 12</td>
<td>49 (28.3)</td>
<td>123 (61.5)*</td>
<td>122 (51.9)*</td>
</tr>
<tr>
<td>Week 24</td>
<td>63 (47.4)</td>
<td>151 (74.0)*</td>
<td>143 (69.8)*</td>
</tr>
<tr>
<td><strong>CDAI (≤2.8)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 12</td>
<td>2 (16.7)</td>
<td>4 (28.7)</td>
<td>12 (42.9)</td>
</tr>
<tr>
<td>Week 24</td>
<td>6 (30.0)</td>
<td>17 (41.5)</td>
<td>24 (43.6)</td>
</tr>
<tr>
<td><strong>SDAI (≤3.3)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 12</td>
<td>1 (12.5)</td>
<td>3 (21.4)</td>
<td>13 (43.3)</td>
</tr>
<tr>
<td>Week 24</td>
<td>4 (21.1)</td>
<td>17 (41.5)</td>
<td>25 (50.0)*</td>
</tr>
<tr>
<td><strong>DAS28-CRP (≤2.6)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 12</td>
<td>5 (26.3)</td>
<td>25 (34.7)</td>
<td>40 (43.5)</td>
</tr>
<tr>
<td>Week 24</td>
<td>9 (22.5)</td>
<td>59 (53.2)*</td>
<td>69 (50.7)*</td>
</tr>
</tbody>
</table>

CDAI, clinical disease activity index; HAQ-DI, HAQ-Disability Index; q2w, every 2 weeks; SDAI, simplified disease activity index.  
*P<0.0001, †P<0.001, ‡P<0.01, *P<0.05.  
*Indicates number and percentage of patients who were responders at a specified visit (week 12 or 24) and sustained a response to study end.

Disclosure: M. C. Genovese, Roche, Sanofi, GlaxoSmithKline, R-Pharm, and Bird Rock Bio. 2, Roche, Sanofi, GlaxoSmithKline, R-Pharm, and Bird Rock Bio. 5; E. K. Mangan, Regeneron Pharmaceuticals, Inc. 1, Regeneron Pharmaceuticals, Inc. 3; T. Kimura, Regeneron Pharmaceuticals. 3, Regeneron Pharmaceuticals. 1; M. Iglesias-Rodriguez, Sanofi Genzyme. 1, Sanofi Genzyme. 3; T. W. J. Huizinga, Sanofi, Roche, and Abblynx. 5.
Improvements in Remission and Low Disease Activity Are Achieved with Ongoing Sarilumab Treatment, in Patients with Rheumatoid Arthritis in 2 Phase 3 Studies

Mark C. Genovese¹, Erin K. Mangan², Jonathan Fay², Toshio Kimura², Hubert van Hoogstraten³ and Roy Fleischmann⁴, ¹Stanford University Medical Center, Palo Alto, CA, ²Regeneron Pharmaceuticals, Inc., Tarrytown, NY, ³Sanofi Genzyme, Bridgewater, NJ, ⁴Metroplex Clinical Research Center, University of Texas Southwestern Medical Center, Dallas, TX

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Sarilumab is a human mAb blocking the IL-6Ra. Efficacy and safety of sarilumab (150 or 200 mg subcutaneously every 2 wks [q2w]) + conventional synthetic (cs)DMARDs were demonstrated in patients with active, moderate-to-severe RA in 2 phase 3 studies: the 52-wk MOBILITY study (NCT01061736) in patients with inadequate response to MTX (MTX-IR) and the 24-wk TARGET study (NCT01709578) in patients with inadequate response to or intolerance of TNF inhibitors (TNF-IR). The most common treatment-emergent adverse events in both studies included infections, neutropenia, injection site reactions, and increased transaminases. This post hoc analysis assessed benefit of sarilumab treatment by examining the proportion of patients who achieved treat-to-target goals of remission or low disease activity (LDA) by 1 year in MOBILITY and 6 months in TARGET.

Methods: Adults with active RA were randomized 1:1:1 to receive sarilumab 150 or 200 mg q2w or placebo + background MTX (MOBILITY) or csDMARDs (TARGET). Clinical efficacy was evaluated for remission and LDA using DAS28-CRP (<2.4 and ≤2.9),¹,² clinical disease activity index (CDAI; ≤2.8 and ≤10), and simplified disease activity index (SDAI; ≤3.3 and ≤11) at wks 4, 8, 12, and 24 in TARGET and additionally at week 52 in MOBILITY. Functional remission (HAQ–Disability Index [HAQ-DI] <0.5)³ was also assessed.

Results: In both studies, more sarilumab-treated patients achieved remission (DAS28-CRP only) and LDA (all criteria) vs placebo (Table). Although remission and LDA generally became evident between wks 4 and 8 in most patient groups (nominal P<0.05 vs placebo, both doses), with ongoing sarilumab treatment (both doses), additional patients achieved remission and LDA at each successive time point assessed through wk 24 in both studies; some additional patients achieved remission and LDA between wks 24 and 52 in MOBILITY. Normalization of physical function (HAQ-DI <0.5) was evident in both sarilumab-treated groups in MOBILITY by wk 12 (nominal P<0.05 vs placebo, both doses); a slight increase in the number of patients achieving normalization was observed by wk 52. In TARGET, a small numerical difference in HAQ-DI normalization was seen in favor of sarilumab treatment at all time points even though this endpoint did not achieve nominal significance.

Conclusion: In MTX-IR and TNF-IR patients with RA treated with sarilumab, efficacy became evident as early as wk 4. The numbers of patients who achieved remission or LDA increased through wk 24 with ongoing sarilumab treatment in both studies, with some further increases observed up to wk 52 in MOBILITY.
References:


<table>
<thead>
<tr>
<th></th>
<th>MOBILITY</th>
<th>TARGET</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo + MTX (N=395)</td>
<td>150 mg q2w + 200 mg q2w + csDMARDs (N=181)</td>
</tr>
<tr>
<td><strong>DAS28-CRP &lt;2.4, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wk 4</td>
<td>6 (1.5)</td>
<td>16 (4.0)*</td>
</tr>
<tr>
<td>Wk 8</td>
<td>14 (3.5)</td>
<td>41 (10.3)*</td>
</tr>
<tr>
<td>Wk 12</td>
<td>17 (4.3)</td>
<td>60 (14.8)*</td>
</tr>
<tr>
<td>Wk 24</td>
<td>30 (7.5)</td>
<td>89 (22.3)*</td>
</tr>
<tr>
<td>Wk 52</td>
<td>30 (7.5)</td>
<td>109 (27.3)*</td>
</tr>
<tr>
<td><strong>DAS28-CRP ≤2.9, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wk 4</td>
<td>12 (3.0)</td>
<td>35 (8.8)*</td>
</tr>
<tr>
<td>Wk 8</td>
<td>20 (5.0)</td>
<td>75 (18.8)*</td>
</tr>
<tr>
<td>Wk 12</td>
<td>30 (7.5)</td>
<td>103 (25.8)*</td>
</tr>
<tr>
<td>Wk 24</td>
<td>55 (13.8)</td>
<td>133 (33.3)*</td>
</tr>
<tr>
<td>Wk 52</td>
<td>46 (11.0)</td>
<td>154 (38.5)*</td>
</tr>
<tr>
<td><strong>CDAI ≤2.8, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wk 4</td>
<td>3 (0.8)</td>
<td>5 (1.3)</td>
</tr>
<tr>
<td>Wk 8</td>
<td>7 (1.8)</td>
<td>16 (4.0)</td>
</tr>
<tr>
<td>Wk 12</td>
<td>12 (3.0)</td>
<td>15 (3.8)</td>
</tr>
<tr>
<td>Wk 24</td>
<td>20 (5.0)</td>
<td>41 (10.3)*</td>
</tr>
<tr>
<td>Wk 52</td>
<td>19 (4.6)</td>
<td>55 (14.5)*</td>
</tr>
<tr>
<td><strong>CDAI ≤10, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wk 4</td>
<td>25 (6.3)</td>
<td>36 (9.5)</td>
</tr>
<tr>
<td>Wk 8</td>
<td>28 (7.0)</td>
<td>88 (22.0)*</td>
</tr>
<tr>
<td>Wk 12</td>
<td>55 (13.8)</td>
<td>111 (27.8)*</td>
</tr>
<tr>
<td>Wk 24</td>
<td>75 (18.1)</td>
<td>150 (37.5)*</td>
</tr>
<tr>
<td>Wk 52</td>
<td>70 (19.1)</td>
<td>106 (41.5)*</td>
</tr>
<tr>
<td><strong>SDAI ≤3.3, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wk 4</td>
<td>1 (0.3)</td>
<td>5 (1.3)</td>
</tr>
<tr>
<td>Wk 8</td>
<td>5 (1.3)</td>
<td>15 (3.8)*</td>
</tr>
<tr>
<td>Wk 12</td>
<td>8 (2.0)</td>
<td>14 (3.5)</td>
</tr>
<tr>
<td>Wk 24</td>
<td>19 (4.6)</td>
<td>41 (10.3)*</td>
</tr>
<tr>
<td>Wk 52</td>
<td>16 (4.0)</td>
<td>60 (15.0)*</td>
</tr>
<tr>
<td><strong>SDAI ≤11, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wk 4</td>
<td>22 (5.5)</td>
<td>37 (9.3)*</td>
</tr>
<tr>
<td>Wk 8</td>
<td>27 (6.8)</td>
<td>89 (22.3)*</td>
</tr>
<tr>
<td>Wk 12</td>
<td>52 (13.1)</td>
<td>112 (28.0)*</td>
</tr>
<tr>
<td>Wk 24</td>
<td>74 (18.6)</td>
<td>148 (37.0)*</td>
</tr>
<tr>
<td>Wk 52</td>
<td>73 (18.3)</td>
<td>174 (43.5)*</td>
</tr>
<tr>
<td><strong>HAQ-DI ≤0.5, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wk 0</td>
<td>26 (6.5)</td>
<td>19 (4.8)</td>
</tr>
<tr>
<td>Wk 4</td>
<td>30 (7.5)</td>
<td>34 (8.5)</td>
</tr>
<tr>
<td>Wk 8</td>
<td>34 (8.5)</td>
<td>50 (12.5)</td>
</tr>
<tr>
<td>Wk 12</td>
<td>36 (9.0)</td>
<td>68 (17.0)*</td>
</tr>
<tr>
<td>Wk 24</td>
<td>40 (10.1)</td>
<td>72 (18.0)*</td>
</tr>
<tr>
<td>Wk 52</td>
<td>34 (8.5)</td>
<td>80 (20.0)*</td>
</tr>
</tbody>
</table>

CDAI, clinical disease activity index; csDMARD, conventional synthetic DMARD; HAQ-DI, HAQ–disability index; SDAI, simplified disease activity index; q2w, every 2 wks.

*Nominal P=0.06 vs placebo.

Disclosure: M. C. Genovese, Roche, Sanofi, GlaxoSmithKline, R-Pharm, and Bird Rock Bio, 2, Roche, Sanofi, GlaxoSmithKline, R-Pharm, and Bird Rock Bio, 5; E. K. Mangan, Regeneron Pharmaceuticals, Inc., 1, Regeneron Pharmaceuticals, Inc., 3; J. Fay, Regeneron Pharmaceuticals, 3; Regeneron Pharmaceuticals, 1; T. Kimura, Regeneron Pharmaceuticals, 3; Regeneron Pharmaceuticals, 1; H. van Hoogstraten, Sanofi Genzyme, 3; Sanofi Genzyme, 1; R. Fleischmann, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, EMD Serono, Genentech, GlaxoSmithKline, Janssen, Eli Lilly, Pfizer, Roche, Sanofi, and UCB, 2; AbbVie, Akros Pharma, Amgen, Bristol-Myers Squibb, Genentech, GlaxoSmithKline, Janssen, Eli Lilly, Pfizer, Sanofi, and UCB, 5.
Long-Term Safety of Adalimumab (HUMIRA) in Adult Patients from Global Clinical Trials across Multiple Indications: An Updated Analysis in 29,987 Patients Representing 56,951 Patient-Years

Gerd R. Burmester¹, Remo Panaccione², Kenneth B. Gordon³, James T. Rosenbaum⁴, Dilek Arikan⁵, Winnie L. Lau⁵ and Rita Tarzynski-Potempa⁵, ¹Charité - University Medicine Berlin, Berlin, Germany, ²University of Calgary, Calgary, AB, Canada, ³Medical College of Wisconsin, Milwaukee, WI, ⁴Ophthalmology, Oregon Health & Science University and Legacy Devers Eye Institute, Portland, OR, ⁵AbbVie Inc., North Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Adalimumab is an anti–tumor necrosis factor-α (TNF-α) agent indicated for the treatment of immune-mediated diseases. The long-term safety of adalimumab was previously reported in 23,458 patients representing up to 12 years of clinical trial exposure in rheumatoid arthritis (RA), juvenile idiopathic arthritis, ankylosing spondylitis (AS), psoriatic arthritis (PsA), plaque psoriasis (Ps), and Crohn’s disease (CD). Here we report an updated analysis examining the long-term safety of adalimumab in adult patients with RA, AS, non-radiographic axial spondyloarthritis (nr-axSpA), peripheral SpA (pSpA), PsA, Ps, hidradenitis suppurativa (HS), CD, ulcerative colitis (UC), and non-infectious uveitis (UV).

Methods: Safety data from 78 clinical trials of adalimumab (RA, 33; AS, 5; nr-axSpA, 2; pSpA, 1; PsA, 3; Ps, 13; HS, 3; CD, 11; UC, 4; UV, 2; other, 1) were included in these analyses, including randomized controlled, open-label, and long-term extension studies conducted in Europe, North America, South America, Asia, Australia, New Zealand, and South Africa through December 31, 2016. Adalimumab postmarketing surveillance data were not included in this analysis. Safety assessments included all adverse events (AEs) and serious AEs (SAEs) that occurred after the first adalimumab study dose and up to 70 days (5 half-lives) after the last study dose.

Results: This analysis included 29,987 patients, representing 56,951 patient-years of exposure (Table 1). The majority of adalimumab exposure was in RA studies. The most frequently reported SAE of interest was infection (highest incidences in CD, RA, UV, and UC). Overall and for most of the adalimumab populations (AS, PsA, Ps, UC, CD, and RA), the observed number of deaths was below what would be expected in an age- and sex-adjusted population (Table 2). For HS, nr-axSpA, pSpA, and UV studies, the small size of these trials precluded accurate assessment of the standardized mortality ratio, and the 95% CIs all included 1.0.
Table 2. Standardized Mortality Ratios Across Indications

<table>
<thead>
<tr>
<th>Indication</th>
<th>SMR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA (n=15,511)</td>
<td>0.74</td>
<td>0.63, 0.87</td>
</tr>
<tr>
<td>AS (n=2026)</td>
<td>0.14</td>
<td>0.00, 0.77</td>
</tr>
<tr>
<td>nr-axSpA (n=863)</td>
<td>1.22</td>
<td>0.14, 4.40</td>
</tr>
<tr>
<td>pSpA (n=165)</td>
<td>1.84</td>
<td>0.21, 6.65</td>
</tr>
<tr>
<td>PsA (n=837)</td>
<td>0.34</td>
<td>0.04, 1.24</td>
</tr>
<tr>
<td>Ps (n=3732)</td>
<td>0.34</td>
<td>0.15, 0.64</td>
</tr>
<tr>
<td>HS (n=733)</td>
<td>1.50</td>
<td>0.40, 3.84</td>
</tr>
<tr>
<td>CD (n=3896)</td>
<td>0.44</td>
<td>0.14, 1.02</td>
</tr>
<tr>
<td>UC (n=1739)</td>
<td>0.37</td>
<td>0.12, 0.87</td>
</tr>
<tr>
<td>UV (n=464)</td>
<td>1.23</td>
<td>0.45, 2.68</td>
</tr>
<tr>
<td>Total (N=29,986)</td>
<td>0.65</td>
<td>0.57, 0.74</td>
</tr>
</tbody>
</table>

Conclusion: This analysis of data from clinical trials of adalimumab demonstrated an overall safety profile consistent with previous findings and with the TNF inhibitor class. No new safety signals or tolerability issues with adalimumab treatment were identified and, for most indications, the mortality rate was below what would be expected in an age- and sex-adjusted population. Efficacy and safety data continue to support the well-established benefits of adalimumab for the approved indications.

Disclosure: G. R. Burmester, AbbVie, Bristol-Myers Squibb, MedImmune, Merck, Pfizer, Roche, and UCB; 2, AbbVie, Bristol-Myers Squibb, MedImmune, Merck, Pfizer, Roche, and UCB, 5, AbbVie, Bristol-Myers Squibb, Merck, Pfizer, Roche, and UCB, 8; R. Panaccione, Abbott Laboratories, Axcan, Bristol-Myers Squibb, Centocor, Elan, Millenium, and Procter and Gamble, 2, Abbott Laboratories, AstraZeneca, Bristol-Myers Squibb, Centocor, Elan, Ferring, GlaxoSmithKline, Procter and Gamble, Schering-Plough, Shire, and UCB, 5, Abbott Laboratories, AstraZeneca, Byk Solvay, Centocor, Elan, Janssen, Procter and Gamble, Prometheus, Schering-Plough, and Shire, 9; K.
Efficacy and Safety of Switching from Adalimumab to Sarilumab in an Open-Label Extension of a Phase 3 Monotherapy Trial in Patients with Active Rheumatoid Arthritis

Gerd R. Burmester1, Stefano Fiore2, Chih-Chi Hu3, Jonathan Fay4, Eun Bong Lee5 and Mark C. Genovese6,
1Department of Rheumatology and Clinical Immunology, Charité - University Medicine Berlin, Free University and Humboldt University Berlin, Berlin, Germany, 2Sanofi Genzyme, Bridgewater, NJ, 3Sanofi Genzyme, Bridgewater, NJ, 4Regeneron Pharmaceuticals, Inc., Tarrytown, NY, 5Division of Rheumatology, Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea, Republic of (South), 6Stanford University Medical Center, Palo Alto, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Sarilumab is a human mAb blocking the IL-6Ra. Efficacy and safety of sarilumab as monotherapy and combination therapy have been reported.1-3 In MONARCH (NCT02332590), adults intolerant of, inappropriate for, or inadequate responders to methotrexate received subcutaneous sarilumab (200 mg every 2 weeks [q2w]) or adalimumab (40 mg) monotherapy for 24 weeks.2 Sarilumab monotherapy demonstrated superiority to adalimumab monotherapy in reducing disease activity and improving physical function in patients with active RA.2 Safety profiles of both therapies were consistent with published data. Patients in MONARCH who completed the initial double-blind phase could continue in the open-label extension (OLE) in which all patients received sarilumab 200 mg q2w monotherapy.

Methods: Disease activity, physical function, and safety were assessed regularly (Table). Data were used as observed.

Results: A total of 321 patients completed MONARCH, 320 of whom entered the OLE; 155 switched from adalimumab to sarilumab (switch group), and 165 remained on sarilumab (continuation group). At OLE entry, mean DAS28-ESR was 4.46 and DAS28-ESR ≤3.2 was 16.1% in the switch group vs 3.45 and 47.9%, respectively, in the continuation group (P<0.0001 for both endpoints). By week 24 of the OLE, the proportion of patients in the switch and continuation groups who achieved DAS28-ESR ≤3.2 was 49.7% vs 58.8% (P=0.1033), DAS28-ESR <2.6 was 40.0% and 42.4% (P=0.6586), CDAI remission was 12.3% and 18.8% (P=0.1054), and improvement in HAQ-DI of ≥0.3 was 63.9% and 66.7% (P=0.6004), respectively. At week 24 of the OLE, treatment-emergent adverse events (TEAEs; 63.9% vs 57.9%), serious TEAEs (9.0% vs 1.2%), infections (34.2% vs 23.6%), and serious infections (1.9% vs 0%) were
observed in the switch and continuation groups, respectively, with 1 death in the switch group (malignancy) and no deaths in the continuation group. Discontinuations due to TEAEs occurred in 5.8% of patients in the switch group and 3.6% in the continuation group.

**Conclusion:** In the OLE of a randomized clinical trial, patients switching from adalimumab 40 mg monotherapy to open-label sarilumab 200 mg q2w monotherapy demonstrated improvements in physical function and in the signs and symptoms of RA, which became numerically similar to patients who were initially randomized to sarilumab 200 mg q2w. Safety observations in the OLE were generally consistent with what was observed in the randomized portion of the study.

**References:**


**Table. Efficacy Endpoints in the Open-label Extension of MONARCH (ITT Population)**

<table>
<thead>
<tr>
<th>Disease activity</th>
<th>Baseline MONARCH</th>
<th>Week 9 OLE</th>
<th>Week 24 OLE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Switch group (adalimumab 40 mg → sarilumab 200 mg q2w) (n=165)</td>
<td>Continuation group (adalimumab 200 mg q2w) (n=165)</td>
<td>Switch group (adalimumab 40 mg → sarilumab 200 mg q2w) (n=165)</td>
</tr>
<tr>
<td></td>
<td>155</td>
<td>165</td>
<td>155</td>
</tr>
<tr>
<td></td>
<td>6.74 (0.83)</td>
<td>6.81 (0.76)</td>
<td>4.46 (1.23)</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td></td>
<td>-1.053 (-1.34)</td>
</tr>
<tr>
<td></td>
<td><strong>p</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily HAI-60 improvement ≥0.3, N (%)</td>
<td>155 (104)</td>
<td>165 (105)</td>
<td>155 (104)</td>
</tr>
<tr>
<td></td>
<td>6 (0.9)</td>
<td>7 (1.0)</td>
<td>6 (0.9)</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td></td>
<td>-2.88 (0.91)</td>
</tr>
<tr>
<td></td>
<td><strong>p</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Disclosure:**

G. R. Burmester, AbbVie, Bristol-Myers Squibb, MedImmune, Merck, Pfizer, Roche, and UCB, 2,AbbVie, Bristol-Myers Squibb, MedImmune, Merck, Pfizer, Roche, and UCB, 5,AbbVie, Bristol-Myers Squibb, Merck, Pfizer, Roche, and UCB, 8; S. Fiore, Sanofi Genzyme, 1,Sanofi Genzyme, 3; C. C. Hu, Sanofi-Genzyme, 1,Sanofi Genzyme, 3; J. Fay, Regeneron Pharmaceuticals, 3,Regeneron Pharmaceuticals, 1; E. B. Lee, Pfizer Inc, 5; M. C. Genovese, Roche, Sanofi, GlaxoSmithKline, R-Pharm, and Bird Rock Bio, 2,Roche, Sanofi, GlaxoSmithKline, R-Pharm, and Bird Rock Bio, 5.


**Abstract Number:** 2483
Cycling Versus Swapping in Patients with Rheumatoid Arthritis with an Inadequate Response to at Least One Tumor Necrosis Factor Alpha Inhibitor: A Systematic Review and Meta-Analysis of Observational Studies

Maria A. Lopez-Olivo, Aliza Matusevich and Maria Suarez-Almazor, Section of Rheumatology and Clinical Immunology, Department of General Internal Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA, Houston, TX

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: In patients with rheumatoid arthritis (RA) who do not respond or lose response to a tumor necrosis factor inhibitor (TNFi), opinions are divided on whether it is better to try an alternative TNFi (cycling) or switch to a therapy with a different mode of action (swapping). The purpose of the review was to compare the effectiveness and safety of the cycling versus the swapping strategies as reported in observational studies.

Methods: We searched 4 electronic databases, sources of gray literature, and bibliographic references of relevant articles for observational studies evaluating the efficacy and safety of targeted therapies in adult RA patients who failed to respond to at least one TNFi. Studies were excluded if they were single-arm or had insufficient data to evaluate the outcomes of interest. Two independent reviewers selected studies, extracted data and evaluated study quality using the Newcastle-Ottawa Scale (NOS). Our primary outcome measure was change in Disease Activity Score of 28 joints (DAS28). We also evaluated the modified American College of Rheumatology 20%, 50% and 70% response criteria (mACR which excludes acute phase reactants) and total serious adverse events. All analyses were based on the random-effects model.

Results: Of 33,716 citations, 24 observational studies (n=10,074 patients) representing 14 countries, met the inclusion criteria. Eight were conference abstracts. Most publications (13 of 24) were based on registries. Most studies had a NOS score equal to or greater than 7 (out of 9) with comparability being the weakest domain. The mean age of patients was 48.7-62.8 years, the majority were females (78%) with a disease duration of 6-17.3 years and a baseline disability score 0.6-2.0. Sixteen studies evaluated cycling versus swapping directly of which 13 were suitable for analysis. Most compared TNFi to rituximab (10 of 13) with two studies investigating tocilizumab or abatacept and one comparing non-TNFi as a group. Other comparisons reported were: (i) cycling vs. another cycling alternative, (ii) swapping vs. another swapping alternative, and (iii) swapping monotherapy vs. swapping combined with cDMARDs. At 12 and 24 weeks, DAS28 score improved significantly in those swapping compared to those cycling (mean difference (MD) 0.89, 95% confidence interval (CI) 0.05 to 1.74 and MD 0.34 95% CI: 0.2, 0.48; respectively). Similar results were observed for the mACR50 favoring the swapping strategy at 24 weeks (OR = 1.45 95%CI: 1.06, 1.98). However, at 52 weeks no difference was observed. No statistically significant differences were observed between groups in the odds of achieving DAS28 remission, mACR20 or mACR70, or experiencing a serious adverse event.

Conclusion: Current evidence from observational studies shows greater improvements with the swapping strategy compared with the cycling strategy in terms of efficacy for RA patients failing their first TNFi. No differences were observed regarding safety. Data were not available for anakinra, certolizumab pegol, golimumab, or tofacitinib.

Disclosure: M. A. Lopez-Olivo, Rheumatology Research Foundation, 2; A. Matusevich, None; M. Suarez-Almazor, Pfizer Inc, 5.
Abstract Number: 2484

**When Etanercept Switch Fails – Clinical Considerations**

Oliver Hendricks and **Kim Hørslev-Petersen**, King Christian X's Hospital for Rheumatic Diseases, University of Southern Denmark, Institute of Regional Health Research, Denmark, Graasten, Denmark

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

On January 14th 2016 EMA approved the biosimilar Etanercept (SB4, Benepali) for clinical use. A non-medical switch from originator Etanercept (ETA, Enbrel) to SB4 was conducted in all Danish outpatient clinics in 2016. Disease activity was largely unaffected in the majority of patients; however 9 patients stopped treatment during the follow-up. There is limited outcome data in switch failures.

**Methods:**

At King Christian X’s Hospital for Rheumatic Diseases, a non-medical switch from ETA to SB4 was carried out in June 2016. Clinical assessment was performed at baseline, after 4 and 8 month. We recorded clinical outcome measurements according to the Danish DANBIO registry for RA and AS. In case of a lack of effect (LOE) and/or adversive events (AE) during the first 4 month after switch, we altered the biologic treatment based on the following objectives:

A. The clinical situation on Enbrel was stable, but Flare (ASDAS >2.1 or DAS28CRP > 3.2) observed at least once during a 24 month period before switch.

B. The clinical situation on Enbrel was characterized by complete remission (ASDAS rate < 1.2 or DAS28CRP < 2.6) for at least 24 months.

**Results:** We registred unchanged efficacy after switch in 76 out of 85 cases. In nine cases we recorded significant LOE and/or AE during the first 4 month after switch. Four of the nine cases matched scenario A. The treatment with Benepali continued in two of those cases. In the other two cases a change to a third biologic treatment was performed due to prolonged disease activity. Five cases matched scenario B (One case of AE, three cases of LOE and one case of combined AE & LOE).The patients had experienced complete remission at least for 2 (and up to 9) years. In these cases we interpreted Benepali to be potentially causative and performed the switch back to Enbrel. All five patients regained complete remission without further adversive events.

**Conclusion:**

No studies exist, that investigate the outcome of Etanercept switch on an individual level. In our study, 89% of the patients experienced the non-medical switch to Benepali as the uncomplicated continuation of a successful treatment. For the last 11 % the situation was different. From the patient’s perspective, it is obvious that experienced AE’s and/ or LOE’s are suspicious to be a consequence of the switch. A meticulous assessment and documentation before
performing the switch is crucial. It is our experience that a prolonged SB4 treatment was adequate in those cases, where the doctor was able to illustrate that episode(s) of Flares also previously had occurred.

In contrast, complete remission before switch followed by significant LOE’s or AE’s after switch, led to considerations about the structural differences of the compounds. Furthermore, it has to be taken into account, that the patient’s willingness to continue with Benepali is limited in this situation.

Explaining the patient that “the same current comes out of the socket, even though the new factory creates the electricity” keeps true in almost 90 % of the cases, but switch failure is a challenge. We switched back to Enbrel in five cases of significant contrast of clinical outcome before and after switch. The Switch back was successful in these cases.

Disclosure: O. Hendricks, Abbvie, Roche, Novartis, 2; K. Hørslev-Petersen, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/when-etanercept-switch-fails-clinical-considerations

Abstract Number: 2485

Outcomes of Switching from TNF Inhibitors to Subcutaneous Golimumab in Patients with Rheumatoid Arthritis to Control Disease Activity or Adverse Events

Hiroki Wakabayashi1, Hitoshi Inada2, Yosuke Nishioka3, Masahiro Hasegawa1,4, Kusuki Nishioka5 and Akihiro Sudo6, 1Department of Orthopaedic Surgery, Mie University Graduate School of Medicine, Tsu City, Mie, Japan, 2Orthopaedic Surgery, Suzuka General Hospital, Suzuka, Japan, 3Clinical Research Institute for Rheumatic Disease, Shima, Japan, 4Mie University Graduate School of Medicine, Tsu, Japan, 5Tokyo Medical University, Shinjuku, Japan, 6Department of Orthopaedic Surgery, Mie University Graduate School of Medicine, Tsu City, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Tumor necrosis factor alpha (TNFα) inhibitors have been used to treat rheumatoid arthritis (RA) for >10 years. The outcomes has revolutionized the treatment goal of RA to clinical remission, structural remission and functional remission. Although the efficacy of this drug as a treatment for patients with active RA has been widely demonstrated, some RA patients initially respond to treatment but subsequently their responsiveness decreases. One of the alleged reasons for this phenomenon is immunogenicity associated with the drug itself. Thus, it is useful to switch to a less immunogenic biologic agent to maintain disease activity and minimize adverse events. Golimumab is less immunogenic compared other TNF inhibitors.

The purpose of this study was to evaluate the efficacy and safety of switching from tumor necrosis factor (TNF) inhibitor to subcutaneous golimumab (GLM-SC) in RA patients for maintenance of disease activity or adverse events.

Methods: Thirty-seven patients who had treated with infliximab, etanercept or certolizumab pegol were switched to GLM-SC for maintenance of disease activity or adverse event. The patients were divided into three groups: the LDA group and the LDAq8w group, which included patients with low disease activity or remission who switched to GLM therapy at 50 mg at 4-week and 8-week intervals, respectively; and the MDA group, which included patients with
moderate disease activity who switched to GLM therapy at 50 mg at 4-week intervals. Effects of TNF inhibitors to GLM-SC switch were evaluated at week 12, 24 and 52 after switching.

Results: A total of 37 patients were analyzed during the survey period: 16 in the LDA group, 14 in the LDAq8w group, and 7 in the MDA group. The mean DAS28-ESR and -CRP values in the LDA and LDAq8w groups maintained from baseline throughout the 52-week treatment period. The proportions of patients who achieved DAS28-ESR remission (defined as < 2.6) in the LDA group and the LDAq8w group were maintained over time from 75.0% (12/16) and 78.6% (11/14) at baseline to 93.8% (15/16) and 92.3% (13/14) at week 52, respectively. There were no patients in flare to moderate or high disease activity. In the MDA groups, the mean (± SD) DAS28-ESR values improved significantly from 4.2 (± 0.6) at baseline to 3.1 (±0.7) and 2.8 (± 0.8) at 24 and 52 weeks, respectively. There were no patients in flare to high disease activity. Treatment discontinuations due to adverse events occurred 1 patient in the MDA group, and no serious adverse events occurred during the observation period in the LDA group or the LDAq8w group. Treatment continuation rate at 52 weeks was 100% in the LDA and LDAq8w group and 85.7% in the MDA group.

Conclusion: Clinical efficacy in GLM-SC treated patients were sustained or improved in patients switched from TNF inhibitors without serious safety concerns. The present results indicate that therapeutic efficacy is adequately maintained in the majority of Japanese RA patients who switch from TNF inhibitors to GLM-SC. We also consistently demonstrated the safety of this therapy. These results provide supportive evidence for use of GLM-SC for continued control of RA disease activity.

Disclosure: H. Wakabayashi, None; H. Inada, None; Y. Nishioka, None; M. Hasegawa, None; K. Nishioka, None; A. Sudo, None.


Abstract Number: 2486

Rituximab Is an Attractive Proposition to Treat Difficult Active RA in Indian (Asia) Patients: Initial Results of a Non Commercial Initiative Using an Initial Regimen of Two 500 Mg Infusions (fortnightly) and a Third 500 Mg Infusion at 6 Weeks in Case of Inadequate Response(ACR 50)

Arvind Chopra1, KIRAN ADAM2, NACHIKET KULKARNI3, Anuradha Venugopalan4, Toktam Kainifard5 and Manjit Saluja6, 1Center for Rheumatic Diseases, Pune, India, Pune, India, 2Rheumatology physician, PUNE, India, 3MD, DNB, PUNE, India, 4Rheumatology, R & D, Lab, Center for Rheumatic Diseases, Pune, India, 5Rheumatology, Consultant research and Dietitian, Pune, India, 6Rheumatology, Co-ordinator Research, Pune, India

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Considering the huge burden of RA in India, the use of biologic DMARDs is miniscule. The major deterrents are cost, poor awareness and few rheumatologists. Despite an inherent appeal, Rituximab (RTX) is yet to find favour. Encouraged by a generous donation of Rituximab (Ristovos™/ RTX) vials, we designed a protocol driven
observational study to determine the response to RTX in RA and optimize outcome. We present initial results. The study is ongoing.

**Methods:** 60 consenting patients (ACR 1987 classified, 80% women, mean age 45.2 years, 100% seropositive RF/anti CCP, 92% erosive, 35% deformities) with active severe RA (mean disease duration 92 months, mean DAS 28 ESR 6.5) despite prolonged methotrexate (mean dose 18.5 mg weekly) and often steroid intake (8.5 mg daily) were enrolled to receive RTX (2 infusions, 500 mg each, fortnightly) in a community rheumatology centre; standard screening included that for TB. We use ACR recommended 68/66 joint count and efficacy measures in routine practice; validated Indian HAQ version. Clinical status and background medication (especially methotrexate and steroids) was monitored at week 6, 12, 24 and 36 as per protocol. 31 Patients failed ACR 50 (primary response) at week 6 and were randomized into 2 arms [500 mg RTX infusion (third) plus 120 mg injectable methylprednisolone (M-Pred) in 14 patients or only 120 mg M-Pred in 17 patients]. At subsequent evaluations, all ACR 50 non-respondents received single 120 mg M-Pred. Comprehensive laboratory work up included CD 19 cell count (Beckman Coulter FC 500). Standard statistical analysis was performed; significant p < 0.05. 54 patients completed 24 weeks and 50 patients completed 36 weeks.

**Results:** Patients improved significantly in joint counts, pain VAS and HAQ by week 24 & 36 (p<0.05), mean DAS 28 reduced to 3.1 (low disease activity). General Health improved from 5.2 to 7.3 [mean VAS, 0 (poor) to 10 cm (optimum)]. Patients with ACR 50 response at week 6 had least CD 19 count and were likely to maintain response by week 34. Patients receiving 3 infusions had the lowest CD 19 count at week 12. Table shows (percent patients) ACR 50 & 70 response. The additional RTX infusion did not seem to confer any obvious benefit. Two patients withdrew soon after the initial infusions (1 developed severe febrile cytopenia, anaemia and mucositis). None of the patients completing 36 weeks withdrew due to AE, albeit mild (dyspepsia, skin rash, mucositis, upper respiratory infections and headaches). We admit several confounders and limitations.

**Conclusion:** In this true to life Indian study, patients with difficult RA were treated with a relatively lower dose Rituximab but showed a significant sustained improvement for least 36 weeks. The ACR 50 and 70 response was strikingly encouraging. The role of Rituximab in certain subjects (RA) may be profound. We beseech an early validation study by the innovator.
<table>
<thead>
<tr>
<th>Patient Category / Evaluation visit (weeks)</th>
<th>R II (n=23)</th>
<th>NR II (n=17)</th>
<th>NR III (n=14)</th>
<th>TOTAL (n=54)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 6 *</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>43</td>
</tr>
<tr>
<td>Week 12 83 (43)</td>
<td>71 (31)</td>
<td>71 (14)</td>
<td>80 (35)</td>
<td></td>
</tr>
<tr>
<td>Week 24 80 (38)</td>
<td>65 (6)</td>
<td>64 (14)</td>
<td>76 (37)</td>
<td></td>
</tr>
<tr>
<td>Week 36 78 (47)</td>
<td>63 (20)</td>
<td>86 (14)</td>
<td>80 (36)</td>
<td></td>
</tr>
</tbody>
</table>

*Patients were classified as per ACR 50 response and Rituximab infusion regimen at week 6; R II: ACR 50 respondent at week 6 after two infusion of Rituximab (RTX) at baseline; NR II: ACR 50 Non-respondent at week 6 after two infusion of RTX at baseline (randomized); NR III: ACR50 Non-respondent at week 6 after two infusion of Rituximab (RTX) at baseline and randomized to receive third infusion; ACR 70 response shown in parenthesis above; n: number of patients of RA in study

**Disclosure:** A. Chopra, None; K. ADAM, None; N. KULKARNI, None; A. Venugopalan, None; T. Kainifard, None; M. Saluja, None.


**Abstract Number:** 2487

**Comparison the Long-Term Clinical Outcomes between Non Anti-TNF Versus Anti-TNF in RA Patients Who Failed to a First Anti-TNF**

**Patricia Bogas**¹, Chamaida Plasencia-Rodriguez¹, Alejandro Balsa¹, Victoria Navarro-Compán², Gema Bonilla¹, Enrique Moral Coro¹, Carolina Tornero¹, Laura Nuño¹ and Diana Peiteado³, ¹Hospital Universitario La Paz, Madrid, Spain, ²Rheumatology, Hospital Universitario La Paz, Madrid, Spain, ³Rheumatology, La Paz University Hospital, Madrid, Spain

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** There are many biological therapies for Rheumatoid Arthritis (RA) with different mechanisms of action and good efficacy rate; however, up to 40% of patients (pts) fail to respond to the 1st biologic agent, and it is still not clear what strategy to follow after showing inadequate response to tumor necrosis factor α inhibitors (TNFi). Our objective was to assess the clinical response and survival (SVV), in our cohort of RA pts that discontinued the 1st
TNFi, of a 2nd TNFi vs a nonTNFi, both in the global cohort and in the subpopulation that dropped out the 1st TNFi due to inefficacy

Methods: This observational study included 149 pts in the RA-Paz cohort who previously suspended Infliximab, Adalimumab, Etanercept and Certolizumab between 1999-2016. Two groups were established as they switched to a TNFi or nonTNFi. Clinical response was evaluated by DAS28, Delta-DAS28 (ΔDAS28) and EULAR response (E-resp). The assessments were performed at 6 (v-6) and 12 months (v-12) since initiating 2nd biological agent and during the last visit prior to drug discontinuation or ending of the study for those who did not interrupt the drug (v-end). T tests and Fisher’s exact test were used to test statistical differences. Analysis was performed using SPSS 20.0

Results: Of the 149 pts who had stopped their 1st TNFi, 61% changed to a 2nd TNFi. The 81% of the overall pts were women. The mean age was 62±14 years and the mean time of 2nd biologic drug was 3.03±3.2 years. 58% associated methotrexate at the beginning of 2nd biologic agent, without differences between groups. At v-6 and v-12, there was no difference in ΔDAS28 [at v-6: 1.3±1.4 in TNFi and 1.2±1.2 in nonTNFi (p=0.95), at v-12: 1.3±1.4 in TNFi and 1.4±1.1 in nonTNFi (p=0.88)]. In contrast, at v-end, pts with nonTNFi showed a higher clinical improvement (ΔDAS28: 0.8±1.7 in TNF-i, 1.7±1.2 in nonTNFi, p=0.001). At v-6, the TNFi group achieved higher good E-resp rate (39% vs 18%, p=0.01), but there was no difference at v-12 (34% in TNF-I vs 23% in nonTNFi, p=0.42). However, at v-end, the nonTNFi group achieved better E-resp (good resp: 37% in nonTNFi vs 26% in TNFi, no resp 18% in nonTNFi vs 50% in TNFi, p=0.005). Likewise, 100% (n=9) of the pts that finished 2nd biologic agent by remission, had changed to a nonTNFi (p<0.00001). There were no differences regarding 2nd biologic drug SVV (mean SVV time of 5.2±0.6 in TNFi, 4.4±0.5 in nonTNFi, p=0.507). A multivariate analysis adjusted for possible confounding factors (sex, age, smoking, RF, anti-CCP and basal DAS28 and DMARDs) was performed; same behavior as in the main analysis was observed. When analyzing the cohort that discontinued 1st TNFi because of inefficacy, at v-6 and v-12 there were no differences between switchers to TNFi and nonTNFi in ΔDAS28 (p=0.192), but at v-end, the nonTNFi group reached a higher ΔDAS28 (0.9±1.5 in TNFi, 1.7±1 in nonTNFi, p=0.031)

Conclusion: In our sample of RA patients who suspended Ifx/Ada/Etn/Ctz as 1st TNFi, switching to a 2nd biologic agent did not show relevant clinical differences between a TNFi and a nonTNFi within the 1st year of treatment. However, in the long-term, switching to a nonTNFi shows enhanced clinical benefits with no impact on survival vis-à-vis a 2nd TNFi. Despite the efficacy of TNFi, new therapeutic targets are needed.

Disclosure: P. Bogas, None; C. Plasencia-Rodriguez, None; A. Balsa, None; V. Navarro-Compán, None; G. Bonilla, None; E. Moral Coro, None; C. Tornero, None; L. Nuño, None; D. Peiteado, None.


Abstract Number: 2488

Golimumab Retention Rate in Patients with Rheumatoid Arthritis. Predictors of Long-Term Retention

Belen Serrano1, Carlos M Gonzalez2, Roberto González3, Julia Martinez-Barrio4, Juan Gabriel Ovalles-Bonilla5, Juan Carlos Nieto2, Justina Janta2, Larissa Valor3, Francisco Javier López Longo6 and Indalecio Monteagudo2, 1Rheumatology, Hospital General Universitario Gregorio Marañón, Genoa, Italy, 2Rheumatology, Hospital General Universitario Gregorio Marañón, Madrid, Spain, 3Rheumatology, Hospital general Universitario Gregorio Marañón, Madrid, Spain, 4Servicio de Reumatologia, Hospital General Universitario Gregorio Marañón, Madrid, Spain, 5Instituto de Investigación Sanitaria Gregorio Marañón, Madrid, Spain, 6Facultad de Medicina, Universidad Complutense de Madrid, Madrid, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The efficacy of Golimumab (GLM) treatment in rheumatoid arthritis (RA) has been widely documented. The aim of this study was to analyse the long-term retention of GLM and to identify independent predictors of drug retention in patients with AR.

Methods: Prospective monocentric cohort of RA patients treated with GLM according with clinical practice. Study was approved by local Ethics Committee. Demographic and clinical variables were analyzed with Cox proportional hazard regression model.

Results: 61 patients were included. The baseline characteristics of the patients are shown in Table 1. Mean follow-up time 26.8 months (SD 26.1). Mean survival time was 46.3 months (95% CI: 35.6-57.1) Age, gender, DAS28 at baseline, rheumatoid factor (RF), antibodies anti-cyclic citrullinated peptide (anti-CCP), concomitant DMARD and previous treatment with biological therapy were considered in the univariate analysis.

Table 1. Baseline demographic and clinical characteristics of the patients.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age -mean (SD)- years</td>
<td>55.1 (14.1)</td>
</tr>
<tr>
<td>Female gender %</td>
<td>85.2%</td>
</tr>
<tr>
<td>Mean evolution time (SD) years</td>
<td>10.2 (8.1)</td>
</tr>
<tr>
<td>SCJ -mean-(SD)</td>
<td>4.1 (3.6)</td>
</tr>
<tr>
<td>DAS28 -mean-(SD)</td>
<td>4.7 (1.4)</td>
</tr>
<tr>
<td>RF+ %</td>
<td>70%</td>
</tr>
<tr>
<td>Anti-CCP + %</td>
<td>78%</td>
</tr>
<tr>
<td>Concomitant DMARD %</td>
<td>74.6%</td>
</tr>
<tr>
<td>Biological therapy naïve %</td>
<td>53.3%</td>
</tr>
</tbody>
</table>

Upon Cox regression analysis, concomitant DMARD [HR 2.6 (95% CI 1.2-5.8)] and use of GLM as first biological [HR 6.3 (95% CI 2.5-15.8)] were predictors of better GLM retention rate. When analyzing the number of previous biologics, GLM retention rate was not statistically different as first or second biologic [HR 5.3 (95% CI: 0.8-32.4)]. GLM retention rate was significantly worst when used as third or fourth biological [HR 19.8 (95% CI 4.3-89.9)]. Figure 1. 27/61 (44.3%) patients discontinued GLM, 18/27 (66.7%) due to lack of efficacy, 8/27 (29.6%) due to adverse event and 1/27 (3.7%) for other reasons.
Conclusion: Real life long term Golimumab retention rate was good. Golimumab survival time was better when used as first or second biological and with concomitant DMARD.

Disclosure: B. Serrano, None; C. M. Gonzalez, MSD, Celgene, Novartis, Abbvie, Janssen, 5, MSD, Celgene, Novartis, Janssen, UCB Pharma, 8; R. González, None; J. Martínez-Barrio, None; J. G. Ovalles-Bonilla, Pfizer, Roche, BMS, Asacpharma, Nordic Pharma, 8, Sanofi-Aventis Pharmaceutical, 5; J. C. Nieto, Roche Pharmaceuticals, MSD, Abbvie, Novartis, Celgene, BMS, 8; I. Janta, None; L. Valor, Roche, Novartis, Celgene, Janssen; Sanofi, 8; F. J. López Longo, None; I. Monteagudo, None.


Abstract Number: 2489

Efficacy and Survival of Biologic DMARD Therapies As Monotherapy: Real World Data

Jose A Gómez-Puerta¹,², Natalia Duque Zapata¹, Luis Alonso Gonzalez¹,³, Carmen Cerón¹, Monica Vásquez¹ and Oscar Jair Felipe Diaz¹,⁴,¹ Medicarte IPS, Medellín, Colombia, ²Grupo de Reumatología, Universidad de Antioquia, Medellín, Colombia, ³Grupo de Reumatología, Universidad de Antioquia, Medellín, Colombia, ⁴Clinica Las Vegas, Medellín, Colombia

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM
**Background/Purpose:** According to different international registries, around one third of patients under biologic DMARD (bDMARD) with rheumatoid arthritis (RA) are receiving bDMARD as monotherapy (1-4). In Latin-American countries, the efficacy and survival of bDMARD as monotherapy is less well known (5). Our aim was to analyze efficacy and survival rates of bDMARD therapies (either anti TNF and non anti TNF) in a cohort of Colombian RA patients.

**Methods:** We conducted a cross-sectional study including patients with diagnosis of RA treated at Medicarte IPS from March 2009 to December 2016. Medicarte is a referral center for the integral medical care and pharmaco-surveillance of patients under biologic therapies in 13 cities in Colombia. Clinical information was obtained from electronic clinical records. Only those patients with complete information including disease activity indexes at baseline and at the last follow-up were included. We defined remission if DAS-28 (ESR) was < 2.6. Survival rates were analyzed using Kaplan-Meier survival curve. Patients were censored if fail to maintain remission or due to loss of follow-up.

**Results:** From 1,020 patients with RA under bDMARD, we identified 139 (13.6%) patients treated as monotherapy. 90% of them were female with a mean age of 56.6 ± 10.9 years. Mean disease duration was 16.8 ± 9.9 years and mean time under bDMARD was 3.3 ± 2.4 years. Eighty three percent of patients were seropositive (FR and/or CCP) and mean DAS28 at baseline of bDMARD therapy was 4.23 ± 1.0. 102 (73%) out of 139 patients in monotherapy were on non anti TNF and 37 (27%) on anti TNF. From non-anti TNF therapies, tocilizumab was used in 52 patients, rituximab in 25 and abatacept in 25 patients. At last visit, remission rates were higher in patients under non-anti TNF vs anti TNF (70.6 vs 54%, p=0.069). Low disease activity rates were similar in both groups (77.5% vs 70.3%, p=0.384). Five year survival rates were significantly higher in patients treated with non-anti TNF vs anti TNF therapies. Among non-anti TNF therapies, survival rates were significantly higher in patients treated with tocilizumab, than in patients treated with rituximab or abatacept.

**Conclusion:** In our cohort of RA patients under bDMARD, 13% of patients are receiving biologic as monotherapy. Survival rates in terms of remission, were higher in patients under non anti TNF therapies, especially in patients treated with tocilizumab.


**Disclosure:** J. A. Gómez-Puerta, AbbVie,BMS, Pfizer, Roche, 8; N. Duque Zapata, None; L. A. Gonzalez, Abbvie, Janssen, Pfizer, 8; C. Cerón, Pfizer Inc, Novartis, 8; M. Vásquez, None; O. J. Felipe Diaz, Abbvie, BMS, Pfizer, Janssen, Roche, 8.


Abstract Number: 2490

**Sustained Clinical Response in Refractory Rheumatoid Arthritis Patients with a Low-Dose Rituximab Retreatment Regimen. a Single Center Experience**

**Sebastian C Rodriguez-Garcia,** Raul Castellanos-Moreira Sr., M. Victoria Hernández, Andrea Cuervo, Virginia Ruiz-Esquide, Julio Ramírez, Juan Cañete and Raimon Sanmartí, Rheumatology Service, Hospital Clinic de Barcelona, Barcelona, Spain

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Tuesday, November 7, 2017
Background/Purpose: The standard dose of rituximab (RTX) in rheumatoid arthritis (RA) is two intravenous (iv) 1 g infusions, separated by two weeks. Recently, the efficacy of a low-dose of RTX for retreatment in RA patients has been reported (1). Our aim is to assess the long-term sustained effectiveness of a low-dose of RTX in daily clinical practice.

Methods: Observational retrospective study in a tertiary hospital. We included all RA patients that have received at least one cycle of RTX, at a standard dose, between May 2006 and May 2017. We selected those patients who achieved a good or moderate EULAR response, and thereafter were down-titrated to a low-dose regimen (1 g), according to clinical judgment. Variables analyzed: age, sex, duration of RA, presence of ACPA (antiCCP2) and rheumatoid factor (RF), use and dosage of glucocorticoids (GC) and synthetic DMARD (csDMARD) before and after RTX treatment, number of biologic DMARD (bDMARD) used prior to initiate RTX. Disease activity was measured using the DAS28-ESR index (at baseline, at initiation and during the low-dose RTX period, and at the last follow-up visit).

Results: From 2006 until 2017, 53 RA patients received, at least, one cycle of 2g RTX. Thirty-seven patients (69.8%) achieved a good or moderate EULAR response (mean initial pre-RTX DAS-28: 5.79 ± 1.17) and were step-down to a low dose re-treatment regimen. Baseline characteristics of patients receiving low-dose RTX: mean age 56.4 ± 10.9 years; 13.5% male, mean disease duration 12.7 ± 9.8 years, 91.9% RF + and 97.3 % ACPA +; mean pre-low dose RTX DAS-28: 4.08 ± 1.39. Thirty-four patients (91.9%) were on cs-DMARDs (51.4% with methotrexate (MTX) and 37.8% with leflunomide (LEF)), and 32 (86.5%) received concomitant GC. RTX was the first biologic only in 10 patients (27%). In the remaining cases, the mean number of previous b-DMARDs was 2.52 ± 1.5. Twenty-seven patients (73%) received only one standard cycle (2g) before RTX dose reduction.

A statistically significant reduction in the mean DAS-28 was observed between the first visit on 1g RTX (4.08 ± 1.39) with the last follow-up visit (3.04 ± 0.95; p< 0.0001), as well as, with the mean DAS-28 during the low-dose RTX period (3.63 ± 0.92; p<0.006).

11 were able to reduce dosage (8 MTX, 3 LEF), with a significant reduction for MTX (16.5 ± 4.4 mg vs. 11.92 ± 8.0 mg; p<0.01). From the 32 patients initially receiving GC, 18 (56.3%) were able to reduce dose (9.36 ± 5.06 vs 4.80 ± 4.04; p< 0.0001), and 9 (28%) discontinued GC therapy.

After a follow-up of 3 ± 1.8 years, only 10 (25%) patients have withdrawn RTX. Reasons were: recurrent infections in 4 cases (11%), loss of efficacy in 2 cases (5.6%), and adverse event and patient preferences in one case, respectively.

Conclusion: A sustained clinical response was observed with the 1 gr retreatment of RTX over a long term period.

Reference:

Disclosure: S. C. Rodriguez-García, None; R. Castellanos-Moreira Sr., None; M. V. Hernández, None; A. Cuervo, None; V. Ruiz-Esquide, None; J. Ramírez, Gebro, 2; J. Cañete, None; R. Sanmartí, None.

Abstract Number: 2491

Real-World Effectiveness and Safety of Subcutaneous Abatacept in Biologic-Naive Vs. Biologic-Experienced RA Patients: The Abatacept Best
Care Study

B Haraoui, Janet E. Pope, Isabelle Fortin, Emmanouil Rampakakis, John S. Sampalis, Francoise Romeyer, Joseph Atallah and Louis Bessette, 1 Institut de Recherche en Rhumatologie de Montréal (IRRM), Montreal, QC, Canada, 2 Department of Medicine, Division of Rheumatology, University of Western Ontario, St Joseph's Health Care, London, ON, Canada, 3 Centre de Rhumatologie de l'Est du Quebec, Rimouski, QC, Canada, 4 JSS Medical Research, Montreal, QC, Canada, 5 McGill University, Montreal, QC, Canada, 6 JSS Medical Research, St-Laurent, QC, Canada, 7 Bristol-Myers Squibb, Montreal, QC, Canada, 8 Centre d'Osteoporose et de Rhumatologie de Quebec, Quebec, QC, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The efficacy and safety of subcutaneous (SC) abatacept in the management of rheumatoid arthritis (RA) has been demonstrated in numerous controlled clinical trials. However, real-world data of SC abatacept in routine care are scarce. The aim of this interim analysis is to compare the effectiveness and safety of SC abatacept used as first line or second biologic agent in Canadian patients enrolled thus far in Abatacept Best Care (ABC).

Methods: ABC is a prospective, multicenter, randomized study aimed at comparing a T2T approach vs. standard of care in real-life management of patients with RA starting SC abatacept as first line or second line biologic agent, and describing the adherence of physicians to the recommended T2T treatment guidelines while collecting data on the real-life use of SC abatacept. General linear models were used to assess the impact of prior biologic use on treatment effectiveness.

Results: 276 patients (74.3% females) were included with a mean (SD) age of 59.7 (11.7) years and duration since RA diagnosis of 7.5 (8.9) years; of these 214 (77.5%) and 189 (68.5%) had available follow-up data at 6 and 12 months, respectively. Prior biologic use was reported for 39.5% while 60.5% were biologic-naive. Overall, baseline disease parameters were comparable with the exception of time since RA diagnosis (9.0 vs. 6.4 years; P<0.001) which was significantly higher in biologic experienced patients and TJC28 (10.5 vs. 9.1; P=0.062) which was numerically higher. After 6 months of treatment, both patient groups experienced significant improvements in all disease parameters which were maintained or further enhanced by 12 months. However, upon adjusting for baseline disease activity, improvements in CDAI (P=0.020), physician global (P=0.011), TJC28 (P=0.031), SJC28 (P=0.009), and HAQ (P=0.037) at 6 months were significantly higher in biologic experienced patients and TJC28 (10.5 vs. 9.1; P=0.062) which was numerically higher.

A total of 533 AEs were reported for 162 (58.7%) patients, 67.0% of biologic-experienced patients and 53.3% of biologic-naive patients (256.1 vs. 211.2 events/100 PY). The most common AEs were upper respiratory infections (biologic-experienced vs. biologic-naive: 4.6% vs. 9.0%; 5.2 vs. 14.6 events/100 PY) and bronchitis (7.3% vs. 7.8%; 8.4 vs. 10.2 events/100 PY). Serious AEs and serious infections were reported for 26 (9.4%) patients (10.1% vs. 9.0%; 16.8 vs. 13.2 events per 100/PY) and 5 (1.8%) patients (0.9% vs. 2.4%; 0 vs. 1.5 events/100 PY), respectively.

Conclusion: The results of the current analysis suggest that SC abatacept has similar safety in biologic-naive and -experienced patients with more improvement in outcome measures in the former.
Table 1: Baseline-Adjusted Improvements in Disease Activity at 6 and 12 Months by Previous Biologic Experience

<table>
<thead>
<tr>
<th>Variable</th>
<th>6 Months*</th>
<th>12 Months*</th>
<th>P-Value</th>
<th>6 Months*</th>
<th>12 Months*</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔPain: VAS mm</td>
<td>-17.5</td>
<td>-11.8</td>
<td>0.119</td>
<td>-25.0</td>
<td>-15.7</td>
<td>0.022</td>
</tr>
<tr>
<td>ΔPatient Global (ΔPtGA): VAS mm</td>
<td>-15.6</td>
<td>-13.6</td>
<td>0.585</td>
<td>-24.1</td>
<td>-14.6</td>
<td>0.016</td>
</tr>
<tr>
<td>ΔMorning Stiffness: VAS mm</td>
<td>-20.4</td>
<td>-13.8</td>
<td>0.076</td>
<td>-22.2</td>
<td>-14.1</td>
<td>0.059</td>
</tr>
<tr>
<td>ΔFatigue: VAS mm</td>
<td>-14.0</td>
<td>-15.6</td>
<td>0.676</td>
<td>-23.6</td>
<td>-14.2</td>
<td>0.023</td>
</tr>
<tr>
<td>ΔPhysician Global (ΔMDGA): VAS mm</td>
<td>-35.9</td>
<td>-27.4</td>
<td>0.011</td>
<td>-43.8</td>
<td>-37.2</td>
<td>0.029</td>
</tr>
<tr>
<td>ΔTJC28</td>
<td>-6.1</td>
<td>-4.4</td>
<td>0.031</td>
<td>-7.1</td>
<td>-6.2</td>
<td>0.255</td>
</tr>
<tr>
<td>ΔSJ28</td>
<td>-5.7</td>
<td>-4.4</td>
<td>0.009</td>
<td>-6.8</td>
<td>-5.2</td>
<td>0.003</td>
</tr>
<tr>
<td>ΔHAQ</td>
<td>-0.43</td>
<td>-0.26</td>
<td>0.037</td>
<td>-0.50</td>
<td>-0.28</td>
<td>0.021</td>
</tr>
<tr>
<td>ΔRAPID3</td>
<td>-3.0</td>
<td>-2.8</td>
<td>0.833</td>
<td>-4.5</td>
<td>-2.3</td>
<td>0.007</td>
</tr>
<tr>
<td>ΔDAS28</td>
<td>-1.8</td>
<td>-1.4</td>
<td>0.053</td>
<td>-2.0</td>
<td>-1.6</td>
<td>0.109</td>
</tr>
<tr>
<td>ΔCDAI</td>
<td>-16.8</td>
<td>-12.8</td>
<td>0.020</td>
<td>-20.7</td>
<td>-16.6</td>
<td>0.012</td>
</tr>
<tr>
<td>ΔSDAI</td>
<td>-13.6</td>
<td>-11.0</td>
<td>0.153</td>
<td>-15.0</td>
<td>-12.6</td>
<td>0.140</td>
</tr>
</tbody>
</table>

*Adjusted for baseline levels, least square mean

Acknowledgments: The authors would like to thank Dr. Kristina Sladojevic and Dr. Eleonora Muratti for their contributions in the study.

Disclosure: B. Haraoui, BMS, Janssen, Roche Speakers bureau: Pfizer, UCB, 2, AbbVie, Amgen, BMS, Celgene, Janssen, Merck, Pfizer, Roche, Sandoz, UCB, 5; J. E. Pope, AbbVie, Amgen, Bayer, BMS, Celtrion, Eli Lilly and Company, Merck, Novartis, Pfizer, Roche, UCB, 5, AbbVie, Amgen, Bayer, BMS, Celtrion, Eli Lilly and Company, Merck, Novartis, Pfizer, Roche, UCB, 5, Amgen, Bayer, BMS, GSK, Merck, Novartis, Pfizer, Roche, UCB, 2, Amgen, Bayer, BMS, GSK, Merck, Novartis, Pfizer, Roche, UCB, 2; I. Fortin, UCB, 2; E. Rampakakis, JSS Medical Research, 3; J. S. Sampalis, JSS Medical Research, 3; F. Romeyer, Bristol-Myers Squibb, 3; J. Atallah, Bristol-Myers Squibb, 3; L. Bessette, Janssen, Roche, UCB, AbbVie, Pfizer, Celgene, Lilly, Novartis, 5, Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Lilly, Novartis, 8.


Abstract Number: 2492

The Long-Term Safety and Durability of Response of Chs-0214, a Proposed Biosimilar to Etanercept: An Open-Label Safety Extension Study

Ingrid Louw1, Alan J. Kivitz2, Tsutomu Takeuchi3, Yoshiya Tanaka4, Satoshi Nakashima5, Jennifer Hodge6, Hong Tang6, Paula O’Connor6 and Barbara Finck6, 1Panorama Medical Centre, Cape Town, South Africa, 2Department of Rheumatology, Altoona Center for Clinical Research, Duncansville, PA, 3Keio University School of Medicine, Tokyo, Japan, 4School of Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan, 5Daiichi Sankyo, Tokyo, Japan, 6Coherus BioSciences, Inc., Redwood City, CA

First publication: September 18, 2017

SESSION INFORMATION
Background/Purpose: CHS-0214 is a proposed biosimilar to etanercept for the treatment of rheumatoid arthritis and other auto-immune diseases. Two randomized, double-blind studies demonstrated equivalence of CHS-0214 to etanercept in patients with rheumatoid arthritis (RA) and chronic plaque psoriasis (PsO). This ongoing, open-label, safety extension study evaluates the long-term safety of and durability of response to CHS-0214 in patients who completed Week 48 of a prior trial.

Methods: All patients are to receive open-label CHS-0214 50 mg weekly for at least 48 weeks. Patients are evaluated at 1 and 3 months post enrollment and every 3 months thereafter. Patients had to have achieved an ACR20 or a PASI50 at Week 48 in the prior trial. The primary endpoints are maintenance of response (ACR20 or PASI50) at Week 4, Week 12 and every 3 months thereafter during the study.

Results: This interim analysis included 359 patients with a mean duration of treatment of 31.45 weeks of open-label CHS-0214 in addition to 48 weeks of treatment in the prior study. Of those, 56.5% were female, 49.6% were Asian, and 44.3% were white. Mean age was 49.9 years, and mean body mass index was 27.1. Of the 359 (225 with RA and 134 with PsO), 357 received ≥1 dose of study drug.

Overall, 197 (87.9%) patients with RA had achieved a durable response (maintenance of ACR20), and 118 (90.1%) of patients with PsO had achieved a durable response (maintenance of PASI50) as of the data cut-off date. Loss of efficacy was a factor in study discontinuation for 5 patients. Treatment-emergent adverse events were reported in 216 (60.5%) patients, and serious TEAE were reported in 14 (3.9%) patients. Four (1.1%) patients had a TEAE that led to study drug discontinuation. The most common (>5%) TEAEs were nasopharyngitis and upper respiratory tract infection.

Conclusion: The majority of patients maintained an efficacious response to treatment with CHS-0214. Treatment was well tolerated and the incidence of TEAEs did not increase with ongoing drug exposure. No new safety signals were identified in these patients with an average of 80 weeks of treatment.

Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). Patients (pts) with RA generally receive conventional synthetic DMARDs (csDMARDs) as first-line therapy, and inadequate responders (IR) to csDMARDs generally receive biological DMARDs (bDMARDs). We evaluated the efficacy and safety of tofacitinib in 3 RA pt populations (popns) who had incomplete response or were intolerant to prior lines of therapy (both referred to as IR).

Methods: Data from pts who were 1) non-MTX csDMARD-IR but not bDMARD-IR; 2) MTX-IR but not bDMARD-IR; and 3) bDMARD-IR (referred to as non-MTX csDMARD-IR, MTX-IR, and bDMARD-IR) were pooled from 8 Phase 2 and 6 Phase 3 trials evaluating the efficacy and safety of tofacitinib 5 or 10 mg BID vs placebo (PBO) in RA. Pts may have received >1 prior csDMARD, and in ~60% of the studies tofacitinib was given in combination with a csDMARD, commonly MTX. Month (M)3 efficacy outcomes included % of pts achieving ACR20/50/70 responses or Disease Activity Score in 28 joints, erythrocyte sedimentation rate (DAS28-4[ESR])<2.6 (remission), and change from baseline (BL) in DAS28-4(ESR) or HAQ-DI scores. No multiplicity adjustments were made. Crude incidence rates (CIR; unique pts with events/100 pt-yrs) based on adverse events (AEs) through M24 were calculated as safety outcomes.

Results: The non-MTX csDMARD-IR, MTX-IR, and bDMARD-IR popns comprised a total of 537, 3113, and 782 pts, respectively (Table; the non-MTX csDMARD-IR and bDMARD-IR popns were substantially smaller). Prior csDMARDs received by the total non-MTX csDMARD-IR, MTX-IR, and bDMARD-IR popns were chloroquine (17.7%, 13.8%, 4.1%), hydroxychloroquine (37.2%, 21.2%, 19.8%), leflunomide (19.4%, 20.5%, 24.2%), MTX (7.3% [not IR to MTX], 100%, 95.5%), sulfasalazine (31.1%, 26.8%, 18.0%), and others (8.0%, 10.7%, 10.4%), respectively. BL characteristics were similar between non-MTX csDMARD-IR, MTX-IR, and bDMARD-IR popns except for mean RA duration (5.2–7.2, 8.1–8.6, and 11.6–12.2 yrs, respectively). Most pts were female (80.3–85.4%), mean age range was 49.7–54.6 yrs, and mean DAS28-4(ESR) score ranged from 6.2–6.5. Significantly higher ACR response rates and greater changes from BL in DAS28-4(ESR) and HAQ-DI scores at M3 were recorded with tofacitinib 5 and 10 mg BID in all popns vs PBO (Table). A trend was observed for numerically higher proportions of non-MTX csDMARD-IR pts achieving efficacy outcomes vs MTX-IR and bDMARD-IR popns. CIRs for TEAEs, SAEs, and DC due to AEs were numerically lower in the non-MTX csDMARD-IR popn vs the MTX-IR popn and both popns had lower CIRs vs the bDMARD-IR popn. For numerical differences, 95%CIs generally overlap. AEs of special interest are reported (Table).

Conclusion: Tofacitinib is associated with improved efficacy and most safety outcomes vs PBO in each of the non-MTX csDMARD-IR, MTX-IR, and bDMARD-IR popns, and may be more efficacious when used in earlier lines of therapy.
Disclosure: J. Tesser, Pfizer Inc, 2; Pfizer Inc, 5; Pfizer Inc, 8; A. Gül, AbbVie, Bristol-Myers Squibb, MSD, Novartis, Pfizer Inc, Roche, Servier, UCB, Xoma, 5; E. Olech, Aurinia, Biogen Idec, Bristol-Myers Squibb, Pfizer Inc, 2; AbbVie, Amgen, Crescendo, Pfizer Inc, 8; K. Oelke, Novartis, 5; AbbVie, Amgen, Bristol-Myers Squibb, Novartis, Pfizer Inc, Regeneron, Sanofi, UCB, 8; T. Lukic, Pfizer Inc, 1; Pfizer Inc, 3; C. W. Murray, Pfizer Inc, 1; Pfizer Inc, 3; C. Zang, Pfizer Inc, 1; Pfizer Inc, 3; L. Takiya, Pfizer Inc, 1; Pfizer Inc, 3.


Analysis of the Efficacy, Safety and Continuation Rate of Abatacept in Elderly Patients with Rheumatoid Arthritis

Mayumi Matsuda 1, Yu Funakubo Asanuma 2, Noritsune Kouzu 3 and Toshihide Mimura 2, 1Department of Rheumatology and Applied Immunology, Saitama Medical University, Moroyama-machi, Japan, 2Department of Rheumatology and Applied Immunology, Faculty of Medicine, Saitama Medical University, Saitama, Japan, 3Saitama Medical University, Moroyama, Japan

First publication: September 18, 2017
In these 2 groups, we examined the retrospective evaluation of the patients’ background, disease activity, decline in physical performance, reduction of methotrexate (MTX) or prednisolone (PSL) dose, safety and continuation rate of ABT.

**Results:** In the patients background (younger group/elderly group), mean age of onset (46/60 year-old), rate of female (83.9/84.4%), naïve rate of biological DMARDs (51.6/28.1%), mean disease duration (7.9/12.1 years), rate of MTX use (64.5/37.5% \( p=0.045 \)), rate of PSL use (64.5/87.5% \( p=0.041 \)), mean dose of MTX (5.4/3.1mg/week), mean dose of PSL (5.0/5.1mg/day), DAS28-ESR4 (5.53/5.84), and HAQ (1.13/1.67 \( p=0.046 \)), positive rate of RF (74.2/93.8% \( p=0.043 \)) were observed. The elderly group showed higher HAQ \( p=0.046 \) than the younger group. In effectiveness, DAS28-ESR4 and HAQ significantly decreased in both groups for the observational period of one year after initiation of ABT therapy \( (P<0.05) \). ABT therapy did not reduce the dose of MTX for one year, while reduction of the dose of PSL was observed in both groups. There were no significant differences in the continuation rate between the younger (87.1%) and the elderly group (75.0%). The cancellation reason of ABT (younger group/elderly group) were due to adverse events (6.5/12.5%), ineffective (6.5/6.3%), remission (0.0/3.1%) one year after ABT started.

**Conclusion:** The ABT treatment in the elderly RA patients was suggested useful as much as in the younger patients regarding the effectiveness, the reduction of PSL dose, and the continuation rate.

**Disclosure:** M. Matsuda, None; Y. F. Asanuma, None; N. Kouzu, None; T. Mimura, Abbvie, 5, Astellas, 5, Eisai, 5, Janssen Pharmaceutica Product, L.P., 5, Novartis Pharmaceutical Corporation, 5, Ono Pharma, 5, Pfizer Inc, 5, Sanofi-Aventis Pharmaceutical, 5, Takeda Pharmaceutical, 5, Tanabe-Mitsubishi Pharma, 5.


**Abstract Number:** 2495

**Biosimilarity between Humira® and the Biosimilar Candidate SB5 in Product Quality**

Nayoung Lee, Minlee Kim, JongAh Joanne Lee, Soohwan Kim and Hahymn Yang, Samsung Bioepis, Incheon, Korea, Republic of (South)

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** A biosimilar is a biopharmaceutical product that is highly similar to an already licensed one in terms of quality, safety, and efficacy. We (Samsung Bioepis) have been developing a biosimilar of Humira® (adalimumab), designated as SB5. To demonstrate its biosimilarity in quality to Humira®, we performed a comprehensive characterization in terms of structure, heterogeneity in size and charge, and biological properties following the ICH, FDA, and EMA guidelines.

**Methods:** We analyzed all available lots of SB5 and more than 70 US- or EU-sourced lots of Humira®, using state-of-the-art methods whenever desirable, and compared the two sets of data. The structural properties comprised primary and higher-order structures and N-glycosylation. The physicochemical characteristics were categorized into liquid chromatographic patterns and electrophoretic pattern concerning size and charge heterogeneity. The biological properties were examined by *in vitro* functional assays.
**Results**: Amino acid sequence and modification were demonstrated by peptide mapping analysis using mass spectrometry, which resulted in the identity in amino acid sequence and the identical site of N-glycosylation between SB5 and Humira®. All N-glycan species were also identical to each other. To testify 3-dimension structural similarity, the butterfly plots of hydrogen/deuterium exchange (HDX) was conducted and showed that SB5 and Humira® are highly similar in terms of solvent accessibility. These results demonstrated a high degree of structural similarity.

The %contents of High Molecular Weights (%HMWs) were determined by size-exclusion HPLC (SE-HPLC) and were shown to be highly similar between SB5 and Humira®. The %contents of Low Molecular Weights (%LMWs) were determined by capillary-electrophoresis sodium dodecyl sulfate, with reduced samples and non-reduced samples (CE-SDS-R, and CE-SDS-NR, respectively). Non-glycosylated heavy chain (NGHC) by CE-SDS-R was the impurity that the amounts are not highly similar between SB5 and Humira®; however, the difference is not considered to be significant clinically.

The charge heterogeneity was investigated not only for the %contents of the variants, by cation-exchange HPLC (CEX-HPLC) and imaged capillary isoelectric focusing (icIEF) but also for the structural identities. The variants were found to contain identical structures, and although the %contents showed difference but it will not considered to be significant clinically based on the result of clinical study.

With regard to TNF-α binding and neutralization, which are the primary modes of action of adalimumab, SB5 was similar to Humira®. The levels of apoptosis, another Fab-related function, and all the Fc-related functions analyzed, including Fc receptor binding, antibody-dependent cell-mediated cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC) were found similar between SB5 and Humira®.

**Conclusion**: A comprehensive set of physicochemical and biological characterizations has demonstrated that SB5 is highly similar to Humira® in product quality.

**Disclosure**: N. Lee, Samsung Bioepis, 3; M. Kim, Samsung Bioepis, 3; J. J. Lee, Samsung Bioepis, 3; S. Kim, Samsung Bioepis, 3; H. Yang, Samsung Bioepis, 3.

**Abstract Number**: 2496

**The Disease Course in Daily Clinical Practice in Radiographic and Non-Radiographic Axial Spondyloarthritis Patients; One-Year Follow-up Results of National-Subgroup of a Worldwide Observational Cohort Study**

Servet Akar¹, Ilhan Sezer², Yasemin Yumusakhuylu³, Ayşen Akinci⁴, Kemal Erol⁵, Kenan Akgun⁶, Hatice Bodur⁷, Sebnem Ataman⁸, Omer Kuru⁹, Meltem Melikoglu¹⁰, Murat Karkucak¹¹, Nazlı Derya Bugdaycı¹², Duygu Ersozlu Bakırli¹³, Murat Birtane¹⁴, Tuncay Duruoz¹⁵, Sukran Erten¹⁶, Ediz Dalkılıç¹⁷, Gülay KINIKLİ¹⁸, Cemal Bes¹⁹, Ahmet Omma²⁰ and Aylin Rezvani²¹, ¹Rheumatology, Izmir Katip Celebi University, School of Medicine, Rheumatology, Izmir, Turkey, ²Physical Medicine and Rehabilitation-Rheumatology, Antalya Training and Research Hospital, Antalya, Turkey, ³Department of Physical Medicine and Rehabilitation, Istanbul Medeniyet University, Göztepe Training and Research Hospital, Istanbul, Turkey, ⁴Hacettepe University Medical School Department of Physical Medicine and Rehabilitation, Ankara, Turkey, ⁵Department of Physical Medicine and Rehabilitation, Division of Rheumatology, Erciyes University Faculty of Medicine, Kayseri, Turkey, ⁶Department of Physical Medicine and Rehabilitation, Istanbul University, Cerrahpasa Faculty of Medicine, Istanbul, Turkey, ⁷Department of Physical Medicine and Rehabilitation, Ankara Numune Training and Research Hospital, Ankara, Turkey, ⁸Department of Physical Medicine and Rehabilitation, Division of Rheumatology, Ankara University Faculty of Medicine, Ankara, Turkey, ⁹Department...
SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
The natural history of axial spondyloarthritis (axSpA) has not been clearly established yet. The aim of this study is to evaluate the natural course of axSpA patients and compare it between radiographic [ankylosing spondylitis (AS)] and non-radiographic (nr-axSpA) sub-groups of the Turkish population of the PROOF study.

Methods:
PROOF is a large observational study, ongoing in 29 countries, aiming to reveal the long-term clinical and radiographic outcomes of patients classified as axSpA according to ASAS criteria. Patients were eligible if diagnosed within ≤1 year prior to the study initiation. Besides assessing disease activity, function, productivity and quality of life (QoL), nr-axSpA patients were followed up annually with sacroiliac joint (SIJ) radiographs. In addition to the treating physician, a central evaluator assessed the SIJ images. In the presence of discrepancy between the two readings, the images were inspected third time by the 2nd central reader and the final result corresponded to 2/3 readings.

Results:
PROOF cohort is consisted of 2126 participants worldwide and 274 axSpA patients were included from 24 centers in Turkey. In total 167 (60.9%) patients were classified as AS and 107 (39%) as nr-axSpA by local investigator. According to the central SIJ readings (n=229), 146 patients (63.8%) were evaluated as AS and 83 (36.2%) as nr-axSpA. The demographic and disease-related characteristics of the study groups are summarized in Table 1. In the first visit, patients were under non-steroidal anti-inflammatory drugs (78.5%), sulfasalazine (22.6%), corticosteroids (5.5%), and TNF inhibitors (9.9%) treatment. In one-year follow-up visit, disease activity measures (physician assessed or patients reported and composite outcome measures) and the percentage of current smokers showed a similar decrease independent of disease subgroup. QoL was improved and overall total activity impairment was decreased during one year of observation. Based on local X-ray grading 1/23 (4.3%) of AS patients are reclassified as nr-axSpA and 9/39 (23.1%) of nr-axSpA patients as AS.

Conclusion:
Although there were differences between the AS and nr-axSpA groups, such as female gender and CRP, baseline disease burden of AS and nr-axSpA patients were quite similar. During one-year follow-up; disease activity and QoL were improved similarly in both subgroups. Based on local X-ray readings, substantial proportion of nr-axSpA patients seemed to be progressed to AS, even in one-year period.

**Table 1:** Demographic and disease related characteristics of ankylosing spondylitis and non-radiographic axial spondyloarthritis patients on baseline and one year of follow-up.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Ankylosing Spondylitis (n=146)</th>
<th>Non-radiographic axSpA (n=83)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, mean ±SD</td>
<td>33.1 ± 9.5</td>
<td>32.8 ± 8.0</td>
</tr>
<tr>
<td>Gender, % Male</td>
<td>57.5</td>
<td>43.4</td>
</tr>
<tr>
<td>HLA-B27 positivity, %</td>
<td>44.4</td>
<td>33.3</td>
</tr>
<tr>
<td>Time since diagnosis in months, mean ± SD</td>
<td>Not applicable</td>
<td>2.0 ± 3.1</td>
</tr>
<tr>
<td>Time since beginning of chronic lumbar pain in months, mean ± SD</td>
<td>67.7 ± 83.9</td>
<td>40.7 ± 43.0</td>
</tr>
<tr>
<td>Current smoker, %</td>
<td>41.8</td>
<td>30.4</td>
</tr>
<tr>
<td>Inflammatory back pain, %</td>
<td>94.5</td>
<td>43.8</td>
</tr>
<tr>
<td>Arthritis, %</td>
<td>21.9</td>
<td>5.5</td>
</tr>
<tr>
<td>Enthesitis, %</td>
<td>46.6</td>
<td>21.9</td>
</tr>
<tr>
<td>Dactylitis, %</td>
<td>2.7</td>
<td>2.1</td>
</tr>
<tr>
<td>Uveitis, %</td>
<td>8.2</td>
<td>2.7</td>
</tr>
<tr>
<td>Psoriasis, %</td>
<td>0.7</td>
<td>0.7</td>
</tr>
<tr>
<td>Inflammatory bowel disease, %</td>
<td>0</td>
<td>0.7</td>
</tr>
<tr>
<td>CRP, mg/L, mean± SD</td>
<td>19.1 ± 26.7</td>
<td>10.0 ± 18.4</td>
</tr>
<tr>
<td>ESR, mm/h, mean ± SD</td>
<td>22.2 ± 17.5</td>
<td>13.7 ± 10.0</td>
</tr>
<tr>
<td>ASDAS (CRP and ESR combined), mean ± SD</td>
<td>3.3 ± 1.0</td>
<td>2.2 ± 1.1</td>
</tr>
<tr>
<td>BASDAI, mean ± SD</td>
<td>4.7 ± 2.3</td>
<td>3.3 ± 2.2</td>
</tr>
<tr>
<td>BASFI, mean ± SD</td>
<td>3.3 ± 2.4</td>
<td>2.3 ± 2.2</td>
</tr>
<tr>
<td>SF-12v2 physical component score, mean ± SD</td>
<td>41.1 ± 8.8</td>
<td>46.9 ± 9.1</td>
</tr>
<tr>
<td>SF-12v2 mental component score, mean ± SD</td>
<td>40.0 ± 11.9</td>
<td>44.6 ± 11.0</td>
</tr>
<tr>
<td>WPAI-SHP, Total activity impairment, %, mean ± SD</td>
<td>46.5 ± 29.5</td>
<td>31.3 ± 27.7</td>
</tr>
</tbody>
</table>

CRP: C-Reactive Protein; ESR: Erythrocyte Sedimentation Rate; ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; SF-12v2: Short Form 12 Item Version 2 Health Survey; WPAI-SHP: Work Productivity and Activity Impairment Questionnaire Specific Health Problem; SD: Standard deviation

**Disclosure:** S. Akar, Abbvie; Pfizer, 2,Abbvie; Merck, Novartis, Pfizer, UCB, 5; I. Sezer, Abbvie, 2,Abbvie; Merck; Pfizer, 5; Y. Yumusakhuylu, Abbvie, 2; A. Akinci, Abbvie, 2,Merek; Amgen; Pfizer, 5; K. Erol, AbbVie, 2; K. Akgun, Abbvie; Pfizer, 2,Abbvie; Merck; Pfizer, 5; H. Bodur, AbbVie; Pfizer, 2,Glaxo; Pfizer; Roche; UCB; Lilly, 5; S. Ataman, AbbVie; Pfizer, 2,Merek; Roche; Novartis; Roche; UCB, 5; O. Kuru, AbbVie; Pfizer, 2,Abbvie; Pfizer; Merek; BMS; Roche; UCB; Aman; 5; M. Melikoglu, AbbVie, 2; M. Karkucak, AbbVie, 2,Abbvie; Lilly; Pfizer, 5; N. D. Bugdayci, AbbVie, 2,AbbVie; Pfizer; Merek; UCB, 5; D. Ersozlu Bakirli, AbbVie, 2,Pfizer Inc, 5; M. Birtane, AbbVie, 2,Pfizer; Merek; Roche; Lilly, 5; T. Duruoz, AbbVie, 2,Sanovel, 5; S. Ertun, AbbVie, 2,Pfizer Inc, 5; E. Dalkilic, Abbvie, 2,Abbvie; Merck; Roche; UCB; Pfizer, 5; G. KINIKLI, AbbVie, 2,Pfizer; Roche, 5; C. Bes, AbbVie, 2; A. Omma, Abbvie, 2,Merck; Pfizer, 5; A. Rezvani, Abbvie, 2.

The Role of Individual and Country-Level Socio-Economic Factors in Work Participation in Patients with Spondyloarthritis across 22 Countries Worldwide: Results from the Comospa Study

Santiago Rodrigues Manica1,2, Alexandre Sepriano3,4, Sofia Ramiro5,6, Fernando Pimentel-Santos1,2, Polina Putrik7, Elena Nikiphorou8,9, Anna Moltó10,11, Maxime Dougados11,12, Désirée van der Heijde13, Robert B.M. Landewé14, Filip van Den Bosch15 and Annelies Boonen7, 1CEDOC, NOVA Medical School, Lisbon, Portugal, 2Rheumatology, Hospital Egas Moniz, Centro Hospitalar de Lisboa Ocidental, Lisbon, Portugal, 3CEDOC, NOVA Medical School, Lisboa, Portugal, 4Rheumatology, Leiden University Medical Center, Leiden, Netherlands, 5Rheumatology, Department of Rheumatology, LUMC, Leiden, Netherlands, Leiden, Netherlands, 6R. Câmara Pestana 6, CEDOC, NOVA Medical School, Lisboa, Portugal, 7MUMC+, Maastricht, Maastricht, Netherlands, 8Whittington Hospital, London, United Kingdom, 9Academic Rheumatology Department, King's College London, London, United Kingdom, 10Rheumatology B Department, Paris Descartes University, Cochin Hospital, AP-HP,Paris, Paris, France, 117 INSERM (U1153), Clinical Epidemiology and Biostatistics, PRES Sorbonne Paris-Cité, Paris, France, 12Paris, Paris, France, 13Leiden University Medical Center, Leiden, Netherlands, 14Clinical Immunology & Rheumatology, Academic Medical Center, University of Amsterdam and Atrium Medical Center, Heerlen, Netherlands, 15Rheumatology, Ghent University Hospital, Gent, Belgium

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Spondyloarthritis (SpA) carries substantial financial costs, including direct costs (use of medical services and treatments) and indirect costs (loss of work productivity). While disease related factors have been repeatedly shown to be associated with work outcomes, information on the role of individual socio-economic (SE) factors (education) and country wealth is scarce.

To explore the role of individual and country SE factors on employment, absenteeism and presenteeism, across 22 countries, from different world regions.

Methods: Patients with a clinical diagnosis of SpA, fulfilling the ASAS SpA criteria and in working age (≤65 years old) from the evaluation of co-morbidities in spondyloarthritis (COMOSPA) were included. Outcomes explored were employment-status, absenteeism and presenteeism (the last 2 only in employed patients, in the last 7 days) according to the Work Productivity and Activity Impairment Specific Health Problem (WPAI-SHP) questionnaire. Three multivariable models were built (one for each outcome) using a multilevel mixed-effects binomial regression (for work status) and ordinal regression (for absenteeism and presenteeism), with country as random-effect.

Independent contribution of individual (education) and country level socio-economic factors (human development index (HDI), country healthcare expenditures and gross domestic product (GDP) (all low vs medium/high tertiles) were assessed in models adjusted for clinical factors.

Results: In total 3,114 patients were included (mean (SD) age 40.9 (11.8) years; 66% males; and 63% employed). Unadjusted employment rates ranged from 28% (Colombia) to 83% (Canada). After adjustment for relevant confounders, differences between countries in work status persisted (p<0.01). At the individual level, higher education was positively associated with being employed (OR=4.21 [95%CI 3.14;5.64]) and lower presenteeism (OR=0.61
At a country level, a higher healthcare expenditure was associated with being employed (OR=2.32 [95%CI=1.48;3.63]) and a higher HDI was associated with a higher employment (OR=1.89 [95%CI=1.19;3.27]) and lower absenteeism (OR=0.48 [95%CI=0.24;0.95]). No significant association was found for GDP. No significant association between any country SE indicators and presenteeism was found.

Conclusion: Individual- and country-level SE factors are associated with work participation in SpA. Work outcomes vary significantly across countries and better socio-economic wealth and welfare seem to be associated with more SpA patients remaining at work and productive.

Disclosure: S. Rodrigues Manica, None; A. Sepriano, None; S. Ramiro, None; F. Pimentel-Santos, None; P. Putrik, None; E. Nikiphorou, None; A. Moltó, None; M. Dougados, None; D. van der Heijde, None; R. B. M. Landewé, None; F. van Den Bosch, None; A. Boonen, None.


Abstract Number: 2498

Rheumatologists Use Different Cut-Offs for Disease Activity in Real Life – the Experience with Golimumab in Ankylosing Spondylitis- Subanalysis from a Non-Interventional German Study

Jürgen Braun, Xenofon Baraliakos, Uta Kiltz, Klaus Krüger, Gerd R. Burmester, Siegfried Wassenberg and Matthias H. Thomas, 1Rheumazentrum Ruhrgebiet, Herne, Germany, 2Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany, 3Praxiszentrum St. Bonifatius München, München, Germany, 4Department of Rheumatology and Clinical Immunology, Charité - University Medicine Berlin, Free University and Humboldt University Berlin, Berlin, Germany, 5Rheumazentrum Ratingen, Ratingen, Germany, 6Medical Affairs, MSD Sharp & Dohme GmbH, Bünde, Germany

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM
Background/Purpose:

International recommendations for the management of axial spondyloarthritis including ankylosing spondylitis (AS) suggest a BASDAI level of disease activity of ≥4 to indicate treatment with biologics. Other cut-offs have rarely been studied so far. Therefore, we were interested to learn about the level of disease activity used in daily routine to start anti-TNF therapy.

Methods:

In a posthoc subanalysis of the non-interventional, prospective, study GO-NICE that has been performed in a real life setting in Germany we used data from biologic naïve patients with established AS to study the initial BASDAI values before the start of therapy with Golimumab 50mg SC once monthly. Established standardized outcome measures were used.

Results:

Out of a total of 543 AS-patients (pts.) documented in 126 German centers, 244 biologic-naïve pts. were eligible. A total of 134 pts. (54.9%) completed the 24 month observational period. The majority of pts. (70.5%), had a BASDAI ≥4 (group (gr.)1), while 14.3% had a BASDAI of ≥2.8 - <4 (gr.2) and 15.1% even had a BASDAI <2.8 (gr.3, Table). The patient demographics did not differ much between these 3 groups, the proportion of males was numerically somewhat lower in gr.1. The proportion of pts. with an elevated CRP was highest in gr.2 at BL. The BASDAI in gr.1,2 and 3 was initially 5.9±1.3, 3.4±0.4 and 2.0±0.8, dropped significantly to 2.2*±2.0, 1.9*±1.2 and 1.0±1.2 within 3 months (*p<0.0001 vs. BL), and decreased significantly (p<0.005) to 2.2±1.7, 1.9±1.7 and 1.4±1.0 at month 24, respectively (fig.). The BASDAI 50% improvement was 68.8%, 44.8%, and 45.2% at month 3, and increased to 84.9%, 61.9%, and 55.0% at month 24, respectively.

<table>
<thead>
<tr>
<th>Demographics and baseline characteristics</th>
<th>BASDAI ≥4; n=172</th>
<th>BASDAI 2.8 - &lt;4; n=35</th>
<th>BASDAI &lt;2.8; n=37</th>
<th>total AS patients; n = 244</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age [years] ± SD (range)</td>
<td>41.9±12.5 (18-72)</td>
<td>44.7±11.6 (20-69)</td>
<td>39.1±12.5 (23-69)</td>
<td>41.9±12.4 (18-72)</td>
</tr>
<tr>
<td>Proportion males n (%)</td>
<td>117 (68.0%)</td>
<td>29 (82.9%)</td>
<td>27 (73.0%)</td>
<td>173 (70.9%)</td>
</tr>
<tr>
<td>Mean time since first diagnosis [years] ± SD (range)</td>
<td>8.8±9.5 (0-49.2)</td>
<td>10.1±10.2 (0.1-37.9)</td>
<td>8.7±9.0 (0.2-36.5)</td>
<td>9.0±9.5 (0-49.2)</td>
</tr>
<tr>
<td>Mean C-reactive protein (CRP) [mg/l] ± SD (range)</td>
<td>18.4±52.8 (0.3-660.0)</td>
<td>27.7±74.1 (0.3-426.0)</td>
<td>18.3±17.8 (1.0-60.6)</td>
<td>19.7±52.7 (0.3-660.0)</td>
</tr>
<tr>
<td>Outside normal range? yes, no, missing, n (%)</td>
<td>75 (45.2%)</td>
<td>21 (65.6%)</td>
<td>18 (51.4%)</td>
<td>114 (48.9%)</td>
</tr>
<tr>
<td></td>
<td>91 (54.8%)</td>
<td>11 (34.4%)</td>
<td>17 (48.6%)</td>
<td>119 (51.1%)</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>3</td>
<td>2</td>
<td>11</td>
</tr>
</tbody>
</table>
Conclusion: The most interesting observation of this real life study and posthoc analysis is certainly that almost a third of the pts. were included in the study who did not reach the recommended BASDAI cut-off of ≥4. Furthermore the data show that the patients with a BASDAI 2.8 < 4 seem to have significant benefit of antiTNF treatment, while this was not really the case with in pts. with a BASDAI <2.8. This finding should lead to a reevaluation of the established BASDAI cut-off of ≥ 4. Future studies should also evaluate the performance of an ASDAS cut-off. It seems likely that especially pts. with elevated CRP levels and a BASDAI < 4 will benefit from this new strategy. We think that in light of the rather weak correlation of pain and ‘objective’ parameters of inflammation such as CRP and MRI the here reported observation does make some sense.

Regarding the treatment with Golimumab no new safety signals were detected.

Disclosure: J. Braun, AbbVie (Abbott), Amgen, Biogen, Boehringer Ingelheim, BMS, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Epirus, Hospira, Janssen, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis and UCB, 5; X. Baraliakos, AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Novartis, Pfizer, Roche, MSD and UCB, 5; U. Kiltz, AbbVie, Chugai, Janssen, MSD, Novartis, Pfizer, Roche and UCB, 5; K. Krüger, AbbVie, BMS, Celgene, Janssen Biologics, MSD, Pfizer, Roche and Sanofi-Aventis, 5; G. R. Burmester, AbbVie, BMS, MSD, Pfizer, Roche, and UCB, 5; S. Wassenberg, AbbVie, Chugai, Janssen Biologics, MSD, Novartis, Pfizer, Roche, and UCB, 5; M. H. Thomas, MSD Sharp Dohme GmbH Germany, 3.


Abstract Number: 2499

Gender Differences in Axial and Peripheral Spondyloarthritis: Results from the Esperanza Cohort

Claudia Urrego¹, Victoria Navarro-Compán², Eugenio De Miguel³, Juan Mulero Mendoza⁴, Teresa Ruiz Jimeno⁵, Cristina Campos Fernandez⁶ and Pablo Zurita Prada ¹, ¹Rheumatology, Hospital General de Segovia., Segovia, Spain, ²Rheumatology, Hospital Universitario La Paz, Madrid, Spain, ³Rheumatology, Hospital La Paz - IdiPaz, Madrid, Spain, ⁴Rheumatology, Hospital Puerta de Hierro. Madrid, Madrid, Spain, ⁵Rheumatology, Hospital Sierrallana. Torrelavega, Santander, Santander, Spain, ⁶Rheumatology, Hospital Universitario de Valencia., Valencia, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
**Background/Purpose:** In patients with spondyloarthritis, published data indicate different manifestations and outcomes between genders. The evidence in this regard in patients with early and peripheral disease is lacking. The aim of this study is to describe if there are differences in the presentation between genders in patients with early axial and peripheral spondylarthritis (axSpA, pSpA).

**Methods:** This study was carried out within the framework of the ESPeranza program, which was a national multicenter initiative aiming to facilitate early diagnosis and follow-up of patients with spondylarthritis in Spain between 2008-2011. Out of 775 patients referred, 377 patients fulfilled the ASAS classification criteria for SpA: 291 (77%) axSpA and 86 (23%) pSpA. Demographic and disease characteristics were compared between genders using a descriptive analysis through Student t test (for continuous variables) and Chi-square test (for categorical variables).

**Results:** In total, 241 (64%) patients were males (191 axSpA and 50 pSpA). In axSpA, males had significantly more frequently radiographic sacroiliac damage, elevated CRP, HLA-B27+ and morning stiffness, while females had higher values of ESR and more frequency of peripheral arthritis (Table1-2). In pSpA, male gender was significantly associated with diagnostic delay, psoriasis and elevated CRP while women had higher rates of functional limitation.

**Conclusion:** There are differences in the manifestations between genders already from the onset of the disease. In patients with axSpA, males have worst prognostic factors compared with females. However, in pSpA, females report poorer functionality despite being diagnosed earlier than male patients. This difference in phenotypes may influence on therapeutic decision-making.

Table 1.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Axial Spondylarthritis n: 291</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males 191</td>
<td>Females 100</td>
</tr>
<tr>
<td>Age (years)</td>
<td>31.6 ± 7.1</td>
<td>32.8 ± 6.8</td>
</tr>
<tr>
<td>Family history</td>
<td>67 (35.1)</td>
<td>34 (34.0)</td>
</tr>
<tr>
<td>Symptoms duration (months)</td>
<td>13.1 ± 6.9</td>
<td>12.7 ± 6.4</td>
</tr>
<tr>
<td>Morning stiffness</td>
<td>138 (72.3)</td>
<td>60 (60.0)</td>
</tr>
<tr>
<td>IBP (ASAS criteria)</td>
<td>74 (38.7)</td>
<td>38 (38.0)</td>
</tr>
<tr>
<td>Arthritis</td>
<td>42 (22.0)</td>
<td>11 (11.0)</td>
</tr>
<tr>
<td>Enthesitis</td>
<td>38 (19.9)</td>
<td>19 (19.0)</td>
</tr>
<tr>
<td>Dactylitis</td>
<td>13 (6.8)</td>
<td>3 (3.0)</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>23 (12.0)</td>
<td>10 (10.0)</td>
</tr>
<tr>
<td>IBD</td>
<td>8 (4.2)</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Uveitis</td>
<td>11 (5.8)</td>
<td>12 (12.0)</td>
</tr>
<tr>
<td>Diarrhea, cervicitis, urethritis</td>
<td>5 (2.6)</td>
<td>6 (6.0)</td>
</tr>
<tr>
<td>HLA-B27</td>
<td>151 (79.1)</td>
<td>68 (68.0)</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>12.4 ± 16.6</td>
<td>7.8 ± 11.7</td>
</tr>
<tr>
<td>ESR (mmHg)</td>
<td>12.3 ± 13.9</td>
<td>16.0 ± 12.5</td>
</tr>
<tr>
<td>SJC (0-68)</td>
<td>0.3 ± 1.6</td>
<td>0.2 ± 0.6</td>
</tr>
<tr>
<td>VAS (0-100) physician</td>
<td>30 ± 22</td>
<td>28 ± 22</td>
</tr>
<tr>
<td>VAS (0-100) patient</td>
<td>40 ± 26</td>
<td>45 ± 29</td>
</tr>
<tr>
<td>BASDAI (0-10)</td>
<td>3.7 ± 2.2</td>
<td>4.0 ± 2.3</td>
</tr>
<tr>
<td>BASFI (0-10)</td>
<td>2.2 ± 2.3</td>
<td>2.6 ± 2.4</td>
</tr>
<tr>
<td>BASMI (0-10)</td>
<td>1.4 ± 1.3</td>
<td>1.5 ± 1.1</td>
</tr>
<tr>
<td>MASES (0-13)</td>
<td>0.5 ± 1.2</td>
<td>0.5 ± 1.5</td>
</tr>
<tr>
<td>Sacroiliitis on x Ray (m NY criteria)</td>
<td>81 (42.4)</td>
<td>28 (28.0)</td>
</tr>
<tr>
<td>Sacroiliitis on MRI (ASAS criteria)</td>
<td>72 (37.7)</td>
<td>53 (53.0)</td>
</tr>
<tr>
<td>Disability to work (%)</td>
<td>24 (12.5)</td>
<td>7 (7.0)</td>
</tr>
<tr>
<td>ASQoL (0-18)</td>
<td>5.5 ± 4.9</td>
<td>6.6 ± 4.5</td>
</tr>
</tbody>
</table>

Table 2.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Periferical Spondylarthritis n: 377</th>
<th>Spondylarthritis n: 86</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Males 50</td>
<td>Females 36</td>
<td>0.7</td>
</tr>
<tr>
<td></td>
<td>33.1 ± 8.4</td>
<td>32.4 ± 6.9</td>
<td></td>
</tr>
<tr>
<td>Family history</td>
<td>15 (30.0)</td>
<td>16 (44.4)</td>
<td>0.2</td>
</tr>
<tr>
<td>Symptoms duration (months)</td>
<td>10.4 ± 6.4</td>
<td>7.7 ± 5.5</td>
<td>0.04</td>
</tr>
<tr>
<td>Morning stiffness</td>
<td>3 (6.0)</td>
<td>3 (8.3)</td>
<td>0.7</td>
</tr>
<tr>
<td>IBP (ASAS criteria)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthritis</td>
<td>48 (96.0)</td>
<td>35 (97.2)</td>
<td>0.8</td>
</tr>
<tr>
<td>Enthesitis</td>
<td>28 (56.0)</td>
<td>15 (41.7)</td>
<td>0.2</td>
</tr>
<tr>
<td>Dactylitis</td>
<td>17 (34.0)</td>
<td>11 (30.6)</td>
<td>0.7</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>21 (42.0)</td>
<td>7 (19.4)</td>
<td>0.03</td>
</tr>
<tr>
<td>IBD</td>
<td>6 (12.0)</td>
<td>4 (11.1)</td>
<td>0.9</td>
</tr>
<tr>
<td>Uveitis</td>
<td>1 (2.0)</td>
<td>0 (0)</td>
<td>0.4</td>
</tr>
<tr>
<td>Diarrhea, cervicitis, urethritis</td>
<td>4 (8.0)</td>
<td>1 (2.8)</td>
<td>0.3</td>
</tr>
<tr>
<td>HLA-B27</td>
<td>16 (32.0)</td>
<td>12 (33.3)</td>
<td>1.0</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>17.4 ± 39.5</td>
<td>8.6 ± 11.5</td>
<td>0.1</td>
</tr>
<tr>
<td>ESR (mmHg)</td>
<td>11.9 ± 14.1</td>
<td>17.4 ± 11.6</td>
<td>0.09</td>
</tr>
<tr>
<td>SJC (0-68)</td>
<td>1.4 ± 2.4</td>
<td>1.3 ± 2.3</td>
<td>0.8</td>
</tr>
<tr>
<td>VAS (0-100) physician</td>
<td>22 ± 19</td>
<td>27 ± 25</td>
<td>0.4</td>
</tr>
<tr>
<td>VAS (0-100) patient</td>
<td>29 ± 22</td>
<td>35 ± 29</td>
<td>0.4</td>
</tr>
<tr>
<td>BASDAI (0-10)</td>
<td>3.2 ± 2.1</td>
<td>3.8 ± 2.4</td>
<td>0.2</td>
</tr>
<tr>
<td>BASFI (0-10)</td>
<td>1.3 ± 1.4</td>
<td>2.3 ± 2.3</td>
<td>0.04</td>
</tr>
<tr>
<td>BASMI (0-10)</td>
<td>1.2 ± 1.1</td>
<td>1.4 ± 1.0</td>
<td>0.5</td>
</tr>
<tr>
<td>MASES (0-13)</td>
<td>0.2 ± 0.6</td>
<td>0.2 ± 0.4</td>
<td>0.6</td>
</tr>
<tr>
<td>Sacroilitis on x Ray (m NY criteria)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sacroilitis on MRI (ASAS criteria)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disability to work (%)</td>
<td>13 (26.0)</td>
<td>6 (16.7)</td>
<td>0.5</td>
</tr>
<tr>
<td>ASQoL (0-18)</td>
<td>4.1 ± 4.7</td>
<td>4.9 ± 5.3</td>
<td>0.5</td>
</tr>
</tbody>
</table>
Are Work Outcomes Improved in Axial Spondyloarthritis (axSpA) Patients with Biologic Therapy? Results from the British Society for Rheumatology Register

Gary J. Macfarlane, Gareth T. Jones and Joanna Shim, Epidemiology Group, School of Medicine, Medical Sciences and Nutrition, University of Aberdeen, Aberdeen, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Patients with axial spondyloarthritis (axSpA) identify the ability to stay at work as a priority. Biologic therapy improves disease activity and quality of life but evidence is equivocal on whether it improves work outcomes.

Methods: BSRBR-AS is a prospective study of patients with axSpA, recruited from eighty five centres throughout Great Britain, who are naïve to biologic therapy. Patient recruitment commenced in December 2012. We compared work outcomes (using the Work Productivity and Activity Impairment Index (WPAI:SHP)) in those commencing biologic therapy at the time of recruitment with those who did not. Adjustment for differences in characteristics (age, Bath indices of disease activity (BASDAI) function (BASFI) global status (BAS-G), and smoking) was by propensity score matching to obtain estimates of treatment effect one year after commencing such therapy.

Results: A total of 201 patients commencing biologics and 627 not commencing biologics have been followed up for one year and were eligible for the current analysis. The study population had a mean age of 53.5 years, a mean duration since diagnosis of 14.6 years, 71.6% were male and 67.8% were HLA-B27 positive. Patients who were commencing biologic therapy were younger (47.9 v. 55.3 years), more likely to be current smokers (22% v. 11.5%), with greater disease activity (BASDAI mean 6.3 v. 3.8), poorer function (BASFI mean 6.3 v. 3.8), and worse global status (BAS-G mean 7.0 v.3.8)(all p < 0.001). At recruitment they reported more absenteeism (13.0% v. 3.0%); more presenteeism (41.5% v. 19.9%); greater productivity impairment (43.3% v. 20.6%); and greater overall activity impairment (59.9% v. 32.5%). At follow-up, biologics patients reported improvements across absenteeism (-7.5%), presenteeism (-30.0%), productivity impairment (-32.2%), and overall activity impairment (-41.3%). After adjustment, biologics patients demonstrated a significantly greater improvement (compared to those not starting biologic therapy) in presenteeism (-12.4%; 95% CI=-22.7, -2.0). There was also greater improvement in absenteeism (-3.9%; -14.4, 6.6); greater reduction in productivity impairment (-8.6%; -20.1, 2.8) and greater reduction in overall activity impairment (-7.3%, -15.2, 0.5) although these differences were not statistically significant.

Conclusion: After taking account of differences between groups, treatment with biologic therapy was associated with greater improvement in measures of work (particularly a reduction in presenteeism) amongst patients with axSpA, compared to those not starting biologic therapy. Thus biologic therapy delivers improved outcomes likely to have important economic benefits.
Disclosure: G. J. Macfarlane, Pfizer Inc; AbbVie; UCB, 2; G. T. Jones, AbbVie; Pfizer; UCB, 2; J. Shim, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/are-work-outcomes-improved-in-axial-spondyloarthritis-axspa-patients-with-biologic-therapy-results-from-the-british-society-for-rheumatology-register

Abstract Number: 2501

**Potential Differences in Axial Spondyloarthritis Disease Activity Categorization Using Different Minimum Values for High-Sensitivity CRP in Ankylosing Spondylitis Disease Activity Score Calculation and Different Definitions of Disease Flare**

Robert B.M. Landewé, Joachim Sieper, Uta Kiltz, Xin Wang, Mei Li, and Jaclyn K. Anderson, 1University of Amsterdam, Amsterdam, Netherlands, 2Charité Universitätsmedizin Berlin, Berlin, Germany, 3Rheumazentrum Ruhrgebiet, Herne, Germany, 4AbbVie Inc., North Chicago, IL

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Tuesday, November 7, 2017

Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities

Session Type: ACR Poster Session C

Session Time: 9:00AM-11:00AM

Background/Purpose: It has been recommended that the lower limit of high-sensitivity CRP (hsCRP) be restricted to 2 in the Ankylosing Spondylitis Disease Activity Score (ASDAS) calculation. Also, a definition of flare of ASDAS increase ≥0.9 was recently proposed. Using non-radiographic axial SpA (nr-axSpA) trial data, this analysis evaluated potential differences in patient (pt) categorization using different minimum values for hsCRP in the ASDAS calculation and different definitions of disease flare.

Methods: ABILITY-3 (NCT01808118) assessed the impact of continuation versus withdrawal of adalimumab (ADA) in nr-axSpA pts who achieved sustained remission with open-label ADA. All pts received open-label ADA 40 mg every other wk during a 28-wk lead-in period. Pts who achieved remission, defined as ASDAS inactive disease (ID, ASDAS<1.3) at wks 16, 20, 24, and 28 were randomized to 40-wk, double-blind ADA (continuation) or PBO (withdrawal). ASDAS was calculated with the full range of hsCRP (protocol-defined) and limiting hsCRP to the lowest possible value of 2 mg/L (rederived). Flare was calculated as 2 consecutive study visits with ASDAS> 2.1 (protocol definition) or with ASDAS increase ≥0.9 (modified definition). Data are reported as observed (open label) and by nonresponder imputation (double blind).

Results: 673 pts were enrolled. At open-label baseline, mean ASDAS using the protocol-defined ASDAS calculation was 3.6 vs 3.7 when rederived. At wk 28, 295 (43.8%) pts achieved protocol-defined ASDAS ID vs 272 (40.4%) pts using the rederived ASDAS; mean ASDAS at double-blind baseline was 0.7 vs 0.9, respectively. At wk 68, significantly more pts treated with ADA vs PBO had no flare per protocol definition (69.7% vs 47.1%; P<0.001; Table). Similar results were observed with modified definitions (Table). At wk 68, significantly greater proportions of ADA vs PBO pts achieved ASDAS endpoints (all P<0.001), with similar results for protocol-defined and rederived ASDAS calculations, respectively: ID (57.2% vs 33.3% and 52.0% vs 29.4%), major improvement (58.6% vs 32.0% and 50.0% vs 30.7%), and clinically important improvement (67.1% vs 45.1% and 67.1% vs 44.4%).
Table. Percentage of patients not experiencing disease flare at week 68 using protocol-defined or rederived ASDAS and/or modified flare definitions

<table>
<thead>
<tr>
<th>Variable, n (%)</th>
<th>Adalimumab (40 mg EOW)</th>
<th>Placebo</th>
<th>Difference, %</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protocol-defined ASDAS and flare</td>
<td>106 (69.7)</td>
<td>72 (47.1)</td>
<td>22.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Rederived ASDAS, protocol-defined flare</td>
<td>100 (65.8)</td>
<td>69 (45.1)</td>
<td>20.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Protocol-defined ASDAS, modified flare definition</td>
<td>97 (63.8)</td>
<td>56 (36.6)</td>
<td>27.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Rederived ASDAS and modified flare definition</td>
<td>99 (65.1)</td>
<td>65 (42.5)</td>
<td>22.6</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

ASDAS, Ankylosing Spondylitis Disease Activity Score; EOW, every other week; ID.

Nonresponder imputation; P value using 2-sided Pearson chi-square test.

*Efficacy outcomes were calculated based on the number of patients randomized, rather than those who would have qualified for randomization based on rederived ASDAS calculations.

**Conclusion:** At both open-label and double-blind baseline, mean ASDAS was similar, regardless of the hsCRP value cut-off used. Fewer pts in both treatment groups were categorized as not experiencing a flare when limiting the lowest possible hsCRP value to 2 mg/L in the ASDAS calculation and/or using a modified flare definition. However, treatment differences remained similar compared with the protocol-defined methodology. Results suggest infrequent clinically relevant differences in ASDAS values with use of either definition for minimum hsCRP and that the use of ASDAS >2.1 or ASDAS increase ≥0.9 as the definition of flare is reasonable.

**Disclosure:** R. B. M. Landewé, Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, and Wyeth, 2,Abbott/AbbVie, Ablynx, Amgen, Astra-Zeneca, Bristol Myers Squibb, Celgene, Janssen (formerly Centocor), Galapagos, GlaxoSmithKline, Novartis, Novo-Nordisk, Merck, Pfizer, Roche, Schering-Plough, TiGenix, UCB, and Wyeth, 5,Abbott/AbbVie, Amgen, Bristol Myers Squibb, Janssen (formerly Centocor), Merck, Pfizer, Roche, Schering-Plough, UCB, and Wyeth, 8; J. Sieper, AbbVie, Janssen, Lilly, Merck, Novartis, Pfizer, Sun Pharma and UCB, 5,AbbVie, Janssen, Lilly, Merck, Novartis, and Pfizer, 8; U. Kiltz, Pfizer Inc, 2,AbbVie, Grunenthal, Novartis, and UCB, 5,AbbVie, Chugai, Janssen, Lilly, MSD, Novartis, Pfizer, and Roche, 8; X. Wang, AbbVie, 1,AbbVie, 3; M. Li, AbbVie, 1,AbbVie, 3; J. K. Anderson, AbbVie, 1,AbbVie, 3.

Defining Clinically Important Worsening Based on ASDAS-CRP for Axial Spondyloarthritis: A Data-Based Consensus By the Assessment in Spondyloarthritis International Society (ASAS)

Anna Molto1, Laure Gossec2, Robert B.M. Landewé3, Désirée van der Heijde4 and Maxime Dougados5, 1Hôpital Cochin, Department of Rheumatology, Paris Descartes University, Paris, France, 2UPMC University Paris 06, Pitié-Salpêtrière Hospital, Paris, France, 3Amsterdam Rheumatology & Immunology Center, Netherlands, Amsterdam, Netherlands, 4Rheumatology, Leiden University Medical Center, Leiden, Netherlands, 5Department of Rheumatology, Paris Descartes University, Hôpital Cochin, Paris, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Time: 9:00AM-11:00AM
Session Title: Spondyloarthopathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C

Background/Purpose: Disease flares are increasingly used as outcomes in axial spondyloarthritis (axSpA) trials or observational studies. The objective of this initiative was to define a cutoff for the ASDAS score that best defines the concept of ‘worsening in axSpA’, to be used in the context of clinical trials and longitudinal observational studies.

Methods:
Various steps were followed between 2014 and 2017. after an SLR and a vignette-exercise among ASAS members: a theoretical 'paper' patient-vignette. After presentation of the results at the ASAS 2015 meeting it was decided that the proposed cut-off needed to be validated with real-life data. A real-life multicenter international study: data necessary to calculate different outcomes were collected from real patients at 2 consecutive visits (spaced 7 days to 6 months): the external standard was defined as a patient’s report that he/she had worsened and he/she felt there was a need for treatment intensification. Different changes in the outcomes against both external standards for worsening (phy-worsening (vignettes) and pt-worsening) were tested followed by a consensus and voting procedure among ASAS members in January 2017.

Results:
(a) There was consensus about worsening being an absolute change between 2 time-points (without defining time between the 2 time-points) and about exploring cutoffs for 3 outcomes: ASDAS-CRP, BASDAI and pain. (b) The literature review had yielded 27 different cutoffs in 38 studies indicating important heterogeneity. (c) The vignette-exercise yielded 12 preliminary definitions for worsening to be tested (as previously reported (ref)). (d) In the prospective study the sensitivity and specificity of each cutoff was tested against pt-worsening and judged by the ASAS-community. (e) No consensus was reached for a BASDAI-based definition due to limited performance of all cut-offs, and it was decided to not define a value for a pain-based definition for worsening. Based on aggregated data (Table), a consensus was reached among the ASAS-members to define worsening as a deterioration in ASDAS of at least 0.9 points. While this cutoff led to only moderate sensitivity when tested against pt-worsening, the overall balance of sensitivity and specificity as well as the overall face validity of this cut-off value for ASDAS was deemed most acceptable.

Table. Sensitivity and specificity of different ASDAS cutoffs to define worsening, against phy-worsening and pt-worsening considered as external standards.
Cutoff values for change in ASDAS

<table>
<thead>
<tr>
<th>Cutoff values for change in ASDAS</th>
<th>Vignette exercise study (N=1150 physician judgments) against the external standard 'phys-worsening' (worsening in N=591)</th>
<th>Prospective real-life study (N=1169 patients), against the external standard 'pt-worsening' (worsening in N=127)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;=0.6</td>
<td>Sensitivity (%) 97</td>
<td>Specificity (%) 65</td>
</tr>
<tr>
<td>&gt;=0.9</td>
<td>Sensitivity (%) 85</td>
<td>Specificity (%) 87</td>
</tr>
<tr>
<td>&gt;=1.1</td>
<td>Sensitivity (%) 60</td>
<td>Specificity (%) 94</td>
</tr>
</tbody>
</table>

Conclusion:

This data-driven ASAS consensus process has allowed to propose an ASDAS-based cutoff value defining worsening in axSpA. As has been observed in other settings, the change defining worsening (at least 0.9) is smaller than the change defining improvement which is 1.2 for ASDAS. This definition should now be applied in trials.

Disclosure: A. Molto, None; L. Gossec, None; R. B. M. Landewé, Abbott/Abb Vie, Ablynx, Amgen, Astra-Zeneca, Bristol Myers Squibb, Celgene, Janssen, Galapagos, Glaxo-Smith-Kline, Novartis, Novo-Nordisk, Merck, Pfizer, Roche, Schering-Plough, TiGenix, UCB, Wyeth, 5,Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, Wyeth, 2,Director of Rheumatology Consultancy BV, 4,Board Member Merit Foundation, 3; D. van der Heijde, None; M. Dougados, Abbvie, Pfizer, Eli Lilly and Company, Novartis, UCB, Merck, Roche, BMS UCB, 2,Abbvie, Pfizer, Eli Lilly and Company, Novartis, UCB, Merck, Roche, BMS, UCB, 5.

Abstract Number: 2503

Does Maastricht Ankylosing Spondylitis Enthesitis Scores Differ between Ankylosing Spondylitis, Psoriatic Arthritis and Rheumatoid Arthritis Patients?

Steffan Robstad Nilssen1, Jintana B: Andersen1, Hanne K. Vestaby1, Glenn Haugeberg2 and Brigitte Michelsen3,
1Dept. of Rheumatology, Hospital of Southern Norway Trust, Kristiansand, Norway, 2Martina Hansens Hospital, Bærum, Norway, 3Dept. of Rheumatology, Hospital of Southern Norway Trust, kristiansand, Norway

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthopathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) is an enthesitis index developed and validated as an outcome measure in ankylosing spondylitis (AS), but is also commonly used in patients...
with psoriatic arthritis (PsA). We aimed to compare the MASES scores between AS, PsA and rheumatoid arthritis (RA) patients.

Methods: From January 2016 to April 2017 AS, PsA and RA patients treated with tumor necrosis factor inhibitors (TNFi) were included in a random manner at the outpatient clinic of the Hospital of Southern Norway Trust, Norway. All RA patients fulfilled the ACR/EULAR, the PsA patients the Classification criteria for Psoriatic Arthritis (CASPAR) and the AS patients the Assessment of SpondyloArthritis International Society (ASAS) diagnostic criteria. MASES scores (range 0-13) were measured by a trained nurse. Tenderness was recorded as absent (0) or present (1). The unadjusted analyses of MASES were conducted using a one way analysis of variance (ANOVA) with post hoc tests (Tukey HSD: homogeneity of variance). The adjusted analyses were conducted using analysis of covariance (ANCOVA) with adjustments for age, sex, disease duration as well as with and without body mass index (BMI). Adjustment for multiple comparisons (Bonferroni) was performed.

Results: A total of 90 AS, 46 PsA and 94 RA patients were included. Mean (SD) age was 48.4 (11.4)/ 54.9 (11.0)/ 54.9 (12.6) years, disease duration 12.6 (9.8) / 14.4 (7.3)/ 13.8 (9.1) years, BMI 27.9 (12.7)/ 27.0 (3.5)/ 26.8 (10.7) kg/m² and percentages females 33.3/ 32.6/ 62.8%, respectively. Both in unadjusted as well as in adjusted analyses, no statistically significant differences in MASES scores between the AS, PsA and RA patients were found (table). Additional adjustment for BMI did not change the main findings.

<table>
<thead>
<tr>
<th></th>
<th>AS (n=90)</th>
<th>PsA (n=46)</th>
<th>RA (n=94)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MASES scores</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted analyses</td>
<td>2.64 (2.00-3.29)</td>
<td>3.44 (2.50-4.37)</td>
<td>2.87 (2.33-3.42)</td>
<td>0.857&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>MASES scores</td>
<td></td>
<td></td>
<td></td>
<td>0.534&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Adjusted analyses</td>
<td>2.91 (2.22-3.60)</td>
<td>3.79 (2.93-4.65)</td>
<td>2.59 (1.92-3.24)</td>
<td>0.088&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Data are shown as mean estimate (95% confidence interval)

a: AS-RA, b: PsA-RA, c: AS-PsA

Conclusion: Enthesitis is a clinically important feature of spondyloarthritis, in contrast to RA. Nevertheless, no significant differences were found in MASES scores between the AS, PsA and RA patients, even after adjusting for BMI.

Disclosure: S. R. Nilssen, None; J. B. Andersen, None; H. K. Vestaby, None; G. Haugeberg, None; B. Michelsen, None.


Abstract Number: 2504

The Validation of Istanbul Back Disability Index (IBDI) in Axial Spondyloarthritis Patients

Tuncay Duruoz, Hatice Sule Baklacioglu, Sevtap Acer Kasman and Didem Erdem, PMR Department, Rheumatology Division, Marmara University School of Medicine, Istanbul, Turkey

First publication: September 18, 2017

SESSION INFORMATION
Background/Purpose: The IBDI was developed to assess the disability in patients with mechanical low back pain (1) which contains the 18 daily activities questions. The main symptom in Axial Spondyloarthritis (Ax-SpA) is inflammatory back pain which makes patient disabled in daily living. To assess the functional disability concerning to inflammatory back pain is important for accurate clinical approach to patients in daily practice. The aim of this study is to investigate the validation of Istanbul Back Disability Index (IBDI) in Ax-SpA patients.

Methods: The patients with Ax-SpA according to ASAS criteria were recruited into the study. Demographic, clinical and functional characteristics of patients were evaluated. Face and content validities were assessed via cognitive debriefing interviews with Ax-SpA patients. Classical psychometrics assessed, convergent validity (correlation of IBDI with Dougados Functional Index (DFI), Health Assessment Questionnaire (HAQ), ASAS Health Index (ASAS-HI), BASDAI, BASFI) and discriminative validity (correlation of IBDI with disease duration (month), Body Mass Index (BMI), Schöber’s test (cm), finger-floor distance (cm), tragus-wall distance (cm), chest expansion (cm), MASES enthesitis score,). Spearman’s correlation coefficient was used to assess the relation between quantitative variables. The SPSS 24.0 statistical package was used for analysis. P<0.05 was accepted as significant.

Results: Sixty patients (37 male, 23 female) with mean of age 39.18 (SD:8.95) years were recruited. The 43.3 % of patients were smoking. The mean of disease duration was 85.93 (SD:79,06) months and the mean of BMI was 26.98 (SD: 4.18) kg/m². The means of BASDAI and the BASFI were 4,49 (SD: 2,37) and 2,83 (SD: 2,67) respectively. Cognitive debriefing showed the IBDI to be clear, relevant, and comprehensive which shows its face and content validity. The IBDI has good correlation with DFI (rho: 0,809; p<0,0001), HAQ (rho: 0,770; p<0,0001), ASAS-HI (rho:0,673; p<0,0001), BASDAI (rho:0,572; p<0,0001) and BASFI (rho:0,821; p<0,0001). This results show that IBDI has good convergent validity. The IBDI has not significant correlation with non functional parameters such as disease duration (rho: 0,202; p:0,121), BMI (rho: -0,142; p:0,280), Schöber’s test (rho:-0,150; p:0,252), finger-floor distance (rho: 0,189; p:0,149), tragus-wall distance (rho: 0,157; p:0,230), chest expansion (rho: -0,232; p:0,075) and MASES (rho: 0,168; p:0,200). These results show that IBDI has discriminative validity.

Conclusion: The IBDI is practical, accurate and not time consuming scale which is valid to evaluate the functional disability in patients with Axial Spondyloarthritis.


Disclosure: T. Duruoz, Abbvie, 2, Sanovel, 6; H. S. Baklacioglu, None; S. Acer Kasman, None; D. Erdem, None.


Abstract Number: 2505

Trends in Time to Diagnosis in Spondyloarthritis Patients. Association with 2009 ASAS Classification Criteria and Clinical Presentation at Disease Onset. Data from Comospa Study

Rodolfo Perez-Alamino1, Hernán Maldonado Ficco2, Christian A. Waimann3, José Antonio Maldonado-Cocco4,5, Anna Moltó6, Maxime Dougdas7, Désirée van der Heijde8, Robert B.M. Landewé9 and Filip van Den Bosch10, 1Rheumatology Department, Hospital de Clínicas Pte. Dr. Nicolás Avellaneda, Tucumán, Argentina, 2section of
SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Diagnostic delay is one of the greatest challenges in Spondyloarthritis (SpA).

Methods: We designed a cross-sectional study, including adult patients fulfilling ASAS SpA criteria from a multicentric international study for the ASAS-COMOSPA study. We evaluate trends in time to diagnosis of SpA during last decades, and its association with 2009 ASAS SpA classification criteria and clinical presentation. Disease onset was defined as first SpA-related musculoskeletal manifestation and/or diagnosis of extraarticular disease [uveitis, inflammatory bowel diseases (IBD) or psoriasis]. In those patients who developed an isolate extraarticular disease as initial manifestation, we performed a secondary analysis defining disease onset at first musculoskeletal manifestations. Time to diagnosis was defined as the gap between SpA diagnosis and disease onset. We stratified patients according decade of disease onset and initial clinical presentation and developed a multivariate logistic model, using early diagnosis (<2 years) as dependent variable and decade of disease onset, initial clinical presentation, sacroiliitis on x-ray, sex and age at disease onset, as independent variables. We estimated predicted probabilities for different clinical presentations.

Results: We included 3984 patients. Median time to diagnosis was 2.9 (p25-75= 0.3 Ð 9.8) years. This delay in diagnosis showed a progressive decrease during last decades (Graph 1A). Patients with disease onset after 2010, showed a shorter delay in diagnosis than those with disease onset in 2000-2010 decade. More frequent clinical presentations at disease onset were: isolated axial involvement (46%), isolated peripheral disease (20%), isolated extra-articular disease (19%), and multiple manifestations (15%). According to multivariate analysis, the probability to have an early diagnosis increased from 8% in patients before 1980 to 67% after 2010. Initial clinical presentation were independent predictors of time to diagnosis (Graph 1B).

Conclusion: Recognition and diagnosis of SpA have improved during the last decades. Type and number of initial clinical presentation were independent predictors of time to diagnosis.

Graph 1A-1B.
In Ankylosing Spondylitis/Axial Spondyloarthritis Smoking Is Associated with a Dose Related Elevation in CRP, Worse Disease Activity and Worse Quality of Life over One Year

Simon Stebbings¹, Mary Wallace², Andrew A. Harrison³, Nicola Dalbeth⁴, Douglas White⁵, Lisa K. Stamp⁶, Daniel Ching⁷ and John Highton⁸, ¹Dunedin Hospital, Department of Rheumatology, Dunedin, New Zealand, ²Surgical Sciences, University of Otago, Dunedin, New Zealand, ³Department of Medicine, University of Otago Wellington, Wellington, New Zealand, ⁴University of Auckland, Auckland, New Zealand, ⁵Department of Rheumatology, Waikato Clinical School, Hamilton, New Zealand, ⁶University of Otago, Christchurch, New Zealand, ⁷Timaru Medical Specialists Ltd, Timaru, New Zealand, ⁸Dept of Medicine, Univ of Otago Med Sch, Dunedin, New Zealand

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Analysis of data from several cohort studies of patients with ankylosing spondylitis (AS) / axial spondyloarthritis (AxSpA) have confirmed earlier suggestions that current smokers have worse outcomes in relation to disease activity, quality of life, radiographic progression and response to biologic therapies. To date studies have not used pack years to assess if there is a dose related effect. The effect of smoking on quality of life has only been studied in a cross sectional analysis.

The aim of the current study was to investigate the effect of smoking on disease activity and quality of life in patients with AxSpA and determine if continued smoking worsens outcomes over time.

Methods:
The Spondyloarthritis Genetics and the Environment (SAGE) study is a longitudinal multicenter study established in 2010 in New Zealand. Annual assessments were performed on a total of 368 patients fulfilling the ASAS criteria for AxSpA. A smoking history, including pack years, was obtained by interview from all participants. Standard outcome measures were recorded at each annual visit including BASDAI, BASFI, AS disease activity score (ASDAS-CRP) and quality of life measures both generic (EuroQol) and specific to AS (ASQol). The association between smoking and outcomes was assessed by linear regression analysis (statistical program R).

Results:
At baseline (visit 1) complete smoking data was available for 361 participants: 189 (52%) had never smoked, 117 (33%) were previous smokers and 55 (15%) were current smokers which is similar to national population data for current smokers in New Zealand (17%).

At baseline, there was a significant association between current cigarette smoking, and worse disease activity and physical function (ASDAS-CRP $\beta=0.95$, 95% $P=0.018$, BASDAI $\beta=0.95$ 95% $P=0.012$, BASFI $\beta=1.19$, 95% $P=0.0032$).

There was a linear relationship between quantity smoked (recorded as pack years/age) and higher CRP: $\beta 0.59$ 95% $P=0.047$.

After 12 months (visit 2), complete smoking data were available for 191 participants: 97 had never smoked, 71 were previous smokers, and 23 were current smokers. At visit 2, there was a significant association between cigarette smoking and higher disease activity as measured by the ASDAS-CRP ($\beta=0.60$, 95% $P=0.0097$). This remained significant even after adjusting for ASDAS-CRP at baseline ($P<0.05$).

Quality of life (Qol) measures showed that current smokers compared to those who never smoked had significantly worse health related Qol: ASQol $\beta 3.35$ $P=6.66e-05$, EuroQol $\beta -0.189 [-0.28- -0.097] P=6.02e-05$. At one year of follow up current smokers continued to record worse Qol measured by EuroQol: -0.12 [-0.22- -0.028] $P=0.012$.

**Conclusion:**

Smoking is associated with higher disease activity and worse quality of life at baseline. After one year of follow up these differences persist. Furthermore, there is a linear relationship between amount smoked and CRP, a marker for worse outcome. Patients with AS/AxSpA should be encouraged to quit smoking.

**Disclosure:** S. Stebbings, Johnson & Johnson, Abbvie, 8; M. Wallace, None; A. A. Harrison, None; N. Dalbeth, Takeda, AstraZeneca, Abbvie, 9; D. White, Abbvie, Pfizer, 5,Abbvie, 8; L. K. Stamp, Amgen, 8; D. Ching, AbbVie, Boehringer-Ingelheim, Celgene, Galapagos, Gilead, GlaxoSmithKline, Lilly, Merck Sharpe & Dhome, MedImmune, Pfizer, Roche, Sanofi, and UCB, 2,AbbVie, Boehringer-Ingelheim, Celgene, Galapagos, Gilead, GlaxoSmithKline, Lilly, Merck Sharpe & Dhome, MedImmune, Pfizer, Roche, Sanofi, and UCB, 5,AbbVie, 8; J. Highton, None.


**Abstract Number:** 2507

**Dactylitis and Enthesitis Predict Uveitis in Large Axial Spondyloarthritis Cohort**

**Gillian Fitzgerald**¹, Phil Gallagher², Catherine Sullivan³, Killian O Rourke⁴, Claire Sheehy⁵, Frances Stafford⁶, Carmel Silke⁷, Muhammad Haroon⁸, Ronan Mullan⁹, Sandy Fraser¹⁰, Grainne Murphy¹¹, Shawn Chavrimootoo¹², Oliver FitzGerald¹³ and Finbar O’Shea¹⁴, ¹Rheumatology, St James's Hospital, Dublin 8, Ireland, ²St. Vincent's University Hospital, Department of Rheumatology, Dublin, Ireland, ³ASRI, Dublin, Ireland, Cork, Ireland, ⁴Rheumatology, Midlands Regional Hospital, Tullamore, Co Offaly, Ireland, ⁵Rheumatology, University Hospital Waterford, Waterford, Ireland, ⁶Rheumatology, Blackrock Clinic, Co Dublin, Ireland, ⁷Rheumatology, Sligo University Hospital, Sligo, Ireland, ⁸Rheumatology, Kerry General Hospital, Co Kerry, Ireland, ⁹Department of Rheumatology, Dublin Academic Medical Centre, St. Vincent's University Hospital, Dublin, Ireland, ¹⁰Department of Rheumatology, University Hospitals Limerick, Ireland, Limerick, Ireland, ¹¹Rheumatology, Cork University Hospital, Cork, Ireland, ¹²Rheumatology, Our Lady's Hospital, Co Meath, Ireland, ¹³ASRI, Dublin, Ireland, Dublin, Ireland, ¹⁴St Jame, Dublin, Ireland

First publication: September 18, 2017
Background/Purpose:

ASRI (Ankylosing Spondylitis Registry of Ireland) is a national registry, designed to provide descriptive epidemiological data on the axial spondyloarthopathy (axSpA) population of Ireland. Uveitis is a common extra-articular manifestation in patients with axSpA. The exact prevalence and associated characteristics are not clearly defined in the literature. The aim of this study was to determine the prevalence of uveitis in a large axSpA cohort and identify associated characteristics.

Methods:

Patients enrolled in ASRI from 2013 until June 2017 were included in this study. A standardised detailed clinical assessment is performed on each patient at their inclusion. Structured interviews provide patient-reported data, including the presence of previous diagnosis of uveitis. Disease activity is assessed by Bath AS Disease Activity Index (BASDAI), spinal mobility by Bath AS Metrology Index (BASMI), function by the Bath AS Functional Index (BASFI) and Health Assessment Questionnaire (HAQ) and quality of life by AS Quality of Life (ASQoL). Statistical analysis is performed using SPSS.

Results:

As of June 2017, 683 patients have been entered in the database: 77% (n=526) male, mean age 45.9 years (SD 12.4), mean disease duration 19 years (SD 12.2), mean delay to diagnosis 8.6 years (SD 8.1), 78.8% fulfil modified New York criteria. Mean BASDAI is 3.9 (SD 2.5), BASMI is 3.6 (SD 2.5), BASFI is 3.6 (SD 2.7), HAQ is 0.52 (SD 0.52) and ASQoL is 6.4 (SD 5.5). HLA-B27 status is available for 74.1% (n=506) of the cohort: 92.7% of these are HLA-B27 positive.

The prevalence of uveitis in this cohort is 36.5%. With regards to other extra-articular manifestations, 6.9% have dactylitis, 18.3% have psoriasis, 9.2% have inflammatory bowel disease, 17.6% have enthesitis and 34.1% have peripheral arthritis.

Patients with uveitis are older (47 v 45 years, p=0.04) and have a longer duration of axial symptoms (21.7 v 17.3 years, p<0.01). There is no significant difference in markers of disease severity. Patients with uveitis have a higher prevalence of dactylitis (11.6% v 4.3%, p<0.01), enthesitis (25.9% v 13.5%, p<0.01), hypertension (26.1% v 18.6%, p=0.02) and HLA-B27 positivity (95.9% v 90.4%, p=0.02). There is a lower prevalence of smoking (22.2% v 32.2%, p=0.01) in patients with uveitis. Use of biologics is similar in patients with and without uveitis (30.7% v 26.8%, p=0.3). There is no difference in the use of NSAIDs (54.8% v 48.4%, p=0.1). There is a trend towards lower prevalence of IBD (12.1% v 7.6%, p=0.06) in patients with uveitis.

In multivariable regression analysis, disease duration, dactylitis and enthesitis are independently associated with the presence of uveitis, with dactylitis the strongest predictor (OR 3.2, 95% CI 1.5-6.8, p<0.01), followed by enthesitis (OR 1.8, 95% CI 1.1-2.9, p=0.02).

Conclusion:

In this axSpA cohort, 36.5% of patients have ever had an episode of uveitis. Uveitis is independently associated with dactylitis, enthesitis and longer disease duration. There is a higher prevalence of smokers in patients without uveitis.
Obese Axial Spondyloarthritis Patients Have Worse Disease Outcomes

Gillian Fitzgerald¹, Phil Gallagher², Catherine Sullivan³, Killian O Rourke⁴, Claire Sheehy⁵, Frances Stafford⁶, Carmel Silke⁷, Muhammad Haroon⁸, Ronan Mullan⁹, Sandy Fraser¹⁰, Grainne Murphy¹¹, Shawn Chavrimootoo¹², Oliver FitzGerald¹³ and Finbar O’Shea¹, ¹Rheumatology, St James's Hospital, Dublin 8, Ireland, ²St. Vincent's University Hospital, Department of Rheumatology, Dublin, Ireland, ³Rheumatology, UCHG Ireland, Galway, Ireland, ⁴Rheumatology, Midlands Regional Hospital, Tullamore, Co Offaly, Ireland, ⁵Rheumatology, University Hospital Waterford, Waterford, Ireland, ⁶Rheumatology, Blackrock Clinic, Co Dublin, Ireland, ⁷Rheumatology, Sligo University Hospital, Sligo, Ireland, ⁸Rheumatology, Kerry General Hospital, Co Kerry, Ireland, ⁹Department of Rheumatology, Tallaght Hospital, TCD, Dublin 24, Ireland, ¹⁰Department of Rheumatology, University Hospitals Limerick, Ireland, Limerick, Ireland, ¹¹Rheumatology, Cork University Hospital, Cork, Ireland, ¹²Rheumatology, Our Lady's Hospital, Co Meath, Ireland, ¹³St. Vincent's University Hospital, Department of Rheumatology. UCD Conway Institute of Biomolecular and Biomedical Research, University College Dublin, Dublin, Ireland

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Obesity is a worldwide public health concern, due to its association with morbidity and mortality. Existing literature looking at obesity in axial spondyloarthritis (axSpA) is sparse, but indicates increased BMI is prevalent. The impact of obesity on disease outcome is less well known. We aimed to determine the prevalence of obesity in a large axSpA cohort and describe its association with disease outcomes.

Methods:

Ankylosing Spondylitis Registry of Ireland (ASRI) provided the cohort for this study. The objectives of ASRI are to provide descriptive epidemiological data on the Irish axSpA population. A standardised clinical assessment is performed on each patient. Structured interviews provide patient-reported data. Weight is recorded in kilograms (kg) and height in centimetres (cm). BMI is categorised per the World Health Organisation criteria: normal weight <25 kg/m², overweight 25-29.9 kg/m² and obese ≥ 30 kg/m². Statistical analysis is performed using SPSS.

Results:

As of June 2017, 683 patients have been enrolled: 77% (n=526) male, mean age 45.9 ± 12.4 years, mean disease duration 19±12.2 years, mean delay to diagnosis 8.6±8.1 years, 78.8% fulfil modified New York criteria. Mean BASDAI is 3.9±2.5, BASMI is 3.6 ± 2.5, BASFI is 3.6± 2.7 and HAQ is 0.52 ±0.52.
Mean BMI in this cohort is 27.8±5.3 kg/m²: 1.1% (n=7) underweight, 31.6% (n=205) normal BMI, 38.9% (n=252) overweight, 28.4% (n=184) obese. Overall, 67.3% are overweight or obese: these patients are significantly older, have longer disease duration and more comorbidities, especially hypertension and hyperlipidaemia, than normal weight patients. Obese patients have significantly higher disease activity and worse physical function, spinal mobility and quality of life than both normal weight and overweight patients (table 1). The prevalence of smoking is lower in obese patients than normal weight patients. In univariable linear regression, BMI and obesity are associated with higher BASDAI, ASQoL, BASMI, BASFI and HAQ scores (table 2). In multivariable regression analysis, obesity remains an independent predictor of higher disease activity and worse function.

Conclusion:

Over two thirds of this axSpA cohort are overweight or obese. Higher BMI and obesity independently predicts worse disease outcomes. Strategies should be put in place to actively reduce axSpA patient’s BMI.

Table 1: Patient characteristics stratified according to BMI categories. Values are mean (±SD) or n (%).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Normal weight n=212</th>
<th>Overweight n=252</th>
<th>Obese n=184</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>41.6 (±12.3)</td>
<td>47.4 (±11.8)*</td>
<td>48.7 (±11.8)*</td>
</tr>
<tr>
<td>Male</td>
<td>156 (73.6%)</td>
<td>202 (80.2%)</td>
<td>143 (77.3%)</td>
</tr>
<tr>
<td>Disease duration, years</td>
<td>16.5 (±11.2)</td>
<td>20.1 (±11.9)*</td>
<td>20.6 (±12.9)*</td>
</tr>
<tr>
<td>HLA B-27 positive</td>
<td>151 (95%)</td>
<td>177 (93.2%)</td>
<td>116 (89.9%)</td>
</tr>
<tr>
<td>BMI, kg/m²²</td>
<td>22.6 (±1.7)</td>
<td>27.3 (±1.4)</td>
<td>34.4 (±4.5)</td>
</tr>
<tr>
<td>ASQoL (0-18)</td>
<td>6 (±5.5)</td>
<td>6 (±5.5)</td>
<td>8 (±5.4)* †</td>
</tr>
<tr>
<td>HAQ (0-3)</td>
<td>0.47 (±0.5)</td>
<td>0.57 (±0.5)</td>
<td>0.68 (±0.57)* †</td>
</tr>
<tr>
<td>BASDAI (0-10)</td>
<td>3.7 (±2.5)</td>
<td>3.8 (±2.4)</td>
<td>4.5 (±2.3)* †</td>
</tr>
<tr>
<td>BASFI (0-10)</td>
<td>2.9 (±2.5)</td>
<td>3.6 (±2.6)*</td>
<td>4.6 (±2.6)* †</td>
</tr>
<tr>
<td>BASMI (0-10)</td>
<td>3 (±2.3)</td>
<td>3.5 (±2.5)</td>
<td>4.6 (±2.5)* †</td>
</tr>
<tr>
<td>Uveitis</td>
<td>76 (35.8%)</td>
<td>88 (34.9%)</td>
<td>67 (36.4%)</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>33 (15.6%)</td>
<td>49 (19.4%)</td>
<td>39 (21.2%)</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>17 (8%)</td>
<td>30 (11.9%)</td>
<td>14 (7.6%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>19 (9%)</td>
<td>53 (21%)* †</td>
<td>71 (38.6%)* †</td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td>15 (7.1%)</td>
<td>40 (15.9%)* †</td>
<td>56 (30.4%)* †</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3 (1.4%)</td>
<td>11 (4.4%)</td>
<td>15 (8.2%)*</td>
</tr>
<tr>
<td>Current smoker</td>
<td>81 (38.2%)</td>
<td>78 (31%)</td>
<td>33 (17.9%)* †</td>
</tr>
<tr>
<td>Current alcohol intake</td>
<td>160 (75.5%)</td>
<td>189 (75%)</td>
<td>116 (63%)* †</td>
</tr>
<tr>
<td>Biologic use</td>
<td>155 (73.1%)</td>
<td>182 (72.2%)</td>
<td>129 (70.1%)</td>
</tr>
<tr>
<td>NSAID use</td>
<td>113 (53.3%)</td>
<td>109 (43.3%)</td>
<td>106 (57.6%)* †</td>
</tr>
</tbody>
</table>

*p value <0.05 compared to BMI <25 kg/m²²; † p value <0.05 compared to BMI 25-30 kg/m²².

Table 2: Linear regression analysis of association between BMI and obesity with clinical outcome.
### Table 1: Association of BMI and Obesity with Disease Outcomes

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Predicting variable</th>
<th>Univariable analysis, B (95% CI)</th>
<th>P</th>
<th>Multivariable analysis, B (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>BASDAI</td>
<td>BMI</td>
<td>0.089 (0.01-0.08)</td>
<td>0.02</td>
<td>0.07 (0.00-0.07)</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>Obesity</td>
<td>0.13 (0.29-1.1)</td>
<td>&lt;0.01</td>
<td>0.13 (0.25-1.1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ASQoL</td>
<td>BMI</td>
<td>0.14 (0.07-0.23)</td>
<td>&lt;0.01</td>
<td>0.14 (0.06-0.23)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>Obesity</td>
<td>0.16 (1.1-2.9)</td>
<td>&lt;0.01</td>
<td>0.17 (1.14-3.08)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>BASMI</td>
<td>BMI</td>
<td>0.26 (0.09-0.16)</td>
<td>&lt;0.01</td>
<td>0.17 (0.05-0.11)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>Obesity</td>
<td>0.22 (0.8-1.63)</td>
<td>&lt;0.01</td>
<td>0.18 (0.62-1.38)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>BASFI</td>
<td>BMI</td>
<td>0.24 (0.08-0.16)</td>
<td>&lt;0.01</td>
<td>0.17 (0.05-0.12)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>Obesity</td>
<td>0.21 (0.78-1.66)</td>
<td>&lt;0.01</td>
<td>0.17 (0.58-1.45)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>HAQ</td>
<td>BMI</td>
<td>0.14 (0.01-0.02)</td>
<td>&lt;0.01</td>
<td>0.1 (0-0.02)</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>Obesity</td>
<td>0.16 (0.1-0.28)</td>
<td>&lt;0.01</td>
<td>-0.15 (0.09-0.27)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

**Disclosure:** G. Fitzgerald, Abbvie, 9; P. Gallagher, None; C. Sullivan, None; K. O Rourke, None; C. Sheehy, None; F. Stafford, None; C. Silke, None; M. Haroon, None; R. Mullan, None; S. Fraser, None; G. Murphy, None; S. Chavrimootoo, None; O. FitzGerald, Pfizer, Abbvie, BMS, Novartis, UCB, Janssen, Celgene and Lilly, 2; F. O' Shea, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/obese-axial-spondyloarthropathy-patients-have-worse-disease-outcomes](http://acrabstracts.org/abstract/obese-axial-spondyloarthropathy-patients-have-worse-disease-outcomes)

**Abstract Number:** 2509

**High Prevalence of Sarcopenia in Axial Spondyloarthropathy Cohort**

**Gillian Fitzgerald**¹ and Finbar O' Shea², ¹Rheumatology, St James's Hospital, Dublin 8, Ireland, ²St Jame, Dublin, Ireland

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**
Sarcopenia, or age-related loss of muscle mass, is well documented in the general population and is associated with functional limitation and increased mortality. Literature on sarcopenia in axial spondyloarthritis (axSpA) is sparse and therefore the extent of the problem is virtually unknown. The aim of this study is to determine the prevalence of sarcopenia in patients with axSpA and determine associations with severity of disease.

Methods:

Forty-three consecutive patients (79.1% male, 97.7% Caucasian) with axSpA were included. Demographic data, spinal metrology, anthropometric measures, serum markers and patient-reported outcome measures were collected. Body composition analysis was performed using bioelectrical impedance analysis (BIA): fat mass, fat-free mass and predicted skeletal muscle mass were collected. Height was measured to the nearest 0.1 cm. Skeletal muscle mass index (SMI) was calculated by appendicular skeletal muscle mass (sum of predicted muscle mass in all 4 limbs) divided by height squared. Sarcopenia was defined as per the European Working Group on Sarcopenia in Older People definition as SMI ≤ 8.87 kg/m² in men and ≤ 6.42 kg/m² in women. BMI was categorised as normal if <25kg/m², overweight if >25kg/m² and obese if >30kg/m². SPSS was used for statistical analysis.

Results:

Baseline characteristics are outlined in table 1, along with significant differences between genders. Mean BMI is 28.8kg/m² (SD 6.3). A high BMI is present in 72.1% of the cohort: 27.9% have normal weight, 37.2% are overweight and 34.9% are obese. Sarcopenia is present in 41.9% (n=18) of the cohort (50% of men and 11.1% of women). In the males with sarcopenia compared to those without, BMI (24 v 34.1 kg/m², p<0.01), waist circumference (88.9 v 105.1 cm, p=0.01), hip circumference (95.6 v 109.9 cm, p<0.01) and fat percentage (20% v 30%, p<0.01) are significantly lower. Testosterone is significantly higher in patients with sarcopenia (18.5 v 13.8, p<0.05). There is no significant difference in disease activity parameters, although there is a trend towards lower BASMI in patients with sarcopenia (3.7 v 4.8, p=0.09). There is no significant difference in number of co-morbidities between patients with and without sarcopenia.

Only 58.8% of men with sarcopenia have normal weight. The remaining 41.2% are overweight. No men with sarcopenia are obese, but all men with normal weight are sarcopenic.

Conclusion:

Almost 42% of this axSpA cohort has sarcopenia. There is no association with disease outcome measures. Of the sarcopenic patients, just under half are overweight, which is at odds with our usual perception of sarcopenia. Physicians need to consider sarcopenia in axSpA, even in patients with high BMI.

Table 1: Baseline and anthropometric characteristics of cohort, along with significant differences between genders.
<table>
<thead>
<tr>
<th></th>
<th>Total (n=44)</th>
<th>Male (n=34)</th>
<th>Female (n=9)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (mean±SD)</td>
<td>50.8±11.1</td>
<td>51±10.5</td>
<td>50.4±13.7</td>
<td>0.9</td>
</tr>
<tr>
<td>Disease duration, years (mean±SD)</td>
<td>24±11.7</td>
<td>24.5±11.6</td>
<td>22.2±12.7</td>
<td>0.6</td>
</tr>
<tr>
<td>Delay to diagnosis, years (mean±SD)</td>
<td>8±7.3</td>
<td>7.8±7.3</td>
<td>9.7±7.7</td>
<td>0.6</td>
</tr>
<tr>
<td>BASDAI (mean±SD)</td>
<td>4.2±2.1</td>
<td>4.1±2.2</td>
<td>5±1.6</td>
<td>0.2</td>
</tr>
<tr>
<td>BASMI (mean±SD)</td>
<td>4.2±1.9</td>
<td>4.3±1.9</td>
<td>4.3±1.9</td>
<td>0.9</td>
</tr>
<tr>
<td>BASFI (mean±SD)</td>
<td>4.1±2.6</td>
<td>4.1±2.6</td>
<td>4±2.8</td>
<td>0.9</td>
</tr>
<tr>
<td>ASQoL (mean±SD)</td>
<td>7.1±5</td>
<td>6.7±4.9</td>
<td>8.8±5.1</td>
<td>0.3</td>
</tr>
<tr>
<td>BMI, kg/m² (mean±SD)</td>
<td>28.8±6.3</td>
<td>29±6.9</td>
<td>27.8±3.4</td>
<td>0.6</td>
</tr>
<tr>
<td>Fat percentage,% (mean±SD)</td>
<td>27.6±8.9</td>
<td>25±7.8</td>
<td>37.5±4.9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Waist circumference, cm (mean±SD)</td>
<td>95.1±0.17</td>
<td>97±18</td>
<td>87.9±12.6</td>
<td>0.2</td>
</tr>
<tr>
<td>Hip circumference, cm (mean±SD)</td>
<td>103.2±11.4</td>
<td>102.8±12.5</td>
<td>104.9±6</td>
<td>0.6</td>
</tr>
<tr>
<td>Waist:hip ratio (mean±SD)</td>
<td>0.93±0.18</td>
<td>0.95±0.18</td>
<td>0.84±0.1</td>
<td>0.07</td>
</tr>
<tr>
<td>Smooth muscle index (SMI), kg/m² (mean±SD)</td>
<td>8.7±1.7</td>
<td>9.18±1.6</td>
<td>6.98±0.55</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Disclosure: G. Fitzgerald, Abbvie, 9; F. O' Shea, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/high-prevalence-of-sarcopenia-in-axial-spondyloarthropathy-cohort](http://acrabstracts.org/abstract/high-prevalence-of-sarcopenia-in-axial-spondyloarthropathy-cohort)

Abstract Number: 2510

**Prevalence of and Factors Associated with Sarcopenia in Patients of Ankylosing Spondylitis**

Ran Song¹, Sang-Hoon Lee¹, Ji-Young Choi², Yeon-Ah Lee², Seung-Jae Hong² and Hyung-In Yang³, ¹Rheumatology, Kyung Hee University Hospital at Gang dong, Seoul, Korea, Republic of (South), ²Rheumatology, Kyung Hee University Hospital, Seoul, Korea, Republic of (South), ³Kyung Hee University Hospital at Gang dong, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Tuesday, November 7, 2017

Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities

Session Type: ACR Poster Session C

Session Time: 9:00AM-11:00AM

Background/Purpose:
Sarcopenia is characterized by progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability and poor quality of life. Sarcopenia is a common feature of all chronic inflammatory diseases and is related to elevated circulating proinflammatory cytokines like tumor necrosis factor. Low lean mass and sarcopenia are common in patients with inflammatory bowel disease and rheumatoid arthritis. However, the studies about sarcopenia in ankylosing spondylitis (AS) were lack. The aim of this study was to evaluate the prevalence and risk factors of sarcopenia in patients with ankylosing spondylitis.

Methods:

Cross-sectional data were collected on 60 male patients with AS who fulfilled the modified New York criteria. For measurement of body composition, dual energy X-ray absorptiometry (DXA) for bone mineral density (BMD) of the lumbar spine, total femur and whole body was performed. Sarcopenia was defined by low skeletal muscle mass (SMI<7.0 kg/m$^2$) and a low muscle strength (handgrip strength<26 kg) according to Asian working group for sarcopenia (AWGS) criteria. We also define the sarcopenia according to Korean criteria based on the Korea National Health and Nutrition Examination Survey (KNHANES) 2008-2009. Clinical data (age, BMI, disease duration, BASDAI, BASMI, use of anti-TNFα agent and use of glucocorticoid) and laboratory data (ESR, CRP, Hemoglobin and level of vitamin D) were compared for AS patients without sarcopenia versus those with sarcopenia.

Results:

The prevalence of sarcopenia by AWGS and Korea criteria based on KNHANES was 15% and 26.7% for patients with AS. The mean age of patients with sarcopenia according to the Korea criteria was 48.8±15.6 years and the sarcopenia occurred at a relatively young age in AS. Mean age was higher in the sarcopenia groups both by AWGS criteria and Korea criteria (p=0.02 and 0.004) and the level of ESR was higher in the sarcopenia group by Korea criteria (16.8±13.6 vs. 14.8±6.0, p=0.03). The patients with sarcopenia tended to show lower BMI, lower disease duration, more cumulative dose of glucocorticoid than the patients without sarcopenia, but there was no statistical significance. The older age (p=0.007), longer disease duration (p=0.008) and lower BMI (p<0.001) were significantly associated with lower skeletal muscle mass in AS.

Conclusion:

Sarcopenia occurred at a relatively young age in patients with AS. Mean age and level of ESR were higher in patients with sarcopenia. The older age, longer disease duration and lower BMI were significantly associated with lower skeletal muscle mass in AS.

Disclosure: R. Song, None; S. H. Lee, None; J. Y. Choi, None; Y. A. Lee, None; S. J. Hong, None; H. I. Yang, None.


Abstract Number: 2511

Irritable Bowel Syndrome and Its Impact on Patient-Reported Outcomes in Axial Spondyloarthritis: Is It an Overlooked Comorbidity?

Tor Olofsson1, Elisabeth Mogard1, Jan Marsal2, Mats Geijer3, Lars Erik Kristensen4, Elisabet Lindqvist1 and Johan K Wallman5, 1Department of Clinical Sciences Lund, Rheumatology, Lund University, Lund, Sweden, 2Department of Clinical Sciences Lund, Gastroenterology, Lund University, Lund, Sweden, 3Department of Radiology, Faculty of Medicine and Health, Örebro University, Örebro, Sweden, 4Department of Rheumatology, Copenhagen University Hospital, Frederiksberg and Bispebjerg, The Parker Institute, Copenhagen, Denmark, 5Department of Clinicial Sciences Lund, Rheumatology, Lund University, Lund, Sweden

First publication: September 18, 2017
Background/Purpose: While inflammatory bowel disease (IBD) is a well-known comorbidity in axial spondyloarthritis (SpA), little is known about functional bowel problems, such as irritable bowel syndrome (IBS), in these patients. In the general population, the IBS prevalence has been estimated to be around 11%. [1] In the present study, we examined the frequency of IBS-symptoms and their relation to patient-reported outcomes in an ongoing survey of axial SpA patients.

Methods: Consecutive axial SpA patients were examined and classified as non-radiographic axial SpA (nr-axSpA; ASAS criteria; n=37) or ankylosing spondylitis (AS; modified New York criteria; n=68). Patients with known IBD were excluded. The ROME III questionnaire was used to assess IBS criteria fulfillment, [2] and faecal (F) calprotectin was measured by a commercially available ELISA kit.

Results: Overall, 30% of patients fulfilled the IBS criteria (n=31; 32%/28% of nr-axSpA/AS patients, no significant between-group difference; Figure 1). In 11 of these subjects (35%), F-calprotectin was, however, also elevated (≥50 mg/kg; F-calprotectin was available in 86 of the 105 patients; Figure 2), making it hard to rule out inflammation rather than functional disease as cause of the symptoms. Applying a stricter definition of IBS, i.e. a combination of fulfilled IBS criteria and a non-pathologic F-calprotectin level (<50 mg/kg), this was met by 19% of the patients (n=16; 23%/16% of nr-axSpA/AS patients, no significant between-group difference; Figure 1). Irrespective of F-calprotectin levels, the presence of IBS symptoms was associated with worse patient-reported outcomes, especially regarding disease activity and health-related quality of life (Table).

Conclusion: In axial SpA patients without known IBD, IBS-symptoms were substantially more common than described for the general population, affecting almost 1/3 of patients, and were linked to worse patient-reported outcomes. To establish the true IBS prevalence in the cohort would require colonoscopy of certain subjects, although even based on a highly conservative definition (fulfillment of IBS criteria and F-calprotectin <50 mg/kg) the observed prevalence was >1.5 times higher than that reported in the general population.

2. Drossman DA. Gastroenterology 2006;130:1377-90
Figure 1.

IBS prevalence in axial spondyloarthritis

<table>
<thead>
<tr>
<th></th>
<th>Nr-axSpA</th>
<th>AS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Filling IBS criteria</td>
<td>12/37</td>
<td>19/68</td>
</tr>
<tr>
<td>Filling IBS criteria + F-Calprotectin &lt;50 mg/kg</td>
<td>7/30</td>
<td>9/56</td>
</tr>
</tbody>
</table>

Non-significant between-group difference (Nr-axSpA vs AS; Chi-2 test) regardless of IBS definition, with reservation for small groups.

Figure 2.

F-calprotectin distributions in patients fulfilling IBS criteria

Non-significant between-group difference (Nr-axSpA vs AS; Mann-Whitney U-test, based on Log10 F-calprotectin values), with reservation for small groups. n(Nr-axSpA/AS)=10/17. Patients missing F-calprotectin data, n (%): Nr-axSpA 2 (17%), AS 2 (11%). Lines represent median values, boxes 25th and 75th percentiles, whiskers 10th and 90th percentiles and dots outliers.
Impact of Inflammatory Bowel Disease in Early Spondyloarthritis in a Prospective Longitudinal Cohort

Daniel Wendling, Xavier Guillot, Clément Prati, Rik Lories and Maxime Dougados, 1Service de Rhumatologie, CHU Jean Minjoz, Besançon, France, 2EA 4267 FDE, FHU INCREASE, Université de Bourgogne FrancheComté, Besançon, France, 3Service de Rhumatologie, CHU J Minjoz, Besançon, France, 4Skeletal Biology and Engineering Research Center, KU Leuven, Leuven, Belgium, 5Rheumatology Department, Paris-Descartes University and Cochin Hospital, Paris, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Inflammatory bowel disease (IBD) is a classical extra articular feature of spondyloarthritis (SpA), with increasing evidence of a pathophysiological relationship.

The aims of this study were to evaluate in the DESIR cohort (1) The prevalence of IBD at baseline, and factors (epidemiological, clinical, imaging, biological data available in the database) associated with IBD, (2) The occurrence of new cases of IBD during the M0-M60 follow-up, and factors associated.

Methods:
DESIR is a prospective observational cohort of patients with recent onset (less than 3 years) inflammatory back pain, beginning before 50 years, suggestive of axial SpA, with a planned follow up of ten years. At baseline: identification of patients with IBD (with medical confirmation), analysis of factors (clinical, biological, imaging, treatment) associated with IBD: comparison of patients with and without IBD, for categorical variables: odds-ratio +/- 95% CI and chi-square/Fisher tests, for continuous variables: unpaired t-tests / Mann-Whitney, in uni and then multivariate analysis (logistic regression). Occurrence of new cases of IBD over the five first years of follow-up (database locked on June 20th 2016), and factors associated with IBD at M60 were assessed using uni- and multivariate analysis by logistic regression. Significance: p less than 0.05.

Results:

At baseline, 706 patients were analyzed, 35 had a past history or a concomitant IBD: prevalence 4.94% [CI 95%: 3.3 – 6.5]. IBD was significantly associated (univariate) with ESSG criteria (OR = infinite [2.8-infinite], familial history of IBD (OR = 3.56 [1.01-110.22]) and negatively associated with psoriasis (OR = 0.09 [0.02-0.24]), HLA-B27 (OR = 0.47 [0.21-0.98]) and NSAID score (mean 30.25 (IBD) versus 45.49; p = 0.005). In multivariate analysis IBD was associated positively with familial history of IBD (OR = 5.69 [3.57-7.82]) and negatively with psoriasis (OR = 0.04 [0.035-0.048]) and HLA-B27 (OR = 0.28 [0.26-0.31]). IBD was not associated with phenotypic presentation (peripheral arthritis, enthesitis, dactylitis, uveitis) or baseline serum levels of cytokines (TNF, IL-6, IL-17 A, IL-17 F, IL-23, IL-23). At M60, 617 patients were analyzed, 58 with IBD: prevalence 9.4 %. 23 incident cases of IBD were recorded, giving an estimated occurrence rate of 0.7/100 patient-years in this population. In univariate analysis on prevalent cases, IBD was associated with lower NSAID score (mean 17 versus 19.9, p = 0.029) and a less frequent NSAID response (OR = 0.30 [0.13-0.76]), worse activity and function indexes (ASDAS-CRP mean 2.28 versus 2.02; p = 0.038, BASFI mean 29 versus 22; p = 0.019, SF-36 mean 39 versus 44; p = 0.004, HAQ mean 0.75 versus 0.5; p = 0.004, ASQoL mean 8.7 versus 6.6; p = 0.012), and with more family history of IBD (OR = 6.6 [1-40]), more sick leave (mean 21 versus 11 days; p = 0.029), and fulfillment of ESSG criteria. In multivariate analysis, IBD was associated with fulfillment of modified New York criteria (p = 0.04).

Conclusion:

IBD occurs with a rate of 0.7/100 patient-years over 5 years in DESIR cohort, with a negative association at baseline with psoriasis and HLA-B27. At five years, IBD is associated with more severe disease and classification criteria.

Disclosure: D. Wendling, None; X. Guillot, None; C. Prati, None; R. Lories, None; M. Dougados, Abbvie, Pfizer, Lilly, Merck, Novartis, 5, Abbvie, Pfizer, Lilly, Merck, Novartis, 2.


Abstract Number: 2513

The Effect of Alcohol on Disease Activity in Axial Spondyloarthritis

Sizheng Zhao1,2, Daniel Thong3, Stephen Duffield1, David Hughes3 and Nicola Goodson1,2, 1Musculoskeletal Biology 1 Department, University of Liverpool, Liverpool, United Kingdom, 2Aintree University Hospital, Liverpool, United Kingdom, 3University of Liverpool, Liverpool, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Background/Purpose: There has been much interest in smoking as a modifiable risk factor for increased disease severity in rheumatic diseases. However, the effects of alcohol consumption remain unclear. Alcohol intake has been associated with increased disease susceptibility in psoriatic arthritis but also with reduced disease severity in rheumatoid arthritis. Its role in axial spondyloarthritis (axSpA) has not been studied in detail. The aim of this study was to explore whether alcohol consumption is associated with disease severity in axSpA.

Methods: Alcohol histories were obtained from axSpA patients meeting the ASAS criteria. Participants were categorised as current drinkers or non-drinkers. Quantity of intake was estimated using units per week with heavy consumption defined as >14 u/week. Disease activity (BASDAI, spinal pain, ASDAS) and functional impairment (BASFI) were compared between alcohol drinkers and non-drinkers, using multivariable linear models adjusting for age, gender, TNF inhibition therapy (TNFi), smoking, index of deprivation and self-reported anxiety and depression (A&D). Given their recognised link, interaction terms between alcohol and A&D were included in these models. Association between heavy alcohol consumption and disease severity was explored within drinkers using multivariable models with the above covariates.

Results: We studied 229 axSpA patients: 76% were male with mean age 46.5 (SD±13.8) years. A third were treated with TNFi. The median BASDAI was 5.7 [interquartile range (IQR) 3.3, 7.6] and BASFI 5.7 [IQR 3.3, 7.6]. ASDAS was available for 79% of patients with mean of 2.7 (SD±1.1). Ever-smoking was reported by 47% and A&D by 54%. Alcohol drinking was reported by 64%, with drinkers reporting median intake of 6 u/week [IQR 2 to 20]. Compared with non-drinkers, drinkers had lower BASDAI, ASDAS and BASFI (Table 1). There were no differences in disease severity between heavy and moderate drinkers. Stratified by smoking status, associations between alcohol and disease severity were stronger in never-smokers. There was a significant interaction between alcohol and A&D in smokers: drinkers had lower BASDAI and BASFI in the absence of A&D.

Conclusion: Alcohol consumption appears to be associated with reduced axSpA disease severity in this cross-sectional cohort. These associations were influenced by smoking status and A&D. This novel finding supports the need for further investigation to explore whether lifestyle modification could lead to better disease outcomes in axSpA.

Table 1. Multivariable linear models of association between alcohol-drinking and measures of disease activity.

<table>
<thead>
<tr>
<th></th>
<th>ß coefficient (95%CI) without interaction terms</th>
<th>ß coefficient (95%CI) in never-smokers</th>
<th>ß coefficient (95%CI) in ever-smokers if A&amp;D is absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>BASDAI</td>
<td>-0.80 (-1.47, -0.38)</td>
<td>-1.35 (-2.26, -0.45)</td>
<td>-1.68 (-3.28, -0.07)</td>
</tr>
<tr>
<td>ASDAS</td>
<td>-0.34 (-0.65, -0.03)</td>
<td>-0.51 (-0.93, -0.10)</td>
<td>-0.69 (-1.40, 0.01)</td>
</tr>
<tr>
<td>Spinal pain</td>
<td>-0.76 (-1.54, 0.02)</td>
<td>-1.70 (-2.74, -0.66)</td>
<td>-0.45 (-2.37, 1.46)</td>
</tr>
<tr>
<td>BASFI</td>
<td>-1.39 (-2.11, -0.67)</td>
<td>-2.22 (-3.18, -1.26)</td>
<td>-2.48 (-4.21, -0.75)</td>
</tr>
</tbody>
</table>

Total sample sizes for each regression model were 213 for BASDAI, BASFI and spinal pain, and 181 for ASDAS.

BASDAI, Bath ankylosing spondylitis disease activity index; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASFI, Bath AS functional index.

Disclosure: S. Zhao, None; D. Thong, None; S. Duffield, None; D. Hughes, None; N. Goodson, None.
When Should Lateral DEXA be Used to Measure Spine Bone Mineral Density in Axial Spondyloarthritis Patients: A Cross-Sectional Study

Sizheng Zhao1,2, Daniel Thong3, Eleanor Quilliam2, Stephen Duffield1, Kai-Wei Yin3 and Nicola Goodson1,2,
1Musculoskeletal Biology 1 Department, University of Liverpool, Liverpool, United Kingdom, 2Aintree University Hospital, Liverpool, United Kingdom, 3University of Liverpool, Liverpool, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Osteoporosis and vertebral fractures are recognized complications in axial spondyloarthritis (axSpA). Anteroposterior (AP) DEXA is commonly used to assess spinal bone mineral density (BMD) but can become inaccurate in the presence of syndesmophyte formation. The 2015 European League Against Rheumatism (EULAR) imaging guidelines highlight the importance of assessing for osteoporosis in axSpA and suggest use of lateral DEXA to assess spinal BMD [1]. However, it is unclear when lateral DEXA should be performed. The aims of this study were 1) to explore AP-BMD changes with axSpA symptom duration, and 2) to identify when optimum assessment of spinal BMD should include lateral spinal DEXA.

Methods: A cross-sectional study was conducted with axSpA patients fulfilling the ASAS criteria and not using bisphosphonates. Each patient underwent AP-DEXA of the lumbar spine (L1-L4) and total hip. Simultaneous lateral lumbar DEXAs were performed in a random subgroup of patients. AP-BMD was plotted against symptom duration using lowess smoothing. Piecewise linear regression was used to estimate a transition point after which AP-BMD began to increase. The difference between AP and lateral spinal BMDs was compared against symptom duration using scatter plots.

Results: AP-DEXAs were performed in 259 patients, 32 also underwent lateral DEXAs. 75% were male with mean age of 38.8 (SD±12.7) years. Median symptom duration was 16.6 years [interquartile range (IQR) 8, 28.4]. Mean BMI was 28.4 (SD±5.7). TNFi was used by 30% and 7% were taking calcium and vitamin D supplements. The median BASDAI was 6.4 [IQR 4.6, 7.7] and BASFI 6.4 [IQR 3.7, 8.2]. Osteopenia and osteoporosis of the spine were present in 27% and 5% and for the hip 29% and 3%, respectively, on AP-DEXA. In the first decade after symptom onset, patients with longer symptom duration had lower AP-BMD (Fig 1). However after 20 years, AP-BMD was higher with increasing symptom duration. Piecewise regression for spine g/cm² and T-score estimated the transition point to be 13 years (95%CI 2.7, 23.0). The difference between AP and lateral BMD increased with increasing symptom duration (Fig 2).

Conclusion: After 13 years, AP-BMD was higher with increasing symptom duration which likely reflects accrual of pathological new bone in this bisphosphonate-naïve cohort. This was supported by the increasing discrepancy between AP and lateral spinal BMD with increasing symptom duration. AP-DEXA can be used to assess BMD during the first decade of symptom duration, but lateral DEXA should be considered after 13 years, particularly for those with known syndesmophytes.
Prevalence and Risk Factors for Osteoporotic Fractures and Low Bone Mineral Density in Axial Spondyloarthritis: A Systematic Review and Meta-Analysis

Julio Ramírez1, Juan Carlos Nieto2, Rafael Curbelo3, Santos Castañeda4 and Loreto Carmona5, 1Rheumatology, Hospital Clinic, Barcelona, Spain, 2Rheumatology, Hospital General Universitario Gregorio Marañón, Madrid, Spain, 3Instituto de Salud Musculoesquelética, Madrid, Spain, 4Hospital Universitario de La Princesa, Madrid, Spain, Madrid, Spain, 5Instituto de Salud Musculoesquelética (InMusc), Madrid, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
To describe the prevalence of osteoporosis (1), the prevalence and incidence of fractures (2), and the frequency of risk factors for low bone mineral density (BMD) (3) in axial spondyloarthritis (Ax-SpA).

Methods:

A systematic review and meta-analysis of observational studies was conducted. Medline, Embase, and Cochrane Library databases were searched with a sensitive strategy. Cross-sectional and longitudinal studies with representative samples of patients with Ax-SpA estimating the frequency of osteoporosis or fractures were selected for objectives 1 and 2. For objective 3, large cross-sectional or longitudinal studies in patients with Ax-SpA published in the last 10 years (Jan 2006 to 2016) were selected.

Results:

After screening 3597 titles and abstracts, 46 studies were reviewed in detail, of which 35 studies had a cross-sectional design, 5 were prospective and 6 retrospective; 21 studies compared Ax-SpA patients with a control group—either healthy individuals (18 studies) or subjects with other diseases (6 studies)—. The prevalence of osteoporosis varied from 11.7% to 34.4% and that of fractures from 11% to 24.6%. Alcohol intake (58-61%), use of corticosteroids (11.7-66-9%), and 25-OH vitamin D deficiency (26-76%) were unexpectedly high in Ax-SpA patients.

Conclusion:

The prevalence of osteoporosis and fractures in Ax-SpA varies between 11.7% and 34.4% and 11-24.6%, respectively. These wide ranges reflect inconsistency of the prevalence estimates. Alcohol intake, steroid use and low levels of 25-OH-vitamin D should be taken into account in osteoporosis assessment in patients with Ax-SpA. Inconsistent results, lack of bone quality assessment, and high likelihood of bias in the majority of the published studies confirm the need for well-designed studies.

Disclosure: J. Ramírez, Gebro, 2; J. C. Nieto, None; R. Curbelo, None; S. Castañeda, None; L. Carmona, None.

Abstract Number: 2516

Trabecular Bone Score As an Assessment Tool to Identify the Risk of Osteoporosis in Axial Spondyloarthritis: A Case-Control Study

Kwi Young Kang, Internal Medicine, Catholic University of Korea, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017

Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities

Session Type: ACR Poster Session C

Session Time: 9:00AM-11:00AM

Background/Purpose: The trabecular bone score (TBS) is a novel tool used to evaluate bone microarchitecture. It is a textural index that evaluates pixel gray-level variations in the lumbar spine DXA image, thereby providing an indirect index of trabecular microarchitecture. To date, no studies have compared TBS between patients with axSpA and matched controls. Therefore, the present study was conducted to assess TBS in these two groups and to identify the risk factors related to a low TBS in patients with axSpA.
Methods: TBS and bone mineral density (BMD) were assessed in the two groups (axSpA and control) using dual-energy X-ray absorptiometry (DXA). Osteoporosis risk factors and inflammatory markers were also assessed. Disease activity and radiographic progression in the sacroiliac joint and spine were evaluated in the axSpA group. Multivariate linear regression analysis was performed to identify risk factors associated with TBS.

Results: In the axSpA group, 248 subjects were enrolled; an equal number of age- and sex-matched subjects comprised the control group. The mean TBS was 1.43±0.08 and 1.38±0.12 in the control and axSpA groups, respectively (p<0.001); BMD at the lumbar spine did not differ between the two groups. The TBS was negatively correlated with erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels in the axSpA group only (p<0.001 and p=0.007, respectively). Syndesmophytes in the axSpA group was associated with lower TBS (p<0.001) but higher lumbar BMD (p=0.021) versus controls. In the multivariate analyses, ESR, CRP, and spinal radiographic progression were significantly associated with TBS.

Conclusion: TBS assessments revealed poor bone quality in patients with axSpA compared with the matched controls. In axSpA, systemic inflammatory markers were negatively correlated with TBS and spinal radiographic progression and inflammatory markers were independently correlated with low TBS. TBS may, therefore, be a useful clinical tool to identify the risk of osteoporosis in patients with axSpA.

Disclosure: K. Y. Kang, None;


Abstract Number: 2517

The Usefulness of Trabecular Bone Score in Assessing the Bone Strength and Fracture Risk of Patients with Ankylosing Spondylitis

Seoung Wan Nam1, Yoon-Kyoung Sung2, Dam Kim2, Soo-Kyung Cho3, Yoonah Song4, Yun Young Choi5 and Tae-Hwan Kim2, 1Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), 2Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), 3Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), 4Department of Radiology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), 5Department of Nuclear Medicine, Hanyang University Medical Center, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Ankylosing spondylitis (AS) is a disease characterized by spinal osteoproliferation (syndesmophytois) and the general trabecular bone loss with increased fracture risk. Syndesmophyts in spine leads overestimation of the anteroposterior (AP) lumbar spine BMD measured by dual-energy X-ray absorptiometry (DXA) which is a gold standard of diagnostic tool for osteoporosis. Thus, more accurate fracture risk assessment tool is needed in AS patients.

Objectives: We aimed to compare various fracture risk assessment tools according to modified Stoke AS Spine Score (mSASSS), and to identify the tool which can best reflect the risk of fracture in AS patients.
Methods: Total of 215 AS patients were enrolled from a single university hospital in Korea. Demographic and clinical information was collected by questionnaires and physical exams. They completed simple X-ray of L-spine, AP and lateral BMD by DXA. FRAX was measured and TBS was obtained from DXA using TBS iNsight software. Quantification of spine ankyloses were determined by mSASSS. We classified patients into two groups: 1) high mSASSS group with mSASSS ≥19, which is median value of study population, and 2) low mSASSS group with mSASSS <19. We compared the clinical characteristics and fracture risk assessment tools between two groups. In addition, fracture risk assessment tools were compared according to history of fracture, which is known to be the strongest risk factor for fracture, using ANCOVA.

Results: The 109 patients (50.7%) were classified to high mSASSS group. Female patients were more in low mSASSS group (p<0.01), and smoking history were more prevalent in high mSASSS group (p<0.01). L-spine lateral BMD and TBS were lower, while right hip and L-spine AP BMD were significantly higher in high mSASSS group. After adjustment, mean TBS of L2-L3 was significantly lower and L-spine AP BMD was significantly higher in high mSASSS group (p=0.02 and p<0.01, respectively). Total 53 patients (24.7 %) had fracture history of any type. Patients with fracture history showed higher 10-year probability of major osteoporotic fracture by FRAX (p=0.01) and lower TBS of L2-L3 in patients with fracture history (p<0.04 after adjustment).

Conclusion: TBS was lower in patients with advanced syndesmophytes, and it was significantly associated with history of fracture. TBS can be a useful method in measuring bone strength and also predicting fracture risk in AS patients.

Table 1. Demographic and clinical characteristics, comparison of bone strength measurement methods in patients with ankylosing spondylitis

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total All patients</th>
<th>High mSASSS (n=109)</th>
<th>Low mSASSS (n=106)</th>
<th>p</th>
<th>adjusted p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>49.9±10.4</td>
<td>50.9±10.4</td>
<td>49.0±10.5</td>
<td>0.18</td>
<td>0.18</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>52 (24.2)</td>
<td>17 (15.6)</td>
<td>35 (33.0)</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Disease duration (months)</td>
<td>188.5±217.7</td>
<td>199.5±247.0</td>
<td>181.1±223.1</td>
<td>0.63</td>
<td>0.63</td>
</tr>
<tr>
<td>BMD (g/cm²)</td>
<td>24.5±4.3</td>
<td>25.3±3.8</td>
<td>23.7±3.0</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>142 (65)</td>
<td>88 (80.7)</td>
<td>54 (50.9)</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Never</td>
<td>73 (34.9)</td>
<td>31 (29.3)</td>
<td>42 (49.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of fracture, n (%)</td>
<td>9 (4.2)</td>
<td>7 (6.4)</td>
<td>2 (2.3)</td>
<td>0.10</td>
<td>0.10</td>
</tr>
<tr>
<td>Vertebral fracture</td>
<td>44 (20.5)</td>
<td>25 (22.9)</td>
<td>19 (17.9)</td>
<td>0.49</td>
<td>0.49</td>
</tr>
<tr>
<td>Non-vertebral fracture</td>
<td>3 (1.4)</td>
<td>0 (0.0)</td>
<td>3 (2.9)</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td>History of known osteoporosis, n (%)</td>
<td>1 (0.5)</td>
<td>0 (0.0)</td>
<td>1 (0.9)</td>
<td>0.62</td>
<td>0.62</td>
</tr>
<tr>
<td>BASMI (L2)</td>
<td>3.3±1.8</td>
<td>3.3±1.8 (n=104)</td>
<td>3.6±1.6 (n=103)</td>
<td>0.24</td>
<td>0.24</td>
</tr>
<tr>
<td>BASMI score</td>
<td>2.9±1.6</td>
<td>4.0±1.6</td>
<td>1.7±1.3</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>mSASSS (n=214)</td>
<td>19.9±7.2 (n=194)</td>
<td>24.9±11.6 (n=184)</td>
<td>12.5±3.6 (n=183)</td>
<td>0.20</td>
<td>0.20</td>
</tr>
<tr>
<td>Previous use of NSAIDs, n (%)</td>
<td>100 (48.1)</td>
<td>48 (44.4)</td>
<td>52 (50.5)</td>
<td>0.24</td>
<td>0.24</td>
</tr>
<tr>
<td>Previous use of DMARDs, n (%)</td>
<td>36 (16.8)</td>
<td>5 (4.6)</td>
<td>31 (30.8)</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>History of significant glucocorticoid use*, n (%)</td>
<td>15 (30.2)</td>
<td>10 (9.0)</td>
<td>5 (5.0)</td>
<td>0.06</td>
<td>0.06</td>
</tr>
<tr>
<td>TBS of L2-L3 (g/cm²)</td>
<td>1.3±0.10</td>
<td>1.3±0.10</td>
<td>1.3±0.10</td>
<td>0.54</td>
<td>0.54</td>
</tr>
<tr>
<td>Right hip BMD (g/cm²)</td>
<td>0.74±0.13</td>
<td>0.74±0.13</td>
<td>0.72±0.10</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td>Right hip tissue BMD (g/cm²)</td>
<td>0.87±0.11</td>
<td>0.83±0.15</td>
<td>0.85±0.11</td>
<td>0.07</td>
<td>0.07</td>
</tr>
<tr>
<td>Lumbar spine BMD, AP, L1-L4 (g/cm²)</td>
<td>1.03±0.21</td>
<td>1.11±0.22</td>
<td>0.96±0.15</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Lumbar spine BMD, AP, L1-L3 (g/cm²)</td>
<td>1.04±0.23</td>
<td>1.11±0.23</td>
<td>0.95±0.18</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Lumbar spine BMD, Lateral L1-L3 (g/cm²)</td>
<td>0.62±0.17</td>
<td>0.61±0.11</td>
<td>0.63±0.16</td>
<td>0.66</td>
<td>0.66</td>
</tr>
<tr>
<td>TBS, L1-L4</td>
<td>1.37±0.10</td>
<td>1.37±0.10</td>
<td>1.37±0.10</td>
<td>0.24</td>
<td>0.24</td>
</tr>
<tr>
<td>TBS, L2-L3</td>
<td>1.39±0.10</td>
<td>1.37±0.10</td>
<td>1.40±0.10</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td>10-year probability of major osteoporotic fracture (%)</td>
<td>4.5 (2.8-7.1)</td>
<td>4.2 (2.8-7.1)</td>
<td>4.9 (3.3-7.3)</td>
<td>0.15</td>
<td>0.15</td>
</tr>
<tr>
<td>10-year probability of hip fracture (%)</td>
<td>1.9 (0.9-3.7)</td>
<td>1.0 (0.5-2.3)</td>
<td>1.0 (0.5-2.3)</td>
<td>0.69</td>
<td>0.69</td>
</tr>
</tbody>
</table>

AS, Ankylosing Spondylitis; mSASSS, modified Stoke AS Spine Score; BMD, bone mineral density; BASMI, Body Mass Index; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BAI, Bath Ankylosing Spondylitis Beliefs Index; NSAID, nonsteroidal anti-inflammatory drug; DMARD, disease modifying antirheumatic drug; TBS, trabecular bone score; FRAX, fracture risk assessment method. *history of glucocorticoid use equivalent to <5 mg or more of prednisolone for more than 3 months.
Racial Differences in Clinical Characteristics and Co-Morbidities of Ankylosing Spondylitis

Dilpreet Singh¹ and Marina N. Magrey², ¹Rheumatology, Case Western Reserve University School of Medicine at MetroHealth Medical Center, Cleveland, OH, ²Case Western Reserve University School of Medicine at MetroHealth Medical Center, Cleveland, OH

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthopathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Ethnic heterogeneity of the United States (US) population makes it imperative to study the racial differences in clinical characteristics of Ankylosing Spondylitis (AS) patients, a disease mainly considered to be of Caucasians with HLA-B27 predominance. We hypothesize that African Americans (AA) have more severe disease compared to Caucasians in the US.

Methods:

Data was collected using Explorys universe, a clinical research informatics tool that uses unified medical language system ontologies to standardize, normalize and aggregate clinical data from 26 US major healthcare systems that use Epic from 1999 to present comprising of over 50 million patients. De-identified data are presented through a secure web interface. The Power Search tool was utilized to create refined cohorts with specific search criteria. We identified 28, 520 patients with AS. This was further stratified by having at least two rheumatology visits; adding race, gender, clinical characteristics, medication use or co-morbidity diagnoses to the search tool. Data sets were recorded as proportions, which were compared using chi-squared test (p<0.05).
Results:

10,990 AS patients with at least two rheumatology visits of all races were identified of whom 50% were males. 84% of AS patients were Caucasian, whereas 8% were AA. Half of both races were males (p=0.17). 25% of the AS cohort tested for HLA-B27 were positive (26% Caucasians vs 20% AA, p = 0.11). Subgroup analysis of 101 AS patient records at our institution identified 78% HLA-B27 positive patients (64% Caucasians vs 42% AA, p=0.0018).

65% of AS patients were smokers (67% Caucasians vs 59% AA, p<0.0001). A greater proportion of AA had elevated erythrocyte sedimentation rate (62% AA vs 48% Caucasians, p < 0.0001) and C-reactive protein levels (68% AA vs 54% Caucasians, p < 0.0001). 73% of AS patients had peripheral arthritis (74% Caucasians vs 76% AA, p= 0.15), 25% had enthesopathy (26% Caucasian vs 27% AA, p = 0.18), 10% had psoriasis (10% Caucasians vs 7% AA, p=0.0002) and inflammatory bowel disease (11% Caucasian vs 12% AA, p = 0.23), 4% had anterior uveitis (4% Caucasians vs 8% AA, p < 0.0001) and 5% had dactylitis (5% Caucasian vs 7% AA, p = 0.09). Majority (87%) of the AS patients were treated with nonsteroidal antiinflammatory drugs (87% Caucasians vs 89% AA, p=0.62) and 39% used TNF-α inhibitors (40% Caucasian vs 37% AA, p<0.08). AA compared to Caucasians had higher prevalence of hypertension (29% vs 22%, n=2,350, p<0.0001), diabetes (27% vs 17%, n=1,940, p<0.0001), depression (36% vs 32%, n=3,380, p=0.02) and heart disease (24% vs 22%, n=2,290, p=0.11). Caucasians compared to AA had higher prevalence of fibromyalgia (14% vs 12%, n=1,480, p=0.07) and osteoporosis (18% vs 16%, n=1890, p=0.36).

Conclusion:

Our findings from a large US electronic database confirm that AS is more prevalent in Caucasians with equal proportion of males and females between both races. Markers of inflammation, anterior uveitis and co-morbidities were significantly higher in AA. There was no significant difference in the use of TNF-α inhibitors. Study limitation was that Explorys could not capture the true proportion of HLA-B27 positivity due to it being a send out test with results not being electronically available in Epic.

Disclosure: D. Singh, None; M. N. Magrey, Amgen, AbbVie, and UCB Pharma, 2,UCB and Janssen, 5.

Characteristics of Eye Diseases in Patients with Ankylosing Spondylitis in Korea: A Single-Center Survey

Seunghun Lee¹, Bon San Koo², Ji Hui Shin³ and Tae-Hwan Kim⁴, ¹Department of Radiology, Hanyang University Hospital, Seoul, Korea, Republic of (South), ²rheumatology, Inje University College of Medicine, seoul, Korea, Republic of (South), ³rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), ⁴Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM
Uveitis is the most common extra-articular manifestation occurring in patients with ankylosing spondylitis (AS). The purpose of this study is to evaluate the characteristics of uveitis in patients with AS using questionnaire survey.

Methods: A questionnaire-based survey was conducted for patients enrolled in AS registry at a rheumatology clinic in a tertiary hospital between September 2015 and December 2015. Patients responded to 10 questions, with several sub-questions related to eye disease including uveitis.

Results: A total of 750 patients participated in the survey. Among them, 266 (35%) answered that they had an eye disease including uveitis (64%), conjunctivitis (8%), dry eye (6%), and iritis (5%). The number of patients who were diagnosed with uveitis in the ophthalmology department was 218 (29%). The number of patients who experienced a flare of uveitis more than once a year was 109 (50%). In addition, at the time of the study, only 53 (24%) had been recommended to undergo testing for autoimmune disease. The most common symptoms of patients with uveitis were ocular congestion (61%), eye pain (54%), and decreased visual acuity (51%). Interestingly, 91 of the 532 patients (17%) who had not been diagnosed with uveitis before also experienced similar symptoms.

Conclusion:

We identified various eye-related problems and the clinical characteristics of uveitis in patients with AS. Our survey revealed not only information about AS-related eye diseases but also the need for cooperation between rheumatologists and ophthalmologists.

Disclosure: S. Lee, None; B. S. Koo, None; J. H. Shin, None; T. H. Kim, None.


Abstract Number: 2520

Incidence of Extra-Articular Manifestations in PsA and As Patients Treated with Golimumab in Canadian Real-World

Michelle Teo1, Derek Haaland2, John Kelsall3, Isabelle Fortin4, Pauline Boulos5, Raman Rai6, Sanjay Dixit7, B Harauou8, Dalton Sholter9, Eliofoistis Psaradellis10, Emmanouil Rampakakis10, Brendan Osborne11, Francois Nantel11 and Allen J Lehman12, 1Balfour Medical Clinic, Penticton, BC, Canada, 2Rheumatology, Clinical Immunology & Allergy, McMaster University, Barrie, ON, Canada, 3Rheumatology, University of British Columbia, Vancouver, BC, Canada, 4Centre de Rhumatologie De l’Est du Quebec, Rimouski, QC, Canada, 5Rheumatology, McMaster University, Hamilton, ON, Canada, 6Private Practice, Hamilton, ON, Canada, 7Rheumatology, McMaster University Hamilton, Burlington, ON, Canada, 8Institut de Recherche en Rhumatologie de Montréal (IRRM), Montreal, QC, Canada, 9Rheumatology Associates, Edmonton, AB, Canada, 10JSS Medical Research, Montreal, QC, Canada, 11Medical Affairs, Janssen Inc., Toronto, ON, Canada, 12Janssen Inc., Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Spondyloarthropathies (SpA) encompass a heterogeneous group of chronic inflammatory diseases affecting axial and peripheral joints. Besides articular symptoms, patients also experience extra-articular
manifestations (EAMs) including uveitis, psoriasis, inflammatory bowel disease (IBD) and multiple organ involvement. The aim of this analysis was to describe the incidence of new onset EAMs focusing on uveitis and IBD among SpA pts over 6 and 12 months of treatment with golimumab (GLM).

**Methods:** BioTRAC is an ongoing, prospective registry of patients initiating treatment with infliximab or GLM for RA, AS, or PsA, or with ustekinumab for PsA. Eligible participants for this analysis comprised GLM-treated AS (n=395) and PsA (n=257) patients. Presence of EAMs was defined as patients with uveitis or IBD. IBD data, however, was not collected for PsA pts. Results were based on patients with available data. Safety was ascertained by the incidence of adverse events (AEs) and serious adverse events (SAEs), reported per 100 pt years (PY) of follow-up.

**Results:** Among AS pts, at baseline, the mean (SD) age was 45.3 (13.5) years and CRP was 14.1 (30.5) mg/L. Positive HLA B27 status was reported for 174 (174/264; 65.9%) pts. History of uveitis was reported among 14.2% (n=50/352) of AS pts. EAMs are reported over time in Table 1. New-onset uveitis and IBD was reported for 2.3% (3.2 events/100 PY) and 1.1% (1.5 events/100 PY) of pts during follow-up, respectively. Results showed that CRP and HLA B27 status were not significantly associated with presence of EAMs at baseline. Overall, 419 AEs and 26 SAEs were reported by 199 (50.4%) and 16 (4.1%) pts by 12 months of treatment, respectively, for a total of 144.1 AEs/100 PY and 8.9 SAEs/100 PY. A total of 5 AEs of uveitis were reported all of which were of mild severity, and either not (n=4) or unlikely related (n=1) to the study drug.

Among PsA pts, the mean (SD) age was 52.7 (13.2) years and CRP was 13.2 (32.4) mg/L at baseline. A total of 9 (9/80; 11.3%) pts had positive HLA B27 status. Patients with a history of uveitis was reported for 1.8% (n=4/224) of PsA pts. New-onset uveitis was reported for 0.4% (0.5 events/100 PY) of patients during follow-up. Overall, 254 AEs and 15 SAEs were reported by 123 (47.9%) and 12 (4.7%) patients by 12 months of treatment, respectively, for a total of 135.0 AEs/100 PY and 8.0 SAEs/100 PY.

Table 1. EAMs over Time and New Onset since Baseline

| Diagnosis | EAM     | Patients with EAMs | New Onset at 6 Months | New Onset at 12 Months | New Onset over Follow-up
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>n/N</td>
<td>6 Months</td>
<td>12 Months</td>
<td></td>
</tr>
<tr>
<td>AS</td>
<td>Uveitis</td>
<td>4/390</td>
<td>8/278</td>
<td>1/197</td>
<td>8/272</td>
</tr>
<tr>
<td></td>
<td>No uveitis</td>
<td>386/390</td>
<td>270/278</td>
<td>196/197</td>
<td>NA</td>
</tr>
<tr>
<td>IBD</td>
<td></td>
<td>22/393</td>
<td>16/277</td>
<td>10/195</td>
<td>4/256</td>
</tr>
<tr>
<td></td>
<td>No IBD</td>
<td>371/393</td>
<td>261/277</td>
<td>185/195</td>
<td>NA</td>
</tr>
<tr>
<td>PsA</td>
<td>Uveitis</td>
<td>0/256</td>
<td>1/187</td>
<td>0/131</td>
<td>1/186</td>
</tr>
<tr>
<td></td>
<td>No uveitis</td>
<td>256/256</td>
<td>186/187</td>
<td>131/131</td>
<td>NA</td>
</tr>
</tbody>
</table>

Patients with unknown EAM were excluded from the analysis. *Denominator (N) represents patients at risk at the respective visit relative to the previous visit. **Average follow-up per patient was 8.8 months for AS and 9.8 months for PsA. NA=not applicable

**Conclusion:** In patients with AS, development of uveitis and IBD was 2.3% and 1.1% during 12-month follow-up of GLM-treatment. Among PsA patients, lower rates of new-onset uveitis were observed with 0.4%. The current results should be interpreted with caution given the low number of cases of uveitis and IBD.
Metabolic Syndrome Is Associated with Active Disease in Psoriatic Arthritis and May Contribute to Development of Syndesmophytes

Pervin Sanci\textsuperscript{1}, Gokce Kenar\textsuperscript{2}, Berrin Zengin\textsuperscript{2}, Sadettin Uslu\textsuperscript{3}, Aydan Koken\textsuperscript{3}, Handan Yarkan\textsuperscript{3}, Gerçek Can\textsuperscript{3}, Merih Birlik\textsuperscript{3} and Fatos Onen\textsuperscript{2}, \textsuperscript{1}Internal Medicine, Dokuz Eylul University Faculty of Medicine, İzmir, Turkey, \textsuperscript{2}Rheumatology, Dokuz Eylul University Faculty of Medicine, İzmir, Turkey, \textsuperscript{3}Rheumatology, Dokuz Eylul University Faculty of Medicine, İzmir, Turkey

First publication: September 18, 2017

Background/Purpose:

An increased prevalence of metabolic syndrome (MetS) has been reported in psoriatic arthritis (PsA) suggesting an association between the inflammation and MetS. The aim of this study is to investigate its relationship with disease activity in patients with PsA. We also evaluated whether an association exists between MetS and axial involvement in PsA.

Methods:

This study included patients with PsA followed in the Rheumatology outpatient clinic at Dokuz Eylul University. Age-matched patients with Takayasu arteritis (TA), an inflammatory systemic disease, were enrolled as diseased controls. The NCEP-ACT III criteria were used to identify subjects with MetS. Disease activity was assessed in patients with PsA by using several parameters including BASDAI, ASDAS, VAS patients’ and physician’ global, Tender and Swollen joint assessment (28/68), DAS28, DAPSA, CPDAI and SPARCC Enthesitis Index. ESR and serum CRP levels were measured. BASFI and BASMI were used to evaluate functional status and HAQ, ASQoL and DLQI to evaluate health and PASI to measure the severity of psoriasis. Hand and pelvis X-rays and sacroiliac joint MRIs were performed when indicated.
Results: There were 104 PsA patients (63.5% F; mean age: 50.9±13.0 years; mean disease duration: 8.69 ±6.5 years) who fulfilled the CASPAR criteria and 28 TA patients (89% F, mean age: 46.3±9.1) who fulfilled the ACR 1990 criteria. The prevalence of MetS was found to be considerably higher in PsA patients compared to TA patients (45.2% and 21.4% respectively, p<0.001). In the comparison of PsA patients with and without MetS, no differences were found regarding treatment frequencies of NSAIDs, glucocorticoids, DMARDs and anti-TNFs and also mean glucocorticoid dosages. PsA patients with MetS had higher BASDAI, BASFI, BASMI, VAS, ASqOL, CPDAI, ASDAS and HAQ scores compared to PsA patients without MetS (Table 1). More patients with syndesmophytes were found among PsA patients with MetS compared to those without MetS (p=0.027). There were no differences in indexes related predominantly peripheral involvement, such as tender and swollen joint counts, enthesitis score and presence of dactylitis.

Conclusion: This study demonstrates a higher prevalence of MetS in PsA patients compared to TA. It also suggests that MetS might be associated with high disease activity and more severe disease especially in patients with axial involvement.

Table 1. Clinical features and disease activity parameters in PsA patients with and without MetS.
<table>
<thead>
<tr>
<th></th>
<th>PsA Patients with MetS (n:47)</th>
<th>PsA Patients without MetS (n:57)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean, yrs)</td>
<td>55.49</td>
<td>47.28</td>
<td>0.001</td>
</tr>
<tr>
<td>Sex (F%)</td>
<td>34/47 (72%)</td>
<td>32/57 (56%)</td>
<td>0.88</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>25/47 (53%)</td>
<td>17/57 (29%)</td>
<td>0.016</td>
</tr>
<tr>
<td>Exsmoker</td>
<td>13/47 (27%)</td>
<td>14/57 (24%)</td>
<td></td>
</tr>
<tr>
<td>Active smoker</td>
<td>9/47 (19%)</td>
<td>26/57 (45%)</td>
<td></td>
</tr>
<tr>
<td>BMI (med, IQR)</td>
<td>30.3 (6.6)</td>
<td>26.4 (5.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Disease duration (yrs) (med/IQR)</td>
<td>7 (6)</td>
<td>9 (8)</td>
<td>0.386</td>
</tr>
<tr>
<td>BASDAI (med, IQR)</td>
<td>22 (34)</td>
<td>11 (25)</td>
<td>0.042</td>
</tr>
<tr>
<td>BASFI (med, IQR)</td>
<td>18 (36)</td>
<td>5 (14)</td>
<td>0.009</td>
</tr>
<tr>
<td>BASMI (med, IQR)</td>
<td>20 (20)</td>
<td>10 (20)</td>
<td>0.001</td>
</tr>
<tr>
<td>VAS (med, IQR)</td>
<td>31 (33)</td>
<td>20 (31)</td>
<td>0.030</td>
</tr>
<tr>
<td>DAS28 (med, IQR)</td>
<td>2.6 (1.2)</td>
<td>2.1 (1.4)</td>
<td>0.059</td>
</tr>
<tr>
<td>PASI (med, IQR)</td>
<td>0.1 (4.8)</td>
<td>1.5 (7.2)</td>
<td>0.164</td>
</tr>
<tr>
<td>CPDAI (med, IQR)</td>
<td>6.3 (6.0)</td>
<td>3.6 (7.4)</td>
<td>0.049</td>
</tr>
<tr>
<td>ASqOL (med, IQR)</td>
<td>7 (8)</td>
<td>3.0 (6)</td>
<td>0.017</td>
</tr>
<tr>
<td>DLQI (med, IQR)</td>
<td>0 (4)</td>
<td>1 (2)</td>
<td>0.794</td>
</tr>
<tr>
<td>ASDAS (med, IQR)</td>
<td>2.5 (1.8)</td>
<td>1.7 (1.2)</td>
<td>0.008</td>
</tr>
<tr>
<td>HAQ (med, IQR)</td>
<td>0.375 (1.125)</td>
<td>0.125 (0.438)</td>
<td>0.011</td>
</tr>
<tr>
<td>VAS physician (med, IQR)</td>
<td>16 (17)</td>
<td>13 (16)</td>
<td>0.151</td>
</tr>
<tr>
<td>DAPSA (med, IQR)</td>
<td>15.8 (13.4)</td>
<td>10.6 (19.9)</td>
<td>0.190</td>
</tr>
<tr>
<td>Tender joint count (med, IQR)</td>
<td>1(2) min:0 max:9</td>
<td>0 (1) min:0 max:6</td>
<td>0.31</td>
</tr>
<tr>
<td>Swollen joint count (med, IQR)</td>
<td>0 (1) min:0 max:5</td>
<td>0 (1) min:0 max:4</td>
<td>0.83</td>
</tr>
<tr>
<td>ESR (med, IQR) (mm/h)</td>
<td>11(13)</td>
<td>10 (15)</td>
<td>0.478</td>
</tr>
<tr>
<td>CRP (med, IQR) (mg/L)</td>
<td>5.5 (9.6)</td>
<td>3.8 (5.6)</td>
<td>0.280</td>
</tr>
<tr>
<td>Dactylitis (n, %)</td>
<td>2/47 (4.2%)</td>
<td>7/56 (12.5%)</td>
<td>0.140</td>
</tr>
<tr>
<td>Enthesitis (n, %)</td>
<td>3/46 (6.5%)</td>
<td>6/56 (10.7%)</td>
<td>0.458</td>
</tr>
<tr>
<td></td>
<td>Uveitis (n, %)</td>
<td>Syndesmophytes (%)</td>
<td>Sacroilitis (radiographic) (%)</td>
</tr>
<tr>
<td>--------------------------</td>
<td>---------------</td>
<td>--------------------</td>
<td>-------------------------------</td>
</tr>
<tr>
<td></td>
<td>1/47 (2.1%)</td>
<td>22/36 (61%)</td>
<td>8/44 (18%)</td>
</tr>
<tr>
<td></td>
<td>2/56 (3.5%)</td>
<td>16/44 (36%)</td>
<td>13/53 (24%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

|                          |               |                    |                               |                         |                            |                        |                           |                        |

**Disclosure:** P. Sanci, None; G. Kenar, None; B. Zengin, None; S. Uslu, None; A. Koken, None; H. Yarkan, None; G. Can, None; M. Birlik, None; F. Onen, None.


Abstract Number: 2522

**Metabolic Syndrome, NAFLD and LIVER Stiffness in Psoriatic Arthritis and Psoriasis Patients: A CROSS-Sectional Study**

Augusta Ortolan¹, Mariagrazia Lorenzin¹, Giulia Tadiotto¹, Francesca Oliviero¹, Ariela Hoxha¹, Marta Favero², Stefano Piaserico³, Leonardo Punzi¹ and Roberta Ramonda¹, ¹Rheumatology Unit, Department of Medicine DIMED, University of Padova, Padova, Italy, ²Rheumatology Unit, Department of Medicine DIMED, University of Padova, Padova, Italy, ³Dermatology Clinic, University of Padova, Padova, Italy

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Metabolic syndrome (MetS) and non-alcoholic fatty liver disease (NAFLD, potentially evolving into liver fibrosis-LF), are more frequent in patient with psoriasis (PsO) with respect to general population. Nevertheless, data about psoriatic arthritis (PsA) are lacking. Aims of the study were: 1) investigating if the presence of arthritis, other
than PsO, could determine any difference with respect to the prevalence of these comorbidities. 2) assess the presence of NALFD and LF and their determinants in PsA/PsO.

**Methods:** PsA patients with concomitant PsO and PsO patients without history or manifestation of arthritis were consecutively enrolled in the period October 2015-June 2016. Exclusion criteria were: liver diseases potentially causing LF except for NAFLD, alcohol consumption≥20 g/day, daily use of non-steroidal anti-inflammatory drugs, use of methotrexate currently/ in the previous year. Anamnestic, biochemical, metrological data were collected, thus defining insulin-resistance index HOMA (Homeostatic Model Assessment) and the presence of MetS. All patients underwent 1) liver ultrasound to assess the presence of steatosis (therefore NAFLD) 2) transient elastography, which measures liver stiffness, to evaluate presence and grading of LF (stiffness≥7 kPa=fibrosis). Disease activity was assessed through Psoriasis Area Severity Index-PASI and Disease Activity index for Psoriatic Arthritis-DAPSA. Statistical analysis included Mann-Whitney and Chi-square test to evaluate differences between PsA/PsO patients, regression analysis to identify predictors of NALFD and liver stiffness, Spearman’s coefficient to examine correlations; p≤0.05 was considered as significant.

**Results:** PsA/PsO patients (43/33 individuals) had similar characteristics: age 60.2±8.4/54.5±19.6 years, male 74.4/63%, PsA/PsO duration 12.6±8.5/18.2±14.2 years. Significant differences were found in: Body Mass Index (BMI) (25.7±3.4/29.1±6.3, p=0.0092), PASI (1.5±2.5/5±4, p=0.03556), uric acid (4.9±1.5/5.7±1.4 mg/dL, p=0.0001), all higher in PsO. MetS and LS prevalence was similar between AP/PsO: 34.9%/33.3% and 30.8%/27.6% (p=ns). NALFD was significantly higher in PsO (64.7% vs 35.3% in PsA, p=0.044). Multivariate regression analysis identified glycosylated haemoglobin as independent predictor of NALFD (RRR 8.34, p=0.016) and HOMA of liver stiffness grading (beta 0.33, p=0.046) (Table). A strong correlation emerged between uric acid and HOMA (p=0.0001, r=0.80) and uric acid-liver stiffness (p<0.0001, r=0.73) in PsO.

**Conclusion:** In our study population the prevalence of MetS and LF was similar between PsA/PsO, while NALFD was more prevalent in PsO. Insuline resistance, which has a key role in MetS, seems the main determinants to liver disease (in terms of NALFD and LF) in PsA/PsO. In this scenario hyperuricemia could be a relevant co-factor.

<table>
<thead>
<tr>
<th>Table: Logistic and linear regression models to identify predictors of NALFD and Liver stiffness grading</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NALFD</strong></td>
</tr>
<tr>
<td>Insulin resistance</td>
</tr>
<tr>
<td>HOMA (Homeostatic Model Assessement)</td>
</tr>
<tr>
<td>Disease activity</td>
</tr>
</tbody>
</table>

**Disclosure:** A. Ortolan, None; M. Lorenzin, None; G. Tadiotto, None; F. Oliviero, None; A. Hoxha, None; M. Favero, None; S. Piaserico, None; L. Punzi, None; R. Ramonda, None.


**Abstract Number:** 2523
The Prevalence, Incidence and Associated Factors for Liver Abnormalities in Psoriatic Arthritis: Results from a Longitudinal Observational Cohort

Rattapol Pakchotanon 1, Justine (Yang) Ye 1, Richard J. Cook 2, Vinod Chandran 3 and Dafna D Gladman 3, 1University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, 2Statistics and Actuarial Science, University of Waterloo, Waterloo, ON, Canada, 3Rheumatology, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is a chronic inflammatory disease which affects the skin and musculoskeletal system. PsA patients frequently suffer from comorbidities: cardiovascular disease, metabolic syndrome, inflammatory bowel disease, liver disease, osteoporosis, malignancy, and ophthalmic disease. Among PsA patients, the prevalence of biochemical liver abnormalities has been reported as 24-36%. We aimed to determine the prevalence and incidence of liver abnormalities and identify the factors associated with liver abnormalities in PsA patients.

Methods: Patients with PsA have been followed prospectively according to a standard protocol which includes detailed clinical and laboratory tests collected at 6-12 month intervals. From this longitudinal cohort study we identified PsA patients with either elevated (>1.5x normal) serum transaminase or alkaline phosphatase levels or liver disease (fatty liver, viral hepatitis, autoimmune liver disease, alcoholic liver disease, liver fibrosis, and cirrhosis) after the first visit to the PsA clinic (cases). Controls were subjects from the same cohort who never had such abnormalities or liver disease. Cases and controls were then matched 1:1 by sex, age at the first clinic visit, and follow-up duration. Variables at the first appearance of liver test abnormality were evaluated using univariable and multivariable regression analyses to identify the factors associated with liver biochemical abnormalities after controlling for demographic variables, disease activity, and treatment.

Results: Among 1061 patients followed in the PsA clinic, 343 had liver abnormalities. 256 patients who developed liver abnormalities after the first visit were identified as cases, 718 patients were identified as controls. The prevalence of liver abnormalities was 32% and the incidence was 39/1000 patient-years. Among 256 cases, the mean age (s.d.) of PsA patients at the onset of liver abnormalities was 50.5 ± 12.8 years. Liver abnormalities were detected after mean (s.d.) follow up duration of 8.3 ±7.8 years. Twenty-nine percent of cases had an identified cause of liver biochemical abnormalities. The common causes of liver abnormalities were drug induced hepatitis (14%) and fatty liver (13%). Multivariable analysis in matched case-control study (204 pairs) revealed that higher BMI, daily alcohol intake, more damage joint count, elevated CRP, use of methotrexate (MTX), leflunomide (LFN) or TNF inhibitors were independent factors associated with liver abnormalities (Table 1).

Table 1. Multivariable analysis of factors associated with liver abnormalities in psoriatic arthritis (PsA) in matched case-control study (204 pairs).

<table>
<thead>
<tr>
<th>Variables</th>
<th>OR (95%CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body mass index</td>
<td>1.07 (1.02–1.12)</td>
<td>0.007</td>
</tr>
<tr>
<td>Daily alcohol intake</td>
<td>4.46 (1.30-15.28)</td>
<td>0.02</td>
</tr>
<tr>
<td>Damage joint count</td>
<td>1.04 (1.01–1.08)</td>
<td>0.01</td>
</tr>
<tr>
<td>Elevated CRP</td>
<td>2.00 (1.04-3.85)</td>
<td>0.04</td>
</tr>
<tr>
<td>Use of MTX/LFN</td>
<td>4.39 (1.67-11.54)</td>
<td>0.003</td>
</tr>
<tr>
<td>Use of TNF inhibitors</td>
<td>10.56 (3.63-30.69)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Conclusion: The prevalence of liver abnormalities among PsA was 32% and the incidence was 39/1000 patient-years. Higher BMI, daily alcohol intake, more damage joint count, elevated CRP, use of MTX/LFN or TNF inhibitors are
associated with liver abnormalities in PsA patients. Monitoring liver function tests in these high risk patients is recommended.

Disclosure: R. Pakchotanon, None; J. Ye, None; R. J. Cook, None; V. Chandran, None; D. D. Gladman, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-prevalence-incidence-and-associated-factors-for-liver-abnormalities-in-psoriatic-arthritis-results-from-a-longitudinal-observational-cohort

Abstract Number: 2524

Weight Change before and after Diagnosis in Patients with Psoriatic Arthritis, Rheumatoid Arthritis, and Ankylosing Spondylitis

Alexis Ogdie1, Michael D. George2, Joel Gelfand3, Maureen Dubreuil4, Thorvardur Love5 and Joshua Baker6; 1Medicine/Rheumatology and Epidemiology, University of Pennsylvania, Philadelphia, PA, 2Division of Rheumatology, University of Pennsylvania, Philadelphia, PA, 3University of Pennsylvania Health System, Philadelphia, PA, 4Clinical Epidemiology, Boston University School of Medicine, Boston, MA, 5Landspitali University Hospital, Reykjavik, Iceland, 6Rheumatology, University of Pennsylvania, Philadelphia, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Rheumatoid arthritis (RA) has been associated with weight loss around the time of diagnosis; little is known about weight change around diagnosis in psoriatic arthritis (PsA) and ankylosing spondylitis (AS). Furthermore, while obesity is a risk factor for RA and PsA, little is known about the importance of weight change as a disease risk factor. We examined weight change before, around, and after diagnosis compared to matched controls in a population-based cohort.

Methods: Data between 1994-2015 from The Health Improvement Network were used. Patients age 18-89 with incident PsA, RA, and AS and population controls matched on start date and general practice and with at least one body mass index (BMI) in each of intervals surrounding diagnosis were eligible. Change in BMI over time was examined using linear regression models incorporating generalized estimating equations with cubic splines with two knots (one year prior to diagnosis and one year after diagnosis) and adjusting for age and sex. Mean BMI over the 10-year study interval was plotted. We examined the significance of slope (compared to zero) at each interval (t1-t3) for each disease group and differences in slope for each interval in the disease groups compared to controls.

Results: Among patients with incident PsA, RA or AS, and matched controls, 2,591, 11,380, 919, and 21,903 respectively met the inclusion criteria. Among those included, the mean number of BMI measurements over 7.5 years of follow up was 8.5. Sex was 58%, 71%, 40%, and 62% female for patients with PsA, RA, AS, and controls respectively. The mean BMI at diagnosis was 29.8, 28.0, 27.6, and 27.9 respectively. Patients with PsA had the highest BMI in all time intervals (Figure 1) although the absolute difference in mean BMI was small. Controls gained a modest amount of weight over all intervals. Patients with PsA, RA, and AS had greater fluctuations in weight (Figure 2). Patients with PsA and RA lost weight around the time of diagnosis, but this was not statistically significant in PsA. Prior to diagnosis, patients with PsA gained weight at a higher rate than controls and patients with AS and RA lost weight at higher rates than controls. Patients with PsA and RA gained more weight after diagnosis than the other groups.
**Conclusion**: This population-based natural history study suggests that weight fluctuates around the diagnosis of inflammatory arthritis and in some cases these weight changes preceded the diagnosis by 5 years or more. Further studies to understand the importance of weight change as a risk factor for these diseases are needed.

**Disclosure**: A. Ogdie, Pfizer, Novartis, 2,Takeda, Pfizer, Novartis, 5; M. D. George, Bristol Myers Squibb, 2; J. Gelfand, Abbvie, Coherus, Janssen Biologics (formerly Centocor), Merck, Novartis Corp, Valeant, and Pfizer Inc, 5,Abbvie, Eli Lilly, Janssen, Novartis Corp, Regeneron, Sanofi, and Pfizer Inc, 2; M. Dubreuil, None; T. Love, None; J. Baker, None.

**Abstract Number**: 2525
Influence of Cardiovascular Comorbidity on Achieving Therapeutic Goals: A Comparative Study between Recent-Onset Psoriatic Arthritis and Established Disease

Rubén Queiro1 and Juan D. Cañete2, 1Rheumatology Department. Hospital Universitario Central de Asturias, Oviedo, Spain, 2Rheumatology Department, Arthritis Unit, Rheumatology Dpt, Hospital Clinic of Barcelona, Barcelona, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthopathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Some cardiovascular risk factors (CVRF) have been associated with a lower probability of achieving a good therapeutic response in PsA1. However, the reason for this association is not known. We aimed to evaluate the potential link between the minimal disease activity (MDA)2 response and the presence of CVRF in PsA patients treated with DMARDs.

Methods: Cross-sectional study carried out at 25 rheumatology departments from Spain. All patients fulfilled CASPAR criteria, had an established disease (disease duration 9.6 ± 7.6 yr), and were receiving biological or synthetic DMARDs. The relationship between MDA and CVRF was evaluated by uni and multivariate analyses. To test the influence of CVRF on MDA achieving, an age-matched cohort of patients with recent-onset PsA (< 2 yr of evolution) not exposed to systemic treatment was selected.

Results: 227 patients were included and 133 (58.6%) achieved a MDA response. Among the classic CVRF, tobacco (crude OR: 0.54), sedentary lifestyle (crude OR: 1.95), hyperuricemia (crude OR: 2.01) and obesity (crude OR: 1.54) were related to the likelihood of MDA in the univariate model (p <0.25). The only CVRF related to the MDA response in the multivariate analysis was a sedentary lifestyle (OR 3.13, 95%CI: 1.50-6.53; p=0.002). No association was found between the number of CVRF and MDA. No differences were found in the prevalence of cardiovascular comorbidity between the two cohorts.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Treated cohort N: 227</th>
<th>Not treated cohort N: 210</th>
<th>p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>53.2 ± 12.4 yr</td>
<td>49.8 ± 13.9 yr</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension</td>
<td>27.3%</td>
<td>22.4%</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes</td>
<td>12.1%</td>
<td>10.5%</td>
<td>NS</td>
</tr>
<tr>
<td>Obesity</td>
<td>21.1%</td>
<td>27.1%</td>
<td>NS</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>30.4%</td>
<td>30.9%</td>
<td>NS</td>
</tr>
<tr>
<td>Tobacco</td>
<td>27.3%</td>
<td>30.4%</td>
<td>NS</td>
</tr>
<tr>
<td>CV events</td>
<td>5.8%</td>
<td>6.2%</td>
<td>NS</td>
</tr>
</tbody>
</table>

Conclusion: Contrary to what has been found in other studies, in this multicenter study we could not find any relationship between CVRF (except for sedentary lifestyle) and MDA. In any case, patients with psoriatic disease should be encouraged to maintain healthy lifestyle habits.
Baseline Data from the Recent-Onset Psoriatic Arthritis Registry of the Spanish Society of Rheumatology

Rubén Queiro1, Ana Laiz2, Carlos Alberto Montilla-Morales3, Eva Galindez-Agirregoikoa4, Juan J. Bethencourt5 and Daniel Seoane6

1Rheumatology Department. Hospital Universitario Central de Asturias, Oviedo, Spain,
2Rheumatology, HU. Santa Creu i San Pau, Barcelona, Spain,
3Hospital Clínico Universitario de Salamanca, Salamanca, Spain,
4Rheumatology Division, Hospital Universitario de Basurto, Bilbao, Spain,
5Rheumatology, HU. Canarias, Sta. Cruz de Tenerife, Spain,
6Research Unit, Spanish Foundation of Rheumatology, Madrid, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
The natural history of psoriatic arthritis (PsA) is hardly known and the information regarding PsA prospective cohorts is very scarce worldwide. The information obtained from prospective cohorts of rheumatic diseases of recent onset is the only way to unravel the true natural history of these diseases. Our objective was to describe the baseline characteristics of the REAPSER (Recent-Onset PsA Registry of the Spanish Society of Rheumatology) cohort, a prospective cohort that seeks to know the natural history and the impact that the disease generates in Spanish patients with PsA.

Methods:
REAPSER is an observational, multicenter study, with consecutive recruitment, which includes adults of both sexes aged 18 yr or older that meet CASPAR criteria for PsA, and have less than two years of disease evolution (recent-onset PsA). Annual follow-up visits will be carried out for 5 years. Measurements include socio-demographic data, employment status, impact of disease, family history of PsA and other inflammatory diseases, comorbidities, lifestyle, use of health...
services, clinical status at disease presentation and during follow up, anthropometric data, clinical evaluation, radiographic progression, lab determinations, and treatment of the disease. The study has been approved by the ethical committees of the participating centers.

The statistical analysis is limited to describing percentages for qualitative variables and central measurements with dispersion values for the quantitative ones.

Results:

Two hundred and fifteen consecutive patients were included, mean age 49.8 ± 13.9 years.
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N: 215</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>67.4%</td>
</tr>
<tr>
<td>Women</td>
<td>32.6%</td>
</tr>
<tr>
<td>Active worker</td>
<td>59.5%</td>
</tr>
<tr>
<td>Unemployed</td>
<td>12.1%</td>
</tr>
<tr>
<td>Retired / pensioner</td>
<td>17.7%</td>
</tr>
<tr>
<td>Job change last year</td>
<td>4.7%</td>
</tr>
<tr>
<td>University studies</td>
<td>20%</td>
</tr>
<tr>
<td>Smoking</td>
<td>30.2%</td>
</tr>
<tr>
<td>BMI</td>
<td>27.7 ± 5.2</td>
</tr>
<tr>
<td>Weekly alcohol consumption (SDU)</td>
<td>0 SDU (0-4)</td>
</tr>
<tr>
<td></td>
<td>41.4%</td>
</tr>
<tr>
<td>Family history of psoriasis</td>
<td>9.3%</td>
</tr>
<tr>
<td>Family history of PsA</td>
<td>6.5%</td>
</tr>
<tr>
<td>Family history of other arthritis</td>
<td>0: 46.5%. 1-2: 35.3%. 3-4: 14.4%. &gt;4: 3.8%</td>
</tr>
<tr>
<td>Charlson's Comorbidity Index</td>
<td>88%</td>
</tr>
<tr>
<td>Psoriasis at baseline</td>
<td>1.5 (0.6-4.3)</td>
</tr>
<tr>
<td>PASI</td>
<td></td>
</tr>
<tr>
<td>Joint pattern</td>
<td></td>
</tr>
<tr>
<td>Peripheral</td>
<td>81.5%</td>
</tr>
<tr>
<td>Axial</td>
<td>5.2%</td>
</tr>
<tr>
<td>Mixed</td>
<td>13.3%</td>
</tr>
<tr>
<td>TJC68</td>
<td>4 (2-8)</td>
</tr>
<tr>
<td>SJC66</td>
<td>2 (1-4)</td>
</tr>
<tr>
<td>BASDAI</td>
<td>3.9 (3-4.4)</td>
</tr>
<tr>
<td>Dactylitis</td>
<td>41.9%</td>
</tr>
<tr>
<td>Enthesitis</td>
<td>25%</td>
</tr>
<tr>
<td>Uveitis</td>
<td>0.5%</td>
</tr>
<tr>
<td>Pain VAS</td>
<td>5 (3-7)</td>
</tr>
<tr>
<td>Patient´s global disease activity</td>
<td>5 (3-7)</td>
</tr>
<tr>
<td>HAQ</td>
<td>0.5 (0.1-4)</td>
</tr>
<tr>
<td>PsAID</td>
<td>3.8 (1.8-6)</td>
</tr>
<tr>
<td>Steinbrocker Index (0-168)</td>
<td>0 (0-4)</td>
</tr>
<tr>
<td>Cardiovascular events</td>
<td>5.7%</td>
</tr>
</tbody>
</table>
Conclusion:

The baseline situation of Spanish patients with recent-onset PsA corresponds to that of a disease with slight cutaneous involvement and predominance of oligoarticular arthritis. Unsurprisingly, structural damage is scarce but not zero. The impact of the disease is still low in these early stages, however 18% of patients have a high Charlson’s comorbidity index (> 3) and almost 5% of patients changed their employment status in the last year due to their PsA.

Disclosure: R. Queiro, None; A. Laiz, None; C. A. Montilla-Morales, None; E. Galindez-Agirregoikoa, None; J. J. Bethencourt, None; D. Seoane, None.


Increased Prevalence of Subclinical Atherosclerosis in Moderate-Severe Plaque Psoriasis Patients

Nuria Vegas-Revenga1, José Luis Martín-Varillas1, Susana Armesto2, Marcos A González- López3, Virginia Portilla2, Patricia Fuentevilla1, Javier Rueda-Gotor2, Carlos Fernández-Díaz1, Lucia C. Domínguez-Casas1, Belén Atienza-Mateo1, Jose L. Hernández4, Ricardo Blanco1, Miguel Angel González-Gay1 and Alfonso Corrales1, 1Rheumatology, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, 2Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, 3Dermatology, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, 4Internal Medicine, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM
**Background/Purpose:** Surrogate markers of subclinical atherosclerosis and cardiovascular (CV) mortality such as carotid plaques (CP), arterial stiffness (AS) and carotid intima-media thickness (c-IMT), have been studied by carotid ultrasound (US) examination. In most studies done before, the results have shown an increased prevalence of CP and high values of c-IMT associated to greater CV risks. The same happens with the pulse wave velocity (PWV), which has become the gold standard to determine AS.

Our aim was to compare the prevalence of CP, PWV and c-IMT measurements between patients with moderate-severe psoriasis and the general population.

**Methods:** A cross-sectional study that included 40 patients with moderate-severe psoriasis (PASI >10, BAS >10 %), that fulfilled definitions for initiating treatment with a biological agent according to the Clinical Practice guidelines and 40 age-, sex- and traditional CV risk factors- matched healthy control subjects. Psoriatic arthritis (PsA) was present in 11 of 40 patients. Patients with history of CV events, diabetes mellitus, and chronic kidney disease or body max index > 35 were excluded. US was performed in the common carotid by a MyLab 70 scanner (Esaote; Genoa, Italy), QAS-RF and Q-IMT Maastricht (Holland). The results were obtained according to the Manheim Consensus Conference criteria. Statistical analysis: Qualitative data were expressed as number and percentages and quantitative data as mean (SD). Student's t test or Mann-Whitney U were used to compare continuous variables, as appropriate. Chi2 test or Fisher test were used for qualitative variables.

**Results:** The main data of the patients are summarized in the **TABLE**. It is important to highlight that the study was based on a young population (mean age <40 years). Thus, the two groups did not present significant differences regarding the classic CV risks factors and other parameters studied, except for high sensitivity C-reactive protein (hsCRP).

As expected given the age of the group, CV risk measured by SCORE was low (0%) in most patients, with a mean of 0.2 (in the plaque psoriasis group) and 0.15 in the control group. No patient had a high-very high CV risk as measured by SCORE (≥ 5%). Patients with psoriasis had a long-standing disease (17.05 ± 11.63 years). The presence of carotid plaques was found in a total of 10 patients with plaque psoriasis (25%), 5 of them had bilateral plaques) and one in the control group (2.5%) without bilateral plaques), p <0.003. Even if patients with psoriasis had a higher PWV (6.33 m/sec) and c-IMT (0.579 mm) compared to the control group (6.13 m/sec and 0.549 mm), the difference was not significant (p = 0.72 and p = 0.17). It could be explained by the age of the study population and the sample size.

**Conclusion:** Moderate-severe psoriasis is associated with increased prevalence of CP, but PWV and c-IMT shows no differences.

**TABLE**
<table>
<thead>
<tr>
<th>Variable</th>
<th>Plaque Psoriasis (n = 40)</th>
<th>Controls (n = 40)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: Mean (SD)</td>
<td>37.68 (11.83)</td>
<td>38.63 (11.83)</td>
<td>0.75</td>
</tr>
<tr>
<td>Sex (Male): n (%)</td>
<td>18 (45)</td>
<td>18 (45)</td>
<td>1.0</td>
</tr>
<tr>
<td>Psoriasis duration (years):</td>
<td>17.05 (11.63)</td>
<td>ND</td>
<td>-</td>
</tr>
<tr>
<td>BSA: Mean (SD)</td>
<td>38.99 (17.08)</td>
<td>ND</td>
<td>-</td>
</tr>
<tr>
<td>PASI: Mean (SD)</td>
<td>19.33 (8.89)</td>
<td>ND</td>
<td>-</td>
</tr>
<tr>
<td>hsCRP (mg/L): Mean (SD)</td>
<td>3.26 (3.31)</td>
<td>1.69 (2.62)</td>
<td>0.001</td>
</tr>
<tr>
<td>ESR (mm/h): Mean (SD)</td>
<td>13.79 (13.23)</td>
<td>8.53 (7.01)</td>
<td>0.17</td>
</tr>
<tr>
<td>Systolic hypertension (mm Hg):</td>
<td>121.33 (13.91)</td>
<td>120.08 (11.73)</td>
<td>0.86</td>
</tr>
<tr>
<td>Cholesterol (mg/dl): Mean (SD)</td>
<td>196.08 (34.31)</td>
<td>193 (36.42)</td>
<td>0.69</td>
</tr>
<tr>
<td>HDL-C (mg/dl): Mean (SD)</td>
<td>55.58 (17.05)</td>
<td>63.88 (20.7)</td>
<td>0.051</td>
</tr>
<tr>
<td>Smoking: n (%)</td>
<td>13 (33)</td>
<td>9 (22.5)</td>
<td>0.32</td>
</tr>
<tr>
<td>Dyslipidemia: n (%)</td>
<td>21 (53)</td>
<td>17 (42.5)</td>
<td>0.37</td>
</tr>
<tr>
<td>Arterial hypertension: n (%)</td>
<td>2 (5)</td>
<td>3 (7.5)</td>
<td>0.99</td>
</tr>
<tr>
<td>Obesity (BMI&gt; 35) n (%)</td>
<td>7 (18)</td>
<td>3 (7.5)</td>
<td>0.18</td>
</tr>
<tr>
<td>SCORE (%): Mean (SD)</td>
<td>0.2 (0.46)</td>
<td>0.15 (0.43)</td>
<td>0.55</td>
</tr>
<tr>
<td>Carotid plaques: n (%)</td>
<td>10 (25)</td>
<td>1 (2.5)</td>
<td>0.003</td>
</tr>
<tr>
<td>Bilateral carotidplaques: n (%)</td>
<td>5 (13)</td>
<td>0 (0)</td>
<td>0.02</td>
</tr>
<tr>
<td>Arterial stiffness (PWV m/sec):</td>
<td>6.33 (1.47)</td>
<td>6.13 (1.18)</td>
<td>0.72</td>
</tr>
<tr>
<td>Carotid IMT (mm): Mean (SD)</td>
<td>0.579 (0.11)</td>
<td>0.549 (0.10)</td>
<td>0.17</td>
</tr>
</tbody>
</table>

**Disclosure:** N. Vegas-Revenga, None; J. L. Martín-Varillas, None; S. Armesto, None; M. A. González- López, None; V. Portilla, None; P. Fuentevilla, None; J. Rueda-Gotor, None; C. Fernández-Díaz, None; L. C. Domínguez-Casas, None; B. Atienza-Mateo, None; J. L. Hernández, None; R. Blanco, None; M. A. González-Gay, None; A. Corrales, None.


**Abstract Number:** 2528
Prevalence of Depression and Attention Deficit Hyperactivity Disorder in Female Patients at a Combined Psoriasis-Psoriatic Arthritis Center

Soumya M. Reddy1, Rebecca Haberman2, Eileen Lydon3, Andrea L. Neimann4, Malavika Attur3, Mark Butler5, Tanya M. Spruill5 and Jose U. Scher6, 1Department of Medicine, Division of Rheumatology *contributed equally, New York University School of Medicine, New York, NY, 2Department of Medicine (*contributed equally), New York University School of Medicine, New York, NY, 3Department of Medicine, Division of Rheumatology, New York University School of Medicine, New York, NY, 4Department of Dermatology, New York University School of Medicine, New York, NY, 5Department of Population Health, New York University School of Medicine, New York, NY, 6New York University School of Medicine, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Psoriatic arthritis (PsA) is a heterogeneous inflammatory arthritis affecting multiple clinical domains. Untreated, PsA has the potential for significant morbidity and disability. Psychiatric disorders have been described as a major comorbidity in PsA. Although anxiety and depression are known to co-occur in PsA, the prevalence of attention deficit hyperactivity disorder (ADHD) in this population has not been reported. Further, little is known about the impact of psychiatric disorders on disease severity and patient reported outcomes. The objective of this study was to characterize the prevalence and gender-driven differences of psychiatric disorders among PsA patients followed at a combined psoriasis-PsA clinic in the US.

Methods:
Two-hundred and fifty-three consecutive adult patients meeting CASPAR criteria for PsA were prospectively recruited at the New York University Psoriatic Arthritis Center and assessed for demographic characteristics, presence of psychiatric comorbidities, including anxiety, depression and ADHD. Diagnosis was defined by patients report and/or current use of psychiatric medications. Objective measures of disease severity included swollen and tender joint counts (SJC/TJC) and %body surface area (BSA) covered by psoriasis. A physician global assessment was recorded at the time of the visit, along with arthritis, skin and nail global scores. A RAPID3 score was also recorded. Data was analyzed with SPSS version 23. Associations between variables were evaluated by t-tests for continuous variables and chi-squared tests for categorical variables.

Results:
Participants were 54% male, had mean age 47 years, and majority were Caucasians (73.1%). A psychiatric diagnosis was reported in 27.8% of PsA patients: depression (18.7%), anxiety (14.7%), and/or ADHD (4.8%). When stratified by gender, female PsA patients had significantly higher prevalence of overall psychiatric diagnosis (34.5% vs 22.1%; p=0.028), depression (25% vs 13.2%; p=0.017) and use of antidepressants (22.2% vs 11.8%; p=0.048). Males had higher use of medications for bipolar disorder (9.1% vs 2.1%; p=0.037). While there were no significant differences in disease severity, female patients reported a significantly higher RAPID3 scores than males (12.09 vs 8.95; p=0.007). Intriguingly, male PsA patients (but not females) with any psychiatric diagnosis had a significantly lower SJC compared to those without these comorbidities (0.79 vs 1.82; p=0.14). Similarly, female PsA patients with psychiatric diagnosis has a lower %BSA affected with psoriasis (1.46 vs 2.40; p=0.054).

Conclusion:
We report, for the first time, a relatively high prevalence of ADHD in a cohort of PsA patients managed in a Psoriasis and PsA clinic. We further validate prior reports of significantly increased levels of depression and antidepressant use in female patients with PsA. Higher RAPID3 scores in women, independent of disease activity or presence of comorbidities, represents a significant gap in how patients perceive their disease symptoms. Further understanding of these gender-driven differences is needed to evaluate the impact on PsA disease burden, adherence and management.

**Disclosure:** S. M. Reddy, None; R. Haberman, None; E. Lydon, None; A. L. Neimann, None; M. Attur, None; M. Butler, None; T. M. Spruill, None; J. U. Scher, NIAMS-NIH, 2.


**Abstract Number: 2529**

**Appraisal of the Contest Questionnaire in the Screening for Psoriatic Arthritis**

Amir Haddad1, Joy Feld1,2, Lihi Eder3, Idit Lavi4, Oxana Zlazhover5 and Devy Zisman1,6, 1Rheumatology Unit Carmel Medical Center, Haifa, Israel, 2Rheumatology Unit, Carmel Medical Center, Haifa, Israel, 3Women's College Research Institute, Women's College Hospital, Toronto, ON, Canada, 4Epidemiology Unit Carmel Medical Center, Haifa, Israel, 5Bnei Zion Medical Center, Haifa, Israel, 6The Ruth and Bruce Rappaport Faculty of Medicine, Technion, Haifa, Israel

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Early diagnosis of psoriatic arthritis (PsA) is critical to prevent poor outcome. Several validated screening questionnaires have been developed to identify PsA patients in the psoriasis population in dermatology and general practice settings. We aimed to test the performance of the CONTEST questionnaire in diagnosing PsA compared to the other existing tools.

**Methods:** Psoriasis patients from a primary dermatology clinic and combined rheumatology-dermatology clinics in one medical center completed the Psoriatic Arthritis Screening and Evaluation tool (PASE), Toronto Psoriatic Arthritis Screen2 (ToPAS2), Psoriasis Epidemiology Screening Tool (PEST) and Early Arthritis for Psoriatic Patients(EARP) questionnaires prior to rheumatologic evaluation. A composite score was calculated by abstracting the score of each discriminatory item from the original tools that constitute the CONTEST questionnaire. The results were compared to the diagnosis of PsA according to CASPAR criteria. The sensitivity and specificity of the different instruments were calculated using the defined cut offs of each instrument. The association between questionnaires’ performance and age, gender, level of education, and systemic therapy was assessed using non-parametric statistics as appropriate.

**Results:** Of the 208 patients screened, 108 fulfilled the CASPAR criteria. The sensitivity of PASE, ToPAS2, PEST and EARP and CONTEST was 57.9%,60%,79.4%,78.5% and 70%, respectively. The specificity was 93%,93.2%,94.9%,91.8% and 91%, respectively. The performance of the tools was not affected by age, gender or educational level. Patients on systemic therapy obtained significantly higher scores on the PASE (p=0.03), PEST (p=0.003), EARP (p=0.01) and CONTEST (p=0.0001) questionnaires, but not on the ToPAS2.
**Conclusion:** All screening questionnaires are helpful in excluding PsA, but cannot serve as substitutes for clinical diagnosis. The CONTEST questionnaire had no additive diagnostic value to the other screening questionnaires of which the PEST had the highest sensitivity and specificity.

**Disclosure:** A. Haddad, None; J. Feld, None; L. Eder, None; I. Lavi, None; O. Zlazhover, None; D. Zisman, None.

**Abstract Number:** 2530

**Clinical Specialty Setting As a Determinant for Disease Management in Patients with Psoriatic Arthritis: An Interim Analysis of the Cross-Sectional Observational Study**

Wolf-Henning Boehncke¹, Rudolf Horváth², Ediz Dalkiliç³, Sônia A L Lima⁴, Masato Okada⁵, Maja Hojnik⁶, **Fabiana Ganz**⁷ and Ennio Lubrano⁸, ¹Geneva University Hospital and University of Geneva, Geneva, Switzerland, ²Department of Pediatric and Adult Rheumatology, University Hospital Motol, Prague, Czech Republic, ³Department of Internal Medicine, Division of Rheumatology, Uludag University School of Medicine, Gorukle, Bursa, Turkey, ⁴ABC Medical School, Santo André, Brazil, ⁵Immuno-Rheumatology Center, St. Luke's International Hospital, Tokyo, Japan, ⁶AbbVie, Ljubljana, Slovenia, ⁷AbbVie AG, Baar, Switzerland, ⁸Department of Medicine and Health Sciences Vincenzo Tiberio, University of Molise, Campobasso, Italy

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Evidence suggests that timely and effective management can improve long-term outcomes in patients (pts) with psoriatic arthritis (PsA); however factors influencing treatment management decisions are not well understood. The objective of this study is to evaluate the association between the clinical specialty setting and time from inflammatory musculoskeletal symptom onset to PsA diagnosis and to different management steps in pts with a diagnosis of PsA.

**Methods:** LOOP is a large cross-sectional, multi-center observational study currently being conducted in 19 countries across Western and Eastern Europe, Latin America, and Asia. Adult pts (≥18 years) with a suspected or an established diagnosis of PsA who are routinely visiting a rheumatologist (rheum), dermatologist (derm) or non-rheum/non-derm site are eligible to participate in this study. Each enrolled patient is being assessed by both rheum and derm in the study. The present interim analysis included pts enrolled by 23 May 2017, which corresponded to approximately 50% of the total protocol specified sample size.

**Results:** Of the 602 pts enrolled by database cut-off date, 518 pts with a confirmed diagnosis of PsA were included in this interim analysis. A majority of pts were recruited by rheums (308, 59.5%), followed by derms (210, 40.5%) and physiatrists (19, 3.7%). PsA was first diagnosed by a rheum in 372 (71.8%) pts and by a derm in 100 pts (19.3%). Baseline demographics and disease characteristics were mostly comparable between PsA pts in rheum and derm settings (Table 1). The timing of different disease management steps by clinical specialty is reported in Table 2. The mean time
from symptom onset to PsA diagnosis was 23 months (mo) in the rheum setting and 2 mo longer for derms. The mean time from PsA diagnosis to first conventional synthetic DMARD (csDMARD) and first biologic DMARD (bDMARD) for rheums were 9 and 53 mo, respectively. Compared with Rheums, Derms required additional 16 and 14 mo to prescribe first csDMARD (P = 0.015 vs Rheum) and first bDMARD, respectively. The mean time from first csDMARD to first bDMARD was 46 mo for rheum; while it was 6 months shorter for derm.

**Conclusion:** Although the duration from musculoskeletal symptom onset to PsA diagnosis was similar between rheum and derm setting, there were differences in the timing of introduction of different DMARD classes. Notably, mean time to first csDMARD was significantly and mean time to first bDMARD numerically shorter in rheum setting. The data lend further support to the need for rheum-derm collaborative approach to optimize management of pts with PsA.

### Table 1. Baseline Demographic and Clinical Characteristics of PsA Patients in LOOP Study by Clinical Specialty.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Rheum (N=368)</th>
<th>Demi (N=210)</th>
<th>Overall (N=578)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean (SD)</td>
<td>50.9 (12.6)</td>
<td>50.4 (12.8)</td>
<td>50.4 (12.8)</td>
</tr>
<tr>
<td>Gender, male, n (%)</td>
<td>149 (49.4)</td>
<td>104 (49.5)</td>
<td>253 (49.6)</td>
</tr>
<tr>
<td>Weight, kg, mean (SD)</td>
<td>78.2 (15.7)</td>
<td>79.0 (17.6)</td>
<td>78.5 (16.4)</td>
</tr>
<tr>
<td>BMI, mean (SD)</td>
<td>27.6 (5.3)</td>
<td>27.9 (5.9)</td>
<td>27.7 (5.5)</td>
</tr>
<tr>
<td>Time from PsA diagnosis to recruiting site visit, months, mean (SD)</td>
<td>68.8 (81.5)</td>
<td>86.8 (107.7)</td>
<td>87.6 (93.3)</td>
</tr>
<tr>
<td>Current Skin symptoms, n (%)</td>
<td>301 (97.7)</td>
<td>298 (98.5)</td>
<td>599 (97.9)</td>
</tr>
<tr>
<td>Current Enthesitis, n (%)</td>
<td>143 (46.4)</td>
<td>108 (57.7)</td>
<td>248 (48.2)</td>
</tr>
<tr>
<td>Current Dactyliasis, n (%)</td>
<td>188 (61.9)</td>
<td>191 (74.4)</td>
<td>380 (68.4)</td>
</tr>
<tr>
<td>Current Swollen joints, n (%)</td>
<td>282 (91.6)</td>
<td>174 (82.9)</td>
<td>456 (80.0)</td>
</tr>
<tr>
<td>Family history of psoriasis, n (%)</td>
<td>106 (34.6)</td>
<td>97 (41.6)</td>
<td>193 (37.6)</td>
</tr>
<tr>
<td>Medical history, any, n (%)</td>
<td>304 (93.7)</td>
<td>299 (98.1)</td>
<td>603 (98.6)</td>
</tr>
<tr>
<td>Current Comorbidities, any, n (%)</td>
<td>200 (63.9)</td>
<td>143 (98.3)</td>
<td>343 (99.2)</td>
</tr>
<tr>
<td>Any PsA treatment, n (%)</td>
<td>300 (97.4)</td>
<td>178 (94.8)</td>
<td>478 (92.3)</td>
</tr>
<tr>
<td>Currently still on csDMARD, Methotrexate, n (%)</td>
<td>115 (44.8)</td>
<td>40 (88.9)</td>
<td>155 (55.6)</td>
</tr>
<tr>
<td>Currently still on bDMARD, TNFi, n (%)</td>
<td>85 (36.9)</td>
<td>91 (91.0)</td>
<td>176 (53.9)</td>
</tr>
</tbody>
</table>

### Table 2. Timing of Disease Management Steps in LOOP Study by Clinical Specialty.

<table>
<thead>
<tr>
<th>Duration</th>
<th>Rheum</th>
<th>Demi</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time from inflammatory musculoskeletal symptom onset to PsA diagnosis, months, (SD)</td>
<td>23.3 (71.0)</td>
<td>25.3 (70.2)</td>
<td>.1195</td>
</tr>
<tr>
<td>Time from PsA diagnosis to first csDMARD, months, (SD)</td>
<td>6.6 (28.2)</td>
<td>24.9 (94.2)</td>
<td>.0150</td>
</tr>
<tr>
<td>Time from PsA diagnosis to first bDMARD, months, (SD)</td>
<td>52.6 (73.7)</td>
<td>66.5 (99.9)</td>
<td>.7957</td>
</tr>
<tr>
<td>Time from first csDMARD to first bDMARD, months, (SD)</td>
<td>46.1 (65.0)</td>
<td>39.9 (64.9)</td>
<td>.2625</td>
</tr>
</tbody>
</table>

*P-value from Wilcoxon rank sum test. Dermatologist vs Rheumatologist.

**Disclosure:** W. H. Boehncke, Abbvie, Biogen Idec, Celgene, Covagen, Galderma, Janssen, Leo, Lilly, MSD, Novartis, Panteck Biosolutions, Pfizer, and UCB; 2, Abbvie, Biogen Idec, Celgene, Covagen, Galderma, Janssen, Leo, Lilly, MSD, Novartis, Panteck Biosolutions, Pfizer, and UCB; 5, Abbvie, Biogen Idec, Celgene, Covagen, Galderma, Janssen, Leo, Lilly, MSD, Novartis, Panteck Biosolutions, Pfizer, and UCB; 9. R. Horváth, Abbvie, MSD, Novartis, Pfizer, and UCB; 2, Abbvie, MSD, Novartis, Pfizer, and UCB; 5, Abbvie, MSD, Novartis, Pfizer, and UCB; 9. E. Dalkiliç, Abbvie, 2, Abbvie, MSD, Pfizer, Roche, and UCB; 8. S. A. L. Lima, Abbvie, BMS, and Janssen; 5, Abbvie, BMS, and
Utilization of the Psoriasis Epidemiology Screening Tool to Identify Signs and Symptoms of Early Psoriatic Arthritis Among Those with Psoriasis: Analysis from the Corrona Psoriasis Registry

Philip J Mease¹, Jacqueline B. Palmer², Mark Lebwohl³, Chitra Karki⁴, George W. Reed⁵, Carol J. Etzel⁶, Jeffrey D. Greenberg⁷ and Philip S. Helliwell⁸, ¹Swedish Medical Center and University of Washington, Seattle, WA, ²Novartis Pharmaceuticals Corporation, East Hanover, NJ, ³Icahn School of Medicine at Mount Sinai, New York, NY, ⁴Corrona, LLC, Southborough, MA, ⁵University of Massachusetts Medical School, Worcester, MA, ⁶The University of Texas MD Anderson Cancer Center, Houston, TX, ⁷New York University School of Medicine, New York, NY, ⁸School of Medicine, University of Leeds, Leeds, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The Psoriasis Epidemiology Screening Tool (PEST) is a 5-item questionnaire developed to help identify psoriatic arthritis (PsA) at an early stage, with a score ≥ 3 indicative of PsA.¹ A recent Korean study found that a PEST score of 2 may be a more favorable cutoff for screening patients with psoriasis (PsO).² The objectives of this study were to assess the risk of undiagnosed PsA among patients with PsO and characterize patients based on PEST scores in the US-based Corrona Psoriasis Registry.

Methods: This study included all patients enrolled in the Corrona Psoriasis Registry with data on all 5 PEST questions. Demographics, disease characteristics, patient-reported outcomes and medication use were analyzed at the time of enrollment and stratified by PEST score (0, 1, 2 or ≥ 3). Pairwise comparisons were made between PEST score = 0 (reference) and other PEST score groups using t tests for continuous variables and χ² tests for categorical variables.

Results: As of June 2016, 99.1% (1516/1529) of patients in the Corrona Psoriasis Registry had data on all 5 PEST questions; 612 patients (40.4%) had dermatologist-reported PsA at enrollment. Among the remaining 904 patients, 421 patients (46.6%) had a PEST score = 0, 225 (24.9%) had a PEST score = 1, 146 (16.2%) had a PEST score = 2 and 112 (12.4%) had a PEST score ≥ 3. Of patients with a PEST score ≥ 3, patients most commonly answered “yes” to “have you ever had a swollen joint (or joints)?” (89%) and “has a doctor ever told you that you have arthritis?” (86%). Compared with patients with a PEST score = 0, patients with a PEST score ≥ 1 all had a higher body mass index, longer duration of PsO, increased family history of PsA, increased prevalence of nail PsO and worse EQ VAS at enrollment (all P < 0.05; Table 1). In addition, patients with PEST scores ≥ 2 were older, more likely to be female, less likely to be employed and
had an increased family history of PsO, worse pain and fatigue, worse dermatology-related quality of life and higher percentage impairment of daily activities due to psoriasis at enrollment vs patients with a PEST score = 0 (all \( P < 0.05 \)). There were no significant differences across PEST scores in affected body surface area or PASI scores.

**Conclusion:** In this cohort of PsO patients with no diagnosis of PsA, patients with PEST scores \( \geq 2 \) were significantly different from those with PEST scores = 0 for many characteristics at enrollment, including body mass index and patient-reported outcomes. These findings highlight the value of screening for PsA among patients with PsO in order to potentially improve patient outcomes.

**References:**


**Table 1. Baseline Characteristics of Patients With PsO and No Diagnosis of PsA Stratified by PEST Scores (0-5)**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PEST Score = 0</th>
<th>PEST Score = 1</th>
<th>PEST Score = 2</th>
<th>PEST Score ( \geq 3 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>48.0 (15.5)</td>
<td>48.5 (14.9)</td>
<td>53.7 (13.9)</td>
<td>52.9 (14.4)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>164 (39.0)</td>
<td>103 (45.8)</td>
<td>72 (49.3)</td>
<td>62 (55.4)</td>
</tr>
<tr>
<td>Currently employed, n (%)</td>
<td>311 (74.0)</td>
<td>169 (75.1)</td>
<td>81 (55.9)</td>
<td>60 (53.6)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>28.6 (6.9)</td>
<td>29.7 (6.8)</td>
<td>31.4 (7.0)</td>
<td>32.2 (8.0)</td>
</tr>
<tr>
<td>BMI (in kg/m²) classifications, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal/underweight (&lt; 25.0)</td>
<td>133 (31.8)</td>
<td>63 (28.1)</td>
<td>22 (15.2)</td>
<td>22 (19.8)</td>
</tr>
<tr>
<td>Overweight (25.0 to &lt; 30.0)</td>
<td>145 (34.7)</td>
<td>73 (32.6)</td>
<td>50 (34.5)</td>
<td>26 (23.4)</td>
</tr>
<tr>
<td>Obese (( \geq 30.0 ))</td>
<td>140 (33.5)</td>
<td>88 (39.3)</td>
<td>73 (50.3)</td>
<td>63 (56.6)</td>
</tr>
<tr>
<td>Family history of PsO, n (%)</td>
<td>13 (3.1)</td>
<td>12 (5.4)</td>
<td>11 (7.5)</td>
<td>14 (12.6)</td>
</tr>
<tr>
<td>Family history of PsA, n (%)</td>
<td>126 (30.9)</td>
<td>65 (28.9)</td>
<td>67 (45.9)</td>
<td>46 (41.4)</td>
</tr>
<tr>
<td>Duration of PsO, years</td>
<td>12.8 (12.0)</td>
<td>15.3 (13.2)</td>
<td>19.1 (15.6)</td>
<td>17.3 (14.8)</td>
</tr>
<tr>
<td>Nail PsO, n (%)</td>
<td>30 (7.1)</td>
<td>35 (15.6)</td>
<td>21 (14.4)</td>
<td>24 (21.4)</td>
</tr>
<tr>
<td>BSA, % involvement</td>
<td>8.8 (12.2)</td>
<td>9.0 (12.0)</td>
<td>9.3 (13.9)</td>
<td>10.2 (13.3)</td>
</tr>
<tr>
<td>PASI (0-72)</td>
<td>5.5 (6.0)</td>
<td>6.1 (6.9)</td>
<td>6.2 (7.1)</td>
<td>6.3 (6.5)</td>
</tr>
<tr>
<td>Pain (VAS 0-100)</td>
<td>20.1 (28.3)</td>
<td>21.5 (29.1)</td>
<td>24.2 (29.2)</td>
<td>28.3 (30.6)</td>
</tr>
<tr>
<td>Fatigue (VAS 0-100)</td>
<td>24.2 (27.0)</td>
<td>23.0 (25.1)</td>
<td>30.4 (28.1)</td>
<td>41.7 (27.8)</td>
</tr>
<tr>
<td>EQ VAS (0-100)</td>
<td>76.7 (19.6)</td>
<td>73.9 (22.9)</td>
<td>73.8 (22.4)</td>
<td>67.0 (22.9)</td>
</tr>
<tr>
<td>DLQI (0-30)</td>
<td>5.8 (6.0)</td>
<td>6.6 (6.1)</td>
<td>6.9 (5.3)</td>
<td>6.1 (5.3)</td>
</tr>
<tr>
<td>Work Productivity and Activity Impairment domain, % of daily activities impaired by PsO</td>
<td>14.2 (23.3)</td>
<td>14.8 (23.4)</td>
<td>17.8 (24.9)</td>
<td>24.0 (28.6)</td>
</tr>
</tbody>
</table>

*BMI, body mass index; BSA, body surface area; DLQI, Dermatology Life Quality Index; EQ VAS, EQ visual analogue scale; PASI, Psoriasis Area and Severity Index; PEST, Psoriasis Epidemiology Screening Tool, PsA, psoriatic arthritis; PsO, psoriasis; VAS, visual analog scale; WPAl-GH, Work Productivity and Activity Impairment questionnaire: general health.

*a* All values are presented as “mean (SD)” unless otherwise indicated.

\( P < 0.05 \) unless otherwise indicated.

4 Family history, but patient had no current diagnosis.

Disclosure: P. J. Mease, Celgene, Novartis, AbbVie, Amgen, BMS, Lilly, Pfizer and UCB, 2, Celgene, Corrona, Novartis, AbbVie, Amgen, BMS, Crescendo, Genentech, Janssen, Lilly, Merck, Pfizer and UCB, 5, AbbVie, Amgen, BMS, Crescendo, Celgene, Genentech, Janssen, Pfizer and UCB, 8; J. B. Palmer, Novartis Pharmaceuticals Corporation, 3; M. Lebwohl, Mount Sinai Medical Center, 3, AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen Research & Development, LLC, Kadmon, LEO Pharma, Novartis, Pfizer and ViDac, 2; C. Karki, Corrona, LLC, 3; G. W. Reed, Corrona, LLC, 3, Corrona, LLC, 1; C. J. Etzel, Corrona, LLC, 3, Merck Human Health, 9; J. D. Greenberg, Corrona, LLC, 1, Corrona, LLC, 3, Eli Lilly, Genentech, Janssen, Novartis, Pfizer, 5; P. S. Helliwell, AbbVie, Janssen and Pfizer, 2, AbbVie, Amgen, Janssen, Pfizer and UCB, 9.


Abstract Number: 2532

The Relationship between the Degree of Skin Involvement and Joint Activity in Patients with PsA: Experience from the Corrona Registry
Background/Purpose: Prior studies have shown an inconsistent relationship between skin and joint symptoms in patients with comorbid PsO and PsA\(^1\)\(^-\)\(^3\). The objective of the study is to characterize the relationship between skin severity and joint activity in patients with comorbid PsA and PsO at enrollment.

Methods: Enrollment visit data from Corrona PsA/SpA registry were obtained from 3/21/2013-9/30/2016. To be included in the analysis, patients had to have a diagnosis of PsA and a history of PsO. PsA patients were evaluated for skin severity as defined by Body Surface Area (BSA) and joint activity as defined by the level of CDAI. Patient characteristics, including current and prior PsA medication use, were obtained during the enrollment visit. We evaluated the relationship of skin severity and joint activity with linear regression. Factors that modify the relationship between BSA and CDAI were separately evaluated using the likelihood ratio test.

Results: 1,542 patients met inclusion criteria. Most were female 816 (52.9%), mean (SD) age was 53.7 (13.2) years, median duration with PsA disease 9.0 years and with PsO disease 18.0 years, and 71 (4.6%) had fibromyalgia. Of the 1484 patients with known DMARD therapy, 266 (18%) patients were on no DMARD therapy, 430 (29%) were on csDMARDs only, 616 (42%) were on first line biologic/tsDMARD therapy, and 172 (12%) were on second line biologic/tsDMARD therapy. The correlation between the skin severity and joint activity was positive and statistically significant 0.183 (p<0.0001). (Figure 1). The relationship between skin severity and joint activity was stronger in patients of younger age, on current treatment of DMARDs and TNFs, with history of MTX use, a higher dactylitis count, not achieving MDA, working from home or being a student, and with higher scores of HAQ, patient reported pain, and fatigue.

Conclusion: Skin severity is directly and significantly related to joint activity. The relationship is modified by age, gender, current therapy, work status, MDA, HAQ, patient reported pain and fatigue. The findings underscore the importance of treating both skin and joint among patients with both PsO and PsA.


Disclosure: P. J. Mease, AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 2,AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 5,AbbVie, Amgen, BMS, Celgene, Genentech, Janssen, Novartis, Pfizer, UCB, 8; C. J. Etzel, Corrona, LLC, 3,Merck Human Health, 9; J. Lisse, Eli Lilly and Company, 1,Eli Lilly and Company, 3; A. W. Armstrong, AbbVie, Amgen, Janssen, Merck, Lilly, Celgene, Novartis, and Pfizer, 5,AbbVie, Janssen, Lilly, 2,AbbVie, Lilly, 8; W. J. Huster, Eli Lilly and Company, 1,Eli Lilly and Company, 3; S. Rebello, Corrona, LLC, 3; R. Dodge, Corrona, LLC, 3; T. M. Muram, Eli Lilly and Company, 1,Eli Lilly and Company, 3; S. Al Sawah, Eli Lilly and Company, 1,Eli Lilly and Company, 3; M. J. Murage, Eli Lilly and Company, 1,Eli Lilly and Company, 3; J. D. Greenberg, corrona, LLC, 1,Corrona, LLC, 3,Genentech, Janssen, Novartis, Pfizer, Eli Lilly, 5; W. Malatestinic, Eli Lilly and Company, 1,Eli Lilly and Company, 3.


Abstract Number: 2533

Current PsA Therapy Impacts the Relationship between the Degree of Skin Involvimento and Joint Activity

Philip J Mease1, Carol J. Etzel2, Jeffrey Lisse3, April W Armstrong4, William J Huster3, Sabrina Rebello2, Rhiannon Dodge2, Talia M Muram3, Sarah Al Sawah3, Mwangi J Murage3, Jeffrey D Greenberg2 and William Malatestinic3, 1Swedish Medical Center and University of Washington, Seattle, WA, 2Corrona, LLC, Southborough, MA, 3Eli Lilly and Company, Indianapolis, IN, 4Keck School of Medicine, University of Southern California, Los Angeles, CA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Simultaneous control of joint symptoms and degree of skin involvement has been linked to improvement in health-related quality of life in patients with coexistent PsA and psoriasis (PsO). The objective of this analysis was to understand how the relationship between skin and joint severity is impacted by PsA therapy.

Methods: Enrollment visit data from Corrona PsA/SpA registry were obtained from 3/21/2013-9/30/2016. To be included in the analysis, patients had to have a diagnosis of PsA and history of PsO. Patients were subsequently stratified into three subgroups based on therapy at enrollment: a) not on DMARD therapy, b) on csDMARDS, or c) on anti-TNFs. Patient demographic and disease characteristics were compared.

The relationship of skin severity (BSA) and joint activity (CDAI) was evaluated using linear regression. To evaluate whether factors modified the relationship between CDAI and BSA, multiple linear regression was performed.
Results: 1,542 patients met inclusion criteria and 1484 had known therapy status. 266 (18%) patients were on no DMARD therapy, 430 (29%) were on csDMARDs only, and 765 (52%) were on anti-TNFs at time of enrollment. Patients on no DMARD therapy were more likely to be female, younger, have shorter PsA duration, more likely to have dactylitis, enthesitis and higher levels of joint activity, skin severity, and HAQ, and less likely to have MDA. (Table). Patients on TNFi therapy had better disease control (CDAI and BSA) than other therapy subgroups, but proportion of patients with MDA was similar to those on csDMARDS.

In the no DMARD therapy group, no variables tested resulted in a significant impact on the relationship. In both csDMARD and TNFi groups, age, BMI, SPARCC, HAQ, patient reported pain and fatigue significantly impacted the relationship between joint activity and skin severity. In csDMARDs group, dactylitis modified the relationship and in TNFi group, PsO onset and MDA modified the relationship.

Table: Descriptive statistics for patient characteristics, disease characteristics and PROs stratified by current drug therapy

<table>
<thead>
<tr>
<th></th>
<th>No DMARDs</th>
<th>csDMARDs only</th>
<th>1st or 2nd Line T</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs):</td>
<td>51.9 ±14.0</td>
<td>57.5 ±14.1</td>
<td>52.7 ±12.0</td>
</tr>
<tr>
<td>(SD)</td>
<td>N=266</td>
<td>N=430</td>
<td>N=765</td>
</tr>
<tr>
<td>Sex:</td>
<td>N=266</td>
<td>N=430</td>
<td>N=765</td>
</tr>
<tr>
<td>n(%) Female</td>
<td>157 (59.5)</td>
<td>237 (55.5)</td>
<td>361 (47.6)</td>
</tr>
<tr>
<td>Insurance Type:</td>
<td>N=266</td>
<td>N=430</td>
<td>N=765</td>
</tr>
<tr>
<td>Private</td>
<td>209 (78.6)</td>
<td>310 (72.1)</td>
<td>645 (84.3)</td>
</tr>
<tr>
<td>Medicare</td>
<td>58 (21.8)</td>
<td>127 (29.5)</td>
<td>127 (16.6)</td>
</tr>
<tr>
<td>Medicaid</td>
<td>7 (2.6)</td>
<td>24 (5.6)</td>
<td>31 (4.1)</td>
</tr>
<tr>
<td>None</td>
<td>6 (2.3)</td>
<td>8 (1.9)</td>
<td>12 (1.6)</td>
</tr>
<tr>
<td>Smoking Status:</td>
<td>N=257</td>
<td>N=420</td>
<td>N=753</td>
</tr>
<tr>
<td>Never: n(%)</td>
<td>131 (51.0)</td>
<td>222 (52.9)</td>
<td>402 (53.4)</td>
</tr>
<tr>
<td>Former: n(%)</td>
<td>90 (35.0)</td>
<td>160 (38.1)</td>
<td>269 (35.7)</td>
</tr>
<tr>
<td>Current: n(%)</td>
<td>36 (14.0)</td>
<td>38 (9.0)</td>
<td>82 (10.9)</td>
</tr>
<tr>
<td>BMI:</td>
<td>N=266</td>
<td>N=430</td>
<td>N=765</td>
</tr>
<tr>
<td>Mean</td>
<td>31.5 ±7.8</td>
<td>31.4 ±7.3</td>
<td>31.5 ±6.9</td>
</tr>
<tr>
<td>PsA Disease Duration (years):</td>
<td>Median</td>
<td>6.0(2.0,13.0)</td>
<td>7.0(3.0,14.5)</td>
</tr>
<tr>
<td>(IQR)</td>
<td>15.0(8.0,27.0)</td>
<td>16.0(9.0,29.0)</td>
<td>18.0(10.0,28.0)</td>
</tr>
<tr>
<td>Work Status: N=266</td>
<td>266</td>
<td>423</td>
<td>756</td>
</tr>
<tr>
<td>Full or Part-time: n(%)</td>
<td>174 (65.4)</td>
<td>233 (55.1)</td>
<td>502 (66.4)</td>
</tr>
<tr>
<td>Student/Not Working Outside Home: n(%)</td>
<td>15 (5.6)</td>
<td>25 (5.9)</td>
<td>56 (7.4)</td>
</tr>
<tr>
<td>Retired: n(%)</td>
<td>52 (19.5)</td>
<td>131 (31.0)</td>
<td>133 (17.6)</td>
</tr>
<tr>
<td>Disabled: n(%)</td>
<td>25 (9.4)</td>
<td>34 (8.0)</td>
<td>65 (8.6)</td>
</tr>
<tr>
<td>CDAI:</td>
<td>N=266</td>
<td>N=430</td>
<td>N=765</td>
</tr>
<tr>
<td>Mean</td>
<td>14.9 ±8.9</td>
<td>11.9 ±9.3</td>
<td>10.5 ±7.2</td>
</tr>
<tr>
<td>BSA:</td>
<td>N=266</td>
<td>N=430</td>
<td>N=765</td>
</tr>
<tr>
<td>Mean</td>
<td>7.5 ±14.3</td>
<td>5.2 ±10.0</td>
<td>5.2 ±10.3</td>
</tr>
<tr>
<td>Enthesitis SPARCC Score:</td>
<td>Mean (SD)</td>
<td>3.9 ±2.9</td>
<td>4.8 ±3.5</td>
</tr>
<tr>
<td>Dactylitis: N=266</td>
<td>266</td>
<td>430</td>
<td>765</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>2.2 ±1.5</td>
<td>2.7 ±2.2</td>
<td>1.9 ±1.5</td>
</tr>
<tr>
<td>Minimal Disease Activity:</td>
<td>n(%)</td>
<td>57 (22.9)</td>
<td>172 (43.8)</td>
</tr>
<tr>
<td>28 Tender Joints Count:</td>
<td>Mean (SD)</td>
<td>4.0 ±5.3</td>
<td>2.6 ±4.8</td>
</tr>
<tr>
<td>28 Swollen Joints Count:</td>
<td>Mean (SD)</td>
<td>2.7 ±3.7</td>
<td>2.0 ±3.7</td>
</tr>
<tr>
<td>Nail PsO VAS (0-100):</td>
<td>Mean (SD)</td>
<td>9.1 ±16.0</td>
<td>8.1 ±21.4</td>
</tr>
<tr>
<td>HAQ (0-3):</td>
<td>Mean (SD)</td>
<td>0.7 ±0.7</td>
<td>0.6 ±0.7</td>
</tr>
<tr>
<td>Patient Pain VAS (0-100):</td>
<td>Mean (SD)</td>
<td>46.0 ±29.0</td>
<td>37.4 ±28.7</td>
</tr>
<tr>
<td>Patient Reported Fatigue (0-100):</td>
<td>Mean (SD)</td>
<td>45.3 ±29.0</td>
<td>39.3 ±29.0</td>
</tr>
</tbody>
</table>
Proportions are calculated among patients with non-missing response. Enthesiits SPARCC Score and Dactylitis Counts are among patients with enthesitis and dactylitis, respectively.

**Conclusion:** There were significant differences in disease characteristics and patient reported outcomes in PsA patients with PsO history when stratified by type of therapy. The relationship between joint activity and skin severity is influenced by age, SPARCC, patient reported pain, fatigue, and HAQ among patients on DMARDs and TNFi therapies. Dactylitis and PsO onset also modified the relationship among csDMARD and TNFi therapy groups, respectively. For improved disease management of PsA patients with a history of PsO, consideration of these factors is important when determining type of therapy.

**Disclosure:** P. J. Mease, AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 2,AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 5,AbbVie, Amgen, BMS, Celgene, Genentech, Janssen, Novartis, Pfizer, UCB, 8; C. J. Etzel, Corrona, LLC, 3;J. Lisse, Eli Lilly and Company, 1,Eli Lilly and Company, 3; A. W. Armstrong, AbbVie, Amgen, Janssen, Merck, Lilly, Celgene, Novartis, and Pfizer, 5,AbbVie, Janssen, Lilly, 2,AbbVie, Lilly, 8; W. J. Huster, Eli Lilly and Company, 1,Eli Lilly and Company, 3; S. Rebello, Corrona, LLC, 3;R. Dodge, Corrona, LLC, 3; T. M. Muram, Eli Lilly and Company, 1,Eli Lilly and Company, 3; S. Al Sawah, Eli Lilly and Company, 1,Eli Lilly and Company, 3; M. J. Murage, Eli Lilly and Company, 1,Eli Lilly and Company, 3; J. D. Greenberg, Corrona, LLC, 1,Corrona, LLC, 3,Genentech, Janssen, Novartis, Pfizer, Eli Lilly, 5; W. Malatestinic, Eli Lilly and Company, 1,Eli Lilly and Company, 3.


**Abstract Number:** 2534

**the Relationship between Biological Therapy, Work Productivity, and Activity Impairment in Patients with Psoriatic Arthritis: Prospective Multicentre Observational Study**

**Jiri Stolfa**¹, Tomas Mlcoch², Jan Tuzil², Liliana Sedova³, Jitka Jircikova⁴, Monika Gregova⁵, Tomas Dolezal⁴ and Karel Pavelka⁶, ¹Institute of Rheumatology Prague, Rheumatology, Prague, Czech Republic, ²Institute of Health Economics and Technology Assessment (iHETA), Statistician, Prague, Czech Republic, ³Institute of Rheumatology Prague, rheumatologist, Prague, Czech Republic, ⁴Institute of Health Economics and Technology Assessment (iHETA), statistician, Prague, Czech Republic, ⁵Instituite of Rheumatology Prague, rheumatologist, Prague, Czech Republic, ⁶Institute of Rheumatology, Prague, Czech Republic, Prague, Czech Republic

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Psoriatic arthritis (PsA) is a progressive disease bringing substantial socioeconomic burden. Gradual loss of productivity (PL) and daily activities can be modified by effective therapy, e.g. biological treatment (BT).

**Methods:** We described the cohort and methods elsewhere. 228 PsA patients diagnosed with CASPAR criteria were followed over 873 appointments in 6-month intervals. Activity (AI) and work impairment (WI) were assessed using WPAI questionnaire. Predictors of WI were explored with linear mixed-effect regression (ME) and statistical differences
between groups using Kruskal-Wallis test. PL was monetized via Human Capital Approach (HCA; costs until retirement at 62.7 years; discount rate 3%) with average gross wage of €1493.

**Results:** 53.5% patients were working and 25.4% were disabled. Mean baseline AI and WI in working patients (± SD) were 0.28 (± 0.24) and 0.33 (± 0.32). Similarly to HAQ score (0.74 ± 0.70), WI and AI worsened with growing PsA activity measured either by DAPsA score or cDAPsA (excluding serum CRP) with p ≤ 0.0001. The mean time to retirement was 14.0 ± 9.9 years.

38.2% patients had BT (anti-TNF) in the 12 months prior to enrolment with the mean costs of €981 per patient-month. Compared to non-BT population, BT patients were younger (50.7 vs. 59.4) and more frequently disabled (17.1% vs. 8.3%). They had lower DAPsA at baseline (14.43 vs. 17.14; p = 0.02) due to lower serum CRP (5.72 vs. 7.12; p = 0.0035) contrarily to cDAPsA which differed neither in baseline (8.60 vs. 9.97; p= 0.075) nor in longitudinal population (8.2 vs. 9.5; p = 0.056). Number of swollen joints dropped in the longitudinal population (1.02 vs. 1.23; p = 0.0015) while WI raised (0.38 vs. 0.41; ≤ 0.0001).

HAQ, AI and time from diagnosis were the best predictors of WI. ME models translated into productivity costs using HCA showed that increase in either HAQ or AI (as sole predictors) by 0.1 represent a growth of PL by €2387 or €5367 (Figure 1). In the most robust model, increase of HAQ and AI together by 0.1 correspond to the growth of indirect costs by €6212. Both DAPsA and cDAPsA were significant, yet weak predictors of WI.

**Conclusion:** In view of the BT indication criteria (severity, failure of previous treatment), the clinical parameters of the BT population suggest that BT effectively slows PsA progression. Primary response was observed as attenuation of acute inflammation measured by CRP. HAQ and AI are the best predictors of WI in PsA. Therefore, we can conclude that decreasing HAQ, e.g. via more effective BT, will undoubtedly increase working productivity and thus decrease productivity losses in PsA patients.

**Figure 1. Fitted values of productivity costs predicted by HAQ or Activity impairment (WPAI questionnaire) using the mixed regression model**

**Disclosure:** J. Stolfa, None; T. Mlcoch, None; J. Tuzil, None; L. Sedova, None; J. Jircikova, None; M. Gregova, None; T. Dolezal, None; K. Pavelka, None.
Patient Outcomes from a Tertiary Center Combined Rheumatology-Dermatology Clinic

Charis G1, Delaney Conway2, Joanne Cunha3, Abrar Qureshi4, So Yeon Paek5 and Anthony M. Reginato6, 1Division of Rheumatology, The Warren Alpert Medical School of Brown University, Providence, RI, 2Internal Medicine, Rhode Island Hospital, The Warren Alpert Medical School of Brown University, Providence, RI, 3Division of Rheumatology, The Warren Alpert Medical School of Brown University, East Providence, RI, 4Dermatology, Rhode Island Hospital, The Warren Alpert Medical School of Brown University, Providence, RI, 5Department of Dermatology, The Warren Alpert Medical School of Brown University, Providence, RI, 6Rhode Island Hospital, The Warren Alpert School of Medicine at Brown University, Providence, RI

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Many autoimmune diseases have both musculoskeletal and cutaneous manifestations, which historically have been managed separately by rheumatologists and dermatologists. Given the complex presentation of autoimmune dermatologic and rheumatologic diseases, new tools are now available for proper workup and diagnosis, and access to a wide array of novel targeted therapies, combined Rheumatology-Dermatology clinics have been developed across the country. These clinics are unique in that both rheumatologists and dermatologists work together to provide multi-disciplinary care for patients with skin and musculoskeletal diseases. In this study, we retrospectively reviewed the records from a our combined Rheumatology-Dermatology clinic at Rhode Island Hospital, a tertiary care medical center in the Northeast.

Methods: We conducted a retrospective chart review of 324 patient visits to the newly formed Rhode Island Hospital Center for Skin and Musculoskeletal Diseases during the period from July 2014 to February 2016. A total of 167 new patients were identified. We collected data on patient demographics, past medical history, family history, referring physician, presenting diagnoses, change in diagnoses, escalation or reduction of pharmacologic management including biologic medication use, and development of adverse events.

Results:

Of 167 new patients seen in the combined Rheumatology-Dermatology Clinic between July 2014 and February 2016, 105 (63%) were female and the average age was 50 years. The average number of visits per patient over this period was 2.5. The majority (68%) of patients were referred by either dermatology or rheumatology for further evaluation and management. The most frequent diagnosis referred to the clinic was psoriasis, comprising 60% of referrals. Other diagnoses seen in the clinic included psoriatic arthritis, systemic lupus erythematosus, cutaneous lupus, dermatomyositis, scleroderma, vasculitis, pyoderma gangrenosum, and mixed connective tissue disease. 44 (26%) patients reported a history of a co-morbid autoimmune condition such as inflammatory bowel disease (IBD), thyroid disease, or pernicious anemia. 118 (71%) patients denied a family history of similar autoimmune condition. As a result of their consultation in the combined dermatology-rheumatology clinic, 55 (37%) patients received a change in diagnosis. One fifth of patients presenting with psoriasis were diagnosed with concomitant psoriatic arthritis. Treatment was changed in 94 (56%) patients overall. 68 (41%) patients had escalation of treatment, while 12 (7%) had treatment reduction. A small minority of patients 18 (11%) experienced adverse events from these treatments.

Conclusion: This study provides evidence to support improved patient outcomes by evaluation in a unique combined rheumatology-dermatology multidisciplinary setting. Patients with complex autoimmune diseases, including those with psoriasis and psoriatic arthritis, experienced benefits from co-management of their condition.
Abstract Number: 2536

Comparison of Quality-of-Life, Function and Psoriasis Measures in Minimal Disease Activity and DAS28 States in Routine Care of Patients with Psoriatic Arthritis

Catherine Hughes, Nora Ng, Toby Garrood and Bruce Kirkham, Rheumatology, Guy's & St Thomas NHS Foundation Trust, London, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Psoriatic arthritis (PsA) often occurs with skin psoriasis (PsO). Disease activity can be measured using several tools including Minimal Disease Activity (MDA/VLMDA) or 28 joint disease activity (DAS28). The Psoriasis Area and Severity Index (PASI) assess the severity of PsO. Patient reported outcome measures (PROMs) are increasingly accepted as key outcome measures (new OMERACT guidelines) including the Dermatology Quality of Life Index (DLQI) and EuroQol 5 dimensions questionnaire (EQ-5D). Our objective was to compare PROMs in MDA and DAS28 disease states, including severe psoriasis, defined as PASI >10 or DLQI>10 or Body Surface Area >10.

Methods:
Patients with PsA attending our center completed PROMs and had clinician assessment. The following data was recorded: age, diagnosis, MDA components, DAS28 components, PASI, DLQI, EQ-5D-3L and Health Assessment Questionnaire (HAQ-DI), in a IRB approved cross-sectional analysis. Statistics were performed using SPSS Version 23.

Results:
129 sequential patients attending between February and November 2016 were included. Population characteristics are outlined in Table 1. 82% of patients had psoriasis, with a DLQI score available for 88% (n=93). MDA and DAS28 low disease activity identified similar patients, with similar arthritis outcomes, generally better in MDA (Tables 1 and 2). Our population generally did not have high PASI (mean 1.38). DLQI scores were higher in active PsA. The DAS28 remission group had 11% of patients with a DLQI >10, in contrast the MDA group had fewer with DLQI >10 (3%).

Conclusion:
MDA and DAS28 measures identify patients with similar arthritis outcomes. Patients in MDA and low DAS28 states have lower DLQI values. MDA is associated with significantly fewer patients with high DLQI. This suggests that MDA identifies patients who have a better overall psoriatic disease outcome.

Table 1: Patient Characteristics, MDA and Very Low (VL)-MDA

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>VL-MDA N=19</th>
<th>MDA N=46</th>
<th>Not-MDA N=83</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age years</td>
<td>51 (19.4)</td>
<td>47 (13.44)</td>
<td>52 (14.15)</td>
<td>0.92 *</td>
</tr>
<tr>
<td>Gender (%F)</td>
<td>32% (6/19)</td>
<td>33% (15/46)</td>
<td>36% (30/83)</td>
<td>0.686**</td>
</tr>
<tr>
<td>Mean DAS28</td>
<td>1.6 (0.46)</td>
<td>1.86 (0.54)</td>
<td>3.88 (1.25)</td>
<td></td>
</tr>
<tr>
<td>DAS28 remission</td>
<td>100% (19/19)</td>
<td>91% (42/46)</td>
<td>12% (10/83)</td>
<td>&lt;0.0001 **</td>
</tr>
<tr>
<td>DAS28 2.6-3.2</td>
<td>0</td>
<td>4% (2/46)</td>
<td>17% (14/83)</td>
<td>0.388**</td>
</tr>
<tr>
<td>DAS28 3.2-5.1</td>
<td>0</td>
<td>0</td>
<td>53% (44/83)</td>
<td></td>
</tr>
<tr>
<td>DAS28 &gt;5.1</td>
<td>0</td>
<td>0</td>
<td>18% (15/83)</td>
<td></td>
</tr>
<tr>
<td>EQ5D Utility Index</td>
<td>0.86</td>
<td>0.78</td>
<td>0.45</td>
<td>&lt;0.0005 *</td>
</tr>
<tr>
<td>EQ5D VAS</td>
<td>84</td>
<td>79</td>
<td>50</td>
<td>&lt;0.0005 *</td>
</tr>
<tr>
<td>PASI&gt;10</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>0.222**</td>
</tr>
<tr>
<td>DLQI &gt;10</td>
<td>0</td>
<td>3% (1/36)</td>
<td>34% (20/59)</td>
<td>0.001**</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>0.0789</td>
<td>0.22</td>
<td>1.32</td>
<td>&lt;0.0005 *</td>
</tr>
<tr>
<td>VAS Pain (0-100)</td>
<td>15</td>
<td>25</td>
<td>63</td>
<td>&lt;0.0005 *</td>
</tr>
</tbody>
</table>

P Value calculated comparing MDA and not-MDA groups using:*Mann Whitney U test; ** Chi Squared test

Table 2: MDA and QoL measures compared to DAS28 scores

<table>
<thead>
<tr>
<th>Total number</th>
<th>DAS remission N=50</th>
<th>DAS 2.6-3.2 N=17</th>
<th>DAS 3.2-5.1 N=45</th>
<th>DAS&gt;5.1 N=15</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PsO</td>
<td>40/50 (80%)</td>
<td>15/17 (88%)</td>
<td>37/45 (82%)</td>
<td>12/15 (80%)</td>
<td>1.00**</td>
</tr>
<tr>
<td>MDA</td>
<td>80% (40/50)</td>
<td>18% (3/17)</td>
<td>2% (1/45)</td>
<td>0</td>
<td>0.000**</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>0.432</td>
<td>0.583</td>
<td>1.49</td>
<td>1.86</td>
<td>0.000*</td>
</tr>
<tr>
<td>EQ5D Utility Index</td>
<td>0.77</td>
<td>0.687</td>
<td>0.53</td>
<td>0.138</td>
<td>0.000*</td>
</tr>
<tr>
<td>EQ5D VAS</td>
<td>70</td>
<td>71</td>
<td>53.4</td>
<td>36</td>
<td>0.000*</td>
</tr>
<tr>
<td>VAS Pain 0-100</td>
<td>29</td>
<td>55</td>
<td>60</td>
<td>81</td>
<td>0.000*</td>
</tr>
<tr>
<td>PASI &gt;10</td>
<td>1/50 (2%)</td>
<td>0</td>
<td>3/45 (7%)</td>
<td>1/15 (7%)</td>
<td>0.662**</td>
</tr>
<tr>
<td>DLQI &gt;10</td>
<td>4/38 (11%)</td>
<td>3/13 (23%)</td>
<td>8/32 (25%)</td>
<td>5/10 (50%)</td>
<td>0.033**</td>
</tr>
<tr>
<td>DLQI 5-10</td>
<td>8/38 (21%)</td>
<td>1/13 (8%)</td>
<td>8/32 (25%)</td>
<td>3/10 (30%)</td>
<td></td>
</tr>
<tr>
<td>DLQI &lt;5</td>
<td>26/38 (68%)</td>
<td>9/13 (69%)</td>
<td>16/32 (50%)</td>
<td>2/10 (20%)</td>
<td></td>
</tr>
</tbody>
</table>

P Value calculated comparing DAS28 remission and non DAS28 remission groups using: *Mann Whitney U; **chi squared test

Disclosure: C. Hughes, None; N. Ng, None; T. Garrood, None; B. Kirkham, Eli Lilly and Company, 2, Abbvie, 2, Novartis Pharmaceutical Corporation, 2, Arthritis Research UK, 2, Roche, 2, UCB, 2, Celgene, 9, Pfizer Inc, 9, Janssen Pharmaceutica Product, L.P., 9, Sandoz, 9.

Abstract Number: 2537

Changes in Severity, Functional Status, and Wellbeing over Time Among Individuals with Ankylosing Spondylitis (AS) in Canada: Results from the RHUMADATA® Multicentre Registry

Shelagh Szabo1, Sara Chehab2, Louis Coupal3 and Denis Choquette4, 1Broadstreet HEOR, Vancouver, BC, Canada, 2Novartis Pharmaceuticals Canada Inc., Montreal, QC, Canada, 3Institut de Recherche en Rhumatologie de Montréal (IRRMM), Montréal, QC, Canada, 4University of Montreal Hospital Research Centre (CRCHUM), Notre Dame Hospital Montreal, Montreal, QC, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: While changes in disease severity, functional status, and patient wellbeing are commonly measured in AS trials, longitudinal data from real-world cohorts are fewer; particularly considering the impact of anti-tumor necrosis factor (TNF) therapy. The objective was to estimate changes in severity, function, and wellbeing over time, from a population of Canadians undergoing active management for AS.

Methods: This real-world analysis used up to 15 years of clinical and patient-reported outcomes (PRO) data from the broad set of patients treated at the IRRM and CORQ (RHUMADATA®). The frequency of use of anti-TNFs was tabulated. AS severity (by BASDAI), functional impact (by BASFI), and wellbeing (by BAS-G) were assessed; at the baseline visit, within the first year of follow-up (e.g. from second visit to 52 weeks), and at least annually thereafter. From those with PRO data post-baseline, mean (standard deviation [SD]) scores were plotted over the next 4 years; stratified by anti-TNF status (treatment-naïve; or treated with 1, 2, or ≥3 anti-TNFs over the period). A sensitivity analysis was performed to limit the cohort to those with ≥2 PRO measures post-baseline.

Results: Mean (SD) age at baseline was 36.0 (12.6) years, and 60.0% were male; median follow-up was 9.7 (10.6) years. Of the 341 patients with post-baseline PRO measures, 116 (34.0%) were never treated, 144 patients (42.2%) were treated with 1, 47 patients (13.8%) were treated with 2, and 34 (10.0%) patients were treated with ≥3, anti-TNFs. Mean (SD) baseline PRO scores were higher with greater anti-TNF treatment (table); for example, BASDAI scores ranged from 4.1 (2.2; anti-TNF-naïve), to 5.5 (1.9; ≥3 anti-TNFs). Mean (SD) scores decreased over time, in each anti-TNF treatment category. As an example for the BASDAI, scores decreased to 3.0 (2.1) during year four (anti-TNF-naïve), and to 4.0 (1.7) for those with ≥3 anti-TNFs. Mean changes from baseline were less among those with more severe disease who received more anti-TNF treatment (data not shown). While the sample for the sensitivity analysis was smaller, the findings were consistent with the base case: improvements on the BASDAI, BASFI, and BAS-G were lower for patients exposed to ≥2 anti-TNFs, compared to those treated with 0 or 1 (data not shown).

Conclusion: The need for re-treatment was common in this Canadian cohort; almost 25% were treated with ≥2 anti-TNFs over 4 years. PROs showed improvements in disease severity, function, and patient wellbeing over time; although consistent with observations from rheumatoid arthritis, these were less pronounced for more severely affected AS patients (treated more heavily with anti-TNFs). These data are useful for demonstrating the clinical and functional burden experienced by AS patients, and suggest a potential role for newer treatments not targeting TNF.
Table: Mean (SD) scores over time, BASDAI, BASFI, and BAS-G; according to number of anti-TNFs (naïve, 1, 2, or ≥3 therapies)

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
<th>Year 4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Anti-TNF-naïve</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BASDAI</td>
<td>116</td>
<td>4.1</td>
<td>2.2</td>
<td>81</td>
<td>3.3</td>
</tr>
<tr>
<td>BASFI</td>
<td>116</td>
<td>2.6</td>
<td>2.4</td>
<td>81</td>
<td>1.8</td>
</tr>
<tr>
<td>BAS-G</td>
<td>92</td>
<td>4.9</td>
<td>2.4</td>
<td>78</td>
<td>3.4</td>
</tr>
<tr>
<td>One anti-TNF</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BASDAI</td>
<td>126</td>
<td>5.2</td>
<td>2.4</td>
<td>122</td>
<td>3.2</td>
</tr>
<tr>
<td>BASFI</td>
<td>124</td>
<td>4.5</td>
<td>2.7</td>
<td>122</td>
<td>2.9</td>
</tr>
<tr>
<td>BAS-G</td>
<td>90</td>
<td>5.9</td>
<td>2.3</td>
<td>106</td>
<td>3.4</td>
</tr>
<tr>
<td>Two anti-TNFs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BASDAI</td>
<td>39</td>
<td>5.2</td>
<td>2.0</td>
<td>47</td>
<td>4.1</td>
</tr>
<tr>
<td>BASFI</td>
<td>39</td>
<td>4.4</td>
<td>2.6</td>
<td>44</td>
<td>4.0</td>
</tr>
<tr>
<td>BAS-G</td>
<td>29</td>
<td>5.8</td>
<td>2.1</td>
<td>38</td>
<td>4.9</td>
</tr>
<tr>
<td>Three or more anti-TNFs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BASDAI</td>
<td>26</td>
<td>5.5</td>
<td>1.9</td>
<td>34</td>
<td>5.5</td>
</tr>
<tr>
<td>BASFI</td>
<td>26</td>
<td>5.0</td>
<td>2.5</td>
<td>34</td>
<td>5.0</td>
</tr>
<tr>
<td>BAS-G</td>
<td>21</td>
<td>6.3</td>
<td>1.8</td>
<td>31</td>
<td>5.9</td>
</tr>
</tbody>
</table>

Disclosure: S. Szabo, None; S. Chehab, Novartis Pharmaceutical Canada Inc., 3; L. Coupal, None; D. Choquette, Abbvie, Amgen, BMS, Celgene, Eli Lilly, Hospira, Merck, Novartis, Pfizer, Roche, Sanofi-Genzyme, UCB, Janssen, Sandoz, 8, Abbvie, Amgen, BMS, Celgene, Eli Lilly, Hospira, Merck, Novartis, Pfizer, Roche, Sanofi-Genzyme, UCB, Janssen, Sandoz, 5, Abbvie, Amgen, BMS, Celgene, Eli Lilly, Hospira, Merck, Novartis, Pfizer, Roche, Sanofi-Genzyme, UCB, Janssen, Sandoz, 2.


Abstract Number: 2538

**Change in Self-Reported Health Status and Fatigue before and after the Diagnosis of Psoriatic Arthritis- the Nord-Trondelag Health Study (HUNT)**

Mari Hoff1, Tom Ivar Lund Nilsen2, Ruth Stoklund Thomsen3, Agnete Malm Gulati4, Arthur Kavanaugh5 and Glenn Haugeberg4, 1Rheumatolgy, University Hospital, St. Olavs Hospital, NTNU, Trondheim, Norway, 2Faculty of medicine, Department of public health and nursing, NTNU, Norwegian University of Science and Technology, Trondheim, Norway, 3Faculty of Medicine, Department of Public Health and Nursing, NTNU, Norwegian University of Science and Technology, Trondheim, Norway, 4NTNU, Norwegian University of Science and Technology, Trondheim, Norway, 5Medicine, University of California, San Diego, La Jolla, CA

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM
Background/Purpose:

Psoriatic arthritis (PsA) is a systemic inflammatory disease that can involve skin, nails, joints, enthuses, and can be associated with systemic symptoms such as fatigue.

The disease may have a negative impact on patients, including their quality of life.

The aim of this study was to examine the effect of PsA on self-reported health status and fatigue.

Methods:

We present longitudinal data on 36,973 participants of the population-based HUNT Study, Norway (HUNT2, 1995-97 and HUNT3, 2006-08). Overall, 0.67% of participants in HUNT3 was validated to have PsA according to the Caspar criteria, and 151 were diagnosed with PsA between HUNT2 and HUNT3.

We examined health status and fatigue before and after the PsA diagnosis, compared with people without PsA, excluding persons diagnosed with PsA before HUNT2.

Self-reported health was measured as “How is your health at the moment (1: Very Good; 2: Good; 3: Fair 4: Poor)”. The question on fatigue was “Do you feel, for the most part, strong and fit or tired and worn out (graded from 1: Very strong and fit to 7: Very tired and worn out). Variables were also dichotomized to classify people as having poor health (response option 3-4) and fatigue (option 5-7).

We used linear regression to estimate adjusted mean differences in outcome variables at HUNT3, and logistic regression to estimate adjusted odds ratios (OR) for poor health and fatigue. All estimates were adjusted for baseline health or fatigue, gender, age, BMI, education, and smoking.

Sensitivity analyses were performed excluding people who reported poor health or fatigue in HUNT2.

Results:

There was no large differences at baseline in sex (57.6 vs. 55.2% women), age (43.9 vs. 46.8 years), BMI (27.3 vs. 26.2 kg/m²), or attainment of higher education (21.2% vs. 22.0%) between people developing PsA and those who did not. However, PsA developers smoked more (41.1 vs. 25.4%) and reported muscle and joint pain (66.9% vs. 46.5%).

Self-reported health status and fatigue before and after the PSA diagnosis are presented in Table. Compared to the controls, people developing PsA reported poorer health (30.5% vs. 23.3%) and more fatigue (31.8% vs. 19.4%).

After adjustment, they scored 0.37 (95% CI 0.28-0.47) higher on poor health and 0.40 (0.23-0.58) higher on fatigue compared to controls. Correspondingly, people developing PsA had an OR of 4.37 (2.95-6.46) for reporting poor health and 1.80 (1.22-2.65) for fatigue at HUNT3. The sensitivity analyses gave ORs of 3.72 (2.37-5.83) and 1.97 (1.31-2.96), respectively.

Conclusion:

Individuals who developed PsA were four times more likely to report poor health and the risk of perceived fatigue was almost doubled. This shows that developing PsA has a negative impact on patients and could contribute to an impaired quality of life in these patients.

The Contribution of Skin and Joint Improvements to the Health-Related Quality of Life of Patients with Active Psoriatic Arthritis

Arthur Kavanaugh\(^1\), Alice B Gottlieb\(^2\), Akimichi Morita\(^3\), Joseph Merola\(^4\), Julie Birt\(^5\), Chen-Yen Lin\(^5\), Catherine Shuler\(^5\) and Diamant Thaçi\(^6\), \(^1\)Medicine, University of California, San Diego, La Jolla, CA, \(^2\)Department of Dermatology, New York Medical College, Valhalla, NY, \(^3\)Dept of Geriatric & Environmental Dermatology, Nagoya City Univ Medical School, Nagoya, Japan, \(^4\)Clinical Unit for Research Innovation & Trials, Harvard Medical School, Boston, MA, \(^5\)Eli Lilly and Company, Indianapolis, IN, \(^6\)Comprehensive Center for Inflammation Medicine, University Hospital Schleswig-Holstein Campus Luebeck, Ratzeburger Allee, Germany

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is a chronic immune-mediated inflammatory disease affecting peripheral and axial joints. For patients with active psoriasis, the added burden of skin disease can further reduce the health-related quality of life (HRQoL) of patients with joint disease. The objective of this analysis is to determine the contribution of joint and skin improvements in the HRQoL of patients with active PsA during phase 3 clinical trials investigating ixekizumab (IXE) treatment.
Methods: The SPIRIT trials are double-blinded phase 3 trials investigating the treatment of IXE, a high affinity monoclonal antibody selectively targeting interleukin-17A, for patients with active PsA. The integrated database of 2 SPIRIT trials consisted of patients who were biologic DMARD-naive (SPIRIT-P1, NCT01695239) or were inadequate responders to TNF-inhibitors (SPIRIT-P2, NCT02349295). Patients were randomized to 80 mg IXE every 4 weeks (Q4W, N=229) or 2 weeks (Q2W, N=226) after a 160 mg starting dose or placebo (PBO, N=224). At baseline and Week 24, joint and skin disease were measured by the Disease Activity index for Psoriatic Arthritis (DAPSA; calculated post-hoc) and Psoriasis Area and Severity Index (PASI), respectively. HRQoL was measured by the EuroQol 5 Dimensions Visual Analog Scale (EQ-5D VAS), Short Form-36 Health Survey (SF-36), and the Work Productivity and Activity Impairment-Specific Health Problem (WPAI). The synergistic contribution of skin and joint improvements to HRQoL was modeled using smoothing spline method and depicted with response surface (Figure 1). Missing data were imputed using last observation carried forward.

Results: Of the 679 PBO- and IXE-treated patients in the SPIRIT trials, 402 (65%) and 224 (36%) patients had ≥3% body surface area (BSA) and ≥10% BSA psoriasis at baseline, respectively. In these patients, we applied response surface modeling to investigate the relationship between DAPSA, PASI, and change from baseline in EQ-5D VAS at Week 24. The greatest improvement in EQ-5D VAS was associated with the largest percent improvements in both DAPSA and PASI together, rather than DAPSA or PASI alone (Figure 2). Similar observations, regardless of ≥3% or ≥10% BSA baseline psoriasis, were made in domains of SF-36 (General Health, Physical Functioning, Social Functioning, and Vitality; data not shown) and WPAI (Activity Impairment; data not shown).

Conclusion: For PsA patients with psoriasis, optimal improvements in patients’ HRQoL, as measured by select domains of patient reported outcomes, were dependent on successful treatment of both joint and skin symptoms.

![Figure 1](image_url). Response surface modeling of the contribution of skin and joint improvements to patient HRQoL. (A) Three dimensional scatterplot of skin (y-axis; PASI – percent improvement), joint (x-axis; DAPSA – percent improvement), and HRQoL (z-axis; EQ-5D – change from baseline) improvement at Week 24. A color spectrum is applied to HRQoL improvements (blue [least improvement] to red [greatest improvement]). (B) Response surface of scatterplot estimated by smoothing spline method.
Abstract Number: 2540

Impact of Sleep on Measures of Disease Activity in Psoriatic Arthritis

Sayanika Kaur1 and Martin J. Bergman2,3, 1Internal Medicine, Mercy Catholic Medical Center, Lansdowne, PA, 2Drexel University College of Medicine, Philadelphia, PA, 3Drexel University College of Medicine, Ridley Park, PA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM
**Background/Purpose:** The impact that sleep has on patients’ perception of disease activity in Psoriatic Arthritis (PsA) has been poorly understood. We assessed the association between sleep, as measured with a 21-point VAS, and various measures of disease activity.

**Methods:** All patients seen in the clinic of MB are asked to complete a questionnaire (MDHAQ) with additional questions regarding sleep, as part of the routine care in this practice. After a clinical exam, including a 28 tender (TJC) and swollen (SJC) joint count, the physician records an MDGlobal score, using a 21 point VAS (0-10). From these values, the RAPID3 (a composite score of Pt Pain+PtGlobal+Function) is calculated. Additionally, the CDAI can also be calculated (TJC+SJC+PtGlobal+MDGlobal). While neither measure has been extensively studied in PsA, they provide insight into the levels of disease activity as perceived by the patient and by the treating physician. We performed multiple regressions, using the Sleep VAS as the dependent variable, to investigate its impact on the various independent variables and composite scores.

**Results:** Random visits of 49 patients (45% male, mean age=59.36yrs, mean disease duration=6.63yrs, mean Sleep VAS=3.83)) were included for study. Multiple regressions were performed “controlling for” age, sex and disease duration. Based on our results, Sleep VAS has a significant impact on TJC, Pain and PtGlobal scores (p<0.05), with a trend toward significance for SJC (p=0.058) (Table1). The composite scores were also significantly impacted: RAPID3 (p=0.018) and CDAI (p=0.003). When the PtGlobal score is removed from the CDAI (“C3”=TJC+SJC+MDGlobal), the significance remained (p=0.014), suggesting that the impact of sleep was not only observed by the patient, but also by the treating physician.

**Conclusion:** Patients with PsA often report difficulty with sleep. We demonstrate a strong association between patient reported sleep problems and multiple measures of disease activity. While it might be assumed that this association would impact patient reported outcomes (PROs), there is also a strong association between sleep and physician measures, including the CDAI. While neither the RAPID3 nor CDAI have been validated for the monitoring of PsA, we feel that this study provides insight into the impact of sleep on disease activity. Based on this study, one cannot determine whether sleep disturbances influence disease activity or vice versa. Nevertheless, by monitoring a Sleep VAS, one can accurately assess levels of disease activity in PsA patients.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Regress. Coefficient</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TJC</td>
<td>0.372</td>
<td>0.134; 0.611</td>
<td>0.003</td>
</tr>
<tr>
<td>SJC</td>
<td>0.715</td>
<td>-0.025; 1.455</td>
<td>0.058</td>
</tr>
<tr>
<td>MDGlobal</td>
<td>0.179</td>
<td>-0.051; 0.409</td>
<td>0.124</td>
</tr>
<tr>
<td>Function</td>
<td>0.216</td>
<td>-0.064; 0.496</td>
<td>0.156</td>
</tr>
<tr>
<td>Pain</td>
<td>0.403</td>
<td>0.094; 0.712</td>
<td>0.012</td>
</tr>
<tr>
<td>PtGlobal</td>
<td>0.322</td>
<td>0.026; 0.619</td>
<td>0.034</td>
</tr>
<tr>
<td>RAPID3</td>
<td>0.977</td>
<td>0.180; 1.77</td>
<td>0.018</td>
</tr>
<tr>
<td>CDAI</td>
<td>1.79</td>
<td>0.652; 2.92</td>
<td>0.003</td>
</tr>
<tr>
<td>C3</td>
<td>1.31</td>
<td>0.275; 2.34</td>
<td>0.014</td>
</tr>
</tbody>
</table>

Sleep VAS=dependent variable C3=TJC+MDGlobal

**Disclosure:** S. Kaur, None; M. J. Bergman, None.


**Abstract Number:** 2541
The Relationship between the Patient Acceptable Symptom State (PASS) and Disease Activity in Patients with Psoriatic Arthritis (PsA)

Jeanie Z. Fei1, Justine (Yang) Ye1, Anthony V. Perruccio2, Dafna D Gladman3 and Vinod Chandran4, 1University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, 2Krembil Research Institute, University Health Network, Toronto, ON, Canada, 3Rheumatology, Toronto Western Hospital, University of Toronto, Toronto, ON, Canada, 4Medicine, Krembil Research Institute, Toronto Western Hospital, University of Toronto, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
PASS is the highest level of symptoms beyond which patients consider themselves well. Psoriatic Arthritis Disease Activity Score (PASDAS) is a recently developed composite disease activity measure that summarizes a patient’s disease in a single 0-10 score. Disease Activity index for Psoriatic Arthritis (DAPSA) is a score recently validated for its utilization in PsA, focusing on the evaluation of disease activity in the joints. In this study, we aimed to 1) identify the PASDAS and DAPSA cut-off points for PASS, 2) to examine the agreement between PASS and the published PASDAS thresholds for low (<3.2), moderate (3.2-5.4), and high disease activity (>5.4), and 3) to examine the agreement between PASS and the defined DAPSA thresholds for disease remission (≤4), low (>4 and ≤14), moderate (>14 and ≤28), and high (>28) disease activity.

Methods: Patients were prospectively recruited from a PsA clinic. A standard protocol including physician assessment and patient-reported outcomes was used to record variables required to calculate PASDAS and DAPSA. In addition, each patient was asked, “Think about all the ways your PsA has affected you during the last 48 hours. If you were to remain in the next few months as you were during the last 48 hours, would this be acceptable to you?” to assess PASS. For analysis, the PASDAS and DAPSA thresholds for PASS were identified using ROC curve analyses to maximize specificity and sensitivity. Furthermore, the agreement between PASS and low, moderate, and high PASDAS disease activity cut-offs; as well as between PASS and disease remission, low, moderate, and high DAPSA disease activity cut-offs were evaluated.

Results: 229 patients [58.5% male, mean age 55.5, mean disease duration 17.2 years] were recruited. 1) The PASDAS threshold for the patient acceptable symptoms state (PASS+) was identified to be 3.79 (AUC: 0.86, sensitivity 0.75, specificity 0.82), and the DAPSA threshold for PASS+ was 13.53 (AUC: 0.85, sensitivity 0.88, specificity 0.72) using ROC curve analyses. 2) When examining the agreement between PASS and PASDAS, 90.3% of patients with low disease activity considered their symptoms state acceptable compared to 55.0% with moderate disease activity and 16.7% with high disease activity. The mean difference in PASDAS between those reporting unacceptable versus acceptable PASS was significantly different (p<0.001), with mean (SD) PASDAS of 4.4 (1.0) and 2.7 (1.1), respectively. 3) With DAPSA, 97.0% of patients in disease remission considered their symptoms state acceptable compared to 89.4% with low, 45.4% with moderate, and 35.7% with high disease activity. The mean difference in DAPSA between those reporting unacceptable vs acceptable PASS was also significantly different (p<0.001), with mean (SD) DAPSA of 25.3 (16.3) and 11.6 (13.2) respectively.

Conclusion:
The PASDAS threshold for patient acceptable symptoms state is 3.79, which is within the moderate disease activity range. Meanwhile, the DAPSA threshold for patient acceptable symptoms state is 13.53, in the low disease activity range. Theses cut-offs should be considered for shared decision making regarding initiating, changing, and/or escalating treatments in PsA patients.
Measuring Psoriasis Specific Impact on Quality of Life: Performance of Dlqi and Skindex-17 in Early Psoriatic Arthritis

Kim Wervers1, Jolanda J. Luime2, Ilja Tchetverikov3, Andreas H. Gerards4, Marc R Kok5, Cathelijne W. Y. Appels6, Wiebo L. van der Graaff7, Johannes H. L. M. van Groenendaal8, Lindy-Anne Korstwagen9, Jozien Veris10, J.M.W. Hazes2 and Marijn Vis2, 1Erasmus Medical Centre, Rotterdam, Netherlands, 2Rheumatology, Erasmus Medical Centre, Rotterdam, Netherlands, 3Albert Schweitzer Hospital, Dordrecht, Netherlands, 4Sint Franciscus Vlietland Group, Schiedam, Netherlands, 5Rheumatology, Maasstad Hospital, Rotterdam, Netherlands, 6Rheumatology, Amphia Hospital, Breda, Netherlands, 7Rheumatology, Rivas hospital, Gorinchem, Netherlands, 8Rheumatology, Reumazorg Zuid West Nederland, Roosendaal, Netherlands, 9Sint Franciscus Vlietland Group, Rotterdam, Netherlands, 10Rheumatology, Reumazorg Zuid West Nederland, Goes, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthopathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Impact of dermatological disease is measured with the Dermatology Life Quality Index (DLQI) and Skindex-17. DLQI is commonly used in dermatology trials but the Skindex-17 has better psychometric properties and less floor effect. We aim to describe health-related quality of life (HRQoL) related to skin involvement using the DLQI and Skindex-17 and to assess impact of replacing DLQI by the Skindex-17 in determining overall PsA disease activity.

Methods: Data collected in the ongoing Dutch south-west Early Psoriatic Arthritis CohoRt (DEPAR) and used for this analysis were Psoriasis Area and Severity Index (PASI), DLQI (range 0-30) and the Skindex-17 (Domains: Psychosocial 0-24 and Symptoms 0-10). Spearman’s correlation was used to calculate correlation between questionnaires and correlation between change in questionnaire-score and change in PASI. The latter was performed within subgroups of psoriasis severity (PASI<7, 7-12 and >12) using change in the first three months after baseline. In the Composite Psoriatic Disease Activity Index (CPDAI), skin involvement is considered not involved, mild, moderate or severe. Using cutoff values of Skindex-17 Symptoms >5 and/or Skindex-17 Psychosocial >9, reclassification of skin assessment was analyzed.

Results: In total 1657 questionnaires of 390 patients were available (mean age 50 years, 51% male). At baseline, median DLQI was 1 (interquartile range, IQR 0-5), Skindex-17 Symptoms 4 (IQR 2-6) and Skindex-17 Psychosocial 2 (IQR 0-8). Correlation between DLQI and Skindex-17 domains was 0.78 (p<0.05). In mild psoriasis (PASI 0-7, n=200), change in PASI had a significant but low correlation with change in HRQoL (Table 1). In moderate psoriasis (PASI 7-12, n=27) the correlation was higher. 269 cases (16%) had CPDAI reclassification, the majority changing from mild with DLQI to moderate with Skindex-17 (n=250, Table 2).

Conclusion: In early PsA with mild/moderate psoriasis, impact of psoriasis is best reflected in the Skindex-17. Using the Skindex-17 in the CPDAI leads to higher rating of skin involvement than using the DLQI. Both suggest a more
subtle impact on HRQoL is missed in the DLQI and the Skindex-17 is preferred in PsA.

| Table 1. Correlations between change in PASI score and change in DLQI/Skindex-17 domains |
|----------------------------------|----------------------------------|----------------------------------|----------------------------------|
| | PASI = 0 (n=41) | PASI >0-7 (n=200) | PASI 7-12 (n=27) | PASI >12 (n=8) |
| Change in DLQI | -0.01 | 0.18* | 0.48* | 0.25 |
| Change in Skinindex17-Symptoms | 0.00 | 0.25* | 0.44* | 0.64 |
| Change in Skinindex17-Psychosocial | 0.17 | 0.17* | 0.64* | 0.08 |

Change between baseline and 3 months assessment. *significant correlation

| Table 2. Classification in skin domain of CPDAI |
|----------------------------------|----------------------------------|----------------------------------|----------------------------------|
| Skin involvement using DLQI | Skin involvement using Skindex-17 | Not involved | Mild | Moderate | Severe |
| Not involved | 450 | 0 | 0 | 0 |
| Mild | 0 | 836 | 250 | 0 |
| Moderate | 0 | 3 | 85 | 16 |
| Severe | 0 | 0 | 0 | 20 |

Not involved (PASI=0); Mild (PASI=10 & Patient-reported outcome, PRO low); Moderate (PASI=10 & PRO high or PASI=10 & PRO low); Severe (PASI>10 & PRO high). PRO low: DLQI=10, Skinindex17-Symptoms=5, Skindex17-Psychosocial =9; PRO high: DLQI>10, Skinindex17-Symptoms>5 or Skindex17-Psychosocial>9

Disclosure: K. Wervers, None; J. J. Luime, None; I. Tchetverikov, None; A. H. Gerards, None; M. R. Kok, None; C. W. Y. Appels, None; W. L. van der Graaff, None; J. H. L. M. van Groenendael, None; L. A. Korswagen, None; J. Veris, None; J. M. W. Hazes, None; M. Vis, None.

Agreement between Paper and Pencil VAS at the Clinic and Electronic VAS at Home in Psoriatic Arthritis and Its Impact on Minimal Disease Activity

**Kim Wervers** ¹, Jolanda J. Luime ², Ilja Tchetverikov ³, Andreas H. Gerards ⁴, Marc R Kok ⁵, Cathelijne W. Y. Appels ⁶, Wiebo L. van der Graaff ⁷, Johannes H. L. M. van Groenendael ⁸, Lindy-Anne Korswagen ⁹, Jozien Veris ¹⁰, J.M.W. Hazes ² and Marijn Vis ², ¹Erasmus Medical Centre, Rotterdam, Netherlands, ²Rheumatology, Erasmus Medical Centre, Rotterdam, Netherlands, ³Albert Schweitzer Hospital, Dordrecht, Netherlands, ⁴Sint Franciscus Vlietland Group, Schiedam, Netherlands, ⁵Rheumatology, Maasstad Hospital, Rotterdam, Netherlands, ⁶Rheumatology, Ampthia Hospital, Breda, Netherlands, ⁷Rheumatology, Rivas hospital, Gorinchem, Netherlands, ⁸Rheumatology, Reumazorg Zuid West Nederland, Roosendaal, Netherlands, ⁹Sint Franciscus Vlietland Group, Rotterdam, Netherlands, ¹⁰Rheumatology, Reumazorg Zuid West Nederland, Goes, Netherlands

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017

Session Title: Spondyloarthopathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities

Session Type: ACR Poster Session C

Session Time: 9:00AM-11:00AM
Background/Purpose: Presence of Minimal Disease Activity (MDA) in Psoriatic Arthritis (PsA) is determined using a patient Visual Analogue Scale (VAS) global PsA activity and VAS pain. Electronic questionnaires for patients to complete at home have great advantages for both patient, researcher and physician, but this implies that physical examination and VAS does not occur simultaneously. We aim to compare a paper VAS at the clinic and electronic VAS at home in psoriatic arthritis and to assess impact of replacing VAS at the clinic by the at-home questionnaires.

Methods: Questionnaires collected in the Dutch south-west Early Psoriatic Arthritis CohoRt (DEPAR) were analyzed. Patients filled out the VAS during their appointment and received a link to the online data-base a week in advance. Patients without an email-address received questionnaires by post. The VAS questionnaire contains a VAS global, VAS joints, VAS psoriasis and VAS pain. Data with both visit- and home VAS present within two weeks of each other were used.

The number of patients without a clinically important difference in the two scores were calculated in two ways: difference of <0.5 SD and <10 mm. Impact on determining disease activity was analyzed using MDA (5/7 equals remission, with VAS criteria VAS-Global ≤20 and VAS-Pain ≤15). Reclassification of being in MDA based on VAS-Visit vs. VAS-Home was analyzed.

Results: In total 839 questionnaires of 221 patients were available for analysis (Table 1). The VAS-Home had significantly higher scores than the VAS-visit, with the biggest difference in the VAS-Global (mean difference 4 mm, 95%CI 3-5, P<0.05). No significant differences were observed between the paper (n=86) and electronic (n=753) groups. In 66%, the two VAS-Global measurements were within 0.5 SD and in 60% within 10 mm. Using the VAS-Global remission criteria of MDA (≤20) resulted in 12% low at visit and high at home and the reverse in 8%. Similar percentages are seen in the VAS-Pain assessment. Using different VAS scores in MDA reclassified 87 assessments (10%): in 54 measurements the patient was in MDA when using VAS-Visit but not when using VAS-Home and the reverse in 33.

Conclusion: In 1 out of 3 measurements replacing paper clinic VAS by electronic at home VAS would result in a difference that reaches clinical importance. Patients report higher scores at home than during a clinical visit, resulting in a lower number of patients reaching MDA and a reclassification of 10%.

Table 1. VAS-Scores
Psoriatic Arthritis Impact of Disease (PSAID12) in Early Psoriatic Arthritis: Pain As One of the Main Determinants of Disease Impact

Kim Wervers1, Jolanda J. Luime2, Ilja Tchetverikov3, Andreas H. Gerards4, Marc R Kok5, Cathelijne W. Y. Appels6, Wiebo L. van der Graaff7, Johannes H. L. M. van Groenendaal8, Lindy-Anne Korswagen9, Jozien Veris10, J.M.W. Hazes2 and Marijn Vis2, 1Erasmus Medical Centre, Rotterdam, Netherlands, 2Rheumatology, Erasmus Medical Centre, Rotterdam, Netherlands, 3Albert Schweitzer Hospital, Dordrecht, Netherlands, 4Sint Franciscus Vlietland Group, Schiedam, Netherlands, 5Rheumatology, Maasstad Hospital, Rotterdam, Netherlands, 6Rheumatology, Amphia Hospital, Breda, Netherlands, 7Rheumatology, Rivas hospital, Gorinchem, Netherlands, 8Rheumatology, Reumazorg Zuid West Nederland, Roosendaal, Netherlands, 9Sint Franciscus Vlietland Group, Rotterdam, Netherlands, 10Rheumatology, Reumazorg Zuid West Nederland, Goes, Netherlands

First publication: September 18, 2017
Background/Purpose: The Psoriatic Arthritis Impact of Disease 12-item questionnaire (PsAID12) has been developed to measure impact of Psoriatic Arthritis (PsA) for purposes of monitoring and clinical management. We aim to investigate the relation between change in disease activity and change in PsAID, and which domains of the PsAID are main drivers of change in score.

Methods: Newly diagnosed PsA patients were included in the Dutch southwest Early Psoriatic Arthritis cohort (DEPAR). For this analysis, patients that have answered the PsAID12 (range 0-10) at two consecutive visits (i.e. 3 months apart) within the first year were included. In case longer periods per patients were available, data from the first period of three months was used. The change in PsAID was compared to the change in disease activity over this period, measured with the Composite Psoriatic Disease Activity Index (CPDAI) using Spearman’s correlation. Change in score on PsAID domains was analyzed in subgroups of patients that perceived improvement in health and those that perceived worsening. The Short Form-36 question on self-perceived change in health was used to determine these subgroups.

Results: 143 unique patients had at least one period with two PsAID and CPDAI measurements (Table 1). Mean age was 51 (SD 13.7) and 70 (49%) were male. The difference in PsAID score was significantly but moderately correlated with the difference in CPDAI (Spearman’s rho 0.267, P=0.0013). 58 patients (41%) reported a better health status compared to 3 months ago and 29 worsening of health status. Figure 1 shows that improved patients had higher scores in almost all domains, with the biggest improvement in pain. Domains of skin problems and embarrassment/shame did not improve significantly. Worsened patients only had significantly lower scores in fatigue, discomfort and social domains.

Conclusion: Improvement in CPDAI disease activity was significantly but moderately associated with improvement in PsAID score. This reflects that the PsAID partially measures disease activity, but measures other constructs of disease as well. In early PsA, a state of improved health is reflected in the PsAID in almost all domains, with the strongest effect in pain.

<table>
<thead>
<tr>
<th></th>
<th>First score</th>
<th>Second score (+3 months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total CPDAI</td>
<td>4 (2, 7)</td>
<td>3 (1, 5)*</td>
</tr>
<tr>
<td>Total PsAID</td>
<td>3.35 (1.4, 5.1)</td>
<td>2.25 (0.85, 4.8)*</td>
</tr>
<tr>
<td>Pain</td>
<td>5 (2, 7)</td>
<td>3 (1, 6)*</td>
</tr>
<tr>
<td>Fatigue</td>
<td>4 (1, 7)</td>
<td>3 (1, 7)</td>
</tr>
<tr>
<td>Skin Problems</td>
<td>2 (0, 5)</td>
<td>2 (0, 4)*</td>
</tr>
<tr>
<td>Work/Leisure</td>
<td>3 (0, 6)</td>
<td>2 (0, 5)*</td>
</tr>
<tr>
<td>Function</td>
<td>3 (1, 8)</td>
<td>2 (0, 5)*</td>
</tr>
<tr>
<td>Discomfort</td>
<td>4 (1, 6)</td>
<td>2 (1, 5)*</td>
</tr>
<tr>
<td>Sleep</td>
<td>3 (0, 7)</td>
<td>1 (0, 5)*</td>
</tr>
<tr>
<td>Coping</td>
<td>2 (0, 5)</td>
<td>1 (0, 5)*</td>
</tr>
<tr>
<td>Anxiety</td>
<td>2 (0, 5)</td>
<td>1 (0, 4)*</td>
</tr>
<tr>
<td>Embarrassment/Shame</td>
<td>0 (0-1)</td>
<td>0 (0-1)</td>
</tr>
<tr>
<td>Social Participation</td>
<td>1 (0.4)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Depression</td>
<td>0 (0, 3)</td>
<td>0 (0, 2)</td>
</tr>
</tbody>
</table>

N=143, data shown as median (IQR). *P<0.05, significant change in three months
Can Achieving Sustained Minimal Disease Activity (MDA) Prevent Progression of Subclinical Atherosclerosis? a Two-Year Prospective Cohort Study in Psoriatic Arthritis

Lydia Ho Pui Tam¹, Tsz Ho CHENG¹, Qing SHANG², Edmund Li³, Priscilla WONG³, Tracy Y. ZHU⁴, M Mimi CHANG⁵, JW Jack LEE⁶, Chun-Kwok WONG⁷, PW Alex LEE¹ and Lai-Shan Tam², ¹Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong, Hong Kong, ²Department of Medicine & Therapeutics, The Chinese University of Hong Kong, Hong Kong, Hong Kong, ³Department of Medicine & Therapeutics, The Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong, Hong Kong, ⁴Bone Quality and Health Center of the Department of Orthopedics & Traumatology, The Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong, Hong Kong, ⁵Department of Medicine & Therapeutics, Prince of Wales Hospital, Hong Kong, Hong Kong, ⁶Biostatistics Division, School of Public and Primary Care, The Chinese University of Hong Kong, Hong Kong, Hong Kong, ⁷Department of Chemical Pathology, The Chinese University of Hong Kong, Hong Kong, Hong Kong

First publication: September 18, 2017
Background/Purpose:

PsA patients have higher cardiovascular disease risk due to underlying inflammation. While achieving MDA was associated with articular benefits, its effect on CVD risk remained uncertain. This study aimed to investigate the effect of achieving sustained MDA (sMDA) on subclinical atherosclerosis.

Methods:

100 consecutive PsA patients without overt CVD were followed for 2 years with clinical assessment every 4 months. Protocolized treatment aiming at MDA were given. sMDA was defined as achieving MDA over 1 year. Carotid IMT at bilateral distal, bulb and proximal internal carotid artery were evaluated annually using high-resolution ultrasound. Carotid plaque progression was defined as increased number of plaque since baseline.

Results:

54 PsA patients [male:29 (53.7%); 50 +/- 12 years] who completed 24-months follow-up were included in this analysis. After 2-year intensive treatment, significantly more patient could achieve MDA [9 (16.7%) at baseline, 35 (64.8%) at 2 years, \( p<0.001 \)]. 23/54 (43%) patients achieved sustained MDA. Baseline characteristics were comparable between subjects who could or couldn’t achieve sMDA. Numeric differences were observed in change in mean IMT between sMDA and non-sMDA group [-0.03mm +/- 0.9 vs +0.01mm +/- 0.08, \( p=0.061 \)]. In multivariate analysis, sMDA was associated with less progression of mean IMT \([\text{EO}=0.045, 95\% CI:-0.082 \text{ to } -0.009, \ p=0.017\] after adjusting age, gender, disease duration, baseline CRP, PASI, dyslipidemia, NSAIDs use, and bDMARDs use throughout the year. 28/54 (52%) patient had plaque progression. The prevalence of plaque progression was numerically higher in non-sMDA group [19 (61%) vs 9 (39%), \( p=0.107 \)]. In multivariate analysis, there was a trend suggesting achievement of sMDA might have protective effect on plaque progression \([\text{OR}=0.2, 95\% CI: 0.036 \text{ to } 1.112, \ p=0.066\]).

Conclusion:

Effective suppression of inflammation by achieving sustained MDA may prevent progression of subclinical atherosclerosis in PsA patients.

Funding: We would like to acknowledge the Health and Medical Research Fund (HMRF) for funding support (HMRF Project No. 01120496)

Figures - Change in IMT and plaque progression in subjects with and without achieving sustained MDA
Disclosure: L. H. P. Tam, None; T. H. CHENG, None; Q. SHANG, None; E. Li, None; P. WONG, None; T. Y. ZHU, None; M. M. CHANG, None; J. J. LEE, None; C. K. WONG, None; P. A. LEE, None; L. S. Tam, None.


Abstract Number: 2546
Secukinumab Decreases Arterial Wall Inflammation in Patients with Peripheral Spondyloarthritis

Leonieke van Mens1, Simone Verweij2, Arno van Kuijk3, Erik Stroes2 and Dominique Baeten1, 1AMC, Amsterdam Immunology and Rheumatology Center, Amsterdam, Netherlands, 2Vascular Medicine, Academisch Medisch Centrum, Amsterdam, Netherlands, 3Reade, Amsterdam Immunology and Rheumatology Center, Amsterdam, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Patients with spondyloarthritis (SpA), a chronic inflammatory disease, have an increased cardiovascular risk, which is partly due to increased inflammatory activity in the arterial wall. IL-17A blockade with secukinumab is an effective treatment for SpA. The role of IL-17A in atherogenesis is controversial, some studies suggest that IL-17A is pro-atherogenic, while others indicate that IL-17A is athero-protective. The effect of secukinumab on arterial wall inflammation is unknown. Therefore, we assessed the effect of 3 months treatment with secukinumab on arterial wall inflammation in SpA patients. To assess the effect of 3 months treatment with secukinumab on arterial wall inflammation in SpA patients with peripheral disease (pSpA).

Methods: 20 SpA patients with peripheral disease (pSpA) were treated in a 12 week open-label trial. Treatment consisted of 300 mg secukinumab once a week during the first 4 weeks and then every 4 weeks thereafter. EULAR DAS response was used to define a responder/non responder state. To measure arterial wall inflammation we performed 18-fluorodeoxyglucose positron emission tomography with computed tomography (18F-FDG PET/CT) imaging in 18 patients at baseline and at week 12.

Results: Sufficient quality scans were available for analysis in 16 patients (age 44±12, 72% male, no previous cardiovascular events). Overall, three months treatment with secukinumab resulted in a significant improvement of disease activity, with 15 patients achieving a EULAR DAS response (9 good and 6 moderate responders). Correspondingly, CRP levels decreased significantly (baseline: 3.2[1.2–12.40] mg/dl vs. wk 12: 2.0[1.1-5.8] mg/dl, p=0.011). Treatment with secukinumab did not affect cholesterol levels (LDL-c from 3.2±0.8 mmol/l to 3.5±0.9 mmol/l, p=0.219). Arterial wall inflammation as measured by PET-CT did not change over the course of the 12 weeks treatment with secukinumab (carotid TBRmax baseline: 1.88±0.6 vs. wk 12: 1.76±0.4, p=0.067). Patients with a good response on secukinumab (n=9) showed a high TBR at baseline with a significant decrease of arterial wall inflammation, while there was a lower TBR in the patients with a moderate (n=6) or poor (n=1) response on secukinumab and there was no effect on arterial wall inflammation in these patients.

Conclusion: This pilot study in 16 patients with pSpA shows a successful clinical response upon secukinumab treatment for three months, with no change in arterial wall inflammation on group level. Sub analysis shows us a significant decrease of arterial wall inflammation in patients with a high TBR at baseline. Further research in larger patient groups, over a longer period of treatment remains warranted to fully elucidate the effect of secukinumab on vascular inflammation.

Disclosure: L. van Mens, None; S. Verweij, None; A. van Kuijk, UCB, Pfizer, MSD, Janssen, 2,Novartis, Celgene, 5; E. Stroes, None; D. Baeten, UCB, 3.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/secukinumab-decreases-arterial-wall-inflammation-in-patients-with-peripheral-spondyloarthritis
the Ideal Target for Psoriatic Arthritis? Comparison of Remission and Low Disease Activity States in a Real Life Cohort

Leonieke van Mens¹, Arno van Kuijk², Dominique Baeten¹ and Laura C Coates³, ¹AMC, Amsterdam Immunology and Rheumatology Center, Amsterdam, Netherlands, ²Reade, Amsterdam Immunology and Rheumatology Center, Amsterdam, Netherlands, ³LIRMM, University of Leeds, Leeds, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Recommendations on psoriatic arthritis (PsA) state that the target of treatment should be remission or inactive disease with an alternative target of minimal or low disease activity (LDA). Multiple potential targets have been developed, each with a different composition of clinical measurements. Our aim is to use an existing real life dataset of a large group of patients in a low disease activity state, to compare different targets for LDA and provide further evidence to choose a target.

Methods: 250 PsA patients considered in an acceptable disease state according to their rheumatologist were included. Targets for remission were the DAPSA and cDAPSA remission (≤4), VLDA and PASDAS ≤ 1.9 (NR). LDA targets analyzed were the DAPSA LDA ≤14, clinical cDAPSA≤13, MDA, adjusted MDA targets: MDAjoints with both TJC and SJC cut-offs mandated, MDAskin where PASI was mandated, MDAjoint&skin where the TJC, SJC and PASI cut-offs mandated.

Results: Of the remission targets, DAPSA/cDAPSA and VLDA show the highest agreement (kappa of 0.516 and 0.544 resp.). The agreement between PASDAS NR and DAPSA/cDAPSA/VLDA was lower, (kappa of 0.403, 0.321, 0.319 resp). PASDAS NR was more stringent than DAPSA/cDAPSA remission. All patients who met VLDA were in DAPSA/cDAPSA remission.

Of the LDA targets, the highest agreement is seen between the DAPSA/cDAPSA and the MDA5/7 (kappa of 0.596 and 0.611 respectively). Agreement between the DAPSA and the alternative MDA measures (MDA joints, MDA skin and MDA joints and skin) is lower as these targets are more stringent (0.356, 0.372, 0.227 resp.).

Comparison of the several candidate measures demonstrates that VLDA is achieved by the lowest proportion of patients and includes patients with the lowest residual disease activity compared with the other remission measures. The modified MDA measures are the most stringent targets for low disease activity in terms of residual disease on joints, psoriasis and enthesis within patients achieving the target. (see graph) In both remission and LDA measures the inclusion of CRP did not show an added value. A PASI>1 was more prevalent in (c)DAPSA in comparison with the 4 MDA measures. Patients with active psoriasis in the DAPSA group report significantly larger impact of skin disease on dermatology related quality of life (DLQI) (DLQI 0-1: 1,25(SD2,4) v.s. DLQI >1: 1,55(2,7).

Conclusion: The different remission and low disease activity targets show that despite significant overlap between the measures, measures targeting the same definition do differ from one another in terms of allowance of residual disease present within the patients. Inclusion of laboratory markers seems unnecessary although exclusion of a skin domain might result in negligence of skin disease in some patients despite a QoL impact.
Disclosure: L. van Mens, None; A. van Kuijk, UCB, Pfizer, MSD, Janssen, 2,Novartis, Celgene, 5; D. Baeten, UCB, 3; L. C. Coates, None.


Abstract Number: 2548

Validation of New Potential Targets for Remission and Low Disease Activity in Psoriatic Arthritis in Patients Treated with Golimumab

Laura C Coates1, Proton Rahman2, Eliofotisti Psaradellis3, Emmanouil Rampakakis3, Brendan Osborne4, Allen J Lehman5 and Francois Nantel4, 1LIRMM, University of Leeds, Leeds, United Kingdom, 2Rheumatology, St Claires
Background/Purpose: Treat to target recommendations in PsA state that the target of treatment should be remission or low disease activity (LDA). So far, the only validated target available was the minimal disease activity (MDA) criteria. Other potential targets have been developed including very low disease activity (VLDA) and the Disease Activity in PsA (DAPSA) score remission. Potential targets for LDA include DAPSA and clinical (cDAPSA) or the minimal disease activity (MDA) criteria for which modifications have been suggested to mandate individual components.

Using an existing real World cohort, the objectives were to calculate the proportion of patients achieving these criteria, their prognostic value and the overall patient impact of these disease states.

Methods: BioTRAC is an ongoing, prospective registry of inflammatory arthritis patients initiating treatment with infliximab, golimumab (GLM) or ustekinumab. PsA patients treated with GLM were included. Data collected at baseline, 6 and 12 months were used. The definition for MDA, remission and LDA outcomes are described in Table 1.

Results: A total of 188 patients (53% female) were included with a mean (SD) disease duration of 5.5 years. The proportion of patients achieving MDA, remission and LDA at baseline, 6 and 12 months is shown in Figure 1. 75% and 53.3% of patients in DAPSA and cDAPSA remission, respectively, also achieved VLDA (p<0.001). Patients who did not achieve cDAPSA nor DAPSA never achieved VLDA. Higher HAQ scores (p<0.03) were observed in patients achieving remission with remaining dactylitis or active skin disease (BSA≤10%; cDAPSA only). The proportions of patients achieving MDA also achieving MDA Joints, MDA Skin, MDA Joints & Skin and DAPSA LDA were 83.8%, 86.9%, 70.7% and 98.7%, respectively. Patients achieving any MDA target had significantly lower SJC, TJC, PASI, dactylitis and enthesitis scores compared to non-achievers (p<0.006). Patients achieving DAPSA or cDAPSA LDA showed significant reductions in SJC, TJC, PASI, dactylitis and enthesitis scores compared to non-achievers (p<0.05).

Conclusion: VLDA is the most stringent new potential targets for remission in PsA. There was a high level of correlation between scores although residual activity in dactylitis and skin despite DAPSA remission has some impact on patients’ function. MDA Joints, MDA Skin, MDA Joints & Skin, DAPSA LDA and cDAPSA LDA represent new potential targets for LDA in PsA. Patients achieving either DAPSA endpoints, however, did not show a significant reduction in skin disease indicating that those two endpoints are more restricted to joint symptoms.
<table>
<thead>
<tr>
<th>Target</th>
<th>Outcome</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDA</td>
<td>MDA</td>
<td>5/7 of TJC28≤1, SJC28≤1, PASI≤1, Pain (VAS) ≤15mm, PtGA (VAS ) ≤20mm, HAQ ≤0.5, tender enthesal points ≤1</td>
</tr>
<tr>
<td>Remission</td>
<td>VLDA</td>
<td>All 7/7 MDA criteria</td>
</tr>
<tr>
<td></td>
<td>DAPSA Remission</td>
<td>TJC + SJC + PtGA + Pain + CRP ≤4</td>
</tr>
<tr>
<td></td>
<td>cDAPSA Remission</td>
<td>TJC + SJC + PtGA + Pain ≤4</td>
</tr>
<tr>
<td>LDA</td>
<td>DAPSA LDA</td>
<td>TJC+SJC+PtGA+Pain+CRP ≤14</td>
</tr>
<tr>
<td></td>
<td>cDAPPSA LDA</td>
<td>TJC+SJC+PtGA+Pain ≤13</td>
</tr>
<tr>
<td></td>
<td>MDA Joint</td>
<td>TJC and SJC cut-offs mandated. 3/5 remaining MDA criteria</td>
</tr>
<tr>
<td></td>
<td>MDA Skin</td>
<td>PASI cut-off mandated. 4/6 remaining MDA criteria</td>
</tr>
<tr>
<td></td>
<td>MDA Joint &amp; Skin</td>
<td>TJC, SJC and PASI cut-offs mandated. 2/4 remaining MDA criteria</td>
</tr>
</tbody>
</table>


Abstract Number: 2549

Achievement of Minimal Disease Activity Is Associated with Improvements in Health-Related Quality of Life and Productivity in Psoriatic Arthritis Patients

Laura C Coates¹, Ana-Maria Orbai², Julie Birt³, Lisa Kerr³, Olivier Benichou⁴ and Philip S. Helliwell⁴, ¹University of Oxford, Leeds, Great Britain, ²Johns Hopkins University School of Medicine, Baltimore, MD, ³Eli Lilly and Company, Indianapolis, IN, ⁴School of Medicine, University of Leeds, Leeds, United Kingdom

First publication: September 18, 2017
SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Treatment goals in psoriatic arthritis (PsA) are moving toward attainment of absolute therapeutic thresholds rather than relative improvement. Minimal disease activity (MDA), a composite endpoint of up to 7 individual measures, has been recommended as an appropriate aim in PsA.

Methods: Data were analyzed from an integrated database of 2 double-blind, phase III SPIRIT trials investigating the efficacy and safety of ixekizumab (IXE), a high-affinity monoclonal antibody selectively targeting interleukin-17A, for patients with active PsA. The integrated database consisted of patients who were biologic DMARD naive (SPIRIT-P1, NCT01695239) or who had an inadequate response or were intolerant to TNF inhibitors (SPIRIT-P2; NCT02349295). Patients were randomized to placebo (n = 224) or 80 mg IXE every 4 weeks (IXEQ4W, n = 229) or every 2 weeks (IXEQ2W, n = 226) after a 160 mg starting dose. Health-related quality of life (HRQoL) and productivity were evaluated using the 36-Item Short Form Health Survey (SF-36; higher scores indicate better functioning), European Quality of Life 5 Dimension 5 Level Health Questionnaire (EQ-5D-5L; higher values indicate better health utility), EQ-5D visual analog scale (EQ-5D VAS; 0-100 scale; higher scores indicate better health), and Work Productivity and Activity Impairment—Specific Health Problem (WPAI-SHP; higher scores indicate higher impairment). MDA was achieved if 5 of 7 criteria were met: tender joint count ≤1; swollen joint count ≤1; Psoriasis Area and Severity Index total score ≤1 or body surface area ≤3%; patient’s assessment of pain VAS ≤15; patient’s global assessment of disease activity VAS ≤20; Health Assessment Questionnaire Disability Index ≤0.5; and tender entheseal points ≤1 (assessed by the Leeds Enthesitis Index).

Results: At Week 24, 474 of 679 patients had nonmissing MDA and HRQoL data. At Week 24, MDA responders had significantly improved SF-36 Physical Component Scores (PCS), EQ-5D-5L index values, and EQ-5D VAS scores but similar SF-36 Mental Component Scores (MCS) relative to MDA nonresponders (Table 1). MDA responders also had a significantly improved percentage of presenteeism, overall work impairment, and percentage of activity impairment on the WPAI-SHP relative to MDA nonresponders at Week 24 (Table 1). MDA responders were more likely to achieve the minimal clinically important difference on the SF-36 PCS, EQ-5D-5L index score, and EQ-5D VAS score but not the SF-36 MCS (Table 2).

Conclusion: Achievement of MDA is associated with improvement of patient-reported HRQoL and productivity.

<table>
<thead>
<tr>
<th>Table 1. Mean (SD) Change from Baseline at Week 24 by MDA Responder Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDA Nonresponder (n = 322)</td>
</tr>
<tr>
<td>SF-36, Physical Component Summary</td>
</tr>
<tr>
<td>SF-36, Mental Component Summary</td>
</tr>
<tr>
<td>EQ-5D-5L Health State Index</td>
</tr>
<tr>
<td>EQ-5D VAS</td>
</tr>
<tr>
<td>WPAI-SHP: Percentage of absenceism</td>
</tr>
<tr>
<td>Percentage of presenteeism</td>
</tr>
<tr>
<td>Overall work impairment</td>
</tr>
<tr>
<td>Percentage of activity impairment outside work</td>
</tr>
</tbody>
</table>

Abbreviations: EQ-5D-5L, European Quality of Life 5 Dimension 5 Level Health Questionnaire; MDA, minimal disease activity; SF-36, 36-Item Short Form Health Survey; VAS, visual analog scale; WPAI-SHP, Work Productivity and Activity Impairment—Specific Health Problem.

*P-values based on one-way analysis of variance (change from baseline = MDA responder status) using observed data. Missing data were excluded.

\*: n = 142; †: n = 84; *: n = 134; #: n = 62; †: n = 321
A New and Simpler Tool for Global Psoriatic Arthritis Assessment: Simplified Composite Psoriatic Disease Activity Index (sCPDAI)

Maria Laura Acosta Felquer, Musaab Elmamoun, Agnes Szentpetery, Phil Gallagher, Oliver FitzGerald and Enrique R. Soriano, Instituto Universitario Hospital Italiano de Buenos Aires, Argentina. 

First publication: September 18, 2017
with PsA. The Composite Psoriatic Disease Activity Index (CPDAI) is one of the more comprehensive, taking into account the assessment of five different domains. One of the problems with CPDAI is its complexity and the large number of instruments that need to be applied for a full assessment.

The aim of this study was to evaluate the performance of a simplified CPDAI (sCPDAI) in a large group of PsA patients.

**Methods:** We evaluated consecutive PsA patients included in the MOPSA database. Measuring Outcome in Psoriatic Arthritis (MOPsA) is a new web-based tool which calculates both MDA and CPDAI based on patient reported outcomes and assessment by physicians. Data collected included: joint counts, patient pain and global activity ratings, HAQ, PASI, BASDAI, DLQI, PsAqol. Clinical DAPSA (Disease Activity for Psoriatic Arthritis), MDA (Minimal Disease Activity) and CDAI (Clinical Disease Activity Index) were also calculated. Pearson’s correlations between CPDAIs and different measures of disease activity were calculated. CPDAI values between patients fulfilling and not fulfilling MDA were compared using Mann-Whitney U test. The area under the ROC curve (AUC) was calculated to quantify the discriminative performance for MDA.

**Results:** 214 PsA patients, fulfilling CASPAR criteria, with mean age of 49 years (SD: 12), and 111 (52%) females, were included. Seventy-six (35.5%) patients were in MDA. Median (IQR) CDAI, cDAPSA, CPDAI, and PASI were 7 (4-16), 10 (5-18), 3 (2-5), and 0.8 (0-3), respectively. Table 1 shows the variables used to construct sCPDAI, and table 2 shows sCPDAI correlation with different variables. Patients in MDA had significantly lower sCPDAI than patients not in MDA (mean (SD) 1.7 (1.4) vs 5.3 (2.8); p<0.0001). The sCPDAI AUC of the ROC curve for MDA was 0.87 (95% CI: 0.83-0.92), with 4 as the best cut off value to discriminate among patients not in MDA status (sensitivity: 68.42%; specificity: 87.67%; +LR: 5.55, -LR: 0.36).

**Table 1:** Simplified CPDAI variables

<table>
<thead>
<tr>
<th></th>
<th>Not Involved (0)</th>
<th>Mild (1)</th>
<th>Moderate (2)</th>
<th>Severe (3)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Peripheral arthritis</strong></td>
<td>Not involved</td>
<td>≤ 4 joints (TJC or SJC) &amp; HAQ ≤ 0.5</td>
<td>≤ 4 joints (TJC or SJC) &amp; HAQ &gt; 0.5 OR &gt;4 joints (TJC or SJC) &amp; HAQ &lt;0.5</td>
<td>&gt; 4 Joints (TJC or SJC) &amp; HAQ &gt; 0.5</td>
</tr>
<tr>
<td><strong>Skin disease</strong></td>
<td>Not involved</td>
<td>BSA ≤3</td>
<td>BSA &gt; 3 ≤30</td>
<td>BSA &gt;30</td>
</tr>
<tr>
<td><strong>Enthesitis</strong></td>
<td>Not involved</td>
<td>≤ 3 sites &amp; HAQ &lt; 0.5</td>
<td>≤ 3 sites &amp; HAQ &gt; 0.5 OR &gt;3 sites &amp; HAQ &lt; 0.5</td>
<td>&gt;3 sitios &amp; HAQ &gt; 0.5</td>
</tr>
<tr>
<td><strong>Dactylitis</strong></td>
<td>Not involved</td>
<td>≤ 3 digits &amp; HAQ &lt; 0.5</td>
<td>≤ 3 digits &amp; HAQ &gt; 0.5 OR &gt;3 digits &amp; HAQ &lt; 0.5</td>
<td>&gt;3 digits &amp; HAQ &gt; 0.5</td>
</tr>
<tr>
<td><strong>Spinal Disease</strong></td>
<td>Not involved</td>
<td>BASDAI &lt; 4 &amp; HAQ &lt; 0.5</td>
<td>BASDAI &lt; 4 &amp; HAQ &gt; 0.5 BASDAI &gt; 4 &amp; HAQ &lt;0.5</td>
<td>BASDAI &gt;4 &amp; HAQ &gt; 0.5</td>
</tr>
</tbody>
</table>

**Table 2:** Spearman correlation between sCPDAI and different outcome measures.
Conclusion: A simplified CPDAI, that includes only HAQ and BASDAI over usual daily clinical practice assessment, showed very good correlation with most outcome measurements used in PsA, and a very good discriminatory power for patients not in remission by MDA.

Disclosure: M. L. Acosta Felquer, None; M. Elmamoun, None; A. Szentpetery, None; P. Gallagher, None; O. FitzGerald, AbbVie, Bristol-Myers Squibb, Novartis, Pfizer Inc, 2,Amgen, Celgene, Eli Lilly, Janssen, 5; E. R. Soriano, Abbvie, BMS, Novartis, Janssen, Pfizer, Roche, UCB, 2,Abbvie, BMS, Novartis, Janssen, Pfizer, Roche, UCB, 5,Abbvie, BMS, Novartis, Janssen, Pfizer, Roche, UCB, 8.


Abstract Number: 2551

Comparison between Two Cut-Off Values of Disease Activity in Psoriatic Arthritis Index and Validation of Its Simplified Clinical Version in Patients with Psoriatic Arthritis

Osvaldo Luis Cerda1, Emilce E Schneeberger1, Cecilia Zaffarana1, Andrea Lujan Coronel Ale1, Marina Natalia Fornaro2, Margarita Landi1, Marcos Rosemffet1, Fernando Dal Pra1, Javier Rosa3 and Gustavo Citera4, 1Section of Rheumatology, Instituto de Rehabilitación Psicofísica, Buenos Aires, Argentina, Buenos Aires, Argentina, 2Section of Rheumatology, Instituto de Rehabilitación Psicofísica, Buenos Aires, Argentina, buenos aires, Argentina, 3Rheumatology Unit, Internal Medicine Service, Hospital Italiano de Buenos Aires, CABA, Argentina, 4Section of Rheumatology, Instituto de Rehabilitación Psicofísica, Buenos Aires, Argentina, Buenos Aires, Argentina

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
**Background/Purpose:** Two groups established cut-off values for Disease Activity Index for Psoriatic Arthritis (DAPSA)\(^1\). The clinical DAPSA (cDAPSA) excludes CRP from its calculation and the authors recommend the use of the same cut-off values as DAPSA. To evaluate the concordance between the two cut-off values established for DAPSA and to validate cDAPSA and develop its cut-off values. **Methods:** Patients \(^3\) 18 years of age with Psoriatic Arthritis (PsA) according to CASPAR criteria belonging to RAPSODIA cohort were included. We recorded clinical data. DAPSA and cDAPSA were calculated. Patients were classified according to both cut-off values. Those patients who showed disagreement in the classification between both cut-off values were re-evaluated by the opinion of four rheumatologists with experience in the evaluation of PsA patients. **Results:** 119 patients were included, 62 males (52.1%), median age 54 years old (IQR 42-63), median disease duration 8 years (IQR 3-15). 49.6% of patients had pure peripheral involvement and 48.7% had mixed involvement. Median value for DAPSA was 12 (IQR 7-19) and for cDAPSA was 13 (IQR 7-19). Correlation between both DAPSA versions was very good Rho=0.85. Table 1 shows the classification of patients according to our cut-off values and those proposed by Schoels et al. A high agreement between cut-off values of both versions was observed K: 0.85 (p= 0.0001). Only 7 patients were discordant, and according to experts' opinion, the performance of Schoels' DAPSA cut-off values was better. A lower agreement was observed between DAPSA and clinical DAPSA K: 0.79 (p = 0.0001), with 10 discordant patients. For this reason, we established new cut-off values for cDAPSA: Remission< 2.5, low disease activity 2.5 to < 11.5 (AUC: 0.94, Se: 92.6% and Sp: 100%), moderate disease activity >11.5 to < 23 (AUC: 0.99, Se: 100% and Sp: 96.3%) and high disease activity > 23 (AUC: 0.99, Se: 100% and Sp: 95.5%). These cut-off values showed a better balance in sensitivity and specificity than those previously proposed. **Conclusion:** The concordance between the two cut-off values of DAPSA was good, although Schoels' DAPSA cut-off values showed better discrimination according to expert opinion. The cut-off values for cDAPSA should be reviewed for better sensitivity and specificity.


**Table 1.**

<table>
<thead>
<tr>
<th>Index</th>
<th>Remission</th>
<th>Low Disease Activity</th>
<th>Moderate Disease Activity</th>
<th>High Disease Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAPSA-IREP n (%)</td>
<td>8 (11.8)</td>
<td>27 (39.7)</td>
<td>22 (32.4)</td>
<td>11 (16.2)</td>
</tr>
<tr>
<td>DAPSA-Schoels n (%)</td>
<td>11 (16.2)</td>
<td>25 (36.8)</td>
<td>24 (35.3)</td>
<td>8 (11.8)</td>
</tr>
<tr>
<td>Discordant patients n</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>

**Disclosure:** O. L. Cerda, None; E. E. Schneeberger, None; C. Zaffarana, None; A. L. Coronel Ale, None; M. N. Fornaro, None; M. Landi, None; M. Rosemffet, None; F. Dal Pra, None; J. Rosa, None; G. Citera, Novartis, Pfizer Inc, 2,AbbVie, Bristol-Myers Squibb, Janssen, Novartis, Pfizer Inc, 5.


**Abstract Number:** 2552
Inter-Connections between Fatigue, Pain and Patient Global Assessment in Patients with Active Spondyloarthritis Followed in the Daily Clinic

Ole Rintek Madsen, Center for Rheumatology and Spine Diseases & The DANBIO Registry, Copenhagen University Hospital Rigshospitalet Gentofte and Glostrup, Denmark, Hellerup, Denmark

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The Assessment of SpondyloArthritis international Society (ASAS) has selected fatigue, pain and patient global assessment (PaGl) as key patient-reported outcome measures in clinical trials and clinical practice. However, although associations between fatigue, pain and PaGl have been examined to some extent on the group level, studies focusing on the agreement between these patient-reported measures in individual patients are missing. A better understanding of how tight the measures are bounded in individuals may improve our ability to deal with them in the daily clinic. The purpose of the study was to examine associations on the group level and agreements on the individual patient level between fatigue, pain and PaGl as scored on visual analogue scales (VAS) in the daily clinic by patients with active spondyloarthritis (SpA).

Methods: Data on 118 SpA patients with active disease planned to initiate treatment with a biological agent were extracted from the Danish registry for biological treatment in rheumatology (DANBIO). Data included fatigue, pain, PaGl, BASDAI, BASFI and physician global assessment assessed on VAS-scales (0-100) and age and CRP. Associations between variables were examined using simple and multiple regression analysis (all mentioned variables including sex was incorporated as independent variables). Agreements between fatigue, pain and PaGl on the individual patient level were examined by Bland-Altman analyses yielding 95% lower and upper limits of agreement (LLoA and ULoA) between intra-individual assessments. The difference between the scores on the group level was expressed as the bias.

Results: Mean age was 42.9±12.6 years, mean BASDAI 56.0±19.0, mean CRP 12.9 mg/l and mean PaGl 65.7±22.6. Significant differences in BASDAI, fatigue, pain, PaGl between men (n= 76) and women were not demonstrated. Fatigue, pain and PaGl were significantly but only moderately inter-correlated with high standard errors of estimation (SEE): Fatigue vs. PaGl (r = 0.57, p < 0.0001, SEE = 21.4), fatigue vs. pain (r = 0.55, p < 0.0001, SEE = 21.6), and pain vs. PaGl (r = 0.81, p < 0.0001, SEE = 15.1). In multiple regression analyses, pain was independently predicted by PaGl (beta = 0.52, p < 0.0001) and BASDAI (beta = 0.36, p < 0.0001) [R = 0.82, SEE = 14.1, p < 0.0001], PaGl by pain (beta = 0.54, p < 0.0001) and BASDAI (beta = 0.33, p < 0.001) [R = 0.81, SEE = 12.7, p < 0.0001], and fatigue by BASDAI (beta = 0.44, p < 0.0001) and PaGl (beta = 0.23, p < 0.05) [R = 0.63, SEE = 20.2, p< 0.0001]. Biases between the patient-reported VAS-scores were small but intra-individual differences were substantial: LLoA and ULoA [bias] for fatigue vs. PaGl were -45.5 and 43.5 [-0.97], for fatigue vs. pain -42.3 and 52.9 [5.3], and for pain vs. PaGl -35.7 and 23.3 [-6.3]. LLoA and ULoA remained constant over the whole range of the VAS-scales.

Conclusion: In patients with SpA, fatigue, pain and PaGl scores were poorly associated and only poorly explained by other potential explanatory variables. On the individual level, disagreements between the scores were substantial. The findings emphasize the complexity of understanding patient-reported outcome measures and their diverging interplay across individuals.

Disclosure: O. Rintek Madsen, None;

Patient and Physician Global Assessment Are Poorly Inter-Connected and Poorly Explained By Other Clinical Markers of Disease Activity in Individual Patients with Psoriatic Arthritis

Ole Rintek Madsen, Center for Rheumatology and Spine Diseases & The DANBIO Registry, Copenhagen University Hospital Rigshospitalet Gentofte and Glostrup, Denmark, Hellerup, Denmark

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Assessment of disease activity is important in the evaluation and monitoring of patients with psoriatic arthritis (PsA) in clinical care and research. As there is no single ‘gold standard’ variable for assessment of disease activity several markers of disease activity are used, among these “global assessment” by the patient (PaGl) and by the physician (PhGl). The agreement and interplay between PaGl and PhGl are not well clarified in patients with PsA, however. The objective of the study was to examine associations on the group level and agreements on the individual patient level between PaGl and PhGl as scored on visual analogue scales (VAS) in the daily clinic by patients with active PsA and by their rheumatologists.

Methods:

Traditional disease activity data on 76 PsA patients with active disease planned to initiate biological treatment were extracted from the Danish DANBIO registry for biological treatment in rheumatology. Data comprised PaGl, PhGl and pain (0 - 100 VAS), 28 swollen and tender joint count, CRP, HAQ-DI and DAS28-CRP(4v). Analyses were performed using parametric statistics. The association between PaGl and PhGl was examined by simple linear regression analysis. The predictability of PaGl and PhGl, respectively, by all other disease markers mentioned and by age and sex was examined using stepwise multiple regression analysis. Agreement between the VAS scores was expressed as the bias (mean difference between intra-individual scores) and the 95% lower and upper limits of agreement (LLoA;ULoA) according to the Bland-Altman method.

Results:

Mean age was 52.2±11.1 years and mean DAS28-CRP 4.7±1.1. 59.2% of the patients were women. Mean PaGl was 63.7±23.2 and mean PhGl 39.9±19.8 (p < 0.0001). Thus the difference between PaGl and PhGl was substantial on the group level. Differences between PaGl and PhGl were even more pronounced on the individual level, however. The average difference was 23.8 (bias) but differences on the individual level ranged from -21.9 (LLoA) to +69.5 (ULoA). The corresponding results for PaGl vs. pain was 4.9 (bias), -17.1 (LLoA) and 22.0 (ULoA), and for pain vs. PhGl 18.9 (bias), -23.0 (LLoA) and 60.8 (ULoA). PaGl was significantly but weakly correlated with PhGl (R = 0.42, p < 0.0001) with a high standard error of estimation (SEE) = 21.2. PaGl was independently predicted by pain (beta = 0.76, p < 0.0001) and HAQ-DI (beta = 0.19, p < 0.01) and was not predicted by PhGl (p = 0.61) (R = 0.78, SEE = 10.5, p < 0.0001). PhGl was independently predicted by SJC (beta = 0.43, p < 0.0001) followed by pain (beta = 0.41, p < 0.0001) and CRP (beta = 0.20, p < 0.05) (R = 0.70, SEE = 14.4, p < 0.0001) with no significantly contribution by PaGl (p = 0.49).

Conclusion:
In patients with active PsA initiating biological treatment, PaGl was in general scored considerably higher than PhGl. On the individual patient level, differences between PaGl and PhGl varied substantially. PaGl was best explained by pain, and PhGl by SJC. The findings reflect strongly diverging attitudes between PsA patients and their rheumatologists to severity of disease and to the relative importance of different outcome measures.

Disclosure: O. Rintek Madsen, None;


Abstract Number: 2554

Disease Activity in Psoriatic Arthritis-ESR Index Maybe a Valid Tool to Evaluate Disease Activity in Patients with Psoriatic Arthritis When CRP Is Not Available

Andrea Lujan Coronel Ale¹, Emilce E Schneeberger¹, Osvaldo Luis Cerda¹, Cecilia Zaffarana¹, Marina Natalia Fornaro², Margarita Landi¹ and Gustavo Citera³, ¹Section of Rheumatology, Instituto de Rehabilitación Psicofísica, Buenos Aires, Argentina, Buenos Aires, Argentina, ²Section of Rheumatology, Instituto de Rehabilitación Psicofísica, Buenos Aires, Argentina, buenos aires, Argentina, ³Section of Rheumatology, Instituto de Rehabilitación Psicofísica, Buenos Aires, Argentina, Buenos Aires, Argentina

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Time: 9:00AM-11:00AM

Background/Purpose: DAPSA is a composite index to assess disease activity in patients with Psoriatic Arthritis (PsA) which includes joint count 66/68, pain and patient’s global assessment (PtGA) and CRP. Since ESR is a more accessible acute phase reactant (APR), our aim was to develop a version of DAPSA using ESR instead of CRP and to estimate its cut-off values.

Methods: Patients with PsA according to CASPAR criteria ≥ 18 years old were included. Sociodemographic data, presence of comorbidities and current treatment were recorded. Morning stiffness, pain, PtGA, physician’s global assessment (PGA) and fatigue were evaluated by Visual Numerical Scale (VNS). Joint count (66/68), presence of dactylitis and enthesitis by MASES. Psoriasis was assessed by PASI and axial mobility by BASMI. APR (ESR in mm/h and CRP in mg/dl) were consigned. Self-questionnaires were performed to assess, quality of life (PsAQoL, ASQoL), functional capacity (HAQ-A and BASFI), and disease activity (BASDAI). Three different DAPSA versions were calculated: DAPSA-CRP, DAPSA-ESR. We also evaluated DAS28, CDAI, SDAI, and CPDAI, and minimal disease activity (MDA). Statistical analysis: Student's T test and ANOVA. Chi² test, Fisher exact test. Spearman test. Multiple linear regression model. ROC curves with AUC.

Results: A total of 119 patients were included, 62 were males (52.1%), with a median age of 54 years (IQR: 42-63) and a median disease duration of 8 years (IQR: 3-15). 58 (48.7%) of the patients presented mixed involvement, 57 (49.6%) peripheral joint involvement and 2 (1.7%) axial involvement. Median DAPSA-CRP was 12 (IQR: 7-19), median DAPSA-ESR was 14.2 (IQR: 8.2-21.1). DAPSA-ESR showed a very good correlation with: DAPSA-CRP (Rho: 0.97), SDAI (Rho: 0.9), CDAI (Rho: 0.92), DAS28 (Rho: 0.91) and CPDAI (Rho: 0.69); number of swollen joints (Rho: 0.73),
Disease activity in psoriatic arthritis: ESR index maybe a valid tool to evaluate disease activity in patients with psoriatic arthritis when CRP is not available.

**Conclusion:** DAPSA-ESR is a valid alternative index to measure peripheral joint activity in patients with PsA, in those places where the CRP can mean a higher additional cost. We determined its cut-off values, which should be validated in other cohorts.

**Disclosure:** A. L. Coronel Ale, None; E. E. Schneeberger, None; O. L. Cerda, None; C. Zaffarana, None; M. N. Fornaro, None; M. Landi, None; G. Citera, None.

**Abstract Number:** 2555

**Clinical History of Psoriatic Arthritis over Four Decades**

Dafna D Gladman¹, Justine Y. Ye² and Vinod Chandran³, ¹Rheumatology, Toronto Western Hospital, University of Toronto, Toronto, ON, Canada, ²Toronto Western Hospital, University of Toronto, Toronto, ON, Canada, ³Medicine, Krembil Research Institute, Toronto Western Hospital, University of Toronto, Toronto, ON, Canada

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Psoriatic arthritis (PsA) is an inflammatory musculoskeletal disease associated with psoriasis. Over the past several decades it was recognized that PsA is more common and more severe than previously thought. It has also been noted that patients who present earlier to a rheumatologist do better. However, whether patients have been treated earlier and more aggressively over the decades is not clear. The objective of this analysis was to describe the demographic, clinical features of inflammation and damage, as well as comorbidities and therapies provided over 4 decades in a single clinic.

**Methods:** A special clinic for psoriatic arthritis initiated in 1978. Patients are included if they have psoriasis and an inflammatory arthritis and other forms of arthritis have been excluded. Patients are followed at 6-12 month intervals according to a standard protocol which includes demographic, clinical, and laboratory evaluations and detailed drug treatment. Radiographic assessments are done at 2 year intervals and include peripheral joints according to the modified Steinbrocker, and axial disease according to NY criteria. Patients who entered the cohort in the past 4 decades were included. Descriptive statistics are used.

**Results:** Over the 40 year period 1428 patients were entered into the clinic and recorded in the database. 635 females 793 males, mean age at diagnosis of psoriasis 28.8 and at PsA 38 years. Information on the clinical, laboratory, radiographic and therapeutic features is provided in the table. As can be seen age at diagnosis remains in the mid-40s, and disease duration of psoriasis remains similar across the decades. However, PsA disease duration has decreased over the decades, suggesting that patients are referred earlier in their course. Patients presented with similar degree of disease...
activity but less patients had evidence of damage at presentation in more recent decades. This is also reflected in the radiographic evidence of damage and the functional class ¼. More patients have comorbidities in more recent decades. While NSAIDs use remains stable, there has been an increased in use of DMARDs, particularly biologics. This is partly related to the availability of the drugs since 2000, but also to the more aggressive approach to the management of the disease.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>44.1 (14.5)</td>
<td>41.3 (11.8)</td>
<td>44.3 (12.9)</td>
<td>46.1 (12.8)</td>
</tr>
<tr>
<td>Disease duration Psoriasis</td>
<td>15.8 (12.6)</td>
<td>13.0 (10.6)</td>
<td>15.3 (12.5)</td>
<td>16.8 (13.6)</td>
</tr>
<tr>
<td>Disease duration PsA</td>
<td>8.3 (9.1)</td>
<td>6.2 (7.1)</td>
<td>6.6 (7.7)</td>
<td>4.7 (7.2)</td>
</tr>
<tr>
<td>Married</td>
<td>64%</td>
<td>70%</td>
<td>63%</td>
<td>57%</td>
</tr>
<tr>
<td>Post-secondary education</td>
<td>49%</td>
<td>73%</td>
<td>71%</td>
<td>74%</td>
</tr>
<tr>
<td>No. of actively inflamed joints</td>
<td>10.4 (9.3)</td>
<td>11.0 (9.7)</td>
<td>11.1 (9.9)</td>
<td>8.9 (10.3)</td>
</tr>
<tr>
<td>PASI score (at presentation)</td>
<td>NA</td>
<td>7.2 (8.3)</td>
<td>6.1 (8.8)</td>
<td>5.0 (6.6)</td>
</tr>
<tr>
<td>Elevated CRP</td>
<td>NA</td>
<td>NA</td>
<td>9%</td>
<td>28%</td>
</tr>
<tr>
<td>Clinically damaged joints</td>
<td>40%</td>
<td>34%</td>
<td>37%</td>
<td>26%</td>
</tr>
<tr>
<td>No. damaged joints</td>
<td>3.1 (6.9)</td>
<td>2.7 (7.2)</td>
<td>3.3 (7.9)</td>
<td>1.5 (4.5)</td>
</tr>
<tr>
<td>Sacroiliitis</td>
<td>24%</td>
<td>16%</td>
<td>24%</td>
<td>19%</td>
</tr>
<tr>
<td>Functional class ¼</td>
<td>11%</td>
<td>13%</td>
<td>11%</td>
<td>7%</td>
</tr>
<tr>
<td>Radiographic damage</td>
<td>59%</td>
<td>47%</td>
<td>54%</td>
<td>39%</td>
</tr>
<tr>
<td>HAQ</td>
<td>NA</td>
<td>0.6 (0.6)</td>
<td>0.7 (0.6)</td>
<td>0.6 (0.6)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3%</td>
<td>3%</td>
<td>7%</td>
<td>8%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>12%</td>
<td>11%</td>
<td>20%</td>
<td>22%</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>70%</td>
<td>77%</td>
<td>71%</td>
<td>68%</td>
</tr>
<tr>
<td>DMARDs</td>
<td>30%</td>
<td>62%</td>
<td>65%</td>
<td>59%</td>
</tr>
<tr>
<td>Biologics</td>
<td>NA</td>
<td>NA</td>
<td>26%</td>
<td>45%</td>
</tr>
</tbody>
</table>

**Conclusion:** Over the past 4 decades similar patients have been admitted to the PsA clinic. However, patients seem to be referred earlier in the course of their disease, and this is reflected in less damage both clinically and radiologically. This may also reflect the increased use of DMARDs both conventional and biologic in this patient population. Education regarding the severity of PsA and the need for early diagnosis and treatment is working. However, further efforts are required to have patients with PsA diagnosed earlier and treated more aggressively to prevent untoward outcomes.

**Disclosure:** D. D. Gladman, None; J. Y. Ye, None; V. Chandran, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/clinical-history-of-psoriatic-arthritis-over-four-decades](http://acrabstracts.org/abstract/clinical-history-of-psoriatic-arthritis-over-four-decades)

**Abstract Number:** 2556

**Were Moll and Wright Right?**
Sergio Schwartzman1, Madeline Epsten2, Jackie Szymonifka2, Stephen A. Paget3 and Lisa A. Mandl1, 1Rheumatology, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, 2Rheumatology, Hospital for Special Surgery, New York, NY, 3Division of Rheumatology, Hospital for Special Surgery/Weill Cornell Medicine, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: In 1973 Moll and Wright published the first paper on the classification criteria for Psoriatic Arthritis (PsA). In their pioneering work, these authors additionally described 5 subtypes of PsA: Oligoarticular (Oli), Polyarticular (Pol), Axial (Axi), DIP form (DIP) and Mutilans (Mut). The classification criteria have been replaced by the CASPAR criteria, and as a consequence there has been a loss of emphasis on the importance of the subtypes. Arguments for decreased significance have been based on claims that these subclasses may overlap, are not stable, and can change over time.

The hypothesis of this study is that with some exceptions, the Moll and Wright subtype classification criteria are stable over time and may have important therapeutic implications.

Methods: This was a retrospective cohort study. All patients with ICD-9 or ICD-10 PsA codes seen at a single center from January 1, 2013 through December 31, 2016 were identified. Patients who met CASPAR classification criteria and who had a Moll and Wright subtype identified and at least a 2 year follow up were studied and described. The distribution of continuous variables was assessed using the Shapiro-Wilk test. Categorical variables are summarized as frequency (percent).

Results: 104 patients were identified. Pertinent demographics are presented in table 1. Distribution and persistence of PsA subtype are presented in tables 2a and 2b. As there is evidence that the Oli and Pol subtypes may overlap and be influenced by therapy, a subanalysis combined these forms and the persistence was 87.5%.

Conclusion: In this retrospective analysis, a striking persistence of the subtype of PsA was noted over time. This was particularly noted with the non-Oli forms of this disease. With the advent of therapeutically targeted therapy that may differentially affect the unique subtypes of PsA, this concept needs to be resurrected and perhaps modified. We would argue that Moll and Wright were right.

Table 1. Demographics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N=104</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at latest visit, years, mean ± SD</td>
<td>59.1 ± 13.1</td>
</tr>
<tr>
<td>Years between earliest/latest visit, median [IQR]</td>
<td>5.2 [3.6, 6.8]</td>
</tr>
<tr>
<td>Male</td>
<td>49 (47.1%)</td>
</tr>
<tr>
<td>Race (White)</td>
<td>92 (88.0%)</td>
</tr>
<tr>
<td>Psoriatic nail dystrophy</td>
<td>34 (32.7%)</td>
</tr>
<tr>
<td>Dactylitis</td>
<td>24 (23.1%)</td>
</tr>
</tbody>
</table>

Table 2a. Percentages of each subtype, by first/last visit

<table>
<thead>
<tr>
<th>Subtype</th>
<th>First visit</th>
<th>Last visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oli</td>
<td>28 (26.9%)</td>
<td>18 (17.3%)</td>
</tr>
<tr>
<td>Pol</td>
<td>57 (54.8%)</td>
<td>60 (57.7%)</td>
</tr>
<tr>
<td>Oli or Pol</td>
<td>85 (81.7%)</td>
<td>78 (75.0%)</td>
</tr>
<tr>
<td>Axi</td>
<td>4 (3.9%)</td>
<td>3 (2.9%)</td>
</tr>
<tr>
<td>DIP</td>
<td>30 (28.9%)</td>
<td>27 (26.0%)</td>
</tr>
<tr>
<td>Mut</td>
<td>3 (2.9%)</td>
<td>4 (3.9%)</td>
</tr>
</tbody>
</table>
Table 2b. Percentages unchanged from first to last visit for each subtype

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Unchanged from first to last visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oli</td>
<td>17/28 (60.7%)</td>
</tr>
<tr>
<td>Pol</td>
<td>48/57 (84.2%)</td>
</tr>
<tr>
<td>Oli or Pol</td>
<td>76/85 (89.4%)</td>
</tr>
<tr>
<td>Axi</td>
<td>3/4 (75.0%)</td>
</tr>
<tr>
<td>DIP</td>
<td>26/30 (86.7%)</td>
</tr>
<tr>
<td>Mut</td>
<td>3/3 (100.0%)</td>
</tr>
<tr>
<td>Overall</td>
<td>82/104 (78.9%)</td>
</tr>
<tr>
<td>Overall, combining 1, 2</td>
<td>91/104 (87.5%)</td>
</tr>
</tbody>
</table>

Disclosure: S. Schwartzman, None; M. Epsten, None; J. Szymonifka, None; S. A. Paget, None; L. A. Mandl, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/were-moll-and-wright-right](http://acrabstracts.org/abstract/were-moll-and-wright-right)

Abstract Number: 2557

**Do Psoriatic Disease Patients Who Participate in Clinical Research Differ from Those Who Do Not?**

Vivian G. Szeto¹², Justine Y. Ye¹, Vinod Chandran³, Dafna D Gladman⁴ and Cheryl F. Rosen⁵, ¹Toronto Western Hospital, University of Toronto, Toronto, ON, Canada, ²University of Alberta, Edmonton, AB, Canada, ³Medicine, Krembil Research Institute, Toronto Western Hospital, University of Toronto, Toronto, ON, Canada, ⁴Rheumatology, Toronto Western Hospital, University of Toronto, Toronto, ON, Canada, ⁵Dermatology, Toronto Western Hospital, University of Toronto, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster III: Outcomes, Outcome Measures, and Comorbidities
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Psoriatic arthritis (PsA) is an inflammatory musculoskeletal disease that affects 30% of people with psoriasis. The current understanding of these diseases involves patients who agree to participate in clinical studies. Therefore, it is not clear whether or not information gained from these studies is generalizable to all patients with psoriatic disease. The aim of this study was to determine whether the clinical features and outcomes of psoriatic disease patients who participate in clinical research are the same as those who do not.

Methods:

Two cohorts of research patients were studied: patients with psoriatic arthritis (PsA cohort) and patients with psoriasis without psoriatic arthritis (PsC cohort). The PsA and PsC cohorts are defined as patients enrolled in clinical research whose follow-up assessments are based on a standardized protocol. A third cohort was studied which included patients who are not enrolled in research (Clinic cohort).
The information on the patients’ disease history (age of onset, extent of psoriasis), demographic and social history (gender, smoking, employment), medication (past and current), and comorbidities (cardiovascular, respiratory, autoimmune) was collected from their charts. The Clinic cohort information was compared to both the PsA and PsC cohorts using one-way ANOVAs, Pearson’s Chi – square, and logistic regression analysis to test association of variables.

**Results:**

A total of 200 patients were included in each cohort studied. Of the 200 patients collected in the Clinic Cohort, 46 patients had PsA while 154 patients did not. The Clinic Cohort data was subsequently split into a PsA Clinic cohort and Psoriasis Clinic cohort to be compared to their respective research cohorts.

The average age of PsA patients studied was 53.3 for the Clinic cohort and 51.0 for the PsA cohort; whereas the average age of PsC patients included in the study was 52.0 for the Clinic cohort and 55.5 for the PsC cohort. The psoriasis disease duration varied among the cohorts with the average being 13.1 y for the PsA Clinic Cohort, 21.6 y for PsA cohort, 17.0 y for the Psoriasis Clinic cohort and 22.9 y for the PsC cohort. In terms of the comorbidities, 32% of the PsA Clinic cohort and 29% of PsA Cohort have cardiac disease while 32% of Psoriasis Clinic Cohort and 33% of the PsC Cohort have been diagnosed with heart disease. Analysis of the therapies and outcomes of the three cohorts is underway.

| Table 1. Comparison of the demographic, social history variables, comorbidities and clinical features between the Clinic cohort and the research cohorts (PsA cohort and PsC cohort). The demographic and social variables were statistically analyzed using the Chi-square distribution. The Pearson’s Chi-square test was performed on the comorbidities variables while an One-way ANOVA was used to analyze the clinical features, *significant difference at p < 0.05. |
| --- | --- | --- |
| **Variables** | **PsA Cohort vs. PsA Clinic Cohort** | **PsC Cohort vs. Psoriasis Clinic Cohort** |
| | *p*-value | *p*-value |
| Demographic & Social History Variables |  |  |
| Gender | 0.2456 | 0.7796 |
| Smoking | 0.0216* | 0.0084* |
| Employment | 0.8474 | 0.4318 |
| Comorbidities |  |  |
| Cardiovascular | 0.63 | 0.92 |
| Respiratory | 0.13 | 0.45 |
| Autoimmune | 0.08 | <0.001* |
| Clinical Features |  |  |
| Average Age of Patients in the Study | 0.33 | 0.022* |
| Average Age of Psoriasis Diagnosis | <0.001* | 0.22 |
| Psoriasis Disease Duration | <0.001* | <0.001* |
Conclusion:

These preliminary results show similarities between the research cohorts and the cohort of patients not involved in clinical research, suggesting generalization of the results of clinical research to all patients with psoriatic disease may be possible. Patients are still being actively recruited to the Clinic Cohorts.

Disclosure: V. G. Szeto, None; J. Y. Ye, None; V. Chandran, None; D. D. Gladman, None; C. F. Rosen, None.


Abstract Number: 2558

DNA Methylation-Dependent Regulation of Cathepsin E Gene Expression
By the Transcription Factor Kaiso in MRL/Lpr Mice

Sumie Hiramatsu1, Katsue S. Watanabe1, Yoshinori Matsumoto2, Yosuke Asano2, Sonia Zeggar1, Keiji Ohashi1, Michiko Morishiata3, Eri Katsuyama1, Takayuki Katsuyama1, Haruki Watanabe1, Mariko Narazaki1, Noriko Tatebe1, Tomoko Kawabata1, Ken-ei Sada1 and Jun Wada1, 1Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan, 2Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan, 3Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Animal Models Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: To identify new candidate genes regulated by DNA methylation and involved in the pathogenesis of systemic lupus erythematosus (SLE), we integrated genome-wide DNA methylation analysis and mRNA expression profiling in CD4+ splenic T cells derived from MRL/lpr lupus-prone mice (MRL) and C57BL6/J mice (B6) as a control.

Methods: Chromatin immunoprecipitation (ChIP)-PCR was used to investigate the transcription factors binding to CGCG methylation sites. Murine T lymphoma cell line, EL-4, was treated with DNA methyltransferase inhibitor, 5-Azacytidine (5-azaC) or histone deacetylase (HDAC) inhibitor, Trichostatin A (TSA) for in vitro study. To analyze the expression levels of mRNAs, quantitative real-time PCR (qPCR) was performed on a Step One Plus Real-Time PCR System (Applied Biosystems) using the TaqMan Gene Expression assays. To identify the function of Ctse, the Ctse gene was depleted by siRNA in EL4 cells stimulated with phorbol 12-myristate 13-acetate (PMA) and ionomycin, and measured IL-10 in cell culture supernatants by ELISA . To examine the expression levels of Il-10 and Ctse in CD4+ T cell subsets in peripheral blood mononuclear cell (PBMC) from 15 SLE patients and 6 healthy controls.

Results: We show that expression levels of Ctse transcripts are elevated in MRL T cells compared to that in B6 T cells and that the 583 bp region in the 1st intron in the Ctse gene is hypomethylated. Bisulfite sequencing show that the CGCG
motif in this region is hypomethylated in MRL cells. Kaiso, known to specifically recognize the methylated DNA motif (mCGCG) through the C2H2 zinc-finger domains, recruits the SMRT (Silencing Mediator of Retinoic acid and Thyroid hormone receptors) / N-CoR (Nuclear hormone receptor Co-Repressor) HDAC3 (Histone deacetylase 3) complex, leading to suppression of its target gene. To demonstrate that Kaiso and HDAC3 are components of the transcriptional complex regulating Ctse expression, we performed ChIP of the endogenous Ctse promoter in CD4+ T cells and observed strong enrichment of a Ctse-derived amplicon including the CGCG motif in both Kaiso and HDAC3 chromatin immunoprecipitates. Moreover, we found that the recruitment of Kaiso to the Ctse promoter was suppressed in MRL cells compared to B6 cells. Additionally, EL4 cells treated with 5-azaC or TSA showed the reduced recruitment of both Kaiso and HDAC3 to the motif. Moreover, we observed that depletion of the Ctse gene by siRNA in EL4 cells results in reduction of IL-10 expression in cell culture supernatants by ELISA and that the expression level of IL-10 transcripts are up-regulated in MRL T cells compared to B6. Lastly, we observed that in CD4+ T cell subsets in PBMC from SLE, the expression levels of CTSE and IL-10 transcripts were elevated in CD4+ T cells from SLE patients compared to that in healthy controls.

**Conclusion:** Our present study provides evidence that DNA methylation-mediated recruitment of both Kaiso and HDAC3 to the Ctse promoter regulates expression of Ctse and that demethylation of this promoter and subsequent elevation of Ctse and IL-10 expression may be the pathogenesis of SLE.

**Disclosure:** S. Hiramatsu, None; K. S. Watanabe, None; Y. Matsumoto, None; Y. Asano, None; S. Zeggar, None; K. Ohashi, None; M. Morishiata, None; E. Katsuyama, None; T. Katsuyama, None; H. Watanabe, None; M. Narazaki, None; N. Tatebe, None; T. Kawabata, None; K. E. Sada, None; J. Wada, None.

**Abstract Number:** 2559

**KZR-616, a Selective Inhibitor of the Immunoproteasome, Blocks the Disease Progression in Multiple Models of Systemic Lupus Erythematosus (SLE)**

Tony Muchamuel1, Janet Anderl2, R Andrea Fan2, Henry W. B. Johnson3, Christopher J Kirk4 and Eric Lowe2, 1Pharmacology and Toxicology, Kezar Life Sciences, South San Francisco, CA, 2Biology, Kezar Life Sciences, South San Francisco, CA, 3Medicinal Chemistry, Kezar Life Sciences, South San Francisco, CA, 4Kezar Life Sciences, South San Francisco, CA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** Systemic Lupus Erythematosus – Animal Models Poster  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** The proteasome inhibitor bortezomib has been used successfully to treat patients with SLE. The immunoproteasome is a distinct class of proteasome found predominantly in immune effector cells. Here we describe KZR-616, an analog of ONX 0914 (Nature Medicine 2009 15;781-788), that selectively targets the LMP7 and LMP2 subunits of the immunoproteasome and examine its potential as a novel therapeutic for the treatment of SLE and lupus nephritis (LN).

**Methods:** Cytokine release was measured in human PBMCs stimulated with endotoxin and in CD4+ T-cells stimulated with antibodies to CD3 and CD28. Human peripheral blood B-cells were stimulated with IL-21 and antibodies to CD40

**Disclosure:** None
and IgM to induce plasmablast differentiation. Cytokines and IgG were measured by mesoscale detection. Immunoproteasome inhibition was measured in human PBMCs and in mice following administration of KZR-616 by measuring proteasome active site occupancy. The therapeutic effect of KZR-616 treatment alone or in combination with mycophenylate mofetil (MMF) was evaluated in the NZB/W F1 model of SLE. Nephritis was monitored by proteinuria. Kidneys were harvested and stained with H&E and anti-IgG. Serum anti-dsDNA were measured by ELISA. Spleen and bone marrow cells were analyzed by flow cytometry. T-dependent antibody responses (TDAR) were measured in mice and monkeys following 1, 4, or 13 weekly administrations.

**Results:** At a concentration resulting in inhibition of LMP7 and LMP2 by 89% and 59%, respectively, KZR-616 induced a decrease in pro-inflammatory cytokine production in human PBMCs, including TNF-α, GM-CSF, IL-6, and IL12/IL-23 p40. In lymphocytes, KZR-616 blocked T-cell production of IFN-γ, TNF-α and GM-CSF, and the differentiation of B-cells to plasmablasts. KZR-616 administration to mice resulted in selective inhibition of LMP7 and LMP2 similar to levels *in vitro*. KZR-616 treatment in diseased mice resulted in a complete resolution of proteinuria and significant reductions in autoantibody production and renal IgG deposition. The halt in disease progression was durable as proteinuria levels did not significantly increase 8 weeks after treatment discontinuation. Histologic analysis following 12 weeks of treatment revealed a complete prevention in glomerular nephritis and sclerosis. Administration of KZR-616 in combination with MMF resulted in significantly greater disease inhibition and prolonged survival compared to either treatment alone. Levels of activated T-cells, B-cells and plasma cells were effectively depleted in diseased animals following KZR-616 treatment. KZR-616 had no significant effect on TDAR in mice or monkeys and did not affect the number of circulating lymphocytes in monkeys.

**Conclusion:** KZR-616 is a novel and selective covalent inhibitor of the immunoproteasome that potently blocks inflammatory cytokine production *in vitro* and disease progression in mouse models of SLE. Durable disease remission in animals was achieved at well tolerated doses without affecting normal T-cell dependent immune responses. KZR-616 is currently being developed for the treatment of LN and Phase 1 safety and pharmacokinetics results are presented elsewhere at this meeting.

**Disclosure:** T. Muchamuel, Kezar Life Sciences, 3; J. Anderl, Kezar Life Sciences, 3; R. A. Fan, Kezar Life Sciences, 3; H. W. B. Johnson, Kezar Life Sciences, 3; C. J. Kirk, Kezar Life Sciences, 3; E. Lowe, Kezar Life Sciences, 3.


**Abstract Number:** 2560

**Spleen Tyrosine Kinase Inhibition Reveals Immune Cell Subsets of Diseased NZB/W F1 Mice That Are Reflected in Systemic Lupus Erythematosus Patient Peripheral Blood Mononuclear Cells**

Christopher Pohlmeyer¹, Zhi-Hua Cui², Christian Franci¹, Gundula Min-Oo¹, JiYun Kim³ and Julie Di Paolo¹, ¹Immunology and Inflammation Biology, Gilead Sciences, Foster City, CA, ²Fibrosis Biology, Gilead Sciences, Foster City, CA, ³Biomarkers, Gilead Sciences, Foster City, CA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Systemic Lupus Erythematosus – Animal Models Poster

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM
**Background/Purpose:** Spleen tyrosine kinase (SYK) is a driver of B cell receptor and Fc receptor signaling pathways, which have central roles in initiating and driving pathogenesis of systemic lupus erythematosus (SLE). NZB/W F1 mice develop spontaneous lupus-like disease and are a model system for testing potential targeted therapies in SLE. Treatment of NZB/W F1 mice with SYK inhibitors has been previously reported to ameliorate symptoms of progressive disease (Bahjat et al., *Arth & Rheum* 2008). Since key pathological manifestations in studies using NZB/W F1 mice correlate with human SLE, we examined the immune cell populations that are affected in this model in order to translate to human SLE phenotypes. We compared splenic populations of healthy and diseased NZB/W F1 mice treated with a highly selective SYK inhibitor, SYKi-A, to PBMCs of healthy donors and SLE patients experiencing flares.

**Methods:** Spleens were harvested from NZB/W F1 mice without disease symptoms (16 weeks old, control), with progressive disease (40 weeks old), or from SYKi-A treated mice (40 weeks old with treatment initiated at 28 weeks). Splenic cells were analyzed by flow cytometry to identify B and T cell subpopulations modulated by disease and SYKi-A treatment. PBMCs isolated from blood of non-SLE and SLE patients were analyzed by flow cytometry to assess disease-mediated changes in disease-relevant lymphocyte populations.

**Results:** Treatment of NZB/W F1 mice with SYKi-A increased overall survival, reduced proteinuria, prevented renal inflammation, and preserved glomerular structure in the kidney. Immune cell populations were examined in the NZB/W F1 mouse cohorts. Splenic B cells from both control mice and SYKi-A treated mice showed a more naïve B cell phenotype than untreated mice with progressive disease as measured by the ratio of transitional B cells (IgM⁺IgD⁺) to class switched cells (IgM⁻IgD⁻) (p<0.0001 and p=0.007, respectively). In human PBMCs, non-SLE individuals showed a more naïve B cell phenotype as measured by the ratio of transitional B cells (CD24⁺CD38⁺) to class switched cells (CD27⁺IgD⁻IgM⁺) compared to SLE subjects (p = 0.034). Additionally, splenic T cells from both control mice and SYKi-A treated mice showed a more naïve T cell phenotype than untreated mice with progressive disease as measured by the ratio of naïve (CD44⁻CD62L⁺) to memory (CD44⁺CD62L⁻) T cells (CD4⁺: p=0.015 and p=0.002, respectively; CD8⁺: p=0.0003 and p=0.0003, respectively). In human PBMCs, non-SLE individuals showed a more naïve CD8⁺ T cell phenotype as measured by the ratio of naïve (CD45RA⁺CCR7⁺CD27⁺) to memory (CD45RO⁺CCR7⁻) CD8⁺ T cells compared to SLE subjects (p=0.042).

**Conclusion:** SYK inhibition following disease onset shifts the balance of lymphocyte subsets to a more naïve phenotype identified in pre-disease NZB/W F1 mice. T and B cell subsets identified in PBMCs from SLE subjects reflect a similar phenotype to those observed in NZB/W F1 diseased mice.

**Disclosure:** C. Pohlmeyer, Gilead Sciences, 3; Z. H. Cui, Gilead Sciences, 3,Gilead Sciences, 1; C. Franci, Gilead Sciences, 1,Gilead Sciences, 3; G. Min-Oo, Gilead Sciences, 3,Gilead Sciences, 1; J. Kim, Gilead Sciences, 3,Gilead Sciences, 1; J. Di Paolo, Gilead, 3.


**Abstract Number:** 2561

**BTK Inhibition Ameliorates Renal Disease in Spontaneous Murine Lupus Nephritis**

Samantha Chalmers¹, Elizabeth Glynn², Mark Panzenbeck², Josephine Pelletier², Todd Bosanac², Sara Khalil², Evan Der³, Leal Herlitz³, Deborah Webb³, Gerald Nabozny⁵, Jay S. Fine², Elliott Klein², Donald Souza⁶, Chaim Putterman⁷ and Meera Ramanujam², ¹Microbiology and Immunology, Albert Einstein College of Medicine, Bronx, NY, ²Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT, ³Albert Einstein College of Medicine, Bronx, NY, ⁴Cleveland Clinic, Cleveland, OH, ⁵gerald.nabozny@boehringer-ingelheim.com, Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT, ⁶Immunology & Inflammation, Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT, ⁷Division of Rheumatology, Albert Einstein College of Medicine, Bronx, NY, USA, Bronx, NY
Background/Purpose: Bruton's tyrosine kinase (BTK) plays an important role in B cell and FcR mediated myeloid cell activation. We recently described a selective BTK inhibitor, BI-BTK-1, that attenuates nephrotoxic serum nephritis, an induced model of renal disease mediated by passively transferred pathogenic antibodies. In the current study, we examined the efficacy of BI-BTK-1 in SLE and lupus nephritis, using the classical NZB × NZW F1 and MRL/lpr mouse models of spontaneous lupus.

Methods: NZB/W F1 female mice were treated with BI-BTK-1 via medicated chow at doses of 0.3, 1, 3, and 10 mg/kg (from 22-51 weeks of age). MRL/lpr female mice were treated with only the 10 mg/kg dose (weeks 9-27). Mice were monitored for proteinuria and serum autoantibodies. Extensive cytometric characterization of B cell subsets in the spleen and bone marrow, and qPCR of kidney RNA, were performed to understand the effects of BTK inhibition on kidney inflammation and the mechanisms of protection.

Results: Treatment with BI-BTK-1 significantly protected NZB/WF1 and MRL/lpr mice from the development of proteinuria (p<0.05 in NZB/WF1 at all doses and p<0.0001 in MRL/lpr mice at 10mg/kg and above) as well as renal dysfunction (serum BUN) at the time of sacrifice (p<0.05 for all doses of BI-BTK-1 vs control chow fed mice in NZB/WF1, and p<0.0004 in MRL/lpr mice). These beneficial effects of BI-BTK-1 were also reflected in the marked histological protection observed in both NZB/WF1 and MRL/lpr strains in glomerular as well as interstitial pathology scores. Mechanistically, BTK inhibition significantly reduced total B cell numbers and all B cell subsets (immature, transitional, follicular, marginal zone, and class switched) in the spleen (p<0.05 for BI-BTK-1 (3 mg/kg and 10 mg/kg) vs control chow fed mice in NZB/WF1 mice). Anti-dsDNA antibody titers were significantly decreased in the NZB/WF1 mice (p<0.05 for BI-BTK-1 (at doses of > 1 mg/kg) vs control treated mice), but surprisingly not significantly affected in the MRL/lpr strain. qPCR of kidney RNA showed that BI-BTK-1 treated mice displayed a significant decrease in several nephritis associated serum biomarkers, including NGAL and MCP-1. Studies to examine the effects of BI-BTK-1 treatment on survival are currently in progress.

Conclusion: Treatment with BI-BTK-1 was dramatically effective in two different spontaneous lupus strains, supporting the potential use of BTK inhibition as a novel approach for the treatment of lupus nephritis.

Disclosure: S. Chalmers, None; E. Glynn, Boehringer Ingelheim, 3; M. Panzenbeck, Boehringer Ingelheim, 3; J. Pelletier, Boehringer Ingelheim, 3; T. Bosanac, Boehringer Ingelheim, 3; S. Khalil, Boehringer Ingelheim, 3; E. Der, None; L. Herlitz, None; D. Webb, Boehringer Ingelheim, 3; G. Nabozny, Boehringer Ingelheim, 3; J. S. Fine, Boehringer Ingelheim, 3; E. Klein, Boehringer Ingelheim, 3; D. Souza, Boehringer Ingelheim, 3; C. Putterman, Boehringer Ingelheim, 2; M. Ramanujam, Boehringer Ingelheim, 3.


Abstract Number: 2562

Inhibition of Spleen Tyrosine Kinase Improves Renal Pathology and Reduces Lymphocyte Activation in the MRL/Lpr and NZB/NZW Murine Models of Systemic Lupus Erythematosus
Julie Di Paolo1, Christopher Pohlmeyer1, Zhi-Hua Cui2, Gundula Min-Oo1, Igor Mikaelian3, Robert Brockett3, Bernard Murray4, Roy Bannister5, JiYun Kim6 and Franziska Matzkies7, 1Immunology and Inflammation Biology, Gilead Sciences, Foster City, CA, 2Fibrosis Biology, Gilead Sciences, Foster City, CA, 3Biology Core Support, Gilead Sciences, Foster City, CA, 4DMPK, Gilead Sciences, Foster City, CA, 5Drug Safety, Gilead Sciences, Foster City, CA, 6Biomarkers, Gilead Sciences, Foster City, CA, 7Gilead Sciences, Foster City, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Animal Models Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Spleen tyrosine kinase (SYK) mediates immunoreceptor signaling in hematopoietic cells important in the initiation and progression of systemic lupus erythematosus (SLE), including those from the B cell receptor (BCR) and Fc receptors (FcR) in B cells, monocytes, and dendritic cells1. SLE is a heterogeneous autoimmune disease characterized by immune system hyperactivation leading to the production of autoantibodies and immune attack on multiple organs including skin, kidney, and others. SYK inhibition is expected to reduce adaptive as well as innate immune cell activation, and immune complex signaling, which are all key drivers in SLE pathology. This work characterizes the disease modifying activity and mechanism of action of SYK inhibition in two spontaneous in vivo murine models of lupus: the MRL/lpr and NZB/W F1 models and estimates the required target engagement needed for efficacy in SLE. In vitro studies focused on GS-9876, a novel, highly selective, once-daily SYK inhibitor that Gilead Sciences is developing for the chronic treatment of rheumatoid arthritis and SLE. In vivo studies were performed with SYKi-A, a structurally similar analog that exhibits better mouse pharmacokinetics. In vitro properties of SYKi-A are similar to those of GS-9876.

Methods:
SYK inhibition was characterized in biochemical and cellular assays demonstrating potency and selectivity. To determine the disease-modifying activity of SYK inhibition, SYKi-A was tested in the MRL/lpr and NZB/W F1 models of lupus. Efficacy was determined by measuring anti-dsDNA titers, proteinuria, renal histopathology, and survival. Splenic cell populations were analyzed by flow cytometry to measure changes in lymphocyte subsets and activation status following SYK inhibition. An in vitro murine whole blood pSYK assay and PK was used to estimate target engagement and correlate with efficacy.

Results:
SYK inhibitors potently inhibited BCR-induced B cell signaling and activation, BCR and CD40 co-stimulation-induced B cell proliferation, and immune-complex stimulated cytokine production in human macrophages. In the murine models of SLE, SYKi-A decreased anti-dsDNA antibody titers, prevented the progression of proteinuria, reduced B cell activation, altered B cell subsets, and reduced T cell activation. In the NZB/W F1 model, there was a significant reduction of renal SYK immunolabeling, decreased renal inflammation, and improved glomerular morphology concurrent with decreased proteinuria, and increased survival. Average SYK target coverage of >50% was required for significant changes in disease activity.

Conclusion:
Building on previously reported studies2-3, these results further support the role of SYK in SLE pathogenesis, provide important information about target coverage needed for efficacy in the murine model, and identify the therapeutic potential for SYK inhibition by GS-9876 in human SLE.

SH3BP2 Gain-of-Function Mutation Ameliorates Lupus in B6.MRL-Faslpr Mice

Akiko Nagasu¹, Tomoyuki Mukai¹, Masanori Iseki², Hajime Nagasu³, Shunichi Fujita¹, Takafumi Mito¹, Shoko Kodama¹, Yumi Sasae⁴, Naoki Kashihara³, Katsuhiro Ishihara², Yasuyoshi Ueki⁵ and Yoshitaka Morita¹, ¹Department of Rheumatology, Kawasaki Medical School, Kurashiki, Okayama, Japan, ²Department of Immunology and Molecular Genetics, Kawasaki Medical School, Kurashiki, Okayama, Japan, ³Department of Nephrology and Hypertension, Kawasaki Medical School, Kurashiki, Okayama, Japan, ⁴Department of Rheumatology, Kawasaki Medical School, Kurashiki, Okayama, Japan, ⁵Department of Oral and Craniofacial Sciences, School of Dentistry, University of Missouri-Kansas City, Missouri-Kansas City, MO

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Animal Models Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by the production of autoantibodies, leading to multiple organ dysfunction. SH3BP2 (Src homology domain 3 binding protein 2) is an adaptor protein, which is dominantly expressed in immune cells and regulates intracellular signaling pathways such as Syk and PLCγ. We have previously reported that SH3BP2 deficiency suppresses autoantibody production and subsequent arthritis induction in a murine collagen-induced arthritis model (Mukai T, et al. Arthritis Rheumatol 2015). To further investigate the role of SH3BP2 in autoimmune inflammatory diseases, we here examine the effect of SH3BP2 gain-of-function in a murine SLE model. We hypothesized that the SH3BP2 gain-of-function exacerbates autoantibody production and organ damage in lupus-prone mice, contrasting the phenotype observed in the SH3BP2 deficient arthritis model.

Methods: SH3BP2 gain-of-function mutant (P416R knock-in; SH3BP2KI/+ ) mice and lupus-prone (B6.MRL-Faslp/lpr/j) mice were crossed to yield the double mutant (SH3BP2KI/+ /Faslp/lpr) mice. Body weight and proteinuria were assessed until 12 months of age. At the end of the observation, mice were euthanized, and serum and organs were collected. Anti-double-stranded DNA (anti-dsDNA) antibody levels in sera were measured by ELISA. Organ involvement was assessed histologically. B-cell and T-cell subsets were analyzed by flow cytometry. To determine the role of SH3BP2 in B cells to mediate proliferation following cross-linking of the B-cell receptor (BCR), resting splenic B cells were isolated from wild-type and SH3BP2KI/+ mice and stimulated with either anti-IgM antibody, anti-IgM antibody plus anti-CD40 antibody or LPS.

Results: Unexpectedly, we found that SH3BP2 gain-of-function mutation suppressed the development of renal disease. According to the amelioration of disease, SH3BP2KI/+ /Faslp/lpr mice had lower titers of anti-dsDNA antibodies than...
Fas\textsuperscript{lpr/lpr} mice. The B220\textsuperscript{+}CD4\textsuperscript{−}CD8\textsuperscript{−} (double-negative) T cell population characteristic of Fas\textsuperscript{lpr/lpr} mice in the lymph nodes was decreased in the SH3BP2\textsuperscript{KI/+}/Fas\textsuperscript{lpr/lpr} mice. In vitro experiments, B-cell proliferation in response to BCR cross-linking with anti-IgM antibody was comparable between wild-type and SH3BP2\textsuperscript{KI/+} cells, suggesting that the mechanism of suppression of disease was not B cell mediated.

**Conclusion:** Contrary to our initial hypothesis, SH3BP2 gain-of-function mutation ameliorated clinical and immunological phenotypes of the lupus-prone mice. Further analyses are required to reveal the immunoregulatory role of SH3BP2 in the autoimmune disease.

**Disclosure:** A. Nagasu, None; T. Mukai, Takeda Pharmaceutical Co., Ltd., 2,Pfizer Japan Inc., 2,Mitsubishi Tanabe Pharma Co., 2,Chugai Pharmaceutical Co., Ltd., 2,AbbVie GK, 2,TEIJIN Pharma Ltd., 2,Astellas Pharma Inc., 2,Japan Blood Products Organization, 2,Shionogi & Co., Ltd., 2,Actelion Pharmaceuticals Japan Ltd., 2,Eli Lilly Japan K.K., 2,DAIICHI SANKYO Co., Ltd., 2,UCB Japan Co. Ltd., 2; M. Iseki, None; H. Nagasu, None; S. Fujita, None; T. Mito, None; S. Kodama, None; Y. Sasa, None; N. Kashihara, None; K. Ishihara, None; Y. Ueki, None; Y. Morita, Takeda Pharmaceutical Co., Ltd., 2,Pfizer Japan Inc., 2,Mitsubishi Tanabe Pharma Co., 2,Chugai Pharmaceutical Co., Ltd., 2,AbbVie GK, 2,TEIJIN Pharma Ltd., 2,Astellas Pharma Inc., 2,Japan Blood Products Organization, 2,Shionogi & Co., Ltd., 2,Actelion Pharmaceuticals Japan Ltd., 2,Eli Lilly Japan K.K., 2,DAIICHI SANKYO Co., Ltd., 2; M. Iseki, None; H. Nagasu, None; S. Fujita, None; T. Mito, None; S. Kodama, None; Y. Sasa, None; N. Kashihara, None; K. Ishihara, None; Y. Ueki, None; Y. Morita, Takeda Pharmaceutical Co., Ltd., 2,Pfizer Japan Inc., 2,Mitsubishi Tanabe Pharma Co., 2,Chugai Pharmaceutical Co., Ltd., 2,AbbVie GK, 2,TEIJIN Pharma Ltd., 2,Astellas Pharma Inc., 2,Japan Blood Products Organization, 2,Shionogi & Co., Ltd., 2,Actelion Pharmaceuticals Japan Ltd., 2,Eli Lilly Japan K.K., 2,DAIICHI SANKYO Co., Ltd., 2.


Abstract Number: 2564

**Inhibition of Neutrophil Elastase Protects Against Glomerulonephritis and Thrombosis in a Mouse Model of Lupus**

**Gautam Sule**\textsuperscript{1}, Levi F. Mazza\textsuperscript{1}, Nayef M. Kazzaz\textsuperscript{1}, Srilakshmi Yalavarthi\textsuperscript{1}, He Meng\textsuperscript{1} and Jason S. Knight\textsuperscript{2},\textsuperscript{1}University of Michigan, Ann Arbor, MI, \textsuperscript{2}, University of Michigan, Ann Arbor, MI

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Systemic Lupus Erythematosus – Animal Models Poster

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Neutrophils are potential instigators of autoimmunity and effectors of organ damage in lupus. However, there is presently no consensus as to whether inhibition of neutrophil effector functions can be pursued as a therapeutic strategy. For example, NADPH oxidase inhibition prevents neutrophil extracellular trap release (NETosis), but exacerbates lupus (likely by interfering with the function of suppressive neutrophil subsets). Similarly, peptidylarginine deiminase inhibitors prevent NETosis and protect against lupus-mediated vascular damage, but raise the levels of key autoantibodies such as anti-double-stranded DNA. Here, we characterize neutrophil elastase, a key effector of neutrophil-mediated organ damage. Neutrophil elastase is required for NETosis and has also been reported to circulate at high levels in lupus patients; however, this key serine protease has been surprisingly little studied in lupus.

**Methods:** We tested the effects of specific inhibition of the serine protease neutrophil elastase in a mouse model of lupus, namely NZWxBXSB F\textsubscript{1} mice (which develop immune-complex nephritis, and also display a strong prothrombotic diathesis). NZWxBXSB F\textsubscript{1} mice were treated with daily oral administration of the potent, selective elastase inhibitor GW311616A. Endpoints assessed NETosis efficiency, circulating autoantibody levels, glomerulonephritis, cardiac fibrosis, and venous thrombosis.
Results: In vitro, the neutrophil elastase inhibitor GW311616A mitigated NETosis in response to stimulation with either phorbol 12-myristate 13-acetate (PMA) or lupus serum. Neutrophils isolated from GW311616A-treated mice also demonstrated reduced NETosis when challenged with stimuli such as PMA and lipopolysaccharide. In NZWxBXSB F₁ mice, a six-week course of daily oral GW311616A or vehicle control (n=24 per group) protected against several aspects of the lupus phenotype. Specifically, treated mice demonstrated reduced levels of autoantibodies against cathelicidin-related antimicrobial peptide (CRAMP, the mouse orthologue of LL-37) and beta-2 glycoprotein I (β₂GPI, the key autoantigen in antiphospholipid syndrome); in contrast, the levels of anti-double-stranded DNA antibodies were not affected. GW311616A-treated mice demonstrated improved proteinuria-free survival, reduced deposition of complement C3 in kidneys, and reduced expansion of CD4⁺ CD44⁺ CD62L⁻ effector T cells in spleens. Cardiac fibrosis (a measure of the prothrombotic phenotype of NZWxBXSB F₁ mice) was reduced by GW311616A. Finally, a brief course of GW311616A in aged NZWxBXSB F₁ mice was effective in mitigating macroscopic venous thrombosis in response to inferior vena cava flow restriction.

Conclusion: These data reveal neutrophil elastase as a novel therapeutic target in lupus. Administration of the specific neutrophil elastase inhibitor GW311616A reduced autoantibody levels, and protected against nephritis as well as both arterial and venous thrombosis. This work once again emphasizes that the method of neutrophil inhibition must be carefully considered in lupus.

Disclosure: G. Sule, None; L. F. Mazza, None; N. M. Kazzaz, None; S. Yalavarthi, None; H. Meng, None; J. S. Knight, None.

Abstract Number: 2565

Pharmacodynamic Modeling of BTK Occupancy Versus Efficacy in Ra and SLE Models Using the Novel Specific BTK Inhibitor Evobrutinib

Philipp Haselmayer¹, Monsterrat Camps², Lesley Liu-Bujalski³, Federica Morandi⁴, Jared Head⁴, Simone C. Zimmerli⁵, Lisa Bruns⁶, Andrew Bender⁷, Patricia Schroeder⁸ and Roland Grenningloh⁹, ¹CBD, Merck KGaA, Darmstadt, Germany, ²Immunology, Merck Serono S.A., Geneva, Switzerland, ³Medicinal Chemistry, EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA, ⁴Biomolecular Pharmacology, EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA, ⁵Immunology, EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA, ⁶Immunology, Merck KGaA, Darmstadt, Germany, ⁷TIP Immunology, EMD Serono Research and Development Institute, Billerica, MA, ⁸Translational Pharmacology, EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA, ⁹EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Animal Models Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Bruton’s tyrosine kinase (BTK) is a clinically-proven target in several hematological indications. Due to its role in mediating the signaling of both B cell receptors (BCR) and Fc receptors (FcR), BTK is also a potential
target for the treatment of autoimmune diseases such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), where B cell and innate immune cell activation are key drivers of pathology. We are developing evobrutinib, a novel, highly selective irreversible BTK inhibitor that may be suitable for the treatment of chronic diseases. This work aimed to characterize the activity of evobrutinib in various in vitro cellular assays and in disease models of RA and SLE. In vivo efficacy and target occupancy data were used to build a pharmacokinetic and pharmacodynamic (PKPD) model describing the correlation between BTK inhibition and disease severity reduction.

**Methods:** The potency and specificity of evobrutinib was characterized using biochemical and cellular assays. The SLE disease-modifying potential of evobrutinib was assessed in a NZB/W F1 mouse model induced using replication-deficient interferon (IFN)-alpha-expressing adenovirus. Efficacy was determined by measuring proteinuria and histological kidney damage. The RA disease-modifying potential of evobrutinib was tested in a mouse collagen-induced arthritis (CIA) model, with efficacy evaluated by paw scores. A biochemical assay was developed to determine BTK occupancy rates in blood cells and splenocytes. These assays were used to build a translational PKPD model relating target occupancy to efficacy.

**Results:** Evobrutinib potently inhibited BCR- and FcR-mediated signaling and subsequent activation and function of B cells and certain myeloid cells. In mouse models of RA and SLE, evobrutinib displayed robust efficacy as demonstrated by a marked reduction of disease severity. In the NZB/W F1 IFN-accelerated SLE model, efficacy correlated with B cell inhibition, reduction of autoantibodies, and decreased circulating memory B and T cells. In addition to SLE, RA-like symptoms were inhibited in a collagen-induced arthritis model. In order to translate preclinical efficacious doses to humans, we determined the degree of target occupancy necessary to achieve disease reduction. Pharmacodynamic modeling showed that BTK occupancy of 60 and 80% was linked to 80% and near complete disease inhibition, in both the RA and SLE models, respectively.

**Conclusion:** These results demonstrate the potential of evobrutinib to treat autoimmune disease and may inform rational dose decisions as evobrutinib is advanced for development in rheumatologic diseases.

**Disclosure:** P. Haselmayer, Merck KGaA, 3; M. Camps, Merck Serono S.A., 3; L. Liu-Bujalski, EMD Serono, Inc, 3; F. Morandi, EMD Serono, Inc, 3; J. Head, EMD Serono, Inc, 3; S. C. Zimmerli, EMD Serono, Inc, 3; L. Bruns, Merck KGaA, 3; A. Bender, EMD Serono, Inc, 3; P. Schroeder, EMD Serono, Inc, 3; R. Grenningloh, EMD Serono, Inc, 3.


**Abstract Number:** 2566

**Myxomavirus-Derived Serpin (Serp-1) Reduces Diffuse Alveolar Hemorrhage in a Murine Model of Lupus**

**Haoyang Zhuang**1, Shuhong Han1, Lijun Yang2, Sriram Ambadapadi3, Alexandra Lucas4 and Westley Reeves5,

1Medicine, University of Florida, Gainesville, FL, 2Pathology, Immunology and laboratory medicine, University of Florida, Gainesville, FL, 3Arizona state University, Tempe, AZ, 4Arizona State University, Tempe, AZ, 5Rheumatology & Clinical Immology, University of Florida, Gainesville, FL

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Systemic Lupus Erythematosus – Animal Models Poster

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM
Diffuse alveolar hemorrhage (DAH) is an unusual complication of lupus with over 50% mortality. In both humans and mice, DAH is associated with ANCA-negative pulmonary capillaritis and hemosiderin-laden lung macrophages (Mϕ). C57BL/6 (B6) mice develop lupus with severe DAH after intraperitoneal injection of pristane. We have shown that the pathogenesis of pristane-induced DAH requires Mϕ and the uptake of dead cells opsonized by immunoglobulin and complement via complement receptor 3 (CD11b/CD18). Serpins, such as the rabbit myxomavirus-derived Serp1 protein, regulate coagulation and inflammation by binding serine proteases. Serp1 inhibits both thrombolytic (e.g. urokinase plasminogen activator) and thrombotic (Factor Xa) proteases and downregulates inflammation in part via its effects on Mϕ. We asked if Serp-1 protects mice from pristane-induced DAH.

Methods:

Pristane-treated B6 mice (21 per group) were given recombinant Serp1 or PBS i.p. from day 1 until d-14. In some experiments, Serp1 treatment was delayed until d-4 or Serp1 was given on days 1-3 only. The severity of DAH was evaluated by gross pathology and histology. Peritoneal cells and alveolar Mϕ collected by bronchoalveolar lavage (BAL) were analyzed by flow cytometry.

Results: DAH developed in 60% of pristane-treated mice with a 14-d mortality of 15%. In mice treated with pristane+Serp1, DAH developed in 10% and mortality was 0% (P<0.001). The interferon signature and numbers of peritoneal Ly6C<sup>hi</sup> inflammatory Mϕ were reduced by Serp1 treatment (P<0.0001). We recently identified a novel M2-like Mϕ expressing CD138 that promotes the resolution of inflammation. Serp1 significantly increased the number of pro-resolution (CD138<sup>+</sup>) Mϕ in both the peritoneum and the lung (P<0.01). When Serp1 treatment was delayed by 3-d, the mice were not protected from DAH, even though hemorrhage does not become apparent until 7-d after pristane treatment. Interestingly, Serp1 treatment from days 1-3 after pristane reduced the incidence of DAH to 20%. High Ly6C<sup>hi</sup> inflammatory Mϕ and low CD138<sup>+</sup> Mϕ numbers correlated with lung hemorrhage. In addition, Serp1 treatment up-regulated the activity of liver X receptor-α (LXRα), a transcription factor that promotes M2 Mϕ polarization, in both peritoneal and lung (alveolar) Mϕ. Mice that are resistant to DAH consistently exhibited higher levels of LXRα activity than susceptible mice.

Conclusion:

The myxomavirus-derived protein Serp1 (effective in Phase IIa clinical trials for treating acute coronary syndromes) protects mice from DAH and is a potential candidate for treating this severe complication of lupus. Its mechanism of action appears to involve activation of LXRα.

Disclosure: H. Zhuang, None; S. Han, None; L. Yang, None; S. Ambadapadi, None; A. Lucas, Viron, 1; W. Reeves, None.


Abstract Number: 2567

Type I IFN Blockade Restores Normal Transitional B Cell Development Post-Anti-CD20 Depletion

Jennie Hamilton<sup>1</sup>, Qi Wu<sup>2</sup>, PingAr Yang<sup>3</sup>, Bao Luo<sup>4</sup>, Shanrun Liu<sup>5</sup>, Huixian Hong<sup>6</sup>, Jun Li<sup>7</sup>, Hui-Chen Hsu<sup>2</sup> and John D. Mountz<sup>8</sup>, <sup>1</sup>Medicine/Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL, <sup>2</sup>Department of Medicine, University of Alabama at Birmingham, Birmingham, AL, <sup>3</sup>Department of Medicine, Clinical Immunology & Rheumatology, University of Alabama at Birmingham, Birmingham, AL, <sup>4</sup>Division of Clinical Immunology and Rheumatology, Department of Medicine, University of Alabama at Birmingham, Birmingham, AL, <sup>5</sup>Biochemistry & Molecular Genetics, University of Alabama at Birmingham, Birmingham, AL,
SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Animal Models Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Application of B cell depletion therapy (BCDT) for treatment of SLE has shown promise in some patients, but some patients exhibit disease relapses. Anti-type I interferon (IFN) receptor therapy has recently been shown to be effective in SLE. We previously showed that type I IFN plays an important role in promoting autoimmune disease in the BXD2 mouse model of lupus. Here, we address the question of whether type I IFN blockade can prevent the relapse and return of autoreactive B cells after anti-CD20 depletion therapy using the BXD2 mouse model of lupus.

Methods: Groups of BXD2 mice (4 weeks old) were either untreated or treated with anti-CD20 and followed by treatment with control antibody, neutralizing antibody against IFNβ, or neutralizing antibody against IFNαR beginning at the time of B cell repopulation. FACS analysis was carried out using validated antibodies. Confocal imaging was carried out to determine areas of repopulation in the spleen. Sera antibody levels of anti-DNA, anti-La, and rheumatoid factor were determined by ELISA analysis.

Results: Compared to normal B6 mice, there was rapid repopulation of transitional and mature B cells in the spleens of BXD2 mice at weeks 2 and 3, after BCDT. Interestingly, treatment with anti-IFNαR normalized the kinetics of repopulation in BXD2 mice and decreased the rapid development from transitional B cells to more mature B cells, suggesting a “window of opportunity” to normalize B cell repopulation after BCDT. To determine superiority of anti-IFNαR during this “window”, groups of mice were treated with either anti-IFNβ or anti-IFNαR, during from 2 to 4 week (MOD, ip) and short and longterm effects of interferon inhibition were determined at week 4 and 12, after BCDT. Early repopulation, determined by confocal imaging at week 4 after BCDT showed a significant inhibition of class-switched (IgM, IgD⁺) transitional B cells in the MZ zone and outer follicles of anti-IFNβ-treated mice compared to IFNαR-treated mice. Decreased development of early-stage transitional (CD93⁺) La₁₃₋₁₃-2₃ tetramer⁺ autoreactive B cells accompanied by decreased Ki67+ proliferation was observed in both anti-IFNβ-treated and anti-IFNαR-treated mice with no significant difference between treatment groups. At week 12 after BCDT, there was a significant decrease in the percent of Fas⁺ GL7 GC-B cells after short-term treatment with anti-IFNAR and anti-IFN-β. Sera levels of anti-DNA, La and rheumatoid factor were reduced in anti-IFN-β and anti-IFNαR blockade treated mice compared to anti-CD20 therapy alone.

Conclusion: Type I interferons exert a prominent effect on the development of autoreactive B cells during a critical “window of opportunity” where transitional B cells are repopulating the periphery following B cell depletion therapy. Importantly, transient blockade of type I IFN during B cell repopulation was sufficient to prevent development of autoreactive B cells and antibodies long-term. These results suggest that blockade of type I IFN may be an effective therapeutic option to enhance and prolong the effects of B cell depletion therapy in lupus. Also, specific inhibition of IFN-β may be sufficient as blockade of all type I IFN signaling in B cells using anti-IFNαR did not offer additional benefit.

Disclosure: J. Hamilton, None; Q. Wu, None; P. Yang, None; B. Luo, None; S. Liu, None; H. Hong, None; J. Li, None; H. C. Hsu, None; J. D. Mountz, None.

Prophylactic and Therapeutic Administration of a JAK1-Selective Inhibitor Blocks and Reverses Nephritis and Sialadenitis in NZB/W-F1 Mice

Rachel Twomey1, Stuart Perper1, Susan Westmoreland1, Terry Melim1, Soumya Mitra1, Zheng Liu1, Manuel Duval1, Carolyn Cuff2, Andrew Long1, Anthony Slavin2 and Stephen Clarke1, 1AbbVie Inc, AbbVie Bioresearch Center, Worcester, MA, 2Immunology Discovery, AbbVie Inc, AbbVie Bioresearch Center, Worcester, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Animal Models Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Signaling of most cytokine receptors occurs through the JAK-STAT pathway. This is true of cytokines linked to the etiology of systemic lupus erythematosus (SLE) and Sjogren’s syndrome (SS), such as type I interferon (IFN-I), IFNg, and IL-6. Thus, the JAK-STAT pathway is a potential target for the treatment of these diseases. IFN-I is of particular interest because a majority of SLE and SS patients have an IFN signature suggesting that levels of IFN are high in these patients. SLE is ameliorated in mice lacking the receptor for IFN-I (IFNAR) indicating that this cytokine is essential to the development of disease. In human SLE, blocking IFN-I binding to IFNAR with an anti-IFNAR mAb was efficacious in a phase 2 clinical trial in SLE patients that exhibited a high IFN signature. We show here that prophylactic and therapeutic treatment with a JAK1-selective inhibitor prevents and reverses disease in lupus-prone mice.

Methods: NZB/W-F1 mice were prophylactically or therapeutically administered a JAK-1 inhibitor daily by gavage. Prophylactic treatment of NZB/W-F1 mice began at 26 weeks of age, while therapeutic treatment was initiated after mice developed high proteinuria. Proteinuria was monitored weekly by urinalysis, and at study termination blood and spleen cells were analyzed by flow cytometry. Additionally, histological and gene transcription analyses of kidney, spleen, and salivary glands were performed.

Results: Prophylactic and therapeutic administration significantly impacted the number of splenic naïve B cells, germinal center B cells and plasmablasts. It also impacted splenic CD4 T cells, but not CD8 T cells. Daily administration of inhibitor prophylactically blocked development of proteinuria and extended survival in NZB/W-F1 mice. Most significantly, JAK1 inhibition reversed established, severe proteinuria and extended survival. In agreement, the kidneys of therapeutically treated mice exhibited reduced inflammation compared to control mice, and the kidney and blood exhibited a lower IFN-I signature compared to controls. JAK1 inhibition also prevented a loss of saliva production and salivary gland inflammation.

Conclusion: JAK1 inhibition is efficacious in preventing the onset of nephritis and sialadenitis, and can reverse already ongoing nephritis in NZB/W-F1 mice. Resolution of ongoing nephritis results in low or normal urine protein levels. Thus, JAK1 inhibition may be an efficacious therapeutic strategy in the treatment of SLE and SS.

Disclosure: R. Twomey, None; S. Perper, None; S. Westmoreland, AbbVie, Inc., 3,AbbVie, Inc., 1; T. Melim, None; S. Mitra, None; Z. Liu, None; M. Duval, None; C. Cuff, None; A. Long, None; A. Slavin, None; S. Clarke, None.

Serine/Arginine-Rich Splicing Factor 1 (SRSF1) Is a Novel Regulator of T Cell Function and Its Selective Deficiency in T Lymphocytes Leads to Autoimmunity and Lupus-like Nephritis

Vaishali R. Moulton1, Takayuki Katsuyama1, Hao Li1, Michael W. Mosho1, Andrew R. Gillooly2 and George C. Tsokos1, 1Division of Rheumatology, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, 2Medicine/ Rheumatology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Animal Models Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

T cells from patients with systemic lupus erythematosus (SLE) exhibit defects in signaling including a reduced expression of the CD3 zeta signaling chain, and defects in cytokine production such as decreased IL-2 production. We used a discovery approach namely mass spectrometry analysis of proteins “pulled-down” by a CD3 zeta mRNA-defined oligonucleotide, and identified the splicing regulator serine arginine-rich splicing factor 1 (SRSF1). We showed that SRSF1 promotes normal expression of CD3 zeta chain, and upregulates IL-2 production in human T cells. We found that SRSF1 expression levels are decreased in SLE T cells, and associates with worse disease. Force expression of SRSF1 into SLE T cells rescued IL-2 production. These results suggest that SRSF1 deficiency is important in the SLE T cell dysfunction. However, it is unknown how SRSF1 deficiency contributes to immune-mediated disease. To this end, we have generated mice with a T cell-restricted deletion of SRSF1, and our goal is to evaluate the mechanistic role of SRSF1 in T cell dysfunction and the development of immune-mediated disease in vivo.

Methods:

T cell Srsf1 conditional knockout (Srsf1-cko) mice were generated by crossing Srsf1-flox mice with d.Lck.Cre (distal promoter) transgenic mice to delete SRSF1 in mature T cells. Mice were euthanized at 10-20 weeks of age, or aged to >1 year. Central (thymus) and peripheral (spleen, lymph nodes) lymphoid organs were analyzed for immune cell phenotype and function by flow cytometry. Serum and urine were collected to assess autoantibody levels and proteinuria respectively. Kidney tissues were fixed, sectioned and stained with hematoxylin and eosin to evaluate histopathology. To assess regulatory T cells (Treg) function in vivo, adoptive transfer of Tregs followed by induction of colitis in two models - dextran sodium sulfate (DSS)-induced colitis in B6 mice, and the naïve CD4 transfer-induced colitis in RAG-ko mice, were utilized.

Results:

Srsf1-cko mice develop peripheral T cell lymphopenia at younger ages, whereas aged mice exhibit lymphocytosis and lymphoproliferation. CD4 T cells exhibit an activated phenotype and produce increased amounts of IFN-γ and IL-17 but lower amounts of IL-2 upon ex vivo stimulation. The Srsf1-cko mice develop autoantibodies, and exhibit increased proteinuria compared to control mice. Kidney histopathology shows evidence of glomerular damage with glomerular hyperproliferation, glomerular capillary hyperplasia, and interstitial infiltration of mononuclear cells. Tregs from Srsf1-cko mice are dysfunctional and are unable to suppress colitis in vivo. These results indicate that a lack of SRSF1 selectively in T cells, leads to impaired T cell function with reduced IL-2 production, increased inflammatory cytokine production, and aberrant Treg function, resulting in autoantibody development and tissue damage.
Conclusion: SRSF1 is a novel regulator of T cell function, and its deficiency leads to autoimmunity and lupus-like nephritis. Therefore, deficiency of SRSF1 in T cells may represent a molecular defect that contributes to the pathogenesis of systemic autoimmune disease.

Disclosure: V. R. Moulton, None; T. Katsuyama, None; H. Li, None; M. W. Mosho, None; A. R. Gillooly, None; G. C. Tsokos, GSK, 5.


Abstract Number: 2570

The Functional Consequence of Human (hu)TLR8 on Macrophage Immunometabolism and Renal Inflammation in Murine Systemic Lupus Erythematosus

Naomi I. Maria1, Megan Woods2, Shani Martinez3, Weiqing Huang4 and Anne Davidson4, 1Center for Autoimmune and Musculoskeletal Diseases, Feinstein Institute for Medical Research, Manhasset, NY, 2Center for Autoimmunity and Musculoskeletal Diseases, Feinstein Institute for Medical Research, Manhasset, NY, 3Feinstein Institute for Medical Research, Manhasset, NY, 4Autoimmunity and Musculoskeletal Diseases, Feinstein Institute for Medical Research, Manhasset, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Animal Models Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Infiltrating macrophages are one of the hallmarks of renal inflammation and kidney damage in lupus nephritis. Increasing evidence suggests the crucial role of cell-specific metabolic reprogramming to regulate and modify inflammatory and immune responses. Inflammatory M1-like [TLR4/LPS] macrophages show enhanced glycolysis – which directly drives their inflammatory phenotype – and impaired oxidative phosphorylation (OXPHOS). In contrast, OXPHOS is prominent in tolerogenic M2-like [IL-4] macrophages. Using a systems approach we recently integrated immunologic and molecular profiles of murine LN kidney macrophages with human SLE renal biopsies, identifying shared pathways that link phagocytosis with disposal of excess cellular debris, activation of TLRs and metabolic pathways. Surprisingly, we observed overexpression of TLR8, but not other endosomal TLRs, in these resident renal macrophages. TLR8 overexpression was also detected in lupus nephritis kidneys. TLR8 is expressed primarily by myeloid cells; its role in systemic autoimmunity, and on macrophage immunometabolism, remains elusive as TLR8 function differs from mouse to man. Mice transgenic for multiple copies of human TLR8 develop spontaneous autoimmunity but do not reflect normal physiology. Herein, we aimed to evaluate the functional consequence of one or two copies of human (huTLR8) on macrophage immunometabolism and renal inflammation in murine SLE.

Methods: NZW/B6.Yaa and Sle1.Yaa mice expressing huTLR8 as a BAC transgene (huTR8tg) were generated and followed clinically. HuTLR8 DNA copy number and mRNA expression was confirmed by qDigital and qRT-PCR respectively. 24-week-old huTLR8tg NZW/B6.Yaa mice were administered TL-506 (TLR8-agonist) subcutaneously for 4 weeks and spleen and kidney were harvested for analysis at 8 weeks. Using the Seahorse XF Analyzer, mitochondrial respiration and glycolytic capacity of LPS(TLR4)-, TLR7- and TLR8-stimulated bone marrow-derived macrophages (BMDMs) was assessed.
**Results:** TL-506-stimulated BMDMs from huTLR8tg mice show enhanced TNF production and glycolysis and impaired mitochondrial respiration compared to wild-type littermates, which was comparable to the profiles observed for LPS- and TLR7-stimulated wt BMDMs. A single copy of huTLR8 in NZW/B6.Yaa mice did not exacerbate/accelerate disease however subcutaneous TLR8-agonist administration appeared to enhance germinal center formation and plasma cell generation in male huTLR8tg mice. To generate lupus mice with 2 copies of huTLR8 we bred the huTLR8tg into the Sle1.Yaa strain. Preliminary findings in these mice show accelerated renal disease and mortality in the males.

**Conclusion:** One copy of huTLR8 does not seem to exacerbate lupus in NZW/B6.Yaa mice but disease is enhanced by a TLR8 agonist or by the introduction of two copies of the transgene. Interestingly, TLR8-stimulated huTLR8tg BMDMs have a similar immunometabolic profile to LPS-[M1-like] and TLR7-induced macrophages. Further elucidating how TLR8 influences macrophage immunometabolism and phenotype will improve our understanding in how reprogramming macrophage metabolic state might be a potential new avenue of therapeutic targeting in systemic autoimmunity.

**Disclosure:** N. I. Maria, None; M. Woods, None; S. Martinez, None; W. Huang, None; A. Davidson, None.


**Abstract Number:** 2571

**IL23 Deficiency Alters Thymic Selection in Lupus Prone Mice**

**Hoang Dai** and Vasileios C. Kyttaris, 1Rheumatology, BIDMC, Boston, MA, 2Rheumatology, Beth Israel Deaconess Medical Center, Boston, MA

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Tuesday, November 7, 2017
**Session Title:** Systemic Lupus Erythematosus – Animal Models Poster
**Session Type:** ACR Poster Session C
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** We have previously reported that IL-23 receptor deficiency in MRL. *lpr* mice ameliorates lupus by altering the balance of pro- and anti-inflammatory cytokines in secondary lymphoid organs. As IL-23 also may also impact thymic selection, we evaluated the effect of IL-23 on thymic selection in lupus prone mice.

**Methods:** We generated MRL. *lpr* mice that lack the IL-23p19 subunit by backcrossing with a B6.II23p19 deficient mice for 11 generations. Thymic tissue was harvested from 6-8 week old mice and used for flow cytometry.

**Results:** IL23p19−/−MRL. *lpr* mice had decreased proteinuria when compared to wild type mice. IL-23p19 deficiency resulted in reduced expression of both IL-7Ra and RORγt in thymocytes. This was associated with reduction of CD3 and TCRβ expression on thymocytes by 35% and 50% respectively. Overall IL-23p19−/−MRL. *lpr* mice had as much as 50% reduction in cells that underwent positive selection. On the contrary IL23p19 deficiency did not affect T cells lineage commitment, nor changed CCR7 expression, a major determinant of cortex-medulla intra-thymic migration. The resulting, post positive and negative selection, T lymphocytes in IL23p19 deficient mice displayed an immature phenotype as measured by CD44 and CD62L expression in both thymus and spleens.

**Conclusion:** IL-23 deficiency in lupus prone mice strongly influences thymic selection resulting in T lymphocytes exiting the thymus with an immature phenotype. We propose that IL-23 not only promotes the development of lupus like autoimmunity through T cell polarization and cytokine production in the peripheral lymphoid organs but also by influencing T cell selection in the thymus.
Rab4a Control over Glycolytic Metabolism and T-Cell Lineage Specification Protects from Intra-Alveolar Hemorrhage in Mouse Model of SLE

Nick Huang1, Zachary Oaks2, Sarah Blair2, Thomas Winans2, Zhi-Wei Lai1, Katalin Banki3 and Andras Perl1,
1Medicine, SUNY Upstate Medical University, Syracuse, NY, 2SUNY Upstate Medical University, Syracuse, NY, 3Clinical Pathology, SUNY Upstate Medical University, Syracuse, NY
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Animal Models Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Systemic lupus erythematosus (SLE) is a potentially fatal autoimmune disease that involves all organs of the body. Without a known cure, a detailed understanding of pathogenesis is vital for development of new treatments. The polymorphic Rab4a locus has been associated with genetic susceptibility and protection from lung disease in patients with SLE (Arthritis Rheum 58: 532-540). Rab4a is overexpressed in T cells of patients and mice with SLE (J Immunol 182: 2063-73). To determine the role of Rab4a in pathogenesis, its impact on intra-alveolar hemorrhage (IAH), a fatal complication of pulmonary involvement, was investigated in Rab4A-KOCD4Cre (KO) mice lacking expression of Rab4a in T cells relative to wild-type (WT) controls. Additionally, the role of Rab4a in T-cell lineage specification and underlying metabolic pathways was investigated in mice and human T-cell lines with modulated Rab4a activity.

Methods:
Mice matched for age and gender were injected intraperitoneally with 0.5 ml per 20 g of body weight of pristane and evaluated for pulmonary capillaritis. 14 days after injection, spleen and lung tissues were harvested and examined for lineage specification within the adaptive and innate arms of the immune system by flow cytometry. CD4+CD25+ T cells were analyzed for regulatory T cell (Treg) function. Metabolic studies were completed using the Seahorse Metabolic Flux Analyzer.

Results:
Pulmonary vasculitis scores were increased in Rab4A-KOCD4Cre mice relative to WT controls, which was underlain by 5.7-fold (p=0.0003) expansion of Gr-1+ neutrophils in the lung of KO mice. Among infiltrating T lymphocytes, CD4+ cells were increased by 42% (p=0.0018) and CD8+ cells were depleted by 45% (p=0.0037). T111 cells, CD4+CD25+ and CD8+CD25+ Tregs were expanded by 9.4-fold (p=0.002), 4.6 fold (p=0.0009) and 2.6-fold (p=0.017), respectively. mTORC1 activities were decreased in all CD4+ T cells and CD4+CD25+ Tregs of the KO mice by 45% (p=0.01) and 29% (p=0.027), respectively. CD4+CD25+ FoxP3+/Akt+ Tregs were depleted by 45% (p=0.02). The suppressor activity of CD4+CD25+ Tregs was diminished 3.8-fold (±0.05, p=0.04) in KO mice. Glycolysis in CD4+ T111 cells and Tregs of
Rab4A-KO^{CD4Cre} mice was diminished by 27% (p=0.02) and 35% (p=0.029). Along this line, glycolysis was also reduced by 22% in Jurkat T cells overexpressing dominant negative Rab4a^{S27N} (p=0.004). In contrast, overexpression of wild-type Rab4a enhanced glycolysis in Jurkat cells by 72% (p=5.41E-06). 1 mg/kg of rapamycin, which blocked nephritis in lupus-prone mice (Ann Rheum Dis 73: 1888-97), failed to prevent pristane-induced IAH.

**Conclusion:**

Rab4a controls metabolic fitness and mTORC1-dependent expansion and function of Tregs, and thus it protects against IAH in a mouse model of SLE.

---

**Disclosure:** N. Huang, None; Z. Oaks, None; S. Blair, None; T. Winans, None; Z. W. Lai, None; K. Banki, None; A. Perl, Pfizer, 2.


**Abstract Number:** 2573

**Lack of CD137-CD137 Ligand Signalling Aggravates Glomerulonephritis and Reduces the Survival of Lupus-Prone B6.MRL{lpr} Mice**

Anselm Mak\(^1\), Bhushan Dharmadhikari\(^2\) and Herbert Schwarz\(^2\), \(^1\)Medicine, National University of Singapore, Singapore, Singapore, \(^2\)Physiology, National University of Singapore, Singapore, Singapore

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Systemic Lupus Erythematosus – Animal Models Poster

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Costimulatory molecules, which are expressed on leukocytes that facilitate their cross-talks via stimulatory and inhibitory signalling, play a potentially important role in the inflammatory processes involved in SLE. Disappointment in clinical trials which tested the efficacy and safety of costimulatory molecule manipulation in SLE treatment prompts more in-depth understanding of the mechanistic impact of costimulatory molecules on the pathophysiology of SLE. We aimed to investigate the effect of the lack of CD137-CD137 ligand (CD137L) signalling in the phenotype and immunological profiles in a murine SLE model, based on our understanding that cognate interaction between CD137 expressed on activated T cells and CD137L constitutively present on antigen presenting cells potently drives pro-inflammatory response.

**Methods:** To generate C57BL/6-MRL.Fas\(^{lpr-/-}\) (B6.lpr) lupus-prone mice devoid of CD137L, B6.lpr mice were crossed with B6.CD137L\(^{-/-}\) mice to generate the B6.lpr\(^{-/-}\)CD137L\(^{-/-}\) double knockout (DKO) mice. The DKO and B6.lpr mice were phenotypically and immunologically compared to each other, and to B6 WT mice which served as a reference. Phenotypes including survival, lupus dermatitis by clinical scoring and glomerulonephritis by semi-quantitative urinalyses and light microscopy were compared between the DKO and B6.lpr mice. Frequencies, activation status and Th polarization of splenic T lymphocytes as studied by flow cytometry, and serum cytokine levels as measured by the multiplex platform were compared between the 3 groups of mice.

**Results:** After a 22-month observation, DKO mice (n=226) had significantly shorter survival than B6.lpr mice (n=137) (median ± SE: 44±4.5 vs. 74±3.3 weeks [p<0.001]). Significantly more DKO mice had severe cutaneous lesions, microscopic haematuria and proteinuria than their B6.lpr counterparts. Renal histopathological studies revealed that endocapillary proliferation (2.96±1.08 vs. 0.16±0.1, p=0.013) and glomerular proliferative lesions (33.3% vs. 7.9%,
p = 0.005) were significantly more frequent in the DKO compared to the B6.lpr mice. Furthermore, DKO mice had a significantly higher mean activity index of lupus nephritis (LN) than their B6.lpr counterparts (0.48±0.1 vs. 0.08±0, p=0.002). While significantly higher frequencies of double negative T cells (CD3+CD4-CD8-) and activated T cells (CD3+CD69+), particularly the CD3+CD8+CD69+ population, were found in the B6.lpr mice as compared to the DKO and B6 WT mice, the frequencies of Th17 cells (CD3+CD4+RORγt+[±Tbet+]) were significantly higher in the DKO than the B6.lpr and B6 WT mice. No difference in the frequencies of regulatory T cells (CD3+CD4+CD25+FoxP3+) was found amongst the mice. Cytokine analyses demonstrated significantly lower mean serum IL-10 levels in the DKO mice compared to the B6.lpr and B6 WT counterparts (p=0.017).

**Conclusion:** Abrogation of bidirectional CD137-CD137L signalling which interrupts CD137-CD137L costimulation resulted in more severe dermatitis and LN and reduced survival in the B6.lpr mouse model. More severe SLE phenotype in B6.lpr mice without CD137-CD137L signalling is potentially mediated by Th17 polarization and lower serum anti-inflammatory IL-10 levels.

**Disclosure:** A. Mak, None; B. Dharmadhikari, None; H. Schwarz, None.


**Abstract Number:** 2574

**Interleukin-33 Ameliorates Murine Lupus Via Induction of Regulatory T Cells and M2 Macrophage Polarisation**

**Mo Yin Mok**1, Ka Sin Law2, Wing Yin Kong1, Ge Liu1, Wallace Lau2, C Luo2, FP Huang3, GC Chan4 and Kwok Wah Chan3, 1Department of Biomedical Sciences, City University of Hong Kong, Hong Kong, Hong Kong, 2Department of Medicine, Queen Mary Hospital, Hong Kong, Hong Kong, 3Department of Pathology, University of Hong Kong, Hong Kong, Hong Kong, 4Department of Paediatrics, University of Hong Kong, Hong Kong, Hong Kong

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Systemic Lupus Erythematosus – Animal Models Poster

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

The levels of IL-33, a Th2 promoting cytokine, and the soluble form of its receptor ST2 were reported to be elevated in serum of patients with active systemic lupus erythematosus (SLE), suggesting a role of the IL-33/ST2 axis in the pathogenesis of SLE. This study aims to examine the effect of IL-33 in disease severity of murine lupus.

**Methods:**

IL-33 was injected intraperitoneally 3 times per week to pre-diseased MRL/lpr mice aged 12 weeks for 6 weeks. Control group was given 1% BSA injection. Urine protein was monitored weekly by albustix and protein assay. Immunophenotyping of splenocytes was examined by flow cytometry. Splenic CD11b+ monocytic cells were isolated by microbeads for mRNA examination.

**Results:**
IL-33-treated mice (n=9) developed significantly less proteinuria compared to BSA-treated group (n=9). Kidney histology of the IL-33-treated group showed remarkably less mesangial deposit, diffuse proliferative glomerular changes and crescents, and had significantly lower renal composite score compared to controls (median 2.0 vs 9.9, p<0.001). Kidneys of these mice expressed lower mRNA levels of TNF-α (32.1+14.7 vs 77.0+27.8, p<0.001), IL-6 (median 0.6 vs 4.7, p=0.003), IL-1β (31.1+10.1 vs 77.8+24.6, p<0.001) and iNOS (p=0.006). Immunophenotyping of splenocytes showed significantly increased CD4+CD25+ regulatory T (Treg) cells (4.0+1.2% vs 2.2+0.2%, p<0.001) that expressed remarkably higher Foxp3 (76.0+5.0% vs 59.3+12.6%, p=0.002). Splenic extracts showed predominant Gata3 (0.37+0.2 vs 0.12+0.09, p=0.01) and Foxp3 (0.42+0.16 vs 0.17+0.11, p=0.002) mRNA in IL-33-treated mice. These Treg cells expressed high cell surface ST2 (8.9+2.7% vs 4.5+2.0%, p=0.008). There was significant expansion of splenic CD11b+ population in IL-33-treated mice (17.8+10.5 vs 8.8+3.0, p=0.01) with reduced expression of iNOS (p=0.02). Kidney extracts of IL-33 treated mice also had elevated mRNA levels of M2 markers including Arg1 (median 199.8 vs 36.1, p=0.004) and FIZZI (median 25.0 vs 2.7, p<0.001) and reduced MCP-1 (12.7+6.5 vs 35.1+12.0, p<0.001). There was also significantly higher levels of mRNA of Foxp3 (median 43.0 vs 20.8, p=0.006) and Gata 3 (1.7+0.5 vs 0.9+0.5, p=0.008) but lower Rorc (2.6+1.0 vs 3.8+0.8, p=0.008) and Tbx21 (12.6+6.0 vs 29.6+13.7, p=0.003) in the kidneys.

Conclusion: Exogenous IL-33 led to significantly less proteinuria and renal inflammation. These mice had significantly higher splenic Treg cells with prominent Foxp3 expression. Isolated CD11b+ cells from spleen and kidney extracts demonstrated mRNA levels of M2 macrophage polarisation.

Disclosure: M. Y. Mok, None; K. S. Law, None; W. Y. Kong, None; G. Liu, None; W. Lau, None; C. Luo, None; F. Huang, None; G. Chan, None; K. W. Chan, None.

Abstract Number: 2575

The Role of Interferon in Autoimmune-Susceptible Ro60 Knockout Mice

Masaoki Kawasumi1, Daiki Rokunohe1, Edward Chiou2, Xizhang Sun2, Lena Tanaka2, Sandra L. Wolin3 and Keith B. Elkon4, 1Medicine/Dermatology, University of Washington, Seattle, WA, 2Medicine/Rheumatology, University of Washington, Seattle, WA, 3RNA Biology Laboratory, National Cancer Institute, Frederick, MD, 4Division of Rheumatology, Department of Medicine, University of Washington, Seattle, WA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Animal Models Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The Ro60 protein is a prominent autoantigen in systemic lupus erythematosus (SLE) and Sjogren’s syndrome (SS). Anti-Ro antibodies are strongly associated with UV-mediated skin rashes in lupus, especially in subacute cutaneous lupus erythematosus (SCLE), the most photosensitive form of lupus. Surprisingly, Ro60 knockout (KO) mice spontaneously develop a lupus-like syndrome associated with autoantibodies and glomerulonephritis. An association with type I interferon (IFN) has not previously been investigated. While it is known that Ro binds to small non-coding Y RNAs, it was recently reported that Ro also binds to Alu RNAs derived from short interspersed retroelements (SINEs). Loss of Ro60 in human cell lines resulted in the accumulation of Alu RNAs and the
dysregulation of IFN-stimulated genes (ISGs). Since SINE transcripts have been shown to be increased following DNA damage, we examined the relationship between Ro60, SINEs, and the inflammatory response after UV irradiation in mice.

**Methods:** C57BL/6 and Ro60 KO mice (n = 3) were irradiated with UVB 500 mJ/cm² once. Skin biopsies were performed at baseline and 1 day following UVB exposure. RNA was extracted from the skin, and RNA expression of retroelements [B1 and B2 SINEs (rodent equivalents of human Alu)], inflammatory markers including type I IFNs, ISGs and Y RNAs were quantified by RT-qPCR.

**Results:** At baseline, Ro60 KO mice exhibited increased expression of ISGs compared to C57BL/6 mice with a 7-fold increase found in Isg15, 4-fold increase in Isg20, and 18-fold increase in Mx1. Y1 and Y3 RNAs were virtually undetectable in Ro60 KO mice even after UVB irradiation. This supports the current theory that Ro60 is involved in RNA processing and quality control including the stabilization of RNA polymerase III transcripts as seen with La protein. While B1 and B2 SINEs were not elevated in Ro60 KO mice compared to C57BL/6 mice at baseline, SINEs were increased in both Ro60 KO and C57BL/6 mice after UVB. These results are consistent with the possibility that retroelements play a role in the inflammatory response following UVB irradiation, although a causal relationship remains to be determined.

**Conclusion:** Increases in ISGs observed at baseline in Ro60 KO mice compared to control C57BL/6 mice may contribute to autoimmunity and lupus-like syndrome reported previously. Furthermore, the accumulation of SINE transcripts after UV irradiation may overwhelm the binding capacity of Ro60, leading to stimulation of innate immune response. A clearer understanding of the relationship between autoimmunity in Ro60 KO mice and changes in the relative amounts of SINEs versus Ro60 protein could provide a new paradigm of how environmental stimuli trigger lupus.

**Disclosure:** M. Kawasumi, None; D. Rokunohe, None; E. Chiou, None; X. Sun, None; L. Tanaka, None; S. L. Wolin, None; K. B. Elkon, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-role-of-interferon-in-autoimmune-susceptible-ro60-knockout-mice

**Abstract Number:** 2576

**Caspase 8 in Dendritic Cells Suppresses IRF5 Activation through Endosomal TLR Signaling to Prevent SLE-like Disease**

FuNien Tsai1, Harris Perlman2 and Carla Cuda2, 1Medicine-Rheumatology, Northwestern University-Feinberg School of Medicine, Chicago, IL, 2Department of Medicine Division of Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Systemic Lupus Erythematosus – Animal Models Poster

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Previous studies implicate dendritic cells (DCs) in the pathogenesis of systemic lupus erythematosus (SLE), yet the mechanisms underlying this involvement are not yet clear. Genome-wide association studies and experimental mouse models provide evidence of toll-like receptor (TLR) involvement in SLE. Immune complexes containing self nucleic acids activate endosomal TLRs 7/9, which require signaling adaptor MyD88 for subsequent up-regulation of proinflammatory gene expression, in part through the action of transcription factor IRF5.
Functional polymorphisms in TLRs 7/9, MyD88 and IRF5 are linked to SLE susceptibility, and mice with an underlying defect in Fas (MRL/lpr) on a TLR7-, MyD88- or IRF5-deficient background are protected from disease. We have shown that DC-specific loss of caspase 8, an enzyme in the Fas pathway classically linked to programmed cell death, induces a SLE-like disease that originates from heightened DC activation. The increased activation of caspase 8-deficient DCs is in part controlled by a MyD88-dependent mechanism, as DC-specific loss of MyD88 reduces disease. We therefore examined the interaction between DC-specific caspase 8, endosomal TLR signaling and IRF5 in disease development.

Methods: Mice lacking caspase 8 specifically in DCs were generated (CreCD11cCasp8flox/flox) and crossed with TLR7−/−TLR9−/− (TLR7−/−TLR9−/−CreCD11Casp8flox/flox), TRIFmut/mutMyD88flox/flox (TRIFmut/mutMyD88flox/floxCreCD11Casp8flox/flox) and IRF5flox/flox (IRF5flox/floxCreCD11Casp8flox/flox) mice. Flow cytometric analysis was used to characterize cell populations. ELISA and Luminex bead-based assays detected serum antibody and cytokine levels. Immunohistochemical and immunofluorescent analyses were used to evaluate spleen and kidney pathology.

Results: CreCD11Casp8flox/flox develop a SLE-like disease characterized by splenomegaly, lymphadenopathy, autoantibodies, elevated serum cytokines, glomerulonephritis, immune complex deposition in the kidney and proteinuria. Caspase 8-deficient DCs are highly activated, leading to lymphocyte hyperactivation in a paracrine manner. Further, we observe a disruption of the splenic architecture in CreCD11Casp8flox/flox mice, with a severe reduction in the marginal zone and metallophilic macrophage populations. Moreover, kidney pathology correlates with increased influx of myeloid populations. Strikingly, TLR7−/−TLR9−/−CreCD11Casp8flox/flox, TRIFmut/mutMyD88flox/floxCreCD11Casp8flox/flox and IRF5flox/floxCreCD11Casp8flox/flox mice are virtually protected from all inflammatory phenotypes.

Conclusion: Our previous studies showed that DC-specific loss of MyD88 reduced, but not ablated, SLE-like disease pathogenesis associated with DC-specific deletion of caspase 8. We now show that deletion of TLR7/9, TRIF/MyD88 or IRF5 in caspase 8-deficient DCs prevents SLE-like disease in CreCD11Casp8flox/flox mice. These data substantiate a novel DC-specific mechanism whereby caspase 8 interacts with and regulates the action of endosomal TLR signaling and IRF5 to control DC activation and subsequent autoimmune disease development.

Disclosure: F. Tsai, None; H. Perlman, None; C. Cuda, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/caspase-8-in-dendritic-cells-suppresses-irf5-activation-through-endosomal-trlr-signaling-to-prevent-sle-like-disease

Abstract Number: 2577

Segmented Filamentous Bacteria Colonization Exacerbate Lupus Nephritis in NZM2410 Mice and Causes an Expansion of Intestinal Group 3 Innate Lymphoid Cells

Giancarlo R. Valiente1, Jeffrey Hampton2, Takuma Wada3, Perry Blough3, William Willis4, Nicholas A. Young4, Lai-Chu Wu5 and Wael Jarjour6, 1Rheumatology & Immunology, The Ohio State University Wexner Medical Center, Columbus, OH, 2Immunology and Rheumatology, The Ohio State University Wexner Medical Center, Columbus, OH, 3The Ohio State University, Columbus, OH, 4Immunology and Rheumatology, The Ohio State University Wexner Medical Center, Columbus, OH, 5Biological Chemistry and Pharmacology, The Ohio State University Wexner Medical Center, Columbus, OH, 6Department of Rheumatology/Medicine, Ohio State University, Columbus, OH

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Animal Models Poster
Session Type: ACR Poster Session C  
Session Time: 9:00AM-11:00AM  

Title: Segmented Filamentous Bacteria Colonization Exacerbate Lupus Nephritis in NZM2410 Mice and Causes an Expansion of Intestinal Group 3 Innate Lymphoid Cells  

Background/Purpose: Innate Lymphoid Cells (ILC3s) represent a newly described innate immune cell with parallel function and phenotype to Th17 cells. ILC3s primarily populate mucosal tissue such as the small intestine and tonsils. ILC3s secrete distinct cytokines such as IL-17, IL-22, and TNF that are thought to play an important role in autoimmunity. Moreover, gut-residing commensals such as Segmented Filamentous Bacteria (SFB) can significantly augment ILC3s and Th17 cells. Furthermore, SFB enhances Th17 cell presence and ILC3 secretion of IL-22 in the intestinal lamina propria of exposed mice. Because these cytokines have been shown to be important in Systemic Lupus Erythematosus (SLE), we examined the effects of SFB on NZM2410 disease phenotype.  

Methods: We examined the presence of ILC3s in the gut of NZM2410 mice with and without intestinal colonization with SFB. Mice were colonized with fecal homogenates containing SFB or no SFB using oral gavage. Serum was collected from mice once per month and Blood Urea Nitrogen was calculated. Upon meeting removal criteria, the kidneys of these mice were processed for immunohistochemistry. Small intestine was digested and then processed for ILC3s and Th17 cells.  

Results: Because of their rarity and lack of source material, SLE mucosal ILC3s are inherently challenging to study in humans. We examined, IIC3 in the mucosa of NZM2410 and utilized SFB to observe any effect that the microbiota may have on mucosal ILC3s in the setting of this mouse model of lupus. We observed that mucosal Th17 and ILC3s were expanded in the small intestine and that kidney damage was exacerbated in SFB exposed mice as compared to unexposed mice.  

Conclusion: These findings support the hypothesis that the microbiota are able to negatively impact lupus clinical course, potentially through activation of ILC3s and Th17 cells and these mechanisms are the subject of ongoing investigations. Moreover, we are examining ILC3-like cells in the peripheral blood of NZM2410 mice and in patients with SLE.  

![Figure 1. The NZM2410 lupus model and exposure to the commensal organism segmented filamentous bacteria (SFB). (A) BUN elevates over the natural lifespan NZM2410 mice. (B) BUN of SFB-exposed mice is elevated as compared to unexposed mice. (C) H&E staining of kidney tissue reveals evidence of mild glomerulonephritis in the unexposed NZM2410 mouse (left) as compared to marked glomerular hypercellularity and interstitial tubulitis in an SFB exposed mouse (right). The same magnification was used in both images.](image-url)
RAB4A Protects from Antinuclear Antibody Production and Nephritis in the Pristane-Induced Model of SLE

Gourav Choudhary¹, Nick Huang², Thomas Winans³, Ryan Kelly⁴, Sarah Blair³, Miguel Beckford³ and Andras Perl²,
¹Department of Biochemistry and Mol. Biology, SUNY Upstate Medical University, Syracuse, NY, ²Medicine, SUNY Upstate Medical University, Syracuse, NY, ³SUNY Upstate Medical University, Syracuse, NY, ⁴SUNY, Syracuse, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Animal Models Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a multisystem chronic inflammatory disease characterized by circulating antinuclear autoantibodies and dysfunction of B cells, T cells, and dendritic cells. Polymorphism of the HRES-1/RAB4 genomic locus has been associated with disease manifestations, such as nephritis, in SLE patients (Arthritis Rheum. 58:532-520), and its Rab4A gene product is overexpressed in T cells of SLE patients and in mice prior to disease onset and, remarkably, inhibition of Rab geranylgeranyl transferase prevented antinuclear antibody (ANA) production and nephritis in lupus-prone mice (Ann. Rheum. Dis. 73:1887-1897). To determine the role of Rab4a in lupus pathogenesis, its impact on ANA production and nephritis was investigated in Rab4A-KO CD4Cre (Rab4AKO) mice lacking expression of Rab4A in T cells relative to wild-type (WT) and floxed Rab4AQ72L knock-in (Rab4AQ72L) controls.

Methods: Four WT, three Rab4AQ72L and four Rab4AKO female mice matched for age were injected intraperitoneally with 0.5 ml per 20 g of body weight of pristane. 14 days after injection, ANA levels were measured in sera by ELISA and immunoglobulin G (IgG) and M (IgM) and complement 3 (C3) deposition as well as infiltration by CD11b+ macrophages, CD11c+ dendritic cells, CD138+ plasma cells, and CD3+ T cells were assessed by immunofluorescence using confocal microscopy. Statistical analyses were performed by t-test; two-tailed p<0.05 was considered significant.

Results: ANA levels were increased in Rab4AKO relative to Rab4AQ72L controls. Deposition of IgG and IgM was increased 2-fold, and C3 deposition was increased 4-fold in glomeruli of Rab4AKO relative to WT and Rab4AQ72L controls. Further, T cells (12-fold), plasma cells (2-fold), and macrophages (7-fold), but not dendritic cells, were accumulated in glomeruli and tubular interstitium of Rab4AKO mice relative to WT and Rab4AQ72L controls.

Conclusion: Based on these results, Rab4A protects against ANA production and nephritis in the pristane-induced model of SLE.
Rock-Mediated Pkca Nuclear Translocation Is Important in Neutrophil Netosis and UVB Induced-Skin Inflammation

Ming-Lin Liu1, Yubin Li2, Meena Sharma3 and Victoria P. Werth4, 1Department of Dermatology, Philadelphia V.A. Medical Center, Philadelphia, PA, 2Dermatology, University of Pennsylvania, Philadelphia, PA, 3Department of Dermatology, Philadelphia V.A. Medical Center, Philadelphia, PA, 4Department of Dermatology, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA

First publication: September 18, 2017

Background/Purpose:

Neutrophils are the most abundant circulating leukocytes and the earliest inflammatory cells to be recruited to the site of photodamage after ultraviolet B (UVB) exposure. However, little is known about the role of the neutrophils in UVB-induced skin inflammation. Neutrophil NETosis is a newly characterized neutrophil cell death that releases neutrophil extracellular traps (NETs), which have been shown to be important in autoimmune inflammation, including lupus. Recent studies from our and other groups indicate the importance of actin cytoskeleton in neutrophil NETosis. Since actin-myosin cytoskeleton is known to be regulated by Rho kinase (ROCK), our recent studies have demonstrated the role of ROCK in PMA-induced neutrophil NETosis in vitro and NETotic neutrophils in UVB-induced skin inflammation in vivo. However it not clear how ROCK and its regulated cytoskeleton is involved in neutrophil NETosis.

Methods:

To explore the effects of ROCK on neutrophil NETosis, we investigated the effects of ROCK inhibition on neutrophil NETosis in vitro in human neutrophils and UVB-induced neutrophil NETosis in the inflamed skin in mice.

Results:

Following PMA stimulation, cytosolic PKCa is gradually translocated to the nuclear membrane. In particular, activated PKCa (phosphor-PKCa at ser657) accumulated at the site of nuclear membrane rupture in the NETotic neutrophils in our confocal analysis. Inhibition of actin, myosin, or MLCK (myosin light chain kinase) of actomyosin networks with cytochalasin D, Blebbistatin, or ML7 can attenuate nuclear translocation of PKCa and neutrophil NETosis. Similarly, the dual ROCK1/2 inhibitor HA1077 attenuated nuclear translocation of PKCa and PMA-induced NETosis. In addition, application of HA1077 intraperitoneally (i.p.) can also reduce UVB-exposure-induced NETosis among the infiltrated neutrophils in the inflamed skin.

Conclusion:

Our preliminary studies therefore elucidated a novel mechanism that ROCK-mediated nuclear translocation of PKCa regulates neutrophil NET formation, and confirmed the protective role of ROCK inhibition in neutrophil NETosis in vitro and in vivo. Our findings may provide insights into a novel therapeutic target for treatment of UVB-induced skin inflammation.
Exploiting Inhibition of PD1 Signaling in a Murine Model of Anti-SSA/Ro Associated Congenital Heart Block

Robert M. Clancy¹, Glenn Fishman¹, Colin Phoon¹, Marc Halushka², Tanisha Jackson¹, Kimberly Robins¹ and Jill P. Buyon¹, ¹NYU School of Medicine, New York, NY, ²Johns Hopkins University School of Medicine, Baltimore, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Animal Models Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The most serious manifestation of fetal exposure to maternal anti-Ro antibodies is the development of heart block. This work addresses the hypothesis that fetal disease occurs in the absence of check point inhibition of inflammation initiated by anti-Ro. This study describes a novel murine model in which deficient PD1 signaling exacerbates mild conduction defects induced by anti-Ro and results in histologic evidence of fibrosis and multinucleated giant cells paralleling observations in human autopsies. Accordingly, these data suggest that checkpoint inhibition may play a role in the pathogenesis of CHB.

Methods: To inhibit PD1 signaling, pregnant wild type CD1 mice treated with anti-CD274 (anti-PD1) Abs, or pregnant PD1 knock out (KO) mice were selected. For both models, mice were injected at E12 and E15 with IgG fractions from either a healthy donor or a mother with anti-52Ro, 60Ro and La (anti-Ro) and 3 children with CHB. As controls, other pregnant CD1 mice received CHB IgG or anti-CD274 Abs alone.

Results: To assure access of autoantibodies to the fetal circulation, blood from embryos (N = 14) dissected from the uterus of a CHB IgG treated pregnant CD1 mouse contained antibody reactivities to all Ro/La components, which were not detected in embryos of mothers injected with control IgG. Exposure of mice to CHB IgG resulted in a prolonged PR interval (5.28 + 0.3, p=0.004 vs control), a result not obtained with anti-PDL1 alone (3.39 + 0.3, p=0.69 vs control). Exposure of CD1 mice to CHB IgG + anti-PDL1 resulted in an even more pronounced conduction defect as reflected by lengthening of the PR interval (PR/√RR, 81 total pups) versus Control IgG (11.3 + 0.2 and 3.4+ 0.1, respectively, p<0.0001). Histology of anti-Ro injected mice showed diffuse positive staining using anti-CD274 Abs (for detection of PDL1 ligand) but not isotype control. Injection of the PD1KO mouse with CHB IgG resulted in the most advanced conduction abnormality as reflected by the PR interval (36 total pups) versus Control IgG (16.24 + 1.56 and 4.55+ 0.11, respectively, p<0.0001). In one of the pups in this group, the block resembled retrograde V-A conduction and the heart removed for histologic evaluation. Consistent with autopsies of human fetuses dying with CHB, there was focal injury with myocyte calcifications, multinucleated giant cells and fibrosis, findings never demonstrated in any previous CHB murine model.

Conclusion: Diminished PD1 signaling exacerbates mild conduction defects induced by anti-Ro/La, which supports the hypothesis that checkpoint inhibitors may play a role in the pathogenesis of CHB.
Safety of Hydroxychloroquine Withdrawal in Older Adults with Systemic Lupus Erythematosus

**Anna Zezon**1, Peter M. Izmirly2, Nicole Bornkamp3, Chung-E Tseng4, H. Michael Belmont3, Anca Askanase5, Jane E. Salmon6, Michael Lockshin7 and Jill P. Buyon3, 1Rheumatology, New York University School of Medicine, Division of Rheumatology, New York, NY, 2New York University School of Medicine, New York, NY, 3Medicine, New York University School of Medicine, New York, NY, 4Rheumatology, New York University School of Medicine, New York, NY, 5Rheumatology, Columbia University College of Physicians & Surgeons, New York, NY, 6Rheumatology, Hospital for Special Surgery, New York, NY, 7Barbara Volcker Center for Women & Rheumatic Disease, Hospital for Special Surgery, New York, NY

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Tuesday, November 7, 2017

Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design

Session Type: ACR Poster Session C

Session Time: 9:00AM-11:00AM

Background/Purpose: Although hydroxychloroquine (HCQ) is a mainstay of treatment for patients with Systemic Lupus Erythematosus (SLE), ocular toxicity can result from accumulated exposure. The introduction of highly sensitive tools has engendered even more concern. As the longevity of patients with SLE improves, additional data will help physicians accurately balance the risk of ocular toxicity and the risk of disease flare, especially in older patients who have stable/quiescent disease. Accordingly, this study was initiated to examine the safety of HCQ withdrawal in older SLE patients.

Methods: Data were obtained by retrospective chart review at three lupus centers. Twenty-seven patients met the following inclusion criteria: ≥ 4 ACR criteria, disease duration ≥ 5 years, HCQ use of 200-400mg per day ≥ 5 years, and discontinuation of hydroxychloroquine at age ≥ 55 years. The comparator group comprised 39 age, gender and racial/ethnic matched patients who remained on HCQ. The primary outcome was a clinically meaningful flare within one year of HCQ withdrawal, defined as moderate or severe, using a revised version of the SELENA-SLEDAI Flare composite that separates mild from moderate flares, evaluates each organ system separately, and incorporates increases in corticosteroid dose and/or addition of immunosuppressive agents. Mild flares were considered secondary outcomes.

Results: Demographics are provided in Table 1. There was a trend toward longer disease duration in the HCQ withdrawal group but no difference in prevalence of prior lupus nephritis between the groups. The reasons for HCQ withdrawal were maculopathy (N=13), presumed/biopsy proven cardiomyopathy (N=2), patient request (N=4), and miscellaneous other reasons (N=8). There was no difference in the primary or secondary outcomes between the groups (Table 1). Two patients had a moderate flare after discontinuing HCQ, of whom one had arthritis treated with methotrexate and one had thrombocytopenia (>30K) and proteinuria of 2 grams/d (baseline 700 mg). Three patients had severe flares while continuing HCQ, of whom two were hospitalized, one for seizures and one for pericarditis; the third had worsening nephritis (urinary protein >4 g/d, requiring treatment). Two patients had moderate flares while remaining on HCQ, one of whom had a rash and arthritis treated with tofacitinib and one a rash treated with prednisone.

Conclusion: In this retrospective study of older patients with SLE on long-term HCQ, withdrawal did not increase the risk of moderate or severe flares. These data provide reassurance regarding the safety of withdrawing HCQ in stable older SLE patients.
<table>
<thead>
<tr>
<th></th>
<th>HCQ Withdrawal (N=27)</th>
<th>HCQ Continuation (N=39)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>59.9</td>
<td>60.6</td>
<td>0.52</td>
</tr>
<tr>
<td>Gender (% Female)</td>
<td>92.6%</td>
<td>97.4%</td>
<td>0.56</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td></td>
<td></td>
<td>0.78</td>
</tr>
<tr>
<td>White</td>
<td>33.3%</td>
<td>35.9%</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>29.6%</td>
<td>25.6%</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>18.5%</td>
<td>20.5%</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>18.5%</td>
<td>17.9%</td>
<td></td>
</tr>
<tr>
<td>Duration of SLE (years)</td>
<td>26.7</td>
<td>21.1</td>
<td>0.087</td>
</tr>
<tr>
<td>(N=61)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of HCQ Use (years)</td>
<td>19.3</td>
<td>17.6</td>
<td></td>
</tr>
<tr>
<td>(N=52)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior Renal Disease (N,%</td>
<td>12 (44.4%)</td>
<td>13 (33.3%)</td>
<td>0.34</td>
</tr>
<tr>
<td>Moderate/Severe Flares (N,%</td>
<td>2 (7.4%)</td>
<td>5 (12.8%)</td>
<td>0.69</td>
</tr>
<tr>
<td>Moderate Flare</td>
<td>2 (7.4%)</td>
<td>2 (5.1%)</td>
<td></td>
</tr>
<tr>
<td>Severe Flare</td>
<td>0 (0%)</td>
<td>3 (7.7%)</td>
<td></td>
</tr>
<tr>
<td>Mild Flare</td>
<td>5 (18.5%)</td>
<td>3 (7.7%)</td>
<td>0.26</td>
</tr>
<tr>
<td>All Flares</td>
<td>7 (25.9%)</td>
<td>8 (20.5%)</td>
<td>0.77</td>
</tr>
</tbody>
</table>

**Disclosure:** A. Zezon, None; P. M. Izmirly, None; N. Bornkamp, None; C. E. Tseng, None; H. M. Belmont, None; A. Askanase, Exagen, 2; J. E. Salmon, None; M. Lockshin, None; J. P. Buyon, None.


**Abstract Number:** 2582

**Compliance and Persistence with Hydroxychloroquine in Patients with Systemic Lupus Erythematosus**

Seong-Min Kweon¹, Seung-Geun Lee², Ji-Heh Park², Eun-Kyoung Park³, Yun-Kyung Kim⁴, Geun-Tae Kim⁵ and Dong Hyun Sohn⁶, ¹Internal Medicine, Pusan National University School of Medicine, Pusan National University Hospital, Busan, South Korea, Busan, Korea, Republic of (South), ²Internal Medicine, Pusan National University School of Medicine, Pusan National University Hospital, Busan, Korea, Republic of (South), ³Division of Rheumatology, Department of Internal Medicine, Pusan National University School of Medicine, Busan, Korea, Republic of (South), ⁴Internal Medicine, Kosin University College of Medicine, Busan, South Korea, Busan, Korea, Republic of (South), ⁵Kosin University College of Medicine, Busan, Korea, Republic of (South), ⁶Microbiology and Immunology, Pusan National University School of Medicine, Yangsan, Korea, Republic of (South)

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM
Compliance and persistence with hydroxychloroquine in patients with systemic lupus erythematosus

**Background/Purpose:** Lifelong treatment with hydroxychloroquine (HCQ) is now recommended for all patients with systemic lupus erythematosus (SLE) irrespective of disease severity or other therapy mainly due to its efficacy in preventing flare, achieving remission and reducing the risk of damage accrual. However, there is lack of data regarding adherence of HCQ treatment in SLE patients. We investigated compliance and persistence with HCQ treatment in SLE patients in clinical practice and analyzed the risk factors for poor adherence.

**Methods:** We conducted a retrospective longitudinal study including 235 SLE patients undergoing HCQ treatment between 2002 and 2016 at a university rheumatology center in South Korea. Compliance was assessed using 1-year medication possession ratio (MPR) and non-compliance was defined as 1-year MPR < 0.8. Persistence was determined as time from HCQ treatment initiation to discontinuation without interruption for longer than 56 days. The reasons for HCQ discontinuation were categorized as poor health literacy, adverse events, pregnancy or unknown factors. Poor health literacy was indicated as the discontinuation of HCQ due to lack of knowledge about its significance in SLE management.

**Results:** Mean age and median baseline SLEDAI-2K of participants were 31.5 years and 8, respectively. Mean 1-year MPR and the frequency of non-compliance were 88.4% and 19.9%, respectively. During the study period, HCQ discontinuation occurred in 115 (48.9%) patients and 1-year, 2-year and 5-year persistence rates were 80, 67.6 and 46.3%, respectively. The most common reason of non-persistence with HCQ treatment was poor health literacy (73%) followed by adverse events (10.4%), unknown factors (10.4%) and pregnancy (6.1%). SLE patients with SLEDAI-2K score < 6 showed significantly worse persistence with HCQ than those with SLEDAI-2K score >= 6, while SLE patients with biopsy-proven lupus nephritis had better HCQ persistence than those without this feature (Fig. 1). SLEDAI-2K score < 6 was a significant risk factor for non-compliance (OR=2.98, p=0.001) and non-persistence (HR=1.55, p=0.046) with HCQ after adjusting confounding factors. In addition, older age was significantly associated with better persistence with HCQ (HR=0.97, p=0.005) and biopsy-proven lupus nephritis had a trend with better HCQ retention (HR=0.66, p=0.076) in multivariable Cox regression model. But, neither HCQ dose nor concomitant immunosuppressive agents showed significant association with HCQ adherence.

**Conclusion:** Overall adherence with HCQ in SLE patients was suboptimal in real practice and SLEDAI-2K score < 6 was a risk factor for poor HCQ treatment adherence. Our data suggest the need to improve adherence with HCQ treatment in SLE patients, especially for those with low disease activity.

**Disclosure:** S. M. Kweon, None; S. G. Lee, None; J. H. Park, None; E. K. Park, None; Y. K. Kim, None; G. T. Kim, None; D. H. Sohn, None.

Effects of Mycophenolate Mofetil (MMF) on Immunogenicity of Ppsv-23 Vaccine in Patients with Systemic Lupus Erythematosus and Other Autoimmune Diseases

Priya Prakash1, Mark Tratenberg2, Slavica Bobic3, Rui Zhang4, Kirk Sperber5, Amy Wasserman6 and Julia Ash7,
1Medicine-Rheumatology, New York Medical College / Westchester Medical Center, Valhalla, NY, 2New York Medical College / Westchester Medical Center, Valhalla, NY, 3Medicine-Rheumatology, New York Medical College / Westchester Medical Center, Valhalla, NY, 4Medicine -Rheumatology, New York Medical College / Westchester Medical Center, Valhalla, NY, 5New York Medical College / Westchester Medical Center, Valhalla, NY, 6Medicine - Rheumatology, New York Medical College / Westchester Medical Center, VALHALLA, NY, 7Medicine -Rheumatology, New York Medical College / Westchester Medical Center, Valhalla, NY

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: MMF suppresses immune function by inhibiting T cell dependent and independent humoral immune responses. This study investigates the humoral immune response to the PPSV23 vaccine by MMF in a larger sample size. Furthermore, this study explores the effect of MMF dose and concurrent steroid use on the anti-pneumococcal antibody responses.

Methods: In this observational cross-sectional study, patients treated with immune suppressive medications who had received PPVS23 were identified and stratified based on receiving MMF or non-MMF immunosuppressants (control group). The humoral response was assessed in both groups using serum IgG titers against 14 pneumococcal polysaccharides (ELISA) as a surrogate marker. The stimulation index (SI) was calculated by dividing the post by the pre immunization titer, which was compared between the MMF and non-MMF groups. The primary endpoints of the study were protective titers of >1.3 µg/ml or either a 4-fold, 3-fold, or 2-fold increase in the SI for 70% of the 14 pneumococcal polysaccharides.

Results: The total study subjects included 39 patients. The MMF group included 23 patients: 21 with SLE, 1 with uveitis, and 1 with DM. The control group included 16 patients: 12 with SLE, 2 with RA, 1 with uveitis, and 1 with PsA. The humoral responses in the MMF group were significantly lower compared to the control group. 40 % of patients in the MMF group vs. 60 % of the control group had protective antibody levels (> 1.3 ug/ml). However, statistically significant differences were only observed in serotypes 51 and 4 (p = 0.05 & p = 0.025). Suppressed antibody responses were observed in the MMF group as defined by a lack of a 4-fold (p = 0.0001), 3-fold (p = 0.001), and 2-fold (p = 0.0163) increase in the SI vs. the control group. 20 %(n=3) of the study group and 50% (n=8) in the control group had more than a 2-fold increase in post-immunization antibody titers to 10 of the 14 serotypes. Patients receiving more than 1.5 g of MMF daily had more suppressed antibody responses defined as a lack of a 4-fold increase (p = 0.04) in the SI compared to patients taking less than 1.5 g of MMF daily. Patients in both the MMF and control groups received less than 10 mg of prednisone that had no effect on the anti-pneumococcal antibody responses.

Conclusion: This data suggests that humoral responses to pneumococcal polysaccharides are more blunted in patients receiving MMF compared to other immunosuppressants. There was a dose effect of MMF on the humoral response. However, no effect of steroids was observed. Evaluation of post-vaccination humoral immunity should be considered in patients receiving MMF.
Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>MMF</th>
<th>Non-MMF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Patients</td>
<td>23</td>
<td>16</td>
</tr>
<tr>
<td>Female</td>
<td>20</td>
<td>14</td>
</tr>
<tr>
<td>Age (yrs.)</td>
<td>48</td>
<td>49</td>
</tr>
<tr>
<td>Disease Duration (yrs)</td>
<td>3.9</td>
<td>3.2</td>
</tr>
<tr>
<td>SLE</td>
<td>21</td>
<td>12</td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Psoriatic Arthritis</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Dermatomyositis</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Uveitis</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Prednisone -mean</td>
<td>13</td>
<td>7</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>18</td>
<td>7</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Effect of MMF on anti-pneumococcal antibody response

![Graph showing effect of MMF on antibody response]

Disclosure: P. Prakash, None; M. Tratenberg, None; S. Bobic, None; R. Zhang, None; K. Sperber, None; A. Wasserman, None; J. Ash, None.


Abstract Number: 2584

**Apremilast in Patients with Lupus Rashes**

Robert S. Katz, Rush University Medical Center, Chicago, IL

First publication: September 18, 2017
Background/Purpose: Apremilast has been approved by the FDA for treatment of psoriasis and psoriatic arthritis. Because side effects are few, we decided to use it off-label in a number of patients with extensive cutaneous lupus rashes resistant to topical therapy and hydroxychloroquine, and as a steroid-sparing method.

Methods: We describe 6 patients with significant cutaneous lupus. 2 had subacute cutaneous lupus, and 4 had significant cutaneous lupus rashes which were chronic and associated with systemic lupus. All were treated with the topical corticosteroid clobetasol, and sometimes less-potent corticosteroid preparations for facial involvement. 2 patients were taking oral corticosteroids with a dosage range of 5 to 15. All 6 patients were taking hydroxychloroquine, 400 mg per day. The etiology of the rashes was confirmed by skin biopsy and/or Dermatology and Rheumatology clinical agreement. The mean age was 48; age range was 24 to 74. There were 3 men and 3 women.

Results: Of the 6 patients, 4 responded to apremilast, 30 mg bid, with a significant reduction in erythema and the size and extent of lesions within a 1-month period. Patients were satisfied with the amount of clearing of the lupus rash, and no significant side effects were noted. The 2 patients who did not have a significant reduction in their erythema discontinued apremilast after 6 weeks, and were placed on higher doses of steroids to help control their active lupus rash.

Conclusion: Apremilast may be an effective therapy for patients with resistant extensive rashes due to systemic lupus and subacute cutaneous lupus.

Disclosure: R. S. Katz, None;


Abstract Number: 2585

Safety Profile in SLE Patients Treated with Atacicept in a Phase IIb Study (ADDRESS II) and Its Extension Study

Joan T. Merrill1, Daniel J. Wallace2, Cristina Vazquez-Mateo3, Amy H. Kao3, Patricia Fleuranceau-Morel3, Peter Chang4 and David A. Isenberg5, 1Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 2Cedars-Sinai Medical Center, UCLA, Los Angeles, CA, 3EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA, 4EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA, 5Centre for Rheumatology Research, University College London, London, England

First publication: September 18, 2017
**Background/Purpose:** Atacicept targets the B-cell stimulating factors, BLyS and APRIL, and has demonstrated a clinical response in SLE patients (pts) with high disease activity (HDA; SLEDAI-2K ≥10) at Screening in the Phase IIb ADDRESS II study.

**Methods:** In ADDRESS II (NCT01972568), pts received weekly atacicept (75 or 150 mg SC injection) or placebo (PBO) for 24 weeks (wks) (1:1:1 randomization). Those who completed treatment were eligible to enter a long-term extension (LTE), to either continue on the same atacicept dose (atacicept groups), or switch from PBO to atacicept 150 mg (PBO/150 mg). The LTE primary objective was to determine the long-term safety and tolerability of atacicept in SLE pts. Current cumulative safety results from ADDRESS II and the LTE are reported here.

**Results:** Of the 306 pts in ADDRESS II, 253 (95% of completers) entered the LTE, of which 132 (52%) had HDA. By 48 wks (from start of Day 1 in ADDRESS II), most pts had ≥1 treatment-emergent adverse event (TEAE), with a slight increase in the atacicept groups vs PBO/150 mg. Herpes zoster incidence was low. Only one patient with asthma and allergic rhinitis on chronic inhaled corticosteroids developed a non-serious opportunistic infection (candida esophagitis, grade 1), which resolved with oral anti-fungal treatment. The most frequent serious TEAEs were infections (Table 1). There was no increase in the atacicept groups vs PBO/150 mg in the incidence of serious infections or exposure-adjusted annualized rates of serious/severe infections in the modified intention to treat population (Table 2) or the HDA subpopulation (data not shown). Serious/severe infections in the PBO/150 mg group occurred more frequently during the PBO-treatment period (15/18 [83%]). Serum IgG reductions (including IgG <3 g/L) were not associated with infections. Four pts in the atacicept 150 mg group developed IgG < 3 g/L after 36 wks of treatment, which resolved without treatment discontinuation; 1 patient in the atacicept 75 mg group developed IgG <3 g/L after treatment discontinuation due to lupus nephritis flare. No safety new signals were identified. The two deaths reported in the LTE occurred after 48 wks; overall exposure-adjusted mortality rate of atacicept treatment was 0.57 /100 pt-years.

**Conclusion:** Cumulative data demonstrate an acceptable safety profile for atacicept, with no increased risk of serious/severe infections, or mortality. This was also seen in the HDA subpopulation, in which a greater atacicept treatment effect has been observed. IgG decreases were not associated with infections but should continue to be monitored.
Table 1. Summary of Cumulative Treatment Emergent Adverse Events in ADDRESS II and LTE by 48 weeks (mITT)

<table>
<thead>
<tr>
<th>Adverse events, n (%)</th>
<th>PBO/150 mg* (n=100)</th>
<th>Atacicept 75mg (n=102)</th>
<th>Atacicept 150mg (n=104)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any TEAEs</td>
<td>82 (82.0)</td>
<td>88 (86.3)</td>
<td>90 (86.5)</td>
</tr>
<tr>
<td>TEAEs leading to treatment discontinuation</td>
<td>9 (9.0)</td>
<td>7 (6.9)</td>
<td>8 (7.7)</td>
</tr>
<tr>
<td>Infections and infestations</td>
<td>53 (53.0)</td>
<td>55 (53.9)</td>
<td>64 (61.5)</td>
</tr>
<tr>
<td>Herpes zoster</td>
<td>1 (1.0)</td>
<td>0 (0.0)</td>
<td>2 (1.9)</td>
</tr>
<tr>
<td>Influenza</td>
<td>1 (1.0)</td>
<td>4 (3.9)</td>
<td>4 (3.8)</td>
</tr>
<tr>
<td>Serious TEAEs</td>
<td>16 (16.0)</td>
<td>12 (11.8)</td>
<td>11 (10.6)</td>
</tr>
<tr>
<td>Serious/severe infections</td>
<td>7 (7.0)</td>
<td>7 (6.9)</td>
<td>6 (5.8)</td>
</tr>
<tr>
<td>Death</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

PBO, placebo; TEAE, treatment-emergent adverse event; LTE, long-term extension; mITT, modified intention to treat.

*Patients receiving PBO in ADDRESS II who entered LTE at Week 24 switched immediately to atacicept 150 mg.

Table 2. Exposure-Adjusted Annualized Rate of Serious/Severe Infections in ADDRESS II and LTE by 24-Week Intervals (mITT)

<table>
<thead>
<tr>
<th>ADDRESS II (24 weeks)</th>
<th>PBO (n=100)</th>
<th>Atacicept 75 mg (n=102)</th>
<th>Atacicept 150 mg (n=104)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects with serious/severe infections, n (%)</td>
<td>7 (7.0)</td>
<td>9 (8.8)</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Total number of serious/severe infections</td>
<td>15</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>Annualized rate (95% CI)*</td>
<td>0.35 (0.21, 0.58)</td>
<td>0.23 (0.12, 0.43)</td>
<td>0.09 (0.03, 0.23)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LTE (24 weeks)</th>
<th>Switched to 150 mg (n=83)</th>
<th>Atacicept 75 mg (n=82)</th>
<th>Atacicept 150 mg (n=81)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects with serious/severe infections, n (%)</td>
<td>2 (2.4)</td>
<td>2 (2.4)</td>
<td>5 (5.7)</td>
</tr>
<tr>
<td>Total number of serious/severe infections</td>
<td>3</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Annualized rate (95% CI)*</td>
<td>0.08 (0.02, 0.24)</td>
<td>0.05 (0.01, 0.20)</td>
<td>0.14 (0.06, 0.32)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PBO/150 mg* (n=100)</th>
<th>Atacicept 75 mg (n=102)</th>
<th>Atacicept 150 mg (n=104)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects with serious/severe infections, n (%)</td>
<td>9 (9.0)</td>
<td>11 (10.8)</td>
</tr>
<tr>
<td>Total number of serious/severe infections</td>
<td>18</td>
<td>12</td>
</tr>
<tr>
<td>Annualized rate (95% CI)*</td>
<td>0.22 (0.14, 0.36)</td>
<td>0.15 (0.08, 0.26)</td>
</tr>
</tbody>
</table>

CI, confidence interval; PBO, placebo; LTE, long-term extension; mITT, modified intention to treat.

The treatment period started with the first dose of study medication [in ADDRESS II or LTE and ended 7 days after the last dose of study medication.

*Patients receiving PBO in ADDRESS II who entered LTE at Week 24 switched from PBO to atacicept 150 mg at Week 24

Table 2. Exposure-Adjusted Annualized Rate of Serious/Severe Infections in ADDRESS II and LTE by 24-Week Intervals (mITT)

Disclosure: J. T. Merrill, Anthera Pharmaceuticals, Lilly, EMD Serono, GlaxoSmithKline and Biogen, 5; D. J. Wallace, EMD Serono, Inc, 5; C. Vazquez-Mateo, EMD Serono, Inc, 3; A. H. Kao, EMD Serono, Inc, 3; P. Fleuranceau-Morel, EMD Serono, Inc, 3; P. Chang, EMD Serono, Inc, 3; D. A. Isenberg, EMD Serono, Inc, 5.


Abstract Number: 2586

Exposure-Response Modelling and Exposure-Safety Modelling Analyses in Two Phase II Studies of Atacicept in SLE
Orestis Papasouliotis, Oezkan Yalkinoglu, Cristina Vazquez-Mateo, Stephen Wax, Amy H. Kao, Peter Chang, Patricia Fleuranceau-morel and Lisa Mahnke, 1Merck KGaA, Darmstadt, Germany, 2EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA, 3EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Atacicept targets the B-cell stimulating factors BLyS and APRIL, and has been shown to reduce SLE disease activity. Our analyses evaluated the exposure-response and exposure-safety relationships for atacicept 75 mg and 150 mg doses.

Methods: APRIL-SLE (NCT00624338) and ADDRESS II (NCT01972568) were phase II, placebo-controlled multicenter studies in patients (pts) with autoantibody-positive SLE. Pts were randomized (1:1:1) to weekly SC injections of atacicept (75 or 150 mg) or placebo (PBO). In APRIL-SLE, pts had BILAG A/B flare at Screening that was reduced to BILAG C/D before randomization using corticosteroids with taper; the primary endpoint was BILAG A/B flare over 52 weeks. In ADDRESS II, pts had SLEDAI-2K ≥ 6 at Screening; the primary endpoint was SRI-4 response at Week 24. SLE responder index (SRI)-6 response was analysed post-hoc in pts with high disease activity (HDA; SLEDAI-2K ≥10). Population pharmacokinetic (PK) model-derived exposure vs the probability of response (BILAG A/B flare, SRI-4, SRI-6), exploratory analysis of exposure vs safety, and population model simulations of serum IgG were analyzed.

Results: Exposure-response modelling suggests a relationship between atacicept exposure and SLE clinical response [Fig. 1], including serum IgG changes from baseline [Fig. 2]. The optimal atacicept exposure was AUC$_{\text{tau,ss}}$ ≥ ~1 mg.hr/mL, which is more achievable with weekly SC doses of atacicept 150 mg than 75 mg across a range of body weights. Body weight-based dosing is unlikely to offer any value over a fixed 150 mg dose, based on comparable predicted clinical response. In HDA pts, serum IgG change from baseline was linked to the probability of SRI-6 response. Greater IgG reductions from baseline were associated with higher atacicept exposure [Fig.2]; however, even at the highest exposure range, mean IgG reductions did not exceed ~ 40%. There was no association between serious/severe infections and exposure by PK quartile.

Conclusion: Exposure-response modelling indicated that there are robust relationships between atacicept exposure and clinical response or IgG levels in SLE pts over time; this supports the proposed mechanism of action for atacicept. Atacicept 150 mg weekly SC is likely to provide an effective level of exposure with an acceptable safety profile. There was no evidence of an increased risk of severe or serious infections at higher exposures. Based on these results, the 150 mg dose merits further evaluation.
Disclosure: O. Papasouliotis, Merck KGaA, 3; O. Yalkinoglu, Merck KGaA, 3; C. Vazquez-Mateo, EMD Serono, Inc, 3; S. Wax, EMD Serono, Inc., 3; A. H. Kao, EMD Serono, Inc, 3; P. Chang, EMD Serono, Inc, 3; P. Fleuranceau-
KZR-616, a Selective Inhibitor of the Immunoproteasome, Shows a Promising Safety and Target Inhibition Profile in a Phase I, Double-Blind, Single (SAD) and Multiple Ascending Dose (MAD) Study in Healthy Volunteers

Jason Lickliter¹, Janet Anderl², Christopher J Kirk³, Jinhai Wang⁴ and Darrin Bomba⁵, ¹Nucleus Network, Melbourne, Australia, ²Biology, Kezar Life Sciences, South San Francisco, CA, ³Kezar Life Sciences, South San Francisco, CA, ⁴DMPK, Kezar Life Sciences, South San Francisco, CA, ⁵Clinical Operations, Kezar Life Sciences, South San Francisco, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Proteasome inhibition is a standard of care for plasma cell malignancies. The first-generation inhibitor, bortezomib (BTZ), targets the constitutive proteasome and immunoproteasome and has been used in the treatment of Systemic Lupus Erythematosus and lupus nephritis (LN). However, BTZ therapy is associated with hematologic (thrombocytopenia, anemia, neutropenia) and constitutional (fatigue, peripheral neuropathy) adverse events (AEs). We report here the safety, pharmacokinetics (PK) and pharmacodynamics (PD) of KZR-616, a first-in-class selective inhibitor of the immunoproteasome, in healthy volunteers (HV) following single or repeat subcutaneous (SC) or single intravenous (IV) administration (ACTRN12616001040459).

Methods:
Cohorts of HV (6 drug:2 placebo) received single SC or IV (30-minute infusion) doses or 4 weekly SC doses. Safety assessments, PK and PD were measured to Day 7 (SAD) or Day 28 (MAD). SAD cohorts included 7.5, 15, 30 and 60 mg (SC) and 7.5 and 15 mg (IV). MAD cohorts (all SC) included 30, 45, 60 mg and 2 intrasubject escalation cohorts with 1 dose at 30 mg and 3 subsequent doses at 45 mg. PK was measured by LC/MS². PD was measured using enzymatic and active site binding assays.

Results:
42 HV (31:11) were enrolled in 6 SAD cohorts. The most common AEs with SC administration were injection site reactions (ISRs), which were generally mild and transient. No clinically-significant laboratory or ECG abnormalities or dose limiting toxicities were observed in the SAD subjects.

Following SC administration, drug exposure increased dose proportionally and was characterized by rapid absorption (Tₘₐₓ 15 – 30 minutes) and clearance (T₁/₂ ~2 hours). SC bioavailability was ~100%. Dose dependent and selective
inhibition of the immunoproteasome exceeded 80% at ≥ 30 mg with significant recovery noted over 7 days. Constitutive proteasome inhibition was <37% in all cohorts.

40 HV (30:10) were enrolled in 5 SC MAD cohorts. In the initial cohort of 60 mg, an infusion reaction-like syndrome (chills, elevated heart rate, nausea) occurred ~8 hours after the first dose in 4 subjects. Further dosing in this cohort was withheld. Subsequent MAD cohorts (initiated at 30 mg) received prophylactic treatment with antihistamines +/- prednisone 1 hour prior to the first and second dose. No similar AEs occurred with repeat dosing of 30 or 45 mg. No clinically-significant laboratory or ECG abnormalities were seen in the remaining 4 MAD cohorts. ISRs did not increase in severity or frequency with repeat SC dosing, there were no AEs of peripheral neuropathy or infection, and 45 mg was well tolerated across 3 cohorts.

Consistent PK was noted following repeat administration and no drug accumulation was observed. At 45 mg, inhibition of 2 key subunits of the immunoproteasome, LMP7 and LMP2, was ~95% and ~70%, respectively.

Conclusion:

KZR-616 was well tolerated in HV and demonstrated consistent PK and PD. Selective immunoproteasome inhibition did not induce hematologic or constitutional toxicities associated with dual proteasome inhibitors. This study has identified candidate doses of KZR-616 to explore the safety, tolerability and efficacy of KZR-616 in patients with rheumatic diseases, such as LN, in an upcoming Phase 1b/2 study.

Disclosure: J. Lickliter, Kezar Life Sciences, 5; J. Anderl, Kezar Life Sciences, 3; C. J. Kirk, Kezar Life Sciences, 3; J. Wang, Kezar Life Sciences, 3; D. Bomba, Kezar Life Sciences, 3.

Abstract: Early Exposure to Hydroxychloroquine Predicts Good Renal Response in Japanese Patients with Lupus Nephritis Class III or IV

Tomofumi Kiyokawa, Hironari Hanaoka, Harunobu Iida, Yukiko Takakuwa and Kimito Kawahata, 1Division of Rheumatology and Allergology, Department of Internal Medicine, St. Marianna University School of Medicine, Kawasaki, Japan, 2Division of Rheumatology and Allergology, Department of Internal Medicine, St. Marianna University School of Medicine, Kawasaki, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The guideline or recommendation for lupus nephritis (LN) has been recently established by both ACR and EULAR, and hydroxychloroquine (HCQ) is recommended for all patients unless there is a contraindication. Although HCQ improves outcomes by reducing renal flares and limiting the accrual of renal damage, its therapeutic effect on renal response has been rarely investigated. In this study, we evaluated its therapeutic effect by focusing on the renal response in Japanese patients with LN class III or IV.
Methods: Patients who were diagnosed as LN class III or IV and treated with mycophenolate mofetil (MMF) as induction therapy were retrospectively investigated. We divided them into two groups according to whether HCQ was received. In this study, we selected patients who were treated with HCQ from early phase of induction therapy, within 4-weeks from high-dose glucocorticoid initiation for HCQ users. Clinical features including renal pathological findings and cumulative complete renal response (CR) were compared.

Results: We identified 7 (38.9%) patients with HCQ and 11 (61.1%) patients without. Although a significantly higher percentage of LN class III was determined in HCQ users comparing to non-HCQ users, there was no other difference in two groups at baseline. A significantly higher cumulative CR rate was detected in HCQ users comparing to non-HCQ users for 1 year (p=0.02) (Figure 1). Multivariate analysis indicated that HCQ use was the independent factor correlated with CR achievement (OR 15.9, 95%CI 1.76-380.1, p=0.02).

Conclusion: HCQ use from early phase of induction therapy may have additional therapeutic effect on renal response in Japanese LN patients with MMF treatment.

Figure 1

![Graph showing cumulative CR rate (%) over weeks]

Disclosure: T. Kiyokawa, None; H. Hanaoka, None; H. Iida, None; Y. Takakuwa, None; K. Kawahata, None.


Abstract Number: 2589

Functional and Mechanistic Characterization of Anifrolumab, a Fully Human Monoclonal Antibody Targeting the Interferon Alpha Receptor 1 for the Treatment of SLE

Gary P. Sims¹, Jeffrey Riggs², Richard Hanna¹, Bhargavi Rajan³, Jodi Karnell¹, Kamelia Zerrouki¹, Divya Sagar¹, Inna Vainshtein³, Erika Farmer¹, Meina Liang³, Miguel A. Sanjuan¹ and Roland Kolbeck¹, ¹Respiratory, Inflammation and Autoimmunity (RIA), MedImmune, LLC, Gaithersburg, MD, ²Respiratory, Inflammation and Autoimmunity (RIA), MedImmune LLC, Gaithersburg, MD, ³MedImmune, LLC, Mountain View, CA, ⁴Analytical Sciences, MedImmune, LLC, Gaithersburg, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Increased type I interferon (IFN) activity is associated with the pathogenesis of SLE. Anifrolumab, a fully human immunoglobulin (Ig) G1 κ monoclonal antibody in clinical development for the treatment of SLE and lupus nephritis, targets the interferon alpha receptor 1 (IFNAR1) and blocks IFNAR1-dependent signaling. Here we characterize the mechanistic and functional properties of anifrolumab.

**Methods:** Binding between anifrolumab and the IFNAR1 was measured by surface plasmon resonance. IFNAR1 internalization on monocytes was assessed by flow cytometry and confocal microscopy. The effect of three mutations in the fragment crystallizable region (Fc) of anifrolumab on Fcγ receptor–dependent cytotoxicity was assessed in antibody-dependent cell-mediated cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC) assays. IFNAR1-dependent signaling induced by recombinant human type I IFN (including IFN-α, -β, and -ω) and by plasmacytoid dendritic cell (pDC)–derived type I IFN was assessed in signal transducer and activator of transcription 1 (STAT1) phosphorylation and IFN-stimulated response element–luciferase reporter assays. Production of IFN-α, TNF, IL-6, and IL-8 by stimulated pDC was measured by enzyme-linked immunosorbent assay or Meso Scale Diagnostics, and expression of cluster of differentiation 80 and 86 was measured by flow cytometry. Expression of type I IFN–regulated genes was measured by quantitative PCR. B-cell differentiation in pDC-/B-cell cocultures was assessed by flow cytometry and Ig production.

**Results:** Anifrolumab blocked type I IFN–dependent IFNAR dimerization and STAT1 phosphorylation with high affinity and specificity. Anifrolumab elicited rapid IFNAR1 internalization and markedly reduced IFNAR1 cell surface levels. Fc mutations on anifrolumab reduced Fcγ receptor–dependent cytotoxicity. Anifrolumab potently inhibited recombinant human type I IFN (including 12 subtypes of α, β, and ω) and pDC-derived type I IFN activities. Anifrolumab suppressed IFN-α, proinflammatory cytokine induction, and upregulation of costimulatory molecules from stimulated pDCs and type I IFN–inducible genes in peripheral blood mononuclear cells. Blockade of IFNAR1 also suppressed plasma cell differentiation and Ig production.

**Conclusion:** Anifrolumab inhibits type I IFN–dependent signaling by sterically inhibiting and rapidly internalizing IFNAR1 on target cells. Anifrolumab has no detectable CDC or ADCC activity. Blockade of type I IFN signaling suppresses pDC functions and B-cell differentiation. Anifrolumab has the potential to be a promising therapeutic agent for treating SLE and other diseases that demonstrate chronic dysfunctional type I IFN signaling.

**Disclosure:** G. P. Sims, MedImmune, LLC, 3,AstraZeneca, 1; J. Riggs, MedImmune, LLC, 3,AstraZeneca, 1; R. Hanna, MedImmune, LLC, 3,AstraZeneca, 1; B. Rajan, MedImmune, LLC, 3,AstraZeneca, 1; J. Karnell, MedImmune, LLC, 3,AstraZeneca, 1; K. Zerrouki, MedImmune, LLC, 3,AstraZeneca, 1; D. Sagar, MedImmune, LLC, 3,AstraZeneca, 1; I. Vainshtein, MedImmune, LLC, 3,AstraZeneca, 1; E. Farmer, MedImmune, LLC, 3,AstraZeneca, 1; M. Liang, MedImmune, LLC, 3,AstraZeneca, 1; M. A. Sanjuan, MedImmune, LLC, 3,AstraZeneca, 1; R. Kolbeck, MedImmune, LLC, 3,AstraZeneca, 1.


**Abstract Number:** 2590

**Subcutaneous Belimumab Plus Standard of Care Demonstrated Improvement in Multiple Organ Domains Versus Placebo Plus Standard of Care in Patients with Active Systemic Lupus Erythematosus (SLE)**

**Andrea Doria**1, Bonnie Pobiner2, William Eastman3, Milena Kurtinecz4, Anne Hammer2, James Groark5 and Damon Bass5, 1Division of Rheumatology, University of Padova, Padova, Italy, 2GSK Research Triangle Park, Research Triangle Park, NC, 3GSK, Research Triangle Park, NC, 4GSK, Philadelphia, PA, 5GSK Collegeville, Collegeville, PA
SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Organ manifestation domain score improvement was assessed with subcutaneous (SC) belimumab (BEL) plus standard SLE care (SoC) in active, autoantibody-positive SLE.

Methods: BLISS-SC (BEL112341; NCT01484496) was a randomized, double-blind, multicenter (177 centers in 30 countries across North, Central and South America, Western and Eastern Europe and Asia) 2-week trial of weekly BEL 200 mg SC or placebo (PBO), plus SoC, in patients with SLE with a SELENA-SLEDAI ≥8 at screening (where randomization to PBO would be to maintain treatment with SoC). The primary endpoint was the SLE Responder Index 4 (SRI4; ≥4-point decrease in SELENA-SLEDAI, <0.3 increase in Physician’s Global Assessment, and no new BILAG A or ≤1 B organ domain scores, from baseline) at Week 52. Efficacy and safety data (including adverse events) have been published1; here, organ-specific responses by BILAG and SELENA-SLEDAI are reported. Analyses included improvements in patients with BILAG baseline A or B scores, measured at each visit (every 4 weeks) between baseline and Week 52 (improvement defined as a shift to B, C, or D; worsening defined as a shift from BILAG E, D, or C to B or A, or from B to A). An increase in total SELENA-SLEDAI domain scores between baseline and Week 52 defined worsening; a decrease defined improvement.

Results: 836 patients comprised the intent-to-treat population. BILAG (Grade A/B) and SELENA-SLEDAI organ system involvement at baseline were similar for both treatment groups, with mucocutaneous and musculoskeletal domains most prominent. The SELENA-SLEDAI immunologic domain was also prominent (not recorded by BILAG).

BEL demonstrated significant improvement versus PBO in the BILAG mucocutaneous, musculoskeletal and vasculitis domains at Week 52 (Table). No statistically significant differences were observed between BEL and PBO for worsening in any BILAG domain. Among patients with baseline SELENA-SLEDAI organ involvement, a statistically significant improvement was observed at Week 52 for BEL versus PBO for the immunologic, mucocutaneous, musculoskeletal, and vascular domains (Table). No statistically significant differences were observed between BEL and PBO for worsening in any SELENA-SLEDAI domain.

<table>
<thead>
<tr>
<th>BILAG</th>
<th>BEL (n=556)</th>
<th>p value</th>
<th>SELENA-SLEDAI</th>
<th>BEL (n=556)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General</strong></td>
<td>22/29 (75.9)</td>
<td>32/39 (82.1)</td>
<td>0.5586</td>
<td>10/18 (55.6)</td>
<td>20/29 (68.9)</td>
</tr>
<tr>
<td>Cardiovascular and respiratory</td>
<td>4/7 (57.1)</td>
<td>7/13 (53.8)</td>
<td>1.0000</td>
<td>Cardiovascular and respiratory</td>
<td>9/25 (36.0)</td>
</tr>
<tr>
<td>Hematologic</td>
<td>33/48 (69.6)</td>
<td>32/91 (35.2)</td>
<td>0.3492</td>
<td>Hematologic</td>
<td>9/25 (36.0)</td>
</tr>
<tr>
<td>Mucocutaneous</td>
<td>88/201 (43.6)</td>
<td>201/368 (55.4)</td>
<td>0.0107</td>
<td>Mucocutaneous</td>
<td>835/248 (54.4)</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>116/209 (55.5)</td>
<td>273/413 (66.1)</td>
<td>0.0110</td>
<td>Musculoskeletal</td>
<td>110/218 (50.5)</td>
</tr>
<tr>
<td>Neurological</td>
<td>0/0 (0.0)</td>
<td>4/4 (100.0)</td>
<td>–</td>
<td>Neurological</td>
<td>1/2 (50.0)</td>
</tr>
<tr>
<td>Renal</td>
<td>19/30 (63.3)</td>
<td>30/53 (56.6)</td>
<td>0.6446</td>
<td>Renal</td>
<td>15/41 (36.6)</td>
</tr>
<tr>
<td>Vasculitis</td>
<td>9/24 (37.5)</td>
<td>35/47 (74.5)</td>
<td>0.0341</td>
<td>Vasculitis</td>
<td>5/18 (27.8)</td>
</tr>
<tr>
<td><strong>Immunologic</strong></td>
<td>34/211 (16.1)</td>
<td>127/427 (29.7)</td>
<td>0.0002</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Conclusion:** Weekly BEL 200 mg SC plus SoC improved organ manifestations in mucocutaneous, musculoskeletal, vascular, and immunologic domains after 52 weeks of therapy, compared with PBO (SoC).


Study funded/conducted by GSK. Medical writing assistance was provided by Louisa Pettinger, PhD, of Fishawack Indicia, funded by GSK.

**Disclosure:** A. Doria, GSK, Pfizer, 8, Italian Association of Lupus Patients, 2, GSK, Pfizer, AstraZeneca, Celgene, Eli Lilly, Baxalta, 5; B. Pobiner, GSK, 1, GSK, 3; W. Eastman, GSK, 1, GSK, 3; M. Kurtinecz, GSK, 1, GSK, 3; A. Hammer, GSK, 1, GSK, 3; J. Groark, GSK, 1, GSK, 3; D. Bass, GSK, 1, GSK, 3.


**Abstract Number:** 2591

**Association of Smoking and Cutaneous Manifestations in Systemic Lupus Erythematosus (SLE): Post-Hoc Results from Phase IIb Studies of Anifrolumab and Sifalimumab**

Victoria P Werth1, Gabor Illei2, Gabriel Abreu3, Liangwei Wang2 and Warren Greth2, 1University of Pennsylvania and the VA Medical Center, Philadelphia, PA, 2MedImmune, Gaithersburg, MD, 3AstraZeneca, Gothenburg, Sweden

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Studies have demonstrated an association between smoking and more severe cutaneous lupus erythematosus, resulting in decreased health-related quality of life and treatment response.1 We analyzed the influence of smoking on cutaneous manifestation severity post hoc in adults with moderate to severe SLE who enrolled in either of two Phase IIb randomized, placebo-controlled studies of anifrolumab or sifalimumab.

**Methods:** Baseline mucocutaneous disease activity in current smokers (stopped for <1 year) and never/past smokers (stopped for >1 year) enrolled in randomized placebo-controlled studies of anifrolumab (NCT01438489; MUSE)2 or sifalimumab (NCT01283139)3 was evaluated by the Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) and SLE Disease Activity Index 2000 (SLEDAI–2K) mucocutaneous descriptors. Disease activity was compared between smoking status-defined subgroups. Smoking status was collected as part of the baseline cardiovascular risk assessment.
**Results:** A total of 736 patients were randomized in both studies. Patients were mostly female (92.8%), with a median age of 39 years and median disease duration of 5.9 years. Baseline CLASI and SLEDAI–2K scores, and smoking status, were available for 729 patients. At baseline, 81.5%, 70.8%, and 44.6% of patients had SLEDAI–2K-defined rash, alopecia, or mucosal ulcers, respectively. Current smokers had significantly greater CLASI activity and damage scores, compared with never/past smokers (table). Where group numbers were large enough to make sufficient evaluations, CLASI activity scores were consistently greater in current smokers irrespective of race, ethnicity, or SLE medication. There was no significant difference in CLASI activity scores between never and past smokers (6.9±5.8, 7.5±6.3, respectively; \( p=0.4857 \)). A significantly greater percentage of current smokers had a moderate or severe rash, defined by CLASI \( \geq 10 \) (\( p<0.0001 \)).

**Conclusion:** Cutaneous disease activity was consistently greater in current smokers compared with never/past smokers, irrespective of race, ethnicity, or SLE medication; this suggests that smoking may actively worsen skin disease. CLASI appears to be a more sensitive measure of inflammatory skin involvement than the SLEDAI–2K mucocutaneous descriptors. As CLASI activity was similar in never/past smokers, smoking cessation should be encouraged in SLE inflammatory skin management.

**References:**

Macrocuteaneous disease activity and smoking status at baseline.

<table>
<thead>
<tr>
<th>Smoking status</th>
<th>Never/ past (n=623)</th>
<th>Current (n=106)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean activity score (SD)</td>
<td>6.9 (5.9)</td>
<td>11.2 (30.2)</td>
<td>0.0001^a</td>
</tr>
<tr>
<td>Mean damage score (SD)</td>
<td>2.1 (4.5)</td>
<td>3.6 (6.6)</td>
<td>0.0332^a</td>
</tr>
<tr>
<td>Activity &gt;10, n (%)</td>
<td>152 (24.4%)</td>
<td>48 (45.3%)</td>
<td>&lt;0.0001^b</td>
</tr>
<tr>
<td>SLEDAI-2K</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rash, n (%)</td>
<td>599 (81.7%)</td>
<td>85 (80.2%)</td>
<td>0.7109^a</td>
</tr>
<tr>
<td>alopecia, n (%)</td>
<td>441 (70.8%)</td>
<td>75 (70.8%)</td>
<td>0.9947^a</td>
</tr>
<tr>
<td>mucosal ulcers, n (%)</td>
<td>282 (45.3%)</td>
<td>43 (40.6%)</td>
<td>0.5083^a</td>
</tr>
</tbody>
</table>

^a Two sample t-test; ^b Chi-square test.

CLASI: Cutaneous Lupus Activity and Severity Index; SD: standard deviation; SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index 2000.

Disclosure: V. P. Werth, MedImmune, 5; G. Illei, AstraZeneca, 1,MedImmune, 3,Regenxbio, 3; G. Abreu, AstraZeneca, 3; L. Wang, AstraZeneca, 1,MedImmune, 3; W. Greth, AstraZeneca, 1,AstraZeneca, 3,AstraZeneca, 5.


Abstract Number: 2592

Safety, Tolerability, and Pharmacokinetics of Subcutaneous and Intravenous Anifrolumab in Healthy Volunteers

Raj Tummala^1, Tomas Rouse^2, Anna Berglind^2 and Linda Santiago^3, ^1AstraZeneca, Gaithersburg, MD, ^2AstraZeneca, Gothenberg, Sweden, ^3MedImmune, LLC, Mountain View, CA

First publication: September 18, 2017
Background/Purpose: Anifrolumab is a fully human anti–interferon-α receptor 1 monoclonal antibody in Phase III development as an intravenous (IV) therapeutic for systemic lupus erythematosus (SLE). In Phase IIb trials, IV anifrolumab (300 mg every 4 weeks) significantly decreased SLE disease activity and was well-tolerated.\(^1\) In this Phase I, blinded, randomized, controlled study (NCT02601625), we profiled the pharmacokinetics (PK), safety, and tolerability of anifrolumab administered subcutaneously (SC) and IV to healthy volunteers.

Methods: Thirty male and female adults were assigned to three sequential treatment cohorts of equal size (anifrolumab 300 mg SC injection, anifrolumab 300 mg IV, anifrolumab 600 mg SC by infusion). Individuals were randomized within each cohort to receive a single dose of either anifrolumab \((n=6/\text{cohort})\) or placebo (PBO) \((n=4/\text{cohort})\). Serial blood samples were collected up to Day 84. Serum anifrolumab concentrations were analyzed with a validated assay. PK parameters were estimated by noncompartmental analysis. Immunogenicity of anifrolumab was assessed by measuring serum anti-drug antibodies (ADAs).

Results: Anifrolumab serum concentration–time profiles and PK parameters in healthy volunteers are presented in the figure and table, respectively. Anifrolumab serum concentrations were below the limit of detection in all individuals by 84 days post dose. Maximum serum concentrations in the SC cohorts occurred after 4–7 days. Exposure to SC anifrolumab increased approximately dose proportionally from 300 mg to 600 mg based on AUC. Anifrolumab exposure after SC administration of the 300-mg dose reached approximately 87% of the IV administration exposure. SC administration of anifrolumab 300 mg and PBO elicited minimal injection-site reactions. Transient injection-site induration occurred in five of six individuals in the anifrolumab 600-mg group and two of four in the PBO group. Transient, mild to moderate injection-site induration and pruritus occurred simultaneously in two of six individuals in the anifrolumab 600-mg group, but not in those in the PBO group. Adverse events were reported by 50% \((n=9)\) of anifrolumab-treated and 33% \((n=4)\) of PBO-treated individuals. No serious adverse events were observed. ADAs were detected in only one individual in the anifrolumab 300-mg IV group at the Day-84 assessment.

Conclusion: Exposure of anifrolumab 300 mg SC was approximately 87% of IV administration, with single SC administrations of anifrolumab being generally well-tolerated in healthy volunteers.

Reference:

Baseline Characteristics of Patients Diagnosed with Systemic Lupus Erythematosus Initiating Treatment with Intravenous Belimumab

Christopher F Bell¹, Julie Priest²,³, Justyna Amelio⁴, Xue Song⁵, Hong Kan⁶, Marni Stott-Miller⁷, Brendan Limone⁵, Virginia Noxon⁵ and Karen H. Costenbader⁸, ¹GSK US Value, Evidence and Outcomes, Research Triangle Park, NC, ²GSK US Value, Evidence and Outcomes (at the time of Study)*, Research Triangle Park, NC, ³US Health Outcomes Durham, *ViiV Healthcare (Present), Durham, NC, ⁴GSK Real World Evidence & Epidemiology, Stevenage, United Kingdom, ⁵Truven Health Analytics, an IBM company, Ann Arbor, MI, ⁶Department of Health Policy and Management, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, ⁷GSK Real World Evidence & Epidemiology, Uxbridge, United Kingdom, ⁸Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Background/Purpose: Belimumab, an inhibitor of B lymphocyte stimulator, is approved in adults with active, autoantibody-positive systemic lupus erythematosus (SLE) receiving standard of care.

Methods: Retrospective analysis was conducted in the Truven Health MarketScan® Commercial Claims and Encounters database (Sept 01, 2010 to Dec 31, 2015) (study 206345). Patients 18–64 years of age at first belimumab infusion (index) with a SLE diagnosis (ICD-9: 710.0 or ICD-10: M32) and continuous enrollment of 6 months pre-index and ≥3 post-index were analyzed. Patients diagnosed with lupus nephritis were excluded. The 6-month pre-index period was analyzed to characterize patients initiating treatment with intravenous belimumab. A previously published disease activity algorithm, developed based on claims data, was used to estimate the frequency of mild, moderate or severe flare symptoms.1

Results: This analysis comprised 2067 patients; 94.7% were female, mean (standard deviation [SD]) age was 43.9 (11.1) years and mean (SD) length of follow-up was 649.7 (434.8) days. In the 6-month pre-index period, mean (SD) Charlson Comorbidity Index score was 1.4 (0.9). Commonly observed comorbid conditions included hypertension (23.4%), myositis/myalgia (21.0%), and pulmonary disease (18.3%). The most frequent SLE-related clinical manifestations included arthralgia (28.4%) and hematologic disorders (20.8%). SLE-related organ involvement included diseases of the musculoskeletal (98.5%), nervous (46.7%) and respiratory systems (40.5%).

Pre-index concomitant medications prescribed included corticosteroids (80.2%), antimalarials (66.0%), nonsteroidal anti-inflammatory drugs (38.2%), immunosuppressive agents (59.1%), and rituximab (1.1%). Mean (SD) daily prednisone-equivalent dose was 27.7 mg (87.5), with 12.7%, 25.7% and 40.9% receiving ≤7.5 mg/day, >7.5 to ≤15 mg/day and >15 mg/day, respectively. Patients had a mean (SD) of 2.9 (5.9) primary care visits and 4.2 (7.0) rheumatologist visits in the 6-month pre-index period (Table). The proportions experiencing a mild, moderate or severe flare pre-index were 43.9%, 91.2% and 12.7% (92.9% had a moderate/severe flare).

Conclusion: In this large sample of belimumab IV initiators in usual care settings, patients with SLE demonstrated substantial SLE-related clinical manifestations in the 6 months prior to initiating, with approximately 90% having evidence of a moderate/severe flare. Concomitant medications included many commonly prescribed therapies, with corticosteroids being the most frequently prescribed, and per patient monthly costs were high. Future studies will investigate whether belimumab treatment reduces healthcare utilization and costs.

Table: Six-month pre-index all-cause healthcare resource utilization and costs among patients with SLE initiating belimumab (n=2067)

<table>
<thead>
<tr>
<th>Resource</th>
<th>Patients with ≥1 utilization, n [%]</th>
<th>PPPPM healthcare costs, US$, mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient admissions</td>
<td>371 (17.9)</td>
<td>1067 (4623)</td>
</tr>
<tr>
<td>Outpatient services</td>
<td>2064 (99.9)</td>
<td>2759 (4899)</td>
</tr>
<tr>
<td>Emergency room visits</td>
<td>813 (39.3)</td>
<td>146 (518)</td>
</tr>
<tr>
<td>Physician office visits</td>
<td>2059 (99.6)</td>
<td>299 (223)</td>
</tr>
<tr>
<td>Hospital-based outpatient visits</td>
<td>1706 (82.5)</td>
<td>1178 (2855)</td>
</tr>
<tr>
<td>Laboratory services</td>
<td>1910 (92.4)</td>
<td>130 (175)</td>
</tr>
<tr>
<td>Other outpatient services</td>
<td>2024 (97.9)</td>
<td>983 (5664)</td>
</tr>
<tr>
<td>Outpatient pharmacy prescriptions</td>
<td>2016 (97.2)</td>
<td>966 (2276)</td>
</tr>
</tbody>
</table>

Conclusion: In this large sample of belimumab IV initiators in usual care settings, patients with SLE demonstrated substantial SLE-related clinical manifestations in the 6 months prior to initiating, with approximately 90% having evidence of a moderate/severe flare. Concomitant medications included many commonly prescribed therapies, with corticosteroids being the most frequently prescribed, and per patient monthly costs were high. Future studies will investigate whether belimumab treatment reduces healthcare utilization and costs.

Study funded/conducted by GSK. Editorial assistance provided by Jennie McLean, PhD, of Fishawack Indicia Ltd, UK, funded by GSK.


Disclosure: C. F. Bell, GSK, 1,GSK, 3; J. Priest, GSK, 1,GSK, 3; J. Amelio, GSK, 1,GSK, 3; X. Song, Truven Health Analytics, 3; H. Kan, GSK, 1; M. Stott-Miller, GSK, 1,GSK, 3; B. Limone, None; V. Noxon, Truven Health Analytics, 3; K. H. Costenbader, GSK, 5,Merck Pharmaceuticals, 2,Biogen Idec, 5,AstraZeneca, 5.
Abstract Number: 2594

**Frequency of Infusions Among Patients Diagnosed with Systemic Lupus Erythematosus Initiating Treatment with Intravenous Belimumab**

*Christopher F Bell*¹, Julie Priest²,³, Marni Stott-Miller⁴, Hong Kan⁵, Justyna Amelio⁶, Xue Song⁷, Brendan Limone⁷, Virginia Noxon⁷ and Karen H. Costenbader⁸, ¹GSK US Value, Evidence and Outcomes, Research Triangle Park, NC, ²GSK US Value, Evidence and Outcomes (at the time of Study)*, Research Triangle Park, NC, ³US Health Outcomes Durham, *ViiV Healthcare (Present), Durham, NC, ⁴GSK Real World Evidence & Epidemiology, Uxbridge, United Kingdom, ⁵Department of Health Policy and Management, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, ⁶GSK Real World Evidence & Epidemiology, Stevenage, United Kingdom, ⁷Truven Health Analytics, an IBM company, Ann Arbor, MI, ⁸Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Belimumab, an inhibitor of B lymphocyte stimulator, is approved for the treatment of adult patients with active, autoantibody-positive systemic lupus erythematosus (SLE) receiving standard of care. The recommended dosing regimen for intravenous belimumab is 10 mg/kg at 2-week intervals for the first 3 doses (loading dose period) and at 4-week intervals thereafter (maintenance period), for a total of 15 doses in the first year of therapy. However, in routine clinical practice, many patients may not be receiving the recommended number of loading or maintenance doses. This study evaluated the frequency of infusions in patients with SLE under routine care settings, using data from a US administrative claims database.

**Methods:** A retrospective analysis (study 206345) was conducted using the Truven Health MarketScan® Commercial Claims and Encounters database (Sept 01, 2010 to Dec 31, 2015). The analysis cohort comprised patients 18–64 years of age with a SLE diagnosis (ICD-9: 710.0 or ICD-10: M32) and ≥1 belimumab infusion. The index date was defined as the date patients received their first belimumab infusion. Continuous enrollment was required for 6 months pre-index and ≥3 months post-index date. The loading dose period was defined as the 34-day period post-index date; patients were divided into subgroups according to the number of infusions received in this time (1–2 or ≥3). Here we present data for those patients with 12 months of follow-up data.

**Results:** Overall, there were 2067 patients; the majority were female (94.7%) and had a mean (standard deviation [SD]) age of 43.9 (11.1) years. From this population, 1537 patients had 12 months of follow-up data; 877 (57.1%) received 1–2 infusions during the loading dose period and 660 (42.9%) received ≥3 infusions. The mean number of infusions and time between infusions are summarized (Table).
Conclusion: In this sample of US patients with SLE in a routine care setting, a high proportion did not receive the recommended number of belimumab loading doses. Furthermore, compared with those who completed the recommended loading dose period, patients who did not complete the loading dose period received significantly fewer belimumab infusions during the maintenance period. This study provides valuable information on belimumab treatment patterns in a real-world setting using a US claims database. These data suggest that belimumab is not always administered as recommended; the effects of this on treatment outcomes remain to be determined.

Study funded/conducted by GSK. Editorial assistance provided by Jennie McLean, PhD, of Fishawack Indicia Ltd, UK, funded by GSK.

Disclosure: C. F. Bell, GSK, 1,GSK, 3; J. Priest, GSK, 1,GSK, 3; M. Stott-Miller, GSK, 1,GSK, 3; H. Kan, GSK, 1; J. Amelio, GSK, 1,GSK, 3; X. Song, Truven Health Analytics, 3; B. Limone, None; V. Noxon, Truven Health Analytics, 3; K. H. Costenbader, Glaxo Smith Kline, 5,Merck Pharmaceuticals, 2,Biogen Idec, 5,AstraZeneca, 5.

Abstract Number: 2595

The Role of Hydroxychloroquine in the Treatment of Undifferentiated Connective Tissue Disease

Hayley Epstein1, Diana P. Pena2, Bianca Di Cocco1, Teja Kapoor3 and Anca Askanase4, 1Rheumatology, CUMC, New York, NY, 2Rheumatology, Universidad Militar Nueva Granada, Bogotá, Colombia, 3Rheumatology, Columbia University College of Physicians & Surgeons, New York, NY, 4Rheumatology, Columbia University Medical Center, New York, NY

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017

Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design

Session Type: ACR Poster Session C

Session Time: 9:00AM-11:00AM
Background/Purpose: To evaluate the change in ANA titers as a proxy for progression in patients with undifferentiated connective tissue disease (UCTD) treated with hydroxychloroquine (HCQ) in a large academic clinical practice.

Methods: This study included all patients diagnosed with UCTD according to the preliminary classification criteria (Mosca et al 1999) seen at the Columbia University Lupus Center in New York from January 2015 to December 2016 that had at least 6 months of follow-up. Clinical and immunological variables were ascertained. Chi squared tests were used to compare the characteristics between treated and untreated patients: demographic characteristics, number of ACR criteria, SLICC criteria, individual symptoms and laboratory values.

Results: 114 patients were identified; 94% female, mean age at diagnosis of 44 years (range 19 – 81); 42% were Caucasian, 16% Hispanic and 12% Black/African American; median disease duration of 5.6 years (1-27). The most prevalent symptoms that required medical attention are described in Figure 1.

51 % of patients had a family history of autoimmune diseases.

94% of patients had positive antinuclear antibody (ANA) titers and 6% were ANA negative Ro/SSA+, 88.6% had titers ≥ 1:160. Interestingly, 17.5 % of the patients studied met SLICC SLE criteria. Over half of the patients, 65(57%) were treated with HCQ and 49(43%) were not treated. The patients treated with HCQ were more likely to also meet SLICC criteria (16 vs. 4, p=0.04), have arthritis (33 vs. 12; p=0.03), have a history of low complements (19 vs. 5, p=0.03); arthralgia and fatigue were common but not different between groups, arthralgia (52 vs. 34; p=NS), and fatigue (36 vs. 15; p=NS).

Of 62 patients that had follow-up ANA testing in the same laboratory, 40 had no change in ANA titer (ANA titer within +/- one dilution was considered stable), 10 had an increase, and 11 had a decrease in ANA titer. 35/62 (56 %) patients had been treated with HCQ for ≥5 months, the majority remained ANA+ with stable/decreased titers. Of patients with dsDNA+ on HCQ 4/5 became negative.

Conclusion: Data from this single-center cohort of patients with UCTD show that patients treated with HCQ have multiple clinical criteria and low complement, suggesting that rheumatologists treat pre-clinical autoimmunity in the setting of clinical symptoms. Follow-up ANA/dsDNA testing suggests that HCQ may prevent increase in ANA titers or dsDNA autoantibodies and disease progression in UCTD. Longitudinal studies are needed to evaluate the long-term impact of HCQ on clinical and serologic outcomes in UCTD.

Disclosure: H. Epstein, None; D. P. Pena, None; B. Di Cocco, None; T. Kapoor, None; A. Askanase, None.
Background/Purpose: The antimalarial drug hydroxychloroquine (HCQ) has been used for decades to treat various rheumatic diseases including systemic lupus erythematosus (SLE). The efficacy of HCQ in lupus is well-demonstrated, and leads to a decreased number of lupus flares. Although multiple mechanisms have been proposed for HCQ, the systemic immunologic effects of HCQ treatment still remains ill-defined in human lupus and may help elucidate the immune mechanisms of HCQ in SLE.

Methods: SLE patients receiving HCQ (n=9) or not receiving HCQ (n=9) were matched and assessed in a cross-sectional design. Single-cell analysis of surface markers were completed by mass cytometry on PBMCs and cellular heterogeneity was visualized using viSNE and manual gating in Cytobank. Further, phospho-specific flow cytometry was used to measure basal levels of pERK, pPLCγ2, pSTAT5 and p38 and expression following CD3/CD28 (TCR) and anti-IgG and IgM (BCR) stimulation. Soluble mediator levels in plasma were assessed using a 51-plex (Affymetrix) and by ELISA (eBioscience). All SLE patients met ACR criteria for SLE classification.

Results: In PBMCs of SLE patients taking HCQ, there was a small non-significant trend towards fewer total cells/mL compared to SLE patients not receiving HCQ (p=0.1200) (Figure 1). There was a significant reduction in the number of B cells (p=0.0269) and CD4+ T Cells (p=0.0124), most significantly transitional B cells (p=0.0053) and effector T cells (p=0.0039) (Th1-type, Th17-type, and Tfh-type) in HCQ patients compared to non-HCQ patients (Figure 1). Cell activation was also reduced in SLE patients receiving HCQ with lower expression of HLA-DR and CD38 on B cells, IL-2 receptor and CCR6 on T cells, and CD86 expression in dendritic cells (p<0.05). Plasma soluble mediators produced primarily by monocyte, platelet and endothelial cells were significantly reduced in patients receiving HCQ, namely PDGF-BB (p=0.0009), MCP-1 (p=0.0041), PAI-1 (p=0.0114), sEselectin (p=0.0118), resistin (p=0.0360) and IL-7 (p=0.0380). No significant differences were observed in TCR and BCR signaling following stimulation, but reduced levels of PLCγ in CD4+ effector T cells were found in SLE patients receiving HCQ following BCR stimulation (p=0.0275).

Conclusion: Our results indicate that SLE patients on HCQ have reductions in circulating lymphocytes, HLA-DR expression on antigen-presenting cells, and monocyte and platelet derived soluble mediators compared to patients off HCQ. In addition, reduced T cell signaling following B cell stimulation suggests that the effects of HCQ on T cells may be a result of altered antigen presentation and reduced IL-7 levels. Together these data provide potential insights into HCQ mechanisms of action in SLE patients, while suggesting use lowers the risk of thrombotic events by reducing platelet activation.
Disclosure: S. Slight-Webb, None; R. Lu, None; H. Chen, None; H. T. Maecker, None; P. J. Utz, None; J. M. Guthridge, None; J. A. James, None.


Abstract Number: 2597

Explorer Study: Rituximab Use in Systemic Lupus Erythematosus, a New Look on Old Data

Marc Scherlinger1,2,3, Claire Carcaud2,4, Thomas Barnetche1,5, Lionel Couzy2,6, Pierre Duffau3,7,8, Estibaliz Lazaro2,9 and Christophe Richez2,10,11, 1Rheumatology, Centre hospitalier universitaire de Bordeaux - Service de Rhumatologie, Bordeaux, France, 2FHU ACRONIM, Bordeaux, France, 3UMR CNRS 5164 - Immunoconcept, Bordeaux, France, 4Internal Medicine, Centre hospitalier universaire de Bordeaux, Bordeaux, France, 5FHU ACRONIM, Pellegrin Hospital, Bordeaux University, Bordeaux, France, 6Nephrology, Centre hospitalier universitaire de Bordeaux - Néphrologie, Bordeaux, France, 7Internal Medicine, Centre hospitalier universaire de Bordeaux - Médecine interne, Bordeaux, France, 8FHU ACRONIM, bordeaux, France, 9Department of Internal Medicine and Clinical Immunology, Bordeaux University Hospital, Pessac, France, 10Department of Rheumatology, Bordeaux University Hospital, Bordeaux, France, 11UMR CNRS 5164 - Immunoconcept, bordeaux, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Even if randomized trials EXPLORER and LUNAR failed to prove the superiority of rituximab versus placebo in patients with systemic lupus erythematosus, several encouraging indications as refractory lupus nephritis and new clinical trials renewed interest for this molecule.
We hypothesized that SLE response criteria used in EXPLORER were not sensible enough to show rituximab efficacy and that new response criteria could show a significant difference. Our objective was to reanalyze EXPLORER trial’s raw data using the newly described SLE response criteria.

Methods:

We proceeded to a pre-specified re-analyze of EXPLORER trial’s raw data. The patients included in EXPLORER study had active SLE disease defined by a British Isles Lupus Assessment Group (BILAG) score A or 2 BILAG B despite immunosuppressive regimen. Renal and neurological SLE were excluded. Patients were randomized through a 2/1 ratio to receive either two 1gr rituximab infusion (day 0 and day 15) repeated at month 6 or a placebo. Standard SLE treatment including immunosuppressants were continued. Patients received in a stratified manner prednisone ranging from 0.5 to 1.0 mg/kg depending on disease severity at inclusion. The original efficacy criterion was a composite clinical score using BILAG at week 52.

In our new analysis, rituximab efficacy was assessed at week 52 using 4 criteria: SRI-4 (Systemic lupus erythematosus Responder Index) with and without a concomitant oral prednisone tapering objective of < 10mg at months 6 (SRI-4 with and without OCS tapering), Lupus Low Disease Activity Score (LLDAS) and BILAG-based Combined Lupus Assessment (BICLA).

Results:

Data from all 257 patients were available. There was 234 women (91%) with a mean age of 40.3 years among which 177 (69%) received hydroxychloroquine.

At week 52, SRI-4 response rate was 27.2% in the rituximab group vs 22.7% in the placebo group (p=0.43); SRI-4 with OCS tapering was 16% in the rituximab group vs 13.6% in the placebo group (p=0.62); LLDAS was 16% in the rituximab group vs 12.5% in the placebo group (p=0.46) and BICLA was 15.4% in the rituximab group vs 15.9% in the placebo group (p=0.91).

Subgroup analyses demonstrated a trend for better efficacy of rituximab compared to placebo in the subgroup of patients co-treated with methotrexate: SRI-4 of 30.6% in the rituximab group vs 12% in the placebo group (n=74, p=0.08). This trend was not found in the subgroup of patients co-treated with azathioprine: SRI-4 of 26.7% in the rituximab group vs 30.6% in the placebo group (p=0.68), nor in the subgroup treated with mycophenolic acid: SRI-4 of 23.1% in the rituximab group vs 21.6% in the placebo group (p=0.86). In the subgroup of patients with an BILAG A/B in hematological system or vasculitis at baseline, there was a significantly higher SRI-4 response rate with rituximab: 28.6% vs 5.3% in the hematological group (p=0.047) and 39.3% vs 0% in the vasculitis group (p=0.037).

Cumulative dose of steroids at week 52 were not statistically different: 4223mg in the rituximab group vs 4390mg in the placebo group (p=0.65).

Conclusion:

Our study confirms the results from the original EXPLORER Study. These results might be partly related to the study’s design, notably the additional daily oral prednisone.

Disclosure: M. Scherlinger, None; C. Carcaud, None; T. Barnetche, None; L. Couzy, None; P. Duffau, None; E. Lazaro, None; C. Richez, Roche Pharmaceuticals, 5.


Abstract Number: 2598

The Effects of Tai Chi on Inflammatory Mediator Secretion in Systemic Lupus Erythematosus
Juliette Yedimenko1, Evelyn Thomas2, Brian Snod3, Juhi Sharma2, Misha Mobeen2, Holly Steigelman1, Alexa Meara4, Giancarlo R. Valiente5, Stacy P. Ardoin6, Nicole Powell7, John Sheridan7, Wael Jarjour8 and Nicholas A. Young3, 1The Ohio State University Wexner Medical Center, Columbus, OH, 2The Ohio State University, Columbus, OH, 3Department of Internal Medicine, Division of Immunology and Rheumatology, The Ohio State University Wexner Medical Center, Columbus, OH, 4Internal Medicine/Rheumatology, The Ohio State University Wexner Medical Center, Columbus, OH, 5Rheumatology & Immunology, The Ohio State University Wexner Medical Center, Columbus, OH, 6Pediatric & Adult Rheumatology, The Ohio State University Wexner Medical Center, Columbus, OH, 7Institute for Behavioral Medicine Research, The Ohio State University, Columbus, OH, 8Immunology and Rheumatology, The Ohio State University Wexner Medical Center, Columbus, OH

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Exercise and psychological stress have been shown to produce opposite effects on immunomodulation. Prior studies in patients with Systemic Lupus Erythematosus (SLE) have demonstrated a decrease in inflammatory cytokine expression with exercise and improved disease activity with psychological stress reduction. In agreement, our prior study in a murine model of lupus nephritis showed an increase in inflammatory cytokine secretion with psychosocial stress induction, while exercise correlated with decreased inflammation and disease pathology. Therefore, to translate our previous findings, this study aims to utilize Tai Chi in exploring the effects of moderate exercise and psychological stress reduction on cytokine levels and perceived stress in SLE patients.

Methods: A cohort of 12 SLE patients >18 years of age participated in Tai Chi group classes twice a week and completed a Tai Chi DVD the remaining 5 days for 2.5 months. Selected participants scored low on a physical activity questionnaire and above average on the perceived stress scale. They were provided with FitBit activity trackers to monitor activity, sleep and caloric expenditure. Data collection included bi-weekly blood samples, monthly questionnaires, and weekly FitBit data compared to baseline measurements.

Results: Relative to baseline data, questionnaires revealed a significant increase in metabolic equivalent of task (MET) and physical activity, and a decrease in perceived stress in SLE patients. FitBit data showed an increase in steps, distance and activity calories, without significant change in body mass index or vigorous activity levels. Analysis of pro-inflammatory serum cytokines in Tai Chi patients demonstrated a relative suppression of IL-6 by 23% (p=0.05), IL-8 by 30% (p=0.006), IFN-γ by 21% (p=0.05) and TNF-α by 11% (Figure 1).

Conclusion: Our results suggest that moderate exercise and psychological stress reduction have clinically detectable immunosuppressive properties. We see a reduction in pro-inflammatory cytokine expression with Tai Chi along with a decrease in perceived stress levels. Thus, we propose Tai Chi as an adjuvant therapy to current pharmacologic interventions in the treatment of SLE, although larger studies are needed given the limitations herein, including a small sample size and short duration.

Figure 1. Average decrease in cytokine expression in SLE patients 2.5 months after participation in a Tai Chi exercise program.
Efficacy and Toxicity of Antimalarials in Systematic Lupus Erythematosus: A Systematic Review

Gaurav Sharma¹, Jasvinder A. Singh², Mohammed Sohaib Khaleel³ and Shristi Shrestha⁴, ¹Department of Medicine, Division of Immunology and Rheumatology, UAB School of Medicine, Birmingham, AL, ²Rheumatology, University of Alabama at Birmingham, Birmingham, AL, ³Department of Molecular Cardiology, University of Louisville, Louisville, KY, ⁴Internal Medicine, Kathmandu Medical College Teaching Hospital, Kathmandu, Nepal

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: To determine the efficacy and adverse effects of antimalarials in patients with systematic lupus erythematosus (SLE).

Methods: A literature search from inception to December 2016 was performed using MEDLINE, EMBASE, Cochrane, CINAHL and ClinicalTrials.gov. All randomized control trials, clinical control trials, cohort, case control and cross-sectional studies of interest were included. Duplicate, independent screening of titles and abstracts was done to identify relevant studies. The primary outcome were effects of antimalarials (AMs) on lupus activity, irreversible organ damage, survival and adverse effects. Secondary outcomes were thrombosis, atherosclerosis, cardiovascular disease, neuropsychiatric disease, effect on bone metabolism.

Results: 5364 abstract and titles were screened for studies assessing the efficacy and toxicity of antimalarial therapy in patients of SLE. 406 full texts were screened and 51 studies with 17349 patients qualified for final analyses. Mean ages were 6-70 years and mean follow-up was 6 months to 10 year.

We found that antimalarials significantly reduce the number of flares and disease activity in SLE patients (high level evidence). Patients on HCQ have increased odds of achieving remission (weak evidence) (Table 1). Outcomes remained similar and significant in pregnant women. We also found that antimalarials have significant toxic effects on skin, eyes and GI tract. Of these, most severe is retinal toxicity which is more evident in patients on Chloroquine as compared to HCQ (p=0.001). Risk of retinal toxicity is more at high doses of chloroquine (>4 mg/kg/day) and longer duration exposure (>7 years). We found weak evidence for antimalarials in preventing/delaying development of new organ damage in patients with SLE. High evidence was found for role of AMs in reducing the risk of mortality in patients with SLE (HR, 0.32 95% CI 0.16 to 0.66, I² of 81%; 4 studies). Antimalarial use also improves lipid profile, bone mineral density and have better cardiovascular outcomes (data is not presented).

Conclusion: Broad spectrum effects and safety profile of AMs qualifies them as a drug of choice in management of patients with SLE. They are effective in preventing flares, reducing systemic disease activity, mortality and have also shown preventive effect on irreversible end organ damage in SLE patients. They do have some adverse effects on long
term use, which can be prevented by appropriate screening practices and using less toxic formulations like hydroxychloroquine.

Table 1: Summary of results for major outcomes
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number of studies</th>
<th>Design of Included studies</th>
<th>Number of participants</th>
<th>Age range (mean)</th>
<th>Gender</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLE activity</td>
<td>23</td>
<td>5 RCT; 16 cohort; 1 cross sectional and 1 case control study</td>
<td>4849</td>
<td>17 -70 years</td>
<td>Females: 4278; Males: 485</td>
<td><strong>Low SLE disease activity is associated with high serum HCQ concentration</strong> based on data from three studies (p &lt; 0.0001; p=0.005; p=0.04). AMs use reduce SLICC/ACR DAI (r=0.22, p=0.015), SLAM R (p=0.0157, and p &lt;0.001) sores and general symptoms and swollen/painful joint counts (p=0.02). <strong>Flares on AMs:</strong> A randomized trial showed that patients on antimalarials have significantly less numbers of SLE flares (defined by American Rheumatic association criteria) (p&lt;0.02). Antimalarial drugs increase the odds of clinical quiescent phase (HR, 2.8 95% CI 1.4 to 5.57, p=0.004). In one cohort study patients with high number of flares during follow up had significantly low serum</td>
</tr>
</tbody>
</table>
concentration of HCQ (p=0.006). On multivariate analysis low HCQ concentration is a risk factor for SLE flares (OR: 3.82, 95% CI 1.16 to 2.58, p=0.027. One trial showed significantly lower incidence of disease exacerbation in chloroquine group as compared to placebo (p<0.01).

**Remission:**
Antimalarial use was significantly associated with remission in SLE patients (OR: 12.91, 2.87 to 58.13).

**HCQ vs Corticosteroids:**
HCQ have less number of flares, severity of flare and better economic outcomes as compared to patients on corticosteroids.

**HRQOL:** Blood HCQ concentration is not predictive of HRQOL.

**Pregnancy outcomes:**
Holding HCQ during pregnancy can lead to 3.6 times more flares and use of HCQ.
during pregnancy have significant improvement in SLEDAI score during pregnancy (p<0.038).

**Time lag:** In one study early HCQ use was associated with increase time lag between 1st symptom and full SLE criteria as compared to controls (p<0.018).

### Adverse reactions

<table>
<thead>
<tr>
<th>RCT</th>
<th>Case control studies</th>
<th>Cohort studies</th>
<th>Cross sectional</th>
<th>3893</th>
<th>Females 2470; Males: 1423</th>
</tr>
</thead>
</table>

**Cutaneous side effects:** Three studies described cutaneous pigmentation as adverse effect of antimalarials. In one case control study, 159/209 chloroquine users had skin toxicity.

**Cardiotoxicity:** No significant changes in heart rate, premature beats, heart rate variability and repolarization after treatment with chloroquine.

**Retinal toxicity:** Retinopathy developed in 21 out of 85 patients (24.7%), patients on CQ (13) had significantly higher risk compared to on HQ(8) treatment (p=0.001). In
two studies, 2/58 and 7/2000 developed retinal toxicity with the use of HCQ. Risk of retinal toxicity increase significantly after 7 years of exposure.

**Retinal nerve fibre layer thickness:**
Patients on Chloroquine in dose of 4mg/kg/day have significantly lower thickness. Retinal function improves after discontinuations of drug for 6 months.

**All adverse effect:** One trial and one retrospective cohort study showed that HCQ is associated with dermatological, gastrointestinal and ocular toxicity. Significant difference between incidence of HCQ and CQ toxicities was found (p<0.00001).

| Irreversible organ damage | 6 studies | 6 cohort studies | 5107 | 36 to 44.1 years | Females: 4573, Males: 534 | HCQ user have low hazard ratio for development of new organ damage (SDI score); HR 0.57, 95% 0.37 to 0.88. Similarly, HCQ delays the time to first |
Non-AM user have longer disease duration and high SDI (p<0.001).

Based on data from two cohort studies showed that HCQ use was associated with reduced risk for new organ damage (SDI >= 1), but the results did not reach statistical significance.

Disclosure: G. Sharma, None; J. A. Singh, Takeda, Savient, 2,consultant fees from Savient, Takeda, Regeneron, Merz, Iroko, Bioiberica, Crealta and Allergan pharmaceuticals, WebMD, UBM LLC and the American College of Rheumatology, 5., JAS serves as the principal investigator for an investigator-initiated study funded by Horizon pharmaceuticals through a grant to DINORA, Inc., a 501 (c)(3) entity. JAS is a member of the executive of OMERACT, an organization that develops outcome mea, 9; M. S. Khaleel, None; S. Shrestha, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/efficacy-and-toxicity-of-antimalarials-in-systematic-lupus-erythematosus-a-systematic-review

Abstract Number: 2600

Plasma Cell and T-Cell Activity Downregulation during MMF Therapy in SLE May be Necessary for Successful Immunosuppression

Cristina Arriens1, Rufeii Lu2, Teresa Aberle2, Stan Kamp2, Wade DeJager2, Melissa E. Munroe2, Eliza Chakravarty1, Katherine Thanou2, Joan T. Merrill3, Joel M. Guthridge4 and Judith A. James3, 1Arthritis & Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, 2Arthritis and Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, 3Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 4Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, OKC, OK

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Background/Purpose: MMF is a key therapy for moderate to severe SLE. MMF inhibits inosine monophosphate dehydrogenase, an enzyme needed in nucleotide synthesis required for lymphocyte proliferation. MMF can also inhibit B-cell activation and plasma cell differentiation. Antibody production, interferon elevation, dysregulated inflammatory soluble mediators, and altered lymphocyte activity are molecular features of SLE. One soluble mediator, stem cell factor (SCF), was recently noted to be elevated in patients who transitioned from pre-SLE to SLE. Examination of cellular activity in patients undergoing MMF therapy may elucidate ongoing immune processes in patients who fail to respond, as up to 50% of MMF-treated LN patients are non-responders.

Methods: Immunologic profiling was conducted on 194 patients who met ACR classification criteria for SLE. Molecular assessments included whole blood gene expression profiling (microarray, analyzed as modules normalized to healthy controls, described by Chaussabel) and plasma soluble mediator assessment (24 cytokines, chemokines, and soluble receptors which passed quality control). We used these data for 3 key analyses. Patients who demonstrated clinical response to MMF (n=12) were compared to those with inadequate response (n=12). High disease activity (SLEDAI ≥ 6) patients on MMF (n=17) were compared to those on AZA (n=19). Wilcoxon test was used to analyze patients with one visit while taking MMF and another while not receiving MMF (n=8 pairs) (Table 1).

Results: The patients in the cohort whose biospecimens were assayed while on MMF (n=32) were younger (p=0.01) and had more Hispanic and Asian patients with less white patients (p=0.04) than those without MMF exposure (n=162). No significant differences in gender, race, or age were present between the other comparison groups. Plasma cell downregulation differentiated responders from non-responders and T-cell downregulation differentiated MMF from AZA treated patients. MMF was less effective at controlling elevated interferon and elevated SCF than AZA (Figure 1). Additionally, in the paired data, monocyte chemoattractant protein 1 was lower while on MMF as compared to off (p=0.04, not shown).

Conclusion: In this translational study of SLE, we showed that resistance to plasma cell suppression in some patients likely contributed to their ineffective MMF treatment. Also, we demonstrated that MMF differentially modulated T-Cell and IFN pathways compared to AZA. Understanding these distinct molecular profiles responding to MMF and AZA can lead to more effective personalized combination therapies.
Table 1. Patient Characteristics. Basic demographic data and SLEDAI scores shown, as represented by number and % for categorical data assessed by Fisher’s exact test, or median and interquartile range (IQR) for continuous data assessed by Mann-Whitney test. Response was defined by SLEDAI ≥6 at the time of biospecimen analysis and at the next clinic visit and Non-Response was defined by SLEDAI ≥6 for the timepoint and at the follow-up visit. Patients with SLEDAI ≥6 on MMF were compared to those with SLEDAI ≥6 on AZA. Patients with one timepoint on MMF and another off MMF (and not on another immunosuppressive) were compared as paired data.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>MMF (n=2)</th>
<th>No MMF (n=12)</th>
<th>P-value (2-tailed)</th>
<th>IQR (MMF)</th>
<th>IQR (No MMF)</th>
<th>On MMF</th>
<th>Off MMF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>6 (35.3)</td>
<td>2 (16.7)</td>
<td>0.065</td>
<td>10 (9.6)</td>
<td>10 (9.6)</td>
<td>16 (9.1)</td>
<td>16 (9.1)</td>
</tr>
<tr>
<td>Race/Ethnicity (%)</td>
<td>3 (15)</td>
<td>37 (23.5)</td>
<td>0.18</td>
<td>3 (15)</td>
<td>3 (15)</td>
<td>6 (31)</td>
<td>6 (31)</td>
</tr>
<tr>
<td>Hispanic/Latinos</td>
<td>1 (21.2)</td>
<td>14 (88.5)</td>
<td>0.1</td>
<td>2 (10)</td>
<td>2 (10)</td>
<td>1 (5.4)</td>
<td>1 (5.4)</td>
</tr>
<tr>
<td>White/Caucasian</td>
<td>3 (26.1)</td>
<td>12 (50)</td>
<td>0.3</td>
<td>4 (30.3)</td>
<td>4 (30.3)</td>
<td>6 (41)</td>
<td>6 (41)</td>
</tr>
<tr>
<td>Native American</td>
<td>3 (12.5)</td>
<td>21 (13.5)</td>
<td>0.6</td>
<td>1 (6.4)</td>
<td>1 (6.4)</td>
<td>2 (12)</td>
<td>2 (12)</td>
</tr>
<tr>
<td>Asian</td>
<td>1 (12.5)</td>
<td>9 (1.9)</td>
<td>0.6</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Age (median, IQR)</td>
<td>52 (23.1)</td>
<td>39 (28.2, 48.7)</td>
<td>0.002</td>
<td>42 (26.9, 55.2)</td>
<td>39 (30.4, 42.0)</td>
<td>0.047</td>
<td></td>
</tr>
<tr>
<td>SLEDAI (median, IQR)</td>
<td>5.5 (2.0)</td>
<td>4 (2, 7)</td>
<td>0.01</td>
<td>2 (2.5)</td>
<td>2 (2.5)</td>
<td>9 (8.1)</td>
<td>9 (8.1)</td>
</tr>
</tbody>
</table>

Figure 1. Modular gene expression and soluble mediator results. The plasma cell gene expression module was downregulated in those responsive to MMF (median -0.11) compared to those non-responsive to MMF (median 0.07) using Mann-Whitney, p=0.035. Two T-Cell modules, 4.1 and 4.15, were significantly downregulated in MMF (median -0.034 and -0.025), compared to AZA (median 0.017 and 0.025), using Mann-Whitney, p=0.018 and p=0.006. Multiple interferon modules noted higher modular scores for interferon and interferon activity in MMF, module 5.12 shown (median 0.19) compared to AZA (median 0.083), p=0.047. SCF was also higher in MMF (median 0.89) compared to AZA (median 1.27), p=0.039.

Disclosure: C. Arriens, None; R. Lu, None; T. Aberle, None; S. Kamp, None; W. DeJager, None; M. E. Munroe, None; E. Chakravarty, None; K. Thanou, None; J. T. Merrill, None; J. M. Guthridge, None; J. A. James, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/plasma-cell-and-t-cell-activity-downregulation-during-mmf-therapy-in-sle-may-be-necessary-for-successful-immunosuppression

Abstract Number: 2601

**Novel Anti-Malarial Drug Derivative Inhibited Type I Interferon Production and Autoimmune Inflammation in SLE Patient PBMC and in Trex1-/- Mouse Spleen and Heart**

Jie An1, Weinan Lai2,3, Joshua Woodward4, Xizhang Sun1, Lena Tanaka1, Tomikazu Sasaki5 and Keith B. Elkon6,

1Division of Rheumatology, University of Washington, Seattle, WA, 2Department of Medicine/Division of Rheumatology, University of Washington, Seattle, WA, 3Department of Rheumatology, Nanfang Hospital, Southern Medical University, Guangzhou, China, 4Department of Microbiology, University of Washington, Seattle, WA, 5Department of Chemistry, University of Washington, Seattle, WA, 6Division of Rheumatology, Department of Medicine, University of Washington, Seattle, WA

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM
**Background/Purpose:** Type I interferon (IFN-I) is strongly implicated in the pathogenesis of Systemic Lupus Erythematosus (SLE) as well as rare monogenic ‘interferonopathies’ such as Aicardi-Goutieres Syndrome (AGS) caused by mutations in the DNA exonuclease, TREX1. A recently described DNA-activated IFN-I pathway, cyclic GMP-AMP (cGAMP) synthase (cGAS), was linked to subsets of AGS and Lupus. Because of these clinical associations, we performed in silico screening for cGAS inhibitors and synthesized a novel drug we named X6, that belongs to the antimalarial drug (AMD) class of aminoacridines. Our previous data showed that, X6, blocked cGAS in vitro and, in a proof of principle in vivo experiment, it significantly reduced the interferon stimulated genes (ISGs) and cGAMP production in the Trex1-/- mouse model of AGS. Here, we compared X6 to a standard care AMD for SLE, Hydroxychloroquine (HCQ), for the treatment of murine AGS and also examined the effects on ISG expression in Peripheral Blood Mononuclear Cell (PBMC) from SLE patients.

**Methods:** Trex1-/- mice were treated orally with either X6 or HCQ 25mg/kg/day (n=10 in each group) for 8 weeks from birth. ISGs expressions from mouse heart and spleen tissues were quantified by qPCR. Multiple Reaction Monitoring (MRM) by Ultra-Performance Liquid Chromatogram coupled with tandem Mass Spectrometer (UPLC-MS/MS) was used to quantify cGAMP. SLE PBMCs (n=7) were incubated with X6 or HCQ for 20 hours at different dose concentrations. ISG expression was quantified by qPCR.

**Results:** Trex1 deficiency in mice leads to an autoimmune myocarditis and lupus-like systemic autoimmunity with increased ISG expression and cGAMP production. When efficacy of X6 was compared with HCQ, X6 was significantly more effective than HCQ in attenuating cGAMP (p<0.05) production in the heart and ISGs expression in both the spleen (ISG15: p<0.01 and ISG20: p<0.01) and the heart (ISG15: p<0.05, Mx1: p<0.05, CXCL10: p<0.01, IFNb: p<0.05). Surprisingly, HCQ in contrast to X6, increased cGAMP production and certain ISGs were also increased compared to vehicle control treated mice. To explore the potential application of drug X6 in complex autoimmune diseases such as SLE and to examine whether X6 is superior to HCQ at reducing IFN signature genes in SLE PBMC, we incubated SLE PBMC with X6 or HCQ for 20 hours and quantified ISG expression by qPCR. We observed that X6 was superior to HCQ in reducing ISG expression (IFI27: p<0.05, IFI44L: p<0.01, PKR: p<0.01, MX1: p<0.05) in SLE PBMC. Interestingly HCQ increased rather than reduced ISG expression compared to untreated controls.

**Conclusion:** Our studies demonstrate that X6 is superior to HCQ for the treatment of a cGAS-STING (Stimulator of Interferon Genes) mediated autoimmune myocarditis in vivo. Furthermore, X6 was superior to HCQ in the suppression of ISGs expression (Interferon activity) in SLE PBMC. These results indicate that the drug X6 could potentially be beneficial for the treatment of AGS and/or Lupus.

**Disclosure:** J. An, None; W. Lai, None; J. Woodward, None; X. Sun, None; L. Tanaka, None; T. Sasaki, None; K. B. Elkon, None.


**Abstract Number:** 2602

**Identification of Clinical and Serological Predictive Factors of Response to Rituximab Treatment in Systemic LUPUS Erythematosus (SLE) Patients**

Hiurma Sanchez-Perez¹ and David A. Isenberg², ¹Rheumatology, Rheumatology Division, Hospital Universitario de Canarias, La Laguna. Tenerife, Spain, ²Centre for Rheumatology Research, Division of Medicine, University College London, London, United Kingdom

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017
Background/Purpose: Response to Rituximab (RTX) varies significantly between Systemic Lupus Erythematosus (SLE) patients. Ethnicity may play a role in these differences, and a possible relationship has been suggested between the clinical response to RTX and the presence of certain auto-antibodies (ab), such as anti-ENA and anti-dsDNA ab, and C3 levels at baseline. The aim of this study was to identify biomarkers that could predict the response to RTX treatment in SLE patients.

Methods: This was a cross-sectional study of 121 SLE patients treated with RTX in UCLH between 2000 and 2016. Demographic, clinical and serological data were analysed. Disease activity was evaluated using the BILAG index. Patients were categorised as “Responders” if all or some of the As and Bs from the BILAG score at the time the RTX was given were lost at 6 and at 12 months, and as “Non-Responders” if none of the As and Bs were lost. Relapse after RTX treatment was defined as development of a new BILAG Grade A or B in any system. A uni and multivariate regression analysis were performed to identify predictive factors of response to RTX utilising a combination of clinical and biological markers.

Results: At 6 and at 12 months, 85% and 70% respectively of our patients had responded clinically to the RTX treatment. 24% of patients relapsed during the year after RTX. In the univariate analysis, constitutional symptoms at diagnosis (crude OR (95% CI): 5.66 (1.53-20.88), p=0.009) and the absence of musculoskeletal disease at the time of RTX (0.27, (0.09-0.81), p=0.019) were related to response at 6 months. In the multivariate analysis, both remained significant, (adjusted OR (95% CI)): 5.33 (1.39-20.41), p=0.014 and 0.26 (0.08-0.81), p=0.021 respectively. With respect to the response at 12 months, in the univariate analysis the presence of arthritis as the main indication for RTX (3.16 (1.31-7.58), p=0.010), the absence of renal disease at diagnosis (0.36 (0.15-0.86), p=0.022) and of cardiorespiratory disease at the time of RTX (0.29 (0.09-0.89), p=0.031), less than one anti-ENA ab (0.28 (0.12-0.66), p=0.003), low levels of C3 at diagnosis (0.29 (0.09-0.89), p=0.031), increased anti-dsDNA ab levels (0.38 (0.17-0.89), p=0.025) and decreased C3 levels (0.27 (0.11-0.63), p=0.002) before RTX were related to the response. In the multivariate analysis, only the absence of more than one anti-ENA showed significance (0.30 (0.11-0.75), p=0.010).

Conclusion: There is a relation between the presence of more than one anti-ENA ab and a worse response to treatment at 12 months and a higher risk of flaring. Having arthritis at the time of RTX leads to a negative response at 6 months but a lower risk of flare before 1 year.

Disclosure: H. Sanchez-Perez, None; D. A. Isenberg, None.


Abstract Number: 2603

Induction of Lupus Nephritis in Real Situation: Cyclophosphamide or Mycophenolate Mofetil?

Gabriela Munhoz1, Maira Lacerda1, Michelle Lopes1, Eduardo Ferreira Borba1, Luciana Seguro2 and Eloisa Bonfa3,

1Rheumatology, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, 2Rheumatology Division, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, 3Rheumatology Division, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil

First publication: September 18, 2017
Background/Purpose: Low-dose intravenous cyclophosphamide (Euro-lupus) and Mycophenolate mofetil (MMF) are well established in lupus nephritis induction therapy, but there are few studies comparing both treatments. Our aim was to compare their efficacy and safety after 6-month induction therapy.

Methods: Retrospective analysis of a prospective cohort of a single tertiary center. Patients with active lupus nephritis were treated with Euro-lupus (500mg, 15/15 days for 3 months, followed by MMF / azathioprine) or MMF (3g/day) as induction therapy. Clinical and laboratory data were evaluated at baseline and after 6 months. Serious infectious were defined as infections requiring hospitalization and/or intravenous antibiotics. Exclusion: creatinine clearance <10mL/min and pregnancy.

Results: 40 patients received Euro-lupus and 70 patients received MMF. Euro-lupus and MMF groups were comparable in age (35.23 ± 10.32 vs. 37.43 ± 11.43 years, p=0.316), female gender (85.0 vs. 84.2%, p=1.0), white race (75.0 vs. 62.9%, p=0.212) and disease duration (5.65 ± 5.64 vs. 6.20 ± 6.44 years, p=0.653). Baseline laboratory parameters, SLEDAI and glucocorticoid therapy data are shown in table 1. The frequency of previous nephritis (70.0 ± 60.0%, p = 0.312), systolic blood pressure (BP) levels (p=0.597) and diastolic BP (p=0.217) were comparable in the two groups. Six-month laboratory parameters, SLEDAI and glucocorticoid therapy data are shown in table 2. After 6 months, Euro-lupus had a higher increase in C3 (p=0.038) and C4 (p=0.046) levels and a greater reduction in prednisone daily dose (-24.69 ± 14.72 vs. -18.43 ± 13.97 mg/day, p=0.029) than MMF. Euro-lupus presented higher frequency of serious infections (22.5 vs. 7.1%, p=0.034) than MMF.

Conclusion: Euro-lupus and MMF protocols were effective as induction therapy for active lupus nephritis with a comparable frequency of patients achieving the proteinuria target and in spite of worse baseline parameters in the former group. The higher frequency of serious infection in Euro-lupus group may be associated with more aggressive glucocorticoid regimen in these patients.

Table 1: Baseline laboratory parameters, SLEDAI and glucocorticoid therapy data of Euro-lupus vs. MMF

<table>
<thead>
<tr>
<th></th>
<th>Euro-lupus</th>
<th>MMF</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine, mg/dL</td>
<td>1.08 ± 0.82</td>
<td>0.85 ± 0.32</td>
<td>0.039*</td>
</tr>
<tr>
<td>Albumin, g/dL</td>
<td>3.20 ± 0.56</td>
<td>3.35 ± 0.59</td>
<td>0.243</td>
</tr>
<tr>
<td>Positive anti-dsDNA</td>
<td>31 (77.5%)</td>
<td>46 (65.7%)</td>
<td>0.279</td>
</tr>
<tr>
<td>C3, mg/dL</td>
<td>64.93 ± 29.59</td>
<td>72.27 ± 29.42</td>
<td>0.212</td>
</tr>
<tr>
<td>C4, mg/dL</td>
<td>10.10 ± 8.17</td>
<td>12.05 ± 9.17</td>
<td>0.267</td>
</tr>
<tr>
<td>24-hour proteinuria, g</td>
<td>2.46 ± 1.84</td>
<td>2.21 ± 1.39</td>
<td>0.434</td>
</tr>
<tr>
<td>Presence of hematuria</td>
<td>35 (87.5%)</td>
<td>43 (61.4%)</td>
<td>0.004*</td>
</tr>
<tr>
<td>SLEDAI</td>
<td>13.80 ± 5.64</td>
<td>11.69 ± 5.87</td>
<td>0.068</td>
</tr>
<tr>
<td>Prednisone dose, mg/day</td>
<td>44.00 ± 15.20</td>
<td>37.71 ± 16.37</td>
<td>0.049*</td>
</tr>
<tr>
<td>IV methylprednisolone</td>
<td>32 (80.0%)</td>
<td>42 (60.0%)</td>
<td>0.036*</td>
</tr>
</tbody>
</table>

Table 2: 6-month laboratory parameters, SLEDAI and glucocorticoid therapy data of Euro-lupus vs. MMF
<table>
<thead>
<tr>
<th></th>
<th>Euro-lupus</th>
<th>MMF</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine, mg/dL</td>
<td>0.89 ± 0.47</td>
<td>0.82 ± 0.34</td>
<td>0.342</td>
</tr>
<tr>
<td>Albumin, g/dL</td>
<td>3.88 ± 0.46</td>
<td>3.61 ± 0.74</td>
<td>0.070</td>
</tr>
<tr>
<td>Positive anti-dsDNA</td>
<td>18 (45.0%)</td>
<td>24 (34.3%)</td>
<td>0.310</td>
</tr>
<tr>
<td>C3, mg/dL</td>
<td>97.03 ± 26.03</td>
<td>91.32 ± 28.06</td>
<td>0.300</td>
</tr>
<tr>
<td>C4, mg/dL</td>
<td>19.42 ± 10.77</td>
<td>16.87 ± 9.09</td>
<td>0.190</td>
</tr>
<tr>
<td>24-hour proteinuria, g</td>
<td>0.64 ± 0.48</td>
<td>0.89 ± 1.19</td>
<td>0.216</td>
</tr>
<tr>
<td>24-hour proteinuria &lt;0.8g/day</td>
<td>29 (72.5%)</td>
<td>47 (67.1%)</td>
<td>0.669</td>
</tr>
<tr>
<td>Presence of hematuria</td>
<td>13 (32.5%)</td>
<td>18 (25.7%)</td>
<td>0.511</td>
</tr>
<tr>
<td>SLEDAI</td>
<td>4.75 ± 3.44</td>
<td>4.51 ± 4.06</td>
<td>0.751</td>
</tr>
<tr>
<td>Prednisone dose, mg/day</td>
<td>19.31 ± 10.99</td>
<td>19.28 ± 13.08</td>
<td>0.991</td>
</tr>
</tbody>
</table>

Disclosure: G. Munhoz, None; M. Lacerda, None; M. Lopes, None; E. F. Borba, None; L. Seguro, None; E. Bonfa, None, 2.


Abstract Number: 2604

**The Effect of Subcutaneous Belimumab on Corticosteroid Use in Patients with Systemic Lupus Erythematosus (SLE): A Phase 3, Randomized, Placebo-Controlled Study**

Ronald F van Vollenhoven¹, April Thompson², Bonnie Pobiner², Joe Eastman², Anne Hammer², James Groark³ and Damon Bass³, ¹Amsterdam Rheumatology and Immunology Center, Amsterdam, Netherlands, ²GSK Research Triangle Park, Research Triangle Park, NC, ³GSK Collegeville, Collegeville, PA

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Tuesday, November 7, 2017

Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design

Session Type: ACR Poster Session C

Session Time: 9:00AM-11:00AM

**Background/Purpose:** Reduced corticosteroid use is considered a key goal in SLE treatment. This concept of ‘steroid-sparing’, seen with intravenous (IV) belimumab based on cumulative steroid use over 52 weeks¹, was investigated in patients with SLE treated with subcutaneous (SC) belimumab.

**Methods:** This was a Phase 3, multicenter, double-blind, 52-week study (112341/NCT01484496) in adult patients with active SLE (SELENA-SLEDAI score ≥8). Patients were randomized (2:1) to weekly belimumab 200 mg SC or placebo, plus standard care (SoC). The primary endpoint was SLE Responder Index response rate at Week 52²; efficacy and safety data have been published³. Here, the effects on corticosteroid use (prednisone equivalent) are reported, evaluating multiple pre-specified measures including the proportion of patients (>7.5 mg/day at baseline) with a ≥25% reduction from baseline to ≤7.5 mg/day during Weeks 40–52 (key secondary endpoint).
Results: Baseline corticosteroid use was comparable between groups (belimumab, 481 [86.5%]; placebo, 241 [86.1%]), with most patients receiving >7.5 mg/day (60.2%). A numerically greater proportion of patients with baseline dose >7.5 mg/day in the belimumab group had a dose reduction of ≥25% to ≤7.5 mg/day during Weeks 40–52 compared with patients receiving placebo (belimumab, 18.2%; placebo, 11.9%; OR [95% CI] 1.65 [0.95, 2.84]; p=0.0732). Fewer patients in the belimumab group versus the placebo group required ≥50% increase (min ≥5 mg/day) in dose during Weeks 40–52 (Week 52: belimumab, 4.9%; placebo, 7.9%; OR [95% CI] 0.56 [0.31, 1.02]; p=0.0574) or any increase in corticosteroid from Weeks 20–28 and 36–52 (Week 52: belimumab, 8.1%; placebo, 13.2%; OR [95% CI] 0.55 [0.34, 0.87]; p=0.0117). The percentage of patients with ≥50% reduction in corticosteroid dose by Week 52 was similar in the belimumab (range: 0.2–15.2%) and placebo (range: 0–14.1%) groups. A small number of patients in each group required an increase (≥50%, min ≥5 mg/day) in dose from baseline (range: belimumab 2.7–5.2%; placebo, 1.4–8.6%). Mean (SD) cumulative corticosteroid dose at Week 52 was 3933.8 mg (3600.76) in the belimumab group and 4567.3 mg (5981.53) in the placebo group; the median (IQR) was the same in both groups (3650.0 [1825–5475]; p=0.4299). Median (IQR) corticosteroid dose at baseline was 10 mg/day (IQR 5–15) in both groups; no meaningful change occurred in either group by Week 52. Mean dose at baseline was 10.8 mg/day and 11.2 mg/day in the belimumab and placebo groups, with mean changes at Week 52 of -1.76 mg and -0.03 mg, respectively. Adverse events incidence (≥1) was similar (belimumab, 80.8%; placebo 84.3%).

Conclusion: SC belimumab decreased the need for raising corticosteroid dose during the study. Other outcomes showed trends towards a corticosteroid-sparing effect of belimumab, consistent with IV studies of belimumab.1,4


Study funded/conducted by GSK. Editorial assistance: Sam Halliwell, PhD, Fishawack Indicia Ltd, funded by GSK.
Background/Purpose:

There is a pressing need for novel biologic therapies in systemic lupus erythematosus (SLE). We sought to systematically review the outcomes of recent phase 3 clinical trials of biologic therapies for SLE and lupus nephritis, and conduct a meta-analysis of steroid sparing effect in these trials.

Methods:

A systematic review of the outcomes of phase 3 clinical trials of biologic therapies for SLE and lupus nephritis was undertaken. Studies were identified by searching the Medline (via Pubmed), EMBASE, CINAHL and SCOPUS databases, the Cochrane library, and clinicaltrials.gov. Adult human studies published in English in the last ten years (until 18 April 2017) were included. All articles that reported outcomes of phase 3, randomized, placebo-controlled clinical trials of biologic therapies for SLE or lupus nephritis were included. A random-effects meta-analysis to compare a common corticosteroid reduction endpoint in the trials of rituximab, belimumab, tabalumab and epratuzumab in SLE, was conducted.

Results:

A total of twenty-eight studies were identified, with nine being conducted in SLE, five in lupus nephritis and the remaining fourteen being post hoc analyses of phase 3 trials in SLE. All biologic therapies trialed targeted B cells (rituximab, belimumab, tabalumab, epratuzumab, atacicept, ocrelizumab), except for abetimus sodium and abatacept. Only the three phase 3 trials of belimumab in SLE met their primary endpoints, although benefit in secondary endpoints and reduction in serological activity was often seen in the other studies. In particular, the meta-analysis (Figure 1) showed that most therapies (belimumab IV and SC, tabalumab and epratuzumab) had a steroid sparing effect, compared to placebo (pooled relative risk 0.76; 95% CI: 0.64, 0.91). Therapies were generally well tolerated, however, three studies were terminated prematurely due to serious side effects, and another due to discontinuation of drug supply. Several ongoing phase 3 trials of B cell and non-B cell agents are currently underway.

Figure 1. Meta-analysis of percentage of patients with decrease in corticosteroid dose from baseline:-

- to ≤ 7.5mg/day, by ≥ 25% from baseline between weeks 40-52 (BLISS-SC, BLISS-52, BLISS-76)
- to ≤ 7.5mg/day, between weeks 24-52 for ≥ 3 consecutive months without an increase in antimalarial or immunosuppressant therapy (ILLUMINATE-1 and -2)
- to ≤ 10mg/day or ≤ 7.5mg/day by week 24 (ALLEVIATE-1 and -2)
- < 10mg/day between week 24-52 in addition to a major clinical response (EXPLORER)
Conclusion:

Although almost all phase 3 clinical trials (with the exception of belimumab) have failed to meet their primary efficacy endpoint, meta-analysis shows a significant steroid sparing effect for novel biologic therapies in SLE. This highlights allowance of background steroid dose as a major methodologic consideration in the design of future SLE clinical trials.

Disclosure: S. Oon, None; M. Huq, None; T. Godfrey, None; M. Nikpour, None.


Abstract Number: 2606

**Pneumococcal Vaccination in Patients with Systemic Lupus Erythematosus: A Multicenter Placebo-Controlled Randomized Double-Blind Study**

Sophie Grabar1, Matthieu Groh2, Mathilde Bahuaud3, Nathalie Costedoat-Chalumeau4, Veronique Le Guern5, Renato Fior6, Boris Bienvenu7, eric hackulla8, Mohamed Hamidou9, Jean Sibilia10, Alexis Mathian11, Thomas Hanslik12, Loïc Guillemin for the French Vasculitis Study Group13, Frédéric Batteux3 and Odile Launay14, 1Université Paris Descartes, Sorbonne Paris Cité AP-HP, Unité de Biostatistique et Épidémiologie, Groupe Hospitalier Cochin Broca Hôtel-Dieu, Paris, France; INSERM, UPMC Université Paris 06, Institut Pierre Louis d’Épidémiologie et de Santé Publique (IP, Paris, France, 2National Referral Center for Rare Systemic Autoimmune Diseases, Hôpital Cochin, AP–HP, Université Paris Descartes, Sorbonne Paris Cité AP-HP, Département d’Immunologie Biologique, Groupe Hospitalier Cochin Broca Hôtel-Dieu, Paris, France, 3Université Paris Descartes, Sorbonne Paris Cité AP-HP, Department of Internal Medicine, Department of Internal Medicine, Cochin University Hospital, Paris, France, 4Université Paris-Sud, AP-HP, Service de Médecine Interne et Immunologie Clinique, Hôpital Antoine Béclère, Clamart, France, 5Internal Medicine, Hôpital de la côte de Nacre, Caen, France, 6chru lille hospital, lille, France, 7Medecine Interne, CHU Hôpital Dieu, Nantes, France, 8Medecine Interne, Centre de Référence Maladies Auto-Immunes et Auto-Inflammatoires Systémiques Rares, Hôpital Cochin, Paris, France, 9Medecine Interne, Chinoin, Paris, France, 10Department of Rheumatology, Strasbourg University Hospital, Strasbourg, France, 11Université Pierre et Marie Curie, Sorbonne Paris Cité AP-HP, Service de Médecine Interne 2, Centre de Référence National pour le Lupus et le Syndrome des Antiphospholipides, institut E3M, Paris, France, 12Université Versailles Saint-Quentin-en-Yvelines, APHP, Service de Médecine Interne, Hôpital Ambroise Paré, Boulogne-Billancourt, France, 13Service de Médecine Interne, Centre de Référence Maladies Auto-Immunes et Auto-Inflammatoires Systémiques Rares, Hôpital Cochin, Paris, France, 14Université Paris Descartes, Sorbonne Paris Cité AP-HP, Groupe Hospitalier Cochin Broca Hôtel-Dieu, Fédération d'Infectiologie, Paris, France; Inserm, F-CRIN I-REIVAC., Paris, France

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**
Invasive pneumococcal disease and respiratory tract infections are both frequent and severe in patients with systemic lupus erythematosus (SLE). This study aimed to compare the immunological efficacy and safety of pneumococcal vaccination with the 23-valent polysaccharide (PPS) vaccine alone to a sequential immunization with the 7-valent pneumococcal conjugate (PnCj) vaccine followed by PPS in patients with SLE and stable disease.

Methods:

Multicenter randomized placebo-controlled double-blind trial: PPS vaccine alone (placebo-PPS group) or PnCj vaccine followed by PPS vaccine (PnCj-PPS group) 24 weeks later. The primary endpoint was the rate of responders at week 28 to at least 5 of the 7 serotypes (4, 6B, 9V, 14, 18C, 19F and 23F) shared by both PPS and PnCj. The response to each serotype was defined as both a two-fold increase between inclusion and week 28 of pneumococcal IgG antibody titers (ELISA) and an antibody titer ≥ 1 µg/mL at week 28. Pneumococcal IgG antibodies’ opsonophagocytic activity (OPA) was also assessed at baseline and at week 28, and the response to a specific serotype was defined by both ≥ four-fold increase of the opsonization index (OI, defined by the serum dilution killing 50% of the bacterial inoculum) between baseline and week 28, and an OI ≥ 8 at week 28.

Results:

Twenty-five patients in the placebo-PPS group and 17 in the PnCj-PPS group were included in a modified intention-to-treat analysis. The primary endpoint was reached in 72% (18/25) in the placebo-PPS and 76% (13/17) in the PnCj-PPS group (p = 0.75). There was no difference in the rates of responders with OPA. At week 52, 13/18 (72%) patients in the placebo-PPS group and 10/13 (77%) patients in the PnCj-PPS group (p=0.77) that met the primary endpoint at week 28 were still responders to ≥ 5/7 serotypes shared by both PPS and PnCj vaccines. Nine SLE flares were reported in 6 patients (4 in the placebo-PPS and 2 in the PnCj-PPS groups respectively, p=0.70).

Conclusion:

Sequential administration of PnCj vaccine followed by PPS vaccine is safe and shows short-term immunological efficacy in patients with SLE but was not superior to the PPS vaccine alone. Future studies with new vaccines and/or innovative schedule designs are warranted in order to better protect SLE patients against pneumococcal infections.

Disclosure: S. Grabar, None; M. Groh, Pfizer Inc, 2; M. Bahuaud, None; N. Costedoat-Chalumeau, None; V. Le Guern, None; R. Fior, None; B. Bienvenu, None; E. hachulla, None; M. Hamidou, None; J. Sibilia, None; A. Mathian, None; T. Hanslik, None; L. Guillevin for the French Vasculitis Study Group, None; F. Batteux, Pfizer, 2; O. Launay, Pfizer Inc, 2.
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
BDCA2 is a plasmacytoid dendritic cell (pDC)-specific receptor that, upon activation, inhibits the production of inflammatory factors by human pDCs, including IFN-α a major player in the pathogenesis of SLE. This 3-Part Phase 1 study evaluated the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD) and clinical efficacy of single and multiple ascending doses (SAD-MAD) of BIIB059 in HV and SLE subjects (NCT02106897). Comparison of PK and PD parameters between HV and SLE as well as final PK-PD results from the SAD in SLE and MAD results are presented.

Methods:
In the SAD part, 12 subjects with active SLE were randomized 2:1 to receive a single IV dose level of BIIB059 (20mg/kg) or placebo. In the MAD part, HV received either 2 (Cohort 9 to 11) or 3 (Cohort 12) SC administrations of Placebo or BIIB059 20, 50 or 150mg (Cohort 9 , 10, 11) Q4W or 3 SC 300mg (Cohort 12) Q2W. Subjects with active SLE , received either 2 (Cohort 13) or 3 (Cohort 14) SC placebo or BIIB059 50 mg (Cohort 13) or 300 mg (Cohort 14). The dose levels were selected based on emerging data from the Part 1 in HV and was not to exceed the maximum tolerated dose or the highest evaluated and tolerable dose. Blood samples were obtained before and after each dose administration to characterize PK and PD (BDCA2 on pDC) relationship for BIIB059.

Results:
Part 1 PK and PD results (SAD) in healthy volunteers, HV) and Part 2 PD results have been previously presented (single dose in SLE)\(^1\)-\(^2\). In Part 2 of the study, following IV administration, mean \(t_{1/2}\) in SLE subjects was 18.1 days, with a mean CL of 0.251 L/day and a mean volume of distribution \(V_{ss}\) of 5.41 L. Following SC administration, in Part 3a, mean \(t_{1/2}\) in HV subjects ranged from 13.3 to 19.5 days, mean CL\(_{ss}/F\) ranged from 0.28 to 0.367 L/day and \(V_{z}/F\) ranged from 7.23 to 9.36 L. In Part 3b, mean \(t_{1/2}\) in SLE subjects ranged from 12.6 to 20.5 days with a mean CL\(_{ss}/F\) of 0.455 to 0.485 L/day and a mean \(V_{z}/F\) of 5.93 and 12.8 L. Exposure (AUC and Cmax) for BIIB059 increased with dose in both HV and SLE subjects. However exposure in SLE subjects was approximately 40% lower compared to HV which could not be attributed to body weight. The observed mean accumulation ratio for AUC was slightly lower in SLE subjects (2.58) compared to HV (2.66) after BIIB059 SC administration. Complete BDCA2 internalization was achieved at all dose levels, the duration of which was dose dependent, and was similar for HV and SLE subjects. Reappearance of BDCA2 on circulating pDCs occurred when serum concentrations of BIIB059 dropped to ~1 μg/mL. BIIB059 was generally well tolerated; the incidence of adverse events (AEs) was similar between BIIB059- and placebo-treated HV and/or SLE subjects in both SAD and MAD.

Conclusion:
BIIB059 was well tolerated with an acceptable safety profile.

Exposure in SLE subjects was lower compared to HV while BDCA2 internalization was similar. Based on the Phase 1 data, BIIB059 is currently evaluated in a Phase 2 trial (NCT02847598).

References:
Abstract Number: 2608

Tacrolimus in Non-Asian Systemic Lupus Erythematosus Patients: A Real-Life Experience from Three European Centers

Chiara Tani1, Miguel Martin-Cascon2, Mériem Belhocine3, Roberta Vagelli1, Chiara Stagnaro4, Guillermo Ruiz-Irastorza5, Nathalie Costedoat-Chalumeau3 and Marta Mosca1, 1Rheumatology Unit, University of Pisa, Pisa, Italy, 2Autoimmune Diseases Research Unit, BioCruces, Hospital Universitario Cruces, Barakaldo, Spain, 3Service de médecine interne Pôle médecine, Hôpital Cochin, Centre de référence maladies auto-immunes et systémiques rares de l’île de France, Paris, France, 4Rheumatology Unit, University of Pisa, PISA, Italy, 5Autoimmune Diseases Research Unit, BioCruces, Hospital Universitario Cruces, Baracaldo, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: there is no consensus on the use of Tacrolimus (TAC) in patients with SLE; clinical studies on TAC, including all the RCT, are mostly limited to patients of Asian ethnicity and hampered by significant heterogeneity. To analyze the real-life practice on the use of TAC in SLE from 3 European referral centers.

Methods: this is a retrospective analysis of prospectively collected data. Adult patients with SLE, according to the 1997 ACR criteria, followed at 3 European referral centers were included. For each patient, demographics, organ involvement and treatment history were collected; concomitant medications, SLEDAI, laboratory features and physician’s global assessment (PGA) were collected at baseline and at 3-6-12 months after starting TAC. Renal response was defined as complete (CR) in case of 24-hour proteinuria <500 mg/dl + inactive urinary sediment + normal creatinine.

Results: 29 patients were included in this analysis (89% female, mean age 38±9 years, mean disease duration 12.9±6 years). Ethnicity was White (82%), Black (14.5%), Hispanic (3.5%). The main indication for TAC prescription was renal involvement (79%), joint (7%), skin (7%), hematological (7%), serositis (3.5%). The median daily dose of TAC was 4.5 mg (IQR 3-5.5). When renal involvement was the main indication, TAC was prescribed for a renal flare in 72% of cases, and for renal disease onset in the remaining cases. In 65.5% of patients, TAC was a second-choice treatment either for the failure of, or for the intolerance of a previous IS therapy. The median number of previous IS was 2 (IQR 1-3). Concomitant medications at TAC institution included GC (89.6 %; median daily dose 7.5 IQR 3.75-12.5), HCQ (67%),
MMF (30%), AZA (11%), RTX (3%), belimumab (14%). At 3 months, according to the PGA, there was a complete resolution of symptoms in 8 pts (32%), partial resolution in 11 pts (44%) and no improvement in 6 pts (24%). This corresponds to: 1) a significant decrease in the mean SLEDAI, (p=0.0006); 2) a significant decrease in the mean 24-hour proteinuria (p=0.001); a significant increase in C3 (p=0.009) and stable creatinine values. In patients with renal involvement, a CR was documented in 6 pts (27.3%), a PR in 7 (31.8%) and no response in 7 (31.8%). At 6 months, the physician declared a complete resolution in 47%, a partial resolution in 29% and no improvement in 23%. The same trend was maintained at 12 months of follow-up. Four patients discontinued the therapy before 3 months. At the time of this analysis, TAC was discontinued in 9 pts (31%); reasons for discontinuation were inefficacy (13 %), drug intolerance (10%), disease remission (6.8 %) and infections (3.4 %), (table 1).

**Conclusion:** this study describes the use of TAC in a multicenter cohort of non-Asian SLE patients. Despite the limitation due to the small number of patients and the uncontrolled nature of the study, these data show that TAC can be considered a valid therapeutic option in SLE patients, especially in renal involvement.

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>3 months</th>
<th>6 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>N of patients tot-renal</td>
<td>29-23</td>
<td>25-17</td>
<td>18-17</td>
<td>18-16</td>
</tr>
<tr>
<td>SLEDAI (median±IQR)</td>
<td>8 (5.5-12)</td>
<td>4 (3-6)</td>
<td>4 (2-7)</td>
<td>5 (2-8)</td>
</tr>
<tr>
<td>PGA (complete resolution %)</td>
<td>33.3%</td>
<td>47%</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>C3 (median, IQR) mg/dl</td>
<td>74 (61-83)</td>
<td>78 (71-95)</td>
<td>83 (72-99)</td>
<td>84 (79-95)</td>
</tr>
<tr>
<td>Creatinine mg/dl (median±IQR)</td>
<td>0.7 (0.5-0.88)</td>
<td>0.82 (0.6-1.1)</td>
<td>0.9 (0.6-1.17)</td>
<td>0.8 (0.6-1.07)</td>
</tr>
<tr>
<td>24hproteinuria mg (median±IQR)</td>
<td>1425 (710-2630)</td>
<td>700 (140-1370)</td>
<td>330 (115-1100)</td>
<td>380 (140-1500)</td>
</tr>
</tbody>
</table>

**Disclosure:** C. Tani, None; M. Martin-Cascon, None; M. Belhocine, None; R. Vagelli, None; C. Stagnaro, None; G. Ruiz-Irastorza, None; N. Costedoat-Chalumeau, None; M. Mosca, None.


**Abstract Number:** 2609

**A Systematic Literature Mining and Gene Expression Analysis Identifies Possible Drug Candidates for Repositioning in Lupus**

Peter E. Lipsky, Matt Ryals, Adam Labonte, Sarah Heuer, James Dittman, Michelle Catalina and Amrie Grammer, AMPEL BioSolutions and RILITE Research Institute, Charlottesville, VA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM
Background/Purpose:

Since new therapies for lupus have been extremely slow to develop and lupus patients have a great unmet medical need, an independent pharma-external effort has been undertaken to evaluate drugs for potential use in this autoimmune disease. In addition, bioinformatic analyses of gene expression profiles were used to confirm the potential utility of identified drug candidates.

Methods:

A comprehensive effort to identify possible drug candidates for repositioning into lupus was initiated in 2013 by crowdsourcing suggestions from the lupus community (www.linkedin.com/lrxlstat) in conjunction with a comprehensive effort at literature mining for information relevant to the more than 1000 compounds approved for human use by the FDA. In 2013, the evidence-based Composite Lupus Treatment Scoring (CoLTs) of each of 157 therapies considered potentially appropriate for lupus was carried out\(^1\). Since the initial evaluation, the FDA has approved > 125 new drug indications, 7 of which targeted a rheumatic disease, but none of which was approved for in lupus. Additionally, >50 drugs-in-development for other indications were identified as possible lupus treatments. All drugs were ranked by the CoLT scoring system that takes into account scientific rationale, experience in lupus mice/human cells, previous clinical experience in autoimmunity, drug properties and adverse event profile. In addition, potential utility of a drug target in SLE was gauged by bioinformatic analysis of gene expression from tissues (kidneys, skin, synovium) and the periphery (whole blood, B cells, T cells, myeloid cells) from both active and inactive patients. Microarray and RNASeq data were analyzed for differentially expressed genes compared with healthy patients and for correlations with clinical parameters.

Results:

Of the >125 newly FDA–approved drug indications, fifty were judged to be potentially relevant for lupus and were evaluated in detail and nine were identified as high-priority candidates for repositioning including drugs targeting cellular metabolism, cell cycle checkpoints, kinases and various pathways in the immune system. Scoring of drugs-in-development added 25 high priority candidates including inhibitors of complement, HDAC, PARP, ubiquitin ligases and as well as antagonists of cell surface receptors and cytokines. In each circumstance, evidence from literature mining was confirmed by gene expression analysis.

Conclusion:

Independently scoring the properties of newly approved drugs and potential drug targets has not only identified unique candidates that could be useful in lupus and possibly other autoimmune/inflammatory conditions, but has also yielded a rigorous evidence-based process by which therapies can be objectively rated for possible clinical application to treat these conditions, thereby mitigating risk in drug development.

References:


Disclosure: P. E. Lipsky, None; M. Ryals, None; A. Labonte, None; S. Heuer, None; J. Dittman, None; M. Catalina, None; A. Grammer, None.


Abstract Number: 2610

Quantiferon Testing in a Clinical Trial of Systemic Lupus Erythematosus

Niti Goel\(^1\), Stephen Wax\(^2\), Amy Kao\(^2\), Russell Reeve\(^3\) and Marsha Mackey\(^4\), \(^1\)QuintilesIMS, Duke University School of Medicine, Durham, NC, \(^2\)EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA), Billerica, MA, \(^3\)QuintilesIMS, Durham, NC, \(^4\)QuintilesIMS, Rockville, MD
Background/Purpose: Tuberculosis (TB) has been reported to occur at a higher rate in SLE patients than in the general population. As a result, most clinical trials of new therapeutic agents in SLE seek to exclude patients with untreated latent or active TB. Unfortunately, there is no gold standard test for the detection of latent TB infection (LTBI). Interferon gamma release assays (IGRAs) are potentially confounded by underlying immunologic impairments, e.g., lymphopenia, immunosuppressant use and disease activity, which can lead to indeterminate (IND) results even in the presence of LTBI. There can also be technical error impacting the results. A common resolution to resolve IND results involves repeat testing. In this post hoc analysis, we sought to evaluate the utility of the QuantiFERON-TB GOLD test (QFT) and repeat testing for IND results in the screening of patients entering an SLE clinical trial.

Methods: Patients with active SLE who had signed informed consent to enter the Phase IIb ADDRESS II study (NCT01972568) with no prior history of TB infection were evaluated for LTBI either locally via IGRA or TB skin test; or QFT centrally. Data for those who received centralized QFT were evaluated. Patients with a positive (POS) QFT result were excluded from trial participation. Patients with an IND QFT result were to be retested: only if negative (NEG) on repeat was a patient eligible for inclusion.

Results: Ninety-nine patients from sites in Bulgaria, Chile, Germany, Poland, Russia and the United Kingdom received QFT centrally. Of these, 84 (84.8%) had a NEG QFT, 8 (8.1%) were POS and 7 (7.1%) were IND on the initial test (Table). Nine patients with an initial NEG result underwent repeat testing for various reasons, and all remained NEG. Of the 7 patients who were initially IND: 2 were IND on repeat testing; 1 had no repeat result since screen failed; 1 was NEG based on a repeat QFT performed locally, and 3 were NEG on repeat QFT centrally. Three of the 4 patients NEG on repeat QFT were enrolled. Even if meeting exclusion criterion for LTBI, patients were often screen failed for another reason, minimizing the impact of the exclusion criterion on overall enrollment. No patients developed TB during the study. In those patients who had IND results, the absolute lymphocyte count was numerically lower with a higher percentage of patients having lymphocyte counts below the lower limit of normal, than in those with POS or NEG results (p-values by t-test > 0.05).

<table>
<thead>
<tr>
<th>Initial screening QFT results</th>
<th>Repeat QFT indeterminate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD, y</td>
<td>44.1 ± 12.56</td>
</tr>
<tr>
<td>Females, n (%)</td>
<td>79 (94.0)</td>
</tr>
<tr>
<td>Lymphocyte count*, mean ± SD, x 10^3/µL (n)</td>
<td>1.46 ± 0.747 (82)</td>
</tr>
<tr>
<td>Lymphocyte count below normal limits*, n (%)</td>
<td>23 (28.0)</td>
</tr>
<tr>
<td>Screen failed for LTBI, n (%)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Enrolled, n (%)</td>
<td>39 (46.4)</td>
</tr>
</tbody>
</table>

* Normal range 1.02 – 3.36 x 10^3/µL

Conclusion: In our study, repeat IND QFT results for TB occurred infrequently. Consistent with previous reports, low lymphocyte counts may contribute to generation of IND results. Limitations of evaluating only screening data include not being able to evaluate the impact of disease activity or immunosuppressants on the QFT results. As only 2 of 99 patients had IND results twice, excluding patients on this basis should be considered a viable approach to confirm eligibility for a clinical trial in SLE.
**Disclosure:** N. Goel, QuintilesIMS, 3; S. Wax, EMD Serono, Inc., 3; A. Kao, EMD Serono, Inc., 3; R. Reeve, QuintilesIMS, 3; M. Mackey, Marsha Mackey, 3.


**Abstract Number:** 2611

**Walk SLE – a Pilot Study Exploring Walk with Ease (WWE), a Self-Directed Walking Program, in Lupus Patients**

Brittany-Belle E. Gordon1, Katherine Kaufman2, Sean T. Hicks1, Julie A. Norfleet1, Rebecca J. Cleveland1, Leigh F. Callahan3 and Saira Z. Sheikh1, 1Thurston Arthritis Research Center, University of North Carolina School of Medicine, Chapel Hill, NC, 2Department of Pediatrics, Duke University School of Medicine, Durham, NC, 3Thurston Arthritis Research Center, University of North Carolina at Chapel Hill, Chapel Hill, NC

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Tuesday, November 7, 2017
**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
**Session Type:** ACR Poster Session C
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Fatigue and arthritis are common sources of impairment in SLE patients that persist despite lifestyle and pharmacologic interventions. Walk with Ease (WWE) is the Arthritis Foundation’s 6-week evidence-based walking program developed for adults with arthritis that has been shown to improve physical function, pain, stiffness and fatigue in individuals with arthritis. WWE is offered in two formats – group (instructor led) or self-directed. The goal of this study was to examine the feasibility of self-directed WWE in SLE patients.

**Methods:** In an interim analysis, pre- and post-6 week evaluation with no usual care comparison group was conducted in 48 patients with SLE in North Carolina. Self-reported outcomes including symptoms (pain, stiffness and fatigue visual analog scales [VAS]) and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-fatigue) scale were evaluated. Means and effect sizes (ES) with 95% confidence intervals were computed for changes in symptoms between baseline and 6 weeks, adjusted for gender, age, race, and baseline outcome. Participant satisfaction measures with WWE are reported as percentages.

**Results:** Two participants were screen failures, 29 participants completed the WWE program at the time of analysis, 7 discontinued the study and 6 were lost to follow-up. There were no statistically significant differences between those who did not complete the study and those who did. Participants were mainly women (90%), aged ≥ 40 years, self-identified as black (48%) and 11 years from initial SLE diagnosis. Three participants also had a physician diagnosis of OA, while four participants had concurrent fibromyalgia. At the end of 6 weeks, participants reported having reduced FACTT-fatigue scores (ES=0.33), and having less VAS pain, stiffness and fatigue (ES=0.42, 0.24 and 0.10, respectively). Most participants reported walking for at least 30 minutes/day (46%), ≥3 days/week (89%) and utilized the workbook for motivation (74%). Participants also reported increased physical activity (86%), confidence to continue exercising (100%) and satisfaction from the program (97%).

**Conclusion:** WWE is a feasible, low-cost program that may decrease SLE-related fatigue, pain and stiffness, improve activity and promote long-term lifestyle changes.
Disclosure: B. B. E. Gordon, None; K. Kaufman, None; S. T. Hicks, None; J. A. Norfleet, None; R. J. Cleveland, None; L. F. Callahan, None; S. Z. Sheikh, None.


Abstract Number: 2612

Disparities in Antimalarial Prescribing for Systemic Lupus Erythematosus Using a Real-World, Electronic Health Record

J.B. Boone, Wendy Xiong, Cecilia P. Chung, Leslie Crofford and April Barnado, Medicine, Vanderbilt University Medical Center, Nashville, TN

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Antimalarials (AMs) reduce disease activity and improve survival in patients with systemic lupus erythematosus (SLE) and are recommended regardless of disease severity. Prior studies using mostly patient self-reported medication data showed that AMs are not universally prescribed. Using a real-world electronic health record (EHR) cohort, we investigated if patient or prescriber characteristics impacted AM prescribing frequency in SLE.

Methods: We identified potential SLE cases from a de-identified EHR with over 2.8 million subjects using a previously validated and published algorithm. A subject was a case if diagnosed with SLE by a specialist (rheumatologist, dermatologist, or nephrologist). Subjects excluded had alternative autoimmune diagnoses (i.e. cutaneous or drug-induced lupus), uncertainty in diagnosis, or missing notes. On chart review, we collected current age at time of analysis, sex, race, presence of SLE nephritis, and specialist managing SLE. SLE nephritis was defined as a positive renal biopsy or clinical diagnosis by a specialist. We assessed for ever use of AMs from inpatient and outpatient electronic prescribing and natural language processing that searched for medications in clinic notes and phone messages. We evaluated for
differences in SLE cases prescribed AMs vs. those not prescribed using the Mann-Whitney U test for continuous variables and chi-square or Fisher’s exact test for categorical variables.

**Results:** We identified 566 cases confirmed on chart review. The SLE cases had a mean current age of 50 ± 18 years and were predominantly female (89%) with race breakdown of 63% Caucasian, 30% African American, 5% Hispanic, and 2% Asian. Of the 566 cases, 534 (94%) patients were ever prescribed an AM. Of the 32 (6%) patients not prescribed an AM, no contraindications were found on chart review. There were no differences in sex or race between SLE cases prescribed AMs vs. cases who were not (Table 1). SLE cases prescribed AMs were younger compared to cases not prescribed AMs (49 ± 18 vs. 57 ± 21, p = 0.05). SLE cases who primarily saw a nephrologist were less likely to have AMs prescribed compared to cases who saw a rheumatologist or dermatologist (64% vs. 98% vs. 100%, p < 0.001). SLE nephritis cases trended towards having less AMs prescribed compared to cases without nephritis (91% vs. 95%, p = 0.06).

**Conclusion:** Using a large EHR cohort, we found 94% of SLE patients were ever prescribed an AM. Our high rate of AM prescribing compared to prior studies suggests that prescribing AMs is becoming more standard practice. SLE patients that were older, primarily followed with a nephrologist, and had nephritis were less likely to have AMs prescribed. Recognizing prescribing practices for AMs in SLE can target future quality improvement efforts.

<table>
<thead>
<tr>
<th>Table 1. Subject Characteristics</th>
<th>Ever Prescribed Antimalarials</th>
<th>Not Prescribed Antimalarials</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Current age, mean ± SD</strong></td>
<td>49 ± 18</td>
<td>57 ± 21</td>
<td>0.05</td>
</tr>
<tr>
<td><strong>Sex, n (%)</strong></td>
<td>478 (94%)</td>
<td>28 (6%)</td>
<td>0.72</td>
</tr>
<tr>
<td>Female</td>
<td>56 (93%)</td>
<td>4 (7%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Race/ethnicity, £ n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>307 (94%)</td>
<td>20 (6%)</td>
<td>0.69</td>
</tr>
<tr>
<td>Black</td>
<td>150 (95%)</td>
<td>8 (5%)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>19 (90%)</td>
<td>2 (10%)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>13 (100%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td><strong>SLE nephritis, n (%)</strong></td>
<td></td>
<td></td>
<td>0.06</td>
</tr>
<tr>
<td>Absent</td>
<td>411 (95%)</td>
<td>20 (5%)</td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>123 (91%)</td>
<td>12 (9%)</td>
<td></td>
</tr>
<tr>
<td><strong>Prescribing Specialty, n (%)</strong></td>
<td></td>
<td></td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Rheumatology</td>
<td>520 (98%)</td>
<td>9 (2%)</td>
<td></td>
</tr>
<tr>
<td>Nephrology</td>
<td>9 (64%)</td>
<td>5 (36%)</td>
<td></td>
</tr>
<tr>
<td>Dermatology</td>
<td>5 (100%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
</tbody>
</table>

*Mann-Whitney U test for continuous variables and chi-square or Fisher’s exact test for categorical variables.*
47 cases had missing race data and were not included.

Disclosure: J. B. Boone, None; W. Xiong, None; C. P. Chung, None; L. Crofford, None; A. Barnado, None.


Abstract Number: 2613

Antimalarial Drug Toxicities in Rheumatic Skin Disease Patients

Lavanya Mittal1, Lingqiao Zhang2, Rui Feng2 and Victoria Werth1, 1Department of Dermatology, Corporal Michael J. Crescenz VAMC, Department of Dermatology, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, 2Department of Biostatistics and Epidemiology at the Hospital of the University of Pennsylvania, Philadelphia, PA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Although existing evidence demonstrates the efficacy of antimalarials for rheumatic skin disease, the safety of these medications, and particularly quinacrine, remain debated. Quinacrine may soon become increasingly difficult to prescribe as a result of these concerns. We investigate the toxicity risk associated with various antimalarial combinations in rheumatic skin disease patients.

Methods: 532 patients (mean age=52.29 years, female=85.15%, male=14.85%) were selected from two ongoing databases of cutaneous lupus erythematosus (69.92%) and dermatomyositis (30.08%). Details regarding antimalarial treatment and toxicities were extracted and five different treatment courses were defined [i.e., hydroxychloroquine, chloroquine, and quinacrine monotherapies, as well as hydroxychloroquine+quinacrine and chloroquine+quinacrine combinations]. The hazard ratio of each major toxicity on the five different treatment courses was estimated using the Cox proportional hazard model to compare the risk associated with each type of treatment to that of hydroxychloroquine.

Results:

Over 90% of patients had a history of hydroxychloroquine, and nearly half (42.9%) had a history of hydroxychloroquine+quinacrine. Only 21.3% of patients had a history of chloroquine either as monotherapy (11.1%) or as chloroquine+quinacrine combination (10.2%). Over half of the patients had a history of quinacrine, usually in combination with hydroxychloroquine or chloroquine, but also as monotherapy (11.8%).

The most prevalent side effects included cutaneous eruption (n=61), gastrointestinal upset (n=38), mucocutaneous dyspigmentation (n=26), neurologic toxicities [i.e., including dizziness and headache (n=10), ototoxicity (n=5), sleep disturbances (n=5), mental fog (n=5), peripheral neuropathy (n=4), tremors (n=2), and psychosis (n=1)], and retinopathy (n=17). Compared to hydroxychloroquine, the hazards of cutaneous eruption, gastrointestinal upset, and neurologic toxicities were lower with hydroxychloroquine+quinacrine. However, based on a post-hoc analysis, this may represent the selection of patients able to tolerate hydroxychloroquine in the cohort of those who received hydroxychloroquine+quinacrine. Although there was increased risk of retinopathy with chloroquine and chloroquine+quinacrine relative to hydroxychloroquine, ophthalmic toxicity was not seen with quinacrine (Table I).
Conclusion: Our study provides evidence that the safety profile of quinacrine is comparable to that of first-line hydroxychloroquine and that quinacrine has an advantage over hydroxychloroquine and chloroquine for patients at risk of retinopathy. Furthermore, adding quinacrine to hydroxychloroquine or chloroquine does not increase the risk of toxicities, and limiting access to quinacrine may leave patients without alternatives to this safe drug.

Table I.
<table>
<thead>
<tr>
<th>Treatment Course</th>
<th>Adjusted HR(^a)</th>
<th>95% Confidence Interval for Adjusted HR</th>
<th>Un-adjusted HR</th>
<th>95% Confidence Interval for Un-adjusted HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chloroquine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin Eruption</td>
<td>0.277</td>
<td>0.038-2.028</td>
<td>0.563</td>
<td>0.135-2.341</td>
</tr>
<tr>
<td>Dyspigmentation</td>
<td>†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GI Upset</td>
<td>0.400</td>
<td>0.054-2.961</td>
<td>0.354</td>
<td>0.048-2.606</td>
</tr>
<tr>
<td>Neurologic</td>
<td>†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quinacrine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin Eruption</td>
<td>†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyspigmentation</td>
<td>4.047</td>
<td>0.956-17.139</td>
<td>3.278</td>
<td>0.787-13.646</td>
</tr>
<tr>
<td>GI Upset</td>
<td>1.273</td>
<td>0.380-4.266</td>
<td>1.028</td>
<td>0.312-3.388</td>
</tr>
<tr>
<td>Neurologic</td>
<td>0.459</td>
<td>0.061-3.461</td>
<td>0.455</td>
<td>0.061-3.386</td>
</tr>
<tr>
<td>Ophthalmic</td>
<td>†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCQ+Quinacrine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin Eruption</td>
<td>0.231 ****</td>
<td>0.082-0.651</td>
<td>0.236 ****</td>
<td>0.084-0.664</td>
</tr>
<tr>
<td>Dyspigmentation</td>
<td>1.517</td>
<td>0.485-4.746</td>
<td>1.416</td>
<td>0.462-4.343</td>
</tr>
<tr>
<td>GI Upset</td>
<td>0.260 **</td>
<td>0.078-0.863</td>
<td>0.227 **</td>
<td>0.069-0.747</td>
</tr>
<tr>
<td>Neurologic</td>
<td>0.195 **</td>
<td>0.045-0.840</td>
<td>0.199 **</td>
<td>0.047-0.845</td>
</tr>
<tr>
<td>Ophthalmic</td>
<td>2.248</td>
<td>0.136-37.028</td>
<td>1.152</td>
<td>1.104-12.753</td>
</tr>
<tr>
<td>CQ+Quinacrine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin Eruption</td>
<td>0.849</td>
<td>0.260-2.771</td>
<td>0.865</td>
<td>0.266-2.812</td>
</tr>
<tr>
<td>Dyspigmentation</td>
<td>1.299</td>
<td>0.160-10.529</td>
<td>1.234</td>
<td>0.154-9.878</td>
</tr>
<tr>
<td>GI Upset</td>
<td>0.446</td>
<td>0.060-3.314</td>
<td>0.170</td>
<td>3.001</td>
</tr>
<tr>
<td>Neurologic</td>
<td>0.471</td>
<td>0.063-3.519</td>
<td>0.451</td>
<td>0.061-3.345</td>
</tr>
</tbody>
</table>

HCQ = hydroxychloroquine; CQ = chloroquine; HCQ+Quinacrine = hydroxychloroquine+quinacrine; CQ+Q = chloroquine+quinacrine

\(^a\) Cox proportional hazard ratios (HR) of toxicities while on various antimalarial regimens, with risk of toxicities on hydroxychloroquine monotherapy as the reference level; adjusted for sex, age, race, and smoking status (never vs. current and past smokers)

** P < 0.05
**** P < 0.01
† = No observations of toxicity
Disclosure: L. Mittal, None; L. Zhang, None; R. Feng, None; V. Werth, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/antimalarial-drug-toxicities-in-rheumatic-skin-disease-patients

Abstract Number: 2614

Hydroxychloroquine Initiation Dosing Trends and Predictors in Systemic Lupus Erythematosus

April Jorge¹, Leo Lu², Yuqing Zhang³, Sharan K. Rai⁴, Lucy H. Young⁵, Ronald B. Melles⁶, Michael F. Marmor⁷, Karen H. Costenbader⁸, Rosalind Ramsey-Goldman⁹, S. Sam Lim¹⁰, John M. Esdaile¹¹, Ann E. Clarke¹², Murray Urowitz¹³, Anca Askanase¹⁴, Cynthia Aranow¹⁵, Michelle Petri¹⁶ and Hyon K. Choi⁴, ¹Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, ²Allergy, Immunology, and Rheumatology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, ³School Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, ⁴Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, ⁵Department of Ophthalmology, Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston, MA, ⁶Department of Ophthalmology, Kaiser Permanente, Redwood City, CA, ⁷Department of Ophthalmology and Byers Eye Institute, Stanford University School of Medicine, Palo Alto, CA, ⁸Brigham and Women's Hospital, Harvard Medical School, Boston, MA, ⁹FSM, Northwestern University, Chicago, IL, ¹⁰Division of Rheumatology, Emory University School of Medicine, Atlanta, GA, ¹¹Arthritis Research Canada, Richmond, BC, Canada, ¹²Division of Rheumatology, University of Calgary, Calgary, AB, Canada, ¹³Centre for Prognosis Studies in the Rheumatic Diseases, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, ¹⁴Rheumatology, Columbia University College of Physicians & Surgeons, New York, NY, ¹⁵Autoimmune and Musculoskeletal Disease, The Feinstein Institute for Medical Research, Manhasset, NY, ¹⁶Medicine (Rheumatology), Division of Rheumatology, Johns Hopkins University School of Medicine, MD, USA, Baltimore, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Hydroxychloroquine (HCQ) is a cornerstone of systemic lupus erythematosus (SLE) care. The major long-term adverse event risk is vision-threatening toxic retinopathy. The 2012 EULAR, 2009 Royal College of Ophthalmology, and 2011 American Academy of Ophthalmology (AAO) guidelines recommended a maximum dosing of the lower of 6.5mg/kg/day of ideal body weight (IBW) or 400 mg daily to minimize the risk of retinopathy, whereas the 2016 AAO guidelines revised this to a maximum of 5mg/kg/day of actual body weight (ABW). We assessed the trend of HCQ prescribing patterns for treating SLE in relation to these dosing guidelines over the past two decades in a general population context. Furthermore, we examined associations with purported risk factors of HCQ retinopathy.

Methods: Using a United Kingdom general population database, we conducted an incident user study of adult SLE patients, identified by Read codes, who initiated HCQ between January 1, 1996 and December 31, 2015. We examined the secular trend of the proportion of initial prescribed HCQ doses exceeding 6.5mg/kg/day IBW as well as 5mg/kg/day ABW and assessed whether excess doses according to these guidelines varied by age, sex, body mass index (BMI; lean, overweight, and obese), and chronic kidney disease (CKD; defined by a eGFR <60).
Results: Of 2741 SLE patients who initiated HCQ over this 20-year period, 36.2% of the prescribed doses were > 6.5mg/kg/day IBW, and 38.12% were > 5mg/kg/day ABW. There was no significant change in the rate of initial excess dosing over time for either dose cut-off (p for trends=0.09 and 0.25, respectively) (Table 1). Women had an increased risk of excess initial dosing compared with men, with OR=12.28 (95% CI, 7.46-20.23) for IBW and 2.00 (95% CI, 1.50-2.66) for ABW dose recommendations. Obesity was associated with a lower risk of excess HCQ dosing using ABW (OR=0.14 for obese vs. lean (95% CI, 0.10-0.18), and a higher risk of excess dosing using IBW (OR 1.30 [95% CI, 1.06-1.59]). Age had no effect on the risk of excess HCQ dosing according to either recommendation (OR 1.11; 95% CI, 0.93-1.32 for IBW, and OR=1.07, 95% CI, 0.89-1.27 for ABW). For the subgroup with available eGFR data (n=657), CKD was associated with an increased risk of excess dosing per ABW (OR 1.85, 95% CI, 1.02-3.37) after adjusting for BMI.

Conclusion: In this general population-based study, over one-third of SLE patients were initiated on HCQ doses exceeding both dosing guidelines, and these rates have not changed over the past two decades. This rate of excess dosing is strikingly higher among women. Obesity posed opposing risk of excess dosing between the two weight-based dosing guidelines. Furthermore, excess dosing is also higher amongst CKD patients per the recent ABW-based guidelines. These findings highlight the potential need to improve excess HCQ dosing, and call for unifying, robust, and evidence-based recommendations.

| Table 1. Initial Hydroxychloroquine Prescription Dose in Relation to Dosing Recommendations |
|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|
| Characteristics | > 6.5mg/kg/day, Ideal Body Weight | > 6.5mg/kg/day, Actual Body Weight | > 5mg/kg/day, Ideal Body Weight | > 5mg/kg/day, Actual Body Weight |
| Year of incident Prevalence | N (%) | Cude OR (95% CI) | Adjusted OR (95% CI) | N (%) | Cude OR (95% CI) | Adjusted OR (95% CI) |
| 1996-2003 (n=619) | 157 (50.9) | 1.00 | 1.00 | 75 (45.2) | 1.00 | 1.00 |
| 2004-2010 (n=187) | 268 (57.1) | 1.02 | 1.00 (0.79-1.32) | 267 (57.7) | 0.86 | 0.68 (0.46-1.32) |
| 2006-2010 (n=113) | 389 (53.9) | 1.11 | 1.00 (0.82-1.31) | 322 (56.4) | 0.82 | 0.67 (0.45-1.04) |
| 2011-2015 (n=89) | 322 (69.0) | 1.10 | 1.00 (0.81-1.34) | 268 (58.5) | 0.90 | 0.80 (0.56-1.15) |
| Age | | | | | | |
| <=55 years (n=2241) | 851 (33.2) | 1.00 | 1.00 | 826 (38.5) | 1.00 | 1.00 |
| > 55 years (n=1219) | 762 (50.2) | 1.10 | 1.00 | 716 (57.7) | 1.00 | 1.00 |
| BMI (kg/m^2) | | | | | | |
| Lean (18.5-24.9) (n=1312) | 488 (37.0) | 1.00 | 1.00 | 635 (48.0) | 1.00 | 1.00 |
| Overweight (25-29.9) (n=483) | 321 (63.4) | 1.10 | 1.00 | 337 (60.9) | 0.63 | 0.63 (0.40-0.99) |
| Obesity (>30) (n=504) | 292 (58.3) | 1.10 | 1.00 | 270 (54.0) | 0.61 | 0.61 (0.40-0.98) |

Disclosure: A. Jorge, None; L. Lu, None; Y. Zhang, None; S. K. Rai, None; L. H. Young, None; R. B. Melles, None; M. F. Marmor, None; K. H. Costenbader, None; R. Ramsey-Goldman, None; S. S. Lim, None; J. M. Esdaile, None; A. E. Clarke, UCB, 2; M. Urowitz, UCB, 2; A. Askanase, Exagen, 2; C. Aranow, None; M. Petri, Anthera Inc, 5,GlaxoSmithKline, 5,EMD Serono, 5,Eli Lilly and Company, 5,Bristol Meyer Squibb, 5,AstraZeneca, 5,Global Rheumatology, 5,Global Academy, 5,Exagen, 2; H. K. Choi, Selecta, Horizon, 5,AstraZeneca, 2.

Non-Pharmacological Treatment on Fatigue, Depression, Disease Activity, and Quality of Life of Systemic Lupus Erythematosus: A Systematic Review

Monthida Fangtham1, Jacob Louis Nash2, Stephanie Hyon3, Raveendhara R. Bannuru4 and Chenchen Wang3,
1Internal Medicine, University of New Mexico, Albuquerque, NM, 2Health Sciences Library and Informatics Center, University of New Mexico, Albuquerque, NM, 3Rheumatology, Center of Integrative Medicine and Division of Rheumatology, Tufts Medical Center, Boston, MA, Boston, MA, 4Center of Integrative Medicine and Division of Rheumatology, Tufts Medical Center, Boston, MA, Boston, MA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: In recent years, non-pharmacological therapies have been deemed as potentially beneficial for patients with systemic lupus erythematosus (SLE). These include complementary and integrative approaches, physical and psychological interventions. We conducted the systematic review to determine the effects of these therapies to inform practice in SLE patients.

Methods: Literature search was performed using PubMed (MEDLINE), EMBASE, Cochrane, PsychINFO, CINAHL, Web of Science, and Google Scholar until March 2017. We included any randomized controlled trials (RCTs) of non-pharmacologic interventions in SLE patients with sample size > 10 and measuring outcomes including fatigue, depression, disease activity, and quality of life. SLE was defined by 1982 or 1997 ACR criteria in all studies. Articles in both English and Chinese were included. Due to the heterogeneity of interventions and comparisons, a meta-analysis was not performed.

Results: Nine RCT studies totaling 651 participants met the inclusion criteria and were included in this review. SLE disease duration ranged between 2.5 to 12 years, mean age ranged from 13 to 48 years, and 96% were female. Table 1 summarizes the randomized controlled trials evaluating the effects of non-pharmacological treatment in patients with SLE. Of the 9 trials, 4 used exercise interventions, 4 used psychological interventions (1 group psychotherapy, 2 cognitive behavioral therapies, 1 psychoeducation intervention) and 1 used electro-acupuncture. Three of 9 studies utilized control groups consisting of usual medical care. Other studies included control interventions of relaxation, attention placebo, symptom monitoring support, minimal needling, and isotonic and resistance exercise. Compared with the control conditions, non-pharmacological interventions were associated with a significant improvement in fatigue in 3 out of 4 studies (1 exercise, 1 psychological and 1 acupuncture intervention). Four studies reported improvement in overall quality of life as measured by SF-36, compared to control. Two out of six studies also reported improved anxiety and depression, and 3 studies improved pain after interventions. However, one psychotherapy study did not find any clinically important improvement in psychological distress, disease activity, and quality of life compared to usual care. Also, no studies demonstrated a greater improvement in disease activity with 6-20 weeks of non-pharmacological interventions.

Table 1. Non-pharmacological Treatment on Fatigue, Depression, Disease Activity and Quality of Life of SLE
<table>
<thead>
<tr>
<th>Author, Yr, Country</th>
<th>N</th>
<th>Intervention</th>
<th>Control</th>
<th>Outcomes Measure</th>
<th>Duration (Weeks)</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tench 2003, UK</td>
<td>93</td>
<td>Home exercise (walking, cycling, swimming), 30-50 min x 3 times/wk, x 12 weeks</td>
<td>1. Relaxation audiotape, 30 min x 3 times/wk + supervised relaxation session q 2 wk x 12 wks 2. Usual medical care</td>
<td>- Fatigue (Chalder Fatigue Scale)  - Depression, anxiety (HADS)  - Disease activity (SLAM)  - Quality of Life (SF-36)</td>
<td>12</td>
<td>-Greater improvement in fatigue (P=0.04) for exercise than relaxation or usual medical care  - No improvement in depression and anxiety, disease activity, quality of life, between 2 exercise groups</td>
</tr>
<tr>
<td>Bogdanovic 2015, Serbia</td>
<td>60</td>
<td>Aerobic exercise, 15 min x 3 times/wk x 6 weeks</td>
<td>Isotonic exercises, 30 min x 3 times/wk x 6 weeks</td>
<td>- Fatigue (FSS)  - Depression (BDI)  - Quality of Life (SF-36)</td>
<td>6</td>
<td>- No significant difference in fatigue  - No significant difference in depression between 2 exercise groups  - Improvement in Quality of Life (P&lt;0.05)</td>
</tr>
<tr>
<td>Abrahão 2016, Brazil</td>
<td>63</td>
<td>Cardiovascular exercise (CT), 50 min x 3 times/wk x 12 weeks</td>
<td>1. Resistance exercise (RT), 50 min x 3 times/wk x 12 weeks 2. Usual medical care</td>
<td>- Depression (BDI)  - Disease Activity (SLEDAI)  - Quality of Life (SF-36)  - Aerobic Capacity</td>
<td>12</td>
<td>- No significant different in depression or disease activity between groups  - Improvement in Quality of Life in CT and RT groups (P&lt;0.05)  - Improvement in aerobic capacity in CT and RT groups (P&lt;0.05)</td>
</tr>
<tr>
<td>Prado 2013, Brazil</td>
<td>19</td>
<td>Supervised Aerobic exercise, 30-60 min 2x weekly x 12 weeks</td>
<td>Usual medical care</td>
<td>- Disease activity (SLEDAI-2K)  - Exercise tolerance</td>
<td>12</td>
<td>- No change in disease activity  - Improvement in exercise tolerance (P&lt;0.05)</td>
</tr>
<tr>
<td>Karlson 2004, USA</td>
<td>122</td>
<td>Psychoeducational intervention 1 time, followed by a phone call once a month x 5 months</td>
<td>Attention Placebo + Video presentation about lupus, 45 min once</td>
<td>- Fatigue  - Disease activity (SLAQ, SLAM)  - Quality of Life (SF-36)  - Self efficacy</td>
<td>20</td>
<td>- Reduction in fatigue score in experimental group (P&lt;0.05)  - No improvement in disease activity  - Improvement in quality of life (P=0.03), global mental health status (P=0.03), and self-efficacy (P=0.004)</td>
</tr>
<tr>
<td>Dobkin 2002, Canada</td>
<td>133</td>
<td>Group psychotherapy, 90 mins x weekly x 3 months + booster session, 1</td>
<td>Usual medical care</td>
<td>- Psychological symptoms (SCL-90-R)  - Disease activity (SLAM-R)</td>
<td>12</td>
<td>- No significant group differences in psychological symptoms, disease activity, and quality of life</td>
</tr>
</tbody>
</table>
| Greco 2004, USA | Biofeedback-assisted/Cognitive-behavioral therapy + relaxation techniques (BF/CBT), 6 sessions x 3 months | 1. Symptom monitoring support intervention (SMS)  
2. Usual medical care | - Psychological Functioning (CES-D, STRESS, ASES)  
- Disease Activity (SLEDAI, SLAM-R)  
- Quality of life: Physical function (SF-36-PF)  
- Pain (AIMS2-pain) | - Greater improvement for BF/CBT in long-term psychological function (P=0.02)  
- No improvement in disease activity in all groups (P>0.05)  
- Greater improvement for BF/CBT in physical function (SF-36-PF) (P<0.05) and pain reduction (P=0.04) |
| Navarrete 2010, Spain | Cognitive-behavioral therapy + relaxation techniques + social skill training, 120 min/wk x 10 weeks | Usual medical care | - Psychological parameters (SVI, BDI, Anxiety Spielberger’s STAI)  
- Disease activity (SLEDAI)  
- Quality of Life (SF-36) | - Improvement in stress (P<0.04), depression (P<0.002) and anxiety (P<0.001)  
- No improvement in disease activity  
- Improvement in SF-36 scales (P<0.05) including physical role (P<0.05), pain (P<0.013), social function (P<0.04), mental health (P<0.02), general health (P<0.05) |
| Greco 2008, USA | Electrical Acupuncture 10 sessions x 5 wks 30 min/session  
Minimal needling, 10 sessions x 2 times over 5 wks  
Usual medical care | 1. Minimal needling, 10 sessions x 2 times over 5 wks  
2. Usual medical care | - Fatigue (FSS)  
- Disease activity (SLAM-R)  
- Pain (AIMS2-pain, MPI, SF-36 body pain) | - Both acupuncture and needling improvement in fatigue compared to usual care  
- No improvement in disease activity  
- Both acupuncture and needling improvement in pain compared to usual care |

Conclusion: The review showed promising results for physical exercise and psychological interventions as an adjunct to traditional medical therapy for improvement in fatigue and quality of life. However, many studies had small sample sizes and short intervention durations. Further high-quality RCTs with longer follow-up periods are warranted.

Disclosure: M. Fangtham, None; J. L. Nash, None; S. Hyon, None; R. R. Bannuru, None; C. Wang, None.
Abstract Number: 2616

Mesenchymal Stem Cells Induce CD1c+ Tolerogenic Dendritic Cells Via up-Regulating FLT3L in Systemic Lupus Erythematosus

Xinran Yuan¹, Dandan Wang² and Lingyun Sun³, ¹Department of Rheumatology and Immunology, The Affiliated Drum Tower Hospital of Nanjing University Medical School, Nanjing, China, ²Department of Rheumatology and immunology, The Affiliated Drum Tower Hospital of Nanjing University Medical School, Nanjing, China, ³Department of Rheumatology and Immunology, the Affiliated Drum Tower Hospital, Nanjing University Medical School, nanjing, China

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Several tolerogenic dendritic cell (DC) subsets have been identified in human such as CD1c+ DCs, which could be elevated by injection of Flt-3 ligand (FLT3L). CD1c+ tolerogenic DCs play important roles in the induction of peripheral tolerance and control of adaptive immune response, hence, they have become appealing targets in the treatment of systemic lupus erythematosus (SLE). Umbilical cord (UC)-derived mesenchymal stem cells (MSCs) also exhibit immunoregulatory effects in SLE. However, the underlying immunosuppression mechanism of MSCs via tolerogenic DCs in SLE remains largely unknown. The aim of this study is to examine tolerogenic DCs levels in SLE patients, and to further investigate the mechanism of MSCs in the regulation of tolerogenic DCs.

Methods: Tolerogenic DCs were isolated as Lin(CD3/19/56/14)-HLA DR+CD11c+CD1c+ from peripheral blood mononuclear cells (PBMCs). Level of tolerogenic DCs was determined by flow cytometry, and serum concentration of FLT3L was assessed by ELISA from 17 healthy controls and 25 SLE patients. Eight SLE patients were given UC MSCs transplantation. PBMCs from 8 patients were collected and co-cultured with UC MSCs at ratios of 1:1, 10:1 and 50:1, for 24 hours, 48 hours and 72 hours, respectively, to detect the level of tolerogenic DCs. The level of FLT3L in the supernatant solution was analyzed. FLT3L siRNA was added to the co-culture system, and the level of tolerogenic DCs was detected.

Results: The levels of peripheral CD1c+ DCs and serum FLT3L were significantly decreased in SLE patients compared to healthy controls. Moreover, the level of CD1c+ DCs was remarkably negatively correlated with SLE disease activity index (SLEDAI) scores. After UC MSCs transplantation, the level of CD1c+ DCs increased, along with an increase in serum FLT3L. In vitro studies showed that UC MSCs time-dependently up-regulated peripheral CD1c+ DCs, but not dose-dependently. The supernatant FLT3L level significantly increased after co-cultured with MSCs. However, the addition of FLT3L siRNA significantly abrogated the up-regulation of CD1c+ DCs by MSCs, which could be reversed by adding extra FLT3L to the co-culture system.

Conclusion: UC MSCs induce CD1c+ tolerogenic DCs through up-regulating FLT3L in lupus patients.

Disclosure: X. Yuan, None; D. Wang, None; L. Sun, None.
Electrocardiogram Abnormalities Related to Antimalarials in Systemic Lupus Erythematosus

Taneisha McGhie1, Paula Harvey2, Jiandong Su1, Nicole Anderson3, George A. Tomlinson4 and Zahi Touma5,
1University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, 2Cardiology, Women's College Hospital, University of Toronto, Toronto, ON, Canada, 3Rheumatology, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, 4Medicine, Mount Sinai Hospital, Toronto, ON, Canada, 5Rheumatology, University of Toronto, Division of Rheumatology, Institute of Health Policy, Management and Evaluation, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Anti-malarials (AM), such as hydroxychloroquine (HCQ) and chloroquine (CQ), have long been used for the treatment of systemic lupus erythematosus (SLE). However, despite their general safety, both drugs have the potential to cause serious toxicity. These drugs have significant lysosomal affinity and induce the prominent development of autophagic vacuoles in several tissues. Cardiotoxicity with potential conduction/structural abnormalities on electrocardiogram (ECG) have been reported with AM. We aimed to study whether cumulative AM is associated with ECG abnormalities.

Methods:
A standard resting supine ECG was performed on consecutive patients attending the Lupus Clinic since 2012. ECGs were analyzed and tracings were coded by a single cardiologist blinded to identifying data and previous AM exposure on the basis of the Minnesota criteria. ECG abnormalities were grouped into structural [left ventricular hypertrophy or atrial enlargement] and conduction abnormalities [prolonged corrected QT interval (QTc), short PR interval, left bundle branch block (LBBB), right bundle branch block (RBBB) and atrioventricular block (AVB), bradycardia, tachycardia, premature atrial complex, ectopic atrial rhythm, atrial fibrillation, premature ventricular complex and ventricular bigeminy].

Clinical and laboratory variables from the baseline (corresponds to the ECG visit) were studied as potential factors associated with ECG abnormalities. Associations between cumulative AM [calculated after equating 3.0 mg of CQ with 6.5 mg of HCQ] and ECG abnormalities (structural or conduction) were assessed using logistic regression analysis (after adjusting for baseline patient characteristics) and in a nested case control study (1:3) [matching for sex, SLE duration at ECG within 5 years, ECG testing year within 5 years and hypertension status].

Results:
Of 453 patients treated with AM, the median cumulative AM was 1207 grams at ECG. The mean age at ECG was 49.2 ± 13.8 years and SLE duration was 19.8 ± 10.4 years. CQ or HCQ had been used by 409 (90.3%) before the ECG.

Conduction abnormalities were more prevalent than structural abnormalities, 71 (15.7%) vs. 58 (12.8%). AM cumulative dose did not show a statistical significant association with ECG structural abnormalities, (OR 1.82, p=0.07) while it was
protective for conduction ECG abnormalities (OR 0.42, p=0.006) (table 1). The nested case control analysis also found that AM cumulative dose is protective against conduction ECG abnormalities (OR 0.36; 95% CI: 0.17-0.75; p=0.007). SLE duration was a risk factor for both structural and conduction ECG abnormalities.

**Conclusion:**

This study suggests an association between cumulative AM dose above the median (1207 g) and structural ECG abnormalities. More importantly, cumulative AM decreases the odds of ECG conduction abnormalities.

**Table 1: Multivariable logistic regression analysis for structural or conduction abnormalities**

<table>
<thead>
<tr>
<th>ECG Abnormality</th>
<th>Variables</th>
<th>OR 95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECG structural abnormality</td>
<td>SLE duration at ECG test (years)</td>
<td>1.03 (1.004, 1.06)</td>
<td>0.0248</td>
</tr>
<tr>
<td></td>
<td>Hypertension vs. normotension</td>
<td>2.21 (0.98, 4.99)</td>
<td>0.0567</td>
</tr>
<tr>
<td></td>
<td>eGFR at ECG (each 10 mL/min/173 m2)</td>
<td>0.83 (0.76, 0.92)</td>
<td>0.0002</td>
</tr>
<tr>
<td></td>
<td>Cumulative AM dose prior to ECG higher than median dose (1207 grams)</td>
<td>1.82 (0.95, 3.47)</td>
<td>0.0707</td>
</tr>
<tr>
<td>ECG conduction abnormality</td>
<td>SLE duration at ECG test</td>
<td>1.03 (1.01, 1.06)</td>
<td>0.0080</td>
</tr>
<tr>
<td></td>
<td>Hypertension</td>
<td>1.66 (0.85, 3.25)</td>
<td>0.1357</td>
</tr>
<tr>
<td></td>
<td>Pulmonary hypertension</td>
<td>2.37 (0.82, 6.80)</td>
<td>0.1090</td>
</tr>
<tr>
<td></td>
<td>Treatment with N-CBB or beta-blockers</td>
<td>2.75 (1.42, 5.33)</td>
<td>0.0026</td>
</tr>
<tr>
<td></td>
<td>Cumulative prednisone 3 years before ECG (each 100 grams)</td>
<td>1.05 (1.01, 1.09)</td>
<td>0.0147</td>
</tr>
<tr>
<td></td>
<td>Cumulative AM prior to ECG higher than median dose (1207 grams)</td>
<td>0.42 (0.22, 0.77)</td>
<td>0.0057</td>
</tr>
</tbody>
</table>

N-CCB; non-dihydropyridine calcium channel blocker

Disclosure: T. McGhie, None; P. Harvey, None; J. Su, None; N. Anderson, None; G. A. Tomlinson, None; Z. Touma, None.
Why Aren’t All Patients with SLE Taking Hydroxychloroquine? A Retrospective Chart Review

Caroline H. Siegel¹, Jennifer M. Grossman¹, John Fitzgerald¹, Bevra H. Hahn¹,², Lori Sahakian¹, Eloise Olmos² and Maureen A. McMahon¹, UCLA David Geffen School of Medicine, Los Angeles, CA, ²Division of Rheumatology, UCLA David Geffen School of Medicine, Los Angeles, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Although previous SLE treatment guidelines recommended judicious use of antimalarials, there is a growing body of evidence demonstrating that HCQ prevents flares, protects against irreversible organ damage, and increases long-term survival in SLE patients. As a result, there has been a paradigm shift: current guidelines recommend treatment with HCQ for all patients with SLE unless there are specific contraindications. Nonetheless, the rates of HCQ use in many SLE cohorts remain at 65% or less. We reviewed a large, diverse cohort of SLE patients at an academic center in order to identify reasons why many SLE patients are not on HCQ.

Methods: A retrospective chart review was conducted of patients in our longitudinal SLE cohort. There were 287 SLE patients reviewed at baseline (2004-2006), 229 at first follow-up (2008-2010), and 102 at second follow-up (2015-present). Active medications were recorded at each time point as well as the primary reason for HCQ non-use when applicable. SLICC Damage Index (SDI) was measured at baseline.

Results: 67% of patients in our cohort were taking HCQ at baseline, 66.8% at first follow-up, and 73.5% at second follow-up (p=NS). Overall, patient preference (43%) was the most common reason for HCQ non-use, followed by physician preference (21%) and allergy/side effects (11%). Although less than 2% of patients had documented eye toxicity as a reason for HCQ discontinuation at baseline and first follow-up, this increased to 9.8% at second follow-up (p=0.001).

We compared SDI at baseline among patients who were actively taking HCQ (n=194), those who had never taken HCQ (n=52), and those who discontinued HCQ for any reason (n=41). We found evidence of SLE-related damage (SDI ≥ 1) in 54.6% of patients on HCQ, 75.6% of HCQ never users and 78.8% of former users (p=0.001 by Chi-squared analysis).

Conclusion: Although the rate of HCQ use in our longitudinal SLE cohort has remained stable, the percentage of patients who discontinued HCQ due to eye-related toxicity has increased. Further studies are required to determine whether this increase in eye-related toxicity can be attributed solely to cumulative HCQ dose, or whether adherence to ophthalmology guidelines and availability of more sensitive testing modalities has led to earlier and more frequent detection. Our data also demonstrate that rates of damage accumulation are comparable between HCQ never and former users and lowest in patients taking HCQ, which reinforces the importance of consistent HCQ use in SLE. This study elucidates an important disconnect between current evidence and clinical practice. Quality improvement initiatives are needed to address this discrepancy in an effort to improve patient outcomes.
Hemophagocytic Syndrome in Patients from SLE Registry from the Spanish Society of Rheumatology (RELESSER)

Ana Lois-Iglesias¹, Francisco J. de Toro², Antonio Zea³, Maria Galindo⁴, Esther Uriarte⁵, Iñigo Rúa-Figueroa⁶ and JM Pego-Reigosa⁷, ¹Rheumatology, University Hospital A Coruña, A Coruña, Spain, ²Rheumatology Division, INIBIC-Complejo Hospitalario Universitario A Coruña (CHUAC), A Coruña, Spain, ³Hospital Ramón y Cajal. Madrid, Madrid, Spain, ⁴Servicio de Reumatología, Hospital 12 de Octubre, Madrid, Spain, ⁵Reumatología, Hospital de Donosti, Donosti, Spain, ⁶Rheumatology Division, Hospital Doctor Negrín, Las Palmas GC, Spain, ⁷Rheumatology Section, Hospital de Meixoeiro, Pontevedra, Spain, Vigo, Spain

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is an autoimmune systemic rheumatic disease that, in our area, presents hematologic manifestations in approximately 70% of cases¹. Some of them are very rare so there are no large series whose analysis could provide relevant information.

Objectives: To study the characteristics of patients with Hemophagocytic Syndrome (HS) in a large sample of SLE patients.

Methods: SLE patients from RELESSER database were studied. We analysed the SLE manifestations present at 12 different domains (mucocutaneous, renal, musculoskeletal, constitutional, hematologic, vascular, cardiac, respiratory, neuropsychiatric, gastrointestinal, ophthalmic and serological) before, during and after HS diagnosis and until the last available assessment. We also studied activity (SELENA-SLEDAI) and damage (SLICC/ACR DI) indices in each of those moments. We evaluated the treatment received, HS recurrences and the number of deaths by this entity.

Results: 3,656 patients from 45 Rheumatology Units across Spain were studied. Seven patients with SLE and HS were identified. 71.4% were women, with a mean age (± S.D.) at the diagnosis of SH of 35.1 (± 17.1) years. In 5 of the 7 cases the HS occurred 115.5 (± 162.9) months after the diagnosis of SLE. In the remaining 2 cases the diagnosis of both entities was simultaneous. The main triggers of HS were infections, followed by SLE activity flares. At the time of HS diagnosis, they had high SLE activity with a mean SLEDAI score of 13.1 (± 11.3) and 1.4 (± 2.3) SDI scores. Clinically, 100% of the patients presented fever and alterations of the liver profile, 85.8% cytopenias and 71.5% dermatological manifestations. Respiratory manifestations and hemolytic anemia were present in 57.2% of the cases. Lymph nodes and coagulopathy in 42.9%. Hepatomegaly was detected in 28.6%, as well as neuropsychiatric, digestive and renal manifestations. Splenomegaly was detected in 14.3%. The mean hemoglobin level was 8.6 (± 1.1) g / dl, platelets 85,585 (± 83,390), ferritin 7,410 (± 6,470) ng / ml and triglycerides 404.7 (± 235.6) mg/dl. All patients underwent a bone marrow study. All patients were admitted. They required an average of 2.2 (± 1.5) treatment lines, using 2.8 (± 1.7) drugs. One patient died during the HS episode and another 2 patients had 2 and 3 recurrences respectively.
The following table shows the characteristics of each patient.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Number of organ systems affected by SLE before HS diagnosis</th>
<th>Number of organ systems affected by SLE at HS diagnosis</th>
<th>Number of organ systems affected by SLE until last assessment</th>
<th>SLEDAI/SLICC-ACR DI at HS diagnosis</th>
<th>SLEDAI/SLICC-ACR DI 1 year after HS</th>
<th>SLEDAI/SLICC-ACR DI at last assessment</th>
<th>Number of treatment lines</th>
<th>Treatments administered</th>
<th>Relapses</th>
<th>Deaths</th>
<th>Follow-up time (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9</td>
<td>4</td>
<td>Died</td>
<td>4//6</td>
<td>*</td>
<td>*</td>
<td>1</td>
<td>GC and CsA</td>
<td>0</td>
<td>Yes</td>
<td>Died</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>1</td>
<td>2</td>
<td>4//0</td>
<td>0//0</td>
<td>0//0</td>
<td>2</td>
<td>GCs, etoposide, iv Ig, CsA, platelets, red cells</td>
<td>2</td>
<td>No</td>
<td>45</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>1</td>
<td>2</td>
<td>5//0</td>
<td>*</td>
<td>*</td>
<td>2</td>
<td>GC, CYP and iv Ig</td>
<td>3</td>
<td>No</td>
<td>80</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>2</td>
<td>2</td>
<td>5//3</td>
<td>*</td>
<td>*</td>
<td>2</td>
<td>Amphotericin B, miltefosine</td>
<td>3</td>
<td>No</td>
<td>Follow-up lost</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td>2</td>
<td>2</td>
<td>4//1</td>
<td>2//1</td>
<td>0//1</td>
<td>2</td>
<td>GC, iv Ig, CsA, MM</td>
<td>4</td>
<td>No</td>
<td>Unknown</td>
</tr>
<tr>
<td>6</td>
<td>3</td>
<td>2</td>
<td>4</td>
<td>4//2</td>
<td>2//0</td>
<td>2//0</td>
<td>4</td>
<td>GC, CsA, anakinra and CYP</td>
<td>4</td>
<td>No</td>
<td>26</td>
</tr>
<tr>
<td>7</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>21//0</td>
<td>2//13</td>
<td>2//13</td>
<td>4</td>
<td>GC, CsA, anakinra and CYP</td>
<td>No</td>
<td>No</td>
<td>24</td>
</tr>
</tbody>
</table>

Simultaneous diagnosis of HS and SLE

Conclusion: HS is a rare life-threatening SLE manifestation (<0.5%). It must be suspected in patients with persistent fever who do not respond to antibiotics, cytopenias and evidence of multiorgan involvement.


Disclosure: A. Lois-Iglesias, None; F. J. de Toro, None; A. Zea, None; M. Galindo, None; E. Uriarte, None; I. Rúa-Figueroa, None; J. Pego-Reigosa, None.


Abstract Number: 2620
The Value of Repeat Biopsy in the Management of Lupus Nephritis Flares

Javier Narváez1,2, Milagros Ricse2, Montserrat Goma3, Francesca Mitjavila4, Xavier Fulladosa5, Olga Capdevila4, Joan Torras5, Xavier Juanola2,6, Ramon Pujol4 and Joan Miquel Nolla1, 1Rheumatology Department, Hospital de Bellvitge. Barcelona. Spain, L’Hospitalet de Llobregat, Spain, 2Rheumatology, Hospital Universitario de Bellvitge, Barcelona, Spain, 3Pathology, Hospital Universitario de Bellvitge, Barcelona, Spain, 4Internal Medicine, Hospital Universitario de Bellvitge, Barcelona, Spain, 5Nephrology, Hospital Universitario de Bellvitge, Barcelona, Spain, 6Rheumatology, University Hospital Bellvitge, Barcelona, Spain

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Whether a repeat renal biopsy is helpful during lupus nephritis (LN) flares remains debatable. Our objective was to analyze the clinical utility of repeat renal biopsy in this complex situation.

Methods: From a total of 190 patients with LN treated between 1988 and 2014 at Bellvitge University Hospital (Barcelona, Spain), we selected for analysis 54 patients with two or more renal biopsies. Renal biopsy was repeated only on the basis of one of these clinical indications: 1) increase, persistence, or recurrence of proteinuria, nephrotic syndrome, or active urinary sediment (hematuria and/or cellular casts), or 2) increase in serum creatinine level or unexplained progression to renal failure. This study did not include patients with protocol biopsies performed to evaluate the response to therapy.

Additionally, we reviewed 686 well-documented similar cases previously reported (PubMed 1990-2016).

Results: The analysis of all patients reviewed showed that histological transformations are common during a LN flare, ranging from 40% to 76% of cases. However, the prevalence of transformations and the clinical value of repeat biopsy vary when they are analyzed according to proliferative or non-proliferative lesions.

The great majority of patients with class II (78% in our series and 77.5% in the literature review) progressed to a higher grade of nephritis (classes III, IV or V), resulting in worse renal prognosis. The frequency of pathological conversion in class V is lower (33% and 43%, respectively) but equally clinically relevant, since almost all cases switched to a proliferative class. Therefore, repeat biopsy is highly advisable in patients with non-proliferative LN at baseline biopsy, because these patients have a reasonable likelihood of switch to a proliferative LN that may require more aggressive immunosuppression.

In contrast, the majority of patients (82% and 73%) with proliferative classes in the reference biopsy (III, IV or mixed III/IV + V), remained into proliferative classes on repeat biopsy. Although rebiopsy in this group does not seem as necessary, it is still advisable since it will allow us to identify the 18% to 20% of patients that switch to a non-proliferative class. In addition, consistent with the reported clinical experience, repeat biopsy might also be helpful to identify selected cases with clear progression of proliferative lesions despite the initial treatment, for whom it is advisable to intensify immunosuppression. Thus, our experience and the literature data support that repeat biopsy also brings more advantages than threats in this group.

Conclusion: Although there is still a need for new randomized, prospective studies to confirm clinical observations, in daily practice kidney repeat biopsies are useful in guiding treatment of LN flares. The results of the repeat biopsy led to a change in the immunosuppressive treatment in more than half of the patients on average, intensifying it in the majority of the cases, but also reducing it in 5% to 30%.
Disclosure: J. Narváez, None; M. Ricse, None; M. Goma, None; F. Mitjavila, None; X. Fulladosa, None; O. Capdevila, None; J. Torras, None; X. Juanola, None; R. Pujol, None; J. M. Nolla, None.


Abstract Number: 2621

**Minimal Renal Affection in Patients with Systemic LUPUS Erythematosus: Characteristics and Evolution**

TC Salman-Monte1, Eva Rodriguez2, José Luis Arevalos3, María José Soler3, Clara Barrios3, Jordi Carbonell4 and Julio Pascual3, 1Rheumatology, Hospital del Mar/Parc de Salut Mar, Barcelona, Spain, 2Nephrology, Hospital del Mar/Parc de Salut Mar, Barcelona, Spain, 3Nephrology, Hospital del Mar/Parc de Salut Mar, Barcelona, Spain, 4Rheumatology Unit, Hospital del Mar/Parc de Salut Mar, Barcelona, Spain

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Lupus nephritis (LN) is the most common organ involvement in Systemic Lupus Erythematosus (SLE). Indications of renal biopsy (RB) are deterioration of renal function and / or activity in sediment and / or proteinuria> 0.5g / 24h or urine protein: creatinine ratio (P:C ratio) > 0.5 (SEN consensus 2012). There are patients who show data of "minimal renal involvement" (MRI) without indication of RB. Our objective is to determine if these patients present clinical and analytical characteristics that allow them to differentiate from patients with LN.

Methods:

We reviewed 171 patients with SLE diagnosis, classifying them as MRI if they showed> 3 occasions at least 1 year, proteinuria determinations = 0.3 g / 24h or P:C ratio= 0.3, ruling out urologic pathology. We have compared clinical and analytical variables of MRI vs LN at the time of SLE diagnosis, at renal involvement diagnosis and last visit.

Results:

We identified 38 (18.7%) patients with MRI and 41 (24%) patients with LN. At the time of SLE diagnosis, the MRI group had a lower titer of anti-DNAds (14.8% vs 42.1%, p = 0.01), anti-Sm (12% vs 32.2%, p = 0.04), presence of lupus anticoagulant (38%, p = 0.01) and anticardiolipin IgG (11% vs 38%, p = 0.01), less severe C3 hypocomplementemia (70 ± 34 vs 86.9 ± 32.7 mg / dl, p = 0.04), C4 (14 ± 10 vs 17 (p = 0.04) and CH50 (33.3 ± 15 vs 49.6 ± 17.4 mg / dl, p = 0.04); and lower inflammatory parameters: ESR (23.1 ± 20 vs 58.9 ± 42 mg / dl, p = 0.01), CRP (12.7±11.8 vs 27.3±17 mg/dl, p=0.02). At the diagnosis of the renal involvement, these results were confirmed (Table) and we observed that, in MRI patients, proteinuria appeared at an older age, with a higher evolution of SLE (12.7 ± 11.8 vs 27.3 ± 17 mg / dl, p = 0.02) and with absence of previous immunosuppressant therapy. After a mean follow-up of 10 ± 6.6 years, no MRI patient presented a renal flare, maintaining stable the renal function.
<table>
<thead>
<tr>
<th></th>
<th><strong>LUPUS NEPHRITIS</strong> (n=41)</th>
<th><strong>MINIMAL RENAL INVOLVEMENT (MRI)</strong> n=38</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (Female/Male)</td>
<td>30/11</td>
<td>29/3</td>
<td>0.05</td>
</tr>
<tr>
<td>Age (years)</td>
<td>38 ± 16</td>
<td>45 ± 17</td>
<td>0.07</td>
</tr>
<tr>
<td>Follow up time (years)</td>
<td>3.4 ± 5.5</td>
<td>5.8 ± 4</td>
<td>0.01</td>
</tr>
<tr>
<td>Creat (mg/dl)</td>
<td>1.3 ± 1.3</td>
<td>0.7 ± 0.2</td>
<td>0.02</td>
</tr>
<tr>
<td>URINE SEDIMENT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Negative</td>
<td>3 (7.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Hematuria</td>
<td>9 (22.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Leukocyturia</td>
<td>14 (35%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Changes in sediment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proteinuria (mg/24h)</td>
<td>2044 ± 2700</td>
<td>266 ± 71.6</td>
<td>NA</td>
</tr>
<tr>
<td>(P:C ratio) (mg/gr)</td>
<td>1761,7 ±1446</td>
<td>232 ± 172</td>
<td>NA</td>
</tr>
<tr>
<td>HT (n, %)</td>
<td>3 (13%)</td>
<td>2 (6%)</td>
<td>0.6</td>
</tr>
<tr>
<td>DM2 (n, %)</td>
<td>2 (8%)</td>
<td>2 (6%)</td>
<td>0.7</td>
</tr>
<tr>
<td>DNA-crithiida</td>
<td>26 (74.3)</td>
<td>9 (37.5)</td>
<td>0.005</td>
</tr>
<tr>
<td>Anti-SSARO (IA)</td>
<td>13 (38.2%)</td>
<td>12 (38.7%)</td>
<td>0.5</td>
</tr>
<tr>
<td>Anti-La (IA)</td>
<td>8 (23.5%)</td>
<td>5 (16.1%)</td>
<td>0.3</td>
</tr>
<tr>
<td>Anti-RNP (IA)</td>
<td>13 (39.4%)</td>
<td>7 (24.1%)</td>
<td>0.1</td>
</tr>
<tr>
<td>Anti-Sm (IA)</td>
<td>13 (39.4%)</td>
<td>4 (14.3%)</td>
<td>0.002</td>
</tr>
<tr>
<td>C3 (mg/dl)</td>
<td>70±21.9</td>
<td>130±10</td>
<td>0.001</td>
</tr>
<tr>
<td>C4 (mg/dl)</td>
<td>16.1±3.9</td>
<td>26±10.8</td>
<td>0.001</td>
</tr>
<tr>
<td>C1q (mg/dl)</td>
<td>16.5±11</td>
<td>26±12.3</td>
<td>0.001</td>
</tr>
<tr>
<td>CH50 (U/mL)</td>
<td>34±5.3</td>
<td>71.0±15</td>
<td>0.001</td>
</tr>
<tr>
<td>Immunosuppressants</td>
<td>15 (38.5%)</td>
<td>25 (78.1%)</td>
<td>0.001</td>
</tr>
<tr>
<td>- Micophenolic acid</td>
<td>20%</td>
<td>4%</td>
<td>0.1</td>
</tr>
<tr>
<td>- Azathioprine</td>
<td>13%</td>
<td>88%</td>
<td>0.001</td>
</tr>
<tr>
<td>- Hydroxychlorochine</td>
<td>20%</td>
<td>32%</td>
<td>0.003</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>19 (50%)</td>
<td>15 (46.9%)</td>
<td>0.4</td>
</tr>
</tbody>
</table>

**Conclusion:**
Our results showed that patients with MRI had a lower clinical and biological SLE activity, both at SLE diagnosis and at the diagnosis of renal involvement. No MRI patients presented a LN flare during the follow-up although it is difficult to know the role played by the immunosuppressant treatment.

Disclosure: T. Salman-Monte, None; E. Rodriguez, None; J. L. Arevalos, None; M. J. Soler, None; C. Barrios, None; J. Carbonell, None; J. Pascual, None.


Abstract Number: 2622

The Benefit of Vitamin D on SLE Disease Activity Is Largely Explained By Renal Activity

Michelle Petri,1 Daniel Goldman2 and Laurence S Magder3, 1Medicine (Rheumatology), Division of Rheumatology, Johns Hopkins University School of Medicine, MD, USA, Baltimore, MD, 2Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, 3Epidemiology and Public health, University of Maryland School of Medicine, Baltimore, MD
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Low vitamin D is commonly found in SLE. In previous studies, supplementation of vitamin D resulted in improvement in the Physician Global Assessment and SLEDAI. We now present the first analysis of the relationship between vitamin D and individual organ activity, based on a large clinical cohort.

Methods: This analysis is based on cohort visits where vitamin D was measured starting in 2010. There were 16,519 visits from 1,345 different patients (92% female, 50% Caucasian, 41% African American). If the patient received any score for an organ system component on the SELENA-SLEDAI, then the patient was defined as having that type of activity.

Results: The following activities were observed (percentage of visits): immunologic (33%), cutaneous (32%), renal (7%), musculoskeletal (5%), hematologic (5%), serologic (2%), vasculitic (1%), CNS (<1%), and constitutional (<1%). The association between levels of Vitamin D and disease activity in the top three organs is shown in Table 1.

Table 1. Estimated association between vitamin D levels and odds of organ-specific lupus disease activity, adjusting for age, race, sex, calendar year, prednisone use and plaquenil use.
<table>
<thead>
<tr>
<th>Vitamin D Level (ng/mL)</th>
<th>Cutaneous Activity</th>
<th>Renal Activity</th>
<th>Musculoskeletal Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>P-value</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>&lt;10 (n=163)</td>
<td>1.4 (1.0, 2.1)</td>
<td>0.049</td>
<td>3.1 (2.0, 4.9)</td>
</tr>
<tr>
<td>10 - &lt;20 (n=1039)</td>
<td>0.9 (0.8, 1.1)</td>
<td>0.41</td>
<td>2.2 (1.5, 3.1)</td>
</tr>
<tr>
<td>20 - &lt;30 (n=2760)</td>
<td>1.0 (0.9, 1.2)</td>
<td>0.53</td>
<td>1.6 (1.2, 2.0)</td>
</tr>
<tr>
<td>30 - &lt;40 (n=3959)</td>
<td>1.1 (1.0, 1.2)</td>
<td>0.13</td>
<td>1.2 (0.9, 1.5)</td>
</tr>
<tr>
<td>40 - &lt;50 (n=3578)</td>
<td>1.0 (Ref Grp)</td>
<td>1.0 (Ref Grp)</td>
<td>1.0 (Ref Grp)</td>
</tr>
<tr>
<td>50 - &lt;60 (n=2308)</td>
<td>1.1 (0.9, 1.3)</td>
<td>0.19</td>
<td>1.0 (0.7, 1.3)</td>
</tr>
<tr>
<td>60 - &lt;70 (n=929)</td>
<td>1.0 (0.8, 1.3)</td>
<td>0.74</td>
<td>0.8 (0.5, 1.3)</td>
</tr>
<tr>
<td>70 - &lt;80 (n=504)</td>
<td>1.3 (1.0, 1.7)</td>
<td>0.072</td>
<td>0.8 (0.4, 1.4)</td>
</tr>
<tr>
<td>80+ (n=356)</td>
<td>1.4 (1.0, 1.9)</td>
<td>0.072</td>
<td>0.6 (0.3, 1.6)</td>
</tr>
</tbody>
</table>

For cutaneous activity, there was a significantly elevated risk among those in the very extreme low level of vitamin D. For Renal Activity, vitamin D > 40 ng/mL lowered the risk of renal disease activity. For musculoskeletal activity, there was no association with vitamin D levels.

We then conducted a “within person” analysis between vitamin D and renal disease activity. In this analysis, each person serves as her own control, and the question is: “When a person has a vitamin D level lower than his/her average, are they more likely to have renal disease activity”. This analysis implicitly adjusts for race, sex, and all variables (measured and unmeasured) that are invariant within a person. The results are shown in Table 2.

**Table 2.** Within-person analysis of the relationship between vitamin D levels and renal activity adjusting for prednisone use, plaquenil use, and implicitly for all time-invariant characteristics.

<table>
<thead>
<tr>
<th>Vitamin D Level (ng/mL)</th>
<th>Renal Activity</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 ng/mL or more lower than personal average</td>
<td>1.5 (1.3, 1.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Within 10 ng/mL of the personal average</td>
<td>1.0 (Ref Grp)</td>
<td></td>
</tr>
<tr>
<td>10 ng/mL or more higher than personal average</td>
<td>0.8 (0.7, 1.0)</td>
<td>0.080</td>
</tr>
</tbody>
</table>
There was a relationship between vitamin D and all three components of SELENA-SLEDAI Renal Activity: hematuria, proteinuria, or pyuria.

**Conclusion:** Low vitamin D was associated with mucocutaneous activity only at extremely low vitamin D levels. The major association was with renal activity. This association held true in “within person” analysis and held true for proteinuria, hematuria and pyuria, as well. Given the safety of vitamin D supplementation, this immunomodulator should now be considered standard of care for lupus nephritis.

**Disclosure:** M. Petri, Anthera Inc, 5,GlaxoSmithKline, 5,EMD Serono, 5,Eli Lilly and Company, 5,Bristol Meyer Squibb, 5,Amgen, 5,United Rheumatology, 5,Global Academy, 5,Exagen, 2; D. Goldman, None; L. S. Magder, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/the-benefit-of-vitamin-d-on-sle-disease-activity-is-largely-explained-by-renal-activity](http://acrabstracts.org/abstract/the-benefit-of-vitamin-d-on-sle-disease-activity-is-largely-explained-by-renal-activity)

**Association Number:** 2623

**Association between Smoking Status and the Clinical and Serological Characteristics at the Onset of Systemic Lupus Erythematosus. an Inception Cohort Analysis**

**Jorge Sanchez-Guerrero**¹, Afra Al Dhaheri², Stacey Morrison³, Jiandong Su⁴, Dafna D Gladman⁵ and Murray Urowitz⁶, ¹Division of Rheumatology, Toronto Western Hospital, Toronto, AB, Canada, ²Tawam Hospital, Al Ain, United Arab Emirates, ³Rheumatology, Krembil Research Institute, Toronto, ON, Canada, ⁴University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, ⁵Department of Medicine, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, ⁶Centre for Prognosis Studies in the Rheumatic Diseases, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Cigarette smoking regulates both innate and adaptive immunity and is associated with numerous diseases. In some inflammatory diseases smoking is associated with deleterious effects but in others, i.e. Ulcerative Colitis, with beneficial effects. The effect in SLE is controversial. This study aims to investigate the associations of current smoking and clinical and serological characteristics of patients with systemic lupus erythematosus at the onset of the disease.

**Methods:** We included patients with SLE of recent onset (within 12 months of diagnosis), participating in an ongoing lupus cohort since 1970. We analyzed the information of Never Smokers (NS) and Current Smokers (CS) gathered at entry into the cohort, including demographic (age, sex, ethnicity), clinical (lupus criteria, SLEDAI-2K score, treatment, SLICC-DI), and laboratory (ANA, anti-ds-DNA, -Sm, -RNP, -Ro,-La, -aCL, lupus anticoagulant, C3, C4). We also analyzed these variables at one and two years of follow-up. **Statistical analysis:** Descriptive statistics, chi-square, t-test; multivariable analysis included linear and logistic regression. A p-value of <0.05 indicated statistical significance.

**Results:** The study included 467 patients [317 (68%) NS, and 150 (33%) CS]; 87% female; mean age 36.1 ± 13.3 years; SLE duration at entry into the cohort 0.2 ± 0.3 years; Caucasian 60%, Black 14%, Other 26%. Males (21.5%) and Caucasians (85.3%) predominated CS (p < 0.001). At entry into the cohort, CS had significantly lower values of ACR
criteria (4.1 ± 1.6 vs 5.1 ± 1.3), SLEDAI-2K score (7.7 ± 6.4 vs 9.9 ± 7.8), fewer showed positive ANA (82% vs 95%), anti-dsDNA (35% vs 67%), anti-Sm (11% vs 31%), anti-RNP (29% vs 47%), anti-Ro (34% vs 49%), low C3 or C4 (39% vs 53%), and fewer used steroids (47% vs 61%), anti-malarials (30% vs 44%), and immunosuppressants (12% vs 26%) than NS (all p < 0.03). In multivariable analyses, adjusting for age, sex, and ethnicity, smoking was independently associated with lower values of ACR criteria, ANA, anti-Sm antibodies, and abnormal C3/C4 (all 0.0001 < p < 0.05).

After one-year (n = 376) and two-years (n = 336) of follow-up, CS continued with lower frequency of positive ANA (p < 0.0001), anti-dsDNA (p < 0.001), and use of steroids (p < 0.05), anti-malarials (p < 0.0001), and immunosuppressants (p < 0.0001). The adjusted mean SLEDAI-2K at one year was lower among CS than NS (5.7 vs 6.6, p = 0.05), but not at two years (5.3 vs 5.6, p = NS), likely due to treatment.

**Conclusion:** Smoking status seems to be associated with differences in clinical and serological phenotype at the onset of lupus. If these results are confirmed, the underlying mechanisms need to be elucidated.

**Disclosure:** J. Sanchez-Guerrero, None; A. Al Dhaheri, None; S. Morrison, None; J. Su, None; D. D. Gladman, AbbVie, Amgen, BMS, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, UCB, 2,AbbVie, Amgen, BMS, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, UCB, 5; M. Urowitz, None.

**Abstract Number:** 2624

**A Renal Biopsy Should Not Delay Treatment Initiation in Suspected Lupus Nephritis**

Astrid Baumann¹, Angela Pakozdi², Andrea Cove-Smith², Debashis Pyne², Michael Sheaff¹ and Ravindra Rajakariar²,

¹Barts Lupus Centre, London, United Kingdom, ²Barts Lupus Centre, Barts Health NHS Trust, London, United Kingdom

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Renal biopsies are considered the gold standard in diagnosing lupus nephritis (LN). ALMS (1), the largest randomized trial in LN, reported the non-inferiority of mycophenolate mofetil (MMF) compared to cyclophosphamide. The mean serum creatinine in this trial was 100micromoles/L. Since its publication, MMF has been standard therapy in proliferative LN, but there may be delays in obtaining a histological diagnosis due to practical considerations. Renal biopsy also has a recognized complication rate. We therefore investigated whether histological findings influenced treatment in patients with SLE and clinical features consistent with LN.

**Methods:**

Histopathology and renal databases were used to identify all cases of new biopsy-proven active LN, diagnosed between February 2012 and November 2016 and managed at the Barts Lupus Centre (n=62). Demographic and clinical data were
collected using case records and pathology systems. LN classes based on glomerular pathology were defined according to the ISN/RPS 2003 classification. Patients were divided into sub groups based on their renal function (eGFR above or below 50 ml/min/1.73m$^2$).

**Results:** The mean age at LN diagnosis was 37 years (+-13 SD). 55 patients were female (89%) whilst 7 were male (11%). The ethnic distribution was the following: 46% South Asian, 34% Black, and 11% Caucasian. The histological class was either pure proliferative (class III or IV) or mixed proliferative (with additional class V) in 24 cases (39%). 42 (64%) patients had an eGFR > 50mL/min at presentation with a mean albumin and urine PCR of 30 g/dL and 520 mg/mmol respectively. Of this group, 37 patients (88%) received MMF, and only 3 patients were treated with cyclophosphamide (1- clinician decision, 2- severe extra renal manifestations). The remaining two patients received Azathioprine and both had sub-nephrotic proteinuria. At six months, 85% of LN patients were either in partial remission, defined as proteinuria below 200 mg/mmol (44%), or complete remission defined as proteinuria below 50 mg/mmol (41%). The treatment choice was different in the group with eGFR ≤ 50mL/min, with 65% of these patients receiving cyclophosphamide.

**Conclusion:**

Current guidelines strongly recommend performing a kidney biopsy in every patient presenting with suspected LN. Our findings indicate that in patients with preserved renal function (eGFR > 50mL/min) and significant proteinuria, treatment decision is not influenced by biopsy result. We therefore propose that induction treatment with MMF should not be delayed until a renal biopsy result is available. This study also questions the necessity of baseline histology in LN patients with preserved renal function, as the majority respond to standard therapy, and raises the possibility that biopsy could be reserved for patients who are resistant to induction therapy.

**References**


**Disclosure:** A. Baumann, None; A. Pakozdi, None; A. Cove-Smith, None; D. Pyne, None; M. Sheaff, None; R. Rajakariar, None.


**Abstract Number:** 2625

**Predicting Flares in Patients with Stable Systemic Lupus Erythematosus**

Jiacai Cho¹, Manjari Lahiri¹, Lay Kheng Teoh¹, Preeti Dhanasekaran²,³, Pak Moon Peter Cheung¹ and Aisha Lateef¹, ¹Medicine, Division of Rheumatology, National University Hospital of Singapore, Singapore, Singapore, ²National University of Singapore, singapore, Singapore, ³National University Hospital of Singapore, Singapore, Singapore

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM
Background/Purpose:

The course of systemic lupus erythematosus (SLE) varies with periods of quiescence punctuated by flares. Predicting exacerbations allows clinicians to select patients who need closer monitoring and guides therapy. However, such data are limited, especially in Asians. We aim to identify the clinical predictors of flares in patients with stable SLE.

Methods:

We enrolled patients ≥ 21 years old with SLE into a prospective observational study. All patients fulfilled either the 1997 ACR Criteria or the 2012 SLICC Classification Criteria. We collected demographic and clinical data by examination and chart review at baseline and three-monthly intervals for up to 5 years. We defined stable disease as SLE Disease Activity Index-2K (SLEDAI-2K) of ≤ 4 and flares using the SLE Flare Index. We determined the predictors of flare in patients with stable disease using Cox proportional hazards. We included variables with P<0.2 on univariate analysis in the multivariate model. Results are expressed as hazard ratios (HR) and 95% confidence intervals (CI).

Results:

We followed 210 patients for a median (IQR) of 31.5 months (24.1, 36.3). The median age (IQR) was 30.6 years (22.3, 42.5) and 91.4% were female. The majority were Chinese (70.5%). The median (IQR) disease duration from diagnosis was 9.96 years (4.5, 15.5). The median baseline SLEDAI-2K was 2 (2, 6) and the baseline SLICC damage score was 0 (0, 2). 152 (72.4%) patients had stable disease at baseline. Table 1 shows the baseline demographic and disease variables. In 5729 patient-months of follow-up, 109 (51.9%) patients had a flare. Median time to first flare was longer in patients with stable disease (10.7 vs. 8.3 months). Figure 1 shows the Kaplan-Meier Failure Curve of the risk of first flare in patients with stable versus active SLE. In the multivariate model of patients with stable SLE, younger age, longer disease duration, thrombocytopenia, hypocomplementemia and higher baseline prednisolone dose predicted flares. Table 2 shows the results of the univariate and multivariate analysis.

Conclusion:

Rheumatologists should closely monitor patients with stable SLE who are (i) younger; (ii) have longer disease duration; (iii) thrombocytopenic; (iv) hypocomplementemic; (iv) requiring higher baseline prednisolone doses; as these patients are more likely to develop flares.
<table>
<thead>
<tr>
<th></th>
<th>Baseline Active Disease (SELDAI-2k &gt;4)</th>
<th>Baseline Stable Disease (SLEDAI-2k ≤4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>58</td>
<td>152</td>
</tr>
<tr>
<td><strong>Demographic Variables</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median Age of Onset (IQR)</td>
<td>29.2 (22.4- 37.6)</td>
<td>31.3 (22.0- 43.9)</td>
</tr>
<tr>
<td>Females (%)</td>
<td>86.2%</td>
<td>93.4%</td>
</tr>
<tr>
<td>Ethnicity (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chinese</td>
<td>65.52</td>
<td>72.37</td>
</tr>
<tr>
<td>Malays</td>
<td>17.24</td>
<td>13.16</td>
</tr>
<tr>
<td>Indians</td>
<td>8.62</td>
<td>8.55</td>
</tr>
<tr>
<td>Others</td>
<td>8.62</td>
<td>5.92</td>
</tr>
<tr>
<td>Education Level (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td>25.86</td>
<td>27.63</td>
</tr>
<tr>
<td>Secondary</td>
<td>34.48</td>
<td>33.55</td>
</tr>
<tr>
<td>Tertiary</td>
<td>39.66</td>
<td>38.82</td>
</tr>
<tr>
<td>Positive Family History (%)</td>
<td>5.17</td>
<td>11.18</td>
</tr>
<tr>
<td>Current Smokers (%)</td>
<td>3.45</td>
<td>2.63</td>
</tr>
<tr>
<td><strong>Disease Variables</strong></td>
<td>Median (IQR)</td>
<td>Median (IQR)</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>20 (5-29)</td>
<td>5 (2-21)</td>
</tr>
<tr>
<td>ESR (mm/hr)</td>
<td>36 (18-63)</td>
<td>22.5 (16-36)</td>
</tr>
<tr>
<td>Complement 3 (mg/dL)</td>
<td>71.5 (58-91.5)</td>
<td>87 (75-100)</td>
</tr>
<tr>
<td>Complement 4 (mg/dL)</td>
<td>15.5 (9.5-25)</td>
<td>19 (14-25.5)</td>
</tr>
<tr>
<td>Hemoglobin (10^9/L)</td>
<td>12.2 (11.3-13.4)</td>
<td>11.7 (10.4- 13.1)</td>
</tr>
<tr>
<td>Total White Cell (10^9/L)</td>
<td>6.58 (4.74- 8.47)</td>
<td>5.44 (4.31-7.01)</td>
</tr>
<tr>
<td>Lymphocyte (10^9/L)</td>
<td>1.06 (0.7-1.43)</td>
<td>1.25 (0.88-1.89)</td>
</tr>
<tr>
<td>Platelet (10^9/L)</td>
<td>247 (186-287)</td>
<td>230 (194-279)</td>
</tr>
<tr>
<td>Estimated Glomerular Filtration Rate (ml/min)</td>
<td>76 (60- 116)</td>
<td>94 (60-114)</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>37 (33-41)</td>
<td>40 (37-42)</td>
</tr>
<tr>
<td>Variable</td>
<td>Median values (IQR)</td>
<td>Univariate Analysis</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------</td>
<td>---------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td></td>
<td>Hazard Ratio (CI)</td>
<td>P value</td>
</tr>
<tr>
<td></td>
<td>Hazard Ratio (CI)</td>
<td>P value</td>
</tr>
<tr>
<td>Young age (Lowest tertile vs. top two tertiles in years)</td>
<td>31.9 (25.7, 34.5) vs 50.0 (46.6, 54.1)</td>
<td>2.03 (1.28-3.21) 0.003</td>
</tr>
<tr>
<td>Females (vs. males)</td>
<td>N.A.</td>
<td>1.15 (0.42-3.15) 0.79</td>
</tr>
<tr>
<td>Current smoker (vs. ex-smoker or non-smoker)</td>
<td>N.A.</td>
<td>2.29 (0.72-7.33) 0.16</td>
</tr>
<tr>
<td>Malay (vs. Chinese)</td>
<td>N.A.</td>
<td>0.73 (0.35-1.53) 0.41</td>
</tr>
<tr>
<td>Indians (vs. Chinese)</td>
<td>N.A.</td>
<td>0.72 (0.31-1.67) 0.44</td>
</tr>
<tr>
<td>Other Ethnicities (vs. Chinese)</td>
<td>N.A.</td>
<td>1.04 (0.38-2.87) 0.94</td>
</tr>
<tr>
<td>Early disease (Lowest tertile vs. top two tertiles in years)</td>
<td>2.4 (1.12, 4.53) vs 14.6 (11.6, 18.3)</td>
<td>0.61 (0.36-1.04) 0.07</td>
</tr>
<tr>
<td>Leukopenia (&lt;3.84 x10^9/L) vs. normal white cell count</td>
<td>2.23 (1.81, 2.72) vs 5.73 (4.52, 7.54)</td>
<td>0.91 (0.22-3.71) 0.89</td>
</tr>
<tr>
<td>Lymphopenia (&lt;0.91 x10^9/L) vs. normal lymphocyte count</td>
<td>0.70 (0.54, 0.88) vs 1.6 (1.25, 1.98)</td>
<td>1.09 (0.69-1.75) 0.71</td>
</tr>
<tr>
<td>Thrombocytopenia (&lt;100 x 10^9/L) vs. normal platelet count</td>
<td>70 (63, 84) vs 246 (204, 283)</td>
<td>3.22 (1.16-8.89) 0.02</td>
</tr>
<tr>
<td>Low complement 3 or complement 4 vs. normal complement (mg/dL)</td>
<td>C3: 56 (48, 62) vs 80 (89, 102)</td>
<td>2.38 (1.34-4.21) 0.003</td>
</tr>
<tr>
<td>C4: 9 (8, 13) vs 20 (15, 27)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive anti-dsDNA vs. negative anti-dsDNA</td>
<td>N.A.</td>
<td>1.20 (0.93-1.56) 0.16</td>
</tr>
<tr>
<td>ESR (Highest tertile vs. lowest tertile in mm/hr)</td>
<td>60 (43, 70) vs 14 (12, 16)</td>
<td>0.66 (0.27-1.57) 0.35</td>
</tr>
<tr>
<td>Renal involvement vs no renal involvement</td>
<td>N.A.</td>
<td>1.43 (0.91-2.22) 0.12</td>
</tr>
<tr>
<td>High prednisolone dose (Highest tertile vs lowest two tertiles in mg/day)</td>
<td>7.5 (5, 10) vs 1.5 (1.25, 2.25)</td>
<td>2.78 (1.62-4.78) &lt;0.001</td>
</tr>
<tr>
<td>Presence of SLICC Damage vs. no SLICC Damage</td>
<td>2 (1, 4) vs 0</td>
<td>0.87 (0.55-1.36) 0.54</td>
</tr>
<tr>
<td>Current hydroxychloroquine use vs not on hydroxychloroquine</td>
<td>N.A.</td>
<td>1.11 (0.51-2.42) 0.79</td>
</tr>
</tbody>
</table>
Proton Pump Inhibitor Induced Subacute Cutaneous Lupus Erythematosus: Clinical Characteristics and Outcomes

Yih Jia Poh¹, Shirish Sangle¹, Eleanor Higgins¹, Emma Benton¹, David McGibbon¹ and David D'Cruz², ¹Louise Coote Lupus Unit, Guy's and St Thomas' Hospital, London, United Kingdom, ²Louise Coote Lupus Unit, Guy's and St. Thomas' Hospital, London, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Drug induced subacute cutaneous lupus erythematosus has rarely been described. There is a growing literature reporting the association between proton pump inhibitor use and subacute cutaneous lupus erythematosus (SCLE). We aim to describe the clinical characteristics of a cohort of patients with proton pump inhibitor induced subacute cutaneous lupus erythematosus, their clinical course and treatment options.

Methods: We retrospectively reviewed twelve patients with proton pump inhibitor induced subacute cutaneous lupus erythematosus at the Louise Coote Lupus Unit. Clinical details recorded included presence of underlying systemic lupus erythematosus (SLE) and SCLE, extent of cutaneous involvement, time to presentation, type of proton pump inhibitor and dosage, histological characteristics, immunological characteristics, treatment and time to resolution.
**Results:** There were 12 patients of whom 10 were female (83%). Eleven patients were Caucasians (92%). The median age at diagnosis was 61 years (range 37-71). Nine patients (75%) had underlying SLE. In this subgroup, only one patient had SCLE as part of their initial SLE presentation. Patients with coexisting SLE were younger with a median age of 53 years compared to patients without coexisting SLE. There were 8 patients with omeprazole, 3 patients with lansoprazole and 1 patient with pantoprazole induced SCLE.

All patients developed typical SCLE lesions clinically. The extent of SCLE was widespread involving the sun-exposed areas of the trunk, upper extremities and the lower limbs in 50% of the patients. Eleven (92%) demonstrated antinuclear antibody positivity and 9 patients (75%) anti-Ro (SS-A) antibody positivity. Seven patients underwent a skin biopsy and 6 patients had histological results in keeping with SCLE. The median time to presentation was 12 months (range 3 weeks -10 years) and the median resolution period was 19 days (range 3 days- 2 months). Proton pump inhibitors were stopped in all patients. Five patients (42%) received concurrent oral corticosteroids and 3 patients (25%) were newly initiated on hydroxychloroquine. Two patients received adjunctive topical therapy including topical steroids alone or in combination with topical tacrolimus. Four patients were re-exposed to proton pump inhibitors and 3 experienced a similar SCLE flare, which resolved following cessation of the proton pump inhibitor. (Table 1)

**Conclusion:** Proton pump inhibitor induced subacute cutaneous lupus may be commonly associated with anti-Ro (SS-A) antibody and this is likely a class effect with all proton pump inhibitors. In July 2015, the European Medicines Agency issued a warning that SCLE is likely to be a class effect for proton pump inhibitors. We recommend judicious use of proton pump inhibitors particularly in SLE patients with anti-Ro (SS-A) antibody positivity.
<table>
<thead>
<tr>
<th>Patient, sex/age (years)</th>
<th>Presence of underlying Systemic Lupus Erythematosus</th>
<th>Antibody Profile (Extractable Nuclear Antigen, ENA)</th>
<th>Proton pump inhibitor/dose (mg)</th>
<th>Extent of SCLE skin lesion</th>
<th>Incubation period</th>
<th>Treatment</th>
<th>Resolution period</th>
</tr>
</thead>
<tbody>
<tr>
<td>1; F, 53</td>
<td>Yes</td>
<td>Anti Ro (SS-A) and anti La (SS-B)</td>
<td>Lansoprazole, 30</td>
<td>Arms, anterior and posterior chest and legs</td>
<td>12 months</td>
<td>Cessation of lansoprazole, oral prednisone 7.5 mg, topical steroid (clobetasol)</td>
<td>3-7 days</td>
</tr>
<tr>
<td>2; F, 63</td>
<td>Yes</td>
<td>Anti Ro (SS-A) and anti La (SS-B)</td>
<td>Omeprazole, 20</td>
<td>Face, arms, torso and legs</td>
<td>No data</td>
<td>Cessation of omeprazole, hydroxychloroquine, oral prednisone</td>
<td>2 months</td>
</tr>
<tr>
<td>3; F, 60</td>
<td>No</td>
<td>Negative</td>
<td>Omeprazole, 20</td>
<td>Chest, upper back, abdomen and legs</td>
<td>3 weeks</td>
<td>Cessation of omeprazole</td>
<td>7 days</td>
</tr>
<tr>
<td>4; F, 71</td>
<td>Yes</td>
<td>Anti Ro (SS-A) and anti La (SS-B)</td>
<td>Omeprazole, 20</td>
<td>No data available</td>
<td>No data</td>
<td>Cessation of omeprazole</td>
<td>No data</td>
</tr>
<tr>
<td>5; F, 48</td>
<td>Yes</td>
<td>Anti Ro (SS-A)</td>
<td>Omeprazole, 20</td>
<td>Upper torso, arms and legs</td>
<td>2-3 months</td>
<td>Cessation of omeprazole, oral prednisone 20 mg (background mycophenolate mofetil 1.5 gram for SLE)</td>
<td>2-3 weeks</td>
</tr>
<tr>
<td>6; F, 37</td>
<td>Yes</td>
<td>Anti Ro (SS-A) and anti La (SS-B)</td>
<td>Pantoprazole, 40</td>
<td>Upper chest and back</td>
<td>No data</td>
<td>Cessation of pantoprazole (background mycophenolate mofetil and hydroxychloroquine)</td>
<td>No data</td>
</tr>
<tr>
<td>7; F, 65</td>
<td>Yes</td>
<td>Anti-Sm and anti-RNP</td>
<td>Omeprazole, 20</td>
<td>Face and neck</td>
<td>24 months</td>
<td>Cessation of omeprazole, hydroxychloroquine (background methotrexate for SLE)</td>
<td>2 months</td>
</tr>
<tr>
<td>8; M, 67</td>
<td>Yes</td>
<td>Anti Ro (SS-A) and anti La (SS-B)</td>
<td>Lansoprazole, 30</td>
<td>Face, torso, arms and legs</td>
<td>12 months</td>
<td>Cessation of lansoprazole, oral prednisone 20 mg</td>
<td>2 months</td>
</tr>
<tr>
<td>9; F, 45</td>
<td>Yes</td>
<td>Anti-Sm and anti-RNP</td>
<td>Omeprazole, 20</td>
<td>Neck, arms, hands and torso</td>
<td>3-5 weeks</td>
<td>Cessation of omeprazole, oral prednisone 20 mg, topical tacrolimus, topical steroid (background hydroxychloroquine and mycophenolate mofetil 2.5 gram)</td>
<td>No resolution, SCLE lesions waxes and wanes</td>
</tr>
</tbody>
</table>
Table 1: Clinical characteristics and outcome of patients with proton pump inhibitor induced SCLE

<table>
<thead>
<tr>
<th>No.</th>
<th>Sex</th>
<th>Age</th>
<th>History of Autoimmune Disease</th>
<th>Treatment</th>
<th>Lesion Location</th>
<th>Duration</th>
<th>Cessation of Treatment</th>
<th>Duration of Cessation</th>
</tr>
</thead>
<tbody>
<tr>
<td>10; F; 61</td>
<td>No</td>
<td></td>
<td>Anti-Ro 60 and Anti La (SS-B)</td>
<td>Omeprazole, 40</td>
<td>Face and torso</td>
<td>6 months</td>
<td>Cessation of omeprazole, hydroxychloroquine</td>
<td>2-4 weeks</td>
</tr>
<tr>
<td>11; F; 50</td>
<td>Yes</td>
<td></td>
<td>Anti-Ro (SS-A) and anti-La (SS-B), anti C1q</td>
<td>Lansoprazole, 30</td>
<td>Upper back (annular polycyclic)</td>
<td>8 years</td>
<td>Cessation of lansoprazole (background hydroxychloroquine)</td>
<td>No data</td>
</tr>
<tr>
<td>12; M; 62</td>
<td>Yes</td>
<td></td>
<td>Anti-Ro and Anti-Ro60</td>
<td>Omeprazole, 20</td>
<td>Neck, arms, hands and torso</td>
<td>10 years</td>
<td>Cessation of omeprazole</td>
<td>2 weeks</td>
</tr>
</tbody>
</table>

**Disclosure:** Y. J. Poh, None; S. Sangle, None; E. Higgins, None; E. Benton, None; D. McGibbon, None; D. D'Cruz, None.


**Abstract Number:** 2627

### Characterization of Emergency Department Visits in an Urban Underserved Lupus Cohort

**Justin Levinson**, Maushmi Savjani, Diane Zisa and Ellen M. Ginzler, Internal Medicine, Division of Rheumatology, Department of Medicine, SUNY Downstate Medical Center, Brooklyn, NY; **Division of Rheumatology, Department of Medicine, SUNY Downstate Medical Center, Brooklyn, NY**; **Rheumatology, Division of Rheumatology, Department of Medicine, SUNY Downstate Medical Center, Brooklyn, NY**

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

#### Background/Purpose:

SLE patients frequently utilize the Emergency Department (ED), impacting the cost of care and quality of life. We performed a retrospective analysis of ED visits over a 5.5 year period among SLE patients from an urban, underserved population. Aims were to: 1) define most common complaints 2) examine sociodemographic statistics 3) analyze most common complaints resulting in admission.

#### Methods:

Charts of patients who met ACR criteria for SLE presenting to the ED or Rheumatology clinic between 1/1/2010 and 6/20/2015 were reviewed for demographics, chief complaint, and ED course. In evaluating level of admissions over the 5.5 year period, patients were classified as Non-users (no ED visits, only clinic visits), Occasional Users (1-5 ED visits) or Frequent Users (>5 visits). Excluded charts were those for pediatrics, medication refills, social work needs, and those for the dialysis or renal transplant services.
Results:

Of an initial cohort of 363 patients and 1700 ED visits, 359 patients were reviewed. 258 patients (72%) had ≥1 visits with a total of 1451 ED visits (range 1-72). Patient demographics are shown in Table 1, with mean age at ED visit of 39.4 years with 31 men, 328 women. The mean number of visits was 6.24 ± 6.40 (±SEM) with 44% of all patients as Occasional Users. Shown in Table 2, most visits were related to musculoskeletal pain (MSK) in 196 patients (13.5%), chest pain in 147 (10.1%), and shortness of breath (SOB) in 112 (7.7%). The most common complaints to prompt hospital admission were fever (80.9%), SOB (75.0%), and syncope (70.0%). 62.3% of chest pain complaints led to admission compared to 27.0% of MSK. Only 36 visits (2.5%) were recorded as complaining of lupus flare, with resulting admissions in 55.6%.

<table>
<thead>
<tr>
<th>Table 1. Sociodemographic Features of SLE Patient Cohort over 5.5 Year Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-users (0 ED visits)</td>
</tr>
<tr>
<td>-------------------------</td>
</tr>
<tr>
<td><strong>Total Number of Patients</strong></td>
</tr>
<tr>
<td><strong>Age</strong></td>
</tr>
<tr>
<td>&lt;30</td>
</tr>
<tr>
<td>&gt;80</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
</tr>
<tr>
<td>Asian</td>
</tr>
<tr>
<td>Black</td>
</tr>
<tr>
<td>Caucasian</td>
</tr>
<tr>
<td>Hispanic</td>
</tr>
<tr>
<td>Undisclosed</td>
</tr>
<tr>
<td><strong>Marital Status</strong></td>
</tr>
<tr>
<td>Single</td>
</tr>
<tr>
<td>Married</td>
</tr>
<tr>
<td>Other (separated, widowed, divorced)</td>
</tr>
<tr>
<td><strong>Employment Status</strong></td>
</tr>
<tr>
<td>Employed</td>
</tr>
<tr>
<td>Unemployed</td>
</tr>
<tr>
<td>Retired/Disability</td>
</tr>
<tr>
<td><strong>Insurance</strong></td>
</tr>
<tr>
<td>Insurance</td>
</tr>
<tr>
<td>Self-pay</td>
</tr>
<tr>
<td><strong>Disease Duration</strong></td>
</tr>
<tr>
<td>&lt;1 year</td>
</tr>
<tr>
<td>Between 1 and 5 years</td>
</tr>
<tr>
<td>&gt;5 years</td>
</tr>
<tr>
<td>Unknown</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2. Chief Complaints of ED Presentation and Number of Resulting Admissions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chief Complaint</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Musculoskeletal Pain</td>
</tr>
<tr>
<td>Chest Pain</td>
</tr>
<tr>
<td>Shortness of Breath</td>
</tr>
<tr>
<td>Abdominal Pain</td>
</tr>
<tr>
<td>OB/Gyn/GU Pain or Bleeding</td>
</tr>
<tr>
<td>Dermatologic</td>
</tr>
<tr>
<td>Neurologic</td>
</tr>
<tr>
<td>URI Symptoms</td>
</tr>
<tr>
<td>Headache</td>
</tr>
<tr>
<td>Vomiting</td>
</tr>
<tr>
<td>Trauma/Laceration</td>
</tr>
<tr>
<td>Fever</td>
</tr>
<tr>
<td>Lab Abnormality</td>
</tr>
<tr>
<td>&quot;Lupus Flare&quot;</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Lower Extremity Swelling</td>
</tr>
</tbody>
</table>

Conclusion:
We present an analysis of characteristics of ED presentation and rate of resulting admissions of SLE patients. Physicians should be aware that the average SLE patients will present to the ED roughly yearly. Unnecessary ED visits of SLE patients can be avoided with patient education and outpatient symptomatic control for the most common complaints.

Disclosure: J. Levinson, None; M. Savjani, None; D. Zisa, None; E. M. Ginzler, GlaxoSmith Kline, Aurinia, Genentech, Ablynx, Janssen, 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/characterization-of-emergency-department-visits-in-an-urban-underserved-lupus-cohort

Abstract Number: 2628

Raynaud’s Symptoms and Pregnancy Induced Hypertension in Patients with Systemic Lupus Erythematosus

Sakiko Isojima, Mayu Saito, Yoko Miura and Nobuyuki Yajima, Showa university, Tokyo, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Several reports suggested that the incidence of obstetric complications such as pregnancy induced hypertension (PIH) and preterm birth was higher in a pregnant woman with systemic lupus erythematosus (SLE) than in a healthy woman. Dysplasia of placental vessels was thought to be one of the putative cause for PIH. It followed by maternal vascular endothelial dysfunction, which lead to vasospasm and hypercoagulation. As a result, maternal blood pressure rose and renal impairment occurred. In the meantime, vascular endothelial dysfunction is also involved in the mechanism of Raynaud's symptoms, which is often seen in patients with SLE. Therefore, there may be an association between the high incidence of PIH and Raynaud’s symptoms in pregnant women with SLE. However, there is no report investigating the association. To that end, we studied the association between PIH and Raynaud's symptoms in women with SLE.

Methods: We conducted a questionnaire survey to SLE patients aged 20 to 50 who visited Showa University Hospital between December 2015 and April 2017. We investigated the following three contexts: 1) Raynaud's symptoms before pregnancy 2) Pregnancy experience 3) PIH and preterm birth.

Results: In total, 109 female SLE patients were applicable, and 43 patients had experienced pregnant. Among 43 patients with SLE, 17 patients developed SLE before pregnancy. Of 17 patients, Raynaud's symptoms were observed in 5 patients, of whom 4 was complicated with PIH during pregnancy. In contrast, among 12 people without Raynaud's symptoms, only one person had experienced PIH. There was significant different occurrence of PIH between those with and without Raynaud’s symptoms (p= 0.0099 Fisher exact test). We found that PIH occurred more frequently in patients with SLE when Raynaud's symptoms were seen before pregnancy. The mechanism of this association was beyond our scope, but we speculate the involvement of endothelin-1. It is considered that high serum concentration of endothelin-1 contributed to the development of PIH. On the other hand, serum concentrations of endothelin-1 were reported to be high in patients with SLE having Raynaud's symptoms. As we could not examine the activity of SLE in this study, we are planning to investigate prospective study for uncovering the detailed association and underlying causative mechanism.
Conclusion: We identified the association between PIH and Raynaud’s symptoms in patients with SLE for the first time. We should pay attention to the onset of PIH in SLE-associated pregnant women who have Raynaud’s symptoms before pregnancy.

Disclosure: S. Isojima, None; M. Saito, None; Y. Miura, None; N. Yajima, None.


Abstract Number: 2629

Systemic Lupus Erythematosus Patients Not Complaining Raynaud’s Phenomenon Display Lower Skin Blood Perfusion Than Healthy Subjects

Barbara Ruaro¹, Alberto Sulli¹, Sabrina Paolino², Carmen Pizzorni³, Veronica Tomatis¹, Massimo Patanè¹ and Maurizio Cutolo¹, ¹Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, Genoa, Italy, Genoa, Italy, ²University of Genova, IRCCS San Martino, Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, Genoa, Italy, Genoa, Italy, ³Research Laboratory and Academic Unit of Clinical Rheumatology, Department of Internal Medicine, University of Genova, Genova, Italy, Genoa, Italy

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: A clinical feature of patients with primary Raynaud's phenomenon (PRP) is the presence of low skin blood perfusion (BP) at the level of hands (1-3). Conversely, few studies investigated skin BP in patients with systemic lupus erythematosus (SLE) (4,5). The aim of this study was to investigate skin BP in different skin areas of hands and face in three groups of subjects: SLE patients not complaining clinical symptoms of Raynaud's phenomenon, PRP patients and healthy subjects (CNT).

Methods: Fourteen SLE patients without Raynaud's phenomenon (ACR criteria) (mean age 51±14 years, mean disease duration 7±4 years), 14 PRP patients (LeRoy, criteria) (mean age 53±21 years, mean Raynaud duration 6±5 years) and 14 CNT, (mean age 53±17 years), after informed consent (6,7). Skin BP was assessed by laser speckle contrast analysis (LASCA) at the level of hands and face, and the mean BP reported as perfusion units (PU) (4). Patients were not taking vasodilator drugs at the time of the study. Statistical analysis was performed by non parametric tests.

Results: BP was found significantly lower in both SLE and PRP patients when compared with CNT at the level of fingertips (median PU 113, 84, 187, respectively; p<0.0001), periungual (median 102, 72, 143, respectively; p<0.0001), dorsal (median 73, 60, 122, respectively; p<0.0001) and palm areas of hands (median 93, 74, 117, respectively; p<0.0001). However, PRP patients showed lower BP values than SLE patients in all areas of hands (fingertips p=0.03, palm p=0.02, periungual p=0.006, dorsum p=0.05), but not at the level of face (p=0.90). SLE, PRP and CNT subjects displayed similar BP values at the level of face (median PU 145, 147, 125, respectively; p=0.40).

Conclusion: Statistically significant differences in skin BP were detected between SLE patients and controls. BP of hands was found lower in SLE patients not complaining clinical symptoms of RP than in healthy subjects. The clinical value of this new finding need to be investigated by further analysis.
Utility of the Korean Version of Systemic Lupus Activity Questionnaire, in Clinical Practice: Its Correlation with Disease Activity Indices of Systemic Lupus Erythematosus

Eun Young Ahn¹, Wonho Lee², Jin Young Moon², Jin Kyun Park², Eun Young Lee³, Eun Bong Lee², Sang-Cheol Bae⁴ and Kichul Shin⁵. ¹Division of Rheumatology, Department of Internal Medicine, Pusan National University Yangsan Hospital, Yangsan, Korea, Republic of (South), ²Division of Rheumatology, Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea, Republic of (South), ³Division of Rheumatology, Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea, Republic of (South), ⁴Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), ⁵Division of Rheumatology, Department of Internal Medicine, SMG-SNU Boramae Medical Center, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Assessing patient-reported outcomes validated to be associated with disease activity has helped clinicians better understand treatment response of patients with systemic rheumatic disease. Such questionnaire for systemic lupus erythematosus (SLE) are rarely used in daily practice; the utility of out-patient targeted questionnaire for SLE has never been studied in Korea.

Methods: The Systemic Lupus Activity Questionnaire, or SLAQ, was translated in Korean (K-) and back-translated, then reviewed by a committee specifically organized for this purpose. This K-SLAQ was then applied to SLE patients followed (out-patient) at institute 1 (SMG-SNU); SELENA-SLEDAI and Systemic Lupus Activity Measure (SLAM)-R was measured on the same day. K-SLAQ was measured again 2 weeks later to assess its reliability. Finally, K-SLAQ was validated in the same manner at a separate institute (2, SNUH). The receiver operating characteristic (ROC) curve was obtained to study K-SLAQ cut-off values in relation to those indicating high disease activity in SELENA-SLEDAI and SLAM-R.

Results: Forty-two patients were enrolled at institute 1, where the median (min-max) age of patients were 40 (19-70), and disease duration was 3.0 (0-18.1) years. The mean K-SLAQ, SELENA-SLEDAI, SLAM-R values were 10 (10-29), 7 (0-26), 5 (1-18), respectively. The correlation between K-SLAQ and the disease activity indices are depicted in the presented table. These results were validated at institute 2 (N= 44). The interclass correlation between repeated K-SLAQ
measures was 0.912 (95% CI 0.847-0.949, \( p < 0.0001 \)), and the area under the ROC curve of SLAQ for SELENA-SLEDAI \( \geq 6 \) was 0.705 (95% CI 0.59-0.82, \( p = 0.002 \)), and SLAM-R \( \geq 7 \) was 0.704 (95% CI 0.595-0.812, \( p = 0.001 \)).

**Conclusion:** K-SLAQ is a useful tool which correlated well with commonly used SLE disease activity indices. This may also facilitate identifying key determinants of flares in daily clinical practice.

### Table. Correlation between SLAQ and SELENA-SLEDAI or SLAM-R

<table>
<thead>
<tr>
<th>Measures</th>
<th>Institute 1 SLAM-R</th>
<th>Institute 2 SLAM-R</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( r )</td>
<td>( p )-value</td>
</tr>
<tr>
<td>SLAQ</td>
<td>0.439</td>
<td>0.004</td>
</tr>
<tr>
<td>Symptom score</td>
<td>0.446</td>
<td>0.003</td>
</tr>
<tr>
<td>Patient global assessment</td>
<td>0.174</td>
<td>0.271</td>
</tr>
<tr>
<td>Patient NRS</td>
<td>0.272</td>
<td>0.082</td>
</tr>
</tbody>
</table>

\( r \), Spearman\(^{-1} \)'s coefficient; NRS, numerical rating scale

---

**Disclosure:** E. Y. Ahn, None; W. Lee, None; J. Y. Moon, None; J. K. Park, None; E. Y. Lee, None; E. B. Lee, None; S. C. Bae, None; K. Shin, None.

---

**Abstract Number:** 2631

**Validation of Clinically Relevant Improvement in Children and Adolescents with cSLE**

**Pinar Ozge Avar Aydin\(^1\), Michael J. Holland\(^2\), Simone Appenzeller\(^3\), Stacy P. Ardoin\(^4\), Tadej Avcin\(^5\), Michael W. Beresford\(^6\), Brian M. Feldman\(^7\), Francisco Flores\(^8\), Marisa S. Klein-Gitelman\(^9\), Beatrice Goilav\(^10\), Raju Khubchandani\(^11\), Deborah M. Levy\(^12\), Angelo Ravelli\(^13\), Nicolino Ruperto\(^14\), Clovis A Silva\(^15\), Scott E. Wenderfer\(^16\), Jun Ying\(^17\) and Hermine I. Brunner\(^1\), \(^1\)Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, \(^2\)Pediatric Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, \(^3\)Pediatric Rheumatology Unit, State University of Campinas, Campinas, Brazil, \(^4\)Pediatric & Adult Rheumatology, The Ohio State University Wexner Medical Center, Columbus, OH, \(^5\)Istituto Giannina Gaslini - Pediatria II, Reumatologia - PRINTO, Genoa, Italy, \(^6\)On Behalf of the UK JSLE Study Group, Liverpool, United Kingdom, \(^7\)Rheumatology, The Hospital for Sick Children, Toronto, ON, Canada, \(^8\)Nephrology and Hypertension, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, \(^9\)Division of Pediatric Rheumatology/PDD PTD, Lurie Children's Hospital of Chicago/Northwestern University, Chicago, IL, \(^10\)Albert Einstein College of Medicine/Montefiore Medical Center, New York, NY, \(^11\)Department of Paediatrics, Jaslok Hospital and Research Center, Mumbai, India, \(^12\)Division of Rheumatology, The Hospital for Sick...
SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Childhood-onset systemic lupus erythematosus (cSLE) is a multisystem autoimmune disease that is characterized by episodes of flares followed by improvement in response to therapy. To assess the clinically relevant response and the efficiency of therapies in cSLE, sensitive and well-correlated criteria with changes in improvement are needed.

Objective: To prospectively validate the PRINTO/ACR Criteria of Response to Therapy (PCI) & assess their ability to capture clinically relevant improvement (CRI).

Methods: Consensus formation methodology (Delphi, nominal group technique; 77 % consensus level) was used to newly define CRI. Using prospective cSLE data, patient profiles (PPs) were developed which provided information at a baseline & follow-up visit, including the cSLE core response variables [CRVs: SLEDAI, the urinary protein-creatinine ratio (PCR), physician global assessments of cSLE disease activity, patient global assessment of well-being, quality of life score]. Twelve experts (>10 yrs experience managing cSLE) were asked to rate disease courses of up to 200 PPs using 2 scales: (1) no change/worsening, minor, moderate, or major improvement; and (2) clinically relevant improved, yes/no. Each PP was determined of the “true” course based upon the majority opinion of the raters. Multinomial logistic regression models (MLRs) were used to predict the true course and develop algorithms to calculate the continuous “improvement score” using absolute or percentage changes of the CRVs. ROC curves were analyzed for the MLR algorithms and AUC, specificity, sensitivity, and kappa statistics were calculated to assess the improvement scores for accuracy. Results were reviewed by the expert panel for further discussion and recommendation.

Results: The consensus definition of CRI was: “A clinically relevant improvement has occurred in a child with lupus if there are reduced signs of disease from active lupus. Although there may not be an improvement of lupus activity in all organ systems, there cannot be increased lupus activity in major organ systems (neuropsychiatric, hematological, gastrointestinal, renal, ophthalmological, and cardiopulmonary). Patient symptoms must be at least stable, and immunosuppressive therapy should be unchanged or decreased” (100 % consensus). All 4 top PCI were highly sensitive and moderately accurate but specificity was lacking to various degrees of improvement or CRI. The MLR-based algorithms appeared more accurate than the PCI for CRI and minor/moderate/major improvement (Table 1).

Conclusion: The PCI are moderately accurate in this validation data set, but the MLR-derived criteria considering absolute CRV changes perform better in capturing CRI and cSLE improvement in general. If confirmed in larger validation studies, MLR-based algorithms may allow for a more effective assessment of response to therapy in cSLE.

Table 1. Multivariate Models for Improvement Criteria
The Southern California Lupus Registry: I. Baseline Characteristics of Patients with Systemic Lupus Erythematosus in an Uncharted Territory

Joshua Liu¹, Kathleen Teves², Van La², Arlene Bravo³, Sheila Lezcano⁴, Talha Khawar⁴, Ebrahim Sadeghi⁴, Cong-Bin Wang⁵, Karina Torralba⁶, Howard Yang⁵ and Vaneet K. Sandhu⁷, ¹Internal Medicine, Loma Linda University Medical Center, Loma Linda, CA, ²Internal Medicine, University of California, Riverside, Riverside, CA, ³Internal Medicine, Loma Linda University, Loma Linda, CA, ⁴Rheumatology, Loma Linda University Medical Center, Loma Linda, CA, ⁵Loma Linda University Medical Center, Loma Linda, CA, ⁶Internal Medicine/Rheumatology, Loma Linda University, Loma Linda, CA, ⁷Division of Rheumatology, Loma Linda University, Loma Linda, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The Southern California Lupus Registry (SCOLR) is a population-based, longitudinal, multi-ethnic cohort of subjects with SLE directed toward studying health and healthcare disparities in the Inland Empire, an under-recognized region of southern California inhabiting more than 3 million individuals where the percentage population living below the federal poverty line exceeds the general population in California. We report herein a
preliminary analysis of baseline characteristics and clinical manifestations to establish a platform for future studies on regional disparities.

**Methods:** Subjects were enrolled into the SCOLR study from June 2016 to June 2017 using the Systemic Lupus International Collaborating Clinic (SLICC) classification criteria for SLE. Retrospective review of medical records as well as clinical visits yielded more than 80 variables including demographic and clinical data, disease activity, comorbidities, serologic identifiers for SLE, and treatment history. Data involving clinical manifestations including renal involvement were analyzed with descriptive statistics.

**Results:** Of the 147 subjects enrolled, the majority resided in the surrounding geographic areas of the participating institution (Loma Linda University Medical Center). Ninety-two percent (135) were women and 8% (12) were men (female:male ratio, 11) with a mean age of 42 years (range 19-85). Thirty-seven percent were White non-Hispanic, 37% White Hispanic, 10% Asian, and 16% Black. Positive antinuclear antibody was demonstrated in 90%, dsDNA antibody in 52%, and Smith antibody in 34% of subjects. Lupus nephritis was noted in 46 subjects, of whom greater than 50% were of Hispanic origin. SLEDAI score was also notably greater in the Hispanic population compared to other subsets.

**Conclusion:** Subjects with SLE residing in the Inland Empire demonstrate findings in line with other cohorts with greater disease activity and severity among non-White groups compared to Whites and Hispanic subjects specifically in our cohort appearing to be at greater risk of morbidity and mortality. Our preliminary data warrants further analysis of racial/ethnic subsets in serologies and disease manifestations.
<table>
<thead>
<tr>
<th><strong>Table 1. Baseline Characteristics</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Current age, average (range)</strong></td>
</tr>
<tr>
<td><strong>Disease duration, average (range)</strong></td>
</tr>
<tr>
<td><strong>Female, n (%)</strong></td>
</tr>
<tr>
<td><strong>Race / Ethnicity (n)</strong></td>
</tr>
<tr>
<td>White Hispanic</td>
</tr>
<tr>
<td>White non-Hispanic</td>
</tr>
<tr>
<td>Black</td>
</tr>
<tr>
<td>Asian/Pacific-Islander</td>
</tr>
<tr>
<td><strong>Serologies (n, %)</strong></td>
</tr>
<tr>
<td>Antinuclear Antibody</td>
</tr>
<tr>
<td>dsDNA Antibody</td>
</tr>
<tr>
<td>Smith Antibody</td>
</tr>
<tr>
<td>Anti-Ro/SSA antibody</td>
</tr>
<tr>
<td>Anti-La/SSB antibody</td>
</tr>
<tr>
<td>Ribonucleoprotein antibody</td>
</tr>
<tr>
<td>Lupus anticoagulant</td>
</tr>
<tr>
<td>Beta-2gp IgM</td>
</tr>
<tr>
<td>Beta-2gp IgG</td>
</tr>
<tr>
<td>Cardiolipin IgM</td>
</tr>
<tr>
<td>Cardiolipin IgG</td>
</tr>
<tr>
<td><strong>Clinical manifestations (%)</strong></td>
</tr>
<tr>
<td>Mucocutaneous abnormalities</td>
</tr>
<tr>
<td>Serositis</td>
</tr>
<tr>
<td>Arthritis</td>
</tr>
<tr>
<td>Hematologic abnormalities</td>
</tr>
<tr>
<td><strong>Lupus nephritis</strong></td>
</tr>
<tr>
<td><strong>Treatment history (current or prior)</strong></td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
</tr>
<tr>
<td>Azathioprine</td>
</tr>
<tr>
<td>Mycophenolate</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
</tr>
<tr>
<td>Belimumab</td>
</tr>
<tr>
<td>Prednisone</td>
</tr>
<tr>
<td><strong>SLEDAI score</strong></td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>1-5 (mild)</td>
</tr>
</tbody>
</table>
Patients with Secondary Sjögren’s Syndrome to SLE Are Characterized By Typical Autoantibodies and a Pro-Inflammatory State

Marika Kvarnstrom¹, Guillermo Ruacho², Johanna Gustafsson³, Agneta Zickert⁴, Vilija Oke⁵, Johan Rönnelid⁶, Kerstin Elvin⁷, Iva Gunnarsson⁸ and Elisabet Svenungsson⁸, ¹Unit of Rheumatology, Department of Medicine, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, Stockholm, Sweden, ²Department of Medicine, Unit of Rheumatology,, Stockholm, Sweden, ³Dep. of Medicine, Karolinska Institutet, Karolinska University Hospital, Unit of rheumatology,, Stockholm, Sweden, ⁴Department of Medicine, Rheumatology Unit, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, ⁵Department of Medicine, Rheumatology Unit, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, ⁶Unit of Rheumatology Unit, Department of Medicine, Karolinska Institute, Karolinska University Hospital, Stockholm, Sweden, ⁷Department of Immunology Genetics and Pathology, Uppsala University, Uppsala, Sweden, ⁸Rheumatology Unit, Department of Medicine, Karolinska Institute, Karolinska University Hospital, Stockholm, Sweden

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Sjögren’s syndrome occurs in isolation (primary Sjögren’s syndrome, pSS), but it is also often secondary (sSS) to, and sometimes difficult to delineate from, other rheumatic diseases, in particular from systemic lupus erythematosus (SLE). Consequently there is a need to investigate similarities and differences between SLE patients with (SLE-sSS) and without sSS (SLE-noSS).

Objective s was to investigate the occurrence of sSS in a large cohort of SLE patients and to explore clinical and laboratory characteristics associated with SLE-sSS as compared to SLE-noSS and controls.

Methods:

We included 504 consecutive SLE patients and 322 population controls, individually matched for age and gender to the first patients. All patients fulfilled the 1982 revised ACR criteria for SLE. SLE-sSS was defined according to the American-European consensus criteria (AECC). Accordingly, subjective and objective quantifications of sicca symptoms were recorded on all subjects. All underwent a thorough clinical investigation. SLE-associated autoantibodies, (ANA screening by BioPlex 2200 system, Bio-Rad) and Rheumatoid factor (Rf, Phadia Immunocap 250) were
determined with standardized methods for all subjects. Routine laboratory workup and a panel of cytokines (MSD 30-plex cytokine assays, performed on samples from 433 consecutive SLE patients and 319 controls) were measured on fasting blood samples.

Results:

SLE-SS, as defined by AECC, occurred in 23% of the SLE patients. Compared to SLE-noSS the SLE-SS group was older, both at inclusion (55 vs 43 yrs, p<0.0001) and at disease onset (40 vs. 32 yrs p<0.0001), and more enriched in females (96 vs. 83 %, p=0.0007), patients with leucopenia (57 vs. 45 %, p=0.02) and peripheral neuropathy (15 vs 7 %, p=0.01). Nephritis was less common in SLE-SS (32 vs 43 %, p= 0.03). Higher levels of total IgG, positivity for anti-SSA/Ro52, anti-SSA/Ro60, anti-SSB antibodies, Rf IgM and Rf IgA further characterized the SLE-SS group. 20/30 investigated cytokines were detectable, of these 19/20 were higher in SLE than in controls. 6/20 cytokines (TNF-a, IL-6, MCP-4, MIP-1β, IL12/IL-23p40 and IP-10) were upregulated in SLE-SS vs. SLE-noSS (see table for figures).

Conclusion:

Through strictly applying the AECC criteria we report that the frequency of SLE-SS increases with age and affects roughly ¼ of SLE patients. Nephritis was less common while leucopenia and peripheral neuropathy were more common among SLE-SS patients. In addition to excess of well-known SS-associated autoantibodies we report higher levels of six pro-inflammatory cytokines in SLE-SS as compared to SLE-nonSS. These findings demonstrate that, though often regarded as a milder version of SLE, patients with SLE-SS are characterized by a state of chronic systemic inflammation.

| Immunoglobulins, autoantibodies and pro-inflammatory cytokines |
|-----------------|-----------------|-----------------|-----------------|-----------------|
|                 | Controls N=322  | SLE-SS N=117    | SLE-noSS N=387  | p-value         |
| IgG total g/L   | median (IQR) or N(%) | median (IQR) or N(%) | median (IQR) or N(%) | SLE-SS vs. SLE-noSS |
| anti-dsDNA % positive (+) | 10.9 (9.5-12.2) | 14.5 (10.4-18.3) | 12.4 (9.8-15.8) | 0.009 |
| anti-Ro52 % +   | 5 (1.6) | 36 (31.3) | 154 (41) | 0.06 |
| anti-Ro60 % +   | 3 (0.9) | 56 (47.9) | 84 (21.8) | <0.0001 |
| anti-La/SSB % + | 69 (59) | 137 (35.9) | 96 (18) | <0.0001 |
| Rf IgG % +      | 10 (3.1) | 44 (37.6) | 69 (18) | <0.0001 |
| Rf IgM % +      | 10/261 (3.8) | 17/80 (21.2) | 35/259 (13.5) | 0.09 |
| TNF-α pg/mL     | 14/283 (4.9) | 32/83 (38.6) | 56/281 (19.9) | 0.0005 |
| IL-6 pg/mL      | 2.3 (2.0-2.8) | 4.9 (3.6-7.1) | 4.4 (3.0-6.0) | 0.008 |
| IL12/IL-23p40 pg/mL | 0.5 (0.4-0.7) | 1.5 (0.8-3.0) | 1.1 (0.6-2.0) | 0.009 |
| IP-10 pg/mL     | 313.2 (99.8-179.5) | 211.3 (141.4-363.8) | 177.1 (119.6274.5) | 0.032 |

Disclosure: M. Kvarnstrom, None; G. Ruacho, None; J. Gustafsson, None; A. Zickert, None; V. Oke, None; J. Rönnelid, None; K. Elvin, None; I. Gunnarsson, None; E. Svenungsson, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/patients-with-secondary-sjogrens-syndrome-to-sle-are-characterized-by-typical-autoantibodies-and-a-pro-inflammatory-state

Abstract Number: 2634
The Prevalence of Autoimmune Disease in Families of Patients with Systemic Lupus Erythematosus (SLE). a Single Centre Study

Oseme Etomi1, Andrea Cove-Smith2, Ravindra Rajakariar3, Myles J. Lewis2,4,5,6, Angela Pakozdi2 and Debasish Pyne2, 1heumatology Department, Barth Health NHS foundation trust, London, United Kingdom, 2Barts Lupus Centre, Barts Health NHS Trust, London, United Kingdom, 3Bart's Lupus Center, Barts Health NHS Foundation Trust, London, United Kingdom, 4Experimental Medicine & Rheumatology, Queen Mary University of London, London, United Kingdom, 5Myles Lewis (myles.lewis@qmul.ac.uk), London, United Kingdom, 6Rheumatology, Centre for Experimental Medicine and Rheumatology, William Harvey Research Institute, Barts and The London, School of Medicine and Dentistry, Queen Mary University of London, London, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster III: Therapeutics and Clinical Trial Design
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Studies to date have reported that up to 30% of lupus patient have a first degree relative with an autoimmune disorder (AD). The most recent study from the Danish registry (1) reports an increase in risk of lupus, rheumatoid arthritis (RA), type 1 diabetes (T1DM) and inflammatory bowel disease in individuals with an SLE-affected first-degree relative. Here we describe the prevalence of ADs amongst family members in a multi ethnic lupus cohort.

Methods:

Questionnaires were distributed to consecutive lupus patients attending our Lupus clinic between April 2017 and June 2017. All patients fulfilled the 2012 SLICC ACR criteria for lupus. Patients were asked about their family history with specific questions on the presence of a range of ADs.

Results:

74 patients completed questionnaires. 24 were incomplete, the remaining 50 were analysed. The average age of patients with SLE was 41.6years (21- 78) 90% of the patients were female. South east Asians (40%) and afro- Caribbean (36%) represented the majority of our cohort. Others included Caucasian (14%), Turkish (4%), oriental (2%), Malaysian (2%) and one mixed race (2%) Caucasian-afro Caribbean.

13 (26%) patients with SLE had another autoimmune condition with RA the most common (n= 7 ,14%), followed by antiphospholipid syndrome (APS) (n =4 , 8%) , sjogrens (n=1) and hashimotos (n=1).

The prevalence of a second AD in lupus patients was highest in Afro-Caribbeans (n=16, 89%). Afro-Caribbean patients were significantly more likely to have another AD than South East Asians (n=7, 35%) (p=0.001) and Caucasians (n=1, 14%) (p=0.001).

A family history of AD was found in 17 patients (34%). SLE was the most prevalent AD in relatives with 8 cases (16%) identified, followed by RA in 5 (10%), T1DM (n=3), graves’ disease (n=3) and multiple sclerosis (n =2 ). Other AD identified were sjogrens, hashimotos and psoriasis (n=1). In 54% the family history was in a first degree relative, second degree relative in 37.5% and 3rd degree relatives in 8.3%. The majority of relatives with an autoimmune history were female ( 70.8%). There was no significant difference in the incidence of a family history of autoimmune disease between the various ethnic groups.

Conclusion:
Within our multi-ethnic cohort of patients with SLE, RA was the most common second AD followed by APS. Afro-Caribbean were more likely to have a second AD than either south-east Asians or Caucasians. SLE, RA, T1DM and Graves’ disease were the most common ADs found in family members. Ethnicity did not affect the likelihood of patients having a relative with an AD. Larger sampling is warranted for future studies.

Disclosure: O. Etomi, None; A. Cove-Smith, None; R. Rajakariar, None; M. J. Lewis, None; A. Pakozdi, None; D. Pyne, None.

Abstract Number: 2635

Dosechecker: Solving the Hydroxychloroquine Dosing Dilemma with a Smart Phone App

Elliot Perlman¹, Robert Friday², Paul Greenberg³, David Browning⁴ and Joan Miller⁵, ¹Rhode Island Eye Institute, Providence, RI, ²Division of Rheumatology, Department of Medicine, Newton-Wellesley Hospital, Newton, MA, ³Division of Ophthalmology, Alpert Medical School, Brown University, Providence, RI, ⁴Charlotte Eye, Ear, Nose, and Throat Associates, Charlotte, NC, ⁵Department of Ophthalmology, Harvard Medical School and Massachusetts Eye and Ear Institute, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: ARHP Systemic Lupus Erythematosus – Clinical Aspects and Treatment Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Hydroxychloroquine retinopathy (HCR) is a potentially blinding but largely preventable disease. The true prevalence of HCR is unknown among the 350,000 Americans who take the drug,¹ but it appears to be rising, related in part to changes in the definition of HCR. Despite improvements in diagnostic testing, it is still challenging to detect early signs of hydroxychloroquine toxicity.²,³ Moreover, once the disease is detected, there is no treatment and retinopathy often continues to progress even when the medication is stopped. Thus, primary prevention offers the best chance of managing HCR. Critical parameters that increase risk for HCR include the magnitude of dose and duration of therapy. Prescribing providers may not routinely calculate the optimal dose of hydroxychloroquine due to a number of factors, including: (1) toxicity is a cumulative effect and takes years to develop; (2) the calculations are cumbersome and time during a clinical encounter is short; (3) lack of familiarity with recommended dosing guidelines; and (4) controversy exists over how to calculate appropriate dosages.

Methods: Equations for calculating a low-risk hydroxychloroquine dose based on a patient’s actual body weight (ABW) and ideal body weight (IBW) were used to develop a novel iOS app to compare the two calculation methods and recommend a dosing strategy to maximize patient safety. The Smart BASIC iOS app was used for programming to devise a hydroxychloroquine dose calculating app compatible with the iOS operating system.

Results: We developed a free iOS App, DoseChecker, to provide a tool for rapid comparison of ABW and IBW hydroxychloroquine dose calculations for a patient at the point of care. Calculated data for an individual patient’s height and weight are reported for the two methods on a single screen output. The DoseChecker app recommends a maximum weekly hydroxychloroquine dose based on whichever dosing strategy (ABW vs. IBW) yields the lower weekly dose. The app then proposes an optimal weekly dosing strategy using a combination of 200mg and 400mg daily doses to reduce the risk of HCR by safely maximizing dosing of hydroxychloroquine.
**Conclusion:** By using *DoseChecker* to engage the patient in clinical decision making, the prescribing provider can educate patients regarding the risk factors for HCR and reinforce the critical need for ongoing ophthalmologic monitoring for HCR. We therefore anticipate that using the *DoseChecker* app in clinical practice will provide a convenient and practical bedside tool to facilitate the safe prescribing of hydroxychloroquine for primary prevention of HCR.

**References:**


**Disclosure:** E. Perlman, None; R. Friday, None; P. Greenberg, None; D. Browning, None; J. Miller, None.


Abstract Number: 2636

**EZH2 Modulates the DNA Methyolome and Controls T Cell Adhesion through Junctonal Adhesion Molecule-a in Lupus Patients**

Pei-Suen Tsou¹, Patrick Coit¹, Nathan Kilian² and Amr H Sawalha¹, ¹Division of Rheumatology, University of Michigan, Ann Arbor, MI, ²Rheumatology, University of Michigan, Ann Arbor, MI

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster II

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** EZH2 is an epigenetic regulator that trimethylates lysine 27 of histone 3 (H3K27me3) and modulates DNA methylation patterns. We have previously suggested that EZH2 might be mediating a pro-inflammatory epigenetic reprograming in naïve CD4+ T cells as an early event in lupus flares. The aim of this study is to characterize the role of EZH2 in CD4+ T cells upon lupus pathogenesis.

**Methods:** Naïve CD4+ T cells were isolated from lupus patients and healthy controls. EZH2 expression levels were determined, and the epigenetic effects of EZH2 overexpression in CD4+ T cells was evaluated using a genome-wide DNA methylation approach. Gene expression and miRNAs were assessed by qPCR while protein expression was examined by Western blotting. A cell adhesion assay was used to assess adhesion of CD4+ T cells to human microvascular endothelial cells (HMVECs).

**Results:** EZH2 expression and H3K27me3 levels were increased in naïve CD4+ T cells in lupus compared to healthy controls. Both miR-26a and miR-101 downregulate EZH2, and were reduced in lupus CD4+ T cells. Overexpressing EZH2 in naïve CD4+ T cells followed by T cell stimulation *in vitro* resulted in significant DNA methylation changes. Genes involved in leukocyte adhesion and migration, such as *F11R* encoding JAM-A (junctonal adhesion molecule A), and *SELPLG* encoding PSGL-1 (P-selectin glycoprotein ligand 1), become hypomethylated in CD4+ T cells when EZH2 is overexpressed. Indeed, overexpression of EZH2 resulted in increased JAM-A expression and ~2 fold increased adhesion of CD4+ T cells to endothelial cells. Pre-incubation of EZH2-transfected CD4+ T cells with neutralizing antibodies against JAM-A significantly blunted cell adhesion. Similarly, CD4+ T cells from lupus patients overexpressed JAM-A and adhered significantly more to endothelial cells compared to T cells from healthy controls. Blocking JAM-A
via neutralizing antibodies or blocking EZH2 using an inhibitor significantly reduced endothelial cell adhesion of lupus CD4+ T cells.

**Conclusion:** We identified a novel role for EZH2 in T cell adhesion mediated by epigenetic remodeling and upregulation of JAM-A. EZH2 is overexpressed in lupus naïve CD4+ T cells and leads to increased T cell adhesion mediated by JAM-A. Blocking EZH2 or JAM-A might have a therapeutic potential in lupus by reducing T cell adhesion, migration, and extravasation.

**Disclosure:** P. S. Tsou, None; P. Coit, None; N. Kilian, None; A. H. Sawalha, None.


Abstract Number: 2637

**A Novel Regulatory Antigen Presenting B Cell and Memory Regulatory T Cell Subsets Are Enriched during the Quiescent Phase of Childhood Onset Systemic Lupus Erythematosus**

Joo Guan Yeo1,2, Thaschawee Arkachaisri1,3, Lena Das1, Justin Hung Tiong Tan1, Jing Yao Leong2, Yun June Angela Tan4, Liyun Lai5, Loshinidevi D/O Thana Bathi2, Phyllis Chen2, Seck Choon Elene Lee1, Yun Xin Book1 and Salvatore Albani5,6, 1Rheumatology and Immunology Service, KK Women's and Children's Hospital, Singapore, Singapore, 2Singhealth Translational Immunology and Inflammation Centre (STIIC), Duke-NUS Medical School, Singapore, Singapore, 3Duke-NUS Medical School, Singapore, Singapore, 4Department of Paediatric Anaesthesia, KK Women's and Children's Hospital, Singapore, Singapore, 5SingHealth Translational Immunology and Inflammation Centre (STIIC), Duke-NUS Medical School, Singapore, Singapore, 6KK Women's and Children's Hospital, Singapore, Singapore

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster II

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Systemic Lupus Erythematosus (SLE) is a multi-factorial disease and the conventional oligo-dimensional investigative approach involving one or a few cell subsets at a time is inadequate for its study. We hypothesize that multiple immunological abnormalities contribute to lupus pathogenesis and hence, a comprehensive holistic interrogative strategy is required. To address these issues, we employ a multi-dimensional, deep immunophenotyping approach using mass cytometry to unravel the pathogenic mechanism underpinning childhood onset SLE (cSLE).

**Methods:**

Peripheral blood mononuclear cells from 14 cSLE patients and 14 healthy paediatric controls, were stained with 37 immune phenotypic markers for mass cytometry. Subsequent analysis of the data was done with dimensional reductions followed by automated cell classification, clustering and visualization using an in-house customized machine learning software (MARVis: Multi-dimensional Automated Reduction and Visualization). Unique nodes representing immune subsets enriched in cSLE patients were statistically evaluated with reference to the healthy cohort and the association with lupus disease activity determined (Mann Whitney U Test, $p < 0.05$).
**Results:**

A statistically significant enrichment of a memory IL10 positive B cell subset (CD19^+CD27^+) with CD11c^+CD25^+HLA-DR^+CD40^hiCD86^hi was found in the SLE cohort. This cell population was significantly associated with an inactive lupus disease state, suggestive of an immunoregulatory function. In the healthy cohort, a reciprocal increase in the transitional/naive B cell population negative for CD11c, CD25, CD40 and CD86 was found.

Secondly, a significant enrichment of the memory regulatory T cell population (CD4^+CD45RO^+CD25^+Foxp3^+) was present in the diseased cohort, especially during disease inactivity, with some of these cells being positive for CXCR5, a homing chemokine receptor to the lymph node germinal centre. Expression of CXCR5 is mechanistically relevant and signifies a potential regulatory role of these cells as the lymph node is an important lupus related microenvironment.

**Conclusion:**

A holistic multi-dimensional approach was able to distill the immunoregulatory components of the cSLE immunome. The identification of a novel regulatory B cell subset, typified by the presence of IL10, with phenotypic markers for antigen presentation (HLA-DR, CD86) and T-B cell interaction (CD25, CD40) suggests its potential regulatory role during direct cell-to-cell interaction. In addition, the concomitant increase in the memory regulatory T cell subset suggests at least a dual regulatory mechanism responsible for quiescent disease. Further mechanistic study of these subsets is necessary and have the dual translational potential of being used as a predictor of clinical fate and identification of new therapeutic targets.

**Disclosure:** J. G. Yeo, None; T. Arkachaisri, None; L. Das, None; J. H. T. Tan, None; J. Y. Leong, None; Y. J. A. Tan, None; L. Lai, None; L. D. T. Bathi, None; P. Chen, None; S. C. E. Lee, None; Y. X. Book, None; S. Albani, None.

**Abstract Number:** 2638

**Inducible cAMP Early Repressor Promotes Glycolysis By Inhibiting the Pyruvate Dehydrogenase Phosphatase Catalytic Subunit 2 in Th17 Cells**

Michihito Kono, Nobuya Yoshida, Nicole E. Skinner and George C. Tsokos, Beth Israel Deaconess Medical Center, Boston, MA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster II

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Th17 cells are key players in SLE. Because Th17 cells use mainly glycolysis, blocking glycolysis can inhibit Th17 cell differentiation and treatment of lupus-prone mice with a combination of glycolysis and mitochondrial metabolism inhibitors reverses disease manifestations. In Th17 cells, pyruvate dehydrogenase (PDH), the enzyme which converts pyruvate to acetyl coenzyme A, is decreased. PDH kinase (PDHK) inactivates PDH whereas PDH phosphatase (PDP) activates PDH. Although previous reports showed PDHK was increased in Th17 and inhibition of PDHK suppressed Th17 differentiation, the underlying molecular mechanisms have not been elucidated yet. cAMP response element modulator (CREM) modulates the transcription of c-AMP responsible genes. We have shown that the
inducible cAMP early repressor (ICER) isoform of CREM promotes Th17 cell differentiation and ICER/CREM deficient mice have less autoimmune disease and CD4+ T cells from the patients with SLE have more ICER/CREM expression than those from health donors\(^1\). Because many genes associated with cell metabolism have cAMP response element (CRE) sites, to which ICER/CREM binds, we sought to identify metabolic enzymes controlled directly by ICER/CREM in Th17 cells.

**Methods:** Naïve CD4\(^+\) T cells from ICER/CREM sufficient or deficient mice were cultured under Th17 conditions. Glycolysis and glycolytic capacity were analyzed by extracellular flux analyzer. PDHK and PDP catalytic subunit 2 (PDP2) expression were measured by qPCR and Western blotting. These experiments were repeated after ICER\(\gamma\) overexpression. Then the effect of ICER to Pdp2 promoter was assessed by luciferase reporter and chromatin immunoprecipitation assays. We also analyzed the effect of PDP2 overexpression on glycolysis and Th17 cell differentiation \textit{in vitro}. Finally, CD4\(^+\)CD45RA\(^-\)CCR6\(^+\)CCR4\(^+\) cells (memory Th17 cells) were sorted from patients with SLE or healthy donors and Pdp2 gene expression was assessed by qPCR.

**Results:** ICER/CREM deficiency decreased glycolysis and glycolytic capacity in Th17 polarized cells and this was reversed by ICER\(\gamma\) overexpression. PDP2 expression increased in ICER/CREM-deficient Th17 polarized cells compared to that recorded in ICER/CREM-sufficient counterparts. ICER\(\gamma\) overexpression corrected the increased levels of PDP2 in ICER/CREM-deficient Th17 cells. On the other hand, decreased PDHK was observed in ICER/CREM-deficient Th17 cells, however, ICER\(\gamma\) overexpression did not restore its expression. Furthermore, Pdp2 promoter reporter assay revealed that Pdp2 activity was increased by site-directed mutation of putative ICER binding site. ICER accumulation at those CRE sites was confirmed by chromatin immunoprecipitation assays. PDP2 overexpression reduced glycolysis and Th17 differentiation. Pdp2 gene expression in memory Th17 cells tended to be decreased in lupus compared to healthy donors.

**Conclusion:** ICER increases glycolysis and promotes Th17 differentiation by inhibiting directly the expression of PDP2. Because PDP2 overexpression reduces Th17 cell differentiation, PDP2 might be a new therapeutic target.

**Reference**


**Disclosure:** M. Kono, None; N. Yoshida, None; N. E. Skinner, None; G. C. Tsokos, GSK, 5.

**Pathological Relevance of T Follicular Helper Cell and Plasmablast in Patients with Systemic Lupus Erythematosus**

**Shingo Nakayamada**\(^1\), Satoshi Kubo\(^2\), Maiko Yoshikawa\(^2\), Yusuke Miyazaki\(^2\), Shigeru Iwata\(^3\), Ippei Miyagawa\(^4\), Shunsuke Fukuyo\(^5\), Kazuhisa Nakano\(^1\) and Yoshiya Tanaka\(^6\), \(^1\)First Department of Internal Medicine, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, \(^2\)The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, \(^3\)First Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, \(^4\)University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, \(^5\)University of Occupational and Environmental Health, Japan, Fukuoka, Japan, \(^6\)The First Department of Internal Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017
Background/Purpose: Increasing evidence points to immunological heterogeneity in the pathogenesis of SLE. Indeed, targeted therapy for SLE showed considerable variability of efficacy. Thus, it seems to be important to explore the characteristic and interaction among the immune cell phenotypes in this disease. The aim of this study was to assess the comprehensive peripheral immunophenotyping in a correlation with clinical manifestations in patients with SLE.

Methods: Peripheral blood mononuclear cells were obtained from 143 SLE patients and 49 healthy controls (HC) and the phenotype of circulating B, T, NK and dendritic cells was defined based on flow cytometric analysis for human immune system termed "the Human Immunology Project". The correlation of immune cell phenotypes with clinical characteristics and responsiveness to immunosuppressive therapies, such as cyclophosphamide, mycophenolate mofetil, or calcineurin, in addition to high-dose glucocorticoids, were evaluated.

Results: The frequency of CD3+CD4+CXCR5+ICOS+CD69+ activated T follicular helper (Tfh) cell, but not CD3+CD4+CXCR3+CCR6-Th1 cell and CD3+CD4+CXCR3+CCR6+ Th17 cell, were higher in SLE than that in HC (mean 0.4 vs 0.2, p=0.03). The frequency of CD19+CD20+IgD-CD27+ class-switched memory B cell and CD19+CD20+IgD+CD27+ double negative B cell were higher in SLE than that in HC (mean 23.6 vs 13.2 and 10.7 vs 5.5, p=0.03 and p=0.04, respectively). The largest difference relative to the HC was observed in the proportion of CD19+CD20+CD27+CD38+ plasmablast, which was higher in SLE (mean 16.2 vs 3.3, p=0.01) and correlated with BILAG index (r=0.24, p<0.001). The proportion of activated Tfh cell significantly correlated with serum IgG level (r=0.20, p=0.02) and with serum anti-Sm antibody level (r=0.26, p=0.01). Among helper T cell subsets (Th1, Th17, Treg and Tfh), the proportion of Tfh cell or activated Tfh cell showed positive correlation with that of plasmablast (r=0.21, p=0.02). Treatment resulted in significant decreased proportions of plasmablast and Tfh cell (plasmablast; mean 17.6 to 10.1, p<0.01, Tfh; mean 1.1 to 0.7, p<0.01). The percentage of patients who showed treatment resistance was highest among patients with high percentage of Tfh cell (p=0.03).

Conclusion: Peripheral immunophenotyping indicated the pathological relevance of Tfh cell and plasmablast in patients with SLE, i.e. activation of Tfh cell correlated with autoantibody production while plasmablast did with disease activity of SLE. The peripheral immunophenotyping might be useful in evaluating the pathogenesis and in determining the therapeutic target of each patient.

Disclosure: S. Nakayamada, Bristol-Myers Squibb, 8; S. Kubo, Bristol-Myers Squibb, 8,Pfizer Inc, 8,Takeda Pharmaceutical Company Ltd, 8; M. Yoshikawa, None; Y. Miyazaki, None; S. Iwata, None; I. Miyagawa, None; S. Fukuyo, None; K. Nakano, None; Y. Tanaka, Mitsubishi-Tanabe, Takeda, Bristol-Myers, Chugai, Astellas, AbbVie, MSD, Daiichi-Sankyo, Pfizer, Kyowa Kirin, Eisai, Ono, 2,Daiichi-Sankyo, Astellas, Pfizer, Mitsubishi-Tanabe, Bristol-Myers, Chugai, YL Biologics, Eli Lilly and Company, Sanofi, Janssen, UCB, 8.


Abstract Number: 2640

Response Gene to Complement-32 Expression Is Upregulated in Lupus T Cells and Promotes IL-17A Expression

Vinh Nguyen1, Alexandru Tatomir2, Cornelia Cudrici3, Horea Rus2 and Violeta Rus1, 1Medicine, University of Maryland School of Medicine and Veteran Affairs Medical Center, Baltimore, MD, 2Neurology, University of Maryland School of Medicine and Veteran Affairs Medical Center, Baltimore, MD, 3NIAMS, NIAMS, NIH, Bethesda, MD

First publication: September 18, 2017
Background/Purpose: RGC (Response Gene to Complement)-32 is a cell cycle regulator widely expressed in normal tissues including brain, kidney, spleen, thymus, multiple tumors and in a variety of cell lines. RGC-32 is localized in the cytoplasm and translocates to the nucleus upon upregulation by complement activation, growth factors and cytokines. RGC-32 is induced by TGFβ in fibroblasts, astrocytes and human renal proximal tubular cells and mediates TGFβ dependent profibrotic pathways. Depending on the cell type, physiological or pathological conditions, RGC-32 can either stimulate or suppress cell growth. We have shown that RGC-32 is preferentially upregulated in murine Th17 cells and promotes their differentiation in vitro and in vivo. Patients with Systemic Lupus Erythematosus (SLE) display increased serum levels, expanded frequency of IL-17 producing cells in blood and organs such as the kidney. Whether RGC-32 is expressed in human CD4⁺ T cells and whether it plays a role in the Th17 pathway abnormalities in lupus patients has not yet been investigated.

Methods: RGC-32 mRNA expression was first assessed with the Autoimmune Disease Profiling cDNA Array (BD Bioscience) spotted with cDNA from CD3⁺, CD19⁺ and CD14⁺ cells from 10 lupus patients and 10 controls. PBMC were obtained from 20 patients with lupus and 18 controls. RGC-32 expression was determined by RT-PCR and flow cytometry in CD4⁺ T cells and CD19⁺ B cells. RGC-32 expression in naïve CD4⁺ T cells from normal controls stimulated under Th1, Th2, Th17 and Treg conditions was determined by RT-PCR. RGC-32 overexpression and silencing was performed by nucleofection and the effect on IL-17A mRNA levels in CD4⁺ T cells under Th17 conditions was determined by RT-PCR.

Results: RGC-32 mRNA expression was significantly increased in CD19⁺ B cells, CD14⁺ monocytes and CD3⁺ T from lupus patients compared to controls. By intracellular staining, CD4⁺ and CD19⁺ cells SLE lupus patients display higher intracellular RGC-32 expression ex vivo (1.5± 0.5 fold and 1.9 ± 0.7 fold, respectively) as compared to controls. By RT-PCR, RGC-32 mRNA expression was significantly higher in CD4⁺ T cells from patients vs. controls. In vitro, RGC-32 mRNA expression increased upon TCR stimulation and was further increased by TGFβ in CD4⁺ T cells from healthy controls. Other cytokines such as IFNα, IL-1β, TNFα did not upregulate RGC-32 mRNA either alone or in combination with TCR stimulation. RGC-32 mRNA upregulation was more robust under Th17 (3.2 ± fold) and Treg (2.6 ± 0.8 fold) as compared to Th1 (1.3 ± 0.4 fold) and Th2 (1.8 ± 0.1 fold) conditions. Overexpression of RGC-32 in CD4⁺ T cells upregulated IL-17A mRNA expression while RGC-32 silencing significantly downregulated IL-17A transcript levels under Th17 polarizing conditions.

Conclusion: These results suggest that T cells from patients with SLE exhibit increased expression of RGC-32 compared to normal controls. In vitro, RGC-32 promotes the differentiation of human Th17 cells. These data support the idea that RGC-32 signaling may enhance disease expression in SLE by promoting abnormalities in the Th17 pathway and provide a compelling rationale for further investigating the therapeutic potential of blocking RGC-32 in SLE.

Disclosure: V. Nguyen, None; A. Tatomir, None; C. Cudrici, None; H. Rus, None; V. Rus, None.
Hsin-Hsuan Juo1, Edward Chiou2, Keith B. Elkon3 and Christian Lood4, 1Rheumatology, University of Washington, Seattle, WA, 2University of Washington, Seattle, WA, 3Department of Medicine & Immunology, University of Washington, Seattle, WA, 4Department of Medicine, Division of Rheumatology, University of Washington, Seattle, WA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Neutrophil activation is linked to inflammation and autoimmune diseases, including systemic lupus erythematosus (SLE) where nucleic acid-containing immune complexes (ICs) drive inflammation through engagement of immune cells, including neutrophils. We recently demonstrated that neutrophils, upon internalization of ICs, undergo a programmed form of necrosis, NETosis, with extrusion of neutrophil extracellular traps (NETs) exposing key lupus autoantigens such as DNA, histones, and mitochondrial components, including oxidized inflammatory mitochondrial DNA. Further, activated neutrophils release proteases able to shed FcgRIIA restricting IC-mediated phagocytosis, while promoting NETosis. The aim of this study was to investigate the clinical utility of neutrophil-derived biomarkers in SLE patients.

Methods: Markers of neutrophil activation (S100A8/A9) and NETosis (8-OHdG DNA, MPO-DNA complexes, cell-free DNA, peroxidase activity) were analyzed by ELISA, fluorimetry and enzymatic assays in healthy controls (HC, n=20) and SLE patients (n=44). The SLE patients were female (91%), of non-Caucasian origin (66%), with an average SLEDAI score of 6 (range 0-22). FcgRIIA shedding was analyzed by flow cytometry. Mitochondria were isolated by density gradient and, upon incubation with macrophages, analyzed for inflammatory potential in presence of SLE autoantibodies.

Results: SLE patients had significantly increased levels of NET-related markers as compared to HCs (p<0.0001), with many of the markers, including 8-OHdG DNA and MPO-DNA complexes being increased in patients with active disease (p<0.05), and related to active kidney involvement and complement consumption (p<0.05). Considering the elevation of mitochondrial components (e.g. 8-OHdG DNA, p<0.01) in SLE, we next asked if SLE patients had antibodies to mitochondrial surface antigens (MSA). Using a novel in house developed flow cytometry technique we demonstrated the presence of anti-MSA antibodies in 35/44 of SLE patients, with the antibody level correlating with SLEDAI (r=0.55, p<0.0001). Further, in vitro, presence of anti-MSA antibodies promoted inflammatory clearance of mitochondria by macrophages with generation of IL-6 and IL-8 (p<0.05), suggesting a pathological role of those autoantibodies. As NETosis is mediated through IC uptake, we analyzed the capacity of lupus serum to induce FcgRIIA internalization and shedding in vitro by flow cytometry. FcgRIIA internalization was highly increased in lupus patients (p<0.0001) and related to disease activity (r=-0.35, p=0.02). Further, FcgRIIA internalization could distinguish SLE patients from HC and RA patients with good sensitivity and specificity (HC: 79.5%, 95%, p<0.0001; RA: 79.5%, 69%, p<0.0001). Finally, FcgRIIA shedding was a better predictor of disease activity as compared to anti-dsDNA antibodies (OR 5.5 p<0.0001 vs OR 2.0 p=0.19).

Conclusion: Our data demonstrate a clear contribution of IC-mediated neutrophil activation in the SLE pathogenesis and identifies several novel, and superior, biomarkers able to monitor disease activity and severity in lupus patients.

Disclosure: H. H. Juo, None; E. Chiou, None; K. B. Elkon, None; C. Lood, None.


Abstract Number: 2642
Lupus Serum Induces Glomerular Endothelial Cell Neutrophil Adhesion in Association with Soluble Mediators of Chemotaxis and Adhesion

Dayvia Russell1, Margaret Markiewicz2 and Jim C. Oates3,4, 1Research Service, Ralph H. Johnson VA Medical Center, Charleston, SC, 2Division of Rheumatology and Immunology, Department of Medicine, Medical University of South Carolina, Charleston, SC, 3Division of Rheumatology & Immunology, Department of Medicine, Medical University of South Carolina, Charleston, SC, 4Medical Service, Ralph H. Johnson VA Medical Center, Charleston, SC

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is associated with endothelial dysfunction, which can accelerate inflammation. Ingress of neutrophils into tissue requires chemotaxis and adhesion to endothelial cells. The goal of this project was to explore possible mechanisms leading to increased adhesion of neutrophils to glomerular endothelial cells induced by lupus serum.

Methods:
SLE patients in a longitudinal cohort that met four or more ACR criteria had serum collected and stored at -80°C during paired clinic visits with less activity (SLE Disease Activity Index (SLEDAI) score 0-6) and more activity (SLEDAI score 4-14 but always 4 points higher than inactive visit). Primary human renal glomerular endothelial cells (HRGECs) were cultured according to the manufacturer’s protocol and used at passages 3-4 and were seeded at 8 x 10^4 cells per fibronectin-coated well and grown to 90% confluence. HRGECs were cultured in SLE serum (2.5% in culture medium) for 3 hours in triplicate. Serum was removed and replaced with culture medium. Calcein AM-stained neutrophils isolated from healthy controls were cultured with HRGECs for 20 minutes. Neutrophil adherence to serum-treated HRGECs after five washes was measured as percent of cells (in fluorescence units) adhering relative to a TNFα positive control. Supernatant from “active disease” cultures was collected after neutrophil culture and analyzed for mediators of inflammatory cell vascular adhesion and transmigration (intracellular adhesion molecule-1 (ICAM), vascular CAM-1 (VCAM), neural CAM (NCAM), platelet-derived growth factor, myeloperoxidase, cathepsin D, plasminogen activator inhibitor-1, and interleukin 8 (IL8)) by commercial multiplex bead array. Associations between variables were determined using Spearman correlation and Mann-Whitney U test. Group values were reported as the median (interquartile range).

Results:
32 SLE patients (13 with lupus nephritis) were enrolled with paired active/inactive visits. Patients were 95% female and 73% African-American and had a median age of 40 (18). To explore factors that associated with increased adhesion, supernatant concentrations of mediators were correlated with relative neutrophil adherence and the fold change adherence from inactive to active disease visits. Cathepsin D (r=-0.46, p=0.05) and IL8 (r=0.77, p<0.001) correlated significantly with relative neutrophil adherence. NCAM (r=-0.54, p=0.002), cathepsin D (r=-0.63, p=0.005), and IL8 (r=0.50, p=0.03) correlated significantly with fold change in adherence with high versus low disease activity.

Conclusion: This study suggests that lupus serum induces expression of mediators that affect neutrophil adhesion. The association of neutrophil adhesion with IL8 is consistent with reports of elevation of IL8 in lupus nephritis and induction by anti-dsDNA antibodies. The negative association with soluble NCAM (not previously reported in HRGECs) may be the result of soluble NCAM competing with the membrane-bound form. Cathepsin D can both induce neutrophil apoptosis and increase the adhesiveness of fibronectin. Neither of these hypotheses was tested in this study.

Disclosure: D. Russell, None; M. Markiewicz, None; J. C. Oates, None.
HO-1 Expression in Monocytes Might Regulate Kidney Damage in Lupus Nephritis Patients

Loreto Cuitino1,2, Javiera Obreque1,2, Patricia Gajardo-Meneses1,2, Gonzalo P. Méndez2,3, Alexis M. Kalergis2,4 and Carolina Llanos1,2, 1Departamento de Inmunología Clínica y Reumatología, Santiago, Chile, 2Escuela de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile, 3Departamento de Anatomía Patológica, Santiago, Chile, 4Millennium Institute on Immunology and Immunotherapy and Departamento de Endocrinología, Santiago, Chile

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: It is well established that up to 70% of systemic lupus erythematosus (SLE) patients will develop Lupus Nephritis (LN). Recent studies have revealed that infiltrating monocytes and macrophages are associated with LN pathogenesis. Studies by our group and others have studied the potential role of HO-1, a haem-degrading enzyme with anti-inflammatory properties, in the modulation of immune cells and SLE development. Therefore, we decided to explore the contribution of HO-1 expression to LN pathogenesis.

Methods: All patients were recruited at Hospital Clínico of Pontificia Universidad Católica de Chile, fulfilled the ACR SLE classification criteria and had proliferative LN confirmed by renal biopsy (Class III, IV or V ISN/RPS). All individuals signed an informed consent form. Monocytes were purified using pan-monocytes MACS kit from peripheral blood mononuclear cells (PBMCs) of LN patients and healthy controls (HC). The CD16+ inflammatory monocytes were quantified. FACS was used to measure phagocytosis, HO-1 expression and ROS levels. The latter were determined using a CellRox Kit.

Results: We found that monocytes purified from LN patients show significant differences as compared to healthy controls (HC) in all parameters analyzed. LN patients have increased the CD16+ inflammatory monocytes (LN: 6.72±0.98%, HC: 4.07±0.48%; p<0.05). HO-1 protein expression is decreased in monocytes from LN patients compared with HC (LN: 1572±481, HC: 4789±911; p=0.005). ROS levels are elevated in LN monocytes showing similar values to monocytes from HC treated with a ROS inducer (HC: 3509±584, HC+TBHP: 8436±1909, LN: 8355±1714). Furthermore, the phagocytic activity is increased in LN monocytes (77.97±3.31%) compared to HC (39.63±2.75%). Moreover, our preliminary data indicate that HO-1 induction leads to down regulation of ROS production in LN (~60%) and HC (~40%) leaving both in similar ROS production. In addition, phagocytic activity is also decreased in LN and HC monocytes in the presence of HO-1 inducer (~30%). Furthermore, in renal biopsies of LN patients we observed that HO-1 expression is increased in renal tubular epithelial cells compared to HC.

Conclusion: Decreased HO-1 expression in circulating monocytes of LN patients leads to higher ROS production and higher phagocytic activity, which contributes to renal injury. We propose that increased HO-1 levels in epithelial renal cells might be an attempt of the kidney to protect itself from damage. Since ROS levels and phagocytosis are reduced when a HO-1 inducer is used, we also speculate that HO-1 induction in monocytes might exert a cytoprotective role in LN by regulating innate immunity. FONDECYT N°1150173.

Acknowledgements: We would like to extend our appreciation to all the volunteers that participated in this study.
Increased Toll-like Receptor 7 Expression Promotes B Cell Abnormalities and Skewing of Cytokine and Autoantibody Profiles in SLE Patients

Ting Wang¹², John Marken², Van Tran², Mengtao Li³, Karen Cerosaletti⁴, Keith B. Elkon², Xiaofeng Zeng⁵ and Natalia V. Giltiay², ¹Department of Rheumatology, Peking Union Medical College and Chinese Academy of Medical Sciences, Peking Union Medical College Hospital, Beijing, WA, China, ²Division of Rheumatology, Department of Medicine, University of Washington, Seattle, WA, ³Peking Union Medical College and Chinese Academy of Medical Sciences, Peking Union Medical College Hospital, Beijing, China, ⁴Translational Research Program Benaroya Research Institute at Virginia Mason, Seattle, WA, USA, Seattle, WA, ⁵Rheumatology, Peking Union Medical College and Chinese Academy of Medical Sciences, Peking Union Medical College Hospital, Beijing, China

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Toll-like receptor 7 (TLR7) is implicated in the production of type I IFNs and the activation of B cells in systemic lupus erythematosus (SLE). Genetic studies support a link between TLR7 rs3853839 C/G polymorphism, associated with an increase in TLR7 expression and SLE susceptibility. While much has been reported on TLR7 in murine lupus, very little is known about how increased TLR7 signaling may contribute to human B cell function and to SLE pathology. This study was undertaken to determine how variations in TLR7 expression affects peripheral B cell populations, auto-Ab production and cytokine expression levels in SLE patients.

Methods:
Human peripheral blood mononuclear cells (PBMCs) were collected from SLE patients and healthy controls (HC) and analyzed for the expression of TLR7 and IFN-stimulated genes (ISGs) by real-time PCR. SLEDAI scores were obtained from clinical records. Frequencies of peripheral B cell population were analyzed by multicolor flow cytometry. Autoreactive cells were identified by fluorescently-labeled SmRNP. Autoantibody profiles were quantified by protein microarray and analyzed by Significance Analysis of Microarrays (SAM). Cytokines in the serum were measured by bead-based ELISA.

Results:
High TLR7 expression in SLE patients was associated with a more pronounced IFN signature. 75.0% of TLR7⁺ SLE patients were TLR7 rs3853839 G (risk) allele-carriers, compared to 47.06% in TLR7norm/lo SLE and 33.33% in HC. High TLR7 expression correlated with an increase in IFNα and IFNγ levels in the serum but did not correlate with serum BAFF levels. Analysis of peripheral B cell subsets in TLR7⁺ SLE patients showed an increase of CD19⁺ B cells, expansion of transitional B cells and pre-plasma cells as compared to TLR7norm/lo and HCs. TLR7⁺ B-cells showed an
increase in IL-6 and a decrease in IL-10 gene expression. TLR7\textsuperscript{hi} SLE patients displayed increased frequencies of Sm/RNP-specific B cells, which were found mostly within the CD27\textsuperscript{-}IgD\textsuperscript{+} naïve B cell pool. IgG microarray revealed an increase in auto-Ab titers, enrichment for more autoantibody specificities, and skewing towards Sm/RNP specificities in the TLR7\textsuperscript{hi} SLE group. Importantly, TLR7\textsuperscript{hi} SLE patients had a higher disease activity (mean ± SD SLEDAI 6.56 ± 0.95 versus 3.07 ± 0.6 in TLR7\textsuperscript{norm/lo}, p=0.007) and were more likely to develop lupus nephritis, supporting the clinical significance of our findings.

Conclusion:

Our studies provide new insights into the role of TLR7 signaling in human SLE. Variation in TLR7 expression dictated by genetic variation affecting TLR7 RNA turnover appears to “shape” B cell maturation and the auto-Ab repertoire. In addition, high TLR7 is associated with IFN production, possibly linked to immune complex production. TLR7 expression may, therefore, serve as a useful biomarker in SLE. TLR7\textsuperscript{hi} SLE patients, particularly the TLR7 rs3853839 G (risk) allele-carriers, represent a distinct population who could respond well to anti-TLR7 and/or type I and type II IFN – targeted therapies.

Disclosure: T. Wang, None; J. Marken, None; V. Tran, None; M. Li, None; K. Ceroaletti, None; K. B. Elkon, Celgene, 5,AstraZeneca, 5,Merck Human Health, 5,Resolve Therapeutic, 4,Amdax Therapeutics, 4; X. Zeng, None; N. V. Giltiay, None.


Abstract Number: 2645

The Internalization of DNA-Antibodies By Podocytes during Lupus Nephritis

Anja Römer-Hillmann\textsuperscript{1}, Elisabeth Jung\textsuperscript{2}, Annika Engbers\textsuperscript{1}, Marcel Reinhardt\textsuperscript{1}, Hedda Wardemann\textsuperscript{3}, Thomas Pap\textsuperscript{4} and Annett Jacobi\textsuperscript{5}, \textsuperscript{1}Institute of Musculoskeletal Medicine, University Hospital Muenster, Muenster, Germany, \textsuperscript{2}Department of Internal Medicine D, Rheumatology, University Hospital Muenster, Muenster, Germany, \textsuperscript{3}Deutsches Krebsforschungszentrum, Heidelberg, Germany, \textsuperscript{4}Institute for Musculoskeletal Medicine, University Hospital Muenster, Muenster, Germany, \textsuperscript{5}Internal Medicine, Ruppiner Kliniken GmbH, Neuruppin, Germany

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Podocytes are postmitotic visceral epithelial cells, located at the Bowmans capsule of the kidney building up the slit diaphragm with their foot processes to filtrate the blood and keep valuable large proteins in the vessels. Loss of these cells leads to proteinuria.

In Systemic Lupus Erythematosus (SLE) different organs are affected by autoantibodies which results in chronic inflammation and a high percentage of patients develop Lupus nephritis (LN) resulting in podocyte damage and disruption of the slit diaphragm. The risk for LN correlates directly with the level of anti-double stranded DNA antibodies (adsDNAabs).
Methods:

In this study, we wanted to identify the direct effect of adsDNAabs on podocytes.

We established an in vitro system to investigate the specific impact of monoclonal antibodies and their immune complexes directly on podocytes (AB8 cell line). Monoclonal antibodies were generated by transfecting HEK293T cell line with Ig heavy and corresponding light chain encoding plasmid DNA obtained from single B cells of patients with SLE and LN. Podocytes were incubated with the produced monoclonal antibodies and the internalization process and functional consequences were analyzed by immunofluorescence, Western Blot, FACS and electron microscopy. For comparison, primary podocytes were isolated from LN patient urine and analyzed by immunofluorescence. To clarify the endocytotic pathway of antibody internalization, cells were treated either with chlorpromazine, MDC or nystatin.

Results:

The recombinantly produced adsDNAabs from LN patients were specific against nuclear structures and build complexes with double stranded DNA, essential for the internalization by cultivated podocytes. Interestingly, viability and migratory capacity were not influenced by the exposure to adsDNAabs for 48h. The internalized antibodies were enclosed by membranous structures and reach the cytosol via clathrin dependent endocytosis. The process of internalization was time and dose dependent and reversible. Furthermore, internalized antibody complexes could also be detected in primary human LN podocytes.

Conclusion:

In our in vitro model the specific uptake of adsDNAabs was observed, in line with human LN data. Podocytes from patients with LN show IgG positive aggregates in the cytosol. The internalization depends on the complex formation of the antibodies with dsDNA and could be important part of the LN pathogenesis.

Disclosure: A. Römer-Hillmann, None; E. Jung, None; A. Engbers, None; M. Reinhardt, None; H. Wardemann, None; T. Pap, Orthogen, 5; A. Jacobi, None.

Abstract Number: 2646

Premature Senescence of Naive CD4+ T-Cells in Systemic Lupus Erythematosus

Patrizia Fasching1, Johannes Fessler2, Andrea Raicht3, Angelika Lackner2, Rusmir Husic1, Winfried Graninger2, Wolfgang Schwinger3, Martin Stradner1 and Christian Dejaco1, 1Department of Rheumatology and Immunology, Medical University of Graz, Graz, Austria, 2Rheumatology and Immunology, Medical University of Graz, Graz, Austria, 3Division of Pediatric Hemato-Oncology, Medical University of Graz, Graz, Austria

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
The pool of naïve CD4+ T-cells is reduced in patients suffering from systemic lupus erythematosus (SLE). We aimed to study if the occurrence of early thymic involution and premature senescence potentially contributes to reduced naïve CD4+ T-cell numbers.

Methods:

 Peripheral blood mononuclear cells were obtained from 50 SLE patients and 50 healthy controls (HC) in a prospective, cross-sectional study. Prevalence of memory and naïve CD4+ T-cells was assessed by flow cytometry. Naïve CD4+ T-cells were isolated by MACS technology for telomere length and T-cell receptor excision circle (TREC) assessment by real-time PCR. Telomere length was chosen as parameter for cellular senescence and TREC for the evaluation of thymic function and replicative history. Moreover, telomerase activity was analyzed according to the Telomeric Repeat Amplification Protocols (TRAP). Patients and HC were separated into two distinct age-groups for analysis of age-dependent differences (≤48 years [SLE n=34, HC n=26]; >48 years [SLE n=16, HC n=24]).

Results:

Naïve CD4+ T-cells were significantly reduced in older SLE patients as compared to HCs (SLE 2.06% [0.99-4.47] vs. HC 4.89 [0.55-21.90], p=0.003); no difference was observed between young patients and respective controls. We observed a drastic decline in the number of TRECs in naïve CD4+ T-cells of SLE patients compared to age-matched HC. TREC numbers were already reduced in younger SLE patients (SLE 168 copies/ng DNA [16-893] vs. HC 2058 [5-64444], p=0.000) and similar results were obtained for older patients (SLE 33 [6-1477] vs. HC 117 [0-2347], p=0.006). Telomeres were shorter in young SLE patients compared to age-matched controls (SLE mean 6.5kbp [±0.5], vs. HC 7.0 [±0.9], p=0.011). In healthy individuals shortening of telomeres induces an increase in telomerase activity resulting in an inverse correlation of telomere length and telomerase activity. We found such a correlation in naïve CD4+ T-cells of HCs (corr coeff=-0.532, p=0.000) but not in naïve CD4+ T-cells of SLE patients.

Conclusion:

Our data indicate extensive replicative history of naïve CD4+ T cells of SLE patients leading to a premature decline in telomere length. Unlike in HC naïve CD4+ T cells of SLE patients are unable to respond with increased enzymatic function of telomerase. These findings may partially explain the abnormally low number of naïve CD4+ T cells found in older SLE patients.

Disclosure: P. Fasching, None; J. Fessler, None; A. Raicht, None; A. Lackner, None; R. Husic, None; W. Graninger, None; W. Schwinger, None; M. Stradner, None; C. Dejaco, None.

Abstract Number: 2647

Epstein Barr Virus Interleukin-10 (vIL10) in Systemic Lupus Erythematosus

Neelakshi R. Jog1, Eliza Chakravarty1, Joel M. Guthridge2 and Judith A. James3,4, 1Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 2Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 3Arthritis & Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 4Department of Pathology, University of Oklahoma Health Sciences Center, Oklahoma City, OK

First publication: September 18, 2017

SESSION INFORMATION
Background/Purpose: Systemic Lupus Erythematosus (SLE) is a systemic autoimmune disease characterized by autoantibody production and periods of elevated and suppressed disease activity. Various genetic and environmental factors likely contribute to disease pathogenesis. Epstein Barr Virus (EBV) is one such environmental factor that has been consistently associated with SLE. EBV maintains latency in infected B cells and shows frequent reactivation, which can be measured indirectly in terms of antibodies to EBV Early Antigen (EA). Our data show that elevated concentrations of EA IgG increase the probability of transitioning to SLE in unaffected SLE family members, suggesting that viral reactivation may contribute to development or worsening of SLE autoimmune responses. EBV encodes homologs of cellular cytokines to escape host anti-viral response and establish latency. One such protein is a late lytic phase protein encoded by BCRF-1 gene and is an IL10 homolog. Monocytes are one of the first cells to respond following infection and dysregulation of monocytes plays a dynamic role in the initiation and continuation of the systemic autoimmune response in SLE. However, the effects of vIL-10 on monocyte function have not been studied. In this study we examine whether vIL10 has similar inhibitory effects on monocytes as hIL10.

Methods: Plasma from 8 SLE patients with varying disease activity and 6 healthy unrelated controls were concentrated and vIL10 was detected by western blotting. The band intensities were normalized to known concentration of recombinant vIL10. Monocytes were enriched from peripheral blood mononuclear cells from healthy donors and stimulated with human or viral IL10. STAT phosphorylation, expression of cell surface markers, and uptake of apoptotic Jurkat cells were determined by flow cytometry. Gene expression was performed using microfluidics quantitative PCRs (Fluidigm).

Results: SLE patients showed significantly higher levels of plasma vIL10 (25423±5968 vs 12968±8432, p<0.05). No correlation was observed between vIL10 and hIL10. To determine whether this increased vIL10 has functional consequences, we performed in vitro stimulation of healthy monocytes with human or viral IL10. vIL-10 induced significantly lower STAT-3 phosphorylation compared to hIL-10, and failed to downregulate IL10R1 gene expression, suggesting differences in signaling cascades activated by vIL10. Although less efficient in downregulating pro-inflammatory gene expression, vIL-10 significantly reduced the expression of scavenger receptor CD163 compared to hIL-10, suggesting inhibition of M2 polarization. In line with inhibition of M2 polarization, vIL10 stimulated monocytes were less efficient in clearance of apoptotic cells.

Conclusion: Our data show that lupus patients have increased levels of vIL-10 which may be a result of increased EBV reactivation. We show that vIL-10 increases pro-inflammatory cytokine secretion by monocytes while reducing the phagocytic capability. The reduced clearance may lead to accumulation of cell debris and fuel the autoimmune response through death associated molecular patterns prior to initial disease flare.

Disclosure: N. R. Jog, None; E. Chakravarty, None; J. M. Guthridge, None; J. A. James, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/epstein-barr-virus-interluekin-10-vil10-in-systemic-lupus-erythematosus

Abstract Number: 2648

The SLE Risk Variant, Reference Single Nucleotide Polymorphism (rs)10499197, Upstream of Tumor Necrosis Factor Alpha-Induced Protein 3 (TNFAIP3) Modulates Enhancer Function and TNFAIP3 Gene Expression
Genome Wide Association studies (GWAS) have identified several variants in the tumor necrosis factor alpha-induced protein 3 (TNFAIP3) gene associated with autoimmune disease. TNFAIP3 encodes A20, an ubiquitin-editing enzyme that inhibits Nuclear Factor-kappa B (NF-κB) signaling to modulate innate and adaptive immune responses. Loss of TNFAIP3 expression is implicated in the pathogenesis of autoimmune disease; however, mechanisms responsible for impaired expression remain unclear. Encyclopedia of DNA Elements (ENCODE) and Chromatin Interaction analysis by paired-end Tag Sequencing (ChIA-PET) suggests TNFAIP3 expression is regulated through a long-range interaction with a putative upstream enhancer. In this study, we investigated the functional importance of a predicted SLE risk variant reference single nucleotide polymorphism (rs)10499197 situated near this enhancer.

Methods:

Electrophoretic Mobility Shift Assays (EMSA) and affinity purification of nuclear factors were performed to screen for specific proteins with altered affinity for the rs10499197 risk allele. Results were validated using Epstein-Barr Virus (EBV) transformed B cell lines carrying non-risk or risk genotypes by Chromatin Immuno-Precipitation (ChIP) followed by quantitative PCR. To investigate the regulatory function of the putative enhancer, we cloned the non-risk and risk alleles into a minimal promoter vector containing the luciferase gene, and performed luciferase assays on immune cells (Jurkat and Tamm-Horsfall Protein 1(THP-1)).

Results:

The rs10499197 risk allele bound the nuclear-protein complex with reduced affinity in EBV-B cells and Jurkat T cells, and increased affinity in THP-1 monocytes, suggesting a cell-specific affect. Affinity purification and ChIP studies revealed reduced binding of the risk allele to NF-κB subunits, NF-kB p50 Subunit (p50) and NF-kB p65 Subunit (p65), and enhanced binding for the risk allele to transcription factors, E2 Transcription Factor1 (E2F1) and Cyclic adenosine monophosphate Responsive Element Binding protein1 (CREB1). E2F1 and CREB1 negatively regulate NF-κB signaling by disrupting NF-kB p50-p65 heterodimer formation, thereby affecting NF-κB-mediated transcription of TNFAIP3. Consistently, luciferase assays demonstrated that the regulatory element functions as an enhancer of TNFAIP3 expression and that the risk allele impaired enhancer activity.

Conclusion:

Results suggest that the SLE risk variant rs10499197 is likely a causal variant that disrupts the function of a putative enhancer upstream of TNFAIP3. Disrupting the enhancer may impair TNFAIP3 expression, enhance NF-κB signaling, and heighten immune responses in a cell type specific manner. Following our work on the TT>A enhancer, this is the second likely causal variant to impact TNFAIP3 expression. Future Chromatin Conformation Capture assay (3C) will determine how the upstream DNA element physically interacts with the TNFAIP3 promoter, and help establish a comprehensive mechanistic understanding for how TNFAIP3 transcriptional regulation is modulated by SLE risk alleles.
Anti-Suprabasin Antibody; A Novel Autoantibody May Contribute to the Pathogenesis of Neuropsychiatric Systemic Lupus Erythematosus

Kunihiro Ichinose¹, Kaname Ohyama², Kaori Furukawa¹, Osamu Higuchi³, Shunya Nakane⁴, Masataka Umeda¹, Tomohiro Koga¹, Takashi Igarashi¹ and Atsushi Kawakami¹,

¹Department of Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, ²Department of Pharmaceutical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, ³Department of Clinical Research, Nagasaki Kawatana Medical Center, Nagasaki, Japan, ⁴Department of Neurology, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Systemic lupus erythematosus (SLE), an autoimmune disorder characterized by the production of pathogenic autoantibodies and inflammatory mediators, involves multiple organ systems. Neuropsychiatric systemic lupus erythematosus (NPSLE) is often difficult to diagnose and distinguish from other diseases, partly because no NPSLE-specific antibodies have been identified. Suprabasin (SBSN) gene was originally identified in mouse and human differentiating keratinocytes as an epidermal differentiation marker. SBSN also plays a role in the growth and invasiveness of tumors. It was demonstrated that the knockdown of SBSN inhibited cell migration and tube formation in tumor endothelial cells, but the pathological role of SBSN in autoimmune disease is not well understood.

Methods:

We developed a novel proteomic strategy for identifying and profiling antigens in immune complexes (ICs) in the cerebrospinal fluid (CSF), and we used this strategy for 26 NPSLE patients. As controls, 25 SLE patients without neuropsychiatric manifestations (SLE), 15 with relapsing remitting multiple sclerosis (RRMS) and 10 normal pressure hydrocephalus (NPH) patients were included. We analyzed the titer of anti-SBSN antibodies in CSF, using a luciferase immunoprecipitation system (LIPS) assay. Real-time quantitative polymerase chain reaction (qPCR) and microarray analysis following exposure of astrocytes to anti-SBSN antibodies were performed. We also performed a multiplex cytokine bead assay using undiluted CSF supernatants and the Bio-Plex Pro Human Cytokine Group I 27-Plex Panel analyzed with a Bio-Plex® MAGPIX™ Multiplex Reader.

Results:

We identified ICs of SBSN in the CSF of the NPSLE group. We also analyzed the CSF of a total of 103 patients (NPSLE=31, SLE=22, MS=30 and NPH=20) from another cohort for anti-SBSN antibodies, using a luciferase immunoprecipitation system (LIPS) assay. The LIPS assay showed that the CSF an antibody index (A.I.) of anti-SBSN antibodies was significantly higher in the NPSLE group compared to the A.I. values of the SLE, MS and NPH groups. Among them, the CSF of 41.9% (13 of 31) NPSLE patients was positive for anti-SBSN antibodies. Of note, the CSF concentrations of IL-10, IL-13, GM-CSF, IP-10 and MCP-1 were significantly higher in the CSF anti-SBSN antibodies-
positive group of NPSLE patients compared to those of the negative group. The expression of SERPINE1 mRNA was significantly upregulated as measured by a qPCR, and microarray data showed that the senescence and autophagy pathways were significantly changed in astrocytes exposed to anti-SBSN antibody compared to normal immunoglobulin G exposure.

**Conclusion:** Our findings indicate that SBSN could be a novel autoantibody for the evaluation of suspected NPSLE, and its use may help elucidate the pathogenesis underlying this disease.

**Disclosure:** K. Ichinose, None; K. Ohyama, None; K. Furukawa, None; O. Higuchi, None; S. Nakane, None; M. Umeda, None; T. Koga, None; T. Igawa, None; A. Kawakami, None.


**Abstract Number:** 2650

**Analysis of C9Orf72 Expansions in Patients with Systemic Lupus Erythematosus and Rheumatoid Arthritis: Preliminary Data**

Micaela Fredi¹, Giorgio Biasiotto², Franco Franceschini³, Massimiliano Filosto⁴, Alessandro Padovani⁴, Angela Tincani⁵, Isabella Zanella² and Ilaria Cavazzana³, ¹Department of Rheumatology and Clinical Immunology, Rheumatology and Clinical Immunology, Rheumatology and Clinical Immunology, Spedali Civili of Brescia, Brescia, Italy, ²Department of Molecular and Translational Medicine and Biotechnology Laboratory, Department of Diagnostics, University of Brescia and Spedali Civili, Brescia, Italy, ³Rheumatology and Clinical Immunology, Spedali Civili of Brescia, Brescia, Italy, ⁴Clinical Neurology, Section for Neuromuscular Diseases and Neuropathies, Spedali Civili and University of Brescia, Brescia, Italy, ⁵Rheumatology and Clinical Immunology, Spedali Civili and University of Brescia, Brescia, Italy

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster II

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

The most frequent genetic cause of Amyotrophic Lateral Sclerosis (ALS) and Frontotemporal Lobar Dementia (FTLD) is a large hexanucleotide expansion (>30, mostly hundred/thousand repeats) within a non-coding region of the C9orf72 gene (1). The cut-off to distinguish normal and pathogenic expansions has not yet been defined, but most healthy individuals have 2-20 repeats on both alleles (usually 2, 5, 8). The pathogenic mechanism of the dominant mutation is most probably toxic gain of functions, through the production of repetitive transcripts and proteins. Nonetheless, C9orf72 reduced expression has been observed in post-mortem brains of mutated ALS/FTLD patients (2). Interestingly, while C9orf72 haploinsufficiency alone seems insufficient to cause neurodegeneration, decreased transcriptional activity with increasing numbers (7-24) of repeats has been demonstrated in vitro (3) and knockout mice exhibit immune dysregulations, developing features of autoimmunity, reminiscent of systemic lupus erythematosus (SLE), suggesting a protective role for the C9orf72 protein against autoimmune diseases (4). Recently, increased prevalence of autoimmune diseases has been observed in C9orf72 expansion-positive FTLD patients (5). We hypothesized that normal but in the upper range C9orf72 expansions could influence the immune system and investigated their size in a cohort of patients with rheumatoid arthritis (RA) and SLE. As a control group we studied a cohort of 49 ALS patients without pathogenic expansion.
Methods:

29 SLE and 6 RA pts were screened for C9orf72 expansion, by the use of a PCR-based protocol, validated in our laboratory (6). Clinical and serological data were collected from clinical charts. A cut-off of ≥9 repeat units was considered in our analysis.

Results:

As expected, no patients with large expansions were found. The average and median values of repeat units were 5.29 (SD 2.87) and 5.08 (SD 4.14) and 3.5 (range 2-15) in RA and 4.8 (SD 3.05) and 5 (range 2-19) in the control population. We individuated ≥9 repeat units in 5/30 (16.7%) SLE patients and 2/6 (33.3%) RA patients; a prevalence higher than what found in ALS group (8.16%). We searched for clinical or serological differences among SLE pts with the normal and ≥9 repeat size expansion. Although those differences were not statistically significant, we reported a higher prevalence of kidney involvement in patients with a number of repeats ≥9 (5/6; 83.3% versus 7/23; 30.4%), p=0.056.

Conclusion:

Conclusion: our preliminary results indicate that ≥9 repeats within the C9orf72 gene are detectable in a non negligible number of patients with systemic autoimmune disease, confirming the possible role of C9orf72 in autoimmune system. The possible association with specific subset of disease must be confirmed in a larger cohort of patients.

References

2-Rohrer JD et al. Lancet Neurol 2015,14:291-301
3-Gijselinck I et al. Mol Psychiatry 2016,21:1112-24
4-Atanasio A et al. Sci Rep 2016,6:23204
5-Miller ZA et al. Neurol Neuroimmunol Neuroinflamm 2016,3(6):e301

Disclosure: M. Fredi, None; G. Biasiotto, None; F. Franceschini, None; M. Filosto, None; A. Padovani, None; A. Tincani, None; I. Zanella, None; I. Cavazzana, None.


Abstract Number: 2651

Association of ITGAM Polymorphism rs1143679 with Susceptibility to Systemic Lupus Erythematosus in North Indian Population

Sandeep Kumar1, Vikas Gupta1, Avadhesh Pratap2, Rajeev Singh3, Reena Kumari3, Amita Aggarwal1 and Ramnath Misra1, 1Clinical Immunology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, 2Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, 3Biochemistry, King George Medical University, Lucknow, India

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
ITGAM (Integrin-α-M, also known as CD11b) gene located at chromosome 16p11.2, encodes for the α-chain of Integrin-αMβ2, a leucocyte specific integrin receptor, also known as complement receptor 3 (CR3). It is important in the adherence of leucocytes to stimulate endothelium and in the phagocytosis of complement coated particles such as apoptotic cells. Single nucleotide polymorphism (SNP) rs1143679 G/A in ITGAM gene encodes an amino-acid change from arginine to histidine at position 77 (R77H) which impairs the integrin-mediated cell adhesion of ligands and reduces phagocytosis of complement-coated particles, hence, predisposing to SLE. SNP rs1143679 has been shown to be associated with SLE in European, African, Hispanic or native American populations. We aimed to verify this association in North Indian population and to study the genetic relations between this SNP and sub-phenotypes of SLE.

Methods:

395 SLE patients (classified according to the 1997 ACR classification criteria for SLE) and 593 controls were enrolled. All samples were genotyped for SNP rs1143679 using TaqMan genotyping assay in Roche LC480 real-time polymerase chain reaction (PCR) system. A case-control association study and a genotype phenotype correlation were performed.

Results:

The mean age of the SLE patients was 30.7 years, and 94.3% were females. Allelic and genotypic frequencies did not deviate from Hardy-Weinberg equilibrium in the controls (p > 0.05). Allele contrast showed that the variant allele A was associated with increased risk for SLE when compared with the G allele (OR = 1.63, 95% CI = 1.23 - 2.17, p < 0.001). A significant difference was detected both under recessive model [AA vs (GA + GG): OR = 4.31, 95% CI = 1.90 - 9.79, p < 0.01] and dominant model [(AA + GA) vs GG: OR = 1.18, 95% CI = 0.85 - 1.64] with regard to the distribution of genotype frequencies between SLE patients and healthy controls. On sub-phenotype analysis, an association was observed between SNP rs1143679 and oral ulcers, under the dominant model (OR = 1.65, 95% CI = 1.01 - 2.70, p < 0.05). None of the other clinical manifestations showed association with SNP rs1143679.

Conclusion:

SNP rs1143679 in ITGAM gene predisposes to SLE in North Indian population. In accordance with the results of the previous studies conducted in European, African, and Hispanic populations, ITGAM rs1143679 polymorphism is associated with SLE susceptibility in different ethnic groups.

Disclosure: S. Kumar, None; V. Gupta, None; A. Pratap, None; R. Singh, None; R. Kumari, None; A. Aggarwal, None; R. Misra, None.


Abstract Number: 2652

Abnormal Expression of Long Noncoding RNA Lncrna-CMPK2 Facilitates Neutrophils Interferon Production By TLR7/8 Agonist Stimulation in SLE

Zhixin Xue, Yuanjia Tang and Nan Shen, Shanghai Institute of Rheumatology, Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

First publication: September 18, 2017
**Background/Purpose:** Interferon plays prominent role in systemic lupus erythematosus (SLE) pathogenesis while the source of high interferon in SLE is still confused, several cell types can produce interferon, neutrophils as one of important interferon source cells have been arousing growing attention, however the interferon production capacity of neutrophils in SLE and the regulation of neutrophils interferon production still remain unclear. Many long noncoding RNAs (lncRNAs) have been identified abnormally expressed in SLE that act on multiple signal pathways, we presume that there could be a role of lncRNAs in neutrophils interferon production regulation.

**Methods:** Interferon production was measured by qPCR and ISRE reporter gene assay, neutrophils interferon production capacity enhanced after interferon prime. We aimed to find out LncRNA that work in it. RNA-seq was performed in two sets of samples, interferon stimulated neutrophils samples and SLE versus healthy controls neutrophils samples. LncRNA-CMPK2 was screened out by cross-reference the two RNA-seq results. Expression of lncRNA-CMPK2 was knocked down in primary neutrophils using antisense oligos (ASO) by electroporation. To dissect the mechanism that lncRNA-CMPK2 act on TLR7/8 pathway interferon production, western blot was conducted to measure expression of key molecules in this pathway.

**Results:** 1. Neutrophils from SLE patients produced two fold more interferon than that from healthy controls by TLR7/8 agonist R848 stimulation. 2. Neutrophils interferon production capacity enhanced after interferon prime. 3. LncRNA-CMPK2 highly expressed in SLE neutrophils, it was the top 2 differently expressed lncRNA in lupus versus healthy controls and was also among the top significantly interferon stimulated lncRNAs according to the two sets of RNA-seq profiling. 4. LncRNA-CMPK2 expression level correlated with lupus interferon score and disease activity. 5. Knockdown of LncRNA-CMPK2 in neutrophils can attenuate interferon production. The mechanism may rely on reducing expression of IRAK4 and IRF7.

**Conclusion:** LncRNA-CMPK2 facilitates neutrophils interferon production in lupus. Over expression status of lncRNA-CMPK2 may provide new understanding of high interferon in the disease, targeting lncRNA-CMPK2 could probably help to control high interferon level in lupus.

**Disclosure:** Z. Xue, None; Y. Tang, None; N. Shen, None.


**Abstract Number:** 2653

**Exposure to a Periodontal Pathogen Aggregatibacter Actinomycetemcomitans Is Associated with Increased SLE Severity**

**Harini Bagavant**¹, Nina Wolska¹, Paulina Rybakowska¹, Magdalena Sroka¹, Astrid Rasmussen¹, Indra Adrianto¹, Felicia Qi², Courtney Montgomery¹, Kathy L. Sivils¹, Joel M. Guthridge³, Judith A. James¹, Joan T. Merrill¹ and Umesh Deshmukh¹, ¹Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, ²University of Oklahoma Health Sciences Center, Oklahoma City, OK, ³Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, OKC, OK

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017
Background/Purpose: Infections are linked to morbidity in systemic lupus erythematosus (SLE). This study was undertaken to evaluate oral infections by dental plaque bacteria in SLE patients and the influence of this bacterial exposure on disease in patients and in lupus mice.

Methods: Circulating IgG antibodies against dental plaque bacteria identify exposure to the organism. In a pilot study, sera from 72 SLE patients in the Lupus Family Registry and Repository (LFRR) were tested for antibodies to 7 dental plaque bacteria by ELISA. Antibodies to Aggregatibacter actinomycetemcomitans (Aa) were measured in a confirmatory study of 587 patients from the Oklahoma Lupus Cohort and 75 healthy volunteers. Correlations between anti-Aa antibody titers and autoantibodies, complement levels, and clinical features of lupus were studied. NZM2328 lupus mice were infected orally with Aa and the effects on disease severity was evaluated.

Results: SLE patients show varying levels of serum antibodies to plaque bacteria. Of the antibodies tested, only anti-Aa antibody levels were significantly associated with anti-dsDNA titers, a hallmark of SLE. This association was confirmed in patients from the Oklahoma Lupus Cohort. Absorption of anti-Aa with Aa did not affect anti-dsDNA reactivity, indicating that this association was not solely due to cross-reactivity. An exploratory analysis of clinical variables showed that higher anti-Aa titers in SLE patients were associated with low C4 complement levels and increased disease activity as measured by SLEDAI and BILAG scores. In lupus mice, Aa activated histone reactive T cells and accelerated onset lupus nephritis.

Conclusion: Exposure to the periodontal pathogen, Aa, is associated with higher autoantibodies and increased disease activity in SLE patients. Evidence from mouse studies suggests that this worsening of disease may be driven by exacerbated auto-reactivity.

Disclosure: H. Bagavant, None; N. Wolska, None; P. Rybakowska, None; M. Sroka, None; A. Rasmussen, None; I. Adrianto, None; F. Qi, None; C. Montgomery, None; K. L. Sivils, None; J. M. Guthridge, None; J. A. James, None; J. T. Merrill, None; U. Deshmukh, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/exposure-to-a-periodontal-pathogen-aggregatibacter-actinomycetemcomitans-is-associated-with-increased-sle-severity

Abstract Number: 2654

Treatment-Associated DNA Methylation Patterns in Systemic Lupus Erythematosus

Juliana Imgenberg-Kreuz1,2, Jonas Carlsson Almlöf1, Dag Leonard3, Gunnel Nordmark2, Maija-Leena Eloranta3, Leonid Padyukov4, Iva Gunnarsson5, Elisabet Svennungsson6, Christopher Sjöwall5, Lars Rönnblom2, Ann-Christine Syvänen1 and Johanna K Sandling1,2, 1Department of Medical Sciences, Molecular Medicine and Science for Life Laboratory, Uppsala University, Uppsala, Sweden, Uppsala, Sweden, 2Department of Medical Sciences, Section of Rheumatology, Uppsala University, Uppsala, Sweden, Uppsala, Sweden, 3Rheumatology and Science for Life Laboratory, Department of Medical Sciences, Uppsala University, Sweden, Uppsala, Sweden, 4Department of Medicine Solna, Rheumatology Unit, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, Stockholm, Sweden, 5Department of Clinical and Experimental Medicine, Rheumatology/AIR, Linköping University, Linköping, Sweden, Linköping, Sweden

First publication: September 18, 2017
DNA methylation has emerged as an important contributing factor in the pathogenesis of systemic lupus erythematosus (SLE). SLE typically requires continuous treatment to control the disease, but the effect of different treatments on DNA methylation is still elusive. Therefore the aim of this study was to investigate the association between methylation levels in SLE patients and the most commonly prescribed medications in SLE.

Methods:

Whole blood samples were obtained from 347 SLE patients in a discovery cohort and from 201 SLE patients in a replication cohort, all fulfilling at least four ACR criteria for SLE. Clinical data regarding medication were collected at the time of blood sampling, and treatment with glucocorticoids, chloroquines, azathioprine, mycophenolate mofetil and methotrexate were included in the analysis. DNA methylation profiles were generated on the Illumina HumanMethylation 450k BeadChip array, interrogating 485,000 CpG sites across the genome. The association model included differential cell count estimations, age and sex as covariates. Differential methylated CpG sites (DMCs) were called in the discovery phase if they had a \( p < 1.3 \times 10^{-7} \) and an average difference in methylation-beta between treated and untreated cases of \( >0.05 \). For the replication phase significance was determined as \( p<6.8 \times 10^{-6} \) and the same direction of effect as observed in the discovery phase.

Results:

We identified and replicated treatment-associated DMCs at a total of 5,177 CpG sites. The vast majority of medication DMCs (n=5,046) were observed by comparing SLE patients that received glucocorticoid treatment at time of blood sampling (n=347) to those who did not (n=201). Glucocorticoid treatment was typically associated with decreased methylation, where the strongest effect was observed at the \( \text{FK506 binding protein 5 (FKBP5)} \) involved in immune regulation. The top DMCs with increased methylation in glucocorticoid treated patients were located in \( \text{RUNX3} \), \( \text{TMEM63A} \), \( \text{ZFP36L1} \) and \( \text{LTA} \). In addition, we identified 130 DMCs for azathioprine and one DMC for mycophenolate mofetil treatment, all of these with decreased methylation levels in the treated patients. We were not able to replicate any DMCs associated with methotrexate or chloroquine treatment.

Conclusion:

Our results indicate a role for treatment-associated DNA methylation patterns in SLE, although the possible impact of clinical manifestations and disease activity on methylation levels must be taken into account. Changes in methylation may reflect exposure to treatment and contribute to treatment response and adverse effects. Additional studies including analyses of longitudinal medication data will further elucidate the potential functional impact of treatment-associated changes in DNA methylation in patients with SLE.

Disclosure: J. Imgenberg-Kreuz, None; J. Carlsson Almlöf, None; D. Leonard, None; G. Nordmark, None; M. L. Eloranta, None; L. Padyukov, None; I. Gunnarsson, None; E. Svenungsson, None; C. Sjöwall, None; L. Rönnblom, None; A. C. Syvänen, None; J. K. Sandling, None.
Vivo Treatment with Rituximab

Carlos Perez-Sanchez¹, Irene Cecchi², Massimo Radin³, Maria Ángeles Aguirre Zamorano¹, Patricia Ruiz-Limon⁴, Nuria Barbarroja¹, Yolanda Jiménez-Gómez¹, Maria Carmen Abalos-Aguilera⁴, Ivan Arias de la Rosa⁴, Eduardo Collantes-Estévez¹, Maria Jose Cuadrado⁵, Savino Sciascia⁶ and Chary Lopez-Pedrera¹, ²Rheumatology service, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain, ²Center of Research of Immunopathology and Rare Diseases- Coordinating Center of Piemonte and Valle d’Aosta Network for Rare Diseases, Department of Clinical and Biological Sciences, University of Turin, Italy, Turin, Italy, ³Department of Clinical and Biological Sciences, Center of Research of Immunopathology and Rare Diseases- Coordinating Center of Piemonte and Valle d’Aosta Network for Rare Diseases, Department of Clinical and Biological Sciences, University of Turin, Italy, Turin, Italy, ⁴Rheumatology Service, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain, ⁵Louise Coote Lupus Unit, St Thomas' Hospital, London, United Kingdom, ⁶Center of Research of Immunopathology and Rare Diseases- Coordinating Center of Piemonte and Valle d’Aosta Network for Rare Diseases, Department of Clinical and Biological Sciences, University of Turin, Italy, Center of Research of Immunopathology and Rare Diseases- Coordinating Center of Piemonte and Valle d’Aosta Network for Rare Diseases, Department of Clinical and Biological Sciences, University of Turin, Italy, Torino, Italy

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Despite emerging data on disease-specific associations for various blood- and plasma-derived miRNAs, consensus is lacking as to whether a cellular, extracellular, or a mixed sample might be utilized to define disease mechanisms and serve as biomarkers for therapeutic response. Although studies showed that B-cells are relevant in the development of CVD, the effect of RTX in the context of CVD in SLE patients has not been fully elucidated yet. Objective: To identify and characterize the microRNA profile in SLE monocytes, along with their association with cardiovascular disease (CVD)-related factors, their contribution to the altered miRNA profile in plasma, and their modulation by in vivo RTX treatment.

Methods: Fifty-three SLE patients, and 27 healthy donors were included in the study. Among them, 20 patients were treated with RTX for 3 months. Blood samples were obtained before and at the end of treatment. nCounter microRNA Expression Arrays (NanoString Technologies) and HTG Edgeseq system (Next generation sequencing) were performed, respectively, to analyze miRNA expression profiles on isolated monocytes and plasma. Target genes of the differentially expressed miRNAs were identified by using the Ingenuity Pathway Analysis Software (IPA). A number of altered miRNAs were validated by RT-PCR on the whole cohorts of SLE patients. Extensive clinical/analytical evaluation was performed, and inflammatory, atherosclerosis and pro-thrombotic profiles were quantified by RT-PCR. Then, correlation and association studies were performed.

Results: MicroRNA profiles showed significantly differential expression of 37 microRNAs in SLE monocytes. Functional analysis showed that those miRNAs were mainly related to connective tissue disorders, inflammatory response and reproductive system disease. The expression of several of these miRNAs (i.e. miR-30, miR-149, miR-199) correlated with parameters related to inflammation (i.e. STAT3, PPARg, IL-6, CRP), oxidative stress (mitochondrial membrane potential) and microvascular dysfunction. Moreover, associations of these miRNAs with the occurrence and type of thrombotic events, obstetric complications and presence of early atherosclerosis were demonstrated. Transfection studies further confirmed the relationship between these identified target genes and specific miRNAs. miRNA profile in plasma demonstrated differential expression of 335 microRNAs in SLE patients of which a 60% were reversed by RTX. Among them, 12 miRNAs were found simultaneously deregulated in monocytes and plasma. Interestingly, those 12 miRNAs displayed a number of CVD-related target genes, and were further reversed by in vivo RTX treatment.
Conclusion: We have identified and characterized a specific miRNA profile in monocytes from SLE patients, mostly related to CVD. Although expression from cellular vs circulating miRNAs was mostly divergent in SLE, there was an intriguing association between monocytes and plasma in terms of common deregulated miRNAs involved in CVD, further reversed by RTX treatment.

Funded by CTS7940 and ISCIII (PI15/01333 and RIER RD16/0012/0015)

Disclosure: C. Perez-Sanchez, None; I. Cecchi, None; M. Radin, None; M. Á. Aguirre Zamorano, None; P. Ruiz-Limon, None; N. Barbarroja, None; Y. Jiménez-Gómez, None; M. C. Abalos-Aguilera, None; I. Arias de la Rosa, None; E. Collantes-Estévez, None; M. J. Cuadrado, None; S. Sciascia, None; C. Lopez-Pedrera, None.


Abstract Number: 2656

Alterations of the Splicing Machinery Components in Leukocytes from Systemic Lupus Erythematosus Patients Influences Its Development and Atherothrombotic Profile and Drives the Therapeutic Response

Carlos Perez-Sanchez¹, Maria Ángeles Aguirre Zamorano¹, Sergio Pedraza-Arévalo², Mercedes del Río-Moreno², Irene Cecchi³, Patricia Ruiz-Limon⁴, Nuria Barbarroja¹, Yolanda Jiménez-Gómez¹, Ivan Arias de la Rosa⁴, Maria Carmen Abalos-Aguilera⁴, Pedro Segui³, Eduardo Collantes-Estévez¹, Justo P Castaño², Raul M Luque⁶, Maria Jose Cuadrado⁷ and Chary Lopez-Pedrera¹, ¹Rheumatology service, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain, ²Department of Cell Biology, Physiology and Immunology. University of Cordoba, Reina Sofia Hospital, IMIBIC, Córdoba, Spain, ³Center of Research of Immunopathology and Rare Diseases- Coordinating Center of Piemonte and Valle d’Aosta Network for Rare Diseases, Department of Clinical and Biological Sciences, University of Turin, Italy, Turin, Italy, ⁴Rheumatology Service, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain, ⁵Radiology, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain, ⁶Department of Cell Biology, Physiology and Immunology. University of Cordoba, Hospital Universitario Reina Sofia (HURS), Instituto Maimónides de Investigación Biomédica de Córdoba (IMIBIC), CIBERobn, and ceiA3, Córdoba, Spain, ⁷St Thomas Hospital, Lupus Research Unit, London, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Recent studies emphasize the relevance of alternative splicing in the development of genetic and autoimmune diseases. The aim of this study was to identify alterations in the leukocyte splicing machinery of systemic lupus erythematosus (SLE) patients and to evaluate its influence on the development and activity of the disease, its atherothrombotic profile, and the response to specific therapies.

Methods: An array of selected components of the major- (n=12) and minor-spliceosome (n=4) and associated splicing factors (n=28) was developed, and their expression levels were evaluated using a Fluidigm methodology, in purified leukocytes from 36 SLE patients and 29 healthy donors (HD). In parallel, an extensive clinical/serological evaluation was performed. Carotid intimate media thickness (CIMT) was used as atherosclerosis marker. Endothelial activity was...
monitored by laser-doppler flowmetry, and pro-inflammatory and oxidative stress markers were quantified by flow cytometry and RT-PCR. In a parallel cohort of SLE patients (n = 12), the effects of in vivo treatment with ubiquinol on spliceosome components was evaluated. Transfection studies with splicing machinery components were also carried out on lupus leukocytes.

**Results:** As a general feature, a significant reduction in splicing machinery components was found in all the SLE leukocyte subtypes. Interestingly, we found a specific altered profile of splicing factors and spliceosome components when compared monocytes (U2AF1, FBP11, SRSF9), lymphocytes (RBM22, PRP8, SRSF5) and neutrophils (RNU4, CA150). The reduced levels of some components of spliceosome in both monocytes and neutrophils were linked to the occurrence of thrombotic events, foetal loss and arterial hypertension. In lymphocytes, those reduced levels were strongly related to the positivity for anti-dsDNA antibodies in SLE patients, thus suggesting that reduced spliceosome machinery would contribute to increase in altered autoantigen assembly, inducing increased autoantibody production. Correlation studies demonstrated an inverse relationship among reduced levels of spliceosome components/splicing factors and high activity of the disease (SLEDAI), endothelial dysfunction, and increased peroxide and peroxynitrite levels, as well as of altered mitochondrial membrane potential in monocytes and neutrophils. In vitro treatment of leukocytes from HDs with anti-dsDNA promoted a reduction in spliceosome components associated with the expression of proinflammatory and oxidative mediators. In vivo treatment with ubiquinol reversed the SLE expression of spliceosome components related to their proatherothrombotic profile. Finally, transfections with splicing machinery components were translated in the modulation of the expression of markers related to inflammation and oxidative stress in lupus.

**Conclusion:** These results reveal the existence of SLE-associated spliceosome alterations -promoted by anti-dsDNA antibodies- which could be related to the development and activity of this autoimmune condition and have influence on the induction of mechanisms that drive atherothrombosis as well as the therapeutic response.

**Disclosure:** C. Perez-Sanchez, None; M. Á. Aguirre Zamorano, None; S. Pedraza-Arévalo, None; M. del Río-Moreno, None; I. Cecchi, None; P. Ruiz-Limon, None; N. Barbarroja, None; Y. Jiménez-Gómez, None; I. Arias de la Rosa, None; M. C. Abalos-Aguilera, None; P. Segui, None; E. Collantes-Estévez, None; J. P. Castaño, None; R. M. Luque, None; M. J. Cuadrado, None; C. Lopez-Pedrera, None.

**Abstract Number: 2657**

**Single Cell Expression Quantitative Trait Loci (eQTL) Analysis of Established Systemic Lupus Erythematosus (SLE)-Risk Loci in Lupus Patient Monocytes**

Yogita Ghodke-Puranik1, Zhongbo Jin2, Wei Fan3, Mark A. Jensen1, Jessica M. Dorschner2, Danielle Vsetecka2, Shreyasee Amin4, Ashima Makol5, Floranne C. Ernst6, Thomas Osborn4, Kevin Moder4, Vaidehi Chowdhary7 and Timothy Niewold8, 1Colton Center for Autoimmunity, New York University, New York, NY, 2Division of Rheumatology and Department of Immunology, Mayo Clinic, Rochester, MN, 3Department of Rheumatology, Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University, China, Shanghai, China, 4Rheumatology, Mayo Clinic, Rochester, MN, 5Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, MN, 6Division of Rheumatology, Mayo Clinic Rochester, Rochester, MN, 7Internal Medicine, Division of Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, MN, 8New York University, New York, NY

**First publication:** September 18, 2017
Background/Purpose: Most confirmed SLE-risk loci are found near or in genes with immune function, yet how these loci influence diverse immune cell subsets remains unknown.

Methods: We performed single cell eQTL analysis in SLE monocytes to determine the impact of SLE-risk loci in single human monocytes. Purified classical (CL) and non-classical (NCL) monocytes from SLE patients were analyzed for expression of 90 genes, and patients were genotyped for 7 SLE-risk SNPs. Each monocyte subset was analyzed separately using non-parametric analyses.

Results: We observed a large number of significant eQTL associations that surpassed the 5% FDR. The SLE-associated SNPs demonstrated more eQTLs in NCLs as compared to CLs (p=2.5x10^{-8}). For a given SNP, the eQTL associated transcripts differed between monocyte subsets (p<0.001 for all 7 SNPs for discordance). For NCLs, TNFAIP3, IRF5, IRF7, PTPN22, and SPP1 shared a significant proportion of eQTL associations. For CLs, TNFAIP3 shared many eQTLs with SPP1 and ITGAM, while SPP1 and ITGAM showed limited overlap. Thus, SLE-associated risk loci exert coordinated effects on gene expression within individual human monocytes, and the risk loci interact in different ways in different cell types.

Conclusion: Our study revealed striking differences, using single cell gene expression, in the occurrence and interaction of SLE risk associated eQTLs within different but closely related cell types. This suggests pleiotropic effects from each locus across various immune cell types, and a high degree of complexity when considering how these loci impact the immune system.

Disclosure: Y. Ghodke-Puranik, None; Z. Jin, None; W. Fan, None; M. A. Jensen, None; J. M. Dorschner, None; D. Vsetecka, None; S. Amin, None; A. Makol, None; F. C. Ernste, None; T. Osborn, None; K. Moder, None; V. Chowdhary, None; T. Niewold, None.


Abstract Number: 2658

4-Hydroxy-2-Nonenal Serum Protein-Adducts and Anti-4-Hydroxy-2-Nonenal-Protein Adduct Antibodies in SLE

Biji T Kurien1,2,3 and R. Hal Scofield4, 1Arthritis and Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, 2U.S. Department of Veterans Affairs Medical Center, Oklahoma City, OK, 3College of Medicine, University of Oklahoma Health Sciences Center, Oklahoma City, OK, 4Arthritis & Clinical Immunology Program, Oklahoma Medical Research Foundation; Department of Medicine, University of Oklahoma Health Sciences Center; US Department of Veterans Affairs Medical Center, Oklahoma City, OK

First publication: September 18, 2017
Background/Purpose:

Systemic lupus erythematosus (SLE) is a chronic, complex disease and autoantibodies to self-antigens are a characteristic feature of the disorder. Our group and others have observed free radical mediated oxidative damage in SLE. Our previous data implicated red cell membrane catalase as a target of 4-hydroxy-2-nonenal (HNE; a by-product of oxidative damage) modification in SLE subjects. Here, we tested the hypothesis that HNE- or malondialdehyde- (MDA) modification occurs in the sera of SLE subjects and that antibodies to HNE would be present in SLE sera, and may precede lupus autoantibodies.

Methods:

Serum proteins from 8 SLE subjects and 8 age and sex-matched normal subjects were analyzed for HNE- or MDA protein-adducts by ELISA. Three additional SLE subjects, who had sera collected longitudinally for 12- 15 years, were tested for the presence of anti-HNE antibodies by ELISA. One SLE subject developed anti-Ro60 under observation and another developed anti-P similarly (after disease diagnosis). The third SLE subject had anti-Sm from time of diagnosis. Ro60, Sm and a multiple antigen peptide synthesized from the P autoantigen were coated on ELISA plates, HNE-modified and used as substrate for anti-HNE ELISA. Unmodified Ro60, Sm and P multiple antigen peptide served as control. To test for HNE or MDA-protein adducts in sera from SLE subjects or normal controls, the sera were coated on ELISA plates as antigen. HNE or MDA adducts in sera was determined with rabbit anti-HNE or anti-MDA antibodies. HNE-modified proteins in sera from SLE or normal controls were also studied by immunoblotting.

Results:

We found significantly increased oxidative damage in the sera of SLE subjects compared to normal controls by ELISA and immunoblotting. There was significantly more HNE-protein adducts in SLE sera compared to controls as determined by ELISA (0.084 ± 0.022 versus 0.055 ± 0.012, p=0.0044; average OD±SD). But, we did not observe any significant difference in MDA-modified proteins between SLE subjects and controls. Analysis of SLE sera by immunoblotting showed HNE modification of two proteins migrating at 24 kD and 38 kD respectively. Anti-HNE P autoantibodies preceded anti-P autoantibodies in the SLE subject that developed anti-P antibodies several months after SLE diagnosis. Anti-HNE P antibodies developed strongly in the anti-P SLE subject in the 68th month (1.2 OD), while anti-P response developed only by month 112. Anti-P response was strong by 125th month (1.7 OD). Anti-HNE P response at this time point was 3.0 OD, almost twice as the anti-P response. Anti-HNE Ro60 response preceded anti-Ro60 antibody response by 20 months in the subject developing anti-Ro60 under observation. Anti-HNE Ro60 response correlated with anti-Ro60 response in this subject for the rest of the dates for which samples were available for testing. However, there was no difference in anti-Sm or anti-HNE Sm antibody levels over time for the subject that had anti-Sm autoantibodies right from the time of diagnosis.

Conclusion:

Increased HNE-modified protein occur in sera of SLE subjects. Anti-HNE antibody may precede anti-Ro60 or anti-P autoantibodies in SLE. HNE-products are potential neoantigens and thus could be involved in the pathogenesis of SLE.

Disclosure: B. T. Kurien, None; R. H. Scofield, None.


Abstract Number: 2659

Deepak Rao1, Celine C. Berthier2, Arnon Arazi3, Anne Davidson4, Yanyan Liu5, Edward Browne3, Thomas Eisenhaure3, Adam Chicoine6, David Lieb7, Dawn Smilek7, Patti Tosta7, James Lederer8, Michael Brenner5, David Hildeman9, E. Steve Woodle10, David Wofsy11, Jennifer H. Anolik12, Matthias Kretzler13, Nir Hacohen14 and Betty Diamond15, 1Division of Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 2Nephrology, Division of Nephrology, University of Michigan Medical Center, Ann Arbor, MI, 3Broad Institute, Cambridge, MA, 4Autoimmunity and Musculoskeletal Diseases, Feinstein Inst for Med Rsch, Manhasset, NY, 5Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 6Brigham and Women's Hospital, Boston, MA, 7Immune Tolerance Network, San Francisco, CA, 8Department of Surgery, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 9University of Cincinnati, Cincinnati, OH, 10University of Cincinnati College of Medicine, Cincinnati, OH, 11Rheumatology, UCSF, San Francisco, CA, 12Medicine- Allergy, Immunology and Rheumatology, University of Rochester Medical Center, Rochester, NY, 13Internal Medicine, Division of Nephrology, University of Michigan, Ann Arbor, MI, 14Harvard Medical School, Boston, MA, 15Autoimmune and Musculoskeletal Diseases, The Feinstein Institute for Medical Research, Manhasset, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: There is a critical need to define the cells that mediate tissue damage in lupus nephritis. Here we aimed to establish a protocol to preserve lupus nephritis kidney biopsies and urine cell samples obtained at multiple clinical sites for subsequent isolation and transcriptomic analysis of single cells.

Methods: We developed a method to cryopreserve intact, viable kidney tissue in a 10% DMSO-containing solution. Viable cryopreserved kidney tissue from tumor nephrectomies and lupus nephritis kidney biopsies were disaggregated by enzymatic digestion and compared to freshly processed tissues. Cell yields and cell composition were assessed by flow cytometry. Transcriptomes of flow-sorted CD45+ leukocytes and CD10+ kidney epithelial cells were evaluated by low-input and single cell RNA-seq.

Results: Cryopreserved kidney tissue from tumor nephrectomies and lupus nephritis biopsies can be thawed and dissociated to yield intact, viable leukocytes and epithelial cells. Cryopreservation of intact kidney tissue provides higher epithelial cell yields compared to cryopreservation of single cell suspensions from dissociated kidneys. Epithelial cell and leukocyte lineage markers are easily detected on cells from cryopreserved kidney tissue by flow cytometry (Figure 1). Cell yields and flow cytometric cell phenotypes are comparable between cryopreserved kidney samples and paired kidney samples shipped overnight on wet ice. High-quality single cell and low-input transcriptomic data were generated from flow-sorted leukocytes from both cryopreserved lupus nephritis kidney biopsies and urine, typically with 3000-4000 genes detected in single cell transcriptomes (Figure 2).

Conclusion: We propose that this method of acquisition of viable cells from cryopreserved intact kidney tissue may serve as a model for robust, centralized cellular analyses of kidney samples acquired in multi-site clinical studies. More broadly, this strategy enables accumulation of a valuable biobank of tissues containing viable cells that can be used for multiple downstream analyses.
Disclosure: D. Rao, None; C. C. Berthier, None; A. Araziz, None; A. Davidson, None; Y. Liu, None; E. Browne, None; T. Eisenhaure, None; A. Chicoine, None; D. Lieb, None; D. Smilek, None; P. Tosta, None; J. Lederer, None; M. Brenner, None; D. Hildeman, None; E. S. Woodle, None; D. Wofsky, None; J. H. Anolik, None; M. Kretzler, None; N. Hacohen, None; B. Diamond, None.


Abstract Number: 2660

**Endothelin-1 and Interleukin-6 Serum Levels Are Associated with More Severe Vasculopathy in Patients with Systemic Sclerosis**

Ana Maria Gheorghiu1, Roxana Sfrent-Cornateanu2, Daciana Marta3, Raida Oneata4, Mihai Bojinca4, Stefania Magda5, Tudor Constantinescu6, Rucsandra Dobrota7, Alina Soare8, Liviu Macovei1, Victor Stoica4, Constantin Bara2 and Carina Mihaia9, 1Carol Davila University of Medicine and Pharmacy, Internal Medicine and Rheumatology Department „Dr. I. Cantacuzino“ Clinical Hospital, Bucharest, Romania, 2Immunology and Physiopathology Department, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania, 3Victor Babes National Institute of Research and Development, Bucharest, Romania, 4Carol Davila University of Medicine and Pharmacy, Internal Medicine and Rheumatology Department, Cantacuzino Clinical Hospital, Bucharest, Romania, 5Cardiology Department, University Emergency Hospital, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania, 6Marius Nasta National Pneumology Institute, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania, 7Department of Rheumatology, Center of Experimental Rheumatology, University Hospital Zurich, Zurich, Switzerland, 8Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Erlangen, Germany, 9Internal Medicine and Rheumatology Dept., Cantacuzino Clinical Hospital, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Tuesday, November 7, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM
Background/Purpose:

Systemic sclerosis (SSc) is a severe connective tissue disease characterized by vascular and fibrotic changes in the skin and various internal organs. Pathogenesis of SSc includes early-onset vasculopathy with endothelial cell activation, microvascular injury and impaired angiogenesis.

Objectives: We aimed to determine the association of several biological molecules reflecting endothelial cell activation or dysfunction: E-selectin (E-sel), inter-cellular adhesion molecule 1 (ICAM-1), endothelin 1 (ET-1), von Willebrand factor (vWF) and interleukin 6 (IL-6), with distinct capillaroscopic SSc patterns and with more severe disease.

Methods:

Forty consecutive SSc patients attending our EUSTAR SSc clinic, aged [median (IQR)] 52 (18) years, male gender 4/40 (10%), diffuse cutaneous subset (dcSSc) 14/40 (35%) were enrolled in this study. Extensive clinical and nailfold capillaroscopy (NFC) pattern assessment, as well as quantification of serum E-sel, ICAM-1, ET-1, vWF, IL-6 and C-reactive protein (CRP) were performed on all patients. Associations between vascular biomarkers and disease characteristics were evaluated by Mann-Whitney U-test and Spearman correlations. We analyzed the confounding effect of CRP on the association between vascular markers and NFC pattern by multivariable logistic regression.

Results:

NFC “late” pattern was found in 21 patients, while 6 had “early” and 13 had “active” NFC pattern. All 5 vascular biomarkers correlated with each other good to moderately, with r indices varying between 0.660 and 0.332, the only exception being ET-1 which did not correlate with E-sel. Good correlations (r 0.465 to 0.727) were also found between all 5 biomarkers and CRP. Patients with severe vasculopathy, as reflected by the NFC “late” pattern, had higher levels of IL-6 (median 12.06 vs. 3.08 pg/mL, p=0.001), ET-1 (median 2.06 vs 1.59 pg/mL, p=0.029), vWF (median 3284 vs 2730 IU/mL, p=0.013) and E-sel (median 52.6 vs. 42.3 ng/mL, p>0.05), compared to patients with NFC “early” or “active” patterns (Mann-Whitney U-test). In the logistic regression analysis, IL6 (OR (95% CI) 1.175 (1.005, 1.374), p=0.04), ET1 (2.802 (1.157, 6.784), p=0.022) and vWF (1.001 (1.000, 1.003), p=0.034) were significantly associated with “late” capillaroscopy pattern even after adjustment for CRP.

There was a significant, negative correlation between lung transfer for carbon monoxide (DLCO) and E-sel, ICAM-1 (both p<0.001) and vWF (p=0.013). ET-1 was higher in patients with more severe disease (dcSSc, patients positive for anti-topoisomerase antibodies and patients with a history of digital ulcers – all p<0.05).

Conclusion:

Serum biomarkers reflecting endothelial cell activation and/or dysfunction are elevated in patients with more severe SSc-associated vasculopathy even when adjusting for inflammation markers. Together with NFC data they might be used for assessing vasculopathy severity in SSc and identifying patients who would benefit from more aggressive vasoactive treatment.

This work was performed as part of the QUANTICAP project, financed by the UEFISCDI PN-II-PT-PCCA-2013-4-1589 grant.

Disclosure: A. M. Gheorghiu, None; R. Sfrent-Cornateanu, None; D. Marta, None; R. Oneata, None; M. Bojinca, None; S. Magda, None; T. Constantinescu, None; R. Dobrota, None; A. Soare, None; L. Macovei, None; V. Stoica, None; C. Bara, None; C. Mihai, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/endothelin-1-and-interleukin-6-serum-levels-are-associated-with-more-severe-vasculopathy-in-patients-%e2%80%a8with-systemic-sclerosis

Abstract Number: 2661

Clinical Impact of Selenium and Vitamin C Deficiency in Systemic Sclerosis
Malnutrition is a major concern in systemic sclerosis (SSc) however literature is scarce on the subject, especially on micronutriment or vitamin deficiency and its relationship to disease outcomes. The aim of our study was to determine the prevalence and the risk factors associated with malnutrition, selenium (Se) and vitamin C (vitC) deficiency in SSc patients.

Methods: We included all unselected and consecutive adult SSc patient fulfilling the 2013 ACR/EULAR criteria the Toulouse University Hospital cohort between 2011 and 2016 who underwent a nutritional workup including (albumin, vitC and selenium plasma/serum levels). Patients were followed according to standard clinical guidelines with visits at least every 6 months. Data collected included clinical characteristics, organ involvement, pulmonary function tests, echocardiography parameters and drug exposure. Se deficiency was defined as serum Se < 70ng/mL. VitC deficiency was defined as serum vitC (determined by HPLC) < 0.4mg/dL. Comparisons were done using the Fisher’s exact test and the Wilcoxon signed-rank test and Association between malnutrition, Se or vitC deficiency was analyzed with logistic regression model.

Results: 82 consecutive SSc patients were included, mostly men (76%), mean aged was 59.7 ±13.5 years. SSc was limited, diffuse or sine scleroderma in 75%, 24% and 1% of cases respectively, with Scl-70 or centromere antibodies in 32% and 44% of cases. Mean disease duration was 9.4 ±9.9 years. 67.1% had a digital ulcer history. The mean modified rodnan skin score (mRSS) at baseline was 11 ±10. Cardiac, pulmonary or GI tract were involved in 19%, 63% and 39% of patients respectively; of whom 9% had pulmonary artery hypertension (PAH). Overt malnutrition was present in 13 (15.9%) patients. Micronutrient deficiencies included Se 19 (23.2%), vitC (26.8%), B6 37(45.1%), folate 11 (23%) and/or B1 4 (4.9%). Malnourished patients were significantly older (68.4 vs 58.1 y., p=0.01) and had more frequently PAH (27% vs 6%, p=0.05). Cardiac involvement was significantly associated with Se deficiency with an OR 6.2, IC95[1.48-32.7], p=0.02. Risk factors associated with vitC deficiency were BMI (OR 0.72 per point, IC95[0.54-0.89], p=0.01), Rodnan ≤ 14 (OR 0.16, IC95[0.03-0.68], p=0.02), interincisive distance (OR 0.91 per mm, IC95[0.81-0.99], p=0.04), esophagitis or Barrett’s mucosa (OR 4.85, IC95[1.48-17.0], p=0.01), pulmonary artery systolic pressure by echocardiography (OR 1.05 per mmHg, IC95[1.00-1.11], p=0.04), (OR 0.95 per %, IC95[0.90-0.99], p=0.04), DLCO (OR 0.95 per %, IC95[0.91-0.99], p=0.01), hemoglobin (OR 0.38 per g/dL, IC95[0.21-0.60], p=0.0002), albumin (OR 0.91 per g/L, IC95[0.82-0.99], p=0.05) and proton-pump inhibitor (OR 4.7, IC95[1.33-22.3], p = 0.03).

Conclusion: Se testing should be considered as soon as heart involvement is suspected. We believe that targeted Se supplementation could be beneficial to patients with heart involvement. VitC testing should be considered in SSc patients with extensive skin involvement and severe disease, and its supplementation should be a part of SSc close management.

Disclosure: R. Dupont, None; G. Moulis, None; L. Astudillo, None; P. Arlet, None; L. Sailler, None; G. Pugnet, None.
The EULAR Systemic Sclerosis Impact of Disease (ScleroID) Score – a New Patient-Reported Outcome Measure for Patients with Systemic Sclerosis – Preliminary Results from the Ongoing Validation Study

Rucsandra Dobrota1, Mike Oliver Becker1, Kim Fligelstone2, Jaap Fransen3, Ann Kennedy4, Yannick Allano5, Patricia Carreira6, László Czirják7, Christopher Denton8, Roger Hesselstrand9, Gunnel Sandqvist10, Otylia Kowalc-Bielecka11, Marco Matucci-Cerinic12, Carina Mihai13, Ana Maria Gheorghiu14, Ulf Müller-Ladner15, MC Vonk16, Turid Heiberg17 and Oliver Distler18, 1Department of Rheumatology, Center of Experimental Rheumatology, University Hospital Zurich, Zurich, Switzerland, 2Royal Free Hospital, Scleroderma Unit and Scleroderma Society, London, United Kingdom, 3Department of Rheumatology, Radboud University Medical Center, Nijmegen, Netherlands, 4Federation of European Scleroderma Associations (FESCA), Tournai, Belgium, 5Department of Rheumatology, Cochin Hospital, Paris Descartes University, Paris, France, 6Department of Rheumatology and Immunology, University of Pécs, Faculty of Medicine, Pécs, Hungary, 8Department of Rheumatology, University College London, Royal Free Hospital, London, United Kingdom, 9Lund University, Lund, Sweden, 10Department of Rheumatology, Lund University Hospital, Lund, Sweden, 11Department of Rheumatology and Internal Medicine, Medical University of Bialystok, Bialystok, Poland, 12Dept of Medicine/Div of Rheum, University of Florence, Florence, Italy, 13Internal Medicine and Rheumatology Dept., Cantacuzino Clinical Hospital, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania, 14Carol Davila University of Medicine and Pharmacy, Internal Medicine and Rheumatology Department „Dr.I.Cantacuzino“ Clinical Hospital, Bucharest, Romania, 15Justus-Liebig-University Giessen, Department of Internal Medicine and Rheumatology, Kerckhoff-Klinik, Bad Nauheim, Germany, Bad-Nauheim, Germany, 16Rheumatology, Radboud University Medical Centre, Nijmegen, Netherlands, 17Department of Health and Social Sciences, Oestfold University College, Oslo, Norway, 18Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Patient reported outcome measures (PROM) are acknowledged a key role in clinical trials in systemic sclerosis (SSc). Given the unmet need of a validated, comprehensive PROM in SSc, the ScleroID questionnaire was developed by a team of patients with SSc and medical experts in the field. This is intended as a brief, disease-specific, patient-derived, disease impact score for research and clinical use in SSc. Here, we present the preliminary analysis from the ongoing ScleroID validation study.

Methods:

This EULAR-endorsed project involves 11 European expert SSc centers. Patients fullfilling the ACR/EULAR 2013 criteria were prospectively included since 05/16 in the ongoing observational cohort study. Patients filled in the ScleroID questionnaire (Figure 1), as well as selected comparators SHAQ, EQ5D, SF36. Additionally, they weighted the 10 dimensions of the ScleroID by distributing 100 points according to the perceived impact on their health. The final score calculation will be based on the ranking of the weights. The study includes a reliability arm (follow-up questionnaire 7-10 days from baseline), as well as a longitudinal arm, looking at sensitivity to change at follow-up visits after 6 and 12 months from baseline.
Results:

As of 01/2017 the study cohort included 224 patients with valid baseline data, 44 also had a reliability visit and 6 a 6-months follow-up visit. 84.4% of patients were female, 54.4% had limited SSc, median age 58, and median disease duration 8 years. The highest preliminary median weights for ScleroID domains were for Raynaud, impaired hand function, fatigue and pain (Table 1). Except for pain, these dimensions were also scored most highly in the ScleroID questionnaire at baseline. As of 06/2017, 362 patients (72.4% of target) were enrolled into the study.

Conclusion:

The EULAR ScleroID score is a novel tool designed for use in clinical practice and clinical trials to display the disease impact of SSc. In this preliminary analysis, Raynaud syndrome, impaired hand function, and fatigue were the main patient reported drivers of disease impact. However, further recruitment and validation of this new instrument is ongoing.

Figure 1. The EULAR Scleroderma Impact of Disease Score (ScleroID)

How much have the different aspects of systemic sclerosis affected you during the last week? Please mark your responses on the scale by choosing the appropriate number for each of the following dimensions:

Raynaud's phenomenon:
Circle the number that best describes the severity of your Raynaud's phenomenon during the last week:
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Hand function:
Circle the number that best describes your hand function limitations due to your systemic sclerosis during the last week:
No limitation 0 1 2 3 4 5 6 7 8 9 10 Extreme limitation

Upper gastrointestinal tract symptoms (e.g. swallowing difficulties, reflux, vomiting):
Circle the number that best describes the severity of your upper gastrointestinal tract symptoms due to your systemic sclerosis during the last week:
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Pain:
Circle the number that best describes the pain you felt due to your systemic sclerosis during the last week:
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Fatigue:
Circle the number that best describes the impact of overall fatigue due to your systemic sclerosis during the last week:
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Lower gastrointestinal tract symptoms (e.g. bloating, diarrhea, constipation, anal incontinence):
Circle the number that best describes the severity of lower gastrointestinal tract symptoms during the last week:
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Limitations of life choices and activities (e.g. social life, personal care, work):
Circle the number that best describes how severe the limitations of life choices and activities due to your systemic sclerosis were during the last week:
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Body mobility:
Circle the number that best describes how much your body mobility was affected due to your systemic sclerosis during the last week:
Not affected 0 1 2 3 4 5 6 7 8 9 10 Extremely affected

Breathlessness:
Circle the number that best describes how severe your breathlessness due to systemic sclerosis was during the last week:
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Digital ulcers:
Circle the number that best describes how much your digital ulcers affected you overall during the last week:
None 0 1 2 3 4 5 6 7 8 9 10 Extreme
Disclosure: R. Dobrota, None; M. O. Becker, None; K. Fligelstone, None; J. Fransen, None; A. Kennedy, None; Y. Allanore, Actelion Pharmaceuticals US, 2,Bayer AG, 2,Bristol-Myers Squibb, 2,Inventiva, 2,Medac, 2,Pfizer Inc, 2,Roche Pharmaceuticals, 2,Genentech and Biogen IDEC Inc., 2,Sanofi-Aventis Pharmaceutical, 2,Server, 2,Actelion Pharmaceuticals US, 5,Bayer AG, 5,Bristol-Myers Squibb, 5,Inventiva, 5,Medac, 5,Pfizer Inc, 5,Roche Pharmaceuticals, 5,Genentech and Biogen IDEC Inc., 5,Sanofi-Aventis Pharmaceutical, 5; P. Carreira, None; L. Czirják, None; C. Denton, None; R. Hesselstrand, None; G. Sandqvist, None; O. Kowal-Bielecka, None; M. Matucci-Cerinic, None; C. Mihai, Actelion Pharmaceuticals Ltd., Geneva Romfarm, Abbvie, Roche, 5; A. M. Gheorghiu, None; U. Müller-Ladner, None; M. Vonk, Actelion Pharmaceuticals Ltd, Therabel and United Therapeutics., 5; T. Heiberg, None; O. Distler, 4 D Science, Actelion, Active Biotec, Bayer, Biogen Idec, Boehringer Ingelheim Pharma, BMS, ChemomAb, Epipharm, Ergonex, espeRare foundation, GSK,Roche-Genentech, Inventiva, Lilly, medac, MedImmune, Mitsubishi Tanabe, Pharmaceuticals, Pfizer, Sanofi, Seroda, 2.


Abstract Number: 2663

Changes in Disability over Time, and Their Relationship with Degree of Skin Thickening, in Patients with Limited and Diffuse Cutaneous Systemic Sclerosis: A Retrospective Cohort Study

Sébastien Peytrignet1, Joanne Manning2, Elizabeth Wragg3, Tonia Moore4, Muditha Samaranayaka3 and Ariane L. Herrick5, 1Manchester Academic Health Sciences Centre, Centre for Musculoskeletal Research, Institute of Inflammation and Repair, The University of Manchester, Manchester, United Kingdom, 2Rheumatology Department, Salford Royal NHS Foundation Trust, Salford, United Kingdom, 3Salford Royal NHS Foundation Trust, Salford, United
SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
The burden of disability of systemic sclerosis (SSc) is increasingly recognised. What is less known are the factors driving this disability and how it changes over time. At a tertiary centre for SSc, clinical and disability data (including the Health Assessment Questionnaire Disability Index, HAQ-DI) have been collected systematically at annual review visits for over 20 years and stored electronically. This allowed us to test the hypothesis that disability is greater in patients with diffuse (dcSSc) compared to limited cutaneous disease (lcSSc) and that disability is associated with the degree of skin thickening in patients with dcSSc but not with lcSSc.

Methods:
This was a retrospective analysis of data collected from 1994 to 2016. For each patient, data were retained from the first simultaneous record of the HAQ-DI (0-3) and modified Rodnan skin score (mRSS, 0-51), measuring skin fibrosis. For each patient, HAQ-DI and mRSS trajectories were assessed separately for the early and late stages of the disease (with 5 years post first non-Raynaud’s manifestation as the cut-off). For the first visit, HAQ-DI and mRSS scores were compared according to disease stage and subtype. The yearly change in HAQ-DI and mRSS was computed for each patient using linear regressions for early and late disease phases and Spearman correlations were computed between changes in HAQ-DI and mRSS.

Results:
401 patients were included in the analysis, 292 (72.8%) with lcSSc and 109 (27.2%) with dcSSc. The mean disease duration at the first visit was 8.0 years (SD 7.9) and mean length of follow-up 5.9 years (SD 3.6). 73 patients were followed during early disease, 218 during late disease and 110 during both stages. At the first visit, patients with dcSSc had higher mean HAQ-DI scores (indicating more disability) than patients with lcSSc for early disease (1.4 vs. 0.9, p=0.003) but there was no difference in ‘late’ patients (1.6 vs. 1.4, p=0.221). The yearly change in HAQ-DI was very variable, with approximately half of the cohort improving while the other half deteriorated. In dcSSc, the changes in disability were associated with changes in mRSS in early (p=0.38, p=0.002) but not in late disease (p=0.11, p=0.382). In lcSSc, changes in mRSS did not associate with changes in disability in early or late disease (p=0.173 for early and p=0.203 for late) (Figure).

Conclusion:
These findings further benchmark the high disability in patients with SSc, and confirm that patients with the diffuse subtype tend to exhibit higher levels of musculoskeletal disability than those with limited disease. In early dcSSc, disability tracks over time with skin thickening, suggesting that in this subgroup skin fibrosis is a driver of disability, whereas in late dcSSc and in lcSSc other factors (e.g. severity of digital ischaemia) may contribute more.

Figure. Yearly changes in HAQ-DI and mRSS, according to disease subtype and stage.
Disclosure: S. Peytrignet, None; J. Manning, None; E. Wragg, None; T. Moore, None; M. Samaranayaka, None; A. L. Herrick, None.


Abstract Number: 2664

Anti-SSA (Ro52/Ro60) and SSB Autoantibodies in Patients with Systemic Sclerosis

Myo-Pale' Aye¹, Ghaith Noaiseh², Thomas A. Medsger Jr.¹, Robert A. Lafyatis³, Maureen Laffoon¹, Lei Zhu¹ and Robyn T. Domsic⁴, ¹Rheumatology, University of Pittsburgh Medical Center, Pittsburgh, PA, ²University of Pittsburgh Medical Center, Pittsburgh, PA, ³Medicine, Rheumatology, University of Pittsburgh Medical Center, Pittsburgh, PA, ⁴Medicine - Rheumatology, University of Pittsburgh Medical Center, Pittsburgh, PA

First publication: September 18, 2017
**Background/Purpose:** Anti-SSA (Ro52/Ro60) and anti-SSB autoantibodies are the cardinal serological markers for Sjogren's syndrome. They are also present in other systemic autoimmune diseases. There is a limited data on their prevalence in systemic sclerosis (SSc). The objectives of this study were to: 1) determine the prevalence of SSA (Ro-52 and Ro-60) and SSB antibodies in consecutive SSc patients using immunoprecipitation (IP) testing, and 2) compare the clinical features and survival among these subsets of SSc patients.

**Methods:** We studied an inception cohort of consecutive new SSc patients first evaluated at the UPMC Scleroderma Center between 2006 and 2011. All patients underwent complete serologic testing using ANA, protein, and RNA immunoprecipitation (IP) testing to detect SSc-associated antibodies, Ro52, Ro60 and SSB antibodies. Prevalence, demographic, clinical features, and survival were compared between SSA/SSB positive and negative SSc patients. Statistical analyses were done using SAS 9.4.

**Results:**

There were 474 patients met the inclusion criteria. The mean age of cohort at first SSc visit was 53.7± 14.9 years, 79% were female, 90% were Caucasian, and 40% had diffuse skin thickening. Of all patients, 65 (14%) were positive for anti-SSA/SSB antibodies (22 had Ro-52, 45 had Ro-60, and 2 had both, 4 had SSB). There was no patient with SSB-only serotype. There were no significant differences in demographics and frequency of major SSc-related internal organ involvement between seropositive and seronegative groups (Table 1). SSA/SSB positive patients had higher frequency of overlap syndrome (22% vs. 13%, p=0.05). The distribution of other SSc-associated autoantibodies did not differ. Over time, SSA/SSB positive patients developed higher rates of photosensitivity (9% vs 4%; p=0.03) and peripheral neuropathy (16% vs 7%; p=0.02). Among the SSA/SSB subsets, Ro-60 only patients developed more frequent gastrointestinal involvement compared to Ro52-only and seronegative patients (85% vs. 37% vs. 75%; p=0.001). No other clinical or serological differences existed between these three groups. Five-year survival was not significantly reduced in the SSA/SSB positive group (p=0.38).

**Conclusion:** In this inception cohort of SSc patients, 14% had SSA/SSB antibodies. These patients at presentation were less likely to have key phenotypic features of Sjogren's syndrome compared to seronegative patients. The seropositive group developed more photosensitivity and neuropathy over time; however, objective Sjogren's evaluation testing was not performed systematically. A previously unreported association of GI complications and Ro60 status was observed. Further studies are needed to confirm this association.

*Table I. First SSc center visit characteristics of SSc with and without anti-SSA/SSB antibodies*
<table>
<thead>
<tr>
<th></th>
<th>SSA/SSB positive (n=65)</th>
<th>SSA/SSB negative (n=409)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age (±SD) at first visit</td>
<td>53.0 ± 15.5</td>
<td>53.8 ± 14.7</td>
<td>0.67</td>
</tr>
<tr>
<td>Female</td>
<td>51 (78%)</td>
<td>325 (79%)</td>
<td>0.85</td>
</tr>
<tr>
<td>Caucasian</td>
<td>55 (85%)</td>
<td>372 (91%)</td>
<td>0.36</td>
</tr>
<tr>
<td>Disease characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median disease duration (IQR)</td>
<td>4.0 (1.4,11.4)</td>
<td>5.0 (1.3,13.5)</td>
<td>0.17</td>
</tr>
<tr>
<td>Diffuse skin disease</td>
<td>24 (38%)</td>
<td>142 (35%)</td>
<td>0.67</td>
</tr>
<tr>
<td>Overlap</td>
<td>14 (22%)</td>
<td>52 (13%)</td>
<td>0.05</td>
</tr>
<tr>
<td>Raynaud's phenomenon</td>
<td>63 (97%)</td>
<td>394 (96%)</td>
<td>0.81</td>
</tr>
<tr>
<td>Dry eyes</td>
<td>25 (39%)</td>
<td>130 (33%)</td>
<td>0.32</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>26 (41%)</td>
<td>139 (35%)</td>
<td>0.40</td>
</tr>
<tr>
<td>Joint Tenderness or Swelling</td>
<td>3 (5%)</td>
<td>39 (10%)</td>
<td>0.20</td>
</tr>
<tr>
<td>Gastrointestinal involvement*</td>
<td>18 (28%)</td>
<td>97 (25%)</td>
<td>0.53</td>
</tr>
<tr>
<td>ILD</td>
<td>13 (20%)</td>
<td>70 (17%)</td>
<td>0.63</td>
</tr>
<tr>
<td>Renal Crisis</td>
<td>2 (3%)</td>
<td>12 (3%)</td>
<td>0.94</td>
</tr>
<tr>
<td>Labs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rheumatoid Factor positive</td>
<td>14/37 (38%)</td>
<td>62/221 (28%)</td>
<td>0.22</td>
</tr>
</tbody>
</table>

*=abnormal objective motility testing or use of antibiotics for small bowel bacterial overgrowth

Disclosure: M. P. Aye, None; G. Noaiseh, None; T. A. Medsger Jr., None; R. A. Lafyatis, None; M. Laffoon, None; L. Zhu, None; R. T. Domsic, None.


Abstract Number: 2665

**Mortality in an Early Diffuse Cutaneous Systemic Sclerosis Cohort—Data from the Prospective Registry for Early Systemic Sclerosis**

Tracy M. Frech\(^1\), Shervin Assassi\(^2\), Elana J. Bernstein\(^3\), Flavia V. Castelino\(^4\), Robyn T. Domsic\(^5\), Jessica K. Gordon\(^6\), Faye Hant\(^7\), Monique Hinchliff\(^8\), Bernie LaSalle\(^9\), Victoria K. Shanmugam\(^10\), Virginia D. Steen\(^11\) and Dinesh Khanna\(^12\), \(^1\)Division of Rheumatology, University of Utah, Salt Lake City, UT, \(^2\)University of Texas McGovern Medical School, Houston, TX, \(^3\)Department of Medicine, Division of Rheumatology, Columbia University, New York, NY,
SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The Prospective Registry of Early Systemic Sclerosis (PRESS) cohort is an early diffuse cutaneous systemic sclerosis (dcSSc) that provides an opportunity to assess the causes of mortality in this decade. The objective of this analysis was to assess the causes of death and describe the clinical features associated with mortality in the PRESS cohort.

Methods: The PRESS cohort includes dcSSc patients with < 2 years’ duration (from 1st non-RP) who are recruited at 11 U.S. Scleroderma Centers. Patients participate in detailed baseline and biannual clinical and laboratory assessments that permit characterization of patient characteristics and patient-reported clinical outcomes (PRO) measures.

Results: As of May 2017, of 194 patients, 12 have died (6.2%) at median follow-up of 9.6 months (1-20 months). The characteristics of the 12 deceased patients are described in Table 1. In these deceased patients, 6 (50%) had interstitial lung disease (ILD) on a high resolution computed tomography (HRCT) of the chest with abnormal pulmonary function tests (PFT) [mean FVC% 52.4 (range 29-77); DLCO% 51.3 (24-82)]. Ten of the deceased patients had a baseline ECG at enrollment, and 40% had either arrhythmia or conduction block. Echocardiogram in 11 of the deceased population had a mean ejection fraction of below or at the lower limit of normal 57.5% (24-68%). Almost all patients who had a right heart catheterization (RHC, n=5) had an abnormality of either pulmonary hypertension or an elevated pulmonary capillary wedge pressure. The etiology of death was attributed to SSc in 11 of the patients (64% cardio-pulmonary) and esophageal cancer in one of the patients. The mean Patient Global Assessment for Overall Health was 6.4 (4-10), but extensive PRO was not complete at the last PRESS visit in the deceased patients.

Conclusion: In this early dcSSc cohort, we found a 6.2% mortality at median follow up 9.6 months. When compared to data from a single U.S. cohort (Steen and Medsger 1997-2001), cardio-pulmonary involvement continues to be leading cause of mortality in dcSSc. This underscores the importance of screening dcSSc patients with PFT, echocardiogram, and ECG, and confirmatory testing with HRCT chest and RHC. While PRO is an important component of research, the burden of questionnaire-based assessments on patients with significant disease features needs to be better clarified.
Table 1: PRESS patient characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Number (n=12) of deceased patients</th>
<th>Number (n=182) of alive patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Female</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, mean (range)</td>
<td>58 (24-77)</td>
<td>49 (19-78)</td>
</tr>
<tr>
<td>Disease duration in years, mean (range)</td>
<td>0.8 (0.1-2)</td>
<td>2.5 (0.1-5.2)</td>
</tr>
<tr>
<td><strong>Race:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- African American</td>
<td>1</td>
<td>30</td>
</tr>
<tr>
<td>- White or Caucasian</td>
<td>9</td>
<td>147</td>
</tr>
<tr>
<td>- Other</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>- Unknown</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>ANA positive, N</strong></td>
<td>11</td>
<td>137</td>
</tr>
<tr>
<td><strong>Autoantibody in ANA positive patients:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- RNA polymerase III</td>
<td>6</td>
<td>71</td>
</tr>
<tr>
<td>- Scl70</td>
<td>1</td>
<td>44</td>
</tr>
<tr>
<td><strong>Clinical Features at last PRESS visit:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Modified Rodnan Skin Score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- 0</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>- 1-14</td>
<td>1</td>
<td>79</td>
</tr>
<tr>
<td>- 15-29</td>
<td>5</td>
<td>72</td>
</tr>
<tr>
<td>- 30-39</td>
<td>4</td>
<td>20</td>
</tr>
<tr>
<td>- &gt;40</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>- Modified Rodnan Skin Score, mean (range)</td>
<td>27 (15-46)</td>
<td>25 (0.48)</td>
</tr>
<tr>
<td>- Tension Friction Tests</td>
<td>7</td>
<td>67</td>
</tr>
<tr>
<td>- ILD (HRCT)</td>
<td>6</td>
<td>68</td>
</tr>
<tr>
<td>- FVC%, mean (range)*</td>
<td>64.5 (29-108)</td>
<td>80.5 (35-122)</td>
</tr>
<tr>
<td>- DLCO%, mean (range)*</td>
<td>51.3 (24-82)</td>
<td>67.5 (25-124)</td>
</tr>
<tr>
<td>- Mean pulmonary pressure (mmHg), mean (range)*</td>
<td>31.3 (21-41)</td>
<td>34.6 (14-125)</td>
</tr>
<tr>
<td>- PCWP (mmHg), mean (range)</td>
<td>12.8 (10-16)</td>
<td>11.2 (3-26)</td>
</tr>
<tr>
<td>- CO (L/min), mean (range)</td>
<td>7.1 (5.4-7.92)</td>
<td>6.5 (3-10)</td>
</tr>
<tr>
<td>- CI (L/min), mean (range)</td>
<td>3.9 (3.5-4.8)</td>
<td>3.4 (1.9-4.6)</td>
</tr>
<tr>
<td>- Echocardiogram*, mean (range)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Ejection fraction %</td>
<td>57.5 (24-68)</td>
<td>61.5 (24-75)</td>
</tr>
<tr>
<td>- Small pericardial effusion</td>
<td>1</td>
<td>14</td>
</tr>
<tr>
<td>- Global wall motion abnormality</td>
<td>3</td>
<td>103</td>
</tr>
<tr>
<td>- ECGP*</td>
<td>3</td>
<td>19</td>
</tr>
<tr>
<td>- Conduction defect</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Etiology of Death Determined by PI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Scleroderma Related</td>
<td>11</td>
<td>N/A</td>
</tr>
<tr>
<td>- Progressive ILD</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>- Pulmonary hypertension</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>- Cardiac involvement (due to conduction defect or muscle involvement)</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>- Kidney</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>- Sepsis due to wounds</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Patient Global Assessment Overall Health</td>
<td>6.4 (4-10)</td>
<td>4.0 (0-10)</td>
</tr>
</tbody>
</table>

*HRCT (n=10 dead, n=124 alive); Echocardiogram within 6 months of last visit (n=11 dead, n=132 alive), PFT within 6 months of last visit (n=12 dead, n=187 alive), Baseline ECG (n=10 dead, n=85 alive).

Disclosure: T. M. Frech, None; S. Assassi, None; E. J. Bernstein, None; F. V. Castelino, NIH, 2; R. T. Domsic, None; J. K. Gordon, None; F. Hant, None; M. Hinchcliff, None; B. LaSalle, None; V. K. Shanmugam, Multiple, 9; V. D. Steen, None; D. Khanna, Bristol-Myers Squibb, 2,Genentech/Roche, 2,NIH/NIAMS, 2,NIH/NIAID, 2,Patient-Centered Outcomes Research Institute, 2,Scleroderma Foundation, 2,Actelion Pharmaceuticals US, 5,Bayer AG, 5,Cytori, 5,EMD Serono, 5,Genkyotex, 5,Gilead, 5,GlaxoSmithKline, 5,Genentech/Roche, 5,Sanofi-Aventis Pharmaceutical, 5,Seattle Genetics, 5.


Abstract Number: 2666

The Clinical Utility of Flow-Mediated Dilation in Systemic Sclerosis Digital Ulcer Assessment
SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic sclerosis (SSc, scleroderma) patients can have the end-stage vasculopathy manifestation of a digital ulcer (DU). Brachial artery flow mediated dilation (FMD) is an established non-invasive vascular marker of endothelial function in SSc. We hypothesized that FMD could stratify the timeline of DU development and role of vasodilators in management.

Methods: Patients were recruited from our scleroderma center at the time of a routine care visit. All vascular measures were assessed by duplex ultrasound Doppler at baseline and after 6 months follow-up for up to two years. Specifically, resting brachial artery blood flow, shear rate, and diameter and BP cuff induced ischemia, vascular reactivity (peak reactive hyperemia), vascular shear rate (peak hyperemia/area under the curve [AUC]), and FMD (Δmm and %) were measured for 2 min after cuff release. We examined FMD variables in SSc patients that (1) had a DU at baseline, (2) developed a new DU, and (3) never had DU in up to 24 months of follow-up. General linear models were used to compare these continuous variables between SSc patients with and without DU controlling for the days from baseline FMD measurement and use of any vasodilatory drug.

Results: FMD was determined in 136 SSc patients at baseline and 55 patients in follow-up. Baseline SSc clinical features are described in Table 1. In those patients with follow-up FMD, 10 (48%) with a baseline DU healed over the course of two years. The timeline for healing for initial DU patients included 3 within 12 month and 4 within 18 months. Seven of 115 patients with no DU at baseline developed a DU at the time of repeat FMD measures. Resting blood flow differed between patients with healed DU and developed DU, in that they had higher blood flow at baseline (p=0.03), which correlated to vasodilator use. When FMD variables were analyzed over time, resting arterial wall shear rate increased over time for all patients and was lowest for those with no DU. The difference in the DU groups (developed and no DU) trended towards significance (p=0.10, Figure 1).

Conclusion: FMD applied to routine clinical care of SSc patients identified that DU trial length may require up to 18 months to document complete healing. FMD variables may be important secondary outcome measures in DU trials. Higher resting blood flow in individuals with a healed DU and those who never had a DU supports the role of vasodilators for this indication. The role of therapeutics that reduce vascular shear rate may be an opportunity for both SSc-DU prevention and healing.

Figure 1: Follow-up vascular shear rate of SSc patients (mean, SEM) that never had DU (n=41) versus developed DU (n=7).
Disclosure: T. M. Frech, None; D. Machin, None; M. Murtaugh, None; A. Donato, None.


Abstract Number: 2667

The Association between Two Non-Invasive Methods for the Assessment of Severity of Gastrointestinal Involvement and Malnutrition in Systemic Sclerosis: Self-Reported Questionnaires and Nail Fold Video-Capillaroscopy

Yasemin Yalçinkaya1, Zeynep Erturk1, Ozlem Pehlivan2, Ali Uグル Unal3, Pamir Atagunduz1, Haner Direskeneli1 and Nevsun Inanc1, 1Departement of Internal Medicine, Division of Rheumatology, Marmara University, Istanbul, Turkey, 2Department of Internal Medicine, Division of Rheumatology, Umraniye Education and Research Hospital, Istanbul, Turkey, 3Department of Internal Medicine, Division of Rheumatology, Marmara University, Istanbul, Turkey

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster III
Background/Purpose: Gastrointestinal (GI) system involvement is commonly seen in systemic sclerosis (SSc) up to 90% of the patients during disease duration and one of the substantial causes of morbidity and mortality in SSc. We aimed to investigate self-reported questionnaires and capillaroscopy in terms of severity of GI involvement and malnutrition in SSc patients.

Methods: GI involvement and nutrition status were evaluated by UCLA SCTC GIT 2.0 questionnaire and ‘malnutrition universal screening tool (MUST) in SSc patients fulfilling ACR/EULAR classification criteria (2013). Simultaneously; early, active and late scleroderma patterns (Cutolo et al.) were determined qualitatively and capillary number (CN) was calculated per linear mm at distal row quantitatively by using nail fold video-capillaroscopy (NVC) in all patients.

Results:

In 126 SSc patients (115 female) with the mean age of 50±12, duration of non-Raynaud symptom of 10±9 years and follow-up of 53±58 months; diffuse cutaneous form was found to be 25% (n=32), anti-Scl70 positivity 32% (n=37), telangiectases 81%(n=102), digital ulcers 44% (n=55), lung disease 40% (n=49) and flexion contractures 15% (n=18). Of the NVC patterns, early was found in 31 (25%), active was in 18 (14%), late was in 68 (54%) and normal in 9 (7%). The scores of skin, telangiectasia, disease activity and UCLA SCTC GIT 2.0 total, reflux and distension items were shown to be higher in patients with late NVC pattern (table-1). The patients with CN≤5 were found to be have higher scores of UCLA SCTC GIT 2.0 total, reflux, distension, soilage, social items and MUST (p<0,001, p<0,001, p=0,001, p=0,002 and p=0,002) and scores of skin, telangiectasia, disease activity and severity (p<0,001, p<0,001, p=0,001 and p=0,003). Of the patients with MUST score of ≥1 (n=18), 16 had late, 1 early NVC pattern and 1 normal pattern.

Conclusion: This SSc cohort predominantly had vascular manifestations. Late scleroderma pattern and decreased capillary density was found to be related to severe GI complaints, disease activity, skin severity and telangiectases. Undernutrition was also frequently seen in patients with late pattern. NVC might be useful to predict the severity of GI and malnutrition.

Table-1: The scores of disease activity and severity and UCLA SCTC GIT 2.0 in SSc patients

<table>
<thead>
<tr>
<th></th>
<th>NVC (normal)</th>
<th>NVC (early)</th>
<th>NVC (active)</th>
<th>NVC (late)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modified Rodnan skin score</td>
<td>2,2±2,5</td>
<td>3,9±4,6</td>
<td>7,3±5,9</td>
<td>9,6±6,9</td>
<td>P&lt;0,001</td>
</tr>
<tr>
<td>Telangiectasis score</td>
<td>1,1±1,6</td>
<td>2,4±2,6</td>
<td>4,9±2,5</td>
<td>5,6±3,4</td>
<td>P&lt;0,001</td>
</tr>
<tr>
<td>Disease activity score</td>
<td>1,1±0,7</td>
<td>0,7±0,9</td>
<td>1,2±1,0</td>
<td>1,6±1,4</td>
<td>P=0,010</td>
</tr>
<tr>
<td>Disease severity score</td>
<td>3,3±1,2</td>
<td>4,5±5,9</td>
<td>4,7±2,2</td>
<td>5,9±2,7</td>
<td>NS</td>
</tr>
<tr>
<td>UCLA SCTC GIT 2.0-total</td>
<td>0,08±0,11</td>
<td>0,09±0,12</td>
<td>0,21±0,24</td>
<td>0,33±0,31</td>
<td>P&lt;0,001</td>
</tr>
<tr>
<td>reflux</td>
<td>0,26±0,36</td>
<td>0,35±0,39</td>
<td>0,57±0,50</td>
<td>0,85±0,65</td>
<td>P&lt;0,001</td>
</tr>
<tr>
<td>Distension</td>
<td>0,17±0,42</td>
<td>0,06±0,20</td>
<td>0,20±0,41</td>
<td>0,50±0,84</td>
<td>P=0,015</td>
</tr>
<tr>
<td>soilage</td>
<td>0±0</td>
<td>0±0</td>
<td>0±0</td>
<td>0,18±0,49</td>
<td>NS</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>0±0</td>
<td>0,10±0,40</td>
<td>0,31±0,62</td>
<td>0,23±0,52</td>
<td>NS</td>
</tr>
<tr>
<td>social functioning</td>
<td>0,04±0,11</td>
<td>0±0</td>
<td>0,06±0,19</td>
<td>0,14±0,31</td>
<td>NS</td>
</tr>
<tr>
<td>emotional wellbeing</td>
<td>0,02±0,07</td>
<td>0±0</td>
<td>0,13±0,30</td>
<td>0,10±0,28</td>
<td>NS</td>
</tr>
<tr>
<td>constipation</td>
<td>0,22±0,46</td>
<td>0,15±0,42</td>
<td>0,18±0,34</td>
<td>0,15±0,36</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS=not significant

Disclosure: Y. Yalçinkaya, None; Z. Erturk, None; O. Pehlivan, None; A. U. Unal, None; P. Atagunduz, None; H. Direskeneli, None; N. Inanc, None.
Abstract Number: 2668

Responsiveness of University of California Los Angeles Scleroderma Clinical Trial Consortium (GIT2.0) and Intestinal Visual Analogue Scale to Change in Systemic Sclerosis Patients

Yossra A Suliman1, Suzanne Kafaja2, Mohamed Alemam3, yasser Shaweesh4, Kasra Tavakoli5 and Daniel E. Furst6,
1Rheumatology and Rehabilitation dept., Rheumatology and Rehabilitation dept. Assiut university hospital, Assiut Egypt, Assiut, Egypt, 2Department of Internal Medicine, University of California Los Angeles, David Geffen School of Medicine, Division of Rheumatology, Los Angeles, CA, 3Clinical Pathology and Laboratory Medicine Department, Assistant Lecturer, Qena, Egypt, 4John H. Stroger Jr. Hospital of cook county, chicago, IL, 5Department of medicine, university of California Los Angeles, Los Angeles, CA, 6David Geffen School of Medicine at UCLA, Los Angeles, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Gastrointestinal tract (GIT) involvement in systemic sclerosis (SSc) is the most common internal organ involvement. Among the few validated patient-reported outcome measures for GI involvement are the University of California Los Angeles Scleroderma Clinical Trial Consortium (GIT2.0) and intestinal visual analogue scale (GI-VAS) The latter is a component of the Scleroderma Health Assessment Questionnaire[SHAQ]). Our aim was to evaluate the comparative responsiveness of these outcome measures when pts are treated and to evaluate the correlation between UCLA-SCTC GIT 2.0 and GI-VAS in our SSc population.

Methods:
115 SSc pts with two or more consecutive visits were enrolled in our study. Values of UCLA-SCTC GIT 2.0 and GI-VAS were completed by all patients at both visits.; any change in GI medication at the baseline visit was reported. ). UCLA-SCTC GIT2.0 includes 34 questions in 7 domains (reflux, distension, soilage, diarrhea, social function, emotional wellbeing and constipation). GI-VAS is a 100 mm VAS that asks the patient, how did GI symptoms interfere with patient function. Paired T test was used to detect the change between the two visits in both GIT 2.0 and GI-VAS. Pearson correlation was used to correlate tests at base line.

Results:
Ninety eight (85%) of SSc pts were females, Mean age 52 yrs (SD ± 12.9); median disease duration 7 (4-11), diffuse subtype 57 pts (50%), (47%), median baseline GIT 2.0 is 0.3 (0.1-0.7) and median baseline GI-VAS 0.8 (0-4.1) table 1.

Out of the 115 pts, only 41 pts needed a change of GI medication at base line visit (37.0%). A statistically significant difference was noted when comparing GIT scores before and after adding a new GI treatment (p=0.006, 95% CI= .05956 to 0.29258). On the other hand, GI-VAS did not show statistical differences between baseline visit and follow-up after adding medications (p=0.963, 95% CI =-0.937 to 0.89588).Baseline correlation between GIT2.0 (total score) and GI-VAS were (r= 0.657 ) moderate.
Conclusion:
Both UCLA-SCTC GIT2.0 and GI -VAS reflect GIT involvement. Unlike the GI-VAS, the UCLA-SCTC GIT2.0 was responsive to treatment. These results also, shows that both tests may represent different aspects of GI involvement and might be considered separately in clinical evaluation of GI system in SSc patients. Discussion: More patients are to be included in this cohort, as the pts had low GIT scores (few symptoms), multiple GI treatments were used and this is a retrospective evaluation of prospectively gathered data.

Table 1: Baseline characteristics of systemic sclerosis patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean(SD, Range), number (percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>52 (12.9)</td>
</tr>
<tr>
<td>females</td>
<td>98 (85%)</td>
</tr>
<tr>
<td>Body mass index (BMI), mean (SD)</td>
<td>24.1 (5.7)</td>
</tr>
<tr>
<td>Disease duration</td>
<td>7 (4-11)</td>
</tr>
<tr>
<td>Intestinal GI- VAS</td>
<td>0.8 (0-9.5)</td>
</tr>
<tr>
<td>UCLA GIT 2.0</td>
<td>0.3 (0.1-2.15)</td>
</tr>
<tr>
<td>Interstitial lung disease</td>
<td>66 (57%)</td>
</tr>
<tr>
<td>FVC</td>
<td>89% (23.2)</td>
</tr>
<tr>
<td>Pulmonary artery hypertension</td>
<td>19 (16%)</td>
</tr>
</tbody>
</table>

Disclosure: Y. A. Suliman, None; S. Kafaja, None; M. Alemam, None; Y. Shaweesh, None; K. Tavakoli, None; D. E. Furst, None.


Abstract Number: 2669

Microvascular Flow Assessed By Dynamic Optical Coherence Tomography: First Non-Invasive Quantitative Outcome Measure of Microvascular Disease in Systemic Sclerosis

Giuseppina Abignano\textsuperscript{1,2}, Alexandra Daniel\textsuperscript{1,3}, Lorraine Green\textsuperscript{1,3}, Sookhoe Eng\textsuperscript{1,3}, Paul Emery\textsuperscript{1,3} and Francesco Del Galdo\textsuperscript{1,3}, \textsuperscript{1}Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom, \textsuperscript{2}Rheumatology Department of Lucania, San Carlo Hospital of Potenza and Madonna delle Grazie Hospital of Matera, Rheumatology Institute of Lucania (iReL), Potenza, Italy, \textsuperscript{3}Leeds Musculoskeletal Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster III
Session Type: ACR Poster Session C
Background/Purpose: Virtual skin biopsy by Optical Coherence Tomography (OCT) has been proposed as quantitative outcome measure of fibrosis in Systemic Sclerosis (SSc). Dynamic OCT (D-OCT) is a newly developed technology that allows quantification of blood flow in vivo during OCT scans. Here we aimed to determine the validity of skin D-OCT as outcome measure of the skin microvascular disease, employing as comparator nailfold video-capillaroscopy (NVC) capillary patterns in SSc patients, and as clinical gold standard the presence of digital ulcers (DU).

Methods: One hundred and four subjects were enrolled in this study in 2 independent cohorts. In cohort 1 (Criterion Validity), 40 SSc patients fulfilling the ACR/EULAR 2013 criteria with different NVC pattern (10 for each normal/non-specific, early, active, ad late NVC pattern) and 10 healthy volunteers (HV) underwent nailfold D-OCT. In cohort 2 (Face/Content Validity) 36 SSc patients with (18) or without (18) DU and 18 patients with Raynaud's phenomenon (RP) and SSc specific ANA, who did not fulfill ACR/EULAR 2013 criteria (SRP group) underwent D-OCT of index and middle fingers on the proximal phalanx. Microvascular flow (MVF) was analyzed using the proprietary software from Michelson Diagnostics Ltd.

Results: Nailfold D-OCT allowed visualization of the corresponding SSc patterns seen at NVC. Furthermore, within D-OCT images, MVF measurements were significantly different between HV and SSc patients with any specific capillary pattern (0.16±0.02 vs 0.10±0.01, p=0.0028) and between SSc patients without and with specific capillary pattern (0.14±0.01 vs 0.10±0.01, p=0.02). Concordantly, MVF was significantly lower in patients displaying capillary loss as main feature compared with those with remarkable angiogenesis (p=0.03). Skin D-OCT showed a median MVF significantly different among the 3 groups: 0.134 (DU) vs 0.153 (no DU) vs 0.167 (SRP) (p<0.0001), and in the DU vs no DU (p<0.001) or vs SRP (p<0.001). Further, DU patients on Sildenafil (n=6) had a significantly higher MVF than DU patients on no Sildenafil (p<0.01).

Conclusion: MVF assessed by D-OCT shows face/content and criterion validity as biomarker of skin microvascular disease in SSc. Future longitudinal studies are needed to evaluate its sensitivity to change over time.

Disclosure: G. Abignano, None; A. Daniel, None; L. Green, None; S. Eng, None; P. Emery, Pfizer, MSD, Abbvie, BMS, UCB, Roche, Novartis, Samsung, Sandoz, Eli Lilly and Company, 5; F. Del Galdo, None.


Abstract Number: 2670

Trigeminal Neuralgia in Systemic Sclerosis

Nancy Maltez1, Marie Hudson2, Yves Troyanov3, May Choi4, Mianbo Wang5, Marvin J. Fritzler6, Murray Baron7 and Doug Smith8. 1Rheumatology, The Ottawa Hospital, Ottawa, ON, Canada, 2Division of Rheumatology, Jewish General Hospital, Lady David Institute for Medical Research, Montreal, QC, Canada, 3Rheumatology, Hôpital du Sacré-Coeur de Montréal, Montréal, QC, Canada, 4University of Calgary, Calgary, AB, Canada, 5Lady Davis Institute for Medical Research, Montreal, QC, Canada, 6Medicine, University of Calgary, Calgary, AB, Canada, 7Rheumatology, McGill University, Jewish General Hospital, Montreal, QC, Canada, 8Division of Rheumatology, Department of Medicine, The Ottawa Hospital - University of Ottawa, Ottawa, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Trigeminal neuralgia (TN) is characterized by pain and spasms affecting one or more divisions of the fifth cranial nerve. Of note, TN is one of the peripheral nervous system manifestations of systemic sclerosis (SSc), reported to be present in approximately 4% of patients. Proposed pathophysiologic mechanisms in this context have included nerve entrapment and compression from mandibular bone resorption, a phenomenon seen in SSc due to pressure ischemia from overlying tight sclerotic skin compromising blood supply to the bone. Previous studies of TN identified an association with overlap syndromes notably in patients with inflammatory myositis (IM), arthritis and interstitial lung disease (ILD). It has also been suggested that facial numbness can precede or follow other manifestations of SSc. However, since there is a paucity of evidence concerning TN in SSc, we undertook a nested case-control study to identify associations between SSc and TN in a multi-centered SSc cohort.

Methods:

Data were retrieved from the Canadian Scleroderma Research Group (CSRG) registry, an open cohort of 1652 SSc subjects enrolled since 2004. Subjects with a physician-reported diagnosis of TN were identified at the baseline study visit (prevalent cases) and during follow-up (incident cases). Four SSc subjects without TN and matched to each case on study visit were identified as controls for either prevalent or incident cases. Sociodemographic, clinical and serological characteristics of cases and controls were compared. P values < 0.05 were considered statistically significant.

Results:

43 (43/1652; 2.6%) prevalent and 36 incident (36/6193 total person-years follow-up; incidence rate 5.8 per 1000 person-years) TN cases were identified and matched to 144 and 172 controls, respectively. There were no significant differences in mean age, gender distribution and mean disease duration between cases and controls. Compared to controls, prevalent cases had more IM (24.4% vs. 5.2%, p<0.001) and arthritis (46.5% vs. 30.2%, p=0.043). Similarly, incident cases also had more IM (19.4% vs. 6.3%, p=0.033) and arthritis (50.0% vs. 16.2%, p<0.001) compared to controls. There was a trend towards more ILD in prevalent (32.6% vs 23.8%, p=0.241) and incident (55.6% vs 40.6%, p=0.105) cases compared to controls. U1RNP was numerically more frequent in cases versus controls (prevalent cases vs controls 9.4% vs 5.4%; incident cases vs controls 17.1% vs 5.8%). Pm/Scl antibodies were infrequent and similar in prevalent (2.9% vs 3.5%) and incident (5.9% vs 5.7%) cases compared to controls.

Conclusion:

This study provides novel evidence for a syndrome linking TN, IM, arthritis and possibly ILD. We propose that TN could be a consequence of active inflammation and represent a sign of disease activity in SSc.

Disclosure: N. Maltez, None; M. Hudson, None; Y. Troyanov, None; M. Choi, None; M. Wang, None; M. J. Fritzler, None; M. Baron, None; D. Smith, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/trigeminal-neuralgia-in-systemic-sclerosis

Abstract Number: 2671

Bosentan in Scleroderma Renal Crisis: A National Open Label Prospective Study

Alice Bérezné1,2, Hendy ABDOUL3, Alexandre Karras4, Isabelle Marie5, Antoine Huart6, Maxence Ficheux7, Viviane Queyrej8, Bernard Imbert9, Xavier Puéchal1, Arnaud Hot10, Boris Bienvenu11, Elisabeth Diot12, Bruno Moulin13,
First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Scleroderma renal crisis (SRC), a life-threatening complication of systemic sclerosis (SSc), arises despite therapy combining an angiotensin-converting–enzyme inhibitor (ACEI) and/or dialysis. Endothelin-1 (ET-1), a powerful endothelium-derived vasoconstrictor peptide, has been implicated in SSc pathogenesis. Plasma ET-1 levels are elevated in SSc patients with SRC. Bosentan, a non-selective ET-1–receptor antagonist, was approved to treat pulmonary arterial hypertension and prevent SSc ischemic digital ulcers. Those findings suggested that bosentan could have therapeutic benefits on other vascular manifestations of SSc, particularly SRC. This open-label national prospective study evaluated the efficacy and tolerance of bosentan for 6 months combined with an ACEI and/or dialysis on renal and overall survival of SSc patients with SRC.

Methods:

SRC was defined as rapidly progressive oliguric renal insufficiency and/or rapidly progressive arterial hypertension. All patients received Bosentan 62.5 mg twice daily for 4 weeks and 125 mg twice daily thereafter for 5 months, in addition to the usual recommended treatments. The primary end-point was kidney survival at 12 months. Secondary endpoints were patient survival and Bosentan side effects at 12 months.

Results:

Between March 2011 and April 2014, 16 patients (10 (62.5%) females; median age 65.3 [range 46.3–71.3] years) were enrolled. Twelve (75%) patients had diffuse SSc, 1 (6.3%) had limited cutaneous SSc and 3 (18.8%) had limited SSc. Four (25%) had pulmonary fibrosis, 3 (18.8%) left ventricular insufficiency and 3 (18.8%) severe bowel involvement. Renal biopsies obtained from 14 patients showed specific vascular SRC lesions. Prior to SRC, 11 (68.8%) patients had taken corticosteroids and 6 (37.5%) were taking an ACEI for hypertension. SRC recurred in 1 patient 2 years after kidney transplantation. Four (25%) patients had normotensive SRC. Seven (43.8%) patients achieved the primary end-point of dialysis-free status. Only 9 (56.3%) patients were alive at 12 months. Seven (43.8%) patients were dialyzed, 6 of them within the first 10 days of inclusion. One patient was dialyzed at month 4 for multivisceral failure and septic shock. No patients on dialysis at baseline came off dialysis. One patient developed an SRC relapse at 6 months. Renal function of dialysis-free survivors did not improve on bosentan, with a mean [range] estimated glomerular filtration rate at entry of 22 [22–49] vs. 16 [11.5–23.5] ml/min/1.73 m² at SRC onset. Seven (43.8%) patients died; 4 (57.1%) of those deaths were not SSc-related. The 3 SSc-related deaths resulted from severe organ involvement (lung fibrosis, intestinal involvement or associated myositis). No patient suffered serious adverse effects requiring bosentan withdrawal.
Conclusion:

Bosentan does not seem to improve renal outcomes and survival is no better than in historical series. However, the high non-SSc–attributable mortality makes drawing any definitive conclusion difficult. Further investigations are needed.


Disclosure: A. Bérezné, Actelion Pharmaceuticals US, 9; H. ABDOUN, None; A. Karras, None; I. Marie, None; A. Huart, None; M. Ficheux, None; V. Queyrel, None; B. Imbert, None; X. Puéchal, None; A. Hot, None; B. Bienvenu, None; E. Diot, None; B. Moulin, None; T. Quémeneur, None; J. E. Kahn, None; L. Mouton, None; L. Guillevin for the French Vasculitis Study Group, None.


Abstract Number: 2672

Perceived Barriers to Mental Health Care Among Patients with Systemic Sclerosis: A Qualitative Study

Karima Becetti, Laura Robbins, Carol Mancuso, Jessica K. Gordon and Robert F. Spiera. 

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud’s – Clinical Aspects and Therapeutics Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic Sclerosis (SSc) is characterized by disfigurement, morbidity, and increased mortality. The diagnosis carries significant psychosocial impact on patients, and many suffer with depression, anxiety, and body image distress. Interventions to address this impact are recommended as an essential aspect of care. However, previous studies identified mental health care as an unmet need for many SSc patients. Using a qualitative approach, this study aimed to evaluate perceived barriers to mental health care in SSc.

Methods: A qualitative study was conducted in a sample of consecutive SSc patients presenting to a single center. After obtaining informed consent, one-to-one interviews were conducted in-person using open-ended questions on individual patients’ experience with SSc and barriers to mental health care. Demographic and clinical data were obtained to characterize the study sample. A grounded theory approach was used to code interview transcripts and identify emergent concepts, categories, and themes. Interviews were continued until data saturation was reached.

Results: Twenty SSc patients with a median (range) age of 56.5 years (21-74) and disease duration of 4.5 years (1-34) were interviewed. 100% were female, 55% were white, 60% had private insurance, and 70% had diffuse SSc. Patients reported multiple psychological symptoms in association with SSc including sadness, anxiety, anger, uncertainty, and suicidal ideations at the time of diagnosis. Interview analysis identified four major themes relating to barriers to mental health care; patient-related, physician-related, system-related, and disease-specific factors (Figure 1). Patient-related factors included stigma about mental illness, avoidance of symptoms, fear of being vulnerable or burdening others, fear of other’s reaction, and lack of need due to available coping mechanisms. Lack of physicians’ rapport, empathy, and interest in emotional symptoms, and their subspecialty (non-mental health) emerged as barriers. System-related factors
included high cost, lack of insurance, division within the healthcare system, and limited access and appointment time. Patients identified disease severity, physical limitations due to SSC, poor understanding of disease process, paucity of effective treatments, lack of SSC-specialized mental health services, and the numerous SSC-related appointments as barriers. The heterogeneity of SSC, variable patient experiences, and fear of contact with other patients with more aggressive disease were barriers to SSC group therapy.

**Conclusion:** In addition to the known barriers to mental health care such as access, cost, and stigma, SSC patients also identified disease-specific barriers. Identifying, understanding, and addressing these barriers are important for the effective dissemination of psychosocial interventions in this unique patient population.

**Figure 1.** Conceptual framework

---

**Disclosure:** K. Becetti, None; L. Robbins, None; C. Mancuso, None; J. K. Gordon, Corbus Pharmaceuticals, 2, Cumberland Pharmaceuticals, 2, Bayer Pharmaceuticals, 2; R. F. Spiera, Roche-Genetech, 2, GSK, 2, BMS, 2, Celgene, 2, Boehringer Ingelheim, 2, Cytori, 2, Chemocentryx, 2, Corbus Pharmaceuticals, 2, Prism, 2, Roche-Genetech, 5, GSK, 5, Boehringer Ingelheim, 5.


**Abstract Number:** 2673

**Real-Life Treatment Strategies for Systemic Sclerosis According to Experts**

Andreu Fernández-Codina$^{1,2}$, Kyle M Walker$^{3}$ and Janet E. Pope$^{4}$, $^{1}$Rheumatology, University of Western Ontario, London, ON, Canada, $^{2}$Systemic Autoimmune Diseases, Hospital Universitari Vall d'Hebron, Barcelona, Spain, $^{3}$Dept. of Medicine, Division of Rheumatology, University of Ottawa, Ottawa, ON, Canada, $^{4}$University of Western Ontario, London, ON, Canada

**First publication:** September 18, 2017

**SESSION INFORMATION**
Background/Purpose:

Second line treatment options for Systemic Sclerosis (SSc) are limited, and scarce data are available for choosing the order of treatment. The aim of this study is to update the SSc treatment algorithms obtained in 2012\(^1\), based on SSc experts’ daily practice.

Methods:

An initial survey was designed based on the 2012 algorithms. The survey asked experts whether they agreed with the 2012 algorithms or not, and which changes should be considered. The questionnaire was completed by 62 of 168 surveyed (67% response) between August and October 2016.

Results:

For scleroderma renal crisis (SRC), there was 65% to 69% agreement with the previous algorithms (1st line angiotensin converting enzyme inhibitors [ACEI], 2nd and 3rd adding: calcium channel blockers [CCB] or angiotensin receptor blockers [ARB], and 4th alpha-blocker). In mild pulmonary arterial hypertension (PAH), only 45% of the experts agreed with the old algorithm. The majority suggested first phosphodiesterase 5 inhibitors (PDE5i) or endotelin receptor antagonists (ERA) plus PDE5i, then prostanoids. In severe PAH, 65% agreed with the preexistent scheme (1st prostanoids, 2nd ERA plus PDE5i, 3rd ERA plus prostanoids). For mild Raynaud’s phenomenon (RP) 66% agreed with the previous algorithm (1st CCB, 2nd adding PDE5i, 3rd ARB or switching to another CCB, 4th prostanoids). Regarding severe RP, 52% agreed with previous (1st CCB, 2nd adding PDE5i, 3rd ERA, 4th prostanoids). Conversely, 60% of the experts did not agree with the prior active digital ulcer (DU) treatment, suggesting 1st CCB, 2nd PDE5i, 3rd prostanoids. For interstitial lung disease (ILD), for induction only 24% agreed with the older proposal. There was a 65% agreement on ILD maintenance. Both algorithms are shown in figure 1. For skin involvement, agreement for patients with a modified Rodnan skin score (mRSS) of 10 was 57% (1st methotrexate [MTX], 2nd MMF); if the mRSS was 24, 32% suggested 1st MMF, 2nd MTX; and mRSS 32, 36% chose 1st MTX, 2nd MMF, 3rd IV CYP, 4th autologous stem cell transplantation (ASCT). In inflammatory arthritis 45% agreed with the previous algorithm, whereas others suggested 1st MTX, 2nd low dose steroids, 3rd hydroxychloroquine, 4th rituximab or tocilizumab.

Conclusion:

There remains some disagreement for 2nd line treatment of SSc. Combination of PDE5i and ERA are prescribed now in mild PAH treatment. Prostanoids have been incorporated as 3rd line agents in active DU treatment. MMF is the new 1st line treatment for ILD induction and rituximab the 3rd. IV CYA and ASCT were recommended as 3rd and 4th line treatments in patients with severe skin involvement. Rituximab and tocilizumab have been incorporated into inflammatory arthritis treatment. This can guide therapy in SSc.

Reference:

The Association between the Extent of Skin Thickness and Organ Involvement, Function and Quality of Life in Early Diffuse Cutaneous Systemic Sclerosis

Janet E. Pope¹, Murray Baron², Tatiana Nevskaya³, Carl Baxter⁴ and Dena Ramey⁵, ¹Medicine, Division of Rheumatology, Schulich School of Medicine and Dentistry, Western University, London, ON, Canada, ²Rheumatology, McGill University, Jewish General Hospital, Montreal, QC, Canada, ³Rheumatology Division, St. Joseph’s Health Care London, London, ON, Canada, ⁴Global Outcomes Research, MSD Ltd, Hoddesdon, United Kingdom, ⁵Epidemiology, Merck & Co., Upper Gwynedd, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: To estimate whether severity of skin thickness is associated with disease severity, function, quality of life (QoL) and progression of internal organ involvement over 12 months in early diffuse cutaneous systemic sclerosis (dcSSc).

Methods: We included dcSSc patients from the Canadian Scleroderma Research Group (CSRG) database with disease duration of ≤5 years from the onset of first non-Raynaud’s symptom at initial visit and 1-year follow-up (FU). We assessed severity of skin involvement with the modified Rodnan skin score (mRSS); internal organ involvement with the Medsger organ severity scores; global measures of disease status with patient- and physician-reported 11 point numerical rating scales (NRS); disease activity with the European Scleroderma Study Group (EScSG) activity index; function with
the HAQ and S-HAQ 11 point NRS scales; and QoL with the SF-36. Bivariate, ANOVA, linear and logistic regression analyses were used to study the associations between mRSS and outcomes, adjusted for potential confounding factors.

**Results:** At baseline (N=204, 74% female, mean age 51±12 yrs, disease duration 2.1±1.3 yrs), higher mRSS was significantly associated with worse total disease severity (Medsger’s score without skin component, physician and patient global NRS, S-HAQ overall disease rating), functional disability (HAQ-DI) and worse QoL (SF-36 PCS) (p<0.0001 for all). Higher mRSS was also associated with the presence and severity of tendon involvement (p<0.0001), severity of gastrointestinal disease (p=0.021), S-HAQ digital ulcer severity (p=0.008) and S-HAQ intestinal problems (p=0.008) by adjusted regression analysis.

At 1-year FU visit (N=174, 74% female, mean age 51±12 yrs, disease duration 2.1±1.3 yrs) we found a significant reduction in mRSS (22.51±9.27 vs 19.42±10.45, p=0.006). There was also a decrease in disease activity by both EScSG-activity index (3.06±1.8 vs 2.41±1.8, p=0.003) and physician-assessed disease activity on NRS scale (4.61±2.37 vs 3.52±2.17, p<0.0001). There were no changes in other measures of disease characteristics.

We also examined the associations between baseline mRSS and outcomes at 1-year FU visit using adjusted regression analysis. Higher baseline mRSS was associated with worse HAQ-DI (p=0.0001) and SF-36 PCS (p=0.0001), higher total Medsger’s severity score (p=0.014), physician-assessed disease damage (p=0.001), severity (p=0.008) and joint involvement (p=0.0001) at FU. Baseline mRSS was not associated with presence/severity of kidney, lung or heart disease at baseline or 1-year FU visit, nor predictive of new/progression of organ involvement over time.

**Conclusion:** Greater skin involvement at baseline was associated with worse joint and GI involvement, worse function and QoL. Baseline mRSS also predicted function, severity of joint involvement and QoL at 1-year FU. No association between skin involvement and burden of other organ-based complications was found, but follow-up was limited to 1-year in this analysis.

**Disclosure:** J. E. Pope, AbbVie, Amgen, Bayer, BMS, Celtrion, Eli Lilly and Company, Merck, Novartis, Pfizer, Roche, UCB, S.Amgen, Bayer, BMS, GSK, Merck, Novartis, Pfizer, Roche, UCB, 5,Amgen, Bayer, BMS, GSK, Merck, Novartis, Pfizer, Roche, UCB, 2; M. Baron, None; T. Nevskaya, None; C. Baxter, MSD Ltd, 3; D. Ramey, Merck and Co., Inc., 3.


**Abstract Number:** 2675

**Lung Transplant Trends in Patients’ with Systemic Sclerosis Using UNOS (United Network Organ Sharing) Database from 2000-2014**

Osman Bhattiy, 1 Rouhin Sen1, Douglas Moore2 and Joseph Nahas3, 1Department of Medicine, CHI Creighton University Medical Center, Omaha, NE; 2Department of Pulmonary/Critical Care, CHI Creighton University Medical Center, Omaha, NE; 3Department of Rheumatology, CHI Creighton University Medical Center, Omaha, NE

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Tuesday, November 7, 2017
**Session Title:** Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster III
**Session Type:** ACR Poster Session C
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**
Systemic sclerosis (SSc) is a chronic autoimmune disease once characterized by high mortality rates now with better outcomes. Pulmonary disease has overtaken renal failure as the leading cause of death. Unfortunately medical therapies are still lacking in this regard and lung transplantation ultimately becomes the most viable option. For many years these patients were not offered lung transplants due to the perception that they would do poorly. In 2006 the International Society of Heart and Lung Transplantation (ISHLT) endorsed Lung transplant (LT) as an option for SSc although many programs still considered SSc a contraindication due to concerns of poor allograft function and presumed low patient survival due to the extra pulmonary organ involvement. Since then retrospective cohort studies [1] have shown survival data post transplant very similar to other similar processes i.e IPF and IPAH which have well-established indications for lung transplant and acceptable outcomes. The question remains if this new literature is resulting in more patients with systemic sclerosis being waitlisted for or actually undergoing transplant since for those that are not mortality is high.

Methods:

We looked retrospectively at all patients with a scleroderma, scleroderma – restrictive, and scleroderma – pulmonary hypertension diagnosis within The United Network Organ Sharing Database from the years 2000 to 2014. This database captures the lung transplants in the United States including those that are waitlisted. The diagnoses above will be used to trend the rates of patients with SSc being waitlisted and undergoing transplants from 2000-2014.

Results:

The data shows that since the year 2000 the percent of patients on the UNOS waitlist and those actually undergoing lung transplantation with a diagnosis of systemic sclerosis has risen. Percent of patients in 2000 with SSc on the waitlist was .29 percent which increased to 2.54 percent in 2014. Percent of patients with SSc who received lung transplant was zero in 2000 increasing to 1.67 in 2014.

Conclusion:

Since the ISHLT endorsed LT as an option for SSc the number of patients with this diagnosis make up a higher proportion of those being waitlisted and undergoing transplant. As data continues to show that these patients do better than what was once believed, efforts should focus on assessing clinical phenotypes and investigating how this may influence not only waitlisting itself, but time to transplant and other outcomes such as mortality.


Disclosure: O. Bhatti, None; R. Sen, None; D. Moore, None; J. Nahas, None.
Reduction of DLco and FVC in Patients with GERD and Systemic Sclerosis

Rodrigo Aguila Maldonado¹, Pierina Sansinanea², Claudia Elizabeth Pena¹, Ana Carolina Costi¹, Ariel Vulcano², Adriana Testi², Mariana Pera³, Lucila Garcia², Valeria Arturi³, Viviana Nagua² and Mercedes Garcia¹, ¹Rheumatology, HIGA General San Martin La Plata, La Plata, Argentina, ²Rheumatology, HIGA General San Martin La Plata, la plata, Argentina, ³HIGA General San Martin La Plata, la plata, Argentina

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Esophageal involvement is common in Systemic Sclerosis (SSc). It is estimated to occur in 70-90% of patients. Esophageal motor dysfunction is characterized by hypotonia of lower esophageal sphincter (LES) and mild peristalsis or aperistalsis in 2/3 of the esophagus. There is evidence that interstitial lung disease (ILD) and pulmonary fibrosis in SSc are associated with episodes of microaspirations secondary to gastroesophageal reflux disease (GERD).

The aim of this study was to determine if GERD is associated with ILD in SSc patients.

Methods: An observational retrospective cohort study was conducted during the period 1983-2016 in a single hospital centre. Diagnosis of GERD was established by typical clinical symptoms of heartburn and regurgitation. Esophageal manometry was performed to evaluate motility and was classified as: hypotensive LES (<10mmHg) and ineffective or absence of peristalsis at the distal esophagus. Pulmonary involvement was performed by high resolution computed tomography. Pulmonary function tests were performed with carbon monoxide diffusing capacity (DLCO) and forced vital capacity (FVC). Demographic, serological, clinical, and respiratory functional tests were analyzed. For quantitative and qualitative variables, Student's T, Mann-Whitney, and Chi-2 were used, respectively. The hazard ratio values were obtained with a 95% confidence interval. Values of p≤0.05 were considered statistically significant.

Results: 125 patients with SSc were included, of whom 91 (72.8%) had GERD, with female predominance in both groups. Comparatively between the groups that presented GERD and those that did not, the age at diagnosis was similar and the time of evolution of the disease was 7 years vs 2 (p <0.001) respectively. In terms of disease subtypes, no statistically significant differences were found between patients with GERD and those who did not. Among the clinical characteristics analyzed, the presence of GER was not associated with cardiac involvement while it was for digital ulcers (36/91 vs 4/34; p=0.003). There were no significant differences in the immunological profile. The decrease in DLCO <70% and FVC <70% were more frequent in patients with GERD (49.4% vs 23.5%, 47.2% vs 23.5%; p=0.009). Alterations in esophageal manometry were more frequent in patients with GERD 59.34% (p=0.035) All data are detailed in the table below.

Conclusion: Significant differences were found when evaluating complementary studies such as DLCO <70%, FVC <70% and esophageal manometry, indicating that there is an association between GERD and ILD. A statistically significant finding was the association between the presence of digital ulcers and the presence of GERD.
<table>
<thead>
<tr>
<th></th>
<th>Patients with GERD (91)</th>
<th>Patients without GERD (34)</th>
<th>P</th>
<th>OR (IC 95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis (years)</td>
<td>47,5±15</td>
<td>48±15</td>
<td>0,84</td>
<td>0,85 (-5,47-6,64)</td>
</tr>
<tr>
<td>Evolution (years)</td>
<td>7 (2-11)</td>
<td>2 (1-5)</td>
<td>&lt; 0,001</td>
<td></td>
</tr>
<tr>
<td>Gender Male</td>
<td>12</td>
<td>6</td>
<td>0,003</td>
<td>4,9 (1,59-15,1)</td>
</tr>
<tr>
<td>Female</td>
<td>79</td>
<td>28</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diffuse type</td>
<td>33</td>
<td>9</td>
<td>0,302</td>
<td>1,58 (0,66-3,79)</td>
</tr>
<tr>
<td>Limited type</td>
<td>57</td>
<td>25</td>
<td>0,254</td>
<td>0,6 (0,52-1,44)</td>
</tr>
<tr>
<td>DLCO &lt; 70%</td>
<td>45</td>
<td>8</td>
<td>0,009</td>
<td>3,18 (1,39-7,76)</td>
</tr>
<tr>
<td>FVC &lt; 70%</td>
<td>43</td>
<td>8</td>
<td>0,016</td>
<td>2,91 (1,19-7,11)</td>
</tr>
<tr>
<td>Manometry:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypotensive LES / aperistalse</td>
<td>54</td>
<td>13</td>
<td>0,035</td>
<td>2,36 (1,05-5,29)</td>
</tr>
<tr>
<td>Digital Ulcers</td>
<td>36</td>
<td>4</td>
<td>0,003</td>
<td>4,91 (1,59-5,12)</td>
</tr>
<tr>
<td>Cardiac involvement</td>
<td>44</td>
<td>16</td>
<td>0,898</td>
<td>1,05 (0,48-2,13)</td>
</tr>
<tr>
<td>Anti scl70</td>
<td>21</td>
<td>4</td>
<td>0,159</td>
<td>2,25 (0,71-7,12)</td>
</tr>
<tr>
<td>Anti centromere</td>
<td>37</td>
<td>17</td>
<td>0,348</td>
<td>0,69 (0,31-1,51)</td>
</tr>
</tbody>
</table>

Disclosure: R. Aguila Maldonado, None; P. Sansinanea, None; C. E. Pena, None; A. C. Costi, None; A. Vulcano, None; A. Testi, None; M. Pera, None; L. Garcia, None; V. Arturi, None; V. Nagua, None; M. Garcia, None.


Abstract Number: 2677

Impact of Rheumatologic Evaluation and Serologic Testing on Patients with Fibrotic Interstitial Lung Disease: A Single Center Retrospective Experience

Lindsey A. MacFarlane and Paul F. Dellaripa, 1Rheumatology, Brigham & Women's Hospital, Boston, MA, 2Rheumatology, Brigham and Women's Hospital, Boston, MD

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Background/Purpose:

The evaluation of patients who develop interstitial lung disease (ILD) includes an assessment for underlying rheumatic disease or connective tissue disease (CTD). Delineating a CTD phenotype in patients with ILD is important as these patients may have a different prognosis compared to idiopathic pulmonary fibrosis (IPF) and other idiopathic interstitial pneumonias (IP). The subset of patients with ILD and predominantly fibrotic radiographic features are particularly challenging as they may be mislabeled as IPF. This study focused on the utility of a Rheumatologist’s clinical diagnosis and serologic testing in identifying those with CTD/ILD in a cohort of patients with fibrotic features.

Methods:

We retrospectively identified 100 new patients who presented to our multidisciplinary ILD clinic from 2013-2014. All were evaluated by a Pulmonologist and the same experienced Rheumatologist who stratified the likelihood of a CTD into 3 groups (no evidence, possible diagnosis or definite diagnosis). Age, sex and serologic data including ANA, RF, CCP, myositis panel, Scl-70, and muscle enzymes were recorded. Each patient was given an initial clinical diagnosis and a final diagnosis based on multidisciplinary consensus from chest CT, biopsy results, and serologic testing.

Results:

Of the 100 patients, 34% had a final diagnosis of IPF, 39% had CTD/ILD, and 27% other IP. (Table) In a subgroup of patients with fibrosis based on CT, a final diagnosis of IPF was made in 48% and final diagnosis of CTD/ILD was noted in 34%. Patients with CTD/ILD were younger and more likely to be female. However, there was no significant difference in age for females with fibrotic features between CTD/ILD and IPF. (Table) Amongst patients with no evidence of CTD on Rheumatologist evaluation, the final diagnosis was IPF in 79%. Serologic testing was positive in 9% but did not change the final diagnosis. In those with possible CTD a final diagnosis of CTD/ILD was made in 56%. Serologic testing was positive in 50% and resulted in a change in diagnosis for 3 patients. In those with a certain CTD all had CTD/ILD and positive serologic testing, but no changes in diagnoses. (Table)

Conclusion: In patients with fibrotic forms of ILD based on CT, CTD is present in a significant number of cases and when the Rheumatologist’s evaluation does not suspect a CTD diagnosis, serologic data is of no significant benefit. In patients where a rheumatologic diagnosis is suspected but not certain, serologic testing does offer benefit diagnostically. Assessment by a rheumatologist is a valuable aspect of the evaluation of the patient with ILD and may obviate the need for extensive serologic testing in a subset of patients.
# Table: Demographics and Diagnoses for Patients with Interstitial Lung Disease

## Entire Cohort
(N=100)

<table>
<thead>
<tr>
<th></th>
<th>Idiopathic Pulmonary Fibrosis</th>
<th>Connective Tissue Disease associated Interstitial Lung Disease</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>34</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>Age (SD)</td>
<td>72.0 (6.9)</td>
<td>62.9 (13.3)</td>
<td>P&lt;0.01</td>
</tr>
<tr>
<td>Female, N (%)</td>
<td>16 (47)</td>
<td>31 (79.5)</td>
<td>P&lt;0.01</td>
</tr>
</tbody>
</table>

## Fibrotic Lung Disease on CT scan
(N=64)

<table>
<thead>
<tr>
<th></th>
<th>No Evidence of Rheumatologic Disease</th>
<th>Possible Rheumatologic Disease</th>
<th>Definite Rheumatologic Disease</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>34</td>
<td>18</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Age (SD)</td>
<td>71.1 (7.3)</td>
<td>64.1 (12.9)</td>
<td>67.3 (10.3)</td>
<td></td>
</tr>
<tr>
<td>Female, N (%)</td>
<td>12 (35)</td>
<td>16 (89)</td>
<td>9 (75)</td>
<td></td>
</tr>
<tr>
<td>Patients with + serologies, N (%)</td>
<td>3 (9)</td>
<td>9 (50)</td>
<td>12 (100)</td>
<td></td>
</tr>
</tbody>
</table>

## Females with Fibrotic Lung Disease on CT scan
(N=33)

<table>
<thead>
<tr>
<th></th>
<th>No Evidence of Rheumatologic Disease</th>
<th>Possible Rheumatologic Disease</th>
<th>Definite Rheumatologic Disease</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>15</td>
<td>18</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Age (SD)</td>
<td>71.9 (7.7)</td>
<td>66.4 (13.6)</td>
<td>P=0.17</td>
<td></td>
</tr>
<tr>
<td>Female, N (%)</td>
<td>15 (48)</td>
<td>18 (82)</td>
<td>P=0.02</td>
<td></td>
</tr>
<tr>
<td>idiopathic IP</td>
<td>Change in diagnosis due to serologies, N (%)</td>
<td>0 (0)</td>
<td>3c (17)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

SD: Standard deviation

CTD/ILD: Connective tissue disease associated interstitial lung disease

IPF: Idiopathic pulmonary fibrosis
IP: interstitial pneumonia

a. Hypersensitivity pneumonitis, emphysema/fibrosis, ILD NOS (2)

b. Hypersensitivity pneumonitis (3), emphysema/fibrosis (1), ILD NOS (3)

c. 1 patient with + Ro had change of diagnosis from RA ILD to interstitial pneumonia with autoimmune features. 1 patient with +myositis panel and +ANA and 1 patient with + myositis panel and + muscle enzymes had change of diagnosis from interstitial pneumonia with autoimmune features to antisynthetase syndrome.

Disclosure: L. A. MacFarlane, None; P. F. Dellaripa, Up to date, 7,Genentech and Biogen IDEC Inc., 9.


Abstract Number: 2678

**Comparison of Scleroderma Associated Isolated Pulmonary Arterial Hypertension and Pulmonary Hypertension with Concomitant Interstitial Lung Disease**

Alexander Hannan1, Raed Dweik2, Kristin B. Highland3, Gustavo Heresi4, Adriano Tonelli5, William Messner6 and Soumya Chatterjee1,7, 1Rheumatic and Immunologic Diseases, Cleveland Clinic, Cleveland, OH, 2Respiratory Institute, Cleveland Clinic, Cleveland, OH, 3Rheumatology.org, Cleveland Clinic, Cleveland, OH, 4Respiratory Institute - Pulmonary Medicine, Cleveland Clinic, Cleveland, OH, 5Pulmonary Medicine - Respiratory Institute, Cleveland Clinic, Cleveland, OH, 6Quantitative Health Sciences, Cleveland Clinic, Cleveland, OH, 7Rheumatic and Immunologic Ds, Cleveland Clinic, Cleveland, OH

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster III

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM
Background/Purpose: Relatively little data exist in the literature to characterize the differences between patients with scleroderma-associated isolated pulmonary arterial hypertension (SSc-PAH, WHO Group 1) and pulmonary hypertension that coexists with interstitial lung disease (SSc-ILD-PH, WHO Group 3). Our aim was to compare the characteristics of SSc-PAH and SSc-ILD-PH patients from the Cleveland Clinic Pulmonary Hypertension Database to help define differences that may exist between these two groups.

Methods: We performed a retrospective chart-review comparing demographic, laboratory, and hemodynamic data from a total of 176 patients (155 with SSc-PAH and 21 with SSc-ILD-PH) enrolled in the Cleveland Clinic Pulmonary Hypertension Database. The diagnosis of PAH was confirmed by right-heart cardiac catheterization (RHC). The diagnosis of SSc was confirmed by a rheumatologist and that of ILD was confirmed by a pulmonologist. Thirty-three variables were ultimately chosen for evaluation; the decision to include a given variable was based either on previous evidence in the literature that said variables were relevant in predicting outcomes in SSc-PAH or SSc-ILD-PH patients. Multivariate and univariate evaluations were performed using ANOVA, the Kruskal-Wallis test, Pearson's chi-square test, and Fisher's Exact test. A p-value of <0.05 was considered significant.

Results: Statistically significant differences between the SSc-PAH and SSc-ILD-PH groups were found for age, forced vital capacity (% estimated), pulmonary vascular resistance, cardiac index by thermodilution, and NT-proBNP level. Additionally, we observed that in our cohort SSc-ILD-PH patients tended to live longer than those with SSc-PAH. Among SSc-ILD-PH, the estimated median time-to-death was 13.19 years (95% CI: 3.79 – 20.72 years), whereas in SSc-PAH patients, the estimated median time-to-death was 4.89 years (95% CI: 4.01 – 6.98 years). However, this difference in survival was not statistically significant ($P = 0.1743$).
<table>
<thead>
<tr>
<th>Factor</th>
<th>Total (N=176)</th>
<th>SSc-PAH (N=155)</th>
<th>SSc-ILD-PH (N=21)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><em><em>BMI</em>†</em>*</td>
<td></td>
<td></td>
<td></td>
<td>0.64a</td>
</tr>
<tr>
<td>Patient Age</td>
<td>63.8±11.9</td>
<td>64.5±11.3</td>
<td>58.0±14.7</td>
<td></td>
</tr>
<tr>
<td><em><em>Forced Vital Capacity Percent</em>‡</em>*</td>
<td>69.8±20.5</td>
<td>71.2±21.0</td>
<td>60.6±14.2</td>
<td>0.027a</td>
</tr>
<tr>
<td><em><em>Forced Expiratory Vol Percent</em>‡</em>*</td>
<td>69.7±19.9</td>
<td>70.8±20.4</td>
<td>61.6±14.4</td>
<td>0.047a</td>
</tr>
<tr>
<td><em><em>Total Lung Capacity Percent</em>‡</em>*</td>
<td>76.7±17.3</td>
<td>77.2±17.0</td>
<td>72.5±19.4</td>
<td>0.29a</td>
</tr>
<tr>
<td><em><em>Ejection Fraction, TTE</em>‡</em>*</td>
<td>57.9±6.6</td>
<td>57.8±6.4</td>
<td>20.0±5.8</td>
<td>0.21a</td>
</tr>
<tr>
<td><em><em>Right Atrial Area, TTE</em>‡</em>*</td>
<td>24.1±8.2</td>
<td>24.4±8.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em><em>Systolic Blood Pressure</em>‡</em>*</td>
<td>131.4±21.6</td>
<td>130.7±21.4</td>
<td>137.4±22.7</td>
<td>0.21a</td>
</tr>
<tr>
<td><em><em>Diastolic Blood Pressure</em>‡</em>*</td>
<td>77.9±13.4</td>
<td>77.7±13.9</td>
<td>79.6±8.7</td>
<td>0.57a</td>
</tr>
<tr>
<td><em><em>Pulmonary Cap. Wedge Pressure</em>‡</em>*</td>
<td>12.1±7.0</td>
<td>12.1±7.2</td>
<td>12.0±5.9</td>
<td>0.96a</td>
</tr>
<tr>
<td><em><em>Pulmonary Vascular Resistance</em>‡</em>*</td>
<td>8.0±5.2</td>
<td>8.4±5.3</td>
<td>5.2±3.8</td>
<td>0.013a</td>
</tr>
<tr>
<td><em><em>Systemic Vascular Resistance</em>‡</em>*</td>
<td>1644.7±678.3</td>
<td>1650.8±699.3</td>
<td>1590.7±465.5</td>
<td>0.74a</td>
</tr>
<tr>
<td><em><em>Uric Acid Level</em>‡</em>*</td>
<td>7.1±3.4</td>
<td>7.5±3.3</td>
<td>3.7±3.7</td>
<td>0.13a</td>
</tr>
<tr>
<td><em><em>Walking Test Distance</em>‡</em>*</td>
<td>272.9±105.3</td>
<td>269.4±108.7</td>
<td>295.1±79.8</td>
<td>0.32a</td>
</tr>
<tr>
<td><em><em>FEV1/FVC Percent Ratio</em>‡</em>*</td>
<td>78.1±9.6</td>
<td>77.8±9.6</td>
<td>80.2±9.9</td>
<td>0.28a</td>
</tr>
<tr>
<td><em><em>Right Vent. Pressure, TTE</em>‡</em>*</td>
<td>71.1±23.2</td>
<td>72.3±22.9</td>
<td>61.7±24.1</td>
<td>0.062a</td>
</tr>
<tr>
<td><strong>Cardiac Output (THERMO)*‡</strong></td>
<td>4.6±1.6</td>
<td>4.6±1.7</td>
<td>5.1±1.6</td>
<td>0.23a</td>
</tr>
<tr>
<td><strong>Cardiac Index (THERMO)*‡</strong></td>
<td>2.5±0.79</td>
<td>2.5±0.76</td>
<td>2.9±0.90</td>
<td></td>
</tr>
<tr>
<td><strong>Cardiac Output (FICK)*‡</strong></td>
<td>4.7±1.6</td>
<td>4.6±1.6</td>
<td>4.8±1.2</td>
<td>0.72a</td>
</tr>
<tr>
<td><strong>Cardiac Index (FICK)*‡</strong></td>
<td>2.6±0.83</td>
<td>2.5±0.84</td>
<td>2.7±0.71</td>
<td>0.49a</td>
</tr>
<tr>
<td><em><em>DLCO on PFT</em>‡</em>*</td>
<td>29.0[0.48,45.0]</td>
<td>29.0[0.49,46.0]</td>
<td>32.0[0.43,42.0]</td>
<td>0.59b</td>
</tr>
<tr>
<td><em><em>C-Reactive Protein Level</em>‡</em>*</td>
<td>1.00[0.40,2.8]</td>
<td>1.2[0.45,2.9]</td>
<td>0.60[0.30,1.7]</td>
<td>0.24b</td>
</tr>
<tr>
<td><em><em>NT-proBNP Level</em>‡</em>*</td>
<td>1079.5[381.0,4099.0]</td>
<td>1485.5[512.0,4248.5]</td>
<td>187.0[110.0,597.0]</td>
<td>0.002b</td>
</tr>
<tr>
<td><em><em>Serum Creatinine Level</em>‡</em>*</td>
<td>0.92[0.79,1.2]</td>
<td>0.97[0.80,1.2]</td>
<td>0.83[0.68,1.05]</td>
<td>0.10b</td>
</tr>
<tr>
<td><em><em>Serum Ferritin Level</em>‡</em>*</td>
<td>96.8[35.0,227.0]</td>
<td>95.8[35.0,227.0]</td>
<td>105.2[85.0,178.6]</td>
<td>0.84b</td>
</tr>
</tbody>
</table>

**Patient Gender**
- Female: 148(84.1) 131(84.5) 17(81.0)
- Male: 28(15.9) 24(15.5) 4(19.0)

**Patient Race*‡**
- Caucasian: 149(86.1) 135(88.8) 14(66.7)
- Other: 24(13.9) 17(11.2) 7(33.3)

**Smoking Status**
- No: 89(50.6) 81(52.3) 8(38.1)
- Unknown: 30(17.0) 27(17.4) 3(14.3)
- Yes: 57(32.4) 47(30.3) 10(47.6)

**IPF Status**
- No: 120(68.2) 107(69.0) 13(61.9)
- Unknown: 33(18.8) 30(19.4) 3(14.3)
- Yes: 23(13.1) 18(11.6) 5(23.8)

**ANA Status**
- Negative: 15(8.5) 13(8.4) 2(9.5)
<table>
<thead>
<tr>
<th>Factor</th>
<th>Total (N=176)</th>
<th>SSc-PAH (N=155)</th>
<th>SSc-ILD-PH (N=21)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>. Unknown</td>
<td>55(31.3)</td>
<td>50(32.3)</td>
<td>5(23.8)</td>
<td></td>
</tr>
<tr>
<td>. Positive</td>
<td>106(60.2)</td>
<td>92(59.4)</td>
<td>14(66.7)</td>
<td></td>
</tr>
</tbody>
</table>

*Data not available for all subjects. Missing values: BMI = 1, Forced Vital Capacity Percent = 9, Forced Expiratory Vol Percent = 9, Total Lung Capacity Percent = 36, Ejection Fraction, TTE = 10, Right Atrial Area, TTE = 99, Systolic Blood Pressure = 9, Diastolic Blood Pressure = 9, Pulmonary Cap. Wedge Pressure = 2, Pulmonary Vascular Resistance = 9, Systemic Vascular Resistance = 9, Uric Acid Level = 155, Walking Test Distance = 37, FEV1/FVC Percent Ratio = 10, Right Vent. Syst. Pressure, TTE = 8, Cardiac Output (THERMO) = 22, Cardiac Index (THERMO) = 22, Cardiac Output (FICK) = 21, Cardiac Index (FICK) = 21, DLCO on PFT = 30, C- Reactive Protein Level = 116, Brain Natriuretic Peptide = 80, NT-proBNP Level = 106, Serum Creatinine Level = 5, Serum Ferritin Level = 118, Patient Race = 3, NYHA class (at diagnosis) = 51, NYHA class (at 3 months) = 105, NYHA class (at 6 months) = 119.

Statistics presented as Mean ± SD, Median [P25, P75], Median (min, max) or N (column %).

p-values: a=ANOVA, b=Kruskal-Wallis test, c=Pearson's chi-square test, d=Fisher's Exact test.

**Conclusion:** In our study, statistically significant differences were found between SSc-PAH and SSc-ILD-PH patients. The suggestion of longer survival in SSc-ILD-PH patients may be explained by some lurking variables that were not available for analysis, such as autoantibody subsets. SSc-PAH patients were older and possibly were more likely to have limited SSc with positive anti-centromere antibody, representing a subpopulation that is distinct from the SSc-ILD-PH patients. More research is necessary to elucidate these differences.

**Disclosure:** A. Hannan, None; R. Dweik, None; K. B. Highland, None; G. Heresi, None; A. Tonelli, None; W. Messner, None; S. Chatterjee, None.


Abstract Number: 2679

**Mortality Is Increased in Scleroderma Associated Pulmonary Arterial Hypertension Patients with Younger Age, Lower Systolic Blood Pressure,**
and Lower Cardiac Index, but Not in Idiopathic Pulmonary Arterial Hypertension

Alexander Hannan1, Raed Dweik2, Kristin B. Highland3, Gustavo Heresi4, Adriano Tonelli5, William Messner6 and Soumya Chatterjee1, 1Rheumatic and Immunologic Diseases, Cleveland Clinic, Cleveland, OH, 2Respiratory Institute, Cleveland Clinic, Cleveland, OH, 3Rheumatology.org, Cleveland Clinic, Cleveland, OH, 4Respiratory Institute - Pulmonary Medicine, Cleveland Clinic, Cleveland, OH, 5Pulmonary Medicine - Respiratory Institute, Cleveland Clinic, Cleveland, OH, 6Quantitative Health Sciences, Cleveland Clinic, Cleveland, OH

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Survival in scleroderma associated pulmonary arterial hypertension (SSc-PAH) is known to be significantly worse compared to that in idiopathic pulmonary arterial hypertension (iPAH). However, specific factors contributing to the worse survival in SSc-PAH is currently unknown. Our objective was to investigate how the age at diagnosis of PAH and systolic blood pressure may influence mortality in these patients.

Methods: A retrospective chart-review was conducted comparing demographic, clinical and hemodynamic data from a total of 862 patients (686 with iPAH and 176 with SSc-PAH) enrolled in the Cleveland Clinic Pulmonary Hypertension Database. The diagnosis of PAH was confirmed by RHC, and the diagnosis of SSc was confirmed by a rheumatologist. We focused on the characteristics of age, systolic blood pressure (SBP) and cardiac output/cardiac index (on right heart catheterization) with regards to their effect on mortality in both the SSc-PAH and the iPAH groups.

Results: Among younger patients (age < 63) those with SSc-PAH had significantly worse survival compared to those with iPAH. Interestingly, a similar difference in mortality between the 2 groups was not seen in patients of age ≥ 63 years.

<table>
<thead>
<tr>
<th>PAH Status Group</th>
<th>Age</th>
<th>P-value*</th>
<th>N</th>
<th>Est. Median Time-to-Death (years)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Idiopathic PAH</td>
<td>Any non-missing</td>
<td>0.0002</td>
<td>598</td>
<td>10.26</td>
<td>(8.45, 12.00)</td>
</tr>
<tr>
<td>Scleroderma Associated</td>
<td>Any non-missing</td>
<td>0.0087</td>
<td>159</td>
<td>5.33</td>
<td>(4.22, 7.59)</td>
</tr>
<tr>
<td>Idiopathic PAH</td>
<td>&lt; 63</td>
<td>0.0002</td>
<td>439</td>
<td>14.41</td>
<td>(10.81, 16.49)</td>
</tr>
<tr>
<td>Scleroderma Associated</td>
<td>&lt; 63</td>
<td>0.0087</td>
<td>76</td>
<td>6.74</td>
<td>(4.22, 20.72)</td>
</tr>
<tr>
<td>Idiopathic PAH</td>
<td>≥ 63</td>
<td>0.0002</td>
<td>159</td>
<td>5.11</td>
<td>(4.58, 6.62)</td>
</tr>
<tr>
<td>Scleroderma Associated</td>
<td>≥ 63</td>
<td>0.0001</td>
<td>83</td>
<td>4.75</td>
<td>(3.78, 5.79)</td>
</tr>
<tr>
<td>Scleroderma Associated</td>
<td>&lt; 63</td>
<td>0.1061</td>
<td>76</td>
<td>6.74</td>
<td>(4.22, 20.72)</td>
</tr>
<tr>
<td>Scleroderma Associated</td>
<td>≥ 63</td>
<td>0.0001</td>
<td>83</td>
<td>4.75</td>
<td>(3.78, 7.59)</td>
</tr>
<tr>
<td>Idiopathic PAH</td>
<td>&lt; 63</td>
<td>0.0001</td>
<td>439</td>
<td>14.41</td>
<td>(10.81, 16.49)</td>
</tr>
<tr>
<td>Idiopathic PAH</td>
<td>≥ 63</td>
<td>0.0001</td>
<td>159</td>
<td>5.11</td>
<td>(4.58, 6.62)</td>
</tr>
</tbody>
</table>

A statistically significant difference in survival was also noted when comparing SSc-PAH patients with SBP >125 mmHg with those with SBP < 125 mmHg; the group with lower SBP had worse survival. A similar mortality difference was not noted in the iPAH patients.
To determine if SBP served as a surrogate for cardiac output, we assessed Kendall tau-b correlations of SBP versus cardiac output and cardiac index (CI) (both by thermodilution and by the Fick equation); no strong correlation was noted. However, a correlation between CI < 2.5 L/min/m² and mortality was noted. A similar mortality difference was not noted in the iPAH patients.

<table>
<thead>
<tr>
<th>PAH Status Group</th>
<th>Systolic Blood Pressure</th>
<th>P-value*</th>
<th>N</th>
<th>Est. Median Time-to-Death (years)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Idiopathic PAH</td>
<td>Any non-missing</td>
<td>0.0007</td>
<td>559</td>
<td>10.02</td>
<td>(8.24, 11.84)</td>
</tr>
<tr>
<td>Scleroderma Associated</td>
<td>Any non-missing</td>
<td>&lt; 0.0001</td>
<td>151</td>
<td>5.33</td>
<td>(4.24, 7.68)</td>
</tr>
<tr>
<td>Idiopathic PAH</td>
<td>&lt; 125</td>
<td>&lt; 0.0001</td>
<td>277</td>
<td>9.48</td>
<td>(6.98, 12.31)</td>
</tr>
<tr>
<td>Scleroderma Associated</td>
<td>&lt; 125</td>
<td>0.2313</td>
<td>63</td>
<td>4.01</td>
<td>(2.51, 6.03)</td>
</tr>
<tr>
<td>Idiopathic PAH</td>
<td>≥ 125</td>
<td>0.0099</td>
<td>282</td>
<td>10.26</td>
<td>(8.23, 12.75)</td>
</tr>
<tr>
<td>Scleroderma Associated</td>
<td>≥ 125</td>
<td>0.8082</td>
<td>88</td>
<td>7.68</td>
<td>(4.70, 18.60)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PAH Status Group</th>
<th>Cardiac Index (FICK) [L/min/m²]</th>
<th>P-value*</th>
<th>N</th>
<th>Est. Median Time-to-Death (years)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Idiopathic PAH</td>
<td>Any non-missing</td>
<td>0.0126</td>
<td>470</td>
<td>9.38</td>
<td>(7.72, 11.50)</td>
</tr>
<tr>
<td>Scleroderma Associated</td>
<td>Any non-missing</td>
<td>0.0003</td>
<td>142</td>
<td>5.59</td>
<td>(4.24, 8.19)</td>
</tr>
<tr>
<td>Idiopathic PAH</td>
<td>&lt; 2.5</td>
<td>0.9208</td>
<td>261</td>
<td>9.38</td>
<td>(7.51, 14.41)</td>
</tr>
<tr>
<td>Scleroderma Associated</td>
<td>&lt; 2.5</td>
<td>0.192</td>
<td>73</td>
<td>4.10</td>
<td>(3.38, 6.03)</td>
</tr>
<tr>
<td>Idiopathic PAH</td>
<td>≥ 2.5</td>
<td>0.5030</td>
<td>209</td>
<td>9.92</td>
<td>(6.81, 11.84)</td>
</tr>
<tr>
<td>Scleroderma Associated</td>
<td>≥ 2.5</td>
<td>0.5030</td>
<td>69</td>
<td>10.74</td>
<td>(5.37, 18.59)</td>
</tr>
<tr>
<td>Idiopathic PAH</td>
<td>&lt; 2.5</td>
<td>0.4199</td>
<td>73</td>
<td>4.10</td>
<td>(3.38, 6.03)</td>
</tr>
<tr>
<td>Scleroderma Associated</td>
<td>&lt; 2.5</td>
<td>0.5030</td>
<td>69</td>
<td>10.74</td>
<td>(5.37, 18.59)</td>
</tr>
</tbody>
</table>

**Conclusion:** Younger age, lower SBP, and lower CI influences survival in SSc-PAH patients, but not in iPAH patients. Younger SSc-PAH patients have markedly lower survival times than similarly aged iPAH patients for unclear reasons. The relationship between lower SBP, decreased CI, and increased mortality has been previously noted in some smaller studies. These data may have important implications for treatment of SSc-PAH especially since some PAH therapies may decrease SBP.

**Disclosure:** A. Hannan, None; R. Dweik, None; K. B. Highland, None; G. Heresi, None; A. Tonelli, None; W. Messner, None; S. Chatterjee, None.


Abstract Number: 2680

**Analysis of Prognostic Determinants of Scleroderma-Associated Pulmonary Arterial Hypertension and Idiopathic Pulmonary Arterial Hypertension**
Alexander Hannan, Raed Dweik, Kristin B. Highland, Gustavo Heresi, Adriano Tonelli, William Messner and Soumya Chatterjee. Rheumatic and Immunologic Diseases, Cleveland Clinic, Cleveland, OH, Respiratory Institute, Cleveland Clinic, Cleveland, OH, Rheumatology.org, Cleveland Clinic, Cleveland, OH, Respiratory Institute - Pulmonary Medicine, Cleveland Clinic, Cleveland, OH, Pulmonary Medicine - Respiratory Institute, Cleveland Clinic, Cleveland, OH, Quantitative Health Sciences, Cleveland Clinic, Cleveland, OH

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic sclerosis (SSc) associated pulmonary arterial hypertension (SSc-PAH) is a serious and often life-threatening complication of SSc. Perhaps the most important enigma in the context of SSc-PAH care is the fact that the prognosis of SSc-PAH patients is substantially worse than that of demographically similar patients with idiopathic PAH (iPAH). Moreover, it has been shown that these differences in survival are not related to a higher prevalence of left-heart disease in SSc-PAH patients. Previous studies have not extensively compared demographic, laboratory, and hemodynamic data from cohorts of iPAH and SSc-PAH patients to determine which specific characteristics of these groups may explain the worsened clinical course and prognosis of SSc-PAH sufferers. The aims of our study were to identify specific characteristics that distinguish these two groups in a large cohort of SSc-PAH and iPAH patients.

Methods: A retrospective chart-review was conducted comparing demographic, laboratory, and hemodynamic [echocardiographic and right heart catheterization (RHC)] data from a total of 862 patients (686 with iPAH and 176 with SSc-PAH) enrolled in the Cleveland Clinic Pulmonary Hypertension Database. The diagnosis of PAH was confirmed by RHC, and the diagnosis of SSc was confirmed by a rheumatologist. Thirty variables were chosen for evaluation; the decision to include a given variable was based either on inclusion of the variables in previous studies on SSc-PAH or on theoretical suspicion that specific variables may be relevant in distinguishing the two conditions. Multivariate and univariate analyses were completed utilizing ANOVA, the Kruskal-Wallis test, Pearson's chi-square test, and Fisher's Exact test.

Results: Statistically significant differences between the SSc-PAH and iPAH groups were found for the variables of age, gender, forced vital capacity, total lung capacity, 6-minute walk distance, FEV1/FVC ratio, transfer factor (DLCO), right ventricular systolic pressure (on transthoracic echocardiogram), mean pulmonary artery pressure and pulmonary vascular resistance (on RHC), systolic blood pressure, BNP and NT-proBNP level, and mortality status.
<table>
<thead>
<tr>
<th>Factor</th>
<th>Total (N=862)</th>
<th>Idiopathic PAH (N=686)</th>
<th>Scleroderma Associated (N=176)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI*</td>
<td>29.0±7.8</td>
<td>29.2±7.9</td>
<td>28.2±7.6</td>
<td>0.11a</td>
</tr>
<tr>
<td>Patient Age</td>
<td>54.7±16.3</td>
<td>52.4±16.5</td>
<td>63.8±11.9</td>
<td>&lt;0.001a</td>
</tr>
<tr>
<td>Forced Vital Capacity Percent*</td>
<td>74.1±20.4</td>
<td>75.3±20.2</td>
<td>69.8±20.5</td>
<td>0.002a</td>
</tr>
<tr>
<td>Forced Expiratory Vol Percent*</td>
<td>70.1±19.9</td>
<td>70.2±19.9</td>
<td>69.7±19.9</td>
<td>0.75a</td>
</tr>
<tr>
<td>Total Lung Capacity Percent*</td>
<td>83.4±17.9</td>
<td>85.4±17.6</td>
<td>76.7±17.3</td>
<td>&lt;0.001a</td>
</tr>
<tr>
<td>Ejection Fraction, TTE*</td>
<td>57.1±7.8</td>
<td>56.9±8.1</td>
<td>57.9±6.6</td>
<td>0.16a</td>
</tr>
<tr>
<td>Right Atrial Area, TTE*</td>
<td>25.5±8.8</td>
<td>25.9±8.9</td>
<td>24.1±8.2</td>
<td>0.098a</td>
</tr>
<tr>
<td>Systolic Blood Pressure*</td>
<td>127.5±24.2</td>
<td>126.5±24.7</td>
<td>131.4±21.6</td>
<td>0.018a</td>
</tr>
<tr>
<td>Diastolic Blood Pressure*</td>
<td>76.7±14.7</td>
<td>76.4±15.0</td>
<td>77.9±13.4</td>
<td>0.24a</td>
</tr>
<tr>
<td>Pulmonary Cap. Wedge Pressure*</td>
<td>12.9±7.1</td>
<td>13.1±7.2</td>
<td>12.1±7.0</td>
<td>0.086a</td>
</tr>
<tr>
<td>Mean Pulmonary Artery Pressure*</td>
<td>49.1±14.7</td>
<td>50.9±14.8</td>
<td>42.3±11.8</td>
<td>&lt;0.001a</td>
</tr>
<tr>
<td>Pulmonary Vascular Resistance*</td>
<td>9.3±6.1</td>
<td>9.7±6.3</td>
<td>8.0±5.2</td>
<td>0.002a</td>
</tr>
<tr>
<td>Systemic Vein Resistance*</td>
<td>1606.0±665.8</td>
<td>1595.4±662.5</td>
<td>1644.7±678.3</td>
<td>0.41a</td>
</tr>
<tr>
<td>Uric Acid Level*</td>
<td>7.3±3.8</td>
<td>7.3±3.9</td>
<td>7.1±3.4</td>
<td>0.86a</td>
</tr>
<tr>
<td>Walking Test Distance*</td>
<td>305.5±115.4</td>
<td>313.8±116.5</td>
<td>272.9±105.3</td>
<td>&lt;0.001a</td>
</tr>
<tr>
<td>FEV1/FVC Percent Ratio*</td>
<td>76.0±9.5</td>
<td>75.3±9.3</td>
<td>78.1±9.6</td>
<td>&lt;0.001a</td>
</tr>
<tr>
<td>Right Vent. Pressure, TTE*</td>
<td>75.3±24.6</td>
<td>76.5±24.9</td>
<td>71.1±23.2</td>
<td>0.012a</td>
</tr>
<tr>
<td>Cardiac Output (THERMO)*</td>
<td>4.8±2.0</td>
<td>4.9±2.1</td>
<td>4.6±1.6</td>
<td>0.12a</td>
</tr>
<tr>
<td>Cardiac Index (THERMO)*</td>
<td>2.6±0.96</td>
<td>2.6±1.00</td>
<td>2.5±0.79</td>
<td>0.45a</td>
</tr>
<tr>
<td>Cardiac Output (FICK)*</td>
<td>4.8±1.9</td>
<td>4.8±2.0</td>
<td>4.7±1.6</td>
<td>0.27a</td>
</tr>
<tr>
<td>Cardiac Index (FICK)*</td>
<td>2.6±1.02</td>
<td>2.6±1.07</td>
<td>2.6±0.83</td>
<td>0.74a</td>
</tr>
<tr>
<td>DLCO on PFT*</td>
<td>36.0[0.76,60.0]</td>
<td>41.0[0.81,65.0]</td>
<td>29.0[0.48,45.0]</td>
<td>&lt;0.001b</td>
</tr>
<tr>
<td>C-Reactive Protein Level*</td>
<td>1.00[0.40,2.9]</td>
<td>1.1[0.40,2.9]</td>
<td>1.00[0.40,2.8]</td>
<td>0.78b</td>
</tr>
<tr>
<td>Brain Natriuretic Peptide*</td>
<td>167.0[45.0,557.0]</td>
<td>134.0[41.0,494.0]</td>
<td>339.5[124.5,975.5]</td>
<td>&lt;0.001b</td>
</tr>
<tr>
<td>NT-proBNP Level*</td>
<td>680.0[232.0,2621.0]</td>
<td>619.0[202.0,2513.0]</td>
<td>1079.5[381.0,4099.0]</td>
<td>0.013b</td>
</tr>
<tr>
<td>Serum Creatinine Level*</td>
<td>0.90[0.74,1.2]</td>
<td>0.90[0.73,1.1]</td>
<td>0.92[0.79,1.2]</td>
<td>0.22b</td>
</tr>
<tr>
<td>Serum Ferritin Level*</td>
<td>85.0[35.8,210.4]</td>
<td>82.7[36.0,210.0]</td>
<td>96.8[35.0,227.0]</td>
<td>0.83b</td>
</tr>
<tr>
<td>Patient Gender</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001c</td>
</tr>
<tr>
<td>. Female</td>
<td>616(71.5)</td>
<td>468(68.2)</td>
<td>148(84.1)</td>
<td></td>
</tr>
<tr>
<td>. Male</td>
<td>246(28.5)</td>
<td>218(31.8)</td>
<td>28(15.9)</td>
<td></td>
</tr>
<tr>
<td>Patient Race*</td>
<td></td>
<td></td>
<td></td>
<td>0.088c</td>
</tr>
<tr>
<td>. Caucasian</td>
<td>690(81.7)</td>
<td>541(80.5)</td>
<td>149(86.1)</td>
<td></td>
</tr>
<tr>
<td>. Other</td>
<td>155(18.3)</td>
<td>131(19.5)</td>
<td>24(13.9)</td>
<td></td>
</tr>
<tr>
<td>Smoking Status</td>
<td></td>
<td></td>
<td></td>
<td>0.75c</td>
</tr>
<tr>
<td>. No</td>
<td>414(48.0)</td>
<td>325(47.4)</td>
<td>89(50.6)</td>
<td></td>
</tr>
<tr>
<td>. Unknown</td>
<td>157(18.2)</td>
<td>127(18.5)</td>
<td>30(17.0)</td>
<td></td>
</tr>
<tr>
<td>. Yes</td>
<td>291(33.8)</td>
<td>234(34.1)</td>
<td>57(32.4)</td>
<td></td>
</tr>
<tr>
<td>Factor</td>
<td>Total (N=862)</td>
<td>Idiopathic PAH (N=686)</td>
<td>Scleroderma Associated (N=176)</td>
<td>p-value</td>
</tr>
<tr>
<td>-------------------------</td>
<td>---------------</td>
<td>------------------------</td>
<td>-------------------------------</td>
<td>---------</td>
</tr>
<tr>
<td><strong>IPF Status</strong></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001c</td>
</tr>
<tr>
<td>. No</td>
<td>640(74.2)</td>
<td>520(75.8)</td>
<td>120(68.2)</td>
<td></td>
</tr>
<tr>
<td>. Unknown</td>
<td>179(20.8)</td>
<td>146(21.3)</td>
<td>33(18.8)</td>
<td></td>
</tr>
<tr>
<td>. Yes</td>
<td>43(5.0)</td>
<td>20(2.9)</td>
<td>23(13.1)</td>
<td></td>
</tr>
<tr>
<td><strong>ANA Status</strong></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001c</td>
</tr>
<tr>
<td>. Negative</td>
<td>300(34.8)</td>
<td>285(41.5)</td>
<td>15(8.5)</td>
<td></td>
</tr>
<tr>
<td>. Unknown</td>
<td>334(38.7)</td>
<td>279(40.7)</td>
<td>55(31.3)</td>
<td></td>
</tr>
<tr>
<td>. Positive</td>
<td>228(26.5)</td>
<td>122(17.8)</td>
<td>106(60.2)</td>
<td></td>
</tr>
<tr>
<td><strong>NYHA class (at diagnosis)</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.11c</td>
</tr>
<tr>
<td>. Class 1 or 2</td>
<td>186(30.9)</td>
<td>157(33.0)</td>
<td>29(23.2)</td>
<td></td>
</tr>
<tr>
<td>. Class 3</td>
<td>314(52.2)</td>
<td>242(50.8)</td>
<td>72(57.6)</td>
<td></td>
</tr>
<tr>
<td>. Class 4</td>
<td>101(16.8)</td>
<td>77(16.2)</td>
<td>24(19.2)</td>
<td></td>
</tr>
<tr>
<td><strong>NYHA class (at 3 months)</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.77c</td>
</tr>
<tr>
<td>. Class 1 or 2</td>
<td>137(42.4)</td>
<td>109(43.3)</td>
<td>28(39.4)</td>
<td></td>
</tr>
<tr>
<td>. Class 3</td>
<td>147(45.5)</td>
<td>114(45.2)</td>
<td>33(46.5)</td>
<td></td>
</tr>
<tr>
<td>. Class 4</td>
<td>39(12.1)</td>
<td>29(11.5)</td>
<td>10(14.1)</td>
<td></td>
</tr>
<tr>
<td><strong>NYHA class (at 6 months)</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.040c</td>
</tr>
<tr>
<td>. Class 1 or 2</td>
<td>142(48.0)</td>
<td>116(48.5)</td>
<td>26(45.6)</td>
<td></td>
</tr>
<tr>
<td>. Class 3</td>
<td>131(44.3)</td>
<td>109(45.6)</td>
<td>22(38.6)</td>
<td></td>
</tr>
<tr>
<td>. Class 4</td>
<td>23(7.8)</td>
<td>14(5.9)</td>
<td>9(15.8)</td>
<td></td>
</tr>
<tr>
<td><strong>Mortality Status</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.016c</td>
</tr>
<tr>
<td>. Alive</td>
<td>368(42.7)</td>
<td>307(44.8)</td>
<td>61(34.7)</td>
<td></td>
</tr>
<tr>
<td>. Dead</td>
<td>494(57.3)</td>
<td>379(55.2)</td>
<td>115(65.3)</td>
<td></td>
</tr>
</tbody>
</table>

*Data not available for all subjects. Missing values: BMI = 5, Forced Vital Capacity Percent = 113, Forced Expiratory Vol Percent = 112, Total Lung Capacity Percent = 269, Ejection Fraction, TTE = 97, Right Atrial Area, TTE = 505, Systolic Blood Pressure = 57, Diastolic Blood Pressure = 61, Pulmonary Cap. Wedge Pressure = 42, Mean Pulmonary Artery Pressure = 9, Pulmonary Vascular Resistance = 89, Systemic Vascular Resistance = 136, Uric Acid Level = 771, Walking Test Distance = 177, FEV1/FVC Percent Ratio = 116, Right Vent. Pressure, TTE = 93, Cardiac Output (THERMO) = 194, Cardiac Index (THERMO) = 194, Cardiac Output (FICK) = 169, Cardiac Index (FICK) = 171, DLCO on PFT = 215, C-Reactive Protein Level = 650, Brain Natriuretic Peptide = 401, NT-proBNP Level = 557, Serum Creatinine Level = 19, Serum Ferritin Level = 615, Patient Race = 17, NYHA class (at diagnosis) = 261, NYHA class (at 3 months) = 539, NYHA class (at 6 months) = 566. Statistics presented as Mean ± SD, Median [P25, P75], Median (min, max) or N (column %). p-values: a=ANOVA, b=Kruskal-Wallis test, c=Pearson's chi-square test, d=Fisher's Exact test.

**Conclusion:** Our analysis confirms findings from previous studies that have shown that SSc-PAH patients demonstrate important differences in hemodynamic and pulmonary function parameters compared to iPAH patients (table). Additionally, patients with SSc-PAH demonstrated much higher BNP and NT-proBNP levels compared to iPAH patients with similar hemodynamic parameters. Further research will be necessary to help delineate other relevant factors that may aid in caring for these patients.

**Disclosure:** A. Hannan, None; R. Dweik, None; K. B. Highland, None; G. Heresi, None; A. Tonelli, None; W. Messner, None; S. Chatterjee, None.

Epidemiology and Survival of Systemic Sclerosis-Systemic Lupus Erythematosus Overlap Syndrome

Samar Alharbi, Zareen Ahmad, Zahi Touma, Arthur Bookman, Jorge Sánchez-Guerrero and Sindhu Johnson

Division of Rheumatology, University of Toronto, Toronto Scleroderma Program, Sinai Health System, University Health Network, Toronto, ON, Canada, Toronto Scleroderma Program, Division of Rheumatology, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada, Rheumatology, University of Toronto, Division of Rheumatology, Institute of Health Policy, Management and Evaluation, Toronto, ON, Canada, Division of Rheumatology, University Health Network, University of Toronto, Toronto, ON, Canada, Institute of Health Policy, Management and Evaluation, Toronto, ON, Canada, Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, Mexico, Division of Rheumatology, University of Toronto, Toronto Scleroderma Program, Sinai Health Systems and University Health Network, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic sclerosis (SSc) is an immune disorder characterized by vasculopathy and fibrosis. SSc may overlap with another disease such as systemic lupus erythematosus (SLE). Little is known about the epidemiology, clinical characteristics, and survival of SSc-SLE overlap syndrome (also called lupoderma). We evaluated the prevalence of SSc-SLE overlap syndrome, differences in SSc clinical characteristics and survival compared with SSc without SLE.

Methods: A retrospective cohort study was conducted between 1970 – 2017 including subjects who fulfilled the ACR/EULAR classification criteria for SSc and/or who fulfilled the ACR classification criteria for SLE. The primary outcome was the time from diagnosis to death from all causes. Survival was evaluated using Kaplan Meier curves and Cox proportional hazard models. Secondary outcomes included the prevalence of SSc-SLE overlap syndrome, and differences in clinical characteristics.

Results: We identified 1252 subjects (SSc n=1166, SSc-SLE n=86) with a SSc-SLE prevalence of 6.8%. SSc-SLE subjects were more frequently female (92% versus 81%, p=0.02), had lupus anticoagulant (6% versus 0.3%, p<0.001), antiphospholipid antibody (6% versus 0.9%, p<0.001), and pulmonary hypertension (52% versus 31%, p<0.001). SSc-SLE subjects less frequently had calcinosis (13% versus 27%, p=0.007), telangiectasia (49% versus 75%, p<0.001) and diffuse subtype (12% versus 35%, p<0.001). There were no significant differences in the occurrence of renal crisis (7% versus 7%), interstitial lung disease (40% versus 34%), digital ulcers (38% versus 32%), hypertension (19% versus 21%), diabetes (6% versus 6%), dyslipidemia (5% versus 7%) or cancer (7% versus 11%) between groups.
The Kaplan Meier curves suggest that SSc-SLE overlap subjects have better survival, but this was not statistically significant (log rank p=0.06). Accounting for female sex and diffuse subtype attenuated survival differences between the two groups (Hazard Ratio 0.70, 95%CI 0.45, 1.11).

**Conclusion:** SSc-SLE subjects are more frequently female and less frequently have cutaneous manifestations of SSc. However, these subjects should be monitored for serious complications of SSc including pulmonary hypertension, interstitial lung disease, renal crisis and digital ulcers.

**Disclosure:** S. Alharbi, None; Z. Ahmad, None; Z. Touma, None; A. Bookman, None; J. Sánchez-Guerrero, None; S. Johnson, None.


**Abstract Number:** 2682

**Correlation between Capillaroscopic Patterns of Nailfold Microangiopathy and Three Different Methods to Assess Dermal Thickness in Systemic Sclerosis Patients**

**Background/Purpose:** Systemic sclerosis (SSc) is characterized by increase of dermal thickness (DT) and impairment of microvascular system (1). Several studies demonstrate that nailfold capillaroscopy (NVC) patterns of microangiopathy correlate with organ involvement, but few studies investigated the correlation between nailfold microangiopathy and skin involvement. The modified Rodnan skin score (mRss) is the validated method to assess the severity of skin damage (2,3), high frequency skin ultrasound (US) is able to detect skin damage in SSc (4,5), and the plicometer skin test (Plicometry) is a further method to evaluate cutaneous involvement in SSc patients (6). The aim of this study was to identify possible correlations between different patterns of nailfold microangiopathy and three different methods (mRss, US and Plicometry) to assess DT in SSc patients.

**Methods:** Sixty-three SSc patients (ACR/EULAR criteria) (mean age 64±11SD years, mean disease duration 7±6 years, 43 lcSSc and 20 dcSSc) and 63 sex and age matched healthy subjects were enrolled, after written informed consent. All subjects were assessed by mRss, US and Plicometry to evaluate DT in the seventeen skin areas of the body usually evaluated by mRss (zygoma, fingers, dorsum of hands, forearms, upper arms, chest, abdomen, thighs, legs, feet) (1-6).
NVC was performed to assess the proper pattern of microangiopathy ("Early", "Active" or "Late" pattern) and to calculate the microangiopathy evolution score (MES) (7-8). Statistical evaluation was performed by non-parametric tests.

Results: There was a statistically significant positive correlation between DT values and severity of nailfold microangiopathy: all methods detected a progressively higher DT in patients with “Early”, “Active” and “Late” pattern of microangiopathy (p<0.005), and a positive correlation was observed also with MES (r=0.71 p<0.001). Finally, a positive correlation was observed in SSc patients between the three method to evaluate DT (Plicometry vs mRss r=0.98, p=0.0001; Plicometry vs US r=0.53, p=0.0001; US vs mRss r=0.53, p=0.0001). As expected, the group of SSc patients had a statistically significant higher DT at level of all areas, as evaluated by the three methods, when compared to the control group (p=0.0001).

Conclusion: This study demonstrates a relationship between skin damage and microangiopathy impairment in SSc patients, as well as a correlation between different methods to assess DT.


Disclosure: B. Ruaro, None; A. Sulli, None; C. Pizzorni, None; E. Alessandri, None; S. Paolino, None; M. Ghio, None; V. Tomatis, None; V. Smith, None; M. Cutolo, None.


Abstract Number: 2683

Factors Associated with Disease Progression in Early-Diagnosed Pulmonary Arterial Hypertension Associated with Systemic Sclerosis

Carina Mihai1, Milos Antic2, Rucsandra Dobrota3, Diana Bonderman4, Harbajan Chadha-Boreham5, J. Gerry Coghlan6, Christopher Denton7, Martin Doelberg5, Ekkehard Gruenig8, Dinesh Khanna9, Vallerie McLaughlin10, Ulf Muller-Ladner11, Janet E. Pope12, Daniel M Rosenberg5, James R Seibold13, Madelon C Vonk14 and Oliver Distler15,
1Internal Medicine and Rheumatology Dept., Cantacuzino Clinical Hospital, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania, 2University Hospital Zurich, Zurich, Switzerland, 3Department of Rheumatology, Center of Experimental Rheumatology, University Hospital Zurich, Zurich, Switzerland, 4Department of Internal Medicine II, Division of Cardiology, Medical University of Vienna, Vienna, Austria, 5Actelion Pharmaceuticals Ltd., Alschwil, Switzerland, 6National Pulmonary Hypertension Service, Royal Free Hospital, London, United Kingdom, 7Department of Rheumatology, University College London, Royal Free Hospital, London, United Kingdom, 8Centre for Pulmonary Hypertension, Thoraxclinic, University Hospital Heidelberg, Heidelberg, Germany, 9Division of Rheumatology and Clinical Autoimmune Center of Excellence, University of Michigan, Ann Arbor, MI, Ann Arbor, MI, 10Internal Medicine, Division of Cardiology, University of Michigan, Ann Arbor, MI, 11Justus-Liebig-University Giessen, Department of Internal Medicine and Rheumatology, Kerckhoff-Klinik, Bad Nauheim, Germany, Bad-Nauheim, Germany, 12Department of Medicine, Division of Rheumatology, University of Western Ontario, St Joseph's Health Care, London, ON, Canada, 13Scleroderma Research Consultants LLC, Litchfield, CT, 14Rheumatology, Radboud University Medical Centre, Nijmegen, Netherlands, 15Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland

First publication: September 18, 2017
Background/Purpose: Pulmonary arterial hypertension (PAH) is a severe complication of systemic sclerosis (SSc), and its diagnosis requires right heart catheterization (RHC). The DETECT study developed an algorithm to select SSc patients with high suspicion of PAH for referral to RHC, identifying patients with early stage PAH and minimizing missed diagnoses. In this longitudinal follow up study, we aimed to identify factors associated with PAH progression in the DETECT cohort.

Methods: DETECT enrolled patients with SSc fulfilling the 1980 ACR classification criteria with a disease duration <3 years since the first non-Raynaud symptom, and who had a pulmonary diffusing capacity for carbon monoxide (DLCO) < 60% of the predicted value. Patients who had been previously diagnosed with pulmonary hypertension (PH) by RHC, who received treatment for PH, and who were at risk for developing PH other than PAH were excluded. A broad range of clinical and laboratory parameters potentially associated with PAH were assessed and PAH was assessed and RHC was performed in all patients at baseline. Patients diagnosed with PAH at baseline were followed up for up to 3 years in centers that agreed for the longitudinal part of the DETECT study, collecting data on survival, World Health Organization (WHO) Functional Class (FC), hospitalization, and PAH-specific treatment. Disease progression was defined as the occurrence of any of the following: WHO-FC worsening, PAH therapy with a drug combination, PAH-related hospitalization, or death. Associations between baseline variables and disease progression were assessed by univariable logistic regression.

Results: Of the 145 SSc patients with PH enrolled in the DETECT study, 87 patients were diagnosed with group I PH (PAH), of whom 57 participated in the longitudinal follow up study (median follow-up time 12.6 months, interquartile range 10.7-21.7 months). Among these 57 patients, 33 (57.9%) had mild PAH, in WHO FC I or II, and 52 received PAH-specific therapy. During follow-up, 25/57 (43.9%) patients had disease progression (4 deaths, 11 hospitalizations for PAH, 14 with worsening in WHO FC, and 8 received PAH-specific combination treatment), with a 1-year survival rate of 93%. The following factors [odds ratio, (95% confidence interval, CI)] were associated with disease progression: male gender [4.1 (1.1-14.1)], high Forced Vital Capacity (FVC) % predicted/ DLCO % predicted ratio [3.6 (1.2-10.7)], and high Borg dyspnoea index [1.7 (1.1-2.6)]. Low DLCO (% predicted) was also significantly associated with progression [area under the curve (95% CI) 0.8 (0.6-0.9)], but the relationship was not linear. A sensitivity analysis, excluding 4 patients with missing outcome data, was also performed and found similar results.

Conclusion: Although the large majority of these patients with early-diagnosed SSc-PAH were treated with PAH-specific drugs, more than 40% had disease progression during a rather short follow-up time, with male gender, functional capacity, and pulmonary function tests (low DLCO, high FVC/DLCO % predicted ratio) at PAH diagnosis being associated with progression. This suggests that even mild and early detected PAH should be regarded as a high-risk complication of SSc.

Disclosure: C. Mihai, Actelion Pharmaceuticals Ltd., Geneva Romfarm, Abbvie, Roche, 5; M. Antic, None; R. Dobrota, Actelion Pharmaceuticals Ltd., Pfizer, 2; D. Bonderman, Actelion Pharmaceuticals Ltd, GlaxoSmithKline, Merck Sharp & Dohme, Bayer, Pfizer, AOP Orphan, United Therapeutics, 5; H. Chadha-Boreham, Actelion Pharmaceuticals Ltd., 3; J. G. Coghlan, Actelion Pharmaceuticals Ltd, GlaxoSmithKline, United Therapeutics, Bayer, Endotronics, 5; C. Denton, Actelion Pharmaceuticals Ltd, Pfizer, GlaxoSmithKline, Sanofi-Aventis, Novartis, 5; M. Doelberg, Actelion Pharmaceuticals Ltd., 3; E. Gruenig, Actelion Pharmaceuticals Ltd, GlaxoSmithKline, Merck Sharp & Dohme, Bayer, United Therapeutics, Pfizer, OMT, AOP Orphan, Novartis, 5; D. Khanna, Actelion Pharmaceuticals Ltd, Bayer, Bristol-Myers Squibb, Covis, Cytori, EMD Serono, Genentech/Roche, Gilead, GSK, Sanofi-Aventis, 5, NIH K24AR063120, 2; V. McLaughlin, Actelion Pharmaceuticals Ltd, Bayer, Gilead, Novartis and United Therapeutics, 5; U. Müller-Ladner, Actelion Pharmaceuticals Ltd, Pfizer and GlaxoSmithKline, 5; J. E. Pope, Actelion Pharmaceuticals Ltd, Bayer, Bristol-Myers Squibb, Merck, Roche, 5; D. M. Rosenberg, Actelion Pharmaceuticals Ltd., 3; J. R. Seibold, Athersys, BriaCell Therapeutics, Pacific Therapeutics, Cytori, 1,Actelion Pharmaceuticals, Bayer, Boehringer-Ingelheim, Covis, Cytori, Eiger, Eicos, EMD Serono, Ironwood, Octapharma, Medac, 5; M. C. Vonk, Actelion Pharmaceuticals Ltd, Therabel and United Therapeutics, 5; O. Distler, 4 D Science, Actelion, Active Biotec, Bayer, Biogen Idec, Boehringer Ingelheim Pharma, BMS, ChemomAb, EpiPharm, Ergonex, espeRare foundation,
Regional and Whole Gut Transit Times in Patients with Systemic Sclerosis Using the Wireless Motility Capsule

Neetu Bali¹, Isela Valera², Aly Aly³, Jeffrey Conklin⁴, Daniel E. Furst⁵ and Suzanne Kafaja⁶, ¹Pediatric Gastroenterology, Hepatology, and Nutrition, David Geffen School of Medicine at UCLA, Los Angeles, CA, ²Autoimmunity and Tolerance Laboratory, Division of Rheumatology, Department of Medicine, David Geffen School of Medicine at University of California Los Angeles, Los Angeles, CA, ³Chamblion St., Alexandria Faculty of Medicine, Alexandria, Egypt, ⁴Medicine, Division of Digestive Diseases at UCLA, Los Angeles, CA, Los Angeles, CA, ⁵David Geffen School of Medicine at UCLA, Los Angeles, CA, ⁶Department of Internal Medicine, University of California Los Angeles, David Geffen School of Medicine, Division of Rheumatology, Los Angeles, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The Gastrointestinal tract (GI) is one of the most commonly affected systems in systemic sclerosis (SSc), impacting the lives of up to 90% of patients, irrespective of their disease subtype. Of the GI manifestations in SSc, GI dysmotility impacts as many as 90% of patients with SSc. Various GI modalities are used to assess and aid in the diagnosis of GI tract motility compromise. The wireless motility capsule (WMC) is an ambulatory, noninvasive and ingestible device that measures intraluminal pressure, pH, and temperature changes as it moves through the GI tract. This helps evaluate regional and whole gut transit times, as well as phasic GI motor activity.

Objective: To describe the regional and whole gut transit times in patients with SSc and to evaluate relationship between GI transit time and other organ manifestation in SSc disease.

Methods: This was a retrospective analysis of all SSc patients from the UCLA SSc program and the UCLA- database, meeting the 2013 ACR/EULAR SSc classification criteria, ≥ 18 y.o, and having had a WMC test performed from July 1, 2013 to July 1, 2016. We reported both regional (gastric emptying, small bowel, and colonic transit times) as well as whole gut transit times. We evaluated other rheumatologic manifestations, including: interstitial lung disease (ILD), pulmonary arterial hypertension (PAH), creatinine clearance (CrCl), and diffuse vs. limited disease. Additionally, we reported patient-reported symptoms related to upper and lower GI transit, including GERD, heartburn, regurgitation, vomiting, dysphagia, constipation, and diarrhea. Statistical analyses of numerical variables were assessed using Wilcoxon rank sum tests and T-tests and categorical variables were assessed using Fisher’s exact tests.

Results: A total of 35 patients met our inclusion criteria. The median age was 57.5 years. There were 34 (97%) women; 23 (65%) were white/Caucasian; 28 (80%) were non-Hispanic/Latino; 25 (71.4%) had limited SSc; 22 (62.9%) had ILD; 16 (45.7%) had PAH. The mean CrCl was 78.1 with SD of 24.8. No statistically significant correlation was noted between regional and/or whole gut motility and other SSc organ manifestation. We found that 42.9% had decreased gastric emptying; 37.5% had decreased small bowel transit time; 33.3% had decreased colonic transit time.
**Conclusion:** In this small cohort, we did not find a significant correlation between regional and whole gut transit times and other manifestations of SSc. Interestingly, we found a discrepancy between patient-reported symptoms and WMC transit times, indicating that symptomatology may not be correlated with a decrease in regional GI transit times. A larger cohort study is needed to verify our findings.

**Disclosure:** N. Bali, None; I. Valera, None; A. Aly, None; J. Conklin, None; D. E. Furst, Grant/Research Support: Amgen, BMS Novartis, Pfizer, Roche/Genentech, Corbus. Consultant: AbbVie, Amgen, BMS, Corbus, Cytori, , Novartis, Pfizer, Roche/Genentech, Speakers Bureau (CME or non-promotional only): BMS, Abbvie NO stocks, royalties, direct fina, 2, see above, 5, see above, 8; S. Kafaja, None.


Abstract Number: 2685

**Sensitivity and Specificity of YKL-40 for the Presence of Pulmonary Arterial Hypertension in Systemic Sclerosis**

Tetsuya Furukawa¹, Kiyoshi Matsui², Masayasu Kitano², Yuichi Yokoyama³, Naoto Azuma² and Hajime Sano²,

¹Division of Rheumatology Department of internal medicine, Hyogo College of Medicine, Nishinomiya, Japan,
²Division of Rheumatology, Department of Internal Medicine, Hyogo College of Medicine, Nishinomiya, Japan,
³Division of Rheumatology, Department of internal medicine, Hyogo College of Medicine, Nishinomiya, Japan

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Tuesday, November 7, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

**Background/Purpose:** Systemic sclerosis (SSc) is an intractable connective tissue disease that causes fibrosis of the skin and organs. The prognosis of this disease is affected by interstitial pneumonia (IP) and pulmonary arterial hypertension (PAH). Chitinase-like protein YKL-40 has been implicated in inflammation and tissue remodeling. A previous study in our department demonstrated elevated blood levels of YKL-40 in Japanese SSc patients. Examinations of the relationship between YKL-40 and PAH in SSc using immunohistochemistry (IHC) have yet to be reported in detail.

**Methods:** Subjects comprised 50 SSc patients without complications examined in our department between August 2014 and April 2017 (Group 1), 18 SSc patients with IP (Group 2), 5 SSc patients with PAH (Group 3), and 5 SSc patients with both IP and PAH (Group 4), as well as a control group of 17 healthy individuals (Group 0). IHC was performed on 7 samples of normal skin and 7 stored samples of SSc skin. Serum levels of YKL-40 were measured by Enzyme Linked Immuno Sorbent Assay and age-adjusted reference levels were calculated [age-percentile strata for YKL-40 = 100/(1+ (YKL-40-3)×(1.062^age)×5000)].

**Results:** We first examined Groups 0, 1 and 2. The YKL-40 age-percentile was 23.9±17.1 in Group 0, significantly higher than in Group 1 (46.3±26.6) or Group 2 (54.2±26.7) (Steel-Dwass test between Groups 0, 1 and 2, p<0.01). No significant difference was evident between Groups 1 and 2 (p=0.52). We then performed immunostaining with YKL-40 antibody for specimens from healthy individuals and SSc patients. All normal skin remained unstained by IHC, whereas subcutaneous vascular endothelium showed prominent staining in all SSc samples. Finally, we examined SSc patients with PAH. YKL-40 age-percentile was 89.7±10.4 in Group 3 and 94.0±11.2 in Group 4. No significant difference was seen between Groups 3 and 4 (Steel-Dwass test between Groups 1-4, p=0.63), or between Groups 1 and 2 (p=0.69). A
significant difference was found between the other groups (p<0.05). YKL-40 age-percentile was more increased with PAH than with other conditions. SSc patients were divided based on presence or absence of PAH and ROC analysis was performed. SSc complicated with PAH could be diagnosed with 80.0% sensitivity and 94.1% specificity.

**Conclusion:** YKL-40 appears to reflect regeneration from capillary injury in SSc, as capillary vessels of the superficial dermis showing staining under IHC. PAH may reflect angiogenesis due to capillary injury in SSc, along with significant rises in YKL-40 in Groups 3 and 4 that complicated PAH and IHC results. YKL-40 may offer a useful and easily applied diagnostic biomarker for SSc and complicated PAH.

**Disclosure:** T. Furukawa, None; K. Matsui, None; M. Kitano, None; Y. Yokoyama, None; N. Azuma, None; H. Sano, None.


Abstract Number: 2686

**In Established Pulmonary Arterial Hypertension the Follow-up Cardiac Catheterization-Derived Pulmonary Artery Systolic Pressure and Vascular Resistance May be Predicted By Echocardiography- a Longitudinal Study in Two Connective Tissue Disease Cohorts**

Vasiliki-Kalliopi Bournia¹, Iraklis Tsangaris², Loukianos Rallidis², Anastasia Anthi², Stylianos Orfanos², Eftychia Demerouti³, Panayiotis Karyofyllis³, Vasilis Voudris³, Stylianos Panopoulos and Petros P Sfikakis⁴,5, ¹First Department of Propedeutic and Internal Medicine and Joined Rheumatology Program, National and Kapodistrian University of Athens Medical School, Athens, Greece, ²Pulmonary Hypertension Clinic, National and Kapodistrian University of Athens Medical School, Athens, Greece, ³Cardiology Department, Onassis Cardiac Surgery, Athens, Greece, ⁴First Department of Propaedeutic and Internal Medicine and Joint Rheumatology Program, National and Kapodistrian University of Athens Medical School, Athens, Greece, ⁵First Department of Propaedeutic and Internal Medicine and Joint Rheumatology Program, National and Kapodistrian University of Athens Medical School, Athens, Greece

First publication: September 18, 2017

SESSION INFORMATION

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster III

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Pulmonary arterial hypertension (PAH) associated with connective tissue disease should always be diagnosed with the gold-standard method of right heart catheterization (RHC). On the other hand, transthoracic echocardiography (TTE) is well validated for initial assessment when PAH is suspected. Whether TTE has a role in the follow-up of PAH is less known. The purpose of this study was to test the hypothesis that TTE can predict follow-up RHC-derived hemodynamic measurements in connective tissue disease-associated PAH.

**Methods:** This retrospective study included two independent cohorts of 30 and 14, patients, respectively, with systemic sclerosis (n=34) and mixed connective tissue disease (n=10) (mean age±SD: 59.09±12.16 years, 86% women), in whom PAH had been suggested by baseline TTE and confirmed by RHC [pulmonary artery systolic pressure (PASP): 59.3±16.8, range 25-90mmHg; pulmonary vascular resistance (PVR): 6.2±3.2, range 0.7-14.5 Wood units]. All 44 patients underwent a second RHC and TTE at follow-up after 9.6±5.7 (range 4-29) months. Seventeen patients had a 3rd
follow-up RHC and TTE 18.7±7.1 (range 10-37) months from baseline, thus producing in all 50 and 28 pairs of baseline/follow-up measurements, in each cohort, respectively. By considering as the gold-standard the follow-up RHC, we examined whether clinically meaningful hemodynamic changes from baseline (i.e. greater than +15% change) in either RHC-derived PASP or PVR could be predicted by the corresponding TTE-derived PASP changes from baseline to follow-up. RHC and TTE were always performed, each, by the same examiner.

Results: In 72% and 93% of comparisons between baseline and follow-up, in the first and second cohort respectively, the latter TTE measurements could safely replace RHC in terms of PASP estimation. Using Mc Nemar’s test we confirmed that the two methods did not differ significantly in either cohort (p=0.79 and p=0.48 for the first and the second cohort, respectively). When in addition to changes in PASP, PVR changes were also considered, follow-up TTE could again safely replace the second RHC in terms of PASP and PVR estimation in 74% and 89% of patients retests (p=0.58 and p=0.25 for the first and the second cohort, respectively). Of note, baseline hemodynamic values or TTE measurements did not differ between patients in whom TTE could predict RHC-derived PASP and PVR and those in whom the results of the two methods at follow-up were divergent.

Conclusion: In a study where operator-dependent methodological errors are limited, we found, in two independent cohorts, that 4 out of 5 patients with connective tissue disease-associated PAH, PASP and PVR can be safely monitored in the long-term non-invasively. Further studies to help identify those patients at need for follow-up RHC are warranted.

Disclosure: V. K. Bournia, None; I. Tsangaris, None; L. Rallidis, None; A. Anthi, None; S. Orfanos, None; E. Demerouti, None; P. Karyofyllis, None; V. Voudris, None; S. Panopoulos, None; P. P. Sfikakis, None.


Abstract Number: 2687

Characteristic of Pulmonary Arterial Hypertension in Patients with Anti-U1RNP Antibody-Positive-Connective Tissue Diseases Is Determined By the Underlying Disease Rather Than Autoantibody Profile

Hidekata Yasuoka¹, Hiroshi Takei¹, Yuichiro Shirai², Kunihiro Yamaoka¹, Masataka Kuwana¹,² and Tsutomu Takeuchi¹, ¹Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, ²Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Patients with connective tissue diseases (CTDs) positive for anti-U1RNP antibody (U1) is characterized by overlapping feature of systemic sclerosis (SSc), systemic lupus erythematosus (SLE), and/or polymyositis/dermatomyositis (PM/DM). Anti-U1RNP antibody is reported to associate with development of pulmonary arterial hypertension (PAH), which is an important organ involvement that determines the prognosis of these patients. The aim of this study was to clarify whether the antibody profile or underlying disease component can determine the characteristic of PAH in this group of patients.
Methods: Thirty-two patients with U1(+)CTD-PAH were involved and 7 U1(-)SLE patients complicated with PAH were used as controls. Patients with SSc, SLE, PM/DM were fulfilled 2013 ACR/EULAR classification criteria, 2012 SLICC classification criteria, and Bohan and Peter’s criteria, respectively. Baseline clinical information retrospectively collected from records, the changes of parameters of right heart catheterization (RHC) within 12 months as a response to the initial treatment and survival rate were compared among patients with overlap syndrome (OL), U1(+)SLE and U1(-) SLE.

Results: Of 32 patients with U1(+)CTD-PAH, underlying diseases were OL (58 %), SLE (29 %), Sjogren’s syndrome (9 %), and SSc (6 %). Interestingly, all patients with OL fulfilled criteria of SSc and SLE components. Age at diagnosis of PAH was tended to be higher in OL (44 ± 14 years) compared to U1(+)-SLE (36 ± 14 years) or U1(-) SLE (35 ± 10 years), and frequency of having ILD was higher in OL compared to U1(+) or U1(-)-SLE (72 % versus 11 %, P < 0.001 or 14 %, P < 0.03, respectively). The change of RHC parameters from baseline such as mean pulmonary arterial pressure (-3.3 ± 8.4 versus -13.3 ± 10.0 mmHg, P < 0.04), pulmonary vascular resistance (0.2 ± 9.2 versus -5.5 ± 2.0 wood units, P < 0.05), or cardiac output (0.4 ± 1.6 versus 1.0 ± 2.3 L/min) were worse in patients with OL compared to those with U1(+)-SLE. There was no difference in survival rate among patients with OL, U1(+)-SLE, and U1(-) SLE. However, all 4 deceased cases with SLE-PAH, both U1(+) and U1(-), were observed within 13 months, but those with OL-PAH were distributed through the course and only 1 of 6 patients died within 13 months (P < 0.05).

Conclusion: Characteristic of PAH complicated with OL patients, who had clinical features of SSc and SLE, was different from those with SLE patients, irrespective of U1-positivity, suggesting that clinical characteristic of PAH complicated with CTD patients with anti-U1RNP antibody was determined by underlying disease components rather than autoantibody profile.

Disclosure: H. Yasuoka, None; H. Takei, None; Y. Shirai, None; K. Yamaoka, None; M. Kuwana, None; T. Takeuchi, None.


Abstract Number: 2688

Collagen Metabolite Biomarker Levels Are Associated with the Amount of Fibrosis in Internal Organs in Systemic Sclerosis Patients

Anne Sofie Siebuhr1, Satoshi Kubo2, Pernille Juhl3, K Nakano4, S Nakayamada5, Morten Karsdal6, Anne-C. Bay-Jensen7 and Yoshiya Tanaka8, 1 the first department of internal medicine, University of occupational and environmental health, Fukuoka, Japan, 2The first department of internal medicine, University of Occupational and environmental Health, Fukuoka, Japan, 3Nordic Bioscience, Herlev, Denmark, 4the first department of internal medicin, University of occupational and environmental health, fukuoka, Japan, 5The first department of internal medicine, University of Occupational and environmental Health, fukuoka, Japan, 6Biomarkers and Reseacrh, Nordic Bioscience, Herlev, Denmark, 7Biomarkers and Reseacch, Nordic Bioscience, Herlev, Denmark, 8The First Department of Internal Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Biomarkers that can monitor the fibrotic burden will aid in trial enrichment and personalized health care in SSc. SSc is associated with internal organ involvement (lung, renal, and gastrointestinal) in the form of fibrosis. Fibrosis is unbalance in extracellular matrix (ECM) turnover and protease specific protein fragments are released during fibrosis. The main family of protein in ECM is collagen, with type I, III and VI localized to interstitial matrix and type IV collagen localized to basement membrane. The aim of our study was investigating biomarker levels relation to the amount of internal organ involvement. 

**Methods:**

Serum from 79 SSc and 19 asymptomatic individuals were included in the study. Biomarkers of type I, III, IV, V and VI collagen formation (P1NP, PRO-C3, P4NP7S, PRO-C5, PRO-C6) and degradation (C3M, C4M2, C5M, C6M) and citrullinated and MMP-degraded vimentin (VICM) were detected by ELISA. Modified Rodnan skin score (mRSS) and extent of internal organ involvement (renal, lung, vasculopathy, and upper and lower gastrointestinal) were recorded for SSc patients with a scoring between 0 and 4 with 0 being no involvement and 4 being severe involvement. Patients were categorized as having no internal organ involvement when 0 and minor with 1. A score of 2, 3 or 4 were classified as definite. Statistics was Mann-Whitney t-test, Spearman’s and trend analysis. 

**Results:**

SSc patients had a mean age of 63.0 years, mean disease duration of 98.3 months and a mean mRSS of 11.1. Patients compared to controls had higher levels of C5M, C6M and PRO-C6 (p=0.0001, p<0.0001, p<0.0001, respectively). Type VI collagen formation and degradation (PRO-C6 and C6M) were twice that of healthy controls (12.6 vs. 5.4 and 26.0 vs 16.7 ng/ml, respectively). C4M2, PRO-C3 and PRO-C6 was associated with skin fibrosis assessed by mRSS (Spearman’s rho=0.24, 0.39 and 0.29, respectively). mRSS was significantly increased with the amount in internal organ involvement (p<0.005). C3M, C4M2 and P4NP7S levels were lowest in the group of patients with some internal organ involvement (p<0.05) and PRO-C6 trended to increase with the number of organs involved (p=0.035). 

**Conclusion:**

Biomarkers of collagen turnover, a surrogate of fibrosis, were increased in SSc and were related to the number of internal organs involved. This study illustrates that biomarker levels of ECM turnover needs to be carefully evaluated in SSc patients in regards to the amount of internal fibrosis.
Troponinemia Independently Associates with Mortality in Systemic Sclerosis
Troponinemia independently associates with mortality in systemic sclerosis

**Title:** Troponinemia independently associates with mortality in systemic sclerosis

**Background/Purpose:** Cardiac involvement is common in systemic sclerosis (SSc) and in the early asymptomatic stages, elevated troponin, or troponinemia, may be the only sign of ongoing myocardial disease.

**Methods:** This retrospective, cross-sectional study included SSc patients with any troponin measurement in the past 10 years, as identified using our institution’s electronic medical record system. Elevated troponin was defined as any value above or at the cut off of normal value in a commercially available laboratory. Clinical data including SSc subtype, disease duration, maximum modified Rodnan skin score (mRSS), maximum serum creatine kinase, aldolase, pro-B-type natriuretic peptide (BNP), echocardiographic and right heart catheterization data were compared between those with elevated troponin and normal troponin. Survival analyses including Cox proportional hazards regression analyses were used to compare both groups.

**Results:** 272 patients were identified with a troponin evaluated during the study period. 83 (31%) had an elevated troponin. Compared to those with a normal troponin, SSc patients with troponinemia were more likely to have the diffuse SSc subtype (55% vs. 37%, p=0.004), shorter disease duration since first non-Raynaud’s symptom (5.8 ± 8.4 vs. 6.1 ± 7.6 years; p=0.30), lower ejection fraction (EF) (49.8 ± 12 vs. 54.8 ± 7.3, p<=0.0001), lower FVC (61.2 ± 18.8 vs. 66.8 ± 20.4, p=0.03), higher RVSP (51.7 ± 21.2 vs. 43.8 ± 16.2, p=0.002), more renal crisis (8.4% vs. 2.6%, p=0.04), higher Medsger muscle (p=0.001) and heart severity scores (p=0.001). Patients with troponinemia also have higher CK values (514 ± 783 vs. 300 ± 553, p=0.01) and higher aldolase (15 ± 11 vs. 11.3 ± 6.3, p=0.002). There was higher frequency of death (28% vs. 9.5%, p=<0.0001). Cox proportional regression analyses demonstrated that patients with troponinemia are 3.2 times (95% confidence interval, 1.33 to 7.7, p=0.009) more likely to have death than those without an elevated troponin even after controlling for SSc subtype, age, gender, race, duration of disease, diabetes, coronary artery disease, smoking, CK, BNP, and World Health Organization dyspnea classification.

**Conclusion:** SSc patients with troponinemia have increased all-cause mortality when compared to those without an elevated troponin even after controlling for demographic and disease-specific confounders.
<table>
<thead>
<tr>
<th>Clinical Characteristics</th>
<th>Troponin Positive (N=83)</th>
<th>Troponin negative (N=189)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease duration defined by 1st non-Raynaud's (at first visit)</td>
<td>5.8 ± 8.4 years</td>
<td>6.1 ± 7.6 years</td>
<td>0.79</td>
</tr>
<tr>
<td>Age at SSc diagnosis defined by 1st non-Raynaud's</td>
<td>45.7 ± 14.2 years</td>
<td>44 ± 13.9 years</td>
<td>0.34</td>
</tr>
<tr>
<td>Female</td>
<td>60 (72.3%)</td>
<td>154 (81.5%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Diffuse skin subtype</td>
<td>46 (55.4%)</td>
<td>70 (37%)</td>
<td>0.004</td>
</tr>
<tr>
<td>Renal crisis</td>
<td>7 (8.4%)</td>
<td>5 (2.6%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>34 (41%)</td>
<td>59 (31%)</td>
<td></td>
</tr>
<tr>
<td>African-American</td>
<td>3 (3.6%)</td>
<td>8 (4.2%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximum Heart Severity Score</td>
<td></td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>0</td>
<td>4 (4.9%)</td>
<td>11 (6.0%)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>10 (12.4%)</td>
<td>22 (11.9%)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2 (2.5%)</td>
<td>5 (2.7%)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>40 (49.4%)</td>
<td>45 (24.3%)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximum Muscle Severity Score</td>
<td>32 (38.6%)</td>
<td>123 (65.1%)</td>
<td>0.001</td>
</tr>
<tr>
<td>0</td>
<td>37 (44.6%)</td>
<td>48 (25.4%)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>10 (12.1%)</td>
<td>12 (6.4%)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2 (2.4%)</td>
<td>2 (1.1%)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2 (2.4%)</td>
<td>4 (2.1%)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximum RVSP</td>
<td>51.7 ± 21.2</td>
<td>43.8 ± 16.2</td>
<td>0.002</td>
</tr>
<tr>
<td>Max pro-BNP</td>
<td>6205 ± 22110</td>
<td>896 ± 1833</td>
<td>0.003</td>
</tr>
<tr>
<td>Lowest Ejection Fraction</td>
<td>49.8 ± 12</td>
<td>54.8 ± 7.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Lowest FVC</td>
<td>61.2 ± 18.8</td>
<td>66.8 ± 20.4</td>
<td>0.03</td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td>16 (19.5%)</td>
<td>21 (11.2%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Ever Smoker</td>
<td>34 (41%)</td>
<td>74 (39.2%)</td>
<td>0.44</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>30 (37%)</td>
<td>68 (37%)</td>
<td>0.53</td>
</tr>
<tr>
<td>Diabetes</td>
<td>9 (10.8%)</td>
<td>8 (4.3%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Peripheral artery disease</td>
<td>10 (12.2%)</td>
<td>12 (6.5%)</td>
<td>0.09</td>
</tr>
<tr>
<td>History of myopathy</td>
<td>48 (52%)</td>
<td>57 (30.2%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Maximum CK</td>
<td>514 ± 783</td>
<td>300 ± 553</td>
<td>0.01</td>
</tr>
<tr>
<td>Maximum aldolase</td>
<td>15.0 ± 11</td>
<td>11.3 ± 6.3</td>
<td>0.002</td>
</tr>
<tr>
<td>Deceased</td>
<td>23 (27.7%)</td>
<td>18 (9.5%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Anti-centromere</td>
<td>12 (23.5%)</td>
<td>32 (23.9%)</td>
<td>0.56</td>
</tr>
<tr>
<td>Anti-topoisomerase I</td>
<td>13 (26.5%)</td>
<td>27 (21.3%)</td>
<td>0.29</td>
</tr>
<tr>
<td>Anti-U1RNP</td>
<td>4 (10.8%)</td>
<td>9 (8.9%)</td>
<td>0.50</td>
</tr>
</tbody>
</table>
Plasma D-Dimer Levels Are More Frequently Elevated in Limited Than Diffuse Cutaneous Systemic Sclerosis but Do Not Reflect Disease Duration or Vasculopathy

Anna Gill¹, Svetlana I. Nihtyanova², Pratima Chowdary³ and Christopher Denton¹, ¹Division of Medicine, Centre for Rheumatology and Connective Tissue Disease, University College London, London, United Kingdom, ²Division of Medicine, Centre for Rheumatology and Connective Tissue Diseases, University College London, London, United Kingdom, ³Department of Haematology, Royal Free Hospital, London, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
D-dimers are degradation products of cross linked fibrin and are biomarkers of activation of the coagulation system. Plasma D-dimer levels can be raised in physiological and pathological non-thrombotic conditions and are thought to be related to a pro-thrombotic state.

Studies have shown raised D-dimer levels in systemic sclerosis (SSc), particularly in diffuse SSc (DcSSc). An association between raised D-dimer level and peripheral ischaemia in SSc has also been described, suggesting that this could be related to a pro-thrombotic state.
Methods:

Blood samples were drawn from 60 outpatients who met the 2013 ACR/EULAR classification criteria for SSc. Samples were analysed for Factor XIII (FXIII) activity (U/dL), D-dimer (ng/ml), and fibrinogen (g/L) levels, and activated partial thromboplastin time (aPTT) (s). Clinical data gathered included age, gender, disease subtype, autoantibody details, duration of SSc and complications of SSc. Associations of demographic and clinical characteristics with FXIII were assessed using linear regression, while associations with D-dimer were analysed using Fisher’s exact test and logistic regression.

Results:

Of the 60 patients assessed, 83.3% were female. Age range was 20-82 years, with a mean age of 60.4 years. In terms of SSc subtype, 51.7% had limited SSc (LcSSc). The duration of SSc ranged from 0.62 to 50.6 years, with a mean duration of 14 years. Antibody status was collected; 36.7% were anti-centromere antibody positive, 11.7% were anti-Scl 70 antibody positive, 16.7% were anti-RNA polymerase antibody positive, and 35% had other positive autoantibodies. An overlapping rheumatological condition was found in 15% of patients. Of all patients, 25% had diagnosis of pulmonary fibrosis (PF), 31.7% had a history of digital ulceration (DU), and 8.3% had active DU at the time of blood draw.

D-dimers were raised in 62.7% of the patients. Raised D-dimer was seen more frequently in lcSSc patients (77.4%) compared to dcSSc (46.4%, p=0.017). In addition, older age increased the odds of having raised D-dimer (OR 1.1, p=0.001). Higher fibrinogen was associated with increased odds for raised D-dimer (OR 6.5, p=0.001). There was no association between raised D-dimer level and PF, current or previous digital ulceration (DU).

Factor XIII activity was positively associated with age (for each year older, this increased by 0.75, p=0.007) but did not associate with diffuse subset, disease duration, autoantibody specificity, fibrinogen level or APTT. There was evidence for a weak association between raised D-dimer and FXIII, where patients with raised D-dimer had on average 13.4 U/dL higher FXIII levels compared to those with normal D-dimer, p=0.089.

Conclusion:

This study confirms that D-dimer levels are frequently elevated in SSc. In contrast to previous studies, our data suggest raised D-dimer level is more commonly associated with LcSSc.

There was no correlation between raised D-dimer level and duration of SSc. This is in contrast with other inflammatory markers such as CRP, which are raised in early SSc only. There was no association between D-dimer level and current or previous DU, suggesting that this feature of vascular dysfunction in SSc is not related to a thrombotic state.

Disclosure: A. Gill, None; S. I. Nihtyanova, None; P. Chowdary, None; C. Denton, Actelion, Pfizer, GlaxoSmithKline, Bayer, Sanofi-Aventis, Boehringer Ingelheim, Genentech-Roche, CSL Behring, Biogen, 5,Actelion, GlaxoSmithKline, Bayer, Genentech-Roche, CSL Behring, 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/plasma-d-dimer-levels-are-more-frequently-elevated-in-limited-than-diffuse-cutaneous-systemic-sclerosis-but-do-not-reflect-disease-duration-or-vasculopathy

Abstract Number: 2691

Increased Circulating Cadherin-11 Levels in Patients with Systemic Sclerosis

Bochra Jandali1, Grace H. Lo2, Robert L. Welschhans3, Julio Charles4, Ramona Mihu3,5, Maureen D. Mayes6, Shervin Assassi7 and Sandeep K. Agarwal3, 1Medicine, Section of Immunology, Allergy and Rheumatology, Baylor College of Medicine, Houston, TX, 2Immunology, Allergy, Rheumatology, Baylor College of Medicine, Houston, TX, 3Medicine, Section of Immunology, Allergy and Rheumatology, Baylor College of Medicine, Houston, TX, 4Internal
SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic sclerosis (SSc) is a chronic systemic disease characterized by skin and internal organs fibrosis along with vasculopathy. Previous studies have reported increased cadherin-11 (Cad11) levels in skin of SSc patients and identified Cad11 as a mediator of skin and lung fibrosis. The aim of this study is to determine if circulating Cad11 levels are increased in SSc patients as compared to healthy controls.

Methods: 300 SSc patients with early SSc enrolled in the Genetics versus Environment in Scleroderma Outcome Study (GENISOS) were studied. All patients fulfilled the ACR/EULAR for SSc and had disease duration < 5 years at the time of enrollment. Baseline or the earliest available serum samples from SSc patients were compared to 153 healthy controls matched for age, gender and race. Serum Cad11 levels were determined by ELISA. Sera with Cad11 levels above the lowest test standard in the ELISA (156 pg/ml) were considered positive for Cad11. Categorical variables were analyzed using the Chi-square method and the Fisher’s Exact Test. P value of <0.05 was considered significant.

Results:

SSc patients were enrolled with the median age of 50.1 +/- 13.1 years of which 83% were females. Average disease duration was 3.9 +/- 2.9 year. 42% of patients had limited SSc and 57% had diffuse SSc. SSc-associated autoantibodies were positive for anti-centromere (ACA) in 14%, for anti-topoisomerase (ATA) in 16% and anti-polymerase III (POLIII) in 22% of patients.

SSc patients had increased levels of serum Cad11 (574.8 +/- 140.7 pg/ml) compared to healthy controls (80.1 +/- 45.1 pg/ml). Serum Cad11 levels were above the lower limit of detection of the ELISA in 16.1% of SSc patients compared to 4.6% of controls. SSc patients were more likely to have detectable levels of serum Cad11 than controls (OR 4.1, 95%CI 1.9-8.8), which remained significant after adjusting for age, gender and race. Compared to patients with limited SSc, patients with diffuse SSc were less likely to have detectable levels of Cad11 in serum samples (limited 24%, diffuse 14%, OR 0.5, 95% CI 0.3-0.9). Chi squared analyses comparing ACA, ATA, and POLIII positivity did not reveal any differences between the autoantibody positive subsets or between the autoantibody positive subset versus the autoantibody negative subsets. Compared to healthy controls, the ACA+ and POLIII+ patients were more likely to have detectable Cad11 levels (p value 0.0006 and 0.027 respectively

Conclusion:

SSc patients are more likely to have detectable levels of serum cadherin-11 compared to healthy controls. These data add to the paradigm that suggests an important role for cadherin-11 in systemic sclerosis.

Disclosure: B. Jandali, None; G. H. Lo, None; R. L. Welschhans, None; J. Charles, None; R. Mihu, None; M. D. Mayes, None; S. Assassi, None; S. K. Agarwal, Roche Pharmaceuticals, 1.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/increased-circulating-cadherin-11-levels-in-patients-with-systemic-sclerosis

Abstract Number: 2692
Vitamin D Deficiency in Systemic Sclerosis Patients: Relations with Multiple Clinical Parameters and Standard Treatment

Amelia Chiara Trombetta1, Vanessa Smith2, Emanuele Gotelli1, Massimo Ghio1, Sabrina Paolino1, Carmen Pizzorni3, Amber Vanhaecke4, Barbara Ruaro5, Alberto Sulli3 and Maurizio Cutolo3
1Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, IRCCS San Martino, Genoa, Italy, Genoa, Italy, 2Faculty of Internal Medicine, Ghent University, Ghent, Belgium, 3Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, IRCCS Policlinico San Martino, University of Genoa, Genoa, Italy, Genoa, Italy, 4Department of Rheumatology, Ghent University Hospital, Ghent University, Ghent, Belgium, Gent, Belgium, 5Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genoa, Genoa, Italy, Genoa, Italy

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster III
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Vitamin D Deficiency In Systemic Sclerosis Patients:

Relations With Multiple Clinical Parameters and Standard Treatment

Background/Purpose: In SSc patients, low 25-hydroxyvitamin D (25(OH)D) serum concentrations have been shown [1]. Primary aim of the study was to evaluate possible correlations between 25(OH)D serum levels and multiple clinical parameters, in patients with systemic sclerosis (SSc). Secondary aim was the evaluation of the effectiveness of standard vitamin D replacement therapy.

Methods: 154 SSc patients were recruited in all seasons of the year. 25(OH)D serum concentrations were evaluated using LIAISON 25-OH system (Diasorin, Italy). In addition, Medsger’s disease severity scale (DSS), nailfold video capillaroscopy (NVC) and all examinations covered by the international guidelines were evaluated [2]. Treatments assumption, including oral colecalciferol, was considered. Non-parametric tests were used for statistical analysis.

Results: 25(OH)D mean serum concentration was 18.7 ±9 ng/ml (<20 classified as a deficiency). A statistically significant correlation was found with presence/absence of fibrotic abnormalities at lung CT scan (16.1 ±8 ng/ml and 20 ±10 ng/ml respectively, p= 0.04) (Figure 1A). DSS parameters correlating with serum concentrations of 25(OH)D were: peripheral vascular (p= 0.03), kidney (p= 0.02), gastrointestinal (p= 0.05) (Figure 1B, 1C, 1D). No significant correlation was observed with digital ulcers incidence, which was closely related to NVC patterns (p<0.0001).

As expected, a statistically significant difference was observed between 25(OH)D serum concentrations in different seasons (winter: 14.6 ±7.8 ng/ml, spring: 17.2 ±7.9 ng/ml, summer: 21.43 ±10 ng/ml, autumn: 20.2 ±10 ng/ml, p= 0.032) (Figure 1E).

No effect of oral colecalciferol (1000 UI per day for at least 6 months) was observed on serum 25(OH)D both in treated (18.8 ±10 ng/ml) or untreated patients (18.7 ±9 ng/ml, p= 0.81) (Figure 1F).
Conclusion: 25(OH)D deficiency correlated with advanced lung involvement and peripheral vascular system, kidney, and gastrointestinal tract involvement (according to the Medsger's DSS). Supplementation with standard doses of oral colecalciferol was not effective in increasing serum concentrations of 25(OH)D. Therefore, for substitutive therapy, higher doses of colecalciferol should be evaluated [3].


Disclosure: A. C. Trombetta, None; V. Smith, None; E. Gotelli, None; M. Ghio, None; S. Paolino, None; C. Pizzorni, None; A. Vanhaecke, None; B. Ruar, None; A. Sull, None; M. Cutolo, None.


Abstract Number: 2693

Relationships between Levels of Patient Activation, Self-Efficacy, and Demographic Variables in Systemic Sclerosis

Janet L. Poole1, Veronica J. Berrocal2, Jennifer Serrano3, Erica Bush3 and Dinesh Khanna3, 1Health Sciences Ctr OT Program, 1 University of New Mexico, Albuquerque, NM, 2Div of Rheumatology, University of Michigan, Ann Arbor, MI, 3University of Michigan, Ann Arbor, MI

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: ARHP Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Patient activation refers to the ability and confidence people have to be engaged in managing their health care [Hibbard, 2004]. Knowledge and beliefs about one’s chronic condition and self-efficacy are both part of patient activation. In a rare, disease, such as systemic sclerosis (SSc), patients must manage their symptoms and advocate for their treatment. Patients with SSc were reported to have low self-efficacy compared to other chronic conditions [Thombs, 2017], they
may also have low patient activation. Thus, the purpose of this study was to examine relationships between patient activation, self-efficacy and demographic variables that could influence patient activation.

**Methods:**

SSc participants, who were part of a larger study on self-management, completed the Patient Activation Measure (PAM). The PAM is a 13 item questionnaire that measures confidence in self-management of one’s chronic condition [Hibbard, 2005]. Higher scores indicate more confidence and knowledge in managing their condition. Based on total scores, patients are categorized into 4 levels: Level 1 (beginning to take role), Level 2 (building knowledge), Level 3 (taking action) and Level 4 (maintaining behaviors). Patients also completed a demographic questionnaire, the Patient Health Questionnaire (PHQ), the PROMIS-29 and PROMIS self-efficacy scales. Significant differences in PAM scores between subgroups were determined using t-tests, Wilcoxon tests or Fisher’s exact tests depending on the distribution of the variables. t-tests were used for variables that were approximately normally distributed, non-parametric Wilcoxon tests for non-normally distributed variables and Fisher’s exact tests for discrete, categorical variables. Pearson correlation coefficients were calculated to determine relationships between the PAM, PROMIS-29, PHQ-8 and PROMIS self-efficacy scales.

**Results:**

267 participants completed the questionnaires. Mean age was 53.7 years, disease duration from onset of first SSc symptoms was 11.9 yrs. 91% were women and 82.8 % were white. On the PAM, the majority of our sample (60%) were at Level 4 with 18.7% at Level 3, 11.2% at Level 2 and 10.5% at Level I. There were significant differences in PAM scores between patients without depressed mood (PHQ-8 <10) vs depressed mood (PHQ-8 >10) and for employment status (working full time vs not working full time). PAM activation scores moderately correlated with PROMIS self-efficacy scales for managing emotions (r=0.54, p<.0001), symptoms (r=0.65, p<.0001), social interactions (r=.58, p<.0001) and medications and treatment (r = 0.57, p<.0001). Correlations between the PAM and PROMIS self-efficacy for managing daily activities (r = .38, p < .0001) and all PROMIS-29 subscale scores were fair [r = -0.23 (PROMIS-29 pain intensity) to -0.49, p < .0001 (PROMIS-29 social and PROMIS-29 anxiety)]. Participants in Levels 3 or 4 had significantly better PROMIS-29 and PROMIS self-efficacy scores than participants at Levels 1 or 2.

**Conclusion:**

Conclusion: Our cohort with SSc had high levels of activation. The moderate correlations with self-efficacy suggest Participants with high activation had high self-efficacy but that they are still conceptually distinct constructs.

**Disclosure:** J. L. Poole, PCORI grant, 2; V. J. Berrocal, PCORI grant, 2; J. Serrano, PCORI, 2; E. Bush, PCORI, 2; D. Khanna, Actelion, Bayer, BoehringerIngelheim, Chemomab, Corbus, Covis, Cytori,Eicos, EMD Serono, Genentech/Roche, Gilead, GSK, Sanofi-Aventis,UCB Pharma, 5,NIH/NIAMS, NIH/NIAID,Bayer, BMS, Genentech/Roche, Pfizer, 2,Eicos, 4.


**Abstract Number:** 2694


Janet L. Poole\(^1\), Veronica J. Berrocal\(^2\), Jennifer Serrano\(^3\), Erica Bush\(^3\) and Dinesh Khanna\(^3\), \(^1\)Health Sciences Ctr OT Program, 1 University of New Mexico, Albuquerque, NM, \(^2\)Div of Rheumatology, University of Michigan, Ann Arbor, MI, \(^3\)University of Michigan, Ann Arbor, MI

**First publication:** September 18, 2017
Background/Purpose: Patient reported outcomes are important to measure the effectiveness of non-pharmacological and pharmacological interventions. The goal of PROMIS is to develop standardized items banks for use across different conditions [1]. The PROMIS-29, which assesses difficulty with activities and symptom severity, has been shown to be valid for patients with SSc [2]. However, other PROMIS measures, such as the PROMIS Self-Efficacy scales may be important to the management of a chronic disease such as SSc.

Methods: Participants with SSc, who were part of a larger study on self-management, completed the PROMIS Self-Efficacy Scales and PROMIS-29. PROMIS-29 includes physical function, anxiety, depression, fatigue, sleep disturbance, pain interference, and satisfaction with social roles, while the PROMIS self-efficacy scales measure self-efficacy for emotions, symptoms, daily activities, social interactions, and medication and treatment. Patients also completed a demographic questionnaire and the Patient Health Questionnaire (PHQ). Significant differences in PROMIS and PROMIS-29 scales between subgroups were determined using t-tests, Wilcoxon tests or Fisher’s exact tests depending on the distribution of the variables. t-tests were used for variables that were approximately normally distributed, non-parametric Wilcoxon tests for non-normally distributed variables and Fisher’s exact tests for discrete, categorical variables.

Results:
267 participants completed the questionnaires. Mean age was 53.7 years, disease duration from onset of first SSc symptoms was 11.9 yrs. 91% were women and 82.8 % were white. There were significant differences in all PROMIS self-efficacy and all PROMIS-29 scale scores between patients without depressed mood (PHQ-8 <10) vs depressed mood (PHQ-8 >10). Married patients had significantly better PROMIS Self-Efficacy for social interaction and PROMIS-29 scores for social role, anxiety, depression, and fatigue. Participants who were employed full time had significantly better scores on the PROMIS self-efficacy scales for managing symptoms, daily activities and medications and treatment compared to participants not employed full time. For the PROMIS-29, significant differences were found for scales relative to physical function, social role, depression, fatigue, pain interference and pain intensity.

Disease duration (< median value or > median value) significantly affected PROMIS self-efficacy scales only with respect to managing daily activities and physical function. No significance differences in PROMIS self-efficacy or PROMIS-29 scores were observed between patients with different subtypes of SSc (diffuse vs limited/sine), education level (< or > 12th grade) or race (white versus non-white).

Conclusion:
Patients with SSc who did not have depressed mood, had education above the 12th grade, were married and employed full time had higher PROMIS-29 and PROMIS Self-Efficacy scores.

References:

Disclosure: J. L. Poole, PCORI grant, 2; V. J. Berrocal, PCORI grant, 2; J. Serrano, PCORI, 2; E. Bush, PCORI, 2; D. Khanna, Actelion, Bayer, BoehringerIngelheim, Chemomab, Corbus, Covis, Cytori,Eicos, EMD Serono, Genentech/Roche, Gilead, GSK, Sanofi-Aventis,UCB Pharma, 5,NIH/NIAMS, NIH/NIAID,Bayer, BMS, Genentech/Roche, Pfizer, 2,Eicos, 4.
Latent Profile Analysis-Derived Typologies of Systemic Sclerosis Patients Using Body Image Indicators: A Scleroderma Patient-Centered Intervention Network (SPIN) Cohort Study

Shadi Gholizadeh1, Linda Kwakkenbos2, Marie-Eve Carrier3, Sarah D. Mills1, Rina S. Fox4, Lisa Jewett2, Karen Gottesman5, Scott Roesch1, Brett D. Thombs2 and Vanessa L. Malcarne1, 1SDSU/UC San Diego Joint Doctoral Program in Clinical Psychology, San Diego, CA, 2McGill University; Lady David Institute for Medical Research, Jewish General Hospital, Montreal, QC, Canada, 3McGill University, Montreal, QC, Canada, 4Department of Medical Social Sciences, Northwestern University Feinberg School of Medicine, Chicago, IL, 5Scleroderma Foundation, Los Angeles, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: ARHP Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: A common and distressing manifestation of systemic sclerosis (SSc, or scleroderma) is disfigurement in socially relevant areas of the body, including the face and hands. Disease-related changes in appearance have been associated with body image dissatisfaction and social anxiety. Although there have been studies identifying correlates of body image dissatisfaction, there is a need for an examination that considers the complex relationships among the personal and social aspects of appearance changes. The present study used latent profile analysis (LPA) to identify body image typologies based on variables representing body image and social anxiety. Identified groups were compared on key sociodemographic, medical, and psychosocial variables.

Methods: The sample consisted of 942 patients with physician-confirmed SSc enrolled in the Scleroderma Patient-centered Intervention Network (SPIN) Cohort who completed study questionnaires from April 2014 through October 2016. Patients in the SPIN Cohort were enrolled at 28 centers from Canada, the United States, and the United Kingdom. The sample was randomized into two groups (Sample 1: N = 469; Sample 2: N = 473) in order to conduct the analysis and provide an opportunity to replicate the findings. For the first aim, exploratory LPA was used to derive categorical latent variables that signified profiles of similarly scoring individuals using three indicators of subjective body image (i.e., dissatisfaction with appearance, social discomfort, and body concealment) and three indicators of social anxiety (i.e., social interaction anxiety, social appearance anxiety, and fear of negative evaluation). For the second aim, differences in groups derived from the LPA were examined for select sociodemographic, medical, and psychosocial variables.

Results: The combined samples were predominantly female (87.4%) and White (79.8%), with limited disease (59%) and an average age of 55 years. In both samples, a two-profile solution was derived. These two classes were substantively analyzed for patterns of scores and termed the Appearance Comfortable (n = 336 and n = 375 in Samples 1 and 2, respectively) and Appearance Distressed (n = 133 and n = 98 in Samples 1 and 2, respectively) groups. In both samples, younger age, diffuse disease subtype, and the presence of hypo/hyper-pigmentation were associated with membership in the Appearance Distressed group. The mean modified Rodnan skin scores for patients in the Appearance Comfortable groups were 7.05 (SD = 7.3) and 7.67 (SD = 8.3) in Samples 1 and 2, respectively. The mean modified Rodnan skin scores for patients in the Appearance Distressed groups were 9.83 (SD = 9.6) and 9.60 (SD = 9.7), in Samples 1 and 2.
respectively. Additionally, patients in the Appearance Distressed group had significantly higher scores on measures of depressive and anxious symptoms and disability.

**Conclusion:** This analysis was the first study to identify typologies of patients based on indicators of body image in any disfiguring condition. Two distinct groups were identified distinguishing between an Appearance Comfortable group and an Appearance Distressed group. The results also elucidated variables that can indicate likely group membership.

**Disclosure:** S. Gholizadeh, None; L. Kwakkenbos, None; M. E. Carrier, None; S. D. Mills, None; R. S. Fox, None; L. Jewett, None; K. Gottesman, None; S. Roesch, None; B. D. Thombs, None; V. L. Malcarne, None.


**Abstract Number:** 2696

**Things Left Unsaid: Important Topics That Are Not Discussed between Patients with Systemic Sclerosis, Their Carers and Their Healthcare Professionals**

Christopher Denton¹, Bee Laird², Lizette Moros³ and José Luis Luna Flores⁴, ¹Department of Rheumatology, University College London, Royal Free Hospital, London, United Kingdom, ²Reframe Research, East Sussex, United Kingdom, ³Boehringer-Ingelheim, Ingelheim, Germany, ⁴Boehringer Ingelheim, Ingelheim, Germany

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** ARHP Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Systemic sclerosis (SSc) is a serious rare condition that can be complicated by internal organ damage including interstitial lung fibrosis (SSc-ILD), which is a major cause of mortality. The prognosis and course of disease is unpredictable and treatment is difficult with no approved treatment options for SSc-ILD. It is very challenging for patients and carers to get a clear understanding of the disease, treatment options and likely outcomes. This study explored and identified the information and communication needs of patients with SSc-ILD and their carers.

**Methods:** Qualitative research with 42 physicians who treat patients with SSc (rheumatologists, pulmonologists, internal medicine specialists, dermatologists), 21 patients with diagnosed SSc-ILD, 16 specialist nurses and 5 carers across 5 countries. Included individual in-depth interviews and observed conversations between pairs of patients, physicians and nurses discussing their experiences of SSc-ILD. All interactions were audio recorded, transcribed and analysed using linguistic techniques based on interactional sociolinguistic discourse analysis, to understand whether the information and emotional needs of patients and carers were met.

**Results:** Prognosis and mortality were the main unspoken topics acknowledged by patients, carers and healthcare professionals. These questions were difficult for physicians and nurses to definitively address, especially early in the disease. Patients and carers felt afraid to ask their physicians about mortality, and were unsure how to ask. Most physicians said that they tried to avoid the question because their duty was to give patients some optimism and hope, and not to cause them any additional distress. Other key questions for patients and carers were about relationships, family, and work. These were questions patients were often unable to ask their physicians because of time constraints or because
they felt these were not topics their physicians should or would be concerned about. Often, specialist nurses felt that they had insufficient disease information or knowledge to provide sufficient support.

**Conclusion:** Topics of key importance to patients, carers, physicians and nurses, such as mortality and disease course, are rarely openly discussed, leaving patients uncertain and anxious about the future. By proactively facilitating communication about difficult but important topics, physicians and nurses could help patients and carers manage and plan their lives with SSc. This study shows that a multi-professional team based approach is likely to give better communication and address patient needs and priorities.

**Disclosure:** C. Denton, None; B. Laird, None; L. Moros, None; J. L. Luna Flores, None.

**View Abstract and Citation Information Online** - [http://acrabstracts.org/abstract/things-left-unsaid-important-topics-that-are-not-discussed-between-patients-with-systemic-sclerosis-their-carers-and-their-healthcare-professionals](http://acrabstracts.org/abstract/things-left-unsaid-important-topics-that-are-not-discussed-between-patients-with-systemic-sclerosis-their-carers-and-their-healthcare-professionals)

**Abstract Number:** 2697

**Systemic Sclerosis Quality of Life Questionnaire (SScQoL) Captures the Complex Problems Experienced By Patients with Scleroderma**

**Matylda Sierakowska**1, Stanislaw Sierakowski2, Marzena Olesinska3, Marek Brzosko4, Piotr Leszczynski5, Katarzyna Pawlak-Bus5, Bogdan Batko6, Piotr Wiland7, Maria Majdan8, Małgorzata Bykowski-Sochacka9, Wojciech Romanowski10, Aleksandra Zon-Giebel11, Sławomir Jeka12 and Mwidimi Ndosi13,  
1Department of Integrated Medical Care, Medical University of Bialystok, Białystok, Poland, 2Department of Rheumatology and Internal Diseases, Medical University of Bialystok, Białystok, Poland, 3Department of Connective Tissue Disease, National Institute of Geriatrics, Rheumatology and Rehabilitation., Warsaw, Poland, 4Department of Rheumatology and Internal Diseases, Pomeranian Medical University, Szczecin, Poland, 5Department of Rheumatology and Rehabilitation, Medical University in Poznan, Poznan, Poland, 6Center of Rheumatology, J. Dietl Hospital in Krakow, Krakow, Poland, 7Department and Clinic of Rheumatology and Internal Medicine, Medical University, Wrocław, Poland, 8Department of Rheumatology and Connective Tissue Diseases, Medical University in Lublin, Lublin, Poland, 9Dr J. Titz-Kosko Regional Hospital for Rheumatic Diseases in Sopot, Sopot, Poland, 10Poznan Centre of Rheumatology in Srem, Srem, Poland, 11Silesian Center of Rheumatology, Rehabilitation and Prevention of Disability, Ustron, Poland, 122nd University Hospital, CM UMK, Department of Rheumatology and Connective Tissue Diseases., Bydgoszcz, Poland, 13Department of Nursing and Midwifery, University of the West of England, Bristol, United Kingdom

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** ARHP Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics Poster  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Systemic sclerosis (SSc) is a chronic rheumatic disease that disturbs the patients’ biological, social, emotional spiritual, and physical functioning; resulting in reduced quality of life. The objective of this study was to assess if the newly adapted and validated tool, the Systemic Sclerosis Quality of Life (SscQoL) tool captures the complex health problems experienced by people with SSc.

**Methods:**
This was a cross-sectional analytical study, which included patients with SSc from 11 rheumatology clinics in Poland. We used the SScQoL (score range 0-29) to assess quality of life in people with SSc. We also assessed their functional status (Health Assessment Disability Index, HAQ-DI); psychological status (Hospital Anxiety and Depression Scale, HADS) and severity of other health problems (0-100 mm Visual Analogue Scale, VAS).

Results:

Patient characteristics are summarised in Table 1. Age was correlated with physical functioning domain QoL ($r_p=0.171; p=0.009$) and breathing problems ($r_p=0.168; p=0.011$). There was a correlation between disease duration and the following health problems: breathing problems ($r_p=0.217; p=0.001$), Raynaud's phenomenon ($r_p=0.184; p=0.005$), fingers ulceration ($r_p=0.168; p=0.011$), pain ($r_p=0.154; p=0.019$) and the level of disability ($r_p=0.153; p=0.020$).

Quality of life (SScQoL) was correlated with: HAQ-DI ($r_p=0.735; p<0.001$), HADS-Anxiety ($r_p=0.631; p<0.001$), HADS-Depression ($r_p=0.596; p<0.001$), Pain-VAS ($r_p=0.593; p<0.001$), Fatigue-VAS ($r_p=0.592; p<0.001$) and the severity of Raynaud's phenomenon (0-100 mm VAS) ($r_p=0.417; p<0.001$).

Conclusion:

With the duration of SSc, the severity of clinical symptoms significantly reduced the quality of life of patients. The results suggest that SscQoL captures a range of complex health problems experienced by people with SSc. The improvement of the QoL in patients with SSc should be a priority objective for health professionals.

Table I. Patient characteristics, health problems and quality of life in patients with SSc

<table>
<thead>
<tr>
<th>Variables studied (score range)</th>
<th>Mean (SD) – except where stated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>55.82 (12.55)</td>
</tr>
<tr>
<td>Disease duration</td>
<td>8.39 (8.18)</td>
</tr>
<tr>
<td>HAQ-DI (0 to 3)</td>
<td>0.99 (0.75)</td>
</tr>
<tr>
<td>Pain VAS (0 to 100)</td>
<td>33.08 (28.36)</td>
</tr>
<tr>
<td>Fatigue VAS (0 to 100)</td>
<td>43.00 (29.04)</td>
</tr>
<tr>
<td>Raynaud's attacks (0 to 100)</td>
<td>38.10 (31.90)</td>
</tr>
<tr>
<td>Intestinal problems (0 to 100)</td>
<td>20.18 (27.73)</td>
</tr>
<tr>
<td>Breathing problems (0 to 100)</td>
<td>26.57 (27.59)</td>
</tr>
<tr>
<td>Finger ulceration (0 to 100)</td>
<td>17.50 (27.85)</td>
</tr>
<tr>
<td>HADS A (0 to 21)</td>
<td>8.96 (4.67)</td>
</tr>
<tr>
<td>HADS D (0 to 21)</td>
<td>6.70 (4.12)</td>
</tr>
<tr>
<td>SScQoL (0 to 29)</td>
<td>14.81 (5.08)</td>
</tr>
<tr>
<td>SScQoL (domain)</td>
<td>* Degree of QoL</td>
</tr>
<tr>
<td>Function (0-6)</td>
<td>3.66 (1.57)</td>
</tr>
<tr>
<td>Emotional (0-13)</td>
<td>6.43 (3.04)</td>
</tr>
<tr>
<td>Social (0-6)</td>
<td>2.25 (1.87)</td>
</tr>
<tr>
<td>Sleep (0-2)</td>
<td>0.96 (0.91)</td>
</tr>
<tr>
<td>Pain (0-2)</td>
<td>0.98 (0.84)</td>
</tr>
</tbody>
</table>

*SScQoL domains have different number of items, therefore the degree of QoL is determined by average score divided by the maximum possible score for that domain

Disclosure: M. Sierakowska, None; S. Sierakowski, None; M. Olesinska, None; M. Brzosko, None; P. Leszczynski, None; K. Pawlak-Bus, None; B. Batko, None; P. Wiland, Celltrion Inc., 2; M. Majdan, None; M. Bykowska-Sochacka, None; W. Romanowski, None; A. Zon-Giebel, None; S. Jeka, None; M. Ndosi, None.

Abstract Number: 2698

IL-21-mTOR Axis Blocks the Differentiation and Function of SLE Tregs Via Suppression of Autophagy

Hiroshi Kato¹ and Andras Perl², ¹Division of Rheumatology/Internal Medicine, SUNY Upstate Medical University, Syracuse, NY, ²Dept of Medicine, SUNY Upstate Medical University, Syracuse, NY

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: T Cell Biology and Targets in Autoimmune Disease Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Mechanistic target of rapamycin (mTOR) activation has emerged as a prominent mediator of pro-inflammatory T-cell expansion and regulatory T (Treg) cell depletion in systemic lupus erythematosus (SLE). While Treg dysfunction has been documented in SLE, it is unknown i) whether the mTOR pathway is activated within Tregs, ii) what pro-inflammatory cues regulate mTOR in Tregs, and iii) how mTOR controls their function.

Methods: Naïve CD4⁺ T cells from matched SLE and healthy control (HC) subjects were cultured for 3 days in the presence of anti-CD3/CD28, TGF-β, and IL-2 with or without IL-6, IL-21, or rapamycin. Next, CD4⁺CD25⁺ Treg function was determined in the presence or absence of IL-21 or IL-2 by assessing the % suppression of proliferation of CFSE-stained autologous CD4⁺CD25⁻ responder T cells cultured for 5 days in the presence of anti-CD3 and irradiated PBMCs. In some experiments, Tregs were expanded in vitro for 4 weeks with or without rapamycin before coculture. Upon Treg isolation, -polarization, and -suppression assay, expression of FOXP3, GATA-3, and CTLA-4 in the Treg were determined by flow cytometry. Using lysates of naïve CD4⁺ T cells cultured under Treg-polarizing conditions with or without IL-21, or SLE Tregs expanded in the presence or absence of rapamycin, phosphorylation of STAT3 at tyrosine 705, Akt at Serine 473, S6K1 at Threonine 389, and 4E-BP1 at Threonine 37 and 46, FOXP3, and LC3 were detected by immunoblotting. Cytokine secretion by CD3⁺ T cells cultured in the presence or absence or rapamycin was determined by LUMINEX assay. Statistical analyses were done using Student’s t-test.

Results: SLE Treg exhibits increased mTOR complex 1 (mTORC1) and 2 (mTORC2) activities, but diminished autophagy, GATA-3 and CTLA-4 expression (% CTLA-4⁺ cells among CD4⁺CD25⁺FOXP3⁺ cells, HC: 6.96±0.79%, SLE: 5.11±0.75%; p=0.034), and function. IL-21, but not IL-6, activates mTORC1 and mTORC2, inhibits autophagy, and abrogates Treg differentiation and function (% suppression with or without IL-21, HC: 38.21±3.78%, 46.63±4.90%; p=0.013, SLE: 18.99±4.95%, 30.25±4.48%; p=0.042) although both of these cytokines phosphorylate STAT3 to comparable levels. IL-2 upregulates while IL-21 constrains GATA-3 and CTLA-4 expression selectively in CD4⁺CD25⁺FOXP3⁺ Tregs (% GATA-3⁺ cells with or without IL-21, HC: 47.78±6.12%, 71.20±4.14%; p=0.0075, SLE: 33.49±5.28%, 66.85±6.29%; p=8.15x10⁻⁵, % CTLA-4⁺ cells with or without IL-21, HC: 36.18±2.31%, 43.92±3.87%; p=0.016, SLE: 39.82±4.38%, 52.11±5.66%; p=0.0058). mTORC1 blockade by three-day rapamycin treatment reverses TGF-β deficiency, while dual blockade of mTORC1 and mTORC2 by four-week rapamycin treatment induces autophagy and restores GATA-3 and CTLA-4 expression selectively in CD4⁺CD25⁺FOXP3⁺ cells (GATA-3⁺ cells with or without rapamycin, 25.48±5.73%, 10.78±3.31%; p=0.037, CTLA-4⁺ cells, 23.11±9.08%, 7.51±5.88%; p=0.035), and Treg function (% suppression with or without rapamycin, 57.77±9.62%, 45.41±8.83%; p=0.04).

Conclusion: The data identify IL-21-driven mTOR activation as a pharmacologically targetable checkpoint of deficient autophagy and diminished expression of TGF-β, GATA-3, and CTLA-4 which underlie Treg dysfunction in SLE.

Disclosure: H. Kato, None; A. Perl, None.
Abstract Number: 2699

Mosaic, a Novel Gene, Mediating Autoimmunity in Mice

Alice Chan¹, Mark Anderson², Hong-Erh Liang³ and Elizabeth Li², ¹Pediatrics, UCSF, San Francisco, CA, ²Diabetes Center, UCSF, San Francisco, CA, ³Department of Medicine, UCSF, San Francisco, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: T Cell Biology and Targets in Autoimmune Disease Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: A novel candidate gene, Mosaic (Multi-Organ System Autoimmunity in Canines), was identified as the culprit causing an early and severe multiorgan autoimmunity in a unique subset of dogs. Affected dogs develop early onset Addison’s disease, arthritis, autoimmune cytopenias, hepatitis and uveitis. Adrenal tissue from affected dogs reveal a T cell infiltrate suggesting a T cell mediated autoimmune process. Little is known about Mosaic function. It is conserved across all known vertebrae species including humans and mice, and it is highly expressed in immune cells, particularly in T regulatory cells based on BioGPS. Thus, we hypothesize that disruption of Mosaic function results in a breach in T cell tolerance and leads to multiorgan autoimmunity.

Methods: To assess the effects of Mosaic deficiency, two mouse models were produced. First, Mosaic knockout mice were generated using a B6 ES cell line by deleting at 2.5kb region containing the start codon and inserting a reporter cassette. This reporter will allow tracing of the endogenous gene expression pattern. The 5’ and 3’ regions of the targeted locus was confirmed using long-range PCR and Mosaic transcript was absent. Second, floxed Mosaic mice were generated using CRISPR-Cas9 by inserting two LoxP sequences flanking exon 3 which contains the start codon. Two gRNAs, two oligonucleotides, and Cas9 protein were injected into B6 fertilized eggs. Mice were screened for insertion of LoxP sequences that were in cis position and had no other indels in the targeted region. 3 founders were generated and bred to the CD4-Cre strain to generate deletion of Mosaic in the T cell compartment. Mosaic transcript was absent in the T cells. These mouse models were phenotyped using flow cytometry and histology.

Results: Using the reporter cassette, Mosaic was identified to have the highest expression level in memory T cells and T regulatory cells. Global deletion of Mosaic resulted in partial embryonic lethality. However, viable knockout pups showed increased memory T cells and decreased naïve T cells. Aged mice showed lymphocytic infiltrates in the adrenal and lacrimal glands compared to littermate controls. Analysis of the Mosaic²/²CD4-Cre mice also showed a skewed memory T cell compartment in mice as young as 1 month of age.

Conclusion: Deletion of Mosaic in mice resulted in an autoimmune phenotype with lymphocytic infiltrates in the adrenal and lacrimal glands. These mice also have a skewed memory T cell phenotype which is consistent with other autoimmune mouse models. Further investigation on Mosaic will reveal the molecular mechanism on how Mosaic functions in tolerance.

Disclosure: A. Chan, None; M. Anderson, None; H. E. Liang, None; E. Li, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/mosaic-a-novel-gene-mediating-autoimmunity-in-mice
Abstract Number: 2700

**Fra-2 Overexpression Leads to Systemic Autoimmunity By Affecting IL2 Dependent Treg Homeostasis**

Florian Renoux¹, Mara Stellato¹, Daniela Impellizzeri², Alexander Vogtseder³, Przemyslaw Blyszczuk¹, Riyun Huang⁴, Arun Subramaniam⁵, Clara Dees⁶, Jörg Distler⁷, Gabriela Kania¹, Onur Boyman² and Oliver Distler⁸,  
¹Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland, ²Division of Clinical Immunology, University Hospital Zurich, Zurich, Switzerland, ³Department of Pathology, Cantonal Hospital Lucerne, Lucerne, Switzerland, ⁴Immune Mediated Diseases, Sanofi-Genzyme, Framingham, MA, ⁵Sanofi-Genzyme, Framingham, MA, ⁶Department of Internal Medicine 3 and Institute for Clinical Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Erlangen, Germany, ⁷Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätshospital, Erlangen, Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Erlangen, Germany, ⁸Department of Rheumatology, Center of Experimental Rheumatology, University Hospital Zurich, Zurich, Switzerland  

**First publication:** September 18, 2017

**SESSION INFORMATION**  
**Session Date:** Tuesday, November 7, 2017  
**Session Title:** T Cell Biology and Targets in Autoimmune Disease Poster II  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Fos-related antigen 2 (Fra-2) is a transcription factor belonging to the Fos family proteins which is part of the AP-1 transcription factor complex. We recently described a fra-2 transgenic (tg) mouse model which develops a multi-organ inflammatory phenotype. We have observed abnormalities in the T cell compartment, which led us to hypothesize that fra-2tg mice develop a T cell-driven autoimmune phenotype. Here we aimed to assess the autoimmune nature of the phenotype in fra-2tg mice and to characterize the potential role of Treg cells.

**Methods:** We used previously generated fra-2tg overexpressing mice. T lymphocyte populations were analyzed by flow cytometry for expression of activation markers (CD62L, CD44 and CD25) and secretion of cytokines. We transferred purified CD4+ T cells into Rag2−/− mice lacking T and B cells, and we generated Rag2−/−fra-2tg mice. We used IL-2-IL-2 antibody complexes (JES6.1A12 clone) to induce the proliferation of CD25+ cells in vivo.

**Results:** Rag2−/−fra-2tg did not develop inflammatory manifestations (n=10), demonstrating that the phenotype in fra-2tg mice is autoimmune and requires the presence of T and/or B cells to develop. Accordingly, we tested the ability of CD4+ T cells to induce the phenotype. We found that the transfer of 1*10⁶ purified CD4+ cells from 16 week-old fra-2tg mice into Rag2−/− recipients was sufficient to induce the phenotype (n=3).

Analysis of T cell populations from fra-2tg mice confirmed the presence of activated CD4+ and CD8+ cells in spleen and lung (n=6). After in vitro stimulation, CD4+ T cells from fra-2tg mice had increased Th2 cytokines production (IL-4, IL-5 and IL-13) and we observed an increase in IgE levels in the serum of fra-2tg mice. Thus, these data strongly suggest a Th2 T cell-driven autoimmune disease in these mice.

We also observed a striking decrease of Treg cells in fra-2tg mice, which might explain the observed autoimmune phenotype. Supporting this hypothesis, we found that 3 week-old mice, which were devoid of organ manifestations and of T cell activation, showed already the same defect in the Treg cell population as older mice (n=6, p<0.001).

Interestingly, we also found that in vivo stimulation with IL-2-IL-2 antibody complexes failed to induce the proliferation of Treg cells in fra-2tg mice compared to WT mice, suggesting that fra-2 overexpression affects IL-2 dependent...
proliferation of fra-2	extsuperscript{tg} Tregs. These data indicate that Fra-2 affects Treg homeostasis by modulating IL-2 responsiveness, resulting in the development of an autoimmune phenotype.

**Conclusion:** Our data suggest that Fra-2 controls Treg cell development or homeostasis, possibly by modulating IL-2 signaling in T cells, which leads to autoimmunity in this mouse model. This new pathway could be targeted in a translational approach to modulate the capacity of T cells to differentiate in Tregs during autoimmune disease.

**Disclosure:** F. Renoux, None; M. Stellato, None; D. Impellizzieri, None; A. Vogtsseder, None; P. Blyszczuk, None; R. Huang, Sanofi-genzyme, 3; A. Subramaniam, Sanofi-genzyme, 3; C. Dees, None; J. Distler, 4D Science, 1, Anamar Medical, Active Biotech, Array Biopma, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, GSK, Novartis, Sanofi-Aventis, UCB, 2, Actelion Pharmaceuticals US, Active Biotech, Anamar, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi, UCB, 5; G. Kania, Bayer, 2; O. Boyman, None; O. Distler, Actelion, Bayer, BiogenIdec, Boehringer Ingelheim, ChemomAb, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Novartis, Pfizer, Sanofi, Sinoxa and UCB, 2, Actelion, Bayer, BiogenIdec, Boehringer Ingelheim, ChemomAb, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Novartis, Pfizer, Sanofi, Sinoxa and UCB, 5, mir-29 for the treatment of systemic sclerosis, 9.


**Abstract Number:** 2701
TNFR2+ Regulatory T Cell subpopulations ARE Highly Suppressive and Are Increased on Anti-TNF Treatment

Francois Santinon¹, Maxime Batignes², Benoit Salomon³, Patrice Decker², Marie-Christophe Boissier⁴, Luca Semerano⁵ and Natacha Bessis², ¹INSERM UMR 1125 University of Paris 13, Sorbonne Paris Cité, bobigny, France, ²INSERM UMR 1125 University of Paris 13, Sorbonne Paris Cité, Bobigny, France, ³Sorbonne Universités, UPMC Université Paris 06, INSERM, CNRS, Centre d'Immunologie et des Maladies Infectieuses (CIMI-Paris), Paris, France, ⁴Rheumatology Department, Assistance Publique – Hôpitaux de Paris (AP-HP), Avicenne Hospital, Bobigny, France, ⁵INSERM UMR 1125 University of Paris 13, Sorbonne Paris Cité and Assistance Publique – Hôpitaux de Paris (AP-HP), Avicenne Hospital, Rheumatology Department, France, Bobigny, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: T Cell Biology and Targets in Autoimmune Disease Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: In rheumatoid arthritis (RA), regulatory T cells (Tregs) are defective in their suppressive capacities and fail to control chronic inflammation. TNF-α is involved in inhibition of Treg differentiation and activation, likely via activation of TNF-α type 1 receptor (TNFR1)¹. Conversely, activation of TNFR2 on Tregs is critical for their phenotypic and functional stability in the inflammatory environment². Moreover, it has been shown that therapeutic TNF blockade with the anti-TNF monoclonal antibodies restores the potency of Treg cell suppression in RA by binding to membrane TNF-α on monocytes and promoting Treg cell expansion through enhanced TNFR2 signaling³.

In the present work, we studied the role of TNFR2 on Tregs in control of inflammation at multiple levels, by: 1) studying the action of TNF on Treg function in the presence and absence of TNFR2 in vitro, 2) testing the severity of a model of skin inflammation in TNFR2KO mice, 3) evaluating the evolution of TNFR2-expressing Tregs from RA patients during anti-TNF treatment.

Methods: Mice deficient in the TNFR2 gene (TNFR2 KO) and TNFR2 lox/lox mice to conditionally delete TNFR2 specifically in Tregs were used. CD4⁺CD25⁺Treg cells were purified by magnetic sorting. Cell phenotype was evaluated by flow cytometry. Tregs stability was evaluated by analyzing methylation status of 9 CpG motifs of the Foxp3 locus, assessed by bisulfite sequencing of CD4⁺CD25⁺ purified cells. Skin inflammation was induced by cutaneous application of an imiquimod-containing ointment. Peripheral blood Tregs were characterized before and after 3 months of anti-TNF treatment in 12 RA patients and in 19 patients with axial spondyloarthritis (AxSpA) that were used as control.

Results: In vitro, TNF-α enhanced Foxp3 maintenance in cultured Tregs. With two models of TNFR2 inactivation (a TNFR2-blocking antibody and a TNFR2 knock-out mouse) this effect was mediated by TNF-TNFR2-and not TNFR1-interaction. In vivo, TNFR2-negative Treg cells, from both TNFR2KO and TNFR2 lox/lox mice, had lower spontaneous suppressive capacities (lower inhibition of effector T cell proliferation and IFN-γ production). FoxP3 methylation was higher in Tregs from TNFR2KO mice than wt mice. This suggested that TNFR2 expression confers higher stability to Tregs.

Compared to wt mice, TNFR2KO mice had enhanced skin-inflammation and decreased Tregs and CD39⁺ Tregs frequencies in lymph nodes. In RA patients responding to anti-TNF treatment, an increase in the frequency of TNFR2-expressing Tregs was evident at 3 months of treatment vs. the baseline. Conversely, no variation in the frequency of these cells was observed in AxSpA patients

Conclusion: TNFR2 signaling on Tregs may play a major role in controlling inflammation and can be activated both by TNF-α and anti-TNF treatment. Further studies to dissect TNFR2 dependent pathways on Tregs are warranted.
References


Disclosure: F. Santinon, None; M. Batignes, None; B. Salomon, None; P. Decker, None; M. C. Boissier, None; L. Semerano, None; N. Bessis, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/tnfr2-regulatory-t-cellsubpopulations-are-highly-suppressive-and-are-increased-on-anti-tnf-treatment

Abstract Number: 2702

Tissue-Invasive T Cells in Rheumatoid Arthritis

Cornelia M. Weyand1, Yi Shen2, Yinyin Li1, Eric L. Matteson3, Stuart Goodman4 and Jorg Goronzy5, 1Medicine: Immunology and Rheumatology, Stanford University, Stanford, CA, 2Medicine: Immunology and Rheumatology, Stanford University School of Medicine, Stanford, CA, 3Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, MN, 4Orthopaedic Surgery, Stanford Medical Center Outpatient Clinic, Redwood City, CA, 5Medicine/Division of Immunology & Rheumatology, Stanford University School of Medicine, Stanford, CA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: T Cell Biology and Targets in Autoimmune Disease Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: A key pathogenic event in rheumatoid arthritis (RA) is the formation of lasting lymphoid microstructures in the synovial tissue. It requires the transmigration of T cells from blood vessels into the tissue and the maneuvering of such T cells through the tissue matrix. T cells move in the tissue microenvironment by assembling cell membrane extensions, so-called podosomes. Regulation of podosome formation in T cells from RA patients is unexplored.

Methods: CD4 T cells were isolated from patients with seropositive RA and age-matched healthy controls. Tissue-residing T cells were examined in synovial biopsies. T cell motility was tested in 3D-collagen gels and in vivo by measuring T cell invasion into synovial tissue in a human synovium-SCID chimera model. Cellular metabolism of T cells was evaluated by quantifying stores of pyruvate, ATP, acetyl-CoA, and neutral fatty acids. We defined a module of 10 genes involved in regulation of the actin cytoskeleton and podosome formation, which was analyzed by RT-PCR, flow cytometry and immunohistochemistry.

Results: Compared to age-matched controls, RA T cells were high expressers of the Tyrosine Kinase Substrate with Five SH3 Domains (TKS5), an adaptor molecule critically involved in podosome formation, migrated more efficiently through 3D-gels and rapidly invaded into synovial tissues. TKS5 overexpression was sufficient to render T cells tissue-invasive; TKS5 knockdown abrogated the tissue-invasive behavior of RA T cells. TKS5 overexpression was associated with arthritogenic effector functions in the synovial tissue site, was regulated as part of a motility gene module and was found to be under metabolic control. Specifically, dampened glycolytic flux, resulting in low cellular pyruvate and ATP, induced TKS5 production and enhanced T cell hypermobility. T cells responded to energy deprivation with the
accumulation of cytoplasmic lipid droplets, a prominent feature of tissue-resident synovial T cells. Restoring pyruvate stores or inhibiting fatty acid synthesis was sufficient to correct for the hypermobility of RA T cells in vitro and in vivo.

**Conclusion:** Synovial tissue invasion and arthritogenic T cell effector functions in RA patients are associated with dysregulated membrane function, specifically the formation of tissue-invasive podosomes. Defects in the T cell locomotion program are mechanistically linked to metabolic reprogramming, which diverts RA T cells from energy production to synthetic and proliferative functions. Understanding tissue invasiveness of RA T cells provides new opportunities to interfere with T cell trafficking and T cell invasion into specific tissue sites.

**Disclosure:** C. M. Weyand, None; Y. Shen, None; Y. Li, None; E. L. Matteson, None; S. Goodman, None; J. Goronzy, None.

**View Abstract and Citation Information Online** - [http://acrabstracts.org/abstract/tissue-invasive-t-cells-in-rheumatoid-arthritis](http://acrabstracts.org/abstract/tissue-invasive-t-cells-in-rheumatoid-arthritis)

**Abstract Number:** 2703

**Single Cell Analysis of TCRs from CD8+ T Cells in Sjogren’s Syndrome**

Michelle L. Joachims1, Christina Lawrence1, Richard C. Pelikan1, Kerry M. Leehan1, Lida Radfar2, David M. Lewis3, Astrid Rasmussen1, R. Hal Scofield1, Kiely Grundahl1, Kathy L. Sivils1, Linda F. Thompson1 and A. Darise Farris1,

1Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK,

2Department of Oral Diagnosis and Radiology, University of Oklahoma College of Dentistry, Oklahoma City, OK,

3Department of Oral Pathology, University of Oklahoma College of Dentistry, Oklahoma City, OK

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** T Cell Biology and Targets in Autoimmune Disease Poster II

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Sjögren’s syndrome (SS) is an autoimmune exocrinopathy characterized by focal lymphocytic infiltration of the salivary and lacrimal glands, severe dry eyes and mouth, fatigue and musculoskeletal pain. How the T cell-dominated salivary gland (SG) inflammation is connected to pathologic and clinical features of SS is poorly understood. We reported that SG CD4+ T cell clonal expansion is antigen-driven and correlated with reduced salivary flow and increased SG fibrosis. To determine whether the extent of SG CD8+ T cell clonal expansion is related to pathologic features of disease, we evaluated the CD8+ TCR repertoire of the same subjects.

**Methods:** Multiplex single cell RT-PCR was used to retrieve paired TCR α and β sequences from SG and peripheral blood (PB) memory CD8+ T cells from 11 subjects meeting the 2016 ACR/EULAR classification criteria for primary Sjögren’s syndrome. The extent of SG and PB CD8+ T cell clonal expansion was compared between SG and PB and evaluated for relationships with pathologic and clinical disease features using Mann-Whitney and Spearman rank correlation tests.

**Results:** Our cohort repertoire consisted of over 2,800 TCR sequences isolated from a median of 28 (range 4-67) SG and 19 (range 4-52) PB cells evaluated per subject. Clonal expansions of SG and PB CD8+ T cells were detected in all subjects. Expansions were extensive in both tissue compartments, ranging from 8.3-66.3% in SG (mean 34.9) and 5-48.5% in PB (mean 23.1). Although the percentage of clonally expanded CD8+ T cells did not differ significantly between SG and PB, there were significantly higher levels of clonally expanded SG CD8+ T cells compared to SG CD4+ T cells from the same individuals. Further, many subjects exhibited large expansions, with 60% of individuals having at
least one clonal expansion of 4 or more cells. In contrast to our prior observations in CD4+ T cells, the degree of SG CD8+ T cell clonal expansion did not significantly correlate with measures of oral disease. However, identical clonal expansions were detected in SG and PB in 5/11 patients (45%), indicating significant trafficking of CD8+ T cells in both tissues. Further, several clonotypes of expanded cells shared between SG and PB were identified as viral-specific, indicating the presence of activated viral-specific T cells in the SG of SS patients.

**Conclusion:** Although relatively small numbers of T cells were evaluated in this study, clonally expanded CD8+ T cells were abundant in both the SG and PB of SS patients but did not obviously correlate with measures of disease. Known viral-specific T cells were found in SG and PB from SS patients, adding evidence for viral-initiated or -driven CD8+ T cell proliferation in SS.

**Disclosure:** M. L. Joachims, None; C. Lawrence, None; R. C. Pelikan, None; K. M. Leehan, None; L. Radfar, None; D. M. Lewis, None; A. Rasmussen, None; R. H. Scofield, None; K. Grundahl, None; K. L. Sivils, None; L. F. Thompson, None; A. D. Farris, None.

**Abstract Number:** 2704

**Skin Migratory Dendritic Cells Targeted and Tolerized By Calcitriol-Peptide Liposomes Supress Antigen-Specific Autoreactive T Cell Expansion and Memory Differentiation to Regulate Autoimmune Arthritis**

Ryan Galea1,2, Hendrik Nel1,2, Meghna Talekar1,2, Suzanne Cole3, Karyn Cochlin4, Shannon Hitchcock5, Bijun Zeng1,2, Suman Yekollu1,2, Jamie Rossjohn6, Hugh Reid7, Ravi Malaviya5, Dave Shealy8, Brendan O'Sullivan1,2 and Ranjeny Thomas1,2, 1Dendright Pty Ltd, Brisbane, Australia, 2University of Queensland Diamantina Institute, Brisbane, Australia, 3Immunology, Janssen Research and Development, Spring House, PA, 4Immunology, Janssen Research and Development, Springhouse, PA, 5Janssen Research and Development, Springhouse, PA, 6Infection and Immunity Program, Biomedicine Discovery Institute and Department of Biochemistry and Molecular Biology, Monash University, Clayton, Australia, 7Monash University, Melbourne, Australia, 8Janssen Research and Development, Spring House, PA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** T Cell Biology and Targets in Autoimmune Disease Poster II  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:**

Current treatments to control autoimmune arthritis and vasculitis use broadly immunosuppressive drugs, associated with undesirable side effects. Antigen-specific immunological tolerance strategies are preferable to control both cellular and humoral immune responses in autoimmune diseases, using the natural process of antigen presentation by dendritic cells (DCs) to control the balance of regulatory T cells (Treg) relative to pathogenic effector (Teff) T cells and B cells. In a phase I clinical trial, intradermally-injected autologous DCs exposed to citrullinated peptides and BAY11-7082 reduced circulating Teff and increased the ratio of Treg to Teff in rheumatoid arthritis. However, simpler strategies are desirable for widespread clinical use. In skin draining lymph nodes (dLN), migratory but not resident DCs are required for tolerance. We developed a strategy for passive targeting of DCs in situ after s.c. delivery of a nanoparticulate liposome formation encapsulating peptide and NF-kB inhibitor.
Methods:

Egg phosphatidylcholine liposomes encapsulating 1,25 dihydroxycholecalciferol (calcitriol) and OVA\textsubscript{323-339} or aggrecan\textsubscript{89-103} peptide were prepared by thin film hydration. Distribution of DiI-labeled liposomes was assessed with in vivo imaging and flow cytometry. DO11.10 OVA-specific memory T cells were generated ex vivo. The response of transferred T cells to liposomes administered i.v. or s.c. was assessed by flow cytometry. Proteoglycan-induced arthritis (PGIA) was induced with recombinant human proteoglycan and DDA adjuvant. IAd-aggrecan tetramers identified aggrecan-specific T cells.

Results:

Liposomes encapsulating calcitriol and peptide were 90-130 nm. After s.c. administration, liposomes encapsulating calcitriol and peptide rapidly distributed to the subcapsular sinus then penetrated dLN, with the majority taken up by CD11b+CD11c+MHC class II+ migratory DCs. Two s.c. injections of OVA323-336/calcitriol liposomes suppressed antigen-specific CD4+ T cell expansion and IFN-g production and induced antigen-specific Foxp3+ peripheral (p)Treg. The induced pTreg suppressed proliferation of and promoted IL-10 production by a second cohort of OVA-specific Teff. In the proteoglycan-induced arthritis (PGIA) model, s.c. aggrecan\textsubscript{89-103}/calcitriol but not OVA\textsubscript{323-339}/calcitriol liposomes prevented disease development and suppressed the severity of established arthritis, associated with reduced autoreactive T cell expansion and reduced memory and follicular-helper T cell differentiation relative to naïve T cells.

Conclusion:

Skin migratory DCs are targeted and tolerized by calcitriol-peptide liposomes, triggering “infectious” antigen-specific tolerance mechanisms to regulate autoimmune arthritis.

Disclosure: R. Galea, None; H. Nel, None; M. Talekar, None; S. Cole, Janssen, 3; K. Cochlin, Janssen Pharmaceutica Product, L.P., 3; S. Hitchcock, Johnson & Johnson, 3; B. Zeng, None; S. Yekollu, None; J. Rossjohn, Janssen Pharmaceutica Product, L.P., 2; Janssen Pharmaceutica Product, L.P., 5; H. Reid, Janssen Pharmaceutica Product, L.P., 2; Janssen Pharmaceutica Product, L.P., 3; H. Reid, Johnson & Johnson, 1; B. O'Sullivan, None; R. Thomas, Janssen Pharmaceutica Product, L.P., 2; Janssen Pharmaceutica Product, L.P., 5.


Abstract Number: 2705

Aberrant Expression and Function of Human Circulating T Follicular Helper Cells and Its Subsets in IgG4 Related Disease

Yu Chen\textsuperscript{1}, Wen Zhang\textsuperscript{2}, Panpan Zhang\textsuperscript{3}, Yanan Zhu\textsuperscript{1} and Hongxian Yang\textsuperscript{3}, \textsuperscript{1}Rheumatology, Peking Union Medical College Hospital, Chinese Academy of Medical Science & Peking Union Medical College, Beijing, China, \textsuperscript{2}Rheumatology, Peking Union Medical College Hospital, Beijing, China, \textsuperscript{3}Rheumatology, Peking Union Medical College Hospital, Chinese Academy of Medical Science & Peking Union Medical College, Beijing, China

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: T Cell Biology and Targets in Autoimmune Disease Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM
**Background/Purpose:** To study the expression and function of T follicular helper cells and its subsets in IgG4-related disease (IgG4-RD).

**Methods:** Flow cytometry was performed to analyze the expression of Tfh cells and its subsets in untreated IgG4-RD patients (n=46) and healthy controls (n=33). With RT-PCR technique, the mRNA levels of Bcl-6, Blimp-1 and IL-21 from IgG4-RD patients were tested. The immunohistochemistry and immunofluorescence technique were used to assess the location of IL-21 and Tfh cells in the involved tissues of IgG4-RD patients, respectively. Furthermore, by cells coculture in vitro, the abilities of cTfh and its subsets to help B cells proliferation, apoptosis, differentiation, and producing IgG4 in IgG4-RD were explored.

**Results:** The frequencies of (CD4+CXCR5+)T, (CD4+CXCR5+ICOS+)T, (CD4+CXCR5+PD-1+)T, PD-1 in (CD4+CXCR5+ICOS+)T and (CD4+CXCR5+ICOS+PD-1) T in IgG4-RD patients were significantly higher in the peripheral blood and involved tissues of IgG4-RD patients compared with healthy controls, and the expression of these cells in those involved tissues were significantly higher than blood. Especially, the percentages of PD-1 in (CD4+CXCR5+ICOS+) cTfh cells was positively correlated to the serum levels of IgG, IgG4, IgG4/IgG%, the number of organ involved, and (CD19+CD24-CD38hi) B cell subset, which has been proved producing higher IgG4 than other B cells. mRNA Bcl6 in CD4+ T cells of IgG4-RD showed no difference with healthy controls while the mRNA Blimp-1 did. mRNA IL-21 in PBMCs of IgG4-RD was also higher compared with healthy controls, and positively correlated with serum levels of IgG4, IgG, IgG4/IgG%. In the involved tissues of IgG4-RD, both of the Tfh cells and IL-21 showed highly expression, mainly distributed around glandular cells or ectopic GC. Importantly, compared to healthy controls, cTfh cells in IgG4-RD patients could more efficiently facilitate B cells proliferation but inhibit cell apoptosis, and enhanced naive B cells differentiate into S memory B cells and (CD19+CD24-CD38hi) B cells, which resulted in much more IgG4 secretion. Furthermore, it was mainly cTfh1 and cTfh2 were significantly higher in IgG4-RD patients compared with healthy controls, and it was mainly cTfh1 and cTfh17 enhanced the ability of B cells proliferation but inhibited apoptosis, while it was mainly cTfh2, as well as cTfh1 promote B cells differentiate into plasma B cells and producing much more IgG4 antibodies in IgG4-RD.

**Conclusion:** Tfh cells, especially the expression of PD-1 in (CD4+CXCR5+ICOS+) T, as well as IL-21 play vital roles in the pathogenesis of IgG4-RD. Compared to healthy control, Tfh cells from IgG4-RD patient could more efficiently facilitate B cells proliferation but inhibit cell apoptosis, and promote B cells differentiation into S memory B and (CD19+CD24-CD38hi)B cells, which result in strong immune response and more IgG4 secretion. And it was cTfh2, as well as cTfh1 mainly performing the function.

**Disclosure:** Y. Chen, None; W. Zhang, None; P. Zhang, None; Y. Zhu, None; H. Yang, None.

**Abstract Number:** 2706

**T Follicular-Helper CELLS (TFH) Enrichment and T Follicular-Regulatory CELLS (TFR) Exclusion from Ectopic Germinal Centers in Salivary Glands of Sjogren’s Syndrome Patients**

Elena Pontarini1, William Murray Brown2, Cristina Croia2, Elisa Corsiero3, Davide Lucchesi2, Elisa Astorri2, Nurhan Sutcliffe2, Anwar Tappuni2, Costantino Pitzalis4 and Michele Bombardieri5, 1William Harvey Research Institute, London, United Kingdom, 2Queen Mary University of London, London, United Kingdom, 3Centre for Experimental Medicine & Rheumatology, William Harvey Research Institute, Queen Mary University of London, London, United Kingdom, 4Centre for Experimental Medicine and Rheumatology, William Harvey Research Institute, Barts and The London, School of Medicine and Dentistry, Queen Mary University of London, London, United Kingdom, 5Centre for Experimental Medicine and Rheumatology, William Harvey Research Institute, Queen Mary University of London, London, United Kingdom

**First publication:** September 18, 2017
Lymphocytic aggregates in the salivary glands (SG) of Sjögren’s syndrome (SS) can organize in ectopic lymphoid structures (ELS) forming functional germinal centers (GCs), which are linked to the development of MALT lymphoma (MALT-L). T follicular-helper cells (Tfh) and follicular T regulatory cells (Tfr) are specialized CD4+ T helper cells that positively and negatively regulate, respectively, the magnitude of the GC response and possibly the development of autoimmunity. We aimed to characterize the infiltration of Tfh and Tfr in the SG of patients with SS in the presence/absence of ectopic GCs and MALT-L.

Methods:

SG biopsies with matching histology and RNA from 37 SS and 38 non-specific chronic sialadenitis (NSCS) patients were stratified as ELS-/ELS+ based on CD3/CD20/CD21/CD138 immunostaining (IHC). Histological samples and mRNA from 12 parotid MALT-L were also studied. Gene expression was performed with Taqman rt-PCR. Multicolor immunofluorescence/confocal microscopy for CD3, CD4, CD45RO, ICOS, PD1, BCL6 and FoxP3 was used to identify Tfh and Tfr.

Results:

Tfh cells (CD4+CD45RO+PD1+ICOS+Bcl6+) and Tfr cells (CD4+CD45RO+PD1+ ICOS+FoxP3+) were significantly increased in the ELS+ SG tissues from SS patients vs ELS- and NSCS. Tfh cells densely infiltrated the B cell rich areas and preferentially localized within ectopic GCs in the SG tissues. Furthermore, Tfh infiltration correlated with SG IL-21 mRNA expression, which in turn was strongly correlated with CD3, CD20 and CD138 IHC scores and with CXCL13, LTb, BAFF, AID and Pax5 gene expression. Finally, MALT-L samples displayed 10-fold higher IL-21 mRNA and twice as many PD1+ICOS+BCL6+ Tfh-cells/field compared to ELS+ SS samples. The Tfh:Tfr ratio in ELS+ SG was approximately 2:1. Interestingly, while in tonsils Tfr were routinely detected within GC, in ELS+ SG Tfr were predominantly excluded from the B cell follicles and accumulated in the T cell rich areas at the periphery of the B-cell aggregates.

Conclusion:

Within the SG of SS patients Tfh cells closely segregate with lesional IL-21 expression, localize within ELS and are strongly enriched during MALT-L development. Conversely, although Tfr cells are also present in ELS+ SG in SS patients, they are excluded from ectopic GCs. This suggests that Tfr in SS SG fail to exert their physiological immunoregulatory function in controlling the magnitude of the GC response and B cell autoreactivity, as observed in secondary lymphoid organs.

Disclosure: E. Pontarini, None; W. Murray Brown, None; C. Croia, None; E. Corsiero, None; D. Lucchesi, None; E. Astorri, None; N. Sutcliffe, None; A. Tappuni, None; C. Pitzalis, None; M. Bombardieri, None.


Abstract Number: 2707

Estrogen Downregulates the Expression of Serine Arginine Splicing Factor 1 (SRSF1) in Human T Lymphocytes
Systemic lupus erythematosus (SLE) is a complex autoimmune disease with multifactorial etiopathogenesis that primarily affects women in the childbearing years. Hormones especially estrogen are implicated in the pathogenesis of disease, however the precise molecular events regulated by estrogen in immune cells are not well understood. T cells play a key role in SLE pathogenesis and display abnormalities in gene expression and function. We previously identified a novel role for the multifunctional protein serine arginine rich splicing factor 1 (SRSF1) in T cell gene regulation and function. We showed that SRSF1 promotes IL-2 production in normal T cells, and its overexpression into SLE T cells rescues IL-2 production. SRSF1 expression is decreased in SLE T cells, and associates with severe disease activity. We recently generated a T cell specific Srsf1-conditional knockout mouse, which exhibits defects in T cell function and develops autoimmune disease. These results suggest that the deficiency of SRSF1 is an important molecular defect in immune-mediated disease. However, not much is known about the regulation of SRSF1 in T cells, and if or how hormones may contribute to its expression. Here we asked whether estrogen regulates the expression of SRSF1 in human T cells.

**Methods:**

Peripheral blood was collected from healthy women in the follicular phase of the menstrual cycle. T cells were isolated by negative selection from peripheral blood. T cells were cultured (in RPMI without phenol red supplemented with charcoal-stripped serum), with increasing concentrations (0, 1nM, 10nM, 100nM) of beta-estradiol for 18 – 24 hours. Total protein and RNA were isolated and the expression of SRSF1 assessed by Western blotting and RT-qPCR. To assess mRNA stability, transcription was blocked with actinomycin D, and cells collected at 0, 0.5, 1, 1.5 and 2 hours, and Srsf1 expression assessed by RT-qPCR. To assess posttranslational protein degradation mechanisms, the proteasome inhibitor MG132 or the lysosome inhibitor Bafilomycin A1 were added to cultures.

**Results:**

We found that exposure to beta-estradiol led to a dose dependent increase in Srsf1 mRNA expression, but a decrease in protein levels in T cells. This discrepancy between mRNA and protein expression suggests that estrogen may downregulate protein levels via post-transcriptional mechanisms such as mRNA decay, translation or protein degradation. The discrepancy between high mRNA versus low protein levels was not due to reduced mRNA stability because the rate of Srsf1 mRNA decay in control versus estrogen-treated T cells did not show significant differences. Culturing estrogen-treated T cells in the presence of inhibitors of the lysosome or proteasome showed that the proteasome but not the lysosome is involved in the degradation of SRSF1. In silico analysis of the Srsf1 3’UTR revealed microRNA (miR) target sites, of which miR-21-5p, miR-27, and miR-200b-3p are known to be regulated by estrogen and to be dysregulated in SLE.

**Conclusion:**

Our results suggest that estrogen can modulate the expression of SRSF1 via posttranscriptional mechanisms in human T lymphocytes, thus revealing a potential molecular link between hormones, immune cells and autoimmune disease.
Placental Growth Factor Regulates the Generation of T-Helper 17 Cells to Link Angiogenesis with Autoimmunity

Seung-Ah Yoo Sr.¹, Min-cheol Kang Sr.², Mingyo Kim Sr.³, Jin-Sun Kong Sr.¹, Ki-Myo Kim Sr.¹, junghee Koh Sr.¹, Chul-Soo Cho⁴, Seung-Hyo Lee Sr.⁵, Jae Young Ryoo Sr.⁶ and Wan-Uk Kim Sr.¹,⁷, ¹The Catholic University of Korea, Center for Integrative Rheumatoid Transcriptomics and Dynamics, seoul, Korea, Republic of (South), ²School of Life Sciences, BK21 Plus KNU Creative BioResearch Group, Kyungpook National University, seoul, Korea, Republic of (South), ³Graduate School of Medical Science and Engineering, BioMedical Research Center, KAIST Institute for the BioCentury, seoul, Korea, Republic of (South), ⁴Internal Medicine, Yeouido St. Mary's Hospital, The Catholic University of Korea, Seoul, Korea, Republic of (South), ⁵Graduate School of Medical Science and Engineering, BioMedical Research Center, KAIST Institute for the BioCentury, SEOUL, Korea, Republic of (South), ⁶School of Life Sciences, BK21 Plus KNU Creative BioResearch Group, Kyungpook National University, SEOUL, Korea, Republic of (South), ⁷The Catholic University of Korea, Department of Internal Medicine, seoul, Korea, Republic of (South)

First publication: September 18, 2017

Background/Purpose: T-helper (Th) cells actively communicate with adjacent cells by secreting soluble mediators, and yet crosstalk between Th cells and endothelial cells is poorly understood. Here, we demonstrated that the placental growth factor (PlGF), an angiogenic factor, was selectively secreted by Th17 cells, and promoted angiogenesis in vitro and in vivo.

Methods: Concentrations of PlGF and interleukin-17 (IL-17) in culture supernatants of stimulated T cells were measured using Enzyme-linked immunosorbent assay (ELISA). The angiogenic effect of PlGF produced by CD4⁺ T was assessed by measuring the tube formation, wounding migration, and chemotaxis of endothelial cells. Expression of Th17, Treg, and phospho Stat was analyzed by flow cytometry. Experimental Th17 disease model was induced in mice either by immunization with type II collagen (CII) or by injection of MOG₃₅-₅₅ peptide.

Results: Angio-lymphokin' PlGF, in turn, specifically induced Th17 cell differentiation and plasticity by activating STAT3 via binding to the FLT1 and NRP1 receptors and substituted for IL6 activity in IL-17 production, whereas it suppressed FOXP3⁺ Treg cell generation. The disruption of PlGF attenuated the severity of delayed-type hypersensitivity and experimental autoimmune encephalomyelitis in mice by reducing IL-17 production; the adoptive transfer of PlGF-overexpressing CD4⁺ T cells to these mice restored their disease phenotypes. On the contrary, selective overexpression of PlGF in T cells increased disease severity and IL-17 and STAT3 expressions in mice with autoimmune arthritis. Finally, we observed a correlation between concentrations of PlGF and IL17 in the synovial fluids of rheumatoid arthritis patients.

Conclusion: Our findings provide novel insights into the PlGF-dictated links between angiogenesis, Th17 cell development, and autoimmunity, indicating that PlGF inhibitors could be used to control autoimmune and inflammatory diseases in hope of dual inhibition of angiogenesis and Th17 cell generation.
Histone Deacetylase 1 (HDAC1): A Novel Therapeutic Target for Patients with Rheumatoid Arthritis

Lisa Goschl¹-², Michael Bonelli³, Victoria Saferding⁴, Teresa Peglej², Sylvia Knapp⁵, Johan Bäcklund⁶, Christoph Bock⁵, Patrick Matthias⁷, Kiyoshi Hirahara⁸, Clemens Scheinecker¹, Günter Steiner⁹, Josef S. Smolen¹ and Wilfried Ellmeier², ¹Medical University of Vienna, Devision of Rheumatology, Vienna, Austria, ²Medical University of Vienna, Institute of Immunology, Center for Pathophysiology, Infectiology and Immunology, Vienna, Austria, ³Rheumatology, Medical University of Vienna, Vienna, Austria, ⁴Medical University of Vienna, Austria, Vienna, Austria, ⁵CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences, Vienna, Austria, ⁶Karolinska Institute, Department of Medical Biochemistry and Biophysics, Stockholm, Sweden, ⁷Friedrich Miescher Institute for Biomedical Research, Basel, Switzerland, ⁸Department of Immunology, Graduate School of Medicine, Chiba University, Chiba, Japan, ⁹Medical University of Vienna, Division of Rheumatology, Vienna, Austria

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: T Cell Biology and Targets in Autoimmune Disease Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Autoreactive T cells drive the inflammatory process, which leads to an irreversible destruction of the joints. Gene transcription and regulation of proinflammatory cytokine production in T cells is regulated by epigenetic mechanisms. Among them histone deacetylases (HDACs) modify the epigenetic landscape by removing acetyl groups of lysine residues of histones, resulting in chromatin condensation and repression of transcription. The application of pan-HDAC inhibitors has been shown to be a potential therapeutic strategy. However, major side effects limited the clinical use and underline the need of more specific HDAC inhibitors. Therefore we addressed the effects of selective HDACs on the development of autoimmune diseases.

Methods: Mice with a T cell specific deletion of HDAC1 (HDAC1cKO) were generated by using the CD4Cre/LoxP system. The clinical and the histological phenotype were assessed in the collagen-induced arthritis (CIA) and the experimental autoimmune encephalitis (EAE) model. Anti-collagen antibody levels were determined by ELISA. Qualitative and quantitative analysis of T cell subsets of the spleen and draining LN were assessed using flow cytometry. Additionally comparative RNA-sequencing of CD4⁺ T cells from wild type (WT) and HDAC1cKO mice was performed.

Results: To address whether HDAC1 is involved in the pathogenesis of autoimmune diseases we induced the CIA and the EAE in WT and HDAC1cKO mice. Surprisingly, despite the presence of serum anti-CII antibodies, HDAC1cKO mice did not develop any clinical or histological signs of inflammation in the CIA model. These data were confirmed in an additional T cell dependent model, the EAE model. HDAC1cKO mice were completely protected against the development of EAE. The total number of cells isolated from the CNS, consisting predominately of CD4⁺ T cells, was significantly reduced in the absence of HDAC1. Molecular analysis of HDAC1cKO CD4⁺ T cells revealed diminished
expression of CCR6, which is an essential chemokine receptor for the development of arthritis and EAE. This was accompanied with an increased production of IFNγ and with an enhancement of STAT1 phosphorylation in activated HDAC1cKO CD4^+ T cells in comparison to WT cells. In line with this finding we observed increased expression of CCR6 in STAT1^-/- CD4^+ T cells. This indicates a negative role of STAT1 in the regulation of CCR6 expression in HDAC1cKO CD4^+ T cells, suggesting an impairment to migrate to the site of inflammation to initiate arthritis and EAE.

**Conclusion:** Our data show the importance of HDAC1 as a key immune regulator in the pathogenesis of the CIA and EAE model. Therefore it might be considered as an interesting novel therapeutic target in autoimmune diseases, in particular patients with RA.

**Disclosure:** L. Goschl, None; M. Bonelli, None; V. Saferding, None; T. Peglej, None; S. Knapp, None; J. Bäcklund, None; C. Bock, None; P. Matthias, None; K. Hirahara, None; C. Scheinecker, None; G. Steiner, None; J. S. Smolen, AbbVie, Amgen, Astra-Zeneca, Astro, BMS, Celgene, Celltrion, Chugai, Gilead, Glaxo, ILTOO, Janssen, Eli Lilly and Company, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi-Aventis, UCB, 5,AbbVie, Janssen, Eli Lilly and Company, MSD, PChizer, Roche, 2,AbbVie, Amgen, Astra-Zeneca, Astro, BMS, Celgene, Celltrion, Chugai, Gilead, Glaxo, ILTOO, Janssen, Eli Lilly and Company, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi-Aventis, UCB, 8; W. Ellmeier, None.


**Abstract Number:** 2710

**CXCR3+CCR6+CD4+ T Cells (Th1Th17) and RF As Novel Predictive Markers for Clinical Response to Abatacept Treatment in Patients with Rheumatoid Arthritis: The 52-Week Analysis**

Koji Mishima¹, Shunichiro Ota², Kazuhiko Higashioka¹, Tsuyoshi Nakayama³, Masahiro Ayano¹, Yasutaka Kimoto⁴, Hiroki Mitoma¹, Mitsuteru Akahoshi¹, Yojiro Arinobu¹, Yasushi Inoue⁵, Kensuke Oryoji⁶, Takuya Sawabe⁷, Shuji Nagano⁸, Hiroaki Nishizaka⁹, Seiji Yoshizawa¹⁰, Shigeru Yoshizawa¹¹, Takeshi Otsuka¹², Akira Ueda¹³, Yoshifumi Tada¹⁴, Hitoshi Nakashima¹⁵, Takahiko Horiuchi¹⁶, Koichi Akashi¹ and Hiroaki Niro³, ¹Department of Medicine and Biosystemic Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan, ²Department of Rheumatology, Shimonoseki City Hospital, Yamaguchi, Japan, ³Department of Medical Education, Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan, ⁴Department of Internal Medicine, Kyushu University Beppu Hospital, Oita, Japan, ⁵Department of Rheumatology, Japanese Red Cross Fukuoka Hospital, Fukuoka, Japan, ⁶The Center for Rheumatology, Matsuyama Red Cross Hospital, Ehime, Japan, ⁷Hiroshima Red Cross Hospital and Atomic-bomb Survivors Hospital, Hiroshima, Japan, ⁸Center for Rheumatology, Iizuka Hospital, Fukuoka, Japan, Iizuka City, Japan, ⁹Kitakyushu Municipal Medical Center, Kitakyushu, Japan, ¹⁰Hamanomachi Hospital, Fukuoka, Japan, ¹¹Department of Rheumatology, Fukuoka Hospital, National Hospital Organization, Fukuoka, Japan, ¹²Munakata Medical Association Hospital, Munakata, Japan, ¹³Department of Internal Medicine, Miyazaki Prefectural Hospital, Miyazaki, Japan, ¹⁴Rheumatology, Saga University, Saga, Japan, ¹⁵Div of Nephrol & Rheumatol, Dept of Int Med, Faculty of Medicine, Fukuoka University, Fukuoka, Japan, ¹⁶Department of Internal Medicine, Kyushu University Beppu Hospital, Beppu, Japan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** T Cell Biology and Targets in Autoimmune Disease Poster II

**Session Type:** ACR Poster Session C
Background/Purpose: The advent of biological therapy has made a remarkable progress in the management of rheumatoid arthritis (RA). Abatacept (ABA), a non-TNF inhibitor, is a CTLA4-Ig and ameliorates synovial inflammation and bone damage in RA. Recent findings showed that anti-cyclic citrullinated peptide antibody (ACPA)-positive RA patients are good responders to ABA therapy in comparison with TNFi therapy, however the temporal impact of ABA on immune cells, particularly T and B cells, and its relationship with clinical response remain to be fully elucidated. In this study, we have sought to uncover these aspects by analyzing immunological changes in RA patients treated with ABA.

Methods: Twenty-five RA patients initiated with ABA as first biologic between May 2014 and March 2015 were prospectively studied with informed consent. Effects of ABA were evaluated sequentially from baseline to 52 weeks by the proportions and activation of lymphocyte subsets in peripheral blood and the titers of autoantibodies including rheumatoid factor (RF) and ACPA, along with the assessment of clinical activity.

Results: In the treatment of ABA, the proportion of CD4^CCR7^CD45RA^ (central memory) T cells enriching T follicular helper (Tfh) cells and CD4^CCR7^CD45RA^- (effector memory) T cells significantly decreased, while that of CD4^CCR7^-CD45RA^ (naive) T cells increased. Overall, activation of pathogenic Th subsets was remarkably suppressed by ABA therapy. Additionally, the proportion of CD4^CD25^CD127^loCCR4^+ T cells (Treg) decreased. On the other hand, the proportion of B cell subsets, activation state of CD8^+ T cells and titers of autoantibodies were minimally affected. Notably, a change in RF levels correlated well with that in Tfh numbers and disease activity (DAS28-CRP). By comparing patients who achieved good EULAR response (GR) with patients who didn't achieve good EULAR response (non-GR) at 3 month after ABA therapy, higher RF titers and lower proportion of CD4^CXCR3^CCR6^+ T cells (Th1Th17) among CD4^+ T cells at baseline were significantly noted in the GR group (p=0.01, p=0.04, respectively). Generation of Th1Th17 cells can be induced by myeloid cells stimulated with endogenous TLR4 ligands including various citrullinated proteins at joints. Using ROC curve, the cutoff values of RF and proportion of Th1Th17 were defined as 144IU/mL and 3.25%, respectively. A subpopulation of RA patients with RF titer≧144IU/mL or Th1Th17≧3.25% at baseline clearly achieved lower disease activity and better GR rates to ABA therapy.

Conclusion: Together, these findings suggest that clinical response to ABA therapy is prospectively predicted by RF titers and the proportion of a novel T cell subset in RA patients, thus helping to choose the optimal treatment strategy with the use of this biologic.

Disclosure: K. Mishima, None; S. Ota, None; K. Higashioka, None; T. Nakayama, None; M. Ayano, None; Y. Kimoto, None; H. Mitoma, None; M. Akahoshi, None; Y. Arinobu, None; Y. Inoue, None; K. Oryoji, None; T. Sawabe, None; S. Nagano, None; H. Nishizaka, None; S. Yoshizawa, None; S. Yoshizawa, None; T. Otsuka, None; A. Ueda, None; Y. Tada, None; H. Nakashima, None; T. Horiuchi, None; K. Akashi, None; H. Niro, None.


Abstract Number: 2711

Mucosal-Associated Invariant T Cells Are an Important Source of TNF in Rheumatoid Arthritis

Diahann Jansen1, Elizabeth Klinken1, Hendrik Nel1, Soi Cheng Law1, Hester Koppejan2, Marjolijn Hameetman3, Ligong Liu4, Alexandra Corbett5, Sidonia Ecke5, David Fairlie4, Rene E.M. Toes6, Floris van Gaalen7, Jamie Rossjohn8,9,10, James McCluskey5 and Ranjeny Thomas1,1The University of Queensland Diamantina Institute, Translational Research Institute, Woolloongabba, Australia, 2Department of Rheumatology, Department of
Background/Purpose: CD8+ T cells have been described to comprise up to 40% of the rheumatoid arthritis (RA) synovial T cell compartment but their pathogenic function is largely unknown. Mucosal associated invariant T (MAIT) cells are predominantly CD4-CD8+ innate-like lymphocytes which comprise up to 10% of circulating T cells and enter mucosal sites. They express a semi-invariant T cell receptor restricted to the MHC class I-like molecule, MR1. MR1 presents ligands derived from the riboflavin synthesis pathway, common to a range of bacteria and yeast. There is evidence for oral and gastrointestinal microbial dysbiosis in RA, and the majority of abundant bacterial species in RA patients are capable of riboflavin synthesis. However, the mechanisms underlying these disease associations are unclear. Furthermore, TNF is both an effector cytokine produced by activated MAIT cells and a key cytokine driver of RA. Therefore, we investigated the relationship between MAIT cells and TNF response to the riboflavin ligand 5-OPRU in RA patients and healthy controls (HC).

Methods: We identified the proportion of MAIT cells based on the expression of CD3, CD4, CD161 and TRAV1-2 or positivity for MR1-5-OPRU tetramers using flow cytometry in peripheral blood (PB) of 14 RA patients and 12 HC and synovial fluid of 8 RA patients. We analysed cellular activation of MAIT cells after stimulation with 5-OPRU by defining the expression of activation markers CD25 and CD69 and the production of TNF and IFN-gamma.

Results: MAIT cells comprised 0.5-17.5% of the CD4-CD3+ T cells in RA PB. MR1-tetramer+ MAIT cell frequencies in PB of HC and RA patients were comparable and on average 85% of MAIT cells were CD4 negative. CD161 expression decreased after MAIT cell stimulation, indicating that the MAIT cells are incompletely identified by the expression of TRAV1-2 and CD161. MAIT cells in RA patients were constitutively more activated than conventional T cells suggesting prior ligand exposure. MAIT cells produced multiple cytokines after PMA and ionomycin stimulation. However, after stimulation with MR1 ligand 5-OPRU, MAIT cells from PB and synovial fluid produced predominantly TNF. In RA patients, disease activity score was negatively correlated with the proportion of PB MAIT cells and with 5-OPRU-stimulated TNF production.

Conclusion: MAIT cells account for a substantial proportion of CD4- T cells. RA PB and synovial MAIT cells produce TNF in response to 5-OPRU ligand derived from microbial riboflavin synthesis. Reduction of TNF-competent MAIT cells in PB of patients with high disease activity suggests migration to tissue inflammatory sites, where the TNF they secrete may drive RA pathology.

Disclosure: D. Jansen, None; E. Klinken, None; H. Nel, None; S. C. Law, None; H. Koppejan, None; M. Hameetman, None; L. Liu, None; A. Corbett, None; S. Eckle, None; D. Fairlie, None; R. E. M. Toes, None; F. van Gaalen, None; J. Rossjohn, None; J. McCluskey, None; R. Thomas, Janssen Pharmaceutica Product, L.P., 2; Janssen Pharmaceutica Product, L.P., 5.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/mucosal-associated-invariant-t-cells-are-an-important-source-of-tnf-in-rheumatoid-arthritis
Autoimmune Arthritis in IL-1 Receptor Antagonist-Deficient Mice Is Associated with a Pathogenic Conversion of Foxp3+ Regulatory T Cells into Th17 Cells

Anais Levescot1, Nathan Nelson-Maney2, Allyn Morris3, Ricardo Grieshaber Bouyer4, Pui Lee5 and Peter Nigrovic6,
1Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Harvard Medical School, boston, MA, 2Division of Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital, Boston, MA, 3Division of Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital, Boston, MA, 4Division of Rheumatology, Immunology, and Allergy, BWH, Boston, MA, 5Harvard Medical School, Boston, MA, 6Division of Rheumatology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: T Cell Biology and Targets in Autoimmune Disease Poster II
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: IL-1β blockade is a highly effective therapy for systemic juvenile idiopathic arthritis (sJIA). However, the rate of inactive disease attained in these trials is lower than reported in sJIA patients treated with IL-1 blockade at disease onset. We have hypothesized that sJIA is a biphasic process in which an initial IL-1β-driven systemic phase directly promoting Th17 differentiation from both Th0 and T regulatory T (T_{reg}) cells and gives rise to IL-17-driven chronic inflammatory arthritis. We sought to test this hypothesis in the IL-1ra^{−/−} model, a spontaneous T cell-mediated murine arthritis dependent upon both IL-1β and IL-17.

Methods: Synovial tissue, lymph nodes and spleen from Il-1ra^{−/−} were characterized via flow cytometry for FOXP3, RORγt expression and cytokine production. In addition, we examined the transcriptomic landscape of sorted T_{reg} cells from newly generated IL-1ra^{−/−} Foxp3-eGFP mice and WT Foxp3-eGFP controls. We sorted 50,000 WT and IL-1ra^{−/−} T_{reg} cells from 3 mice and performed low-input RNA-Sequencing. Differential expression testing was performed using EdgeR. Additionally, we performed Gene Set Enrichment Analysis between WT and IL-1ra^{−/−} groups. In order to assess osteoclastogenic potential, sorted T_{reg} cells where co-culture with macrophage precursors cells (1:2 ratio) in presence of anti-CD3/CD28 beads, M-CSF and RANK-L. After 5 days of co-culture, TRAP^{+} multinucleated cells (more than three nuclei) were counted.

Results: The percentage of T_{reg} cell among CD4^{+} cells in periphery and locally in synovial tissue was similar between WT and IL-1ra^{−/−} mice. However, T_{reg} cells from IL-1ra^{−/−} synovium showed an up-regulation of RORγt expression. Interestingly, a significant number of FOXP3^{+} cells also produced IL-17 upon in vitro stimulation. To gain molecular insight into the mechanism underlying T_{reg} cell plasticity in our model, we performed RNAseq-driven characterization of T_{reg} cells from IL-1ra^{−/−} and WT mice. Notably, Gene Set Enrichment Analysis revealed distinct metabolic programs between both subsets. The oxidative phosphorylation gene set was enriched in WT T_{reg}. On the other hand, mTOR and glycolysis pathways that orchestrate a metabolic checkpoint for the differentiation of Th17 cells were enriched in IL-1ra^{−/−} T_{reg} cells. This finding confirms the ongoing conversion of Foxp3^{+} cells into Th17 cells. In addition to this Th17-skewed phenotype, T_{reg} from IL-1ra^{−/−} mice over-expressed RANK-L and facilitate osteoclastogenesis in vitro whereas WT T_{reg} inhibited osteoclast differentiation, suggesting a novel pathogenic role for IL-1ra^{−/−} T_{reg} cells.
**Conclusion:** All together our results suggest that chronic inflammatory arthritis in IL-1ra−/− mice is associated with the conversion of Foxp3+ Treg cells into pathogenic Th17 cells. These findings suggest that early IL-1β blockade could modulate the development of arthritogenic T cells in IL-1-driven arthritis, a result that may inform the understanding and treatment of sJIA.

**Disclosure:** A. Levescot, None; N. Nelson-Maney, None; A. Morris, None; R. Grieshaber Bouyer, None; P. Lee, None; P. Nigrovic, Novartis Pharmaceutical Corporation, 2, Novartis Pharmaceutical Corporation, 5, Sobi, 2, Sobi, 5, UCB, 5, Pfizer Inc, 5, Casebia, 5, UpToDate, 7, American Academy of Pediatrics, 7.


**Abstract Number:** 2713

**CD318 Is a New Ligand for CD6**

Gospel Enyindah-Asonye1, Yan Li1, Danislav Spassov2, Katie Hebron3, Andries Zijlstra4, Mark Moasser2, Benlian Wang5, Nora Singer6, David A. Fox7 and Feng Lin8, 1Department of Immunology, Lerner Research Institute of the Cleveland Clinic, Cleveland, OH, 2Department of Medicine, University of California, San Francisco, San Francisco, CA, 3Department of Pathology, Microbiology, and Immunology, Vanderbilt University, Nashville, TN, 4Department of Pathology, Microbiology and Immunology, Vanderbilt University, Nashville, TN, 5Center for Proteomics and Bioinformatics, Case Western Reserve University, Cleveland, OH, 6Division of Rheumatology, MetroHealth Medical Center, Cleveland, OH, Cleveland, OH, 7Rheumatology/Internal Medicine, University of Michigan Medical Center, Ann Arbor, MI, 8Department of Immunology, Cleveland Clinic Foundation, Cleveland, OH

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** T Cell Biology and Targets in Autoimmune Disease Poster II

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** CD6, an important regulator of T cells, has one known ligand, CD166, but studies performed during the treatment of autoimmune conditions and in vitro experiments suggest that the CD6-CD166 interaction might not account for important functions of CD6 in autoimmune diseases. The antigen recognized by mAb 3A11 has been proposed as a new CD6 ligand distinct from CD166, yet the identity of this ligand is hitherto unknown.

**Methods:** To determine the identity of the antigen recognized by mAb 3A11, we investigated HBL-100 cell surface proteins pulled down by this mAb by mass spectrum (MS) analysis. We then probed whole HBL-100 cell lysates with an anti-CD318 Ab in western blot and assessed CD318 expression levels on HBL-100 cells by flow cytometry before and after IFNγ stimulation. We next studied transfected MDA-468 cells that overexpress CD318 after doxycycline induction and transfected MDA-468 cells knocked down for CD318 expression using shRNA, by flow cytometry using a commercial anti-CD318 mAb and mAb 3A11. We also studied binding of CD6 to HT-1080 sarcoma cells in which expression of CD166 but not CD318 was selectively ablated by CRISP-R technology, and measured binding of rCD318 to CHO-C6D transfectants. We then assessed the role of CD318 in autoimmunity in vivo using CD318-knockout mice and the experimental autoimmune encephalomyelitis (EAE) model of multiple sclerosis.

**Results:** CD318-related peptides were abundant in mAb 3A11 precipitates from HBL-100 cells. Mab 3A11 and anti-CD318 immunoprecipitated identical bands at 130kDa, and binding of each mAb to the cell surface was identically upregulated by pre-exposure of cells to IFNγ. Moreover, each mAb bound to CD318 in western blots. In a CD318-
inducible system, staining with mAb 3A11 resulted in exactly the same pattern as seen with anti-CD318 mAbs, while in CD318 knockdown cells neither mAb showed detectable staining. An HT-1080 CD166 KO cell line was developed that expresses CD318 but not CD166 -binding of CD6 to the surface of these cells was attenuated but still evident, and was further reduced by rCD318 in a dose-dependent manner. Recombinant CD6 precipitated a protein from lysates of these cells that was recognized by anti-CD318. Recombinant CD318 bound to human CD6-expressing CHO cells but not control CHO cells. Moreover, CD318 KO mice had markedly attenuated disease severity of EAE, with reduced antigen-specific Th1 and Th17 responses and significantly decreased inflammation and CD4+ T cell infiltration in the central nervous system.

**Conclusion:** These data establish CD318 as a novel second ligand of CD6, and indicate a previously unknown role for CD318 in regulation of T cell driven autoimmunity. The engagement of CD6 by CD318 is an unusual example of a ligand-receptor interaction between a lymphocyte-specific cell surface glycoprotein that can participate in T cell activation (CD6) and a molecule (CD318) that is found only on cells that are traditionally considered not to be components of the immune system. This interaction points to an ability of T cells to specifically recognize distinct signals from “non-immune system” tissue cells that may be important in organ-targeted autoimmune diseases.

**Disclosure:** G. Enyindah-Asonye, None; Y. Li, None; D. Spassov, None; K. Hebron, None; A. Zijlstra, None; M. Moasser, None; B. Wang, None; N. Singer, Merck, EMD Serono, 2, Pfizer Inc, 5; D. A. Fox, None; F. Lin, None.

**Abstract Number: 2714**

**The Paracaspase MALT1 Plays a Central Role in the Pathogenesis of Rheumatoid Arthritis**

Elisabeth Gilis¹, Jens Staal², Rudi Beyaert² and Dirk Elewaut³, ¹Molecular Immunology and Inflammation Unit, VIB Inflammation Research Center, Ghent, Belgium, Gent, Belgium, ²Molecular Immunology and Inflammation Unit, VIB Inflammation Research Center, Ghent, Belgium, ³VIB Inflammation Research Center, University of Ghent, Gent, Belgium

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** T Cell Biology and Targets in Autoimmune Disease Poster II

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** One of the hallmarks of many inflammatory arthritides is their strong linkage with MHC-signalling, which is mirrored by the marked role for adaptive immunity. Accordingly, rheumatoid arthritis (RA) is characterized by the activation of auto-reactive T-cells and the development of auto-antibodies. T-cells may additionally respond to non-TCR mediated signals, which are essential in driving their effector functions. Pathways leading to the modulation of both innate and adaptive signals are therefore of marked interest to study in arthritic diseases. The paracaspase MALT1 is a key player in the activation and proliferation of immune and non-immune cells. These cells include the lymphoid, myeloid and mast cells, indicating MALT1’s crucial role in both innate and adaptive signaling. Therefore, MALT1 is regarded a promising target for the treatment of autoimmune diseases and defining its role in the pathogenesis of inflammatory arthritis is a critical first step.

**Methods:** To unravel MALT1’s role in inflammatory arthritis, we initially assessed MALT1-activation in mice that were challenged with collagen-induced arthritis (CIA), the prototype model for antigen-induced RA. We then addressed the role of MALT1 in the pathogenesis of inflammatory arthritis by challenging MALT1-deficient mice to distinct models of arthritis (CIA and CAIA). Additionally, CIA was induced in CD4-specific MALT1-deficient mice to determine the
importance of MALT1 in T-cells. Bone homeostasis was assessed by micro-CT analysis, a 3 point bending test to test bone strength and by osteoclastogenesis assays using RANKL induced osteoclastogenesis and resorption pit assays. Immunophenotyping of T cell and regulatory T cell subsets was conducted in spleen and lymph nodes and anti-collagen II specific antibody development was measured by ELISA.

**Results:** We provide evidence that MALT1 plays a crucial role in the pathogenesis of RA as MALT1-deficient mice were completely protected against CIA. This complete protection was additionally observed in CD4-specific MALT1-deficient mice, indicating that the selective ablation of MALT1 in CD4-positive cells is sufficient for the observed resistance against CIA. This was reflected by markedly lower induction of anti-collagen type II antibodies. CAIA on the other hand, which is a T- and B-cell independent model of RA, did not depend on the presence of MALT1, since both MALT1+/+ and MALT1-/- mice showed comparable symptoms of RA. MALT1 deficient mice show an osteoporotic phenotype but osteoclastogenesis was normal suggesting an indirect effect. MALT1 deficient mice lack natural Tregs which could account for the osteoporotic phenotype. Accordingly, CD4-specific MALT1-deficient mice also had an osteoporotic phenotype on microCT with impaired bone strength.

**Conclusion:** Overall, our data highlight that MALT1 plays a crucial role in the pathogenesis of inflammatory arthritis but has a dual role on inflammation versus bone homeostasis. Our data indicate an osteoporotic phenotype in the absence of MALT1 caused by lack of Tregs.

**Disclosure:** E. Gilis, None; J. Staal, None; R. Beyaert, None; D. Elewaut, Scientific Research Flanders; Research Council Ghent University; Interuniversity Attraction Pole., 2,Boehringer Ingelheim; Pfizer; UCB; Merck; Novartis; Janssen; Abbvie, 5.


**Abstract Number:** 2715

**NKTR-358: A Selective, First-in-Class IL-2 Pathway Agonist Which Increases Number and Suppressive Function of Regulatory T Cells for the Treatment of Immune Inflammatory Disorders**

**John Langowski,** Peter Kirk, Murali Addepalli, Thomas Chang, Vidula Dixit, Grace Kim, Yolanda Kirksey, Peiwen Kuo, Myong Lee, Mekhala Maiti, Werner Rubas, Paul Sims, Yuan Song, Yinyan Tang, Laurie VanderVeen, Ping Zhang, Stephen Doberstein and Jonathan Zalesky, Nektar Therapeutics, San Francisco, CA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** T Cell Biology and Targets in Autoimmune Disease Poster II

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Impaired IL-2 production and regulatory T cell (Treg) dysfunctions have been implicated as an immunological mechanism in multiple autoimmune diseases. While low-dose IL-2 can be used to stimulate Tregs for clinical benefit, poor pharmacokinetics necessitates daily delivery, adverse events are dose-limiting, and Treg increases are modest and short-lived. Nektar Therapeutics is developing NKTR-358, a novel product which utilizes the aldesleukin (Proleukin®) amino acid sequence chemically conjugated with stable polyethylene glycol (PEG) moieties, intended for low dose subcutaneous administration to selectively restore Treg homeostasis with no impact on Tcon function.
Methods: The affinity to the IL-2 receptor was assessed by surface plasmon resonance. Activity in cynomolgus and human PBMC was measured by pSTAT5 induction in multiple lymphocyte populations utilizing flow cytometry. In vivo activity after subcutaneous administration in C57BL/6 mice or cynomolgus monkey was measured by changes in lymphocyte numbers and activation by flow cytometry. Ex vivo Treg function was determined by the inhibition of Tcon proliferation by isolated splenic Treg. Efficacy was examined in a model of cutaneous hypersensitivity in mice using keyhole limpet hemocyanin (KLH), and in cynomolgus monkey using tetnoid toxin. Efficacy in a model of systemic lupus erythematosus (SLE) was assessed using MRL/MpJ-Faslpr mice.

Results: NKTR-358 has greatly attenuated affinity for human IL-2Rβ relative to IL-2Rα and IL-2Rαβ complexes, suggesting biological engagement favors activation of Treg which express the high affinity IL-2Rαβγ over Tcon, which express the low-affinity IL-2Rβγ. In vitro, Treg were far more sensitive to NKTR-358 stimulation relative to all other lymphocyte subsets in cynomolgus or human PBMC. In mice, a single administration led to sustained Treg mobilization for 7 to 10 days in blood and spleen without Tcon activation, an effect concomitant with increased Treg activation and suppressive capacity. In cynomolgus monkey, plasma exposure was even more prolonged leading to sustained Treg mobilization and activity for over 14 days after a single administration - a response superior in magnitude, duration and specificity compared to an equivalent total dose of rhIL-2 administered daily for five days. NKTR-358 administration suppressed the antigen-induced inflammatory response in the KLH hypersensitivity model, an effect which was antigen-specific and associated with establishment of Treg memory. Similar results were achieved in cynomolgus monkey using tetanus toxoid. Finally, NKTR-358 was efficacious a mouse model of SLE, with repeat administration over 12 weeks sustaining Treg elevation, significantly reducing blood urea nitrogen and returning urine protein levels and kidney histopathology to normal.

Conclusion: NKTR-358 delivers sustained, preferential activation of Tregs. Currently, NKTR-358 is being studied in a Phase 1 study in healthy subjects to measure Treg mobilization, functional activity, pharmacokinetics and safety, with the goal of establishing a range of dose levels to be advanced into a multiple-ascending dose trial in patients with SLE.

Disclosure: J. Langowski, Nektar Therapeutics, 3; P. Kirk, Nektar Therapeutics, 3; M. Addepalli, Nektar Therapeutics, 3; T. Chang, None; V. Dixit, Nektar Therapeutics, 3; G. Kim, Nektar Therapeutics, 3; Y. Kirksey, Nektar Therapeutics, 3; P. Kuo, Nektar Therapeutics, 3; M. Lee, Nektar Therapeutics, 3; M. Maiti, Nektar Therapeutics, 3; W. Rubas, Nektar Therapeutics, 3; P. Sims, Nektar Therapeutics, 3; Y. Song, Nektar Therapeutics, 3; Y. Tang, Nektar Therapeutics, 3; L. VanderVeen, Nektar Therapeutics, 3; P. Zhang, Nektar Therapeutics, 3; S. Doberstein, Nektar Therapeutics, 3; J. Zalevsky, Nektar Therapeutics, 3.


Abstract Number: 2716

Gastrointestinal Involvement in Adult IgA Vasculitis (Henoch–Schönlein purpura): Initial Manifestations and Outcomes

Alexandra Audemard-Verger1, Aurélie Baldoli2, Zahir Amoura3, Patrice Cacoub4, Sébastien Sanges5, Francois Maurie6, Bertrand Lioger7, Nihal Martis8, Etienne Rivière9, Geoffroy Urbanski10, Evangeline Pillebout11, Loïc Guillevin for the French Vasculitis Study Group12 and Benjamin Terrier13, 1Internal Medicine, Caen, France, 2Internal Medicine, CHU, Caen, France, 3Department of Internal Medicine 2, Referal center for SLE/APS, Hôpital Pitié-Salpêtrière, AP-HP, UPMC Univ Paris 06 & French National Reference Center For Systemic Lupus and Antiphospholipid Syndrome, Paris, France, 4Department of Internal Medicine and Clinical Immunology, Groupe Hospitalier Pitié-Salpêtrière, Paris, France, 5Université Lille Nord de France, Faculté de Médecine Henri Warembourg, Lille, Lille, France, 6Internal Medicine, Sainte-Blandine de Metz Hospital, Metz, France, 7GICC UMR 7292, University François Rabelais, Tours, France, 8Internal medicine, Nice, France, 9Internal Medicine, CHU, Bordeaux, France, 10Internal Medicine, CHU, Angers, France, 11Nephrology, Saint Louis, Paris, France, 12Service de Médecine Interne,
Background/Purpose: Gastrointestinal (GI) involvement during adult IgA vasculitis (IgAV) occurs in roughly half the cases. In many other systemic vasculitides, GI involvement represents a poor-prognosis factor, leading to the use of immunosuppressive agents combined glucocorticoids. This study was undertaken to describe the first manifestations and prognoses of GI involvement in adult IgAV patients.

Methods:

This nationwide, retrospective study analyzed the data from 260 adult IgAV patients to describe and compare the initial symptoms and outcomes of those with GI involvement (GI+) vs. those without it (GI–).

Results: Among the 260 patients analyzed, 137 (53%) were GI+ vs. 123 (47%) GI–. The initial GI manifestations included: abdominal pain for 135/137 (99%), intestinal bleeding for 43/137 (31%) and diarrhea for 36/137 (26%). Abdominal computed-tomography (CT) scans and/or ultrasonography were obtained for 65% of GI+ patients. The most frequent imaging finding was thickening of the intestinal wall (61%). Upper and/or lower GI endoscopies of 78 (57%) patients revealed abnormalities in 77%, including mucosal ulceration (53%), erythema (34%) and/or purpura (26%). In contrast, intestinal biopsies were obtained from only 8 (6%) patients. The most frequent histological finding was nonspecific inflammatory infiltrates seen in all biopsies, but specific vasculitis features were rarely described (e.g., fibrinoid necrosis seen in only 1). At diagnosis, GI+ patients vs. GI– patients, respectively, were younger (mean±SD age 46.3±1.5 vs. 54.5±1.7 years; P=0.0004), had more constitutional symptoms (43% vs. 23%; P=0.0005), more frequent joint manifestations (72% vs. 50%; P=0.0002) and higher C-reactive protein (3.7 vs. 1.9 mg/dL; P=0.001). Renal involvement frequency and severity were similar for the 2 groups. Finally, GI+ patients vs. GI– patients, respectively, had comparable overall clinical response rates (80% vs. 76%; P=0.53); minor (12% vs. 13%; P=0.91) or major relapse rates (6% vs. 9%, P=0.54); renal outcomes (1 transplanted vs. 1%, P=1.00; 4 on dialysis vs. 2%, P=0.42); and vasculitis-related mortality (2% vs. 3%; P=0.68). None of the cohort patients had life-threatening GI manifestations at diagnosis, but 2 patients developed GI perforations 1 and 3 months after starting glucocorticoids.

Conclusion: GI involvement is a frequent manifestation of adult IgAV but does not seem to negatively impact overall prognosis. Therapeutic management should not necessarily include immunosuppressive agents as first-line therapy, as for systemic necrotizing vasculitis, but more data are needed to confirm these findings.

Disclosure: A. Audemard-Verger, None; A. Baldoli, None; Z. Amoura, None; P. Cacoub, None; S. Sanges, None; F. Maurier, None; B. Lioger, None; N. Martis, None; E. Riviere, None; G. Urbanski, None; E. Pillebout, None; L. Guillevin for the French Vasculitis Study Group, None; B. Terrier, None.


Abstract Number: 2717

Late Onset of IgA Vasculitis Is Associated with More Severe Renal Involvement
**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** Vasculitis Poster III: Other Vasculitis Syndromes  
**Session Type:** ACR Poster Session C  
**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Immunoglobulin A vasculitis (IgAV), formerly called Henoch–Schönlein purpura, is a small-vessel vasculitis characterized by immune-complex deposits with predominant IgA. Although the disease is often benign in children, adult IgAV has been described as being more severe. Moreover, renal involvement represents the main cause of morbidity and mortality in adults. This study was undertaken to determine whether age could impact IgAV initial manifestations and outcomes.

**Methods:** In this nationwide retrospective study, data from 260 IgAV patients were analyzed to describe their first symptoms and outcomes according to age at IgAV onset: 90 (35%) >60 years (late-onset) and 170 (65%) <60 years.

**Results:** Mean±SD age at IgAV diagnosis for the entire cohort was 50.1±18 years and 63% were male. Baseline manifestations included: purpura (100%), renal involvement (70%), arthralgias or arthritis (62%), gastrointestinal involvement (53%) and renal failure (30%), defined as estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m². Patients with late-onset IgAV, compared to those <60 years old, respectively, had more frequent renal involvement (89% vs. 60%; P<0.0001), more frequent microscopic hematuria (78% vs. 53%; P=0.0001); and more severe disease at diagnosis, with a higher renal failure rate (44% vs. 10%; P<0.0001) and higher urine protein excretion (1.20 vs 0.45 g/day; P=0.002). Only tubulointerstitial lesions in renal biopsies were more frequent in patients >60 years (44% vs. 21%; P=0.003). Median serum IgA was significantly higher for patients >60 years than those <60 years (4.4 vs. 3.3 g/L; P=0.0007). Therapeutic management was similar for both groups: glucocorticoids (70% vs. 60%; P=0.20) and cyclophosphamide (23% vs. 24%; P=0.85). Renal failure at the end of follow-up was more frequent for late-onset patients (42% vs. 13%; P<0.0001) and their vasculitis-related mortality was higher (4% vs. 0%; P=0.02). However, percentage±SD eGFR variation (deltaGFR) and annual DeltaGFR variation were similar for patients >60 and <60 years, respectively: 0.05±5.2% vs. 14.2±8.9% (P=0.27) and −2.2±10.9% vs. 11.1±8.3% (P=0.34).

**Conclusion:** Late onset of IgAV is associated with more frequent and severe renal involvement, and more frequent tubulointerstitial lesions. Comorbidities and physiological age might be involved.

**Disclosure:** A. Audemard-Verger, None; A. Baldolli, None; N. Le Gouellec, None; L. Raffray, None; A. Deroux, None; J. Goutte, None; B. Lioger, None; Z. Amoura, None; P. Cacoub, None; S. Sanges, None; E. Pillebout, None; L. Guillemin for the French Vasculitis Study Group, None; B. Terrier, None.

Is Smoking Important in Adult IgA Vasculitis?

Alojzija Hočevar1, Ziga Rotar1, Vesna Jurcić2 and Matija Tomšič3, 1Department of Rheumatology, University Medical Centre Ljubljana, Ljubljana, Slovenia, 2Institute of Pathology, University of Ljubljana, Faculty of Medicine, Ljubljana, Slovenia, 3University of Ljubljana, Faculty of Medicine, Ljubljana, Slovenia

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Vasculitis Poster III: Other Vasculitis Syndromes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Nicotine may predispose to kidney injury by increasing the oxidative stress, and there is known association between smoking and the progression of chronic kidney disease, including IgA nephropathy. Currently, there is no information about the influence of smoking on the presentation of IgA vasculitis (IgAV) in adults. The aim of our study was to evaluate the role of smoking on the clinical manifestations of acute adult IgA vasculitis.

Methods: We analyzed medical records of histologically proven, adult IgAV cases, diagnosed between January, 1 2010 and April, 30 2017 at our at our secondary/tertiary rheumatology center. The disease activity was assessed using Birmingham vasculitis activity score-3 (BVAS-3). Renal disease was defined severe in case of nephrotic syndrome or nephritic syndrome with acute renal failure. Gastrointestinal (GI) disease was severe in case of bloody diarrhoea, ileus or bowel perforation. We looked at the potential differences in the clinical manifestations of acute IgAV with regard to smoking habits at the time of IgAV presentation (nonsmokers vs. ever smokers vs. current smokers).

Results: During the 76 month period we identified 207 new IgAV cases (56.5 % males, median (IQR) age 64.6 (44.6; 77.3) years). Skin, GI, renal and joint involvement were present in 207 (generalized purpura above the waist in 102 and necrotic in 98), 68 (severe in 17), 94 (severe in 23), and 87 patients, respectively. 87 patients (42.0%) had a positive history of smoking, and 38 of them were current smokers, smoking daily on average (SD) 13 (± 8) cigarettes (range 1 to 30).

Clinical characteristics of nonsmokers vs. ever vs. current smokers are presented in the Table 1. There were no significant differences regarding the frequency of overall GI tract, renal or joint involvement between the groups. However, current smokers had 4.5 times higher risk of clinically severe renal involvement vs. nonsmokers (95%CI 1.8 - 11.0; p=0.001). Past smokers developed severe renal involvement as frequent as nonsmokers (p= 0.202)

Conclusion: Current smoking was associated with the clinically more severe kidney involvement in adult IgAV. This increased risk disappeared with smoking cessation.

Table 1.
<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>Nonsmokers (120)</th>
<th>Ever smokers (87)</th>
<th>Current smokers (38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>44.2</td>
<td>73.6</td>
<td>65.8</td>
</tr>
<tr>
<td>Age (years)*</td>
<td>69.2 (41.4;80.6)</td>
<td>62.0 (49.5;74.9)</td>
<td>50.3 (39.6;64.2)</td>
</tr>
<tr>
<td>Disease duration (days)*</td>
<td>10 (5;21)</td>
<td>8 (5;14)</td>
<td>9(5;16)</td>
</tr>
<tr>
<td>Prior infection (%)</td>
<td>35.8</td>
<td>34.5</td>
<td>44.7</td>
</tr>
<tr>
<td>Generalized purpura</td>
<td>48.3</td>
<td>50.6</td>
<td>47.4</td>
</tr>
<tr>
<td>Skin necroses (%)</td>
<td>46.7</td>
<td>48.3</td>
<td>52.6</td>
</tr>
<tr>
<td>Joint involvement (%)</td>
<td>40.8</td>
<td>43.7</td>
<td>52.6</td>
</tr>
<tr>
<td>Arthritis (%)</td>
<td>15.0</td>
<td>18.4</td>
<td>21.1</td>
</tr>
<tr>
<td>GI tract involvement (%)</td>
<td>32.5</td>
<td>33.3</td>
<td>39.5</td>
</tr>
<tr>
<td>Severe GI tract involvement (%)</td>
<td>7.5</td>
<td>9.2</td>
<td>13.2</td>
</tr>
<tr>
<td>Renal involvement (%)</td>
<td>41.7</td>
<td>50.6</td>
<td>57.9</td>
</tr>
<tr>
<td>Severe renal involvement (%)</td>
<td>5.8</td>
<td>18.4</td>
<td>26.3</td>
</tr>
<tr>
<td>IgA level (g/l)*</td>
<td>3.7 (3.0;4.8)</td>
<td>4.5 (3.1; 5.7)</td>
<td>3.9 (2.9;5.2)</td>
</tr>
<tr>
<td>BVAS-3</td>
<td>8 (3;14)</td>
<td>9 (4;16)</td>
<td>12 (5;17)</td>
</tr>
</tbody>
</table>

Legend: * median and IQR; severe GI tract involvement - bloody diarrhea or ileus or surgical intervention; severe renal involvement - acute renal failure or nephrotic syndrome; BVAS-3 - Birmingham vasculitis activity score;

**Disclosure:** A. Hočevar, None; Z. Rotar, None; V. Jurcic, None; M. Tomšič, None.

**View Abstract and Citation Information Online** - [http://acrabstracts.org/abstract/is-smoking-important-in-adult-iga-vasculitis](http://acrabstracts.org/abstract/is-smoking-important-in-adult-iga-vasculitis)

**Abstract Number:** 2719

**Can Annexin A1 Expression on Neutrophils Distinguish Adult IgA Vasculitis from Other Small Vessel Vasculitides?**

Tadeja Kuret¹, Katja Lakota¹,², Polona Žigon¹, Manca Ogrič¹, Boris Lestan¹, Snezna Sodin Semrl¹,², Saša Čučnik¹,³, Matija Tomšič¹,⁴ and Alojzija Hočevar¹, ¹Department of Rheumatology, University Medical Centre Ljubljana, Ljubljana, Slovenia, ²Faculty of Mathematics, Natural Science and Information Technology, University of Primorska, Koper, Slovenia, ³Faculty of Pharmacy, University of Ljubljana, Ljubljana, Slovenia, ⁴University of Ljubljana, Faculty of Medicine, Ljubljana, Slovenia

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Vasculitis Poster III: Other Vasculitis Syndromes

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM
Background/Purpose: Immunoglobulin A vasculitis (IgAV, formerly Henoch–Schönlein purpura) is a small vessel, immune complex vasculitis characterized by dominant IgA deposits in the vascular wall. Clinical symptoms include skin, joint, gastrointestinal (GI) or renal involvement. Adults frequently develop more severe disease than children\(^1\). Recently, the neutrophil to lymphocyte ratio (NLR) has been proposed as a potential marker for predicting systemic involvement in adult IgAV\(^2\). Moreover, neutrophil phenotypes have been shown to be differentially involved in disease progression of other vasculitides\(^3\). We aimed to determine the percentage of neutrophils, T- and B-cells, NLR and mean fluorescence intensity (MFI) of CD62L and Annexin A1 (AnxA1) on CD16\(^+\) neutrophils in peripheral blood of newly diagnosed, biopsy-proven adult patients with IgAV compared to other small vessel vasculitides (non-IgAV) and healthy blood donors (HBD).

Methods: Flow cytometry of stained, lysed and fixed whole blood was performed in IgAV (n=15; n=9 for AnxA1), non-IgAV patients (n=11; n=6 for AnxA1) and HBD (n=16; n=7 for AnxA1). The diagnoses of non-IgAV included infection-associated small vessel vasculitis, vasculitis associated with tubulointerstitial nephritis and uveitis, ANCA vasculitis and, cryoglobulinemic vasculitis. IgAV patients were further divided into two groups based on organ involvement (patients with isolated skin involvement; n=9 and patients with concomitant renal or GI involvement; n=6). In the IgAV group only one patient had concomitant infection (of urinary tract).

Results: Percentage of CD16\(^+\) neutrophils and NLR were significantly higher, while percentages of T- (CD3\(^+\)) and B-cells (CD19\(^+\)) were significantly lower in newly diagnosed IgAV and non-IgAV cases compared to HBD. Expression of AnxA1 was significantly elevated on CD16\(^+\) neutrophils in IgAV (16.1 (12.9-19.4); median (IQR)) compared to non-IgAV (10.0 (8.1-15.2); p=0.029 (Table 1)). IgAV patients with skin and renal or GI involvement had a significantly higher percentage of CD16\(^+\) neutrophils (77.1 (67.2-83.6)) compared to skin limited IgAV cases (64.5 (57.1-69.1); p=0.012).

| Table 1: Neutrophil/Lymphocyte percentages, their ratio and expression of AnxA1 and CD62L in IgAV patients as compared to HBD and non-IgAV patients |
|-----------------------------------------------|-----------------|-----------------|-----------------|
|                                | HBD             | IgAV            | Non-IgAV         |
| Neutrophils (%)                 | 51.0 (47.1-56.9)| 67.5 (63.6-73.3)| 69.0 (59.4-78.2)|<0.0001          |<0.0001          |0.9586          |
| T-cells (%)                     | 26.4 (23.0-31.8)| 16.6 (10.2-21.4)| 17.8 (19.2-21.4)|0.0004           |0.0096           |0.8355          |
| B-cells (%)                     | 3.8 (2.9-4.7)   | 2.4 (1.6-2.9)   | 1.5 (0.9-2.7)   |0.0042           |0.0083           |0.3502          |
| NLR                             | 1.7 (1.4-2.1)   | 3.3 (2.8-5.8)   | 3.4 (2.2-7.1)   |0.0001           |0.0043           |0.8967          |
| Annexin A1 (MFI)                | 21.3 (18.4-23.7)| 16.1 (12.9-19.4)| 10.0 (8.1-15.2)|0.0549           |0.0023           |0.0290          |
| CD62L (MFI)                     | 56.4 (44.9-72.0)| 83.7 (58.6-102.8)| 92.2 (61.0-127.1)|0.0575           |0.0256           |0.4743          |

Conclusion: Our study reports that neutrophil AnxA1 might represent a good surface marker for distinguishing IgAV from other small vessel vasculitides.

References:


Disclosure: T. Kuret, None; K. Lakota, None; P. Žigon, None; M. Ogrič, None; B. Lestan, None; S. Sodin Semrl, None; S. Čučnik, None; M. Tomšíč, None; A. Hočevar, None.

Abstract Number: 2720

Behçet’s Disease in Southeastern Michigan: A Single Center Comparative Study

Nathan Kilian1 and Amr H Sawalha2, 1Rheumatology, University of Michigan, Ann Arbor, MI, 2Division of Rheumatology, University of Michigan, Ann Arbor, MI

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Vasculitis Poster III: Other Vasculitis Syndromes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Behçet’s disease is a heterogeneous immune-mediated disease, with clinical variability across ethnicities and geographic locations. In this study, we describe and analyze the clinical characteristics of our multi-ethnic Behçet’s disease cohort and provide a comparative analysis comparing the International Criteria for Behçet’s Disease (ICBD) with the International Study Group (ISG) criteria in our patients.

Methods: A retrospective analysis was performed, in which the presence and absence of common Behçet’s disease manifestations were recorded in our cohort. Differences in disease characteristics between men and women, and between ICBD and ISG derived cohorts were determined using chi square tests and Yates’ correction. In addition, the associations between major and minor disease manifestations were also calculated.

Results: A total of 114 patients with a male to female ratio of ~ 1:4 were included. All patients met the ICBD criteria, including 76 who also met the ISG criteria. Over 95% of patients had recurrent genital ulcers, which is higher than generally reported. Retinitis was 5.3 times more common in men than women (p-value= 0.009), and arthralgia was 3.3 times more likely in women than men (p-value= 0.048). When comparing cohorts derived from the two different criteria, the ISG cohort had more skin manifestations (OR= 3.3, p-value= 0.0006). Acne was associated with ~8 times higher odds of developing retinitis in our patients (p-value= 0.0008), and superficial thrombophlebitis was associated with a trend for higher odds of developing uveitis (OR= 4.1, p-value= 0.057). Using the ICBD criteria, 38 additional patients were identified compared to only using the ISG criteria. Of these patients, 28 presented with only mucosal ulceration with or without joint involvement.

Conclusion: We characterize Behçet’s disease in a multi-ethnic cohort from North America. Using the ICBD criteria in the United States significantly increases the likelihood of identifying Behçet’s disease patients, particularly in patients with isolated mucosal involvement, who constitute a substantial subset of our patients in this region.

Disclosure: N. Kilian, None; A. H. Sawalha, None.
Abstract Number: 2721

Anti-IL6-Receptor Tocilizumab in Refractory Uveitis Associated to Extraocular Manifestations in Patients with Behçet’s Disease. Multicenter Study

Belén Atienza-Mateo1, José Luis Martín-Varillas1, Lucia C. Domínguez-Casas1, Nuria Vegas-Revenga1, Vanesa Calvo-Rio1, Natalia Palmou Fontana2, Ricardo Blanco3, Javier Loricera1, MC Gonzalez-Vela4, Emma Beltrán5, Lucia Martínez Costa6, Elia Valls Pascual6, Marisa Hernández Garfella5, Antonio Atanes7, Miguel Cordero Coma8, Joan Miquel Nolla Solé9, Carmen Carrasco Cubero10, Enar Pons11 and Miguel Angel González-Gay2

1Rheumatology, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain,
2Rheumatology, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria., Santander, Spain,
Hospital Universitario Marqués de Valdecilla, Santander, Spain, 3Hospital Universitario Marqués de Valdecilla, Santander, Spain, 4Pathology Anatomy, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, 5Hospital General Universitario de Valencia, Valencia, Spain, 6Hospital Peset, Valencia, Spain, 7Hospital Universitario de A Coruña, A Coruña, Spain, 8Hospital de León, León, Spain, 9Hospital Universitari de Bellvitge, Barcelona, Spain, 10Hospital Universitari Germans Trias i Pujol, Barcelona, Spain, 11Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria., Santander, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Vasculitis Poster III: Other Vasculitis Syndromes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: To assess the efficacy of Tocilizumab (TCZ) in refractory uveitis associated to extraocular manifestations due to Behçet’s disease (BD).

Methods: Multicenter study of patients with BD refractory to standard systemic treatment (conventional immunosuppressive drugs and/or anti-TNF-α agents).

Results: We studied 11 patients (7 men/4 women) (20 affected eyes); mean age 38.4±20.4 years. Uveitis was bilateral in 9 patients. The pattern of ocular involvement was: panuveitis (n=8; with retinal vasculitis in 4), anterior uveitis (n=2) and posterior uveitis (n=1). Cystoid macular edema (CME) was present in 7 patients. The clinical course was recurrent (n=7) or chronic (n=4). Apart from the visual complications, at TCZ onset the following extraocular manifestations were present: oral and/or genital ulcers (n=7), arthritis (n=4), folliculitis/pseudofolliculitis (n=4), erythema nodosum (n=2), livedo reticularis (n=1), and neurological involvement (n=2). Before TCZ, they had received systemic corticosteroids, conventional immunosuppressive drugs and biologic agents, adalimumab (n=8), infliximab (n=4), golimumab (n=3), canakinumab (n=1), or etanercept (n=1). TCZ was used in monotherapy or combined with conventional immunosuppressive drugs at 8 mg/kg/iv/4 weeks (n=10) or 162 mg/sc/week (n=1). TCZ yielded rapid and maintained improvement in all ocular parameters (TABLE). After a mean follow-up of 9.5±8.05 months using TCZ, all patients experienced ocular improvement, with complete remission in 8 of them. However, TCZ was only effective in 3 of the 11 patients with extraocular manifestations. This biologic agent had to be withdrawn in 2 cases, 1 due to a severe infusion reaction and 1 due to arthritis impairment.
**Conclusion:** TCZ appears to be useful in highly refractory BD-related uveitis. However, there are controversial results regarding its efficacy in the treatment of extraocular manifestations of BD.

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex / Age (years)</th>
<th>Ocular pattern and course</th>
<th>Extraocular manifestations</th>
<th>Manifestations that improved with TCZ therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male / 27</td>
<td>Bilateral posterior uveitis + unilateral CME</td>
<td>Oral ulcers, asymptomatic white matter lesions on MRI, arthritis, folliculitis</td>
<td>Uveitis and CME</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chronic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Female / 42</td>
<td>Bilateral panuveitis + unilateral CME</td>
<td>Oral and genital ulcers, erythema nodosum</td>
<td>Uveitis and CME</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chronic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Male / 50</td>
<td>Bilateral panuveitis/papillitis + unilateral CME</td>
<td>Papillitis, arthritis</td>
<td>All of them (uveitis, papillitis, CME and arthritis)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Relapsing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Male / 35</td>
<td>Bilateral panuveitis + retinal vasculitis</td>
<td>Oral ulcers, folliculitis</td>
<td>Uveitis and retinal vasculitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Relapsing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Female / 67</td>
<td>Bilateral panuveitis + retinal vasculitis + bilateral CME</td>
<td>Livedo reticularis</td>
<td>Uveitis, retinal vasculitis and CME</td>
</tr>
<tr>
<td>6</td>
<td>Male / 31</td>
<td>Unilateral panuveitis + retinal vasculitis + unilateral CME</td>
<td>Oral and genital ulcers, folliculitis</td>
<td>Uveitis, retinal vasculitis and CME</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Relapsing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Female / 22</td>
<td>Bilateral panuveitis + bilateral CME</td>
<td>None</td>
<td>Uveitis and CME</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chronic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Male / 75</td>
<td>Bilateral panuveitis + retinal vasculitis + unilateral CME</td>
<td>Oral and genital ulcers, arthritis, folliculitis</td>
<td>Uveitis, retinal vasculitis and arthritis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Relapsing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Male / 10</td>
<td>Bilateral anterior uveitis</td>
<td>Oral and genital ulcers, hemorrhagic stroke, erythema nodosum</td>
<td>Uveitis, oral and genital ulcers and erythema nodosum</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Relapsing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Female / 48</td>
<td>Bilateral anterior uveitis</td>
<td>Oral and genital ulcers, arthritis, pseudofolliculitis, erythema nodosum, intestinal involvement</td>
<td>Uveitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Relapsing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Male / 16</td>
<td>Unilateral panuveitis</td>
<td>Oral ulcers, arthritis</td>
<td>Uveitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chronic</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CME, cystoid macular edema; MRI, magnetic resonance imaging.

**Disclosure:** B. Atienza-Mateo, None; J. L. Martín-Varillas, None; L. C. Domínguez-Casas, None; N. Vegas-Revenga, None; V. Calvo-Rio, None; N. Palmou Fontana, None; R. Blanco, None; J. Loricera, None; M. Gonzalez-Vela, None; E. Beltrán, None; L. Martínez Costa, None; E. Valls Pascual, None; M. Hernández Garfella, None; A. Atanes, None; M. Cordero Coma, None; J. M. Nolla Solé, None; C. Carrasco Cubero, None; E. Pons, None; M. A. González-Gay, None.
Abstract Number: 2722

Long Term Follow-up and Optimization of Infliximab in Refractory Uveitis of Behçet’s Disease. Multicenter Study of 103 Cases


1Rheumatology, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, Hospital General Universitario de Valencia, Valencia, Spain, Hospital de Valme, Sevilla, Spain, Hospital Clinic, Barcelona, Spain, Hospital Gregorio Marañón, Madrid, Spain, Hospital Peset, Valencia, Spain, Hospital Vall d´Hebron, Barcelona, Spain, Hospital San Cecilio, Granada, Spain, Hospital Universitario IOBA, Valladolid, Spain, Hospital de Cruces, Bilbao, Spain, Hospital Donostia, San Sebastian, Spain, Hospital Universitario Donostia. San Sebastian, Spain, Hospital Basurto, Bilbao, Spain, Hospital Universitario de Móstoles, Madrid, Spain, Hospital General Alicantino, Alicante, Spain, Hospital Universitario La Paz, Madrid, Spain, Hospital Clínico San Carlos, Madrid, Spain, Hospital Pontevedra, Pontevedra, Spain, Hospital Sierrallana, Torrelavega, Spain, Hospital La Princesa, Madrid, Spain, Hospital Córdoba, Córdoba, Spain, Hospital Universitario de A Coruña, A Coruña, Spain, Hospital Doctor Negrín, Las Palmas de Gran Canaria, Spain, Hospital Universitario Santiago de Compostela, Santiago de Compostela, Spain, Hospital Cabuérniga, Gijón, Spain, Hospital Lucus Augusti, Lugo, Spain, Hospital Arrixaca, Murcia, Spain, Fundación Jiménez Díaz, Madrid, Spain, Hospital 12 de Octubre, Madrid, Spain, Hospital Universitario Fundación Alcorcón, Madrid, Spain, Hospital Clínico Zaragoza, Zaragoza, Spain, Hospital Universitari Germans Trias i Pujol, Barcelona, Spain, Hospital Severo Ochoa, Madrid, Spain, Hospital General Universitario de Elda, Alicante, Spain, Complejo Asistencial de Palencia, Palencia, Spain, Pathology Anatomy, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, Internal Medicine, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, Rheumatology, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain.

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Vasculitis Poster III: Other Vasculitis Syndromes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM
Background/Purpose: Uveitis is a severe manifestation of Behçet Disease (BD). The treatment is based on corticosteroids and conventional immunosuppressive drugs. In refractory cases, anti-TNFα had demonstrated efficacy. Our aim was to study the efficacy in long-term treatment with Infliximab (IFX) and its optimization.

Methods: Multicenter study of 178 patients diagnosed with Uveitis associated with BD refractory to high-dose of corticosteroids and at least one conventional immunosuppressive drug. IFX was used in 103 of these patients. The degree of ocular inflammation was evaluated with “the SUN working Group” (Am J Ophthalmol 2005; 140: 509-516) and the macular thickening with the optical coherence tomography (OCT). A comparison between baseline, 1st and 2nd week, 1st, 3rd and 6th month and 1st, 2nd, 3th and 4th year was performed. The statistical analysis was performed with the software STATISTICA Statsoft Inc. Tulsa, Oklahoma, USA. Results are expressed in mean±SD for variables with a normal distribution, or median [25-75 IQR] when distribution is not normal. The comparison of continuous variables was performed with the Wilcoxon test.

Results: We studied 103 patients/185 affected eyes (55 men/48 women), mean age 40.4±10.1. The ocular pattern was panuveitis (n=64), posterior uveitis (n=28) and anterior (n=11). Before IFX and besides oral corticosteroids, patients received: iv metilprednisolone (n=30), cyclosporine A (CyA) (n=77), azathioprine (AZA) (n=58), metotrexate (MTX) (n=45) and other treatments (n=34). IFX was administrated in monotherapy (n=24) or combined with other drugs (n=78): CyA (n=32), MTX (26), AZA (17), Cyclophosphamide (1), tacrolimus (1) and mycophenolate (1). The maintenance dose of IFX ranged between 3-5 mg/kg every/4 or 8 weeks. The evolution of the main ocular parameters is summarized in TABLE. Once achieved the remission we optimized treatment with IFX in 28 patients. a) In 23, the interval of dose was increased. b) In the other 5 patients the dose was reduced. After a mean follow-up of 32.29±23.35 months, IFX was stopped in 56 patients for the following reasons: remission (n=20), preference for other way of administration (n=11), inefficacy (n=15), infusional reaction (n=5), TBC (n=1), cutaneous reaction (n=1), oral ulcers (n=1), colon carcinoma (n=1) and desire of pregnancy (n=1).

Conclusion: IFX is effective in short and long term treatment of refractory uveitis associated to BD. Optimization and even discontinuation of IFX after remission is possible.

Table.
<table>
<thead>
<tr>
<th></th>
<th>BCVA (mean±S.D.)</th>
<th>AC cells (median [IQR])</th>
<th>Vitritis (median [IQR])</th>
<th>OCT (µ) (mean±S.D.)</th>
<th>Retinal Vasculitis (% affected eyes)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td>0.50±0.35</td>
<td>1 [0-2]</td>
<td>1 [0-2]</td>
<td>331.7±134.0</td>
<td>53.84%</td>
</tr>
<tr>
<td><strong>1st week</strong></td>
<td>0.53±0.34</td>
<td>0 [0-1]</td>
<td>0.25 [0-1.5]</td>
<td>325.8±124.2</td>
<td>42.30%</td>
</tr>
<tr>
<td><strong>2nd week</strong></td>
<td>0.58±0.33</td>
<td>0 [0-1]</td>
<td>0 [0-1]</td>
<td>319.6±115.3</td>
<td>33.17%</td>
</tr>
<tr>
<td><strong>1st month</strong></td>
<td>0.63±0.33</td>
<td>0 [0-0]</td>
<td>0 [0-0]</td>
<td>301.4±103.7</td>
<td>22.11%</td>
</tr>
<tr>
<td><strong>3rd month</strong></td>
<td>0.68±0.34</td>
<td>0 [0-0]</td>
<td>0 [0-0]</td>
<td>283.2±83.5</td>
<td>10.57%</td>
</tr>
<tr>
<td><strong>6th month</strong></td>
<td>0.68±0.34</td>
<td>0 [0-0]</td>
<td>0 [0-0]</td>
<td>265.7±66.5</td>
<td>7.21%</td>
</tr>
<tr>
<td><strong>1st year</strong></td>
<td>0.66±0.33</td>
<td>0 [0-0]</td>
<td>0 [0-0]</td>
<td>264.1±61.3</td>
<td>2.40%</td>
</tr>
<tr>
<td><strong>2nd year</strong></td>
<td>0.66±0.33</td>
<td>0 [0-0]</td>
<td>0 [0-0]</td>
<td>263.6±65.1</td>
<td>1.92%</td>
</tr>
<tr>
<td><strong>3rd year</strong></td>
<td>0.66±0.33</td>
<td>0 [0-0]</td>
<td>0 [0-0]</td>
<td>239.8±26.8</td>
<td>0.48%</td>
</tr>
<tr>
<td><strong>4th year</strong></td>
<td>0.67±0.32</td>
<td>0 [0-0]</td>
<td>0 [0-0]</td>
<td>231.2±35.6</td>
<td>0.48%</td>
</tr>
</tbody>
</table>

**Disclosure:** B. Atienza-Mateo, None; J. L. Martín-Varillas, None; L. C. Domínguez-Casas, None; N. Vegas-Revenga, None; V. Calvo-Río, None; E. Beltrán, None; J. Sánchez-Burson, None; M. Mesquida, None; A. Adán, None; M. V. Hernández, None; J. L. Martín-Varillas, None; M. Hernández Garfella, None; E. Valls Pascual, None; L. Martínez Costa, None; A. Sellas-Fernandez, None; J. L. Garcia-Serrano, None; J. L. Callejas-Rubio, None; N. Ortego, None; J. M. Herreras, None; A. Fonollosa, None; O. Maíz, None; A. Blanco, None; I. Torre, None; C. Fernandez-Espartero, None; V. Jovani, None; D. Peiteado Lopez, None; D. Díaz Valle, None; E. Pato, None; J. Cruz, None; C. Fernandez-Cid, None; E. Aurrecooecha, None; M. García, None; M. A. Caracuel, None; A. Atanes, None; F. Francisco, None; S. Insúa, None; S. Gonzalez-Suárez, None; A. Sánchez-Andrade, None; L. Linares, None; F. Romero-Bueno, None; A. J. García, None; R. Almodovar, None; E. Mínguez, None; C. Carrasco Cubero, None; E. Raya Álvarez, None; M. Alcalde-Villar, None; C. Fernández-Carbadillo, None; F. Pagés, None; M. Gonzalez-Vela, None; R. Demetrio, None; E. Pons, None; J. L. Hernández, None; M. A. González-Gay, None; R. Blanco, None.


Abstract Number: 2723

**Adalimumab Therapy Optimization in Refractory Uveitis Due to Behçet’s Disease after Achieving Remission. interventional Versus Control Group**

Belén Atienza-Mateo¹, José Luis Martín-Varillas¹, Nuria Vegas-Revenga¹, Lucía C. Domínguez-Casas¹, Vanesa Calvo-Río¹, Emma Beltrán², Juan Sánchez-Burson³, Marina Mesquida⁴, Alfredo Adán⁴, M Victoria Hernández⁴, Marisa
Hernández Garfella², Elia Valls Pascual³, Lucía Martínez Costa⁵, Agusti Sellas-Fernandez⁶, Miguel Cordero Coma⁷, Manuel Díaz-Llopis⁸, Roberto Gallego⁸, David Salom⁸, Norberto Ortega⁹, José L. García-Serrano⁹, José-Luis Callejas-Rubio⁹, José M. Herreras¹⁰, Ángel M García-Aparicio¹¹, Olga Maiz¹², Ana Blanco¹³, Ignacio Torre¹⁴, David Díaz Valle¹⁵, Esperanza Pato¹⁵, Elena Aurrecoechea¹⁶, Miguel A. Caracuel¹⁷, Fernando Gamero¹⁸, Enrique Mínguez¹⁹, Carmen Carrasco Cubero²⁰, Alejandro Olive²¹, Julio Vázquez²², Oscar Ruiz Moreno²³, Fernando Jiménez-Zorzo²⁴, Javier Manero²⁴, Myriam Gandía Martínez²⁵, Esteban Rubio-Romero²⁶, F. Javier Toyes-Sáenz de Miera²⁷, Javier López-Longo²⁸, JM Nolla²⁹, Marcelino Revenga³⁰, Rosalia Demetrio³¹, Enar Pons³¹, Miguel Angel González-Gay¹ and Ricardo Blanco³², ¹Rheumatology, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, ²Hospital General Universitario de Valencia, Valencia, Spain, ³Hospital de Valme, Sevilla, Spain, ⁴Hospital Clinic, Barcelona, Spain, ⁵Hospital Peset, Valencia, Spain, ⁶Hospital Vall d’Hebron, Barcelona, Spain, ⁷Hospital de León, León, Spain, ⁸Hospital Universitario La Fe, Valencia, Spain, ⁹Hospital San Cecilio, Granada, Spain, ¹⁰Hospital Universitario IOBA, Valladolid, Spain, ¹¹Hospital Donostia, San Sebastián, Spain, ¹²Hospital Donosti, San Sebastian, Spain, ¹³Ophthalmology, Hospital Universitario Donostia. San Sebastian. Spain, San Sebastián, Spain, ¹⁴Hospital Basurto, Bilbao, Spain, ¹⁵Hospital Clínico San Carlos, Madrid, Spain, ¹⁶Hospital Sierrallana, Torrelavega, Spain, ¹⁷Hospital Córdoba, Córdoba, Spain, ¹⁸Hospital San Pedro Alcántara, Cáceres, Spain, ¹⁹Hospital Clínico Zaragoza, Zaragoza, Spain, ²⁰Hospital Universitari Germans Trias i Pujol, Barcelona, Spain, ²¹Hospital Universitari Germans Trias i Pujol, Barcelona, Spain, ²²Hospital de Ferrol, A Coruña, Spain, ²³Ophthalmology and Rheumatology, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria., Santander, Spain, ²⁴Hospital Miguel Servert, Zaragoza, Spain, ²⁵Hospital Puerta del Mar, Cádiz, Spain, ²⁶Hospital Universitario Virgen del Rocío, Sevilla, Spain, ²⁷Hospital Universitario Virgen Macarena, Sevilla, Spain, ²⁸Hospital Gregorio Marañón, Madrid, Spain, ²⁹Hospital Universitari de Bellvitge, Barcelona, Spain, ³⁰Hospital Universitario Ramón y Cajal, Madrid, Spain, ³¹Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria., Santander, Spain, ³²Hospital Universitario Marqués de Valdecilla, Santander, Spain

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Vasculitis Poster III: Other Vasculitis Syndromes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Adalimumab (ADA) therapy has been approved by the EMA and the FDA in non-infectious and non-anterior uveitis. After loading, the maintenance dose is 40 mg subcutaneously every other week. However, the duration of ADA therapy is not well established. Our purpose is to assess the long-term follow-up of a large series of patients with refractory uveitis due to Behçet Disease (BD) undergoing ADA therapy who experienced clinical remission and to compare the outcome of BD patients in whom ADA treatment was optimized when clinical remission was achieved with those in whom ADA optimization was not performed (control group).

Methods: Multicenter study that included 74 patients with BD uveitis refractory to glucocorticoids and conventional immunosuppressive drugs who required treatment with ADA. BD uveitis remission was defined if there was not apparent anterior and posterior chamber inflammation for at least 3 months. Based on a shared decision between the patient and the physician, once ocular remission was achieved, ADA therapy was optimized. It was performed increasing the interval between ADA doses progressively as follows: Initially every 3 weeks and then every 4, 6, 7 and 8 weeks up to discontinuation. Ocular inflammation was evaluated according to “SUN” (Am J Ophthalmol 2005; 140: 509-516). Macular thickening was evaluated with Optical Coherence Tomography (OCT).

Results: Ocular remission was achieved in 65 of 74 (86.6%) patients. ADA was optimized in 23 of these 65 patients (35.3%). In the remaining 42 patients ADA was maintained at standard dose (40 mg/sc/2 weeks). No demographic or ocular differences between the optimized (n=23) and the control group (n=42) were observed at the onset of ADA therapy. At last follow-up BCVA was significantly higher in the optimized group when compared to the control (non-optimized) group. No other significant clinical differences between both groups were seen (TABLE). No relevant
adverse effects were seen in the optimized group. It was not the case in the non-optimized BD patients who had the following complications: 1 lymphoma, 1 pneumonia, 1 severe local reaction at the injection site and 1 bacteremia by E. coli. After 34.7±13.3 months follow-up, ADA intervals at last visit in the optimized group (n=23) were as follows: every 3 weeks (n=6), 4 weeks (10), 5 weeks (1), 8 weeks (2), and discontinued (n=4). ADA dose (40 mg/sc/2 weeks) has to be reinitiated at the standard dose (40 mg/sc/2 weeks) due to ocular relapses in only 2 of 23 patients had a, achieving again remission. Results were expressed as mean±SD for normally distributed variables or as median [25-75 IQR] for those that did not follow a normal distribution.

**Conclusion:** Most patients with refractory uveitis due to BD undergoing ADA therapy achieve remission. ADA optimization can be successfully performed.

**Table.**

<table>
<thead>
<tr>
<th></th>
<th>Optimized Group</th>
<th>Non Optimized Group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic features</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>37.2±13.1</td>
<td>39.1±9.3</td>
<td>0.5</td>
</tr>
<tr>
<td>Sex (n, ♂/♀)</td>
<td>15/8</td>
<td>19/23</td>
<td>0.13</td>
</tr>
<tr>
<td>Positive HLA-B51(%)</td>
<td>61</td>
<td>74</td>
<td>0.26</td>
</tr>
<tr>
<td>Duration of uveitis (months) prior to ADA(median [IQR])</td>
<td>43 [23-74.5]</td>
<td>24 [6-36]</td>
<td>0.1</td>
</tr>
<tr>
<td>Previous Immunosuppressants (n) (mean±S.D.)</td>
<td>2±1.1</td>
<td>1.7±1.1</td>
<td>0.3</td>
</tr>
<tr>
<td><strong>Ocular pattern at ADA onset</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BCVA (mean±S.D.)</td>
<td>0.61±0.36</td>
<td>0.56±0.33</td>
<td>0.46</td>
</tr>
<tr>
<td>AC cells (median [IQR])</td>
<td>0 [0-2]</td>
<td>1 [0-2]</td>
<td>0.85</td>
</tr>
<tr>
<td>Vitritis (median [IQR])</td>
<td>1 [0-2]</td>
<td>1 [0-2]</td>
<td>0.66</td>
</tr>
<tr>
<td>OCT (mean±S.D.)</td>
<td>306.7±122.9</td>
<td>332.8±129.1</td>
<td>0.51</td>
</tr>
<tr>
<td><strong>Ocular pattern at last visit</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BCVA (mean±S.D.)</td>
<td>0.89±0.19</td>
<td>0.77±0.25</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>AC cells (median [IQR])</td>
<td>0 [0-0]</td>
<td>0 [0-0]</td>
<td>0.7</td>
</tr>
<tr>
<td>Vitritis (median [IQR])</td>
<td>0 [0-0]</td>
<td>0 [0-0]</td>
<td>0.3</td>
</tr>
<tr>
<td>OCT (mean±S.D.)</td>
<td>250.5±17.9</td>
<td>249±26.1</td>
<td>0.87</td>
</tr>
</tbody>
</table>

**Disclosure:** B. Atienza-Mateo, None; J. L. Martín-Varillas, None; N. Vegas-Revenga, None; L. C. Domínguez-Casas, None; V. Calvo-Rio, None; E. Beltrán, None; J. Sánchez-Burson, None; M. Mesquida, None; A. Adán, None; M. V. Hernández, None; M. Hernández Garfella, None; E. Valls Pascual, None; L. Martínez Costa, None; A. Sellas-Fernandez, None; M. Cordero Coma, None; M. Díaz-Llopis, None; R. Gallego, None; D. Salom, None; N. Ortego, None; J. L. García-Serrano, None; J. L. Callejas-Rubio, None; J. M. Herreras, None; Á. M. García-
Apremilast for Refractory Mucocutaneous Ulcers of Behçet’s Disease. National Multicenter Study of 14 Cases

Belén Atienza-Mateo, José Luis Martín-Varillas, Javier Loricera, Nuria Vegas-Revenga, Lucia C. Domínguez-Casas, Jose L. Hernández, Clara Moriano, Maria Dolores García-Armario, Iván Castelvi, Francisca Sivera, Jaime Calvo-Alen, Isabel de la Morena, Francisco Ortiz-Sanjuán, José Andrés Román-Ivorra, Ana Pérez-Gómez, MC Gonzalez-Vela, Miguel Angel González-Gay and Ricardo Blanco.

Background/Purpose: Behçet’s disease (BD) is characterized by recurrent oral and/or genital ulcers accompanied by ocular, cutaneous, articular, gastrointestinal, and/or neurologic manifestations. Oral and/or genital aphthous ulcers are often refractory to conventional treatment. Apremilast is an orally-active small molecule which inhibits phosphodiesterase-4 (PDE-4) that modulates some inflammatory pathways. Our aim was to assess the efficacy of apremilast in BD patients with oral and/or genital ulcers refractory to conventional treatment.

Methods: Retrospective national multicenter open-label study on 14 BD patients treated with apremilast at standard dose of 30 mg twice daily. The main outcome was resolution of oral and/or genital ulcers.

Results: We included 14 patients (10 women/4 men), with a mean age of 44.3±14.4 years. Before apremilast, all patients had also received several systemic conventional drugs: oral corticosteroids (n=13), colchicine (n=14), NSAIDS (n=7), methotrexate (n=7), azathioprine (n=5), cyclosporine (n=4), infliximab (n=3), adalimumab (n=3), dapsone (n=3), mycophenolate mofetil (n=1), tocilizumab (n=1), etanercept (n=1), secukinumab (n=1). The main clinical symptoms for starting apremilast were oral aphthous ulcers (n=14) and genital ulcers (n=10). Other manifestations present at apremilast onset were arthralgia/arthritis (n=4), folliculitis (n=4), furunculosis (n=1), erythematous and scaly skin lesions (n=1), psoriasis (n=1), erythema nodosum (n=1), deep venous thrombosis (n=1), ileitis (n=1), asthenia (n=3). Ten patients experienced improvement in the first two weeks after starting apremilast. TABLE shows the evolution of the
After a median follow-up of 3.5 [interquartile range, 3-9] months, most of the patients experienced a total or partial clinical improvement. In this period of time, 7 patients developed side-effects: dyspepsia (n=4), nausea (n=3), diarrhea (n=3), headache (n=1), abdominal pain (n=1), anorexia (n=1), and halitosis (n=1). However, only 2 of 6 patients had to reduce the dose of apremilast to 30 mg/day. In 3 patients (21%) apremilast was withdrawn after 3 months of treatment due to unsatisfactory response.

**Conclusion:** Apremilast leads to a rapid and maintained improvement in many patients with refractory mucocutaneous ulcers of BD. Even in patients refractory to several systemic drugs including biologic therapy.

<table>
<thead>
<tr>
<th>Table.</th>
<th>Baseline</th>
<th>Week 1-2</th>
<th>Week 4</th>
<th>Week 12</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n= 14</td>
<td>n= 14</td>
<td>n= 11</td>
<td>n= 10</td>
</tr>
</tbody>
</table>

**Resolution of main symptom, oral and/or genital ulcers n, (%):**

<table>
<thead>
<tr>
<th></th>
<th>Complete</th>
<th>Partial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 1-2</td>
<td>4/14 (29)</td>
<td>6/14 (43)*</td>
</tr>
<tr>
<td>Week 4</td>
<td>8/11 (73)</td>
<td>2/11 (18)</td>
</tr>
<tr>
<td>Week 12</td>
<td>7/10 (70)</td>
<td>0/10 (0)</td>
</tr>
</tbody>
</table>

**Resolution of others symptoms n, (%):**

<table>
<thead>
<tr>
<th></th>
<th>Complete</th>
<th>Partial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 1-2</td>
<td>3/8 (37)</td>
<td>1/8 (12)</td>
</tr>
<tr>
<td>Week 4</td>
<td>4/8 (50)</td>
<td>2/8 (25)</td>
</tr>
<tr>
<td>Week 12</td>
<td>3/7 (43)</td>
<td>3/7 (43)</td>
</tr>
</tbody>
</table>

**Dose of prednisone (mg/day), median [IQR]:**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 1-2</th>
<th>Week 4</th>
<th>Week 12</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>7.5 [0-15] (14)</td>
<td>5.0 [0-10] (14)</td>
<td>7.5 [0-15] (11)</td>
<td>5 [0-5] (9)</td>
</tr>
</tbody>
</table>

The number of patients with available data is shown in parentheses.

**Disclosure:** B. Atienza-Mateo, None; J. L. Martín-Varillas, None; J. Loricera, None; N. Vegas-Revenga, None; L. C. Domínguez-Casas, None; J. L. Hernández, None; C. Moriano, None; M. D. García-Armario, None; I. Castelvi, None; F. Sivera, None; J. Calvo-Alen, None; I. de la Morena, None; F. Ortiz-Sanjuán, None; J. A. Román-Ivorra, None; A. Pérez-Gómez, None; M. Gonzalez-Vela, None; M. A. González-Gay, None; R. Blanco, None.

**View Abstract and Citation Information Online**: [http://acrabstracts.org/abstract/apremilast-for-refractory-mucocutaneous-ulcers-of-behcets-disease-national-multicenter-study-of-14-cases](http://acrabstracts.org/abstract/apremilast-for-refractory-mucocutaneous-ulcers-of-behcets-disease-national-multicenter-study-of-14-cases)

**Abstract Number:** 2725

**Understanding Vasculitis Patients’ Ability to Work with Numbers**

**Cole Rodman**¹, Mary-Kate Tompkins¹, Holly Steigelman², Brad H. Rovin³, Stacy P. Ardoin⁴, Ellen Peters⁵ and Alexa Meara⁶, ¹The Ohio State University, Columbus, OH, ²The Ohio State University Wexner Medical Center, Columbus, OH, ³Ohio State University Medical Center, Columbus, OH, ⁴Pediatric & Adult Rheumatology, The Ohio State University Wexner Medical Center, Columbus, OH, ⁵Decision Research, Eugene, OR, ⁶Internal Medicine/Rheumatology, The Ohio State University Wexner Medical Center, Columbus, OH

**First publication:** September 18, 2017
SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Vasculitis Poster III: Other Vasculitis Syndromes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: In the case of a complex disease like vasculitis, the patient is often tasked with understanding complicated care plans and managing myriad medications. Without appropriate support for these tasks, however, poor health outcomes may result. Recently, shared decision-making (SDM) has become a strategy for effective disease management, with the focus on the physician’s ability to communicate. However, little attention has been paid to the manner in which the abilities and background of the patient interact with the communication and decision-making process. For this project, the following measures were obtained: patient activation (PAM), a measure of patient engagement, objective numeracy (ONS), a measure of objective math skills, subjective numeracy (SNS), a measure of self-reported math skills, health literacy (sTOFHLA), the Brigham Vasculitis Activity Score (BVAS), and the Vasculitis Damage Index (VDI), measures of activity and damage respectively.

Methods: Participants (N=43) were recruited from the Ohio State University Lupus, Vasculitis, and Glomerulonephritis (LVG). Subjects completed each of the measures indicated above. Pearson’s correlation coefficient (PCC), r, was calculated for each of the variable pairs shown in Table 1. Some subjects were missing data. All available data for each variable were used.

Results: 37 out of the 43 patients had ANCA associated-vasculitis and 3 patients had Takayasu’s vasculitis, one patient each had eosinophilic polyangiitis, CNS vasculitis and Behcet’s syndrome. The ONS scores were relatively low (mean = 3.85 out of a possible 8 maximum score) while the mean PAM score was high (mean = 3.23 out of a possible 4 maximum score). All but one subject had above normal health literacy scores (sTOFHLA > 23). Table 1 illustrates correlations between variables.

Conclusion: Currently, very little evidence exists about the relations between patient activation, numeracy, and disease outcomes in vasculitis patients. Interestingly, although many patients had high patient activation and adequate health literacy scores, they had low math and numerical skills. Subjective and objective numerical ability were correlated, indicating patients who believed they were skilled numerically actually were. Higher activation scores were strongly negatively correlated with both disease damage and activity, indicating that greater engagement in care corresponded to lower disease damage and activity. Surprisingly, higher ONS scores trended with higher disease damage, a relationship that, if it proves robust, merits future investigation.
<table>
<thead>
<tr>
<th></th>
<th>Health Literacy</th>
<th>SNS</th>
<th>ONS</th>
<th>Patient Activation</th>
</tr>
</thead>
<tbody>
<tr>
<td>SNS</td>
<td>Pearson’s r</td>
<td>0.068</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>p value</td>
<td>0.736</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>N=</td>
<td>27</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ONS</td>
<td>Pearson’s r</td>
<td>0.372</td>
<td>0.399</td>
<td></td>
</tr>
<tr>
<td></td>
<td>p value</td>
<td>0.061</td>
<td>0.043</td>
<td></td>
</tr>
<tr>
<td></td>
<td>N=</td>
<td>26</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Patient Activation Measure</td>
<td>Pearson’s r</td>
<td>0.263</td>
<td>0.280</td>
<td>0.215</td>
</tr>
<tr>
<td></td>
<td>p value</td>
<td>0.195</td>
<td>0.166</td>
<td>0.291</td>
</tr>
<tr>
<td></td>
<td>N=</td>
<td>26</td>
<td>26</td>
<td>26</td>
</tr>
<tr>
<td>Disease Activity (BVAS)</td>
<td>Pearson’s r</td>
<td>-0.194</td>
<td>-0.166</td>
<td>-0.056</td>
</tr>
<tr>
<td></td>
<td>p value</td>
<td>0.332</td>
<td>0.408</td>
<td>0.786</td>
</tr>
<tr>
<td></td>
<td>N=</td>
<td>27</td>
<td>27</td>
<td>26</td>
</tr>
<tr>
<td>Disease Damage (VDI)</td>
<td>Pearson’s r</td>
<td>0.011</td>
<td>-0.034</td>
<td>0.199</td>
</tr>
<tr>
<td></td>
<td>p value</td>
<td>0.957</td>
<td>0.866</td>
<td>0.329</td>
</tr>
<tr>
<td></td>
<td>N=</td>
<td>27</td>
<td>27</td>
<td>26</td>
</tr>
</tbody>
</table>

SNS= Subjective Numeracy; ONS= Objective numeracy

Disclosure: C. Rodman, None; M. K. Tompkins, None; H. Steigelman, None; B. H. Rovin, None; S. P. Ardoin, not applicable, 9; E. Peters, None; A. Meara, None.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/understanding-vasculitis-patients-ability-to-work-with-numbers](http://acrabstracts.org/abstract/understanding-vasculitis-patients-ability-to-work-with-numbers)

Abstract Number: 2726

**Differentiating Features of Primary Angiitis of Central Nervous System and Reversible Cerebral Vasoconstriction Syndrome: Clinical and Radiological Evaluation**

Didem Saygin¹, Russell Cerejo², Priya Sundaram-Simonelli³, Gabor Toth⁴, Stephen Jones³, Leonard H. Calabrese⁵ and Rula A Hajj-Ali⁶, ¹Internal Medicine, Department of Internal Medicine, Cleveland Clinic, Cleveland, Cleveland, OH, ²Cleveland Clinic, Cleveland, OH, ³Neuroradiology, Cleveland Clinic, Cleveland, OH, ⁴Cerebrovascular Center, Cleveland Clinic, Cleveland, OH, ⁵Rheumatic & Immunologic Disease and Infectious Disease, Cleveland Clinic Foundation, Cleveland, OH, ⁶Rheumatic and Immunologic Disease, Cleveland Clinic, Cleveland, OH

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Vasculitis Poster III: Other Vasculitis Syndromes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM
**Background/Purpose:** Primary angitis of central nervous system (PACNS) is an isolated vasculitis affecting small-sized cerebral blood vessels. One of the major mimickers of PACNS is reversible cerebral vasoconstriction syndrome (RCVS). Both entities have distinctive pathophysiology, prognosis and therapeutic implications and differentiation between both is prudent. In this study, we aimed to compare the clinical and imaging characteristics of PACNS and RCVS cases at the presentation to better differentiate these entities.

**Methods:** Patients from Cleveland Clinic prospective RCVS-PACNS registry were included in the study. PACNS cases were included if they had a biopsy consistent with vasculitis or positive angiography and inflammatory cerebrospinal fluid pattern. Patients were asked to fill out questionnaires regarding their symptoms at presentation, headache impact test (HIT-6) and migraine disability assessment test (MIDAS). Brain MRI and cerebral angiography performed near the time of presentation were blindly evaluated by one neuroradiologist and two interventional radiologists, respectively.

**Results:** Our study included 28 PACNS and 45 RCVS cases. Main results are summarized in table. Female patients were more commonly affected by RCVS compared to males (3:5:1). RCVS cases more commonly presented with headache than PACNS cases. Headache was often insidious and dull in PACNS, whereas it was sudden and thunderclap in RCVS. Time for headache to peak was reported as seconds and intensity of headache was higher in RCVS cases. Neurologic deficit was more commonly associated with headache in PACNS than RCVS cases.

Appearance of vascular abnormality on cerebral angiogram was sausage-like in most of the RCVS and irregular in most of the PACNS cases. Subarachnoid hemorrhage was more common on MRI of RCVS cases, while nonspecific white matter changes were more common in PACNS cases. Lesions were superficial (involving cortex and subcortical white matter) in RCVS and deep (deep and periventricular white matter) in PACNS cases. Total score of MIDAS was higher in RCVS indicating more disability due to headache in these cases (p=0.01). Results of HIT-6 are shown in the figure.

**Conclusion:** PACNS cases experience insidious-onset and dull headache, while RCVS cases often experience sudden, more severe and disabling headache. Radiologic signs such as nonspecific white matter changes, deep location of lesion, and irregular appearance of the vessel on angiogram are more commonly seen in PACNS cases, and can help guide clinicians in differential diagnosis.

<table>
<thead>
<tr>
<th></th>
<th>PACNS (n=28)</th>
<th>RCVS (n=45)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>46.7±14.3</td>
<td>45.8±13.3</td>
<td>0.9</td>
</tr>
<tr>
<td>Gender (F:M)</td>
<td>13:15</td>
<td>35:10</td>
<td>0.006</td>
</tr>
<tr>
<td>Race (White/Black/Other)</td>
<td>27/0/1</td>
<td>38/6/1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Headache characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence of headache</td>
<td>18 (69.2%)</td>
<td>36 (97.3%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Insidious/Thunderclap headache</td>
<td>6/3</td>
<td>3/30</td>
<td>0.0002</td>
</tr>
<tr>
<td>Time for headache to peak (hours/minutes/seconds)</td>
<td>3/2/1</td>
<td>1/4/21</td>
<td>0.002</td>
</tr>
<tr>
<td>Intensity of headache (0-100)</td>
<td>51.1±22.6</td>
<td>75.4±25.1</td>
<td>0.01</td>
</tr>
<tr>
<td>Dull headache</td>
<td>3 (30%)</td>
<td>1 (2.94%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Neurologic deficit associated with headache</td>
<td>15 (83.33%)</td>
<td>19 (52.77%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Exposure to vasoactive substance</td>
<td>3 (18.75%)</td>
<td>15 (53.12%)</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>Imaging characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Appearance of irregularity on cerebral angiogram (sausaging/irregular, notched)</td>
<td>4/7</td>
<td>27/1</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Subarachnoid hemorrhage on MRI</td>
<td>1 (4.76%)</td>
<td>14 (41.17%)</td>
<td>0.004</td>
</tr>
<tr>
<td>Non-specific white matter changes on MRI</td>
<td>7 (33.33%)</td>
<td>3 (8.82%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Superficial location of lesion on MRI</td>
<td>5 (15.15%)</td>
<td>14 (45.16%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Deep location of lesion on MRI</td>
<td>12 (36.36%)</td>
<td>5 (16.12%)</td>
<td>0.02</td>
</tr>
</tbody>
</table>
Disclosure: D. Saygin, None; R. Cerejo, None; P. Sundaram-Simonelli, None; G. Toth, None; S. Jones, None; L. H. Calabrese, Bristol-Myers Squibb, 5; R. A. Hajj-Ali, Abbvie, 8, Novartis Pharmaceutical Corporation, 5, GlaxoSmithKline, 5.


Abstract Number: 2727

Assessment of Damage and Prognosis in Patients with Adult IgA Vasculitis: Retrospective Multicentered Cohort Study

Fatma Alibaz-Oner1, Ahmet Omma2, Alper Sari3, Omer Karadag4, Dondu Uskudar Cansu5, Cemal Bes6, Fatih Yildiz7, Mustafa Ferhat Oksuz8, Sema Yilmaz9, Atalay Dogru10, Ayse Balkarli8, Sibel Bakirci11, and Haner Direskeneli12.

1Marmara University, School of Medicine, Rheumatology, Istanbul, Turkey, 2Department of Internal Medicine, Division of Rheumatology, Ankara Numune Training and Research Hospital, Ankara, Turkey, 3Rheumatology, Hacettepe University, School of Medicine, Ankara, Turkey, 4Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Turkey, 5Rheumatology, Osmangazi University, School of Medicine, Eskisehir, Turkey, 6Rheumatology, Bakirköy Dr. Sadi Konuk Training and Research Hospital, Istanbul, Turkey, 7Rheumatology, Van EAH, Adana, Turkey, 8PsART study group, Ankara, Turkey, 9Department of Rheumatology, Selcuk University School of Medicine, Konya, Turkey, 10Rheumatology, Suleyman Demirel University, School of Medicine, Isparta, Turkey, 11Fellow in Rheumatology, Antalya, Turkey, 12Rheumatology, Marmara University, School of Medicine, Rheumatology, Istanbul, Turkey

First publication: September 18, 2017

SESSION INFORMATION
IgA Vasculitis is a leukocytoclastic vasculitis involving small vessels with depositions of immune complexes containing IgA. IgA Vasculitis is a predominantly pediatric vasculitis. There is limited data for the prognosis of adult IgA Vasculitis, with also no damage assessment. In this study, we aimed to evaluate the clinical characteristics, treatment, outcome and damage of patients with adult IgA Vasculitis.

Methods: We assembled a retrospective cohort of patients with adult IgA Vasculitis from tertiary Rheumatology Centers in Turkey. The demographics, clinical characteristics, treatment and outcomes of patients were abstracted from medical records. Birmingham Vasculitis Activity Score (BVAS), prognostic Five Factor Score (FFS) and vasculitis damage index (VDI) were calculated.

Results: The study included 52 (male/ female: 40/12) patients with adult IgA Vasculitis. The mean age was 42.2±17 years. Infection history within 6 weeks before presentation was present in 22 (42.3%) patients (18 upper respiratory tract, 3 gastrointestinal and one urinary tract). Cutaneous manifestations and arthritis/arthralgia were the most common clinical manifestations (Table 1). All patients were treated with oral glucocorticoids (GC). Pulse GC treatment was also given to 12 (23.1%) patients. As additional immunosuppressive agents, azathiopirine was given to 21 (40.4%) and pulse cyclophosphamide to 11 (21.2%) patients. Twenty-eight patients (53.9%) had follow-up of 28.6 months. Five (17.8%) patients relapsed during follow-up. While 3 relapses were major, 2 of them were minor relapses. At the last visit, disease status was evaluated as active or treatment failure by the treating physician in 6 (21.4%) patients. Mortality was 3.6% (n=1) during follow-up, due to pneumonia. The mean VDI score was 0.6 in the last visit. Nine (32.1%) patients had at least one damage item at the end of follow-up period.

Conclusion: Our results showed that approximately one fifth of patients with adult IgA Vasculitis had relapses during follow-up. At the end of follow-up, one third of patients had at least one damage item. Although, 45% of patients had FFS≥1, the mortality rate was observed to be low in the present study.

Table 1: Baseline clinical characteristics of patients with adult Henoch Schönlein Purpura
**Adult Henoch Schönlein Purpura**

(n=52)

<table>
<thead>
<tr>
<th>Laboratory parameters</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/dL)*</td>
<td>13.5±2</td>
</tr>
<tr>
<td>Erythrocyte Sedimentation Rate (mm/hour) *</td>
<td>32.7 ± 22</td>
</tr>
<tr>
<td>C-reactive protein (mg/l)†</td>
<td>25.2 (1-94.9)</td>
</tr>
<tr>
<td>Proteinuria (&gt;300mg/24 hours)</td>
<td>28 (53.9%)</td>
</tr>
<tr>
<td>Creatinine (mg/dl)*</td>
<td>0.9±0.4</td>
</tr>
<tr>
<td>Hepatitis B positivity (n)</td>
<td>4/47 (8.5%)</td>
</tr>
<tr>
<td>Hepatitis C positivity (n)</td>
<td>0/47</td>
</tr>
<tr>
<td>ANA positivity</td>
<td>8/47 (17%)</td>
</tr>
<tr>
<td>RF Positivity</td>
<td>0/48</td>
</tr>
<tr>
<td>c-ANCA positivity</td>
<td>1/48 (2.1%)</td>
</tr>
<tr>
<td>p-ANCA positivity</td>
<td>1/47 (2.1%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical Manifestations, n/52 (%)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>7 (13.5%)</td>
</tr>
<tr>
<td>Weight loss</td>
<td>14 (26.9%)</td>
</tr>
<tr>
<td>Myalgia/Weakness/Leg tenderness</td>
<td>24 (46.2%)</td>
</tr>
<tr>
<td>Arthritis and/or arthralgia</td>
<td>46 (88.5%)</td>
</tr>
<tr>
<td>Neurologic manifestations</td>
<td>1 (1.9%)</td>
</tr>
<tr>
<td>Testicular pain or tenderness</td>
<td>3 (5.8%)</td>
</tr>
<tr>
<td>Recent onset or severe hypertension</td>
<td>2 (3.8%)</td>
</tr>
<tr>
<td>Cutaneous Manifestations</td>
<td>48 (92.3%)</td>
</tr>
<tr>
<td>Peripheral limb edema</td>
<td>8 (15.4%)</td>
</tr>
<tr>
<td>Gastrointestinal manifestations</td>
<td>39 (75%)</td>
</tr>
<tr>
<td>Cardiac manifestations</td>
<td>2 (3.8%)</td>
</tr>
</tbody>
</table>

| FFS=0                                        | 29 (55.8%)    |
| FFS=1                                        | 15 (28.8%)    |
| FFS≥2                                        | 8 (15.4%)     |

**BVAS score at diagnosis***  

4.1± 1.7

**Disclosure:**  
F. Alibaz-Oner, None; A. Omma, Abbvie, 2,Merck; Pfizer, 5; A. Sari, None; O. Karadag, None; D. Uskudar Cansu, None; C. Bes, Roche Pharmaceuticals, 2; F. Yildiz, None; M. F. Oksuz, None; S. Yilmaz, None; A. Dogru, None; A. Balkarli, None; S. Bakirci, None; H. Direskeneli, None.


**Abstract Number:** 2728

**Serum Levels of Interleukin-36 Receptor Antagonist in Behçet’s Patients**
Behcet's disease (BD) is a systemic vasculitis disorder of unknown etiology with recurrent exacerbations and remissions. The etiopathogenesis of the disease is still unclear. The most investigated cytokine in the pathogenesis of the disease is interleukin (IL) -1 family. A new member of the IL-1 cytokine family, IL-36Ra (Receptor Antagonist), stimulates dendritic cells from the host cells of innate and acquired immunity. In this study we investigated whether the level of serum IL-36Ra increase or not in the etiopathogenesis of Behcet's disease, its effect on disease activity and clinical findings.

Methods:
Serum IL-36Ra levels were measured by (ELISA) kits following the manufacturer’s instructions. All BD patients recruited for this study met the 1990 international criteria for classification of BD.

Results:
31 of the patients were active disease (51.7%). Demographic and clinical parameters are shown in Table 1.

Table 1: Demographic and clinical characteristics of Behcet’s patients and healthy controls

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All BD Patients (n:60)</th>
<th>Active BD Patients (n:31)</th>
<th>Healthy Controls (n:20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>41 ± 11,1 (mean+SD)</td>
<td>38,4 ± 11,3</td>
<td>40,2 ± 13</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>29/31</td>
<td>14/17</td>
<td>10/10</td>
</tr>
<tr>
<td>Oral ulcers</td>
<td>59 (98.3%)</td>
<td>25 (80.6%)</td>
<td>-</td>
</tr>
<tr>
<td>Genital ulcers</td>
<td>48 (80%)</td>
<td>23 (74.2%)</td>
<td>-</td>
</tr>
<tr>
<td>Thrombophlebitis</td>
<td>14 (23.3%)</td>
<td>7 (22.6%)</td>
<td>-</td>
</tr>
<tr>
<td>Arthritis</td>
<td>22 (36.6%)</td>
<td>11 (35.5%)</td>
<td>-</td>
</tr>
<tr>
<td>Uveitis</td>
<td>30 (50%)</td>
<td>11 (35.5%)</td>
<td>-</td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>18 (30%)</td>
<td>6 (19.4%)</td>
<td>-</td>
</tr>
<tr>
<td>CNS involvement</td>
<td>5 (8.3%)</td>
<td>4 (12.9%)</td>
<td>-</td>
</tr>
</tbody>
</table>

Serum IL-36Ra levels were found to be $15.36 ± 13.26$ pg / ml in the patient group and $17.90 ± 13.03$ pg / ml in the control group ($p = 0.677$). Serum IL-36Ra levels were found to be $17.80 ± 10.63$ pg / ml in the active patient group and serum IL-36 Ra level in the inactive patient group was found to be $12.77 ± 7.12$ pg / ml. A statistically significant difference was found between IL-36Ra levels in active and inactive patient groups ($p = 0.037$). There was no statistically significant difference between IL-36Ra levels ($p = 0.636$ and $p = 0.207$, respectively) between active patient and inactive patient group and control group. Serum IL-36Ra levels were significantly higher in patients with Behçet's disease than those without oral ulcers ($p = 0.018$). In addition, serum IL-36Ra levels ($24.45 ± 11.58$ pg / ml) were higher in patients with neurological involvement than those without neurological involvement ($14.45 ± 8.71$ pg / ml) ($p = 0.011$). No statistically significant difference was found between serum IL-36Ra and other systemic manifestations.

Conclusion:
According to our results, there was a statistically significant difference between IL-36Ra and oral ulcers, neurological involvement, disease activity and CRP. More study is needed to determine the role of IL-36Ra in the pathogenesis of Behcet's disease.

Disclosure: P. Ünsal, None; P. Cerci, None; Ş. A. Açıkgöz, None; G. Keskin, None; Ü. Ölmez, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/serum-levels-of-interleukin-36-receptor-antagonist-in-behcets-patients

Abstract Number: 2729

Surgical Therapies in the Treatment of Pulmonary Artery Involvement in Behcet’s Syndrome

Hasan Tuzun1, Gul Guzelant2, Ozkan Demirhan3, Buge Oz4, Izzet Fresko2, Vedat Hamuryudan2, Hasan Yazici2 and Emire Seyahi2, 1Istanbul University, Cerrahpasa Medical Faculty, Department of Cardiovascular Surgery, Istanbul, Turkey, 2Istanbul University, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey, 3Istanbul Bilim University, Medical Faculty, Department of Thoracic Surgery, Istanbul, Turkey, 4Istanbul University, Cerrahpasa Medical Faculty, Department of Pathology, Istanbul, Turkey

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Vasculitis Poster III: Other Vasculitis Syndromes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The mainstay treatment of pulmonary artery involvement (PAI) in Behcet’s syndrome (BS) is immunosuppression and corticosteroids (1). The role of surgical intervention in the management of PAI can be questionable in many cases considering the severe outcome of our previous attempts (2-3). For the past few years we observed that there are indeed several conditions associated with PAI which require surgical operations. In this study, we described disease characteristics, management and outcome of a group of BS patients who underwent surgical procedures for complications due to PAI.

Methods: There were 9 patients with BS (8 M/1 F) who underwent surgery for PAI from 2003 to 2016 at the Department of Thoracic and Cardiovascular Surgery, Cerrahpasa Medical Faculty. The medical records, outpatient charts, radiological and pathological studies of these patients were reviewed retrospectively.

Results: The mean age of the patients was 24.8±7.5 years (range: 12-35). The mean duration of the disease at the time of the surgery was 4.3±3.8 years. The main symptom was haemoptysis. The most common surgery type was lobectomy which was done in 6 patients, followed by decortications in 3. The reason for the surgical procedures were variable as shown in Table. It was giant pulmonary arterial aneurysms refractory to the medical treatment in 4 patients (patients no. 1, 2, 3 and 4), hydropneumothorax due to cavitary lesions in two (patients no. 5 and 6), pleural effusions refractory to the medical treatment in one (patient no. 7), bronchopleural fistula after embolization in one (patient no. 8) and bronchiectasis in another (patient no. 9). All patients received cyclophosphamide treatment with different total doses. Seven patients (patient no. 2, 4, 5, 6, 7, 8 and 9) are still alive and are being followed in our clinic for a median of 7.5 years (IQR:1.5-11). Patient no. 1 had died because of hepatic failure due to Budd-Chiari syndrome after 1 year from the surgery and patient no. 3 had died because of massive haemoptysis within 2 months of lobectomy.

Conclusion: We now think that lobectomies in patients with giant aneurysms refractory to medical treatment can be done with successful results. Also, complications such as refractory pleural effusions, bronchiectasies and bronchopleural fistula can be managed with surgical interventions successfully in patients with PAI.
References:

Table. Main symptom and type of surgical intervention in 9 patients

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age</th>
<th>Presentation</th>
<th>Preoperative treatment</th>
<th>Surgical procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12</td>
<td>Haemoptysis</td>
<td>Cyclophosphamide 1.5 gr</td>
<td>Left lower lobectomy</td>
</tr>
<tr>
<td>2</td>
<td>21</td>
<td>Haemoptysis</td>
<td>Cyclophosphamide 3 gr, infliximab 300 mg (first dose)</td>
<td>Right lower lobectomy</td>
</tr>
<tr>
<td>3</td>
<td>16</td>
<td>Haemoptysis</td>
<td>Cyclophosphamide 2 gr</td>
<td>Left lower lobectomy</td>
</tr>
<tr>
<td>4</td>
<td>28</td>
<td>Haemoptysis</td>
<td>Cyclophosphamide 1 gr</td>
<td>Right lower lobectomy</td>
</tr>
<tr>
<td>5</td>
<td>28</td>
<td>Hydropneumothorax</td>
<td>Cyclophosphamide 6 gr</td>
<td>Left lower lobectomy</td>
</tr>
<tr>
<td>6</td>
<td>23</td>
<td>Hydropneumothorax</td>
<td>Cyclophosphamide 8 gr</td>
<td>Capitonnage</td>
</tr>
<tr>
<td>7</td>
<td>29</td>
<td>Empyema</td>
<td>Cyclophosphamide 12 gr, after than azathioprine</td>
<td>Decortication and wedge resection</td>
</tr>
<tr>
<td>8</td>
<td>32</td>
<td>Empyema</td>
<td>Cyclophosphamide 2 gr</td>
<td>Decortication</td>
</tr>
<tr>
<td>9</td>
<td>35</td>
<td>Haemoptysis</td>
<td>Cyclophosphamide 7 gr, after than azathioprine</td>
<td>Left lower lobectomy</td>
</tr>
</tbody>
</table>

Disclosure: H. Tuzun, None; G. Guzelant, None; O. Demirhan, None; B. Oz, None; I. Fresko, None; V. Hamuryudan, None; H. Yazici, None; E. Seyahi, None.


Abstract Number: 2730

Clinical Features and Treatment of Central Nervous System Vasculitis Associated with Acute Posterior Multifocal Placoid Pigment Epitheliopathy

Hiromichi Tamaki¹ and Rula A Hajj-Ali², ¹Department of Rheumatic and Immunologic Diseases, Cleveland Clinic Foundation, Cleveland, OH, ²Rheumatic and Immunologic Disease, Cleveland Clinic, Cleveland, OH

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Vasculitis Poster III: Other Vasculitis Syndromes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Acute posterior Multifocal Placoid Pigment Epitheliopathy (APMPPE) is a rare inflammatory eye disease and some appear to develop central nervous system vasculitis (CNSV). This entity is poorly described in the medical literature and little is known about treatment and prognostic factors.

Methods:

We present a case series of 23 patients with CNSV in association with APMPPE; 21 cases have been reported in the literature in addition to our experience with two cases. Patients were identified after a systematic literature search using Pubmed and Scopus for key words including APMPPE, stroke, neurological and CNSV. The cases were classified into definite (confirmed by pathology) or probable (inflammatory cerebrospinal fluid (CSF), imaging evidence of stroke/vasculopathy, and/or steroid response). The clinical features were described.

Results:

Total 23 articles and 24 articles were found in pubmed and scoupus respectively. Total 54 cases were described in these articles. Two cases met the criteria for definitive case and 19 cases met the criteria for probable case. Total 23 cases were analyzed after adding our two cases. The clinical features of these patients were summarized in table 1.

Thirteen patients treated only with glucocorticoids (GC) resulted in 2 deaths and 2 relapses. One of these two relapses was treated with cyclophosphamide (CYC) with improvement. One patient received GC and CYC with improvement, however, a relapse occurred after switching to azathioprine (Aza). The other 4 patients who received GC and Aza improved without relapse or death. Two patients were treated with GC and MMF without relapse or death. One patient was treated with GC and mitotoxin successfully. Two patients without any treatment resulted in one death. Two patients without any treatment resulted in one death. The prognostic factors were compared (Table 2).
The death and relapse free survival curve of the entire cohort was also drawn (Figure 1).

![Survival Curve](image)

**Conclusion:**

The treatment outcome varies widely among the patients. No clinical variables can predict relapse or death. The longer duration from an onset of eye symptoms to CNS disease may have a better prognosis, although this did not reach statistical significance. We successfully treated CNS vasculitis with MMF and MMF can be used to treat this severe complication of APMPPE.

**Disclosure:** H. Tamaki, None; R. A. Hajj-Ali, Abbvie, 8, Novartis Pharmaceutical Corporation, 5.


**Abstract Number:** 2731

**The Utility of Unbiased Metagenomic Next Generation Sequencing in the Management of Patients with CNS Vasculitis**

Hiromichi Tamaki¹, Michael R Wilson², Leonard H. Calabrese³, Joseph L. DeRisi⁴, and Rula A Hajj-Ali⁵, ¹Department of Rheumatic and Immunologic Diseases, Cleveland Clinic Foundation, Cleveland, OH, ²Department of Neurology, UCSF, San Francisco, CA, ³Rheumatic & Immunologic Disease, Cleveland Clinic Foundation, Cleveland, OH, ⁴Biochemistry and Biophysics, UCSF, San Francisco, CA, ⁵Rheumatology, Cleveland Clinic Foundation, Cleveland, OH
In the clinical approach to CNS vasculitis, exclusion of infection is of major concern as some microbes can cause vasculitis, and infections can complicate immunosuppressive therapy for CNS vasculitis. The yields of conventional microbiologic techniques to detect CNS infections from cerebrospinal fluid (CSF) are suboptimal, particularly for unusual organisms that may not be part of the differential diagnosis. Unbiased metagenomic next-generation sequencing (mNGS) is an emerging technique that offers an alternative, hypothesis-free approach for detecting CNS infections. Here we report on a pilot study to examine the utility of mNGS in the management of patients with CNS vasculitis.

Methods:

Patients were recruited from our CNS registry at Cleveland Clinic. Total RNA was extracted from 250 uL of CSF, and cDNA sequencing libraries were prepared using random hexamer primers. NGS was performed on an Illumina HiSeq 2500 machine, and the resulting 10-20 million paired-end 150 nucleotide sequences were analyzed by a rapid computational pipeline for identifying all known viruses, bacteria, fungi and parasites. The patients received a regular medical care otherwise. The results of mNGS were compared with regular medical care.

Results:

The main results are summarized in Table 1.

<table>
<thead>
<tr>
<th>ID</th>
<th>Clinical scenario</th>
<th>CSF WBC</th>
<th>CSF Protein</th>
<th>CSF Glucose</th>
<th>CSF Cultures</th>
<th>mNGS</th>
<th>Final Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A 37 year-old man with recurrent transient ischemic stroke, partial aphasia, and multiple intracranial arterial stenoses. A negative CSF analysis for infectious CNS vasculitis.</td>
<td>343 (83% lymph)</td>
<td>34</td>
<td>56</td>
<td>negative</td>
<td>Aspergillus</td>
<td>Aspergillus CNS infection</td>
</tr>
<tr>
<td>2</td>
<td>A 55 year-old man with relapsing polyneuritis and bowel pseudo-obstruction developed fever and headache 6 days after cyclophosphamide. A question of infection versus reactive CNS vasculitis.</td>
<td>29 (60% neutrophil)</td>
<td>34</td>
<td>47</td>
<td>negative</td>
<td>negative</td>
<td>A flare up of CNS vasculitis</td>
</tr>
<tr>
<td>3</td>
<td>A 57 year-old man with cognitive deficit and partial facial numbness presumptively diagnosed with CNS vasculitis was initially misdiagnosed as developing a new onset of systemic lupus erythematosus with MRI while on cyclophosphamide. A question of infection versus persistent SLE vasculitis.</td>
<td>3 (66% lymph)</td>
<td>54</td>
<td>70</td>
<td>negative</td>
<td>negative</td>
<td>A flare up of CNS vasculitis</td>
</tr>
<tr>
<td>4</td>
<td>A 60 year-old woman with cognitive decline, diffuse white matter lesions on MRI, and encephalopathy. A question of CNS vasculitis in Susac’s syndrome with retinal vasculopathy with cerebral leukoencephalopathy (RLCVL).</td>
<td>11 (93% lymph)</td>
<td>61</td>
<td>48</td>
<td>negative</td>
<td>negative</td>
<td>Atypical Susac’s syndrome</td>
</tr>
<tr>
<td>5</td>
<td>A 41 year-old woman with a history of diabetes and hypertension developed acute ischemic stroke and a 3 stage immunosuppressive regimen was started. A question of CNS vasculitis in the setting of known systemic autoimmune disease.</td>
<td>1 (88% lymph)</td>
<td>23</td>
<td>70</td>
<td>negative</td>
<td>negative</td>
<td>Atherosclerotic ischemic stroke</td>
</tr>
</tbody>
</table>

mNGS was useful in the following cases. Patient 1 was presumptively diagnosed with an autoimmune CNS disease based on a negative extensive infectious work-up. The CSF fungal cultures were negative 3 times, but research-based mNGS detected Aspergillus spp. This result was confirmed with a clinical 18s rRNA fungal PCR. Two patients (2, 3) with established CNS vasculitis clinically deteriorated while appropriately treated with glucocorticoids and cyclophosphamide. mNGS did not identify an infection. The patients were treated successfully with escalation of immunosuppression. Patient 4 did not have the typical triad for Susac’s syndrome, and as a result, a viral etiology was of great concern. To the degree that mNGS can be shown to have good sensitivity, the negative mNGS result in this case, would help exclude any lingering concerns about a potential infectious etiology.

Conclusion:
While these data are preliminary, mNGS may be useful to detect infectious pathogens that are novel or associated with a low yield with conventional diagnostic techniques in patients with CNS vasculitis. mNGS may be also useful to exclude opportunistic infections in patients with CNS vasculitis arising in those treated with aggressive immunosuppression therapy. This technique is worth exploring in the larger cohort of patients with CNS vasculitis and patient recruitment is ongoing.

Disclosure: H. Tamaki, None; M. R. Wilson, None; L. H. Calabrese, None; J. L. DeRisi, None; R. A. Hajj-Ali, Abbvie, 8,Novartis Pharmaceutical Corporation, 5.


Abstract Number: 2732

Recommendations for the Management of Neuro-Behcet’s Disease By the Japanese National Research Committee for Behcet’s Disease

Hirotoshi Kikuchi1, Tetsuji Sawada2, Masato Okada3, Mitsuhiro Takeno4, Masataka Kuwana4, Yoshiaki Ishigatsubo5, Izumi Kawachi6, Hideki Mochizuki7, Susumu Kusunoki8 and Shunsei Hirohata9, 1Department of Internal Medicine, Teikyo University School of Medicine, Tokyo, Japan, 2Rheumatology, Tokyo Medical University, Shinjuku Tokyo, Japan, 3Immuno-Rheumatology Center, St. Luke’s International Hospital, Tokyo, Japan, 4Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan, 5Department of Internal Medicine and Clinical Immunology, Yokohama City University Graduate School of Medicine, Yokohama, Japan, 6Department of Neurology, Niigata University Medical and Dental Hospital, Niigata, Japan, 7Department of Neurology, Osaka University Graduate School of Medicine, Osaka, Japan, 8Department of Neurology, Kinki University School of Medicine, Osaka, Japan, 9Rheumatology and Infectious Diseases, Kitasato University School of Medicine, Kanagawa, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Vasculitis Poster III: Other Vasculitis Syndromes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Central nervous system involvement is one of the most serious complications in Behçet’s disease (BD). This condition is referred to as neuro-Behçet’s disease (NB) and can be classified into acute type (ANB) and chronic progressive type (CPNB) based upon differences in the clinical course and responses to corticosteroid treatment. Diagnostic criteria were generated in 2013 based on a multicenter clinical survey performed by the Behçet’s Disease Research Committee of the Ministry of Health, Labor and Welfare of the Japanese Government. Although ‘Guidelines for Treatment of NB’ was also proposed based on the survey, it is still preliminary. The aim of the current study is to develop evidence-based recommendations for the management of NB supplemented by expert opinions where necessary.

Methods: First, clinical questions (CQs) on NB were extracted from a literature search for problem areas and related keywords, and draft CQs and a flow chart were prepared. The expert committee, a task force of the research subcommittee for NB, consisted of 7 board-certified rheumatologists (one was also a board-certified neurologist) and 3 board-certified neurologists. A systematic literature search was performed using Medline and the Japan Medical Abstract Society databases from 1997 to 2016. A total of 15 initial CQs were generated. These yielded the final recommendations developed from 3 blind Delphi rounds, in which the rate of agreement scores on CQs (range 1[strongly disagree]-5[strongly agree]) was determined though voting by the whole committee.
Results: Thirteen recommendations were developed for the management of NB (general 1, ANB 7, CPNB 5). The strength of each recommendation was established based on the evidence level as well as rate of agreement. There was excellent concordance between the level of agreement of rheumatologists and that of neurologists. Based on these recommendations, a flow chart was established for the management for ANB and CPNB (Figure).

Conclusion: The recommendations generated in this study are mainly based not only on expert opinions but on the results of uncontrolled evidence from open trials and retrospective cohort studies. Nevertheless, such guidelines that can be used for international studies would be needed, for which verification by further properly designed controlled clinical trials is required.

Disclosure: H. Kikuchi, Mitsubishi Tanabe Pharma, 2; T. Sawada, Mitsubishi Tanabe Pharma, 2; M. Okada, Mitsubishi Tanabe Pharma, 2; M. Takeno, Mitsubishi Tanabe Pharma, 2; M. Kuwana, Mitsubishi Tanabe Pharma, 2; Y. Ishigatsubo, Mitsubishi Tanabe Pharma, 2; I. Kawachi, None; H. Mochizuki, None; S. Kusunoki, None; S. Hirohata, Mitsubishi Tanabe Pharma, 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/recommendations-for-the-management-of-neuro-behcects-disease-by-the-japanese-national-research-committee-for-behcects-disease

Abstract Number: 2733

Clinical Characteristics and Treatment Outcomes of Patients with Behçet’s Disease and Vascular Involvement

In Young Kim1, Yeong Hee Eun2, Ji young Chai3, Hyungjin Kim1, Jaejoon Lee1, Eun-Mi Koh1, Duk-Kyung Kim4 and Hoon-Suk Cha1, 1Department of Medicine, Division of Rheumatology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, Republic of (South), 2Department of Medicine, Division of Rheumatology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, MN, Korea, Republic of (South), 3Department of Rheumatology, Bundang Jesaeng Hospital, Seongnam, Korea, Republic of (South), 4Department of Medicine, Division of Cardiology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, Republic of (South)

First publication: September 18, 2017
Background/Purpose: The international Chapel Hill Consensus Conference (CHCC) categorized Behçet’s disease (BD) as variable vessel vasculitis, which was defined as vasculitis that can affect vessels of any size and type. Vascular manifestations have been reported in up to 50% of patients with BD, most commonly as venous thrombosis. The aim of this study is to investigate characteristics and treatment outcomes of patients with vascular BD, particularly with large vessel involvement.

Methods: A retrospective review was performed on 2,496 patients with ICD-10 code of Behçet’s disease and/or aortic disease who visited Samsung Medical Center between 2004 and 2014. Patients who were suspected to have BD and vascular involvement were enrolled.

Results: Eighty-three patients with clinical features of BD and vascular involvement were identified. Although less than half satisfied the classic International Study Group (ISG) criteria, greater proportion fulfilled the International Criteria for BD (ICBD), and all of the patients satisfied at least “suspected BD” according to the Japanese criteria. Fifty patients had arterial lesions including 34 with aorta involvement. Another 33 patients had venous thrombosis without arterial lesions. Patients showed a male predominance (87%) and a predilection of young age with the median of 42 years old. The most prominent type of arterial lesions was aneurysm (80%) with a high frequency of pseudoaneurysms. Among the aorta, the thoracic aorta was most commonly involved and 18 patients had aortic valve regurgitation. Seventy-five (90%) patients received glucocorticoids with a median initial dose of prednisolone of 30 mg per day and 68 (82%) received immunosuppressive treatment. Half of the patients had more than one relapse after stabilization of the first vascular event. During the course, 44 patients underwent surgery and/or endovascular treatment and 60% of these patients had repeated treatment for the relapse. These included 31 aortic valve replacement on 13 patients.

Conclusion: Patients with vascular BD showed a predilection of young male and 60% of patients had arterial involvement. The aorta was affected in more than half of the patients who had arterial involvement. Aneurysmal change was frequent finding and relapse rate was high during disease course. Further studies into a practical and specialized diagnostic tool for vascular BD and optimal treatment strategies are required.

Disclosure: I. Y. Kim, None; Y. H. Eun, None; J. Y. Chai, None; H. Kim, None; J. Lee, None; E. M. Koh, None; D. K. Kim, None; H. S. Cha, None.


Abstract Number: 2734

A Comparison of Current Practice to New Vasculitis Treatment Guidelines

Ishrat Gill1, Norman Madsen2, Imran Hassan3 and Elaine Yacyshyn4, 1Medicine, University of Alberta, Sherwood Park, AB, Canada, 2Medicine, Rheumatology, University of Alberta, Edmonton, AB, Canada, 3EPICORE Centre, University of Alberta, Edmonton, AB, Canada, 4Medicine, University of Alberta, Edmonton, AB, Canada

First publication: September 18, 2017
Background/Purpose: Appropriate treatment for Anti-Neutrophilic Cytoplasm Antibodies (ANCA) Associated Vasculitis (AAV) requires induction and maintenance of remission, while balancing side effects from treatment. The CanVasc (Canadian Vasculitis Research Consortium) guidelines (2015) recommend use of corticosteroids and other immunosuppressive therapies for adequate treatment. However, clinical practices may vary significantly under different models of care. We analyzed the current clinical state of practice for treating ANCA related vasculitides within three different subspecialties, to compare differences in prescribing, in contrast to CanVasc guidelines.

Methods: This study was a retrospective cohort study; patient information was retrieved from databases of rheumatology, pulmonology and nephrology clinics under Alberta Health Services (AHS) in Edmonton. Diagnosis of patients with ANCA-associated systemic vasculitis was based according to the 2012 Chapel Hill Guidelines and use of corticosteroid therapy at diagnosis was the inclusion criteria. Data on demographics, corticosteroid dosage and time to taper, concurrent therapies, and management of recurrences was recorded. The medical subspecialty most responsible for steroid prescribing was also identified.

Results:

<table>
<thead>
<tr>
<th>Subspecialty</th>
<th>Nephrology</th>
<th>Pulmonology</th>
<th>Rheumatology</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td># Patients</td>
<td>59</td>
<td>9</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>% Males</td>
<td>46%</td>
<td>22%</td>
<td>50%</td>
<td>0.426</td>
</tr>
<tr>
<td>% Females</td>
<td>54%</td>
<td>78%</td>
<td>50%</td>
<td>0.426</td>
</tr>
<tr>
<td>% receiving pulse steroid on initial diagnosis</td>
<td>20.3%</td>
<td>11.1%</td>
<td>25%</td>
<td>0.778</td>
</tr>
<tr>
<td>% of patients experiencing flares (≥1)</td>
<td>20.3%</td>
<td>55.6%</td>
<td>45%</td>
<td>0.018</td>
</tr>
<tr>
<td>% of patients receiving pulse steroid during a flare</td>
<td>25%</td>
<td>0%</td>
<td>22.2%</td>
<td>0.0006</td>
</tr>
<tr>
<td># receiving any steroid therapy during flare</td>
<td>7</td>
<td>6</td>
<td>9</td>
<td>0.002</td>
</tr>
<tr>
<td>Time from start of therapy to taper (days)</td>
<td>32</td>
<td>50</td>
<td>39</td>
<td>0.411</td>
</tr>
</tbody>
</table>

Conclusion: Differences in clinical practice persist within subspecialties, when managing AAV patients. Our data highlights a shorter duration on initial dose of prednisone dose after diagnosis in Nephrology patients with taper within 1 month, compared to a longer duration of the initial prednisone dose in Pulmonology patients. CanVasc guidelines recommend glucocorticoids should be gradually tapered to a dose of 5-10 mg/day within 3-6 months of achieving remission. Our data shows that most patients remained on their initial prednisone dose for a much longer period than recommended, although this may be due to remission not being achieved. During recurrences/flares, adjustment to concurrent therapy was preferred over increasing corticosteroid dose instead. Our study highlights that subspecialties have a different approach to managing AAV patients than CanVasc recommendations. Ensuring that patients receive standard best practice for treatment should be a future goal in vasculitis patient management. Further studies are required to assess the effectiveness and knowledge translation of these practice modules, in support of CanVasc guidelines.
Is There an Association between Adult IgA Vasculitis and Cancer?

Jaka Ostrovrsnik¹, Ziga Rotar¹, Rok Jese¹, Matija Tomšič¹, ²and Alojzija Hočevar¹, ¹Department of Rheumatology, University Medical Centre Ljubljana, Ljubljana, Slovenia, ²University of Ljubljana, Faculty of Medicine, Ljubljana, Slovenia

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Vasculitis Poster III: Other Vasculitis Syndromes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: An increased incidence rate of cancer has been reported in adult patients with IgA vasculitis (IgAV). These conclusions are mostly based on observations in severely ill, hospitalized subgroup of patients. Most of the studies allowed for a wide time interval between IgAV and cancer appearance, not necessarily reflecting a causative link. The aim of our longitudinal prospective study was to look for the potential association between IgAV and cancer in an unselected adult IgAV population.

Methods: We analysed medical records of prospectively followed, histologically proven adult IgAV cases at our secondary/tertiary rheumatology centre form a well-defined referral region between 1 January 2010 and 31 May 2016, who were followed until 31 May 2017. Patients with at least 6-month follow up were included in the analysis. We identified cancer as concurrent with IgAV, if the patients had active cancer or a relapse of cancer or newly-diagnosed cancer diagnosed up to 6 months prior or 6 months after IgAV diagnosis. Cancers developing after 6 months of follow up were labelled as unrelated to IgAV. We used appropriate descriptive statistical methods, and the Fisher’s exact and Mann-Whitney U tests to assess differences of clinical characteristics in acute phase of IgAV, between the cancer and non-cancer groups. The national prevalence and age adjusted incidence rates of cancer from a well-defined referral region were obtained from National cancer registry (NCR).

Results: During the 77-month observation period we identified 171 new IgAV cases. 2 patients died in the acute disease phase due to vasculitis, and 7 during the first 6 months of follow-up for reasons other than IgAV or cancer. 18 patients were lost to follow-up. The remaining 144 patients (55% male, median (IQR) age 66 (44-77) years) were followed for a median (IQR) of 23 (13-34) months. At the time of IgAV diagnosis, 4/144 (2.8%) had active, previously-diagnosed malignant disease. In 2/144 patients (1.4%) a new cancer was diagnosed. One of the patients with an active cancer of urinary bladder, was treated with antibiotics for urinary tract infection prior to IgAV diagnosis, and was also on chemotherapy. The patients with cancer were older (median age (IQR) 82 (80-83) vs. 64 (44-76) years; p=0.003) but their presenting features of IgAV, and the initial IgAV treatment did not significantly differ from those without cancer. At the end of the observation period, the prevalence of cancer in our cohort was 4.2%. Compared to the 4.6% prevalence of cancer in our general population and the relative risk of cancer in our IgAV cohort was 0.91 (p=0.817; 95% CI 0.42-2.00). The age adjusted incidence rate of cancer was 13.9 per 1000 patient years. The annual age adjusted incidence rate of cancer in our citizens, acquired from NCR, was 31.2 per 1000 patient years and the standardised incidence ratio for our IgAV cohort was 0.89 (p=0.781; CI 0.11-3.21).

Conclusion: In our cohort of unselected adult IgAV cases, we did not confirm the previous observations of the association of IgAV and cancer.
Abstract Number: 2736

Long-Term Survival in Systemic Necrotizing Vasculitides

Sabine Jardel1, Xavier Puéchal2, Alain Le Quellec3, Matthieu Groh2, Mohamed Hamidou4, Francois Maurier5, Olivier Aumaître6, Achille Aouba7, Thomas Quémeneur8, Jean-François Subra9, Vincent Cottin10, Pascal Godmer11, Patrice Cacoub12, Philippe Delaval13, Anne-Laure Fauchais14, Eric Hachulla15, Delphine Maucourt-Boulch16, Loïc Guillemin2 and Jean-Christophe Lega17, 1Lyon 1 University, Lyon, France, 2National Referral Center for Rare Systemic Autoimmune Diseases, Hôpital Cochin, AP–HP, Université Paris Descartes, Paris, France, 3Montpellier, Montpellier, France, 4Internal Medicine Department, Internal Medicine Department, Nantes University Hospital, Nantes, France, 5Internal Medicine, Sainte-Blandine de Metz Hospital, Metz, France, 6CHU Pitié-Salpêtrière - Department of Internal Medicine 2. Referral center for SLE/APS, Paris, France, 7Department of Internal Medicine, Caen University Hospital, Caen, France, 8Service de néphrologie, médecine interne et vasculaire, Hôpital de Valenciennes, Valenciennes, France, 9Angers, Angers, France, 10Louis Pradel Hospital, Claude Bernard University Lyon 1, Lyon, France, 11Medecine Interne, CH Vannes, Vannes, France, 12Department of Internal Medicine and Clinical Immunology, Groupe Hospitalier Pitié-Salpêtrière, Paris, France, 13Rennes, Rennes, France, 14Internal Medicine, Internal Medicine, Limoges, France, 15CHU Lille, Département de Médecine Interne et Immunologie Clinique, F-59000 Lille, France, Lille, France, 16Biostatistics and bioinformatics, Centre Hospitalier Lyon Sud - Claude Bernard University Lyon 1, Lyon, France, 17Department of Internal and Vascular Medicine, Lyon Sud Hospital, Hospices Civils de Lyon, Lyon, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Vasculitis Poster III: Other Vasculitis Syndromes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
The aim of the study was to describe the evolution of mortality over recent decades in systemic necrotizing vasculitides, including polyarteritis nodosa (PAN), granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA).

Methods:
The date of diagnosis and the cause of death for patients with PAN, GPA, MPA, and EGPA were analyzed from the French Vasculitis Study Group database. Patients were divided into 5 groups: diagnosis before 1980, 1980-1989, 1990-1999, 2000-2010, and after 2010. The causes of death were classified as either vasculitis, infection, cardiovascular, malignancy, miscellaneous, or unknown.

Results:
Among the 2243 included patients (PAN 16%, GPA 42%, EGPA 23%, MPA 19%), 301 (13%) deaths were reported (Table 1). The 5-year overall survival rate increased from 72.2% (95% confidence interval [CI] 59.7-87.2) for patients diagnosed before 1980, to 94.5% (95% CI 90.4-98.8) after 2010 (p<0.001; Figure 1). The incidence of 5-year mortality between 1980-1989 and the last decade (>2010) decreased from 2.18 to 0.11 per 100 person-years for vasculitis-related
deaths (p=0.004), from 1.09 to 0.11 for cardiovascular-related deaths (p=0.03), and from 0.82 to 0.25 (p=0.03) for deaths caused by infection. No death by infection occurred in patients diagnosed after 2010. For deaths related to malignancy, the incidence of 5-year mortality was 0.41 per 100 person-years in 1980-1989, 0.17 in 2000-2009 (p=0.21), and 0.32 after 2010 (p=0.78).

**Conclusion:**

The results indicate that survival has dramatically improved since the 1980s due to the decrease of vasculitis flares and infections, but that cancer-related mortality remained stable. These results highlight the current targets to improve the overall prognosis.
Table 1 - Baseline characteristic of patients

<table>
<thead>
<tr>
<th></th>
<th>TOTAL (n = 2243)</th>
<th>&lt;1980 (n = 51)</th>
<th>1980-1989 (n = 196)</th>
<th>1990-1999 (n = 610)</th>
<th>2000-2009 (n = 986)</th>
<th>2010 (n = 400)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex, %</td>
<td>53.5</td>
<td>52.9</td>
<td>53.1</td>
<td>56.2</td>
<td>52.0</td>
<td>54.3</td>
<td>0.6</td>
</tr>
<tr>
<td>Mean age at diagnosis, years ± SD</td>
<td>52.6 ± 16.8</td>
<td>38.6 ± 16.2</td>
<td>48.4 ± 16.3</td>
<td>53.8 ± 16.6</td>
<td>55.6 ± 16.6</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Diagnosis, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PAN</td>
<td>358</td>
<td>28</td>
<td>84</td>
<td>118</td>
<td>93</td>
<td>35</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GPA</td>
<td>938</td>
<td>0</td>
<td>17</td>
<td>245</td>
<td>493</td>
<td>183</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>EGPA</td>
<td>511</td>
<td>15</td>
<td>64</td>
<td>125</td>
<td>212</td>
<td>95</td>
<td>0.004</td>
</tr>
<tr>
<td>MPA</td>
<td>436</td>
<td>8</td>
<td>31</td>
<td>122</td>
<td>188</td>
<td>87</td>
<td>0.48</td>
</tr>
<tr>
<td>Mean duration of follow-up, years ± SD</td>
<td>6.2 ± 5.8</td>
<td>9.6 ± 10.1</td>
<td>8.2 ± 5.6</td>
<td>5.6 ± 4.2</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total number of deaths at 5 years (%)</td>
<td>185</td>
<td>11</td>
<td>37</td>
<td>80</td>
<td>48</td>
<td>9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vasculitis (%)</td>
<td>60</td>
<td>3</td>
<td>16</td>
<td>29</td>
<td>11</td>
<td>1</td>
<td>0.18</td>
</tr>
<tr>
<td>Infection (%)</td>
<td>34</td>
<td>1</td>
<td>6</td>
<td>18</td>
<td>9</td>
<td>0</td>
<td>0.57</td>
</tr>
<tr>
<td>Cardiovascular (%)</td>
<td>34</td>
<td>1</td>
<td>8</td>
<td>13</td>
<td>11</td>
<td>1</td>
<td>0.79</td>
</tr>
<tr>
<td>Malignancy (%)</td>
<td>19</td>
<td>0</td>
<td>3</td>
<td>7</td>
<td>6</td>
<td>3</td>
<td>0.19</td>
</tr>
<tr>
<td>Miscellaneous (%)</td>
<td>19</td>
<td>0</td>
<td>3</td>
<td>8</td>
<td>6</td>
<td>2</td>
<td>0.54</td>
</tr>
<tr>
<td>Unknown (%)</td>
<td>19</td>
<td>6</td>
<td>1</td>
<td>5</td>
<td>5</td>
<td>2</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>


a Percentage calculated from the total number of patients.

b Percentage calculated from the total number of deaths at 5 years in the same decade.
Pulmonary Manifestations of Primary Systemic Vasculitides

Abstract Number: 2737
Jean-Paul Makhzoum1, Raashid Luqmani2, Richard A. Watts3, Anthea Craven4, Peter A. Merkel5 and Christian Pagnoux6, 1Rheumatology, Vasculitis Clinic, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada, 2Botnar Research Centre, University of Oxford, Oxford, United Kingdom, 3Rheumatology Department, The Ipswich Hospital, Ipswich, Great Britain, 4Nuffield Department of Orthopaedics Rheumatology and Musculoskeletal Sciences, Botnar Research Centre, Oxford University Hospitals, Oxford, United Kingdom, 5Division of Rheumatology, University of Pennsylvania; Perelman School of Medicine, Philadelphia, PA, 6Rheumatology-Vasculitis clinic, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Vasculitis Poster III: Other Vasculitis Syndromes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Pulmonary involvement in systemic primary vasculitides is diverse and occurs with variable incidence depending on the type of vasculitis. This study aimed to describe the spectrum and extent of lung manifestations in systemic vasculitides.

Methods: A large, cross-sectional study describing, comparing, and contrasting the lung manifestations of adults with Takayasu arteritis (TAK), giant cell arteritis (GCA), granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), eosinophilic granulomatosis with polyangiitis (EGPA), polyarteritis nodosa (PAN), and IgA vasculitis (IgAV, Henoch Schönlein) was performed using data from the Diagnostic and Classification Criteria in Vasculitis (DCVAS) study. The DCVAS study is an international, collaborative project that has collected comprehensive clinical data on a large cohort of patients with vasculitis to help in the development of new classification and diagnostic criteria. Data from the baseline and 6-month DCVAS visits were used for analysis.

Results: 1952 patients with primary vasculitides were included: 170 TAK, 657 GCA, 555 GPA, 223 MPA, 146 EGPA, 153 IgAV, and 48 PAN. The presence of respiratory symptoms was frequent in GPA (64.5%), MPA (65.9%), and EGPA (89.0%), but less so in TAK (21.8%), GCA (15.8%), PAN (27.1%) and IgAV (5.9%). Hemoptysis occurred mainly in patients with GPA (26.7%), MPA (23.3%), and EGPA (8.2%) and was rare in TAK (n=3), GCA (n=2), and PAN (n=2); no hemoptysis was reported in IgAV. Intubation for respiratory failure was infrequent and only seen in ANCA-associated vasculitis (AAV; 2.7% in GPA, 2.7% in MPA, 3.4% in EGPA).

Abnormal lung imaging was reported in GCA (19.7%), TAK (12.3%), GPA (59%), MPA (73%), EGPA (70%), PAN (36%), and IgAV (11%). Lung nodules were present in 25%, 11.7%, and 13.3% of patients with GPA, MPA, and EGPA, respectively. Lung imaging in PAN and IgAV revealed non-specific inflammation, consolidation, or pleural effusion. Pulmonary function tests (done in 32% of patients with AAV) revealed a restrictive pattern in GPA (16.6%), MPA (28.3%), and EGPA (4.6%), and an obstructive pattern in 70% of patients with EGPA. Bronchoscopy was done in 23% of patients with AAV, abnormal in 74% of them (mucosal changes, alveolar hemorrhage, hypersecretion). Lung biopsy, performed in 14% of patients with AAV, showed vasculitis in GPA (60.6%), EGPA (63.2%), but not in MPA (0/6).

At 6 months, lung damage items on the Vasculitis Damage Index (VDI) were present in patients with TAK (4.1%), GCA (3.3%), GPA (15.4%), MPA (28.7%), EGPA (52.7%), PAN (6.2%), and IgAV (1.3%). Only 3 patients with lung damage had died by the 6-month follow-up visit, all with MPA. Death was lung- and vasculitis-related in 1 patient only (alveolar hemorrhage). In GPA, lung damage at month 6 was associated with more frequent baseline gastrointestinal (30.6% vs. 16.7%) and neurological (49.4% vs. 30.3%) symptoms.

Conclusion: Pulmonary manifestations occur in many primary systemic vasculitides, including PAN and IgAV, but are more frequently severe and the source of permanent damage in AAV.

Disclosure: J. P. Makhzoum, Royal College of Physicians and Surgeons of Canada, 2, Association des spécialistes en médecine interne du Québec (ASMIQ), 2; R. Luqmani, None; R. A. Watts, None; A. Craven, None; P. A. Merkel, None;
Abstract Number: 2738

Infectious Complications in Systemic Necrotizing Vasculitides: Pooled Analysis of Five Prospective, Randomized, Controlled Trials

Lafarge Antoine¹, Christian Pagnoux², Xavier Puéchal³, Maxime Samson⁴, Mohamed Hamidou⁵, Alexandre Karras⁶, Thomas Quémeneur⁷, Matthieu Groh⁸, Luc Mouthon⁹, Loïc Guillemin for the French Vasculitis Study Group and Benjamin Terrier¹⁰, ¹Medecine Interne, Hôpital Cochin, Paris, France, ²Mount Sinai Hospital, Toronto, ON, Canada, ³Service de Médecine Interne, Centre de Référence Maladies Auto-Immunes et Auto-Inflammatoires Systémiques Rares, Hôpital Cochin, Paris, France, ⁴Department of Internal Medicine and Clinical Immunology, Hôpital François Mitterrand, CHU de Dijon, Dijon, France, ⁵Medecine Interne, CHU Hôtel Dieu, Nantes, France, ⁶Nephrology, HEGP, Paris, France, ⁷Service de néphrologie, médecine interne et vasculaire, Hôpital de Valenciennes, Valenciennes, France, ⁸National Referral Center for Rare Systemic Autoimmune Diseases, Hôpital Cochin, AP-HP, Université Paris Descartes, Paris, France, ⁹Université Paris Descartes Sorbonne Paris, Paris, France, ¹⁰Internal Medicine, Cochin University Hospital, Paris, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Vasculitis Poster III: Other Vasculitis Syndromes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Prognosis of patients with systemic necrotizing vasculitides has been markedly improved during the last 2 decades. However, infectious complications remain a major cause of morbidity and mortality. In majority of therapeutic studies on systemic vasculitides, number of patients is estimated to assess treatment efficacy and not tolerance. The aim of this study is to describe and analyse infectious complications in patients with systemic necrotizing vasculitides.

Methods:

Data from 5 prospective, randomized, controlled trials conducted by the French Vasculitis Study Group (FVSG) (CHUSPAN 1, CHUSPAN 2, WEGENT, CORTAGE, MAINRITSAN), were pooled and analysed. These studies evaluated therapeutic strategy for the treatment of polyarteritis nodosa (PAN), granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA). Primary endpoint of this study was the occurrence of a severe infection, defined by the need of a hospitalization, intravenous treatment or leading to death.

Results:

Seven hundred and thirty-three patients were included between 1993 and 2012, including 398 men (54.3%), with a median age of 60 years old (IQR 47-70). Vasculitis diagnoses were MPA in 231 (31.5%) patients, GPA in 226 (30.8%), GEPA in 186 (25.4%) and PAN in 85 (11.6%). Five Factor Score was greater than or equal to 1 in 289 patients (39.4%), and median Birmingham Vasculitis Activity Score at inclusion was 4.5 (0-14).
After a median follow-up of 5.2 years (IQR 3-9.7), 269 (36.7%) patients experienced 431 infections, among which 148 (20.2%) patients having 174 severe infections, including 84 (48.3%) bronchopulmonary infections, among which 2 aspergillosis and 2 nocardiosis, 28 (16.1%) gastrointestinal infections, 12 (6.9%) urinary infections, 11 (6.3%) septicemias, 11 (6.3%) cutaneous infections, 7 (4%) ENT infections, 6 zoster infections (3.4%), 2 Candida oesophagitis (1.1%), 2 endocarditis (1.1%) and 1 malignant anguiillulosis (0.6%).

Proportion of patients with severe infection remained stable over time. All patients developing at least one severe infection (n=148) received glucocorticoids, including pulses of methyprednisolone initially in 68 (45.9%) patients. Median glucocorticoid dose at the time of severe infection was 10 mg/day (IQR 5-25.8). Fifty-five percent of patients were also receiving immunosuppressive agents: including cyclophosphamide (16.9%), azathioprine (14.8%), rituximab (10.6%) or methotrexate (8.5%).

Median time from treatment initiation to first severe infection was 14.5 months (IQR 4.1-55.1). Finally, 22 severe infections directly led to death, representing 19.3% of all causes of death.

Statistical analysis of variables associated with severe infections is ongoing in order to identify high-risk patients.

Conclusion:

Severe infections are a frequent adverse in systemic necrotizing vasculitides, mostly occurring after 12 months, and with a substantial impact on morbidity and mortality. These findings highlight the need for better preventive measures in these immunocompromised patients. Statistical analysis will enable us to identify patients at risk of severe infections.

Disclosure: L. Antoine, None; C. Pagnoux, None; X. Puéchal, None; M. Samson, None; M. Hamidou, None; A. Karras, None; T. Quémeneur, None; M. Groh, None; L. Mouthon, None; L. Guillemin for the French Vasculitis Study Group, None; B. Terrier, None.


Abstract Number: 2739

Onco-Hematological Malignancies in Systemic Necrotizing Vasculitides: Pooled Analysis of Five Prospective, Randomized, Controlled Trials

Lafarge Antoine1, Christian Pagnoux2, Xavier Puéchal3, Maxime Samson4, Mohamed Hamidou5, Alexandre Karras6, Thomas Quémeneur7, Matthieu Groh8, Luc Mouthon9, Loïc Guillemin for the French Vasculitis Study Group3 and Benjamin Terrier10, 1Medecine Interne, Hôpital Cochin, Paris, France, 2Mount Sinai Hospital, Toronto, ON, Canada, 3Service de Médecine Interne, Centre de Référence Maladies Auto-Immunes et Auto-Inflammatoires Systémiques Rares, Hôpital Cochin, Paris, France, 4Department of Internal Medicine and Clinical Immunology, Hôpital François Mitterrand, CHU de Dijon, Dijon, France, 5Medecine Interne, CHU Hôtel Dieu, Nantes, France, 6nephrology, HEGP, Paris, France, 7Service de néphrologie, médecine interne et vasculaire, Hôpital de Valenciennes, Valenciennes, France, 8National Referral Center for Rare Systemic Autoimmune Diseases, Hôpital Cochin, AP–HP, Université Paris Descartes, Paris, France, 9Université Paris Descartes Sorbonne Paris, Paris, France, 10Internal Medicine, Cochin University Hospital, Paris, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Vasculitis Poster III: Other Vasculitis Syndromes
Session Type: ACR Poster Session C
Background/Purpose:

The use of long-term immunosuppressive agents in patients with systemic necrotizing vasculitides has dramatically improved the overall prognosis, but expose patients to potential severe adverse events. Also, pro-oncogenic effects of these drugs have been previously showed, but data on onco-hematological malignancies in this patient population are scarce. The aim of this study is to describe and analyse solid cancers and malignant hemopathies in patients with systemic necrotizing vasculitides.

Methods:

Data from 5 prospective, randomized, controlled trials conducted by the French Vasculitis Study Group (FVSG) (CHUSPAN 1, CHUSPAN 2, WEGENT, CORTAGE, MAINRITSAN), were pooled and analysed. These studies evaluated therapeutic strategy for the treatment of polyarteritis nodosa (PAN), granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA). Primary endpoint of this study was the occurrence of a solid cancer or a malignant hemopathy.

Results:

Seven hundred and thirty-three patients were included between 1993 and 2012, including 398 men (54.3%), with a median age of 60 years old (IQR 47-70). Vasculitis diagnoses were MPA in 231 (31.5%) patients, GPA in 226 (30.8%), GEPA in 186 (25.4%) and PAN in 85 (11.6%).

After a median follow-up of 5.2 years (IQR 3-9.7), 39 (5.3%) patients developed an onco-hematological complication, including solid cancer in 34 (4.6%) cases and malignant hemopathy in 5 (0.7%). Solid cancers included gastrointestinal cancers in 9 (26.5%), skin cancers in 8 (23.5%), pulmonary cancers in 6 (17.7%), urinary tract cancers in 5 (14.7%), gynecologic cancers in 4 (11.8%), and cerebral tumor and metastatic cancer of unknown origin in 1 (2.9%) case each. In one-third of patients, synchronous metastases were present at cancer diagnosis. Malignant hemopathies included myelodysplastic syndrome in 2 cases, and multiple myeloma, myeloproliferative syndrome and kidney lymphoma in 1 case each. Proportion of patients experiencing onco-hematological complications decreased over time: 7.7% for patients included between 1993-1999, 6.3% between 2000-2005 and 3% between 2006-2012. Immunosuppressive agents that patients received prior the occurrence of solid cancer or malignant hemopathy were cyclophosphamide in 26 (66.7%), azathioprine in 18 (46.2%), methotrexate in 10 (25.6%), and mycophénolate mofetil and rituximab in 3 (7.7%) cases each.

Median time from treatment initiation to onco-hematological malignancies was 4.1 years (IQR 1.4-7.9). Finally, 19/39 patients died because of their onco-hematological complications, representing 16.7% of all causes of death.

Conclusion:

Onco-hematological complications represent a rare complication in systemic necrotizing vasculitides with a decreasing frequency over the last decades. These complications occur lately after vasculitis diagnosis, stressing the importance of thinking about it in patients in remission. Although rare, onco-hematological complications account for almost 20% of causes of deaths. Statistical analysis will enable us to identify patients at risk of such complications.

Disclosure: L. Antoine, None; C. Pagnoux, None; X. Puéchal, None; M. Samson, None; M. Hamidou, None; A. Karras, None; T. Quémeneur, None; M. Groh, None; L. Mouthon, None; L. Guillevin for the French Vasculitis Study Group, None; B. Terrier, None.


Abstract Number: 2740
Cyclophosphamide Treatment Modulates Circulating Cell Populations in Patients with Vasculitis and Autoimmune Systemic Diseases

Martina Skácelová1, Gabriela Gabčová2, Pavel Horak3, Zuzana Mikulková2, František Mrázek4, Eva Kriegová5 and Andrea Smržová6, 1III. Department of Internal Medicine, Faculty of Medicine and Dentistry, Palacký University of Olomouc, Olomouc, Czech Republic, 2Department of Immunology, Faculty of Medicine and Dentistry, Palacky University Olomouc, Olomouc, Czech Republic, 3III. Department of internal medicine, III. Department of Internal Medicine, Faculty of Medicine and Dentistry, Palacký University of Olomouc, Olomouc, Czech Republic, 4Department of Immunology, Faculty of Medicine and Dentistry, Palacky University of Olomouc, Olomouc, Czech Republic, 5Department of Immunology, Department of Immunology, Faculty of Medicine and Dentistry, Palacky University of Olomouc, Olomouc, Czech Republic, 6III. Department of Internal Medicine, III. Department of Internal Medicine, Faculty of Medicine and Dentistry, Palacký University of Olomouc, Olomouc, Czech Republic

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Vasculitis Poster III: Other Vasculitis Syndromes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Although cyclophosphamide (CFA) remain the cornerstone for treatment of patients with severe manifestations of systemic autoimmune diseases, the knowledge about the effect of CFA on circulating cell populations in these diseases is limited.

Objectives: To investigate the effect of CFA administration on circulating immune cell subpopulations in patients with vasculitis and autoimmune systemic diseases.

Methods: We analysed major immune cell populations in peripheral blood (PB) from 13 patients (vasculitis n=7; autoimmune systemic diseases n=6). Paired samples from each patient were analysed before CFA administration, and after one and six months’ follow-up. Using 6-colour flow cytometer (BD FACSCanto II) we characterized T lymphocytes (CD3, CD4, CD8, CD25, CD127, HLA-DR), B lymphocytes (CD19, CD20, CD27, HLA-DR), NK cells (CD3, CD16, CD56, CD69), neutrophils (CD15, CD11b, CD16, CD54, CD62L, CD64), and monocytes (CD11b, CD14, CD16, CD64, HLA-DR). Statistics was done by software GraphPad Prism.

Results: After single dose of CFA, the percentage of CD69+ NK cells increased and CD4+/CD8+ ratio decreased compared with their percentage before administration (P=0.01; P=0.03, respectively). After six months of CFA administration, decreased percentage of activation marker HLA-DR on CD4+ cells (P=0.004), decreased percentage of CD19+ B cells (P=0.04) and increased percentage of activation marker CD69 on NK cells (P=0.004) was observed comparing with paired samples obtained before CFA therapy. Different patterns were observed in subgroups of patients with vasculitis and autoimmune systemic diseases. Clinical evaluation of treatment response and observed changes in immune cell populations in individual patients is ongoing.

Conclusion: In our patients, CFA therapy resulted in changes of activation markers on CD4+, CD8+, B and NK cells, as well as neutrophils. Further investigation of selected markers may lead to identification of new biomarkers for prediction of the treatment effectiveness.

Acknowledgement: MZ CR VES15-28659A, IGA_LF_2017_009

Disclosure: M. Skácelová, None; G. Gabčová, None; P. Horak, None; Z. Mikulková, None; F. Mrázek, None; E. Kriegová, None; A. Smržová, None.

Rheumatoid Factor (RF) Levels Remain Persistently Elevated 24 Weeks after Interferon (INF) Free Direct Antiviral Agents (DAA) Therapy in the Majority of RF+ HCV Infected Persons

Corinne Kowal, Carey Shive, Elizabeth Zebrowski, Lenche Kostadinova, Brianna Fuller, Elane Reyes, Kelsey Rife, Amy Hirsch, Anita Compan, Shyam Kottilil, Yngve Falck-Ytter, Leonard H. Calabrese, Donald Anthony, and Maya Mattar. 1Department of Medicine, Louis Stokes VA Medical Center, Cleveland, OH, 2Department of Medicine and Pathology, Case Western Reserve University, Cleveland, OH, 3VA Geriatric Research and Education Clinical Center (GRECC), Louis Stokes VA Medical Center, Cleveland, OH, 4Louis Stokes VA Medical Center, Cleveland, OH, 5Department of Medicine, Case Western Reserve University, Cleveland, OH, 6Case Western Reserve University, Cleveland, OH, 7IHV Clinical Research Unit, University of Maryland, Baltimore, MD, 8Internal Medicine/ Division of gastroenterology, Louis Stokes VA Medical Center, Cleveland, OH, 9Rheumatic & Immunologic Disease and Infectious Disease, Cleveland Clinic Foundation, Cleveland, OH, 10Division of Medicine and Pathology, Divisions of Infectious and Rheumatic diseases, University Hospitals Cleveland Medical Center, Cleveland, OH, 11VA Geriatric Research and Education Clinical Center (GRECC), Cleveland, OH, 12Internal Medicine/ Division of Rheumatology, University Hospitals Cleveland Medical Center, Cleveland, OH

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Vasculitis Poster III: Other Vasculitis Syndromes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Cryoglobulinemic vasculitis (CV) is an extrahepatic manifestation of chronic HCV infection. It varies in severity from mild to life threatening. Some but not all patients with HCV infection and CV harbor B cell clonal expansions that are somatically hypermutated and show features of an antigen-driven response, with IgM+CD27+ B cell subset overrepresentation of \( V_{H}1-69 \) and \( V_{\kappa}3-20 \) variable genes that encode RFs of the Wa cross-reactive idiotype, Rearrangement of the \( bcl-2 \) gene via a t (14:18) translocation has also been observed. To begin to determine mechanisms underlying B cell derangement during chronic HCV infection we assessed the variability of decline rate of rheumatoid factor (RF) levels in HCV infected patients treated with interferon free DAA therapy.

Methods:
130 Chronic HCV infected participants undergoing IFN free HCV therapy (Sofosbuvir/ledipivir for 8 weeks or Sofosbuvir/Ledipivir/Ribavirin for 12 weeks) were enrolled from the Cleveland VA . They had chronic HCV infection (>6 months seropositive and RNA positive) with absence of serum Hepatitis B surface antigen and HIV antibody, and they were treated with IFN free DAA HCV. Serum IgM RF and soluble CD14 (sCD14) were determined by ELISA.

After identifying 44 RF+ participants, we measured RF levels longitudinally in 44 RF+, 6 RF intermediate, and 3 RF-participants at weeks 0, 4, 8, 12 and 20-24 after initiating curative IFN free DAA HCV therapy, and clinical parameters correlating with RF decline were evaluated.

Results:
All participants achieved a sustained virologic response at week 12 after therapy cessation (SVR12), and all also achieved a SVR24. After DAA therapy initiation, all RF- and RF intermediate participants remained RF- and intermediate respectively. 100%, 73%, 80% and 69% of RF+ participants remained RF+ at weeks 0, 4, 8 and 20-24. 10% of these had no evidence of declining RF level, while RF decline rate appeared similar between those that remained RF positive and those that became RF negative at the completion of the study. Before therapy RF level was associated with albumin level after completion of therapy \((r=0.417, p=0.013)\), and albumin level after completion of therapy was also associated with RF decline magnitude \((r=0.504, p=0.002)\). Additionally, baseline sCD14 was correlated with week 4 RF level \((r=0.654, p=0.002)\), thus factors that induce Kupffer cell production of sCD14 may also participate in hepatic support for RF production.

**Conclusion:**

These data indicate wide variability in RF decline rate, and provide support for a model where factors other than HCV itself participate in determining RF level during chronic active HCV infection, as well as RF decline during IFN free DAA therapy. Further definition of factors contributing to persistence of RF may help guide therapeutic approaches for HCV associated cryoglobulinemic vasculitis.

**Disclosure:**

C. Kowal, None; C. Shive, None; E. Zebrowski, None; L. Kostadinova, None; B. Fuller, None; E. Reyes, None; K. Rife, None; A. Hirsch, None; A. Compan, None; S. Kottill, None; Y. Falck-Ytter, None; L. H. Calabrese, Celgene, Crescendo, 2, Celgene, Crescendo, 5, Celgene, Crescendo, 8; D. Anthony, None; M. Mattar, None.


**Abstract Number:** 2742

**A Retrospective Study Comparing the Phenotype and Outcomes of Patients with Polyarteritis Nodosa between UK and Turkish Cohorts**

Omer Karadag1,2, Abdulsamet Erden2, Yelda Bilginer2, Seerapani Gopaluni1, Alper Sari2, Berkan Armagan2, Ilhan Ertendi2, Seza Ozen2 and David Jayne3, 1Vasculitis and Lupus Clinic, Addenbrooke’s Hospital, University of Cambridge, Cambridge, United Kingdom, 2Hacettepe University Vasculitis Center (HUVAC), Ankara, Turkey, 3Vasculitis and Lupus Clinic, Department of Medicine, University of Cambridge, Cambridge, United Kingdom

First publication: September 18, 2017

**SESSON INFORMATION**

Session Date: Tuesday, November 7, 2017
Session Title: Vasculitis Poster III: Other Vasculitis Syndromes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

**Background/Purpose:** Polyarteritis Nodosa (PAN) is a rare subgroup of the primary vasculitides. There are only two published cohorts describing demographic and clinical features of the disease. Furthermore, various subgroups of PAN have been described, such as hepatitis B virus (HBV)-related, cutaneous and monogenic forms. There is a paucity of information on the current phenotypes and geographic differences of PAN. This study aimed to compare disease characteristics between PAN cohorts from the UK and Turkey (TR).

**Methods:** A retrospective survey of databases from two vasculitis centres between 1990-2016 for PAN patients fulfilling the EMEA Vasculitis Classification algorithm. All paediatric-onset adult patients met the Ankara 2008 (EULAR/PReS endorsed) criteria for childhood PAN. Patients with typical angiographic and/or histopathologic findings consistent with PAN were included. We evaluated demographics, organ involvement, treatment, patient survival and time to first relapse
**Results:** 93 (M/F: 51/42) patients (UK: 47, TR: 46) were included in the study. Median age at disease onset was 36.0 (20.0-49.8) years. Three were HBV-related, 20 (21.5%) had paediatric onset and 16 (16.5%) had cutaneous PAN. TR patients had younger age of disease onset (p=0.002). Twelve (26%) of TR patients had a monogenic form of disease (Familial Mediterranean Fever association in seven, deficiency of adenosine deaminase 2, DADA2, in five). Cutaneous PAN was more frequent in the UK (12 vs. four patients, p=0.031) whereas renal involvement was higher in the TR group (76.1% vs. 40.4%, p<0.001). Further analyses showed female predominance in cutaneous PAN when compared to systemic involvement (68.8% vs. 40.3% p=0.037). No difference was found in phenotype between paediatric and adult onset patients except frequency of cutaneous lesions (100% vs. 64.3%, p=0.002). In both cohorts, most patients received a combination of glucocorticoids and cyclophosphamide. During a median 67.5 (32-126) months follow up, 13 patients died (12.7% in the UK vs. 15.2% in TR cohorts). No difference was found between the two cohorts in relation to relapse rate, death and vasculitis damage index. Five factor score was significantly related to mortality (p=0.019).

**Conclusion:** This is the largest study defining diagnoses of PAN according to the EMEA algorithm. The TR group had a younger age of disease onset and more cases of monogenic disease; however disease extent, relapse rate, damage index and death rates were similar between groups.

**Table:** Comparison of Demographic, clinical characteristics and outcomes between the UK and Turkish Cohorts
<table>
<thead>
<tr>
<th></th>
<th>UK cohort (n:47)</th>
<th>Turkish cohort (n: 46)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age at onset, years</strong></td>
<td>44 (28.5-59.0)</td>
<td>24.5 (11.8-40.5)</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td>43.0 (18.0)</td>
<td>28.7 (17.8)</td>
<td></td>
</tr>
<tr>
<td><strong>Paediatric onset,</strong>%</td>
<td>17.0</td>
<td>26.0</td>
<td>0.287</td>
</tr>
<tr>
<td><strong>Sex, male,</strong> %</td>
<td>44.7%</td>
<td>65.2%</td>
<td>0.047</td>
</tr>
<tr>
<td><strong>Time to diagnosis, months</strong></td>
<td>2 (1-5)</td>
<td>3 (2-8)</td>
<td>0.041</td>
</tr>
<tr>
<td><strong>Constitutional symptoms,</strong> %</td>
<td>87.1</td>
<td>88.1</td>
<td>0.898</td>
</tr>
<tr>
<td><strong>Cutaneous Manifestations,</strong> %</td>
<td>68.1</td>
<td>75.6</td>
<td>0.426</td>
</tr>
<tr>
<td><strong>Musculoskeletal manifestations,</strong> %</td>
<td>76.7</td>
<td>82.6</td>
<td>0.278</td>
</tr>
<tr>
<td><strong>Neurologic manifestations,</strong> %</td>
<td>32.5</td>
<td>54.3</td>
<td>0.089</td>
</tr>
<tr>
<td><strong>Gastrointestinal manifestations,</strong> %</td>
<td>48.8</td>
<td>45.0</td>
<td>0.733</td>
</tr>
<tr>
<td><strong>Renal involvement,</strong> %</td>
<td>40.4</td>
<td>76.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Testicular pain/tenderness (men only),</strong> %</td>
<td>28.5</td>
<td>16.7</td>
<td>0.310</td>
</tr>
<tr>
<td><strong>DEI</strong></td>
<td>5.3 (2.5)</td>
<td>6.35 (2.3)</td>
<td>0.05</td>
</tr>
<tr>
<td><strong>Distribution of patients</strong></td>
<td></td>
<td></td>
<td>0.641</td>
</tr>
<tr>
<td>· FFS=0</td>
<td>51.0%</td>
<td>41.3%</td>
<td></td>
</tr>
<tr>
<td>· FFS=1</td>
<td>36.2%</td>
<td>43.5%</td>
<td></td>
</tr>
<tr>
<td>· FFS&gt;=2</td>
<td>12.8%</td>
<td>15.2%</td>
<td></td>
</tr>
<tr>
<td><strong>ESR, mm/hr</strong></td>
<td>29 (15.5-49)</td>
<td>57 (35.3-78.3)</td>
<td>0.035</td>
</tr>
<tr>
<td><strong>CRP, mg/L</strong></td>
<td>24 (9.8-117.3)</td>
<td>40.5 (18-40.5)</td>
<td>0.128</td>
</tr>
<tr>
<td><strong>WBC , /mm3</strong></td>
<td>11450 (7500-15525)</td>
<td>9875 (7800-12500)</td>
<td></td>
</tr>
<tr>
<td><strong>Haemoglobin, g/L</strong></td>
<td>12.6 (11.2-13.4)</td>
<td>11.9 (10.4-13.2)</td>
<td>0.238</td>
</tr>
<tr>
<td><strong>Serum Creatinine, Umol/l</strong></td>
<td>73 (60.5-98)</td>
<td>81.3 (64.0-88.4)</td>
<td>0.41</td>
</tr>
<tr>
<td><strong>Follow up, months</strong></td>
<td>79.0 (35.0-43.0)</td>
<td>65 (29.5-108)</td>
<td>0.669</td>
</tr>
<tr>
<td><strong>Response to treatment,</strong> %</td>
<td></td>
<td></td>
<td>0.838</td>
</tr>
<tr>
<td>· Complete</td>
<td>60.4</td>
<td>54.5</td>
<td></td>
</tr>
<tr>
<td>· Partial</td>
<td>30.2</td>
<td>31.8</td>
<td></td>
</tr>
<tr>
<td>· No response</td>
<td>9.4</td>
<td>13.7</td>
<td></td>
</tr>
<tr>
<td><strong>Any relapse,</strong>%</td>
<td>58.9</td>
<td>52.9</td>
<td>0.675</td>
</tr>
<tr>
<td><strong>Death,</strong> %</td>
<td>12.7</td>
<td>15.2</td>
<td>0.733</td>
</tr>
<tr>
<td><strong>VDI</strong></td>
<td>1 (0-1)</td>
<td>1 (0-2)</td>
<td>0.632</td>
</tr>
</tbody>
</table>

Values are labeled as mean (SD) or median (IQR 25%-75%). DEI: disease extent index; FFS: Five factor score, ESR: Erythrocyte
Objective is to study clinical features and treatment responses of PAN patients needing biologic therapy.

**Background/Purpose:** Recent studies highlight the usefulness and necessity of biologic agents in the treatment of primary vasculitides. Evidence for the use of biologics in PAN is limited. Objective is to study clinical features and treatment responses of PAN patients needing biologic therapy.

**Disclosure:** O. Karadag, None; A. Erden, None; Y. Bilginer, None; S. Gopaluni, None; A. Sari, None; B. Armagan, None; I. Ertenli, None; S. Ozen, None; D. Jayne, None.


**Abstract Number:** 2743

**Requirement and Response Rates of Biologic Agents in Polyarteritis Nodosa (PAN)**

**Omer Karadag**1,2, Berkan Armagan2, Abdulsamet Erden2, Seerapani Gopaluni1, Alper Sari2, Sedat Kiraz2 and David Jayne3, 1Vasculitis and Lupus Clinic, Addenbrooke’s Hospital, University of Cambridge, Cambridge, United Kingdom, 2Hacettepe University Vasculitis Center (HUVAC), Ankara, Turkey, 3Vasculitis and Lupus Clinic, Department of Medicine, University of Cambridge, Cambridge, United Kingdom

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Vasculitis Poster III: Other Vasculitis Syndromes

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM
Methods: A retrospective survey of databases from two vasculitis centres (Addenbrooke’s hospital in the UK & Hacettepe University, Turkey) between 1990-2016 for PAN patients fulfilling the EMEA Vasculitis Classification algorithm was done. Hepatitis B related PAN patients were excluded (n=3). Previous therapies including biologics were recorded. Response to therapy was determined according to the documentation by physicians.

Results: 90 (M/F: 48/42) patients (UK: 45, TR: 45) were included in the study. 16 patients had cutaneous PAN and 12 of the TR patients had a monogenic form of disease (Familial Mediterranean Fever: 7 patients, deficiency of adenosine deaminase 2, DADA2: 5 patients). During a median follow up of 79 (35.5-128) months, 28 patients (31.1%) (8 from TR, 20 from the UK, p = 0.004) were exposed to biologics. Seven of them had more than one biologic. Four of the 16 cutaneous PAN (25%) and 24 of the 74 systemic PAN (32.4%) patients received biologics (p=0.684). Except for one patient with cutaneous PAN, all patients had corticosteroids and cyclophosphamide before biologics. In patients with cutaneous PAN; RTX was used in two patients (one had good response), CAMPATH in two patients (one with no response), Infliximab (IFX) in one patient (with good response).

RTX and IFX were the most commonly used agents in systemic PAN patients. Complete or partial response was observed in more than half of the patients. Etanercept (ETN) was used in 5 patients; of the 4 patients with DADA2 three responded well, one had partial response and one patient did not respond. Adalimumab was used in two patients but was prematurely stopped in both cases due to serious infection. Interferon alpha was used in two patients and resulted in good response in both. TCZ was used in one patient without any benefit. Distribution of biologics used in patients with systemic PAN is shown in Table.

Response could not be evaluated in 6 patients; due to missing data of two patients, and short duration usage in 4 patients (withdrawal due to adverse effects: 3). Biologics were stopped in four of the patients; due to severe infections in three and anaphylactic reaction in one.

Conclusion: There is an unmet need to establish evidence for biologics in the treatment of PAN as 30 per cent of the patients in this study needed escalation in therapy to biologics. The experiences of RTX and IFX has been mixed with some very good responses and some not responses. Patients with DADA2 responded well to ETN. This probably reflects the fact that PAN is a more heterogeneous condition in terms of genetic background and clinical course.

Table. Distribution of biologics used in patients with systemic PAN

<table>
<thead>
<tr>
<th>Type of biologics and number of patients</th>
<th>Good response</th>
<th>Partial response</th>
<th>No response</th>
<th>Response not evaluated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rituximab (n=9)</td>
<td>4</td>
<td>0</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Infliximab (n=9)</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Etanercept (n=5)</td>
<td>3*</td>
<td>1*</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>CAMPATH (n=2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adalimumab (n=2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interferon Dalpha (n=2)</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tocilizumab (n=1)</td>
<td></td>
<td></td>
<td></td>
<td>1*</td>
</tr>
</tbody>
</table>

*: Patients with DADA2

Disclosure: O. Karadag, None; B. Armagan, None; A. Erden, None; S. Gopaluni, None; A. Sari, None; S. Kiraz, None; D. Jayne, None.

Long-Term Remission in Severe Behcet’s Disease Following Withdrawal of Successful Anti-TNF Treatment

Petros P Sfikakis¹, Aikaterini Arida¹, Stylianos Panopoulou², Kalliopi Fragkiadaki², George Pentazos³, Katerina Laskari³, Maria Tektonidou¹ and Nikos Markomichelakis², ¹First Department of Propaedeutic and Internal Medicine and Joint Rheumatology Program, National and Kapodistrian University of Athens Medical School, athens, Greece, ²First Department of Propaedeutic and Internal Medicine and Joint Rheumatology Program, National and Kapodistrian University of Athens Medical School, Athens, Greece, ³Rheumatology Unit, 1st Dept. of Propaedeutic Internal Medicine, Joined Academic Rheumatology Program, Athens University Medical School, Athens, Greece

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Vasculitis Poster III: Other Vasculitis Syndromes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Anti-TNF treatment has been shown to be effective in inducing complete remission in many Behcet’s disease (BD) patients with eye, large vessel, intestine and central nervous system involvement, but data on patients’ outcomes after their discontinuation are currently lacking. We examined whether remission of BD with severe vital organ involvement is maintained after withdrawal of successful anti-TNF treatment.

Methods:
In this retrospective longitudinal outcome study we examined the records of all patients with BD who have been followed up in our center at least once yearly since 2000. The final follow-up visit and review of flow-charts was conducted during the first trimester of 2017. Patients eligible for the study’s analysis were those who, a) achieved complete and sustained remission during long-term anti-TNF treatment given for refractory to conventional immnosuppressive therapy disease, b) discontinued anti-TNF treatment at some point, and, c) were followed-up at least 3 years after discontinuation. The study’s endpoint was the proportion of patients achieving complete remission of BD, sustained for at least 3 years after withdrawal of the anti-TNF agent.

Results: Of our BD cohort comprising 87 patients, 29 were eligible for analysis (median anti-TNF treatment of 2 years, IQR 1.1-2.0). Of them, 12 (41%) achieved the study’s end-point. The remaining patients relapsed within 1 year (median, IQR 0.6-1.5) after discontinuation. Re-treatment with anti-TNF was safe and effective in the long-term in 14/17 (82%); 4 of them have also achieved the study’s end-point, so far. Overall, 16/29 patients (55%) remain currently in complete remission lasting for a median of 6.5 years (IQR 5.5-8); 34% are any drug-free, all treated with anti-TNF mainly for sight-threatening disease, and 21% are on low-dose maintenance with azathioprine only, treated initially with anti-TNF for ocular (n=4), intestinal and central nervous system involvement. Notably, patients remaining in drug-free remission were younger (p<0.03) and had shorter (p<0.03) BD duration at anti-TNF treatment initiation than patients on azathioprine maintenance.

Conclusion:
Drug-free, long-term remission after withdrawal of successful anti-TNF treatment is feasible in patients with severe BD. Since an anti-TNF-induced ‘cure’ cannot be differentiated from a spontaneous remission by natural history, prospective studies should examine whether anti-TNF should be used first-line for remission induction in every patient with vital organ involvement.
Prevalence of Vasculitides As Extraintestinal Manifestation of Inflammatory Bowel Disease (IBD)

Sarah Ifteqar1, Jason Springer2 and Mehrdad Maz3, 1Department of Medicine, Division of Allergy, Clinical Immunology and Rheumatology, University of Kansas Medical Center, Kansas City, KS, 2Department of Internal Medicine, Division of Allergy, Clinical Immunology, & Rheumatology, Kansas University Medical Center, Kansas City, KS, 3Allergy, Clinical Immunology, and Rheumatology, Division of Allergy, Clinical Immunology and Rheumatology, Department of Internal Medicine, University of Kansas Medical Center, Kansas City, KS

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Vasculitis Poster III: Other Vasculitis Syndromes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: The extraintestinal manifestations of Inflammatory Bowel Disease (IBD) are identified in 6%-40% of patients. Systemic vasculitides may present as extraintestinal manifestations of IBD. The purpose of this study was to determine the frequency of vasculitides (large, medium or small vessel) in a cohort of patients with IBD.

Methods: This is a retrospective chart review of patients from 12/2006 to 12/2016 at a single tertiary medical center. A cohort of patients with diagnosis codes for inflammatory bowel disease including Crohn’s disease (CD), Ulcerative colitis (UC) and Microscopic colitis (MC) was identified. Patients with vasculitides including giant cell arteritis (GCA), Takayasu’s arteritis (TA), PAN, aortitis, ANCA associated vasculitis, GPA, MPA, EGPA, CNS vasculitis, cryoglobulinemic vasculitis, cutaneous vasculitis, Leukocytoclastic vasculitis (LCV), Pulmonary vasculitis, Rheumatoid vasculitis, small vessel vasculitis (SVV), and retinal vasculitis were identified. One sided student’s t-tests were used for statistical analysis.

Results: An EMR query yielded a total of 1686 patients, of whom 913 patients were diagnosed with CD, 695 with UC and 78 with MC. A search for a concomitant diagnosis code for vasculitis yielded 10 patients (10/1687=0.59%). Of the 10 patients, 6 had CD (60%), 3 had UC (30%) and 1 had MC (10%). Both genders had equal representation. The mean age at diagnosis of IBD was 29.4 years with males being diagnosed at a younger age; 26.8 vs 32 years (p=0.28). Vasculitis presented later, at a mean age of 42. The difference in the age at diagnosis of IBD and vasculitis was statistically significant overall (12.6 years; p=0.038). The most common extraintestinal manifestation of vasculitis was LCV (3, 30%) followed by SVV (2, 20%) and CNS vasculitis (2, 20%). Immunological evaluation did not reveal increased incidence of ANCA antibodies (table 1). Only 3 patients (30%) were ANCA positive, 5 were ANCA negative and data was missing for 2 patients. In this cohort of patients with IBD about 0.6% developed vasculitis with an estimated prevalence of extraintestinal manifestations of vasculitis of 590 per 100,000 which is higher compared to reported prevalence rates of vasculitides such as GPA and GCA which has which have a prevalence of 13.5 and 278 per 100,000 based on population studies in the UK and Minnesota, USA respectively.

Conclusion: In this cohort of patients with IBD, a small percentage of patients developed vasculitis. However, in the majority of cases vasculitis was diagnosed after the onset of IBD suggesting that vasculitis may be secondary to IBD or IBD-related treatments.
Comparison between IgG and IgM Type Anti-Alpha-Enolase Antibody in Patients with Behcet’s Disease According to the Disease Severity

Shin Eui Kang\textsuperscript{1}, Sang Jin Lee\textsuperscript{1,2}, Hyun Jung Yoo\textsuperscript{1,3}, Jeong Yeon Kim\textsuperscript{1}, Ji Soo Park\textsuperscript{1}, Sehui Shon\textsuperscript{4}, Eun Young Lee\textsuperscript{3}, Eun Bong Lee\textsuperscript{3} and Yeong Wook Song\textsuperscript{1,3,4}\textsuperscript{*}

\textsuperscript{1}Department of Molecular Medicine and Biopharmaceutical Sciences, Seoul National University School of Medicine, Seoul, Korea, Republic of (South); \textsuperscript{2}Division of Rheumatology, Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea, Republic of (South); \textsuperscript{3}Division of Rheumatology, Department of Internal Medicine, Kyungpook National University School of Medicine, Daegu, Korea, Republic of (South); \textsuperscript{4}Department of Molecular Medicine and Biopharmaceutical Sciences, Graduate School of Convergence Science and Technology, Seoul National University, Seoul, Korea, Republic of (South)

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Vasculitis Poster III: Other Vasculitis Syndromes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Behcet’s disease (BD) is a chronic inflammatory disease of unknown etiology, characterized by recurrent oral and genital ulcers, skin lesions, uveitis, and arthritis. It is regarded as vasculitis and anti-endothelial cell antibodies are found in BD. One of the endothelial cell antibodies was reported to recognize alpha-enolase and serum IgM anti-alpha-enolase antibody (AEA) was associated with involvement of the vascular system in BD in previous study. This study was aimed
to investigate expression of alpha-enolase in the surface of peripheral blood cells and serum IgM or IgG AEA, and their association with clinical manifestations or disease activity of BD.

**Methods:**

Cell surface alpha-enolase expression was examined from several cell types of peripheral blood, including lymphocytes, monocytes, and granulocytes using flow cytometry in patients with BD and healthy controls (HCs). Serum AEA levels were measured by enzyme-linked immunosorbent assay (ELISA) in 110 BD patients and age/sex matched 110 HCs. Association of alpha-enolase or AEA with clinical manifestation was analyzed.

**Results:**

The frequency of surface alpha-enolase-expressing cells was increased in BD in lymphocytes and monocytes. Serum IgG AEA levels were increased in BD patients (median [IQR], 0.360 [0.268-0.482], \( p < 0.0001 \)), particularly in active patients (BDCAF ≥ 2) (0.375 [0.274-0.537], \( p < 0.0001 \)) compared to HCs (0.274 [0.231-0.357]). The levels of IgG AEA were correlated with the number of oral ulcer, ESR, and CRP. There was no difference of IgM AEA in sera from BD compared to HCs (0.538 [0.351-0.763] vs. 0.504 [0.344-0.823], \( p = 0.764 \)) and no association of AEA levels and clinical manifestations in patients with BD.

**Conclusion:**

Serum IgG AEA was increased in BD patients and correlated with oral ulcer, ESR and CRP.

**Disclosure:** S. E. Kang, None; S. J. Lee, None; H. J. Yoo, None; J. Y. Kim, None; J. S. Park, None; S. Shon, None; E. Y. Lee, None; E. B. Lee, None; Y. W. Song, None.


**Abstract Number:** 2747

**Long Term Follow-up of Behcet’s Syndrome Patients Treated with Cyclophosphamide**

Mert Gurcan¹, Sinem Nihal Esatoglu¹, Vedat Hamuryudan¹, Caner Saygin², Didem Saygin³, Serdal Ugurlu⁴, Emire Seyahi¹, Melike Melikoglu¹, Izzet Fresko¹, Sebahattin Yurdakul¹, Hasan Yazici¹ and Gulen Hatemi¹, ¹Istanbul University, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey, ²Department of Hematology and Oncology, Taussig Cancer Institute, Cleveland Clinic, Cleveland, Cleveland, OH, ³Internal Medicine, Department of Internal Medicine, Cleveland Clinic, Cleveland, Cleveland, OH, ⁴Rheumatology, Istanbul University, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Vasculitis Poster III: Other Vasculitis Syndromes

**Session Type:** ACR Poster Session C

**Session Time:** 9:00AM-11:00AM

**Background/Purpose:** Cyclophosphamide (CYC) remains an important treatment option for Behçet’s syndrome (BS) pts with life threatening conditions such as arterial aneurysms. However, several adverse events are associated with CYC
treatment and this has led to increased use of biologic agents such as rituximab in other vasculitides. The aim of this study is to survey the outcome and short and long term adverse events with CYC use among BS pts.

**Methods:** We conducted a retrospective chart review of all BS patients treated with oral or intravenous CYC between 1972 and 2006. Patients were called and a standard form was used for collecting demographic characteristics, indication for CYC use, the reason for the cessation of therapy, cumulative dose of CYC, short and long term adverse events and outcome.

**Results:** We evaluated 99 pts who had an available contact information. After a median follow up of 18 (12-26) yrs after the initiation of CYC therapy, 27 pts had died within a median follow-up of 4 (0-10) yrs, 13 were lost after a median follow-up of 2.5 (0-11) yrs, and 59 were reached. CYC was prescribed for vascular involvement in 62 pts, eye involvement in 24, central nervous system involvement in 2, both vascular and eye involvement in 8 and both vascular and central nervous system involvement in 2. The median duration of CYC use and cumulative dose of CYC were 16 (6-63) gr and 12 (3-26) mo respectively. The reasons for death among the pts were shown in Table.

Twelve pts experienced serious adverse events associated with short term CYC use and 1 of them died due to infection. Among these adverse events, hemorrhagic cystitis occurred in 3 pts, infections in 5, ischemic stroke, acute myocardial infarction, anaphylactic reaction and grand mal epileptic seizure in 1 patient each. CYC treatment was terminated due to refractory disease in 30 pts and adverse events in 13. CYC induction was completed with beneficial results in the remaining 56 pts. During long term follow-up, malignancies and/or cardiovascular disease occurred in 27% of the pts. Overall, 9 malignancies were observed in 8 pts after a median follow up of 20 (12-25) yrs. The malignancies were t-MDS-AML, bladder carcinoma (n=2), lymphoma (n=2), HCC, colon adenocarcinoma, squamous cell carcinoma and prostate adenocarcinoma. Sixteen pts had cardiovascular disease and 3 had stroke.

**Conclusion:** CYC treatment was effective in about half of the pts. Serious adverse events including infections and malignancies occurred in 12% of the pts during CYC treatment and malignancies and cardiovascular events in 27% of the pts during long term follow-up. Other immunosuppressives used by these pts may also have contributed to these results and concomitant use of high dose corticosteroids may be responsible for the cardiovascular events. These results underline the need for safer and effective alternatives to CYC for serious organ involvement in BS, similar to that in other vasculitides.

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular involvement</td>
<td></td>
</tr>
<tr>
<td>Pulmonary artery aneurysm</td>
<td>7</td>
</tr>
<tr>
<td>Abdominal aorta aneurysm</td>
<td>2</td>
</tr>
<tr>
<td>Budd-Chiari syndrome</td>
<td>3</td>
</tr>
<tr>
<td>Malignancy</td>
<td>3</td>
</tr>
<tr>
<td>t-MDS/AML</td>
<td>1</td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
<td>1</td>
</tr>
<tr>
<td>SVCT due to high grade lymphoma</td>
<td>1</td>
</tr>
<tr>
<td>Infection</td>
<td>4</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>3</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>1</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>1</td>
</tr>
<tr>
<td>Traffic accident</td>
<td>1</td>
</tr>
<tr>
<td>Unknown</td>
<td>6</td>
</tr>
</tbody>
</table>

Table. The reasons for death in 27 of the surveyed 99 BS patients treated with cyclophosphamide

SVCT: superior vena cava thrombosis; t-MDS/AML: therapy related myelodysplastic syndrome-acute myeloid leukemia
Immunogenicity of Infliximab Among Patients with Behcet’s Syndrome: A Controlled Study

Sinem Nihal Esatoglu¹, Fatma Nihan Akkoc¹, Yesim Ozguler¹, Fatma Ozbakir², Okan Kadir Nohut², Dilsen Cevirgen³, Vedat Hamuryudan¹, Ibrahim Hatemi⁴, Aykut Ferhat Celik⁵, Hasan Yazici¹ and Gulen Hatemi¹, ¹Istanbul University, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey, ²Istanbul University, Cerrahpasa Medical Faculty, Central Research Laboratory, Istanbul, Turkey, ³Istanbul University, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of and Rheumatology, Istanbul, Turkey, ⁴Istanbul University, Cerrahpasa Medical School, Istanbul University, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Gastroenterology, Istanbul, Turkey, ⁵Istanbul University, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Gastroenterology, Istanbul, Turkey

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Vasculitis Poster III: Other Vasculitis Syndromes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:

Immunogenicity of anti-TNFs has been recognized as an important problem that may cause loss of response and adverse events such as infusion reactions. We aimed to investigate the prevalence of anti-drug antibodies against infliximab (IFX) in patients with Behçet’s syndrome (BS) together with controls.

Methods:

We collected serum samples from 66 consecutive BS patients (51 M, 15 F and mean age 37±9 years) who were receiving IFX. IFX was used for severe eye involvement in 43, vascular involvement in 12, nervous system involvement in 8 and arthritis in 2 patients. Additionally, 53 ankylosing spondylitis (AS), 25 Crohn’s disease (CD) and 27 rheumatoid arthritis (RA) patients, and 31 healthy subjects were included as controls. We included patients who had received at least 4 cycles of IFX. Samples were collected just before an infusion, stored at -80°C until analysis, and serum IFX trough levels and anti-IFX antibodies were measured by ELISA at the same time. We reviewed the charts of these patients regarding demographic and clinical characteristics, concomitant DMARDs, the number of IFX treatment cycles, responsiveness to IFX and allergic reactions. We used a cut-off value of 0.5 μg/mL for serum IFX trough level, extrapolating from RA studies. After serum sampling, we continued to follow up patients regarding allergic reactions and treatment efficacy.

Results:

Anti-IFX antibodies were detected in 4 (6%) BS, 5 (18.5%) RA, 3 (12%) CD, and 1 (2%) AS patient, and in none of the healthy subjects. The mean number of IFX cycles was 19±14 in BS, 21±13 in RA, 19±21 in CD, and 33±18 in AS patients. During follow up, 2/4 BS patients with anti-IFX antibodies had flares. Allergic reactions occurred in 9 (14%)
BS, 6 (22%) RA, 5 (20%) CD, and 4 (7.5%) AS patients. 3/5 RA patients and 3/3 CD patients who experienced an allergic reaction had anti-IFX antibodies whereas none of BS and AS patients did.

Concomitant DMARDs were used in 46 (74%) BS, 17 (67%) RA, 22 (84%) CD, and 7 (13%) AS patients. Overall, 6 (46%) patients with anti-IFX antibodies were not on DMARDs. The median serum IFX trough level was significantly lower in patients with anti-IFX antibodies compared to those without antibodies (0.17 (IQR: 0.08-0.28) vs 0.12 (IQR: 0.03-1.18; p=0.042). The serum IFX trough level was lower than the cut off value in all of the 13 patients with anti-IFX antibodies and in 89% of patients without anti-IFX antibodies (p=0.64).

We were able to get samples before at least 2 consecutive infusions in 27 BS patients and the presence of anti-IFX antibodies was consistent across the samples in all of these patients. We were able to get samples before the infusion and at week 2 in 5 BS patients. Serum IFX level was below 0.5 μg/mL before IFX and above 0.5 μg/mL at week 2 in all of these 5 patients.

Conclusion:

BS patients had a lower frequency of anti-IFX antibodies compared to RA and CD patients and similar to AS patients. This might be related to the similar comparative low B cell activity in these 2 conditions. Due to the small number of BS patients with anti-IFX antibodies, we could not conclude on the effect of immunogenicity on the treatment response. The low serum IFX levels even in patients without anti-IFX antibodies and good drug response deserves further attention.

Disclosure: S. N. Esatoglu, None; F. N. Akkoc, None; Y. Ozguler, None; F. Ozbakir, None; O. K. Nohut, None; D. Cevirgen, None; V. Hamuryudan, None; I. Hatemi, None; A. F. Celik, None; H. Yazici, None; G. Hatemi, None.

Abstract Number: 2749

Four-Distinct Phenotypes of Patients with Necrotizing Arteritis of Medium and Small Arteries

Tsuyoshi Shirai¹, Hiroshi Fujii¹, Yoko Fujita², Yuko Shiroti¹, Tomonori Ishii¹ and Hideo Harigae¹, ¹Department of Hematology and Rheumatology, Tohoku University Graduate School of Medicine, Sendai, Japan, ²Department of Hematology and Rheumatology, Tohoku University Graduate School of Medicine, Sendai, Japan

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Vasculitis Poster III: Other Vasculitis Syndromes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose: Polyarteritis nodosa (PAN) is a necrotizing arteritis of medium and small arteries. PAN is divided into systemic and cutaneous PAN (cPAN). cPAN can be further classified into mild cPAN or severe cPAN in which ulcer, necrosis, or neuritis is observed. However, it is sometimes difficult to set a boundary between severe cPAN and systemic PAN, and their optimal treatments are still unclear. The aim of this study is to evaluate clinical characteristics of patients with necrotizing arteritis of medium and small arteries.

Methods: 50 patients who were diagnosed as necrotizing arteritis of medium and small arteries without glomerulonephritis or vasculitis in arterioles, capillaries, or venules during 2008-2016 in our institution were enrolled to this study. Clinical backgrounds, symptoms, laboratory findings including inflammatory markers and antineutrophil
cytoplasmic antibodies (ANCA), affected organs, treatments, and the rates of relapse and death were retrospectively evaluated.

Results: Among 50 patients with necrotizing arteritis of medium and small arteries, 39 patients were classified as cPAN (mild, 18; ulcer or necrosis, 8; neuritis, 9; both, 4), and 11 cases manifested systemic vasculitis. One case of cPAN developed renal involvement. Clinical characteristics of mild cPAN included female predominance (94.4%) and younger age (median, 33), while severe cPAN and systemic type had no sex difference. The characteristics of systemic type included older age (median, 69), general symptoms, higher levels of inflammatory markers, lower levels of serum proteins, and organ damages. Severe cPAN manifested intermediate phenotypes. The positivity of autoantibodies in cPAN was about 30%, while 81.8% of systemic type possessed some autoantibodies. Particularly, 54.5% of systemic type possessed myeloperoxidase (MPO)-ANCA though the titers were significantly lower than those of microscopic polyangiitis, suggesting non-specific elevation of MPO-ANCA in Japanese population. The median doses of PSL for mild cPAN, severe cPAN, and systemic type were 20, 40, 40 mg/day, respectively. Immunosuppressants were used in 20% of mild cPAN, 90% of severe cPAN, and 73% of systemic type. Although the mortality rates were indistinguishable, the relapse rates of cPAN with ulcer or necrosis were significantly higher than other types (p=0.0032, figure 1).

Conclusion: 22% of patients with necrotizing arteritis of medium and small arteries presented systemic vasculitis. The clinical characteristics of mild cPAN, cPAN with ulcer or necrosis, cPAN with neuritis, and systemic vasculitis were distinct from each other, suggesting that they should be managed differently. Particularly, cPAN with ulcer or necrosis showed high relapse rates, indicating unmet need to establish adequate treatments such as rituximab.

Disclosure: T. Shirai, None; H. Fujii, None; Y. Fujita, None; Y. Shirota, None; T. Ishii, Chugai, Ono, Pfizer, Mitsubishi-Tanabe, Astellas, 8; H. Harigae, None.


Abstract Number: 2750

A Serum Metabolomic Analysis in Behcet’s Disease: A Preliminary Study

Wenjie Zheng1, Xiuhua Wu1,2, Maryam Goudarzi3, Hua Chen1, Jingjing Liu1, Jing Shi1, Chaoran Li1, Mengyu Zhou4, Wen Zhang1, Xuan Zhang1 and Henghong Li3, 1Rheumatology, Peking Union Medical College Hospital, Beijing, China, 2Rheumatology, General Hospital of Tianjin Medical University, Tianjing, China, 3Georgetown University Medical Center, Georgetown University, Washington, DC, WA, 4Peking Union Medical College Hospital, Beijing, China
First publication: September 18, 2017
Background/Purpose: The diagnosis of Behçet's disease (BD) is mainly based on clinical manifestations and remains a challenge in clinical practice, due to the fact that there are no diagnostic biomarkers available currently. Recently metabolomics has been applied in discovering and validating biomarkers of inflammatory diseases. This study aims to identify serum metabolites associated with BD and to search for the metabolites responsive to treatment using metabolomics approach.

Methods: Medical records and serum samples of 24 pre-treated BD patients (15 men and 9 women) and 12 post-treated patients were collected. Serums from 25 gender- and age-matched healthy volunteers were also collected. Metabolomics and lipidomics profiling were carried out by using UPLC-QTOFMS and UPLC-QTOFMS respectively. Raw mass spectrometric data were processed using Progenesis QI software. Statistical analysis and putative ion identification on the post-processed data were conducted utilizing MetaboLyzer.

Results: Unsupervised principal component analysis (PCA) plots of the lipidomics and metabolomics data showed clear separation of profiles from BD patients and healthy controls. Statistical analysis of the data revealed statistically differential metabolites between BD patients and healthy controls. Identification of selected metabolites was confirmed by comparing MS/MS fragmentation pattern with authentic standards. The serum levels of several phosphatidylcholines (PCs) were found significantly lower in BD patients compared to healthy controls. We also observed a marked increased levels of polyunsaturated fatty acids (PUFAs) including two omega-6 fatty acids, linoleic acid and arachidonic acid, and oleic acid, a n-9 PUFA in BD patients compared with those in the healthy control group. It is of interest to note that treatment recovered two omega-6 fatty acids (linoleic acid and arachidonic acid) but not the other differential metabolites.

Conclusion: Our study shows altered serum metabolomics profile in BD patients and suggests that levels of PCs, and PUFAs may be indicative in the diagnosis of BD. Two omega-6 fatty acids, linoleic acid and arachidonic acid, may provide insights for therapeutic effects.

Disclosure: W. Zheng, None; X. Wu, None; M. Goudarzi, None; H. Chen, None; J. Liu, None; J. Shi, None; C. Li, None; M. Zhou, None; W. Zhang, None; X. Zhang, None; H. Li, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/a-serum-metabolomic-analysis-in-behcets-disease-a-preliminary-study

Abstract Number: 2751

Tocilizumab in the Treatment of Severe and/or Refractory Behcet’s Disease: a Single-Centre Experience in China

Wenjie Zheng1, Yanxia Ding1,2, Di Wu1, Jiaxin Zhou1, JinJing Liu1, Dong Yan1, Mengyu Zhou3, Yan Zhao1 and Fengchun Zhang3, 1Rheumatology, Peking Union Medical College Hospital, Beijing, China, 2Rheumatology, The First Affiliated Hospital of Zhengzhou, Zhengzhou, China, 3Peking Union Medical College Hospital, Beijing, China

First publication: September 18, 2017
Session Type: ACR Poster Session C  
Session Time: 9:00AM-11:00AM

Background/Purpose:
To report the efficacy and safety of tocilizumab (TCZ) for the treatment of severe and/or refractory Behçet's disease (BD).

Methods:
We retrospectively analyzed the efficacy and safety profile of BD patients with severe and/or refractory BD treated with tocilizumab in our medical center between 2014 and 2017.

Results:
Ten BD patients (9 male and 1 female) were enrolled, with a mean age and median course of 34.6±8.6 year and 80 month (range 35 to 132), respectively. Vascular, cardiac and neurological involvements were presented in 7, 2 and 1 patients, respectively. Of the seven vascular BD patients, pseudoaneurysms were presented in five patients, including one patients with recurrent venous thrombosis and arterial pseudoaneurysms, one patient with internal leakage after the stent placement of abdominal aortic pseudoaneurysm, one patient with coronary sinus rupture and pseudoaneurysm formation, two patients with aortic pseudoaneurysm and multiple artery stenosis or occlusion. Two patients with severe aortic regurgitation developed post-operative paravalvular leakage (PVL) after valve surgery. One neuro-BD patient presented with brainstem, spinal cord and peripheral involvements.

Prior to TCZ therapy, all patients experienced disease progression and elevated serum inflammation markers despite of high-dose glucocorticoids in combination with multiple immunosuppressants. They were then treated with TCZ, 8mg/kg every 4 weeks, in combination with background low- or medium-dose glucocorticoids and immunosuppressants, for a median of 6 (range 3-15) months.

After a median follow-up of 10 month (range 3 to 22), all patients achieved improvement both in clinical symptoms and serum inflammation markers (ESR and hsCRP). Vascular lesions were stable and no recurrent aneurysm was observed. No PVL were observed in both patients with valvular involvement after repeated surgery at 6 and 8 months, respectively. The neuro-BD patient achieved both clinical and imaging improvement. The corticosteroid dose was tapering in most cases, indicating a potential steroid-sparing effect. TCZ was well-tolerated and no serious adverse event was observed.

Conclusion:
Our data suggest that TCZ is safe and effective for the treatment of patients with severe and/or refractory BD. Further controlled studies are warranted to confirm the therapeutic potential of TCZ in BD patients.

Disclosure: W. Zheng, None; Y. Ding, None; D. Wu, None; J. Zhou, None; J. Liu, None; D. Yan, None; M. Zhou, None; Y. Zhao, None; F. Zhang, Xian Janssen, 8.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/tocilizumab-in-the-treatment-of-severe-and-or-refractory-behcets-disease%ef%bc%9a-single-centre-experience-in-china](http://acrabstracts.org/abstract/tocilizumab-in-the-treatment-of-severe-and-or-refractory-behcets-disease%ef%bc%9a-single-centre-experience-in-china)
Risk of Hospitalizations for Venous Thromboembolism Among Patients with Selected Systemic Vasculitides: A Nationwide Analysis

Yiming Luo¹, Jiehui Xu², Yumeng Wen¹, Alvaro Ramos-Rodriguez¹, Changchuan Jiang¹, Shuyang Fang¹, Mustafa Kagalwalla¹ and Neha Ohri³, ¹Department of Medicine, Mount Sinai St Luke's and Mount Sinai West Hospitals, Icahn School of Medicine at Mount Sinai, New York, NY, ²Department of Biostatistics, Mailman School of Public Health, Columbia University Medical Center, New York, NY, ³Division of Rheumatology, Department of Medicine, Mount Sinai St Luke's and Mount Sinai West Hospitals, Icahn School of Medicine at Mount Sinai, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Vasculitis Poster III: Other Vasculitis Syndromes
Session Type: ACR Poster Session C
Session Time: 9:00AM-11:00AM

Background/Purpose:
Venous thromboembolism (VTE) contributes significantly to in-hospital morbidity and mortality. Previous studies have suggested that certain vasculitides, including granulomatosis with polyangiitis (GPA) and giant cell arteritis (GCA) are associated with increased risk of VTE. However, there is mixed evidence in the literature about the risk of VTE in patients with polyarteritis nodosa (PAN) and Takayasu’s arteritis (TA). Some of these studies were limited by not adjusting for common cofounders, in this case VTE risk factors. We sought to explore the association of VTE as primary reason for hospitalization in patients with GPA, GCA, PAN and TA using a national inpatient database.

Methods:
We conducted a retrospective cross-sectional study using the National Inpatient Sample (NIS) database for the year 2014. Diagnoses were identified using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes. Patients with a principal admission diagnosis of VTE and a secondary diagnosis of GPA, GCA, PAN and TA were included in the study. There were no exclusion criteria. Univariate and multivariate logistic regression models were used to adjust for potential confounders.

In this study, we adjusted for age, gender, race, length of stay and selected common risk factors for VTE such as active smoking, cancer, heart failure, stroke, sepsis, thrombophilia, obesity, nephrotic syndrome, inflammatory bowel disease, pregnancy, postpartum and long bone fracture.

Results:
A total of 287,790 hospitalizations with a principal diagnosis of VTE were identified. Among this cohort, the number of hospitalizations with a secondary diagnosis of GPA, GCA, PAN and TA were 11,285, 16,480, 4,450 and 1,350, respectively. The unadjusted OR for a principal diagnosis of VTE and a secondary diagnosis of any of these four vasculitides reached statistical significance for GPA (OR 2.76, 95% CI 2.10 - 3.64, p < 0.001), GCA (OR 2.45, 95% CI 1.91 - 3.13, P < 0.001), PAN (OR 1.81, 95% CI 1.04 - 3.13, p = 0.035). There was no difference for TA (OR 2.30, 95% CI 0.95 - 5.56, p = 0.065). When adjusting for confounding variables, there was statistical significance for GPA (OR 2.54, 95% CI 1.90 - 3.40, p < 0.001), GCA (OR 1.53, 95% CI 1.18 - 1.98, p = 0.001) and TA (OR 2.46, 95% CI 1.01 - 5.97, p = 0.047), though not for PAN (OR 1.47, 95% CI 0.83 - 2.60, p = 0.183).

Conclusion:
Our study suggests that GPA and GCA are independently associated with increased risk of hospitalizations for VTE, which is consistent with previously published studies in the literature. We found that PAN is associated with increased risk of VTE hospitalizations but is not considered an independent risk factor, which confers a possible explanation for the conflicting results in previous investigations. TA was associated with an increased risk of VTE after adjusting for confounders. Further studies are needed to clarify these relationships further.

Disclosure: Y. Luo, None; J. Xu, None; Y. Wen, None; A. Ramos-Rodriguez, None; C. Jiang, None; S. Fang, None; M. Kagalwalla, None; N. Ohri, None.

Brain Functional Connectivity Features of Pain Centralisation Relate to Degree of ‘Fibromyalgianess’ in Rheumatoid Arthritis

Neil Basu1, Chelsea Cummiford2, Eric Ichesco2, Tony Larkin2, Richard E. Harris2, Alison Murray3, Gordon Waiter4 and Daniel J. Clauw5
1Institute of Applied Health Sciences, University of Aberdeen, Aberdeen, United Kingdom, 2Chronic Pain and Fatigue Research Center, University of Michigan, Ann Arbor, MI, 3Aberdeen Brain Imaging Center, University of Aberdeen, Aberdeen, United Kingdom, 4Aberdeen Brain Imaging Centre, University of Aberdeen, Aberdeen, United Kingdom, 5Anesthesiology, University of Michigan, Ann Arbor, MI

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Plenary Session III
Session Type: ACR Plenary Session
Session Time: 11:00AM-12:30PM

Background/Purpose:
Many rheumatoid arthritis (RA) patients continue to report pain despite excellent control of inflammation with immunotherapy regimes. Variable degrees of co-existing fibromyalgia (FM) may explain this disparity.

Patients diagnosed with FM are characterised by features of pain centralisation. For example they exhibit aberrant inter-regional brain communications, as measured by functional connectivity MRI (fcMRI). We and others have suggested that part of the neural signature for pain centralisation is enhanced connectivity between the insula (a region implicated in the affective processing of pain) and the Default Mode Network (DMN, a network related to self-referential thinking).

We hypothesised that RA patients reporting the highest 2011 ACR FM survey criteria scores - a continuous measure of FM degree also known as fibromyalgianess (FMness) – would demonstrate fcMRI features of pain centralisation as observed in FM.

Methods:
Consecutive clinic attending RA patients fulfilling ACR/EULAR 2012 criteria were recruited and underwent a 9min fcMRI brain scan. In addition, they undertook a clinical evaluation which included a measure of FMness (ACR FM survey criteria) and inflammation (CRP). Images were acquired by a 3 Tesla, 8 channel phased array head coil using a T2*-weighted gradient-echo echo-planar imaging pulse sequence. FcMRI data were preprocessed and analyzed using SPM8, Conn and GIFT running on MATLAB 7.10. Group independent component analysis selected out the brain networks of interest (DMN, salience, dorsal attention, sensorimotor). Network to whole brain functional connectivity analyses were then conducted for each patient followed by group level multiple linear regression which correlated connectivity of each network to FMness. Finally, corrections for age, sex and CRP were applied. Analyses were significant on the cluster level with a false discovery rate p value <0.05 derived from an uncorrected voxel level p value <0.001.

Results:
54 patients participated (mean age 54.9years; 75.9% female; mean disease duration 11.5 years; mean FMness score 13.3 [range 1-29]; mean DAS28 3.6 [range 1.5-6.4]). They demonstrated a significant (p=0.002) positive correlation between DMN connectivity to the left mid/posterior insula and FMness (r=0.55). This observation remained significant after adjusting for age, sex and CRP. No other significant functional connections were identified with the DMN or among the other selected networks.

Conclusion:
Rheumatoid arthritis patients who report high levels of FMness appear to share neurobiological features with ‘primary’ FM patients. This study is the first to provide neuroimaging evidence that RA is a mixed pain state with a centralised pain component (which demands alternative therapeutic strategies to standard RA immunotherapies). The ACR FM survey appears to be a strong surrogate for neurobiological evidence of centralised pain and, in the future, could be a useful tool to support clinicians’ evaluation of pain and subsequent personalised management.

Disclosure: N. Basu, None; C. Cummiford, None; E. Ichesco, None; T. Larkin, None; R. E. Harris, None; A. Murray, None; G. Waiter, None; D. J. Clauw, Abbott Pharmaceutical, 5,Aptinyx, 5,Astellas Phamaceutical, 5,Cerephex, 5,Daiichi Sankyo, 5,Pfizer Inc, 5,Pierre Fabre, 8,Samumed, 5,Theravance, 5,Tonix, 5.
Comparison of Individually Tailored Vs Systematic Rituximab Regimens to Maintain ANCA-Associated Vasculitis Remissions: Results of a Prospective, Randomized-Controlled, Phase 3 Trial

Pierre Charles1, Benjamin Terrier2, Elodie Perrodeau3, Pascal Cohen2, Stanislas Faguer4, Antoine Huart5, Mohamed Hamidou6, Christian Agard7, Bernard Bonnotte8, Maxime Samson8, Alexandre Karras9, Noémie Jourde-Chiche10, François Lifermann11, Pierre Gobert12, Catherine Hanrotel-Saliou13, Pascal Godmer14, Nicolas Martin Silva15, Grégory Pugnet16, Marie Matignon17, Olivier Aumaître18, Estibaliz Lazaro19, Xavier Puéchal20, Philippe Ravaud21, Luc Mouthon22 and Loïc Guillemin20, 1Service de Médecine Interne, Hôpital Cochin, Paris, France, 2Service de Médecine Interne, Hôpital Cochin, Centre de référence national pour les maladies systémiques autoimmunes rares d’Ile de France, DGHU Authors, Assistance Publique-Hôpitaux de Paris (AP-HP), Paris, France, Paris, France, 3Epidemiology, Hôpital Hotel Dieu, Paris Descartes University, Paris, France, 4Service de Néphrologie et Immunologie Clinique, Centre Hospitalier Universitaire (CHU) de Toulouse, Toulouse, France, 5CHU, Toulouse, France, 6Internal Medicine Department, Internal Medicine Department, Nantes University Hospital, Nantes, France, 7Internal Medicine Department, Nantes University Hospital, Nantes, France, 8Department of Internal Medicine and Clinical Immunology, Hôpital Francois Mitterrand, CHU de Dijon, Dijon, France, 9Nephrology, HEGP, Paris, France, 10Vascular Research Center of Marseille, Aix-Marseille Univ., Vascular Research Center of Marseille, Marseille, France, 11Dax, Dax, France, 12Nephrology, Centre Hospitalier d’Avignon, Avignon, France, 13Brest, Brest, France, 14Medecine Interne, CH Vannes, Vannes, France, 15Department of Internal Medicine, Caen University Hospital, Caen, France, 16Department of Internal Medicine, Toulouse University Hospital, University of Toulouse, INSERM UMR 1027, Toulouse, France, 17Service de Néphrologie, Hôpital Henri-Mondor, Créteil, Créteil, France, 18CHU Pitié-Salpêtrière - Department of Internal Medicine 2. Referral center for SLE/APS, Paris, France, 19service de médecine interne et maladies infectieuses, CHU de Bordeaux, Pessac, France, 20National Referral Center for Rare Systemic Autoimmune Diseases, Hôpital Cochin, AP–HP, Université Paris Descartes, Paris, France, 21Hôpital Hôtel Dieu, Paris, France, 22Service de Médecine Interne, Hôpital Cochin, Centre de référence national pour les maladies systémiques autoimmunes rares d’Ile de France, DGHU Authors, Assistance Publique-Hôpitaux de Paris (AP-HP), Paris, France ;Université Paris Descartes Sorbonne Paris, Paris, France

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Plenary Session III
Session Type: ACR Plenary Session
Session Time: 11:00AM-12:30PM

Background/Purpose:

Once ANCA-associated vasculitis (AAV) remission was obtained, rituximab (RTX) superiority to azathioprine (AZA) to maintain remission was shown.1 In that study, at month 28, only 5% of RTX recipients vs 29% taking AZA suffered major relapses. However, at present, neither ANCA-positivity and/or titers (status) nor peripheral blood CD19 B-cell–detection are considered reliable AAV-relapse predictors. The MAINRITSAN2 trial (ClinicalTrials.gov, no. NCT01731561) was designed to evaluate RTX infusions individually tailored to ANCA status and/or circulating CD19 B-cell reappearance to maintain AAV remission.

Methods:

Patients with granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) in complete remission after induction therapy (glucocorticoids and cyclophosphamide, rituximab or methotrexate) were included in an open-label, multicenter, randomized–controlled trial to compare RTX regimens: given according to ANCA status and/or circulating CD19 B-cell reconstitution vs systematically infused (controls). The experimental arm received fixed, 500-mg RTX infusions on day-0 postrandomization, then every 3 months until month 18, when CD19 lymphocytes exceeded 0/mm3 or ANCA status (reappearance)/titer (higher) differed from the previous determination. Controls received 500 mg of RTX on days 0 and 14 postrandomization, then 6, 12 and 18 months after the first infusion. The primary endpoint was the number of relapses (new or reappearing symptom or worsening disease with BVAS>0) at month 28, as assessed by an independent Adjudication Committee blinded to treatment arms.
Results: The 162 patients included [117 (72.2%) GPA and 45 (27.8%) MPA] were equally allocated to the experimental (n=81; 50%) and control (n=81; 50%) groups. Prerandomization induction therapy was cyclophosphamide for 100 (61.7%) patients, RTX for 61 (37.7%) or methotrexate for 1 (0.6%). Median RTX-infusion numbers were: 3 (interquartile range (IQR) 2–4) for the experimental arm and 5 (IQR 5–5) for controls. Twenty-one (13%) patients suffered 22 relapses: 14 (17.3%) in 13 experimental arm patients and 8 (9.9%) in 8 controls (P=0.22). The relapse-free-survival rate was 83.8% (95% confidence interval [CI], 76.1–92.3%) for the experimental arm and 86.4% (95% CI, 79.2–94.2) for controls (P=0.58). Twenty-six (32.1%) experimental arm patients experienced at least 1 severe adverse event vs 31 (38.3%) controls (P=0.51). Four patients died, 1 of an infectious complication. No association between ANCA status and/or circulating CD19 B cells and relapses was observed.

Conclusion: AAV-relapse rates for patients given individually tailored or systematic RTX-infusion schedules did not differ significantly. However, ANCA and circulating CD19 B cells could be considered useful tools to decide to reinfuse because they achieved lower RTX total doses (i.e., 3 vs 5 infusions) to prevent relapses in the experimental arm.


Disclosure: P. Charles, None; B. Terrier, None; E. Perrodeau, None; P. Cohen, None; S. Faguer, None; A. Huart, None; M. Hamidou, None; C. Agard, None; B. Bonnotte, None; M. Samson, None; A. Karras, None; N. Jourde-Chiche, None; F. Lifermann, None; P. Godmer, None; C. Hanrotel-Saliou, None; N. Martin Silva, None; G. Pugnet, None; M. Matignon, None; O. Aumaître, None; E. Lazaro, None; X. Puéchal, None; P. Ravaud, None; L. Mouton, None; L. Guillevin, Hoffmann-La Roche, Inc., 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/comparison-of-individually-tailored-vs-systematic-rituximab-regimens-to-maintain-anca-associated-vasculitis-remissions-results-of-a-prospective-randomized-controlled-phase-3-trial

Abstract Number: 2755

Comparative Risk of Biologic Therapies in Patients with Rheumatoid Arthritis Undergoing Elective Arthroplasty

Michael D. George1, Joshua Baker2, Kevin Winthrop3, E Alemay4, Lang Chen5, SE Connolly4, TA Simon4, Qufei Wu6, Fenglong Xie7, Shuo Yang7 and Jeffrey R. Curtis8, 1Division of Rheumatology, University of Pennsylvania, Philadelphia, PA, 2Rheumatology, University of Pennsylvania, Philadelphia, PA, 3Oregon Health Sciences University, Portland, OR, 4Bristol-Myers Squibb, Princeton, NJ, 5University of Alabama at Birmingham, Birmingham, AL, 6Biostatistics and Analysis Center, University of Pennsylvania, Philadelphia, PA, 7Division of Clinical Immunology & Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 8Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Plenary Session III
Session Type: ACR Plenary Session
Session Time: 11:00AM-12:30PM

Background/Purpose: Biologic DMARDs have varying mechanisms of action and may be associated with different infection risks. The perioperative time period is a particularly high-risk time for infections, which can carry significant morbidity. This study compared risk of post-operative infections after arthroplasty in patients with RA exposed to different biologic DMARDs or to methotrexate.

Methods: A retrospective cohort study using U.S. Medicare data from 2006-2014 evaluated adults with ≥ 2 ICD9 codes for RA undergoing elective inpatient primary or revision total knee or hip arthroplasty. Eligible patients received an infusion of infliximab, abatacept, or tocilizumab or prescription for adalimumab, or etanercept within 8 weeks, or a rituximab infusion within 16 weeks of surgery. Methotrexate treated patients with previous biologic treatment but no biologic within 6 months of surgery were also included. Patients with hip fracture, malignancy, pre-existing infection, or non-elective surgery (admission through the emergency department or as a hospital transfer) were excluded. Multivariable logistic or Cox regression evaluated associations between medication exposure and risk of 1) serious (hospitalized) infection within 30 days using a validated set of discharge diagnoses from inpatient discharge diagnoses and 2) rate of prosthetic joint infection (PJ, ICD9 996.66) within 1 year, adjusting for confounders.

Results: Among 8694 surgeries in 7831 patients, serious infection occurred in 844 (9.7%), most commonly urinary infection, skin/soft tissue infection, and pneumonia. Infection incidence ranged from 9.7% to 10.0%, and risk was similar across medication exposure groups after adjustment for confounders (Table). Glucocorticoids were associated with a dose-dependent increase in risk, with
significantly increased risk even at 5-10mg per day (Table). The overall rate of PJI within 12 months was 3.1/100 person-years (n = 228 infections), with crude rates ranging from 1.8 (rituximab) to 6.4 (tocilizumab) per 100 person-years (Figure). After adjustment, risk of PJI remained elevated in tocilizumab vs. TNF inhibitors [HR 2.16 (1.14-4.10), p = 0.02] (Table).

**Conclusion**: Short-term risk of serious post-operative infection after arthroplasty was similar in patients with RA treated with different biologics. Rates of PJI were low, with small variations in PJI risk between biologics possibly related to differences in disease severity. Glucocorticoids showed a strong dose-dependent association with infection, with a larger impact on post-operative infection risk than choice of biologic.

| Table: Crude incidence of serious infection within 30 days of prosthetic joint infection within 1 year after elective hip and knee arthroplasty and results of multivariable logistic regression and Cox model. |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                 | N               | 30 day infection n (%) | 30 day infection adjusted OR* (95% CI) | PJI n (incidence/100py) | PJI adjusted HR* (95% CI) | Glucocorticoid average daily dose |
| **DMARD exposure** |                 |                 |                 |                 |                 |
| TNF inhibitor   | 5766            | 559 (9.7%)      | Reference       | 347 (3.1)       | Reference        |
| Abatacept       | 1330            | 131 (9.8%)      | 0.99 (0.80-1.23) | 28 (2.1)        | 0.96 (0.60-1.58) |
| Rituximab       | 392             | 39 (10.0%)      | 0.57 (0.38-0.81) | 6 (1.5)         | 0.55 (0.24-1.26) |
| Tocilizumab     | 215             | 25 (11.6%)      | 1.08 (0.69-1.72) | 3 (1.4)         | 2.16 (1.14-4.10) |
| Methotrexate    | 1035            | 100 (9.7%)      | 0.36 (0.22-0.59) | 7 (0.7)         | 0.88 (0.49-1.59) |

*Models include DMARD exposure and glucocorticoid dose. Also adjusted for age, sex, race, year, surgery type, region, urban, zip code based median household income, disability, Charlson score, diabetes, congestive heart failure, COPD/emphysema, obesity, extraarticular RA, number of previous biologic DMARDS, antibiotics use, past year, hospitalization past year, hospitalized infection past year, skilled nursing facility stay past year, number of outpatient visits, surgeon volume.
Effect of Baseline and Change in Effusion-Synovitis on Cartilage Damage over 18 Months in Patients with Osteoarthritis and Meniscal Tear

Lindsey A. MacFarlane1, Heidi Y. Yang2, Jamie E. Collins3, Mohamed Jararaya4, Ali Guermazi5, Lisa A. Mandl6, Elena Losina3 and Jeffrey N. Katz7, 1Rheumatology, Brigham & Women's Hospital, Boston, MA, 2Orthopaedic and Arthritis Center for Outcomes Research, Brigham & Women's Hospital, Boston, MA, 3Orthopaedic and Arthritis Center for Outcomes Research, Department of Orthopedic Surgery, Brigham & Women's Hospital, Boston, MA, 4Musculoskeletal Radiology, Boston University School of Medicine, Boston, MA, 5Boston University School of Medicine, Boston, MA, 6Department of Rheumatology, Hospital for Special Surgery, New York, NY, 7Rheumatology, Immunology, and Allergy, Brigham & Women's Hospital, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Plenary Session III
Session Type: ACR Plenary Session
Session Time: 11:00AM-12:30PM

Background/Purpose:
Synovitis is a common feature in meniscal tear (MT) and osteoarthritis (OA). Synovitis has been associated with progression of cartilage damage in persons with OA, as has arthroscopic partial meniscectomy (APM), a frequent treatment for MT. It is unknown whether the presence or the persistence of effusion-synovitis is associated with changes in cartilage damage in patients with concurrent MT and OA.

Methods:
We used data from the Meniscal Tear in Osteoarthritis Research (MeTeOR) Trial of APM vs. physiotherapy (PT). Subjects were ≥45 years old, had MT on MRI, OA on MRI or radiograph, and knee symptoms. Subjects crossing-over between treatment groups or without both baseline and 18mo MRI were excluded. MRIs were read using the MRI OA Knee Score (MOAKS). Baseline effusion-synovitis was dichotomized as none/mild (0) and moderate/severe (1). Change in effusion-synovitis over 18mo was categorized as never developed (0 at baseline, 0 at 18mo), intermittent (1 at only 1 time point), and persistent (1 at baseline, 1 at 18mo). Change in cartilage damage over 18mo was examined in 14 subregions and assessed by a) number of subregions with worsening (subregions grade ≥1 at baseline with increased surface area affected by full thickness loss) and b) number of additional subregions affected (subregions grade 0 at baseline with new full thickness loss). Both outcomes were specified as binary (0 regions vs. 1+). We used logistic regression to investigate the associations between a) baseline effusion and b) change in effusion on both cartilage damage outcomes over 18mo in 4 individual models – with adjustment for differences in treatment (APM vs. PT), sex, BMI, and baseline cartilage damage.

Results:
We analyzed 174 knees (1/person), 102 had APM and 72 PT. Moderate/severe effusion was observed in 48% patients at baseline and 29% at 18mo. Fifty-six percent of subjects had subregions with worsening and 45% had additional subregions affected. Over 18mo, 44% subjects never developed effusion, 35% had intermittent effusion, and 21% had persistent effusion. Overall participants were 59% female, 58 years old, with a BMI of 30 kg/m². Compared to subjects who never developed effusion, those with intermittent effusion had 2.6-fold (95% CI 1.2, 5.5) greater odds of worsening cartilage damage, while those with persistent effusion had 4.5-fold (95% CI 1.6, 12.8) greater odds. Similar results were obtained for analyses of baseline effusion and number of additional subregions affected (Table).

Conclusion:
Effusion-synovitis status at baseline and 18mo was associated with worsening of cartilage damage at 18mo in patients with MT and OA, independent of study treatment. The risk of cartilage damage was greater in those with persistent effusion than in those with intermittent effusion. If confirmed in other studies, these findings would support research on the structural effects of interventions to reduce effusion in this population.

**Table:** Odds ratios from logistic regression of A) Baseline and B) Change in Effusion-Synovitis on Cartilage Damage over 18 months

<table>
<thead>
<tr>
<th>A. Baseline Effusion-synovitis</th>
<th>1+ subregion with worsening cartilage damage*</th>
<th>1+ additional subregion affected by cartilage damage*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds Ratio (95% CI)</td>
<td>Odds Ratio (95% CI)</td>
</tr>
<tr>
<td>None/mild</td>
<td>92</td>
<td>REF</td>
</tr>
<tr>
<td>Moderate/severe</td>
<td>84</td>
<td>2.9 (1.4, 5.9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.8 (1.4, 5.5)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>B. 18 Month Change in Effusion-synovitis</th>
<th>1+ subregion with worsening cartilage damage*</th>
<th>1+ additional subregion affected by cartilage damage*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds Ratio (95% CI)</td>
<td>Odds Ratio (95% CI)</td>
</tr>
<tr>
<td>Never Developed</td>
<td>77</td>
<td>REF</td>
</tr>
<tr>
<td>Intermittent</td>
<td>61</td>
<td>2.6 (1.2, 5.5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.2 (1.1, 4.7)</td>
</tr>
<tr>
<td>Persistent</td>
<td>36</td>
<td>4.5 (1.6, 12.8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.0 (1.5, 10.3)</td>
</tr>
</tbody>
</table>

*all models adjusted for treatment (APM vs PT), sex, BMI and baseline cartilage damage

Change in effusion-synovitis: never developed (none/mild at baseline and 18mo), intermittent (mod/severe at only 1 time point), persistent (mod/severe at baseline and 18mo)

Disclosure: L. A. MacFarlane, None; H. Y. Yang, None; J. E. Collins, None; M. Jarraya, None; A. Guermazi, BICL, LLC, 1,MerckSerono, TissueGene, OrthoTrophix, AstraZeneca and Genzyme, 5; L. A. Mandl, Boehringer Ingelheim, 2,American College of Physicians, 3,Up To Date, 7; E. Losina, None; J. N. Katz, None.


**Abstract Number:** 2757

**Kidney and Skin Single-Cell RNA Sequencing in Lupus Nephritis Provides Mechanistic Insights and Novel Potential Biomarkers**

Evan Der¹, Hemant Suryawanshi², Saritha Ranabothu³, Beatrice Goilav⁴, H. Michael Belmont⁵, Peter M. Izmirlý⁶, Nicole Bornkamp⁵, Nicole Jordan⁷, Tao Wang¹, Meng Wu⁶, Judith A. James⁸, Joel M. Guthridge⁹, Soumya Raychaudhuri¹⁰, Thomas Tuschl¹¹, Jill P. Buyon¹² and Chaim Putterman¹³, ¹Albert Einstein College of Medicine, Bronx, NY, ²The Rockefeller University, New York, NY, ³Nephrology, Children's Hospital at Montefiore, Bronx, NY, ⁴Albert Einstein College of Medicine/Montefiore Medical Center, New York, NY, ⁵Medicine, New York University School of Medicine, New York, NY, ⁶New York University School of Medicine, New York, NY, ⁷Montefiore Medical Center, New York, NY, ⁸Arthritis & Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, ⁹Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, ¹⁰Divisions of Genetics and Rheumatology, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ¹¹Rockefeller
ScRNAseq was performed on ~2 mg kidney tissue collected from clinically indicated renal biopsies, and skin biopsies obtained at the time of renal biopsies, in 20 SLE patients. ScRNAseq was performed using Fluidigm C1 HT Integrated Fluidic Circuits and cDNA libraries were prepared using the Nextera XT DNA Library Prep Kit followed by NextSeq (Illumina) sequencing.

Results: A total of 1616 renal cells and 2392 skin cells were sequenced from LN and healthy control skin and kidney biopsies. Cell-types were determined using principal component analysis and tSNE plotting, resulting in the definitive identification of keratinocytes (N = 2004 cells), tubular cells (N=936 cells), fibroblasts (N=422), endothelial cells (N=154), and leukocytes (N=129). Genes identified by differential expression analysis of tubular cells (Fig. 1) and keratinocytes originating from patients with proliferative (class III or IV) (N=7 patients) and membranous (class V) nephritis (N=6 patients) were subjected to gene ontology pathway analysis. Tubular cells in patients with proliferative nephritis demonstrated upregulated TNF signaling (p<.001), including the transcription factor FOS, as compared to patients with membranous nephropathy. Moreover, the VEGF signaling (p<.001) pathway was upregulated, as was chemokine activity (p<.001) including CCL2 and CXCL3. Interestingly, keratinocytes from non-lesional skin of patients with proliferative nephritis also demonstrated upregulated TNF signaling (p<.01) as compared to those with membranous nephritis.

Conclusion: ScRNAseq from small amounts of renal biopsy tissue in SLE can differentiate between the different classes of LN, and provide important insights into potential pathogenic mechanisms. Further, due to the systemic nature of the disease, transcriptomic changes in the skin of LN patients can provide a useful source of biomarkers and may reflect important information concerning concurrent kidney pathological events.
Response to JAK1/2 Inhibition with Baricitinib in “Candle”, “Savi” and “Candle-like” Diseases. A New Therapeutic Approach for Type I IFN-Mediated Autoinflammatory Diseases

Gina A. Montealegre Sanchez1, Adam Reinhardt2, Suzanne Ramsey3, Helmut Wittkowski4, Philip J Hashkes5, Sara Murias6, Yackov Berkun7, Susanne Schalm8, Jason A Dare9, Diane Brown10, Deborah L. Stone11, Ling Gao9, Thomas L. Klausmeier12, John D. Carter13, Robert Colbert14, Dawn C. Chapelle15, Hanna Kim15, Samantha Dill15, Adriana Almeida de Jesus1, Paul Wakim16, A. Zlotogorski17, Seza Ozen18, Paul Brogan19 and Raphaela Goldbach-Mansky1, 1Translational Autoinflammatory Disease Studies (TADS), Laboratory of Clinical Investigation and Microbiology (LCIM), NIAID/NIH, Bethesda, MD, 2Faculty of Physicians of the University of Nebraska Medical Center, College of Medicine, Nebraska, NE, 3Pediatric Rheumatology, IWK Health Centre, Dalhousie University, Halifax, NS, Canada, 4Department of Pediatric Rheumatology and Immunology, University of Muenster, Muenster, Germany, 5Pediatrics Rheumatology; Shaare Zedek Medical Center, Jerusalem, Israel, 6Hospital Infantil La Paz, Madrid, Spain,
Monogenic autoinflammatory interferonopathies, including chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperatures (CANDLE) and STING-associated vasculopathy with onset in infancy (SAVI), present with a prominent interferon (IFN)-response gene signature (IRS) in the blood, systemic inflammation, and organ-specific damage often associated with increased morbidity and mortality in childhood. An Expanded Access Program with baricitinib, a JAK kinase inhibitor with \textit{ex vivo} IFN blocking capacity, was developed to provide baricitinib to patients (pt.) with no comparable or satisfactory treatment options.

**Methods:**
Potential benefit was assessed by reductions in daily symptom diary to <0.5 (CANDLE and CANDLE-like pt.) and to <1.0 (SAVI pt.) and reductions of steroid doses to <0.15mg/kg/day or by at least 50% from baseline. Quality of life assessments, linear growth, and changes in IRS and IFN-induced biomarkers are also reported. Drug safety was longitudinally followed. Paired t-tests were used to compare daily mean daily symptom diary and prednisone doses at the last clinic visit to baseline data.

**Results:**
Between October 2011 and October 2016, 18 pt. were enrolled and treated, 10 CANDLE pt., 4 SAVI pt., and 4 CANDLE-like pt. Mean follow-up duration 3.0 years. The median daily symptom diary score decreased from 1.3 (IQR 0.93-1.78) to 0.25 (IQR 0.1-0.63) \((p<0.001)\) with responses most significant in CANDLE patients. In 14 patients receiving steroids at baseline, daily prednisone doses decreased from 0.44 mg/kg/day (IQR 0.31-1.9) to 0.11 mg/kg/day (IQR 0.02-0.24) \((P<0.005)\); 5 of 10 CANDLE patients achieved lasting clinical remission. All active patients \((n=16)\), except two, reported improvement in quality of life. 9 of the 13 patients with growth potential improved their Z-scores from -4.34 to -2.83 \((p=0.02)\). DEXA Z-scores also improved from -4.0 to -3.1 \((p=0.006)\). IFN scores significantly dropped and durably normalized in 5 CANDLE patients. Treatment-related serious adverse events included infections; 2 patients with genetically undefined interferonopathies discontinued due lack of efficacy, one also had avascular necrosis. One CANDLE patient developed BK viremia and azotemia and was discontinued from the program. The most common adverse events included upper respiratory infections and BK viruria (baseline screening for BK virus in blood and urine was not performed).

**Conclusion:**
Daily doses of baricitinib significantly improved clinical disease manifestations, laboratory parameters, linear growth, and bone mineral density, and decreased IFN signaling in patients with CANDLE, SAVI and 2 other autoinflammatory interferonopathies. Monitoring safety and efficacy is important in benefit-risk assessment.

Acknowledgements: This work was supported by the NIH IRP of NIAID and NIAMS.
Disclosure: G. A. Montealegre Sanchez, Eli Lilly and Company, 9, Regeneron, 9; A. Reinhardt, None; S. Ramsey, None; H. Wittkowski, None; P. J. Hashkes, None; S. Murias, None; Y. Berkun, None; S. Schalm, None; J. A. Dare, None; D. Brown, None; D. L. Stone, None; L. Gao, None; T. L. Klausmeier, None; J. D. Carter, None; R. Colbert, Eli Lilly and Company, 9; D. C. Chapelle, None; H. Kim, None; S. Dill, None; A. Almeida de Jesus, None; P. Wakim, None; A. Zlotogorski, None; S. Ozen, None; P. Brogan, Eli Lilly and Company, 9; R. Goldbach-Mansky, Eli Lilly and Company, 9, SOBI, 9, Regeneron, 9, Novartis Pharmaceutical Corporation, 9.


Abstract Number: 2759

**The Risk of Ischaemic Stroke in Primary APS Patients: A Prospective Study**

Massimo Radin¹, Karen Schreiber², Irene Cecchi³, Dario Roccatello⁴, Maria Jose Cuadrado⁵ and Savino Sciascia⁶, ¹Department of Clinical and Biological Sciences, Center of Research of Immunopathology and Rare Diseases- Coordinating Center of Piemonte and Valle d’Aosta Network for Rare Diseases, Department of Clinical and Biological Sciences, University of Turin, Italy, Turin, Italy, ²Department of Thrombosis and Haemophilia, Guy's and St Thomas' Hospital, London, United Kingdom, London, United Kingdom, ³Center of Research of Immunopathology and Rare Diseases- Coordinating Center of Piemonte and Valle d’Aosta Network for Rare Diseases, Department of Clinical and Biological Sciences, University of Turin, Italy, Turin, Italy, ⁴Center of Research of Immunopathology and Rare Diseases- Coordinating Center of Piemonte and Valle d’Aosta Network for Rare Diseases, Department of Clinical and Biological Sciences, University of Turin and S. Giovanni Bo, Turin, Italy, ⁵St Thomas Hospital, Lupus Research Unit, London, United Kingdom, ⁶Center of Research of Immunopathology and Rare Diseases- Coordinating Center of Piemonte and Valle d’Aosta Network for Rare Diseases, Department of Clinical and Biological Sciences, University of Turin, Italy, Center of Research of Immunopathology and Rare Diseases- Coordinating Center of Piemonte and Valle d’Aosta Network for Rare Diseases, Department of Clinical and Biological Sciences, University of Turin, Italy, Torino, Italy

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Antiphospholipid Syndrome
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:

The antiphospholipid syndrome (APS) is an autoimmune condition characterized by thrombosis and/or pregnancy morbidity and persistent positivity for antiphospholipid antibodies (aPL). The most common neurological manifestation of APS is ischaemic stroke (1). Identifying patients with APS at high risk for developing any thrombotic event remains a major challenge. In this study, we aimed to identify predictive factors of ischaemic stroke in a cohort of primary APS (PAPS) patients who presented with new onset symptoms suggestive of acute stroke.
Methods:
This prospective multicenter study included 36 consecutive PAPS patients [mean age 32 years old (SD 33·7), female (86%)] who presented with new onset symptoms suggestive of an acute stroke. Data on cardiovascular risk factors and aPL positivity were collected and aGAPSS score was calculated. Patients were prospectively followed up for 12 months. Demographic, clinical and laboratory characteristics are summarized in Table 1 and Table 2.

Results:
In ten (28%) out of 36 PAPS patients [mean age 41 years old (SD 13·4), female (70%)], the suspicion of an acute stroke was confirmed by brain MRI. Sixty percent of these patients were < 50 years old. Six out of the ten patients had a history of previous venous thrombosis and were receiving vitamin K antagonist (VKA), with INR target 2-3; one patient had a history of a previous arterial event receiving treatment with VKA target INR 2-3 plus low dose aspirin (LDA), and one patient had a history of previous pregnancy morbidity receiving only LDA. Time in therapeutic range for patients receiving VKA was 77·7 (S.D. 6·6). Hypercholesterolemia was significantly higher in patients with confirmed stroke when compared to those without (p < 0·05). Similarly, we found a significantly higher rate of anti-ß2GPI antibodies (IgG/IgM) (p < 0·05) and higher aGAPSS values in patients with a confirmed stroke [mean aGAPSS 8·9 (S.D. 4·7) Vs. mean aGAPSS 6·4 (S.D. 2·5); p < 0·05].

Conclusion:
Patients with PAPS, including young patients, have a high risk of recurrent thrombosis despite anticoagulation treatment. A careful risk assessment is mandatory to identify patients at risk for recurrence. Modifiable risk factor reduction may be a first step to prevent recurrence.

References:

<table>
<thead>
<tr>
<th>Patients Characteristics</th>
<th>All (n=36)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>31</td>
<td>86</td>
</tr>
<tr>
<td>Age, mean (S.D.), years</td>
<td>32 (33·7)</td>
<td></td>
</tr>
<tr>
<td>Age &lt; 50 years</td>
<td>25</td>
<td>69</td>
</tr>
<tr>
<td>Age &lt; 40 years</td>
<td>15</td>
<td>42</td>
</tr>
<tr>
<td>Caucasians, n</td>
<td>31</td>
<td>86</td>
</tr>
<tr>
<td>Stroke</td>
<td>10</td>
<td>28</td>
</tr>
<tr>
<td>Small vessel changes</td>
<td>8</td>
<td>22</td>
</tr>
<tr>
<td>Hyperintensive lesions</td>
<td>5</td>
<td>14</td>
</tr>
<tr>
<td>increased for age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haematoma</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>PAPS, n</td>
<td>36</td>
<td>100</td>
</tr>
<tr>
<td>Arterial Hypertension, n</td>
<td>9</td>
<td>25</td>
</tr>
<tr>
<td>Hyperlipidemia, n</td>
<td>7</td>
<td>19</td>
</tr>
<tr>
<td>LA, n</td>
<td>33</td>
<td>92</td>
</tr>
<tr>
<td>aCL IgG/M, n</td>
<td>12</td>
<td>33</td>
</tr>
<tr>
<td>Anti-Beta2GPI IgG/IgM, n</td>
<td>6</td>
<td>17</td>
</tr>
<tr>
<td>Triple aPL positivite</td>
<td>4</td>
<td>11</td>
</tr>
</tbody>
</table>

Table 2
<table>
<thead>
<tr>
<th></th>
<th>Stroke (10)</th>
<th>No stroke (26)</th>
<th>p (Chi Square test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean, SD)</td>
<td>43.4 ±10.4</td>
<td>39.2 ±12.5</td>
<td>0.183</td>
</tr>
<tr>
<td>Sex (females)</td>
<td>7 (70%)</td>
<td>23 (88%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>6 (60%)</td>
<td>3 (12%)</td>
<td>0.075</td>
</tr>
<tr>
<td>Arterial Hypertension</td>
<td>4 (30%)</td>
<td>3 (12%)</td>
<td>1.00</td>
</tr>
<tr>
<td>LA</td>
<td>9 (90%)</td>
<td>24 (92%)</td>
<td>1.00</td>
</tr>
<tr>
<td>aCL IgG/M</td>
<td>3 (30%)</td>
<td>9 (35%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Anti-Beta2GPI IgG/IgM</td>
<td>5 (50%)</td>
<td>1 (4%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Triple aPL positivity</td>
<td>2 (20%)</td>
<td>2 (8%)</td>
<td>0.305</td>
</tr>
</tbody>
</table>

Disclosure: M. Radin, None; K. Schreiber, None; I. Cecchi, None; D. Roccatello, None; M. J. Cuadrado, None; S. Sciascia, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-risk-of-ischaemic-stroke-in-primary-aps-patients-a-prospective-study

Abstract Number: 2760

Antiphospholipid Syndrome Alliance for Clinical Trials & International Networking (APS ACTION) Clinical Database and Repository (“Registry”) Analysis: First and Recurrent Thrombosis Risk after 1201 Patient-Years of Follow-up

Ozan Unlu1, Daniela Andrade2, Alessandra Banzato3, D. Ware Branch4, Paul R. Fortin5, Maria Gerosa6, Roger A. Levy7, Michelle Lopes8, Michelle Petri9, Ignasi Rodriguez10, Maria Tektonidou11, Amaia Ugarte12, Rohan Willis13, Doruk Erkan14 and, on Behalf of APS ACTION.15

Background/Purpose: APS ACTION Registry was created to study the natural course of disease over 10 years in persistently antiphospholipid antibody (aPL)-positive patients with/without other systemic autoimmune diseases. Previously, based on 16 new thrombotic events, we reported the annual recurrent and first thrombosis risk in persistently aPL-positive patients as 2.38 and 1.86%, respectively (Arthritis Rheumatol. 2016; 68 [suppl 10]).

Methods: A web-based data capture system is used to store patient demographics, history, and medications. Inclusion criteria are positive aPL based on the Updated Sapporo Classification Criteria at least twice within one year prior to enrollment. Patients are followed every 12±3 months with clinical data and blood collection; they also receive advice on cardiovascular disease and thrombosis prevention at each visit. In this descriptive analysis, we report additional thrombotic events based on patients who completed one-, two-, three-, and four-year follow-up visits.
Results: As of 4/2017, 671 patients were included (aPL/APS without any other autoimmune disease [AIDx]: 436 [no thrombosis: 88; thrombotic APS [TAPS]: 241; obstetric APS [OAPS]: 47; and TAPS+OAPS: 60]; and aPL/APS associated with another AIDx: 235 [no thrombosis: 67; TAPS: 118; OAPS: 18; and TAPS+OAPS: 32]). Of 671 patients, 515 (77%), 391 (58%), 243 (36%), and 52 (8%) completed their one-, two-, three-, and four-year follow-up visits, respectively. Mean follow up were 2.38 years (844 patient-years [pt-y]) and 2.23 years (357 pt-y) for those with and without a history of thrombosis, respectively. Table demonstrates the demographic, clinical, and laboratory characteristics of 13 patients who had new thrombosis since our most recent analysis. Based on a total of 22 recurrent events (10 events during the 1st year; 5 during the 2nd; 6 during the 3rd; and 1 during 4th) and six initial (3 events during the 1st year; 2 during the 2nd; and 1 during the 3rd) since the inception of the registry, the incident thrombosis risk was 2.60 and 1.68 per 100 pt-y in patients with and without history of thrombosis, respectively (annual thrombosis risk 2.63% and 1.68%, respectively). In a subgroup analysis, the incident thrombosis risk was: a) 3.13 and 1.50 per 100 pt-y in patients with and without history of thrombosis, respectively for those with other AIDx and b) 2.38 and 1.79 per 100 pt-y in patients with and without history of thrombosis, respectively for those without other AIDx.

Conclusion: The incident thrombosis risk remains relatively low and commonly associated with LA- and/or triple aPL-positivity as well as non-aPL thrombosis risk factors. The risk is similar between aPL-positive patients with and without other AIDx. Annual and risk stratified analysis of APS ACTION registry will better determine the risk of thrombosis in persistently aPL-positive patients based on different risk profiles.

<table>
<thead>
<tr>
<th>Age/sex/</th>
<th>Baseline Data</th>
<th>Follow-Up Data</th>
<th>Other AIDx</th>
<th>Other APS Risk Factors</th>
<th>PT-Thrombosis Risk Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>24/PM</td>
<td>No</td>
<td>Triple aPL,</td>
<td>DPT</td>
<td>No (15%)</td>
<td>DVT (10%)</td>
</tr>
<tr>
<td>48/PM</td>
<td>No</td>
<td>No aPL,</td>
<td>DPT</td>
<td>No (15%)</td>
<td>DVT (10%)</td>
</tr>
<tr>
<td>46/LAM</td>
<td>No</td>
<td>LA,</td>
<td>PE</td>
<td>No (15%)</td>
<td>DVT (10%)</td>
</tr>
<tr>
<td>25/KM</td>
<td>No</td>
<td>LA,</td>
<td>No,</td>
<td>No (15%)</td>
<td>DVT (10%)</td>
</tr>
<tr>
<td>37/LAF</td>
<td>No</td>
<td>Triple aPL,</td>
<td>Stroke, DVT</td>
<td>No (15%)</td>
<td>DVT (10%)</td>
</tr>
<tr>
<td>38/ML</td>
<td>No</td>
<td>Other AIDx</td>
<td>PE</td>
<td>No (15%)</td>
<td>DVT (10%)</td>
</tr>
<tr>
<td>11/18</td>
<td>No</td>
<td>LA,</td>
<td>Stroke,</td>
<td>No (15%)</td>
<td>DVT (10%)</td>
</tr>
<tr>
<td>20/12</td>
<td>No</td>
<td>Triple,</td>
<td>Stroke</td>
<td>No (15%)</td>
<td>DVT (10%)</td>
</tr>
</tbody>
</table>

 Disclosure: O. Unlu, None; D. Andrade, None; A. Banzato, None; D. W. Branch, None; P. R. Fortin, None; M. Gerosa, None; R. A. Levy, None; M. Lopes, None; M. Petri, Exagen, 2; I. Rodriguez, None; M. Tektonidou, None; A. Ugarte, None; R. Willis, None; D. Erkan, None; O. B. O. A. , None.

Adenosine Receptor Agonism Protects Against Antiphospholipid Antibody-Mediated Netosis and Venous Thrombosis

Ramadan A. Ali¹, He Meng¹, Srilakshmi Yalavarthi¹, Yogendra Kanthi¹ and Jason S. Knight², ¹University of Michigan, Ann Arbor, MI, ²University of Michigan, Ann Arbor, MI

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Antiphospholipid Syndrome
**Background/Purpose:** We have previously reported that antiphospholipid antibodies (aPL) activate neutrophils and thereby exaggerate neutrophil extracellular trap release (NETosis), which potentially contributes to the thrombotic events inherent to antiphospholipid syndrome (APS). Recent evidence suggests that the second messenger cyclic AMP (cAMP) suppresses NETosis. Here, we hypothesized that surface adenosine receptors (which trigger cAMP formation in neutrophils) serve as an endogenous counterpoint to thrombo-inflammatory disease, and that pharmacological agonism of adenosine receptors may therefore mitigate the thrombotic manifestations of APS. In particular, our data led us to investigate the adenosine 2A receptor and its downstream pathways.

**Methods:** For *in vitro* studies, control neutrophils were prepared from healthy volunteers and stimulated with (i) total IgG pooled from primary APS patients, (ii) affinity-purified anti-β2GPI antibodies, or (iii) phorbol 12-myristate 13-acetate (as a positive control). NETs were quantified by chromogenic detection of the enzymatic activity of NET-associated myeloperoxidase, or by SytoxGreen-based fluorescence measurement of extracellular DNA. For *in vivo* studies, thrombosis was triggered by surgical restriction of blood flow through the inferior vena cava, with resulting macroscopic thrombi assessed 48 hours later (a model of thrombosis that our group and others has shown to be accentuated by NETs).

**Results:** We began by assessing the effect of cAMP on aPL-mediated NETosis. 8-Br-cAMP (a cell-permeable, degradation-resistant cAMP derivative) significantly inhibited NETosis in dose-dependent fashion. As extracellular adenosine receptors are key regulators of neutrophil cAMP levels, we assessed agonism of the adenosine 2A, 2B, and 3 receptors. While CGS21680 (A2A agonist) suppressed NETosis with nanomolar potency, BAY60-6583 (A2B agonist) and 2-Cl-IB-MECA (A3 agonist) had minimal effect, even at micromolar concentrations. The antithrombotic agent dipyridamole is known to potentiate adenosine-mediated signaling by (i) increasing extracellular concentrations of adenosine, and (ii) interfering with the breakdown of cAMP. Indeed, dipyridamole suppressed aPL-mediated NETosis in a dose-dependent manner. Finally, in a mouse model of macroscopic venous thrombosis, CGS21680 (A2A agonist) was highly effective in mitigating thrombosis (3-fold reduction in thrombus weight; p=0.028 with 15 mice per group).

**Conclusion:** We demonstrate for the first time that adenosine 2A receptor agonism can attenuate aPL-mediated NETosis *in vitro* and venous thrombosis in mice. Furthermore, dipyridamole (a drug known to potentiate adenosine-mediated signaling) phenocopies adenosine 2A receptor agonism in terms of suppressing *in vitro* NETosis. Studies are underway to fully characterize relevant signaling pathways in neutrophils, and to assess the therapeutic potential of dipyridamole against aPL-accelerated thrombosis.

**Disclosure:** R. A. Ali, None; H. Meng, None; S. Yalavarthi, None; Y. Kanthi, None; J. S. Knight, None.


**Abstract Number:** 2762

**Study of 60 Patients with Intrauterine Fetal Deaths Related to Antiphospholipid Syndrome**

Mériem Belhocine1, Laetitia Coutte2, Nicolas Martin Silva3, Nathalie Morel4, Gaelle Guettrot-Imbert4, Romain Paule4, Michel Dreyfus5, Micaela Fredi6, Odile Souchaud-Debouverie7, Jean Charles Piette8, Veronique Le Guern4 and Nathalie Costedoat-Chalumeau1. 1Service de médecine interne Pôle médecine, Hôpital Cochin, Centre de référence maladies auto-immunes et systémiques rares de l’île de France, Paris, France; 2Department of Internal Medicine, Department of Internal Medicine, Cochin University Hospital, Paris, France; 3Department of Internal Medicine, Department of Internal Medicine, University Hospital Center of Caen, Caen, France; 4Department of Internal Medicine, Department of Internal Medicine, Cochin University Hospital, Paris, France; 5Department of Gynecology and Obstetrics, Department of Gynecology and Obstetrics, University Hospital Center of Caen, Caen, France; 6Department of Rheumatology and Clinical Immunology, Rheumatology and Clinical Immunology, Rheumatology and Clinical Immunology, Spedali Civili di Brescia, Brescia, Italy; 7Department of Internal Medicine, Department of Internal Medicine, Poitiers University Hospital, Poitiers, France; 8Department of Internal Medicine, Department of Internal Medicine, University Hospital Pitié-Salpêtrière, Paris, France

**First publication:** September 18, 2017
**Background/Purpose:** The antiphospholipid syndrome (APS) is defined by a combination of arterial and/or venous thrombosis, pregnancy morbidity, and persistent antiphospholipid antibodies. There is a real gap in knowledge on intrauterine fetal death (IUFD) in APS patients because there are no large published series. Moreover, heterogeneous gestational ages and varying definitions of APL assays positivity are used in the literature.

**Methods:** We retrospectively analysed the history and clinical data of women followed in 4 French university hospitals for a diagnosis of APS (Sydney criteria) who experienced an IUFD at or after 10 weeks of gestation (WG) between 2000 and 2016. According to the classification criteria, if the IUFD was otherwise explainable by a fetal or obstetrical complication not related to APS, the patient was excluded. The patients were included when at least 2 positive antibodies were found 12 weeks apart or more and within 5 years of the obstetrical event.

**Results:** Sixty patients were included. Their mean age at the IUFD was 29 ± 5 years (Table 1). Prior to the IUFD, 10 patients (17%) had a previous live birth, 8 (13%) had an early miscarriage, 5 (8%) an abortion while 37 (62%) were nulligest. APS was already known in 9 patients (15%) and systemic lupus erythematosus (SLE) in 8 patients (13%). There was a high prevalence of triple positive (38%) and double positive (25%) women.

During the index IUFD, treatment consisted of low dose aspirin (LDA) (n=7), low molecular weight heparin (LMWH) (n=3) or a combination of both (n=5). IUFD occurred at a mean gestational age of 22.3 ± 7 WG. It was associated in 16 cases to obstetrical complications, namely preeclampsia (n=12), HELLP syndrome (n=6) and/or placental abruption (n=5). There was no maternal mortality associated. Placental infarctions were found in 25 out of 34 available histologic examinations.

Regarding the following pregnancy, 34 out of the 43 patients (79%) who received a treatment (LDA and/or LMWH started before 12 WG) had a live birth versus 1 out of 9 patients (11%) who did not receive such treatment.

Overall, including the follow up period of 5 years [IQR: 3-10], 26 patients (43%) experienced one or more thrombosis, among which half before the index IUFD, and 28% were diagnosed with SLE. Ultimately, 51 patients had at least one live birth, including 48 after experiencing the IUFD. The median age at last follow-up of the childless women was 33 years old [IQR: 30-45].

**Conclusion:** The IUFD was mostly inaugural in the APS and unrelated to other obstetrical complications. The strong autoimmune biology, significant occurrence of SLE and thrombosis suggest that these IUFD events happened in patients with a solid APS diagnosis and are not randomly associated with weak autoantibodies. A majority of women succeeded in having at least one live birth when treated.

**Table 1. Patients' characteristics**
<table>
<thead>
<tr>
<th></th>
<th>Our series</th>
<th>Cervera et al.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>29±5</td>
<td></td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>19 (32)</td>
<td></td>
</tr>
<tr>
<td>Follow-up since IUFD (years)</td>
<td>5[3;10]</td>
<td></td>
</tr>
<tr>
<td>Gestational age at IUFD (WG)</td>
<td>22.3±7</td>
<td></td>
</tr>
<tr>
<td>History of live birth before the IUFD, n (%)</td>
<td>10 (17)</td>
<td></td>
</tr>
<tr>
<td>History of live birth overall, n (%)</td>
<td>51 (85)</td>
<td></td>
</tr>
<tr>
<td>Antibodies profile</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anticardiolipin, n (%)</td>
<td>44 (73)</td>
<td>(87.9)</td>
</tr>
<tr>
<td>Anticardiolipin IgG, n (%)</td>
<td>41 (68)</td>
<td></td>
</tr>
<tr>
<td>Anticardiolipin IgM, n (%)</td>
<td>8 (13)</td>
<td></td>
</tr>
<tr>
<td>Lupus anticoagulant, n (%)</td>
<td>43 (72)</td>
<td>(53.6)</td>
</tr>
<tr>
<td>Lupus anticoagulant -aPTT-based assay, n (%)</td>
<td>29 (48)</td>
<td></td>
</tr>
<tr>
<td>Lupus anticoagulant-dRVVT assay, n (%)</td>
<td>33 (55)</td>
<td></td>
</tr>
<tr>
<td>Unknown assay, n (%)</td>
<td>5 (8)</td>
<td></td>
</tr>
<tr>
<td>Anti-β2GP1, n (%)</td>
<td>32 (53)</td>
<td></td>
</tr>
<tr>
<td>Anti-β2GP1 IgG, n (%)</td>
<td>30 (50)</td>
<td></td>
</tr>
<tr>
<td>Anti-β2GP1 IgM, n (%)</td>
<td>7 (12)</td>
<td></td>
</tr>
<tr>
<td>Unknown , n (%)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>Triple positive, n (%)</td>
<td>23 (38)</td>
<td></td>
</tr>
<tr>
<td>History of thrombosis before the IUFD, n (%)</td>
<td>13 (22)</td>
<td></td>
</tr>
<tr>
<td>History of thrombosis overall, n (%)</td>
<td>26 (43)</td>
<td></td>
</tr>
<tr>
<td>Associated systemic lupus erythematosus before the IUFD, n (%)</td>
<td>8 (13)</td>
<td></td>
</tr>
<tr>
<td>Associated systemic lupus erythematosus overall, n (%)</td>
<td>17 (28)</td>
<td>(36.2)</td>
</tr>
</tbody>
</table>

Disclosure: M. Belhocine, None; L. Coutte, None; N. Martin Silva, None; N. Morel, None; G. Guettrot-Imbert, None; R. Paule, None; M. Dreyfus, None; M. Fredi, None; O. Souchaud-Debouverie, None; J. C. Piette, None; V. Le Guern, None; N. Costedoat-Chalumeau, None.


Abstract Number: 2763

**mTORC1 Blockade with Rapamycin and N-Acetylcyesteine Reduces Anti-Phospholipid Antibody Levels in Controlled Clinical Trials of Patients with SLE**

Thomas Winans¹, Ryan Kelly², Zhi-Wei Lai³, Stephen Faraone², Paul E. Phillips⁴, Katalin Banki⁵ and Andras Perl³, ¹SUNY Upstate Medical University, Syracuse, NY, ²SUNY, Syracuse, NY, ³Medicine, SUNY Upstate Medical University, Syracuse, NY, ⁴Dept of Medicine/Div of Rheum, SUNY-Upstate Medical Univ, Syracuse, NY, ⁵Clinical Pathology, SUNY Upstate Medical University, Syracuse, NY

First publication: September 18, 2017

SESSION INFORMATION

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Antiphospholipid Syndrome
Background/Purpose: Anti-phospholipid antibodies (aPL) constitute a diagnostic criterion and source of morbidity, termed anti-phospholipid syndrome (APS), in patients with or without systemic lupus erythematosus (SLE). Oxidization causes the immunogenicity of phospholipid antigens, such as β2GPI and cardiolipin (Arthritis Rheumatol. 63, 2774-82). Mitochondrial dysfunction-connected mechanistic target of rapamycin complex 1 (mTORC1) activation has been recently found to trigger aPL in mice (Arthritis Rheumatol. 68, 2728). Blockade of mTORC1 with rapamycin (Arthritis Rheumatol. 54:2983-8; J Immunol. 191:2236-46) and the antioxidant, N-acetylcysteine (NAC) has shown clinical efficacy in SLE (Arthritis Rheumatol. 64:2937-46). Therefore, we measured aPL levels in sera collected during clinical trials with rapamycin and NAC (ClinicalTrials.gov Identifiers: NCT00779194 and NCT00775476).

Methods: 40 SLE patients meeting eligibility criteria were started on 2 mg of rapamycin (sirolimus) with the dose adjusted to tolerance and trough levels of 6-15 ng/ml, and sera were collected before 1st rapamycin dose and 1 month, 3 months, 6 months, 9 months, and 12 months after initiation of treatment. 36 patients were enrolled in the NAC trial, and sera were collected before 1st NAC dose and 1 month, 2 months, and 3 months after initiation of treatment. At each study visit, blood samples were obtained from 42 healthy controls (HC) matched for patients’ age, gender, and ethnicity for parallel analyses. IgA, IgG, and IgM antibodies to β2GPI (anti-β2GPI) and cardiolipin (ACLA) were measured by ELISA (Arthritis Rheumatol. 63, 2774-82). Statistical analyses of drug efficacy was assessed relative to pretreatment samples with paired t-test using GraphPad. Patients and HC were compared with unpaired t-test. For hypothesis testing, differences were considered significant at p <0.05.

Results: IgG, but not IgM or IgA, anti-β2GPI (unpaired t-test p=0.014) and ACLA were elevated in untreated SLE patients relative to HC (unpaired t-test p=0.029). With respect to baseline, NAC, but not placebo, reduced IgG and IgM anti-β2GPI levels after 1 month intervention. NAC also reduced IgM, but not IgG or IgA, ACLA after 1 month intervention. Rapamycin reduced IgM and IgA, but not IgG, anti-β2GPI and ACLA production after 1 month, which was sustained after treatment for 12 months.

Conclusion: These ancillary studies suggest that rapamycin and NAC limit aPL production which should be included as an efficacy outcome in clinical trials of mTORC1 blockade in patients with SLE and APS.

Disclosure: T. Winans, None; R. Kelly, None; Z. W. Lai, None; S. Farame, None; P. E. Phillips, None; K. Banki, None; A. Perl, Pfizer, 2.


Abstract Number: 2764

Gene Expression Profile in Monocytes of Antiphospholipid Syndrome Patients Reveals Novel Altered Genes and Pathways Involved in the Pathophysiology of the Disease

Patricia Ruiz-Limon1, Carlos Perez-Sanchez2, Maria Ángeles Aguirre Zamorano2, Irene Cecchi3, Nuria Barbarroja2, Yolanda Jiménez-Gómez2, Ivan Arias de la Rosa1, Maria Carmen Abalos-Aguilera1, Pedro Segui4, Eduardo Collantes-Estévez2, Maria Jose Cuadrado5 and Chary Lopez-Pedrera2, 1Rheumatology Service, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain, 2Rheumatology service, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain, 3Center of Research of Immunopathology and Rare Diseases- Coordinating Center of Piemonte and Valle d’Aosta Network for Rare Diseases, Department of Clinical and Biological Sciences, University of Turin, Italy, Turin, Italy, 4Radiology, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain, 5St Thomas Hospital, Lupus Research Unit, London, United Kingdom

First publication: September 18, 2017
their specific molecular profile of activation in the pathogenesis of Antiphospholipid syndrome patients (APS) has not been yet evaluated. Thus, the aim of this study was to characterize the monocytes molecular signature of altered genes and pathways involved in the pathology of APS patients.

**Methods:** Monocytes from peripheral blood of six subject including APS and healthy donors (HDs) were purified by negative immunomagnetic selection (Miltenyi). Total RNA was extract and microarray studies were performed in an Agilent G4112F platform (Whole Human Genome Microarray 44k) using the One-Color gene expression system. Functional categorisation of the altered gene signature and molecular pathways and networks, was carried out by using the Ingenuity Pathway Analysis Software (IPA). The most differentially expressed genes were validated by RT-PCR in monocytes purified from 30 APS and 30 HDs. Correlation and association studies were performed with clinical and analytical variables. The effect of antiphospholipid antibodies (aPL) in the expression of a number of genes were also evaluated by in vitro studies on healthy monocytes.

**Results:** Gene expression array identified 518 significantly altered genes in monocytes from APS patients in relation to the control group (p<0.05 and fold change>2), including 352 up-regulated and 166 down-regulated. IPA analysis showed that the main canonical pathways integrated by these genes were leukocyte adhesion, diapedesis and extravasation signaling (CLDN16, ACTC1, CLDN12, CCL26, CCL23, FPR1 and FPR2), interleukin signaling (IL18, IL12B, IL22RA, NFATC1), IFN, TNF and TFGbeta signaling (IFNAR1, TNFRSF1A, SMAD6), relevant intracellular signaling pathways involved in signal transduction such as p38, Erk, STAT, TLR, JAK and NFkB, and oxidative stress production and antioxidant reponse (GPX8, CYBB, SLC2A/2,3 and 5). This analysis further identified that the most relevant disease and function in which these altered genes are involved, were leukocyte migration, inflammatory response, cardiovascular disease and free radical scavenging. In addition the alteration of several of these genes was validated by RT-PCR and associated to clinical parameters of all the patients included in the study. In vitro studies demonstrated the specific modulation of several genes by direct effect of aPLs.

**Conclusion:** Gene expression profile allows the identification of relevant genes and pathways altered in monocytes of APS patients, which are associated with the pathogenesis of the disease and modulated, at least partially, by aPLs. Thus, the identification of novel biomarkers, might contribute to the development of targeted therapies. Acknowledgements: Supported by FIS (PI01333/2015) and CTS-7940.

**Disclosure:** P. Ruiz-Limon, None; C. Perez-Sanchez, None; M. Á. Aguirre Zamorano, None; I. Cecchi, None; N. Barbarroja, None; Y. Jiménez-Gómez, None; I. Arias de la Rosa, None; M. C. Abalos-Aguilera, None; P. Segui, None; E. Collantes-Estévez, None; M. J. Cuadrado, None; C. Lopez-Pedrera, None.


**Abstract Number:** 2765

**Centre of Pressure Characteristics during Walking in Individuals with and without First Metatarsophalangeal Joint Osteoarthritis**

**Hylton Menz**¹, Maria Auhl², Jade Tan² and Shannon Munteanu¹, ¹La Trobe University, Bundoora, Australia, ²School of Allied Health, La Trobe University, Bundoora, Australia

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** ARHP Rehabilitation Science  
**Session Type:** ARHP Concurrent Abstract Session  
**Session Time:** 2:30PM-4:00PM

**Background/Purpose:** Osteoarthritis of the first metatarsophalangeal joint (1st MTPJ OA) is a common and disabling condition characterised by symptoms of joint pain and stiffness, formation of a dorsal exostosis, and progressive reduction in range of motion of 1st MTPJ dorsiflexion. Because the 1st MTPJ plays an important role in transferring the body’s centre of mass over the foot during the propulsive phase of gait, individuals with 1st MTPJ OA frequently adopt an apropulsive walking pattern. The objective of this study was to compare centre of pressure characteristics during walking in individuals with and without 1st MTPJ OA, in order to provide insights into alterations in foot function associated with this condition.
Methods: Twenty people with 1st MTPJ OA and 20 asymptomatic controls matched for age, sex and body mass index underwent gait analysis using the emed®-x400 plantar pressure system (Novel GmbH, Germany). Average and maximum centre of pressure velocity and lateral-medial force index during loading, midstance, terminal stance and preswing were compared between the groups, adjusting for contact time.

Results: During the preswing phase of gait, maximum centre of pressure velocity was significantly slower in individuals with 1st MTPJ OA (0.78 ± 0.19 vs 1.13 ± 0.36 m/sec; p=0.003), and both average and maximum lateral-medial force indices were significantly higher in individuals with 1st MTPJ OA (0.98 ± 0.14 vs 0.82 ± 0.13; p<0.001 and 1.37 ± 0.29 vs 1.15 ± 0.15; p=0.008, respectively). See Figures 1 and 2. Non-weightbearing 1st MTPJ dorsiflexion range of motion was significantly associated with maximum centre of pressure velocity (r=0.54, p<0.001) and average lateral-medial force index (r=-0.44, p=0.004) during preswing.

Conclusion: These findings suggest that individuals with 1st MTPJ OA may generate less forward momentum when walking due to a lateral transfer of force during propulsion, possibly due to decreased range of 1st MTPJ dorsiflexion.

Disclosure: H. Menz, None; M. Auhl, None; J. Tan, None; S. Munteanu, None.


Abstract Number: 2766
Physical Therapy Vs. Internet-Based Exercise Training for Patients with Knee Osteoarthritis: Results of a Randomized Controlled Trial

Kelli Allen1, Liubov Arbeeva2, Leigh F. Callahan3, Yvonne M. Golightly4, Adam P. Goode5, Bryan Heiderscheit6, Carla Hill7, Kim Huffman8, Herbert Seversen9, and Todd A. Schwartz10, 1Rheumatology, University of North Carolina at Chapel Hill and Durham VA Medical Center, Durham, NC, 2Thurston Arthritis Research Center, University of North Carolina at Chapel Hill, Chapel Hill, NC, 3Thurston Arthritis Research Center, University of North Carolina, Chapel Hill, NC, 4Epidemiology, University of North Carolina at Chapel Hill, Chapel Hill, NC, 5O, Duke University, Durham, NC, 6Department of Orthopedics and Rehabilitation, University of Wisconsin, Madison, WI, 7University of North Carolina at Chapel Hill, Chapel Hill, NC, 8School of Medicine, Division of Rheumatology, Immunology and Molecular Physiology and Durham VA Medical Center, Duke University, Durham, NC, 9Oregon Research Institute, Durham, OR, 10Biostatistics, University of North Carolina at Chapel Hill, Chapel Hill, NC

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: ARHP Rehabilitation Science
Session Type: ARHP Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: The majority of adults with osteoarthritis (OA) are inactive, highlighting the need for continued efforts to promote regular engagement in exercise. Few studies have directly compared different strategies, ranging in intensity of resources required, for improving exercise and related outcomes among patients with OA. The objective of this study was to compare the effectiveness of physical therapy (PT) (with an emphasis on a home exercise program) and internet-based exercise training (IBET) among individuals with knee OA.

Methods: This was a randomized controlled trial of 350 participants with symptomatic knee OA, allocated to PT, IBET and a wait list (WL) control group in a 2:2:1 ratio, respectively. The PT group received up to 8 individual visits within 4 months. The IBET program provided tailored exercises, video demonstrations, and guidance on progression. The primary outcome was the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and four physical performance tests were included as secondary outcomes: unilateral stand test, 30-second chair stand, 2-minute march, and Timed Up-and-Go. Outcomes were assessed at baseline, 4 months and 12 months. General linear mixed effects modeling compared changes in outcomes among study groups, using an intent-to-treat paradigm.

Results: At 4-months, both the PT and IBET groups improved in WOMAC score, but mean differences compared to WL were not statistically significant (PT: -3.36, 95% Confidence Interval (CI) = -6.84, 0.12, p=0.06; IBET: -2.70, 95%CI = -6.24, 0.85, p=0.14). Similarly, at 12-months mean differences compared to WL were not statistically significant for either group (PT: -1.59, 95% Confidence Interval (CI) = -5.26, 2.08, p=0.39; IBET: -2.63, 95%CI = -6.37, 1.11, p=0.17). Results for WOMAC subscales and physical performance tests are shown in Table 1.

Conclusion: Modest improvements in outcomes following both PT and IBET were observed in comparison to a WL control group. Initial gains were better for the PT group, but the IBET group maintained improvements in WOMAC better over time. A combination of these two interventions, with IBET used as a tool to facilitate home exercise following PT, may result in more robust effects and maintenance over time.
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Baseline to 4-Month Difference (95% CI)</th>
<th>Difference in Baseline to 4-Month vs. WL (95% CI), p-value</th>
<th>Baseline to 12-Month Difference (95% CI)</th>
<th>Difference in Baseline to 12-Month vs. WL (95% CI), p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WOMAC Total (N=348)*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WL</td>
<td>-3.37 (-6.33,-0.41)</td>
<td>--</td>
<td>-2.83 (-5.93,0.27)</td>
<td>--</td>
</tr>
<tr>
<td>PT</td>
<td>-6.73 (-8.86,-4.6)</td>
<td>-3.36 (-6.84,0.12), 0.06</td>
<td>-4.42 (-6.66,-2.17)</td>
<td>-1.59 (-5.26,2.08), 0.39</td>
</tr>
<tr>
<td>IBET</td>
<td>-6.06 (-8.29,-3.84)</td>
<td>-2.70 (-6.24,0.85), 0.14</td>
<td>-5.46 (-7.82,-3.09)</td>
<td>-2.63 (-6.37,1.11), 0.17</td>
</tr>
<tr>
<td>WOMAC Function (N=348)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WL</td>
<td>-2.30 (-4.46,-0.14)</td>
<td>--</td>
<td>-1.51 (-3.76,0.74)</td>
<td>--</td>
</tr>
<tr>
<td>PT</td>
<td>-4.77 (-6.32,-3.23)</td>
<td>-2.48 (-5.02,0.07), 0.06</td>
<td>-3.3 (-4.91,-1.68)</td>
<td>-1.79 (-4.45,0.87), 0.19</td>
</tr>
<tr>
<td>IBET</td>
<td>-3.74 (-5.36,-2.12)</td>
<td>-1.44 (-4.03,1.15), 0.27</td>
<td>-3.4 (-5.11,-1.7)</td>
<td>-1.90 (-4.61,0.82), 0.17</td>
</tr>
<tr>
<td>WOMAC Pain (N=350)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WL</td>
<td>-0.66 (-1.41,0.09)</td>
<td>--</td>
<td>-0.64 (-1.38,0.09)</td>
<td>--</td>
</tr>
<tr>
<td>PT</td>
<td>-1.11 (-1.65,-0.58)</td>
<td>-0.45 (-1.33,0.42), 0.31</td>
<td>-0.70 (-1.23,-0.16)</td>
<td>-0.05 (-0.92,0.81), 0.90</td>
</tr>
<tr>
<td>IBET</td>
<td>-1.59 (-2.15,-1.02)</td>
<td>-0.93 (-1.82,-0.03), 0.04</td>
<td>-1.15 (-1.71,-0.59)</td>
<td>-0.51 (-1.39,0.38), 0.26</td>
</tr>
<tr>
<td>Unilateral Stand Time (N=350)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WL</td>
<td>0.04 (-0.75,0.82)</td>
<td>--</td>
<td>-0.09 (-0.88,0.69)</td>
<td>--</td>
</tr>
<tr>
<td>PT</td>
<td>-0.59 (-1.15,-0.03)</td>
<td>-0.63 (-1.56,0.30), 0.19</td>
<td>-0.05 (-0.6,0.50)</td>
<td>0.04 (-0.89,0.98), 0.93</td>
</tr>
<tr>
<td>IBET</td>
<td>0.02 (-0.57,0.61)</td>
<td>-0.02 (-0.97,0.93), 0.97</td>
<td>-0.05 (-0.64,0.53)</td>
<td>0.04 (-0.91,1.00), 0.93</td>
</tr>
<tr>
<td>30 Second Chair Stand (N=350)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WL</td>
<td>0.18 (-0.87,1.23)</td>
<td>--</td>
<td>0.66 (-0.27,1.58)</td>
<td>--</td>
</tr>
<tr>
<td>PT</td>
<td>-0.13 (-0.87,0.61)</td>
<td>-0.31 (-1.55,0.94), 0.63</td>
<td>0.16 (-0.49,0.82)</td>
<td>-0.49 (-1.58,0.60), 0.37</td>
</tr>
<tr>
<td>IBET</td>
<td>0.50 (-0.29,1.28)</td>
<td>0.32 (-0.95,1.59), 0.62</td>
<td>0.90 (0.20,1.60)</td>
<td>0.24 (-0.87,1.35), 0.67</td>
</tr>
<tr>
<td>2 Minute March Test (N=350)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WL</td>
<td>-8.43</td>
<td>--</td>
<td>0.00 (-6.49,6.48)</td>
<td>--</td>
</tr>
</tbody>
</table>
**Active Yet Sedentary: The Association of Moderate to Vigorous Physical Activity and Sedentary Behavior with Incident Functional Limitation in Knee OA**

**Hiral Master**¹, Louise Thoma¹, Meredith Christiansen¹, Dana Mathews² and Daniel White³, ¹Physical Therapy and Biomechanics and Movement Science, University of Delaware, Newark, DE, ²Physical Therapy, Biomechanics and Movement Science, University of Delaware, Newark, DE, ³Department of Physical Therapy, University of Delaware, Newark, DE

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** ARHP Rehabilitation Science  
**Session Type:** ARHP Concurrent Abstract Session  
**Session Time:** 2:30PM-4:00PM

**Background/Purpose:**

Engaging in adequate levels of moderate to vigorous physical activity (MVPA) reduces the risk of functional limitation in people with knee osteoarthritis (OA). Sedentary behavior (SED) is common in those with either high or low level of MVPA, and is also linked to poor health outcomes in people with knee OA. However, it remains unclear whether being sedentary regardless of MVPA level increases one's risk of developing functional limitation in people with knee OA. The purpose of this study was to examine the association of MVPA and SED with incident functional limitation 4 years later in people with knee OA.

**Methods:**

We used publically available data from the Osteoarthritis Initiative (OAI). Our primary exposures were time spent in MVPA and SED that were collected at the 48-month OAI visit (baseline) using an accelerometer (Actigraph GT1M) worn for >10 hours/day for ≥4 days. We classified people as having at least one 10 min bout/week in MVPA defined as ≥2020 counts/min. SED was defined as time spent at <100 counts/minutes standardized to wear time. We classified people as being Active-Low SED (≥1 MVPA bouts and lowest SED tertile), Active-High SED (≥1 MVPA bouts and top two SED tertiles, i.e. more sedentary), Inactive-Low SED (No MVPA bout and lowest SED tertile), and Inactive-High SED (No MVPA bout and top two SED tertiles). We defined our outcome, incident...
functional limitation, as >12 sec for the 5 repetition sit-to-stand test (STS) and <1.22 m/sec gait speed during a 20-meter walk at the 96-month OAI visit (4 years later). To examine the association of MVPA and SED with incident function limitation, we calculated risk ratios and 95% confidence intervals [RR (95%CI)] adjusted for potential confounders.

**Results:**

We included 1927 people with valid exposure data (55% female, age [mean±(SD)] 65.1±8.8 years, BMI 28.4±4.9 kg/m²) at baseline. Of those free of the outcome at baseline and had follow-up data, 15% (n=162/1091) and 21% (n=236/1133) developed functional limitation 4 years later measured by STS and gait speed, respectively. The Active-High SED group had a similar risk of functional limitation compared with the Active-Low SED group. The Inactive-High SED group had 1.5 times the risk of incident functional limitation compared with the Active-Low SED group. The Inactive-Low SED group had 1.5 to 1.6 times the risk of incident functional limitation compared with the Active-Low SED group (Table).

**Conclusion:**

For active people, high SED was not associated with incident functional limitation compared to those who were low SED. However, those who were inactive had an increased risk of incident functional limitation regardless of SED compared with people who were Active-Low SED. Thus, being active may potentially offset the functional consequences of SED. Effective clinical interventions to improve MVPA are needed for people with knee OA.

**Table:** Risk Ratios (RR) of the incident functional limitation at the 4-year follow-up as measured by STS and gait speed.

<table>
<thead>
<tr>
<th></th>
<th>Baseline Mean (SD)</th>
<th>Incident Function Limitation/total* %</th>
<th>Unadjusted RR (95% CI)</th>
<th>**Adjusted RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active-Low SED</td>
<td>9.9 (2.7)</td>
<td>31/293</td>
<td>10.6</td>
<td>Reference</td>
</tr>
<tr>
<td>Active-High SED</td>
<td>9.9 (2.6)</td>
<td>49/412</td>
<td>11.9</td>
<td>1.1 (0.7-1.8)</td>
</tr>
<tr>
<td>Inactive-Low SED</td>
<td>11.1 (3.2)</td>
<td>20/106</td>
<td>18.9</td>
<td>1.9 (1.1-3.2)</td>
</tr>
<tr>
<td>Inactive-High SED</td>
<td>11.2(2.9)</td>
<td>62/280</td>
<td>22.1</td>
<td>2.2 (1.4-3.3)</td>
</tr>
<tr>
<td><strong>Gait speed</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active-Low SED</td>
<td>1.4 (0.2)</td>
<td>45/311</td>
<td>14.4</td>
<td>Reference</td>
</tr>
<tr>
<td>Active-High SED</td>
<td>1.4 (0.2)</td>
<td>75/434</td>
<td>17.3</td>
<td>1.3 (0.9-1.8)</td>
</tr>
<tr>
<td>Inactive-Low SED</td>
<td>1.3 (0.2)</td>
<td>31/120</td>
<td>25.8</td>
<td>1.9 (1.3-2.9)</td>
</tr>
<tr>
<td>Inactive-High SED</td>
<td>1.2 (0.2)</td>
<td>85/268</td>
<td>31.7</td>
<td>2.3 (1.7-3.2)</td>
</tr>
</tbody>
</table>

*Incident function limitation is defined as STS > 12 sec or Gait speed < 1.22 m/sec.

**Adjusted for education, race, sex, baseline age, BMI and comorbidities; 95% CI = 95% confidence interval

**Disclosure:** H. Master, None; L. Thoma, None; M. Christiansen, None; D. Mathews, None; D. White, None.


**Abstract Number:** 2768

**Effects of a Home-Based Telephone-Supported Physical Activity Program on Physical Function Among Older Adults with Chronic Low Back Pain**

Adam P. Goode¹, Shannon Taylor², Susan Hastings³, Catherine Stanwyck³, Cynthia Coffman³ and Kelli Allen⁴, ¹O, Duke University, Durham, NC, ²Health Services Research and Development, Durham VA Medical Center, Durham, NC, ³Durham VA Medical Center, Durham, NC, ⁴Rheumatology, University of North Carolina at Chapel Hill and Durham VA Medical Center, Durham, NC
Background/Purpose: The majority of older adults with chronic low back pain (cLBP) are inactive and have significant functional limitations, highlighting the need for continued efforts to promote regular engagement in exercise and physical activity. Few studies have directly compared different strategies, including behavioral interventions (i.e., cognitive behavioral therapy) for improving physical function-related outcomes among older adults with cLBP. The objective of this trial was to collect preliminary data on the efficacy of physical activity (PA) only and PA + cognitive behavioral therapy for pain (CBT-P) programs for improving functional outcomes among older adult Veterans with cLBP. We hypothesized that home-based telephone-supported PA only and PA + CBT-P program would produce a significant increase in older adults’ physical function.

Methods: Older adult Veterans with cLBP at the Durham VA HealthCare System were randomized to 12-week telephone-supported PA only or PA + CBT-P interventions or a wait list (WL) control group. A physical therapist conducted the initial evaluation and established the PA and exercise program in person with the participant. Follow up telephone calls were delivered by a physical therapist (n=3) and an exercise counselor (n=10). The PA intervention included stretching, strengthening, and aerobic activities; CBT-P was tailored for older adults with cLBP. Outcomes measured at baseline and 12-weeks were: physical performance (timed up-and-go; TUG), self-report physical function (PROMIS Health Assessment Questionnaire (iHAQ)), self-reported LBP-specific disability (Roland-Morris Low Back Pain and Disability Questionnaire (RMDQ)), the Satisfaction with Physical Function Scale, and pain catastrophizing (from the Coping Strategies Questionnaire). General linear mixed models were used to compare outcomes over 12-weeks of follow-up among groups. Effect sizes were calculated using Cohen’s d.

Results: Mean age of participants was 70.3 years; 53% were Non-white, 93% Male, and 83% had back pain symptoms lasting longer than 5 years. No significant differences were found for the PA or PA + CBT-P group, compared with the WL group, for primary outcomes of TUG or PROMIS HAQ; however, effect sizes were moderate to large (d= -0.64) for improving physical function on the PROMIS HAQ in the PA only group and small for improvements in the TUG for both the PA only (d= -0.28) and PA+CBT-P (d= -0.31) groups. A significant difference was found for the RMDQ at 12 week follow-up for the PA only group (-4.10 ((95% CI -6.85, -1.34; p<0.01)) compared to WL, with a moderate to large effect size (d= -0.78). Small effect sizes were found for Satisfaction with Physical Function Scale and Coping Strategies Questionnaire Catastrophizing scores in both the PA and PA+CBT-P.

Conclusion: Results from this pilot trial suggest that a home-based telephone-supported PA program may be effective for improving some aspects of physical functioning among inactive older adults with cLBP. The addition of CBT-P did not result in a significant additive affect for increasing physical function or changes in behavioral outcomes. Results provide support for a larger trial investigating telephone-supported PA for older adults with cLBP.

Disclosure: A. P. Goode, None; S. Taylor, None; S. Hastings, None; C. Stanwyck, None; C. Coffman, None; K. Allen, None.

Abstract Number: 2769

Predictive Value of Leisure-Time Physical Activity in Women with Systemic Erythematosus Lupus on Physical and Mental Health

Alix St-Aubin¹, Anne-Sophie Julien², Carolyn Neville³, Ellie Aghdassi⁴, Stacey Morrison⁵, Jiandong Su⁶, Janet E. Pope⁷, Sara Hewitt⁸, Christian Pineau⁹, Paula Harvey¹⁰, Michal Abrahamowicz¹¹, Deborah Da Costa¹², Paul Poirier¹³ and Paul R. Fortin¹⁴, ¹Division of Rheumatology, Department of Medicine, CHU de Québec – Université Laval, Quebec, QC, Canada, ²CHU de Quebec - Universite Laval, Quebec City, QC, Canada, ³Department of Medicine, McGill University Health Center, Montreal, QC, Canada, ⁴Epidemiology Division, The Toronto Western Hospital, Toronto, ON, Canada, ⁵Rheumatology, Krembil Research Institute, Toronto, ON, Canada, ⁶Rheumatology, Centre for Prognosis Studies in the Rheumatic Diseases, Toronto Western Hospital and University of Toronto, Toronto, ON, Canada, ⁷Department of Medicine, Division of Rheumatology, University of Western Ontario, St Joseph's Health Care, London, ON, Canada, ⁸Department of Medicine, Division of Rheumatology, University of Western Ontario, St-Joseph Health Care, London, ON, Canada, ⁹Rheumatology, McGill University Health Center, Montreal, QC, Canada, ¹⁰Cardiology, Women's College
SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: ARHP Rehabilitation Science
Session Type: ARHP Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that is associated with a higher mortality due to higher risk of cardiovascular events. Although physical activity is known to decrease cardiovascular morbidity and mortality, sedentary behavior highly prevails in SLE patients. The purpose of this study was to determine whether leisure-time physical activity level is associated with a better quality of life at one year.

Methods: Patients (n=287) in the Health Improvement and Prevention Program in SLE (HIPP) were randomized either into the « now » group (n=144) which received a comprehensive behavioral intervention including a supervised exercise program in the first 12 months or the « later » group (n=143) which received the intervention after 12 months. At baseline, 12 and 24 months, patients were asked to complete questionnaires assessing leisure-time physical activity (LTPA) measured by the Aerobics Centre Longitudinal Study physical activity questionnaire or ACLS, quality of life using the physical (PCS) and mental (MCS) component scales of the Short-Form 36, disease damage (Systemic Lupus International Collaborating Clinics Damage Index or SLICC), disease activity (Systemic Lupus Erythematosus Disease Activity Index or SLEDAI) and coronary heart disease risk factor using the Framingham risk score. LTPA levels were separated on the basis of hour of metabolic equivalent (MET) performed weekly: 1) sedentary group (no LTPA activity), 2) insufficiently active (<7.5 MET-h/week) and 3) active (>7.5 MET-h/week). Logistic and linear regressions were used to assess the effect of LTPA level, study group and their interactions on dichotomous and continuous outcomes respectively. Models were also adjusted for age at baseline.

Results: A total of 276 patients were included in this analysis. At baseline, no associations with the LTPA level were found regarding the SLEDAI, SLICC and Framingham scores. However, for the PCS, there was a significant difference for the LTPA levels (p<0.001). The active group reported statistically and clinically better physical health (43.78±0.92 vs. 36.97±1.30, p<0.001) when compared with the insufficiently active group and the sedentary group (37.12±1.35, p=0.0002), while there were no differences between the insufficiently active and the sedentary groups. At one year, those same associations are found between the LTPA levels (p=0.003). For the MCS , there was no statistical difference between the study groups but there was a difference between the LTPA level only in the unadjusted analysis, where the active group (47.97±0.99) had a significantly better score than the insufficiently active (43.60±1.38, p<0.05)

Conclusion: Our data suggests that the LTPA level is associated with better physical activity at baseline and a good predictor of the physical activity status at one year but is only associated with mental status at baseline. Further research are needed to better understand the LTPA level in SLE patients and to tailor appropriate exercise-based interventions.

Disclosure: A. St-Aubin, None; A. S. Julien, None; C. Neville, None; E. Aghdassi, None; S. Morrison, None; J. Su, None; J. E. Pope, AbbVie, Amgen, Bayer, BMS, Celtrion, Eli Lilly and Company, Merck, Novartis, Pfizer, Roche, UCB, 5.Amgen, Bayer, BMS, GSK, Merck, Novartis, Pfizer, Roche, UCB, 2; S. Hewitt, None; C. Pineau, None; P. Harvey, None; M. Abrahamowicz, None; D. Da Costa, None; P. Poirier, None; P. R. Fortin, None.


Abstract Number: 2770

Using Fitbits. Fitabase®, and Remote Coaching to Increase Physical Activity in Employees with Knee Osteoarthritis Symptoms

Pamela Semanik¹, Julia (Jungwha) Lee², Christine Pellegrini³, Jing Song⁴ and Rowland W. Chang⁵, ¹College of Nursing, Rush University, Chicago, IL, ²Preventive Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, ³Department of Preventive Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, ⁴Center for Healthcare Studies, Northwestern
SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: ARHP Rehabilitation Science
Session Type: ARHP Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Knee osteoarthritis (OA) affects approximately 6% of adults and is a leading cause of disability among U.S. adults. Physical activity (PA) is known to improve the health status of those with knee OA. In 2007-2008, 49% of all employed adults failed to meet U.S. PA recommendations. This pilot study examined the feasibility of a scalable worksite PA program for employees with knee OA symptoms working at a large insurance firm.

Methods: After exclusion criteria, 61 subjects were randomized to either the MobilWise (MW) lifestyle intervention (n=20), the Fitbit Only (FO) intervention (n= 21), or waitlist control (WC) group (n= 20). Randomization was stratified based on current PA tracker ownership/use and meeting/not meeting PA recommendations of 150 minutes/week of moderate-vigorous PA. MW and FO received an education session including detailed instruction on PA/benefits and the Fitbit Flex monitor. MW group also received weekly individual motivational interviewing-based personalized coaching sessions by phone for 12 weeks. MW and FO groups were asked to synchronize their Fitbit at least twice weekly using the Fitbit App to transfer data to a storage service (Fitabase®), but only MW data were viewed weekly for coaching feedback. WC received the education session and a Fitbit at study’s end. Measures at baseline and 3 month follow-up included demographics, PA assessed by triaxial accelerometer (average 7-day vector magnitude counts), and WOMAC pain and function. Feasibility of conducting a larger RCT was assessed by tracking enrollment/retention. Acceptability of MW and FO interventions was assessed by tracking the personal monitor synchronization frequency on Fitabase® and the number of completed coaching encounters.

Results: Participants at baseline were primarily obese (59%), female (73%), Caucasian (44%), with mean age 51 years, BMI 33 kg/m². Of 10 participants not completing the study, 6 left the company and 4 dropped. Completing participants were not different (BMI and waist circumference) from non-completers.

Feasibility assessment revealed 63% of those screened via web tool signed consents. Proportion of monitored participants who regularly synchronized Fitbits with Fitabase® was 93%. Retention ranged from 80% (WC), 80% (FO) to 95% (MW), with 100% completing MW coaching calls.

Conclusion: MobilWise was moderately successful at improving PA levels and self-reported function in employees with knee OA symptoms, but may not be required to produce change in all those at risk. The Fitbit Only group had equally good/better (improved pain) results at 3 months.
NOMID-Associated Complications in Mice Are Prevented By CDD-450, a Small Molecule Inhibitor of the Mitogen-Activated Protein Kinase-Activated Protein Kinase 2 (MK2) Pathway

Gabriel Mbalaviele, Chun Wang, Susan Hockerman, Jon Jacobsen, Jeff Hirsch, Steve Mnich, Matt Saabye, Hal Hoffman and Joseph Monahan

Medicine, Washington University School of Medicine, St. Louis, MO, Confluence Life Sciences, Inc, St. Louis, MO, University of California, San Diego, San Diego, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Innate Immunity and Rheumatic Disease
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: NLRP3-activating mutations cause cryopyrinopathies of which NOMID is the most severe phenotype. NLRP3 assembles a protein complex, responsible for the maturation of IL-1β and IL-18. NOMID-associated inflammation, not bone phenotype is resolved by IL-1 biologics, but these drugs require parenteral injection and are costly. Engineered mice harboring a mutation found in NOMID patients exhibit several features of the human disease, including excessive IL-1β and IL-18 secretion and low bone mass. Here, we tested the hypothesis that the p38 MAPK/MK2 (p38) axis is central in the biosynthesis of pro-IL-1β and NLRP3, and as a result, inhibition of this pathway may provide efficacy in NOMID mice. We used our proprietary p38/MK2 pathway inhibitor, CDD-450 that is predicted to be safer and more efficacious than global p38 inhibitors.

Methods: CDD-450 selectivity for the p38/MK2 complex was evaluated by comparing p38 phosphorylation of MK2 vs other substrates including PRAK. CDD-450 efficacy was assessed in vitro and in vivo. For in vivo studies, floxed mice expressing NLRP3 carrying D301N substitution, ortholog of human D303N, were crossed with Cre-ER for postnatal conditional activation of NLRP3 upon exposure to tamoxifen, injected for 3 consecutive days over 2 weeks to generate NOMID mice. Mice were fed with normal or 1000 ppm CDD-450-formulated chow beginning 3 days before Tam exposure. This formulation yielded steady-state serum CDD-450 levels, which in pilot studies suppressed LPS-induced cytokine production by >80%. The studies were carried for up to 7 weeks.

Results: CDD-450 inhibited p38 phosphorylation of MK2 with low nanomolar potency and was >700-800x less potent at inhibiting p38 phosphorylation of PRAK and ATF2. NOMID mice produced excessive amounts of IL-1β; approximately 35% of these mice died during the course of the study. However, mice who survived, exhibited severe body weight loss and developed neutrophilia, thrombocytosis, lymphopenia, anemia, and splenomegaly. Remarkably, all CDD-450-treated mice survived and exhibited reduced weight loss as a result of abrogated or at least attenuated disease severity. NOMID mice also exhibited osteopenia, coincident with increased numbers of osteoclasts, responses that were inhibited >95% by CDD-450. Furthermore, in vitro osteoclast differentiation of...
mouse bone marrow-derived macrophages and IL-1β production by these cells were also blocked by CDD-450. From a translational prospective, human peripheral blood mononuclear cells (PBMC) were isolated from a cryopyrin-associated periodic syndrome (CAPS) patient, in which the disease is triggered upon exposure to low temperatures. CAPS PBMC, but not WT PBMC produced large amounts of IL-1β at 32°C, an event that was inhibited by CDD-450 in a dose-dependent manner. In contrast, WT PBMC cultured at 37°C produced IL-1β only when they were exposed to LPS, a response that was also reduced by CDD-450.

**Conclusion:** CDD-450 is a selective inhibitor of the p38/MK2 axis. Importantly, this compound exhibits sustained efficacy in NOMID mice and human cell systems. These results support ongoing efforts for clinical development of this compound for the treatment of inflammatory disorders.

**Disclosure:** G. Mbalaviele, Conuence Life Sciences, 4, Confluence Life Sciences, 5; C. Wang, Confluence Life Sciences, 3; S. Hockerman, Confluence Life Sciences, 3; J. Jacobsen, Confluence Life Sciences, 3; J. Hirsch, Confluence Life Sciences, 3; S. Mnich, Confluence LifeSciences, 3; H. Hope, Confluence Life Sciences, 3; M. Saabye, Confluence Life Sciences, 3; H. Hoffman, None; J. Monahan, Confluence Life Sciences, 3.


**Abstract Number:** 2772

**Unbound IL-18 Distinguishes Human Macrophage Activation Syndrome from Familial Hemophagocytic Lymphohistiocytosis and Affects Innate Versus Adaptive Murine Lymphocytes Differently**

Paul Tsoukas¹, Eric Weiss², Dirk Holzinger³, Charlotte Girard⁴, Dirk Foell⁵, Alexei A. Grom⁶, Sandra Ammann⁷, Stephan Ehl⁷, Eduardo Schiffrin⁸, Adriana Almeida de Jesus⁹, Raphaela Goldbach-Mansky⁹, Cem Gabay¹⁰ and Scott Canna¹¹, ¹Pediatric Rheumatology, Children’s Hospital of Pittsburgh, Pittsburgh, PA, ²RK Mellon Institute, Children’s Hospital of Pittsburgh, Pittsburgh, PA, ³Department of Pediatric Rheumatology and Immunology, University of Muenster, Muenster, Germany, ⁴Division of Rheumatology, Department of Internal Medicine Specialties, University Hospital of Geneva, Geneva, Switzerland, ⁵University of Muenster, Muenster, Germany, ⁶Pediatric Rheumatology, Cincinnati Children’s Hospital, Cincinnati, OH, ⁷Center for Chronic Immunodeficiency, Faculty of Medicine, University of Freiburg, Freiburg, Germany, ⁸AB2 Bio, Lausanne, Switzerland, ⁹Translational Autoinflammatory Disease Studies (TADS), Laboratory of Clinical Investigation and Microbiology (LCIM), NIAID/NIH, Bethesda, MD, ¹⁰SCQM, Geneva, Switzerland, Geneva, Switzerland, ¹¹Richard King Mellon Foundation Institute for Pediatric Research, Children’s Hospital of Pittsburgh, Pittsburgh, PA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** Innate Immunity and Rheumatic Disease  
**Session Type:** ACR Concurrent Abstract Session  
**Session Time:** 2:30PM-4:00PM

**Background/Purpose:**

Persistently and extremely elevated serum IL-18 has been associated with Macrophage Activation Syndrome (MAS). Chronic IL-18 is hypothesized to contribute to excessive interferon (IFN)-γ and MAS-like inflammation. However, NK cells in systemic juvenile idiopathic arthritis (sJIA) fail to increase IFN-γ production in response to IL-18. In contrast to IL-18 insensitivity in sJIA, acutely blocking IL-18 successfully treated a patient with NLRC4-MAS.[1] Due to the complex role of IL-18 in MAS and related diseases, we proposed to 1) characterize IL-18 in hyperferritinemic diseases, and 2) characterize NK and other IL-18 responsive cells in murine models of chronic IL-18 exposure.

**Methods:**

Serum from patients with active sJIA, sJIA-MAS, Infection-Associated Hemophagocytic Lymphohistiocytosis or familial HLH (fHLH) was assayed by ELISA for total IL-18 and related cytokines. Transcriptional and flow cytometric assessment of lymphocytes from WT, Nlrc4 mutant (N4-TS), and IL-18 transgenic (118tg) mice was also performed.

**Results:**
Disease activity markers were comparable across the human cohort. Total IL-18 was substantially higher in sJIA-MAS than fHLH. IL-18 Binding Protein (IL-18BP) was not significantly different between hyperferritinemic syndromes, resulting in substantial free IL-18 in sJIA-MAS. By contrast, CXCL9 (a marker of IFN-g activity) was somewhat higher in fHLH. The ratio of total IL-18 to CXCL9 provided a basis for distinguishing sJIA-MAS from fHLH (ROC area under the curve = 0.93). A ratio > 2.3 provided 83% sensitivity and 100% specificity in distinguishing MAS from fHLH. (Figure 1)

Though we have observed increased serum IL-18 in N4-TS mice, we detected free IL-18 only in Il18tg mice. Consistent with this finding, we identified downregulation of the IL-18 receptor (IL-18R) in NK cells of Il18tg but not WT or N4-TS mice. Il18tg NKs had increased transcription of genes encoding perforin, IL-12R, and STAT1 but not IFN-g, suggesting a poised state of activation. The pattern of IL-18R expression in T cells differed from NKs in that we observed cell surface upregulation of IL-18R on activated tissue-resident CD8+ T cells in both N4-TS and Il18tg mice, but not WT.

Conclusion:

Delays in precise diagnosis in hyperferritinemic syndromes may contribute to increased morbidity and mortality. We found that a diagnostic approach balancing assessment of inflammasome activity (represented by IL-18) with IFN-g activity (represented by CXCL9) impressively distinguished MAS from fHLH in this retrospective cohort. Whereas high IL-18 induces insensitivity in NKs, our data suggest it may promote exuberant responses by CD8+ T cells. Though the downstream effects of increased IL-18 on T cells requires further analysis, our data raise the possibility that the pathogenic effects of IL-18 in MAS are mediated through activated T cells.

Reference:

[1] Canna SW et al., JACI, 2017

Disclosure: P. Tsoukas, None; E. Weiss, None; D. Holzinger, None; C. Girard, None; D. Foell, None; A. A. Grom, Novartis, NovImmune and AB2bio Ltd, 5; S. Ammann, None; S. Ehl, None; E. Schiffrin, AB2bio Ltd, 3; A. Almieda de Jesus, None; R. Goldbach-Mansky, None; C. Gabay, Roche, Pfizer, AB2 Bio, 2, Sanofi, AB2 Bio, AbbVie, Pfizer, BMS, MSD, Roche, Novartis, 5; S. Canna, None.


Abstract Number: 2773

Severe Juvenile Arthritis Associated with a De Novo Gain-of-Function Germline Mutation in MYD88

Keith A. Sikora1, Joshua R. Bennett2, Laurens Vyncke3, Zuoming Deng4, Wanxia Li Tsai2, Ewald Pauweles5, Gerlinde Layh-Schmitt2, April D. Brundidge2, Fatemeh Navid2, Kristien Zaal6, Eric Hanson2, Massimo G. Gadina7, Louis M. Staudt8, Thomas A. Griffin9, Jan Tavernier3, Frank Peelman3 and Robert Colbert2, 1Pediatric Translational Research Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, 2National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, 3Department of Biochemistry, Ghent University, Ghent, Belgium, 4Biodata Mining & Discovery, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, 5Center for Molecular Modeling, Ghent University, Ghent, Belgium, 6Light Imaging Section, Office of Science and Technology, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, 7Translational Immunology, Office of Science and Technology, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, 8National Cancer Institute, National Institutes of Health, Bethesda, MD, 9Levine Children’s Hospital at Carolinas Medical Center, Charlotte, NC
**SESSION INFORMATION**

Session Date: Tuesday, November 7, 2017
Session Title: Innate Immunity and Rheumatic Disease
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

**Background/Purpose:** Using whole exome sequencing, we discovered a *de novo* heterozygous germline mutation in *MYD88* (myeloid differentiation primary response 88) (c.666T>G, p.S222R) in a child with destructive small-to-medium joint polyarticular juvenile arthritis (JA) exhibiting persistent neutrophil-predominant synovial infiltrates and rash. MyD88 is a critical adaptor protein that connects Toll-like and IL-1 receptor signaling to activation of NF-κB. Germline loss-of-function mutations in MyD88 cause immunodeficiency, while somatic gain-of-function mutations have been linked to lymphoma. We asked whether the MyD88 S222R mutation causes gain-of-function effects that could contribute to the development of destructive arthritis.

**Methods:** The patient was evaluated for peripheral blood immunophenotype, cytokine and chemokine production, and monocyte osteoclastogenesis, compared to family and other healthy controls. Functional studies in monocytes and dermal fibroblasts included gene/protein expression, quantitation of neutrophil chemotaxis, and siRNA-mediated knockdown of MyD88 and p65. Wild type (WT) or S222R MyD88-AU1 fusion proteins were re-expressed in MyD88-deficient THP-1 cells. NF-κB activity was measured via p65 subunit phosphorylation and using a reporter system. Effects on MyD88 structure were predicted via molecular dynamics modeling, and mechanistic studies were performed to assess the capacity of S222R MyD88 to oligomerize, which is necessary for signaling, using IF microscopy and proximity ligation assay (PLA).

**Results:** MyD88 S222R results in increased NF-κB p65 phosphorylation and NF-κB reporter activity in THP-1 cells compared to WT MyD88. IF microscopy and PLA demonstrated increased MyD88-S222R oligomerization compared to WT MyD88, indicating a behavior similar to MyD88-L265P, which is the most common lymphoma-associated MyD88 gain-of-function mutation. Immunophenotyping showed a persistent absence of CD16 on monocytes, an expansion of CD4+ Th17 T cells, and the presence of a previously uncharacterized CD123+CD11c+ dendritic cell population, as well as markedly increased basal and stimulated p-STAT3 in monocytes and T and B lymphocytes in the patient. Peripheral monocytes exhibited baseline interferon and chemokine gene expression signatures, while monocyte-derived osteoclasts exhibited enhanced survival and were morphologically larger than those cultured from a control. Fibroblasts exhibited significantly greater baseline expression of CXCL chemokines compared to controls, which abated upon MyD88 or p65 knockdown.

**Conclusion:** This is the first description of a *de novo* germline MyD88 mutation (S222R) associated with severe polyarticular JA. We demonstrate clear gain-of-function effects of the S222R mutation using THP-1 cells which are consistent with biologic effects in hematopoietic and non-hematopoietic cells derived from the patient, and likely to be a consequence of increased oligomerization. These effects offer plausible mechanisms for neutrophil-predominant, destructive arthritis, and support a role for single gene defects contributing to extreme JA phenotypes.

**Disclosure:** K. A. Sikora, None; J. R. Bennett, None; L. Vyncke, None; Z. Deng, None; W. L. Tsai, None; E. Pauwels, None; G. Layh-Schmitt, None; A. D. Brundidge, None; F. Navid, None; K. Zaal, None; E. Hanson, None; M. G. Gadina, None; L. M. Staudt, None; T. A. Griffin, None; J. Tavernier, None; F. Peelman, None; R. Colbert, None.


**Abstract Number:** 2774

**Activation of a Cytosolic DNA Sensor Pathway in the Etiopathogenesis of Sjögren’s Syndrome**

Harini Bagavant1, Joanna Papinska1, Grezgorz Gmyrek1, Magdalena Sroka1, Indranil Biswas2, Sai Tummala2 and Umesh S Deshmukh1, 1Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 2Oklahoma Medical Research Foundation, Oklahoma City, OK

**First publication:** September 18, 2017

**SESSION INFORMATION**

Session Date: Tuesday, November 7, 2017
Background/Purpose: Patients with Sjögren’s syndrome (SjS) often present with a heightened type I IFN response. Recognition of DNA within the cytosol by a multitude of cytosolic DNA sensors and downstream activation of the stimulator of interferon gene (STING) protein is a key pathway for the induction of type I IFN. So far, only indirect evidence suggests that this pathway might be involved in the pathophysiology of SjS. Thus, the major objective of this study was to investigate the role of STING activation in the etiopathogenesis of SjS.

Methods: Female C57BL/6 mice (10-12 weeks old) were injected with a STING agonist dimethylxanthenone-4-acetic acid (DMXAA) and control mice were treated similarly with the vehicle. Salivary glands were monitored for gene expression by real time PCR and for inflammatory cell infiltration by immunohistochemistry and flow cytometry. Salivary gland function was evaluated by measuring pilocarpine-induced salivation. Sera were analyzed for cytokines and autoantibodies. Cultured primary salivary gland cells were used to study the expression and activation of STING in vitro.

Results: DMXAA treatment rapidly upregulated the expression of Ifnβ and pro-inflammatory cytokines, both systemically and locally in the salivary glands. In the murine submandibular glands, STING expression was detected only in the acinar, but not in the ductal cells. In vitro activation of STING in cultured primary salivary gland cells rapidly phosphorylated TBK1, IRF3 and induced the expression of Ifnβ and TNFa. Within 4 weeks of treatment, in comparison with the vehicle group, DMXAA treated mice developed significantly higher incidence of sialoadenitis (1/17 versus 10/21, p=0.009). The inflammatory cell infiltrates were mainly composed of CD4+ T cells and F4/80+ activated macrophages. At early stages of the disease, significantly increased numbers of Lin- NK1.1+: NK cells (CD49b+CD49a-), tissue resident type I innate lymphoid cells (ILC1) (CD49a+CD49b-) and salivary gland ILC1 (CD49a+CD49b+) were observed in the salivary glands. The mean saliva amount in DMXAA treated group (56±14 mg) was significantly lower (p=0.001) than the untreated (80±20 mg) and the vehicle treated groups (78±25). The incidence of high titer ANA (>400) was significantly higher (p=0.02) in the DMXAA group (8/16) than in the vehicle treated group (0/8).

Conclusion: This study demonstrates that activation of STING protein induces certain features of SjS in mice. Our study also suggests that IFN-γ producing ILC1s might be involved in the initial stages of salivary gland disease in SjS. We would like to propose that apart from viral infections, conditions that cause cellular perturbations and accumulation of host DNA within the cytosol should be considered as possible endogenous triggers for SjS.

Disclosure: H. Bagavant, None; J. Papinska, None; G. Gmyrek, None; M. Sroka, None; I. Biswas, None; S. Tummala, None; U. S. Deshmukh, None.

Critical Role of Neutrophil Extracellular Traps (NETs) in Patients with Behcet’s Disease

Alexandre LE JONCOUR1,2, Stephane Loyau3, Nicolas Lelay4, Marie-Christine Bouton5, Antoine Dossier6, Anne-Claire Desbois7, Fanny Domon8, Thomas Papo9, Martine Jandrot-Perrus5, Patrice Cacoub10, Nadine Ajzenberg5, David saadoun7 and Yacine Boulaftali2, 1Département Hospitalo-Universitaire Inflammation-Immunopathologie-Biotherapie (DHU i2B), F-75005, Paris, France, 2National center for Autoimmune and Systemic rare diseases and for AutoInflammatory diseases, Paris, France, 3INSERM 1148, CHU Xavier Bichat, paris, France, 4Unité INSERM 1148, CHU Xavier Bichat, Faris, France, 5Service de Médecine Interne, CHU Xavier Bichat, Paris, France, 6Département Hospitalo-Universitaire Inflammation-Immunopathologie-Biotherapie, National center for Autoimmune and Systemic rare diseases and for AutoInflammatory diseases, Paris, France, 7Département Hospitalo-Universitaire Inflammation-Immunopathologie-Biotherapie, National center for Autoimmune and Systemic rare diseases and for AutoInflammatory diseases, Paris, France, 8Service de Médecine Interne, CHU Xavier Bichat, Paris, France, 9Département de Médecine Interne et Immunoologie Clinique, National center for Autoimmune and Systemic rare diseases and for AutoInflammatory diseases, Paris, France

First publication: September 18, 2017
Behçet's disease (BD) is a chronic systemic vasculitis characterised by muco-cutaneous, ocular, gastrointestinal, cerebral recurrent lesions. Venous thrombosis, a frequent and life-threatening complication. The etiology of BD is poorly understood but activated neutrophils have been proposed to contribute to the disease. However, evidence supporting a role for primed neutrophils in BD-associated thrombotic risk is scant. To respond to inflammatory insults, neutrophils release web-like structures, known as neutrophil extracellular traps (NETs), which are prothrombotic.

We aim to evaluate the role of NETs in the thrombotic complications in BD disease.

**Methods:**

Blood samples were collected from BD patients according to the ACR International Study Group Criteria for Behçet's disease and healthy controls (HC). Cell free DNA (CfDNA), myeloperoxidase (MPO) and DNA complexes were measured in serum using Picogreen assay and ELISA. NETosis was assessed in purified neutrophils from BD patients and HC, and analyzed by microscopy after immunostaining of MPO and DNA. Thrombin generation assay were performed in plasma of patients and HC.

**Results:**

Active BD patients (n=16) had elevated serum CfDNA levels compared to inactive BD patients (n=23) and to HC (n=8) (2105 ± 249, 1379 ± 79 and 951 ± 64 ng/ml respectively p<0.0001). MPO-DNA complexes were significantly increased in Active BD serum (n=15) compared to inactive BD (n=19) and to HC serum(n=8) (2.84 ± 0.21, 1.92 ± 0.26, and 0.32 ± 0.08 OD, respectively, p<0.001). In addition, levels of cfDNA and MPO-DNA complexes were significantly higher in Angio BD serum (n=17) compare to non-angio BD serum(n=22) (2073 ± 237 vs 1390± 0.83 ng/ml p=0.008 and 2,96 ± 0.13 vs 1.80 ± 0.26 OD p=0.004, respectively). Purified neutrophils from BD patients exhibited spontaneous NETosis compared to HC (31.7 ± 4.4% vs 5.4 ± 1.9% respectively, p=0.004). Consistently, PMA-activated neutrophils from BD patients have increased NET formation compared to neutrophils from HC (41.8 ± 2.7% vs 18 ± 3.8% respectively, p=0.002). Thrombin generation in BD plasma was significantly increased and positively correlated with MPO-DNA complexes (r² = 0.84, p=0.001 and cfDNA (r²= 0.9, p=0.002). Importantly, DNase treatment significantly decreased thrombin generation in BD plasma but had no effect in HC plasma suggesting a procoagulant role of NETs.

**Conclusion:**

Our data show for the first time the critical role of circulating NETs in BD patients. NETs may be involved in thrombi formation. Targeting NETs may represent a potential therapeutic option in BD.

**Disclosure:**

A. LE JONCOUR, None; S. Loyau, None; N. Lelay, None; M. C. Bouton, None; A. Dossier, None; A. C. Desbois, None; F. Domont, None; T. Papo, None; M. Jandrot-Perrus, None; P. Cacoub, None; N. Ajzenberg, None; D. saadoun, None; Y. Boulaftali, None.


**Abstract Number:** 2776

**Plasmacytoid Dendritic Cells in Systemic Fibrosis: Pathogenic Role in Bleomycin-Induced Fibrosis Model and Correlation with Disease in Patients with Systemic Sclerosis**

**Suzanne Kafaja**1, Isela Valera2, Anagha Divekar3, Rajan Saggar4, Dinesh Khanna5, Daniel E. Furst6 and Ram R. Singh7, 1Department of Internal Medicine, University of California Los Angeles, David Geffen School of Medicine, Division of Rheumatology, Los Angeles, CA, 2Autoimmunity and Tolerance Laboratory, Division of Rheumatology, Department of Medicine, David Geffen School of Medicine at University of California Los Angeles, Los Angeles, CA, 3Biolegend, Sa Diego, CA, 4Medicine, University of California, Los Angeles, David Geffen School of Medicine, Los Angeles, CA, 5University of Michigan, Ann Arbor, MI, 6David Geffen School of Medicine at UCLA, Los Angeles, CA, 7Autoimmunity and Tolerance Laboratory, Department of Medicine/Rheumatology, David Geffen School of Medicine at University of California Los Angeles, Los Angeles, CA

**First publication:** September 18, 2017
Fibrosis is the end-result of most inflammatory conditions, but its pathogenesis remains unclear. Studies in patients and animal models suggest a role for T-cells and innate immune cells including dendritic cells (DC) in the development of fibrosis. DCs play a role in T-cell priming and differentiation also infiltrate the lung in response to bleomycin injection in animals. DCs also accumulate in lungs of patients with idiopathic pulmonary fibrosis and in skin of patients with systemic sclerosis (SSc). However, the exact role of DCs in the pathogenesis of fibrotic diseases including SSc is unclear. We investigated the role of plasmacytoid dendritic cells (pDC) in the pathogenesis of systemic fibrosis using the bleomycin model and clinical samples from patients with systemic sclerosis (SSc).

**Methods:**
Female C57BL/6 mice were depleted of pDCs using anti-pDCA1 and were compared to mice depleted with isotype control IgG2b. Clinical observation and analyses were carried of draining LN, spleen, lungs and skin including flow cytometry, pathology, collagen production and RT PCR array. In our work, we evaluated human data (HRCT and BAL) from SSc Imatinib trial. We also examined pDCs in Peripheral blood, skin and lung in controls as well as SSc patients.

**Results:**
pDCs were more profoundly increased than other immune cells in the lung and lung-draining lymph nodes, but not in the spleen, of bleomycin-injected mice compared to control animals. Depletion of pDCs improved the clinical score, lung histopathology score, skin thickness, and collagen content compared to control antibody-treated animals. B-cells, T-cells and natural killer T-cells were reduced in the lungs, but unaffected/increased in the spleen, of pDC-depleted mice as compared to controls. pDC-depleted mice also had a reduced expression of genes involved in chemotaxis, dendritic cell differentiation, inflammation, and fibrosis in the lungs as compared to controls. In humans, while pDCs were reduced in the peripheral blood of patients with SSc compared to healthy donors, their numbers were increased in the lung and skin of patients with SSc. The frequencies of pDCs in the bronchoalveolar lavage (BAL) correlated with SSc-lung disease scores and with IL-4+ and CD4+ T-cells in BAL.

**Conclusion:**
Taken together, our observations identify the increased trafficking to pDCs to the affected organs as a potential therapeutic target in fibrotic diseases.

**Disclosure:** S. Kafaja, None; I. Valera, None; A. Divekar, None; R. Saggar, None; D. Khanna, Actelion, Bayer, BoehringerIngelheim, Chemomab, Corbus, Covis, Cytori,Eicos, EMD Serono, Genentech/Roche, Gilead, GSK, Sanofi-Aventis,UCB Pharma, NIH/NIAMS, NIH/NIAID,Bayer, BMS, Genentech/Roche, Pfizer, 2,Eicos, 4; D. E. Furst, Grant/Research Support: Amgen,BMS Novartis, Pfizer, Roche/Genentech,Corbus. Consultant:AbbVie, Amgen, BMS, Corbus, Cytori, Novartis, Pfizer, Roche/Genentech., Speakers Bureau(CME or non-promotional only): BMS, Abbvie NO stocks, royalties, direct fina, 2,see above, 5,see above, 8; R. R. Singh, None.

**Abstract Number:** 2777

**Factors Associated with Readiness for Adopting Osteoporosis Treatment Change**

**Maria I. Danila**, 1 Elizabeth J. Rahn2, Amy S. Mudano1, Ryan C. Outman3, Peng Li4, David T. Redden4, Fred A. Anderson5, Susan L. Greenspan6, Andrea Z. LaCroix7, Jeri W. Nieves8, Stuart L. Silverman9, E.S. Siris10, Nelson B. Watts11, Sigrid Ladores12, Karen Meneses12, Jeffrey R. Curtis3 and Kenneth Saag3, 1University of Alabama at Birmingham, Birmingham, AL, 2Department of Medicine, Division of Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 3Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 4Department of Biostatistics, University of Alabama at Birmingham, Birmingham, AL, 5University of Alabama at Birmingham, Birmingham, AL, 6University of Massachusetts Medical School, Worcester, MA, 7Group Health Cooperative, Seattle, WA, 8Helen Hayes, West Haven, NY, 9Cedars-Sinai Medical
SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes II
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Understanding factors associated with the readiness for adopting osteoporosis treatment change may inform the design of behavioral interventions to improve osteoporosis treatment uptake in women at high risk for fracture.

Methods: US women in the Global Longitudinal Study of Osteoporosis (GLOW) with prior self-reported fractures and not currently using osteoporosis therapy were eligible to participate in the Activating Patients at Risk for OsteoPOroSis (APROPOS) Study. Participants’ readiness for behavior change was assessed using a modified form of the Weinstein Precaution Adoption Process Model (PAPM). We defined pre-contemplative participants as those who self-classified in the unaware and unengaged stages of PAPM. Contemplative participants were defined by the undecided, decided not to act, and decided to act stages of PAPM. Bivariate tests and stepwise multivariable logistic regression evaluated the following factors associated with these two levels of readiness for behavior change: sociodemographic characteristics, health literacy, self-reported history of depression and dementia, previous treatment for osteoporosis, whether participants had been told they had osteoporosis/osteopenia, and whether they had concerns about osteoporosis.

Results: A total of 2,684 women were enrolled in APROPOS. Participants were 95% Caucasian, with a mean(SD) age 74.9(8.0) years and 77% had some college education. Overall, 25% (N=544) self-classified in the contemplative stage of behavior change. Compared to women who self-classified as pre-contemplative, contemplative women were more likely to be concerned about osteoporosis (adjusted OR[aOR]=3.2, 95% CI 2.3-4.4) and to report prior osteoporosis treatment (aOR 4.3, 95% CI 3.1-6.0). Individuals who had been told they had osteoporosis had a 12.4 fold odds to be in the contemplative group (95% CI 8.5-18.1), while those who had been told they had osteopenia had 4.1 fold odds to be in the contemplative group (95% CI 2.9-5.9).

Conclusion: Among women with high risk of future fracture, having been told by a health care provider that they had osteoporosis/osteopenia was independently associated with considering taking medications for osteoporosis. Our results suggest that in considering osteoporosis intervention design efficiency and effectiveness, women’s recognition of a diagnosis of osteoporosis/osteopenia are critical components to be considered when attempting to influence stage of behavior transitions.

Disclosure: M. I. Danila, None; E. J. Rahn, None; A. S. Mudano, None; R. C. Outman, None; P. Li, None; D. T. Redden, None; F. A. Anderson, Millenium Pharmaceuticals, 5; S. L. Greenspan, Amgen, 2,Lilly, 2; A. Z. LaCroix, Amgen, Pfizer, Sermonix, 9; J. W. Nieves, None; S. L. Silverman, Amgen, Lilly, 2,Amgen, 5; E. S. Siris, None; N. B. Watts, OsteoDynamics, 1,Shire, 2,OsteoDynamics, 4,AbbVie, Amgen, Janssen, Merck, Radius, Sanofi, 5,Amgen, Shire, 9; S. Ladores, None; K. Meneses, None; J. R. Curtis, Amgen, 2,Amgen, 5; K. Saag, Amgen, Lilly, Merck, 5,Amgen, Lilly, Merck, 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/factors-associated-with-readiness-for-adopting-osteoporosis-treatment-change

Abstract Number: 2778

Preventing Rheumatoid Arthritis: North American Perspectives of Patients and First-Degree Relatives on the Risk of Developing the Disease and of Potential Preventative Interventions

Mark Harrison1, Luke Spooner2, Marie Hudson3, Katherine Milbers4, Cheryl L. Koehn5, Axel Finckh6 and Nick Bansback7,
1Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada, 2University of British Columbia, Vancouver, BC, Canada, 3Division of Rheumatology, Jewish General Hospital, Lady David Institute for Medical Research, Montreal, QC, Canada, 4Centre for Health Evaluation and Outcomes Sciences, Vancouver, BC, Canada, 5Arthritis Consumer Expert, Vancouver, BC, Canada, 6University Hospital of Geneva, Geneva, Switzerland, 7School of Population and Public Health, University of British Columbia, Vancouver, BC, Canada

First publication: September 18, 2017
Background/Purpose: Increasingly, evidence suggests that treatment of people at risk of rheumatoid arthritis (RA) with anti-rheumatic drugs could prevent the onset of disease. Ongoing randomized controlled trials of treatments to prevent RA are starting to report their findings. There will be uncertainty about preventative treatment in practice, arising from the ability to predict who is at risk of RA, uncertain benefits and risks with preventative treatment and the convenience of treatment to the recipient. The aim of this study was to determine the preferences of pre-symptomatic, at risk people, for preventative treatment and the likely uptake of preventative treatment.

Methods: A discrete choice experiment was administered using a web survey to North American patients and first-degree relatives of patients, asking participants to first choose between sets of 2 hypothetical preventative RA treatments, then choose between their preferred treatment and 'no treatment for now'. Focus groups of RA patients, first-degree relatives of RA patients and rheumatologists identified 5 key attributes of treatment (reduction in risk of RA, how treatment is taken, chance of side effects, certainty in estimates, health care providers opinion). An experimental design using SAS developed 18 choice sets blocked into 4 sets of 11 choices, which included 2 consistency checks. DCE data was analyzed using a conditional logit regression model to estimate the significance and relative importance of attributes in influencing preferences.

Results: 597 people (25% of whom reported having RA) started and completed all tasks in the survey. The majority of the sample were from the USA (88%), aged between 25 and 64 years, modal age category was 30 to 39 years (52%), and 59% female. All attributes levels significantly influenced preferences for treatments, but how treatment is taken (oral vs. infusion $\beta=0.971$, p<0.001) was the most influential, followed in similar magnitude by reducing risk of side effects ($\beta=0.862$, p=0.001), matching of patient and health care professional preferences ($\beta=0.859$, p<0.001), and increasing risk reduction ($\beta=0.839$, p<0.001). The strength of preference for reducing uncertainty in evidence was statistically significant but smaller in magnitude (moderate from very little certainty $\beta=0.487$, P=0.005).

Respondents would be most willing to trade a reduction in risk of RA for an oral route of administration followed by a treatment preferred by their health care professional. The preferred preventative treatment was chosen over no treatment in 67% of choices.

Conclusion: Our survey suggests that the most important feature of preventative strategy for RA will be the convenience of taking treatment, followed by the potential risks and benefits of treatments, but equally the recommendation or preference of their health care provider. The degree of confidence in estimates of risks and benefits of treatments is also important in people’s decisions to accept treatment. The uptake of a preventative strategy will depend on these key factors. This evidence will help policy makers understand whether different preventative treatment strategies are likely to be acceptable to people to whom they might be offered.

Disclosure: M. Harrison, Pfizer Inc, 5,Roche Pharmaceuticals, 5,Multiple, indirect, 9; L. Spooner, None; M. Hudson, Roche Pharmaceuticals, 2,Bristol-Myers Squibb, 5; K. Milbers, None; C. L. Koehn, F. Hoffmann-La Roche Ltd, 9; A. Finckh, AbbVie, A2BIO, BMS, MSD, Pfizer, and Roche, 5; N. Bansback, None.


Abstract Number: 2779

The Patient Perspective on Bdmard Dose Reduction: A Mixed Methods Study

L.M. Verhoef1, E.M.H. Selten1, J.E. Vriezekolk1, A.J.L. de Jong2, F.H.J. van den Hoogen1,3, A.A. Den Broeder1,3 and M.E.J.L. Hulscher4, 1Rheumatology, Sint Maartenskliniek, Nijmegen, Netherlands, 2Department of Rheumatology, Rijnstate Arnhem, Arnhem, Netherlands, 3Rheumatology, Radboud university medical centre, Nijmegen, Netherlands, 4Radboud Institute for Health Sciences, IQ healthcare, Radboud university medical centre, Nijmegen, Netherlands

First publication: September 18, 2017
**Background/Purpose:** biological DMARDs (bDMARDs) are effective in the treatment of RA, but are also associated with side-effects and high costs. Dose reduction of bDMARDs, after low disease activity is reached, is safe and effective. To date, few studies have focused on bDMARD dose reduction from the patient perspective. Therefore, the aim of this study was to identify the factors that play a role for patients when considering dose reduction, and to determine their relative importance.

**Methods:** A mixed methods design was used in which we 1) identified influencing factors by performing qualitative interviews and 2) ranked these factors using a Maximum Difference Scaling questionnaire.

Phase 1: We performed semi-structured interviews with RA patients. Interviews were transcribed verbatim and two researchers analyzed the transcriptions by inductive thematic analysis.

Phase 2: The influencing factors were derived from the interviews and used in a Maximum Difference Scaling experiment with RA patients from 3 different centers in the Netherlands (an academic hospital, a specialized hospital and a large general hospital). The survey included 18 questions in which patients were asked to choose the most and least important factor from a subset of 5 factors. The mean relative importance score (RIS) for each factor was calculated using hierarchical Bayes modeling.

**Results:** For phase 1 and phase 2, 22 and 195 patients were included respectively (table 1). Thirty factors were identified from the interviews and used in the questionnaire. The 10 factors that were ranked the highest, are shown in table 2. Most respondents had a positive attitude towards bDMARD dose reduction. The results show that patients are concerned that dose reduction will lead to a disease flare that affects their daily life (pain, function). It is important for them to know that it is possible to increase the dose if (further) reduction is not possible and that the bDMARD will be effective again. Patients value the opinion of their rheumatologist, and being involved in the decision to start tapering is highly ranked as well.

<table>
<thead>
<tr>
<th>Table 1. Patient characteristics (mean (SD) or N (%))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Disease duration (years)</td>
</tr>
<tr>
<td>Number of respondents per center</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Experience with bDMARD dose reduction</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>General attitude towards bDMARD dose reduction</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>
Table 2. Top-10 factors from the Maximum Difference Scaling questionnaire

<table>
<thead>
<tr>
<th>Nr.</th>
<th>Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>The possibility to increase the dose when disease symptoms worsen</td>
</tr>
<tr>
<td>2</td>
<td>The risk that my disease activity will increase</td>
</tr>
<tr>
<td>3</td>
<td>My current disease activity</td>
</tr>
<tr>
<td>4</td>
<td>The risk that my physical function will deteriorate (e.g. I won’t be able to work)</td>
</tr>
<tr>
<td>5</td>
<td>The confidence I have in my rheumatologist</td>
</tr>
<tr>
<td>6</td>
<td>To what extent I’m involved in the decision on bDMARD dose reduction</td>
</tr>
<tr>
<td>7</td>
<td>Whether the bDMARD is (still) necessary for the RA</td>
</tr>
<tr>
<td>8</td>
<td>What my rheumatologist advises regarding bDMARD dose reduction</td>
</tr>
<tr>
<td>9</td>
<td>The risk that I will experience more pain</td>
</tr>
<tr>
<td>10</td>
<td>The effect of the bDMARD after increasing the dose</td>
</tr>
</tbody>
</table>

Conclusion: Although preferences will vary between individual patients, the results from this study could facilitate implementation of bDMARD dose reduction by informing care providers on what is important for patients and providing a basis for shared decision making.


Disclosure: L. M. Verhoef, None; E. M. H. Selten, None; J. E. Vrieseckolk, None; A. J. L. de Jong, None; F. H. J. van den Hoogen, Biogen Idec, 5,Celltrion, 5,Janssen Pharmaceutica Product, L.P., 5,Mundipharma, 5,Sandoz, 5; A. A. Den Broeder, CZ, 2,Menzis, 2,ZonMW, 2,Amgen, 5,Boehringer Ingelheim, 5,Bristol-Myers Squibb, 8,Pfizer Inc, 8; M. E. J. L. Hulscher, None.


Abstract Number: 2780

Preference Phenotypes Can be Used to Support Shared Decision Making at the Point-of-Care

Liana Fraenkel¹, Pauline Binder-Finnema², Betty Hsiao², Carole Wiedmeyer³, George Michel² and W. Benjamin Nowell⁴, 
¹Rheumatology, Rheumatology, Yale University School of Medicine, New Haven, CT, New Haven, CT, ²Yale University School of Medicine, New Haven, CT, ³CreakyJoints/Global Health Living Foundation, Upper Nyack, NY, ⁴Global Healthy Living Foundation, Upper Nyack, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes II
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Many important treatment decisions for patients with rheumatoid arthritis (RA) are conditional on patient preferences and mandate a shared decision making (SDM) approach. Furthermore, SDM is being increasingly recognized as an important quality measure. One of the most common preference sensitive decisions in RA is how to escalate care when response to
methotrexate monotherapy is inadequate. The objective of this study was to examine whether preference phenotypes can be used to promote SDM at the point-of-care.

**Methods:** 1314 subjects completed a conjoint analysis survey (1048 in English, 266 in Spanish) designed to elicit preferences for triple therapy, FDA-approved biologics and tofacitinib. Five distinct phenotypes were generated using latent class analysis (See Figure). We subsequently created a pamphlet to describe the phenotypes and their implications. To examine the feasibility of using preference phenotypes to promote SDM in the clinic, we performed a pre-post-test study. Consenting RA patients received the pamphlet once roomed by a nurse in the post-phase. Visits in both phases were audiotaped, and those in which there was evidence of active disease were transcribed and analyzed.

**Results:** 50 visits were transcribed in the pre-phase and 46 in the post phase of the study. The mean age of the study population was 59 years; 85% were female, 68% were Caucasian, and 65% were seropositive. The pamphlet was used in 38 of the 46 visits in the post phase. Thirty-six out of the 38 patients were able to identify with one or more of the phenotypes presented in the pamphlet. A greater number of treatment decisions were concordant with patients’ preferences in the post-phase compared to pre-phase (12% vs 35%). Addition of the pamphlet did not increase the time of the visits. The average time of visits in the pre- and post-phases was 29 and 25 minutes respectively.

**Conclusion:** The results of this feasibility study suggest that patients can identify with preference phenotypes representing variability in patient values and that introduction of this tool at the point-of-care may increase the likelihood that treatment decisions are concordant with patients’ values.

**Figure 1. Variability in What Matters Most to Patients**

![Figure 1](image)

**Figure 2. Which group most closely matches how you think about RA medications?**

![Figure 2](image)

**Disclosure:** L. Fraenkel, None; P. Binder-Finnema, None; B. Hsiao, None; C. Wiedmeyer, None; G. Michel, None; W. B. Nowell, Global Healthy Living Foundation, 3.

View Abstract and Citation Information Online - [http://acrabstracts.org/abstract/preference-phenotypes-can-be-used-to-support-shared-decision-making-at-the-point-of-care](http://acrabstracts.org/abstract/preference-phenotypes-can-be-used-to-support-shared-decision-making-at-the-point-of-care)

**Abstract Number:** 2781

**Assessing RA Disease Activity with Promis Measures Using Smartphone Technology**
Huifeng Yun1, Shuo Yang2, W. Benjamin Nowell3, Cooper Filby1, Lang Chen1 and Jeffrey R. Curtis4, 1University of Alabama at Birmingham, Birmingham, AL, 2Division of Clinical Immunology & Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 3Global Healthy Living Foundation, Upper Nyack, NY, 4Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes II
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Health information technology has enabled efficient measurement of PROs using Computer Adaptive Testing (CAT) methods, which have been shown to minimize missing data and reduce participant burden. The bridge between PROMIS and traditional patient-reported PROs (e.g. RAPID3) is not clear, and it might be possible that some instruments in PROMIS might proxy for measuring more lengthy PROs.

Methods: Four PROMIS CAT instruments: Pain Interference, Physical Function, Sleep Disturbance, Fatigue, and a visual analog scale (Pain Intensity); and the Routine Assessment of Patient Index Data 3 (RAPID3) were administered to participants in the PCORI-funded ArthritisPower patient registry via a mobile application (App) on their smartphone or computer. The RAPID3 was evaluated in terms of multiple correlations (Pearson) with PROMIS and total variance explained using mixed models. Both the RAPID3 score and category was predicted using the selected 4 PROMIS instruments and pain intensity to form a new predicted score (“CAT-PROMIS RAPID3”). Kappa statistics and Bland-Altman 95% limits of agreement (LOA) were used to measure agreement between the measured RAPID3 and the predicted CAT-PROMIS RAPID3.

Results: At the time of analysis, 2,376 patients had answered all five PROMIS instruments and the RAPID3 and contributed 3906 observations. Mean +/-SD age was 51.6 +/- 10.5 years; 90% were women. Most (81%) had high RAPID3 scores. The mean assessment time for each of the PROMIS instruments ranged from a low of 16 seconds (sleep disturbance) to a high of 105 seconds (RAPID3). As single pairwise comparisons, the 4 PROMIS CATs examined were only modestly correlated (r ~ 0.2-0.4) to one other and the RAPID3. However, in aggregate, the PROMIS instruments explained a very high fraction of total variance ($R^2=80\%$) of the RAPID3. The measured RAPID3 was very highly correlated with the CAT-PROMIS predicted RAPID3 ($r=0.97$). Overall agreement (table) between categories of the RAPID3 vs. CAT-PROMIS RAPID3 also was very high (kappa = 0.81). Bland-Altman 95% limits of agreement shows minimal residual differences and no systematic biases.

Conclusion: There was excellent agreement between the measured RAPID3 and a predicted RAPID3 score estimated using several PROMIS instruments. Few if any questions in the RAPID3 may need to be measured if PROMIS scores are available.

<table>
<thead>
<tr>
<th>Table. Cross Classification of Patient-reported RAPID3 versus predicted PROMIS-CAT RAPID3</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAPID3</td>
</tr>
<tr>
<td>Near remission</td>
</tr>
<tr>
<td>Near remission</td>
</tr>
<tr>
<td>Low</td>
</tr>
<tr>
<td>Moderate</td>
</tr>
<tr>
<td>High</td>
</tr>
</tbody>
</table>

Disclosure: H. Yun, BMS, 2; S. Yang, None; W. B. Nowell, Global Healthy Living Foundation, 3; C. Filby, None; L. Chen, None; J. R. Curtis, UCB Pharma, Janssen-Cilag, Amgen, Roche, Myriad Genetics, Lilly, Novartis, BMS, Pfizer, 2,UCB Pharma, Janssen-Cilag, Amgen, Roche, Myriad Genetics, Lilly, Novartis, BMS, Pfizer, 5.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/assessing-ra-disease-activity-with-promis-measures-using-smartphone-technology

Abstract Number: 2782
Patient Beliefs and Preference to Initiate a Proposed Medication in Rheumatoid Arthritis

Richard W Martin¹, Rohit Nallani², Andrew D Head¹, Aaron T Eggebeen¹, James D Birmingham¹ and Eric T Slavin¹, ¹Medicine, Rheumatology, Michigan State University, College of Human Medicine, Grand Rapids, MI, ²Michigan State University, College of Human Medicine, Grand Rapids, MI

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes II
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Normative economic theory assumes that people making decisions have complete information of the options, rationally weigh the opportunity costs, expected outcomes and optimize their net benefit¹. However, rheumatoid arthritis (RA) patients facing medication decisions during a doctor-patient dialogue often do not have all the information needed to make a rational decision. In addition, patients primed with pharmaceutical industry (pharma) ‘decision guides’ may choose to escalate DMARD therapy based on the social influence of testimonials² rather than increased knowledge². In the current study, we evaluate how patient beliefs about antirheumatic medicines influence choice to add or change medications when patients are not primed with pharma decision guides.

Methods: We conducted a prospective observational study of doctor-patient discussions about adding or changing medications in consecutive RA patients attending routine rheumatology clinic visits. All patients completed written surveys immediately after medication discussions as well as a 30-day post-visit telephone survey. We evaluated patient beliefs about the proposed medicines from the perspective of the Integrated Model of Behavioral Prediction which included: expected outcomes, as well as perceived social norms and behavioral control².

Results: Of 580 RA patients seen during the observation period, 104 (17.9%) patients discussed starting a new medication. 91 (87.5%) completed the follow up survey. Demographics: Mean age 55.4 years, RA duration 7.5 years, CDAI 20 (range 0-50), 65.4% of discussions involved escalating DMARD therapy. Baseline patient belief about medication (0-5) were that they would: Improve symptoms 4.14 (sd .92), Slow progression 3.76 (sd 1.20), Cause serious adverse effect (SAE) 2.43 (sd 0.77), Others like me would choose to start the medication (Social Norm) 3.95 (sd 0.97), and Self-efficacy to take medication 4.68 (sd .53). A linear regression model of these 5 predictor variables on intention to take the proposed medication had an R² = .143. Standardized β were significant for ‘Belief would have SAE’ - .245 (P=.01) and ‘self-efficacy’ .222 (P=.02) but not ‘Improve symptoms’, ‘Slow progression’ or ‘Social Norm’. 30 days after the doctor-patient dialogue patient beliefs the medication would cause improvement and slow progression increased (P<.01), Self-efficacy to take the medication decreased (P< .01) and beliefs would have SAE and Social Norm were stable (NS).

Conclusion: Patients making real life decisions had high expectations that anti-rheumatics would improve their symptoms, but their preference to initiate therapy was more dependent on the belief they would have a SAE and beliefs of their behavioral control to take the medication. When not primed with pharma materials, patient perception of social norms did not demonstrate a significant effect on preference.

References:


Disclosure: R. W. Martin, None; R. Nallani, None; A. D. Head, None; A. T. Eggebeen, None; J. D. Birmingham, None; E. T. Slavin, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/patient-beliefs-and-preference-to-initiate-a-proposed-medication-in-rheumatoid-arthritis

Abstract Number: 2783
Medications Associated with Osteoporotic Fracture Risk in Patients with Rheumatoid Arthritis

Gulsen Ozen1, Sofia Pedro2, Frederick Wolfe2 and Kaleb Michaud1, 1Rheumatology, University of Nebraska Medical Center, Omaha, NE, 2National Data Bank for Rheumatic Diseases, Wichita, KS

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects IV: Medications and Risk
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Osteoporotic (OP) fractures are a major cause of disability, cost, and mortality in RA. Besides increased OP fracture risk, chronic inflammation and pain predispose RA patients to several comorbidities including cardiovascular, mental, and gastrointestinal disorders that lead to the frequent use of multiple medications. Some of these medications have been reported to influence OP fracture risk in the general population, but these associations have not been studied in RA patients. We examined the association of DMARDs, statins, antidepressants, proton pump inhibitors (PPI), opioids, NSAIDs, anticonvulsants, and antipsychotics with OP fracture risk in a US-wide observational RA cohort.

Methods: RA patients (≥40 years old) without prior OP fracture from 2001 through 2016 in the National Data Bank for Rheumatic Diseases (NDB) were assessed for OP fractures (fractures resulting from any fall from a standing height or less). DMARDs were categorized into 4 mutually exclusive groups: (1) MTX monotherapy-reference (2) TNF inhibitors (TNFi) (3) Non-TNFi biologics (4) Others; along with a separate glucocorticoid (GC) variable. Statins, antidepressants (selective serotonin reuptake inhibitors [SSRI] and others), PPI, opioids (weak and strong opioids), NSAIDs, anticonvulsants, and antipsychotics were evaluated separately as current use vs. nonuse and based on the treatment duration. Cox proportional hazard models were used to adjust for sociodemographics, comorbidities, BMI, fracture risk by FRAX, and RA severity measures.

Results: During a median (IQR) 5.4 (2.3-9.7) years of followup in 11,002 RA patients, 863 (7.8%) OP fractures were observed. Patients who developed fractures were significantly older, had higher disease duration and activity, GC use, comorbidity and FRAX scores at baseline than who did not. Crude incidence rates (95% CI) in each medication group are presented in the Table. The adjusted models showed a significant OP fracture risk increase with GC use of ≥3 months of any dose, SSRI (HR 1.35 [1.10-1.64], P=0.003), opioids of any strength (weak: HR 1.48 [1.26-1.74]; strong: HR 1.78 [1.41-2.26], P<0.001 for both) (Table). OP fracture risk increase started even after 1-30 days of opioid use (HR 1.99 [1.59-2.48], P<0.001), whereas SSRI-associated risk increase started after 3 months of use (HR 1.25 [0.99-1.59], P= 0.061).

Conclusion: SSRI and opioids were associated with increased OP fracture risk in RA patients. This risk increase might be associated with increased fall risk caused by these medications. Given the frequent occurrence of chronic pain, mood disorders and polypharmacy in RA patients, the necessity of the medications should regularly be reviewed in RA patients, particularly who have high fracture risk and long-term GC use. When managing pain with opioids, even in the short-term, clinicians should be aware of the fracture risk.
<table>
<thead>
<tr>
<th></th>
<th>No. of failures/No. of exposure</th>
<th>Patient-years</th>
<th>Incidence rates (95% CI) per 1000 patient-years</th>
<th>Adjusted HR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All patients</strong></td>
<td>863/11,002</td>
<td>52,323</td>
<td>16.5 (15.4-17.6)</td>
<td>-</td>
</tr>
<tr>
<td><strong>DMARD groups</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MTX monotherapy</td>
<td>166/3,199</td>
<td>8,886</td>
<td>18.7 (16.0-21.7)</td>
<td>Reference</td>
</tr>
<tr>
<td>TNFi</td>
<td>263/4,976</td>
<td>17,449</td>
<td>15.1 (13.4-17.0)</td>
<td>0.81 (0.65-1.02)</td>
</tr>
<tr>
<td>Non-TNFi biologics</td>
<td>54/1,201</td>
<td>2,618</td>
<td>20.6 (15.8-26.9)</td>
<td>0.82 (0.58-1.17)</td>
</tr>
<tr>
<td>Other DMARDs</td>
<td>380/6,876</td>
<td>23,369</td>
<td>16.3 (14.7-17.9)</td>
<td>0.85 (0.69-1.04)</td>
</tr>
<tr>
<td><strong>GC use</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>513/8,681</td>
<td>37,946</td>
<td>13.5 (12.4-14.7)</td>
<td>Reference</td>
</tr>
<tr>
<td>&lt;7.5mg/d for &lt;3 months</td>
<td>9/792</td>
<td>651</td>
<td>13.8 (7.2-26.5)</td>
<td>1.01 (0.45-2.26)</td>
</tr>
<tr>
<td>&lt;7.5mg/d for ≥3 months</td>
<td>209/3,259</td>
<td>9,676</td>
<td>21.6 (18.9-24.7)</td>
<td>1.27 (1.06-1.53)*</td>
</tr>
<tr>
<td>≥7.5mg/d for &lt;3 months</td>
<td>15/757</td>
<td>617</td>
<td>24.3 (14.7-40.3)</td>
<td>1.57 (0.84-2.95)</td>
</tr>
<tr>
<td>≥7.5mg/d for ≥3 months</td>
<td>117/1,876</td>
<td>3,431</td>
<td>34.1 (28.4-40.9)</td>
<td>1.74 (1.37-2.22)*</td>
</tr>
<tr>
<td><strong>Statins</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>243/4,003</td>
<td>14,391</td>
<td></td>
<td>16.9 (14.9-19.1)</td>
<td>0.96 (0.81-1.13)</td>
</tr>
<tr>
<td><strong>Antidepressants</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSRIs</td>
<td>173/2,280</td>
<td>6,590</td>
<td>26.3 (22.6-30.5)</td>
<td>1.35 (1.10-1.64)*</td>
</tr>
<tr>
<td>Others</td>
<td>76/1,259</td>
<td>3,386</td>
<td>22.4 (17.9-28.1)</td>
<td>1.04 (0.80-1.36)</td>
</tr>
<tr>
<td><strong>PPI</strong></td>
<td>319/4,800</td>
<td>15,886</td>
<td>20.1 (18.0-22.4)</td>
<td>0.93 (0.79-1.09)</td>
</tr>
<tr>
<td><strong>Opioids</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weak opioids</td>
<td>305/4,432</td>
<td>11,609</td>
<td>26.3 (23.5-29.4)</td>
<td>1.48 (1.26-1.74)*</td>
</tr>
<tr>
<td>Strong opioids</td>
<td>108/1,417</td>
<td>2,674</td>
<td>40.4 (33.4-48.8)</td>
<td>1.78 (1.41-2.26)*</td>
</tr>
<tr>
<td><strong>NSAIDs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>COX2 inhibitors</td>
<td>113/2,897</td>
<td>7,140</td>
<td>15.8 (13.2-19.0)</td>
<td>0.91 (0.72-1.16)</td>
</tr>
<tr>
<td>NonCOX2 inhibitors</td>
<td>289/5,874</td>
<td>18,070</td>
<td>16.0 (14.3-17.9)</td>
<td>1.13 (0.96-1.33)</td>
</tr>
<tr>
<td><strong>Anticonvulsants</strong></td>
<td>107/1,949</td>
<td>4,751</td>
<td>22.5 (18.6-27.2)</td>
<td>0.95 (0.75-1.20)</td>
</tr>
<tr>
<td><strong>Antipsychotics</strong></td>
<td>29/619</td>
<td>1,279</td>
<td>22.7 (15.8-32.6)</td>
<td>1.05 (0.69-1.58)</td>
</tr>
</tbody>
</table>

*Stratified by FRAX risk categories for MOF and adjusted for age, sex, ethnicity, disease duration, education level, insurance, , rural residency, smoking, comorbidity index, BMI, HAQ, pain and patient global scores, prior osteoporosis diagnosis, calcium/vitamin D use, HRT, exercise, prior sDMARD and bDMARD counts, and calendar year

*P<0.05
Are We over-Testing for Liver Enzyme Abnormalities in Rheumatoid Arthritis Patients Prescribed Methotrexate?

Chi Chi Lau\textsuperscript{1}, Syeda Maria Sayeed\textsuperscript{1}, Amanda Kennedy\textsuperscript{2}, Joan Skelly\textsuperscript{3} and Sheldon Cooper\textsuperscript{4}, \textsuperscript{1}Rheumatology/ Medicine, University of Vermont, Burlington, VT, \textsuperscript{2}Internal Medicine, University of Vermont, Burlington, VT, \textsuperscript{3}Biostatistics, University of Vermont, Burlington, VT, \textsuperscript{4}Department of Medicine/Rheumatology, University of Vermont, Burlington, VT

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects IV: Medications and Risk
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Methotrexate (MTX) is a first line drug for Rheumatoid Arthritis (RA) that is associated with elevated liver function tests (LFTs) in 10-20% of patients though only 2-3% of patients stop MTX for this side effect. Current guidelines advise LFT testing every 2 to 3 months with little data to support the utility of such monitoring. Our goal was to describe changes made to MTX dosing in response to elevated aspartate aminotransferase (AST) levels and define any correlation between elevated AST to MTX dose and duration of therapy.

Methods: The electronic health records of RA patients on MTX from 7/1/2009 to 12/31/2015 were reviewed for elevated AST values (>46 U/L,) which were categorized as mild ( >1- < 2x upper limits of normal,ULN) or severe (³2x ULN). We recorded the MTX dose and duration, and action taken on the dose (continued, decreased, stopped, or stopped for other reason than MTX) at the time of the AST elevation. The last AST observed for each patient while on MTX was used for analysis. Fisher’s Exact test was used to compare the proportions of actions taken in each AST category. A Spearman correlation was used to assess the correlation between MTX dose and AST levels; t-tests were used to compare MTX duration between the AST levels.

Results: Of 1158 RA patients taking MTX, 235 (20.2%) had at least one elevated AST value. Sixteen (6.8%) patients with elevated AST stopped MTX, because of provider concern for hepatotoxicity from the drug. Most patients (78%) with mild AST elevation continued MTX (p<0.0005), although 18% of patients continued MTX despite severe AST elevation (Figure 1). Providers stopped MTX for other reasons (infection, malignancy, cardiac event, cholelithiasis) in 76% of patients with severe AST elevation. There was no correlation between MTX dose and elevated AST (Spearman correlation = -0.015). Patients with mild AST elevation were on MTX for a mean (SD) of 73.3 (60.7) months which was no different from those with severe AST elevation at 69.5 (47.2) months, p=0.736 (Figure 2, AST level vs MTX duration).

Conclusion: Liver enzyme elevation, as measured by AST level, rarely resulted in MTX cessation for suspected MTX toxicity. The most common reason for stopping MTX was for AST elevation in the presence of an acute illness not related to RA. We advocate less frequent LFT testing for patients on MTX when the patient is clinically stable due to lack of evidence that monitoring leads to meaningful change in provider prescribing practice.
**Serious Infections Associated with Tofacitinib in Rheumatoid Arthritis Patients Previously Treated with Methotrexate**

Marina Amaral de Avila Machado¹, Cristiano S. Moura², Steve Ferreira Guerra¹, Jeffrey R. Curtis³, Michal Abrahamowicz⁴, Hassan Behloul¹ and Sasha Bernatsky⁵. ¹Department of Medicine, McGill University Health Centre, Montreal, QC, Canada, ²Division of Clinical Epidemiology, McGill University Health Centre, Montreal, QC, Canada, ³Rheumatology & Immunology, University of Alabama at Birmingham, Birmingham, AL, ⁴Department of Medicine, McGill University Health Centre, Montrecream, QC, Canada, ⁵Divisions of Rheumatology and Clinical Epidemiology, McGill University Health Centre, Montreal, QC, Canada

**First publication:** September 18, 2017
SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects IV: Medications and Risk
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Little is known about the real-world safety of tofacitinib, an oral Janus kinase inhibitor. We compared serious infections associated with tofacitinib, disease-modifying antirheumatic drugs (DMARDs), tumor necrosis factor inhibitors (TNFi) and non-TNF biologics in rheumatoid arthritis (RA) patients previously treated with methotrexate (MTX).

Methods: We performed a retrospective cohort study using MarketScan® Databases from 2010-2014. We studied adults with RA, previously treated with MTX, and newly prescribed one of the medications under study between January 2011 and December 2014. Cohort entry was the date of first prescription or infusion of drug. We required subjects to be continuously enrolled with medical and pharmacy coverage for 12 months before cohort entry and to have had no use of biologics or tofacitinib at any point prior to cohort entry. We defined serious infection as one associated with a hospitalization. We assessed current drug exposure considering prescription days’ supply or infusion intervals in a time-dependent manner, thereby classifying patients into one of the five groups: 1) DMARDs without biologics or tofacitinib; 2) TNFi +/- DMARDs, 3) non-TNF biologics +/- DMARDs; 4) tofacitinib +/- DMARDs, or 5) non-use (time within none of the previous groups). Subjects remained exposed for the most recently presented drug group until 90 days or until the start of a new drug. This classification was independent of whether the patient did or did not continue to use MTX, including the group 5. We estimated the rate of serious infection and hazard ratios (HR) with 95% confidence intervals (CI) to assess the risk of serious infections between the exposure groups, using group 5 as a reference. We adjusted the analysis for covariates such as sex, age, year of cohort entry, current use of MTX, and confounders in the one-year prior to cohort entry: Charlson comorbidity index; use of selective COX-2 inhibitors, nonsteroidal anti-inflammatory drugs, and oral glucocorticoid (none, ≤7.5mg/day; >7.5mg/day); hospitalization for infection and for all reasons; physician, rheumatology, and emergency department visits. Patients were followed from cohort entry until the earliest date of loss of medical or pharmacy coverage, death, end of the study, or the first hospitalized infection.

Results: We included 21,832 RA patients; 0.8% with tofacitinib, 24.7% with other DMARDs, 61.2% with TNFi, and 13.3% with non-TNF biologics. Among all patients, 77.0% were female and the median age was 56 (interquartile interval 48-63) years. The incidence of serious infection with tofacitinib was 3.7 per 100 patient-years. The adjusted HR for hospitalized infection was 1.81 (95% CI 1.08-3.01) for tofacitinib compared to the reference group (Table 1).

<table>
<thead>
<tr>
<th>Exposure groups</th>
<th>Events</th>
<th>Total person-years</th>
<th>Incidence (per 100 patient-year)</th>
<th>Adjusted Hazard Ratio</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non use</td>
<td>134</td>
<td>6,833.71</td>
<td>1.96</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>DMARDs</td>
<td>103</td>
<td>5,157.20</td>
<td>2.00</td>
<td>0.82</td>
<td>0.62; 1.07</td>
</tr>
<tr>
<td>TNFi +/- DMARDs</td>
<td>484</td>
<td>22,351.79</td>
<td>2.17</td>
<td>1.13</td>
<td>0.92; 1.38</td>
</tr>
<tr>
<td>Non-TNF biologic +/- DMARDs</td>
<td>168</td>
<td>6,648.01</td>
<td>2.53</td>
<td>1.10</td>
<td>0.87; 1.38</td>
</tr>
<tr>
<td>Tofacitinib +/- DMARDs</td>
<td>17</td>
<td>464.32</td>
<td>3.66</td>
<td>1.81</td>
<td>1.08; 3.01</td>
</tr>
</tbody>
</table>

Conclusion:
Tofacitinib was associated with more hospitalized infections, but this could represent channelling. Further analyses are underway.

Disclosure: M. A. D. A. Machado, None; C. S. Moura, None; S. Ferreira Guerra, None; J. R. Curtis, None; M. Abrahamowicz, None; H. Behlouli, None; S. Bernatksy, None.


Abstract Number: 2786

Timing of Abatacept Infusions before Elective Arthroplasty and the Risk of Post-Operative Infection
SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects IV: Medications and Risk
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Current guidelines recommend holding biologic DMARDs before major surgery, despite limited data. Few studies have examined perioperative timing of individual biologic therapies. This study evaluated whether holding abatacept infusions before elective hip or knee arthroplasty is associated with a decreased risk of serious post-operative infection.

Methods: This retrospective cohort study using U.S. Medicare claims data from 2006-2014 evaluated adults with ≥ 2 ICD9 codes for RA who received abatacept by infusion (precisely dated in claims data) within 6 months of elective inpatient primary or revision total hip or knee arthroplasty. Patients with hip fracture, malignancy, pre-existing infection, non-elective procedures (admission through the emergency department or as a hospital transfer), or with surgery after hospital day 3 were excluded. Multivariable logistic regression evaluated associations of abatacept stop timing (time between most recent infusion and surgery categorized in 4 week intervals based on dosing interval) with serious (hospitalized) infection within 30 days using a validated set of discharge diagnoses from inpatient hospitalizations, adjusting for potential confounders. Associations of abatacept stop time with rate of prosthetic joint infection (PJI, ICD9 996.66) within 1 year were examined using Kaplan-Meier curves.

Results: Among 1476 surgeries in 1358 patients, serious infection within 30 days occurred in 10.1% (n = 149). Urinary infection, skin/soft tissue infection, and pneumonia were the most common infections. In adjusted analyses, stop timing of 4-8 weeks (held for one dosing interval) vs. < 4 weeks was not associated with a significant decrease in the risk of infection [OR 0.91 (0.62-1.33), p = 0.62] (Table). Glucocorticoid dose > 7.5mg/day vs. none was associated with increased risk of infection [OR 2.38 (1.42-3.98), p = 0.001]. Over 12 months, the rate of PJI was 2.7 per 100 person-years (n = 33 infections). Rates of PJI within 1 year were similar in patients with abatacept stop timing < 4 weeks vs. longer stop timing (Figure).

Conclusion: Holding abatacept for one dosing interval (i.e. one month) was not associated with a decrease in the risk of post-operative infection. In contrast, glucocorticoid dose > 7.5mg per day was associated with a substantial increase in the risk of post-operative infection. Given the potential risk of flare, holding abatacept prior to elective joint procedures may not be warranted.
Disclosure: M. D. George, Bristol Myers Squibb, 2; J. Baker, None; K. Winthrop, BMS, 2, UCB Pharma, Roche, Lilly, Pfizer, GSK, AbbVie, Galapagos, BMS, 5; E. Alemao, Bristol-Myers Squibb, 3, Bristol-Myers Squibb, 1; L. Chen, None; S. Connolly, Bristol-Myers Squibb, 3, Bristol-Myers Squibb, 1; T. Simon, Bristol-Myers Squibb, 3, Bristol-Myers Squibb, 1, 9; Q. Wu, None; F. Xie, None; S. Yang, None; J. R. Curtis, UCB Pharma, Janssen-Cilag, Amgen, Roche, Myriad Genetics, Lilly, Novartis, BMS, Pfizer, 2, UCB Pharma, Janssen-Cilag, Amgen, Roche, Myriad Genetics, Lilly, Novartis, BMS, Pfizer, 5.
Tuberculosis, Potential Opportunistic Infections, and Other Infections of Interest in Patients with Moderate to Severe Rheumatoid Arthritis in the Baricitinib Program

Kevin Winthrop, Stephen Lindsey, Masayoshi Harigai, John D. Bradley, Lei Chen, David L. Hyslop, Maher Issa, Atsushi Nishikawa, Sarah Witt, Christina L. Dickson and Maxime Dougados

1Oregon Health & Science University, Portland, OR,
2Ochsner Health Center, Baton Rouge, LA, 3Division of Epidemiology and Pharmacoepidemiology of Rheumatic Diseases, Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan, 4Eli Lilly and Company, Indianapolis, IN, 5Lilly Japan K.K., Kobe, Japan, 6Rene Descartes University, Cochin Hospital, Paris, France

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects IV: Medications and Risk
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Baricitinib (bira) is an oral selective Janus kinase (JAK) 1 and JAK2 inhibitor approved in the EU for the treatment (trt) of moderately to severely active rheumatoid arthritis (RA) in adults. Compared to the general population, RA patients (pts) have an increased rate of tuberculosis (TB) and other potential opportunistic infections (OI). This analysis evaluated reported potential OI in RA pts treated with bira across 8 completed studies (4 Phase [Ph] 3, 3 Ph2, 1 Ph1) and 1 ongoing long-term extension (LTE) study, with data up to September 1, 2016.

Methods: The All bira RA analysis set included pts exposed to any bira dose, with exposure up to 5.5 years (yrs) (Ph 1-3 and LTE studies); the comparison with placebo (PBO) was based on 6 studies (Ph 2-3) with bira 4 mg QD and PBO up to week (wk) 24 (PBO-bira 4 mg set); dose-response assessment was based on 4 studies (Ph 2-3) with bira 2 and 4 mg QD, including the LTE (bira 2mg-4mg-extended set); the methotrexate (MTX) and adalimumab (ADA) data were based on the individual studies RA-BEGIN and RA-BEAM, respectively, up to wk 52. Reported potential OI were identified using Lilly-defined preferred terms from the Infections and infestations system organ class of the Medical Dictionary for Regulatory Activities (MedDRA) and pre-specified pairings of infecting organism and infection site. Sponsor medical review of these events was conducted to identify potential OI.

Results: Forty-five events, including TB, were identified in the All bira RA set (Table). There were 10 reported cases of TB (incidence rate [IR]=0.15/100 pt-yrs [PY]); all occurred in TB-endemic regions and 6 were associated with extra-pulmonary involvement. Bira was associated with an increased risk of trt emergent herpes zoster (HZ) compared to PBO in the PBO-bira 4 mg set (PBO IR=1.0/100PY, bira IR=4.3/100PY). In the All bira RA set, 18 HZ cases had distribution beyond the primary or adjacent dermatomes (considered potential OI), with 194 additional cases (overall IR=3.2/100PY). There were no visceral cases; 4 were associated with facial palsy (3) or other motor nerve palsy (1) and 3 had ocular involvement. Single cases of cytomegalovirus and Epstein-Barr virus infection were reported. Fungal events of candidiasis involving the esophagus (6), lung (1), and soft tissue (1), Pneumocystis jirovecii pneumonia (3, all in Japan) and single cases of histoplasmosis, paracoccidioidomycosis, and cryptococcal lung infections, and aspergillosis skin infection were reported. Few events occurred in the randomized, controlled portion of the studies, or with active comparator trt (MTX: none; ADA: 1 TB). Progressive multifocal leukoencephalopathy was not seen in the bira RA program.

Conclusion: Trt with bira was associated with an increased risk of HZ. TB and other potential OI, including HZ with distribution of infection beyond the primary or adjacent dermatomes, were uncommon with bira trt.
The Risk of Major Toxicity with Aspirin for Primary Cardiovascular Prevention in Rheumatoid Arthritis Patients Using Nsaids: A Secondary Cohort Analysis of a Randomized Controlled Clinical Trial

Daniel H. Solomon¹, Peter Libby², Qiuquing Wang³, Katherine E Wolski⁴, Lisa M Wisniewski⁴, Neville Yeomans⁵, Michael Lincoff⁶, Steven E Nissen⁷ and M. Elaine Husni⁸, ¹Brigham and Women’s Hospital and Harvard Medical School, Boston, MA, ²Cardiology, Brigham and Women’s Hospital, Boston, MA, ³Cleveland Clinic, Cleveland, OH, ⁴Cardiovascular Medicine, Cleveland Clinic, Cleveland, OH, ⁵Western Sydney Medical School, Sydney, Australia, ⁶Cardiology, Cleveland Clinic Foundation, Cleveland, OH, ⁷Cardiovascular Medicine, Chair, Cleveland Clinic, Cleveland, OH, ⁸Rheumatology Dept A50, Cleveland Clinic Foundation, Cleveland, OH

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects IV: Medications and Risk
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM
Background/Purpose: There are relatively clear guidelines for the use of low dose aspirin in the general population for primary cardiovascular (CV) prevention, but the risk-benefit calculation may differ in RA. While RA confers an increased CV risk compared with age and gender matched controls, such patients more likely use NSAIDs and corticosteroids. Since these therapies associate with bleeding, they might counterbalance potential benefits of low dose aspirin. We re-analyzed data from the PRECISION trial, in which all patients received an NSAID, to determine the risk-benefit ratio of low dose aspirin for primary CV prevention in RA.

Methods: We conducted a cohort study using data from the PRECISION RCT, including RA patients without a known history of CVD. From this group, we compared the potential risks and benefits for those using low dose aspirin to those not. Patients were censored at the first outcome or loss to follow-up. The primary outcome was major NSAID toxicity, including major adverse CV event (MACE: CV death, non-fatal myocardial infarction, or non-fatal stroke, re-vascularization, hospitalization for unstable angina or transient ischemic attack), clinically significant gastrointestinal events, renal events, and all-cause mortality. We estimated incidence rates and hazard ratios (HR) using Cox regression. Covariates considered for entry into the model included CV risk factors, prior ulcer disease, use of steroids, use of statins, use of DMARDs, HAQ score, serum creatinine, and body mass index (BMI).

Results: We found 1852 subjects with RA in PRECISION without known CVD; 540 reported using low dose aspirin for CV prevention and 1312 did not. They had an average age of 60 years, 77% were female and 52% used tobacco. The mean BMI was 31kg/m² and CV risk factors were common: 34% had diabetes, 76% had hypertension, and dyslipidemia in 56%. The randomized NSAID treatment assignments were well balanced across the aspirin users and non-users. Any major NSAID toxicity was observed in 79 (6.0%) of non-aspirin users and 37 (6.9%) of aspirin users (p = 0.50) (see Table). Aspirin users experienced all components of the primary outcome at a similar rate to non-users (see Table). In age and gender adjusted Cox regression models, low dose aspirin did not associate with a reduction in major NSAID toxicity (HR 0.95, 95% CI 0.64 - 1.40) or with MACE (HR 1.23, 95% CI 0.72 - 2.10)(see Table). Fully adjusted models yielded very similar results for the primary outcome (HR 1.08, 95% 0.69 – 1.69).

Conclusion: RA patients using low dose aspirin had similar risk of major NSAID toxicity and MACE as patients not. Even among this cohort of RA patients with known CV risk factors, the use of low dose aspirin for primary CV prevention appears not to confer clear benefits. A larger cohort will be needed to confirm, but low dose aspirin may not promote primary prevention of CV events in RA despite their increased risk.

Table: Influence of low-dose aspirin treatment at baseline on adjudicated major NSAID toxicity in RA subjects without known cardiovascular disease in PRECISION

<table>
<thead>
<tr>
<th></th>
<th>Rates of events</th>
<th>Hazard ratio (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major NSAID toxicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin (N=540)</td>
<td>Non-aspirin (N=1312)</td>
<td></td>
</tr>
<tr>
<td>MACE</td>
<td>22 (4.1)</td>
<td>1.23 (0.72, 2.10)</td>
</tr>
<tr>
<td>Clinically significant GI</td>
<td>8 (1.5)</td>
<td>1.72 (0.68, 4.40)</td>
</tr>
<tr>
<td>events</td>
<td>3 (0.6)</td>
<td>0.39 (0.11, 1.34)</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>12 (2.2)</td>
<td>0.72 (0.37, 1.40)</td>
</tr>
</tbody>
</table>

NA, not available as there were too few outcomes to include more than age, gender and aspirin status.* Comparing aspirin users to non-users (reference). Variables included in fully adjusted model: age, gender, treatment assignment (celecoxib, naproxen, ibuprofen), hypertension, diabetes, hyperlipidemia, BMI, statin use, DMARD use, Health Assessment Questionnaire, and LDL.

Disclosure: D. H. Solomon, Pfizer Inc, 9; P. Libby, None; Q. Wang, Pfizer, 2; K. E. Wolski, Pfizer, 2; L. M. Wisniewski, Pfizer, 2; N. Yeomans, Pfizer Inc, 5; M. Lincoff, Lilly, Astra Zeneca, Pfizer, AbbVie, CSL, Esperion, Amgen, 2; S. E. Nissen, Pfizer Inc, 9; M. E. Husni, Pfizer Inc, 6, AbbVie, Novartis, Eli Lilly, UCB, Janssen, Bristol-Myers Squibb, Regeneron, Amgen, 5, PASE Questionnaire, 7.


Abstract Number: 2789
Deficiency of the Novel Rheumatoid Arthritis (RA) Risk Gene, LBH, Induces Replication Stress in RA Fibroblast-like Synoviocytes (FLS) and Exacerbates Arthritis Severity

Shinji Matsuda, Deepa Hammaker, Katheryn Topolewski, Karoline Briegel, Steven Dowdy, David L. Boyle, Wei Wang, and Gary S. Firestein, Medicine, UC San Diego, La Jolla, CA; Division of Rheumatology, Allergy and Immunology, UCSD School of Medicine, La Jolla, CA; UC San Diego, La Jolla, CA; University of Miami, Miami, FL; UC San Diego School of Medicine, La Jolla, CA; University of California San Diego, La Jolla, CA; Chemistry and Biochemistry, UC San Diego, La Jolla, CA; Medicine, University of California San Diego, La Jolla, CA

Background/Purpose: LBH (Limb-bud and heart development) was recently identified as an RA risk gene that has abnormally methylated loci and a functional enhancer SNP in RA FLS. These genetic and epigenetic marks decrease LBH expression, which is associated with increased RA risk. Subsequent studies showed that LBH deficiency unexpectedly leads to S phase arrest. The present studies define the mechanism of S-phase arrest and assess the effect of LBH deficiency in an animal model of rheumatoid arthritis.

Methods: Cultured FLS were derived from RA synovium obtained at the time of arthroplasty. DNA damage was assayed using a comet assay, which is a single cell method that measures diffusion of DNA fragments from the nucleus. Male Rosa-26-Cre; Lbh+/+ (WT) and conditional knockout Rosa-26-Cre; Lbhlox/lox mice (LBH−/−) were injected i.p. with 80 μl of pooled adult K/BxN mice serum on day 0 and 2. The clinical scores were determined until day 12. Western blots qPCR assays were performed on synovial tissue and cultured FLS extracts to assay protein and mRNA levels. LBH deficiency in FLS (LBHlow) was induced using siRNA transfection.

Results: Because S-phase arrest is often due to DNA replication damage, we determined whether LBH deficiency in FLS increases DNA damage. Comet assays showed that LBHlow cells had comets with significantly longer tails than control cells, indicating increased in DNA strand breaks (p = 0.001). DNA damage in LBHlow cells led us to assess the activation status of the checkpoint kinases, CHK1 and CHK2, which are activated in response to DNA damage during S phase and induces growth arrest. Western blot analysis showed that CHK1 phosphorylation increased 4-fold greater in LBH deficient cells than control cells, while CHK2 was not activated (p=0.03). Three main polymerases are responsible for DNA synthesis in S phase and were assayed in control and LBHlow cells. LBH deficiency reduced POLA1 protein by 86% (p < 0.01) compared with control. However, POLD1 and POLE were not affected by LBH deficiency. To examine the contribution of LBH in inflammatory arthritis, passive K/BxN arthritis was studied in WT and LBH−/− mice. LBH−/− mice had a significantly increased peak clinical score of arthritis (mean = 8±3, p = 0.02) compared to WT (mean = 6±2), primarily in the later stages of the model. IL-1ß gene expression, which plays an essential role in this model, was significantly increased in the joints of the LBH−/− mice with arthritis (2.1±0.7) compared with arthritic WT mice on day 12 (0.7±0.1, p<0.05). To determine whether checkpoint arrest occurred in the joints of LBH−/− mice with arthritis, western blot analysis was performed for phospho-CHK1. LBH-deficient mice had 2±0.5-fold higher levels of phospho-CHK1 compared with WT in the arthritis model (p < 0.05).

Conclusion: These findings indicate that LBH regulates the cell cycle in vitro and induces cell cycle arrest due to decreased POLA1 expression in response to DNA damage and decreases DNA repair. LBH deficiency allows DNA damage to accumulate in vivo leading to S phase arrest. Because accumulation of DNA fragments is known to exacerbate murine arthritis, the LBH RA risk allele likely contributes to disease severity in RA by suppressing LBH expression and increasing DNA damage.

Disclosure: S. Matsuda, None; D. Hammaker, None; K. Topolewski, None; K. Briegel, None; S. Dowdy, None; D. L. Boyle, None; W. Wang, None; G. S. Firestein, None.

Regulation of ASK1 Expression and Its Role in Rheumatoid Arthritis (RA)
Background/Purpose: Rheumatoid arthritis (RA) fibroblast-like synoviocytes (FLS) reside in the synovial intimal lining. They display a unique aggressive phenotype, invading the articular cartilage and promoting inflammation. Elevated mitogen activated protein kinase (MAPK) signaling occurs in RA, but targeting downstream MAPKs like p38 has had minimal success. As an alternative approach, we focused on the upstream MAPK kinase, apoptosis signal regulating kinase-1 (ASK1). ASK1 can regulate p38 and JNK, and aberrant ASK1 signaling has been implicated in cancer, neurodegenerative diseases and inflammatory and cardiovascular disorders. We examine the regulation of ASK1 expression in RA FLS and its role in the collagen-induced arthritis (CIA) model using a novel ASK1 inhibitor.

Methods: Synovial tissue was obtained from RA and osteoarthritis (OA) patients during joint replacement surgery or synovectomy. Gene expression was assessed by qPCR. ASK1 promoter activity was measured using minimal promoter luciferase reporter constructs that included a 1.3 kb (Full Length) region, a 994 kb lacking the RelA binding site (Truncated), or a full length region with a mutated upstream RelA-binding site. A novel selective ASK1 inhibitor (ASK1i) was used in the rat collagen induced arthritis (CIA) model, and animals received treatment by oral gavage from day 10 through day 16. Ankle diameters were measured and histology was evaluated for inflammation, pannus formation, cartilage damage, and bone resorption.

Results: A strong correlation was found between ASK1 and IL-1β mRNA expression in synovium (n = 20, r² = 0.62, p = 0.00003), and to a lesser degree between ASK1 and TNF mRNA (r² = 0.45, p = 0.001). No correlation was found between ASK1 and IL-6 mRNA (r² = 0.01, p = 0.61). Because previous studies showed that IL-1 increases ASK1 expression in FLS, the mechanism behind the increased gene expression was explored using ASK1 reporter constructs. ASK1 promoter activity for the Full Length construct was significantly increased by IL-1β (40-fold ±10 increase, n = 6, p = 0.012) and TNF (15-fold ± 3, 6 hr, n = 3, p = 0.011) compared with control construct. Increased transcription was eliminated in the Truncated construct and in the construct with the mutated RelA binding motif. These results confirm that ASK1 is induced at the transcriptional level after IL-1β and TNF stimulation and identifies the RelA motif as the primary regulatory region. To determine if ASK1 plays a role in inflammatory arthritis, CIA rats were treated with ASK1i. The inhibitor significantly decreased ankle swelling in the CIA rat model in a dose-dependent fashion, resulting in a 46 ± 8.8% and 48 ± 9.9% decrease at day 16 for animals treated with 3 mg and 10 mg/kg, respectively, compared with vehicle (n = 8 per group, p < 0.05). ASK1i decreased histologic severity, with 36 ± 12% reduction in total histology score for 10 mg/kg compared with vehicle (n = 8, p < 0.05).

Conclusion: IL-1β and TNF regulate ASK1 through the RelA binding motif in the ASK1 promoter and synovial cytokine expression correlates with synovial ASK1 mRNA. A novel small molecule ASK1 inhibitor significantly decreased disease severity in CIA. The data support advancing an ASK1 inhibitor as a potential therapeutic target for RA.

Disclosure: G. Nygaard, None; D. Hammaker, None; D. L. Boyle, None; L. Li, Gilead, 3; J. Di Paolo, Gilead, 3; G. S. Firestein, Gilead, 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/regulation-of-ask1-expression-and-its-role-in-rheumatoid-arthritis-ra

Abstract Number: 2791

Receptor Activator of Nuclear Factor Kappa-B Ligand (RANKL) and Marginal Jawbone Loss Predates the Onset of Rheumatoid Arthritis

Elin Kindstedt1, Linda Johansson2, Py Palmqvist3, Cecilia Koskinen Holm1, Heidi Kokkonen4, Ingegerd Johansson3, Pernilla Lundberg3 and Solbritt Rantapaa-Dahlqvist5, 1Department of Odontology/Molecular Periodontology, Umeå University, Umeå, Sweden, 2Public Health and Clinical Medicine/Rheumatology, Umeå University, Umeå, Sweden, 3Department of...
SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis I
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:

Previous studies have shown a higher incidence of alveolar bone loss in patients with rheumatoid arthritis (RA) and that patients with periodontitis are at a greater risk for developing RA. Periodontitis, displayed as marginal jawbone loss was analysed in individuals prior to symptom onset of RA and related to plasma levels of receptor activator of nuclear factor kappa-B (RANKL), a cytokine crucial for bone resorption.

Methods:

A case-control study performed within the Medical Biobank of Northern Sweden included 232 pre-symptomatic individuals with blood samples donated before symptom onset and 194 controls. A questionnaire on self-assessed dental status and smoking status was retrieved. Dental radiographs to evaluate marginal jawbone levels were available from 93 pre-symptomatic individuals (mean age; 56.8 95%CI 55.9, 57.7 years and pre-dating time; -5.3 95%CI -12.2, -0.2, 74.2% females) and 83 controls (mean age; 55.5 95%CI 54.6, 56.5, 73.5% females). Of these individuals 45 had radiograph documentations prior to development of RA symptoms and to whom sex, age and smoking status could be matched among the controls. Plasma were analysed for RANKL (BioVendor, Karasek, Czech Republic), and anti-citrullinated peptide antibodies (ACPA) (anti-CCP2 test, Eurodiagnostics, Sweden) from similar time points.

Results:

Compared to matched controls, total bone loss was significantly higher in never-smokers who developed RA but not in smokers and increasing levels on total jawbone loss was associated with a significantly higher odds to be diagnosed with RA later (OR=1.06, 95%CI 1.01, 1.11). Regardless of smoking status, the number of unaffected teeth did not differ significantly between those who were subsequently diagnosed with RA and their matched controls. In the pre-symptomatic individuals RANKL positive individuals had significantly higher extent of marginal jawbone loss, which was further increased in ACPA positive individuals. Previously documented association between smoking and ageing and marginal jawbone loss was verified.

Conclusion:

Marginal jawbone loss preceded onset of symptoms of RA but the difference was only manifested in non-smokers. Moreover, marginal jawbone loss and plasma RANKL levels were related in the pre-symptomatic individuals particularly in ACPA positive individuals.

Disclosure: E. Kindstedt, None; L. Johansson, None; P. Palmqvist, None; C. Koskinen Holm, None; H. Kokkonen, None; I. Johansson, None; P. Lundberg, None; S. Rantapaa-Dahlqvist, None.


Abstract Number: 2792

Th22 Cells Are a Potent Inducer of Osteoclastogenesis in Rheumatoid Arthritis

Yusuke Miyazaki1, Shingo Nakayamada2, Satoshi Kubo1, Kazuhiisa Nakano2, Kei Sakata3, Shigeru Iwata4, Ippei Miyagawa5 and Yoshiya Tanaka6, 1The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, 2First Department of Internal Medicine, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, 3The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, 4First Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, 5University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, 6The First Department of Internal Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan

First publication: September 18, 2017
Background/Purpose: CD4+ T cells can differentiate into functionally distinct subsets and play a pivotal role in rheumatoid arthritis (RA). Th22 cells have been identified as a new subset secreting IL-22. Although elevated levels of IL-22 in the synovial fluids of RA patients were reported, its pathological roles remain unclear. In this study, we examined the function of human Th22 cells, the distribution of Th22 cells in synovial tissues in RA patients, and the influences of Th22 cells on osteoclast differentiation in order to elucidate the role of Th22 cells in RA pathogenesis.

Methods: CD3+CD4+CXCR3+CCR6- (Th1) cells, CD3+CD4+ CXCR3−CCR4+CCR6−CCR10− (Th17) cells, and CD3+CD4+CXCR3−CCR4+CCR6+CCR10+ (Th22) cells were sorted from the peripheral blood of healthy individuals and the ability of these subsets to produce cytokines were compared. CD3+CD4+IL-22+IL-17−IFN-γ−Th22 cells and chemokine receptor-ligands (CCL17, CCL20, CCL28) in synovial tissues in patients with RA and osteoarthritis (OA) were evaluated by immunohistochemistry. Human monocytes were cultured with IL-22, IL-17 or IFN-γ in the presence of M-CSF and RANKL for 12 days. Th1 cells, Th17 cells or Th22 cells were sorted from peripheral blood and co-cultured with monocytes in the presence of M-CSF and RANKL.

Results: CD3+CD4+CCR4+CCR6+CCR10+ cells produced neither IFN-γ nor IL-17, but characteristically produced IL-22 alone, and that their ability to produce IL-22 exceeded that of other helper T cell subsets. Th22 cells were markedly infiltrated in synovial tissue in patients with active RA, but not in patients with OA. CCL17, CCL20 and CCL28 were abundantly expressed in RA synovial tissue compared to OA. Actually, by in vitro Trans-well migration assay, Th22 cells efficiently migrated towards CCL28. Addition of IL-22 to the in vitro culture of monocytes with M-CSF and RANKL markedly increased numbers of tartrate-resistant acid phosphatase (TRAP)-positive osteoclasts formation. Contrarily, the addition of IFN-γ to the culture significantly decreased TRAP-positive osteoclasts number, whereas IL-17 had marginal effects. The gene expression of NFATc1 and cathepsin K was significantly increased by addition of IL-22 to the culture in a dose dependent manner. Co-culture of Th22 cells, which were sorted from peripheral blood, with monocytes in the presence of M-CSF and RANKL induced TRAP-positive osteoclasts formation more efficiently than that of either Th1 cells or Th17 cells. IL-22 neutralizing antibody completely inhibited osteoclast formation in co-culture of Th22 cells with monocytes.

Conclusion: Th22 cells, which co-express chemokine receptors CCR4, CCR6 and CCR10, possess strong potency of tissue migration and accumulate into inflamed synovial tissues where the ligands such as CCL28 are highly expressed. The results indicated that Th22 cells have the capacity to promote osteoclast differentiation through production of IL-22. Thus, Th22 cells may play a pivotal role in the pathogenesis of RA by bone resorption in RA synovitis.

Disclosure: Y. Miyazaki, None; S. Nakayamada, Bristol-Myers Squibb, 8; S. Kubo, Bristol-Myers Squibb, 8,Pfizer Inc, 8,Takeda Pharmaceutical Company Ltd, 8; K. Nakano, None; K. Sakata, None; S. Iwata, None; I. Miyagawa, None; Y. Tanaka, Mitsubishi-Tanabe, Takeda, Bristol-Myers, Chugai, Astellas, Abbvie, MSD, Daiichi-Sankyo, Pfizer, Kyowa Kirin, Eisai, Ono, 2, Daiichi-Sankyo, Astellas, Pfizer, Mitsubishi-Tanabe, Bristol-Myers, Chugai, YL Biologics, Eli Lilly, Sanofi, Janssen, UCB, 8.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/th22-cells-are-a-potent-inducer-of-osteoclastogenesis-in-rheumatoid-arthritis

Abstract Number: 2793

Joint Location-Specific JAK-STAT Signaling in Rheumatoid Arthritis (RA) Fibroblast-like Synoviocytes (FLS)

Deopa Hammaker1, Gyrid Nygaard1, David L. Boyle2, Rizi Ai3, Wei Wang4 and Gary S. Firestein5, 1Medicine, UC San Diego, La Jolla, CA, 2University of California San Diego, La Jolla, CA, 3UC San Diego, La Jolla, CA, 4Chemistry and Biochemistry, UC San Diego, La Jolla, CA, 5Medicine, University of California San Diego, La Jolla, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis I
Session Type: ACR Concurrent Abstract Session
Aberrant epigenetic marks in RA FLS contribute to disease pathogenesis and aggressive FLS behavior. Computational data also suggest that RA FLS isolated from different joint locations display distinct epigenetic states and transcriptomes that implicate joint-specific pathogenic pathways. For example, IL-6 signaling and JAK-STAT epigenetic marks differ in RA hips and knees. This suggests that hip and knee FLS might have differential responses to IL-6 stimulation and JAK inhibitors like tofacitinib, which could contribute to asynchronous clinical responses between joints in RA patients treated with targeted agents. In this study, the joint-specific biology of IL-6 and JAK in RA hip and knee FLS were explored to biologically validate the computational data using IL-6-induced monocyte chemoattractant protein 1 (MCP1) gene expression as a primary differential function.

Methods:

FLS lines were established from synovial tissue of RA patients undergoing total hip or knee replacement surgery. The cells were expanded in 10% fetal calf serum/DMEM and used at passages 3 – 7. FLS were plated, serum starved for 18 hours and then stimulated with various concentrations of IL-6 for 2h. In some experiments, the cells were pre-treated with tofacitinib prior to IL-6 stimulation. RNA was isolated and GAPDH-normalized gene transcripts were quantified by qPCR.

Results:

Under basal conditions, hip FLS expressed significantly less MCP1 than knee FLS (1.37±0.22 and 2.5±0.27, respectively; n=15/group, p=0.003). At low doses of IL-6 (<20ng/ml), MCP1 expression for hip FLS remained lower than for knee FLS, but the fold increase was greater for hip. For example, at 7.5 ng/ml of IL-6, MCP1 increased 2.4±0.4 fold for hip FLS and 1.2±0.07 fold for knee FLS). At high concentrations of IL-6 (40-100ng/ml) hip and knee MCP1 gene expression were similar, suggesting that the differences under basal conditions could be overcome. Because JAK-STAT signaling in RA hips and knee FLS was predicted to be different based on our computational data, we performed dose responses with the JAK inhibitor tofacitinib. Pre-incubation of FLS with various concentrations of tofacitinib prior to IL-6 stimulation reduced IL-6-induced MCP1 expression for both hip and knee FLS, but with greater sensitivity in hip FLS (EC50 of 30 nM for hip FLS and 80 nM for knee FLS). These results suggest that knee FLS required higher concentrations of tofacitinib for the same degree of MCP1 inhibition as hip FLS. Inhibition of basal expression of MCP1 in the absence of exogenous IL-6 was greater for hip compared with knee FLS (50% and 13% inhibition, respectively, n=4/group) suggesting that JAK-STAT-related signaling differs in the joint-specific FLS.

Conclusion:

These studies biologically validate the prediction that RA hip and knee FLS are imprinted with distinct functions related to IL-6 signaling and the JAK-STAT pathway. Differential sensitivity to JAK inhibition could be related to the unique epigenetic imprinting due to joint location and could contribute to variable clinical responses to tofacitinib. Additional studies that profile the epigenome and transcriptome in individual joints could create opportunities for personalized therapy.

Disclosure: D. Hammaker, None; G. Nygaard, None; D. L. Boyle, None; R. Ai, None; W. Wang, None; G. S. Firestein, None.


Abstract Number: 2794

**Apolipoprotein B Binds to Enolase-1 and Aggravates Inflammation in Rheumatoid Arthritis**

**Joo Youn Lee**¹, Min Jueng Kang¹, Yi Jong Choi², Ji Soo Park³, Jin Kyung Park¹,², Eun Young Lee⁴, Eun Bong Lee⁵, Thomas Pap⁶, Eugene Yi⁷ and Yeong Wook Song¹,². ¹Department of Molecular medicine and biopharmaceutical science, Seoul National University, seoul, Korea, Republic of (South), ²Division of Rheumatology, Department of Internal Medicine, Seoul National University, Seoul, Korea, Republic of (South), ³Department of Molecular medicine and biopharmaceutical science, Seoul National University, Seoul, Korea, Republic of (South), ⁴Division of Rheumatology, Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea, Republic of (South), ⁵Division of Rheumatology, Department of Internal Medicine, Seoul National University, Seoul, Korea, Republic of (South), ⁶Institute of Experimental Musculoskeletal Medicine, University Hospital Münster, Münster, Germany

First publication: September 18, 2017
**Background/Purpose:** Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease characterized by synovial inflammation and joint destruction. Monocytes and synovial macrophages are key players in inflammatory process of RA. Enolase-1 (ENO1) is a multifunctional glycolytic enzyme in cytoplasm of cells and it is also found on the cell surface as plasminogen receptor. The majority of cells expressing ENO1 in peripheral blood mononuclear cells (PBMCs) and synovial fluid mononuclear cells (SFMCs) derived from RA patients were known to be CD14-positive monocytes and macrophages. This study was aimed to discover and investigate a novel ligand of cell surface expressed ENO1 and biological role of the interaction between ENO1 and its novel ligand, apolipoprotein B (apoB).

**Methods:** ENO1 binding protein was identified present in RA synovial fluid (SF) using affinity-base mass spectrometry analysis. The interaction between ENO1 and apoB was evaluated using physical characterization, such as ligand blotting assay, ligand binding assay, surface plasmon resonance (SPR), and confocal microscopy. The production of pro-inflammatory cytokines in PBMCs from RA or healthy control (HC) after stimulation with apoB were evaluated using cytokines ELISA. The pro-inflammatory effect of apoB was evaluated in K/BxN serum transfer arthritis mouse model.

**Results:** Characterization of physical interaction between ENO1 and apoB using various binding assay, ligand blotting assay, ligand binding assay, SPR, and confocal microscopy showed that apoB is a novel ligand of ENO1. Interaction between surface ENO1 and apoB induced higher levels of pro-inflammatory cytokines in RA PBMCs than HC PBMCs. When surface ENO1 expression was down-regulated after transfection with ENO1-specific siRNA, production of inflammatory cytokines by RA PBMCs in response to apoB stimulation decreased. Moreover, in K/BxN serum transfer arthritis model, mice were immunized with K/BxN serum and apoB induced exacerbation of arthritis with increased ankle thickness, arthritis score, and production of pro-inflammatory cytokines. LDLR knockout mice are known to have high levels of serum LDL and apoB. The arthritis score and ankle thickness were markedly higher in low density lipoproteins receptor (LDLR) knockout mice compared to wild type after K/BxN serum transfer.

**Conclusion:** In this study, we discovered apoB as a novel ligand of ENO1. ApoB may enhance chronic inflammation in RA patients.

**Disclosure:** J. Y. Lee, None; M. J. Kang, None; J. Y. Choi, None; J. S. Park, None; J. K. Park, None; E. Y. Lee, None; E. B. Lee, None; T. Pap, None; E. Yi, None; Y. W. Song, None.

**Abstract Number:** 2795

**Comparison of Switching from the Originator Rituximab to the Biosimilar Rituximab GP2013 or Re-Treatment with the Originator Rituximab in Patients with Active Rheumatoid Arthritis: Safety and Immunogenicity Results from a Multicenter, Randomized, Double-Blind Study**

Hans-Peter Tony, Hendrik Schulze-Koops, Klaus Krüger, Stanley B Cohen, Alan J. Kivitz, Slawomir Jeka, Edit Vereckei, Liyi Cen and Dmitrij Kollins. 1 Department of Internal Medicine 2, Rheumatology and Clinical Immunology, University Hospital Würzburg, Würzburg, Germany, 2 Division of Rheumatology and Clinical Immunology, Department of Internal Medicine IV, University of Munich, Munich, Germany, 3 Praxiszentrum St. Bonifatius München, München, Germany, 4 Metroplex Clinical Research Centre, Dallas, TX, 5 Altoona Center for Clinical Research, Duncansville, PA, 6 2nd University Hospital, CM UMK, Department of Rheumatology and Connective Tissue Diseases, Bydgoszcz, Poland, 7 National Institute of Rheumatology and Physiotherapy, Budapest, Hungary, 8 Clinical Development, Sandoz, a Novartis Division, Holzkirchen, Germany

**First publication:** September 18, 2017
Session Time: 2:30PM-4:00PM

Background/Purpose: GP2013, a biosimilar to European Union (EU) approved reference rituximab (RTX), developed in a stepwise approach that adheres to stringent biosimilar development guidelines. The biosimilarity of GP2013 and RTX has been confirmed preclinically and in patients with RA and follicular lymphoma. Switching patients from a reference product to its biosimilar has to be shown for regulatory approval in some regions. In this study, the safety and immunogenicity of the switch from RTX to GP2013 was compared with the continued RTX in patients with active RA.

Methods: This randomized, double-blind, parallel-group study in adult patients with active RA was conducted across the United States (US; 28 centers) and the EU (26 centers), who had received the last treatment with RTX 6-18 months prior to randomization and required RTX re-treatment. Patients were randomized (1:1) to receive 1000 mg intravenous infusions of either GP2013 (switch group) or continue RTX (control group) on days 1 and 15. Methotrexate (7.5-25 mg/week) and folic acid were given in the same stable dose as before randomization. Safety assessments included the incidence of hypersensitivity; infusion-related and anaphylactic reactions; immunogenicity (antidrug antibody [ADA] development); the incidence of adverse events (AE), and other safety parameters (vital signs and laboratory parameters). Patients were followed up for 24 weeks.

Results: Of the 107 patients randomized to the switch group (n=53) or control group (n=54), majority of patients completed the study up to 24 weeks (94.3% vs 96.3%). Demographic and baseline characteristics were well balanced between the groups. The incidence of hypersensitivity (9.4% vs 11.1%) and infusion-related reactions (11.3% vs 18.5%) were low and similar in both groups. In the control group, 1 patient developed an anaphylactic reaction within 24 h of infusion. Among the patients, who tested negative for ADA at screening, only 1 patient in the control group tested positive for ADAs in all visits after the first infusion (Table 1). No patient had ADA of neutralizing capacity. The rate of AEs was similar between the groups, serious AE occurred only in the control group (Figure 1). Although more patients in the switch group had AEs in some AE categories, these differences could not be attributed to a cluster of specific events. The majority of patients in both treatment groups did not have newly occurring laboratory abnormalities.

Conclusion: The safety profile, in particular hypersensitivity reactions and occurrence of ADAs, of patients who switched from RTX to GP2013 was comparable with the patients who received continued treatment with RTX.

<table>
<thead>
<tr>
<th>Table 1. Summary of key safety assessments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Switch group (GP2013), ( N=53 ) n/N (%)</td>
</tr>
<tr>
<td>------------------------------------------</td>
</tr>
<tr>
<td>Hypersensitivity reactions⁴</td>
</tr>
<tr>
<td>Infusion-related reactions²</td>
</tr>
<tr>
<td>Anaphylactic reactions³</td>
</tr>
<tr>
<td>ADA¹ positive after screening</td>
</tr>
</tbody>
</table>

⁴Standardized MedDRA Query (SMQ) was used to identify hypersensitivity reactions in the database of adverse events.

²Redefined Query compiling 262 MedDRA Preferred Terms (PT) was used to identify potential infusion-related reactions in the database of Adverse Events occurred on the day of or day after GP2013/RTX infusions.

¹2006 NIAID/FAAN criteria were used to identify anaphylactic reactions within 24 h of the start of GP2013/RTX infusions.

²Patients with negative ADA results at screening and at least an evaluable post-randomization ADA assessment were included in the analysis.

ADA: Antidrug antibodies; CI: confidence interval; MedDRA: Medical Dictionary for Regulatory Activities; n: number of patients with an event; after treatment: N: total number of patients who received respective treatment; NIAID/FAAN: National Institute of Allergy and Infectious Disease and Food Allergy and Anaphylaxis Network; RTX: reference rituximab.
A Randomized, Double Blind Trial over 52 Weeks to Demonstrate Bioequivalence of GP2013 and Reference Rituximab in Patients with Rheumatoid Arthritis

Josef S. Smolen¹, Stanley B Cohen², Morton Scheinberg³, Tamas Shisha⁴, Dmitrij Kollins⁴, Peijuan Zhu⁵, Liyi Cen⁴, Alan J. Kivitz⁶, Andra Rodica Balanescu⁷, Juan J. Gomez-Reino⁸ and Hans-Peter Tony⁹, ¹Medical University Vienna, Division of Rheumatology, Department of Internal Medicine III, Vienna, Austria, ²Metroplex Clinical Research Centre, Dallas, TX, ³Rheumatology, Hospital Israelita Albert Einstein, Sao Paulo, Brazil, ⁴Clinical Development, Sandoz, a Novartis Division, Holzkirchen, Germany, ⁵Clinical Pharmacology, Sandoz, a Novartis Division, NJ, NJ, ⁶Altoona Center for Clinical Research, Duncansville, PA, ⁷Research Center of Rheumatic Diseases, “Sf. Maria” Hospital, University of Medicine and Pharmacy “Carol Davila”, Bucharest, Romania, ⁸BIOBADASER, Santiago, Spain, Santiago de Compostela, Spain, ⁹Department of Internal Medicine 2, Rheumatology and Clinical Immunology, University Hospital Würzburg, Würzburg, Germany

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy III: Biosimilars Therapy
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Rituximab (RTX) is a mAB indicated for the treatment of RA in patients with inadequate response to anti-TNF therapy. The current study compares the biosimilar GP2013 with the reference medicine approved in Europe, RTX-EU and in the US, RTX-US.

Methods: Eligible patients were randomized to GP2013, RTX-EU or RTX-US. The primary endpoint was the area under the serum concentration–time curve from study drug infusion to infinity (AUC₀-inf). The read-out for primary and all key secondary analyses were
performed at week 24 (results submitted for publication). Patients were then followed up to week 52.

**Results:** A total of 312 patients (262 female and 50 male) were randomized. Demographics and baseline characteristics were comparable between the groups. The 90% CI of the ratio of the geometric mean were within the predefined range of 80-125% for the primary and key secondary pharmacokinetic and pharmacodynamic (PD) endpoints demonstrating three-way bioequivalence of GP2013, RTX-EU and RTX-US at week 24 (Table 1). Data was pooled for RTX-US and RTX-EU for efficacy assessments. A similar proportion of patients were retreated in both the groups (GP2013: 70% and RTX: 74%). PD responses remained similar up to the end of the observation period at week 52 (Figure 1). Change from baseline in DAS28 (CRP) at week 24 was -2.07 (Standard error [SE] =-0.108) and -2.11 (SE=0.095) in the GP2013 and the RTX groups, respectively. The difference of 0.04 (95% CI: -0.241, 0.323) was below the pre-defined non-inferiority margin of 0.6. ACR20 response rate was 72.3% (95% CI: 64.2%, 80.3%) and 67.3% (95% CI: 59.9%, 74.7%) in the GP2013 and RTX groups at week 24, respectively. Efficacy outcome remained similar up to week 52 (Figure 2). The rates of adverse events were similar between the groups. Anti-drug antibodies (ADAs) were detected in 16.5% of GP2013 and in 15.1% of RTX-treated patients up to last visit. The ADAs were transient in the majority of patients and neutralizing ADAs were detected in 5 and 1 patient in GP2013 and RTX group, respectively.

**Conclusion:** The study met its primary objective by demonstrating 3-way PK bioequivalence of GP2013, RTX-EU and RTX-US. Three-way PD equivalence, as measured by the depletion of peripheral B cells was also demonstrated. Furthermore, GP2013 and RTX were similar in terms of efficacy, safety and immunogenicity up to week 52.

**Table 1. Summary of primary and key secondary PK/PD results**

<table>
<thead>
<tr>
<th>PK parameter (unit)</th>
<th>Treatment</th>
<th>n</th>
<th>Adjusted geometric mean</th>
<th>Comparison</th>
<th>Geometric mean ratio</th>
<th>90% CI of mean ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary PK endpoints</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AUC_last (day*mcg/mL)</td>
<td>GP2013</td>
<td>124</td>
<td>7627.44</td>
<td>RTX-US vs RTX-EU</td>
<td>1.903</td>
<td>(0.998, 1.208)</td>
</tr>
<tr>
<td></td>
<td>RTX-US</td>
<td>86</td>
<td>7536.89</td>
<td>GP2013 vs RTX-US</td>
<td>1.912</td>
<td>(0.925, 0.103)</td>
</tr>
<tr>
<td></td>
<td>RTX-EU</td>
<td>79</td>
<td>6896.07</td>
<td>GP2013 vs RTX-EU</td>
<td>1.136</td>
<td>(1.010, 1.210)</td>
</tr>
<tr>
<td><strong>Key secondary PK endpoints</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C_max (mcg/mL)</td>
<td>GP2013</td>
<td>120</td>
<td>361.53</td>
<td>RTX-US vs RTX-EU</td>
<td>1.090</td>
<td>(0.948, 1.167)</td>
</tr>
<tr>
<td></td>
<td>RTX-US</td>
<td>82</td>
<td>335.60</td>
<td>GP2013 vs RTX-US</td>
<td>1.076</td>
<td>(0.979, 1.154)</td>
</tr>
<tr>
<td></td>
<td>RTX-EU</td>
<td>79</td>
<td>319.60</td>
<td>GP2013 vs RTX-EU</td>
<td>1.131</td>
<td>(1.027, 1.244)</td>
</tr>
<tr>
<td><strong>Key secondary PD endpoint (B cell depletion)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AUEC_{0-52} (mcg*day)</td>
<td>GP2013</td>
<td>119</td>
<td>12313.53</td>
<td>RTX-US vs RTX-EU</td>
<td>1.033</td>
<td>(1.016, 1.050)</td>
</tr>
<tr>
<td></td>
<td>RTX-US</td>
<td>86</td>
<td>1210.57</td>
<td>GP2013 vs RTX-US</td>
<td>0.989</td>
<td>(0.974, 1.004)</td>
</tr>
<tr>
<td></td>
<td>RTX-EU</td>
<td>76</td>
<td>1201.15</td>
<td>GP2013 vs RTX-EU</td>
<td>1.021</td>
<td>(1.003, 1.040)</td>
</tr>
</tbody>
</table>

**Figure 1. Arithmetic mean (± standard deviation) of percent B-cell relative to baseline**

![Figure 1](image-url)
Disclosure: J. S. Smolen, None; S. B. Cohen, None; M. Scheinberg, None; T. Shisha, Sandoz, a Novartis division, 3; D. Kollins, Sandoz, a Novartis division, 3; P. Zhu, Sandoz, a Novartis division, 3; L. Cen, Sandoz, a Novartis division, 3; A. J. Kivitz, None; A. R. Balanescu, None; J. J. Gomez-Reino, None; H. P. Tony, None.


Abstract Number: 2797

Etanercept Biosimilar GP2015 Has Equivalent Efficacy and Safety to Etanercept Originator in Patients with Moderate to Severe Rheumatoid Arthritis: The Phase 3 Equira Study

Arthur Kavanaugh1, Yannick Allanore2, Eugeniusz J. Kucharz3 and Goran Babic4, 1Medicine, University of California, San Diego, La Jolla, CA, 2Department of Rheumatology, Cochin Hospital, Paris Descartes University, Paris, France, 3Department of Internal Medicine and Rheumatology, Medical University of Silesia, Katowice, Poland, 4Clinical development, Biopharmaceuticals, Hexal AG, a Sandoz company, Holzkirchen, Germany

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy III: Biosimilars Therapy
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: The biosimilarity of GP2015 and etanercept originator product (ETN) has been previously demonstrated in patients with chronic plaque-type psoriasis.1 The randomized, double-blind, phase 3 study, EQUIRA (NCT02638259) compared the efficacy and safety of GP2015 versus ETN in patients with moderate-to-severe RA and an inadequate response to DMARDs. Here, we present the 24-week results (TP1).

Methods: Patients (aged ≥ 18 years) with active RA (diagnosed according to the ACR 1987 or ACR/EULAR 2010 criteria for ≥ 6 months before baseline and active disease defined as DAS28-CRP ≥ 3.2, and CRP >5 mg/L or ESR ≥28 mm/h), who had an inadequate clinical response to MTX at a dose of 10 - 25 mg/week, were randomized 1:1 to self-administer 50 mg GP2015 or ETN subcutaneously, once weekly, for 24 weeks. All patients continued to receive concomitant MTX (10 - 25 mg/week), at a stable dose throughout the study and folic acid (≥ 5 mg/week until end of study). The primary endpoint was change from baseline in DAS28-CRP at week 24.

Results: The baseline demographic and disease characteristics were comparable between the GP2015 (n=170) and ETN (n=156) groups. In the per-protocol set, GP2015 was determined to be equivalent to ETN in the LS mean change from baseline to week 24 in DAS28-CRP, as the 95% CI was within the pre-specified equivalence margin of -0.6; 0.6 (LS means difference between GP2015 vs
ETN: -0.04, 95% CI: -0.24, 0.15). At week 24, the ACR 20/50/70 response rates and the mean change from baseline in DAS28-CRP scores were comparable between GP2015 and ETN groups (Table). In the GP2015 (n=186) vs ETN (n=190) groups (safety set), treatment-emergent adverse events (AEs) occurred in 43.5% vs 49.5% patients, respectively; SAEs occurred in 0.5% vs 3.2% patients, respectively. One patient died in the ETN group. Injection site reactions, as a part of all AEs, were reported in 7.0% of patients in GP2015 and 17.9% of patients in ETN group. Using a very sensitive assay, very low titers of ADAs were transiently detected, however at week 24 none of the patients had significant levels detected.

### Table. Efficacy response over 24 weeks (per-protocol set)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Time</th>
<th>GP2015 N = 170</th>
<th>ETN N = 156</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAS28-CRP, LS means difference (95% CI)</td>
<td>Week 24</td>
<td>-0.04 (-0.24, 0.15)</td>
<td></td>
</tr>
<tr>
<td>DAS28-CRP (mean change)</td>
<td>Week 4</td>
<td>-1.61</td>
<td>-1.71</td>
</tr>
<tr>
<td></td>
<td>Week 12</td>
<td>-2.23</td>
<td>-2.21</td>
</tr>
<tr>
<td></td>
<td>Week 24</td>
<td>-2.78</td>
<td>-2.81</td>
</tr>
<tr>
<td>EULAR good response, n* (%)</td>
<td>Week 24</td>
<td>83 (48.8)</td>
<td>75 (48.1)</td>
</tr>
<tr>
<td>EULAR moderate response, n* (%)</td>
<td>Week 24</td>
<td>83 (48.8)</td>
<td>77 (49.4)</td>
</tr>
<tr>
<td>ACR20 (% responders)</td>
<td>Week 4</td>
<td>48.8</td>
<td>53.5</td>
</tr>
<tr>
<td></td>
<td>Week 12</td>
<td>79.2</td>
<td>76.8</td>
</tr>
<tr>
<td></td>
<td>Week 24</td>
<td>88.8</td>
<td>93.6</td>
</tr>
<tr>
<td>ACR50 (% responders)</td>
<td>Week 4</td>
<td>15.5</td>
<td>19.4</td>
</tr>
<tr>
<td></td>
<td>Week 12</td>
<td>33.9</td>
<td>44.5</td>
</tr>
<tr>
<td></td>
<td>Week 24</td>
<td>63.9</td>
<td>71.2</td>
</tr>
<tr>
<td>ACR70 (% responders)</td>
<td>Week 4</td>
<td>4.8</td>
<td>5.2</td>
</tr>
<tr>
<td></td>
<td>Week 12</td>
<td>13.1</td>
<td>16.8</td>
</tr>
<tr>
<td></td>
<td>Week 24</td>
<td>33.7</td>
<td>42.9</td>
</tr>
</tbody>
</table>

*total number of patients achieving responses/remission

BL, baseline; ETN, etanercept originator product

**Conclusion:** GP2015 demonstrated equivalent efficacy to ETN in patients with RA who had an inadequate response to DMARDs. Overall, the safety profile was comparable between GP2015 and ETN.


**Disclosure:** A. Kavanaugh, Sandoz, Merck, Boehringer Ingelheim, 5; Y. Allanoore, Sandoz, Sanofi, Pfizer, Roche Genentech, 5,Sanofi, Pfizer, Roche Genentech, 2; E. J. Kucharz, Hexal AG, a Sandoz company, 5; G. Babic, Hexal AG, a Sandoz company, 3.


**Abstract Number:** 2798

**A Randomized, Double-Blind Study Comparing PF-06438179/GP1111, a Potential Infliximab Biosimilar, and Infliximab, Both in Combination with MTX, As Treatment for Patients with Moderate to Severe Active RA Who Have Had an Inadequate Response to MTX Therapy**

Stanley B Cohen¹, Rieke Alter², Hideto Kameda³, Muhammad I. Rehman⁴, Karl Schumacher⁵, Susanne Schmitt⁵, Steven Y. Hua⁶ and K. Lea Sewell⁷, ¹Metroplex Clinical Research Center, Dallas, TX, ²Schlosspark-Klinik, University Medicine Berlin, Berlin, Germany, ³Division of Rheumatology, Department of Internal Medicine, Toho University Ohashi Medical Center, Tokyo, Japan, ⁴Pfizer Inc, Andover, MA, ⁵Global Clinical Development, Biopharmaceuticals, Hexal AG, Holzkirchen, Germany, ⁶Pfizer Inc, San Diego, CA, ⁷Biosimilars Development, Pfizer Inc, Cambridge, MA

**First publication:** September 18, 2017
Background/Purpose: This double-blind, randomized study evaluated efficacy, safety and immunogenicity of PF-06438179/GP1111, a potential infliximab biosimilar, vs infliximab sourced from the EU (infliximab-EU) in patients (pts) with moderate to severe active RA with inadequate response to MTX and ≤2 doses of 1 non-depleting, non-infliximab biologic. We report results after the first 30 wks of treatment.

Methods: Pts (N=650), stratified by geographic region, were randomized 1:1 to PF-06438179/GP1111 or infliximab-EU (3 mg/kg IV at wks 0, 2, 6 and then every 8 wks), both given with MTX (10-25 mg/wk). Dose escalation to 5 mg/kg was allowed starting at wk 14 for pts with inadequate response. Primary endpoint was ACR20 response rate at wk 14. Secondary efficacy endpoints included ACR20 response rate, Disease Activity Score-28, 4 components based on high-sensitivity C-reactive protein (DAS28-CRP) and other measures of clinical response or remission up to wk 30. Therapeutic equivalence was declared if the 2-sided 95% confidence interval (CI) for the difference between groups in ACR20 at wk 14 was within the symmetric equivalence margin of ±13.5%. A 2-sided 90% CI was also calculated, as requested by the FDA, using the asymmetric equivalence margin of –12.0% to +15.0%.

Results: Pts (80.3% female; 79.4% seropositive) had a mean RA duration of 6.9 yrs; mean baseline DAS28-CRP was 6.0 in both groups. Wk 14 ACR20 response rates in the intent-to-treat population were 62.7% for PF-06438179/GP1111 and 64.1% for infliximab-EU. Using non-responder imputation for missing data (n=23; 3.5%), the treatment difference was –2.39%; corresponding CIs (95%: –9.92%, +5.11%; 90%: –8.75%, +4.02%) were entirely contained within the pre-specified equivalence margins (symmetric and asymmetric). Response rates through wk 30 were similar, with the ACR20 treatment difference ranging from –5.81% to –0.83% at the specified visits. Mean change in DAS28-CRP from baseline was –2.1 at wk 30 for both groups. ACR50, ACR70 and European League Against Rheumatism (EULAR) response as well as DAS remission (DAS28 <2.6) and ACR/EULAR remission were similar between groups at each study visit. Eighty-three pts each in the PF-06438179/GP1111 (25.7%) and infliximab-EU (25.5%) groups dose escalated at or after wk 14. Incidences of all-causality treatment-emergent adverse events (57.3% vs 54.0%) and serious adverse events (any event: 5.0% vs 6.1%; infections: 1.9% vs 2.8%) were similar between PF-06438179/GP1111 and infliximab-EU, respectively. Infusion related reactions (5.9% vs 6.4%), hypersensitivity (13.6% vs 15.6%), pneumonia (0.9% vs 0.9%) and latent/active tuberculosis (0.3% vs 0.3%) were also similar between PF-06438179/GP1111 and infliximab-EU, respectively. Overall post-dose anti-drug antibody rates through wk 30 were 48.6% for PF-06438179/GP1111 and 51.2% for infliximab-EU.

Conclusion: PF-06438179/GP1111 and infliximab-EU showed similar efficacy, safety and immunogenicity in pts with moderate to severe active RA on background MTX. This ongoing trial will evaluate clinical efficacy, safety and immunogenicity after a single transition from infliximab-EU to PF-06438179/GP1111 after 30 or 54 wks of treatment.


Efficacy, Safety and Immunogenicity in Randomized, Double-Blind (DB) and Open-Label Extension (OLE) Studies Comparing FKB327, an Adalimumab Biosimilar, with the Adalimumab Reference Product (Humira®; RP) in Patients (pts) with Active Rheumatoid Arthritis (RA)

Mark C. Genovese1, Josephine Glover2, Nobuhito Matsunaga3, Diane Chisholm4 and Rieke Alten5, 1Stanford University Medical Center, Palo Alto, CA, 2Coephycient Pharmaceutical Consultancy, Guildford, United Kingdom, 3Fujifilm Kyowa Kirin Biologics,
SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy III: Biosimilars Therapy
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: FKB327 is a proposed biosimilar of the adalimumab RP. A randomized, DB, Phase 3 study (NCT02260791) compared the efficacy, safety, pharmacokinetics (PK) and immunogenicity of FKB327 and RP in pts with active RA inadequately controlled on methotrexate (MTX). This was followed by a randomized OLE study with treatment switching (NCT02405780) which assessed long-term safety, efficacy, PK and immunogenicity.

Methods: Pts aged ≥18 years with moderate to severe, active RA (2010 ACR criteria) for ≥3 months and taking MTX for ≥3 months (10–25 mg/week stable dose for ≥8 weeks) were enrolled. In the DB study, pts were randomized 1:1 to FKB327 or RP (40 mg subcutaneously [sc]) every other week (eow) with continuing MTX. The primary endpoint was ACR20 response rate at Week 24 with prespecified equivalence margins of −12 to +15% for a two-sided 90% confidence interval (CI), recommended by the FDA. Secondary endpoints included DAS28-CRP at Week 24 and ACR20/50/70 response rates over time. Safety was assessed by the incidence/severity of adverse events (AEs) and laboratory abnormalities. In the OLE, pts completing the DB study with clinical response and no serious AEs were immediately re-randomized to FKB327 or RP so that two-thirds of pts remained on the same treatment as in the DB study and one-third switched to the alternate treatment (40 mg sc eow) for Weeks 0–28 (Part 1), then all received FKB327 to Week 76 (Part 2). The primary endpoint was safety. Interim analysis of the OLE was performed when results of approximately 100 patient-years’ continuous treatment were available on both products.

Results: In the DB study, 728 pts from 12 countries were treated with FKB327 (n=366) or RP (n=362). Demographics and baseline RA characteristics were similar between the groups, with mean MTX dose of 15.8 mg/week (standard deviation [SD] 4.8) and mean RA duration of 8.5 years (SD 8.0). ACR20 response rate at Week 24 (non-responder imputation, full analysis set) was comparable (FKB327 72.5%; RP 74.3%); 90% CI (−7.3, 3.6) fell within prespecified equivalence margins. DAS28-CRP at Week 24 and ACR20/50/70 response rates over time were highly comparable. Safety profiles, mean serum trough drug concentration at steady state, and prevalence/titer of anti-drug antibodies (ADAs) were all well-matched. Re-randomization in the OLE resulted in 645 pts receiving the following treatment sequences across the DB then OLE (Part 1) studies: FKB327–FKB327, n=216; RP–RP, n=213; FKB327–RP, n=108; and RP–FKB327, n=108. At interim analysis, safety profiles were comparable for all treatment sequences, although group sizes were reduced after switching. ACR20 response rate at Week 30 was comparable after continuous (FKB327–FKB327, 82.5%; RP–RP, 84.3%) and switched (FKB327–RP, 86.5%; RP–FKB327, 89.1%) treatment. No consistent differences in PK and ADA profiles were seen between continuous and switched treatments.

Conclusion: The DB study met its primary equivalency endpoint for ACR20 response rate at Week 24; safety, ADA and PK profiles also supported the comparability of FKB327 and RP in pts with active RA. Interim OLE results suggested that long-term safety, efficacy, PK and immunogenicity of FKB327 and RP were comparable on continuous and switched treatment.

Disclosure: M. C. Genovese, Fujifilm Kyowa Kirin Biologics, 5; J. Glover, Fujifilm Kyowa Kirin Biologics, 5; N. Matsunaga, Fujifilm Kyowa Kirin Biologics, 3; D. Chisholm, Fujifilm Kyowa Kirin Biologics, 3; R. Alten, None.


Abstract Number: 2800

Long-Term Safety and Efficacy of Biosimilar Infliximab (CT-P13) after Switching from Originator Infliximab: Results from the 26-Week Open Label Extension of a Randomized Norwegian Trial

Guro Løvik Goll¹, Kristin Kaasen Jørgensen², Joe Sexton¹, Inge C Olsen³, Nils Bolstad⁴, Merete Lorentzen⁵, Espen A. Haavardsøl⁶, Cato Mork⁷, Jorgen Jahnson⁸ and Tore K Kvien⁹, ¹Dept Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, ²Dept Gastroenterology, Akershus University Hospital, Lørenskog, Norway, ³Department of Rheumatology, Diakonhjemmet Hospital,
SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy III: Biosimilars Therapy
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:
TNF-inhibitors (TNFi) have improved treatment of rheumatoid arthritis (RA), spondyloarthritis (SpA), psoriatic arthritis (PsA), Crohn’s disease (CD), ulcerative colitis (UC), and chronic plaque psoriasis (Ps). The NOR-SWITCH study was funded by the Norwegian government to investigate if switching from originator infliximab (Remicade®, INX) to CT-P13 (biosimilar infliximab, Remsima®) is safe.

Methods:
The study was designed as a 52-week randomized, double-blind, non-inferiority, phase IV trial with a 26 week open label extension in which all patients received CT-P13. Adult patients with a diagnosis of RA, SpA, PsA, CD, UC, or Ps on stable treatment with originator infliximab were randomized 1:1 to either continued INX or switch to CT-P13 treatment in the main study. Patients on CT-P13 throughout the 78-week study period (maintenance group) and patients switched to CT-P13 at week 52 (switch group) were assessed for treatment efficacy, safety and immunogenicity. The primary endpoint was disease worsening during follow-up according to disease-specific composite measures and/or a consensus between investigator and patient leading to major change in treatment.

Results:
Between October 2014 and July 2016, 481 patients (INX 241, CT-P13 240, Full Analysis Set, FAS) were randomized, received treatment and were followed for 52 weeks. Results from the main trial showed that CT-P13 is non-inferior to continued treatment with originator infliximab. 380 patients entered the extension phase of the trial. The main demographic and baseline (52w) characteristics of the extension study population are shown in the table. Disease worsening occurred in 16.8% and 11.6% of patients in the maintenance and switch arms, respectively (Per Protocol Set, PPS). The frequency of disease worsening in each specific diagnosis is shown in the table (exploratory analyses). Changes in the generic disease variables and disease specific composite measures were similar in both arms (table). During the extension study, 3/197 and 5/183 patients in the maintenance and switch groups (FAS), respectively, developed anti-drug antibodies. Trough drug levels and the frequencies of reported adverse events were comparable between the two groups (data not shown).

Conclusion:
The open-label extension of the NOR-SWITCH trial did not show any difference between patients who maintained CT-P13 vs patients who switched from INX to CT-P13.
<table>
<thead>
<tr>
<th>Demographics and baseline characteristics</th>
<th>Maintenance group</th>
<th>Switch group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients (FAS)</td>
<td>197</td>
<td>183</td>
</tr>
<tr>
<td>Age (years)</td>
<td>47.8 (14.9)</td>
<td>47 (14.3)</td>
</tr>
<tr>
<td>Females</td>
<td>64 (32.5%)</td>
<td>78 (42.6%)</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>17.1 (10.6)</td>
<td>16.3 (10.4)</td>
</tr>
<tr>
<td>Duration of ongoing infliximab treatment (years)</td>
<td>6.7 (3.8)</td>
<td>6.4 (3.5)</td>
</tr>
<tr>
<td>Concomitant immunosuppressive therapy</td>
<td>103 (52.3%)</td>
<td>82 (44.8%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diagnoses</th>
<th>Maintenance group</th>
<th>Switch group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid arthritis</td>
<td>27 (13.7%)</td>
<td>28 (15.3%)</td>
</tr>
<tr>
<td>Spondyloarthritis</td>
<td>38 (19.3%)</td>
<td>29 (15.8%)</td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
<td>9 (4.6%)</td>
<td>11 (6%)</td>
</tr>
<tr>
<td>Crohn’s disease</td>
<td>65 (33%)</td>
<td>62 (33.9%)</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>42 (21.3%)</td>
<td>38 (20.8%)</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>16 (8.1%)</td>
<td>15 (8.2%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Disease characteristics</th>
<th>Maintenance group</th>
<th>Switch group</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAS 28 (RA and PsA)</td>
<td>2.3 (1.0)</td>
<td>2.8 (1.2)</td>
</tr>
<tr>
<td>ACPA positive (RA)</td>
<td>13/27 (48.1%)</td>
<td>18/28 (64.3%)</td>
</tr>
<tr>
<td>ASDAS (SpA)</td>
<td>1.9 (0.8)</td>
<td>1.7 (0.7)</td>
</tr>
<tr>
<td>BASDAI (SpA)</td>
<td>3.2 (1.8)</td>
<td>2.6 (1.6)</td>
</tr>
<tr>
<td>Harvey-Bradshaw Index</td>
<td>1 (0 – 4)</td>
<td>1 (0.2 – 4)</td>
</tr>
<tr>
<td>Partial Mayo Score</td>
<td>0 (0 – 0)</td>
<td>0 (0 – 1)</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate (mm/h) (all)</td>
<td>8 (4-17)</td>
<td>7 (4-15)</td>
</tr>
<tr>
<td>C-reactive protein (mg/L) (all)</td>
<td>2 (1 – 5)</td>
<td>2 (1 – 5)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Disease worsening</th>
<th>Maintenance group</th>
<th>Switch group</th>
<th>Risk difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>32 (16.8%)</td>
<td>20 (11.6%)</td>
<td>-5.9% (-12.9-1.1)</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>9 (34.6%)</td>
<td>6 (22.2%)</td>
<td>-10.5% (-34.6-13.6)</td>
</tr>
<tr>
<td>Spondyloarthritis</td>
<td>3 (7.9%)</td>
<td>2 (7.1%)</td>
<td>-0.6% (-13.5-12.2)</td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
<td>1 (12.5%)</td>
<td>3 (33.3%)</td>
<td>20.8% (-17.6-59.1)</td>
</tr>
<tr>
<td>Crohn’s disease</td>
<td>13 (20.6%)</td>
<td>8 (13.1%)</td>
<td>-7.9% (-21-5.2)</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>6 (15.1%)</td>
<td>1 (2.9%)</td>
<td>-12.4% (-25-0.1)</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0% (0-0)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Disease measures at week78</th>
<th>Maintenance group</th>
<th>Switch group</th>
<th>Adjusted difference week 78 (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 78</td>
<td>Week 78</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physician Global Assessment of Disease Activity (0-10)</td>
<td>1.45 (1.55)</td>
<td>1.15 (1.51)</td>
<td>0.13 (-0.13-0.4)</td>
</tr>
</tbody>
</table>
### Data Table:

<table>
<thead>
<tr>
<th></th>
<th>Mean (SD)</th>
<th>Median (25–75 percentiles)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient Global Assessment of Disease Activity (0-10)</strong></td>
<td>2.58 (2.26)</td>
<td>0.48 (0.16-0.8)</td>
</tr>
<tr>
<td><strong>Log(_{10}) erythrocyte sedimentation rate (mm/h)</strong></td>
<td>0.89 (0.4)</td>
<td>0 (-0.05-0.05)</td>
</tr>
<tr>
<td><strong>Log(_{10}) C-reactive protein (mg/L)</strong></td>
<td>0.31 (0.48)</td>
<td>-0.02 (-0.1-0.05)</td>
</tr>
<tr>
<td><strong>Harvey-Bradshaw Index (CD)</strong></td>
<td>2.93 (3.24)</td>
<td>0.57 (-0.2-1.33)</td>
</tr>
<tr>
<td><strong>Partial Mayo Score (UC)</strong></td>
<td>0.88 (1.55)</td>
<td>0.44 (-0.13-1.01)</td>
</tr>
<tr>
<td><strong>ASDAS (SpA)</strong></td>
<td>2.13 (0.85)</td>
<td>0.2 (-0.06-0.46)</td>
</tr>
<tr>
<td><strong>DAS28 (RA, PsA)</strong></td>
<td>2.48 (1.54)</td>
<td>0.19 (-0.33-0.71)</td>
</tr>
<tr>
<td><strong>CDAI (RA, PsA)</strong></td>
<td>6.81 (7.47)</td>
<td>1.92 (-1.07-4.91)</td>
</tr>
<tr>
<td><strong>SDAI (RA, PsA)</strong></td>
<td>7.41 (7.95)</td>
<td>2.13 (-1.86-6.12)</td>
</tr>
<tr>
<td><strong>PASI (Ps)</strong></td>
<td>1.49 (0.89)</td>
<td>-0.28 (-0.87-0.31)</td>
</tr>
</tbody>
</table>

Data are n (%), mean (SD) or median (25 – 75 percentiles). 95% CI, 95% confidence interval of the adjusted treatment difference. BASDAI, Bath Ankylosing Spondylitis Disease Activity Index. ASDAS, Ankylosing Spondylitis Disease Activity Score. DAS28, Disease Activity Score in 28 joints. CDAI, Clinical Disease Activity Index. SDAI, Simplified Disease Activity Index. PASI, Psoriasis Area and Severity Index.

---

### Notes:


### Disclosure:


### Abstract Number:

2801

### Effects of Anti-IL17 Blockade with Secukinumab on Systemic and Local Immune Responses: A Mechanism-of-Action Study in Peripheral Spondyloarthritis

**Leonieke van Mens**1, Marleen van de Sande2, Silvia Menegatti3, Iris Blijdorp4, Jet de Jong2, Inka Fluri4, Talia Latuhihin1, Arno van Kuijk5, Nataliya Yeremenko4 and Dominique Baeten1, AMC, Amsterdam Immunology and Rheumatology Center, Amsterdam, Netherlands, 2Clinical Immunology and Rheumatology, Amsterdam Rheumatology and immunology Center, Academic Medical Center/University of Amsterdam, Amsterdam, Netherlands, 3Immunology, Immunoregulation Unit, Institut Pasteur, Paris, France, 4Amsterdam Immunology and Rheumatology Center, Amsterdam, Netherlands, 5Reade, Amsterdam Immunology and Rheumatology Center, Amsterdam, Netherlands

**First publication:** September 18, 2017

### SESSION INFORMATION
**Background/Purpose:** IL-17A blockade is an effective therapy for AS and PsA, the prototypical forms of spondyloarthritis (SpA). How IL-17A blockade affects the systemic and local immune responses in SpA remains incompletely understood. Our aim was to assess the effect of anti-IL17A treatment with secukinumab on the systemic cytokine responses and the synovial immunopathology in SpA patients with peripheral disease (pSpA).

**Methods:** 20 active SpA patients were included in a 12wk open-label trial followed by 2yrs non-investigational extension. All patients received secukinumab 300mg/wk from baseline (bsl) to wk4 and then every 4wks. TruCulture tubes with SEB and zymosan were drawn at bsl, day3, and wk12. Synovial biopsies were obtained by needle arthroscopy at bsl and wk12, analyzed by immunohistochemistry (IHC) and qPCR.

**Results:** The 20 pSpA patients were 13 PsA, 3 undifferentiated SpA, 2 AS with peripheral arthritis, 1 reactive arthritis and 1 IBD associated pSpA. There were no SAEs in the 12wk core study. Two SAEs occurred in the extension: tonsillitis (suspected related to study drug) and myocardial infarction (non related), both fully recovered. Secukinumab induced a rapid and highly significant improvement in SJC (median bsl: 2,5[IQR1-4] vs wk12: 0,5[IQR0-1]p=0.001), TJC(6[2-8] vs 0,5[0-3]p=0.001); VAS pt global(46[28-65] vs 13[6-24]p<0.001). 18/20 patients reached EULAR good or moderate DAS response (Resp) at wk 12(10 good, and 8 moderate Resp). In parallel, improvements of BASDAI(53[25-63] vs 20[9-40]p=0.001) and PASI(5,7[4,5-7,1] vs 0,6[0,1-1,8]p=0.001), CRP(3,85[1,35-16,6] vs 2[1,15-6,3]p=0.001) and ESR(16[6-35] vs 6[2,8-16,3]p=0.001) was seen. This was associated with decreased production of MMP-3, a validated biomarker of inflammation in pSpA (VanDooren, A&R, 2004) by peripheral blood cells in the TruCulture system (figure). With exception of a decrease in IL-17A, the TruCulture system did not reveal any impact of secukinumab on the capacity of peripheral blood cells to produce a broad panel of cytokines and chemokines. Contrasting this preserved systemic immune response, IHC confirmed the positive impact of 12wks of secukinumab on peripheral joint immunopathology as reflected by a significant decrease of macrophage infiltrate of the synovial sublining (2[1-3] vs 1,5[1-2]p=0.028) and neutrophils (1[0,5-3,5] vs 0[0-1]p=0.004), sensitive synovial biomarkers of treatment response in pSpA (Kruithof, A&R, 2005) mRNA analysis of synovial biopsies before and after 12wks of secukinumab shows a decrease in IL-17A but not TNF expression.

**Conclusion:** This mechanistic study indicates that IL-17A blockade with secukinumab has a profound beneficial clinical and biological impact on pSpA without compromising systemic immune responses. Further gene expression analysis will delineate which inflammatory pathways are blocked by secukinumab in the diseased target tissue.
Sustained Remission of Inflammation Is Associated with Reduced Structural Damage on SI Joint MRI in Patients with Early Axial Spa: Evidence to Support the Concept of Treat-to-Target

Walter P. Maksymowych, Pascal Claudepierre, Manouk de Hooge, Robert G. Lambert, Robert B.M. Landewé, Anna Molto, Désirée van der Heijde, Jack F Bukowski, Heather Jones, Isabelle Logeart, Lisa Marshall, Ronald Pedersen, Annette Szumski, Bonnie Vlahos, Maxime Dougados, Radiology & Diagnostic Imaging, University of Alberta, Edmonton, AB, Canada, Universite Paris Est Creteil, Paris, France, Leiden University Medical Center, Leiden, Netherlands, Department of Radiology & Diagnostic Imaging, University of Alberta, Edmonton, AB, Canada, Amsterdam Rheumatology & Immunology Center, Amsterdam, Netherlands, Hopital Cochin, Department of Rheumatology, Paris Descartes University, Paris, France, Clinical Affairs, Pfizer, Collegeville, PA, Inflammation & Immunology Global Medical Affairs, Pfizer, Collegeville, PA, Medical Affairs, Pfizer, France, Paris, France, Department of Biostatistics, Pfizer, Collegeville, PA, Biostatistics, inVentiv Health, Princeton, NJ, Clinical Sciences, Pfizer, Collegeville, PA, Hopital Cochin, Paris Descartes University, Paris, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment III
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:
Treat-to-target is an accepted strategy in RA; however, it is unknown whether it will reduce/prevent disability, impairment of mobility, and structural damage in patients with early axial SpA (axSpA) who do not meet modified New York criteria for radiographic sacroiliitis. We evaluated the impact of sustained clinical remission on MRI structural parameters. We hypothesized that patients with sustained inactive disease (Ankylosing Spondylitis Disease Activity Score [ASDAS] <1.3) are more likely to achieve reduction in erosion (structural damage) and increase in backfill (a reparative process) on MRI of the SI joints (SIJ).

Methods:
The EMBARK (NCT01258738) and DESIR (NCT01648907) studies enrolled patients with early axSpA. EMBARK included a 12-week double-blind placebo-controlled period, then open-label etanercept for 92 weeks. DESIR patients had no history of biologic therapy and did not receive biologics for 2 years. T1 weighted MRI images of the SIJ at baseline (BL) and 104 weeks were combined and anonymized; readers were unaware of film chronology and original patient cohort. Three experienced readers evaluated the MRI images using the SpondyloArthritis Research Consortium of Canada (SPARCC) SIJ Structural Score (SSS). Change in erosion or backfill was considered present if 2 of 3 readers measured change in the same direction. ASDAS endpoints were: sustained inactive disease (Ankylosing Spondylitis Disease Activity Score [ASDAS] <1.3) are more likely to achieve reduction in erosion (structural damage) and increase in backfill (a reparative process) on MRI of the SI joints (SIJ).

Results:
In EMBARK and DESIR, 150 and 68 patients, respectively, had BL and 104-week MRI images and ASDAS measurements every 6 months. For the patients in EMBARK with sustained ASDAS inactive disease, the proportion with a decrease in erosion was significantly greater than with an increase, and the proportion with an increase in backfill was significantly greater than with a decrease, in both the unadjusted and adjusted analyses (Table). In the adjusted analysis, this was also the case for patients with MDA. This trend was also present for patients with sustained ASDAS inactive disease in DESIR; the difference between proportions was not as great as in EMBARK.

Conclusion:
These results are important because, for the first time, the data demonstrate a link between achieving sustained ASDAS inactive disease and MRI structural endpoints. The clinical relevance of change in MRI erosion and backfill in the SIJ and their relationship to the development of ankylosis requires further study.

Table. Patients in EMBARK with a decrease or increase in MRI structural lesion according to sustained ASDAS response type
<table>
<thead>
<tr>
<th>Sustained ASDAS response type</th>
<th>Lesion decreased n/N (%)</th>
<th>Lesion increased n/N (%)</th>
<th>Net % patients with increase (95% CI)</th>
<th>P-value</th>
<th>Net % patients with increase (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Erosion (Damage)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASDAS inactive disease (&lt;1.3)</td>
<td>Response</td>
<td>33/100 (33.0)</td>
<td>5/100 (5.0)</td>
<td>-28.0 (-38.8, -17.2)</td>
<td>&lt;0.0001</td>
<td>-22.8 (-37.9, -7.7)</td>
</tr>
<tr>
<td></td>
<td>Non-response</td>
<td>9/50 (18.0)</td>
<td>2/50 (4.0)</td>
<td>-14.0 (-28.7, 0.7)</td>
<td>0.06</td>
<td>-17.1 (-34.9, 0.7)</td>
</tr>
<tr>
<td>ASDAS &lt;2.1</td>
<td>Response</td>
<td>39/129 (30.2)</td>
<td>6/129 (4.7)</td>
<td>-25.6 (-35.0, -16.1)</td>
<td>&lt;0.0001</td>
<td>-25.7 (-37.3, -14.0)</td>
</tr>
<tr>
<td></td>
<td>Non-response</td>
<td>3/21 (14.3)</td>
<td>1/21 (4.8)</td>
<td>-9.5 (-31.8, 12.7)</td>
<td>0.39</td>
<td>-8.4 (-35.8, 18.9)</td>
</tr>
<tr>
<td>Best sustained ASDAS response</td>
<td>Inactive disease</td>
<td>33/100 (33.0)</td>
<td>5/100 (5.0)</td>
<td>-28.0 (-38.8, -17.2)</td>
<td>&lt;0.0001</td>
<td>-22.8 (-37.9, -7.7)</td>
</tr>
<tr>
<td></td>
<td>MDA (≥1.3 to &lt;2.1)</td>
<td>6/29 (20.7)</td>
<td>1/29 (3.4)</td>
<td>-17.2 (-37.7, 3.3)</td>
<td>0.10</td>
<td>-41.6 (-69.5, -13.7)</td>
</tr>
<tr>
<td></td>
<td>Non-response</td>
<td>3/21 (14.3)</td>
<td>1/21 (4.8)</td>
<td>-9.5 (-31.5, 12.5)</td>
<td>0.39</td>
<td>-8.8 (-34.0, 16.3)</td>
</tr>
<tr>
<td><strong>Backfill (Repair)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASDAS inactive disease (&lt;1.3)</td>
<td>Response</td>
<td>0/100 (0)</td>
<td>2/210 (22.0)</td>
<td>22.0 (13.9, 30.1)</td>
<td>&lt;0.0001</td>
<td>19.5 (7.7, 31.3)</td>
</tr>
<tr>
<td></td>
<td>Non-response</td>
<td>1/50 (2.0)</td>
<td>3/50 (6.0)</td>
<td>4.0 (-5.0, 13.0)</td>
<td>0.38</td>
<td>8.1 (-3.4, 19.7)</td>
</tr>
<tr>
<td>ASDAS &lt;2.1</td>
<td>Response</td>
<td>0/129 (0)</td>
<td>23/129 (17.8)</td>
<td>17.8 (11.3, 24.4)</td>
<td>&lt;0.0001</td>
<td>17.0 (8.5, 25.5)</td>
</tr>
<tr>
<td></td>
<td>Non-response</td>
<td>1/21 (4.8)</td>
<td>2/21 (9.5)</td>
<td>4.8 (-12.1, 21.7)</td>
<td>0.57</td>
<td>9.4 (-11.5, 30.4)</td>
</tr>
<tr>
<td>Best sustained ASDAS response</td>
<td>Inactive disease</td>
<td>0/100 (0)</td>
<td>22/210 (22.0)</td>
<td>22.0 (13.9, 30.1)</td>
<td>&lt;0.0001</td>
<td>19.5 (7.7, 31.3)</td>
</tr>
<tr>
<td></td>
<td>MDA (≥1.3 to &lt;2.1)</td>
<td>0/29 (0)</td>
<td>1/29 (3.4)</td>
<td>3.4 (-5.9, 12.8)</td>
<td>0.46</td>
<td>15.5 (0.4, 30.6)</td>
</tr>
<tr>
<td></td>
<td>Non-response</td>
<td>1/21 (4.8)</td>
<td>2/21 (9.5)</td>
<td>4.8 (-11.1, 20.6)</td>
<td>0.55</td>
<td>9.5 (-9.0, 28.0)</td>
</tr>
</tbody>
</table>

*Adjusted for covariates at baseline: sex, symptom duration, smoking status, human leukocyte antigen-B27 status, ASDAS, SPARCC MRI SIJ score, total SIJ score based on modified New York grade.

MDA, moderate disease activity.

**Disclosure:** W. P. Maksymowych, Abbvie, Pfizer, 2,Abbvie, Janssen, Lilly, Merck, Novartis, Pfizer, UCB, 5; P. Claudepierre, Pfizer, Roche-Chugai, MSD, 2,Abbvie, BMS, Celgene, Janssen, Novartis, Merck, Pfizer, Roche, UCB; M. de Hooge, MdH Research, 3; R. G. Lambert, BioClinica, 5,AbbVie, 8; R. B. M. Landewé, Abbott/AbbVie, Ablynx, Amgen, Astra-Zeneca, Bristol Myers Squibb, Celgene, Janssen (formerly Centocor), Galapagos, GlaxoSmithKline, Novartis, Novo-Nordisk, Merck, Pfizer, Roche, Schering-Plough, TiGenix, UCB, and Wyeth, 5,Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, and Wyeth, 2,Abbott/AbbVie, Amgen, Bristol Myers Squibb, Janssen (formerly Centocor), Merck, Pfizer, Roche, Schering-Plough, UCB, and Wyeth, 8; A. Molto,
None; D. van der Heijde, AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, Glaxo-Smith-Kline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB; AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer, Director: Imaging Rheumatology bv; J. F. Bukowski, Pfizer Inc, 1, Pfizer Inc, 3; H. Jones, Pfizer Inc, 1, Pfizer Inc, 3; I. Logeat, Pfizer Inc, 1, Pfizer Inc, 3; L. Marshall, Pfizer Inc, 1, Pfizer Inc, 3; R. Pedersen, Pfizer Inc, 1, Pfizer Inc, 3; A. Szmuski, inVentiv Health, 3; B. Vlahos, Pfizer Inc, 1, Pfizer Inc, 3; M. Dougados, Pfizer, AbbVie, UCB, Merck and Lily, 2, Pfizer, AbbVie, UCB, Merck and Lily, 5.


Abstract Number: 2803

Predictors of Remission Maintenance up to Week 68 and Successful Therapy Discontinuation in Patients with Non-Radiographic Axial Spondyloarthritis Who Achieved Sustained Remission on 28-Week Open-Label Adalimumab Treatment

Joachim Sieper¹, Robert B.M. Landewé², Marina N. Magrey³, Jaclyn K. Anderson⁴, Sheng Zhong⁴, Xin Wang⁴ and Apinya Lertratanakul⁴, ¹Charité Universitätsmedizin Berlin, Berlin, Germany, ²University of Amsterdam, Amsterdam, Netherlands, ³Case Western Reserve University School of Medicine at MetroHealth Medical Center, Cleveland, OH, ⁴AbbVie Inc., North Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment III
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Sustained remission is an important treatment goal in patients (pts) with non-radiographic axial SpA (nr-axSpA). Factors predicting successful remission maintenance are unknown. We sought to identify predictors of remission maintenance in nr-axSpA pts who achieved remission after open-label (OL) adalimumab (ADA) treatment in the ABILITY-3 trial (NCT01808118) and were subsequently randomized to continuation or withdrawal of ADA therapy.

Methods: ABILITY-3 enrolled adult pts with nr-axSpA with objective evidence of active MRI inflammation in the SI joints or spine or elevated high-sensitivity CRP at screening, active disease at baseline (ASDAS ≥2.1, BASDAI ≥4, and Patient's Assessment of Total Back Pain score ≥ 4), and inadequate response to ≥2 NSAIDs (Table). Pts received ADA 40 mg every other wk during a 28-wk OL lead-in period. Pts who achieved sustained remission, defined as ASDAS inactive disease [ID] score <1.3 at wks 16, 20, 24, and 28, were randomized to double-blind withdrawal (placebo; PBO) or continued ADA for 40 wks during period 2 (study wk 68). Stepwise logistic regression was used to identify predictors of sustained remission in those in the continued ADA and withdrawal (PBO) groups who did not experience a flare (defined as ASDAS ≥2.1 at 2 consecutive study visits) during period 2. Remission maintenance in period 2 was assessed with the following: ASAS partial remission (PR; score ≤ 2.0) and ASDAS ID at wk 68, ASAS PR and ASDAS ID at every visit, and ASDAS ID for ≥5 of 10 visits.

Results: By wk 68, 100/145 (69%) ADA pts had not flared; shorter symptom duration and very low wk 28 ASDAS were associated with absence of flare. Of those without flare, 58% achieved ASAS PR and 78% ASDAS ID at wk 68; 33% achieved ASAS PR and 42% ASDAS ID at every visit. Very low wk 28 ASDAS predicted sustained remission at all subsequent visits (Figure 1A). By wk 68, 70/148 (47%) PBO pts had not flared; lower wk 28 ASDAS was associated with absence of flare. Of those without flare, 59% achieved ASAS PR and 70% ASDAS ID at wk 68; 29% achieved ASAS PR and 31% ASDAS ID at every visit (Figure 1B).
<table>
<thead>
<tr>
<th>Variable</th>
<th>Adalimumab (40 mg EOW)</th>
<th>Placebo</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline, mean (SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>n=152</td>
<td>n=153</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>34.7 (10.3)</td>
<td>35.3 (10.2)</td>
<td>0.611</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>56 (37)</td>
<td>60 (39)</td>
<td>0.724</td>
</tr>
<tr>
<td>SpA symptom duration, y</td>
<td>6.4 (6.9)</td>
<td>7.1 (6.8)</td>
<td>0.358</td>
</tr>
<tr>
<td>HLA-B27 positive, n (%)</td>
<td>132 (87)</td>
<td>134 (88)</td>
<td>0.866</td>
</tr>
<tr>
<td>ASDAS</td>
<td>3.5 (0.9)</td>
<td>3.5 (0.8)</td>
<td>0.851</td>
</tr>
<tr>
<td>BASDAI</td>
<td>6.8 (1.4)</td>
<td>6.8 (1.5)</td>
<td>0.851</td>
</tr>
<tr>
<td>BASFI</td>
<td>5.1 (2.3)</td>
<td>5.0 (2.3)</td>
<td>0.776</td>
</tr>
<tr>
<td>Hs-CRP, mg/L</td>
<td>9.9 (14.1)</td>
<td>9.1 (13.3)</td>
<td>0.576</td>
</tr>
<tr>
<td>Pt total back pain</td>
<td>7.0 (1.7)</td>
<td>7.0 (1.8)</td>
<td>0.946</td>
</tr>
<tr>
<td>PGA</td>
<td>6.6 (1.5)</td>
<td>6.4 (1.4)</td>
<td>0.150</td>
</tr>
<tr>
<td>SPARCC SI joint score*</td>
<td>8.5 (12.8)</td>
<td>10.3 (13.4)</td>
<td>0.226</td>
</tr>
<tr>
<td>SPARCC spine score</td>
<td>3.3 (7.5)</td>
<td>3.6 (7.2)</td>
<td>0.671</td>
</tr>
<tr>
<td>Wk 28, mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASDAS</td>
<td>0.7 (0.4)</td>
<td>0.6 (0.4)</td>
<td>0.355</td>
</tr>
<tr>
<td>BASDAI</td>
<td>0.8 (0.8)</td>
<td>0.7 (0.7)</td>
<td>0.145</td>
</tr>
<tr>
<td>BASFI</td>
<td>0.7 (1.0)</td>
<td>0.7 (1.2)</td>
<td>0.994</td>
</tr>
<tr>
<td>Hs-CRP, mg/L</td>
<td>1.5 (2.4)</td>
<td>1.4 (1.8)</td>
<td>0.647</td>
</tr>
<tr>
<td>Pt total back pain</td>
<td>1.1 (1.4)</td>
<td>1.0 (1.4)</td>
<td>0.567</td>
</tr>
<tr>
<td>PGA</td>
<td>0.8 (1.0)</td>
<td>0.9 (1.1)</td>
<td>0.386</td>
</tr>
<tr>
<td>SPARCC SI joint score‡</td>
<td>2.6 (6.1)</td>
<td>2.5 (4.0)</td>
<td>0.775</td>
</tr>
<tr>
<td>SPARCC spine score‡</td>
<td>1.2 (3.8)</td>
<td>1.2 (3.8)</td>
<td>0.889</td>
</tr>
</tbody>
</table>

ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; EOW, every other week; HLA-B27, human leukocyte antigen B27; hs-CRP, high-sensitivity C-reactive protein, PGA, physician global assessment of disease activity; Pt, patient; SI, sacroiliac; SpA, spondyloarthritis; SPARCC, Spondyloarthritis Research Consortium of Canada.

*Adalimumab, n=150; placebo, n=151
‡Adalimumab, n=145; placebo, n=148
Conclusion: In nr-axSpA pts who achieved remission after 28-wk OL ADA therapy, very low ASDAS at week 28 predicted absence of flare in both the continued ADA and withdrawal group. With continued ADA, shorter symptom duration also predicted absence of flare, and achievement of very low ASDAS at week 28 predicted sustained remission using most remission definitions, suggesting early aggressive treatment may be beneficial in achieving sustained remission. No consistent predictors of sustained remission after ADA withdrawal were identified.

Disclosure: J. Sieper, AbbVie, Janssen, Lilly, Merck, Novartis, Pfizer, Sun Pharma and UCB, 5,AbbVie, Janssen, Lilly, Merck, Novartis, and Pfizer, 8; R. B. M. Landewé, Abbott/AbbVie, Ablynx, Amgen, Astra-Zeneca, Bristol Myers Squibb, Celgene, Janssen (formerly Centocor), Galapagos, GlaxoSmithKline, Novartis, Novo-Nordisk, Merck, Pfizer, Roche, Schering-Plough, TIGenix, UCB, and Wyeth, 5,Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, and Wyeth, 2,Abbott/AbbVie, AbbVie, 5,Abbott, Amgen, and UCB Pharma, 2,UCB and Janssen, 5, J. K. Anderson, Abbvie, 3,Abbvie, 1; S. Zhong, AbbVie, 1,AbbVie, 3; X. Wang, Abbvie, 3,Abbvie, 1; A. Lertratanakul, AbbVie, 1,AbbVie, 3.

Abstract Number: 2804

Pregnancy Outcomes in Patients with Ankylosing Spondylitis: A Nationwide Population Study
Pregnancy outcomes in patients with ankylosing spondylitis: a nationwide population study.

**Background/Purpose:** Autoimmune inflammatory diseases influence on pregnancy outcomes. But rare studies have focus on the ankylosing spondylitis (AS) and pregnancy outcomes.

**Methods:** The primary data source was the National Health Insurance database and national birth registry of Taiwan. We obtained records of all pregnancies in Taiwan between 2001 and 2012 from a national insurance database. Maternal and fetal outcomes were obtained from national birth registry.

**Results:** We analyzed data from 2,350,339 women between 2001 and 2012 categorized into 2 groups. Subjects in the reference group (2,347,847 women) had no AS diagnosis, and those in the AS group (2,492 women) had diagnosed with AS before pregnancy. Maternal outcomes in patients with AS revealed a higher adjusted odds ratio for Puerperal cerebrovascular disorders (OR 4.05 95% CI 2.02 to 8.12), Preterm labor (OR 1.18 95% CI 1.00 to 1.38), cesarean delivery (OR 1.08 95% CI 1.01 to 1.15), pulmonary edema (OR 4.99 95% CI 1.24 to 20.10) and gestational diabetes (OR 1.16 95% CI 1.02 to 1.34). The neonatal outcomes in AS group showed a higher adjusted OR for poorer 1 minute Apgar score (<7) (OR 1.38 95% CI 1.10 to 1.75), poorer 5 minute Apgar score (<7) (OR 1.60 95% CI 1.02 to 2.52), fetal abnormalities (OR 1.20 95% CI 1.03 to 1.39), chromosomal abnormalities (OR 1.72 95% CI 1.15 to 2.59) and unspecific abnormalities (OR 1.28 95% CI 1.01 to 1.62).

**Conclusion:** Patients with AS were associated with higher prevalence of adverse birth outcomes.
<table>
<thead>
<tr>
<th>Overall outcomes</th>
<th>Pregnancies N (%)</th>
<th>Crude Odds ratio (95% CI)</th>
<th>Adjusted Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Without AS</td>
<td>With AS</td>
<td></td>
</tr>
<tr>
<td>Death _30 days post-partum</td>
<td>314 (0.01)</td>
<td>0 (0.00)</td>
<td>N/A</td>
</tr>
<tr>
<td>Death _1 year post-partum</td>
<td>793 (0.03)</td>
<td>0 (0.00)</td>
<td>N/A</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute myocardial</td>
<td>111 (0.00)</td>
<td>0 (0.00)</td>
<td>N/A</td>
</tr>
<tr>
<td>Aneurysm</td>
<td>52 (0.00)</td>
<td>0 (0.00)</td>
<td>N/A</td>
</tr>
<tr>
<td>Cardiac arrest/ventricular fibrillation</td>
<td>116 (0.00)</td>
<td>0 (0.00)</td>
<td>N/A</td>
</tr>
<tr>
<td>Heart failure</td>
<td>144 (0.01)</td>
<td>2 (0.08)</td>
<td>1.58 (0.40-6.28)</td>
</tr>
<tr>
<td>Shock</td>
<td>1,191 (0.05)</td>
<td>2 (0.08)</td>
<td>4.59 (0.65-32.3)</td>
</tr>
<tr>
<td>Pregnancy-related hypertenstion</td>
<td>53,984 (2.30)</td>
<td>65 (2.61)</td>
<td>1.14 (0.89-1.48)</td>
</tr>
<tr>
<td>Gestational hypertension</td>
<td>23,028 (0.98)</td>
<td>25 (1.00)</td>
<td>1.03 (0.69-1.54)</td>
</tr>
<tr>
<td>Puerperal cerebrovascular disorders</td>
<td>1,705 (0.07)</td>
<td>8 (0.32)</td>
<td>4.33 (2.12-8.85)*</td>
</tr>
<tr>
<td>Thrombotic embolism</td>
<td>214 (0.01)</td>
<td>2 (0.08)</td>
<td>4.59 (0.65-32.3)</td>
</tr>
<tr>
<td>Complication during delivery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amniotic fluid embolism</td>
<td>232 (0.01)</td>
<td>0 (0.00)</td>
<td>N/A</td>
</tr>
<tr>
<td>Antepartum hemorrhage</td>
<td>209,662 (8.93)</td>
<td>257 (10.31)</td>
<td>1.18 (1.03-1.34)*</td>
</tr>
<tr>
<td>Postpartum hemorrhage due to atony</td>
<td>12,621 (0.54)</td>
<td>19 (0.76)</td>
<td>1.43 (0.91-2.24)</td>
</tr>
<tr>
<td>Postpartum hemorrhage not due to atony</td>
<td>3,501 (0.15)</td>
<td>4 (0.16)</td>
<td>1.08 (0.41-2.88)</td>
</tr>
<tr>
<td>Severe postpartum hemorrhage</td>
<td>63,287 (2.70)</td>
<td>83 (3.33)</td>
<td>1.24 (0.99-1.56)</td>
</tr>
<tr>
<td>Preterm labor</td>
<td>106,014 (4.52)</td>
<td>148 (5.94)</td>
<td>1.34 (1.13-1.59)*</td>
</tr>
<tr>
<td>Premature rupture of membranes</td>
<td>83 (0.00)</td>
<td>0 (0.00)</td>
<td>N/A</td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>8,057 (0.34)</td>
<td>7 (0.28)</td>
<td>0.80 (0.38-1.67)</td>
</tr>
<tr>
<td>Cesarean delivery</td>
<td>781,237 (33.27)</td>
<td>992 (39.81)</td>
<td>1.33 (1.23-1.44)*</td>
</tr>
<tr>
<td>Induction of labor</td>
<td>117 (0.00)</td>
<td>0 (0.00)</td>
<td>N/A</td>
</tr>
<tr>
<td>Surgical complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe anesthesia</td>
<td>302 (0.01)</td>
<td>0 (0.00)</td>
<td>N/A</td>
</tr>
<tr>
<td>Complications</td>
<td>Cases</td>
<td>Rate (%)</td>
<td>Control Cases</td>
</tr>
<tr>
<td>---------------------------------------------------</td>
<td>-------</td>
<td>----------</td>
<td>---------------</td>
</tr>
<tr>
<td>Thorax, abdomen, and pelvis injuries</td>
<td>5,585</td>
<td>0.24</td>
<td>4(0.16)</td>
</tr>
<tr>
<td>Intracranial injuries</td>
<td>13,296</td>
<td>0.57</td>
<td>15(0.60)</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>1,859</td>
<td>0.08</td>
<td>3(0.12)</td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>1,605</td>
<td>0.07</td>
<td>2(0.08)</td>
</tr>
<tr>
<td>Operations on heart and pericardium</td>
<td>1,011</td>
<td>0.04</td>
<td>2(0.08)</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adult respiratory distress syndrome</td>
<td>5,867</td>
<td>0.25</td>
<td>8(0.32)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>1,541</td>
<td>0.07</td>
<td>2(0.08)</td>
</tr>
<tr>
<td>Disseminated intravascular coagulation</td>
<td>37,046</td>
<td>1.58</td>
<td>49(1.97)</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>330</td>
<td>0.01</td>
<td>2(0.08)</td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>103</td>
<td>0.00</td>
<td>0(0.00)</td>
</tr>
<tr>
<td>Temporary tracheostomy</td>
<td>19,810</td>
<td>0.84</td>
<td>31(1.24)</td>
</tr>
<tr>
<td>Ventilation</td>
<td>1,690</td>
<td>0.07</td>
<td>0(0.00)</td>
</tr>
<tr>
<td>Gestational diabetes</td>
<td>126,485</td>
<td>5.39</td>
<td>204(8.19)</td>
</tr>
</tbody>
</table>

_Adjusted for age, infant sex, Charlson comorbidity index, urbanization, income, occupation, birth year, maternal nationality

*p<0.05

Table 2. Comparison of neonatal outcomes between pregnancies associated with maternal AS or not.
<table>
<thead>
<tr>
<th>Category</th>
<th>Without AS (n=2,347,847)</th>
<th>With AS (n=2,492)</th>
<th>Crude Odds ratio (95% CI)</th>
<th>Adjusted Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stillbirth</strong></td>
<td>17,346 (0.74)</td>
<td>17 (0.68)</td>
<td>0.93 (0.57-1.49)</td>
<td>0.81 (0.50-1.30)</td>
</tr>
<tr>
<td><strong>Stillbirth</strong> explained</td>
<td>1,766 (0.08)</td>
<td>3 (0.12)</td>
<td>1.60 (0.52-4.97)</td>
<td>1.38 (0.44-4.28)</td>
</tr>
<tr>
<td><strong>Stillbirth</strong> unexplained</td>
<td>15,580 (0.66)</td>
<td>14 (0.56)</td>
<td>0.85 (0.50-1.44)</td>
<td>0.75 (0.44-1.26)</td>
</tr>
<tr>
<td><strong>Low birth weight (&lt;2500 g)</strong></td>
<td>151,048 (6.43)</td>
<td>173 (6.94)</td>
<td>1.19 (1.03-1.38)*</td>
<td>1.06 (0.91-1.22)</td>
</tr>
<tr>
<td><strong>Prematurity (&lt;37 week)</strong></td>
<td>178,059 (7.58)</td>
<td>219 (8.79)</td>
<td>1.10 (0.94-1.30)</td>
<td>1.10 (0.96-1.26)</td>
</tr>
<tr>
<td><strong>Small for gestational age</strong></td>
<td>227,984 (9.71)</td>
<td>221 (8.87)</td>
<td>0.91 (0.78-1.05)</td>
<td>0.97 (0.85-1.11)</td>
</tr>
<tr>
<td><strong>Large for gestational age</strong></td>
<td>231,066 (9.84)</td>
<td>227 (9.11)</td>
<td>0.91 (0.79-1.05)</td>
<td>0.85 (0.74-0.97)</td>
</tr>
<tr>
<td><strong>APGAR SCORE 1 min (&lt;7)</strong></td>
<td>46,844 (2.00)</td>
<td>71 (2.85)</td>
<td>1.45 (1.14-1.83)*</td>
<td>1.38 (1.10-1.75)*</td>
</tr>
<tr>
<td><strong>APGAR SCORE 5 min (&lt;7)</strong></td>
<td>12,194 (0.52)</td>
<td>19 (0.76)</td>
<td>1.48 (0.94-2.32)</td>
<td>1.60 (1.02-2.52)*</td>
</tr>
<tr>
<td><strong>Fetal distress</strong></td>
<td>116,442 (4.96)</td>
<td>125 (5.02)</td>
<td>1.00 (0.83-1.20)</td>
<td>1.00 (0.84-1.19)</td>
</tr>
<tr>
<td><strong>Fetal abnormalities, any</strong></td>
<td>105,705 (4.50)</td>
<td>165 (6.62)</td>
<td>1.52 (1.29-1.79)*</td>
<td>1.20 (1.03-1.39)*</td>
</tr>
<tr>
<td><strong>Central nervous system malformations</strong></td>
<td>10,085 (0.43)</td>
<td>8 (0.32)</td>
<td>0.73 (0.36-1.48)</td>
<td>0.67 (0.33-1.34)</td>
</tr>
<tr>
<td><strong>Chromosomal abnormalities</strong></td>
<td>10,207 (0.43)</td>
<td>23 (0.92)</td>
<td>2.15 (1.40-3.30)*</td>
<td>1.72 (1.15-2.59)*</td>
</tr>
<tr>
<td><strong>Hereditary disease in family possible affecting fetus</strong></td>
<td>1,863 (0.08)</td>
<td>4 (0.16)</td>
<td>1.95 (0.66-5.71)</td>
<td>1.55 (0.58-4.12)</td>
</tr>
<tr>
<td><strong>Suspected damage due to viral or other disease in the mother</strong></td>
<td>3,122 (0.13)</td>
<td>7 (0.28)</td>
<td>2.26 (1.09-4.69)*</td>
<td>1.62 (0.77-3.40)</td>
</tr>
<tr>
<td><strong>Suspected damage due to drugs or radiation decreased fetal movements</strong></td>
<td>923 (0.04)</td>
<td>0 (0.00)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Suspected damage due to drugs or radiation other/unspecified abnormalities</strong></td>
<td>33,970 (1.45)</td>
<td>59 (2.37)</td>
<td>1.66 (1.28-2.17)*</td>
<td>1.17 (0.91-1.51)</td>
</tr>
<tr>
<td><strong>Other/unspecified abnormalities</strong></td>
<td>42,411 (1.81)</td>
<td>69 (2.77)</td>
<td>1.59 (1.24-2.04)*</td>
<td>1.28 (1.01-1.62)*</td>
</tr>
</tbody>
</table>

_Adjusted for age, infant sex, Charlson comorbidity index, urbanization, income, occupation, birth year, maternal nationality

*p<0.05

Disclosure: Y. F. Fang. None;


Abstract Number: 2805
Juvenile-Onset Ankylosing Spondylitis Has a Lower Rate of Radiographic Progression Than Adult-Onset Ankylosing Spondylitis

Anthony So¹, Ammepa Anton², Florence Tsui³, Ismail Sari⁴, Renise Ayerst⁵, Robert D Inman⁶ and Nigil Haroon⁴, ¹University of British Columbia, Vancouver, BC, Canada, ²University Health Network, Toronto, ON, Canada, ³University of Toronto, Toronto, ON, Canada, ⁴Rheumatology, Toronto Western Hospital, University of Toronto, Spondylitis Clinic, Toronto, ON, Canada, ⁵Medicine, University Health Network, Toronto, ON, Canada, ⁶Department of Immunology, University of Toronto, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment III
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: There are no large radiographic follow up studies assessing progression in juvenile-onset Ankylosing Spondylitis (JoAS) as compared to adult-onset Ankylosing Spondylitis (AoAS). The purpose of this study is to examine the clinical and imaging aspects of JoAS in a large spondylitis clinic.

Methods: The spondylitis clinic has a database of around 1300 patients with confirmed ankylosing spondylitis (AS) as defined by the modified New York criteria. AS patients with symptom onset of back pain at 16 years of age or under were classified as JoAS. They were then matched by gender and duration of back pain to patients with symptom onset of back pain over 16 years old, defined as AoAS, in a 1:2 ratio. Clinical and radiographic data were then extracted. The analysis utilized linear or logistic regression analysis to correct for disease duration, gender, prior anti-TNF exposure, ESR, and HLA-B27 status as appropriate.

Results: 158 JoAS patients were identified and matched to 316 AoAS patients. There was a total of 365 males and 106 females. Baseline mean BASDAI was 4.36 for JoAS and 5.00 for AoAS and was not significantly different when adjusted for prior anti-TNF use. However, patient global disease activity was 4.38 for JoAS and 5.16 for AoAS, which was significantly different (p=0.032) after adjusting for prior anti-TNF use. Current and previous history of smoking exposure, iritis, and psoriasis did not differ between JoAS and AoAS. There was more associated Crohn’s disease in JoAS (13%) versus AoAS (4%), p=0.001. There was no difference in B27 status between the two groups. Baseline mSASSS was lower in JoAS (3.9%) vs AoAS (11.6%), and was statistically different when corrected for prior anti-TNF, duration of back pain, gender, baseline ESR, and B27 status (p<0.001). When followed over time, progression of 1 mSASSS unit or more yearly was lower in the JoAS (11%) vs AoAS (24%), and was still significant when corrected for gender, prior anti-TNF use, ESR, and HLA-B27 status, p=0.018. Progression of 4 mSASSS units or more over any time period was lower in the JoAS (14%) vs AoAS (35%), and was still significant when corrected for the covariates above, p=0.001. More JoAS (65%) were on biologics compared to AoAS (47%), p<0.001. Of the patients on biologics, more JoAS (52%) had switched biologics compared to AoAS (33%), p=0.006.

Conclusion: The rate of axial radiographic progression over time was lower in the JoAS cohort when corrected for covariates. JoAS patients were also on more biologics and switched biologics more regularly compared to AoAS patients.

Disclosure: A. So, None; A. Anton, None; F. Tsui, None; I. Sari, None; R. Ayerst, None; R. D. Inman, None; N. Haroon, Abbvie, Amgen, Janssen, Novartis, 5.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/juvenile-onset-ankylosing-spondylitis-has-a-lower-rate-of-radiographic-progression-than-adult-onset-ankylosing-spondylitis

Abstract Number: 2806

Integrated Longitudinal Analysis Increases Precision and Reduces Bias: A Comparative 5-Year Analysis in the DESIR Cohort

Alexandre Sepriano¹, Sofia Ramiro², Désirée van der Heijde¹, Maxime Dougados³, Pascal Claudepierre⁴, Antoine Feydy⁵, M. Reijnierse⁶, Damien Loueille⁷ and Robert B.M. Landewé⁸, ¹Leiden University Medical Center, Leiden, Netherlands, ²Rheumatology, Department of Rheumatology, LUMC, Leiden, Netherlands, Leiden, Netherlands, ³Paris-Descartes University,, Paris, France, ⁴Hôpital Henri Mondor, Créteil, France, ⁵Univ. Paris Descartes, PRES Sorbonne Paris Cité, Service de radiologie B, Hôpital Cochin, Assistance Publique - Hôpitaux de Paris, Paris, France, ⁶Department of Radiology, Leiden University Medical Center, Leiden,
SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthopathies and Psoriatic Arthritis – Clinical Aspects and Treatment III
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Evaluation of imaging is important in spondyloarthritis (SpA) research, but loss to follow up often jeopardizes interpretation of the evaluation. The Interpretation may further be challenged by the fact that often different readers have contributed to scores, in multiple read ‘waves’. A common approach is to evaluate patients (pts) with complete follow up (completers analysis), and aggregate scores of individual readers (eg. agreement ≥ 2 out of 3 readers). These approaches are not assumption-free, may cause non-random data loss, and may as such provide spurious estimates and loss of external validity. We investigated if the use of all data in an assumption-free manner (a so called ‘integrated analysis’) affects the precision of estimates for imaging outcomes in pts with axial SpA (axSpA), with completers analysis as reference standard.

Methods: Pts from the DESIR cohort fulfilling the ASAS axSpA criteria were included. Radiographs and MRIs of the SIJ and spine were obtained at baseline (BL), 1, 2 and 5 years. Each film was scored by 2 or 3 readers in 3 ‘reading-waves’ (wave 1: BL only; wave 2: BL, 1, 2 years; wave 3: BL, 2, 5 years). Each outcome was analyzed in two ways: i. according to a ‘combination algorithm’ (’2 out of 3’ for binary and mean of 3 readers for continuous variables); and ii. per individual reader. The change of each outcome was analyzed by generalized estimating equations (GEE) with ‘time’ as explanatory variable. Three analytical approaches were pursued: i) ‘integrated-analysis’ (including all pts with ≥ 1 score from ≥ 1 reader from all waves); ii) completers-only analysis (including only pts with complete 5-year follow-up, using scores from individual readers from wave 3); iii) aggregated completers analysis using a combination algorithm (the same as ii but using combined scores).

Results: In total, 413 pts were included (mean (SD) symptom duration: 1.6 (0.9) years) and 366 completed the 5-year follow up. An analysis with all data from different readers and ‘waves’ (‘integrated analysis’) was more inclusive, but did not result in a meaningful loss of precision (width of 95%Cs) of the change-estimates as compared to both completers analyses (table). In fact, for low-incident outcomes (e.g. the formation of new syndesmophytes), an increased incidence was ‘captured’ by the ‘integrated analysis’ but not by the completers analysis with combined scores (% change/year (95% CI): 0.67 (0.34; 1.01) vs 0.39 (-0.10; 0.90), respectively). The same results were seen using continuous outcomes.

Conclusion: An efficient and entirely assumption-free usage of all data from different readers and ‘read-waves’ does not compromise precision of the estimates of change in imaging parameters, and may yield increased statistical power for detecting changes with low incidence. In addition, integrated analysis may protect against attrition bias and avoid bias by ‘convenient choices’.

Disclosure: A. Sepriano, None; S. Ramiro, None; D. van der Heijde, None; M. Dougados, None; P. Claudepierre, None; A. Feydy, None; M. Reijnierse, None; D. Louille, None; R. B. M. Landewé, None.

Can the Automated Neuropsychological Assessment Metrics (ANAM) Predict Cognitive Impairment Compared to a Comprehensive Neuropsychological Battery in Patients with Lupus?

Zahi Touma1, Dorcas Beaton2, Carmela Tartaglia3, Lesley Ruttan4, Sabrina Lombardi4, Nicole Anderson5, Jiandong Su6, Kenneth Colosimo7, Michelle Vitti7, Dennisse Bonilla8, Joan E. Wither9, Marvin J. Fritzler10 and Robin Green11. 1Rheumatology, University of Toronto, Division of Rheumatology, Institute of Health Policy, Management and Evaluation, Toronto, ON, Canada, 2Mobility Program Clinical Research Unit, St Michael's Hospital, Toronto, ON, Canada, 3University of Toronto, Krembil Neurosciences Centre, Toronto, ON, Canada, 4Toronto Rehabilitation Institute, Toronto, ON, Canada, 5Division of Rheumatology, Toronto Western Hospital and University of Toronto, Toronto, ON, Canada, 6Rheumatology, Centre for Prognosis Studies in the Rheumatic Diseases, Toronto Western Hospital and University of Toronto, Toronto, ON, Canada, 7University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, 8Krembil Research Institute, University Health Network, Toronto, ON, Canada, 9Rheumatology, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, 10Medicine, University of Calgary, Calgary, AB, Canada, 11Brain and Therapeutics, Toronto Rehabilitation Institute, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment IV: Neuropsychiatric Disease and Health Economics
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Currently, the diagnosis of cognitive impairment (CI) is often delayed requiring use of a comprehensive battery (CB) which imposes a time- and cost-burden. It would therefore be beneficial to have a more expedient CI screening tool that can be used in the ambulatory clinic setting. The Automated Neuropsychological Assessment Metrics (ANAM) is a computerized tool that can be used to screen for CI. We determined the ability of ANAM (v4) GNS Battery to predict CI in patients with systemic lupus erythematosus (SLE).

Methods: Consecutive consenting SLE patients (n=98), aged 18-65 years, who attended a single center between July 2016 and April 2017 were recruited. Participants were administered the ANAM and CB on the same day. ANAM throughput scores were used to provide an estimate of ‘cognitive efficiency’. Patient scores on the ANAM and CB were compared to a normative sample of age- and gender-matched healthy controls to obtain z-scores.

The CB evaluates the following major cognitive domains: manual motor speed and dexterity, simple attention and processing speed, visual-spatial construction, verbal fluency, learning and memory (visuospatial and memory), and executive functioning (untimed and timed). ANAM evaluates the following major cognitive domains: attention and processing speed, memory, visual-spatial processing, executive functioning, abstract language function and fine motor processing. Tests comprising the CB and ANAM are listed in Table 1.

CI was operationalized on the CB and ANAM as a z-score of ≤ -1.5 on ≥2 domains or a z-score ≤-2.0 on ≥1 domains, or either (Table 2).

The performance of ANAM was compared against the CB using different CI definitions. Descriptive analysis was used to determine prevalence, sensitivity (Sn), specificity (Sp), Positive Predictive Value (PPV) and Negative Predictive Value (NPV).

Results: Of the 98 patients (90.8% female), the mean age at SLE diagnosis was 28.5 ± 10.2 and disease duration at enrolment was 15.5 ± 10.0 years. Prevalence of CI using CB ranged between 40.0-44.8 % (z≤-1.5 in ≥2 domains and z≤-2.0 in ≥1 domains, respectively) and 55.2% for either. Prevalence of CI using the ANAM ranged between 30.8-39.3% % (z≤-1.5 in ≥2 domains and z≤-2.0 in ≥1 domains, respectively) and 43.0% for either.

ANAM sensitivity/specificity was 52/73% and PPV/NPV was 70/55% [based on z≤-1.5 in ≥2 domains or z≤-2.0 in ≥1 domains for ANAM and CB (corresponding for A+B and E+F in Table 2)].
Conclusion: ANAM is a promising tool for the assessment of CI in SLE. Future studies are required to determine if the sensitivity of the ANAM can be improved against the current CB.
<table>
<thead>
<tr>
<th>Table 1. Comprehensive battery and ANAM domains and subtests</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Comprehensive Battery</strong></td>
</tr>
<tr>
<td><strong>Domains</strong></td>
</tr>
<tr>
<td>Manual motor speed and dexterity</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Simple attention and processing speed</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Visual-spatial construction</td>
</tr>
<tr>
<td>Verbal fluency</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Learning and memory</td>
</tr>
<tr>
<td>Visuospatial</td>
</tr>
<tr>
<td>Verbal</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Executive Functioning</td>
</tr>
<tr>
<td>Untimed</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Executive timed</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Fine motor</td>
</tr>
</tbody>
</table>
Table 2. Performance of ANAM against the comprehensive battery

<table>
<thead>
<tr>
<th>Definitions of CI</th>
<th>Comprehensive Battery</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>z≤-1.5 in ≥2 domains</td>
<td>z≤-2.0 in ≥1 domains</td>
</tr>
<tr>
<td></td>
<td>E</td>
<td>F</td>
</tr>
<tr>
<td></td>
<td>Sn/Sp</td>
<td>Sn/Sp</td>
</tr>
<tr>
<td></td>
<td>PPV/NNV</td>
<td>PPV/NNV</td>
</tr>
<tr>
<td>ANAM</td>
<td>A</td>
<td>45/81%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>62/68%</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>55/76%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>61/71%</td>
</tr>
<tr>
<td></td>
<td>A+B</td>
<td>55/69%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>55/69%</td>
</tr>
</tbody>
</table>

Sn sensitivity; Sp specificity; PPV Positive Predictive Value/ NPV Negative Predictive Value

Disclosure: Z. Touma, None; D. Beaton, None; C. Tartaglia, None; L. Ruttan, None; S. Lombardi, None; N. Anderson, None; J. Su, None; K. Colosimo, None; M. Vitti, None; D. Bonilla, None; J. E. Wither, None; M. J. Fritzler, Inova Diagnostics, Inc., 5; R. Green, None.


Abstract Number: 2808

Longitudinal Assessment of Cognitive Function in SLE: Identification of Trajectories

Zahi Touma1, Jiandong Su2 and Patricia P. Katz3, 1Rheumatology, University of Toronto, Division of Rheumatology, Institute of Health Policy, Management and Evaluation, Toronto, ON, Canada, 2University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, Medicine/Rheumatology, University of California, San Francisco, San Francisco, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment IV: Neuropsychiatric Disease and Health Economics
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:
Cognitive function may change over time in patients with SLE, and cognitive function trajectories (CFTs) have not well been studied. This is the first study to identify CFTs in SLE and their correlates.

Methods:
Data were from the University of California San Francisco Lupus Outcomes Study, in which participants are followed longitudinally via annual telephone surveys. The Hopkins Verbal Learning Test-Revised (HVLT-R; measures verbal memory) was administered in years 2-7 and the Controlled Oral Word Association Test (COWAT; verbal fluency) in years 4-7, providing up to 6 and 4 years of observation, respectively. Individuals with at least 2 assessments were included in analysis. Age- and education-stratified z-scores were derived for HVLT delayed recall and COWAT.

Proc Traj (SAS) was used to identify group-based trajectory models. One model each was fitted for the HVLT-R and COWAT. To select the best model, models with 2-5 trajectories were examined by graphic shapes, number of patients in each group, and model fitting statistics according to Bayesian Information Criterion. Separate univariate/multivariable logistic regression analyses (for HVLT-R and COWAT) were then performed to look for factors at baseline associated with CFT, including sex, ethnicity, disease duration, renal problems, treatments, fatigue, depressive symptoms (CESD), and self-reported disease activity.

Results:
815 patients (92.4% female) with mean age 34.5±13.3 years at SLE diagnosis were studied. 761 and 658 individuals had at least 2 HVLT-R and COWAT scores, respectively. Two CFTs were identified for each measure (see Figure): persistently low (29% in HVLT-R, 55% in COWAT) and persistent normal (71% in HVLT-R, 44.6% in COWAT). In multivariable analyses, persistently normal HVLT-R was associated with Caucasian race; renal problems, intravenous glucocorticoids use in the prior year, and higher CESD scores were associated with persistently low HVLT-R (Table). Persistently normal COWAT was associated with longer disease duration, while higher CESD score was associated with persistently low COWAT.

Conclusion:
Cognitive function followed particular trajectories over time in SLE, with some patients having persistently low scores while others had normal scores. Depressive symptoms were associated with persistently low function in both measures. Other factors associated with persistently low function were measure-specific. Additional longitudinal studies including more nuanced measures of cognitive function are needed to further explore long-term patterns of cognitive function in SLE.
Table. Baseline factors associated with better cognitive function trajectories in univariate and multivariate analysis

<table>
<thead>
<tr>
<th></th>
<th>HVLT-R delayed recall</th>
<th>COWAT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Univariate</td>
<td>Multivariate</td>
</tr>
<tr>
<td>Female</td>
<td>1.3 (0.7, 2.3)</td>
<td>---</td>
</tr>
<tr>
<td>Caucasian</td>
<td>1.6 (1.1, 2.2)</td>
<td>1.5 (1.02, 2.2)</td>
</tr>
<tr>
<td>Disease duration, year</td>
<td>1.0 (0.98, 1.02)</td>
<td>---</td>
</tr>
<tr>
<td>Renal problems</td>
<td>0.5 (0.4, 0.8)</td>
<td>0.6 (0.4, 0.9)</td>
</tr>
<tr>
<td>Smoking, ever</td>
<td>0.8 (0.6, 1.2)</td>
<td>---</td>
</tr>
<tr>
<td>Oral glucocorticoids during baseline year</td>
<td>0.8 (0.6, 1.1)</td>
<td>---</td>
</tr>
<tr>
<td>Intravenous steroids during baseline year</td>
<td>0.4 (0.2, 0.8)</td>
<td>0.5 (0.2, 0.4)</td>
</tr>
<tr>
<td>Plaquenil use</td>
<td>0.8 (0.6, 1.1)</td>
<td>---</td>
</tr>
<tr>
<td>CESD score</td>
<td>0.96 (0.95, 0.97)</td>
<td>0.97 (0.96, 0.98)</td>
</tr>
</tbody>
</table>

Tabled values are odds ratios (95% confidence intervals).

Disclosure: Z. Touma, None; J. Su, None; P. P. Katz, Bristol-Myers Squibb, 2.


Abstract Number: 2809

**Spatial Navigation Impairment Associated with Anti-NMDA Receptor Antibodies in Systemic Lupus Erythematosus**

Erik Anderson¹, Elisabeth J. Ploran², Betty Diamond³, Bruce Volpe⁴, Cynthia Aranow⁵ and Meggan Mackay⁶,⁷, ¹Autoimmune and Musculoskeletal Disease, The Feinstein Institute for Medical Research, Manhasset, NY, ²Department of Psychology, Hofstra University, Hempstead, NY, ³Autoimmune and Musculoskeletal Diseases, The Feinstein Institute for Medical Research, Manhasset, NY, ⁴Biomedical Sciences, The Feinstein Institute for Medical Research, Manhasset, NY, ⁵The Feinstein Institute for Medical Research, Manhasset, NY, ⁶Autoimmune & Musculoskeletal Disease, The Feinstein Institute for Medical Research, Manhasset, NY, ⁷Autoimmune and Musculoskeletal Disease, The Feinstein Institute for Medical Research, Manhasset, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment IV: Neuropsychiatric Disease and Health Economics
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:

Cognitive impairment is well-documented in SLE with considerable impact on quality of life but attribution is limited by a lack of biomarkers that distinguish SLE disease-related mechanisms from other causes (medications, infection, mood disorders, thrombosis). Cross-reactive anti-dsDNA/NMDA receptor antibodies (DNRAb) have been shown to bind neurons in the mouse hippocampus, specifically place cells, with resulting synaptic signaling changes promoting neuron dysfunction or death and difficulties in spatial tasks¹. The purpose of this study was to evaluate serum DNRAb associations with spatial memory in SLE using a novel spatial navigation task (SNT).
Methods:

21 SLE patients that met ACR criteria, had no history of CNS insult and low disease activity and 9 age, gender and ethnically matched healthy controls (HC) were recruited. SLE disease activity was assessed by SLEDAI within 2 weeks of testing. The SNT utilizes a desktop virtual environment to assess spatial memory. Participants were placed at a start point and asked to navigate through a computerized virtual city of 30 intersections (Fig. 1), with one unmarked target intersection set to trigger a congratulatory screen upon entry. Subjects were given a maximum of 5 minutes to complete each of 4 trials to find the target. Serum DNRAb assays were performed by ELISA with the DWEYS consensus sequence. Analyses included the Chi Square and student t tests.

Results:

Table 1 shows relevant subject characteristics with SLE subjects grouped by DNRAb titer. DNRAB- SLE subjects had slightly higher SLEDAI scores and frequency of anti-DNA antibody titers compared to the DNRAb+ group. Over 4 trials, 77.7% of HC found the target compared to 20% of DNRAb+ subjects (p=.01). DNRAb- SLE behaved like HC with a 60% success rate (p=.41). Differences between DNRAb+ and – did not reach statistical significance (p=.07). These differences in success occurred despite all three groups making the same number of movements (p=.83) and turns (p=.49) during the trials, covering the same amount of search area (p=.76), having a similar amount of computer experience (p=.15), and no differences in simple reaction time tasks (p=.7).

Conclusion:

DNRAb+ subjects perform poorly on the SNT compared to DNRAb- SLE subjects who perform similarly to HC. The lack of group differences for mood disturbances, medications and demographics and that the DNRAb- group performed similar to HC despite having higher disease activity and anti-DNA titers suggest that this SNT may provide an objective measure of DNRAb-mediated brain toxicity that will need to be replicated in future studies.

\(^{1}\) Chang, EH. EBioMedicine. 2015;2(7)
Table 1. Subject Characteristics

<table>
<thead>
<tr>
<th></th>
<th>SLE n=21</th>
<th>Healthy control n=9</th>
<th>p</th>
<th>SLE DNRAb+ n=10</th>
<th>SLE DNRAb- n=11</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>42.3 ± 10.5</td>
<td>38.6 ± 11.7</td>
<td>.455</td>
<td>45.6 ± 9.5</td>
<td>38.1 ± 10.4</td>
<td>.099</td>
</tr>
<tr>
<td>Gender: male</td>
<td>2 (9.5%)</td>
<td>0</td>
<td>.338</td>
<td>0</td>
<td>2 (18%)</td>
<td>.156</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latino/ Hispanic</td>
<td>4 (20%)</td>
<td>3 (37.5%)</td>
<td>.59</td>
<td>3 (30%)</td>
<td>1 (9%)</td>
<td>.313</td>
</tr>
<tr>
<td>Asian</td>
<td>1 (5%)</td>
<td>1 (12.5%)</td>
<td></td>
<td>0</td>
<td>1 (9%)</td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>14 (70%)</td>
<td>4 (50%)</td>
<td></td>
<td>6 (60%)</td>
<td>9 (82%)</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>1 (5%)</td>
<td>0%</td>
<td></td>
<td>1 (10%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td>13.4 ± 2.4</td>
<td>15.3 ± 2.4</td>
<td>.08</td>
<td>13.1 ± 2.3</td>
<td>13.4 ± 2.5</td>
<td>.808</td>
</tr>
<tr>
<td>Computer experience; some/none</td>
<td>10 (48%)</td>
<td>1 (11%)</td>
<td>.057</td>
<td>7 (70%)</td>
<td>3 (27%)</td>
<td>.05*</td>
</tr>
<tr>
<td>Disease duration</td>
<td>16 ± 9.1</td>
<td>11.1 ± 8.9</td>
<td>.227</td>
<td>1.1 ± 1.4</td>
<td>3.1 ± 2.3</td>
<td>.026*</td>
</tr>
<tr>
<td>SLEDAI</td>
<td>1.1 ± 1.4</td>
<td>3.1 ± 2.3</td>
<td>.227</td>
<td>1.1 ± 1.4</td>
<td>3.1 ± 2.3</td>
<td>.026*</td>
</tr>
<tr>
<td>SLICC DI</td>
<td>.9 ± 1.0</td>
<td>.91 ± 1.2</td>
<td>.985</td>
<td>.9 ± 1.0</td>
<td>.91 ± 1.2</td>
<td>.985</td>
</tr>
<tr>
<td>Beck Depression Index</td>
<td>7.1 ± 5.4</td>
<td>1.8 ± 2.4</td>
<td>.001</td>
<td>5.5 ± 5</td>
<td>8.6 ± 5.5</td>
<td>.204</td>
</tr>
<tr>
<td>STA-Y (anxiety)</td>
<td>30.7 ± 9.2</td>
<td>25.1 ± 5.2</td>
<td>.1</td>
<td>32.3 ± 10.1</td>
<td>29.2 ± 8.4</td>
<td>.45</td>
</tr>
<tr>
<td>Medications</td>
<td></td>
<td></td>
<td></td>
<td>Current HCQ</td>
<td>Current DMARDa</td>
<td></td>
</tr>
<tr>
<td>Current .1 (mg/day)</td>
<td>1.8 ± 2.9</td>
<td>3.2 ± 4.2</td>
<td>3.79</td>
<td>100%</td>
<td>8 (73%)</td>
<td>.074</td>
</tr>
<tr>
<td>Current DMARDa</td>
<td>5 (50%)</td>
<td>6 (55%)</td>
<td>.835</td>
<td>2 (20%)</td>
<td>8 (73%)</td>
<td>.016*</td>
</tr>
<tr>
<td>anti-dsDNA ab +</td>
<td>2 (20%)</td>
<td>8 (73%)</td>
<td>.696</td>
<td>8 (80%)</td>
<td>8 (73%)</td>
<td>.696</td>
</tr>
<tr>
<td>anti-Ro+</td>
<td>2 (20%)</td>
<td>3 (27%)</td>
<td>.696</td>
<td>2 (20%)</td>
<td>3 (27%)</td>
<td>.696</td>
</tr>
<tr>
<td>anti-La+</td>
<td>1 (10%)</td>
<td>3 (27%)</td>
<td>.314</td>
<td>1 (10%)</td>
<td>3 (27%)</td>
<td>.314</td>
</tr>
<tr>
<td>Anti-cardiolipin/LAC+</td>
<td>0</td>
<td>0</td>
<td></td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Disclosure: E. Anderson, None; E. J. Ploran, None; B. Diamond, None; B. Volpe, None; C. Aranow, None; M. Mackay, None.


Abstract Number: 2810

The Impact of Psychiatric Comorbidity on Health Care Utilization for Youth with Systemic Lupus Erythematosus

Andrea M. Knight1,2, Alaina M. Davis3, Marisa S. Klein-Gitelman4, Zuleyha Cidav5 and David Mandell6, 1Division of Rheumatology, Center for Pediatric Clinical Effectiveness & PolicyLab, Children's Hospital of Philadelphia, Philadelphia, PA, 2Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, 3Pediatric Rheumatology, Monroe Carell Junior Children's Hospital at Vanderbilt, Division of Pediatric Rheumatology, Nashville, TN, 4Division of Pediatric Rheumatology/PDD PTD, Lurie Children's Hospital of Chicago/Northwestern University, Chicago, IL, 5Perelman School of Medicine, Center for Mental Health Policy and Services Research, University of Pennsylvania, Philadelphia, PA, 6Psychiatry and Pediatrics, Center for Mental Health Policy and Services Research, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment IV: Neuropsychiatric Disease and Health Economics
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM
**Background/Purpose:** Youth with systemic lupus erythematosus (SLE) have high health care utilization, which may be exacerbated by psychiatric disorders, a common comorbidity in this group. We examined the impact of psychiatric diagnoses on utilization of medical services in youth with SLE.

**Methods:** We conducted a retrospective cohort study using administrative claims for 2000 to 2013 from Clinformatics™ DataMart (OptumInsight, Eden Prairie, MN), a large US database of privately insured enrollees. We included youth ages 10-24 years with an incident diagnosis of SLE (³3 International Classification of Diseases, Ninth Revision codes for SLE 710.0, each >30 days apart, with ≥1 year of preceding continuous enrollment without a code for SLE). We categorized mutually exclusive groups of youth with SLE as those with: 1) no psychiatric diagnosis, 2) a psychiatric diagnosis in the 12 months preceding SLE diagnosis, and 3) an incident psychiatric diagnosis in the 12 months after SLE diagnosis. We calculated mean ambulatory, emergency and inpatient visits for medical services in the year after SLE diagnosis, and used Poisson regression to compare the number of visits among the 3 groups, adjusting for demographic and disease variables.

**Results:** We identified 650 youth with an incident diagnosis of SLE, with mean age of 18.4 years (SD 3.7), composed of 88% females and 25% with nephritis. Depression was diagnosed in 144 (22%), anxiety in 93 (14%), and other psychiatric disorders in 210 (32%). A psychiatric diagnosis was present preceding SLE diagnosis in 122 (19%) and diagnosed in the year after SLE diagnosis in 105 (16%); 423 (65%) had no psychiatric diagnosis. In adjusted models, mean ambulatory visits in the year after SLE diagnosis were higher for those with preceding (14.4, SD 11.7, p=0.01) and incident (18.1, SD 14.6, p=0.0001) psychiatric diagnoses than among those without a psychiatric diagnosis (11.6, SD 9.9) (Figure). Those with an incident psychiatric diagnosis had more acute care visits compared to those without a psychiatric diagnosis: 9.5 (10.9) vs 5.1 (8.6) for emergency (p=0.0001), and 4.9 (10.7) vs 2.8 (7.8) for inpatient (p=0.03). Those with a preceding psychiatric diagnosis had 6.9 (13.1) mean emergency and 3.5 (8.2) mean inpatient visits, which were not significantly statistically different from the other groups.

**Conclusion:** In youth with SLE, psychiatric comorbidity is associated with higher utilization of medical services in ambulatory settings in the year after SLE diagnosis, and those with a new psychiatric diagnosis during this period had higher utilization of acute medical care. Interventions to address existing and newly identified psychiatric disorders may decrease health care burden for youth with SLE.

**Disclosure:** A. M. Knight, Childhood Arthritis & Rheumatology Research Alliance, Lupus Research Alliance, 2; A. M. Davis, None; M. S. Klein-Gitelman, Janssen Pharmaceutical Product, L.P., 2, Pfizer Inc, 2, UCB biosciences, 2, Abbvie, 2, Lupus Foundation of America, 2, NIH/LFA/Cure JM/Arthritis Foundation, 2, Up to Date, 7; Z. Cidav, None; D. Mandell, None.


**Abstract Number:** 2811

---

**Economic Evaluation of Damage Accrual in a Nationwide Canadian SLE Cohort**

May Choi1, Yvan St. Pierre2, Murray Urowitz3, Dafna D Gladman4, Sasha Bernatsky5, Evelyne Vinet6, Christian Pineau7, John G Hanly8, Christine A. Peschenk9, Paul R. Fortin10, Michelle Jung11, Claire Barber12, Susan Elliott13, Jenna Dixon14 and Ann E. Clarke11, 1University of Calgary, Calgary, AB, Canada, 2Clinical Epidemiology, Research Institute of the McGill University Health Centre, Montreal, QC, Canada, 3Centre for Prognosis Studies in the Rheumatic Diseases, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, 4Centre for Prognosis Studies in The Rheumatic Diseases, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, 5Divisions of Rheumatology and Clinical Epidemiology, Research Institute of the McGill University Health Centre, Montreal, QC, Canada, 6Divisions of Rheumatology and Clinical Epidemiology, McGill University Health Centre,
Montreal, QC, Canada, 7Rheumatology, MUHC, Montreal, QC, Canada, 8Division of Rheumatology, Department of Medicine and Department of Pathology, Queen Elizabeth II Health Sciences Centre and Dalhousie University, Halifax, NS, Canada, 9RR 149G, Univ of Manitoba, Winnipeg, MB, Canada, 10Medicine, CHU de Quebec - Universite de Laval, Quebec, QC, Canada, 11Division of Rheumatology, University of Calgary, Calgary, AB, Canada, 12Medicine, University of Calgary, Calgary, AB, Canada, 13GEOGRAPHY AND ENVIRONMENTAL MANAGEMENT, University of Waterloo, Waterloo, ON, Canada, 14Geography and Environmental Management, University of Waterloo, Waterloo, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment IV: Neuropsychiatric Disease and Health Economics
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:

We describe the costs associated with damage states in a Canadian-wide SLE cohort using multi-state modeling, which provides a dynamic representation of damage accrual in real time.

Methods:

Patients fulfilling the revised ACR or Systemic Lupus International Collaborating Clinics (SLICC) Classification Criteria for SLE from 6 Canadian centres were enrolled. Participants completed validated health resource utilization (including hospitalizations, medications, physician visits, tests, and emergency room visits) and lost productivity questionnaires. Direct costs were calculated by multiplying health resources by their 2017 Canadian prices. Indirect costs included time loss and impaired productivity in labour force and non-labour force activities and were valued using age-sex specific wages from Statistics Canada. Annual costs associated with damage states (SLICC/ACR Damage Index [SDI]) were obtained from multiple regressions adjusting for age, race/ethnicity, and disease duration. To compute long-term estimates of direct/indirect costs, annual costs associated with each level of disease damage were multiplied by the expected duration in each state, forecasted using a multi-state Markov model (Bruce IN. Ann Rheum Dis 2015;74:1706-13). Future costs were discounted at a yearly rate of 3%.

Results:

1361 patients participated, 90.4% female, 71.0% Caucasian, mean age at diagnosis 33.1 years (SD 13.5), mean SLE duration at completion of economic questionnaire 16.8 years (SD 11.6), mean SLE Disease Activity Index (SLEDAI-2K) 2.71 (SD 3.21), and mean SDI 1.54 (SD 1.87). Annual direct and total costs were higher in those with an SDI ≥5 (Table 1).

Table 1. Predicted Annual Health Costs Stratified by SDI

<table>
<thead>
<tr>
<th>SDI State</th>
<th>Direct Costs, Mean, 95% CI 2017 Canadian $</th>
<th>Indirect Costs, Mean, 95% CI 2017 Canadian $</th>
<th>Total Costs, Mean, 95% CI 2017 Canadian $</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>4379 (2859, 5900) 24768 (21439, 28098) 29147 (24997, 33298)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>5846 (4266, 7427) 26625 (23032, 30218) 32472 (28085, 36858)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>6743 (4899, 8587) 31285 (26910, 35661) 38028 (32845, 43212)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>10885 (8530, 13240) 23786 (18044, 29528) 34671 (28006, 41336)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>9427 (6015, 12840) 30272 (21892, 38652) 39699 (30158, 49241)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥5</td>
<td>18620 (15850, 21390) 27903 (21565, 34241) 46523 (39048, 53997)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Five and 10-year cumulative direct and total costs increased with increasing baseline SDIs, while indirect costs did not differ when stratified by baseline SDI (Table 2).

Table 2. Predicted 5 and 10-Year Cumulative Costs Stratified by Baseline SDI
### Table

<table>
<thead>
<tr>
<th>SDI</th>
<th>Total 5-Year Cumulative Costs, Mean, 95% CI</th>
<th>Total 10-Year Cumulative Costs, Mean, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2017 Canadian $</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Direct</td>
<td>Indirect</td>
</tr>
<tr>
<td>0</td>
<td>20094</td>
<td>115192</td>
</tr>
<tr>
<td></td>
<td>(98809, 131575)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>29167</td>
<td>126431</td>
</tr>
<tr>
<td></td>
<td>(107292, 145569)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>37925</td>
<td>133252</td>
</tr>
<tr>
<td></td>
<td>(109369, 157281)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>52647</td>
<td>117893</td>
</tr>
<tr>
<td></td>
<td>(87927, 147858)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>62796</td>
<td>133923</td>
</tr>
<tr>
<td></td>
<td>(99189, 168657)</td>
<td></td>
</tr>
<tr>
<td>≥ 5</td>
<td>85629</td>
<td>128038</td>
</tr>
<tr>
<td></td>
<td>(98415, 157662)</td>
<td></td>
</tr>
</tbody>
</table>

### Conclusion:

Patients with the highest baseline SDIs incurred cumulative direct costs that were 4.2-fold higher and total costs almost 2-fold higher than those with the lowest baseline SDIs. Indirect costs did not vary with SDI and patients with no or minimal damage still experienced considerably reduced productivity. Indirect costs exceeded direct, on average, by 3.9-fold, underscoring the importance of lost workforce productivity, and the need for actionable workplace and systems-level (i.e., government, policies, and society) interventions to improve the employment outcomes of those living with SLE.

**Disclosure:** M. Choi, None; Y. St. Pierre, None; M. Urowitz, None; D. D. Gladman, None; S. Bernatsky, None; E. Vinet, None; C. Pineau, None; J. G. Hanly, None; C. A. Peschken, None; P. R. Fortin, None; M. Jung, None; C. Barber, None; S. Elliott, None; J. Dixon, None; A. E. Clarke, None.

Background/Purpose: Belimumab, an inhibitor of B lymphocyte stimulator, is approved in adults with active, autoantibody-positive systemic lupus erythematosus (SLE) receiving standard of care. There is limited information on all-cause healthcare resource utilization (HCRU) and costs before/after initiation of belimumab treatment. Data from privately-insured US administrative claims databases can provide valuable descriptive information on HCRU and costs under routine care settings.

Methods: A retrospective analysis (study 206345) was conducted using the Truven Health MarketScan® Commercial Claims and Encounters database (Sept 01, 2010 to Dec 31, 2015). Patients were 18–64 years of age with a SLE diagnosis (ICD-9: 710.0 or ICD-10: M32) and ≥1 belimumab infusion. The index date was the date of the first belimumab infusion. Continuous enrollment was required 6 months pre-index and ≥3 post-index date. Here, we present data from patients with 6 months of post-index follow-up.

Results: This analysis comprised 1879 patients with 6 months of post-index follow-up. The proportion of patients utilizing healthcare services was significantly lower after belimumab initiation versus the pre-index period for inpatient admissions, and for some outpatient services such as emergency room visits, hospital-based outpatient visits and laboratory services (all p<0.001; Table). The number of healthcare services utilized was also significantly lower after initiation versus the pre-index period for inpatient admissions and several outpatient services, including emergency room visits, physician office visits, hospital-based outpatient visits, laboratory services and outpatient pharmacy prescriptions (all p<0.001). Total all-cause healthcare costs were significantly higher following belimumab initiation, compared with the pre-index period (p<0.001). Outpatient service costs, including hospital-based outpatient visits and other outpatient costs, were significantly higher following initiation (all p<0.001). However, inpatient admissions, physician office visits and laboratory costs were significantly lower after initiation (all p<0.001).

Conclusion: This study provides valuable real-world information about HCRU and costs before and after initiation of intravenous belimumab in a large sample of US patients with SLE. While total costs increased in the 6-month follow-up period, in part due to the cost of belimumab, significant reductions in inpatient admissions, emergency room visits and physician office visits, as well as the costs associated with these services were observed. The effect of belimumab treatment on HCRU and costs, particularly beyond the first 6 months, requires further exploration.

Study funded/conducted by GSK. Editorial assistance provided by Jennie McLean, PhD, of Fishawack Indicia Ltd, UK, funded by GSK

Disclosure: C. F. Bell, GSK, 1,GSK, 3; J. Priest, GSK, 1,GSK, 3; M. Stott-Miller, GSK, 1,GSK, 3; H. Kan, GSK, 1; J. Amelio, GSK, 1,GSK, 3; X. Song, Truven Health Analytics, 3; B. Limone, None; V. Noxon, Truven Health Analytics, 3; K. H. Costenbader, Glaxo Smith Kline, 5,Merck Pharmaceuticals, 2,Biogen Idec, 5,AstraZeneca, 5.

Interferon-Induced APOL1 over-Expression Causes Autophagic Dysfunction and Mitochondrial Stress in Risk Variant-Carrying Endothelial Cells

Ashira Blazer1, Sara Rasmussen2, Androo Markham3, Shilpi Mehta-Lee4, Jill P. Buyon4 and Robert M. Clancy2, 1Division of Rheumatology, NYU School of Medicine, New York, NY, 2Department of Medicine, Division of Rheumatology, NYU School of Medicine, New York, NY, 3Medicine, NYU School of Medicine, New York, NY, 4NYU School of Medicine, New York, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis I
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:
In SLE Apolipoprotein L1 (APOL1) risk variants (RV) associate with cardiovascular and end stage renal disease. APOL1 induction initially promotes cellular maintenance through autophagy; but when prolonged disrupts lipid bilayers causing ion flux, mitochondrial stress, and cell death. We hypothesized that cytokine-induced RV expression impairs autophagy favoring pore formation in endothelial cells (ECs) implicating endothelial dysfunction as a mechanism for broader organ damage.

Methods: ECs were isolated from umbilical cords of 11 healthy African American subjects and genotyped for APOL1 by PCR sequencing (G0/G0 n=4, RV/G0 n=4 RV/RV n=3). CD31+ ECs (confirmed by FACS) were treated with IFNγ (100 units/mL) for 24 hours and subsequent assessments included: APOL1 and autophagy marker LC3B protein measurements by immunoblot, LC3B staining by immunofluorescence, angiogenesis capacity on Matrigel matrix, and bioenergetic profiling by the Seahorse mitochondrial stress test method.

Results:
EC were >98% CD31 positive by flow cytometry. Across the genotypes, exposure to IFNγ increased APOL1 protein expression 13.3±9.2 fold (p=0.012). To assess the ability of APOL1 over-expression to initiate autophagy, LC3B positive autophagosomes were counted by immunofluorescence. As expected, in G0/G0 ECs autophagosomes increased 41% when APOL1 was over-expressed. By contrast, autophagosomes decreased 7.1% in RV/G0 and 35.5% RV/RV ECs suggesting an autophagy defect. This result was confirmed by immunoblot. Autophagy-dependent angiogenesis was evaluated by plating resting and IFNγ treated ECs on Matrigel matrix. At baseline, RV/RV ECs showed impaired angiogenesis capacity forming fewer junctions (J) and tubules (T) than RV/G0 and G0/G0 ECs (RV/RV: J: 539.9, T: 484.8; RV/G0: J: 841.8, T: 727.7, G0/G0: J: 810.8 T: 719.0, p=0.07). Overexpressing APOL1 with IFNγ, impaired angiogenesis in both the RV/RV and RV/G0 ECs but not G0/G0 ECs (RV/RV: J: 353.0 T: 319.8; RV/G0: J: 297.8, T: 296.0, G0/G0: J: 739.0 T: 657.8, p=0.001). As a proof of concept, autophagy inhibitor ABT-737 was added to G0/G0 ECs resulting in a 42% decrease in junctions (p=0.036) and 52% decrease in tubules (p=0.012). Mitochondrial oxygen consumption of resting and IFNγ treated ECs, was next assessed by bioenergetic profiling. For baseline, there were genotype-dependent differences in spare capacity (SC) and coupling efficiency (CE) (G0/G0: SC: 41.0±22.0 pmol/min CE: 439.8%; RV/G0: SC: 22.75 pmol/min CE:119.9%; RV/RV SC: 24.6±4.71 pmol/min CE:100.35%). Upon adding IFNγ, Proton leak increased 1.89 pmol/min in the G0/G0 ECs, 1.49 pmol/min in the RA/G0 ECs, and 7.50 pmol/min in the RA/RA ECs. This pattern is consistent with genotype dependent increased cation pore formation with electron escape across the inner mitochondrial membrane.

Conclusion:
IFNγ increases both ancestral and variant APOL1 intracellular accumulation in cultured ECs across genotype. In RV carrying ECs, this increased expression results in aberrant autophagy, angiogenesis, and mitochondrial energy production, all of which likely contribute to endothelial dysfunction, representing an underpin of broader organ damage.

Disclosure: A. Blazer, None; S. Rasmussen, None; A. Markham, None; S. Mehta-Lee, None; J. P. Buyon, Exagen, 2; R. M. Clancy, None.

Interferon-β Production By B Cells Promotes B Cell Survival and Is Strongly Associated with Active Disease in African Americans with SLE

Jennie Hamilton1, Qi Wu2, PingAr Yang3, Bao Luo4, Shanrun Liu5, Jun Li6, Ignacio Sanz7, W. Winn Chatham8, Hui-Chen Hsu2 and John D. Mountz9, 1Medicine/Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 2Department of Medicine, University of Alabama at Birmingham, Birmingham, AL, 3Department of Medicine, Clinical Immunology & Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 4Division of Clinical Immunology and Rheumatology, Department of Medicine, University of Alabama at Birmingham, Birmingham, AL, 5Biochemistry & Molecular Genetics, University of Alabama at Birmingham, Birmingham, AL, 6Medicine, University of Alabama at Birmingham, Birmingham, AL, 7Rheumatology and Lowance Center for Human Immunology, Emory University School of Medicine and Lowance Center for Human Immunology, Atlanta, GA, 8Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 9University of Alabama at Birmingham, Department of Medicine, Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis I
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Plasmacytoid dendritic cells are considered the main source of pathogenic IFN in SLE. However, recent work found that elevated serum type I IFN protein was not accompanied by increased type I IFN in circulating pDCs, suggesting the importance of other cellular sources of type I IFN in some patients. Developing transitional B cells are important targets of type I IFN in SLE, and were recently shown to produce IFNα. IFNβ expression has not been investigated in SLE B cells; in mice, however it has been identified as a prerequisite for efficient TLR stimulation, suggesting that autocrine stimulation of developing B cells with high-affinity IFNβ may be a prerequisite for subsequent immune-competence to respond to TLR challenges.

Methods: Peripheral blood mononuclear cells (PBMCs) from 34 SLE patients and 9 healthy controls were recruited; all SLE patients met the ACR 1997 revised criteria for SLE. Comprehensive clinical data was recorded for each SLE subject in a double-blind fashion. Intracellular analysis of endogenous IFNβ was carried out using validated reagents on FACS isolated B cells.

Results: There was a significant increase in endogenous IFNβ in transitional (p = 0.002), naive (p = 0.004) and memory (p = 0.031) B cell subpopulations of SLE patients compared to healthy controls. Endogenous IFN-β in B cells was significantly higher than endogenous IFN-β in CD4 T cells, with levels equivalent to that seen in pDCs. Endogenous IFNβ was highly correlated with clinical disease including renal disease (p = 0.0072) and autoantibodies including anti-dsDNA (p = 0.036), anti-Sm (p = 0.011) and anti-SSA (p=0.04). Notably, T1/T2 B cell IFNβ expression was significantly increased in African-American patients (p=0.011) with more severe disease manifestations. T1/T2 IFNβ expression was also significantly correlated with the percent of 9G4+ autoreactive B cells (p = 0.0001) and CD19hiCD38hiCD27+ plasma cell formation (p = 0.031). Upregulation of CD69 after TLR7 stimulation with CL264 was highly dependent upon B cell endogenous secretion IFNβ and could be significantly inhibited in the presence of anti-IFNβ antibody. The specific requirement for IFNβ was demonstrated by the lack of additional inhibition in the presence of anti-IFNαR neutralizing antibody, which blocks signaling from all type I IFNs. In vitro survival of purified B cells was also dependent on IFNβ after TLR7 stimulation and was significantly decreased with blockade of IFNβ.

Conclusion: Intracellular IFNβ production by early-stage transitional B cells is a novel and important B cell intrinsic factor that regulates B cell survival and sensitivity to TLR7 stimulation. B cell endogenous IFNβ may be an essential factor for their development into autoantibody producing B cells. The present work suggests a need for future human lupus studies into type I IFN dysregulation that pioneer beyond the view of pDC produced IFNα. These results also provide a mechanistic basis for development of more effective therapies to dampen the type I IFN cascade by specifically targeting the high-affinity IFNβ or the enhanceosome components that promote its induction in a subgroup of lupus patients.

Disclosure: J. Hamilton, None; Q. Wu, None; P. Yang, None; B. Luo, None; S. Liu, None; J. Li, None; I. Sanz, None; W. W. Chatham, None; H. C. Hsu, None; J. D. Mountz, None.

Pathological Roles By Siglec and Type I Interferons for the Development of Autoimmune Congenital Heart Block

Robert M. Clancy¹, Marc Halushka² and Jill P. Buyon¹, ¹NYU School of Medicine, New York, NY, ²Johns Hopkins University School of Medicine, Baltimore, MD
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis I
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Given that diseases associated with anti-SSA/Ro such as SLE and Sjögren’s syndrome associate with an upregulation of type I interferons, recent attention has focused on a potential role for IFN in the pathogenesis of congenital heart block (CHB). Based on the consistent demonstration of macrophages and multinucleated giant cells in areas of injury, it is relevant that Sialic Acid Binding Ig Like Lectin 1 (SIGLEC1), a receptor on monocytes/macrophages, is upregulated by IFN. Functionally, Siglec-1 expressing macrophages might play an important role as effector cells in fibrosis. Accordingly, this study leveraged both autopsy tissue and freshly isolated macrophages from a fetal heart dying with CHB to address whether IFN-α contributes to the pathogenesis of CHB by regulating activated macrophages in affected cardiac tissue.

Methods: Three approaches were taken to evaluate Siglec-1 expression. Transcriptomic analysis was performed on macrophages freshly isolated from a fetal heart dying with CHB at 19 weeks and a heart from an otherwise healthy electively terminated fetus using (DAPI negative cells with isolation by flow using antibodies to CD45). Immunohistochemistry was performed on another fetal heart dying with CHB. In vitro experiments utilized cultured healthy human macrophages transfected with anti-SSA/Ro- associated ssRNA as a proxy for the in vivo conditions.

Results: Transcriptomes of the two hearts for each isolated leukocyte fraction were compared. By following 213 IFN inducible genes, there was enrichment of targeted transcripts in CHB vs control (p=0.0001) and SIGLEC1, which was 200-fold more abundant in CHB vs control and ranked among the top three differentially expressed candidates. In another fetal heart dying with CHB, Siglec1 staining as detected by antibody HPA053457 was prominent in areas of injury. By morphology, the two cell types expressing Siglec 1 were macrophages and dendritic cells. In vitro experiments were performed in accordance with previous laboratory work, in which a model of anti-SSA/Ro-associated injury exploits macrophages stimulated with the ssRNA component (hY3) of the SSA/Ro immune complex. IFN inducible genes (15 transcripts) were among the 30 most highly upregulated genes in hY3 stimulated conditions and SIGLEC1 was two-fold more abundant in CHB vs control. Given the enrichment of type I IFN-responsive genes in the macrophage transcriptome, a WISH cell line was selected to evaluate supernatants from macrophages transfected with hY3. IFIT1, MX1, and EIF2AK2 transcripts were significantly increased in the WISH cells treated with hY3 macrophage supernatants, but not macrophage supernatants alone (N = 7, P =0.02).

Conclusion: These data now provide a link between IFN and the inflammatory and possibly fibrosing component of CHB and position Siglec-1 positive macrophages as integral to the process.

Disclosure: R. M. Clancy, None; M. Halushka, None; J. P. Buyon, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/pathological-roles-by-siglec-and-type-i-interferons-for-the-development-of-autoimmune-congenital-heart-block

Prediction of Connective Tissue Disease in an at-Risk Cohort Using a Novel Interferon Stimulated Gene Expression Score

Md Yuzaiful Md Yusof¹,², Yasser M El-Sherbiny¹,³, Antonios Psarras¹, Elizabeth M.A. Hensor¹,⁴, Adewonuola Alase¹, Alaa Mohamed¹, Miriam Wittmann¹,⁴, Paul Emery¹,⁴ and Edward M Vital¹,⁴, ¹Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom, ²NIHR Leeds Biomedical Research Unit, Leeds Teaching Hospitals NHS Trust, Leeds,
Prediction of connective tissue disease in an at-risk cohort using a novel interferon stimulated gene expression score

**Background/Purpose:** A period of ANA positivity and other immune dysregulation precedes autoimmune connective tissue disease (CTD), providing a potential opportunity for disease prevention. Type I interferons (IFN-I) are important mediators of CTDs but their role in disease initiation is unclear. The objective of this study was to develop biomarkers of progression to CTDs, with a view to enabling early intervention for disease prevention.

**Methods:** A prospective observational study was conducted in 150 patients. At Risk of CTD was defined by (i) ANA; (ii) ≤1 clinical SLE criteria; (iii) symptom duration <12 months and (iv) treatment-naïve. Progression was defined by meeting 2012 ACR/SLICC SLE, 2016 ACR/EULAR Primary Sjogren’s, or other diagnostic criteria. Using factor analysis, we previously reported a novel IFN score which comprised 30 selected IFN stimulated genes (ISGs), as measured using TaqMan, into two factors scores: (i)“Score A” (composed of IFN-α responsive genes) and (ii)“Score B” (genes responsive to IFN-α, β and γ). 50 healthy controls and 150 SLE patients were used as negative and positive controls. Penalised logistic regression using Lasso method was used to identify baseline predictors of CTD progression.

**Results:** 118 patients with 1-year follow-up data were included in this analysis. 104 were female with median age (range) 48 (20-84) years. 20 (17%) patients progressed to CTD (SLE=14, Sjogren’s=5) in the following 12 months. At baseline, in At Risk CTD vs healthy controls, only IFN Score A was increased; p=0.002. IFN Score B was only increased in true established SLE. In At Risk patients, IFN Score B was low in patients who did not progress and increased in those who did progress; p<0.001. ROC indicated that a Score B level of >0.126 yielded Area Under the Curve (AUC) of 0.82 with 58% sensitivity, 85% specificity, 46% positive predictive value and 90% negative predictive value in predicting progression. However, there was only a trend to difference in IFN Score A between these two groups; p=0.058 (Figure 1). A positive family history of autoimmune rheumatic disease (ARD); OR 4.22 95% CI (1.07 - 16.73) and Score B; 2.70 (1.38 - 5.28) increased the odds of CTD progression at 12 months in multivariable analysis.

**Conclusion:** A novel ISG score and family history of ARD predict progression from ANA+ to clinical autoimmune disease. These may allow early intervention to prevent CTD. Analyses of other immunological biomarkers and longitudinal tests are in progress as well as a validation cohort.
Expression Patterns of Interferon Induced Genes in Newborns Exposed to Ro/SSA Autoantibodies in Utero

Gudny Ella Thorlacius¹, Malin Hedlund¹, Margarita Ivanchenko¹, Vijole Ottosson¹, Amina Ossoinak¹, Linda Lagnefeldt¹, Lars Rönnblom², Sven-Erik Sonesson³, Maija-Leena Eloranta¹ and Marie Wahren-Herlenius¹, ¹Unit of Experimental Rheumatology, Department of Medicine, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, Stockholm, Sweden, ²Department of Medical Sciences, Section of Rheumatology, Uppsala University, Uppsala, Sweden, Uppsala, Sweden, ³Pediatric Cardiology Unit, Department of Women’s and Children’s Health, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, Stockholm, Sweden, ⁴Rheumatology and Science for Life Laboratory, Department of Medical Sciences, Uppsala University, Sweden, Uppsala, Sweden

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis I
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose: Women with Sjögren’s syndrome and autoantibodies against Ro/SSA are at risk for pregnancy complications, including neonatal lupus erythematosus (NLE) and a congenital heart block in the baby. Ro/SSA autoantibodies are also associated with expression of interferon (IFN) regulated genes. Treatment with hydroxychloroquine (HCQ), which alters type 1 IFN activity, is thought to reduce the risk of NLE. The pattern and magnitude of IFN expression and responses in Ro/SSA autoantibody exposed newborns has not been investigated.

Methods: Thirteen Ro/SSA autoantibody positive mothers either receiving no medication (Ro/SSA+) or treated with HCQ and/or azathioprine (Ro/SSA+T), and their newborn babies were included in the study, together with 8 healthy mother-baby pairs (HC). Blood was drawn from the mother and baby (cord) at birth, with immediate separation into plasma and PBMC. mRNA expression levels were measured using microarrays and used for calculating IFN scores. Cell surface expression of molecules was investigated by flow cytometry, and IFN-α in plasma and supernatants was analyzed by immunoassay. The ability of PBMCs from newborns to produce IFN-α in response to autoantibody exposure was tested by stimulation with 10% plasma in cell culture for 24h.

Results: As expected, mRNA expression patterns in cells of SSA+ mothers showed enrichment of type I IFN pathways compared to HC mothers, and mothers from the Ro/SSA+ group had a higher IFN score and higher levels of IFN-α than HC mothers. Notably, also in newborns of Ro/SSA+ mothers, there was an enrichment of type I IFN pathways and high IFN score compared to newborns of HC mothers, and maternal and baby IFN scores had a significant, positive correlation (Pearson r=0.8128, p<0.0001). However, babies in the Ro/SSA+T group, whose mothers received immunomodulatory treatment, had an IFN score with values comparable to HC babies, while the maternal Ro/SSA+T IFN scores did not differ from those of non-treated mothers. Activation of CD14+ monocytes, in the form of increased MHC class II surface expression was observed in the Ro/SSA+ exposed newborns. PBMCs from both HC and Ro/SSA+ newborns cultured with Ro/SSA+ plasma produced IFN-α.

Conclusion: Babies exposed to Ro/SSA autoantibodies in utero have circulating IFN-α, an IFN-signature in their PBMCs and increased MHC class II expression on the cell surface of monocytes, which was partly reversed by maternal treatment with HCQ or other immunomodulatory drugs. PBMCs from babies are capable of producing IFN-α after exposure to Ro/SSA+ plasma. There is a measurable activation of the type I IFN system in Ro/SSA autoantibody exposed fetuses which may contribute to the risk of NLE.

Disclosure: G. E. Thorlacius, None; M. Hedlund, None; M. Ivanchenko, None; V. Ottosson, None; A. Ossoinak, None; L. Lagnefeldt, None; L. Rönnblom, None; S. E. Sonesson, None; M. L. Eloranta, None; M. Wahren-Herlenius, None.


Gene Expression Analysis Demonstrates That Multiple Type 1 Interferons Are Involved in Lupus Pathogenesis

Abstract Number: 2818
SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis I
Session Type: ACR Concurrent Abstract Session
Session Time: 2:30PM-4:00PM

Background/Purpose:
A role for interferon (IFN) in lupus pathogenesis has been inferred from the prominent IFN gene signature (IGS) found in lupus peripheral blood. However, the identification of the major type of IFN up-regulating gene expression in SLE has not been determined. The current experiments were undertaken to differentiate the subtype of IFN driving gene expression perturbations in lupus.

Methods:
Raw data from lupus cells and tissues were derived from the GEO repository and collaborators. Determination of differentially expressed (DE) genes was done for each dataset. Gene Set Variation Analysis (GSVA) was used as a non-parametric, unsupervised method for estimating the variation of pre-defined gene sets in gene expression samples. Upstream regulator analysis was employed to identify possible upstream regulators of lupus DE genes. For each potential regulator, an activation z-score was calculated from the experimentally observed information provided for the downstream targets. The first reference dataset used was from Chiche et al, 2014, the second was the DE analysis of the in vitro treatment of PBMC with individual IFNs (Waddell et al, 2010) and the third was the IFNB signature in the whole blood of Multiple Sclerosis patients treated with IFNB (Nickles et al, 2013).

Results:
The IGS was detected in most lupus samples. Comparison of lupus DE genes with previously reported IGS modules or with gene expression data sets obtained by stimulating PBMC with specific IFNs indicated better separation of lupus patient samples from controls using the latter and, additionally, identified patients with TNF and IL12 signatures lacking IFN signatures. Z score calculations to determine the most likely upstream regulator predicted IFNB1 and IFNW as the major IFNs inducing the IGS for SLE skin and kidney. Confirmation of the strong IFNB1 signal was carried out using published microarray data of the IFNB1 signature in Multiple Sclerosis (MS) patients (MS IFNB1). The MS IFNB1 had superior overlap to SLE datasets compared to both IFN-M and the in vitro PBMC IFN Signature. Z score calculations using the MS IFNB1 signature showed high Z scores for all active lupus cells and tissues. The data indicate that IFNB and IFNW are likely IFN family member upstream regulators accounting for the IGS in SLE cells and tissues.

Conclusion:
The type I and type II IGS overlap significantly and are not distinguishable by previously defined interferon modules. In contrast, GSVA using individual cytokine / interferon signatures from in vitro stimulation of PBMC allows interrogation and stratification of individual lupus patient IGS and separates lupus patient from control samples. Z score calculations demonstrate the likely role of IFNB1 and IFNW1 in SLE pathogenesis and suggest that targeting these interferons may have therapeutic value for SLE.

References:


Abstract Number: 2819
Association of Socioeconomic Status with Osteoarthritis-Induced Disability Progression

Divya Narayanan\textsuperscript{1}, Rebecca J. Cleveland\textsuperscript{2}, Joanne M. Jordan\textsuperscript{3}, Eric Seaberg\textsuperscript{4} and Leigh F. Callahan\textsuperscript{1}, \textsuperscript{1}Thurston Arthritis Research Center, University of North Carolina at Chapel Hill, Chapel Hill, NC, \textsuperscript{2}Thurston Arthritis Research Center, University of North Carolina School of Medicine, Chapel Hill, NC, \textsuperscript{3}Thurston Arthritis Research Center, University of North Carolina at Chapel Hill, Chapel Hill, NC, \textsuperscript{4}Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: ARHP: Exemplary Abstracts
Session Type: ARHP Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Osteoarthritis (OA) is the number one chronic condition of the joints. Social determinants associated with disability progression due to OA are largely unknown. Efforts to determine if socioeconomic status (SES) is associated with OA disability progression may aid in prevention efforts. This study aims to describe the relationship between SES measures with disability progression among individuals with radiographic knee and/or hip OA from the Johnston County OA (JoCo OA) Project in rural North Carolina.

Methods: We examined the association between disability progression and each of four individual SES variables (education, occupation, income, and home ownership) and one community level SES measure (household (HH) poverty) using data from 541 participants in the JoCo OA cohort. In the time to event analysis, disability progression was defined as a change of ≥ 0.22 points in the Health Assessment Questionnaire (HAQ) disability score between baseline and last follow-up. Risk of disability progression was evaluated using a parametric time to event Weibull model that accounted for interval censoring. Change in HAQ score was assessed using linear mixed models (LMM). Interaction terms were included to examine disability progression by age. All analyses simultaneously adjusted for other SES measures, as well as age, race, and gender.

Results: Based on the time to event analysis, individuals who reported making ≤ $30,000 were more likely to experience disability progression compared to those with an income > $30,000 (aHR = 1.45; 95% CI: 1.03, 2.04). In contrast, the LMM analysis showed that lack of home ownership was the only SES covariate that had an independent association with disability after accounting for interaction terms (β: 0.14; 95% CI: 0.02, 0.25). Additionally, the interaction between age and HH poverty indicated that as an individual aged, the effect of a 10% increase in HH poverty on increases in HAQ scores was greater (β = 0.03; 95% CI: 0.01, 0.05). This suggests an increased risk of disability progression among individuals living in areas of higher HH poverty as they age.

Conclusion: Lower income, lack of home ownership and increased household poverty are independently associated with increased risk of disability progression, suggesting that societal interventions to address these specific SES factors could help to mitigate OA-related disability.

TABLE 1. Association between Disability Progression and SES Measures and Demographic Factors by Age
**Model 1: Disability Progression Analysis**  
(Multivariable Time-to-Event Analysis)†

<table>
<thead>
<tr>
<th>Category</th>
<th>aHR (95% CI)</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Education (&lt; HS)</td>
<td>1.06 (0.81, 1.39)</td>
<td>0.00</td>
<td>0.96</td>
</tr>
<tr>
<td>Household Poverty (per 10% change)</td>
<td>1.06 (0.93, 1.22)</td>
<td>0.05</td>
<td>0.08</td>
</tr>
<tr>
<td>Occupation Category (Low SES)</td>
<td>1.00 (0.77, 1.30)</td>
<td>0.05</td>
<td>0.22</td>
</tr>
<tr>
<td>Income (≤ $30K)</td>
<td>1.45 (1.03, 2.04)</td>
<td>-0.00</td>
<td>0.99</td>
</tr>
<tr>
<td>Home Ownership (Don't Own)</td>
<td>1.10 (0.81, 1.48)</td>
<td>-0.03</td>
<td>0.16</td>
</tr>
<tr>
<td>Age * Education</td>
<td>-0.03 (-0.07, 0.01)</td>
<td>0.03</td>
<td>0.004</td>
</tr>
<tr>
<td>Age * Household Poverty</td>
<td>-0.01 (-0.05, 0.03)</td>
<td>0.01</td>
<td>0.58</td>
</tr>
<tr>
<td>Age * Occupation</td>
<td>-0.01 (-0.05, 0.04)</td>
<td>0.04</td>
<td>0.11</td>
</tr>
<tr>
<td>Age * Home Ownership</td>
<td>-0.00 (-0.05, 0.04)</td>
<td>0.00</td>
<td>0.96</td>
</tr>
</tbody>
</table>

**Model 2: Linear Change in HAQ Score**  
(Linear Mixed Models Analysis)†

<table>
<thead>
<tr>
<th>Category</th>
<th>β (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Education (&lt; HS)</td>
<td>0.00</td>
<td>0.10</td>
</tr>
<tr>
<td>Household Poverty (per 10% change)</td>
<td>0.05</td>
<td>0.01</td>
</tr>
<tr>
<td>Occupation Category (Low SES)</td>
<td>0.05</td>
<td>0.13</td>
</tr>
<tr>
<td>Income (≤ $30K)</td>
<td>0.14</td>
<td>0.05</td>
</tr>
<tr>
<td>Home Ownership (Don't Own)</td>
<td>-0.00</td>
<td>0.04</td>
</tr>
</tbody>
</table>

†Note: All analyses accounted for age, race, and gender.

**Disclosure:** D. Narayanan, None; R. J. Cleveland, None; J. M. Jordan, None; E. Seaberg, None; L. F. Callahan, None.


**Abstract Number:** 2820

**Disease Activity By the Sledai in Lupus Patients Who Self Report Sleep Disturbance and Sleep Impairment Using the Patient-Reported Outcomes Measurement Information System Instruments**

Teresa Aberle¹, Rufei Lu², Sarah Cioli³, Stan Kamp¹, Wade DeJager¹, Stephen Apel⁴, Cristina Arriens⁵, Eliza Chakravarty⁶, Aikaterini Thanou¹, Joel M. Guthridge⁷, Joan T. Merrill⁸ and Judith A. James⁹, ¹Arthritis and Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, ²Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, ³Arthritis and Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, ⁴Oklahoma Medical Research Foundation, Oklahoma City, OK, ⁵Arthritis & Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, ⁶Oklahoma Medical research af, Edmond, OK, ⁷Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, OKC, OK, ⁸Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, ⁹Arthritis & Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** ARHP: Exemplary Abstracts  
**Session Type:** ARHP Concurrent Abstract Session  
**Session Time:** 4:30PM-6:00PM

**Background/Purpose:** Lupus patients commonly report sleep dysfunction, which is associated with upregulation of inflammatory cytokines in healthy people. Studies exploring relationships between self-reported sleep dysfunction and SLE have yielded conflicting results. The objective of our study was to evaluate the relationship between sleep and SLE disease activity in a large, ethnically diverse cohort of adult lupus patients.
Methods: 141 patients meeting ACR classification criteria for SLE completed the Patient-Reported Outcomes Measurement Information System (PROMIS) Sleep Disturbance Short Form 8b and Sleep Related Impairment Short Form 8a. Correlations between sleep scores and the SLE Disease Activity Instrument (SLEDAI) were tested by Spearman correlation. Upper and lower quartile proportions and associations were compared by Chi-square. Patients completing sleep assessments at ≥2 visits (n=69) were examined for intra-patient variability with mixed linear regression to model relationships between SLEDAI and sleep disturbance or impairment.

Results:
Participants were mostly Caucasian (50.4%) or African American (29.1%) and female (90.1%), with median age of 42. Sleep disturbance and impairment was increased compared to the national average (median T-scores of 56.3 and 55.6, respectively, vs. average of 50). Patients in the upper quartile of SIS and SDS did not differ in SLEDAI score compared to patients in the lowest quartile of SIS and SDS. However, SLE patients with the poorest sleep were more likely to have anti-dsDNA (OR 3.33, 95% CI 1.43, 10.0; p<0.01) and less likely to be scored for arthritis than those with the least sleep impairment (OR 0.185, 0.050, 0.690; p<0.05). Within individuals, sleep disturbance and sleep impairment did not correlate with total SLEDAI scores (r² = -0.0859 and r = -0.125, respectively; p>0.05). Adding medication usage covariates showed that sleep inducing agents (coefficient = -2.02; p<0.05) were associated with a decreased SLEDAI score, and steroid use (0.707; p<0.05) was associated with an increased SLEDAI score.

Conclusion: We found higher rates of sleep dysfunction in SLE than the national average which was not accounted for by SLEDAI scores. The possibility of immune phenotypes (anti-dsDNA) or medications contributing to sleep dysfunction should be further studied as improved sleep may be associated with health benefits such as decreased pain, less depression or minimization of co-morbid fibromyalgia.

Disclosure: T. Aberle, None; R. Lu, None; S. Cioli, None; S. Kamp, None; W. DeJager, None; S. Apel, None; C. Arriens, Exagen, 2; E. Chakravarty, None; A. Thanou, None; J. M. Guthridge, None; J. T. Merrill, Anthera Pharmaceuticals, Lilly, EMD Serono, GlaxoSmithKline and Biogen., 5; J. A. James, None.

A Multidisciplinary Telemedicine Program for Identification of Spondyloarthritis in Medically Underserviced Communities

Christopher Hawke1, Laura Passalent1, Nigil Haroon2, Robert D Inman3 and Y. Raja Rampersaud4, 1Allied Health, Toronto Western Hospital, Toronto, ON, Canada, 2Rheumatology, Toronto Western Hospital, University of Toronto, Spondylitis Clinic, Toronto, ON, Canada, 3Department of Immunology, University of Toronto, Toronto, ON, Canada, 4Arthritis Program, Krembil Research Institute, University Health Network, Toronto, ON, Canada
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: ARHP: Exemplary Abstracts
Session Type: ARHP Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose:
Early diagnosis is critical for optimal management of patients with inflammatory arthritis. Axial spondyloarthritis (AxSpA) has the longest delay in diagnosis among inflammatory joint diseases. Timely access to rheumatological assessment is particularly challenging in remote areas.

Objectives: To evaluate the impact of an alternate model of care on detection of AxSpA in remote areas and determine patient satisfaction with the model.

Methods:
To improve access to assessment of AxSpA, a satellite inter-professional AxSpA screening clinic (SpASC) was established 1000 kilometers away from the parent spondylitis clinic. Two Advanced Practice Physiotherapists (APPs) with extended scope training in
inflammatory arthritis provided standardized assessment onsite for patients with chronic back pain of more than 3 months duration and onset less than age 50. Patients with a previous diagnosis of SpA or those with leg-dominant pain were excluded. A telemedicine platform (OTN) allowed for APPs to consult with the staff Rheumatologist at the parent site at the end of the assessment.

The following investigations were obtained prior to the assessment: X-rays of the pelvis, lumbar, and cervical spine; testing for HLA B27, CRP and ESR levels.

The APP and Rheumatologist independently diagnosed patients as; AxSpA, non-specific back pain or other. The Rheumatologist and APP rated the probability of AxSpA as low, medium or high, scoring confidence of the classification on a 0-10 Likert scale. Radiographs of the sacroiliac joints were scored independently by the APP and rheumatologist using New York grading. For patients thought likely to have AxSpA despite non-diagnostic X-rays, an MRI was ordered. Access was measured by wait time in days and by the geographic area of patients based on postal code. Each patient that attended the satellite clinic was asked to complete a multidimensional patient satisfaction questionnaire.

Results:

In this analysis, 43 patients who completed the study protocol were assessed. Another 17 patients are awaiting MRI. The patients had a mean age of 36.8 (IQR 27.5-41) years and 28 (68.3%) were female. Nine (20.9%) patients were diagnosed with AxSpA (5 Ankylosing Spondylitis and 4 non-radiographic AxSpA). Thirty-two (74.4%) had non-specific back pain. One patient (2.3%) had a pedicle fracture and one (2.3%) was referred to a specialist clinic, with a subsequent diagnosis of lupus.

Diagnostic agreement between the APP and Rheumatologist was moderate-good (kappa 0.63 (0.38-0.87)). Median wait times were 162 days (July 2016, IQR, 69-176 days) and 131 days (March 2017, IQR, 99-180 days). With local wait time up to 2 years. Of the 60 patients seen in the clinic 47 (78%) travelled less than 50km to the clinic, with 13 (21.6%) travelling between 120-350kms.

Twenty-three patients (51%) returned satisfaction questionnaires after the consultation: 21 (95%) either agreed or strongly agreed that overall they were satisfied with the consultation.

Conclusion:

Establishing a satellite clinic with ACPAC-trained APPs consulting rheumatologists via telemedicine can offer improved access to care and effective diagnosis of AxSpA. Overall, patients were satisfied and accepting of the alternative consultation process.

Disclosure: C. Hawke, None; L. Passalent, None; N. Haroon, None; R. D. Inman, None; Y. R. Rampersaud, None.

A Randomized Controlled Effectiveness Trial of the Enhance-Fitness® Physical Activity Program in People with Arthritis

Dina L. Jones¹, Jennifer L. Eicher¹, Hannah M. Ludwick² and Kayéromi D. Gomez³, ¹Orthopaedics, West Virginia University, Morgantown, WV, ²Biostatistics, West Virginia University, Morgantown, WV, ³Office of Research, University of Illinois College of Medicine at Rockford, Rockford, IL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: ARHP: Exemplary Abstracts
Session Type: ARHP Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: EnhanceFitness® (EF) is an evidence-based, community-delivered intervention for older adults; however, its effectiveness in people with arthritis is unknown. The purpose of this pragmatic, community-based, randomized controlled trial was to determine the effectiveness of 12 weeks of EF in improving arthritis symptoms, physical and psychosocial function, and physical activity (PA) in adults with arthritis as compared to a 12-week, wait-list control group.
Methods: Community-dwelling adults, aged 18 years or older, were eligible if they were sedentary/low-active (≤ 60 minutes/week of moderate/vigorous-intensity PA), had self-reported physician-diagnosed arthritis, and were medically cleared for exercise. Participants were randomly assigned to the EF (immediate exercise) or wait-list control group. Participants exercised thrice weekly for 12 weeks (36 classes), and completed self-reported and performance-based assessments at baseline and 12 weeks. The outcomes were arthritis symptoms (pain, stiffness, fatigue on a visual analogue scale), physical and psychosocial functioning (SF-12, Self-Efficacy Questionnaire), upper/lower extremity strength (arm curl and 5 times sit-to-stand tests), aerobic endurance (2-minute step test), functional mobility (timed up-and-go test), and PA (minutes/week and kilocalories/week for all PA, CHAMPS Physical Activity Questionnaire). Analysis of Covariance was performed to determine if outcomes improved from baseline to 12 weeks after adjusting for group, age, sex, body mass index, site (northern vs. southern state county), and outcome score at baseline. The proportion of participants meeting national PA guidelines (≥ 150 minutes/week of moderate/vigorous-intensity exercise, National Health Interview Survey Questionnaire) was compared between groups at 12 weeks using a Chi-square test.

Results: Twenty-two EF classes were held at 15 community sites in 4 urban and 5 rural counties. Of the 134 participants, 68 were randomized to EF and 66 to the control group. Participants were primarily female (87%) and white (95%), with osteoarthritis (75%) and a mean ± SD age of 67 ± 11 years (range 35-89). The EF group experienced significantly lower stiffness (Effect Size [d] -0.9, p<0.001) and fatigue (d -0.8, p=0.03), and improved performance on the arm curl (d 0.9, p<0.001) and timed up-and-go (d -0.8, p=0.03) tests at 12 weeks as compared to the control group. A significantly greater proportion of the EF group were meeting PA guidelines (67%) at 12 weeks as compared to the control group (34%) (p<0.001). There were no significant differences between groups in the remaining variables.

Conclusion: A 12-week EF program was effective in improving arthritis symptoms, upper extremity strength, functional mobility, and the proportion meeting PA guidelines in adults with self-reported arthritis. This study demonstrated that an exercise program including the four key components for reducing pain and enhancing physical function (aerobic, strengthening, balance, and flexibility exercises) can substantially improve health in adults with arthritis when delivered in real-world community settings.

Disclosure: D. L. Jones, None; J. L. Eicher, None; H. M. Ludwick, None; K. D. Gomez, None.

Abstract Number: 2823

Preliminary Comparison of Patient-Centered Weight Loss Programs Starting before Versus after Knee Replacement

Christine Pellegrini1,2, Rowland W. Chang3, Dorothy D. Dunlop4, David Conroy1,5, Julia (Jungwha) Lee6, Linda VanHorn6, Bonnie Spring1 and Kenzie Cameron7, 1Northwestern University Feinberg School of Medicine, Chicago, IL, 2Exercise Science, University of South Carolina's Arnold School of Public Health, Columbia, SC, 3Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL, 4Center for Healthcare Studies, Northwestern University Feinberg School of Medicine, Chicago, IL, 5Kinesiology, The Pennsylvania State University, University Park, PA, 6Preventive Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, 7General Internal Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: ARHP: Exemplary Abstracts
Session Type: ARHP Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Most patients risk gaining weight in the years after knee replacement, adding further concern to a population that is mostly overweight/obese prior to surgery. Based on patient and stakeholder input and the Self-Determination Theory, we adapted the Diabetes Prevention Program to create the Patient-Centered Weight Loss Program (PACE). The purpose of the study was to compare changes in weight, function, and patient-reported outcomes between PACE programs initiated either before or after knee replacement.

Methods: Consented patients scheduled for knee replacement were randomized to a 14 session weight loss program starting either ≤6 weeks before surgery (PACE) or at 12 weeks post-op (Delayed PACE). All participants were provided a calorie goal to facilitate a 5% weight loss and were encouraged to increase physical activity. Patients were encouraged to self-monitor diet and activity using their preferred method (paper, web, app, Fitbit) and selected weekly or biweekly coaching sessions based on preference. Weight, function,
and patient-reported outcomes using Patient-Reported Outcomes Measurement Information System (PROMIS) were assessed at baseline (pre-op), 12, and 26 weeks after surgery. Repeated measures ANOVAs were used to examine changes in outcomes across time and group.

**Results:** Ten participants (5 randomized to PACE and 5 to Delayed PACE) completed the PACE intervention (mean±SD 62.2±7.9 years, 60% female, 80% White, BMI 35.2±5.4 kg/m²). Participants completed an average of 9.6±2.2 coaching sessions that were 15.2±3.4 minutes in duration. A significant effect for time ($P<0.001$) and a time by group interaction ($P=0.01$) were observed on weight change. Improvements over time were seen for all functional outcomes and patient-reported outcomes with the exception of sleep disturbance. No baseline differences were seen between groups.

**Conclusion:** Starting a patient-centered weight loss program either before or after knee replacement resulted in significant weight losses at 12 and 26 weeks post-op. Patients appear to naturally lose weight immediately post-op; hence waiting to start a weight loss program 12-weeks post-op may initiate greater weight loss during the first 6 months after surgery as compared to those who start ≤6 weeks pre-op.
<table>
<thead>
<tr>
<th>Outcome</th>
<th>PACE (n=5)</th>
<th>Delayed (n=5)</th>
<th>Mean Group Difference (95% CI)</th>
<th>Group</th>
<th>Time</th>
<th>Group x Time</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Body Weight</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (lbs)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>220.3 ± 24.1</td>
<td>213.8 ± 22.2</td>
<td>2.7 (-10.8, 16.2)</td>
<td>0.50</td>
<td>&lt;0.001**</td>
<td>0.01*</td>
</tr>
<tr>
<td>12 Weeks</td>
<td>211.0 ± 25.7</td>
<td>207.2 ± 25.0</td>
<td>-14.1 (-24.9, -3.2)</td>
<td>0.50</td>
<td>&lt;0.001**</td>
<td></td>
</tr>
<tr>
<td>26 Weeks</td>
<td>211.0 ± 23.8</td>
<td>190.4 ± 20.5</td>
<td>21.6 (-10.8, 63.0)</td>
<td>0.50</td>
<td>&lt;0.001**</td>
<td></td>
</tr>
<tr>
<td><strong>Physical Function</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Timed Up &amp; Go (secs)</td>
<td>9.2 ± 1.9</td>
<td>8.0 ± 2.8</td>
<td></td>
<td>0.35</td>
<td>0.03*</td>
<td>0.79</td>
</tr>
<tr>
<td>Baseline</td>
<td>8.3 ± 1.0</td>
<td>7.2 ± 1.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 Weeks</td>
<td>7.8 ± 0.7</td>
<td>7.1 ± 1.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>26 Weeks</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 Minute Walk (Feet)</td>
<td>1173.5 ± 323.1</td>
<td>1333.5 ± 314.1</td>
<td>-54.7 (-221.1, 111.7)</td>
<td>0.57</td>
<td>&lt;0.001**</td>
<td>0.79</td>
</tr>
<tr>
<td>Baseline</td>
<td>1393.7 ± 365.1</td>
<td>1499.0 ± 370.9</td>
<td>-6.8 (-266.7, 253.1)</td>
<td>0.57</td>
<td>&lt;0.001**</td>
<td></td>
</tr>
<tr>
<td>12 Weeks</td>
<td>1489.0 ± 430.9</td>
<td>1642.2 ± 445.5</td>
<td>-153.2 (-423.6, 117.2)</td>
<td>0.57</td>
<td>&lt;0.001**</td>
<td></td>
</tr>
<tr>
<td>26 Weeks</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chair Stands (stands/30 secs)</td>
<td>10.4 ± 2.4</td>
<td>10.6 ± 2.9</td>
<td></td>
<td>0.42</td>
<td>&lt;0.001**</td>
<td>0.09</td>
</tr>
<tr>
<td>Baseline</td>
<td>11.0 ± 3.7</td>
<td>14.2 ± 4.1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 Weeks</td>
<td>13.2 ± 3.1</td>
<td>15.0 ± 3.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>26 Weeks</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PROMIS Outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain Intensity (t score)</td>
<td>51.7 ± 5.8</td>
<td>51.6 ± 5.1</td>
<td>-0.3 (-9.4, 8.8)</td>
<td>0.88</td>
<td>&lt;0.001**</td>
<td>0.98</td>
</tr>
<tr>
<td>Baseline</td>
<td>44.1 ± 4.4</td>
<td>43.6 ± 7.9</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 Weeks</td>
<td>38.0 ± 4.2</td>
<td>37.0 ± 9.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>26 Weeks</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain Interference (t score)</td>
<td>58.8 ± 5.6</td>
<td>60.3 ± 4.0</td>
<td>-2.9 (-11.5, 5.6)</td>
<td>0.60</td>
<td>0.001*</td>
<td>0.46</td>
</tr>
<tr>
<td>Baseline</td>
<td>54.4 ± 3.2</td>
<td>53.0 ± 8.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 Weeks</td>
<td>49.4 ± 7.2</td>
<td>44.5 ± 8.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>26 Weeks</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mobility (t score)</td>
<td>36.2 ± 5.1</td>
<td>37.6 ± 3.4</td>
<td>1.4 (-5.2, 8.5)</td>
<td>0.30</td>
<td>&lt;0.001**</td>
<td>0.43</td>
</tr>
<tr>
<td>Baseline</td>
<td>40.6 ± 7.2</td>
<td>43.7 ± 5.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 Weeks</td>
<td>42.2 ± 3.5</td>
<td>47.8 ± 7.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>26 Weeks</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Sleep Disturbance (t-score) | Baseline | 12 Weeks | 26 Weeks |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep Disturbance (t-score)</td>
<td>52.0 ± 9.2</td>
<td>51.7 ± 10.4</td>
<td>44.7 ± 5.5</td>
</tr>
<tr>
<td>26 Weeks</td>
<td>53.2 ± 6.0</td>
<td>52.3 ± 4.5</td>
<td>49.4 ± 9.1</td>
</tr>
<tr>
<td>26 Weeks</td>
<td>-0.5 (-11.6, 10.5)</td>
<td>3.5 (-8.1, 15.0)</td>
<td>-0.5 (-11.6, 10.5)</td>
</tr>
<tr>
<td>26 Weeks</td>
<td>0.60</td>
<td>0.07</td>
<td>0.68</td>
</tr>
</tbody>
</table>

Disclosure: C. Pellegrini, None; R. W. Chang, None; D. D. Dunlop, None; D. Conroy, None; J. Lee, None; L. VanHorn, None; B. Spring, Actigraph, 9, Arrivale, 9; K. Cameron, None.


Abstract Number: 2824

**Sleep and Depression Mediate the Relationship between Pain and Cognitive Dysfunction in Lupus Patients**

Teresa A. Lillis¹, Vanessa Tirone¹, Stacy Weinberg², Nisarg Gandhi³, Ailda Nika⁴, Winston Sequeira⁴, Stevan E. Hobfoll¹, Joel A. Block⁵ and Meenakshi Jolly⁴

¹Behavioral Sciences, Rush University Medical Center, Chicago, IL, ²Division of Rheumatology, Rush University Medical Center, Chicago, IL, ³Rush University Medical Center, Chicago, IL, ⁴Rheumatology, Rush University Medical Center, Chicago, IL

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Tuesday, November 7, 2017

Session Title: ARHP: Exemplary Abstracts

Session Type: ARHP Concurrent Abstract Session

Session Time: 4:30PM-6:00PM

**Background/Purpose:** Cognitive Dysfunction (CD) is seen among 20-80% of patients with Systemic Lupus Erythematosus (SLE) and adversely affects their quality of life and productivity. Pain, a known correlate of CD, may occur in SLE from the disease itself or concurrent fibromyalgia (FM). Sleep issues and depression, also encountered in SLE, may impact both pain and CD. With the goal of a potential intervention for CD, we explored whether sleep issues and depression mediated the relationship between pain and CD in SLE patients.

**Methods:** 115 consenting SLE patients were recruited from a Rheumatology outpatient clinic. Patients completed questionnaires on demographics, pain (Pain Inventory), stress [(Perceived Stress Scale (PSS)), depression (PHQ2), sleep (LupusPROv1.8), and cognition (LupusPROv1.8)]. Diagnosis of concurrent FM and current steroid use were identified via chart review. Physicians performed disease activity (SELENA-SLEDAI) and damage (SLICC-ACR/ SDI) assessment. Bivariate correlations were used to determine relationships between above variables. Relationships among pain, sleep, depression and CD (primary variables) were assessed with bootstrapped mediation models controlling for race/ethnicity, FM status, current steroid use, SLEDAI, SDI, and stress (covariates).

**Results:** The sample was 90% female: average age was 40 years (SD 13). Racial composition was 52% African-American, 24% White, 11% Hispanic, 5% Asian, and 8% other. There were significant relationships noted among the variables (Table 1), including a positive relationship between pain and CD (r 0.39). Mediation analyses (Figure 1) indicated that the effect of pain on CD was mediated by depression (B 0.33) and sleep (B 0.30). These effects were maintained even after controlling for aforementioned covariates, of which, only SLEDAI (B 0.20) and stress (B 0.22) were significantly linked to CD [all p’s < .05] in the full model.

**Conclusion:** Even after controlling for disease activity and stress, both sleep and depression accounted for the relationship between pain and CD in SLE. These relationships need validation in longitudinal studies with additional measurement modalities. Our findings indicate promising, non-pharmacologic intervention avenues for SLE patients with pain and CD. Cognitive-behavioral therapies for depression and sleep are known to reduce distress and enhance functioning across various psychosocial domains. Given the symptom burden of SLE, interventions that maximize potential benefits without additional pharmacologic treatments may be of particular utility.
Table 1. Correlations among primary study variables and covariates.

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Total Pain Index</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Lupus PRO Sleep</td>
<td>.65**</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>PHQ 2</td>
<td>.42**</td>
<td>.52**</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Lupus PRO Cog</td>
<td>.39**</td>
<td>-.56**</td>
<td>.57*</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>African American Race</td>
<td>.21*</td>
<td>.20*</td>
<td>.26**</td>
<td>.22*</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Comorbid FM</td>
<td>.25**</td>
<td>.18</td>
<td>.30**</td>
<td>.30**</td>
<td>.06</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Takis Drioids</td>
<td>.24*</td>
<td>.04</td>
<td>.15</td>
<td>-.01</td>
<td>.12</td>
<td>-.18</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>SLEDAI</td>
<td>.26*</td>
<td>.01</td>
<td>.03</td>
<td>-.15</td>
<td>.09</td>
<td>-.09</td>
<td>.42**</td>
<td>1</td>
</tr>
<tr>
<td>9</td>
<td>SDI</td>
<td>-.08</td>
<td>.12</td>
<td>-.07</td>
<td>.13</td>
<td>.13</td>
<td>-.10</td>
<td>.13</td>
<td>.11</td>
</tr>
<tr>
<td>10</td>
<td>Perceived Stress</td>
<td>.34**</td>
<td>.37**</td>
<td>.57**</td>
<td>.49**</td>
<td>.19*</td>
<td>.15</td>
<td>.05</td>
<td>.10</td>
</tr>
</tbody>
</table>

Note: "p<.05; "**p<.01. For ease of interpretation of results, signs for Lupus PRO Sleep and Lupus PRO Cog scores were reversed. Accordingly, higher Lupus PRO Sleep scores = worse sleep and higher Lupus PRO Cog scores = worse cognition.

Figure 1: Path Diagram for Mediation Model of Pain and Cognition.
Note: Insignificant covariate paths (i.e., FM diagnosis, current steroid use, race/ethnicity, SDI) not shown.

Abstract Number: 2825

A Possible Environmental Origin for a Proportion of the Genetic Risk of Rheumatoid Arthritis and Systemic Lupus Erythematosus

John B. Harley¹, Xiaoting Chen¹, Mario Pujato², Daniel Miller¹, Avery Maddox¹, Carmy Forney³, Albert Magnusen³, Arthur Lynch¹, Kashish Chetal⁴, Masashi Yukawa⁵, Artem Barski⁶, Nathan Salomonis⁴, Kenneth Kaufman⁷, Leah C. Kottyan⁸ and Matthew Weirauch⁹. ¹Center for Autoimmune Genomics and Etiology (CAGE), Cincinnati Children's Hospital Medical Center, Cincinnati, OH, ²Center of Autoimmunity Genomics and Etiology (CAGE), Cincinnati Children's Hospital Medical Center, Cincinnati, OH, ³Center of Autoimmunity Genomics and Etiology (CAGE), Cincinnati Children's Hospital Medical Center; US Department of Veterans Affairs Medical Center, Cincinnati, OH, ⁴Division of Biomedical Informatics, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, ⁵Divisions of Allergy and Immunology and Human Genetics, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, ⁶Divisions of Allergy and Immunology and Bioinformatics, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, ⁷Center for Autoimmunity Genomics and Etiology (CAGE), Cincinnati Children's Hospital Medical Center, Cincinnati, OH, ⁸Center for Autoimmunity Genomics and Etiology (CAGE), Division of Allergy and Immunology, Cincinnati Children's Hospital, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, ⁹Center for Autoimmunity Genomics and Etiology (CAGE) and Divisions of Biomedical Informatics and Developmental Biology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

Disclosure: T. A. Lillis, None; V. Tirone, None; S. Weinberg, None; N. Gandhi, None; A. Nika, None; W. Sequeira, None; S. E. Hobfoll, None; J. A. Block, None; M. Jolly, Pfizer Inc, 2,LupusPRO, 7.
Background/Purpose: Nearly 150 genetic loci are convincingly associated with lupus (SLE) or rheumatoid arthritis (RA) and underlie their incompletely understood mechanisms of pathogenesis. Since 90% of complex disease genetic loci fall in genomic regulatory regions, since we suspect that regulatory elements may be shared across loci, and since other evidence is consistent with Epstein-Barr virus (EBV) contributing to SLE and RA pathogenesis, we tested the hypothesis for both SLE and RA that transcription factors and co-factors (TFs) encoded by EBV selectively bind the human genome at disease risk loci. We also evaluated over 212 TFs in over 150 cell lines and types in 1544 datasets. We selectively evaluated examples of allele specific TF binding.

Methods: We used published results, defining disease risk loci for RA and SLE as all variants with disequilibrium r²>0.8 to the most highly associated locus variant. The location of TF binding was taken from 1544 available TF chromatin immunoprecipitation with sequencing (ChIP-seq) datasets. By assigning loci to random sites in the human genome (or to open chromatin in EBV infected B cells) while preserving their locus structure, we used simulation to generate a normal distribution to estimate probability of the observed intersections of TF ChIP-seq binding and the risk loci for 213 diseases or phenotypes. We explored individual variants in ChIP-seq datasets for distorted TF binding to alleles.

Results: After Bonferroni correcting for 1544 comparisons we found powerful associations of the Epstein-Barr virus nuclear antigen 2 (EBNA2) ChIP-seq data with the loci of European SLE (26 of 53 loci, OR=6, Pc<10E-6, with the risk loci from 94 diseases or phenotypes, including other rheumatic disorders. Nearly 150 genetic loci are convincingly associated with lupus (SLE) or rheumatoid arthritis (RA) and underlie their incompletely understood mechanisms of pathogenesis. Since 90% of complex disease genetic loci fall in genomic regulatory regions, since we suspect that regulatory elements may be shared across loci, and since other evidence is consistent with Epstein-Barr virus (EBV) contributing to SLE and RA pathogenesis, we tested the hypothesis for both SLE and RA that transcription factors and co-factors (TFs) encoded by EBV selectively bind the human genome at disease risk loci. We also evaluated over 212 TFs in over 150 cell lines and types in 1544 datasets. We selectively evaluated examples of allele specific TF binding.

Conclusion: The indirect binding of EBNA2 to human DNA is associated with the genetic risk loci of both SLE and RA, as also are an associated set of human TFs clustering with EBNA2 at particular genetic loci, identifying different subsets of loci for RA and SLE. In the data now available these relationships in both diseases are found virtually exclusively in EBV-infected B cells. EBNA2 and human TFs bind alleles differentially at some plausibly causal variants. These results are consistent with EBV, the EBV infected B cell, and EBNA2 encoded by EBV DNA participating in SLE and RA pathogenesis.

Disclosure: J. B. Harley, None; X. Chen, None; M. Pujato, None; D. Miller, None; A. Maddox, None; C. Forney, None; A. Magnusen, None; A. Lynch, None; K. Chetal, None; M. Yukawa, None; A. Barski, None; N. Salomonis, None; K. Kaufman, None; L. C. Kottyan, None; M. Weirauch, None.


Abstract Number: 2826

**Fine-Mapping Identifies Causal Variants for RA and T1D in DNASE1L3, Sirpg, MEG3, TNFAIP3 and CD28/CTLA4 Loc**

Harm-Jan Westra¹, Marta Martinez-Bonet², Suna Onengütor³, Annette Lee⁴, Yang Luo¹, Nikola Teslovich¹, Jane Worthington⁵, Javier Martin⁶, TWJ Huizinga⁷, Lars Klaraesko⁸, Solbritt Rantapää Dahlqvist⁹, Wei-Min Chen³, Aaron Quinlan³, John Todd⁴, Stephen Eyre², Peter Nigrovic², Peter Gregerson⁴, Stephen Rich³ and Soumya Raychaudhuri¹². ¹Division of Genetics and Rheumatology, Department of Medicine, Harvard Medical School, Boston, MA, ²Division of Rheumatology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, ³Department of Public Health Sciences, University of Virginia, Charlottesville, VA, ⁴The Feinstein Institute for Medical Research, Northwell Health, Manhasset, NY, ⁵Arthritis Research UK Centre for Genetics and Genomics, Centre for Musculoskeletal Research, Faculty of Biology, Medicine and Health, Manchester Academic Health Science Centre, The University...
SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Genetics, Genomics and Proteomics
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: While genome-wide association studies have identified risk loci for rheumatoid arthritis and other autoimmune diseases, in very few instances have causal variants driving risk been precisely defined.

Methods: We fine-mapped 76 autoimmune disease loci outside of the MHC, combining genotype data from rheumatoid arthritis (RA) and type 1 diabetes (T1D) case-control studies. After sequencing 799 1kb regulatory (H3K4me3) regions within these loci in 568 individuals, we observed accurate imputation for 89% of common variants. We applied Bayesian fine-mapping for these loci in RA (11,475 cases, 15,870 controls), T1D (9,334 cases and 11,111 controls) and combined datasets.

Results: We reduced the number of potential causal variants to ≤5 in 8 RA and 11 T1D loci. We identified causal missense variants in five loci (Table, DNASE1L3, SIRPG, PTPN22, SH2B3 and TYK2) and likely causal non-coding variants in six loci (Table, MEG3, TNFAIP3, CD28/CTLA4, ANKR55, IL2RA, REL/PUS10). In the DNASE1L3 locus, the previously reported missense RA lead SNP rs35677470 (posterior=0.81) causes a R206C change in DNASE1L3, which abolishes its nuclease function. In SIRPG, we identified the rs6043409 missense variant, causing a V263A substitution (posterior=0.25). For the loci with non-coding causal candidates, we performed stringent filtering based on allelic function and enhancer activity. Using this approach, in the CD28/CTLA4 locus, we identified independent variants associated with RA and T1D: the rs117701653 SNP near CD28, associated with RA (posterior=0.82), and the rs3087243 SNP associated with both RA and T1D (posterior=0.91). Functional assays including EMSA and luciferase assay showed allele specific, cell type specific activity for rs117701653 but not rs3087243. Additionally, in the TNFAIP3 locus in RA, we identified allele specific and cell type specific enhancer activity for the rs35926684 indel (posterior=0.24), but not the previously reported lead variant rs6920220. Finally, in the MEG3 locus, we identified the rs34552516 indel (posterior=0.37) for T1D with allele specific and cell type specific enhancer activity.

Conclusion: This study demonstrates the potential for dense genotyping and imputation to pinpoint missense and non-coding causal alleles.

Disclosure: H. J. Westra, None; M. Martinez-Bonet, None; S. Onengut, None; A. Lee, None; Y. Luo, None; N. Teslovich, None; J. Worthington, None; J. Martin, None; T. Huizinga, Abbott Laboratories, Biotest AG, Bristol-Myers Squibb, Crescendo Bioscience, Novartis Pharmaceuticals Corporation, Pfizer Inc, Roche, sanofi-aventis, Schering-Plough, UCB, Eli Lilly, 5,METEOR Board, 6,EU & Dutch Arthritis Foundation, 2,Abbott Laboratories, Biotest AG, Bristol-Myers Squibb, Novartis Pharmaceuticals Corporation, Pfizer Inc, Roche, sanofi-aventis, Schering-Plough, 8,Abbott Laboratories, Roche, 9; L. Klareskog, None; S. Rantapää Dahlqvist, None; W. M. Chen, None; A. Quinlan, None; J. Todd, None; S. Eyre, None; P. Gregersen, None; S. Rich, None; S. Raychaudhuri, Pfizer Inc, 2,Roche Pharmaceuticals.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/fine-mapping-identifies-causal-variants-for-ra-and-t1d-in-dnase1l3-sirpg-meg3-tnfaip3-and-cd28ctla4-loc
A Novel Statistical Method to Resolve Cellular Heterogeneity in Disease Tissues: Integrating Transcriptomic Data in Accelerating Medicines Partnership (AMP) – RA Network Phase 1 Data

Fan Zhang1, Kamil Slowikowski2, Chamith Fonseka1, Kevin Wei3, Maria Gutierrez-Arcelus4, James Lederer5, Nir Hacohen6, Vivian P. Bykerc7, Michael Holers8, Peter Gregersen9, Mandy J. McGeeachy10, Larry W. Moreland11, Andrew Filer12, Costantino Pitzalis13, Yvonne C. Lee14, Jennifer H. Anolik15, Michael Brenner4 and Soumya Raychaudhuri16

1Divisions of Genetics and Rheumatology, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 2Division of Medicine and Rheumatology, Brigham and Women's Hospital, Harvard Medical Schoo, Boston, MA, 3Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 4Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 5Department of Surgery, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 6Harvard Medical School, Boston, MA, 72-005, Mt Sinai Hospital, Toronto, ON, Canada, 8Medicine, Division of Rheumatology, University of Colorado Denver, Aurora, CO, 9The Feinstein Institute for Medical Research, Northwell Health, Manhasset, NY, 10Medicine, University of Pittsburgh, Pittsburgh, PA, 11Rheumatology & Clinical Immunology, University of Pittsburgh, Pittsburgh, PA, 12Institute of Inflammation and Ageing (IIA), University of Birmingham, Birmingham, United Kingdom, 13Centre for Experimental Medicine and Rheumatology, William Harvey Research Institute, Barts and The London, School of Medicine and Dentistry, Queen Mary University of London, London, United Kingdom, 14Rheumatology Immunology & Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 15Medicine- Allergy, Immunology and Rheumatology, University of Rochester Medical Center, Rochester, NY, 16Division of Medicine and Rheumatology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Genetics, Genomics and Proteomics
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Detecting distinct cellular subsets in disease tissues is key to understanding the pathogenesis of immune diseases, for example in synovial tissues in rheumatoid arthritis (RA). Yet this task is complicated by the highly heterogeneous nature of the immune system. Recently, advances in single-cell technologies have enabled us to increase the power to resolve this heterogeneity to find disease relevant and cell type subsets. Integration of single-cell data with bulk data will help identify differentially abundant cell subsets.

Methods: We develop a novel statistical method for integrative analysis of any single-cell assay (flow cytometry, single-cell RNA-seq, or mass cytometry) with bulk RNA-seq (Figure 1). Our method has three steps. (1) We find the principal components (PCs) in the bulk RNA-seq data. (2) We model cell type abundances as a linear combination of bulk PCs. With single-cell data, we model a single-cell measurement with each PC to identify important signatures of bulk RNA-seq. The identified subsets are reflected as distinct clusters of cells in single-cell data and explain the variance in the bulk data. In mass cytometry data, we use a logistic model that includes the PC as a variable to predict the cluster identity of a cell. (3) To assess significance, we use permutations to test statistical significance of model coefficients.

Results: Using this integrative method, we are able to identify cellular subsets and statistically significant marker genes (permutation P < 1e-5) in fibroblasts, B cells, and T cells in AMP Phase 1 RA data (Bulk RNA-seq: 40 RA and 14 OA; Single-cell RNA-seq: 22 RA and 3 OA; Mass cytometry: 15 RA and 11 OA). Synovial fibroblasts separate into lining fibroblasts marked by CD55 and PRG4, and sublining fibroblasts marked by THY1 and CD74. B cells were separated into two distinct subsets: activated B cells that express HLA-DR, CD37, and CD83 and plasma cells that express XBP1 and FKBPI1. T cells were also separated into CD4+ helper that express CD4, IL7R, and SELL and CD8+ cytotoxic that express CD8A, CCL5, and HLA-DQA1. We tested subsets of these populations for disease association. We found that fibroblast subset marked by THY1 were significantly associated with RA (logistic regression P < 2e-5) when we integrated bulk data with mass cytometry. Derived from the bulk PCs, we observed that a PD1+ subset of CD4 memory T cells which have been recently described as peripheral T helper cells also expanded in RA (P < 0.01).

Conclusion: This computational strategy integrates multiple transcriptomic data types from fresh synovial tissue, giving us a view of the cellular heterogeneity relevant to RA. This method may also have promise in integrating single-cell and bulk data from other sources, for example kidney biopsies from systemic lupus erythematosus (SLE) or tumor biopsies. Acknowledgements: We acknowledge AMP RA/SLE network and AMP funding NIH UH2AR067677-01.
Disclosure: F. Zhang, None; K. Slowikowski, None; C. Fonseka, None; K. Wei, None; M. Gutierrez-Arcelus, None; J. Lederer, None; N. Hacohen, None; V. P. Bykerk, None; M. Holers, None; P. Gregersen, None; M. J. McGechy, None; L. W. Moreland, None; A. Filer, None; C. Pitzalis, None; Y. C. Lee, Express Scripts, 1, Pfizer Inc, 2; J. H. Anolik, None; M. Brenner, None; S. Raychaudhuri, Pfizer Inc, 2, Roche Pharmaceuticals, 2.


Abstract Number: 2828

**A Graph-Theoretic-Approach Applied to Modular-Repertoire-Analysis Identifies Shared Gradual Whole Blood Interferon Signatures in Systemic Lupus Erythematosus and Primary Sjögren’s Syndrome Patients and Reveals New Interferon-Related Modules in Disease Progression**

Ilya Korsunski¹, Noémie Jourde-Chiche², Peter Gregersen³, Damien Chaussabel⁴, Laurent Chiche⁵ and Naomi I. Maria⁶, ¹Center for Genomics and Human Genetics, Feinstein Institute for Medical Research, Manhasset, NY, ²Nephrology, AP-HM, Department of Nephrology, CHU Conception, Marseille, France, ³Robert S. Boas Center for Genomics and Human Genetics, Feinstein Institute for Med Res, Manhasset, NY, ⁴Translational Medicine, Sidra Medical and Research Center, Doha, Qatar, ⁵Internal medicine, Hopital européen, Marseille, France, ⁶Center for Autoimmune and Musculoskeletal Diseases, Feinstein Institute for Medical Research, Manhasset, NY

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Genetics, Genomics and Proteomics

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 4:30PM-6:00PM

**Background/Purpose:** There is significant clinical and molecular heterogeneity among patients suffering from systemic autoimmune diseases, such as systemic lupus erythematosus (SLE) and primary Sjögren’s Syndrome (pSS). Deciphering this heterogeneity could allow the molecular stratification of patients in terms of prognosis and therapeutic targets. Our previous work using a modular repertoire analysis (MRA) has demonstrated that the IFN signature observed in SLE patients is not restricted to a mere type I IFN signature, but involves the gradual activation of 3 distinct IFN modules driven by various IFN types including IFNy. Although a type I IFN signature
has been described in patients with pSS, a detailed MRA in pSS is still lacking. Here we aimed to refine MRA and discover new transcriptional signatures in SLE and pSS, by applying a novel graph-theoretic-approach (GTA) to reveal the progression of module activation patterns in these diseases.

**Methods:** Blood transcriptomic microarray datasets, including that of SLE patients (n=157 samples; LUPUCE cohort) fulfilling ACR-criteria and pSS patients (n=133; UKPSSR) fulfilling American European Consensus Group (AECG)-criteria, were analyzed using MRA followed by GTA. MRA was performed using a blood modular framework comprising 260 modules. A novel GTA, based on the Extended Suppes Bayes Causal Network (ESBCN), was used to generate an ordered, branching progression model of modular activation. Disease-specific causal graphs in selected datasets were built in order to generate hypotheses regarding disease progression for a particular disease. Significance to clinical characteristics was evaluated using Fisher’s exact test and ANOVA, for categorical and continuous characteristics, respectively.

**Results:** The GTA-to-MRA analysis confirmed the previously described pattern of gradual activation of IFN modules in SLE patients: first M1.2 (81.5%), then M3.4 (67.5%) and finally M5.12 (22.3%). Interestingly, this gradual IFN signature was also observed in pSS patients who exhibited activation of I (64%), 2 (37%) or all 3 (8%) IFN modules. Additionally, GTA-to-MRA identified a dual mode of disease progression in SLE after the activation of the IFN modules M1.2 and M3.4: either completion of the IFN signature, to include the more IFNγ-related module M5.12 and with completion of a newly identified 4th IFN-related module M8.59, or the activation of a neutrophil module M5.15 associated with renal involvement. In pSS, a dual mode of progression identified comparable completion of IFN signature to include M5.12, ending with the new IFN module M8.59, or activation of a 5th IFN-related module M8.95. Solely 6% of pSS patients portrayed a neutrophil signature, not linked to IFN progression, possibly identifying a relevant new pSS subgroup.

**Conclusion:** The application of GTA to blood MRA reveals for the first time the sharing of gradual activation of IFN modules between SLE and pSS, identifies new IFN-related modules through the observation of progression patterns, and discerns a pattern of progression involving a neutrophil signature associated with renal involvement in patients with SLE. Defining distinct molecular subgroups will aid in development of more tailored therapeutic regimens.

**Disclosure:** I. Korsunski, None; N. Jourde-Chiche, None; P. Gregersen, None; D. Chaussabel, None; L. Chiche, None; N. I. Maria, None.

**Abstract Number:** 2829

**Complete Epigenetic Landscape of Rheumatoid Arthritis Fibroblast-like Synoviocytes Reveals Unanticipated Critical Pathogenic Pathways**

Rizi Ai1, Teresina Laragione2, Deepa Hammaker3, David L. Boyle4, Andre Wildberg5, Keisuke Maeshima3, Emmanuele Palescandolo6, Vinod Krishna6, Bryan Linggi7, David Pocalyko8, John W. Whitaker9, Percio S. Gulkö2, Wei Wang10 and Gary S. Firestein11, 1UC San Diego, La Jolla, CA, 2Medicine/Rheumatology, Icahn School of Medicine at Mount Sinai, New York, NY, 3Division of Rheumatology, Allergy and Immunology, UCSD School of Medicine, La Jolla, CA, 4University of California San Diego, La Jolla, CA, 5Chemistry and Biochemistry, UNIVERSITY OF CALIFORNIA SAN DIEGO, LA JOLLA, CA, 6Janssen Pharmaceuticals, Spring House, PA, 7Janssen Pharmaceuticals, Spring House, PA, 8Janssen Research, Spring House, PA, 9Janssen Pharmaceuticals, La Jolla, CA, 10Chemistry and Biochemistry, UC San Diego, La Jolla, CA, 11Medicine, University of California San Diego, La Jolla, CA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Genetics, Genomics and Proteomics

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 4:30PM-6:00PM

**Background/Purpose:** Epigenetics participates in the pathogenesis of rheumatoid arthritis (RA). Epigenetic marks, gene expression and DNA polymorphisms have been investigated but the analyses are limited to few marks and simple combination methods. In the present study, we used a novel algorithm (Episeq) to integrate epigenomes for RA FLS in an unbiased fashion combining whole genome histone modifications, open chromatin, RNA expression and DNA methylation. By focusing on the chromatin states of
regulatory elements and using a new computational platform, we identified unexpected pathways that contribute to the pathogenesis of RA.

**Methods:** We applied multiple omics technologies on 11 RA and 11 osteoarthritis [OA] FLS: ChIPseq for histone modifications, ATACseq for open chromatin, RNAseq for transcriptomes and whole genome bisulfite sequencing (WGBS) for DNA methylation. The complex multidimensional relationships were addressed with our novel unbiased method, EpiSig, which is a flexible framework for integrative analysis of any type of sequencing data and identifies epigenomically co-modified regions that share similar patterns. Common epigenetic modification patterns were identified on a global genome scale and the genome was segmented into regulatory/functional elements. The epigenetic state of each element was defined and differentially modified epigenetic regions (DMER) between RA and OA were identified. Pathway evaluation used Ingenuity Pathway Analysis. Bostatistical analyses used Benjamini-Hochberg corrections.

**Results:** 218 genome-wide datasets were generated across FLS samples, including 152 histone modification datasets (H3K27ac, H3K4me1, H3K4me3, H3K36me3, H3K27me3, H3K9me3), 22 DNA methylation datasets, 22 open chromatin datasets and 22 transcriptome datasets. Eighteen epigenomic states were defined with distinct FLS chromatin signatures, including 4 promoter states, 6 enhancer states, 2 transcribed states, 2 states with zinc finger protein genes and 4 repressed states. The genome was segmented into 5 kb regions, and 125 epigenetic clusters with similar epigenetic patterns were determined across FLS. We identified regions that were differentially marked when comparing OA and RA. 13 clusters with significant DMER enrichment in RA were identified, which were grouped into biological pathways based on genes associated with these promoters and enhancers. Among the pathways that were significantly different in RA FLS, Phospholipase C Signaling, p53 Signaling, Integrin Signaling, and Protein Kinase A signaling were particularly notable. Other pathways were unexpected, such as Huntington’s Disease Signaling (HDS). To biologically validate the HDS pathway, we showed that one key member of HDS, namely HIP1, is expressed in FLS. HIP1 deficiency induced by siRNA knockdown decreased cultured RA FLS invasion into an artificial matrix by 56% (p<0.001).

**Conclusion:** We developed the first high-resolution global epigenomic landscape for RA and using a novel method to prioritize RA-specific biological pathways. Biologic validation of one unanticipated target in HDS pathway confirms that this unbiased method can identify novel therapeutic targets.

**Disclosure:** R. Ai, None; T. Laragione, None; D. Hammaker, None; D. L. Boyle, None; A. Wildberg, None; K. Maeshima, None; E. Palescandolo, Janssen Pharmaceutica Product, L.P., 3; V. Krishna, Janssen RD LLC, 3; B. Linggi, Johnson & Johnson, 3; D. Pocalyko, Johnson & Johnson, 1, Johnson & Johnson, 3; J. W. Whitaker, Johnson & Johnson, 3; P. S. Gulko, None; W. Wang, None; G. S. Firestein, Janssen Pharmaceutica Product, L.P., 2.


**Abstract Number:** 2830

**Epigenetic Cell Counting: A Novel Tool to Quantify Immune Cells in Salivary Glands Detects Robust Correlations of T Follicular Helper Cells with Immunopathology**

**Joel A.G. van Roon**1, Frederique M. Moret1, Sofie L.M. Blokland1, Aike A. Kruize2, Gerben Bouma3, Andre van Maurik3, Sven Olek4, Ulrich Hoffmueller4 and Timothy R.D.J. Radstake5, 1Rheumatology & Clinical Immunology/ Laboratory of Translational Immunology, University Medical Center Utrecht, Utrecht, Netherlands, 2Rheumatology & Clinical Immunology, University Medical Center Utrecht, Utrecht, Netherlands, 3ImmunoInflammation TAU, GlaxoSmithKline, Stevenage, United Kingdom, 4Epiontis GmbH, Berlin, Germany, 5Laboratory of Translational Immunology, University Medical Center Utrecht, Utrecht, Netherlands

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Tuesday, November 7, 2017
**Session Title:** Genetics, Genomics and Proteomics
**Session Type:** ACR Concurrent Abstract Session
**Session Time:** 4:30PM-6:00PM

**Background/Purpose:** Histological analysis of salivary glands for decades has been a valuable tool in the characterization of patients with primary Sjögren’s syndrome (pSS) and non-Sjögren’s sicca (nSS) patients. Importantly, it has helped in understanding the immunopathology of sicca patients. Nonetheless, standardization of histological assessments, e.g. to quantify lymphocytic foci or germinal centers is lacking, contributing to improper classification of disease and assessment of risk of lymphoma for example. Also, detailed and reproducible quantification of the heterogeneity of inflammatory cells and their contribution to immunopathology is
Methods: DNA was isolated from frozen tissue sections of 13 nSS, 12 probable SS, 29 pSS and 7 overlap SS patients. Bisulfite conversion of demethylated DNA sites was followed by cell specific qPCR that was used to calculate the percentage of cell subsets related to the total number of cells quantified by housekeeping gene expression. Percentages of epigenetically counted cells were correlated to gene expression generated by RNA-seq analysis of matched salivary gland tissue and histological and clinical parameters (lymphocytic focus score (LFS), %IgA+ plasma cells, serum IgG, SSA positivity).

Results: Strongly increased percentages of epigenetically quantified percentages of CD3, CD4, CD8, B cells, T follicular helper (Tfh) cells and Treg cells in pSS vs nSS patients were observed (all p<0.001, CD8 p=0.05, B cells p=0.01). These inflammatory cell types all strongly correlated with LFS (at least p<0.001, CD8 p=0.015), local B cell hyperactivity (% IgA+ cells, all p<0.001, except CD8 p=0.060 and B cells p=0.127) and systemic B cell hyperactivity (all at least p<0.01, except CD8 p=0.052). Th17 cells were not significantly different between nSS and pSS patients. Only CD8 T cells were significantly increased in probable SS patients as compared to nSS patients (p<0.05). Percentages of CD3 and B cells positively correlated with CD3 and CD19 RNA expression (r=0.608, p<0.0001; r=0.598, p<0.0001, resp.). Interestingly, percentages of Tfh cells correlated with CXCL13 (r=0.789, p<0.0001), IL7R, CXCR5 and ICOS RNA expression (all p<0.0001) and were strongly associated with autoimmunity (SSA positivity, p<0.001).

Conclusion: Epigenetic cell counting is a promising novel tool to reproducibly and easily quantify immune cells in the (inflamed) labial salivary gland of sicca patients with relatively low amount of tissue needed (<1 mm³). Considering the potential of this technique to include a huge number of (cell-specific) biomarkers we believe this opens up new standardized ways for salivary gland analysis with high relevance for patient classification, understanding of immunopathology and clinical trials.

Disclosure: J. A. G. van Roon, None; F. M. Moret, None; S. L. M. Blokland, None; A. A. Kruize, None; G. Bouma, None; A. van Maurik, None; S. Olek, None; U. Hoffmueller, None; T. R. D. J. Radstake, None.


Abstract Number: 2831

Real-World Experience with Tofacitinib Versus Adalimumab and Etanercept in Biologic-Naive Patients with RA Previously Treated with Methotrexate: Data from a US Administrative Healthcare Insurance Claims Database

Tim Smith1, James Harnett1, David Gruben2, Connie Chen1, Ekta Agarwal1 and John Woolcott3, 1Pfizer Inc, New York, NY, 2Pfizer Inc, Groton, CT, 3Pfizer Inc, Collegeville, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Health Services Research I: Cost Drivers in Rheumatic Disease
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor for the treatment of RA. Tofacitinib access has been restricted by many US payers to use after treatment with ≥1 injectable biologic DMARD (bDMARD); there are limited real-world data comparing tofacitinib with bDMARDs in biologic-naive RA patients (pts). This study compared pt characteristics, treatment patterns, and costs in pts initiating tofacitinib vs adalimumab (ADA) or etanercept (ETN) in a US population with commercial healthcare insurance.

Methods: This retrospective cohort study included pts aged 18–64 years with ≥1 tofacitinib or bDMARD healthcare insurance claim (Truven MarketScan® Commercial Claims and Encounters database) during 1/1/2014–1/1/2017, ≥1 MTX claim within 12 months prior to index, and ≥1 diagnosis of RA at index or within 12 months prior. Pts had to be continuously enrolled for ≥12 months pre-/post-index with no pre-index claims for tofacitinib or a bDMARD. Monotherapy was defined as absence of select conventional synthetic DMARDs within 90 days post-index. Outcomes were treatment persistence at 12 months (index refills with <60-day gap after supply expiration), adherence at 12 months (proportion of days covered [PDC]), and 12-month post-index RA-related costs. Statistical analyses were performed using t-statistics (continuous variables) or chi-squared statistics (binary variables) in pairwise comparisons.
**Results:** Pts who met selection criteria and initiated tofacitinib (n=184), ADA (n=1771), or ETN (n=1472) had similar baseline characteristics except for age which was higher in tofacitinib pts (mean 52.6 [SD 9.3], 49.9 [9.5], and 49.9 [10.0] years, respectively), and tofacitinib pts were more often located in the Northeast vs Southern region vs ADA. Tofacitinib pts had higher 12-month pre-index costs vs ADA (mean $4296 [SD $8159] vs $2880 [SD $5497], respectively; p=0.0225), more rheumatologist visits 90 days pre-index (mean 1.80 [SD 0.86] vs 1.96 [1.11]; p=0.0435), and higher (worse) Quan Charlson comorbidity index scores (mean 1.65 [SD 0.91] vs 1.50 [0.91]; p=0.0300). Tofacitinib pts had higher monotherapy use (34.2%) vs ADA (21.7%; p=0.0001) and ETN (26.5%; p=0.0263). Persistence at 12 months was similar for tofacitinib pts (46.2%) vs ADA (49.5%) and ETN (50.5%), although more tofacitinib pts restarted index treatment during 12 months post-index (17.9%) vs ADA (9.8%; p=0.0006) and ETN (7.1%; p<0.0001), and fewer tofacitinib pts switched treatment (16.9%) vs ADA (26.5%; p=0.0044) and ETN (29.6%; p=0.0003). Adherence (PDC) at 12 months was also similar between tofacitinib (0.63), ADA (0.67), and ETN (0.67) pts. Total post-index RA-related costs were lower with tofacitinib pts (mean $29,938 [SD $19,287]) vs ADA ($38,733 [SD $17,096]; p<0.0001) and ETN ($38,534 [SD $16,261]; p<0.0001).

**Conclusion:** Among biologic-naïve patients with RA and prior MTX, there was higher baseline monotherapy use among those receiving tofacitinib vs ADA and ETN. Persistence and adherence were similar for tofacitinib, and total RA-related costs were lower vs ADA and ETN, despite tofacitinib pts having higher pre-baseline costs.

**Disclosure:** T. Smith, Pfizer Inc, 1,Pfizer Inc, 3; J. Harnett, Pfizer Inc, 1,Pfizer Inc, 3; D. Gruben, Pfizer Inc, 1,Pfizer Inc, 3; C. Chen, Pfizer Inc, 1,Pfizer Inc, 3; E. Agarwal, Pfizer Inc, 1,Pfizer Inc, 3; J. Woolcott, Pfizer Inc, 1,Pfizer Inc, 3.

**Abstract Number:** 2832

**Finding the Optimal Treatment Strategy for Disease Activity-Guided Dose Reduction of Adalimumab and Etanercept in Rheumatoid Arthritis: A Modelling Study**

D.P.G. Bos, L.M. Verhoef, C.H.M. van den Ende, F.H.J. van den Hoogen, Bruno Fautrel, M.E.J.L. Hulscher, W. Kievit and A.A. Den Broeder, 1Rheumatology, Sint Maartenskliniek, Nijmegen, Netherlands, 2Rheumatology, Radboud university medical centre, Nijmegen, Netherlands, 3UPMC University Paris 06, Pitié-Salpêtrière Hospital, Paris, France, 4Paris VI Pierre et Marie Curie University, Paris, France, 5Radboud Institute for Health Sciences, IQ healthcare, Radboud university medical centre, Nijmegen, Netherlands, 6Department for Health Evidence, Radboud university medical centre, Nijmegen, Netherlands

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Health Services Research I: Cost Drivers in Rheumatic Disease

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 4:30PM-6:00PM

**Background/Purpose:** Although bDMARDs are often able to control the RA, they are expensive and associated with adverse effects. Therefore, it is important to use the lowest effective dose in each patient. Several studies have shown that, disease activity-guided dose reduction without deterioration of disease activity is possible, while saving costs in patients with stable and low disease activity. Despite these positive results, questions remain on the optimal tapering strategy. Different strategies are conceivable, with varying results regarding the balance between the number of flares, utilities and costs. Therefore, the objective of this study was to investigate the most cost-effective TNFi dose reduction strategy for RA patients using a modelling design.

**Methods:** In a cost-utility analysis using Markov modelling based on data from the DRESS study, STRASS study, and the RA Nijmegen cohort, the following strategies were tested: 1. four steps DRESS tapering (figure 1: 100%-67%-50%-0%); 2. Tapering with an extra dosage step of 33%; 3. Tapering without withdrawal; 4. Use of a stricter flare criterion; and 5. Use of a predictor (biomarker: 80% specific, 80% sensitive, €100 per test) for successful tapering. Also, a continuation group (strategy 0) was modelled and used as comparator. Scenario analyses with 30% and 50% drug price discount (biosimilars) and no discounting were executed. In addition, it was examined how well a biomarker should be able to predict to become cost-effective.
Results: All examined tapering strategies were found to be cost saving, but yielded more short-lived flares compared to strategy 0. The change in utilities was minimal (large overlap in credible intervals) (table 1). Strategy 2 is cost-effective compared to all other strategies (highest incremental net monetary benefit (iNMB)). Due to the large overlap in credible intervals of the NMBs of strategy 1, 2 and 3, the chance that they are actually not different in terms of cost-effectiveness is high. Scenario analyses did not change results. A biomarker becomes cost-effective when it has a sensitivity and specificity of 96% or higher.

Table 1: Main outcomes of each strategy

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>0. continuation (comparator)</th>
<th>1. DRESS strategy</th>
<th>2. DRESS 33% strategy</th>
<th>3. Tapering without withdrawal</th>
<th>4. Use of a stricter flare criterion</th>
<th>5. Strategy with a predictor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Costs ($)</td>
<td>21072 (20803-21357)</td>
<td>13192 (12445-13953)</td>
<td>13966 (12774-14928)</td>
<td>13839 (13199-14949)</td>
<td>15947 (15195-16761)</td>
<td>16024 (15001-15961)</td>
</tr>
<tr>
<td>QALYs</td>
<td>1.82 (1.166-1.199)</td>
<td>1.177 (1.160-1.192)</td>
<td>1.181 (1.160-1.197)</td>
<td>1.192 (1.166-1.198)</td>
<td>1.197 (1.175-1.204)</td>
<td>1.199 (1.180-1.200)</td>
</tr>
<tr>
<td>Mean number of short-lived flares</td>
<td>0.53 (0.35-0.73)</td>
<td>0.97 (0.83-1.12)</td>
<td>0.74 (0.58-0.92)</td>
<td>0.69 (0.52-0.89)</td>
<td>2.09 (1.79-2.40)</td>
<td>0.55 (0.53-0.56)</td>
</tr>
<tr>
<td>RMB</td>
<td>73513 (72212-74723)</td>
<td>86958 (79454-82468)</td>
<td>81023 (79492-82494)</td>
<td>80735 (79294-82205)</td>
<td>79455 (77648-80688)</td>
<td>79781 (78170-81420)</td>
</tr>
<tr>
<td>RMB***</td>
<td>-</td>
<td>7509</td>
<td>7509</td>
<td>7223</td>
<td>5652</td>
<td>6248</td>
</tr>
</tbody>
</table>

Conclusion: All dose reduction strategies dominated the continuation strategy. For use in clinical practice, we recommend a choice between strategy 1, 2 and 3, based on shared decision making.


Disclosure: D. P. G. Bos, None; L. M. Verhoef, None; C. H. M. van den Ende, None; F. H. J. van den Hoogen, None; B. Fautrel, AbbVie, Biogen, BMS, Celgene, Hospira, Janssen, Eli Lilly and Company, Novartis, Pfizer, Roche, SOBI Pharma, UCB, 5; M. E. J. L. Hulscher, None; W. Kievit, None; A. A. Den Broeder, None.
Cost-Effectiveness of Competing Anticoagulation Strategies in Knee Replacement Patients

Savannah R. Smith1,2, Jeffrey N. Katz3,4 and Elena Losina3,4, 1Orthopedics, Brigham and Women's Hospital, Boston, MA, 2George Washington University School of Medicine and Health Sciences, Washington, DC, 3Orthopaedics, Brigham and Women's Hospital, Boston, MA, 4Harvard Medical School, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Health Services Research I: Cost Drivers in Rheumatic Disease
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Total knee replacement (TKR) patients are routinely prescribed anticoagulation therapy to prevent deep vein thrombosis (DVT) and pulmonary embolism (PE). Clinical guidelines are ambiguous regarding the specific agent and duration of prophylaxis. We conducted a cost-effectiveness analysis to evaluate the benefits and risks of 14- and 35-day therapy with the most commonly prescribed anticoagulants post-TKR.

Methods: We built a probabilistic, state-transition computer simulation model to assess clinical and economic outcomes of 14-day and 35-day anticoagulation therapy after TKR. Complications of TKR and therapy included DVT, PE, bleeding, and prosthetic joint infection (PJI). DVTs could progress to PE and were classified as symptomatic or asymptomatic, with asymptomatic carrying a greater risk of PE. Operative site bleeds were associated with an increased risk of PJI (RR = 11), while non-operative site bleeds (CNS, GI) carried a quality of life decrement and risk of death. We evaluated 5 anticoagulation agents: rivaroxaban, low molecular weight heparin (LMWH), fondaparinux, warfarin, and aspirin. Each was associated with a unique reduction in DVT risk and an increased risk of bleeding compared with no anticoagulation; these risks were estimated from published literature. Costs included the agent and, when applicable, injection administration or monitoring costs (Table). We assumed a 1 year horizon and a willingness to pay (WTP) threshold of $100,000 per quality adjusted life year (QALY). Strategies with incremental cost-effectiveness ratios (ICERs) below WTP were deemed cost-effective.

Results: Aspirin at any duration was associated with the highest incidence of DVT and PE (28% and 5%, respectively). Extended fondaparinux resulted in the largest reduction in thromboses (DVT + PE) and greatest increase in bleeds (14% and 3%, respectively). Extended rivaroxaban reduced DVT incidence to 18% while increasing bleeds to 6%. Extended LMWH was associated with DVT and bleeding incidence of 19% and 4%, respectively. Both extended fondaparinux and rivaroxaban resulted in 0.74 QALYs; all other strategies, including no prophylaxis, resulted in fewer QALYs and higher costs and were therefore dominated (Table). The ICER for extended fondaparinux ($16.3M) greatly exceeded WTP; thus, extended rivaroxaban was the preferred strategy.

Conclusion: Extended rivaroxaban therapy after TKR is a cost-effective strategy to prevent DVT and PE while minimizing bleeding risk. The high cost and risk of bleeding of fondaparinux precluded it from being cost-effective. While there has been increased interest in using lower potency therapies, such as aspirin, these results demonstrate that aspirin’s low bleeding risk and low cost do not compensate for its poor efficacy in preventing DVT post-TKR.

Table.
### Characteristics of Anticoagulation Therapies

<table>
<thead>
<tr>
<th>Anticoagulant</th>
<th>RR DVT</th>
<th>RR Bleeds</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rivaroxaban</td>
<td>0.12</td>
<td>2.12</td>
<td>$7.90</td>
</tr>
<tr>
<td>LMWH</td>
<td>0.20</td>
<td>1.23</td>
<td>$40.90b</td>
</tr>
<tr>
<td>Fondaparinux</td>
<td>0.08</td>
<td>2.21</td>
<td>$46.77b</td>
</tr>
<tr>
<td>Warfarin</td>
<td>0.36</td>
<td>1.21</td>
<td>$7.23/$3.60a</td>
</tr>
<tr>
<td>Aspirin</td>
<td>0.62</td>
<td>1.00</td>
<td>$0.14</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Anticoagulant Strategy</th>
<th>Cost</th>
<th>QALY</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extended Rivaroxaban</td>
<td>$2,660</td>
<td>0.7398</td>
<td></td>
</tr>
<tr>
<td>Extended VKA</td>
<td>$2,820</td>
<td>0.7395</td>
<td>Dominated</td>
</tr>
<tr>
<td>Standard Rivaroxaban</td>
<td>$2,870</td>
<td>0.7392</td>
<td>Dominated</td>
</tr>
<tr>
<td>Extended ASA</td>
<td>$2,970</td>
<td>0.7389</td>
<td>Dominated</td>
</tr>
<tr>
<td>Standard VKA</td>
<td>$3,000</td>
<td>0.7390</td>
<td>Dominated</td>
</tr>
<tr>
<td>Standard ASA</td>
<td>$3,130</td>
<td>0.7386</td>
<td>Dominated</td>
</tr>
<tr>
<td>Standard LMWH</td>
<td>$3,370</td>
<td>0.7392</td>
<td>Dominated</td>
</tr>
<tr>
<td>Standard Fondaparinux</td>
<td>$3,390</td>
<td>0.7393</td>
<td>Dominated</td>
</tr>
<tr>
<td>No prophylaxis</td>
<td>$3,410</td>
<td>0.7382</td>
<td>Dominated</td>
</tr>
<tr>
<td>Extended LMWH</td>
<td>$3,700</td>
<td>0.7398</td>
<td>Dominated</td>
</tr>
<tr>
<td>Extended Fondaparinux</td>
<td>$3,780</td>
<td>0.7399</td>
<td>$16,300,000</td>
</tr>
</tbody>
</table>

- Includes cost of monitoring, presented as Week 1/Weeks 2+ due to extra monitoring during first week of treatment
- Includes cost of injection administration

RR = Relative risk, as compared with no anticoagulation
QALY = Quality-adjusted life year
ICER = Incremental cost-effectiveness ratio
Dominated = Strategy increased cost and decreased quality-adjusted life years

**Disclosure:** S. R. Smith, None; J. N. Katz, None; E. Losina, None.


**Abstract Number:** 2834

### Healthcare Cost Drivers in Rheumatoid Arthritis

**Nina Mars**, Anne M Kerola, Markku J Kauppi, Matti Pirinen, Outi Elonheimo and Tuulikki Sokka-Isler, Institute for Molecular Medicine Finland (FIMM), University of Helsinki, Helsinki, Finland; Department of Internal Medicine, Päijät-Häme Central Hospital, Lahti, Finland; University of Helsinki, Helsinki, Finland; School of Medicine, University of Tampere, Tampere, Finland; Department of Rheumatology, Päijät-Häme Central Hospital, Lahti, Finland; FCG Finnish Consulting Group Ltd., Helsinki, Finland; Rheumatology, Jyväskyla Central Hospital, Jyväskyla, Finland

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Health Services Research I: Cost Drivers in Rheumatic Disease

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 4:30PM-6:00PM
Background/Purpose: Rheumatoid arthritis (RA) is associated with high healthcare resource utilization, but knowledge about factors determining healthcare costs is limited. The aim was to identify healthcare cost drivers in RA.

Methods: RA patients attending Jyvaskyla Central Hospital (JCH) rheumatology unit, Finland, are as of 2007 prospectively enrolled in a structured digital database. We combined this clinical data with well-recorded administrative data on all primary and specialty healthcare in visits in Jyvaskyla area from fiscal year 2014. We excluded 46 outliers, defined as patients with annual costs exceeding the geometric mean by two standard deviations. For each patient, we considered the median of time dependent clinical variables: disease activity score (DAS28-3), health assessment questionnaire index (HAQ index, 0-3), and pain on visual analogue scale (VAS, 0-100). In patients with non-zero costs, factors affecting annual costs (€) were assessed with an age-stratified multivariate generalized linear model using Gamma distribution and a log link function. Variables were selected by statistical significance in univariate analyses. All multivariate analyses were adjusted for age in years or disease duration, and sex. To increase interpretability, we calculated marginal effects at the means of the independent variables. This displays how the annual costs are affected when a variable increases by one unit, while the other variables remain unchanged.

Results: Three age groups were analysed separately: 18-50 (n = 179), 51-70 (n = 477) and 71-100 (n = 300), with mean per-patient annual healthcare costs being 2,942€, 2,914€ and 4,026€, respectively. The main factor associated with healthcare costs across all age groups was disease activity: an increase in the long-term median level of DAS28(3) of an individual yielded up to a 848€ to 1,063€ increase in annual costs (Table 1). In terms of other clinical measures, strong evidence of an association was present for pain in those 18-50 (31€ per one point increase in VAS, p = 0.002) and for number of comorbidities in those 51-70 (317€ per comorbidity, p < 0.001).

Conclusion: A main cost driver in all age groups was disease activity.

Table 1. Multivariate generalized linear model for annual costs, stratified by age. The marginal effects were calculated at the means of the independent variables. For continuous variables, the marginal effect displays how the annual costs are affected when the variable increases by one unit, while the other variables remain unchanged. For dichotomous variables, the change represents comparison to the reference group.

<table>
<thead>
<tr>
<th>Age group</th>
<th>Marginal effect (€)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-50 (n = 179)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>-118</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DAS28(3)</td>
<td>1063</td>
<td>0.03</td>
</tr>
<tr>
<td>Male* (n = 41)</td>
<td>-146</td>
<td>0.09</td>
</tr>
<tr>
<td>VAS (0-100)</td>
<td>31</td>
<td>0.002</td>
</tr>
<tr>
<td>51-70 (n = 477)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>0.23</td>
<td>0.99</td>
</tr>
<tr>
<td>Erosions**</td>
<td>688</td>
<td>0.04</td>
</tr>
<tr>
<td>Male* (n = 139)</td>
<td>684</td>
<td>0.05</td>
</tr>
<tr>
<td>Median DAS28(3)</td>
<td>848</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median HAQ index (0-3)</td>
<td>-16</td>
<td>0.76</td>
</tr>
<tr>
<td>Median VAS (0-100)</td>
<td>11</td>
<td>0.27</td>
</tr>
<tr>
<td>Number of comorbidities</td>
<td>317</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>71-100 (n = 300)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>-12</td>
<td>0.70</td>
</tr>
<tr>
<td>Erosions**</td>
<td>810</td>
<td>0.19</td>
</tr>
<tr>
<td>Male* (n = 93)</td>
<td>1687</td>
<td>0.007</td>
</tr>
<tr>
<td>Median DAS28(3)</td>
<td>1042</td>
<td>0.005</td>
</tr>
<tr>
<td>Median HAQ index (0-3)</td>
<td>125</td>
<td>0.07</td>
</tr>
<tr>
<td>Median VAS (0-100)</td>
<td>13</td>
<td>0.41</td>
</tr>
<tr>
<td>Number of comorbidities</td>
<td>205</td>
<td>0.08</td>
</tr>
</tbody>
</table>

* Reference group: females  
** Reference group: no erosions

Disclosure: N. Mars, None; A. M. Kerola, None; M. J. Kauppi, None; M. Pirinen, None; O. Elonheim, Finnish Consulting Group Ltd, 3; T. Sokka-Istler, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/healthcare-cost-drivers-in-rheumatoid-arthritis

Abstract Number: 2835

5-Year Evolution Patterns of Physical Activity and Sedentary Behavior of Patients with Symptomatic Hip and/or Knee Osteoarthritis, and Their Sociodemographic and Clinical Correlates
Sarah Bitar¹, Abdou Y Omourou²,³, Aurélie Van-hoye¹, Francis Guillemin⁴,⁵ and Anne-Christine Rat⁴,⁵,⁶, ¹Université de Lorraine, EA 4360 APEMAC, Nancy, France, ²Université de lorraine, EA 4360 APEMAC, Nancy, France, ³Inserm, CIC-1433 Clinical epidemiology, Nancy, France, ⁴Université de Lorraine, EA4360, APEMAC, Nancy, France, ⁵Inserm, CIC-1433 Epidémiologie Clinique, Vandoeuvre-lès-Nancy, France, ⁶Rheumatology Department, CHRU Nancy, Vandoeuvre-lès-Nancy, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Health Services Research I: Cost Drivers in Rheumatic Disease
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Regular Physical Activity (PA) at a moderate level of intensity for approximately 2.5 hours per week is recommended in the management of hip and/or Knee osteoarthritis (OA). We aimed to identify evolution patterns of PA components (frequency, duration, intensity, type (weight bearing or not)) and Sedentary Behavior (SB) over five years and to determine baseline predictors for each trajectory in a representative cohort of patient with hip and/or knee OA.

Methods: Patients from the KHOALA cohort, a population-based multicenter cohort of 878 patients with symptomatic knee and/or hip OA, aged between 40 and 75 years old were included. For the purpose of the study, we used data collected between inclusion and the fifth year of follow-up. PA and SB were measured by the Modifiable Activity Questionnaire (MAQ). Evolution patterns of PA components and SB were identified using group-based trajectory analysis. Association of socio-demographic and clinical characteristics with PA and SB patterns were identified by multivariate logistic regression.

Results: Two groups of trajectories were identified for each PA component and three for the SB (figure1). Baseline sociodemographic and clinical characteristics were associated with Frequency and Type component trajectories: women were more often in the “moderate and stable duration” of PA group and in the “low and stable frequency of weight bearing PA” group than in the high groups; patients aged 60 years and older were in the “high and decreasing frequency” of PA group (OR= 3.2 [1.2-8.1]). Patients with impaired patients reported outcome variables (womac, pain VAS, SF36 vitality) were more often in the group of “low frequency of weight bearing PA” than in the high frequency group. Factors associated with moderate and high SB trajectories were all sociodemographic: being a male, below 60 year’s old, single (OR=1.5 [1.1-2.1]), obese (OR=2.1 [1.4-3.1]), smoking (OR=2.0 [1.1-3.7]), less physical jobs.

Conclusion: The determinants of the 5-year evolution of PA were different according to its components. Sociodemographic and clinical characteristics were associated with the frequency and type of PA while symptoms were not associated with SB. Sociodemographic factors associated with SB define populations to target for interventions promoting decrease of SB. Factors associated with components of PA allow for adapting PA practice or can be targets for interventions (e.g. on fatigue or mental health).
Figure 1. Trajectories of physical activity component’s and sedentary behavior.

Disclosure: S. Bitar, None; A. Y. Omourou, None; A. Van-hoye, None; F. Guillemin, None; A. C. Rat, None.


Abstract Number: 2836

The Additional Economic Burden of Depression Among Adults with Rheumatoid Arthritis in the United States

Nan Li and Steven Peterson, Janssen Research & Development, LLC, Spring House, PA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Health Services Research I: Cost Drivers in Rheumatic Disease
Session Type: ACR Concurrent Abstract Session
Background/Purpose: Depression is significantly more prevalent in patients with rheumatoid arthritis (RA) compared with the general population.\(^1\) It has a significant effect on RA patients, compromising clinical outcomes and increasing mortality. The objective of this study is to compare the healthcare utilization, expenditures, and work productivity among patients with RA to patients with RA and depression.

Methods: The Truven Health MarketScan® Research Databases were used in the analysis. Patients \(\geq\) 18 years of age with at least 2 RA visits, at least 2 months apart, between January 1, 2013 and December 31, 2013 were eligible for inclusion. The date of the first observed claim with an RA diagnosis was defined as the “index date.” Depression was defined as at least 2 visits for depressive disorder, at least 14 days apart, during the 12-month pre-index period in eligible patients. Outcomes were measured during the 12-month post-index period. Propensity score was calculated and controlled in logistics regression or Poisson regression. The incremental adjusted annual cost and 95% confidence interval (CI) were calculated using the bootstrapping method.

Results: A total of 46,700 RA patients were eligible for the analysis. Of this sample, 3,478 (7%) patients had RA and depression. The mean age of the study sample was 52 (standard deviation = 9.7) years and 78% were female. Patients with and without depression were significantly different \((P < 0.05)\) in terms of age, gender, residence area, relationship to primary insured, joint aspirations/injections, extra-articular manifestations, and difficulty walking, and had a wide variety of heterogeneous comorbidities at baseline. These covariates were used to calculate propensity score. After adjustment for propensity score, RA patients with depression used more healthcare resources annually compared with those without depression (relative risk and rate ratio > 1 with \(P < 0.05\) for all outcomes in Table 1). The incremental adjusted annual direct cost was $8,488 (95% CI, $6,793-$10,223); while the RA-related incremental adjusted annual direct cost was $578 (95% CI, $-98-$1,243).

Conclusion: This study highlights economic burden due to the presence of depression in RA patients. These findings underline the importance of managing RA when treatment algorithms are devised for these patients.


| Table 1. Relative Risk/Rate Ratios for Healthcare Utilization Comparing Patients With RA and Depression and Patients With RA Only |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
| **Logistic regression**         | **Unadjusted**  | **Adjusted**    | **Unadjusted**  | **Adjusted**    |
|                                 | Relative Risk  | \(P\) value     | Relative Risk  | \(P\) value     |
| RA-related surgery              | 1.96 (1.51, 2.55) | <0.0001         | 1.77 (1.34, 2.34) | <0.0001         |
| Hospitalization                 | 1.80 (1.66, 1.94) | <0.0001         | 1.47 (1.35, 1.60) | <0.0001         |
| RA-related hospitalization      | 1.41 (1.19, 1.67) | <0.0001         | 1.26 (1.05, 1.50) | 0.0113          |
| Emergency visits                | 1.41 (1.36, 1.47) | <0.0001         | 1.24 (1.17, 1.31) | <0.0001         |
| Short-term disability           | 1.50 (1.17, 1.92) | 0.0012          | 1.36 (1.05, 1.76) | 0.018           |
| **Poisson regression**          | **Rate Ratio**  | **(95% CI)**    | **Rate Ratio**  | **(95% CI)**    |
|                                 | **(95% CI)**    | \(P\) value     | **(95% CI)**    | \(P\) value     |
| Number of RA-related surgeries  | 2.95 (2.59, 3.36) | <0.0001         | 2.56 (2.23, 2.95) | <0.0001         |
| Number of hospitalizations      | 2.16 (2.02, 2.31) | <0.0001         | 1.70 (1.55, 1.80) | <0.0001         |
| Days of hospitalization         | 2.31 (2.24, 2.39) | <0.0001         | 1.79 (1.73, 1.85) | <0.0001         |
| Number of RA-related hospitalizations | 1.44 (1.23, 1.70) | <0.0001         | 1.28 (1.08, 1.52) | 0.0048          |
| Days of RA-related hospitalization | 1.62 (1.48, 1.77) | <0.0001         | 1.37 (1.25, 1.51) | <0.0001         |
| Number of physician visits      | 1.75 (1.74, 1.76) | <0.0001         | 1.51 (1.50, 1.52) | <0.0001         |
| Number of RA-related physician visits | 1.19 (1.17, 1.20) | <0.0001         | 1.12 (1.10, 1.13) | <0.0001         |
| Number of short-term disability events | 1.33 (1.29, 1.39) | 0.0005          | 1.41 (1.09, 1.91) | 0.0079          |
| Days of short-term disability   | 1.37 (1.33, 1.41) | <0.0001         | 1.22 (1.19, 1.26) | <0.0001         |

RA, rheumatoid arthritis; CI, confidence interval.

Disclosure: N. Li, Johnson & Johnson, 3; Johnson & Johnson, 1; S. Peterson, Johnson & Johnson, 3; Johnson & Johnson, 1.


Abstract Number: 2837
Cross-Sectional Analysis of Chikungunya Arthritis Patients 22-Months Post-Infection Demonstrates a Lack of Viral Persistence in Synovial Fluid

Aileen Chang1, Karen Martins* Contributed equally2, Liliana Encinales3, St. Patrick Reid4, Marlon Acuña3, Carlos Encinales3, Christian Matranga5, Nelly Pacheco3, Carlos Cure3, Bhavarth Shukla6, Teofilo Arteta Ruiz3, Richard Amdur7, Lisa Cazares8, Melissa Gregory8, Michael Ward8, Alexandra Porras9, Alejandro Rico Mendoza9, Lian Dong8, Tara Kenny8, Ernie Brueggemann8, Lydia Downey8, Priyanka Kamalapathy7, Paola Lichtenberger6, Orlando Falls3, Gary Simon7, Jeffrey Bethony7 and Gary S. Firestein10,
1Medicine, George Washington University, Washington, DC, 2United States Army Medical Research Institute for Infectious Disease, Frederick, MD, 3Allied Research Society, Baranquilla, Colombia, 4University of Nebraska, Omaha, NE, 5Broad Institute, Boston, MA, 6University of Miami, Miami, FL, 7George Washington University, Washington, DC, 8United States Army Medical Research Institute of Infectious Disease, Frederick, MD, 9Allied Research Society, Bogota, Colombia, 10Medicine, UCSD, La Jolla, CA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Infection-related Rheumatic Disease
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Chikungunya virus infection is a mosquito-borne disease that causes chronic joint pain for months to years in approximately one half of infected patients. The study objective was to determine if chikungunya virus (CHIKV) persists in the synovial fluid, potentially serving as a causative mechanism of persistent arthritis.

Methods:

Design: Cross-sectional

Setting: Atlántico and Bolívar Departments, Colombia

Participants: Thirty-eight patients with CHIKV infection during the 2014-2015 epidemic with chronic arthritis, including in the knee joint, and ten healthy controls without prior CHIKV infection were included.

Measures: Participants completed a symptom questionnaire. Prior infection with CHIKV was confirmed by serological analysis. The presence of chikungunya viral RNA in blood and synovial fluid were measured by qPCR.

Results: Prior CHIKV infection was serologically confirmed in 33/38 (87%) of the cases based on IgM (3%) and IgG ELISA (100%). Confirmed chikungunya arthritis patients were predominantly women (82%), Afro-Colombian (55%), or White-Colombian (33%) with high school or less level of education (94%). CHIKV arthritis patients were a median 22 (IQR 21-23) months post CHIKV infection. Initial symptoms of CHIKV infection included joint pain (97%), joint swelling (97%), joint stiffness (91%), fever (91%), and rash (88%). The most commonly affected joints during initial infection were knees (87%), elbows (76%), wrists (75%), fingers (56%), and toes (56%). None of the participants were qPCR positive for persistent virus in the serum or synovial fluid. Furthermore, no viral proteins were identified in synovial fluid by mass spectrophotometry and synovial fluid was also culture negative. Participants reported an effect on their activities of daily living from their arthritis (82%) and disease severity was moderate, as shown by an average Disease Activity Score-28 of 4.52 ± 0.77.

Conclusion: This is one of the largest observational studies involving chikungunya arthritis patients. Synovial fluid analysis revealed no evidence of CHIKV by PCR, mass spectrometry, or culture. This suggests that immunomodulating medications may be safe in the treatment of chikungunya arthritis and suggests a possible mechanism whereby CHIKV causes arthritis through induction of host autoimmune pathology.

Disclosure: A. Chang, None; K. Martins* Contributed equally, None; L. Encinales, None; S. P. Reid, None; M. Acuña, None; C. Encinales, None; C. Matranga, None; N. Pacheco, None; C. Cure, None; B. Shukla, None; T. Arteta Ruiz, None; R. Amdur, None; L. Cazares, None; M. Gregory, None; M. Ward, None; A. Porras, None; A. Rico Mendoza, None; L. Dong, None; T. Kenny, None; E. Brueggemann, None; L. Downey, None; P. Kamalapathy, None; P. Lichtenberger, None; O. Falls, None; G. Simon, None; J. Bethony, None; G. S. Firestein, None.

Apoptotic Bodies Containing dsDNA Covalently Modified By Parvovirus B19 Non-Structural Protein NS1 Induce dsDNA Autoantibodies and End Organ Damage in Non-Autoimmune Mice

Stanley J. Naides1, Kanoktip Puttaraksa2, Heidi Pirttinen2, and Leona Gilbert2, 1Immunology, Quest Diagnostics Nichols Institute, San Juan Capistrano, CA, 2Department of Biological and Environmental Science and Nanoscience Center, University of Jyvaskyla, Jyvaskyla, Finland

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Infection-related Rheumatic Disease
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Persistent viral infections can induce aberrant immune responses and are implicated in the development of autoimmunity. Parvovirus B19 (B19V) non-structural protein, NS1, a helicase, covalently modifies self dsDNA and induces apoptosis. This study was undertaken to determine whether resulting apoptotic bodies (ApoBods) containing virally modified dsDNA could induce autoimmunity in an animal model.

Methods: Non-autoimmune BALB/c mice were inoculated with B19V NS1, pristane or staurosporine induced ApoBods and serum tested for dsDNA autoantibodies by Crithidia luciliae staining and ELISA. Brain, heart, liver and kidney pathology was examined by bright field and confocal microscopies. Deposition of self-antigens and ApoBods in glomeruli was examined by staining with labeling antibodies to dsDNA, histones H1 and H4, and TATA-binding protein.

Results: Innoculation with B19V NS1-induced ApoBods induced dsDNA autoantibodies in a dose dependent fashion, whereas staurosporine induced ApoBods did not. Histopathological features of immune mediated organ damage was evident in pristane-induced and B19V NS1-induced ApoBod groups and severity score was significantly higher in these groups than in staurosporine treated groups, and was B19V NS1-induced ApoBod dose dependent. Nucleosomal antigens were deposited in pristane-induced and B19V NS1-induced ApoBod groups, but not in the staurosporine-induced ApoBod group.

Conclusion: This study demonstrated proof of principle in an animal model that virally modified dsDNA in apoptotic bodies could break tolerance to self dsDNA and induce dsDNA autoantibodies and end-organ damage. The study helps explain observations suggesting a viral contribution to the development of systemic lupus erythematosus.

Disclosure: S. J. Naides, Quest Diagnostics, 3; K. Puttaraksa, None; H. Pirttinen, None; L. Gilbert, Te?ted Oy, 4.

Practice Patterns of Pneumocystis Pneumonia Prophylaxis in Connective Tissue Diseases: a Survey of Infectious Disease Physicians

Rachel M. Wolfe1, Susan E. Beekmann2, Philip M. Polgreen2 and James E. Peacock Jr.3, 1Internal Medicine, Section on Rheumatology and Immunology, Wake Forest Baptist Health, Winston-Salem, NC, 2Internal Medicine, Division of Infectious Diseases, Carver College of Medicine, Iowa City, IA, 3Internal Medicine, Section on Infectious Disease, Wake Forest Baptist Health, Winston-Salem, NC

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Infection-related Rheumatic Disease
Session Type: ACR Concurrent Abstract Session
**Background/Purpose:** Potent immunosuppressive therapy for connective tissue diseases (CTDs) imparts an increased risk for opportunistic infections including Pneumocystis pneumonia (PCP). High mortality rates have been reported in CTD patients with PCP which raises the question as to if and when prophylaxis for PCP is indicated. Unfortunately, the specific risk factors and precise indications for PCP prophylaxis in CTD patients remain poorly defined and are guided only by expert opinion and personal experience. Wide variations in PCP prophylaxis patterns among rheumatologists have been previously established. This study was aimed to evaluate patterns among infectious disease physicians.

**Methods:** An electronic survey on PCP prophylaxis in CTD patients was emailed to 1,264 adult infectious disease physicians who are members of the Infectious Diseases Society of America Emerging Infections Network.

**Results:** 631 (50%) physicians responded to the survey. Respondents were significantly more likely to work in an academic/university system (p = 0.02) and either be early (<5 years) or late (≥25 years) in their careers (p = 0.0002). Almost half (43%) reported that they did not make recommendations for PCP prophylaxis in non-HIV patients. Of those making recommendations for prophylaxis, there was little agreement on indications for prophylaxis. The greatest consensus for specific CTDs was for granulomatosis with polyangiitis (GPA) with 53% advocating for PCP prophylaxis. Only about a third recommended prophylaxis for other vasculitides, lupus, lupus nephritis, inflammatory myositis and rheumatoid arthritis on high dose corticosteroids. Interestingly, the most frequent single response was “Not Sure” (35%) but this option was also often selected along with other specific CTDs (41% of total respondents). When questioned about specific therapies, corticosteroids ≥20 mg/day was the most frequently cited indication for PCP prophylaxis (87%). Few recommended PCP prophylaxis with DMARD therapy (both biologic and non-biologic) without concurrent high dose corticosteroids (2-12% versus 69-77%). Surrogate laboratory markers were not routinely used to guide decisions about prophylaxis (21%). There was no consensus for the specific indices although CD4 alone was the most frequent response. While the majority recommended discontinuation of PCP prophylaxis with tapering of corticosteroids (65%), there was considerable variability in the specific dose at which it should be discontinued. The most frequent response was below 16-20 mg/daily. 89% of respondents felt that guidelines about PCP prophylaxis would be helpful in their practice.

**Conclusion:** There is little consensus about PCP prophylaxis in CTDs among infectious disease physicians although certain diseases (GPA) and immunosuppressants (higher dose corticosteroids) are common indications to recommend prophylaxis. There remains much uncertainty in clinical practice with respect to the role for PCP prophylaxis in patients with CTD, both by infectious disease physicians and rheumatologists. Guidelines for PCP prophylaxis would be an important adjunct in caring for these complex patients.

**Disclosure:** R. M. Wolfe, None; S. E. Beekmann, None; P. M. Polgreen, None; J. E. Peacock Jr., None.


**Abstract Number:** 2840

**Clinical Presentation and Outcomes in Patients with Prosthetic Joint Septic Arthritis Who Had One-Stage Versus Two-Stage Joint Replacement**

Mary Louise Fowler1, Kevin Byrne2, Sarah Lieber3, Robert Shmerling4 and Ziv Paz3, 12Boston University School of Medicine, Boston, MA, 2Boston University School of Medicine, Boston, MA, 3Beth Israel Deaconess Medical Center, Boston, MA, 4Rheumatology, Beth Israel Deaconess Medical Center, Boston, MA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Infection-related Rheumatic Disease

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 4:30PM-6:00PM

**Background/Purpose:** Prosthetic joint septic arthritis (PJSA) complicates about 1 to 2 percent of joint replacement surgeries. The management of PJSA usually includes a combination of surgery and antibiotics. Resection arthroplasty with re-implantation for PJSA may be performed in one or two stages. There is a lack of comparative trials comparing the two strategies and there is no consensus regarding which option should be recommended.
Objective: To define the epidemiology, clinical characteristics and outcomes of patients with PJSA for whom a one-stage procedure was performed as compared with patients with PJSA for whom a two-stage procedure was performed.

Methods: We conducted a retrospective study that included all patients aged 18 years and older admitted to a single, tertiary-care hospital between 1998 and 2015 who were diagnosed with monoarticular PJSA and were surgically treated with either a one-stage or two-stage joint replacement. We excluded cases of native joint infection or septic bursitis.

Results: Of the 65 patients with PJSA treated with either one- or two-stage procedure, 18 had a one-stage procedure while 47 had a two-stage procedure. There were no differences in average age or gender between the two groups [Table 1]. Chronic kidney injury and end-stage liver disease were significantly more common in patients who had a two-stage procedure (p=0.006 and p=0.02 respectively) while patients who had a one-stage replacement were more often febrile (50% vs. 27.7%; p=0.11), had higher peripheral white blood cell (WBC) counts (14.6 vs. 10.7 thousand cells/mm$^3$; p=0.01) and had a greater mean percentage of peripheral polymorphonuclear (PMN) leukocytes (85.5% vs. 76.5%, p<0.001). While one-stage procedures were split evenly between knee and hip replacements, two-stage knee replacements were more common (75% of cases) than two-stage hip replacements (25% of cases) [Table 2]. Outcomes between the two strategies were similar [Table 2].

Conclusion: In our institution, two-stage joint revision for PJSA is more common than one-stage procedures, especially when the knee is involved. Although this study might have been underpowered to detect small differences, there were no clear differences in clinical features or outcomes of patients with PJSA undergoing revision arthroplasty based on the type of operation. Surgeons seem to favor two-stage for patients with comorbidities while preferring one-stage for patients presenting with early PJSA infection. Larger prospective trials are needed to identify which circumstances should lead surgeons to choose one strategy over the other.

Table 1. Demographic and clinical features of patients with PJSA who had one-stage or two-stage joint replacement surgery.

<table>
<thead>
<tr>
<th>Demographic and clinical features of patients with PJSA who had one-stage or two-stage joint replacement surgery.</th>
<th>One-stage (n=18)</th>
<th>Two-stage (n=47)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr), mean (SD)</td>
<td>61 (11.42)</td>
<td>61.2 (12.28)</td>
<td>0.96</td>
</tr>
<tr>
<td>Female gender, N (%)</td>
<td>11 (61.1)</td>
<td>20 (42.5)</td>
<td>0.19</td>
</tr>
<tr>
<td>Risk Factors for SA:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DM, N (%)</td>
<td>5 (27.8)</td>
<td>14 (29.8)</td>
<td>0.87</td>
</tr>
<tr>
<td>CKI, N (%)</td>
<td>0 (0)</td>
<td>7 (14.9)</td>
<td>0.006</td>
</tr>
<tr>
<td>HIV, N (%)</td>
<td>0 (0)</td>
<td>2 (4.3)</td>
<td>0.16</td>
</tr>
<tr>
<td>ESLD, N (%)</td>
<td>0 (0)</td>
<td>5 (10.6)</td>
<td>0.02</td>
</tr>
<tr>
<td>IVDD, N (%)</td>
<td>1 (5.6)</td>
<td>4 (8.5)</td>
<td>0.67</td>
</tr>
<tr>
<td>OA, N (%)</td>
<td>10 (55.6)</td>
<td>25 (53.2)</td>
<td>0.87</td>
</tr>
<tr>
<td>Recent joint trauma, N (%)</td>
<td>1 (5.6)</td>
<td>1 (2.1)</td>
<td>0.57</td>
</tr>
<tr>
<td>Recent procedure in joint, N (%)</td>
<td>13 (72.2)</td>
<td>30 (63.8)</td>
<td>0.52</td>
</tr>
<tr>
<td>Clinical features:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever (&gt;100 F), N (%)</td>
<td>9 (50)</td>
<td>13 (27.7)</td>
<td>0.11</td>
</tr>
<tr>
<td>Sepsis (defined by SIRS criteria), N (%)</td>
<td>7 (38.9)</td>
<td>11 (23.4)</td>
<td>0.17</td>
</tr>
<tr>
<td>Mean peripheral WBC (in thousands), (SD)</td>
<td>14.59 (5.51)</td>
<td>10.7 (4.51)</td>
<td>0.01</td>
</tr>
<tr>
<td>Mean peripheral PMN (%), (SD)</td>
<td>85.47 (6.11)</td>
<td>76.5 (11.05)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean ESR (mm/hr), (SD)</td>
<td>64.2 (60.13)</td>
<td>80.1 (33.04)</td>
<td>0.18</td>
</tr>
<tr>
<td>Mean CRP (mg/L), (SD)</td>
<td>109.94 (100.6)</td>
<td>140.33 (107.34)</td>
<td>0.35</td>
</tr>
<tr>
<td>Mean synovial WBC (in thousands), (SD)</td>
<td>87.36 (114.89)</td>
<td>104.35 (149.5)</td>
<td>0.66</td>
</tr>
<tr>
<td>Mean synovial fluid PMN (%), (SD)</td>
<td>82.25 (18.37)</td>
<td>90 (17)</td>
<td>0.17</td>
</tr>
</tbody>
</table>

SD: Standard deviation; DM: Diabetes Mellitus; CKI: Chronic Kidney injury; HIV: Human Immunodeficiency Virus; ESLD: End Stage Liver Disease; IVDD: Intravenous Drug Use; RA: Rheumatoid arthritis; WBC: White Blood cell; PMN: Polymorphonuclear leukocyte; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein.
Infection Is the Major Trigger of Adult Hemophagocytic Syndrome, an Orphan Systemic Hyperinflammatory, Life-Threatening Disease: Analysis in 147 Patients (GEAS-SEMI Registry)

Pilar Brito-Zerón1, Alejandra Flores-Chavez2,3,4, Pedro Moral Moral5, A. Martínez-Zapico6, Pilar Hernández-Jimenez7, Guadalupe Fraile Rodriguez8, Patricia Perez Guerrero9, Eva Fonseca10, Angel Robles11, Maria Vaquero Herrero12, Angela Ruiz de Temiño de la Peña13, Maria José Forner14, José Ramón Larrañaga15, Mónica Rodriguez Carballeira16, Luis Fernando Viejo Llorente17, Manuel Ruiz Muñoz18, Roberto Hurtado19, César Morcillo20, Soledad Retamozo21 and Manuel Ramos-Casals22,23, 1Laboratory of Systemic Autoimmune Diseases “Josep Font”, CELLEX, Institut d’Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Department of Systemic Autoimmune Diseases, ICMID, Hospital Clinic, Barcelona, Barcelona, Spain, 2Department of Autoimmune Diseases, ICMiD, Hospital Clinic Barcelona, Barcelona, Spain, 3Programa de Doctorado en Ciencias Médicas, Centro Universitario de Investigaciones Biomédicas (CUIB), Universidad de Colima, Colima, Mexico, Mexico, Mexico, 4Unidad de Investigación en Epidemiología Clínica, UMAE, Hospital de Especialidades, Centro Médico Nacional de Occidente, Instituto Mexicano del Seguro Social, Jalisco, Mexico, 5Hospital La Fè Valencia, Valencia, Spain, 6Hospital Universitario de Asturias, Oviedo, Oviedo, Spain, 7Internal Medicine, Hospital 12 de Octubre, Madrid, Spain, 8Internal Medicine, Hospital Ramón y Cajal, Madrid, Madrid, Spain, 9Department of Internal Medicine, Hospital Universitario Puerta del Mar, Cádiz, Cádiz, Spain, 10Internal Medicine, Hospital de Cabueñes, Gijón, Gijón, Spain, 11Internal Medicine, Hospital La Paz, Madrid, Madrid, Spain, 12Complejo Asistencial Universitario de Salamanca, Salamanca, Spain, 13Hospital Rio Hortega Valladolid, Valladolid, Spain, 14Department of Internal Medicine, Hospital Clínico de Valencia, Valencia, Spain, 15Department of Internal Medicine, Hospital Xeral, Vigo, Vigo, Spain, 16Hospital Mutua de Terrasa, Terrasa, Spain, 17Hospital Virgen de la Salud Toledo, Toledo, Spain, 18Department of Internal Medicine, Hospital Universitario Fundacion Alcorcón, Madrid, Spain, 19Hospital Vega Baja de Orihuela, Alicante, Spain, 20Department of Medicine, Hospital CIMA-Sanitas, Barcelona, Barcelona, Spain, 21Rheumatology Unit, Hospital Privado Universitario de Córdoba, Institute University of Biomedical Sciences University of Córdoba (IUCBC), Cordoba, Argentina, 22Laboratory of Systemic Autoimmune Diseases “Josep Font”, CELLEX, Institut d’Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Department of Systemic Autoimmune Diseases, ICMID, Hospital Clinic, Barcelona, Spain, 23Department of Medicine, University of Barcelona, Barcelona, Spain

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Infection-related Rheumatic Disease
Background/Purpose: Hemophagocytic syndrome or hemophagocytic lymphohistiocytosis (HLH) is an increasingly-recognized condition in adults, characterized by a wide range of etiologies, symptoms and outcomes, but with a common etiopathogenic pathway leading to organ damage: an excessive hyperinflammatory response. We analyzed the role of infections as triggers of adult hemophagocytic syndrome in a National Cohort Registry.

Methods: In June 2013, the Study Group on Autoimmune Diseases (GEAS) of the Spanish Society of Internal Medicine created the national registry of patients with HLH. Patients fulfilled the diagnostic guidelines for HLH proposed by the Histiocyte Society in 1991 and updated in 2004. We investigated infections (viruses, bacteria, parasites and fungi) as causative external factors potentially involved in initiate the disease.

Results: On June 15, 2017, a total of 147 patients with HLH were included in the GEAS-SEMI Registry, 87 (59%) men and 60 (41%) women, with a mean age at diagnosis of HLH of 44; 18% were not born in Spain. The main signs and symptoms at presentation consisted of fever in 132 (90%) patients, splenomegaly in 80 (54%), polyadenopathies in 71 (48%) and hepatomegaly in 22 (15%) patients. The main internal organ involvements included pulmonary in 49 (33%) patients, renal in 46 (31%), gastrointestinal in 41 (28%) and CNS in 32 (22%) patients. The main analytical markers consisted of ferritin > 500 ng/mL in 143 (97%, mean 15498 ng/mL), thrombocytopenia <100,000/mm3 in 123 (84%), anemia < 9 g/dL in 106 (72%), and neutropenia <1000/mm3 in 65 (44%). Tissular hemophagocytosis was confirmed in 133/143 (93%) patients. Death occurred in 79 (54%) patients; a higher mortality rate was found in patients with an underlying neoplasia (33% vs 16% in survivals, p=0.023) and in those with severe anemia (85% vs 60%, p=0.001) and thrombocytopenia (95% vs 72%, p<0.001). Mean age at diagnosis was higher in patients who died in comparison with survivors (56.8 vs 42.1 yrs, p<0.001). An infectious trigger was detected in 88 (60%) of patients, mainly viruses in 37 (25%, Epstein-Barr virus infection in 16 cases), bacteria in 23 (16%, mycobacterium infection in 9 cases), fungi in 14 (10%, candida in 5 cases) and parasites in 9 (6%, leishmaniasis in 8 cases).

Conclusion:
The rate of mortality of adult patients diagnosed with hemophagocytic syndrome exceeds 50% of cases, especially in patients with underlying hematological diseases and in those with advanced age. An infection as trigger of the hyperinflammatory response was demonstrated in 60% of cases, with EBV, mycobacterium and leishmanial being the microorganisms more frequently isolated. Active infections in a patient with suspected HLH should always be treated appropriately.

Disclosure: P. Brito-Zerón, None; A. Flores-Chavez, None; P. Moral Moral, None; A. Martínez-Zapico, None; P. Hernández-Jimenez, None; G. Fraile Rodríguez, None; P. Perez Guerrero, None; E. Fonseca, None; A. Robles, None; M. Vaquero Herrero, None; A. Ruiz de Temiño de la Peña, None; M. J. Forner, None; J. R. Larrañaga, None; M. Rodriguez Carballéa, None; L. Fernando Viejo Llorente, None; M. Ruiz Muñoz, None; R. Hurtado, None; C. Morcillo, None; S. Retamozo, None; M. Ramos-Casals, None.

Usefulness of Polymerase Chain Reaction for Diagnosing Whipple’s Disease in Rheumatology

Marion Herbette1, Jean Baptiste Cren2, Laurie Joffres3, charlotte lucas4, Emilie Ricard5, Carine Salliot6, Jerome Guinard7, Aleth Perdriger8, Elisabeth Solau-Gervais9, Béatrice Bouvard10 and Alain Sarraux11, 1Rheumatology, University Hospital, Brest, France, 2Rheumatology, University Hospital of Angers, Angers, France, 3University Hospital de Poitiers, Poitiers, France, 4Rheumatology, University Hospital, Rennes, France, 5Rheumatology, University Hospital, Orleans, France, 6department of Rheumatology, Orleans, France, 7Microbiology, CHU Angers, Angers, France, 8Service de Rhumatologie, CHRU de Rennes, Rennes, France, 9Rhumatologie, University Hospital, Poitiers, France, 10rheumatology, CHU Angers, Angers, France, 11Rheumatology, Brest University Medical School Hospital, Brest, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Infection-related Rheumatic Disease
Background/Purpose: Whipple's disease should be considered in patients with recurrent episodes of seronegative arthritis in the large limb, various symptoms (fever, uveitis,...) or biological abnormalities (eosinophilia, C-reactive protein elevation, anaemia, thrombocytosis...) but none of these findings is specific. To determine when Tropheryma whippelii polymerase chain reaction (PCR) is appropriate in patients evaluated for rheumatological symptoms.

Methods: In a retrospective observational study done in five hospitals, we assessed the clinical and radiological signs that prompted T. whippelii PCR testing between 2010 and 2014, the proportion of patients diagnosed with Whipple’s disease, the number of tests performed and the number of diagnoses according to the number of tests, the patterns of Whipple’s disease, and the treatments used. Diagnosis of Whipple’s disease was based on 1- at least one suggestive clinical finding; 2- at least one positive PCR test; and 3- a dramatic response to antibiotic therapy. There were divided in: CWD: Classic Whipple’s disease (duodenal biopsy PAS staining + or T. whippelii immunohistochemistry, or as blood positive by PCR); FWD: Focal Whipple’s disease (joint fluid positive by PCR but duodenal biopsy negative by PAS staining and immunohistochemistry); CTWAA: Chronic T. whippelii-associated arthritis (duodenal biopsy, stool, or saliva positive by PCR but duodenal biopsy and joint fluid negative).

Results: At least one PCR test was performed in each of 267 patients. Rheumatic signs were peripheral arthralgia (n=239, 89%), peripheral arthritis (n=173, 65%), and inflammatory back pain (n=85, 32%). The main extra-articular signs were constitutional symptoms (n=111, 41.8%), diarrhoea (n=70, 26.5%), fever (n=53, 20%), lymphadenopathy (n=14, 5.3%), and neurological signs (n=11, 4.2%). Whipple’s disease was diagnosed in 13 patients (4.9%). The main samples tested and the more frequently positive tests in the centres with diagnoses of Whipple’s disease were saliva and stool. In the centres with no diagnoses of Whipple’s disease, arthritis was less common, whereas constitutional symptoms, fever, and lymphadenopathy were more common. 11 patients with Whipple’s disease had CRP elevation. The annual incidence ranged across centres from 0 to 3.6/100000 inhabitants. The group with Whipple’s disease had a higher proportion of males, older age, and greater frequency of arthritis. When both stool and saliva PCR are positive the predictive value is 91%. When both stool and saliva PCR are negative the negative predictive value is 99%.

Conclusion: Males aged 40-75 years with unexplained intermittent seronegative peripheral polyarthritis, including those without constitutional symptoms, should have T. whippelii PCR tests on saliva, stool and, if possible, joint fluid. When both stool and saliva PCR are positive the predictive value is 91%.

Disclosure: M. Herbette, None; J. B. Cren, None; L. Joffres, None; C. Lucas, None; E. Ricard, None; C. Salliot, None; J. Guinard, None; A. Perdriger, None; E. Solau-Gervais, None; B. Bouvard, None; A. Saraux, None.

The Relationship between Serum Urate Concentration and Incident Gout: An Individual Participant Data Analysis

Nicola Dalbeth1, Amanda Phipps-Green2, Christopher Frampton3, Tuhina Neogi4, William J. Taylor5 and Tony R. Merriman6,
1University of Auckland, Auckland, New Zealand, 2University of Otago, Dunedin, New Zealand, 3University of Otago, Christchurch, New Zealand, 4Boston University School of Medicine, Boston, MA, 5University of Otago, Wellington, New Zealand, 6Biochemistry Dept, PO Box 56, University of Otago, Dunedin, New Zealand

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Metabolic and Crystal Arthropathies I: Gout Risk of Disease Activity, Cardiovascular Disease and Mortality
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Elevated serum urate concentration (hyperuricemia) is considered to be a key risk factor for developing gout. However, the relationship between serum urate and incident gout is unclear, with variation in estimates of risk depending on different published studies. We undertook the largest individual participant data analysis to date to examine the relationship between serum urate concentration and incident gout.
**Methods:** Publically available cohort studies with both baseline serum urate and incident gout data were identified through a systematic search of PubMed and the Database of Genotype and Phenotype, and individual participant data were extracted for analysis. Kaplan-Meier plots were generated and the cumulative incidence of gout was calculated according to the baseline serum urate category. We evaluated the relation of serum urate categories (<6mg/dL as referent group) to risk of gout using Cox proportional hazards modelling, adjusted for potential confounders (age, sex, ethnicity, cohort).

**Results:** Four cohorts with publically available data were identified (Atherosclerosis Risk in Communities Study, Coronary Artery Risk Development in Young Adults Study, and the Original and Offspring cohorts of the Framingham Heart Study), with a total of 18,889 participants who were gout-free at baseline, mean (SD) 11.2 (4.2) years of follow-up, and 212,363 total patient-years included in the analysis. The overall cumulative incidence (95% CI) of gout by 5 years was 1.1 (0.9-1.3)%, by 10 years was 2.4 (2.2-2.6)% and by 15 years was 3.2 (2.8-3.6)%. The cumulative incidence at each time point varied according to baseline serum urate concentrations, with 15 year cumulative incidence (95% CI) ranging from 1.1 (0.9-1.4)% for <6mg/dL to 48.6 (30.5-66.6)% for 10mg/dL or more (Figure and Table). Compared with baseline serum urate <6mg/dL, the adjusted hazard ratio (95% CI) for baseline serum urate 6.0-6.9 mg/dL was 2.7 (2.0-3.6), for 7.0-7.9 mg/dL was 6.6 (5.0-8.8), for 8.0-8.9 mg/dL was 14.9 (11.1-20.1), for 8.0-8.9 mg/dL was 29.7 (20.8-42.3), and for 10mg/dL or more was 64.0 (42.5-96.1).

**Conclusion:** Serum urate is a strong concentration-dependent predictor of incident gout. Nonetheless, only about half of those with serum urate concentrations of 10mg/dL or more develop gout over 15 years, implying a role for additional factors in the pathogenesis of gout and a long duration of hyperuricemia preceding the onset of clinical gout. This analysis provides cumulative incidence estimates to guide discussions with hyperuricemic individuals about their risk of developing gout over time.

**Disclosure:** N. Dalbeth, Takeda, AstraZeneca, Abbvie, 9; A. Phipps-Green, None; C. Frampton, None; T. Neogi, None; W. J. Taylor, Pfizer Inc, 5; T. R. Merriman, Ardea Biosciences, 2.


**Abstract Number: 2844**

**Risk of Cardiovascular Events in Older Patients with Gout Initiating Febuxostat Versus Allopurinol: A Population-Based Cohort Study**

MaryAnn Zhang1, Jun Liu2, Eun Ha Kang3, Rishi J. Desai4, Tuhina Neogi5, Daniel H. Solomon1 and Seoyoung C. Kim1, 1Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA, 2Division of Pharmacoepidemiology and Pharmacoeconomics, Brigham and Women's Hospital, Boston, MA, 3Division of Rheumatology, Department of Internal Medicine, Division of Rheumatology, Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, Korea, Republic
SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Metabolic and Crystal Arthropathies I: Gout Risk of Disease Activity, Cardiovascular Disease and Mortality
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Gout, a disorder of uric acid deposition, is commonly treated with xanthine oxidase inhibitors like febuxostat and allopurinol. While it is well-known that patients with gout are at increased risk of cardiovascular (CV) disease, little evidence is available with regard to comparative CV safety of febuxostat and allopurinol in the general older population.

Methods: Using claims data from U.S. Medicare (2008-2013), we conducted a cohort study among gout patients aged ≥65 initiating febuxostat versus allopurinol. All patients were continuously enrolled in Medicare parts A/B/D for ≥1 year free of a given drug prior to the 1st dispensing date (index date). The primary outcome was a composite CV endpoint of myocardial infarction (MI) or stroke. Secondary outcomes comprised MI, stroke, coronary revascularization, and new and recurrent heart failure (HF) requiring hospitalization. Follow-up time began the day after index date to the earliest day of the following: drug discontinuation, insurance disenrollment, occurrence of outcome, death, nursing home admission or last day of the study period. To adjust for ≥55 baseline covariates and index year, we used propensity score (PS) matching with a 1:3 ratio. Cox proportional hazards regression compared the risk of primary and secondary outcomes in the PS-matched cohorts of febuxostat and allopurinol initiators.

Results: We included 24,900 febuxostat initiators PS-matched on 74,700 allopurinol initiators. The median age was 76 years, 52% were male, and 32% had CV disease at baseline. During the mean (SD) follow-up time of 1.1 (1.1) years among febuxostat initiators and 1.2 (1.2) years among allopurinol initiators, the incidence rate (IR) per 100 person-years for the primary endpoint (MI or stroke) was 3.45 (95% CI, 3.24-3.68) in febuxostat and 3.34 (95% CI, 3.23-3.46) in allopurinol initiators. Hazard ratios (HR) for MI or stroke were 1.02 (95% CI, 0.95-1.10) in the febuxostat versus allopurinol groups. The risk of developing secondary outcomes was also similar in both groups (Table). For new-onset HF hospitalization, the IR in the febuxostat group was 5.72 (95% CI, 5.39-6.08) per 100 person-years with a HR of 1.04 (95% CI, 0.97-1.12) compared to allopurinol. Among patients with baseline HF, the IR of first-time HF exacerbation was 42.66 (95% CI, 41.12-44.26) per 100 person-years among febuxostat initiators with a HR of 0.95 (95% CI, 0.91-0.99) versus allopurinol.

Conclusion: Among 99,600 older patients with gout enrolled in Medicare, there was no difference in CV risk (including MI, stroke, coronary revascularization and new/recurrent HF) between patients initiating febuxostat compared to allopurinol.
Table. Risk of overall cardiovascular events and heart failure (HF) in febuxostat initiators versus allopurinol:

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Febuxostat (n=24,900)</th>
<th>Allopurinol (n=74,700)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Event (n)</td>
<td>Person-years</td>
</tr>
<tr>
<td><strong>Primary:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MI or stroke</td>
<td>941</td>
<td>27,261</td>
</tr>
<tr>
<td><strong>Secondary:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MI</td>
<td>601</td>
<td>27,450</td>
</tr>
<tr>
<td>Stroke</td>
<td>372</td>
<td>27,630</td>
</tr>
<tr>
<td>Coronary revascularization</td>
<td>723</td>
<td>27,225</td>
</tr>
<tr>
<td>New-onset HF a</td>
<td>1,057</td>
<td>18,472</td>
</tr>
<tr>
<td>HF exacerbation b</td>
<td>2,848</td>
<td>6,676</td>
</tr>
</tbody>
</table>

PS matched covariates included demographic factors, medical comorbidities, use of gout-related medications, use of cardiovascular drugs, and markers of healthcare utilization intensity (i.e. number of emergency room visits).

* IR is per 100 person-years

a among the subgroup of patients with no baseline history of HF

b among the subgroup of patients with baseline history of HF, with HF as the primary diagnosis

Disclosure: M. Zhang, None; J. Liu, None; E. H. Kang, None; R. J. Desai, None; T. Neogi, None; D. H. Solomon, AstraZeneca, 2; S. C. Kim, Pfizer Inc, 2,Bristol-Myers Squibb, 2,Roche/Genentech, 2,AstraZeneca, 2,Merck Human Health, 2.


Abstract Number: 2845

Association between Serum Urate As a Surrogate Endpoint and Flares in People with Gout: An Ecological Study Based on a Systematic Review of Trials and Open Label Extensions
Background/Purpose: The primary efficacy measure in urate lowering therapy (ULT) trials is usually serum urate (SU). However, it is unknown whether the strength of the association between SU and clinically relevant outcomes is sufficient for SU to be considered a surrogate. The aim of this study was to examine the strength of a possible association between SU and flares, indirectly providing support for SU as an important biomarker in clinical practice.

Methods: A systematic literature review was undertaken to identify all relevant studies. First, randomized controlled trials (RCTs) comparing any ULT in people with gout with any control or placebo, ≥3 months duration were included. The maximum RCT duration of 12 months and studies where the proportion of individuals with SU < 6 mg/dL and the proportion having a flare were assessed in close temporal proximity may obscure any relationship. Therefore, open label extension (OLE) and longitudinal observational studies were included in secondary analyses. Standardized data elements were extracted by two independent reviewers. Association between the variables were analyzed by simple correlation between gout flare rate either as a proportion or converted into events over patient-years (dependent variable[s]), scattered against the proportion achieving SU < 6 mg/dL and the duration of the trial. The CORR procedure (SAS) provided a nonparametric measure of association between the variables; we used Spearman’s rank-order correlation to test the potential association between variables.

Results: Of the 2,775 records, 9 RCTs were identified. 3 OLE studies and 11 observational studies were identified. Using data from the 9 RCTs, of which the maximum trial duration was 12 months, meta-regression analysis did not reveal a statistically significant association between the proportion of individuals with SU < 6 mg/dL and the observed flare rate (P = 0.82). The ratio of the time in months at which the proportion of individuals having a flare was reported/time in months at which the proportion of individuals with SU < 6 mg/dL was reported was calculated and those studies where the ratio was < 2 were excluded. Using the remaining 5 studies (incl. 11 data points) there was a clear association between proportion of individuals achieving SU < 6 mg/dL and the observed gout flares (over patient years; Fig A; Spearman rho = -0.888, P = 0.0003). Duration of ULT was also strongly inversely associated with the proportion of patients experiencing a flare (Fig B; Spearman rho = -0.878, P = 0.0004).

Conclusion: From observational data, SU < 6 mg/dL is strongly associated with reduced gout flares but the duration of the RCTs needed to reveal possible causation, with clinically relevant benefit takes longer than the usual RCT duration. These associations provide some support that SU may be a suitable biomarker for gout clinical trials.

Disclosure: L. K. Stamp, Amgen, 8; M. Morillon, None; W. Taylor, Pfizer NZ, 5; N. Dalbeth, Takeda, AstraZeneca, Abbvie, 9; M. Lassere, None; J. A. Singh, Takeda, Savient, 2, consultant fees from Savient, Takeda, Regeneron, Merz, Iroko, Bioiberica, Crealta and Allergan pharmaceuticals, WebMD, UBM LLC and the American College of Rheumatology, 5. JAS serves as the principal investigator for an investigator-initiated study funded by Horizon pharmaceuticals through a grant to DINORA, Inc., a 501 (c)(3) entity. JAS is a member of the executive of OMERACT, an organization that develops outcome mea, 9; R. Christensen, None.

Abstract Number: 2846

**Cause-Specific Mortality in Gout: Novel Findings of Elevated Risk of Renal-Related and Decreased Risk of Dementia-Related Death**

Ana Beatriz Vargas-Santos¹, Tuhina Neogi², Geraldo Castelar-Pinheiro¹ and Aleksandra Turkiewicz³, ¹Internal Medicine - Rheumatology, State University of Rio de Janeiro, Rio de Janeiro, Brazil, ²Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA, ³Clinical Sciences Lund, Orthopedics, Clinical Epidemiology Unit, Lund University, Lund, Sweden

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Metabolic and Crystal Arthropathies I: Gout Risk of Disease Activity, Cardiovascular Disease and Mortality

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 4:30PM-6:00PM

**Background/Purpose:**

There is recognized higher mortality among gout patients, with cardiovascular (CV) mortality having been previously reported. The present study aimed to examine cause-specific mortality beyond CV diseases in patients with gout compared to general population.

**Methods:**

We used the Swedish Skåne Healthcare Register, which contains data regarding healthcare visits for all residents of the large region, and the Causes of Death Register (high validity), both with diagnoses registered according to International Classification of Diseases, version 10 (ICD-10) system. We identified subjects with incident gout (ICD-10: M10) diagnosed between 2003 and 2013. We matched each person with gout with up to 10 comparators free of gout by age and sex. Subjects were followed from the date of gout diagnosis or a matching index date for the comparators until relocation outside Skåne, death or end of study period (12/31/14). Using information on the underlying cause of death, we estimated hazard ratios (HR) of mortality for specific causes of death in a multi-state Cox model accounting for competing risks, adjusting for potential confounders (Table), and also stratified by sex.

**Results:**

Among a source population of 832,258 subjects, there were 19,497 persons with an incident gout diagnosis who were matched with 194,947 comparators free of gout. Persons with gout had higher prevalence of chronic kidney disease, metabolic and CV comorbidities, but lower prevalence of dementia than comparators. The all-cause mortality rate per 1000 person-years was 63.6 among those with gout and 47.3 among those without gout. The causes of death among those with and without gout, respectively, were: CV diseases, 49.5% and 41.4%; neoplasms, 18.2% and 21.9%; diabetes, 3.4% and 2.2%; infections, 5.7% and 5.8%; kidney diseases, 1.6% and 0.8%; dementia, 3.8% and 8.4%. Gout was associated with an 18% increased risk of all-cause mortality (HR 1.18, 95% CI 1.14-1.21). In terms of cause-specific mortality, the largest association was seen for the relation of gout to risk of death due to renal disease (HR of 1.47) (Table). Gout was associated with lower risk of death due to dementia (HR 0.80), while elevated risk of CV-related mortality in gout was confirmed (HR 1.25). While men had higher mortality overall, in the stratified analyses, the effect of gout on cause-specific CV-, infection-, neoplasm-, and renal-related mortality was modestly higher among women than men, potentially reflecting generally lower baseline risk of mortality in women (Table). Similar results were obtained with the Fine & Gray method.
Conclusion:

A novel finding is the ~50% increased risk of renal-related mortality among gout patients that highlights the need for improved understanding and management of gout and kidney disease. The finding of ~20% lower dementia-related mortality calls for attention to the relation between hyperuricemia and dementia.

Disclosure: A. B. Vargas-Santos, None; T. Neogi, None; G. Castelar-Pinheiro, None; A. Turkiewicz, None.

The Sons of Gout Study. Ultrasonographic Evaluation of Asymptomatic Monosodium Urate Crystal Deposition in Sons of People with Gout

Abhishek Abhishek¹, Wendy Jenkins¹, Philip Courtney², Adrian Jones³, Weiya Zhang⁴ and Michael Doherty⁵, ¹Devision of Rheumatology, University of Nottingham, NG5 1PB, England, ²Department of Rheumatology, Notingham, United Kingdom, ³Rheumatology Unit, Nottingham City Hospital, Nottingham Notts, United Kingdom, ⁴Division of Rheumatology, Orthopaedics and Dermatology, School of Medicine, University of Nottingham, Nottingham, United Kingdom, ⁵Academic Rheumatology, University of Nottingham, Nottingham, Great Britain

First publication: September 18, 2017

SEASON INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Metabolic and Crystal Arthropathies I: Gout Risk of Disease Activity, Cardiovascular Disease and Mortality
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Hyperuricemia and gout aggregate in families. The objectives of this study were to estimate the prevalence of asymptomatic monosodium urate (MSU) crystal deposition in men with a parent with gout, and to describe the sites involved in early crystal deposition.

Methods: People with gout who participated in previous research at Academic Rheumatology, University of Nottingham, UK, were mailed a letter about the study accompanied by a study pack to be posted to their son(s) ≥20 years in age. Sons interested in participating returned a reply slip and underwent telephone screening to exclude gout or inflammatory arthritis. Eligible sons were invited for a study visit at which information about disease and demographic characteristics was obtained, musculoskeletal assessment
performed and venesection undertaken. A trained ultrasonographer (AA) performed ultrasound of 1st meta-tarsophalangeal joints (MTPJs), talar domes, femoral condyles, patella and triceps tendons, wrist triangular cartilage and 2nd meta-carpophalangeal joints (MCPJs) blinded to the SUA level person specific characteristics [1]. The images were scored for double contour sign (DCS), tophus, calcification, hyaline linear bodies and effusion. Doubtful images were scored blindly by a second sonographer with >10 years’ experience (PC). This study was approved by the Nottinghamshire Research Ethics Committee-II. N (%), mean (standard deviation (SD)) were used for descriptive purpose. Chi-square tests were used to compare categorical values.

Results: 1435 parents were invited to post the study packs to their sons if applicable. 249 replies were received, 134 sons agreed to participate, and 130 of these completed assessments to date. Their mean (SD) age, body mass index, and SUA were 43.86 (11.22) years, 27.10 (4.76) kg/m², and 6.42 (1.13) mg/dl respectively. 64.6% sons had SUA >6 mg/dl, and 30% of them had MSU crystal deposition defined as presence of either DCS or tophus. All had MSU deposition at either 1st MTPJ, and one participant had DCS at the ankle. None of the other joints had a tophus or a DCS. The prevalence of MSU deposit was 0%, 18.8%, 35.7%, 38.3% and 34.2% in those with SUA <5, 5-5.66, 5.67-6.33, 6.33-7 and >7 mg/dl respectively. Participants with MSU crystal deposition were more likely to have calcification at patellar tendons (23.1% vs. 7.7%, p=0.01).

Conclusion: Sons of people with gout frequently have asymptomatic MSU deposits. MSU crystal deposits appear at the MTPJs and in the tendons before appearing in other joints such as the ankle or the knee. In this high risk population MSU crystal deposition occurred at SUA <6.3 mg/dl which suggests that pro-nucleating changes in the connective tissue matrix may have a role in crystal deposition.

References:

Disclosure: A. Abhishek, AstraZeneca, 7; W. Jenkins, None; P. Courtney, None; A. Jones, None; W. Zhang, Grunenthal, 9, Husin-pharm, 9; M. Doherty, AstraZeneca, 9, AstraZeneca, Grunenthal, Mallinckrodt and Roche., 9.

Abstract Number: 2848

Improving Gout Outcomes: The Randomized Evaluation of an Ambulatory Care Pharmacist-Led Intervention to Optimize Urate Lowering Pathways (RAMp-Up) Study

Ted R. Mikuls¹, TC Cheetham², Gerald D. Levy³, Nazia Rashid⁴, Kimberly Low⁵, Brian W Coburn⁶, Kenneth Saag⁷, Lang Chen⁸ and Jeffrey R. Curtis⁹, ¹Internal Medicine, Division of Rheumatology, University of Nebraska Medical Center, Omaha, NE, ²Research and Evaluation, Kaiser Permanente Southern California, Pasadena, CA, ³Internal Medicine/Rheumatology, Kaiser Permanente Southern California, Downey, CA, ⁴Pharmacy Analytic Services, Kaiser Permanente Southern California, Downey, CA, ⁵Kaiser Permanente Southern California, Panorama City, CA, ⁶Division of Rheumatology, University of Nebraska Medical Center, Omaha, NE, ⁷Department of Medicine, University of Alabama at Birmingham, Birmingham, AL, ⁸University of Alabama at Birmingham, Birmingham, AL, ⁹Rheumatology & Immunology, University of Alabama at Birmingham, Birmingham, AL

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Metabolic and Crystal Arthropathies I: Gout Risk of Disease Activity, Cardiovascular Disease and Mortality
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Allopurinol is a cornerstone therapy in gout management. Despite this, allopurinol use is suboptimal as providers often fail to follow the treat-to-target paradigm endorsed as a best practice in gout. We conducted a large cluster-randomized study to examine the impact of a pharmacist-driven intervention to optimize allopurinol therapy in gout.

Methods: Medical offices in the Kaiser Permanente Southern California health system were cluster randomized (n = 103 clusters) to deliver either a pharmacist-led intervention or usual care to patients receiving new allopurinol prescriptions. The intervention allowed
the study pharmacist to assume responsibility for most elements of allopurinol prescribing. Patient outreach was conducted primarily via telephone interactive voice recognition (IVR) system to assess adherence, encourage serum urate (sUA) and other gout-related lab monitoring, provide patient-focused gout education, and adjust allopurinol dosing. Primary outcomes were achievement of a sUA <6.0 mg/dl and allopurinol treatment adherence at one year. Patients were considered adherent if the proportion of days covered (PDC), based on allopurinol prescription fills, was ≥ 0.8. Treatment (n=77) and control (n=147) patients without a follow-up sUA were assumed not to have reached sUA goal (i.e. non-responder imputation).

**Results:** Usual care (n=782) and intervention (n=630) patients were similar in age, sex, mean household income, BMI, baseline sUA (mean 8.4 mg/dl in both groups), creatinine, and starting allopurinol dose (mean 188 mg/day in both groups). Intervention patients were more often Caucasian (45% vs. 38%) and less often reported Asian race (20% vs. 26%) than those receiving usual care (p=0.01). The proportion achieving sUA goal, 1-year adherence, ending allopurinol dose, and changes in sUA are shown in the Table. The intervention met all primary outcomes and showed significant improvements compared to usual care. With a mean of 2.4 (±2.4) IVR/pharmacist contacts, intervention patients were approximately 3-times more likely than usual care patients to receive allopurinol dose escalation (32% vs. 12%, p<0.001).

**Conclusion:** A relatively simple intervention leveraging ambulatory pharmacists and automated telephone technology led to improved treatment adherence and achievement of sUA goal in gout patients initiating allopurinol. However, almost 7 of 10 intervention patients failed to achieve a sUA < 6.0 mg/dl. Thus, while this light-touch, low-tech intervention was effective for some patients, additional efforts will be needed to optimize allopurinol administration in gout care.

**Table:** Study outcomes

<table>
<thead>
<tr>
<th></th>
<th>Control (n=782)</th>
<th>Treatment (n=630)</th>
<th>P-value</th>
<th>Adjusted OR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>sUA &lt; 6.0 mg/d</td>
<td>20.6%</td>
<td>31.3%</td>
<td>&lt;0.001</td>
<td>1.75 (1.37, 2.24)</td>
</tr>
<tr>
<td>PDC ≥ 0.8 at 1 year</td>
<td>35.4%</td>
<td>47.6%</td>
<td>&lt;0.001</td>
<td>1.69 (1.30, 2.19)</td>
</tr>
<tr>
<td>Change in sUA, mg/d</td>
<td>-1.35 (1.86)</td>
<td>-1.67 (1.84)</td>
<td>&lt;0.001</td>
<td>N/A</td>
</tr>
<tr>
<td>PDC at 1 year</td>
<td>0.59 (0.29)</td>
<td>0.66 (0.29)</td>
<td>&lt;0.001</td>
<td>N/A</td>
</tr>
<tr>
<td>Ending allopurinol dose, mg/d</td>
<td>203 (103)</td>
<td>235 (104)</td>
<td>&lt;0.001</td>
<td>N/A</td>
</tr>
</tbody>
</table>

OR = odds ratio; CI = confidence interval; *Multivariable logistic regression; adjusted for race and calendar year

**Disclosure:** T. R. Mikuls, BMS, 2,Ironwood Pharm, 2,Pfizer Inc, 5,NIH, VA, 2; T. Cheetham, None; G. D. Levy, None; N. Rashid, None; K. Low, None; B. W. Coburn, None; K. Saag, Ironwood/AstraZeneca, 5,Horizon, 2,Takeda, 2,Ironwood/AstraZeneca, 5,Horizon, 5,Takeda, 5; L. Chen, None; J. R. Curtis, None.


**Abstract Number:** 2849

**Pain and Functional Trajectories in Symptomatic Knee Osteoarthritis over a 12-Week Period of Non-Pharmacological Exercise Interventions**

Augustine Lee1, William F. Harvey2, Xingyi Han1, Lori Lyn Price3,4, Jeffrey B. Driban1, Raveendhara R. Bannuru1 and Chenchen Wang2,1Rheumatology, Tufts Medical Center, Boston, MA, 2Rheumatology, Center of Integrative Medicine and Division of Rheumatology, Tufts Medical Center, Boston, MA, 3Institute for Clinical Research and Health Policy Studies, Tufts Medical Center, Boston, MA, 4Tufts Clinical and Translational Science Institute, Tufts University, Boston, MA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017
**Session Title:** Orthopedics, Low Back Pain and Rehabilitation
**Session Type:** ACR Concurrent Abstract Session
**Session Time:** 4:30PM-6:00PM
**Background/Purpose:** Exercise is the recommended treatment for knee osteoarthritis (OA). However, heterogeneous patterns in treatment response are poorly understood. Our purpose was to identify pain and functional trajectories from exercise interventions among adults with symptomatic knee OA, and to determine their association with baseline factors.

**Methods:** Secondary analysis of a single-blind, randomized trial comparing 12-week Tai Chi and Physical Therapy exercise programs among adults with symptomatic knee OA (ACR Criteria). We used weekly measures of WOMAC pain (0-500) and function (0-1700) to identify trajectories using group-based trajectory models. Associations between baseline factors and trajectories were examined using multinomial logistic regression.

**Results:** We examined 171 participants (mean age 61 years, BMI 32kg/m$^2$, 71% female, 57% white), and identified four pain trajectories: Lower-Early Improvement (43.3%), Moderate-Early Improvement (32.2%), Higher-Delayed Improvement (15.2%), and Higher-No Improvement (9.4%) (Figure). We found similar trajectories for function, except that the lower function trajectories diverged into gradual (11.7%) or delayed improvement (14.6%). Compared with the Lower-Early Improvement pain trajectory, moderate and higher pain trajectories were significantly associated with younger age, obesity, black race, and poorer physical health (Table). Importantly, psychological morbidities, such as greater depressive symptoms were significantly associated with Higher-Delayed (Odds Ratio [OR]: 1.06; 95% CI, 1.004-1.12) and Higher-No Improvement pain trajectories (OR: 1.07; 95% CI, 1.01-1.13) compared with the Lower-Early Improvement group. A similar pattern of significant associations were found among the functional trajectories (data not shown).

**Conclusion:** Using innovative analytical techniques, we found four distinct trajectories for pain and function over 12-week exercise interventions among adults with symptomatic knee OA. While most participants experienced early improvements, subgroups with greater baseline pain/physical disability had either gradual, delayed, or no improvements. Notably, psychological morbidities tended to distinguish non-responders or delayed-responders from early responders. These findings help disentangle the heterogeneity of treatment response and may advance patient-centered care for these patients.

![Figure A. Pain Trajectories](image1.png)

![Figure B. Function Trajectories](image2.png)

**Figure A. Pain Trajectories**

**Figure B. Function Trajectories**

**Figure. Pain and Functional Trajectories from Exercise Interventions:** WOMAC= Western Ontario and McMaster Universities Osteoarthritis Index. **Panel A:** Pain Trajectories. WOMAC Pain subscale range: 0-500, higher scores = greater pain. **Panel B:** Function Trajectories. WOMAC Function subscale range: 0-1700, higher scores = poorer physical function.
Table. Associations Between Pain Trajectories and Baseline Participant Factors

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Lower Pain, Early Improvement n= 74</th>
<th>Moderate Pain, Early Improvement n= 55</th>
<th>Higher Pain, Delayed Improvement n= 26</th>
<th>Higher Pain, No Improvement n= 16</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds Ratio (95% CI)</td>
<td>Odds Ratio (95% CI)</td>
<td>Odds Ratio (95% CI)</td>
<td>Odds Ratio (95% CI)</td>
</tr>
<tr>
<td>Age, years</td>
<td>Reference</td>
<td>0.98 (0.94, 1.01)</td>
<td>0.95 (0.90, 0.99)</td>
<td>0.95 (0.90, 1.00)</td>
</tr>
<tr>
<td>Female Sex</td>
<td>Reference</td>
<td>1.10 (0.51, 2.36)</td>
<td>1.50 (0.53, 4.24)</td>
<td>1.35 (0.39, 4.65)</td>
</tr>
<tr>
<td>Black (vs. White and Others)</td>
<td>Reference</td>
<td>2.48 (1.09, 5.61)</td>
<td>4.02 (1.52, 10.68)</td>
<td>7.82 (2.41, 25.35)</td>
</tr>
<tr>
<td>Body Mass Index, kg/m², &gt;30 (vs. ≤ 30)</td>
<td>Reference</td>
<td>2.78 (1.33, 5.78)</td>
<td>3.93 (1.41, 10.98)</td>
<td>1.24 (0.42, 3.67)</td>
</tr>
<tr>
<td>Duration of knee pain, years</td>
<td>Reference</td>
<td>0.97 (0.93, 1.01)</td>
<td>1.01 (0.98, 1.05)</td>
<td>0.91 (0.81, 1.03)</td>
</tr>
<tr>
<td>Highest Level of Education</td>
<td>Reference</td>
<td>0.62 (0.23, 1.66)</td>
<td>1.06 (0.26, 4.26)</td>
<td>0.23 (0.07, 0.79)</td>
</tr>
<tr>
<td>Some College or more (vs. High school Graduate or Less)</td>
<td>Reference</td>
<td>1.67 (0.83, 3.39)</td>
<td>1.78 (0.72, 4.44)</td>
<td>1.43 (0.48, 4.25)</td>
</tr>
<tr>
<td>Intervention assignment</td>
<td>Reference</td>
<td>1.67 (0.83, 3.39)</td>
<td>1.78 (0.72, 4.44)</td>
<td>1.43 (0.48, 4.25)</td>
</tr>
<tr>
<td>Physical Health</td>
<td>Reference</td>
<td>1.49 (1.28, 1.73)</td>
<td>2.06 (1.65, 2.57)</td>
<td>2.18 (1.69, 2.82)</td>
</tr>
<tr>
<td>WOMAC Physical Function, (Range: 0-1700)</td>
<td>Reference</td>
<td>1.41 (1.17, 1.70)</td>
<td>2.33 (1.71, 3.19)</td>
<td>1.71 (1.27, 2.31)</td>
</tr>
<tr>
<td>Patient Global Assessment, (Range: 0.0-10.0cm)</td>
<td>Reference</td>
<td>2.16 (1.06, 4.39)</td>
<td>18.61 (4.09, 84.75)</td>
<td>4.66 (1.37, 15.83)</td>
</tr>
<tr>
<td>SF-36 Physical Component Summary, &lt;40 points (vs. ≥40 points) (Range: 0-100)</td>
<td>Reference</td>
<td>0.97 (0.66, 1.41)</td>
<td>2.52 (1.45, 4.39)</td>
<td>2.33 (1.22, 4.45)</td>
</tr>
<tr>
<td>PROMIS Sleep Disturbance Short Form, v.8a (Range; T-score: 28.9-76.5)</td>
<td>Reference</td>
<td>0.81 (0.66, 0.99)</td>
<td>0.63 (0.49, 0.82)</td>
<td>0.62 (0.46, 0.84)</td>
</tr>
<tr>
<td>SF-36 Energy and Vitality, (Range: 0-100)#</td>
<td>Reference</td>
<td>1.70 (0.83, 3.5)</td>
<td>1.74 (0.67, 4.53)</td>
<td>3.35 (0.99, 11.39)</td>
</tr>
<tr>
<td>CHAMPS Physical Activity, mod-high calories/week# &lt;1123.3 (vs. ≥1123.3)</td>
<td>Reference</td>
<td>0.76 (0.61, 0.95)</td>
<td>0.63 (0.46, 0.84)</td>
<td>0.64 (0.45, 0.89)</td>
</tr>
<tr>
<td>6-Minute Walk Test, meters, (Normal Range: 400-700)#</td>
<td>Reference</td>
<td>2.19 (0.89, 5.38)</td>
<td>4.27 (1.51, 12.09)</td>
<td>2.13 (0.57, 7.93)</td>
</tr>
<tr>
<td>Leg Extensor Muscle Strength **, newtons #, 1RM</td>
<td>Reference</td>
<td>0.92 (0.84, 1.01)</td>
<td>0.91 (0.80, 1.04)</td>
<td>0.89 (0.76, 1.04)</td>
</tr>
<tr>
<td>Muscle Contraction Velocity ** meters/second (40% of 1RM)#</td>
<td>Reference</td>
<td>0.96 (0.78, 1.18)</td>
<td>0.69 (0.51, 0.92)</td>
<td>0.70 (0.50, 0.98)</td>
</tr>
<tr>
<td>Berg Balance, ≤50 points (vs. &gt;50 points) (Range: 0-56)</td>
<td>Reference</td>
<td>2.19 (0.89, 5.38)</td>
<td>4.27 (1.51, 12.09)</td>
<td>2.13 (0.57, 7.93)</td>
</tr>
<tr>
<td>Psychosocial Health</td>
<td>Reference</td>
<td>0.98 (0.94, 1.02)</td>
<td>0.95 (0.90, 0.99)</td>
<td>0.95 (0.90, 1.01)</td>
</tr>
<tr>
<td>Measure</td>
<td>Reference</td>
<td>0.88 (0.70, 1.11)</td>
<td>0.77 (0.58, 1.01)</td>
<td>0.71 (0.52, 0.97)</td>
</tr>
<tr>
<td>----------------------------------------------</td>
<td>-----------</td>
<td>-------------------</td>
<td>-------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>SF-36 Mental Health; (Range: 0-100)</td>
<td>Reference</td>
<td>1.03 (0.98, 1.08)</td>
<td>1.06 (1.004, 1.12)</td>
<td>1.07 (1.01, 1.13)</td>
</tr>
<tr>
<td>Beck-II Depression, (Range: 0-63)</td>
<td>Reference</td>
<td>0.99 (0.94, 1.05)</td>
<td>1.06 (0.99, 1.13)</td>
<td>1.12 (1.03, 1.22)</td>
</tr>
<tr>
<td>Perceived Stress; (Range: 0-40)</td>
<td>Reference</td>
<td>1.00 (0.99, 1.02)</td>
<td>0.99 (0.98, 1.01)</td>
<td>1.01 (0.98, 1.04)</td>
</tr>
<tr>
<td>MOS Social Support; (Range: 19-95)</td>
<td>Reference</td>
<td><strong>0.80 (0.67, 0.96)</strong></td>
<td><strong>0.66 (0.52, 0.84)</strong></td>
<td><strong>0.53 (0.39, 0.72)</strong></td>
</tr>
<tr>
<td>Arthritis Self-Efficacy Scale-8 (Range: 0-10)</td>
<td>Reference</td>
<td>0.93 (0.49, 1.73)</td>
<td>0.85 (0.38, 1.89)</td>
<td>0.79 (0.30, 2.06)</td>
</tr>
<tr>
<td>Outcome Expectations; (Range: 1.0-5.0)</td>
<td>Reference</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1RM= one-repetition maximum; CHAMPS= Community Healthy Activities Model Program for Seniors; CI= Confidence Interval; MOS= Medical Outcomes Survey; PROMIS= Patient-Reported Outcomes Measurement Information Systems; SF-36= Short Form-36; WOMAC= Western Ontario and McMasters Osteoarthritis Index. *Normal range reported for the general population. **For muscle strength, and velocity, total n= 165 to 168: 86 to 88 for Tai Chi and 78 to 80 for Physical Therapy. #Higher score indicates greater health. Note: Odds ratios >1.00 favor the first category in dichotomized comparisons.

Disclosure: A. Lee, None; W. F. Harvey, None; X. Han, None; L. L. Price, None; J. B. Driban, None; R. R. Bannuru, None; C. Wang, None.


Abstract Number: 2850

**Jakinibs Decrease Chronic Low Back Pain and Increase Function: A Proof of Concept Trial**

Maria Greenwald¹ and JoAnn Ball², ¹Desert Medical Advances, Palm Desert, CA, ²rheumatology, Desert Medical Advances, Palm Deseret, CA

First publication: September 18, 2017

**SESSION INFORMATION**
Session Date: Tuesday, November 7, 2017
Session Title: Orthopedics, Low Back Pain and Rehabilitation
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM
**Background/Purpose:** Low back pain (LBP) is ubiquitous and estimated to affect 26% of Americans in any 3 month period. Why would rheumatoid arthritis patients be any different? We noted improvement in chronic LBP among patients using JAK inhibitors (JAKinibs) in a prospective program.

**Methods:** Sequential RA patients over age 40 were first educated, to explain that RA is not a typical cause chronic LBP. Patients with over 3 months of chronic LBP with or without radiculopathy, then signed informed consent and completed questionnaires. At baseline, patients scored > 6 on the LBP intensity score (out of 11 maximum score), a disability score of 12 (max score 24), and a response of fair, poor, or very poor in the Leikert patient’s global assessment (PGA). These responses were specific to the back. Often LBP had been present for a decade proceeding RA. Excluded for thirty days prior and during the study were narcotics, corticosteroids, gabapentin, pregabalin, anti-depressants, acetaminophen, and muscle relaxants. All patients had moderate to severe RA where JAKinibs were appropriate treatment. Patients answered questionnaires specific to LBP every 2 weeks for a 12 week period. They were randomized by birth year. This phase 1 study was single blind. All assessments of LBP were by the patient (blinded to therapy). This was a phase 1 exploratory trial for improvement in LBP with JAKinibs.

**Results:** 74 patients enrolled; 37 each to JAKinhib and placebo for 12 weeks. There were 74% women, average age 59.6 years, BMI 27.4, Caucasian 58%, Hispanic 41% and Asian 1%. Despite no differences at baseline, chronic LBP in the JAKinib group improved compared to placebo. The pain score decreased 2.1 (31%), p< 0.01; the disability score improved 3.9 (21%), p< 0.01; the PGA improved 0.8 (19%), p< 0.01; and stiffness in the back improved 0.7 (16%), p< 0.02. Originally, patients reported 4.5 lost work hours due to chronic LBP, out of a 40 hour week. The JAKinib group reported no loss in work hours after 12 weeks. The improvements began at 2 weeks and were sustained during the 12 week observation period.

**Conclusion:** This is a proof of concept trial evaluating JAKinibs for the treatment of LBP. In the past decade, many trials have attempted to find LBP therapy among anti-inflammatory and anti-cytokine therapies, including a study with etanercept as an epidural injection therapy. None have been found effective. In recent large RA trials where JAKinibs are being evaluated for the treatment of RA, adverse events of LBP were less frequent in the JAKinibs groups than the placebo. Given that LBP is ubiquitous and RA patients are susceptible to mechanical LBP, we prospectively tracked in randomized patients, pain, disability, PGA, stiffness and work loss. In each category, the JAKinhib group improved compared to placebo in LBP. Perhaps this immunotherapy JAKinib, can provide mild to moderate benefit in the treatment of chronic LBP.

**JAKinibs net improvement effect on chronic LBP (compared to placebo)**

<table>
<thead>
<tr>
<th>Pain</th>
<th>Stiffness of Back</th>
<th>Disability</th>
<th>PGA</th>
<th>Work</th>
</tr>
</thead>
<tbody>
<tr>
<td>-2.1</td>
<td>-0.7</td>
<td>3.9</td>
<td>0.8</td>
<td>-4.5</td>
</tr>
</tbody>
</table>

- All results were statistically significant (p<0.01 for pain, disability, PGA and p<0.02 for stiffness).
- Results record improvements in the JAKinhib group compared to the placebo group.
- The WOMAC recorded pain and stiffness, the Roland-Morris questionnaire recorded disability (24-point scale), and the patient global assessment (PGA) was a 5-point Likert scale. Pain and stiffness improvement is recorded as a negative.
- Both improvement in disability and PGA is recorded as positive in these scales.
- 37 patients were randomized to JAKinhib, and 37 were randomized to placebo for 12 weeks.

**Disclosure:** M. Greenwald, None; J. Ball, None.


**Abstract Number:** 2851

**General and Abdominal Obesity As Risk Factors for Late-Life Mobility Limitation Among Women with Total Knee or Hip Replacement for Osteoarthritis**

Aladdin Shadyab¹, Wenjun Li², Charles Eaton³ and Andrea LaCroix⁴, ¹Family Medicine and Public Health, University of California, San Diego, La Jolla, CA, ²Medicine, University of Massachusetts Medical School, Worcester, MA, ³Family Medicine and Epidemiology, Warren Alpert Medical School, School of Public Health, Brown University, Providence, RI, ⁴Family Medicine and Public Health, University of California, San Diego School of Medicine, La Jolla, CA

**First publication:** September 18, 2017
Background/Purpose: The population is rapidly aging, and by 2060, more than 12 million women will be ages 85 years and older in the United States. As millions of women with total knee (TKR) and total hip (THR) replacements for osteoarthritis (OA) reach old age, it is important to understand which modifiable factors predict disability-free survival after surgery. Although indicators of adiposity, such as high body mass index (BMI), waist circumference (WC), and waist-hip ratio (WHR) are associated with increased risk of OA and utilization of total joint replacement (TJR), their associations with late-life mobility after TJR are unknown. The purpose of this study was to examine associations of BMI, WC, and WHR with mobility limitation at age 85 among women with TKR or THR for OA.

Methods: This was a prospective study of women (aged 65-79 years at baseline) from the Women’s Health Initiative (WHI) recruited during 1993-1998 and followed through 2012. WHI data were linked to Medicare claims data to determine TKR (n=1,867) and THR (n=944) for OA. Women were followed for up to 18 years after undergoing TJR to determine mobility status at age 85. Women who reported that their health limited their ability to walk one block or climb one flight of stairs were classified as having mobility limitation. BMI was defined as normal-weight (≤24.9 kg/m²), overweight (25-29.9), obese I (30-34.9), or obese II (≥35.0). WC and WHR were defined according to cutpoints for abdominal obesity. Multinomial logistic regression models were used to evaluate associations of adiposity measures with mobility limitation at age 85 and death before age 85 (reference category=mobility intact at age 85).

Results: Among women with THR, 45.7% had mobility limitation at age 85, 34.8% had intact mobility at age 85, and 19.6% died before age 85. Among women with TKR, 47.9% had mobility limitation at age 85, 30.4% had intact mobility at age 85, and 21.8% died before age 85. Compared with normal-weight women with THR, overweight (odds ratio [OR]=1.53; 95% confidence interval [CI]=1.04-2.25), obese I (OR=2.40; 95% CI=1.49-3.85), and obese II (OR=4.37; 95% CI=1.96-9.74) women had increased risk of late-life mobility limitation. Obese II women also had increased risk of death before age 85 (OR=6.08; 95% CI=2.39-15.49). Women with THR and WC >88 cm relative to ≤88 cm had increased risk of mobility limitation (OR=1.65; 95% CI=1.17-2.33). WHR was not associated with survival outcomes among women with THR. Among women with TKR, associations of BMI and WC with survival outcomes varied by age at TKR and were strongest in the youngest age group (67-74 years at TKR; OR for mobility limitation=3.24; 95% CI=1.40-7.50 for obese II vs. normal-weight). In the oldest age group (80-82 years at TKR), obesity was associated with increased risk of mobility limitation at age 85 (OR=1.78; 95% CI=1.03-3.06) and death (OR=3.78; 95% CI=1.23-11.67), and WC >88 cm was associated with risk of mobility limitation (OR=1.61; 95% CI=1.07-2.43) but not death.

Conclusion: Among women with THR or TKR for OA, general and abdominal obesity were associated with increased risk of late-life mobility limitation and death. These findings support maintenance of healthy body weight among women with THR or TKR to lessen mobility loss in late life.

Disclosure: A. Shadyab, None; W. Li, None; C. Eaton, None; A. LaCroix, None.


Abstract Number: 2852

Widespread Pain Prior to Total Knee Replacement (TKR) Is Associated with Increased Risk of No Clinical Improvement in Pain Among Women

Ernest Vina1, Di Ran2, Erin L. Ashbeck2 and C. Kent Kwoh3, 1Rheumatology, University of Arizona, Tucson, AZ, 2The University of Arizona Arthritis Center, Tucson, AZ, 3University of Arizona, Tucson, AZ

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Orthopedics, Low Back Pain and Rehabilitation
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM
Background/Purpose:

Up to 47% of individuals may not have clinically significant improvement following joint replacement surgery. Evidence also suggests that women are less likely to benefit from TKR surgery than men, but the reasons are unclear. The objective of this study is to evaluate the association between pre-operative widespread pain (WP) and failure to experience clinical improvement 2 years following TKR separately for men and women.

Methods:

Osteoarthritis Initiative participants who underwent TKR surgery prior to the 7-year follow-up visit were included in the analysis. WP was defined based on a modified ACR definition of chronic WP and was assessed with a questionnaire which included a homunculus figure. Pain and disability were assessed at the clinic visit prior to TKR as well as 2 years later, using WOMAC pain, WOMAC disability, and Knee Injury and Osteoarthritis Outcome (KOOS) pain scores. Medication use for osteoarthritis (OA)-related symptoms was also determined. Clinically significant improvement was defined as improvement in WOMAC subscale (or KOOS pain) score ≥ to the minimal important difference (based on previously published literature). Relative risk (RR) of no clinical improvement was estimated using log-binomial regression, comparing participants with and without WP, stratified by gender.

Results:

Our sample consists of 120 with and 178 without WP who underwent TKR surgery. Those with WP, compared to those without, were more likely to be women (70.0% vs. 56.2%), with <$50K/year income (48.2% vs. 37.1%), and obese (55.3% vs. 46.8%). Two years after their pre-operative pain assessment, ~12% of men and ~15% of women reported no clinical improvement in knee pain. OA-related medication use after surgery was also more common in women with WP than those without (69.2% vs. 50.0%, p=0.0311).

Among women, WP prior to surgery was significantly associated with an increased risk of no clinically significant improvement following TKR based on WOMAC pain (RR 2.35, 95% CI [1.06-5.20], p=0.0351) and results were suggestive, though not significant, for KOOS pain (RR 1.93, 95% CI [0.97-3.85], p=0.0626). After adjustment for sociodemographic and clinical characteristics, the magnitudes of association were stronger (WOMAC pain, RR 3.50, 95% CI [1.05-11.65], p=0.0409; KOOS pain, RR 2.49, 95% CI [1.00-6.18], p=0.0490). No association among men was observed between pre-TKR WP and failure to improve in WOMAC or KOOS pain score following surgery (Table 1). No strong evidence for an association between WP and failure to improve in WOMAC disability was seen for either gender.

Conclusion:

WP prior to TKR was significantly associated with increased risk of no clinical improvement in knee OA pain 2 years later among women. However, no evidence of an association between WP and TKR outcome was found among men, though the prevalence of WP pain among men was also limited. WP assessment may help identify patients at risk of failure to benefit from TKR surgery.

Table 1. Widespread Pain Prior to TKR and Risk of No Clinically Significant Improvement Two Years Later, Stratified by Gender

<table>
<thead>
<tr>
<th>Widespread Pain</th>
<th>No Improvement</th>
<th>Unadjusted Model</th>
<th>Adjusted Model*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No/Tot Eval (%)</td>
<td>RR (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>WOMAC pain</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>575 (21.8)</td>
<td>1.00 Ref</td>
<td>1.00 Ref</td>
</tr>
<tr>
<td>W</td>
<td>1675 (68.6)</td>
<td>0.71 (0.41-1.24)</td>
<td>0.291</td>
</tr>
<tr>
<td>WOMAC disability</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>575 (21.8)</td>
<td>1.00 Ref</td>
<td>1.00 Ref</td>
</tr>
<tr>
<td>W</td>
<td>1675 (68.6)</td>
<td>0.87 (0.52-1.45)</td>
<td>0.577</td>
</tr>
</tbody>
</table>

*Adjusted for age, gender, race, education, income, marital status, employment, body mass index, depression, WOMAC disability score, knee pain medication use, and baseline score

RR: relative risk; CI: confidence interval

KOOS: Knee Injury and Osteoarthritis Outcome Score

Disclosure: E. Vina, NIH/NIAMS, 2; D. Ran, None; E. L. Ashbeck, None; C. K. Kwoh, NIH/NIAMS, 2, EMD Serono, 2, Abbvie, 2.


Abstract Number: 2853
Is Frailty Associated with Adverse Events after Total Joint Arthroplasty?

Lisa A. Mandl¹,², Abigail M. Schmucker³, Nathaniel Hupert⁴, Mayu Sasaki³, Charles N. Cornell⁵,⁶, Michael B. Cross⁵,⁶, Alejandro Gonzalez Della Valle⁵,⁶, Mark P. Figgie⁶,⁷, Seth A. Jerabek⁵,⁶, Jackie Szymonifka¹ and Steven K. Magid⁸,⁹, ¹Rheumatology, Hospital for Special Surgery, New York, NY, ²Medicine - Rheumatology, Weill Cornell Medicine, New York, NY, ³Quality Research Center, Hospital for Special Surgery, New York, NY, ⁴Medicine, Healthcare Policy and Research, Weill Cornell Medicine, New York, NY, ⁵Surgery, Hospital for Special Surgery, New York, NY, ⁶Surgery, Weill Cornell Medicine, New York, NY, ⁷Orthopaedics, Hospital for Special Surgery, New York, NY, ⁸Medicine - Rheumatology, Hospital for Special Surgery, New York, NY, ⁹Medicine, Weill Cornell Medicine, New York, NY

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Orthopedics, Low Back Pain and Rehabilitation
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: The increased volume of TJA due to the aging population requires a better understanding of the effect of physiological frailty, in addition to chronological age, on TJA-associated complications. If frailty is associated with poor outcomes, it is potentially modifiable.

Methods: Community-dwelling patients ≥65yo scheduled for elective total knee (TKA) or hip (THA) arthroplasty were recruited from a musculoskeletal specialty hospital. All patients were medically approved for surgery. Pre-operative frailty was defined as at least 3/7 frailty characteristics based on the Fried frailty phenotype and a composite frailty score previously validated in surgical populations (Table 1). Pre-operatively subjects completed the PROMIS-29, SF-12, Depression Screening (CES-D 10), Lubben Social Network Scale (LSNS-18), Katz Index of Independence in Activities of Daily Living (ADL), and Hip/Knee Injury and Osteoarthritis Outcome Score (HOOS/KOOS). Grip strength was measured and normalized by age and gender. Adverse events were obtained from medical records and by phone 30 days post-discharge. Stepwise multivariable logistic regressions were performed to ascertain if frailty, or any of its components, were independent risk factors for short-term adverse events (AEs).

Results: 464 subjects enrolled (mean age 73 (range 65-94), 95% white, 61% female, 60% TKA, 40% THA). 8% were frail (9% THA, 8% TKA). 17% had difficulty with at least 1 Katz ADL (14% THA, 19%TKA).

Among patients who reached 30-day follow-up, 180/373 (48%) had 263 AEs and 35/373 (9%) had 51 severe AEs. There were no significant differences in AEs or severe AEs between frail and non-frail patients. Controlling for gender, age, and which joint was replaced, independent predictors of having ≥1 AEs included pre-operative anemia (OR=3.14; 95% CI 1.08-9.15) and PROMIS-29 Anxiety (OR=1.05; 95% CI 1.02-1.08). Having a hip rather than knee replaced decreased the risk of severe AEs (OR=0.39; 95% CI 0.17-0.88).

For THA patients, older age was associated with increased risk of AEs (OR=1.07; 95% CI 1.01-1.13), while better SF-12 PCS was protective (OR=0.94; 95% CI 0.90-0.98).

For TKA patients, a higher PROMIS Anxiety score was associated with an increased risk of AEs (OR=1.04; 95% CI 1.003-1.08). Having ≥1 Katz ADL dependency was associated with an increased risk of severe AEs (OR=2.51; 95% CI 1.03-6.11).

Our composite measure of frailty did not predict AEs in any model.

Conclusion: A substantial proportion of medically-cleared TJA patients at this high-volume center were frail. Having ADL dependency was associated with a 2.5x increased risk of severe AEs among TKA. Whether frailty is associated with long-term AEs, pain, or function needs to be established in longitudinal trials.
Table 1: Frailty Characteristics

<table>
<thead>
<tr>
<th>Individual Frailty Characteristics, %</th>
<th>Total Hip Replacement (N=277)</th>
<th>Total Knee Replacement (N=187)</th>
<th>All (N=464)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unintentional weight loss of ≥ 10lbs in last year</td>
<td>2.7</td>
<td>2.6</td>
<td>2.6</td>
</tr>
<tr>
<td>≥1 Dependency on the Katz ADL</td>
<td>13.5</td>
<td>18.5</td>
<td>16.5</td>
</tr>
<tr>
<td>Weakness (grip strength &gt;1 SD below mean for age/gender norm)</td>
<td>33.2</td>
<td>39.4</td>
<td>36.9</td>
</tr>
<tr>
<td>Anemia (pre-operative hematocrit &lt;35%)</td>
<td>6.1</td>
<td>5.8</td>
<td>6.0</td>
</tr>
<tr>
<td>Poor nutrition (pre-operative albumin &lt;3.4 g/dL)*</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>≥1 falls in past 6 months</td>
<td>16.6</td>
<td>14.2</td>
<td>15.2</td>
</tr>
<tr>
<td>Exhaustion (answered “moderate” or “most” for CES-D 10 questions about effort and getting going)</td>
<td>29.5</td>
<td>20.4</td>
<td>24.0</td>
</tr>
<tr>
<td>Frailty: &gt;3 characteristics, %</td>
<td>8.6</td>
<td>8.1</td>
<td>8.3</td>
</tr>
</tbody>
</table>

* 277/464 (115 THA, 162 TKA) patients had albumin levels recorded.

Disclosure: L. A. Mandl, None; A. M. Schmucker, None; N. Hupert, None; M. Sasaki, None; C. N. Cornell, Exactech, 5,HSS Journal, 6; M. B. Cross, Acelity, 5,Acelity Surgical Advisory Board, 5,Bone and Joint Journal 360, 6,Exactech, Inc, 5,Intellijoint, 5,Intellijoint, 1,Journal of Orthopaedics and Traumatology, 6,Link Orthopaedics, 5,Smith & Nephew, 5,Techniques in Orthopaedics, 6,Theravance Biopharma, 5,Zimmer, 5; A. Gonzalez Della Valle, None; M. P. Figgie, Lima, 7,Mekanika, 1; S. A. Jerabek, Stryker, 5; J. Szymonifka, None; S. K. Magid, None.

Abstract Number: 2854

**Optimizing Data Capture for Performance – Metrics Using Smartphone App Technology**

James Willig¹, Jeffrey R. Curtis², Andrew Westfall³, Donald Lein⁴, Christian Ray Smith⁴, Jonathan Cortis⁵, Clayton Rice⁵ and Christopher Hunt⁶, ¹Med - Infectious Diseases, University of Alabama at Birmingham, Birmingham, AL, ²Rheumatology & Immunology, University of Alabama at Birmingham, Birmingham, AL, ³Department of Biostatistics, School of Public Health, University of Alabama at Birmingham, Birmingham, AL, ⁴University of Alabama at Birmingham, Birmingham, AL, ⁵CTS, Inc, Birmingham, AL

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** Orthopedics, Low Back Pain and Rehabilitation  
**Session Type:** ACR Concurrent Abstract Session  
**Session Time:** 4:30PM-6:00PM

**Background/Purpose:** Gait speed has been associated with many clinical outcomes (e.g. frailty, mortality, joint replacement need, etc.) relevant for rheumatologic conditions. Measuring Gait speed (stride length x step count/time) typically requires significant clinician/staff time or a gait lab with specialized equipment. Our formative work was to measure “step count” via smartphones as a first step in making gait speed measurement available for patient home follow-up.

**Methods:** We developed and tested a mobile App-based method to count steps, comparing a hardware (pedometer) vs. software (“Shake algorithm”) approach. Shake algorithm software allows for adjustment of amplitude (how big a shake equates a step) and refresh rate (how often the software counts a shake/step). We conducted calibration and validation phases. In both, subjects carried iOS devices to walk in a walkway while the App was recording step count. The App was then compared to a hardware pedometer. We used a variety of walking surfaces and distances to test the feasibility of the hardware vs. software counting methods. We used the CES-D 10 questions to assess exhaustion and a gait speed test to assess clinical outcomes.

**Results:** There was agreement between the hardware and software methods (Pearson R=0.90, p<0.001). The hardware method was more expensive and labor intensive than the software method. Our results will be used to create a research grade smartphone app for use in a future clinical trial.
and Android phones (one in each front pants pocket) simultaneously, and electronic gait timers measured the time it took to cover pre-measured distances.

Calibration phase: Subjects walked a 20m course at normal and slow (<1.0 m/s) speeds for 9 different shake algorithm settings (x3 walks for each). We determined which setting most closely matched investigator observed step counts. Validation phase: we used the selected shake algorithm settings for the smartphones and recruited subjects to each complete walks (x3) of 6, 10 and 20m at both slow and normal (>1.0m/s) speeds.

We compared step difference (absolute difference) from observed step counts to hardware (pedometers) and software (shake algorithm) derived step counts. We used generalized estimated equation adjusted (participant level) negative binomial regression models of absolute step difference from observed step counts, to determine optimal settings (calibration) and subsequently to gauge performance of the shake algorithm settings and pedometers across different distances and speeds (validation).

**Results:** Calibration: 270 observations across 5 individuals were used to determine optimal smartphone shake algorithm settings for slow and fast walking speeds. Validation: Compared to observed step count, the shake service outperformed pedometer across all distances at slow, and at 6m for normal speed on iOS. On the Android phone, the shake service outperformed the pedometer at slow speed for 6 and 20m, and at 20m for normal speed (Table).

**Conclusion:** Software based approaches such as the shake algorithm, which can have parameters adjusted for optimized measurement of step can be adjusted to outperform fixed hardware such as pedometers. These results will facilitate bringing the capture of performance based metrics such as gait speed to patient home follow-up, using technology users already own (smartphones) to optimize data capture for research and clinical care across rheumatologic conditions.

<table>
<thead>
<tr>
<th>OS</th>
<th>Slow Speed (n=153)</th>
<th>P-value</th>
<th>Normal Speed (n=156)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Shake</td>
<td>Pedometer</td>
<td>Shake</td>
<td>Pedometer</td>
</tr>
<tr>
<td>iOS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6m</td>
<td>2.16±1.97</td>
<td>8.15±4.48</td>
<td>&lt;0.001</td>
<td>1.93±1.60</td>
</tr>
<tr>
<td>10m</td>
<td>2.85±2.77</td>
<td>5.38±4.84</td>
<td>&lt;0.001</td>
<td>2.48±2.19</td>
</tr>
<tr>
<td>20m</td>
<td>5.22±5.22</td>
<td>7.41±7.89</td>
<td>0.029</td>
<td>4.32±3.87</td>
</tr>
<tr>
<td>Android</td>
<td>Slow Speed (n=153)</td>
<td>P-value</td>
<td>Normal Speed (n=156)</td>
<td>P-value</td>
</tr>
<tr>
<td></td>
<td>Shake</td>
<td>Pedometer</td>
<td>Shake</td>
<td>Pedometer</td>
</tr>
<tr>
<td>6m</td>
<td>2.15±1.92</td>
<td>2.92±2.88</td>
<td>0.006</td>
<td>1.79±1.61</td>
</tr>
<tr>
<td>10m</td>
<td>2.52±2.50</td>
<td>2.89±3.49</td>
<td>0.374</td>
<td>2.03±2.28</td>
</tr>
<tr>
<td>20m</td>
<td>4.34±4.57</td>
<td>3.01±3.78</td>
<td>0.033</td>
<td>3.47±4.41</td>
</tr>
</tbody>
</table>
Abstract Number: 2855

Subcutaneous Abatacept in Patients Aged 2–17 Years with Polyarticular Juvenile Idiopathic Arthritis and Inadequate Response to Biologic or Non-Biologic Disease-Modifying Antirheumatic Drugs: Pharmacokinetics, Effectiveness, Safety and Immunogenicity over 2 Years

Hermine I. Brunner¹, N Ruperto², G Vega-Cornejo³, A Berman⁴, Inmaculada Calvo⁵, R Cuttica⁶, F Ávila-Zapata⁷, Michael Henrickson¹, DJ Kingsbury⁸, D Viola⁹, V Keltsey¹⁰, K Minden¹¹, John F. Bohnsack¹², X Li¹³, M Nys¹⁴, R Wong¹³, S Banerjee¹³, Daniel J Lovell¹ and Alberto Martini¹⁵, ¹Cincinnati Children’s Hosp. Medical Center, Cincinnati, OH, ²Istituto G. Gaslini Pediatria II Reumatologia, Genoa, Italy, ³Clinica de Reumatología y Enfermedades Autoinmunes (CREA), Hospital México Americano, Guadalajara Jalisco, Mexico, ⁴Universidad Nacional de Tucuman and Centro Médico Privado de Reumatología, Tucuman, Argentina, ⁵Hospital Univ. La Fe, Valencia, Spain, ⁶Hospital General de Niños Pedro de Elizalde, Buenos Aires, Argentina, ⁷Star Medica Hospital, Yucatán, Mexico, ⁸Randall Children’s Hospital at Legacy Emanuel, Portland, OR, ⁹CAICI Institute, Rosario City, Santa Fe State, Argentina, ¹⁰GBUZ Samara region "Togliatti City Clinical Hospital No.5" Rheumatology Department, Togliatti, Russian Federation, ¹¹German Rheumatism Research Center and Charité University Medicine, Berlin, Germany, ¹²University of Utah School of Medicine, Salt Lake City, UT, ¹³Bristol-Myers Squibb, Princeton, NJ, ¹⁴Bristol-Myers Squibb, Braine-l’Alleud, Belgium, ¹⁵Istituto G. Gaslini Pediatria II Reumatologia and University of Genova, Genoa, Italy

First publication: September 18, 2017
Table 1. Demographics, Disease Characteristics and Concomitant Medication at Baseline and Study Drug Exposure

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients aged 2–5 years (n=46)</th>
<th>Patients aged 6–17 years (n=173)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years</strong></td>
<td>4.0 (3.0, 5.0)</td>
<td>13.0 (10.0, 15.0)</td>
</tr>
<tr>
<td><strong>Female, n (%)</strong></td>
<td>28 (60.9)</td>
<td>136 (78.6)</td>
</tr>
<tr>
<td><strong>Weight, kg</strong></td>
<td>18.0 (15.0, 21.1)</td>
<td>45.0 (31.5, 57.0)</td>
</tr>
<tr>
<td><strong>Number of active joints</strong></td>
<td>7.0 (6.0, 12.0)</td>
<td>10.0 (6.0, 19.0)</td>
</tr>
<tr>
<td><strong>JIA disease onset, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polyarthritis RF-negative</td>
<td>29 (63.0) 3 (6.5) 10 (21.7) 0 4 (8.7) 0 0</td>
<td>94 (54.3) 46 (26.6) 19 (11.0) 5 (2.9) 0 4 (2.3) 5 (2.9)*</td>
</tr>
<tr>
<td>Polyarthritis RF-positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extended oligoarthritis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systemic arthritis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enthesitis-related arthritis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Oral corticosteroid use, n (%)</strong></td>
<td>9 (19.6)</td>
<td>56 (32.4)</td>
</tr>
<tr>
<td><strong>Oral corticosteroid dose, mg/day†</strong></td>
<td>3.1 (2.5, 6.3)†</td>
<td>5.0 (3.4, 5.6)§</td>
</tr>
<tr>
<td><strong>Concomitant MTX use, n (%)</strong></td>
<td>37 (80.4)</td>
<td>136 (78.6)</td>
</tr>
<tr>
<td><strong>MTX dose, mg/m²/week</strong></td>
<td>13.3 (10.9, 15.3)</td>
<td>11.6 (9.7, 14.4)</td>
</tr>
<tr>
<td><strong>Route of MTX administration, n (%)</strong></td>
<td>18 (39.1) 19 (41.3) 0 0</td>
<td>76 (43.9) 51 (29.5) 8 (4.6) 1 (0.6)</td>
</tr>
<tr>
<td><strong>Prior biologic use, n (%)‡</strong></td>
<td>10 (21.7)</td>
<td>46 (26.6)</td>
</tr>
<tr>
<td><strong>Abatacept exposure, months, mean (SD)</strong></td>
<td>18.8 (7.3)</td>
<td>21.8 (6.9)</td>
</tr>
</tbody>
</table>

Values represent median (25th percentile, 75th percentile), unless otherwise specified *Protocol deviation: persistent oligoarthritis (n=4), undifferentiated (n=1) †Prednisone equivalent ‡n=8 §n=52 ‡Including etanercept, adalimumab, tocilizumab JIA=juvenile idiopathic arthritis
### Table 2. Summary of AEs Over 2 Years (All Treated Patients)

<table>
<thead>
<tr>
<th>Event</th>
<th>Patients aged 2–5 years (n=46)</th>
<th>Patients aged 6–17 years (n=173)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Deaths</strong></td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>SAEs*</td>
<td>3 (6.5)</td>
<td>14 (8.1)</td>
</tr>
<tr>
<td>Related SAEs†</td>
<td>1 (2.2)</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Discontinued due to SAEs‡</td>
<td>0</td>
<td>4 (2.3)</td>
</tr>
<tr>
<td><strong>AEs</strong></td>
<td>43 (93.5)</td>
<td>152 (87.9)</td>
</tr>
<tr>
<td>Related AEs</td>
<td>27 (58.7)</td>
<td>54 (31.2)</td>
</tr>
<tr>
<td>Discontinued due to AEs</td>
<td>1 (2.2)</td>
<td>7 (4.0)</td>
</tr>
<tr>
<td><strong>AEs of special interest§</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malignancies¶</td>
<td>0</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Autoimmune disorders**</td>
<td>0</td>
<td>3 (1.7)</td>
</tr>
<tr>
<td>Local injection-site reactions</td>
<td>2 (4.3)</td>
<td>12 (6.9)</td>
</tr>
<tr>
<td><strong>Infections</strong></td>
<td>36 (78.3)</td>
<td>118 (68.2)</td>
</tr>
</tbody>
</table>

Data are n (%)

*2–5-year cohort: overdose, tendon disorder, febrile convulsion (each n=1, 2.2%); 6–17-year cohort: sepsis, abdominal pain, and upper respiratory tract infection (occurred in one patient), appendicitis, pneumonia, pyelonephritis, concussion, radius fracture, urinary calculus, nephrolithiasis, anemia, vertigo, chest pain, synovitis, hypomagnesemia and ovarian germ cell teratoma stage III (occurred in one patient), autonomic nervous system imbalance  †2–5-year cohort: overdose; 6–17-year cohort: sepsis ‡6–17-year cohort: sepsis, vertigo, ovarian germ cell teratoma stage III, autonomic nervous system imbalance §No opportunistic infections related to study drug occurred during the study in either cohort ††6–17-year cohort: ovarian germ cell teratoma stage III **6–17-year cohort: pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS), psoriasis, Takayasu’s arteritis SAE=serious adverse event

**Disclosure:** H. I. Brunner, Novartis, Genentech, Pfizer, UCB, Lilly, Janssen, Ablynx, AbbVie, BMS, EMD Serono, AstraZeneca, 5; N. Ruperto, The G. Gaslini Hospital, BMS, Hoffman-La Roche, Janssen, Novartis, Pfizer, Sobi, 2,AbbVie, Ablynx, Amgen, AstraZeneca, Baxalta Biosimilars, Biogenidec, Boehringer, Bristol Myers Squibb, Celgene, Eli-Lilly, EMD Serono, Hoffman-La Roche, Janssen, Novartis, Pfizer., R-Pharm, Sanofi, Servier, Sinergie, Takeda, 8,AbbVie, Ablynx, Amgen, AstraZeneca, Baxalta Biosimilars, Biogenidec, Boehringer, Bristol Myers Squibb, Celgene, Eli-Lilly, EMD Serono, Hoffman-La Roche, Janssen, Novartis, Pfizer., R-Pharm, Sanofi, Servier, Sinergie, Takeda, 5; G. Vega-Cornejo, None; A. Berman, None; I. Calvo, Novartis Pharmaceutical Corporation, 2,AbbVie, Roche, Novartis, Sobi, 8; R. Cuitica, None; F. Ávila-Zapata, None; M. Henrickson, None; D. Kingsbury,
Evaluation of a Dosing Regimen for Tocilizumab in Patients Younger Than Two Years of Age with Systemic Juvenile Idiopathic Arthritis

Navita L. Mallalieu 1, Joy Hsu 1, Karen Wang 1, Sunethra Wimalasundera 2, Wendy Douglass 2, Chris Wells 2, Inmaculada Calvo 3, Rubén Cuttica 4, Hans-Iko Huppertz 5, Rik Joos 6, Yukiko Kimura 7, Diana Milojevic 8, Margalit Rosenkrantz 9, Kenneth Schikler 10, Tamas Constantin 11 and Carine Wouters 12, 1 Roche Innovation Center, New York, NY, 2 Roche Products, Ltd., Welwyn Garden City, United Kingdom, 3 Hospital Universitario y Politécnico La Fe, Valencia, Spain, 4 Hospital Gral de Niños Pedro Elizalde, Buenos Aires, Argentina, 5 Professor Hess Children's Hospital, Bremen, Germany, 6 ZNA, Antwerp, and UZ, Gent, Belgium, 7 Hackensack University Medical Center, Hackensack, NJ, 8 Tufts Medical Center, Boston, MA, 9 Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA, 10 University of Louisville Medical School, Louisville, KY, 11 Semmelweis University, Budapest, Hungary, 12 University Hospital Gasthuisberg, Leuven, Belgium

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects II: Juvenile Arthritis
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Tocilizumab (TCZ) is approved for the treatment of systemic juvenile idiopathic arthritis (sJIA) based on clinical trials in patients ≥2 years of age. This phase 1 study (NP25737), the first of a biologic in patients with sJIA <2 years of age, evaluated the pharmacokinetics (PK), pharmacodynamics (PD), efficacy, and safety of TCZ.

Methods: Patients with uncontrolled sJIA and symptoms for ≥1 month prescreening whose treatment with corticosteroids and NSAIDs failed and who had no history of allergy to TCZ or other biologics received open-label TCZ 12 mg/kg intravenously every 2 weeks (dose calculated each visit based on body weight). Patients were treated up to Week 12 and could continue until they reached 2 years of age or were treated for 1 year from baseline. End points included PK (primary), safety (secondary), PD, and efficacy (exploratory) at Week 12. Comparison was made with data from a previous trial in sJIA patients ≥2 years of age (WA18221) that formed the basis for approval of TCZ in sJIA.

Results: Eleven patients were enrolled; mean (SD) age was 1.3 (0.33) years, and weight was 9.97 (1.38) kg. Serum TCZ concentrations, estimated using population PK analysis, peaked immediately after infusion; median (range) maximum concentration was 282 (195-347) mcg/mL (steady state reached by Week 12), and median (range) trough concentration was 34.3 (19.2-59.7) mcg/mL. Peak and trough exposures were within the exposure range in older children (244 [109-382] to 54.3 [10.9-117] mcg/mL) (Figure). Observed mean±SD soluble IL-6 receptor levels increased from 47.65±16.40 ng/mL at baseline to 1461.14±852.71 ng/mL at Day 85. CRP and ESR levels, which were elevated at baseline, decreased to 3.35±3.77 mg/L and 3.50±0.84 mm/h, respectively. Mean±SD Juvenile Arthritis Disease Activity Score-71 improved from 22.27±10.09 at baseline to 4.90±6.11 at Day 85. By Week 12, 10 patients had 32 adverse events (AEs); 4 withdrew due to AEs. Infections or infestations were the most frequently reported AEs (10 events, 9 patients). Five serious AEs (SAEs) occurred in 3 patients; all had SAEs of hypersensitivity that led to treatment withdrawal, and 1 of these 3 patients then experienced SAEs of foot and mouth disease and sJIA flare after study withdrawal. No deaths occurred during the study.

Conclusion: TCZ exposures achieved in this study fell within the exposure range of the previous trial in sJIA patients ≥2 years of age. This study provides evidence that TCZ is effective in sJIA patients <2 years of age and achieves PK and efficacy similar to those demonstrated previously in older patients. The safety profile was similar to that observed in patients ≥2 years of age in types of AEs observed, with the exception of a higher incidence of serious hypersensitivity events.
Disclosure: N. L. Mallalieu, Roche, 3; J. Hsu, Roche, 3; K. Wang, Roche, 3; S. Wimalasundera, Roche, 3; W. Douglass, Roche, 1, Roche, 3; C. Wells, Roche, 3; L. Calvo, None; R. Cuttica, Roche, Novartis, Lilly, GSK, BMS, Janssen, 5; Roche, Novartis, Lilly, GSK, BMS, Janssen, 8; H. I. Huppertz, Novartis Pharmaceutical Corporation, 5; R. Joos, None; Y. Kimura, Novartis, SOBI, 5; D. Milojevic, Abbvie, 5; M. Rosenkranz, None; K. Schikler, None; T. Constantin, None; C. Wouters, Roche, Pfizer, GSK, 5.


Abstract Number: 2857

**Short and Long-Term Follow-up of Tocilizumab for Severe Juvenile Idiopathic Arthritis-Associated Uveitis**

**Nuria Vegas-Revenga**1, Vanesa Calvo-Río1, Montserrat Santos-Gómez2, Inmaculada Calvo3, Mª Isabel González- Fernández3, Berta López- Montesinos3, Marina Mesquida4, Alfredo Adan4, M. Victoria Hernández4, Olga Maiz5, Antonio Atanes6, Beatriz Bravo7, Consuelo Modesto8, Gisela Díaz-Cordovés9, Natalia Palmou-Fontana1, Javier Loricera1, MC Gonzalez-Vela10, Rosalia Demetrio11, Carlos Fernández-Díaz1, Lucia C. Dominguez-Casas1, José Luis Martín-Varillas1, Belén Atienza-Mateo1, Jose L. Hernández12, Miguel Angel González-Gay1 and Ricardo Blanco1, 1Rheumatology, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, 2Rheumatology, Hospital de Sierrallana. Torrelavega. Spain, Torrelavega, Spain, 3Rheumatology, Hospital Universitario i Politecnico La Fe. Valencia. Spain, Valencia, Spain, 4Hospital Clinic. Barcelona. Spain, Barcelona, Spain, 5Hospital Donostia. Spain, San Sebastian, Spain, 6Rheumatology, Complejo Hospitalario Universitario A Coruña (CHUAC). Spain, A Coruna, Spain, 7Rheumatology, HU Virgen de las Nieves. Granada. Spain, Granada, Spain, 8Hospital Universitari Vall d'Hebron. Barcelona. Spain, Barcenola, Spain, 9Rheumatology, Hospital Regional Universitario de Málaga. Spain, Málaga, Spain, 10Pathology Anatomy, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, 11Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain, 12Internal Medicine, Hospital Universitario Marqués de Valdecilla. IDIVAL. Santander. Universidad de Cantabria. Spain, Santander, Spain

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Tuesday, November 7, 2017

Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects II: Juvenile Arthritis

Session Type: ACR Concurrent Abstract Session
**Session Time:** 4:30PM-6:00PM

**Background/Purpose:** Our objective was to assess the efficacy of tocilizumab (TCZ) at short and long term follow-up for severe juvenile idiopathic arthritis-associated uveitis.

**Methods:** A Multicentre study of 25 patients who had inadequate response or intolerance to traditional treatment with corticosteroids and at least one conventional immunosuppressive drug including biological therapy. The outcome variables were the degree of inflammation of the anterior chamber and vitreous, visual acuity and macular thickness. The results are expressed as mean ±SD for normally distributed variables, or as median [IQR] when are not. Comparison of continuous variables was performed using the Wilcoxon test.

**Results:** We studied 25 patients (21 women/ 4 men); mean age; 18.6±8.3. Uveitis was bilateral in 22. JIA subsets were oligoarthritis (n=17), polyarthritis (5), psoriatic (2) and enthesitis-related arthritis (1). Ocular sequelae found at initiation of TCZ included cataracts (13), glaucoma (7), synechiae (10), band keratopathy (12), maculopathy (9), and amblyopia (5). Pattern of uveitis was: anterior (17), panuveitis (4), intermediate (2) and posterior (2). Before TCZ, patients had received corticosteroids, conventional immunosuppressive drugs (Methotrexate (MTX) 24) and biologic agents, including adalimumab (24), etanercept (8), infliximab (7), abatacept (6), rituximab (2), anakinra (1), and golimumab (1). TCZ dosage regimen was 8 mg/kg IV every 4 weeks (21), every 2 weeks (2), every 8 weeks (1), or 2.9 mg/kg subcutaneously every week (1). It was used in combination with conventional immunosuppressive drugs in 22 patients. All of the outcome variables showed rapid and maintained improvement in all ocular parameters (TABLE) after a follow up of one year (n=21), 2 years (n=11), and 3 years (n=5). A reduction in the daily median dose of prednisone from 10 mg [0-15 mg] to 0 mg [0-0 mg] in 3 years, (p<0.05) was observed. After a median follow-up of 20.5±11.7 months in 4 patients, the interval between TCZ doses was increased to 5 weeks (n=2), 6 weeks (1) and 7 weeks (1) because of sustained clinical remission. TCZ had to be withdrawn due to articular inefficiency (1) or articular and ocular inefficiency (1). The main adverse effects were severe autoimmune thrombocytopenia, autoimmune anemia and thrombocytopenia, pneumonia, viral conjunctivitis and bullous impetigo in 1 patient each.

**Conclusion:**

TCZ is useful at short and long term follow-up for severe Juvenile Idiopathic Arthritis-associated uveitis. It is possible to optimize the TCZ dose.

**TABLE.**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>1st week</th>
<th>2nd week</th>
<th>1st month</th>
<th>3rd month</th>
<th>6th month</th>
<th>1st year</th>
<th>2nd year</th>
<th>3rd year</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Visual acuity mean ± SD</strong></td>
<td>0.57±0.35</td>
<td>0.55±0.35</td>
<td>0.56±0.35</td>
<td>0.59±0.33</td>
<td>0.6±0.32*</td>
<td>0.63±0.32*</td>
<td>0.63±0.35*</td>
<td>0.59±0.32*</td>
<td>0.45±0.34*</td>
</tr>
<tr>
<td><strong>Anterior chamber cells [median (IQR)]</strong></td>
<td>1 [0-1]</td>
<td>0.75 [0-1]*</td>
<td>0.5 [0-1]*</td>
<td>0 [0-0.5]*</td>
<td>0 [0-0]*</td>
<td>0 [0-0]*</td>
<td>0 [0-0]*</td>
<td>0 [0-0]*</td>
<td>0 [0-0]*</td>
</tr>
<tr>
<td><strong>Vitritis [median (IQR)]</strong></td>
<td>0 [0-0]</td>
<td>0 [0-1]</td>
<td>0 [0-0]</td>
<td>0 [0-0]</td>
<td>0 [0-0]*</td>
<td>0 [0-0]*</td>
<td>0 [0-0]*</td>
<td>0 [0-0]*</td>
<td>0 [0-0]</td>
</tr>
<tr>
<td><strong>OCT (microns) mean ± SD</strong></td>
<td>358.69±92.17</td>
<td>351.4±108.29</td>
<td>336.5±100.9*</td>
<td>313.4±91.28*</td>
<td>280.7±35.03*</td>
<td>274.9±101.33*</td>
<td>245.4±29.4*</td>
<td>239.6±33.5</td>
<td>ND</td>
</tr>
</tbody>
</table>

*p <0.05 compared with basal data

**Disclosure:** N. Vegas-Revenga, None; V. Calvo-Río, None; M. Santos-Gómez, None; I. Calvo, Novartis Pharmaceutical Corporation, 2,AbbVie, Roche, Novartis, Sobi, 8; M. I. González- Fernández, None; B. López- Montesinos, None; M. Mesquida, None; A. Adan, AbbVie, Santen and Allergan, 9; M. V. Hernández, None; O. Maiz, None; A. Atanes, None; B. Bravo, None; C. Modesto, None; G. Díaz-Cordovés, None; N. Palmou-Fontana, None; J. Loriceria, None; M. Gonzalez-Vela, None; R. Demetrio, None; C. Fernández- Diaz, None; L. C. Domínguez-Casas, None; J. L. Martín-Varillas, None; B. Atienza-Mateo, None; J. L. Hernández, None; M. A. González-Gay, None; R. Blanco, None.

Validation of Biomarkers to Predict Flare in Polyarticular JIA upon Stopping Anti-TNF Therapy

Daniel J Lovell¹, Sarah Ringold² and P. Scott Eastman³, ¹PRCSG, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH, ²Seattle Children's Hospital, Seattle, WA, ³Senior Director, New Product Development, Crescendo Bioscience, South San Francisco, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects II: Juvenile Arthritis
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: More than 40% of children with polyarticular forms of Juvenile Idiopathic Arthritis (JIA) experience clinical inactive disease on medication (CR). No clinical variable or biomarker has been identified to predict which patients in CR can effectively stop anti-TNF biologic therapy.

Methods: In a 16 center, prospective protocol driven clinical trial, 106 JIA pts. (polyarticular RF+/RF- and extended oligoarticular) in CR while on anti-TNF treatment stopped anti-TNF therapy (all other meds remained stable) and were followed prospectively for up to 10 mos. Flare was determined by prespecified criteria. Serum drawn at the time of stopping anti-TNF therapy were analyzed for 12 individual biomarkers included in the multi-biomarker disease activity score (MBDA; Vectra DA) using multiplexed immunoassay methods previously described ¹,²: vascular cell adhesion molecule-1 [VCAM-1], epidermal growth factor [EGF], vascular endothelial growth factor A [VEGF-A], interleukin-6 [IL-6], tumor necrosis factor receptor 1 [TNF-R1], matrix metalloproteinase-1 [MMP-1], matrix metalloproteinase-3 [MMP-3], human cartilage glycoprotein-39 [YKL-40], leptin, resistin, serum amyloid A [SAA], and CRP (1,2). The Vectra DA score (range 1 to 100) was calculated with a validated algorithm. Six additional biomarkers were also assayed: interleukin-8 [IL-8], interleukin-1B [IL-1B], macrophage-derived chemokine [MDC], interleukin-6 receptor [IL-6R], intercellular adhesion molecule 1 [ICAM-1] with a custom multiplex assay (MSD, Bethesda, MD). S100A12 levels were determined as previously described ³,⁴. Univariate analysis with students t-test for significance and multivariate discriminant analysis was used to calculate relationship of clinical and biomarker variables with risk for flare.

Results:

39/106 (37%) of the pts. flared, mean/median/SEM for time to flare was 212/250/9.8 days. Univariate analysis of correlations with flare/no flare status shown in Table 1. Multivariate discriminant analysis identified a model that includes 7 variables (MMP-3, JIA duration, JIA Dx age, VCAM-1, CR duration, VEGF, and resistin) with an AUC 0.80, correct prediction in 79% of cases, sensitivity 79%, specificity 79%, PPV 91%, NPV 79%.

Table 1.

<table>
<thead>
<tr>
<th>Metric</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ln MMP-3</td>
<td>0.014</td>
</tr>
<tr>
<td>Ln Disease Duration</td>
<td>0.016</td>
</tr>
<tr>
<td>Age Diagnosis</td>
<td>0.037</td>
</tr>
<tr>
<td>VCAM-1</td>
<td>0.063</td>
</tr>
<tr>
<td>ID duration at baseline (yrs)</td>
<td>0.069</td>
</tr>
<tr>
<td>VEGF-A</td>
<td>0.21</td>
</tr>
<tr>
<td>Resistin</td>
<td>0.38</td>
</tr>
<tr>
<td>MBDA</td>
<td>0.97</td>
</tr>
<tr>
<td>IL-6</td>
<td>1.00</td>
</tr>
<tr>
<td>Ln S100A12</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Conclusion:

37% of the pts. flared ≤ 10 mos of stopping anti-TNF. The MBDA did not discriminate significantly flare/no flare. A combination of clinical and lab biomarkers predicted not flaring accurately in 79% of cases.
References.


Disclosure: D. J. Lovell, AbbVie Inc., AstraZeneca, Centocor, Bristol-Myers Squibb, Pfizer, Regeneron, Hoffman La-Roche, Novartis, UBC, Xoma, and Genentech, 5,Wyeth Pharmaceuticals, 8,Amgen and Forest Research, 9; S. Ringold, Crescendo Bioscience, 2; P. S. Eastman, Crescendo Bioscience, 3.


Abstract Number: 2859

Development of New Juvenile Arthritis Disease Activity Score Cut-Offs for Oligoarthritis and RF-Negative Polyarthritis from a Large Multinational Cohort of Children with Juvenile Idiopathic Arthritis

Alessandro Consolaro1,2, Pieter Van Dijkhuizen1, Graciela Espada3, Boriana Varbanova4, Sheila Oliveira5, Paivi Miettunen4, Gaëlle Chédeville5, Michaël Hofer5, Pavla Dolezalová5, Ivan Foeldvari5, Gerd Horneff5, Anne Estmann5, Chris Pruunsild5, Rosa Merino5, Inmaculada Calvo Penades5, Pablo Mesa del Castillo5, Pekka Lahdenne5, Maka Ioseliani5, Maria Trachana5, Olga Vougiouka5, Miroslav Harjacek5, Ilonka Orban5, Tamás Constantín5, Nahid Shafaie5, Violeta Vladislava Panaviene5, Marite Rygg5, Elzbieta Smolewska5, Jose Antonio Melo Gomes5, Jelena Vojinovic5, Ekaterina Alexeeva5, Tadej Avcin5, Veronika Vargova5, Nuray Akty Ayaz5, Ozgur Kasapcopur5, Yaryna Boyko5, Sarah Ringold5, Mariangela Rinaldi5, Marco Garrone5, Nicolino Ruperto7 and Angelo Ravelli5, 1Pediatria II, Reumatologia, Istituto Giannina Gaslini, Genoa, Italy, 2University of Genoa, GENOA, Italy, 3Istituto Giannina Gaslini - Pediatria II, Reumatologia - PRINTO, Genova, Italy, 4Istituto Giannina Gaslini - Pediatria II, Reumatologia - PRINTO, Genoa, Italy, 5Istituto Giannina Gaslini - Pediatria II, Reumatologia - PRINTO, Gernoa, Italy, 6Istituto Giannina Gaslini - Pediatria II, Reumatologia - PRINTO, Genoa, Italy, 7Istituto Giannina Gaslini, Genoa, Italy, 8University of Genova, IRCCS Istituto Giannina Gaslini, Genova, Italy, 9University of Genova, Genova, Italy

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects II: Juvenile Arthritis
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose:

The measurement of the level of disease activity plays a pivotal role in the care of patients with juvenile idiopathic arthritis (JIA). To serve this purpose, the Juvenile Arthritis Disease Activity Score (JADAS) was developed in 2009. More recently, a version excluding the acute phase reactant was tested (cJADAS). Cutoff values for the state of remission, low disease activity (LDA), moderate disease activity (MDA) and high disease activity (HDA) were recently developed for the original JADAS score and for the clinical version. These cutoff values are ideally suited for pursuing tight disease control in a treat-to-target strategy, with treatment escalation if the desired JADAS score is not reached. However, although cutoffs were validated in a large and multinational cohort of patients, they were developed in a dataset of patients from a single pediatric rheumatology center an partly before the advent of the so-called biologic era. Aim of the study is to develop the JADAS and cJADAS cut-off values of remission, LDA, MDA, and HDA for oligoarthritis and RF-negative polyarthritis in a large multinational cohort of JIA patients

Methods: The EPidemiology, treatment and Outcome of Childhood Arthritis (EPOCA) study is aimed to obtain information on the frequency of JIA subtypes in different geographic areas, the therapeutic approaches adopted by pediatric rheumatologists practicing in diverse countries or continents, and the disease and health status of children with JIA currently followed worldwide. More than 9.000 patients with JIA from 118 pediatric rheumatology centres in 49 countries were collected so far. For the development of cut-offs,
patients with oligoarthritis and polyarthritis followed in the 20 Centres with the highest frequency of these 2 subtypes were retained. In each centre, the 75th centile of JADAS and cJADAS distribution in patients who were subjectively rated by the attending physician as being in remission and LDA, and the 25th centile of JADAS and cJADAS in patients rated as in HDA, were calculated. The obtained values at each centre were then averaged to obtain the preliminary cut-offs for each disease activity state.

Results: The cutoffs validation cohorts were made of 930 patients with oligoarthritis from 20 pediatric rheumatology Centres and 1,004 patients with RF-neg polyarthritis from 20 pediatric rheumatology Centres. Preliminary cut off values for each versions of JADAS and cJADAS are presented in table.

<table>
<thead>
<tr>
<th>Oligoarthritis</th>
<th>JADAS10</th>
<th>JADAS27</th>
<th>JADAS71</th>
<th>cJADAS10</th>
<th>cJADAS27</th>
<th>cJADAS71</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remission</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.2</td>
<td>1.2</td>
<td>1.2</td>
</tr>
<tr>
<td>LDA</td>
<td>3.9</td>
<td>3.7</td>
<td>3.9</td>
<td>3.4</td>
<td>3.3</td>
<td>3.4</td>
</tr>
<tr>
<td>HDA</td>
<td>16.4</td>
<td>16.2</td>
<td>16.4</td>
<td>14.3</td>
<td>14.1</td>
<td>14.3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Polyarthritis</th>
<th>JADAS10</th>
<th>JADAS27</th>
<th>JADAS71</th>
<th>cJADAS10</th>
<th>cJADAS27</th>
<th>cJADAS71</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remission</td>
<td>2.6</td>
<td>2.6</td>
<td>2.6</td>
<td>2.4</td>
<td>2.3</td>
<td>2.4</td>
</tr>
<tr>
<td>LDA</td>
<td>5.1</td>
<td>4.9</td>
<td>5.1</td>
<td>5.1</td>
<td>4.9</td>
<td>5.1</td>
</tr>
<tr>
<td>HDA</td>
<td>18.9</td>
<td>18.9</td>
<td>22.7</td>
<td>19.0</td>
<td>20.0</td>
<td>25.3</td>
</tr>
</tbody>
</table>

Conclusion: New JADAS and cJADAS temptative cut-offs for remission, LDA, and HDA were calculated. Obtained values will be tested in the validation analysis. The preliminary values are higher than currently available cut-offs.

Disclosure: A. Consolaro, None; P. Van Dijkhuizen, None; G. Espada, None; B. Varbanova, None; S. Oliveira, None; P. Miettunen, None; G. Chédeville, None; M. Hofer, Novartis and AbbVie, 5; P. Dolezalová, None; I. Foeldvari, AbbVie and Novartis, 9; G. Horneff, AbbVie, Pfizer, Novartis, and Roche, 2,AbbVie, Novartis, Sobi, Pfizer, and Roche, 9; A. Estmann, None; C. Pruunsild, None; R. Merino, None; I. Calvo Penades, None; P. Mesa del Castillo, None; P. Lahdenne, None; M. Ioseliani, None; M. Trachana, None; O. Vougiouka, None; M. Harjacek, None; I. Orban, None; T. Konstantin, None; N. Shaaf, None; V. V. Panaviene, None; M. Rygg, None; E. Smolewska, None; J. A. Melo Gomes, None; J. Vojinovic, AbbVie, 8; E. Alexaeva, None; T. Avcin, None; V. Vargova, None; N. Aktay Ayaz, None; O. Kasapcopur, Novartis Pharmaceutical Corporation, 8, Roche Pharmaceuticals, 8; Y. Boyko, None; S. Ringold, Crescendo Bioscience, 2; M. Rinaldi, None; M. Garrone, None; N. Ruperto, BMS, Hoffman-La Roche, Janssen, Novartis, Pfizer and Sobi, 2,Abbvie, Ablynx, AstraZeneca, Baxalta Biosimilars, Biogen Idec, Boehringer, Bristol Myers Squibb, Eli-Lilly, EMD Serono, Gilead Sciences, Janssen, Medimmune, Novartis, Pfizer, Rpharm, Roche, Sanofi, 5, Abbvie, Ablynx, AstraZeneca, Baxalta Biosimilars, Biogen Idec, Boehringer, Bristol Myers Squibb, Eli-Lilly, EMD Serono, Gilead Sciences, Janssen, Medimmune, Novartis, Pfizer, Rpharm, Roche, Sanofi, 8; A. Ravelli, None.


Abstract Number: 2860

Enthesitis-Related Arthritis: Axial -Pattern Is Associated with an Expansion of Peripheral Th17 Populations .

Maria M. Katsicas1, Carolina Carrara2 and Ricardo Russo3, 1Service of Immunology & Rheumatology., Hospital de Pediatria Prof Dr JP Garrahan, Buenos Aires, Argentina, 2Immunoology & Rheumatology, Hospital de Pediatria Prof Dr JP Garrahan, Buenos Aires, Argentina, 3Service of Immunology/Rheumatology, Hospital de Pediatria Garrahan, Buenos Aires, Argentina

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017

Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects II: Juvenile Arthritis

Session Type: ACR Concurrent Abstract Session

Session Time: 4:30PM-6:00PM
Background/Purpose: Enthesitis-related arthritis (ERA) is a category of juvenile idiopathic arthritis encompassing most cases of juvenile spondyloarthropathy. Two different clinical patterns (axial /peripheral) have been recognized, possibly identifying distinct subpopulations. Different pro-inflammatory cytokines linked to Th1 and Th17 T-cell subsets have been implicated in the pathogenesis of ERA. Our objectives were to assess Th1 and Th17 cell subsets in ERA patients and to examine the association between clinical features and Th1 / Th17 cell subsets.

Methods: Patients with ERA (ILAR criteria) were included in a cross sectional study. Patients were classified according to their pattern of joint involvement into axial or peripheral as per ASAS criteria. Patients were clinically assessed on the same day blood samples were collected. Recorded features: active joint count (AJ), pain score (0-10), sacroiliac pain (SIP), lumbar pain (LP), lumbar limitation (LL) by Schöber’s test, patient wellbeing using a visual analogue scale (VASp, 0-10), disease activity according to the physician (VASphy), JADAS-10, JSpADA (Juvenile Spondyloarthritis Disease Activity index), ESR/CRP, active enthesitis (AE), functional capacity (CHAQ), radiologic sacroiliitis (MRI/X-rays) and therapy with TNF inhibitors (TNFi). Inactive disease was defined as JADAS-10 ≤ 1 and JSpADA =0. Quantification of Th-1 and Th17 cells was done by flow cytometry in PBMCs stimulated with PMA/IO in the presence of Brefeldin A. Staining with surface and intracellular components defined Th1 and Th17 phenotypes (CD4+ IFN+ and CD4+ IL-17+ respectively). Mann-Whitney U-test and Chi² were used as appropriate.

Results: 30 patients (90 % M) were included. HLA-B27 was positive in 13 (45%). Median age was 12 years, disease duration was 4 years. Clinical features (medians): AJ 1 (0-16), pain 0 (0-8.5), VASp 0.75 (0-8.5), VASphy 0 (0-8.5), JADAS-10 4.75 (0-25.8), JSpADA 1.75 (0-5.5); LL 4.5 (3-7) cm, ESR 15 (4-95) mm/h; CRP 1.64 (0-57) mg/dl. SIP in 13 (43%), LP in 18 (60%), AE in 1 (3%), CHAQ ≥ 0.5 in 7 (23%), and sacroiliitis in 18(60%) children. All patients fulfilled ASAS criteria: 17 (57%) ASAS-peripheral and 13 (43%) ASAS-axial; 8 patients (27%) met modified New York Criteria for Ankylosing Spondylitis (AS). Twenty (67%) patients were treated with TNFi. Ten (33%) patients showed inactive disease according to JADAS-10 and 6 (20%) according to JSpADA. Th1 cell percentage was 8.5±3.4 (4-17.4), Th17 cell % 0.90±0.44 (0.39-2.34%) in the whole group. Patients with peripheral and axial involvement showed similar Th1 cell percentage: 7.55±2.83 (4.3-14.9) and 10.1± 3.84 (4-17.4) and different Th17 cell percentage: 0.70±0.32 (0.39-1.72) and 1.10±0.44 (0.82-2.34) respectively (p=0.0009). Patients with AS exhibited higher Th17 cell percentage (p=0.01). LP (p=0.0001) and sacroilitis (p=0.0024) showed significant associations with Th17 cell.

Conclusion: ERA patients with axial pattern exhibit peripheral Th17 cell expansion. These findings suggest a pathogenic role for Th17 cells and support the potential use of IL-17 blocking strategies for the treatment of these patients.


Disclosure: M. M. Katsicas, None; C. Carrara, None; R. Russo, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/enthesitis-related-arthritis-axial-pattern-is-associated-with-an-expansion-of-peripheral-th17-populations

Abstract Number: 2861

Treat-to-Target in Rheumatoid Arthritis: What Level of Treatment Response Is Necessary By 3 Months in Order to Achieve the Treatment Target By 6 Months? Results from the Real Life NOR-DMARD Study

Vibeke Norvang1, Inge C Olsen2, Joseph Sexton1, Eirik K Kristianslund1, Till Uhlig1, Tore Kvien3, Daniel Aletaha4, Josef S. Smolen4 and Espen A. Haavardsholm1, 1Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, 2Department of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, 3Diakonhjemmet Hospital, Oslo, Norway, 4Medical University Vienna, Division of Rheumatology, Department of Internal Medicine III, Vienna, Austria

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects V: Predicting Treatment Response
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: In a treat-to-target strategy in rheumatoid arthritis (RA) treatment adoptions are recommended in case of poor improvement in disease activity 3 months after initiating therapy with disease modifying anti-rheumatic drugs (DMARDs), or if remission or low disease activity (LDA) has not been reached by 6 months.¹ A pooled analyses from several pivotal RCTs showed that...
RA patients who did not achieve a minor treatment response within 3 months were unlikely to reach the treatment target by 6 months.² We aimed to investigate which response levels at 3 months are predictive of achieving the treatment targets at 6 months in a routine clinical setting.

**Methods**: Data were provided by NOR-DMARD, a prospective, multicentre, observational study. We selected biological DMARD-naïve RA-patients enrolled in the period 2000-2012, who had at least moderate disease activity according to the Simplified Disease Activity Index (SDAI) when initiating therapy. All analyses were performed for the total group of included patients (n=1610), as well as for the following sub-groups: disease duration more/less than 12 months (n=895/681), baseline SDAI moderate/high disease activity (n=825/785), DMARD-naïve patients starting methotrexate (n=237) and biological DMARD-naïve patients starting a tumour necrosis factor inhibitor (n=248). We used a diagnostic test approach with receiver operating characteristic curves to explore the association between SDAI 50/70/85 response at 3 months and achievement of the treatment targets of SDAI remission or SDAI LDA at 6 months.

**Results**: At inclusion mean (SD) SDAI was 28.3 (12.8) and median (25-75% percentile) disease duration was 2 (0.2-8.8) years. At 6 months 46.8% of all patients had achieved LDA and 10.8% had reached remission. Not achieving at least 50% SDAI response at 3 months was associated with failing to reach remission, with low negative likelihood ratios (LRs) for all analysed groups (LR- 0.15-0.36). Patients with high disease activity at baseline were likely to fail reaching remission at 6 months if they achieved less than SDAI 70% response at 3 months (LR- 0.25), and to not reach LDA if they achieved less than SDAI 50% response (LR- 0.30). Achieving SDAI 85% response at 3 months was associated with reaching the treatment targets in all analysed groups, with high positive LRs for both remission (LR+ 4.77-9.64) and LDA (LR+ 4.56-8.06).

**Conclusion**: These results from a routine clinical setting confirm results from RCTs demonstrating a predictive association between levels of treatment response at 3 months and achievement of the treatment target after 6 months in RA-patients. Assessments at 3 months can inform clinicians to continue or adjust ongoing DMARD-therapy in a treat-to-target strategy aiming for remission or LDA within 6 months.

**References:**
Diverse Disease Activity Measures Demonstrate That the Routine Assessment of Patient Index Data with 3 Measures (Rapid-3) Assesses Only Non Inflammatory Components of Disease and Should Not be Utilized in a Treat to Target Strategy in Rheumatoid Arthritis

Craig Wiesenhutter, Coeur d'Alene Arthritis Clinic, Coeur D Alene, ID
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects V: Predicting Treatment Response
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose:
Treating Rheumatoid Arthritis (RA) patients to target (T2T) has been shown to result in better outcomes in patients with RA. Surrogate measures of disease activity help decision making in the clinic. The ACR has published recommendations for use in clinical practice. One of the five recommended measures included the Routine Assessment of Patient Index Data with 3 Measures (Rapid-3).

The Rapid-3 has been a popular choice for such a purpose. It is a patient questionnaire and requires no provider input or lab data. Also validity has been felt to be “good” and moderate correlations are found with more rigorous but time consuming tools, such as the Clinical Disease Activity Score with 28-joint counts (DAS28). However, the concern remains that this tool measures subjective, not inflammatory components of disease activity. The purpose of this paper is to analyze numerous disease activity measures (DAMs) and lab test, including more “objective” diverse DAMs, to determine whether the RAPID-3 measures predominately inflammatory, or subjective non inflammatory components of disease.

Methods:
Patients at a community based rheumatology clinic undergo disease activity measures (DAMs) and many other clinical and lab assessments on a routine basis as part of the implementation of T2T strategy. These assessments include the disease activity score in 28 joints (DAS28), a power Doppler joint count (UPDJC), which is an objective measurement of hyper vascularization of the synovium, and the 12-multibiomarker disease activity test (MBDA), as well as several other commonly assessed DAMs including the Rapid-3, Health Assessment Questionnaire. (HAQ), etc. The UPDJC includes scoring at six dorsal wrist and six dorsal MCP sites. The average duration of RA in patients at this clinic is > 10 years. Correlations were determined by Pearson’s coefficients, and linear regression models were employed.

Results:
Rapid-3 VS Prob

<table>
<thead>
<tr>
<th>Measure</th>
<th>N</th>
<th>Rapid-3 VS</th>
<th>Prob</th>
<th>Measure</th>
<th>N</th>
<th>Rapid-3 VS</th>
<th>Prob</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAS28CRP</td>
<td>378</td>
<td>r=0.398</td>
<td>p&lt;0.0001</td>
<td>CDAI</td>
<td>378</td>
<td>r=0.329</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>DAS28ESR</td>
<td>360</td>
<td>r=0.357</td>
<td>p&lt;0.0001</td>
<td>Pt Pain</td>
<td>360</td>
<td>r=0.902</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>USPDJC</td>
<td>336</td>
<td>r=0.002</td>
<td>NS</td>
<td>SAA</td>
<td>336</td>
<td>r=0.042</td>
<td>NS</td>
</tr>
<tr>
<td>CRP</td>
<td>338</td>
<td>r=0.012</td>
<td>NS</td>
<td>MBDA</td>
<td>338</td>
<td>r=0.071</td>
<td>NS</td>
</tr>
<tr>
<td>ESR</td>
<td>342</td>
<td>r=0.025</td>
<td>NS</td>
<td>BMI</td>
<td>342</td>
<td>r=0.238</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>HAQ</td>
<td>333</td>
<td>r=0.776</td>
<td>p&lt;0.0001</td>
<td>SJC</td>
<td>333</td>
<td>r=0.008</td>
<td>NS</td>
</tr>
<tr>
<td>Pt Global</td>
<td>329</td>
<td>r=0.585</td>
<td>p&lt;0.0001</td>
<td>RF</td>
<td>329</td>
<td>r=0.047</td>
<td>NS</td>
</tr>
<tr>
<td>Dr Global</td>
<td>378</td>
<td>r=0.175</td>
<td>p&lt;0.004</td>
<td>Anti CCP</td>
<td>378</td>
<td>r=0.035</td>
<td>NS</td>
</tr>
<tr>
<td>IL6</td>
<td>271</td>
<td>r=0.068</td>
<td>NS</td>
<td>Leptin</td>
<td>333</td>
<td>r=0.110</td>
<td>NS</td>
</tr>
<tr>
<td>TJC</td>
<td>371</td>
<td>r=0.330</td>
<td>p&lt;0.0001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusion:

Correlations between separate components of numerous disease activity measures including two diverse disease activity measures (UPDJC and Vectra DA 12-biomarker test), laboratory studies including phase reactants, serologies, and interleukins versus the Routine Assessment of Patient Index Data with 3 Measures (Rapid-3) clearly shows a complete lack of association with measures of inflammation.

Correlations with valid disease activity measures, such as the DAS28, are with the subjective components of the measurement, i.e. patient global, and and painful joint count, not with the objective components.

Linear multivariate regression analysis demonstrates that the vast majority of the Rapid-3 measure can be explained by two very subjective components, Patient pain, and the HAQ, neither of which pertain to inflammatory processes.

The Rapid-3 should not be used in a treat to target strategy in the management of rheumatoid arthritis.

Disclosure: C. Wiesenhutter, None;


Abstract Number: 2863

Serum Proteomic Signatures Predict Relapse in Rheumatoid Arthritis Patients Undergoing DMARD Withdrawal

Liam O’Neil¹, Victor Spicer², Carol A Hitchon², Juergen Rech³, Axel J. Hueber⁴, John Wilkins⁵, Hani El-Gabalawy¹ and Georg Schett³, ¹Rheumatology, University of Manitoba, Winnipeg, MB, Canada, ²University of Manitoba, Winnipeg, MB, Canada, ³Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätssklinikum Erlangen, Erlangen, Germany, ⁴Department of Medicine 3, Rheumatology and Immunology, University of Erlangen-Nuremberg, Erlangen, Germany

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects V: Predicting Treatment Response
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Early and targeted treatment strategies have led to increasing numbers of patients with RA achieving sustained clinical remission. If and when to taper Disease Modifying Anti-Rheumatic Drug (DMARD) therapy is an emerging question for both clinicians and patients. Unfortunately, data on clinical, biochemical or imaging modalities that can reliably predict relapse following therapy withdrawal are limited to date. The objectives of our study were two-fold; first to generate unsupervised serum proteomic
profiles using baseline samples from patients with RA in remission. We also aimed to identify serum biomarkers that predict relapse following DMARD withdrawal.

**Methods:** The RETRO (Reducing therapy in Rheumatoid Arthritis Patients in ongoing Remission) study is a multicentre, randomized, prospective trial enrolling RA patients in sustained clinical remission (DAS28 2.6) to undergo DMARD withdrawal. 130 baseline serum samples from the RETRO study were analyzed using SOMAscan (SOMAlogic Inc.), allowing the generation of comparative quantitative levels of > 1300 proteins. Unsupervised clustering analysis was performed to identify subgroups of patients. Unique clusters were analyzed with Ingenuity Pathway Analysis (QIAGEN). Differentially expressed proteins between patients who relapsed, and those who remained in remission were combined to synthesize a predictive biomarker scoring algorithm. A multivariate logistic regression model that included seropositive status, current treatment, both disease and remission duration, and the biomarker score was used to analyze predictors of relapse.

**Results:** Unsupervised clustering analysis distinguished 4 unique subpopulations of patients. Compared to the remaining population, Cluster 3 (n = 14) had shorter disease duration (p = 0.012), higher seropositivity rates (p = 0.02) and no use of biologic DMARDs (p = 0.001). Cluster 3 had 145 proteins with significantly (p <0.05) reduced expression (log2 difference = 0.50 - 1.17) compared to the remaining population. Pathway analysis of these proteins suggested downregulation of Acute Phase Response signaling. Additionally, we created a predictive biomarker withdrawal score (SOMA score; range = 1.5 to 26.0) comprised of 8 unique biomarkers using our data. Patients failing DMARD withdrawal had higher mean SOMA scores compared to those who sustained remission (13.4 vs 8.0, p < 0.001). 83.7% of patients who failed withdrawal had scores greater than a cut off of 9.64, while only 25.6% of those remaining in remission had scores above this cut off. Multivariate regression analysis identified SOMA score as the only independent predictor for relapse after DMARD withdrawal (OR = 15.5, 4.5 - 53.4, p < 0.001).

**Conclusion:** Unsupervised proteomic analysis of RA patients in sustained clinical remission generates distinct clusters of subpopulations. We discovered a unique protein signature in a group of patients who, despite being seropositive, achieved sustained clinical remission without requiring biologic therapy. We constructed a serum protein biomarker score that successfully predicts failure of DMARD withdrawal. Validation of our predictive score will be undertaken to assess its use as a clinical decision-making tool.

**Disclosure:** L. O’Neil, None; V. Spicer, None; C. A. Hitchon, None; J. Rech, None; A. J. Hueber, None; J. Wilkins, None; H. El-Gabalawy, None; G. Schett, None.


**Abstract Number:** 2864

**Anti-Acetylated Peptide Antibodies Positive Rheumatoid Arthritis Patients Show a More Favorable Response to Tumor-Necrosis-Factor Inhibitor Treatment and Better Disease Activity Control over Time**

Paul Studenic1, Stephan Blüml1, Holger Bang2, Daniela Sieghart1, Daniel Aletaha1, Helmuth Haslacher3, Josef S. Smolen1,4 and Günter Steiner1,1Medical University Vienna, Division of Rheumatology, Department of Internal Medicine III, Vienna, Austria, 2Orgentec Diagnostika GmbH, Mainz, Germany, 3Medical University Vienna, Department of Laboratory Medicine, Vienna, Austria, 4Department of Internal Medicine, Hietzing Hospital, Vienna, Austria

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017  
**Session Title:** Rheumatoid Arthritis – Clinical Aspects V: Predicting Treatment Response  
**Session Type:** ACR Concurrent Abstract Session  
**Session Time:** 4:30PM-6:00PM

**Background/Purpose:** Anti-acetylated-peptide antibodies (AAPA) have been found in rheumatoid arthritis (RA) patients and may be additional markers for diagnosis, particularly in rheumatoid factor (RF)/ anti-citrullinated protein antibodies (ACPA) negative patients. Here we investigated whether the presence of AAPA may be useful for prediction of Tumor-Necrosis-Factor-inhibitor (TNFi) treatment response.

**Methods:** RA patients starting their first TNFi treatment were identified and tested for AAPA (by ELISA using two acetylated peptides derived from vimentin), RF (by nephelometry), and ACPA (by ELISA) at baseline. Based on logistic regression analysis, Odds Ratios
Including 95% confidence intervals (95% CI) for association with a 50% response of the Simplified disease activity index (SDAI50) and for reaching SDAI low disease activity (LDA) or remission at 6 months were calculated. We also performed longitudinal analysis by General Estimated Equation analyses (GEE) and Cox-regression.

**Results:** Among the 93 patients starting on a TNFi (85% female, mean disease duration: 7.7±7 years; mean SDAI: 20±13), 53% were positive for AAPA, 57% for ACPA and 61% for RF; 35.5% were triple positive, and 7.5% only for AAPA. There was a higher proportion of RF+ and ACPA+ patients in the AAPA+ group.

Presence of AAPA was associated with significantly higher rates of SDAI50 response (44% vs. 18%; OR 3.58 95%CI: 1.1-11.6; p=0.034) and LDA (72% vs. 48%; OR: 3.01; 1.05-8.64; p=0.041). Analogous analysis for RF or ACPA did not show such association either with achieving SDAI50 (RF: 35% vs. 30%; OR: 1.15; 0.39-3.39; p=0.796; ACPA: 38% vs. 25%; OR: 1.66; 0.53-5.21; p=0.282) or LDA (RF: 68% vs. 52%; OR: 2.08, 0.74-5.82; p=0.163; ACPA: 67% vs. 52%; OR: 2.17; 0.75-6.27; p=0.155).

AAPA+ patients showed significantly higher relative changes in SDAI (p=0.021), CDAI (p=0.025), DAS-ESR (p=0.022) and DAS-CRP (p=0.014) compared to AAPA- patients. Respective analyses for RF and ACPA were not significant for any of the indices.

Longitudinal analyses of the SDAI in patients on TNFi revealed significant difference in SDAI over time between AAPA+ vs. AAPA- patients (p=0.045); again, this was not seen in the analyzes of RF (p=0.597) or ACPA (p=0.407). Treatment retention was significantly higher for AAPA+ patients (Hazard Ratio, HR: 0.506; 0.310-0.829; p=0.007); this effect remained significant after adjustment for RF and ACPA (HR=0.556; 0.327-0.946; p=0.03; **Figure**). For RF or ACPA the crude HR were 0.689 (0.420-1.131; p=0.141) and 0.613 (0.376-1.000; p=0.050), respectively.

**Conclusion:** Although validations in other cohorts are warranted for confirmation, in this observational cohort, AAPA positivity appeared to be good discriminator of response to the first TNFi-treatment and associated with more favorable long-term control of disease activity and treatment retention.

**Disclosure:** P. Studenic, None; S. Blüml, None; H. Bang, None; D. Sieghart, None; D. Aletaha, None; H. Haslacher, None; J. S. Smolen, None; G. Steiner, None.


**Abstract Number:** 2865
The Utility and Limitations of Serum C-Reactive Protein in Appraising Synovial Inflammation

Carl Orr¹, Aurélie Najm², Francis Young¹, Trudy McGarry³, Monika Biniecka⁴, Ursula Fearon⁵ and Douglas J. Veale⁶,

¹Centre for Arthritis and Rheumatic Diseases, Dublin Academic Medical Centre, University College Dublin, Dublin 4, Ireland, ²INSERM U1238 University of medicine, PHY-OS Laboratory, Nantes, France, ³St. Vincent's University Hospital, Dublin, Ireland, ⁴Dublin Academic Medical Centre, Dublin, Ireland, ⁵Trinity College Dublin, Department of Molecular Rheumatology, Trinity College Dublin, Dublin, Ireland, ⁶Rheumatology, St. Vincent's University Hospital, Dublin 4, Ireland

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects V: Predicting Treatment Response
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose:

Despite the clinical role of synovial histology in the differential diagnosis of arthritis, there are still profound unmet needs regarding predictors for diagnosis, disease progression and response to treatment. Nevertheless, histological examination of the synovium allows for the most robust appraisal of levels of local synovial inflammation.

The most common validated disease activity score is the DAS28, incorporating either CRP or ESR. As CRP is now widely accessible, and is responsive in a more timely manner to changes in systemic inflammatory activity, the DAS28—CRP is widely used today.

It is noteworthy that RA registry data for over 9000 patients has shown that more than half did not have elevation of ESR or CRP, but had ongoing disease activity as determined by joint counts and global assessments (1).

Methods:

223 consecutive subjects with RA with knee arthralgia underwent arthroscopy. Serum samples were taken and serum CRP levels measured, immediately before the procedure. A macroscopic score of synovitis on a visual analogue scale ranging from 0-100mm was recorded by the operator at arthroscopy. Based on the Haematoxylin and Eosin staining, a tissue inflammatory score for each biopsy was applied by a hospital pathologist with extensive experience examining synovial biopsies (1=normal synovium, 2=mildly inflamed and 3=moderately to severely inflamed).

Results:

A statistically significant positive correlation was observed between the CRP as well as the DAS28-CRP, and the level of inflammation in the biopsy retrieved (n=197, rho=0.42, CI 0.30 to 0.53, p<0.0001; n=189, rho=0.23, CI 0.09 to 0.36, p=0.0011 respectively) and these results are depicted in figure 1 a and b.

Tissue inflammation scores were available for 75 subjects with a normal CRP (<5mg/l). 49.3% of patients had histological evidence of inflammation in their synovium, despite having normal serum CRP levels, and 10.6% had moderate to severe synovitis as assessed at arthroscopy. Tissue inflammation scores were available for 14 subjects defined as being in clinical remission by DAS28-CRP criteria (<2.6), and 71.4% of these subjects had histological evidence of inflammation in their synovium. Despite being classified as being in remission by these criteria, 21.4% had moderate to severe synovitis at arthroscopy.

Conclusion:
Better biomarkers are required in RA to accurately appraise CRP. It is conceivable that there are a subset of RA patients where disease cannot be normally monitored by CRP; more work is needed to determine if such patients can be identified at the outset.

References:

Disclosure: C. Orr, None; A. Najm, None; F. Young, None; T. McGarry, None; M. Biniecka, None; U. Fearon, None; D. J. Veale, AbbVie, Actelion, Bristol-Myers Squibb, Janssen, MSD, Novartis, Pfizer Inc, Roche, UCB, 2,AbbVie, Actelion, Bristol-Myers Squibb, Janssen, MSD, Novartis, Pfizer Inc, Roche, UCB, 8.


Abstract Number: 2866

**Microarray Pathway Analysis Comparing Baricitinib and Adalimumab in Moderate to Severe Rheumatoid Arthritis Patients, from a Phase 3 Study**

Paul Emery1, Peter C. Taylor2, Michael Weinblatt3, Yoshiya Tanaka4, Edward C. Keyston5, Ernst R. Dow6, Richard Higgs6, William L. Macias6, Guilherme Rocha6, Terence P. Rooney6, Douglas E. Schlichting6, Steven H. Zuckerman6 and Iain B. McInnes7, 1Leeds MSK Biomed/Chapel Allerton Hospital, Leeds, United Kingdom, 2NDORMS, University of Oxford, Oxford, United Kingdom, 3Brigham and Women’s Hospital, Boston, MA, 4The First Department of Internal Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan, 5University of Toronto, Toronto, ON, Canada, 6Eli Lilly and Company, Indianapolis, IN, 7University of Glasgow, Glasgow, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy IV: Pharmacodynamic Markers and Therapeutic Intervention
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: In RA-BEAM (NCT01710358), baricitinib (BARI), an oral selective inhibitor of Janus kinase (JAK) 1 and JAK 2, yielded significant improvements in patients (pts) with active RA who had an inadequate response to methotrexate compared to placebo (PBO) or adalimumab (ADA).1 We analyzed molecular pathways modulated by BARI compared with ADA after 4 and 12 weeks (wks) of treatment relative to PBO.

Methods: Pts (N=1307) were randomized 3:3:2 (PBO [switched to BARI after 24 wks], BARI 4 mg once daily, ADA 40 mg every other week) for 52 wks. Total RNA extracted from whole blood collected at baseline (BL), wk 4, and wk 12 was analyzed using the GeneChip Human Transcriptome Array 2.0 (Affymetrix). Probeset level data were summarized to a data-driven transcript level and analyzed using a mixed effects model on a log2 transformed response. Multiplicity was adjusted for by testing both within and between transcripts.

Results: Pathway analysis revealed that there was little overlap of the immune pathways modulated by both BARI and ADA at wk 4 with no significant overlap by wk 12 (Table). BARI downregulated JAK/Signal Transducer and Activator of Transcription (STAT) signaling pathways, such as those induced by IFNs, IL-6, GM-CSF, IL-5, and IL-3. Expression of interferon responsive genes (IRGs) was downregulated by BARI and upregulated by ADA. BARI reduced IRGs by 75% at wk 4 in pts that had high IFN gene expression at BL. ADA modulated complement pathways. Of interest, STAT transcripts were reduced at wk 4 by BARI (STAT1, 2, 5A, 5B, 6); by wk 12 several STATs (STAT 1, 2, 5A) did not differ from PBO. In addition to different pathways being modulated, there were additional differences noted in the number of genes modulated by each treatment (Figure). Using PBO as standard, BARI modulated more genes than ADA at wks 4 and 12; BARI resulted in more gene modulation at wk 12 than at wk 4, whereas ADA gene modulation was similar.
at wks 4 and 12. In addition, both the numbers and types of genes modulated by BARI diverged further from ADA at wk 12 than at wk 4.

**Conclusion:** While BARI and ADA both showed significant benefits compared to PBO in the RA-BEAM trial, gene expression profiling revealed significant differences between treatments. Notably, BARI and ADA modulated JAK/STAT or complement pathways, respectively, and the drugs had opposite effects on interferons. This analysis indicates that different, and possibly complementary mechanisms of action underlie each targeted therapy.


---

**Disclosure:** P. Emery, Pfizer, MSD, Abbvie, BMS, UCB, Roche, Novartis, Samsung, Sandoz, Eli Lilly and Company, 5; P. C. Taylor, Abbvie, Eli Lilly and Company, Galapagos, GlaxoSmithKline, Pfizer, UCB, Biogen, Sandoz, Novartis, Janssen, 5; Celgene, Eli Lilly and Company, Galapagos, UCB, Abide Therapeutics, 2; M. Weinblatt, Amgen, BMS, Crescendo Bioscience, UCB, Genzyme, 2, Amgen, Abbvie, BMS, Eli Lilly and Company, Gilead, Merck, Pfizer, Novartis, Roche, UCB, Crescendo Bioscience, Genzyme, Samsung, 5; Y. Tanaka, Mitsubishi-Tanabe, Takeda, Bristol-Myers, Chugai, Astellas, Abbvie, MSD, Daiichi-Sankyo, Pfizer, Kyowa-Kirin, Eisai, Ono, 2, Daiichi-Sankyo, Astellas, Pfizer, Mitsubishi-Tanabe, Bristol-Myers, Chugai, YL Biologics, Eli Lilly and Company,
CD39 Positive Regulatory T Cells As a Biomarker of Responsiveness to Methotrexate in Rheumatoid Arthritis

Vikas Gupta1, Shobhita Katiyar2, Ankita Singh2, Ramnath Misra1 and Amita Aggarwal1, 1Clinical Immunology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, 2Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy IV: Pharmacodynamic Markers and Therapeutic Intervention
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose:

About 30-40% of patients with RA do not respond to MTX, the first-line therapy in RA. Early identification of responders may allow the use of alternative DMARDs in patients unlikely to respond, thus preventing long-term damage. CD39, an ectonucleotidase highly expressed on regulatory T cells (Tregs), is responsible for the production of adenosine, an important anti-inflammatory mediator of MTX action. CD39 expression on Tregs improves their suppressive capacity. Therefore, we aimed to study the role of CD39+ regulatory T cell (CD39+ Treg) frequency as a biomarker for MTX responsiveness in RA.

Methods:

Patients with active RA (fulfilling 2010 ACR/EULAR classification criteria and having DAS28-CRP >3.2) who were naive to DMARDs were enrolled. Frequency of CD39+ Tregs (CD39+CD4+CD25+FoxP3+ T cells) and CD39+CD4+CD25+ cells was determined by flow cytometry in peripheral blood before start of therapy. After 4 months of treatment with MTX monotherapy (no corticosteroids were given), patients were classified into two groups based on EULAR response criteria: responders (moderate/good response; MTX-R) and non-responders (MTX-NR). All patients who needed rescue therapy after 2 months were classified as non-responders. All patients were genotyped for single nucleotide polymorphism (SNP) rs11188513 in CD39 gene using TaqMan probe method. The data (median and IQR) was analyzed using non-parametric tests.

Results:

Among the 70 patients who completed at least 2 months follow-up (60 females, median age: 39 years and median disease duration: 24 months), 53 patients were RF positive and 57 were anti-CCP positive. The baseline median DAS-28 CRP was 5.15 (4.45-5.89). After 4 months of follow-up, 54 patients were classified as MTX-R and 16 as MTX-NR.

There was no difference in the two groups as regards age, disease duration, disease activity or baseline frequency of Tregs [1.4% (1.0%-2.3%) vs 1.1% (0.7%-1.8%), p = NS]. However, the baseline CD39+Treg frequency was significantly higher in the MTX-R compared with the MTX-NR [78.0% (68.3%-87.4%) vs 67.8% (24.7%-84.3%), p < 0.05]. At a cut-off of CD39+ Treg frequency of 75.1%, the positive predictive value (PPV) to identify responders was 86%.
As Foxp3 staining takes time we also saw if the frequency of CD39+CD4+CD25+ T cells could be utilized for prediction of MTX response. The baseline CD39+CD4+CD25+ T cells frequency was also significantly higher in the MTX-R compared with the MTX-NR [43.6% (36.0%-52.7%) vs 32.6% (25.0%-39.7%), p < 0.01]. At a cut-off frequency of 41.7%, PPV to identify responders was 91%. MTX treatment did not alter the CD39+ Treg frequency [75.9% (61.8%-87.0%) vs 67.2% (51.3%-84.0%), p = NS].

CC genotype at SNP rs11188513 of CD39 gene was associated with a significantly lower frequency of both CD39+ Tregs (p < 0.01) as well as CD39+CD4+CD25+ T cells (p < 0.01).

Conclusion:

Higher frequency of CD39+ Tregs in the peripheral blood is associated with response to MTX in RA and hence, this should be considered as a potential biomarker for prediction of response to MTX treatment.

Disclosure: V. Gupta, None; S. Katiyar, None; A. Singh, None; R. Misra, None; A. Aggarwal, None.


Abstract Number: 2868

Pharmacodynamic Analysis of Whole Blood Gene Expression over 2 Years in a Phase IIIb Head-to-Head Trial of Abatacept and Adalimumab in Patients with RA

O Jabado1, MA Maldonado1, Michael Schiff2, Michael Weinblatt3, Roy Fleischmann4, William H. Robinson5, A Greenfield1 and SE Connolly1, 1Bristol-Myers Squibb, Princeton, NJ, 2University of Colorado, Denver, CO, 3Brigham and Women’s Hospital, Boston, MA, 4Metroplex Clinical Research Center Dallas, Dallas, TX, 5Stanford University, Palo Alto, CA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy IV: Pharmacodynamic Markers and Therapeutic Intervention
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: The head-to-head AMPLE study compared the safety and efficacy of abatacept (co-stimulatory modulator) versus adalimumab (TNFα inhibitor) for treatment of RA over 2 years. The objective of this initial analysis was to determine molecular pharmacodynamic (PD) changes in whole blood associated with abatacept and adalimumab treatment; this is the first step toward defining predictive biomarkers of response. Methods: RNA was isolated from the whole blood of patients at baseline, Day 85, Year 1, and Year 2, then profiled using Affymetrix U219 GeneChip (628 patients, 2049 total samples). Differential expression between study arms over time was assessed using a linear model with clinical covariates and a multiple testing correction. Single-sample Gene Set Enrichment Analysis (ssGSEA)1 was used to calculate enrichment for gene modules derived from literature. Transcription profiling of naïve and activated immune cell types was used to generate immune gene signatures as a proxy for cell abundance measurements.2

Results: Differential gene expression analysis revealed many changes that fit with expected mechanisms of action (MoA). Genes that encode proteins associated with T-cell co-stimulation and antibody production were lower in the abatacept arm; genes transcribed in response to pro-inflammatory signals were lower in the adalimumab arm (Table). Some of the most differentially expressed genes have not been previously associated with RA (e.g. PI3/elafin, ALPL, PROK2, GBP5, ZNF683) or are poorly studied. Using immune cell type gene expression signatures as proxies for abundance, we found plasma cells, B cells and natural killer cells were all lower in the abatacept arms by Year 2; conversely, polymorphonuclear leukocytes were higher in the abatacept arm (Figure).

Conclusion: This first analysis shows PD differences consistent with the expected MoA of abatacept and adalimumab. Further analysis of this rich time course dataset may reveal predictive biomarkers of response and disease progression, and novel targets for therapeutics.

Table 1. Selected List of Differentially Expressed Genes and Gene Modules Between Treatment Arms at Year 2

<table>
<thead>
<tr>
<th>Genes</th>
<th>Lower in abatacept</th>
<th>Lower in adalimumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>ID</td>
<td>Function</td>
<td>ID</td>
</tr>
<tr>
<td>IGHA1</td>
<td>Antibody production</td>
<td>CXCL1</td>
</tr>
<tr>
<td>IGHA2</td>
<td></td>
<td>IL1b</td>
</tr>
<tr>
<td>IGKC</td>
<td></td>
<td>MMP9</td>
</tr>
<tr>
<td>CTLA4</td>
<td>Cell co-stimulatory</td>
<td>LCN2</td>
</tr>
<tr>
<td></td>
<td>signaling</td>
<td>CAMP</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CEACAM3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ADM</td>
</tr>
<tr>
<td>HLA-DPB1</td>
<td>Antigen presentation</td>
<td></td>
</tr>
<tr>
<td>CCR4</td>
<td>Chemokine receptors</td>
<td></td>
</tr>
<tr>
<td>CCR5</td>
<td></td>
<td>ORM1</td>
</tr>
<tr>
<td>CXCR6</td>
<td></td>
<td>M8.16</td>
</tr>
<tr>
<td>M3.6</td>
<td>IL2 activated NK</td>
<td>M9.42</td>
</tr>
<tr>
<td>M4.10</td>
<td>Plasma cells</td>
<td></td>
</tr>
<tr>
<td>Estimated</td>
<td>B cells</td>
<td>Granulocytes</td>
</tr>
<tr>
<td>immune cell</td>
<td></td>
<td></td>
</tr>
<tr>
<td>types</td>
<td>B cells</td>
<td></td>
</tr>
<tr>
<td>NK cells</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

IL, interleukin; NK=natural killer

Disclosure: O. Jabado, Bristol-Myers Squibb, 3; M. Maldonado, Bristol-Myers Squibb, 1; Bristol-Myers Squibb, 3; M. Schiff, AbbVie, BMS, Eli Lilly, JNJ, UCB, 5; AbbVie, BMS, 8; M. Weinblatt, Amgen, BMS, Crescendo Bioscience, UCB, DxtTerity, Sanofi, 2, Amgen, BMS, Crescendo Bioscience, UCX, AbbVie, Lilly, Pfizer, Roche, 5; R. Fleischmann, AbbVie, Amgen, Astellas, AstraZeneca, BMS, Celgene, EMD-Serono, Janssen, Eli Lilly, Merck, Novartis, Pfizer, Roche, Sanofi-Genzyme, UCB, 2, AbbVie, Amgen, BMS, Celgene, GSK, Janssen, Eli Lilly, Novartis, Pfizer, Roche, Sanofi-Genzyme, UCX, 5; W. H. Robinson, None; A. Greenfield, Bristol-Myers Squibb, 3; S. Connolly, Bristol-Myers Squibb, 3; Bristol-Myers Squibb, 1.


Abstract Number: 2869

Significant Decrease of T-Cells but Not Macrophages in the Synovium of Patients with Active Rheumatoid Arthritis after Treatment with Tocilizumab

Katerina Chatzidionysiou¹, Marianne Engström¹, Erik af Klint¹, Aase Hensvold¹ and Anca I Catrina², ¹Rheumatology Unit, Department of Medicine, Karolinska Institute, Karolinska University Hospital, Stockholm, Sweden, ²Department of Medicine, Rheumatology Unit, Department of Medicine, Karolinska Institute, Karolinska University Hospital, Stockholm, Sweden

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy IV: Pharmacodynamic Markers and Therapeutic Intervention
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Tocilizumab (TCZ) is an anti-IL6R monoclonal antibody approved for the treatment of Rheumatoid Arthritis (RA). There is limited data on synovial tissue histology changes. The aim of this study was to characterize the synovial tissue histological changes after treatment with TCZ and to investigate the effect of treatment on citrullination.
**Methods:** 15 patients with definite RA, according to ACR 1987 criteria, independent of disease duration, who failed treatment with at least one conventional synthetic or biologic disease modifying anti-rheumatic drug (DMARD) were included. Synovial biopsies were obtained before and after 8 weeks of treatment with TCZ from all patients. Clinical evaluation was performed at baseline and at the time of the second synovial biopsy. We evaluated by immunohistochemistry (IHC) expression of citrullinated proteins (CP) and protein arginine deiminase (PAD) enzymes in synovial tissue before and after treatment with TCZ (C03, B09, BVCA1, PAD2, PAD4). Negative controls were used for each antibody. Expression of CD68, CD3 and CD55 was also evaluated. Evaluation of all IHC variables was performed by two blinded independent observers using a semiquantitative score on a 0–3 scale (0, no staining; 1, low amounts of staining; 2, moderate amounts of staining; 3, high amounts of staining). Paired-wised Wilcoxon Signed Ranks Test was used to compare the median value before and after treatment.

**Results:**

The median (IQR) age, disease duration, N. prior biologic DMARDs and DAS28 at baseline was 66 (58-79), 4 (1-13), 1 (0-2), 6 (5-7), respectively. 93% were female, 53% were RF + and 60% ACPA+, 53% had concomitant glucocorticoids and only 27% had concomitant conventional synthetic DMARDs. Significant reductions in DAS28, swollen and tender joint count (SJC and TJC, respectively), and acute phase reactants (ESR and CRP) were observed between baseline and 8 weeks (table 1). By IHC, TCZ induced significant decrease in the number of CD3, C03 and CD55, but not in the number of the other CP, PAD2, PAD4 and CD68 (table 1). No significant correlations between reduction in disease activity (by ΔDAS28, ΔSJC, ΔTJC, ΔESR, ΔCRP) and reduction in CP, CD68 or CD3 were found.

**Conclusion:** IL6R blockade leads to significant decrease in synovial T-cell count. No clear impact on citrullination was observed. Interestingly, no effect on the number of macrophages was found.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>12 weeks</th>
<th>Wilcoxon Signed Ranks Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAS28 BL</td>
<td>5.9 (4.7-6.8)</td>
<td>2.98 (2.0-3.8)</td>
<td>0.028</td>
</tr>
<tr>
<td>SJC BL</td>
<td>9 (3-14)</td>
<td>1 (0-4.25)</td>
<td>0.009</td>
</tr>
<tr>
<td>TJC BL</td>
<td>10 (4-15)</td>
<td>1 (0-2.25)</td>
<td>0.017</td>
</tr>
<tr>
<td>ESR BL</td>
<td>34 (15-69)</td>
<td>6 (5-16)</td>
<td>0.001</td>
</tr>
<tr>
<td>CRP BL</td>
<td>11 (5-27)</td>
<td>1 (1-2)</td>
<td>0.005</td>
</tr>
<tr>
<td>CD68</td>
<td>2 (1-3)</td>
<td>2 (0.75-3)</td>
<td>0.41</td>
</tr>
<tr>
<td>CD3</td>
<td>2 (1-3)</td>
<td>1 (0-2)</td>
<td>0.046</td>
</tr>
<tr>
<td>G09 (cit)</td>
<td>0 (0-2)</td>
<td>0 (0-2)</td>
<td>0.862</td>
</tr>
<tr>
<td>C03 (cit)</td>
<td>1 (0-1)</td>
<td>0 (0-1)</td>
<td>0.025</td>
</tr>
<tr>
<td>BVCA1 (cit v/im)</td>
<td>1 (0-1)</td>
<td>0 (0-1)</td>
<td>0.18</td>
</tr>
<tr>
<td>B09 (cit)</td>
<td>2 (1-2)</td>
<td>2 (1-2)</td>
<td>0.20</td>
</tr>
<tr>
<td>PAD2</td>
<td>3 (2-3)</td>
<td>2 (1.5-3)</td>
<td>0.16</td>
</tr>
<tr>
<td>PAD4</td>
<td>2 (2-3)</td>
<td>2 (2-3)</td>
<td>0.37</td>
</tr>
<tr>
<td>CD55</td>
<td>2 (2-3)</td>
<td>1.5 (1-2)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Table 1. Clinical and IHC changes between 0 and 8 weeks after treatment with TCZ.

**Disclosure:** K. Chatzidionysiou, Lilly, AbbVie, Roche, Pfizer, 5; M. Engström, None; E. af Klint, None; A. Hensvold, None; A. I. Catrina, None.


**Abstract Number:** 2870

**Ex Vivo Comparison of Baricitinib, Upadacitinib, Filgotinib, and Tofacitinib for Cytokine Signaling in Human Leukocyte Subpopulations**

Iain B. McInnes1, Richard Higgs2, Jonathan Lee2, William L. Macias2, Songqing Na2, Robert A. Ortmann2, Guilherme Rocha2, Thomas Wehrman3, Xin Zhang2, Steven H. Zuckerman2 and Peter C. Taylor4, 1University of Glasgow, Glasgow, United Kingdom, 2Eli Lilly and Company, Indianapolis, IN, 3Primity Bio, Fremont, CA, 4NDORMS, University of Oxford, Oxford, United Kingdom
Background/Purpose: Baricitinib (babi), an oral selective Janus kinase (JAK) 1/2 inhibitor, has been approved in the EU for the treatment of adults with moderately to severely active RA. We compared the in vitro cellular pharmacology of bari to upadacitinib (ABT), filgotinib (filgo), and tofacitinib (tofa), three JAK inhibitors (JAKis) currently approved or in clinical development.

Methods: Peripheral blood mononuclear cells from healthy donors (n=6-12) were incubated with different JAKis over a 7-point concentration range. Following cytokine stimulation, levels of phosphorylated signal transducer and activator of transcription (pSTAT) were measured and IC50 calculated in phenotypically gated leukocyte subpopulations. Therapeutic dose relevance of the in vitro analysis was assessed using calculated mean concentration-time (CT) profiles over 24 h obtained from JAKi-treated subjects (bari 4 mg QD; ABT 15 & 30 mg QD; filgo 100 & 200 mg QD; tofa 5 & 10 mg BID). Time above IC50 (T>IC50; h/day) and average daily % inhibition of pSTAT formation (%SI) were calculated for each JAKi, cytokine, and cell type.

Results: The cytokines tested did not signal in all cell types (Table 1). When signaling was detected, IC50, %SI, and T>IC5 for a particular JAKi were similar across cell types and exhibited dose dependent inhibition (Tables 1 & 2). For JAK1/3 dependent signaling across 4 cytokines (IL-2, 4, 15, 21), IC50 for ABT and tofa were more potent than bari; filgo was the least potent. Overlaid on CT profiles, these results indicated generally higher %SI and longer T>IC for ABT and tofa compared to bari and filgo. For IL-6 (JAK1/2), %SI and T>IC was tofa > bari/ABT > filgo and for IL-10 (JAK1/TYK2), %SI was tofa > bari/ABT > filgo. IFN-γ (JAK1/2) was modulated by bari, ABT, and tofa, but not by filgo. IFN-α (JAK1/TYK2) signaling was most potently inhibited with bari and ABT, and less with filgo. Filgo did not appear to modulate GM-CSF signaling (JAK2/2), while %SI and T>IC were similar between bari and ABT.

Conclusion: JAKis display different in vitro pharmacologic profiles which, coupled to their in vivo pharmacokinetics, suggest that they modulate distinct cytokine pathways to differing degrees and durations over 24 h. Bari and filgo inhibited JAK1/3 signaling to a lesser extent than ABT and tofa. Consistent across JAKis, no agent potently or continuously inhibited an individual cytokine signaling pathway throughout the dosing interval as assessed by %SI or T>IC, respectively. These observations may have implications for the varying efficacy and safety profiles observed with JAKIs across disease states.


Abstract Number: 2871

Anti-RA33 (hnRNP-A2/B1) Autoantibodies Are Associated with the Therapeutic Response to Methotrexate and Anti-TNF Treatment in Patients with Rheumatoid Arthritis

Daniela Sieghart1, Paul Studenic1, Farideh Alasti2, Daniel Aletaha3, Josef S. Smolen1 and Günter Steiner2, 1Medical University Vienna, Division of Rheumatology, Department of Internal Medicine III, Vienna, Austria, 2Rheumatology, Medical University of Vienna, Vienna, Austria, 3Department of Medicine III, Division of Rheumatology, Medical University of Vienna, Vienna, Austria

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy IV: Pharmacodynamic Markers and Therapeutic Intervention
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose:

Besides the determination of rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA), anti-RA33 antibodies (which are directed to the nuclear antigen hnRNP-A2/B1) could be of additional diagnostic and/or prognostic value in patients with rheumatoid arthritis (RA) because they are also found in RF/ACPA negative patients.

Abstract:

Anti-RA33 (hnRNP-A2/B1) Autoantibodies Are Associated with the Therapeutic Response to Methotrexate and Anti-TNF Treatment in Patients with Rheumatoid Arthritis

Daniela Sieghart1, Paul Studenic1, Farideh Alasti2, Daniel Aletaha3, Josef S. Smolen1 and Günter Steiner2, 1Medical University Vienna, Division of Rheumatology, Department of Internal Medicine III, Vienna, Austria, 2Rheumatology, Medical University of Vienna, Vienna, Austria, 3Department of Medicine III, Division of Rheumatology, Medical University of Vienna, Vienna, Austria

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy IV: Pharmacodynamic Markers and Therapeutic Intervention
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose:

Besides the determination of rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA), anti-RA33 antibodies (which are directed to the nuclear antigen hnRNP-A2/B1) could be of additional diagnostic and/or prognostic value in patients with rheumatoid arthritis (RA) because they are also found in RF/ACPA negative patients.
Methods:
To determine the diagnostic sensitivity and specificity of anti-RA33 subtypes sera from 255 RA patients, 258 disease controls and 100 healthy subjects were tested by a prototype anti-RA33 EliA® (Thermo Fisher Scientific) for the presence of anti-RA33 IgG, IgA and IgM antibodies. ACPA and RF were routinely measured by EliA® and nephelometry, respectively. All RA patients had initially been treated with conventional synthetic drugs (mostly methotrexate, MTX) and were subsequently treated with at least one TNF inhibitor (TNFi). Therapeutic responses to MTX and TNF blocking biologicals were analyzed in an inception cohort (n=104) who had started their DMARD therapy at our clinic. To define therapeutic responses the simplified disease activity index (SDAI) and American College of Rheumatology (ACR) responses were calculated.

Results:
Diagnostic specificity was >96% for all 3 anti-RA33 subtypes. Among the 255 RA patients, 11% tested positive for anti-RA33 IgG antibodies, 15% for IgM antibodies and 6% for IgA antibodies. Altogether, 62 patients (24%) had at least one type of anti-RA33 antibody: 24 patients were RF-negative, 26 were ACPA-negative and 18 were RF/ACPA double negative. Thus, in 32 patients (13%), anti-RA33 was the only antibody specificity. Regarding response to therapy, the percentage of SDAI50 responders (24%) was significantly lower (p=0.0117) in the group of patients testing positive for anti-RA33 antibodies of any isotype (with or without concomitant RF and/or ACPA) than in anti-RA33 negative (but RF/ACPA positive) patients (42% responders) and similar to the group of completely seronegative patients (21% responders). In contrast, regarding responses to MTX the percentage of SDAI50 responders was significantly higher (p<0.0001) among anti-RA33 positive patients (with or without concomitant RF and/or ACPA) (59% responders) compared to anti-RA33 negative (but RF/ACPA positive) patients (37% responders) and seronegative patients (24% responders).

Conclusion:
Apart from their added diagnostic value anti-RA33 antibodies of any isotype may have also prognostic value for prediction of therapeutic responses to MTX and TNFi treatment. Therefore anti-RA33 antibodies may be taken into consideration as additional diagnostic and prognostic markers that might become helpful tools in therapeutic decision making.

Disclosure: D. Sieghart, None; P. Studenic, None; F. Alasti, None; D. Aletaha, None; J. S. Smolen, AbbVie, Eli Lilly, Janssen, MSD, Pfizer Inc, Roche, 2,AbbVie, Amgen, AstraZeneca, Astro, Celgene, Celtrion, Eli Lilly, GSK, ILTOO, Janssen, MedImmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, UCB, 5,AbbVie, Amgen, AstraZeneca, Astro, Celgene, Celtrion, Eli Lilly, GSK, ILTOO, Janssen, MedImmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, UCB, 8; G. Steiner, Thermo Fisher Scientific (Phadia GmbH), 2.


Abstract Number: 2872

Elevated mTORC1 Signature in B Cells from Sjögren’s Syndrome Patients: mTOR Inhibition As a Novel Therapeutic Strategy to Halt B Cell Hyperactivity

Sofie L.M. Blokland1,2, Maarten R. Hillen3,4, Rina G.K. Kommer-Wichers4, Aike A. Kruize2, Timothy R.D.J. Radstake2,5, Jasper C.A. Broen2,4 and Joel A.G. van Roon2,4, 1Rheumatology & Clinical Immunology/ Laboratory of Translational Immunology, University Medical Center Utrecht, Utrecht, Netherlands, 2Department of Rheumatology & Clinical Immunology, University Medical Center Utrecht, Utrecht, Netherlands, 3Rheumatology & Clinical Immunology, University Medical Center Utrecht, Utrecht, Netherlands, 4Laboratory of Translational Immunology, UMC Utrecht, Utrecht, Netherlands, 5Laboratory of Translational Immunology, University Medical Center Utrecht, Utrecht, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Sjögren's Syndrome II: Pathogenesis, Autoantibodies and T-Cells
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose:
A hallmark feature of primary Sjögren’s syndrome (pSS) is B cell hyperactivity, including presence of autoantibodies, aberrant presence of B cells and plasma cells in the salivary glands, elevated serum IgG levels and increased risk of lymphoma development. The mTOR pathway is essential for cell growth, survival and proliferation of B cells and mTOR inhibition has been shown to be effective in immune B cell suppression in transplant patients and in treatment of B cell lymphomas. Interestingly, in a murine pSS model mTOR targeting inhibited lymphocytic infiltration in the lacrimal gland. However, mTOR activation in B cells has not been studied in pSS patients.

**Methods:** The expression of mTOR pathway related genes (MTOR, RPTOR, RICTOR, DEPTOR, AKT1, IGF1R, IGF1, PTEN) was measured in purified peripheral blood B cells and monocytes from pSS patients (n=12), non-Sjögren’s sicca patients (n=17) and healthy controls (HC, n=9). Gene expression was scrutinized for correlation with clinical parameters (lymphocytic focus scores (LFS), anti-SSA/SSB auto-antibodies, EULAR Sjögren’s Syndrome Disease Activity Index (ESSDAI), EULAR Sjögren’s Syndrome Patient Reported Index (ESSPRI), serum IgG levels, ESR), as well as correlation with B cell subset distribution, utilizing Flow Cytometry. Next, culture experiments were performed to study inhibition of the mTORC1 pathway by rapamycin (phosphorylated S6, kinase activity downstream of mTORC1) and its effect on B cell proliferation and IgG production by mTOR inhibition. Immunofluorescence was performed on pSS salivary gland tissue using colocalizing CD20 and pS6.

**Results:** RPTOR and IGF1R expression were significantly increased in B cells from pSS patients (p=0.019 and p=0.018, respectively) and correlate with serum IgG levels (r=0.429, p=0.020, and r=0.462, p=0.012). We did not observe a significant difference in monocytes. To better gauge the combined upregulation of mTOR related genes, we calculated a combined index statistic to indicate an mTOR signature. This signature was significantly elevated in pSS (p=0.027), correlating with serum IgG levels (r=0.463, p=0.011). Frequencies of memory and naïve B cells did not differ between pSS and HC in this cohort. Activation of B cells in culture resulted in phosphorylation of S6, B cell proliferation and IgG production in both HC and pSS. In the salivary glands of pSS patients immunofluorescent colocalization showed presence of large percentages of B cells with mTORC1 activity (pS6) at the lymphocytic loci. Inhibition of mTOR by rapamycin reduced B cell proliferation (80.8±9.9 vs 19.1±15.8%, p<0.001), IgG+ B cells (39.5±15.5 vs 11.1±5.7%, p=0.001) and IgG production (800.0±321.8 vs 37.9±70.4 ng/mL, p=0.0014).

**Conclusion:**

The increased mTORC1 signature in peripheral and salivary gland B cells from pSS patients correlates with B cell hyperactivity and IgG levels and can be targeted by rapamycin in vitro, representing a novel potential therapeutic strategy for pSS.

**Disclosure:** S. L. M. Blokland, None; M. R. Hillen, None; R. G. K. Kommer-Wichers, None; A. A. Kruize, None; T. R. D. J. Radstake, None; J. C. A. Broen, None; J. A. G. van Roon, None.


**Abstract Number:** 2873

**DNA Microarray Analysis Identifies Nuclear Receptor Subfamily 4 Group a Member 2 (NR4A2) As a Novel Molecule Involved in the Pathogenesis of Sjögren’s Syndrome**

Hiroyuki Takahashi, Hiroto Tsuboi, Hiromitsu Asashima, Hanae Kudo, Yuko Ono, Saori Abe, Yuya Kondo, Isao Matsumoto and Takayuki Sumida, Department of Internal Medicine, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Sjögren's Syndrome II: Pathogenesis, Autoantibodies and T-Cells

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 4:30PM-6:00PM

**Background/Purpose:** Some reports on DNA microarray analysis in labial salivary glands (LSGs) of Sjögren’s syndrome (SS) and healthy controls (HCs) showed that the genes associated with mononuclear infiltration were up-regulated in SS. However, since the controls were healthy individuals, it is possible that the results reflected nonspecific gene expression due to inflammatory cell infiltration. The purpose of this study was to examine the genes expressed specifically in LSGs of patients with SS by comparing them with those of patients with IgG4-related disease (IgG4-RD), which also show mononuclear inflammation and to identify the genes involved in the pathogenesis of SS.

**Methods:**
1) Gene expression in LSGs of SS patients (n=5), IgG4-RD patients (n=5) and HCs (n=3) was analyzed by DNA microarray. All patients with SS and IgG4-RD fulfilled the Japanese Ministry of Health criteria for the diagnosis of SS (1999) and the diagnostic criteria for IgG4-RD proposed in 2011 by the All Japan IgG4 team, respectively. After the obtained microarray data were normalized by FARMS algorithm, differentially expressed genes (DEGs) up-regulated in SS were identified in pairwise comparisons with IgG4-RD (false discovery rate<0.05) by rank products method. Approval for this study was obtained from the local ethics committee and a signed informed consent was obtained from each subject.

2) Validation of the results was performed by quantitative PCR (qPCR) using LSGs obtained from other patients with SS (n=15), IgG4-RD (n=12), and HC (n=6) than those examined by DNA microarray.

3) Protein production of the validated gene in LSGs was examined by immunofluorescence (IF) assay.

4) The molecular functions of the validated gene under the pathological condition of SS were examined using peripheral blood CD4+ T cells in vitro.

**Results:**

1) In patients with SS, 1785 up-regulated probe sets (corresponding to 1320 up-regulated genes) were identified as DEGs in comparison with those with IgG4-RD.

2) CXCL9, NR4A2, CD26, SGK1, IRF4 and PDK1 were selected as candidate genes for validation, according to rank<150, high expression levels, small variance and relation to T cell functions. qPCR confirmed up-regulation of NR4A2 in LSGs of SS compared with IgG4-RD.

3) IF staining showed higher production of NR4A2 in nuclei of CD4+ T cells and IL-17-producing cells in LSGs of SS, compared with IgG4-RD.

4) Overexpression of NR4A2 mRNA was observed in peripheral CD4+ T cells of SS patients, compared with HCs. The percentage of IL-17-producing peripheral CD4+ T cells under Th17-polarizing conditions correlated significantly with NR4A2 mRNA expression at baseline. Nuclear NR4A2 expression in Th17-polarized CD4+ T cells determined by cellular IF was significantly higher in SS than in HC. Importazole, an inhibitor of importin-β, inhibited nuclear transport of NR4A2 and Th17 polarization via suppression of IL-21 expression in naïve CD4+ T cells under Th17-polarizing conditions, but did not alter RORC expression.

**Conclusion:** NR4A2 seems to promote Th17 polarization via increased expression and intranuclear localization in CD4+ T cells of SS patients, which could play a critical role in the pathogenesis of SS.

**Disclosure:** H. Takahashi, None; H. Tsuboi, None; H. Asashima, None; H. Kudo, None; Y. Ono, None; S. Abe, None; Y. Kondo, None; I. Matsumoto, None; T. Sumida, None.

Thymic Stromal Lymphopoietin (TSLP) Expression Is Associated with Lymphoproliferation and Lymphoma in Primary Sjögren’s Syndrome

**Abstract Number:** 2874

**Thymic Stromal Lymphopoietin (TSLP) Expression Is Associated with Lymphoproliferation and Lymphoma in Primary Sjögren’s Syndrome**

Saviana Gandolfo1, Cinzia Fabro1, Michela Bulfoni2, Sabino Russi3, Luca Quartuccio1, Domenico Ettore Sansonno3, Carla Di Loreto2, Daniela Cesselli2 and Salvatore De Vita1, 1Rheumatology Clinic, Academic Hospital S. M. della Misericordia, Medical Area Department, University of Udine, Italy, Udine, Italy, 2Institute of Anatomic Pathology, Academic Hospital S. M. della Misericordia, Medical Area Department, University of Udine, Italy, Udine, Italy, 3Department of Biomedical Sciences and Human Oncology, University of Bari, Italy, Bari, Italy

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Sjögren’s Syndrome II: Pathogenesis, Autoantibodies and T-Cells

**Session Type:** ACR Concurrent Abstract Session
**Background/Purpose:** Primary Sjögren’s syndrome (pSS) is an autoimmune and lymphoproliferative systemic disease with B cell hyperactivity and increased risk of non-Hodgkin lymphoma (NHL) evolution. In pSS, the salivary gland (SG) epithelium plays a crucial role in modulating the autoimmune response. Thymic stromal lymphopoietin (TSLP) is an epithelial lymphopoietic cytokine involved in the maintenance of immune tolerance at interfaces with the environment and in regulating lymphocyte homeostasis, acting also as a B cell growth factor. The aim of this study is to investigate TSLP expression in serum and SG biopsies, as well as TSLP function on peripheral blood lymphocytes (PBLs) in pSS patients, stratified according to their lymphoproliferative histopathologic status, from fully benign MALT lesions (fbSS) to myoepithelial sialadenitis (MESA) and to NHL.

**Methods:** Serum TSLP levels were determined by ELISA in 38 pSS patients (13 fbSS, 13 MESA, 12 NHL; all positive for the latest pSS ACR/EULAR Classification Criteria and for anti-SSA antibodies) and 33 controls (20 healthy blood donors, HBDs, and 13 non-autoimmune sicca, nSS). TSLP expression was also studied by RT-PCR and by immunohistochemistry in SG biopsies of all the pSS patients and nSS controls. Immunofluorescence double-staining was performed to characterize TSLP positive cells in SG. Correlations with clinical and histopathologic parameters were investigated. Finally, PBLs from both patients and controls were cultured and stimulated with TSLP and phenotypic changes evaluated by flow cytometry.

**Results:** TSLP serum levels were significantly higher in fbSS compared to nSS (p=0.048) and to HBDs (p<0.0001). A significant increase in TSLP levels occurred from fbSS to MESA (p=0.0015) and to NHL (vs fbSS p<0.0001; vs MESA p=0.0025), where the increase was dramatic. A positive significant correlation between serum TSLP and ESSDAI was found (p<0.0001). By contrast, in SG biopsies TSLP showed a pattern opposite to the serum by immunohistochemistry both in the salivary epithelium and in the whole inflammatory infiltrate: a significant declining staining of TSLP was in fact found from fbSS to MESA and NHL. Strikingly, however, the number of TSLP positive B cells progressively increased with the progression of lymphoproliferation, with the maximum number of TSLP positive B cells being detected in NHL. *In vitro* stimulation assays on cultured pSS PBLs showed a marked TSLP ability to promote proliferation and activation of B cells, and to induce IgG production.

**Conclusion:** A pathogenetic role of TSLP is herein suggested in pSS for the first time. Overall TSLP, which promotes B cell expansion, shows a progressive increase from benign to malignant B cell lymphoproliferation in pSS. The increasing serum levels of TSLP, coupled with the increasing expression by B cells themselves, may support a possible autocrine pathogenetic mechanism. By contrast, the observed decreasing production by the salivary epithelium suggests an insufficient response to regulate B cell expansion. Further studies are definitely worthwhile, including the analysis of TSLP as a biomarker to stratify pSS.

**Disclosure:** S. Gandolfo, None; C. Fabro, None; M. Bulfoni, None; S. Russi, None; L. Quartuccio, None; D. E. Sansonno, None; C. Di Loreto, None; D. Cesselli, None; S. De Vita, None.

**Abstract Number:** 2875

**Molecular Features Define Unique Sjögren’s Syndrome Patient Subsets**

Judith A. James1, Joel M. Guthridge2, Hua Chen3, Rufei Lu3, Rebecka L. Bourn3, Alan N. Baer4, Ghaith Noaiseh5, Anne Parke6, Andreea Coca7, Tammy Utset8, Mark C. Genovese9, Teresa Aberle3, Daniel J. Wallace10, Karen Boyle11, Lynette Keyes-Elstein12, Nathalie Franchimont13, Eugene St. Clair14, Virginia Pascual15, Paul J. Utz16 and Kathy L. Sivils2, 1Arthritis & Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 2Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 3Arthritis and Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, 4Medicine (Rheumatology), Johns Hopkins University School of Medicine, Baltimore, MD, 5University of Pittsburgh Medical Center, Pittsburgh, PA, 6University of Connecticut, Farmington, CT, 7University of Rochester Medical Center, Rochester, NY, 8University of Chicago, Chicago, IL, 9Stanford University Medical Center, Palo Alto, CA, 10UCLA, Beverly Hills, CA, 11Rho Federal Systems, Inc, Chapel Hill, NC, 12Rho Federal Systems, Inc., Chapel Hill, NC, 13Biogen, Cambridge, MA, 14Department of Medicine, Duke University Medical Center, Durham, NC, 15Baylor Institute for Immunology Research, Baylor Research Institute, Dallas, TX, 16Medicine, Stanford University School of Medicine, Stanford, CA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Sjögren's Syndrome II: Pathogenesis, Autoantibodies and T-Cells
**Session Type:** ACR Concurrent Abstract Session  
**Session Time:** 4:30PM-6:00PM

**Background/Purpose:** Immunologic heterogeneity in primary Sjogren’s syndrome (pSS) poses a challenge when selecting a therapeutic for a given patient or when assembling patient cohorts for research or clinical trials. Heterogeneity in the IFN pathways within pSS is established, but little is known about potential variations in other immune pathways that may influence the disease course or response to treatment. This study characterized and clustered pSS patients by molecular phenotypes.

**Methods:** All pSS patients (n=52) met AECG classification criteria, had at least one systemic manifestation and had stimulated salivary flow of >0.1 mL/min. Patients were assessed for proteomic and genomic markers to enable systems level molecular phenotyping of these patients. Proteomic analysis included 30 serum cytokines, chemokines, soluble receptors which passed stringent quality control measures, and 13 anti-nuclear autoantibodies (anti-dsDNA, chromatin, ribosomal P, Sm, Sm/RNP, RNP, centromere B, Scl-70, and Jo-1) by multiplex, bead-based assay and ELISAs. Correlated gene expression signatures were derived from gene expression microarray data based on the most informative molecular variables by random forest methods.

**Results:** Expression modules identified three distinct clusters of pSS patients. Cluster 1 showed no significantly elevated gene expression signatures in interferon or inflammation and only modest elevations in platelet or erythrocyte expression profiles. Cluster 2 showed the strongest interferon and inflammation signatures. Patients in Cluster 3 had a moderate interferon signature, but with a weak inflammation signature. Anti-Ro and anti-La responses were present in patients in all three clusters. Cluster 2 showed the highest levels of IP-10, MIG, LIGHT, and BLyS, corresponding to the strong interferon and inflammation signatures. Cluster 3, characterized by a weak inflammatory signature and mixed interferon patterns, showed increased IP-10 compared to Cluster 1, and non-significant increases in IL-2RA, IL-1α, and sEselectin compared to Clusters 1 and 2 (Figure).

**Conclusion:** Molecular profiles encompassing interferon, inflammation, and other molecular signatures can be used to separate patients with pSS into distinct groups. Profiles correlating with treatment effects may be useful for clinical trial design or treatment selection.

**Disclosure:** J. A. James, None; J. M. Guthridge, None; H. Chen, None; R. Lu, None; R. L. Bourn, None; A. N. Baer, Novartis, Boston Pharmaceuticals, and Bristol-Myers, 5; G. Noaiseh, None; A. Parke, None; A. Coca, None; T. Utset, None; M. C. Genovese, None; T. Aberle, None; D. J. Wallace, None; K. Boyle, None; L. Keyes-Elstein, None; N. Franchimont, None; E. St. Clair, Bristol-Myers Squibb, 2,Bristol-Myers Squibb, 5,AbbVie, 5,UpToDate, 7; V. Pascual, None; P. J. Utz, None; K. L. Sivils, None.


**Abstract Number:** 2876

**Analysis of Autoantibody Reactivity to the Complete Human Peptidome By Phage Immunoprecipitation Sequencing Does Not Identify a Predominant Novel Autoantibody in Sjogren’s Syndrome**

Tiezheng Yuan¹, Michelle Petri², Alan N. Baer³ and H. Benjamin Larman¹, ¹Pathology (Immunology), Johns Hopkins University School of Medicine, Baltimore, MD, ²Medicine (Rheumatology), Division of Rheumatology, Johns Hopkins University School of Medicine, MD, USA, Baltimore, MD, ³Medicine (Rheumatology), Johns Hopkins University School of Medicine, Baltimore, MD
SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Sjögren's Syndrome II: Pathogenesis, Autoantibodies and T-Cells
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose:
An unbiased and comprehensive approach to the analysis of Sjögren’s syndrome (SS) antibody repertoires would provide important data on its pathogenesis. Phage ImmunoPrecipitation sequencing (PhIP-seq) utilizes next generation DNA sequencing analysis of a phage-displayed human peptidome to characterize the binding specificities of autoantibody repertoires. We utilized PhIP-seq to define the serum autoantibody repertoire in SS, with the goal of revealing novel, shared SS-specific, self-antigens, which are involved in disease pathogenesis.

Methods:
The study cohort consisted of 193 SS patients consecutively evaluated in the Hopkins Sjögren’s Center, each with independent anti-Ro60 [immunoprecipitation (IP) using IVTT generated S35-Ro60] and anti-Ro52/-SSB (ELISA) antibody testing and positive results in 181 (94%). Control cohorts included 47 SLE patients with positive anti-SSA/SSB serology but without SS (Hopkins Lupus Center) and 301 healthy individuals (United Kingdom repository). Serum from each individual was screened against an overlapping 90-mer human peptidome library using automated PhIP-seq. Peptide enrichments were quantified as number of standard deviations from expected abundance, based on analysis of negative control (no serum) IPs (‘z-scores’). For each protein, analyses of the most enriched peptide were used to identify autoantibodies that associate non-randomly among these subsets of SS patients and controls.

Results:
The top SS-associated antibodies were anti-Ro60 and anti-Ro52, the benchmark SS autoantibodies. When analyzed using a z-score cutoff of 10 and compared to conventional assay results, the sensitivity and specificity of PhIP-seq autoantibody detection in the SS cohort was 49% and 88% for anti-Ro60, 84% and 88% for anti-Ro52, and 32% and 99% for anti-SSB. By PhIP-seq, most anti-SSA positive SS patients had either anti-Ro52 alone (40.6%) or both anti-Ro52 and -Ro60 (58.6%), but rarely anti-Ro60 alone (0.8%). In both SS and SLE controls, anti-Ro52 was directed primarily to the 1-90 and 136-205 amino acid epitopes and anti-Ro60 to the 181-270 and 226-295 amino acid epitopes. Using a minimum frequency cut-off of 3% and a SS-association of 3-fold versus lupus and healthy controls, we identified antibodies to 4 autoantigens, including 2 previously discovered SS-associated minor antigens.

Conclusion:
A comprehensive analysis of the antibody repertoire to the complete human peptidome in SS using PhIP-seq did not reveal a predominant novel autoantigen. This technology is limited to detection of antibodies that recognize linear epitopes, and thus may fail to reveal antibodies directed against conformational or post-translationally modified epitopes. In this SS cohort, antibodies to linear Ro60 epitopes were rarely formed in the absence of antibodies targeting linear Ro52 epitopes. The two novel SS-associated autoantigens are undergoing additional validation.

Supported by the Sjogren’s Syndrome and Jerome L. Greene Foundations.

Disclosure: T. Yuan, None; M. Petri, Exagen, 2; A. N. Baer, None; H. B. Larman, None.

Abstract Number: 2877

Premature Senescence of Naive CD4+ T-Cells in Primary Sjogren’s Syndrome

Patrizia Fasching1, Johannes Fessler2, Andrea Raicht3, Angelika Lackner2, Josef Hermann2, Rusmir Husic1, Sabrina Hammerl4, Winfried Graninger2, Wolfgang Schwinger2, Christian Dejaco1 and Martin Stradner1, 1Department of Rheumatology and Immunology,
SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Sjögren's Syndrome II: Pathogenesis, Autoantibodies and T-Cells
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose:
Lymphopenia is a frequent finding in primary Sjögren’s syndrome (pSS) affecting mostly the CD4+ T-cell population. Here we examine possible underlying defects in thymic output and premature senescence of CD4+ T-cells.

Methods:
We included 47 pSS patients and 50 healthy controls (HCs) in a prospective, cross-sectional study. Patients and HCs were separated into two distinct age-groups for analysis of age-dependent differences (≤48 years [SS n=10, HC n=26]; >48 years [pSS n=37, HC n= 24]). Prevalence of T-cell subpopulations was assessed by flow cytometry according to standard surface staining protocols. Naive CD4+ T-cells were isolated by MACS technology for telomere length and T-cell receptor excision circle (TREC) assessment by real-time PCR. Moreover, telomerase activity was analyzed according to the Telomeric Repeat Amplification Protocols (TRAP).

Results:
We found lower numbers of CD4+ T-cells in pSS patients compared to age matched healthy controls (560/µl vs. 943/µl, p<0.0001). The reduced naïve subset accounted for most of this difference (203/µl vs. 429/µl, P=0.0001). Furthermore, the number of TRECs in naïve CD4+ T-cells was already reduced in young pSS patients (58 copies/ng DNA vs. 2058 copies/ng DNA, p<0.0001) and was furthermore decreased in older patients (14 copies/ng DNA vs. 117 copies/ng DNA, p=0.000) suggesting reduced thymic output or extensive proliferative history. To test for a proliferative history we performed telomere length as well as telomerase activity analysis. Young patients displayed significantly shortened telomeres compared to age-matched controls (6.5kbp vs. 7.0kbp, p=0.011) while telomeres of old patients were not significantly different from age-matched controls. In healthy individuals shorter telomeres resulted in an elevation of telomerase activity, a finding that we could not observe in pSS patients.

Conclusion:
Our data indicate an extensive replicative history of naïve CD4+ T-cells in pSS resulting in premature shortening of telomeres. In contrast to HC, naïve CD4+ T-cells in pSS are unable to induce telomerase activity. This may lead to the reduction of the naïve CD4+ T-cell pool resulting in CD4+ T-cell lymphopenia.

Disclosure: P. Fasching, None; J. Fessler, None; A. Raicht, None; A. Lackner, None; J. Hermann, None; R. Husic, None; S. Hammerl, None; W. Graninger, None; W. Schwinger, None; C. Dejaco, None; M. Stradner, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/premature-senescence-of-naive-cd4-t-cells-in-primary-sjogrens-syndrome

Abstract Number: 2878

Efficacy and Safety Results of Guselkumab in Patients with Active Psoriatic Arthritis over 56 Weeks from a Phase 2a, Randomized, Double-Blind, Placebo-Controlled Study

Atul A. Deodhar1, Alice B Gottlieb2, Wolf-Henning Boehncke3, Bin Dong4, Yuhua Wang4, Yanli Zhuang4, William Barchuk5, Xie L. Xu5 and Elizabeth Hsia4, 1Division of Arthritis & Rheumatic Diseases OP09, Oregon Health & Science University, Portland, OR, 2Department of Dermatology, New York Medical College, Valhalla, NY, 3Geneva University Hospital and University of Geneva, Geneva, Switzerland, 4Janssen Research & Development, LLC, Spring House, PA, 5Janssen Research & Development, LLC, San Diego, CA

First publication: September 18, 2017
Background/Purpose: Evaluate efficacy and safety of guselkumab (GUS) in patients (pts) with active psoriatic arthritis (PsA) over 56 weeks (wks).

Methods: Pts w/active PsA (defined as ≥3 tender & ≥3 swollen joints, C-reactive protein ≥3 mg/L) and ≥3% body surface area (BSA) of plaque psoriasis despite current or previous treatment w/standard-of-care therapies, including previous TNF inhibitor therapy, were eligible to participate and were randomized 2:1 to receive GUS 100 mg subcutaneously or placebo (PBO) at wk 0, 4, and every 8 wks thereafter through wk44. At wk16, pts from either group with <5% improvement from baseline in both swollen and tender joint counts were eligible for early escape (EE) to open-label ustekinumab. All remaining PBO pts crossed-over to receive GUS 100 mg at wks24, 28, 36, and 44. At wk56, a post-treatment follow-up visit was conducted. Efficacy post wk24 through wk44 and wk56 was evaluated in pts who did not EE and continued treatment at wk24 (post wk24 efficacy analysis set) based on observed data. The wk24 data in this population were included as a reference.

Results: 149 pts were randomized to receive study agent (PBO: 49, GUS: 100). The study met its primary and all secondary endpoints through wk24. At wk24, 29 pts in the PBO group crossed over to receive GUS, of which 28 completed treatment through wk44. 86 pts in the GUS group continued treatment at wk24 and 84 pts completed treatment through wk44. Post wk24, ACR 20/50/70 and PASI 75/90/100 responses improved in PBO to GUS crossover pts and were well-maintained in GUS pts through wk44 (last efficacy assessments while on drug) and wk56 (final follow-up visit) (Table). The efficacy results from wk24 through wk44 and wk56 are summarized in Table.

Through wk56, 17.2% of PBO—GUS, 46.0% of GUS, and 39.5% of the combined GUS pts had ≥1 AEs, of which infections and infestations were the most commonly reported (3.4%, 27.0%, and 21.7%, respectively). Post wk24, there was no disproportional increase in overall AE frequency, or infections and infestations among GUS pts with longer exposure. Through wk56, among 129 pts who received GUS, there was 1 pt with malignancy (basal cell carcinoma), 1 pt with 2 serious infections (both pneumonia), 6 pts reported ≥1 SAEs (myocardial infarction, osteoarthritis, pupils unequal, radius fracture, pneumonia, ulcerative keratitis), 2 pts discontinued treatment due to AEs, 1 pt had neutropenia meeting NCI-CTCAE toxicity grade 3, and 6 pts were positive for antibodies to GUS. No deaths occurred through wk56.

Conclusion: In pts with active PsA and ≥3% BSA of psoriasis, GUS demonstrated substantial benefits on joint symptoms, physical function, psoriasis, enthesitis, dactylitis, and quality of life, and efficacy was well-maintained through wk56. GUS was well-tolerated with no unexpected safety findings in this population after ~1 year of exposure.
<table>
<thead>
<tr>
<th>Efficacy Endpoints</th>
<th>Week 24*</th>
<th>Week 44</th>
<th>Week 56</th>
<th>Week 24</th>
<th>Week 44</th>
<th>Week 56</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACR 20</td>
<td>9/29 (31.0%)</td>
<td>21/28 (75.0%)</td>
<td>22/27 (81.5%)</td>
<td>57/86 (66.3%)</td>
<td>65/84 (77.4%)</td>
<td>61/83 (73.5%)</td>
</tr>
<tr>
<td>ACR 50</td>
<td>5/29 (17.2%)</td>
<td>13/28 (46.4%)</td>
<td>18/27 (66.7%)</td>
<td>34/86 (39.5%)</td>
<td>39/84 (46.4%)</td>
<td>44/83 (53.0%)</td>
</tr>
<tr>
<td>ACR 70</td>
<td>1/29 (3.4%)</td>
<td>7/28 (25.0%)</td>
<td>8/28 (28.6%)</td>
<td>14/86 (16.3%)</td>
<td>22/84 (26.2%)</td>
<td>27/83 (32.5%)</td>
</tr>
<tr>
<td>PASI 75</td>
<td>6/29 (20.7%)</td>
<td>23/28 (82.1%)</td>
<td>22/27 (81.5%)</td>
<td>71/86 (82.6%)</td>
<td>75/83 (90.4%)</td>
<td>70/82 (85.4%)</td>
</tr>
<tr>
<td>PASI 90</td>
<td>3/29 (10.3%)</td>
<td>21/28 (75.0%)</td>
<td>20/27 (74.1%)</td>
<td>61/86 (70.9%)</td>
<td>68/83 (81.9%)</td>
<td>64/82 (78.0%)</td>
</tr>
<tr>
<td>PASI 100</td>
<td>3/29 (10.3%)</td>
<td>19/28 (67.9%)</td>
<td>15/27 (55.6%)</td>
<td>38/86 (44.2%)</td>
<td>53/83 (63.9%)</td>
<td>47/82 (57.3%)</td>
</tr>
<tr>
<td>Mean (SD) change from baseline in HAQ-DI score</td>
<td>-0.19 (0.581)</td>
<td>-0.63 (0.612)</td>
<td>-0.67 (0.558)</td>
<td>-0.46 (0.530)</td>
<td>-0.54 (0.598)</td>
<td>-0.55 (0.621)</td>
</tr>
<tr>
<td>Median (IQR) percent change from baseline in Enthesitis Score&lt;sup&gt;a&lt;/sup&gt;</td>
<td>-50.0 (-100.0, 0.0)</td>
<td>-100.0 (-100.0, -60.0)</td>
<td>-100.0 (-100.0, -35.0)</td>
<td>-100.0 (-100.0, -50.0)</td>
<td>-100.0 (-100.0, -50.0)</td>
<td>-100.0 (-100.0, -50.0)</td>
</tr>
<tr>
<td>% of patients with unresolved enthesitis&lt;sup&gt;a&lt;/sup&gt;</td>
<td>12/18 (66.7%)</td>
<td>8/17 (47.1%)</td>
<td>6/16 (37.5%)</td>
<td>26/67 (38.8%)</td>
<td>25/66 (37.9%)</td>
<td>19/65 (29.2%)</td>
</tr>
<tr>
<td>Median (IQR) percent change from baseline in dactylitis&lt;sup&gt;b&lt;/sup&gt;</td>
<td>-45.0 (-70.8, 0.0)</td>
<td>-100.0 (-100.0, -100.0)</td>
<td>-100.0 (-100.0, -100.0)</td>
<td>-100.0 (-100.0, -100.0)</td>
<td>-100.0 (-100.0, -100.0)</td>
<td>-100.0 (-100.0, -100.0)</td>
</tr>
<tr>
<td>% of patients with unresolved dactylitis&lt;sup&gt;b&lt;/sup&gt;</td>
<td>13/16 (81.3%)</td>
<td>2/16 (12.5%)</td>
<td>1/16 (6.3%)</td>
<td>20/50 (40.0%)</td>
<td>10/49 (20.4%)</td>
<td>12/48 (25.0%)</td>
</tr>
<tr>
<td>Mean (SD) change from baseline in SF-36 physical component summary (PCS) score</td>
<td>2.13 (7.365)</td>
<td>8.02 (8.647)</td>
<td>N/A</td>
<td>7.40 (7.448)</td>
<td>8.34 (8.783)</td>
<td>N/A</td>
</tr>
<tr>
<td>Mean (SD) change from baseline in SF-36 mental component summary (MCS) score</td>
<td>0.51 (6.770)</td>
<td>5.53 (9.013)</td>
<td>N/A</td>
<td>5.45 (9.081)</td>
<td>4.56 (9.548)</td>
<td>N/A</td>
</tr>
<tr>
<td>% of patients achieving Minimal Disease Activity (MDA)</td>
<td>1/29 (3.4%)</td>
<td>8/28 (28.6%)</td>
<td>N/A</td>
<td>23/86 (26.7%)</td>
<td>29/84 (34.5%)</td>
<td>N/A</td>
</tr>
</tbody>
</table>
Among the patients with enthesitis at baseline

Among the patients with dactylitis at baseline

*Measured prior to receiving guselkumab


Switching from Adalimumab to Chs-1420: A Randomized, Double-Blind Global Clinical Trial in Patients with Psoriasis and Psoriatic Arthritis

Jennifer Hodge, Hong Tang, Paula O'Connor and Barbara Finck, Coherus BioSciences, Inc., Redwood City, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment IV
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: CHS-1420 is a proposed biosimilar to adalimumab. A phase 3, randomized, double-blind, multicenter study evaluated the equivalence of CHS-1420 to adalimumab in patients with moderate-severe plaque PsO, including patients with psoriatic arthritis (PsA).

Methods: Male and female patients (aged ≥18 years) were randomized 1:1 to CHS-1420 or adalimumab (80 mg, then 40 mg every other week) for 16 weeks (Treatment Period 1). At Week 16, half the patients receiving adalimumab were switched to CHS-1420, and half continued adalimumab; all patients receiving CHS-1420 continued CHS-1420 for 8 weeks (Treatment Period 2).

Results: 545 patients were randomized into the study. A total of 503 patients (92.3%) completed Treatment Period 2, including 250 patients in the CHS-1420/CHS-1420 group, 124 subjects in the switching group, and 129 subjects in the adalimumab/adalimumab group. Equivalence of CHS-1420 to adalimumab was established based on the primary endpoint (PASI75 at Week 12). A PASI75 at Week 24 was achieved by 84.6%, 81.6%, and 88.3% of patients in the CHS-1420/CHS-1420, switching, and adalimumab/adalimumab groups, respectively, demonstrating maintenance of response. No statistically significant difference was found between treatment groups.

Conclusion: This randomized, double-blind, global clinical trial demonstrated equivalence of CHS-1420 to adalimumab based on the primary endpoint (PASI75 at Week 12). Patients who switched from adalimumab to CHS-1420 at Week 16 had similar efficacy and safety results at Week 24 compared to patients who received only CHS-1420 or adalimumab. Results in patients with PsA were similar across treatment groups.
Clinical Evolution of Patients with Inflammatory Back Pain: A Population-Based Longitudinal Cohort Study

Runsheng Wang¹, Cynthia S. Crowson², Kerry Wright³ and Michael Ward⁴, ¹Rheumatology, Columbia University Medical Center, New York, NY, ²Health Sciences Research, Mayo Clinic College of Medicine and Science, Rochester, MN, ³Rheumatology, Mayo Clinic, Rochester, MN, ⁴NIH/NIAMS, Bethesda, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment IV
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Title: Clinical Evolution of Patients with Inflammatory Back Pain: a Population-Based Longitudinal Cohort Study

Authors: Runsheng Wang¹, Cynthia Crowson², Kerry Wright³, Michael Ward³

1. Columbia University Medical Center, New York, NY
2. Mayo Clinic, Rochester, MN
3. NIH/NIAMS, Bethesda, MD

Background/Purpose: Inflammatory back pain (IBP) is an early manifestation and a key feature of spondyloarthritis (SpA). However, the natural history of IBP has not been well defined. Significant differences exist between the prevalence of IBP (3-6%) and prevalence of SpA (0.5-1%), suggesting either that IBP often resolves or is due to conditions other than SpA. The objective of this study was to investigate the long-term outcomes of IBP, and clinical predictors of progression to SpA.

Methods: A population-based cohort of patients with incident IBP in 2000-2003 among residents of a geographically defined area was established retrospectively. Using diagnostic codes for back pain on clinic visits, we screened and validated the presence of new-onset IBP among patients age 16 to 35 via manual medical record review. Verified patients either met the Calin, Berlin, or ASAS criteria, or were considered by their treating rheumatologist to have IBP. We collected data on clinical SpA features, HLA-B27 status, inflammatory markers, and imaging, and followed their outcomes until July 2016. Aalen-Johansen methods (a multistate generalization of cumulative incidence with adjustment for competing risks) were used to examine their evolution to one of 3 outcomes: progression to SpA, progression to a non-SpA diagnosis, or resolution of back pain. Recursive partitioning with a time to event outcome was used to identify predictors for progression to SpA.

Results: After screening 5304 patients, we identified 124 subjects with new-onset IBP from 2000 to 2003. After a median of 13.2 years of follow up, progression to SpA occurred in 39 patients (Figure). The probability of having SpA at 5, 10, 15 years was 24%, 30%, and 33%, respectively. In almost half of the patients, their IBP resolved during follow up. Progression was seen in 85% of 13 patients with a history of uveitis, and 26% of 111 patients without history of uveitis by 15 years after IBP incidence. Among those without a history of uveitis, progression was seen in 32% of men and 14% of women by 15 years.

Conclusion: Less than 1/3 of patients with new-onset IBP progress to SpA over more than a decade of follow up, while many resolve. History of uveitis is the most important predictor for progression.
Pre-Existing Psoriasis Is Predictive for Clinical Relapse after Drug-Free Remission Induced By Therapy with Golimumab in Early Peripheral Spondyloarthritis

Philippe Carron¹, Gaëlle Varkas², Thomas Renson³, Roos Colman⁴, Dirk Elewaut⁵ and Filip van Den Bosch⁶, ¹Rheumatology, Department of Rheumatology Ghent University Hospital, Ghent, Belgium, ²Laboratory for Molecular Immunology and Inflammation, Department of Rheumatology, VIB, Ghent University and Ghent University Hospital, Ghent, Belgium, ³Rheumatology, Ghent University Hospital, GENT, Belgium, ⁴Department of Public Health, Ghent University, Ghent, Belgium, Biostatistics Unit,Ghent University, Ghent, Belgium, Ghent, Belgium, ⁵VIB Inflammation Research Center, University of Ghent, Ghent, Belgium, ⁶Rheumatology, Ghent University Hospital, Gent, Belgium

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment IV
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: The use of new treatment strategies in early stages of spondyloarthritis (SpA) makes it possible to achieve remission or low disease activity in more patients than before. Furthermore, one could speculate that there is a possibility of a “window of opportunity” for drug-free remission in peripheral SpA (pSpA), referring to the existence of a transient time frame in which the disease is more susceptible to treatment leading to better outcomes. The objective is to evaluate drug-free clinical remission after induction therapy with golimumab (GLM) in patients with active pSpA in a very early stage of the disease. To identify patient characteristics predicting sustained remission or occurrence of relapse after drug withdrawal.

Methods: CRESPA (Clinical REmission in peripheral SPondyloArthritis) is an ongoing monocentric study of golimumab treatment in pSpA patients. Eligible patients were ≥18 years and fulfilled the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for pSpA. All patients had a symptom duration <12 weeks. Clinical remission was defined as the absence of arthritis, enthesitis and dactylitis on clinical examination. If patients were in clinical remission at two consecutive major visits (at week 12, 24, 36 and 48), treatment was withdrawn. Patients were prospectively followed to assess the rate of sustained drug-free clinical remission and clinical relapse.

Results: Patient demographics, baseline characteristics and 24-week results of the placebo-controlled phase have been described previously¹. 82% (49/60) of patients fulfilled sustained clinical remission criteria. At week 24, 30 patients already fulfilled criteria for sustained remission; at weeks 36 and 48, respectively 11 and 8 patients additionally reached this status. At present, 53% (26/49) of these patients are still in drug-free sustained clinical remission (follow-up between 18 and 58 months). The mean time for clinical relapse upon medication withdrawal was 31 weeks. Pre-existing psoriasis at baseline was predictive for clinical relapse whereas polyarticular disease (SJC>5) and psoriasis were not predictive for sustained clinical remission after treatment withdrawal. Fig 1 shows
the percentages of patients that achieved sustained clinical remission, that are still in drug-free remission or experienced clinical relapse after treatment withdrawal for the total group and by subtype SpA.

**Conclusion:** Very early treatment with GLM resulted in sustained clinical remission in more than 80% of patients with pSpA, including PsA. Upon drug withdrawal, more than 50% remain in drug-free remission (with a minimum follow-up of 18 months). Clinical relapse is more often observed in PsA patients. Retreatment with golimumab upon clinical relapse resulted in similar responses.


<table>
<thead>
<tr>
<th>Total population</th>
<th>Fulfilling Sustained Clinical Remission Criteria</th>
<th>Still in Drug-free Clinical Remission</th>
<th>Clinical relapse upon Treatment Withdrawal</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SpA subtype</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PsA (fulfilling CASPAR criteria)</td>
<td>60/60 (100%)</td>
<td>49/60 (81.7%)</td>
<td>26/49 (53%)</td>
</tr>
<tr>
<td>Reactive Arthritis</td>
<td>23/60 (38.3%)</td>
<td>17/23 (73.9%)</td>
<td>5/17 (29.4%)</td>
</tr>
<tr>
<td>Reactive Arthritis</td>
<td>2/60 (3.3%)</td>
<td>2/2 (100%)</td>
<td>2/2 (100%)</td>
</tr>
<tr>
<td>Reactive Arthritis</td>
<td>3/60 (5%)</td>
<td>3/3 (100%)</td>
<td>0/3 (0%)</td>
</tr>
<tr>
<td>Reactive Arthritis</td>
<td>1/60 (1.7%)</td>
<td>0/1 (0%)</td>
<td>NA</td>
</tr>
<tr>
<td>Reactive Arthritis</td>
<td>1/60 (1.7%)</td>
<td>1/1 (100%)</td>
<td>0/1 (0%)</td>
</tr>
<tr>
<td>pSpA HLA B27+</td>
<td>32/60 (53.3%)</td>
<td>29/32 (90.6%)</td>
<td>18/29 (62.1%)</td>
</tr>
<tr>
<td>pSpA HLA B27-</td>
<td>28/60 (46.7%)</td>
<td>20/28 (71.4%)</td>
<td>8/20 (40%)</td>
</tr>
</tbody>
</table>

**Disclosure:** P. Carron, None; G. Varkas, None; T. Renson, None; R. Colman, None; D. Elewaut, Scientific Research Flanders; Research Council Ghent University; Interuniversity Attraction Pole., 2,Boehringer Ingelheim; Pfizer; UCB; Merck; Novartis; Janssen; Abbvie, 5; F. van Den Bosch, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/pre-existing-psoriasis-is-predictive-for-clinical-relapse-after-drug-free-remission-induced-by-therapy-with-golimumab-in-early-peripheral-spondyloarthritis

**Abstract Number:** 2882

**IgG Galactosylation Status Combined with MYOM2 SNP Precisely Predicts Anti-TNF Response in Ankylosing Spondylitis**

Jing Liu¹, Shifang Ren², Zhenmin Niu¹, Qi Zhu³, Wei Wan⁴, Jing Han⁵, Yanyun Ma⁵, Weilin Pu⁶, Yuan Li¹, Xia Xu⁴, Yi Wang⁵, Dongbao Zhao⁴, Hui Zhang⁷, Feng Qian⁵, Xiaodong Zhou⁸, John D. Reveille⁹, Li Jin¹³¹, Dong-yi He⁵, Hejian Zou¹¹¹²¹, Jianxin Gu² and Jucun Wang¹⁰¹²¹³. ¹State Key Laboratory of Genetic Engineering, Collaborative Innovation Center for Genetics and Development, School of Life Sciences, Fudan University, Shanghai, China, ²Department of Biochemistry and Molecular Biology, Key Laboratory of Glycoconjugate Research Ministry of Public Health, School of Basic Medical Sciences, Fudan University, Shanghai, China, ³Institute of Arthritis Research, Shanghai Academy of Chinese Medical Sciences, Guanghua Integrative Medicine Hospital, Shanghai, China, ⁴Department of Rheumatology and Immunology, Shanghai Hospital, Shanghai, China, ⁵Ministry of Education Key Laboratory of Contemporary Anthropology, School of Life Sciences, Fudan University, Shanghai, China, ⁶State Key Laboratory of Genetic Engineering, Collaborative Innovation Center for Genetics and Development, School of Life Sciences, Fudan University, Shanghai, China, ⁷State Key Laboratory of Genetic Engineering, Collaborative Innovation Center for Genetics and Development, School of Life Sciences, Fudan University, Shanghai, China, ⁸National Center for Rheumatology, University of Texas McGovern Medical School, Houston, TX, ⁹University of Texas McGovern Medical School, Houston, TX, ¹⁰Fudan-Taizhou Institute of Health Sciences, Taizhou, China, ¹¹Division of Rheumatology,
Ankylosing spondylitis (AS) is an immune-mediated inflammatory disorder of spine and sacroiliac joints, which could lead to bony fusion of vertebral joints. TNF-blockers have a high efficacy in treating AS, yet up to 40% of AS patients show poor or even no response to this treatment. We aim to build an approach to predict the response prior to clinical treatment.

Methods: Ninety-two AS patients undergoing etanercept treatment were recruited and patients who did not fulfill BASDAI50 or ASAS40 at week 12 after starting treatment were considered poor-responders. The IgG galactosylation (IgG-Gal) ratio was calculated and candidate SNPs in patients treated with etanercept were examined. Machine-learning models and cross-validation were conducted to predict responsiveness.

Results: Both IgG-Gal ratio at each drug delivery and differential IgG-Gal ratios between week 0 and weeks 2, 4, 8, 12 showed significant differences between responders and poor-responders (Fig. 1A, B). AUC of the IgG-Gal ratio prediction model was 0.8 after cross-validation, significantly higher than current clinical indices, including CRP, ESR, BASDAI, BASFI and ASDAS. In addition, one MYOM2 SNP was found significantly associated with drug response (Table 1) (p=0.000576). Thus, a three-stage approach consisting of baseline IgG-Gal ratio, differential IgG-Gal ratio in 2 weeks, and the MYOM2 SNP genotype was conducted as follows (Fig. 2): **Stage I**: The IgG-Gal ratio of all AS patients were evaluated prior to etanercept treatment. Patients whose IgG-Gal ratio values were over 0.8 were predicted to be responders. **Stage II**: The others were examined after one dose of etanercept and repetitive IgG-Gal ratio evaluation was performed at week 2, among which patients whose |Δ|IgG-Gal ratio value were below -0.1 were predicted to be responders. **Stage III**: The remains were subjected to MYOM2 SNP genotyping, revealing patients with CT/TT genotype to be poor-responders and patients with CC genotype to be responders.

Conclusion: We propose a novel three-stage approach to combine genetic markers and post-translational modifications to predict precisely the response to the TNF blocker (Etanercept) in AS patients with an accuracy of 100% for poor-responders and 98% for responders.
Figure 1. A: IgG-Gal ratio variance during treatment; B: ΔIgG-Gal ratio change during treatment; Red line: poor-responders, blue line: responders.

p values between responders and poor-responders of each time point were listed.

Figure 2. Flowchart of the novel three-stage method in prediction of etanercept patient response. IgG-Gal ratio: IgG galactosylation ratio, ΔIgG-Gal ratio: The difference of IgG-Gal ratio between weeks 0 and 2.

Table 1. Distribution of a single nucleotide polymorphism in MYOM2 between responders and poor-responders

<table>
<thead>
<tr>
<th>Genotype</th>
<th>CC (%)</th>
<th>CT (%)</th>
<th>TT (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responder</td>
<td>52 (81.3)</td>
<td>11 (17.2)</td>
<td>1 (1.5)</td>
<td>5.76 x 10^-4</td>
</tr>
<tr>
<td>Poor-responder</td>
<td>12 (42.9)</td>
<td>15 (33.6)</td>
<td>1 (3.5)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Allele</th>
<th>Freq</th>
<th>P value</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responder</td>
<td>115</td>
<td>13</td>
<td>1.10 x 10^-3</td>
</tr>
<tr>
<td>Poor-responder</td>
<td>39</td>
<td>17</td>
<td></td>
</tr>
</tbody>
</table>

Disclosure: J. Liu, None; S. Ren, None; Z. Niu, None; Q. Zhu, None; W. Wan, None; J. Han, None; Y. Ma, None; W. Pu, None; Y. Li, None; X. Xu, None; Y. Wang, None; D. Zhao, None; H. Zhang, None; F. Qian, None; X. Zhou, None; J. D. Reveille, Janssen, 5; L. Jin, None; B. He, None; H. Zou, None; J. Gu, None; J. Wang, None.
Prevalence of Cardiovascular Risk Factors and Subclinical Cardovacular Disease in Psoriatic Arthritis

Maria Paz Martínez-Vidal1, Cristina Fernández-Carballido2, Mariano Andres3, Vega Jovani4, Carlos Santos5, Maria Nieves Martínez Alberola6, Francisca Sivera7 and Raquel Martín-domenech6, 1Rheumatology, Hospital general universitario de Alicante, Alicante, Spain, 2Hospital General Universitario de Elda, Elda, Spain, 3RHEUMATOLOGY, Hospital general universitario de Alicante, Alicante, Spain, 4Reumatología, Hospital general universitario de Alicante, Alicante, Spain, 5Rheumatology, Hospital de Alcoy, Alcoy, Spain, 6Rheumatology, Hospital General Universitario de Elda, Elda, Spain, 7Sección de Reumatología, Hospital General Universitario de Elda., Elda, Spain
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment IV
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: SCORE tables underestimate the Cardiovascular Risk (CVR) for patients with Rheumatoid Arthritis (RA) and EULAR recommends multiplying by 1.5 the CVR obtained from them in RA patients [1]. A concern exists that CVR in Psoriatic Arthritis (PsA) might be underestimated [2,3]. Several studies show that the carotid intima-media thickness (CIMT) and the presence of cholesterol plaques (CP) detected with Ultrasound (US) are significantly associated with CVR [4,5]. The objective of this study was too assess the CVR profile in PsA patients using the SCORE/European recommendations, and to study the presence of subclinical CV disease by US techniques.

Methods: Transversal descriptive multicenter study of PsA patients followed up in Rheumatology Units. Variables: Age, gender, psoriasis and PsA duration, PsA type and therapy; classic CVR factors (BMI, hypertension, dyslipidaemia, smoking, diabetes); prevalent personal and familiar CV events (coronary, cerebrovascular and thromboembolic events, sudden death). The probability of fatal atherosclerotic CV events over a 10 year period was calculated (Spanish SCORE chart/European recommendations). Then all patients underwent bilateral US carotid study (GE LOGIQ S7 Expert US Equipment). The common CIMT was measured in both common carotids using an automatized lecture of the distal intima-media wall in a surface of 1.39 cm or 300 points, 1 cm caudal to the carotid bulb. Plaques were defined according to the Mannheim consensus [6]. Statistical analysis: Descriptive, univariate and multivariate analyses (ANOVA) were performed.

Results: 176 PsA patients from three hospitals were included: mean age 55.2 yo (SD11.8) (50.6% male). Clinical characteristics summarized in Table 1. 62% of the patients had at least one classical CV risk factor. In the US study, a CIMT greater than 0.9 mm or the presence of plaques were found in 55 patients (31.2%). Cardiovascular Risk was upgraded to very high because of the US results in 53 patients (30.1%). Finally, 33.5% of the patients were considered as very high risk. The risk distribution before and after the US study is depicted in Table 2.

Conclusion: CV risk factors are frequent among PSA patients. A substantial proportion of patients with PsA are at a very high risk of a fatal CV event. The SCORE/European classification seems to underestimate the CV risk, as 30.1% of the patients were upgraded to a higher risk after the US study.

Table 1. Clinical characteristics of the PsA patients included
<table>
<thead>
<tr>
<th><strong>DISEASE TYPE</strong></th>
<th>Only axial</th>
<th>8 (4.5%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral</td>
<td>168 (95.5%)</td>
<td></td>
</tr>
<tr>
<td>Only peripheral</td>
<td>124 (70.5%)</td>
<td></td>
</tr>
<tr>
<td>Psoriasis duration (months)</td>
<td>222.61</td>
<td></td>
</tr>
<tr>
<td>PsA duration (months)</td>
<td>132.89</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>TREATMENT</strong></th>
<th>NSAID only</th>
<th>9 (5.1%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMARDs</td>
<td>90 (51.1%)</td>
<td></td>
</tr>
<tr>
<td>Anti-TNFα</td>
<td>73 (41.5%)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>3 (1.7%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>CARDIOVASCULAR EVENTS</strong></th>
<th>Personal</th>
<th>4 (2.3%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Familiar</td>
<td>55 (31.3%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>CLASSICAL CVR FACTORS</strong></th>
<th>DM</th>
<th>27 (15.3%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>51 (29%)</td>
<td></td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td>41 (23.3%)</td>
<td></td>
</tr>
<tr>
<td>Tobacco</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2. CV risk stratification according to the SCORE tables/European recommendations and after the carotid US study.
A Phase 2 Study of Safety and Efficacy of Anabasum (JBT-101), a Cannabinoid Receptor Type 2 Agonist, in Diffuse Cutaneous Systemic Sclerosis

Robert F. Spiera¹, Laura K. Hummers², Lorinda Chung³, Tracy M. Frech⁴, Robyn T. Domsic⁵, Vivien Hsu⁶, Daniel E. Furst⁷, Jessica K. Gordon¹, Maureen D. Mayes⁸, Robert W. Simms⁹, Scott Constantine¹⁰ and Barbara White¹⁰.

¹Rheumatology, Hospital for Special Surgery, New York, NY, ²Medical and Rheumatology, Johns Hopkins University, Baltimore, MD, ³Rheumatology, Stanford University Medical Center, Palo Alto, CA, ⁴Division of Rheumatology, University of Utah, Salt Lake City, UT, ⁵Rheumatology, University of Pittsburgh, Pittsburgh, PA, ⁶Rheumatology, Robert Wood Johnson University Scleroderma Program, New Brunswick, NJ, ⁷David Geffen School of Medicine at UCLA, Los Angeles, CA, ⁸University of Texas McGovern Medical School, Houston, TX, ⁹Rheumatology, Boston University School of Medicine, Boston, MA, ¹⁰Corbus Pharmaceuticals, Inc., Norwood, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics II
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Systemic sclerosis (SSc) is characterized in part by chronic activation of the innate immune system with fibrosis. Anabasum is a non-immunosuppressive, synthetic, orally administered selective CB2 agonist that activates resolution of innate immune responses in animal models of SSc and healthy humans. This study evaluated safety and efficacy of anabasum in diffuse cutaneous SSc (dcSSc).

Methods: A double-blind, randomized placebo (PBO)-controlled 16-week Phase 2 trial (JBT101-SSc-001) enrolled subjects with dcSSc ≤ 6 years duration on stable medications including immunosuppressive drugs. Subjects received anabasum 5 mg QD, 20 mg QD, or 20 mg BID x 4 weeks, then 20 mg BID x 8 weeks, or PBO x 12 weeks. Subjects were followed off study drug x 4 weeks. The primary efficacy outcome was ACR Combined Response Index in diffuse cutaneous Systemic Sclerosis (CRISS).

Results: Forty-two subjects received study drug: anabasum N = 27 and PBO N = 15. Baseline patient characteristics were similar in both groups. There were no serious, severe or unexpected adverse events (AEs) related to anabasum. Severity and relationship of AEs to study drug were similar in both groups. AEs in ≥10% of anabasum subjects were dizziness and fatigue. Anabasum subjects had greater improvement in ACR CRISS scores than PBO subjects over 16 weeks (Fig. 1, p = 0.044, 1-sided, mixed model repeated measures included baseline mRSS and disease duration). Anabasum subjects had greater improvement and less worsening in individual CRISS core measures including modified Rodnan Skin Score (mRSS), Patient Global Assessment (PtGA), Physician Global Assessment (MDGA), and HAQ-DI (Fig. 2).

Figure 1. CRISS Scores
There were strong correlations of CRISS scores with change from baseline in mRSS (r = -0.894, p < 0.0001) and MDGA (r = -0.591, P < 0.0001) with weaker correlations with FVC % predicted (r = 0.280, P = 0.0006), PtGA (r = -0.270, P = 0.0008), and HAQ-DI (r = -0.294, P = 0.0003). Patient-reported outcomes of SSc skin symptoms, itch, and PROMIS-29 physical function, pain interference, and sleep also improved (P < 0.05 for all). Evaluation of gene transcripts in skin biopsies showed anabasum but not placebo reduced expression of key genes implicated in SSc and gene ontology pathways associated with inflammation and fibrosis.

**Conclusion:** Anabasum had acceptable safety and tolerability in this Phase 2 trial in dcSSc and demonstrated consistent evidence of clinical benefit. Changes in gene expression were consistent with biologic effects of anabasum on pathways relevant to SSc. Further evaluation of anabasum in treatment of dcSSc is warranted.

**Disclosure:**
- **R. F. Spiera,** Roche-Genetech, 2, GSK, 2, BMS, 2, Boehringer Ingelheim, 2, Cytori, 2, Chemocentryx, 2, Corbus Pharmaceuticals, 2, Prism, 2, Roche-Genetech, 5, GSK, 5, Boehringer Ingelheim, 5; **L. K. Hummers,** None; **L. Chung,** Cytori, Actelion, Reata, 5; **T. M. Frech,** None; **R. T. Domsic,** None; **V. Hsu,** None; **D. E. Furst,** Grant/Research Support: Amgen, BMS Novartis, Pfizer, Roche/Genentech, Corbus. Consultant: AbbVie, Amgen, BMS, Corbus, Cytori, Novartis, Pfizer, Roche/Genentech. Speakers Bureau (CME or non-promotional only): BMS, AbbVie NO stocks, royalties, direct fina, 2, see above, 5, see above, 8; **J. K. Gordon,** Corbus Pharmaceuticals, 2, Cumberland Pharmaceuticals, 2, Bayer Pharmaceuticals, 2; **M. D. Mayes,** None; **R. W. Simms,** None; **S. Constantine,** Corbus Pharmaceuticals, Inc., 1, Corbus Pharmaceuticals, Inc., 3; **B. White,** Corbus Pharmaceuticals, 1, Corbus Pharmaceuticals, 3.

**Tadalafil Reduces Skin Fibrosis and Profibrotic Genes Expression in Patients with Systemic Sclerosis**

**Sakir Ahmed,** Mohit Kumar Rai, Durga Prasanna Misra and Vikas Agarwal, Clinical Immunology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India

**Abstract Number:** 2885
Background/Purpose:
Currently, drugs that modify skin fibrosis in Systemic Sclerosis (SSc) have efficacy in certain subgroups of patients only.
Phosphodiesterase-5 inhibitors (PDE5i) are known to reduce fibrosis in Peyronie’s disease and renal fibrosis. We studied the efficacy of Tadalafil, a long acting PDE5i, in reducing the skin fibrosis in SSc.

Methods:
In this prospective open-labeled study, 24 patients meeting ACR 2013 classification criteria for systemic sclerosis were recruited. Twelve received Tadalafil in addition to standard of care whereas the rest were continued on standard of care. Demographic and clinical details including Modified Rodnan Skin Score (mRSS) were recorded at baseline and at 6 months. Paired forearm skin biopsies of 5mm diameter were taken at baseline and at 6 months. Expression of profibrotic genes COMP, THBS1, SIGLEC1, IFI44, TN-C, COL1A1, COL1A2, ACTA2 and CTGF [Abbreviations in Table 2] in skin biopsies were compared to housekeeping gene GAPDH using real time polymerase chain reaction.

Results:
Baseline characteristics were similar in both the groups [Table 1]. One patient was lost to follow-up in each group. Amongst patients on Tadalafil, median mRSS decreased from 22 to 13 (p= 0.005) whereas median mRSS in the other group had a statistically non-significant increase from 15 to 19 (p=1) at 6 months [Figure 1].

In the Tadalafil group, there was decrease in the expression of COMP, SIGLEC1, CTGF and IFI44 that was statistically significant (Table 2). In the other group, there was significant increase in the expression of IFI44, THBS1 and TN-C that was absent in the Tadalafil group. Overall change in mRSS (ΔmRSS) correlated with change in SIGLEC1, IFI44, TBHS1 and COL1A1 (Spearman; p<0.05).

Conclusion:
Tadalafil significantly reduced the skin fibrosis in SSc with down-regulation or prevention of upregulation (or both) in 6 of the 9 profibrotic genes tested.

<table>
<thead>
<tr>
<th></th>
<th>No Tadalafil (11)</th>
<th>Tadalafil (11)</th>
<th>Non-parametric comparisons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age [years]</td>
<td>34 (22-38)</td>
<td>29 (22-38)</td>
<td>p=0.332&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Females: Males</td>
<td>7:4</td>
<td>10:1</td>
<td>p=0.311&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Diffuse/Limited</td>
<td>8/3</td>
<td>9/2</td>
<td>p=1&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Duration of Skin thickening [months]</td>
<td>24 (12-48)</td>
<td>36 (18-48)</td>
<td>p=0.356&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Duration of Raynaud [months]</td>
<td>36 (14-48)</td>
<td>36 (22.5-54)</td>
<td>p=0.549&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>mRSS</td>
<td>15 (9-32)</td>
<td>22 (16-29)</td>
<td>p=0.401&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>ANA positivity</td>
<td>9</td>
<td>9</td>
<td>-</td>
</tr>
<tr>
<td>Immunosuppressants (concurrent)</td>
<td>Cyclophosphamide 2</td>
<td>Cyclophosphamide 2</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Mycophenolate 1</td>
<td>Mycophenolate 1</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Steroids 2</td>
<td>Steroids 1</td>
<td>-</td>
</tr>
<tr>
<td>Other Drugs (concurrent)</td>
<td>Proton pump inhibitors 9</td>
<td>Proton pump inhibitors 9</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Nifedipine 2</td>
<td>Nifedipine 3</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Losartan 2</td>
<td>Losartan 1</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 1: Baseline Characteristics
<sup>1</sup>Mann-Whitney U test
<sup>2</sup>Fisher Exact Test
IGR: Interquartile Range
Table 2: Changes in gene expression (as compared to glyceraldehyde 3-phosphate dehydrogenase) from baseline to 6 months in skin biopsies

<table>
<thead>
<tr>
<th>Gene</th>
<th>Full name of gene</th>
<th>Change in Expression Median (Interquartile Range)</th>
<th>Wilcoxon Signed rank</th>
<th>Changes in Expression Median (Interquartile Range)</th>
<th>Wilcoxon Signed rank</th>
</tr>
</thead>
<tbody>
<tr>
<td>COMP</td>
<td>Collagen Glycine</td>
<td>-2.40 [-1.79] [-0.87]</td>
<td>-0.033</td>
<td>0.50 [-2.11] [-1.25]</td>
<td>p=0.722</td>
</tr>
<tr>
<td>SOLLEC1</td>
<td>None</td>
<td>-1.33 [-1.02] [-0.35]</td>
<td>p=0.041</td>
<td>-0.99 [-1.25] [-1.24]</td>
<td>p=0.274</td>
</tr>
<tr>
<td>COL1F</td>
<td>Connective Tissue</td>
<td>-1.33 [-1.02] [-0.35]</td>
<td>p=0.041</td>
<td>0.00 [-1.25] [-2.03]</td>
<td>p=0.041</td>
</tr>
<tr>
<td>IRA4</td>
<td>Interferon Induced</td>
<td>-0.69 [-1.23] [-0.91]</td>
<td>p=0.041</td>
<td>0.79 [-1.25] [-1.20]</td>
<td>p=0.049</td>
</tr>
<tr>
<td>Thbs1</td>
<td>Thrombospondin 1</td>
<td>0.00 [-1.53] [-0.02]</td>
<td>p=0.033</td>
<td>0.79 [-1.25] [-1.20]</td>
<td>p=0.049</td>
</tr>
<tr>
<td>Tgf-beta</td>
<td>Tumor Necrosis</td>
<td>-0.00 [-0.43] [-0.69]</td>
<td>p=0.722</td>
<td>0.77 [-1.25] [-1.49]</td>
<td>p=0.003</td>
</tr>
<tr>
<td>COL1A1</td>
<td>Collagen Type I</td>
<td>-1.29 [-1.54] [-0.06]</td>
<td>p=0.033</td>
<td>0.58 [-0.43] [-1.38]</td>
<td>p=0.248</td>
</tr>
<tr>
<td>COL1A2</td>
<td>Collagen Type I</td>
<td>-1.01 [-1.04] [-1.73]</td>
<td>0.01 [-0.43] [-1.38]</td>
<td>0.10 [-0.43] [-1.38]</td>
<td>0.248</td>
</tr>
<tr>
<td>ACTA2</td>
<td>Alpha Smooth Muscle Actin</td>
<td>-0.31 [-1.45] [-0.54]</td>
<td>p=0.528</td>
<td>-0.05 [-0.58] [-0.44]</td>
<td>p=0.657</td>
</tr>
</tbody>
</table>

Disclosure: S. Ahmed, None; M. K. Rai, None; D. P. Misra, None; V. Agarwal, None.


Abstract Number: 2886

**Safety and Efficacy of Long-Time Intensified Rituximab Treatment in Patients with Systemic Sclerosis**

**Hans-Peter Brezinschek**¹, Sonja Kielhauser², Winfried Graninger³ and Florentine Moazed-Fürst², ¹Internal Medicine/Division of Rheumatology and Immunology, Rheumatology and Immunology, Medical University Graz, Austria, Graz, Austria, ²Rheumatology and Immunology, Medical University Graz, Austria, Graz, Austria, ³Rheumatology and Immunology, Medical University of Graz, Graz, Austria

First publication: September 18, 2017

**SESSION INFORMATION**
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics II
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM
**Background/Purpose:** Rituximab (RTX), a monoclonal B cell depleting antibody, is one of the few new drugs that has been shown to have beneficial effects on the fibrotic process in patients with systemic sclerosis (SSc). Whether long-time treatment with RTX might lead to hypogammaglobulinemia or lymphopenia that increase the susceptibility to infections in these patients is unknown. The purpose of this observational study was to analyse the levels of IgG and IgM as well as the number of lymphocytes and the frequency of serious infections in our cohort of SSc patients.

**Methods:** SSc patients (n=24; 18 female) with signs of alveolitis in the CT scan where started on a continuous intensified RTX treatment (500mg within 2 weeks every 3 months). The serum levels of IgG, IgM and the total lymphocyte counts were determined before the first RTX application and before the last RTX cycle within this year. Mean duration (95%CI) of RTX therapy was 40 months (30-50). Serious infections were evaluated by analyzing the medical records for hospitalisation because of infections. In addition, the European Scleroderma Study Group (EStSG) activity index as well as the modified Rodnan skin score (mRSS) and the diffusing capacity for carbon monoxide (DLCO) were used to estimate the therapeutic efficacy of RTX.

**Results:** The EStSG activity index decreased significantly (p<0.0001), with a mean (±SE) of 3.5 (±0.3) at baseline and 0.4 (±0.1) after the last RTX cycle. In addition, the mean (±SE) mRSS was significantly lower in the last visit (8.0 ±1.4) compared to baseline value (23.9 ±2.4; p<0.0001). The DLCO (95% CI) value improved from 69.2% (61.4-77.5%) to 72.3% (64.5-80.1%), but did not reach significant levels (p=0.1612). The mean number of lymphocytes per 10⁹/L (±SE) was not significantly altered during the treatment period (p=0.0890) and ranged from 1.58 ±0.12 at the beginning and 1.42 ±0.1 after the last cycle (normal range 1.0 to 4.8). The mean IgG and IgM levels ±SE decreased significantly from 12.9g/L ±0.4 and 1.3g/L ±0.1 to 10.4 ±0.4 (p=0.0002) and 0.7 ±0.1 (p<0.0001), respectively. Interestingly, only 3 patients had IgM levels below the normal range of 0.4g/L. None of our patient had to be admitted to the hospital because of serious infections.

**Conclusion:** The intensified RTX protocol is an effective and safe therapeutic option for SSc patients. In contrast to patients with rheumatoid arthritis, in our SSc patients the total number of lymphocytes was not related to the clinical response to RTX.

**Disclosure:** H. P. Brezinschek, None; S. Kielhauser, None; W. Graninger, None; F. Moazedi-Fürst, None.

Methods: Intra-venous CY (4 g/m²) and recombinant human granulocyte colony-stimulated factor. HSCT was performed after treatment with intra-venous CY (200 mg/kg, divided into four days). We used the modified Rodman total thickness skin score (mRTSS) to assess the improvement of skin sclerosis. Good response was defined as more than a 50% decrease in mRTSS from baseline within six months after HSCT. Pulmonary function was also evaluated using spirometry, high resolution CT, and serum KL-6 level.

Results: Between 2000 and 2012, 15 patients who met the criteria and signed the informed consent were enrolled in the trial and 14 patients were given HSCT; one was not transplanted because of her mobilization failure. Median follow-up period was 137 months. Eight patients (57%) showed a good response to HSCT in the improvement of skin sclerosis, but skin sclerosis relapsed in two patients and interstitial lung disease progressed in another patient. Five patients (36%) kept a long-term efficacy of HSCT. Four in six patients without a good response to HSCT required additional treatments due to progression of diffuse skin sclerosis or interstitial lung disease. Adverse effects related to HSCT occurred in five patients (36%). Engraftment syndrome developed in two patients and hemophagocytic syndrome in one patient, successfully treated with corticosteroids. Hemorrhagic cystitis associated with Adeno Virus occurred in one patient, leading to irreversible vesicoureteral reflux requiring urinary catheter. Cardiopulmonary arrest due to severe cardiomyopathy occurred in two patients. One patient could be rescued after intensive care including percutaneous cardiopulmonary support and intra-aortic balloon pumping, but another one couldn’t.

Conclusion: Although HSCT brings the favorable results to some patients with severe SSc, we should carefully consider the selection of the patients for HSCT as the treatment of SSc.

Disclosure: H. Nakamura, None; S. Yasuda, Bristol-Myers Squibb, MSD, 2, Chugai Pharmaceutical, Mitsubishi-Tanabe Pharma, Bristol-Myers Squibb, Astellas Pharma, 8; A. Noguchi, None; T. Odani, None; Y. Fujieda, None; M. Kato, None; K. Oku, None; J. Sugita, None; T. Bohgaki, None; T. Endo, None; T. Teshima, None; T. Atsumi, None.


Abstract Number: 2888

Corticosteroid-Sparing Benefit of Intravenous Immunoglobulins in Systemic Sclerosis-Associated Inflammatory Myopathy: A Retrospective Study of 54 Patients

Benjamin Chaigne1, Simao Rodeia2, Nouria Benmostefa2-3,4, Alice Bérezné5, Pascal Cohen6, Alexis Regent7, Benjamin Terrier6, Nathalie Costedoat-Chalumeau8, Loïc Guillevin9, Claire Le Jeunne6 and Luc Mouthon10, 1Service de Médecine Interne, Centre de Référence Maladies Systémiques Autoimmunes Rares d’Ile de France, hôpital Cochin, DHU Authors, Assistance Publique-Hôpitaux de Paris, Paris, France, 2Service de Médecine Interne, Centre de Référence Maladies Systémiques Autoimmunes Rares d’Ile de France, DHU Authors, hôpital Cochin, Assistance Publique-Hôpitaux de Paris, Paris, France, 3Service de Médecine Interne CHU de Sétif, Algérie, Sétif, Algeria, 4Faculté de Médecine, Université de Sétif 1, Sétif, Algeria, 5Internal Medicine, National Referral Center for Rare Systemic Autoimmune Diseases, Hôpital Cochin, Paris, France, 6Service de Médecine Interne, Hôpital Cochin, Centre de référence national pour les maladies systémiques autoimmunes rares d’Ile de France, DHU Authors, Assistance Publique-Hôpitaux de Paris (AP-HP), Paris, France, 7National Referral Center for Rare Systemic Autoimmune Diseases, Hôpital Cochin, AP-HP, Université Paris Descartes, Paris, France, 8Service de médecin interne Pôle médecine, Hôpital Cochin, Centre de référence maladies auto-immunes et systémiques rares de l’Ile de France, Paris, France, 9Internal medicine, Cochin University Hospital, paris, France, 10Service de Médecine Interne, Hôpital Cochin, Centre de référence national pour les maladies systémiques autoimmunes rares d’Ile de France, DHU Authors, Assistance Publique-Hôpitaux de Paris (AP-HP), Paris, France, Université Paris Descartes Sorbonne Paris, Paris, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics II
Session Type: ACR Concurrent Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Little is known about systemic sclerosis (SSc)-associated myopathy (SScAM) treatment. Intravenous immunoglobulin (IVIg) are used off-label in SScAM. Herein we aimed to evaluate the use of IVIg in SScAM.

Methods: We conducted a retrospective study of patients with SScAM followed between 1993 and 2017 who received IVIg in the department of internal medicine of Cochin University Hospital. All patients fulfilled the ACR/EULAR criteria for SSc. SScAM was
defined as a histologically proven myopathy or the association of myalgia and/or muscle impairment associated with elevation of muscle enzymes or myositis alteration at MRI.

**Results**: Fifty-four patients were included in the study comprising 23 (42.6%) with limited cutaneous SSc and 27 (50%) with diffuse cutaneous SSc. SScAM occurred at a median [interquartile range (IQR)] time of 1 month [0 – 13] after the diagnosis of SSc. Thirty-six patients (66.7%) had muscle impairment, 29 (53.7%) had myalgia and 24 (44.4%) had dysphagia. Fifty-two patients (96.3%) had increased creatine kinase level. An electromyography was performed in 26 patients (48.1%) and was normal in 22 patients (44.6%). A MRI was performed in 13 patients (24.1%) and was pathological in 10 patients (76.9%). A muscle biopsy was performed in 52 patients (96.3%) and showed muscle involvement in 50 patients (92.6%), mainly inflammatory infiltrates (65.3% of the biopsies), and necrosis (57.4% of the biopsies). Twenty patients (37%) received IVIg. IVIg was initiated to treat SScAM because of worsening muscle involvement in 18 patients (90.0%) and was given in combination with corticosteroids in all patients. Adverse events (AEs) occurred in 7 patients (38.9%) including serious AEs in 2 patients (10%). After a median follow-up of 9 years [range 61-164], 18 patients (90%) had achieved clinical remission, every patient (100%) had achieved biological remission. When compared to patients who did not receive IVIg, there was no difference in remission rates, modified Rodnan skin score, lung function tests but patients who were treated with IVIg had a statistically significant higher decrease of corticosteroids at 6 and 12 months after treatment initiation (Figure 1).

**Conclusion:** This study shows the benefit of IVIg as adjunctive therapy, with an acceptable tolerance profile, and supports its use, especially as a corticosteroid-sparing agent, in SScAM.

**Figure 1. Corticosteroid sparing after intravenous immunoglobulin infusion in patients with systemic sclerosis-associated myopathy**

Box and whiskers show the minimum to the maximum corticosteroid decreased dose of 20 patients who received IVIg for systemic sclerosis-associated myopathy (SScAM) at 3, 6, 12 months and at the end of the follow-up period (>M12). Controls (n=34) were patients with SScAM who did not receive IVIg. Mann-Whitney test was used for comparisons. * p-value < 0.05, *** p-value < 0.001

**Disclosure: B. Chaigne**, None; **S. Rodeia**, None; **N. Benmostefa**, None; **A. Bérezné**, None; **P. Cohen**, None; **A. Regent**, None; **B. Terrier**, None; **N. Costedoat-Chalumeau**, None; **L. Guillevin**, None; **C. Le Jeune**, None; **L. Mouthon**, None.

**Abstract Number: 2889**

**Aminaphtone Ameliorates Clinical Symptoms and Increases Skin Blood Perfusion in Patients with Both Primary and Secondary Raynaud Phenomenon: A Six-Month Open Study**

**Alberto Sulli**1, Maurizio Cutolo2, Carmen Pizzorni2, Sabrina Paolino2, Elisa Alessandro2, Emanuele Gotelli2 and Barbara Ruaro2,

1Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, IRCCS San Martino, Genoa, Italy, Genova, Italy, 2Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, IRCCS San Martino, Genoa, Italy

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Tuesday, November 7, 2017

**Session Title:** Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics II

**Session Type:** ACR Concurrent Abstract Session
Background/Purpose: Current treatments for Raynaud's phenomenon (RP) have limited efficacy, which was mainly demonstrated by physician/patient reported outcomes. Aminaphtone is a vasoactive drug recently suggested to improve RP symptoms and among other mechanism is also able to down-regulate endothelin-1 production by endothelial cells (1-3). The aim of this study was to evaluate the clinical symptoms related to RP and skin blood perfusion changing, during aminaphtone treatment in primary RP (PRP) and secondary RP (SRP) patients, during a six-month follow-up.

Methods: Forty-six patients with active RP were enrolled in November 2015 after informed consent (11 PRP, mean age 49±19 SD years, mean RP duration 6±3 years; 35 SRP in systemic sclerosis (SSc) (ACR/EULAR criteria) (mean age 61±17 SD years, mean RP duration 11±9 years). Aminaphtone was administered off label 75 mg twice daily in addiction to current treatments (patients were on stable drug regimen from at least two months, and they did not modify it during follow-up). Blood perfusion was measured, in perfusion units (PU), in all patients by Laser speckle contrast analysis (LASCA) (4,5) at the level of fingertips, periungual areas, dorsum and palm of hands and face at baseline (W0), after one (W1), four (W4), twelve (W12) and twenty-four (W24) weeks of treatment. Raynaud condition score (RCS) and both Raynaud's attack frequency and duration were also assessed at the same times. Forthy-six patients with RP (9 PRP, mean age 56±12 SD years, mean RP duration 8±4 years; 37 SRP in SSc, mean age 63±11 SD years, mean RP duration 12±10 years) were also enrolled as control group, and evaluated at T0 and T24. Statistical analysis was performed by non parametric tests.

Results: A progressive statistically significant decrease of RCS (median at W0, W1, W4, W12, W24 respectively: 7, 6, 4, 4, 4; p<0.0001), Raynaud's frequency (median 2, 2, 1, 1, 1 attacks/day; p<0.0001) and duration (median: 20, 20, 10, 4, 4 minutes; p<0.0001) was observed from W0 to W12. A progressive statistically significant increase of blood perfusion was observed from W0 to W12 in all skin areas (median PU at W0, W1, W4, W12, W24 respectively: fingertips 55, 88, 101, 107, 98; periungual areas 44, 88, 91, 92, 92; dorsum of hands 38, 61, 75, 75; palm of hands 56, 85, 89, 82; face 127, 138, 144, 159, 129; p<0.001 for all areas). No further statistically significant amelioration of either RP symptoms of or blood perfusion was observed from W12 to W24. The results were similar for both PRP and SRP patients (p=0.4). In the control group no statistically significant changes regarding blood perfusion from W0 to W24 were observed (p=0.9 for all areas).

Conclusion: Aminaphthone treatment improves RP-related clinical symptoms and rapidly increases skin blood perfusion, also in SSc patients. A randomized blind clinical trial need to confirm these results.


Disclosure: A. Sulli, None; M. Cutolo, Laboratory Baldacci, 2; C. Pizzorni, None; S. Paolino, None; E. Alessandri, None; E. Gotelli, None; B. Ruaro, None.


Abstract Number: 2890

Performance of Machine Learning Methods Using Electronic Medical Records to Predict Varicella Zoster Virus Infection

Milena Gianfrancesco1, Gabriela Schmajuk2, Sara Murray3, Dana Ludwig3, Awni Hannun4, Anand Avati4, Suzanne Tamang5 and Jinoos Yazdany6. 1Medicine/Rheumatology, University of California, San Francisco, San Francisco, CA, 2San Francisco VA Medical Center, University of California San Francisco, San Francisco, CA, 3University of California, San Francisco, San Francisco, CA, 4Computer Science, Stanford University, Palo Alto, CA, 5Stanford Center for Population Health Science, Stanford University, Palo Alto, CA, 6Medicine/Rheumatology, University of California San Francisco, San Francisco, CA

First publication: September 18, 2017
**Background/Purpose:** Varicella zoster virus infections (VZV) can be associated with significant morbidity in immunosuppressed hosts. However, methods do not exist to systematically identify which patients with rheumatic diseases are at highest risk for VZV, information critical for implementing preventive strategies such as vaccination or antiviral prophylaxis. Machine learning methods that can combine large amounts of information from across the electronic health record (EHR) are increasingly being explored in healthcare. In this study, we derived and compared machine learning algorithms to classify the development of VZV using health system wide EHR data.

**Methods:** We used data from an EHR with over 800,000 patients from a university-based health system from 2012-2016. We identified incident VZV using a combination of ICD code (B02.xx) and a text string processing algorithm (terms: “zoster” and/or “shingles”). All structured (immunizations, vital signs, allergies, medications, laboratories, insurance, encounters, providers, demographics) and unstructured data (i.e. text from clinical notes) from before the VZV event were used. A sample of 201 patients was selected and chart reviewed to validate case status (n=100 cases, 101 controls). We used a supervised approach to identify predictors of VZV and compared performance metrics of 6 machine learning algorithms, including: logistic regression, elastic net, random forests, support vector machine, generalized boosted models, and naïve Bayes. Various datasets were evaluated using information at 1, 3, 6, 12, and 18 months prior to index date with repeated cross-fold validation.

**Results:** Preliminary results indicate that generalized boosted models based on 3 months of data prior to VZV outperformed all other algorithms (AUC 0.85; accuracy 0.80; Kappa 0.60) (Table 1). Random forest models also performed well (AUC 0.81; accuracy 0.72), but had a lower reliability (Kappa =0.44). Logistic regression and naïve Bayes models performed the poorest (AUC 0.58 and 0.50, respectively). Top variables associated with VZV included sociodemographics (age, sex, race), clinical (blood pressure, BMI, medications), and health care utilization (number of encounters).

**Conclusion:** Generalized boosted models outperformed other algorithms in identifying VZV in a large university health system, with algorithms that used 3 months of data prior to infection as having the best performance. Further refinement of algorithms with a larger sample size and incorporating more data will assist in developing a highly accurate classification algorithm for VZV that can be used to inform clinical decision making in real-time. This proof-of-concept study highlights the promise of leveraging all the data available through EHR to flag patients who may be at risk for adverse drug events or medical complications before they occur.

**Table 1. Algorithm performance results using 3 months of electronic medical record data (n=201)**

<table>
<thead>
<tr>
<th></th>
<th>Logistic Regression</th>
<th>Elastic Net</th>
<th>Random Forest</th>
<th>Support Vector Machine</th>
<th>Generalized Boosted Models</th>
<th>Naïve Bayes</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC</td>
<td>0.58</td>
<td>0.70</td>
<td>0.81</td>
<td>0.70</td>
<td>0.85</td>
<td>0.50</td>
</tr>
<tr>
<td>Accuracy</td>
<td>0.58</td>
<td>0.70</td>
<td>0.72</td>
<td>0.58</td>
<td>0.80</td>
<td>0.50</td>
</tr>
<tr>
<td>Reliability</td>
<td>0.16</td>
<td>0.40</td>
<td>0.44</td>
<td>0.16</td>
<td>0.60</td>
<td>0.00</td>
</tr>
<tr>
<td>F-score</td>
<td>0.46</td>
<td>0.75</td>
<td>0.72</td>
<td>0.57</td>
<td>0.80</td>
<td>0.67</td>
</tr>
<tr>
<td>Sens.</td>
<td>0.36</td>
<td>0.88</td>
<td>0.72</td>
<td>0.56</td>
<td>0.80</td>
<td>1.00</td>
</tr>
<tr>
<td>Spec.</td>
<td>0.80</td>
<td>0.52</td>
<td>0.72</td>
<td>0.60</td>
<td>0.80</td>
<td>0.00</td>
</tr>
<tr>
<td>PPV</td>
<td>0.64</td>
<td>0.65</td>
<td>0.72</td>
<td>0.58</td>
<td>0.80</td>
<td>0.50</td>
</tr>
<tr>
<td>NPV</td>
<td>0.56</td>
<td>0.81</td>
<td>0.72</td>
<td>0.50</td>
<td>0.80</td>
<td>0.00</td>
</tr>
</tbody>
</table>

**Disclosure:** M. Gianfrancesco, None; G. Schmajuk, None; S. Murray, None; D. Ludwig, None; A. Hannun, None; A. Avati, None; S. Tamang, None; J. Yazdany, None.


**Abstract Number:** 2891

**Do Certain Dmards Increase Risk of New-Onset Type 2 Diabetes in RA Patients? a Disease Risk Score Analysis Using Administrative Databases**

E Alemao, Z Guo and L Burns, Bristol-Myers Squibb, Princeton, NJ
Background/Purpose: Data on the association between RA and type 2 diabetes mellitus (T2DM) are inconsistent, suggesting RA treatments such as glucocorticoids (GCs) and hydroxychloroquine could impact T2DM risk.\textsuperscript{1–3} Recent randomized controlled trials\textsuperscript{4,5} demonstrated that biologic (b)DMARDs such as abatacept (ABA) improve pancreatic beta cell function in T1DM and have a lower risk of T2DM in RA patients (pts) in clinical practice.\textsuperscript{4,5} The objective of this analysis was to evaluate the development of T2DM in RA pts treated with ABA, other bDMARDs and conventional (c)DMARDs. \textbf{Methods:} Administrative claims data from Optum Clininformatics Data Mart (database A) and QuintilesIMS\textsuperscript{TM} PharMetrics Plus (database B) from 2006 to 2016 were used. Study inclusion criteria were: 2 diagnosis codes for RA plus 1 DMARD prescription; aged ≥18 yrs; and ≥3 mths baseline (pre-index date) and 3 mths of follow-up (post-index date). Mutually exclusive treatment groups were created based on the first prescription (index date) using hierarchy of ABA, other bDMARD and cDMARD. Also, an RA group without record of DMARD (NoDMARD) was identified. The index date for NoDMARD was first diagnosis date for NoDMARD. Incident T2DM was identified using 1 ICD-9 or ICD-10 diagnosis code for T2DM. Assessment of T2DM risk between treatment groups was based on traditional regression and a disease risk score (DRS) approach. DRS is the probability of developing T2DM estimated using a Cox model with a pre-specified list of 27 covariates. Adjusted incidence rate for T2DM was based on Cox model (stratified by DRS groups categorized into 4 equal groups based on quartile scores) with treatment as independent variable. \textbf{Results:} From database A, 105,683 (72.8% female, 58.3 [16.0] yrs) and from database B, 266,842 (73.1% female, mean [SD] age 51.6 [13.3] yrs) RA pts were included. Respectively, 2.9%, 10.4%, 34.8% and 51.8% were prescribed ABA, bDMARD, cDMARD and NoDMARD in database A; and 2.7%, 13.0%, 35.4% and 48.9% in database B. Based on the overall pooled sample size of 372,525 RA pts, the incidence rate per 1000 pt-yrs for new-onset T2DM was 37.8 (95% CI 37.4, 38.1). Pooled hazard ratios (HRs) for T2DM were significantly higher for bDMARD vs ABA in both DRS-based and regression-based approaches; HRs for cDMARDs were also higher (vs ABA) but were significant only in the regression approach. NoDMARD group (vs ABA) had the highest HRs for incidence of T2DM (Table).

\textbf{Conclusion:} We observed a lower incident risk of T2DM in RA pts treated with abatacept (vs risk in pts treated with other bDMARDs and cDMARDs) in two large real-world databases, warranting further comparisons. NoDMARD group should be interpreted with caution as it comprises a heterogeneous pt population.


\begin{table}[h]
\centering
\begin{tabular}{|l|l|l|}
\hline
 & HR (95% CI) & \textit{p} value \\
\hline
Pooled data of databases A and B – disease risk score method & & \\
\hline
bDMARD (vs abatacept) & 1.12 (1.04, 1.20) & 0.003 \\
\hline
cDMARD (vs abatacept) & 1.06 (0.99, 1.14) & 0.079 \\
\hline
NoDMARD (vs abatacept) & 1.29 (1.21, 1.38) & <0.001 \\
\hline
Pooled data of databases A and B – regression method & & \\
\hline
bDMARD (vs abatacept) & 1.14 (1.05, 1.22) & <0.001 \\
\hline
cDMARD (vs abatacept) & 1.08 (1.01, 1.16) & 0.028 \\
\hline
NoDMARD (vs abatacept) & 1.33 (1.24, 1.42) & <0.001 \\
\hline
\end{tabular}
\caption{HRs for Incidence of New-Onset Type 2 Diabetes Mellitus in Patients with RA by DMARD Treatment}
\end{table

\textbf{Disclosure:} E. Alemao, Bristol-Myers Squibb, 1,Bristol-Myers Squibb, 3; Z. Guo, Bristol-Myers Squibb, 3; L. Burns, Bristol-Myers Squibb, 1,Bristol-Myers Squibb, 3.
Persistently Frequent Emergency Department (ED) Utilization Among Systemic Lupus Erythematosus (SLE) Patients

Jiha Lee1, Lisa Gale Suter1,2 and Liana Fraenkel1,3

1Rheumatology, Rheumatology, Yale University School of Medicine, New Haven, CT, New Haven, CT, 2Medicine, Rheumatol., TAC S541, Rheumatology, VA Connecticut Healthcare System, West Haven, CT, New Haven, CT, 3Medicine, Section of Rheumatology, Rheumatology, VA Connecticut Healthcare System, West Haven, CT, New Haven, CT

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Health Services Research II: Methods and Technology in Care and Research
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose: SLE patients frequently utilize the ED irrespective of their access to care, which raises concern for inadequate quality of care in the outpatient setting. In the general population, previous studies have shown that most high-utilizers only use the ED frequently for a brief period of time (<12 months), however, a subgroup continue to use the ED persistently over years. We sought to investigate the characteristics and patterns of healthcare resource utilization among SLE patients who persistently frequent the ED in order to identify opportunities to improve outpatient care.

Methods: We identified SLE patients who persistently frequented the ED from 2013-2016. Persistent use was defined as having 3 or more ED visits during the 12 months in a calendar year, for at least 2 out of the 4 years, consecutive or non-consecutive, during the study period. Patient demographics, general health status, SLE history, long-term opioid therapy (LOT), encounter specific information and disposition were collected through retrospective electronic health record review. Each ED encounter was categorized into the following groups; SLE-, infection-, pain-related, or other. We used multivariate logistic regression to evaluate patient characteristics associated with each encounter category group. Variables with p-value <0.1 in univariate analysis were included in the multivariate model.

Results: Seventy-seven SLE patients having 1143 encounters were identified as persistently frequent ED users. Most were female (91%) and had SLE for longer than 10 years (54%). The mean age was 42 (SD 15), and 69% were African American, 14% were Caucasian, and 17% were Hispanic. All had some form of insurance with 49% having Medicaid as their primary insurance. Approximately one third had diagnosis of depression (31%) and 38% were on LOT. Most were on hydroxychloroquine (77%) and/or an additional disease modifying rheumatic drug (51%). Of all ED encounters, 32% were pain-related (Figure 1), and of these most were either discharged from the ED (69%) or within 48 hours of admission (20%). In multivariate analysis, SLE patients with pain-related encounters accounting for >10% of ED use were more likely to be obese, have more comorbid conditions, and be on LOT (Table 1).

Conclusion: Pain is major cause of ED use among SLE patients, and associated with LOT. SLE patients who utilize the ED for pain are more likely to be non-critically ill, as evidenced by frequent discharges from the ED and short stay admissions. Thus, SLE patients who persistently frequent the ED for pain may represent a viable target for interventions to improve outpatient care and care co-ordination.
Table 1: Multivariate analysis of factors associated with SLE patient who persistently frequented the ED having pain-related encounters account for more than 10% of total ED utilization

<table>
<thead>
<tr>
<th>Variables</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.00 (0.95-1.06)</td>
<td>0.870</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>0.25 (0.02-3.09)</td>
<td>0.283</td>
</tr>
<tr>
<td>Hispanic</td>
<td>0.02 (0.00-0.17)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Area of Deprivation Index</td>
<td>1.05 (0.98-1.12)</td>
<td>0.201</td>
</tr>
<tr>
<td>No. of co-morbidities</td>
<td>0.54 (0.33-0.89)</td>
<td>0.015</td>
</tr>
<tr>
<td>Long-term opioid therapy</td>
<td>7.50 (1.19-47.43)</td>
<td>0.032</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>1.12 (1.01-1.24)</td>
<td>0.034</td>
</tr>
<tr>
<td>Additional DMARD</td>
<td>2.55 (0.50-12.97)</td>
<td>0.258</td>
</tr>
</tbody>
</table>

OR = odds ratio, 95% CI = 95% confidence interval, No. of co-morbidities = number of co-morbidities, Additional DMARD = disease modifying antirheumatic drug (excluding hydroxychloroquine)

Disclosure: J. Lee, None; L. G. Suter, CMS, 3; L. Fraenkel, None.


Abstract Number: 2893

The Use of Natural Language Processing to Identify, Retrieve, Report, and Correct Observational Data on US Veterans Enrolled in the Veterans Affairs Rheumatoid Arthritis Registry

Grant Cannon1, Jorge Rojas1, Neill Bell2, Andreas Reimold3, Ted R. Mikuls4, Namrata Singh5, Gail S. Kerr6, Pascale Schwab7, Jennifer Barton7, Liron Caplan8, Joshua Baker9, Angelo L. Gaffo10, J. Steuart Richards11, Deana Lazaro12, Vikas Majithia13 and Brian Sauer1, 1Salt Lake City VA Medical Center and University of Utah, Salt Lake City, UT, 2Salt Lake City VA Medical Center and University of Utah, Dallas VA Medical Center, Dallas, TX, 3Dallas VA Medical Center and Texas Western University, Dallas, TX, 4VA Nebraska-Western Iowa Health Care System and University of Nebraska Medical Center, Omaha, NE, 5VA Nebraska-Western Iowa Health Care System and University of Iowa, Omaha, IA, 6Washington DC VA Medical Center, Georgetown and Howard University Hospitals, Washington, DC, 7Portland VA Medical Center and University of Oregon, Portland, OR, 8Denver VA Medical Center and University of Colorado, Denver, CO, 9Philadelphia VA Medical Center and University of Pennsylvania, Philadelphia, PA, 10Birmingham VA Medical Center and University of Alabama at Birmingham, Birmingham, AL, 11Pittsburgh VA Medical Center and
Background/Purpose: The Veterans Affairs (VA) Rheumatoid Arthritis (RA) (VARA) registry is an observational cohort study at 12 VA medical centers that prospectively collects clinical and laboratory outcome measures, which are recorded in the VARA database. To replace manual entry and reduce missing data, a Natural Language Processing (NLP) system was developed to extract outcome measures recorded in standardized text templates embedded in the electronic health record (EHR) notes for US Veterans enrolled in the registry. This study compared pre- and post-implementation experiences with this system.

Methods: VARA database entries for follow-up observations between January 1, 2016 and April 30, 2016 (pre-implementation) were compared to similar entries after NLP implementation January 1, 2017 to April 30, 2017 (post-implementation) with the number of notes containing outcome measures reported. Laboratory measure were automatically collected from EHR reports. At six VARA sites, missing data reports were provided to VARA investigators and clinic notes were reviewed to determine if outcome measures could be retrieved from documentation outside the standardized template. Note addendums were then entered to provide additional data when available.

Results: In comparison to 640 notes on 540 patients from 8 VARA sites in the pre-implementation period, 798 notes on 671 unique patients were recorded in the VARA database from 11 VARA sites during the post-implementation period. This represents an increase of 24.7%, 24.3%, and 37.5% in the number of notes, unique patients captured, and sites engaged, respectively. This increase in data capture was much larger than the 8.3% increase in VARA patient enrollment during the same period. The successful capture of specific outcome measures is listed in the Table, which shows an absolute increase in all elements between observation periods. In a pilot effort to do data corrections at six VARA test sites, missing data on 31 notes were evaluated to see if corrections were possible. Investigators were able to retrieve additional information for 10 (32%) notes from data outside the standard template and use note addendums to report these data. An automated NLP extraction was then employed to add this additional information to the database. Permanently missing data were universally due to the failure to document information at the point-of-care, as opposed to failure of the algorithm.

Conclusion: This study demonstrates that NLP can be leveraged in conjunction with standardized EHR templates to successfully retrieve patient data from across a national health care system, eliminate the need for manual data entry, and substantially increase the rate of data capture. By facilitating the collection of clinical and laboratory measures in RA patients, these efforts will further enhance the feasibility of conducting epidemiologic and outcomes studies of RA.

Disclosure: G. Cannon, None; J. Rojas, None; N. Bell, None; A. Reimold, None; T. R. Mikulcs, None; N. Singh, None; G. S. Kerr, None; P. Schwab, None; J. Barton, None; L. Caplan, None; J. Baker, None; A. L. Gaffo, None; J. S. Richards, None; D. Lazarz, None; V. Majithia, None; B. Sauer, None.


Abstract Number: 2894
Synchronous Telemedicine Care in Rheumatology for a Dispersed Veterans Affairs Health System

Patrick R. Wood¹ and Liron Caplan², ¹Rheumatology, University of Colorado School of Medicine, Aurora, CO, ²Division of Rheumatology, University of Colorado School of Medicine, Aurora, CO

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Wednesday, November 8, 2017
Session Title: Health Services Research II: Methods and Technology in Care and Research
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose: Rural Veterans with inflammatory arthritis (IA) lack access because of geographic and other barriers. A national shortage of rheumatologists exists, particularly in rural settings, and recent data suggest rural IA patients have poorer outcomes than those in close proximity to large cities and tertiary care. Synchronous Telemedicine (TM) is an emerging care delivery modality which has been employed in a variety of disease settings which holds great promise in relieving some of these disparities. Limited program evaluation of TM in rheumatologic care has been conducted, including examination of specialty-specific and patient centered outcomes, quality of care, patient satisfaction, or cost-effectiveness longitudinally for care delivered in this fashion.

Methods: Veterans with IA (including crystalline, rheumatoid arthritis (RA), and spondyloarthritis) in a widely disbursed VA health care system were enrolled in periodic TM follow-up. Data were collected longitudinally before and after entering the program, including patient-centered outcomes (e.g. RAPID3), and select patient satisfaction instruments adapted from the Survey of Health Experience for Patients (SHEP). Demographics were recorded. Similar data were collected on a convenience sample of concurrent IA patients enrolled in usual care (UC) clinics. Descriptive statistics, linear regression, and t-tests were performed.

Results: 60 patients were observed, including 19 in an initial TM cohort, and 41 UC patients. Mean age was 64.2, 90% were male, and 70% carried a clinical diagnosis of RA. No differences in these demographics were noted between groups. RAPID3 scores did not vary between TM and UC groups at baseline, with mean scores of approximately 11 (moderately active). Multiple SHEP instrument scores varied between groups initially (e.g. 8.3 vs 5.7 on a 1-10 Likert scale, p<0.01) and the TM cohort initially travelled greater distance (459.4mi vs 86.9mi, p<0.01) and spent more money ($157.72 vs $40.27, p<0.01) per visit than UC patients. Multivariate regression analyses suggest SHEP scores were predicted by disease activity status (β=-0.10, p=0.04) only when also accounting for additional patient-centered factors including cost (β=0.01, p<0.01) and distance (β=-0.01, p<0.01). In longitudinal follow-up via TM, SHEP instrument scores improved significantly among TM patients (β=3.54, p<0.01). Distance travelled (-454.4mi/visit, p<0.01) and costs ($-134.78/visit, p<0.01) were also significantly reduced in this group, with no significant changes in RAPID3 observed.

Conclusion: Synchronous TM may be a viable alternative to routine follow-up for IA care in rural settings and represents a radical change towards patient-centered care paradigms. Long-term follow-up and additional study including outcomes validation in TM care in rheumatology are warranted.

Disclosure: P. R. Wood, None; L. Caplan, None.


Abstract Number: 2895

Predictors of Hospitalization, Length of Stay and Costs of Care Among Children with Juvenile Dermatomyositis in the United States

Michael C. Kwa¹, Jonathan I. Silverberg² and Kaveh Ardalan³,⁴, ¹Dermatology, Northwestern University Feinberg School of Medicine, Chicago, IL, ²Dermatology, Preventive Medicine and Medical Social Sciences, Northwestern University Feinberg School of Medicine, Chicago, IL, ³Departments of Pediatrics and Medical Social Sciences, Northwestern University Feinberg School of Medicine, Chicago, IL, ⁴Division of Rheumatology, Ann & Robert H. Lurie Children’s Hospital of Chicago, Chicago, IL

First publication: September 18, 2017

SESSION INFORMATION
Juvenile dermatomyositis (JDM) is a rare autoimmune disease that causes significant morbidity and quality of life impairment. Little is known about JDM inpatient burden in the US. This study analyzes the prevalence and predictors of hospitalization, length of stay (LOS), and cost of care in US patients with JDM.

Methods:

Data on 14,401,668 pediatric hospitalizations from the 2002-2012 Nationwide Inpatient Sample (NIS), a 20% stratified sample of all acute-care hospitalizations in the US was analyzed. Previously validated ICD-9-CM codes were used to identify hospitalizations with a primary (i.e. condition chiefly responsible for inpatient admission) vs. secondary diagnosis of JDM. The control group included all hospitalizations without any diagnosis of JDM. Survey logistic regression models evaluated predictors of hospitalization for JDM. Adjusted ORs were obtained via multivariate regression including age, sex, race/ethnicity, season, insurance, number of chronic conditions, and hospital location. Linear regression models with log transformed cost of care or LOS evaluated predictors of cost of hospitalization and LOS using the aforementioned covariates.

Results:

There were 909 and 495 weighted admissions with a primary or secondary diagnosis of JDM, respectively. In multivariable analysis, older age, female sex, non-winter season, metropolitan area and Western geographic region, and other types of financial coverage aside from Medicaid and private insurance (i.e. Childrens Health Insurance Program (CHIP), other federal/state/local government programs) were all associated with higher rates of hospitalization for JDM (Table 1). The weighted total LOS and inflation-adjusted cost of care for patients with a primary diagnosis of JDM was 19,159 days and $49,339,995 with geometric means [95% CI] of 2.50 [2.27-2.76] days and $7,350 [$6,228-$8,674]. LOS in secondary JDM and cost in primary and secondary JDM were significantly higher compared to no JDM. Hispanic and other non-white race/ethnicity were associated with increased LOS (log-linear regression; adjusted beta [95% confidence interval]) (Hispanic: 0.28 [0.14-0.41]; other non-white: 0.59 [0.31-0.86]). Hispanic patients had higher cost of care (0.30 [0.05-0.55]) (Table 2).

Conclusion:

JDM adds to inpatient burden in the US, especially via increased LOS and cost of care. Rates of hospitalization for JDM differed by age, gender, season, form of financial coverage, and geography/region, while Hispanic patients had increased LOS and cost of care.
Human Cartilage Influences the Crystallization of Monosodium Urate; Understanding the Link between Gout and Osteoarthritis

Ashika Chhana1, Bregina Pool2, Ally Choi1, Ryan Gao1, Mark Zhu1, Jillian Cornish2, Jacob Munro3 and Nicola Dalbeth4, 1Medicine, University of Auckland, Auckland, New Zealand, 2Department of Medicine, University of Auckland, Auckland, New Zealand,
Background/Purpose: Monosodium urate (MSU) crystal deposition and gout flares frequently affect joints that have been damaged or are affected by osteoarthritis. The aim of this study was to examine the effects of healthy, osteoarthritic and degraded human cartilage on the three key steps of MSU crystallization; reduced urate solubility, crystal nucleation (appearance of MSU crystals), and crystal growth.

Methods: Paired macroscopically-healthy and macroscopically-diseased knee cartilage samples were obtained from patients undergoing orthopedic surgery. Cartilage was homogenized using the FreezerMill 6870 (SPEX CertiPrep Ltd) and the resulting powder dispersed in sterile water for preparation of cartilage homogenates. In crystallization assays, cartilage homogenates were added to solutions of sodium urate at 37°C and pH adjusted to 8.9. The cartilage-urate solutions were sampled over 24 hours for assessment of urate concentration (Cobas c311 autoanalyser, Roche Diagnostics), and crystal growth and morphology (by polarizing microscopy and ImageJ software). After 24 hours, total MSU crystal weight was determined. In separate assays, time to nucleation was determined by polarizing microscopy. The following cartilage preparations were tested: 1%, 5% and 10% healthy homogenized cartilage; 5% healthy and 5% diseased homogenized cartilage; and 5% healthy homogenized cartilage and 5% healthy enzyme-degraded cartilage.

Results: The addition of 5% and 10% healthy cartilage homogenates increased the total weight of MSU crystals formed compared to control (no added cartilage) (1-way ANOVA, P=0.0007, Figure A). Addition of healthy cartilage did not change urate solubility or time to nucleation compared to control. MSU crystals grown in the presence of healthy cartilage homogenates were significantly shorter (2-way ANOVA, P<0.0001). In morphological analysis, MSU crystal bow-like structures were observed both in the presence and absence of healthy cartilage homogenates, and the bows formed in the presence of healthy cartilage were also significantly shorter compared to control (Figure B and C). There were no differences between healthy cartilage and diseased cartilage homogenates in all assessments. For the enzyme-degraded cartilage, the lengths of MSU crystals and MSU crystal bows grown in the presence of degraded cartilage were significantly shorter than those grown in the presence of homogenized cartilage (2-way ANOVA, P<0.0001 for both), with no difference in other measures.

Conclusion: In crystallization assays, addition of human cartilage increases the amount of MSU crystals formed and also influences MSU crystal size. These findings may provide an explanation for the clinical presentation of gout in osteoarthritic joints.

Disclosure: A. Chhana, None; B. Pool, None; A. Choi, None; R. Gao, None; M. Zhu, None; J. Cornish, None; J. Munro, None; N. Dalbeth, Takeda, AstraZeneca, Abbvie, 9.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/human-cartilage-influences-the-crystallization-of-monosodium-urate-understanding-the-link-between-gout-and-osteoarthritis
A Non-Coding Genetic Variant Maximally Associated with Serum Urate Levels Is Functionally Linked to HNF4A-Dependent PDZK1 Expression

Tony R. Merriman\textsuperscript{1}, Sarada Ketharnathan\textsuperscript{2}, James Boocock\textsuperscript{3}, Amanda Phipps-Green\textsuperscript{2}, Jisha Antony\textsuperscript{2}, Megan Leaask\textsuperscript{2}, Justin O'Sullivan\textsuperscript{4} and Julia Horsfield\textsuperscript{2}, \textsuperscript{1}Biochemistry Dept, PO Box 56, University of Otago, Dunedin, New Zealand, \textsuperscript{2}University of Otago, Dunedin, New Zealand, \textsuperscript{3}University of California Los Angeles, Los Angeles, CA, \textsuperscript{4}University of Auckland, Auckland, New Zealand

\textbf{First publication:} September 18, 2017

\textbf{SESSION INFORMATION}
\textbf{Session Date:} Wednesday, November 8, 2017
\textbf{Session Title:} Metabolic and Crystal Arthropathies II: Mechanisms of Crystal Inflammation and Metabolism
\textbf{Session Type:} ACR Concurrent Abstract Session
\textbf{Session Time:} 9:00AM-10:30AM

A non-coding genetic variant maximally associated with serum urate levels is functionally linked to HNF4A-dependent PDZK1 expression

\textbf{Background/Purpose:} Genome-wide association studies have revealed several dozen genetic variants associated with serum urate levels. These loci are dominated by genes encoding renal and gut uric acid transporters (\textit{SLC2A9}, \textit{ABCG2}, \textit{SLC17A1-4}, \textit{SLC22A11}, \textit{SLC22A12}) and auxiliary molecules such as \textit{PDZK1}. The precise molecular mechanisms by which causal genetic variant(s) affect serum urate are largely unknown, although the majority of influence will be through control of gene expression. Here we functionally link the maximally associated genetic variant (\textit{rs1967017}) at the \textit{PDZK1} locus to elevated \textit{PDZK1} expression via the HNF4A transcription factor, revealing a new mechanism for serum urate control.

\textbf{Methods:} We performed expression quantitative trait locus (eQTL) and likelihood analyses (PAINTOR and COLOC) followed by gene expression assays in zebrafish and human cell lines. Zebrafish were used to determine the ability of \textit{rs1967017} to direct tissue-specific gene expression, and luciferase assays in HEK293 and HepG2 cells were used to detect the effect of \textit{rs1967017} on transcription amplitude.

\textbf{Results:} PAINTOR analysis revealed \textit{rs1967017} to be the most likely causal variant in the region (\textit{Posterior Prob}=0.93). \textit{Rs1967017} is a cis-acting eQTL for \textit{PDZK1} in the colon and small intestine with a high probability for the association signal with urate levels and the association signal with \textit{PDZK1} to be the same (COLOC \textit{Posterior Prob}=0.93), meaning that \textit{rs1967017} likely influences urate levels through an influence on \textit{PDZK1} expression. The region harboring \textit{rs1967017} was capable of directly driving green fluorescent protein expression in the kidney and intestine of zebrafish embryos, indicating a conserved ability to confer tissue-specific expression. The urate-increasing T-allele of \textit{rs1967017} introduces a binding site for the transcription factor HNF4A. siRNA depletion of HNF4A reduced endogenous \textit{PDZK1} expression in HepG2 cells. Luciferase assays showed that the T-allele of \textit{rs1967017} gains enhancer activity relative to the C-allele, with T-allele enhancer activity abrogated by HNF4A depletion (Figure).

\textbf{Conclusion:} Our data predict that the urate-raising T-allele of \textit{rs1967017} enhances HNF4A binding to the \textit{PDZK1} promoter, thereby increasing \textit{PDZK1} expression. Because \textit{PDZK1} is a scaffold protein for uric acid transporters, its increased expression may contribute to reduced excretion of uric acid.
Abstract Number: 2898

New Mouse Model of Gout Risk Variant, ABCG2 Q141K, Reveals Unexpectedly Severe Molecular and Functional Defect in ABCG2 Mediated Intestinal Uric Acid Secretion

Kazi M. Hoque and Owen M. Woodward, Physiology, University of Maryland School of Medicine, Baltimore, MD
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Metabolic and Crystal Arthropathies II: Mechanisms of Crystal Inflammation and Metabolism
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose:
Gout is a common arthritic disease resulting from deposition of monosodium urate crystals in joints and is a consequence of having elevated circulating uric acid (UA) levels (hyperuricemia). Previously, we discovered that \textit{ABCG2} codes a high-capacity UA efflux transporter, that when dysfunctional causes hyperuricemia and significantly increases the risk for gout. Recent work from others has demonstrated ABCG2 mediated secretion is important in extra-renal, specifically, intestinal excretion of UA. Although ABCG2 is thought to be important for both renal and extra-renal UA excretion, in human cohort studies, ABCG2 dysfunction confers a disproportionate risk for the Renal Overload (ROL) type of hyperuricemia (Matsuo et al 2014), a finding highlighting a disconnect in our understanding of the ABCG2 risk alleles and extra-renal UA excretion.

Methods:
To study the molecular and physiological consequences of a common gout causing \textit{ABCG2} mutation on intestinal UA excretion, we created a mouse model of the Q141K mutation (Q140K in mouse) using CRISPR Cas9 gene editing techniques on a C57BL6 mouse background.

Results:
In a comparison of wildtype and mutant litter mates, we found in the wild type mice ABCG2 expression varies along the GI track with the highest levels in the jejunum and ileum, but surprisingly low levels in the colon. These data are consistent with the observed low level of ABCG2 expression in the human colonic Caco-2 cell line. The localization of the wild type ABCG2 protein was exclusive to the brush border of villus cells and luminal membrane of the crypt cells, optimized to facilitate UA secretion into the intestinal lumen. In contrast, both one or two copies of the Q140K \textit{Abcg2} allele resulted in significant decreases (53% and 88% respectively) in total intestinal expression and apical membrane staining in villus cells. Using an intestinal ligation loop model, we tested the acute UA secretion of the small intestines and found the Q140K mutation reduced UA flux 40%. The reduction in the UA flux in the Q140K loop model was comparable to the reduction observed when the wild type ABCG2 loop was treated with the ABCG2 inhibitor FTC (30%), suggesting the Q140K mutation approximates a complete loss of ABCG2 function in the small intestines.

Conclusion:
We conclude that the Q141K gout causing ABCG2 mutation (Q140K mouse) results in severe loss of ABCG2 mediated UA secretion in the small intestine, contrary to the current dogma that the Q141K ABCG2 is a less severe mutation with only partial (50%) loss of function. Our findings illustrate a potential explanation as to why just one copy of the Q141K ABCG2 allele dramatically increases risk of the ROL type of hyperuricemia.

Disclosure: K. M. Hoque, None; O. M. Woodward, None.
Trapped Crystals in Synovial Fluid: Neutrophil Extracellular Traps (NETs) from Bench to Bed-Side

Estrella Garcia Gonzalez, Orso Maria Luccherini, Alessandra Gamberucci, Alessandra Ali, Antonella Simpatico, Sauro Lorenzini, Marco Bardelli, Mauro Galeazzi and Enrico Selvi, Rheumatology Unit - Policlinico le Scotte, Siena, Italy

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Metabolic and Crystal Arthropathies II: Mechanisms of Crystal Inflammation and Metabolism
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose: Recent data show that neutrophils are able to release chromatin and granular enzymes in web-like structures called neutrophil extracellular traps (NETs). The release of NETs has a physiological role in the innate immunity response by trapping microbes. However, further data indicate that neutrophils are able to release NETs under different conditions such as in the presence of monosodium urate (MSU) and calcium pyrophosphate dihydrate (CPPD) crystals. In particular, it has been postulated that an increasing release of NETs up to a critic threshold during gout attack may lead to the rapid resolution of the disease by packaging MSU crystals and degrading proinflammatory cytokines. Nowadays, the gold standard for the diagnosis of crystal-induced arthropathies remains the identification of crystals in synovial fluid. Interestingly, at standard wet synovial fluid analysis, besides cells and crystals, clumps of non-refractile fibril-like material are commonly observed. These fibrillar aggregates, primarily composed by fibrin and collagen fibrils, appear as ragged and angulated meshes where crystals remain often trapped, making their identification easier. Since crystals appear concentrated on these networks, we found intriguing to understand whether these clumps of non-refractile fibril-like material may contain NETs.

Methods: Synovial fluid samples from MSU and CPPD arthropathies (n=3 for each group) were collected for wet analysis by polarizing, compensated microscopy and then immediately fixed and processed for fluorescence microscopy. Samples were stained on poly-L-lysine-coated glass coverslips with DAPI nucleic acid stain and with anti-neutrophil elastase (NE, rabbit polyclonal) and anti-histone H3 citrullinated antibodies (H3, mouse monoclonal) (Abcam, UK and LS-Bio, US, respectively) in order to visualize NETs' components.

Results: The definitive diagnosis of crystal-induced arthropathy was confirmed by the identification of MSU or CPPD crystals in synovial fluid. In addition, fibril-like aggregates trapping crystals and cells were observed in all the samples analyzed. After immunostaining, web-like NET structures containing DNA, NE and H3-histone were visualized by immunofluorescence. NET structures appeared as networks trapping MSU or CPPD crystals.

Conclusion: NETs can be visualized in synovial fluid from MSU and CCPD crystal-induced arthropathies. NETs appear as part of the clots of fibril-like material frequently observed in synovial fluid trapping crystals.

Disclosure: E. Garcia Gonzalez, None; O. M. Luccherini, None; A. Gamberucci, None; A. Ali, None; A. Simpatico, None; S. Lorenzini, None; M. Bardelli, None; M. Galeazzi, None; E. Selvi, None.


Abstract Number: 2900
Osteoarthritis-Associated Calcium-Containing Crystals and Biomaterial Microparticles Both Drive M1 Macrophage Polarization in a Syk and MAP Kinase-Dependent Manner

Geraldine M. McCarthy1, Olwyn Mahon2, Sarah O’Hanlon3, Daniel Kelly4 and Aisling Dunne5, 1Div of Rheumatology, Mater Misericordiae University Hospital, Dublin, Ireland, 2School of Biochemistry and Immunology, , Trinity College Dublin, Dublin, Ireland, 3School of Biochemistry and Immunology, Trinity College Dublin, Dublin, Ireland, 4Trinity Center for Bioengineering, , Trinity College Dublin, Dublin, Ireland, 5School of Biochemistry and Immunology, Trinity College Dublin, Dublin 2, Ireland

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Metabolic and Crystal Arthropathies II: Mechanisms of Crystal Inflammation and Metabolism
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose: Intra-articular basic calcium phosphate (BCP) crystals are associated with advanced osteoarthritis (OA) and synovitis. OA-associated synovium exhibits increased numbers of macrophages compared with non-OA joints. Total joint replacements (TJR) are performed for advanced OA but periprosthetic osteolysis remains a complication. The local generation of prosthesis-associated wear particles (WP) over time leads to an inflammatory cascade which culminates in implant loosening. Studies suggest that WP-activated macrophages assume a classically activated M1 inflammatory phenotype that overcomes the M2 macrophage-associated activities required for healing. This in turn contributes to the initiation and progression of peri-implant inflammation. Modulating macrophage cytokine production could be a treatment option for periprosthetic inflammation and also OA synovitis. However, the effect of BCP crystals and hydroxyapatite (a component of BCP crystals and commonly used biomaterial) on macrophage polarization has not been previously reported.

We sought to examine 1) macrophage polarization in response to BCP crystals and 2) the signalling pathways involved in BCP crystal, hydroxyapatite (HA) and polymethyl methacrylate (PMMA) bone cement-induced macrophage polarization in primary human macrophages and to determine whether pharmacological blockade of these pathways can impact on M1 macrophage phenotype and inflammatory gene induction.

Methods: Primary human macrophages were stimulated with PMMA (500 µg/ml) or hydroxyapatite particles (250 µg/ml) over the course of 30 minutes. Activated Syk, p38 and ERK were detected by immunoblotting using phospho-specific antibodies. mRNA expression levels of M1 and M2 macrophage markers were analysed by q-PCR 24 hrs post-stimulation while cytokine production was measured by ELISA. Statistical analysis was performed by one way analysis of variance (ANOVA) with Tukey post-test where applicable or student’s t test when comparing only two observations.

Results: We demonstrate that BCP crystals as well as PMMA and HA particles promote macrophage polarization and pro-inflammatory cytokine production via activation of the membrane proximal kinase, Syk, and members of the mitogen-activated protein kinase (MAPK) family of signaling molecules. Pre-treatment of macrophages with Syk or MAPK inhibitors, not only prevents macrophage polarization, but also attenuates production of key pro-inflammatory mediators implicated in periprosthetic osteolysis (Fig) as well as OA synovitis. However, the effect of BCP crystals and hydroxyapatite (a component of BCP crystals and commonly used biomaterial) on macrophage polarization has not been previously reported.

Conclusion: Both BCP crystal and WP-induced macrophage polarization and cytokine production is dependent on activation of specific intracellular signalling molecules. Improved understanding of the biological cascades activated by microparticles could lead to new treatments to modulate OA synovitis as well as aseptic implant loosening.

Disclosure: G. M. McCarthy, None; O. Mahon, None; S. O’Hanlon, None; D. Kelly, None; A. Dunne, None.
Anti-Inflammatory Mechanism of Lubricin/Proteoglycan 4 (PRG4) in Monosodium Urate (MSU)-Crystal Induced Arthritis in THP-1 Macrophages Is Mediated By NALP3 Inflamasome.

Anthony M. Reginato¹, Changqi Sun², Tannin Schmidt³, Elsaid Khalid⁴ and Gregory Jay⁵, ¹Division of Rheumatology, The Warren Alpert School Of Medicine of Brown University, Providence, RI, ²Division of Rheumatology, Rhode Island Hospital/The Warren Alpert School of Medicine of Brown University, Providence, RI, ³Kinesiology and Schulich School of Engineering, University of Calgary, Calgary, AB, Canada, ⁴Department of Biomedical and Pharmaceutical Science, Chapman University School of Pharmacy, Irvine, CA, ⁵Emergency Medicine and Engineering, The Warren Alpert Medical School Brown University, Providence, RI

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Metabolic and Crystal Arthropathies II: Mechanisms of Crystal Inflammation and Metabolism
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose: Lubricin/proteoglycan-4 (PRG4) is a mucinous glycoprotein secreted by synovial fibroblast and superficial zone chondrocytes. PRG4 has a multifaceted homeostatic role in the joint including boundary lubrication, friction lowering of apposed cartilage surfaces and prevention of synovial overgrowth. PRG4 is abundant in the synovial fluid (SF) and its levels are reduced in SF from patients with inflammatory arthropathies. Therapeutically, the recombinant and native form of PRG4 has been shown to exhibit a disease a disease-modifying effect in pre-clinical osteoarthritis (OA) models. Recent studies have suggested that PRG4 may have anti-inflammatory properties in MSU-crystal induced arthritis. Inflamasomes are proteins platforms linking recognition of danger-associated molecular patterns such as MSU by cytosolic sensory proteins to caspase-1 activation. The objective of this study was to further evaluate the anti-inflammatory mechanisms of rhPRG4 in the inflammasome in MSU in acute gout inflammation.

Methods: We evaluated the impact of recombinant human PRG4(rhPRG4) on MSU-induced release, secretion and expression of interleukin-1 beta (IL-1b), tumor necrosis factor alpha (TNF-a), interleukin-8 (IL-8), by ELISA, immunohistochemistry, and western-blot analysis in MSU-stimulated THP-1 cell. Cytosolic and nuclear levels of nuclear factor kappa B (NFkB) p50 and p65 subunits, IkB were studied using western blot. We also evaluated the role of rhPRG4 in the expression of the NLRP3 inflammasome components using qPCR, immunohistochemistry and western-blot analysis. Immunoprecipitation experiments were performed to evaluate if rhPRG4 inhibited NALP3 inflammasome assembly by binding to ASC and prevent caspase-1 activation and cytokine release.

Results: In THP-1 cell line, rhPRG4 significantly inhibited IL-1b, TNF-a and IL-8 production to MSU-crystals using ELISA, western blot analysis and immunohistochemistry in a dose dependent manner. rhPRG4 inhibited the expression of NALP3, PYCARD, Caspase-1 and IL-18 using immunohistochemistry, western blot analysis and qPCR in a dose dependent manner compared to colchicine. rhPRG4 inhibited nuclear factor kappa B (NfkB) and IkB. Considering the activation of the NALP3 inflammasome requires oligomerization of the proteins NALP3, ASC and procaspase, we explored changes in the association of these proteins in response to rhPRG4 in MSU-stimulated THP-1 cells. After immunoprecipitation of ACS, there was a decrease in association of NALP3, activated (cleaved) caspase-1 in rhPRG4 treated THP-1 cells exposed to MSU-crystals.

Conclusion:
Our findings advance our understanding of the complex anti-inflammatory mechanisms of PRG4 in joint homeostasis. rhPRG4 retards the progression MSU-crystal induced inflammatory arthritis by inhibiting the expression and assembly of the NALP3 inflammasome. Our findings provide a better understanding of the molecular mechanism(s) of PRG4 in MSU-crystal induced arthritis with important implications in the development of novel biological strategies in gout.

Acknowledgements
This work is support from a grant from the Arthritis Foundation and COBRE grant P20GM104937 from the National Institutes of Health.
Inflammatory Arthritis Due to Immune Checkpoint Inhibitors: A Persistent Problem Requiring Immunosuppression

Laura Cappelli¹, Clifton O. Bingham III² and Ami A. Shah³, ¹Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, ²Rheumatology, Johns Hopkins University, Baltimore, MD, ³Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases II
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose: Immune checkpoint inhibitors (ICIs) have emerged as an important treatment for advanced malignancies. ICIs are a form of immunotherapy which block negative co-stimulation of T-cells, thereby causing generalized immune activation. De novo inflammatory arthritis (IA) is a potential consequence of ICI use, but there is limited information to guide management of this often severe immune-related adverse event.

Methods: We evaluated clinical data from our longitudinal cohort of patients with ICI-induced IA. Patients with rheumatologist-confirmed IA occurring during or after ICI treatment with no prior history of IA or other systemic autoimmune disease were included. Patients were excluded if they were missing initial joint counts/description of clinical phenotype, or their ICI agent was unknown (e.g. blinded clinical trial). Data was analyzed by ICI treatment regimen to evaluate for differences in presentation and treatment response.

Results: Of the 31 patients included, 18 received anti-PD-1 or anti-PD-L1 monotherapy, 13 received anti-CTLA-4/anti-PD-1 combination therapy and none received anti-CTLA-4 monotherapy (table 1). Median age was 59, and 41.9% were female. Melanoma and non-small cell lung cancer were the most common tumors. Eighty-four percent (26/31) required systemic immunosuppression (corticosteroids, DMARDs). The other 5 patients received NSAIDs and intra-articular steroids. Initial joint involvement and CRP differed significantly by treatment regimen; those treated with combination therapy had higher CRP levels and were less likely to have initial small joint involvement. All cases of reactive arthritis (arthritis plus urethritis/conjunctivitis) were in the combination therapy group. Six patients received therapy with TNF-inhibitors (TNF-i), 4 received methotrexate, and 1 received leflunomide. Of those treated with TNFi, 4 had a persistent anti-tumor response to ICIs, and none lost the response while on TNF-inhibition. Duration of treatment with TNFi ranged from 2-21 months. 3-month follow up data was available on 20 patients after cessation of ICIs (7 still on therapy, 4 died/lost to follow up). Of these 18 had continued IA symptoms requiring treatment.

Conclusion: Baseline clinical features of ICI-induced IA differ by ICI regimen, specifically CRP levels, initial joints affected, and presence of the reactive arthritis triad. The majority of patients referred to rheumatology required systemic immunosuppression to manage their IA symptoms. Tumor progression was not seen in patients requiring TNFi.
<table>
<thead>
<tr>
<th>Variable</th>
<th>All patients (n = 31)</th>
<th>PD-1/PD-L1 mono Rx (n=18)</th>
<th>Combination CTLA-4/ PD-1 Rx (n=13)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: median (IQR)</td>
<td>59 (54-68)</td>
<td>62 (55-73)</td>
<td>57 (45-59)</td>
<td>0.02</td>
</tr>
<tr>
<td>Female sex: N (%)</td>
<td>13 (41.9%)</td>
<td>10 (55.6%)</td>
<td>3 (23.1%)</td>
<td>0.07</td>
</tr>
<tr>
<td>Tumor Type: N (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Melanoma: 8 (25.8%)</td>
<td>Melanoma: 2 (11.1%)</td>
<td>Melanoma: 6 (46.2%)</td>
<td>0.08</td>
<td></td>
</tr>
<tr>
<td>NSCLC: 12 (38.7%)</td>
<td>NSCLC: 9 (50%)</td>
<td>NSCLC: 3 (23.1%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other: 11 (35.5%)</td>
<td>Other: 7 (38.9%)</td>
<td>Other: 4 (30.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Partial/complete tumor response: N (%)</td>
<td>Yes: 17 (63%)</td>
<td>Yes: 9 (64.2%)</td>
<td>Yes: 8 (61.5%)</td>
<td>0.60</td>
</tr>
<tr>
<td>(Total N=27)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Additional IRAE present: N (%)</td>
<td>Yes: 22 (71%)</td>
<td>Yes: 11 (84.6%)</td>
<td>Yes: 11 (61.1%)</td>
<td>0.36</td>
</tr>
<tr>
<td>First joint/s affected: N (%)</td>
<td>Knee: 16 (51.6%)</td>
<td>Knee: 7 (38.9%)</td>
<td>Knee: 9 (69.2%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Other large: 7 (22.6%)</td>
<td>Other large: 3 (16.7%)</td>
<td>Other large: 4 (30.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small joint/s: 8 (25.8%)</td>
<td>Small joint/s: 8 (44.4%)</td>
<td>Small joint/s: 0 (0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td># Swollen joints: median (IQR)</td>
<td>7 (4-10)</td>
<td>8.5 (5-11)</td>
<td>5 (4-7)</td>
<td>0.41</td>
</tr>
<tr>
<td>Reactive arthritis triad: N (%)</td>
<td>3 (9.7%)</td>
<td>0 (0%)</td>
<td>3 (23%)</td>
<td>0.10</td>
</tr>
<tr>
<td>CRP (mg/dL) median (IQR)</td>
<td>1.5 (0.2-7.2)</td>
<td>0.7 (0.2-3.3)</td>
<td>4.8 (2.5-9.2)</td>
<td>0.02</td>
</tr>
<tr>
<td>Required systemic corticosteroids: N (%)</td>
<td>26 (84%)</td>
<td>14 (77.8%)</td>
<td>12 (92.3%)</td>
<td>0.33</td>
</tr>
<tr>
<td>Required additional immunosuppression: N (%)</td>
<td>10 (32.3%)</td>
<td>3 (16.7%)</td>
<td>7 (53.9%)</td>
<td>0.09</td>
</tr>
<tr>
<td>Persistent IA 3 months after ICI cessation: N (%)</td>
<td>18 (90%)</td>
<td>8 (80%)</td>
<td>10 (100%)</td>
<td>0.47</td>
</tr>
<tr>
<td>(Total N= 20)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Comparison of PD-1/PD-L1 monotherapy to combination therapy. Wilcoxon Rank Sum test used for continuous data and Fisher’s exact tests for categorical. Bold values indicate statistical significance. CRP: C-reactive protein

Disclosure: L. Cappelli, Bristol-Myers Squibb, 2; C. O. Bingham III, Bristol-Myers Squibb, 2,Bristol-Myers Squibb, 5; A. A. Shah, Bristol-Myers Squibb, 5.


Abstract Number: 2903
Serum CC-Chemokine Ligand 18 Level Is a Potential Biomarker of Disease Activity in IgG4-Related Disease

Mitsuhiro Akiyama, Hidekata Yasuoka, Keiko Yoshimoto and Tsutomu Takeuchi, 1Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, 2Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases II
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose: IgG4-related disease (IgG4-RD) is a systemic disorder characterized by severe fibrosis in lesions. In previous reports, CC-chemokine ligand 18 (CCL18) level is a substantial biomarker for fibrotic diseases such as idiopathic pulmonary fibrosis and systemic sclerosis. However, the possible involvement of CCL18 in fibrotic pathogenesis of IgG4-RD remains unknown. The objective of this study was to investigate association between serum CCL18 levels and clinical and laboratory findings including treatment response in patients with IgG4-RD.

Methods: Twenty-eight consecutive treatment-naïve patients with IgG4-RD and 16 healthy volunteers were enrolled. The patients were diagnosed as IgG4-RD according to the 2011 comprehensive IgG4-RD diagnostic criteria. Disease activity of the patients was assessed based on the IgG4-RD responder index (IgG4-RD RI). Serum concentration of CCL18 was measured by using human CCL18/PARC Quantikine ELISA Kit (R&D Systems Inc., Minneapolis, MN, USA). The correlation between serum CCL18 levels and clinical and laboratory parameters were examined by Spearman correlation coefficient.

Results: The mean age of patients with IgG4-RD was 59.7 years, and the proportion of female was 50% (14/28). The involved organs of the patients were lacrimal gland and orbits (22 cases, 78.6%), salivary gland (19 cases, 67.9%), lymph node (11 cases, 39.3%), lung (7 cases, 25%), pancreas (7 cases, 25%), kidney (5 cases, 17.9%), retroperitoneum (3 cases, 10.7%), aorta (2 cases, 7.1%), skin (2 cases, 7.1%), breast (1 case, 3.6%) and paravertebral mass (1 case, 3.6%). Serum concentration of CCL18 in patients with IgG4-RD (mean 44.7 ng/mL, range 3.6–120.9 ng/mL) was significantly higher than that of healthy volunteers (mean 18.5 ng/mL, range 0.1–63.8 ng/mL; P = 0.01). Of note, serum CCL18 concentrations positively correlated with IgG4-RD RI scores (ρ = 0.54, P < 0.005), number of affected organs (ρ = 0.56, P < 0.005), or serum levels of IgG4 (ρ = 0.50, P < 0.01), but not serum IgE levels (ρ = -0.05, P = 0.79) or blood eosinophil counts (ρ = 0.18, P = 0.38), suggesting that serum CCL18 concentrations reflect IgG4-RD state rather than allergic condition. Moreover, serum CCL18 concentrations significantly decreased after glucocorticoid treatment in patients with IgG4-RD (44.7 ng/mL vs. 12.7 ng/mL, P < 0.01), which were paralleled with disease improvement.

Conclusion: Serum CCL18 concentration is a novel biomarker potentially valuable for evaluating disease activity and treatment response in IgG4-RD. Our results suggest that CCL18 contribute to the fibrotic process in IgG4-RD.

Disclosure: M. Akiyama, None; H. Yasuoka, None; K. Yoshimoto, None; T. Takeuchi, Mitsubishi Tanabe Pharma Corporation, 2.

Efficacy and Tolerance of TNF Alpha Inhibitor (TNFI) Treatment in Cardiac Sarcoidosis (CS)

Deborah Puyraimond-Zemmour, Catherine Chapelon-Abric, David Saadoun, Diane Bouvry, Marc Ruivard, Marc Andre, Laurent Perard, Pascal Sève and Patrice Cacoub, 1Sorbonne Universités, UPMC Univ Paris 06, UMR 7211, and Inflammation-Immunopathology-Biotherapy Department (DHU iiB), F-75005, Paris, France, Paris, France, 2AP-HP, Groupe Hospitalier Pitié-Salpêtrière, Department of Internal Medicine and Clinical Immunology, F-75013, Paris, France, Paris, France, 3Department of Internal Medicine and clinical Immunology. French National Reference Center for Autoimmune Diseases. DHU I2B (Inflammation, Immunotherapy and Biotherapy), UPMC, Paris VI, Hôpital Pitié Salpêtrière, AP-HP, UPMC, Univ Paris 06, Paris, France, 4Hôpital Avicenne, Department of Pneumology, Bobigny, France, Bobigny, France, 5CHU Estaing, Department of Internal Medicine, Clermont-
SESSION INFORMATION

Session Date: Wednesday, November 8, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases II
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose: CS is a life-threatening condition that accounts for 85% of sarcoidosis-related deaths in Japan and 13-25% in America. The objective is to evaluate the effectiveness and tolerance of TNFI treatment in CS.

Methods: From a French multicenter cohort of patients with extra-thoracic sarcoidosis, we retrospectively analyzed patients who fulfilled following inclusion criteria 1) a definite histologically proven extra-thoracic sarcoidosis, 2) a CS based on the 2011-Heart Rhythm Society consensus and 3) who received a TNFI. The response to TNFI treatment was analyzed on multiple criteria including (i) cardiac clinical symptoms/signs i.e. New York Heart Association (NYHA) class for dyspnea, heart failure, and cardiac rhythm or conduction disturbances; (ii) NT-pro-BNP and BNP serum levels, and (iii) cardiac imaging abnormalities on echography, scintigraphy, MRI, or 18 FDG PETscan. Patients were classified as complete responders when they showed a complete normalization of all baseline abnormal exams (clinical, biological and imaging). Non responders were defined by the absence of improvement of all baseline abnormal exams or an aggravation of at least one exam. All other cases were defined as partial responders.

Results: We analyzed 25 patients, aged 38 years, 36.4% had chest pain/heart failure, and abnormal findings on EKG (73%), cardiac MRI (55%), echocardiography (40%), 18 FG PETscan (30%) and scintigraphy (10%). 42% had > 4 organs involved by sarcoidosis. Sarcoidosis duration before starting TNFI was 136 months [19; 311]. CS was refractory to other immunosuppressants i.e. methotrexate (n=24/25), cyclophosphamide (n=12/25), azathioprine (n=8/25), and mycophenolate mofetyl (n=6/25). After a follow up of 50.7 months after starting TNFI (infliximab n=24, etanercept n=1), 36% patients were complete responders, 48% partial responders and 16% non-responders. 8% had a CS relapse and were treated by a second course of TNFI with a good response. Corticosteroids were given at baseline in all patients; mean daily dose of steroids was 21 mg [5;50] at baseline versus 10 mg [1;40] at the last visit, and they were stopped in 28%. Eight patients had to withdraw TNFI because of adverse events, i.e. infection (n=5), allergy (n=1), and cardiac arrest (n=2). Two patients died, from a sudden death and an unknown cause (two months after stopping TNFI).

Conclusion: TNF alpha inhibitors showed a complete/partial cardiac response in 84% of patients with cardiac sarcoidosis refractory to immunosuppressive therapy, with a steroid sparing-effect. Adverse events led to TNF alpha inhibitors withdrawal in one third of patients.

Disclosure: D. Puyraimond-Zemmour, None; C. Chapelon-Abric, None; D. Saadoun, None; D. Bouvry, None; M. Ruivard, None; M. Andre, None; L. Perard, None; P. Sève, None; P. Cacoub, None.

Abstract Number: 2905

TET2 Mutation Is Significantly Associated with the Development of Autoimmune Disorder in Patients with Myelodysplastic Syndrome

Yoon-Jeong Oh1, Dong-Yeop Shin2, Sang Mee Hwang3, Eun Young Lee4, Yeong Wook Song5, Dong-Soon Lee3 and Jin Kyun Park6,

1Division of Rheumatology, Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea, Republic of (South), 2Cancer Research Institute, Seoul National University College of Medicine, Seoul, Korea, Republic of (South), 3Department of Laboratory Medicine, Seoul National University College of Medicine, Seoul, Korea, Republic of (South), 4Seoul National University College of Medicine, Seoul, Korea, Republic of (South), 5Department of Molecular Medicine and Biopharmaceutical Sciences, Graduate School of Convergence Science and Technology, Seoul National University, Seoul, Koer, Seoul, Korea, Republic of (South), 6Division of Rheumatology, Seoul National University Hospital, Seoul, Korea, Republic of (South)

First publication: September 18, 2017
Background/Purpose: Myelodysplastic syndrome (MDS) is characterized by ineffective hematopoiesis in bone marrow and peripheral cytopenia. Various genetic mutations contribute to MDS. Common mutations affect genes regulating epigenetic control, protein translation among others. A recent study demonstrated that certain autoimmune manifestations were associated with specific karyotypic abnormalities in patients with MDS. The aim of this study was to investigate whether particular genetic mutations are associated with the occurrence of autoimmune disorders in MDS.

Methods: A total of 88 genetic mutations that are commonly associated with MDS were sequenced in 73 MDS patients. The association of each mutation with autoimmune disease (AID) was analysed.

Results: The mean age of MDS patients was 65.1 years, and 49 (67.1%) were male. During the follow-up duration, 19 (26.0%) developed AIDs; 7 (9.6%) thyroiditis, 5 (6.8%) immune thrombocytopenia (ITP) and haemolytic anemia (HA), and 1 (1.4%) rheumatoid arthritis (RA), 1 (1.4%) ankylosing spondylitis (AS), 1 (1.4%) systemic lupus erythematosus (SLE), 1 (1.4%) panniculitis, 1 (1.4%) psoriasis, 1 (1.4%) neutrophilic dermatosis, and 1 (1.4%) uveitis. Baseline demographic and laboratory parameters did not differ between patients with AID.

Of 73 MDS patients, 57 (78.1%) carried mutation at least in 1 of the 88 selected genes. The presence of mutation (73.7% vs. 79.6%, p=0.75) and the number of mutations (2.32 vs. 2.04, p=0.56) were similar between the patients with or without AID. Strikingly, the TET2 mutation was significantly higher in patients with AID compared to those without AID (26.3% vs. 5.6%, p=0.017). Five (62.5%) of 8 MDS patients with TET-2 mutation exhibited AID (RA, AS, ITP, panniculitis, and neutrophilic dermatosis).

Conclusion: Mutation of TET2, an epigenetic regulator, might be associated with increased risk of developing autoimmune diseases in patients with MDS.

Table. Baseline characteristics in patients with MDS
<table>
<thead>
<tr>
<th>Age at diagnosis, mean (SD)</th>
<th>MDS(N=73)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (%)</td>
<td>65.1 (14.6)</td>
</tr>
<tr>
<td>Female (%)</td>
<td>49 (67.1%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Autoimmune abnormalities</th>
<th>MDS(N=73)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid arthritis (%)</td>
<td>1 (1.4%)</td>
</tr>
<tr>
<td>Ankylosing spondylitis (%)</td>
<td>1 (1.4%)</td>
</tr>
<tr>
<td>Autoimmune thyroiditis (%)</td>
<td>7 (9.6%)</td>
</tr>
<tr>
<td>SLE (%)</td>
<td>1 (1.4%)</td>
</tr>
<tr>
<td>ITP/Hemolytic anemia (%)</td>
<td>5 (6.8%)</td>
</tr>
<tr>
<td>Panniculitis (%)</td>
<td>1 (1.4%)</td>
</tr>
<tr>
<td>Psoriasis (%)</td>
<td>1 (1.4%)</td>
</tr>
<tr>
<td>Neutrophilic dermatosis (%)</td>
<td>1 (1.4%)</td>
</tr>
<tr>
<td>Uveitis (%)</td>
<td>1 (1.4%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MDS, subtypes</th>
<th>MDS(N=73)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refractory anemia, n (%)</td>
<td>5 (6.8%)</td>
</tr>
<tr>
<td>RCMD, n (%)</td>
<td>15 (20.5%)</td>
</tr>
<tr>
<td>RAEB-1 and2, n (%)</td>
<td>28 (38.4%)</td>
</tr>
<tr>
<td>MDS/MPN, n (%)</td>
<td>7 (9.6%)</td>
</tr>
<tr>
<td>Unclassifiable, n (%)</td>
<td>15 (20.5%)</td>
</tr>
<tr>
<td>Others, n (%)</td>
<td>3 (4.1%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genetic mutation</th>
<th>MDS(N=73)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>57 (78.1%)</td>
</tr>
<tr>
<td>No</td>
<td>16 (21.9%)</td>
</tr>
</tbody>
</table>

Figure. Gene mutations features in MDS with or without autoimmune diseases
Disclosure: Y. J. Oh, None; D. Y. Shin, None; S. M. Hwang, None; E. Y. Lee, None; Y. W. Song, None; D. S. Lee, None; J. K. Park, None.


Abstract Number: 2906

Use of Disease-Modifying Antirheumatic Drugs, Biologic Response Modifiers and Corticosteroids, and Subsequent Risk of Coccidioidomycosis Infection Among Medicare Beneficiaries

Dominick Sudano1, C. Kent Kwoh2, Lili Zhou3, Erin L. Ashbeck4 and Wei-Hsuan Lo-Ciganic5, 1University of Arizona Arthritis Center, University of Arizona, Tucson, AZ, 2University of Arizona, Tucson, AZ, 3Department of Pharmacy, Practice and Science, University of Arizona, College of Pharmacy, Tucson, AZ, 4The University of Arizona Arthritis Center, Tucson, AZ, 5Department of Pharmacy, Practice and Science, College of Pharmacy, University of Arizona, Associate professor, TUCSON, AZ
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases II
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose: Coccidioidomycosis (Cocci) is a fungal infection endemic to seven states in the US. Biologic response modifiers (BRMs) have been shown to increase the risk of serious infections including fungal infections, but data are limited on the risk of Cocci with BRMs and corticosteroids (CSTs). Our objective was to examine the association between use of DMARDs, BRMs, and CSTs and subsequent risk of Cocci infection among Medicare beneficiaries with rheumatic or autoimmune diseases.

Methods: In a retrospective cohort study using 2011-2013 Medicare claims data (5% representative sample), we restricted the analyses to continuously enrolled, fee-for-service beneficiaries who resided in Arizona, California, New Mexico, Nevada, Texas, Utah, and Washington. Among beneficiaries having any of ten rheumatic/autoimmune diseases (i.e., RA, SLE, psoriasis, PsA, AS, PM, DM, IBD, ReA, and SSc), we identified those who initiated DMARDs, BRMs, CSTs or did not use any DMARDs/BRMs/ CSTs. The index date was defined as the earliest date of the rheumatic/autoimmune disease diagnosis or first prescription of CSTs, DMARDs, or BRMs. Individuals with diagnosed Cocci infection prior to the index date were excluded. Based on the refill days supplied, we created time-varying exposure variables of DMARDs, BRMs, and CSTs, and applied a 90 day lag period following drug cessation. We used multivariable Cox proportional hazard regression to examine DMARD, BRM, and CSTs use and the risk of subsequent Cocci infection, adjusted for age, sex, race, Medicaid eligibility, low income subsidy, RxHCC risk score, Elixhauser comorbidity index, disability, metropolitan area, opioid use, and NSAID use within 3 months of the index date. Cox models included indicator variables for CSTs, DMARDs, and BRMs simultaneously.

Results: Among 14,931 beneficiaries (mean age: 68.7; white: 75.3%, black: 7.6%), 51 individuals were diagnosed with Cocci during the study period (1.6 per 1,000 person-years). Increased risk of Cocci was observed among beneficiaries prescribed any CSTs (HR=1.94, 95%CI: 1.10, 3.42) and any BRMs (HR=2.25, 95%CI: 1.02, 4.95), though not for individuals prescribed any DMARDs/BRMs/ CSTs. The index date was defined as the earliest date of the rheumatic/autoimmune disease diagnosis or first prescription of CSTs, DMARDs, or BRMs. Individuals with diagnosed Cocci infection prior to the index date were excluded. Based on the refill days supplied, we created time-varying exposure variables of DMARDs, BRMs, and CSTs, and applied a 90 day lag period following drug cessation. We used multivariable Cox proportional hazard regression to examine DMARD, BRM, and CSTs use and the risk of subsequent Cocci infection, adjusted for age, sex, race, Medicaid eligibility, low income subsidy, RxHCC risk score, Elixhauser comorbidity index, disability, metropolitan area, opioid use, and NSAID use within 3 months of the index date. Cox models included indicator variables for CSTs, DMARDs, and BRMs simultaneously.

Conclusion: The overall incidence of Cocci was low among Medicare beneficiaries with rheumatic or autoimmune diseases in the southwestern United States from 2011 to 2013. Our findings suggest that BRM and CSTs users may have higher risk of Cocci compared to non-users, but no evidence of increased risk was observed for those who used DMARDs. Cocci is a serious infection, and warrants consideration for regular screening among clinicians for individuals on BRMs and CSTs.
Table 1. Use of Disease-Modifying Antirheumatic Drugs, Biologic Response Modifiers and Corticosteroids, and Subsequent Cocci risk: Multivariable Cox Models

<table>
<thead>
<tr>
<th>No. Cocci Cases</th>
<th>Crude Rate (per 1,000 person-years)</th>
<th>Unadjusted HR (95% CI)</th>
<th>Adjusted HR(^a) (95% CI)</th>
<th>Adjusted HR(^b) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSTs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>29</td>
<td>1.2</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Yes</td>
<td>22</td>
<td>2.5</td>
<td>1.95 (1.11, 3.42)</td>
<td>1.94 (1.10, 3.42)</td>
</tr>
<tr>
<td>DMARDs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>35</td>
<td>1.5</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Yes</td>
<td>16</td>
<td>1.8</td>
<td>1.05 (0.56, 1.94)</td>
<td>1.02 (0.54, 1.91)</td>
</tr>
<tr>
<td>BRMs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>43</td>
<td>1.5</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Yes</td>
<td>8</td>
<td>3.1</td>
<td>2.20 (1.01, 4.83)</td>
<td>2.25 (1.02, 4.95)</td>
</tr>
</tbody>
</table>

**Abbreviations:** BRMs: biologic response modifiers; Cocci: Coccidioidomycosis; CSTs: corticosteroids

\(^a\) Adjusted HRs were estimated by including sociodemographics and health status covariates and indicator variables for CSTs, DMARD, and BRM, simultaneously. For example, the HR for BRMs compares the risk of Cocci for those exposed to BRMs compared to participants not exposed to BRMs, adjusted for concurrent CSTs exposure and DMARD exposure.

Disclosure: D. Sudano, None; C. K. Kwoh, NIH/NIAMS, 2,EMD Serono, 2,Abbvie, 2; L. Zhou, None; E. L. Ashbeck, None; W. H. Lo-Ciganic, None.


Abstract Number: 2907

**Salivary Gland Enlargement in IgG4-Related Disease Is Associated with Multiorgan Involvement and Higher Basal Disease Activity**

**Eduardo Martín Nares\(^1\), Jacobo Guerrero Castillo\(^2\), Arturo Angeles Angeles\(^2\) and Gabriela Hernandez-Molina\(^1\), \(^1\)Department of Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, \(^2\)Department of Pathology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico**

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Wednesday, November 8, 2017
Session Title: Miscellaneous Rheumatic and Inflammatory Diseases II
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

**Background/Purpose:**

IgG4-related disease (IgG4-RD) is an immune-mediated condition which clinical spectrum encompasses single or multiple organ involvement. Enlargement of major and minor salivary glands is one of the main disease features. Whether salivary gland enlargement is associated with systemic involvement has not been previously evaluated. The purpose of this study was to elucidate if salivary gland enlargement is associated with systemic disease.

**Methods:** We included patients with an established diagnosis (definitive: organ involvement, biopsy proven and high IgG4 levels; probable: organ involvement, biopsy proven without high IgG4 levels; possible: organ involvement, high IgG4 levels without histology) of IgG4-RD according to the Comprehensive Diagnostic Criteria, who regularly attend a tertiary referral center in Mexico City (2000-2017). We retrospectively collected demographics, clinical (organ involvement, disease activity and damage assessed by the IgG4-RD
Responder Index [IgG4-RD RI] at basal and at 6 months of follow-up, number of relapses, remission and treatment, basal laboratory (C3, C4, ESR, PCR, total eosinophil count, IgG4 levels) as well as imaging and histologic data.

Results:

We included 32 patients, 17 (53.1%) men, mean age 50.2 ± 14.1 years and median disease duration 20.5 months. Seven (21.9%) have a definitive diagnosis, 12 (37.5%) probable and 13 (40.6%) possible. Overall we identified 21 anatomic sites affected, mainly pancreas 56.2%, lymph nodes 56.2%, lacrimal glands 37.5% and bile duct 34.3%. Salivary gland involvement was present in 12 (37.5%) patients (2 parotid, 3 minor salivary gland and 7 both). Among these patients, only 5 (41.6%) referred dry mouth and in 7 patients (58.3%) glandular enlargement was the onset disease feature. Salivary glandular enlargement was identified only radiologically in 5 patients (41.6%) and both clinical and radiologically in 7 (58.3%) patients. When we compared patients with (n=12) vs. without (n=20) salivary gland enlargement, the first group had a higher number of affected organs (6.5 vs. 2, p=0.0001) and absolut eosinophil’s count (348 vs. 137.5/mm³, p=0.05), a higher prevalence of lacrimal glands (75% vs. 15%, p=0.002), lymph nodes (91.7% vs. 35%, p=0.002) and lung involvement (33.3% vs. 0%, p=0.01), azathioprine use (83.3% vs. 30%, p=0.003), as well as a higher basal IgG4-RD RI (12 vs. 6, p=0.001) and a longer delay in diagnosis (64 month vs. 6.5 months, p=0.001). We did not find differences regarding gender, age, IgG4 serum levels, C3, C4, ESR, PCR, antinuclear antibodies, rheumatoid factor, anti-Ro/SSA and anti-La/SSB antibodies (negative in all patients), number of relapses, remission at 6 months and damage. We performed a logistic regression analysis (only including the number of organs, the basal IgG4-RD RI and time of follow-up) and found an association of salivary gland enlargement with the basal IgG4-RD RI (OR 1.63, 95% CI 1.12-2.35, p=0.009).

Conclusion: Our study highlights the systemic nature of IgG4-RD. Patients with salivary gland enlargement should be routinely screened for systemic involvement.

Disclosure: E. Martín Nares, None; J. Guerrero Castillo, None; A. Angeles Angeles, None; G. Hernandez-Molina, None.

Abstract Number: 2908

High Disease Activity Is a Predictor of Depression and Persistent Depression in Early Rheumatoid Arthritis: Results from a Rheumatoid Arthritis Cohort

Raman Joshi1, Mohammad Movahedi2, Bindee Kuriya3, Emmanouil Rampakakis4, Angela Cesta2, Xiuying Li2, Sandra Couto2, John S. Sampalis5 and Claire Bombardier2, 1William Osler Health Centre-Brampton Civic Hospital, Brampton, ON, Canada, 2Toronto General Hospital Research Institute, University Health Network, Toronto, ON, Canada, 3Sinai Health System, University of Toronto, Toronto, ON, Canada, 4JSS Medical Research, Montreal, QC, Canada, 5McGill University, Montreal, QC, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects VI: Comorbidities of Rheumatoid Arthritis
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose:
The prevalence of depression among individuals with rheumatoid arthritis (RA) may be as high as 40% but persistence of depression over time is relatively unknown. Uncontrolled inflammation may drive severe disease and, in turn, inflammation and high disease activity are hypothesized to mediate depressive symptoms. The aims of this analysis were to: (1) describe the prevalence of depression at baseline and determine how often depression persists over time; (2) determine whether there is an association between changes in disease activity and depression over time among individuals with early RA (ERA).

Methods:
ERA patients enrolled in the Ontario Best Practices Research Initiative (OBRI) with ERA (≤ 1 year disease duration) and >/= 2 years of follow-up were included. Persistent depression was defined as self-reported depression at baseline and at >50% of visits over the first 2 years. The association between baseline disease activity, measured by the Clinical Disease Activity Index (CDAI), and depression at
baseline or persistent depression was evaluated with multivariate logistic regression. The General Estimation Equation was also used to explore the association between changes in CDAI disease activity over time and risk of depression.

**Results:**

469 patients with ERA (72.9% female) were included with a mean (SD) age of 56.8 (13.6) years. Mean (SD) disease parameters were: CDAI: 22.9 (14.1); DAS28: 4.6 (1.5); and HAQ disability Index: 1.1 (0.75). At baseline, the prevalence of depression was 26%, and 23% reported persistent depression. Persistent depression was significantly higher in patients with moderate CDAI (19%) and high CDAI (29%) compared to those in CDAI low disease activity (LDA) or remission (16%, p=0.02). After adjusting for potential confounders (sex, rheumatoid factor status, prior use of csDMARDs, current use of bDMARDs, HAQ disability index, number of comorbidities), increased CDAI at baseline was significantly associated with both baseline depression and persistent depression (OR: 1.04; 95%CI: 1.01-1.06, p=0.002). Female gender (OR: 3.17; 95%CI: 1.50-6.68 p=0.002) and greater number of comorbidities at baseline (OR: 1.68; 95%CI: 1.47-1.93, p<0.001) were also associated with persistent depression. Over the course of follow-up, the risk of depression was significantly higher among patients with moderate disease activity compared to those in CDAI LDA or remission (OR: 1.16; 95%CI: 1.04-1.29, p=0.006). The risk of depression was substantially greater for those with high disease activity (OR: 1.32; 95%CI: 1.15-1.52) over time compared to those achieving LDA or remission states.

**Conclusion:**

Depression in ERA is common and initial high disease activity increases the risk of depression as well as its persistence. High CDAI during the early years of follow-up was also an independent predictor of depression. This highlights the importance of intervening during the “window of opportunity” to control disease activity and the potential to mitigate adverse health outcomes, including depression.

Disclosure: R. Joshi, None; M. Movahedi, None; B. Kuriya, None; E. Rampakakis, Janssen Inc., 9; A. Cesta, None; X. Li, None; S. Couto, None; J. S. Sampalis, None; C. Bombardier, Canada Research Chair in Knowledge Transfer for Musculoskeletal Care and a Pfizer Research Chair in Rheumatology, 6.

**Abstract Number: 2909**

**Only Very High Radiographic Progression Affects HAQ-DI, Results from the Swiss Scqm Cohort**

**Ruediger Mueller**1, Reto Thalmann2, Hendrik Schulze-Koops3, Nicole Graf4 and Johannes von Kempis2, 1Rheumatology, MD, St. Gallen, Switzerland, 2Rheumatology, Kantonsspital St. Gallen, St. Gallen, Switzerland, 3Division of Rheumatology and Clinical Immunology, Department of Internal Medicine IV, University of Munich, Munich, Germany, 4Graf Biostatistics, Winterthur, Switzerland

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Wednesday, November 8, 2017  **Session Title:** Rheumatoid Arthritis – Clinical Aspects VI: Comorbidities of Rheumatoid Arthritis  **Session Type:** ACR Concurrent Abstract Session  **Session Time:** 9:00AM-10:30AM

**Background/Purpose:**

The aim of treatment of rheumatoid arthritis is to control disease activity and to inhibit joint damage. Progression of damage is analysed by conventional radiographs. High radiographic progression has, to our knowledge, not been analysed in detail.

**Objectives:** To analyse RA patients depending on their individual peak radiographic progression.

**Methods:** We selected for the highest (peak) radiographic progression in every individual patient of the Swiss registry SCQM with at least two scored sets of radiographs of hands and feet. The individual radiographic progression was analysed as change of Ratingen erosion scores/year (follow up 1998 – 2015). The baseline disease characteristics were compared using standard descriptive statistics (Kruskal-Wallis or Chi-square tests). The change of DAS 28 and HAQ-DI scores before and after peak progression was analysed with the Wilcoxon signed rank tests.
Results:

Of the 4'033 patients in the analysis 3'049 patients had a peak radiographic progression rate between 0 and ≤10/year, 773 between 10 and ≤20, 150 between 20 and ≤30, and 61 of >30 (defining groups 1-4). Rheumatoid factor and ACPA were more frequent in patient groups with higher peak radiographic progression (RF: 73.6, 80.0, 88.9, 90.0; ACPA: 66.8, 73.4, 74.3, 82.1, groups 1-4, respectively). Peak radiographic progression at a rate >20/year (groups 3 and 4) were not detected after December 2012. When the rate of radiographic progression before and after peak progression was analysed, 69.7%, 74.7%, 76.9%, and 93.3% of the patients had a radiographic progression of 25% or lower as compared to peak progression before and 76.1%, 81.8%, 91.1%, and 93.8% after this peak progression, respectively for patients in groups 1 to 4 (Figure A).

The disease activity, as assessed by DAS 28, was significantly higher in all patient groups before peak progression and lower thereafter (p < 0.001). Average HAQ-DI scores increased after peak radiographic progression in group 4 (p = 0.005) whereas it is stable or even decreases among the patients of the other patient groups.

Conclusion: These data show that high radiographic progression is rare and gets less frequent over the last years. Higher disease activity precedes radiographic peak progression. Radiographic progression before and after the individual peak radiographic progression was far lower as compared to the time of radiographic peak progression. Only the highest individual peak (change of Ratingen score >30/year) radiographic progression was followed by an increase of HAQ-DI scores.

Disclosure: R. Mueller, None; R. Thalmann, None; H. Schulze-Koops, None; N. Graf, None; J. von Kempis, None.

Abstract Number: 2910

Comparison of Clinical and Ultrasound Measures of Disease Activity in a Large National ‘Real Life’ Cohort of RA Patients

Pascal Zufferey1, Delphine Couvoisier2, Hans Ruedi Ziswiler3, Laure Brulhart4, Giorgio Tamborini5, Michael Nissen6, Adrian Ciurea7, Burkhard Moeller8, Maria Antonietta D’Agostino9,10 and Axel Finckh2, 1Department of Rheumatology, University Hospital Lausanne, Lausanne, Switzerland, 2geneva university hospital, Geneva, Switzerland, 3Osteorheuma, Bern, Switzerland, 4médecine, hôpital neuchateuloi, La chaux de fond, Switzerland, 5UZR, Basel, Switzerland, 6rheumatology, geneva university hospital, Geneva, Switzerland, 7Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland, 8Department for Rheumatology, Immunology and Allergology, University Hospital of Bern, Bern, Switzerland, 9Department of Rheumatology, Assistance publique-Hôpitaux de Paris Ambroise Paré Hospital, Boulogne-Billancourt, Université Versailles Saint Quentin en Yvelines, Paris, France, 10University of Paris, Paris, France

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Wednesday, November 8, 2017
Session Title: Rheumatoid Arthritis – Clinical Aspects VI: Comorbidities of Rheumatoid Arthritis
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose: Clinical measures of disease activity, such as the DAS-score and ultrasound (US) scores of disease activity can be sometimes yield discordant results. Little research has attempted to understand the reasons for these discordances. Moreover, it is not well known what the implications of such discordances are or how clinical and US assessments evolve over time in this situation

Objectives: First: to determine the percentages of patients presenting discordances between DAS and US assessments in a real-life cohort. Second: to describe associated factors. Third: to evaluate the evolution of both measures of disease activity over time.

Methods: All patients with at least one concomitant US- and DAS-score assessment, performed since the introduction of validated US (SONAR) score in the SCQM between 2009 and January 2017 were included. Disease activity was categorized as remission, low, moderate and high activity based on previously established cut-offs for the DAS and the US-score. Potential predictors of discordance were extracted from the SCQM database, including age, gender, seropositivity, duration of illness, number of swollen and tender joints, global physician assessment of disease activity, HAQ, presence of fibromyalgia, type of treatment, patients followed in private practice and other. A longitudinal analysis was performed in all the patients with at least two subsequent visits with US and DAS assessment performed simultaneously.
**Results:** 2367 assessments could be analyzed, of which 1072 (45%) were considered concordant based on identical disease activity states with the DAS- and the US score. The proportion concordant assessments significantly differed by clinical disease status (p<0.001); more frequent in clinical remission (78.4% of agreement) compared to active disease status (21% in low or moderate DAS, 45% in high DAS). Among the discordant assessments, disease activity state tended to be more frequently over-estimated by the DAS compared to US-score (38%), than the other way round (17%), (p<0.05).

Factors associated with the presence of discordant results were the swollen joint count (p <0.001), the overall estimation of the disease activity (p<0.001) by the clinician, the duration of the disease (p<0.02).

For 1181 patients, several DAS and US assessments were available during follow-up. The proportion of discordances during the follow-up was similar to the initial evaluation. Initial discordance/concordances could however change status without obvious reason, especially in the moderate and low disease activity subgroup (75 % new discordancess).

**Conclusion:** Discordances between DAS and US assessments appear to be higher than expected in real life. Both outcome measures can lead to over- or under-estimations of the true disease activity. Discordant assessments seem to be linked essentially to inaccuracies in the clinical evaluation in particular (inadequate swollen joint counts) and/or to limitations of the US procedure (especially poor distinction between moderate and low activity disease).

**Disclosure:** P. Zufferey, None; D. Couvoisier, None; H. R. Ziswiler, None; L. Brulhart, None; G. Tamborrini, None; M. Nissen, None; A. Ciurea, None; B. Moeller, None; M. A. D'Agostino, None; A. Finckh, None.

**Abstract Number: 2911**

**Low Appendicular Bone Mass Predicts Mortality in Patients with Rheumatoid Arthritis**

**Mark Edward Hall**

1. Internal Medicine, University of Texas Health Science Center at San Antonio, San Antonio, TX,
2. Internal Medicine-Rheumatology, University of Texas Health Science Center at San Antonio, San Antonio, TX,
3. Medicine, San Antonio Military Medical Center, San Antonio, TX,
4. Sectra AB, Linköping, Sweden

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Wednesday, November 8, 2017

**Session Title:** Rheumatoid Arthritis – Clinical Aspects VI: Comorbidities of Rheumatoid Arthritis

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 9:00AM-10:30AM

**Background/Purpose:** Rheumatoid Arthritis (RA) is a multi-system disease which causes joint damage and is associated with increased cardiovascular (CV) morbidity and osteoporosis. Our purpose is to examine the relationship between bone mass and mortality in patients with RA.

**Methods:** We recruited patients with RA from public and private rheumatology practices in San Antonio, Texas. In addition to demographic data, baseline measures were obtained including the extent and severity of joint involvement, the presence of CV risk factors (such as the presence of diabetes, tobacco use, hypercholesterolemia, and hypertension), and the bone mineral density (BMD), calculated from appendicular bone mass via Digital X-ray Radiogrammetry (DXR) of anteroposterior hand radiographs (Sectra AB, Linköping, Sweden). During annual follow-up, all deaths were identified from relatives, physicians, obituaries, or national databases. We obtained certificates for all deaths. Patients were divided into groups according to BMD quartile. We used the Kaplan-Meier method to examine the association of BMD with mortality. We then adjusted for potential confounding variables using Cox proportional hazards regression analysis.

**Results:** Our study included 653 patients with RA. Their mean age ± standard deviation [SD] was 58.1±12.7 years and 72% were women. We had a total of 8,653 person-years [PY] of observation and noted 252 deaths over the course of the study for a mortality rate of 2.9 per 100 PY. Mortality was highest in the lowest BMD quartile at 5.2 per 100 PY (95% confidence interval [95% CI] 4.3-6.3). Higher BMD quartiles had less mortality, most notably in the two highest quartiles with a mortality rate of 1.9 per 100 PY (95% CI 1.4-2.6) and 1.6 per 100 PY (95% CI 1.2-2.2), respectively. The mortality hazard ratio (HR) was 0.74 per each decigram/cm² increase in
BMD (95% CI 0.62-0.90, P-value less than or equal to 0.01) after adjusting for age, sex, ethnicity, CV risk factors, and measures of RA inflammatory disease activity (counts of tender and swollen joints and erythrocyte sedimentation rate) and joint damage (Sharp score of radiographic erosions and joint space narrowing).

**Conclusion:** Low BMD in RA patients is independently associated with increased mortality rate. Together with other known risks factors and comorbidities, the presence of a low BMD suggests worse outcomes in patients with RA. BMD measurements via DXR may be of utility in the clinic as hand radiographs are routinely trended over time and readily obtained. Further research is needed to understand the mechanisms underlying the association between BMD and mortality in RA.

**Disclosure:** M. E. Hall, None; I. del Rincon, None; J. F. Restrepo, None; D. F. Battafarano, None; J. Algulin, Sectra AB, 3; A. Escalante, None.


**Abstract Number:** 2912

**The Neural Correlates of Inflammation in RA: A Multi-Modal MRI Study**

*Andrew Schrepf¹, Chelsea Cummiford¹, Eric Ichescuo¹, Tony Larkin¹, Steven E. Harte¹, Richard E. Harris¹, Alison Murray², Gordon Waiter³, Daniel J. Clauw⁴ and Neil Basu⁵, ¹Chronic Pain and Fatigue Research Center, University of Michigan, Ann Arbor, MI, ²Aberdeen Brain Imaging Center, University of Aberdeen, Aberdeen, United Kingdom, ³Aberdeen Brain Imaging Centre, University of Aberdeen, Aberdeen, United Kingdom, ⁴Chronic Pain & Fatigue Research Center, University of Michigan, Ann Arbor, MI, ⁵Institute of Applied Health Sciences, University of Aberdeen, Aberdeen, United Kingdom*

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Wednesday, November 8, 2017

**Session Title:** Rheumatoid Arthritis – Clinical Aspects VI: Comorbidities of Rheumatoid Arthritis

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 9:00AM-10:30AM

**Background/Purpose:**

Inflammation is the hallmark of disease activity in rheumatoid arthritis (RA). RA is characterized by fatigue and cognitive/affective disturbances, and these symptoms often worsen during a disease flare. However, surprisingly little is known about the neural correlates of inflammation in autoimmune disease. Here we used MRI to investigate how neuroimaging outcomes are associated with levels of peripheral inflammation in this patient population.
**Methods:** RA patients, fulfilling ACR/EULAR 2012 criteria, were recruited and underwent a multi-modal MRI brain scan which was repeated 6 months later to validate our findings. Recruitment was stratified (1:1) by disease activity (swollen joint count ≥1). The clinical evaluation included measures of inflammation (ESR) and self-reported levels of fatigue and pain (VAS) as well as depression (Hospital Anxiety and Depression Scale). Images were acquired by a 3 Tesla, 8 channel phased array head coil using a T2*-weighted gradient-echo echo-planar imaging pulse sequence. Functional connectivity was assessed during a simple cognitive task and conducted through Independent Components Analysis (ICA) to investigate the relationship of established neural networks with other brain regions. Structural analyses were conducted using voxel-based morphometry (VBM). The primary outcomes of interest were brain regions where connectivity varied with levels of ESR. These regions were then examined post-hoc for associations with VBM findings, and clinical symptoms. Primary results were significant on the cluster level with a false discovery rate (FDR) p value <0.05 derived from an uncorrected voxel level p value <0.001.

**Results:** Fifty-four subjects participated (mean age 54.9 years; 75.9% female; mean disease duration 11.5 years; mean ESR 19.4 [2-62]; mean DAS28 3.6 [range 1.5-6.4]). Several regions were identified that showed positive connections to the Dorsal Attention Network (DAN), Salience Network (SLN), and Default Mode Network (DMN) as ESR increased. The right (R) frontal pole (r= .56, p=.002 FDR), and left (L) inferior/superior parietal junction (r=.58, p=.001) showed positive connections to the DAN while the L inferior parietal lobule, L mid-temporal gyrus and several frontal regions, demonstrated positive connections to the DMN and SLN (all p < .05 FDR). Positive connections between the R frontal pole and L parietal with the DAN were replicated at the second time point (p<.05). In the same parietal region, higher inflammation was associated with decreased grey matter volume. The degree of connectivity in most of the identified regions was associated with more severe fatigue and pain scores.

**Conclusion:** The neurobiology of fatigue, cognitive dysfunction, and pain in RA, and their relationship with inflammation are poorly understood, yet these are some of the most common and debilitating symptoms in rheumatic diseases. The present study identified brain regions that may serve as inflammatory “hubs” in RA. Several of these regions play important roles in higher-order cognitive processing and therefore may represent key areas underpinning the development of symptoms such as fatigue and cognitive impairment in RA.

**Disclosure:** A. Schrepf, None; C. Cummiford, None; E. Ichesco, None; T. Larkin, None; S. E. Harte, None; R. E. Harris, None; A. Murray, None; G. Waiter, None; D. J. Clauw, Abbott Pharmaceutical, 5;Aptinyx, 5;Astellas Pharmaceutical, 5;Cerephex, 5;Daiichi Sanyko, 5;Pfizer Inc, 5;Samumed, 5;Theravance, 5;Tonix, 5; N. Basu, None.


**Abstract Number:** 2913

**the Periodontal Pathogen Aggregatibacter Actinomycetemcomitans Is Associated with Subclinical Coronary Atherosclerosis in Rheumatoid Arthritis**

**Jon T. Giles**1, Jesper Reinholdt2, Joan Bathon3, Felipe Andrade4 and Maximilian F. König5. 1Division of Rheumatology, Columbia University, College of Physicians and Surgeons, New York, NY, 2Department of Biomedicine, Aarhus University, Aarhus, Denmark, 3Division of Rheumatology, Columbia University, College of Physicians & Surgeons, New York, NY, 4Medicine/Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, 5Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Wednesday, November 8, 2017

**Session Title:** Rheumatoid Arthritis – Clinical Aspects VI: Comorbidities of Rheumatoid Arthritis

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 9:00AM-10:30AM

**Background/Purpose:** The oral pathogen Aggregatibacter actinomycetemcomitans (Aa) generates citrullinated proteins targeted by autoantibodies in RA through its pore-forming toxin leukotoxin A (LtxA). Aa-derived LtxA is implicated in atherogenesis and atherosclerotic plaque instability, conditions over-represented in RA. No prior studies have explored the potential link between Aa, Aa-derived LtxA, and atherosclerosis in RA.

**Methods:** RA patients underwent cardiac computed tomography (CT) with coronary arterial calcification (CAC), a measure of coronary atherosclerosis, assessed. Serum levels of IgG antibodies against Aa serotype b and purified LtxA were measured by ELISA. Healthy controls cutoffs for seropositivity were used. Multivariable robust regression was used to model the associations of anti-Aa and anti-LtxA with CAC, adjusting for pertinent confounders.
Results: A total of 194 RA patients [mean age=59 years; 60% female; median RA duration=9 years; 79% RF or anti-CCP seropositive] were studied. Anti-Aa was detected in n=41 (21%) and anti-LtxA in n=82 (42%). Adjusting for relevant confounders (listed in Fig), those with anti-LtxA had a mean CAC score 65% higher than those without anti-Aa or anti-LtxA (61 vs. 37 units, respectively; p=0.005 (Fig1a)). Those anti-Aa+/anti-LtxA had a mean adjusted CAC score 262% higher than those with neither antibody (134 vs. 37 units, respectively; p<0.001) and 120% higher than those with anti-LtxA, with or without concomitant anti-Aa. Among CAC-associated features, swollen joint count (SJC) was differentially associated with CAC depending on the context of anti-LtxA. In anti-LtxA- patients, SJC was not associated with CAC (Figure 1B, open circles). However, in anti-LtxA+ patients, each swollen joint was associated, on average, with a 6 unit higher CAC score (p<0.001). The interaction of anti-LtxA and swollen joints was significant (p=0.002). The association was not linear, with a marked difference noted in those with>10 swollen joints (Figure 1B, solid diamonds). Combining the two above groups with higher CAC scores [i.e. anti-Aa+/anti-LtxA- and anti-LtxA+ and>10 swollen joints; n=32 (16% of the cohort)], the adjusted mean CAC was 171% higher vs. those without these features (114 vs. 42 units, respectively; p<0.001).

Conclusion: Infection with the periodontal pathogen Aa may contribute to atherosclerosis in RA. Anti-LtxA, a marker of exposure to leukotoxic Aa strains, was significantly associated with more CAC and identified patients in which synovitis was robustly and independently associated with the extent of CAC. A subgroup of RA patients with isolated antibody positivity to the leukotoxic Aa serotype b showed markedly higher risk of atherosclerosis. Additional studies are warranted to elucidate the underlying mechanism, and whether Aa-specific screening and treatment may reduce CVD risk in RA patients.

Disclosure: J. T. Giles, None; J. Reinholdt, None; J. Bathon, None; F. Andrade, None; M. F. Konig, None.


Abstract Number: 2914

Anti-CCP Antibody Levels Are Elevated in Cervicovaginal Fluid in Association with Local Inflammation in Premenopausal Women without RA

Sonia Khatter1, Heather Berens-Norman2, Courtney Anderson1, Justin August1, Marie L. Feser1, Chelsie Fleischer1, Ashley Visser1, Jill M. Norris3, V. Michael Holers1, Kevin D. Deane1 and M. Kristen Demoruelle1, 1Division of Rheumatology, University of Colorado School of Medicine, Aurora, CO, 2University of Colorado School of Medicine, Aurora, CO, 3Department of Epidemiology, Colorado School of Public Health, Aurora, CO

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis II
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose: Data support that anti-CCP antibodies likely originate at a mucosal site prior to the onset of inflammatory arthritis (IA) in the development of RA. Our group identified anti-CCP in the lungs of subjects without IA who are At-Risk for future RA. However, a portion of serum CCP+ subjects did not exhibit anti-CCP in the lung, suggesting another mucosal site of generation. Based on a higher incidence of RA in women, the dynamic nature of immune responses in the cervicovaginal (CV) mucosa and our
preliminary data that serum anti-CCP-IgG is associated with intrauterine device (IUD) use in first-degree relatives (FDR) of RA patients, we sought to evaluate anti-CCP antibodies in the CV mucosa of women with and without RA.

**Methods:** We studied premenopausal women: 11 serum CCP+ with classified RA, 18 At-Risk for RA (15 serum CCP- FDRs and 3 serum CCP+ from clinics) and 35 serum CCP- healthy Controls. A CV fluid (CVF) sample was collected between days 14-28 of the menstrual cycle. Paired serum and CVF was tested by ELISA for CCP3 (IgG, Inova). In 24 of the non-RA women, CVF was also tested for 11 inflammatory cytokines/chemokines (Meso Scale). In addition, 7 Controls collected serial CVF samples from 3 different menstrual cycle phases. No interference by hemolysis was found on CVF CCP results.

**Results:** CVF anti-CCP levels were higher in RA (Figure Panel A). In non-RA subjects, CVF anti-CCP levels were higher in current IUD users (p=0.04 in all non-RA; p=0.04 in Controls only; Panel B). There was no association between CVF anti-CCP levels and self-report of smoking, pregnancy, genital infection or other contraception type. In non-RA subjects, CVF anti-CCP significantly correlated with CVF markers of inflammation including IL-6, monocyte chemoattractant protein (MCP)-1, macrophage inflammatory protein (MIP)-1α and MIP-1β (p<0.001 for all; Panel C). In addition, CVF anti-CCP was higher in the early follicular phase compared to ovulatory and luteal phases (p<0.001, Panel D), and in 4 Controls that were tested, CVF IL-6, MIP-1α and MIP-1β increased with anti-CCP levels in the early follicular phase.

**Conclusion:** We demonstrate for the first time that anti-CCP antibodies are elevated in CVF of women with and without RA. Importantly, these elevations were associated with markers of local CV inflammation. Furthermore, the 2 factors associated with higher CVF anti-CCP levels were IUDs and the early follicular phase, and both have previously been associated with local CV inflammation (Shanmugasundaram 2016; Macneill 2012). Of note, several serum CCP- women had elevated CVF anti-CCP levels suggesting that the CV mucosa may be a unique site of anti-CCP generation in some women, which could provide insight into the higher rates of RA in women. Additional studies are needed to identify specific mechanisms of CV anti-CCP generation and factors associated with transitions to systemic autoimmunity.

**Disclosure:** S. Khatter, None; H. Berens-Norman, None; C. Anderson, None; J. August, None; M. L. Feser, None; C. Fleischer, None; A. Visser, None; J. M. Norris, None; V. M. Holers, None; K. D. Deane, Inova Diagnostics, Inc., 5; M. K. Demoruelle, None.

**Abstract Number:** 2915

**Increased Expression of Malondialdehyde-Acetaldehyde Adducts (MAA) and Anti-Maa Antibody in Rheumatoid Arthritis-Interstitial Lung Disease**
Background/Purpose: Generated under oxidative stress, malondialdehyde-acetaldehyde adducts (MAA), and antibody responses to MAA appear to facilitate loss of immune tolerance and generate pro-inflammatory responses in rheumatoid arthritis (RA). Both MAA adduct formation and anti-MAA antibody levels are enriched in joint tissues of RA patients compared to those with non-inflammatory arthritis, and MAA appears to co-localize with citrullination in joint tissue. Because oxidative stress and autoimmunity are also key components of extra-articular complications of RA, including interstitial lung disease (ILD), we assessed MAA and anti-MAA antibody responses in RA-ILD.

Methods: Using banked serum from the Veterans Affairs Rheumatoid Arthritis (VARA) registry, we assessed serum anti-MAA antibody concentrations (IgA, IgM, and IgG via ELISA) in RA patients with and without diagnosis codes for ILD. Log-transformed anti-MAA antibody concentrations were compared by group using t-tests and linear regression models adjusted for age, sex, smoking status, disease activity, and anti-CCP antibody positivity. Additionally, we analyzed lung tissue sections from subjects with RA-ILD, non-RA ILD, emphysema, and controls (n=2 per group) available through the NIH’s Lung Tissue Resource Consortium. Sections were stained using a MAA-specific rabbit polyclonal antibody and a citrulline-specific mouse IgM monoclonal antibody, and imaged with a confocal laser scanning microscope.

Results: In a male predominant (90%), established RA patient cohort (mean duration 11 years) with frequent smoking history (78%), 103 subjects had a diagnosis code for ILD. Serum concentrations of IgA and IgM anti-MAA antibody were significantly higher in RA-ILD subjects, even after adjustment for anti-CCP antibody positivity, disease activity, and smoking status (Table 1). IgG anti-MAA antibody concentrations were also marginally higher in RA-ILD subjects, but were not statistically significant. Lung tissue demonstrated staining for MAA in non-RA ILD and emphysema; however, qualitatively, staining was highest in RA-ILD (Figure 1). In addition, staining demonstrated that MAA and citrulline co-localized in lung tissue from RA-ILD.

Conclusion: Anti-MAA antibodies, IgA and IgM, are higher in RA patients with a diagnosis of RA-ILD. Along with the enhanced staining of MAA-modified proteins in lung tissue samples from RA-ILD, our findings suggest that MAA adduct formation and resulting adaptive immune responses could play an important role in the pathogenesis of RA-ILD and also serve as informative disease biomarkers.
Table 1. Associations of RA-ILD with serum anti-MAA antibody expression.

<table>
<thead>
<tr>
<th></th>
<th>RA-ILD N=103</th>
<th>RA, no lung disease N=1468</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgA anti-MAA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concentration</td>
<td>6.96 (1.07)</td>
<td>6.40 (1.42)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>β coefficient</td>
<td>0.503 (0.224, 0.782)</td>
<td>Referent</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IgM anti-MAA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concentration</td>
<td>8.18 (1.40)</td>
<td>7.41 (2.00)</td>
<td>0.002</td>
</tr>
<tr>
<td>β coefficient</td>
<td>0.718 (0.324, 1.112)</td>
<td>Referent</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IgG anti-MAA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concentration</td>
<td>7.59 (1.15)</td>
<td>7.33 (1.45)</td>
<td>0.08</td>
</tr>
<tr>
<td>β coefficient</td>
<td>0.232 (-0.056, 0.521)</td>
<td>Referent</td>
<td>0.11</td>
</tr>
</tbody>
</table>

± log transformed

Concentrations mean (SD)

Regression models with RA-ILD predicting serum anti-MAA antibody titer; adjusted for age, sex, smoking status, anti-CCP positivity, DAS28.

Disclosure: B. R. England, None; G. M. Thiele, None; M. J. Duryee, None; D. P. Ascherman, None; L. Caplan, None; M. K. Demoruelle, None; K. D. Deane, Inova Diagnostics, Inc., 5; T. R. Mikuls, BMS, 2, Ironwood Pharm, 2, Pfizer Inc, 5, NIH, VA, 2.


Abstract Number: 2916

The Presence of a Large Number of Autoantibodies at Baseline Is Favourable for Early Treatment Response but Unfavourable for Drug-Free Remission in RA Patients

Emma de Moel¹, Veerle Derksen¹, LA Trouw¹, Holger Bang², R.J. Goekoop³, I Speyer⁴, TWJ Huizinga¹, CF Allaart¹, REM Toes¹ and Diane van der Woude⁵, ¹Rheumatology, Leiden University Medical Center, Leiden, Netherlands, ²Orgentec Diagnostika GmbH, Mainz, Germany, ³Haga Hospital, The Hague, Netherlands, ⁴Haaglanden Medical Center, The Hague, Netherlands, ⁵Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Background/Purpose: The autoantibody response of seropositive RA is very diverse and consists of various numbers of isotypes and antibodies to multiple post-translational modifications. It is yet unknown whether this varying breadth of the autoantibody profile associates with treatment outcomes. Therefore, we aimed to comprehensively characterize the number of isotypes and anti-modified peptide antibodies (AMPAs) present in RA and investigate whether the breadth of the autoantibody profile, as a reflection of the underlying immunopathology, associates with early treatment response and rates of sustained drug-free remission (SDFR).

Methods: In baseline sera of 399 seropositive RA patients in the IMPROVED study\(^1\), we measured IgG, IgM, and IgA isotypes for anti-cyclic citrullinated peptide-2, rheumatoid factor, and anti-carbamylated protein antibodies, and reactivity against 4 citrullinated peptides (vimentin 59-74, fibrinogen β 36-52 and α 27-43, enolase 5-20) and 2 acetylated peptides (lysine and ornithine). We investigated associations between autoantibody profile and 1) change in disease activity score (DAS)-44 between 0 and 4 months and 2) sustained drug-free remission (SDFR) (drug-free DAS44<1.6 lasting ≥1 year).

Results: A broad baseline autoantibody isotype profile dose-dependently associated with a favourable early treatment response: ΔDAS 0-4 months of 7-8 vs 1-2, 3-4, and 5-6 isotypes, respectively: -2.2 vs -1.5 [p<0.001], -1.7 [p=0.04], and -1.8 [p=0.04] (Figure 1). A similar trend was observed for AMPA-number. Conversely, a broad autoantibody profile was associated less chance of achieving early SDFR between 1-2 years (Figure 2). In the long run (2-5 years), not the breadth of the autoantibody response, but rather seropositivity per se was associated with not achieving SDFR.

Conclusion: Not only the presence of autoantibodies, but also the breadth of the autoantibody profile has prognostic value in RA. Seropositive patients with a broader autoantibody profile have a better early response to immunosuppression, likely reflecting an active but readily suppressible humoral immunity. However, in the long-term this autoimmunity cannot be quenched without continued therapy.

References: \(^1\)Heimans, AR&T 2016, 18:23

Disclosure: E. de Moel, None; V. Derksen, None; L. Trouw, None; H. Bang, None; R. J. Gockoop, None; I. Speyer, None; T. Huizinga, None; C. Allaart, None; R. Toes, None; D. van der Woude, None.

Neutrophil Activation in Rheumatoid Arthritis – Potential Biomarkers of Disease Activity and Severity

Mary Bach¹, Daniel Moon², Marcel Bach², Marcus Bach² and Christian Lood³, ¹VA Puget Sound Health Care System, Seattle, WA, ²University of Washington, Seattle, WA, ³Department of Medicine, Division of Rheumatology, University of Washington, Seattle, WA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis II
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose: Neutrophil activation is associated with inflammation and autoimmunity, including rheumatoid arthritis (RA), where neutrophil infiltration to joints participates in tissue destruction and development of arthritis. In RA, neutrophils may spontaneously, or upon engagement with inflammatory cytokines and autoantibodies, undergo a programmed form of necrosis, NETosis, upon which neutrophil extracellular traps (NETs) are extruded. Due to their inflammatory capacity in vitro, as well as containing key autoantigens, such as citrullinated histones and vimentin, NETs have been suggested to be an important contributor to the RA pathogenesis. However, the clinical utility of NETs has not been carefully addressed. The aim of the current study was to investigate if markers of neutrophil activation and NETosis were increased in RA, and related to disease activity and severity.

Methods: Markers of neutrophil activation (S100A8/A9) and NETosis (8-OHdG DNA, MPO-DNA complexes, cell-free DNA, citrulline) were analyzed by ELISA, fluorimetry and enzymatic assays in healthy controls (HC, n=24) and RA patients (n=101). Serum-mediated neutrophil activation was analyzed by flow cytometry. The RA patients were female (74%), age 53 (range 20-78) of Caucasian origin (64%), with an average CDAI score of 13.8 (range 0-46) and 80% of the patients being seropositive.

Results: RA patients had significantly elevated levels of NET-related markers as compared to HCs (p<0.0001), with several markers, including S100A8/A9 and cell-free DNA, being increased in patients with active disease (p<0.01 and p<0.05, respectively). Further, S100A8/A9 correlated with CDAI (r=0.52, p<0.0001) as well as number of swollen joints (r=0.55, p<0.0001). In contrast to CRP (p=0.16), S100A8/A9 and NETs predicted active disease in seropositive RA patients (OR 9.2, p<0.05, and OR 6.6, p<0.05, respectively). The sensitivity and specificity was 56.9% and 87.5% (S100A8/A9), and 68.6% and 75% (NETs), suggesting superior clinical utility of NETs and S100A8/A9 as compared to CRP in determining active disease. Further, levels of NETs, but not S100A8/A9, were able to distinguish seronegative RA from HCs (OR 20.8, p=0.007). Consistent with the hypothesis of NETosis being a major source of citrullinated proteins in RA, we found that patients with elevated NET levels had increased citrulline levels in the circulation (OR 5.1, p=0.006). Further, NETosis was associated with increased levels of inflammatory 8-OHdG DNA (p<0.0001). As autoantibodies and inflammatory cytokines have been suggested to induce NETosis in RA we next assessed the capacity of RA serum to support neutrophil activation in vitro. RA sera induced increased neutrophil activation (p<0.0001) as compared to HC sera, partly dependent on FcgRIIA activation (p<0.05), with serum-mediated neutrophil activation being in particular elevated in patients with erosive disease (p=0.02).

Conclusion: Our results demonstrate a clear contribution of neutrophils in the RA pathogenesis, and identifies several biomarkers able to monitor disease activity and severity in RA patients, with superior clinical utility as compared to CRP.

Disclosure: M. Bach, None; D. Moon, None; M. Bach, None; M. Bach, None; C. Lood, None.

The Appearance of IgA RF Followed By IgG RF Is Associated with Transition to Classifiable RA in a Large Preclinical RA Cohort

Lindsay B. Kelmenson¹, Brandie D. Wagner², M. Kristen Demoruelle¹, V. Michael Holers¹, Ted R. Mikuls³, Jess D. Edison⁴ and Kevin D. Deane¹, ¹Rheumatology Division, University of Colorado Denver, Aurora, CO, ²Department of Biostatistics and Informatics,
SESSION INFORMATION

Session Date: Wednesday, November 8, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis II
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose:

Autoantibodies including rheumatoid factor (RF) and antibodies to citrullinated protein antigens (ACPA) are known to be present in the serum of individuals prior to the development of rheumatoid arthritis (RA) (Majka, 2008). These autoantibodies may initially be generated at a mucosal surface given their discovery in the induced sputum of RA and arthritis-free subjects (Willis, 2013). However, there is limited knowledge of the temporal evolution of RF isotypes prior to RA onset, although appearance in the circulation of IgA prior to IgG autoantibody isotypes would support a possible early role for mucosal triggering of autoimmunity in RA.

Methods:

Using the resources of the Department of Defense Serum Repository (DoDSR), we evaluated 214 RA Cases and 158 matched Controls. All RA Case and Control samples were tested for IgA and IgG RF isotypes (Inova). In addition, cut-off for these antibodies were determined using a level that was positive in <5% of a separate group of 58 military controls. The time at which IgA and IgG RF levels differed between RA Cases and Controls prior to diagnosis of RA was evaluated using a linear mixed model after log transformation of IgA and IgG levels. Linear contrasts were used at various times to estimate what time point prior to diagnosis of RA that mean levels of each RF isotype differed between RA Cases and Control, with this analysis serving to identify the earliest time point at which these autoantibodies could be considered abnormal when compared to Controls. For RA Cases, the mean time prior to diagnosis of first positivity of each isotype was also compared using a t-test.

Results:

Descriptions of the RA Cases and Controls are presented in the Table. RF-IgA levels were significantly elevated in Cases compared to Controls at 13 years 7 months prior to RA diagnosis. In contrast, RF-IgG levels were significantly higher in Cases compared to Controls at 11 years 1 month prior RA diagnosis. These differences in time of elevation of autoantibodies in Cases compared to Controls, 13 years 7 months vs. 11 years 1 month were statistically significant (p<0.01). Moreover, among RA Cases IgA RF positivity occurred first (mean -1671 days, SD 1761), followed by IgG RF (mean -1359 days, SD 1461) prior to RA diagnosis (p=0.30).

Conclusion:

In analyses of these preclinical RA samples, we found IgA RF to be present prior to the appearance of IgG RF. Given the known relationship of IgA with mucosal inflammation in general, these findings support a potential early mucosal origin for RF generation. In addition, the transition to IgG RF may also play a role in the development of joint symptoms. Future studies should evaluate the role of other factors on the evolution of RF isotypes, as well as the evolution of ACPA isotypes.

<table>
<thead>
<tr>
<th>Age, mean (SD)</th>
<th>Controls</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA Cases n=214</td>
<td>Controls n=158</td>
<td></td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>38.0 (7.9)</td>
<td>34.1 (8.0)</td>
</tr>
<tr>
<td>Female, N (%)</td>
<td>102 (48%)</td>
<td>76 (48%)</td>
</tr>
<tr>
<td>Non-Hispanic White, N (%)</td>
<td>124 (58%)</td>
<td>89 (56%)</td>
</tr>
<tr>
<td>Ever Smoker, N (%)</td>
<td>67 (31%)</td>
<td>35 (22%)</td>
</tr>
<tr>
<td>RF isotypes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IgA, mean level (SD)</td>
<td>22.4 (33.0)</td>
<td>1.8 (2.1)</td>
</tr>
<tr>
<td>IgA, % positive</td>
<td>126 (59%)</td>
<td>13 (10%)</td>
</tr>
<tr>
<td>IgG, mean level (SD)</td>
<td>14.3 (29.9)</td>
<td>5.48 (7.2)</td>
</tr>
<tr>
<td>IgG, % positive</td>
<td>65 (30%)</td>
<td>8 (5%)</td>
</tr>
</tbody>
</table>
Number and Type of ACPA Fine Specificities Are Correlated to High Resolution Computed Tomography Parenchymal Lungs Changes in Patients with Early Untreated Rheumatoid Arthritis

Vijay Joshua¹, Aase Hensvold¹, Gudrun Reynisdottir¹, Monika Hansson¹, Guy Serre², Johan Grunewald³, Katerina Chatzidionysiou¹ and Anca I. Catrina¹, ¹Rheumatology Unit, Department of Medicine, Karolinska Institute, Karolinska University Hospital, Stockholm, Sweden, ²Unité Différenciation Épidermique et Autoimmunité Rhumatoïde, Unité Mixte de Recherche, INSERM, Toulouse, France, ³Division of Respiratory Medicine, Department of Medicine, Karolinska University Hospital, Karolinska Institutet, Stockholm, Sweden

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Rheumatoid Arthritis – Human Etiology and Pathogenesis II
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose:
Airways abnormalities that are consistent with inflammation are common in anti-CCP2 positive subjects without inflammatory arthritis. Anti-CCP2 antibodies are associated with HRCT parenchymal lung abnormalities in patients with early RA. This study aims to examine the association between ACPA fine specificities and HRCT lung changes in an early RA cohort and to assess these changes after 6 months.

Methods:
Patients (n=106) with newly diagnosed RA according to the ACR 1987 criteria and naïve to treatment with oral glucocorticoids or DMARDs were included. HRCT was performed in order to assess the presence parenchymal (nodules, ground-glass opacities, opacities, fibrosis, emphysema) and airway abnormalities (bronchiectasis, air trapping, air wall thickening). EliA system (Phadia) was used to detect RF IgA and IgM, anti-CCP2 IgA and IgG, and peptide microarray (Phadia) was used to detect antibodies against 10 citrullinated (Cit) peptidic antigens: CCP-1 (Filaggrin), CEP-1 (α-enolase), Vim 2-17, Vim 60-75 (Vimentin), Fib α 36-50, Fib α 573, Fib α 591, Fib α 621-635, Fib β 36-52, Fib β 60-74 (Fibrinogen). Most of the patients (n=93) were followed up after 6 months. Logistic regression analysis was performed to examine associations between HRCT lung changes at the time of RA diagnosis and autoantibodies.

Results:

HRCT parenchymal and airway changes was present in 58 (54.7%) and 68 (64.2%) patients, respectively. The forced vital capacity (FVC) was significantly lower in the presence of airway abnormalities, while the ratio FEV<sub>1</sub>/FVC was significantly lower in patients with parenchymal lung changes. Higher age, RF IgA, CCP2 IgG, ever smoking and pack-years above 24 were significant predictors of parenchymal lung changes. Some ACPA fine specificities, especially against Cit Fib and Vim peptides, were associated to parenchymal lung changes in ever smokers. The risk of having parenchymal changes increased parallel to the increase in number of ACPA specificities. Having more than 5 ACPA specificities at the time of diagnosis increased the risk of having parenchymal lung abnormalities in current smokers (OR=13.8, 95% CI=1.9-196.2, p=0.05). Of the patients that were followed up after 6 months 4 had progression of fibrosis and 3 had new fibrosis. No difference in airway changes were observed at follow-up. There was a significant decrease in DAS28 at follow-up (Mean±SD: 5.5 ± 1.1 vs 3.2±1.3 P value < 0.001). The titers of some but not all of the ACPA fine specificity was significantly decreased after 6 months of treatment CCP-1 (Mean±SD 46.6±289.7 vs 101.6±235.3), CEP-1 (59.1±120.1 vs 35.9±76.3), Vim 60-75 (338±488.1 vs 220.3±327.2), Vim 2-17 (25.7±59.3 vs 17±37.8), Fib β 60-74 (237.3±411 vs 136.4±241.5), Fib α 621-635 (187.3±306.3 vs 115.9±203.2).

Conclusion:

The presence of RF IgA, anti-CCP2 IgG and antibodies to Cit Fib and Vim peptides were associated with parenchymal lung changes in early-untreated RA. The more ACPA fine specificities, the higher the risk of having parenchymal lung changes already at the time of RA diagnosis. Treatment with DMARDs significantly reduces the disease activity and titers of some of the ACPA fine specificities.

Abstract Number: 2920

**Comparative Rates of Osteoporotic Fractures Among U.S. Medicaid Enrollees with and without Systemic Lupus Erythematosus**

Sara K. Tedeschi¹, Beatrice Pan¹, Hongshu Guan¹, Seoyoung C. Kim², Daniel H. Solomon¹ and Karen H. Costenbader¹, ¹Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA; ²Division of Pharmacoepidemiology and Pharmacoeconomics, Brigham and Women's Hospital, Boston, MA

First publication: September 18, 2017

**SESSION INFORMATION**

**Session Date:** Wednesday, November 8, 2017  
**Session Title:** Systemic Lupus Erythematosus – Clinical Aspects and Treatment V: Longterm Outcomes  
**Session Type:** ACR Concurrent Abstract Session  
**Session Time:** 9:00AM-10:30AM  

**Background/Purpose:** Fractures are potentially avoidable and highly morbid. We studied non-vertebral fracture rates among SLE patients enrolled in Medicaid, the U.S. health insurance program for low-income people, and compared them to age- and sex-matched Medicaid patients without SLE.

**Methods:** Among patients aged 5-65 years enrolled >180 days during 2007-2010, we identified an SLE and a lupus nephritis (LN) cohort using previously described algorithms (SLE: ≥3 ICD-9 codes for SLE ≥30 days apart; LN: SLE + ≥2 ICD-9 codes for kidney
disease ≥30 days apart). Four age- and sex-matched non-SLE patients were included for each SLE patient. Subjects were followed from index date (SLE definition met, or a matched date for non-SLE patients) through end of follow-up (12/31/10) or censoring (death or disenrollment). During the baseline period (180 days before index date), we assessed sociodemographics, SLE- and prescriptions, and comorbidities. Incident fractures of the pelvis, hip, wrist, and humerus were identified via validated algorithms using ICD-9 + current procedural terminology codes. Within each cohort, we calculated cumulative incidence rates (IRs) and 95% confidence intervals (CI) for any fracture and for each fracture type. Poisson regression models, adjusted for all covariates, estimated cumulative IR ratios (IRRs), comparing SLE and LN to non-SLE patients. Age-stratified analyses investigated differences in fracture rates, using age 45 years as a cutoff based on mean age at menopause in SLE.

**Results:** 39,918 SLE patients were matched to 159,672 non-SLE patients. Mean age was 40.1 (±13.4) years and 92.2% were female. 9,096 SLE patients (22.8%) had LN. Black race comprised 43.3% of SLE, 53.1% of LN, and 23.1% of the non-SLE cohort. Average prednisone equivalent during baseline was ≥7.5mg/day in 11.5% of SLE, 20.1% of LN, and 0.3% of non-SLE patients. Fracture IRs were 1.48/100,000 person-years in SLE (Table) and 2.06/100,000 person-years in LN. Compared to matched non-SLE patients, fracture rates were 39% higher in SLE patients and 69% higher in LN patients, even after adjusting for medications associated with bone density loss. Hip fracture rates were almost 3.5 times higher and pelvic fracture rates were more than doubled among SLE patients ≤ age 45 compared to matched non-SLE patients after adjustment. Hip fracture rates were 5 times higher among LN patients ≤ age 45 compared to matched non-SLE patients (adjusted IRR 5.02 [1.46-17.19]).

**Conclusion:** Compared to age- and sex-matched Medicaid enrollees without SLE, SLE and LN patients had much higher non-vertebral fracture rates, particularly hip and pelvic fractures in patients ≤ 45 years of age. These results highlight the need for fracture prevention measures among young SLE patients.
### Fracture Events and Incidence Rates Ratios (IRR) among Medicaid enrollees with SLE (n=39,918) and without SLE (n=159,672), 2007-2010

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Events/person-years</th>
<th>IRR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Any Fracture</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLE cohort</td>
<td>489/32,933,916</td>
<td><strong>1.39 (1.20-1.62)</strong></td>
</tr>
<tr>
<td>Non-SLE cohort</td>
<td>955/110,109,578</td>
<td>Ref.</td>
</tr>
<tr>
<td>≤45 years old</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLE</td>
<td>189/19,974,373</td>
<td><strong>1.63 (1.31-2.04)</strong></td>
</tr>
<tr>
<td>Non-SLE</td>
<td>292/63,949,145</td>
<td>Ref.</td>
</tr>
<tr>
<td>&gt;45 years old</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLE</td>
<td>300/12,959,543</td>
<td>1.33 (0.84-2.10)</td>
</tr>
<tr>
<td>Non-SLE</td>
<td>663/46,160,433</td>
<td>Ref.</td>
</tr>
<tr>
<td><strong>Pelvic Fracture</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLE cohort</td>
<td>224/32,933,916</td>
<td><strong>1.73 (1.68-2.17)</strong></td>
</tr>
<tr>
<td>Non-SLE cohort</td>
<td>330/110,109,578</td>
<td>Ref.</td>
</tr>
<tr>
<td>≤45 years old</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLE</td>
<td>97/19,974,373</td>
<td><strong>2.11 (1.51-2.96)</strong></td>
</tr>
<tr>
<td>Non-SLE</td>
<td>104/63,949,145</td>
<td>Ref.</td>
</tr>
<tr>
<td>&gt;45 years old</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLE</td>
<td>127/12,959,543</td>
<td>1.59 (0.79-3.18)</td>
</tr>
<tr>
<td><strong>Hip Fracture</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLE cohort</td>
<td>70/32,933,916</td>
<td>1.44 (0.95-2.20)</td>
</tr>
<tr>
<td>Non-SLE cohort</td>
<td>90/110,109,578</td>
<td>Ref.</td>
</tr>
<tr>
<td>≤45 years old</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLE</td>
<td>17/19,974,373</td>
<td><strong>3.40 (1.31-8.81)</strong></td>
</tr>
<tr>
<td>Non-SLE</td>
<td>8/63,949,145</td>
<td>Ref.</td>
</tr>
<tr>
<td>&gt;45 years old</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLE</td>
<td>53/12,959,543</td>
<td>1.30 (0.19-8.73)</td>
</tr>
<tr>
<td>Non-SLE</td>
<td>82/46,160,433</td>
<td>Ref.</td>
</tr>
</tbody>
</table>

*Adjusted for age (continuous), sex, race/ethnicity (White, Black, Hispanic, Other), calendar year of index date (2007-2009), U.S. Census tract median household income by zip code (continuous), cumulative average prednisone equivalent/day (0, >0 to <7.5, ≥7.5 to <20, ≥20mg), hydroxychloroquine prescription (yes/no), other immunosuppressant prescription (azathioprine, cyclophosphamide, cyclosporine, tacrolimus, lefunomide, methotrexate, and/or rituximab) (yes/no), anticoagulant prescription (heparin, low-molecular weight heparin, and/or warfarin) (yes/no), bisphosphonate prescription (yes/no), cholecalciferol, ergocalciferol and/or calcium prescription (yes/no), Charlson-Deyo comorbidity index (continuous).

+Age-stratified models are not adjusted for age

---

**Disclosure:** S. K. Tedeschi, None; B. Pan, None; H. Guan, None; S. C. Kim, None; D. H. Solomon, None; K. H. Costenbader, None.


**Abstract Number:** 2921

---

**Improved Survival Following Renal Transplantation in Waitlisted Patients with Systemic Lupus Erythematosus in the United States**

April Jorge¹, Zachary S. Wallace², NaLu³, Yuqing Zhang⁴ and Hyon K. Choi⁵, ¹Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, ²Division of Rheumatology, Allergy and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, ³Department of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, ⁴School Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, ⁵Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA.
SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment V: Longterm Outcomes
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose:
Lupus nephritis is a major complication of systemic lupus erythematosus (SLE), occurring in up to half all SLE patients and progressing to end-stage renal disease (ESRD) in 20% of those affected. Renal transplantation is a preferred treatment, but this is a limited resource, and the survival benefit of transplantation has not been well-characterized in this population. We assessed survival impact following waitlisting for a renal transplant in patients with SLE in the US.

Methods:
We identified all incident cases of ESRD due to SLE (ICD9=710.0) in the United States Renal Data System (USRDS) between 1995 and 2014. The USRDS captures nearly all patients with ESRD in the US and includes the cause of ESRD by ICD9 code as well as demographics, comorbidities, and dates of waitlist entry, transplantation and death including its causes. We included all patients with ESRD due to SLE who were waitlisted for a renal transplant during the study period and followed patients until death or January 1, 2016. We restricted our analysis to patients waitlisted for transplant to limit the potential bias of confounding by indication. We used a time-varying Cox regression analysis to estimate the hazard ratio (HR) for death following renal transplantation compared to those who remained on the waitlist, while adjusting for age, sex, body mass index, tobacco use, comorbidities, and first ESRD treatment modality at baseline. We also assessed differences in cause of death using cause-specific hazard models.

Results:
During the study period, 9,852 patients with ESRD due to SLE were waitlisted for a renal transplant, and 5,914 (60%) of these patients received a transplant. The majority were female (82.1%) and non-white (59.3%). The average age at ESRD onset, waitlisting, and transplant were 35.7 years, 37.7 years, and 38.5 years, respectively, and the average time from ESRD diagnosis to being waitlisted was 1.5 years. Over a mean follow up time of 7.6 years following waitlisting, 2,722 died. Transplantation was associated with a 67% reduction in overall mortality (HR 0.33 (95% CI 0.29-0.38) among those waitlisted.

In cause-specific analyses, patients who remained on the waitlist had a higher risk of cause-specific death from CVD (adjusted HR, 9.2 [95% CI, 7.9-10.7]) cancer (adjusted HR, 3.8 [95% CI, 2.3-6.1]) and infection (adjusted HR, 7.4 [95% CI 5.8-9.3]).

Conclusion:
In this nationwide study of transplantation for ESRD due to SLE, renal transplantation was associated with a 67% reduction in mortality. Patients who were waitlisted but never received a transplant were more likely to die from CVD, cancer, and infection. Our findings highlight the survival benefits associated with renal transplantation for patients with SLE ESRD and call for the need to improve access to transplantation in this patient population. Patients on the waitlist may benefit from improved interventions to minimize CVD, cancer and infection risk.

Disclosure: A. Jorge, None; Z. S. Wallace, None; N. Lu, None; Y. Zhang, None; H. K. Choi, Selecta, Horizon, 5, AstraZeneca, 2.

Outcomes of Lupus Nephritis in Vulnerable Populations

Christine Peschken1, Rebecca Gole2, Carol A Hitchon3, David Robinson3, Ada Man4, Annaliee Tisseverasinghe4 and Hani El-Gabalawy1, 1 Medicine & Community Health Sciences, University of Manitoba, Winnipeg, MB, Canada, 2 University of Manitoba, Winnipeg, MB, Canada, 3 Arthritis Center, University of Manitoba, Winnipeg, MB, Canada, 4 Rheumatology, University of Manitoba, Winnipeg, MB, Canada

First publication: September 18, 2017
Background/Purpose:
Lupus nephritis is a known predictor of mortality; we have previously shown an increased frequency of nephritis in North American Indian (NAI) and Asian (ASN) lupus patients. We examined the risks of end-stage renal disease (ESRD) and death among lupus nephritis patients, and included the impact of ethnicity, low income (LowInc), lack of education (LowEduc), and living >500 km from rheumatology care (Remote).

Methods:
Patients from a single academic center were followed from 1990-2016 using a custom database. Records of all SLE patients were abstracted. Variables included birthdate, diagnosis date, ethnicity, ACR classification criteria (ACRc), SLICC Damage Index (SDI) including ESRD, treatment and date of death. Ethnicity was categorized into NAI, Caucasian (CAU), ASN and Other. In patients who had developed nephritis, Kaplan Meier and Cox proportional hazard models were used to compare ESRD and survival between vulnerable groups.

Results:
Nine hundred forty-four SLE patients were identified: 240 (25%) NAI, 576(60%) CAU, 104(11%) ASN and 24(2.5%) Other. “Other” patients were excluded. Mean disease duration was 14 years, 89% female. Nephritis developed in 39% of CAU (n= 224), 57% of NAI (n=136; OR 2.1; 95%CI 1.5-2.8), and 75% of ASN (n=76; OR 4.7; 95%CI 2.9-7.6), p<0.001. Twenty percent of patients had not completed high school, 20% were LowInc, and 11% were Remote; LowInc, LowEduc, and Remote did not increase the odds of nephritis. Among nephritis patients, ESRD developed in 11%, and 17% died. Comparing nephritis patients (N=436), NAI (29±15) and ASN (29±13) years were younger at diagnosis; CAU (36±16), p<0.001. Disease duration was similar in NAI and ASN, both (11years±13); and longer in CAU (16±11); p<0.001.There were no differences in additional ACRc met between ethnic groups. SDI in addition to ESRD was similar in NAI (1.8±2.2) and CAU (2.0±2.5) and lower in ASN (1.2±1.4), p=0.04. Odds of ESRD were increased in NAI (OR 2.6; 95%CI 1.3-5.5) and ASN (OR 3.7; 95%CI 1.6-8.2) compared to CAU. LowInc, LowEduc, and Remote did not increase odds of ESRD. Odds of death were increased in NAI (OR 1.9; 95%CI 1.1-3.2), but not in ASN (OR 0.6; 95%CI 0.2-1.4) compared to CAU. LowInc also did not increase odds of death, but LowEduc (OR 3.2; 95%CI 1.8-5.5), and Remote (OR 2.9; 95%CI 1.4-6.0) did. In separate models, after adjustment for age, gender, SDI, ACRc, and age at diagnosis, risk of ESRD was increased in NAI (HR 2.8; 95%CI 1.0-8.1) and ASN (HR 4.0; 95%CI 1.6-10.3) compared to CAU. LowInc, LowEduc, and Remote did not increase risk of ESRD. Only LowEduc (HR 2.1; 95%CI 1.1-3.9) increased the adjusted risk of death; ethnicity, LowInc and Remote were not significant.

Conclusion:
Compared to CAU, NAI and ASN not only have a higher risk of nephritis, but among those with nephritis, risk of ESRD is 3-4 fold higher in NAI and ASN. Lack of education, rather than ethnicity, was the major risk factor for death. Reasons for these differences may include renal pathology, care pathways, comorbid conditions and additional socioeconomic factors and need to be further explored.

Disclosure: C. Peschken, None; R. Gole, None; C. A. Hitchon, None; D. Robinson, None; A. Man, None; A. Tisseverasinghe, None; H. El-Gabalawy, None.

Abstract Number: 2923

A Propensity Score-Matched Study of Organ Damage in Patients with Systemic Lupus Erythematosus from the BLISS Long-Term Extension Trials Versus the Toronto Lupus Cohort: A Post Hoc Longitudinal Analysis

Murray Urowitz, Robert L. Ohsfeldt, Ron Wielage, Kari A. Kelton, Yumi Asukai and Sulabha Ramachandran, Medicine, Centre for Prognosis Studies in the Rheumatic Diseases, Toronto Western Hospital and University of Toronto, Toronto, ON, Canada,
SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment V: Longterm Outcomes
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose: Two Phase 3, randomized controlled trials (BLISS 52/76) studied the efficacy and safety of belimumab plus standard of care (SoC) in systemic lupus erythematosus (SLE) over 52/76 weeks. A pooled analysis (201223) of the BLISS long-term extension (LTE) studies (BEL112233/NCT00724867; BEL112234/NCT00712933) reported low levels of organ damage accrual in patients who received belimumab plus SoC for 5 years (measured by the Systemic Lupus International Collaborating Clinics [SLICC]/American College of Rheumatology Damage Index [SDI]).1 These studies were open-label with no SoC arm. In order to compare belimumab plus SoC to SoC alone, we conducted a post hoc, propensity score-matched (PSM) analysis (BEL206347) of changes in SDI scores of US patients treated with belimumab plus SoC in the BEL112233 LTE versus patients treated with SoC alone in the Toronto Lupus Cohort (TLC) over 5 years.

Methods: The TLC was identified as the most suitable source of SoC comparator data for the LTE studies.2 A literature review identified potential patient and disease characteristics that impact organ damage for use in the PSM. Propensity scores for each LTE and TLC patient were compared to find an acceptable match (1:1 match, 20% caliper). The primary endpoint was the difference in change in SDI from baseline to Year 5 between patients treated with belimumab plus SoC versus SoC alone, based on the US BLISS LTE and the TLC. A regression augmented inverse PS weighting (IPSW) model tested the robustness of the results. Secondary analyses included parametric hazard models of the time to first increase in SDI score and a proportions test of the magnitude of year-to-year increases in SDI.

Results: 17 clinical variables were used to calculate the PS; all were well balanced in the sample after PSM. The primary outcome results (5-year SDI change) demonstrated that belimumab was associated with a 0.444 smaller increase (95% confidence interval [CI]: -0.697, -0.191) compared with SoC (Table). The regression augmented IPSW model demonstrated a similar treatment effect estimate (coefficient, -0.450; standard error (SE) 1.115; p>0.001).

Belimumab was associated with a significantly slower rate of organ damage progression (any increase) compared with SoC (hazard ratio: 0.312; SE: 0.087; 95% CI: [0.226, 0.605], p<0.001). Among patients with SDI increases, those treated with SoC alone were more likely to experience an increase of 2+ compared to belimumab plus SoC (30.56% vs 6.06%; p=0.006).

Table. Summary of 5-year SDI change in patients with ≥5-year follow-up: PS 1:1 match with caliper

<table>
<thead>
<tr>
<th></th>
<th>z-value</th>
<th>Baseline (SE) [95% CI]</th>
<th>5 years (SE) [95% CI]</th>
<th>Change from baseline (SE) [95% CI]</th>
<th>Treatment effect (SE) [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belimumab + SoC (N=99)</td>
<td>-5.46</td>
<td>0.768 (0.125) [0.582, 1.015]</td>
<td>1.051 (0.153) [0.748, 1.355]</td>
<td>0.283 (0.059) [0.166, 0.340]</td>
<td>-0.444 (0.128) p&lt;0.001</td>
</tr>
<tr>
<td>SoC (N=99)</td>
<td></td>
<td>0.717 (0.099) [0.522, 0.911]</td>
<td>1.444 (0.150) [1.149, 1.740]</td>
<td>0.727 (0.114) [0.503, 0.952]</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: This longitudinal PSM study comparing belimumab plus SoC to SoC alone indicates that belimumab had a clinically significant impact in slowing the rate of organ damage, measured by SDI.


Study funded/conducted by GSK. Editorial assistance provided by Emma Hargreaves, of Fishawack Indicia Ltd, funded by GSK.

Disclosure: M. Urowitz, GSK, 2; R. L. Ohsfeldt, a GSK contractor (Medical Decision Modelling Inc.), 5,Astra Zeneca, 5,Amgen, 5,Hygieia, 5; R. Wielage, a GSK contractor (Medical Decision Modelling Inc.), 3; K. A. Kelton, a GSK contractor (Medical Decision Modelling Inc.), 3; Y. Asukai, GSK, 1,GSK, 3; S. Ramachandran, GSK, 3,GSK, 1.

Effect of Antimalarials over the Different Domains of the Damage INDEX in Latin American SLE Patients

Guillermo J. Pons-Estel1, Daniel Wojdyla2, Graciela S. Alarcón3, Rosa Maria Serrano4, Rosana Quintana4, Manuel Ugarte-Gil5, Víctor Pimentel-Quiroz5, Enrique R Soriano6, Marina Scollnik7, Monica Sacnun4, José A. Gómez-Puerta8, Mario H. Cardiel9, Virginia Pascual-Ramos10, Ignacio García de la Torre11, Leonor Barile9, Luis H. Silveira12, Mary Carmen Amigo13, Maria Josefina Sauza del Pozo14, Marlene Guibert-Toledano15, Gil A. Reyes16, Antonio Iglesias Gamarra17, Luis Alonso Gonzalez18, Rosa Chacón-Diaz19, María H Esteva Spinetti20, Isaac Abadi20, Eduardo M. Acevedo-Vásquez21, Jose Alfaro-Lozano22, María Ines Segami23, Loreto Massardo24, Oscar Neira25, Emilia Sato26, Eloisa Bonfa27, Lilian Costallat28, Ricardo Xavier29, Fernando Cavalcanti30, Nilizio A. Da Silva31, Eduardo Ferreira Borba32, Luis J. Catoggio33, Joao C. Tavares Brenol29, Verónica Saurit34, Francisco Caeiro35, Alejandro Alvarellos34, Judith Sarano36, Mercedes García37, Laura Onetti38, Cristina Drenkard39, Guillermo Berbottó40, Hugo R. Scherbarth41, Sergio Jacobelli24, Jose F Molina42, Gloria Vásquez42 and Bernardo Pons-Estel43, 1GLADEL, Rosario, Argentina, 2GLADEL consultant, Rosario, Argentina, 3University of Alabama at Birmingham, Birmingham, AL, 4Argentina, GLADEL, Rosario, Argentina, 5Peru, GLADEL, Lima, Peru, 6Argentina, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina, 7Rheumatology Unit, Internal Medicine Service, Hospital Italiano de Buenos Aires, CABA, Argentina, 8Colombia, GLADEL, Medellín, Colombia, 9GLADEL, Mexico, Mexico, 10Instituto Nacional de Ciencias Médicas y Nutrición, Mexico City, Mexico, 11Hospital General de Occidente, Guadalajara, Mexico, 12Rheumatology, Instituto Nacional de Cardiología Ignacio Chavez, Mexico City DF, Mexico, 13Centro Medico ABC, Mexico, Mexico, 14Servicio de Reumatología, Instituto Mexicano de Seguro Social, Hospital de Especialidades No 25, Monterrey, Mexico, 15Centro de Investigaciones Médico Quirúrgicas, Habana, Centro de Investigaciones Médico Quirúrgicas, Habana, La Habana, Cuba, 16GLADEL, Havana, Cuba, 17Grupo de Inmunología Celular e Inmunogenética, Facultad de Medicina, Universidad de Antioquia, medellín, Colombia, 18Medicarte IPS, Medellín, Colombia, 19Servicio de Reumatología, Hospital Universitario de Caracas, Centro Nacional de Enfermedades Reumáticas, Caracas, Venezuela, 20GLADEL, Caracas, Venezuela (Bolivarian Republic of), 21Hospital Nacional Guillermo Almenara Irigoyen, Lima, Peru, 22Rheumatology, Hospital Guillermo Almenara Irigoyen. EsSalud, Lima, Peru, 23GLADEL, Lima, Peru, 24GLADEL, Santiago, Chile, 25Rheumatology Unit, Hospital del Salvador. Facultad de Medicina. Universidad de Chile, Santiago, Chile, 26Rheumatology Division, Universidade Federal de Sao Paulo, Sao Paulo, Brazil, 27Rheumatology Division, Facultad de Medicina da Universidade de São Paulo, São Paulo, Brazil, 28GLADEL, Brazil, Brazil, 29GLADEL, Porto Alegre, Brazil, 30GLADEL, Fernambuco, Brazil, 31GLADEL, Goias, Brazil, 32Rheumatology, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, 33Rheumatology Unit, Internal Medicine Service. Hospital Italiano de Buenos Aires, Buenos Aires, Argentina, 34Rheumatology, Rheumatology Unit, Hospital Privado Universitario de Córdoba, Cordoba, Argentina, 35Rheumatology, Hospital Privado Centro Médico de Córdoba, Córdoba, Argentina, 36Rheumatology Unit, Instituto de Investigaciones Medicas Alfredo Lanari, Buenos Aires, Argentina, 37Rheumatology, HIGA General San Martin La Plata, La Plata, Argentina, 38GLADEL, Cordoba, Argentina, 39Division of Rheumatology, Emory University School of Medicine, Atlanta, GA, 40Sanatorio Británico, Rosario, Argentina, 41GLADEL, Mar del Plata, Argentina, 42GLADEL, Medellín, Colombia, 43GLADEL, Rosario, Santa Fe, Argentina

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Wednesday, November 8, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment V: Longterm Outcomes
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose:

We have previously shown that Latin American SLE patients treated with Antimalarials (AMs) have a 25% lower risk of damage accrual than patients not receiving them1. The present study was conducted to assess the effects of AMs over the 12 items of the SLICC Damage Index, (SDI).

Methods:

Patients with a recent SLE diagnosis (≤2 years) from the GLADEL cohort were studied. End-point: Increase in the 12 items SDI since cohort entry.
Independent (socio-demographic, clinical laboratory and treatment) variables were included. The effect of AMs as a time dependent variable on items of the SDI (adjusting for potential confounders) was examined with a multivariable Cox regression model. Multivariate models were developed for the most common SDI items.

Results:

Of the 1,466 patients included in this analysis 1049 (72%) received AMs during follow-up (as defined); median exposure time: 30 months (Q1-Q3: 11–57 months). Total damage accrual occurred in 665 (45%) patients during a median follow up time of 24 months (Q1-Q3: 8–55) months. Within the 12 items of the SDI there were 301 integument, 208 renal, 149 neuropsychiatric, 98 musculoskeletal, 88 cardiovascular, 65 ocular, 43 pulmonary, 42 peripheral vascular, 33 gastrointestinal, 22 premature gonadal failure, 16 diabetes and 9 malignancy. After adjusting for potential confounders, at any time during follow-up a patient on AMs had a 35% and 30% lower risk of renal and neuropsychiatric damage accrual respectively than a patient not on AMs (adjusted HR 0.65, 95%CI 0.47–0.90 and HR 0.70, 95% CI 0.48–1.02). Such protective effect was not evident for integument, musculoskeletal and cardiovascular damage.

Conclusion:

After adjustment for possible confounding factors related to AMs use and damage accrual, AMs were independently associated with a reduced risk of renal and neuropsychiatric damage accrual in this cohort.

References:


Table 1. Multivariable Cox proportional hazard model: Time-to-items damage accrual.

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Unadjusted HR (95% CI)</th>
<th>p-value</th>
<th>Adjusted HR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Integument Damage</td>
<td>0.987 (0.763 – 1.277)</td>
<td>0.9223</td>
<td>0.971 (0.734 – 1.286)</td>
<td>0.8381</td>
</tr>
<tr>
<td>Renal Damage</td>
<td>0.516 (0.385 – 0.692)</td>
<td>&lt; 0.0001</td>
<td>0.652 (0.472 – 0.901)</td>
<td>0.0094</td>
</tr>
<tr>
<td>Neuropsychiatric Damage</td>
<td>0.651 (0.458 – 0.925)</td>
<td>0.0167</td>
<td>0.701 (0.481 – 1.024)</td>
<td>0.0660</td>
</tr>
<tr>
<td>Musculoskeletal Damage</td>
<td>0.838 (0.524 – 1.340)</td>
<td>0.4612</td>
<td>0.909 (0.561 – 1.473)</td>
<td>0.6977</td>
</tr>
<tr>
<td>Cardiovascular Damage</td>
<td>0.562 (0.357 – 0.886)</td>
<td>0.0130</td>
<td>0.690 (0.430 – 1.107)</td>
<td>0.1240</td>
</tr>
</tbody>
</table>

1 Hazard ratio for any antimalarial vs. no antimalarial in the previous month.

2 Adjusted for integument domain SDI at entry, hypertension, malar rash, discoid rash, proteinuria/cilindruria, hematologic disorder, glucocorticoid pulse and SLEDAI at cohort entry.

3 Adjusted for renal domain SDI at entry, age at diagnosis, socio-economic level, hypertension, proteinuria/cilindruria, immunosuppressants and SLEDAI at cohort entry.

4 Adjusted for neurologic domain SDI at entry, glucocorticoid pulse, NSAIDs and SLEDAI at cohort entry.

5 Adjusted for musculoskeletal domain SDI at entry, gender, hypertension, discoid rash, oral/nasopharyngeal ulcerations, arthritis, neurologic disorder, glucocorticoids at cohort entry.

6 Adjusted for cardiovascular domain SDI at entry, disease duration, hypertension and serositis at cohort entry.

Disclosure: G. J. Pons-Estel, None; D. Wojdyla, None; G. S. Alarcón, None; R. M. Serrano, None; R. Quintana, None; M. Ugarte-Gil, None; V. Pimentel-Quiroz, None; E. R. Soriano, AbbVie, Janssen, Novartis, Pfizer Inc, UCB, 2,AbbVie, Janssen, Novartis, Pfizer Inc, UCB, 5,AbbVie, Bristol-Myers Squibb, Janssen, Novartis, Pfizer Inc, Roche, UCB, 8; M. Scolnik, None; M. Sacnun, None; J. A.
Economic Evaluation of Damage Accrual in the Systemic Lupus International Collaborating Clinics (SLICC) Inception Cohort

Ann E. Clarke1, Ian N. Bruce2, Murray Urowitz3, John G. Hanly4, Yvan St.Pierre5, Sang-Cheol Bae6, Sasha Bernatsky7, Dafina D Gladman8, Jorge Sanchez-Guerrero9, Paul R. Fortin10, Juanita Romero-Diaz11, Michelle Petri12, Rosalind Ramsey-Goldman13, Cynthia Aranow14, Søren Jacobsen15, Daniel J. Wallace16, Joan T. Merrill17, S. Sam Lim18, Ola Nived19, Andreas Jönsen20, Susan Manzi21, Thomas Stoll22, Christine A. Peschken23, David A. Isenberg24, Anisur Rahman25, Li Su26 and Vernon Farewell27, 1Division of Rheumatology, University of Calgary, Calgary, AB, Canada, 2Central Manchester University Hospital NHS Foundation Trust and Manchester Academic Health Science Centre, Arthritis Research UK Epidemiology Unit, The University of Manchester, Manchester Academic Health Sciences Centre, Manchester, United Kingdom, 3Centre for Prognosis Studies in the Rheumatic Diseases, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, 4Rheumatology, Division of Rheumatology, Capital Health and Dalhousie University, Halifax, NS, Canada, 5McGill University Health Centre, Montreal, QC, Canada, 6Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of (South), 7Divisions of Rheumatology and Clinical Epidemiology, Research Institute of the McGill University Health Centre, Montreal, QC, Canada, 8Centre for Prongosis Studies in The Rheumatic Diseases, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada, 9Division of Rheumatology, Toronto Western Hospital, Toronto, AB, Canada, 10Medicine, CHU de Quebec - Universite de Laval, Quebec, QC, Canada, 11Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico city, Mexico, 12Medicine (Rheumatology), Division of Rheumatology, Johns Hopkins University School of Medicine, MD, USA, Baltimore, MD, 13FSM, Northwestern University, Chicago, IL, 14Autoimmune and Musculoskeletal Disease, The Feinstein Institute for Medical Research, Manhasset, NY, 15Rheumatology, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark, 16Rheumatology, Cedars-Sinai Medical Center, Beverly Hills, CA, 17Oklahoma Medical Research Foundation, Oklahoma City, OK, 18Division of Rheumatology, Emory University School of Medicine, Atlanta, GA, 19Department of Rheumatology, University Hospital, Lund, Sweden, 20Lund University, Department of Clinical Sciences, Rheumatology, Lund, Sweden, 21Medicine, Allegheny Health Network, Pittsburgh, PA, 22Abteilung Rheumatologie/Rehab, Kantonsspital Schaffhausen, Schaffhausen, Switzerland, 23RR 149G, Univ of Manitoba, Winnipeg, MB, Canada, 24Centre for Rheumatology, Division of Medicine, University College London, London, United Kingdom, 25Rayne Institute, Centre for Rheumatology Research, UCL Division of Medicine, London, United Kingdom, 26Nova Scotia Rehab Site, Division of Rheumatology, Capital Health and Dalhousie University, Halifax, NS, Canada, 27Medicine, Division of Rheumatology, Capital Health and Dalhousie University, Halifax, NS, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment V: Longterm Outcomes
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose:
Little is known about the association of healthcare costs and damage accrual. We describe the costs associated with damage progression using multi-state modeling.

Methods:
Patients fulfilling the revised ACR Criteria for SLE from 32 centres in 11 countries were enrolled in the SLICC Inception Cohort within 15 months of diagnosis. To supplement the primary data collection, patients were sampled cross-sectionally at a single time between 4 and 17 years of disease duration on healthcare use and lost labour force/non-labour force productivity over the preceding year. Healthcare use was costed using 2017 Canadian prices (direct costs) and lost productivity using 2017 Statistics Canada age-sex specific wages (indirect costs). Annual costs associated with damage states (SLICC/ACR Damage Index [SDI]) were estimated from multiple regressions adjusting for age, sex, race/ethnicity, and disease duration. Five and 10-year cumulative costs were estimated by multiplying annual costs associated with each SDI state by the expected duration in each state, forecasted using a multi-state model and longitudinal SDI data from the SLICC Inception Cohort (Bruce IN. Ann Rheum Dis 2015;74:1706-13). Future costs were discounted at a yearly rate of 3%.

**Results:**

457 patients participated, 88.2% female, 44.6% Caucasian, mean age at diagnosis 33.6 years, mean disease duration at time of the economic data 10.0 years, mean SLE Disease Activity Index (SLEDAI-2K) 2.97, and mean SDI 1.07. Annual direct costs were higher in those with an SDI ≥5 (Table 1). At SDI ≥2, hospitalizations and medications accounted for 54.3% of direct costs, whereas at SDI ≥3, dialysis was responsible for 55.6%.

<table>
<thead>
<tr>
<th>SDI State</th>
<th>Direct Costs, Mean, 95% CI</th>
<th>Indirect Costs, Mean, 95% CI</th>
<th>Total Costs, Mean, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>4642 (3187, 6098)</td>
<td>22611 (16130, 29091)</td>
<td>27253 (20394, 34112)</td>
</tr>
<tr>
<td>1</td>
<td>5937 (4472, 7401)</td>
<td>28 934 (22358, 35509)</td>
<td>34870 (27911, 41830)</td>
</tr>
<tr>
<td>2</td>
<td>5895 (3763, 8027)</td>
<td>30 573 (21 839, 39 307)</td>
<td>36 468 (27223, 45713)</td>
</tr>
<tr>
<td>3</td>
<td>9074 (5387, 12760)</td>
<td>26 743 (12937, 40549)</td>
<td>35 817 (21204, 50429)</td>
</tr>
<tr>
<td>4</td>
<td>4241 (0, 9825)</td>
<td>24197 (3364, 45029)</td>
<td>28437 (6387, 50488)</td>
</tr>
<tr>
<td>≥5</td>
<td>20014 (14270, 25757)</td>
<td>26758 (6481, 47035)</td>
<td>46771 (25310, 68233)</td>
</tr>
</tbody>
</table>

Cumulative 5 and 10-year direct costs increased with increasing baseline SDI (Table 2). Indirect costs did not vary with baseline SDI.

<table>
<thead>
<tr>
<th>SDI</th>
<th>Total 5-Year Cumulative Costs, Mean, 95% CI</th>
<th>Total 10-Year Cumulative Costs, Mean, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Direct</td>
<td>Indirect</td>
</tr>
<tr>
<td></td>
<td>2017 Canadian $</td>
<td>2017 Canadian $</td>
</tr>
<tr>
<td>0</td>
<td>23014 (15922, 30106)</td>
<td>118083 (84236, 151931)</td>
</tr>
<tr>
<td>1</td>
<td>29434 (20395, 38472)</td>
<td>143253 (104234, 182272)</td>
</tr>
<tr>
<td>2</td>
<td>33649 (19783, 47516)</td>
<td>142868 (88570, 197166)</td>
</tr>
<tr>
<td>3</td>
<td>44852 (24207, 65497)</td>
<td>130030 (53562, 206499)</td>
</tr>
<tr>
<td>4</td>
<td>55181 (28482, 81879)</td>
<td>126324 (30008, 222641)</td>
</tr>
<tr>
<td>≥5</td>
<td>94406 (67311, 121501)</td>
<td>132694 (38272, 227116)</td>
</tr>
</tbody>
</table>
Conclusion:

Patients with the highest baseline SDIs incurred cumulative 5 and 10-year direct costs approximately 4-fold higher than those with the lowest SDIs. However, indirect costs were influenced by factors other than SDI (potentially disease activity, quality of life, fatigue, plateauing of expectations regarding productivity later in the disease) and patients incurred considerable indirect costs even with no or minimal damage. This work demonstrates the substantial increase in direct costs in patients with higher damage, highlighting the cost savings potentially achieved by earlier introduction of therapies more effective at attenuating damage progression.

Disclosure: A. E. Clarke, UCB, 2; I. N. Bruce, UCB, 2; M. Urowitz, UCB, 2; J. G. Hanly, None; Y. St.Pierre, None; S. C. Bae, None; S. Bernatsky, None; D. D. Gladman, None; J. Sanchez-Guerrero, None; P. R. Fortin, None; J. Romero-Diaz, None; M. Petri, UCB, 5; R. Ramsey-Goldman, None; C. Aranow, UCB, 2; S. Jacobsen, None; D. J. Wallace, None; J. T. Merrill, UCB, 5; S. S. Lim, None; O. Nived, None; A. Jönsen, None; S. Manzi, None; T. Stoll, None; C. A. Peschken, None; D. A. Isenberg, None; A. Rahman, None; L. Su, None; V. Farewell, None.


Abstract Number: 2926

Fucosyltransferase-1 Mediates Macrophage Driven Myofibroblast Differentiation and TGF-β Signaling in Systemic Sclerosis and Bleomycin-Induced Fibrosis

W. Alexander Stinson1, Ellen Cealey1, Pei-Suen Tsou1, Ray A. Ohara1, Yuxuan Du2, Jonatan Hervoso1, Nicholas Lepore1, Sarah Arwani1, Dinesh Khanna1, David A. Fox1 and M. Asif Amin1, 1Division of Rheumatology and Clinical Autoimmune Center of Excellence, University of Michigan, Ann Arbor, MI, Ann Arbor, MI, 2Division of Rheumatology and Clinical Autoimmune Center of Excellence, University of Michigan, Ann Arbor, MI, Ann Arbor, MI, MI

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics II
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose: Systemic sclerosis (SSc) is a connective tissue disease characterized by dysregulated fibrosis of the skin. During fibrosis, macrophage release of transforming growth factor (TGF-β) and resistin like-alpha (RELM-α) leads to myofibroblast over-activation and excessive extracellular matrix deposition. However, the role of post-translational fucosylation in fibrosis has yet to be examined. Herein, we demonstrate mechanisms by which fucosyltransferase-1 (Fut1) contributes to macrophage driven fibrosis and to TGF-β signaling in murine and SSc DFs.

Methods: Wild type (WT) and Fut1 knockout (Fut1−/−) mice were intradermally injected with bleomycin or PBS and euthanized at days 1, 3, 5, and 9 to evaluate the longitudinal involvement of macrophages in skin fibrosis. Following euthanasia, fibrotic murine skin was harvested to assess cytokine expression by qPCR or pro-fibrotic macrophage ingress by immunofluorescence. To determine whether Fut1 was critical to macrophage-induced myofibroblast differentiation, WT and Fut1−/− macrophages were co-cultured with WT DFs for 48h. Co-culture supernatants were collected for ELISAs for pro-fibrotic cytokines TGF-β, RELM-α, IL-6, and MCP-1. DF alpha smooth muscle actin (α-SMA) and type 1 collagen (Col1a1) expression were assessed via qPCR. WT and Fut1−/− DFs were stimulated with TGF-β and downstream transcription factor expression assessed via qPCR. Fucosylation of TGF-βR1 by Fut1 was confirmed by ulex europaeus agglutinin 1 (UEA1) immunoprecipitation. Lastly, α-1,2 fucosidase treatment of SSc DFs was performed to determine whether Fut1-added fucose was critical to TGF-βR1 function.

Results: Fut1−/− mice were resistant to bleomycin-induced fibrosis. At day 5, Col1a1, TGF-β, and RELM-α mRNA were significantly reduced in Fut1−/− compared to WT fibrotic skin. Additionally, at day 5 and 9, Fut1−/− mice exhibited significantly fewer F4/80+ RELM-α+ macrophages in skin lesions, suggesting the involvement of Fut1 in pro-fibrotic macrophage function. IL-6, MCP-1, M-CSF, and RELM-α expression in supernatant were significantly reduced in WT DF co-culture with Fut1−/− compared to WT macrophages.

Fucosyltransferase-1 Mediates Macrophage Driven Myofibroblast Differentiation and TGF-β Signaling in Systemic Sclerosis and Bleomycin-Induced Fibrosis

W. Alexander Stinson1, Ellen Cealey1, Pei-Suen Tsou1, Ray A. Ohara1, Yuxuan Du2, Jonatan Hervoso1, Nicholas Lepore1, Sarah Arwani1, Dinesh Khanna1, David A. Fox1 and M. Asif Amin1, 1Division of Rheumatology and Clinical Autoimmune Center of Excellence, University of Michigan, Ann Arbor, MI, Ann Arbor, MI, MI

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics II
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose: Systemic sclerosis (SSc) is a connective tissue disease characterized by dysregulated fibrosis of the skin. During fibrosis, macrophage release of transforming growth factor (TGF-β) and resistin like-alpha (RELM-α) leads to myofibroblast over-activation and excessive extracellular matrix deposition. However, the role of post-translational fucosylation in fibrosis has yet to be examined. Herein, we demonstrate mechanisms by which fucosyltransferase-1 (Fut1) contributes to macrophage driven fibrosis and to TGF-β signaling in murine and SSc DFs.

Methods: Wild type (WT) and Fut1 knockout (Fut1−/−) mice were intradermally injected with bleomycin or PBS and euthanized at days 1, 3, 5, and 9 to evaluate the longitudinal involvement of macrophages in skin fibrosis. Following euthanasia, fibrotic murine skin was harvested to assess cytokine expression by qPCR or pro-fibrotic macrophage ingress by immunofluorescence. To determine whether Fut1 was critical to macrophage-induced myofibroblast differentiation, WT and Fut1−/− macrophages were co-cultured with WT DFs for 48h. Co-culture supernatants were collected for ELISAs for pro-fibrotic cytokines TGF-β, RELM-α, IL-6, and MCP-1. DF alpha smooth muscle actin (α-SMA) and type 1 collagen (Col1a1) expression were assessed via qPCR. WT and Fut1−/− DFs were stimulated with TGF-β and downstream transcription factor expression assessed via qPCR. Fucosylation of TGF-βR1 by Fut1 was confirmed by ulex europaeus agglutinin 1 (UEA1) immunoprecipitation. Lastly, α-1,2 fucosidase treatment of SSc DFs was performed to determine whether Fut1-added fucose was critical to TGF-βR1 function.

Results: Fut1−/− mice were resistant to bleomycin-induced fibrosis. At day 5, Col1a1, TGF-β, and RELM-α mRNA were significantly reduced in Fut1−/− compared to WT fibrotic skin. Additionally, at day 5 and 9, Fut1−/− mice exhibited significantly fewer F4/80+ RELM-α+ macrophages in skin lesions, suggesting the involvement of Fut1 in pro-fibrotic macrophage function. IL-6, MCP-1, M-CSF, and RELM-α expression in supernatant were significantly reduced in WT DF co-culture with Fut1−/− compared to WT macrophages.
Consequently, WT DF expression of α-SMA and Col1a1 mRNA was significantly diminished in Fut1⁻/⁻ compared to WT macrophage co-culture, suggesting the involvement of Fut1 in macrophage-induced myofibroblast differentiation. TGF-βR1 is fucosylated by Fut1 in murine and SSc DFs, as suggested by UEA1 immunoprecipitation. Fut1⁻/⁻ DFs exhibit diminished expression of TGF-β associated transcription factors compared to WT, pointing to the involvement of Fut1 in TGF-β-mediated functions. Finally, α-1,2 fucosidase diminished TGF-βR1 expression detected by flow cytometry, indicating that Fut1 regulates TGF-β signaling via the critical addition of α-1,2 fucose to TGF-βR1.

**Conclusion:** Overall, this work provides novel evidence that Fut1 mediates macrophage-driven fibrosis and that Fut1-catalyzed fucosylation of TGF-βR1 regulates TGF-β signaling. The multi-faceted involvement of Fut1 in fibrosis points to its candidacy as a novel therapeutic target in the treatment of SSc.

**Disclosure:** W. A. Stinson, None; E. Cealey, None; P. S. Tsou, None; R. A. Ohara, None; Y. Du, None; J. Hervoso, None; N. Lepore, None; S. Arwani, None; D. A. Fox, None; M. A. Amin, None.


**Abstract Number:** 2927

**Interferon Regulatory Factor (IRF) 7 in Type I IFN Signaling Represents As a Key Upstream Regulator in Early Diffuse SSc Patients and Plays Critical Role in Pathogenesis of Fibrosis**

Minghua Wu¹, Gloria Salazar¹, Jun Ying¹, Julio Charles², Xiaodong Zhou³, Maureen D. Mayes² and Shervin Assassi², ¹Department of Internal Medicine - Rheumatology, University of Texas McGovern Medical School, Houston, TX, ²University of Texas McGovern Medical School, Houston, TX, ³Internal Medicine-Rheumatology, University of Texas McGovern Medical School, Houston, TX

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Wednesday, November 8, 2017  
**Session Title:** Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics II  
**Session Type:** ACR Concurrent Abstract Session  
**Session Time:** 9:00AM-10:30AM

**Background/Purpose:** Previous global gene expression studies of SSc patients revealed presence of a prominent type I interferon (IFN) signature. IRF7 is a key transcription factor in the IFN signaling pathway. Polymorphisms in IRF7 gene are associated with SSc susceptibility. In our more recent global gene expression studies examining established disease, IRF7 was predicted to be the most activated upstream transcription factor in SSc skin and blood cells. Therefore, IRF7 might play a key role in the interplay between inflammation and fibrosis in this multifaceted disease. However, the specific role of IRF7 in SSc pathogenesis and fibrosis has not been identified.

**Methods:** Skin punch biopsies were collected from early diffuse SSc patients (n=57) and age-, gender-, and ethnicity-matched healthy controls (n=33) for global gene expression studies. IRF7 activation was also determined in tight skin 1 (TSK1/+ mouse) model. Next, we investigated the impact of IRF7 KO on skin fibrosis in TSK1 mice. We utilized loss-of-function approaches in TSK1/+ mice, to generate TSK1/+ IRF7⁻/- double transgenic mouse model. Twelve weeks old TSK1/+IRF7 KO mice skin tissue (n=7) was analyzed for collagen, α-SMA and fibronectin mRNA and protein expression.

**Results:** In agreement with our data in established disease, the global gene expression profiling of early diffuse SSc skin (median disease duration = 1.1 years) revealed that IRF7 was the top activated upstream transcription factor (activation z-score=8.101, p=1.3x10⁻²⁵). Several other transcription factors in type I IFN signaling pathway such as STAT1, STAT4, IRF1, and IRF3 were also among top 10 activated transcription factors. Consistent with our previous data in bleomycin induced dermal fibrosis model, TSK1/IRF7 KO transgenic mice showed reduced type I collagen mRNA and protein expression compared to TSK1/+ mice. Col1a2 mRNA levels were lower in TSK1/IRF7 KO mice (1.41 ± 0.21 folds) vs. in TSK1/+ mice (2.64 ± 1.06 folds) compared to control wildtype mice. Hypodermal thickness in TSK1/IRF7 KO mice was also significantly reduced compared to TSK1/+ mice (303.4 ± 72.5 μm Vs. 715.2 ± 161.9 μm; p=0.036). Finally, the myofibroblast marker α-SMA and fibronectin in the skin tissue was also significantly reduced in the TSK1/IRF7 double transgenic mice compared to TSK1/+ mice skin on immunohistochemistry.
Conclusion: Activation of IRF7 might play a pivotal role in the type I IFN driven inflammatory response followed by fibrosis in SSc. IRF7 may therefore represent a promising novel therapeutic target in SSc.

Disclosure: M. Wu, None; G. Salazar, None; J. Ying, None; J. Charles, None; X. Zhou, None; M. D. Mayes, None; S. Assassi, Bayer Healthcare, 2,Biogen Idec, 2,Reata, 5,Boehringer Ingelheim, 5.


Abstract Number: 2928

STAT3 As an Important Integrator of Profibrotic Pathways in Systemic Sclerosis

Debomita Chakraborty1, Barbora Šumová2, Tatjana Mallano3, Chih-Wei Chen3, Alfiya Distler3, Christina Bergmann3, Andreas Ramming4, Oliver Distler5, Georg Schett3, Ladislav Senolt6 and Jörg Distler3, 1Department of Internal Medicine 3- Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Erlangen, Germany, 2Institute of Rheumatology, Prague, Czech Republic, Prague, Czech Republic, 3Department of Internal Medicine 3 – Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Erlangen, Germany, 4Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Erlangen, Germany, 5Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland, 6Institute of Rheumatology and Department of Rheumatology, 1st Faculty of Medicine, Charles University in Prague, Prague, Czech Republic

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Wednesday, November 8, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics II
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose: Signal transducer and activator of transcription 3 (STAT3) is a transcription factor that regulates key cellular processes such as proliferation, apoptosis, invasion, angiogenesis, metastasis and immune responses. STAT3 can be phosphorylated and activated by various kinases, several of which have been implicated in aberrant fibroblast activation in fibrotic diseases including systemic sclerosis (SSc). We hypothesized that profibrotic signals converge on STAT3 and that STAT3 may be an important molecular checkpoint for tissue fibrosis.

Methods: Activation of STAT3, JAK1, JAK2, SRC, c-ABL and JNK was analyzed in SSc patients and in experimental models of SSc by real-time PCR, Western Blot and immunohistochemistry. Selective inhibitors in conjunction with knockdown and knockout strategies were used to target STAT3 signaling and its upstream kinases in vitro and in vivo. The anti-fibrotic potential of genetic and pharmaceutical inactivation of STAT3 was evaluated in two mouse models of SSc: bleomycin-induced fibrosis and fibrosis induced by overexpression of a constitutively active TGFβ receptor type I (TBRact).

Results: Accumulation of phosphorylated and thus active STAT3 (P-STAT3) was detected in fibroblasts in the skin of SSc patients as compared to healthy volunteers. Enhanced STAT3 signaling was also found in murine models of SSc. The upregulation of P-STAT3 was found to be mediated by TGFβ signaling. Expression profiling and functional studies in vitro and in vivedemonstrated that the activation of STAT3 is mediated by the combined action of JAK, SRC, c-ABL and JNK kinases. STAT3-deficient fibroblasts were less sensitive to the profibrotic effects of TGFβ. Fibroblast-specific knockout of STAT3 also ameliorated experimental fibrosis. In the model of bleomycin-induced fibrosis, dermal thickening was decreased by 77%, collagen content by 52% and myofibroblast counts by 58% compared to compared to littermates with normal expression of STAT3. STAT3 knockout mice were also protected from TBRact-induced fibrosis. Pharmacological inhibition of STAT3 using the small molecule inhibitor S3I-201 exerted potent anti-fibrotic effects and inhibited TGFβ-induced fibroblast activation, bleomycin- and TBRact-induced experimental fibrosis in pharmacologically relevant and well tolerated doses.

Conclusion: We demonstrate that STAT3 integrates several profibrotic signals in SSc and might thus be a novel core mediator of fibrosis. Inhibition of STAT3 prevented fibroblast activation and demonstrated potent anti-fibrotic effect in different preclinical models of SSc. Considering the potent anti-fibrotic effects observed in this study and the fact that several STAT3 inhibitors are currently tested in clinical trials, STAT3 might be an interesting candidate for molecular targeted therapies of SSc.
WNT5A Promotes Tissue Fibrosis By Wnt/PCP-Dependent Activation of Latent TGF-β

Chih-Wei Chen1, Thuong Trinh-Minh2, Neng-Yu Lin2, Yun Zhang3, Florian Groeber4, Christian Beyer5, Georg Schett6 and Jörg Distler7, 1Department of Internal Medicine 3 – Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Erlangen, Germany, Erlangen, Germany, 2Department of Internal Medicine 3 – Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Erlangen, Germany, 3Department of Internal Medicine 3 and Institute for Clinical Immunology, Friedrich-Alexander-University of Erlangen-Nuremberg and University Hospital Erlangen, Erlangen, Germany, 4Translational Center Würzburg, Fraunhofer Ins. IGB, Würzburg, Germany, 5Department of Internal Medicine 3 and Institute for Clinical Immunology, Friedrich-Alexander-University of Erlangen-Nuremberg and University Hospital Erlangen, Erlangen, Germany, 6Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, Erlangen, Germany, Erlangen, Germany, 7Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Erlangen, Germany

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics II
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose: Canonical Wnt/β-catenin signaling has emerged as a core pathway of fibrosis. They role of non-canonical Wnt signaling, however, has not been systematically studied. In this study we aimed to characterize the role of non-canonical WNT signaling in the pathogenesis of fibrotic diseases such as systemic sclerosis (SSc).

Methods: The expression of Wnt ligands was analyzed in patients with SSc, idiopathic pulmonary fibrosis (IPF) and sclerodermatous chronic graft-versus-host disease (cGvHD). The functional role of non-canonical WNT signaling was evaluated in full thickness skin grafts, in bleomycin-induced fibrosis and in experimental cGvHD. WNT signaling was modulated in vitro and in vivo using small molecule inhibitors, siRNA mediated knockdown, fibroblasts specific recombination and soluble decoy receptors.

Results:
Profiling of all non-canonical WNT ligands demonstrated that WNT5A is the predominant non-canonical Wnt ligand in skin and lungs with pronounced overexpression in patients with SSc, IPF and cGvHD as compared to non-fibrotic controls. WNT5A induced fibroblast-to-myofibroblast transition and collagen release in conventional cell culture and in full-thickness skin models in vitro and was sufficient to induce dermal and pulmonary fibrosis in vivo. Fibroblast-specific knockout of Wnt5a ameliorated bleomycin-induced fibrosis and experimental cGvHD. WNT signaling was modulated in vitro and in vivo using small molecule inhibitors, siRNA mediated knockdown, fibroblasts specific recombination and soluble decoy receptors.

Activation of latent TGF-β by WNT5A/PCP signaling required MMPs, thrombospondin-
Conclusion: We characterize WNT5A-induced PCP signaling as a novel pro-fibrotic mediator in fibrotic diseases. WNT5A contributes to the increased activation of TGF-β signaling in fibrotic diseases. We also provide evidence that WNT5A/PCP signaling may be a potential target for therapeutic intervention in fibrotic diseases.

Disclosure: C. W. Chen, None; T. Trinh-Minh, None; N. Y. Lin, None; Y. Zhang, None; F. Groeber, None; C. Beyer, None; G. Schett, None; J. Distler, 4D Science, 1, Anamar Medical, Active Biotech, Array Biopma, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, GSK, Novartis, Sanofi-Aventis, UCB, 2, Actelion Pharmaceuticals US, Active Biotech, Anamar, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi, UCB, 5.

Abstract Number: 2930

Transforming Growth Factor Beta 3 (TGFB3) – a Novel Systemic Sclerosis Susceptibility Locus Involved in Fibrosis and Th17 Cell Development Identified By Genome-Wide Association Study in African Americans from the Genome Research in African Scleroderma Patients Consortium

1NIAMS-Rheumatology, National Institutes of Health (NIH), National Institute of Arthritis and Musculoskeletal and Skin Diseases, Bethesda, MD, 2National Institutes of Health (NIH), National Human Genome Research Institute, Bethesda, MD, 3Stanford University, Stanford, CA, 4National Institutes of Health (NIH), National Institute on Deafness and Other Communication Disorders, Bethesda, MD, 5Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, 6Division of Rheumatology, Johns Hopkins University, Baltimore, MD, 7Northwestern University, Feinberg School of Medicine Scleroderma Program, Chicago, IL, 8Rheumatology, Stanford University Medical Center, Palo Alto, CA, 9Medicine/Rheumatology, University of California, San Francisco, San Francisco, CA, 10Rheumatology, University of Pennsylvania, Philadelphia, PA, 11Medicine - Rheumatology, University of Pittsburgh, Pittsburgh, PA, 12Rheumatology, Arthritis and Osteoporosis Consultants of the Carolinas, Charlotte, NC, 13NYU Langone Medical Center, New York, NY, 14Rheumatology, Hospital for Special Surgery, New York, NY, 15Rheumatology, Robert Wood Johnson University Scleroderma Program, New Brunswick, NJ, 16Medicine, Rheumatology, University of Chicago, Chicago, IL, 17University of Michigan, Ann Arbor, MI, 18University of Texas McGovern Medical School, Houston, TX, 19Medicine/Rheumatology, Univ of Pittsburgh, Pittsburgh, PA, 20Department of Public Health Sciences, Medical University of South Carolina, Charleston, SC, 21Boston University, Boston, MA, 22Tulane, New Orleans, LA, 23Rheumatology, The George Washington University, Washington, DC, 24Division of Rheumatology and Immunology, Department of Medicine, Medical University of South Carolina, Charleston, SC, 25Rheumatology, MedStar Georgetown University Hospital, Washington, DC, 26Stanford University School of Medicine, Stanford, CA, 27Rheumatology and Dermatology, Northwestern University, Feinberg School of Medicine Scleroderma Program, Chicago, IL, 28Rheum Div/Mason F Lord, Johns Hopkins University, Baltimore, MD, 29Rheumatology, University California, San Francisco, San Francisco, CA, 30Inflammatory Disease Section, National Human Genome Research Institute, National Institutes of Health, Bethesda, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Pathogenesis, Animal Models and Genetics II
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM
Background/Purpose: Systemic sclerosis (SSc) is a multisystem disease that has a higher prevalence in African Americans (AA), with a more severe phenotype, internal organ involvement, and increased mortality. Genetic risk factors contributing to the AA SSc phenotype are largely unknown.

Methods: The Genome Research in African American Scleroderma Patients consortium (GRASP) was established to recruit AA patients to investigate the genetic basis of SSc. The Illumina MEGA array was used to genotype 934 patients and 946 controls to conduct the first genome-wide association study (GWAS) of SSc in AA. A total of 1.7 million variants were genotyped and after quality control filtering 1.4 million variants remained and were imputed into the 1000 Genomes Phase 3 v5 reference panel. We utilized HiChIP, a protein-centric chromatin conformation method, to elucidate the role of these variants.

Results: Admixture and principal component analysis (PCA) confirmed that the patients and controls were well-matched. λGC was 1.03, suggesting no major population stratification. The MHC region demonstrated the strongest association after accounting for the top 10 PCAs (Figure 1). The rs35915063 was the top scoring variant in the HLA-DQB1 gene \( P=2.2 \times 10^{-17} \), \( OR=1.96 \) (95% CI 1.7-2.3). Stepwise conditional regression analysis using an additive model revealed the DQA1 gene variant rs9271620 \( P=1.01 \times 10^{-8} \) and the DPB1 gene variant rs2071354 \( P=5.8 \times 10^{-8} \) as independent risk variants. eQTL databases revealed a reduction in DQB1, DQA1, and DRB1 expression and an increase in DPB1 and DQA2 expression based on the associated allele of these three variants. The rs59063398 variant showed the strongest non-MHC association with \( P=2.0 \times 10^{-8} \), \( OR=0.47 \) (95% CI 0.4-0.6) (Figure 2A). This variant is part of an evolutionarily conserved haploblock in the IFT43 gene region that is African ancestry specific. Overlaying our GWAS data on the H3K27ac HiChIP data in Th17 and Treg cells highlighted IFT43 intronic variants falling under the TGFβ3 promoter peak, suggesting potential alteration of TGFβ3 promoter activity and in turn regulation of TGFβ3 expression (Figure 2B).

Conclusion: This first GWAS of SSc in AA confirms MHC as a susceptibility locus and identifies a novel (TGFβ3), non-MHC locus, as a SSc susceptibility gene. IFT43/TGFβ3 region variants are non-polymorphic in Europeans, suggesting an explanation for the increased prevalence and severity of SSc in AA. TGFβ3 has a role in fibrosis and in development of effector Th17 cells, raising the possibility of therapies targeting these pathways.

![Figure 1: GWAS of Illumina MEGA array using 934 SSc cases and 946 controls. Data shown here are from trend test after correcting for the top ten PCAs. Pink line denotes \( p \)-value for genome-wide significance \( (P=5 \times 10^{-8}) \) and purple line denotes \( P=10^{-8} \).](image1)

![Figure 2A: Chr 14 region association analysis showing genotyped (red) and imputed (blue) variants in 934 SSc cases and 946 controls. Data shown here are from trend test after correcting for the top ten PCAs. B: Imputed Chr 14 GWAS data overlaid with H3K27ac HiChIP data in Th17 and Treg cells. The tall peak is anchored on TGFβ3 promoter. Pink arrow highlights the IFT43 variants that fall under the TGFβ3 promoter peak.](image2A)

Disclosure: P. Gourh, None; E. F. Remmers, None; A. Satpathy, None; S. Boyden, None; N. D. Morgan, None; A. A. Shah, None; A. Adeyemo, None; A. Bentley, None; M. A. Carns, None; S. C. Chandrasekharappa, None; L. Chung, Cytori, Actelion, Reata, 5; L. A. Criswell, None; C. T. Derk, None; R. T. Domsic, None; A. Doumatey, None; H. Gladue, None; A. Goldberg, None; J. K. Gordon, Corbus Pharmaceuticals, 2, Cumberland Pharmaceuticals, 2, Bayer Pharmaceuticals, 2; V. Hsu, None; R. Jan, None; D. Khanna, Bristol-Myers Squibb, 2, Genentech/Roche, 2, NIH/NIAMS, 2, NIH/NIAID, 2, Patient-Centered Outcomes Research Institute,
Intrinsic Subsets Are Conserved across Organ Systems

Multi-Organ RNA-Sequencing of Patients with Systemic Sclerosis (SSc) Finds That Intrinsic Subsets Are Conserved across Organ Systems

Background/Purpose: While skin fibrosis is a hallmark of systemic sclerosis (SSc), internal organ involvement is the primary cause of morbidity and mortality, often related to pulmonary disease and gastrointestinal (GI) dysfunction. Here we tested the hypothesis, generated from a meta-analysis of ten different SSc datasets, that any single patient with SSc would have the same deregulated molecular signatures across multiple organ systems, consistent with the systemic nature of the disease.

Methods: RNA sequencing (RNA-seq) was performed on at least four organ biospecimens (skin, esophagus, fundus, duodenum, and/or blood) from 14 patients who met 2013 ACR/EULAR criteria for SSc. RNA was sequenced by 75bp paired-end RNA-seq at >80 million reads per sample and aligned to the reference genome (hg19). Each sample was assigned to an intrinsic subset (inflammatory, proliferative, or normal-like) using Support Vector Machine (SVM) classification and unsupervised hierarchical clustering with profiles of normalized Reads Per Kilobase of transcript per Million mapped reads (RPKM) values.

Results: Hierarchical clustering of the RPKM data showed that samples from a single tissue type cluster tightly together. Analysis of skin and esophagus individually also recapitulated the intrinsic subsets previously observed in these organs. Furthermore, for the first time, the inflammatory, proliferative, and normal-like intrinsic subsets were identified in the fundus and duodenum. The blood of patients with SSc also displayed gene expression signatures of the inflammatory, proliferative, and normal-like intrinsic subsets. Subsequent normalizing for tissue type in an agglomerative analysis of all tissues results in the identification of intrinsic gene expression subsets across organ systems. Importantly, all five organs assessed were represented in each intrinsic subset. The majority of patients (9/14) showed >60% concordance of intrinsic subset assignment across the multiple organs analyzed. Moreover, tissues from the gastrointestinal tract tended to belong to the same subset (5/14 with 100% concordance).

Conclusion: We have performed the first molecular analysis of biospecimens from multiple organs within an individual patient with SSc. Our data suggest that SSc molecular subsets are reproducible in different tissues and that deregulated molecular pathways are conserved across organ systems within the same patient. These data indicate that intrinsic subsets are common feature of end-organ pathology in SSc. We cannot rule out the possibility that pathogenic mechanisms of disease activity and progression are discordant in
mTOR Pathway Is Activated in Endothelial Cells from Patients with Takayasu Arteritis and Is Modulated By Serum IgG

Jérôme Hadjadj1, Guillaume Canaud2, Tristan Mirault3, Maxime Samson4, Patrick Bruneval5, Alexis Regent6, Claire Goulvestre7, Veronique Witko-Sarsat8, Nathalie Costedoat-Chalumeau9, Loïc Guillemin for the French Vasculitis Study Group10, Luc Mouthon11 and Benjamin Terrier12, 1Department of Internal Medicine, National Referral Center for Rare Autoimmune and Systemic Diseases, Hospital Cochin, Assistance Publique-Hôpitaux de Paris (AP-HP), Team Neutrophils and Vasculitis, INSERM U1016, Cochin Institute, Paris, France, Paris, France, 2Department of Nephrology and Transplantation, Necker-Enfants Malade, Université Paris Descartes, Sorbonne Paris Cité, INSERM U1151, Necker-Enfants Malades Hospital, Paris, France AP-HP, Paris, France, PARIS, France, 3Department of Vascular Medicine, Georges Pompidou European Hospital, AP-HP, Université Paris Descartes, Sorbonne Paris Cité, Paris, France, Paris, France, 4Dijon University Hospital, Dijon, France, 5HEGP, Paris, France, 6National Referral Center for Rare Systemic Autoimmune Diseases, Hôpital Cochin, AP–HP, Université Paris Descartes, Paris, France, 7Department of Immunology, Hospital Cochin, Assistance Publique-Hôpitaux de Paris (AP–HP), Paris, France, Paris, France, 8Team Neutrophils and Vasculitis, INSERM U1016, Cochin Institute, LABEX Inflamex, Université Sorbonne Paris Cité, 75013, Paris, France, Paris, France, 9Service de médecine interne Pôle médecine, Hôpital Cochin, Centre de référence maladies auto-immunes et systémiques rares de l’Île de France, Paris, France, 10Service de Médecine Interne, Centre de Référence Maladies Auto-Immunes et Auto-Inflammatoires Systémiques Rares, Hôpital Cochin, Paris, France, 11Service de Médecine Interne, Hôpital Cochin, Centre de référence national pour les maladies systémiques autoimmunes rares d’Île de France, DHU Authors, Assistance Publique-Hôpitaux de Paris (AP-HP), Paris, France ;Université Paris Descartes Sorbonne Paris, Paris, France, 12Service de Médécine Interne, Hôpital Cochin, Centre de référence national pour les maladies systémiques autoimmunes rares d’Île de France, DHU Authors, Assistance Publique-Hôpitaux de Paris (AP-HP), Paris, France, Paris, France

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Wednesday, November 8, 2017
Session Title: Vasculitis III: Pathogenesis
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose: Takayasu arteritis (TA) and giant cell arteritis (GCA) are large-vessel vasculitis characterized by vascular remodelling involving endothelial cells (ECs) and vascular smooth muscle cells, leading to ischemic events. We hypothesized that mammalian target of rapamycin (mTOR) pathway could drive vascular inflammation and remodelling in large-vessel vasculitis.

Methods: To study activation of mTOR pathway in injured vessels from patients with TA and GCA, we evaluated phosphorylation of S6RP (p-S6RP) and AKT (p-AKT Ser 473) by immunofluorescence analysis on aorta and temporal arteries biopsies, which reflect activation of mTORC1 and mTORC2, respectively. To investigate the potential role of antibodies binding to ECs in the activation of mTOR pathway, sera from patients with TA, GCA and healthy controls (HCs) were screened for the presence of antibodies against ECs (AECA) using indirect immunofluorescence (IIF) and cellular ELISA. We evaluated in vitro the effect of purified IgG from patients with AECA on mTOR pathway activation and cell proliferation. Target antigens of AECA were investigated by Western-blotting.

Results: Immunofluorescence analysis on tissues revealed that adventitial vessels from aorta’s vasa vasorum from TA patients were strongly positive for both p-S6RP and p-AKT (Ser 473) in ECs but not in vascular smooth muscle cells, showing that both mTORC1 and mTORC2 were specifically activated in ECs in TA, but not in ECs from GCA patients and HCs (Figure 1). Using IIF and cellular
ELISA, we observed higher levels of AECA in TA patients compared to GCA and healthy controls (HCs) with these two techniques. Using Western blot, we demonstrated that purified IgG from TA patients caused mTORC1 activation in ECs, whereas this effect was not observed with purified IgG from GCA or HCs. mTORC1 was activated through PI3K-AKT pathway, suggesting that recruitment of AKT to the cell membrane is necessary for activation of the mTOR pathway induced by serum IgG in TA. Finally, purified IgG from TA induced a significant ECs proliferation compared to GCA and HCs IgG, and this effect was decreased after ECs exposure with sirolimus, a specific mTOR inhibitor, and PI3K inhibitor. Sera obtained from TA patients with positive screening of AECA bound predominantly to an endothelial cell antigen with a molecular weight between 60 and 65 kDa.

Conclusion: Our results suggest that antibodies against ECs drive vascular inflammation leading then to vascular remodelling in TA through activation of mTOR pathway in ECs, but not in GCA. Inhibition of mTOR pathway could represent an alternative therapeutic option in TA.

Figure 1:

Disclosure: J. Hadjadj, None; G. Canaud, None; T. Miraunt, None; M. Samson, None; P. Bruneval, None; A. Regent, None; C. Goulvestre, None; V. Witko-Sarsat, None; N. Costedoat-Chalumeau, None; L. Guillemin for the French Vasculitis Study Group, None; L. Mouthon, None; B. Terrier, None.

Abstract Number: 2933

The Microvascular Niche Instructs Pathogenic T Cells in Medium and Large Vessel Vasculitis

Cornelia M. Weyand¹, Zhenke Wen², Yi Shen², Gerald Berry³, Joyce Liao⁴ and Jorg Goronzy⁵, ¹Medicine: Immunology and Rheumatology, Stanford University, Stanford, CA, ²Medicine: Immunology and Rheumatology, Stanford University School of Medicine, Stanford, CA, ³Pathology, Stanford University School of Medicine, Stanford, CA, ⁴Byers Eye Institute at Stanford, Stanford University, Palo Alto, CA, ⁵Medicine/Division of Immunology & Rheumatology, Stanford University School of Medicine, Stanford, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Vasculitis III: Pathogenesis
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM
Background/Purpose: Adventitial microvascular networks (vasa vasora) control the access to the wall structure of medium and large arteries and thus guard the immune privilege of the aorta and its branches. In giant cell arteritis (GCA), CD4 T helper 1 (Th1) and Th17 cells obtain access to the arterial wall layers, where together with macrophages they form granulomatous infiltrates. Whether the small adventitial vessels have a pathogenic role in GCA is unknown.

Methods: Tissue transcriptomes were examined in tissue biopsies of patients with temporal arteritis or GCA aortitis, and genes-of-interest were confirmed by immunohistochemical staining. Unprimed CD4 T cells were collected from peripheral blood of patients with active GCA and age-matched healthy controls. Effector cell differentiation was analyzed by detecting intracellular cytokines by flow cytometry or immunohistochemistry. Microvascular endothelial cell (mvEC)-T cell interactions were studied in an ex vivo and in vivo system. Relevant signaling pathways were identified by iRNA technology (Notch1, Raptor), small molecule inhibitors (NOTCH and mTORC1 inhibitors) and monoclonal antibodies.

Results: Microvascular endothelial cells (mvEC) in the adventitia of GCA-affected temporal arteries and aortas expressed abundant Jagged1, a ligand for the cell-fate-regulating receptor Notch1. Patients with active GCA had high frequencies of Notch1+ CD4 T cells, which had left the quiescent state and acquired effector cell characteristics. Jagged1-expressing mvEC were able to instruct CD4 T cells to enter differentiation and commit to Th1 and Th17 differentiation. In vivo, upregulation of Jagged1 on adventitial microvessels intensified the inflammatory activity of the vasculitogenic lesions by increasing the frequency of tissue-residing IFN-γ–producing effector cells. Jagged1-induced T cell instruction was dependent on the mTORC1 signaling pathway; commitment to either the Th1 or the Th17 lineage was sensitive to mTORC1 inhibitors.

Conclusion: Adventitial microvessels form an instructive tissue niche, that protects medium and large arteries from inflammatory attack. In GCA, this immune-protective mechanism fails and Jagged1-expressing mvEC stimulate and instruct Notch1+ CD4 T cells. This signal is sufficient for CD4 T cells to invade into the tissue site and acquire pathogenic effector functions. Vasculitogenic functions depend on the mTORC1 signaling pathway. Overall, these findings identify multiple actionable steps in the pathogenesis of GCA.

Disclosure: C. M. Weyand, None; Z. Wen, None; Y. Shen, None; G. Berry, None; J. Liao, None; J. Goronzy, None.

Comparative Analysis of the Macrophage Glycolytic Machinery in Giant Cell Arteritis (GCA) and in Coronary Artery Disease (CAD)

Cornelia M. Weyand¹, Ryu Watanabe², Tsuyoshi Shirai³, Hui Zhang⁴, Gerald Berry⁵ and Jorg Goronzy⁶, ¹Medicine: Immunology and Rheumatology, Stanford University, Stanford, CA, ²Medicine: Immunology/Rheumatology, Stanford University School of Medicine, Stanford, CA, ³Department of Hematology and Rheumatology, Tohoku University Graduate School of Medicine, Sendai, Japan, ⁴Medicine: Immunology and Rheumatology, Stanford University School of Medicine, Stanford, CA, ⁵Pathology, Stanford University School of Medicine, Stanford, CA, ⁶Medicine/Division of Immunology & Rheumatology, Stanford University School of Medicine, Stanford, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Vasculitis III: Pathogenesis
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose: Macrophages are key effector cells in the vessel wall inflammation of the atherosclerotic plaque as well as in the intramural infiltrates of giant cell arteritis (GCA). The histomorphology of both diseases is distinct; GCA macrophages are arranged in granulomatous lesions and form giant cells, whereas plaque-residing macrophages facilitate lipid uptake and participate in a fibro-inflammatory reparative process. Whether the profile of inflammatory macrophage functions is comparable in both conditions and which signaling pathways drive macrophage activation in the vessel wall lesions is insufficiently understood.

Methods: Tissue-residing macrophages were analyzed in biopsies from atherosclerotic plaques and from GCA-affected temporal arteries. Monocyte-derived macrophages were generated from peripheral blood CD14+ precursor cells by differentiating the cells with
M-CSF over a 5-day culture. Macrophages were stimulated with 100 U/ml IFN-γ and 100 ng/ml LPS. Patients were enrolled if they had (a) at least one documented myocardial infarct or (b) a temporal artery biopsy positive for GCA. Tissue transcriptomes and gene expression panels from macrophages were established by RT-PCR. Protein expression was examined by flow cytometry and by immunohistochemical staining of tissue sections.

**Results:** In macrophages from patients with CAD glucose transporters and enzymes of the glycolytic pathway were strongly upregulated (Glut1, HK2, GAPDH, PKM1, PGM1, HIF1α, and c-myc). Glucose and its breakdown product pyruvate directly controlled the production of inflammatory cytokines (IL-1β, IL-6) and regulated the expression of co-stimulatory (CD80, CD86) and co-inhibitory ligands (PD-L1). Most plaque-residing macrophages were PD-L1<sup>hi</sup> expressors. In contrast, the glycolytic machinery was not upregulated in GCA macrophages. Profiling for chemokines and cytokines revealed high expression of CXCL9, 10 and 11 in GCA macrophages, but the inflammatory cytokines IL-1, IL-6 and TNF were indistinguishable in GCA patients versus normal controls. Opposite to CAD macrophages, GCA macrophages were characterized by low expression of the co-inhibitory ligand PD-L1. Tissue-residing cells in temporal artery lesions also had the PD-L1<sup>low</sup> phenotype.

**Conclusion:** Signaling pathways driving the activation of macrophages in the atherosclerotic plaque and in GCA lesions are fundamentally different. CAD macrophages are characterized by a metabolic defect, over-utilize glucose and are functionally a hybrid between excess cytokine release and high expression of PD-L1. GCA macrophages are biased towards chemokine production. The low expression of the immuno-inhibitory ligand PD-L1 enables them to strongly promote T cell effector functions.

**Disclosure:** C. M. Weyand, None; R. Watanabe, None; T. Shirai, None; H. Zhang, None; G. Berry, None; J. Goronzy, None.


**Abstract Number:** 2935

**Nasal Microbiota in Patients with Granulomatosis with Polyangiitis Compared to Healthy Controls**

**Rennie L. Rhee**<sup>1</sup>, Antoine G. Sreih<sup>1</sup>, Catherine E. Najem<sup>1</sup>, Peter C. Grayson<sup>2</sup>, Chunyu Zhao<sup>3</sup>, Kyle Bittinger<sup>3</sup>, Ronald G. Collman<sup>4</sup> and Peter A. Merkel<sup>5</sup>, <sup>1</sup>Rheumatology, University of Pennsylvania, Philadelphia, PA, <sup>2</sup>National Institute of Arthritis, Musculoskeletal and Skin Disease (NIAMS), Bethesda, MD, <sup>3</sup>Gastroenterology, Hepatology, and Nutrition, Children's Hospital of Philadelphia, Philadelphia, PA, <sup>4</sup>Medicine & Microbiology, University of Pennsylvania, Philadelphia, PA, <sup>5</sup>Division of Rheumatology, University of Pennsylvania, Philadelphia, PA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Wednesday, November 8, 2017  
**Session Title:** Vasculitis III: Pathogenesis  
**Session Type:** ACR Concurrent Abstract Session  
**Session Time:** 9:00AM-10:30AM

**Background/Purpose:**

Prior studies have suggested a potential link between nasal microbes, in particular *Staphylococcus aureus*, and granulomatosis with polyangiitis (GPA; Wegener’s) but these studies relied on culture-dependent methods. This study comprehensively examined the entire community of nasal microbiota in patients with GPA compared to healthy controls using deep sequencing methods.

**Methods:**

The nasal microbiota of 61 patients with GPA and 41 healthy controls was sampled using nasal swabs and analyzed by sequencing of the bacterial 16S rRNA gene (V1-V2 region). The abundance profiles of the 11 most abundant bacterial taxa were compared using the Wilcoxon rank sum test, correcting for multiple comparisons. Additional comparative analyses within the GPA cohort were performed by ANCA type (PR3 vs MPO), presence or absence of sinonasal Vasculitis Damage Index items (VDI), and disease activity (active vs remission). The effects of antibiotics and immunosuppressive therapies (both current and within the past 6 months) were evaluated using generalized linear models.

**Results:**
Corynebacterium, Propionibacterium, and Staphylococcus featured as prominent bacterial taxa in the nasal swab samples, consistent with previous reports. After clustering the sequence reads into operational taxonomic units, we identified two abundant groups of Staphylococcus in the data: one closely related to S. aureus and the other similar to S. epidermidis. The S. epidermidis cluster and Propionibacterium were decreased in abundance in GPA vs controls (Figure 1A). In multivariate analyses, patients with GPA receiving non-glucocorticoid immunosuppressive therapy had a higher abundance of Propionibacterium (p = 0.01) that was similar to the abundance seen in healthy controls. Among patients with GPA, there was a lower abundance of the S. aureus cluster in i) subjects with PR3- vs MPO-ANCA; and ii) subjects with at least 1 sinonasal VDI item vs. those without a sinonasal VDI item (Figure 1B). In multivariate analyses, ANCA type remained significantly associated with abundance of S. aureus independent of medications and presence of a sinonasal VDI item (p = 0.01).

**Conclusion:**

Nasal microbial communities differ between patients with GPA and controls as well as between clinically-distinct subsets of GPA. Interestingly, a lower abundance of Propionibacterium (which prior studies have suggested may negatively interact with S. aureus) was found in patients with GPA, particularly among those off immnosuppressive therapies, raising the possibility that a loss of the “protective” effect of Propionibacterium may increase susceptibility to colonization by pathogens such as S. aureus. These data support the theory that microbes are involved in the disease process of GPA and that a deeper understanding of dysbiotic microbial communities in GPA could lead to novel preventative or therapeutic strategies.

**Disclosure:** R. L. Rhee, None; A. G. Sreih, None; C. E. Najem, None; P. C. Grayson, None; C. Zhao, None; K. Bittinger, None; R. G. Collman, None; P. A. Merkel, None.


**Abstract Number:** 2936

**B-Cell Depletion By Rituximab Affects the Distribution of Effector Th-Cell Subsets in Patients with ANCA Associated Vasculitis**

Wayel H. Abdulahad1, Ulrich Specks2, Theo Bijma3, Deborah J. Phippard4, Fredrick Karnell5, Noha Lim5, John H. Stone6 and Cees G.M. Kallenberg1, 1Rheumatology and Clinical Immunology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, 2Mayo Clinic College of Medicine, Rochester, MN, 3UMCG, Groningen, Netherlands, 43 Bethesda Metro Center., Suite 400, Bethesda, MD, 5Immune Tolerance Network, Bethesda, MD, 6Rheumatology Unit, Massachusetts General Hospital, Boston, MA

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Wednesday, November 8, 2017

**Session Title:** Vasculitis III: Pathogenesis

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 9:00AM-10:30AM
Background/Purpose:

The current study is aimed to assess the effect of B-cell depletion on the distribution of effector T-cell subsets in AAV-patients. Alterations in CD4\(^+\) Th effector cell (Th1/Th2/Th17/T\(_{FH}\)) homeostasis may contribute to the therapeutic effect of rituximab (RTX) as Th-effector imbalances are involved in the emergence of autoimmune diseases.

Methods:

Patients with active AAV were treated in a randomized, controlled trial with corticosteroids combined with RTX 375 mg/m\(^2\) weekly x 4 or oral cyclophosphamide (CYC) 2m/kg/d for 6 months as induction therapy. Blood samples from 69 of these AAV-patients were obtained at baseline, 2 months, and 6 months (primary endpoint), and time of assessment for clinical remission. The frequency of circulating Th1 (producing IFN\(\gamma\)), Th2 (producing IL-4), Th17 (producing IL-17), and T\(_{FH}\) (producing IL-21) cells were assessed at all time-points using flow cytometry upon \textit{in vitro} stimulation with PMA and Calcium Ionophore.

Results:

At baseline, the four circulating effector Th-cell subsets were comparable in frequency between the RTX-group and the CYC-group. Among the RTX-treated patients, the frequency of Th2 cells decreased steadily, whereas, no significant changes were seen in frequencies of Th1, Th17, and T\(_{FH}\) cells. The frequencies of Th2 and T\(_{FH}\) cells in CYC-treated patients remained unchanged during the follow-up compared to baseline; whereas, a significant increase was observed in Th17 and Th1 cells at 2 and 6 months, respectively. Interestingly, the decrease in the percentage of Th2 cells among the RTX-treated patients at 6 months was restricted to patients who achieved complete and sustained remission up to 18 months (n=24); whereas, no such changes were observed in patients who relapsed after the achievement of complete remission at 6 months (n=9). Moreover, among the CYC treated patients, the increases in Th17 cells at 2 and 6 months were restricted to patients who achieved complete and sustained remission (n=15) in comparison to those who experienced relapses (n=7).

Conclusion:

In patients with active AAV, B-cell depletion therapy, as well as treatment with oral CYC influences blood Th cell homeostasis. Changes in Th cell during induction therapy with RTX or CYC may contribute to long-term clinical outcome.

Disclosure: W. H. Abdulahad, None; U. Specks, None; T. Bijma, None; D. J. Phippard, None; F. Karnell, None; N. Lim, None; J. H. Stone, None; C. G. M. Kallenberg, None.

Abstract Number: 2937

**Genetic Variants in HLA-C and Class I Pathway Genes Influence Susceptibility to Kawasaki Disease**

Chisato Shimizu\(^1\), Jihoon Kim\(^2\), Hariklia Eleftherohorinou\(^3\), Victoria Wright\(^3\), Long Hoang\(^4\), Adriana Tremoulet\(^5\), Alessandra Franco\(^6\), Martin Hibberd\(^4\), Atsushi Takahashi\(^7,8\), Michiaki Kubo\(^9\), Kaoru Ito\(^10\), Toshihiro Tanaka\(^10,11\), Yoshihiro Onouchi\(^10,12\), Lachlan Coin\(^3\), Michael Levin\(^3\), Jane Burns\(^13\) and Hiroko Shike\(^14\), \(^1\)Pediatrics, University of California San Diego, School of Medicine, La Jolla, CA, \(^2\)Medicine, University California San Diego, School of Medicine, La Jolla, CA, \(^3\)Imperial College London, London, United Kingdom, \(^4\)Genome Institute of Singapore, Singapore, Singapore, \(^5\)Pediatrics, University California San Diego, School of Medicine, La Jolla, CA, \(^6\)Pediatrics, University of California San Diego School of Medicine, La Jolla, CA, \(^7\)Laboratory for Statistical Analysis, RIKEN Center for Integrative Medical Sciences, Yokohama, Japan, \(^8\)Department of Genomic Medicine, National Cerebral And Cardiovascular Center, Suita, Japan, \(^9\)RIKEN Center for Integrative Medical Sciences, Yokohama, Japan, \(^10\)Laboratory for Cardiovascular Diseases, RIKEN Center for Integrative Medical Sciences, Yokohama, Japan, \(^11\)Department of Human Genetics and Disease Diversity, Graduate School of Medical and Dental Sciences, Tokyo, Japan, \(^12\)Department of Public Health, Chiba University Graduate School of Medicine, Chiba, Japan, \(^13\)Pediatrics, University California San Diego, School of Medicine, San Diego, CA, \(^14\)Penn State Hershey Medical Center, Hershey, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Background/Purpose:

Host genetics influence susceptibility to Kawasaki disease (KD), an acute pediatric vasculitis, and genome wide association studies (GWAS) have detected variants with modest effects on disease susceptibility. Recently we performed a pathway analysis using a European descent KD GWAS dataset. We reported that the antigen processing and presentation pathway was one of the top 50 pathways associated with KD susceptibility with 9 single nucleotide variants (SNVs) located near HLA-B and C in the HLA class I region driving the association. We speculated that these SNVs in the HLA class I region influence antigen presentation and KD susceptibility.

Methods:

Nine SNVs in the HLA region from our European descent GWAS were tested for association with KD using a Japanese GWAS dataset. To explore the influence of these SNVs on KD susceptibility, we performed expression quantitative trait loci (eQTL) analysis using a US multi-ethnic cohort (n=146) and analyzed the associated polymorphic amino acid sequence of HLA-B and –C by HLA typing an independent U.S. multi-ethnic cohort (n=78) and a Japanese cohort (subset of Japanese GWAS n=275).

Results:

Two SNVs (rs6906846 upstream of HLA-C and rs2254556 upstream of HLA-B) were significantly associated with KD susceptibility in both the European descent and Japanese GWAS datasets (combined nominal p=1.0xE-04 for rs6906846 and p=7.0xE-05 for rs2254556). HLA typing in both our U.S. multi-ethnic cohort (n=78) and the Japanese cohort (n=275) revealed association of the risk allele at this locus with specific HLA-C types (e.g. HLA-C*07:02 U.S. and Japanese combined p=2.8xE-30) and with specific amino acid sequences at multiple HLA-C positions, including several in the peptide binding groove that could influence peptide binding and presentation. The risk allele (A) at rs6906846 was associated with higher expression of HLA-C by microarray (n=146, AA vs. GG p<1.0xE-04) and targeted amplification of whole blood RNA in an independent U.S. multi-ethnic cohort (n=42, AA vs. GG p<5.0xE-02). We extended the eQTL analysis using our U.S. multi-ethnic array data (n=146) to 5 previously reported SNVs associated with KD that were located in/near genes in the HLA class I pathway from the Japanese GWAS: rs2854251 (proximal to antigen peptide transporter (TAP) 1/2 and proteasome subunit beta (PSMB) 8/9) and a Taiwanese GWAS: rs149481 (Endoplasmic reticulum aminopeptidase (ERAP)1/2 region), and rs1873668, rs4243399, and rs16849083 (coatomer protein complex subunit beta 2 (COPB2) region). In our U.S. multi-ethnic cohort (n=146), we found increased transcript levels of TAP2 (GG vs. AA p<5.0xE-03) and PSMB8 (GG vs. AA p<5.0xE-02), and reduced ERAP2 transcripts (AA vs. AC p<5.0xE-03) associated with the corresponding risk alleles.

Conclusion: SNVs that influence the amino acid sequence in the HLA peptide binding groove and that serve as eQTL for HLA-C pathway proteins influence KD susceptibility in diverse ethnic groups. These findings suggest the importance of HLA-C antigen presentation to CD8+ T cells and/or NK cell regulation in KD pathogenesis.

Disclosure: C. Shimizu, None; J. Kim, None; H. Eleftherohorinou, None; V. Wright, None; L. Hoang, None; A. Tremoulet, None; A. Franco, None; M. Hibberd, None; A. Takahashi, None; M. Kubo, None; K. Ito, None; T. Tanaka, None; Y. Onouchi, None; L. Coin, None; M. Levin, None; J. Burns, None; H. Shike, None.


Abstract Number: 2938

Is Synovial Hypertrophy without Doppler Activity in Rheumatoid Arthritis Joints Sensitive to Change ? – Results of a Longitudinal Ultrasound Study

Lene Terslev 1, Mikkel Østergaard 1, Joseph Sexton 2 and Hilde B Hammer 2, 1Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Rigshospitalet, Denmark, Copenhagen, Denmark, 2Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Imaging of Rheumatic Diseases II: Focus on Rheumatoid Arthritis and Systemic Sclerosis
Backgound/Purpose: Ultrasound (US) is used to assess diseases activity in rheumatoid arthritis (RA). Gray scale (GS) US shows the synovial hypertrophy (SH) and Doppler the amount of hyperemia which is believed to reflect disease activity. Some joints with SH may have no Doppler activity despite the use of high-end US equipment and these joints are generally believed to be inactive without potential to change. The aim is to investigate if joints with SH but no Doppler activity is sensitive to change during treatment with biological DMARD (bDMARD) in RA patients.

Methods:

RA patients initiating or changing bDMARD treatment were included. US examination was performed at baseline, 3 and 6 months using Siemens Antares US equipment with Doppler settings for slow flow. 36 joints were evaluated at each visit. SH and Doppler activity was graded from 0-3 according to the US atlas by Hammer et al. The GS score for SH in joints without Doppler activity was registered for the individual joints using GS SH>1 as threshold. The changes were compared to changes in SH in joints with Doppler activity.

Results:

157 patients (83.2% women, 81.3% seropositive for anti-CCP and 75.8% for rheumatoid factor) were included, with a mean (SD) age of 51.5 (13.3) years and mean disease duration of 9.9 (8.1) years. At baseline, 52.2% used prednisolone (mean (SD) 7.7 (4.6) mg, range 2.5-25mg). The patients had a mean (SD) baseline DAS28 of 4.5 (1.5). At baseline 27% of the joints had SH without Doppler activity and 28% of the joints had SH with Doppler activity. Joints without Doppler had overall lower grades of SH (mean 0.72) than joints with Doppler (mean 1.21).

Of the joints that had SH without Doppler at baseline, 54% had a decrease in SH at 3 months, and 56% at 6 months. For joints with SH with Doppler at baseline, 52% had a decrease in SH at 3 months, and 60% at 6 months. The overall proportion of joints improving in SH was similar in joint with and without Doppler activity but when adjusting for the baseline score of SH, SH in joints without Doppler activity had a higher tendency towards decrease than those with Doppler activity (3 months: p <0.0001; 6 months < 0.0005).

Conclusion:

SH in joints without Doppler activity improves during bDMARD, i.e is sensitive to change. Thus, SH without Doppler activity is not a sign of inactive disease. These findings document that both Doppler and SH should be evaluated when assessing disease activity by US.

Disclosure: L. Terslev, None; M. Østergaard, Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Centocor, GSK, Hospira, Janssen, Mercck, Mundipharma, Novartis, Novo, Orion, Pfizer, Regeneron, Schering-Plough, Roche, Takeda, UCB, and Wyeth, 5; J. Sexton, None; H. B. Hammer, AbbVie Norway, 2,Abbvie, 8,Novartis Pharmaceutical Corporation, 5,Pfizer Inc, 8,Roche Pharmaceuticals, 8.


Abstract Number: 2939

Clinical Correlate of Synovial Proliferation in Early Rheumatoid Arthritis

Fan XIAO1, JIANG YUE2, Queenie Mak3, Lai-Shan Tam4 and James F Griffith5, 1Department of Imaging and Interventional Radiology, The Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong, Hong Kong, 2Department of Medicine and Therapeutics, Prince of Wales Hospital, The Chinese University of Hong Kong, HONG KONG, Hong Kong, 3Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong, Hong Kong, 4Department of Medicine & Therapeutics, The Chinese University of Hong Kong, Hong Kong, Hong Kong, 5Department of Imaging and Interventional Radiology, The Prince of Wales Hospital, The Chinese University of Hong Kong, HONGKONG, Hong Kong

First publication: September 18, 2017
Clinical Correlate of Synovial Proliferation in Early Rheumatoid Arthritis

**Background/Purpose:** To determine whether semi-quantitative, quantitative assessment of synovitis severity or synovial perfusion data correlates best with clinical symptoms and inflammatory markers.

**Methods:** 116 patients (88 females, 28 males, mean age, 53±13 years) with early (i.e. symptoms < 24 months) RA underwent 3T dynamic contrast-enhanced (DCE) MRI of the most symptomatic wrist. Sequences obtained were: fat-saturated T1-weighted axial; fat-saturated T2-weighted coronal; T1-weighted coronal and fat-saturated post-contrast T1-weighted axial.

Analyses undertaken included:

1. Semi-quantitative grading of (a) synovial proliferation (RAMRIS) and (b) tenosynovitis.
2. Quantitative measurement of enhancing synovial volume using segmentation method (cm$^3$) (Fig 1).
3. Maximum enhancement (ME) and enhancement slope (ES) of enhancing synovium derived from time-intensity curves of DCE MRI data (Fig 2).
4. Clinical assessment (Simple Disease Activity Index) and inflammatory markers (erythrocyte sedimentation rate, C-reactive protein).

Clinical evaluation included a determination of morning stiffness (minutes), pain score (0-10), disease activity by the Simple Disease Activity Index (which reflects the number of swollen ± tender joints) and serological inflammatory markers (ESR, CRP).

**Results:** Synovitis and tenosynovitis was present in 113 (97%) and 81 (70%) of the 116 wrists examined. Tenosynovitis was associated with more severe synovial proliferation. Regarding clinical correlation, quantitative parameters correlated much better with patient symptoms than semi-quantitative parameters. Morning stiffness and pain correlated with total synovial and tenosynovial volume ($r=0.407$, $p=0.028$) but not with RAMRIS ($r=0.165$, $p=0.196$). SDAI best correlated with ME and ES ($r=0.502$, $p<0.001$). ESR ($r=0.380$, $p=0.002$) and CRP ($r=0.469$, $p<0.001$) only correlated with ES.

**Conclusion:** Quantitative correlated with patient symptoms and serological inflammatory markers better than semi-quantitative parameters. Synovial volume was more related to morning stiffness and pain while perfusion parameters were more related to disease activity and inflammation.

**Fig 1.** Automated segmentation of enhancing synovium of the distal radioulnar joint (A) and following manual removal of adjacent vasculature (B). Joint synovial proliferation is seen as red, tenosynovial proliferation as green.
**Fig 2.** ERA patient (SDAI=40.46) with severe synovitis. The DCE perfusion curve was fit and $E_{\text{max}} = 102.37$, $E_{\text{slope}} = 526.08$ respectively.

**Disclosure:** F. Xiao, None; J. Yue, None; Q. Mak, None; L. S. Tam, None; J. F. Griffith, None.


**Abstract Number:** 2940

**Outcome of Power Doppler Ultrasound-Detected Residual Synovitis in Rheumatoid Arthritis Patients with Clinical Remission: A 1 Year Longitudinal Study with Consecutive Ultrasound Examinations**

Gaël Mouterde¹, Cédric Lukas², Nathalie Filippi¹, Gregory Marin³, Nicolas Molinari³, Jacques Morel¹ and Bernard Combe¹,
¹Rheumatology, Montpellier University, Lapeyronie Hospital, Montpellier, France, ²Rheumatology, Lapeyronie Hospital and EA2415 Montpellier University, Montpellier, France, ³Statistics, Montpellier University, Lapeyronie Hospital, Montpellier, France

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Wednesday, November 8, 2017

**Session Title:** Imaging of Rheumatic Diseases II: Focus on Rheumatoid Arthritis and Systemic Sclerosis

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 11:00AM-12:30PM

**Background/Purpose:** Some studies revealed an association of Power Doppler (PD) ultrasound (US)-detected residual synovitis (PDUSS) and risk of relapse and radiographic progression (RP), in rheumatoid arthritis (RA). However, the longitudinal relationship between clinical remission and repeated US residual lesions during follow-up is not so well-known.

**Objectives:** 1/ to determine the longitudinal relationship between clinical course and US findings in RA in remission; 2/ to evaluate the ability of PDUSS to predict relapse or RP at 1 year.

**Methods:** RA patients ≥18 years fulfilling 2010 ACR-EULAR criteria, treated with synthetic (cs) or biologic (b) DMARDs and in clinical remission (DAS28-ESR<2.6 and no clinically active synovitis) ≤6 months, were included in the longitudinal prospective SONORE study (ClinicalTrials.gov identifier: NCT02618954). Clinical and biological characteristics of patients were collected at baseline, and every 3 months (M) during 1 year. RA treatment had to be stable during follow-up. A standard US examination on 40 joints for the presence of synovial hypertrophy and PD signal was performed by an independent investigator blinded to clinical and radiographic data at each visit during 1 year. Presence of US synovitis was defined by a PD signal≥1 in ≥1 joint. Radiographs of hands, wrists and feet were scored at baseline and 1 year. Outcome measures: RP was defined by an increase ≥1 point of the modified total Sharp score. A relapse was defined by a DAS28≥3.2 at ≥1 follow-up visits AND a change of DMARDs, excluding change due to safety issues; or an increase in the DMARD or Corticosteroid (CS) dosage (≥5mg/d). Baseline variables, including PDUSS and its persistence during the follow-up, were assessed for their association with time to progression to relapse or RP using univariate then stepwise multivariate Cox regression analyses to obtain adjusted HRs.

**Results:** The 115 included patients had a mean (SD) age of 58.9 (±12.8) years, mean disease duration of 9.3 (±9.3) years, a mean duration of remission of 2.1 (±2.3) months. 74.8% were female, 79.1% were anti-CCP positive, 51.4% had erosive disease. The mean DAS28-ESR was 2.03 (±0.63). 79.5% received csDMARD, 63.3% bDMARD and 26.5% CS. PDUSS was detected in ≥1 joint in 75 patients (72.1%) at baseline, 60 at M3, 53 at M6, 40 at M9, 27 at M12. 41/75 (54.7%) had persistence of at least one PDUSS during the follow-up. 19 (17.1%) had a relapse (1 at M3, 6 at M6, 10 at M9, 2 at M12) and 12 (11.7%) had a RP at 1 year. In multivariate analysis, persistence of at least one PDUSS during the follow-up (HR= 5.24 [1.74-22.5], p=0.009) and baseline number of tender joints (HR=1.32 [0.95-1.68], p=0.052) were predictors of relapse or RP at 1 year. Duration of remission, other baseline US findings including baseline PDUSS, autoantibodies, and erosive disease had no additional predictive value.
Conclusion: PDUSS slowly decrease with time in RA patients in remission. Persistence of a PDUSS during the follow-up, rather than baseline PDUSS, predicts unfavorable outcome at 1 year. This suggests that initial US findings are not sufficient to justify therapeutic change, but that the persistence of a residual PDUSS requires careful follow-up, and might even potentially merit strategy adaptation.

Disclosure: G. Mouterde, None; C. Lukas, None; N. Filippi, None; G. Marin, None; N. Molinari, None; J. Morel, None; B. Combe, None.

Abstract Number: 2941

Effect of Achieving Sustained SDAI Remission on Erosion Repair in Patients with Early RA: A Prospective HR-pQCT Study

Jiang Yue1, James F Griffith2, Fan XIAO3, Ling Qin4 and Lai-Shan Tam5, 1Department of Medicine & Therapeutics, The Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong, Hong Kong, 2Department of Imaging and Interventional Radiology, The Prince of Wales Hospital, The Chinese University of Hong Kong, HONGKONG, Hong Kong, 3Department of Imaging and Interventional Radiology, The Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong, Hong Kong, 4Bone Quality and Health Centre of the Department of Orthopaedics and Traumatology, The Prince of Wales Hospital, The Chinese University of Hong Kong, hongkong, Hong Kong, 5Department of Medicine & Therapeutics, The Chinese University of Hong Kong, Hong Kong, Hong Kong

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Imaging of Rheumatic Diseases II: Focus on Rheumatoid Arthritis and Systemic Sclerosis
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose:
To assess whether achieving sustained SDAI remission in patients with early rheumatoid arthritis (ERA) facilitates repair of existing bone erosions as measured by high-resolution peripheral quantitative computed tomography (HR-pQCT).

Methods:
In this prospective study, 63 ERA patients were treated with a tight-control protocol aiming at remission using csDMARDs. HR-pQCT examinations were performed at baseline and one-year post-baseline. Changes in erosion size (maximal width, depth, volume) and density of the surrounding bone (marginal osteosclerosis) of erosion near the second metacarpal-phalangeal joint (MCP2) were quantified using HR-pQCT at baseline, 6 months and 12 months. Patients were sub-grouped according to whether or not they achieved sustained simplified disease activity score (SDAI) remission (SDAI< 3.3) at month 6, 9 and 12.

Results:
19 (31%) patients achieved (Group 1) and 44 (69%) patients did not achieve (Group 2) sustained SDAI remission. At baseline, no significant differences in erosion size and marginal osteosclerosis were present between the two groups. In group 1, significant reduction in erosion volume and increase in marginal osteosclerosis was observed between baseline and 12 months (Table 1). In contrast, erosion width significantly increased in group 2 at 6 and 12 months compared to baseline. At 12 months, change in erosion volume was significantly different between the two groups.

Conclusion:
In ERA patients who achieved sustained SDAI remission, HR-pQCT revealed a reduction in erosion volume and an increase in marginal osteosclerosis, indicating that partial erosion repair seems to be possible as long as effective reduction of inflammation is achieved.

Acknowledgement
We would like to acknowledge the Health and Medical Research Fund (HMRF) for funding support (HMRF Project No. 10110071).

Disclosure: 
J. Yue, None; J. F. Griffith, None; F. XIAO, None; L. Qin, None; L. S. Tam, None.

Abstract Number: 2942

One Year Changes in Ultrasound Findings in the Feet Are Associated with Patient Reported Outcomes but Not Clinical Examination: a Prospective Observational Study of Patients with Early Rheumatoid Arthritis

Hanyan Zou1, Karen A. Beattie2, George Ioannidis3 and Maggie Larche2, 1McMaster University, Hamilton, ON, Canada, 2Medicine, McMaster University, Hamilton, ON, Canada, 3St Joseph's Healthcare Hamilton, Hamilton, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Imaging of Rheumatic Diseases II: Focus on Rheumatoid Arthritis and Systemic Sclerosis
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose:
Despite extensive involvement of the feet in early RA, few studies report clinical and imaging changes in the feet over time. In this observational study, we aimed to 1) characterize 1-year changes in the feet using US, physical exam, and patient-reported outcomes; and 2) determine the associations between 1-year changes in these assessments.

Methods:
Patients with early RA (ACR criteria, DMARD naïve) were examined at baseline, 6 weeks, 3 months, 6 months, and 1 year. At each time point, the 2nd-5th MTP joints were examined by a rheumatologist [swollen joint count (SJC), tender joint count (TJC)], and imaged using US. Synovial thickening (ST) and power Doppler (PD) on US were graded semiquantitatively (0-3, max. score=24/patient for each). Patients also completed the Leeds Foot Impact Scale (LFIS) and Health Assessment Questionnaire (HAQ) at each visit.

Results:
Forty patients were enrolled [mean (SD) age=52.1(10.4) years, n=32 female]. Paired t-tests revealed significant 1-year improvements in inflammation on US (ST and PD), SJC and TJC, and patient-reported outcomes (Table 1). Over 1-year, ST scores improved in 30 patients and worsened in 7; PD scores improved in 16 patients and worsened in 5. Total ST and PD scores significantly correlated with each other at baseline (r=0.53, p<0.05) and 1-year (r=0.37, p<0.05); 1-year change scores were also correlated (r=0.42, p<0.05). Changes in PD scores, but not ST scores, significantly correlated with changes in LFIS and HAQ (Table 2). US findings did not significantly correlate with clinical exam at any time point or over 1-year. Associations between changes in SJC and TJC and patient reported outcomes are shown in Table 2.

Table 1: Mean scores of US, joint counts, and patient-report questionnaires at baseline and 1-year, and their respective paired t-test results.

<table>
<thead>
<tr>
<th></th>
<th>Baseline (Mean (SD))</th>
<th>One year (Mean (SD))</th>
<th>Paired Differences (Mean (SD))</th>
<th>t-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD</td>
<td>2.17 (4.11)</td>
<td>0.44 (1.05)</td>
<td>1.73 (4.01)</td>
<td><strong>t=2.76</strong></td>
</tr>
<tr>
<td>ST</td>
<td>9.07 (5.37)</td>
<td>5.12 (3.96)</td>
<td>3.95 (5.97)</td>
<td><em><strong>t=4.24</strong></em></td>
</tr>
<tr>
<td>SJC</td>
<td>1.27 (1.70)</td>
<td>0.61 (1.16)</td>
<td>0.66 (1.93)</td>
<td><em>t=2.18</em></td>
</tr>
<tr>
<td>TJC</td>
<td>3.98 (2.89)</td>
<td>2.93 (3.06)</td>
<td>1.05 (3.02)</td>
<td><em>t=2.23</em></td>
</tr>
<tr>
<td>LFIS</td>
<td>23.33 (14.00)</td>
<td>19.44 (13.33)</td>
<td>3.90 (9.87)</td>
<td><em>t=2.47</em></td>
</tr>
<tr>
<td>HAQ</td>
<td>1.12 (0.69)</td>
<td>0.72 (0.62)</td>
<td>0.40 (0.55)</td>
<td><em><strong>t=4.61</strong></em></td>
</tr>
</tbody>
</table>
Table 2: Correlations between 1 year change in US findings, joint counts, and patient-reported questionnaires, accounting for their respective baseline values as covariates.

<table>
<thead>
<tr>
<th>Standardized β</th>
<th>Change in LFIS</th>
<th>Change in HAQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in PD</td>
<td>0.42**</td>
<td>0.34*</td>
</tr>
<tr>
<td>Change in ST</td>
<td>0.19</td>
<td>0.25</td>
</tr>
<tr>
<td>Change in SJC</td>
<td>0.42**</td>
<td>0.20</td>
</tr>
<tr>
<td>Change in TJC</td>
<td>0.81</td>
<td>0.05</td>
</tr>
</tbody>
</table>

* p<0.05, ** p<0.01

**Conclusion:** Although all indicators of disease activity showed significant improvements after 1-year, only change in PD and change in SJC significantly correlated with change in patient-reported outcomes. Changes in ST may take longer to develop than 1-year, which may account for its insignificance. The lack of association between US and joint counts suggests that swelling and tenderness in the feet may be influenced by factors other than inflammation.

**Disclosure:** H. Zou, None; K. A. Beattie, None; G. Ioannidis, None; M. Larche, None.


**Abstract Number:** 2943

**Ultrasound Scoring of One Parotid and One Submandibular Gland in Primary Sjogren’s Syndrome – Further Increasing Feasibility in Outpatient Clinics**

**Esther Mossel**¹, Suzanne Arends², Jolien F. van Nimwegen², Konstantina Delli³, Alja J. Stel¹, Frans G.M. Kroese², Fred K.L. Spijkervet⁴, Arjan Vissink⁵ and Hendrika Bootsma², ¹Rheumatology and Clinical Immunology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, ²Rheumatology and Clinical Immunology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, ³Department of Oral and Maxillofacial Surgery, University of Groningen, University Medical Center Groningen, the Netherlands, Groningen, Netherlands, ⁴Oral and Maxillofacial Surgery, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, ⁵Department of Oral and Maxillofacial Surgery, University of Groningen, University Medical Center Groningen, Groningen, Netherlands

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Wednesday, November 8, 2017

**Session Title:** Imaging of Rheumatic Diseases II: Focus on Rheumatoid Arthritis and Systemic Sclerosis

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 11:00AM-12:30PM

**Background/Purpose:**

To assess whether ultrasonographic scoring of (i) both parotid and submandibular salivary glands and (ii) all components of the Hocevar scoring system¹, is needed for classifying patients as primary Sjögren’s syndrome (pSS).

**Methods:**

Ultrasound examination of the major salivary glands (sUS) was performed in 204 consecutive outpatients, diagnosed or clinically suspected with pSS.
Parenchymal echogenicity, homogeneity, hypoechoic areas, hyperechogenic reflections and salivary gland posterior border were scored in the right and left parotid and submandibular glands\textsuperscript{1}. Univariate and multivariate logistic regression analyses were performed to assess which salivary glands and sUS components significantly predicted classification as pSS or non-pSS according to the 2016 ACR-EULAR criteria\textsuperscript{2}.

**Results:**

116 (57\%) patients were classified as pSS, the remaining 88 (43\%) patients as non-pSS. The correlation between the sUS scores of both parotid glands ($\rho$=0.909), both submandibular glands ($\rho$=0.868) and between the left and right glands ($\rho$=0.926) was excellent. The correlation between the sUS scores of the left parotid and left submandibular gland ($\rho$=0.731) and between the right parotid and right submandibular gland ($\rho$=0.734) was slightly lower.

Multivariate analysis showed that sUS scores of one parotid gland and one submandibular gland contributed independently to ACR-EULAR classification. Instead of scoring both sides (area under the curve, AUC=0.856; Nagelkerke $R^2=0.527$), sUS scoring of only the right (AUC=0.850; $R^2=0.518$) or left (AUC=0.852; $R^2=0.511$) parotid and submandibular glands is enough to significantly predict classification of patients according to the ACR-EULAR criteria.

In univariate analysis, all individual components of the Hocevar scoring system significantly predicted ACR-EULAR classification. Hypoechogenic areas showed the highest explained variance ($R^2=0.508$). Multivariate analysis showed that only parenchymal echogenicity and hypoechogenic areas independently predicted ACR-EULAR classification (AUC=0.857; $R^2=0.539$). Taking only the sUS scores of the right glands into account, multivariate analysis showed that only parenchymal echogenicity and hypoechogenic areas contributed independently to ACR-EULAR classification (AUC=0.855; $R^2=0.539$). However, when scoring only hypoechoic areas on one side, results were comparable (AUC=0.846; $R^2=0.498$). Similar results were found when the analyses were repeated for the left glands.

**Conclusion:**

sUS examination of a parotid and submandibular gland on one side is enough to predict classification of patients according to the ACR-EULAR criteria.

Presence of hypoechoic areas is the best predictor of ACR-EULAR classification. Although parenchymal echogenicity also independently predicted ACR-EULAR classification, its reliability is limited.\textsuperscript{3} Therefore, we conclude that sUS scoring of only hypoechoic areas in one parotid and submandibular gland is enough to predict ACR-EULAR classification. These finding may increase the feasibility of sUS in outpatients clinics worldwide.

**References:**

1 Hocevar et al. Rheumatology 2005.

**Disclosure:** E. Mossel, None; S. Arends, None; J. F. van Nimwegen, None; K. Delli, None; A. J. Stel, None; F. G. M. Kroese, None; F. K. L. Spijkervet, None; A. Vissink, None; H. Bootsma, None.


**Abstract Number:** 2944

### Patterns and Characteristics of Accelerated Hand Osteoarthritis: Data from the Osteoarthritis Initiative

**Julie Davis\textsuperscript{1}, Lena Franziska Schaefer\textsuperscript{2}, Timothy E. McAlindon\textsuperscript{3}, Charles B. Eaton\textsuperscript{4}, Mary Roberts\textsuperscript{5}, Ida K. Haugen\textsuperscript{6}, Stacy Smith\textsuperscript{7}, Jeffrey Duryea\textsuperscript{2}, Bing Lu\textsuperscript{8} and Jeffrey B. Driban\textsuperscript{1}, 1Rheumatology, Tufts Medical Center, Boston, MA, 2Radiology, Brigham & Women's Hospital/ Harvard Medical School, Boston, MA, 3Division of Rheumatology, Tufts Medical Center, Boston, MA, 4Family Medicine and Community Health( Epidemiology), Alpert Medical School of Brown University, Pawtucket, RI, 5Center for Primary Care and Prevention, Memorial Hospital of Rhode Island, Pawtucket, RI, 6Diakonhjemmet Hospital, Oslo, Norway,
Background/Purpose: Epidemiology for hand osteoarthritis (OA) incidence is lacking and few large cohorts have sufficient size to explore subsets. We previously characterized a subset of adults who develop an accelerated form of knee OA, in which they progress from normal radiographic appearance to advance-stage disease within 4 years and often in < 12 months. It is unknown whether such a novel subset exists among adults with hand OA. We aimed to characterize individuals who develop accelerated hand OA (AHOA) and compare them to those who do not.

Methods: We evaluated 3489 participants in the Osteoarthritis Initiative (OAI) with complete data for baseline and 48-month radiographic hand OA. One reader scored posteroanterior radiographs of the dominant hand using a modified Kellgren-Lawrence (KL) scale (weighted kappa > 0.84) and another reader scored the presence of central or marginal erosions (kappa > 0.79). We defined hand OA as a hand with at least 1 joint with KL grade ≥ 2 on at least 2 fingers (digits 2 to 5). We defined AHOA as a hand with at least 1 joint that progressed from a KL grade of 0 or 1 at baseline to KL 3 or 4 at 48 months. We ran descriptive statistics to characterize AHOA.

Results: The overall rate of AHOA was 1.12% over 4 years, with 38 hands having 1 joint affected and 1 hand with 2 joints affected. At baseline, adults who developed AHOA were more likely to have radiographic hand OA (69% vs 36%), central erosions (21% vs 7%), and marginal erosions (8% vs 2%) in other joints compared to those who did not develop AHOA (see Table). Only 1 joint that developed accelerated OA had an erosion (marginal) at baseline. Adults with AHOA were more likely to develop new erosions in either the same or any other joint over 48 months (central n = 13, 34%; marginal n = 3, 8%) than those who did not develop AHOA (central n = 162, 5%; marginal n = 51, 1%). Eight (21%) people who developed AHOA had an incident erosion in the same joint that worsened. Only 1 person (3%) with AHOA had a fracture during the observation period, compared to 48 people (2%) with fractures in the control group. The most common locations of accelerated OA were the thumb and second digit (Figure 1).

Conclusion: Adults who developed AHOA were more likely to have erosive hand OA than those without AHOA, confirming that erosive hand OA is a more rapid progressing phenotype. Furthermore, the majority of those who developed AHOA were affected at the second metacarpophalangeal joint (28%) or the first carpometacarpal joint (26%). This suggests the digits commonly used for pinching and fine motor skills are particularly susceptible to accelerated OA compared to other digits.
Table 1. Baseline Characteristics of Adults Who Develop Accelerated Hand Osteoarthritis (OA)

<table>
<thead>
<tr>
<th></th>
<th>No Accelerated OA</th>
<th>Accelerated OA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 3489</td>
<td>n = 39</td>
</tr>
<tr>
<td></td>
<td>mean (SD) or n (%)</td>
<td>mean (SD) or n (%)</td>
</tr>
<tr>
<td>Female n (%)</td>
<td>2020 (58%)</td>
<td>24 (62%)</td>
</tr>
<tr>
<td>Pre-menopause n (%)</td>
<td>295 (15%)</td>
<td>3 (13%)</td>
</tr>
<tr>
<td>Peri-menopause n (%)</td>
<td>291 (14%)</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>Post-menopause n (%)</td>
<td>1423 (71%)</td>
<td>19 (79%)</td>
</tr>
<tr>
<td>Physician Diagnosed Hand OA n (%)</td>
<td>581 (17%)</td>
<td>6 (15%)</td>
</tr>
<tr>
<td>Prevalent Hand Pain n (%)</td>
<td>835 (24%)</td>
<td>6 (15%)</td>
</tr>
<tr>
<td>Radiographic Hand OA n (%)</td>
<td>1246 (36%)</td>
<td>27 (69%)</td>
</tr>
<tr>
<td>Central Erosions (≥ 1 joint) n (%)</td>
<td>239 (7%)</td>
<td>8 (21%)</td>
</tr>
<tr>
<td>Marginal Erosions (≥ 1 joint) n (%)</td>
<td>84 (2%)</td>
<td>4 (11%)*</td>
</tr>
<tr>
<td>Metabolic Syndrome (2-4 components) n (%)</td>
<td>1933 (58%)</td>
<td>26 (67%)</td>
</tr>
<tr>
<td>Self-Reported Diabetes n (%)</td>
<td>268 (8%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Use of Lipid Medications n (%)</td>
<td>988 (28%)</td>
<td>7 (18%)</td>
</tr>
<tr>
<td>High Blood Pressure n (%)</td>
<td>2110 (60%)</td>
<td>28 (72%)</td>
</tr>
<tr>
<td>Large Waist Circumference n (%)</td>
<td>2553 (74%)</td>
<td>31 (79%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>60.9 (9.2)</td>
<td>60.6 (9.1)</td>
</tr>
<tr>
<td>Body Mass Index (kg/m²)</td>
<td>28.7 (4.8)</td>
<td>29.1 (5.0)</td>
</tr>
<tr>
<td>Body Weight (kg)</td>
<td>81.6 (16.4)</td>
<td>81.2 (15.7)</td>
</tr>
</tbody>
</table>

Notes on missing data: Only included people with body weight, and status of self-reported hand pain (yes or no) and physician diagnosed hand OA (yes and no or unknown) at baseline. Missing data: Less than 3% missing data for menopause status, central erosions, marginal erosions, diabetes status, and waist circumference. Metabolic syndrome (n missing = 137 controls). No other missing data. * 1 marginal erosion occurred in the same joint that developed accelerated hand osteoarthritis and 3 had marginal erosions in a different joint.

Figure 1. Patterns of Accelerated Hand Osteoarthritis by Location

Disclosure: J. Davis, None; L. F. Schaefer, None; T. E. McAlindon, None; C. B. Eaton, None; M. Roberts, None; I. K. Haugen, None; S. Smith, None; J. Duryea, None; B. Lu, None; J. B. Driban, NIAMS-NIH, 2, AXSOME Therapeutics, Inc., 5.


Abstract Number: 2945

Incident Hand OA Is Strongly Associated with Reduced Peripheral Blood Leukocyte Telomere Length

Timothy E. McAlindon¹, Mary Roberts², Lena Franziska Schaefer³, Jeffrey B. Driban⁴, Jeffrey Duryea³, Francisco J Blanco⁵, Jose-Luis Fernandez-Garcia⁶ and Charles Eaton⁷, ¹Division of Rheumatology, Tufts Medical Center, Boston, MA, ²Center for Primary Care
SESSION INFORMATION

Session Date: Wednesday, November 8, 2017
Session Title: Osteoarthritis – Clinical Aspects II: Structural Progression and Incidence
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose: Hand OA (HOA) is a painful, destructive and deforming polyarticular disorder that impairs an individual’s ability to perform manipulative activities of daily life and has a strong association with increasing age. Telomeres are specialized chromatin structures at the end of linear eukaryotic chromosomes that perform a capping function, protecting chromosomes from degradation, recombination, and fusion between chromosomes. After each round of DNA replication there is a progressive loss of terminal telomere sequences, so telomeres progressively shorten with ageing in replicating somatic cells. There is also evidence that telomeric structure may be damaged as a result of oxidative stress. Ultimately, the telomeric sequence array may become critically shortened and trigger replicative senescence or apoptosis, contributing to processes related to aging. Peripheral blood leukocyte (PBL) telomere length is a biomarker for biological age and longevity. Data from cross-sectional studies are conflicting on whether telomere length is shorter in subjects with OA.

Methods: This used a convenience sample of Caucasian participants in the Osteoarthritis Initiative who had right hand x-rays at 0 and month 48; and PBL telomere length measured at baseline using real-time quantitative PCR. We defined interphalangeal OA (IPOA) as KL ≥2 in a finger or thumb joint (excluding thumb-base); and incidence if KL score increased from ≤1 to ≥2. We defined symptomatic IPOA as KL≥2 in ≥1 joint on 2 different fingers and report of hand pain (“During the past 30 days, pain, aching or stiffness on most days”) after baseline. We analyzed the standardized log of telomere length as a predictor for OA incidence at a joint level and across all joints using generalized linear mixed models to control for confounders and account for within-person correlation among joints.

Results: 275 participants were eligible for the analysis (mean baseline age 59.1y [s.d.8.7], 56.7% female, BMI 27.4 Kgm⁻²[4.4], 39 [14.2%] physician-diagnosed hand OA). 494 joints had OA at baseline and 47 developed incident IPOA. Prevalent IPOA at baseline was cross-sectionally associated with older age (OR=2.2; 95% CI 1.8, 2.6) and shorter telomere length (OR=1.3; 1.1, 1.6) but not with gender or BMI (all mutually adjusted). In prospective analyses with adjustment for age, BMI and gender, shorter telomere length predicted IPOA incidence in a joint (OR=1.5, 1.07, 2.1 -i.e. for every s.d. decrease in log of telomere length there is 50% increase in the likelihood of OA incidence); and the increase in number of affected joints (β=0.06, p=0.02), as well as incidence of symptomatic IPOA (OR=1.7, 1.1, 2.7). This association was consistent in the smaller subset without HOA at baseline (OR=1.7, 0.99, 2.8).

Conclusion: Shorter PBL telomere length is strongly and independently associated with prevalent and incident OA in finger joints and development of symptomatic IPOA. This may indicate an accelerated ageing phenotype associated with impaired chondrocyte function and capacity of cartilage and joint structures to maintain health and respond to biomechanical and inflammatory/metabolic stressors, leading to OA.

Disclosure: T. E. McAlindon, None; M. Roberts, None; L. F. Schaefer, None; J. B. Driban, NIAMS-NIH, 2,AXSOME Therapeutics, Inc., 5; J. Duryea, None; F. J. Blanco, Pfizer Inc, 5; J. L. Fernandez-Garcia, None; C. Eaton, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/incident-hand-oa-is-strongly-associated-with-reduced-peripheral-blood-leukocyte-telomere-length

Abstract Number: 2946

Identifying Rapid Structural Disease Progression in Knee Osteoarthritis

Jamie E. Collins¹², Jeffrey N. Katz²³ and Elena Losina¹², ¹Orthopaedic and Arthritis Center for Outcomes Research, Department of Orthopedic Surgery, Brigham & Women's Hospital, Boston, MA, 2Harvard Medical School, Boston, MA, 3Rheumatology, Immunology, and Allergy, Brigham & Women's Hospital, Boston, MA

First publication: September 18, 2017
Background/Purpose: Knee OA is a heterogeneous disease, with some patients experiencing rapid deterioration and others experiencing slow disease progression. Identifying patients likely to experience rapid disease worsening is a top research priority; this would allow better recruitment strategies for clinical trials, optimizing the execution of trials focused on disease modifying drugs, and would help physicians make better treatment decisions.

Methods: We used data from the Osteoarthritis Initiative (OAI), a multicenter, longitudinal, observational study of knee OA. We selected patients with baseline (BL) Kellgren-Lawrence (KL) grade 1 - 3, with knee pain, and with joint space width (JSW) assessed at BL and ≥1 follow-up. Medial minimum JSW was assessed with a fixed-flexion knee radiograph annually through year 4; total follow-up was 9 years. We used latent class growth analysis (LCGA) to identify distinct subgroups of JSW progression. LCGA allows for the modeling of distinct subgroups based on longitudinal trajectory. We included random effects for intercept and slope to allow for within-subject variability. After identifying the number of trajectories, we used logistic regression to assess the association between BL characteristics and JSW trajectory group.

Results: We used data from 1,755 OAI study participants. BL radiographic severity was KL1 in 16%, KL2 in 52%, and KL3 in 32%. The mean (SD) JSW was 4.0mm (1.3) and the range was 0.7 – 8.5mm. LCGA identified 2 distinct JSW trajectories [Figure]. The majority of patients (90%) had stable JSW over 4 years of follow-up (Non-progressor group) with a mean (SD) JSW of 4.1 (1.2) at BL and 3.9 (1.4) at 4 year follow-up, for a yearly decrease of 0.05mm. A subgroup of patients experienced rapid disease progression (Progressor group), with a BL mean (SD) JSW of 3.8 (1.5) and a 4 year follow-up JSW of 1.7 (1.3), for a yearly decrease of 0.53mm. 5% of the Non-progressors went on to have total knee replacement between years 5 and 9, compared to 23% of the Progressors. BL KL, obesity, and alignment were associated with progression group: in a multivariable model, the odds of being a Progressor were 2.4 (95% CI: 1.4, 3.9) times higher for participants with KL 3 vs. KL 1; 1.6 (1.1, 2.1) times higher for obese participants vs. non-obese, and 1.2 (0.8, 1.8) times higher for those with varus alignment vs. neutral. 30% of the cohort had 0 risk factors, 6% were Progressors; 43% had 1 risk factor, 10% were Progressors; 23% had 2 risk factors, 15% were Progressors; 5% had 3 risk factors, 26% were Progressors.

Conclusion: We found a subgroup of patients experiencing rapid structural progression in JSW. These patents may be appropriate candidates for clinical trials of disease modifying drugs. A strategy that required 2 or 3 risk factors for inclusion into a trial could enrich the cohort for progressors by two-fold compared to a strategy of enrolling non-selectively.

Disclosure: J. E. Collins, None; J. N. Katz, None; E. Losina, None.
Do Bone Marrow Lesions Reactivate Endochondral Ossification Leading to Osteophyte Genesis? Data from the Osteoarthritis Initiative

Leticia Deveza1, Laurence Teoh2, Elena Ochoa-Albiztegui3, Ali Guermazi4, Frank Roemer4,5 and David Hunter1, 1Rheumatology, Institute of Bone and Joint Research, Kolling Institute, University of Sydney, Sydney, Australia, 2Department of General Medicine, Middlemore Hospital, Auckland, New Zealand, Auckland, New Zealand, 3Department of Radiology, Memorial Sloan Kettering Cancer Center, New York, NY, USA, New York, NY, 4Department of Radiology, Boston University School of Medicine, Boston, MA, USA, Boston, MA, 5Department of Radiology, University of Erlangen-Nuremberg, Erlangen, Germany, Erlangen, Germany

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Osteoarthritis – Clinical Aspects II: Structural Progression and Incidence
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose: Osteophytes are formed through reactivation of endochondral ossification. In adults, reactivation of endochondral ossification may occur in the context of fracture repair. As yet, the rationale for the genesis of osteophytes in osteoarthritis (OA) remains unclear. We investigated whether bone marrow lesions (BMLs) (representing subchondral remodeling due to increased loading) and inflammation (assessed as effusion-synovitis on non-contrast-enhanced MRI) were associated with the presence and progression of osteophytes in OA knees.

Methods: We analyzed data from 600 participants included in the FNIH Biomarkers study within the Osteoarthritis Initiative. Osteophytes and BMLs were scored according to size (0-3) on MRI in the medial and lateral femur and tibia, and effusion-synovitis was scored in the whole knee according to severity (0-3, where 0 means absent) using the MRI OA Knee Score (MOAKS). BMLs and effusion-synovitis were considered present when a score ≥ 1 for each feature was given. Osteophyte severity was categorized into grades 0 (absent), 1 (small) and 2-3 (medium to large). We examined the cross-sectional and longitudinal relation between the baseline presence of BMLs and effusion-synovitis to osteophyte severity and progression (increase in size in ≥ 1 grade) in each joint compartment on MRI over 24 months. Ordinal regression was used for the cross-sectional analysis and binary logistic regression for the longitudinal analysis adjusted for covariates. We assessed the interaction effect between BMLs and knee alignment, measured by goniometer on physical examination (neutral, varus or valgus), using interaction terms.

Results: At baseline, BMLs were present in 10.8% to 53.3% depending on the knee compartment and effusion-synovitis was present in 61% of the knees. Presence of BMLs was strongly associated with baseline osteophytes in all four knee compartments (Table), with odds ratios (OR) ranging from 1.63 (95% confidence interval [CI] 1.15, 2.30) in the medial femur to 7.13 (4.92, 10.93) in the lateral femur. Presence of effusion-synovitis was also associated with osteophytes, except in the medial tibia. At baseline, the interaction analysis showed no effect of alignment in the association between BMLs and osteophytes. Over 24 months, osteophyte progression mostly occurred in the medial tibia (7.3%) and was strongly associated with the presence of baseline BMLs in the same joint compartment (OR 3.89 [1.84, 8.23]). Baseline effusion-synovitis was also associated with an increase in osteophyte size in the medial femur and tibia.

Conclusion: Bone marrow lesions were strongly associated with the presence of osteophytes and with osteophyte progression on MRI over 24 months. Although inflammation may also play a role in the development of osteophytes, BMLs appear to be more strongly related to the reactivation of endochondral ossification process.
Distinct Trajectories of Medial Fixed Joint Space Width Loss over Four Years of Follow-up Among Knees with and at Risk for Knee Osteoarthritis

C. Kent Kwoh1,2, Di Ran2,3, Erin L. Ashbeck2 and Jeffrey Duryea4, 1Division of Rheumatology, Department of Medicine, The University of Arizona, Tucson, AZ, 2The University of Arizona Arthritis Center, Tucson, AZ, 3Department of Epidemiology and Biostatistics, Mel and Enid Zuckerman College of Public Health, Tucson, AZ, 4Radiology, Brigham & Women's Hospital/ Harvard Medical School, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Osteoarthritis – Clinical Aspects II: Structural Progression and Incidence
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose: Knee OA (KOA) is typically described as a slowly progressive disease, though it is recognized that some patients experience rapid structural deterioration. Identification of knees at risk for rapid structural deterioration would be useful for recruitment to randomized controlled trials (RCTs) and observational studies of KOA. Our objectives were to identify distinct trajectories of medial fixed joint space width (fJSW) loss and estimate the expected percentage of knees in each trajectory based on two measures of KOA severity, Kellgren-Lawrence grade (KLG) and knee pain.

Methods: Osteoarthritis Initiative participants with baseline radiographs centrally read as KLG 0-3, measured medial fJSW (location x=0.250), and participant-reported knee pain severity in the past 30 days based on a numerical rating scale (NRS; 0-10) were selected. One knee per participant was randomly selected when two knees were available, providing a sample size of 3,163 knees. Distinct trajectories of medial fJSW loss over 4 years of follow-up were identified using a group-based discrete mixture model for clustering of longitudinal data. Predicted probability of loss trajectories based on combinations of baseline KLG and NRS were generated with multinomial logistic regression, with NRS categorized as 0, 1-3, and 4-10.

Results: Three distinct trajectories of medial fJSW loss were identified (Figure 1), including knees that remained stable over 4 years (2,030; 64.2%, mean posterior probability of group membership 0.92); knees that experienced slow loss (960; 30.4%, mean probability 0.88); and knees with fast radiographic worsening (173; 5.5%, mean probability 0.94). Among KLG 2 knees, the proportion that experienced slow progression was 28.6-31.8%, while 3.3-7.3% of knees underwent fast progression, depending on the baseline NRS (Figure 2). Among KLG 3 knees, 42.1-49.0% had slow progression, while 6.8-13.0% underwent fast progression. The combination of KLG 3 and knee pain severity 4-10 yielded the highest estimated proportion of knees that experienced subsequent fast progression.
Conclusion: Three distinct trajectories of medial fJSW loss, representing stable, slow, and fast loss of joint space, were identified across the spectrum of KOA disease severity. Recruitment based on KLG and knee pain severity enriches the proportion of expected progressors, both slow and fast, though fast progressors are still not highly represented. Additional risk factors are needed to enrich studies for participants at high risk of rapid structural deterioration.

Disclosure: C. K. Kwoh, EMD Serono, 2, Abbvie, 2; D. Ran, None; E. L. Ashbeck, None; J. Duryea, BICL, LLC, 5.
The Relation of Cumulative Load to Prevalent Cartilage Damage in the Knee

Dana Mathews1, Tuhina Neogi2, Joshua Stefanik2, Ali Guermazi3, Frank Roemer3, Louise Thoma4, Hiral Master4, Meredith Christiansen4, Cora E. Lewis5, Michael C. Nevitt6, James Torner7 and Daniel White8, 1Physical Therapy, Biomechanics and Movement Science, University of Delaware, Newark, DE, 2Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA, 3Department of Radiology, Boston University School of Medicine, Boston, MA, USA, Boston, MA, 4Physical Therapy and Biomechanics and Movement Science, University of Delaware, Newark, DE, 5University of Alabama Birmingham, Birmingham, AL, 6Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, CA, 7University of Iowa, Iowa City, IA, 8Department of Physical Therapy, University of Delaware, Newark, DE

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Osteoarthritis – Clinical Aspects II: Structural Progression and Incidence
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose: Cartilage damage, which is a precursor and feature of knee osteoarthritis (OA), has been linked to both obesity and excessive joint loading. Assessment of the combined effect of obesity and repetitive joint load as experienced during daily walking to represent cumulative load may provide additional insights into the risk for cartilage pathology in OA. The purpose of our study was to examine the relation of cumulative load to prevalent cartilage damage in the tibiofemoral (TF) and patellofemoral (PF) joints in people with or at high risk of knee OA.

Methods: Data from the 60-month visit of the Multicenter Osteoarthritis (MOST) Study, a NIH-funded longitudinal cohort of persons with or at risk of knee OA, was used for this study. Subjects had accelerometry data over 7 days (StepWatch Activity Monitor, Orthocare Innovations) and knee MRIs (1.0T, OrthOne) obtained at this visit. The primary exposure of interest was categories of cumulative load, defined using BMI and objectively measured physical activity (i.e. average steps/day). We categorized participants as Non-obese (BMI<30 kg/m²) or Obese (BMI³30 kg/m²), and then into tertiles of daily walking as High, Middle, and Low steps/day. Cartilage morphology was scored in 14 subregions (10 TF, 4 PF) using the Whole Organ Magnetic Resonance Imaging Score (WORMS). We examined the relation of cumulative load to the presence of cartilage damage, defined as any WORMS score ≥2, using logistic regression with generalized estimating equations (GEE) to account for the correlation between subregions within a knee. Analyses were adjusted for age, sex, and frontal plane knee alignment.

Results: We included 987 MOST subjects (62% women, age 66.9 ± 7.5 years, BMI 29.7 ± 4.8) that contributed 9610 TF observations and 3734 PF observations. The prevalence of TF cartilage damage was 27% (2619/9610 subregions) and 48% (1791/3734 subregions) for PF cartilage damage. Cumulative load was not associated with TF cartilage damage (see Figure 1). In the PF joint, there was a higher likelihood of prevalent PF cartilage damage for those in the Obese-High 1.3(0.99-1.7), Obese-Low 1.6(1.2-2.2), and Non-obese-Low 1.5(1.1-1.9) groups compared with the reference (Non-obese, High steps/day) group (see Figure 2).

Conclusion: Greater cumulative load may be associated with prevalent cartilage damage in the PF, but not TF joint. Insufficient cumulative load (i.e. low steps/day) may also be associated with prevalent PF cartilage damage. These preliminary findings support the need to encourage weight loss for people who are obese and at risk of knee OA in addition to an active lifestyle.
**Validation of a Definition for Flare in Patients with Established Gout**

**Angelo L. Gaffo**<sup>1</sup>, Nicola Dalbeth<sup>2</sup>, Kenneth Saag<sup>3</sup>, Jasvinder A. Singh<sup>4</sup>, Elizabeth J. Rahn<sup>1</sup>, Amy S. Mudano<sup>5</sup>, Yi-Hsing Chen<sup>6</sup>, Ching-Tai Lin<sup>7</sup>, Sandra Bourke<sup>2</sup>, Worawit Louthrenoo<sup>8</sup>, Janitzia Vazquez-Mellado<sup>9</sup>, Hansel Hernández-Llinas<sup>10</sup>, Tuhina Neogi<sup>11</sup>, Ana Beatriz Vargas-Santos<sup>12</sup>, Geraldo Castelar-Pinheiro<sup>13</sup>, Rodrigo B. Chaves-Amorim<sup>13</sup>, Till Uhlig<sup>14</sup>, Hilde B Hammer<sup>14</sup>, Maxim Eliseev<sup>15</sup>, Fernando Perez-Ruiz<sup>16</sup>, Lorenzo Cavagna<sup>17</sup>, Geraldine M. McCarthy<sup>18</sup>, Lisa K. Stamp<sup>19</sup>, Martijn Gerritsen<sup>20</sup>, Viktoria Fana<sup>21</sup>, Francisca Sivera<sup>22</sup> and William J. Taylor<sup>23</sup>, 1Department of Medicine, Division of Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 2University of Auckland, Auckland, New Zealand, 3Division Clinical Immunology & Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 4Rheumatology, University of Alabama at Birmingham, Birmingham, AL, 5University of Alabama at Birmingham, Birmingham, AL, 6Taichung Veterans General Hospital, Taichung, Taiwan, 7Division of Allergy, Immunology and Rheumatology, Taichung Veterans General Hospital, Taichung, Taiwan, 8Div of Rheumatology, Dept of Internal Medicine, Chiang Mai University, Chiang Mai, Thailand, 9Rheumatology, Hospital General de Mexico, Mexico City, Mexico, 10Hospital General de Mexico, Mexico City, Mexico, 11Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA, 12Internal Medicine Department, Division of Rheumatology, Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil, 13Universidade do Estado do Rio de Janeiro - UERJ, Rio de Janeiro, Brazil, 14Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, 15V. A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation, 16Servicio de Reumatología, Vizcaya, Spain, 17Division of Rheumatology, University and IRCCS Policlinico S. Matteo Foundation, Pavia, Italy, 18Div of Rheumatology, Mater Misericordiae University Hospital, Dublin, Ireland, 19University of Otago, Christchurch, New Zealand, 20Westfries Gasthuis, Hoorn, Netherlands, 21Center for Rheumatology and Spine Diseases, Rigshospitalet , Glostrup, Copenhagen Center for Arthritis Research (COPECARE), Copenhagen, Denmark, 22Sección de Reumatología, Hospital General Universitario de Elda., Elda, Spain, 23University of Otago, Wellington, New Zealand

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Wednesday, November 8, 2017

**Session Title:** Patient Outcomes, Preferences, and Attitudes III

**Session Type:** ACR Concurrent Abstract Session
Background/Purpose: A standardized validated definition for gout flares (or attacks) is not available. Two provisional definitions published in 2012 were based on patient-reported elements (patient-defined attack, pain at rest greater than 3 in a 0-10 numeric rating scale, presence of at least one swollen joint, presence of at least one warm joint). These definitions had acceptable sensitivity and specificity but lacked external validation which would facilitate its adoption in gout clinical studies. Our objective was to perform external validation of previously published preliminary gout flare definitions in patients with gout.

Methods: We enrolled 509 participants with gout from 17 international sites in a cross-sectional study performed during routine clinical care. All patients met the 2015 ACR/EULAR classification criteria for gout. Criteria from the previously published gout flare definitions were collected by a site investigator and the final adjudication of a gout flare status was done by a local expert rheumatologist, through an evaluation independent from that of the site investigator. Logistic regression, Bayesian statistics, and receiver-operator curves were used to calculate the final diagnostic performance of the gout attack definitions which were based on number of criteria and a classification and regression tree (CART) approaches.

Results: The mean age of participants was 57.5 years (standard deviation [SD] 13.9) and 89% were men. Mean disease duration was 12.3 (SD 10.3) years, 35.4% had tophi, and 75% were taking urate-lowering therapies. The previously published and favored number of criteria definition requiring the presence of 3 or more out of 4 criteria was found, using the current study data, to be 85% sensitive and 95% specific in confirming the presence of flare in patients with gout (Table). The concurrent logistic regression model had an area under the curve of 0.97. The previously published definition based on a CART algorithm (entry point pain at rest > 3 followed by patient-defined attack “yes”) was 73% sensitive and 96% specific using the current study data (Table). The number of criteria approach with a cut-point at 3 or more out of 4 criteria had higher diagnostic accuracy using the current study data than in its initial 2012 description (92% versus 84%). Finally, using current study data the number of criteria approach at 3 or more out of 4 criteria had higher accuracy to the CART algorithm based approach (92% versus 89%) but with a much better sensitivity (85% versus 73%).

Conclusion: The definition requiring the presence of 3 or more out of 4 patient-reported criteria is validated to be sensitive, specific, and accurate in identifying flares in patients with gout using an independent large international sample. Having a validated gout flare definition will improve ascertainment of outcomes in gout clinical studies.

Table. Diagnostic performance of gout attack (flare) definitions: *number of criteria* and classification and regression tree (CART)

<table>
<thead>
<tr>
<th>Number of criteria</th>
<th>Patients with gout flare (n=157)</th>
<th>Patients without gout flare (n=382)</th>
<th>Sensitivity% (95% CI)</th>
<th>Specificity% (95% CI)</th>
<th>PPV% (95% CI)</th>
<th>NPV% (95% CI)</th>
<th>Accuracy% (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 or more</td>
<td>157</td>
<td>119</td>
<td>100 (96.1-100)</td>
<td>66 (61.7-71)</td>
<td>57 (51.6-63)</td>
<td>100 (100)</td>
<td>77 (72.8-80)</td>
</tr>
<tr>
<td>2 or more</td>
<td>152</td>
<td>43</td>
<td>97 (93.9-99)</td>
<td>88 (84.9-91)</td>
<td>78 (73.8-83)</td>
<td>98 (96.9-99)</td>
<td>91 (88-93)</td>
</tr>
<tr>
<td>3 or more</td>
<td>134</td>
<td>18</td>
<td>85 (79-90)</td>
<td>95 (92.9-97)</td>
<td>88 (83.9-93)</td>
<td>94 (91.9-96)</td>
<td>92 (89-94)</td>
</tr>
<tr>
<td>All 4</td>
<td>96</td>
<td>6</td>
<td>61 (55-69)</td>
<td>98 (96.9-99)</td>
<td>94 (93.9-97)</td>
<td>85 (82.8-87)</td>
<td>87 (84-90)</td>
</tr>
<tr>
<td>CART†</td>
<td>114</td>
<td>13</td>
<td>73 (65-79)</td>
<td>96 (94-98)</td>
<td>90 (86-94)</td>
<td>89 (86-92)</td>
<td>89 (86-92)</td>
</tr>
</tbody>
</table>

CI = confidence interval, PPV = positive predictive value, NPV = negative predictive value, CART = classification and regression tree

*Criteria include: patient-defined gout flare, pain at rest > 3 on a 0-10 numeric rating scale, presence of at least one swollen joint, presence of at least one warm joint
†CART rule: Pain at rest > 3 followed by patient-defined gout flare positive

Disclosure: A. L. Gaffo, SOBI, 5, Amgen, 2; N. Dalbeth, AstraZeneca, 2, Takeda, Pfizer, AstraZeneca, Cymbay, Crealta, 5, Takeda, AstraZeneca, 9; K. Saag, AstraZeneca, Horizon, Ironwood, SOBI, Takeda, 5; J. A. Singh, Takeda, Savient, 2, Savient, Takeda, Regenon, Merz, Bioiberica, Crealta, Allergan, WebMD, UBM LLC, American College of Rheumatology, 5; E. J. Rahn, None; A. S. Mudano, None; Y. H. Chen, None; C. T. Lin, None; S. Bourke, None; W. Louthrenoo, None; J. Vazquez-Mellado, None; H. Hernández-Llinas, None; T. Neogi, None; A. B. Vargas-Santos, None; G. Castela-Pinheiro, None; R. B. Chaves-Amorim, None; T. Uhlig, None; H. B. Hammer, None; M. Eliseev, None; F. Perez-Ruiz, Ardea Biosciences, AstraZeneca, Cymbay, Grunenthal, Menarini, 5; L. Cavagna, None; G. M. McCarthy, None; L. K. Stamp, None; M. Gerritsen, None; V. Fana, None; F. Sivera, AstraZeneca, 5; W. J. Taylor, AstraZeneca, Pfizer, Abbvie, Roche, 5.

Responsiveness of the Patient Reported Outcomes Measurement Information System to Golimumab Intravenous and Infliximab Treatment in a Real World Clinical Trial in Rheumatoid Arthritis Patients

Jeffrey R. Curtis¹, Douglas Conaway², Jay Schechtman³, Aaron Broadwell⁴, Alan J. Kivitz⁵, Vance Bray⁶, Shelly Kafka⁷, Dennis Parenti⁷, Shawn Black⁷, Stephen Xu⁸, Wayne Langhoff⁹ and Clifton O. Bingham III⁹, ¹Rheumatology & Immunology, University of Alabama at Birmingham, Birmingham, AL, ²Rheumatology/Medicine, Carolina Health Specialists, Myrtle Beach, SC, ³Sun Valley Arthritis Center LTD, Peoria, AZ, ⁴Rheumatology Osteoporosis Specialists, Shreveport, LA, ⁵Altoona Arthritis & Osteoporosis Center, Altoona, PA, ⁶Denver Arthritis Clinic, Denver, CO, ⁷Janssen Scientific Affairs, LLC, Horsham, PA, ⁸Janssen Research & Development, LLC, Spring House, PA, ⁹Rheumatology, Johns Hopkins University, Baltimore, MD

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes III
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose: The Patient (Pt) Reported Outcomes Measurement Information System (PROMIS [P]) questionnaires developed by the NIH have been validated and are a feasible assessment tool for rheumatoid arthritis (RA) patients (pts) (Bartlett 2015). AWARE (Comparative and Pragmatic Study of Golimumab Intravenous [IV] Versus Infliximab in RA) is a large, pragmatic multi-center United States based, real-world evidence study of golimumab IV (GLM) vs. infliximab (IFX) in RA, and is using PROMIS assessments as one measure of pt response to therapy. Here we report interim results of the responsiveness of multiple PROMIS short forms and profiles with treatment of RA using GLM or IFX.

Methods: AWARE is a prospective, noninterventional study in which 1,200 adult pts will be enrolled upon initiation of treatment with GLM or IFX. PRO assessments of pt response to treatment include use of PROMIS-29 Profile v2.0 (P29v2), P Pain Interference Short Form-6b (SF6b) and P Fatigue Short Form-7a (SF7a), 36-Item Short Form Health Survey (SF-36v2) and the Clinical Disease Activity Index (CDAI). We report results of an interim analysis of pt response to PROMIS questionnaires. PROMIS questionnaire results are normalized to the US population and reported as a “T-score” (mean of 50 and standard deviation (SD) of 10). Data shown are mean ± standard deviation baseline score (month 0) and change from baseline (months 2 and 5), and interpreted as an effect size.

Results: GLM pts were 61.0 ± 13.0 years and IFX pts were 57.2 ± 13.0 years. RA disease duration of GLM pts was 9.0 ± 9.3 years and IFX pts was 6.8 ± 9.7 years. Mean baseline CDAI score for GLM pts was 31.1 ± 14.6 and for IFX pts was 34.3 ±16.2. with most starting in high (71.4% GLM/72.0% IFX) or moderate disease activity (21.8% GLM/23.4% IFX). A total of 573-586 pts contributed data at the 2 month time point, and 169-173 pts at the 5 month time point. PROMIS domain T-scores of GLM and IFX pts at baseline and mean change from baseline are shown (Table). The mean changes in PROMIS T-scores were generally in the 1-4 unit range, consistent with a small to moderate size effect, with all mean changes in the expected direction that reflected clinical improvement.
<table>
<thead>
<tr>
<th>PROMIS Domain</th>
<th>Mon. of Tx</th>
<th>GLM</th>
<th>IFX</th>
<th>PROMIS Domain</th>
<th>Mon. of Tx</th>
<th>GLM</th>
<th>IFX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue SF7a</td>
<td>0</td>
<td>59.4 (8.5)</td>
<td>377</td>
<td>59.2 (8.6)</td>
<td>305</td>
<td>0</td>
<td>58.7 (9.7)</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>-1.9 (6.1)</td>
<td>317</td>
<td>-1.1 (5.5)</td>
<td>269</td>
<td>2</td>
<td>-1.6 (7.0)</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>-2.3 (6.0)</td>
<td>74</td>
<td>-2.7 (6.6)</td>
<td>101</td>
<td>5</td>
<td>-2.6 (7.5)</td>
</tr>
<tr>
<td>Pain Interference SF 6b</td>
<td>2</td>
<td>-2.4 (5.7)</td>
<td>319</td>
<td>-2.6 (5.9)</td>
<td>270</td>
<td>2</td>
<td>1.1 (4.6)</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>-3.3 (6.9)</td>
<td>74</td>
<td>-3.8 (6.7)</td>
<td>101</td>
<td>5</td>
<td>2.3 (4.7)</td>
</tr>
<tr>
<td>Pain Interference P29v2</td>
<td>2</td>
<td>-2.6 (6.6)</td>
<td>319</td>
<td>-2.6 (6.6)</td>
<td>267</td>
<td>2</td>
<td>-1.4 (6.5)</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>-2.4 (6.9)</td>
<td>73</td>
<td>-3.7 (7.6)</td>
<td>100</td>
<td>5</td>
<td>-1.8 (7.9)</td>
</tr>
<tr>
<td>Depression P29v2</td>
<td>2</td>
<td>-1.3 (6.8)</td>
<td>315</td>
<td>-1.6 (6.6)</td>
<td>266</td>
<td>2</td>
<td>1.6 (6.2)</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>-2.9 (6.9)</td>
<td>72</td>
<td>-2.3 (8.4)</td>
<td>101</td>
<td>5</td>
<td>3.0 (6.8)</td>
</tr>
<tr>
<td>Anxiety P29v2</td>
<td>2</td>
<td>-1.3 (7.6)</td>
<td>316</td>
<td>-2.0 (7.0)</td>
<td>262</td>
<td>2</td>
<td>-0.9 (2.0)</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>-2.4 (7.5)</td>
<td>72</td>
<td>-2.9 (9.4)</td>
<td>101</td>
<td>5</td>
<td>-1.0 (2.5)</td>
</tr>
</tbody>
</table>

Mon. = Month, Tx = Treatment

**Conclusion:** These interim data support the use of PROMIS questionnaires to evaluate RA pts in trials and to measure improvement across a range of domains. As additional pts reach later time points (future interim analyses and primary endpoint assessment), the magnitude of change will become more apparent. Analyses using the fully enrolled AWARE study evaluated over 3 years and analysis of PROMIS changes relative to other outcome measures will further define the practical utilization of PROMIS in RA pts.

**Disclosure:** J. R. Curtis, AbbVie, Roche/Genentech, BMS, UCB, Myraid, Lilly, Amgen, Janssen, Pfizer, Corrona, 5; Amgen, Pfizer, Crescendo Bio, Corrona, 9; D. Conaway, Amgen, Crescendo Bioscience, AbbVie, BMS, CSRO, Interstate Postgraduate Medical Association, Pfizer, Janssen, 8, Crescendo, Janssen, 2, Janssen, 6, Interstate Postgraduate Medical Association, 9; J. Schechtman, None; A. Broadwell, AbbVie, Amgen, Janssen, Celgene, Pfizer, Mallinckrodt, UCB, 8, Amgen, Janssen, Pfizer, 5, Janssen, 2; A. J. Kivitz, Amgen, AbbVie, Celgene, Genentech, Janssen, Merck, Novartis, Pfizer, UCB, Genzyme, Sanofi, Regeneron, Vertex, 8, Amgen, AbbVie, Celgene, Genentech, Janssen, Merck, Novartis, Pfizer, UCB, Genzyme, Sanofi, Regeneron, Vertex, 5; V. Bray, Janssen, AbbVie, Lilly, Astra Zeneca, Gilead, Sun, Reg Pharm, 2; S. Kafka, Janssen, 3, Johnson & Johnson, LLC, 1; D. Parenti, Janssen, 3, Johnson & Johnson, LLC, 1; S. Black, Janssen, 3, Johnson & Johnson, LLC, 1; S. Xu, Janssen, 3, Johnson & Johnson, LLC, 1; W. Langhoff, Janssen, 3, Johnson & Johnson, LLC, 1; C. O. Bingham III, Janssen, 2, Janssen, 5.


**Abstract Number:** 2952

**A Randomized Controlled Trial (RCT) of an Internet-Based Self-Management Program for Adolescents with Juvenile Idiopathic Arthritis (JIA)**
Background/Purpose: Juvenile Idiopathic Arthritis (JIA) is a common chronic childhood illness associated with negative impact on health-related quality of life (HRQL). As teens mature, they are expected to assume greater responsibility in disease management. There is evidence to suggest that psycho-educational treatments can improve health outcomes in teens with JIA. However, the vast majority do not receive comprehensive self-management education. An Internet-based intervention was developed to help improve accessibility and disease self-management for teens with JIA. This intervention consisted of disease education, self-management strategies, and social support. A randomized controlled trial design was used to determine the effectiveness of the intervention.

Methods: Participants were between 12-18 years old with JIA across 11 pediatric centers in Canada. Most teens participated with a parent/caregiver. Intervention participants reviewed 12 modules focused on disease education and self-management strategies. Control participants reviewed standard disease education modules without self-management material. Over the 3-month program, health coaches had monthly check-ins with teens, but only reviewed modules with intervention participants. Parents in both groups reviewed modules on promoting independence and disease self-management in their teen. Participants completed outcome measures at 4 time points: baseline, program completion, 3-months, and 6-months after the program. Primary outcomes were: pain and HRQL. Secondary outcomes were: emotional symptoms, adherence, coping, knowledge, and self-efficacy.

Results: In total, 333 teens (n = 109 male, n = 224 female; mean age = 14.5, SD = 1.7) and 306 parents (n = 52 male, n = 254 female) were enrolled. Of the 164 intervention participants, 62.8% (n = 103) completed the study over an average 189.8 days (SD=113.5). Of the 169 control participants, 87.0% (n = 147) completed the study over 123.6 days (SD=70.6). Analyses indicate a significant overall reduction in pain interference in enjoying daily life for intervention participants compared to control after adjusting for baseline level of interference (intervention: M=1.03, SE=0.16; control: M=1.62, SE=0.13; p=0.004). There was also a significant difference interaction between intervention group and time (p=0.001) for HRQL related to treatment problems. Specifically, the intervention group reported improved HRQL versus control participants by 12 months (Mean difference at 12 months=3.22, SE=1.56, adjusted p=0.040). Participants in both groups showed non-significant improvements over time, compared to baseline, in pain coping, self-efficacy, disease knowledge, and HRQL. The majority of teens in the intervention found the coach calls helpful and were satisfied with call frequency. Most teens also found the website text content, videos, graphics/animations, and relaxation exercises helpful.

Conclusion: Teens and parents enjoyed being part of the study and the program improved aspects of HRQL. Education and social support factors may be key determinants of improving patient reported outcomes. The intervention website has been launched to the general public (URL: teens.aboutkidshealth.ca/jia).

Disclosure: J. N. Stinson, None; S. Campillo, None; T. Cellucci, None; P. Dancey, None; C. M. Duffy, None; J. Ellsworth, None; B. M. Feldman, None; A. Huber, None; N. Johnson, None; P. McGrath, None; A. Rosenberg, None; N. J. Shiff, None; L. R. Spiegel, None; S. M. L. Tse, None; L. Tucker, None; J. C. Victor, None; S. Luca, None.


Abstract Number: 2953
Drivers of Satisfaction with Care in Lupus

Bhavika Sethi1, Ailda Nika2, Winston Sequeira3, Joel A. Block4, Sergio Toloza5, Ana Bertoli6, Ivana Blazevic7, Luis M. Vilá8, Ioana Moldovan9, Karina Torralba10, Davide Mazzoni11, Elvira Cicognani11, Sarfaraz Hasni12, Berna Goker13, Seminur Haznedaroglu13, Josiane Bourré-Tessier14, Sandra V. Navarra15, Chi Chiu Mok16, Ann Clarke17, Michael Weisman18, Daniel J. Wallace19 and Meenakshi Jolly3, 1University of Birmingham, Birmingham, United Kingdom, 2Rheumatology, Rush University Medical Center, Chicago, IL, 3Department of Medicine, Section of Rheumatology, Rush University Medical Center, Chicago, IL, 4Division of Rheumatology, Rush University Medical Center, Chicago, IL, 5Rheumatology, Hospital San Juan Batista, Catamarca, Argentina, Catamarca, Argentina, 6Instituto Reumatológico Strusberg, Córdoba, Argentina, 7Rheumatology, Universidad de Buenos Aires, Buenos Aires, Argentina, 8Department of Medicine, Division of Rheumatology, University of Puerto Rico Medical Sciences Campus, San Juan, Puerto Rico, 9Rheumatology, Beaver Medical Group, Redlands, CA, 10Division of Rheumatology, Department of Internal Medicine, Loma Linda University, Loma Linda, CA, 11Department of Psychology, University of Bologna, Bologna, Italy, 12National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, 13Internal Medicine-Rheumatology, Gazi University Medical School, Ankara, Turkey, 14Rheumatology, University of Montreal, Montreal, QC, Canada, 15Rheumatology, University of Santo Tomas Hospital, Manila, Philippines, 16Medicine, Tuen Mun Hospital, Hong Kong, Hong Kong, 17Division of Rheumatology, University of Calgary, Calgary, AB, Canada, 18Cedars-Sinai Medical Center Division of Rheumatology, Los Angeles, CA, 19Rheumatology, Cedars-Sinai Medical Center, Beverly Hills, CA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Wednesday, November 8, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes III
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose: Although survival in SLE has improved, quality of life (QOL) remains poor. Physicians aim to reduce suffering and improve health outcomes, while maximizing efficiency and reducing costs. Patient satisfaction with care (SC) correlates with adherence, health behaviors and outcomes. However, SC may be influenced by patient, provider, care-processes and disease variables. This study aims to determine the modifiable and non-modifiable correlates of SC in SLE.

Methods: 1262 consenting patients, meeting ACR criteria for SLE, were recruited for this study from 2009-2016. Demographics, disease activity (SELENA-SLEDAI) and QOL (LupusPROv1.7) were collected. LupusProv1.7 includes a four-item domain on SC covering physician accessibility, education, physician discussion and monitoring of medication side effects, and physicians’ understanding of impact of lupus on patients’ lives. Regression analyses were conducted using patient (age, gender, ethnicity, education, social support) and disease (duration, disease activity, damage, medications, QOL) variables as independent predictors. P ≤0.05 was considered significant.

Results: Mean (SD) age was 41.7 (13.5) yrs; 93% were female. Ethnic composition was: African American 10%, Caucasian 23%, Hispanic 18%, Asian 48%. On univariate analysis, age, Asian ethnicity, current steroid use and QOL (desires-goals) were inversely associated with SC, while Hispanic and African-American ethnicity, disease activity (total score, pyuria, proteinuria, hematuria, urine casts), QOL (cognition, social support, coping) were directly associated with SC (Table 1). On multivariate analysis, ethnicity (positive for African Americans and Hispanics, negative for Asians), disease activity (pyuria) and QOL (desires-goals, social support and coping) remained independent predictors of SC.

With stepwise regression modelling (Table 1), African American and Hispanic ethnicity, total SLEDAI and pyuria, and QOL (social support and coping) were positively associated with SC, while Asian ethnicity and QOL (desires-goals) were negatively and independently associated with SC.

Conclusion: Asian patients have worse SC even after adjusting for demographics, disease activity, treatment and QOL. This requires further investigation into the role of culture, health behaviors and healthcare systems, but also suggests physicians need to be more attentive to the needs of Asian patients. Patients with greater disease activity have better SC, perhaps from greater interactions with physicians and ancillary services. SC thus may not be a good surrogate for tracking patients’ health outcomes and quality of care. Social support and coping are potentially modifiable. Evaluation of patients’ external and internal resources (social support and coping) using a bio-psychosocial model of health for SLE is suggested.
Disclosure: B. Sethi, None; A. Nika, None; W. Sequeira, None; J. A. Block, None; S. Tolosa, None; A. Bertoli, None; I. Blazevic, None; L. M. Vilá, None; I. Moldovan, None; K. Torralba, None; D. Mazzoni, None; E. Cicognani, None; S. Hasni, Intramural Research Program of the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health, 2; B. Goker, None; S. Haznedaroglu, None; J. Bourré-Tessier, None; S. V. Navarra, None; C. C. Mok, None; A. Clarke, None; M. Weisman, None; D. J. Wallace, None; M. Jolly, Pfizer Inc, 2, LupusPRO, 7.


Abstract Number: 2954

Achieving Balance and Diversity in Patient Engagement in Research: Perspectives from Patients

Graham Macdonald1, Jenny Leese2, Bao Chau Tran3, Alison Hoens3, Sheila Kerr4, Lianne Gulka5, Wendy Lum5 and Linda Li6,

1Occupational Science and Occupational Therapy, University of British Columbia, Vancouver, BC, Canada, 2Physical Therapy, University of British Columbia, Vancouver, BC, Canada, 3Arthritis Research Canada, Richmond, BC, Canada, 4Arthritis Patient Advisory Board, Richmond, BC, Canada, 5Arthritis Research Canada Arthritis Patient Advisory Board, Richmond, BC, Canada, 6Rheumatology, Arthritis Research Canada, Richmond, BC, Canada

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Wednesday, November 8, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes III
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose:

The movement for patient engagement in research aspires to greater inclusion of and collaboration with patients at virtually every point in the research cycle. Currently there is little empirical evidence concerning how patient engagement in research affects the lives of the patients involved. Our objective was to examine the experience of what it takes to be involved in research as a patient partner, focusing on occupational (relating to activities of daily life) aspects of their involvement, and how the conditions of involvement shape the nature of their participation and who can participate.

Methods:

This project was designed in a collaboration with patients with arthritis who had experience as research partners. Eligible participants were current or past members of a patient advisory board in an arthritis research centre. Participants were invited to take part in an hour-long interview. A semi-structured topic guide with prompts and probes was used to elicit detail about the benefits and challenges of being a patient engaged in research. An iterative thematic analysis of the interviews was conducted using constant comparison method. Discussions with patient partners informed the development of themes.

Results:
In 2015-2016, 22 participants were recruited, 21 (95%) were female, ages ranged from 26 to 68 years, and time spent as a patient engaged in research ranged from 1 month to 10 years. Twelve (55%) had inflammatory arthritis, 5 (23%) had OA, 4 (18%) had both, and one (4%) did not report. Fourteen (64%) had at least one university degree. 12 participants (55%) were employed fulltime, 9 (41%) were retired, 2 (9%) were students and 2 (9%) were on disability benefits. Two themes emerged from the findings, the first concerned maintaining occupational balance as a patient partner, in which many participants described their experience as volunteers in a patient advisory board as being rewarding and purposeful, though sometimes difficult to balance with priorities such as family, work, and health. Some described their volunteer work as akin to a full-time job, drawing on professional skill sets developed in the past. Many emphasized the time and effort it took to develop the knowledge-base to participate. The second theme was drawn from the participants’ concern at the difficulty of making patient engagement more diverse and reaching under-represented populations, specifically noting issues such as gender imbalance, and poorer representation from marginalized communities, lower socio-economic classes and people with limited educational opportunities.

Conclusion:
Our findings show that for patients who have had the opportunity to be partners in research, it can be both rewarding and burdensome. Our participants also identified, with concern for the democratic ideal of inclusivity, that there are populations lacking the opportunity to be engaged in research and are not being reached or represented. This is of concern due to the important role that the social determinants of health play in determining quality of life for people affected by arthritis. Our findings suggest that increased efforts and resources as well as new strategies are needed to bring increased diversity to patient engagement in arthritis research.

Disclosure: G. Macdonald, None; J. Leese, None; B. C. Tran, None; A. Hoens, None; S. Kerr, None; L. Gulka, None; W. Lum, None; L. Li, None.


Abstract Number: 2955

Does Guideline-Based Care Improve Outcomes That Matter to Patients? Tighter Control, Less Suffering, and Greater Well-Being over the Past Decade in Canadian RA Patients

Susan J. Bartlett1,2, Orit Schieir3, Marie-France Valois4, Carol A Hitchon5, Janet E. Pope6, Gilles Boire7, Boulos Haraoui8, Edward C. Keystone9, Diane Tin10, Carter Thorne11 and Vivian P. Bykerk12, 1Department of Medicine, Division of ClinEpi, Rheumatology, Respiriology, McGill University, Montreal, QC, Canada, 2Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, 3Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada, 4McGill University, Montreal, QC, Canada, 5University of Manitoba, Winnipeg, MB, Canada, 6Department of Medicine, Division of Rheumatology, University of Western Ontario, St Joseph's Health Care, London, ON, Canada, 7Rheumatology Division, Centre Hospitalier Universitaire de Sherbrooke and Universite de Sherbrooke, Sherbrooke, QC, Canada, 8Institute de Rheumatologie, Montreal, QC, Canada, 9University of Toronto, Toronto, ON, Canada, 10The Arthritis Program, Southlake Regional Health Centre, Newmarket, ON, Canada, 11University of Toronto, Newmarket, ON, Canada, 122-005, Mt Sinai Hospital, Toronto, ON, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Patient Outcomes, Preferences, and Attitudes III
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose: Best practice recommendations can increase quality of care and improve clinical outcomes, however the impact of recommendations on outcomes that matter most to patients have not been evaluated. We compare changes in patient reported outcomes (PROs) valued most by people with RA in the first year of follow up, as well as prior (2007-10) and subsequent (2011-16) to the 2010 release of Treat to Target and 2011 Canadian RA Treatment Recommendations.

Methods: Data included ERA adults enrolled in CATCH (Canadian early ArThritis CoHort) between 2007-16 who met 1987 or 2010 RA criteria and had active disease at enrolment. Standardized visits included clinical assessments, questionnaires, and laboratory tests
every 3 months. Treatment was at the discretion of the rheumatologist and cohort investigators met annually to discuss ways to improve outcomes. We examined changes in DAS28, pain, fatigue, patient global and HAQ at 6 and 12 months prior to and after guidelines release.

**Results:** The sample included 1942 adults who were mostly female (72%) with a mean (SD) age of 55 (15), 2 (2) comorbidities, and symptom duration of 6 (3) months. At enrollment, almost all (95%) were in DAS28 moderate or high disease activity [MDA (42%), HDA (53%)], and were initially treated with csDMARDS (92%) and MTX (75%). CDAI, DAS28 and PROs by DAS28 disease levels are shown in the Table. As mean DAS28 scores decreased over the first year, similar clinically meaningful improvements in patient global, pain, and fatigue were also evident (-3.0, -2.8, -2.3, -0.6; p’s<.001). When comparing change in PROs in 2007-2010 vs 2011-2016, there were more rapid improvements in patient global and pain at 6 and 12 months (p’s<.001; Figure) and similar improvements in HAQ and fatigue.

**Conclusion:** Results from this large country-wide study suggest that better disease control in the first year of RA translated to similar improvements in pain, fatigue and disability—symptoms that patients identify as important—resulting in greater overall well-being. These data offer additional evidence supporting the importance of early identification and control of disease activity to improve long term outcomes and quality of life in people with RA.

<table>
<thead>
<tr>
<th>Participant characteristics.</th>
<th>Total</th>
<th>LDA</th>
<th>MDA</th>
<th>HDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>1942</td>
<td>93%</td>
<td>42%</td>
<td>53%</td>
</tr>
<tr>
<td>DAS28</td>
<td>5.2 (1.3)</td>
<td>2.9 (0.2)</td>
<td>4.2 (0.5)</td>
<td>6.2 (0.8)</td>
</tr>
<tr>
<td>CDAI</td>
<td>28.1 (13.8)</td>
<td>10.8 (5.3)</td>
<td>19.4 (8.0)</td>
<td>36.9 (11.8)</td>
</tr>
<tr>
<td>Patient Global (0-10)</td>
<td>6.0 (2.8)</td>
<td>3.2 (2.2)</td>
<td>4.9 (2.7)</td>
<td>7.2 (2.4)</td>
</tr>
<tr>
<td>Pain (0-10)</td>
<td>5.7 (2.8)</td>
<td>3.3 (2.3)</td>
<td>4.6 (2.6)</td>
<td>6.8 (2.4)</td>
</tr>
<tr>
<td>Fatigue (0-10)</td>
<td>5.4 (3.0)</td>
<td>3.8 (2.8)</td>
<td>4.6 (2.9)</td>
<td>6.1 (2.9)</td>
</tr>
<tr>
<td>HAQ-DI (0-3)</td>
<td>1.1 (0.7)</td>
<td>0.6 (0.5)</td>
<td>0.8 (0.6)</td>
<td>1.4 (0.7)</td>
</tr>
</tbody>
</table>

**Disclosure:** S. J. Bartlett, None; O. Schieir, None; M. F. Valois, None; C. A. Hitchen, None; J. E. Pope, AbbVie, Amgen, Bayer, BMS, Celtrion, Eli Lilly and Company, Merck, Novartis, Pfizer, Roche, UCB, 5,Amgen, Bayer, BMS, GSK, Merck, Novartis, Pfizer, Roche, UCB, 2; G. Boire, None; B. Harauoi, AbbVie, Amgen, BMS, Celgene, Eli Lilly, Janssen, Merck, Pfizer, Roche, Sandoz, 6,AbbVie, Amgen, BMS, Janssen, Pfizer, Roche, and UCB; 2,Pfizer, and UCB, 8; E. C. Keystone, Abbott Laboratories, Amgen Inc., AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb, F. Hoffmann-La Roche Inc, Janssen Inc, Lilly Pharmaceuticals, Novartis Pharmaceuticals, Pfizer Pharmaceuticals, Sanofi-Aventis, UCB, 2,Abbott Laboratories, AstraZeneca Pharma, Biotest, Bristol-Myers Squibb Company, Crescendo Bioscience, F. Hoffmann-La Roche Inc, Genentech Inc, Janssen Inc, Lilly Pharmaceuticals, Merck, Pfizer Pharmaceuticals, UCB, 5,Amgen, Abbott Laboratories, AstraZeneca LP, Bristol-Myers Squibb Canada,, 8; D. Tin, None; C. Thorne, AbbVie, Amgen, Celgene, Lilly, Novartis, Pfizer, Sanofi, and UCB, 2,Medexus/Medac, 8,AbbVie, Amgen, Celgene, Centocor, Genzyme, Hospira, Janssen, Lilly, Medexus/Medac, Merck, Novartis, Pfizer, Sanofi, and UCB, 5; V. P. Bykerk, Amgen, Bristol-Myers Squibb Company, Gilead, Sanofi-Genzyme/Regeneron, Pfizer Pharmaceuticals, UCB, 5.


**Abstract Number:** 2956

**Evidence Based Recommendations for Corticosteroid Tapering/Discontinuation in New Onset Juvenile Dermatomyositis Patients from the Printo Trial**
Gabriella Giancane, Claudio Lavarello, Angela Pistorio, Francesco Zulian, Bo Magnusson, Tadej Avcin, Fabrizia Corona, Valeria Gerloni, Serena Pastore, Roberto Marini, Silvana Martino, Anne Pagnier, Michel Rodiere, Christine Soler, Valda Stanevicha, Rebecca ten Cate, Yosef Uziel, Jelena Vojinovic, Elena Fueri, Angelo Ravelli, Alberto Martini and Nicolino Ruperto, Istituto Giannina Gaslini - Pediatric I, Reumatologia - PRINTO, Genoa, Italy, Istituto Giannina Gaslini - Pediatric I, Reumatologia - PRINTO, Genoa, Italy, Pediatric Rheumatology, Leiden University Medical Center, Leiden, Netherlands, University of Genova, IRCCS Istituto Giannina Gaslini, Genoa, Italy, Istituto Giannina Gaslini, Genoa, Italy

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Wednesday, November 8, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects III: Lupus, Dermatomyositis, and Scleroderma
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose: At present no clear evidence-based guidelines exist to standardize the tapering and discontinuation of corticosteroids (CS) in juvenile dermatomyositis (JDM). To provide evidence-based recommendations for CS tapering/discontinuation through the analysis of the patients in the PRINTO new onset JDM trial and to identify predictors of clinical remission and CS discontinuation.

Methods: New onset JDM children were randomized to receive either prednisone (PDN) alone or in combination with MTX or CSA, according to a specific steroid protocol. Major therapeutic changes (MTC) were defined as the addition or major increase in the dose of MTX/CSA/other drugs or any other reasons for which patients were dropped from the trial. Patients were divided according to clinical remission into two major groups. Group 1 included those on clinical remission, who could discontinue PDN, with no MTC, and represented the reference standard for the best clinical outcome. Group 1 was compared with those who did not achieve clinical remission, without or with MTC (group 2 and 3, respectively). JDM core set measures (CSM) were compared in the 3 groups. We also calculated the gold standard group (group 1) median change in the CSM in the first 6 and over 24 months and applied a logistic regression model to identify the predictors of clinical remission with PDN discontinuation.

Results: 139 children were enrolled in the trial: 47 on PDN, 46 on PDN+CSA and 46 on PDN+MTX. We identified 30 (21.6%) patients for group 1, 43 (30.9%) for group 2 and 66 (47.5%) for group 3. At baseline all 3 groups had a high level of disease activity with no differences in the CSM. Already in the first 2 months a clear differential trend in disease activity measures, according to clinical remission status and PDN discontinuation, could be identified. From the observation of the median change in the CSM of group 1 in the first 6 months, the following recommendations could be extrapolated: decrease corticosteroids from 2 to 1 mg/kg/day in 2 months if the MD-global, parent-global, CHAQ, DAS, CMAS, MMT or Phs measures have a change of at least 50%; from 1 to 0.5 mg/kg/day in the following 2 months if the MD-global, CHAQ, DAS, CMAS have a change of at least 20%; in the following 2 months (month 4-6) corticosteroids can be tapered up to the safe dose of 0.2 mg/kg/day, if the disease activity measures remain at low/normal values. We finally ran a logistic regression model that showed the achievement of PRINTO criteria 50-70-90 at 2 months from disease onset, an age at onset >9 years and the combination therapy PDN+MTX, increase the probability of clinical remission from 4 to 7 times. (Table 1)

Conclusion: We propose evidence-based specific cut-offs for CS tapering/discontinuation based on the change in JDM CSM of disease activity, and identify the best predictors for clinical remission.

Table 1. Logistic regression model for the outcome remission

<table>
<thead>
<tr>
<th></th>
<th>OR (95% CI)</th>
<th>p#</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responder at 2 months:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Printo-50 (vs. not responder/Printo-20)</td>
<td>5.41 (1.37 - 21.32)</td>
<td>0.0076</td>
</tr>
<tr>
<td>Printo-70 (vs. not responder/Printo-20)</td>
<td>6.90 (1.91 - 24.99)</td>
<td></td>
</tr>
<tr>
<td>Printo-90 (vs. not responder/Printo-20)</td>
<td>4.46 (1.08 - 18.38)</td>
<td></td>
</tr>
<tr>
<td>Age at onset &gt; 8.53 years (8.53 years)</td>
<td>4.64 (1.69 - 12.71)</td>
<td>0.0017</td>
</tr>
<tr>
<td>Treatment group: PDN+MTX (vs. PDN / PDN+CSA)</td>
<td>3.63 (1.30 - 10.09)</td>
<td>0.0116</td>
</tr>
</tbody>
</table>

Disclosure: G. Giancane, None; C. Lavarello, None; A. Pistorio, None; F. Zulian, None; B. Magnusson, None; T. Avcin, None; F. Corona, None; V. Gerloni, None; S. Pastore, None; R. Marini, None; S. Martino, None; A. Pagnier, None; M. Rodiere, None; C. Soler, None; V. Stanevicha, None; R. ten Cate, None; Y. Uziel, None; J. Vojinovic, AbbVie, 8; E. Fueri, None; A. Ravelli, None; A. Martini, GASLINI Hospital, 3,Astellas, AstraZeneca, Bristol-Myers Squibb, Italfarmaco, and MedImmune, 8,AbbVie Inc., AstraZeneca, Bristol-Myers Squibb, Janssen Biologies B.V., Eli Lilly and Co., “Francesco Angelini”, GlaxoSmithKline, Italfarmaco, Novartis, Pfizer, Roche, Sanofi Aventis, Schwarz Biosciences GmbH, Xoma, and Wyeth Pharmaceuticals, 2; N. Ruperto, BMS,
Factors Associated with Cardiac Dysfunction in a Longitudinal Follow-up of Neonatal Lupus

Amit Saxena¹, Peter M. Izmirly², Rebecca Bomar², Shireen Golpanian², Deborah Friedman³ and Jill P. Buyon¹

¹Rheumatology, New York University School of Medicine, New York, NY, ²New York University School of Medicine, New York, NY, ³New York Medical College, Valhalla, NY

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects III: Lupus, Dermatomyositis, and Scleroderma
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose: There are minimal data and no longitudinal studies regarding the long term cardiac health of children with cardiac manifestations of neonatal lupus (NL). This study was performed to evaluate risk factors for morbidity over time and provide evidence based guidance regarding the course of cardiac NL.

Methods: Echocardiograms throughout life were evaluated in 200 individuals born with cardiac NL from the Research Registry for Neonatal Lupus: 111 from ages 0-1 years, 156 ages 1-17 years, and 63 >17 years. A composite adverse outcome defined as qualitatively decreased left ventricular (LV) function or concurrent use of cardiac medications was assessed. Aortic dilation (root or ascending aorta z-score >2.0) was also recorded. Analyses were performed to associate the composite adverse outcome and aortic dilation with maternal medications, pacing, and fetal disease status, including a severity score based on mortality risk factors such as lower fetal heart rate and extranodal disease.

Results: The composite adverse outcome for cardiac dysfunction was identified in 18.9% of echos in children ages 0-1, 11.3% ages 1-17 and 20.6% ages >17. In 89 children in which echos were available at ages 0-1 and 1-17, 4/14 with dysfunction at ages 0-1 were also affected at ages 1-17, while 10 reverted to normal, and only 7/75 developed new dysfunction during age 1-17. In 31 cases with echos at ages 1-17 and >17, 1/2 cases with dysfunction at age 1-17 was also affected >17, and 3/29 developed new dysfunction in adulthood. Earlier age at pacemaker placement was associated with dysfunction in the 0-1 age group (p=0.018), but not in later ages. Cardiac dysfunction was significantly associated with number of years paced at ages >17 (p=0.001), but not earlier. A lower fetal ventricular heart rate at initial heart block detection was associated with cardiac dysfunction in all age groups (p=0.038, 0.009, 0.016 respectively). Fetal extranodal cardiac disease was associated with dysfunction (p=0.046) in ages >17. Higher fetal severity score associated with postnatal dysfunction in all age groups (p=0.063, 0.03, 0.005). Aortic dilation was present in 15.3% at ages 0-1 and 17.6% at ages 1-17, but at >17, dilation only occurred in 7.9%. There was no association of postnatal cardiac dysfunction or aortic dilation with maternal medication use, maternal rheumatic disease, fetal age at heart block detection or gestational age of birth.

Conclusion: Cardiac dysfunction in the first year normalizes by later childhood in the majority of cases, possibly due to the short term effects of cardiac pacing or resolution of inflammation with the clearance of maternal autoantibodies. Aortic dilation can continue for longer periods, but also decreases in frequency with age. Nevertheless, cardiac dysfunction does persist in a fifth of cases and in adulthood there are associations with fetal extranodal disease and heart rate at detection. Patients who develop morbidity in utero may have subclinical damage or be more susceptible to future insults that manifest later in life, which can be exacerbated by prolonged pacing. Close monitoring and aggressive treatment of early extranodal disease in cardiac NL may have long term benefit in preventing subsequent morbidity.

Disclosure: A. Saxena, None; P. M. Izmirly, None; R. Bomar, None; S. Golpanian, None; D. Friedman, None; J. P. Buyon, None.
Validation of Flare Criteria for Children and Adolescents with Systemic Lupus Erythematosus

Hermine I. Brunner1, Michael J. Holland2, Michael W. Beresford3, Nicolino Ruperto4, Stacy P. Ardoin5, Simone Appenzeller6, Clovis A Silva7, Glauzia V. Novak7, Daniela M. Lourenço8, Francisco Flores9, Beatrice Gollay10, Scott E. Wenderfer11, Deborah M. Levy12, Angelo Ravelli13, Raju Khubchandani14, Tadej Avcin15, Marisa S. Klein-Gitelman16, Brian M. Feldman17 and Jun Ying18,

1Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 2Pediatric Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 3On Behalf of the UK JSLE Study Group, Liverpool, United Kingdom, 4Istituto Giannina Gaslini, Genoa, Italy, 5Pediatric & Adult Rheumatology, The Ohio State University Wexner Medical Center, Columbus, OH, 6Pediatric Rheumatology Unit, State University of Campinas, Campinas, Brazil, 7Pediatric Rheumatology Unit, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, 8Pediatric Rheumatology Unit, Faculdade de Medicina da Universidade de São Paulo, Sao Paulo, Brazil, 9Nephrology and Hypertension, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, 10Albert Einstein College of Medicine/Montefiore Medical Center, New York, NY, 11Pediatrics-Renal, Baylor College of Medicine, Texas Children's Hospital, Houston, TX, 12Division of Rheumatology, The Hospital for Sick Children, Toronto, ON, Canada, 13University of Genova, IRCCS Istituto Giannina Gaslini, Genova, Italy, 14Department of Paediatrics, Jaslok Hospital and Research Center, Mumbai, India, 15Istituto Giannina Gaslini - Pediatra II, Reumatologia - PRINTO, Genoa, Italy, 16Division of Pediatric Rheumatology/PDD PTD, Lurie Children's Hospital of Chicago/Northwestern University, Chicago, IL, 17Rheumatology, The Hospital for Sick Children, Toronto, ON, Canada, 18Center for Biostatistical Services, University of Cincinnati College of Medicine, Cincinnati, OH

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Wednesday, November 8, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects III: Lupus, Dermatomyositis, and Scleroderma
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose: Childhood-onset systemic lupus erythematosus (cSLE) is characterized by changing disease activity: episodes of improvement are often followed by episodes of worsening, i.e. flares. Considering changes of previously defined core response variables (proteinuria [mostly from protein creatinine ratio, PCR], disease activity (SLEDAI, BILAG), physician global assessment of cSLE activity), and ESR, preliminary flare algorithms have been derived by Classification Tree Analysis (CART) and multinomial logistic regression (MLR), respectively. International consensus yielded 4 preferred criteria for detection of cSLE flares, based on initial validation in 2010-11. These algorithms yield flare-scores, with higher scores reflecting worse flares. Our objective was to validate the preliminary cSLE flare algorithms, and delineate flare scores that reflect mild/moderate/major flares.

Methods: A total of 1,860 Patient Profiles (PPs) providing relevant data at baseline and follow-up were generated from existing international prospective cSLE cohorts, with systematic imputation of missing algorithm variables. Pediatric rheumatologists (PP-raters) were asked to judge disease courses between baseline and follow-up as: improved, no change, mild flare, moderate flare, or major flare. Based on majority opinion of PP-raters, each PP was assigned a true disease course, against which the flare algorithms were tested for accuracy. Using two complementary approaches (distribution-weighted, MLR-based) potential threshold flare-scores for flare severity (mild, moderate, major) were derived and tested for accuracy via area under the receiver operating characteristic curve (AUC). Analyses were reviewed by an expert panel that used nominal group technique to achieve consensus (≥75% agreement).

Results: Among 503 invited, feedback from 274 PP-raters (53% response rate) was available for analysis. Based on PP-rater feedback, true disease courses were as follows: 540 no change or improved and 510/483/325 PPs as mild flare/ moderate flare/ major flare. There was consensus to use MLR estimates for all flare thresholds. As shown (Table 1), CART-based models, though maintaining very good to excellent accuracy (AUCs for mild/moderate/major flares all >70%), were less suited to discriminate mild and moderate flares. Algorithms from MLR maintained outstanding accuracies (all AUC > 90.79%) and had sensitivities/specificities for mild/moderate/major flares all >82%/>82% in the 2017 validation analyses. This was true for both BILAG and SLEDAI-based algorithms (see Table 1).

Conclusion: The provisional criteria for flare of global disease of cSLE have outstanding accuracy in identifying flare in cSLE with different degrees of severity. Based on our results and consensus, the BILAG and the SLEDAI-based algorithm from MLR are equally acceptable to measure flares in cSLE.
<table>
<thead>
<tr>
<th>Method</th>
<th>Preliminary Flare Algorithms*</th>
<th>Flare severity</th>
<th>Threshold scores from logistic regression</th>
<th>Area under ROC curve 2010 data</th>
<th>Area under ROC curve 2017 data</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Logistic regression</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.5 x SLEDAI + 0.45 X PCR + 0.5 X MD-global + 0.02 x ESR</td>
<td>Major</td>
<td>6.4</td>
<td>95.12%</td>
<td>93.11%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Less than or equal to Moderate</td>
<td>3.0</td>
<td>85.14%</td>
<td>93.94%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Less than or equal to Mild</td>
<td>0.6</td>
<td>85.99%</td>
<td>93.11%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Major</td>
<td>7.4</td>
<td>93.10%</td>
<td>90.79%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Less than or equal to Moderate</td>
<td>3.7</td>
<td>84.92%</td>
<td>92.04%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Less than or equal to Mild</td>
<td>2.2</td>
<td>84.81%</td>
<td>93.06%</td>
</tr>
<tr>
<td><strong>Classification tree analysis (CART)</strong></td>
<td></td>
<td>Major</td>
<td>4</td>
<td>85.14%</td>
<td>76.21%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Less than or equal to SLEDAI; S3 if 0.7 less than or equal to PCR; S2 if 2 less than or equal to MD-global; S1 Other</td>
<td>3</td>
<td>79.52%</td>
<td>80.17%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Less than or equal to Moderate</td>
<td>3</td>
<td>83.86%</td>
<td>89.01%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Less than or equal to Mild</td>
<td>3</td>
<td>85.92%</td>
<td>70.66%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Major</td>
<td>4</td>
<td>85.92%</td>
<td>70.66%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Less than or equal to BILAG; S3 if 0.7 less than or equal to PCR; S2 if 2 less than or equal to MD-</td>
<td>3</td>
<td>79.52%</td>
<td>74.59%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Less than or equal to Moderate</td>
<td>3</td>
<td>82.24%</td>
<td>84.12%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Less than or equal to Mild</td>
<td>3</td>
<td>82.24%</td>
<td>84.12%</td>
</tr>
</tbody>
</table>
Are Patients with Overlap Features Different from Patients without? Results from the Juvenile Systemic Scleroderma Cohort

Ivan Foeldvari1, Jens Klotsche2, Ozgur Kasapcopur3, Amra Adrovic4, Valda Stanevicha5, Maria Teresa Terreri6, Ekaterina Alexeeva7, Maria M. Katsicas8, Vanessa Smith9, Rolando Cimaz10, Mikhail Kostik11, Thomas J. A. Lehman12, Jordi Anton13, Walter A. Sifuentes-Giraldo14, Flavio Sztajnbok15, Tadey Avcin16, Mahesh Janarthanan17, Maria Jose Santos18, Dana Nemkova19, Cristina Battagliotti20, Despina Eleftheriou21, Liora Harel22, Tilman Kallinich23, K Minden24, Susan Mary Nielsen25, Kathryn S. Torok26, Yosef Uziel27, Anne Stevens28, Clarissa Pilkington29 and Nicola Helmus1, 1Hamburg Center for Pediatric and Adolescent Rheumatology, Hamburg, Germany, 2Epidemiology Unit, German Rheumatism Research Center, Berlin, Germany, 3Pediatric Rheumatology, Istanbul University-Cerrahpasa Medical School, Department of Pediatric Rheumatology, Istanbul, Turkey, 4Department of Pediatric Rheumatology, Istanbul University-Cerrahpasa Medical School, Istanbul, Turkey, 5Pediatric cathedra, Riga Stradiņš University, Riga, Latvia, 6Pediatric Rheumatology Unit, Federal University of São Paulo (UNIFESP - Universidade Federal de São Paulo), São Paulo, Brazil, 7Children's Health of RAMS and IM Sechenov First Moscow State Medical University, Moscow, Russian Federation, 8Service of Immunology & Rheumatology, Hospital de Pediatría Prof Dr JP Garrahan, Buenos Aires, Argentina, 9Faculty of Internal Medicine, Ghent University, Ghent, Belgium, 10Pediatrics, Ospedale Pediatrico Anna Meyer, Florence, Italy, 11Hospitalet Pediatrics, State Pediatric Medical University, Saint-Petersburg, Russia, 12Pediatric Rheumatology, Hospital for Special Surgery Weill Cornell Medical College, New York, NY, 13Pediatric Rheumatology, University Children's Hospital, Barcelona, Spain, 14Rheumatology, Hospital Universitario Ramón y Cajal, Madrid, Spain, 15Universidade Federal do Rio de Janeiro, Brazil, 16University Children's Hospital, Ljubljana, Slovenia, 17Pediatric Rheumatology, Chennai, India, 18Reuma.pt, Almada, Portugal, 19Pediatric Rheumatology Unit, Department of Pediatric Rheumatology and Adolescent Medicine, General University Hospital in Prague, Prague, Czech Republic, 20Hospital de Niños Dr Orlando Alasia, Santa Fé, Argentina, 21Infection, Inflammation and Rheumatology, UCL Institute of Child Health, London, United Kingdom, 22Schneider Children's Medical Center of Israel, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel, 23Charité, Humboldt University Medicine Berlin, Berlin, Germany, 24Charité – University of Medicine Berlin, Berlin, Germany, 25Rigshospitalet, Copenhagen, Denmark, 26Pediatric Rheumatology, University of Pittsburgh Med Ctr.

* In all algorithms changes (worsening) of the variables are considered, e.g. change in SLEDAI, change in proteinuria, etc; MD-global: Physician global assessment of disease measured on a visual analog scale (range: 0-10; 0 = inactive disease), PCR proteinuria estimated from 24-hr timed collection or random urine sample; Receiver operating characteristic; A=12; B=8, C=1, D/E = 0

(1) Details about algorithm development are provided in Brunner, H. I., R. Mina, "Preliminary criteria for global flares in childhood-onset systemic lupus erythematosus." Arthritis Care Res (Hoboken) 63(9): 1213-1223.

Disclosure: H. I. Brunner, None; M. J. Holland, None; M. W. Beresford, None; N. Ruperto, BMS, Hoffman-La Roche, Janssen, Novartis, Pfizer and Sobi, 2,Abbvie, Ablynx, AstraZeneca, Baxalta Biosimilars, Biogen Idec, Boehringer, Bristol Myers Squibb, Eli-Lilly, EMD Serono, Gilead Sciences, Janssen, Medimmune, Novartis, Pfizer, Rpharm, Roche, Sanofi., 5,Abbvie, Ablynx, AstraZeneca, Baxalta Biosimilars, Biogen Idec, Boehringer, Bristol Myers Squibb, Eli-Lilly, EMD Serono, Gilead Sciences, Janssen, Medimmune, Novartis, Pfizer, Rpharm, Roche, Sanofi., 8, S. P. Ardoín, not applicable, 9, S. Appenzeller, None; C. A. Silva, Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP #2014/14806-0 and 2015/03756-4 to CAS), Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq 303422/2015-7 - 1A to CAS), 2, G. V. Novak, None; D. M. Lourenço, None; F. Flores, None; B. Goilav, None; S. E. Wenderfer, None; D. M. Levy, None; A. Ravelli, None; R. Khubchandani, None; T. Avcin, None; M. S. Klein-Gitelman, Janssen Pharmaceutica Product, L.P., 2,UCB biosciences, 2,Abbvie, 2,Lupus Foundation of America, 2,NIH/LFA/Cure JM/Arthritis Foundation, 2,Up to Date, 7; M. S. Klein-Gitelman, Janssen Pharmaceutica Product, L.P., 2,UCB biosciences, 2,Abbvie, 2,Lupus Foundation of America, 2,NIH/LFA/Cure JM/Arthritis Foundation, 2,Up to Date, 7; B. M. Feldman, None; J. Ying, None.


Abstract Number: 2959

Are Patients with Overlap Features Different from Patients without? Results from the Juvenile Systemic Scleroderma Cohort

Ivan Foeldvari1, Jens Klotsche2, Ozgur Kasapcopur3, Amra Adrovic4, Valda Stanevicha5, Maria Teresa Terreri6, Ekaterina Alexeeva7, Maria M. Katsicas8, Vanessa Smith9, Rolando Cimaz10, Mikhail Kostik11, Thomas J. A. Lehman12, Jordi Anton13, Walter A. Sifuentes-Giraldo14, Flavio Sztajnbok15, Tadey Avcin16, Mahesh Janarthanan17, Maria José Santos18, Dana Nemkova19, Cristina Battagliotti20, Despina Eleftheriou21, Liora Harel22, Tilman Kallinich23, K Minden24, Susan Mary Nielsen25, Kathryn S. Torok26, Yosef Uziel27, Anne Stevens28, Clarissa Pilkington29 and Nicola Helmus1, 1Hamburg Center for Pediatric and Adolescent Rheumatology, Hamburg, Germany, 2Epidemiology Unit, German Rheumatism Research Center, Berlin, Germany, 3Pediatric Rheumatology, Istanbul University-Cerrahpasa Medical School, Department of Pediatric Rheumatology, Istanbul, Turkey, 4Department of Pediatric Rheumatology, Istanbul University-Cerrahpasa Medical School, Istanbul, Turkey, 5Pediatric Cathedra, Riga Stradiņš University, Riga, Latvia, 6Pediatric Rheumatology Unit, Federal University of São Paulo (UNIFESP - Universidade Federal de São Paulo), São Paulo, Brazil, 7Children's Health of RAMS and IM Sechenov First Moscow State Medical University, Moscow, Russian Federation, 8Service of Immunology & Rheumatology, Hospital de Pediatría Prof Dr JP Garrahan, Buenos Aires, Argentina, 9Faculty of Internal Medicine, Ghent University, Ghent, Belgium, 10Pediatrics, Ospedale Pediatrico Anna Meyer, Florence, Italy, 11Hospital Pediatrics, State Pediatric Medical University, Saint-Petersburg, Russia, 12Pediatric Rheumatology, Hospital for Special Surgery Weill Cornell Medical College, New York, NY, 13Pediatric Rheumatology, University Children's Hospital, Barcelona, Spain, 14Rheumatology, Hospital Universitario Ramón y Cajal, Madrid, Spain, 15Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil, 16University Children's Hospital, Ljubljana, Slovenia, 17Pediatric Rheumatology, Chennai, India, 18Reuma.pt, Almada, Portugal, 19Pediatric Rheumatology Unit, Department of Pediatric Rheumatology and Adolescent Medicine, General University Hospital in Prague, Prague, Czech Republic, 20Hospital de Niños Dr Orlando Alasia, Santa Fé, Argentina, 21Infection, Inflammation and Rheumatology, UCL Institute of Child Health, London, United Kingdom, 22Schneider Children's Medical Center of Israel, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel, 23Charité, Humboldt University Medicine Berlin, Berlin, Germany, 24Charité – University of Medicine Berlin, Berlin, Germany, 25Rigshospitalet, Copenhagen, Denmark, 26Pediatric Rheumatology, University of Pittsburgh Med Ctr,
Juvenile systemic sclerosis (jSSc) patients with overlap features seems to have a better long term outcome. There is currently no data, where the clinical characteristics of patients with and without overlap features were compared.

**Methods:**

Patients, fulfilling the PRES jSSc-classification criteria were included. Organ involvement was assessed using the standardized assessment. Patients were classified to diffuse (dcjSSc) and limited (lcjSSc) subtype and grouped as patients with and without overlap features.

**Results:**

Till April 2016 eighty patients were enrolled. We present data at time point of the enrollment. 11 of the patients had overlap features (oJSSc). 6 of 58 (10%) in the dcjSSc and 5 of 22 (23%) in the lcjSSc. Most patients were Caucasian. Female/male ratio differed in the groups, in the nojSSc 3.9:1 and in the ojSSc 11:1 (p=0.1). Mean disease duration was 3.6 years in the non-overlap features group (noJSSc) and 3.2 years in the ojSSc group. Patients with nojSSc were 35% Scl-70 positive and ojSSc group none (p=0.032). Decreased DLCO occurred in 48% in the nojSSc and in 100% in the ojSSc group (p=0.088). Renal involvement was more frequent in the ojSSc group with 18% compared to 4% in the nojSSc (p=0.078). Swollen joints occurred in 63% in the ojSSc and in 29% in the nojSSc group (p<0.001). Muscle weakness combined with joint contractures occurred in 43% in the ojSSc and in 8% in the nojSSc group (p=0.011).

**Conclusion:**

Patients with overlap features have distinct characteristics compared with patients with nojSSc. This characteristics were no Scl-70 positivity, higher portion of interstitial lung disease, renal involvement, arthritis and muscle involvement accompanied by joint contractures. The future larger patient data collection in our cohort will help to make the differences more accentuated.

**Literature**


**Disclosure:** I. Foeldvari, None; J. Klotsche, None; O. Kasapcopur, None; A. Adrovic, None; V. Stanevicha, None; M. T. Terreri, None; E. Alexeeva, None; M. M. Katsicas, None; V. Smith, None; R. Cimaz, None; M. Kostik, None; T. J. A. Lehman, None; J. Anton, None; W. A. Sifuentes-Giraldo, None; F. Sztajnbok, None; T. Avcin, None; M. Janarthanan, None; M. J. Santos, None; D. Nemkova, None; C. Battagliotti, None; D. Eleftheriou, None; L. Harel, None; T. Kallinich, None; K. Minden, None; S. M. Nielsen, None; K. S. Torok, None; Y. Uziel, None; A. Stevens, None; C. Pilkington, None; N. Helmus, None.
19. Methods:

Data were analyzed from the 2002-2012 Nationwide Inpatient Sample, containing a representative 20% stratified sample of all hospitalizations in the United States. Primary (i.e. condition chiefly responsible for inpatient admission) vs secondary diagnoses of JDM (age <18 years) were identified using the previously validated ICD-9-CM code 710.3. Comorbidities were identified using ICD-9-CM codes in NIS for each patient discharge. Survey weighted logistic regression models were used to determine associations of JDM with comorbidities. Multivariate models included age, sex and race/ethnicity (model-1), as well as obesity, hypertension and diabetes (model-2) as binary covariates. A 2-sided p-value < 0.05 was considered statistically significant.

20. Results:

From 2002-2012, 909 primary and 498 secondary diagnoses of JDM were identified (from 14,535,620 pediatric hospital discharges). JDM inpatients were 34.6% male, 49.0% white, 18.5% black and 24.1% Hispanic. Twelve of 13 cardiovascular comorbidities were significantly associated with JDM (Table 1). Hypertension was the most common comorbidity in children with JDM (8.78% JDM patients vs 0.43% those without JDM, OR [95% CI]: 22.25 [15.51-31.92]). JDM was also associated with higher rates of obesity, uncomplicated diabetes, and lipid abnormalities. JDM inpatients had higher odds of cardio/cerebrovascular disorders, i.e. peripheral/visceral atherosclerosis, late effects of cerebrovascular disease, personal history transient ischemic attack/cerebral infarction, pulmonary circulatory disorder, arrhythmia, bradycardia, and hypotension. In multivariate regression models adjusting for age, gender and race/ethnicity, associations with JDM remained significant in 10 of 13 comorbidities.

21. Conclusion:

JDM is associated with higher odds of cardiovascular and cerebrovascular risk factors and disease. The possible interaction of chronic inflammation, vasculopathy, and treatment side effects with sociodemographic and cardiovascular risk factors requires further study.
Body Composition and Myokine Levels in Juvenile Dermatomyositis and Associations with Physical Function

Birgit Nomeland Witczak1, Kristin Godang2, Jens Bollerslev2,3, Thomas Schwartz4,5, Berit Flate3,6, Ivar Sjaastad3,4,7 and Helga Sanner6,8
1Oslo University Hospital, Institute for Experimental Medical Research, Oslo University Hospital, Oslo, Norway, Oslo, Norway, 
2Section of Specialized Endocrinology, Department of Endocrinology, Oslo University Hospital, Rikshospitalet, Oslo, Norway, Oslo, Norway, 
3Institute for Clinical Medicine, University of Oslo, Oslo, Norway, Oslo, Norway, 
4Institute for Experimental Medical Research, Oslo University Hospital, Oslo, Norway, Oslo, Norway, 
5Department of Infectious Diseases, Oslo University Hospital, Oslo, Norway, Oslo, Norway, 
6Department of Rheumatology, Oslo University Hospital, Rikshospitalet, Oslo, Norway, Oslo, Norway, 
7Department of Cardiology, Oslo University Hospital, Oslo, Norway, Oslo, Norway, 
8Norwegian National Advisory Unit on Rheumatic Diseases in Children and Adolescents, Oslo University Hospital, Rikshospitalet, Oslo, Norway, Oslo, Norway

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Pediatric Rheumatology – Clinical and Therapeutic Aspects III: Lupus, Dermatomyositis, and Scleroderma
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose: JDM presents with proximal muscle weakness and atrophy is frequent. Still, body composition (BC) in JDM has not been widely studied, but is known to be unfavourably altered in other CTDs and associated with physical disability. It has also been proposed that monocyte chemoattractant protein-1 (MCP-1), acting as a myokine, may promote inflammation in skeletal muscle in idiopathic inflammatory myopathies. Aim of study was to compare BC and myokines in JDM patients with controls and explore associations between measures of BC and myokines with physical function outcomes.

Methods: 59 JDM patients and 59 age- and sex-matched controls were included. BC including total and appendicular lean mass (LM) and fat mass (FM), was measured by DXA. MCP-1 and IL-6 in serum were quantified. Functional outcomes were short form-36 physical component summary (SF-36), childhood or adult HAQ (CHAQ/HAQ), manual muscle testing (MMT-8) and 6 minute walking test distance (6 MWD). Multiple linear backward regression was used to identify indicators of appendicular lean mass (ALM) and appendicular fat mass percentage (AFM%) and to assess associations between physical function outcomes and ALM, AFM% and myokines.

Results: Table 1 presents characteristics, BC and myokine levels in patients and controls. Median disease duration was 16.8 years; 61% were female; 28% were on prednisolone or DMARDs at follow-up. Patients had significantly higher ESR, lower SF-36, MMT-8, 6 MWD, and physical activity than controls. BMI was comparable in patients and controls (P=0.752). Patients had 8% lower total lean mass, 10.4% lower appendicular LM and 6% lower trunk LM compared to controls (all P’s ≤0.032). Total body FM% was 10.6% higher, AFM% was 10.6% % higher and android:gynoid fat ratio was 34.3% higher in patients than controls (all P’s ≤0.017). MCP-1 and IL-6 were higher in patients than controls (P’s ≤0.017).

In JDM patients, MCP-1 was an independent indicator of ALM (β=-0.041, 95%CI(-0.081, -0.001)) and CRP and DAS muscle independent indicators of AFM% (β=0.8, 95%CI (0.3, 1.3); β=1.3, 95%CI(0.3, 2.2)).

When identifying independent indicators of physical outcomes, ALM was associated with SF-36 and MMT-8 (β=0.6, 95%CI(0.1, 1.0); β=0.370, 95%CI(0.190-0.550)); AFM% with CHAQ/HAQ, MMT-8 and 6MWD (β= -0.005, 95%CI(0.001, 0.009); β=-0.132, 95%CI(-0.203, -0.062); β= -1.968, 95%CI (-2.931, -1.006)) and MCP-1 with CHAQ/HAQ and 6MWD (β=0.004, 95%CI(0.001, 0.008) and β=1.512, 95%CI(-3.264, -0.241)).

Conclusion: JDM patients assessed after long-term disease duration had unfavorable alterations in BC compared with controls, including lower LM and higher FM percentage. MCP-1 was higher in patients compared with controls, and independently associated
with lower ALM and poorer functional outcomes in patients. Low ALM and high AFM percentage were also independently associated with impaired physical function in patients.
<table>
<thead>
<tr>
<th>Table 1. Characteristics and body composition data in JDM patients and controls.</th>
</tr>
</thead>
<tbody>
<tr>
<td>JDM patients total (n=59)</td>
</tr>
<tr>
<td>Age, years at FU</td>
</tr>
<tr>
<td>DAS muscle at FU</td>
</tr>
<tr>
<td>DAS skin at FU</td>
</tr>
<tr>
<td>Physical exercise, hours/week (n=51)</td>
</tr>
<tr>
<td>hs-CRP, ug/mL</td>
</tr>
<tr>
<td>ESR, mm (n=55)</td>
</tr>
<tr>
<td>CHAQ/HAQ</td>
</tr>
<tr>
<td>SF-36 PCS &gt;13 years (n=51)</td>
</tr>
<tr>
<td>MMT-8</td>
</tr>
<tr>
<td>6MWD, m (n=58)</td>
</tr>
<tr>
<td><strong>Antropometric parameters</strong></td>
</tr>
<tr>
<td>Weight, kg</td>
</tr>
<tr>
<td>Height, cm</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
</tr>
<tr>
<td><strong>DXA-derived measures</strong></td>
</tr>
<tr>
<td>Total body LM, kg</td>
</tr>
<tr>
<td>ALM, kg</td>
</tr>
<tr>
<td>Trunk LM, kg</td>
</tr>
<tr>
<td>LMI, kg/m²</td>
</tr>
<tr>
<td>ALMI, kg/m²</td>
</tr>
<tr>
<td>Total body FM, kg</td>
</tr>
<tr>
<td>AFM, kg</td>
</tr>
<tr>
<td>Total body FM percentage</td>
</tr>
<tr>
<td>Trunk FM percentage</td>
</tr>
<tr>
<td>AFM percentage</td>
</tr>
<tr>
<td><strong>Android:gynoid fat ratio</strong></td>
</tr>
<tr>
<td><strong>Myokines</strong></td>
</tr>
<tr>
<td>IL-6, pg/mL (n=54)</td>
</tr>
<tr>
<td>MCP-1, pg/mL (n=54)</td>
</tr>
</tbody>
</table>

Values are mean (SD) or median(IQR) or number(%); n: =59 pairs of patients and controls, or n=59 patients, unless otherwise stated.

AFM, appendicular fat mass; ALM, appendicular lean mass; ALMI, appendicular lean mass index; BMI, body mass index; CHAQ/HAQ, child and
MRI Results Following Discontinuation of Methotrexate in Patients with Rheumatoid Arthritis Treated with Subcutaneous Tocilizumab: Results from a Randomized Controlled Trial

Charles Peterfy¹, Joel Kremer², William F C Rigby³, Nora Singer⁴, Christine Birchwood⁵, Darcy Gill⁵, William Reiss⁵, Jinglan Pei⁵ and Margaret Michalska⁵
¹Spire Sciences, Inc., Boca Raton, FL, ²Albany Medical College, Albany, NY, ³Geisel School of Medicine at Dartmouth, Lebanon, NH, ⁴Case Western Reserve University School of Medicine, Cleveland, OH, ⁵Genentech, Inc., South San Francisco, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy V: Imaging and Cardiovascular Outcomes Therapy
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose: Although previous studies have established the efficacy of tocilizumab (TCZ) initiated as monotherapy (MONO) for the treatment of rheumatoid arthritis (RA),¹,² changes in active intra-articular inflammation after discontinuation of methotrexate (MTX) in patients achieving good clinical control with TCZ + MTX have not been evaluated. Magnetic resonance imaging (MRI) effectively images synovitis and osteitis and can detect changes in bone erosion with greater sensitivity than radiography.³ This study used MRI to assess differences in joint damage between patients with RA who achieved low disease activity with TCZ + MTX and then continued or discontinued MTX in the COMP-ACT trial (NCT01855789).

Methods: US patients with RA who were inadequate responders to MTX were enrolled; initial combination therapy included MTX (≥ 15 mg/week orally) plus TCZ 162 mg subcutaneous (SC) either weekly or every 2 weeks. Patients who achieved DAS28-ESR ≤ 3.2 at week 24 were randomized 1:1 to receive TCZ-MONO or continue TCZ + MTX until week 52 (double blind). A subset of these patients was included in this MRI substudy; 1.5 Tesla MRI was used to obtain images of bilateral hands and wrists at Weeks 24 and 40. Two independent radiologists evaluated images at a central reading facility using RAMRIS (synovitis, osteitis, erosion) and CARLOS (cartilage loss). Outcomes included changes in MRI scores from Week 24 to 40 and the proportion of patients with progression of each score.

Results: Of the 296 patients who achieved DAS28 ≤ 3.2 at Week 24 and were randomized to TCZ + MTX or TCZ-MONO, 79 were enrolled in the MRI substudy (n = 41 and 38, respectively); 74.7% were women, and the mean (SD) age was 56.3 (12.8) years. Patient demographics in the MRI substudy were similar to overall study demographics. Mean changes from Week 24 to 40 in bone erosion, synovitis, osteitis and cartilage loss scores were not significantly different between the TCZ + MTX and TCZ-MONO groups for both bilateral hands and the dominant hand (Table). There were no significant differences between the groups in the proportion of patients with no progression in each outcome measure (range, 89.7% to 97.4% with TCZ + MTX and 87.9% to 100.0% with TCZ-MONO).
**Conclusion:** In patients who achieved low disease activity with TCZ + MTX, MRI changes were minimal and showed no difference in the response of active intra-articular inflammation in patients who discontinued MTX vs those who continued TCZ + MTX within the period of observation, consistent with the result of similar mean change in DAS28 between the groups in the primary analysis.

**Table.** MRI Changes in Patients Receiving TCZ in Combination With MTX or TCZ as Monotherapy

<table>
<thead>
<tr>
<th></th>
<th>Both Hands</th>
<th>Dominant Hand</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TCZ + MTX (n = 41)</td>
<td>TCZ-MONO (n = 38)</td>
<td>Difference (95% CI) (TCZ-MONO minus TCZ + MTX)</td>
<td>TCZ + MTX (n = 41)</td>
<td>TCZ-MONO (n = 38)</td>
</tr>
<tr>
<td>Bone erosion score (0-250), mean (SE)</td>
<td>−0.06 (0.18)</td>
<td>0.18 (0.19)</td>
<td>0.24 (−0.21 to 0.68)</td>
<td>0.06 (0.25)</td>
<td>0.49 (0.25)</td>
</tr>
<tr>
<td>Synovitis score (0-24), mean (SE)</td>
<td>−0.24 (0.15)</td>
<td>−0.18 (0.15)</td>
<td>0.06 (−0.30 to 0.41)</td>
<td>−0.22 (0.12)</td>
<td>−0.11 (0.12)</td>
</tr>
<tr>
<td>Osteitis score (0-75), mean (SE)</td>
<td>−0.16 (0.34)</td>
<td>0.37 (0.36)</td>
<td>0.53 (−0.30 to 1.36)</td>
<td>−0.39 (0.52)</td>
<td>0.69 (0.54)</td>
</tr>
<tr>
<td>Cartilage loss score (0-100), mean (SE)</td>
<td>0.20 (0.14)</td>
<td>−0.03 (0.15)</td>
<td>−0.23 (−0.58 to 0.11)</td>
<td>0.11 (0.18)</td>
<td>−0.05 (0.19)</td>
</tr>
</tbody>
</table>

MTX, methotrexate; TCZ, tocilizumab; TCZ-MONO, TCZ monotherapy.

* ANCOVA model for estimated means includes Week 24 bone erosion as a covariate, treatment group and the randomization stratification factors: DAS28 remission status at Week 24 (< 2.6, ≥ 2.6 to ≤ 3.2), patient anti-TNF exposure (Yes or No) and baseline weight-by-dosing group (< 80 kg q2w, 80 to < 100 kg q2w, 80 to < 100 kg qw, ≥ 100 kg qw).

**References:**


**Disclosure:** C. Peterfy, Roche Pharmaceuticals, 5,Spire Sciences, LLC, 3; J. Kremer, Corrona, LLC, 1,Corrona, LLC, 3,AbbVie, Amgen, BMS, Genentech, Lilly, Regeneron, Sanofi, Pfizer, 5,AbbVie, Genentech, Lilly, Novartis, Pfizer, 2; W. F. C. Rigby, Roche, 5; N. Singer, Merck, EMD Serono, 2,Pfizer Inc, 5; C. Birchwood, Genentech, Inc., 3; D. Gill, Genentech, Inc., 3; W. Reiss, Genentech, Inc., 3; J. Pei, Genentech, Inc., 3; M. Michalska, Genetech, Inc., 3.


**Abstract Number:** 2963
Sirukumab Improves Synovial Vascularity As Measured By Power Doppler Sonography in Rheumatoid Arthritis Patients from As Early As Week 4 in a Phase 3 Trial

Bidisha Dasgupta1, Kristen Sweet1, Dick DeVries2, Benjamin Hsu1, Ian Gourley1, Matthew Loza1 and Peter C. Taylor3, 1Janssen Research & Development, LLC, Spring House, PA, 2Janssen Biologics Europe, Leiden, Netherlands, 3Kennedy Institute of Rheumatology, University of Oxford, Oxford, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy V: Imaging and Cardiovascular Outcomes Therapy
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose: Ultrasound (US) is an established non-invasive tool for sensitively assessing disease activity at the individual-joint level in rheumatoid arthritis (RA). Synovial thickness is detectable on grey-scale US and synovial vascularity by power Doppler US (PDS).1 Studies have shown that PDS correlates with clinical assessment of disease activity and synovial histopathology.2 Furthermore, PDS can detect subclinical synovitis.3 Sirukumab (SIR), a human monoclonal antibody that selectively binds to IL-6 with high affinity, demonstrated efficacy in RA in several phase 3 studies including SIRROUND-H (active comparator monotherapy study). The ability of grey-scale US and PDS to evaluate changes in synovitis was assessed following SIR and adalimumab (ADA) treatment in patients (pts) with moderate to severe RA in a substudy of SIRROUND-H.

Methods: In SIRROUND-H, US assessment was carried out at 9 clinical sites in a nested subset of 41 pts, with 27 pts pooled from SIR 50mg q4w/SIR 100mg q2w and 14 pts in the ADA 40mg q2w treatment groups. Assessments were performed at baseline (BL), and Wks 2, 4, 8 and 24. 12 joints (10 metacarpal [MCP] plus wrists) were evaluated and synovial vascularity (VASCi), thickness (STI) and tenosynovitis/hyperemia (wrist) scores were reported for each timepoint. Significance of differences between baseline and post-treatment timepoints were tested using Wilcoxon signed-rank and Mann-Whitney tests (α=0.05).

Results: BL VASCi and STI scores correlated with BL disease activity (DAS28[CRP], CDAI, and swollen and tender joint counts). Pts who were ACPA and RF positive had significantly higher BL VASCi and STI scores. Initial analysis of post-treatment changes in PDS outcomes showed no significant differences from BL at the population level. However, a significant proportion of the study cohort (36.6% or 15/41) had a BL VASCi score <1, leaving little room for evaluable improvement. When the analysis of post-treatment changes was restricted to pts with a BL VASCi >1 (n=26), both SIR and ADA treatment showed significant reductions in VASCi starting at Wk 4 and sustained through Wk 24 (P<0.05 vs BL). Wk 24 DAS remission was associated with lower BL VASCi and STI (P<0.05). The Wk 24 changes in VASCi and STI did not correlate with Wk 24 DAS28(CRP) or DAS28(ESR) changes from baseline. STI was not changed with SIR or ADA treatment over the course of the study duration (24 wks) and there was no observed difference in effect on vascularity or thickness between patients treated with SIR vs ADA.

Conclusion: Our study demonstrates the utility of non-invasive PDS of small joints to detect synovial changes following drug treatment in RA patients with high baseline VASCi scores. Both SIR and ADA similarly improved VASCi scores from Wk 4. A correlation between changes in PDS score and disease activity was not observed in this small substudy, consistent with reports in the literature.3 In conclusion, PDS can detect changes in joint pathology with treatment and is feasible for use in global clinical studies.

References:

Disclosure: B. Dasgupta, Johnson & Johnson, 3; K. Sweet, Johnson & Johnson, 3; D. DeVries, Johnson & Johnson, 3,Johnson & Johnson, 1; B. Hsu, Johnson & Johnson, 1,Johnson & Johnson, 3; I. Gourley, Johnson & Johnson, 1,Johnson & Johnson, 3; M. Loza, Johnson & Johnson, 1,Johnson & Johnson, 3; P. C. Taylor, Janssen, 2,Janssen, GSK, AbbVie, 5.


Abstract Number: 2964
Structural Damage in Patients with Very Early RA Is Predicted with Clinical Measures of Baseline Disease Activity: DAS28 (CRP), SDAI, M-DAS28 and RAPID3 but Not CDAI

Edward C. Keystone1, H Ahmad2, Yusuf Yazici3, X Liu2 and MJ Bergman4, 1University of Toronto, Toronto, ON, Canada, 2Bristol-Myers Squibb, Princeton, NJ, 3New York University School of Medicine, New York, NY, 4Drexel University College of Medicine, Philadelphia, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy V: Imaging and Cardiovascular Outcomes Therapy
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose: Clinicians rely on time-efficient, validated disease activity assessments to help accurately predict disease progression in patients with RA. The utility of the Routine Assessment of Patient Index Data 3 (RAPID3) in predicting structural damage progression is largely unknown, while that of DAS28 (CRP) and modified (M-)DAS28 have been previously reported. This post hoc analysis using data from the AVERT (NCT01142726) study investigated the value of baseline clinical measures for predicting structural damage progression with MRI as a measure of progression. Methods: AVERT was a 24-month, active-controlled trial with a 12-month, double-blind treatment period, during which MTX-naïve, ACPA-positive patients with early active RA were randomized (1:1:1) to abatacept 125 mg weekly plus MTX or abatacept or MTX monotherapy, followed by a 12-month withdrawal period, during which all treatment was stopped. Logistic regression analysis, corrected for age, sex and corticosteroid use at baseline, was used to assess the correlation between baseline measures of disease activity (DAS28 [CRP], SDAI, CDAI, M-DAS28 and RAPID3) and the degree of structural joint damage, as assessed by MRI at 6 and 12 months. MRI erosion progression was defined as change from baseline greater than the smallest detectable change, which was calculated as SD/square root (2) x 1.96 (where SD is standard deviation of paired differences of change from baseline in total score between two readers). Results: Logistic regression analysis was carried out for all randomized and treated patients who received abatacept + MTX (n=119) or MTX monotherapy (n=116). For these patients, DAS28 (CRP), M-DAS28 and RAPID3 at baseline were significant predictors of radiographic progression at Months 6 and 12 (Figure). Baseline SDAI was a significant predictor at Month 12 but not Month 6, and baseline CDAI was not a significant predictor at either time point (Figure). At Months 6 and 12, receiver operating characteristic curves showed that RAPID3 had the highest predictive value (area under the curve) for MRI progression (Table).

Table. Area Under ROC Curves for the Impact of Disease Activity at Baseline on MRI Progression at Months 6 and 12 (all Randomized and Treated Patients)

<table>
<thead>
<tr>
<th>Disease activity measure*</th>
<th>AUC at Month 6</th>
<th>AUC at Month 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAS28 (CRP)</td>
<td>0.6322</td>
<td>0.6466</td>
</tr>
<tr>
<td>RAPID3</td>
<td>0.7181</td>
<td>0.7047</td>
</tr>
<tr>
<td>M-DAS28</td>
<td>0.6488</td>
<td>0.6823</td>
</tr>
<tr>
<td>CDAI</td>
<td>0.5666</td>
<td>0.5958</td>
</tr>
<tr>
<td>SDAI</td>
<td>0.6549</td>
<td>0.6647</td>
</tr>
</tbody>
</table>

*M-DAS28 was calculated based on a different statistical model (which also included DAS28 [CRP] and RAPID3) due to a different number of patients with non-missing values. In the other model, the AUC for DAS28(CRP) and RAPID3 at Month 6 were 0.6281 and 0.7157, respectively. At Month 12 the values were the same for both models.

AUC=area under the curve; M-DAS28=modified DAS28; ROC=receiver operating characteristic.

Disclosure: E. C. Keystone, Abbott Laboratories, Amgen Inc., AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb, F. Hoffmann-La Roche Inc., Janssen Inc, Lilly Pharmaceuticals, Novartis Pharmaceuticals, Pfizer Pharmaceuticals, Sanofi-Aventis, UCB, 2,Abbott Laboratories, AstraZeneca Pharma, Biotest, Bristol-Myers Squibb Company, Crescendo Bioscience, F. Hoffmann-La Roche Inc, Genentech Inc, Janssen Inc, Lilly Pharmaceuticals, Merck, Pfizer Pharmaceuticals, UCB, 5,Amgen, Abbott Laboratories, Astrazeneca LP, Bristol-Myers Squibb Canada, F. Hoffmann-La Roche Inc., Janssen Inc., Pfizer Pharmaceuticals, Sanofi Genzyme UCB, 8; H. Ahmad, Bristol-Myers Squibb, 3,Bristol-Myers Squibb, 1, 9; Y. Yazici, Genentech, Celgene, BMS, 2,Celgene, 5; X. Liu, Bristol-Myers Squibb, 3; M. Bergman, Pfizer, JNJ, 1,Norvatis, AbbVie, Celgene, 8,AbbVie, BMS, Amgen, Celgene, Genentech, Pfizer, Janssen, GSK Horizon, 5.


Abstract Number: 2965

Non-Invasive Imaging Methods for Evaluating the Cardiovascular Involvement in Patients with Rheumatoid Arthritis before and after 18 Months of Treatment with Anti-TNF Drugs

Fabiola Atzeni1, Luigi Gianturco2, Laura Boccassini3, Piercarlo Sarzi-Puttini3 and Maurizio Turie4, 1Rheumatology Unit, ASST Fatebenefratelli - Sacco, L. Sacco University Hospital, Milano, Italy, 2Beato Matteo5 Hospital, GSD Foundation, Vigevano, Italy, Vigevano, Italy, 3Rheumatology Unit, ASST Fatebenefratelli - Sacco, L. Sacco University Hospital, Milan, Italy, 4IRCCS, Galeazzi Orthopedic Institute, Dept. Biomedical Sciences for Health, University of Milan, Milan, Italy

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Wednesday, November 8, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy V: Imaging and Cardiovascular Outcomes Therapy
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose: The aim of this study was to evaluate left ventricular myocardial function with two-dimensional speckle tracking echocardiography (STE), in addition to conventional Doppler and tissue Doppler echocardiography, in order to detect subclinical left ventricular myocardial dysfunction in patients with RA.

Methods: The study involved 30 outpatients who fulfilled the 2010 ACR/EULAR criteria for RA (11 males and 19 females; mean age 54.63±9.36 years, median disease duration 2 years), at baseline at after 18 months of treatment with anti-TNF drugs and 30 healthy controls matched in terms of age, gender and other anthropometric characteristics. All patients underwent a complete physical examination and routine laboratory analysis. Disease activity was assessed by means of Disease activity score 28 (DAS 28).
Cardiovascular (CV) risk profiles were assessed by means of standard ECG, conventional and stress trans-thoracic echocardiography with the measurement of CFR, carotid ultrasonography and pulse wave velocity (PWV). Two-dimensional echocardiographic images were obtained using the apical 4-chamber view at a high frame rate of 70-80 frames/s, and three cardiac cycles were stored in cine-loop format for off-line analysis using commercially available QLAB 9 software (Philips Medical System, USA) in order to assess end-systolic LV longitudinal strain (ε).

Results:

None of the patients showed any signs or symptoms of CV disease, pulmonary involvement, or any other complication. The patients’ mean LVEF and E/A ratios were respectively 58.43±3.07% and 0.75±0.35, which were not significantly different from those of the controls (60.45±5.24 % and 0.85±0.29); however, although within the normal range. The results of the speckle tracking analysis were significantly different between the two groups, with global longitudinal strain deformation in the apical 4-chamber view (Long. ε 4c) being significantly lower in the RA patients (Long. ε 4c %: median 18.78, IQR 15.80-20.82 vs 20.16, IQR 19.03-21.89; p<0.05). Right and left pulse wave velocity (PWV) (PWV right, m/sec: median 7.92, IQR 7.14-8.60 vs 6.85, IQR 6.41-7.88; p=0.07 and PWV left, m/sec: median 7.90, IQR 6.99-8.16 vs 6.85, IQR 6.36-7.84; p=0.06) and right and left coronary intima media thickness (cIMT) (cIMT right, mm: median 0.90, IQR 0.75-1.08 vs 0.75, IQR 0.50-0.85; p<0.05 and cIMT left, mm: median 0.89, IQR 0.74-0.99 vs 0.74, IQR 0.49-0.85; p<0.05) values were all higher in the RA patients, and the differences of cIMT were statistically significant. Furthermore a significant improvement in Long. ε 4c of LV in RA patients at 18 months of the biological treatment was observed (Long. ε 4c %: median 18.78, IQR 15.80-20.82 vs 19.24, IQR 17.02-21.29 p<0.01) at FUP, such as a minimal reduction of arterial stiffness and cIMT parameters (p=NS).

Conclusion: LV myocardial longitudinal ε measured by means of speckle tracking echocardiography was impaired in RA patients in the absence of any clinical evidence of CV disease and echocardiographic evaluations negative. This data suggests an early myocardial alteration, but further studies are required to define more precise methods of assessing CV disease in RA population.

Disclosure: F. Atzeni, None; L. Gianturco, None; L. Bocassini, None; P. Sarzi-Puttini, None; M. Turiel, None.


Abstract Number: 2966

Impact of Tofacitinib Treatment Compared with Placebo or Methotrexate on Cardiovascular Risk Scores in Six Phase 3 Randomized Controlled Trials

Michael Nurmohamed1, Ernest Choy2, Christina Charles-Schoeman3, George Kitas4, Paola Accossato5, Piotr Szczypa6, Konstantina Chouchouli7, Tatjana Lukic8 and Pinaki Biswas8, 1VU University Medical Centre, Amsterdam, Netherlands, 2CREATE Center, Division of Infection and Immunity, Cardiff University School of Medicine, Cardiff, United Kingdom, 3University of California, Los Angeles, Los Angeles, CA, 4Arthritis Research UK Centre for Epidemiology, University of Manchester, Manchester, United Kingdom, 5Pfizer S.r.l, Rome, Italy, 6Pfizer Ltd, Walton Oaks, United Kingdom, 7Pfizer Hellas S.A, Neo Psychiko, Greece, 8Pfizer Inc, New York, NY

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Wednesday, November 8, 2017
Session Title: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy V: Imaging and Cardiovascular Outcomes Therapy
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM
Background/Purpose: Patients (pts) with RA are at increased risk of myocardial infarction and stroke not fully explained by usual cardiovascular (CV) risk factors. Tofacitinib is an oral Janus kinase inhibitor for the treatment of RA. Small, dose-dependent increases from baseline in total, LDL-c, and HDL-c have been noted in some pts. Major adverse cardiovascular events (MACE) are infrequent in the tofacitinib clinical program. The Framingham and Reynolds risk scores calculate the 10-year risk of developing CV disease; Reynolds risk score includes high-sensitivity C-reactive protein (hsCRP) as a variable, Framingham risk score does not. We scored pts receiving tofacitinib to investigate the impact of changes in lipids and hsCRP on CV risk scores.

Methods: This was a post-hoc analysis of 6 Phase 3 randomized controlled trials (disease-modifying antirheumatic drug [DMARD]-inadequate responders [IR] in ORAL Standard [NCT00853385; N=471]; ORAL Sync [NCT00856544; N=729]; ORAL Solo
NCT00814307; N=574); ORAL Scan [NCT00847613; N=739]; ORAL Step [NCT00960440; N=353]; methotrexate [MTX]-naïve pts in ORAL Start [NCT01039688; N=906]. Pts received tofacitinib 5 or 10 mg BID either as monotherapy (ORAL Solo, ORAL Start), with background MTX (ORAL Standard, ORAL Scan, ORAL Step), or csDMARDs (ORAL Sync). All trials were placebo (pbo) controlled except ORAL Start (tofacitinib vs MTX). Pts with diabetes were excluded from this analysis. Framingham and Reynolds CV risk scores were calculated at baseline (BL) and Month 3. Change from baseline was assessed using a linear mixed model for repeated measures, controlling for treatment.

Results: 2/5 trials in DMARD-IR pts (ORAL Sync [tofacitinib 5 mg p<0.012; tofacitinib 10 mg p=0.042] and ORAL Step [tofacitinib 10 mg only p=0.041]), showed a significantly higher change from BL to Month 3 in Framingham risk score with tofacitinib vs pbo (Figure); Reynolds risk scores were significantly (all <0.05) reduced from BL to Month 3 with both doses of tofacitinib vs pbo except ORAL Step, in which there was no significant difference in change from BL to Month 3 between tofacitinib 5 mg BID and pbo (Figure). Change from BL to Month 3 in Framingham risk score was significantly higher with tofacitinib 5 mg and 10 mg vs MTX in ORAL Start; however, for Reynolds risk score there was no significant difference between either dose of tofacitinib and MTX.

Conclusion: In this analysis, the 10-year Framingham CV risk score was not significantly increased with tofacitinib vs pbo in 3 out of 5 Phase 3 trials, although a higher CV risk score was identified vs MTX. The 10-year CV risk calculated by Reynolds risk score, which includes hsCRP as a variable, was significantly reduced with tofacitinib vs pbo and there was no difference vs MTX. CV risk with RA treatment is a function of lipid changes and/or hsCRP. An ongoing study will investigate the incidence of MACE with tofacitinib vs etanercept or adalimumab.

Disclosure: M. Nurmohamed, AbbVie, Celgene, Eli Lilly, Janssen, MSD, Pfizer Inc, Roche, Sanofi, UCB, 2,AbbVie, Janssen, Roche, Sanofi, 5,Bristol-Myers Squibb, Roche, 8; E. Choy, BioCancer, Pfizer Inc, Roche, UCB, 2,Amgen, Biogen, Chugai Pharma, Eli Lilly, Janssen, Novartis, Pfizer, Regeneron, Roche, R-Pharm, Sanofi, 5,Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Chugai Pharma, Eli Lilly, Hospira, MSD, Novartis, Pfizer, Regeneron, UCB, 8; C. Charles-Schoeman, Bristol-Myers Squibb, Pfizer Inc, 2,Pfizer Inc, Regeneron, Sanofi, 5; G. Kitas, None; P. Accossato, Pfizer Inc, 1,Pfizer Inc, 3; P. Szczypta, Pfizer Ltd, 1,Pfizer Ltd, 3; K. Chouchouli, Pfizer Inc, 3; T. Lukie, Pfizer Inc, 1,Pfizer Inc, 3; P. Biswas, Pfizer Inc, 1,Pfizer Inc, 3.
Our results, from a non-randomized study, did not suggest an advantage of using US of 7 joints in addition to clinical examination as a T2T benchmark compared to clinical examination alone in getting RA patients into clinical remission.

**Conclusion:** Our results, from a non-randomized study, did not suggest an advantage of using US of 7 joints in addition to clinical examination as a T2T benchmark compared to clinical examination alone in getting RA patients into clinical remission.
<table>
<thead>
<tr>
<th>T2T approach</th>
<th>Outcome</th>
<th>DAS44 remission</th>
</tr>
</thead>
<tbody>
<tr>
<td>No T2T vs T2T-DAS44 alone‡</td>
<td></td>
<td>0.69 (0.42; 1.15)</td>
</tr>
<tr>
<td>T2T-DAS44-US vs T2T-DAS44 alone‡</td>
<td></td>
<td>0.59 (0.39; 0.91)</td>
</tr>
</tbody>
</table>

*Adjusted for age, gender, HAQ-score, RF, ACPA, previous use of DMARDs, smoking-status, education and number of comorbidities. § Clinical definition of T2T (T2T-DAS44) was used as the comparator for each of the presented treatment strategies.

Disclosure: A. Sepriano, None; S. Ramiro, MSD, 2; R. B. M. Landewé, None; D. van der Heijde, None; S. Ohrndorf, None; O. FitzGerald, Abbvie, Novartis, BMS, Pfizer, 3, Cellgene, Pfizer, Abbvie, Lilly, Janssen, Novartis, UCB, BMS, 5; M. Backhaus, None; M. Larche, None; J. Homik, None; A. Saraux, None; H. B. Hammer, None; L. Terslev, None; M. Østergaard, None; G. R. Burmester, None; B. Combe, None; M. Dougados, None; C. A. Hitchon, None; G. Boire, None; R. G. Lambert, None; R. Dadashova, None; J. Paschke, None; E. Hutchings, None; W. P. Maksymowych, None.


Abstract Number: 2968

**Less Fatigue in Psoriatic Arthritis after High Intensity Interval Training, a Randomized Controlled Trial**

Ruth Stoklund Thomsen1, Tom Ivar Lund Nilsen2, Glenn Haugeberg3, Anja Bye3, Arthur Kavanaugh4 and Mari Hoff5, 1Faculty of Medicine, Department of Public Health and Nursing, NTNU, Norwegian University of Science and Technology, Trondheim, Norway, 2Faculty of medicine, Department of public health and nursing, NTNU, Norwegian University of Science and Technology, Trondheim, Norway, 3NTNU, Norwegian University of Science and Technology, Trondheim, Norway, 4Medicine, University of California, San Diego, La Jolla, CA, 5Rheumatology, University Hospital, St. Olavs Hospital, NTNU, Trondheim, Norway

First publication: September 18, 2017

**SESSION INFORMATION**

Session Date: Wednesday, November 8, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment V
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose: Patients with psoriatic arthritis (PsA) have a high disease burden with increased pain and more fatigue than the general population. Physical exercise is recommended for arthritis patients, although little research has been done assessing its utility. A pilot study suggests decreased disease activity in patients with spondyloarthritis (1) after high intensity interval training (HIIT).

The primary aim of this study was to measure the efficacy of HIIT on fatigue, secondly the efficacy on disease activity in PsA.

**Methods:** PsA patients satisfying CASPAR criteria were recruited from clinics to this randomized clinical trial. The intervention group (N=32) performed HIIT, defined as 4 times 4 minutes supervised training at 85-95% of maximum heart rate on a stationary bicycle twice a week, in addition to one additional self-guided HIIT session a week for 11 weeks. The control group (N=31) was instructed not to change their pre-study physical exercise habits during 11 weeks of the study. Before the intervention period, all participants tested their maximum heart rate and VO2max.

Fatigue and Patient Global Assessment (PGA) of overall disease activity were measured on a 100 mm VAS. Activity of arthritis was measured by DAS44. Measurements were performed at baseline and at 3 months. Mean differences within and between groups were analyzed using linear mixed models.

**Results:** Of the 63 patients included, 29 in the intervention group and 28 in the control group completed the trial period. Mean (SD) age was 51(11) years in the intervention group and 45(12) years in the control group. The proportion of women was 68% in the intervention
group and 63% in the control group. HIIT was associated with reduced fatigue at 3 months (mean difference 12.95; 95% CI -25.97 to 0.05), and changed from 48.6 to 32.8 (p=0.002) in the intervention group; from 48.6 to 45.8 (p=0.569) in the control group. There was no effect of HIIT on DAS44 (mean difference 0.08; 95% CI -0.36 to 0.20) or PGA (mean difference 0.56; 95% CI -10.99 to 9.86). DAS44 was reduced from 1.98 to 1.61 (p=0.001) in the intervention group and from 1.98 to 1.69 (p=0.006) among controls, whereas PGA declined from 40.0 to 34.3 (p=0.158) in the intervention group and from 40.0 to 34.9 (p=0.195) in controls. Medication did not change during the study period.

**Conclusion:** Fatigue was significantly reduced at 3 months in the intervention group. HIIT was well tolerated in PsA patients concerning disease activity measured by DAS44 and PGA. This study suggests that HIIT may be of benefit to PsA patients. Thus, HIIT could be an important contribution to cost-efficient treatment strategies as supplementary to medical treatment for this group of patients.

**References:**


**Disclosure:** R. S. Thomsen, None; T. I. L. Nilsen, None; G. Haugeberg, None; A. Bye, None; A. Kavanaugh, None; M. Hoff, None.

**Efficacy and Safety of Ixekizumab in Patients with Active Psoriatic Arthritis and Previous Inadequate Response to TNF Inhibitors: 52-Week Results from a Phase 3 Study**

**Mark C. Genovese**¹, Bernard Combe², Joel Kremer³, David Adams⁴, Chin Lee⁴, Lisa Kerr⁴ and Peter Nash⁵, ¹Stanford University Medical Center, Palo Alto, CA, ²Rheumatology, CHU Lapeyronie and Montpellier University, Montpellier, France, ³St. Peter's Hospital, Albany, NY, ⁴Eli Lilly and Company, Indianapolis, IN, ⁵University of Queensland, Brisbane, Australia

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Wednesday, November 8, 2017

**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment V

**Session Type:** ACR Concurrent Abstract Session

**Session Time:** 11:00AM-12:30PM

**Background/Purpose:** Ixekizumab (IXE) is a high affinity monoclonal antibody that selectively targets interleukin-17A. In patients with active psoriatic arthritis (PsA) who had an inadequate response to tumor necrosis factor inhibitors (TNFi), IXE was superior to placebo (PBO) in improving the signs and symptoms of PsA after 24 weeks of treatment (SPIRIT-P2; NCT02349295).¹ The objective
of this study is to report the Week 52 interim efficacy and safety findings of IXE treatment during the Extension Period (EP) of SPIRIT-P2 (Weeks 24-156).

Methods: SPIRIT-P2 is a phase 3, multicenter, double-blind study. All 363 patients had an inadequate response to one or two TNFi or were intolerant to TNFi. During the Double-Blind Treatment Period (DBTP; Weeks 0-24), patients were randomly assigned 1:1:1 to subcutaneous administration of either 80 mg IXE every 4 weeks (Q4W; N=122) or every 2 weeks (Q2W; N=123) following a 160 mg starting dose at Week 0, or PBO (N=118). Of these, 310 patients completed the DBTP and entered the EP (Weeks 24-156). Patients randomized to IXE at Week 0 continued the same dose regimen in the EP. PBO patients were re-randomized (1:1) to IXE Q4W or Q2W at Week 16 (inadequate responders) or 24. In this interim analysis, efficacy (up to Week 52) and safety (up to Week 156) were analyzed using the EP population, defined as all patients who received at least 1 dose of study drug in the EP. Missing values were considered non-response for categorical data and were imputed by modified baseline observation carried forward for continuous data.

Results: In the DBTP, a significantly higher percentage of patients achieved ACR20 at Week 24 with IXE Q4W (53%) or Q2W (48%) than with PBO (20%). For patients who entered the EP, the mean age was 52 years, 47% were male, the mean time since PsA onset was 12 years, and mean tender and swollen joint counts at baseline (Week 0) were 23 and 12, respectively. For EP patients who were initially randomized to IXE Q4W or Q2W during the DBTP, ACR20 responses at Week 52 were 68% and 59%, respectively. For patients treated with PBO during the DBTP and re-randomized to IXE Q4W or Q2W during the EP, ACR20 responses at Week 52 were 61% and 50%, respectively. Additional efficacy measures are depicted in the Table. The frequency of adverse events (AEs) in the EP are presented in the Table; the majority were mild or moderate in severity. Serious AEs occurred in 15 patients, and one death occurred in the EP population: a myocardial infarction in a PBO/IXE Q2W patient 502 days after starting IXE.

Conclusion: IXE demonstrated sustained improvement in the signs and symptoms of PsA across treatment groups during the EP. The safety profile of IXE observed in the EP population was consistent with the safety profile of the intent-to-treat population in the DBTP of SPIRIT-P2.1


<table>
<thead>
<tr>
<th>Week 52 Respondent Rate, N (%)</th>
<th>IXE Q4W (N=111)</th>
<th>IXE Q2W (N=107)</th>
<th>PBO/IXE Q4W (N=46)</th>
<th>PBO/IXE Q2W (N=46)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACR20</td>
<td>33/111 (30)</td>
<td>32/107 (30)</td>
<td>15/36 (43)</td>
<td>15/36 (43)</td>
</tr>
<tr>
<td>ACR50</td>
<td>20/111 (18)</td>
<td>19/107 (18)</td>
<td>8/36 (22)</td>
<td>8/36 (22)</td>
</tr>
<tr>
<td>ACR70</td>
<td>12/111 (11)</td>
<td>12/107 (11)</td>
<td>6/36 (17)</td>
<td>6/36 (17)</td>
</tr>
<tr>
<td>MDA</td>
<td>32/107 (30)</td>
<td>31/107 (30)</td>
<td>14/36 (39)</td>
<td>14/36 (39)</td>
</tr>
<tr>
<td>LFI (0)†</td>
<td>2/11 (2)</td>
<td>2/10 (2)</td>
<td>0/4 (0)</td>
<td>0/4 (0)</td>
</tr>
<tr>
<td>LDI-B (0)†</td>
<td>21/26 (19)</td>
<td>21/26 (20)</td>
<td>8/22 (18)</td>
<td>8/22 (18)</td>
</tr>
<tr>
<td>PASI63</td>
<td>41/62 (67)</td>
<td>41/62 (67)</td>
<td>18/23 (78)</td>
<td>18/23 (78)</td>
</tr>
<tr>
<td>PASI80°</td>
<td>34/62 (55)</td>
<td>34/62 (55)</td>
<td>15/23 (65)</td>
<td>15/23 (65)</td>
</tr>
<tr>
<td>NAPSI (0)°</td>
<td>41/81 (51)</td>
<td>41/81 (51)</td>
<td>9/29 (32)</td>
<td>9/29 (32)</td>
</tr>
</tbody>
</table>

Week 52 Mean (SD) Change from Baseline

Table: Efficacy and Safety Results of an Interim Analysis of the Extension Period Population of SPIRIT-P2. For efficacy analyses, baseline was defined as assessment recorded on or prior to Week 0. For analyses of TEAEs, baseline was defined as AE that started prior to the study drug injection at Week 26. *Assessed only in patients with enthesitis and LFI-0 at baseline. †Assessed only in patients with psoriatic lesions ≥3% of BSA at baseline. ‡Assessed only in patients with finger/nail psoriasis at baseline.

Disclosures: M. C. Genovese, Eli Lilly and Company, Abbvie, Astellas, Galapagos, Pfizer, Vertex, Crescendo Bioscience, 5; B. Combe, Pfizer, UCB, 2, BMS, Janssen, Lilly, MSD, Pfizer, Roche-Chugai, UCB, 8, Abbvie, BMS, Janssen, Lilly, MSD, Novartis, Pfizer, Roche-Chugai, UCB, 5; J. Kremer, Abbvie, Amgen, BMS, Genentech, GSK, Eli Lilly and Company, Novartis, Pfizer, 5, Abbvie, Genentech,
Inhibition of Radiographic Progression in Psoriatic Arthritis By Adalimumab Independent of the Control of Clinical Disease Activity

Robert B.M. Landewé1, Christopher T. Ritchlin2, Laura C Coates3, Daniel Aletaha4, Benoît Guérette5, Ying Zhang5, Fabiana Ganz6 and Maja Hojnik7, 1University of Amsterdam, Amsterdam, Netherlands, 2Division of Allergy, Immunology and Rheumatology, School of Medicine and Dentistry, Division of Allergy, Immunology and Rheumatology, School of Medicine and Dentistry, University of Rochester, Rochester, New York, USA, Rochester, NY, 3University of Leeds and Leeds Teaching Hospitals NHS Trust, Leeds, Great Britain, 4Department of Medicine III, Division of Rheumatology, Medical University of Vienna, Vienna, Austria, 5AbbVie Inc., North Chicago, IL, 6AbbVie AG, Baar, Switzerland, 7AbbVie, Ljubljana, Slovenia

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment V
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose: Patients (pts) with psoriatic arthritis (PsA) may experience structural damage and irreversible functional impairment if not treated appropriately. Treatment with TNF inhibitors in rheumatoid arthritis (RA) pts showed inhibition of radiographic progression larger than expected based on the control of clinical disease activity.1 Preliminary results showed that such a disconnect phenomenon may also be observed in PsA pts following treatment with adalimumab (ADA).2 The objective of this analysis was to further examine the relationship between inhibition of radiographic progression and control of clinical disease activity using different disease activity measures following treatment with originator ADA versus placebo (PBO) in pts with active PsA.

Methods: ADEPT3 was a 24-week (wk), randomized, double-blind trial comparing the safety and efficacy of ADA with PBO in pts with active PsA. In this post hoc analysis, radiographic progression, defined as change from baseline (BL) to wk 24 in modified total Sharp score (ΔmTSS) >0.5, was calculated in pts with evaluable radiographs at both time points. Pts were classified based on achieving minimal disease activity (MDA) and different subcategories of disease activity (remission, low, moderate, or high) based on time-averaged (TA) DAS28(CRP), DAPSA, and PASDAS. The associations between ΔmTSS and disease activity were assessed by Pearson (r_p) or Phi (r_ϕ) correlation coefficients.

Results: Of the 296 pts (ADA, N=144; PBO, N=152) included in this analysis, higher proportions of pts receiving ADA compared with PBO achieved MDA and remission/low disease activity status across all the outcome measures. There was a significant interaction between treatment and disease activity status with respect to radiographic progression (P<0.001 for all outcome measures). In addition, treatment with ADA for 24 wks compared with PBO resulted in significantly lower mean ΔmTSS even in pts with moderate or high disease activity (TA-DAPSA or TA-PASDAS) or not achieving MDA (Table). Radiographic progression showed a weak, but significant correlation with disease activity status in pts treated with PBO (r_p ≥0.3, P<.001 for TA-DAS[CRP], TA-DAPSA, and TA-PASDAS; r_ϕ=−0.14 [95% CI:−0.20 to −0.09 for MDA]), but not ADA.
Conclusion: The results showed that the relationship between disease activity as determined by various outcome measures differed between ADA and PBO treated pts. ADA provided inhibition of radiographic progression which was somewhat larger and independent of the control of clinical disease activity. This supports the disconnect phenomenon in PsA following ADA treatment.

References:

Table. Change from Baseline to Week 24 in modified Total Sharp Score (ΔmTSS) categorized by Disease Activity Status Across Each Outcome Measure in ADA and PBO Treated Patients.

<table>
<thead>
<tr>
<th>Outcome measure Mean (SD)</th>
<th>ΔmTSS</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>TA-DAS28(CRP)†</td>
<td>ADA</td>
<td>PBO</td>
</tr>
<tr>
<td>Remission (≤2.6)</td>
<td>n = 144</td>
<td>n = 152</td>
</tr>
<tr>
<td>Low disease activity (≥2.6-5.2)</td>
<td>-0.2 (1.3)</td>
<td>0.6 (1.7)</td>
</tr>
<tr>
<td>Moderate disease activity (≥5.2)</td>
<td>0.2 (1.3)</td>
<td>1.5 (3.6)</td>
</tr>
<tr>
<td>High disease activity</td>
<td>1.7 (2.9)</td>
<td>4.9 (8.2)</td>
</tr>
<tr>
<td>TA-DAPSA†</td>
<td>ADA</td>
<td>PBO</td>
</tr>
<tr>
<td>Remission (≤5)</td>
<td>n = 144</td>
<td>n = 152</td>
</tr>
<tr>
<td>Low disease activity (≥5-11)</td>
<td>-0.2 (1.0)</td>
<td>0.0 (0.0)</td>
</tr>
<tr>
<td>Moderate disease activity (≥11-28)</td>
<td>-0.2 (1.4)</td>
<td>0.4 (1.0)</td>
</tr>
<tr>
<td>High disease activity (≥28)</td>
<td>-0.1 (1.8)</td>
<td>1.4 (3.5)</td>
</tr>
<tr>
<td>TA-PASDAS†</td>
<td>ADA</td>
<td>PBO</td>
</tr>
<tr>
<td>Low disease activity (≤3.2)</td>
<td>n = 136</td>
<td>n = 150</td>
</tr>
<tr>
<td>Moderate disease activity (≥3.2-5.4)</td>
<td>-0.4 (1.5)</td>
<td>0.4 (1.3)</td>
</tr>
<tr>
<td>High disease activity (≥5.4)</td>
<td>0.2 (1.9)</td>
<td>2.0 (4.3)</td>
</tr>
<tr>
<td>MDA‡</td>
<td>ADA</td>
<td>PBO</td>
</tr>
<tr>
<td>Yes</td>
<td>n = 139</td>
<td>n = 148</td>
</tr>
<tr>
<td>No</td>
<td>-0.2 (1.3)</td>
<td>1.1 (3.1)</td>
</tr>
</tbody>
</table>

*P-value for difference between treatment groups is based on ANCOVA.
†Time averaged (TA) variable is calculated as area under the curve (AUC) of that variable and standardized by length of study (24 weeks).
‡Minimal disease activity (MDA) was calculated in patients with at least 5 out of 7 MDA components available.
ADA = adalimumab, PBO = placebo; TA = time-averaged; DAS28(CRP) = 28-joint disease activity score based on C-reactive protein, DAPSA = disease activity index for psoriatic arthritis; PASDAS = psoriatic arthritis disease activity score; index; MDA = minimal disease activity; ANCOVA = analysis of covariance.

Disclosure: R. B. M. Landewé, Abbott/AbbVie, Ablynx, Amgen, Astra-Zeneca, BMS, Janssen (formerly Centocor), GSK, Merck, Novo-Nordisk, Novartis, Pfizer, Roche, Schering-Plough, TiGenics, UCB, and Wyeth, 5,Abbott/AbbVie, Ablynx, Amgen, Astra-Zeneca, BMS, Janssen (formerly Centocor), GSK, Merck, Novo-Nordisk, Novartis, Pfizer, Roche, Schering-Plough, TiGenics, UCB, and Wyeth, 9,Rheumatology Consultancy BV, 9,Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB and Wyeth, 2,Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB and Wyeth, 9,C. T. Ritchlin, Amgen, Janssen, Pfizer, and UCB, 9; L. C. Coates, AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Sun Pharma, and UCB, 2,AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Sun Pharma, and UCB, 9; D. Aletaha, AbbVie, BMS, Lilly, Pfizer, Merck, Medac, UCB, Mitsubishi/Tanabe, Janssen, and Roche, 2,AbbVie, BMS, Lilly, Pfizer, Merck, Medac, UCB, Mitsubishi/Tanabe, Janssen, and Roche., 9; B. Guérette, abbvie, 3,Abbvie, 1; Y. Zhang, AbbVie, 3,AbbVie, 1; F. Ganz, Abbvie, 1,AbbVie, 3; M. Hojnik, Abbvie, 1,abbvie, 3.

What Do Reduced 28 Joint Counts Miss in Patients with Psoriatic Arthritis?

Andreas Kerschbaumer1, Josef S. Smolen1,2 and Daniel Aletaha1, 1Medical University Vienna, Division of Rheumatology, Department of Internal Medicine III, Vienna, Austria, 2nd Department of Medicine, Hietzing Hospital, Vienna, Austria

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment V
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose:
Clinical joint assessment by the rheumatologist is a key examination of patients with psoriatic arthritis (PSA). A clinically swollen joint is predicting subsequent joint damage. Since joint assessment is regarded time-consuming, a tension exists between comprehensiveness, e.g. using complete joint counts (JC; 76/78 or 66/68), and feasibility. Reduced JC, such as the 28 joint count, however, may be less valuable in PSA than RA due to differences in joint patterns.

Here, we examined the validity of a reduced 28 swollen and tender JC, using the extended JCas comparators.

Methods:
We analyzed data from a random subset of 80% of patients enrolled in the ADEPT (n=264) and the IMPACT-2 trial (n=163). In ADEPT a 76/78 JC was performed, in IMPACT-2, it was the 66/68 JC only. At week 24 of the two trials, patients with a complete absence of SJC or TJC by the 28-count were analyzed for their residual joint activity. Sensitivity and NPV for each joint count were calculated for each study. Finally, we analyzed the residual tender and swollen joints of 76/78 and 66/68 JC remained active in patients with a 28-joint count of 0 at endpoint.

Results:
As summarized in table 1, investigation of SJC at week 24 in ADEPT showed that 63 of all 264 patients (23.9 %) achieved a SJC28=0; of these 63 patients, 51 (81%) also had a SJC66=0 and 50 (79.4 %) had a SJC76=0. Twelve and 13 patients, respectively, had residual SJC76 or SJC66 while having a SJC28=0. Of the 52 patients with a TJC28=0, 41 and 39, respectively, had also TJC78=0 and TJC68=0, while 11 and 13 patients had residual TJC68 or TJC78.

In IMPACT2, 50 of 163 patients (30.7%) achieved SJC28 remission, with 15 patients (30%) of these remaining active by SJC66. TJC28 remission was achieved by 44 patients, with 17 patients (38.6 %) not achieving complete TJC68 remission.

Exploration of individual residual swollen and tender joints showed mainly foot and ankle joints being active/tender at week 24, as can be seen in figure 1.

Conclusion:
Absence of swelling by the 28 joint count in PsA seems to not adequately reflect the situation of all relevant joints, as in at least one of four patients residual clinical activity is detectable by more comprehensive 76/78 and 66/68 joint counts. Assessment of ankle and foot joints, especially MTPs, contributed numerically most to the missed joints. These limitations should be considered when treating PsA patients to target.
Table 1: 28-joint counts versus 66/68 and 76/78 joint counts in ADEPT and IMPACT-2.

<table>
<thead>
<tr>
<th></th>
<th>ADEPT</th>
<th>SJC 66</th>
<th>SJC 76</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>TotalSensitivity</td>
<td></td>
</tr>
<tr>
<td>SJC28</td>
<td>51</td>
<td>12 63</td>
<td>0.81</td>
</tr>
<tr>
<td>SJC28&gt;0</td>
<td>0</td>
<td>201 201</td>
<td>NPV</td>
</tr>
<tr>
<td>Total</td>
<td>51</td>
<td>213 264</td>
<td>0.94</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>IMPACT-2</th>
<th>SJC 66</th>
<th>SJC 76</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TotalSensitivity</td>
<td></td>
<td>TotalSensitivity</td>
</tr>
<tr>
<td>SJC28</td>
<td>41</td>
<td>11 52</td>
<td>0.79</td>
</tr>
<tr>
<td>SJC28&gt;0</td>
<td>0</td>
<td>212 212</td>
<td>NPV</td>
</tr>
<tr>
<td>Total</td>
<td>41</td>
<td>223 264</td>
<td>0.95</td>
</tr>
</tbody>
</table>

Figure 1: Swollen (red) and tender (blue) joints for all patients at baseline (A+C) and patients JC28=0 at week 24 (B+D).

Disclosure: A. Kerschbaumer, None; J. S. Smolen, None; D. Aletaha, None.
Risk of Myocardial Infarction and Cerebrovascular Accident in Ankylosing Spondylitis: A General Population-Based Study

Anthony So¹, Jonathan Chan², Eric C. Sayre³ and J. Antonio Avina-Zubieta³,4,¹University of British Columbia, Vancouver, BC, Canada, ²Rheumatology, University of British Columbia, Vancouver, BC, Canada, ³Arthritis Research Canada, Richmond, BC, Canada, ⁴Division of Rheumatology, Department of Medicine, University of British Columbia, Vancouver, BC, Canada

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment V
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose: There is conflicting data on the risk of myocardial infarction (MI) and cerebrovascular accidents (CVA) in patients with Ankylosing Spondylitis (AS). This study attempts to assess the future risk of newly recorded MI and CVA events among incident cases of AS compared to non-AS controls from the general population by utilizing physician billing, medication, and hospitalization data that covers the entire province of British Columbia (BC), Canada.

Methods: Our data includes all outpatient visits and hospitalizations (1990-2012) and all dispensed medications (1996-2012) for all BC residents. We conducted a retrospective matched cohort study of all patients > 18 years of age satisfying the following criteria: 1) two ICD-9 or 10 codes (720.0 or M45) for AS at least two months apart and within a 2-year period by any physician or hospitalization; 2) all AS cases had at least a 7-year run-in period before the 1st ICD code for AS in order to consider the case as incident. Each AS patient was matched with up to 10 controls by birth year, sex, and entry cohort time. The outcomes were a newly recorded MI (ICD-9-CM: 410 or ICD-10-CM: I21) or CVA (ICD-9 codes: 433-434, ICD-10 codes: I63-I66) event from hospital or death certificates. We estimated relative risks (RRs), adjusting for age, sex, and entry cohort time as well as multivariable models adjusting for confounders including glucocorticoids and non-steroidal anti-inflammatory drugs using a Cox proportional hazard model.

Results: 7,190 individuals with newly diagnosed AS were identified (48.7% female, mean age of 45.8 yrs). 7,148 and 7,107 were free of previous CVA/MI, respectively. 80 developed CVA (incidence rate= 1.8 per 1000 patient years) and 115 had MI (incidence rate= 2.6 per 1,000 patient years) (Table 1). The age-, sex-, and entry-time-matched RR for CVA was 1.60 (95% CI, 1.25-2.03) and MI was 1.52 (95% CI, 1.24-1.85). When adjusted for cardiovascular risk factors (obesity, angina, COPD, hospitalizations in year before index date, Charlson’s comorbidity index, oral glucocorticoids, cardiovascular drugs, anti-diabetic medication, HRT, contraceptives, fibrates, statins, NSAIDs, and Cox-2 inhibitors), the estimated RR was 1.34 (1.04-1.73) for CVA and 1.21 (0.98-1.49) for MI.

Conclusion: This large population-based study demonstrates an increased risk of CVA, but not for MI. These findings support that increased monitoring for this potentially fatal outcome and its modifiable risk factors is warranted for AS patients.

Table 1: Relative risk of incident CVA and MI according to AS status
<table>
<thead>
<tr>
<th></th>
<th>AS (N=7,148)</th>
<th>Non-AS (N=71,489)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CVA events, n</strong></td>
<td>80</td>
<td>492</td>
</tr>
<tr>
<td><strong>Incidence Rate of CVA /1000 Person-Years</strong></td>
<td>1.81</td>
<td>1.13</td>
</tr>
<tr>
<td><strong>Incidence Rate Ratio of CVA (95% CI)</strong></td>
<td>1.60 (1.25-2.03)</td>
<td>1.0</td>
</tr>
<tr>
<td><strong>Multivariable RR of CVA (95% CI)</strong></td>
<td>1.34 (1.04-1.73)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>AS (N=7,107)</th>
<th>Non-AS (N=71,033)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MI events, n</strong></td>
<td>115</td>
<td>748</td>
</tr>
<tr>
<td><strong>Incidence Rate of MI /1000 Person-Years</strong></td>
<td>2.62</td>
<td>1.73</td>
</tr>
<tr>
<td><strong>Incidence Rate Ratio of MI (95% CI)</strong></td>
<td>1.52 (1.24-1.85)</td>
<td>1.0</td>
</tr>
<tr>
<td><strong>Multivariable RR of MI (95% CI)</strong></td>
<td>1.21 (0.98-1.49)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Disclosure: A. So, None; J. Chan, None; E. C. Sayre, None; J. A. Avina-Zubieta, None.


Abstract Number: 2973

Detection of Clinical Signs of Arthritis and Subclinical Evidence of Inflammation in Psoriasis Patients with Risk for Arthritis: Value of Clinical Examination, Ultrasound and Fluorescence-Optical Imaging – Results from the Prospective Multicentre Xciting Study

**Michaela Koehm**¹, Tanja Rossmannith², Hans-Eckhard Langer³, Marina Backhaus⁴, Gerd R. Burmester⁵, Siegfried Wassenberg⁶, Benjamin Köhler⁶, Harald Burkhardt⁷ and Frank Behrens⁸, ¹Division of Rheumatology and Fraunhofer IME-Project-Group Translational Medicine and Pharmacology, Goethe University, Frankfurt/Main, Germany, ²Fraunhofer Institute for Molecular Biology and Applied Ecology IME, Project Group Translational Medicine & Pharmacology TMP, Frankfurt, Germany, ³RHIO (Rheumatology, Immunology, Osteology) Duesseldorf, Duesseldorf, Germany, ⁴Rheumatology, Park-Klinik Weissensee, Berlin, Germany, ⁵Department of Rheumatology and Clinical Immunology, Charité - University Medicine Berlin, Free University and Humboldt University Berlin, Berlin, Germany, ⁶Rheumazentrum Ratingen, Ratingen, Germany, ⁷Division of Rheumatology and Fraunhofer IME-Project-Group Translational Medicine and Pharmacology, Goethe University, Frankfurt, Germany, ⁸Clinical Research Rheumatology and Fraunhofer Institute IMETranslation, Goethe University, Frankfurt, Germany

**First publication:** September 18, 2017

**SESSION INFORMATION**
**Session Date:** Wednesday, November 8, 2017
**Session Title:** Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment V
**Session Type:** ACR Concurrent Abstract Session
**Session Time:** 11:00AM-12:30PM

**Background/Purpose:** Psoriasis (Pso) is one of the most common chronic inflammatory skin diseases in Europe. Psoriatic arthritis (PsA) is closely associated to Pso whereas the skin manifestation appears usually years before PsA-related symptoms emerge. Biomarkers for its early detection are missing In early PsA manifestations, changes in synovial vascularisation combined with increased...
expression of proangiogenic factors appear first. Therefore, imaging biomarkers for detection of changes in vascularisation can be useful for early detection of joint disease. Fluorescence-optical imaging (FOI) is a new method to detect changes in microvascularisation of the hands and might be of value in early detection of (subclinical) signs of inflammation in Psoriasis patients

**Methods:** 411 patients with dermatologically confirmed Pso were included without diagnosis of PsA but risk factors for its development (nail psoriasis and/or joint pain or swelling within the last 6 months). Clinical examination (CE; swollen (66) and tender (68) joint count, enthesitis, dactylitis assessment) and standardised ultrasound (US) assessment was performed by a qualified rheumatologist to assess PsA symptoms. Additionally, FOI was performed. Data was analysed for an increased vascularisation of musculoskeletal structures of hands as marker of inflammation. In cases of discrepant results (positive FOI and negative results for CE and US), MRI was performed to validate the FOI-surrogate indicator of inflammation. Patients with negative MRI results are followed up over a 24-month period (XTEND) to evaluate rate of PsA-development.

**Results:** 45.5% of the Pso patients (mean age 55.8 years, 57% female, baseline BSA 6.6%, mean duration of Pso 19.1 years) were diagnosed positive for PsA by rheumatologists either by CE (32%) or US. In a total 73.3% of the patients an increase of fluorescence signal intensities of the hands was detectable by FOI (figure 1). In 22% of the patients neither in CE and US nor in FOI any signs of musculoskeletal inflammation could be detected. In 38% of the patients suspected inflammation by FOI was confirmed by MRI scan. 13.1% of the patients were identified for follow-up measurement in XTEND.

**Conclusion:** In this cohort of patients with active Pso and not yet diagnosed PsA, more than 40% of the patients were classified as PsA by CE and US only. Additionally, in another 28.7% signs of inflammation were detected by FOI technique while MRI scan was only positive in 38% of these patients. FOI might have the potential for early detection of musculoskeletal involvement in patients with Pso. Its possible high sensitivity in the detection of inflammation will be further evaluated: patients with positive FOI and negative MRI will be repetitively re-evaluated for a 24-month follow-up period to evaluate the predictive value of positive FOI in development of (clinical) active PsA.

**Disclosure:** M. Koehm, Pfizer Inc, 2; T. Rossmanith, Pfizer Inc, 2; H. E. Langer, Pfizer Inc, 2; M. Backhaus, None; G. R. Burmester, AbbVie Inc., Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB, 5; AbbVie Inc., Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB, 5; S. Wassenberg, AbbVie, Chugai, Janssen Biologics, MSD, Novartis, Pfizer, Roche, and UCB, 5; B. Köhler, None; H. Burkhardt, Pfizer Inc, 2; F. Behrens, Abbvie, Pfizer, Chugai, Prophylux, Bioline, Novartis, 2, Abbvie, Pfizer, Roche, Chugai, UCB, BMS, Celgene, MSD, Novartis, Biotech, Janssen, Genzyme, Eli Lilly and Company, 5; Abbvie, Pfizer, Roche, Chugai, UCB, BMS, Celgene, MSD, Novartis, Biotech, Janssen, Genzyme, Eli Lilly and Company, 8.


**Abstract Number:** 2974

**B Cell Binding Autoreactive VH4.34 Antibodies Are Specific to Lupus, Consist of Diverse Isotypes, and Are Associated with High Disease Activity and Lupus Nephritis**

**Scott Jenks**1, Joseph Marcus2, Kevin Cashman1 and Ignacio Sanz3,

1Emory University School of Medicine and Lowance Center for Human Immunology, Atlanta, GA, 2San Antonio Uniformed Services Health Education Consortium, San Antonio, TX, 3Rheumatology
Background/Purpose: SLE is characterized by the dysregulation of humoral immunity including high levels of autoreactive IgG VH4.34 antibodies recognized by the rat anti-human idiotypic antibody 9G4 (9G4+). VH4.34 antibodies have a germ line encoded anti-self specificity for blood antigen glycolipids and glycolipid epitopes of the B220 isoform of CD45 expressed on naïve B cells. As a consequence, naïve B cells from SLE patients can have high levels of 9G4 staining ex vivo due to surface bound VH4.34 antibodies. Serum 9G4+ IgG is correlated with high disease activity, lupus nephritis and anti-dsDNA. The role of B cell binding (BCB) 9G4+ in lupus pathogenesis and its potential clinical correlates is unclear.

Methods: 161 SLE (4 or more ACR criteria) patients were analyzed, including 24 patients with active nephritis. SLE patients were compared to 30 healthy controls or 15 RA, 15 Dermatomyositis, 26 scleroderma, and 7 pSS patients analyzed as autoimmune controls. 9G4+ BCB was measured ex vivo by flow cytometry and BCB was quantified as the ratio of the median fluorescence intensity of naïve B cells to that of switched memory. The resulting B cell binding ratio (BR) ranged from 1 (no binding) to 20 (very high binding) patients with a BR higher than 2.5 were considered positive. 9G4+ IgG, IgM, and IgA were measured by ELISA, capturing with the rat monoclonal 9G4 and detecting with goat anti-human IgG, IgM, or IgA.

Results:

BCB binding was highly specific for SLE as 33% of SLE patients were BCB positive compared to only 1.6% of autoimmune control patients and none of the HCD. Lupus patients with high disease activity or active nephritis were significantly more likely to have BCB than patients with low disease activity (47% and 54% as compared to 24% for low disease activity). When we compared BR to serum 9G4+ IgG concentration we found only a weak correlation (p=0.04, r=0.26). However, SLE patients had elevated 9G4+ IgM and IgA and the concentration of these isotypes was more strongly correlated with BCB (IgM p >0.001, r= 0.586) (IgA p>0.001, r=0.4602 ). IgA BCB was demonstrated directly by the detection of both surface 9G4 and IgA staining of healthy control donor naïve B cells after incubation with serum from an SLE patient. Patients with high BR had higher disease activity (p=0.021) and were more likely to have a history lupus nephritis (p=0.002) but this was not true for serum 9G4+ isotypes measure in either isolation or combination.

Conclusion:

The degree of B cell bound 9G4+ in some SLE patients is striking. Here we show that this auto-reactivity is specific to lupus and is more common in patients with active disease and active lupus nephritis. Interestingly, this association between B cell bound 9G4+ and disease activity is stronger than the association between serum 9G4+ IgG. As suggested by our data, this may be consequence of BCB measuring 9G4+ antibodies of multiple isotypes. The combination of IgA and IgG anti-dsDNA is more predictive of disease activity than either isotype alone and the same may be true for BCB 9G4+. In this light our finding that 9G4+ IgA is elevated in SLE patients and can bind B cells is intriguing. BCB 9G4+ may be a useful assay for stratifying SLE patients into clinically and immunologically distinct groups in future clinical and mechanistic studies.

Disclosure: S. Jenks, None; J. Marcus, None; K. Cashman, None; I. Sanz, None.


Abstract Number: 2975

Using Immune and Metabolic Phenotyping to Understand the Immunopathogenesis of Juvenile-Onset SLE and Stratify Patient Groups

George Robinson1, Marsilio Adriani1, Ines Pineda Torra2, Yiannis Ioannou3 and Elizabeth Jury4, 1Centre for Rheumatoloy Research, University College London, London, United Kingdom, 2Centre for Clinical Pharmacology, University College London, London, United Kingdom, 3Arthritis Research UK Centre for Adolescent Rheumatology, University College London, London, United Kingdom, 4Division of Medicine, Centre for Rheumatology Research, University College London, London, United Kingdom
**Background/Purpose:**

Juvenile-onset systemic lupus erythematosus (JSLE) is an autoimmune disorder characterized by immune cell dysregulation, chronic inflammation and increased cardiovascular risk. Disease onset dominates mid-puberty and the female to male ratio is 4.5:1, suggesting a hormonal importance in disease pathogenesis. JSLE patients have more aggressive disease, more major organ involvement and increased standardised mortality ratios compared to patients with adult-onset SLE yet research into JSLE is uncommon. Our previous findings show that defects in immune cell lipid metabolism contribute to disease pathogenesis in adult-onset SLE. However, in JSLE little is known about the immune profile or whether abnormal lipid metabolism also contributes to pathogenesis. Here we performed in depth immune and metabolic profiling in a cohort of JSLE patients and age and gender matched healthy donors (HCs).

**Methods:**

Flow cytometry was carried out using two 15-colour panels to immune-phenotype peripheral blood mononuclear cells from 39 healthy donors (HCs, 17 male, 22 female, mean age 18) and 35 JSLE patients (12 male, 23 female, mean age 19). Data was analysed by cluster and phenotype–phenotype correlation. Flow cytometry was also used to measure functional and metabolic marker expression on immune cell subsets. Data was correlated with clinical assessments of disease.

**Results:**

Patients with JSLE were characterised by increased naïve and decreased memory B-cell and T-cell subsets and increased monocyte frequency (p=0.0013) compared to HCs. Furthermore, phenotype-phenotype correlation analysis identified differential associations between naïve and memory immune cell subtypes when comparing the HC and JSLE cohorts.

CD4+ and CD8+ T-cells from JSLE patients had elevated membrane lipid raft (p=0.0185, p=0.0087) and glucose transport receptor (GLUT-1) (p=0.0205, p=0.0017) expression suggesting that they were more metabolically active. Metabolic defects were also found in monocytes and plasmacytoid dendritic cells. The expression of these metabolic markers on different subsets correlated with cell frequency suggesting a role of cell metabolism in driving the JSLE phenotype. Furthermore the metabolic immune-phenotype in JSLE correlated positively with disease activity, erythrocyte sedimentation rate and dsDNA titre and negatively with complement protein C3 supporting the hypothesis that altered metabolism is associated with JSLE development and severity.

Unsupervised hierarchical cluster analysis of patient clinical data revealed that JSLE patients in this cohort could be stratified into 5 groups each with a unique clinical identity mainly associated with disease activity markers and the presence of anti-cardiolipin antibodies. Each group had a unique immune-phenotype and metabolic profile.

**Conclusion:**

Differences in the metabolic profiles of immune cell subsets in JSLE contribute to disease pathogenesis and severity. Cellular metabolic regulators may therefore have therapeutic benefit for JSLE patients. Defining these patient groups further may help to determine the therapeutic benefit of these and other therapeutics and allow for the treatment patients in a more effective and personalised manner.

**Disclosure:** G. Robinson, None; M. Adriani, None; I. Pineda Torra, None; Y. Ioannou, None; E. Jury, None.


**Abstract Number:** 2976

**Identification of Systemic Lupus Erythematosus Causal Risk Variant Candidates Spanning the UBE2L3 Haplotype**

Jaanam Gopalakrishnan1,2, Shaofeng Wang3, Yao Fu4, Satish Pasula1, Ajay Nair1, Mandi Wiley1 and Patrick Gaffney2,4, 1Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 2Department of Pathology,
Molecular Phenotypes Associated with Clinical Disease Activity in Adult Systemic Lupus Erythematosus

Rufei Lu1, Joel M. Guthridge2, Cristina Arriens3, Teresa Aberle4, Stan Kamp4, Melissa E. Munroe4, Tim Gross1, Wade DeJager4, Susan Macwana4, Virginia C. Roberts4, Stephen Apel5, Hua Chen4, Eliza Chakravarty6,7, Katherine Thanou4, Joan T. Merrile7 and Judith A. James8, 1Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 2Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, OKC, OK, 3Arthritis & Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, 4Arthritis and Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK, 5Oklahoma Medical Research Foundation, Oklahoma City, OK, 6Clinical Immunology, Oklahoma

Disclosure: J. Gopalakrishnan, None; S. Wang, None; Y. Fu, None; S. Pasula, None; A. Nair, None; M. Wiley, None; P. Gaffney, None.

Abstract Number: 2977
Background/Purpose: Remarkable clinical and pathophysiological diversity complicate diagnosis, treatment and therapeutic development in systemic lupus erythematosus (SLE). This study used molecular phenotyping to identify more homogeneous subsets of lupus patients.

Methods: Plasma, serum and RNA serial or single samples (n=290) were collected from 184 SLE patients who met ACR classification. Disease activity was assessed by modified SELENA-SLEDAI. Immune pathways were evaluated by modular transcriptional analysis of Illumina Beadchip Microarray gene expression data. Plasma soluble mediators (n=32) and 13 antinuclear autoantibodies (anti-dsDNA, chromatin, ribosomal P, Sm, Sm/RNP, RNP, centromere B, Scl-70 and Jo-1) were assessed by multiplex, bead-based assay and ELISAs. Spearman correlations were used for univariate and multivariate analysis using R. Patients were clustered on transcriptional module scores and soluble mediators using Random Forest and tSNE.

Results: We identified seven clusters of SLE patients with distinct molecular profiles. Cluster 4 had the highest inflammation and interferon (IFN) signatures, followed by Cluster 1. These clusters differed in IFN, T cell and inflammation module scores. Other clusters showed no elevation of IFN nor inflammation modules, but were distinguished by monocyte, neutrophil, plasma cell and T cell module scores. All three IFN expression modules strongly correlated with circulating IFN-related mediators, including IFNa, IFNg, IP10, MCP1, MIG, MIP1a, and MIP1b. The clusters with high IFN and inflammation scores had elevated IL-10, as did Cluster 6, which had the highest plasma cell module score and had only moderate IFN and inflammation module scores. Clinically, Clusters 1 and 4 were similar, displaying the highest SLEDAI scores, as well as increased rates of low complement, DNA binding antibodies, proteinuria and hematuria. Cluster 2 showed slight elevations in IFN and inflammation modules, but had low SLEDAI scores and reduced prevalence of low complement and DNA binding antibodies. Clusters 3, 5, 6, and 7 had higher rates of rash, alopecia and arthritis.

Conclusion: Molecular profiles encompassing IFN, T cell, neutrophil, plasma cell, and inflammation signatures distinguish groups of SLE patients and reveal multiple potential pathways of clinical disease. These profiles can potentially contribute to clinical trial design and individualized treatment.

Disclosure: R. Lu, None; J. M. Guthridge, None; C. Arriens, Exagen, 2; T. Aberle, None; S. Kamp, None; M. E. Munroe, None; T. Gross, None; W. DeJager, None; S. Macwana, None; V. C. Roberts, None; S. Apel, None; H. Chen, None; E. Chakravarty, None; K. Thanou, None; J. T. Merrill, Anthera Pharmaceuticals, Lilly, EMD Serono, GlaxoSmithKline and Biogen., 5; J. A. James, None.
OX40/OX40L Axis Impairs Follicular and Natural Regulatory T Cell Function in Human Systemic Lupus

Christophe Richez1, Jean-Francois Augusto2, Clement Jacquemin3, Estibaliz Lazaro4, Marie-Elise Truchetet1, Noémie Gensous5, Isabelle Douchet5, Thierry Schaeverbeke6, Cécile Contin-Bordes7 and Patrick Blanco7,1

1Department of Rheumatology, Bordeaux University Hospital, Bordeaux, France, 2Department of Nephrology, Angers University Hospital, Angers, France, 3Université de Bordeaux, Bordeaux, France, 4Department of Internal Medicine and Clinical Immunology, Bordeaux University Hospital, Pessac, France, 5UMR CNRS 5164, Bordeaux, France, 6Department of Rheumatology, Bordeaux University Hospital, BORDEAUX, France, 7Immunology, Department of Immunology, Bordeaux University Hospital, Bordeaux, France

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis II
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose:
Regulatory T cells (Treg) are impaired in human Systemic Lupus Erythematosus (SLE) and contribute to T cell activation. However, the mechanisms responsible for the Treg deficiency in SLE remain unclear. Our group recently reported that OX40L was expressed by myeloid APCs in blood and in inflamed tissues of SLE patients. OX40L stimulation induced human CD4+ T cells to express TFH associated molecules, and was sufficient to induce memory and naïve CD4+ T cells to become functional B cell helpers.

OX40L has been also shown to block Treg functions both in mice and in humans. We hypothesized that OX40L/OX40 axis was implicated in Treg and regulatory follicular helper T cell (TFR) dysfunction in human SLE.

Methods: Flow cytometry was used for analysis of cell surface and intracellular molecules expressed on blood cells of SLE patients (n = 61) and healthy donors (HD)(n = 16). Using recombinant sOX40L, in vitro-generated SLE-DCs expressing OX40L, and DCs from patients, the impact of OX40/OX40L axis on the function of cTregs (CD4+CXCR5-CD25high Foxp3+) and TFR (CD4+CXCR5+CD25high Foxp3+) purified from HD was studied in co-culture experiments.

Results:
OX40L/OX40 axis engagement on Tregs and TFR not only specifically impaired their ability to regulate T effector cells proliferation but also their ability to suppress TFH-dependent B cell activation, and immunoglobulin secretion. Indeed, we observed that soluble and membrane-bound OX40L decreased suppressive Treg function (p<0.05), without inducing Treg cell death. Treg suppressive function was restored when in vitro-generated SLE-DCs expressing OX40L were pre-incubated with a blocking anti-OX40L mAb. Furthermore, purified tonsils TFR cells previously cultured or not with sOX40L were cultured with purified TFH and memory B cells in the presence of SEB. We observed a higher immunoglobulin production and an increased differentiation of B cells into CD38+ plasmablasts in co-cultures with TFR exposed to sOX40L.

APCs from active SLE patients (n = 5) mediated Tregs dysfunction in an OX40L-dependent manner (mean % of inhibition 25.5±22 vs 72.9±9.6 with APCs purified from 7 HD, p=0.01). We also observed an inverse correlation between OX40L expression on SLE-APCs and their ability to hamper Tregs cell suppressive function (r=-0.85, p=0.0001).

OX40L-expressing cells co-localized with FoxP3 positive cells in active SLE skin lesions, suggesting that OX40L+ cells-Treg contact actually operates in vivo within inflammatory tissues.

In vitro, engagement of OX40L/OX40 axis resulted in FoxP3 down-regulation in Tregs. FoxP3 expression in SLE Tregs negatively correlated with the proportion of circulating OX40L-expressing mDCs, suggesting that OX40L-dependent Foxp3 down-regulation also operates in vivo.
Conclusion: These data support that OX40L/OX40 signals are implicated in T regulatory cell dysfunction in human SLE. Thus, blocking OX40L/OX40 axis appears as a promising therapeutic strategy.

Disclosure: C. Richez, None; J. F. Augusto, None; C. Jacquemin, None; E. Lazaro, None; M. E. Truchetet, None; N. Gensous, None; I. Douchet, None; T. Schaeverbeke, None; C. Contin-Bordes, None; P. Blanco, None.


Abstract Number: 2979

The Expression of Mitochondrial Molecules in Microparticle Immune Complexes in the Blood of Patients with Systemic Lupus Erythematosus

Fariborz Mobarrez1, Enrico Fuzzi1, Iva Gunnarsson1, David Pisetsky2 and Elisabet Svenungsson1, 1Rheumatology Unit, Department of Medicine, Karolinska Institute, Karolinska University Hospital, Stockholm, Sweden, 2Department of Medicine, Duke University Medical Center, Durham, NC

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Wednesday, November 8, 2017
Session Title: Systemic Lupus Erythematosus – Human Etiology and Pathogenesis II
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a prototypic autoimmune disease characterized by immune complexes, especially those with nuclear molecules bound by antinuclear antibodies. Although the source of these antigens is not fully known, increased apoptosis and defective clearance of dead cells have been proposed. During apoptosis and cell activation, microparticles (MPs) are released extracellularly. MPs are small membrane-bound particles that can contain molecules arising from both the nucleus and cytoplasm. Moreover, these MPs are often covered with immunoglobulins, thus forming MP-immune complexes (mplICs).

Methods: Plasma samples from 47 patients with SLE (4³ of 1982 ACR criteria) and 24 healthy controls were investigated. MPs and mplICs were analyzed by flow cytometry and defined by size; MPs (< 7.0 µm) or mplICs (> 7.0 µm). Samples were labeled with MitoTracker deep red FM to investigate mitochondrial content. Flow cytometry was also used to assess outer mitochondria markers by staining with anti-Tom-20 and anti-hexokinase I. The presence of IgG was evaluated with an anti-IgG reagent.

Results: Levels of both MPs and mplICs in SLE patients were significantly elevated compared to controls (Fig 1A). Although MP concentrations were higher than those of mplICs, mplICs contained more mitochondria compared to MPs (Fig 1B). mplICs also displayed IgG and exposed the outer mitochondria markers. The number of mplICs containing mitochondria correlated strongly to the presence of anti-dsDNA antibodies (Fig 2) as well as to levels of TNF-α (r² 0.2, p<0.05), IL-6 (r² 0.23, p<0.01) and IL-7 (r² 0.24, p<0.01). Moreover, compared to patients with inactive renal disease, patients with active renal disease had significantly higher levels of IgG-coated mplICs containing mitochondria (p<0.01). Patients with SLAM above 6, had significantly higher numbers of mplICs containing mitochondria and exposing outer mitochondria markers Tom-20 and hexokinase I (p<0.05).

Conclusion: MPs and mplICs are significantly more abundant in the blood of SLE patients compared to controls. Importantly, the majority of the mitochondria were present in the larger mplIC sup-population. Moreover, mplICs that contain mitochondria also display outer mitochondria markers, with levels correlating with levels of anti-dsDNA antibodies, disease activity and pro-inflammatory cytokines. mplICs may therefore contribute to SLE pathogenesis, with mitochondria representing a source of cell antigens that can trigger innate and adaptive immune responses as well as deposit in the tissue.
Chemokine CCL21 As a Potential Serum Biomarker for Pulmonary Arterial Hypertension in Systemic Sclerosis

Anna-Maria Hoffmann-Vold1, Roger Hesselstrand2, Håvard Fretheim1, Thor Ueland1, Arne K Andreassen1, Oyvind Midtvedt1, Torhild Garen1, Pål Aukrust1, John A Belperio3 and Øyvind Molberg1, 1Oslo University Hospital, Oslo, Norway, 2Lund University, Lund, Sweden, 3University of California, Los Angeles, Los Angeles, CA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics III
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose: Systemic sclerosis (SSc) is a major cause of pulmonary arterial hypertension (PAH). Murine models indicate key roles of chemokines CCL19/21 and their receptor CCR7 in lung inflammation leading to PAH. We aimed to assess the chemokine CCL19/21 axis in SSc-PAH.
**Methods:** Sera from two independent prospective SSc cohorts including Oslo University Hospital (OUH, n=298) and Lund University Hospital (LU, n=28), idiopathic PAH (n=12) and controls (n=100) were analysed for CCL19/CCL21 by ELISA. Levels were defined as high or low using \([\text{mean} + 2\text{SD}]\) in controls as cut-off. Risk stratification at time of PAH diagnosis was performed according to 2016 European Society of Cardiology guidelines. PAH related events were defined as; (a) PAH progression (b) end-stage PAH (c) hospitalization for PAH worsening and (d) all-cause mortality. Cellular sources of CCL21 and CCR7 within SSc-PAH lung tissue were determined by immunohistochemistry.

**Results:** CCL21 was higher in SSc than controls, and stable across time of PAH diagnosis. Clinical and demographics are shown in Table 1. 129/298 SSc patients underwent RHC at OUH, 41 were diagnosed with PAH and 25 with PH-ILD; at LU 16 patients had PAH. PAH was more frequent in patients with high CCL21 (>0.4 ng/ml) than low CCL21 (33.3\% versus 5.3\%, \(p<0.001\)) and higher than in PH-ILD and idiopathic PH (Figure 1). In multivariate analyses, CCL21 was associated with PAH (HR 5.1 95\% CI 2.39-10.76, \(p<0.001\)) and predictive for new onset PAH (HR 3.3, 95\% CI 1.52-7.10, \(p=0.003\)). CCL21 was associated with occurrence of PAH related events (HR 4.7, 95\%CI 2.12-10.46, \(p<0.001\)). Risk stratification at PAH diagnosis alone did not predict PAH related events, but when combined with CCL21 (HR 1.3, 95\% C 1.03-1.60, \(p=0.027\)). Survival at 5- and 10-years differed between high and low CCL21 subsets (87\% and 71\% versus 96\% and 91\%, \(p<0.001\)). Main cellular sources of CCL21 in SSc-PAH lungs were vascular endothelial cells and circulating mononuclear cells (Figure 2), while CCR7 marked infiltrating vascular wall mononuclear cells.

**Conclusion:** CCL21 appears as a promising marker for SSc-PAH risk prediction and PAH progression. CCL21 may be part of a deregulated immune pathway linked to development of lung vascular damage in SSc.

<table>
<thead>
<tr>
<th>Table 1:</th>
<th>Total</th>
<th>SSc-PH</th>
<th>iPAH</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PAH</td>
<td>PH-ILD</td>
<td></td>
</tr>
<tr>
<td>OUH (n=298)</td>
<td>56 (13.9)</td>
<td>66.8 (8.2)</td>
<td>68.6 (10.3)</td>
</tr>
<tr>
<td>LU (n=16)</td>
<td>12.1 (10.8)</td>
<td>15.2 (6.5)</td>
<td>8.7 (5.6)</td>
</tr>
<tr>
<td>OUH (n=12)</td>
<td>0 (0)</td>
<td>40.3 (14.5)</td>
<td></td>
</tr>
<tr>
<td>Age at onset, yrs</td>
<td>68.6 (10.3)</td>
<td>59.5 (10.2)</td>
<td></td>
</tr>
<tr>
<td>Time from onset to PH, yrs</td>
<td>n.a.</td>
<td>15.2 (6.5)</td>
<td>8.7 (5.6)</td>
</tr>
<tr>
<td>Time from sera sampling to PH, yrs</td>
<td>12.1 (10.8)</td>
<td>15.2 (6.5)</td>
<td>8.7 (5.6)</td>
</tr>
<tr>
<td>Males, no (%)</td>
<td>55 (18.5)</td>
<td>9 (22)</td>
<td>2 (12.5)</td>
</tr>
<tr>
<td>Deceased, no (%)</td>
<td>99 (31.6)</td>
<td>21 (51.2)</td>
<td>11 (68.8)</td>
</tr>
<tr>
<td>Diffuse cutaneous SSc, no (%)</td>
<td>78 (26.2)</td>
<td>4 (9.8)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Anti-centromere Ab, no (%)</td>
<td>127 (46.9)</td>
<td>25 (69.4)</td>
<td>8 (50)</td>
</tr>
<tr>
<td>mPAP at diagnosis, mmHg</td>
<td>99 (31.6)</td>
<td>21 (51.2)</td>
<td>11 (68.8)</td>
</tr>
<tr>
<td>CCL21 at baseline, pg/ml</td>
<td>0.51 (0.2)</td>
<td>0.60 (0.3)</td>
<td>0.33 (0.1)</td>
</tr>
</tbody>
</table>

**Figure 1:**
Disclosure: A. M. Hoffmann-Vold, None; R. Hesselstrand, None; H. Fretheim, None; T. Ueland, None; A. K. Andreassen, None; O. Midtvedt, None; T. Garen, None; P. Aukrust, None; J. A. Belperio, None; O. Molberg, None.
Evaluation of American College of Rheumatology Provisional Composite Response Index in Systemic Sclerosis (CRISS) in the Fasscinate Trial

Dinesh Khanna¹, Veronica J. Berrocal², Christopher Denton³, Angelika Jahreis⁴, Helen Spotswood⁵, Celia J. F. Lin⁴, Jeffrey Siegel⁶ and Daniel E. Furst⁷, ¹University of Michigan, Ann Arbor, MI, ²Div of Rheumatology, University of Michigan, Ann Arbor, MI, ³Department of Rheumatology, University College London, Royal Free Hospital, London, United Kingdom, ⁴Genentech, South San Francisco, CA, ⁵Roche Products Ltd., Welwyn Garden City, CA, United Kingdom, ⁶Roche Products Ltd., Welwyn Garden City, United Kingdom, ⁷University of California, Los Angeles, David Geffen School of Medicine, Los Angeles, CA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics III
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose: Treatment with Interleukin-6R inhibitor, tocilizumab (TCZ), in early progressive systemic sclerosis (SSc; the faSScinate trial) resulted in consistent, but not statistically significant, improvements in skin sclerosis at wks 24 and 48. The CRISS index, a composite outcome measure for trials in SSc, is a 2-step process that assigns a probability of improvement for each subject ranging from 0.0 [no improvement] to 1.0 [marked improvement]. Step 1 assesses clinically meaningful decline in cardio-pulmonary-renal involvement with a probability of 0.0. For remaining subjects, probability of improvement examined 5 variables: FVC%, Rodnan skin score (mRSS), patient (PTGA) and physician global assessments (MDGA), and HAQ-DI. We assessed the performance of CRISS in the faSScinate at wks 24 and 48.

Methods: Pts ≥18 y with active SSc were randomized 1:1 to TCZ 162 mg or placebo (PBO) subcutaneously wkly for 48 wks. Step 1 for CRISS was captured using review of serious adverse event data. Step 2 calculated the CRISS index as previously defined. Non-parametric Wilcoxon test and proportion z-tests were used to assess whether significant differences exist between the CRISS score in both its continuous and binary form in TCZ and PBO. Analyses utilized all subjects, with missing data imputed using the best-fitting linear mixed model determined through Chi-square significance test on the deviance. The linear mixed models selected included a subject-specific random intercept, an indicator for treatment and a function of time. PD Protocol WA27788 Amendment 4 p.50-53,101

Results: 87 pts (43 TCZ, 44 PBO) were enrolled. 14.10.15_CSR WA27788 (Week 24), pg51-54 4 subjects in the PBO and none in TCZ met the pre-defined definition of worsening cardio-pulmonary-renal involvement (Step 1) thus given a score of 0.0. Using the CRISS as a continuous measure, the median scores statistically significantly favored TCZ compared to the PBO at wks 24 and 48 (p=0.01 and 0.002; Table).

Conclusion: In this post-hoc analysis using patient-level data from FaSScinate, CRISS discriminated TCZ from PBO, supporting its validity in an independent cohort from its development cohort.

<table>
<thead>
<tr>
<th></th>
<th>TCZ, N=43</th>
<th>PBO, N=40Ø</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRISS (0.0-1.0), median [IQR] at 24 weeks</td>
<td>0.19 [0.006; 0.92]</td>
<td>0.0006 [0.0001; 0.13]</td>
<td>0.01*</td>
</tr>
<tr>
<td>CRISS (0.0-1.0), median [IQR] at 48 weeks</td>
<td>0.32 [0.01; 0.93]</td>
<td>0.001 [0.0002; 0.16]</td>
<td>0.002*</td>
</tr>
<tr>
<td>mRSS (0-51), mean change at 24 weeks</td>
<td>-4.19</td>
<td>-2.65</td>
<td>0.28</td>
</tr>
<tr>
<td>mRSS (0-51), mean change at 48 weeks</td>
<td>-5.26</td>
<td>-3.0</td>
<td>0.12</td>
</tr>
<tr>
<td>FVC% predicted, mean change at 24 weeks</td>
<td>-0.66</td>
<td>-4.20</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>FVC% predicted, mean change at 48 weeks</td>
<td>-2.21</td>
<td>-6.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>PT GA (0-10), mean change at 24 weeks</td>
<td>-0.36</td>
<td>-0.06</td>
<td>0.51</td>
</tr>
<tr>
<td>PT GA (0-10), mean change at 48 weeks</td>
<td>-0.85</td>
<td>-0.36</td>
<td>0.33</td>
</tr>
<tr>
<td>MD GA (0-10), mean change at 24 week</td>
<td>-1.92</td>
<td>-1.79</td>
<td>0.82</td>
</tr>
<tr>
<td>MDGA (0-10), mean change at 48 weeks</td>
<td>-3.18</td>
<td>-1.88</td>
<td>0.03</td>
</tr>
<tr>
<td>HAQ-DI (0-3), mean change at 24 weeks</td>
<td>0.17</td>
<td>0.18</td>
<td>0.93</td>
</tr>
<tr>
<td>HAQ-DI (0-3), mean change at 48 weeks</td>
<td>0.15</td>
<td>0.23</td>
<td>0.53</td>
</tr>
</tbody>
</table>

*Using Wilcoxon test as CRISS data is not normally distributed

Ø 4 subjects in the placebo met step 1 thus given a score of 0.0. The data were not imputed for these subjects when calculating individual measures over time.

The linear mixed model was expressed either as a categorical variable for week-visit number (HAQ-DI and FVC), or as a polynomial of degree 1 in week-visit used as a continuous variable (PT and MD GA) or as a 2 degree polynomial in
Disclosure: D. Khanna, Actelion, Bayer, BoehringerIngelheim, Chemomab, Corbus, Covis, Cytori,Eicos, EMD Serono, Genentech/Roche, Gilead, GSK, Sanofi-Aventis,UCB Pharma, 5,NIH/NIAMS, NIH/NIAID,Bayer, BMS, Genentech/Roche, Pfizer, 2,Eicos, 4; V. J. Berrocal, None; C. Denton, Bayer, CSL Behring, 2,Genentech-Roche, Actelion, GlaxoSmithKlein, Bayer, Sanofi-Aventis, Inventiva, Boehringer Ingelheim, 5; A. Jahreis, Genentech Inc, 3; H. Spotswood, Roche Products Ltd, 3,Roche Products Ltd, 1; C. J. F. Lin, Genentech Roche, 3; J. Siegel, Genentech, Inc., 3; D. E. Furst, None.


Abstract Number: 2982

Morbidity and Mortality of Scleroderma in African Americans

Duncan F. Moore1, Elisabeth Kramer1, Rami Eltaraboulsi2 and Virginia D. Steen1, 1Division of Rheumatology, Department of Medicine, MedStar Georgetown University Hospital, Washington, DC, 2MedStar Georgetown University Hospital, Washington, DC
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics III
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose:
Retrospective cohorts have demonstrated that African Americans (AAs) with scleroderma are more likely to have severe disease and higher mortality than non-AAs. A prior study concluded that this excess risk was not fully explained by differences in rates of diffuse disease and autoantibody status (Gelber 2013). Our study sought to further evaluate this risk among matched AAs and non-AAs at our site.

Methods:
A single-center, retrospective study comparing AA and non-AA patients with scleroderma was performed. Patients were evaluated by the senior author between 2008 and 2016. AA and non-AAs were matched based on sex, age at first visit, date of first visit, disease duration at first visit, and limited vs. diffuse cutaneous disease. Demographic, serologic, and clinical features were compared. Mortality risks were assessed in an unadjusted manner and by a Cox proportional hazards model with covariates of race, median household income by ZIP code, marital status, education level, employment status, and insurance type.

Results:
AAs comprised 203 of the 402 patients analyzed. The groups were statistically similar regarding all factors by which they were matched. Table 1 shows our findings. AAs had significantly reduced FVC and DLCO, more severe fibrosis per CT, a higher prevalence of any type of pulmonary hypertension, and more severe cardiac involvement. As expected, autoantibody profile statistically differed among the two groups (p<0.001). Death during follow-up was 21.2% in AAs vs. 11.1% in non-AAs (p=0.006). AA status demonstrated an unadjusted hazard ratio for death during follow-up of 2.037 (p=0.007), but when adjusted for the aforementioned socioeconomic covariates, the hazard ratio of AA status declined to 1.256 (95% CI 0.494 – 3.191, p=0.633). The only statistically significant covariate was median income in thousands of dollars by ZIP code, with a hazard ratio of 0.983 (95% CI 0.968 – 0.999, p=0.033).

Conclusion:
African American patients with scleroderma have more severe pulmonary disease and a higher unadjusted risk of mortality than matched non-African Americans. Adjusting for available socioeconomic factors, African American race was not a significant risk factor for mortality, but lower median household income by ZIP code was an independent risk factor for increased mortality.
Table 1 - Morbidity and mortality in African Americans and non-African Americans

<table>
<thead>
<tr>
<th></th>
<th>African American (n = 203)</th>
<th>Non-African American (n = 199)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (female)</td>
<td>176 (86.7)</td>
<td>173 (86.9)</td>
<td>0.944</td>
</tr>
<tr>
<td>Age at first visit, mean ± SD</td>
<td>47.4 ± 13.3</td>
<td>48.5 ± 13.0</td>
<td>0.379</td>
</tr>
<tr>
<td>Disease duration at first visit (years), mean ± SD</td>
<td>7.7 ± 8.1</td>
<td>8.3 ± 9.6</td>
<td>0.512</td>
</tr>
<tr>
<td>SSc type (diffuse)</td>
<td>97 (47.8)</td>
<td>81 (40.7)</td>
<td>0.121</td>
</tr>
<tr>
<td>Autoantibody</td>
<td></td>
<td></td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>anti-centromere</td>
<td>15 (7.4)</td>
<td>43 (21.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>anti-Scl70</td>
<td>43 (21.2)</td>
<td>41 (20.6)</td>
<td>0.886</td>
</tr>
<tr>
<td>anti-U1RNP</td>
<td>26 (12.8)</td>
<td>10 (5.0)</td>
<td>0.006</td>
</tr>
<tr>
<td>isolated nucleolar ANA</td>
<td>50 (24.6)</td>
<td>32 (16.1)</td>
<td>0.033</td>
</tr>
<tr>
<td>anti-RNA polymerase III</td>
<td>7 (3.4)</td>
<td>29 (14.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>non-specific SSc ANA</td>
<td>46 (22.7)</td>
<td>27 (13.6)</td>
<td>0.018</td>
</tr>
<tr>
<td>negative ANA</td>
<td>11 (5.4)</td>
<td>9 (4.5)</td>
<td>0.680</td>
</tr>
<tr>
<td>Inflammatory arthritis</td>
<td>33 (16.3)</td>
<td>43 (21.6)</td>
<td>0.171</td>
</tr>
<tr>
<td>Tendon rubs</td>
<td>25 (12.3)</td>
<td>40 (20.1)</td>
<td>0.034</td>
</tr>
<tr>
<td>Telangiectasia</td>
<td>39 (19.2)</td>
<td>101 (50.8)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Calcinosis</td>
<td>10 (4.9)</td>
<td>33 (16.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Skin score, mean ± SD</td>
<td>14.1 ± 13.2</td>
<td>14.4 ± 12.6</td>
<td>0.803</td>
</tr>
<tr>
<td>FVC (% predicted), mean ± SD</td>
<td>68.4 ± 20.4</td>
<td>84.1 ± 48.7</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>DLCO (% predicted), mean ± SD</td>
<td>45.8 ± 19.8</td>
<td>63.7 ± 20.9</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Fibrosis per CT</td>
<td></td>
<td></td>
<td>0.002</td>
</tr>
<tr>
<td>no fibrosis</td>
<td>38 (18.7)</td>
<td>60 (30.2)</td>
<td>0.008</td>
</tr>
<tr>
<td>mild/moderate fibrosis</td>
<td>77 (37.9)</td>
<td>67 (33.7)</td>
<td>0.373</td>
</tr>
<tr>
<td>severe fibrosis</td>
<td>22 (10.8)</td>
<td>6 (3.0)</td>
<td>0.002</td>
</tr>
<tr>
<td>not performed</td>
<td>66 (32.5)</td>
<td>66 (33.2)</td>
<td>0.889</td>
</tr>
<tr>
<td>Pulmonary hypertension by right heart catheterization</td>
<td>42 (20.7)</td>
<td>25 (12.6)</td>
<td>0.029</td>
</tr>
<tr>
<td>Severe cardiac involvement</td>
<td>35 (17.2)</td>
<td>17 (8.5)</td>
<td>0.009</td>
</tr>
<tr>
<td>Renal crisis</td>
<td>17 (8.4)</td>
<td>6 (3.0)</td>
<td>0.021</td>
</tr>
<tr>
<td>Death during follow-up</td>
<td>43 (21.2)</td>
<td>22 (11.1)</td>
<td>0.006</td>
</tr>
<tr>
<td>Duration from diagnosis to death or end of study (years), mean ± SD</td>
<td>9.5 ± 7.3</td>
<td>9.5 ± 8.9</td>
<td>0.920</td>
</tr>
</tbody>
</table>

Disclosure: D. F. Moore, None; E. Kramer, None; R. Eltaraboulsi, None; V. D. Steen, None.


Abstract Number: 2983

**Predictors for Disease Worsening Defined By Organ Failure in Diffuse Systemic Sclerosis: A European Scleroderma Trials and Research (EUSTAR) Analysis**

Mike Oliver Becker\(^1\), Nicole Graf\(^2\), Rafael Sauter\(^3\), Yannick Allanore\(^4\), John Curram\(^5\), Christopher Denton\(^6\), Dinesh Khanna\(^7\), Marco Matucci-Cerinic\(^8\), Janethe Pena\(^9\), Janet E. Pope\(^10\) and Oliver Distler\(^1\), \(^1\)Department of Rheumatology, Center of Experimental Rheumatology, University Hospital Zurich, Zurich, Switzerland, \(^2\)Graf Biostatistics, Winterthur, Switzerland, \(^3\)Big Data Institute, Li Ka Shing Centre for Health Information and Discovery, Nuffield Department of Medicine, University of Oxford, Oxford, United Kingdom, \(^4\)Department of Rheumatology, Cochin Hospital, Paris Descartes University, Paris, France, \(^5\)Bayer Plc, Newbury, United Kingdom,
Background/Purpose: Mortality and worsening of organ function would be desirable endpoints for clinical trials in systemic sclerosis (SSc). However, these events are relatively rare, making clinical trial design with these endpoints challenging. To enrich for patients with these events, predictive factors have to be identified. The aim of this study was therefore to identify predictive factors in a population of patients with diffuse SSc from the large European Scleroderma Trials and Research (EUSTAR) group database.

Methods: Inclusion criteria were diagnosis of diffuse SSc and a follow-up after 9–15 (12 ± 3) months. This timeframe was chosen to reflect typical clinical trial design. Disease worsening/organ progression was fulfilled if any of the following events occurred: new renal crisis, decrease in forced vital capacity (FVC) ≥10%, new left ventricular ejection fraction (LVEF) <45% or decrease in LVEF by >10% for patients with baseline LVEF <50%, new pulmonary (arterial) hypertension on echocardiography, or death. These parameters had been defined by expert nominal group technique. Methodologically, two main limitations had to be addressed: (1) the problem of missing data and (2) the low number of events, which prohibits the simultaneous exploration of the set of predictors in a regression model. We addressed these issues by (a) imputing multiple predictors on the basis of different algorithms (multiple imputation), and by (b) using least absolute shrinkage and selection operator (LASSO) regression, thus 42 clinical parameters were entered as predictors into the analysis.

Results: Of the 1451 patients who met the inclusion criteria, 706 had complete data available on all parameters for disease worsening; there were no clinically meaningful differences between patients with and without complete data. Of 706 patients originally evaluated, 228 (32.3%) had disease progression, most of which was either a decrease in FVC (103 patients, 14.6%) or death (92 patients, 13.0%) within the observation period (12±3 months). Of the 42 clinical parameters introduced into the model as outcome predictors, eight remained in the final regression model which was chosen by the Bayesian information criterion (Table 1). The probability, in our model, e.g. for a 60-year-old patient with diffuse SSc, lung fibrosis and active digital ulcers as well as muscle weakness to develop organ progression within the next 12 months increased to >60% compared with 32.3% in the total population. Bootstrap with 10000 repetitions successfully validated the model. The Receiver Operating Characteristic was 0.711 for the final model and 0.705 for the validation. The maximum absolute error in predicted probability was 0.026.

Conclusion: The use of the predictive factors presented here could enable cohort enrichment with patients at risk for overall disease worsening in clinical trials.

Table 1: Predictive factors in the final LASSO regression model.

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Estimate</th>
<th>SE</th>
<th>p-value</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Intercept)</td>
<td>-2.74</td>
<td>0.465</td>
<td>&lt;0.0001</td>
<td>0.08</td>
<td>0.03-0.14</td>
</tr>
<tr>
<td>Age (per 1 year)</td>
<td>0.02</td>
<td>0.007</td>
<td>0.001</td>
<td>1.02</td>
<td>1.01-1.04</td>
</tr>
<tr>
<td>Active digital ulcers</td>
<td>0.50</td>
<td>0.222</td>
<td>0.026</td>
<td>1.64</td>
<td>1.00-2.54</td>
</tr>
<tr>
<td>C-reactive protein elevation</td>
<td>0.56</td>
<td>0.194</td>
<td>0.002</td>
<td>1.80</td>
<td>1.23-2.63</td>
</tr>
<tr>
<td>Significant dyspnea</td>
<td>0.18</td>
<td>0.261</td>
<td>0.491</td>
<td>1.20</td>
<td>0.72-2.00</td>
</tr>
<tr>
<td>Lung fibrosis</td>
<td>0.79</td>
<td>0.221</td>
<td>0.0004</td>
<td>2.21</td>
<td>1.43-3.41</td>
</tr>
<tr>
<td>Muscle weakness</td>
<td>0.50</td>
<td>0.204</td>
<td>0.015</td>
<td>1.64</td>
<td>1.10-2.45</td>
</tr>
<tr>
<td>Peripheral effusion</td>
<td>0.50</td>
<td>0.301</td>
<td>0.068</td>
<td>1.65</td>
<td>0.91-2.97</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>0.56</td>
<td>0.301</td>
<td>0.064</td>
<td>1.75</td>
<td>0.97-3.16</td>
</tr>
</tbody>
</table>

| CI, confidence interval; OR, odds ratio; SE, standard error |

Disclosure: M. O. Becker, None; N. Graf, Biotronik AG, 5; R. Sauter, None; Y. Allanore, Actelion Pharmaceuticals US, 2,Bayer AG, 2,Bristol-Myers Squibb, 2,Inventiva, 2,Medac, 2,Pfizer Inc, 2,Roche Pharmaceuticals, 2,Genentech and Biogen IDEC Inc., 2,Sanofi-Aventis Pharmaceutical, 2,Server, 2,Actelion Pharmaceuticals US, 5,Bayer AG, 5,Bristol-Myers Squibb, 5,Inventiva, 5,Medac, 5,Pfizer Inc, 5,Roche Pharmaceuticals, 5,Genentech and Biogen IDEC Inc., 5,Sanofi-Aventis Pharmaceutical, 5; J. Curram, Bayer Plc, 1,Bayer Plc, 3; C. Denton, Actelion Pharmaceuticals US, 5,Bayer AG, 5,GlaxoSmithKline, 5,CSL Behring, 5,Merck-Serono, 5,Roche Pharmaceuticals, 5,Genentech and Biogen IDEC Inc., 5,Sanofi-Aventis Pharmaceutical, 5,Boehringer Ingelheim, 5,Actelion Pharmaceuticals US, 8,Bayer AG, 8,GlaxoSmithKline, 8,CSL Behring, 8,Merck-Serono, 8,Roche Pharmaceuticals, 8,Genentech and Biogen IDEC Inc., 8,Inventiva, 8,Sanofi-Aventis Pharmaceutical, 8,Boehringer Ingelheim, 8; D. Khanna, Bristol-Myers Squibb, 2,Genentech/Roche, 2,NIH/NIAID, 2,NIH/NIAID., 2,NIH/NIAID., 2,Patient-Centered Outcomes Research Institute,
Predictive Value of a Combined Index for Weight Loss in Systemic Sclerosis

Gianluca Bagnato1, Erika Pigatto2, Alessandra Bitto1, Carmelo Pizzino1, Natasha Irrera1, Giuseppina Abignano3, Michele Hutchinson4, Francesco Squadrito1, Maya H. Buch5, Sebastiano Gangemi1, William Neal Roberts6, Antonino Saïta1, Franco Cozzi7 and Francesco Del Galdo8,
1University of Messina, Messina, Italy, 2University of Padova, Padova, Italy, 3Rheumatology Department of Lucania, Rheumatology Institute of Lucania (IReL), San Carlo Hospital of Potenza and Madonna delle Grazie Hospital of Matera, Potenza, Italy, 4University of Leeds, Leeds, United Kingdom, 5NIHR-Leeds Musculoskeletal Biomedical Research Unit, Leeds, United Kingdom, 6University of Louisville, Louisville, LA, 7Division of Rheumatology, Rheumatology Unit, Department of Medicine, University of Padova, Padova, Italy, 8Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds and NIHR Leeds Musculoskeletal Biomedical Research Unit, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Wednesday, November 8, 2017
Session Title: Systemic Sclerosis, Fibrosing Syndromes and Raynaud's – Clinical Aspects and Therapeutics III
Session Type: ACR Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose: Malnutrition and severe gastrointestinal (GI) dysfunction are the cause of mortality in 4-15% of systemic sclerosis (SSc) patients whereas overall GI involvement is observed in 75-90% of cases. Tools, reliable in other metabolic diseases, such as the Malnutrition Universal Screening Tool (MUST), or adiponectin to leptin ratio (A/L), have not yet been explored for the prediction of severe malnutrition in SSc. Our aim was to explore the performance of MUST and A/L to identify a combined index for stratification of risk of weight loss at 12 months in patients with SSc.

Methods: 180 consecutive SSc patients were enrolled in this multicentre longitudinal study (University of Leeds n=70, University of Messina n=60, University of Padova n=50). Serum levels of adiponectin and leptin were measured and their ratio calculated (A/L). Malnutrition risk was evaluated through MUST, which includes BMI and weight loss reported by the patient in the last 3-6 months, and by the score corresponds to the malnutrition risk (0=no, 1=mild, ≥2=moderate/severe). Weight loss ≥10% of baseline weight after 12 months was also calculated.

Results: No statistical differences were observed at baseline among the single centres cohorts. Overall, we observed a BMI decrease over time (24.1 vs 23.1, p<0.0001). 40/180 (22%) SSc patients had a weight loss ≥10% after 12 months. These patients were older (median 63 vs 55, p=0.02), more frequently with the diffuse form (48% vs 31%, p=0.05), Scl70 positive (32% vs 17%, p=0.04), had higher modified Rodnan skin scores (median 10 vs 6, p=0.01), and HRCT evidence of pulmonary fibrosis (55% vs 30%, p=0.003), with concordant lower TLC (mean: 76.7 vs 93.7, p<0.001), and lower FVC (mean: 74.6 vs 83.5, p=0.05). No differences were observed in CK serum levels. In the group of patients with ≥10% weight loss baseline A/L was 2.34 (vs 0.37, p<0.0001), baseline MUST was 1.54 (vs 0.57, p<0.0001), while baseline BMI was 21.4 (vs 24.9, p<0.0001). Using ≥10% weight loss at 12 months as gold standard, we built receiver operating characteristic (ROC) curves for BMI, MUST, A/L and combined indexes. BMI and A/L had a better AUC (0.84; 95% CI: 0.77-0.84) vs MUST (0.77; 95% CI: 0.69/0.77). By combining BMI and A/L in logistic regression, we defined the predictor of malnutrition in systemic sclerosis (PREMASS) with the formula: 3.33 - (0.25 * baseline BMI) + (1.71 * baseline A/L). A PREMASS score >0.21 showed an AUC of 0.80 (95% CI: 0.80 D 0.87), 85% sensitivity (95% CI: 74-96) and 83% specificity (95% CI: 77-89) for
≥10% weight loss with an overall 59% positive predictive value (95% CI: 46-71) and 95% negative predictive value (95% CI: 91-99) and a relative risk of 11.9 (95% CI: 5.3-26.8).

**Conclusion:** Here we propose a novel combined index, PREMASS, for stratification for risk of severe weight loss in the following 12 months in SSc. Further validation in independent cohorts will confirm the clinical value of PREMASS index for the clinical management and risk stratification for weight loss in SSc patients.

**Disclosure:** G. Bagnato, None; E. Pigatto, None; A. Bitto, None; C. Pizzino, None; N. Irrera, None; G. Abignano, None; M. Hutchinson, None; F. Squadrito, None; M. H. Buch, Pfizer Ltd, 2, Roche Pharmaceuticals, 2, Abbott Immunology Pharmaceuticals, 5, Sandoz, 5; S. Gangemi, None; W. N. Roberts, None; A. Saitta, None; F. Cozzi, None; F. Del Galdo, None.


**Abstract Number:** 2986

**Omega Polyunsaturated Fatty Acids and Systemic Lupus Erythematosus (SLE): the Michigan Lupus Epidemiology & Surveillance (MILES) Program**

**Prae Charoenwoodhipong**¹, Suzanna Zick², Wendy Marder³, Afton L. Hassett⁴, W. Joseph McCune⁵, Caroline Gordon⁶, Siobán Harlow⁷ and Emily C. Somers³, ¹University of Michigan, Ann Arbor, MI, ²Department of Family Medicine, University of Michigan, Ann Arbor, MI, ³Internal Medicine-Rheumatology, University of Michigan, Ann Arbor, MI, ⁴Rheumatology, Emory University, Atlanta, GA, ⁵Int Med/ Rheum, University of Michigan, Ann Arbor, MI, ⁶Rheumatology Research Group, Institute of Inflammation and Ageing., College of Medical and Dental Sciences, University of Birmingham, Birmingham, United Kingdom, ⁷Epidemiology Department- School of Public Health, Obstetrics and Gynecology- Medical School, University of Michigan, Ann Arbor, MI

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Wednesday, November 8, 2017
**Session Title:** ARHP Epidemiology and Public Health
**Session Type:** ARHP Concurrent Abstract Session
**Session Time:** 11:00AM-12:30PM

**Background/Purpose:**

Omega fatty acids have immunomodulatory properties; omega-3 (n-3) fatty acids are generally anti-inflammatory and omega-6 (n-6) pro-inflammatory. High n-6:n-3 ratios (up to 16:1) are common in Western diets and are thought to contribute to chronic diseases. In small studies omega-3 supplementation in SLE has been associated with reduction of disease activity in systemic lupus erythematosus (SLE), but no study has examined there impact on patient reported outcomes (PROs). We performed a population-based cross-sectional study based on the MILES Program to examine the association between dietary intake of n-3 and n-6 fatty acids and PROs in SLE.

**Methods:**

The MILES Program includes a population-based cohort of SLE cases from southeast Michigan. Data on dietary intake of omega fatty acids was collected at baseline using questions from the National Cancer Institute’s Diet History Questionnaire II (DHQ II). Patient reported outcome data included the Systemic Lupus Activity Questionnaire (SLAQ), RAND 36 Health Survey, Fibromyalgia (FM) Scale, PROMIS Sleep Disturbance (short form 8b) and PROMIS Depression (short form 8b). Multivariable regression, adjusted for covariates (age, sex, race, energy intake, and body mass index), was used to assess the association between n-3 and n-6 fatty acid intake and patient reported outcomes.

**Results:**

456/462 (98.7%) of SLE cases enrolled in MILES completed dietary questionnaires at baseline. 425 (93.2%) were female, 207 (45.4%) were black, and mean age at baseline visit was 52.9 years. Controlling for covariates, increasing n-6:n-3 ratios were associated with SLE disease activity (SLAQ score); β 0.322 (95% CI 0.069, 0.574; p=0.013). Intake of n-3 fatty acids was significantly associated with better sleep quality (β -1.114, 95% CI -2.029, -0.198) and trended towards significant decreases in depressive symptoms (β -0.884, 95% CI -1.916, 0.148) and presence of comorbid fibromyalgia (OR 0.817, 95% CI 0.655, 1.020). Associations between fatty acid intake and general health-related quality of life were not observed.
Conclusion:

This large, population-based study suggests that dietary intake levels of n-3 and n-6 fatty acids may impact patient reported outcomes in SLE. Future dietary intervention studies modulating the absolute intake and ratios of n-3 and n-6 fatty acids should be considered in SLE.

Disclosure: P. Charoenwoodhipong, None; S. Zick, None; W. Marder, None; A. L. Hassett, None; W. J. McCune, None; C. Gordon, None; S. Harlow, None; E. C. Somers, None.


Abstract Number: 2987

Moderate and Serious Psychological Distress Among US Adults with and without Arthritis, 2002 to 2015

Louise Murphy, Michael Boring, Teresa J. Brady, Kristina Theis, Jennifer M. Hootman, Kamil E. Barbour, and Charles G. Helmick

1Division of Population Health, Centers for Disease Control and Prevention, Atlanta, GA; 2Cutting Edge Technology and Solutions, Mesa, AZ; 3Arthritis Program, Centers for Disease Control and Prevention, Atlanta, GA; 4Centers for Disease Control and Prevention, Atlanta, GA; 5Centers for Disease Control and Prevention, Kennesaw, GA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: ARHP Epidemiology and Public Health
Session Type: ARHP Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose: US population-health surveys frequently measure current mental health status using the Kessler-6 (K-6) which indicates psychological distress level. Among all US adults, moderate and serious psychological distress predict high health care utilization. Higher prevalence of serious psychological distress (SPD) among adults with arthritis compared with those without is well documented; however, little is known about moderate psychological distress (MPD) prevalence by arthritis status. We examined MPD and SPD prevalence, by arthritis status, for 2002 to 2015.

Methods: We analyzed National Health Interview Survey (NHIS) data; NHIS is an ongoing population-based survey designed to provide annual estimates representative of US civilian, non-institutionalized population. Participants had arthritis if they responded “yes” to “Have you ever been told by a doctor or other health care professional that you have arthritis, rheumatoid arthritis, gout, lupus or fibromyalgia?”. Using the K-6, NHIS respondents rated frequency (0 [none of the time] to 4 [all of the time]) that they felt each of 6 items (sad, worthless, nervous, restless, hopeless, and everything was an effort) in the past 30 days. We categorized rating sums into 3 psychological distress levels: none-mild (0-4]; moderate (5-12); serious (≥13-24) and estimated age-standardized (2000 US projected population) prevalence and 95% confidence interval (CI). All analyses accounted for NHIS’ complex design. Moving averages were 3 year means. Tests for trend were conducted using linear orthogonal contrasts (α =0.05).

Results: MPD prevalence was 12 percentage points higher among adults with arthritis (27.4%; CI=25.2-29.7) compared with those without (15.4%; CI=14.8-16.0); SPD was also more prevalent among adults with arthritis (arthritis=8.5%; CI=7.2-10.0; without arthritis=2.6%; CI=2.3-3.0). From 2002 to 2015, only MPD increased significantly (5 percentage points) among adults with arthritis whereas both MPD and SPD prevalence increased significantly for those without arthritis (Figure).

Conclusion: In 2015, approximately 1 in 3 US adults with arthritis experienced either MPD or SPD compared with almost 1 in 5 adults without arthritis. From 2002 to 2015, SPD prevalence remained constant among adults with arthritis but MPD prevalence increased indicating that psychological distress is a growing problem. Mental health issues can reduce adherence to clinical treatment and practicing healthy behaviors. Engaging in physical activity and self-management education (e.g., Chronic Disease Self-Management Program) are proven to reduce arthritis symptoms (e.g., pain) and symptoms of mood disorders, but psychological distress may be a barrier to participation. Thus, ensuring that psychological distress is identified and addressed is an important step in helping adults with arthritis to manage their arthritis well.
Characteristics of People with Work-Related Versus Non-Work Related Carpal Tunnel Syndrome: National Health Interview Survey, 2010 & 2015

Nancy A. Baker, Department of Occupational Therapy, University of Pittsburgh, Pittsburgh, PA
First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: ARHP Epidemiology and Public Health
Session Type: ARHP Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose: The underlying causes of carpal tunnel syndrome (CTS) are complex and may be unrelated to work status. Yet, too often, CTS is viewed and researched only as a work-related disorder. There is almost no research that compares the characteristics of work-related versus non work-related disorders. In this study we used data from the 2010 and 2015 National Health Information Survey (NHIS), representative of the U.S. civilian non-institutionalized population, to determine which characteristics are risk factors for non work-related CTS compared to work-related CTS.

Methods: We analyzed adults (age 18+). CTS cases were defined as “Have you EVER been told by a doctor or other health professional that you have a condition affecting the wrist and hand called carpal tunnel syndrome?” and we designated whether CTS was work/non work-related by the response in those with CTS to the question “Have you ever been told by a doctor or other health professional that your CTS was probably work-related.” Arthritis and diabetes were self-reported in a similar fashion. Obesity was those with Body Mass Index (BMI) \( \geq 30 \), and smoking as those who never or ever smoked. To identify occupational type, respondents were categorized in three major Standard Occupational Classification System categories (SOC): 1) Management, Professional, and Related & Service (MP&S); 2) Sales and Office (SO); 3) Natural Resources, Construction and Maintenance & Production, Transportation, and Material Moving (NCM&PTM), each of which represent progressively greater exposure to high-repetition, forceful tasks which are considered an important risk factor for work-related CTS.

We completed simple descriptive characteristics as well as a logistical regression using appropriate NHIS weights.

Results: Of our sample of 60,759 adults, 8.6% (95%CI: 8.4, 7.8) had CTS. Of these 65.5% (62.4, 68.6) were work-related and 34.5% (31.4, 37.6) were non work-related.
Characteristics associated with non work-related CTS were age greater than 65 (Odds Ratio [OR] 2.5: 95%CI 1.4, 4.3), working in jobs which do not typically have exposure to high-repetition, forceful tasks (MP&S OR 1.9: 1.3, 2.3; SO OR 1.6: 1.0, 2.8) and ever having smoked (OR 1.4: 1.0, 1.9) (See Table 1).

**Conclusion:** While work-related CTS is more common than non work-related CTS, at least a third of CTS cases are non work-related. Characteristic of those with non work-related CTS are similar to those with work-related CTS. The exceptions are age over 65, when people typically are not working, and those who do not generally have high repetition forceful jobs. Although co-morbidities, such as arthritis and obesity did not increase the risk of reporting non work-related CTS, ever having smoked was an independent risk factor. This study supports the need to examine all causes of CTS and consider it as a potential upper extremity issue, regardless of work-status.

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (referent: 18-34 y.o)</td>
<td></td>
</tr>
<tr>
<td>45-64 y.o</td>
<td>1.0 (0.7, 1.4)</td>
</tr>
<tr>
<td>65+ y.o</td>
<td>2.5 (1.4, 4.3)</td>
</tr>
<tr>
<td>Sex: Female (referent: Male)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.8 (0.6, 1.1)</td>
</tr>
<tr>
<td>Race/ethnicity (referent: Non-Hispanic White)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>1.1 (0.7, 1.6)</td>
</tr>
<tr>
<td>Non-Hispanic Black</td>
<td>0.7 (0.5, 1.1)</td>
</tr>
<tr>
<td>Non-Hispanic Other</td>
<td>0.5 (0.2, 1.1)</td>
</tr>
<tr>
<td>Education: ≤ College (referent: &gt; College)</td>
<td>1.1 (0.8, 1.5)</td>
</tr>
<tr>
<td>Employment: Employed (referent: Not employed)</td>
<td>1.4 (0.9, 2.0)</td>
</tr>
<tr>
<td>Work category: (referent: NCM&amp;PTM)</td>
<td></td>
</tr>
<tr>
<td>MP&amp;S</td>
<td>1.9 (1.3, 2.3)</td>
</tr>
<tr>
<td>SO</td>
<td>1.6 (1.0, 2.6)</td>
</tr>
<tr>
<td>Arthritis: no arthritis (referent: arthritis)</td>
<td>1.0 (0.7, 1.3)</td>
</tr>
<tr>
<td>Diabetes: no diabetes (referent: diabetes)</td>
<td>0.9 (0.5, 1.4)</td>
</tr>
<tr>
<td>Obesity: BMI ≤30 (referent: BMI&gt;30)</td>
<td>1.0 (0.7, 1.4)</td>
</tr>
<tr>
<td>Smoke: smoked (referent: never smoked)</td>
<td>1.4 (1.0, 1.9)</td>
</tr>
</tbody>
</table>

Table 1: Multivariable adjusted odds ratios (OR) with 95% confidence intervals (95% CI) for adults with work-related and non work-related carpal tunnel syndrome: NHIS 2010 & 2015 (event = non work-related)

**Disclosure:** N. A. Baker, None;


**Abstract Number:** 2989

**Hydration and Gout: Looking at New Modes of Uric Acid Management**

**Patricia Kachur¹, Chirag Bambholiya², Hong Liang³ and Pramil Cheriyath², ¹Internal Medicine, Ocala Regional Medical Center, Ocala, FL, ²Ocala Regional Medical Center, Ocala, FL, ³North Florida Regional Medical Center, Gainsville, FL**

**First publication:** September 18, 2017

**SESSION INFORMATION**

**Session Date:** Wednesday, November 8, 2017

**Session Title:** ARHP Epidemiology and Public Health

**Session Type:** ARHP Concurrent Abstract Session

**Session Time:** 11:00AM-12:30PM

**Background/Purpose:**

Gout affects more than 4% of adults in the United States, and it is the most common form of inflammatory arthritis among men. Studies show that excessive intake of alcoholic beverages, red meat, soft drinks and fruit juices increase the risk of developing gout. Similarly, dairy products and coffee seem to have a protective effect, as they increase the excretion of uric acid. Water is one of the best universal solvents and may be a readily available remedy for gout. As described in previous papers, water helps in the excretion of excess uric acid from the body and will replenish the dehydrated patient but no causal association has been established. Our objective of the study is to look at the association between water intake and uric acid levels in gout patients

**Methods:**
17,321 individuals from the general population were surveyed by the National Health and Nutrition Examination Survey (NHANES) between 2009-2014. From this data set, 539 participants with a gout diagnosis were selected for the current study after excluding all patients with chronic kidney disease. Our primary definition of hyperuricemia was a serum uric acid level of ≥6.0 mg/dL. While participants with <6.0 mg/dL uric acid were labeled as normal or low Serum uric acid level. Water intake was considered high for men taking ≥ 3000mg and for women taking ≥ 2200mg; while intake was considered low for men taking < 3000mg and for women taking < 2200mg. Statistical modeling adjusted for demographic characteristics, body mass index, alcohol use, hypertension, diabetes mellitus, and other factors. All analyses were performed with use of SAS version 9.4’s (Cary, North Carolina) Proc survey methodology.

Results:

Thirty nine percent of participants had a uric acid level < 6 mg/dL, the remainder had uric acid ≥6.0 mg/dL. The high uric acid group had significantly more obesity and hypertension, as well as having a significantly higher proportion of males. Multivariate logistic regression showed a significant association between low water intake and hyperuricemia. The odds of developing hyperuricemia was 58% less with high water intake (OR = 0.421, 95% CI: 0.262-0.679, p-value = 0.0007) after adjusting for age, sex, race diabetes, BMI, and hypertension.

Table 1. Multivariate Logistic Regression Analysis for Uric Acid (≥ 6 mg/dL vs. < 6 mg/dL)

<table>
<thead>
<tr>
<th>Effect</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water intake (high)</td>
<td>0.421</td>
<td>0.262-0.679</td>
<td>0.0007</td>
</tr>
<tr>
<td>Gender (female)</td>
<td>0.574</td>
<td>0.298-1.107</td>
<td>0.0958</td>
</tr>
<tr>
<td>Race</td>
<td>1.132</td>
<td>0.868-1.478</td>
<td>0.3530</td>
</tr>
<tr>
<td>BMI</td>
<td>1.491</td>
<td>0.955-2.330</td>
<td>0.0779</td>
</tr>
<tr>
<td>Age</td>
<td>0.974</td>
<td>0.956-0.992</td>
<td>0.0054</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.644</td>
<td>0.954-2.834</td>
<td>0.0723</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.153</td>
<td>0.633-2.097</td>
<td>0.6355</td>
</tr>
</tbody>
</table>

Conclusion:

In summary, there is a strong association between low water consumption and hyperuricemia. These findings support the physiology of increased uric acid excretion with excess water intake. High water intake may allow for significant benefits to those suffering from gout and warrants further study as a therapeutic intervention.

Disclosure: P. Kachur, None; C. Bambhroliya, None; H. Liang, None; P. Cheriyath, None.


Abstract Number: 2990

Is Risk of Retinopathy Among Hydroxychloroquine Users of SLE Patients Accurate? a Simulation Study Accounting for Competing Risk of Death

Na Lu1, Hyon K. Choi2, April Jorge3 and Yuqing Zhang4, 1Clinical Epidemiology, Boston University School of Medicine, Boston, MA, 2Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, 3Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, 4School Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Wednesday, November 8, 2017
Session Title: ARHP Epidemiology and Public Health
Session Type: ARHP Concurrent Abstract Session
Background/Purpose: Hydroxychloroquine (HCQ) is used for the long-term treatment of systemic lupus erythematosus (SLE) patients. HCQ is generally well-tolerated with wide-ranging benefits, including reduced disease activity and improved survival; a critical adverse effect is vision-threatening retinopathy. Historically, the risk was considered to be very low. However, a recent retrospective case-control study (N=2,361 taking HCQ for ≥5 years) reported the prevalence estimate of HCQ retinopathy to be 7.5%, which is >3 times higher than that of previous studies (Melles R, et al. JAMA Ophthalmol.; 2017). This study served as the key basis for the 2016 revised American Academy of Ophthalmology (AAO) recommendations for HCQ retinopathy screening. However, this study did not take into account the competing risk of death (e.g., a 2-fold increased mortality risk in SLE) and thus, the reported retinopathy risk could be overestimated. We conducted a simulation study to estimate potential impact of competing risk of death on risk of retinopathy among patients with SLE.

Methods: In the simulation studies we assumed that (1) the hazard rates of toxic retinopathy for three different doses of HCQ (i.e., >5mg/kg), 4-5mg/kg and <4mg/kg) change over time according to a Weibull distribution; (2) the survival rate in the general population from 55 to 75 years old was based on 2013 Life Table in US; (3) mortality rate in SLE patients is 2-fold higher than that in the general population; and (4) the risk of retinopathy was 70%, 40%, and 15% for 25 years, respectively, based on the previous study. We estimated the risk of retinopathy and depicted survival curves using K-M curve with and without accounting for competing risk of death. We simulated 6000 independent observations based on 1000 replications.

Results: As shown in Figure 1, the shape and magnitude of risk of retinopathy for each HCQ dose category were similar to the findings of the previous study. After accounting for competing risk of death, the risk of toxic retinopathy was 29.9% (95% CI: 28.8% to 30.1%), 20.4% (95% CI: 19.4% to 21.5%), 10.7% (95% CI: 9.9% to 11.6%), respectively, for each dose over 25 years. The risk of retinopathy from HCQ without accounting for competing risk death may overestimate the true risk of retinopathy for each category of HCQ by 40.2%, 96.0% and 134.1% over 25 years of use, respectively.

Conclusion: Although high dose and long-term HCQ use increase the risk of toxic retinopathy, the reported risk of retinopathy from the recent study without accounting for competing risk of deaths in SLE patients is likely to be overestimated particularly in the long-term follow-up. Prospective studies are needed to accurately estimate the risk of retinopathy attributed to HCQ.

Disclosure: N. Lu, None; H. K. Choi, None; A. Jorge, None; Y. Zhang, None.

Is a Growing Waistline over 8 Years Associated with Incident Functional Limitation and Low Health-Related Quality of Life in Knee Osteoarthritis?

Meredith Christiansen1, Louise Thoma1, Hiral Master1, Dana Mathews2 and Daniel White3, 1Physical Therapy and Biomechanics and Movement Science, University of Delaware, Newark, DE, 2Physical Therapy, Biomechanics and Movement Science, University of Delaware, Newark, DE, 3Department of Physical Therapy, University of Delaware, Newark, DE

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: ARHP Epidemiology and Public Health
Session Type: ARHP Concurrent Abstract Session
Session Time: 11:00AM-12:30PM

Background/Purpose: A large waist circumference (WC) is associated with walking difficulty in people with or at risk for knee osteoarthritis (OA). To date, it is unclear whether a meaningful increase in WC is also associated with walking difficulty and poor health. This is important to study since minimizing gains in WC may be important to reduce functional limitation and low health-related quality of life (HRQoL), which are common in knee OA. The purpose of this study was to investigate the association of increasing WC with function and HRQoL in people with or at risk for knee OA.

Methods: Data was extracted from the Osteoarthritis Initiative, a large prospective cohort study of people with or at risk for knee OA. Our primary exposures of interest were baseline WC and a meaningful increase in WC. WC was measured around the participant’s mid torso at the largest circumference with a tape measure. Baseline WC was classified into two groups using established thresholds: 1) Large WC (males > 102cm, females > 88cm) and 2) Small WC (males ≤ 102cm, females ≤ 88cm). A meaningful increase in WC over an 8-year timeframe was classified into two groups: 1) Increase (> 5cm) and 2) Maintain (≤ 5cm). Our two outcome measures of interest were function and HRQoL at the 8-year follow up measured by 1) gait speed (m/s) during a 20-meter walk test and 2) Short Form 12 Physical Summary Scale (SF12-P). Gait speed < 1.2 m/s and a SF12-P < 40 indicated functional limitation and poor HRQoL, respectively. We calculated risk ratios and 95% confidence intervals RR(95%CI) to examine the association of increased WC with study outcomes, adjusted for potential confounders.

Results: Of 4796 participants with baseline WC data (58% female, age 61± 9, BMI 28.6 ± 4.8), 2543 and 2238 people were free of the outcome at baseline and had 8-year follow up data for SF12-P and gait speed, respectively. The Large WC-Increase group had the greatest risk of developing functional limitation and poor HRQoL compared with the Small WC-Maintain group (Table 1). Those in the Large WC-Maintain group had a greater risk of developing a functional limitation compared with the Small WC-Maintain group, but were at similar risk for poor HRQoL (Table 1). Participants in the Small WC-Increase group were at similar risk as the Small WC-Maintain group for developing functional limitation and poor HRQoL (Table 1).

Conclusion: People with large WC had greater risk of functional limitation and poor HRQoL 8 years later, irrespective of increasing WC, compared with those with a small WC. Those with a large WC who increase WC had the highest risk compared to those with a small WC who maintained WC. Educating people with knee OA to avoid WC gains, particularly those already with a large WC, may mitigate future functional limitation and poor HRQoL.

<p>| Table 1: Risk Ratios for Functional Limitation and HRQoL |
|-----------------|----------------|------------------|</p>
<table>
<thead>
<tr>
<th><strong>Outcome</strong></th>
<th><strong>Incident Outcome/Total</strong></th>
<th><strong>%</strong></th>
<th><strong>Unadjusted RR (95%CI)</strong></th>
<th><strong>Adjusted RR</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gait speed</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small WC-Maintain</td>
<td>61/446</td>
<td>13.6</td>
<td><strong>REFERENCE</strong></td>
<td><strong>REFERENCE</strong></td>
</tr>
<tr>
<td>Large WC-Increase</td>
<td>138/414</td>
<td>33.3</td>
<td>2.4 (1.8-3.1)</td>
<td>2.2 (1.7-2.9)</td>
</tr>
<tr>
<td>Large WC-Maintain</td>
<td>294/1079</td>
<td>27.2</td>
<td>1.9 (1.5-2.5)</td>
<td>1.7 (1.3-2.2)</td>
</tr>
<tr>
<td>Small WC-Increase</td>
<td>51/269</td>
<td>17</td>
<td>1.2 (0.9-1.7)</td>
<td>1.2 (0.9-1.7)</td>
</tr>
<tr>
<td><strong>SF12-P</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small WC-Maintain</td>
<td>63/476</td>
<td>13.2</td>
<td><strong>REFERENCE</strong></td>
<td><strong>REFERENCE</strong></td>
</tr>
<tr>
<td>Large WC-Increase</td>
<td>121/482</td>
<td>25.1</td>
<td>1.8 (1.4-2.5)</td>
<td>1.7 (1.3-2.3)</td>
</tr>
<tr>
<td>Large WC-Maintain</td>
<td>207/1285</td>
<td>16.8</td>
<td>1.2 (0.9-1.6)</td>
<td>1.1 (0.8-1.4)</td>
</tr>
<tr>
<td>Small WC-Increase</td>
<td>49/339</td>
<td>15.9</td>
<td>1.0 (0.7-1.4)</td>
<td>1.0 (0.7-1.6)</td>
</tr>
</tbody>
</table>

*Incident Outcome defined as gait speed < 1.2 m/s and SF12-P ≤ 40
**Adjusted for age, sex, race, education, comorbidity, knee pain within the day 30 days
Statistically significant at alpha level 0.05
95% CI = 95% confidence interval

Disclosure: M. Christiansen, None; L. Thoma, None; H. Master, None; D. Mathews, None; D. White, None.
Curbing the Opioid Epidemic: Predictors of Opioid Use in Juvenile Fibromyalgia Syndrome

Sabrina Gmuca¹, Rui Xiao², Andrea M. Knight³, David D. Sherry¹, Pamela F. Weiss⁴ and Jeffrey S. Gerber⁵, ¹Pediatric Rheumatology, Children's Hospital of Philadelphia, Philadelphia, PA, ²Department of Biostatistics and Epidemiology, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, ³Division of Rheumatology, Center for Pediatric Clinical Effectiveness & PolicyLab, Children's Hospital of Philadelphia, Philadelphia, PA, ⁴Division of Rheumatology, Center for Pediatric Clinical Effectiveness, Children's Hospital of Philadelphia, Philadelphia, PA, ⁵Children's Hospital of Philadelphia, Philadelphia, PA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: ACR/ARHP Combined: Pediatrics
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose: Despite the lack of evidence to support the use of opioids in the treatment of adult fibromyalgia syndrome, approximately 30% of patients receive an opioid prescription (Fitzcharles, Am J Med. 2011). The prevalence of and risk factors for opioid prescribing for juvenile fibromyalgia syndrome (JFMS), however, have not been established.

Methods: We performed a retrospective cohort study using de-identified healthcare claims data from Clinformatics™ DataMart (OptumInsight, Eden Prairie, MN) from May 2000 - June 2013. The index date was the first ICD-9 code for fibromyalgia (729.1). JFMS was defined as subjects ≥ 2 and < 18 years of age at the index date with ≥2 codes for fibromyalgia within 12 months and continuous enrollment 6 months prior to and 12 months after the index date. Subjects with burns, sickle cell disease, or malignancy were excluded. Opioid exposure was defined as ≥ 1 prescription within 6 months prior to or any time after the index date. Healthcare utilization was assessed by provider type and place of service and defined as ≥ 1 co-variate prior to first opioid prescription. Acute care visit included an urgent care and/or emergency department encounter. Multivariate logistic regression modeling (adjusting for demographics, co-morbidities, and healthcare utilization) was used to identify independent risk factors associated with opioid use.

Results: Of 26516 subjects who met study criteria, 5296 (20%) received an opioid prescription. Subjects were predominantly female (55%) and Caucasian (80%). Median age at index date was 14 years (IQR: 11.0, 16.0) and at first opioid prescription was 16 years (IQR: 13, 17). Codeine (71%), tramadol (21%) and oxycodone (14%) were the most commonly prescribed opioids. Diagnosis of anxiety and depression occurred in 14% and 15% of children, respectively. In multivariate logistic regression (Table 1), opioid exposure was positively associated with female sex (OR =1.26; p<0.001), Caucasian race (OR=1.31; p<0.001), preceding acute care visit (OR: 1.41; p<0.001), hospitalization (OR: 2.38; p<0.001) and anesthesiology encounters (OR: 1.09; p=0.04). Compared to the Northeast, subjects from the Western United States had an increased risk of opioid exposure (OR: 1.20; p<0.01). Presence of a mental health co-morbidity and an encounter with a mental health provider were associated with decreased risk of opioid use (all p<0.05). Children seen by a chiropractor or emergency medicine physician also had a decreased risk of opioid use (OR: 0.35 and OR: 0.83, respectively; both p<0.001).

Conclusion: Opioids were prescribed for 20% of children with JFMS. Increased physician education in acute care and inpatient settings is needed to reduce prescribing of opioids for JFMS. Increased availability of mental health resources and non-pharmacologic treatment options might represent effective strategies to reduce opioid exposure in children with JFMS.
Knee Joint Sounds: A Non-Invasive Modality for Classifying Knee Joint Health in Juvenile Idiopathic Arthritis

Daniel Whittingslow¹, Beren Semiz², Lori Ponder³, Patricia Vega-Fernandez⁴, Omer Inan⁵ and Sampath Prahalad⁶, ¹Department of Biomedical Engineering, Georgia Institute of Technology, Atlanta, GA, ²Electrical and Computer Engineering, Georgia Institute of Technology, Atlanta, GA, ³Emory University, Atlanta, GA, ⁴Pediatrics, Emory University School of Medicine, Atlanta, GA, ⁵Biomedical Engineering, Georgia Institute of Technology, Atlanta, GA, ⁶Pediatrics, Emory Children's Center, Atlanta, GA

First publication: September 18, 2017

SESSION INFORMATION

Session Date: Wednesday, November 8, 2017
Session Title: ACR/ARHP Combined: Pediatrics
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose:

Juvenile Idiopathic Arthritis (JIA) is the most common, chronic, childhood rheumatic disease and an important cause of disability. It is characterized by persistent inflammation of the joints, with onset in childhood. A pronounced improvement in functional outcome has been documented in the past decade - largely due to advances in clinical diagnosis and treatment regimes. However, 5-10% of patients still have serious functional disability five years post diagnosis. Outcomes will be further improved by advances in the standardization of clinical diagnostics, disease tracking, and further refining of the treatment regimen.
The diverse nature of JIA, the lack of specific biomarkers and its concomitant progression have made standardizing diagnosis and tracking of the disease difficult. Currently, diagnosing and tracking JIA relies on subjective physical exams, reported symptoms, and imaging studies. There exists a need for a non-invasive, safe, radiation-free technique for objectively and accurately assessing the status of affected joints.

**Methods:**

Joint sounds can be used to quantitatively assess the joint. Microphones can be used to capture information regarding the underlying physiologic processes of a joint. This technique is safe, radiation-free, objective, and quantitative. The joint sounds change with the biomechanics of the joint: internal friction between articulating structures in the knee create various frequencies of vibrations that can be detected at the surface of the knee. The inflammation and altered biomechanical properties provide the opportunity for utilizing this technology to diagnose and monitor the condition.

We performed joint sound recordings on four JIA patients and seven healthy controls that were age and sex matched. The knee sounds of the subjects were recorded using a custom hardware setup consisting of LED motion tracking and accelerometers for vibration detection (Figure 1A shows a leg in flexion with recording apparatus). The subjects performed ten flexion/extension cycles with the recording apparatus (1B exercise and microphone schematic).

**Results:**

The results can be seen in Figure 1C. The top graph shows the angle of the knee, while the bottom plot shows the sound profile. The plots of JIA patients are more chaotic with periodic peaks. After treatment, the sounds of JIA patient more closely resembled the knee sounds of quiet healthy control. Signal analysis was performed between two groups. We found that RMS power and the standard deviation of the signals were substantially different between the groups (1D).

**Conclusion:**

The substantial differences in joint sound signals between healthy children and children with JIA are encouraging for the further development and refinement of this acoustic recording system and associated knee health algorithm for the diagnosis and objective monitoring of JIA.

**Disclosure:** D. Whittingslow, None; B. Semiz, None; L. Ponder, None; P. Vega-Fernandez, None; O. Inan, None; S. Prahalad, None.


**Abstract Number:** 2994

**Improving Outcomes Using a Treat to Target Approach and Clinical Decision Support in Polyarticular Juvenile Idiopathic Arthritis**
Polyarticular juvenile idiopathic arthritis (Poly-JIA) causes pain, functional disability, and joint damage. Variation in Poly-JIA clinical assessment and treatment likely has a negative impact on outcomes. Our goal was to improve Poly-JIA outcomes by standardizing disease activity scoring, ensuring disease activity review at the point of care, and implementing clinical decision support (CDS) to reduce treatment variation.

Methods: In January 2016, we began documenting JIA disease activity at outpatient visits. For Poly-JIA, we iteratively designed and tested CDS algorithms to standardize medication selection, dosing, and treatment duration. In April 2016, we implemented CDS (Phase 1) for Poly-JIA reactivation. In October-November 2016, we began disease activity target review for all JIA patients and CDS (Phase 2) for patients with new Poly-JIA and those in remission. Process measures included visit-level clinician target attestation (goal > 50%) and CDS use (goal > 15%). The outcome measure was the three-variable clinical Juvenile Arthritis Disease Activity Score (cJADAS), which is the sum of the physician and patient/parent global assessment (both 0-10), and active joint count (maximum 10). We calculated the monthly population cJADAS mean using the patients’ last recorded value in patients with two or more visits. Our goal was to improve the Poly-JIA cJADAS by ≥ 10%. Data were analyzed for special cause variation using standard statistical process control (SPC) and run chart methodology.

Results: From February 2016-March 2017, we longitudinally assessed 112 patients with Poly-JIA and 358 with other JIA subtypes. After October 2016, the mean monthly disease activity target attestation in all JIA patients was 74%. In Phases 1 and 2, we used CDS in 5-17% and 41-88% of Poly-JIA encounters, respectively. From July 2016-June 2017, Poly-JIA cJADAS scores decreased from a baseline of 5.5 to 3.5 (36%) (Figure). Special cause variation was identified in January 2017, when the cJADAS score decreased to 4.0, which was less than the lower confidence limit. During this period, the proportion of patients in clinician-defined remission increased from 31% to 49%. Significantly fewer joint injections were performed from December 2016-June 2017. In other JIA subtypes observed over the same period in whom target attestation was used without CDS, cJADAS scores decreased from 3.9 to 3.4 (13%), which did not achieve special cause variation.

Conclusion: After exceeding our target attestation and CDS use goals, Poly-JIA disease activity improved by 36%. We estimate that approximately 22 more patients are currently in remission. Therefore, using a treat to target approach paired with CDS can improve Poly-JIA disease activity substantially. We plan to study changes medication use, assess pain and functional outcomes, and develop additional CDS algorithms.

Disclosure: L. Buckley, None; E. Ware, None; G. Kreher, None; L. Wiater, None; J. Mehta, None; J. Burnham, None.
Pathogens in the Inflammatory Process of Periodontal Disease and Juvenile Idiopathic Arthritis

Nancy Delnay¹, Neil McNinch² and Mary Toth³, ¹Rheumatology, Akron Children's Hospital, Akron, OH, ²Rebecca Considine Research, Akron Children's Hospital, Akron, OH, ³Rheumatology, Children's Hospital Medical Center, Akron, OH

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: ACR/ARHP Combined: Pediatrics
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose:
Juvenile idiopathic arthritis (JIA) and periodontal disease (PD) are both diseases of inflammation that can result in bone loss when the inflammatory process is prolonged. In periodontal disease redness and swelling to gums represents infection of bacteria such as Porphyromonas gingivalis (Pg). Hitchon (2010) linked anti-p gingivalis antibodies and anti-cyclic citrullinated peptide (CCP) antibodies in adult patients with rheumatoid arthritis. CCP antibodies are linked with erosive joint disease. In 2016 Lange investigated antibody responses to oral pathogens of children with JIA, concluding that children with CCP-positive JIA have higher antibody titers to p. gingivalis. The purpose of this study is to determine the presence of the bacteria (Pg) in children with JIA who are positive for rheumatoid factor (RF) or CCP.

Methods:
A convenience sample of 12 children ages 10-21 with a diagnosis of JIA and either RF positive or CCP positive was selected from a hospital based rheumatology clinic. A full exam, including an oral exam was completed to assess for JIA and PD disease activity. During the exam a saliva sample was collected to identify the presence of common pathogens associated with gum disease and increased risk of systemic disease. Genomic DNA was extracted from the saliva sample and tested for bacteria associated with periodontal disease. The bacteria were tested by PCR amplification followed by fluorescent endpoint detection of sample bacterial concentrations. Pathogenic bacteria were reported as low, moderate or high risk for association with periodontal disease. Differences in the bacterial profile were compared to an age and gender matched control group with periodontal disease. Fisher’s exact test and Wilcoxon test were used to compare the groups.

Results:
Upon physical examination 7 of 12 children (58%) examined showed signs of localized oral inflammation to one or more teeth, none of the 12 had generalized oral inflammation. Only 2 of 12 children (17%) had presence of Pg: neither had bleeding with brushing or flossing and one exhibited localized gum redness. Exploratory analysis of common pathogens associated with periodontal disease: JIA status was not associated with Pg, Fisher’s Exact Test $p = 0.68$. Calculated Pg bacterial load was not different by JIA status, Wilcoxon Rank Sum Test $p = 0.63$. Infection status was associated with JIA status, Fisher’s Exact Test $p < 0.01$. 4 of 12 children (33%) exhibited presence of high risk bacteria: Pg, Aggregatibacter actinomycetemcomitans (Aa), Tannerella forsythia (Tf) and Treponema denticola (Td). There was no significant difference in high risk bacterial counts by JIA status ($p = 0.63, 0.30, 0.35 & 0.61$ respectively). The results of this study were limited by sample size.

Conclusion:
Children with CCP-positive or RF positive JIA have similar bacterial profiles as children with periodontal disease placing them at risk for development of periodontal disease. This reinforces the need for inclusion of oral health exam within the JIA population. Further studies with larger sample sizes are needed to understand the association between oral pathogens and the inflammatory process.

Disclosure: N. Delnay, None; N. McNinch, None; M. Toth, None.


Abstract Number: 2996

Resilience and Transition Readiness in Pediatric SLE Patients
SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: ACR/ARHP Combined: Pediatrics
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose: Childhood onset systemic lupus erythematosus (SLE) is a chronic autoimmune condition with high morbidity that requires long-lasting care through adulthood. Transition from pediatric to adult care is difficult and poor transition can be associated with worse outcomes. Resilience is the ability to respond positively to adversity. It is a mutable trait that can be improved through interventions. In other chronic conditions, resilience has been found to be an important predictor of transition readiness. The purpose of this study is to evaluate if resilience is predictive of transition readiness. A secondary aim is to explore other factors that may influence transition readiness in SLE.

Methods: Sixty-two adolescent SLE patients from the Stanford Children’s Health Pediatric Rheumatology clinic were enrolled in a cross-sectional study. Inclusion criteria included diagnosis of SLE confirmed using American College of Rheumatology or Systemic Lupus International Collaborating Clinics (SLICC) classification criteria before age 18 and disease duration more than 6 months. Participants completed questionnaires on transition readiness, resilience, depression, anxiety and fatigue. Resilience was evaluated using Resilience Scale (RS-14), a validated measure in adolescents and adults. Transition readiness was evaluated using Transition Readiness Assessment Questionnaire (TRAQ), a validated scale in adolescents with chronic disease. Data regarding SLE disease characteristics, disease duration, disease activity and socioeconomic status was obtained. A multivariable linear regression model was created to evaluate association between transition readiness and resilience.

Results: The majority of participants were mostly (87%) and Asian (47%). The mean age was 18.6 years and mean disease duration was 5.1 years. TRAQ scores were significantly correlated with resilience, RS-14 (ρ=0.39, p=0.002) and current age (ρ=0.47, p<0.001). There was no correlation with disease duration, fatigue, anxiety, depressive symptoms, disease damage (SLICC Damage Index) or disease activity (SLEDAI score). A Wilcoxon rank sum test indicated that the TRAQ score was greater for individuals with public insurance (Median=87.5) than for privately insured patients (Median=75), p=0.002. There was no difference in scores between genders, or in individuals with depression or anxiety or history of severe disease. A multiple regression analysis model was calculated to predict TRAQ score based on resilience, controlling for insurance status, age and disease duration. Resilience (β=0.33, p=0.002), age (β=0.49, p=0.001), and insurance status (β=0.31, p=0.004) were significant predictors in this model. The overall model fit was $R^2$ of 0.44 (p=0.0001).

Conclusion: In adolescent SLE patients, preparation for transition is important. Correcting for age, and other confounding factors, resilience score appears predictive of transition readiness. In addition to current care, it may be important to include resilience building into transition programs to assist with improved outcomes.

Disclosure: J. Lai, None; L. Nelson, None; I. Balboni, None; T. Lee, None; J. Hsu, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/resilience-and-transition-readiness-in-pediatric-sle-patients

Abstract Number: 2997

Patient and Family Reported Psychosocial Areas of Concern within Pediatric Rheumatology: Quality Improvement Data and Implications for Practice

Nicole Tennermann and Melissa Hazen, Rheumatology, Boston Children's Hospital, Boston, MA

First publication: September 18, 2017

SESSION INFORMATION
Session Date: Wednesday, November 8, 2017
Session Title: ACR/ARHP Combined: Pediatrics
Session Type: ACR Concurrent Abstract Session
Session Time: 9:00AM-10:30AM

Background/Purpose:

Psychosocial factors greatly impact the subjective disease experience and outcomes of children with rheumatic conditions. Attention to the psychosocial aspects of patients’ needs is essential in the multidisciplinary care of children with rheumatic disease. Such understanding can aid the assessment of presenting and persisting symptoms and shed light on barriers to treatment adherence.

In order to obtain baseline data regarding the psychosocial needs impacting pediatric rheumatology patients at our center, a quality improvement survey was undertaken. Here, we will discuss its implementation, review our findings, and outline modifications made to enhance multidisciplinary, patient-centered rheumatic care.

Methods:

Psychosocial needs assessment questionnaires are administered to every patient seen in the Rheumatology Program beginning in October 2016. We have reviewed 1714 questionnaires to date. Assessments ask about 8 areas of psychosocial concern frequently associated with social determinants of health: insurance, food insecurity, transportation to medical appointments, school concerns, housing instability/homelessness, safety, substance abuse, mental health/behavior, and coping with one’s medical condition. Responses can indicate concerns or no concerns in any area, and a follow-up question asks whether help addressing the concerns is desired. Questionnaires are completed by parents/caregivers or by adolescent/young adult patients. Patients can complete questionnaires at multiple office visits and can select as few or as many areas of concern as indicated. All questionnaires are administered in English.

Results:

Preliminary analysis demonstrates that approximately 25% of all questionnaires indicate concerns in at least one domain. In any given area of psychosocial concern, desires for help with addressing the need ranged from 0% (for assistance with substance abuse) to 100% (for assistance with food insecurity/homelessness). The areas of concern most often identified by families include school (61%), mental health/behavior (54%), and coping with rheumatic disease (46%). Overall, this means that 12% of questionnaires endorsed a concern for which social work assistance was requested.

Conclusion:

This quality improvement initiative demonstrates that a sizeable number of patients and families experience psychosocial stressors that may negatively impact the disease process and health outcomes. While we have a robust survey response rate and reproducible findings, there are limitations like self-presentation bias and the confines of the questionnaire design, including being available only in English. Nonetheless, we suspect these limitations lead to the under-reporting of need and requests for assistance. As a result of these findings, we have implemented programmatic changes to more effectively address our patients’ psychosocial needs. Specifically, the data gleaned from this quality improvement initiative is being used to enhance patient care through increased social work presence in the clinic, development of psychosocial support programs for patients and professional education for providers.

Disclosure: N. Tennermann, None; M. Hazen, None.

Efficacy and Safety of Intra-Articular Sprifermin in Symptomatic Radiographic Knee Osteoarthritis: Results of the 2-Year Primary Analysis from a 5-Year Randomised, Placebo-Controlled, Phase II Study

Marc C. Hochberg¹, Ali Guermazi², Hans Guehring³, Aida Aydemir⁴, Stephen Wax⁵, Patricia Fleuranceau-Morel⁴, Asger Reinstrup Bihlet⁶, Inger Byrjalsen⁶, Jeppe Ragnar Andersen⁶ and Felix Eckstein⁷, ¹University of Maryland School of Medicine, Baltimore, MD, ²Boston Imaging Core Lab, LLC, and Boston University School of Medicine, Boston, MA, ³Merck KGaA, Darmstadt, Germany, ⁴EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA, ⁵EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA, ⁶Nordic Bioscience, Herlev, Denmark, ⁷Institute of Anatomy, Paracelsus Medical University, Salzburg, Austria

First publication: October 19, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: ACR Late-Breaking Abstract Session
Session Type: ACR Late-breaking Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Sprifermin, a novel recombinant human fibroblast growth factor-18 is currently investigated as a potential disease-modifying osteoarthritis (OA) drug. Two-year primary data from a 5-year Phase II trial (FORWARD) is presented.

Methods: Patients (pts) aged 40–85 years with symptomatic radiographic knee OA, KLG 2 or 3, and medial mJSW ≥2.5 mm in the target knee were randomized (1:1:1:1:1) to receive 3 weekly intra-articular injections with double-blinded placebo (PBO) or sprifermin, administered in cycles every 6 or 12 months (Fig 1). The primary endpoint was the change in total tibiofemoral joint (TFJ) cartilage thickness from baseline (BL) to Year 2. The ITT population (all randomized pts) was used for non-MRI endpoints; and the mITT (all ITT pts with BL and ≥1 post-treatment MRI up to Year 2) for MRI endpoints.
**Results:** The ITT population included 549 pts: median age 65 years, 69% women, 80% white, and 69% KLG2. Of these, 12.2% (sprifermin) and 19.4% (PBO) discontinued treatment within 2 years. The primary endpoint was met (Fig 2); there was a dose-dependent increase in total TFJ cartilage thickness, with significant differences for sprifermin 100µg q6 mo (Group 1) and 100µg q12 mo (Group 2) vs PBO (+0.03 vs -0.02 mm; p<0.001, and +0.02 vs -0.02 mm; p<0.001, respectively). Furthermore, significant differences in change of cartilage thickness were observed between sprifermin vs PBO in medial (Group 1: +0.02 vs -0.03 mm; p=0.003) and lateral TFJ compartments (Group 1 and 2: both +0.04 vs -0.01 mm; p<0.001), and in central medial TFJ sub-regions (Group 1: +0.054 vs -0.11; p<0.001). Changes in mJSW observed with X-ray were significantly different between sprifermin Group 1 and PBO in the lateral but not the medial compartment. Total WOMAC scores improved by ~50% in all treatment groups including PBO. AEs and serious AEs were balanced between groups, and an overall acceptable safety profile was observed.

**Conclusion:** To our knowledge, sprifermin is the first investigational agent to show prevention of cartilage loss in both the lateral and medial (including central medial) femorotibial compartments. These structural benefits associated with sprifermin suggest that it may be efficacious for disease-modifying treatment of OA, and should be further evaluated in clinical trials.
Figure 1. FORWARD study design

**Screening**
- Knee osteoarthritis
- KL Grade 2-3

**Randomization**
- Treatment period (2 years)
  - Group 1: Sprifermin 100 μg q6 mo
  - Group 2: Sprifermin 100 μg q12 mo
  - Group 3: Sprifermin 30 μg q6 mo
  - Group 4: Sprifermin 30 μg q12 mo
  - Placebo

**Extended follow-up** (3 years)

**1st endpoint:** Change in cartilage thickness (MRI)
**2nd endpoints:** Patient-reported outcomes of pain and functioning (including WOMAC), JSW (X-ray)

**Major efficacy assessments:** ★ ★ ★ ★ ★ ★ ★ ★ ★ ★ ★

i.a., intra-articular; JSW, joint space width; KL, Kellgren-Lawrence; mo, months; MRI, magnetic resonance imaging; q, every; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index
Figure 2. Primary endpoint: change from baseline in cartilage thickness in the TFJ over 2 years (qMRI)

Analysis population: modified ITT (all subjects with BL and ≥1 post-treatment qMRI in the double-blind treatment period); error bars = 95% CI.

Total qMRI cartilage thickness = total volume divided by total surface area (i.e., average cartilage thickness)

At baseline, qMRI total cartilage thickness was similar in all treatment arms and averaged ~ 1.8 mm.

CI, confidence interval; q6mo, every 6 months; q12 mo, every 12 months; qMRI, quantitative magnetic resonance imaging; TFJ, total femorotibial joint

**Disclosure:** M. C. Hochberg, Bioiberica SA, Bristol Myers Squibb, EMD Serono, Galapagos, IBSA SA, Eli Lilly, Novartis Pharma AG, Pfizer Inc., Plexxikon, Samumed LLC, Theralogix LLC and TissueGene, 5; A. Guermazi, BICL, LLC, 1, Merck Serono, TissueGene, OrthoTrophix, AstraZeneca and Genzyme, 5; H. Guehring, Merck KGaA, 3; A. Aydemir, EMD Serono, Inc, 3; S. Wax, EMD Serono, Inc., 3; P. Fleuranceau-Morel, EMD Serono, Inc, 3; A. R. Bihlet, None; I. Byrjalsen, None; J. R. Andersen, None; F. Eckstein, Chondrometrics GmbH, 1.


**Abstract Number:** 2L

**Efficacy and Safety Results from a Phase 2 Trial of Risankizumab, a Selective IL-23p19 Inhibitor, in Patients with Active Psoriatic Arthritis**
Philip J Mease¹, Herbert Kellner², Akimichi Morita³, Alan J. Kivitz⁴, Kim A. Papp⁵, Stella Aslanyan⁶, Beate Berner⁷, Kun Chen⁸, Ann Eldred⁸, and Frank Behrens⁹, ¹Swedish Medical Center and University of Washington School of Medicine, Seattle, WA, ²Private Practice and Division of Rheumatology KHI Neuwittelsbach, München, Germany, ³Dept of Geriatric and Environmental Dermatology, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan, ⁴Altoona Center for Clinical Research, Duncansville, PA, ⁵K Papp Clinical Research and Probit Medical Research Inc, Waterloo, ON, Canada, ⁶Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT, ⁷Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany, ⁸AbbVie Inc., North Chicago, IL, ⁹CIRI/Rheumatology and Fraunhofer Institute IME, Translational Medicine and Pharmacology, Goethe University, Frankfurt, Germany

First publication: October 19, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: ACR Late-Breaking Abstract Session
Session Type: ACR Late-breaking Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: Interleukin-23 (IL-23), a key regulator of multiple effector cytokines (including IL-17, IL-22, and TNF), has been implicated in psoriatic lesions, synovitis, enthesitis, and bone erosion. Risankizumab (RZB) is a potent humanized IgG1 mAb that inhibits IL-23 by specifically binding its p19 subunit. The purpose of this Phase 2 study was to investigate the safety and efficacy of RZB in patients (pts) with active psoriatic arthritis (PsA).

Methods: Pts with active PsA were randomized in a 2:2:2:1:2 ratio to receive RZB (150 mg at weeks [Wks] 0, 4, 8, 12, and 16 [Arm 1], 150 mg at Wks 0, 4, and 16 [Arm 2], 150 mg at Wks 0 and 12 [Arm 3], 75 mg single dose at Wk 0 [Arm 4]) or matching placebo (PBO, Arm 5) in this ongoing double-blind, parallel-design, dose-ranging Phase 2 study. Pts were stratified at randomization by prior TNFi use and concurrent MTX use. The primary efficacy endpoint was ACR20 response at Wk 16. Additional efficacy endpoints included ACR50/70, minimal disease activity (MDA), DAS28(CRP), dactylitis count, SPARCC enthesitis index, pain on visual analog scale (VAS), and HAQ-DI; PASI responses were assessed only in pts with psoriasis (PsO) affecting ≥3% body surface area (BSA) at baseline (BL).

Results: Among the 185 pts who were randomized and received the study drug, 172 (93.0%) completed 16 wks of treatment. BL demographics and disease characteristics
were similar across treatment arms. The median age was 51 years; 80 (43.2%) pts were female and 89 (49.4%) pts had PsO ≥3% BSA. At BL, dactylitis or enthesitis was present in 56 (30.4%) and 119 (64.7%) pts, respectively; 45 (24.3%) pts had prior TNFi exposure and 106 (57.3%) pts were receiving concomitant MTX. At Wk 16, ACR20 responses were significantly greater in pts receiving RZB (across all arms, 57.1–65.0%) compared with PBO (37.5%, Table 1). PASI75/90/100 responses at Wk 16 were significantly higher in RZB-treated pts compared with PBO. ACR50 responses were numerically higher and improvements in HAQ-DI and enthesitis from BL were numerically greater in RZB arms. At Wk 16, RZB-treated pts achieved significantly higher ACR70 and MDA responses as well as greater improvements in DAS28(CRP) and Pain–VAS. Treatment-emergent adverse events (TEAEs) were comparable across treatment arms (Table 2); the most common TEAE was infection. There were no deaths or cases of tuberculosis in RZB-treated pts; 1 adjudicated major adverse cardiovascular event was reported in RZB arm.

**Conclusion:** In this Phase 2 study, RZB significantly improved joint and skin symptoms in pts with active PsA. RZB was well-tolerated with no new or unexpected safety findings.

Table 1. Summary of Efficacy Results at Week 16a

<table>
<thead>
<tr>
<th>Endpoints</th>
<th>Arm 1 N=42</th>
<th>Arm 2 N=42</th>
<th>Arm 3 N=39</th>
<th>Arm 4 N=20</th>
<th>Arm 1 + 2 N=84</th>
<th>Placebo Arm 5 N=42</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary endpoint</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACR20 (%)</td>
<td>57.1*</td>
<td>61.9**</td>
<td>59.0*</td>
<td>65.0*</td>
<td>59.5**</td>
<td>35.7</td>
</tr>
<tr>
<td><strong>Secondary endpoints</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACR50 (%)</td>
<td>23.8</td>
<td>23.8</td>
<td>38.5**</td>
<td>25.0</td>
<td>23.8</td>
<td>11.9</td>
</tr>
<tr>
<td>ACR70 (%)</td>
<td>14.3*</td>
<td>7.1</td>
<td>25.6***</td>
<td>15.0*</td>
<td>10.7**</td>
<td>0.0</td>
</tr>
<tr>
<td>PASI75 (%)p</td>
<td>75.0***</td>
<td>70.0***</td>
<td>73.9***</td>
<td>66.7***</td>
<td>72.2***</td>
<td>9.5</td>
</tr>
<tr>
<td>PASI90 (%)p</td>
<td>58.3***</td>
<td>66.7***</td>
<td>52.2***</td>
<td>55.6**</td>
<td>63.3***</td>
<td>9.5</td>
</tr>
<tr>
<td>PASI100 (%)b</td>
<td>33.3</td>
<td>50.0**</td>
<td>34.8*</td>
<td>55.6**</td>
<td>43.3**</td>
<td>9.5</td>
</tr>
<tr>
<td>MDA (%)</td>
<td>28.6**</td>
<td>28.6**</td>
<td>33.3**</td>
<td>35.0**</td>
<td>28.6**</td>
<td>7.1</td>
</tr>
<tr>
<td>ΔDAS28(CRP)c</td>
<td>-1.1</td>
<td>-1.6***</td>
<td>-1.5**</td>
<td>-1.9***</td>
<td>-1.3**</td>
<td>-0.8</td>
</tr>
<tr>
<td>ΔDactylitis Countf</td>
<td>-0.5</td>
<td>-2.5</td>
<td>-3.1</td>
<td>-3.6</td>
<td>-1.6</td>
<td>-2.8</td>
</tr>
<tr>
<td>ΔSPARC Enthesitis Indexc</td>
<td>-1.4</td>
<td>-2.4</td>
<td>-1.8</td>
<td>-3.8*</td>
<td>-1.7</td>
<td>-1.2</td>
</tr>
<tr>
<td>ΔPain–VASc</td>
<td>-11.7</td>
<td>-17.5**</td>
<td>-18.1**</td>
<td>-24.3**</td>
<td>-14.6**</td>
<td>-3.3</td>
</tr>
<tr>
<td>ΔHAQ-DIf</td>
<td>-0.18</td>
<td>-0.16</td>
<td>-0.25</td>
<td>-0.16</td>
<td>-0.18</td>
<td>-0.09</td>
</tr>
</tbody>
</table>

Arm 1, 150 mg RZB at weeks 0, 4, 8, 12, and 18; Arm 2, 150 RZB at weeks 0, 4, and 16 (PBO at weeks 8 and 12); Arm 3, 150 mg RZB at weeks 0 and 12 (PBO at weeks 4, 8, and 12); Arm 4, 75 mg RZB at week 0 (PBO at weeks 4, 8, 12, and 16); Arm 5, PBO at weeks 0, 4, 8, 12, and 16.

P-values for comparison versus placebo: *** P < 0.001; ** P < 0.01; * P < 0.05.

*Results for categorical endpoints are based on NRI analyses. Results for continuous variables are based on MMRM analyses.

PASI responses calculated only in patients with psoriasis affecting ≥3% BSA at baseline; Arm 1, N=18; Arm 2, N=20; Arm 3, N=23; Arm 4, N=9; Arm 5, N=21.

δ Mean change from baseline are presented.

ACR20/50/70 = 20/50/70% improvement in American college of rheumatology score; BSA = body surface area; DAS28(CRP) = 28-joint disease activity score based on C-reactive protein; Δ = change from baseline to week 16; HAQ-DI = health assessment questionnaire-disability index; MDA = minimal disease activity; MMRM = mixed effect model repeat measurement; NRI = non-responder imputation; PASI75/90/100 = 75/90/100% improvement in psoriasis area and severity index; PBO = placebo; RZB = risankizumab; SPARCC = Spondyloarthritis Research Consortium of Canada; VAS = visual analog scale.
Disclosure: **P. J. Mease**, AbbVie, Amgen, Bristol Myers, Celgene, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, Sun Pharma, and UCB, 2, AbbVie, Amgen, Bristol Myers, Celgene, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, Sun Pharma, and UCB, 5, AbbVie, Amgen, Bristol Myers, Celgene, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, Sun Pharma, and UCB, 8; **H. Kellner**, AbbVie, BMS, MSD, Novartis, Pfizer, Roche and UCB, 2, AbbVie, BMS, MSD, Novartis, Pfizer, Roche and UCB, 5, AbbVie, BMS, MSD, Novartis, Pfizer, Roche and UCB, 8; **A. Morita**, AbbVie, Eli Lilly Japan K.K., Janssen Pharmaceutical K. K., Kyowa Hakko Kirin Co., Ltd, Leo Pharma, Maruho Co, Ltd, Mitsubishi-Tanabe Pharma, and Novartis, 2, AbbVie, Eli Lilly Japan K.K., Janssen Pharmaceutical K. K., Kyowa Hakko Kirin Co., Ltd, Leo Pharma, Maruho Co, Ltd, Mitsubishi-Tanabe Pharma, and Novartis, 5, AbbVie, Eli Lilly Japan K.K., Janssen Pharmaceutical K. K., Kyowa Hakko Kirin Co., Ltd, Leo Pharma, Maruho Co, Ltd, Mitsubishi-Tanabe Pharma, and Novartis, 8; **A. J. Kivitz**, AbbVie, Amgen, Boehringer Ingelheim, Celgene, Genentech, Genzyme, Horizon, Janssen, Merck, Novartis, Pfizer, Sanofi, Sun Pharma Advanced Research, Regeneron, UCB, and Vertex, 5, AbbVie, Amgen, Boehringer Ingelheim, Celgene, Genentech, Genzyme, Horizon, Janssen, Merck, Novartis, Pfizer, Sanofi, Regeneron, UCB, and Vertex, 8; **K. A. Papp**, AbbVie, Amgen, Astellas, Baxalta, Baxter, BL, BMS, Celgene, Dermira, Lilly, Forward, Galderma, Genentech, GSK, Janssen, Kyowa-Hakko Kirin, Leo, MedImmune, Merck, Novartis,
Secukinumab Demonstrates Low Radiographic Progression and Sustained Efficacy through 4 Years in Patients with Active Ankylosing Spondylitis

Jürgen Braun¹, Xenofon Baraliakos¹, Atul A. Deodhar², Denis Poddubnyy³, Paul Emery⁴, Evie Maria Delicha⁵, Zsolt Taloczy⁶ and Brian Porter⁶, ¹Rheumazentrum Ruhrgebiet, Herne, and Ruhr University Bochum, Herne, Germany, ²Division of Arthritis & Rheumatic Diseases, Oregon Health & Science University, Portland, OR, ³Department of Rheumatology, Charité Universitätsmedizin Berlin, Berlin, Germany, ⁴Leeds Musculoskeletal Biomedical Research Unit/Institute Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom, ⁵Novartis Pharma AG, Basel, Switzerland, ⁶Novartis Pharmaceuticals Corporation, East Hanover, NJ

First publication: October 19, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: ACR Late-Breaking Abstract Session
Background/Purpose: Secukinumab, a fully human anti–interleukin-17A monoclonal antibody, reported improved signs and symptoms of ankylosing spondylitis (AS) in the MEASURE 1 trial. Here, we report efficacy, including imaging outcomes, and safety from the MEASURE 1 extension trial (NCT01863732) out to 4 years (208 weeks [wks]).

Methods: In the core study, 371 patients (pts) with active AS were randomized to secukinumab or placebo (PBO). Pts on secukinumab had a 10 mg/kg iv loading dose at baseline (BL), Wks 2 and 4, and then 150 mg sc (IV→150 mg) or 75 mg sc (IV→75 mg) every 4 wks from Wk 8 (same schedule for PBO). Based on ASAS20 response at Wk 16, PBO pts were re-randomized to secukinumab 150 or 75 mg sc at Wk 16 (non-responders) or Wk 24 (responders). Efficacy data at Wk 208 are reported for pts originally randomized to secukinumab 150 mg (approved dose with sc loading). Lateral radiographs of the cervical and lumbar spine at BL, Wk 104 and Wk 208 were read centrally by 2 independent readers, blinded to treatment arm and radiograph sequence, using the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS). For this analysis, radiographs performed at BL and Wk 104 were re-read for pts who completed 208 wks of treatment. Descriptive statistics on observed or imputed data are provided.

Results: Of the 274 patients in this extension study, 89.7% (78/87) originally assigned to secukinumab 150 mg completed 208 wks. Mean (±SD) change in mSASSS from BL to Wk 208 was lower with secukinumab 150 mg (1.2±3.91) vs 75 mg (1.7±4.70). No radiographic progression was seen in 73% (mSASSS change from BL ≤0) and 79% (mSASSS change from BL <2) of pts with secukinumab over 208 wks (Figure). Mean mSASSS changes at Wk 208 were numerically higher in males vs females, pts with elevated vs normal BL hsCRP, and pts with vs without BL syndesmophytes. Sustained efficacy in signs/symptoms was seen through Wk 208, evidenced by ASAS 20/40, BASDAI, BASFI, BASMI and ASDAS inactive disease (Table). Efficacy responses were numerically lower with secukinumab 75 mg vs 150 mg. Across the entire treatment period (secukinumab exposure [mean±SD]: 3.4±1.44 years), exposure-adjusted incidence rates for serious infections, Crohn's disease, uveitis and malignant/unspecified tumors were 1.0, 0.6, 1.8 and 0.5 per 100 pt-years, respectively.

Conclusion: Secukinumab 150 mg demonstrates lower radiographic progression vs 75 mg at 4 years. These 4-year results confirm the sustained efficacy and known safety profile of secukinumab.


Table. Summary of efficacy data at Wk 208
Secukinumab IV→150mg (N=87)

Radiographic outcomes\(^\text{a,b}\)

mSASSS at BL, mean±SD \(8.8\pm16.23\) (n=71)
Change in mSASSS from BL to Wk 208, mean±SD \(1.2\pm3.91\) (n=71)
Change in mSASSS from BL to Wk 104, mean±SD \(0.6\pm1.84\) (n=57)
Change in mSASSS from Wk 104 to Wk 208, mean±SD \(0.6\pm2.61\) (n=58)

Other efficacy outcomes

ASAS20 / 40,\(^\text{c}\)% \(76.4 / 58.0\)
BASDAI,\(^\text{d}\) change from BL, LS mean±SE \(-3.3\pm0.23\)
ASDAS inactive disease,\(^\text{c}\)% \(11.6\)
BASFI,\(^\text{b}\) change from BL, mean±SD \(-2.9\pm2.39\) (n=80)
BASMI,\(^\text{b}\) change from BL, mean±SD \(-0.52\pm1.12\) (n=76)

BL, baseline; LS, least squares; n, number of pts meeting criteria; N, total number of pts in the extension trial; SD, standard deviation; SE, standard error \(^\text{a}\)Radiographs performed at BL and Wk 104 were re-read for pts who completed 208 wks of treatment; \(^\text{b}\)Observed data; \(^\text{c}\)Estimated using multiple imputation; \(^\text{d}\)MMRM estimates

Figure. Cumulative probability plot of 4 years progression for mSASSS (Full analysis set)
Final Results of an Open Label Phase 2 Study of a Reversible B Cell Inhibitor, Xmab®5871, in IgG4-Related Disease

John H. Stone1, Zach Wallace2, Cory A. Perugino3, Ana D. Fernandes4, Payal Patel5, Paul A. Foster6 and Debra J. Zack6, 1Massachusetts General Hospital Rheumatology Unit, Harvard Medical School, Boston, MA, 2Division of Rheumatology, Allergy and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, 3Ragon Institute of MGH, MIT and Harvard, Cambridge, MA, 4Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Boston, MA, 5Rheumatology, Harvard, Boston, MA, 6Xencor, Inc., San Diego, CA

First publication: October 19, 2017
Background/Purpose: IgG4-related disease (IgG4-RD) is an immune-mediated condition causing fibro-inflammatory lesions that can lead to irreversible organ damage and death. No approved therapies exist. A novel monoclonal antibody, XmAb5871, is a humanized anti-CD19 antibody with an Fc engineered for increased affinity to FcγRIIb. Co-ligation of CD19 and FcγRIIb leads to inhibition of B lineage cells. Because of the importance of B cells and plasmablasts (PB) in IgG4-RD pathogenesis, an open label pilot of XmAb5871 in IgG4-RD was performed.

Methods: IgG4-RD patients with active disease defined by an IgG4-RD Responder Index (RI) of ≥ 3 were administered XmAb5871 (5 mg/kg) IV every 14 days for 12 doses. The primary outcome measure was the proportion of patients on Day 169 with a decrease in the IgG4-RD RI of ≥2 points compared to baseline. Secondary endpoints included the proportion of patients achieving an IgG4-RD RI of 0 with no corticosteroids (CS) after month 2. Other immunosuppressive medications were not allowed. Mechanistic studies were performed at baseline and at selected intervals.

Results: 15 patients enrolled between March 2016 and January 2017. The median age of the 15 patients was 63 years (43 to 77 years). Two-thirds were male. 12 of 15 patients had elevated baseline serum IgG4 concentrations (median IgG4: 220 mg/dL; 25 – 2415). 10 had undergone treatment with other therapy before entry. The median baseline IgG4-RD RI was 12 (2 – 30), with active inflammatory disease in a median of 5 organ systems (1-10). The organs most commonly affected were lymph nodes (73% of patients), submandibular glands (60%), parotid glands (53%), and lacrimal glands (47%). 5 patients (33%) had kidney involvement, 4 (27%) had lung findings and 3 each (20%) had orbital lesions, nasal cavity involvement or heart/pericardium findings. 12 patients (80%) completed the study and all 12 achieved the primary endpoint of at least a 2-point reduction in the IgG4-RD RI on Day 169. None of the 12 required CS after month 2. 8 patients (53%) achieved remission (IgG4-RD RI of 0 and no CS after 2 months) and the other 4 achieved IgG4-RD RI scores of ≤4 at Day 169. 14 of 15 patients (93%) achieved a decrease of ≥ 2 in the IgG4-RD RI, most within 2 weeks. One patient had been on baseline CS for 2 years (15 mg/day) and was able to discontinue CS within 2 months. 4 others received CS at the start of the trial and tapered off within 2 months. 3 patients had minor, transient GI side-effects during the 1st infusion; all completed the study. Two SAEs of pneumonia and recurrence of pneumonia due to lack of compliance were seen in 1 patient (who completed). 3 patients discontinued early. One was an atypical patient with laryngeal involvement only who did not respond to XmAb5871 or to subsequent rituximab. A 2nd responded well, but flared at 12 weeks and did not respond to
subsequent rituximab therapy. The 3rd responded well but developed infusion-related symptoms including transient rash and arthralgias following the 5th infusion. She concurrently developed anti-drug antibodies.

Mean B cell counts decreased to ~40-55% of baseline and circulating PBs decreased by ~70% following XmAb5871.

**Conclusion:** XmAb5871 is tolerated well in patients with active IgG4-RD and is a promising treatment approach for IgG4-RD.

**Disclosure:** J. H. Stone, Xencor, 2; Z. Wallace, None; C. A. Perugino, None; A. D. Fernandes, None; P. Patel, None; P. A. Foster, Xencor Inc, 1,Xencor Inc, 3; D. J. Zack, Xencor Inc, 1,Xencor Inc, 3.

[View Abstract and Citation Information Online](http://acrabstracts.org/abstract/final-results-of-an-open-label-phase-2-study-of-a-reversible-b-cell-inhibitor-xmab5871-in-igg4-related-disease)

**Abstract Number:** 5L

**Rapamycin Vs. Placebo for the Treatment of Inclusion Body Myositis: Improvement of the 6 Min Walking Distance, a Functional Scale, the FVC and Muscle Quantitative MRI**

Olivier Benveniste\(^1\), Jean-Yves Hogrel\(^2\), Melanie Annoussamy\(^2\), Damien Bachasson\(^2\), Aude Rigolet\(^3\), Laurent Servais\(^2\), Joe-Elie Salem\(^4\), Baptiste Hervier\(^3\), Oceane Landon Cardinal\(^5\), Kuberaka Mariampillai\(^1\), Jean-Sebastien hulot\(^4\), Pierre Carlier\(^2\) and Yves Allenbach\(^6\), \(^1\)Assistance Publique - Hôpitaux de Paris, Pitié-Salpêtrière University Hospital, Department of Internal Medicine and Clinical Immunology, Hospital University Department: inflammation, immunopathology and biotherapy (DHU i2B), Paris, France, Paris, France, \(^2\)Institute of Myology, Paris, France, \(^3\)Internal Medicine, Pitié-Salpêtrie University Hospital, Paris, France, \(^4\)INSERM, CIC-1421, Paris, France, \(^5\)Internal Medicine, Assistance Public - Hopitaux de Paris, Pitié-Salpêtrire University Hospital, Paris, France, \(^6\)Internal Medicine, Assistance Public - Hopitaux de Paris, Pitié-Salpêtrie University Hospital, Paris, France

**First publication:** October 19, 2017
SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: ACR Late-Breaking Abstract Session
Session Type: ACR Late-breaking Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose:

Inclusion body Myositis (IBM) is the most frequent myositis in patients over 50 years old. Conventional immunosuppressive drugs are today ineffective or even aggravate muscle deficits. Rapamycin is a mTOR inhibitor used in organ transplantation. Potentially, rapamycin can deplete T effector cells, preserve T regulatory cells and induce autophagy (protein degradation), all parameters impaired during IBM.

Methods:

RAPAMI is a prospective, randomized, controlled, double blind, monocentric, phase IIb trial evaluating the efficacy of rapamycin against placebo (NCT02481453). The primary endpoint was stabilization of maximal voluntary quadriceps isometric strength assessed with a dynamometer (Biodex System3 pro). Secondary endpoints included safety, other muscle groups strength, distance walked in 6 minutes (6MWD), pulmonary functional tests, functional scales, and muscle quality assessed by quantitative nuclear resonance magnetic exams (NRM).

Results:

Forty-four patients were treated by oral rapamycin (2 mg/d, n=22) or placebo (n=22) during 12 months (M12). Twelve months after the initiation of the treatment, the quadriceps strength decreased significantly and similarly in both groups (mean relative change: -11.07% vs. -12.36 %). Nevertheless, in comparison to the placebo group, 6MWD was unchanged (mean change: -4.1 m vs. -38.5 m, p=0.035), IBM weakness composite index was less degraded (11.91% vs. 24.26%, p=0.038) and forced vital capacity significantly improved (mean relative change: +12.3% vs. 1.6%, p=0.016). Additionally, NRM showed significant less fat muscle replacement (difference between M12 and baseline in %) in quadriceps (1.7 vs. 4.4, p=0.025) or hamstrings (0.9 vs. 7.3, p=0.027). Finally in NRM, the loss between M12 and baseline of contractile cross-sectional area (mm²) was less pronounced in quadriceps (-3.7 vs. -10.7, p=0.005).

Conclusion: Even if the primary endpoint was not reached, these first results showed coherent data in favor of rapamycin. Notably for the first time in a RCT, an improvement of the 6MWD is observed during IBM.
Disclosure: O. Benveniste, None; J. Y. Hogrel, None; M. Annoussamy, None; D. Bachasson, None; A. Rigolet, None; L. Servais, None; J. E. Salem, None; B. Hervier, None; O. Landon Cardinal, None; K. Mariampillai, None; J. S. hulot, None; P. Carlier, None; Y. Allenbach, None.


Abstract Number: 6L

Efficacy and Safety of Ustekinumab, an Interleukin 12/23 Inhibitor, in Patients with Active Systemic Lupus Erythematosus: Results of a Phase 2, Randomized Placebo-Controlled Study

Ronald van Vollenhoven1, Bevra H. Hahn2, George C. Tsokos3, Carrie Wagner4, Peter Lipsky5, Benjamin Hsu4, Marc Chevrier4, Robert Gordon4, Manon Triebel6 and Shawn Rose4, 1Amsterdam Rheumatology and Immunology Center ARC, Amsterdam, Netherlands, 2UCLA David Geffen School of Medicine, Los Angeles, CA, 3Division of Rheumatology, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, 4Janssen Research & Development, LLC, Spring House, PA, 5Ampel BioSolutions LLC, Charlottesville, VA, 6Janssen Biologics Europe, Leiden, Netherlands

First publication: October 19, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: ACR Late-Breaking Abstract Session
Session Type: ACR Late-breaking Abstract Session
Session Time: 4:30PM-6:00PM

Background/Purpose: The IL-12/23 pathway has been implicated in the pathogenesis of SLE. The anti-IL12/23 monoclonal antibody ustekinumab (UST) is efficacious in the
treatment of psoriasis, psoriatic arthritis, and Crohn’s disease. Here, we evaluated the safety and efficacy of UST in patients (pts) with active SLE.

**Methods:** We conducted a phase 2, placebo (PBO)-controlled study in 102 adults with seropositive (ANA, anti-dsDNA, and/or anti-Smith antibodies) SLE by SLICC criteria and active disease (SLEDAI score ≥6 and ≥1 BILAG A and/or ≥2 BILAG B scores) despite standard-of-care therapy. Pts (n=102) were randomized (3:2) to receive UST IV ~6 mg/kg or PBO at wk0, followed by SC injections of UST 90mg q8w or PBO, both added to standard care; stratification factors were consent for skin biopsy (y/n), disease features, (eg, presence of lupus nephritis, baseline concomitant SLE medications, SLEDAI score), site/region, and race. The primary endpoint was the proportion of patients achieving SLE response index (SRI)-4 response at wk24. Major secondary endpoints at wk24 included change from baseline in SLEDAI-2K, change from baseline in Physician’s Global Assessment (PGA), and proportion of pts with BICLA response. Endpoint analyses included all pts who received ≥1 dose of study agent, had ≥1 measurement prior to administration, and had ≥1 post-baseline measurement. Patients with missing data and treatment failures were imputed as nonresponders.

**Results:** Baseline pt demographic and disease characteristics were well-balanced between treatment groups (female=91%; mean age=41 (18-66) years; mean SLEDAI-2K= 10.9). At wk24, 60% of pts in the UST group had an SRI-4 response vs 31% in the PBO group (p=0.0046), with a treatment effect favoring UST beginning at wk12. Pts in the UST group had greater median change from wk0 to wk24 in SLEDAI-2K and PGA vs PBO (Table). No difference was observed in the proportion of pts achieving a BICLA composite response at wk24, although among BICLA nonresponders, a greater proportion of UST pts had no BILAG worsening vs PBO. The risk of a new BILAG flare (≥1 new BILAG A or ≥2 new BILAG B) was significantly lower in the UST group vs. PBO (HR 0.11 [95% CI 0.01-0.94]; p=0.0078). UST demonstrated improvement in musculoskeletal and mucocutaneous disease features vs PBO. Improvements in anti-dsDNA and C3 levels were also noted through wk24 with UST. Through wk24, 78% of UST pts and 67% of PBO pts had ≥1 adverse event; 8.3% and 9.5%, respectively, had ≥1 serious adverse event (Table). There were no deaths in the study. Safety events were consistent with the UST safety profile in other studied indications.

**Conclusion:** UST showed significantly better efficacy in clinical and laboratory parameters in the treatment of active SLE compared with placebo, while demonstrating a comparable safety profile. UST may be an effective therapy with a novel mechanism of action in the treatment of SLE.
<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Ustekinumab</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients randomized, n</strong></td>
<td>42</td>
<td>60</td>
</tr>
<tr>
<td><strong>Efficacy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with SRI-4 response, n (%)</td>
<td>13 (31.0)</td>
<td>36 (60.0)</td>
</tr>
<tr>
<td>P value</td>
<td></td>
<td>0.0046a</td>
</tr>
<tr>
<td>Change from baseline in SLEDAI-2K, median (range)</td>
<td>-2.0 (-20; 10)</td>
<td>-6.0 (-10; 3)</td>
</tr>
<tr>
<td>P value</td>
<td></td>
<td>0.0265a,b</td>
</tr>
<tr>
<td>Change from baseline in PGA, median (range)</td>
<td>-1.6 (-5.6; 2.7)</td>
<td>-2.5 (-6.6; 2.8)</td>
</tr>
<tr>
<td>P value</td>
<td></td>
<td>0.2110a,b</td>
</tr>
<tr>
<td>Patients with BICLA response, n (%)</td>
<td>14 (33.3)</td>
<td>21 (35.0)</td>
</tr>
<tr>
<td>P value</td>
<td></td>
<td>0.9939a</td>
</tr>
<tr>
<td>Proportion of BICLA nonresponders with no BILAG worsening, n/N (%)</td>
<td>11/28 (39.2)</td>
<td>29/39 (74.4)</td>
</tr>
<tr>
<td>P value</td>
<td></td>
<td>0.0043</td>
</tr>
<tr>
<td>Patients with 50% improvement from baseline joint disease activity, % (95% CI)</td>
<td>63.2 (61.7-64.6)</td>
<td>87.7 (86.8-88.6)</td>
</tr>
<tr>
<td>P value</td>
<td></td>
<td>0.0208d</td>
</tr>
<tr>
<td>Patients with 50% improvement from baseline CLASI activity score, % (95% CI)</td>
<td>25.2 (23.1-27.4)</td>
<td>58.7 (57.4-60.1)</td>
</tr>
<tr>
<td>P value</td>
<td></td>
<td>0.0429e</td>
</tr>
<tr>
<td>Change from baseline in anti-dsDNA (kIU/L), median (range)</td>
<td>-12.6 (-168.8; 233.1)</td>
<td>-30.7 (-2919.6; 132.9)</td>
</tr>
<tr>
<td>P value</td>
<td></td>
<td>0.1073h</td>
</tr>
<tr>
<td>Change from baseline in</td>
<td>0.15 (-12.4; 21.8)</td>
<td>6.60 (-17; 50.8)</td>
</tr>
<tr>
<td>Complement C3 (mg/dL)≥, median (range)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------------------------------------</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td><strong>P value</strong></td>
<td></td>
<td>0.0636^h</td>
</tr>
<tr>
<td><strong>Adverse events</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with ≥1 TEAE, n (%)</td>
<td>28 (66.7)</td>
<td>47 (78.3)</td>
</tr>
<tr>
<td>Most Common TEAEs, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>9 (21.4)</td>
<td>5 (8.3)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>5 (11.9)</td>
<td>6 (10.0)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>3 (7.1)</td>
<td>6 (10.0)</td>
</tr>
<tr>
<td>Headache</td>
<td>5 (11.9)</td>
<td>4 (6.7)</td>
</tr>
<tr>
<td>Patients with ≥1 SAE, n (%)</td>
<td>4 (9.5)</td>
<td>5 (8.3)</td>
</tr>
</tbody>
</table>

^a Prespecified analyses; all other analyses shown here were post-hoc.

^b One-sided test for no difference between two treatment groups based upon a Wilcoxon non-parametric median test for difference of location

^c Patient subpopulation (67% of total population) with at least 4 joints with pain and signs of inflammation at baseline

^d Patient subpopulation (58% of total population) with CLASI activity score of at least 4 at baseline

^e Proportions of responders and p values based on a modified intention to treat analysis using a multiple imputation model for missing data from weeks 16 to 24

^f Patient subpopulation (42% of total population) with anti-dsDNA autoantibodies present at baseline

^g Patient subpopulation (41% of total population) with low Complement C3 levels present at baseline

^h One-sided test for no difference between two treatment groups based upon a Wilcoxon non-parametric median test for difference of location

BICLA, BILAG-based Combined Lupus Assessment; BILAG, British Isles Lupus Assessment Group; CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; SLEDAI-2K, Systemic Lupus Erythematosus Disease


Abstract Number: 7L

A Phase 2 Study of Safety and Efficacy of Anabasum (JBT-101), a Cannabinoid Receptor Type 2 Agonist, in Refractory Skin-Predominant Dermatomyositis

Victoria P. Werth1, Emily Hejazi2, Sandra M. Pena1, Jessica S. Haber3, Joyce Okawa1, Rui Feng4, Kirubel Gabre2, Josef Concha2, Caitlin Cornwall5, Nancy Dgetluck6, Scott Constantine5 and Barbara White5, 1Department of Dermatology, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, 2University of Pennsylvania, Philadelphia, PA, 3Department of Dermatology, University of Pennsylvania, Philadelphia, PA, 4Department of Biostatistics and Epidemiology at the Hospital of the University of Pennsylvania, Philadelphia, PA, 5Corbus Pharmaceuticals, Inc., Norwood, MA, 6Biostatistics, Corbus Pharmaceuticals, Inc., Norwood, MA

First publication: October 19, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: ACR Late-Breaking Abstract Poster
Background/Purpose: Effective treatment options are limited for refractory skin disease in dermatomyositis (DM). Anabasum is a non-immunosuppressive, synthetic, oral preferential CB2 agonist that triggers resolution of innate immune responses and reduces cytokine production by PBMC from DM patients. This purpose of this study was to test safety and efficacy of anabasum in DM subjects with refractory, moderate-to-severely active skin disease.

Methods: A double-blind, randomized placebo-controlled 16-week Phase 2 trial (JBT101-DM-001) enrolled adults with documented DM and a Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) activity score ≥ 14, minimal active muscle involvement and failure or intolerance to hydroxychloroquine and stable DM medications including immunosuppressants. Subjects received 2 escalating doses of anabasum (20 mg QD X 4 weeks, then 20 mg BID X 8 weeks) or PBO X 12 weeks. Subjects were followed off study drug X 4 weeks. Safety and efficacy outcomes were assessed from Day 1 through end of study at Week 16. The primary efficacy objective was to assess efficacy of anabasum using CDASI activity score.

Results: 11 adults each received anabasum and PBO (N = 22). Demographic and disease characteristics were similar in both cohorts. Both cohorts had mean CDASI activity scores in the severe range (33-35) despite immunosuppressants (19/22 subjects). Anabasum subjects had clinically meaningful improvement in CDASI activity scores with mean reduction ≥ 5 points at all visits after 4 weeks. Improvement had statistical significance at end of study (Fig. 1, P = 0.02, 2-sided MMRM) that first became apparent after 4 weeks. Anabasum provided greater improvement than placebo in CDAI damage index, patient-reported global skin disease and overall disease assessments, skin symptoms including photosensitivity and itch, fatigue, sleep, pain interference with activities, pain, and physical function (examples in Fig. 1). Improvements in secondary efficacy outcomes reached statistical significance (P ≤ 0.1, 1-sided MMRM) at multiple visits after week 4 (Fig. 1). There were no serious, severe or unexpected adverse events (AEs) related to anabasum. Tolerability of anabasum was excellent with no study drop-outs. Subjects in the anabasum cohort had numerically more mild AEs than placebo subjects (29 vs. 19) and fewer moderate AEs (4 vs. 7). AEs in ≥ 3 subjects in any cohort were diarrhea, dizziness (lightheadedness), fatigue and dry mouth.
Conclusion: Anabasum demonstrated consistent evidence of clinical benefit across multiple efficacy outcomes and had acceptable safety and tolerability in this Phase 2 trial in refractory skin disease in DM. Further evaluation of anabasum in the treatment of DM is warranted.

Disclosure: V. P. Werth, None; E. Hejazi, None; S. M. Pena, None; J. S. Haber, None; J. Okawa, None; R. Feng, None; K. Gabre, None; J. Concha, None; C. Cornwall, Corbus Pharmaceuticals, Inc., 1,Corbus Pharmaceuticals, Inc., 3; N. Dgetluck, Corbus Pharmaceuticals, Inc., 1,Corbus Pharmaceuticals, Inc., 3; S. Constantine, Corbus Pharmaceuticals, Inc., 1,Corbus Pharmaceuticals, Inc., 3; B. White, Corbus Pharmaceuticals, 1,Corbus Pharmaceuticals, 3.


Abstract Number: 8L

Prevalence of Blindness in a Cohort of Rheumatologic Patients Treated with Hydroxychloroquine
Hydroxychloroquine (HCQ) is widely used in the treatment of chronic rheumatic diseases. Its long-standing use has been associated with retinopathy in a daily and cumulative dose dependent manner by weight. Less frequently, ‘bull’s eye maculopathy’ may be found, which is irreversible and can result in blindness. We examined the prevalence of ocular toxicity in a large cohort of patients in a tertiary center in the United States treated with HCQ for inflammatory arthritis and systemic lupus erythematosus (SLE).

Methods: Our retrospective cohort study identified 2898 patient from 1999 to August 2017 with diagnoses of rheumatoid arthritis (RA), inflammatory polyarthritis, SLE, subacute cutaneous lupus and discoid lupus erythematosus who had a prescription written for HCQ. 31 patients were identified as having a diagnosis of ‘blindness’ or ‘toxic maculopathy’ in their electronic medical record (Epic) and were chart reviewed. Patient weight and dose of HCQ at initiation and discontinuation, dose of HCQ at the time of any ocular symptoms, duration of HCQ use, rheumatologic diagnosis, reason for blindness or vision impairment, comorbidities and the use of tamoxifen were extracted into REDCap database.

Results:

Of our 31 patients with a diagnosis of ‘blindness’ or ‘toxic maculopathy’, 11 had documented blindness of one or both eyes. In each of these cases, a diagnosis other than HCQ ocular toxicity was confirmed as the cause of blindness: stroke (27%), pre-existing macular disease (18%), diabetic retinopathy (18%), hypertensive retinopathy (9%) and cataracts (9%).
Three out of the 31 patents in our cohort had HCQ retinal toxicity, each without blindness or change in vision.

Two cases were identified with bull’s eye maculopathy attributed to HCQ, diagnosed on fundus and macular optical coherence tomography (OCT) exam. Case one was a 51 year old female who had been treated for SLE with HCQ 400 mg daily for over 20 years at 7.1-8.2 mg/kg dose based on documented weight over 15 years. Case two was a 66 year old female who had been treated for SLE on HCQ 400 mg daily for at least 18 years at 7.3-8.2 mg/kg dose based on documented weight over 13 years. Comorbidity of case one was chronic kidney disease, whereas case two had hypertension and cataracts (not visually significant), both without prior use of tamoxifen.

One patient had HCQ toxicity without bull’s eye maculopathy but with pigmentary changes on fundus exam and loss of photoreceptor inner segment and outer segment junction in mid periphery on OCT exam. She was 57 years old with 25 years use of HCQ 400 mg daily at 6.3 mg/kg dose based on documented weight over 11 years. She had underlying myopia controlled with glasses without vision complaints.

**Conclusion:** There were no cases of blindness attributable to toxic maculopathy from HCQ use in our cohort of 2868 patients. We identified two patients with bull’s eye maculopathy (0.10%) and one with HCQ toxic maculopathy (0.07%) in this cohort; all 3 patients received HCQ for greater than 18 years, and none had functional vision loss at diagnosis. Our findings suggest that comorbid conditions that are common in RA and SLE contribute substantially to vision loss and blindness and should not be ignored.

**Disclosure:** D. Singh, None; L. Muhieddine, None; D. Einstadter, None; S. Ballou, None.


**Abstract Number:** 9L

**Circulating Type I, II and III Interferons (IFNs) Associate with IFN-Scores, but Define Distinct Subsets of Active SLE**
Vilija Oke\textsuperscript{1}, Iva Gunnarsson\textsuperscript{1}, Jessica M. Dorschner\textsuperscript{2}, Agneta Zickert\textsuperscript{1}, Timothy B. Niewold\textsuperscript{3} and Elisabet Svenungsson\textsuperscript{1}, \textsuperscript{1}Department of Medicine, Rheumatology Unit, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, Stockholm, Sweden, \textsuperscript{2}Division of Rheumatology and Department of Immunology, Mayo Clinic, Rochester, MN, \textsuperscript{3}Colton Center for Autoimmunity, New York University, New York, NY

First publication: October 19, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: ACR Late-Breaking Abstract Poster
Session Type: ACR Late-breaking Abstract Session
Session Time: 9:00AM-11:00AM

Background/Purpose:

Serum induced IFN gene expression (IFN-score) is considered a golden standard to assess IFN activity in SLE. So far, IFN-scores have not been compared to serum levels of type I, II and III IFNs. The study aimed to investigate how IFN-scores and SLE manifestations relate to serum levels of IFNs type I(αs), II(γ) and III(λ1).

Methods:

461 SLE patients and 322 controls were included. IFN-score was measured by WISH cell assay. INF-αs and IFN-λ1 were measured by ELISA. IFN-γ was measured by MSD 30-plex assay.

Results:

SLE patients had higher IFN-scores and higher levels of IFN-αs, IFN-γ and IFN-λ1 (p<0.001). IFN-scores correlated with levels of IFN-γ and IFN-α (ρ=0.39, and ρ=0.25, p<0.0001). Further, patients were grouped according to the high levels (≥3\textsuperscript{rd} quartile) of each IFN/IFN-score. The group with high IFN-scores had higher disease activity (SLAM, SLEDAI): weight loss (41%), fatigue (33%), fever (39%), rash (44%), lymphadenopathy (45%), arthritis (40%), nephritis (55%) (p<0.01). Interestingly, incidence of neuropsychiatric SLE, antiphospholipid (aPL) antibodies (abs), and also damage score was lower (p<0.05).

The characteristics of IFN-γ high group included higher disease activity (SLAM, SLEDAI), and specifically: active nephritis (52%), lymphadenopathy (40%), arthritis
(42%), lymphopenia (37%), anemia (35%) and positivity for Sm (41%), SmRNP (36%) and RNP68 (45%), Ro52 (35%) and Ro60 (33%)(p<0.03).

The common features of IFN-α high group included younger age, shorter disease duration, active rash (34%), lymphadenopathy (43%), Ro52 (38%) and La (43%)(p=0.01). Presence of aPL abs and previous vascular events were lower and renal affection was uncommon (p<0.01).

In general, high IFN-scores reflected SLE manifestations that could be further stratified by high IFN-γ levels and to a lesser extent by high IFN-α. High IFN-λ1 did not define any phenotype of active SLE, except presence of anti-nucleosome abs.

**Conclusion:**

We demonstrate that high IFN-score associate more strongly with type II rather than type I IFNs. Importantly, major manifestations of SLE: active nephritis and arthritis, and also anti-Sm/SmRNP antibodies associate with IFN-γ; while rash associate with IFN-α.

Our findings are of major importance while tailoring clinical trials with anti-IFN therapies and demonstrate that importance of IFN-γ has so far been underscored.

**Disclosure: V. Oke, None; I. Gunnarsson, None; J. M. Dorschner, None; A. Zickert, None; T. B. Niewold, None; E. Svenungsson, None.**


Abstract Number: 10L

**Upadacitinib (ABT-494) in Patients with Active Rheumatoid Arthritis and Inadequate Response or Intolerance to Biological Dmards: A Phase 3 Randomized, Placebo-Controlled, Double-Blind Study of a Selective JAK-1 Inhibitor**

Mark C. Genovese¹, Roy Fleischmann², Bernard Combe³, Stephen Hall⁴, Ying Zhang⁵, Yijie Zhou⁵, Mohamed-Eslam F. Mohamed⁶, Sebastian Meerwein⁷ and Aileen L.
Background/Purpose: Upadacitinib (ABT-494, UPA), an oral, selective JAK-1 inhibitor was effective in 2 ph2 trials in rheumatoid arthritis (RA) pts with inadequate response (IR)/intolerance to csDMARDs/ bDMARDs.

Methods: Pts with active RA (TJC≥6, SJC≥6; hsCRP≥3 mg/L) on stable csDMARDs were randomized 2:2:1:1 to receive UPA 15 mg or 30 mg once daily (QD) or PBO for 12 wks followed by UPA 15 mg or UPA 30 mg QD starting at Wk 12. The primary endpoints were the proportion of pts who achieved ACR20 and the proportion who achieved DAS28-CRP ≤3.2 at Wk 12 (NRI).

Results: Of 499 randomized pts, 498 received study drug; 451 (90.6%) and 419 (84.1%) completed Wks 12 and 24 respectively. Baseline disease characteristics indicated long-standing severe, refractory disease: (means) duration since diagnosis 13 yrs; DAS28CRP, 5.8; TJC68, 27.9; SJC66, 16.8; 53% experienced ≥2 prior bDMARDs. At Wk 12, significantly more pts (p<.001) on UPA 15 and 30 vs PBO achieved the primary endpoints (ACR20: 64.6% and 56.4% vs 28.4%; DAS28-CRP≤3.2: 43.3% and 42.4% vs 14.2%) and other secondary endpoints (Table 1). By Wk 1, significantly more pts achieved ACR20 on UPA 15 and 30 vs PBO (27.4% and 24.8% vs 10.7%, p<.001). At Wk 12, significant improvements were observed on UPA 15 and 30 vs PBO for HAQ-DI (LS mean change -0.39 and -0.42 vs -0.17, p<.001). At Wk 24, responses were similar or greater for pts originally on UPA and comparable for pts who switched to UPA after 12 wks of PBO.

In the first 12 wks, frequency of AEs was comparable for PBO and UPA 15, but higher for UPA 30 (Table 2). Overall AE rates (E/100 PY) through Wk 24 for UPA 30 were similar or slightly higher than UPA15; more AEs led to study drug discontinuation in
UPA 30. Occurrence of infections was similar in all arms, but there were more serious infections and herpes zoster cases in UPA 30. Malignancies were observed in 4 pts over 12 wks with 1 additional case through Wk 24. Through Wk 12, pulmonary embolism (PE) was reported in 2 pts (1 each on UPA 15 and 30), none with DVT; through Wk 24, PE were reported in 4 more pts (UPA 15: 3, 1 of whom also had a DVT; UPA 30:1). All had risk factors for DVT/PE. Two deaths were reported (UPA 30: 1 prior to Wk 12; UPA 15:1 after Wk12).

**Conclusion:** In this treatment-refractory, bDMARD-IR RA population, rapid, significant improvements in signs and symptoms were observed with UPA at both doses vs PBO during 12 wks of treatment, and maintained through 24 wks. No new safety signals were identified vs previous ph2 studies. PE and DVT cases observed in this study have not been reported for the only other ph3 study with unblinded data to date. Overall data from the ph3 program will allow a comprehensive evaluation of the benefit:risk profile of UPA in RA.

| Table 1. Efficacy Measures#, Percentage of Patients with a Response |
|-------------------------------------------------|------------------|------------------|------------------|------------------|
|                                                  | Week 12          | Week 24          |
|                                                  | PBO              | UPA 15 mg        | UPA 30 mg        | PBO              |
|                                                  | N=169            | N=164            | N=165            | N=85             |
|                                                  | UPA 15 mg        | UPA 30 mg        | PBO              |
|                                                  | N=164            | N=165            | UPA 15 mg        |
|                                                  | N=85             | N=164            | UPA 30 mg        |
|                                                  |                  |                  | N=165            |
| ACR20                                           | 28.4             | **64.6***        | **56.4***        | 61.2             |
| DAS28-CRP≤3.2                                   | **14.2**         | **43.3***        | **42.4***        | 38.8             |
|                                                 |                  |                  |                  | 56.0             |
| ACR50                                           | 11.8             | **34.1***        | **35.8***        | **35.3**         |
| CDAI ≤10                                        | **14.2**         | **31.7***        | **33.9***        | 34.1             |
| CDAI ≤2.8                                       | 4.7              | **7.9**          | **11.5**         | **12.9**         |
| DAS28-CRP<2.6                                   | **9.5**          | **28.7***        | **23.6***        | **28.2**         |

*Primary endpoints in bold text. Data are presented for 24 wks (period 1) of the ongoing trial. 
#Results for binary endpoints are based on NRI analysis. **p < .001 for comparison vs PBO, conducted for first 12 wks only.**
Table 2. Summary of AEs

<table>
<thead>
<tr>
<th>Pts with AE up to Wk 12, n (%)*</th>
<th>AE over 24 wks for Any UPA Exposure, Events/100PY**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>UPA 15 MG (N=236) (PYs=88.6)</td>
</tr>
<tr>
<td>Any AE</td>
<td>95 (56.2%)</td>
</tr>
<tr>
<td>Serious AE</td>
<td>0</td>
</tr>
<tr>
<td>AE Leading To Study Drug Discontinuation</td>
<td>9 (5.3%)</td>
</tr>
<tr>
<td>Severe AE</td>
<td>3 (1.8%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pts with AESI up to Wk 12, n (%)*</th>
<th>AESI over 24 wks for Any UPA Exposure, Events/100PY**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>51 (30.2%)</td>
</tr>
<tr>
<td>-Serious Infection</td>
<td>0</td>
</tr>
<tr>
<td>-Opportunistic Infection</td>
<td>0</td>
</tr>
<tr>
<td>Herpes Zoster v</td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>GI perforation</td>
<td>0</td>
</tr>
<tr>
<td>Malignancy v</td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>CV event (adjudicated) v</td>
<td>0</td>
</tr>
<tr>
<td>Death v</td>
<td>0</td>
</tr>
</tbody>
</table>

AE, adverse event; AESI, AE of special interest; PY, patient year; E/100PY, events/100 patient years; GI, gastrointestinal; CV, cardiovascular.

*Unique subjects are counted.
**Reported data is based on up to 24 wks of exposure for the original UPA 15 and 30 groups and up to 12 wks of exposure for PBO pts who were switched to UPA at Wk 12. Multiple events occurring in the same pts are counted in the E/100PY calculation.

v Herpes Zoster: most were mild and single dermatome; through wk 12- UPA 30 mg: 2 serious cases

b Malignancies: through wk 12- PBO: 1 hepatic neoplasm; UPA 15 mg: 1 malignant melanoma; UPA 30 mg: 2 pts with prostate cancer. From wk 12-24, UPA 15 mg: 1 pt with bladder cancer

Adjudicated CV events: through wk 12- UPA 15 mg: 1 pt with ischemic stroke. From wk 12-24, UPA 15 mg: 1 pt with cardiovascular procedure, 1 pt with cardiac arrest adjudicated to undetermined/unknown cause of death; UPA30 mg: 1 pt with myocardial infarction

§ Deaths: through wk 12- UPA 30 mg: 1 due to cardiac failure and PE. From wk 12-24, UPA 15 mg: 1 unwitnessed death adjudicated as undetermined/unknown cause of death (see above)

Disclosure: M. C. Genovese, Abbvie, Lilly, Pfizer, Galapagos, Gilead, 2,AbbVie, Lilly, Pfizer, Galapagos, Gilead, 5; R. Fleischmann, AbbVie, 2,AbbVie, 5; B. Combe, Abbvie, BMS, Jansen, Lilly, MSD, Pfizer, Roche Chugai, UCB, 5; S. Hall, None; Y. Zhang, AbbVie Inc, 3,AbbVie Inc, 1; Y. Zhou, Abbvie, 1,AbbVie, 3; M. E. F. Mohamed, AbbVie, 1,AbbVie, 3; S. Meerwein, AbbVie, 1,AbbVie, 3; A. L. Pangan, AbbVie, 1,AbbVie, 3.

View Abstract and Citation Information Online -
http://acrabstracts.org/abstract/upadacitinib-abt-494-in-patients-with-active-rheumatoid-
Risk of Second Malignant Neoplasm and Mortality in Rheumatoid Arthritis Patients Treated with Biological Dmards: A Danish Population-Based Cohort Study

Lene Dreyer¹, René Cordtz², Inger Marie J. Hansen³, Lars Erik Kristensen⁴, Merete Lund Hetland⁵ and Lene Mellemkjær⁶, ¹Center for Rheumatology and Spine Diseases, Gentofte University Hospital, Rigshospitalet, Hellerup, Denmark, ²Center for Rheumatology and Spine Diseases, Gentofte University Hospital, Rigshospitalet, Hellerup, Denmark, ³Department of Reumatology, OUH, Svendborg Hospital, Svendborg, Denmark, ⁴The Parker Institute, Copenhagen University Hospital, Bispebjerg and Frederiksberg, Copenhagen F, Denmark, ⁵DANBIO, Glostrup Hospital. On behalf of all Depts of Rheumatology in Denmark. Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Rigshospitalet, Denmark, Glostrup, Denmark, ⁶Danish Cancer Society Research Center, Copenhagen, Denmark, Copenhagen, Egypt

First publication: October 19, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: ACR Late-Breaking Abstract Poster
Session Type: ACR Late-breaking Abstract Session
Session Time: 9:00AM-11:00AM

Background/Purpose:

The safety of treatment with biological DMARDs (bDMARDs) has been carefully studied for the past 15 years, however, it is still largely unknown whether this treatment is safe in arthritis patients with a history of cancer. We studied the risk of a second malignant neoplasm (SMN) and mortality in rheumatoid arthritis (RA) patients with a history of a primary cancer diagnosis and treated with bDMARDs.

Methods:
In total, 1678 RA patients registered in the DANBIO Register during 2000-2011, had a primary cancer according to the Danish Cancer Registry. Hazard Ratios (HR) for SMN and death were calculated.

**Results:**

There were 190 RA patients who had received bDMARDs *before* their primary cancer diagnosis only, 220 only *after*, 92 both before and after, while 1176 arthritis patients with cancer had *never* received bDMARDs. Among 502 patients ever treated with bDMARDs, the HR (cancer site adjusted) for developing a SMN was 1.11 (95% Confidence interval (CI) 0.74-1.67) compared with never treated, Table 1. The HR for death among patients treated with bDMARDs *before* the primary cancer diagnosis *only*, was 1.53 (95% CI 1.13-2.09). After further adjustment for extent of the primary cancer, the HR for death was 1.20 (95% CI 0.88-1.63) among patients treated with bDMARDs *before* the primary cancer diagnosis only, 1.36 (95% CI 0.78-2.39) among patients treated only *after* the cancer and 1.22 (95% CI 0.70-2.13) among patients treated *both* before and after the cancer.

**Conclusion:**

RA patients with a history of cancer and treated with bDMARDs had no increased risk of a SMN compared with never treated. No clear conclusion can be drawn regarding mortality in bDMARD-treated patients.
Table 1. Risk of a second malignant neoplasm (SMN) in rheumatoid arthritis patients according to biological DMARD treatment

<table>
<thead>
<tr>
<th>Treatment</th>
<th>SMN, Person-years</th>
<th>HR&lt;sup&gt;1&lt;/sup&gt; (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never bDMARDs (N=1176)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ever bDMARDs (N=502)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>bDMARDs only before first cancer</td>
<td>11</td>
<td>1.06 (0.52-2.14)</td>
</tr>
<tr>
<td>bDMARDs after first cancer</td>
<td>27</td>
<td>1.13 (0.71-1.80)</td>
</tr>
<tr>
<td>bDMARDs only after first cancer</td>
<td>21</td>
<td>1.15 (0.68-1.95)</td>
</tr>
<tr>
<td>bDMARDs both before and after first cancer</td>
<td>6</td>
<td>1.09 (0.46-2.57)</td>
</tr>
<tr>
<td>TNF-I after</td>
<td>21</td>
<td>1.21 (0.73-2.03)</td>
</tr>
<tr>
<td>Rituximab after</td>
<td>7</td>
<td>1.05 (0.47-2.34)</td>
</tr>
</tbody>
</table>

Abbreviations: DMARD, Disease modifying anti-rheumatic drug; HR, Hazard Ratio; TNF-I, tumour necrosis factor-alpha inhibitor.

<sup>1</sup> Adjusted for age, gender, calendar time and cancer site
<table>
<thead>
<tr>
<th>Treatment</th>
<th>Deaths Obs</th>
<th>Person-years</th>
<th>Adjusted¹ Deaths Person-years</th>
<th>Further adjusted² Deaths Person-years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never bDMARDs</td>
<td>207</td>
<td>2461</td>
<td>1 (ref.)</td>
<td>1 (ref.)</td>
</tr>
<tr>
<td>Ever bDMARDs</td>
<td>135</td>
<td>1225</td>
<td>1.25 (0.99-1.57)</td>
<td>1.35 (1.04-1.76)</td>
</tr>
<tr>
<td>bDMARDs only before first cancer</td>
<td>93</td>
<td>272</td>
<td>1.50 (1.15-1.97)</td>
<td>1.53 (1.13-2.09)</td>
</tr>
<tr>
<td>bDMARDs only after first cancer</td>
<td>42</td>
<td>953</td>
<td>0.92 (0.64-1.31)</td>
<td>1.08 (0.73-1.61)</td>
</tr>
<tr>
<td>bDMARDs both before and after first cancer</td>
<td>23</td>
<td>760</td>
<td>1.01 (0.62-1.65)</td>
<td>1.19 (0.69-2.04)</td>
</tr>
<tr>
<td>TNF-I after</td>
<td>35</td>
<td>723</td>
<td>0.85 (0.52-1.38)</td>
<td>0.99 (0.57-1.73)</td>
</tr>
<tr>
<td>Rituximab after</td>
<td>9</td>
<td>235</td>
<td>0.96 (0.66-1.41)</td>
<td>1.13 (0.73-1.74)</td>
</tr>
</tbody>
</table>

Abbreviations: DMARD, Disease modifying anti-rheumatic drug; HR, Hazard Ratio; TNF-I, tumour necrosis factor-alpha inhibitor.

¹ Adjusted for age, gender, calendar time, cancer site ² Further adjusted for extent of disease.
Evaluation of Intravenous Injection of Tc 99m Tilmanocept in Static Planar Gamma Emission Imaging and Fused SPECT/CT Imaging for Rheumatoid Arthritis

Arash Kardan¹, Bonnie Abbruzzese², James Sanders², Allison Kissling², David Ralph², Joanna Shuping², Michael Blue², Carley Hartings², Rachael Hershey², Ahmad Ismail², Izabela Gierach², Hannah Bailey², Amelia Spaulding², Matthew Haynam², George Zubal³ and Frederick Cope², ¹Charles F. Kettering Memorial Hospital and Wright State University Boonshoft School of Medicine, Dayton, ND, ²Navidea Biopharmaceuticals, Inc., Dublin, OH, ³Z-Concepts, LLC, East Haven, CT

First publication: October 19, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: ACR Late-Breaking Abstract Poster
Session Type: ACR Late-breaking Abstract Session
Session Time: 9:00AM-11:00AM

Background/Purpose: Activated macrophages play a critical role in RA by perpetuating inflammation via TNFα release and participating in the destruction of bone and cartilage. Notably, macrophages are the dominant cell type in the synovial sublining of RA-affected joints. Thus, specific detection of activated macrophage infiltration in RA patients may
provide valuable immunodiagnostic insight towards joint inflammation, destruction and overall disease progression.

Tc 99m Tilmanocept is a synthetic radiopharmaceutical imaging agent that binds to the activated macrophage mannose receptor (CD206) with high affinity. It is currently under investigation for intravenous (IV) administration in subjects with RA in a dose escalation study. The purpose of this report is to communicate safety and imaging findings from RA subjects who received the maximum study dose of 400 µg tilmanocept/10 mCi Tc 99m.

**Methods:** Nine subjects with clinically diagnosed RA were enrolled in the trial. All subjects received IV administration of 400 µg of tilmanocept radiolabeled with either 10 mCi (n=3), 5mCi (n=3), or 1 mCi (n=3) Tc 99m. Static planar gamma emission images of the whole body and affected joints were acquired at 60 and 180 min post injection with additional SPECT/CT imaging of affected joints.

**Results:** No adverse events were observed after IV administration of 400 µg Tc 99m tilmanocept radiolabeled with 1, 5, or 10 mCi of Tc 99m. There was strong correlation of radiotracer localization to affected joints observed in gamma emission imaging. SPECT/CT imaging further demonstrated that Tc 99m tilmanocept localization is specific to the PIP, MCP, knees, ankle, shoulder, elbow, and periarticular synovial spaces and not in cortical bone or osseous marrow spaces.

**Conclusion:** Overt joint-specific localization of Tc 99m tilmanocept activity was visualized in affected joints of all subjects who had undergone multiple RA flares despite previous successful treatments, which demonstrates macrophage infiltration of these joints as a key component of disease. IV injection of Tc 99m tilmanocept at the maximum study dose was well-tolerated with no adverse events. These findings, in addition to prior biopsy evaluations from other subjects, confirm activated CD206 macrophage infiltration to be a key component of RA pathology which can be safely and effectively visualized on gamma emission imaging with Tc 99m tilmanocept.
Figure 1. Static planar gamma emission imaging (left) and maximum intensity projection (MIP) SPECT/CT imaging (right) demonstrating site-specific localization activity to an affected joint.

Left

Right

Figure 2. Fused SPECT/CT images of RA subjects defining the localization of Tc 99m tilmanocept to the periaricular synovial space of the knee (left) and ankle (right).

Left

Right

Disclosure: A. Kardan, None; B. Abbruzzese, None; J. Sanders, None; A. Kissling, None; D. Ralph, None; J. Shuping, None; M. Blue, None; C. Hartings, None; R. Hershey, None; A. Ismail, None; I. Gierach, None; H. Bailey, None; A. Spaulding, None; M. Haynam, None; G. Zubal, None; F. Cope, None.

Significant, Sustained Improvement in Knee Function after Intra-Articular TPX-100: A Double-Blind, Randomized, Multi-Center, Placebo-Controlled Phase 2 Trial

Dawn McGuire¹, Nancy E Lane², Neil Segal³, Samy Metyas⁴, Hans Richard Barthel⁵, Meghan Miller¹, David Rosen¹ and Yoshi Kumagai¹, ¹OrthoTrophix, Inc, Oakland, CA, ²UC Davis Medical Center, Sacramento, CA, ³University of Kansas, Shawnee, KS, ⁴Medvin Clinical Research, Covina, CA, ⁵Barthel Clinic, Santa Barbara, CA

First publication: October 19, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: ACR Late-Breaking Abstract Poster
Session Type: ACR Late-breaking Abstract Session
Session Time: 9:00AM-11:00AM

Background/Purpose: The current Phase 2 study was designed to evaluate safety, tolerability and preliminary efficacy of TPX-100 by IA administration in subjects with mild to moderate patellofemoral osteoarthritis (PFOA) involving both knees. TPX-100, a 23-amino acid peptide derived from Matrix Extracellular Phosphoglycoprotein (MEPE), has been shown to induce articular cartilage proliferation and improve healing after experimental injury in large and small animal models after IA administration. A unique feature of this clinical trial was the use of each subject as his/her own control, intended to minimize effects of age, sex, genetic factors, and activity levels that can complicate inter-subject comparisons. Knee-specific patient-reported outcomes (PROs) used in this study, including the Knee Osteoarthritis Outcome Score (KOOS), were recorded separately for left and right knees.

Methods: Adult men and women with bilateral PFOA (ICRS grade 1-3, confirmed by screening MRI) were enrolled at 15 sites. One knee was randomly assigned to receive TPX-100 for 4 weekly injections, while the contralateral knee (control) received identical placebo (saline) injections. Investigator, subject, site and sponsor were blinded as to treatment assignment. The study had two parts: in Part A, 4 dose cohorts (n=6-9 subjects/cohort; 20, 50, 100 and 200mg/injection) were enrolled. Safety/tolerability of each cohort was evaluated by a Safety Review Committee (SRC) before the next cohort
was enrolled. There were no dose-limiting toxicities or safety concerns at any dose, and the 200 mg dose was selected dose for Part B of the study.

**Results:** A total of 118 subjects (236 knees) were enrolled, 29 in Part A and 89 in Part B. The study population was fairly representative of the knee OA population in the U.S. regarding age (median 60 years) and Body Mass Index (29.2). There were no drug-related SAEs and no dose-limiting toxicities across doses from 20-200 mg/injection. Common adverse events such as knee pain had virtually identical incidences in control and TPX-100-treated knees. Efficacy results were based on the “per-protocol” population of 93 subjects (186 knees) who received 4 weekly injections of 200mg TPX-100 (from Part A or Part B) in the knee randomly assigned to active drug and had at least one MRI after baseline. Quantitative MRI revealed no measurable between-knee differences in cartilage thickness or volume at 6 or 12 months. However, statistically significant (P<.05) and clinically meaningful differences, per literature criteria, in knee function were demonstrated in favor of TPX-100-treated knees compared with controls at 6 and 12 months, including activities of daily living, sports activities, and knee-related quality of life, and a significant reduction in pain going up or down stairs. Subjects’ use of analgesics, including non-steroidal anti-inflammatory medications, declined markedly during the study. Results will be provided in detail.

**Conclusion:** Improving the functional status of patients with knee OA is a central therapeutic goal of OA treatment. In the present proof-of-concept study, TPX-100, administered in 4 weekly intra-articular injections, was safe and associated with robust functional benefits for up to 12 months.

**Disclosure:** D. McGuire, OrthoTrophix, Inc, 3; N. E. Lane, OrthoTrophix, 9; N. Segal, OrthoTrophix, 9; S. Metyas, OrthoTrophix, 9; H. R. Barthel, OrthoTrophix, 9; M. Miller, OrthoTrophix, Inc, 3; D. Rosen, OrthoTrophix, Inc, 3; Y. Kumagai, OrthoTrophiX, Inc, 3.


Abstract Number: 14L

**Miv-711, a Novel Cathepsin K Inhibitor Demonstrates Evidence of Osteoarthritis Structure Modification:**
Results from a 6 Month Randomized Double-Blind Placebo-Controlled Phase IIA Trial

Philip G. Conaghan¹, Michael A Bowes², Sarah R. Kingsbury¹, Alan Brett², Gwenael Guillard², Åsa Jansson³, Cecilia Wadell³, Richard Bethell³ and John Öhd³, ¹University of Leeds, Leeds, United Kingdom, ²Imorphics Ltd, Manchester, United Kingdom, ³Medivir AB, Huddinge, Sweden

First publication: October 19, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: ACR Late-Breaking Abstract Poster
Session Type: ACR Late-breaking Abstract Session
Session Time: 9:00AM-11:00AM

Background/Purpose:

The need for drugs that achieve structure modification in OA is imminent but their development has been burdened by the need for large, long term studies. New imaging biomarkers using structured machine learning offer opportunity for shorter duration and smaller DMOAD trials. MIV-711, a potent and selective cathepsin K inhibitor reduced CTX-I and CTX-II after once-daily administration for up to 28 days in healthy volunteers. Our aim was to examine the efficacy (symptoms and structure) and safety of MIV-711 in knee OA patients.

Methods:

Patients with ACR knee OA, KL2-3 and pain ≥4 & <10 on 0-10 NRS were enrolled at one of 6 European sites and randomised to receive MIV-711 100mg or 200mg or matched placebo qd. Participants remained on usual analgesic medication. Clinical (pain, function, QoL) and safety data were recorded serially and MRI was performed at baseline and wk26. Primary outcome was change in NRS pain score with the key secondary endpoint of change in MRI bone area (medial femur). The main analyses were conducted using linear mixed models.

Results:

244 participants were enrolled (100mg n=82, 200mg n=82, placebo n=80), 69% women, mean age 62, mean BMI ~32. NRS pain scores; function and QoL measures were not
statistically significantly reduced compared to placebo. However, there was a trend to reduction for MIV-711 on the NRS (Figure 1) and across the majority of patient-reported outcomes. Significant reduction in medial femur bone area change for both MIV-711 doses (unadjusted p-values =0.002 and 0.004) were observed at wk26, with no evident differences between the 2 doses (Figure 2A). MIV-711 treated participants demonstrated reduced loss of cartilage thickness on the medial femur versus placebo (unadjusted p=0.023 for 100mg dose, 0.125 for 200mg dose, Figure 2B); medial tibia cartilage loss was not significant. The reductions observed for the biomarkers CTX-I and –II were substantial and of a similar magnitude, indicating strong target engagement for both doses. There was generally good tolerability and safety, with infrequent musculoskeletal symptoms, infections and rashes.

**Conclusion:**

MIV-711 demonstrated significant reduction in OA bone disease progression, and also reduced cartilage progression, in the femur. Although there was no statistically significant reduction in pain, the study duration required to fully realize the symptom benefits expected from structure modification is unclear. Further evaluation of this novel agent is now warranted.
Disclosure: P. G. Conaghan, Novartis Pharmaceutical Corporation, Flexion Therapeutics, AbbVie, Infirst, Medivir, Merck Serono, ONO Pharmaceutical
A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Titration-to-Effect Study of Orally Administered CR845 in Patients with Osteoarthritis of the Hip or Knee

Sukirti Bagal, Catherine Munera, Patricia Brady and Joseph Stauffer, Cara Therapeutics, Stamford, CT

First publication: October 19, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: ACR Late-Breaking Abstract Poster
Session Type: ACR Late-breaking Abstract Session
Session Time: 9:00AM-11:00AM

Background/Purpose: CR845 is a selective kappa opioid receptor agonist with a peripheral mechanism of action. Here we report preliminary results from a Phase 2b study designed to characterize the analgesic efficacy of orally administered CR845 in patients with osteoarthritis (OA) of the hip or knee (ClinicalTrials.gov NCT02944448).

Methods: 476 male and female patients (ages ≥25 years) with moderate to severe pain (numeric rating scale [NRS] ≥5) associated with hip or knee OA were enrolled at 33 sites in the US. Following a 14-day screening period, patients were randomized 2:1 to CR845 or placebo, respectively. CR845 (1.0, 2.5, or 5.0 mg) or placebo were administered BID for a total of 8 weeks, with doses administered at least 2 hours before or after a meal.
Patients started on 1.0 mg or placebo, then during the 4-week post-randomization period, titrated upward to 2.5 or 5.0 mg to effect in a double-blind fashion and maintained for 4 weeks on the final individualized effective dose. The primary outcome measure was change from baseline in the weekly mean pain intensity score (0-10, NRS) at the index joint with CR845 compared to placebo at Week 8/Day 57. Secondary outcome measures included differences between CR845 and placebo in the Western Ontario and McMaster Osteoarthritis Index (WOMAC) total and sub-scores and in the Patient Global Impression of Change (PGIC) scale. Safety and tolerability measures were also captured over the 8-week treatment period.

**Results:** Efficacy was assessed in 118 hip OA patients (CR845, n=78; placebo, n=40) and 358 patients with knee OA (CR845, n=238; placebo, n=120). The primary efficacy results comparing CR845 (all doses) vs placebo were not statistically significant. However, patients with hip OA maintained on 5.0 mg (n=66) exhibited a statistically significant 69% reduction in mean joint pain score over placebo (p=0.043) accompanied by a 41% reduction over placebo in use of rescue medication at Week 8. The proportion of patients who titrated to the 5.0 mg dose and reported a PGIC score of "very much improved" or "much improved" was statistically higher in patients with knee OA (p<0.005 vs placebo) and hip OA (p<0.006 vs placebo). Patients maintained on the 1.0 and 2.5 mg doses did not exhibit statistically significant reductions in mean joint pain scores compared to placebo nor did patients with knee OA at any dose. Doses were generally well tolerated with no drug-related serious AEs. The most common AEs with ≥5% incidence were constipation (13%), dizziness (8%), and dry mouth (6%). There were no clinically significant changes in serum sodium levels during the 8-week treatment period for any dose group.

**Conclusion:** Post-hoc analyses demonstrated that hip OA patients receiving CR845 5.0 mg had significant pain reduction compared to placebo patients. The PGIC measure of pain in hip and knee patients combined also showed significant benefit of 5.0 mg CR845 while other pain measures showed improvement but not statistical significance. These beneficial effects and a positive safety profile warrant further clinical study.

**Disclosure:** S. Bagal, Cara Therapeutics, 3; C. Munera, Cara Therapeutics, 3; P. Brady, Cara Therapeutics, 3; J. Stauffer, Cara Therapeutics, 3, Cara Therapeutics, 1.


**Abstract Number:** 16L
Incidence of Thromboembolic Events in the Tofacitinib Rheumatoid Arthritis, Psoriasis, Psoriatic Arthritis and Ulcerative Colitis Development Programs

Philip J Mease, Joel Kremer, Stanley Cohen, Jeffrey R. Curtis, Christina Charles-Schoeman, Edward V Loftus, Jeffrey D Greenberg, Niki Palmetto, Keith S Kanik, Daniela Graham, Cunshan Wang, Pinaki Biswas, Gary Chan, Ryan DeMasi, Hernan Valdez, Thijs Hendrikx and Thomas V Jones, 1 Swedish Medical Center and University of Washington, Seattle, WA, 2 Medicine, Albany Medical College and the Center for Rheumatology, Albany, NY, 3 Metroplex Clinical Research Center, Dallas, TX, 4 University of Alabama, Birmingham, AL, 5 University of California, Los Angeles, CA, 6 Mayo Clinic, Rochester, MN, 7 Corrona, LLC, Southborough, MA, 8 Pfizer Inc, New York, NY, 9 Pfizer Inc, Groton, CT, 10 Pfizer Inc, Collegeville, PA

First publication: October 19, 2017

SESSION INFORMATION

Session Date: Tuesday, November 7, 2017
Session Title: ACR Late-Breaking Abstract Poster
Session Type: ACR Late-breaking Abstract Session
Session Time: 9:00AM-11:00AM

Background/Purpose: Tofacitinib is an oral Janus kinase (JAK) inhibitor that preferentially inhibits signaling by JAK3 and JAK1, with functional selectivity over JAK2. Potential increased risk of venous thromboembolic events (VTE) in patients (pts) with rheumatoid arthritis (RA) has been reported for a JAK 1/2 inhibitor.1 To assess VTE risk with tofacitinib, data were reviewed from the tofacitinib development program in RA, psoriasis (PsO), psoriatic arthritis (PsA), and ulcerative colitis (UC).

Methods: Data from Phase (P) 2 (RA, PsO, UC) and P3 (RA, PsO, PsA, UC) randomized clinical studies of tofacitinib as monotherapy or in combination with conventional synthetic (cs)DMARDs were included. Two cohorts were defined; 1) the placebo (PBO)-controlled cohort: pts randomized to tofacitinib 5 or 10 mg BID, or PBO up to Month (M) 3 in RA, PsO, and PsA studies, and pts randomized to tofacitinib 10 mg BID or PBO for the 9-week induction period in UC studies; 2) the dose-comparison cohort: pts randomized to tofacitinib 5 or 10 mg BID, adalimumab (ADA) 40 mg SC Q2W (RA and PsA only) or methotrexate (MTX) 20 mg QW (RA only) throughout the P2/3 studies for RA (up to M24), PsO (up to M12), and PsA (up to M12), and for the 12-month P3 UC
maintenance study. First deep vein thrombosis (DVT) and pulmonary embolism (PE) events were identified using the MedDRA embolic and thrombotic SMQ preferred terms restricted to the respiratory, thoracic, mediastinal, and vascular disorder System Organ Classes; incidence rates (IRs; pts with events/100 pt-years) were based on single events occurring during treatment or ≤28 days after the last dose or up to the cohort cut-off date. IRs for PE in pts with RA were compared with Corrona Registry data.

**Results:** Up to M3 in the PBO-controlled cohort, DVT and PE were both independently reported in 1 pt with RA and 1 with UC, who both received PBO; no pts receiving tofacitinib had DVT or PE events (Table). In the dose-comparison cohort there were 2 DVT events in tofacitinib-treated pts with RA (5 mg BID, n=1; 10 mg BID n=1) and 1 DVT event in a pt with PsA (tofacitinib 10 mg BID) (Table). IRs were 0.1 (95% CI: 0.0, 0.3) for both tofacitinib doses in RA, and 0.5 (95% CI: 0.0, 2.8) for tofacitinib 10 mg BID in PsA. Five PE events occurred in the dose-comparison cohort, all in RA (5 mg BID, n=2; 10 mg BID, n=3). IRs were 0.1 (95% CI: 0.0, 0.4) for tofacitinib 5 mg BID and 0.2 (95% CI: 0.0, 0.4) for 10 mg BID. IRs for PE with tofacitinib in RA were similar to those reported by the Corrona Registry in pts with RA treated with tofacitinib (0.1 [95% CI: 0.0, 0.4]), biologic DMARDs (0.2 [95% CI: 0.1, 0.3]), and csDMARDs (0.2 [95% CI: 0.0, 0.5]). DVT were reported twice with MTX, and none with ADA.

**Conclusion:** Analysis of DVT and PE across randomized clinical studies for RA, PsO, PsA, and UC showed no evidence of an increased risk of events with tofacitinib.

## Table. Incidence rates for deep vein thrombosis and pulmonary embolism across the tofacitinib clinical development program

<table>
<thead>
<tr>
<th>n/N IR (95% CI)</th>
<th>Placebo-controlled cohort</th>
<th>Dose-comparison cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tofacitinib 5 mg BID</td>
<td>Tofacitinib 10 mg BID</td>
</tr>
<tr>
<td><strong>Rheumatoid arthritis (N=5368; PY=4440)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DVT</td>
<td>0.1149</td>
<td>0.2024</td>
</tr>
<tr>
<td></td>
<td>0.01 (0.0, 0.9)</td>
<td>0.01 (0.0, 0.8)</td>
</tr>
<tr>
<td>PE</td>
<td>0.01 (0.0, 0.9)</td>
<td>0.01 (0.0, 0.8)</td>
</tr>
<tr>
<td><strong>Psoriatic arthritis (N=3662; PY=8763)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DVT</td>
<td>0.1123</td>
<td>0.1120</td>
</tr>
<tr>
<td></td>
<td>0.01 (0.0, 1.0)</td>
<td>0.01 (0.0, 1.0)</td>
</tr>
<tr>
<td>PE</td>
<td>0.01 (0.0, 1.0)</td>
<td>0.01 (0.0, 1.0)</td>
</tr>
<tr>
<td><strong>Ulcereative colitis (N=1156; PY [DVT]=1420; PY [PE]=1418)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DVT</td>
<td>0.0238</td>
<td>0.236</td>
</tr>
<tr>
<td></td>
<td>0.00 (0.0, 6.8)</td>
<td>0.00 (0.0, 6.8)</td>
</tr>
<tr>
<td>PE</td>
<td>0.00 (0.0, 6.8)</td>
<td>0.00 (0.0, 6.8)</td>
</tr>
</tbody>
</table>

*Includes Months 0–3 of Phase 2/3 studies for RA, PsO and PsA, and the 8-week induction period of Phase 2/3 UC studies; †Includes Months 0–24 of Phase 2/3 studies for RA, Months 0–12 for PsO and PsA, and the 12-month P3 UC maintenance study; ‡Dose-comparison cohort for tofacitinib 5 mg BID and 10 mg BID comprises patients randomized at baseline to tofacitinib 5 mg BID + patients randomized at baseline to PBO to tofacitinib 5 mg BID, and patients randomized at baseline to tofacitinib 10 mg BID + patients randomized at baseline to PBO to tofacitinib 10 mg BID, respectively.

BID, twice daily; CI, confidence interval; DVT, deep vein thrombosis; IR, incidence rate (patients with event/100 PY); N, number of patients in treatment group; n, number of patients with event; N/A, not applicable; PE, pulmonary embolism; PsA, psoriatic arthritis; PsO, psoriasis; PY, patient-years; QW, once weekly; Q2W, every 2 weeks; RA, rheumatoid arthritis; SC, subcutaneous; UC, ulcerative colitis

### Disclosure: P. J. Mease, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, Sun Pharmaceutical, UCB, 2,AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, Sun Pharmaceutical, UCB, 5,AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Genentech, Janssen, Novartis, Pfizer Inc, UCB, 8; J. Kremer, Corrona, LLC, 1,Corrona, LLC, 3,AbbVie, Amgen, BMS, Genentech, Lilly, Regeneron, Sanofi, Pfizer, 5,AbbVie, Genentech, Lilly, Novartis, Pfizer, 2; S. Cohen, AbbVie, Amgen, Boehringer Ingelheim, Gilead, Merck, Pfizer Inc, 5,AbbVie, Amgen, Boehringer Ingelheim, Gilead, Merck, Pfizer Inc, 9; J. R. Curtis, Amgen, 2,Corrona, 2,Crescendo Bio, 2,Pfizer Inc, 2,AbbVie, 5,Amgen, 5,Bristol-Myers Squibb, 5,Corrona, 5,Eli Lilly and Company, 5,Janssen Pharmaceutica Product, L.P., 5,Myriad, 5,Pfizer Inc, 5,Roche Pharmaceuticals, 5,UCB, 5; C. Charles-Schoeman, AbbVie, Bristol-Myers Squibb, Pfizer Inc, 2,Amgen, Pfizer Inc, Regeneron-Sanofi, 3; E. V. Loftus, AbbVie, 5,Amgen, 5,CVS Caremark, 5,Eli Lilly and Company, 5,Janssen Pharmaceutica Product, L.P., 5,MedImmune, 2,Pfizer Inc, 2,Receptos, 2,Robarts Clinical Trials, 2,Seres, 2,Takeda, 2,UCB, 2; J. D. Greenberg, Corrona, LLC, 1,Corrona, LLC, 3,Eli Lilly, Genentech, Janssen, Novartis, Pfizer, 5; N. Palmetto, Pfizer Inc, 1,Pfizer Inc, 3; K. S. Kanik, Pfizer Inc, 1,Pfizer Inc, 3; D. Graham, Pfizer Inc, 1,Pfizer Inc, 3; C. Wang, Pfizer Inc, 1,Pfizer Inc, 3; P. Biswas, Pfizer Inc, 1,Pfizer Inc, 3; G. Chan, Pfizer Inc, 1,Pfizer Inc, 3; R. DeMasi, Pfizer Inc, 1,Pfizer Inc, 3; H. Valdez, Pfizer Inc, 1,Pfizer Inc, 3; T. Hendrikx, Pfizer Inc, 1,Pfizer Inc, 3; T. V. Jones, Pfizer Inc, 1,Pfizer Inc, 3.
Subcutaneous Secukinumab Inhibits Radiographic Progression in Psoriatic Arthritis: Primary Results from a Large Randomized, Controlled, Double-Blind Phase 3 Study

Philip J Mease1, Désirée van der Heijde2, Robert B.M. Landewé3, Shephard Mpofu4, Proton Rahman5, Hasan Tahir6, Atul Singhal7, Elke Böttcher8, Sandra V. Navarra9, Karin Meiser4, Aimee Readie10, Luminita Pricop10 and Ken Abrams10, 1Swedish Medical Center and University of Washington, Seattle, WA, 2Leiden University Medical Center, Leiden, Netherlands, 3Academic Medical Center, Amsterdam and Atrium Medical Center, Heerlen, Netherlands, 4Novartis Pharma AG, Basel, Switzerland, 5Rheumatology, Memorial University of Newfoundland, St Johns, NF, Canada, 6Whipps Cross Hospital, London, United Kingdom, 7Southwest Rheumatology, Dallas, TX, 8Rheumazentrum Favoriten, Vienna, Austria, 9Rheumatology, University of Santo Tomas Hospital, Manila, Philippines, 10Novartis Pharmaceuticals Corporation, East Hanover, NJ

First publication: October 19, 2017

SESSION INFORMATION
Session Date: Tuesday, November 7, 2017
Session Title: ACR Late-Breaking Abstract Poster
Session Type: ACR Late-breaking Abstract Session
Session Time: 9:00AM-11:00AM

Background/Purpose: Secukinumab, a fully human monoclonal antibody that selectively neutralizes IL-17A, has shown significant and rapid efficacy in psoriatic arthritis (PsA). We present primary results of FUTURE 5 (NCT02404350), the largest randomized controlled trial (RCT) of a biologic conducted to date in PsA, assessing efficacy of
subcutaneous (sc) secukinumab 300 mg and 150 mg, including radiographic inhibition of structural damage, and safety.

**Methods:** Adults (n = 996) with active PsA, stratified by previous anti-TNF use, were randomized 2:2:2:3 to sc secukinumab 300 mg with loading dosage (LD), 150 mg with LD, 150 mg without LD, or placebo (PBO). All groups received secukinumab or PBO at baseline (BL), Wks 1, 2, 3, and 4, and then every 4 wks. At Wk 16, PBO non-responders (patients [pts] with <20% improvement from BL in tender or swollen joint counts) were switched to secukinumab 300 mg or 150 mg; remaining PBO pts were switched at Wk 24. The primary endpoint was ACR20 at Wk 16. The key secondary endpoint was radiographic structural progression, as measured by modified total van der Heijde Sharp score (mTSS), assessed by two blinded readers, based on hand/wrist/foot X-rays obtained at BL, Wk 16 (non-responders), and Wk 24. Statistical analyses used non-responder imputation for binary variables, linear extrapolation for radiographic data, and missing at random assumption for continuous endpoints. Testing results used a pre-defined hierarchical hypothesis testing strategy to adjust for multiplicity.

**Results:** BL characteristics were balanced across arms. Approximately 30% of pts had experienced an inadequate response or intolerance to previous anti-TNF therapy. Secukinumab significantly improved ACR20 at Wk 16 vs. PBO. Radiographic progression (mTSS) was significantly inhibited at Wk 24 in all secukinumab arms vs. PBO (Table). A greater proportion of pts had no radiographic progression (change from BL in mTSS ≤0.5) with secukinumab vs. PBO: 88% (300 mg), 79% (150 mg), 83% (150 mg without LD), and 73% (PBO). All hierarchical endpoints were significant for secukinumab vs. PBO at Wk 16, except for enthesitis and dactylitis resolution for 150 mg without LD (Table).
<table>
<thead>
<tr>
<th>Week 16 Data‡</th>
<th>Secukinumab 300 mg sc (n=222)</th>
<th>Secukinumab 150 mg sc (n=220)</th>
<th>Secukinumab 150 mg sc without LD (n=222)</th>
<th>Placebo (n=332)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACR20 (% responders)</td>
<td>62.6*</td>
<td>55.5*</td>
<td>59.5*</td>
<td>27.4</td>
</tr>
<tr>
<td>mTSS structural progression (mean change from BL to week 24)</td>
<td>0.08¥</td>
<td>0.17∞</td>
<td>–0.09¥</td>
<td>0.50</td>
</tr>
<tr>
<td>PASI 75/90 (% responders)</td>
<td>70.0*/53.6*</td>
<td>60.0*/36.8*</td>
<td>58.1*/31.6*</td>
<td>12.3/9.3</td>
</tr>
<tr>
<td>ACR50 (% responders)</td>
<td>39.6*</td>
<td>35.9*</td>
<td>32.0*</td>
<td>8.1</td>
</tr>
<tr>
<td>HAQ-DI score (LS mean change from BL)</td>
<td>–0.55*</td>
<td>–0.44*</td>
<td>–0.45*</td>
<td>–0.21</td>
</tr>
<tr>
<td>DAS28-CRP score (LS mean change from BL)</td>
<td>–1.49*</td>
<td>–1.29*</td>
<td>–1.29*</td>
<td>–0.63</td>
</tr>
<tr>
<td>Enthesitis resolution (%)</td>
<td>55.7†</td>
<td>54.6†</td>
<td>41.9</td>
<td>35.4</td>
</tr>
<tr>
<td>Dactylitis resolution (%)</td>
<td>65.9*</td>
<td>57.5†</td>
<td>56.3</td>
<td>32.3</td>
</tr>
</tbody>
</table>
Efficacy across all endpoints was greater in pts who were anti-TNF-naïve. The 300 mg and 150 mg groups had an earlier onset of response vs. pts who received 150 mg without LD. Adverse event (AE) rates at Wk 16 were 51.8% (300 mg), 52.7% (150 mg), 52.7% (150 mg without LD) and 58.7% (PBO); non-fatal serious AE rates were 2.3%, 3.2%, 1.4%, and 3.0%, respectively. No deaths were reported.

**Conclusion:** Subcutaneous secukinumab 300 mg with LD and 150 mg with and without LD, inhibited radiographic structural progression and provided rapid and clinically significant improvements in the signs, symptoms and physical function of pts with PsA. The safety profile was consistent with that previously reported with no new safety signals identified.

**Disclosure:** **P. J. Mease,** AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, 2,AbbVie, Amgen, BMS, Celgene, Crescendo Bioscience, Corrona, Demira, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, Zynerba, 5,AbbVie, Amgen, BMS, Celgene, Crescendo Bioscience, Genentech, Janssen, Novartis, Pfizer, UCB, 8; **D. van der Heijde,** AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, Glaxo-Smith-Kline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCBAbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer, 5,Director: Imaging Rheumatology bv, 9; **R. B. M. Landewé,** Abbott/AbbVie, Ablynx, Amgen, Astra-Zeneca, Bristol Myers Squibb, Celgene, Janssen (formerly Centocor), Galapagos, GlaxoSmithKline, Novartis, Novo-Nordisk, Merck, Pfizer, Roche, Schering-Plough, TiGenix, UCB, and Wyeth, 5,Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, and Wyeth, 2,Abbott/AbbVie, Amgen, Bristol Myers Squibb, Janssen (formerly Centocor), Merck, Pfizer, Roche, Schering-Plough, UCB, and Wyeth, 8; **S. Mpofu,** Novartis, 1,Novartis, 3; **P. Rahman,** Janssen Pharmaceutica Product, L.P., 8,Amgen, AbbVie, BMS, Celgene, Pfizer, Janssen, Wyeth, EliLiiy, Novartis, 8,Amgen, AbbVie, BMS, Celgene, Pfizer, Janssen, Wyeth, EliLiiy, Novartis, 5; **H. Tahir,** Abbvie, 5,Novartis Pharmaceutical Corporation, 5,Pfizer Inc, 5,UCB, 5,Eli-Lily, 5,Janssen Pharmaceutica Product, L.P., 5,Novartis Pharmaceutical Corporation, 2,Pfizer Inc, 2; **A. Singhal,** Abbvie, 2,Gilead, 2,Sanofi, 2,Regeneron, 2,Amgen, 2,Roche Pharmaceuticals, 2,BMS, 2,Janssen Pharmaceutica Product, L.P., 2,Lilly, 2,Novartis Pharmaceutical Corporation, 2,Pfizer Inc, 2,UCB, 2,AstraZeneca,
Rituximab As Re-Induction Therapy in Relapsing ANCA-Associated Vasculitis

Rona Smith1, Rachel Jones2, Ulrich Specks3, Carol A McAlear4, Kim Mynard2, Simon Bond2, David Jayne5 and Peter A. Merkel6, 1Department of Medicine, University of Cambridge, Department of Medicine, University of Cambridge, Cambridge, United Kingdom, 2Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom, 3Mayo Clinic College of Medicine, Rochester, MN, 4University of Pennsylvania, Philadelphia, PA, 5Vasculitis and Lupus Clinic, Department of Medicine, University of Cambridge, Cambridge, United Kingdom, 6Division of Rheumatology, University of Pennsylvania, Philadelphia, PA

First publication: October 19, 2017
Background/Purpose:

RITAZAREM (ClinicalTrials.gov: NCT01697267) is an international, randomized, controlled trial comparing rituximab with azathioprine as maintenance therapy after induction of remission with rituximab and glucocorticoids for relapsing ANCA-associated vasculitis (AAV). Since all patients receive rituximab for induction, the RITAZAREM trial is also the largest prospective study of the use of rituximab in patients with relapsing AAV.

Methods:

188 patients with granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) were enrolled and received remission-induction therapy with rituximab (4 x 375 mg/m²) and a higher- or lower-dose glucocorticoid regimen, depending on physician choice: reducing from either prednisone (or prednisolone) 1 mg/kg/day or 0.5 mg/kg/day to 10 mg/day by 4 months. Severe disease was defined as an organ- or life-threatening manifestation. Patients who achieved remission (BVAS/WG ≤1 and prednisone ≤10 mg daily) by month 4 were randomized to either repeat dose rituximab (1 g every 4 months) or azathioprine (2 mg/kg/day) for a total treatment period of 24 months. Preliminary results of the 4-month induction phase are reported.

Results:

95/188 (51%) subjects were male, median age 59 years (interquartile range (IQR) 47.5-68.0), disease duration of 5.0 years (IQR 1.85-10.15). 149/188 (79%) had previously received cyclophosphamide and 67/188 (36%) had previously received rituximab. 137/188 (73%) had PR3-ANCA positive disease, and 51/188 (37%) MPO-ANCA positive disease. 118/188 (63%) of relapses were severe, 56/188 (30%) received the higher-dose glucocorticoid regimen and 132/188 (70%) received the lower-dose glucocorticoid regimen (Table 1). The median BVAS/WG at enrollment was 5, maximum 14.

Data on responses at month 4 was available on 181 patients. 165/181 (91.2%) of patients achieved remission. 11/181 (6.0%) patients failed to achieve remission: 9/11 had PR3-ANCA positive disease; 9/11 had ear, nose, and throat involvement at baseline; 7/11 had severe disease at enrollment; and 9/11 received the lower (0.5 mg/kg) glucocorticoid dosing regimen. 5 (2.8%) patients died in the induction phase; causes of death included: pneumonia (2), cerebrovascular accident (1), alveolar hemorrhage/respiratory failure (1), and colon cancer (1).

53 severe adverse events (SAEs) occurred in 30 patients during the induction phase; 15/53 (28%) SAEs were severe infections. 52/188 (28%) patients developed an IgG level <5g/l in the induction phase.
**Conclusion:**

Data from the first phase of RITAZAREM, the largest reported cohort of patients with relapsing AAV, demonstrates that rituximab, in conjunction with glucocorticoids, is highly effective at re-inducing remission in patients with AAV who have relapsed, with an acceptable safety profile. The maintenance phase of the RITAZAREM trial is ongoing.

<table>
<thead>
<tr>
<th>Glucocorticoid induction regimen (oral prednisone/prednisolone)</th>
<th>Relapse Severity at Enrollment (%)</th>
<th>Totals (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Severe</td>
<td>Non-Severe</td>
</tr>
<tr>
<td>High-dose (starting at 1mg/kg/day)</td>
<td>45 / 188 (24%)</td>
<td>11 / 188 (6%)</td>
</tr>
<tr>
<td>Low-dose (starting at 0.5mg/kg/day)</td>
<td>73 / 188 (39%)</td>
<td>59 / 188 (31%)</td>
</tr>
<tr>
<td>Totals (%)</td>
<td>118 / 188 (63%)</td>
<td>70 / 188 (37%)</td>
</tr>
</tbody>
</table>

**Disclosure:** **R. Smith**, Roche Pharmaceuticals, 2; **R. Jones**, Roche Pharmaceuticals, 2; **U. Specks**, Genentech and Biogen IDEC Inc., 2; **C. A. McAlear**, Genentech and Biogen IDEC Inc., 2; **K. Mynard**, Roche Pharmaceuticals, 2; **S. Bond**, Roche Pharmaceuticals, 2; **D. Jayne**, Roche Pharmaceuticals, 2; **P. A. Merkel**, Genentech and Biogen IDEC Inc., 2.

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Page Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aaby, D</td>
<td>1696</td>
</tr>
<tr>
<td>Aakhus, S</td>
<td>744</td>
</tr>
<tr>
<td>Aaltonen, K</td>
<td>1541</td>
</tr>
<tr>
<td>Abaci, N</td>
<td>169</td>
</tr>
<tr>
<td>Abad, MA</td>
<td>335</td>
</tr>
<tr>
<td>Abad, S</td>
<td>814</td>
</tr>
<tr>
<td>Abad, I</td>
<td>1654, 2924</td>
</tr>
<tr>
<td>Abalos-Aguilera, MC</td>
<td>391, 392, 1466, 2435, 2655, 2656, 2764</td>
</tr>
<tr>
<td>Abbruzzese, B</td>
<td>12L</td>
</tr>
<tr>
<td>Abdo, H</td>
<td>174</td>
</tr>
<tr>
<td>Abdel Mohsen, D</td>
<td>2387</td>
</tr>
<tr>
<td>Abdel-Wahab, N</td>
<td>850, 2128, 2155</td>
</tr>
<tr>
<td>Abdelhafiz, Y</td>
<td>243</td>
</tr>
<tr>
<td>Abdelkader, A</td>
<td>2062</td>
</tr>
<tr>
<td>Abdessemad, A</td>
<td>252</td>
</tr>
<tr>
<td>Abdollahi-Roodsaz, S</td>
<td>402, 1742</td>
</tr>
<tr>
<td>ABDOUL, H</td>
<td>2671</td>
</tr>
<tr>
<td>Abdulahad, WH</td>
<td>782, 807, 1782, 1846, 2936</td>
</tr>
<tr>
<td>Abdulqader, Y</td>
<td>270</td>
</tr>
<tr>
<td>Abe, A</td>
<td>412, 1347</td>
</tr>
<tr>
<td>Abe, N</td>
<td>11</td>
</tr>
<tr>
<td>Abe, S</td>
<td>2873</td>
</tr>
<tr>
<td>Abel, G</td>
<td>700, 701</td>
</tr>
<tr>
<td>Abeles, I</td>
<td>688</td>
</tr>
<tr>
<td>ABELSON, A</td>
<td>2246</td>
</tr>
<tr>
<td>Aberle, T</td>
<td>1657, 1658, 1841, 2600, 2820, 2875, 2977</td>
</tr>
<tr>
<td>Abhishek, A</td>
<td>1104, 2847</td>
</tr>
<tr>
<td>Abhyankar, R</td>
<td>1581</td>
</tr>
<tr>
<td>Abignano, G</td>
<td>734, 2669, 2984</td>
</tr>
<tr>
<td>Abji, F</td>
<td>647</td>
</tr>
<tr>
<td>Abolin, JN</td>
<td>1648, 1872, 1977, 1979</td>
</tr>
<tr>
<td>Abogamal, A</td>
<td>634</td>
</tr>
<tr>
<td>Abraham, B</td>
<td>1809</td>
</tr>
<tr>
<td>Abraham, D</td>
<td>49, 753</td>
</tr>
<tr>
<td>Abraham, H</td>
<td>1097</td>
</tr>
<tr>
<td>Abraham, S</td>
<td>1560</td>
</tr>
<tr>
<td>Abraham, T</td>
<td>1770</td>
</tr>
<tr>
<td>Abraham, V</td>
<td>1825</td>
</tr>
<tr>
<td>Abrahamowicz, M</td>
<td>1839, 2769, 2785</td>
</tr>
<tr>
<td>Abrahante Lloréns, J</td>
<td>1062</td>
</tr>
<tr>
<td>Abram, F</td>
<td>1197, 1208, 2192</td>
</tr>
<tr>
<td>Abrams, K</td>
<td>17L, 606</td>
</tr>
<tr>
<td>Abramson, SB</td>
<td>2198</td>
</tr>
<tr>
<td>Abreu, G</td>
<td>2591</td>
</tr>
<tr>
<td>Abril, A</td>
<td>267, 1990, 2021, 2173</td>
</tr>
<tr>
<td>Abril, I</td>
<td>1990</td>
</tr>
<tr>
<td>Abu Alsaoud, S</td>
<td>1271</td>
</tr>
<tr>
<td>Abu-Mendoza, C</td>
<td>667, 671, 1445, 1975, 2360, 2361, 2393</td>
</tr>
<tr>
<td>Abutiban, F</td>
<td>471, 2366</td>
</tr>
<tr>
<td>Acar, H</td>
<td>266</td>
</tr>
<tr>
<td>Accortt, N</td>
<td>1039, 1342, 1425</td>
</tr>
<tr>
<td>Accortt, NA</td>
<td>989</td>
</tr>
<tr>
<td>Accossato, P</td>
<td>2966</td>
</tr>
<tr>
<td>Acer Kasman, S</td>
<td>2504</td>
</tr>
<tr>
<td>Acevedo-Castañeda, ES</td>
<td>1445, 1975, 2361</td>
</tr>
<tr>
<td>Acevedo-Vásquez, EM</td>
<td>1654, 2924</td>
</tr>
<tr>
<td>Acharya, N</td>
<td>1963</td>
</tr>
<tr>
<td>Achenbach, SJ</td>
<td>32, 1032, 1214</td>
</tr>
<tr>
<td>Açıkgöz, ŞA</td>
<td>2728</td>
</tr>
<tr>
<td>Acosta, C</td>
<td>277</td>
</tr>
<tr>
<td>Acosta Felquer, ML</td>
<td>1557, 2550</td>
</tr>
<tr>
<td>Acosta Peña, G</td>
<td>154</td>
</tr>
<tr>
<td>Acuña, M</td>
<td>2837</td>
</tr>
<tr>
<td>Adachi, J</td>
<td>1886, 1888, 2383</td>
</tr>
<tr>
<td>ADAM, K</td>
<td>2486</td>
</tr>
<tr>
<td>Adams, A</td>
<td>89, 1800, 2313</td>
</tr>
<tr>
<td>Adams, A</td>
<td>1213</td>
</tr>
<tr>
<td>Adams, D</td>
<td>597, 628, 2969</td>
</tr>
<tr>
<td>Adams, E</td>
<td>1112</td>
</tr>
<tr>
<td>Adams, M</td>
<td>2290</td>
</tr>
<tr>
<td>Adams, S</td>
<td>2136</td>
</tr>
<tr>
<td>Adams, W</td>
<td>515</td>
</tr>
<tr>
<td>Adan, A</td>
<td>1155, 1169, 1516, 2297, 2722, 2723, 2857</td>
</tr>
<tr>
<td>Addario, A</td>
<td>787</td>
</tr>
<tr>
<td>Addepalli, M</td>
<td>2715</td>
</tr>
<tr>
<td>Addya, S</td>
<td>754</td>
</tr>
<tr>
<td>Adebajo, AO</td>
<td>634</td>
</tr>
<tr>
<td>Adelowo, O</td>
<td>2069</td>
</tr>
<tr>
<td>Ademola, T</td>
<td>206</td>
</tr>
<tr>
<td>Adeyemi-Fowode, O</td>
<td>1318</td>
</tr>
<tr>
<td>Adeyemo, A</td>
<td>919, 2930</td>
</tr>
<tr>
<td>Adhikari, S</td>
<td>404</td>
</tr>
<tr>
<td>Adinolfi, A</td>
<td>2055</td>
</tr>
<tr>
<td>Adler, B</td>
<td>728</td>
</tr>
<tr>
<td>Adler, S</td>
<td>805</td>
</tr>
<tr>
<td>Adnan, E</td>
<td>1064</td>
</tr>
<tr>
<td>Adriani, M</td>
<td>2975</td>
</tr>
<tr>
<td>Adrianto, I</td>
<td>300, 1811, 2653</td>
</tr>
<tr>
<td>Adrovic, A</td>
<td>368, 369, 746, 1283, 2117, 2305, 2959</td>
</tr>
</tbody>
</table>
Aelion, JA 601
Aeschlimann, C 332
Aeschlimann, FA 1892
Aesif, SW 1171
af Forselles, K 62
af Klint, E 2869
Afeltra, A 1292
Afzali, A 1309
Aga, AB 235, 459, 486
Agard, C 797, 2754
Agarwal, E 1252, 2831
Agarwal, P 1477, 2472
Agarwal, SK 2691
Agarwal, V 1568, 1723, 1920, 2885
Agere, S 962, 1409
Aggarwal, A 580, 2311, 2329, 2330, 2651, 2867
Aggarwal, R 851, 2136, 2171
Aghdassi, E 2769
Agnolucci, J 2295
Agosti, J 1796
Agrawal, R 1696
Aguado, P 1891
Aguado, P 1471, 2422
Á
Águeda, A 611
A
Aguero, S 269
Aguila Maldonado, R 1766, 2237, 2676
Aguilar, G 1225, 2021
Aguilar Galán, R 1158
Aguilar-Salinas, C 1492
Aguilera Barragán-Pickens, G 1445, 1975, 2360, 2361
Aguilera-Cros, C 498
Aguirre, A 1798
Aguirre Zamorano, MA 2655, 2656, 2764
Agustinelli, R 707
Ah Kion, MD 757
Ahearn, J 673, 680, 1673
Ahijado-Guzman, P 1226, 1516, 1518
Ahlman, M 263, 779, 820, 821, 1845
Ahmad, H 608, 609, 2964
Ahmad, H 595, 610, 1424, 1474
Ahmad, I 55, 56
Ahmad, S 2425
Ahmad, Z 733, 2681
Ahmadi, SF 691
Ahmed, S 1723, 2885
Ahmed, S 86, 962, 976, 1409
Ahn, EY 2630
Ahn, GY 1152, 1461
Ahn, HS 982
Ahn, SJ 1565
Ahn, SS 245
Ahola Kohut, S 1259
Ahuja, S 1317, 1625
Ai, R 2793, 2829
Aihara, M 2158, 2172
Aikawa, NE 524, 1268, 1302
Ailioaie, C 2333
Aina, O 1770
Ainsworth, HC 164
Ainsworth, R 166
Aiona, K 1055
Airò, P 1683
Airoldi, C 2021
Aitken, D 1850
Aizawa, A 2427
Aizer, J 89, 92
Ajeganova, S 929
Ajibade, A 634
Ajmone Marsan, N 1693
Ajzenberg, N 2775
Akahoshi, M 36, 77, 2710
Akaikie, H 1279
Akamata, K 31
Akar, S 542, 1455, 1472, 1509, 1514, 1534, 2496
Akasaka, D 1319, 1320
Akasbi, M 209
Akashi, K 551, 861, 1321
Akashi, K 36, 77, 2710
Akdam, H 2353
Akdemir, G 429
Akdogan, A 1174, 1312, 1451, 1522, 2409
Å
Åkerstedt, T 123
A
Akgün, E 2231
Akgun, K 2496
Akhtar, N 962
Akhtari, S 714, 1592
Akil, M 565
Akinci, A 305, 2496
Akintayo, F 2069
Akintayo, R 2069
Akita, Y 1010
Akiyama, M 2903
Akiyama, Y 1776
Akizuki, S 479
Akker, M 2117
Akkoc, FN 2748
Akkoc, N 1776, 1455, 1472, 1514, 1534, 1514, 1534
Akl, E 15
Aksentijevich, I 290, 292, 1892
Aktay Ayaz, N 2859
Akter, T 762
Al Dhaheri, A 2623
Al Hinai, S 62
Al Ohaly, R 151
Al Salmi, I 2399, 2400, 2401
Al Sawah, S 1001, 1555, 2532, 2533
Al Sheik, H 733
Al Snih, S 277
Al-ani, M 270
Al-Awadhi, A 471, 2366
Al-Charakh, M 203
Al-Herz, A 471, 2366
Al-Hosni, R 1936
Al-Kandari, W 471, 2366
Al-Marzooq, A 203
Al-Mossawi, MH 643
Al-Saber, A 471, 2366
Al-Soudi, A 1847
Alabas, O 2214
Alabdurababani, Z 1599
Alachkar, M 2380
AlAhmed, O 2027
Alajmi, S 151
Alam, F 43
Alarcón, E 2021
Alarcón, GS 687, 1606, 1654, 2924
Alarcón-Riquelme, M 41, 178, 1712
Alase, A 2816
Alastü, F 452, 1432, 2871
Alavi, A 264, 2011
Alba, P 1645
Alba-Férez, R 543, 1965
Albani, S 759, 953, 1462, 1577, 1744, 1745, 1941, 2637
Albarrán Hernández, F 1738
Albayda, J 242, 2131
Albert, A 1027
Albert, D 377
Albert Espi, G 2094
Albiero, E 2237
Albiges, L 1741
Alborghetti, F 1969
Albornoz, C 148
Albornoz, MA 148
Albrecht, K 2388
Albric, L 894
Albugami, M 153
Alcalde-Villar, M 2722
Alcañiz Escandell, C 684, 1221, 1224, 2003
Alcazar, LA 420, 538, 1443, 2412, 2419
Aldasoro, V 780
Aldei, A 471, 2366
Aldous, A 2137
Aldunate, L 456, 457
Alegre, JJ 1587, 1612, 1683, 2003, 2094
Alehashemi, S 779, 820
Alekseyenko, A 1786
Alemam, M 2668
Alemao, E 410, 413, 595, 1034, 1035, 1341, 1465, 1817, 2450, 2755, 2786, 2891
Alendry, S 205
Alenizi, A 471, 2366
Alessandri, E 2682, 2889
Alessio, M 376
Aletaha, D 452, 1478, 2245, 2472, 2861, 2864, 2871, 2970, 2971
Alexander, P 896
Alexander, R 673, 680, 682
Alexeeva, E 386, 1283, 2279, 2280, 2333, 2859, 2959
Alexsson, A 182, 1638
Alfaro, J 450, 1378
Alfaro-Lozano, J 687, 1654, 2924
Alfredsson, L 119, 123, 124, 125, 127, 132, 914, 1403
Alguacil, A 209
Algulin, J 2911
Alhajeri, H 471, 2366
Alharbi, S 2681
Alhazzani, A 153
Alhusayen, R 994, 996
Ali, A 2899
Ali, RA 2761
Ali, Y 471, 2366
Ali, Y 1482
Alia, P 2379
Alibaz-Oner, F 2727
Aliko, A 1456
Aliprantis, A 398
Alivernini, S 1898
Aljaberi, N 105, 384
Alkhairi, B 105, 2243
Alkureishi, M 2306
Alaabart, C 2291, 2916
Alaabart, CF 427, 429, 1402
Allam, F 2028, 2036
Allanore, Y 732, 1683, 2662, 2797, 2983
Allbritton, N 49
Allen, J 2005
Allen, K 2766, 2768
Allen, R 2225
Allen, R 1367, 1368
Allenbach, Y 5L
Allez, M 1823
Allia, J 1216
Allman, M 1990
Ally, F 953
Allyn, B 49
Almadori, A 1688
Almagor, O 936, 2188
Almario, C 2266
Almeda-Valdés, P 1492
Almeida, C 745
Almeida de Jesus, A 939, 1024, 1893, 2347, 2349, 2758, 2772
Almirall, M 1535
Almodovar, R 2722
Almodóvar González, R 2130
Alobud, S 153
Alonso, E 1506
Alonso-Ruiz, A 2442
Aloush, V 1648, 1977, 1979
Alperi-López, M 28
Alperin, J 2095
Alqahtani, A 755
Alsina, M 639
Alsouk, R 471, 2366
Alsultan, N 153
Altamirano Ufion, A 2265
Altan, L 2204
Alten, R 356, 414, 500, 1468, 1469, 1909, 2452, 2798, 2799
Altinel, S 1163
Altman, R 980
Altorok, N 755, 1710
Altpeter, M 846
Altymani, Y 153
Alunno, A 571
Alva, M 2021
Alvarellos, A 572, 2008, 2924
Alvarenga, JC 1219
Alvarez, AC 572, 2008
Alvarez, A 1645
Alvarez, B 1448
Alvarez, D 360
Alvarez de Buergo, MC 2112
Alvarez del Castillo Araujo, AL 2021
Á
Álvarez Reyes, F 2402
A
Alvarez Sepúlveda, P 1645
Alvarez-Mon, M 1738
Alvarez-Quiroga, C 1445
Alvarez-Rodriguez, B 498
Alvaro-Gracia, JM 2371
Aly, A 2684
AM, DVG 1379, 2403
Amano, E 1149
Amano, K 507, 1421
Amano, K 2017
Amantini, D 1189
Amanzi, L 255
Amara, K 477, 834
Amariylo, G 1012
Amaya, I 277
Ambadapadi, S 2566
Ambrozic, A 704
Amdur, R 274, 2837
Amelio, J 2593, 2594, 2812
Amengual, O 11
Amezcua-Guerra, LM 154
Amiable, N 466, 1027
Amiaud, J 1940
Amigo, MC 1654, 2924
Amigues, I 525, 2363
Anil, I 2062
Amin, MA 971, 1336, 1705, 2926
Amin, S 1214, 1662, 2657
Amirault, J 398
Amiya, E 795
Ammann, P 48
Ammann, P 2772
Ammar, R 1818
Ammendolia, C 1851
Ammitzbøll-Danielsen, M 246, 1878
Arama, V  997
Aramaki, T  1441
Aramburu, F  2062
Aranow, C  1606, 2614, 2809, 2925
Arape, R  2021
Araujo, E  1112
Araujo, EG  881
Arazi, A  25, 2659
Arbeeva, L  846, 2766
Arboleya, L  498
Arce-Franco, MT  40
Archambault, KA  2931
Archer, A  896
Archer, S  73, 1571
Ardalan, K  1277, 1284, 2252, 2895, 2960
Ardid, D  2228
Ardoin, SP  1594, 1614, 1615, 2598, 2631, 2725, 2958
Ardura, M  2027
Arefayene, M  45
Aren, K  730, 1730
Arenas, MD  2081
Arends, RH  1195
Arends, S  1501, 2943
Arendse, R  612, 629
Areny Micas, R  2021
Arevalo Ruales, K  684, 1221, 1224, 2003
Arevalos, JL  2621
Argila, D  2343
Aria, Y  1568
Arias de la Rosa, I  391, 392, 1466, 2435, 2655, 2656, 2764
Arida, A  2744
Arikan, D  2481
Arima, M  2386
Arimura, Y  795, 1013, 1751, 1762, 1778
Aringer, M  1589, 1622
Arinobu, Y  36, 77, 238, 2710
Arinuma, Y  1761
Arismendi, MI  751, 1691
Arkachaisri, T  953, 1744, 2637
Arkema, EV  134, 1812, 1840
Arlet, P  2661
Armagan, B  1174, 1240, 1312, 1451, 1522, 2110, 2409, 2742, 2743
Armas, E  935, 1204
Armas-González, E  40
Armesto, S  2527
Armitage, C  1584
Armstrong, AW  1555, 2532, 2533
Arnaud, L  1840
Arndt, T  1000
Arnett, D  2429
Arnold, C  2266
Arnoux, F  388
Arntz, OJ  72, 1934
Arock, M  71
Aronow, B  173
Arora, T  828
Arora, VK  409
Arriens, C  673, 680, 1657, 1658, 1841, 2600, 2820, 2977
Arroyo-Ávila, M  442
Arsenault, P  2224
Arteaga, S  210, 2123
Arteta Ruiz, T  2837
Arthur, V  940
Arts, E  147
Arturi, V  1766, 2676
Arvikar, S  494, 949, 1020
Arwani, S  1336, 2926
Aryee, M  184
Asadi-Zeydabadi, M  490
Asai, N  540
Asai, S  540
Asakawa, K  854
Asako, K  1762
Asami, Y  1460
Asano, T  76
Asano, Y  26, 31, 1719
Asano, Y  2558
Asanuma, YF  2494
Asashima, H  2873
Ascherman, DP  2915
Ascone, G  1074
Ash, J  1086, 2583
Ashbeck, E  2183
Ashbeck, EL  2852, 2906, 2948
Ascher, R  2186
Asiri, A  151
Askanase, A  673, 680, 690, 1238, 1482, 1601, 1606, 1632, 1841, 2033, 2344, 2581, 2595, 2614
Asking, J  127, 134, 914, 1403, 1541
Aslam, F  1452
Aslanidis, S  2357
Bachali, P 296, 1026, 2818
Bachasson, D 5L
Bachelez, H 613
Backhaus, M 2007, 2967, 2973
Bäcklund, J 2709
Backman, C 197
Backman, CL 2269
Bacon, K 2218
Bacon, P 1848
Badak, SO 739
Badaracco, A 2253
Badawi, RD 243
Badawi, S 1037
Badley, EM 214, 217
Badoud, I 48
Bae, D 82, 87
Bae, SC 207, 1016, 1474, 1606, 2405, 2630, 2925
Bae, S 2148, 2149
Bae, YJ 2461
Baek, IW 716
Baek, JY 82
Baek, JM 47
Baenas, D 572, 2008
Baer, AN 877, 878, 2875, 2876
Baer, P 614
Baerlecken, NT 581
Baerwald, C 1340, 1465, 2024
Baeten, D 581, 1559, 1571, 1578, 1792, 1831, 2546, 2547, 2801
Baffie, C 1439
Bagal, S 15L
Baganz, L 1430
Bagavant, H 559, 2653, 2774
Bager, CL 489
Bagga, H 1431
Bagheri, A 779, 820, 1845
Bagheri, M 263
Baglaenko, Y 645, 831, 835
Bagnasco, F 2333
Bagnato, G 2984
Bagur, A 320
Bahal, S 685
Bahorski, S 846
Bahuaud, M 2415, 2606
Bai, G 1311
Bai, R 2241, 2242
Baildam, E 366, 2287
Bailey, H 12L
Baillet, A 1584
Bajai, P 2041
Bajema, I 890
Bajuaifer, Y 151
Baker, EJ 385
Baker, K 1853
Baker, MF 545
Baker, NA 2988
Baker Frost, D 768
Bakirci, S 254, 2727
Bakker, J 1693
Bakker, JA 890
Bakker, P 1512
Baklacioglu, HS 2504
Bakshi, R 1870
Bal, A 2204
Balada, E 849
Balandraud, N 388, 2430
Balanescu, AR 2796
Balasubramanian, A 1213
Balbir-Gurman, A 1023, 1731
Balboni, I 2996
Balderia, P 2058
Baldini, C 556, 876, 877, 1479, 1486, 1487, 1488, 1489, 1756
Baldini Campos, R 568
Baldissera, E 1292
Baldo, D 2121
Baldolli, A 2716, 2717
Balevic, S 1296, 1297
Balfour, A 2440
Bali, N 2684
Balkarli, A 2727
Ball, J 2850
Ball, M 1730
Ball, S 2180
Ballabio, M 2332
Ballent, M 1645
Ballina-García, FJ 28
Ballou, S 8L, 1954
Balogh, E 1433
Balsa, A 793, 1450, 1471, 1533, 1891, 2422, 2426, 2487
Bambara, LM 1683
Bambhroliya, C 2989
Bancroft Rizzo, D 1859
Banda, N 404
Bande, JM 1360
Bandoli, G 1313
Bandyopadhyay, S 1818
Banerjee, S 595, 608, 609, 610, 2855
Banerjee, S 1050
Banerjee, S 263, 779, 1153
Bang, H 571, 1402, 2864, 2916
Bang, J 975, 1434
Bang, SY 1016, 1572, 2074, 2405
Bangert, E 2162
Banjari, M 1763
Bank, I 1731
Banak, A 8
Bankhurst, A 309, 310
Banki, K 2572, 2763
Banks, S 1237
Bannister, B 1784, 2024
Bannert, B 1784, 2024
Bannuru, RR 449, 931, 1185, 1194, 2615, 2849
Bansback, N 1045, 2778
Banschbach, K 1280
Banse, C 528
Banzato, A 12, 2760
Banzo, JI 260, 817
Bao, G 844, 987, 2044
Baquero, JL 1361
Bana, C 2660
Barabani, C 1766
Baracat, E 1302
Baraf, HSB 206, 934, 1141, 2054
Barahona-Correa, J 1672
Baraliakos, X 3L, 582, 1511, 1523, 1526, 1529, 1877, 2498
Baranauskaite, A 2446
Barbadillo, C 2130
Barbar-Flaisler, F 2027
Barbrija, N 41, 391, 392, 1466, 2435, 2655, 2656, 2764
Barber, C 1093, 1103, 2811
Barber, M 1855
Barbey, C 2607
Barbhia, M 837, 985, 988, 1628, 1863, 1953
Barbier, J 2228
Barbour, KE 1004, 1857, 2987
Barchechath-Flaisler, F 1453
Barchuk, W 2878
Barclay, M 1105
Bardelli, M 2899
Bardin, T 1137, 1442
Barete, S 71
Baril-Dionne, A 1599
Barile, L 1654, 2924
Barkatz, H 216
Barker, A 91, 94, 99, 907, 908, 909
Barlow, JL 1178
Barnette, T 1223, 1490, 1562, 2597
Barnidge, D 1752
Baron, G 1442
Baron, M 287, 902
Baron, M 945, 1722, 2670, 2674
Barone, F 863, 877, 1784
Barr, E 706
Barr, S 1599, 1641
Barra, L 1325
Barral, C 1449
Barrasa, JI 396
Barrat, FJ 757
Barreia, JC 269, 2237
Barrett-Connor, E 2180
Barrios, B 269, 1007
Barrios, C 2621
Barron, K 367
Barry, O 2374
Barski, A 2825
Barsness Motschenbacher, L 834
Barsotti, S 255, 1488, 1756, 2166
Barth, Z 471, 2366
Barthels, CM 294, 1087, 1088, 1171, 2261
Barthels, W 1245
Barthels-Peculis, L 1801
Barth, Z 1265, 1276
Barthel, HR 13L
Bartholmai, B 1876, 2175
Bartlett, D 1380, 1381
Bartlett, SJ 443, 461, 1082, 1255, 1393, 1814, 2248, 2255, 2390, 2391, 2595
Bartoloni, E 571
Bartoloni-Bocci, E 1292
Barton, A 122, 1017, 1736
Barton, J 1257, 2221, 2378, 2893
Barut, K 368, 369, 746, 2117, 2305
Basher, R 2010
Bashleben, C 700, 701
Basnet, S 879, 1952
Bass, AR 89, 92, 218, 220, 221, 923, 1148
Bass Goldman, T 206
Bastacky, S 898
Bastida, C 1436
Basu, N 2753, 2912
Batat, E 995
Bathi, LDT 953, 2637
Bathon, J 1348, 1482, 2362, 2363, 2913
Bathon, JM 174
Batignes, M 2701
Batko, B 2697
Battafarano, D 2358
Battafarano, DF 869, 2911
Battaglia, MG 1360
Battagliotti, C 269, 1283, 2959
Batterman, A 1263
Batteux, F 2415, 2606
Batthish, M 2317
Batticciotto, A 152, 280, 2015
Battisti, KA 2111
Battistone, MJ 91, 94, 99, 907, 908, 909
Batu, ED 1174, 1892, 2110, 2349
Baudens, G 2464
Bauer, E 1096
Baumann, A 2624
Baumgartner, S 1120
Baumhauer, J 1247
Bautista-Caro, MB 654
Bautista-Molano, W 456, 457, 634, 640
Bawadekar, M 294
Baxter, C 2674
Baxter, D 972
Bay-Jensen, AC 465, 1399, 2207, 2212
Bay-Jensen, AC 489, 740, 771, 969, 1063, 2688
Bayat, N 2140
Baydogan, SN 2305
Baygin, H 2353
Baynton, E 469
Beagley, K 1584
Bean, K 222
Bean, KM 83
Beaton, D 1231, 1621, 1623, 2807
Beattie, KA 2016, 2942
Beattie, SD 502
BEAUDOUIN, C 2415
Beaufort, R 588, 589, 590, 1504
Beauvais, C 216
Bécède, M 452
Becetti, K 2672
Bechman, K 1374
Becic Pedersen, A 2398
Beck, JP 94, 907, 908, 909
Becker, L 2931
Becker, ML 380, 1322, 2296
Becker, MA 1116
Becker, MO 731, 2662, 2983
Becker, Y 1666
Beckett, B 308
Beckford, M 2578
Beckmann, D 865, 966
Becvar, R 766, 1692, 1694, 2153
Bedoya, E 269
Beegle, S 1166
Beek, K 1563
Beekmann, SE 2839
Begley, R 1459
Behlouli, H 2785
Behrens, F 2L, 1825, 2973
Bejarano, M 2237
Bekker, CPJ 4, 1729
Bekkering, P 2291
Belchis, D 878
Belendiuk, K 1600
Belhocine, M 2608, 2762
Belilos, E 964, 1770
Belisle, P 2104
Belkacemi, M 1390
Bell, CF 2593, 2594, 2812
Bell, C 247
Bell, D 1325
Bell, MJ 1262
Bell, M 403
Bell, N 2893
Bell, R 247, 394, 1333
Bellando-Randone, S 1679
<table>
<thead>
<tr>
<th>Name</th>
<th>Pages/References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birdwell, K</td>
<td>1022</td>
</tr>
<tr>
<td>Birlik, M</td>
<td>825, 1472, 1496, 2521</td>
</tr>
<tr>
<td>Birmingham, JD</td>
<td>2782</td>
</tr>
<tr>
<td>Birnbaum, J</td>
<td>878</td>
</tr>
<tr>
<td>Birru Talabi, M</td>
<td>1306</td>
</tr>
<tr>
<td>Birt, J</td>
<td>597, 2539, 2549</td>
</tr>
<tr>
<td>Birt, R</td>
<td>1249</td>
</tr>
<tr>
<td>Birtane, M</td>
<td>2496</td>
</tr>
<tr>
<td>Bishop, E</td>
<td>863</td>
</tr>
<tr>
<td>Bishop, M</td>
<td>206</td>
</tr>
<tr>
<td>Bishop, P</td>
<td>52</td>
</tr>
<tr>
<td>Bisoendial, R</td>
<td>1792</td>
</tr>
<tr>
<td>Bistoni, O</td>
<td>571</td>
</tr>
<tr>
<td>Biswas, I</td>
<td>2774</td>
</tr>
<tr>
<td>Biswas, P</td>
<td>16L, 616, 617, 1427, 1440, 2966</td>
</tr>
<tr>
<td>Bitar, S</td>
<td>2835</td>
</tr>
<tr>
<td>Bitencourt, N</td>
<td>204, 1799</td>
</tr>
<tr>
<td>Bitoun, S</td>
<td>1463, 1823</td>
</tr>
<tr>
<td>Bitter, H</td>
<td>947</td>
</tr>
<tr>
<td>Bittinger, K</td>
<td>2935</td>
</tr>
<tr>
<td>Bitto, A</td>
<td>2984</td>
</tr>
<tr>
<td>Bitton, A</td>
<td>1796</td>
</tr>
<tr>
<td>Bizzaro, N</td>
<td>747</td>
</tr>
<tr>
<td>Bizzarro, S</td>
<td>492</td>
</tr>
<tr>
<td>Björk, A</td>
<td>566</td>
</tr>
<tr>
<td>Blachley, T</td>
<td>1422, 1423, 1815</td>
</tr>
<tr>
<td>Black, S</td>
<td>344, 473, 2951</td>
</tr>
<tr>
<td>Blackmore, D</td>
<td>1025</td>
</tr>
<tr>
<td>Blair, JPM</td>
<td>489</td>
</tr>
<tr>
<td>Blair, S</td>
<td>2572, 2578</td>
</tr>
<tr>
<td>Blake, M</td>
<td>1893</td>
</tr>
<tr>
<td>Blalock, SJ</td>
<td>1860</td>
</tr>
<tr>
<td>Blanchard, C</td>
<td>1619, 1620</td>
</tr>
<tr>
<td>Blanchard, F</td>
<td>1940, 2079</td>
</tr>
<tr>
<td>Blanchard-Delaunay, C</td>
<td>814</td>
</tr>
<tr>
<td>Blanco, A</td>
<td>1516, 2112, 2297, 2722, 2723</td>
</tr>
<tr>
<td>Blanco, FJ</td>
<td>179, 904, 1008, 1011, 1190, 1196, 1535, 1930, 1931, 1949, 2189, 2192, 2945</td>
</tr>
<tr>
<td>Blanco, P</td>
<td>2978</td>
</tr>
<tr>
<td>Blanco, R</td>
<td>260, 498, 644, 780, 816, 817, 1169, 1411, 1516, 1539, 1612, 1828, 2112, 2297, 2343, 2402, 2527, 2721, 2722, 2723, 2724, 2857</td>
</tr>
<tr>
<td>Blanco Madrigal, J</td>
<td>498</td>
</tr>
<tr>
<td>Blanco Madrigal, JM</td>
<td>529, 2343</td>
</tr>
<tr>
<td>Blaney Davidson, EN</td>
<td>1076, 2227</td>
</tr>
<tr>
<td>Blank, M</td>
<td>790</td>
</tr>
<tr>
<td>Blank, N</td>
<td>361</td>
</tr>
<tr>
<td>Blank, U</td>
<td>71</td>
</tr>
<tr>
<td>Blanken, A</td>
<td>239</td>
</tr>
<tr>
<td>Blanqué, R</td>
<td>497</td>
</tr>
<tr>
<td>Blanshan, N</td>
<td>2229</td>
</tr>
<tr>
<td>Blauvelt, A</td>
<td>2440</td>
</tr>
<tr>
<td>Blavnsfeldt, AB</td>
<td>2367</td>
</tr>
<tr>
<td>Blay, S</td>
<td>845</td>
</tr>
<tr>
<td>Blazekovic, A</td>
<td>2334</td>
</tr>
<tr>
<td>Blazer, A</td>
<td>689, 2813</td>
</tr>
<tr>
<td>Blazevic, I</td>
<td>2953</td>
</tr>
<tr>
<td>Blettery, M</td>
<td>226</td>
</tr>
<tr>
<td>Bley, T</td>
<td>783</td>
</tr>
<tr>
<td>Blicharski, T</td>
<td>1193</td>
</tr>
<tr>
<td>Bliddal, H</td>
<td>1188, 1196</td>
</tr>
<tr>
<td>Blijdorp, I</td>
<td>2801</td>
</tr>
<tr>
<td>Bliska, J</td>
<td>942</td>
</tr>
<tr>
<td>Blitz, JR</td>
<td>2321</td>
</tr>
<tr>
<td>Blobel, C</td>
<td>1833</td>
</tr>
<tr>
<td>Block, JA</td>
<td>191, 1353, 2264</td>
</tr>
<tr>
<td>Block, JA</td>
<td>347, 1084, 1101, 1239, 1602, 2824, 2953</td>
</tr>
<tr>
<td>Block, L</td>
<td>2261</td>
</tr>
<tr>
<td>Blockmans, D</td>
<td>783, 796, 893</td>
</tr>
<tr>
<td>Bloem, JL</td>
<td>2208</td>
</tr>
<tr>
<td>Blokland, SLM</td>
<td>553, 2830, 2872</td>
</tr>
<tr>
<td>Blom, AB</td>
<td>903, 1074, 1934, 2227</td>
</tr>
<tr>
<td>Bloom, J</td>
<td>379</td>
</tr>
<tr>
<td>Blough, P</td>
<td>2577</td>
</tr>
<tr>
<td>Blu, A</td>
<td>2008</td>
</tr>
<tr>
<td>Blue, M</td>
<td>12L</td>
</tr>
<tr>
<td>Bluemke, DA</td>
<td>263, 820</td>
</tr>
<tr>
<td>Blüml, S</td>
<td>63, 1338, 2864</td>
</tr>
<tr>
<td>Błyszczuk, P</td>
<td>1718, 1926, 2700</td>
</tr>
<tr>
<td>Bobic, S</td>
<td>2583</td>
</tr>
<tr>
<td>Boccassini, L</td>
<td>2965</td>
</tr>
<tr>
<td>Bock, C</td>
<td>2709</td>
</tr>
<tr>
<td>Bockenholt, U</td>
<td>2251</td>
</tr>
<tr>
<td>Boddi, M</td>
<td>1679</td>
</tr>
<tr>
<td>Bodick, N</td>
<td>934</td>
</tr>
<tr>
<td>Bodur, H</td>
<td>2496</td>
</tr>
<tr>
<td>Body, JJ</td>
<td>320</td>
</tr>
<tr>
<td>Boehm, M</td>
<td>939, 1166</td>
</tr>
<tr>
<td>Boehncke, WH</td>
<td>2530, 2878</td>
</tr>
<tr>
<td>Boehnlein, M</td>
<td>2451</td>
</tr>
<tr>
<td>Boer, AC</td>
<td>1356</td>
</tr>
<tr>
<td>Boers, M</td>
<td>1901, 2365</td>
</tr>
<tr>
<td>Boes, ML</td>
<td>1912</td>
</tr>
<tr>
<td>Boesen, M</td>
<td>236, 248</td>
</tr>
<tr>
<td>Boeters, DM</td>
<td>1386, 1993</td>
</tr>
<tr>
<td>Name</td>
<td>Pages</td>
</tr>
<tr>
<td>---------------------------</td>
<td>----------------</td>
</tr>
<tr>
<td>Budde, P</td>
<td>695, 722, 875, 1182, 1722</td>
</tr>
<tr>
<td>Budgell, B</td>
<td>1851</td>
</tr>
<tr>
<td>Budinger, GRS</td>
<td>174</td>
</tr>
<tr>
<td>Budoff, M</td>
<td>867, 2417</td>
</tr>
<tr>
<td>Budziakowska, M</td>
<td>721</td>
</tr>
<tr>
<td>Budgell, B</td>
<td>1851</td>
</tr>
<tr>
<td>Budiger, GRS</td>
<td>174</td>
</tr>
<tr>
<td>Budoff, M</td>
<td>867, 2417</td>
</tr>
<tr>
<td>Budziakowska, M</td>
<td>721</td>
</tr>
<tr>
<td>Bugdayci, ND</td>
<td>2496</td>
</tr>
<tr>
<td>Bugdayli, K</td>
<td>1168</td>
</tr>
<tr>
<td>Bugrofsky, R</td>
<td>833</td>
</tr>
<tr>
<td>Bui, L</td>
<td>1898</td>
</tr>
<tr>
<td>Bujold, E</td>
<td>1293</td>
</tr>
<tr>
<td>Bujor, A</td>
<td>539</td>
</tr>
<tr>
<td>Bukhari, M</td>
<td>2397</td>
</tr>
<tr>
<td>Bukiri, H</td>
<td>1096</td>
</tr>
<tr>
<td>Bukowski, JF</td>
<td>587, 2273, 2455, 2802</td>
</tr>
<tr>
<td>Bukulmez, H</td>
<td>2018</td>
</tr>
<tr>
<td>Bulhoes, CN</td>
<td>524</td>
</tr>
<tr>
<td>Bulleri, A</td>
<td>1488</td>
</tr>
<tr>
<td>Bulloch, A</td>
<td>121</td>
</tr>
<tr>
<td>Bumbacea, D</td>
<td>997</td>
</tr>
<tr>
<td>Bundy, D</td>
<td>1813</td>
</tr>
<tr>
<td>Burgmeister, L</td>
<td>1847</td>
</tr>
<tr>
<td>Burges, R</td>
<td>1191, 2226</td>
</tr>
<tr>
<td>Burghardt, AJ</td>
<td>1996, 2038</td>
</tr>
<tr>
<td>Burguera, EF</td>
<td>1949</td>
</tr>
<tr>
<td>Burke, J</td>
<td>503</td>
</tr>
<tr>
<td>Burkhardt, H</td>
<td>1825, 2973</td>
</tr>
<tr>
<td>Burkly, L</td>
<td>45, 663</td>
</tr>
<tr>
<td>Burlingame, R</td>
<td>2170</td>
</tr>
<tr>
<td>Burmester, GR</td>
<td>39, 605, 616, 617, 1072, 1418, 1427, 1904, 2006, 2007, 2352, 2463, 2470, 2471, 2481, 2482, 2498, 2967, 2973</td>
</tr>
<tr>
<td>Burns, J</td>
<td>2937</td>
</tr>
<tr>
<td>Burns, L</td>
<td>1035, 2891</td>
</tr>
<tr>
<td>Burr, AM</td>
<td>1195</td>
</tr>
<tr>
<td>Burris, T</td>
<td>1924</td>
</tr>
<tr>
<td>Bursill, D</td>
<td>2064</td>
</tr>
<tr>
<td>Burton, BS</td>
<td>2257</td>
</tr>
<tr>
<td>Buschiazzo, E</td>
<td>1007, 1564</td>
</tr>
<tr>
<td>Bush, E</td>
<td>2693, 2694</td>
</tr>
<tr>
<td>Busquets, N</td>
<td>1467</td>
</tr>
<tr>
<td>Bustabad, S</td>
<td>40, 1383, 2277, 2284</td>
</tr>
<tr>
<td>Butanis, A</td>
<td>1255, 2255</td>
</tr>
<tr>
<td>Butany, J</td>
<td>1592</td>
</tr>
<tr>
<td>Butbul Aviel, Y</td>
<td>375</td>
</tr>
<tr>
<td>Butendieck, R</td>
<td>1990</td>
</tr>
<tr>
<td>Butler, M</td>
<td>2528</td>
</tr>
<tr>
<td>Butler, P</td>
<td>1688</td>
</tr>
<tr>
<td>Butler, PW</td>
<td>323</td>
</tr>
<tr>
<td>Butler, P</td>
<td>1887</td>
</tr>
<tr>
<td>Butler, R</td>
<td>1755</td>
</tr>
<tr>
<td>Butt, A</td>
<td>428</td>
</tr>
<tr>
<td>Buttgereit, F</td>
<td>1946, 2388</td>
</tr>
<tr>
<td>Buyon, JP</td>
<td>164, 673, 680, 681, 689, 719, 1061, 1482, 1786, 1843, 2580, 2581, 2757, 2813, 2815, 2957</td>
</tr>
<tr>
<td>Bye, A</td>
<td>2968</td>
</tr>
<tr>
<td>Bykerk, VP</td>
<td>241, 443, 445, 461, 1241, 1393, 1405, 1406, 1814, 2390, 2391, 2827, 2955</td>
</tr>
<tr>
<td>Bykowska-Sochacka, M</td>
<td>2697</td>
</tr>
<tr>
<td>Byram, K</td>
<td>1764</td>
</tr>
<tr>
<td>Byrd, B</td>
<td>1069</td>
</tr>
<tr>
<td>Byrjalsen, I</td>
<td>1, 1L, 465, 2207, 2212</td>
</tr>
<tr>
<td>Byrne, K</td>
<td>282, 2840</td>
</tr>
<tr>
<td>Byrne, R</td>
<td>966</td>
</tr>
<tr>
<td>Byun Robinson, A</td>
<td>2308</td>
</tr>
<tr>
<td>C</td>
<td></td>
</tr>
<tr>
<td>C. Guthrie, L</td>
<td>1351</td>
</tr>
<tr>
<td>Cabacungan, R</td>
<td>309, 310</td>
</tr>
<tr>
<td>Cabello, A</td>
<td>1939</td>
</tr>
<tr>
<td>Cabez, A</td>
<td>335</td>
</tr>
<tr>
<td>Cabral, AR</td>
<td>16</td>
</tr>
<tr>
<td>Cabral, D</td>
<td>1288, 1289, 2345</td>
</tr>
<tr>
<td>Cabral-Marques, O</td>
<td>84</td>
</tr>
<tr>
<td>Cabrera-Villalba, S</td>
<td>480</td>
</tr>
<tr>
<td>Cacoub, P</td>
<td>71, 281, 894, 1183, 1734, 1746, 2716, 2717, 2736, 2775, 2904</td>
</tr>
<tr>
<td>Cadeg, R</td>
<td>1773</td>
</tr>
<tr>
<td>Cadzow, M</td>
<td>1104</td>
</tr>
<tr>
<td>Caeiro, F</td>
<td>572, 2008, 2237, 2924</td>
</tr>
<tr>
<td>Cai, A</td>
<td>1428</td>
</tr>
<tr>
<td>Cai, G</td>
<td>1850</td>
</tr>
<tr>
<td>Cai, G</td>
<td>729, 756, 775, 1707, 2931</td>
</tr>
<tr>
<td>Cai, Y</td>
<td>2436</td>
</tr>
<tr>
<td>Cai, Z</td>
<td>2219</td>
</tr>
<tr>
<td>Caiello, I</td>
<td>2331, 2332, 2340</td>
</tr>
<tr>
<td>Cailotto, F</td>
<td>1945</td>
</tr>
<tr>
<td>Cairns, E</td>
<td>1325</td>
</tr>
<tr>
<td>Calabrese, C</td>
<td>116, 1156</td>
</tr>
<tr>
<td>Calabrese, LH</td>
<td>112, 116, 1156, 2393, 2726, 2731, 2741</td>
</tr>
</tbody>
</table>
Calamia, K 1990
Calamia, V 1190
Calder, P 913
Calderon, DS 1001, 1513, 1827
Calderón Goercke, M 260, 817
Caldito, G 1687
Caldron, P 1686
Calhoun, V 206
Calich, AL 1757
Ç
Çalışkan, A 305
Callahan, LF 314, 846, 1053, 2611, 2766, 2819
Callejas-Rubio, JL 2722, 2723
Calò, E 1075
Calvet, G 276
Calvo, G 1535
Calvo, I 1169, 2297, 2855, 2856, 2857
Calvo, V 1516
Calvo Aranda, E 2062
Calvo Begueria, E 209
Calvo Penades, I 2859
Calvo Zorrilla, I 529
Calvo-Alen, J 780, 1400, 1587, 1588, 1612, 2724
Calvo-Gutierrez, J 391
Calvo-Río, V 260, 780, 817, 1169, 2112, 2297, 2721, 2722, 2723, 2857
Calza, S 1300
Camacho, M 1190
Camargo, C 837
Camargo, CZ 1691
Cambier, J 1663
Cambry, N 2023
Cameron, K 2823
Camp, HS 505, 1904
Campbell, J 1191, 2225, 2226
Campbell, K 1478
Campbell, PL 971, 1705
Campbell, W 994, 996, 1231
Campillo, S 2952
Campillo-Gimenez, L 2083
Campochiaro, C 770, 1292
Campos, A 2057
Campos, J 863
Campos, J 1518
Campos, LMA 1302
Campos Fernandez, C 2277, 2499
Camps, M 2565
Can, G 542, 825, 1455, 1472, 1496, 1514, 1534, 2521
Canaud, G 2932
Canavatchel, AR 2196
Canessa, P 233
Canestrari, G 741, 742
Cañete, J 480, 864, 2490
Cañete, JD 179, 335, 460, 639, 1416, 2525
Canna, S 938, 1895, 2347, 2772
Cannella, AC 101, 110
Cannella, AC 101, 110
Cannon, G 135, 433, 907, 908, 909, 1036, 1039, 1042, 1342, 1357, 2377, 2378, 2448, 2893
Canovas Olmos, I 684, 1221, 1224, 2003
Cantabrana-Alutiz, A 40
Cantalejo, M 1226
Cantarini, L 365
Cantatore, FP 1292
Cantor, SB 1052
Cantrell, J 926
Canzoni, M 2239
Cao, Y 1883
Ç
Çapa, F 1514
C
Capar, S 1514
Caparbo, VF 1268, 1570, 1961
Capdevila, O 2620
Capila, I 764, 1019
Caplan, L 135, 1036, 1357, 2377, 2378, 2893, 2894, 2915
Caporali, R 1292
Cappa, V 1300
Cappelleri, JC 596, 1246
Cappelli, L 116, 1103, 1363, 2902
Cappucci, A 269
Caprioli, M 1969
Capuccio, AM 1645
Caracciolo, JA 360, 1359, 1360
Caracuel, MA 2722, 2723
Carames, B 904, 1931
Carbonell, J 2621
Carcaud, C 2597
Cardamone, G 650
Cardiel, M 178, 1654
Cardiel, MH 2924
Cardillo, T 511
Cardoso, A 502, 513, 2219
Carette, S 784, 785, 789, 821, 1760, 1767, 1774, 1849, 2120
Caricchio, R 1786, 1919
Carini, C 1292
Carlesso, G 561
Carlesso, L 859
Carlevaris, L Sr. 269
Carlier, P 5L
Carlin, J 19, 951
Carlsson Almlöf, J 2654
Carlsten, H 1413
Carlucci, P 899
Carmona, FD 2343
Carmona, L 1140, 1361, 2379, 2515
Carmona-Rivera, C 290, 292
Carnago, L 1797
Cameiro, S 634
Carns, MA 730, 919, 946, 1730, 2930
Caro, XJ 156
Carpenter, DM 1860
Carr, A 874
Carranza Leon, D 720
Carrara, C 2860
Carrara, G 781, 2055
Carrasco, R 2272
Carrasco Cubero, C 2721, 2722, 2723
Carrasco-cubero, M 2402
Carreia, P 498, 1683, 2662
Carrier, M 15
Carrier, ME 2049, 2695
Carrino, JA 594
Carrion, O 2062
Carroll, R 712
Carron, P 253, 2881
Carruthers, M 1099, 2127
Carsons, SE 876, 964, 1770, 1784
Carter, JD 2758
Carthron, D 846
Cartwright, A 913
Carubbi, F 571
Caruso, A 790
carvajal Alegria, G 574
Carvalho, P 91
Casado, E 320
Casado, G 269, 278
Casado Burgos, E 1467
Casal-Dominguez, M 2131
Casasola, J 456, 457
Cascino, M 1600, 1752
Casciola-Rosen, L 2157
Case, S 1242
Casella, R 735
Caselli, G 408, 955
Casey, C 712
Cashman, K 2974
Casian, A 1773
Casillas, M 502
Caspi, D 1648
Castagnola, E 2333
Castañeda, S 498, 780, 816, 1400, 1411, 2343, 2515
Castano, I 793
Castano, JP 2656
Castelar-Pinheiro, G 276, 350, 1340, 2063, 2846, 2950
Castelino, FV 729, 1922, 2665
Castellano Cuesta, JA 684
Castellanos-Moreira, R Sr. 480, 2490
Castellvi, I 1587, 2094, 2402
Castelvi, I 2724
Castiglioni, A 91
Castillo, R 636
Castillo Gallego, MC 2021
Castrejón, I 191, 347, 1101, 1351, 1353, 2247, 2264
Castro, C 64, 905
Castro-Hernández, J 40
Castro-Viñuelas, R 58, 1930
Catalan Pellet, A 2237
Catalina, M 296, 2609, 2818
Catanoso, M 815
Catay, E 2021
Cathebras, P 797, 814
Catlett, I 503, 514
Catoggio, C 1645
Catoggio, LJ 1772, 2924
Catrina, AI 2869
Catrina, AI 65, 486, 970, 2919
Catrina, SB 970
Cauchie, M 705
Cauley, JA 2199
Causevic, H 567
Cauvin, A 497
Cavagna, L 350, 2950
Cavagnoli, R 2950
Cavalcanti, F 2924
Cavalleri, M 231
Cavalin, C 120
Cavallasca, J 1645
Cavazza, A 790
Cavazza, M 1872
Cavazzana, I 686, 2166, 2650
Cavillon, E 269
Cazares, L 2021, 2055
Cealey, E 1336, 2926
Ceballos, MF 572
Cebon, J 1173
Ceccarelli, F 1300
Cecchettini, A 556
Cecchi, I 5, 391, 1466, 2655, 2656, 2759, 2764
Cecchin, V 2314
Cefle, A 542, 1455, 1472, 1534
Cejas, P 2468
Celik, AF 2748
Celik, AM 803
Celis, R 460, 1416
Cella, D 2252
Cellucci, T 2317, 2952
Cen, L 2795, 2796
Centola, M 2362
Cepeda-Perez, AS 2414
Cerci, P 2728
Cerda, O 269
Cerda, OL 1007, 1564, 2551, 2554
Cerejo, R 2726
Ceribelli, A 650, 1969
Cerón, C 2489
Cerosaletti, K 2644
Cerrahoglu, L 2204
Cerritos, S 196
Cervantes Pérez, EC 498
Cervera, R 12, 15, 1622
Cesak, M 1692
Cesak, P 1692, 1694, 2153, 2154
Cesaroni, M 80
Cesselli, D 2874
Cesta, A 432, 470, 1475, 2383, 2908
Cetin, P 825, 1514
Cevallos, R 1754
Cevallos, S 1094
Cevik, R 2204
Cevirgen, D 2748
Cha, HS 2088, 2733
Chacón-Díaz, R 1654, 2924
Chacon-Garcia, J 211, 998, 999
Chadha, A 1686
Chadha-Boreham, H 2683
Chae, JJ 942
Chae, JN 975, 1434
Chafey, P 769
Chai, JY 2088, 2733
Chaichian, Y 829, 986, 1290, 1291
Chaigne, B 769, 1070, 2888
Chaillet, N 1293
Chakraborty, D 2928
Chakravarty, E 1657, 1658, 1809, 1811, 1841, 2600, 2647, 2820, 2977
Chakravarty, SD 598
Chalhoub, N 1650
Challa, D 792
Chalmers, S 29, 1837, 2561
Chalmeta Verdejo, I 684, 1221, 1224, 2003
Chalom, E 2271
Chalouhi El-Khoury, E 2445
Chambenoit, O 1525
Chambers, CD 1309, 1313, 1785
Chambers, M 1929
Champiat, S 1741
Chan, A 2699
Chan, A 1929
Chan, B 1527
Chan, D 291
Chan, EKH 630, 1530
Chan, EKH 1531
Chan, G 16L
Chan, G 2574
Chan, GYL 1702
Chan, HJK 2574
Chan, JHS 462, 1577
Chan, J 612, 883, 2972
Chan, KL 523
Chan, KW 2574
Chan, LHK 2323
Chandler, H 59, 1937
Chandra, T 673
Chen, R 828
Chen, S 985, 1628, 2230
Chen, S 1192
Chen, S 1251
Chen, SC 1114
Chen, S 1192
Chen, S 1251
Chen, SC 1114
Chen, S 1192, 1202, 1211
Chen, WS 268
Chen, WM 2826
Chen, W 1311
Chen, X 175, 183, 2825
Chen, Y 937, 2326, 2338
Chen, YF 2359
Chen, YH 350, 2950
Chen, YC Sr. 325, 1114, 2014
Chen, Y 2705
Chen, YF 2219
Chen, Z 2146
Chen, Z 710
Cheng, B 2472
Cheng, CW 711
Cheng, K 2180
Cheng, L 503
Cheng, S 994, 996
Cheng, S 517
CHENG, TH 1903, 2244, 2545
Cheon, GJ 2025
Cheon, YH 1332
Cheong, KM 1145
Cheong, SY 1470, 2446, 2467
Cheriyanth, P 1146, 2989
Chernoff, D 1900
Chessa, D 638
Chetaille, AL 1027
Chetal, K 2825
Cheu, M 1752
Cheung, F 1024, 2337
Cheung, M 38
Cheung, PMP 2625
Chevalier, P 1119
Chevret, S 810
Chevrier, M 6L, 80
Chew, CS 865
Chhabra, A 2292
Chhana, A 2896
Chiang, HH 2052
Chiapparoli, I 2166
Chiba, K 1995
Chiba, T 1179
Chische, D 2224
Chiche, L 2828
Chichotky, Y 360
Chicoine, A 2659
Chien, HC 1866
Chien, J 315
Chieze, R 2170
Chighizola, CB 1292
Chijioke, A 2069
Chik, C 1781
Chilaka, S 1948
Chin, C 1090
Chinchilla, S 1115, 1133, 2068
Chinenov, Y 1833
Ching, D 2470, 2506
Chini, E 1724
Chino, K 2017
Chino, K 853
Chinque, H 1713
Chiocchit, G 1579, 1580
Chiostri, M 1679
Chiou, E 2575, 2641
Chiou, MJ 1314
Chipman, J 2143
Chipping, J 868
Chiriboga, L 670
Chirivi, RGS 293
Chisholm, D 2799
Chitnis, M 1556
Chiu, H 430
Chiu, I 1262
Chizzolini, C 41
Chmiel, JS 936, 2188
Cho, CS 716, 2708
Cho, E 1153
Cho, J 2625
Cho, NH 1135
Cho, SK 1016, 2517
Cho, YN 1065
Choate, E 1391
Chock, YP 1611
Choe, JY 139, 557, 2074, 2466
Choi, A 2896
Choi, CB 1016
Choi, D 2689
Choi, D 308
Choi, HK 328, 837, 895, 1104, 1130, 1131, 1610, 1789, 1964, 2067, 2077, 2614, 2921, 2990
Choi, J 2072, 2074
Choi, JY 2145, 2794
Couvoisier, D 2910
Couzy, L 2597
Covarrubias-Cobos, JA 596, 620
Cove-Smith, A 43, 685, 2624, 2634
Cowan, H 968
Cox, G 1760
Cox, T 2321
Coyle, C 1967
Cozzi, F 1683, 2984
Craft, JE 1661
Craig, E 2248
Craig, G 1250
Craven, A 2737
Cravens, EN 2707
Cravo, AR 611
Crego, K 288
Crego, D 923
Crego, DB 218
Cremin, K 1104, 1514
Cremone, G 871
Cren, JB 2842
Crescentini, F 791, 815
Crestani, B 814
Crimston-Smith, L 1231
Criscione-Schreiber, L 89, 910, 911, 1797, 2165
Criswell, LA 229, 230, 919, 946, 983, 1085, 1806, 2930
Crittenden, DB 319
Croci, S 790, 1075
Crofford, L 317, 712, 1689, 2233, 2612
Crofford, LJ 2234
Croft, AP 863, 1339
Croft, J 1004
Croia, C 2706
Croker, B 1832
Cron, RQ 641, 1897, 2320
Cronstein, B 64, 905, 1218, 1932, 1939
Crooks, J 1249
Crooks, J 525
Crosset, M 2187
Cross, MB 2853
Crotti, T 1899
Crouthamel, M 143
Crow, C 2237
Crow, MK 1668
Crow, YJ 2348
Crow-Hercher, R 1298, 1308
Crowson, CS 13, 32, 147, 777, 792, 794, 812, 813, 1032, 1109, 1160, 1161, 1168, 1695, 1749, 1750, 1802, 1816, 1819, 1959, 2105, 2175, 2389, 2880
Crowther, M 15
Cruz, A 2038
Cruz, J 2722
Cruz, J 2297
Cruz Caparrós, G 209
Cruz-Bautista, I 1492
Cruz-Pérez, F 442
Cruz-Rojas, Y 543, 1965
Cruzat, V 360
Cseuz, R 1909
Csuka, ME 1686
Cu, D 34
Cuadrado, MJ 2655, 2656, 2759, 2764
Cucheron, M 787
Cucho-Venegas, M 450, 687, 1378
Č
Čučnik, S 704, 2719
Cuda, C 29, 174, 405, 406, 1709, 1835, 2576
Cudrici, C 2640
Cuellar, C 2116
Cuende, E 1535, 2284
Cuende Quintana, E 1738
Cuervo, A 179, 460, 480, 639, 1416, 2490
Cuevas-Orta, E 1445, 2360
Cuff, C 2568
Cui, C 181
Cui, H 971
Cui, J 172, 1021
Cui, L 1211
Cui, ZH 2560, 2562
Cuitino, L 2643
Cummiford, C 2753, 2912
Cunha, J 2535
Cupps, T 820
Curbelo, R 2515
Cure, C 2837
Curiale, C 356
Curiel, R 2137, 2341
Curiel, RV 1274
Curram, J 732, 2983
Curran, J 2317
Curran, ML 852, 1275, 2252
Curry, M 17, 1318
Curti, A 1645
Curtis, JR 16L
<table>
<thead>
<tr>
<th>Name</th>
<th>Page Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dasic, G</td>
<td>1252</td>
</tr>
<tr>
<td>Dastmalchi, M</td>
<td>2167</td>
</tr>
<tr>
<td>Datto, M</td>
<td>2165</td>
</tr>
<tr>
<td>Daumas, A</td>
<td>796</td>
</tr>
<tr>
<td>Dave, A</td>
<td>1096</td>
</tr>
<tr>
<td>Dave, M</td>
<td>1254</td>
</tr>
<tr>
<td>Davelaar, N</td>
<td>1747, 1792</td>
</tr>
<tr>
<td>Davenport, EK</td>
<td>602</td>
</tr>
<tr>
<td>Davey, JR</td>
<td>2235, 2236</td>
</tr>
<tr>
<td>Davey, R</td>
<td>1231</td>
</tr>
<tr>
<td>Davi, S</td>
<td>2332</td>
</tr>
<tr>
<td>Davidson, A</td>
<td>719, 2570, 2659</td>
</tr>
<tr>
<td>Davidson, N</td>
<td>1615</td>
</tr>
<tr>
<td>Davidson, P</td>
<td>1260</td>
</tr>
<tr>
<td>Davies, A</td>
<td>1567</td>
</tr>
<tr>
<td>Davies, B</td>
<td>95</td>
</tr>
<tr>
<td>Davies, K</td>
<td>874</td>
</tr>
<tr>
<td>Davies, K</td>
<td>565, 1500</td>
</tr>
<tr>
<td>Davies, R</td>
<td>1073</td>
</tr>
<tr>
<td>Davignon, JL</td>
<td>287, 902</td>
</tr>
<tr>
<td>Davin, S</td>
<td>1873, 1976, 1978</td>
</tr>
<tr>
<td>Davis, A</td>
<td>1103</td>
</tr>
<tr>
<td>Davis, AM</td>
<td>2810</td>
</tr>
<tr>
<td>Davis, BN</td>
<td>2418</td>
</tr>
<tr>
<td>Davis, JM III</td>
<td>32, 1032, 1819</td>
</tr>
<tr>
<td>Davis, J</td>
<td>2944</td>
</tr>
<tr>
<td>Davis, L</td>
<td>1036</td>
</tr>
<tr>
<td>Davis, M</td>
<td>899</td>
</tr>
<tr>
<td>Davis, RL</td>
<td>483</td>
</tr>
<tr>
<td>Davis, WE</td>
<td>407, 721</td>
</tr>
<tr>
<td>Dawoud, N</td>
<td>1569</td>
</tr>
<tr>
<td>Dawson, T</td>
<td>1231</td>
</tr>
<tr>
<td>Day, G</td>
<td>1051</td>
</tr>
<tr>
<td>de Agustín, JJ</td>
<td>1467</td>
</tr>
<tr>
<td>De Angelis, R</td>
<td>1608</td>
</tr>
<tr>
<td>De Avila, J</td>
<td>640</td>
</tr>
<tr>
<td>De Benedetti, F</td>
<td>376, 1894, 2270, 2331, 2332, 2333, 2339, 2340</td>
</tr>
<tr>
<td>de Bock, E</td>
<td>352</td>
</tr>
<tr>
<td>de Boer, S</td>
<td>1901</td>
</tr>
<tr>
<td>de Boysson, H</td>
<td>796</td>
</tr>
<tr>
<td>de Bruin, F</td>
<td>582</td>
</tr>
<tr>
<td>de Brum-Fernandes, AJ</td>
<td>1570, 2023</td>
</tr>
<tr>
<td>De Cock, D</td>
<td>141, 366, 547, 1820, 2287, 2439</td>
</tr>
<tr>
<td>De Dios, JR</td>
<td>1448, 1516</td>
</tr>
<tr>
<td>De Escalante Yangüela, B</td>
<td>209</td>
</tr>
<tr>
<td>de Graaf, K</td>
<td>2332</td>
</tr>
<tr>
<td>De Groote, P</td>
<td>1685</td>
</tr>
<tr>
<td>de Gruijter, J</td>
<td>1827</td>
</tr>
<tr>
<td>de Guzman, MM</td>
<td>17, 378</td>
</tr>
<tr>
<td>De Haas, V</td>
<td>1896</td>
</tr>
<tr>
<td>de Hooge, M</td>
<td>253, 587, 1831, 2802</td>
</tr>
<tr>
<td>De Jager, J</td>
<td>1354</td>
</tr>
<tr>
<td>de Jong, A1L</td>
<td>2779</td>
</tr>
<tr>
<td>de Jong, EMGJ</td>
<td>1729</td>
</tr>
<tr>
<td>de Jong, J</td>
<td>1831, 2801</td>
</tr>
<tr>
<td>de Jong, Y</td>
<td>225</td>
</tr>
<tr>
<td>De Keyser, F</td>
<td>752</td>
</tr>
<tr>
<td>de Koning, A</td>
<td>582, 646, 1831</td>
</tr>
<tr>
<td>de Kwant, J</td>
<td>1108</td>
</tr>
<tr>
<td>de la Fuente, D</td>
<td>1467</td>
</tr>
<tr>
<td>de la Loge, C</td>
<td>352</td>
</tr>
<tr>
<td>de la Morena, I</td>
<td>2724</td>
</tr>
<tr>
<td>De la Red, G</td>
<td>209</td>
</tr>
<tr>
<td>De la Rubia Navarro, M</td>
<td>684, 1221, 1224, 2003</td>
</tr>
<tr>
<td>De La Sota, M</td>
<td>269</td>
</tr>
<tr>
<td>de la Torre, I</td>
<td>1821</td>
</tr>
<tr>
<td>de la Vega, M</td>
<td>278, 541</td>
</tr>
<tr>
<td>de La Vega, MC</td>
<td>269</td>
</tr>
<tr>
<td>de Langhe, E</td>
<td>41, 1683</td>
</tr>
<tr>
<td>de Leon, E</td>
<td>1255, 2255</td>
</tr>
<tr>
<td>de Leonardis, F</td>
<td>418</td>
</tr>
<tr>
<td>De Lorenzis, E</td>
<td>741, 742</td>
</tr>
<tr>
<td>De Lorenzo, R</td>
<td>2131</td>
</tr>
<tr>
<td>De Miguel, E</td>
<td>261, 654, 781, 793, 1471, 1506, 1533, 1535, 2021, 2499</td>
</tr>
<tr>
<td>de Min, C</td>
<td>2332</td>
</tr>
<tr>
<td>De Mits, S</td>
<td>253</td>
</tr>
<tr>
<td>de Moel, E</td>
<td>1402, 2916</td>
</tr>
<tr>
<td>de Moreuil, C</td>
<td>814, 1754, 1779</td>
</tr>
<tr>
<td>de Mutsert, R</td>
<td>2209</td>
</tr>
<tr>
<td>de Pablo, P</td>
<td>913</td>
</tr>
<tr>
<td>De Pauw, M</td>
<td>752</td>
</tr>
<tr>
<td>De Peretti, F</td>
<td>1216</td>
</tr>
<tr>
<td>de Peyrecave, N</td>
<td>1515</td>
</tr>
<tr>
<td>De Ranieri, D</td>
<td>2018, 2306, 2319</td>
</tr>
<tr>
<td>de Roock, S</td>
<td>1896</td>
</tr>
<tr>
<td>de Rooij, ENM</td>
<td>890</td>
</tr>
<tr>
<td>De Rycke, Y</td>
<td>2394</td>
</tr>
<tr>
<td>De Santis, M</td>
<td>650, 1969</td>
</tr>
<tr>
<td>De Smet, M</td>
<td>1189</td>
</tr>
<tr>
<td>de Thurah, A</td>
<td>1802, 2367</td>
</tr>
<tr>
<td>de Toro, FJ</td>
<td>2619</td>
</tr>
<tr>
<td>De Toro Santos, FJ</td>
<td>1930</td>
</tr>
<tr>
<td>De Vera, M</td>
<td>1231</td>
</tr>
<tr>
<td>De Vera, MA</td>
<td>1316</td>
</tr>
</tbody>
</table>
De Vicente, M 209
De Vita, S 877, 1300, 1489, 2874
de Vlam, K 596, 614
de Vries, N 1847
de Vries-Bouwstra, J 760
de Vries-Bouwstra, JK 1693
De Waure, C 742
De Wilde, K 67
de Winter, J 581, 1831
de Wit, M 1257
de Zoysa, J 1104
Deakin, C 2336, 2341, 2342
Deane, KD 478, 483, 484, 490, 990, 1055, 1663, 1971, 2914, 2915, 2918
DeBandt, M 226
Debusschere, K 1915
Dechant, C 1184
Decker, M 1781
Decker, P 120, 866, 2701
Decruy, T 1582
Decuman, S 752
Dedeoglu, F 361
Deeb, M 1592
Dees, C 753, 826, 1706, 1714, 1716, 2700
Defrance, T 2348
Degroof, A 41
Degun, R 361
de Guzman, M 1318
DeHaan Ph.D., W 2091
Dehlin, M 2080
Dehoorne, J 2273
DeHoratius, RJ 1057
Dejaco, C 259, 781, 783, 2646, 2877
DeJager, W 1657, 1658, 2600, 2820, 2977
Dejene, S 526
Dekkers, J 492
Dektiarev, I 1144
del Alcazar, D 2420
del Campo-Pérez, V 1587
Del Gaizo, V 1254, 2282
Del Galdo, F 734, 1683, 2669, 2984
Del Giorno, J 1854
Del Pino-Montes, J 2277
del Rincon, I 869, 2358, 2911
Del Rio, L 1448
del Río, T 159, 2129
del Río-Moreno, M 2656
Delaval, L 796, 797
Delaval, P 1758, 2736
Delay, L 2228
Delbrel, X 1779
DeLeon, J 964
Deleuran, B 642, 1077
Deleuze, JF 1579
Delev, N 886, 887
Delgado, C 498
Delgado Dominguez, CJ 998
Delicha, EM 3L, 1539
Deligny, C 226
Del'Orso, S 899
Della Rossa, A 255
Dellaripa, P 2384
Dellaripa, PF 2136, 2677
Dellavance, A 2121
Delle Sedie, A 1373, 1488, 2020, 2055, 2239
Delli, K 2943
Delnay, N 2995
Delorme, P 1197, 1208
Delzell, E 828
Demarchi, J 2237
DeMarco, AG 206
DeMarco, P 206
DeMartino, J 25
DeMartino, JA 1060
DeMasi, R 16L, 424, 495, 522, 533, 884, 1397, 1906
Dematte, J 1696
Demehri, S 242
Demerouti, E 2686
Demetrio, R 2112, 2722, 2723, 2857
Demetrio-Pablo, R 1169, 2297
Demir, S 1174, 2110
Demirhan, O 2729
Demizu, S 1319
Demoruelle, MK 478, 483, 484, 490, 990, 1971, 2914, 2915, 2918
Den Broeder, AA 1205, 2438, 2779, 2832
Den Broeder, AA 421, 422
den Broeder, N 421, 422
den Hollander, W 903, 906
Deng, X 1877
Deng, Z 2773
Denio, A 1100
Denis, L 1779
Denisova, R 386, 2279, 2280
Doody, KM 1456
Dooley, MA 885, 1606
Doorenspleet, ME 1847
Dorais, M 1197
Dore, RK 1890
Dörfler, A 2024
Doria, A 1292, 2590
Dorman, CW 2229
Dorris, E 288
Dorschner, JM 9L, 1662, 2657
Dos Santos, FMM 723
Dossier, A 2775
Dostál, C 6
Douillet, A 1823
Doucet, J 576, 875
Douchet, I 2978
Dougados, M 512, 513, 584, 587, 588, 589, 590, 591, 592, 593, 646, 1442, 1504, 1515, 1521, 1542, 1545, 2415, 2497, 2502, 2505, 2512, 2787, 2802, 2806, 2967
Doughem, K 1505
Douglas, K 147
Douglas, K 1155
Douglass, W 2270, 2856
Douillard, C 1584
Douma, S 2357
Doumatay, A 919, 2930
Dove, D 1581
Dove, D 1915
Dover, SK 1124
Dow, ER 2866
Dowd, T 2148
Dowdy, S 2789
Dowle, S 2342
Downey, C 1100
Downey, L 2837
Doyle, A 345, 1992
Doyle, P 1099
Doyle, R 62
Doyle, RE 302, 387
Doyle, T 2384
Dozmorov, M 178
Drage, LA 1168
Dragone, L 1600
Drake, J 1105
Draper, T 921
Drellichman, G 1225
Drenkard, C 33, 354, 833, 844, 987, 2044, 2924
Dreyer, L 11L, 1541
Dreyfus, M 2762
Driban, JB 917, 931, 978, 2196, 2200, 2201, 2849, 2944, 2945
Driver, T 1098
Drogemoller, B 2345
Drouin, EE 949
Droz, N 343
Drude, B 2006
Drukman, I 1503
Druzin, M 1290, 1291
Drynda, S 1980
Du, Y 971, 1336, 2926
Dua, A 2161
Duan, R 2436
Duan, X 928, 2241, 2242
Duarte, C 2042
Duarte-Garcia, A 13
Dubey, D 1723, 1848
Dubois-Morell, S 1685
Dubost, JJ 873
Dubreuil, M 1536, 2524
Dubrovsky, A 54
Ducreux, J 41
Dudek, A 1909
Dudler, J 521, 2253
Dueckers, G 939
Duffau, P 2597
Duffield, S 2513, 2514
Duffy, CM 2289, 2317, 2952
Dufour, A 41
Dufrost, V 108
Duftner, C 259, 781, 783
Duga, S 650
Dulgeroglu, D 2204
Dumanic, M 61
Dumoitier, N 769
Dumonteil, S 814
Dumortier, H 561
Duncan, C 1948
Dunkel, J 2451
Dunlop, DD 2193, 2194, 2195, 2223, 2823
Dunlop-Thomas, CM 354, 844
Dunn, J 1709
Dunn, P 1349
Dunne, A 2900
Dunsmuir, R 661
Dunstan, R 675
Duong, D 2322
Dupont, R 2661
Dupont, S 497, 1189
Dupuy, C 1784
<table>
<thead>
<tr>
<th>Name</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eleftheriou, D</td>
<td>1283, 2959</td>
</tr>
<tr>
<td>Eleftherohorinou, H</td>
<td>2937</td>
</tr>
<tr>
<td>Elera-Fitzcarrald, C</td>
<td>450, 687, 1378</td>
</tr>
<tr>
<td>Elewaut, D</td>
<td>67, 253, 1582, 1915, 2714, 2881</td>
</tr>
<tr>
<td>Elfishawi, M</td>
<td>1109</td>
</tr>
<tr>
<td>Eliseev, M</td>
<td>350, 2950</td>
</tr>
<tr>
<td>Elkayam, O</td>
<td>1503, 1648, 1977, 1979</td>
</tr>
<tr>
<td>Elewaut, D</td>
<td>67, 253, 1582, 1915, 2714, 2881</td>
</tr>
<tr>
<td>Elkon, KB</td>
<td>485, 2575, 2601, 2020, 2641, 2644</td>
</tr>
<tr>
<td>Ellegaard, K</td>
<td>265, 2020</td>
</tr>
<tr>
<td>Ellingsen, K</td>
<td>2398</td>
</tr>
<tr>
<td>Ellinwood, N</td>
<td>1055</td>
</tr>
<tr>
<td>Elliott, A</td>
<td>1259</td>
</tr>
<tr>
<td>Elliott, J</td>
<td>1642, 1643</td>
</tr>
<tr>
<td>Elliott, S</td>
<td>2811</td>
</tr>
<tr>
<td>Ellis, B</td>
<td>1807</td>
</tr>
<tr>
<td>Ellis, LA</td>
<td>362, 455, 473, 1057</td>
</tr>
<tr>
<td>Ellis, SJ</td>
<td>219</td>
</tr>
<tr>
<td>Ellmeier, W</td>
<td>2709</td>
</tr>
<tr>
<td>Ellsworth, J</td>
<td>2952</td>
</tr>
<tr>
<td>Elmamoun, M</td>
<td>634, 1829, 2550</td>
</tr>
<tr>
<td>Elmesmari, A</td>
<td>972</td>
</tr>
<tr>
<td>Elndy, B</td>
<td>1569</td>
</tr>
<tr>
<td>Elonheiro, O</td>
<td>1054, 2834</td>
</tr>
<tr>
<td>Eloranta, ML</td>
<td>1638, 2654, 2817</td>
</tr>
<tr>
<td>Elloseily, EMA</td>
<td>1897, 2320</td>
</tr>
<tr>
<td>Eltaraboulsi, R</td>
<td>2982</td>
</tr>
<tr>
<td>Elvin, K</td>
<td>1675, 2633</td>
</tr>
<tr>
<td>Elzalabany, MS</td>
<td>2387</td>
</tr>
<tr>
<td>Emamikia, S</td>
<td>1840</td>
</tr>
<tr>
<td>Emery, D</td>
<td>1781</td>
</tr>
<tr>
<td>Emil, NS</td>
<td>309, 310</td>
</tr>
<tr>
<td>Encinales, C</td>
<td>2837</td>
</tr>
<tr>
<td>Encinales, L</td>
<td>274, 2837</td>
</tr>
<tr>
<td>Encinas, L</td>
<td>2237</td>
</tr>
<tr>
<td>Endo, T</td>
<td>2887</td>
</tr>
<tr>
<td>Endo, Y</td>
<td>1882, 2144</td>
</tr>
<tr>
<td>Eng, S</td>
<td>734, 2669</td>
</tr>
<tr>
<td>Engbers, A</td>
<td>2645</td>
</tr>
<tr>
<td>Engel, R</td>
<td>1935</td>
</tr>
<tr>
<td>Engelson, BJ</td>
<td>968</td>
</tr>
<tr>
<td>England, BR</td>
<td>135, 433, 472, 842, 1036, 1357, 1365, 2376, 2377, 2378, 2392, 2915</td>
</tr>
<tr>
<td>Englbrecht, M</td>
<td>414, 633, 848, 881, 2024</td>
</tr>
<tr>
<td>English, C</td>
<td>95</td>
</tr>
<tr>
<td>English, K</td>
<td>2269</td>
</tr>
<tr>
<td>Englund, M</td>
<td>1117, 2019, 2073</td>
</tr>
<tr>
<td>Engström, M</td>
<td>970, 2869</td>
</tr>
<tr>
<td>Eniola-Adefeso, O</td>
<td>8</td>
</tr>
<tr>
<td>Enocsson, H</td>
<td>454, 677</td>
</tr>
<tr>
<td>Enriquez RMA, A</td>
<td>206</td>
</tr>
<tr>
<td>Enriquez Sosa, F</td>
<td>1909</td>
</tr>
<tr>
<td>Ensworth, S</td>
<td>1316, 1599</td>
</tr>
<tr>
<td>Enyindah-Asonye, G</td>
<td>2713</td>
</tr>
<tr>
<td>Epis, O</td>
<td>2239</td>
</tr>
<tr>
<td>Eppler, B</td>
<td>2288</td>
</tr>
<tr>
<td>Epstein, H</td>
<td>2595</td>
</tr>
<tr>
<td>Epsten, M</td>
<td>594, 1263, 1581, 2556</td>
</tr>
<tr>
<td>Eraso, M</td>
<td>634</td>
</tr>
<tr>
<td>Erausquin, C</td>
<td>1587</td>
</tr>
<tr>
<td>Eb, S</td>
<td>1099</td>
</tr>
<tr>
<td>Erd, D</td>
<td>2504</td>
</tr>
<tr>
<td>Erden, A</td>
<td>1174, 1240, 1312, 1451, 1522, 2110, 2409, 2742, 2743</td>
</tr>
<tr>
<td>Erdogan, M</td>
<td>463, 2103</td>
</tr>
<tr>
<td>Ergezen, B</td>
<td>2117</td>
</tr>
<tr>
<td>Erickson, AR</td>
<td>101, 2448</td>
</tr>
<tr>
<td>Erickson, J</td>
<td>624</td>
</tr>
<tr>
<td>Erickstad, K</td>
<td>1687</td>
</tr>
<tr>
<td>Eriksson, P</td>
<td>1479</td>
</tr>
<tr>
<td>Erkan, D</td>
<td>12, 15, 108, 2760</td>
</tr>
<tr>
<td>Erken, E</td>
<td>739</td>
</tr>
<tr>
<td>Ermann, J</td>
<td>398, 660, 1186, 1382</td>
</tr>
<tr>
<td>Ermurat, S</td>
<td>2210</td>
</tr>
<tr>
<td>Ernestam, S</td>
<td>1541</td>
</tr>
<tr>
<td>Ernste, FC</td>
<td>1662, 2082, 2175, 2657</td>
</tr>
<tr>
<td>Erol, K</td>
<td>2496</td>
</tr>
<tr>
<td>Erpelding, ML</td>
<td>1802</td>
</tr>
<tr>
<td>Ersozlu Bakirli, D</td>
<td>2496</td>
</tr>
<tr>
<td>Erten, S</td>
<td>2496</td>
</tr>
<tr>
<td>Ertenli, I</td>
<td>1174, 1312, 1451, 1522, 2409, 2742</td>
</tr>
<tr>
<td>Ertl, P</td>
<td>966</td>
</tr>
<tr>
<td>Erturk, Z</td>
<td>1455, 2667</td>
</tr>
<tr>
<td>Erturk, Z</td>
<td>1472</td>
</tr>
<tr>
<td>Ervin, J</td>
<td>1191</td>
</tr>
<tr>
<td>Esatoglu, SN</td>
<td>463, 746, 802, 803, 2103, 2462, 2747, 2748</td>
</tr>
<tr>
<td>Escalante, A</td>
<td>869, 2358, 2911</td>
</tr>
<tr>
<td>Escamilla Gomez, VA</td>
<td>154</td>
</tr>
</tbody>
</table>
Eschard, JP 1222  
Eschard, JP 2464  
Escobar, A 1448  
Escudero-Contreras, A 391, 392, 1466, 2435, 2475  
Esaile, JM 197, 353, 1839, 2614  
Esmailzadeh, E 750  
Espada, G 2859  
Espesen, J 1550  
Espie, P 1784  
Espinal, J 1097  
Espinosa, G 15, 1159, 2098  
Espinoza, LR 1574  
Essenmacher, L 1304  
Esteva Spinetti, MH 1654, 2924  
Estis, J 867, 2417  
Estmann, A 2859  
Estrada, P 1467  
Estrella, N 2021  
Esvedt, R 1847  
Etcheto, A 584  
Etomi, O 2634  
Etzel, CJ 128, 475, 1019, 1371, 1423, 1555, 1900, 2531, 2532, 2533  
Eudy, AM 49, 911, 1296, 1297, 1298, 1299, 1308, 2165  
Eugénio, G 2012, 2042  
Euller Ziegler, L 1216  
Eun, JS 558, 2122, 2369  
Eun, YH 2733  
Eun, Y 2088  
Eusébio, M 611  
Evans, L 1328  
Evans, M 202, 1089  
Evans, V 1231  
Evans-Marin, H 402, 1742  
Everekliyan, M 2143  
Everett, BM 985, 1628  
Everett, C 874  
Everett, K 1271  
Everist, B 2053  
Everix, D 1103  
Evers, R 1845  
Evitar, T 1648  
Ewarien, B 2114  
Exeni, I 269  
Expósito, R 498, 1517, 1518, 1519  
Expósito Pérez, L 2277  
Eyre, S 2341, 2826  
Ez-Zaitouni, Z 1512  
Ezeugwu, V 2351  
F  
F. Kholef, E 1366  
F. Nemeth, J 1428  
Fabien, N 2348  
Fabro, C 2874  
Fadle, N 1389  
Faerber, P 1784  
Fagerli, KM 342, 1512, 1541  
Faghihi-Kashani, S 2136  
Faguer, S 2754  
Fahey, K 2252  
Fahmi, H 52, 57  
Fahmy, L 294  
Fahoum, S 375  
Fahrleitner-Pammer, A 320  
Faiq, A 2140  
Fair, J 1239  
Fairchild, R 110  
Fairlie, D 2711  
Falahee, M 848  
Falasinnu, T 829, 986  
Falck, R 315  
Falck-Ytter, Y 2741  
Fall, N 1895  
Fallon, L 880  
Falls, O 2837  
Falzon, L 259  
Fan, H 424, 474, 495, 500, 1437  
Fan, J 2  
Fan, M 318  
Fan, RA 81, 2559  
Fan, W 2657  
Fan, W 2241, 2242  
Fana, V 350, 2950  
Fang, MA 1098  
Fang, S 1699, 2085, 2411, 2752  
Fang, YF 1314, 2804  
Fang, YF 1251  
Fang Castro, M 801  
Fangtham, M 309, 310, 2615  
Fanok, M 637  
Faraawi, R 545  
Farag, AM 1784  
Faraone, S 2763  
Fardo, DW 1009  
Faré, R 1416  
Farewell, V 2925
Fernandez-Lopez, C 1011, 2189, 2192
Fernandez-Nebro, A 1587, 1588, 1612
Fernández-Ochoa, A 1712
Fernández-Puente, P 1190
Fernandez-Ruiz, R 1497
Fernández-Tajes, J Sr. 1011
Fernando Molina, J 1654
Fernando Viejo Llorente, L 2841
Ferraccioli, G 609, 741, 742, 1898
Ferrada, MA 1177, 2100
Ferrari, F 408
Ferrari, S 1887
Ferrari, S 319
Ferraz, ML 2121
Ferreira, GRV 1302
Ferreira Guerra, S 2785
Ferrer-Fabregas, B 849
Ferri, D 831, 835
Ferriani, V 95
FERRIERES, J 657
Ferro, F 556, 1486, 1487, 1488, 1489, 1756
Ferry, J 1179
Ferucci, E 924, 1051
Fervenza, F 2339
Fichter, F 1998
Field, E 1497, 2106
Fielding, RA 2197
Fields, R 309, 310
Fifi-Mah, A 1599
Figgie, MP 218, 220, 221, 923, 1029, 2853
Figueiredo, C 414
Figueiredo, CP 1961
Fike, A 899
Filby, C 446, 2781
Filer, A 174, 241, 863, 1405, 1406, 2827
Filhol, E 2364
Filippi, N 2940
Filippou, G 2020, 2055
Filippucci, E 265, 1608, 2020, 2055, 2239
Filkova, M 579, 2434
Filosto, M 2650
Finck, B 2492, 2879
Finckh, A 436, 1034, 2778, 2910
Fine, D 719
Fine, JS 29, 2561
Finn, D 2251
Finnes, H 1880
Finzel, S 414
Finzel, S 881, 1997
Fior, R 2606
Fiore, S 130, 2482
Fiorentino, D 775, 2157, 2931
Fiorentino, S 572
Fiorillo, C 2339
Firat, E 1174, 2110
Firestein, G 1406
Firestein, GS 166, 274, 1339, 1405, 1456, 2789, 2790, 2793, 2829, 2837
Firth, J 186
Fisch, P 1731
Fischbach, M 493
Fischer, A 1323
Fischer, MA 985, 1628
Fischer-Betz, R 1295, 1297
Fish, E 832
Fish, J 2041
Fishbein, M 24
Fisher, B 874, 877, 913, 1784
Fishman, E 355
Fishman, G 2580
Fisk, H 913
Fito Manteca, MC 498
FitzCharles, M 467
Fitzgerald, G 2507, 2508, 2509
Fitzgerald, J 1391, 2086, 2618
FitzGerald, O 608
FitzGerald, O 615, 616, 617, 623, 880, 1826, 2507, 2508, 2550, 2967
Fitzpatrick, LA 1890
Fitzpatrick, R 1807
Flaisler, F 2364
Flake, DD II 1371
Flato, B 2333
Flatø, B 1265, 1276, 2961
Fleck, M 414
Flegel, W 2136
Fleischer, C 2914
Fleischmann, R 10L, 418, 619, 624, 855, 1141, 1196, 1202, 1424, 1437, 1818, 1822, 1906, 2219, 2393, 2470, 2471, 2480, 2868
Fleishaker, D 620
Fleming, D 1429
Fleuranceau-Morel, P 1L, 2585, 2586
Fligelstone, K 2662
Flint, JD 1810
Flint, S 770
FLIPO, RM 1162
Flipo, RM 1439, 1442, 1809, 2464
Floch, D 1784
Flood, J 109
Flood, KS 729
Florence, K 1823
Florentinus, S 1418
Florenzano, M 2116
Flores, F 441, 2631, 2958
Flores, J 572, 2008
Flores, MT 232, 1861
Flores Ramirez, R 667
Flores-Chavez, A 210, 2123, 2841
Florez-Durante, OI 14
Flowers, P 1950
Fluri, I 1559, 2801
Flusser, G 1503
Flynn, A 1809
Focherini, M 638
Foeldvari, I 2272
Foeldvari, I 364, 1282, 1283, 1286, 1894, 2271, 2273, 2307, 2859, 2959
Foell, D 2772
Fokker, C 1901
Foley, C 381, 382
Foltz, V 337, 588, 589, 590, 1234, 1504
Fomina, N 2445
Fong, LS 425, 426, 1808
Fong, W 1577
Fonollosa, A 2722
Fonseca, C 1713
Fonseca, E 2841
Fonseca, JE 2475
Fonseca Aizpuru, E 209
Fonseca, C 1405, 2827
Font Urgelles, J 538, 1443, 2412
Font-Ugalde, P 998
Fontaine, K 2310
Fontana, A 790
Fontana, J 939
Fontana, L 1075
Foo, J 1465
Forbes, LJ 785, 789, 838, 1364
Ford, E 1431
Ford, K 129, 1900
Forejtová, Š 579, 1538, 1549
Foreman, J 118
Förger, F 1309, 1315, 1809
Fornaro, MN 1564, 2551, 2554
Forner, MJ 2841
Fornes Ferrer, V 684, 1224
Forney, C 175, 2825
Forsblad D’Elia, H 1479
Forsman, A 58
Forsyth, AM 2431
Fortes-Gordo, P 2422, 2426
Fortes, N 276
Fortin, I 612, 2491, 2520
Fortin, PR 466, 1027, 1293, 1599, 1606, 1641, 1666, 2760, 2769, 2811, 2925
Foster, CS 1155
Foster, H 95
Foster, HE 107, 186, 366, 2287
Foster, M 62
Foster, PA 4L
Foti, R 1292
Fotouhi, N 1060
Fountaine, RJ 1195
Fouret, P 71
Fourez, JP 1746
Fournier, M 2457
Fowler, J 2440
Fowler, ML 282, 2840
Fox, DA 174, 962, 971, 1336, 1705, 2095, 2713, 2926
Fox, RS 2049, 2695
Fox, T 606, 607, 621, 1529, 1546
Frachette, C 2348
Fradin, J 878
Fraenkel, L 190, 340, 1058, 1236, 1257, 1395, 1536, 1796, 1852, 2780, 2892
Fragio Gil, JJ 684, 1221, 1224, 2003
Fragkakis, EM 661
Funamura, K 1048
Fung, W 1652
Funk, R 1322, 2296
Furer, V 1503, 1648, 1977, 1979
Furey, A 1209, 1210
Furie, R 673, 680, 681, 719, 886, 887
Furnier, A 385
Furst, DE 535
Furst, DE 725, 749, 943, 1371, 1703, 2049, 2668, 2684, 2776, 2884, 2981
Furu, M 551
Furukawa, H 1013, 1751, 1762
Furukawa, K 2649
Furukawa, T 2685
Furuya, H 956, 957, 958, 959, 960, 2135
Furuya, K 1999, 2132
Furuya, T 329, 1343
Fushimi, K 806
Fuzibet, JG 814
Fuzzi, E 2979
G
G M Balbi, G 10
Gabay, C 1825, 1895, 2772
Gabay, O 1068
Gabčová, G 2740
Gaber, T 1946
Gabre, K 7L, 2156
Gabriel, SE 32, 147, 1032
Gabrielli, A 1023, 1292
Gad, I 755
Gadeholt, O 453
Gademsetty, C 102
Gadi, VK 2431
Gadina, MG 292, 1893, 2773
Gaffney, PM 164, 184, 300, 2283, 2648, 2976
Gaffo, AL 350, 357, 2893, 2950
Gager, K 91
Gagnon, F 1271
Gaich, CL 508, 855, 2219
Gaillez, C 618, 621, 622, 1526, 1826
Gajardo-Meneses, P 2643
Galarbos, C 379
Galarza-Delgado, DA 147
Galcerán-Chaves, C 210, 2123
Galdamez, J 1581
Gale, S 527, 550, 778
Galea, R 2704
Galeazzi, M 1468, 1469, 2452
Galeazzi, M 521, 2899
Galien, R 497, 504, 1458
Galimi, F 1456
Galíndez Agirregoiako, E 529
Galíndez-Agirregoiako, E 1232, 2343, 2526
Galindo, M 1587, 1588, 1612, 2619
Galindo-Feria, AS 2167
Gallagher, P 2507, 2508, 2550
Gallardo, M 2237
Gallego, R 2723
Gallizzi, R 1894
Galloway, J 434, 1374, 1807
Gally, S 2464
Galtung, HK 570
Gálvez Elkin, MS 2021
Galvez-Ruiz, D 211, 998, 999
Gamarra-Hilburn, CF 1125
Gamberucci, A 2899
Gamble, G 1108
Gamboa-Cárdenas, R 687, 1378
Gamboa-Cardenas, RV 450
Ganero, F 2723
Gámir-Gámir, ML 1270
Gan, RW 990, 1971
Gandelman, J 1586
Gandhi, K 622, 1523, 1528, 1546
Gandhi, N 2824
Gandhi, R 2235, 2236
Gandia Martinez, M 2723
Gandiga*, PC 2163
Gandino, IJ 269, 2109
Gandjbakhch, F 337, 1234, 1878, 2055
Gandolfi, S 1489, 2874
Ganga, V 991
Gangemi, S 2984
Ganguli, A 358, 1561, 1963
Ganguly, R 1477, 2258
Ganocy, SJ 1954
Ganser, G 2274, 2307
Gantes, M 2723
Ganz, F 2163
Gao, E 1407, 1408
Gao, L 1655
Gao, L 2758
Gao, ML 1251
Gao, R 2896
Garaiman, A 997
Garal-Pantaler, E 195
Garces, K 2477, 2478
Garchon, HJ 1579
Garcia, K 2477, 2478
Garcia, E 1467
García, L 1766, 2676
García, M 2722
Garcia, MV 360, 440
Garcia, M 1766, 2237, 2276, 2924
García, MA 360, 1645
Garcia De La Peña, P 1612, 2062, 2130
Garcia-De La Torre, I 2924
GARCIA DE YEBENES Y PROUS, MJ 2130
García Ferrer, HR 1574
Garcia Gonzalez, E 2899
Garcia Kutzbach, A 1574
García Magallon, B 2284
Garcia Montoya, L 2129
Garcia Morillo, JS 209
Garcia Salinas, R 231, 1007, 1079, 1564
Garcia Vivar, ML 529, 1448
García-Aparicio, A 2112
García-Aparicio, ÁM 2723
García-Armario, MD 2724
García-Carazo, S 1891
García-Carazo, S 793
García-De La Torre, I 178, 1654
Garcia-Espinosa, MA 2257
García-Fernández, A 1270
García-Hernandez, MDLL 1947
García-Moreno, MÁ 326
Garcia-Patos, V 849
García-Portales, R 1517, 1519
García-Puig, J 261
García-Serrano, JL 2722, 2723
García-Vicuña, R 1535, 1612, 2375
Gard, C 1056
Gardet, A 675
Garen, T 743, 744, 947, 1002, 2980
Garg, J 1600
Garg, M 1024
Garg, R 1524, 1525
Garg, V 1038, 2454
Garges, C 1000
Garjo Bufort, M 2003
Garmish, O 2445
Garnier Rodríguez, JL 487, 1383
Garraud, T 2079
Garrett, S 763
Garrido, M 71, 1734, 1746
Garrido-Cumbre, M 211, 998, 999
Garrison, LP 1049
Garrone, M 2859
Garrood, T 2536
Garrote-Corral, S 1270
Garrouste, C 797
Garton, J 300
Gartshteyn, Y 2344
Garza Romero, A 1144
Garzarro-regard, M 814
Gasho, C 98
Gatenholm, P 58
Gatineau, F 877
Gato Diez, A 209
Gato-Calvo, L 1949
Gattorno, M 1744, 1894
Gaubil-Kaladjian, I 1222
Gaudy, A 886, 887
Gaujoux-Viala, C 1223, 1390, 1453, 1490, 2364
Gaumer, S 1580
Gaur, P 2330
Gavasso, S 1073
Gavigan, K 2250
Gavinier, S 668
Gaviola, G 1382
Gavrila, D 913
Gay, S 1335, 1791
Gaylis, N 520
Gaynon, L 1085
Gayvoronskaya, A 386
Gazdhar, A 1715
Gazeley, D 114
Gazitt, T 485
Gehin, J 1990
Geier, J 1427
Geijer, M 2511
Geirsson, AJ 1541
Geiser, T 1715
Gill, D 1905, 2460, 2962
Gill, E 2345
Gill, I 2734
Gill, S 394
Gill, T 1910, 1913
Gillispie, M 90
Gillooly, AR 952, 2569, 2707
Gillooly, K 503
Gilloteau, I 607
Gilmore-Bykovskyi, A 2261
Gilroy, D 298
Giltiay, NV 1667, 2644
Gimenez-Romero, D 684
Gindzienska-Sieskiewicz, E 761
Ginsberg, SD 362, 1298, 1308
Ginsburg, S 1537
Ginzler, EM 1482, 1606, 1633, 2627
Giordano, F 360
Giordano, J 1121
Giovannelli, J 1685
Girard, C 1895, 2772
Girard, E 1444
Girard, N 1741
Girgis, I 514
Girolami, F 1193
Girszyn, N 814, 1779
Giulini, M 266
Gkaliagkousi, E 2357
Gladkikh, V 2279, 2280
Gladman, DD 596, 600, 602, 603, 604, 620, 647, 651, 713, 714, 718, 880, 884, 994, 996, 1590, 1591, 1592, 1599, 1606, 1624, 1826, 1829, 2523, 2541, 2555, 2557, 2623, 2811, 2925
Gladue, H 919, 946, 2930
Glanowski, C 1183
Glanzman, J 22
Glenn, S 184
Glick, K 2182
Gliklich, R 212, 468, 1394
Glimm, AM 2007
Glinatsi, D 236, 246
Glintborg, B 134, 1541, 1550
Gloor, A 805
Glover, C 294
Glover, J 2799
Glowacka-Kulesz, M 1909
Gluzman, I 1023, 1919
Glynn, E 2561
Gmuca, S 2992
Gmyrek, G 2774
Gn, C 2535
Go, DJ 2025
Go, E 1280, 1892
Gobbi, C 2237
Gobert, P 2754
Godang, K 2961
Godeau, B 814, 1779
Godfrey, T 2605
Godinez, F 243
Godmer, P 2736, 2754
Goeb, V 873, 2464
Goeccker, R 185
Goekoop, RJ 2916
Goekoop-Ruiterman, YP 1402
Goel, N 2610
Goel, R 1848
Goemaere, S 1889
Goesling, J 194, 1870
Gogier, C 2469
Goglin, S 189, 1798
Goh, ET 434
Goh, YI 1080
Goilav, B 2631, 2757, 2958
Goin, DE 2432, 2433
Gokcen, N 739
Goker, B 1534, 2953
Goldbach-Mansky, R 939, 1024, 1893, 2337, 2347, 2349, 2758, 2772
Goldberg, A 919, 946, 2930
Goldberg, B 2140
Goldberg, JD 1843
Goldberg, T 1080
Goldblatt, F 1629
Goldenstein-Schmierberg, C 634, 1302
Golder, V 188, 1629
Goldin, J 749, 2009
Goldman, D 7, 663, 664, 665, 666, 1603, 1604, 1605, 2622
Goldmuntz, E 943
Goldscheider, I 1184
Goldsmit, CH 1262
Goldsway, N 1872
Gole, R 2922
Golightly, YM 926, 1950, 2766
Goll, GL 2800
Golpanian, S 2957
Gottenberg, JE 561, 873, 876, 1442, 1491, 1795
Gottesman, K 2049, 2695
Gottheil, S 2390
Gottlieb, AB 607, 2539, 2878
Gottlieb, I 2225, 2226
Goudarzi, M 2750
Goulet, J 1058
Goulvestre, C 2932
Goupille, P 588, 589, 590, 1504
Gourh, P 919, 946, 2930
Gourley, I 2963
Goutte, J 2717
Govind, N 427
Govoni, M 638, 1292, 1300
Goyal, K 455
Goyal, L 504, 1458
Gozek Ocal, A 2108
Gozen, ED 802
Grammer, A 296, 1026, 2609, 2818
Grande Ratti, MF 3
Grandon, B 1580
Granel, A 269
Graninger, W 2268, 2469, 2646, 2877, 2886
Grapinet, J 2203
Gras, P 2083
Grassi, W 1608
Grassia, S 220, 221
Grassin-Delyle, S 1579
Gratacos-Masmitja, J 999, 1533, 1535
Gratal, P 396
Grau-Junyent, JM 849
Grauer, A 318, 319, 1886
Gravallese, EM 241, 1405, 1406
Graver, JC 807
Greene, CS 1014
Greenfield, A 2868
Greenman, D 1668
Greenspan, SL 320, 2256, 2777
Greental, A 1872
Greenwald, M 1909, 2850
Greer, J 1909
Gregersen, P 1405, 1406, 1971, 2826, 2827, 2828
Gregorini, I 2259
Gregory, M 2837
Gregova, M 2534
Gregson, J 361
Greis, K 173
Greloni, G 1772
Gremese, E 741, 742, 1898
Grenningloh, R 774, 2565
Greth, W 2591
Grevich, S 2350
Grewal, N 315
Griep, E 2365
Griep-Wentink, H 2365
Grier, A 394
Griesemer, I 846
Grieshaber Bouyer, R 297, 2712
Griffith, JF 1994, 2939, 2941
Griffiths, CE 613
Griffiths, H 1354
Griffiths, M 73, 1571
Grigoriadou, S 685
<table>
<thead>
<tr>
<th>Name</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haroon, M</td>
<td>2507, 2508</td>
</tr>
<tr>
<td>Haroon, N</td>
<td>176, 656, 2805, 2821</td>
</tr>
<tr>
<td>Haroun, T</td>
<td>1298, 1308, 1797</td>
</tr>
<tr>
<td>Harper, C</td>
<td>45</td>
</tr>
<tr>
<td>Harre Hindmarsh, J</td>
<td>1127</td>
</tr>
<tr>
<td>Harris, BD</td>
<td>80</td>
</tr>
<tr>
<td>Harris, C</td>
<td>1407, 1408</td>
</tr>
<tr>
<td>Harris, K</td>
<td>2451</td>
</tr>
<tr>
<td>Harris, N</td>
<td>1179</td>
</tr>
<tr>
<td>Harris, N</td>
<td>1299</td>
</tr>
<tr>
<td>Harris, RE</td>
<td>2753, 2912</td>
</tr>
<tr>
<td>Harris, T</td>
<td>49</td>
</tr>
<tr>
<td>Harrison, AA</td>
<td>430, 2506</td>
</tr>
<tr>
<td>Harrison, DD</td>
<td>599, 630, 1530, 1531, 1532</td>
</tr>
<tr>
<td>Harrison, M</td>
<td>2778</td>
</tr>
<tr>
<td>Harrison, P</td>
<td>504, 510, 534, 537, 1458, 1909</td>
</tr>
<tr>
<td>Harrold, LR</td>
<td>336, 410, 1341, 1796, 2449, 2450</td>
</tr>
<tr>
<td>Harry, O</td>
<td>2301</td>
</tr>
<tr>
<td>Hart, J</td>
<td>988</td>
</tr>
<tr>
<td>Harte, SE</td>
<td>2912</td>
</tr>
<tr>
<td>Hartings, C</td>
<td>12L</td>
</tr>
<tr>
<td>Hartl, A</td>
<td>578</td>
</tr>
<tr>
<td>Hartvig, W</td>
<td>781</td>
</tr>
<tr>
<td>Hartvig, C</td>
<td>360</td>
</tr>
<tr>
<td>Harvey, BP</td>
<td>961</td>
</tr>
<tr>
<td>Harvey, P</td>
<td>714, 1590, 1592, 2617, 2769</td>
</tr>
<tr>
<td>Harvey, WF</td>
<td>449, 843, 931, 1185, 2849</td>
</tr>
<tr>
<td>Hasan, E</td>
<td>471, 2366</td>
</tr>
<tr>
<td>Haschka, J</td>
<td>414</td>
</tr>
<tr>
<td>Hase, N</td>
<td>395, 2071</td>
</tr>
<tr>
<td>Hasegawa, E</td>
<td>412</td>
</tr>
<tr>
<td>Hasegawa, H</td>
<td>795, 1010, 1064</td>
</tr>
<tr>
<td>Hasegawa, M</td>
<td>2485</td>
</tr>
<tr>
<td>Hasegawa, M</td>
<td>21</td>
</tr>
<tr>
<td>Haseler, L</td>
<td>310</td>
</tr>
<tr>
<td>Haselmayer, P</td>
<td>2565</td>
</tr>
<tr>
<td>Hashiba, Y</td>
<td>273</td>
</tr>
<tr>
<td>Hashimoto, H</td>
<td>1013, 1751, 1762</td>
</tr>
<tr>
<td>Hashimoto, J</td>
<td>311, 1447</td>
</tr>
<tr>
<td>Hashimoto, M</td>
<td>479, 551, 2164</td>
</tr>
<tr>
<td>Hashimoto, T</td>
<td>973</td>
</tr>
<tr>
<td>Hashiramoto, A</td>
<td>299, 973</td>
</tr>
<tr>
<td>Hashkes, PJ</td>
<td>2758</td>
</tr>
<tr>
<td>Haslacher, H</td>
<td>2864</td>
</tr>
<tr>
<td>Hasni, S</td>
<td>2953</td>
</tr>
<tr>
<td>Hasni, SA</td>
<td>899</td>
</tr>
<tr>
<td>Hass, N</td>
<td>2443</td>
</tr>
<tr>
<td>Hassan, I</td>
<td>922, 2734</td>
</tr>
<tr>
<td>Hassett, AL</td>
<td>1003, 1870, 2986</td>
</tr>
<tr>
<td>Hassett, G</td>
<td>1231</td>
</tr>
<tr>
<td>Hastings, S</td>
<td>2768</td>
</tr>
<tr>
<td>Hasturk, H</td>
<td>494</td>
</tr>
<tr>
<td>Hatemi, G</td>
<td>463, 746, 2103, 2462, 2747, 2748</td>
</tr>
<tr>
<td>Hatemi, I</td>
<td>2748</td>
</tr>
<tr>
<td>Hatron, PY</td>
<td>873</td>
</tr>
<tr>
<td>Hatron, PY</td>
<td>1162, 1685</td>
</tr>
<tr>
<td>Hatta, K</td>
<td>507, 1421</td>
</tr>
<tr>
<td>Hattersley, G</td>
<td>59, 1890, 1937</td>
</tr>
<tr>
<td>Hattori, K</td>
<td>324</td>
</tr>
<tr>
<td>Hatzis, C</td>
<td>1856</td>
</tr>
<tr>
<td>Hauber, B</td>
<td>358</td>
</tr>
<tr>
<td>Hauge, EM</td>
<td>262, 799</td>
</tr>
<tr>
<td>Hauge, EM</td>
<td>2367</td>
</tr>
<tr>
<td>Haugeberg, G</td>
<td>342, 2503, 2538, 2968</td>
</tr>
<tr>
<td>Haugen, IK</td>
<td>917, 1202, 2006, 2944</td>
</tr>
<tr>
<td>Haugen, IK</td>
<td>265, 2020</td>
</tr>
<tr>
<td>Häupl, T</td>
<td>39</td>
</tr>
<tr>
<td>Haupt, L</td>
<td>452</td>
</tr>
<tr>
<td>Hausmann, JS</td>
<td>361</td>
</tr>
<tr>
<td>Hawke, C</td>
<td>2821</td>
</tr>
<tr>
<td>Hawker, G</td>
<td>1851</td>
</tr>
<tr>
<td>Hayashi, H</td>
<td>2249</td>
</tr>
<tr>
<td>Hayashi, H</td>
<td>1319</td>
</tr>
<tr>
<td>Hayashi, J</td>
<td>2017</td>
</tr>
<tr>
<td>Hayashi, M</td>
<td>1048</td>
</tr>
<tr>
<td>Hayashi, N</td>
<td>240</td>
</tr>
<tr>
<td>Hayashi, S</td>
<td>299, 965</td>
</tr>
<tr>
<td>Hayat, S</td>
<td>1687</td>
</tr>
<tr>
<td>Hayat, S</td>
<td>471, 2366</td>
</tr>
<tr>
<td>Hayden, H</td>
<td>2350</td>
</tr>
<tr>
<td>Haydon, J</td>
<td>1639</td>
</tr>
<tr>
<td>Haye Salinas, MJ</td>
<td>572</td>
</tr>
<tr>
<td>Hayer, S</td>
<td>61</td>
</tr>
<tr>
<td>Hayes, KW</td>
<td>936, 2188</td>
</tr>
<tr>
<td>Haynam, M</td>
<td>12L</td>
</tr>
<tr>
<td>Haynatzki, G</td>
<td>135</td>
</tr>
<tr>
<td>Hays, K</td>
<td>1813</td>
</tr>
<tr>
<td>Hayward, W</td>
<td>309</td>
</tr>
<tr>
<td>Hazan, E</td>
<td>1977, 1979</td>
</tr>
<tr>
<td>Hazard, ES</td>
<td>1018</td>
</tr>
<tr>
<td>Hazen, M</td>
<td>2997</td>
</tr>
<tr>
<td>Hazes, JMW</td>
<td>1551, 1792, 2048, 2542, 2543, 2544</td>
</tr>
<tr>
<td>Hazlewood, G</td>
<td>1045, 1393</td>
</tr>
<tr>
<td>Haznedaroglu, S</td>
<td>2953</td>
</tr>
<tr>
<td>Name</td>
<td>Page(s)</td>
</tr>
<tr>
<td>-----------------------</td>
<td>---------</td>
</tr>
<tr>
<td>Ho, MF</td>
<td>165</td>
</tr>
<tr>
<td>Hoang, A</td>
<td>1029</td>
</tr>
<tr>
<td>Hoang, L</td>
<td>2937</td>
</tr>
<tr>
<td>Hoang, T</td>
<td>377</td>
</tr>
<tr>
<td>Hobfoll, SE</td>
<td>2824</td>
</tr>
<tr>
<td>Hočevar, A</td>
<td>781, 822, 2718, 2719, 2735</td>
</tr>
<tr>
<td>Hochberg, M</td>
<td>935, 1006, 1204, 2200</td>
</tr>
<tr>
<td>Hochberg, MC</td>
<td>1L</td>
</tr>
<tr>
<td>Hockerman, S</td>
<td>2771</td>
</tr>
<tr>
<td>Hockey, HU</td>
<td>1784</td>
</tr>
<tr>
<td>Hocking, A</td>
<td>19</td>
</tr>
<tr>
<td>Hodge, J</td>
<td>1440, 2492, 2879</td>
</tr>
<tr>
<td>Hoekstra, M</td>
<td>782</td>
</tr>
<tr>
<td>Hoekstra, O</td>
<td>244, 257</td>
</tr>
<tr>
<td>Hoens, A</td>
<td>315, 353, 2240, 2269, 2954</td>
</tr>
<tr>
<td>Hoepken, S</td>
<td>881</td>
</tr>
<tr>
<td>Hofauer, B</td>
<td>876</td>
</tr>
<tr>
<td>Höfel, L</td>
<td>2288</td>
</tr>
<tr>
<td>Hofer, M</td>
<td>376, 1278, 2333, 2859</td>
</tr>
<tr>
<td>Hoff, M</td>
<td>2538, 2968</td>
</tr>
<tr>
<td>Hoffman, AF</td>
<td>1060</td>
</tr>
<tr>
<td>Hoffman, E</td>
<td>525</td>
</tr>
<tr>
<td>Hoffman, GS</td>
<td>1752, 1783, 1844</td>
</tr>
<tr>
<td>Hoffman, H</td>
<td>2771</td>
</tr>
<tr>
<td>Hoffman, S</td>
<td>1725</td>
</tr>
<tr>
<td>Hoffmann, A</td>
<td>1696</td>
</tr>
<tr>
<td>Hoffmann, F</td>
<td>1877</td>
</tr>
<tr>
<td>Hoffmann, PM</td>
<td>1892</td>
</tr>
<tr>
<td>Hoffmann-Vold, AM</td>
<td>1002</td>
</tr>
<tr>
<td>Hoffmann-Vold, AM</td>
<td>743, 744, 749, 947, 2980</td>
</tr>
<tr>
<td>Hoffmueller, U</td>
<td>2830</td>
</tr>
<tr>
<td>Hofmann, M</td>
<td>63</td>
</tr>
<tr>
<td>Hofmann, M</td>
<td>1825</td>
</tr>
<tr>
<td>Hofstetter, C</td>
<td>118</td>
</tr>
<tr>
<td>Hogrel, JY</td>
<td>5L</td>
</tr>
<tr>
<td>Hohlbaum, A</td>
<td>2476</td>
</tr>
<tr>
<td>Hojnik, M</td>
<td>1509, 1521, 2530, 2970</td>
</tr>
<tr>
<td>Hojo, S</td>
<td>1907</td>
</tr>
<tr>
<td>Holden, M</td>
<td>570</td>
</tr>
<tr>
<td>Holers, M</td>
<td>1405, 1406, 2827</td>
</tr>
<tr>
<td>Holers, VM</td>
<td>483, 484, 490, 719, 990, 1364, 1663, 1971, 2914, 2918</td>
</tr>
<tr>
<td>Holinka, J</td>
<td>966</td>
</tr>
<tr>
<td>Holl, J</td>
<td>2251</td>
</tr>
<tr>
<td>Holland, G</td>
<td>2322</td>
</tr>
<tr>
<td>Holland, MJ</td>
<td>2301, 2631, 2958</td>
</tr>
<tr>
<td>Hollema, H</td>
<td>573</td>
</tr>
<tr>
<td>Holman, AJ</td>
<td>1049</td>
</tr>
<tr>
<td>Holmdahl, R</td>
<td>1323</td>
</tr>
<tr>
<td>Holmes, T</td>
<td>758</td>
</tr>
<tr>
<td>Holmsted, K</td>
<td>2382</td>
</tr>
<tr>
<td>Holmström, M</td>
<td>872</td>
</tr>
<tr>
<td>Holt, V</td>
<td>1910</td>
</tr>
<tr>
<td>Holweg, CT</td>
<td>1774</td>
</tr>
<tr>
<td>Holzinger, D</td>
<td>1896, 2772</td>
</tr>
<tr>
<td>Homan, PJ</td>
<td>174, 302, 387, 405, 406, 1709, 1835</td>
</tr>
<tr>
<td>Homer, K</td>
<td>1855</td>
</tr>
<tr>
<td>Homey, B</td>
<td>553</td>
</tr>
<tr>
<td>Homik, J</td>
<td>2967</td>
</tr>
<tr>
<td>Honda, H</td>
<td>974</td>
</tr>
<tr>
<td>Hong, E</td>
<td>1470, 2446, 2467</td>
</tr>
<tr>
<td>Hong, H</td>
<td>34, 2567</td>
</tr>
<tr>
<td>Hong, J</td>
<td>2418</td>
</tr>
<tr>
<td>Hong, S</td>
<td>662, 672, 1110</td>
</tr>
<tr>
<td>Hong, SJ</td>
<td>585, 1868, 2074, 2510</td>
</tr>
<tr>
<td>Hong, S</td>
<td>1910</td>
</tr>
<tr>
<td>Hong, SH</td>
<td>2025</td>
</tr>
<tr>
<td>Hong, YS</td>
<td>401, 1331, 1493</td>
</tr>
<tr>
<td>Honig, S</td>
<td>1217, 1218</td>
</tr>
<tr>
<td>Honne, K</td>
<td>481</td>
</tr>
<tr>
<td>Hootman, JM</td>
<td>234, 1004, 1955, 2216, 2987</td>
</tr>
<tr>
<td>Hoover, J</td>
<td>1328</td>
</tr>
<tr>
<td>Hope, H</td>
<td>2771</td>
</tr>
<tr>
<td>Hoppe, B</td>
<td>577</td>
</tr>
<tr>
<td>Hopping, G</td>
<td>1444</td>
</tr>
<tr>
<td>Hoque, KM</td>
<td>2898</td>
</tr>
<tr>
<td>Horai, Y</td>
<td>2144</td>
</tr>
<tr>
<td>Horak, P</td>
<td>1358, 2740</td>
</tr>
<tr>
<td>Horcada, ML</td>
<td>1587, 1612</td>
</tr>
<tr>
<td>Horga, JF</td>
<td>1187</td>
</tr>
<tr>
<td>Horie, K</td>
<td>395</td>
</tr>
<tr>
<td>Horikoshi, H</td>
<td>279</td>
</tr>
<tr>
<td>Horino, T</td>
<td>271</td>
</tr>
<tr>
<td>Horita, N</td>
<td>1150, 1151</td>
</tr>
<tr>
<td>Horiuchi, T</td>
<td>36, 77, 79, 1154, 2710</td>
</tr>
<tr>
<td>Horne, A</td>
<td>1105, 1108</td>
</tr>
<tr>
<td>Horneff, G</td>
<td>364, 1894, 2271, 2272, 2273, 2274, 2307, 2333, 2859</td>
</tr>
<tr>
<td>Horowitz, D</td>
<td>241</td>
</tr>
<tr>
<td>Horsfield, J</td>
<td>2897</td>
</tr>
<tr>
<td>Horstman, M</td>
<td>198</td>
</tr>
<tr>
<td>Horton, DB</td>
<td>2275, 2278, 2281</td>
</tr>
</tbody>
</table>
Igawa, T 1882, 2144, 2649
Igel, T 1144
Iglesias Gamarra, A 2924
Iglesias-Gamarra, A 1654
Iglesias-Rodriguez, M 2471, 2479
Igoe, A 1134
Iguchi, S 1320
Iida, H 9, 702, 2152, 2588
Ikari, K 329, 1343, 1388
Ikumi, N 555
Ilar, A 119, 914
Illei, G 2591
Im, S 2413
Ima-Edomwonyi, U 634
Imai, T 397, 1414, 1907
Imaizumi, C 240
Imamura, M 240
Imamura, P 1645
Imanaka, H 1279
Imbert, B 1758, 2671
Imboden, JB Jr. 126, 327, 1996, 2038
Imgenberg-Kreuz, J 182, 2654
Imhof, I 403
Impellizzeri, D 2700
Imundo, LF 232, 379
Inada, H 2485
Inan, O 2993
Inanc, M 1606
İ
İnanc, N 542, 1455, 1472, 1534, 2667
İ
İnanici, F 313
Incerti, D 925
Inciarte-Mundo, J 1416
Ingegnoli, F 745
Ingle, JN 165
Inman, RD 645, 1509, 1787, 1914, 2805, 2821
Inokuchi, S 77
Inoo, M 2424
Inotani, S 271, 1149
Inoue, E 329, 1343, 1388
Inoue, K 271
Inoue, N 2325
Inoue, T 272, 1769
Inoue, Y 2710
Inoue, Y 240
Inoue, Y 1494
Insúa, S 2722
Intriago, MJ 1230
Intxaurbe Pellejero, AR 529
Inui, K 464
Ioan-Facsinay, A 2328
Ioannidis, G 2016, 2942
Ioannou, Y 2975
Iorio, A 15
Ioseliani, M 2859
Iraheta, I 1574
Irazoqui-Palazuelos, F 2445
Irie, H 1319
Irisawa, K 1698
irizarry-Caro, JA 292
Irrera, N 2984
Irure-Ventura, J 644, 1411
Isaac, Z 1382
Isaacs, JD 141, 1017, 1736
Isaeva, K 386, 2279, 2280
Isailovic, N 650, 1969
Isayama, T 2160
Iseki, M 79, 2563
Isenberg, DA 876, 885, 889, 1606, 1784, 2585, 2602, 2925
Ishido, M 1151
Ishido, T 1150, 1151
Ishigatsubo, Y 1154, 2732
Ishiguro, N 324, 540, 1435, 2465
Ishihara, K 2563
Ishihara, M 1698
Ishihara, S 389
Ishihara, S 2232
Ishii, N 397
Ishii, S 956, 957, 958, 960, 2135
Ishii, T 511
Ishii, T 412
Ishii, T 772, 891, 1704, 2749
Ishikawa, H 412, 1347
ishikawa, O 1704
Ishikawa, Y 2160
Ishimori, M 2266
Ishizaki, J 1010, 1064
Isla Aguilar, MA 1975
Ismail, A 12L
Ismail, F 1921
Isobe, M 795, 891
Isojima, S 2628
Isozaki, T 956, 957, 958, 959, 960, 2135
Israelsson, L 477, 834
Issa, M 415, 1824, 2787
Issa, S 2243
Issuree, P 1833
Itescu, S 1703
Ito, H 2132, 2220
Ito, H 240
Ito, K 2937
Ito, S 412
Ito, T 1279
Ito, T 2093
Itoh, K 279, 1698
Itoh, Y 1494, 1960
Iturzaeta, JM 1891
Iudici, M 1754, 1757
Ivana, P 6
Ivanchenko, M 941, 2817
Ivardava, M 386
Ivers, N 882
Iversen, L 771
Iversen, MD 931
Ivarro Cortes, J 684, 1221, 1224, 2003
Iwahashi, Y 1751
Iwamoto, M 481, 1154
Iwamoto, N 1882, 1995, 2144, 2421
Iwamoto, T 1662
Iwao, K 2427
Iwasawa, Y 1319, 1320
Iwata, N 370, 1494, 2299
Iwata, S 773, 2639, 2792
Iyer, K 2047
Iyer, R 374
Izadi, Z 189, 1047
Izmird, PM 719, 1482, 1838, 2581, 2757, 2957
Izopet, J 902
Izumikawa, M 1690, 2424
Izzi, S 1092
J
Jabado, O 2868
Jabbari, S 994, 996
Jablonski, K 60
Jackson, E 458
Jackson, RD 2200, 2223
Jackson, T 2580
Jacob, CO 1837
Jacobe, H 1284, 1285
Jacobelli, S 2924
Jacobi, A 2645
Jacobs, JW 167, 1476, 2458
Jacobs, J 1376
Jacobsen, J 2771
Jacobsen, S 1213
Jacobsen, S 236, 1589, 1606, 2925
Jacobson, KA 292
Jacobsson, LT 1117, 1512, 1541, 2073, 2080
Jacquemin, C 337, 1234
Jacquemin, C 2978
Jacques, P 67, 253, 1582, 1915
Jacques, S 1579
Jaeger, VK 1683, 1715, 2253
Jafarzadeh, SR 1783, 1865, 2063
Jaffari, F 2036
Jaffe, E 908
Jafri, K 327, 1047, 2263
Jagemann, L 44
Jagpal, A 357, 1395
Jah, N 1580
Jahnson, J 2800
Jahreis, A 2981
Jain, A 1848
Jain, M 1585, 2265
Jain, M 2141
Jain, M 648
Jain, S 1765, 2010
Jain, S 2034
Jain, S 1735
Jakobi-Brook, K 1023, 1919
Jakobsen, S 1550
Jamal, SM 347, 1084, 1101, 2247, 2264
James, E 951
James, JA 46, 83, 222, 300, 719, 901, 984, 1627, 1644, 1657, 1658, 1811, 1841, 2596, 2600, 2647, 2653, 2757, 2820, 2875, 2977
James, M 448
Jamian, L 1689
Jamilloux, Y 814
Jamin, C 41
Jamoul, C 504, 510, 534, 537, 1458
Jan, R 919, 946, 1116, 2930
Jan, S 6
Janarthanan, M 1283, 1286, 2959
Jandali, B 2691
Jandial, S 95, 107, 186
Jandova, R 78
<table>
<thead>
<tr>
<th>Name</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Juhl, P</td>
<td>465, 740, 771, 2688</td>
</tr>
<tr>
<td>Julien, AS</td>
<td>466, 1666, 2769</td>
</tr>
<tr>
<td>Jun, JH</td>
<td>82</td>
</tr>
<tr>
<td>Jun, JB</td>
<td>1016, 1135, 2074</td>
</tr>
<tr>
<td>June, J</td>
<td>331</td>
</tr>
<tr>
<td>June, RR</td>
<td>1237, 1370</td>
</tr>
<tr>
<td>Jung, E</td>
<td>2645</td>
</tr>
<tr>
<td>Jung, KH</td>
<td>982, 2202</td>
</tr>
<tr>
<td>Jung, M</td>
<td>2811</td>
</tr>
<tr>
<td>Jung, SY</td>
<td>399</td>
</tr>
<tr>
<td>Jung, SM</td>
<td>245</td>
</tr>
<tr>
<td>Jung, G</td>
<td>1894</td>
</tr>
<tr>
<td>Jungel, A</td>
<td>760</td>
</tr>
<tr>
<td>Junker, P</td>
<td>465</td>
</tr>
<tr>
<td>Juo, HH</td>
<td>1457, 2641</td>
</tr>
<tr>
<td>Juric, V</td>
<td>2718</td>
</tr>
<tr>
<td>Jurencak, R</td>
<td>2289</td>
</tr>
<tr>
<td>Jurik, AG</td>
<td>1830</td>
</tr>
<tr>
<td>Jury, E</td>
<td>2423, 2975</td>
</tr>
<tr>
<td>Jusufagic, A</td>
<td>2266</td>
</tr>
<tr>
<td>Jørgensen, KK</td>
<td>2800</td>
</tr>
<tr>
<td>Jørgensen, NR</td>
<td>2382</td>
</tr>
<tr>
<td>Jørgensen, SH</td>
<td>1830</td>
</tr>
<tr>
<td>Jørgensen, TS</td>
<td>1541, 2260</td>
</tr>
<tr>
<td>Kabat, B</td>
<td>1752, 1844</td>
</tr>
<tr>
<td>Kabba, K</td>
<td>1917</td>
</tr>
<tr>
<td>Kabra, H</td>
<td>1929</td>
</tr>
<tr>
<td>Kacar, C</td>
<td>2204</td>
</tr>
<tr>
<td>Kachur, P</td>
<td>1146, 2989</td>
</tr>
<tr>
<td>Kado, D</td>
<td>2180</td>
</tr>
<tr>
<td>Kadowaki, N</td>
<td>1690, 2424</td>
</tr>
<tr>
<td>Kadva, AK</td>
<td>2270</td>
</tr>
<tr>
<td>Kaelber, D</td>
<td>1134</td>
</tr>
<tr>
<td>Kaelber, KL</td>
<td>1134</td>
</tr>
<tr>
<td>Kaeley, GS</td>
<td>254, 1391, 1392, 1874</td>
</tr>
<tr>
<td>Kafaja, S</td>
<td>1703, 2668, 2684, 2776</td>
</tr>
<tr>
<td>Kafka, S</td>
<td>344, 473, 598, 1057, 2951</td>
</tr>
<tr>
<td>Kagalwalla, M</td>
<td>1699, 2085, 2411, 2752</td>
</tr>
<tr>
<td>Kagwiria, R</td>
<td>753, 1714, 1924</td>
</tr>
<tr>
<td>Kahaleh, B</td>
<td>755, 1710, 1923</td>
</tr>
<tr>
<td>Kahlenberg, JM</td>
<td>897</td>
</tr>
<tr>
<td>Kahn, JE</td>
<td>1779, 2671</td>
</tr>
<tr>
<td>Kai, M</td>
<td>250</td>
</tr>
<tr>
<td>Kaieda, S</td>
<td>552</td>
</tr>
<tr>
<td>Kaine, J</td>
<td>424, 500</td>
</tr>
<tr>
<td>Kainifard, T</td>
<td>2486</td>
</tr>
<tr>
<td>Kalabic, J</td>
<td>1038, 1418, 2271</td>
</tr>
<tr>
<td>Kaldas, M</td>
<td>2086</td>
</tr>
<tr>
<td>Kalergis, AM</td>
<td>2643</td>
</tr>
<tr>
<td>Kalisvaart, H</td>
<td>293</td>
</tr>
<tr>
<td>Kallenberg, CGM</td>
<td>1752, 1783, 1844, 2936</td>
</tr>
<tr>
<td>Kallinich, T</td>
<td>361, 1283, 1286, 1894, 2959</td>
</tr>
<tr>
<td>Kalra, S</td>
<td>1876, 2175</td>
</tr>
<tr>
<td>Kalunian, KC</td>
<td>673, 680, 681, 719, 888, 1606, 1838</td>
</tr>
<tr>
<td>Kaly, L</td>
<td>1537</td>
</tr>
<tr>
<td>Kalyoncu, U</td>
<td>447, 1174, 1240, 1312, 1451, 1522, 2110, 2409</td>
</tr>
<tr>
<td>Kalyvas, C</td>
<td>1546</td>
</tr>
<tr>
<td>Kamalapathy, P</td>
<td>274, 2837</td>
</tr>
<tr>
<td>Kamatani, Y</td>
<td>170</td>
</tr>
<tr>
<td>Kamath, R</td>
<td>1211</td>
</tr>
<tr>
<td>Kambara, T</td>
<td>2158</td>
</tr>
<tr>
<td>Kambas, K</td>
<td>293</td>
</tr>
<tr>
<td>Kamed, H</td>
<td>240, 417, 1593, 2798</td>
</tr>
<tr>
<td>Kamed, T</td>
<td>1690, 2424</td>
</tr>
<tr>
<td>Kanen, DL</td>
<td>719, 901, 984, 1589, 1606, 1644, 1697</td>
</tr>
<tr>
<td>Kamerling, S</td>
<td>295</td>
</tr>
<tr>
<td>Kamerling, SWA</td>
<td>890</td>
</tr>
<tr>
<td>Kamiyama, R</td>
<td>237, 1460, 2151</td>
</tr>
<tr>
<td>Kamogawa, Y</td>
<td>772, 1704</td>
</tr>
<tr>
<td>Kamoi, K</td>
<td>1155</td>
</tr>
<tr>
<td>Kamp, P</td>
<td>1627</td>
</tr>
<tr>
<td>Kamp, S</td>
<td>1627, 1657, 1658, 1841, 2600, 2820, 2977</td>
</tr>
<tr>
<td>Kamphuis, SSM</td>
<td>2333</td>
</tr>
<tr>
<td>Kampylafka, E</td>
<td>633</td>
</tr>
<tr>
<td>Kamradt, T</td>
<td>865</td>
</tr>
<tr>
<td>Kan, H</td>
<td>2593, 2594, 2812</td>
</tr>
<tr>
<td>Kanaan, SB</td>
<td>2431</td>
</tr>
<tr>
<td>Kanakaraj, P</td>
<td>462</td>
</tr>
<tr>
<td>Kanamono, T</td>
<td>1048</td>
</tr>
<tr>
<td>Kanaoka, M</td>
<td>2158, 2172</td>
</tr>
<tr>
<td>Kanayama, Y</td>
<td>324</td>
</tr>
<tr>
<td>Kanazawa, T</td>
<td>507, 1421</td>
</tr>
<tr>
<td>Kandane-Rathnayake, R</td>
<td>188, 1629</td>
</tr>
<tr>
<td>Kaneko, M</td>
<td>2017</td>
</tr>
<tr>
<td>Kaneko, R</td>
<td>1319, 1320</td>
</tr>
<tr>
<td>Kaneko, Y</td>
<td>140, 417, 717, 854, 1426</td>
</tr>
<tr>
<td>Kaneshiro, K</td>
<td>973</td>
</tr>
<tr>
<td>Kaneshita, S</td>
<td>272, 1769</td>
</tr>
<tr>
<td>Kang, A</td>
<td>1576</td>
</tr>
</tbody>
</table>
Kang, EH 526, 1113, 1377, 1495, 2009, 2844
Kang, EJ 1123
Kang, GW 982
Kang, J 413
Kang, JH 1595, 1647, 1868, 1869, 2097
Kang, JY 2369
Kang, JW 558, 2369
Kang, KY 2516
Kang, MC Sr. 2708
Kang, R 1050
Kang, SW 1143
Kang, SE 87, 1412, 2746
Kang, S 1417
Kang, S 1152
Kang, W 449, 1185
Kang, YM 558, 2122, 2369
Kania, G 1718, 1721, 1926, 2700
Kanik, KS 16L, 616, 617, 619, 620, 623
Kanan, V 2041
Kanne, JP 1171
Kantarci, A 494
Kanthi, Y 2761
Kao, A 2610
Kao, AH 889, 1642, 1643, 2585, 2586
Kao, SY 2000, 2052
Kao Yang, YH 1866
Kaouk, S 1873, 1976, 1978
Kapetanovic, MC 1117, 2073
Kapila, A 1797
Kaplan, A 368
Kaplan, G 121
Kaplan, MJ 290, 291, 292, 484, 820, 899
Kaplanski, G 71
Kapoor, T 1601, 2344, 2595
Kapudanoglu, E 2204
Kapur, S 629, 631
Kara, E 802
Kara, M 305
Karaaslan, İç 2349
Karabulut, E 58
Karadag, O 376, 1174, 1240, 1312, 1451, 1522, 2110, 2409, 2727, 2742, 2743
Karaman, E 802
Karaman, S 825
Karaplis, A 318
Karas, M 1166
Karasawa, R 2335, 2338
Karasawa, T 481
Karaseva, A 386, 2279, 2280
Karashima, T 271
Karatas, A 542, 1455, 1472
Karatemiz, G 463, 746, 2103
Kardan, A 12L
Karellis, A 467
Kargard, M 1093
Kariya, Y 2427
Karki, C 1422, 1552, 1553, 1554, 2453, 2454, 2531
Karukuçak, M 2496
Karliner, J 403
Karsdal, M 465, 489, 740, 771, 969, 1063, 1929, 2688
Karsdal, MA 1399, 2207, 2212
Karstens, L 1326
Kartman, CE 1824
Kartnig, F 966
Karyofyllis, P 2686
Kasahara, A 272
Kasai, K 2325
Kasama, T 956, 957, 958, 959, 960, 1456, 2135
Kasapcopur, O 368, 369, 746, 1283, 1286, 2117, 2305, 2859, 2959
Kashihara, N 2563
Kasifoglu, T 447
Kasselman, LJ 964
Kastbom, A 454
Karlson, E 172, 837, 915, 988, 1021, 1863, 1953, 1971, 2384
Karmacharya, P 823, 879, 1952
Karnani, DR 1364
Karnell, F 2936
Karnell, J 2589
Karolius, L 249
Karontsch, T 696, 966, 1415
Karouzakis, E 1791
Karp, D 2, 901, 984, 1644, 2041
Karp, J 398, 1186
Karpouzas, G 147, 867, 921, 1261, 1392, 1803, 1908, 2417, 2437
Karras, A 1759, 2671, 2738, 2739, 2754
Karsdal, M 465, 489, 740, 771, 969, 1063, 1929, 2688
Karsdal, MA 1399, 2207, 2212
Karstens, L 1326
Kartman, CE 1824
Kartnig, F 966
Karyofyllis, P 2686
Kasahara, A 272
Kasai, K 2325
Kasama, T 956, 957, 958, 959, 960, 1456, 2135
Kasapcopur, O 368, 369, 746, 1283, 1286, 2117, 2305, 2859, 2959
Kashihara, N 2563
Kasifoglu, T 447
Kasselman, LJ 964
Kastbom, A 454
<table>
<thead>
<tr>
<th>Name</th>
<th>Pages</th>
<th>Name</th>
<th>Pages</th>
<th>Name</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keenan, RT</td>
<td>2165</td>
<td>Kennedy, N</td>
<td>1398</td>
<td>Khalil, S</td>
<td>2561</td>
</tr>
<tr>
<td>Keggereis, B</td>
<td>296</td>
<td>Kennedy, O</td>
<td>905</td>
<td>Khalsa, U</td>
<td>1272</td>
</tr>
<tr>
<td>Kejzar, N</td>
<td>822</td>
<td>Kennedy, S</td>
<td>1201</td>
<td>Khamashta, MA</td>
<td>15, 1606</td>
</tr>
<tr>
<td>Kekeh, C</td>
<td>468, 1394</td>
<td>Kenny, T</td>
<td>2837</td>
<td>Khan, A</td>
<td>319</td>
</tr>
<tr>
<td>Kekow, J</td>
<td>1980</td>
<td>Ker, KJ</td>
<td>1613</td>
<td>Khan, A</td>
<td>1686</td>
</tr>
<tr>
<td>Kelberman, D</td>
<td>2342</td>
<td>Kerbach, M</td>
<td>2391</td>
<td>Khan, C</td>
<td>846</td>
</tr>
<tr>
<td>Keller, KK</td>
<td>262, 799</td>
<td>Kerckhofs, G</td>
<td>1945</td>
<td>Khan, MS</td>
<td>222</td>
</tr>
<tr>
<td>Keller, S</td>
<td>328, 1130, 1131, 2077</td>
<td>Kermani, TA</td>
<td>781, 784, 785, 789, 1392</td>
<td>Khan, MN</td>
<td>55, 56</td>
</tr>
<tr>
<td>Kele, G</td>
<td>314</td>
<td>Kerola, AM</td>
<td>1054, 2834</td>
<td>Khan, NA</td>
<td>991, 1452</td>
</tr>
<tr>
<td>Kelley, K</td>
<td>314</td>
<td>Kerr, GS</td>
<td>135, 433, 1357, 2893</td>
<td>Khan, S</td>
<td>428</td>
</tr>
<tr>
<td>Kelley, S</td>
<td>934, 1200</td>
<td>Kerr, L</td>
<td>628, 2549, 2969</td>
<td>Khanal, R</td>
<td>823, 879, 1952</td>
</tr>
<tr>
<td>Kelley, WJ</td>
<td>8</td>
<td>Kerr, S</td>
<td>2240, 2954</td>
<td>Khanna, D</td>
<td>726, 729, 732, 734, 745, 749, 767, 919, 943, 946, 1248, 1686, 1701, 1705, 1709, 1855, 1922, 2665, 2683, 2693, 2694, 2776, 2926, 2930, 2981, 2983</td>
</tr>
<tr>
<td>Kellner, H</td>
<td>2L</td>
<td>Kerschbaumer, A</td>
<td>452, 2245, 2971</td>
<td>Khanna, P</td>
<td>2070</td>
</tr>
<tr>
<td>Kelly, A</td>
<td>339, 1231</td>
<td>Kerstens, PJSM</td>
<td>429</td>
<td>Khatri, P</td>
<td>1680</td>
</tr>
<tr>
<td>Kelly, D</td>
<td>2900</td>
<td>Kerzberg, E</td>
<td>269, 360</td>
<td>Khat, S</td>
<td>2914</td>
</tr>
<tr>
<td>Kelly, JA</td>
<td>164, 184</td>
<td>Keskin, G</td>
<td>2728</td>
<td>Khawaja, K</td>
<td>95</td>
</tr>
<tr>
<td>Kelly, M</td>
<td>2225, 2226</td>
<td>Ketharnathan, S</td>
<td>2897</td>
<td>Khawar, T</td>
<td>2632</td>
</tr>
<tr>
<td>Kelly, R</td>
<td>2578, 2763</td>
<td>Kevil, C</td>
<td>1404</td>
<td>Khawaja, SS</td>
<td>292</td>
</tr>
<tr>
<td>Kelly, S</td>
<td>2450</td>
<td>Kewans, H</td>
<td>1569</td>
<td>Kheir, JM</td>
<td>222</td>
</tr>
<tr>
<td>Kelly, S</td>
<td>174, 1405, 1406, 1410</td>
<td>Keyes-Ellstein, L</td>
<td>943, 2875</td>
<td>Kherani, R</td>
<td>612</td>
</tr>
<tr>
<td>Kelly, VM</td>
<td>1290</td>
<td>Keysor, J</td>
<td>1853</td>
<td>Khodayari Moez, E</td>
<td>2303</td>
</tr>
<tr>
<td>Kelmenson, LB</td>
<td>478, 484, 2918</td>
<td>Keystone, EC</td>
<td>443, 451, 461, 495, 512, 513, 1352, 1393, 1470, 1814, 2390, 2391, 2466, 2866, 2955, 2964</td>
<td>Khodra, B</td>
<td>924</td>
</tr>
<tr>
<td>Kelsall, J</td>
<td>2520</td>
<td>Khabbush, A</td>
<td>2342</td>
<td>Khong, ZW</td>
<td>200</td>
</tr>
<tr>
<td>Kelso, S</td>
<td>1346</td>
<td>Khadrawy, A</td>
<td>471, 2366</td>
<td>Khoo, C</td>
<td>2119</td>
</tr>
<tr>
<td>Kelton, KA</td>
<td>2923</td>
<td>Khaleel, MS</td>
<td>2599</td>
<td>Khosla, S</td>
<td>1214</td>
</tr>
<tr>
<td>Keltsev, V</td>
<td>2855</td>
<td>Khalid, E</td>
<td>2901</td>
<td>Khouatra, C</td>
<td>1758, 1779</td>
</tr>
<tr>
<td>Khar, G</td>
<td>825, 1496, 1514, 2521</td>
<td>Khalid, O</td>
<td>441</td>
<td>Khraish, M</td>
<td>613</td>
</tr>
<tr>
<td>Kendler, DL</td>
<td>320</td>
<td>Khalidi, NA</td>
<td>784, 785, 789, 821, 1760, 1767, 1774, 1781, 1849</td>
<td>Khraishi, MMM</td>
<td>545, 2276</td>
</tr>
<tr>
<td>Kendler, D</td>
<td>1887</td>
<td>Khalil, C</td>
<td>2266</td>
<td>Khubchandani, R</td>
<td>95, 2304, 2631, 2958</td>
</tr>
<tr>
<td>Kennedy, A</td>
<td>359, 2784</td>
<td></td>
<td></td>
<td>Khuder, S</td>
<td>755, 1409</td>
</tr>
</tbody>
</table>
Kida, T 272, 1769
Kido, D 1090
Kielhauser, S 2886
Kiely, P 2372
Kiener, HP 696, 865, 966, 1415
Kievit, W 2832
Kihara, M 841
Kikly, K 1576
Kikuchi, H 2732
Kikuchi, J 717
Kikuchi, T 70
Kilgore, M 828
Kilian, K 1002
Kilian, N 2636, 2720
Kilic, E 313
Kilic, G 313
Kilic, L 447, 1240, 1312, 1451, 1522, 2110, 2409
Killeen, O 381
Killeen, OG 382
Kilty, I 544
Kiltz, U 1511, 2498, 2501
Kim, A 38, 1243, 1918
Kim, C 765
Kim, C 201
Kim, D 2517
Kim, DW 2074
Kim, DW 2444
Kim, D Sr. 286
Kim, DK 2733
Kim, E 1409
Kim, GT 2002, 2582
Kim, G 749, 2715
Kim, HR 554, 1369, 2065
Kim, H 1893, 2337, 2347, 2758
Kim, H 1369
Kim, HW 2075
Kim, HA 1868
Kim, H 1152
Kim, HJG 2009
Kim, HJ 982
Kim, HS 1677, 1678, 1868
Kim, H 2088, 2733
Kim, IY 2088, 2733
Kim, J 1177
Kim, JY 87, 1412, 1417, 2746
Kim, JH 2369
Kim, JH 1377, 1495
Kim, JM 975, 1434
Kim, JW 401, 1331, 1493, 2396
Kim, J 2936
Kim, J 1143
Kim, J 2088
Kim, J 2560, 2562
Kim, JY 47
Kim, K 2002
Kim, KJ 716, 2404
Kim, KM Sr. 2708
Kim, K 1016, 2405
Kim, L 91
Kim, L 599, 630, 1530, 1531, 1532
Kim, M 1838
Kim, MJ 1152, 1461
Kim, M Sr. 2708
Kim, M 2495
Kim, M 2495
Kim, NR 558, 2122, 2369
Kim, SH 975, 1434, 1868, 2074
Kim, SH 82
Kim, SK 82
Kim, SY 1375
Kim, SH 1868
Kim, SK 139, 557, 1868
Kim, SC 526, 527, 1113, 1864, 2057, 2230, 2844, 2920
Kim, S 2495
Kim, SH 2444
Kim, S 192
Kim, TH 53, 74, 1016, 1565, 1572, 1938, 2444, 2517, 2519
Kim, TJ 643, 1065
Kim, T 1954
Kim, WU Sr. 286, 716, 1334, 2708
Kim, YG 662, 672, 1110
Kim, YM Sr. 286
Kim, Y 2405
Kim, YS 2444
Kim, YK 2002, 2582
Kim, Y 1677, 1678
Kim, Y 1544
Kimball, A 1309
Kimmel, D 54
Kimoto, M 444
Kimoto, Y 36, 77, 2710
Kimura, F 279, 1698
Kimura, T 330
Kimura, T 130, 2471, 2479, 2480
Kimura, Y 1762
Kimura, Y 2282, 2856
Kimyon, U 802
Kinanah, Y 1753, 1873, 1976, 1978
Kindstedt, E 2791
King, E 1671
King, F 2092
King, J 1042
Kingsbury, DJ 2271
Kingsbury, D 2855
Kingsbury, SR 14L
Kinhikar, A 576
KINIKLI, G 2496
Kinjo, N 370
Kinsey, K 186
Kiptoo, P 1322
Kiraz, S 1174, 1240, 1312, 1451, 2110, 2409, 2743
Kirchner, E 1156
Kirchner, L 1349
Kirino, Y 237, 1150, 1151, 1154, 1460, 2150, 2151
Kirk, CJ 81, 2559, 2587
Kirk, P 2715
Kirkham, B 2536
Kirksey, Y 2715
Kirmayr, K 269, 360
Kirou, KA 1264, 1668
Kirresh, O 102
Kish, J 1040, 1041
Kishi, H 481
Kishi, T 1274, 2142, 2143
Kishida, D 1165, 1732
Kishimoto, D 237, 1460, 2150, 2151
Kishimoto, M 1215
Kishimoto, TK 2091
Kishore, S 1317, 1625
Kisluk, B 269
Kissin, EY 110, 111
Kissling, A 12L
Kitagawa, Y 272
Kitagori, K 1066
Kitahara, Y 1907
Kitai, C 882
Kitamori, T 26, 31
Kitamura, N 555, 870
Kitano, M 2685
Kitas, G 2966
Kitas, GD 147
Kitsch, A 374
Kittaka, M 68
Kittelson, A 1854
Kivistö, S 872
Kivitz, AJ 2L, 601, 615, 620, 1141, 1539, 1686, 1784, 1828, 2091, 2492, 2795, 2796, 2951
Kiwalkar, S 103, 104
Kiyokawa, T 9, 702, 2152, 2588
Kjaergaard, H 2432, 2433
Kjelgaard-Petersen, CF 969, 1063
Klain, D 360, 1359, 1360
Klar, R 512, 1821, 1824
Klarenbeek, PL 1847
Klareskog, L 119, 123, 124, 125, 127, 132, 476, 477, 834, 2826
Klassen, LW 289, 400, 488, 1669
Klatzmann, D 71
Klaudivus, I 1473
Klausmeier, TL 2758
Klearman, M 527, 892
Klein, A 2274
Klein, E 29, 2561
Klein, K 1335
Klein, L 206
Klein, M 1692, 2153, 2154, 2176
Klein-Gitelman, MS 1281, 2631, 2810, 2958
Kleinert, S 414, 2388
Kleinman, J 1263
Kleyer, A 414, 633, 655, 2024, 2406
Klimiuk, PA 2442
Klimowicz, A 1581, 1915
Kline, M 2318
Klingel, K 1718, 1926
Klink, T 783
Klinken, E 2711
Klinkert, ER 573
Kloppenburg, M 1875, 2181, 2208, 2209, 2210, 2211, 2328
Klompenburg, M 1202
Klotsche, J 1283, 1286, 2307, 2959
Klünder, B 505, 1418
Knapp, K 1250, 1454
Knapp, S 2709
Knevel, R 172, 1028
Knight, AM 1266, 2810, 2992
Knight, H 961
Knight, JS 8, 12, 2564, 2761
Knight, S 565
Kowlton, N 2362
<table>
<thead>
<tr>
<th>Name</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kornacker, M</td>
<td>1328</td>
</tr>
<tr>
<td>Koroleva, I</td>
<td>576</td>
</tr>
<tr>
<td>Korrer, S</td>
<td>130</td>
</tr>
<tr>
<td>Korsunski, I</td>
<td>2828</td>
</tr>
<tr>
<td>Korswagen, LA</td>
<td>2542, 2543, 2544</td>
</tr>
<tr>
<td>Kortekaas, M</td>
<td>2210</td>
</tr>
<tr>
<td>Kortekaas, M</td>
<td>265, 2020</td>
</tr>
<tr>
<td>Kosarek, N</td>
<td>2931</td>
</tr>
<tr>
<td>Kosinski, M</td>
<td>2258</td>
</tr>
<tr>
<td>Koskinen Holm, C</td>
<td>2791</td>
</tr>
<tr>
<td>Kostadinova, L</td>
<td>1496</td>
</tr>
<tr>
<td>Koster, MJ</td>
<td>777, 781, 786, 794</td>
</tr>
<tr>
<td>Kostik, M</td>
<td>1283, 1286, 2959</td>
</tr>
<tr>
<td>Kostine, M</td>
<td>2126</td>
</tr>
<tr>
<td>Kostov, B</td>
<td>209, 210, 876, 2123</td>
</tr>
<tr>
<td>Kosuva Ozturk, Z</td>
<td>1496</td>
</tr>
<tr>
<td>Kotake, S</td>
<td>2102</td>
</tr>
<tr>
<td>Kotoku, A</td>
<td>870, 2368</td>
</tr>
<tr>
<td>Kottlil, S</td>
<td>2741</td>
</tr>
<tr>
<td>Kottschade, L</td>
<td>1880</td>
</tr>
<tr>
<td>Kottyan, LC</td>
<td>175, 183, 1663, 2429, 2825</td>
</tr>
<tr>
<td>Koumpouras, F</td>
<td>1661</td>
</tr>
<tr>
<td>Koutsogeorgopoulou, L</td>
<td>1646</td>
</tr>
<tr>
<td>Kouzu, N</td>
<td>2494</td>
</tr>
<tr>
<td>Kowal, C</td>
<td>2741</td>
</tr>
<tr>
<td>Kowal, K</td>
<td>761</td>
</tr>
<tr>
<td>Kowal-Bielecka, O</td>
<td>761, 2662</td>
</tr>
<tr>
<td>Koyama, Y</td>
<td>1700</td>
</tr>
<tr>
<td>Kozlova, A</td>
<td>760</td>
</tr>
<tr>
<td>Kraaij, T</td>
<td>295, 890</td>
</tr>
<tr>
<td>Krabbe, S</td>
<td>236, 586</td>
</tr>
<tr>
<td>Kragstrup, TW</td>
<td>642, 1928</td>
</tr>
<tr>
<td>Krajden, M</td>
<td>1099</td>
</tr>
<tr>
<td>Kramer, E</td>
<td>2982</td>
</tr>
<tr>
<td>Kramer, S</td>
<td>385</td>
</tr>
<tr>
<td>Kramkimel, N</td>
<td>2126</td>
</tr>
<tr>
<td>Krasnokutsky Samuels, S</td>
<td>1144, 2198</td>
</tr>
<tr>
<td>Kraus, VB</td>
<td>1200, 1211, 1380, 1381</td>
</tr>
<tr>
<td>Kraus, WE</td>
<td>1380, 1381</td>
</tr>
<tr>
<td>Krause, A</td>
<td>258, 697</td>
</tr>
<tr>
<td>Krause, A</td>
<td>865</td>
</tr>
<tr>
<td>Krause, M</td>
<td>1307, 2407</td>
</tr>
<tr>
<td>Kreher, G</td>
<td>2994</td>
</tr>
<tr>
<td>Kremer, J</td>
<td>16L, 336, 410, 415, 475, 499, 509, 856, 1341, 1422, 1423, 1558, 1815, 1904, 1905, 2449, 2450, 2453, 2454, 2460, 2962, 2969</td>
</tr>
<tr>
<td>Kreetzler, M</td>
<td>1849, 2659</td>
</tr>
<tr>
<td>Krieg, T</td>
<td>769</td>
</tr>
<tr>
<td>Kriegová, E</td>
<td>1358, 2740</td>
</tr>
<tr>
<td>Krischer, J</td>
<td>1774, 1849</td>
</tr>
<tr>
<td>Krishna, V</td>
<td>2829</td>
</tr>
<tr>
<td>Krishnamurthy, A</td>
<td>65, 970</td>
</tr>
<tr>
<td>Krishnaswami, S</td>
<td>1427</td>
</tr>
<tr>
<td>Kriska, A</td>
<td>2200</td>
</tr>
<tr>
<td>Kristensen, LE</td>
<td>11L, 1541, 2260, 2511</td>
</tr>
<tr>
<td>Kristensen, S</td>
<td>1550</td>
</tr>
<tr>
<td>Kristianslund, EK</td>
<td>342, 1541, 2861</td>
</tr>
<tr>
<td>Kristkov, Z</td>
<td>2285</td>
</tr>
<tr>
<td>Kříštková, Z</td>
<td>1538</td>
</tr>
<tr>
<td>Kroeber, G</td>
<td>586, 594</td>
</tr>
<tr>
<td>Kroese, FGM</td>
<td>560, 569, 573, 1501, 2943</td>
</tr>
<tr>
<td>Krogh, NS</td>
<td>236, 1084, 1550</td>
</tr>
<tr>
<td>Kron, M</td>
<td>1155</td>
</tr>
<tr>
<td>Kronenberg, HM</td>
<td>1094</td>
</tr>
<tr>
<td>Kronenberg, M</td>
<td>862</td>
</tr>
<tr>
<td>Krönke, G</td>
<td>1338, 2406</td>
</tr>
<tr>
<td>Kroon, FPB</td>
<td>1875, 2208, 2209, 2210, 2211</td>
</tr>
<tr>
<td>Kroon, F</td>
<td>1202</td>
</tr>
<tr>
<td>Kroon, HM</td>
<td>1875</td>
</tr>
<tr>
<td>Krug, H</td>
<td>2229</td>
</tr>
<tr>
<td>Krüger, K</td>
<td>414, 1473, 2463, 2498, 2795</td>
</tr>
<tr>
<td>Kruize, AA</td>
<td>553, 876, 2830, 2872</td>
</tr>
<tr>
<td>Krupnikova, SS</td>
<td>96</td>
</tr>
<tr>
<td>Kua, SMY</td>
<td>1702</td>
</tr>
<tr>
<td>Kubacki, M</td>
<td>1057</td>
</tr>
<tr>
<td>Kubassova, O</td>
<td>248</td>
</tr>
<tr>
<td>Kubinova, K</td>
<td>1692, 2153, 2154</td>
</tr>
<tr>
<td>Kubo, K</td>
<td>273</td>
</tr>
<tr>
<td>Kubo, M</td>
<td>170, 2937</td>
</tr>
<tr>
<td>Kubo, S</td>
<td>773, 1179, 2639, 2688, 2792</td>
</tr>
<tr>
<td>Kuboi, Y</td>
<td>397</td>
</tr>
<tr>
<td>Kubota, A</td>
<td>2416</td>
</tr>
<tr>
<td>Kubota, T</td>
<td>1737</td>
</tr>
<tr>
<td>Kubota, T</td>
<td>370, 1279, 2299</td>
</tr>
<tr>
<td>Kucerova, I</td>
<td>6</td>
</tr>
<tr>
<td>Kucharz, EJ</td>
<td>2797</td>
</tr>
<tr>
<td>Kucharzewska, P</td>
<td>967</td>
</tr>
</tbody>
</table>
Kyburz, D 301
Kyndt, X 1758
Kyttaris, VC 688, 2571
L
La, V 2632
Labadia, M 1582
Labonte, A 1026, 2609
Labrador Sanchez, E 684, 1221, 1224, 2003
Labrador-Horrillo, M 849
Lac, P 1325
Lacaille, D 197, 1245
Lacassagne, S 372
Lacerda, M 2603
Lachmann, HJ 361
Lachner, N 1576
Lackner, A 2268, 2646, 2877
Lacoste, P 216
Lacour, JP 2440
LaCroix, A 977, 2851
LaCroix, AZ 2256, 2777
Ladd, J 1203
Laden, F 988
Ladjouz Rezig, A 252
Ladores, S 2256, 2777
Lafargue, T 337, 1234
Lafaurie, G 640
Lafeber, FP 167, 1476, 2458
Laffoon, M 944, 2664
Lafforgue, P 322, 1449
Lafian, A 1228
Lafleur, J 1042
Lafon, R 682
Lafontant, A 468, 1394
Lafourcade, A 2394
Lafyatis, RA 765, 1923, 2664
Laghouati, S 1741
Lagier, RJ 2312, 2327
Lagnefeldt, L 2817
Lagoas Gomes, J 35
Lahdenne, P 2859
Lahiri, M 2625
Lahoud, Y 1220
Lai, CC 268
Lai, J 2996
Lai, L 759, 953, 1577, 1941, 2637
Lai, Q 2040
Lai, W 1311, 2601
Lai, X 1311
Lai, Y 2101
Lai, ZW 2572, 2763
Laird, B 1258, 2696
Laiz, A 1232, 2526
Lajam, A 759, 1941
Lajas, C 2419
Lajas Petisco, C 1443
Lakatos, P 320
Lakis, VA 491
Lakota, K 704, 2719
Lakshminarayanan, S 636
Lales, G 2315
Lam, E 871
Lam, HM 2244
Lamas, JR 2419
Lamb, J 853
Lambert, C 2084
Lambert, M 1685, 1758, 2348
Lambert, M 2126
Lambert, N 388
Lambert, RG 586, 587, 1507, 2802, 2967
Lamblin, N 1685
Lambotte, O 1741
Lambrecht, I 1222
Lammertsma, A 244
Lamot, L 2334
Lamot, M 2334
Lampa, J 423, 1344
Lampe, J W 1203
Lampe, PD 1203
Lamua, JR 1517, 1518, 1519
Lamuedra, A 396
Lan, WC 1128
Lanata, C 229, 230, 983, 1085
Lancelot, M 127
Lanchbury, JS 1371
Land, J 1782, 1846
Landesmann, U 452
Landewé, RBM 17L, 427, 587, 591, 592, 593, 640, 1507, 1512, 1523, 1542, 1787, 1831, 1993, 2497, 2501, 2502, 2505, 2802, 2803, 2806, 2967, 2970
Landi, M 1564, 2551, 2554
Landon Cardinal, O 5L
Landron, C 797
Landsberg, P 430
Lane, J 45
Lane, J 303
Lane, NE 13L, 319
Lane, NE 54, 115, 935, 1204, 2180, 2205
Lang, A 1946
Lang, B  2317
Langdahl, B  2367
Langefeld, CD  164, 2429
Langer, HE  2973
Langford, CA  784, 785, 789, 821, 1752, 1755, 1760, 1767, 1774, 1783, 1844, 1849
Langguth, D  1431
Langholff, W  344, 473, 2951
Langley, RGB  627
Langowski, J  2715
Langsetmo, L  2179
LANNA, CC  723
Lanoy, E  1741
Lanyon, P  565, 874
Lanz, S  2084
Lanza, M  408, 955
Lao, C  2095
Lao, N  1080
Lao, VW  1903
Lao, VW  1903
Lapeyre-Mestre, M  819
Lapin, WB  378
Lapunzina, P  1891
Laragione, T  1407, 1408, 2829
Larche, M  2016, 2942, 2967
Lareau, C  184
Laredo, JD  588, 589, 590, 1504
Larena, C  2130
Largo, R  396, 1939, 2056
larici, AR  742
Larkin, T  2753, 2912
Larman, HB  2876
Larmore, CJ  499
Laroche, F  1973
Larosa, M  1292
Larrañaga, JR  2841
Larroche, C  873, 1491
Larroude, M  332
Larroude, MS  269, 1225, 1645
Larsen, E  1830
Larsson, S  1189
LaSalle, B  2665
Lasca, L  2008
Laska, MJ  1077
Laskari, K  1387, 2744
Laskin, C  1310
Laslett, L  1850
Lassere, M  2845
Lateef, A  1629, 2625
Lato, V  1608
Lattermann, C  934
Latuhihin, T  2801
Lau, A  2383
Lau, CS  1629
Lau, CC  2784
Lau, C  1598
Lau, E  980, 1043
Lau, P  2119
Lau, W  2574
Lau, WL  2481
Lau, X  1903
Laufer, VA  2429
Laumann, A  2960
Launay, D  1685, 2348
Launay, JM  71
Launay, O  2415, 2606
Laurent, R  808, 809
Laurindo, IMM  278, 541
Lauver, D  1087, 1088
LaValley, MP  437, 539, 2184
Lavareello, C  2956
Lavazais, S  497
Lavet, C  48
Lavi, I  2529
Lavrovsky, Y  1163
Law, KS  2574
Law, S  1536
Law, SC  2711
Law, WG  1702
Lawrence, C  30, 2703
Lawrence, P  909, 1042
Lawson, C  565, 1500
Lawson, E  1626
Laxer, R  1892
Laxer, RM  373, 1285
Lay, YAE  54
Layh-Schmitt, G  652, 653, 1566, 2773
Layrolle, P  2079
Layton, R  846
Lazaretti-Castro, M  1886
Lazariciu, I  533, 1440
Lazaro, D  2893
Lazaro, E  796, 814, 2597, 2754, 2978
Lazarow, E  1273
Lazowick, E  1566
Lazzari, AA  91
Lazzaroni, MG  1292
Le, L  578, 1998
Le Bars, M  609, 1468, 1469, 2452
Le Bras, A  1759
Leung, E 1326
Leung, J 1243
Leung, J 1173
Leung, YY 1577, 1941
Leung, YT 1660
Levartovsky, D 1648
Levescot, A 297, 2712
Levesque, K 164
Levesque, MC 1196, 1202, 1211
Levi, E 627
Levin, M 2937
Levin, S 1328
Levine, AB 1264
Levine, JS 37
Levinson, BA 1843
Levinson, J 1633, 2627
Levy, DM 1271, 1599, 2317, 2631, 2958
Levy, GD 2848
Levy, G 1196, 1202
Levy, O 398
Levy, RA 10, 2760
Levy, S 398
Lewiecki, EM 1886, 1887
Lewinson, R 121
Lewis, CE 857, 859, 932, 2178, 2184, 2197, 2218, 2949
Lewis, DM 46, 559, 2703
Lewis, J 2041
Lewis, K 1328
Lewis, M 1581
Lewis, M 685
Lewis, MJ 43, 1410, 2634
Lewis, N 25
Lewis, SJ 2235
Lezcano, S 2632
Lezcano-Valverde, JM 420
Lheritier, K 365
Lhoste, Y 50
Li, C 2750
Li, C 102
Li, C 1883
Li, C 544
Li, D 451
Li, D 1060
Li, E 1903, 2545
Li, E 2699
Li, G 2383
Li, H 34, 2569
Li, H 2750
Li, H 2241
Li, H 285
Li, J 449, 1185
Li, J 2146
Li, J 189
Li, J 34, 832, 2567, 2814
Li, L 961, 2790
Li, L 1025
Li, L 197, 315, 353, 2240, 2269, 2954
Li, L 403
Li, M 1507, 1787, 2501
Li, M 42, 2644
Li, N 630, 1477, 1530, 1531, 2836
Li, N 749
Li, P 2256, 2777
Li, Q 518
Li, QK 878
Li, Q 1210
Li, S 2134
Li, S 758, 2157
Li, S 1406
Li, S 136
Li, SC 1285
Li, TK 1903
Li, T 41
Li, T 2146
Li, W 503
Li, W 504, 1458
Li, W 1071
Li, W 977, 2851
Li, X 2855
Li, XY 197
Li, X 1996, 2038
Li, X 876
Li, X 1138
Li, X 1005
Li, X 470, 1475, 2383, 2908
Li, X 2101
Li, Y 2713
Li, Y 1974
Li, Y 2241
Li, Y 1904
Li, Y 2702
Li, Y 1554
Li, Y 2882
Li, Y 2579
Li, Y 1883
Li, Y 2451
Li, Y 1524
Li, ZG 1251
Li, ZG 1629
Li, Z 1005
Li, Z 1821, 2242, 2451
Listing, J 1510
Litinsky, I 1648
Litman, HJ 410, 1341, 1422, 2450
Little, C 808
Littlejohn, G 1354
Liu, A 514
Liu, B 1173
Liu, CC 1673
Liu, E 38
Liu, F 2205
Liu, FC 2000, 2052
Liu, G 2574
Liu, HX 1251
Liu, H 1575
Liu, H 1311
Liu, J 1251
Liu, J 897
Liu, J 2882
Liu, J 2750, 2751
Liu, J 2290
Liu, J 2632
Liu, J 1113, 2844
Liu, L 2711
Liu, M 1425, 1552, 1553, 1554
Liu, M 1209, 1210
Liu, ML 2579
Liu, Q 1005
Liu, Q 1015
Liu, Q 1711, 1727
Liu, R 1875, 2181, 2208
Liu, S 832, 2567, 2814
Liu, T 937
Liu, W 1196, 1202, 1251, 2436
Liu, WC 1251
Liu, W 1246
Liu, X 2964
Liu, XY 2436
Liu, X 2101
Liu, X 1524
Liu, Y 224
Liu, Y 2659
Liu, Y 970
Liu, Y 1326, 2451
Liu, Y 939
Liu, Y 1251
Liu, Y 234
Liu, Y 928
Liu, Y 292
Liu, Z 2568
Liu-Ambrose, T 315
Liu-Bryan, R 2089
Liu-Bujalski, L 2565
Livneh, A 361, 1012
Llamas, P 1939
Llanos, C 2643
Lliso Ribera, G 1410
Llorca, J 644, 1400, 1411, 2343
Llorens, V 1516
Llorente, I 2130
Lloves, N 155, 360
Lloyd, KA 476, 477
Lluch, P 780
Lo, E 1203
Lo, GH 2196, 2199, 2200, 2201, 2691
Lo, KH 599, 630, 1530, 1531, 1532
Lo, YTL 711
Lo Giudice, LF 1557
Lo-Ciganic, WH 1866, 2906
Loaiza Gongora, JL 2003
Lobo, D 1219
Lobo, JL 137
Lobosco, S 456, 457, 1513
Locatelli, F 2166
Lochhead, R 1020
Lockshin, M 108, 2581
Loeuille, D 592, 1373, 2806
Lofek, S 769
Loft, AG 1550
Loftus, EV 16L
Logeart, I 587, 2802
Lohmander, LS 1189
Lohr, KM 1046
Loignon, RC 1666
Lois-Iglesias, A 1587, 2619
Lojacono, A 1300
Lojo, L 2130
Lomakina, O 386, 2279, 2280
Lomax, KG 361
Lombardi, S 1621, 1623, 2807
Lomholt, S 642
Londoño Jiménez, A 683
Long, A 2568
Longchamps, MP 466, 1027
Longman, R 594
Longobardi, S 30
Lönnblom, E 1323
Lood, C 485, 1667, 1916, 2641, 2917
Loogier, L 177
Looney, RJ 1655
Loos, BG 492
Lopes, C 35, 611
Lopes, JB 1961
Lopes, M 668, 1616, 2603, 2760
Lopes Barreto, D 2048
López, AM 2008
Lopez, A 1801
López, P 28
López de Figueroa, P 904
López de Recalde, M 2094
López Dupla, M 209
Lópe Longo, FJ 159, 632, 1520, 1587, 1588, 1612, 1972, 2129, 2130, 2488
Lopez Montesinos, B 2297
López- Montesinos, B 2857
López-Carrasco, G 1492
López-Cerón, A 1972
López-Corbeto, M 498
López-Ferretis, H 1445, 2360, 2361
López-González, R 2112
López-Longo, J 2722, 2723
López-Medina, C 1545
López-Mejías, R 644, 1379, 1400, 1411, 2343, 2403, 2435
Lopez-Olivo, MA 118, 531, 1052, 2128, 2262, 2395, 2483
López-Otin, C 904
Lopez-Pedrera, C 41, 391, 392, 1466, 2435, 2655, 2656, 2764
Lopez-Romero, P 320, 418, 513, 1821
López-Salguero, S 1132, 1140, 1227
Lopez-Velazquez, M 1598
Lopiz, Y 2419
Lorentzen, M 2800
Lorentzon, M 318
Lorenz, HM 1469
Lorenz, HM 414
Lorenz, H 1468, 2452
Lorenzen, T 781
Lorenzi, M 925
Lorenzin, M 2522
Lorenzini, S 2899
Lorenzo, C 2358
Lorenzoni, V 1622
Loricera, J 260, 498, 780, 816, 817, 2721, 2724, 2857
Lories, R 906, 1945, 2512
Lorig, K 2046
Losina, E 1536, 1796, 2756, 2833, 2946
Lotz, M 904
Lou, YQ 1251
Loughin, T 2289
Loughran, T Jr. 485
Lourenço, DM 2958
Lourenco, E 692
Louthrenoow, W 350, 1629, 2950
Louveau, B 2394
Louw, I 2492
Love, T 2524
Lovejoy, T 2221
Lovell, DJ 953, 2270, 2271, 2272, 2290, 2333, 2855, 2858
Low, AHL 759, 1577, 1702
Low, BPL 200
Low, K 2848
Low, P 244
Low, R 1030
Lowder, C 1881
Lowe, D 2322
Lowe, E 81, 2559
Lowerison, M 121
Lowichik, A 379
Loyau, S 2775
Loyd, B 1854
Loyo, E 2306
Loyola-Sánchez, A 228
Loza, E 2098, 2379
Loza, MI 1931
Loza, M 548, 549, 1478, 2963
Lozada, AC 411
Lozano-Rivas, N 1587, 1612
Lu, B 858, 917, 978, 1796, 1863, 1953, 2384, 2944
Lu, CC 2000, 2052
Lu, F 2057
Lu, G 1060
Lu, H 1004
Lu, L 328, 895, 1131, 1610, 1789, 2614
Lu, L 1871
Lu, N 859, 1130, 1212, 1951, 2077, 2921, 2990
Lu, R 1657, 1658, 2596, 2600, 2820, 2875, 2977
Lu, WS 1114
Lu, X 2134
Lu, PhD, X 175
Lubberts, E 1747, 1792, 1944
Luber, M 655, 864
Lubin, O 1872
Mackey, M 2610
MacKrill, K 1107
MacNeill, S 1328
Macovei, L 997, 2660
Macwana, S 1657, 1658, 2977
Madaio, M 1833
Madaio, M 1833
Maddox, A 2825
Maddox, J 318
Mader, R 2182
Madjoun, HM 1615
Magnaguagno, F 2300
Magnusen, R 496
Magnuson, B 2259, 2956
Magnusson, S 1479
Magrey, MN 334, 2518, 2803
Magri, S 1079, 1564
Magro-Checa, C 1587
Maguire, P 576, 875
Maharaj, A 634
Mahato, K 1669
Maher, J 1069
Maheshwari, A 2374
Mahler, EAM 1205
Mahler, M 727, 747, 945, 1722
Mahlch, J 140
Mahmoud, TG 435, 445, 1241
Mahnke, L 2586
Mahomed, N 214, 2235, 2236
Mahon, O 2900
Mahowald, M 2229
Mahr, A 437, 810
Maica, G 435, 445
Maica, GL 1241
Maidhof, A 964
Maier, A 19
Maier, A 1292
Maillard, H 1685
Maiz-Alonso, C 2112, 2297, 2402
Major, G 339
Major, T 1104, 2066
Mak, A 2573
Mak, Q 1903, 2939
Mak, S 1592
Mak, T 1833
Makdissi, J 874
Makhdoum, JP 2737
Makinde, H 29, 1835
Makino, H 1013, 1751, 1762, 1778
Makol, A 1662, 1695, 1816, 2105, 2389, 2657
Makovey, J 2186
Makris, UE 2, 204, 1799, 1852
Maksymowych, M 586
Maksymowych, WP 587, 594, 922, 1025, 1546, 2802, 2967
Malaab, M 1726
Malagon, MDM 391
Malangone-Monaco, E 1057
Malatestinic, W 1555, 2532, 2533
Malättia, C 2300
Malaviya, R 1428, 2704
Malavolta, N 638, 1292
Malayeri, A 263, 779, 820, 1845
Malcarne, VL 2049, 2695
Malcus, C 2348
Maldini, C 437, 810
Maldonado, F 2100
Maldonado, G 1230
Maldonado, I 277
Marengo, F 2021
Margaretten, M 1081, 1798
Marhadour, T 574
Maria, NI 2570, 2828
Mariampillai, K 5L
Mariani, L 1849
MARIANO, RZ 568
Maribo, T 1802
Marie, I 2671
Mariette, X 1463, 1468, 1469, 2452
Mariette, X 873, 876, 877, 1442, 1491, 1795, 1809, 1823
Marighela, T 751
Marin, AI 483
Marin, C 2062
Marin, F 320
Marin, G 2940
Marin, J 1350, 1645, 2021
Marinelli, K 821
Marini, R 2956
Marinsek, N 361
Marion, MC 164
Mariz, H 707
Marken, J 1667, 2644
Markham, A 2813
Markiewicz, M 2642
Marklein, B 1072, 1793
Markomichelakis, N 2744
Markovic, SN 1880
Markusse, IM 429
Marmorstein, M 1166
Maroof, A 73, 1571, 1936
Marotta, A 1366
Marozio, L 1300
Marques, MC 2252
Marques, M 2042
Marra, C 199
Marrache, AM 2459
Marrero, B 939, 2347
Mars, N 1054, 2834
Marsais, F 497
Marsal, J 2511
Marsal, S 649
Marsh, G 675
Marshall, L 587, 2276, 2298, 2455, 2802
Marshall, L 2336, 2341, 2342
Marshall, SW 926
Marston, BA 104
Marta, D 2660
Marte, J 1182
Martel-Pelletier, J 52, 57, 1196, 1197, 1208, 2192
Martens, M 1074
Martin, A 242
Martin, A 997
Martin, J 1411, 1713, 2343, 2826
Martin, MA 1588
Martin, MD 1171
Martin, RS 888
Martin, RW 1385, 2782
Martin, R 1523
Martin, T 814
Martin, T 41
Martin, W 1392
Martín Nares, E 18, 2907
Martin Silva, N 2754, 2762
Martin-Cascon, M 2608
Martín-Domenech, R 2277, 2883
Martín-Esteve, I 2379
Martín-López, M 2402
Martín-Mola, E 654, 2422, 2475
Martín-Varillas, JL 260, 780, 816, 817, 1169, 2112, 2402, 2527, 2721, 2722, 2723, 2724, 2857
Martínez, A 1450
Martínez, A 1448
Martínez, H 1187, 1190, 1203
Martínez, MA 849
Martínez, S 2570
Martínez, S 851
Martínez, S 2126
Martínez Acosta, L 2112
Martínez Alberola, MN 2883
Martínez Cordellat, I 684, 1221, 1224, 2003
Martínez Costa, L 2721, 2722, 2723
Martínez Frances, M 2003
Martínez Osuna, P 513
Martínez P, JM 2109
Martínez Taboada, V 1587
Martínez- Costa, L 1169
Martínez-Barrio, J 159, 632, 1520, 1972, 2129, 2130, 2488
Martínez-Becerra, MJ 1172
Martínez-Bonet, M 2826
Martínez-Flores, G 1445, 1975, 2360, 2361
Martínez-Galla, D 667, 671
Martínez-Lavín, M 154
Martínez-Martínez, LA 154
Martínez-Martínez, MU 667, 671, 1445, 1975, 2360, 2361
Martínez-Quintanilla Jiménez, L 2375
Martínez-Rodríguez, I 260, 817
Martínez-Vidal, MP 2883
Martínez-Zapico, A 2841
Martini, A 1278, 1744, 2259, 2270, 2271, 2272, 2273, 2300, 2333, 2855, 2956
Martini, G 1287, 2295, 2314
Martino, S 2259, 2956
Martins, K 274
Martins, L 723
Martins* Contributed equally, K 2837
Martire, MV 2021
Martis, N 2716
Marton, A 720
Martynov, V 756, 1707, 1730
Marut, W 1729
Marzan, K 2271
Marzan, KA 361
Marzo-Ortega, H 597, 1507, 1529, 1539
Mas, AJ 2112
Masani, N 1770
Masayuki, Y 2220
Mascarenhas, S 2031, 2032
Mascella, F 638
Masetto, A 612
Mashiko, T 395
Maslow, G 910
Massard, C 1741
Massardo, L 1654, 2924
Massarotti, E 673, 680, 719
Massarotti, M 2397
Masse, C 645
Massicotte, F 1817
Master, H 1867, 2767, 2949, 2991
Masui, K 854
Masuoka, S 1414, 2428
Masyan, H 803
Matei, C 780
Mateus, A 1706
Mathews, D 1867, 2767, 2949, 2991
Mathialahan, T 2380
Mathian, A 2606
Mathias, A 1329
Mathiesen, A 265, 2020
Mathieu, A 1300
Mathieu, AL 2348
Mathis, N 1918
Mathsson-Alm, L 486
Matigian, N 1576
Matignon, M 2754
Matmusaev, M 660
Matranga, C 2837
Matsos, M 1599
Matsubara, H 1048
Matsubara, T 703
Matsuda, M 2494
Matsuda, M 2427
Matsuda, S 2789
Matsuda, S 417
Matsueda, Y 1761
Matsui, K 841
Matsui, K 2685
Matsui, S 1157
Matsui, T 1593, 2249
Matsumoto, AK 206, 495
Matsumoto, I 393, 2873
Matsumoto, K 798
Matsumoto, M 70
Matsumoto, T 540, 1010, 1064
Matsumoto, T 1149
Matsumoto, T 319
Matsumoto, Y 2558
Matsunaga, N 2799
Matsunaga, T 1180
Matsuo, H 431, 2441
Matsuo, H 170, 1104, 2087
Matsuo, S 1013, 1751, 1762, 1778
Matsuoka, H 1447
Matsuoka, N 238, 1441
Matsushima, S 1999
Matsushita, I 330
Matsushita, M 1447
Matsushita, T 21
Matsuura, I 692
Matsuzaki, H 79
Mattar, M 2741
Matteson, EL 13, 32, 174, 792, 812, 813, 1032, 1109, 1160, 1161, 1695, 1749, 1750, 1802, 1816, 1819, 1959, 2105, 2389, 2702
Matthias, P 2709
Matthias, T 1969
Mattiello, A 913
McQueen, FM 1992
McQuitty, S 2269
McWherter, C 2089
McWilliams, L 448, 948
Md Yusof, MY 679, 1917, 2816
Meara, A 1231, 1257, 1614, 1615, 2598, 2725
Mease, PJ 2L, 16L, 17L, 595, 596, 602, 603, 604, 605, 606, 607, 608, 609, 610, 614, 618, 620, 621, 622, 626, 1425, 1515, 1552, 1553, 1554, 1555, 1560, 1787, 2531, 2532, 2533
Mecoli, CA 748
Medema, JK 1196, 1202, 1211
Mediero, A 1939, 2056
Medina, G 14
Medina, JP 2056
Medina, MA 360, 1359, 1360
Medina, M 450, 687, 1378
Medina Bornachera, D 1645
Medina-Rodriguez, FG 2445
Medina-Rosas, J 634, 1599
Medsger, TA Jr. 919, 944, 946, 2664, 2930
Meduri, A 741
Meednu, N 22, 561, 1405, 1406
Meehan, R 525
Meerpohl, J 15
Meerwein, S 10L
Mehri, N 1585
Mehta, B 842, 2051
Mehta, BY 218, 220, 221, 923, 1885, 2410
Mehta, BK 775, 2931
Mehta, D 45
Mehta, J 2994
Mehta, NN 899
Mehta-Lee, S 2813
Meier, L 968
Meier-Kriesche, U 1429
Meijboom, L 257
Meinão, I 845
Meini, A 2259
Meiser, K 17L
Meisner, PD 318
Meißner, Y 1430
Melero González, RB 1587, 1612
Melikoglu, M 2462, 2747
Melikoglu, M 2204, 2496
Melim, T 2568
Melki, I 1666
Melkie, A 225
Mellemkjær, L 11L
Meller, S 553
Melles, RB 2614
Mellins, ED 1728
Melnick, J 576, 676, 1372
Melnick, JA 336
Melo, F 269, 360
Melo Gomes, JA 2859
Melo-Gomes, JA 1278
Melsens, K 752
Melsons, K 1248
Melton, LJ III 1214
Meltzer, M 225
Melville, SA 676, 1372
Mena-Vazquez, N 498
Mendel, A 1305
Méndez, GP 2643
Mendez, L 232
Mendez, L 1686
Mendez, M 1645
Mendez-Agrusa, B 1229
Mendoza, FA 754, 1248
Menegatti, S 2801
Meneghel, A 1287, 2295, 2314
Meneses, K 2256, 2777
Meneses, S 2186
Menezes, P 1961
Meng, A 1329
Meng, H 2564, 2761
Meng, QL 1251
Meng, T 356
Mengistu, Y 225
Mennuni, L 955
Menon, S 616, 617, 620
Menon, V 212, 468, 1394
Menor Almagro, R 1158, 2284
Menz, H 2765
Mera, A 780, 816
Mercedes-Núñez, I 543, 1965
Mercer-Rosa, LM 1266
Merciris, D 497
Merino, R 2859
Merkel, PA 18L, 784, 785, 789, 820, 821, 893, 896, 1166, 1752, 1760, 1767, 1774, 1783, 1844, 1849, 2100, 2737, 2935
Merle, H 226
Merlevede, B 1716
Merola, J 2539
Merola, JF 613
Meroni, M 698, 930, 1292
Meroni, PL 12, 1292
Merrien, D 1758
Merrill, JT 681, 888, 889, 1238, 1606, 1627, 1657, 1658, 1664, 1838, 1841, 2585, 2600, 2653, 2820, 2925, 2977
Merriman, ME 1104
Merriman, TR 170, 1104, 1106, 1108, 1127, 2061, 2066, 2087, 2843, 2897
Merritt, K 1668
Mertens, JS 1729
Mertoglu, S 3
Mh, CA 1171
Meyers, KC 1171
Meyers, M 2174
MEYER, N 1491
Mezian, K 305
Mi, C 2241
Mi, Q 2346
Mian, A 1433
Miao, F 2345
Miao, W 645
Miceli, J 1601, 2033
Miceli-Richard, C 584, 646, 1523
Michallet, AS 2348
Michalska, M 550, 1905, 2460, 2962
Michaud, D 913
Michaud, K 131, 135, 144, 472, 508, 546, 842, 1103, 1252, 1357, 1365, 1649, 2051, 2376, 2377, 2392, 2410, 2457, 2783
Michel, G 2780
Michelsen, B 342, 1344, 1345, 2503
Michet, CJ Jr. 1109, 2100
Michot, JM 1741
Michou, L 466, 1027
Micu, MC 1373, 2055
Midtvedt, O 743, 744, 947, 2980
Midtvedt, Ø 1002
Midzic, I 1092
Mieles, M 1230
Miettunen, P 1894, 2316, 2859
Migalovich Sheikhet, H 1731
Migita, K 76
Migli, C 356
Migliore, F 407, 721
Migliorini, P 1486
Mihai, C 997, 2660, 2662, 2683
Mihu, R 2691
Mijares, V 644, 1400, 1411, 2343
Mijnheer, G 953
Mika, O 1980
Mikaelian, I 2562
Mikdashi, JA 715
Mike, E 1836
Miklos, D 1811
Mikulková, Z 2740
Mikuls, TR 135, 144, 289, 400, 433, 472, 488, 1036, 1124, 1357, 1365, 1971, 2376, 2377, 2378, 2392, 2848, 2893, 2915, 2918
Milani, C 1712
Milbers, K 2778
Milchert, M 781
Milic, V 877
Milicescu, M 997
Milisenda, JC 849, 2131
Millan, AM 2402
Millan, M 2094
Millen, A 2355, 2356
Miller, D 183, 2825
Miller, E 117
Miller, FD 2387
Miller, FW 1274, 2136, 2137, 2140, 2141, 2142, 2143, 2337
Miller, J 2635
Mosho, MW 952, 1743, 2569
Moskalev, A 2279, 2280
Mosor, E 848
Mosquera, A 2306
Moss, A 1328
Moss, L 1004
Moss, S 1004
Moss, T 2049
Mossel, E 2943
Mostafa, N 1418
Mota, F 222
Motomura, H 330
Motwani, M 298
Moulin, B 2671
Moulin, P 1784
Moulin, G 819, 2100, 2661
Moulton, VR 952, 1743, 2569, 2707
Mountz, JD 34, 832, 2567, 2814
Moura, CS 443, 461, 2391, 2785
Mouriño-Rodriguez, C 1587
Mourits, MJ 573
Mouterde, G 2055, 2940
Mouthon, L 769, 1070, 1754, 1757, 1758, 1763, 2671, 2738, 2739, 2754, 2888, 2932
Mouyis, M 1810
Movahedi, M 432, 470, 1475, 2908
Movasat, A 1738
Mowrey, W 683
Moya, P 1467
Moya Herraiz, A 1224
Moyano, S 1483, 1557
Moylett, J 288
Mozaffarian, N 1909
Mpofu, S 17L
Mrázek, F 1358, 2740
Mrukowicz, C 1003
Mtiabaa, M 1465, 1817
Mu, J 1669
Mu, R 2242
Muchamuel, T 81, 2559
Mudano, AS 350, 357, 2256, 2777, 2950
Mudri, S 1328
Mudumba, S 2170
Mueller, DL 476, 477, 834
Mueller, E 1250, 2115
Mueller, K 2254
Mueller, R 535, 536, 2469, 2909
Mueller-Lutz, A 1998
Muhiedidine, L 8L
Muiño, G 2008
Mukadam, Z 1171
Mukae, H 2144
Mukai, T 68, 69, 79, 1324, 2563
Mukherjee, D 1433
Mukherjee, R 1568
Mukhtyar, C 781
Muler Mendoza, J 2499
Mulhearn, B 1736
Mulheren, R 2147
Mullan, R 2507, 2508
Mullazehi, M 132
Müller, C 1708
Müller, F 2253
Müller-Ladner, U 1683, 1935, 1943, 2662, 2683
Mullis, S 2029
Mulvihill, E 2027
Mumbach, M 2930
Munera, C 15L
Munhoz, G 2603
Munir, A 1748
Muñoz, A 1158
Muñoz, JS 2021
Muñoz, S 1159, 2098
Muñoz, S 1645
Muñoz-Fernández, S 1361, 1509
Muñoz-Louis, R 543, 1965, 2021
Munro, J 2896
Munro, J 95
Munroe, ME 901, 984, 1644, 1657, 1658, 2600, 2977
Munteanu, S 2765
Muntyanu, A 647
Murage, MJ 1555, 2532, 2533
Muraguchi, A 481
Murakami, K 479, 1066, 2160, 2164
Murakami, M 1568
Murakoshi, D 1698
Muram, D 409, 499, 525
Muram, TM 1555, 2532, 2533
Muraoka, S 1414
Murari-Nascimento, P 276
Murasawa, A 412
Murata, O 2125
<table>
<thead>
<tr>
<th>Name</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muratore, F</td>
<td>790, 791, 815, 1075</td>
</tr>
<tr>
<td>Muratti, E</td>
<td>1817</td>
</tr>
<tr>
<td>Murbæch, K</td>
<td>744</td>
</tr>
<tr>
<td>Murias, S</td>
<td>376, 2758</td>
</tr>
<tr>
<td>Muroasaki, T</td>
<td>1776</td>
</tr>
<tr>
<td>Murphy, CL</td>
<td>371</td>
</tr>
<tr>
<td>Murphy, G</td>
<td>2507, 2508</td>
</tr>
<tr>
<td>Murphy, K</td>
<td>2282</td>
</tr>
<tr>
<td>Murphy, L</td>
<td>234, 1004, 1955, 2216, 2987</td>
</tr>
<tr>
<td>Murphy, PM</td>
<td>1153</td>
</tr>
<tr>
<td>Murphy, R</td>
<td>1104</td>
</tr>
<tr>
<td>Murphy, SL</td>
<td>1855</td>
</tr>
<tr>
<td>Murray, A</td>
<td>2753, 2912</td>
</tr>
<tr>
<td>Murray, A</td>
<td>256, 2005</td>
</tr>
<tr>
<td>Murray, B</td>
<td>2562</td>
</tr>
<tr>
<td>Murray, CW</td>
<td>500, 2493</td>
</tr>
<tr>
<td>Murray, D</td>
<td>1752</td>
</tr>
<tr>
<td>Murray, ET</td>
<td>1800, 2313</td>
</tr>
<tr>
<td>Murray, J</td>
<td>475</td>
</tr>
<tr>
<td>Murray, K</td>
<td>1256</td>
</tr>
<tr>
<td>Murray, S</td>
<td>2890</td>
</tr>
<tr>
<td>Murray Brown, W</td>
<td>2706</td>
</tr>
<tr>
<td>Murtaugh, M</td>
<td>2666</td>
</tr>
<tr>
<td>Muscarà, M</td>
<td>1300</td>
</tr>
<tr>
<td>Musetti, MC</td>
<td>1194</td>
</tr>
<tr>
<td>Mushlin, A</td>
<td>1050</td>
</tr>
<tr>
<td>Muskat, K</td>
<td>1406</td>
</tr>
<tr>
<td>Mussano, E</td>
<td>269</td>
</tr>
<tr>
<td>Musselli, C</td>
<td>45, 675, 2607</td>
</tr>
<tr>
<td>Musset, L</td>
<td>2170</td>
</tr>
<tr>
<td>Muszinsky, P</td>
<td>2008</td>
</tr>
<tr>
<td>Mutebi, A</td>
<td>363, 2448</td>
</tr>
<tr>
<td>Muthana, M</td>
<td>288</td>
</tr>
<tr>
<td>Mutti, A</td>
<td>152</td>
</tr>
<tr>
<td>Mutz, J</td>
<td>2041</td>
</tr>
<tr>
<td>Myasoedova, E</td>
<td>1032, 1802, 1819</td>
</tr>
<tr>
<td>Mydel, P</td>
<td>1456</td>
</tr>
<tr>
<td>Mynard, K</td>
<td>18L</td>
</tr>
<tr>
<td>Mysler, E</td>
<td>1645, 1906</td>
</tr>
<tr>
<td>Myśliński, R</td>
<td>202, 830</td>
</tr>
<tr>
<td>Möller, JM</td>
<td>236</td>
</tr>
<tr>
<td>N</td>
<td>2758, 2870</td>
</tr>
<tr>
<td>Naber, H</td>
<td>188, 195</td>
</tr>
<tr>
<td>Naborzyn, G</td>
<td>29, 1581, 1582, 1915, 2561</td>
</tr>
<tr>
<td>Nada, R</td>
<td>1765</td>
</tr>
<tr>
<td>Nada, S</td>
<td>755, 1710</td>
</tr>
<tr>
<td>Naden, RP</td>
<td>1589</td>
</tr>
<tr>
<td>Naderi, N</td>
<td>811</td>
</tr>
<tr>
<td>Nadkarni, G</td>
<td>1631</td>
</tr>
<tr>
<td>Nagahara, H</td>
<td>272, 1769</td>
</tr>
<tr>
<td>Nagai, H</td>
<td>237, 1460, 2151</td>
</tr>
<tr>
<td>Nagai, K</td>
<td>551</td>
</tr>
<tr>
<td>Nagakura, T</td>
<td>1279</td>
</tr>
<tr>
<td>Nagamine, R</td>
<td>2177</td>
</tr>
<tr>
<td>Nagano, S</td>
<td>238, 1441, 2710</td>
</tr>
<tr>
<td>Nagaraj, S</td>
<td>1093</td>
</tr>
<tr>
<td>Nagaraja, V</td>
<td>1701</td>
</tr>
<tr>
<td>Nagasaka, K</td>
<td>841, 1013, 1751, 1762</td>
</tr>
<tr>
<td>Nagasawa, H</td>
<td>2017</td>
</tr>
<tr>
<td>Nagasawa, K</td>
<td>1154</td>
</tr>
<tr>
<td>Nagasawa, Y</td>
<td>555</td>
</tr>
<tr>
<td>Nagasu, A</td>
<td>68, 69, 79, 1324, 2563</td>
</tr>
<tr>
<td>Nagasu, H</td>
<td>2563</td>
</tr>
<tr>
<td>Nagata, Y</td>
<td>238</td>
</tr>
<tr>
<td>Nagatani, K</td>
<td>1776</td>
</tr>
<tr>
<td>Nagayasu-Tanaka, T</td>
<td>389, 390</td>
</tr>
<tr>
<td>Nagore, D</td>
<td>1448</td>
</tr>
<tr>
<td>Nagpal, S</td>
<td>1899</td>
</tr>
<tr>
<td>Nagua, V</td>
<td>1766, 2676</td>
</tr>
<tr>
<td>Nah, SS</td>
<td>1868</td>
</tr>
<tr>
<td>Nahar, J</td>
<td>2675</td>
</tr>
<tr>
<td>Nahes, SJ</td>
<td>700, 701, 2312, 2327, 2838</td>
</tr>
<tr>
<td>Naidu, S</td>
<td>1765, 2010</td>
</tr>
<tr>
<td>Naik, H</td>
<td>2607</td>
</tr>
<tr>
<td>Naik, P</td>
<td>1363</td>
</tr>
<tr>
<td>Nair, A</td>
<td>2648, 2976</td>
</tr>
<tr>
<td>Nair, D</td>
<td>1680</td>
</tr>
<tr>
<td>Nair, N</td>
<td>1017</td>
</tr>
<tr>
<td>Nair, V</td>
<td>1849</td>
</tr>
<tr>
<td>Najam, S</td>
<td>1686</td>
</tr>
<tr>
<td>Najem, CE</td>
<td>1849, 2935</td>
</tr>
<tr>
<td>Najera Herranz, C</td>
<td>684, 1221, 1224, 2003</td>
</tr>
<tr>
<td>Najera-Aleson, V</td>
<td>2056</td>
</tr>
<tr>
<td>Najm, A</td>
<td>1940, 2079, 2865</td>
</tr>
<tr>
<td>Naka, I</td>
<td>861, 1321</td>
</tr>
<tr>
<td>Naka, T</td>
<td>974</td>
</tr>
<tr>
<td>Nakabayashi, A</td>
<td>272, 1769</td>
</tr>
<tr>
<td>Nakabo, S</td>
<td>479</td>
</tr>
<tr>
<td>Nakachi, Y</td>
<td>1320</td>
</tr>
<tr>
<td>Nakagawa, K</td>
<td>1446</td>
</tr>
<tr>
<td>Nakagawa, N</td>
<td>973</td>
</tr>
<tr>
<td>Nakagishi, Y</td>
<td>370, 2325</td>
</tr>
<tr>
<td>Nakai, A</td>
<td>973</td>
</tr>
<tr>
<td>Nakajima, A</td>
<td>1446</td>
</tr>
<tr>
<td>Nakajima, A</td>
<td>329, 1343, 1388</td>
</tr>
</tbody>
</table>
Nelson, A 400
Nelson, DR 475
Nelson, JL 2431, 2432, 2433
Nelson, L 2996
Nelson, R 1042
Nelson, R 2332
Nelson, S 1042
Nelson, W 1801
Nelson-Maney, N 2712
Nemkova, D 1283, 1286, 2959
Neogi, T 350, 839, 857, 858, 859, 933, 1050, 1111, 1113, 1212, 1536, 1591, 2063, 2178, 2184, 2197, 2843, 2844, 2846, 2949, 2950
Neovius, M 133, 916
Neregard, P 356
Neri, R 1756, 2166
Nerome, Y 1279
Nerviani, A 43, 1401, 1410
Nesbeth, Y 1707
Neuberger, G 1859
Neumann, E 1935, 1943
Neuver, A 1753
Neva, C 2769
Neville, C 1601, 2033
Nevin, K 770
Nevitt, M 857, 2180, 2184
Nevitt, MC 859, 932, 1050, 2197, 2200, 2218, 2949
Nevskaya, T 2674
New, P 853
Newman, E 1100, 1349
Newman, K 1585
Newton, D 661
Nezzer, J 1191
Ng, B 951, 1457
Ng, N 2536
Ng, SC 1702
Ng, WF 182, 563, 565, 874, 877, 1500, 1784
Nghiem, K 2143
Ngo, L 117
Nguyen, Sime, W 1056
Nguyen, B 652, 1566
Nguyen, D 494
Nguyen, D 601
Nguyen, H 171
Nguyen, JT 218, 220, 221, 923
Nguyen, K 808, 809
Nguyen, L 2931
Nguyen, S 1238, 1601, 2033
Nguyen, SH 485
Nguyen, V 2640
Nguyen, Dinh, Q 1137
Niazi, F 1043, 1198, 1199
Nicassio, PM 847, 1261, 1602
Nicholson, AG 1715
Nickerson, K 898
Nicolai, R 2339, 2340
Niddrie, F 339
Niederreiter, B 61, 1323, 1415
Nielsen, BD 262, 799
Nielsen, HB 489
Nielsen, MA 642
Nielsen, S 2333
Nielsen, SM 1283, 2959
Nieman, KM 136
Niemi, E 403
Nieto, JC 159, 632, 1499, 1520, 1972, 2129, 2488, 2515
Nieto, MA 2412
Nieuwenhuis, WP 1993
Nieuwlaat, R 1231
Nieves, JW 2256, 2777
Nieves, Y 1191
Niewold, T 2657
Niewold, TB 9L, 834, 1662
Nigon, D 306, 902, 2001
Nigrovec, P 297, 641, 1739, 2712, 2826
Nihtyanova, SI 737, 2690
Niihata, K 1593
Nika, A 2824, 2953
Niki, Y 70
Nikishorou, E 434, 1542, 2372, 2497
Nikpour, M 188, 945, 948, 1629, 2605
Nikulenkova, N 1909
Nilsen, TIL 2538, 2968
Nilssen, SR 2503
Nilsson, JÅ 811
Nilsson, PB 1117, 2073
Ninaber, MK 1693
Niro, H 36, 77, 2710
Nishikawa, A 2787
Nishikawa, H 271, 1149
Nishikomori, R 79
Nishimori, S 69
Nishimi, A 956, 957, 958, 959, 960, 2135
Nutz, A 2364
Nüßlein, H 1469, 2452
Nüßlein, H 414, 1468
Nye, A 186
Nygaard, G 2790, 2793
Nys, M 2855
Nzuonkwelle, S 203
Nørregaard, J 236
O
O Cuiv, P 491
O Rourke, K 428, 2507, 2508
O' Shea, F 2507, 2508, 2509
O'Beirne, R 336
O'Brien, S 15
O'Brien, S 1307, 2026
O' Connor, P 2492, 2879
O'Dell, JR 289, 472, 488, 546, 1045, 1365, 1669, 1971
O'Donnell, CI 490
O'Dwyer, J 874
O' Hanlon, S 2900
O' Hanlon, TP 2136, 2337
O'Loughlin, C 493
O'Malley, B 673, 682
O'Neil, K 1285
O'Neil, L 2863
O' Neill, A 1398
O'Rourke, K 113, 2029
O'Sullivan, B 2704
O'Sullivan, C 1231
O'Sullivan, J 2897
Oaks, Z 2572
Oates, JC 137, 1018, 1674, 1919, 2642
Oberle, E 2018
Obiora, D 1126
Obreque, J 2643
Ocal, L 2108
Occipinti, ME 742
Ocejo-Vinyals, JG 644, 1411
Ochiai, M 1388
Ochiai, T 389, 390
Ochoa-Albiztegui, E 2947
Ochs, W 2388
Octaria, R 1022
Odani, T 841, 2887
Odds, CV 851, 2136, 2171
Odimayomi, O 1081
Oelke, K 2493
Oelke, KR 1524, 1525
Oelzner, P 453
Oen, K 2289, 2292
Oerlemans, R 1418
Oeser, AM 720, 1609
Oganesian, B 2148, 2149
Ogawa, K 250
Ogawa, Y 2465
Ogbomo, A 455
Ogdie, A 346, 614, 1574, 1805, 2309, 2524
Ogino, Y 1319
Ogrič, M 2719
Ogura, T 240
Oh, JS 672
Oh, K 584
Oh, YJ 2905
Ohara, RA 971, 2926
Ohashi, K 2558
Öh, J 14L
O
Ohkawara, T 974
Ohkuro, M 397
Ohmura, K 479, 1066, 2160, 2164
Ohno, N 788
Ohno, S 237, 1460, 2151
Ohri, N 2085, 2411, 2752
Ohrndorf, S 246, 2006, 2007, 2967
Ohsawa, Y 69
Ohsfeldt, RL 2923
Ohta, A 1154
Ohyama, K 2649
Oi, K 275, 1942
Ojiwa, H 703
Ojeda, I 209
Ojeda-Garcia, C 498
Okabe, T 1215
Okada, A 238, 1441
Okada, M 626, 1215, 2530, 2732
Okada, Y 170
Okado, M 1238, 1601, 2033, 2344
Okamoto, M 552
Okamoto, N 370, 1494, 1960, 2299
Okamoto, Y 484
Okano, T 464
Okano, T 861, 1321
Okawa, J 7L, 2156
Okawa, S 1698
Okayama, A 273, 2427
Okazaki, K 1179
<table>
<thead>
<tr>
<th>Name</th>
<th>Page Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Okazaki, T</td>
<td>9, 795</td>
</tr>
<tr>
<td>Oke, V</td>
<td>9L, 1675, 2633</td>
</tr>
<tr>
<td>Okitsu, S</td>
<td>25</td>
</tr>
<tr>
<td>Okuyama, N</td>
<td>2158</td>
</tr>
<tr>
<td>Okiyama, N</td>
<td>2158</td>
</tr>
<tr>
<td>Oksuz, MF</td>
<td>2727</td>
</tr>
<tr>
<td>Oku, K</td>
<td>11, 2887</td>
</tr>
<tr>
<td>Okubo, N</td>
<td>1435</td>
</tr>
<tr>
<td>Okuda, Y</td>
<td>91, 907</td>
</tr>
<tr>
<td>Okurayama, A</td>
<td>2017</td>
</tr>
<tr>
<td>Olanrewaju, T</td>
<td>2069</td>
</tr>
<tr>
<td>Oldroyd, A</td>
<td>853</td>
</tr>
<tr>
<td>Olech, E</td>
<td>2493</td>
</tr>
<tr>
<td>Olenyová, M</td>
<td>6</td>
</tr>
<tr>
<td>Olek, S</td>
<td>2830</td>
</tr>
<tr>
<td>Olesinska, M</td>
<td>2697</td>
</tr>
<tr>
<td>Olferiev, M</td>
<td>1668</td>
</tr>
<tr>
<td>Oliffe, M</td>
<td>1681</td>
</tr>
<tr>
<td>Olives-Martánez, E</td>
<td>16</td>
</tr>
<tr>
<td>Olivé, A</td>
<td>498, 1587, 1588, 1612, 2723</td>
</tr>
<tr>
<td>Oliveira, I</td>
<td>633</td>
</tr>
<tr>
<td>Oliveira, S</td>
<td>2859</td>
</tr>
<tr>
<td>Oliver, CE</td>
<td>2418</td>
</tr>
<tr>
<td>Oliver, J</td>
<td>607</td>
</tr>
<tr>
<td>Oliver, M</td>
<td>2286</td>
</tr>
<tr>
<td>Oliver, S</td>
<td>576, 875</td>
</tr>
<tr>
<td>Oliveria, S</td>
<td>1031</td>
</tr>
<tr>
<td>Olivieri, I</td>
<td>1292</td>
</tr>
<tr>
<td>Oliviero, F</td>
<td>2522</td>
</tr>
<tr>
<td>Ollier, W</td>
<td>853, 913</td>
</tr>
<tr>
<td>Ok, Ö</td>
<td>2728</td>
</tr>
<tr>
<td>Ölmel, Ü</td>
<td>2728</td>
</tr>
<tr>
<td>Olmos, E</td>
<td>692, 2618</td>
</tr>
<tr>
<td>Olmos, JM</td>
<td>1379, 2403</td>
</tr>
<tr>
<td>Olmos, ME</td>
<td>2008</td>
</tr>
<tr>
<td>Olmos Calvo, I</td>
<td>966</td>
</tr>
<tr>
<td>Olofsson, T</td>
<td>133, 423, 2511</td>
</tr>
<tr>
<td>Olorunfemi, O</td>
<td>103</td>
</tr>
<tr>
<td>Olsen, IC</td>
<td>459, 2800, 2861</td>
</tr>
<tr>
<td>Olsen, J</td>
<td>2432, 2433</td>
</tr>
<tr>
<td>Olsen, NJ</td>
<td>1370</td>
</tr>
<tr>
<td>Olson, C</td>
<td>91</td>
</tr>
<tr>
<td>Olson, J</td>
<td>1444</td>
</tr>
<tr>
<td>Olson, P</td>
<td>1918</td>
</tr>
<tr>
<td>Olsson, H</td>
<td>967</td>
</tr>
<tr>
<td>Olsynzynski, W</td>
<td>631</td>
</tr>
<tr>
<td>Olufemi-Aworinde, K</td>
<td>2069</td>
</tr>
<tr>
<td>Omair, M</td>
<td>153</td>
</tr>
<tr>
<td>Omair, M</td>
<td>151, 153</td>
</tr>
<tr>
<td>Omar, A</td>
<td>316, 2120</td>
</tr>
<tr>
<td>Omarbekova, A</td>
<td>1786</td>
</tr>
<tr>
<td>Ombrello, A</td>
<td>290, 292, 367</td>
</tr>
<tr>
<td>Ombrello, MJ</td>
<td>940</td>
</tr>
<tr>
<td>Omdal, R</td>
<td>182, 1479</td>
</tr>
<tr>
<td>Omerovic, E</td>
<td>1550</td>
</tr>
<tr>
<td>Omieto, F</td>
<td>145</td>
</tr>
<tr>
<td>Ominsky, M</td>
<td>1937</td>
</tr>
<tr>
<td>Omma, A</td>
<td>2496, 2727</td>
</tr>
<tr>
<td>Ommar, OS</td>
<td>2348</td>
</tr>
<tr>
<td>Omourou, AY</td>
<td>2835</td>
</tr>
<tr>
<td>Omoyinmi, E</td>
<td>939</td>
</tr>
<tr>
<td>Oneata, R</td>
<td>997, 2660</td>
</tr>
<tr>
<td>Onel, K</td>
<td>1800, 2306, 2313</td>
</tr>
<tr>
<td>Onen, F</td>
<td>542, 825, 1455, 1472, 1496, 1514, 1534, 2521</td>
</tr>
<tr>
<td>Onengut, S</td>
<td>2826</td>
</tr>
<tr>
<td>Onetti, L</td>
<td>2924</td>
</tr>
<tr>
<td>Ong, K</td>
<td>980, 1043</td>
</tr>
<tr>
<td>Ong, VH</td>
<td>737, 770</td>
</tr>
<tr>
<td>Onenguaert, M</td>
<td>497</td>
</tr>
<tr>
<td>Onishi, A</td>
<td>551, 861, 1321</td>
</tr>
<tr>
<td>Onishi, I</td>
<td>2424</td>
</tr>
<tr>
<td>Onizuka, N</td>
<td>2179, 2206</td>
</tr>
<tr>
<td>Ono, Y</td>
<td>2873</td>
</tr>
<tr>
<td>Onohara, M</td>
<td>2072, 2074</td>
</tr>
<tr>
<td>Onouchi, Y</td>
<td>2937</td>
</tr>
<tr>
<td>Onsel Turk, U</td>
<td>1163</td>
</tr>
<tr>
<td>Onuma, K</td>
<td>1928</td>
</tr>
<tr>
<td>Oommen, P</td>
<td>2274</td>
</tr>
<tr>
<td>Oon, S</td>
<td>2605</td>
</tr>
<tr>
<td>Ooyama, H</td>
<td>170</td>
</tr>
<tr>
<td>Opdenakker, G</td>
<td>1945</td>
</tr>
<tr>
<td>Orange, D</td>
<td>495</td>
</tr>
<tr>
<td>Orba, AM</td>
<td>2549</td>
</tr>
<tr>
<td>Orban, I</td>
<td>376, 2859</td>
</tr>
<tr>
<td>Ordoñez, JC</td>
<td>1227</td>
</tr>
<tr>
<td>Ordoñez, S</td>
<td>498</td>
</tr>
<tr>
<td>Ordoniz-Del Valle, D</td>
<td>1020</td>
</tr>
<tr>
<td>Oreiro, N</td>
<td>1011, 2189, 2192</td>
</tr>
<tr>
<td>Oreskja, S</td>
<td>766, 1692, 1694, 2153, 2154, 2176</td>
</tr>
<tr>
<td>Orfanos, S</td>
<td>2686</td>
</tr>
<tr>
<td>Origuchi, T</td>
<td>1882, 2144, 2421</td>
</tr>
<tr>
<td>Orita, K</td>
<td>464</td>
</tr>
<tr>
<td>Orlandi, M</td>
<td>1486</td>
</tr>
<tr>
<td>Orman, M</td>
<td>2099</td>
</tr>
<tr>
<td>Ormerod, K</td>
<td>491, 1576</td>
</tr>
</tbody>
</table>
Ormseth, MJ 720, 1233, 1367, 1368, 1609, 1764
Ormseth, S 921, 1261, 1803
Ornelas, NM 154
Oron, A 374
Orozco, M 2008
Orozco, S 2008
Orr, C 2865
Orrock, J 2306
Ort, T 1428
Ortega, AG 634
Ortega, L 277
Ortego, N 2722, 2723
Ortego Centeno, N 2343
Ortiz, MA 1467
Ortiz, V 2004
Ortiz Garcia, AM 2284, 2375
Ortego-Sanjuán, F 780, 2724
Ortego-Sanjuán, FM 684, 1221, 1224, 2003
Ortmann, R 513
Ortmann, RA 2870
Ortolan, A 2522
Orwell, E 2180
Oryoji, K 1464, 2710
Orzechowski, N 775
Osada, A 393
Osaki, M 1995
Osani, MC 1194
Osborn, T 1662, 1876, 2657
Osborne, B 545, 612, 629, 631, 2459, 2520, 2548
Oshima, H 250
Oshima, S 1447
Ó
Óskarsdóttir, S 916
O
Oskin, J 1929
Osmon, DR 2082
Osorio, F 904
Ospelt, C 970, 1335
Ossoinak, A 2817
Ostendorf, B 266, 307, 993, 1998
Ostensen, M 1315
Osting, VC 91
Ö
Östör, A 1038
O
Ostrov, B 2283
Ostrovskīns, J 2735
Ostrowski, RA 515, 1112
Ota, S 2710
Ota, T 1154
Ota, Y 36
Otahal, P 1850
Otani, H 412
Otani, K 2220
Otawa, S 1821
Othman, AA 505, 506, 1904
Oto, Y 2220
Oton Sanchez, MT 1587, 1612
Oton-Sanchez, T 1361
Ototake, Y 2172
Otsuka, T 2710
Otten-Mus, AM 1792, 1944
Ottesen, B 2432, 2433
Otto, G 2342
Ottosson, V 941, 2817
Otvos, JD 415
Oude Voshaar, MAH 1078
Ouhaddi, Y 57
Oullette, A 1330
Ousey, K 256
Outman, R 2256
Outman, RC 2777
Ovalles-Bonilla, JG 159, 632, 1520, 1972, 2129, 2488
Overgaard, A 1188
Owada, T 2386
Oz, B 2729
Oz, B 542, 1455, 1472
Oza, A 328, 2077
Ozaki, S 9, 1013, 1751, 1762
Ozawa, T 481
Ozbekir, F 2748
Ozbeklan, Z 447
Ö
Özçakar, L 305
O
Ozçakir, S 2204
Ozdogan, H 376, 2103, 2117, 2462
Ozdolap, S 2204
Ozen, G 542, 842, 1455, 2051, 2410, 2783
Ozen, S 1163
Ozen, S 361, 939, 1174, 1892, 2349, 2742, 2758
Ozguler, Y 463, 2103, 2462, 2748
Ozturk Durmaz, H 1240
O’Donovan, F 468, 1394
Paraboschi, EM 650
Paran, D 1648
Pardeo, M 2331
Pardo Pardo, J 1599
Pardue, S 1404
Paredes, C 1230
Parent, G 466
Parent, I 497
Parenti, D 344, 455, 473, 2951
Parga Vidal, L 1793
parikh, S 1615
Paris, M 600, 601, 604
Pariser, DM 600
Parisi, F 741, 742
Park, C 2461
Park, CK 1143
Park, DJ 1595, 1647, 1868, 1869, 2097
Park, EH 1970, 2025, 2168
Park, EK 2002, 2582
Park, JS 87, 1412, 1417, 2145, 2746, 2794
Park, JH 2582
park, JH 1334
Park, JK 87, 827, 1181, 1547, 2168, 2630, 2794, 2905
Park, J 2266
Park, JS 183
Park, JW 1547
Park, KS 399, 2202, 2404
Park, M 719
Park, MC 2075
Park, SI 2072
Park, SY 625
Park, SY 207
Park, SH 139, 557
Park, SH 401, 1331, 1369, 1493, 2396
Park, W 2074, 2202, 2445, 2461
Park, YS 74, 1938
Park, YH 942
Park, YB 245, 1547, 2074, 2444
Park, YW 1065
Park, Y 1016, 2405
Park, Y 1000, 1524, 1552, 1553
Park, YJ 716, 2404
Parke, A 2875
Parker, M 1681
Parks, C 2131
Parks, CG 915
Parks, D 174
Parks, ML 218, 219, 220, 221, 923
Parmeggiani, M 790, 1075
Parodi, M 930
Parperis, K 203, 270
Parrish, E 92
Parton, H 1482
Partovi, R 1260
Partridge, S 374
Pascal, M 1436
Pascart, T 2084
Pascaud, J 1463, 1795
Paschke, J 586, 594, 2967
Pascual, E 1132, 1140, 2081
Pascual, J 2621
Pascual, M 2094
Pascual, V 2875
Pascual-Ramos, V 147, 348, 411, 1083, 1654, 2013, 2924
Pascual-Salcedo, D 1450, 1471
Pasoto, SG 876, 1499
Pasquale, M 1246
Passalent, L 316, 2120, 2821
Passarelli, C 2331
Pastor-Asurza, CA 450, 687, 1378
Pastore, S 1278, 2956
Pastori, A 300
Pasula, S 2648, 2976
Patarà, M 2629
Patarata, E 1651
Patel, A 113
Patel, D 2257
Patel, H 499, 508
Patel, J 223
Patel, P 4L
Patel, P 2322, 2323
Patel, S 1249
Patel, S 1687
Patel, V 198
Patel, Z 1770
Paterson, M 146, 214, 994, 996
Pathai, S 1155
Pathan, E 1543
Pato, E 2722, 2723
Pato Cour, E 1443, 2412
Patten, S 121
Patterson, K 945
Patterson, SL 327, 2263
Patterson-Lomba, O 1963
Pattoli, M 503
<table>
<thead>
<tr>
<th>Name</th>
<th>Last Name</th>
<th>First Name</th>
<th>Middle Initials</th>
<th>Year(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pau, D</td>
<td></td>
<td></td>
<td></td>
<td>2464</td>
</tr>
<tr>
<td>Paudel, P</td>
<td></td>
<td></td>
<td></td>
<td>1952</td>
</tr>
<tr>
<td>Pauer, L</td>
<td></td>
<td></td>
<td></td>
<td>1974</td>
</tr>
<tr>
<td>Paukkeri, EL</td>
<td></td>
<td></td>
<td></td>
<td>2191</td>
</tr>
<tr>
<td>Paul, A</td>
<td></td>
<td></td>
<td></td>
<td>1254</td>
</tr>
<tr>
<td>Paul, D</td>
<td></td>
<td></td>
<td></td>
<td>1454</td>
</tr>
<tr>
<td>Paule, R</td>
<td></td>
<td></td>
<td></td>
<td>1974</td>
</tr>
<tr>
<td>Pauling, J</td>
<td></td>
<td></td>
<td></td>
<td>745</td>
</tr>
<tr>
<td>Paupitz, J</td>
<td></td>
<td></td>
<td></td>
<td>1268</td>
</tr>
<tr>
<td>Pauwels, E</td>
<td></td>
<td></td>
<td></td>
<td>2773</td>
</tr>
<tr>
<td>PAVAO, R</td>
<td></td>
<td></td>
<td></td>
<td>2021</td>
</tr>
<tr>
<td>Pavelcova, K</td>
<td></td>
<td></td>
<td></td>
<td>2087</td>
</tr>
<tr>
<td>Pavelka, K</td>
<td></td>
<td></td>
<td></td>
<td>78, 170, 579, 766, 992, 1104, 1538, 1549, 1692, 1694, 1828, 2087, 2153, 2154, 2176, 2434, 2534</td>
</tr>
<tr>
<td>Pavelikova, M</td>
<td></td>
<td></td>
<td></td>
<td>2087</td>
</tr>
<tr>
<td>Pawlak-Bus, K</td>
<td></td>
<td></td>
<td></td>
<td>2697</td>
</tr>
<tr>
<td>Payan-Schober, F</td>
<td></td>
<td></td>
<td></td>
<td>719</td>
</tr>
<tr>
<td>Paz, Z</td>
<td></td>
<td></td>
<td></td>
<td>282, 2840</td>
</tr>
<tr>
<td>Pazmino, S</td>
<td></td>
<td></td>
<td></td>
<td>1820</td>
</tr>
<tr>
<td>Peglej, T</td>
<td></td>
<td></td>
<td></td>
<td>906</td>
</tr>
<tr>
<td>Peelen, D</td>
<td></td>
<td></td>
<td></td>
<td>257</td>
</tr>
<tr>
<td>Peed, D</td>
<td></td>
<td></td>
<td></td>
<td>326</td>
</tr>
<tr>
<td>Pedenraza-Arevalo, S</td>
<td></td>
<td></td>
<td></td>
<td>2656</td>
</tr>
<tr>
<td>Pedro, S</td>
<td></td>
<td></td>
<td></td>
<td>131, 144, 842, 1649, 2051, 2410, 2783</td>
</tr>
<tr>
<td>Pedro Martinez, AJ</td>
<td></td>
<td></td>
<td></td>
<td>1445, 1975, 2360, 2361</td>
</tr>
<tr>
<td>Peela, D</td>
<td></td>
<td></td>
<td></td>
<td>257</td>
</tr>
<tr>
<td>Peelman, F</td>
<td></td>
<td></td>
<td></td>
<td>2773</td>
</tr>
<tr>
<td>Peeters, T</td>
<td></td>
<td></td>
<td></td>
<td>906</td>
</tr>
<tr>
<td>Peeters, T</td>
<td></td>
<td></td>
<td></td>
<td>2709</td>
</tr>
<tr>
<td>Pego-Regiosa, J</td>
<td></td>
<td></td>
<td></td>
<td>1587, 1588, 1612, 2619</td>
</tr>
<tr>
<td>Pehlivan, O</td>
<td></td>
<td></td>
<td></td>
<td>2667</td>
</tr>
<tr>
<td>Pehlivan, Y</td>
<td></td>
<td></td>
<td></td>
<td>542, 1455, 1472, 1534</td>
</tr>
<tr>
<td>Pei, J</td>
<td></td>
<td></td>
<td></td>
<td>550, 778, 1905, 2460, 2962</td>
</tr>
<tr>
<td>Peikert, T</td>
<td></td>
<td></td>
<td></td>
<td>23</td>
</tr>
<tr>
<td>Peiteado, D</td>
<td></td>
<td></td>
<td></td>
<td>654, 793, 1450, 1471, 2021, 2422, 2487</td>
</tr>
<tr>
<td>Peiteado Lopez, D</td>
<td></td>
<td></td>
<td></td>
<td>2722</td>
</tr>
<tr>
<td>Pel, S</td>
<td></td>
<td></td>
<td></td>
<td>1503</td>
</tr>
<tr>
<td>Pelagage, F</td>
<td></td>
<td></td>
<td></td>
<td>1360</td>
</tr>
<tr>
<td>Pelikan, RC</td>
<td></td>
<td></td>
<td></td>
<td>184, 2703</td>
</tr>
<tr>
<td>Pellegini, C</td>
<td></td>
<td></td>
<td></td>
<td>2770, 2823</td>
</tr>
<tr>
<td>Pelletier, JP</td>
<td></td>
<td></td>
<td></td>
<td>52, 57, 1196, 1197, 1208, 1817, 2192</td>
</tr>
<tr>
<td>Pelletier, J</td>
<td></td>
<td></td>
<td></td>
<td>2561</td>
</tr>
<tr>
<td>Pelletier, M</td>
<td></td>
<td></td>
<td></td>
<td>466, 1027, 1666</td>
</tr>
<tr>
<td>Pelouquin, C</td>
<td></td>
<td></td>
<td></td>
<td>839, 1111, 1220, 1951</td>
</tr>
<tr>
<td>Pemmarie, A</td>
<td></td>
<td></td>
<td></td>
<td>2191</td>
</tr>
<tr>
<td>Pena, CE</td>
<td></td>
<td></td>
<td></td>
<td>1766, 2676, 2676</td>
</tr>
<tr>
<td>Pena, DP</td>
<td></td>
<td></td>
<td></td>
<td>2595</td>
</tr>
<tr>
<td>Pena, J</td>
<td></td>
<td></td>
<td></td>
<td>732, 2983</td>
</tr>
<tr>
<td>Peña, MS</td>
<td></td>
<td></td>
<td></td>
<td>1516</td>
</tr>
<tr>
<td>Pena, SM</td>
<td></td>
<td></td>
<td></td>
<td>7L, 2156</td>
</tr>
<tr>
<td>Peña-Blanco, R</td>
<td></td>
<td></td>
<td></td>
<td>543, 1965</td>
</tr>
<tr>
<td>Pena-Rossi, C</td>
<td></td>
<td></td>
<td></td>
<td>1822</td>
</tr>
<tr>
<td>Penadés Vidal, M</td>
<td></td>
<td></td>
<td></td>
<td>209</td>
</tr>
<tr>
<td>Pendergraft, W</td>
<td></td>
<td></td>
<td></td>
<td>25, 719</td>
</tr>
<tr>
<td>Pendón, G</td>
<td></td>
<td></td>
<td></td>
<td>360, 1645</td>
</tr>
<tr>
<td>Peng, L</td>
<td></td>
<td></td>
<td></td>
<td>2101</td>
</tr>
<tr>
<td>Peng, Q</td>
<td></td>
<td></td>
<td></td>
<td>2134</td>
</tr>
<tr>
<td>Peng, S</td>
<td></td>
<td></td>
<td></td>
<td>1328</td>
</tr>
<tr>
<td>Peng, Y</td>
<td></td>
<td></td>
<td></td>
<td>136</td>
</tr>
<tr>
<td>Pengo, V</td>
<td></td>
<td></td>
<td></td>
<td>15</td>
</tr>
<tr>
<td>Penkava, F</td>
<td></td>
<td></td>
<td></td>
<td>643</td>
</tr>
<tr>
<td>Pennebaker, J</td>
<td></td>
<td></td>
<td></td>
<td>341, 2250</td>
</tr>
<tr>
<td>Pentazos, G</td>
<td></td>
<td></td>
<td></td>
<td>1387, 2744</td>
</tr>
<tr>
<td>Penteado, M</td>
<td></td>
<td></td>
<td></td>
<td>723</td>
</tr>
<tr>
<td>Penteon, P</td>
<td></td>
<td></td>
<td></td>
<td>2012</td>
</tr>
<tr>
<td>Pera, M</td>
<td></td>
<td></td>
<td></td>
<td>1766, 2021, 2676</td>
</tr>
<tr>
<td>Peral Gutiérrez De Ceballos, E</td>
<td></td>
<td></td>
<td></td>
<td>209</td>
</tr>
<tr>
<td>Perard, L</td>
<td></td>
<td></td>
<td></td>
<td>2904</td>
</tr>
<tr>
<td>Perdriger, A</td>
<td></td>
<td></td>
<td></td>
<td>873, 1491, 2842</td>
</tr>
<tr>
<td>Pereira, D</td>
<td></td>
<td></td>
<td></td>
<td>269, 360</td>
</tr>
<tr>
<td>Pereira, I</td>
<td></td>
<td></td>
<td></td>
<td>456, 457</td>
</tr>
<tr>
<td>Pereira, L</td>
<td></td>
<td></td>
<td></td>
<td>276</td>
</tr>
<tr>
<td>Pereira, RMR</td>
<td></td>
<td></td>
<td></td>
<td>333, 1219, 1268, 1302, 1499, 1570, 1961</td>
</tr>
<tr>
<td>Perel-Winkler, A</td>
<td></td>
<td></td>
<td></td>
<td>1601, 2033</td>
</tr>
<tr>
<td>Perez, CE</td>
<td></td>
<td></td>
<td></td>
<td>529, 1448</td>
</tr>
<tr>
<td>Perez, K</td>
<td></td>
<td></td>
<td></td>
<td>206</td>
</tr>
<tr>
<td>Perez, MO</td>
<td></td>
<td></td>
<td></td>
<td>333</td>
</tr>
<tr>
<td>Perez, N</td>
<td></td>
<td></td>
<td></td>
<td>1632</td>
</tr>
<tr>
<td>Pérez, SK</td>
<td></td>
<td></td>
<td></td>
<td>360, 1359</td>
</tr>
<tr>
<td>Perez, T</td>
<td></td>
<td></td>
<td></td>
<td>690, 1632</td>
</tr>
<tr>
<td>Perez Davila, A</td>
<td></td>
<td></td>
<td></td>
<td>360</td>
</tr>
<tr>
<td>Pérez de Lis, M</td>
<td></td>
<td></td>
<td></td>
<td>210, 2123</td>
</tr>
</tbody>
</table>
Pérez Gómez, A 1738
Perez Guerrero, P 209, 2841
Perez Pampín, E 2277
Perez Sandoval, T 498
Perez Venegas, JJ 1587
Pérez- Pampín, E 816
Perez- Alamino, R 360, 2505
Pérez- Alvarez, R 209, 210, 2123
Perez Baos, S 396, 2056
Pérez- Gómez, A 2724
Pérez Pampin, E 780
Pérez- Ríos, N 442
Perez-Baos, S 396, 2056
Pérez-Gómez, A 2724
Pérez-Pampín, E 780
Pérez- Ríos, N 442
Pere-Baños, S 396, 2056
Pérez- Gómez, A 2724
Pérez Pampín, E 780
Pérez- Ríos, N 442
Perich- Campos, R 450, 687, 1378
Perin, J 2248
Peris, K 600
Perkins, E 855
Perl, A 2028, 2036, 2572, 2578, 2698, 2763
Perlat, A 814
Perlman, K 2635
Perlman, H 29, 174, 302, 387, 405, 406, 1405, 1709, 1835, 2576
Pernis, AB 1406
Perper, S 2568
Perrella, M 408
Perricone, R 1292
Perrodeau, E 1442, 1758, 2754
Perrot, S 1973
Perruccio, AV 214, 217, 2235, 2236, 2541
Pers, JO 23, 41
Persuitte, G 496, 1423, 2449
Pertega, S 2189
Pertuiset, E 1758
Perugino, CA 4L, 1175, 1179
Pesce, M 2259
Peschken, C 2922
Peschken, CA 1599, 1606, 1641, 2811, 2925
Peter, N 2442
Peterfy, C 1196, 1202, 1211, 2962
Peters, E 340, 1236, 1614, 2725
Peters, J 1899
Peters, MS 1168
Petersen, MJL 2365
Petersen, D 1191
Petersen, F 84
Petersen, J 318
Petersen, NJ 2200
Peterson, EJ 1062
Peterson, S 630, 1530, 1531, 2836
Peterson, SK 118
Pethő-Schramm, A 167, 1476, 2458
Petit, M 120
Petkovic, I 269
Pettráčková, A 1358
Petri, M 7, 663, 664, 665, 666, 669, 681, 706, 719, 1297, 1603, 1604, 1605, 1606, 1611, 1634, 1635, 1636, 1842, 1919, 2614, 2622, 2760, 2876, 2925
Petrica, L 1898
Petric, K 341, 1107
Petroiw, L 93
Petrone, T 503
Petru, L 2087
Petitphier, C 1966
Peytriget, S 2663
Pezant, N 1811
Pfeiffenberger, M 1946
Pfeifle, R 1338
Pfeil, A 453
Pfreundschuh, M 1389
Pham, H 1680
Pham, L 867
Pham, M 13
Pham, TP 352
Pham, T 322, 1449
Pham-Ledard, A 2126
Phatak, S 2311
Phialy, L 108
Philip, S 2041
Philipp, T 1549
Phillips, K 2145
Phillips, K 174, 858
Phillips, PE 2763
Phillips, S 1031
Phippard, DJ 2936
Phipps, R 1947
Phipps-Green, A 1104, 1108, 2061, 2843, 2897
Phoon, C 2580
Pialat, JB 2203
Pianta, A 949
Ponce, A 1467
Ponce, J 1227
Ponce, L 1909
Ponder, L 2993
Ponomarev, I 1946
Pons, E 2112, 2721, 2722, 2723
Pons-Estel, B 360, 1645
Pons-Estel, B 1654, 2924
Pons-Estel, GJ 1654, 2924
Pontarini, E 43, 2706
Ponte, C 781, 783
Pontes, C 1535
Ponticos, M 1713
Pool, B 2896
Poole, JL 2693, 2694
Poole, J 400
Poon, KS 711
Poortmans, PMP 1205
Pope, B 85
Pope, E 1285
Pope, JE 146, 201, 432, 443, 461, 502, 732, 945, 1384, 1393, 1599, 1814, 2390, 2391, 2491, 2673, 2674, 2683, 2769, 2955, 2983
Pope, RM 174, 302, 387
Popik, S 1477
Popov, JM 2312, 2327
Popovich, D 1730
Popp, F 536
Porras, A 274, 2837
Porrati, L 1969
Porta, F 2055
Porter, B 3L, 1523, 1526, 1528, 1529, 1828
Porthoghese, P 2231
Portilla, V 644, 1411, 2527
Ports, WC 619
Posadas Martinez, ML 3
Posch, M 1784
Posner, J 358
Possidente, C 359
Posso, S 951
Postema, R 122, 1034, 1465, 1817
Potluri, H 294
Pouchot, J 1734
Poudel, D 823, 879, 1952
Pouplin, S 528
Pourpaki, M 1355
Povedano, J 1158
Powell, N 2598
Power, JD 214, 2235, 2236
Poynard, T 894
Pozo, AS 1172
Prade, J 2024
Pradines, J 764
Prado, M 707
Praetorius, HA 492
Prahalad, S 2322, 2323, 2993
Prajzlerova, K 579, 2434
Prakash, DM 2124
Prakash, G 2029
Prakash, H 2141
Prakash, P 1086, 2583
Praprotnik, S 822, 876
Prasad, P 24
Prasad, S 2262
Pratap, A 2651
Prati, C 2107, 2512
Prato, G 2015
Pratsidou-Gertsi, P 1278
Pratt, G 2262, 2395
Preuss, KD 1389
Prevete, I 1292
Price, A 1807
Price, E 565, 874, 1500
Price, K 1341, 2450
Price, LL 843, 931, 1059, 2196, 2201, 2849
Pricop, L 17L, 606, 618, 621, 622, 1826
Priest, J 2593, 2594, 2812
Prieto Peña, D 260, 817
Prior, A 2284
Priori, R 876, 1300
Pritchard-Wiart, L 2303, 2351
Probert, NJ 1193
Prod'homme, T 1019
Proril, M 2203
Proudfoot, C 2457
Proudman, C 948
Proudman, S 448, 945, 948, 1248, 1899
Provan, SA 1344, 1345
Pruthi, R 13
Pruunsild, C 2859
Pruvost, A 1463
Psaradellis, E 612, 631, 2459, 2520, 2548
Psarras, A 679, 1917, 2816
Pu, W 1727, 2882
Pucci, G 747
Puchner, A 63, 1338
Pudota, K 889
Puéchal, X 1757, 1758, 1759, 1763, 1779, 2671, 2736, 2738, 2739, 2754
Puéchal for the French Vasculitis Study Group, X 1754
Puggina, S 1287
Pugliesi, A 568
Pugnet, G 814, 819, 2661, 2754
Puig, J 1104
Puig-Kröger, A 654, 2422, 2426
Pujato, M 2825
Pujol, M 1467
Pujol, R 2620
Pulicicchio, C 503
Punaro, M 641, 1285
Pundole, X 850
Punj, V 1330
Punzi, L 145, 2522
Puppo, G 1488
Purdom, E 2433
Purdue, E 1581
Purmaletk, M 290, 899
Pusey, C 295
Putrik, P 2497
Puttaraksa, K 2838
Putterman, C 29, 673, 676, 680, 681, 719, 900, 1023, 1372, 1482, 1735, 1836, 1837, 1919, 2561, 2757
Puxeddu, I 1486
Puyade, M 796
Puyraimond-Zemmour, D 2904
Puzas, E 115
Py, G 2021
Pyne, D 43, 685, 2624, 2634
Qi, F 2653
Qian, F 1711, 2882
Qian, H 1060
Qian, Y 1801
Qing, X 1833
Qodsi, M 205
Quadri, SMS 562
Quartier, P 361, 365, 1754, 2271
Quartuccio, L 876, 894, 1489, 2874
Quattrocchi, E 143
Quebe, A 508, 2219
Quehenberger, O 649
Queiro, R 335, 1232, 2525, 2526
Quémeneur, T 2671, 2736, 2738, 2739
Quere, G 2126
Quero, L 301
Quevedo, JC 1506
Quevedo, V 1587
Queryvel, V 2671
Quilliam, E 2514
Quinet, R 407, 721
Quiniou, V 1734
Quinlan, A 2826
Quinn, KA 1845
Quintana, R 269, 360, 2924
Quintanilla-González, L 1618
Quintero, M 2021
Quinteros, A 269
Quirante-Piñé, R 1712
Quirk, C 308
Quirke, AM 913
Qureshi, Q 407
Qureshi, A 2535
R
Ra, J 38
Raats, JMH 293
Rabah, D 675, 2607
Rabelink, T 295, 890
Rabinovich, CE 1285, 2271
Raby, B 837
Racaza, GZ 847
Rademacher, N 294
Rader, T 1599
Radfar, L 30, 46, 559, 2703
Radin, M 5, 1466, 2655, 2759
Radstake, T 1127
Radstake, TRDJ 4, 553, 1656, 1729, 1912, 2830, 2872
Radstake, TR 1104
Radchenko, J 1040, 1041
Radu, A 997
Raffray, L 2717
Raftakis, I 1387
Raga, AC 2189, 2192
Ragab, G 894
Raggi, P 1609
Raghunath, S 1899
Ragina, N 1304
Rahbar, MH 583, 1505
Raheel, S 792, 812, 813
Rahimi, H 247, 394, 1333
Rahman, A 1606, 2925
Rahman, MA 1911
Rahman, P 17L, 176, 629, 1209, 1210, 2548
Rahn, EJ 350, 357, 2256, 2777, 2950
Rai, MK 1723, 1920, 2885
Rai, R 629, 631, 2520
Rai, SK 328, 1130, 1131, 1610, 1964, 2077, 2614
Rai, V 1583
Raicht, A 2646, 2877
Raiti, L 360, 2237
Rajabirostami, E 1585, 2265
Rajagopalan, S 2175
Rajakariar, R 43, 685, 2624, 2634
Rajan, B 2589
Rajmohan, D 308
Rallidis, L 2686
Ralos-Casals, M 877
Ralph, D 12L
Ralston, E 291
Ramachandran, S 2923
Ramadan, I 715
Ramadan, S 921, 1261
Ramakrishnan, S 2423
Raman, C 85
Ramanan, AV 939, 2270
Ramanujam, M 29, 2561
Ramaswamy, M 561
Ramey, D 2674
Ramey, W 1046
Ramires, T 1498
Ramires de Jesus, G 12
Ramirez, AA 378
Ramírez, J 1479
Ramírez, J 460, 480, 639, 1416, 1467, 2490, 2515
Ramirez, M 1367
Ramiro, S 35, 259, 427, 582, 591, 592, 593, 781, 783, 1542, 1560, 2497, 2806, 2967
Ramirez-Santana, C 1672
Ramji, A 1099
Ramly, E 1087, 1088, 2261
Rammel, J 17
Ramming, A 655, 753, 826, 864, 1706, 1925, 2928
Ramonda, R 581, 1512, 1831, 2522
Ramon, V 164, 1292, 1300
Ramon, VL 930
Ramos, PS 919, 946, 1018, 2930
Ramos, YF 903
Ramos-Bello, D 1445, 1975, 2360, 2361
Ramos-Casals, M 209, 210, 876, 1606, 2123, 2841
Ramos-Rodriguez, A 2085, 2411, 2752
Rampakakis, E 432, 467, 629, 631, 2459, 2491, 2520, 2548, 2908
Ramapersaud, YR 214, 1851, 2235, 2236, 2821
Ramsey, S 939, 2758
Ramsey-Goldman, R 233, 673, 680, 681, 1589, 1606, 1622, 1839, 2614, 2925
Ramskay, P 1145
Ran, D 2852, 2948
Ranabothu, S 2757
Rand, J 15
Randell, E 1209, 1210
Randhawa, S 885
Randolph, TW 1203
Ranganath, VK 1391, 1392
Ranganathan, P 1968
Ranganathan, V 176
Rangel-Moreno, J 1834
Ranieri, L 1129, 1227
Rantapää Dahlqvist, S 147, 2826
Rantapaa-Dahlqvist, S 1638, 2354, 2791
Ranza, R 278, 541, 634
Rao, A 1454
Rao, D 241, 1405, 1406, 2659
Rao, P 2141
Rao, R 1478, 2472, 2473
Rapley, T 95, 186
Rasch, LA 1253
Rascón, FJ 278, 541, 634
Rasouliyan, L 621, 622, 1528, 1826
Rastie madabadi, Z 236
Rasulnia, M 2257
Rat, AC 979, 1056, 2835
Ringold, S 2275, 2278, 2281, 2282, 2350, 2858, 2859
Rini, B 1156
Rini, C 846
Rintek Madsen, O 2382, 2552, 2553
Riordan, ME 2282
Ríos, C 846
Ríos, G 442
Riscanevo, N 572, 2008
Rispinto, S 1873, 1976, 1978
Rist Bouillon, S 247, 621, 1947, 2970
Ritcheil, CT 1645
Ritchlin, E 1795
Robert, C 1741
Roberts, C 2005
Roberts, J 474
Roberts, J 1090
Roberts, L 193
Roberts, M 917, 2944, 2945
Roberts, R 1106
Roberts, S 1936
Roberts, VC 222, 1657, 1658, 2977
Roberts, WN 2984
Roberts-Thomson, P 945
Robin-Jagerschmidt, C 497
Robins, K 2580
Robinson, C 2355, 2356
Robinson, D 2922
Robinson, G 2975
Robinson, WH 1405, 1406, 1928, 2868
Robl, R 1026
Robles, A 209, 2123, 2841
Robles Flores, BJ 498
Roblot, P 1758
Robson, J 745
Robusto, M 650
Roccatello, D 5, 27, 1466, 2759
Rocchiccioli, S 556
Rocha, B 179
Rocha, G 2866, 2870
Roche, N 284
Rocio Gil, D 456, 457
Rockette-Wagner, BJ 2200
Roddy, E 1104
Roddy, J 945
Rodeia, S 2888
Rodiere, M 2259, 2956
Rodman, C 2725
Rodrigues, J 896
Rodrigues, M 1292
Rodrigues, SH 707
Rodrigues Manica, S 2497
Rodríguez, AM 352
Rodríguez, E 2621
Rodríguez, I 15, 2760
Rodríguez, M 2306
Rodríguez, MA 277
Rodríguez, S 498
Rodríguez, S 2062
Rodríguez, Y 1672
Rodríguez Aguilar, M 667
Rodríguez Carballeira, M 2841
Rodríguez Fernández, S 209
Rodríguez Gil, G 2021
Rodríguez Heredia, J 1465
Rodríguez Lozano, B 487, 1383
Rodríguez-Bautista, E 543, 1965
Rodríguez-Bellido, Z 450, 687, 1378
Rodríguez-Carrio, J 28
Rodríguez-Cuenca, S 391, 392
Rodríguez-Garcia, SC 480, 2490
Rodríguez-Gómez, M 498
Rodríguez-Jiménez, M 1672
Rodríguez-Lozano, C 1535, 2277
Rodríguez-Nieto, MJ 1172
Rodríguez-Pérez, N 442
Rodríguez-Reyna, TS 18
Rouleau, GW 1696, 2193
Rouse, T 2592
Rousseau, JC 2187
Roussou, E 874, 1433
Rouster-Stevens, KA 2341
Rout, J 874
Routier, E 1741
Rouvet, I 2348
Rouvière, B 41
Roux, C 1887
Rovati, LC 408, 955, 1193
Rovisco, J 611
Roy, M 2303
Roy, S 2031, 2032
Royo, A 1361
Rozenbaum, M 1537
Rozenblyum, E 1259
Rozo, C 1406
Ru, J 2242
Rúa-Figueroa, I 1587, 1588, 1612, 2619
Ruacho, G 2633
Ruan, CJ 1251
Ruaru, B 776, 2629, 2682, 2692, 2889
Rubas, W 2715
Rubenstein, E 810
Rubin, CT 49
Rubin, J 49
Rubinstein, T 2306
Rubio Romero, E 1158
Rubio-Muñoz, P 1518, 2402
Rubio-Romero, E 2112, 2343, 2723
Ruddock, S 874
Ruderman, EM 174, 205, 336, 513
Rudnik, M 1718, 1926
Rudwaleit, M 577, 578
Ruebeck, D 1247
Rueda-Gotor, J 644, 2527
Rueffer, JU 2254
Ruffatti, A 164, 1292, 1300
Rufibach, K 1830
Rui, TS 398
Ruibal Escribano, A 498, 1448
RUIDAVETS, JB Sr. 657
Ruivard, M 1758, 2904
Ruíz, J 1226
Ruíz de Morales, JM 1159, 2098
Ruíz de Temiño de la Peña, A 2841
Ruíz del Agua, A 1448
Ruíz Gutiérrez, L 1738, 2130
Ruíz Jimeno, T 2499
Ruíz Lucea, E 529, 1587, 1612
Ruíz Moreno, O 2297, 2723
Ruíz Muñoz, M 2841
Ruíz-Esquiet, V 460, 480, 1416, 1436, 2490
Ruíz-Irastorza, G 1589, 1606, 2608
Ruíz-Limon, P 391, 392, 1466, 2435, 2655, 2656, 2764
Ruíz-Montesinos, D 2277
Ruíz-Perdomo, Y 196
Ruíz-Ponce, M 392
Ruíz-Romero, C 1190
Ruíz-Romero, C 179
Rumsey, D 2100, 2317, 2351
Rumsey, DG 2303
Runa, M 980
Ruotolo, G 415
Ruperto, N 1823, 2272, 2855
Ruperto, N 2259, 2270, 2271
Ruperto, N 1278, 2273, 2333, 2631, 2859, 2956, 2958
Rus, H 2640
Rus, V 2640
Rush, JS 1784
Rush, S 230, 1806
Russell, D 2642
Russell, JJ 158
Russell, J 728
Russell, LA 218, 220, 221, 923
Russi, S 2874
Russo, L 320
Russo, R 95, 2860
Ruta, S 440, 1350, 1557, 2021, 2109
Rutgers, A 1782, 1846
Ruth, JH 971
Ruth, NM 1813
Ruttan, L 1621, 1623, 2807
Ruus, AK 570
Ruzek, M 961
Ruzickova, O 1692, 1694, 2153, 2154
Ryals, M 2609
Ryan, C 1688
<table>
<thead>
<tr>
<th>Name</th>
<th>Page Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ryan, EM</td>
<td>488, 1124</td>
</tr>
<tr>
<td>Rybak, L</td>
<td>2198</td>
</tr>
<tr>
<td>Rybakowska, P</td>
<td>2653</td>
</tr>
<tr>
<td>Rygg, M</td>
<td>1278, 2859</td>
</tr>
<tr>
<td>Ryoo, ZY Sr.</td>
<td>2708</td>
</tr>
<tr>
<td>Ryu, JH</td>
<td>1695, 2105</td>
</tr>
<tr>
<td>Ryu, JA</td>
<td>2405</td>
</tr>
<tr>
<td>Ryu, KH</td>
<td>82</td>
</tr>
<tr>
<td>S</td>
<td></td>
</tr>
<tr>
<td>S. Akhavan, P</td>
<td>451</td>
</tr>
<tr>
<td>Sa, KH</td>
<td>558</td>
</tr>
<tr>
<td>Saabye, M</td>
<td>2771</td>
</tr>
<tr>
<td>Saad, CGS</td>
<td>524, 1570</td>
</tr>
<tr>
<td>Saadoun, D</td>
<td>71, 281, 894, 1183, 1734, 1746, 2775, 2904</td>
</tr>
<tr>
<td>Saag, K</td>
<td>318, 350, 357, 828, 1141, 1888, 1890, 2256, 2777, 2848, 2950</td>
</tr>
<tr>
<td>Saaiibi, D</td>
<td>2021</td>
</tr>
<tr>
<td>Saavedra, J</td>
<td>1672</td>
</tr>
<tr>
<td>Saavedra Alanis, VM</td>
<td>1975</td>
</tr>
<tr>
<td>Sabbadini, MG</td>
<td>1292</td>
</tr>
<tr>
<td>Sabelli, M</td>
<td>440</td>
</tr>
<tr>
<td>Sacchetti, C</td>
<td>1456</td>
</tr>
<tr>
<td>Saccomani, C</td>
<td>497</td>
</tr>
<tr>
<td>Sace, A</td>
<td>682</td>
</tr>
<tr>
<td>Sacerdote, C</td>
<td>913</td>
</tr>
<tr>
<td>SACHETTO, Z</td>
<td>568</td>
</tr>
<tr>
<td>Sacnun, M</td>
<td>360, 2924</td>
</tr>
<tr>
<td>Sacnun, MP</td>
<td>332</td>
</tr>
<tr>
<td>Sacre, K</td>
<td>796, 814</td>
</tr>
<tr>
<td>Sacrini, F</td>
<td>650</td>
</tr>
<tr>
<td>Sada, KE</td>
<td>1013, 1593, 1751, 1762, 1778, 2558</td>
</tr>
<tr>
<td>Sadatsafavi, M</td>
<td>1316</td>
</tr>
<tr>
<td>Sadeghi, E</td>
<td>2632</td>
</tr>
<tr>
<td>Sadeh, J</td>
<td>1822</td>
</tr>
<tr>
<td>Sadun, R</td>
<td>910</td>
</tr>
<tr>
<td>Sadusky, J</td>
<td>2261</td>
</tr>
<tr>
<td>Saegusa, J</td>
<td>861, 1321</td>
</tr>
<tr>
<td>Saeki, T</td>
<td>1157, 1180, 2093</td>
</tr>
<tr>
<td>Saeki, Y</td>
<td>1447</td>
</tr>
<tr>
<td>Saevarsdottir, S</td>
<td>127, 132, 438, 914</td>
</tr>
<tr>
<td>Saeys, Y</td>
<td>1582</td>
</tr>
<tr>
<td>Saez, C</td>
<td>159, 1972</td>
</tr>
<tr>
<td>Safer, P</td>
<td>1023, 1919</td>
</tr>
<tr>
<td>Saferding, V</td>
<td>63, 1338, 2709</td>
</tr>
<tr>
<td>Saffari, SE</td>
<td>1702</td>
</tr>
<tr>
<td>Safford, MM</td>
<td>336, 1395</td>
</tr>
<tr>
<td>Sagar, D</td>
<td>2589</td>
</tr>
<tr>
<td>Sagawa, R</td>
<td>272</td>
</tr>
<tr>
<td>Saggard, R</td>
<td>2776</td>
</tr>
<tr>
<td>Sagliani, J</td>
<td>520</td>
</tr>
<tr>
<td>Saha, A</td>
<td>1631</td>
</tr>
<tr>
<td>Saha, S</td>
<td>1929</td>
</tr>
<tr>
<td>Sahakian, L</td>
<td>2618</td>
</tr>
<tr>
<td>Sahhar, J</td>
<td>945</td>
</tr>
<tr>
<td>Ş</td>
<td>2204</td>
</tr>
<tr>
<td>Şahin, O</td>
<td>2204</td>
</tr>
<tr>
<td>Ş</td>
<td></td>
</tr>
<tr>
<td>Şahin Onat, Ş</td>
<td>305</td>
</tr>
<tr>
<td>Ş</td>
<td></td>
</tr>
<tr>
<td>Sah, S</td>
<td>1482</td>
</tr>
<tr>
<td>Sahlström, P</td>
<td>476, 834</td>
</tr>
<tr>
<td>Said Nahal, R</td>
<td>1579</td>
</tr>
<tr>
<td>Saidin, S</td>
<td>759, 1577, 1744, 1745, 1941</td>
</tr>
<tr>
<td>Saifan, C</td>
<td>2352</td>
</tr>
<tr>
<td>Saigusa, R</td>
<td>26, 31, 1719</td>
</tr>
<tr>
<td>Saiiki, O</td>
<td>2474</td>
</tr>
<tr>
<td>Sailler, L</td>
<td>819, 2661</td>
</tr>
<tr>
<td>Sainsbury, I</td>
<td>1418</td>
</tr>
<tr>
<td>Sainz, F</td>
<td>2062</td>
</tr>
<tr>
<td>Sainz de la Maza, M</td>
<td>1516</td>
</tr>
<tr>
<td>Saito, K</td>
<td>417, 841</td>
</tr>
<tr>
<td>Saito, L</td>
<td>517</td>
</tr>
<tr>
<td>Saito, M</td>
<td>2628</td>
</tr>
<tr>
<td>saito, S</td>
<td>1704</td>
</tr>
<tr>
<td>Saito, S</td>
<td>412</td>
</tr>
<tr>
<td>Saito, S</td>
<td>2017</td>
</tr>
<tr>
<td>Saitta, A</td>
<td>2984</td>
</tr>
<tr>
<td>Saka, K</td>
<td>1388</td>
</tr>
<tr>
<td>Sakai, R</td>
<td>841</td>
</tr>
<tr>
<td>Sakai, R</td>
<td>2017</td>
</tr>
<tr>
<td>Sakai, Y</td>
<td>299, 973</td>
</tr>
<tr>
<td>Sakamoto, N</td>
<td>2144</td>
</tr>
<tr>
<td>Sakata, K</td>
<td>2792</td>
</tr>
<tr>
<td>Sakata, K</td>
<td>798</td>
</tr>
<tr>
<td>Saketkoo, LA</td>
<td>919, 946, 2096</td>
</tr>
<tr>
<td>Saketkoo, LA</td>
<td>745, 2930</td>
</tr>
<tr>
<td>Sakhardande, S</td>
<td>899</td>
</tr>
<tr>
<td>Sakiyama, M</td>
<td>170</td>
</tr>
<tr>
<td>Sakurai, N</td>
<td>237, 1460</td>
</tr>
<tr>
<td>Salah, S</td>
<td>1366</td>
</tr>
<tr>
<td>Salama, AD</td>
<td>1773</td>
</tr>
<tr>
<td>Salas, R</td>
<td>2306</td>
</tr>
<tr>
<td>Salazar, F</td>
<td>420</td>
</tr>
<tr>
<td>Salazar, G</td>
<td>1721, 2927</td>
</tr>
<tr>
<td>Saldaña-Baarnard, M</td>
<td>1445</td>
</tr>
<tr>
<td>Saldarriaga Rivera, L</td>
<td>411, 2021</td>
</tr>
<tr>
<td>Saleh, A</td>
<td>1363</td>
</tr>
</tbody>
</table>
Saleh, K 471, 2366
Salem, D 37
Salem, JE 5L
Salinas, G 112
Salinas, M 2116
Salinger, A 485
Salliot, C 2842
Salman-Monte, T 2621
Salmon, JH 1056, 1222, 2464
Salmon, JE 1482, 1790, 1812, 1833, 2581
Salinger, A 485
Salliot, C 2842
Salmon, JE 1482, 1790, 1812, 1833, 2581
Salmon, JH 1056, 1222, 2464
Salmon, JE 1482, 1790, 1812, 1833, 2581
Salmon, JH 1056, 1222, 2464
Salmon, JE 1482, 1790, 1812, 1833, 2581
Salmon, JH 1056, 1222, 2464
Salmon, JE 1482, 1790, 1812, 1833, 2581
Salmon, JH 1056, 1222, 2464
Salomon, B 2701
Salome, J 2233, 2234
Salor, B 800
Saluja, M 2486
Salvador, G 480
Salvarani, C 783, 790, 791, 815, 1075, 1292
Salvatierra, G 2237
Salvatorii, F 1079
Samaranayaka, M 2663
Sambandham, G 2124
Samersaw-Lund, MB 1276
Sami, H 2137
Sammaritano, LR 1264
Sammel, A 808, 809
Sampalis, JS 432, 467, 2491, 2908
Sampath, S 168
Sampene, E 1087, 1088, 1171
Sandling, JK 1638, 1675, 2654
Sandoo, A 147
Sandovici, M 807
Sanqvist, G 2662
Sandri, G 638
Sandrock, R 462
Sands, E 2091
Sangani, S 2163
Sanges, S 1685, 2716, 2717
Sangle, S 1773, 2100, 2626
Sangle (Joint First Author), S 1768
Sanguankeo, A 149, 1484, 1485
Sanjuan, MA 2589
Sanjurjo-Rodríguez, C 1930
Sanmartí, R 460, 480, 639, 1416, 1436, 1516, 1535, 2475, 2490
Sanna, G 5
Sanner, H 1276, 2961
Sano, H 2685
Sansinanea, P 1766, 2676
Sanssonno, DE 2874
Santa Cruz, MJ 360, 1359, 1360, 1564, 2021
Santana Suárez, B 1807
Santaniello, A 735, 1712
Santelices, L 1642, 1643
Santelli, E 1456
Santesso, N 1599
Santiago, L 939
Santiago, L 2021
Santiago, L 2592
Santillan-Guerrero, E 1445
Santinon, F 866, 2701
Santos, C 2883
Santos, H 611
Santos, L 1616
Santos, MJ 611, 1283, 1286, 2959
Santos, O 276
Santos Faria, D 611
Santos-Gómez, M 2857
Santos-Soler, G 1612
Santos, A 200, 1702
Sanz, I 33, 833, 2814, 2974
Sanz, J 1535
Sanz Alonso, M 487, 1383
Sarano, J 1645, 2924
Saraux, A 41, 216, 574, 873, 877, 1056, 1438, 1439, 1442, 1491, 2394, 2842, 2967
Sarazin, J 2095
Sargin, G 2353
Sari, A 1174, 1240, 1312, 1451, 1522, 2110, 2409, 2727, 2742, 2743
Sari, I 656, 1514, 2805
Saridogan, M 2204
Sarikaya, S 2204
Sarkar, M 897
Sarkissian, A 1594
Sarmiento-Velasquez, O 450, 687, 1378
Sarode, R 2
Sarpel, T 739
Sarsour, K 352, 527, 778
Sarvagyl-Maman, H 1503, 1648
Sarzi-Puttini, P 521
Sarzi-Puttini, P 152, 280, 2015, 2965
Sasae, Y 2563
Sasaki, E 1319, 1320
Sasaki, M 2853
Sasaki, T 2601
Sasso, EH 438, 1371, 1900
Sasu, M 997
Sato, E 801, 845, 1654, 2924
Sato, H 1414
Sato, S 26, 31, 1719
Sato, S 854
Sato, S 76
Sato, T 1776
Sato, T 2421
Sato, T 2335
Sato, Y 1179
Sato, Y 1700
Sato, Y 237, 1460
Satoh, M 773
Satoh, Y 773
Satpathy, A 2930
Sattar, N 868
Satterwhite, L 2407
Satulu, I 1608
Sauco, C 2021
Sauer, B 433, 1039, 1342, 2377, 2893
Sauer, PhD, BC 2378, 2448
Saunders, KC 475, 1019
Saunders, S 1325
Saunkeah, B 222
Saurit, V 572, 1645, 2008, 2924
Sauter, R 2983
Sauvageau, D 1817
Sauza del Pozo, MJ 1654, 2924
Savary, L 863
Savic, S 1894
Savioli, B 800, 801
Savjani, M 1633, 2627
Savu, A 1957
Sawabe, T 2710
Sawada, T 2249, 2732
Sawalha, AH 178, 767, 1705, 2636, 2720
Sawaya, R 1971
Saxena, A 673, 680, 2957
Saxena, R 669, 1921
Sayeed, SM 2784
Saygin, C 2747
Saygin, D 1598, 2726, 2747
Sayles, H 135, 472, 546, 1124, 1357, 2377
Sayre, EC 315, 883, 1245, 1316, 2972
Sazak, S 369
Scaglioni, V 1772, 1777
Scalbert, C 2126
Scalzi, LV 349, 2283
Scarafia, S 155
Schaal, J 1330
Schadler, AD 1046
Schaefer, LF 917, 2944, 2945
Schaefer, P 886, 887
Schaefer, PH 642
Schäfer, VS 258, 697, 781
Schaffer, D 109, 1858
Schafhalter-Zopoth, I 2174
Schalm, S 2758
Schanberg, LE 1296, 2282
Schechtman, J 2951
Scheepers, LEJM 1117, 2073, 2080
Schein, F 797
Scheinberg, M 888, 2796
Scheinecker, C 2709
Schelin, ME 423
Schell, J 89
Schembri, G 809
Schenk, S 2180
Schenker, H 2024
Schibli, R 1708
Schieir, O 443, 461, 1393, 1814, 2390, 2391, 2955
SCHIEVANO, E 145
Schiff, M 512, 618, 1424, 1818, 2472, 2868
Schippenbauer, A 2136, 2141
Schiffer, P 2253
Schiffrin, E 1895, 2772
Schikler, K 641, 2856
Schiodan, C 1830
Schiopu, E 729, 919, 946, 2095, 2930
Schleich, C 307, 1998
Schleisman, M 1326
Schlenk, EA 109, 1858
Schlesinger, N 60, 1138, 2070
Schlichting, DE 502, 513, 855, 2866
Schlom, J 1182
Schmajuk, G 126, 189, 202, 327, 1047, 1089, 2263, 2890
Schmeling, H 2270, 2316, 2341
Schmets, G 293
Schmidt, C 1365
Schmidt, M 1918
Schmidt, P 2026, 2407
Schmidt, RL 1682
Schmidt, T 2901
Schmidt-Olsen, S 1830
Schmitt, S 2798
Schmitt-Haendle, M 414
Schmittat, G 2007
Schmucker, AM 2853
Schmukler, J 1101, 2264
Schneeberger, E 1645
Schneeberger, EE 231, 1007, 1564, 1802, 2551, 2554
Schweebeiss, S 527
Schneider, C 938
Schneider, M 266, 307, 695, 993, 1295, 1430, 1589, 1998
Schneider, M 1851
Schneider, R 365
Schneiderová, P 1358
Schniering, J 1708, 1717
Schnitzer, TJ 1196
Schnöbel-Müller, E 2288
Schoen, P 2476
Schoenecker, E 1124
Schollaert-Fitch, K 1284, 1728, 2346
Scholz, B 1095
Scholz, G 436
Schonenberg-Meinema, D 2291
Schonfeld, S 1963
Schousboe, J 2180
Schreiber, B 737
Schreiber, K 2759
Schreiter, J 80
Schreiyäck, C 1943
Schreif, A 2912
Schrieb, L 809
Schroder, D 1844
Schroeder, C 175, 183
Schroeder, D 1752
Schroeder, K 1001
Schroeder, LL 1100
Schroeder, P 2565
Schubert, T 50
Schuch, F 414
Schuck, E 2440
Schuler, M 1006
Schulert, G 1895, 2324, 2332
Schulte-Pelkum, J 695
Schulz, H 1663
Schulz-Knappe, P 695, 722, 875, 1182
<table>
<thead>
<tr>
<th>Name</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Şendur, OF</td>
<td>2204</td>
</tr>
<tr>
<td>S</td>
<td></td>
</tr>
<tr>
<td>Sène, D</td>
<td>873, 876</td>
</tr>
<tr>
<td>Senécal, JL</td>
<td>727</td>
</tr>
<tr>
<td>Senel, S</td>
<td>542, 1455, 1472, 1534</td>
</tr>
<tr>
<td>Senger, K</td>
<td>674</td>
</tr>
<tr>
<td>Sengewein, R</td>
<td>307, 1998</td>
</tr>
<tr>
<td>Sengupta, M</td>
<td>1239</td>
</tr>
<tr>
<td>Senolt, L</td>
<td>78, 579, 692, 1694, 1694, 2153, 2154, 2176, 2434, 2928</td>
</tr>
<tr>
<td>_SENTURK, RS</td>
<td>1163</td>
</tr>
<tr>
<td>SENTURK, T</td>
<td>2353</td>
</tr>
<tr>
<td>Seo, P</td>
<td>784, 785, 789, 1752, 1760, 1767, 1774, 1783, 1844, 1849</td>
</tr>
<tr>
<td>Seo, SK</td>
<td>82</td>
</tr>
<tr>
<td>Seo, WJ</td>
<td>662, 1110</td>
</tr>
<tr>
<td>Seoane, D</td>
<td>1232, 2526</td>
</tr>
<tr>
<td>Sepriano, A</td>
<td>35, 259, 591, 592, 593, 2497, 2806, 2967</td>
</tr>
<tr>
<td>Sequeira, W</td>
<td>2824, 2953</td>
</tr>
<tr>
<td>Serada, S</td>
<td>974</td>
</tr>
<tr>
<td>Serafi, S</td>
<td>2137</td>
</tr>
<tr>
<td>Serafin, DS</td>
<td>49</td>
</tr>
<tr>
<td>Serafini, PC</td>
<td>1302</td>
</tr>
<tr>
<td>Sergeant, JC</td>
<td>853</td>
</tr>
<tr>
<td>Sergeeva, M</td>
<td>2024</td>
</tr>
<tr>
<td>Serhan, C</td>
<td>298</td>
</tr>
<tr>
<td>Seror, R</td>
<td>873, 876, 877, 1491</td>
</tr>
<tr>
<td>Serrano, B</td>
<td>159, 632, 1520, 1972, 2129, 2488</td>
</tr>
<tr>
<td>Serrano, J</td>
<td>2693, 2694</td>
</tr>
<tr>
<td>Serrano, RM</td>
<td>2924</td>
</tr>
<tr>
<td>Serratrice, J</td>
<td>1754</td>
</tr>
<tr>
<td>Serre, G</td>
<td>2919</td>
</tr>
<tr>
<td>Sertdemir, Y</td>
<td>739</td>
</tr>
<tr>
<td>Servais, L</td>
<td>5L</td>
</tr>
<tr>
<td>Servick, C</td>
<td>2047</td>
</tr>
<tr>
<td>Servy, H</td>
<td>337, 1234</td>
</tr>
<tr>
<td>Seta, N</td>
<td>575</td>
</tr>
<tr>
<td>Seth, B</td>
<td>111</td>
</tr>
<tr>
<td>Sethi, B</td>
<td>2953</td>
</tr>
<tr>
<td>Setiadi, AF</td>
<td>674</td>
</tr>
<tr>
<td>Seto, A</td>
<td>843</td>
</tr>
<tr>
<td>Seto, N</td>
<td>290</td>
</tr>
<tr>
<td>Setoguchi, S</td>
<td>1032</td>
</tr>
<tr>
<td>Sève, P</td>
<td>814, 2904</td>
</tr>
<tr>
<td>Seversen, H</td>
<td>2766</td>
</tr>
<tr>
<td>Seviola Pérez, B</td>
<td>2343</td>
</tr>
<tr>
<td>Sevim, E</td>
<td>12</td>
</tr>
<tr>
<td>Sewell, KL</td>
<td>2798</td>
</tr>
<tr>
<td>Sewerin, P</td>
<td>266, 307, 993, 1998</td>
</tr>
<tr>
<td>Sexton, J</td>
<td>2800</td>
</tr>
<tr>
<td>Sexton, J</td>
<td>147, 342, 486, 1345, 2861, 2938</td>
</tr>
<tr>
<td>Seyahi, E</td>
<td>746, 802, 803, 2103, 2462, 2729, 2747</td>
</tr>
<tr>
<td>Seyhögolu, E</td>
<td>1312, 2409</td>
</tr>
<tr>
<td>Sezer, I</td>
<td>2496</td>
</tr>
<tr>
<td>Sfikakis, PP</td>
<td>147, 1387, 2686, 2744</td>
</tr>
<tr>
<td>Sfrent-Cornateanu, R</td>
<td>2660</td>
</tr>
<tr>
<td>Sfriso, P</td>
<td>365</td>
</tr>
<tr>
<td>Shabana, K</td>
<td>2299</td>
</tr>
<tr>
<td>Shackleton, M</td>
<td>2119</td>
</tr>
<tr>
<td>Shaddick, G</td>
<td>2039</td>
</tr>
<tr>
<td>Shadick, N</td>
<td>441</td>
</tr>
<tr>
<td>Shadick, NA</td>
<td>75, 435, 445, 1241, 1371, 2384</td>
</tr>
<tr>
<td>Shadyab, A</td>
<td>649, 977, 2851</td>
</tr>
<tr>
<td>Shafaie, N</td>
<td>2859</td>
</tr>
<tr>
<td>Shafer, S</td>
<td>586</td>
</tr>
<tr>
<td>Shah, AA</td>
<td>729, 919, 946, 1922, 2689, 2902, 2930</td>
</tr>
<tr>
<td>Shah, A</td>
<td>137</td>
</tr>
<tr>
<td>Shah, B</td>
<td>1144</td>
</tr>
<tr>
<td>Shah, M</td>
<td>850, 2128, 2155</td>
</tr>
<tr>
<td>Shah, S</td>
<td>495</td>
</tr>
<tr>
<td>Shah, U</td>
<td>719</td>
</tr>
<tr>
<td>Shahbazi, A</td>
<td>1327, 2148</td>
</tr>
<tr>
<td>Shahnawaz, Z</td>
<td>2028</td>
</tr>
<tr>
<td>Shahwan, F</td>
<td>151</td>
</tr>
<tr>
<td>Shakhnovich, V</td>
<td>2296</td>
</tr>
<tr>
<td>Shakhtakhtinskaya, F</td>
<td>386</td>
</tr>
<tr>
<td>Shakoor, N</td>
<td>347, 2247</td>
</tr>
<tr>
<td>Shamim, E</td>
<td>2136</td>
</tr>
<tr>
<td>Shan, J</td>
<td>1267</td>
</tr>
<tr>
<td>Shan, Y</td>
<td>1815, 2453</td>
</tr>
<tr>
<td>Shanahan, W</td>
<td>888</td>
</tr>
<tr>
<td>SHANG, Q</td>
<td>1903, 2545</td>
</tr>
<tr>
<td>Shanmugam, VK</td>
<td>96, 97, 729, 919, 946, 1922, 2665, 2930</td>
</tr>
<tr>
<td>Shao, J</td>
<td>2451</td>
</tr>
<tr>
<td>Shapiro, LS</td>
<td>215, 1166, 1686</td>
</tr>
<tr>
<td>Shardell, M</td>
<td>1006</td>
</tr>
<tr>
<td>Sharma, A</td>
<td>634, 1637, 1765, 2010, 2100, 2124</td>
</tr>
<tr>
<td>Sharma, A</td>
<td>1175</td>
</tr>
<tr>
<td>Sharma, D</td>
<td>1301</td>
</tr>
<tr>
<td>Sharma, E</td>
<td>1142</td>
</tr>
<tr>
<td>Sharma, G</td>
<td>2599</td>
</tr>
<tr>
<td>Sharma, J</td>
<td>60, 2598</td>
</tr>
<tr>
<td>Sharma, K</td>
<td>1765</td>
</tr>
</tbody>
</table>
Sharma, L 932, 936, 1050, 2188, 2193, 2251
Sharma, M 2579
Sharma, N 969, 1063
Sharma, R 2395
Sharma, R 24, 2190
Sharma, S 2124
Sharma, S 1329
Sharma, TS 444
Sharma, V 85
Sharon, H 1872
Sharples, L 874
Shaughnessy, L 1309, 1809
Shaukat, A 170, 1127
Shaw, GM 1290, 1291
Shaw, P 1043, 1198, 1199
Shaw, R 2174
Shaw, S 73, 1571, 1936
Shaw, T 293
Shaweesh, Y 2668
Shbeeib, I 792
Shea, B 1257
Sheaff, M 2624
Sheahan, A 1548
Shealy, D 2704
Sheehy, C 2507, 2508
Sheehy, S 839
Sheets, R 1273
Sheikh, SZ 2611
Shelef, MA 294
Shelley, D 1203
Shemesh Eisen, L 1648
Shen, F 1428
Shen, J 1459
shen, L 1311
Shen, M 2113
Shen, N 180, 181, 954, 1574, 1659, 2652
Shen, S 618
Shen, S 1031
Shen, Y 2702, 2933
Shenavandeh, S 750
Sheng, Q 1367, 1368, 1764
Sheng, S 1477, 1908, 2437
Shergy, W 1397
Sheridan, J 2598
Sherman, N 398, 1186
Sherry, DD 2992
Shesternya, P 2445
Sheth, K 636, 2046
Shi, B 1724
Shi, C 928
Shi, H 436
Shi, H 1, 643, 1567
Shi, J 518
Shi, J 2750
Shi, J 2134
Shi, J 2101
Shi, L 1660
Shi, S 224
Shi, X 2241, 2242
Shibanuma, N 973
Shibata, A 2017
Shiboski, C 877
Shiboski, S 126
Shibutou, N 804
Shields, D 1028
Shiff, NJ 2289, 2292, 2952
Shike, H 2937
Shim, J 2500
Shim, SC 1143, 1474, 2445, 2461
Shimada, H 1690, 2424
Shimizu, C 2937
Shimizu, J 1737
Shimizu, M 370, 2299, 2325
Shimizu, S 1593
Shimizu, S 170
Shimizu, T 1996, 2038
Shimizu, T 170
Shimizu, T 1882, 2144
Shimizu, Y 1388
Shimojima, Y 1165, 1732
Shimokawa, H 1704
Shimonov, D 1770
Shin, DY 2905
Shin, JH 1565, 2519
Shin, JY 1958
Shin, J 82
Shin, K 827, 1547, 2630
Shin, S 2441
Shinomiya, N 170
Shiozawa, S 866
Shipa, M 1433
Shir, Y 467
Shirai, T 772, 1704, 2749, 2934
Shirai, Y 2687
Shirota, Y 1704, 2749
Shisha, T 2796
Shive, C 2741
Shlomchik, M 898
Shmagel, A 2179
Shmagel, AK 834, 2169, 2206
Smith, R 18L
Smith, S 168
Smith, SR 2833
Smith, S 917, 2057, 2944
Smith, S 808
Smith, T 1354
Smith, T 1246, 2831
Smith, V 752, 776, 1248, 1283, 1286, 1683, 2005, 2682, 2692, 2959
Smith, WM 1161
Smitherman, EA 384, 385, 2294
Smithson, G 553
Smolen, JS 61, 63, 452, 502, 511, 571, 621, 622, 848, 966, 1338, 1397, 1415, 1418, 1419, 1420, 1589, 1796, 1821, 2245, 2268, 2456, 2466, 2709, 2796, 2861, 2864, 2871, 2971
Smolewska, E 2859
Smržová, A 1694
Smucrova, H 1694
Smulders, YM 2365
Snoad, B 60, 2598
Snoeck, V 2476
Snow, A 382
Snow, M 2096
Snowden, N 186
Snyder, M 424, 474
Snyder, M 1752
So, A 1104
So, A 883, 2805, 2972
Soare, A 655, 864, 997, 1706, 1925, 2660
Soares de Souza, S 269
Sobanski, V 1685
Sobue, Y 540
Sockalingam, S 1629
Söderling, J 916
Söderling, JK 133
Sodin Semrl, S 704, 2719
Soejima, M 841
Soejima, Y 237, 1460, 2151
Soen, S 1435
Soever, L 316, 2120
Sofue, H 272
Sohani, A 1179
Sohl, B 349
Sohn, D 1645
Sohn, DH 1928, 2582
Sokka-Isler, T 1054, 2834
Sokol, R 1304
Sokolove, J 1357, 1928
Solans, R 876
Solau-Gervais, E 2842
Soldano, S 776
Soler, C 2259, 2956
Soler, MJ 2621
Soler i Ferrer, C 209
Solfietti, L 27
Soliman, S 1664, 1921
Solmaz, D 447, 1514, 1534
Solomon, A 2355
Solomon, D 1348
Solomon, DH 187, 527, 856, 920, 989, 1021, 1044, 1113, 1796, 1862, 1864, 2057, 2060, 2381, 2788, 2844, 2920
Solomon, GE 637
Solomon, JJ 2392
Solomon, K 1895
Solomons, N 885
Soloshenko, M 386, 2279, 2280
Solow, EB 204, 1799, 1860
Solus, JF 1367, 1368, 1609, 1764
Soma, J 1778
Soma, K 1440, 1906, 2393
Somers, EC 1003, 2986
Somma, L 269
Son, CN 975, 1434, 2444
Son, J 2092
Son, MB 1242, 1597
Son, SM 1540
Son, Y 551
Sondag, M 2107
Sone, T 69, 1324
Sonesson, SE 941, 2817
Song, AP 1155
Song, D 2141
Song, H 2241
Song, IH 1560
Song, JJ 245
Song, J 2194, 2195, 2223, 2770
Song, JS 2074
Song, L 1660
Song, M 598
Song, P 1326
Song, R 585, 2510
Song, X 42
Song, X 2593, 2594, 2812
Song, Y 1561
Song, YW 82, 87, 827, 1181, 1377, 1412, 1417, 1474, 1495, 1547, 1970, 2009, 2025, 2122, 2145, 2168, 2441, 2746, 2794, 2905
Stanevica, V 2272
Stanevicha, V 1278, 1283, 1286, 2259, 2273, 2333, 2956, 2959
Stanfield, L 111
Stange, R 63
Stanislavchuk, M 1909, 2370
Stanley, S 669
Stanwyck, C 2768
Stapleton-Gray, K 493
Stark, J 1030, 1527, 1548
Stark, M 775, 2931
Starkebaum, G 485
Starr, M 467, 631
Starzyk, K 468, 1394
Staten, N 1918
Staudt, LM 2773
Stauffer, J 15L
Staunstrup, LM 489
Stavrakis, S 1627, 1841
Ste-Marie, P 467
Stebbens, S 2506
Stebbins, C 663
Steen, J 65, 476, 477, 970
Steen, VD 729, 730, 758, 919, 946, 1686, 1922, 2114, 2665, 2930, 2982
Steere, A 494, 1020
Steere, AC 949
Stefanica, A 1925
Stefanick, M 2180
Stefanik, J 857, 2184, 2949
Steffensen, R 1077, 1514
Stegeman, CA 1782, 1846
Steigelman, H 1594, 1614, 1615, 2598, 2725
Stein, CM 1367, 1368, 1609, 1764
Stein, CM 720, 1022, 1586, 2362
Stein, N 1609
Steiner, G 571, 696, 848, 966, 1323, 1432, 2709, 2864, 2871
Steinfeld, J 1884
Steiniche, T 799
Steinig, E 1239
Steinsson, K 1606
Stel, AJ 2943
Stellato, M 1718, 1926, 2700
Stengaard-Pedersen, K 1077
Stenlund, H 2354
Stepan, J 320
Stepenaskie, S 379
Stephansson, O 916
Stern, E 1713
Stetler-Stevenson, M 2143
Stetsovsky, D 1057
Steunebrink, LMM 1078
Steup-Beekman, G 1402
Stevens, A 924, 1281, 1283, 2350, 2959
Stevens, R 1191, 2225, 2226
Stevens, W 945, 948
Stevens-Lapsley, J 1854
Stevenson, DK 1290
Stevenson, L 2607
Stevenson, R 2316
Stever, JR 1039, 1342, 2096
Stewart, D 198
Stewart, J 631
Stewart, KG 1285
Stewart, L 972
Stewart, S 2050
Stiburkova, B 170, 1104, 2087
Sticherling, M 633
Stiening, C 1918
Stifano, G 1923
Stimec, J 373
Stinson, JN 1259, 2952
Stinson, WA 971, 1336, 2926
Stobbione, P 698, 930
Stock, A 29, 900, 1735, 1836
Stockert, L 2371
Stoenuiu, MS 1373
Stoffer, M 848
Stohl, W 1837
Stoica, V 997, 2660
Stojan, G 706, 1634, 1635, 1636
Stolfa, J 2534
Stoll, ML 641, 2320
Stoll, T 2925
Stolshek, BS 363, 2448
Stone, DL 292, 1892, 2758
Stone, J 1179
Stone, JH 4L, 778, 892, 895, 1175, 1179, 1752, 1783, 1789, 1844, 2936
Stone, V 1096
Storkanova, H 766, 1692, 1694, 2153, 2154
Storms, L 906
Stott-Miller, M 2593, 2594, 2812
Stoten, V 1820
Stoye, C 1448
Stradner, M  2646, 2877
Strand, V  500, 501, 595, 596, 608, 892, 1371, 1477, 1528, 1561, 1839, 1906, 1918, 2258
Strangfeld, A  1295, 1430
Strayhorn, MT  2199, 2201
Strengholt, S  436, 522, 533, 1427, 1437
Striebich, CC  185, 1055
Strienger, E  2317
Strle, K  494, 949, 1020
Stroes, E  2546
Strotmeyer, E  2180
Struglics, A  1189
Su, J  713, 714, 718, 1590, 1591, 1621, 1623, 1624, 1652, 2617, 2623, 2769, 2807, 2808
Su, K  1669
Su, L  2925
Su, L  2420
Su, Y  1725, 1927
Su, Z  212, 468, 1394
Suárez, A  28
Suarez-Almazor, M  118, 531, 850, 1052, 1231, 1252, 2128, 2155, 2200, 2262, 2395, 2483
Subang, R  37
Subash, M  2045
Subedi, A  367, 1153
Subesinghe, S  1768
Suboticki, JL  1352, 1419, 1420, 1422, 2453, 2456
Subra, JF  1758, 2736
Subramaniam, A  2700
Subramanian, A  1330
Subramanian, SV  920, 1862
Suchartlikitwong, S  1480, 1481
Suda, M  389, 390
Sudano, D  2906
Sudharshan, L  1246
Sudo, A  2485
Suehiro, R  2298
Suelo, D  1564
Suemori, K  1010, 1064
Sugahara, K  20
Sugano, E  1388
Sugihara, T  795, 841, 1013, 1751, 1762
Sugimoto, N  1388
Sugioka, Y  464
Sugita, J  2887
Sugitani, N  1388
Sugiura, M  1593
Sugiyama, E  275, 703, 1942
Sugiyama, K  555, 870
Sugiyama, N  431
Sugiyama, Y  237, 1460, 2150, 2151
Suguro, T  2416
Suh, CH  2074, 2445, 2461
Suh, DH  82, 87
Suh, HJ  150
Suh, J  1228
Suitner, M  1599
Sujatha-Bhaskar, S  674
Sulaiman, A  2370
Sule, G  8, 2564
Sule, S  2310
Sulik, A  761
Suliman, YA  2668
Sulli, A  698, 776, 2005, 2629, 2682, 2692, 2889
Sullivan, C  2507, 2508
Sullivan, KE  1167, 1660
Sullivan, K  943
Sumida, T  393, 1013, 1751, 1762, 2873
Sumino, T  412
Sumiyoshi, R  1882, 2144
Sumova, B  78, 2176, 2928
Sumpton, D  1231
Sun, C  177
Sun, C  2901
Sun, CC  1060
Sun, F  1791, 2146
Sun, HW  899
Sun, K  227, 1244
Sun, L  710, 1071, 2616
Sun, L  499
Sun, M  970
Sun, N  1015
Sun, W  22
Sun, X  1883
Sun, X  485, 2575, 2601
Sunada, Y  69
Sundaram, S  2174
Targoff, IN 1274
Targoff, IN 2136, 2142, 2337
Tarn, J 563, 565, 1500
Taroni, JN 1014
Tarp, S 2367
Tarrant, J 504, 1458
Tarrant, TK 49
Tartaglia, C 1621, 1623, 2807
Tas, SW 967, 1847
Tarvin, S 1280
Tarzynski-Potempa, R 2481
Tas, SW 967, 1847
Tashkin, DP 726, 749, 943
Tasset, C 504, 510, 534, 537, 1458
Tate, G 1645
Tate, P 2021
Tate, R 355
Tatebe, N 2558
Tateishi, K 973
Tatomir, A 2640
Tatsis, S 2307
Tatulych, S 1397, 2371
Taulaigo, AV 1498, 1651
Taurog, J 1578, 1910
Tausche, AK 1104, 1127
Tavakoli, K 2668
Tavares Brenol, JC 2924
Tavernier, J 2773
Taxter, AJ 351
Tay, SH 200
Tayama, M 1319
Tayar, J 531, 2155
Taylor, C 256, 2005
Taylor, DCA 1118, 1119, 1120, 1121, 1122, 2059
Taylor, J 2294, 2301
Taylor, PC 504, 508, 855, 1515, 2260, 2352, 2866, 2870, 2963
Taylor, S 2768
Taylor, T 503
Taylor, W 2845
Taylor, WJ 345, 350, 357, 2063, 2064, 2843, 2950
Tazzyman, S 288
Tchetverikov, I 1551, 2542, 2543, 2544
Teague, H 899
Tebib, J 1439
Tebo, AE 1682
Tecson, K 355
Tedeschi, SK 187, 837, 988, 1348, 1589, 1622, 1863, 1953, 2060, 2920
Teeple, A 362
Teerakanok, J 1480, 1481
Teerenstra, S 2438
Tegzova, D 6
Tehrani, R 515
Teil, M 1809
Teitsma, XM 167, 1476, 2458
Teixeira, C 35
Tejada-Reyes, E 543, 1965
Tejera, BS 1379, 2403
Tejón, P 1516
Tektonidou, M 12, 2744, 2760
Telles, RW 723
Tellier, E 71
Tello Winniczuk, N 2414
Temesgen-Oyelakin, Y 899
ten Brinck, RM 482, 918
ten Cate, R 1278, 2259, 2291, 2328, 2956
Tenbrock, K 364
Teng, CC 2378
Teng, GG 200, 1702
Teng, J 1
Teng, L 601, 602, 603, 604
Teng, O 295
Teng, YKO 890
Teng, MS, CC 433, 1039, 1342, 2448
Tenner, C 1217
Tennermann, N 2997
Tenorio, JA 1891
Teo, C 2373
Teo, M 629, 2520
Teoh, L 2947
Teoh, LK 2625
Tepper, M 298
Ter Haar, N 1896
Ter Wee, MM 1253
Terada, Y 271, 1149
Terai, C 2138, 2139
Terao, C 172, 2100
Terbrueggen, R 441
Terkeltaub, R 1142, 2064, 2089
Terreri, MT 1283, 1286, 2959
Terrier, B 796, 797, 814, 1754, 1757, 1758, 1759, 1763, 1779, 2716, 2717, 2738, 2739, 2754, 2888, 2932
Terry, K 522, 533
Terslev, L 236, 246, 249, 265, 781, 1373, 1878, 2020, 2055, 2938, 2967
Teruel, M 178
Tesei, G 1679
Tesher, M 2306
Teshigawara, S 1447
Teshima, T 2887
Tesiram, J 430
Teske, NM 1613
Teslovich, N 2826
Tesser, J 424, 2493
Tessier, PA 466, 1027
Testi, A 1766, 267
Thabane, L 896
Thabut, D 894
Thaci, D 2539
Thakur, M 2455
Thalmann, R 2909
Thanarajasingam, U 1880
Thanoo, N 2194
Thanou, A 1627, 1841, 2820
Thanou, K 1657, 1658, 2600, 2977
Tharp, L 2250
Thawii, G 242
Theander, E 182, 1479
Theis, K 1004, 2987
Theodore, S 1680
Therkildsen, P 262, 799
Therneau, TM 32
Thevissen, K 752
Thibaud, G 216
Thiel, S 1077
Thiele, A 1473
Thiele, GM 289, 400, 488, 1124, 1357, 2915
Thiele, RG 110, 241, 561, 1879
Thiers, B 884
Thirukumaran, C 223
Thom, H 1546
Thom, L 15
Thoma, L 1867, 2767, 2949, 2991
Thomas, E 60, 2598
Thomas, J 763
Thomas, MH 2463, 2498
Thomas, P 2163
Thomas, R 430, 491, 1576, 1584, 1911, 2704, 2711
Thomas, R 1069
Thomas, SM 484
Thomas, T 318
Thomason, J 1916
Thombs, BD 2049, 2695
Thompson, A 2604
Thompson, LF 2703
Thompson, PR 485
Thomsen, MD 2367
Thomsen, RS 2538, 2968
Thomson, J 1092
Thomson, W 168, 366, 940, 2287, 2293, 2302
Thong, D 2513, 2514
Thorlacius, GE 566, 941, 2817
Thorne, C 146, 197, 443, 461, 1103, 1393, 1814, 1908, 2390, 2391, 2437, 2472, 2955
Thornton, S 173, 2324
Thudium, CS 465, 969, 1063, 1399, 2212
Thurlings, R 72, 421, 422
Thurner, L 1389
Tiaden, A 301
Tian, H 227, 1244
Tierney, A 323
Tierney, M 1398
Tietz, L 578
Tiffany, L 1068
Tift, B 354
Tikiz, C 2204
Tillett, W 1560, 2039
Tilstra, J 898
Timilsina, S 472
Timmen, M 63
Timoshchenko, RG 49
Tin, D 443, 461, 1393, 1814, 2390, 2391, 2955
Tincani, A 12, 686, 824, 1292, 1297, 1300, 2166, 2650
Tineo, C 2306
Ting, T 2018, 2301
Tiniakou, E 950, 2131
Tino, J 503
Tio, L 52
Tiongson, M 747
Tiongson, MD 89, 92
Tirone, V 2824
Tison, A 2126
Tisseverasinghe, A 1641, 2922
Titcombe, PJ 476, 477, 834
Titze, J 720
Tkachenko, N 386
Tkacz, J 1030
<table>
<thead>
<tr>
<th>Name</th>
<th>Page Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vittecoq, O</td>
<td>528, 873, 1442</td>
</tr>
<tr>
<td>Vitters, E</td>
<td>1794</td>
</tr>
<tr>
<td>Vitti, M</td>
<td>1621, 1623, 2807</td>
</tr>
<tr>
<td>Vivaldelli, E</td>
<td>1292</td>
</tr>
<tr>
<td>Vives, MJ</td>
<td>209</td>
</tr>
<tr>
<td>Vives, R</td>
<td>1535</td>
</tr>
<tr>
<td>Vivot, A</td>
<td>1757</td>
</tr>
<tr>
<td>Vizzardi, E</td>
<td>686</td>
</tr>
<tr>
<td>Vlach, J</td>
<td>25</td>
</tr>
<tr>
<td>Vlad, V</td>
<td>1373, 2055</td>
</tr>
<tr>
<td>Vlahos, B</td>
<td>587, 2273, 2802</td>
</tr>
<tr>
<td>Vlasakova, V</td>
<td>6</td>
</tr>
<tr>
<td>Vodicka, E</td>
<td>1049</td>
</tr>
<tr>
<td>Vogelsang, P</td>
<td>1073</td>
</tr>
<tr>
<td>Vogetseder, A</td>
<td>2700</td>
</tr>
<tr>
<td>Vogl, T</td>
<td>421, 422</td>
</tr>
<tr>
<td>Voisin, AL</td>
<td>1741</td>
</tr>
<tr>
<td>Vojinovic, J</td>
<td>95, 2259, 2273, 2859, 2956</td>
</tr>
<tr>
<td>Volkmann, ER</td>
<td>749, 943</td>
</tr>
<tr>
<td>Volkov, M</td>
<td>492</td>
</tr>
<tr>
<td>Voll, R</td>
<td>521, 2024</td>
</tr>
<tr>
<td>Vollenweider, CF</td>
<td>876</td>
</tr>
<tr>
<td>Volpe, B</td>
<td>2809</td>
</tr>
<tr>
<td>von Borstel, A</td>
<td>1782, 1846</td>
</tr>
<tr>
<td>von Dalwigk, K</td>
<td>1415</td>
</tr>
<tr>
<td>Von Feldt, JM</td>
<td>1574</td>
</tr>
<tr>
<td>Von Feldt, JM</td>
<td>91, 109</td>
</tr>
<tr>
<td>von Hegedus, JH</td>
<td>2328</td>
</tr>
<tr>
<td>von Kempis, J</td>
<td>535, 536, 2469, 2909</td>
</tr>
<tr>
<td>von Richter, O</td>
<td>2443</td>
</tr>
<tr>
<td>von Scheven, E</td>
<td>1626</td>
</tr>
<tr>
<td>Vonk, MC</td>
<td>2683</td>
</tr>
<tr>
<td>Vonk, M</td>
<td>2662</td>
</tr>
<tr>
<td>Vonkeman, HE</td>
<td>1078</td>
</tr>
<tr>
<td>VoPham, T</td>
<td>988</td>
</tr>
<tr>
<td>Vora, SS</td>
<td>2111</td>
</tr>
<tr>
<td>Vorakanthada, Y</td>
<td>1481</td>
</tr>
<tr>
<td>Voskuyl, A</td>
<td>244, 257, 2365</td>
</tr>
<tr>
<td>Voss, A</td>
<td>1077</td>
</tr>
<tr>
<td>Voss, P</td>
<td>2253</td>
</tr>
<tr>
<td>Voudris, V</td>
<td>2686</td>
</tr>
<tr>
<td>Vougiouka, O</td>
<td>1278, 2859</td>
</tr>
<tr>
<td>Vriezekolk, J</td>
<td>E 2779</td>
</tr>
<tr>
<td>Vrijens, B</td>
<td>1252</td>
</tr>
<tr>
<td>Vsetecka, D</td>
<td>1662, 2657</td>
</tr>
<tr>
<td>Vukatana, G</td>
<td>638</td>
</tr>
<tr>
<td>Vulcano, A</td>
<td>1766, 2676</td>
</tr>
<tr>
<td>Vyncke, L</td>
<td>2773</td>
</tr>
<tr>
<td>Vyse, TJ</td>
<td>43</td>
</tr>
<tr>
<td>W</td>
<td></td>
</tr>
<tr>
<td>Wada, J</td>
<td>2558</td>
</tr>
<tr>
<td>Wada, M</td>
<td>272, 1769</td>
</tr>
<tr>
<td>Wada, T</td>
<td>1698</td>
</tr>
<tr>
<td>Wada, T</td>
<td>2577</td>
</tr>
<tr>
<td>Wada, TT</td>
<td>2017</td>
</tr>
<tr>
<td>Wade, J</td>
<td>1099</td>
</tr>
<tr>
<td>Wade, SW</td>
<td>2448</td>
</tr>
<tr>
<td>Wade, S</td>
<td>2127</td>
</tr>
<tr>
<td>Wadell, C</td>
<td>14L</td>
</tr>
<tr>
<td>Wager, C</td>
<td>675</td>
</tr>
<tr>
<td>Wagh, A</td>
<td>1801</td>
</tr>
<tr>
<td>Wagman, RB</td>
<td>321, 323, 1887, 1888, 1889</td>
</tr>
<tr>
<td>Wagner, BD</td>
<td>2918</td>
</tr>
<tr>
<td>Wagner, C</td>
<td>6L</td>
</tr>
<tr>
<td>Wagner, E</td>
<td>1666</td>
</tr>
<tr>
<td>Wagner, M</td>
<td>173</td>
</tr>
<tr>
<td>Wagner-Weiner, L</td>
<td>2306</td>
</tr>
<tr>
<td>Wähämaa, H</td>
<td>65, 970</td>
</tr>
<tr>
<td>Wahl, D</td>
<td>108</td>
</tr>
<tr>
<td>Wahl, ER</td>
<td>2058</td>
</tr>
<tr>
<td>Wahl, J</td>
<td>1581, 1582</td>
</tr>
<tr>
<td>Wahren-Herlenius, M</td>
<td>566, 876, 941, 1479, 1502, 2817</td>
</tr>
<tr>
<td>Waimann, CA</td>
<td>2021, 2505</td>
</tr>
<tr>
<td>Waiter, G</td>
<td>2753, 2912</td>
</tr>
<tr>
<td>Wakabayashi, H</td>
<td>2485</td>
</tr>
<tr>
<td>Wakabayashi, K</td>
<td>956, 957, 958, 959, 960, 1456, 2135</td>
</tr>
<tr>
<td>Wakai, K</td>
<td>170</td>
</tr>
<tr>
<td>Wakak, K</td>
<td>1347</td>
</tr>
<tr>
<td>Wakefield, RJ</td>
<td>1373, 2012</td>
</tr>
<tr>
<td>Wakhlu, A</td>
<td>251</td>
</tr>
<tr>
<td>Wakiguchi, H</td>
<td>370</td>
</tr>
<tr>
<td>Wakim, P</td>
<td>1893, 2758</td>
</tr>
<tr>
<td>Wakiya, R</td>
<td>1690, 2424</td>
</tr>
<tr>
<td>Walder, M</td>
<td>2253</td>
</tr>
<tr>
<td>Waldheim, E</td>
<td>929</td>
</tr>
<tr>
<td>Walgreen, B</td>
<td>1074, 1793, 1794</td>
</tr>
<tr>
<td>Walker, J</td>
<td>948</td>
</tr>
<tr>
<td>Walker, JG</td>
<td>945, 1899</td>
</tr>
<tr>
<td>Walker, KM</td>
<td>2673</td>
</tr>
<tr>
<td>Walker, P</td>
<td>2224</td>
</tr>
<tr>
<td>Walker, R</td>
<td>1104</td>
</tr>
<tr>
<td>Walker, UA</td>
<td>1683, 1715, 2253</td>
</tr>
<tr>
<td>Wallace, CA</td>
<td>374</td>
</tr>
<tr>
<td>Wallace, DJ</td>
<td>673, 680, 901, 984, 1606, 1644, 2585, 2875, 2925, 2953</td>
</tr>
<tr>
<td>Wallace, M</td>
<td>1106, 2506</td>
</tr>
<tr>
<td>Wallace, S</td>
<td>1023, 1919</td>
</tr>
<tr>
<td>Wallace, ZS</td>
<td>4L, 895, 1175, 1179, 1789, 2921</td>
</tr>
</tbody>
</table>
Wu, W 1068
Wu, W 1727
Wu, X 2750
Wu, YL 1671, 1673, 1675
Wu, YJ 1629
Wu, Y 25, 774
Wu, YH 2436
Wu, Z 2241
Wulffraat, N 2333
Wunderlin, A 1721
Wunderlin, G 1068
Wyllie, R 95
Wysham, KD 327, 2263
Xavier, R 2924
Xhan, X 2345
XIAO, F 1994, 2939, 2941
Xiao, F 928, 1311, 2241, 2242
Xiao, H 928, 2241, 2242
Xiao, R 1266, 2309, 2992
Xiao, W 532
Xie, C 285
Xie, DX 1788
Xie, L 512, 1821
Xie, L 455
Xie, YM 1251
Xin, X 2242
Xin, Y 519, 1459
Xing, L 22
Xiong, W 2612
Xiong, W 515
Xiong, Y 1015
Xu, D 774
Xu, D 852, 1275
Xu, G 1974
Xu, H 1572, 1974, 2451
XU, J 1994
Xu, J 1699, 2085, 2411, 2752
Xu, P 1883
Xu, Q 1326
Xu, R 1313, 1785
Xu, S 344, 473, 2951
Xu, S 1669
Xu, W 605
Xu, X 928, 2882
Xu, X 1792
Xu, XL 2878
Xu, Y 1246
Xu, Y 1556
Xu, Z 1575
Xue, B 2436
Xue, H 2101
Xue, J 1311, 2241
Xue, Z 181, 1659, 2652
Y
Yabe, H 2138, 2139
Yachie, A 2325
Yacyshyn, E 922, 1781, 2734
Yadav, A 2330
Yagüe, J 1436
Yajima, N 1593, 2628
Yaksh, T 860
Yalakki, L 1768
Yalavarthi, S 8, 2564, 2761
Yalçınkaya, Y 542, 2667
Yalkinoglu, O 2586
Yamada, H 9, 1013, 1751, 1762
Yamada, H 861, 1321
Yamada, K 1157, 1180
Yamada, S 1414
Yamada, S 507, 1421
Yamada, Y 464
Yamagata, K 1013, 1751, 1762, 1778
Yamaguchi, R 1388
Yamaguchi, Y 2158, 2172
Yamamoto, K 431
Yamamoto, K 551
Yamamoto, K 170, 1104
Yamamoto, M 1157
Yamamoto, W 395, 551
Yamamura, M 804
Yamanaka, H 329, 1343, 1388, 1435, 1665, 1684, 2102, 2133
Yamaoka, K 798, 2687
Yamasaki, Y 1279
Yamashita, K 1762
Yamashita, T 26, 31, 1719
Yamatou, T 1279
Yamauchi, T 397
Yamazaki, H 2093
Yamazaki, H 841
Yamazaki, H 439
Yamazaki, K 370, 1960
Yamazaki, R 2386
Yan, D 2751
Yan, J 95
Yan, J 398, 1186
Yan, T 963
Yoo, WH 47, 1733
Yoon, BY 2202
Yoon, CH 399
Yoon, EJ 2075
Yoon, S 2072
Yorgin, P 1273
Yorkston, J 242
Yoshida, E 1099
Yoshida, K 187, 1348
Yoshida, K 1999, 2132, 2220
Yoshida, K 973
Yoshida, N 2638
Yoshida, S 891
Yoshida, S 551
Yoshida, Y 275, 1942
Yoshifuji, H 479, 795, 1066, 2100, 2160, 2164
Yoshiga, Y 1320
Yoshii, N 1593
Yoshikawa, H 311, 551
Yoshikawa, H 773, 2639
Yoshikawa, S 2093
Yoshimi, R 237, 1460, 2150, 2151
Yoshimoto, K 20, 798, 1426, 2903
Yoshimura, M 1447
Yoshinaga, Y 271
Yoshinari, H 773
Yoshitama, T 238, 1441
Yoshizaki, A 31
Yoshizaki, A 26, 31, 1719
Yoshizawa, S 2710
Yuan, C 1670
Yuan, K 2093
Yuan, K 798
Yuan, M 245
Yuan, P 449, 1015, 1185
You, Y 598
You, Z 407
Youn, H 1192
Young, A 2372
Young, A 1701
Young, F 2865
Young, KA 901, 984, 1644
Young, L 2100
Young, LH 2614
Young, NA 60, 1748, 2577, 2598
Young-Min, S 565, 1500
Younossi, Z 281
Yourish, J 550
Youssef, P 809, 1354
Youssef, S 2030
Ytterberg, J 476, 1072
Ytterberg, SR 784, 785, 789, 821, 1760, 1767, 1774, 1849, 2136
Yu, CY 1671, 1673, 1675
Yu, G 1671
Yu, H 82
Yu, J 928
Yu, KH 1128, 1136, 1314, 2359
Yu, KS 2072
Yu, N 1837
Yu, S 312
Yu, S 1771
Yu, X 954
Yu, X 84
Yu, Y 1669
Yu, Z 871, 1796, 2057
Yukawa, M 2825
Yumusakhuylu, Y 2496
Yun, C 519
Yun, M 245
Yurdakul, S 2462, 2747
Yuvienco, C 105, 2243
Z
Zaal, K 291, 2773
Zabotti, A 638
Zabulis, X 2357
Zacarias, A 2379
Zacariaz, J 1350
Zack, DJ 4L
Zaffarana, C 2551, 2554
Zahmatkesh, G 691
Zaichko, K 2370
Zaiss, M 864
Zak, A 1796
Zakem, JM 407
Zalazar, MM 360
Zalcman, J 1012
Zalewsky, J 2715
Zaman, A 471, 2366
Zamanian, RT 758
Zamecnik, J 2176
Zammit, D 1337
Zamora, L 1629
Zamora, N 531, 2395
Zamora-Legoff, V 16, 18, 1492
Zamora-Medina, MC 708
Zampeli, E 147
Zanella, I 2650
Zang, C 2493
Zannin, ME 2295
Zanwar, A 1848, 2311
Zapata, P 2100
Zapater, P 1129, 1187
Zapatero, A 1226
Zarco, P 998, 999, 1535
Zarrin, AA 674
Zatti, S 1300
Zavada, J 992, 1538, 1549, 2087
Zbarskaya, O 1576
Zbijewski, W 242
Zbinden, A 1315
Zea, A 2619
Zea Mendoza, A 1270
Zebrowski, E 2741
Zeck, B 670
Zeft, A 2272
Zeger, S 2248
Zeggar, S 2558
Zehender, A 1925
Zeher, M 876, 1784
Zehou, O 2126
Zeidi, M 2159
Zeilinger, M 61
Zeisbrich, M 284
Zejden, A 1830
Zelarney, P 525
Zell, J 1103
Zell, M 2086
Zeltner, M 1046
Zemach, R 1648
Zeman, F 2254
Zen, Y 1179
Zeña-Huancas, P 687
Zeng, B 2704
Zeng, C 1788
Zeng, F 176, 656
Zeng, J 180
Zeng, P 132
Zeng, X 42, 2101, 2644
Zeng, X 2101
Zengin, B 825, 1496, 1514, 1534, 2521
Zerbi, S 955
Zerbini, A 1075
Zerbini, CAF 320
Zerrouki, K 2589
Zervakis, G 836
Zevallos, F 450, 687, 1378
Zezon, A 2581
Zhai, G 1209, 1210
Zhan, Y 1771
Zhang, A 1669
Zhang, A 928
Zhang, B 2436
Zhang, D 1116
Zhang, F 1405, 2019, 2827
Zhang, F 928, 1974, 2101, 2751
Zhang, H 1575
Zhang, H 2882, 2934
Zhang, J 1748
Zhang, J 1015
Zhang, J 1248
Zhang, J 1326
Zhang, JL 1251, 1311
Zhang, K 166
Zhang, L 1196, 1211
Zhang, L 2436
Zhang, L 1311
Zhang, L 2613
Zhang, L 1326
Zhang, M 1113, 2844
Zhang, M 218, 923
Zhang, M 2241
Zhang, M 2196
Zhang, M 788
Zhang, N 834
Zhang, P 2101, 2705
Zhang, P 2715
Zhang, Q 1311
Zhang, R 449, 1015, 1185
Zhang, RM 158
Zhang, R 1086, 2583
Zhang, S 1311
Zhang, S 2134
Zhang, S 2
Zhang, W 2101
Zhang, W 1209, 1210
Zhang, W 2847
Zhang, W 2101, 2705, 2750
Zhang, X 855
Zhang, X 1974
Zhang, X 1185
Zon-Giebel, A 2697
Zou, H 2016, 2942
Zou, H 2882
Zou, J 2242
Zubal, G 12L
Zuber, Z 2273
Zubkova, I 386
Zucchi, A 1969
Zucht, HD 695, 722, 875, 1182
Zuckerman, N 674
Zuckerman, SH 415, 2866, 2870
Zufferey, P 521, 2055, 2253, 2910
Zuily, S 108
Zulian, F 1287, 2259, 2295, 2314, 2956
Zuliani, F 638
Zuliani, L 1292
Zuniga-Pflucker, JC 835
Zuo, Y 2
Zurakowski, D 1242
Zurita Prada, P 2499
Zwezerijnen, B 257
Ø
Øiestad, B 2218
Øijordsbakken, G 570
Ørnbjerg, L 236
Østergaard, M 236, 246, 418, 438, 1371, 1878, 2938, 2967
Keyword Index

1

18FDG PET/CT scan  2003

2

25-hydroxyvitamin D  332

3

3D model  58, 966

A

A3 Adenosine receptor  2068

abatacept  416, 419, 498, 526, 527, 540, 560, 608, 609, 610, 1424, 1429, 1465, 1468, 1469, 1474, 1817, 2272, 2450, 2452, 2491, 2494, 2710, 2786, 2855, 2868, 2891, 2964

academic  2041

access to care  185, 186, 196, 213, 419, 882, 1040, 1051

ACPA  65, 327, 410, 413, 432, 459, 478, 482, 484, 487, 492, 836, 970, 990, 1250, 1341, 1356, 1376, 1383, 1432, 1454, 2012, 2016, 2375, 2406, 2407, 2450, 2791, 2919

ACR  17L, 105, 356, 505, 618, 624, 734, 1556, 2280, 2969

activities of daily living (ADL)  2853

activity score  930, 1431, 1498, 2141, 2630

acute-phase reactants  2117

adalimumab  515, 611, 619, 961, 1038, 1047, 1155, 1352, 1418, 1419, 1420, 1422, 1424, 1431, 1448, 1471, 1521, 1522, 1560, 1906, 2017, 2271, 2280, 2283, 2298, 2393, 2440, 2442, 2443, 2446, 2453, 2456, 2495, 2723, 2799, 2868, 2879, 2970

adaptive immunity  1793, 1922

adenosine receptors  64, 292, 905, 1932, 1939, 2761

adhesion molecules  8, 960, 1921, 2636, 2642

adipocytokines  1943

adipokines  1414, 1935, 2209, 2984

adipose tissue  54, 570, 1961, 2372, 2961

adjuvant arthritis  86, 389, 390, 962

administrative databases  199, 1000, 1039, 1054, 1525, 1593, 1631, 1963, 2593, 2594, 2812, 2834

adolescent  2810

adolescent patients  371, 910, 2996

adult-onset Still's disease  365, 1152, 1154

adverse events  8L, 527, 543, 819, 850, 1173, 1182, 1600, 1755, 1776, 1963, 2078, 2119, 2128, 2155, 2222, 2256, 2320, 2599

Advocacy  362, 1053

aerobic  2822

African-Americans  226, 689, 915, 919, 946, 1018, 1697, 2161, 2518, 2813, 2814, 2930, 2982

Aging  406, 904, 1133, 1854, 1931, 2341, 2455, 2717, 2945

alcohol use  1130, 1610, 2513

allopurinol  1105, 1106, 1111, 1113, 1118, 1120, 1137, 1138, 1144, 2058, 2059, 2265, 2844, 2848

Alternative Activation  287

alternative medicine  227, 1244, 2159

amyopathic dermatomyositis  7L, 2146, 2156, 2160, 2163

ANA  43, 198, 476, 559, 673, 700, 701, 705, 1097, 2104, 2578

anakinra  169, 367, 368, 940, 1142, 2090

analgesics  15L, 389

ANCA  18L, 797, 814, 893, 895, 896, 1010, 1013, 1288, 1289, 1749, 1750, 1751, 1752, 1755, 1758, 1759, 1761, 1762, 1763, 1764, 1767, 1768, 1769, 1770, 1771, 1772, 1773, 1775, 1776, 1778, 1844, 1846, 1849, 2736, 2754, 2935, 2936

anemia  436, 2381

angiogenesis  54, 71, 772, 956, 957, 967, 1705, 1719, 2132, 2708

Angiography  785

angiotensin  1324

animal models  48, 57, 69, 294, 392, 393, 400, 402, 408, 503, 863, 904, 1323, 1325, 1328, 1329, 1339, 1578, 1708, 1720, 1742, 1793,

anti-CCP antibodies 239, 476, 477, 481, 483, 1034, 1402, 1965, 2914, 2916

anti-centromere antibodies (ACA) 575

anti-citrullinated protein/peptide antibodies (ACPA) 293, 413, 476, 477, 480, 486, 951, 1325

anti-depressant 2783

anti-dsDNA 693, 703, 704, 833, 2563, 2645

anti-TNF therapy 133, 287, 423, 543, 546, 550, 598, 599, 606, 630, 632, 638, 654, 1019, 1049, 1057, 1280, 1310, 1312, 1450, 1456, 1520, 1525, 1527, 1530, 1531, 1532, 1538, 1543, 1545, 1548, 1552, 1553, 1554, 1570, 1823, 1825, 1905, 2449, 2451, 2459, 2460, 2462, 2477, 2478, 2487, 2488, 2491, 2721, 2744, 2799, 2858, 2859, 2662

antibodies 46, 132, 521, 730, 944, 1272, 1325, 1428, 1571, 1666, 1667, 1811, 2091, 2136, 2139, 2318, 2876

anticoagulation 2833

antigen RA 834, 951

antigen-presenting cells 176, 2714

antigens 491, 1666, 1731

antimalarial drugs 714, 1590, 1592, 2599, 2612, 2613, 2617, 2924

antinuclear antibodies (ANA) 707, 1096

antiphospholipid 4, 1656
autoantigens 26, 30, 37, 39, 44, 295, 562, 676, 941, 2335, 2658
autoimmune diseases 20, 27, 41, 164, 183, 184, 210, 245, 284, 562, 900, 1002, 1023, 1035, 1064, 1068, 1069, 1156, 1171, 1290, 1328, 1407, 1466, 1479, 1617, 1741, 1747, 1786, 1792, 1911, 1999, 2111, 2121, 2126, 2128, 2142, 2454, 2569, 2601, 2634, 2658, 2708, 2715, 2740, 2826, 2905
autoimmunity 23, 831, 832, 849, 901, 916, 954, 1167, 1408, 2121, 2580, 2583, 2640, 2647, 2699, 2713, 2838
Autoinflammation 79, 939, 1027, 2110, 2347
Autoinflammatory Disease 79, 169, 290, 361, 367, 379, 942, 1027, 1154, 1174, 1892, 1893, 2113, 2348, 2567
autophagy 56, 653, 904, 975, 1434, 1745, 1925, 1926, 1931, 2698
avascular necrosis 270
axial spondyloarthritis 176, 581, 584, 587, 594, 644, 646, 1001, 1315, 1503, 1507, 1509, 1512, 1513, 1515, 1521, 1522, 1538, 1566, 1573, 1787, 1831, 1877, 2438, 2496, 2500, 2501, 2504, 2506, 2507, 2508, 2509, 2513, 2514, 2516, 2521, 2802, 2803, 2860
azathioprine 1022, 1759, 1782
B
B cell targeting 20, 25, 32, 514, 889, 890, 2486, 2585, 2586
B cell tolerance 23, 831, 832, 833, 836, 2348, 2567
back pain 193, 208, 307, 594, 1852
back surgery 193
BAFF 20, 28, 576, 875, 888, 1463, 1667, 1823, 1837
basic research 25
Basic Science 2993
behavioral strategies 315
Behcet's syndrome 77, 1075, 1150, 1151, 1170, 2102, 2720, 2721, 2722, 2723, 2724, 2728, 2729, 2732, 2733, 2744, 2746, 2747, 2748, 2750, 2751, 2775
belimumab 890, 893, 2590, 2593, 2594, 2604, 2812, 2923
best practices 1040
big data 210, 296, 337, 876, 986, 1009, 1014, 1170, 1234, 2609
BILAG 1664, 1986, 2602
bioinformatics 41, 177, 183, 184, 1334, 2405, 2818, 2866, 2931
Biologic agents 6L, 134, 159, 210, 231, 324, 379, 425, 426, 471, 475, 521, 523, 525, 528, 542, 545, 551, 598, 599, 629, 635, 1007, 1046, 1052, 1058, 1158, 1425, 1430, 1439, 1441, 1446, 1453, 1456, 1457, 1471, 1524, 1525, 1530, 1532, 1534, 1539, 1541, 1542, 1543, 1550, 1562, 1564, 1779, 1810, 1826, 1828, 1907, 2014, 2029, 2129, 2266, 2285, 2333, 2382, 2386, 2409, 2444, 2447, 2464, 2487, 2491, 2546, 2743, 2801, 2965
biologic drugs 3L, 27, 196, 238, 278, 280, 421, 422, 470, 520, 524, 605, 606, 624, 628, 631, 636, 842, 1016, 1159, 1432, 1451, 1455, 1478, 1533, 1537, 1558, 1884, 1908, 2098, 2278, 2284, 2290, 2416, 2437, 2454, 2472, 2473, 2500, 2589, 2592
biologic response modifiers 206, 636, 2906
career 912
carpal tunnel syndrome 2092, 2988
cartilage 48, 57, 62, 240, 305, 903, 905, 906, 969, 1928, 1929, 1945, 1946, 2207, 2406, 2896, 2949
case 1153
case-based 2319
Castleman's disease 1179
catastrophic antiphospholipid syndrome 15
cathepsin k inhibitor 14L
CD T cells 85, 1727
CD8 cells 2424, 2425
Cell Migration 865, 1336
Cell Signaling 83, 299, 1073, 2089, 2436, 2870
central nervous system involvement 1781, 2732
CER 468
Cerebritis 2838
cerebrovascular disease 1480, 1485, 2359, 2759, 2972
certolizumab pegol 463, 1030, 1309, 1515, 1516, 1517, 1518, 1809, 2451
cervical spine 1984, 1985, 2053
Chemokine Receptors 40, 397, 553, 724, 958, 961, 1912, 1914, 2231, 2232
chemokines 40, 397, 553, 957, 958, 971, 1379, 1414, 1882, 1907, 1912, 1977, 2135, 2145, 2340, 2642
cholesterol 666, 964, 1074, 1327, 1579
chondrocalcinosis 1126, 1135, 2053, 2083
chondrocytes 55, 904, 905, 1933, 1934, 2191
chondroitin 1190, 1203, 1206, 1208
chronic disease care 419, 1857
chronic low back pain 1831
Chronic pain 149, 927
chronic recurrent multifocal osteomyelitis (CRMO) 374
Churg-Strauss syndrome 1761, 1774, 1779, 1884
citrullination 65, 485, 488, 492, 837, 1072
citrulline 834, 2430, 2915
classification criteria 370, 459, 877, 1154, 1172, 1289, 1376, 1397, 1493, 1496, 1498, 1502, 1589, 1622, 1765, 2048, 2102, 2314, 2556
Clinical 247, 306, 934, 1200, 1274, 2633, 2720, 2805
clinical practice 95, 186, 367, 433, 538, 607, 743, 816, 1046, 1078, 1088, 1118, 1233, 1382, 1443, 1460, 1468, 1511, 1517, 1548, 1555, 1559, 1690, 2059, 2382, 2452, 2454, 2484, 2499, 2530, 2532, 2533, 2862, 2894
clinical practice guidelines 15, 2395
clinical research 13L, 15L, 452, 544, 583, 771, 885, 1147, 1661, 1784, 1854, 2093, 2167, 2625, 2855
clinical research methods 2179, 2610
Clinical Response 159, 347, 421, 422, 432, 522, 885, 1206, 1477, 1518, 1838, 2371, 2454, 2487, 2602
Clinical Science 1846
clinical skills 95
clinical trials 4L, 7L, 13L, 50, 318, 437, 509, 525, 526, 725, 726, 738, 874, 885, 891, 935, 1029, 1201, 1204, 1676, 1827, 1838, 1839, 1884, 1886, 1904, 1909, 2074, 2092, 2156, 2610, 2766, 2799, 2884, 2981, 2983
CNS Lupus 1836
CNS Vasculitis 2730, 2731
Co-morbidities 8L, 135, 136, 723, 981, 1160, 1615, 1617, 1631, 1797, 1959, 2366, 2518, 2921
cosimulation 1328, 2573
cognitive dysfunction 1621, 1623, 1650, 2080, 2807, 2808, 2809, 2824
colchicine 368, 375, 1144, 1445, 2108
collagen 465, 489, 740, 762, 771, 1226, 1725, 1930, 2688, 2709
combination therapies 1329, 1425, 1674, 1906, 2393
communication 358, 1100, 1255, 1260, 1385, 1614, 1857, 1860, 2255
community programs 233, 1860
comorbidity 234, 528, 803, 1004, 1036, 1133, 1451, 1527, 1902, 2307, 2309, 2388
comparative effectiveness and harms 473, 635, 1825, 2282, 2290, 2785
complement 169, 568, 670, 673, 680, 681, 682, 1077, 1157, 1671, 1673, 1842, 1918
complement deficiency 1766
complementary alternative medicine 56, 343
Compliance 352, 434, 920, 1244, 1262, 1601, 1853, 1862, 2033, 2254, 2268, 2582
complications 1618, 1963, 1968, 2147, 2361, 2692, 2853
computed tomography (CT) 243, 582, 585, 731, 783, 1181, 1287, 1877, 2009, 2065, 2088
connective tissue diseases 258, 275, 679, 696, 698, 1172, 1181, 1292, 1687, 1876, 2035, 2097, 2105, 2114, 2116, 2169, 2677
consults 106, 185, 928
copd 837
coping skills 845, 1979
coronary artery disease 723, 1125, 1585, 2934
corticosteroids 206, 787, 795, 819, 934, 1200, 1313, 1442, 1460, 1585, 1788, 1963, 2139, 2319, 2394, 2604, 2906, 2956
cost containment 114, 281, 1043, 1097, 1885, 2439
Counseling 192, 215, 315, 1292
COX inhibitors 1434
creatinine kinase 2161, 2174
CRMO 371, 372, 373
Crohn's Disease 372, 594, 1047, 2748
cross-sectional studies 584, 2194
cryoglobulinemia 2741
crystal-induced arthritis 249, 981, 1091, 1132, 2055, 2081, 2083, 2090, 2896, 2899
CTLA-4 1942, 2095
Curriculum 89, 90, 104, 109, 911, 1858
cutaneous lupus 886, 2591
cutaneous lupus erythematous 33, 675, 833, 1613, 1617, 2613, 2626
cutaneous manifestations 2156, 2157, 2749
CVID 1167
cyclophosphamide 31, 749, 1684, 2603, 2624, 2740, 2747
cyclosporine 2152
CyTOF 83, 297, 759, 953, 1405, 1406, 1577, 1736, 1914, 1941, 2420, 2637
cytokines 20, 22, 32, 36, 38, 60, 67, 71, 72, 73, 78, 81, 83, 404, 466, 521, 565, 652, 658, 758, 800, 956, 957, 958, 960, 962, 965, 969, 1027, 1209, 1348, 1357, 1381, 1412, 1413, 1658, 1672, 1738, 1742, 1743, 1747, 1782, 1792, 1793, 1794, 1844, 1895, 1936, 2132, 2135, 2329, 2332, 2339, 2346, 2353, 2354, 2425, 2559, 2574, 2596, 2598, 2633, 2698, 2701, 2711, 2794, 2801, 2870, 2980
D
data analysis 212, 1014, 1019, 1134, 1712, 1865, 1964, 2827, 2910, 2923
data collection 212, 1475, 2047, 2854
death 829, 986, 987, 1429, 1596, 1804, 2846
decision analysis 411, 1045, 1052, 1078, 1257, 1298, 1589, 2266, 2778
degenerative arthritis 307
Degos Disease 1166
dendritic cells 4, 389, 399, 861, 950, 1064, 1338, 1579, 1656, 1948, 2576, 2616, 2704, 2776, 2978
denosumab 321, 322, 323, 324, 334, 1435, 1850, 1886, 1887, 1888, 1889
deposition 2063
depression 121, 140, 148, 162, 194, 208, 607, 739, 844, 845, 847, 1006, 1086, 1235, 1261,
dermatomyositis

diabetes

diacerein

diagnosis

diagnostic criteria

diagnostic imaging

Diagnostic Tests

dietary supplements

differential diagnosis

diffuse idiopathic skeletal hyperostosis (DISH)

digital technologies

Digital X-ray Radiogrammetry (DXR)

disability

Disease Activity

Disease Sub-phenotyping

disease susceptibility

disease-modifying antirheumatic drugs

DMARDs

DNA degradation

DNA Methylation

doctor-patient relationship

Doppler ultrasound

drug interactions

drug safety

drug therapy

drug toxicity

drug treatment

dry eyes

dual energy x-ray absorptiometry (DEXA)

DXA

Dysmotility

dyspnea

E

Early Rheumatoid Arthritis
Grant writing 115
grants 92
growth factors 1278
guidelines 1599, 2390, 2395, 2414, 2732
GWAS 168, 170, 182, 1009, 1021, 2341, 2343, 2405, 2930
gynecologic issues 573, 1318, 1501
H
hand disorders 266, 917, 1875, 2006, 2181, 2189, 2208, 2210, 2945
Hand function 739
health 312, 1867
Health Assessment Questionnaire 342, 928, 1251, 1360, 2239, 2242, 2244, 2245
Health Care 214, 1050, 1054, 2216, 2834
health care cost 185, 195, 196, 199, 207, 208, 413, 1030, 1043, 1049, 1054, 1098, 1489, 1561, 2260, 2812, 2831, 2834, 2836, 2895
health care disparities 196, 199, 218, 222, 224, 225, 228, 230, 233, 634, 829, 1093, 2922
health education 1813
health equity 2497
Health Information Technology 95, 1362
health literacy 192, 230, 2033
health outcome 218, 342, 980, 1049
health status 2538
healthcare policy 1053
healthcare reform 193
healthcare system 1094
heart 741
heart block 164, 555, 941, 1061, 1300, 2580, 2817
heart disease 258, 1032, 1119, 1125, 1301, 1926
heat-shock proteins 766
Henoch-Schönlein purpura 2716, 2717, 2718, 2727, 2735
hepatitis 369, 384, 385, 472, 523, 1099, 2036, 2385
Hepatitis C 281, 894, 1355, 2036, 2221, 2387, 2741
herbal remedies 2159
Heterogeneous 756
high risk 223, 318
Hip 312, 828, 977, 997, 1029, 1056, 1220, 2186, 2793, 2835
hip disorders 303
Hispanic patients 442, 921
histone acetylation 1660, 2709
Histone Modification 82, 293, 1575, 2709
histopathologic 60, 567, 573, 1347, 2114, 2416
hormones 1308, 2707
human leukocyte antigens (HLA) 164, 271, 1013, 1102, 1514, 1572, 1579, 1580, 1675, 1910, 2000, 2037, 2136, 2430, 2431
human papillomavirus (HPV) 1304, 1318, 1808
hyalurinate 1043, 1198, 1199
hydroxychloroquine 8L, 442, 546, 1296, 1297, 1601, 1651, 1773, 1862, 1964, 2033, 2034, 2035, 2581, 2582, 2588, 2595, 2596, 2599, 2613, 2614, 2618, 2635, 2990
hypermobility 382, 2115
hypertension 670, 678, 720, 1088, 1267, 1558, 1586, 1702, 2067, 2189, 2308, 2361, 2370
hyperuricemia 170, 672, 1021, 1117, 1119, 1120, 1121, 1122, 2057, 2059, 2069, 2071, 2073, 2074, 2078, 2081, 2088, 2989
I
ibandronate 1171
ICD-10 2048
ICD-9 137
Idiopathic Inflammatory Myopathies (IIM) 2136, 2146, 2154, 2162
interdisciplinary rheumatology team 1092
interferons 4, 9L, 80, 85, 181, 300, 566, 675, 679, 754, 831, 832, 860, 866, 873, 897, 939, 941, 1014, 1073, 1369, 1655, 1657, 1658, 1659, 1660, 1662, 1663, 1719, 1727, 1842, 1893, 1916, 2159, 2332, 2336, 2339, 2340, 2347, 2349, 2568, 2575, 2576, 2589, 2592, 2601, 2652, 2758, 2813, 2814, 2815, 2816, 2817, 2818, 2828, 2875, 2927, 2977
interleukins (IL) 2L, 31, 73, 74, 85, 86, 57, 570, 606, 618, 621, 622, 626, 768, 864, 970, 1152, 1187, 1426, 1428, 1461, 1523, 1528, 1529, 1539, 1571, 1793, 1794, 1795, 1826, 1828, 1930, 1936, 2422, 2571, 2705, 2728
internet 1362, 1503, 2186, 2766
Intervention 846, 1086, 1990, 2770, 2823
intima medial thickness 1484, 1585
intravenous immunoglobulin (IVIG) 748, 2320, 2888
investigator 1393
iPS (induced pluripotent stem cells) 58
J
Japanese 431, 806, 1165, 1343, 2588
joint arthroplasty 2900
joint damage 382, 429, 436, 450, 451, 454, 533, 626, 906, 1028, 1101, 1353, 1366, 2245, 2300, 2458, 2964
joint destruction 53, 250, 390, 453, 464, 2792, 2909
joint procedures 309, 2910
juvenile arthritis 339, 364, 381, 382, 937, 2018, 2274, 2277, 2281, 2282, 2289, 2304, 2306, 2310, 2317, 2326, 2328, 2330, 2350, 2993
juvenile dermatomyositis 852, 1274, 1276, 1277, 1278, 1279, 1280, 2137, 2141, 2142, 2143, 2259, 2335, 2336, 2337, 2338, 2339, 2340, 2341, 2342, 2895, 2960, 2961
juvenile idiopathic arthritis-enthesitis (ERA) 371, 2285, 2288, 2296, 2311, 2329, 2333
juvenile myositis 1254, 1275, 2142, 2336, 2341
juvenile scleroderma 1281, 1282, 1283, 1286
juvenile sclerosis 2959
juvenile SLE 369, 1268, 2027, 2975
juvenile spondylarthropathy 2334, 2805, 2860
K
Kawasaki disease 2937
Kidney 322, 1026, 1108, 1122, 1921, 2052, 2061, 2399, 2400, 2401, 2846
kinase 514, 1319, 1320, 1567, 1573, 2771
Knee 1L, 13L, 312, 926, 932, 933, 934, 936, 977, 979, 980, 1006, 1029, 1043, 1050, 1056, 1059, 1191, 1192, 1194, 1198, 1199, 1200, 1201, 1205, 1206, 1207, 1208, 1788, 1853, 2019, 2177, 2178, 2183, 2185, 2189, 2192, 2193, 2197, 2200, 2201, 2204, 2205, 2217, 2251, 2767, 2793, 2823, 2835, 2852, 2948
knowledge 100, 108, 2262, 2265, 2317
L
laboratory and imaging evaluation 1096
laboratory tests 206, 581, 697, 700, 707, 1097, 1102, 1124, 1682, 1954, 1982, 2031, 2037, 2093, 2632
lactation 355, 1298
language 220, 1991
large vessel vasculitis 102, 259, 785, 788, 791, 795, 801, 811, 815, 824, 1845, 2737, 2933
Leadership 233
Lesions 587, 2802
leukocytes 8, 2656, 2659
Leukopenia, leukocytopenia, 515, 1629, 2381
lipids 548, 549, 913, 990, 1095, 1265, 1731, 2328, 2702
liver chemistry 2380, 2523, 2784
liver disease 136, 1099, 1224, 2380, 2522
longitudinal studies 330, 538, 715, 732, 784, 943, 1248, 1277, 1443, 1500, 1613, 1642, 1643, 1668, 1994, 2131, 2138, 2880, 2942, 2946, 2957
low back pain 306, 1508, 1850, 2001, 2233, 2504, 2768, 2850
lung 483, 484, 742, 1682, 2919
Lung Disease 24, 257, 400, 568, 838, 854, 939, 1486, 1488, 1612, 1715, 1722, 1756, 2386, 2566, 2688, 2737, 2776
lupus nephritis 9, 173, 662, 663, 665, 667, 668, 669, 670, 671, 672, 678, 683, 689, 702, 885, 1085, 1267, 1273, 1600, 1611, 1616, 1640, 1641, 1648, 1662, 1668, 1786, 1833, 1837, 1843, 1920, 1921, 2559, 2561, 2570, 2587, 2588, 2603, 2608, 2620, 2624, 2920, 2922
Lyme disease 1020
lymph node 967
lymphocytes 41, 655, 660, 686, 961, 1427, 2125, 2424, 2596, 2874
lymphopenia 952
M
Macrophage 12L, 284, 285, 286, 287, 289, 302, 405, 406, 481, 488, 968, 1584, 2232, 2324, 2580, 2815, 2926, 2934
macrophage activation syndrome 245, 370, 1147, 1597, 1895, 1897, 2324, 2325, 2331, 2332, 2772, 2900
macrophages 174, 301, 387, 403, 782, 1581, 1730, 1791, 2089, 2330, 2570
magnetic resonance imaging (MRI) 1L, 236, 555, 783, 870, 1207, 1208, 1569, 1830, 1875, 1992, 1993, 1999, 2019, 2300, 2962
major histocompatibility complex (MHC) 919, 938
malignancy 273, 1146, 1606, 1896, 2122, 2739
management 279, 347, 1042, 2530, 2731, 2732
Marketing 1857
MAS 938, 1597
mast cells 552, 788, 1401, 2115
matrix metalloproteinase (MMP) 464, 489, 763, 963, 1945
measure 1101, 1349, 1615, 1623, 1802, 2041, 2666, 2958
mechanisms 400, 2589
mediation 837, 2209
medical education 96, 107, 116
medical management 449, 1118
Medical school 93, 96, 97
Medicare 129, 136, 1113
medication 161, 215, 223, 1099, 1500, 1536, 2140, 2194, 2584, 2820
medication side effects 1860, 1964, 2618
meniscus 2756
mental health 213, 630, 998, 1861, 1979, 2672, 2810
mesenchymal stem cells 49, 62, 652, 1566, 1703, 1935, 2419, 2616
messenger RNA (mRNA) 2656
meta-analysis 11, 149, 170, 314, 321, 438, 463, 531, 539, 635, 636, 691, 693, 786, 787, 810, 896, 1034, 1185, 1200, 1223, 1297, 1365, 1480, 1481, 1484, 1485, 1556, 1561, 1562, 2127, 2262, 2367, 2392, 2395, 2429, 2483, 2515
metabolic syndrome 917, 1596, 1609, 2180, 2189, 2521, 2522
metabolism 38, 284, 954, 1061, 1321, 1339, 1663, 1822, 2570, 2572, 2638, 2702, 2934, 2975
metabolomics 38, 648, 667, 1025, 1210, 1712, 1723, 1848, 2750
methotrexate (MTX) 122, 167, 224, 225, 352, 363, 386, 408, 433, 443, 446, 461, 466, 493, 517, 518, 534, 539, 615, 636, 793, 804, 827, 1017, 1252, 1322, 1399, 1419, 1430, 1438, 1445, 1457, 1463, 1476, 1738, 1755, 1815, 1823, 1905, 2271, 2279, 2288, 2295, 2298, 2333, 2380, 2381, 2424, 2449, 2453, 2456, 2458, 2460, 2465, 2479, 2480, 2784, 2867, 2962
methylation 178, 650, 903, 1011, 1017, 1745, 2334
mHealth 1234
microbiome 394, 402, 491, 493, 494, 569, 637, 641, 949, 1068, 1326, 1367, 1574, 1576, 1712, 1717, 1737, 1742, 1786, 1832, 1913, 2075, 2329, 2334, 2350, 2577, 2935
Microchimerism 2431
microparticles 2338, 2900, 2979
MicroRNA 4, 63, 180, 301, 579, 643, 954, 972, 1009, 1012, 1336, 1367, 1368, 1710, 1729, 1764, 2150, 2187, 2326, 2338, 2434, 2435, 2436, 2655
migration inhibitory factor (MIF) 84
miscellaneous 1177, 2100
missing data 2465
mitochondria 64, 284, 966, 1008, 1011, 1417, 1666, 1933, 2192, 2342, 2979
mixed connective tissue disease (MCTD) 339, 1265, 1639, 2094, 2124, 2686
modifiable risk 2217
modified stoke ankylosing spondylitis spinal score (MSASSS) 3L, 1526
monoclonal antibodies 875, 1163, 1195, 1907, 1936, 2445, 2461, 2490
monocytes 77, 302, 960, 1567, 1573, 1680, 1709, 1718, 1948, 2342, 2643, 2764
morbidty and mortality 11L, 145, 203, 303, 308, 420, 524, 812, 944, 987, 993, 1002, 1130, 1317, 1600, 1610, 1625, 1699, 1771, 1885, 1972, 2077, 2109, 2376, 2392, 2412, 2665, 2689, 2736, 2846, 2911, 2921, 2982
morphea 1284, 1287, 1729, 2346
mouse model 26, 52, 53, 391, 406, 497, 660, 860, 866, 1322, 1334, 1568, 1576, 1661, 1915, 1943, 2232, 2568, 2573, 2580, 2700
MSCs 1655
mTor 1321, 1746, 2698, 2763, 2872, 2932
mucosal T cells 402, 1065
multicenter study 584, 1441
multiple imputation 2465
muscle biopsy 948, 1381
muscle strength 1219, 2961
Musculoskeletal 69, 157, 345, 2050, 2418
musculoskeletal curriculum 91, 100, 103, 110, 907
musculoskeletal disorders 49, 157, 2092
musculoskeletal sonography 110, 1608, 2301
mycobacterium 1587
mycophenolate mofetil 1171, 1782, 2152, 2583, 2600, 2603, 2624
myeloperoxidase (MPO) 1769
myocardial involvement 714, 2319
myopathy 850, 2130, 2131, 2153, 2154, 2167, 2173, 2888
ostearticular 1883
osteoblasts 47, 49, 63, 68, 74, 959, 1566, 1655, 1938, 1947
osteoclastogenesis 53, 65, 68, 902, 961, 1320, 1323, 1338, 1570, 1948, 2773, 2792
osteoclasts 47, 53, 63, 69, 1074, 1335, 1435, 1570, 1932, 1942, 1944
osteomyelitis 373
osteonecrosis 54
osteonecrosis of the jaw 2256
osteopenia 1229, 2397
osteoarthritic 1883
osteophytosis 2947
osteoporosis 59, 63, 68, 69, 1074, 1335, 1435, 1570, 1932, 1942, 1944
osteoprotegerin 1126, 2379
outcome measures 229, 235, 338, 350, 357, 726, 1029, 1079, 1093, 1231, 1238, 1247, 1287, 1293, 1356, 1359, 1360, 1384, 1390, 1511, 1556, 1624, 1627, 1638, 1676, 1686, 1805, 1807, 1841, 1875, 1878, 2032, 2039, 2211, 2238, 2245, 2293, 2315, 2484, 2502, 2525, 2536, 2547, 2548, 2550, 2552, 2662, 2781, 2851, 2859, 2893, 2950, 2971, 2981
outcomes 128, 203, 220, 221, 303, 309, 311, 348, 355, 442, 469, 640, 668, 713, 715, 781, 795, 923, 1054, 1231, 1250, 1275, 1288, 1299, 1311, 1316, 1317, 1384, 1391, 1392, 1427, 1457, 1543, 1550, 1616, 1618, 1648, 1702, 1754, 1801, 1839, 1862, 1957, 2137, 2138, 2139, 2157, 2166, 2188, 2193, 2293, 2295, 2302, 2314, 2453, 2497, 2500, 2504, 2608, 2623, 2683, 2717, 2747, 2848, 2853, 2861, 2864, 2957, 2994
outreach 112

P

P. Gingivalis 487, 494, 1072, 2995
PAD 483, 488, 1072, 1363, 2430
pain management 15L, 933, 1206, 1974, 2220, 2221, 2222, 2224, 2225, 2226, 2230, 2235
pannus 1382
paraoxonase 1327, 2148
parathyroid hormone 1937
Participation 118
pathogenesis 387, 401, 483, 557, 569, 573, 649, 658, 661, 953, 1075, 1077, 1713, 1736, 1744, 2337, 2342, 2572, 2650, 2728, 2829, 2914
patient 1856, 2952
patient assistance 196, 1257, 1258, 2696
patient engagement 216, 1254, 1258, 2030, 2240, 2251, 2255, 2257, 2266, 2269, 2611, 2696, 2725, 2780, 2954
patient health 781, 2923
patient participation 216, 1241, 1260, 2725, 2954
patient preferences 211, 340, 345, 358, 1045, 1236, 1237, 1246, 1252, 1856, 2251, 2269, 2283, 2779, 2782
patient questionnaires 353, 475, 1253, 2220, 2862
Patient Satisfaction 1249, 2953

payment 830
PD-1 1173, 2095, 2580, 2705
pediatric medical center 349
pediatric rheumatology 17, 90, 107, 173, 248, 369, 378, 379, 381, 383, 384, 385, 1242, 1259, 1266, 1270, 1272, 1276, 1277, 1280, 1281, 1282, 1283, 1284, 1285, 1286, 1288, 1318, 1728, 1800, 1892, 1893, 2018, 2252, 2259, 2271, 2281, 2286, 2294, 2301, 2305, 2308, 2309, 2315, 2319, 2346, 2858, 2895, 2957, 2959, 2960, 2996
pediatrics 95, 186, 232, 351, 380, 1269, 1271, 1277, 1289, 1494, 1754, 1813, 1960, 2111, 2252, 2276, 2296, 2310, 2321, 2637, 2758, 2855, 2895, 2937, 2960, 2997
performance 588, 589, 590, 1090, 1504, 2854
Periodontitis 487, 492, 494, 640, 1331, 1343, 1383, 2913, 2995
Perioperative management 1457, 2755, 2786
Personalized Medicine 166, 1016, 1022, 1672, 2429, 2600
pharmacists 215, 225, 1046, 1048, 1090, 2848
pharmacokinetics 506, 519, 544, 1163, 1752, 1809, 1893, 2072, 2270, 2296, 2443, 2592, 2607, 2855, 2856
pharmacology 819, 850, 1022, 1296, 1322
pharmacotherapy 1053, 1166, 1929, 2900
phase 3 2605
phenotypes 688, 712, 713, 859, 1591, 1639, 1672, 1689, 1756, 1883, 2574, 2596, 2975
phospholipase 1209
physical activity 234, 315, 337, 846, 1004, 1234, 1398, 1619, 1620, 1692, 1804, 1867, 2153, 2193, 2194, 2195, 2223, 2251, 2351, 2766, 2767, 2768, 2770, 2822, 2835, 2968
physical examination 91
physical function 236, 625, 630, 1277, 1531, 1854, 2303, 2961
physical therapy 931, 1059, 1694, 2154, 2321, 2766, 2849
Physician Assistant 109, 1858
physician data 153
placenta 1809, 2762
plasma cells 1834, 2559
Plasmablasts 4L, 30, 1846, 1882, 2426, 2639
platelets 77, 798, 1719, 1949
Pneumococcal 1256
polyangitis 893, 1770, 1777, 2737
polyarteritis nodosa 2742, 2743, 2749
polyarthritis 276
polychondritis 1149, 1737, 2010
polymerase chain reaction (PCR) 2842
polymorphism 165, 170, 177, 181, 1013, 1127, 1411, 1751, 1762, 1975, 2370, 2651
polymyalgia rheumatica 782, 792, 804, 812, 818, 1176, 1184, 2043, 2107
polymyositis 851, 854, 1732, 2130, 2132, 2145, 2151, 2164, 2165, 2169
polymyositis/dermatomyositis (PM/DM) 1999, 2133, 2134, 2136, 2138, 2139, 2150, 2160, 2163, 2168
population studies 217, 1088, 1093, 1218, 1290, 1957, 1959, 1969, 2105, 2398, 2651, 2880, 2972
post-translational modification 479
poverty 923
PPAR-gamma 399
Practice 2163
practice guidelines 1102, 2037, 2734
prednisolone, prednisone 896, 930, 1422, 1423, 2604, 2734
pregnancy 2, 5, 6, 12, 355, 930, 1031, 1290, 1291, 1292, 1293, 1294, 1295, 1296, 1297, 1298, 1299, 1300, 1301, 1303, 1309, 1310, 1311, 1312, 1313, 1314, 1315, 1316, 1317, 1785, 1809, 1810, 1811, 1812, 1957, 1958, 2432, 2433, 2762, 2804

Preoperative 219

prescribing trends 205, 922, 927, 1542, 2614

prevention 841, 1088, 1217, 1304, 2026, 2121, 2250, 2760, 2778

primary care 186, 909

primary immunodeficiency 378

prior authorization 1046, 1053

PRO 189, 335, 508, 597, 612, 1232, 1395, 1531, 2248, 2463, 2539, 2548, 2549

prognostic factors 66, 122, 451, 583, 608, 671, 702, 727, 787, 854, 1162, 1279, 1361, 1375, 1389, 1393, 1455, 1468, 1843, 1994, 2107, 2125, 2137, 2164, 2198, 2212, 2275, 2289, 2386, 2405, 2421, 2452, 2730, 2816, 2871, 2909

prolactin 1660

PROMIS 227, 344, 1081, 1082, 1244, 1247, 1255, 1263, 1264, 1852, 2248, 2255, 2694, 2781, 2853, 2951

prostaglandins 389, 408, 656, 955, 2328

prosthesis 282, 2082, 2840

proteinuria 662, 1668, 1843, 2621

proteoglycans 962, 1930

proteomics 173, 556, 650, 729, 765, 769, 1010, 1019, 1024, 1190, 1358, 2322, 2335, 2337

pseudogout 187, 1126, 1132, 2053, 2060, 2082, 2090


psychiatric 2810

psychological status 845, 2987

psychological well-being 349, 998, 2288, 2987

psychosocial 2695, 2997

psychosocial factors 843

Puberty 1278

Publication 991

pulmonary complications 24, 526, 529, 735, 737, 743, 758, 1700, 2168, 2678, 2679, 2683

pulmonary fibrosis 732, 974, 1711, 1902, 2114, 2983

Pulmonary Involvement 378, 730, 736, 752, 944, 947, 1276, 1598, 1685, 1697, 1702, 1760, 1769, 2008, 2398, 2676, 2678, 2679, 2680, 2687, 2729, 2737, 2980

Q

qualitative 112, 339, 745, 848, 1238, 1243, 1259, 1263, 2240, 2260, 2262, 2268, 2269, 2317

quality 50, 830, 2041

quality improvement 102, 198, 309, 385, 721, 1042, 1080, 1081, 1087, 1092, 1096, 1097, 1101, 1102, 1229, 1796, 1797, 1798, 1814, 2026, 2027, 2028, 2034, 2037, 2043, 2045, 2046, 2261, 2994, 2997

Quality Indicators 1085, 1593

quality measures 48, 342, 1080, 1084, 1085, 1229, 1797, 2040, 2043, 2046, 2305
quality of care 385, 847, 1229, 2035, 2294
quality of life 7L, 358, 417, 630, 699, 739, 845, 892, 1004, 1083, 1243, 1263, 1284, 1285, 1495, 1511, 1531, 1652, 1653, 1767, 1807, 1867, 2220, 2244, 2252, 2254, 2258, 2259, 2267, 2302, 2315, 2506, 2513, 2536, 2538, 2542, 2544, 2615, 2697, 2769, 2878, 2953, 2955

regulatory cells 21, 71, 87, 866, 1733, 2572, 2574, 2637, 2715

rehabilitation 113, 2111, 2769

reimbursement 2048


renal disease 9, 139, 325, 665, 895, 1111, 1122, 1288, 1586, 1679, 1713, 1766, 1772, 1789, 1849, 1864, 2621, 2622, 2671

Reproductive Health 1291, 1293, 1294, 1303, 1304, 1305, 1306, 1307, 1310, 1812, 1813

research methods 228, 2050, 2557

resolution of disease 298, 864, 1334, 2328

respiratory disease 145, 2003, 2384, 2606

resveratrol 42

Retroperitoneal Fibrosing 1175, 2122

reversible cerebrovascular vasocostriction 2726

rheumatic disease 49, 67, 81, 88, 191, 192, 201, 203, 509, 536, 803, 841, 964, 1023, 1046, 1092, 1099, 1299, 1301, 1303, 1307, 1309, 1809, 1958, 1964, 1972, 2028, 2109, 2253, 2353, 2409, 2587, 2906

rheumatic education 88, 96, 201

rheumatoid arthritis 1256, 1391

rheumatoid arthritis, animal models 61, 394, 396, 398, 399, 400, 401, 407, 861, 865, 1062, 1074, 1319, 1320, 1324, 1326, 1327, 1331, 1335, 1337, 2704
rheumatoid arthritis, pathogenesis 78, 480, 967, 1412, 1902, 2435, 2913
rheumatoid arthritis, synovium 171, 961, 1401, 1412, 1940, 2436, 2869
rheumatoid arthritis, treatment 395, 417, 451, 498, 520, 536, 548, 549, 551, 1049, 1310, 1392, 1394, 1432, 1444, 1445, 1477, 1478, 1908, 2437, 2472, 2473, 2492, 2799, 2871, 2963
Rheumatoid Factor 72, 239, 410, 432, 480, 482, 1250, 1376, 1402, 1432, 1454, 1819, 2016, 2741, 2916, 2918
rheumatologic disease 332, 2119, 2583
rheumatologic practice 172
Rheumatology 97, 115, 912, 2046
ribonucleoprotein (RNP) 1096, 1265
risk 123, 124, 125, 132, 146, 848, 913, 915, 993, 1005, 1483, 2007, 2076, 2309, 2651, 2760
risk assessment 5, 147, 172, 203, 272, 657, 708, 723, 978, 1117, 1119, 1150, 1151, 1227, 1306, 1693, 1863, 2073, 2150, 2151, 2359, 2365, 2759, 2913
risk management 273, 2365
rituximab 18L, 27, 39, 496, 547, 560, 874, 890, 1175, 1346, 1466, 1472, 1687, 1752, 1757, 1759, 2167, 2169, 2320, 2385, 2402, 2445, 2461, 2486, 2490, 2567, 2597, 2602, 2655, 2754, 2795, 2796, 2886, 2936
RNA 181, 302, 387, 770, 1026, 1330, 1721, 1744, 1745, 2075, 2324, 2432, 2575, 2757
Safety issues 278, 538, 1031, 1089, 1443, 2274, 2277, 2886
salivary gland 30, 268, 552, 554, 558, 567, 570, 572, 574, 877, 878, 1487, 1497, 1499, 2703, 2830, 2873, 2907
salivary hypofunction 556, 567
SAPHO syndrome 371, 1883
sarcoidosis 209, 1160, 1161, 1170, 1183, 1959, 2099, 2123, 2125, 2127, 2904
sarcopenia 1901, 1961, 2509, 2510
Scleredema 98, 754, 765, 770, 1258, 1724
scleroderma 257, 727, 728, 733, 736, 737, 750, 761, 763, 767, 774, 775, 776, 919, 945, 948, 1248, 1284, 1285, 1287, 1676, 1680, 1681, 1682, 1686, 1695, 1705, 1706, 1709, 1711, 1713, 1725, 1728, 1729, 1922, 1923, 1957, 2346, 2665, 2666, 2671, 2674, 2678, 2679, 2680, 2681, 2687, 2690, 2691, 2695, 2696, 2926, 2930, 2982
scleroderma-like conditions 748, 2131
self-management 197, 1245, 1857, 1860, 1990, 2693, 2952
Senescent Cells 1931, 2646, 2945
serologic tests 384, 699, 808, 1154, 1389, 1436, 1497, 1881, 2114, 2677
seronegative spondyloarthropathy 1503, 1569, 2518
severity 470, 495, 1407, 1408, 1479, 1613
sex bias 165, 394, 1109, 1479, 1816, 2388
Sexuality 148, 1501, 1637
shared dicision making 1255, 2260, 2725, 2778, 2782
shoulder disorders 2079
sialoadenitis 1497
SICCA 574, 1495, 1497
<table>
<thead>
<tr>
<th>Term</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signal transduction</td>
<td>85, 969, 1330, 1409, 1412, 1732, 2761, 2790, 2928</td>
</tr>
<tr>
<td>Sjögren's syndrome</td>
<td>30, 45, 46, 182, 268, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 568, 569, 570, 571, 572, 573, 574, 575, 576, 722, 873, 874, 875, 876, 877, 878, 1064, 1069, 1073, 1479, 1480, 1481, 1482, 1483, 1484, 1485, 1486, 1487, 1488, 1489, 1490, 1491, 1492, 1493, 1494, 1495, 1496, 1498, 1499, 1500, 1501, 1502, 1784, 1795, 2123, 2237, 2633, 2664, 2703, 2706, 2774, 2816, 2817, 2828, 2830, 2872, 2873, 2874, 2876, 2877, 2943</td>
</tr>
<tr>
<td>Sjögren's</td>
<td>566, 567, 576</td>
</tr>
<tr>
<td>Skill development</td>
<td>103, 1858</td>
</tr>
<tr>
<td>Skin</td>
<td>625, 756, 897, 1026, 1555, 1827, 2532, 2533, 2682, 2757</td>
</tr>
<tr>
<td>Skin fibrosis</td>
<td>729, 732, 764, 770, 1018, 1680, 1701, 1714, 1726, 1728, 2663, 2776, 2884, 2885</td>
</tr>
<tr>
<td>Sleep</td>
<td>123, 933, 1398, 1530, 1644, 1872, 1974, 1989, 2195, 2223, 2540, 2820, 2824</td>
</tr>
<tr>
<td>Sleep apnea</td>
<td>1649</td>
</tr>
<tr>
<td>Sleep disorders</td>
<td>158, 1649, 1653</td>
</tr>
<tr>
<td>Small molecules</td>
<td>16L, 81, 531, 935, 1052, 1204, 1567, 2601</td>
</tr>
<tr>
<td>Social media</td>
<td>105, 118, 2243, 2250</td>
</tr>
<tr>
<td>Social support</td>
<td>844, 846, 1243</td>
</tr>
<tr>
<td>Socio-economic inequities</td>
<td>220, 221, 923, 1542</td>
</tr>
<tr>
<td>Socioeconomic factors</td>
<td>218, 219, 361, 1393</td>
</tr>
<tr>
<td>Socioeconomic status</td>
<td>920, 2534, 2819</td>
</tr>
<tr>
<td>Sonography</td>
<td>254, 2963</td>
</tr>
<tr>
<td>Spine involvement</td>
<td>307, 585, 590, 1851</td>
</tr>
<tr>
<td>Spondylarthropathy</td>
<td>252, 254, 373, 577, 586, 629, 645, 879, 1232, 1567, 1576, 1578, 1580, 2330, 2503, 2525, 2526</td>
</tr>
<tr>
<td>Statins</td>
<td>1095, 1674, 2077, 2149</td>
</tr>
<tr>
<td>Statistical methods</td>
<td>126, 184, 1452, 1838, 1956, 2050, 2051, 2179, 2290, 2806, 2827, 2890, 2946</td>
</tr>
<tr>
<td>Statistics</td>
<td>147, 2050</td>
</tr>
<tr>
<td>Stem cells</td>
<td>1688, 1930, 1934, 1947, 2887</td>
</tr>
<tr>
<td>Steroid-sparing</td>
<td>2605</td>
</tr>
<tr>
<td>Steroids</td>
<td>435, 1112, 1801, 2361, 2604</td>
</tr>
<tr>
<td>Still's disease</td>
<td>364, 1885, 2109</td>
</tr>
<tr>
<td>Strength</td>
<td>1219, 1237, 2218, 2822</td>
</tr>
<tr>
<td>Stress</td>
<td>70, 844, 847, 1008, 1235, 1602, 1983, 2598</td>
</tr>
<tr>
<td>Subchondral bone</td>
<td>48</td>
</tr>
<tr>
<td>Support and Education Groups</td>
<td>118, 1861</td>
</tr>
<tr>
<td>Surgery</td>
<td>219, 282, 1050, 1618, 1816, 2389, 2729</td>
</tr>
<tr>
<td>SYK</td>
<td>1319, 1329, 1337, 2562</td>
</tr>
<tr>
<td>Synovial cells, synovial fluid</td>
<td>86, 299, 481, 962, 965, 976, 1330, 1339, 1407, 1408, 1413, 1456, 1940, 2801</td>
</tr>
<tr>
<td>Synovial fluid</td>
<td>1178, 1366, 1739, 2081, 2086, 2239, 2422, 2899</td>
</tr>
<tr>
<td>Synovial Immune Biology</td>
<td>1020, 1063, 1339, 1405, 1406, 1940</td>
</tr>
</tbody>
</table>
thrombocytopenia 11, 2381
thrombosis 2, 3, 5, 7, 8, 10, 16, 17, 304, 664, 708, 822, 879, 883, 1625, 1750, 1753, 2564, 2752, 2759, 2760, 2761, 2762, 2775
tissue engineering 58, 2418
tissue growth factor (TGF) 1721, 1928
tobacco use 124, 125, 467, 786, 999, 1087, 1370, 1383, 1645, 1683, 2261
tocilizumab 167, 417, 447, 453, 465, 527, 550, 778, 780, 804, 805, 816, 891, 892, 1169, 1399, 1423, 1426, 1436, 1439, 1467, 1476, 1825, 1905, 2270, 2297, 2325, 2449, 2458, 2460, 2464, 2469, 2474, 2475, 2721, 2751, 2856, 2857, 2869, 2962
tolerance 46, 522, 861, 916, 1064, 1463, 1834, 2091, 2704, 2738, 2739, 2974
Toll Like receptors 580
toll-like receptors 43, 301, 757, 860, 898, 1060, 1063, 1323, 1656, 1663, 1670, 2329, 2436, 2570, 2576
tophaceous gout 2054, 2063
total joint replacement 220, 311, 923, 1136, 1210, 1854, 2184, 2851, 2853
Total Knee Arthroplasty (TKA) 221, 317, 2833, 2851
tracking 2993
trainee 98, 99, 100, 111
transcription factor 166, 300, 1661, 1737, 1932
transcriptional regulation 171, 174, 285, 1411, 1579, 2827
transforming growth factor 974, 1706, 1714, 1720, 1924, 1925, 1938, 2926, 2928, 2929
Transition 204, 339, 910, 1242, 1259, 1754, 1799, 2795, 2996
transplantation 322, 895, 1224, 1789, 2675, 2887, 2921
Traps 79, 361
treatment guidelines 634, 1342, 1548, 1955, 2618, 2955
treatment options 192, 368, 972, 1158, 1342, 1430, 2166, 2284, 2291, 2671, 2673, 2743, 2881
Triage 185, 186, 201
tuberculosis 206, 997, 1089, 1966, 2409, 2610, 2787
tumor necrosis factor (TNF) 75, 76, 139, 171, 394, 515, 526, 547, 621, 860, 959, 973, 1036, 1052, 1068, 1338, 1415, 1428, 1433, 1507, 1516, 1523, 1535, 1539, 1540, 1547, 1556, 1787, 1791, 1817, 1826, 1828, 1833, 1942, 1948, 2024, 2127, 2159, 2448, 2450, 2463, 2481, 2485, 2501, 2711, 2803, 2864
Twitter 105
type II collagen 132
tyrosine kinase inhibition 503, 1720
U
ulcers 256, 750, 1704, 1892, 2007, 2666, 2724
2030, 2055, 2210, 2239, 2301, 2527, 2910, 2940, 2942, 2943, 2963, 2967

uric acid 250, 668, 672, 1106, 1108, 1110, 1114, 1120, 1121, 1122, 1123, 1124, 1141, 1145, 1864, 2054, 2057, 2058, 2059, 2063, 2067, 2070, 2071, 2072, 2074, 2075, 2076, 2078, 2080, 2085, 2091, 2366, 2843, 2845, 2848, 2896, 2897, 2898

Urinary Biomarkers 663, 669, 1849

utilization review 188, 214, 1041, 1952

uveitis 271, 1155, 1158, 1159, 1161, 1169, 1170, 1516, 1881, 1963, 2098, 2112, 2295, 2296, 2297, 2298, 2299, 2314, 2318, 2322, 2323, 2507, 2519, 2722, 2723, 2857

V

Vaccination 1256

vaccines 269, 280, 369, 383, 384, 385, 386, 566, 827, 1182, 1400, 1824, 2026, 2027, 2028, 2029, 2393, 2396, 2414, 2415, 2583, 2606

Validity 352, 586, 1284, 1805, 1852, 2211, 2252

vasculitis 18L, 23, 24, 71, 212, 226, 260, 261, 263, 281, 295, 710, 779, 780, 781, 784, 785, 788, 794, 796, 797, 798, 799, 805, 808, 809, 814, 815, 817, 820, 821, 893, 894, 895, 896, 1002, 1010, 1288, 1289, 1734, 1746, 1749, 1751, 1752, 1754, 1755, 1756, 1757, 1758, 1759, 1760, 1763, 1764, 1765, 1766, 1767, 1768, 1769, 1770, 1771, 1773, 1776, 1777, 1782, 1783, 1789, 1844, 1845, 1846, 1847, 1849, 1856, 2023, 2109, 2343, 2345, 2716, 2717, 2718, 2719, 2725, 2728, 2733, 2734, 2735, 2736, 2737, 2738, 2739, 2740, 2741, 2745, 2749, 2752, 2754, 2775, 2932, 2935, 2936, 2937

vasculogenesis 755, 1679

viruses 183, 274, 277, 808, 902, 2428, 2703, 2838

viscosupplementation 980, 1043

Vitamin D 149, 326, 329, 664, 665, 666, 1747, 2400, 2622, 2692

W

website 2120

Wegener's granulomatosis 893, 1010, 1753, 1757, 1765, 1770, 1775, 1777, 1781, 1847

weight loss 1192, 1635, 1955, 2206, 2823, 2984

WNT Signaling 903, 935, 1201, 1204, 1716, 1924, 2929

women's health 1293, 1294, 1306, 1308, 1642, 2205

work 119, 914, 1453, 1973, 2237, 2258, 2500, 2836, 2988

Work Disability 133, 417, 992, 2039, 2244, 2497, 2534

Workforce 96, 97, 119, 914

wounds 255, 1717, 1719

X

x-ray 1L, 3L, 590, 1207, 1526, 1877, 2000

Y

young adults 910, 1214